

Eco-evolutionary dynamics of pathogen virulence

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Outline

1 Overview

- The evolution of host-pathogen theory
- Toy models

2 Transient virulence and emerging diseases

- Overview
- Toy model
- Myxomatosis data

3 Transient virulence and seasonality

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- Toy model
- WNV data

4 More on theory vs. data

- Tradeoff curves
- Conclusions

Acknowledgements

People Arjun Nanda and Dharmini Shah; Christophe Fraser;
Marm Kilpatrick; Anson Wong

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Discovery grant

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Host-pathogen evolutionary biology

Why is it interesting?

- Intellectual merit
 - Coevolutionary loops
 - Cryptic effects
 - Eco-evolutionary dynamics (Luo and Koelle, 2013)
 - Cool stories
 - Lots of data (sometimes)
- Broader applications
 - Medical
 - Conservation and management
 - Outreach

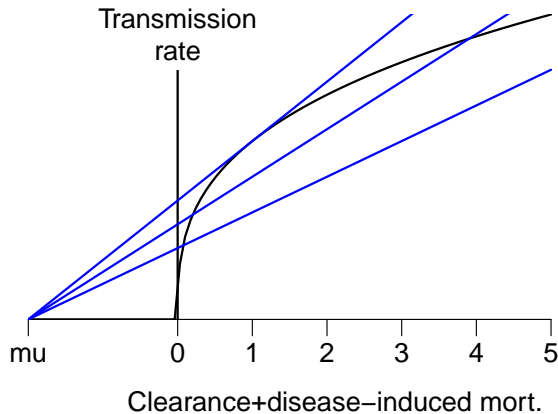
Host-pathogen evolutionary biology

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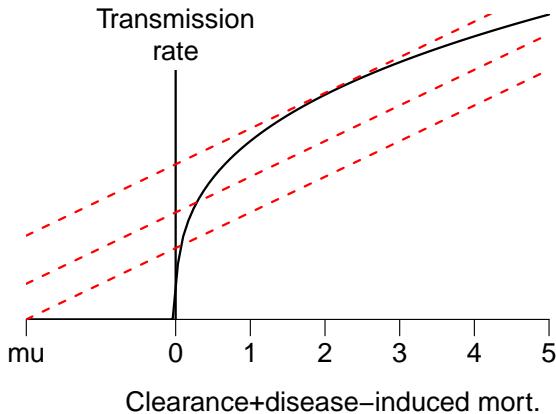
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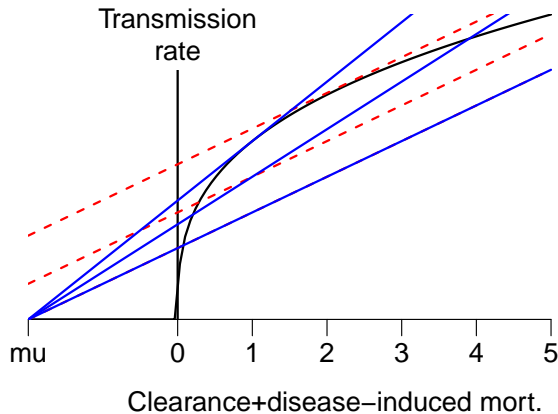
Basic tradeoff theory: assumptions

- Homogeneous, non-evolving hosts
- No superinfection/coinfection
- Horizontal, direct transmission
- Tradeoff between *rate* of transmission and length of infectious period
- Infectious period $\propto 1/\text{clearance}$
(= recovery+*disease-induced mortality*+*natural mortality*)

Tradeoffs, \mathcal{R}_0 , and r 

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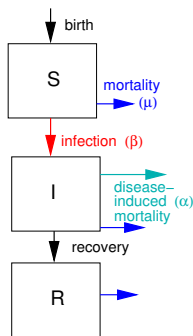
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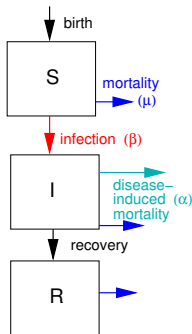
Epidemiological model

- SIR model
- Constant population size (birth=death)
- Ignore recovery
- Rescale: $\mu = 1$, $N = 1$ (time units of host lifespan)



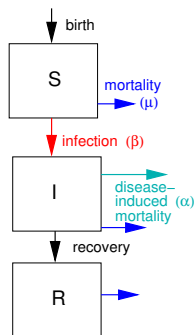
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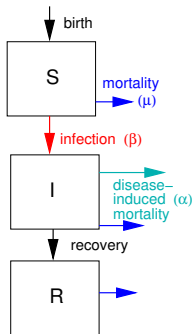
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The model (2): evolutionary dynamics

Incorporate *trait dynamics*

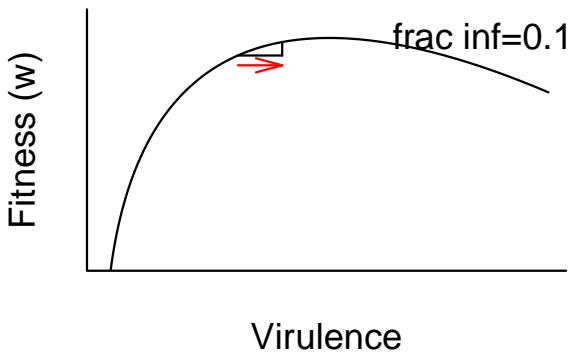
Standard quantitative genetics model (Abrams, 2001):

- Fitness depends on mean trait value ($\bar{\alpha}$)
and ecological context (proportion susceptible)
- Constant additive genetic variance V_g
- Trait evolves toward increased fitness:
rate proportional to $\Delta\text{fitness}/\Delta\text{trait}$

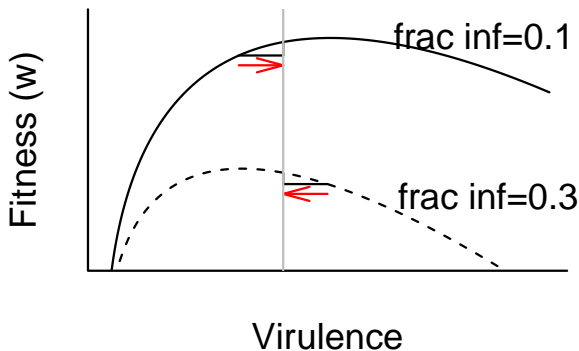
Alternatives:

multi-strain, adaptive dynamics, PDEs, agent-based models ...

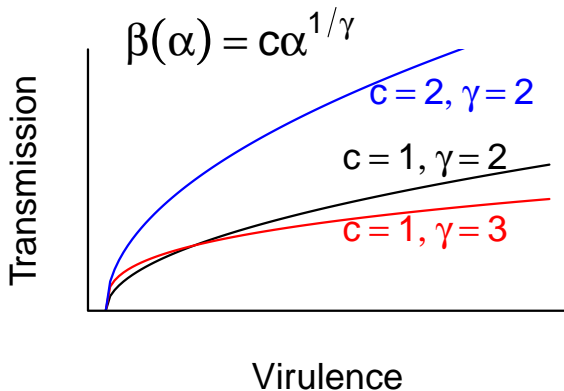
Evolutionary dynamics, cont.



Evolutionary dynamics, cont.



Power-law tradeoff curves



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(Why) are emerging pathogens more virulent?

What might explain initially high, but rapidly decreasing, virulence of emerging pathogens?

- Pathogens with low virulence go unnoticed
- Hosts less resistant to / tolerant of novel parasites
- High transmission → frequent coinfection → selection for virulence
- Disease-induced drop in population density decreases selection for virulence (Lenski and May, 1994)

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Transient emerging virulence

When a parasite previously in eco-evolutionary equilibrium emerges in a new host population (at low density) it will show a transient peak in virulence as it spreads

How big is the peak? Does it matter?

Model parameters

Parameter		Alternative	
c	Transmission scale	\mathcal{R}_0^*	Equilibrium \mathcal{R}_0
γ	Transmission curvature	α^*	Equilibrium virulence
$I(0)$	Initial epidemic size	$1/N_0$	Inverse population size
V_g	Genetic variance		

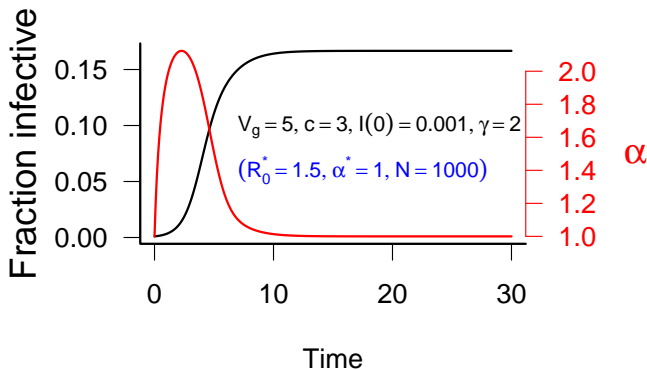
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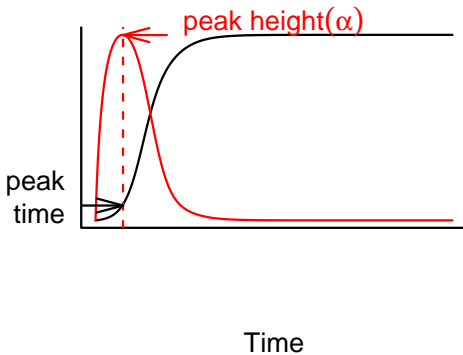
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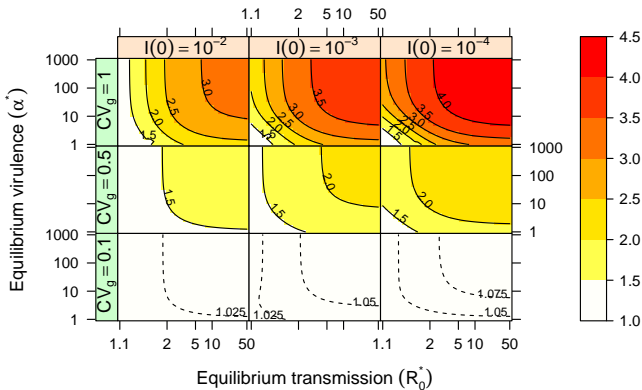
Example



Response variables



Peak height



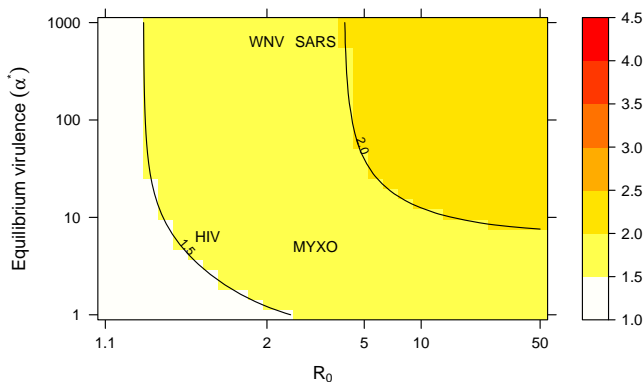
Estimates for emerging pathogens

Order of magnitude estimates for some emerging high-virulence pathogens:

Pathogen	R_0^*	α^*	Reference
SARS	3	640	Anderson et al. (2004)
West Nile	1.61–3.24	639	Wonham et al. (2004)
HIV	1.43	6.36	Velasco-Hernandez et al. (2002)
myxomatosis	3	5	Dwyer et al. (1990)

Emerging pathogens: where are we?

$CV_g = 0.5$, $I(0) = 10^{-3}$ (middle panel):



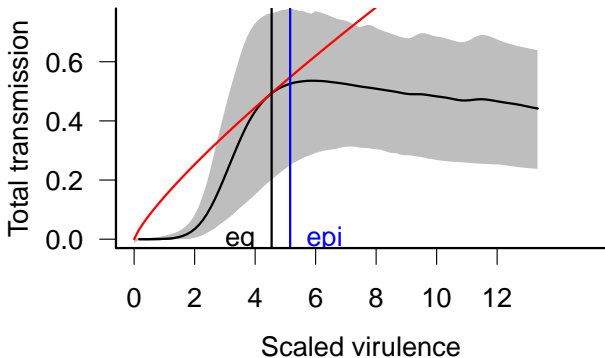
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Overview

- Mosquito-borne viral disease of rabbits
- Benign in South American rabbits, quickly fatal in European rabbits
- Well characterized (Fenner et al., 1956; Dwyer et al., 1990)

Myxomatosis tradeoff curve



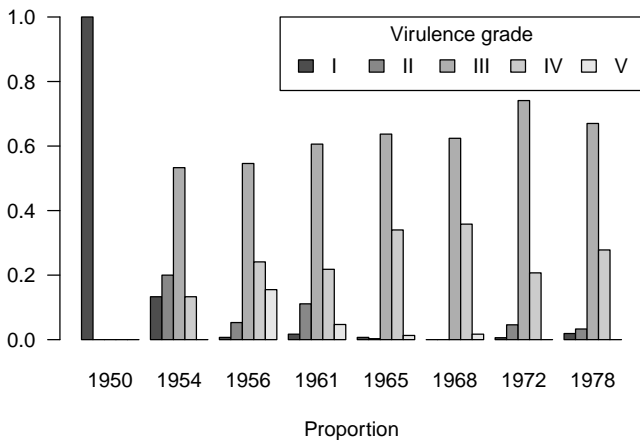
Estimating evolvability (V_g)

- Key parameter: genetic variance in virulence (evolvability)
- Despite case studies of rapid pathogen evolution:
 - myxomatosis (Dwyer et al., 1990)
 - syphilis (Knell, 2004)
 - serial passage experiments (Ebert, 1998)
 - *Plasmodium chabaudi* (Mackinnon and Read, 1999a)

we rarely have enough information to estimate V_g

- Only (?) for myxomatosis do we know the variation in virulence among circulating strains

Myxomatosis grades vs. time



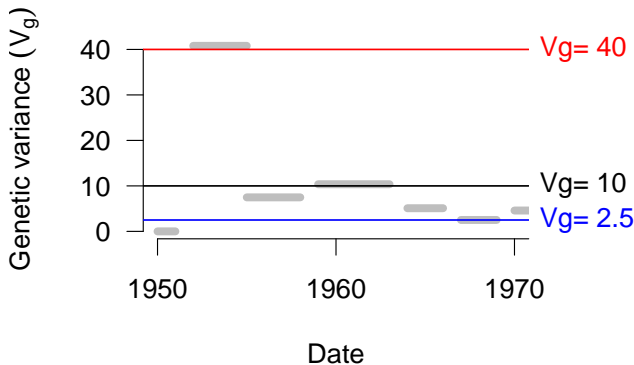
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Myxomatosis variance vs. time



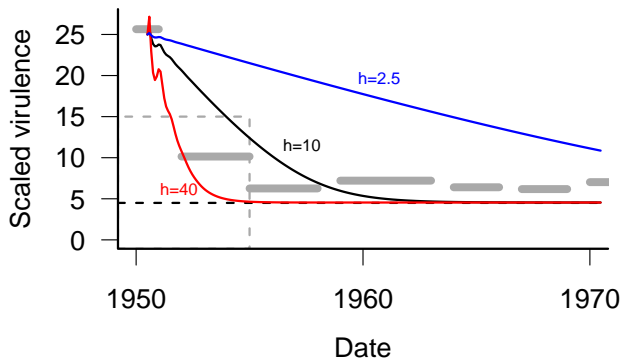
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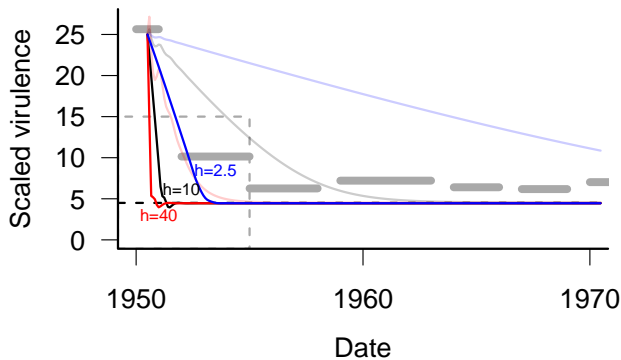
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Myxomatosis virulence dynamics: power-law tradeoff



Myxomatosis virulence dynamics: realistic tradeoff



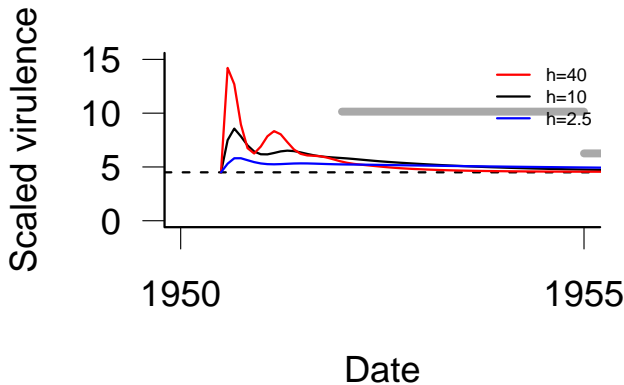
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Myxo virulence: equilibrium start, power-law tradeoff



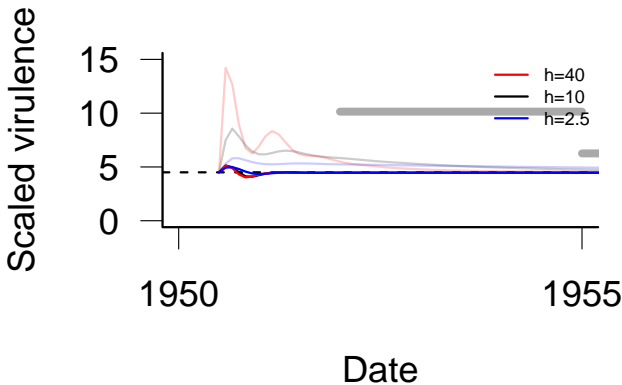
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Myxo virulence: equilibrium start, realistic tradeoff



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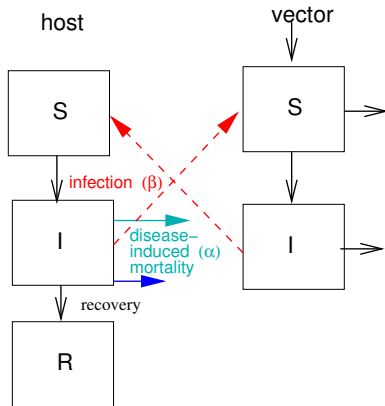
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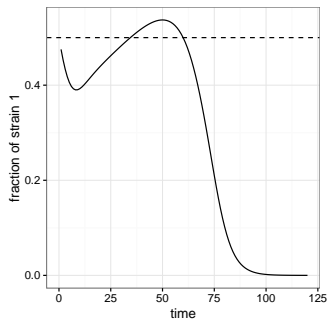
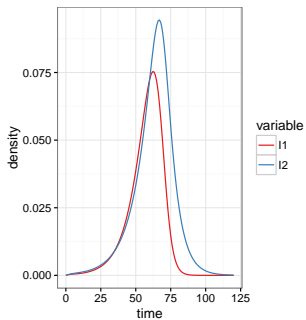
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Toy model

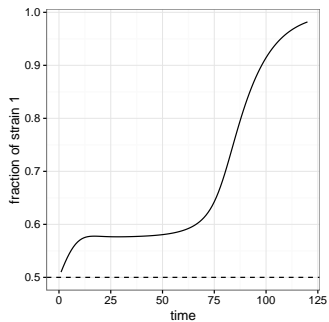
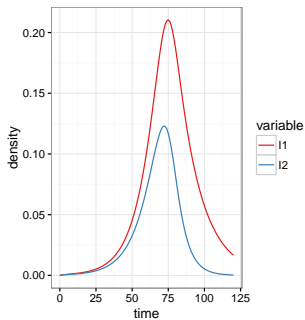
- Basic Ross-MacDonald vector-host model
- Simple vector (mosquito) demography
- No host demography
- Two pathogen strains



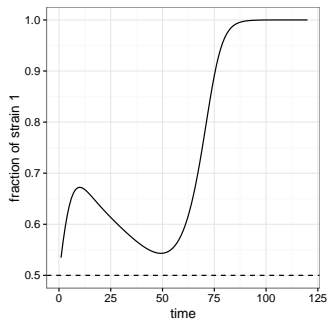
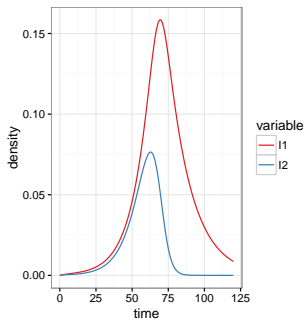
Case I: $r_1 > r_2$, equal \mathcal{R}_0



Case II: $\mathcal{R}_{0,1} > \mathcal{R}_{0,2}$, equal r



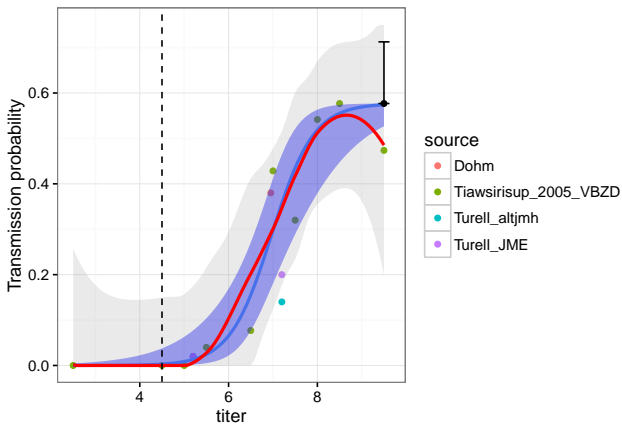
Case III: $\mathcal{R}_{0,1} > \mathcal{R}_{0,2}$, $r_2 > r_1$



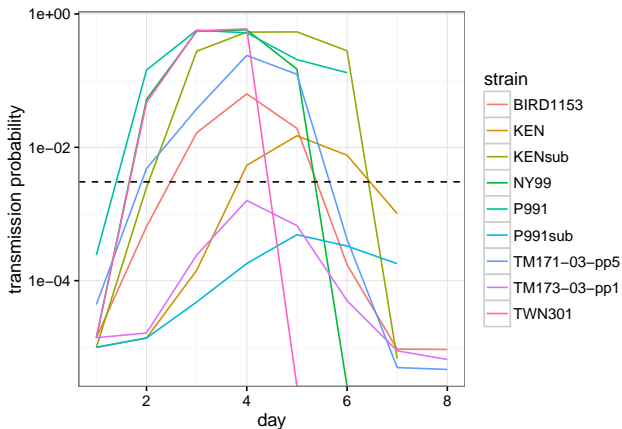
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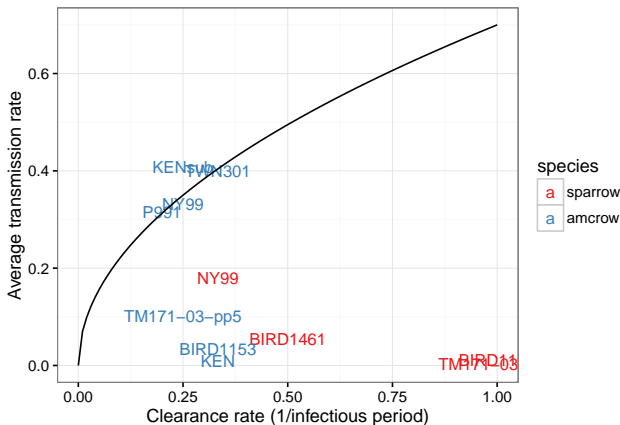
Titer vs infectiousness



Titer curves (American crows)



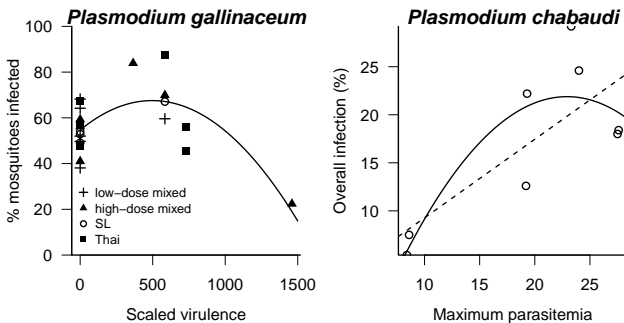
Transmission vs clearance for WNV



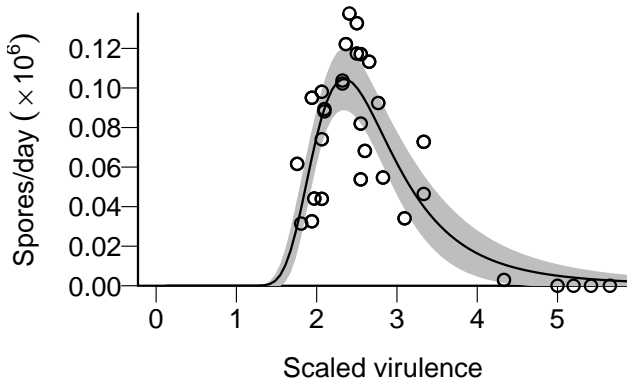
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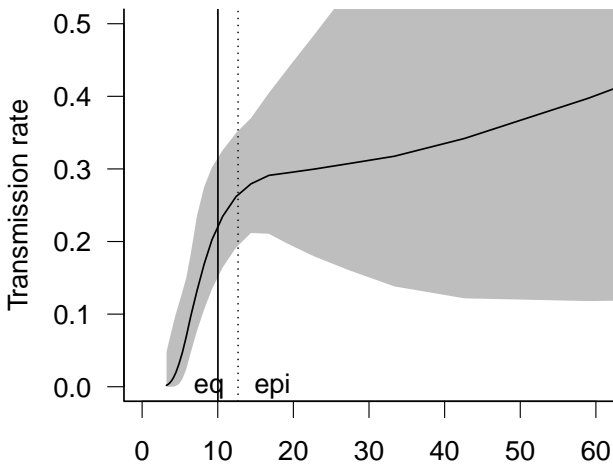
Malaria (Mackinnon and Read, 1999b; Paul et al., 2004)



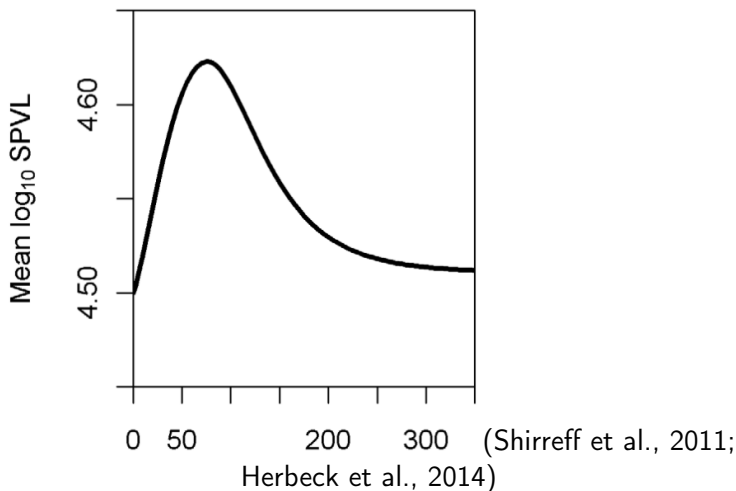
Pasteuria ramosa (Jensen et al., 2006)



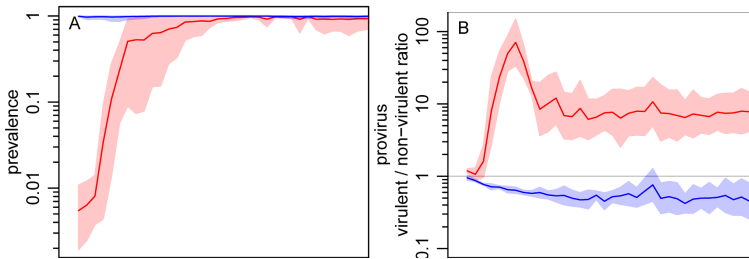
HIV (Fraser et al., 2007)



HIV dynamics (Shirreff et al., 2011)



Phage dynamics (Berngruber et al., 2013)



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- Eco-evolutionary dynamics of virulence are still plausible (Alizon et al., 2009; Luo and Koelle, 2013)
- Sensitive to genetic variance and shape of tradeoff curve
- Theory meets molecular biology: mutations of large effect vs. quantitative variability

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Crome (1997) on theory

When we regard theories as tight, real entities and devote ourselves to their analysis, we can limit our horizons and, worse, attempt to make the world fit them. A lot of ecological discussion is not about nature, but about theories, generalizations, or models supposed to represent nature . . .

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