IDEAS
INFECTIOUS DISEASE EVOLUTION ACROSS SCALES
EEID 2019 PRINCETON

17th Annual Meeting on Ecology and Evolution of Infectious Disease

Princeton University June 10-13, 2019

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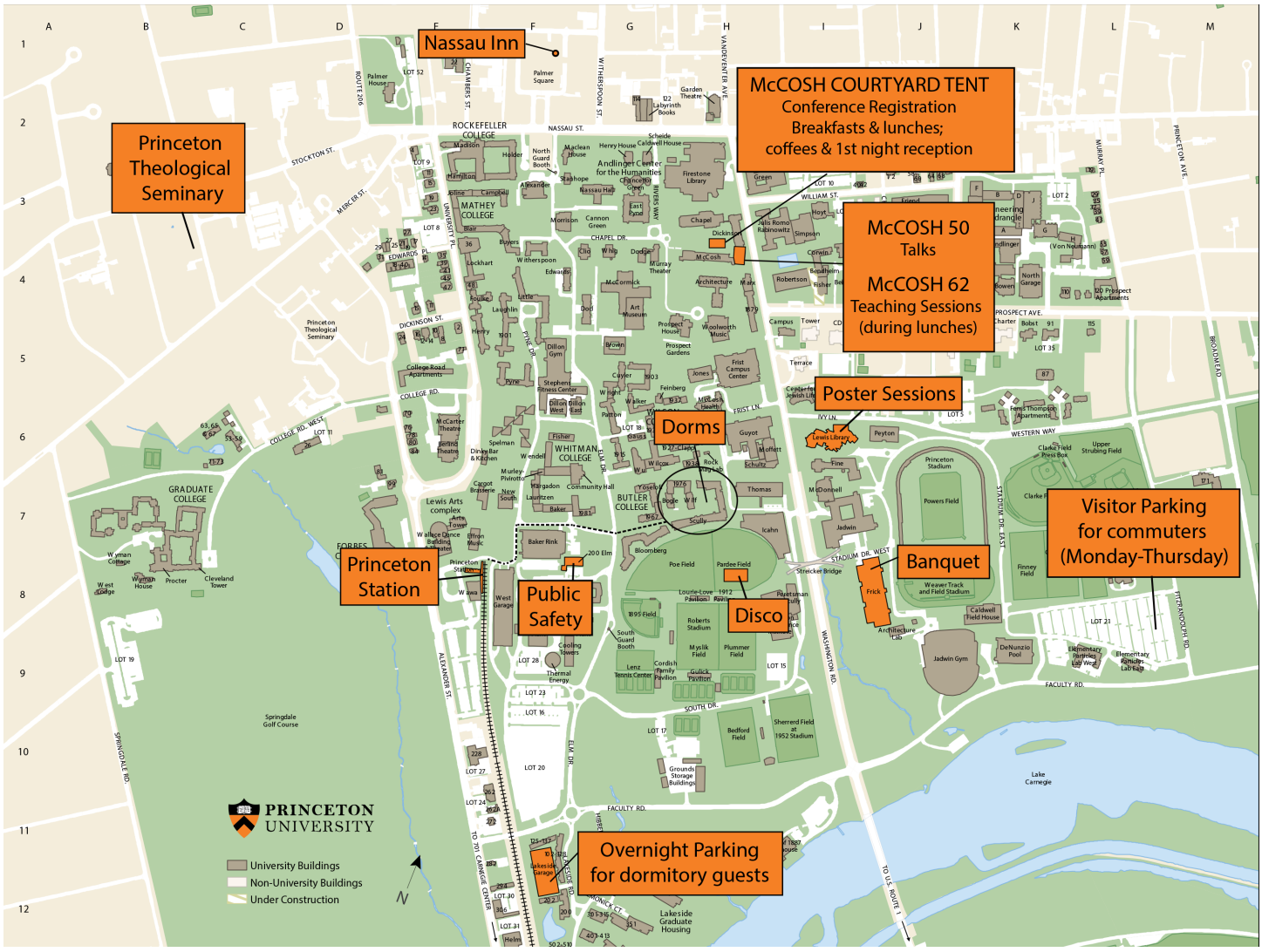


Contents

Schedule

All talks will be in McCosh 50

Monday 10 June

3:00-5:00 pm Registration & VirScan sampling at McCosh tent

5:00-7:00 **Within-host competition in infectious disease dynamics**
(Chair: Nicole Mideo; Sponsor: NSF RCN-IDEAS) See abstracts on pages 17-18

5:00 pm Introduction and welcome, from Princeton University Disease Group
5:05 pm Andrew Read: "The ecology of drug therapy"
5:35 pm Georgiana May: "A defensive symbiont of maize causes selection for greater virulence in a pathogen of Maize"
5:50 pm Katie Gostic: "B cell competition shapes the population-level impacts of broadly protective influenza Immunity"
6:05 pm Megan Greischar: "How ecology across scales influences the evolution of malaria parasites"
6:35 pm Anna Sjodin: "Do viruses interact? Exploring patterns of herpesvirus co-infection at multiple scales"
6:50 pm Hows and whys of VirScan, from Mike Mina

7:00-9:00 pm **Welcome reception with substantial appetizers**, McCosh tent

Tuesday 11 June

8:00-9:00 am **Breakfast**, McCosh tent

9:00 am-noon **Behavioral drivers of infectious disease dynamics** (Chair: Andy Dobson)
See abstracts on pages 19-21

9:00 am Lindy McBride: "Geographic, genetic, and neural origins of human biting in the mosquito vector Aedes aegypti"
9:30 am Jessica Hite: "Feeding colds and starving fevers? Evolutionary theory illustrates why appetite during illness matters"
9:45 am Douglas Kerlin: "Modelling the transmission of Devil facial tumour disease using contact networks"
10:00 am Emily Durkin: "The role of behaviour in parasite evolution"

10:15 am **Coffee break**, McCosh tent

10:45 am Sylvain Gandon: "Evolution and manipulation of vector behavior"
11:15 am Ayesha Mahmud: "When a megacity goes on holiday: the impact of population mobility on the spread of local epidemics"
11:30 am Janis Antonovics: "The perception kernel: vector behavior and disease transmission"
11:45 am Kristin Duffield: "When resistance is futile: age determines host reproductive effort under infection threat "
11:50 am John Giles: "Modeling seasonal commuting behavior for inferring infectious disease dispersal"
11:55 am *Announcements & hike planning info, from Princeton University Disease Group*

12:00-1:00pm **Lunch**, McCosh tent **(Teaching EEID session 1, McCosh 62)**

1:00-4:30 pm **Environmental drivers of infectious disease dynamics** (Chair: Jess Metcalf)
See abstracts on pages 22-24

1:00 pm Jeffrey Shaman: "Climate and influenza: Associations, processes and implications"
1:30 pm Nichar Gregory: "El Niño drought and tropical forest conversion synergistically determine mosquito vectorial capacity"
1:45 pm Ernest Asare: "The influence of birth rate and meteorological indices on the temporal patterns of rotavirus infection in Dhaka (Bangladesh)"
2:00 pm Devin Kirk: "Predicting warming-induced infectious disease epidemics with the metabolic theory of ecology"

2:15 pm **Coffee break**, McCosh tent

2:45 pm Elizabeth Borer: "Vectors as foraging animals: a frame-shift for disease ecology"
3:15 pm Matthieu Domenech de Celles: "Unraveling the seasonal epidemiology of pneumococcus"
3:30 pm David Allen: "Larval blacklegged tick phenology changes with elevation: implications for Lyme disease"
3:45 pm **Teasers for Poster session 1 (50 30-second teasers)**

4:30-7:00 pm **Poster Session 1, with beverages and hearty appetizers in Lewis Library**
(See abstracts pages 33-76)

Dinner independently, in town

Wednesday 12 June

5:30-8:00 am Birding hike
8:00-9:00 am **Breakfast**, McCosh tent
9:00am-noon Further hikes & rows

12:00–1:00pm **Lunch**, McCosh tent **(Teaching EEID session 2, McCosh 62)**

1:00-4:00 pm **Genetics of infectious disease dynamics across scales** (Chair: Bryan Grenfell)
See abstracts on pages 24-26

1:00 pm Christine Carrington: "The West Indies: a popular destination for emerging viruses"
1:30 pm Shai Pilosof: "The dynamic and non-neutral genetic strain structure of Plasmodium falciparum with implications for malaria epidemiology"
1:45 pm Christopher Kozakiewicz: "Phylogeography reveals reduced transmission of feline immunodeficiency virus among bobcats in an urban landscape"
2:00 pm Amanda Gibson: "Does genetic diversity reduce disease risk?"

2:15 pm **Coffee break**, McCosh tent

2:45 pm David Kennedy: "Multiscale Genetic Drift Shapes Pathogen Variation within Hosts"
3:15 pm Pamela Martinez-Vargas: "Prediction of post-vaccine Streptococcus pneumoniae lineage frequencies based on potential accessory genes under selection"
3:30 pm **Teasers for poster session 2 (50 30-second teasers)**

4:00-6:00 pm **Poster Session 2, with beverages and light appetizers** in Lewis Library
(See abstracts pages 77-120)
6:00-8:00 pm **Banquet**, Frick Hall
8:00-11:00pm **Dance party**, Poe Field

Thursday 13 June

8:00-9:00 am **Breakfast**, McCosh tent

9:00am-noon **From wondrous complexity to one health** (Chair: Andrea Graham)
See abstracts on pages 27-32

9:00 am Laura Bergner: "A hyperparasite with a missing viral helper: the ecology and evolutionary history of a novel satellite virus in vampire bats"
9:15 am Steve Ellner: "Individual specialization and disease spread in multi-host communities: Plant-pollinator networks"
9:30 am Jacobus de Roode: "Secondary plant chemicals alter virulence and transmission of herbivore parasites through a combination of toxicity and modulation of immunity and the microbiome"
9:45 am Catherine Herzog: "Management practices and age cohorts that contribute to increased Peste des petits ruminants seroprevalence in sheep goats and cattle in northern Tanzania"
9:50 am Amrita Bhattacharya: "Selection for increased virulence leads to decreased bacteriocin production in insect-pathogenic Xenorhabdus nematophila"
9:55 am Nicholas Skaff: "Thresholds in coastal climate and transcritical variation induce geographic heterogeneity in West Nile virus transmission across Los Angeles"
10:00 am Baptiste Elie: "The role of viral fitness variation in understanding the geographic origins of seasonal influenza"
10:05 am Changes to NSF-EEID, from Sam Scheiner & Katharina Dittmar

10:15 am **Coffee break**, McCosh tent

10:45 am Oliver Brady: “Predicting the spread of Aedes aegypti & Ae. albopictus at local & global scales”

10:50 am Jan Gogarten: “Tropical rainforest flies carrying pathogens form long-term associations with wild non-human primate social groups”

10:55 am Jessica Stephenson: “Dirty lying cheats: male guppies may use behaviour to avoid infection, conceal disease and boost parasite transmission”

11:10 am Allison Shaw: “Parasite richness intensity and prevalence shape the evolution of host seasonal migration”

11:25 am Ariane Düx: “A 1912 measles genome from Berlin gives new insights into the virus' evolutionary history”

11:40 am Skylar Hopkins: “Thermal refugia and ecological traps mediate bat survival after infection with the white-nose syndrome fungus”

11:55 am Poster prize announcements & closing remarks

12:00-1:00 pm **Lunch & Farewell**, McCosh tent, **with thanks from Princeton University Disease Group!**

Stay Connected (Wi-fi)

Option 1 | eduroam

Visitors from other eduroam participating institutions can select eduroam. When prompted, enter your home institution email address and password.

Option 2 | Connect to puvisitor

You will be directed to the web site below. Click on the box to accept the terms of use and then click on the LOG IN button.

Each device must be registered individually. Users cannot register with @princeton.edu email addresses.
Contact the Office of Information Technology helpdesk@princeton.edu, 609-258-4357 (8-HELP) or https://princeton.edu/wireless for more information.

Parking and Transportation

PARKING

A complete campus bus and parking map is available here.

Daily Visitor Parking

Visitor parking is available for free on weekdays in:

Lot 21 (GPS: "Princeton University Lot 21")
Lot 20 (GPS: "Princeton University Lot 20")

Weekend and Evening Parking

Visitors may park in most other lots and garages. View the campus map to find parking closest to the buildings you are visiting.

Metered and pay station parking is also available on streets around campus. Overnight parking is NOT permitted on Princeton streets.

Overnight Parking

Attendees staying in the Princeton University dormitories will receive overnight parking passes at dormitory check-in.

TRANSPORTATION

Rail Routes

Northbound NJ TRANSIT trains passing through Princeton Junction provide direct service to New York City and Newark Liberty International Airport. A southbound transfer to the SEPTA regional rail Trenton Line train at Trenton provides service to Philadelphia. Amtrak trains connect Princeton Junction to Washington, D.C., Boston and the broader region.

Hike Information and Maps

The hike will take place on the morning of Wednesday 12th June. There are a number of options for the hike depending on how far you'd like to walk and what time you want to start. All of the options (with the exception of the birding walk) will be self-guided. While the terrain is almost perfectly flat, Princeton can often be quite hot and humid, so be sure to bring adequate water and sun protection.
Breakfast and lunch will be served from 8-9am and 12-1pm in the tent outside of McCosh Hall. Plan accordingly so you don't miss your chance to eat before talks start at 1pm!

Here is a LINK to the maps: https://bit.ly/2Wd4JEF

5.30am Early birders and ghouls hike! ~4miles round trip

This hike will depart from Fitzrandolph Gate (the main entrance to campus on Nassau Street) at 5.30am prompt and make its way down Witherspoon street to the intersection with Rt206, where we can cross into Mountain Lakes and walk around the lakes, woods and ponds checking out the tail end of the warbler migration and the resident water birds. The map of this hike outlines a basic loop around the lake, but there are plenty of opportunities for further explanation of the other trails (outlined in the Mountain Lakes trail map). The small nature reserve of Mountain lakes was once owned by two of Princeton's most infamous undergraduates, the Menendez brothers, who were admitted to Princeton after their parents were horribly murdered by unknown assailants. Their parents' considerable estate paid for the boys to live a life of luxury at Princeton and they also bought and ran "Chucks Spring street café" in town on Spring street, famous for its excellent chicken wings. When it emerged that the boys were the ones who'd murdered their parents, their sojourn at Princeton was curtailed and they now reside in the "Big House" just outside Los Angeles.
We can return for breakfast at "Chucks" or at the excellent Greek diner on Leigh Avenue, just across from Mountain lakes, or at any of the fine breakfast places on Nassau Street. This should allow us to join the day's main group of hikers who can depart between 8.30 and 10.00 from behind Frist campus center and outside Guyot Hall.

Mid-length hike: Kingston and back, 8 miles round trip

Depart campus around 9:30 am to walk down Washington Road, cross the bridge over Lake Carnegie and then turn immediately left to walk along the old tow path of the Delaware and Raritan canal. The canal was dug by hand and runs all the way from Trenton to Raritan and was used for taking market produce from New Jersey into Newark and Manhattan. The railways instantly made it redundant. The attached nature guide (written by Henry Horn) provides many important insights into the natural history you will see along the canal: the birds will be mainly aquatic although there will be some warblers and

blue birds in the trees and a nesting pair of bald eagles on the right bank as you approach Kingston. The guide also describes many of the plants you will see and some history of the creation of canal.
You can make your way back from Kingston by Uber (wimps!), or by returning to the lake side of the canal footpath and retracing your steps to the Princeton campus. Do not be fooled! The path on the east side of the canal dead-ends before reaching Princeton!

Long hike: Rocky Hill and back, 12 miles round trip

Those wishing to do a longer hike can depart campus around 8:30am. This hike is an extension of the mid-length hike described above. After reaching Kingston, take the path on the east side of the canal to continue onwards to Rocky Hill. One third of the way to Rocky Hill is a possible two hundred yard diversion to Rockingham, the house occupied for several days by George Washington after his defeat of the British army at the Battle of Princeton. The house is preserved in the style of the time that Washington spent there. The section of trail between Kingston and Rocky Hill is more wooded and there will be many warblers and possibly foxes and beavers.

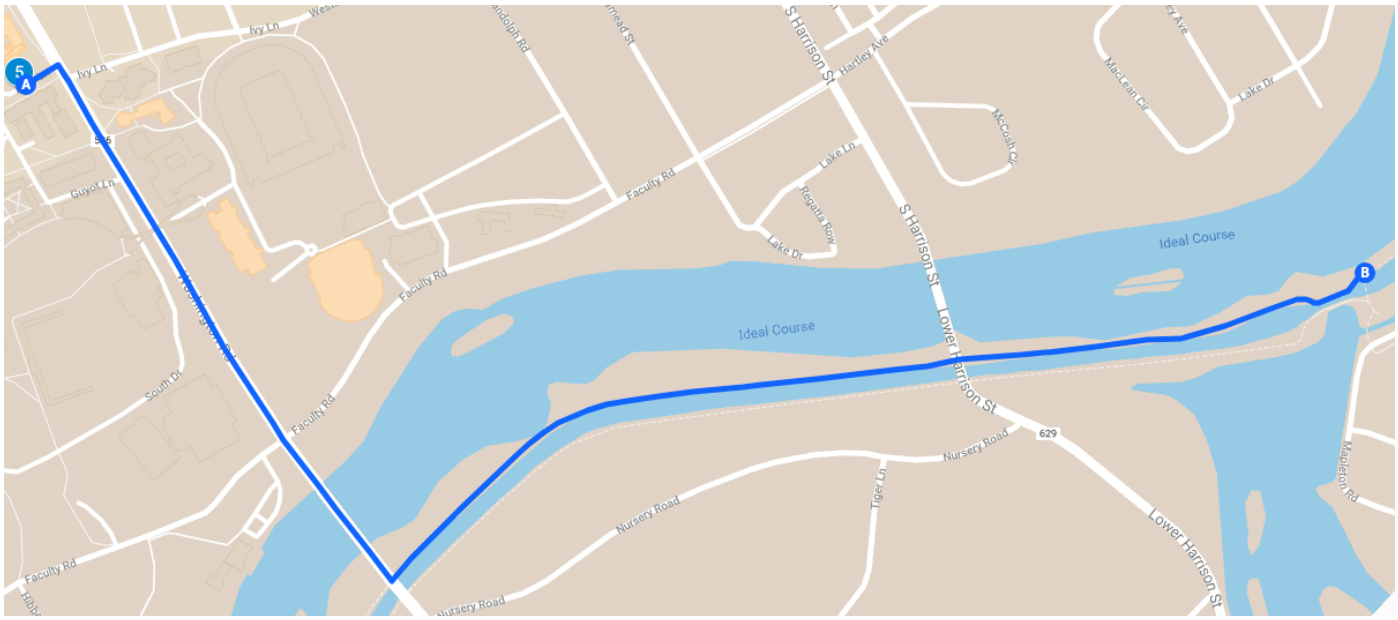
After reaching Rocky Hill, you can either return to Princeton by Uber (wimps!), or make your way back by returning to the path on the lake side (west side) of the canal and heading south. Remember, the path on the east side of the canal south of Kingston dead-ends before reaching Princeton!

Short Hike, Lake Carnegie and back, 4 miles round trip

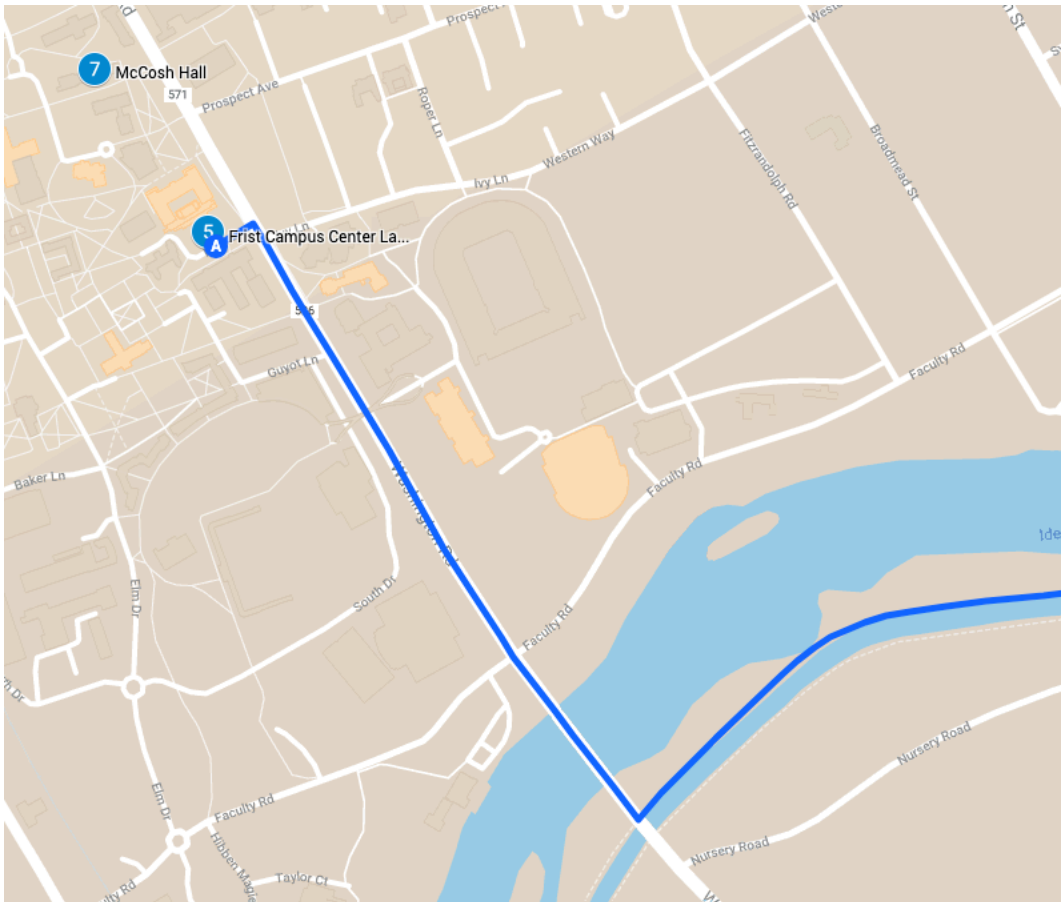
Those wishing to have a slower start to the day (for whatever reason…) can take a short hike along the canal path at their own leisure. After turning onto the lake side of the canal path, continue for about 1 mile to a boardwalk from which you can get a nice view of the lake. Turning around here makes the hike roughly 4 miles round trip.

Canoeing on Lake Carnegie

Princeton Canoe and Kayak Rental is located on Lake Carnegie, entrance on Alexander Road near tow path in Princeton. (609) 452–2403. http://princetoncanoe.com/

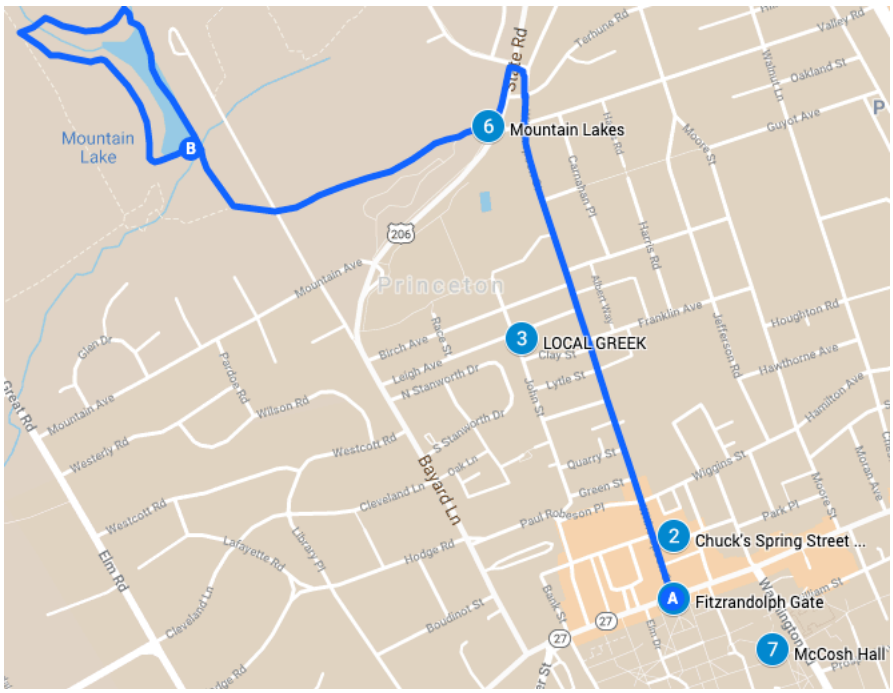


CARNEGIE LAKE HIKE



DIRECTIONS TO CANAL PATH

KINGSTON HIKE



MOUNTAIN LAKES HIKE

MOUNTAIN LAKES HIKE

Restaurants

A FEW RECOMMENDATIONS IN PRINCETON

Rojo's Roastery (coffee), 33 Palmer Square West

Small World Coffee, 14 Witherspoon St & 254 Nassau Street location (Nassau location serves breakfast)

Agricola, 11 Witherspoon

Blue Point Grill (seafood), 258 Nassau Street

Cargot Brasserie (French cuisine), 98 University Place

Dinky Bar & Kitchen (good drinks and a small food menu), 94 University Place

Elements (great, fancy), 66 Witherspoon Street

Jammin' Crepes (casual, good lunch spot), 20 Nassau Street

Local Greek, 44 Leigh Ave

Mediterra (Italian cuisine), 29 Hulfish Street

Mistral (tapa style), 66 Witherspoon Street

Nomad Pizza (brick oven style pizza), 301 N Harrison Street

Tacoria (Mexican), 110 Nassau Street

The Bent Spoon (homemade ice-cream), 35 Palmer Square

Things to do in Princeton

ON PRINCETON CAMPUS

Prospect House and Garden Prospect Mansion was given to the college in 1878 for use as a residence for the president. The Garden was later re-designed by Mrs. Woodrow Wilson, when her husband was president of Princeton University.

Princeton University Art Museum The museum features approximately 70,000 works ranging from ancient to contemporary art. It is located in McCormick Hall on campus and is open Tuesday, Wednesday, Friday, and Saturday, 10:00 a.m. to 5:00 p.m., Thursday, 10:00 a.m. to 9:00 p.m., and Sunday, 12:00 to 5:00 p.m. Admission is free.

POINTS OF INTEREST WITHIN WALKING DISTANCE

Delaware and Raritan Canal towpath

Institute Woods The grounds surrounding The Institute for Advanced Study, can be accessed off Mercer Street, or from the end of Springdale or Olden Lane. There are many walking paths, some leading to the canal, some to the battlefield, and some to a bird sanctuary. Excellent bird watching is possible.

Albert Einstein House The Einstein House is located at 112 Mercer Street. It is a white frame 2-story house with a large front porch in Greek revival style. Please note, this is a private residence; it is not open to the public. Einstein lived in this house from 1933 until his death in 1955.

Speaker abstracts (in chronological order)

Monday 10 June: Within-host competition in infectious disease dynamics

The ecology of drug therapy
Andrew F Read, Center for Infectious Disease Dynamics, Huck Institutes for the Life Sciences, Penn State

Drug-sensitive pathogens have diametrically opposed effects on resistance evolution. Sensitive pathogens empower evolution when they themselves become resistant (via mutation or horizontal gene transfer). But they also provide a potent resistance-retarding force: competitive suppression. Here I will discussion the possibility that in-host ecology can be exploited to improve health outcomes. In silico, in vitro and in vivo, it is possible to use sensitives to contain resistance, and drugs to contain the sensitives. These containment strategies involve unconventional regimens, but they can substantially prolong and even prevent treatment failure. There is a very real prospect that a therapeutic drug can be used to treat a patient even when resistance to the drug is present. Key to such success: a much better understanding of within-host ecology.

A defensive symbiont of maize causes selection for greater virulence in a pathogen of maize
Georgiana May, University of Minnesota

Defensive symbionts provide protection to hosts by reducing pathogen damage and are sought as natural disease-control agents in human-managed systems such as agriculture. However, theory suggests that competition between defensive symbionts and pathogens may cause selection for increased virulence in the pathogen, lessening the benefit of defense over time. We investigated the impacts of a defensive symbiont on pathogen fitness using a plant host (maize), a fungal pathogen (*Ustilago maydis*), and a defensive symbiont (Fusarium). Pathogen strains of varying levels of virulence were generated using crosses, and plants were inoculated with these, with or without the defensive symbiont. Fitness of the pathogen was assessed as spore weight, and of the plant as height growth. Fitness outcomes were evaluated using *aster* models which allow integration of fitness outcomes over disease development stages (infection, latent period, sporulation). Results of the analyses demonstrate that the pathogen's fitness increases with virulence with indication of a trade-off only at the highest virulence levels. The presence of the defensive symbiont lowers pathogen fitness similarly across all virulence levels. Results for analysis of disease development stages separately shows that the defensive symbiont lowers pathogen infection rates likely because the defensive symbiont directly interferes with pathogen growth on the leaf surface. Together, results support a model of defensive symbiont causing selection for increased virulence in a pathogen.

B cell competition shapes the population-level impacts of broadly protective influenza immunity
Katelyn (Katie) Gostic, UCLA

Narrow cross-protection is a hallmark of influenza immunity, but broadly protective antibody responses against conserved influenza epitopes are also possible. Recently, we showed individuals gain broad, lifelong protection against hemagglutinin subtypes in the same phylogenetic "group" as influenza strains encountered in childhood. This broadly protective imprinting strongly shapes population-level impacts from emerging, avian influenza viruses. New analyses of large surveillance datasets support similar broadly protective imprinting effects during the first 2009 pandemic wave, but not during the second pandemic wave, or during normal, seasonal circulation

of H1N1 and H3N2. In other words, population-level impacts of broadly protective immunity rapidly decay as novel influenza strains establish in humans and become familiar to our immune systems.
Together with recent immunological evidence, these results highlight that narrow immunity is not an intrinsic property of the influenza virus, but an emergent property of within-host competition between broadly and narrowly neutralizing B cells. Due to structural properties of the hemagglutinin antigen, whose variable epitopes are exposed and highly immunogenic, narrowly neutralizing antibodies can usually exclude their less-fit, broadly neutralizing competitors. But exposure to novel avian or pandemic strains (whose conserved epitopes may be the only recognizable immune targets) can facilitate competitive release, and broad immune protection. If broad immunity were more common, it could prevent repeated influenza infections and possibly even slow antigenic drift. Ongoing efforts to stimulate broad immunity with universal influenza vaccines, and to understand its existing population-level impacts will hinge on our understanding of the within-host dynamics of B cell selection.

How ecology across scales influences the evolution of malaria parasites
Megan Greischar, University of Toronto

Mosquito populations undergo dramatic seasonal and human-induced changes, ecology that underpins malaria transmission. Understanding how parasites adapt to changing ecology requires integrating their success across scales, linking parasite traits to within-host proliferation, spread through mosquito populations, and transmission back to hosts. We develop a novel, data-driven model of human malaria infections to examine a within host-trait—how parasites allocate to within-host proliferation versus onward transmission—that influences disease severity and transmission success. We find that a trade-off between early and late infectiousness emerges from within-host ecology, rendering the evolution of transmission investment sensitive to ecological dynamics outside the host. The expansion of a human epidemic favors rapid proliferation, and can overwhelm the evolutionary impact of host recovery rates and mosquito population dynamics. However, any association between transmission investment and host recovery (currently unknown) can dramatically alter parasite strategies and determine whether the evolutionary consequences of intervention efforts are beneficial or costly.

Do viruses interact? Exploring patterns of Herpesvirus co-infection at multiple scales
Anna R. Sjodin, University of Connecticut

Most host individuals are simultaneously infected with multiple pathogens, which can affect infection, virulence, or transmission of each co-infecting pathogen. Viruses demonstrate non-random patterns of co-infection within host individuals, providing evidence for the potential of virus-virus interactions such as competition or facilitation. However, we do not yet understand whether viral co-infection patterns are driven by virus-virus interactions or by other factors such as host demographics, transmission mode, or environment. We collected oral swabs from 1,086 wild bats from Puerto Rico, and recorded six individual-level host traits: mass, forearm length, ectoparasite intensity, sex, and reproductive status. The hosts represented eight species roosting in two separate caves on a single nature reserve. We then tested the hosts twice for Herpesvirus infection and developed a Bayesian community-level occupancy model that examined the impact of host traits on viral infection, while accounting for failed detection of viruses. The latent variable, representing true occupancy of viral infection per host individual, was then extracted and used to examine patterns of co-infection at three scales: host population, cave, and nature reserve. By accounting for host demographics and failed viral detection before analyzing co-infection patterns, this study provides robust information about the role of viral competition and facilitation in shaping infection patterns of Herpesviruses across multiple scales of analysis.

Tuesday 11 June: Behavioral drivers of infectious disease dynamics

Geographic, genetic, and neural origins of human biting in the mosquito vector *Aedes aegypti*
Lindy McBride, Princeton University, Ecology & Evolutionary Biology/Princeton Neuroscience Institute

The mosquito *Aedes aegypti* has recently evolved a strong preference for biting humans, making it one of the most important vectors of human arboviral disease. Preference for humans likely arose in Africa ~10,000 years ago, but the geographic distribution, ecological correlates, and genetic/neural determinants of this behavior are largely unknown. I will describe recent work from our group characterizing behavioral variation among *Aedes aegypti* populations across sub-Saharan Africa and taking advantage of this variation to map the genetic and neural basis of human biting. Our results reveal profound heterogeneity in both mosquito and human populations, with implications for understanding the spread of human disease.

Feeding colds and starving fevers? Evolutionary theory illustrates why appetite during illness matters.
Jessica L. Hite, University of Nebraska, Lincoln

A perplexing quirk of many host-pathogen interactions is that hosts typically reduce their food intake when infected, or merely exposed to, infectious agents. The occurrence of this behavior is widely-documented. Yet, the ecological factors that influence it, how it affects disease outcomes, or why it evolved remains poorly resolved. Addressing this gap carries important implications for both basic and applied biology; feeding behavior functions as a 'master switch' that governs within-host energetics, physiology, and immune functions with downstream consequences for host life history — and the pool of resources available to fuel (or inhibit) parasites and pathogens.

We synthesize recent empirical studies and use an adaptive dynamics approach to examine how changes in food intake affects the evolution of virulence (pathogen-induced harm to hosts) and the size of epidemics. We show that, depending on dietary contexts (i.e., ratios of specific macro-nutrients), changes in feeding behavior (e.g., reduced food intake) can select for higher or lower virulence. Importantly, we also find that changes in resource acquisition can have disparate effects at the individual- vs. population-level. Accounting for this resource-driven tug-of-war between hosts and parasites can, therefore, reveal novel and unexpected outcomes that are not captured by classical evolutionary theory. Moreover, this data-theory integration proves essential to pinpointing the key evidence needed to rigorously address this biological mystery.

Modelling the transmission of Devil facial tumour disease using contact networks
Douglas Kerlin, Environmental Futures Research Institute, Griffith University, Brisbane, Australia

The social structure of wildlife populations can play a significant role in the transmission of disease. Devil facial tumour disease (DFTD), a deadly transmissible cancer of Tasmanian devils (*Sarcophilus harrisii*), is spread by the direct transmission of cancer cells by biting. It is generally assumed that DFTD transmission is frequency-dependent. Infected individuals develop aggressive facial tumours, which can cause blindness and interfere with feeding, leading to death. Contacts within a population of wild Tasmanian devils, yet to be affected by DFTD, were recorded over a period of 6 months (January to June, encompassing both mating and non-mating periods) using collars fitted with proximity loggers. Collar data was used to construct contact networks based on the frequency of interactions devils had with other individuals in the population, with network edges weighted by the number of new biting wounds observed on devils. Contact networks were subsequently used to develop exponential random graph models (ERGMs), describing the network structure with reference to the sex and age of devils in the network. A simulation model, incorporating realistic Tasmanian devil population dynamics (based on capture-mark-recapture data) was developed, to model the possible spread of a new DFTD infection into the population, with these ERGMs used to simulate network structure each timestep. Results of this analysis provide insights into pathways of DFTD (and other frequency-dependent infections) transmission and highlight significant behavioural drivers of pathogen spread.

The role of behaviour in parasite evolution
Emily Durkin, University of Florida

Parasitic lifestyles have evolved many times in animals, but how such life- history strategies evolved from free-living ancestors remains a great puzzle. Transitional symbiotic strategies, such as facultative parasitism, are hypothesized evolutionary stepping stones towards obligate parasitism. However, to consider this hypothesis, heritable genetic variation in infectious behaviour of transitional symbiotic strategies must exist. To provide evidence for heritable genetic variation in infectious behaviour we experimentally evolved infectivity and estimated the additive genetic variation in a facultatively parasitic mite*, Macrocheles muscaedomesticae*. Mites responded positively to selection for increased infectivity; realized heritability of infectious behaviour was significantly different from zero and estimated to be 16.6% (4.4% SE). Our study is the first to provide an estimate of heritability and additive genetic variation for infectious behaviour in a facultative parasite, which suggests natural selection can act upon facultative strategies with important implications for the evolution of parasitism. Furthermore, we discuss mite personality types that may be predictive of their parasitic behaviour.

Evolution and manipulation of vector behavior
Sylvain Gandon, DR2 - CNRS Montpellier

The transmission of many animal and plant diseases relies on two main components of the behavior of arthropod vectors: the biting rate and the biting choice of the vector. In particular, the choice to feed on either infected or uninfected hosts can dramatically affect the epidemiology of vector-borne diseases. I will use an epidemiological model to explore the impact of host choice behavior on the dynamics of these diseases and I will examine selection acting on vector behavior, but also on pathogen manipulation of this behavior. This model identifies multiple evolutionary conflicts over the control of vector behavior and generates testable predictions under different scenarios. In general, the vector should evolve the ability to avoid infected hosts. However, if the vector behavior is under the control of the pathogen, uninfected vectors should prefer infected hosts while infected vectors should seek uninfected hosts. But some mechanistic constraints on pathogen manipulation ability may alter these predictions. These theoretical results will be discussed in the light of observed behavioral patterns obtained on a diverse range of vector-borne diseases. These patterns confirm that several pathogens have evolved conditional behavioral manipulation strategies of their vector species. Other pathogens, however, seem unable to evolve such complex conditional strategies. Contrasting the behavior of infected and uninfected vectors may thus help reveal mechanistic constraints acting on the evolution of the manipulation of vector behavior.

When a megacity goes on holiday: the impact of population mobility on the spread of local epidemics
Ayesha Mahmud, Harvard University

Fluctuations in population density and mobility are important drivers of epidemics, but are often difficult to quantify. Understanding the role of population mobility in infectious disease outbreaks is particularly crucial in the context of rapidly growing and highly connected urban centers in low and middle income countries, which can act to amplify and spread local epidemics both nationally and internationally. Here, we combine estimates of population movement from mobile phone data for millions of subscribers in Dhaka, Bangladesh, with epidemiological data from a household survey, to understand the role of population mobility on the spatial spread of chikungunya within and outside Dhaka city during a large outbreak in 2017. The peak of the 2017 chikungunya outbreak in Dhaka coincided with the annual Eid holidays, during which large numbers of people traveled from Dhaka to their native region in other parts of the country. We show that normal population fluxes around Dhaka city played an important role in determining disease risk, and also that travel during Eid was crucial to the spread of the infection to the rest of the country. Our results highlight the impact of large-scale population movements, for example during holidays, on the spread of infectious diseases. These dynamics are difficult to capture using traditional approaches, and we compare our results to a standard diffusion model to highlight the value of real-time data from mobile phones for outbreak analysis and forecasting.

The perception kernel: vector behavior and disease transmission
Janis Antonovics, University of Virginia

Predictions of disease spread in host-pathogen systems have been usually based on fixed dispersal kernels. However, in vector transmitted diseases such assumptions are unlikely to be met because vectors can adjust their visitation and flight behavior in response to host density, for example, by moving further when hosts are further apart. To model vector transmission, we introduce the concept of a perception kernel, where vector behavior is based on simple decisions following the vector's distance dependent perception of the spatial distribution of the host. We show that the perception kernel results in expected patterns of vector transmission in relation to density obtained from mean-field models, but also that it results in counter-intuitive patterns of disease spread in spatially explicit populations. We illustrate how the perception kernel is applicable to experimental and field data using a pollinator-transmitted plant pathogen as a model system.

Food, love, and war: nutrition determines reproductive effort when threatened with infection
Kristin Duffield, School of Biological Sciences, Illinois State University

The threat presented by pathogenic infection can lead to an alteration of life history strategy by hosts. One outcome is increased investment in current reproduction following a cue of impending mortality (e.g., infection), which decreases the expectation of future offspring. This is known as the terminal investment hypothesis. In this framework, it has largely been overlooked that the terminal investment threshold (i.e., the level of cue required to switch reproductive strategy) is likely contingent on an organism's condition and its environmental context, aside from the threat itself. Nutrition is an important factor influencing individual condition, with key effects on life history parameters that could affect the expression of terminal investment. Recent work has revealed the nutritional underpinnings of a trade-off between immunity and reproductive effort in the cricket *Gryllodes sigillatus*. Using diet combinations identified by this study, specifically distinct protein:carbohydrate ratios related to optima for immune and reproductive effort respectively, we addressed if nutrition influences an individual's terminal investment threshold. We reared male *G. sigillatus* on diets maximizing immune function or reproductive effort, before exposing them to one treatment of a spectrum of increasing simulated infection cues. We then quantified male reproductive effort (calling), to comprehensively quantify terminal investment thresholds across diets, and additionally aspects of cellular and humoral immune function, to identify any underlying trade-offs. Our results confirm the prediction that nutrition, with its key link to individual condition, influences shifts in the reproductive strategy of hosts when they are faced with a cue of a survival threat.

Modeling seasonal commuting behavior for inferring infectious disease dispersal
John R. Giles, Johns Hopkins Bloomberg School of Public Health

Movement of human populations can impact disease transmission dynamics through contact heterogeneities of susceptible and infectious individuals. The recent availability of call data records (CDR), which measure mobile phone usage, has enabled spatial models of disease transmission that explicitly model contact heterogeneities based on human mobility. These models rely on the number of trips observed between an origin and destination during a unit of time, however, the length of time spent in the destination (trip duration) also impacts disease dynamics. We analyzed daily CDR for 107 districts in Namibia from 2010–2014, which provide the number of trips made among districts and the duration of each trip. We fit hierarchical Bayesian models to the CDR that describe the exponential decay in trip duration, the joint-distribution of trip duration and trip distance, and a novel gravity formulation that contains a dispersal kernel conditioned on trip duration. We then developed spatial TSIR simulations for influenza and measles that incorporate estimates of trip duration decay and connectivity. Preliminary analyses indicate that trip duration has a positive log-linear relationship with trip distance, where longer durations occur for travel among rural districts compared to travel among urban districts. We also found that when trip duration is incorporated into spatial transmission simulations, the pathogen generation time can have a larger impact on the spatial force of infection based on the temporal

contribution of infectious individuals on each epidemic generation. This work increases our understanding of both spatial and seasonal patterns in disease dynamics due to human mobility.

Tuesday 11 June: Environmental Drivers of Infectious Disease Dynamics

Climate and Influenza: Associations, Processes and Implications
Jeffrey Shaman, Mailman School of Public Health Columbia University

Many pathogens, as part of their natural life cycle, experience periods of time in either the ambient environment or poikilothermic vector intermediaries. During these periods, pathogen survival and transmission may be modulated by physical environmental conditions. For influenza, considerable evidence indicates that atmospheric absolute humidity conditions alter virus viability and transmissibility once expelled from an infected host. The mechanisms underpinning this association remain underdetermined; however, this effect of humidity appears to explain the seasonality of influenza in temperate regions, as well as the timing of outbreaks during pandemic events. This connection of virus viability with ambient absolute humidity conditions has important implications for the control of influenza in indoor environments.

El Niño drought and tropical forest conversion synergistically determine mosquito vectorial capacity
Nichar Gregory, Imperial College London

Extreme warming events can profoundly alter the transmission dynamics of mosquito–borne diseases by affecting the physiology of mosquito vectors. Typically, models used to predict disease transmission use environmental data collected at coarse spatiotemporal scales. However, as small-bodied ectotherms, mosquitoes are more likely to respond to fine-scale temperature dynamics. Vegetation structure is a key mediator of local temperature, and drivers of environmental change (e.g. deforestation) can significantly alter diurnal temperature cycles. Disturbance activities can also hinder the buffering capacity of natural habitats, making them more susceptible to extreme weather events (e.g. droughts). Using field experiments spanning three years in Malaysian Borneo, we investigated the effects of land-use-mediated local temperature on life-history traits of a dominant mosquito vector, *Aedes albopictus*. Combining field-derived measurements with those from the literature, we parameterised a vectorial capacity model to estimate the effects of forest conversion on disease transmission potential. We found that variation in temperature due to forest conversion dramatically increases vectorial capacity, but that this effect was mediated by an El Niño drought. Additionally, we found that laboratory-derived estimates were poor predictors for trait performance under field conditions. This work highlights the importance of scale when using environmental data to drive transmission models, and the synergistic effects of land-use and seasonal climate variations for predicting a key disease transmission-relevant mosquito trait.

The Influence of Birth Rate and Meteorological Indices on the Temporal Patterns of Rotavirus Infection in Dhaka (Bangladesh)
Ernest Asare, Yale School of Public Health

Background: The introduction of rotavirus vaccines in Bangladesh is imminent, but the impact is likely to be low to moderate based on observations from other low-income countries. In order to identify strategies to improve vaccine performance, a better understanding of the drivers of pre-vaccination rotavirus patterns is required. We investigated the importance of seasonal variations in the birth rate and meteorological indices (degree of wetness and diurnal temperature range) as potential drivers of spatio-temporal variations of rotavirus incidence in Dhaka.

Methods: We fit mathematical models to 22 years of rotavirus surveillance data from Dhaka with and without incorporating seasonal variation in the birth rate and meteorological indices. The models were fitted to both the whole time series and subsets of the data (1990-2001 and 2003-2012) to estimate model parameters. The sub-data were used for both in-sample fitting and out-of-sample model validation.

Results: The models showed good agreement with the observed age distribution of rotavirus cases and were able to capture the observed shift in seasonal patterns of rotavirus hospitalizations from biannual to annual peaks, particularly when incorporating seasonality in the birth rate. In addition, models that explicitly incorporate meteorological indices were able to predict out-of-season outbreaks of rotavirus. Models incorporating both the seasonal birth rate and meteorological indices provided the best fit to the data.

Conclusions: Both demographic and environmental factors are important drivers of rotavirus patterns in Dhaka, Bangladesh. Model we developed can be used to evaluate the impact of rotavirus vaccination in Dhaka against the changing patterns of disease incidence.

Predicting warming-induced infectious disease epidemics with the metabolic theory of ecology
Devin Kirk, University of Toronto

Environmental conditions can impact the spread of disease, but there has been debate as to whether warming temperatures will increase the frequency of infectious disease epidemics. The metabolic theory of ecology (MTE) provides a general framework of thermal scaling that may be useful for predicting how climate change will affect disease dynamics. Using *Daphnia magna* and a microsporidian gut parasite, we conducted three experiments across a wide thermal range and fitted mechanistic models of within-host parasite population dynamics and between-host transmission models that utilize MTE submodels for parameters. We found that the MTE models effectively predict host survival, parasite growth, cost of infection, and disease transmission across temperature. We then used these models to parameterize a population-level epidemiological model to predict disease dynamics under both constant and warming environmental conditions. We tested our model predictions by driving experimental *Daphnia* – parasite populations through constant or slowly warming conditions and found that our MTE model is able to accurately forecast disease dynamics and whether or not an epidemic will occur. Our results serve as a proof of concept that linking simple metabolic models with a mechanistic host–parasite framework can be used to predict temperature responses of parasite population dynamics at both the within-host and between-host levels.

Vectors as foraging animals: a frame-shift for disease ecology
Elizabeth Borer, University of Minnesota

Insect vectors of disease are animals that forage in their environment, avoiding predators while seeking nutrition and mates. For pathogens transmitted by insects, such behavioral choices made by individual vectors can create variable risk among host individuals and control the rate of pathogen spread in a host population. For example, an individual host's nutritional value from the perspective of the vector, the local predation risk perceived by the vector, or the local abiotic environment can alter the behavior and foraging decisions of insect vectors. Yet, in disease ecology, models often employ a highly simplified caricature of vectors, such as global dispersal and random host encounter; the relatively rare models that incorporate vector behavior have shown that even relatively simple behavioral rules can improve predictions of infectious disease spread. In part, this mismatch has arisen because experimental studies manipulating vectors, pathogens, hosts, and the biotic and abiotic environment in which vectors make choices is challenging both logistically and ethically for most animal pathogens. I will talk about experimental and modeling work with insect vectors of plant viruses that is unmasking the conditions under which vector behavior will be most likely to generate dynamic outcomes that differ from highly simplified models of vector-borne disease.

Unraveling the seasonal epidemiology of pneumococcus
Matthieu Domenech de Cellès, Institut Pasteur, Université Paris-Saclay

Infections caused by *Streptococcus pneumoniae*—including invasive pneumococcal diseases (IPDs)—remain a significant public health concern worldwide. The marked winter seasonality of IPDs is a striking, but still enigmatic aspect of pneumococcal epidemiology in non-tropical climates. Here we confronted age-structured

dynamic models of carriage transmission and disease with detailed IPD incidence data to test a range of hypotheses about the components and the mechanisms of pneumococcal seasonality. We find that seasonal variations in climate, influenza-like illnesses, and inter-individual contacts jointly explain IPD seasonality. We show that both the carriage acquisition rate and the invasion rate vary seasonally, acting in concert to generate the marked seasonality typical of IPDs. We also find evidence that influenza-like illnesses increase the invasion rate in an age-specific manner, with a more pronounced effect in the elderly than in other demographics. Finally, we quantify the potential impact of seasonally-timed interventions, a new type of control measures that exploit pneumococcal seasonality to help reduce IPDs. Our findings shed new light on the epidemiology of pneumococcus and may have notable implications for the control of pneumococcal infections.

Larval blacklegged tick phenology changes with elevation: implications for Lyme disease
David Allen, Middlebury College

Borrelia burgdorferi, the causative agent of Lyme disease, exists in an enzootic cycle between *Ixodes* ticks and vertebrate hosts. The primary transmission loop is from infected nymphal ticks to vertebrate hosts to larval ticks which molt to nymphal ticks, completing the loop. For *B. burgdorferi* to persist in a system vertebrate hosts must stay infectious between nymphal and larval feeding. To investigate how abiotic conditions affect the timing of that feeding, over three years we sampled for blacklegged ticks, *Ixodes scapularis*, along an elevation gradient in the Green Mountains of Vermont, USA. At low elevations most larval ticks fed in the late summer, while at high elevations most fed in the early summer. At all elevations nymphs fed in the early summer. This could present elevation-based differences in the selective pressure for *B. burgdorferi* persistence in the vertebrate host. We investigated this possibility by developing a strain-specific next-generation matrix model for *B. burgdorferi*, parameterized from our field work and literature sources. We show that the asynchronous larval and nymphal feeding at low elevations may select for strains of *B. burgdorferi* with longer persistence in the host. These strains are also the most parthenogenic to humans. Previous work has shown differences in larval *Ixodes* phenology across continental scales in North America and Europe, but this work demonstrates those differences over much small spatial scales.

Wednesday 12 June: Genetics of Infectious Disease Dynamics Across Scales

The West Indies: a popular destination for emerging viruses
Christine Carrington, Faculty of Medical Sciences, The University of the West Indies, Trinidad and Tobago

Most of the islands of the West Indies are resource poor and severely lack diagnostic and surveillance capacity, thus limiting the region's ability to detect and adequately respond to health threats. The islands are at increasing risk for introduction and rapid spread of viruses, due to high volume tourism, commercial traffic and the effects of climate change. In addition, the southernmost island, Trinidad, lies only 11 km off the Venezuelan coast of South America, where political unrest and an ongoing humanitarian crisis has led to a large and steady influx of undocumented migrants and illegally-trafficked livestock, wildlife and animal products. This increases the risk of animal, zoonotic and human pathogens entering the country and positions Trinidad as a potential gateway and epicentre for the spread of infectious agents from South American hotspots to North America.

The role of the islands as entry points or as hubs for regional dissemination of mosquito-borne viruses that have emerged in the America, both recently (e.g. Chikungunya virus, Zika virus) and historically (e.g. Yellow Fever virus, Dengue virus) will be discussed, including data from recent serosurveys and phylogeographic analyses. The latter reveal patterns of arboviral gene flow driven by human traffic, including long distance links, often reflecting shared colonial histories among countries within the region and with extra-regional hotspots for viral emergence. Additionally, population genetic and phylogeographic analyses of *Desmodus rotundus* (common vampire bat) and rabies viruses from Trinidad

and from the South American mainland will be presented, showing evidence for regular mainland-island bat movement and repeated rabies virus introductions to the island. A serosurvey across several bat species in Trinidad confirming rabies exposure in species capable of migrating long distances will also be presented. Together these data highlight how the islands serve as stepping stones or as direct links between South and North America, and emphasise the need for improved diagnostic and surveillance systems in the West Indies.

The dynamic and non-neutral genetic strain structure of *Plasmodium falciparum* with implications for malaria epidemiology

Shai Pilosof, University of Chicago

In their competition for hosts, parasites with antigens that are novel to host immunity will be at a competitive advantage. The resulting frequency-dependent selection can structure parasite populations into strains of limited genetic overlap. For the causative agent of malaria, *Plasmodium falciparum*, the high recombination rates and associated vast diversity of its highly antigenic and multicopy *var* genes preclude such clear clustering; this undermines the definition of strains as specific, temporally-persisting gene variant combinations. We used temporal multilayer networks to analyze the genetic similarity of parasites in both simulated data and in an extensively and longitudinally sampled population in Ghana. When viewed over time, populations are structured into modules (i.e., groups) of parasite genomes whose *var* gene combinations are more similar within, than between, the modules, and whose persistence is much longer than that of the individual genomes that compose them. Comparison to neutral models that retain parasite population dynamics but lack competition reveals that the selection imposed by host immunity promotes the persistence of these modules. This modular structure is in turn associated with a slower acquisition of immunity by individual hosts. Modules thus represent dynamically generated niches in host immune space, which can be interpreted as strains. Multilayer networks extend the scope of phylodynamics analyses by allowing quantification of temporal genetic structure in organisms that generate variation via recombination or other non-bifurcating processes. The temporal modular structure should enable the formulation of tractable epidemiological models that account for parasite antigenic diversity and its influence on intervention outcomes.

Phylogeography reveals reduced transmission of feline immunodeficiency virus among bobcats in an urban landscape

Christopher Kozakiewicz, University of Tasmania (now at Washington State University)

Spatially heterogeneous landscape factors such as urbanisation can have substantial impacts on the severity and spread of wildlife diseases. It is important to understand how these impacts may vary among populations and among different spatial scales, but research directly linking patterns of transmission to heterogeneous landscapes remains rare. Feline immunodeficiency virus (FIV) is a directly-transmitted retrovirus that infects many felid species and is a model for phylogenetic inference of pathogen transmission at landscape scales. We reconstructed phylogenetic relationships among FIV isolates sampled from five genetically and spatially distinct bobcat (*Lynx rufus*) populations in coastal southern California. We found strong broad-scale FIV phylogeographic structure with respect to major urban barriers among host populations, with divergence dates reflecting historical urban growth patterns in this region. We then implemented a “landscape phylogeographic” approach to explicitly test fine-scale landscape factors affecting FIV phylogenetic relatedness and dispersal velocities within and among populations. We found that FIV isolates sampled from areas that differed in the amount of natural landcover were more distantly related, suggesting reduced transmission among natural and non-natural areas. Further, FIV lineages dispersed more rapidly through areas of higher vegetation density. These multiple lines of evidence demonstrate how urbanisation can change patterns of disease transmission and provide insights into how continued urban development may influence the incidence and management of wildlife disease.

Does genetic diversity reduce disease risk?
Amanda Gibson, University of Virginia

Why does infectious disease sweep through some host populations and not others? One prominent hypothesis proposes that diseases spread more readily through host populations with low genetic diversity. This hypothesis stems from the idea that genetically similar hosts are likely susceptible to the same infections. Hence the transmission rate of an infection will be higher in groups of genetically similar hosts than in groups of genetically dissimilar hosts. This hypothesis has an intuitive appeal, and epidemics in crop monocultures provide dramatic examples of the vulnerability of low diversity populations. Yet results of empirical tests do not consistently support a link between diversity and disease in natural systems. To resolve this uncertainty, we are conducting a meta-analysis of >100 studies to broadly evaluate two key predictions of the hypothesis that genetic diversity limits disease risk. First, we are testing the prediction that infection prevalence declines as genetic diversity of host populations increases. We are comparing our results across observational and experimental studies of natural and agricultural systems. Second, we are testing the prediction that low diversity populations show elevated variation in infection prevalence. Though this prediction is rarely evaluated, variation in disease risk is critical to disease management: a single large epidemic can decimate a crop or drive local host extinctions. The results of this study will answer a fundamental question in the ecology and evolution of infection disease by providing a general quantification of the effect of genetic diversity on disease dynamics.

Multiscale genetic drift shapes pathogen variation within hosts
David Kennedy, Pennsylvania State University

Pathogen genetic variation within hosts can alter the severity and spread of infectious diseases, but little is known about the forces that shape this variation. Infectious disease dynamics inherently occur at multiple scales, requiring both replication within hosts and transmission between hosts. Genetic drift is a consequence of population dynamics, and so pathogen variation may be influenced by multiscale genetic drift. Analyses of drift in pathogens, however, have oversimplified pathogen population dynamics, either by considering dynamics only at a single scale or by making drastic simplifying assumptions. By combining high-throughput sequencing of field isolates with multiscale mathematical modeling of the gypsy moth and its baculovirus, we show that genetic drift imposed by host-pathogen population dynamics that occur at multiple scales explains the levels of pathogen diversity seen in the gypsy moth virus system. When the effects of drift are simplified by neglecting transmission bottlenecks and stochastic variation in virus replication within hosts, the model fails. A de novo mutation model and a purifying selection model similarly fail to explain the data. Our results show that genetic drift can play a strong role in determining pathogen variation and that mathematical models that account for pathogen population growth at multiple scales of biological organization can be used to explain this variation.

Prediction of post-vaccine *Streptococcus pneumoniae* lineage frequencies based on potential accessory genes under selection
Pamela P. Martinez, Harvard T.H. Chan School of Public Health

Predicting how pathogens evolve in response to intervention measures is challenging. In the case of Pneumococcal conjugate vaccines, they modify the population dynamics of *Streptococcus pneumoniae* by targeting only a pool of bacterial serotypes. It has been shown that even though the frequencies of the bacterial lineages are affected by the introduction of the vaccine, the accessory gene frequencies remain relatively constant. Negative frequency-dependent selection has been proposed as one of the mechanisms that explains the maintenance and restoration of loci frequencies post-intervention. By implementing a model that relies on negative frequency-dependent selection on the accessory gene frequencies, we have accurately predicted the effect of vaccination in the frequencies of *Streptococcus pneumoniae* lineages present before the vaccine introduction. We further examined which accessory genes are more likely to be under frequency-dependent selection, their predictive ability, and the implications of these findings in predicting the effect of future interventions on bacterial population dynamics.

Thursday 13 June: From Wondrous Complexity to One Health

A hyperparasite with a missing viral helper: the ecology and evolutionary history of a novel satellite virus in vampire bats
Laura Bergner, University of Glasgow

Satellite viruses are hyperparasites that require an unrelated "helper" virus to spread between cells and transmit. The best known satellite virus, Hepatitis deltavirus, causes the most severe form of viral hepatitis in humans and requires co-infection with Hepatitis B to spread. Recent studies described related satellite viruses in other host groups, but their biology and evolutionary history relative to human deltavirus remain obscure. Using metagenomic sequencing, we discovered a novel deltavirus in the saliva of common vampire bats (Desmodus rotundus), termed DrDV, which is widespread in Peru and infects 17.5% (N=240) of individuals with no detectable age or sex biases in infection. Recaptures of infected individuals over 3 years suggested non-pathogenic infections in bats. Surprisingly, despite genetic similarity to human deltavirus, DrDV was absent from bat livers and DrDV-infected bats were not co-infected with Hepatitis B or any Hepatitis B-like viruses. Finally, we detected an apparent cross-species transmission of DrDV to a fruit bat, which implies that these host species either share a common helper virus or that DrDV can use a variety of helper viruses. Our findings show that both the tissue tropism and transmission mechanism of satellite viruses can be evolutionarily plastic and raise questions about how viruses requiring a helper are transmitted within and between species.

Individual Specialization and Disease Spread in Multi-Host Communities: Plant-Pollinator Networks
Stephen Ellner, Cornell University

Interaction networks for multi-species communities are typically constructed at the species level or above. A link is drawn between, for example, a host species and a vector species if there are contacts between any individuals of those two species, and link strength is measured by the frequency of such contacts. However, generalist species often consist of more specialized individuals having preferences (permanent or time-varying) for different subsets of the resources used by the species as a whole. We use an SIS model for pathogen spread on plant-pollinator networks to explore the epidemiological impacts of individual pollinator specialization on different flower species. We find that modeling and analysis "blind" to individual specialization can badly mis-estimate R0 and steady-state disease prevalence, predicting die-off of a disease that actually is strongly persistent (R0>5). Specialization typically favors disease persistence, but often lowers steady-state prevalence. Effects of dynamic preferences remain substantial so long as typical preference switching times are comparable to the time from infection to death or recovery, or longer. Disease ecologists have long recognized that permanent heterogeneity (superspreaders, central versus peripheral locations in a network, host competence, etc.) can have large effects on epidemiological outcomes. Our results suggest that the same can be true for dynamic heterogeneity, even if all individuals are the same on average over time.

Secondary plant chemicals alter virulence and transmission of herbivore parasites through a combination of toxicity and modulation of immunity and the microbiome
Jacobus de Roode, Emory University

Infectious disease dynamics are not only driven by the interaction between host and parasite, but also by environmental factors. In plant-herbivore-parasite interactions, these environmental factors are largely accounted for by the chemical traits of host plants. Toxic chemicals could theoretically reduce parasite virulence and transmission through multiple mechanisms. Chemicals could directly interfere with parasites, or they could enhance host immunity. Alternatively, they could reduce immunity by providing an alternative defense, or modulate the host's microbiome to reduce parasite infection. Monarch butterflies are specialist feeders of milkweed host plant species, which vary in their toxicity of secondary chemicals called cardenolides. Monarchs are commonly infected with a debilitating protozoan parasite, and infected females preferentially lay their eggs

on high-cardenolide species of milkweed, which reduce infection in their offspring and alter virulence and transmission. Using a series of experiments, including transcriptome analyses and fecal transplants, we found that toxic plants did not enhance immunity, but did down-regulate a small number of immune genes. Additionally, transplanting fecal matter from monarchs reared on toxic milkweed to monarchs reared on non-toxic milkweed resulted in a transfer of anti-parasitic resistance, implying an important role for the monarch gut microbiome. These results show that the chemicals in host plants can be major drivers of infectious disease in herbivores, most likely as a result of direct anti-parasite toxicity and modulation of immunity and the microbiome.

Management practices and age cohorts that contribute to increased Peste des petits ruminants seroprevalence in sheep, goats, and cattle in northern Tanzania

Catherine Herzog, Center for Infectious Disease Dynamics, Penn State University

Peste des petits ruminants virus (PPRV) causes a contagious disease of high morbidity and mortality in sheep and goats and has been shown to elicit seroconversion in cattle. PPRV threatens 80% of the global small ruminant population of nearly 2 billion animals. Using a large serosurvey from 20 villages in northern Tanzania, we investigated PPRV age-seroprevalence and household survey data to determine significant risk factors and specific management practices for increased PPRV circulation, to explore spatial variation in the force of infection at multiple scales, and to identify the age cohort(s) responsible for PPRV transmission among sheep, goats, and cattle. We used generalized linear mixed models within a catalytic framework to calculate the force of infection (FOI, per capita infection rate of susceptible hosts) and reproductive numbers using both an age constant and piecewise constant model. We used a machine learning approach to identify specific management risk factors for PPRV seroconversion such as confinement and grazing practices, seasonal camp and market attendance, herd size, and demographics. We found the dentition-based age group with the highest FOI for sheep and goats was 1.5-2 years of age, and 3.5-4.5 years of age for cattle. Pastoral management systems had higher FOI and a wider range of ages with a higher FOI than agropastoral systems. Insights from this investigation of specific management practices will lead to improved control strategies through feasible changes in non-vaccination practices, geographical areas and host species to target, and discovery of additional ecological mechanisms driving PPRV seroconversion.

Selection for increased virulence leads to decreased bacteriocin production in insect-pathogenic Xenorhabdus nematophila

Amrita Bhattacharya, Indiana University Bloomington

Bacteria exhibit a wide array of social behaviors. For pathogenic bacteria, their social behaviors not only affect their growth within the host but may also influence their effect on their hosts. Here we investigate how a ubiquitous bacterial social trait, bacteriocin production, is associated with the pathogen's ability to harm its host, virulence. Bacteriocins are costly antimicrobial toxins produced by almost all bacteria that can kill even closely related strains. Despite conferring a competitive advantage, bacteriocin production imposes growth costs on the producing lineage. Theory predicts a negative correlation between virulence and bacteriocin production owing to their inverse correlations with growth. We directly test this prediction using experimentally evolved lineages of the insect-pathogenic Xenorhabdus nematophila. We compare bacteriocin production and growth between an ancestral population, and 16 derived lineages that show faster host killing, and thus increased virulence, than the ancestral population. Consistent with predictions, we find that the evolved, more virulent lineages show dramatically reduced bacteriocin production and faster growth relative to the ancestral population. We also find that bacteriocin production is negatively correlated with growth across the examined populations, supporting the underlying assumption of theoretical models. These results, to the best of our knowledge, provide some of the earliest direct insights into how virulence and bacteriocin production coevolve in natural pathogenic populations, and demonstrate how host health may be affected by social traits of pathogenic bacteria.

Thresholds, coastal climate, and transcritical variation induce geographic heterogeneity in West Nile virus transmission across Los Angeles
Nicholas Skaff, University of California, Berkeley

Temperature is widely known to influence the spatiotemporal dynamics of infectious disease transmission, particularly as critical values (e.g., thermal optima, thresholds) are achieved or surpassed. When temperature conditions exhibit such 'transcritical variation', abrupt spatial or temporal discontinuities may result, generating sharp geographic or seasonal boundaries in transmission. Here, we develop a spatiotemporal machine learning algorithm to examine the implications of transcritical variation for West Nile virus (WNV) transmission in the Los Angeles metropolitan area (LA). Analyzing a massive vector and WNV surveillance dataset between 2006-2016, we found that mean temperature lagged one month strongly predicted the probability of WNV presence in Cx. quinquefasciatus pools (Cx. infection probability), forming distinctive inhibitory (10.0°C-21.0°C) and favorable (22.3°C-30.2°C) mean temperature ranges that bound a narrow 1.3°C transitional zone. Temperature during the most intense months of WNV transmission (July-September) had stronger effects on Cx. infection probability in coastal and central LA than inland, because temperature variation in cooler marine-influenced settings was more frequently transcritical, i.e., traversed the narrow transitional temperature range. As a result, temperature, operating through Cx. infection probability, had a stronger effect on human WNV incidence in coastal and central zones, than inland. This contributed to a pronounced expansion in the geographic distribution human cases into coastal and central parts of LA during warm months. Our findings suggest that transcritical variation can generate abrupt, highly localized heterogeneity in WNV transmission, and may determine sensitivity of transmission to future temperatures, especially in locations where current temperatures lie at the cusp of critical values.

The role of viral fitness variation in understanding the geographic origins of seasonal influenza
Baptiste Elie, Emory University

Human influenza viruses circulate globally, with phylogeographic studies indicating that these viruses migrate annually from tropical Asia to temperate regions. Wen et al. (2016) recently showed that a higher R_0 value in tropical regions versus temperate regions was necessary to fully account for the extent of this pattern in influenza subtype H3N2. While variation in R_0 could be due to geographic differences in host contact rates or environmental factors, this variation could also be due to viral genetics. Here, we hypothesize that viruses circulating in temperate regions have lower fitness on average than those circulating in tropical regions due to geographic bottlenecks and the occurrence frequency of deleterious mutations. To test our hypothesis, we use H3N2 hemagglutinin sequences collected between 2012 and 2018, and their metadata. We reconstruct the migration events of this subtype and calculate viral fitness based on site-specific amino acid preferences as inferred through deep-mutational scanning (Lee et al. (2018)). By analyzing the evolution of fitness in the context of migration events, we first show that migrating viruses appear to be randomly sampled from source regions, with no evidence for more fit viruses preferentially seeding sink regions. Second, we ask whether viral populations in sink regions tend to evolve towards lower fitness due to deleterious mutation accumulation. By combining the results from these two analyses, we document the contribution of viral fitness variation on observed patterns of H3N2 geographic spread.

Predicting the spread of Aedes aegypti and Ae. albopictus at local and global scales
Oliver Brady, London School of Hygiene and Tropical Medicine

The mosquito species Aedes aegypti and Ae. albopictus are the principal vectors for a range of growing global viral diseases including dengue, Zika, Yellow fever and chikungunya. One key driver of the expanding distribution of these diseases has been the spread of these mosquitoes to new geographic areas. While we know that human travel and trade networks are the principle means by which these species spread and that environmental drivers dictate whether they will establish on arrival, we have an incomplete understanding of how these two factors interact to determine the invasion process.

Here we illustrate how combining species distribution and geographic spread models can be used to infer historical patterns of spread and make future predictions about where these mosquitoes will spread to next. We focus on two different examples: i) prediction of the global future distribution of Ae. aegypti and Ae. albopictus in 2020, 2050 and 2080 using the latest climate and demographic change projections and ii) prediction of monthly detection of each species in the USA as part of the CDC Aedes Challenge 2019.

These contrasting applications show the importance of different drivers of spread at different spatial and temporal scales. Models and maps such as these can play an important role in targeting surveillance and control efforts to contain the spread of these species, as well as for improving predictions of the spread of the viruses they transmit.

Tropical rainforest flies carrying pathogens form long-term associations with wild non-human primate social groups

Jan F. Gogarten, Robert Koch Institute, Berlin, Germany

Living in groups provides benefits but incurs costs such as attracting disease vectors. For example, synanthropic flies associate with human settlements, and higher fly densities increase pathogen transmission. We investigated whether such associations also occur for mobile non-human primate groups (NHP). We studied flies in a group of wild sooty mangabeys (Cercocebus atys atys) in Taï National Park, Côte d'Ivoire. We observed a 706% higher fly density within the mangabey group than outside the social group. A mark-recapture experiment showed that flies stayed with the group for up to 12 days and for up to 1.3 km. We then tested flies for two pathogens infecting mangabeys in this ecosystem: Bacillus cereus biovar anthracis (Bcbva), causing rainforest anthrax, and Treponema pallidum pertenue, causing yaws. Flies contained treponemal (6/103) and Bcbva (7/103) DNA, and we cultured Bcbva from all PCR-positive flies, confirming bacterial viability. Whole genome sequences revealed a large diversity of Bcbva, likely derived from several sources. To explore whether these fly associations represent a cost of sociality in other NHP, we examined fly densities in the social groups of six species in Kibale National Park, Uganda. We consistently found higher fly densities in social groups than outside social groups and identified a positive relationship between group sizes and fly densities. We conclude that flies carrying bacterial pathogens actively track mangabeys and that such fly associations are widespread across NHP species living in different ecosystems representing a cost to sociality.

Dirty lying cheats: male guppies may use behaviour to avoid infection, conceal disease, and boost parasite transmission

Jessica Stephenson, University of Pittsburgh

Males and females have different agendas. One of the ways this is manifest is in the way they interact with parasites. In general, females appear better defended against parasites than males. How this difference might drive sex differences in behaviour in the presence or absence of infection is poorly understood. Previous research has indicated a negative correlation between behavioural and physiological parasite defence: better-defended individuals engage in behaviours entailing higher infection risk, including social interactions. Here, we use the guppy and a directly transmitted ectoparasite in behavioural experiments testing how this correlation may depend on host sex and infection status. Our results indicate that parasite-induced behavioural plasticity differs substantially between the sexes. Time spent shoaling ('sociality') and activity level did not vary with parasite defence, infection or social context among females. Among males (the less well defended sex), however, sociality was negatively correlated with resistance in the absence and early stages of infection, but positively correlated in late infection, when the parasite is most likely to transmit. Less resistant males may therefore use behaviour to avoid infection, but in late infection become more sociable to increase transmission and mating opportunities. Additionally, males who lost the most mass through the course of infection spent less time swimming, but only in isolation; when in the presence of a shoal, there was no such correlation. These least

tolerant males may mask disease symptoms in order to maintain group membership. We discuss the implications of these patterns for parasite transmission and evolutionary dynamics.

Parasite richness, intensity and prevalence shape the evolution of host seasonal migration
Allison Shaw, University of Minnesota, St. Paul

The role of parasites in determining host ecology and behavior is becoming increasingly recognized. Although parasites (which here we define broadly to include both macroparasites and microparasites) have long been thought to influence the evolution of seasonal migration, precisely determining the conditions under which this occurs by quantifying costs of infection remains a challenge. Furthermore, empirical studies from different systems generate conflicting conclusions of whether migratory behavior is on-the-whole beneficial or costly in terms of infection. Here we developed a model that demonstrates how the metric used to describe infection (richness/diversity, prevalence or intensity) shapes the prediction of whether migration will evolve. Our model shows that predictions based on minimizing parasite richness yield opposite results compared to those based on minimizing infection prevalence. In our model, migration is only selected for when minimizing prevalence, and we find that migrants typically have greater parasite richness but lower infection prevalence than non-migrants (residents). Consistent with these findings, those empirical studies that measure parasite diversity typically find that migrants are worse off than residents, while those measuring prevalence or intensity find the opposite. Our own empirical analysis of fish parasite data finds that migrants (of all types) have higher parasite richness than residents, but with no significant difference in either prevalence or intensity.

A 1912 measles genome from Berlin gives new insights into the virus' evolutionary history
Ariane Düx, Robert Koch Institute, Berlin, Germany

The origins of RNA viruses are notoriously difficult to determine. Molecular dating approaches tend to underestimate divergence times and are often at odds with other information sources (e.g. historical records, endogenous viral elements, phylogeography). This discrepancy can be attributed to differences in short- and long-term substitution rates caused by purifying selection and saturation of nucleotide changes in small genomes with high mutation rates.
For more precise estimates of RNA-viral divergence, we make use of ancient viral sequences and substitution models that account for time dependency of substitution rates (TDR). Here, we re-assess the origin of Measles morbillivirus (MeV) using the to date oldest RNA virus genome, from a fatal measles case from 1912 in Berlin, and a novel TDR model. MeV likely originated in cattle; its closest relative is Rinderpest morbillivirus (RPV). However, dating of this host switch is controversial. Historical considerations favor a scenario where measles was introduced to humans a few thousand years ago. As infection with MeV confers lifelong immunity, a prerequisite for the host switch was a sufficiently large human population, which didn't exist until ~5.000 years ago. Molecular dating, however, has provided a much younger origin placing the most recent common ancestor of MeV and RPV in the 11^{th}-12^{th} century. Our preliminary phylogenetic analyses place the 1912 measles strain basal to all available MeV genomes and push back the divergence date of MeV and RPV. At EEID2019, we will present a new, more precise estimate for the origin of measles which will further our understanding of measles emergence.

Thermal refugia and ecological traps mediate bat survival after infection with the white-nose syndrome fungus
Skylar Hopkins, Virginia Tech

Given environmental conditions that favor disease, pathogens can act as ecological filters that mediate host survival and reproduction. Habitats that were once favorable for hosts across environmental gradients may therefore become refugia and/or population sinks after pathogen invasion. To understand how white-nose syndrome, an emerging infectious disease in North America, and environmental conditions simultaneously influence host survival, we visited 22 hibernacula before, during, and after invasion by the fungus in Michigan

and Wisconsin. During each annual visit in early (November) and late (March) hibernation, we quantified individual bats' roosting temperatures, fungal loads, and survival, focusing on a historically common bat species (Myotis lucifugus). After invasion, we found that relatively warm roosting temperatures were associated with higher observed fungal growth rates on bats between November and March on recaptured bats. Correspondingly, we found that bats that roosted at relatively warm temperatures or had high fungal loads in November were less likely to be recaptured in the spring. Because fungal growth rates are temperature-dependent, relatively cold roosts serve as thermal refugia that allow some infected bats to survive hibernation. In contrast, most bats have continued to use relatively warm roosts after fungal invasion, perhaps because those warmer roosts minimize energy expenditure during hibernation in the absence of disease. Therefore, post-fungal invasion, warmer roosts might be serving as ecological traps for bats. Over time, bat populations might evolve to select cooler roosts, but only if they can do so given their other physiological constraints during hibernation.

POSTER ABSTRACTS

SESSION 1 – Tuesday 11 June (4:30-7:00 pm)

BEHAVIORAL DRIVERS OF INFECTIOUS DISEASE DYNAMICS
(Posters 1-1 → 1-30)

1-1 The inception and evolution of the field of infectious disease ecology
Ellen Brandell, Pennsylvania State University

Infectious disease ecology is a newly established research field. It is growing expeditiously, yet sometimes lacks recognition as a stand-alone field. This is partially due to a lack of knowledge about who comprises the field, major avenues of training and research, and the evolution of research themes through time. To understand who comprises the field, we administered a survey, and present trends in demographics. For instance, the proportion of women earning PhDs nearly doubled from 1980–2000 (30.5%) compared to recent years (~65%). This means that PhD students and postdocs are more likely to be female, but with increasing age, there is approximate gender parity in position held. In another measure of diversity, we find that most graduate degrees are obtained in the USA, but institutional diversity and the frequency of degrees earned in low- and middle-income countries has increased in the last decade. To understand research trends, we conducted a literature review using top journals selected by survey respondents and performed topic detection using non-negative matrix factorization to explore topic frequency over time. For example, the rate of publication on climate change has increased while that of HIV and hantavirus has decreased. This approach helped group commonly occurring words together (e.g., parasite and model) and identify larger trends. Our work characterizes who comprises disease ecology, major avenues of research, and the journals and articles that define the field. We hope our findings influence the development of training programs and the field as a whole.

1-2 Transmissible viral vaccines: opportunities and challenges
Scott Nuismer, University of Idaho

Spillover from wild animal populations fuels the origin and recurrence of many emerging infectious diseases. This observation identifies novel opportunities to decrease the threat of emergence by reducing or eliminating pathogens within their animal reservoirs. Transmissible vaccines are a powerful new technology that capitalizes on this opportunity. Here I provide a brief history of transmissible vaccines and an overview of the methods used to create them. I then present the results of mathematical models grounded in the biology of transmissible vaccines currently being developed for emerging infectious diseases of humans. The results of these models quantify the impact of transmissible vaccines on pathogen populations, and identify key engineering challenges that must be overcome for transmissible vaccines to be both evolutionarily stable and epidemiologically effective.

1-3 A framework for transitioning models developed through usable science collaborations
Katharine A. Owers, Colorado State University & Center for Epidemiology and Animal Health (USDA APHIS)

The United States Animal Movement Model (USAMM) simulates livestock shipments and the US Disease Outbreak Simulation (USDOS) simulates livestock disease spread based on shipments and local transmission, with optional control implementation. The project that developed these models is an example of "usable science", where research is designed in collaboration with decision makers, in this case with researchers in the Center for Epidemiology and Animal Health (CEAH, a unit of USDA|APHIS). Involving decision makers throughout the research process ensures that the project takes into account the full context and constraints of the decision, providing results that can be used to inform policy. There is a growing body of literature on frameworks for usable science and examples of successful collaborations like this one. However, there is little information about the management of project-related output once the initial research project ends. This is an important aspect of usable science because questions from policymakers are rarely solved by a single answer; instead, most need to be repeatedly revisited as new information becomes available. To enable ongoing use of USAMM and USDOS to inform policy after the project funding their development ends, we are now transitioning them to CEAH. We have developed a framework that addresses five requirements for a successful transition: institutional (agency) familiarity with the models, accessible training materials and documentation, appropriate results for agency users, technical infrastructure to run the models, and that all these components are sustainable after the funding ends. We provide example tasks and strategies related to each requirement.

1-4 Algorithms to optimize surveillance of a city for the vector of Chagas disease
Justin Sheen, University of Pennsylvania

Surveillance for houses infested with triatomines, the insect vectors of Chagas disease, is a challenge, especially in cities. Cities are large, complex environments, and the number of infestations is small. With limited personnel and time identifying a good sample of houses to inspect becomes even more complicated. There are at least two objectives in surveillance: achieving high spatial coverage, and visiting houses that we believe to be at higher risk based on their histories of infestation. The realities of the field make it difficult to achieve both.

We present two algorithms that are designed to achieve the objectives of a surveillance campaign with a specific focus on overcoming the challenges of an urban environment. The first algorithm uses k-means clustering and recursion to create groups of houses based on risk. The second algorithm uses a multi-objective optimization approach with Delaunay triangulation to balance risk information with coverage, and suggests houses to inspect in real time in the field. Both algorithms consistently reduce the mean probability of infestation in a search area, compared to rule-of-thumb approaches, as estimated through an INLA spatio-temporal model.

1-5 Are susceptible hosts also more infectious?
Andrew R. Wargo, Virginia Institute of Marine Science

It is well known that there is a high degree of between host variation in susceptibility to infection as well as infectiousness to new hosts. Although recent studies have shown this heterogeneity can heavily impact disease dynamics, it is rarely accounted for in epidemiological inferences. Furthermore, the relationship between these traits is not well established, and they are often assumed to be positively linked or a single parameter. We sought to disentangle susceptibility and infectiousness and determine if they are correlated. To do so we experimental exposed several independent genetic lines of rainbow trout (*Oncorhynchus mykiss*) to infectious hematopoietic necrosis virus, at a range of challenge dosages. This allowed us to use dose response models to quantify the distribution and mean of susceptibility, defined as the proportion of fish becoming infected, for each fish genetic line. We also quantified the amount of virus shed from each fish, to elucidate infectiousness. We examined how heterogeneity in susceptibility and infectiousness would influence disease dynamics, in comparison to typical models that consider the traits to be homogeneous. We demonstrate that this

heterogeneity can have important implications for the efficacy of disease management through strategies such as vaccination and selective breeding.

1-6 Detecting disease emergence using dynamical footprints
Brett S. Tobias, Odum School of Ecology, University of Georgia

Developing methods for anticipating the emergence or re-emergence of infectious diseases is both important and timely, however traditional model-based approaches are stymied by uncertainty surrounding the underlying drivers. We demonstrate an operational, mechanism-agnostic detection algorithm for disease (re-)emergence based on early-warning signals (EWS) derived from the theory of critical slowing down. Specifically, we used computer simulations to train a supervised learning algorithm to detect the dynamical footprints of (re-)emergence present in epidemiological data. Our algorithm was then challenged to forecast the slowly manifesting, spatially-replicated re-emergence of mumps in England and pertussis in the US. Our method successfully anticipated re-emergence many years in advance, during which time mitigation efforts could have been implemented. Additionally, we examined two case studies in which an outbreak unfolded rapidly, namely the emergence in 2014 of MERS in the Middle East and an outbreak of the plague in 2017 in Madagascar. Our algorithm successfully anticipated both events, with a lead time of one year and one month, respectively. In both instances, the outbreak was detected at the midpoint of the first reported case and epidemic take-off. Taken together, these findings illustrate the power of theoretically-informed machine learning techniques to develop early warning systems for the (re-)emergence of infectious diseases.

1-7 Disease Dynamics Inferred from Last Wills and Testaments
Alexandra Bushby, McMaster University

Historical epidemics of infectious diseases are often studied through mortality records. In England, registration of deaths began in 1538, long after the invasion of the Black Death in the 14th century. Some historical research on the Black Death has been based on monthly counts of wills written in London during known plague epidemics. We undertook a systematic analysis of all wills probated in the Court of Husting, London, 1258-1688.

These wills were digitized in 2017 by British History Online. We wrote an R package that scrapes the wills from the web and provides tools to perform a variety of statistical analyses. We aimed to contribute both to historical epidemiology and to other historical work on Medieval and Renaissance London.

There were 4,110 wills probated by Court of Husting. The date of probate is known for all wills, but the date the will was written is indicated in only 64%. Only 11% of testators were women. Of the 51% of wills that mention an occupation, 82% were merchants, and all others were members of the church, municipal government, or nobility. We obtained a daily time series of numbers of wills written, and a weekly time series of numbers of wills probated (because wills were probated only on Mondays). Four large peaks (during known plague epidemics in 1348, 1361, 1368 and 1375) are clear. Plausible epidemic growth rates can be estimated using will dates, but not probate dates. The distribution of lags from writing to probating wills is approximately lognormal.

1-8 Disproportionate species contributions to multi-host dynamics of the generalist amphibian fungal pathogen; *Batrachochytrium dendrobatidis*
Dave Daversa, University of Liverpool

Although most parasites infect multiple host species, each species typically responds distinctly to parasite exposure and infection. There is a therefore a major push to understand (a) how variation in host community composition affects multi-host infection dynamics and (b) the relative contributions of different host species to infection risk in the broader community. We set out to address those issues using a notoriously generalist pathogen, *Batrachochytrium dendrobatidis (Bd),* a fungus that infects the skin of myriad amphibian species worldwide. We ran a mesocosm experiment whereby we introduced *Bd* into tanks that varied in the presence

and abundance of salamander larvae, frog larvae, and toad larvae – host species which co-occupy sites in Central Spain. The experiments showed that communities with proportionally more salamanders had lower community-level *Bd* prevalence by the end of the experiment. A path analysis revealed that *Bd* dynamics was predominantly driven by infections in frogs, but toad infections also had an influence. We then fit the mesocosm data to a mathematical model that estimated the extent to which each species contributed to the community-level R_0. Frog and toad larvae contributed 2-3 times more to R_0 than expected from their abundance alone, while salamanders contributed little. Together, these findings demonstrate disproportionate species contributions to *Bd* maintenance that results in significant effects of species composition on infection dynamics. More broadly, our work illustrates how basic information on host abundance and infection prevalence can be used target hosts that are key contributors to pathogen transmission and maintenance.

1-9 A preliminary agent-based model to explore the coupled natural human system of human-tick interactions.

Maria del Pilar Fernanadez, Earth Institute, Columbia University

Zoonotic vector-borne diseases are determined by a complex set of ecological factors driving transmission in nature and drivers of human disease risk, including social factors. Although these ecological and social factors are interrelated, they are often studied separately. We propose a coupled natural human system to explore the complex interactions between these factors driving transmission of Lyme disease in Northeast U.S. at a neighborhood/local level. Using an agent-based model (ABM), the main goal is to understand how human-tick encounters and the emergence of Lyme in the population is derived from the interaction between the density of infected vectors and individual human behaviors, including those related to adaptation to perceived risk. Herein, we present a preliminary ABM in which we simulated an environment encompassing patches of urban forests and residential properties with different densities of infected Ixodes scapularis nymphs. Human agents were assigned a random movement within this environment and 3 counterfactual scenarios were simulated after a first tick encounter by the agent: i) avoidance of urban parks; ii) use of personal protection measures; iii) and spray against ticks at the household level. These scenarios were compared to a scenario with no adaptive human response. This is part of a broader project to build an empirically-based ABM combining ecological data collected on Staten Island, NY, and human behavioral data derived from a smartphone application (The Tick App). Combining these data will provide insights into the relative importance of factors driven by humans and nature and potential targets for intervention strategies.

1-10 The role of social behavior in modulating immune phenotype: a proposed ecoimmunological experiment in mice

Alexander E. Downie, Princeton University

Sociality and immunity have not commonly been linked, despite the well-studied connections between sociality and infectious disease exposure. Just as organisms have behavioral strategies to avoid disease in social settings, so too might we expect organisms to use immune strategies reflecting these settings. Indeed, gene expression profiles of monkeys suggest that dominance status affects immune phenotype. We propose a detailed study in mice of how individual immune phenotype varies with social position and behavior. Our planned experiment uses groups of mice kept in a semi-wild, outdoor setting, which more closely mirrors a natural environment and also produces immune phenotypes more analogous to those of humans. We will both track behavior and measure several different immune elements, including both constitutive and inducible immune defenses to characterize overall immune phenotypes. We will analyze this immune and social/behavioral data to identify important correlations between social behavior and immune phenotype. Our study, a comprehensive look at how social environment modulates immune function, will reveal how disease vulnerabilities vary within communities and potentially affect the spread of disease. And a sociality-immunity framework can be integrated with life history theory to produce more detailed analyses of organismal strategies. We can also provide valuable methodological insights for ecoimmunologists. We will build detailed immune phenotypes for mice in semi-wild conditions and identify what role sociality plays in generating

the large phenotypic variance seen in wild populations. And we will identify the immune measures most informative for overall immune phenotype and therefore particularly useful for field researchers.

1-11 Deep learning classification of rabies vector behaviours to understand domestic to wild animal transmission
James Foley, University of Oxford

A main driver of zoonotic disease transfer is vector behaviour, yet the level of detail required for informed predictive modelling is rarely collected. Contact rates and transmission rates depend on for example, area or resource preference, routes of travel and the specific behaviour performed yet these types of data are often lacking. With advances in sensor technology and machine or deep learning classification we can now collect and analyse behavioural and movement data at a scale and resolution that was previously impossible. Using custom-built collars with GPS and accelerometer sensors, we obtained high-resolution behavioural data from free roaming domestic dogs living in sympatry with endangered Ethiopian wolves, *Canis simensis*, in the Bale Mountains National Park of southern Ethiopia. As more dogs become free roaming or feral, incorporating the role of behaviour into the transmission of rabies and canine distemper virus to threatened carnivores can deliver more effective management options. Dog behaviours were classified using a recurrent neural network and incorporated into an agent-based model with full parametrisation for habitat preference and activity types. The contribution of behaviours, such as movement speeds and activity, to viral transmission from dogs to the wolves can then be quantified. Combined with 30 years of wolf population data, we trialed interventions aimed at manipulating vector behaviour or vaccination strategies *in silico*. We show how empirical behavioural data can be analysed to provide evidence-based recommendations where vector behaviour is also informing real world policy and management.

1-12 Pitfalls of telemetry-derived contact networks of wildlife
Marie Gilbertson, University of Minnesota

Contact network modeling in wildlife can reveal traits or individuals critical to pathogen transmission and help inform disease management strategies. However, estimates of contact between animals are notoriously difficult to acquire. Researchers often use telemetry technologies to identify animal interactions; such data may have different sampling intervals or capture a small subset of the population. The objective of this study was to understand the consequences of telemetry sampling on our ability to detect contacts and generate estimates of network structure. We simulated individual movement trajectories for wildlife populations using a home range-like movement model, creating full location datasets and corresponding “complete” networks. To mimic telemetry data, we created “sample” networks by subsampling the population (10-100% of individuals) and sampling interval (every minute to every three days). We varied the definition of contact for sample networks, using spatio-temporal or home range overlap. We calculated six network metrics important for disease transmission and assessed ranked correlation coefficients between complete and sample network metrics. Telemetry sampling severely reduced our ability to calculate the network metrics of betweenness and clustering coefficient, with less impact on other metrics. In populations with infrequent interactions, however, high intensity sampling may still be necessary. Defining contact via spatial overlap generally resulted in overly connected networks, but in some instances could optimize otherwise coarse telemetry data. By synthesizing movement ecology, computational, and disease ecology approaches, we found that careful use of telemetry data has the potential to inform network models, fostering improved understanding and management of wildlife infectious disease.

1-13 The influence of mating status and genotype on immunity
Kylie Hampton, Illinois State University

Reproduction and immunity are critical aspects of an organism’s life history, but there is often a conflict between males and females over female investment into these traits post-mating. Sexually antagonistic

coevolution should lead to differences between male genotypes in their ability to manipulate females, and, correspondingly, differences between female genotypes in their ability to resist. How the genotype of the ejaculate donor and the female's own genotype might interact to influence female immune responses remains unknown. The objective of this study was to determine how mating status and genotype of a female interact with the genotype of her mate to affect female immune responses. Female decorated crickets from three distinct genotypic backgrounds were either left unmated or singly mated in a fully reciprocal design to males from the same three genotypic backgrounds. Female immune function was assayed by i) counting circulating hemocytes, ii) measuring prophenoloxidase and iii) assaying antibacterial activity. Data collection for this study is still ongoing; however, preliminary data suggest that male genotype interacts with female genotype, resulting in differences in immune function between mating treatments that are contingent on genetic line. This ongoing work should reveal how male and female genotypes influence female immunity post-mating, and contribute to our understanding of the evolutionary ecology of sexual conflict.

1-14 Behavioral-mediated Resistance of Remnant Northern Long-eared Bat (*Myotis septentrionalis*) Populations

Samantha Hoff, University at Albany

Since the arrival of the disease white-nose syndrome (WNS) to North America, Northern long-eared bat (*Myotis septentrionalis*, hereafter MYSE) populations have experienced precipitous declines. This species exhibits some of the most severe symptoms and rapid extirpation within three years of fungal pathogen detection at traditional hibernacula, factors predicted to lead to its extinction. Our recent work provides evidence that remnant MYSE populations off the coast of the northeastern US are persisting despite WNS infections, and we aim to determine the mechanisms aiding in population survival. We predict this persistence is due to a behaviorally-mediated form of disease resistance, where unique hibernation behaviors reduce pathogen exposure and/or infection severity. Hibernation sites on three islands were acoustically monitored during the winters of 2017-2018 and 2018-2019, with activity documented on average every 3 - 10 days (range of 1 - 50 days); typical torpor bouts for healthy Myotis bats have been documented on average every 12 - 19 days. MYSE were captured during late fall and early spring to test for fungal presence and infection severity from spring of 2017 through spring 2019. Although we observed an increase in prevalence and fungal load over the hibernation season for all sites, overall prevalence (54%) was much lower than the expected near 100% during late hibernation/emergence based on published data from traditional hibernacula. Research investigating the mechanisms allowing for persistence of this species in coastal habitats is critical to informing management decisions of this federally threatened species in response to WNS.

1-15 Cryptic connections illuminate pathogen transmission within community networks

Joseph Hoyt, Virginia Polytechnic Institute

Understanding host interactions that lead to pathogen transmission is fundamental to predicting and controlling epidemics. While the majority of transmission often occurs within social groups, the contribution of connections that bridge groups and species to pathogen dynamics is poorly understood. These cryptic connections, which are often indirect or infrequent, provide transmission routes between otherwise disconnected individuals, and may play a key role in large-scale outbreaks that span multiple populations or species. We quantified the importance of cryptic connections in disease dynamics by simultaneously characterizing social networks and tracing transmission dynamics of surrogate pathogen epidemics through eight communities of bats. We then compared these data to the invasion of the fungal pathogen that causes white-nose syndrome, a recently-emerged disease devastating North American bat populations. We found that cryptic connections increased links between individuals and species by an order of magnitude. Individuals were connected, on average, to less than two percent of the population through direct contact, and only six percent through shared groups. However, tracing surrogate pathogen dynamics showed that each individual was connected to nearly fifteen percent of the population and revealed widespread transmission between solitarily roosting individuals and extensive among-species contacts. Connections estimated from surrogate pathogen epidemics, which include cryptic connections,

explained three times as much variation in transmission of the fungus causing white-nose syndrome as connections based on shared groups. These findings show how cryptic connections facilitate community-wide spread of pathogens and can lead to explosive epidemics.

1-16 Estimating the Effects of Conflict and Mixing on the Effective Reproduction Number for Ebola Virus Disease in the 2018-2019 Outbreak in the Democratic Republic of Congo
James Holland Jones, Stanford University

The current Ebola virus disease (EVD) outbreak that began in 2018 in northeastern Democratic Republic of Congo is now the second largest EVD outbreak in history, with an excess of 1200 probable cases as of of mid-April 2019. Predictions of the epidemic curve are complicated by competing forces that may influence epidemic growth such zones affected by active conflict, vaccination campaigns, and possibly asymmetric mixing by region. Using daily EVD case counts obtained from the DRC Ministry of Health (MOH) between May 8, 2018 and mid-April, we estimate EVD reproduction numbers using the method of Wallinga and Teunis (2004). We extend the analysis in a number of ways, accounting for mixing across regions. In the absence of asymmetric mixing, the initial reproduction number and the estimated epidemic quenching rate are clearly lower than for most previous EVD outbreaks. The details of mixing matter for this result to an extent, suggesting that collecting data on interactions between regions should be a priority. We find mixed evidence for the effect of intensity of conflict on reproduction numbers. We conclude with a discussion of novel network-based approaches to outbreak control. In particular, we adopt the community-bridge-finder algorithm of Salathé and Jones (2010) to target interventions such as vaccination at individuals and communities with high centrality for the spatial spread of the epidemic.

1-17 Disentangling the long-term epidemic dynamics of measles in Japan
Ryo Kinoshita, Hokkaido University

Measles is a completely immunizing viral infection. The simplicity of its natural history has facilitated excellent documentation of measles population dynamics in various contexts. Here we present a case study in Japan, where historical measles dynamics have yet to be thoroughly investigated. We constructed a time-series SIR model to capture the dynamics of measles incidence in Japan after World War II (WWII), using datasets of monthly notified cases of measles, demographic statistics, vaccination coverage, and seroepidemiological surveillance. Given the spatial heterogeneity in epidemic dynamics across the country, we focused this analysis on the single prefecture of Tokyo, from 1949-1984. Broadly, findings were comparable to those in the canonical studies of measles dynamics in England and Wales.

1-18 Concurrent assessment of epidemiological and operational uncertainties for optimal outbreak control: Ebola as a case study
Shouli Li, Pennsylvania State University

Determining how to best manage an epidemiological outbreak may be hindered by both epidemiological uncertainty (i.e. about epidemiological processes) and operational uncertainty (i.e. about the effectiveness of candidate interventions). These two uncertainties are rarely addressed concurrently in epidemic studies, impeding decision-making. Here we present an approach to simultaneously address both sources of uncertainty. Epidemiological uncertainty is represented by a large ensemble of models of the 2014 West African Ebola outbreak. Operational uncertainty about the effectiveness of three classes of intervention is assessed for a wide range of potential effectiveness for each intervention. We ranked each intervention in terms of caseload reduction in each model, initially assuming an unlimited budget. To explore the role of budget limitation, we assessed the influence of three candidate cost functions relating intervention effectiveness and cost for different budget levels. Our results show that appropriate information gain could reduce expected caseload by more than 50%. The ranking of interventions is jointly determined by the underlying epidemiological process, the effectiveness of the interventions and the size of the budget available for the program. Under higher budget

conditions, resolution of epidemiological uncertainty is most valuable. When budgets are tight, however, operational and epidemiological uncertainty are equally important. Overall, our study demonstrates that significant management improvements could result from a careful examination of both epidemiological and operational uncertainties within the same modelling structure. This approach can be applied to decision-making for management of other diseases for which multiple models and multiple interventions are available.

1-19 Treatment of sarcoptic mange in a wildlife population – management implications for an environmentally transmitted pathogen
Alynn M. Martin, US Geological Survey Northern Rocky Mountain Science Center (NOROCK)

Disease outbreak events can significantly reduce host abundance in wildlife populations, but management intervention efforts may ameliorate the impact. In many cases, appropriate methods for control and treatment are either unknown or ineffective for *in situ* disease control. Here, we undertake a disease control regime during a sarcoptic mange (aetiological agent *Sarcoptes scabiei*) outbreak in a bare-nosed wombat (*Vombatus ursinus*) population by employing current best practice treatment methodologies. The program consisted of weekly treatment application for 12 weeks with consistent visual surveys for disease presence and severity through the following year. Using our field results, we parameterised a mechanistic host-disease model that explicitly described indirect-transmission and host behaviour, and explored the impact of alternative practical disease intervention methods on treatment success. Our results suggest that our treatment efforts fell short of locally eradicating *S. scabiei* from the wombat population, but that the incorporation of better application methodologies and a longer lasting treatment is likely to increase treatment success in future management efforts. These results may be more broadly applied to other hosts impacted by sarcoptic mange, as well as other species impacted by environmentally transmitted pathogens.

1-20 Including mosquito biting behavior in models affects estimates of R0: Chikungunya as a case study
Amalie McKee, University of New Mexico

Arboviruses are an emerging problem in North America. Chikungunya, Zika, and dengue are all vectored by *Aedes aegypti* and see repeated introduction into the United States. As such, a lot of effort has been made to characterize the risk of invasion, using temperature-specific data on mosquito life cycle, and the extrinsic incubation period of each virus in the mosquito. This data is used to calculate the vectorial capacity of *Aedes aegypti* and resulting reproductive ratio of a virus at a given place and time. However, this calculation is usually done using formulae derived from the Ross-Macdonald model, which conventionally assumes that mosquito lifespan is exponentially distributed. The exponential distribution on mosquito lifespan assumes that most mosquitos die right away, and some live arbitrarily long and bite an arbitrarily large amount of times. This assumption also presumes that the average number of bites after a mosquito becomes infectious is the same as the average number of bites any mosquito takes – that is, the fact that a mosquito is generally fairly old when it becomes infectious is not considered in the Ross-Macdonald model. We model a bite-structured adult mosquito population that presumes a maximum number of bites. We show that this more detailed model predicts a lower reproductive ratio of the virus than the Ross-Macdonald model, and that model structure affects predictions of the optimal temperature for viral transmission.

1-21 The effects of metapopulation structure on multi-strain disease dynamics
Matthew J. Michalska-Smith, University of Minnesota

Many of the most impactful diseases that affect humans, livestock, and wildlife have clusters in their population-genetic variability that we classify as strains. Importantly, host immunity to one of these strains is neither independent from nor equivalent to immunity to related strains. This partial cross-protective immunity affects disease dynamics across the population as a whole and can dramatically influence intervention strategies. While the study of multi-strain diseases goes back decades, this work has not yet been generalized to a loosely connected collection of subpopulations, i.e. a metapopulation. Starting from the strain theory of host-pathogen

systems proposed by Gupta et al. (1998), we simulate multi-strain disease dynamics on a network of interconnected populations, characterizing the effects of parameterization and network structures on these dynamics. We find that dynamics propagate through the metapopulation network, even if parameterizations vary between populations. Moreover, in chains of connected populations experiencing cyclical dynamics, the movement of (partially) immune individuals dampens the dynamics of populations further along the chain. This work serves as an important first step in extending prior results on multi-strain diseases to a generalized population structure. This extension is particularly apt in the case of livestock production, where a system of mostly isolated populations (farms) is connected through the forced movement of individuals.

1-22 Are dispersal and transmission synonymous? Investigating the overlap of ecological dispersal and disease transmission in theory and application
Janine Mistrick, University of Minnesota

Theoretical frameworks in ecology are used to understand and predict trends we see in nature. Though models used to approximate these trends are applied in different ways across sub-disciplines, commonalities can often be found linking the foundational concepts. Dispersal and disease transmission are two such frameworks which are applied to specific ends in their respective fields but share a common 'conceptual ancestor'. I investigate the theory behind- and the application of these two frameworks in a compare and contrast-type analysis guided by the 'big' question: "are dispersal and transmission synonymous?" To focus my thinking, as both dispersal and disease transmission can be applied to many systems and scales of organization, I primarily consider population-level models (metapopulation models) and individual-based models in my compare-contrast analysis. When comparing dispersal to disease transmission, I limit my questions to the nature of modeling directly-transmitted pathogens among distinct populations/individuals which is the most akin to animal movement as a focus of dispersal. In my analysis, I consider the underlying assumptions, parameters used to build the models, and the research applications for population- and individual-level models under both frameworks to determine: Is the way we approximate movement through space and time in heterogeneous environments synonymous in dispersal and disease transmission? Do these similarities persist across scales of organization (populations versus individuals)? I conclude by suggesting concepts or modeling approaches in dispersal that have been under-utilized in the study of disease transmission and could provide further insight into the questions we ask as disease ecologists.

1-23 Temporal dynamics of multi-host parasite prevalence in species-rich plant and pollinator communities
Wee Hao Ng, Cornell University

How multi-host parasites spread in species-rich communities is challenging to study and poorly understood. One approach is to track parasite prevalence through time, looking for temporal signatures of superspreaders, disease hotspots, and/or dilution effects. Here, we assessed temporal variation in parasite prevalence in a community comprised of 103 species of bees that interact at 86 species of flowering plants. We quantified abundance of each species during a growing season, then screened nearly 6000 bees and flowers for 5 pollinator parasites. We found widespread prevalence of parasites in bees and on flowers: 34% of bee species and 51% of flower species had samples that tested positive for at least one parasite. Mean prevalence of parasites in the genera *Crithidia* and *Apicystis* generally increased over the collection period in the pollinator community. This was almost entirely driven by the late-season increase in the relative abundance of *Bombus* (bumblebees), which exhibit higher parasite prevalence compared to the other pollinator species. In contrast, the mean prevalence of pollinator parasites on flowers decreased over time, which may be caused by dilution effects from higher floral abundance later in the season, counteracting the increased prevalence among pollinators. Our results suggest that *Bombus* may play a disproportionate role in the transmission of parasites in the community, and that temporal variation in floral abundance is an important factor to consider when modelling disease dynamics.

1-24 Fade-Out and Re-Emergence of *Leptospira interrogans* serovar Pomona in a Wildlife Reservoir Host – California sea lions (*Zalophus californianus*)
Katherine Prager, University of California, Los Angeles

Since 1984, *Leptospira interrogans* serovar Pomona has appeared endemic in California sea lions (CSL: *Zalophus californianus*), causing yearly seasonal outbreaks with large outbreaks every 3-5 years. In 2010, we increased efforts to understand CSL-*Leptospira* dynamics by collecting data on exposure (n>3200) and incidence (n>2400) from wild and stranded CSL. We observed an unprecedented absence of detected cases from 2013-2017, suggesting *Leptospira* ceased circulating. Concurrently, antibody titers and prevalence declined to low levels, and animals born 2013-2016 tested seronegative. This apparent fade-out was followed by a small outbreak in 2017 and a major outbreak in 2018. The age distribution of cases in these outbreaks was shifted upward relative to the endemic period, as expected for an immunizing infection after a period of fade-out. Interestingly, re-emergence of leptospirosis in CSL in 2017 was heralded by cases in northern elephant seals (ES: *Mirounga angustirostris*).

We hypothesize that fade-out was driven by recent oceanographic anomalies through the combined action of two mechanisms: (1) reduced susceptible buildup due to reduced pup production and increased pup mortality; and (2) changes in age- and sex-specific movement patterns which altered population mixing and hence transmission dynamics. By 2017, conditions were likely ideal for re-emergence: births had replenished susceptibles, and oceanographic conditions had returned to normal, likely shifting movement patterns back to those conducive to *Leptospira* transmission.

1-25 Free-ranging dog movements in Arequipa Peru and implications for urban rabies control
Brinkley Raynor, University of Pennsylvania

The identification of a rabid dog in 2015 indicated the re-emergence of canine rabies in Arequipa city, Peru after 10 years of epidemiological silence. Most rabid dogs have been detected along water channels transecting the city that are dry most of the year. Our team has also observed numerous dogs spending time or walking along these dry water channels. The aim of this study was to explore how the urban landscape of Arequipa affects the movement patterns of free-ranging dogs, the main host of the rabies virus in the area. We tracked 23 free-ranging dogs with GPS collars and analyzed their spatio-temporal data using the time- local convex hull method. We estimated the space usage by the dogs and directionality of their movements. We found that there was great variation in movement patterns between individual dogs. The movement patterns were affected by the landscape. Specifically, water channels were found to be areas of high movement. Dogs that utilized the water channels had distinct movement patterns: they traveled farther, more linearly, and faster. These findings suggest that water channels could serve as ecological corridors with potential to affect disease spread and control efforts.

1-26 Leveraging census data to unlock insights from changing dynamic of pertussis transmission in London
Arash Saeidpour, Odum School of Ecology, University of Georgia

The incidence of pertussis in London from 1982 to the present are characterized by 3 distinct stages: a period exhibiting declining trends with ~4-year inter-epidemic cycles from 1982 to 1995 (stage 1), followed by a deep trough until 2006 (stage 2) and the subsequent resurgence of disease (stage 3). We sought to identify the drivers of the spatio-temporal evolution of pertussis dynamics in the boroughs of London during this period. We applied the Bandpass Hilbert transform to examine the spatial hierarchy in traveling waves of pertussis across London boroughs. Parallel geographic, demographic and socioeconomic data were used as covariates for the statistical analysis of phases differences among boroughs. We discuss how demographic and socioeconomic differences among boroughs are associated with spatial asynchrony in the period approaching herd immunity, during the nadir of pertussis transmission and its subsequent re-emergence.

1-27 A prudent adaptive behaviour accelerates disease transmission on networks
Samuel Scarpino, Northeastern University

Most aspects of real-world social networks, e.g., clustering and community structure, and of human behaviour, e.g., social distancing and increased hygiene, which have been studied to-date, will slow disease spread. Here, we consider a model where individuals with essential societal roles–such as teachers, first responders, health-care workers, etc.– who fall ill are replaced with healthy individuals. We refer to this process as relational exchange. Relational exchange is also a behaviour, but one whose effect on disease transmission is less obvious. By incorporating this behaviour into a dynamic network model, we demonstrate that replacing individuals can accelerate disease transmission. Furthermore, we find that the effects of this process are trivial when considering a standard mass-action model, but dramatic when considering network structure: featuring accelerating spread, discontinuous transitions, and hysteresis loops. This result highlights another critical shortcoming in mass-action models, namely their inability to account for many behavioural processes. Lastly, using empirical data, we find that this mechanism parsimoniously explains observed patterns across 17 influenza outbreaks at the U.S.A. national-level, 25 years of influenza data at the U.S.A. state-level, and 19 years of dengue virus data from Puerto Rico. We anticipate that our findings will advance the emerging field of disease forecasting, improve our capacity to model the physics of complex behaviours on networks, and will better inform public health decision making during outbreaks.

1-28 Dismantling dogma by modeling mastitis: the impact of asymptomatic infections
Ola Liota Weinbaum, University of New Mexico

Despite widespread compliance with control recommendations, chronic infectious disease remains problematic in animal agriculture. Efforts to disrupt transmission target symptomatic individuals, but disease persists at the population level. *Staphylococcus aureus* mastitis in dairy cows is a painful inflammation of the udder that reduces milk volume and quality. The popularly targeted transmission mechanism is contact between the milk of symptomatic cows and the udders of susceptible cows via milking equipment.

A common control practice is to milk symptomatic cows last, known as the Milk Last Intervention (MLI). However, asymptomatic cows are also infectious. We suspect that they play an important role in maintaining the disease in a herd. In this study, we develop a mathematical model parameterized from the literature, as well as from USDA industry surveys, to address the following question: How does MLI impact transmission dynamics? We classify cows according to infection stage and implement the model in a stochastic discrete time framework. We also investigate how different characteristics of the infectious classes influence our model predictions.

When accounting for asymptomatic transmission, our study predicts that for certain probabilities of infection MLI statistically significantly delays reaching the maximum portion sick in the herd. MLI does not appear to change the total number of sick cow days across a lactation period. Our results highlight the importance of stochasticity and asymptomatic individuals in this system. A broader understanding of *S. aureus* transmission is urgently needed to inspire new non-pharmaceutical interventions, as antibiotic resistant strains like MRSA confound traditional attempts at control.

1-29 Modelling multi-species and multi-mode contact networks: implications for persistence of bovine tuberculosis at the wildlife-livestock interface
Mark Q. Wilber, Colorado State University and National Wildlife Research Center, United States Department of Agriculture

Individual- and species-level heterogeneity in contact rates can alter the ability of a pathogen to invade a host community. Many pathogens have multiple modes of transmission -- by direct or indirect contact. Analyses of epidemiological networks rarely account for multiple modes of contact, which can lead to an incomplete understanding of how individual- and species-level heterogeneity affect disease transmission. We developed a

network-based analysis to explore how individual- and species-level heterogeneity shape multi-mode contact networks. We applied this network-based approach to contact data from proximity loggers collected in a multi-species host community that contributes to the spillover of the disease bovine tuberculosis (bTB) to cattle populations in Michigan, USA. We used this approach to quantify how individual- and species-level heterogeneity influence direct and indirect contacts in this system and predict the role that different wildlife species have in maintaining bTB in the community. We found that individual- and species-level heterogeneity disproportionately influenced indirect and direct contact networks, with individual-level heterogeneity having a greater effect on indirect contact networks and species-level heterogeneity having a greater effect on direct contact networks. We used the results from our network analysis to show that white-tailed deer could act as the sole reservoir host for bTB in this community with important implications for understanding past bTB dynamics and managing the persistence of bTB in the future.

1-30 Detecting spatial inequity in rubella burden using serological data: An Indian case study
Amy Winter, Johns Hopkins University, Bloomberg School of Public Health

Serological surveys that measure immunoglobulin G (IgG) virus-specific antibodies (a correlate of immunity) in blood serum are an increasingly recognized tool used for control of vaccine preventable infections. These data directly capture profiles of immunity that result from the complex interaction of human behavior (i.e., birth rates, connectivity, and vaccination) and pathogen epidemiology. In this analysis, we explore the feasibility of rubella serological data to capture rubella meta-population dynamics of extinction and recolonization. We first draw from meta-population theory to simulate serological age-profiles of immunity across a range of 'community' sizes and connectedness in order to delineate potential summary metrics that capture expected variation in age-specific seroprevalence across communities. We go on to analyze empirical serological data from four districts in India to assess spatial variability in age-specific seroprevalence at the sub-district scale. We estimate the simulation-derived summary metric of variation in the age-profiles of immunity at each sub-district and compare these to typical correlates of immunity over space (i.e., community size and connectivity). The results of this analysis can be used to bound the potential of serological data to estimate spatial variation in transmission as a result of population connectivity and highlight inequity in burden from rubella infection across communities.

Environmental Drivers of Infectious Disease Dynamics (Posters 1-31 → 1-64)

1-31 The Effect of Temperature on the Presence of Wolbachia spp. in *Culex quinquefasciatu*
Megan Fung, University of Massachusetts Boston

The endosymbiotic bacterium *Wolbachia spp.* has the potential to reduce fecundity and transmission ability of infectious disease by some mosquito species. The intracellular Wolbachia is naturally found in species of *Culex pipiens*, including *Culex quinquefasciatus*, commonly known as the Southern house mosquito*. C. quinquefasciatus* is found on every continent except Antarctica and is a known vector for numerous arboviruses, including dengue (DENV). Obligate bacteria symbionts, such as *Wolbachia spp.*, may be affected by rising temperatures, therefore, indirectly affecting the transmission of arbovirus by Wolbachia-carrying mosquitoes. Second instar *C. quinquefasciatus* larvae were raised along a temperature gradient from 35 degrees Celsius to 24 degrees Celsius. Adults were collected upon eclosion and qPCR was run to detect levels of *Wolbachia spp.* infection. Eclosion rates among the larvae raised in the 24-27 degrees Celsius groups were higher than those of the groups raised in 28-33 degrees Celsius. Mortality rates were higher among the larvae raised in 30-35 degrees Celsius. Studying the effects of temperature on arboviral transmission is valuable not only for data on where infection is likely, but also because of the potential effects of climate change globally.

1-32 Mechanistic disease models reveal drivers of divergent epizootic patterns in the amphibian-*Ranavirus* system

Joseph R. Mihaljevic, Northern Arizona University

Mathematical disease models are valuable tools for identifying the mechanisms of divergent epidemic trends. In the amphibian-Ranavirus system, after four months of transmission, we see 100% prevalence of frog virus 3 (FV3) in larval wood frog populations of the northeastern USA. In stark contrast, data from several populations of larval tiger salamanders in the southwestern USA show that the related Ambystoma tigrinum virus (ATV) burns out after three months, with peak prevalence below 60%. We hypothesize that these divergent patterns are linked to: (1) differences in transmission and kill rates, (2) variable host susceptibility, and (3) the effects of seasonally fluctuating water temperature on viral shedding rate. We construct disease models that represent our competing hypotheses, we estimate model parameters from published data, and we compare the fits of our models to the epizootic data. This routine allows us to identify the mechanisms that most strongly influence these ranaviral epizootics. Model comparisons reveal that the divergent epizootic patterns are driven by substantial differences in transmission rates and kill rates of the two viruses. In addition, wood frog populations are more consistently susceptible to FV3, while tiger salamander populations have high variability in susceptibility. This higher heterogeneity drives lower cumulative infection rates in the ATV system. Although we detect a putative effect of temperature on viral shedding rate in experimental data, we could not detect this effect in the epizootic data. Our analysis identifies key areas of future research and demonstrates how mathematical models can evaluate environmental drivers of disease.

1-33 Local density and the mapping of dengue risk in the urban landscape of Delhi

Victoria Romeo-Aznar, University of Chicago

The rapid urbanization of the planet and the environmental, demographic, and socioeconomic heterogeneity of cities challenge the understanding and mathematical modeling of transmission dynamics of vector-borne infections. One fundamental, but systematically neglected, axis of environmental and spatial variation corresponds to human density. Coupled vector-human models, extensions of the Ross-MacDonald equations, do not typically consider the production of vector breeding sites by humans, assuming constant, or linearly increasing, vector abundance with host density. This deep-seated assumption implies a decreasing force of infection with hosts numbers. With a classical dynamical model, we previously demonstrated how the opposite trend can arise from other vector recruitment functions, specifically those with a faster than linear increase. From high-resolution reported dengue cases in Delhi, we also provided evidence for such patterns in the estimated recruitment of *Aedes aegypti* and depending on socioeconomic conditions, including a quadratic dependence in poor areas of the city. We investigate here the consequences of the estimated relations between vector and human abundance, by producing risk maps of the disease based on high-resolution human density and socio-economic typologies. Because temperature also varies within cities, we also examine its joint effect with host density on local risk of dengue transmission. We consider in particular the winter/low transmission season to identify areas where the disease could persist between epidemics. Resulting maps differ considerably from those under standard assumptions. We discuss implications for targeted intervention efforts.

1-34 Predation by crabs improves host population structure for parasitic trematodes in a snail-trematode system

Anieke van Leeuwen, Royal Netherlands Institute for Sea Research and Utrecht University

Parasitism is one of the most common interactions in food webs and parasites can control the outcome of interactions between free-living species. Another interaction, predation, can act against parasites. By targeting infectious parasite life-stages directly, or by preferentially predating infected prey individuals, predators are thought to negatively impact parasite prevalence and improve 'herd health'. While this is intuitive, predation can have non-intuitive impacts. For instance, predation is often size-specific, and, in such cases, predators can positively impact prey populations by imposing mortality. With increased mortality, intraspecific competition

among prey is reduced and the overall effect may be an increase in biomass in specific life-stages or even total prey population biomass, so-called overcompensation effects. When host species are prey, can stage-specific predation have such non-intuitive impacts on parasites?

Here, we use size-structured modelling to reveal that predator-induced, stage-specific overcompensation in snail-hosts can improve host population structure for trematode parasites, resulting in increased parasite production. We qualitatively compare our modeling outcomes of host population structure to field data from a system where both parasitism and predation are both known to impact snail population dynamics. We show that stage-specific biomass overcompensation, occurring in snails as a result of predation, can account for the size-prevalence distribution in this system. Hence, rather than protecting against parasitism, when predation is size structured, it can facilitate parasites.

1-35 Effect of Climate Change on the Microbiome and Potential Defense Against Fungal Pathogens in Developing Lithobates clamitans Tadpoles
Diego Aparicio, University of Massachusetts Boston

Recent work has shown that host health and disease resistance can be affected by the microbiome and that the microbiome can help prime the immune system early in life. The microbiome can be seen as an extension of the host and is influenced by environmental conditions and pathogens, thus impacting disease dynamics. *Batrachochytrium dendrobatidis* (*Bd*) has emerged as a global pathogenic fungus that has led to severe amphibian population declines and several extinctions. The interaction between *Bd* and the amphibian host can also be affected by temperature and precipitation. We explored future climate scenarios of pond drying using mesocosms and characterized the response of the amphibian skin microbiome and its relation to disease susceptibility. We extracted DNA from the skin swabs of green frog (*Lithobates clamitans*) tadpoles exposed to different pond drying regimes during larval development in northern Vermont. Using Illumina Sequencing and bioinformatics tools to examine trends in microbial communities, we explored trends in how future amphibians may be challenged or be able to cope with changing temperatures and faster rates of pond drying. These findings provide a proxy for how future populations will deal with climate change and predict potential shifts in disease dynamics.

1-36 Variation in risk and how it affects the impact of interventions on tuberculosis incidence
Diepreye Ayabina, Liverpool School of Tropical Medicine

In a heterogeneous population, individuals with higher risk are more prominently affected by an infectious disease, leaving a susceptible pool whose average risk decreases as disease prevalence increases. Failure to account for this risk in mathematical models of infectious diseases can lead to biased estimates of the impact of interventions. In this work we estimate risk distributions from suitable transmission models and tuberculosis incidence data for Nepal and Vietnam. Using these risk parameters and models we also assess the impact of interventions such reducing reactivation, improving treatment success and reducing progression to active tuberculosis, on disease incidence towards meeting the WHO 2035 target in these countries.

1-37 Quantifying flying fox food shortages as a mechanism for Hendra virus spillover in Queensland, Australia
Kelsee Baranowski, The Pennsylvania State University

Hendra virus is an emerging zoonotic henipavirus in eastern Australia with high mortality rates in spillover species. Pteropus bats, also known as flying foxes, are the reservoir hosts. Spillover occurs when horses inhale or ingest the excreta of infected bats, causing respiratory and neurological symptoms. Infected horses can transmit the virus to other horses, other domestic animals, and humans. Hendra virus spillovers occur seasonally and are increasing in frequency.1 They are likely associated with environmental changes, bat abundance, and bat foraging behavior.2

To understand mechanistically how changes in reservoir ecology relate to Hendra virus spillover, we evaluated the spatiotemporal variation of food availability for flying foxes in Queensland, Australia. From data collected on the feeding habitats of flying foxes,3 we used flowering productivity and reliability scores of flying fox diet species to estimate potential food availability on a bi-monthly scale. Associating this data with comprehensive Regional Ecosystem maps of Queensland's vegetation, we evaluated the area of diet species lost from 1997 to 2017. The high loss of diet species over 20 years coupled with recurring seasonal blooming reductions, have created winter food shortages that leave flying foxes nutritionally stressed. As deforestation continues to remove critical flying fox diet species, flying foxes must find alternate food resources, particularly during winter bottlenecks, likely drawing them to marginal habitats near humans and domestic horses. This forced change in foraging behavior increases the spatial overlap between reservoir hosts and potential spillover hosts, potentially increasing the frequency of Hendra virus spillovers.

1-38 Understanding the Ecological and Immunological Dynamics of Typhoid and Paratyphoid in Preparation for Typhoid Conjugate Vaccine Roll-out

Ruthie Birger, Yale School of Public Health

In Nepal, incidence of both typhoid and paratyphoid fevers displays seasonal patterns linked to environmental drivers. Both diseases are transmitted fecal-orally with contaminated water as a key mode of transmission, which is strongly impacted by seasonal rainfall. Novel typhoid conjugate vaccines (TCVs), which protect against typhoid but not paratyphoid, are being rolled out in Nepal. However, the immunological interactions between typhoid and paratyphoid may be masked by rainfall's impact. We aimed to anticipate paratyphoid dynamics after TCV roll-out by assessing the marginal association between typhoid and paratyphoid while controlling for rainfall. Using weekly data from 1998-2010, we analyzed the periodicity of rainfall, typhoid and paratyphoid via wavelet analysis. We then fitted ARIMA models to estimate associations between rainfall, typhoid, and paratyphoid at a variety of lags, while controlling for autocorrelation. The dominant periods for all data sets were around 1 year, indicating strong seasonality; there was additional evidence of multi-year periods in the fever data due to an outbreak. The association between rainfall and cases of both typhoid and paratyphoid was highest with a 1-week lag, while the correlation between residuals of rainfall and residuals of cases was strongest at 7 weeks for typhoid and 5 weeks for paratyphoid. Our results indicate that rainfall may impact typhoid and paratyphoid incidence at varying lead times; this complex temporal relationship may have implications for paratyphoid incidence. It is thus crucial to estimate the impact of rainfall on typhoid and paratyphoid to analyze their potential interactions and predict paratyphoid dynamics post-TCV roll-out.

1-39 Investigating persistent measles dynamics in Niger and associations with temperature and rainfall variation

Alexandre Blake, Pennsylvania State University

The regular, defined spatiotemporal patterns of measles that were documented in settings like England and Wales in the pre-vaccination era, are not necessarily seen today in low-income countries where measles persists, such as Niger. Further investigations of mechanisms underlying measles dynamics in current settings could provide valuable insights to these persistent measles hotspots to improve surveillance systems and support targeted interventions.

A large part of Niger follows a seasonal pattern with the variation of population density between rural and urban areas because of agricultural migration. Environmental factors such as temperature and rainfall could then be valuable indicators of drivers of measles transmission. Simultaneously, a heterogeneous vaccination coverage, and the possibility of re-introductions due to contiguity with neighboring countries could lead to chaotic measles dynamics. We investigated weekly measles spatiotemporal patterns in Niger surveillance data from 1995-2001 in association with temperature and rainfall variation.

A better understanding of measles dynamics and its environmental drivers in Niger could cast a new light on how to break or reduce transmission in this setting. Adapting the programmatic response to measles with answers tailored to today's challenges is likely the only way to optimize preparedness to those recurrent outbreaks and the impact of public health interventions

1-40 Susceptibility of rusty crayfish, *Orconectes rusticus,* to two amphibian fungal pathogens
Jennifer L. Boulter, University of Massachusetts Boston

Batrachochytrium dendrobatidis, Bd, is a fungal pathogen linked to global declines of amphibian populations. This pathogen infects the host's keratinized tissue and affects their osmotic and electrolyte regulations, thus drastically decreasing host survival. *Batrachochytrium salamandrivorans*, Bsal; sister taxa to Bd, has recently emerged as a severe threat to salamanders. If introduced, it poses a serious threat to the salamanders in the United States, which is the global hotspot for salamander biodiversity. Both pathogens cause the disease chytridiomycosis in amphibians. Proven to infect amphibians, crayfish have also shown susceptibility to Bd. From a 2017 pilot study we found that mortality occurs when crayfish are exposed to Bd and to Bsal. In these experiments, the invasive crayfish, *Orconectes rusticus*, was exposed to Bd or Bsal. Exposure trials were set up as dose-dependent susceptibility trials (n=10 per treatment) of Bd, Bsal, and a coinfection of Bd and Bsal. Exposed crayfish will also be co-housed with naïve *Lithobates catesbeianus* tadpoles to test whether crayfish are competent hosts to spread the two pathogens. We also exposed several crayfish to a single high dose of Bd, Bsal, and Bd/Bsal and after several weeks, to allow for infection loads to increase, we euthanized the crayfish and dissected them for histological processing. From this data, survival curves were computed and both histology and qPCR were used to confirm infection and susceptibility of crayfish to both Bd and Bsal. These results are ecologically significant due to the invasive nature of this crayfish species, which poses the threat of potentially introducing the pathogens to naïve areas as they expand their range.

1-41 West Nile Virus: 2018 Real Time Forecast
Nicholas DeFelice, Icahn School of Medicine at Mount Sinai

West Nile virus (WNV) is the leading cause of domestically acquired arboviral disease; however, there is considerable inter-annual variation in the number of human cases. As a consequence, effective allocation of public health resources is challenging and often reactive, a circumstance that highlights the need for accurate, real-time forecasts of the burden of disease. Recently, we showed that accurate and reliable predictions of seasonal WNV outbreaks can be made using a mathematical model representing WNV transmission dynamics among mosquitoes and birds, as well as spillover to humans. The mathematical model is optimized using a data assimilation method and two observed data streams: mosquito infection rates and reported human WNV cases. These retrospective forecasts were then used to calibrate estimation of real-time forecast expected accuracies for various predicted features: outbreak peak timing, peak magnitude, and total number of infected mosquitoes for the season and the number of human cases in the next 4 weeks and over the season. Weekly forecasts of WNV were generated in real time using this calibrated system for 4 California Counties during the 2018 outbreak. Overall, the real-time forecasts were able to estimate accurately the peak timing, peak magnitude, and total number of infected mosquitoes for the season in real-time prior to the peak of infected mosquitoes. Forecasts of human WNV cases over the next 4-weeks were able to provide accurate prediction intervals of future observations: the 4-week ahead 50% prediction interval captured 55% of observations. Here we present the models and evaluation of the real-time forecasts.

1-42 Local environmental variation shapes pathogen community composition but does not alter disease burden in a wild plant-pathogen system
Johannah E. Farner, Stanford University

Both environmental conditions and pathogen community structure are likely to mediate the disease burden on hosts. However, how natural gradients of environmental variation influence pathogen community composition

and pathogen pressure on host populations remains a major empirical gap. To better understand how environmental heterogeneity shapes the landscape of disease experienced by plant hosts, we took advantage of the occurrence of the California native bunchgrass *Stipa pulchra* in both benign greenstone and harsh serpentine soil types with differing chemistries and plant communities. We asked whether *S. pulchra* found on different soil types along the same ridgetop would have significantly different disease burdens caused by unique pathogen communities. Additionally, we analyzed the chemical composition of serpentine- and nonserpentine-grown *S. pulchra* to understand potential effects of soil chemistry on plant-pathogen interactions. We found that distinct fungal pathogen communities associated with each soil type caused consistent, low disease burden on *S. pulchra,* and that foliar tissue chemistry reflected the soil type plants grew in. Plant community structure and plant tissue chemistry represent two possible mechanisms by which soil type might shape unique pathogen communities at our study sites. Our findings suggest that local variation in soil type and annual variation in climatic conditions, along with seasonal plant senescence, may protect *S. pulchra* from disease outbreaks and maintain diverse communities of relatively benign fungal pathogens.

1-43 Predicting hotspots and coldspots of global zoonoses in livestock
Ilya R. Fischhoff, Cary Institute of Ecosystem Studies

Livestock diseases represent major economic burdens, as well as posing threats to human health. Understanding the environmental features that predict livestock disease outbreaks is important to managing these threats. Here we present machine learning analyses of human and ecological influences on disease outbreaks in livestock and wildlife. We modeled the locations of all known disease outbreaks as well as the size of each outbreak. Factors that increased the probability of outbreak presence included the interactions between road density and the densities of each of several livestock species (goats, chickens, cattle, and pigs), mean temperature, electrical infrastructure (intensity of nighttime lights), and high background diversity of wild mammal species. These outbreaks tended to be larger in drier locations with high densities of pigs and roads, suggesting that the presence and density of pigs and the high degree of contact supported by primary and secondary roads lead to larger and more frequent disease outbreaks on farms. These results also suggest the need for enhanced disease surveillance in “coldspots”: locations with high predicted probability of outbreaks yet no nearby outbreaks observed to date.

1-44 Cost of parasitism to the malaria vector: a meta-analysis
Amber Gigi Hoi, University of Toronto

The myth that vectors are mere carriers of parasites and do not incur fitness costs has long been discounted for many disease systems. Parasites can reduce survival and reproduction in vectors, and these costs determine duration of transmission and vector density, respectively. However, the precise costs remain elusive even in one of the most studied parasite-vector systems, malaria parasites (*Plasmodium spp.*) and mosquitoes, and empirical studies have generated conflicting results. Infection status is likely to interact with other stressors, such as high temperature, and exacerbate any fitness costs to a vector; such subtle differences in context could lead to divergent experimental outcomes. In order to quantity the costs of *Plasmodium* infection on mosquito fecundity and longevity and to investigate the contribution of environmental factors such as temperature to these effects, we perform a meta-analysis on 26 original studies identified via systematic literature review. We then calculate the effect of parasitism on mosquito mortality risk and fecundity both during and after the extrinsic incubation period (EIP), and incorporate these new estimates into vectorial capacity calculations. This new analysis increases the precision of key parameters in infectious disease models and will greatly benefit disease prediction and control.

1-45 Habitat Types and Environmental Factors Associated with Equines and Ticks
Angela James, USDA APHIS Veterinary Services, Center of Epidemiology and Animal Health

Tick distributions, density, and host-seeking behavior are key components in defining disease risk to equines and these components are influenced by different environmental drivers and habitat associations. Many tick species seek hosts during specific times of the year with the transmission of tick-borne disease occurring at these specific times on a seasonal basis. Dispersal of ticks by their associated hosts, abundance of hosts in the area, environmental conditions, and habitat/host preferences are also factors to consider when determining various pathways that may influence tick-equine contact. Our goals were to identify tick species and infestation rates on horses and to evaluate climate and habitat types among horse properties that may influence seasonal tick-equine contact. As part of the NAHMS Equine Study, ticks were collected from horses during spring and summer months from 26 different states. Based on ecoregions, habitat type was quantified, ticks removed from horses were identified, location on horse recorded, and number of ticks per horse examined. We used spatial regression analyses to investigate the effects of habitat types, horse demographics, and climate on occurrence of ticks on equines. Seven different tick species were collected from equines from May through October 2016. The highest tick infestation rates on equines were in the following ecoregions Western Cordillera, Ozark Mountain forest, Southeastern plains, and Mississippi Alluvial Coastal plains. We will discuss implications of changes to tick-borne disease risk based on seasonal exposure of equines to different tick species based on habitat type and landscape use.

1-46 Scaling dampens the effect of rodent densities on the transmission dynamics of ticks and tick-borne pathogens
Aleksandra Krawczyk, National Institute for Public Health and the Environment, Bilthoven, Netherlands

Rodents contribute to the life cycle of *Ixodes ricinus* by feeding immature stages and act as amplifying hosts for tick-borne pathogens. We tested whether these two processes are rodent density-dependent and for which pathogens they synergistically contribute to disease risk under semi-controlled conditions. Rodent removal decreased and acorn addition increased rodent densities but treatments had no effect on population of nymphs. Remarkably, both experimental conditions didn't change the annual population of nymphs infected with *Borrelia afzelii* and *Neoehrlichia mikurensis*. Nevertheless, the mean monthly transition of larvae to nymphs was consistently positively correlated with rodent densities. The infection rates of *Borrelia afzelii* and *Neoehrlichia mikurensis*, two rodent-associated pathogens were dependent on rodent densities, resulting in an increase in the densities of infected ticks. As expected, the infection rate, but not the density of ticks infected with the bird-associated *B. garinii* decreased with increasing rodent densities. Surprisingly, the infection rates of two other rodent-associated pathogens, *Borrelia miyamotoi* and *Babesia microti*, were independent of rodent densities, and increasing rodent densities only resulted in moderate increases of infected nymphs. This study shows that the feeding of immature *I. ricinus* and the transmission of some, but not all tick-borne pathogens, is dependent on rodent densities, resulting in variable outcomes in disease risks. However, fluctuations in rodents densities alone are insufficient to predict disease risks as additionally other factors affect the transmission dynamics of tick-borne pathogens, including weather conditions, roe deer abundance, transmission modes, and (a)synchrony of tick and rodent activity.

1-47 A Preliminary Study for Spatial Correlations of Farm-level Foot-and-mouth Disease Outbreaks
Xiaoxiao Li, Pennsylvania State University

Foot-and-mouth disease (FMD) is a severe, highly contagious viral disease which causes illness in cloven-footed animals and results in massive losses and hardships for farmers and ranchers. FMD is difficult to control and there is concern about its potential reintroduction into FMD-free countries like the United States. Statistical models for farm-level FMD outbreaks have been developed for predicting the spread of disease with distance-based transmission decay; this statistical model is assumed to account for all the different transmission mechanisms that exist in reality. Applying the same transmission kernel may not be suitable for large maps with

spatial heterogeneity. In this poster, we present a preliminary study on detecting heterogeneity in spatial correlations and investigate changes in spatial correlation across time. The study will provide insights on potential strategies for modeling spatial-temporal dynamics of FMD.

1-48 Deforestation drives malaria transmission and malaria burden reduces forest clearing in the Brazilian Amazon

Andrew MacDonald, Earth Research Institute, University of California, Santa Barbara

Deforestation and other forms of land use change are among the most pressing anthropogenic environmental impacts. In Brazil, a recent resurgence of malaria paralleled rapid deforestation and settlement in the Amazon basin, yet empirical evidence of a deforestation-driven increase in malaria remains surprisingly equivocal. We hypothesize an underlying cause of this ambiguity is that deforestation and malaria influence each other in bi-directional causal relationships, where deforestation increases malaria through ecological mechanisms and malaria simultaneously reduces deforestation through socio-economic mechanisms. We test these hypotheses with a large and robust geospatial dataset encompassing 807 municipalities across 13 years and show that deforestation has a strong positive effect on human malaria incidence, controlling for variation over space and time and across gradients of land use intensification. Our results suggest that a 10% increase in deforestation leads to a 3.7% increase in *Plasmodium falciparum* malaria cases (~1,730 additional cases in 2008). The effect is larger in the interior and absent on the fringe of the Amazon where little forest remains. However, this strong effect is only detectable after controlling for a feedback of malaria burden on forest loss, whereby increased malaria burden significantly reduces forest clearing, possibly mediated by human behavior or economic development. We estimate that for a 1% increase in *P. falciparum* malaria, we expect a 1.5% decrease in forest area cleared (~235 fewer km^2 lost in 2008). This bi-directional socio-ecological feedback between deforestation and malaria, which attenuates as land use intensifies, illustrates the intimate ties between environmental change and human health.

1-49 Environmental Influence on FMDv Persistence Around Cattle Herds in Cameroon

Sarah R. Mielke, The Ohio State University College of Veterinary Medicine

Foot-and-Mouth Disease virus (FMDv) persists in the environment dependent on pH, relative humidity (RH), and temperature. Recently, an analysis of available survival data showed that viral persistence is likely affected in diverse ways from interactions between RH, temperature, and matrix (i.e. soil or air). In endemic regions disentangling these relationships will aid efforts to eliminate FMD, which devastates economies and destabilizes food security. Cameroon, in West Africa, has a dynamic livestock system, where the potential for environmental transmission of FMDv is high, but may vary throughout the year due to the range of environmental conditions. Therefore, we hypothesize that detection in the environment is: (A) inversely related to distance from the center of the herd, (B) inversely related to time from index case, and (C) related directly with decreasing relative humidity (RH) and inversely with decreasing temperature. To investigate viral contamination, samples were collected from individuals, vehicles, and along cattle pathways from three sedentary herds beginning on day one of reported outbreaks and ending by day 30, then tested for the presence of FMD viral RNA using rRT-PCR. Analysis suggests that distance from herd and time from index case decrease detection on soil whereas, time but not distance decreases detection in air. Interaction of RH and temperature suggests increased detection at high temperatures (>24°C) and RH (>75%), indicating the potential for viral persistence to influence transmission in tropical regions. Therefore, analysis of transmission models with and without an environmental component will improve our understanding in this system.

1-50 Mosquito and primate ecology predict human risk of yellow fever virus spillover in Brazil

Erin Mordecai, Stanford University

Predicting pathogen spillover from animals to humans is important both for anticipating public health threats and for understanding the ecology of infectious disease emergence and sylvatic transmission. Because pathogen

spillover is stochastic and infrequent, predicting these events remains a challenge. Here, for the first time we empirically apply and parameterize a theoretical model for predicting pathogen spillover, recently developed by Plowright and colleagues. We model yellow fever virus spillover from non-human primates to humans in Brazil using geospatial data on human vaccine coverage, environmental variables, primate and vector distributions and biology, and human abundance. The model synthesizes disparate data sources to model each of the mechanisms required for pathogen spillover: the distribution and abundance of primate reservoir hosts and sylvatic mosquitoes, mosquito – primate and mosquito – human biting rates, mosquito dispersal, mosquito survival, mosquito infectiousness, human susceptibility, and human abundance. We show that these ecological mechanisms can predict observed yellow fever spillover in humans with high accuracy (AUC = 0.72 – 0.79). We then use boosted regression trees to examine the environmental mechanisms that might be missing in the mechanistic models. We find that the mechanistic ecologically modeled risk in the current and preceding month are the strongest predictors of observed spillover, followed by vaccine coverage, population density, temperature, and precipitation. More broadly, this work shows that for a widespread human viral pathogen, the ecological interactions between environment, vectors, reservoir hosts, and humans can predict spillover with surprising accuracy and potentially improve spillover prevention and control.

1-51 Infection dynamics and ecology of endemic tick-borne relapsing fever in a community of wildlife hosts
Peter J. Motyka, Northern Arizona University

Tick-borne relapsing fever (TBRF) is a debilitating disease that may be emerging as a public health concern in popular mountain areas in the western United States. Human cases of TBRF currently display distinct seasonal patterns within years, and across years they occur as occasional outbreaks. It is unknown if these patterns coincide with oscillating or epidemic infection dynamics in the environment or if they are simply driven by human activities that increase exposure. To address this, we conducted the first long-term surveillance study of TBRF infections within local wildlife host communities at endemic foci. Between 2009-2016, we sampled small mammals using mark-recapture methods at three popular campgrounds in the Eastern Sierra Nevada Mountains. We captured 1653 individual animals of 13 species for an eight-year total of 2367 captures. Blood samples from each capture were tested with qPCR for the presence of *Borrelia hermsii*, the pathogenic spirochete responsible for TBRF in the western US. We calculated infection prevalence at multiple scales to observe the short-term and long-term dynamics and compared them to patterns in human cases. We then modeled the effect of different wildlife host species and the effect of overall biodiversity at each site. Our mark-recapture surveillance also revealed unexpected patterns of infection in individual animals across multiple years. These results will advance our understanding of this potentially emerging disease and help inform management efforts to reduce risk to humans.

1-52 Fungal disease and temperature alter skin microbiome structure in an experimental salamander system
Carly R. Muletz-Wolz, University of Maryland

Pathogens compete with host microbiomes for niche opportunities. The biotic interactions between pathogen and microbiome occur in a shared environment leading to variation in host disease outcome through direct and indirect effects. Previous research on amphibians and the deadly fungal pathogen *Batrachochytrium dendrobatidis* (Bd) have shown that skin microbiomes can reduce Bd infection at enzootic infection levels, with high species richness and high abundance of competitors as putative mechanisms. We used a laboratory experiment to test if host microbiomes can respond similarly at epizootic levels across a range of temperatures, and to quantify host-pathogen-microbiome interactions in an environmental context. We characterized the response of salamanders (n = 87) and their skin microbiomes to temperature (13, 17, 21 °C) and pathogen exposure at epizootic-like loads. We used a novel approach (i) by identifying OTUs that are taxonomically similar to a dataset of culturable bacteria known to kill the pathogen (anti-Bd bacteria), some of which we have cultured and identified as anti-Bd from the same salamander population, and (ii) by using path analysis to test the directionality of pathogen-microbiome interactions on host disease outcome. We found that temperature directly and indirectly impacted skin microbiome structure, but that this did mediate host survival. Instead,

increasing Bd load led to greater dysbiosis in skin microbiomes and ultimately high host mortality through an indirect effect of temperature on Bd load. Our research incorporates a critical element in the study of host microbiomes by identifying the direct and indirect effects of temperature on pathogen-microbiome-host interactions.

1-53 Can the thermal sensitivities of a parasite's basic life-history traits explain its distribution? The case of a rapidly spreading muskox lungworm
Alexander Nascou, University of Toronto

Climate change is altering host-parasite dynamics in complex ways. For parasites, many of which have free-living stages, warming temperatures under climate change can have positive effects, such as reduced development times, and negative effects, such as shortened lifespans. These opposing responses make predicting the net effect of climate change on parasite dynamics challenging. For example, many studies predicting parasite range expansion have relied on overly simplistic models that consider only a positive, linear influence of temperature change on larval development rate, with no consideration of the multiple, interacting, nonlinear, and often opposing, effects of temperature acting elsewhere in the lifecycle. Such approaches necessarily imply range expansion under warming temperatures. We address these limitations by building a life-cycle-based host-parasite model that accounts for the temperature-sensitivity of a large number of vital rates that together determine a parasite's fundamental thermal niche. We explore the effectiveness of this approach for predicting parasite distribution using a case study from the Canadian Arctic, where the specialist muskox lungworm *Umingmakstrongylus pallikuukensis* has been rapidly expanding its range northward over the last two decades. We parameterize the model using a large body of experimental and field data from this system and predict a fundamental thermal niche that corresponds closely with observed parasite occurrence in the field. This approach is easily adaptable to almost any host-parasite system and is a promising way of predicting the impacts of climate change on the spread of parasites.

1-54 Quantifying the Consequences of Measles-Induced Immune Modulation for Whooping Cough Epidemiology
Navideh Noori, Institute for Disease Modeling

Measles, an acute viral disease, continues to be an important cause of childhood mortality worldwide. Infection with the measles virus is thought to be associated with a transient but profound period of immune suppression. Recently, it has been claimed that measles-induced immune manipulation lasts for about 30 months and results in increased susceptibility to other co-circulating infectious diseases and more severe disease outcomes upon infection. We tested this hypothesis using model-based inference applied to parallel historical records of measles and whooping cough mortality and morbidity. Specifically, we used maximum likelihood to fit a mechanistic transmission model to incidence data from three different eras, spanning mortality records from 1904-1912 and 1922-1932 and morbidity records from 1946-1956. Our aim was to quantify the timing, severity and pathogenesis impacts of measles-induced immune modulation and their consequences for whooping cough epidemiology across a temporal gradient of measles transmission. We identified an increase in susceptibility to whooping cough following recent measles infection, though the duration of this effect was variable. Overall, while the immune impacts of measles may be strong and clearly evident at the individual level, their epidemiological signature in these data appears both modest and inconsistent.

1-55 How much can we infer about epidemic processes from historical time series?
Sang Woo Park, McMaster University

Bubonic plague, caused by Yersinia pestis, has been traditionally believed to be spread by rat fleas. Recent experimental and theoretical studies have brought this explanation into question, suggesting human ectoparasites such as lice or human fleas as alternate vectors. In particular, Dean et al. used mathematical models to analyze mortality reports from the Second Pandemic (1400s-1900s), concluding that human

ectoparasites were the predominant drivers of these epidemics. However, their analysis relied on several strong assumptions. Here, we revisit mortality data from the Second Pandemic to study how much can be inferred about the underlying transmission mechanism from time series alone. We develop a model that accounts for all possible combinations of transmission routes and quantify uncertainty in our understanding of the system using biologically realistic prior distributions on all parameters. A simulation study suggests that the true mechanism can sometimes, but not always, be inferred from mortality data alone. Analyses of the Second Pandemic data suggest that combined transmission is likely. When we incorporate information from the Third Pandemic, however, conclusions change for a few individual epidemics. Overall, our results suggest that there remains large uncertainty in our understanding of historical plague epidemics. We suggest that any modeling studies that want to infer unobserved mechanism should take all sources of variability into account.

1-56Temperature-dependent infection dynamics in a butterfly-parasite system

Isabelle Grace Ragonese, Odum School of Ecology, University of Georgia

For ectothermic organisms like insects, environmental temperatures can influence their physiology, survival, behavior, and large-scale distribution. Given that insects are important pollinators and vectors of disease, a growing body of research has focused on the effects of temperature on insect-pathogen interactions. While much of the work so far has emphasized how temperature alters individual host or parasite traits (e.g. immune response or growth), contemporary climate change intensifies the need to quantify how these within-host processes scale up to influence local transmission and regional infection patterns. Monarch butterflies (*Danaus plexippus*) and their protozoan parasite *Ophryocystis elektroscirrha* (OE) are an apt system for studying temperature dependent infection dynamics at multiple scales. During their iconic migration, monarchs recolonize the North American continent in successive generations, exposing the butterflies to a wide range of environmental temperatures. OE forms dormant spores that persist outside of the host, and the longevity of these spores at different temperatures has important implications for transmission. In a past experiment assessing OE spore viability, we found that both exposure time and temperature significantly impact infection prevalence, spore load, and host lifespan. This understanding will help us determine how the monarch-OE interaction responds to temperature. In the future, I aim to (1) quantify thermal responses of within-host infection processes, (2) examine the temperature dependence of local parasite transmission, and (3) use this information to predict regional infection patterns.

1-57 Shifting the paradigm from wildlife disease to wildlife health

Katherine Richgels, US Geological Survey, National Wildlife Health Center

Traditional solutions for wildlife health have often been focused on single host-disease systems; however, the increased emergence and severity of wildlife diseases combined with on-going stressors such as habitat loss and climate change suggest that a more holistic approach is needed. The One Health framework is an obvious choice for finding solutions to disease issues that simultaneously consider the needs of humans, agriculture, and wildlife. Disease issues in wildlife are complicated by numerous factors including that they are free ranging, dispersed across the landscape, and treatment options are often financially or socially (e.g., euthanasia) unacceptable. However, that does not mean that we should 'do nothing' for wildlife diseases. Instead, we propose that the perspective when considering how to manage a wildlife disease needs to consider the population or species health, as this perspective would incorporate all potential stressors and population parameters. We provide a simple simulation model that incorporates density dependent reproduction, natural mortality, and disease-driven mortality to illustrate when managing a population holistically, that is encouraging compensation from other sources of mortality or reproductive rates, may improve population performance despite a disease that may be difficult to manage directly. It is likely that while we cannot treat the disease in the field, we can take mitigating actions to reduce other sources of stress or mortality to make a population or species more robust to the threats posed by an emerging infectious disease.

1-58 Spatiotemporal monitoring of viral dynamics in honey and wild bees in Northern California
Nina Sokolov, University of California – Berkeley

Honey bees have been subject to well publicized die-offs, but the dynamics of most wild bee species remain unknown. The data on wild bees we do have, however, points towards a general decline. Infectious diseases are one of the major contributors to this decline. Work is coming out showing that viruses that were once thought to be honey bee specific, are now being found in other bee species. Overall, wild bees are at a potential risk of disease spillovers due to their proximity to managed bees within their habitats. My proposed research aims to increase monitoring of viral dynamics in managed honey and wild bees in California through time at sites that range in human impact, managed bee density, and participation in crop pollination. I will quantify viral prevalence in bee populations comparatively to examine if honey bees act as source of emerging diseases. Field caught honey and wild bees will be collected once a week across multiple pollinator seasons, processed, and analyzed for their viruses. Collections are underway for this season and samples are beginning to be processed. I hypothesize that if managed honey bee populations are a source of novel viral infections, then there will be a delay but subsequent match in viral dynamics in the wild bees. My proposed work will bring new knowledge of bee virus dynamics and inform how far this spread has gone into wild populations in hopes to design ecologically minded disease management strategies to conserve bee diversity into the future.

1-59 Thermal ecology of malaria transmission and the potential impact of behavioral resistance
Eunho Suh, Pennsylvania State University

A number of studies report changes in the biting time of malaria mosquitoes following the introduction of long-lasting insecticide-treated bed nets (LLINs). Here, we explored whether timing of blood feeding interacts with environmental temperature to influence the vector competence of Anopheles mosquitoes for the human malaria parasite, Plasmodium falciparum. We found no effect of biting time on the proportion of mosquitoes that became infectious at constant temperature. However, the addition of realistic daily temperature fluctuation reduced the vector competence of mosquitoes feeding in the morning and increased the competence of those feeding in the early evening. A transmission dynamics model illustrates that such changes could have important implications for the epidemiological impact of “behavioral resistance”. A shift in mosquito biting to the morning could reduce the transmission probability, and so poses little epidemiological risk. However, an increase in early evening biting could increase transmission not only because people are unprotected by bed nets, but also because there is a higher chance of blood-feeding mosquito becoming infectious.

1-60 Spatiotemporal variation impacts factors driving parasite infection in a natural population
Amy Sweeny, University of Edinburgh

Host-parasite interactions in nature are highly context-dependent, with parasite infection dynamics driven by a range of factors occurring across several ecological scales (e.g. individual, population, or ecosystem). However, it is often difficult to determine the importance of these factors because they can vary profoundly across space and time. Studies in natural populations are also subject to practical limitations, so it is often unclear how our inference of factors influencing parasite dynamics are biased by spatiotemporal resolution of sampling. Here, we used a longitudinal dataset of >1000 individual wood mice (*Apodemus sylvaticus*) which encompasses 6 years of sampling across 6 different field sites. Within this spatially- and temporally- replicated dataset, we aimed to determine which factors, including host characteristics, co-infecting parasites, and the environment, drive infection intensity of an important helminth parasite, *Heligmosomoides polygyrus*. We found that season, host body condition, and sex were the three most important determinants of infection; importantly, however, all three drivers varied temporally in the strength and even direction of the effect. We also show that longitudinal (repeated capture) versus cross-sectional (single capture) sampling increased ability to detect annual variation in these key drivers, and importantly, that longitudinal sampling, within just one year or site, provides a reliable estimation of the drivers of infection found in full-dataset models. Our results demonstrate how spatiotemporal variation can significantly impact both parasite dynamics and the factors that drive infection. In addition, we

show that robust sampling designs are crucial for estimating the key ecological drivers of host-parasite interactions.

1-61 Host immune activation is modulated by environment in co-infected sea fans
Allison M. Tracy, Cornell University

The invertebrate immune system governs host defenses against biotic and abiotic threats in a changing environment. In the face of warming oceans and increasing disease, coral responses span a diversity of innate immune pathways. However, the interplay between environment and pathogenic attacks remains murky. Two parasites of the Caribbean sea fan, *Gorgonia ventalina*, both induced significant increases in the expression of immune genes T5A and NFkB in an experiment using pathogen inoculations. However, increases in cellular immunity and the expression of a third immune gene (MMP) only occurred during copepod infections, perhaps because the parasites exploit different host tissues.

We tested the hypothesis that increased immunity in copepod infections reduces the probability of co-infection by the fungus by surveying 15 reef sites in Puerto Rico. Contrary to our hypothesis, co-occurrence was random, suggesting other factors structure parasite infection. Sea fan colony size strongly predicted the prevalence and severity of copepod infections. Cellular immunity in the field mirrored the parasite profiles in the lab. However, the effect of parasite infection on immunity was small relative to that of site differences. We suggest that host size and the environment have such a large effect on both parasite prevalence and host immunity that they overwhelm effects of the parasites on each other. Thus, host size and site-specific features, such as genetic structure or environmental conditions, emerge as critical drivers in this multi-parasite system. The overwhelming role of the environment argues for the importance of field studies in understanding infection risk and co-infection dynamics.

1-62 Spatial risk of helminth infections and forecasting under climate changes: the case of gastrointestinal helminths of rabbits in the UK
Chiara Vanalli, Pennsylvania State University

Climate changes have been predicted to impact the distribution and severity of infectious diseases. For soil-transmitted parasites climate is expected to alter the abundance of infective stages in the environment. However, the size of these infective pools is also affected by the host intensity of infection and degree of shedding into these pools. Here, we investigated how hosts with single and dual parasite infections contribute to the spatial risk of infection and how this changes under climate warming. As a study case we selected two common helminths in populations of rabbits from the UK and historical data of temperature and relative humidity from EUROCORDEX (European Coordinated Regional Climate Downscaling Experiment). Climatic projections throughout the 21st century were simulated using the IPSL-CM5A-MR model. Simulations indicate that dual infected hosts contribute more heavily to the pool of infective stages, than animals with single infections. For *G. strigosum* the highest risk of infection is found in the more humid north-west England and west-central Scotland, particularly during the winter and spring months. For *T. retortaeformis* temperature drives risk of infection with the highest values in summer and fall, and in south-east England. Long-term climatic changes lead to an increasing risk of *G.strigosum* infection in the western UK, as related to a more humid environment. For *T. retortaeformis* is expected to increase with climate changes this will also be affected by the contribution of single and dual-infected hosts.

1-63 Spatial Occurrence Patterns of the Invading Tick Vector *Haemphysalis longicornis*: Unravelling reported versus established populations
Morgan Wehtje, USDA APHIS Veterinary Services, Center of Epidemiology and Animal Health

Multiple environmental and physical factors can affect both the initial location and subsequent establishment success of vectors such as ticks. Established populations of vectors have a higher likelihood of transmitting

infectious diseases to vertebrate hosts. The Asian longhorned tick (ALHT) or *Haemphysalis longicornis* was identified in 2017 in New Jersey. ALHT is native to portions of Russia and SE Asia, but has invaded Australia, New Zealand and most recently the United States. Though not yet shown to carry or transmit diseases to livestock or humans in the US it is a known vector of several livestock and human diseases in both its native and invaded ranges. Since 2017, identification and documentation of ALHT occurrences have been recorded by state, federal, and private institutions. We examined available records to date and used spatial hot spot analysis to identify geographic areas where the tick appears to be established, areas that need further data collection to determine the ticks status and environmental factors potentially driving these patterns. Analyses reveal that even though the tick has been documented in numerous locations current data are insufficient to qualify it as established or breeding in many of the locations and warrants further investigation and data collection. Furthermore, there may be factors, beyond suitable climate, limiting the establishment of the tick and caution should be used when interpreting ALHT distribution maps generated by climate variables alone.

1-64 Quantifying immune boosting from population transmission: a case study of rubella
Luojun Yang, Princeton University

Immune boosting is known to maintain long-term immune memory in the pre-vaccine era through repeated exposures, and is the principle that underlies booster vaccines. Linking data at the population and individual levels, we show that the effect of boosting on individual serum antibody levels is transient, with an estimated half-life of 5 weeks. We find that individual serum antibodies are tightly coupled to rubella incidence summed at this lag, and we illustrate the underlying immunological mechanisms through dynamics of B cell and antibody populations. We conclude that seasonal rubella transmission drives annual fluctuations in individual serum antibodies. If vaccination reduces natural boosting, waning immunity might pose a great risk of disease resurgence.

GENETICS OF INFECTIOUS DISEASE DYNAMICS ACROSS SCALES (Posters 1-65 → 1-93)

1-65 Cellular heterogeneity underlying poly-functional *Drosophila* fat body tissue
Vanika Gupta, Cornell University

The insect fat body is a multifunctional tissue that can serve as a generic model for how poly-functional organs achieve diversified tasks, including management of immune response to infection. Fat body functions span those of at least three vertebrate organs: immune system, adipose tissue, and liver. The fat body is the primary systemic immune organ in insects, but also serves as the metabolic control organ responsible for storage and release of lipids and other nutrients and produces most of the yolk used to provision developing eggs. This is analogous to vertebrate adipose tissue, which is a cellularly heterogeneous tissue that stores lipids and also produces cytokines and inflammatory reactions in response to infection. We hypothesize that cellular heterogeneity in the fat body allows subsets of cells to specialize in each function, collectively resulting in a tissue with highly varied capabilities. We further hypothesize that stimuli such as bacterial infection alter either the number or identity of sub-functionalized cells, resulting in quantitatively dynamic responses at the tissue level. We are using single-cell RNA sequencing (scRNAseq) on the 10X platform to test the hypothesis of cellular heterogeneity in *Drosophila melanogaster* (fruit fly) fat body. Using tissue-specific drivers, we have tagged adult fat body cells with GFP which are then sorted using FACS to obtain well-dissociated fat body cells. We are using flies which remain either challenged or unchallenged with a gram-negative bacteria *Providencia rettgeri*, both while actively engaged in egg development and in the absence of reproductive investment. We seek to identify cells subpopulations within the fat body which are responsible for specific functions. We further want to identify plasticity in the fat body tissue under different physiological environments. We will use the data to understand how poly-functional tissues

balance competing physiological functions, providing mechanistic understanding for the classical life history tradeoff between immunity and reproduction.

1-66 Genomics of Wildlife Disease Workshop: Training for early and mid career scientists in modern genetic tools for wildlife disease analysis

Jill Pecon Slattery, Smithsonian Conservation Biology Institute-National Zoological Park

Recent technological advances in genomic sciences, and increasingly affordable Next Generation Sequencing (NGS) assay costs, have coalesced to result in powerful tools to monitor, detect, and reconstruct the past, present and future role of pathogens impacting wildlife populations. However, many researchers lack the training and expertise required to use these computationally intensive methodologies. We have conducted two successful training workshops Genomics of Diseases in Wildlife in 2017 and 2018. GDW format consisted of lectures, daily computer labs and analysis of real-world NGS data and provided comprehensive training in the use of genomic tools for investigations of a broad range of interactions between wildlife host species and their pathogens, and provided unique networking opportunities among instructors, guest speakers, and participants. Over the course of two years, 45 participants from diverse backgrounds studying a wealth of disease ecology systems have completed the workshop. Participants ranged from graduate students to mid career PhD, DVM, and DVM-PhD trained individuals from academia, nonprofit organizations, zoos, and government wildlife agencies. Twenty eight percent of participants were from non-US countries on 4 continents; 58% of attendees were women. Excellent course reviews were received and a Horizon Scanning exercise completed by GDW2017 and published in the May 2019 issue of Journal of Heredity. GDW2019 and GDW2020 are underway, providing an opportunity for acquiring skills in genomic solutions to ameliorate the local, regional, and global impact of wildlife disease. Prior and current sponsors include National Science Foundation, American Genetic Association, Morris Animal Foundation, Illumina, SCBI, CSU, and GENEIOUS.

1-67 Molecular typing of *Mycobacterium bovis* isolates to understand transmission patterns of bovine tuberculosis in a multi-host system

Assel Akhmetova, University of Glasgow

Introduction: Bovine tuberculosis (bTB) is an important global zoonotic disease affecting primarily cattle and wildlife. In the United Kingdom, bTB continues to have impact on livestock, with European badgers infected with *Mycobacterium bovis* as a wildlife reservoir. Whole genome sequencing (WGS) has superior discriminatory power and can differentiate individual strains within a conventionally assigned genotype and inform on transmission patterns more accurately than routine genotyping techniques.

Materials and methods: *M. bovis* strains were isolated over 20 years from livestock and badgers living in farmlands and surrounding areas of an endemic area (approximately 100 km^2) in the southeast of Northern Ireland. A total of 1248 isolates (1073 from cattle and 175 badgers) were genotyped by multi locus VNTR analysis (MLVA) and their genetic relatedness evaluated by eBURST. From these, 618 were sequenced and consensus SNPs identified from whole genome alignment using vSNP bioinformatics pipeline. *M. bovis* genomic and temporal data were integrated in a Bayesian inference analysis framework together with the SeqTrack algorithm to reconstruct ancestral genealogies and possible transmission events.

Results: MIRU-VNTR identified 38 genotypes, 36 in cattle and 7 in badgers, respectively. Four genotypes were shared among both species, and the majority clustered in single clonal complex. VNTR typing has identified distinct spatial clustering across both cattle and badger derived isolates in the area. Finer scale clustering identified by WGS data will be used to identify natural scales of local spatial outbreaks, thereby informing our understanding of the underlying processes driving the spread of bTB across the two species.

1-68 Predicting the global mammalian viral sharing network using phylogeography
Greg Albery, EcoHealth Alliance, New York

Many emerging human viruses originate in wild mammals, motivating major ongoing research effort into mammalian viral communities. Much of this research aims to identify whether high viral diversity is associated with specific taxa or species-level traits, typically emphasizing zoonotic spillover rather than viral sharing among mammals themselves. As a result, the processes driving mammalian viral sharing are largely unknown, and there are few general rules for predicting viral sharing patterns. Using a global dataset of mammal-virus associations, we revealed that geographic overlap and phylogenetic similarity account for >20% of the deviance in pairwise viral sharing probability among 600 mammal species. We then predicted global mammalian viral sharing patterns by applying model estimates to phylogeographic data from >4000 mammal species. The resulting network recapitulated multiple known viral sharing patterns: in particular, geographic hotspots of viral sharing were centred in the tropics, and rodents and bats were highly central in the network. Unlike in previous models, no specific genotypic or phenotypic traits were required to generate these patterns, yet our model predicted known hosts at the species level within the top 2% of potential hosts. These results demonstrate major roles of broad macroecological factors in determining mammalian viral sharing, presenting a new "neutral" model of expected sharing patterns which can be leveraged to make useful predictions. Finally, we detail the application of these methods to bird-virus and mammal-helminth networks. We suggest that incorporating macroecological factors and pairwise species interactions can augment future models of parasite sharing, aiding public health and conservation efforts.

1-69 Stochastic establishment of antibiotic resistance
Helen Alexander, University of Oxford

In pathogen populations, drug resistance initially arises in a single individual, and tends to remain rare in drug-free environments, due to competitive suppression by the fitter drug-sensitive genotype. Under drug treatment, resistance is selectively favoured, but rare pre-existing or *de novo* mutants are subject to a high degree of demographic stochasticity: i.e. they may either die out or grow into a large population. This role of stochasticity is well-known in population genetics, but rarely quantified empirically, and arguably under-appreciated in infectious disease contexts. We set out to experimentally assess stochastic loss of resistant lineages during drug treatment, using a bacterial (*Pseudomonas aeruginosa*) model system. We carried out high-replicate *in vitro* experiments assessing growth in cultures inoculated with very few resistant cells, at various antibiotic concentrations. We then estimated the probability that a single resistant cell establishes a surviving lineage by fitting these data to a simple stochastic mathematical model. When resistant cells were inoculated in isolation, we found that their establishment probability dropped dramatically at antibiotic concentrations widely considered "sub-inhibitory" to the resistant strain. Next, we plan to seed rare resistant cells into large sensitive populations, in order to test the hypothesis that competition for resources further limits establishment. Overall, we expect antibiotic dose, ecological interactions, and physiological responses to interact in shaping the outgrowth of resistant lineages. These considerations could redefine optimal drug dosing strategies. More broadly, the experimental and statistical methods we developed could be adapted to study stochastic establishment of other disease-relevant mutants in environments of interest.

1-70 The natural history of RNA viruses impacts the speed of Muller's ratchet
Brent Allman, Emory University

The phenomenon of Muller's ratchet, or the accumulation of deleterious mutations in a finite population, has been understudied in a theoretical context in RNA viruses. The high mutation rates of RNA viruses can make their populations susceptible to Muller's ratchet. Little work, however, explores how the unique population structures and life cycles of viruses may impact this phenomenon. To investigate this, we develop an agent-based intercellular model of viral evolution. We find that coinfection of cells by viruses can result in the sharing of intracellular viral proteins and thereby potentially relax selection on deleterious mutants. This would speed

up Muller's ratchet. However, cellular coinfection also allows for reassortment among segmented viral genomes, potentially producing highfitness viral offspring from complementary parental genotypes. This would slow down Muller's ratchet. We show that high rates of cellular co-infection, gene segment loss, and positive epistasis can hasten Muller's ratchet, while increased population sizes and reduced selection-interference via reassortment can slow the ratchet. These results highlight the need to consider viruses' unique natural histories to understand their evolutionary dynamics.

1-71 Drivers of uneven gene-specific evolutionary rates shaping microbial genomes in highly vaccinated populations

Ana I Ramos Bento, University of Georgia

Microbial genome evolution is shaped by a variety of selective pressures. Understanding how these processes occur can help address important problems in disease (re)emergence by explaining observed differences in genotypic variation, including virulence and potential vaccine escape. Such is the case of pertussis, caused by the bacterium *Bordetella pertussis*. Pertussis eco-epidemiology remains contentious, and while case-based and sero-epidemiological studies have been employed extensively, bacterial sequence data have not been utilized to their full potential. We use a combination of Bayesian coalescent and epidemiological models to understand Bordetella *pertussis* transmission dynamics and investigate drivers of gene-specific rates of evolution. We compare pertussis in England & Wales with the Netherlands spanning the pre-vaccine, the whole cell vaccine and the acellular vaccine eras (1940s-present). We show that vaccination is exerting a stronger positive selection pressure on specific parts of the genome, particularly on cell surface and pathogenicity related sites. We also show that intriguingly, in the Netherlands, despite the resurgence, there is epidemiological evidence indicating that baseline transmission is decreasing. We address implications of these patterns. This framework provides insight into ways in which pathogens may adapt under several driving forces of selection on an epidemiological time scale.

1-72 Spatiotemporal dynamics of RNA viruses associated with white clover (*Trifolium repens L.*)

Lisa Bono, Rutgers University

Although metagenomics reveals that natural virus communities harbor vast genetic diversity, the spatiotemporal dynamics of viral diversity in the wild are seldom tested, especially across small geographic scales. This problem is usefully examined in the above-ground phyllosphere, because terrestrial plants are frequently infected by taxonomically-diverse RNA viruses, whose elevated mutation rates generate abundant allele diversity. Here, we studied the problem by comparative analysis of RNA virus samples over time from three spatially-separated patches of a common perennial legume, white clover (*Trifolium repens*L.), growing in a grassy lawn. We predicted that clover samples would show similarly high levels of virus species (alpha) diversity across space, but differing among-patch diversity of non-dominant virus taxa over time (4 samples spanning 6 weeks). Results showed that recognizable alpha diversity in clover patches was consistently dominated by RNA virus family *Alphaflexiviridae*across space, but that all patches showed inconsistent spatiotemporal presence of a diversity of minority virus families. Also, we observed that white clover mosaic virus (WClMV) dominated all patches across space and time. The high coverage of WClMV fostered an haplotype analysis, which revealed that two strains of the virus consistently infected clover plants during the 6-week period. These results offer insights into viral communities associated a single host species of plant that are asymptomatic.

1-73 Why are juveniles more susceptible to disease? The evolutionary dynamics of age-specific resistance

Emme Louise Bruns, University of Virginia

A large class of human and wildlife diseases are dependent on juvenile hosts for their transmission because younger hosts are typically more susceptible to disease. However the question of *why* species retain such high susceptibility in the juvenile stage remains an evolutionary puzzle. Indeed, life history theory predicts that hosts should evolve to be more resistant as juveniles than as adults since early infection is costlier to the host. Studies of anther-smut, (a pollinator-vectored, sterilizing disease) on wild carnations show that disease persistence in

nature is strongly dependent on the presence of a highly susceptible juvenile class. However, while we find evidence of genetic variation in juvenile and adult resistance, the majority of plant families retain high susceptibility at the juvenile stage, indicating that juvenile resistance may be less beneficial than previously assumed. Using a simple age-structured model, we show that the evolution of juvenile resistance can be limited by ecological feedbacks that lower disease prevalence and increase the age of first contact. This result provides an alternative explanation for the predominance of juvenile susceptibility observed in nature that does not invoke strong physiological constraints.

1-74 The Cost of Virulence in an Evolving Bacterial Pathogen
Justin Critchlow, Vanderbilt University

Pathogens can evolve to increase or decrease the damage to their host (virulence), replicate faster, evade the immune system, or survive longer, but the alteration of one trait can come at a cost to the others. While theory predicts increasing virulence under greater host immune resistance, efforts to empirically quantify this interaction often fail because they neglect to account for variably structured interactions between immunity and microbes at different phenotypic stages. Therefore, to study potential trade-offs between virulence and growth under variable immune pressure, experiments need to isolate their interactions over the course of infection.

In this study we take advantage of natural variation in red flour beetle (*Tribolium castaneum*) susceptibility to *Bacillus thuringiensis* (Bt) infection to quantify the impact of immunological variability on bacterial life history evolution. We passaged Bt through 6 generations of different flour beetle strains while controlling for selection on the force of infection. For experimental and control lines, we measured bacterial virulence, growth rate, and transmission phenotypes as well as the expression of genes associated with virulence factor production and sporulation. Our results suggest that stronger and weaker immune responses select on different aspects of microbial life history. Our study could inform more realistic models of disease transmission and evolution, and aid predictions of pathogen responses to control measures.

1-75 Partitioning interspecific and intraspecific variation of microbicidal activity in mammals
Cynthia J. Downs, Hamilton College

Immune defenses are highly plastic traits, but comparisons among species indicate a strong phylogenetic signal. Here, we investigated how variation in microbicidal capacity is partitioned between and within species. We evaluated the microbiocidal capacity of serum from 31 species of terrestrial mammals against *Escherichia coli, Micrococcus luteus,* and *Salmonella enterica*. We predict that variation within a species will be less than variation among species. We adapted the microbiocidal (a.k.a. BKA) assay to facilitate comparisons of species with vastly different microbiocidal capacities. Serum samples were collected from at least 8 healthy, adult zoo-housed individuals of each species. We found that a comparison of diverse species required assays that captures killing ability across a dilution curve rather than for a single dilution. Mammals varied greatly in their ability to kill microbes and those that effectively killed one microbe were not necessarily good at killing others. We will use phylogenetically-informed mixed effects models to disentangle the effects of within-species and among-species contributions to variation in microbicidal capacity. These methods will allow broad comparisons among species and help us understand the evolutionary and ecological forces shaping immune defenses.

1-76 A reference *Ascaris lumbricoides* genome enables insights into *Ascaris* populations and speciation
Alice Easton, NYU Langone School of Medicine

Research on the molecular makeup and molecular epidemiology of A*. lumbricoides* has been limited. We created a reference quality genome of *Ascaris lumbricoides*, which is highly similar to *A. suum*. Using this genome, we compared whole genome sequences of 68 individual *Ascaris* collected from human study participants in 5 Kenyan villages where pig husbandry is rare. We identified SNPs in these nuclear genomes, and inferred phylogenetic relationships. Similar worms clustered within individual donors and within villages, suggesting

villages may represent local transmission pools. We then assembled and compared the mitochondrial genomes of these 68 worms with 20 publicly available *Ascaris* mitochondrial sequences. The sequences from these worms split into two clades seen worldwide, one of which is more strongly associated with pigs. However, human- and pig-derived samples were found in both clades. There was no evidence of differentiation into separate clades of worms on different continents or countries. The limited nuclear and mitochondrial genome observed in this study, and worldwide, suggests a recent global *Ascaris* population expansion. The mitochondrial phylogeny may be illustrative of a historical association of *Ascaris* lineages with either pigs or humans, whereas introgression among *Ascaris* following the movement and interaction of their pig and human hosts could have scrambled this separation in the nuclear genome. Instead, the large number of SNPs in the nuclear genome elucidate recent transmission patterns, such as a large proportion of transmission occurring within villages. *A. suum* may be of great relevance, and risk, to human populations.

1-77 Diversity of schistosome infections and implications of repeated drug treatments
Christina Faust, University of Glasgow

Hotspots of schistosomiasis persist in Uganda despite over 14 years of mass drug administration (MDA). A key question is how to optimize drug distribution to maximise success by reducing transmission while managing for drug resistance. In this talk we will present a longitudinal cohort survey of *S. mansoni* genetics from three endemic communities along Lake Victoria. We recruited 103 young children (9 mons – 5 yrs), 700 school-aged children (6 – 14 yrs) and 250 adults (≥15 yrs) from communities to compare infection rates and determine their contribution to transmission. At each timepoint, three days of stool samples were used estimate infection intensity as eggs per gram (epg) and larval parasites were stored for genetic analyses. The epidemiological data suggests that school aged children are the most heavily infected group and more rapidly re-infected following a treatment campaign. However, parasites in adults have higher genetic diversity and are both locally acquired and representative of short-term travel. Population structure of parasites across space and time indicates parasites are highly genetically diverse, recover from bottlenecking selection of treatment rapidly, and have little barriers to gene flow across distances of up to 50 km. While we find evidence for resistant genotypes immediately following treatment, these are unlikely to spread because they are rapidly swamped by high rates of local transmission. While school-aged children are often the focus of control programs, we provide genetic evidence that these target groups can be rapidly re-infected by an untreated reservoir of high-risk young adults.

1-78 Retroviral infection dynamics in endangered Florida panthers are shaped by evolutionary history spillover and management
Roderick Gagne, Colorado State University

Habitat destruction is resulting in fragmented populations that are at elevated risk of extinction as a result of multiple factors, such as vulnerability to stochastic events, inbreeding depression, and disease. Management efforts to alleviate inbreeding can require genetic rescue events where animals from outside populations are introduced. The Florida panthers are an iconic example of a successful genetic rescue. We used a modern NGS technology to evaluate the consequences of genetic rescue on transmission patterns of feline foamy virus (FFV), an endemic retrovirus in the panther population and in other pumas. Phylogenetic analysis revealed multiple clades of FFV with limited geographic structuring that included isolates from Florida panthers interspersed with variants from other puma and domestic cat populations. However, we identified a distinct clade consisting entirely of Florida panther isolates, including many from historic samples prior to the genetic rescue. Our results suggest FFV in the contemporary population has arisen from: (1) geographic isolation of FFV and the Florida panther in the early twentieth century, (2) contemporary FFV introductions as a result of an intentional genetic rescue event, and (3) apparent spillover of FFV from domestic cats. Our findings highlight how isolated populations are at risk from the introduction of pathogens, from spillover from closely related species, or via management actions to preserve these populations. The pattern of spillover from domestic cats as well as direct panther to panther transmission reflects that of the pathogenic Feline Leukemia Virus and thus FFV provides a model to inform management of pathogenic outbreaks.

1-79 Limited conditions promote evolutionary rescue in highly pathogenic host-pathogen systems
Ben Golas, Colorado State University

Theoretical models have shown that for populations in decline as a result of an introduced stressor, evolutionary rescue via natural selection can lead to positive growth, but if population size is reduced below a critical threshold, the population is at risk of extinction as a result of demographic stochasticity. While there is evidence for this theory to be applicable to a variety of stressors, we lack demonstration of its applicability in naturally occurring host-pathogen systems. We investigate the conditions necessary for evolutionary rescue from extinction to be possible in host-pathogen systems by allowing evolution of resistance in host populations in an ecologically-validated stochastic model of prairie dogs and the plague-causing bacterium *Yersinia pestis*, highlighting the rate of resistance development and genetic variation of this rate necessary for prairie dogs to be evolutionarily rescued from plague-induced extinction. We then break the plague model down to compare different compartmental disease models, each including evolution of host resistance, exploring the ecological system components that allow evolutionary rescue from extinction to be possible. We find that a SIR compartmental model and many variations thereof lack the potential for evolutionary rescue. The conditions that allow evolutionary rescue in disease systems are a unique combination of sustained, highly pathogenic selective pressure balanced with nonlinear population growth that improves population survival, as seen in plague systems, with moderate population adaptation and variance prior to infection. Thus, we believe evolutionary rescue via natural selection in host-pathogen systems to be a rare but possible event.

1-80 Host tolerance can evolve rapidly in response to an emerging infectious disease
Amberleigh E. Henschen, *Iowa State University*

In response to emerging infectious diseases, mechanisms can rapidly evolve in hosts that reduce the costs of these infections. These mechanisms fall into two main categories: resistance mechanisms, which directly reduce pathogen load, and tolerance mechanisms, which reduce the fitness costs of infection without directly impacting pathogen load. We tested whether free-living house finches (*Haemorhous mexicanus*) have evolved resistance or tolerance to the emerging bacterial pathogen *Mycoplasma gallisepticum* (MG) by comparing populations where MG has been endemic for different amounts of time. We hypothesized that tolerance is evolving to MG in house finches, as host resistance mechanisms (e.g., inflammatory responses) in this system result in tissue damage and severe conjunctivitis, reducing predator avoidance and survival. In accordance with our predictions, when infected with the same pathogen load, finches from populations where MG has been endemic for longer (>20 years) had less severe conjunctivitis than finches from populations where MG has been endemic only a short time (<10 years) or has not been detected. Our results support the hypothesis that tolerance can rapidly evolve in animal hosts in response to an emerging infectious disease. Future work will focus on understanding the mechanisms of tolerance, as well as how tolerance affects pathogen transmission in this system.

1-81 Competence of New York City *Aedes albopictus* mosquitoes for chikungunya virus
Maria Kaczmarek, NYU School of Medicine

Chikungunya virus (CHIKV) is a mosquito-borne virus that emerged out of Africa over 500 years ago. CHIKV is known for the recent acquisition of adaptive mutations resulting in a host-range expansion allowing the virus to be vectored by both *Aedes aegypti* and *Aedes albopictus* mosquitoes. *Ae.albopictus* can be found in temperate climates, including the northeastern United States, providing a potential vehicle for CHIKV expansion into areas outside of the tropical regions where it is currently found. Therefore, we interrogated whether local populations of *Ae.albopictus* found in New York City (NYC) are competent for CHIKV. Mosquito eggs were collected from three sites in NYC and mosquitoes were reared in the laboratory. These mosquitoes (F4, total N = 148) were fed a blood meal spiked with $6x10^6$ plaque forming units of CHIKV and the efficiency of CHIKV infection, dissemination, and transmission were quantified. Specifically, 7 and 14 days post infection bodies, legs and wings, were collected, along with salivary expectorations from individual mosquitoes. Titers from all materials

were quantified using plaque assays and viral RNA was quantified from mosquito saliva using qPCR. Nearly all mosquitoes were infected with CHIKV, and we found no significant differences in titers between populations. Together, our results suggest that local NY *Ae.albopictus*, reared in the laboratory, are susceptible to CHIKV IOL. Here, we only used a single strain of CHIKV, in the future mosquitos will be infected with additional divergent CHIKV strains. Further, differences in susceptibility among individual mosquitoes will be investigated via transcriptome profiling.

1-82 Inoculum dose dependence in innate host responses to malaria infection
Tsukushi Kamiya, University of Toronto

Understanding immune responses across contexts is key to predicting individual infection outcomes. Inoculum dose is one such biotic context that varies widely among infections with a given parasite. In experimental malaria infections in mice, inoculation dose has been shown to impact outcomes including the peak parasite density, severity of anaemia and pace of infection. However, there is a lack of quantitative understanding of if or how inoculation dose influences host responses to infection, despite the likely causal link between variation in host responses and the observed variation in infection outcomes. By incorporating functional host responses during the acute phase of malaria infection (i.e., targeted killing of infected red blood cells, indiscriminate removal of red blood cells, and erythropoiesis) into a mechanistic within-host malaria model, we characterise reaction norms in activation and decay of host responses with respect to inoculation dose. Using a Bayesian hierarchical approach, we fit the model to experimental time-series data of healthy and infected red blood cells during the acute phase of *Plasmodium chabaudi* infection across seven orders of magnitude of inoculation dose. Our results show that the variation in infection outcomes across inoculation doses is best explained by dose-dependent regulation of indiscriminate removal of red blood cells. We also find dose-independent individual-level variation – even among inbred laboratory mice whose environments are highly controlled – in upregulation of responses against malaria parasites.

1-83 Using phylodynamics and machine learning to estimate effects of mutations on viral transmission rates
Lenora Kepler, North Carolina State University

In the context of rapidly evolving and adapting pathogens such as Ebola and HIV, it is crucial to be able to track mutations in the microbial population, and the effects of these mutations on the fitness/transmissibility of a pathogen. The ability to identify the mutations that increase a pathogen's transmission rate would enable enhanced public health planning; targeted research into mechanistic interactions; and identification of potential drug resistance. While phylodynamic methods exist to estimate the fitness of a given genotype of a virus, the methods currently used are too computationally intensive to allow exploration of complex, epistatic interactions between sites.

The aim of this work is two-fold. First, to create flexible and extensible software to simulate a viral outbreak with specified mutation and population parameters, including sequence data and a reconstructed transmission tree. This software should be flexible enough to be adaptable to varying population structure composition, host-vector interaction, epistasis, and differing models of sequence evolution.

Second, we aim to leverage machine learning techniques to make traditional likelihood-based parameter estimation methods faster and more accurate. Boosted regression trees will enable us to partition the feature space in complex ways that allow for non-additive fitness effects such as epistasis, and pooling fitness estimates over multiple regression trees should allow for improved predictive performance.

In the future, we hope to apply methods used on the simulated data to infer information about mutations' effect on viral transmission rate from genomic datasets, and examine how accurately in-vitro methods predict the fitness of a mutation in the natural environment.

1-84 Trait-based modeling of multi-host pathogen transmission: Plant-pollinator networks
Scott H. McArt, Cornell University

Epidemiological models for multi-host pathogen systems often classify individuals taxonomically and use species-specific parameter values, but in species-rich communities, that approach may require intractably many parameters. Trait-based models offer a potential solution, but have not accounted for within-species trait variation or between-species trait overlap. We have recently found empirical evidence that flower and bee traits are associated with disease prevalence and transmission in plant-pollinator networks composed of >100 bee species and >80 flowering plant species. Here, we develop SIS models for disease spread in plant-pollinator networks with continuous trait distributions without regard to species identity. We model trait-dependent contact rates in two common scenarios: nested networks, and specialized plant-pollinator interactions based on trait matching. We find that disease spread in plant-pollinator networks is impacted the most by selective pollinators, universally attractive flowers, and co-specialized plant-pollinator pairs. When extreme pollinator traits are rare, pollinators with common traits are most important for disease spread, whereas when extreme flower traits are rare, flowers with uncommon traits impact disease spread the most. Greater nestedness and specialization both typically promote disease persistence. Given recent pollinator declines caused in part by pathogens, we discuss how trait-based models could inform conservation strategies for wild and managed pollinators. Furthermore, while we have applied our model to pollinators and pathogens, its framework is general and can be transferred to any kind of species interactions, in any community.

1-85 Using genomics and machine learning to predict the zoonotic potential of viruses
Nardus Mollentze, University of Glasgow Centre for Virus Research

With the ever decreasing cost of metagenomic sequencing, the number of known virus species is rapidly growing. However, data on the ecology of such newly discovered species remains unavailable, which means we cannot assess the importance of these viruses to human and animal health. Using a novel dataset of 836 viruses from 34 virus families (spanning RNA and DNA viruses from mammals and birds), we are developing methodology to assess zoonotic potential directly from genome sequences – often the only information available for novel viruses. The zoonotic status of known animal virus species is strongly predicted by virus genome features and the level of similarity to human genes, with sensitivity of 78% and specificity of 59%. Initial results indicate that matching the genomic signatures of human genes involved in the interferon response is important. These human genes have evolved to remain highly expressed in the presence of effectors targeting foreign nucleic acids, which means their mRNA sequences provide a clear signal of what it takes to evade detection by the innate immune system. That viruses which mimic the patterns in these genes are more likely to be zoonotic points to a key role for synonymous changes and mutations outside protein coding regions of the genome to affect the potential of viruses to infect novel hosts. Further, the ability to rank viruses by their probability of being zoonotic using only genome sequences allows more focussed ecological and virological characterisation in the face of ever increasing numbers of newly discovered species.

1-86 Live-attenuated influenza vaccine (LAIV) strains enter the US swine population in 2018 (and you thought making flu vaccines for humans was hard)
Martha Nelson, Fogarty International Center, National Institutes of Health

Developing broadly protective influenza vaccines is a high priority for US infectious disease research. Influenza A viruses (IAVs) in US swine are similar to those circulating in humans, but with even greater genetic diversity. Multivalent inactivated vaccines licensed for US swine fail to protect against the diversity of newly emerging strains. New platforms have been licensed recently that could be implemented in humans in the future, such as the HA subunit vaccine delivered as RNA in an alphavirus vector. Recently, a bivalent live-attenuated influenza vaccine (LAIV) with a truncated NS1 protein was licensed to provide broader protection against heterologous strains in pigs. However, swine are known as ‘mixing vessels’ for their capacity for genomic ‘reassortment’, in which IAVs swap entire genome segments. Here, a phylogenetic analysis of 163 whole-genome sequences

obtained from US swine in 2018 identified genetic signatures of multiple reassortment events between LAIV strains and wildtype viruses. Onward transmission of multiple LAIV/wt reassortant genotypes was observed, indicating that vaccine strain segments are likely to become established in US swine. Patterns of reassortment relate to the underlying population structure of co-circulating IAV lineages. Intensive monitoring is needed to determine how frequently LAIV strains enter the swine population, their spatial spread, associations with clinical disease, and which reassortant genotypes are fit and likely to become established long-term. Overall, these findings demonstrate the unintended evolutionary consequences of an effort to develop more broadly protective vaccines in swine, and the potential of real-world veterinary experiments to guide humans embarking on a similar quest.

1-87 The network structure and eco-evolutionary dynamics of CRISPR-induced immune diversification
Mercedes Pascual, University of Chicago

Immune selection can act as a form of balancing selection to drive the antigenic (and underlying genetic) diversification of pathogens. In bacteria and archaea, the CRISPR system (for Clustered Regularly Interspaced Short Palindromic Repeats) functions as an adaptive immune system by incorporating DNA segments called 'protospacers' of infecting viruses into host genomes. These acquired segments, termed 'spacers' when in the host, constitute bacterial specific immune memory. From this perspective, strain diversification of both host and pathogen emerges from their frequency-dependent co-evolutionary dynamics and involves the large combinatorics of spacers and protospacers. Previous work has shown the possibility of diverse communities with distributed immunity of the host, in which ecological dynamics exhibit two main regimes. In the first one, viruses flourish and diversify under fluctuating abundance and coexistence; in the second one, bacteria dominate under stable abundance leading to the extinction of viruses up to their eventual escape. We describe the network structures of genetic diversity characterizing 'who infects whom' and 'who is protected from whom', that emerge from transmission and immune dynamics including evolution. We show that these structures are different from those expected under neutrality, and explain how they feed back into the dynamics themselves leading to transitions between the two regimes. We discuss how and why these findings differ from those in existing strain theory for immune selection in humans and other non-microbial hosts.

1-88 Impact of influenza antigenic evolution on disease dynamics in the United States
Amanda C. Perofsky, Fogarty International Center, National Institutes of Health

Influenza viruses continually evolve new antigenic variants, primarily through mutations to the HA1 region of the hemagglutinin (HA) gene. Here we study the poorly understood impact of evolutionary changes on annual influenza dynamics. We constructed an A/H3N2 phylogenetic tree using a dataset enriched for U.S. sequences and inferred antigenic and genetic distances between strains circulating in successive seasons, using hemagglutination inhibition data, substitutions at 129 epitope sites in HA1, or substitutions at seven sites adjacent to the receptor-binding site. We obtained weekly epidemiological and virological data from the CDC and explored correlations between A/H3N2 epidemic dynamics (timing, size, peak incidence, effective R, age patterns) and evolutionary distance during 1997 – 2018. We used lasso regression to select predictors of epidemic dynamics, including evolutionary distance, epidemic size in prior seasons, and influenza A/H1N1 and B incidence. We found that epitope change was the most consistent predictor of A/H3N2 epidemiology, and the only variable retained in multivariate analyses. Increased epitope distance between seasons correlated moderately with earlier and larger peaks, larger epidemic sizes, and higher transmission rates. Influenza cases shifted from young children to adults in seasons with high epitope change. In conclusion, the relationship between HA antigenic drift, epidemic impact, and age dynamics is moderate, with genetic distance based on a broad set of epitopes having greater predictive power than hemagglutinin inhibition-based measures. Influenza epidemiological patterns are consistent with increased population susceptibility in high HA epitope change seasons; the impact of vaccination and neuraminidase evolution will be studied next.

1-89 Distributions, abundance, and virus-vector-host interactions for a tick-borne hemorrhagic fever virus
Sergio E. Rodriguez, University of Texas Medical Branch, Galveston

Tick-borne viruses have increased in geographic range over the last several decades due to numerous factors such as globalization and climate shifts. Along with this increase, incidence of human spillover events resulting from pathogenic tick-borne virus infections, are also on the rise. Our lab focuses on the transmission dynamics for a number of tick-borne viruses, with particular emphasis on the Bunyavirus, Crimean-Congo hemorrhagic fever virus (CCHFV). This life-threatening pathogenic tick-borne virus is spreading throughout southeastern Europe, the Middle East, Africa, and parts of Asia. We seek to better understand the distribution, abundance, and virus-vector-host interactions for CCHFV, its tick genera, and animal reservoirs. Herein, we report on our field studies in collection of various species of tick from two hot-spots for CCHFV, the Republics of Turkey and Spain, and our findings in determining tick(specie)-host preferences and resulting viral diversity. In attempt to establish models for these experiments within a laboratory setting, we further report on our results from exploring multiple tick(specie)-host interactions *in vivo* and *in vitro* by establishing a number of animal types and artificial tick tissue systems for CCHFV. These studies of pathogen dynamics from both field and laboratory settings are urgently needed to establish predictive models for human disease risks and tick-borne pathogen spread.

1-90 Genotypes of bacteria and host drive specificity of colonization in a bumble bee gut symbiont system
Logan A. Sauers, Illinois State University

Organisms harbor complex microbial communities that aid in defense against pathogens, among other beneficial functions. However, the function of these communities is reliant on successful colonization, and the factors that influence colonization in these host-beneficial microbe systems remains understudied. In bumble bees, coevolved and vertically transmitted core gut microbes are critical for the health of these important pollinators with many implicated in pathogen defense and immune development. *Snodgrassella alvi* is a key gut bacterial symbiont in the Apid bees, including bumble bees. As the first gut colonizer, *S. alvi* forms a biofilm, which is likely critical for the subsequent establishment of other gut microbes. Thus, understanding *S. alvi* colonization has important implications for microbiota development and bee health. This work aims to investigate the effects of bacterial strain and host genotypes on the colonization of *S. alvi* within bumble bee hosts. Using multiple strains of *S. alvi* isolated from different colonies of the bumble bee *Bombus impatiens,* together with colonization experiments across different host genotypic units, we find a significant genotype-by-genotype interaction determining the colonization of this beneficial gut microbe. These genotype-by-genotype interactions show specificity between microbe and host in this system is much finer than previously demonstrated specificity at the level of host genera. Furthermore, interactions between host and microbial genotypes have many important ecological and evolutionary implications.

1-91 Geographic variation in host immunogenetics and malarial parasite infection in a *Catharus* thrush species complex
Naima C. Starkloff, State University of New York, Albany & New York State Museum

Unlike free-living organisms that generally follow the latitudinal diversity gradient, different avian malaria parasite lineages exhibit contrasting diversity and prevalence gradients with latitude. This may be due to ecological differences among their vector organisms but may also reflect differences in host-parasite interactions mediated by evolved host immunity. Parasites and hosts engage in a co-evolutionary “arms race”, resulting in a tug of war of evolved traits for parasite persistence and host resistance. Host genes involved in immune response are under strong selective pressure to mediate infections that have negative fitness consequences for birds. A classic case is the selection for high copy number and high polymorphism in the Major Histocompatibility Complex (MHC), in which greater allelic diversity enables the recognition of a greater diversity of infective microorganisms. Using next generation sequencing, we identify the diversity of MHC alleles in a large sample of individuals (n=476) of the closely-related Gray-cheeked Thrush (*Catharus minimus*), Bicknell’s Thrush (*C. bicknelli*) and Veery (*C. fuscescens*) from 20 localities spanning >17 degrees of latitude in

eastern North America. We find that the diversity of MHC alleles among the three species of thrushes varies significantly but find no linear relationship between MHC allele diversity and the diversity or prevalence of malaria parasite infections. We also investigate the interaction of avian malaria and the MHC by testing whether the presence or absence of specific MHC alleles affect the likelihood of infection by different malaria parasite lineages.

1-92 Reconstructing the antigenic evolution of influenza A viruses in multiple hosts
Nídia Isabel Sequeira Trovão, Icahn School of Medicine at Mount Sinai & Fogarty International Center, NIH

Influenza A viruses have a remarkable capacity to transmit between species, presenting an ongoing pandemic threat. Influenza A viruses of the H3N2 and H1N1 subtype are particularly adept at host-switching, and currently circulate in birds, humans, pigs, dogs, and horses. These viruses rapidly evolve their surface antigens to evade host immune detection, requiring bi-annual updates to influenza vaccine strains in humans. Vaccines also have been formulated for lineages in other hosts, although the processes for updating animal vaccines strains are ad hoc and infrequent, partly due to lower estimated rates of antigenic evolution. The prohibitive cost of large-scale phenotypic testing of A subtype viruses in animals has impeded a rigorous comparison of rates of nucleotide and antigenic evolution of H3N2 and H1N1 viruses across species. Here, we first attempt to validate whether antigenic characteristics of the hemagglutinin subunits can be effectively applied to predict antigenic evolution across diverse host species. This method harnesses the advantages of the recently developed mixed effects model implemented within the Bayesian genealogical framework, which allows accounting for the viral evolutionary trajectories and superimposing the host transmission history onto the viral phylogeny. We inferred nucleotide and antigenic rates of evolution that varied significantly across host-specific and continent-specific lineages. These findings further our basic understanding of how varying immune-driven selection pressures in different host species relate to host-specific rates of antigenic evolution. Critically, this knowledge advances efforts to predict evolutionary trajectories and evaluate pandemic risks, and informs the required timing of vaccine strain updates in different hosts.

1-93 Spatial structure as a mechanism for pathogen diversity
Senay Yitbarek, University of California, Berkeley

We examine the role of spatial structure between two competing pathogens for a single host. Many competition models assume that populations are well-mixed, but increasingly it has been shown that populations occur in spatially structured environments with limited dispersal abilities. For infectious diseases, theoretical studies predict that spatial host population structure impacts life-history strategies of pathogens by selecting for lower infectivity. However, we lack empirical studies that consider the distribution of multiple pathogen genotypes in spatially structured environments. Bacteriophages are an excellent model system for observing competitive dynamics. In this work, we investigate the effects of spatial structure on pathogen life-history strategies using a joint experimental and theoretical approach. By competing two lytic bacteriophages of the host *Pseudomonas syringae* in experimental microhabitats, ranging from well-mixed to spatially structured environments, we show that the weaker phage competitor is able to persist in spatially structured environments. We further develop a spatially explicit individual-based model using experimentally derived parameters that incorporate key aspects of phage life cycles to examine how changes in phenotype affects fitness across different environments. Our integrated experimental-theoretical approach allows us to explore the possible mechanisms underlying the differences in behavior.

1-94 The scaling of the energetic cost of parasitism from hosts to ecosystems
Rita Grunberg, Rutgers University

Parasites are thought to play a significant role in ecosystem energy flow, but we currently lack a mechanistic framework to integrate parasite energetics at broad scales. Here, we develop a metabolic framework to describe the energetic cost of parasitism from hosts to ecosystems. First, we develop and test theory that link host metabolism ($\boldsymbol{R_h}$) to the energy flux of parasitic communities ($\boldsymbol{F_p}$) spanning 28 host taxa. Specifically, we test whether the fraction of a host's energy budget that is allocated to parasitism is invariant with respect to host body size. Our data affirms an allometric relationship between host metabolic rate and parasite community flux ($p < 0.001$), although the slope of the relationship was shallower than our expected isometric relationship (observed slope: 0.76; 95% CI: 0.56, 0.95). This relationship suggests the fraction of energy taken by parasites declines with host metabolic rate. The empirical equation $\boldsymbol{F_p = 0.002 * R_h^{0.76}}$ implies that the fraction of energy a parasite community uses, $\boldsymbol{\delta}$, varies with host metabolic rate as: $\boldsymbol{\delta = F_p/R_h = 0.002 * R_h^{-0.24}}$. Next, we extend this framework to explain the scaling of host and parasite community energetics at the ecosystem scale. Across ecosystems, we report a strong relationship between the energy flux of parasites communities and the energy flux of their host communities ($R^2 = 0.93$, $p < 0.0001$). A common scaling exponent describes host and parasite energy flux across ecosystems (slope = 0.41; 95% CI: 0.35, 0.48). Overall, energetic-based models outperformed those using biomass when describing parasite community energetics within hosts and ecosystems.

1-95 Parasite-vaccine interactions and their implications for vaccination – a systematic review and (plans for) meta-analysis
Liana F. Wait, Princeton University

Immune responses to vaccination are notoriously heterogeneous between individuals and populations. One factor that could influence an individuals' response to vaccination is their infection history with unrelated parasites. We systematically reviewed the literature on parasite-vaccine interactions, and provide an initial meta-analysis of the results in these papers. We also discuss parasite and vaccine factors that could determine the outcome of such an interaction to determine an individual's response to vaccination and hence their resistance to the vaccine target. Parasite factors include the type of parasite involved, the timing of infection relative to vaccination, while vaccine factors include vaccine formulation, route of administration, and the type of immune response required to provide protection against the target antigen. Finally, we use a mathematical model to explore the potential population dynamic consequences of these effects.

1-96 Implications of Batrachochytrium dendrobatidis for Panamanian Anurans and the Amphibian Microbiome
Eden Abebe, University of Massachusetts Boston

The pathogenic fungus, *Batrachochytrium dendrobatidis* (*Bd*), is negatively impacting populations of amphibians worldwide. *Bd* causes the skin disease chytridiomycosis in amphibians, which leads to keratinization of the skin and is frequently lethal. Some amphibians are able to survive infection or show resistance to *Bd*, drawing interest to the mechanisms that they use to do this. Certain bacteria, such as *Janthinobacterium lividum,* have been shown to reduce the likelihood of the fungus infecting amphibians and increasing their chances of survival. Swab samples were collected from several species and locations of wild anurans throughout Panama. DNA extraction and 16S rRNA sequencing were performed using an Illumina miSeq. The skin microbiome was analyzed in QIIME2, alongside life history traits collected *in situ*. By developing our understanding of *in situ*

factors affecting the microbiome of amphibians, we can develop more effective mitigation strategies for reducing amphibian biodiversity loss globally.

1-97 Dengue after Zika: characterizing impacts of Zika emergence on endemic dengue transmission
Rebecca Borchering, Odum School of Ecology, University of Georgia

In 2015 and 2016, Zika virus (ZIKV) swept through many Latin American countries where dengue virus (DENV) is endemic. Dengue and Zika viruses are of the same family, share a vector and may interact competitively or synergistically through human immune responses. We examine dengue incidence data from Brazil and Colombia from before, during, and after the Zika epidemic. We find evidence that dengue incidence was atypically low in 2017 in both Brazil and Colombia. We investigate whether Zika incidence at the state or department level is associated with changes in dengue incidence and find mixed results. We use simulations to investigate expected impact of cross-protection or enhancement between dengue and Zika. Our simulations show that regardless of the mechanism, low periods of dengue incidence are followed by a resurgence in dengue cases. It is therefore likely that countries currently experiencing low levels of dengue incidence will experience large dengue seasons in the near future.

1-98 Modeling immunity profiles of malaria under superinfection
Lauren M. Childs, Virginia Tech

Regions where malaria is endemic are characterized by stable malaria transmission and high levels of naturally acquired immunity. Children, but not infants, have the highest level of parasites, and many infections, particularly among adults, are asymptomatic. In contrast, other regions are characterized by epidemic, rather than endemic, malaria with minimal levels of immunity in the population. With recent enhanced control efforts, many countries are moving towards malaria elimination, a perturbation of the level of malaria transmission. We build a discrete-time modeling framework of within-host dynamics of malaria infection tracking antigenically varying proteins and the corresponding immune response, which is capable of accommodating superinfection of multiple genotypes. We find that the effect of superinfection depends on the immune response developed, which is a result of the similarity of the genotypes and the timing of superinfection relative to the pre-existing infection. We see effects on the length of infection and the predicted transmissibility of genotypes. We expect individual variation in length of infection and transmissibility due to superinfection to impact the distributions of immunity across a population.

1-99 How does interspecific host competition alter the amplification and dilution of disease?
Michael Cortez, Utah State University

For pathogens that infect multiple host species, the addition or loss of a host species in a community can affect levels of disease in other host species. Using 2-host, 1-pathogen epidemiological models, I explore how interspecific host competition influences whether increased host biodiversity increases (amplifies) or decreases (dilutes) disease, and how those effects are altered by the pathogen transmission mechanism. The two main results I will present are (1) increased interspecific competition promotes dilution for pathogens with frequency dependent direct transmission, environmental transmission, or density dependent direct transmission and (2) the amount of interspecific host competition needed for dilution is highest for density dependent direct transmission, lowest for frequency dependent direct transmission, and intermediate for environmental transmission. I also show how my theoretical framework is a step towards unifying dilution effect theory for environmentally and directly transmitted pathogens.

1-100 Complex effects of coinfection of Mycoplasma gallisepticum and haemosporidian in house finches.
André A. Dhondt, Cornell University

The host jump from poultry to house finches of the bacterium *Mycoplasma gallisepticum* (MG) resulted in a rapid epidemic of mycoplasmal conjunctivitis across house finch populations in the USA and Canada. Given the widespread prevalence of multiple species of haemosporidian across birds (including *Plasmodium spp* and *Leucocytozoon spp* in birds around Ithaca, NY*)*, and given our experience with experimentally infecting birds with MG we are now studying effects of coinfections on these diverse pathogens. Note that while these pathogens impact host survival to some extent, many infected host recover or develop chronic infections.
House finches that are chronically infected with *Plasmodium* develop more severe and longer disease caused by MG. An MG Infection of House finches chronically infected with *Plasmodium* (no circulating merozoites or gametocytes in the blood) causes a relapse of *Plasmodium (*infected erythrocytes re-appear). An experimental MG Infection of House finches chronically infected with *Leucocytozoon* has only a marginal effect on Leucocytozoon prevalence; the presence of *Plasmodium* in the same host, however, causes a major increase in the detection by PCR of *Leucocytozoon* prevalence and infection intensity. The re-emergence of *Plasmodium* is likely the result of an increase in blood corticosterone levels following an MG infection. The increase in *Leucocytozoon* prevalence is probably the result of *Leucocytozoon* being an opportunistic pathogen. All three pathogens seem to benefit from coinfection.

1-101 A macroparasite within-host framework accommodating spatial structure can recapitulate key aspects of influenza A infection dynamics.
Molly Gallagher, Emory University

Classic microparasite models of infectious disease describe the dynamics of different classes of individuals in a population, such as the susceptible, infected, and removed classes in an SIR model. This general framework has been used extensively to model infectious disease dynamics at the between-host level, and has also been applied on a smaller scale to describe the within-host spread of a pathogen through a population of cells. At the within-host level, however, these SIR-type models do not easily allow us to consider the impact of cellular coinfection on infected cell phenotypes and ultimately viral dynamics. Here, we first review recent evidence from collaborators that cellular multiplicity of infection strongly affects infected cell phenotypes in the case of influenza A virus. These phenotypes include overall viral yield, cell death rates, and the occurrence of interferon induction and superinfection exclusion. We then present and build on recently developed within-host 'macroparasite'-type models, which can be modified in a scalable manner to accommodate different functional forms for infected cell phenotypes. Finally, we fit a spatially implicit extension of this within-host model to equine influenza data, and show that it can recapitulate *in vivo* measurements, including viral titer and interferon levels.

1-102 Finding the limits of emerging disease surveillance
Emma E. Glennon, University of Cambridge, Cambridge UK

Every spillover of a transmissible zoonosis has the potential to spark an epidemic. Detecting spillover events early could improve both our understanding of the ecological drivers of zoonoses and our ability to intervene at the most critical moment for outbreak prevention. However, spillovers of rare pathogens are difficult to detect, especially when they occur amid a background of syndromically similar endemic diseases. To estimate, understand, and potentially improve detection rates, we have modelled the processes of transmission and surveillance during the first few generations of an emerging outbreak.

We first used simulations of early transmission chains, informed by published estimates of transmission parameters and all available incidence data for Ebola virus disease and epidemic monkeypox, to estimate detection rates of these diseases. We estimate that the majority of spillover events of both zoonoses are never detected, as well as that detection rarely occurs within the first few generations of an outbreak. To examine this

apparent surveillance failure, we have also modelled the early stages of syndromic surveillance using a Bayesian framework parameterized with symptomatic, diagnostic, and epidemiological data for both rare and common causes of rash and hemorrhagic fever across sub-Saharan Africa. These models demonstrate that a failure to detect small zoonotic outbreaks is a natural feature of resource-limited syndromic surveillance. However, they also demonstrate the potential efficacy of unconventional additions to surveillance programs—including improved diagnostics for more common febrile illnesses and increased consideration of minor or uncharacteristic symptoms.

1-103 Serodynamics of leptospirosis in California Sea Lions
Ana C. R. Gomez, University of California, Los Angeles

California sea lions (*Zalophus californianus;* CSL) have experienced repeated outbreaks of infection by bacterial spirochete *Leptospira interrogans* serovar Pomona since at least 1984. Cases of leptospirosis of varying severity are described among thousands of sea lions that strand along the coast of California each year. Despite a long-standing dataset of incidence, serology, and demography, the overall impact of leptospirosis in this large migratory wildlife population remains difficult to estimate.

We propose a model to scale the time series of observed severe cases of leptospirosis in CSL to the population-wide incidence. Using a biphasic antibody decay model based on longitudinal serology, we estimate the distribution of titers among 1 to 2 year old animals and fit it to observed cross-sectional serology to obtain the scaling factor between the number of observed and total cases in that age class.

Using the full time series of case counts for 1 to 2 years-old CSL we estimate that for every severe case of leptospirosis observed in this age class, around 200 new cases occur. The model performs well on simulated datasets where scaling is known, depending on sampling intensity and duration. Finally, we use serology from animals estimated by length to be 2 to 3 years old to refine our quantitative understanding of titer dynamics, especially in the lower titer range, and discuss the trade-off between the decay parameters and the maximum titer distribution used in the model.

1-104 Heterogeneous serologic responses to pertussis vaccination: efficacy and protection
Christian E. Gunning, University of Georgia, Odum School of Ecology

Worldwide, two main classes of vaccines are used to protect against Bordetella pertussis infection and disease: the original whole-cell vaccines, and the more recent, less reactogenic acellular vaccines. While the population-level efficacy of these vaccines has been repeatedly demonstrated, serological markers of protection in humans from infection and/or disease remain unclear.

Here we employ historical acellular pertussis vaccine trials to evaluate the potential impact of heterogeneous serologic responses to multiple-antigen acellular vaccines. We construct three scenarios that describe alternative hypotheses regarding serologic heterogeneity. The first scenario assumes independence of the within-individual responses to each antigen. We also examine scenarios that assume low and high levels of covariance between antigenic responses. For each scenario, we using published antibody titer sample statistics to draw parametric bootstrap samples of vaccinees.

We introduce a conceptual model where protection from disease is a function of antibody titers to vaccine component antigens. We evaluate this conceptual model using bootstrap samples of vaccinees, above, and compare results to the observed results of vaccine efficacy trials for a range of acellular vaccines. While we cannot directly evaluate the clinical relevance of this model, our results highlight the potentially complex relationship between serologic heterogeneity and population-level estimates of vaccine efficacy.

1-105 Phylogenetic inference of multiscale selection pressures using a continuous state birth-death process
Marco Hamins-Puertolas, North Carolina State University

In host-pathogen systems, pathogen strains can have varying levels of fitness at the within host and between host scales. This can be presented through changes in the ability to compete at the within host scale or through variation in the host's ability to transmit. Here we develop a method to perform inference on the magnitude and direction of selection pressures within and between hosts along with other relevant parameters like effective population size. Hosts in this model are assigned to a value that is an element of some closed and bounded set. In the context of a host-pathogen system, allele frequency or a measure of genetic distance can be used. Given a phylogeny with continuous-valued tip states, we can perform maximum-likelihood inference utilizing a continuous state birth-death branching process.

1-106 Incorporating a dose-response relationship into models of typhoid fever transmission
Yu-Han Kao, Yale School of Public Health

Effective allocation of resources to control typhoid fever requires accurate estimation of disease burden. However, estimating how the burden of disease varies across different populations has been challenging due to the complex nature of the disease. The age distribution of typhoid fever cases generally varies inversely with transmission intensity, but immunity to typhoid is known to be incomplete; thus, the mechanisms underlying this heterogeneity are not fully understood. Human challenge studies suggest that individuals are more likely to show symptoms when exposed to greater doses of Salmonella Typhi. Accounting for increased risk of symptomatic infection at higher force of infection in a transmission model might explain the variation in age-specific incidence of typhoid fever, and can provide better estimates of the impact of vaccination. We incorporated a dose-response function describing the relationship between the force of infection and the probability of developing symptomatic disease into a previously developed typhoid transmission model. We fit the model to incidence data from multiple countries, and evaluated the potential impact of typhoid conjugate vaccine strategies across a range of different transmission settings. The model accounting for a dose-response function produced comparable goodness of fit measures as compared to previous models and required fewer parameters to explain the variation in incidence across settings. Vaccination outcomes from the dose-response inclusive model suggest a larger and more sustained decline in typhoid fever cases. Accounting for a dose-response function in typhoid transmission models has important implications for understanding disease dynamics and the potential impact of vaccination.

1-107 Temporal trends and geographic inequalities in antibiotic prescribing in Massachusetts
Stephen Michael Kissler, Harvard T.H. Chan School of Public Health & University of Cambridge

Antibiotic resistance is strongly associated with antibiotic use. Reducing the prescription of 'unnecessary' antibiotics – which constitute nearly one third of all outpatient antibiotic prescriptions in the US – is a key public health priority. The formulation and evaluation of policies aimed at reducing antibiotic consumption require a detailed knowledge of current spatiotemporal patterns in antibiotic prescribing. We characterise these antibiotic prescribing patterns for Massachusetts from 2011—2015 using a massive All-Payer Claims Database that captures individual outpatient pharmacy claims for over 94% of Massachusetts residents under the age of 65. Overall, the outpatient antibiotic prescription rate dropped by 17%, echoing similar decreases reported across the US. Within this overall trend however lie striking heterogeneities. Prescribing varies markedly by time of year, especially among younger age groups, for whom the wintertime prescribing rate can be up to three times higher than the summertime rate. Due to major shifts in the composition of healthcare providers, nurse practitioners and physician assistants are prescribing antibiotics that might have previously been given by medical doctors. Geographic inequalities in prescribing are explained in part by differences in age structure, median income, and urbanness, though the relative importance of these predictors varies both by time of year and across the five years. Using a mathematical model, we comment briefly on how these prescribing heterogeneities might affect

antibiotic resistance rates in the population, and we discuss important considerations for designing targeted interventions aimed at further reducing antibiotic prescription rates.

1-108 Multiple transmission routes sustain high prevalence of a virulent parasite in a butterfly host
Ania A. Majewska, University of Georgia

Understanding factors that allow virulent parasites to reach high infection prevalence in host populations is important for managing infection risks to human and wildlife health. Multiple transmission routes have been proposed as one mechanism by which virulent pathogens can achieve high prevalence, underscoring the need to investigate this hypothesis through an integrated modeling-empirical framework. Here, we examine a virulent, specialist protozoan infecting monarch butterflies that commonly reaches high prevalence (50-100%) in resident populations. We integrate field and modeling work to show that a combination of three empirically-supported transmission routes (vertical, adult transfer, and environmental transmission) contribute to high end of season infection prevalence in this system. Although horizontal transmission is necessary for parasite invasion, most new infections post-establishment arise from vertical transmission. Our study predicts that multiple transmission routes, coupled with high parasite virulence, can reduce resident host abundance by up to 50%, suggesting that the protozoan could contribute to declines of North American monarchs.

1-109 Cooperative Evolution Leads to Pathogen Attenuation Within Host
Abigail J. Miller, Salk Institute for Biological Studies

Antagonist interactions between hosts and pathogenic microbes can promote disease and result in a Red Queen effect leading to the oscillation of antagonistic traits in both populations. However, we hypothesize that under certain conditions cooperative interactions between host and pathogens may support commensalism over time. Using *Citrobacter rodentium*, an enteric bacteria that causes lethal colonic inflammation in mice, we discovered that a high iron diet promotes host survival during infection. Consistent with our hypothesis, we also found that this diet promotes persistent colonization and attenuation of *C. rodentium* over time. Analysis of *C. rodentium* isolates' genomes reveal stable null mutations in *C. rodentium's* genes responsible for virulence, suggesting a cooperative host-pathogen interaction. To uncover the mechanisms pushing *C. rodentium* towards an attenuated state, we first created antibiotic-tagged versions of both the wild-type and avirulent strains to measure competitive fitness *in vivo*. We found the avirulent isolates to be deficient in initial colonization of the host in comparison to the wild-type strain, however attenuated isolates are able to outcompete wild-type during long-term colonization. Next, we plan to examine the roles, if any, the host immune system or the microbiome play in selecting for avirulent *C. rodentium.* Together these findings reveal a novel aspect of cooperative host-pathogen evolution, and possible alternative methods to alleviating infections without driving damaging antagonistic host-pathogen interactions.

1-110 Do host immune responses slow the development of malaria parasites? Can we tell?
Madeline A. E. Peters, University of Toronto

Malaria parasites have characteristic developmental cycles within a vertebrate host. For example, the main aetiological agent of human malaria, *Plasmodium falciparum*, takes ~48 hours to replicate inside of host red blood cells (RBCs). There is great interest in understanding the extent to which these cycles are controlled by the host or parasite and which party – if either – they benefit. Recent experimental work suggests that the rodent malaria parasite, *Plasmodium berghei*, characterized by a ~24 hour cycle, experiences a substantial delay in its development time when infecting a host with an active immune response. Here, we use mathematical models to test alternative explanations for that inferred effect. Using a delay-differential equation model of within-host malaria infection dynamics, we simulate data assuming a fixed 24-hour cycle. We then fit those data with a published model of parasite maturation, with which the delayed development was inferred, and find that several documented sources of measurement bias (e.g., an inability to distinguish early-stage parasites infecting young RBCs from late-stage parasites) can lead to inferring delayed maturation when there is no such effect. We

caution that the currently available data present an unclear picture and emphasize the key missing data required to overcome these biases, including confirming parasite stage structure via multiple methods and estimating absolute parasite biomass rather than the relative measure of parasitaemia (i.e., percent of RBCs infected). Understanding the extent to which host immune responses alter parasite developmental timing is key for elucidating the evolutionary significance of these characteristic cycles.

1-111 Identity and density of parasite exposures alters the outcome of co-infections in amphibians
Chloe T. Ramsay, University of Notre Dame

Hosts are exposed to numerous parasites simultaneously under natural conditions and these co-infections can threaten host populations and ecosystem stability. Moreover, the spatiotemporal variation in abundance of co-occurring parasites might influence host responses to them and thus infection intensities. We investigated how the parasite density and identity alters within host co-infection dynamics by simultaneously exposing adult Cuban treefrogs (*Osteopilus septentrionalis*) to pairwise combinations of the chytrid fungus (*Batrachochytrium dendrobatidis*, Bd), the nematode *Aplectana hamatospicula,* and Ranavirus over a range of five densities per parasite. We quantified total parasite load, host survival and growth over four weeks. We hypothesized that the competitive advantage of a co-infecting parasite would be positively associated with its exposure dose, and we anticipated that this advantage would be amplified when the co-infecting parasites activate similar immune responses. Bd load was not influenced by exposure dose of the other two parasites, but Ranaviral load decreased with increasing exposure dose of Bd and *A. hamatospicula*. *A. hamatospicula* load was not affected by Ranaviral density but decreased with increasing Bd density. Host survival and growth were reduced by Bd infections relative to unexposed frogs. Higher doses of the non-focal parasite caused a competitive disadvantage for the focal parasite, which decreased the loads in some cases. However, there was less evidence to support that these patterns would be amplified when parasites activate similar immune responses. Potential mechanisms to explain the patterns we found range from the potential for immune-mediated interactions to direct competition between the parasites for space or resources.

1-112 Cross-immunity and immune imprinting in the age distributions of influenza B lineages
Marcos C. Vieira, University of Chicago

The two co-circulating lineages of influenza B have distinct age distributions, with young adults experiencing fewer infections with B/Yamagata (but not B/Victoria) than individuals in other age groups. Because B/Yamagata was the dominant lineage during the 1990s, its lower incidence among young adults might arise from individuals having reduced susceptibility to the lineage they encountered first compared to the other. In addition to this "imprinting" effect, however, protection might arise from cross-immunity to strains encountered later in life as individuals are repeatedly infected. We fit statistical models to the age distributions of B/Victoria and B/Yamagata cases reported in Australia and New Zealand in 2002-2013 and asked whether substantially more protection arises from the first infection than later infections. Preliminary results suggest age distributions can be explained by cross-immunity to previously encountered strains from each lineage, with no clear evidence for a reduction in susceptibility driven by the first exposure (0-40% for B/Victoria, 0-70% for B/Yamagata). Because of B/Yamagata's dominance during the 1990s, young adults would have stronger cross-immunity to past B/Yamagata strains than to previous B/Victoria strains, which only reemerged in the early 2000s. We also found B/Yamagata infections to be more protective against subsequent B/Victoria infections than were B/Victoria infections against subsequent B/Yamagata infections. The lack of clear evidence for immune imprinting suggests the antibody response to primary infection with seasonal influenza does not always preclude effective responses to subsequent infections with other lineages.

1-113 The early evolutionary dynamics of drug-resistance in *Plasmodium falciparum*: What's sex got to do with it?

Alexander O. B. Whitlock, University of Toronto

Plasmodium falciparum has evolved resistance to nearly all of the currently available antimalarials but, despite the impending public health crisis, the origin of resistance remains poorly understood. Despite *falciparum's* enormous population size, resistance can often be traced to a single event. Furthermore, though disease burden is highest in sub-Saharan Africa, most resistance mutations have arisen in Asia, where transmission intensity is lower. This pattern suggests that producing a resistant phenotype is complex, and that high transmission intensity, which is associated with elevated genetic diversity and widespread partial immunity in the host population, exacerbates this complexity. Previous models have demonstrated that recombination, competition, and immune responses impact the spread of resistance. However, few have explored how these factors interact, and none have done so within the full context of the complex *Plasmodium* life cycle. Here, we introduce a stochastic, individual-based, multiscale model of evolving *Plasmodium* populations within host and vector populations to determine how transmission intensity shapes the fate of resistance mutations and the evolution of life history traits. Parasites in this model have discrete genomes which experience random mutations to epistatic loci, allowing the evolution of costly multilocus resistance and compensatory mutations. We examine how within-host diversity shapes effective recombination rate and the conditions in which linkage disequilibrium suppresses, generates, or maintains resistance. We also distinguish within-host selection for reproductive fitness from selection for antigenic novelty. Understanding the ecological factors which facilitate the emergence of resistance will allow us to identify probable origins and intervene before resistance becomes clinically apparent.

SESSION 2 – Wednesday 12 June (4:00-6:00 pm)

BEHAVIORAL DRIVERS OF INFECTIOUS DISEASE DYNAMICS (Posters 2-1 → 2-30)

2-1 A General 'Linear Chain Trick' for building ODE models with flexible dwell times
Paul J. Hurtado, University of Nevada

ODE models have been criticized for their inability to incorporate non-exponential dwell time distributions (e.g. for infectious period). The Linear Chain Trick (LCT; aka the Gamma Chain Trick) is a technique for constructing mean field ODE models with dwell times that are Erlang distributed (i.e., gamma distributed with integer shape parameter), however we lack general theory to facilitate the easy application of this technique, especially for complex models, where ODEs must instead be derived from integral equations or continuous time stochastic models. This shortcoming has forced modelers to either construct ODE models using heuristics with oversimplified dwell time assumptions, or use time consuming derivations from first principles, or to instead use non-ODE models (like integro-differential equations or delay differential equations) which can be cumbersome to derive and analyze.

I will present results that generalize the LCT, and make it easier to construct mean field ODEs that better incorporate appropriate dwell time assumptions, including some conditional dwell time assumptions. Specifically, I will 1) present novel extensions of the LCT to various scenarios found in applications; 2) provide formulations of the LCT and its extensions that bypass the need to derive ODEs from integral or stochastic model equations; and 3) I'll introduce a novel Generalized Linear Chain Trick (GLCT) framework that extends the LCT to a much broader family of distributions, including the flexible phase-type distributions. These results also help clarify connections between individual-level stochastic model assumptions and the structure of corresponding mean field ODE models.

2-2 Co-circulation and misdiagnosis of Zika, dengue, and chikungunya led to underestimation of the 2015-2017 Zika epidemic in the Americas
Rachel J.Oidtman, University of Notre Dame

During the 2015-2017 Zika epidemic, two other viruses also transmitted by *Aedes* mosquitoes – dengue and chikungunya – were also in circulation in many countries in the Americas. Clinical field studies of suspected and confirmed cases during coincident epidemics of all three viruses have shown that diagnostic criteria for both case types are prone to misdiagnosis. Given the importance of case report data for informing estimates of the epidemic's dynamics, our objective was to produce revised estimates of the magnitude of the Zika epidemic that account for misdiagnosis. Our approach used basic principles of probability to translate the observed data (i.e., case reports diagnosed as Zika) into an estimate of the latent variable of interest (i.e., case reports truly attributable to Zika virus). These probabilistic adjustments made use of empirical estimates of diagnostic sensitivity and specificity obtained in northeastern Brazil during a period of co-circulation of Zika, dengue, and chikungunya. Of the nine million cases of dengue and chikungunya reported in the Americas in 2014-2017, we estimated that 252,010 (95% CI: 99,687 - 414,994) cases may have been caused by Zika virus instead. This implies that the Zika epidemic may have been 37% (95% CI: 15% - 61%) larger than case reports alone suggest. The majority of these misdiagnoses were estimated to have occurred in countries with high incidence of all three viruses, such as Brazil, Paraguay, and Mexico.

2-3 PA-Dashboard facilitates analysis of systems evolution of P. aeruginosa biofilm pathways
Christopher Panlasigui, CUNY-Hunter College

Pseudomonas aeruginosa-dashboard (PA-Dashboard) is a web interactive tool to analyze biofilm formation in this important bacterial pathogen causing 51,000 infections in the U.S. annually. The ability of PA to produce biofilm allows it to survive in different ecological niches, escape host defenses, and become resistant to many anti-biotics. Attributable of its large genome size and metabolic plasticity, PA biofilm can infect almost any tissue and exhibit long-term intractable infections particularly to immunocompromised and immunosuppressed individuals. To focus on the genomic and metabolic variabilities, PA-Dashboard is equipped with a heatmap to provide an overview of the abundance of metabolites from 27 clinical strains from cancer patients. Alongside are multiple tabs detailing the distribution of metabolite of each strain represented by a box plot, metabolite name and metabolic pathway from KEGG database, and genome-scale metabolic network from PA14 iPau1129 and PAO1 iPae1146 strains. All these features are laid out to maximize typical computer screen for ease of use, and seamless analysis. It is in our hope that this integration of statistical overview and tabulated details can facilitate the analysis of the genomic and metabolic variabilities to elucidate *P. aeruginosa* biofilm formation.

2-4 Disentangling the key components of tick-borne pathogen transmission: overwintering survival and host-finding success of *Ixodes scapularis* in Eastern United States
Danielle M. Tufts, Columbia University

The blacklegged tick (*Ixodes scapularis*) is the primary vector of *Borrelia burgdorferi*, the Lyme disease agent in North America. The basic reproduction number (R_0) for some tick-borne pathogens is highly sensitive to the probability that engorged larvae survive the winter (S_N), molt into nymphs, and find a host (c). This process is dependent on local environmental variables, including climate, host population size and movement, and tick behavior. We estimated host-finding success (c) and host density via mark-recapture trapping of the primary host, *Peromyscus leucopus*, at two sites on Block Island, RI and two in mainland Connecticut by measuring the abundance of nymphs on hosts in year 2016 and comparing it to the abundance of larvae found on hosts in 2015, taking into account overwintering survival. These abundances were the product of mouse densities and tick burdens on mice. We estimated overwintering survival (S_N) using engorged larvae placed in field enclosures at each location. The result suggests that local host-finding differences may be driven in part by host behavior. Estimating tick overwintering survival (s_N) and the probability a surviving tick successfully finds a host (c) separately allowed for assessments of regional variation in different elements of the Lyme disease system. These calculations contributed to understanding the nuanced effects on tick physiology from those on tick questing behavior and the effects of climate from those of host populations. Characterizing such relationships will eventually allow us to make more reliable predictions of Lyme disease risk in new regions or those undergoing ecological change.

2-5 The macroecology of avian competence for *Borrelia burgdorferi*
Daniel Becker, Indiana University

Zoonotic bacteria of the *Borrelia burgdorferi* sensu lato complex are transmitted to humans by ticks and cause Lyme disease, which has infection foci through North America, Europe, and Asia. Human risk is partly shaped by variation in the relative abundance of competent reservoirs, host species than can transmit bacteria to uninfected larval ticks. While life history strategy is implicated as a driver of competence among mammal reservoirs, competence appears more idiosyncratic among avian reservoirs. Yet because many birds have high tick burdens, can transport infected ticks over long distances, and occupy suburban environments, resolving interspecific drivers of competence could have implications for human risk. Here, we collated competence data (i.e., ability of birds to infect larvae or presence of infected larvae on wild birds) for 162 species. To learn the trait profile of a competent bird, we applied boosted regression trees to binary competence data and a suite of species traits and taxonomic covariates. Our model characterized competent avian species with 90% accuracy. Traits most important for describing competent birds included incubation time, sexual dimorphism in mass,

geographic range size, maximum lifespan, fledging age, and diet, suggesting that competent avian reservoirs are fast-lived, have larger males, are geographically widespread, and are less insectivorous. We applied our model to trait data for 11,000 other bird species to identify at least 22 unsampled species with a high probability of being competent reservoirs. These results highlight potential bird species and geographic regions as high-priority targets for future Lyme disease surveillance.

2-6 Childhood infections in a pre-health care society: epidemic dynamics and the impact of vaccination
Michael Briga, University of Turku, Finland

Childhood infections represent a major socio-economic burden, especially in populations with limited health care. Vaccination is one the most important public health interventions, but decomposing its impact from other public health developments has proven difficult. We here investigate the demographic and epidemiological impact of the first mass vaccination intervention in human history against the childhood infection smallpox in a society with minimal health care improvement, 18th and 19th century Finland, and compare it against that of two 'control' childhood infections without vaccination, pertussis and measles. We show >40 readily identifiable epidemics of smallpox, pertussis and measles over 100 years, responsible in the pre-vaccine era for 20% of all deaths till age 10. The introduction of vaccination promptly halted the rise of smallpox, almost halved smallpox deaths and averted between 9% and 15% of the deaths till age 10, corresponding to 200,000-300,000 lives in 50 years. Ten years after the introduction of smallpox vaccination, smallpox' age at infection doubled, its periodic epidemic structure collapsed and its reproduction number decreased. In contrast, pertussis and measles, for which there was no vaccination, showed dynamics consistent with that of growing pre-health care populations: their death toll almost doubled, their reproduction number increased and pertussis, but not measles, showed a decreasing age at infection and accelerating periodic epidemics. These results show that even in the absence of health care development, mass vaccination programs can have a demographic and epidemiological impact to the extent of altering a population's demographic course.

2-7 The changing epidemiology of the varicella-zoster virus; insights on vaccine efficacy
Jesus Cantu, Columbia University, Mailman School of Public Health

Regional sociocultural and environmental contexts can alter the transmission dynamics of infectious diseases. For common childhood infections, like chickenpox, the changing age and nature of the population have proven particularly important for the continued transmission of the virus and its potential pathogenesis. Varicella is an infectious disease caused by primary infection with the varicella-zoster virus (VZV), an exclusively human virus. A live-attenuated vaccine was first developed in 1974 and first implemented in the US in 1995, as part of their national immunization schedule. Outbreaks of chickenpox in highly vaccinated communities led to the recommendation of a second dose in 2007, a means to boost antibody levels and decrease the experience of breakthrough varicella among vaccinated individuals. At the population-level, some studies have been able to document a decrease in overall varicella-related hospitalizations among children by using outpatient data. However, incomplete and changing reporting makes it difficult to quantify vaccine impact on disease transmission. We have collated what we believe to be the most extensive longitudinal data on VZV cases. These include state-level US data (1972-2014) combined with data for the State of Texas (1920-2016). For each state, we also have VZV vaccination data (1996-2016) and demography data (1930-2016). Our aim is to directly infer VZV vaccine mode of action and efficacy based on the observed differences in the epidemic dynamics pre- and post-vaccine. VZV transmission will be quantified using dynamic transmission models, parameterized via iterated particle filtering. The model-data combination will allow us to reconstruct unobserved VZV transmission within populations and measure the reduction afforded by the vaccine, at first and second dose.

2-8 Urban landscape heterogeneity and the risk of dog-mediated human rabies in Peru
Virginia Micaela De la Puenta Leon, *Universidad Peruana Cayetano Heredia, Perú*

Rabies virus is circulating in the dog population of Arequipa, Peru, putting at risk 1 million people. The complex landscape of the city facilitates and hinders the transmission of rabies virus. Here, we used door-to-door surveys in communities at different stages of urbanization to assess the impact of the urban landscape on two major drivers of human rabies risk: dog population dynamics and access to post-exposure prophylaxis for bitten humans. We surveyed 4,370 households; all visited houses and health facilities in the study area were georeferenced. We found bite rates to be highest in the newest, poorest communities where access to healthcare is lowest and turnover in the dog population highest. Urbanization processes involve ecological, social, and economic changes that in turn directly affect the risk of dog-mediated human rabies through multiple mechanisms. Adaptation of migrants to the new environment delays or even impedes rabies preventative measures including seeking medical attention following a dog bite, increasing their risk of rabies in periurban areas. The high turnover of the dog population in periurban areas compared to urban areas, drastically reduces the proportion of vaccinated dogs in those communities where human experience higher rates of dog bites, increasing the risk of transmission.

2-9 Dynamic modeling of personal protection control strategies for vector-borne disease limits the role of diversity amplification
Jeffrey Demers, University of Maryland

Personal protection measures, such as bed nets and repellents, are important tools for the suppression of vector-borne diseases like malaria and Zika, and the ability of health agencies to distribute protection and encourage its use plays an important role in the efficacy of community-wide disease management strategies. Recent modeling studies have shown that a counterintuitive diversity-driven amplification in community-wide disease levels can result from a population's partial adoption of personal protection measures, potentially to the detriment of disease management efforts. This finding, however, may overestimate the negative impact of partial personal protection as a result of implicit restrictive model assumptions regarding host compliance, access to, and longevity of protection measures. We establish a new modeling methodology for incorporating community-wide personal protection distribution programs in vector-borne disease systems which explicitly accounts for compliance, access, longevity, and control strategies by way of a flow between protected and unprotected populations. Our methodology yields large reductions in the severity and occurrence of amplification effects as compared to existing models, and previous methodologies with no obvious biological connections emerge as slow and rapid transition limits of our methodology. Our methodology applied to a simple SIR model provides mathematical evidence in support of the hypothesis that amplification severity is determined by a balance between vector diversion and consequent bite rate focusing on unprotected hosts versus the time wasted by vectors tracking down unbiteable protected hosts.

2-10 Cannibalism and disease transmission: just what the doctor ordered
Bret D. Elderd, Louisiana State University

Cannibalism, while quite prevalent in the natural world, is often viewed as detrimental to a cannibal's health, especially when they consume a pathogen-infected individual. The general idea being that by cannibalizing weak or sick individuals, the chance of coming into contact with a pathogen and subsequently becoming infected with that pathogen increases. Using a series of experiments and mechanistic models, we demonstrate that cannibalism decreases disease transmission during an outbreak and, therefore, may not be as deleterious as once thought. It may even be advantageous.

2-11 Eco-epidemiological consequences of breastfeeding and vaccination disparities in the United States
Romain Garnier, Georgetown University

Breastfeeding is key to the present and future health of newborns, in high- and low-income settings alike. For instance, access to breast milk has been shown to significantly reduce the risk of hospital admissions in newborns. In the United States, improving breast milk access is a public health priority but analyses of secular trends are largely lacking. Here, we seek to understand the spatio-temporal patterns of breastfeeding in the United States and characterize the interplay between breastfeeding and vaccination for childhood diseases such as rotavirus. Using data on breastfeeding and vaccination rates from the National Immunization Survey of the CDC, we first study associations between breastfeeding, socio-economic variables, and vaccination. We notably find that race and income strongly predict variation in breastfeeding. We then use these associations to parameterize a dynamical model to forecast the epidemiological consequences of the interacting processes of breastfeeding and vaccination. We particularly build this model to fit the epidemiology of rotavirus in children aged 0 to 1-year-old, and include the distinct protective effects of both breastfeeding and vaccination. We explore situations within the range of the variation observed between states in the United States. We show how public health measures differentially targeting populations based on socio-economic characteristics could result in improved eco-epidemiological outcomes at the population level.

2-12 Regulation of post-mating immune response in female *Drosophila melanogaster*
Kathleen E. Gordon, Cornell University

In *D. melanogaster* and many other species, female reproductive investment comes at a cost to immunity and resistance to infection. Within hours of mating, *D. melanogaster* females become more susceptible to bacterial infection. Previous studies showed that females were less resistant to bacterial infection at 2.5 and 26.5 hours after mating, but did not test whether a mated female would eventually recover virgin levels of immunity. We tested whether mated females could recover virgin levels of immunity when infected at 2, 4, 7, or 10 days after mating. We observed no recovery of immune capacity in mated females over time. We conclude that mating has a permanent suppressive effect on the female immune system. Knowing that females mate multiply, we tested whether a second mating further affected immune performance. We hypothesized that females who mated twice might become more susceptible to infection than females mated once. Instead, we found that females mated either once or twice before infection survived at equal proportions and both significantly lower than virgin females. This indicates that effects of a single mating are sufficient to suppress the immune response and a second mating does not compound the effect. During mating, the male transfers seminal fluid proteins, like Sex Peptide, that change female physiology and behavior. Sex Peptide induces the female to produce Juvenile Hormone (JH), which promotes egg development. We and others have previously shown that JH is immunosuppressive and decreases resistance to bacterial infection. We thus hypothesize that JH signaling might control resource allocation between reproduction and immunity. Future experiments will seek to understand whether JH titers in mated and virgin females correlate with our understanding of the dynamics of the post-mating immune response and whether limiting investment in reproduction can improve immune capacity.

2-13 An analysis of the role of virulence on infectiousness and behavior trade-offs and transmission potential for influenza
Andreas Handel, College of Public Health, University of Georgia

While most communicable infectious diseases require a certain level of virulence to induce symptoms that support transmission, too much virulence can cause a reduction in host activity and thus transmission potential. There is very little data regarding the potential impact of different levels of virulence on host symptoms, behavior, and overall transmission potential in human diseases. To study this question, we collected data on symptoms and activity of 326 influenza patients at a university health center during the 2016/2017 influenza season. We classified symptoms as infectiousness-related or morbidity-related, and calculated two corresponding scores. The scores were used to explore the relationship between infectiousness, morbidity, and

host behavior, quantified as activity levels. We found a strong decrease in activity level with increasing morbidity score. There was no consistent pattern between activity level and infectiousness score. We also found a positive correlation between the morbidity and infectiousness score. Our results provide empirical evidence that for influenza, increasing virulence leads to increased infectiousness and altered host behavior with reduced activity and thus forms a trade-off which determines overall transmission potential.

2-14 Pathogen Evolution when Transmission and Virulence are Stochastic
Pooya Aavani, Texas Tech University

Evolutionary processes are inherently stochastic, since we can never know with certainty exactly how many descendants an individual will leave, or what the phenotypes of those descendants will be. Despite this, models of pathogen evolution have nearly all been deterministic, treating values such as transmission and virulence as parameters that can be known ahead of time.

We present a broadly applicable analytic approach for modeling pathogen evolution in which vital parameters such as transmission and virulence are treated as random variables, rather than as fixed values. Starting from a general stochastic model of evolution, we derive specific equations for the evolution of transmission and virulence. We show that adding stochasticity introduces new directional components to pathogen evolution. In particular, two kinds of covariation between traits emerge as important: covariance across the population (what is usually measured), and covariance between random variables within an individual. We show that these different kinds of trait covariation can be of opposite sign and contribute to evolution in very different ways. In particular, probability covariation between random variables within an individual is sometimes a better way to capture evolutionarily important tradeoffs than is covariation across a population.

2-15 Predicting Ebola virus disease risk and the role of African bat birthing
Reed C. Hranac, Hopkirk Research Institute, Massey University, New Zealand

Ebola virus disease (EVD) presents a threat to public health throughout equatorial Africa. Despite numerous 'spillover' events into humans and apes, the reservoirs and mechanism of spillover are poorly understood. Evidence suggests fruit bats play a role in both instances, yet data remain sparse and bats exhibit a wide range of life history traits. Here we pool sparse data and use a mechanistic approach to examine how birthing cycles of African fruit bats, molossid bats, and non-molossid microbats inform the spatio-temporal occurrence of EVD spillover. We use ensemble niche models to predict spatio-temporally varying bat birthing and model outbreaks as spatio-temporal Poisson point processes. We predict three distinct annual birthing patterns among African bats along a latitudinal gradient. Of the EVD spillover models tested, the best by quasi-Akaike information criterion (qAIC) and by out of sample prediction included African fruit bat-related terms. Temporal bat birthing terms fit in the best models for both human and animal outbreaks were consistent with hypothesized viral dynamics in bat populations, but purely spatial models also performed well. Our best model predicted risk of EVD spillover at locations of the 2018 EVD outbreaks in the Democratic Republic of the Congo was within the top 12-35% and 0.1% of all cells analyzed. Results suggest that sparse data can be leveraged to help understand complex systems.

2-16 Consequences of a changing resource landscape: bat nutritional health as a driver of excretion and spillover of Hendra virus
Maureen Kessler, Montana State University

In Australia, flying foxes (*Pteropus* spp. bats) are important pollinators and seed-dispersers in native forests. They are also the reservoir of Hendra virus, a lethal zoonosis transmitted from bats to horses, and subsequently, from horses to humans. Flying fox food resources are changing in complex ways, driven by deforestation that removes native habitat and introduced plantings that supplement alternative food sources. Flying foxes increasingly roost and forage in urban and agricultural landscapes, but changes in diet remain largely

unexplored, despite the potential to profoundly impact Hendra virus spillover through nutritionally and behaviorally- mediated changes in immunity and foraging behavior. Using a combination of repeat roost- and individual-level sampling and GPS tracking of captured flying foxes, we evaluated differences in foraging behavior and health across roosts in eastern Australia. We tested how foraging behaviors, urinary biomarkers, and body condition vary with diet using land-use data within each foraging radius as a proxy for flying fox food resources. Preliminary results demonstrate substantial variation in foraging behavior in native forest compared to agricultural landscapes, and patterns of urinary biomarkers and body condition are roost-specific. Future analyses will incorporate bat diet generated from fecal DNA metabarcoding and microscopy matched with Hendra virus excretion to test whether diet composition associates with the timing, magnitude, or duration of Hendra virus excretion pulses from flying foxes. Understanding the foraging ecology and diet of flying foxes is critical to understanding the role that changing resource landscapes may play in viral excretion and spillover of Hendra virus from flying foxes.

2-17 Compensating for pathogen-induced losses: colony-level disease resilience in ants
Megan A. M. Kutzer, IST Austria

Immune defense is comprised of resistance and tolerance, two contrasting strategies that can improve host survival and fitness. A fascinating aspect of these strategies is that they lead to different coevolutionary trajectories and so have different consequences for epidemiology and pathogen virulence evolution. Despite the obvious advantages of using a eusocial insect model system to investigate how societies use collective defense mechanisms, host tolerance has been understudied in colonial systems. Most work focuses on how these societies use resistance behaviors to reduce pathogen load through nest hygiene and mutual sanitary care. However, under specific conditions, tolerance could represent an alternative colony level defense mechanism. We predict that a tolerant colony will survive a disease outbreak by buffering the effect of pathogen-induced losses. Moreover, the capacity of a colony to return to its original strength (*i.e.* resilience) may be highly caste-specific if queens are more difficult to replace than workers. To test if resilience is affected by pathogen dose and the caste of infected colony members, we performed a series of longitudinal studies using the ant, *Cardiocondyla obscurior*, and the obligate killing fungal pathogen, *Metarhizium robertsii*. Here, we find that colonies show resilience, particularly when pathogen burden is below a critical value and a single caste is infected. We also find that colonies can shift to alternative strategies to guarantee colony reproduction and colony fitness after pathogen exposure.

2-18 Host phenology and parasite transmission
Hannelore Macdonald, University of Pennsylvania

The timing of biological phenomena, or phenology, is a fundamental component of all ecological interactions. Differences in the timing of activity of interacting species dictates changes in their contact rates and corresponding ecological dynamics. These interactions are important for the fitness of one or both interacting species. Interactions among species and species life stages
are also essential for disease transmission. Phenology is a recognized driver of transmission in disease ecology due to the structure it imposes on contacts between hosts over time, yet the impact of host phenology on disease transmission has not been formally evaluated. While it is evident that phenology can affect disease systems, it is less obvious how the exact nature of the differential phenology of hosts affects thresholds for parasite persistence. To address this question theoretically, we have formulated a mathematical model with explicit functions for phenology to investigate the impact of a range of phenological scenarios on transmission dynamics. Here we present a model of the Lyme disease system to illustrate the workings and flexibility of this framework and to provide insight into how differential host phenology affects thresholds for pathogen persistence. We show that this system is most sensitive to the relative timing between the emergence start time of the two tick life stages important for transmission. We also show that the rate that both tick life stages emerge alters transmission efficiency. Our approach provides a straightforward framework for predicting the long-term transmission consequences of differential phenology.

2-19 Zoonotic emergence and control in the era of rising human mobility
Christian Mason, University of California, Los Angeles

From the origins of HIV to the West African Ebola epidemic, recent literature has posed rising human mobility as a key factor underlying the accelerating pace of zoonotic pathogen emergence. Spillover from wildlife often occurs in small settlements far from cities, and historically many outbreaks have been restricted to these rural settings. Movement of infected people to more populated areas will determine the risk of generalized epidemics. So there is much concern about the implications of increased mobility, improved infrastructure, and expanded road networks for emergence risks. Yet despite the vivid and important case studies, there has not yet been a systematic exploration of this problem. We present a general stochastic modeling framework to examine transmission dynamics on a hierarchical network of patches, representing spillover into villages and subsequent movement to towns and cities. Here we analyze the influence of per capita movement rates and increasing connectivity on outbreak dynamics, and explore the interaction with pathogen life history characteristics including infectious period duration and density dependence of transmission. Finally, using our model we assess the efficacy of various approaches to outbreak surveillance and control, providing guidance to public health policy in resource-constrained settings.

2-20 Manipulating vector transmission reveals local processes in bacterial communities of bats
Clifton D. McKee, Colorado State University; Division of Vector-Borne Diseases, Centers for Disease Control and Prevention
For many vector-borne infections in wildlife, a biological vector has not been experimentally verified. Such knowledge is valuable for understanding the ecology of these infections because diversity in infecting communities is maintained within and among hosts through dispersal by vectors. Manipulation of vector populations provides a unique opportunity to test the importance of vectors in infection cycles while also observing changes in pathogen community diversity and species interactions in the absence of dispersal. Using a captive colony of fruit bats in Ghana, we provide experimental evidence that bat flies (Nycteribiidae) are vectors of *Bartonella* bacteria. Simultaneously, we observe changes in the *Bartonella* community over time that are attributable to ecological drift and potentially selection through interspecies competition mediated by host immunity. This work validates long-standing hypotheses about the ecology of bat-associated *Bartonella* and highlights the important mechanisms that maintain diversity in infectious communities across scales, both within and among hosts.

2-21 Social host interactions modify pathogen success in multiple infections
Barbara Milutinović, Institute of Science and Technology Austria

Multiple infections will affect disease outcome and transmission success, yet studies on these important evolutionary traits are still 1) largely limited to theoretical research and 2) neglect that many species live in groups, some with complex interactions that specifically target pathogens. Social insects evolved colony-level disease protection (*social immunity*) characterized by joint behavioral actions of society members that benefit the colony as a whole. In order to transmit successfully, pathogens co-infecting social hosts have to possess strategies that allow them to overcome not only other competitors and individual immune systems, but also the society-level defenses. We explore the effects of social immunity on competitive success and prevalence of fungal pathogens in multiple infections, using Argentine ants and *Metarhizium* fungi. We find that social immunity reduces sporulation success of all genotypes, but shifts relative success in production of transmission stages between species. Hence, similar to the physiological immune systems of individual organisms that can change the relative prevalence of different pathogen genotypes in their bodies (immune-mediated competition), we here show that host behavior that directly affects pathogens can have similar effects at the colony level and could significantly affect epidemiology and evolution of virulence in this system.

2-22 Multi-Host Infection Dynamics in Plant-Pollinator Networks
Chris Myers, Cornell University

The dynamics of multi-host, multi-vector infection in ecosystems are complicated by many factors. Plant-pollinator systems offer a case in point: different species of pollinators visit plants with varying degrees of specialization, the floral makeup of a community changes substantially over the course of a growing season, and the transmission of pollinator parasites among different host species can occur through the deposition and ingestion of contaminated fecal matter on shared flowers. To characterize this sort of infection dynamics, we are analyzing an extensive set of field data we have collected on plant-pollinator interaction networks, along with parasite screens in bees and on flowers, at three old-field wildflower sites. Simple models of transmission dynamics among bees and flowers based on the observed interactions are able to explain only partially the observed prevalence of parasites. We are analyzing and modeling these data to identify possible superspreaders, hotspots, and other heterogeneities in the bee and flower communities, features of interaction networks that are predictive of parasite transmission patterns, and the role of bee and flower traits in shaping these infection dynamics.

2-23 Chagas disease eco-epidemiology: vector host-feeding patterns suggest risk of Chagas disease on the Caribbean island of Trinidad
Jennifer K. Peterson, Princeton University

Chagas disease, (etiological agent *Trypanosoma cruzi*), is not recognized as an epidemiological risk in the Caribbean, due in part to a belief that the triatomine bug vectors in the region do not feed on humans. Lending evidence to the contrary, three studies on the Caribbean island of Trinidad found *T. cruzi*-infected triatomine bugs and *T.* cruzi-seropositive humans with clinical features of Chagas disease. However, there have been no reports of direct contact between humans and triatomine bugs on the island, begging the question, are the bugs feeding on humans? To answer this question and gain a better understanding of the epidemiological risk of Chagas disease in Trinidad, we analyzed blood meals from triatomine bugs collected near human homes from five sites in northern and central Trinidad. For each bug, we diagnosed *T. cruzi* infection, and sequenced its DNA to determine the last host species from which it fed. Out of 55 bugs (54 *Panstrongylus geniculatus* and 1 *Rhodnius pictipes*), 46 (83.6%) were infected with *T. cruzi*. DNA sequencing yielded conclusive host identification for 53 (96.4%) of the 55 bugs. The most common hosts were humans (30 bugs; 56.6%), followed by chickens (10 bugs; 18.9%), sylvatic mammals (9 bugs; 17.0%), and sylvatic birds (4 bugs; 7.5%). Of the 30 bugs that fed on humans, 26 (86.7%) were infected with *T. cruzi.* At least one bug from each of the five collection sites was infected with *T. cruzi*, and at least one bug from each site had taken a human blood meal. *T. cruzi*-infected bugs with human blood meals were found at three of the sites. Ecologically, our findings suggest that in Trinidad, the triatomine bug species *P. geniculatus* feeds on a range of taxa across sylvatic and domestic habitats, which is a common characteristic of epidemiologically relevant *T. cruzi* vector species. Indeed, *P. geniculatus* is a competent vector of *T. cruzi,* and has been implicated in Chagas disease transmission in regions recognized as Chagas-endemic. Epidemiologically, our results suggest that humans are likely to be involved in a vector-borne *T. cruzi* transmission cycle in Trinidad, and that Chagas disease may be a higher epidemiological risk in Trinidad than previously believed.

2-24 Interactions and pathogen transmission between carnivores at the domestic animal and wildlife interface in the Betampona Natural Reserve, Madagascar
Fidisoa Rasambainarivo, Princeton University

Introduced animal species are exerting significant pressure on native animals through different mechanisms, such as predation or competition. This increase in native-exotic animal interactions also presents potential for “pathogen pollution,” the introduction of a pathogen into a new geographic area. We studied the patterns of interactions and assess the risks of disease transmission between introduced and endemic animals in the Betampona natural reserve (BNR) ecosystem, a

lowland tropical forest of eastern Madagascar. Using camera traps, I described the spatio-temporal interactions between carnivore species, and monitored land-use sharing between domestic and endemic wildlife in this unique ecosystem. Secondly, I used serological analyses to estimate the prevalence and identify risk factors for exposure to selected pathogens in introduced and endemic animal species within the BNR. Identifying domestic animal pathogens that have spilled over to wildlife or others that may potentially threaten endangered populations in the wild is a critical step in order to conduct targeted surveillance and better monitoring of animal diseases in the area. Thirdly, using microbial genetics, I investigated the structure of the transmission network for environmentally transmitted microbial agents to identify species or individuals that may act as "super-spreaders". Identifying "key species or individuals" associated with the transmission of these pathogens will facilitate the allocation of limited resources to assess and limit the impact of these diseases on endangered and endemic species. Collectively, our results suggest that the introduction of a pathogen in this community underline the importance of animal health management and disease surveillance.

2-25 Nestling vaccination as a control for enzootic West Nile virus transmission
Suzanne Robertson, Virginia Commonwealth University

West Nile virus (WNV), a vector-borne disease spread primarily between avian hosts and mosquito vectors, is a major public health concern in the United States. While seasonal WNV outbreaks have been widely observed to be associated with the end of the avian nesting season, the ecological mechanisms responsible for this synchronicity are not well understood. Since newly hatched birds, or nestlings, have less feather coverage and fewer defense mechanisms than older birds, they may receive bites from mosquitoes at an increased rate. We use a mathematical model incorporating avian (host) stage-structure and stage-specific mosquito (vector) biting rates to investigate the connection between properties of avian nesting and enzootic WNV transmission, and the implications for public health interventions. In the United States, the primary methods used to control WNV are aimed at reducing the vector population. We explore the viability of a novel control, vaccination of nestling birds. We determine when vaccination is recommended in addition to vector control, and how these results depend on budget, control efficacy, and vector biting rates on nestling birds.

2-26 Ilegal mining and malaria: controlling the emergence of drug resistance in Colombia
Mauricio Santos-Vega, Universidad de Los Andes, Bogotá, Colombia

Despite the progress in malaria control evidenced in south america in recent decades, these mosquito-borne diseases remain as the cause of thousands of coases in Venezuela, Peru, Brazil and Colombia. This reemergence has been attributed to several factors such as the reduction in the funding for eradication and control measures environmental change affecting the temporal and spatial pattern of the disease, political conflicts in endemic zones, the evidence of submicroscopic or asymptomatic infections and the increase in gold mining activities in low transmission regions. Although, climate has been postulated as a driving force for the changing (expanding) epidemiology of Malaria in Colombia. Here we combine, a novel dataset on illegal mining activity using machine learning algorithms and satellite imagery features with a process-based dynamical models for the transmission of the disease confronted to a decades of monthly surveillance malaria data, to address the role of gold mining in the increasing trend in *P. falciparum* cases malaria in Colombia. We show a strong and significant effect of interannual changes in the illegal gold mining on malaria incidence. Simulations of the mining-driven transmission model with the MLE (Maximum Likelihood Estimates) of the parameters accurately capture observed disease incidence over the las decade. These results underscore the important role of illegal gold mining in Colombia in the re-emergence of malaria in Colombia, this increase in malaria prevalence could potentially lead to ideal conditions for the selection of drug resistance mutations which in conjunction with massive migration due to mining could allow for the dissemination of parasite populations carrying resistance genotype.

2-27 Parasite spread in experimental metapopulation: A role for super-spreaders?
Christina Pernice Tadiri, McGill University

Host competence, an individual's propensity to transmit infection, is one of the most important aspects of individual heterogeneity that may impact host-parasite dynamics in a metapopulation, yet it is still underexplored experimentally. This study used data from experimental epidemics of the ectoparasite *Gyrodactylus turnbulli* in metapopulations of guppies to identify the more competent hosts and determine the degree to which they influence epidemic dynamics. We characterized fish as having either intense infections, prolonged infections, both or neither to explore how resistance and tolerance relate to degree of host competence. Fish with both intense and prolonged infections were larger than fish with neither, indicating that an individual's size may influence its tolerance. Fish with prolonged infections had more contacts and were responsible for more transmission than other fish, regardless of infection intensity. We found a positive association between the number of fish with prolonged infections and parasite metapopulation persistence, and a positive interactive effect of the number of fish with both prolonged and intense infections on metapopulation parasite load, indicating tolerant fish contribute the most to metapopulation loads. These findings highlight the importance of disentangling different facets of host competence, particularly the underrecognized mechanism of tolerance in disease transmission.

2-28 A mechanistic, stigmergy model of a territory formation in an asocial predator: consequences for pathogen transmission
Lauren A. White, [1]National Socio-Environmental Synthesis Center (SESYNC)

Mechanistic portrayals of how animals form and maintain territories remain rare, and as a discipline, collective movement ecology has tended to focus on synergistic (e.g., migration, shoaling) rather than agonistic or territorial interactions. Here we ask how different mechanisms of territory formation and maintenance (e.g., land tenure vs. resource dispersion) might contribute to disease dynamics in an asocial territorial predator. We develop a mechanistic individual-based model for an asocial, territorial predator, where stigmergy—the deposition of signals (e.g., scent marking, scraping) dictates local movement choices and long-term territory formation. Our objectives are to explore how these asynchronous, non-local cues contributes to encounter rates and pathogen spread in response to: (1) changes in the permanence of the environmental cue; (2) seasonal changes in aversion/attraction to cue of conspecifics (e.g., mating season); and (3) heterogeneous resources (in the form of kill sites) where predators may exhibit social tolerance. We theorize that seasonal "switching" of cues from aversive to attractive during mating along with social tolerance at kill sites will be critical for the persistence of directly transmitted pathogens. We further hypothesize that the ratio of indirect pathogen survival in the environment to the duration of the signaling cue will be critical for indirect pathogen transmission dynamics.

2-29 Feeding wildlife in urban parks: effects on behavior, species interactions, and infection
Cali A. Wilson, University of Georgia

Feeding wildlife is a popular way for people to engage with, and learn about, wild animals. Food subsidies can have profound impacts on animal health, behavior, and species interactions, although these impacts are not always beneficial, especially when they alter disease transmission. I will investigate how host-parasite dynamics are mediated by variation in individual behavior (e.g., aggressiveness) and community composition (e.g., rate of interspecific contact), along a gradient of human-provided food. I will explore these dynamics in urban populations of American white ibis (*Eudocimus albus*) in South Florida that are habituated to taking human-provided food and host a variety of pathogens. Within species, I will test whether greater supplemental feeding at parks will increase ibis flock sizes and contact rates and alter the behavior of ibis. At the community level, I will test whether sites with greater supplemental feeding have a higher proportion of non-native and domesticated species and more interspecific contact. Lastly, I will build two mathematical models incorporating data collected in the field studies to explore how *i*) individual variation in behavior and *ii*) community

composition affect disease dynamics. These models can be used to understand transmission dynamics occurring in other systems with heterogeneity in host behavior and competency to better predict disease spread and outbreaks.

2-30 Dynamics of bed bug infestations and control under disclosure policies
Xiaoyue (Sherrie) Xie, University of Pennsylvania

Bed bugs have re-emerged in the United States and worldwide over recent decades, presenting a major challenge to both public health practitioners and housing authorities. A number of municipalities have proposed or initiated policies to stem the bed bug epidemic, but little guidance is available to evaluate these. One contentious policy is $disclosure$, whereby landlords are obligated to notify potential tenants of current or prior bed bug infestations. Aimed to protect tenants from leasing an infested rental unit, disclosure also creates a kind of quarantine, partially and temporarily removing infested units from the market. Here we develop a mathematical model for the spread of bed bugs in a generalized rental market, calibrate it to parameters of bed bug dispersion and housing turnover, and use it to evaluate the costs and benefits of disclosure policies to landlords. We find disclosure to be an effective control policy to curb infestation prevalence. Over the short term (within five years), disclosure policies result in modest increases in cost to landlords, while over the long term, reductions of infestation prevalence, lead, on average, to savings. These results are insensitive to different assumptions regarding the prevalence of infestation, rate of introduction of bed bugs from other municipalities, and the strength of the quarantine effect created by disclosure.

ENVIRONMENTAL DRIVERS OF INFECTIOUS DISEASE DYNAMICS (Posters 2-31 → 2-65)

2-31 *Piscirickettsia salmonis* transmission in Atlantic salmon in Chile
Amy Kinsley, University of Minnesota

Piscirickettsia salmonis, the etiological agent of Salmon Rickettsial Septicemia (SRS), is responsible for an overwhelmingly large proportion (50-97%) of disease-related mortality in the Chilean salmon industry. Current control strategies for SRS include a combination of vaccination and antibiotics, each with variable efficacy, leading to the use of large amounts of antibiotics. In this study, we developed a within-farm transmission model to evaluate the efficacy of management practices aimed at reducing the within-farm incidence of SRS. Specifically, we developed a vaccinated-susceptible-infectious-recovered model to assess the impact of early detection and treatment of SRS in Chile. Using surveillance data from 2011-2017, we estimated pre-antibiotic treatment transmission coefficients for 737 Atlantic salmon production cycles.

2-32 Investigation of spatial patterns of human-tick exposure in California through the use of a large-scale citizen science program
Tanner Porter, Northern Arizona University

In the United States, tick-borne diseases (TBD) have traditionally been associated with the northeastern US, where the majority of TBD cases are reported. The west coast of the US, accounts for the minority of cases of TBD, however, active tick and pathogen surveillance in California has revealed sites that have similar tick densities and TBD infection prevalence to the northeastern US. TBDs are the result of spillover of vector borne pathogens from sylvatic cycles into the human population through the bite of an infected tick. Human-tick interactions are rarely considered in this system but impact the distribution and prevalence of reported TBD cases. We utilized GPS coordinates of reported human-tick interactions collected through a citizen science based passive surveillance program to characterize and identify patterns in human exposure to ticks. Variables that were assessed included human population density, general weather patterns, and land cover. Overall, this analysis identifies patterns associated with human-tick interactions in California. These results can be used to

further develop disease risk models and inform the public or public outreach groups on areas with increased risk of human-tick interactions thus TBDs.

2-33 Modeling joint effects of infectious disease and toxicant exposure in wildlife
Cecilia A. Sánchez, Odum School of Ecology, University of Georgia

Exposure to toxicants (e.g. pesticides, heavy metals, pharmaceuticals) can have lethal and sub-lethal effects for wildlife including reduced fecundity, impaired movement, and decreased body condition. Toxicant exposure could also increase susceptibility to infectious diseases, intensify pathogen virulence, or change host contact patterns. I outline a mathematical model that provides a framework to understand the consequences for a wildlife population facing both pathogen infection and exposure to toxicants. I present preliminary model results that explore how wildlife–infection dynamics respond to the proportion of toxic habitat and the costs associated with toxicant exposure. Specifically, I explore three outcomes of interest: population size, infection prevalence, and density of infected animals. As an example of a relevant wildlife–toxicant system, I provide metals concentrations from Australian flying foxes, species that can transmit viruses to animals and humans. Flying foxes are increasingly settling in urban environments due to natural habitat degradation and the availability of fruiting and flowering resources in urban areas. However, they might be exposed to toxicants from human activities in these sites. Mass spectrometry analysis of flying fox fur showed that concentrations of 12 metals varied across 8 sampling locations, which could have implications for differential susceptibility and transmission of infectious agents.

2-34 The effects of daily temperature fluctuations and microclimate temperature variation on mosquito life-history traits and pathogen transmission
Annika Avery, University of California, Berkeley

An increasingly critical question in disease ecology is how climate change will affect infectious disease transmission. These dynamics have been especially well-studied in vector-borne pathogens as it is well known that temperature affects the different life-history traits of both the mosquito and the pathogen. Therefore, there is a relationship between temperature and a mosquito's ability to transmit vector-borne diseases. While there is a large body of literature covering how constant mean temperature affects different life-history traits in mosquitoes and pathogens, there exists limited literature on both daily temperature fluctuations and microclimate temperature variations. Here, we review current empirical and theoretical work that incorporates temporal (daily temperature fluctuation) and spatial (microclimate) variation in temperature and highlight important insights from these works to suggest the necessary next steps to better predict the effects of climate on mosquito-borne pathogen transmission. In empirical studies, daily temperature fluctuations have been found to affect life history traits of the pathogen and mosquito differently than constant mean temperatures do and theoretical studies show that incorporating these fluctuations better predicts disease dynamics. Studies on microclimate variation found varying temperature dynamics between microclimates to impact mosquito life-history traits, and furthermore, disease transmission. In an effort to collect and organize the existing literature on daily temperature fluctuations and microclimate variation and their effects on mosquito and pathogen life-history traits, we conducted an extensive literature search. This review can be used as a guide to understand previously conducted research, as well as help plan future research on daily temperature fluctuations and microclimate temperature variation.

2-35 Climate change and directly-transmitted infections: the implications for RSV
Rachel E. Baker, Princeton University

Understanding how climate change will alter the burden of infectious diseases has clear public health implications. Despite valuable advances in predicting the effect of climate change on vector-borne diseases, the effect on directly-transmitted infections remains understudied. Here we develop a novel methodology to disentangle the climate drivers of these types of infections from other seasonal drivers which allows us to

consider the implications of climate change for future transmission. We apply the method to investigate the climate drivers of respiratory syncytial virus (RSV), a major cause of severe lower respiratory tract infections in infants. Leveraging hospitalization data from both the U.S.A and Mexico, we find evidence of a nonlinear effect of absolute humidity and precipitation on RSV transmission. Our predictions can help explain present variations in timing of onset in RSV across Northern America as well as the types of dynamic pattern observed. Using CMIP5 projections for future climate coupled with our mechanistic disease model, we predict climate change will lead to a northward shift in the patterns of RSV presently observed within the US. In Mexico, we find the likelihood of severe outbreaks of RSV hinge on projections for extreme precipitation.

2-36 Persistent effects of management history on honeybee viriomes
Lewis J. Bartlett, Emory University & University of Exeter

Infectious disease is now recognised as a major threat to both managed and wild pollinators. A key question is how different management regimes determine honeybee disease epidemiology. Here we examined the effect of management history by characterising the viriome of three honeybee populations that had previously different management histories (feral, low intensity management, high intensity "industrial" management) after one year in a standardised common garden. Colonies from a feral population origin showed qualitatively different viral abundance patterns to honeybees from the two managed population origins. Amongst the managed honeybees, colonies from the industrially managed background exhibited higher viral abundances for all viruses than those from lightly managed backgrounds. Interestingly, the difference between the industrially- and lightly managed origins was on the same scale as that between feral and managed honeybees. Our results show that not only does management have long lasting impacts on honeybee disease epidemiology, but moreover, the style of management is critical, suggesting that apicultural intensification could have major impacts on pollinator health. More broadly, our work shows that viriomes or viral burdens within migratory populations are not only a result of the current population ecology, but are also determined by the prior environments and ecologies experienced by those populations.

2-37 Host-parasite interaction recovers after experimental habitat fragmentation
Matthew Evans Bitters, University of Colorado, Boulder

Habitat fragmentation is a leading cause of biodiversity loss worldwide and commonly negatively impacts species at higher trophic levels and parasites. Parasites are increasingly recognized for their importance in maintaining ecosystem function, but few studies have looked at fragmentation's long-term effect on them. Existing studies show that parasites have varied responses to fragmentation and are largely dependent on the responses of their hosts. We asked how a host-parasite interaction involving a skink definitive host (*Lampropholis guichenoti*), amphipod intermediate host (*Arcitalitrus sylvaticus*), and parasitic nematode (*Hedruris wogwogensis*) changed in the short- versus long-term after experimental forest fragmentation in the Wog Wog Habitat Fragmentation Experiment (Wog Wog) in southeastern Australia.

Previously, we determined that fragmentation drove declines in nematode infection rates in remnant fragments and the nonnative pine plantation matrix, compared to undisturbed continuous forest, immediately following fragmentation. These reductions in infection were driven by changes in amphipod abundance, which were, in turn, driven by changes in the abiotic environment of fragments and the matrix. This disruption in the host-parasite relationship ameliorated over time as the matrix matured and amphipods repopulated all parts of the landscape. Necropsied amphipods and skinks sampled 23 years after fragmentation show reinfections of the nematode in remnant forest fragments. We conclude that the intermediate host is critical in maintaining and reestablishing host-parasite interactions that may have been previously disrupted. In addition, short-term responses after large scale disturbance events like habitat fragmentation may not predict how parasites that rely on trophic transmission will respond in the long-term.

2-38 Environmental and demographic drivers of *Leptospira* outbreaks in California sea lions
Benny Borremans, University of California, Los Angeles

The yearly influx of susceptibles in a population (through births) is a key driver of seasonal disease outbreaks in many wildlife species. Environment can have additional effects on outbreak size and seasonality by acting on host immunity, transmission rates, or survival. A key challenge in disease ecology has been to assess the relative importance of such intrinsic and extrinsic drivers of transmission.

California sea lions (*Zalophus californianus*) experience seasonal outbreaks of leptospirosis (caused by *Leptospira interrogans*) with significant interannual variation in intensity. This study aims to reveal the drivers behind outbreak size variation by estimating the relative contributions of environmental conditions and host demography.
Data consist of annual time series (1984-2012) of case counts, population size, and oceanographic variables. Additionally we reconstructed the age- and sex-specific susceptibility of the population through time using results from a long-term mark-resight study. To quantify the relative contributions of extrinsic vs. intrinsic drivers, we fitted generalized additive models.

We find that outbreak size is primarily driven by susceptibility in key juvenile animals, with additional contributions of sea surface temperature and coastal upwelling. Oceanographic processes such as upwelling of nutrient-rich water and El Niño events are known to influence prey availability and location, with potential bottom-up effects on sea lion movement and mixing, body condition and susceptibility to infection. These results provide rare empirical support for the existence of both intrinsic and extrinsic drivers of pathogen transmission, and highlight how climate change might affect disease outbreaks in wildlife populations.

2-39 The influence of multiple stressors of a fungicide and microsporidian parasite on bumble bee health
Austin C. Calhoun, Illinois State University

Pollination services provided by managed and wild bees are essential for agricultural and natural ecosystems. However, threats to pollinator health leading to population declines put these services in jeopardy. Several potential causes of declines have been suggested, including exposure to pathogens and agro-chemicals. Although individual effects are widely studied, interactions between pesticides and immunity may exacerbate the negative effects of individual exposures in environments where they co-occur. In bumble bees (*Bombus spp.*), a landscape analysis demonstrated a correlation between local use of the fungicide chlorothalonil and infection loads of the microsporidian pathogen *Nosema bombi* in declining species. This is suggestive of an interaction, but causation still needs to be established. By exposing microcolonies of *B. impatiens* in a fully reciprocal design to chlorothalonil and/or *Nosema*, we test if a sublethal dose of chlorothalonil influences *N. bombi* infection and exacerbates its negative effects. We predict that chlorothalonil will reduce immune function, leading to increased infection loads and transmission potential, with associated negative effects on health. This study will be the first to experimentally assess the combined stressors of *N. bombi* and chlorothalonil in bumble bees, and will provide information on how bumble bee health will be affected by variability in agro-chemical and pathogen environments.

2-40 St. Louis encephalitis virus activity is not associated with abundance of its main urban avian host, Eared Doves (*Zenaida auriculata*)
Adrian Diaz, Universidad Nacional de Córdoba, Argentina & Instituto de Investigaciones Biológicas y Tecnológicas

The St. Louis encephalitis virus (SLEV), a flavivirus endemic in the Americas, is maintained among multiple avian hosts and mosquitoes vector species. Our aim was to associate viral activity in mosquitoes with the per species abundance of potential avian hosts in Córdoba City, Argentina. We collected mosquitoes with CDC dry ice supplemented light traps. We taxonomically determined mosquitoes and grouped them into pools regarding: capture site, collection date, species, sex and female physiological state. Within areas of 500m radius around the

mosquito traps, we recorded species and abundance of all birds perched and heard. The most abundant mosquito collected was *Culex quinquefasciatus* (61.51%), the main urban vector of SLEV. In 24/100 pools we found at least one mosquito positive for SLEV. We examined the association between bird abundances and SLEV activity applying Generalized and Mixed Linear Models (GLMM). Independent variables were the abundances of House Sparrows (*Passer domesticus*), Spotted-winged Pigeon (*Patagioenas maculosa*) and Eared Dove (*Zenaida auriculata*), which correspond to 70% of overall the avifauna recorded at each site. We compared six models based on the Theory of Information with AICc metrics. The null model differed from the remaining models in approximately 5 AICc units. Hence, SLEV activity was not associated with bird abundances, not even with Eared Doves, the main urban amplifier for the virus. Predicting models of SLEV infection should include vectors abundances and their feeding patterns besides the abundance of potential hosts.

2-41 Does habitat quality 'dilute' disease risk instead of biodiversity? 'Habitat health' an alternate explanation for reduced pathogen prevalence in species-rich communities

Michelle L. Fearon, University of Michigan

Growing evidence suggests that host biodiversity is linked with reduced disease risk in many diverse host-pathogen systems. These findings are commonly explained as the "dilution effect", where species-rich communities have reduced disease risk due to reduced encounters with infected individuals or rates of transmission during species interactions. Here, we propose and test an alternative hypothesis to explain observed dilution effect patterns called "habitat health". The habitat health mechanism proposes that areas with higher habitat quality promote greater host biodiversity and provide higher quality resources to hosts, which may allow for improved resistance to infection and stronger immune function. Therefore, we hypothesize that bees from species-rich communities may be healthier and less susceptible than individuals from species-poor communities due to better resources from the surrounding habitat. We tested the habitat health mechanism in pollinator communities infected with three viruses along a habitat gradient, and compared virus prevalence in four pollinator host species. We found that pollinators had significantly reduced virus prevalence in communities with greater proportions of natural habitat nearby and pollinator biodiversity was positively correlated with surrounding natural habitat. These results support habitat health as an important, alternative mechanism to the dilution effect and suggests that further work will be critical to tease apart how habitat quality and host biodiversity interact to influence disease risk. A better understanding of these links between habitat, biodiversity, and infectious disease could lead to additional promising management strategies that will simultaneously preserve habitats, conserve species, and reduce disease risk among humans and wildlife.

2-42 How to make more from exposure data? An integrated machine learning pipeline to predict pathogen exposure

Nicholas M. Fountain-Jones, University of Minnesota

1. Predicting infectious disease dynamics is a central challenge in disease ecology. Models that can assess which individuals are most at risk of being exposed to a pathogen not only provide valuable insights into disease transmission and dynamics but can also guide management interventions. Constructing such models for wild animal populations, however, is particularly challenging; often only serological data is available on a subset of individuals and non-linear relationships between variables are common.

2. Here we provide a guide to the latest advances in statistical machine learning to construct pathogen-risk models that automatically incorporate complex non-linear relationships with minimal statistical assumptions from ecological data with missing values. Our approach compares multiple machine learning algorithms in a unified environment to find the model with the best predictive performance and uses game theory to better interpret results. We apply this framework on two major pathogens that infect African lions: canine distemper virus (CDV) and feline parvovirus.

3. Our modelling approach provided enhanced predictive performance compared to more traditional approaches, as well as new insights into disease risks in a wild population. We were able to efficiently capture and visualise strong non-linear patterns, as well as model complex interactions between variables in shaping exposure risk from CDV and feline parvovirus. For example, we found that lions were more likely to be exposed to CDV at a young age but only in low rainfall years.

4. When combined with our data calibration approach, our framework helped us to answer questions about risk of pathogen exposure which are difficult to address with previous methods. Our framework not only has the potential to aid in predicting disease risk in animal populations, but also can be used to build robust predictive models suitable for other ecological applications such as modelling species distribution or diversity patterns.

2-43 Exploring host and environmental drivers of population persistence following pathogen invasion
Alexander Grimaudo, Virginia Tech

Emerging infectious diseases have caused dramatic declines in wildlife populations, altered species communities, and changed ecosystem function. Understanding the mechanisms mediating host population declines and persistence following pathogen invasion can provide insight into the long-term coevolutionary dynamics between hosts and pathogens. Here, we investigate how characteristics of the host, environment, and their interaction facilitate population persistence. Utilizing a common garden experiment, we explore the mechanisms of persistence in little brown bats (*Myotis lucifugus*) impacted by white-nose syndrome (WNS). We hypothesize that characteristics of the host conducive to their survival (i.e. host resistance or tolerance) were positively selected for by disease-induced population declines, but that the strength of selection was environmentally mediated. Our data suggest that traits favorable to host survival have been positively selected for by WNS, but that environmental characteristics within hibernacula interact strongly with these traits to determine disease outcome. In the warmest and wettest site, mortality during the WNS epidemic was 100%, but in the persisting little brown bats used in this experiment, we observed only 20% mortality within the same site. However, mortality was significantly higher in this site compared to a cold and wet site, where mortality was <1%. Ultimately, our results show that the coevolutionary dynamics between hosts and pathogens following pathogen invasion can be dependent on the host's environment.

2-44 Resource Provisioning at Urban Gardens Influences Parasite Incidence in Bumblebees
Nicholas A. Ivers, University of Texas at Austin

One of the major factors believed to be driving global pollinator declines is the presence and prevalence of parasites and pathogens in wild populations of bees. Bee communities are known to be affected by a number of generalist pathogen groups, including: Neogregarines (*Apicystis sp.)*, Trypanosomatids (*Crithidia sp.*) , and Microsporidians (*Nosema sp.*). Transmission is believed to occur through indirect contact at floral heads where infected individuals deposit parasites while foraging on flowers which may later infect subsequently foraging bees. Thus, resource availability, especially floral and nesting resources, are hypothesized to have a critical impact on the transmission and overall incidence of parasites within the bee community; this is of particular interest in heterogeneous communities with limited or patchy resources. Resource provisioning may have a positive impact on parasite transmission if hosts become aggregated at the resource, but the opposite could be true if increased bee diversity 'dilutes' parasites and lowers transmission frequency. We surveyed bee and pathogen prevalence in 25 rigorously studied urban gardens in Central Califorina, to provide insight into how floral resource provisioning in these gardens impacts the bee and pathogen community across a gradient of local and regional land management practices. Specifically, we focus on the parasite community of a key pollinator species, *Bombus vosnesenskii*, and determine the relative importance of landscape composition, resource provisioning, and pollinator diversity and abundance on bee health. Infection prevalence varied greatly across the gardens, with a range from 0-70% of bees showing positive signs of infection.

2-45 Environmental reservoirs of a deadly amphibian pathogen
Tatum Katz, University of California, Santa Barbara

Most organisms avoid destroying the place in which they live. Even many diseases, which still harm their hosts, have evolved to decrease their virulence in order to maintain a host that is healthy enough to spread the disease. Unusually, Batrachochytrium dendrobatidis (Bd or chytrid), the chytrid fungus that causes chytridiomycosis, has the ability to decimate the place in which it lives without burning itself out. This pathogen can invade an amphibian population to cause mortality and often extirpation of the host species. Disease ecology theory predicts that density-dependent pathogens will die out when the host population falls below a density threshold, but before the host is driven extinct, making it remarkable that Bd is frequently associated with extirpations of host populations, and in some cases extinctions of host species. One hypothesis for how Bd is able to achieve this destruction is the presence of unknown environmental reservoirs and vectors. To gain a greater understanding of Bd outside of its amphibian hosts, we traveled to 25 sites across the state of California to sample insects, soil, water, and nematodes for the presence of Bd. This project is ongoing, however, results indicate that Bd may be using soil and nematodes as environmental reservoirs.

2-46 Emerging Red Disease of American eels in Chesapeake Bay: Etiology, epidemiology and impacts in the wild and aquaculture
Amanpreet K. Kohli, Virginia institute of Marine Science

American eels (*Anguilla rostrata*) are commercially, recreationally, and ecologically important to the Chesapeake Bay. Stock assessments indicate that eel populations are declining, with infectious diseases implicated as a cause. An eel distributor from Chesapeake Bay reported up to 20% disease-associated mortality in his holding system. Eel fishers indicate that this “red” disease, characterized by severe skin ulceration, has a patchy distribution in the wild.

Our preliminary findings suggest bacteria are a causative agent. However, little is known about the etiology, epidemiology, underlying environmental drivers of this emerging disease, or its significance to the fishery. Our research objectives and associated methodology are -
1) To identify the dominant microbial pathogens associated with red disease of eels using standard bacteriological methods and 16s rRNA sequencing.
2) To elucidate the environmental correlates of this disease in wild eels with bi-weekly sampling in the Rappahannock river. Statistical model will be used to identify correlations between temporal and spatial variability in environmental parameters and prevalence of red disease in wild.
3) To experimentally quantify the impacts of environmental stressors on disease expression by subjecting eels to laboratory challenges and tracking the development and progression of clinical signs and mortality.
There is an urgent need to better understand the role of red disease in the decline of wild populations and the impact it has on the eel fishery and emerging aquaculture industry. Our work will support effective disease mitigation and management of eel losses.

2-47 Interventions on the Planetary Health menu: examples, evidence, and evaluation
Kevin Lafferty, US Geological Survey at UC Santa Barbara

Environmental drivers of disease create the potential for intersections between conservation biology and human health. We tabulated suggested examples of win–win interventions that both reduce human infectious disease and improve ecosystem integrity using a systematic literature review and expert surveys. We found 48 proposed win–win interventions for reducing human infectious disease and improving ecosystem integrity (e.g., controlling invasive rats to reduce predation on endemic birds and reduce rat-borne disease risk for humans). We critically evaluated each intervention using a common set of criteria and eliminated 11 interventions that caused harm to people or conservation targets. We then compared the remaining interventions to find commonalities and identify gaps where new intervention options might await discovery,

and we developed a decision hierarchy to aid practitioners and policy makers in choosing interventions that meet their priorities and resource constraints. Despite a few gaps, the interventions that we found represented many human infectious diseases, regions, conservation threats, and intervention types (e.g., species management, vaccination campaign, etc.). However, most interventions were either hypothetical or supported by limited evidence, and thus most would be seen as too risky for many practitioners and policymakers. Organizations that can afford to implement potentially risky interventions via adaptive-management frameworks and academic researchers can help make these interventions more accessible by improving our knowledge of intervention feasibility and success, thereby reducing risk. And as new win-win interventions for human health and conservation are proposed, our decision-making hierarchy can be used to evaluate and choose amongst them.

2-48 Making soup out of urban greening

Miriam Maas, National Institute for Public Health and the Environment (RIVM)

Greening of cities is a popular concept to improve living conditions in cities. On a small scale, citizens are stimulated to replace tiles in gardens with plants and green roofs are implemented. On a larger scale, green corridors are designed within cities to enable wildlife to move into and within urban areas. In the Netherlands too, urban greening is stimulated, and the presence of a varied urban fauna is regarded as a positive result. Currently, the (presumptive) positive health aspects of greening are emphasized, e.g. cleaner air and mental wellbeing. The potential negative effects of zoonoses from wildlife in green areas are largely overlooked. However, we know that there are multiple animal species in Dutch cities that play a role in transmission of zoonoses, for example urban red foxes (transmission of *Echinococcus multilocularis*), ticks (various tick-borne pathogens) and rats (*Leptospira* spp.).

How urban wildlife communities are influenced by greening, and contribute to the risk of zoonotic diseases is still uncertain. For example, greening may enable rat populations to grow, but may also enable growth of predator populations such as the red fox. Both species carry zoonotic pathogens, and how the balance between these populations and their zoonoses influences ultimately the public health risk, is unknown yet. Several small and unrelated projects on the disease risk of individual animal species have been initiated. Our future aim is to be able to combine projects and collect data more coherently and to make "soup" out of all these different "ingredients of urban greening".

2-49 Phenological synchrony drives disease dynamics in host-parasite system

Travis McDevitt-Galles, University of Colorado, Boulder

A key challenge surrounding ongoing climate shifts is to identify how they alter species interactions, including those between hosts and parasites. Because transmission often occurs during critical time windows, shifts in the phenology of either taxa can alter the likelihood of interaction or the resulting pathology. We quantified how phenological synchrony between susceptible stages of an amphibian host (*Pseudacris regilla*) and infection by the pathogenic trematode (*Ribeiroia ondatrae*), determined infection prevalence, parasite load, and host pathology. By tracking hosts and parasites throughout development between low- and high-elevation regions (San Francisco Bay Area and the Southern Cascades [Mt. Lassen]), we found that when phenological synchrony was high (Bay Area), each established parasite incurred a 33% higher probability of causing severe limb malformations relative to areas with less synchrony (Mt. Lassen). As a result, hosts in the Bay Area had up to a 50% higher risk of pathology even while controlling for mean infection load. Our results indicate that host-parasite interactions and the resulting pathology were the joint product of infection load and phenological synchrony, highlighting the sensitivity of disease outcomes to forecasted shifts in climate.

2-50 Determining the environmental drivers of Japanese encephalitis virus transmission and estimating the size of the population at risk

Sean Moore, University of Notre Dame

Japanese encephalitis virus (JEV) is a major cause of neurological disability in Asia and causes an estimated 68,000 severe encephalitis cases and 13,000 deaths annually. Cases and deaths are significantly underreported and the true burden of the disease is not well understood. Targeting vaccination campaigns to the most vulnerable populations requires a better understanding of both the magnitude and spatial distribution of the disease. We determined the transmission intensity within different JE-endemic countries by estimating the force of infection from existing studies of age-specific seroprevalence or incidence. Because JEV is not transmissible from humans to mosquitoes, a zoonotic reservoir is a necessary component of the transmission cycle and JE is believed to be largely a rural disease. To identify the areas suitable for sustained JEV transmission and the size of the population living in at-risk areas we conducted a spatial analysis of the risk factors associated with JEV. First, we demarcated potential JEV-endemic areas using large-scale spatiotemporal datasets related to suitable climate conditions for the vector species, suitable habitat conditions (rice cultivation or nearby wetlands), and the presence of potential zoonotic hosts (domestic pigs or fowl). JE occurrence was then estimated by fitting an ensemble of Poisson point process boosted regression tree models, which were validated using seroprevalence studies (in both humans and domestic animals) from several different countries. JE occurrence estimates were used to calculate the size of the population-at-risk throughout Asia and combined with force of infection estimates in each country to estimate the annual JE burden.

2-51 The cost of travel: high dispersal limits local adaptation in host-parasite systems

Wynne Moss, University of Colorado at Boulder

Interactions between hosts and parasites exert strong selective pressures on both species, often resulting in higher parasite performance on sympatric relative to allopatric host populations (local adaptation). However, in some trematodes, long-distance dispersal within definitive hosts may increase gene flow to such high rates that local adaptation is not possible. We investigated how two trematode species (*Manodistomum syntomentera* and *Ribeiroia ondatrae*) differ in genetic structure and degree of local adaptation to their amphibian intermediate hosts. The definitive hosts for *R. ondatrae* are birds, which have the potential to disperse parasites over large geographic ranges, whereas *M. syntomentera* is dispersed by water-associated snakes with lower dispersal capability. We conducted cross infection experiments, in which chorus frogs (*Pseudacris regilla*) from one of six populations were crossed with cercariae from one of two locations. Using generalized linear mixed models, we tested how the distance between where hosts and parasites were collected impacted infection success. *R. ondatrae* cercariae were equally successful in infecting hosts, regardless of their location, while *M. syntomentera* performed better on hosts from their own local population, as demonstrated by a significant interaction between parasite species and geographic distance ($\beta = 0.128 \pm 0.046$; $P < 0.01$). The two source populations of *M. syntomentera* differed genetically (10% base pair dissimilarity), but *R. ondatrae* populations did not (< 0.5%). We therefore demonstrate that parasites with high dispersal capabilities may pay a cost in terms of local adaptation, with genetic swamping precluding the ability to adapt to certain host populations.

2-52 Disease dynamics of wild butterfly populations utilizing native and novel host-plant species

Nadya D. Muchoney, University of Nevada, Reno

Incorporation of novel host-plants can result in profound changes for insect herbivores, impacting both physiological processes and interspecific interactions. Investigating the influence of novel host-plant use on interactions with natural enemies may provide insight into the costs and benefits of dietary expansion. Here, we evaluated the hypothesis that improved defense against infectious diseases may promote the incorporation of novel host-plants into herbivore diets. To address this hypothesis, we examined how use of a recently incorporated host-plant, *Plantago lanceolata*, impacted immune performance, chemical defense, and interactions with an infectious pathogen in wild populations of a North American herbivore: the Baltimore

checkerspot butterfly, *Euphydryas phaeton*. The focal pathogen, Junonia coenia densovirus (JcDNV), was found to be widespread in *E. phaeton* populations, but more prevalent in populations utilizing the novel host-plant, *P. lanceolata,* than those utilizing a native host-plant, *Chelone glabra.* Chemical defense varied based on host-plant species and population, with lower levels of iridoid glycoside (IG) sequestration occurring in larvae feeding on *P. lanceolata*. Notably, populations that sequestered higher concentrations of iridoid glycosides exhibited reduced immune performance, but also reduced JcDNV infection loads, compared to populations with lower IG sequestration. Together, these results indicate that sequestration of iridoid glycosides may contribute to suppression of viral infection in herbivorous hosts through non-immunological mechanisms, and that feeding on *P. lanceolata* may compromise *E. phaeton*'s defenses against JcDNV infection. Overall, these findings reveal substantial host-plant mediated variation in herbivore disease dynamics, highlighting the importance of considering interactions with pathogens in investigations of diet breadth evolution.

2-53 Reconstructing the Origins of a Leptospirosis Outbreak in Channel Island Foxes
Riley O. Mummah, University of California, Los Angeles

The Channel Island foxes (*Urocyon littoralis santarosae*) on Santa Rosa Island, California, suffered drastic population declines in the late 1990s, leading to their listing as an endangered species. All 15 remaining foxes were brought into a captive-breeding program beginning in 2000, which culminated in the successful release of all foxes back into the wild between 2003-2009. However, in 2010, two dead foxes exhibited signs of leptospirosis, and subsequent investigation revealed island-wide seroprevalence of *Leptospira interrogans* serovar Pomona. This elicited concern regarding the potential impact of this pathogen on the recovering population and raised questions about the origin of the outbreak. To reconstruct the origin, we tested banked sera collected from 2006-2010 from released foxes for the presence of antibodies. To investigate spatiotemporal exposure patterns prior to the first samples in 2006, we paired extensive data on individual fox movements with a model of MAT titer serodynamics. The foxes have been tracked since 2003 using two methods: precise GPS locations from trapping and direct observations and less precise radio telemetry locations. The imprecise telemetry data were converted into spatial polygons and integrated with the GPS data to calculate a moving-window kernel density for each fox. By overlaying inferred times of infection from MAT titers, we obtained an estimate of the spatiotemporal origin of the outbreak. This is a unique case study in reconstructing the origins of a pathogen emergence event in a wildlife population.

2-54 Quantifying microbiome effects of antibiotics and probiotics in neonates of a NICU
Rene Niehus, Harvard School of Public Health

Antibiotics can disrupt the human gut microbiota and cause amplification of pre-existing resistance genes. High within-patient resistance is associated with higher resistance in infections, and may also contribute to increased population-level spread of resistance. Probiotic bacterial strains have been used successfully in mice to suppress antibiotic-resistant pathogens. However, little is known about the effects of probiotics on the human microbiome. Here, we analyse metagenomic shotgun data from a prospective follow-up study of eleven newborns staying in a neonatal ICU in Siem Reap, Cambodia. In addition to varying antibiotic treatments, six of these patients received daily probiotic treatment with Lactobacillus acidophilus. We build a dynamic model of the within-host resistance dynamics that explicitly models an internal metagenomics standard, enabling us to quantify effects of probiotics on absolute abundance of different resistance markers. Our model allows us to simulate the microbiome dynamics of resistance under varying conditions, and to design an efficient trial to infer probiotic microbiome effects.

2-55 The fungal microbiome of a grass host under natural infections by diverse parasites
Kayleigh R. O'Keeffe, University of North Carolina at Chapel Hill

Parasites can affect and be affected by the host's microbiome, with consequences for host susceptibility, parasite transmission, and both host and parasite fitness. Yet, unraveling the complex relationships among

hosts, parasites, and the microbiome remains a frontier in disease ecology, and investigations under natural conditions are limited. Foliar fungal parasites can serve as a suitable model system to investigate microbiome/parasite interactions under natural settings. We investigated how diversity and composition of the fungal microbiome within a grass host, tall fescue, are associated with infection from three different fungal parasites, *Rhizoctonia solani, Colletotrichum cereale,* and *Puccinia coronata* compared to that of asymptomatic leaves. As a necrotroph, *R. solani* must kill host tissue to extract resources, whereas *P. coronata,* a biotroph, requires host tissue to remain alive to feed. *C. cereale* is a hemibiotroph, initially feeding as a biotroph and then shifting to a necrotrophic phase. A necrotroph may act as a niche modifier, changing its host environment, whereas biotrophs may not. Barcoded amplicon sequencing of the fungal ITS region revealed that leaf segments that were symptomatic of necrotrophic *R. solani* had significantly lower fungal diversity and unique fungal composition compared to segments that were asymptomatic or symptomatic of other parasites. This supports the hypothesis that necrotrophs may act as niche modifiers for the host's microbiome. Together, these results highlight the need to consider parasite species characteristics in order to better understand interactions between parasites and the microbiome.

2-56 Understanding complex larval habitats and the microbiome in *Aedes albopictus*
Amanda A. Tokash-Peters, University of Massachusetts Boston

The spread of the Asian Tiger mosquito (Aedes albopictus) globally continues to be of great concern in regard to vector-borne disease. Advances in the use of microbiome manipulation using organisms like Wolbachia have become promising methods of mosquito and pathogen control, but our understanding of what environmental factors can influence the microbiome remains limited. Here we examined Aedes albopictus larvae in naturally occurring treehole and tire water environments to determine time to eclosion and microbiome composition, as well as comparison to a reference population of Aedes aegypti. Adults, larvae, and water were analyzed for microbial composition. Future work will examine the influence of biological larvicides on the microbiome and the microbiome composition of wild mosquitoes at several sites globally.

2-57 Identifying drivers of *Dracunculus medinensis* infection in the dogs of Chad
Robert Lundell Richards, Odum School of Ecology, University of Georgia

Few human infectious diseases have been driven as close to eradication as *Dracunculus medinensis*, or Guinea worm. By 2010 the number of cases had fallen from 3.5 million in 1986 to 1,797. At the same time the epidemiology of the parasite in Chad began to change. Human cases were no longer clearly associated, and infections arose in domestic dogs, suggesting a canine origin to many cases. Thus, domestic dogs now threaten the viability of *D. medinensis* eradication efforts, making understanding the factors driving infection in dogs essential. In this study, we evaluated what factors of the parasite's environment were most predictive of *D. medinensis* infection in domestic dog populations at the village level in Chad. Using boosted regression tree models to identify covariates of importance for predicting *Dracunculus* infection, we found that local measures such as the presence of infection in a village were mostly predicted by demographic (e.g. prevalence of fishing, dog population size) and geographic (e.g. standard deviation in elevation) factors. In contrast, regional measures of infection, such as presence of a village in a spatial hotspot, were mostly predicted by climatic factors (e.g. precipitation of the warmest quarter). This work provides important new insight into the landscape-scale ecology of a debilitating parasite and can be used to more effectively target ongoing eradication and control efforts.

2-58 Effects of simulated climate change on the development of immune defenses
Veronica Saenz, University of Pittsburgh

Climate change impacts diverse taxonomic groups and ectotherms are particularly at risk because their body temperatures directly reflect environmental temperatures. In amphibians, temperature has effects on metabolism, development, growth, movement, immunity and reproduction. Understanding the relationships

between temperature and immune function is particularly important for amphibians, which are not only exposed to climate change, but also are particularly susceptible to emerging infectious diseases. I tested the effects of the chytrid fungus *Batrachochytrium dendrobatidis (Bd)* in one month old frogs from Vermont and Pennsylvania that developed under current and future climate conditions. Few studies have examined the role of increased environmental temperature during tadpole development and subsequent consequences after metamorphosis on innate defenses such as antimicrobial peptides (AMPs) or adaptive immune defenses, such as splenocytes. As expected, frogs raised at higher temperatures predicted under future climate change scenarios metamorphosed faster and with lower body mass index than frogs raised at lower temperatures. The infection intensity was not higher in the frogs that developed under modeled future temperatures, and body mass index does not seem to be affected due to infection in leopard frogs. However, frogs that developed at higher temperatures had lower splenocyte concentrations relative to those that developed in lower temperatures, which could be due to the stress of metamorphosing quickly. For the frogs exposed to Bd, there were no significant differences between thermal treatments in AMP presence or intensity, which suggests that the production and secretion of AMPs by metamorphs was not affected by temperature.

2-59 Estimating re-emergence probabilities of dengue in Rio de Janeiro, Brazil
Rahul Subramanian, University of Chicago

Understanding mechanisms of vector-borne disease persistence and re-mergence in specific environments can inform local elimination strategies, particularly for "boundary regions" where climate conditions are barely suitable for transmission. We investigate the population dynamics of dengue in the boundary-region metropolis of Rio de Janeiro, Brazil, which experienced sequential serotype invasions as well as their re-emergence. Stochastic epidemiological models were fit to monthly case data from the 1986-1987 invasion of the first serotype (DENV1), which re-emerged in 1995, and to the 2012-2013 invasion of the last serotype (DENV4). The estimated reproductive number (R_0) falls below one during winter and ranges approximately between 1.2-2.5 in summer. The probability of a re-emergent DENV1 epidemic occurring in 1995 was determined, taking into account population growth and R_0 values. Preliminary results indicate a low re-emergence probability for the examined ranges of the reporting rate and R_0. In parallel, the re-emergence time was deterministically estimated by calculating the number of epidemic "skips" expected following the DENV1 invasion using literature R_0 estimates. The methodology of Stone et al (Nature 2007) was extended to take into account population growth and more general seasonality. The number of skips is shown to be very sensitive to small changes in R_0. If dengue's low R_0 is near a threshold for observing large numbers of skips, then small increases to its value from localized spatial structure or within-serotype antigenic variation could facilitate disease persistence. Quantifying factors enabling re-emergence in boundary regions, especially the influence of heterogeneous urban space, would enhance control efforts.

2-60 Environmental and Population Drivers of Respiratory Syncytial Virus (RSV) Transmission in the US
Kaiyuan Sun, Fogarty International Center, National Institutes of Health

Respiratory syncytial virus (RSV) is responsible for 13-22% of deaths from acute lower respiratory tract infections in children under 5 years; annual epidemics exhibit strong seasonal cycles and highly structured spatial patterning in the US. A better understanding of the environmental and demographic drivers of RSV dynamics could help guide intervention strategies, especially with several new RSV vaccines currently under development. Here we apply statistical and mathematical models[1-4] to county-level US hospitalization records spanning 20 years and investigate the predictors of RSV transmission. We find that RSV "epidemic intensity"[1], measured as the inverse of the Shannon entropy, is negatively correlated with average vapor pressure and population density, while RSV activity peaks earlier in warm, humid and populous counties of the US (**Figure 1**). Although vapor pressure is highly correlated with RSV patterns, other environmental drivers, including temperature, potentially contribute to seasonal forcing. In agreement with prior work, mechanistic modeling[3] of weekly RSV incidences indicate that local environmental factors drive seasonal variations in the basic reproduction number, $R_0(t)$ **(Figure 2)**. Our results are also consistent with population density promoting RSV transmission over a wider range of climatic conditions,

in turn reducing epidemic intensity in more crowded counties. We hypothesize that environmental forcing and crowding, along with waning immunity and human mobility, jointly contribute to the observed spatial structure of RSV epidemics in the US; further work will use mechanistic models to explore how these factors may interact to affect the age profile and burden of RSV epidemics.

2-61 Seasonal dynamics by host sex in haemosporidian parasite load in a non-migratory population of dark-eyed juncos

Katie M. Talbott, Indiana University

Understanding seasonal dynamics in parasite load is important in identifying potential points of parasite-imposed selection pressure. Studies investigating seasonal dynamics of avian haemosporidian infection often focus on spring relapse, an increase in parasite load that occurs during reproductive recrudescence in some hosts. Few studies have investigated infection dynamics occurring throughout the breeding season in North American songbirds, and none of these has assessed infection dynamics in terms of parasite load. We predicted a peak in mean parasite load mid-way through the breeding season based on physiological demands associated with reproduction, followed by a decrease in the fall. We predicted a higher mean parasite load in females compared to males during late spring and summer, again based on higher physiological costs of reproduction in females. We sampled free-living male and female adult dark-eyed juncos in eastern North America at four time points (early May, mid-June, late July, and mid-November). We used qPCR to assess haemosporidian infection intensity (*Plasmodium/Haemoproteus spp.*). We found seasonal, sex-based, and age-based trends in parasite load, and will discuss their potential impacts on junco survival and reproduction.

2-62 Hand Foot and Mouth Disease dynamics in Vietnam

Lieu Thi Bich Tran, Oxford University Clinical Research Unit, Vietnam

Hand Foot and Mouth disease (HFMD) is an increasing public health problem which is mainly caused by four serotypes: enterovirus 71, coxsackievirus A16, A10 and A6. Different types of mechanistic models have been utilized to capture and understand the determinants of HFMD dynamics in Malaysia, Taiwan, China and Japan but not yet in Vietnam. Results from these different places using various modelling techniques have shown a variety of factors are important drivers of transmission, including births, seasonality and cross-protection. However, not all of these factors were considered in all studies. In this study, we used a mechanistic modelling approach to rigorously examine the drivers of HFMD dynamics in Ho Chi Minh City (HCMC) in Vietnam. We developed a Susceptible-Infected-Recovered model with cross-immunity between serotypes, seasonality in transmission and births. We fit the model to the HFMD case data from the three main referral hospitals in HCMC from July 2013 to December 2017. We estimated that the transmission rate was significantly associated with holidays, relative humidity and minimum temperature. The model with time-varying transmission rate and births fit the data well. In the next step, we will include cross-protection alone, and then add transmission and births into the model to estimate the duration of cross-protection and to assess how much it is driving dynamics. The highlighted relationships between climatic factors and school seasons and the disease dynamics suggest when there will be periods of high transmission and can therefore suggest the timing of relevant policies to control HFMD in HCMC.

2-63 Modeling the Impact of Climate Drivers on a 2017 Dengue Fever Outbreak in Sri Lanka

Caroline E. Wagner, Princeton University

Vector-borne diseases have enormous global clinical significance, with Dengue fever alone accounting for 96 million apparent infections per year among an at-risk population of nearly four billion people. From a modeling perspective, these diseases are unique because the range of persistence and the biological processes of the vectors that transmit them are dictated by the local climate. Additionally, the transmission landscape of Dengue fever is dependent on the strain of the virus in circulation and human behavioral patterns, among other factors. In this work, we consider the 2017 Dengue fever epidemic in Sri Lanka as a model system for investigating possible climatological and epidemiological drivers of vector-borne disease outbreaks. We show first that the

temporal dynamics of Dengue fever are related to the distinct climatological patterns encountered across the island. Motivated by this, we next develop a predictive model relating the transmission rate of Dengue fever to key climatological variables using the time-series Susceptible-Infected-Recovered (TSIR) model. Using this model, we show that climate variables alone are unable to account for the epidemic case numbers observed in 2017, and that a combination of extreme weather events as well as invasion by a serotype that had been largely absent from the island in recent years may have played an important role. Further, we provide estimates for the future burden of Dengue fever across Sri Lanka using the CMIP5 climate projections. Altogether, this work provides a novel framework for teasing apart and analyzing the various complex drivers of vector-borne disease epidemics.

2-64 Environmental conditions of forest and domestic *Ae. aegypti* oviposition sites in Kenya: potential selection pressures on the evolution of oviposition during local domestication
Siyang Xia, Yale University

The mosquito *Aedes aegypti* is the main disease vector of yellow fever, dengue, chikungunya and Zika virus. Originated in African forests, this species has successfully adapted to domestic habitats, which contributes to its high efficacy as a disease vector. Understanding these domestic adaptations, especially at their initial stage, will provide valuable knowledge for understanding the evolutionary history of *Ae. aegypti* and for developing vector control approaches. An essential step during the forest-to-domestic transition is the change of oviposition sites. Forest *Ae. aegypti* lay eggs in natural containers like tree holes, while their domestic counterparts heavily rely on artificial containers such as plastic buckets. These habitat-specific containers likely have different environmental conditions, which can drive the divergent evolution of oviposition behaviors in the forest- and domestic-living mosquitoes. In order to examine this hypothesis, we conducted field research in Rabi area in Kenya, where forest *Ae. aegypti* recently invaded local villages. We sampled and characterized 68 natural oviposition sites (e.g. tree holes and artificial containers) in both habitats. Forest and domestic sites showed different physical conditions, bacterial community compositions and volatile profiles. In addition, field oviposition experiments placing bamboo (a proxy for tree holes) and artificial containers in the forest and a nearby village suggested slightly different oviposition preference between mosquitoes living in the two habitats. Collectively these results may shed lights on how *Ae. aegypti* adapted to domestic habitats and exemplify how ecological studies may deepen our understanding of vector biology.

2-65 The transmission of Hand, Foot and Mouth Disease in East and Southeast Asia
Jijun Zhao, Qingdao University, China

Hand Foot and Mouth Disease (HFMD) is in endemic in many countries in East and Southeast Asia. The transmission mechanism of HFMD was rarely studied. The cyclic pattern of HFMD incidence is believed to be related to climatic factors, rather than school terms as observed from childhood infectious diseases in developed countries in the pre-vaccination era. Furthermore, the association of incidence and climatic factors in different locales in China are inconsistent and even contradictory. Here we selected countries or regions in typical climatic zones in East and Southeast Asia to study the transmission rate and its seasonality for HFMD. We used Time Series Susceptible Infected Recovered (TSIR) model to estimate the HFMD transmission rate. We then used a linear regression model to analyze the effects of climate factors, seasonal contact rate in children (and seasonal contact rate in population for provinces in China) on the transmission rate of HFMD in selected regions. We found that: 1) transmission rate of HFMD is highly seasonal in the studied countries, SARs and provinces of mainland China, except Singapore; 2) the HFMD transmission rate can be affected by the climatic factors as well as the seasonal contact rate of population, depending on which factor is dominant; 3) The transmission rate in provinces in China increased dramatically during the time period of Chinese Spring Travel Rush that has higher population contact; 4) transmission rate seasonality in Japan, Hong Kong SAR and Macau SAR is affected by climatic factors.

2-66 Estimating generation intervals in heterogeneous populations
Michael Li, McMaster University, Canada

The generation interval is the time between the moment a focal individual is infected and the moment that they infect another. Its distribution provides insight into understanding the relationship between the reproduction number and the exponential rate of growth, which often characterizes infectious disease dynamics. Since infection events are difficult to observe for many infectious diseases, many researchers often use the serial interval (the time between symptom onset in primary and secondary cases, or observation of clinical signs for wildlife diseases) as a proxy for the generation interval; there are theoretical and intuitive arguments why these should be approximately the same. However, our work with data from heterogeneous populations shows that there can be important differences between generation intervals and serial intervals, particularly when incubation period, infectious period and infectiousness can be correlated. We explore these differences through simulations and by using data from rabies contact tracing.

2-67 Increase in host population size facilitated the emergence of a specialist strain in the tick-vectored bacterium, *Anaplasma phagocytophilum*
Matthew Aardema, Montclair State University & Sackler Institute for Comparative Genomics, American Museum of Natural History

In pathogenic organisms, evolutionary processes such as adaptation and divergence may be significantly influenced by demographic processes in host populations. In Europe, the tick-vectored bacterium, *Anaplasma phagocytophilum*, circulates as multiple, distinct strains. Two of the most closely related strains are a host generalist and a roe deer specialist. Using sequence data from the bacteria, we show that the specialist strain is derived and likely diverged from the generalist strain relatively recently. Examining genetic signatures of demographic change in European roe dear, we also show that it underwent a dramatic population expansion also within the last 200 years. Together, these two observations suggest that a substantial host expansion lead to strain divergence in *A. phagocytophilum*. This work has important implications for the recent emergence of multiple novel zoonotic diseases.

2-68 Genomic Insight into the Phylogeographic Diversification of *Borreliella*
Saymon Akther, City University of New York

Lyme disease is the most common vector-borne disease in United States. Transmitted by hard-bodied ticks, the geographic range of the Lyme disease pathogens *Borreliella* are continuously expanding and disease prevalence is rising across the Northern United States, Southern Canada and Europe. Previously constructed genome-based phylogeny of *Borreliella* species support two large species groups, one found in New World and the other found in Eurasia. However, strains belonging to species *B. burgdorferi* are widely distributed in both continents and some North American-Eurasian coexisting species revealed evidence of genomic admixture which is inconsistent with the contemporary biogeographic history. Using 70+ whole genome sequences including many previously un-sequenced species, we show that *Borreliella* has a complex phylogeographic history with previously undocumented history of migration and introgression and an ancestral divergence coinciding with the breakage of the two continents.

2-69 Parasite intensity drives fetus development and sex allocation in an Arctic ungulate
O. Alejandro Aleuy, University of Calgary, Canada

Prenatal development influences individual and population fitness through survival of newborns and their performance against predators at early ages. Despite the mounting evidence of the negative influence of parasites on host fitness, we know very little about how parasite infection in reproductive females might influence factors such as fetus development and sex allocation. Using Dall's sheep as a model system, we used a partial least squares path model approach (PLS-PM) to investigate the associations among ewe characteristics (e.g. age and body condition), gastrointestinal parasite community (richness and infection intensity) and fetus development. The mother and parasite effects on fetus sex were assessed through PCA and linear models. The PLS-PM revealed that fetal development was dominated by the direct negative effect of gastrointestinal parasites, but in particular by the nematode *M. marshalli*. Female fetuses were significantly associated with mothers with fewer parasites and in good condition. Similarly, *M. marshalli* was the parasite with the highest effect on fetus sex through an indirect pathway of decreasing body condition of the mother. Refining our understanding of the impact that individual parasite species, as well as parasite communities, can have on reproductive indicators can be critical to understanding the role of parasites in host populations of ungulates inhabiting the Arctic, and elsewhere.

2-70 Transmission as a co-evolutionary process
Laura Ward Alexander, University of California – Berkeley

Evolutionary changes in disease transmission mode are commonplace. While such evolution may be the result of genetic changes in the pathogen, host traits may be equally important. For example, transmission mode may depend on the susceptibility of host tissues to pathogen entry at a particular site of infection. Using basic population genetics models combined with numerical dynamics, we explore the role of both host and pathogen traits to determine the outcome of evolution of frequency-dependent vs. density-dependent transmission. Conditions under which the transmission mode favored by the host differs from that of the pathogen are of particular interest, as these conflicts may maintain genetic variation regarding transmission mode in both host and pathogen.

2-71 Pathogen evolution in the age of molecular diagnostics
Amy E. Benefield, University of Colorado, Boulder

To what extent can diagnostic processes influence a pathogen's evolutionary trajectory? While diagnostics may rarely have direct impacts on pathogen fitness, the reliability and timing of diagnostic tests impact human behaviors and treatments. As a result, variation in diagnostics may lead to variation in selection pressures. We focus on how molecular diagnostic tests (MDTs) can act as an indirect selective agent driving pathogen evolution. Molecular tests that accurately diagnose infection – leading to treatments that affect the detected pathogen(s) – should cause the pathogen to evolve to avoid detection. MDTs operate by using a reference sequence(s) to detect the pathogen, and thus strains that vary from the reference sequence might be identified and treated less frequently. We use a modified SIR model with explicit population genetics to explore the circumstances under which pathogens experience directional selection to avoid detection by MDTs. We also use sequence data from *Chlamydia trachomatis* to create an empirically-based set of predictions. Our results show the conditions under which pathogens incur mutations that increase the distance from the MDT reference sequence as a result of testing. As molecular tests become more prominent in the diagnostics market, we should be wary of overly-simplistic assays that pathogens can escape – particularly when that test is used more frequently than traditional diagnostic tests.

2-72 Shifts in disease dynamics in a tropical amphibian assemblage are not due to pathogen attenuation
Keely Biggs, University of Nevada, Reno

Infectious diseases rarely end in extinction. Yet the mechanisms that explain how epidemics subside are difficult to pinpoint. We investigated host-pathogen interactions after the emergence of a lethal fungal pathogen in a tropical amphibian assemblage. Some amphibian host species are recovering, but the pathogen is still present and is as pathogenic today as it was almost a decade ago. In addition, some species have defenses that are more effective now than they were before the epidemic. These results suggest that host recoveries are not caused by pathogen attenuation and may be due to shifts in host responses. Our findings provide insights into the mechanisms underlying disease transitions, which are increasingly important to understand in an era of emerging infectious diseases and unprecedented global pandemics.

2-73 Physiology of flight drives viral virulence evolution in bat reservoirs for emerging zoonoses
Cara E. Brook, University of California, Berkeley

Bats have gained attention for their roles as reservoirs for several of the planet's most virulent emerging human diseases, including Ebola filovirus and Nipah henipavirus, which they host without demonstrating apparent morbidity or mortality. Recent work out of our research group confirms that zoonoses derived from bats are significantly more virulent than those derived from any other mammalian order. As the only volant mammal, bats demonstrate several unique physiologies—including constitutively expressed antiviral defenses (i.e. interferons), periodic bouts of flight-induced fever, and daily metabolic torpor events—which have been posited to support their seeming tolerance of viral infections that cause extreme disease in other mammals. We developed and analyzed a theoretical, within-host evolutionary model of a bat immune system, demonstrating how these unique features of flight physiology could drive the evolution of rapid viral replication rates without inducing substantial virulence in bat hosts. We further demonstrate how viruses with high replication rates evolved in perpetually antiviral reservoir hosts—like bats—could be particularly virulent following cross species emergence into secondary hosts lacking the same unique physiology and constitutive immunity. Our work provides an explanation for the extraordinary virulence resulting from bat-derived zoonoses in human spillover hosts.

2-74 Has global viral diversity been overestimated?
Colin Carlson, Georgetown University

Present estimates suggest there are over one million virus species found in mammals alone, with roughly half a million posing a possible threat to human health. Although previous estimates assume linear scaling between host and virus diversity, we show that ecological network theory predicts a nonlinear relationship, produced by broad patterns of plasticity in host-virus associations. In light of this, we re-estimate global viral diversity, using the most comprehensive available dataset of mammal-virus associations. To account for host sharing, we fit a power law scaling relationship for host-virus species interaction networks, adapting a method previously used to estimate helminth species richness. We estimate that there are approximately 40,000 virus species in mammals, a reduction of two orders of magnitude from current projections of viral diversity. Of those, we expect roughly 10,000 viruses to harbor zoonotic potential, the vast majority being RNA viruses. We expect that the increasing availability of host-virus association data will improve the precision of these estimates, and their utility in the sampling and surveillance of pathogens with pandemic potential. More broadly, we suggest host sharing should be widely included in macroecological approaches to estimating biodiversity, and discuss how our approach to estimating affiliate species richness can be used for other applications in disease ecology and other fields.

2-75 A global-scale recombination profile of cassava mosaic viruses
Alvin Crespo-Bellido, Rutgers University

Cassava (*Manihot esculenta*) is a staple food crop throughout Africa, and South and Southeast Asia whose production is severely hindered by whitefly-transmitted geminiviruses. The Cassava mosaic disease (CMD) complex is comprised of 11 viral species exhibiting accelerated rates of evolution, driven by high mutation rates and genetic recombination. Recombination is especially implicated in the emergence of new CMD viral strains; most notably in the emergence of a highly virulent recombinant in the late 1990s that caused severe epidemics through sub-Saharan Africa. While there has been an increase in scientific efforts to understand CMD dynamics and Cassava mosaic virus (CMV) evolution, a revised, global-scaled survey of the frequency and patterns of CMV interspecies recombination is currently lacking. Through bioinformatic analyses, we were able to update the recombination profile of CMVs. We assembled datasets with the genetic sequences of 868 publicly-available CMV isolates implicated in CMD and collected during field surveys throughout Africa and South Asia. Computational analyses using several recombination detection methods revealed putative recombination events in the CMV sequences. The results showed that recombination is featured prominently in the evolutionary histories of most CMV species and that it is not constrained by traditional geographic barriers, suggesting international trade may be an important factor in the spread of CMVs.

2-76 Phylogenetic analysis of suspect bat reservoirs for filoviruses and henipaviruses
Daniel E. Crowley, Montana State University

Zoonotic filoviruses and henipaviruses can be transmitted from bats to humans and domestic animals causing severe disease and onward transmission among recipient hosts. These pathogens are considered of highest concern for future pandemics. There has been substantial effort to conduct surveillance for these pathogens in bats, but less effort to collate surveillance data. Taxonomic patterns in prevalence and seroprevalence of collated data could help guide surveillance and risk assessment efforts. We systematically collected data on filovirus and henipavirus detections and used a machine-learning algorithm, phylofactorization, to flexibly search the bat phylogeny for cladistic patterns in filovirus and henipavirus infection and sampling efforts. Across 143 sampled bat species, evidence for filovirus infection was widely dispersed across the sampled phylogeny. We find major gaps in filovirus sampling in bats, especially in species occurring in the Western Hemisphere. Evidence for henipavirus infection was clustered within Pteropodidae; however, no other clades have been sampled as intensely.

2-77 Viral models for viral phylogenies: a bespoke substitution matrix helps uncover the deep relationships among circular rep-encoding ssDNA viruses
Siobain Duffy, Rutgers, The State University of New Jersey

Large numbers of novel circular Rep-encoding ssDNA viruses (CRESS DNA viruses) have been discovered in the past decade, prompting a new appreciation for the ubiquity and genomic diversity of this group of viruses. Although highly divergent in the eukaryotic hosts they infect or are associated with, CRESS DNA viruses are united by the homologous replication-associated protein (Rep). An accurate genealogy of Rep can therefore provide insights into how these pathogens are related to each other. We worked with a dataset of CRESS DNA RefSeq genomes (n=926), which included representatives from all six established families and unclassified species. To assure an optimal Rep genealogy, we derived and tested a bespoke amino acid substitution model (named CRESS), which outperformed existing protein matrices in describing the evolution of Rep. The CRESS matrix was also selected as the best fitting to describe the evolution of several CRESS DNA families' capsid protein sequences and *Parvoviridae* NS1/Rep sequences, suggesting that the CRESS matrix has captured substitution patterns universal to CRESS DNA viruses (and perhaps ssDNA viral proteins in general). The CRESS model-estimated Rep genealogy revealed several intriguing relationships that had not been previously observed: most significantly a potential single origin of intron-containing Reps, which causes several geminivirus genera to group with *Genomoviridae* (bootstrap support 55%, SH-like support 0.997). While there are numerous

unclassified CRESS DNA viruses throughout the tree, there is significant intermingling with sequences assigned to *Circoviridae*, suggesting a needed expansion of *Circoviridae* or creation of further new CRESS DNA virus families.

2-78 The effects of host genetic diversity on parasite evolution
Alice Ekroth, University of Oxford

The 'monoculture effect' is when genetically homogenous populations are more vulnerable to outbreaks of disease. Such a phenomenon could be predicted to shape parasite evolution such that genetically heterogenous host populations would impose stronger selection on parasites to adapt. We test this idea by experimentally evolving the parasitic bacteria, *Staphylococcous aureus,* in genetically heterogenous and homogenous host populations of wild isolates of the nematode *Caenorhabditis elegans.* When comparing gut colonizations of ancestral to evolved *S. aureus*, we find great variation in infectivity between replicate homogenous host populations to heterogenous ones. We also conduct a meta-analysis to directly test the biological conditions under which host genetic diversity limits disease spread. Overall, we find broad support for the monoculture effect across host species. The effect was independent of host-parasite specialisation (genotypic or species-level), parasite type and diversity, virulence, and experimental environment. Together, these studies highlight the impact of host genetic diversity as a driver of parasite evolution and ecology with relevance to small and at-risk host populations.

2-79 Lassa fever in West Africa: indications of a reverse zoonosis
Elisabeth Fichet-Calvet, Bernhard-Nocht Institute of Tropical Medicine, Hamburg, Germany

Lassa fever is a haemorrhagic fever caused by an arenavirus, the Lassa virus (LASV) and would affect 150-200,000 persons per year in West Africa, mainly in Nigeria, Sierra Leone, Guinea and Liberia. LASV is hosted by the multimammate mice, *Mastomys natalensis*, and *Mastomys erythroleucus*. It is commonly admitted that Lassa Fever is a zoonosis with a rodent-to-human transmission, but a human-to-human transmission is occurring as well.

Here, we seek to phylogenetically infer ancestry and descent between LASV sequences detected in rodents (n = 89) and humans (n = 96), in order to provide increased insight into virus transmission at the rodent-human boundary.

In BEAUTI, the following settings were used: 2 partitions of partial GP and NP linked in their substitution models, clocks and trees, date at the nearest day, 8 taxa, GTR+gamma4, codon partition 1,2,3 and constant size population. MCMC chains were run 50 million states, and sampled every 20,000 states to obtain an effective sample size above 200 for all the parameters. Phylogeny was implemented in BEAST 1.10, and results were examined in Tracer 1.6. The results show that the time of most recent common ancestor (tmrca) was highest in rodent populations located in Mali (80-112 years), and lowest in those inhabiting in forest Guinea (17-23 years). When comparing the sequences in rodents and humans in Kenema and Ekpoma, the tmrca is higher in humans (54-76 years) than in rodents (46-60 years). This suggests than humans were infected before rodents and point into the direction of a reverse zoonosis.

2-80 Disentangling the population biology of mumps re-emergence
Deven Vishwas Gokhale, University of Georgia

Mumps is a childhood viral infection, caused by a collection of genotypic strains belonging to the family paramyxoviridae. Despite high estimated coverage with the Jeryl-Lynn vaccine since 1968, the US has witnessed a re-emergence of mumps in the 21st Century. A critical feature of these recent outbreaks, the causes of which remain contested, is an unusually high proportion of mumps cases among university students and older adults, many of whom have received the complete dose of MMR vaccination. Two principle hypotheses have been proposed to explain contemporary mumps epidemiology: (1) waning

of vaccine-derived immunity, and (2) a mismatch between the dominant circulating strain (genotype G) and the virus used in vaccine production (genotype A) leading to "leakiness" in vaccinal immunity.

To arbitrate among these competing explanations, we formulated age-stratified mechanistic transmission models and used likelihood-based inference to confront them with longitudinal incidence records. We discuss our findings in the context of efficient public health policy strategies for once again bringing mumps transmission under control.

2-81 Host phylogenetic distance drives trends in virulence and transmissibility across the animal-human interface

Sarah Guth, University of California, Berkeley

Historically, efforts to assess "zoonotic risk" have focused only on quantifying the potential for cross-species emergence of viruses from animal hosts. However, viruses clearly differ in relative burden, both in terms of morbidity and mortality ('virulence') incurred and capacity for sustained human-to-human transmission. We compiled a database of 375 virus-mammal associations and delineated host and viral traits predictive of (a) viral zoonotic potential, (b) human mortality associated with viral spillover, and (c) human transmissibility following spillover. We demonstrate elevated zoonotic potential among hosts at both near and far extremes in phylogenetic distance from humans. Increasing host phylogenetic distance positively correlates with human mortality but negatively correlates with human transmissibility, suggesting that the virulence induced by hosts at high phylogenetic distance may facilitate zoonosis but limit viral capacity for human transmission. The most closely related hosts to humans harbor zoonoses of lower impact in terms of morbidity and mortality, while the most distantly related hosts—in particular, order Chiroptera—harbor highly virulent zoonoses with a lower capacity for endemic establishment in human hosts. Our results emphasize the importance of understanding how zoonoses manifest in the human population and also highlight potential risks associated with multi-host transmission chains in spillover.

2-82 Mutation in experimental cassava geminivirus populations

J. Steen Hoyer, Rutgers University

Single-stranded DNA viruses are ubiquitous and infect all three domains of life. They have been studied intensively in plants, where they threaten food security throughout much of the tropical and subtropical world. High-throughput sequencing has been used to discover novel ssDNA viruses and for surveillance of ssDNA pathogens, but rarely applied to characterization of genetic variation within a laboratory population, as has been done for many RNA viruses. ssDNA viruses show similar rapid, mutation-driven evolutionary dynamics, so sequencing-based experimental approaches should improve our understanding of ssDNA virus diversity.

We are measuring evolutionary dynamics in two synergistic whitefly-transmitted ssDNA geminiviruses that limit cassava production across Africa: African cassava mosaic virus (ACMV) and East African cassava mosaic Cameroon virus (EACMCV). Cassava plants are bombarded with infectious clones (individually and jointly) and infection is allowed to proliferate for at least 14 days. Virus DNA is enriched with size selection and rolling circle amplification and sequenced using the Illumina NextSeq 500 platform. Technical replicate libraries are prepared from each DNA sample, allowing systematic quantification of technical variability.

We have completed four independent experiments with two different cassava cultivars and three temperatures. We have recorded tens of thousands of observations of thousands of distinct spontaneous genetic variants across experiments. Concordance among allele frequency estimates for sets of technical replicates is high. Our preliminary data strengthen the hypothesis that ssDNA plant viruses can create diverse populations quickly, underlying their ability to evolve as fast as RNA viruses.

2-83 Stochastic mutation-selection-drift models of parasite virulence evolution
Morgan Kain, McMaster University

Most mathematical models of parasite evolution use a deterministic framework, where stochasticity's only role is to provide raw material for adaptation via mutation. In an attempt to consider parasite virulence evolution from a broader perspective, and in particular to understand the diversity of virulence found in natural communities, we explore two stochastic, discrete-population models for parasite evolution: (1) Parasite evolution in transmission and virulence (modeled here as parasite-induced mortality rate) in the absence of a virulence-transmission tradeoff; (2) Parasite evolution when parasite transmission is constrained by virulence, but where parasites can evolve compensatory mechanisms to stay near the tradeoff frontier. In the absence of a virulence-transmission tradeoff, we find as expected that parasites are strongly selected for increased transmission and decreased virulence, limited only by the effects of mutation and drift. We observe a bimodal distribution of outcomes depending on the mean and standard deviation of the mutational spectrum. When parasite transmission is constrained by virulence, parasites may still evolve high transient virulence. In the unconstrained model smaller host populations evolve parasites with lower transmission and virulence at equilibrium, while in the presence of constraints host population size affects the rate and trajectory of parasite evolution but not its equilibrium.

2-84 Host behavioral diversity and disease dynamics
Nick Keiser, University of Florida

Increased genetic diversity within a host population can reduce the severity of epidemics because diverse populations may harbor more resistant or resilient individuals. However, population diversity in infection resistance *per se* may not alone alter population-level effects of disease, as host behavioral phenotypes play an integral role in disease defenses and genetically diverse populations are not always phenotypically diverse. From a suite of genotypes of the fly *Drosophila melanogaster*, we identified five genotypes that were equally susceptibility to a generalist pathogenic fungus (*Metarhizium robertsii*), but varied in a suite of behavioral traits that alter infection risk. We quantified behavioral differences among genotypes in multi-dimensional trait space using ordination analyses and produced replicated experimental populations that contained one of five genotypes, mixtures of three genotypes with similar behavioral phenotypes, or mixtures of three behaviorally diverse genotypes. Populations were exposed to a 24hr pathogen pulse, and then allowed to interact naturally on pathogen-free food patches for 20 days where we measured mortality daily compared to pathogen-free controls. We found that mixed-genotype populations experienced greater mortality compared to monotypic populations only when made up of phenotypically diverse individuals. Thus, genetic diversity alone did not alter disease dynamics, but phenotypically diverse populations died more rapidly than behaviorally depauperate populations. Potentially, the presence of diverse behavioral phenotypes may increase the number of ways in which individuals can become exposed to infectious agents or transmit them to conspecifics.

2-85 Identification of Host Species of Lyme disease ticks (*Ixodes scapularis*) using DNA Barcoding
Li Li, City University of New York

Ixodes scapularis, or deer tick, is the most common vector of Lyme disease and other tick-borne diseases (TBDs) in eastern North America. It remains unclear the composition of host species serving as reservoirs of pathogens in local transmission cycles. Molecular techniques such as DNA barcoding are a direct method for identifying host species of ticks as well as reservoirs of TBD pathogens. Ticks parasitize multiple host species during their two-year life cycle, adding to the difficulties in determining from its host species. We established a sensitive molecular method for identifying the host species through the leftover blood meal in questing ticks. The method consists of a two-round nested polymerase chain reaction (PCR) followed by Sanger sequencing, targeting a part of mitochondrial 12S rDNA that is vertebrate-specific. The method has been successfully applied to questing adult ticks collected from Long Island, New York, and amplified the marker DNA identified as white-tailed deer (*Odocoileus virginianus*). Currently, we are optimizing the method in order to apply it to nymph ticks and low-

quality samples. We plan to use the method to survey a large sample of ticks from diverse locations and test hypotheses such as diverse host species among different tick stages and populations. Further development of this technique will allow us to combine with the detection of tick-borne pathogens, e.g. *Borrelia burgdorferi* sensu lato to co-identify reservoir hosts of the pathogens as well as the tick vectors.

2-86 The incapacitating effects of chytrid coinfection: a functional genomics analysis of Eastern newt susceptibility to *Batrachochytrium salamandrivorans* (*Bsal*) and *Batrachochytrium dendrobatidis* (*Bd*)
Cait McDonald, Cornell University

The pathogenic chytrid fungus, *Batrachochytrium salamandrivorans* (*Bsal*), is the most recent emerging disease threat to salamanders. *Bsal* is not yet present in North America, which is a global hotspot of salamander biodiversity. While *Bsal* is absent, its sister taxon, *Batrachochytrium dendrobatidis (Bd)*, is widespread, where prevalence may reach more than 80%. Given this prevalence, *Bsal-Bd* coinfection will likely influence future *Bsal* disease emergence. Our current knowledge of host response to *Bsal* is restricted to assessments of clinical signs, histologic lesions, and mortality. Here, we expand this understanding to the level of host gene expression using RNA-sequencing. We compare host transcriptome-wide responses in a highly susceptible species, the Eastern newt (*Notophthalmus viridescens*), to *Bsal*, *Bd*, and *Bsal-Bd* co-infection. We find that coinfection amplifies disease severity relative to single infection with either pathogen, most notably by disabling the host complement system. We further show that host immune response varies significantly with each pathogen treatment. Relative to *Bd* infection, *Bsal* infection elicits more pronounced innate and adaptive gene expression phenotypes. This study is pertinent not only to our understanding of the *Bsal*-salamander system, but it also has management implications in an era wherein globalization has been identified as a means by which virulent pathogen lineages may gain access to previously naïve host populations.

2-87 Quantifying the dynamics of HIV decline in perinatally-infected neonates on antiretroviral therapy
Sinead E. Morris, Columbia University Medical Center

Objective(s): To model the kinetics of HIV decline in perinatally-infected neonates initiating antiretroviral treatment (ART), identify clinical correlates of these kinetics, and assess their concordance with those in other age groups.

Design: From 2014-2017, HIV viral load (VL) was monitored in 122 perinatally-infected infants identified at birth and initiating ART within a median of 2 days. Other pre-treatment infant and maternal covariates, including CD4 T cell counts and percentages, were also measured.

Methods: A subset of the cohort demonstrated consistent decline and achieved VL below the detection threshold (< 20 copies/ml) within one year. For those with sufficient VL data, we fit a mathematical model describing the loss of short- and long-lived infected cells during ART. We then estimated the lifespans of infected cells and the time to viral suppression (< 20 copies/ml), and tested for correlations with pre-treatment covariates.

Results: Data from 43 infants were fit using the mathematical model. All parameters were consistent with those obtained previously from adults and other infants. One exception was the lifespan of short-lived infected cells which was longer than in other cohorts. This discrepancy may reflect insufficient sampling during initial viral decline, when the loss of short-lived cells is most apparent. Infants with higher pre-treatment CD4 percentage or lower pre-treatment VL trended towards more rapid viral suppression.

Conclusions: HIV dynamics in perinatally-infected neonates initiating very early ART are broadly similar to those observed in other age groups. Accelerated viral suppression is also associated with higher CD4 percentage and lower VL.

2-88 Virulence Evolution of Facultative Pathogens
Aakash Pandey, Kansas State University

Various aspects of pathogen life history affect the trajectory of virulence evolution. In addition to infecting hosts, facultative pathogens are able to grow independent of hosts in the environmental reservoirs. These diverse ecological settings could give rise to novel life-history trade-offs altering the course of virulence evolution in these pathogens. Although facultative pathogens cause many human and agricultural diseases, models of virulence evolution often focus on obligate pathogen life-histories. As a result, virulence evolution in the facultative pathogens is under-explored. We used the adaptive dynamics framework to explore the evolution of facultative pathogen virulence. We found that higher carrying capacity in environmental reservoirs can result in higher virulence evolutionary outcomes. Further, increasing the strength of a potential environmental persistence-virulence trade-off leads to lower virulence. We also found that the evolutionary branching is a common phenomenon where pathogens with diverse virulence strategies can co-exist. Our results highlight the need to evaluate whether facultative pathogens have virulence-associated life-history trade-offs and show that the problem of virulence evolution in these systems are a fertile ground for both theoretical and experimental study.

2-89 Limited constraints on RNA virus evolution by isogenic host range mutations at the same amino acid
Mansha Seth-Pasricha, Rutgers University

RNA viruses frequently have significant interactions between mutations – epistasis that constrains the beneficial mutational spectrum, and these effects can be seen in isogenic viruses that differ by as few as 1 mutation. We investigated how mutations on the same amino acid position, those that conferred an expanded host range, affected evolutionary trajectories in the dsRNA bacteriophage phi6. We experimentally evolved isogenic host range mutants, all of which had mutations in the P3 attachment protein on the same amino acid (E8A, E8G, and E8K), on novel hosts for 30 days: each passage on *Pseudomonas syringae pv tomato* (PT), each passage on *P. pseudoalcaligenes ERA* (PE), or daily alternation of those hosts. While there were idiosyncratic substitutions in all evolution experiments, the three different mutants in the same amino acid found the same parallel mutations when evolved on PT (most notably Q130R in P3), and when evolved on alternating PT and PE (K144R and Q130R). Interestingly, the original E8G, E8K, and E8A mutations were retained in all three treatments over the 30-day evolution. A mutation in the P5 peptidoglycan hydrolase protein (G168C or W219C) emerged in most PE evolved lineages. While such a mutation may be biochemically significant based on differences in host morphology, these parallel mutations that are indicative of adaptation in response to natural selection, led to different-fold increases in fitness in novel hosts, but no loss of fitness was indicated in the original host indicative of protagonistic pleiotropy.

2-90 Viral populations in honey bees (Apis mellifera) are disrupted by vector-mediated transmission
Allyson M. Ray, Huck Institutes of the Life Sciences, Department of Entomology, Center for Pollinator Research, and Center of Infectious Disease Dynamics, Pennsylvania State University

Hosts and their associated pathogens can co-evolve for generations, resulting in reciprocal antagonistic adaptations. When a novel selective pressure appears, such as the introduction of a pathogen vector, the co-evolutionary equilibrium can be disturbed, possibly allowing for adaptations to sweep across populations. The *Varroa destructor* mite switched hosts from the Asian honey bee (*Apis cerana*) to the European honey bee (*Apis mellifera*), and in only a few decades, spread across the globe. This host switching event not only introduced a new blood-feeding parasite to bees, but also provided a novel vector for pathogens, including Deformed Wing Virus (DWV), which has become a predominant pathogen of bees worldwide in recent years. Studies suggest that the new transmission route provided by Varroa mites (a direct injection into the hemolymph rather than an oral introduction) results in increased viral titers, decreased variant frequencies, and decreased bee survival over the winter. Understanding how Varroa transmission influences host-pathogen dynamics is both critical for mitigating negative impacts on this critical pollinator species, and provides a model for understanding how vector

introduction influences pathogen evolution. To evaluate how Varroa influenced DWV dynamics and evolution, we serial passaged a population of DWV by injection through *in vitro* reared honey bee pupae and measured viral populations throughout the five passages. Our results suggest that repeated pupal-to-pupal transmission, mimicking mechanical vectoring by Varroa, does alter the proportions of variants in viral populations, possibly simulating the selective pressure imposed by a viral vector and a mechanism for virus evolution.

2-91 Females cope better with cancer: Tasmanian devils and facial tumour disease

Manuel Ruiz-Aravena, University of Tasmania, Australia

A highly-infectious and deadly transmissible cancer affecting wild Tasmanian devils was discovered in 1996. This transmissible cancer, Devil Facial Tumour Disease (DFTD), has spread across 90% of the devil distribution. Mortality is swift, with individuals dying within 12 months of the first signs of infection. Epidemiological models anticipated that the rapid decline of devil populations threatened the species with extinction. However, the persistence of populations in long infected areas suggests that devils may be adapting to the disease. We investigated tolerance and resistance to DFTD between 2014 and 2019 by analysing longitudinal ecological, physiological and histopathological data from two devil populations near the epidemic front. Our results showed that male and female devils responded differently to tumour burden, with females presenting higher levels of tolerance than males. Higher levels of serum antibodies to DFTD correlated with a higher risk of infection in males. There was no relationship between serum antibodies and risk of infection in females, supporting sex-differences in DFTD resistance. We detected tumour growing slower in females than in males. In addition, 6 natural tumour regressions were detected in females and 3 in male devils, again supporting sex-differences. These findings expand the current evidence of hosts rapidly evolving in response to DFTD with potential links to the genomic changes related to disease outbreak. The sex bias in tolerance and resistance of devils suggests that the biology of the devil-cancer interaction differ, and therefore natural selection may operate differently on tumours infecting male and female devils.

2-92 Swarm Biology Reconciles Contrasting Observations of Immunity at Individual-Cell Versus Organismal Scales

Edward C. Schrom, Princeton University

In mammalian immunity, the choice of which weapons to deploy against invading parasites (“effector choice”) is largely orchestrated by T-helper cells. During any given infection, most T-helpers commit to a single effector type (e.g. Th1, Th2, Th17, etc.). This led to the notion that individual T-helpers differentiate into discrete effector lineages, and that this differentiation is uniform at the group level (i.e. organismal scale). However, recent evidence shows that individual T-helpers are plastic in their ability to switch effector types, readily induced to coexpress markers of multiple effector types, and surprisingly variable from cell to cell in their expression of these markers. Thus, flexibility and variability at the scale of individual cells must be reconciled with polarized commitment at the scale of organismal immunity. To do so, we look to the field of collective decision-making, in which swarm decisions are explained by the dynamic accumulation of signals among individuals. By modeling not only T-helpers but also their dynamic communication, we find that cell density modulates the emergence of unified effector choices. Only at biological cell density, and not under in vitro conditions, can individually flexible and variable T-helper cells coordinate polarized effector commitments. Moreover, the surprising stochastic variability in signaling among T-helpers, written off as mere noise in in vitro experiments, may actually serve critical functions in vivo. Finally, we validate key assumptions of our model and offer further insights from continuing experimental work. Developing this framework of a cellular swarm may unlock further cross-scale insights in mammalian immunity.

2-93 Wolbachia for dengue control; will dengue viruses evolve resistance?
Tran Thuy Vi, Oxford University Clinical Research Unit, Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam

Dengue viruses (DENV) are major human pathogens, transmitted between people primarily by *Aedes aegypti* mosquitoes. Recently, the endosymbiont bacteria Wolbachia was horizontally introduced into Ae. Aegypti; Wolbachia infection non-specifically impairs DENV replication in these mosquitoes opening up a potential new strategy for dengue control. This project tests the hypothesis that DENV cannot easily develop resistance to the mechanisms by which Wolbachia blocks virus replication. Using contemporary viruses, we challenged wild type (WT) and Wolbachia-infected *Ae. Aegypti* mosquitoes (wMel strain) with patient-derived viremic blood, and performed serial passaging of DENV through both strains, using microinjection. DENV WGS using the Illumina MiSeq platform was performed at Passage 0 (viremic blood sample), 10, 15 and 20. CLC genomic workbench software was used as a bioinformatics tool to analyse and interpret sequence data. Preliminary results showed that multiple synonymous and non-synonymous mutations were observed in the consensus sequences in both WT and wMel mosquito groups. Within the E-gene, we saw three amino acid changes arise independently in two positions (E483K, G483R, and E664K) across multiple experiments. Further experiments are planned to investigate the whether these mutations affect functionality of the protein.

2-94 The evolution of specialization to host genotype in an insect pathogen
Elisa Visher, University of California, Berkeley

Specific interactions between parasite and host genotypes underlie a breadth of evolutionary theory. Trade-offs between adaptation to different host genotypes are thought to constrain niche breadth, thereby maintaining specialist partners that interact through frequency dependent interactions to maintain genetic diversity. While hugely important for evolutionary theory, experimental evidence for trade-offs between genotypes is rare. Therefore, we measure the trade-off between different host genotypes in our *plodia interpunctella* and baculovirus model system. We experimentally evolved a virus population on inbred lines of moth to measure the evolution of local adaptation to specific host genotypes. By measuring fitness in terms of both viral infectivity and replication on local and foreign genotypes at multiple time points, we assay for local adaption on multiple axes of viral fitness and can distinguish between ecological and evolutionary effects. We find that the evolved baculovirus populations were more infective on the host genotype that they were passaged on than they were on foreign genotypes. This effect was not significant at earlier time points of the experimental evolution, suggesting that viral evolution was the main contributor to local adaptation. Our results demonstrate genotype specific interactions in our baculovirus and plodia system and will therefore underlie future work examining the effects of host genetic diversity on parasite evolution.

WITHIN-HOST COMPETITION IN INFECTIOUS DISEASE DYNAMICS (Posters 2-95 → 2-114)

2-95 Chronic infection with *Babesia microti* leads to systemic changes in immune activity that grant tolerance in a wild rodent
Christopher Taylor, University of Nottingham, UK

Responses to infection fall on a spectrum from resistance, in which the host acts to keep pathogen abundance as low as possible, to tolerance, in which the host acts to minimise damage caused by the pathogen. Of these two strategies, less is currently known about the role that tolerance plays in wild populations. We have investigated the effects of the protozoan haemoparasite *Babesia microti* on a wild population of field voles *Microtus agrestis*, with a view to investigating the roles of resistance and tolerance in the host response. *B. microti* is highly prevalent, infecting around half of the vole population, and establishes long-lasting infections that cause major enlargement of the spleen, and anaemia. Despite this, remarkably we observed no reduction in survival, fecundity or body condition in the infected individuals. We quantified immune activity by measuring

expression levels of a range of immune-related genes in blood, mesenteric lymph node and spleen tissue using qPCR. We found that *B. microti* was associated with a major shift in immune activity in all three tissues, having a stronger effect than other measured factors such as age and condition. The majority of the affected genes were cytokines or transcription factors involved in regulatory arms of the immune response, such as IL-10 and FoxP3, as well as sestrin-3, which is involved in the response to oxidative stress. Taken together, our results show evidence of a strong tolerance response that minimises damage caused by *B. microti* infection in wild voles.

2-96 Modelling the effects of cross-immunity on pandemic risk
Benjamin Singer, University of Oxford

Over the last century, the world has seen an increase in the long-distance travel of people and goods, partially due to the growth of the tourism industry and in agricultural trade. This could plausibly increase the risk of pandemics by allowing pathogens to travel between distant communities. However, cross-immunity, the phenomenon whereby infection with one strain of a pathogen provides some level of immunity against other strains, could mean that this enhanced pathogen spread also leads to widespread immunity to further strains. In this presentation I will discuss a metapopulation model of disease spread consisting of SIR populations connected on a network representing travel routes between populations. This model was developed to explore the relationship between travel rates and pandemic risk. I will discuss the effects of network structure, co-circulation of pathogens, and varieties of immunity on this relationship, focussing on analytic results where possible. I will close with a discussion of how this model applies to the behaviour of various diseases in the modern world.

2-97 Breaking down defenses: a quantitative analysis of malaria infection dynamics reveals distinct immune defense strategies
Nina Wale, University of Michigan

The host immune response both curbs and causes disease and is an important driver of pathogen evolution. To understand the immune response's impact on host and pathogen fitness we need a quantitative picture of its effect on the population dynamics of host and pathogen cells. Here, we use a data-driven modeling approach to quantify the birth and death processes underlying the dynamics of the rodent malaria parasite, *Plasmodium chabaudi*, and the red blood cells (RBCs) it targets. We decompose the host immune response into three components, each with a distinct effect on parasite and RBC vital rates, and quantify the relative contribution of each component to anemia and (the cessation of) parasite population growth. We find that, in addition to killing parasitized cells directly, the host deploys the different immune components to achieve distinct resource-directed defense strategies. Early in the infection, the hosts cuts off the supply of RBCs and actively destroys them; these 'siege' and 'scorched-earth' strategies help to bring the infection under control. Late in the infection, the host employs a strategy that alters not at the availability but the *demography* of RBCs. Specifically, by accelerating the turnover of RBCs, the host achieves a 'juvenilization' strategy that allows it to simultaneously recover from anemia and keep parasite proliferation at bay. Significantly, by quantifying the impact of the different components of the immune response on both parasite fitness and host disease, we reveal that phenomena often interpreted as harmful to the host may in fact be helpful to it.

2-98 Multi-host pathogens and multi-parasitised hosts: an individual-level approach to understanding transmission of two pathogens (*Batrachochytrium dendrobatidis* and Ranavirus) across three amphibian host species
Bryony Allen, University of Liverpool

Many important pathogens circulate within multi-host communities. Equally, many hosts can be infected with multiple pathogens. Recent studies of declining amphibian populations indicate that the two pathogens of global conservation concern, Ranavirus and Batrachochytrium dendrobatidis (Bd), commonly occur as co-infections. Yet, experimental evidence of co-infection dynamics in amphibians remains sparse. Both pathogens are host

generalists with significant heterogeneity seen in the functional roles host species play in transmitting and maintaining either emerging infectious disease.

To help unpick the tangled dynamics of this multi-host, multi-pathogen system we empirically tested how susceptibility, infectiousness and burden of disease changed with infection scenario (single vs coinfection) across a panel of three amphibian host species, that range in their reported susceptibility. We measured the contributions of each host, at an individual level, to the environmental pool of infectious particles, by quantifying *Bd* zoospores and ranavirus virion outputs. Endpoint infection load was also measured to link the hosts' infection burdens with their infectiousness.

We demonstrated that the probability of infection and the resulting infection load is context dependent with host species being a most influential. Exposure sequence was significant for predicting ranaviral infection with, a higher number of individuals infected in co-infection scenarios.

Understanding the susceptibility and infectiousness of each host, at an individual level, allows us to predict how host species community composition influences the establishment and persistence of both pathogens, singularly and as coinfections. Our study provides previously lacking empirical evidence of within-host and between-host dynamics under different infection scenarios.

2-99 A general framework for modeling the impact of coinfections on pathogen evolution

Mary Bushman, Emory University

Theoretical models suggest that mixed-strain infections, or coinfections, are an important driver of pathogen evolution. However, the within-host dynamics of coinfections vary enormously, which complicates efforts to develop a general understanding of how coinfections affect evolution. Here, we develop a general framework which condenses the within-host dynamics of coinfections into a few key outcomes, the most important of which is the overall R_0 of the coinfection. Similar to a phenotype influenced by two different alleles in a diploid organism, we argue that the R_0 of a coinfection is a product of the R_0 values of the coinfecting strains, shaped by the interaction of those strains at the within-host level. Extending the analogy, we propose that the overall R_0 reflects the *dominance* of the coinfecting strains, and that the ability of a mutant strain to invade a population is a function of its dominance in coinfections. To illustrate the utility of these concepts, we use a within-host model to show how dominance arises from the within-host dynamics of a coinfection, and then use an epidemiological model to demonstrate that dominance is a robust predictor of the ability of a mutant strain to save a maladapted wildtype strain from extinction (evolutionary emergence).

2-100 Domestic cats are genetically resistant to feline leukemia virus – evidence from *in vitro* and *in vivo* infections

Elliott Chiu, Colorado State University

Feline leukemia virus (FeLV), a virus native to domestic cats, can infect other felids with devastating consequences following spillover. Little is understood about host factors relating to FeLV susceptibility in novel species. One difference of particular note between domestic cats and wild felids is that domestic cats harbor endogenous FeLV (enFeLV), transmitted genetically from parents to offspring. Previous reports have noted a negative correlation between enFeLV and exogenous FeLV infection in domestic cats. Here, we test the hypothesis that enFeLV confers resistance against exogenous FeLV infection, and thus is a factor in wild felid host susceptibility. We infected primary fibroblasts isolated from domestic cats and pumas (*Puma concolor*) with FeLV and measured infection by proviral quantification and replication by viral antigen production. We further compared proviral load and viral antigen load in naturally infected domestic cats and Florida panthers (*P. concolor coryi*). Our *in vitro* experiments demonstrate that puma fibroblasts are more susceptible to FeLV infection and produce virus at greater levels than domestic cat fibroblasts. Furthermore, domestic cat infection appears to correlate with enFeLV long terminal repeat (LTR) copy number, but not the enFeLV envelope gene

copy number, a proxy for full-length enFeLV integrations. In naturally infected animals, panthers trended to greater viral antigen load in lymphoid tissue, despite similar FeLV proviral load compared to domestic cats. Our findings suggest that enFeLV-LTR may diminish capacity of FeLV to replicate in cells. Other factors such as innate and acquired immunity likely also contribute to trends in infection and disease progression.

2-101 Microbial dysbiosis and its implications for disease in a genetically depauperate species
Alexandra DeCandia, Princeton University

The microbiome is increasingly recognized as a critical player in health and immunity. Symbiotic microbes have been shown to aid immune development, outcompete pathogenic invaders, regulate immune and metabolic processes, and maintain homeostasis in hosts. When these microbes are disrupted, dysbiosis can contribute to disease state and severity. Thus characterizing healthy and disrupted microbial communities in wildlife populations can inform our understanding of disease pathogenesis and aid conservation management. Santa Catalina Island foxes (*Urocyon littoralis catalinae*) present an ideal case study for these analyses due to their extremely high prevalence of ear canal tumors. Though the precise cause is yet unknown, infection with ear mites (*Otodectes cynotis*) has been linked to sustained ear infections, abnormal cell growth, and tumor development. To better understand these connections, we sequenced the ear canal microbiome and five other body sites in healthy and mite-infected foxes. We characterized microbial community composition, diversity, and evenness, and performed differential abundance testing between groups. We found that healthy foxes exhibited rich communities of diverse microbes, with numerous taxa in high abundance. In contrast, mite infection was associated with reduced diversity and evenness, with the opportunistic pathogen *Staphylococcus pseudintermedius* dominating the community. These results support the hypothesis that ear mites disrupt microbial communities and possibly drive sustained inflammation. They provide further insights into the pathogenesis of this complex system, and contribute to the broader effort of applying microbial sequencing techniques to wildlife populations threatened by disease.

2-102 Changing Antimicrobial Resistance Trends in Kathmandu, Nepal: A 23-Year Retrospective Analysis of Bacteraemia
Sabina Dongol, Oxford University Clinical Research Unit, Patan Academy of Health Sciences, Kathmandu, Nepal

Background: A comprehensive longitudinal understanding of the changing epidemiology of the agents causing bacteraemia and their antimicrobial resistance (AMR) profiles in key locations is crucial for assessing the progression and magnitude of the global AMR crisis.

Methods: We conducted a retrospective analysis of standardised microbiological data from April 1992 to December 2014 at a single healthcare facility in Kathmandu, examining time trends of non-*Salmonella* and *Salmonella*-associated bacteraemia and their corresponding antimicrobial susceptibility profiles.

Results: Over the study period 224,741 blood cultures were performed, of which, 30,353 (13.5%) exhibited bacterial growth. *Salmonella enterica* remained the leading cause of bacterial illness and accounted for 65.4% (19,857/30,353) of all positive blood cultures. *S*. Typhi and *S*. Paratyphi A were the dominant serovars, constituting 68.5% (13,592/19,857) and 30.5% (6,057/19,857) of all isolated *Salmonellae*. An increase in fluoroquinolone non-susceptibility and a decrease in the prevalence of MDR were observed in both serovars. We observed a significant increasing trend in the proportion of MDR non-*Salmonella* Enterobacteriaceae ($p < 0.001$), other Gram-negative organisms ($p = 0.006$), and Gram-positive organisms ($p = 0.006$) over time.

Conclusions: This work describes significant changes in the epidemiology of *Salmonella enterica* in the Kathmandu Valley during the last quarter of a century. We highlight the need to examine current treatment protocols for enteric fever. An increasing burden of bacteraemia associated with MDR non-Salmonella organisms in the community underscores the need for preventing the circulation of MDR bacteria within the local population.

2-103 Integrating data across scales to model the within-host dynamics of emerging viruses
Amandine Gamble, University of California, Los Angeles

Determining the potential for a virus to spill over from its reservoir community to humans requires a quantitative understanding of its replication dynamics within and among host species. Modeling can provide valuable insights on viral dynamics at a hierarchy of biological scales, from the intra-cellular to the individual host levels, and can make unique contributions by integrating empirical evidence across disciplines and scales. However, the limited quantity and diversity of experimental data still represents an important bottleneck for models of viral dynamics and their validation. This is especially true for emerging lethal viruses for which biosecurity constraints and ethical considerations limit experimental data collection. A promising approach to bridge this gap is to incorporate data on fine-scale virological processes that can be studied using engineered biological models such as virus-like particles or pseudotyped viruses. In the present study, we discuss how virological data collected at scales from molecules to animals using different biological models can be integrated together to provide insights on the viral dynamics of henipaviruses. Henipaviruses are emerging viruses classified as biosafety level 4. Some of these viruses, such as Nipah and Hendra viruses, are highly lethal to humans but do not appear to cause disease in bats, which are considered as potential reservoirs. Such a framework could help to develop biological insight and practical predictors of the evolutionary and epidemiological risks posed by potential zoonotic viruses, while also identifying data gaps and guiding future empirical studies.

2-104 Evolution of virulence in a natural epidemic
Camden D. Gowler, University of Michigan

Virulence can evolve rapidly, which can be problematic for hosts when parasites become more virulent. The prominent theory on transient virulence evolution suggests that the optimal evolutionary strategy is to maximize the growth rate (r) at the start of an epidemic and to maximize lifetime reproductive fitness (R_0) over time, as the number of susceptible hosts dwindles. Despite a few classic examples, there is little evidence of virulence evolution in a natural system where neither the host nor parasite is introduced. Here, we took advantage of a natural system where both host and parasites could be collected over the course of an epidemic and then maintained in the laboratory for controlled experiments. We collected zooplankton (*Daphnia dentifera*) hosts infected with the bacterial parasite *Pasteuria ramosa* from three different lakes at several timepoints during the epidemic of this parasite. We cured some hosts of their infections with antibiotics and preserved others as a parasite stock, thus capturing host and parasite genotypes over the course of a natural epidemic. Then, under standard conditions in the lab, we assessed the virulence of parasites on contemporary host genotypes in a controlled experiment. Preliminary results show that, for at least one population, virulence is highest at the start of an epidemic and lowest at the end. For another population, preliminary results suggest a more complicated—but still interesting—story.

2-105 Evaluating the frequency and common drivers of within-host priority effects during coinfection
Fletcher Halliday, University of Zurich

A current frontier in disease ecology is understanding how interactions among parasite species influence their epidemics. Interactions among parasites can result when prior infection by one parasite alters host susceptibility to a second parasite, generating priority effects among parasites. The increasing number of laboratory studies that aim to measure priority effects highlights growing interest among disease ecologists to understand these processes. Yet, laboratory studies, which are implemented at the scale of host individuals, are poorly suited to understand parasite epidemics, which occur at the scale of host populations. To evaluate the role of within-host priority effects during parasite epidemics, we compiled longitudinal datasets of coinfection in host individuals across 11 host and 69 parasite species, including over 25,000 observations of host plants, primates, ungulates, small mammals, birds, and invertebrates. To evaluate the role of within-host priority effects, we performed time-

until event analysis, specifically testing whether infection sequence among co-occurring parasites influenced their risk of infection. Consistent with lab studies, microparasites were most commonly facilitated by prior infection with ectoparasites and macroparasites ($p<0.05$), though parasite type did not predict antagonistic interactions ($p=0.12$). However, the sequence of infection predicted only 10% of the nearly 600 pairwise combinations of potentially interacting parasites. This rarity of within-host priority effects may result from a lack of natural variation in infection sequence, indicating that within-host priority effects may be a less common driver of parasite epidemics than previously thought

2-106 Evolution of stage-specific virulence
Ryosuke Iritani, iTHEMS, RIKEN, Japan

The impact of infectious disease is often very different in juveniles and adults, but theory has focused on the drivers of stage-dependent defense in hosts rather than the potential for stage-dependent virulence evolution in parasites. Stage structure has the potential to be important to the evolution of pathogens because it exposes parasites to heterogeneous environments in terms of both host characteristics and transmission pathways. We develop a stage-structured (juvenile–adult) epidemiological model and examine the evolutionary outcomes of stage-specific virulence under the classic assumption of a transmission-virulence trade-off. We show that selection on virulence against adults remains consistent with the classic theory. However, the evolution of juvenile virulence is sensitive to both demography and transmission pathway with higher virulence against juveniles being favored either when the transmission pathway is assortative (juveniles preferentially interact together) and the juvenile stage is long, or in contrast when the transmission pathway is disassortative and the juvenile stage is short. These results highlight the potentially profound effects of host stage structure on determining parasite virulence in nature. This new perspective may have broad implications for both understanding and managing disease severity.

2-107 Impact of antimicrobial use on resistance in non-target bacterial populations
Clare L. Kinnear, University of Michigan

The emergence of, and selection for antimicrobial resistance is a growing concern for effective treatment of infections. While much consideration is given to the best strategies to minimize selection during treatment, resistance management typically focuses on the infection rather than the whole microbiome. Pathogens that live commensally within the gut, and only opportunistically cause infections, provide an even more complex problem for antimicrobial resistance. In these cases, treatment of the infection not only impacts the infecting population, but may also have an unquantified impact on more readily transmitted populations in the gut.
Vancomycin-resistant enterococcus (VRE) is a leading cause of hospital acquired infection. Due to intrinsic multi-drug resistance, *Enterococcus faecium* blood stream infections have limited treatment options, with daptomycin often being the preferred treatment. In hospitalized patients, colonization of the gut with *Enterococcus* is common, and often observed prior to patients developing a symptomatic infection. We conducted a case-control study to compare resistance profiles and within-host variation in resistance from patients with and without prior daptomycin exposure. Prior systemic use of daptomycin resulted in increased resistance in gut populations of *E. faecium,* with significant differences in within-patient variation. Further, we show that this resistance can emerge rapidly following treatment and both the resistance and the diversity can exist within patients for several months once the drug pressure is removed. Understanding the impact of daptomycin use on the non-target population in the gut may enable development of methods to reduce transmitted resistance.

2-108 The Effects of Vaccination on Dengue Virulence Evolution
Ellie Mainou, Emory University

Theory on pathogen virulence evolution posits that parasites face trade-offs between transmission and the duration of infection, as both cannot simultaneously be optimized. A higher transmission rate requires higher parasite replication, whereas longer durations of infection (e.g., via a lower clearance rate) requires lower parasite

production. Under some circumstances, this trade-off can lead to the evolution of an intermediate level of parasite virulence, which maximizes the parasite's reproduction rate. Such fitness trade-offs have been empirically demonstrated in dengue. Further, a quantitative analysis of these trade-offs indicate that viral transmission potential is maximized at intermediate virulence levels and depends on dengue's epidemiological context. Here, we examine how a licensed dengue vaccine (Dengvaxia) may impact the evolution of virulence of this virus. Dengvaxia is a recombinant live-attenuated, imperfect vaccine that is thought to act like a silent infection. As such, vaccination with Dengvaxia would alter the epidemiological context in which dengue transmits, which in turn should impact virulence-associated selection pressures on the virus. To examine the potential effect of Dengvaxia vaccination on dengue virulence evolution, we develop a nested, multi-scale model of viral replication and transmission. The model includes deterministic within-host dynamics, which differ by host infection status and the virulence phenotype of a viral strain. The model also includes epidemiological dynamics simulated through an individual-based model in a dengue-endemic context. By introducing vaccination into the population, we examine whether Dengvaxia would select for higher-virulence or lower-virulence strains. We place our findings in the context of the imperfect vaccine-driven virulence evolution literature.

2-109 Development of a Reservoir Targeted Vaccine to Control Crimean-Congo Hemorrhagic Fever
Megan C. Mears, The University of Texas Medical Branch, Galveston

Crimean-Congo Hemorrhagic Fever virus (CCHFV), the etiologic agent of the tick-borne, severe zoonotic disease Crimean-Congo Hemorrhagic Fever, is considered a priority pathogen by the WHO, and NIH/NIAID. CCHFV is transmitted in enzootic cycles by the *Hyalomma* tick reservoir among mammals and birds, and is endemic to much of western Asia, the Middle East, Southeastern Europe, and Africa. Human infections are often subclinical, but clinical presentation of severe human disease displays multi-organ failure and hemorrhage, with case fatality rates up to 30%. Despite its wide-spread distribution and life-threatening potential, no vaccines or treatments have been licensed for use against CCHFV. We propose a One Health approach to combat CCHFV through the development of a reservoir targeted veterinary vaccine in addition to other countermeasure efforts. This multitargeted approach will utilize a concealed tick antigen and CCHFV antigen within the veterinary licensed vaccine backbone of Myxoma virus to collapse the transmission cycle of CCHFV. We hypothesize that this approach will offer a sustainable and long-term solution for disease reduction in endemic regions. Future studies will assess the immunogenicity and efficacy of our anti-tick and anti-CCHFV vaccine, with a primary focus on licensure for domestic ruminants and wildlife amplifying hosts.

2-110 Asynchrony between virus diversity and immune selection pressure limits influenza virus evolution
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Seasonal influenza viruses evolve to escape existing antibody-mediated immunity in the human population. As few as one or two amino acid substitutions at key residues can suffice to produce virus antigenic variants that partially escape antibody binding. Given this low mutational barrier, the virus's high polymerase error rate, and potential within-host and population-level selective advantages for escape variant viruses, it is surprising that new antigenic variants are rarely observed within individuals and only proliferate at the population level every 3–8 years. Using mathematical models, we show that natural selection for antigenic novelty is inefficient due to asynchrony between within-host virus diversification and the action of adaptive immune responses. We find that immune selection acts principally at the point of initial virus inoculation, when virus population sizes are very small, and that opportunities for selection later in an infection are rare. Incorporating these within-host dynamics into an epidemic framework, we show that new antigenic variants are frequently generated within infected hosts but only rarely spread beyond that first generator host. Explicitly considering realistic timings of within-host virus and immune dynamics provides a simple mechanistic explanation for the punctuated but noisy trajectory of influenza virus antigenic evolution, the strong selection pressure favoring new antigenic variants at the population level, and the absence of observable antigenic novelty in typical influenza virus infections.

2-111 The dynamics of group A streptococcus pharyngeal and skin colonisation in children at high-risk of acute rheumatic fever

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Background: Group A *Streptococcus* (*Streptococcus pyogenes* or Strep A) is a human-restricted, Gram-positive bacterial pathogen. Strep A causes pharyngitis (sore throat) which if left untreated can lead to the autoimmune condition known as acute rheumatic fever (ARF). Repeated ARF can progress to rheumatic heart disease (RHD), a chronic and life-threatening condition resulting in permanent damage to the heart. Aboriginal Australians living in remote communities experience a high burden of Strep A disease and are 55 times more likely to die from RHD than urban non-Aboriginal people. The increased risk is largely due to the lower socio-economic risk factors experienced by people living in remote communities including poverty, household-crowding and increased distance to health care. Effective prevention strategies are urgently needed to alleviate the burden of Strep A disease in Australia and worldwide. Our surveillance studies in Western Australian communities aim to describe the dynamics of Strep A colonisation to inform selection and evaluation of interventions including new vaccines.

Methods: ~3,400 swabs will be collected from the skin and throat of 600 children in remote school-based settings. Clinical swabs will be interrogated with Strep-A specific quantitative PCR, whole genome sequencing and metagenomics. Strep A density, co-colonisation and multi-genotype carriage will be determined in the context of the throat microbiome.

Significance: We will provide important baseline data for Western Australian Aboriginal children at high risk of Strep A disease. We seek advice for the multi-variable longitudinal analysis that will be conducted to advance the value of the molecular data we will generate.

2-112 Stochastic variation in immune activation in host's and its impact on infection outcomes

Radhika Ravikumar, Cornell University

Severity of an infection is often determined by measuring pathogen load within hosts, a trait that is known to be negatively correlated with the probability of surviving an infection. Inter-individual variation in pathogen burden has, for the most part, been assumed to be a result of genetic variation in hosts' ability to manage pathogen loads. However, a few studies in the recent past have found there to be considerable variation in pathogen burden even when genetically similar hosts are infected with the same strain of pathogen. These observations have led us to develop a model of infection progression that characterizes outcomes of infection as at least partially stochastic. Furthermore, hosts, even when genetically similar, were seen to cluster into two distinct groups based on pathogen burden. These two groups also had very different outcomes of infection: hosts that accumulated a high pathogenic load always succumbed to infection while others survived infection by curtailing pathogen proliferation. Our model of infection progression ascribes this stochasticity to the kinetics of immune-activation. According to our model, as the host immune system attempts to outcompete the pathogen and establish effective immunological control of the infection, stochastic variation in the host's ability to control pathogen growth could lead to differences in inter-individual pathogen loads. Here, using AMP production as a proxy to quantify activation of host immune systems, we test the hypothesis that it is indeed stochastic variation in kinetics of infection response that leads to inter-host differences in pathogen loads, and thereby the outcomes of infection (i.e whether a host survives or not).

2-113 Identifying age cohort effects in influenza infections

Diana Vera Cruz, Duke University

Original antigenic sin (OAS) refers to the proclivity of the host immune system to focus on previously recognized viral epitopes during secondary challenges with related viral strains. This preference is sustained by antibody memory and can paradoxically result in suboptimal immune protection. Integral to the OAS hypothesis is the importance of the initial strain we encounter in our childhood that primes the antibody repertoire to contend against further infections. A number of studies have supported the OAS hypothesis for influenza viruses. One clear

case of OAS was documented during the 2013-2014 influenza season, when an atypically large number of middle-aged individuals became infected with influenza A subtype H1N1. Here, our goal is to identify OAS-driven cohort effects more generally by combining phylogenetic analyses with host age metadata. Central to our analysis is our expectation that a focal clade will differ in the distribution of host birth years from other contemporary clades if one or more antigenic mutations occurred on a lineage at the root of the focal clade. Using sequence data and host age information from individuals infected with H1N1 in the U.S. from 2009 to the present, we performed pairwise comparisons of host age distributions between clades from each of the observed seasons to investigate potential age bias. As hoped for, we identified the known 2013-2014 season instance of OAS-driven anomalous age incidence patterns. We further identified several other instances of possible age cohort effects.

2-114 Malaria drug resistance and vector transmission

Manon Villa, CNRS-IRD, Université de Montpellier

Drug resistance is a major issue for human health and economy. The fate of drug resistant mutations depends on factors which we may be able to control (like molecules we use or their administration), but also on factors over which we have no control, the most important of which is the biological costs that resistance imposes on the fitness of parasites. In drug-treated hosts these costs are largely compensated by the benefits conferred by the resistance. In untreated hosts, however, the magnitude of these costs will determine whether these mutations will persist and spread in the population.

Current views about the costs of drug resistance in malaria parasites are almost entirely based on data regarding parasitic infections in the vertebrate host. Yet, the passage through a mosquito is an essential step in the life cycle of *Plasmodium*. Within mosquitoes the parasites reproduce sexually, differentiate, proliferate and migrate to the salivary glands to ensure transmission to the next host. Costs of drug resistance may be expressed at any one of these stages, profoundly impacting the probability of transmission of drug resistant strains.

The purpose of this project is to investigate the impact of the drugs on malaria transmission. For this purpose, we study: 1)The cost of drug resistance in the vertebrate host and in the vector in the field (*P. falciparum*) and in the laboratory (*P. relictum*). 2)The impact of drug on the vector fitness.

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