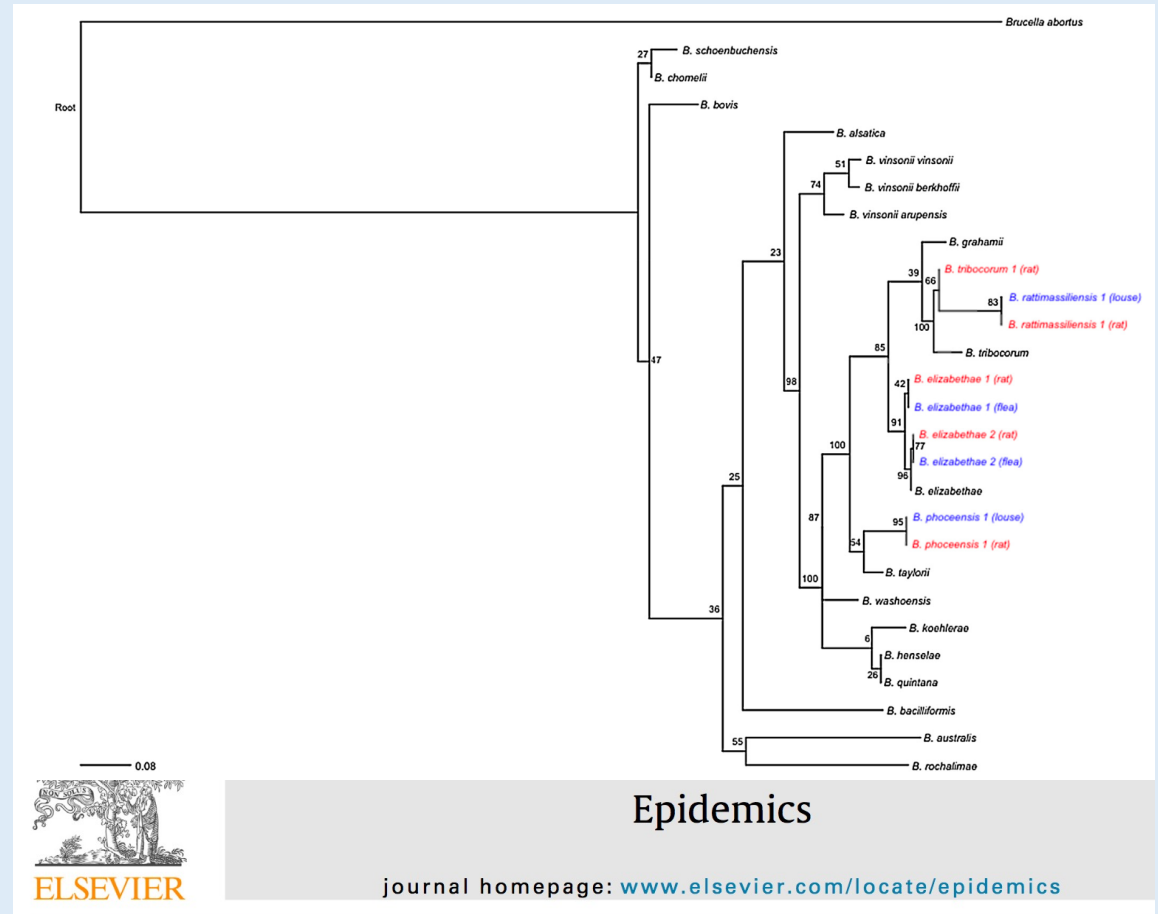


# Transmission dynamics and host-parasite-vector relationships in rodent-borne *Bartonella* spp.

- **Background:** *Bartonella* spp. is an erythrocytic bacterial pathogen of Malagasy rodents with different genotypes which could demonstrate unique transmission mechanisms.
- **Statistical Question:** Is the occurrence of *S. fonquerniei* on Malagasy *R. rattus* related to (a) the indoor/outdoor locality in which the rat is trapped, (b) abundance of *E. gallinacea*, and (c) the abundance of *X. cheopsis* on the same rat?
- **Mechanistic Question:** How can we explain the prevalence of different genotypes of *Bartonella* spp. by age class in Malagasy *Rattus rattus*?
- **Acknowledgements:** Christian and Sophia (readers); Gwen (presentation)

Cara Brook, University of Chicago



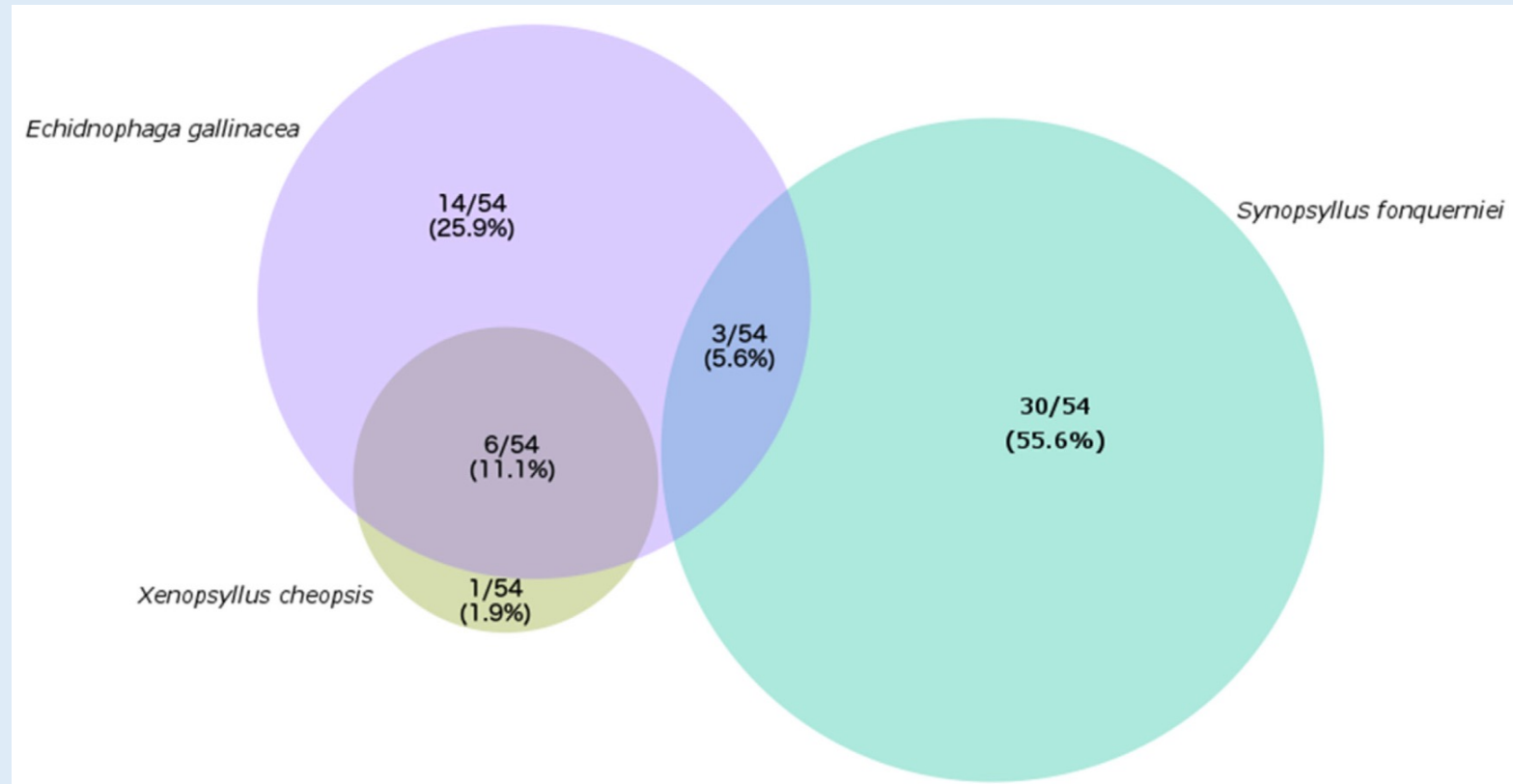
Elucidating transmission dynamics and host-parasite-vector relationships for rodent-borne *Bartonella* spp. in Madagascar

Cara E. Brook<sup>a,\*</sup>, Ying Bai<sup>b</sup>, Emily O. Yu<sup>a</sup>, Hafaliana C. Ranaivoson<sup>c,d</sup>, Haewon Shin<sup>e</sup>, Andrew P. Dobson<sup>a</sup>, C. Jessica E. Metcalf<sup>a,1</sup>, Michael Y. Kosoy<sup>b,1</sup>, Katharina Dittmar<sup>e,1</sup>

## Statistical Question:

Is the occurrence of *S. fonquerniei* on Malagasy *R. rattus* related to (a) the indoor/outdoor locality in which the rat is trapped, (b) abundance of *E. gallinacea*, and (c) the abundance of *X. cheopsis* on the same rat?

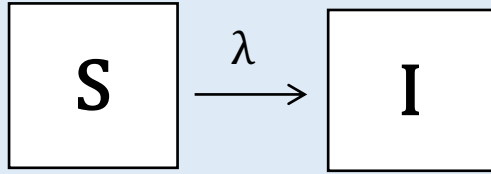
- **Response Variable:** pres/abs *S. fonquerniei*
- **Predictor Variables:** abundance of *E. gallinacea* (numeric); abundance of *X. cheopsis* (factor); indoor/outdoor locality (factor)
- **Family:** “binomial”
- **Link:** logit
- **Hypothesis:** *S. fonquerniei* occurrence is related to low abundance of *X. cheopsis* & outdoor status locality
- **R code:**



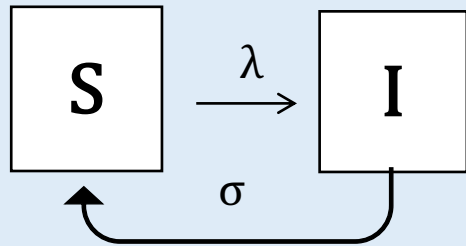
```
glm(pres/abs S. fonquerniei ~ abundance X. cheopsis + abundance E. gallinacea + indoor_outdoor, family="binomial", data = madarat)
```

# Mechanistic Question:

How can we explain the prevalence of different serotypes of *Bartonella* spp. by age class in Malagasy *Rattus rattus*?



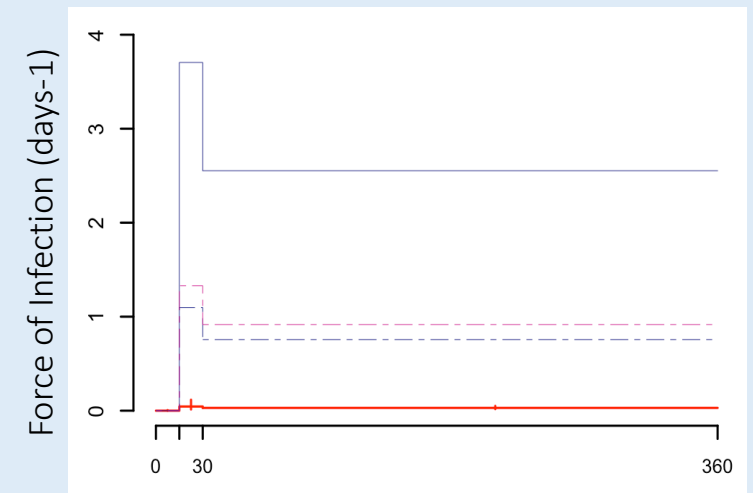
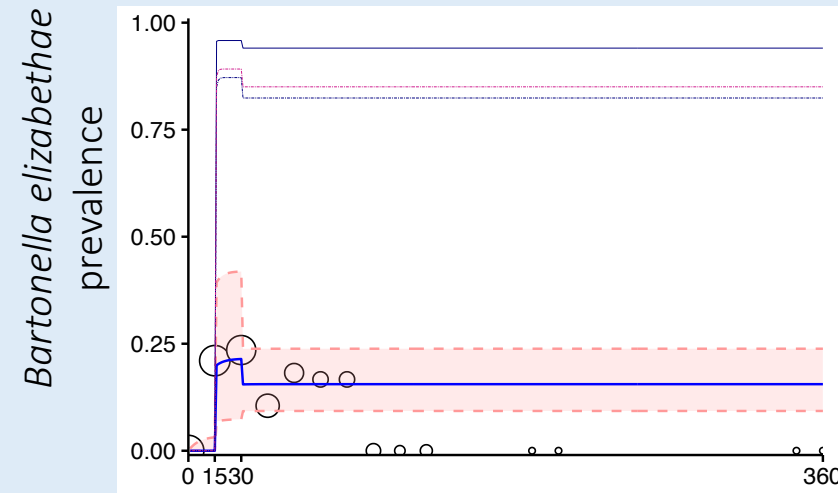
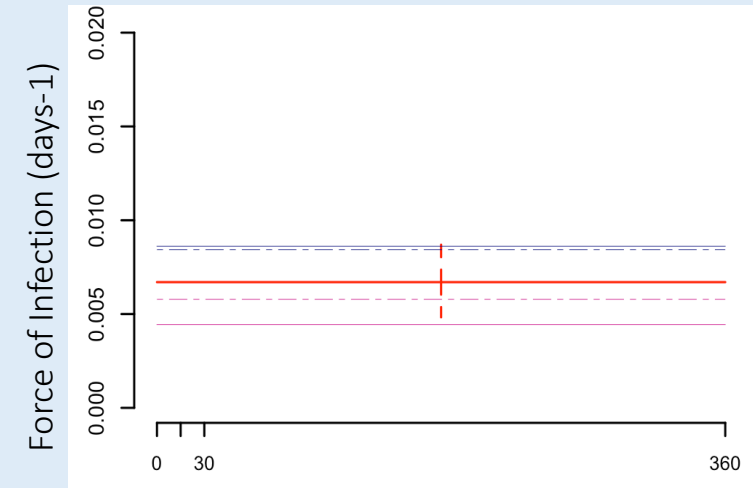
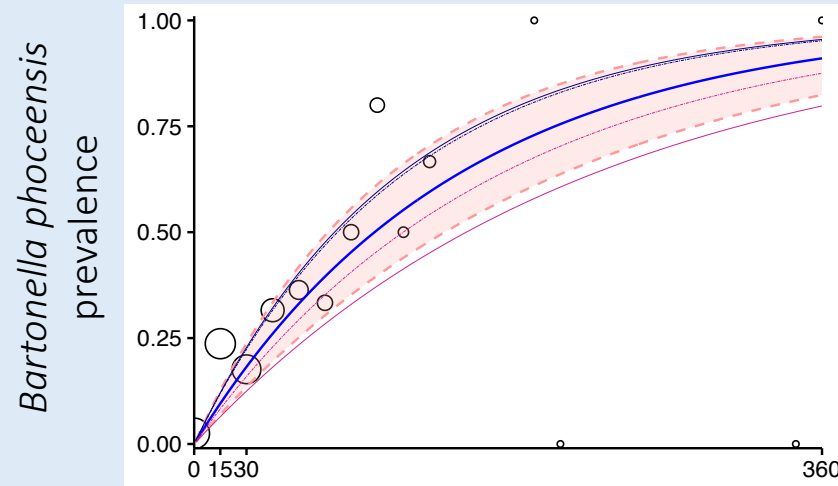
$$\frac{dI(a)}{da} = \lambda(a)(1 - I(a))$$



$$\frac{dI(a)}{da} = \lambda(a)(1 - I(a)) - \sigma I(a)$$

S = susceptible rats  
I = infectious rats

λ = force of infection;  
σ = rate of waning immunity



Age (days)

Age (days)

# Next Steps:

1. Conduct further field studies in lowland regions of Madagascar to determine whether the distribution of *B. elizabethae* is limited to the highland range of *S. fonquerniei*
2. Conduct serological tests on *R. rattus* blood to attempt to identify a whether *Bartonella* spp. negative rats are recovered or susceptible.
3. Fit relevant mechanistic transmission models to age-seroprevalence data.



# Investigating coinfections in the spongy moth-fungus-virus system

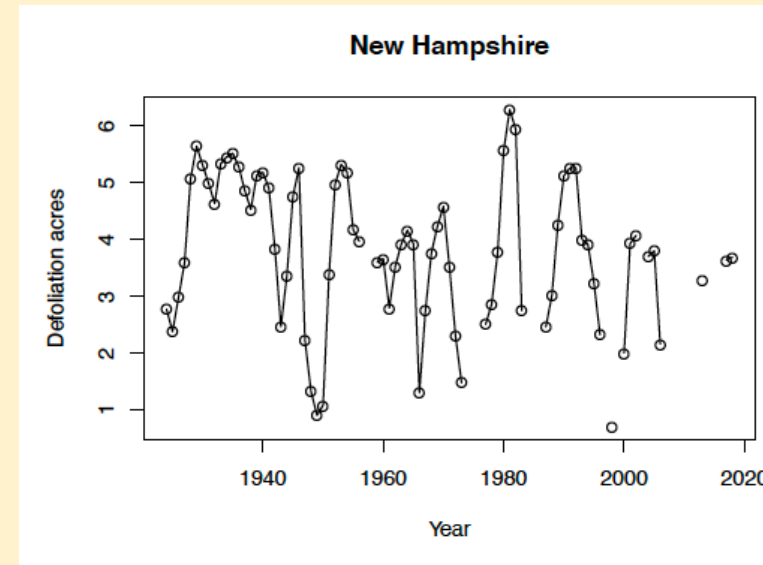
**Background:** The spongy moth, *Lymantria dispar*, is an invasive lepidopteran (family: Lymantriidae) that defoliates hardwood trees across North America. Its population dynamics are driven by epizootics (epidemics in animals) of two fatal, environmentally-transmitted pathogens: a fungus, *Entomophaga maimaiga*, and a baculovirus, *Ld-nucleopolyhedrovirus*. Coinfections are detected in nature, but we do not understand what factors drive the presence of coinfection, or how coinfections influence spongy moth population dynamics.

**Statistical Question:** What is the relationship between environmental factors (rainfall, relative humidity, temperature) and the presence of coinfections?

**Mechanistic Question:** How do coinfections drive spongy moth population dynamics?

**Acknowledgements:** Christian and Cara (readers); Gwen (presentation)

Sophia Horigan, University of Chicago



## Statistical Question:

What is the relationship between environmental factors and the presence of coinfections?

**Response Variable:** cumulative number of coinfections in a population

**Predictor Variable:** temperature, relative humidity, rainfall, site

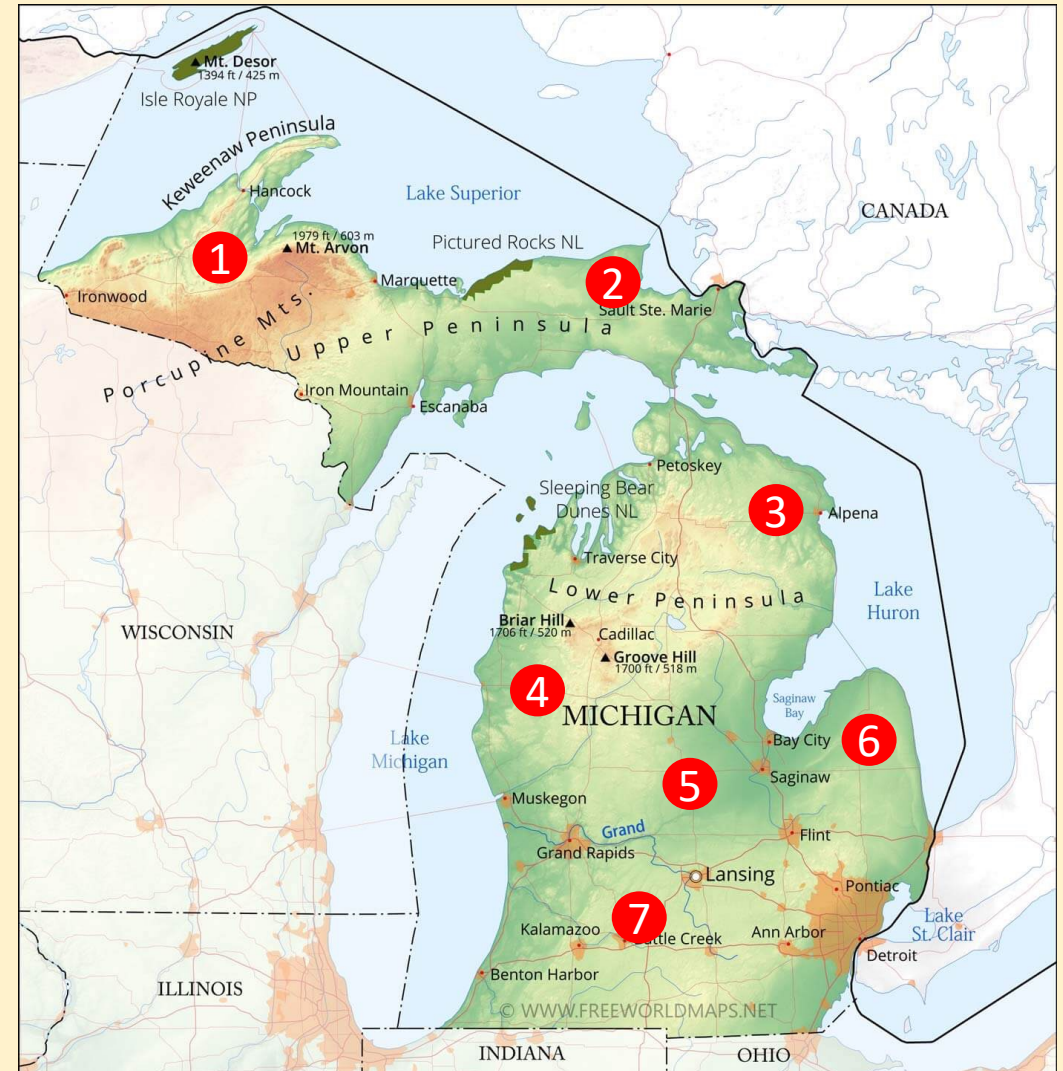
**Family:** “poisson”

**Link:** log

**Hypothesis:** Sites with higher rainfall, higher humidity, and moderate temperatures will have a higher number of cumulative coinfections.

**R code:**

```
glmer(cum. # coinfections~rainfall + temperature + relative humidity + (1| site), family = “poisson”, data=infection.data)
```



## Mechanistic Question:

How do coinfections drive spongy moth population dynamics?

### States

S – susceptible caterpillars

$I_{f,E}$  – early fungus infected

$I_{f,L}$  – late fungus infected

$I_{v,E}$  – early virus infected

$I_{v,L}$  – late virus infected

$I_{fv}$  – coinfecting

F – fungal spores in the environment

V – viral particles in the environment

### Parameters

$\beta_f$  – fungus transmission

$\beta_v$  – virus transmission

$\delta_f$  – progression to late fungus infection

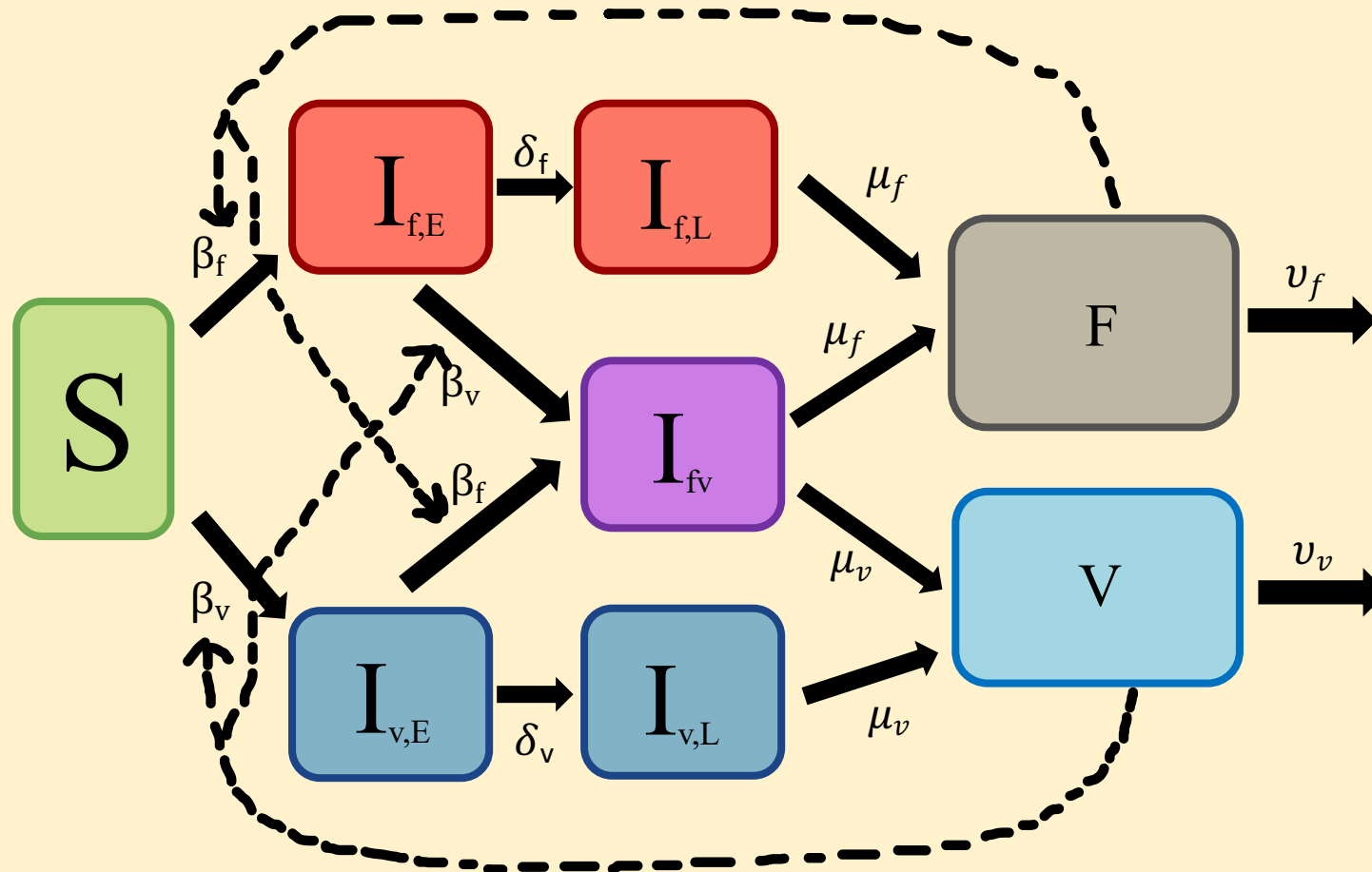
$\delta_v$  – progression to late virus infection

$\mu_v$  – conversion of dead insect to virus particles

$\mu_f$  – conversion of dead insect to fungal spores

$\nu_f$  – fungal spore decay

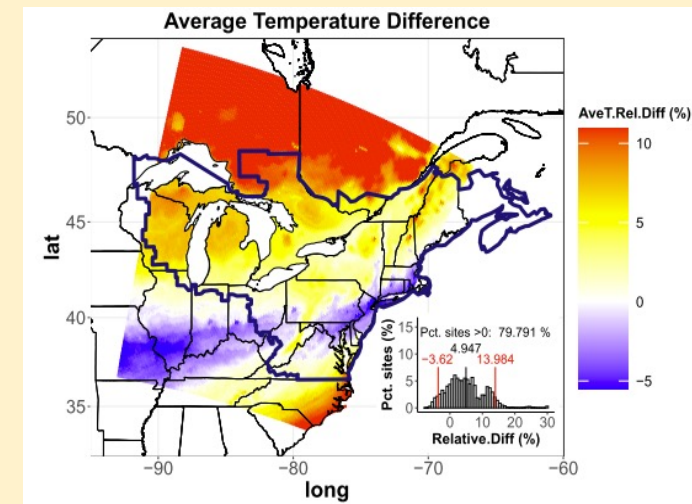
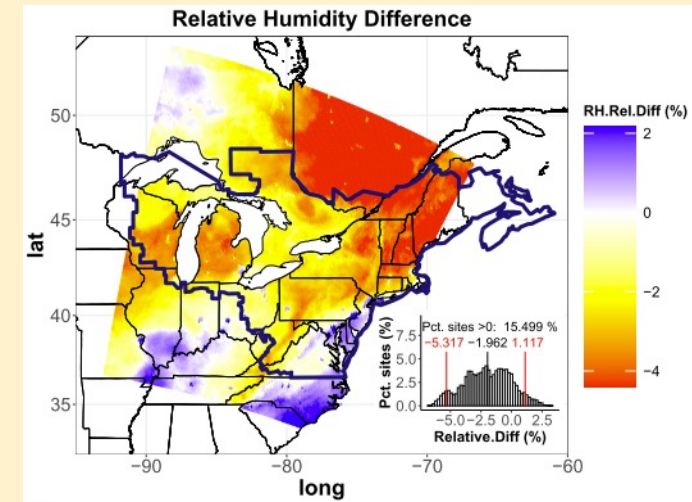
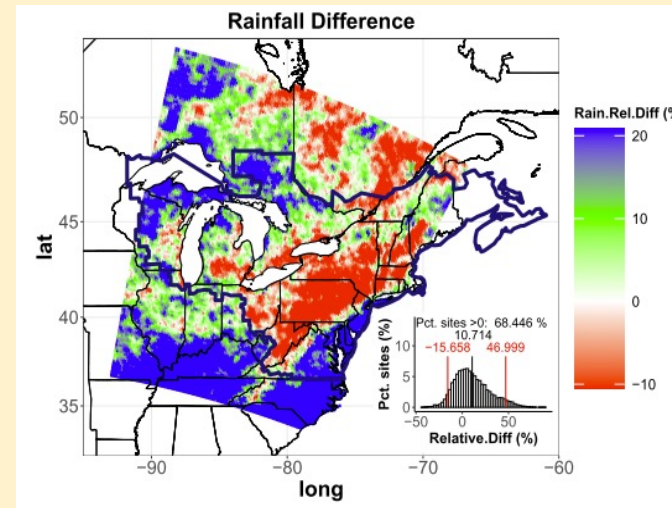
$\nu_v$  – viral particle decay



# Investigating coinfections in the spongy moth-fungus-virus system

## Next Steps:

1. Conduct field sampling at all sites for at least two more years to get infection data across a range of annual weather conditions.
2. Fit the mechanistic model to field data.
3. Extend the model to long-term dynamics by incorporating spongy moth reproduction and pathogen overwintering dynamics.
4. Use the long-term model to predict the future of spongy moth populations under climate change.





# Age mediated viral shedding in Malagasy fruit bats



**Background:** Previous work in our lab has shown that age class and sex of bats impacts seroprevalence for henipaviruses and filoviruses. However, we do not know how viral shedding in bats from active infections impact age-seroprevalence.

**Statistical question:** How does age class drive viral load in Malagasy fruit bats?

**Mechanistic question:** How does viral shedding differ between juvenile and adult Malagasy fruit bats?

Acknowledgement to people who have evaluated these models:  
Cara Brook, Sophia Horigan (readers); Nuzha (presentation)

Disentangling serology to elucidate henipa- and filovirus transmission in Madagascar fruit bats

[Cara E. Brook](#),<sup>1, 8</sup> [Hafaliana C. Ranaivoson](#),<sup>2, 3</sup> [Christopher C. Broder](#),<sup>4</sup> [Andrew A. Cunningham](#),<sup>5</sup>  
[Jean-Michel Héraud](#),<sup>2</sup> [Alison J. Peel](#),<sup>6</sup> [Louise Gibson](#),<sup>5</sup> [James L. N. Wood](#),<sup>7</sup> [C. Jessica Metcalf](#),<sup>1, †</sup> and  
[Andrew P. Dobson](#)<sup>1, †</sup>

# Statistical question: How does age class of Malagasy fruit bats mediate viral load?

**Hypothesis:** Adult bats shed more virus than juvenile bats

**Response variable:** presence/absence of coronavirus, filovirus, lyssavirus, and/or henipavirus

**Predictor variable:** age, bat species, virus family

**Distribution:** “binomial”

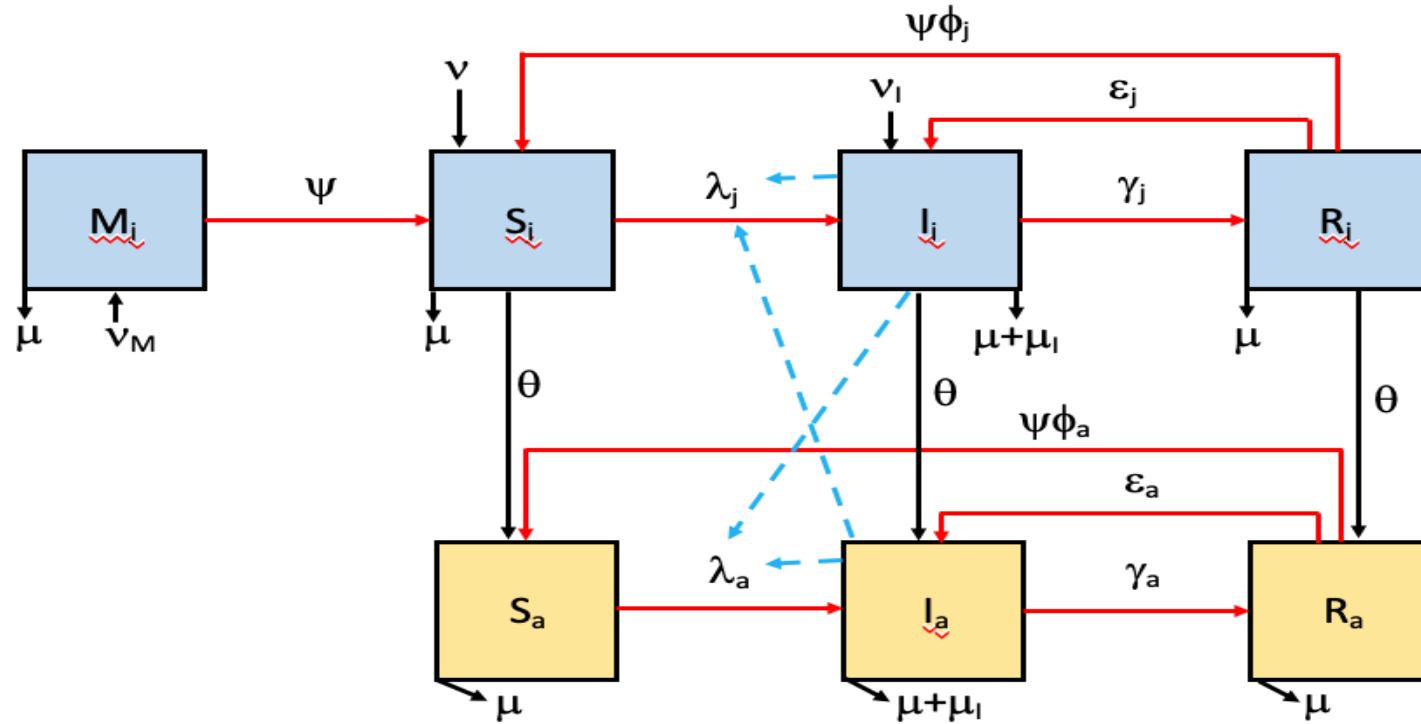
**Linker:** logit

**R function:** `glmer(presence/absence virus~age+(1|bat/virus), family="binomial", data=mada.bat.age.virus.shedding`

Nest virus family in bat fam as rndm effect for glmer

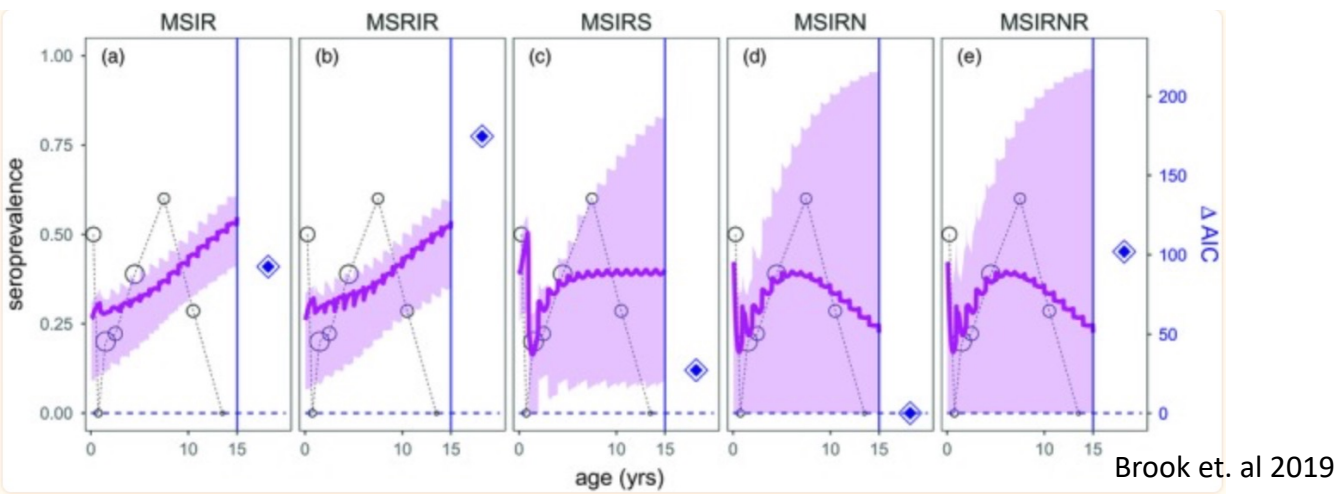
Species	Viral family	PCR pos/neg ratios	Age
E. dupreanum	Coronavirus	10/90 n=100	Each indiv. has an age associated with it
	Filovirus	0/100 n=100	Each indiv. has an age associated with it
	Lyssavirus	12/68 n=100	Each indiv. has an age associated with it
	Henipavirus	25/75 n=100	Each indiv. has an age associated with it
R. madagascariensis	Coronavirus	8/92 n=100	Each indiv. has an age associated with it
	Filovirus	2/98 n=100	Each indiv. has an age associated with it
	Lyssavirus	17/83 n=100	Each indiv. has an age associated with it
	Henipavirus	0/100 n=100	Each indiv. has an age associated with it
P. rufus	Coronavirus	9/91 n=100	Each indiv. has an age associated with it
	Filovirus	0/100 n=100	Each indiv. has an age associated with it
	Lyssavirus	10/90 n=100	Each indiv. has an age associated with it
	Henipavirus	0/100 n=100	Each indiv. has an age associated with it

# Mechanistic question: How does viral shedding differ between juvenile and adult Malagasy fruit bats?



Parameter	Description
M	Maternally immune
S	Susceptible
I	Infectious/infected
R	Recovered

Parameter	Description
$v$	Births
$v_M$	Births from maternally immune adults
$v_i$	Births from infected/infectious adults
$\mu$	Deaths
$\mu_i$	Deaths from infection
$\lambda_j$	Virus transmission rate in juveniles
$\lambda_a$	Virus transmission rate in adults
	Recovery rate in juveniles
$\gamma_a$	Recovery rate in adults
$\psi$	Maternal antibody waning
$N_j$	Juvenile population size
$N_a$	Adult population size
$\phi_j$	Antibody waning, susceptible again in juveniles
	Antibody waning, susceptible again in adults
$\varepsilon_j$	Persistently infected or latent in juveniles, infected->infectious or latent->infectious
$\varepsilon_a$	Persistently infected or latent in adults, infected->infectious or latent->infectious
$\theta$	Aging rate from juvenile to adult



Brook et. al 2019

# Next steps:

- Generate family level PCR data for coronaviruses, lyssaviruses, filoviruses, henipaviruses (presence/absence data)
- Use Sanger sequencing from positive hits to design specific virus primers
- Generate qPCR data for above viruses (quantitative data)
- Fit relevant mechanistic model to relevant age-qPCR data for each viral family.

