HIV virulence evolution in structured epidemic models

Ben Bolker and Sang Woo Park

McMaster University, Hamilton, Ontario, Canada

McMaster University

Michael G. DeGroote
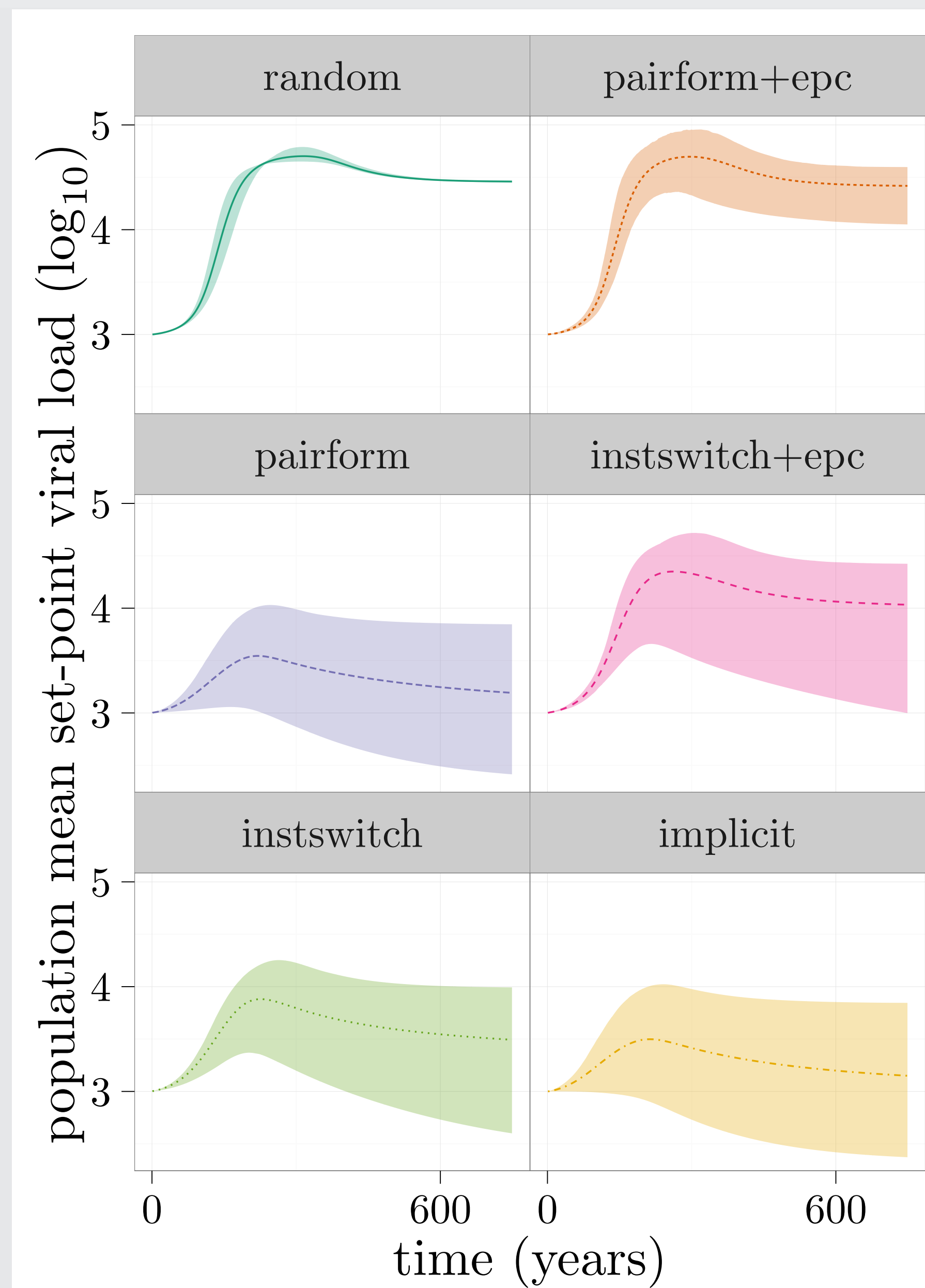INSTITUTE FOR INFECTIOUS DISEASE RESEARCH

Summary

Pathogens can evolve rapidly in response to changing conditions (e.g., epidemic stage or public health interventions). Models of **eco-evolutionary dynamics** often neglect important epidemiological processes, such as the dynamics of sexual partnerships. We compared **models with a range of complexity** of partnership dynamics and extra-partnership contact.
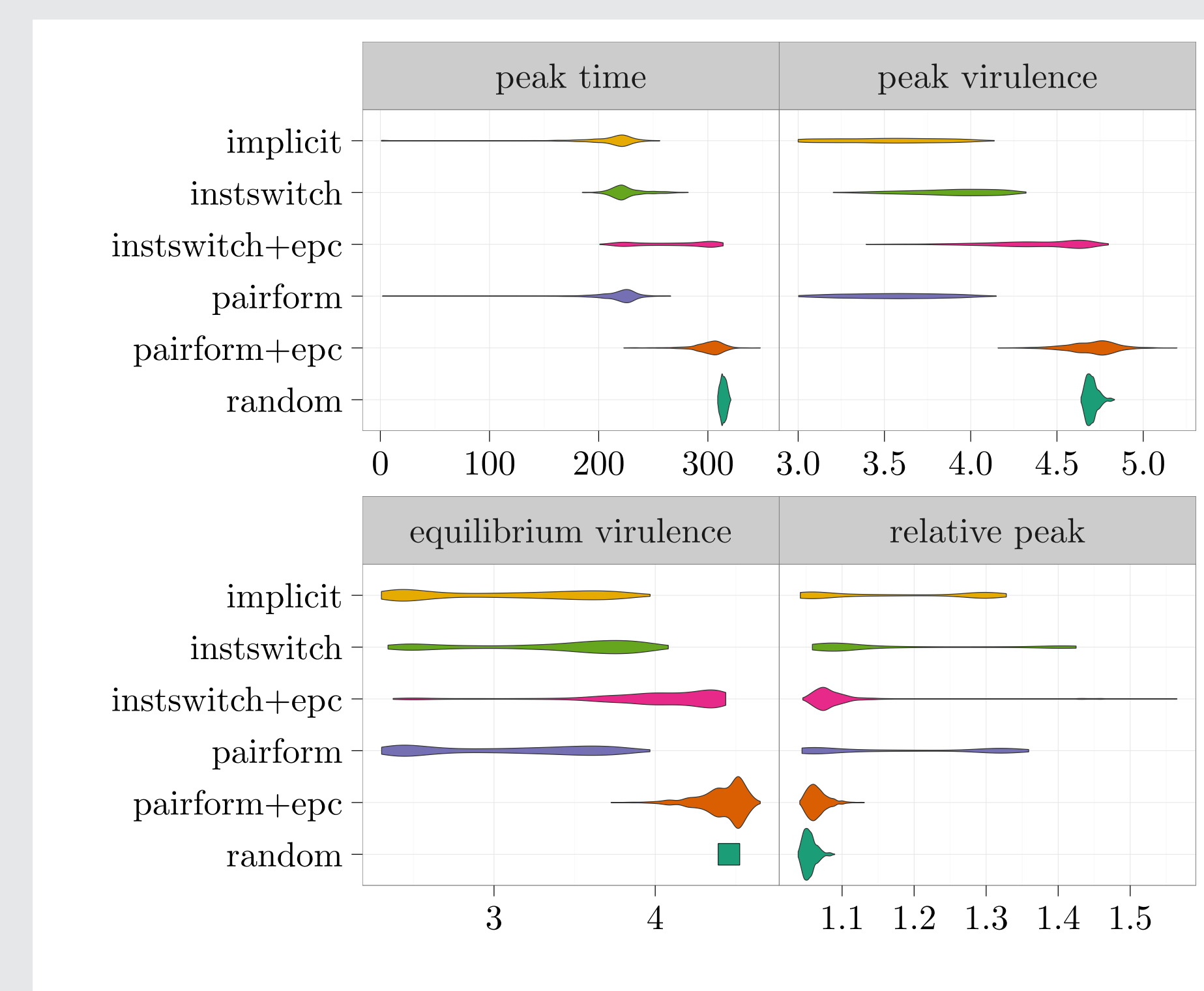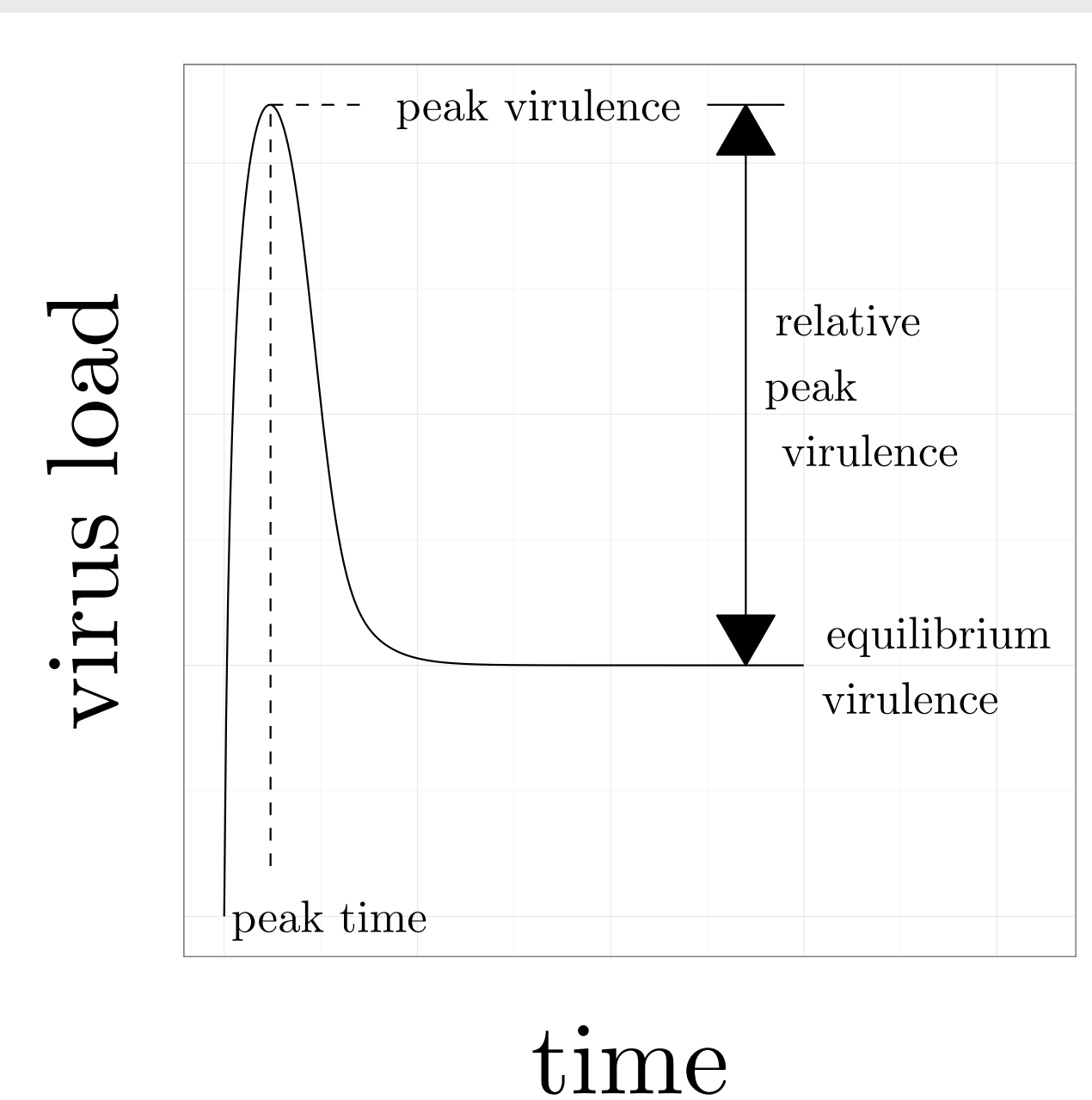
Tradeoff theory
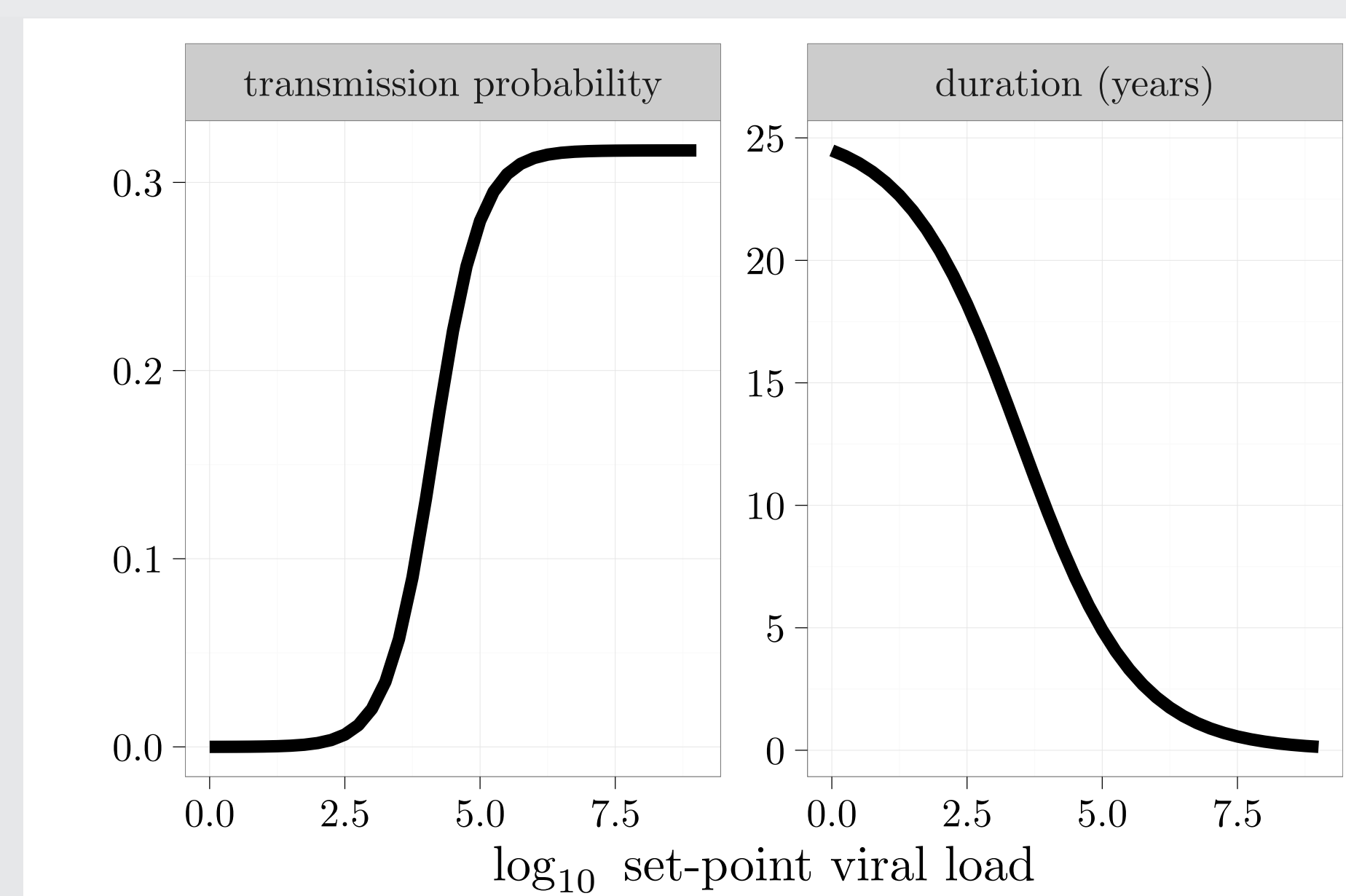
- virulence evolution mediated by transmission-vs-clearance tradeoff
- still debated [1, 2]
- HIV [3]: **set-point viral load** ($\approx$ "virulence") correlated with transmission probability, rate of progression to AIDS (data from Rakai, Uganda)
- eco-evolutionary virulence dynamics: [4]

Epidemiological structure

Champredon *et al.* 2013 [5]

infection from (1) infected partner (*SI* couples); (2) other coupled inf.; (3) uncoupled inf.

Simplified disease model (single stage only)

- **pair formation**: instantaneous or delayed?
- **extra-pair contact** (epc): present or absent?
- **implicit model**: no explicit partnerships, force of infection expression derived from $\mathcal{R}_0$ of pair-formation model (without epc)
- **random-mixing model**: standard SIR model

Parameter uncertainty/exploration

- Latin hypercube sampling: parameters from [5]
- parameters calibrated across models to the same **initial epidemic growth rate** (r)

Eco-evolutionary dynamics
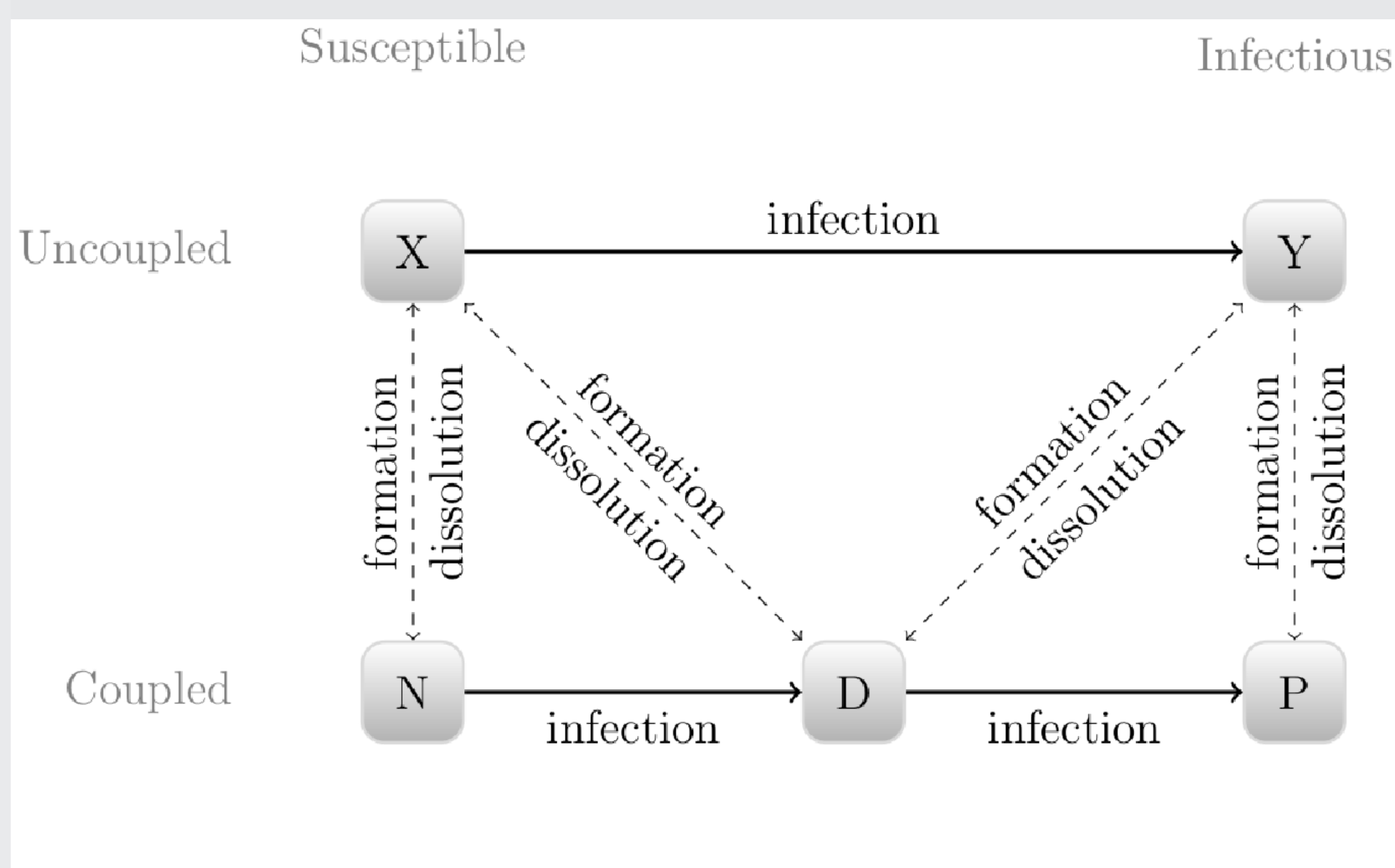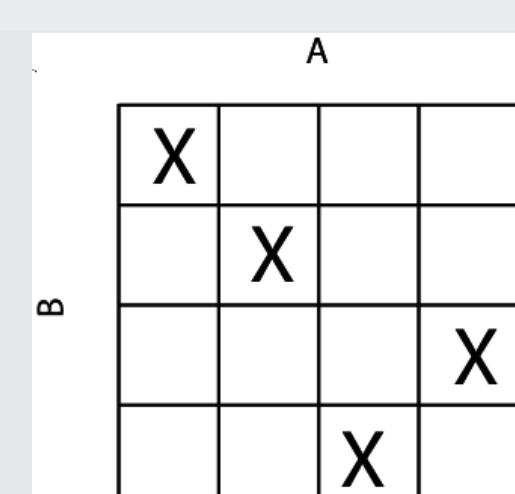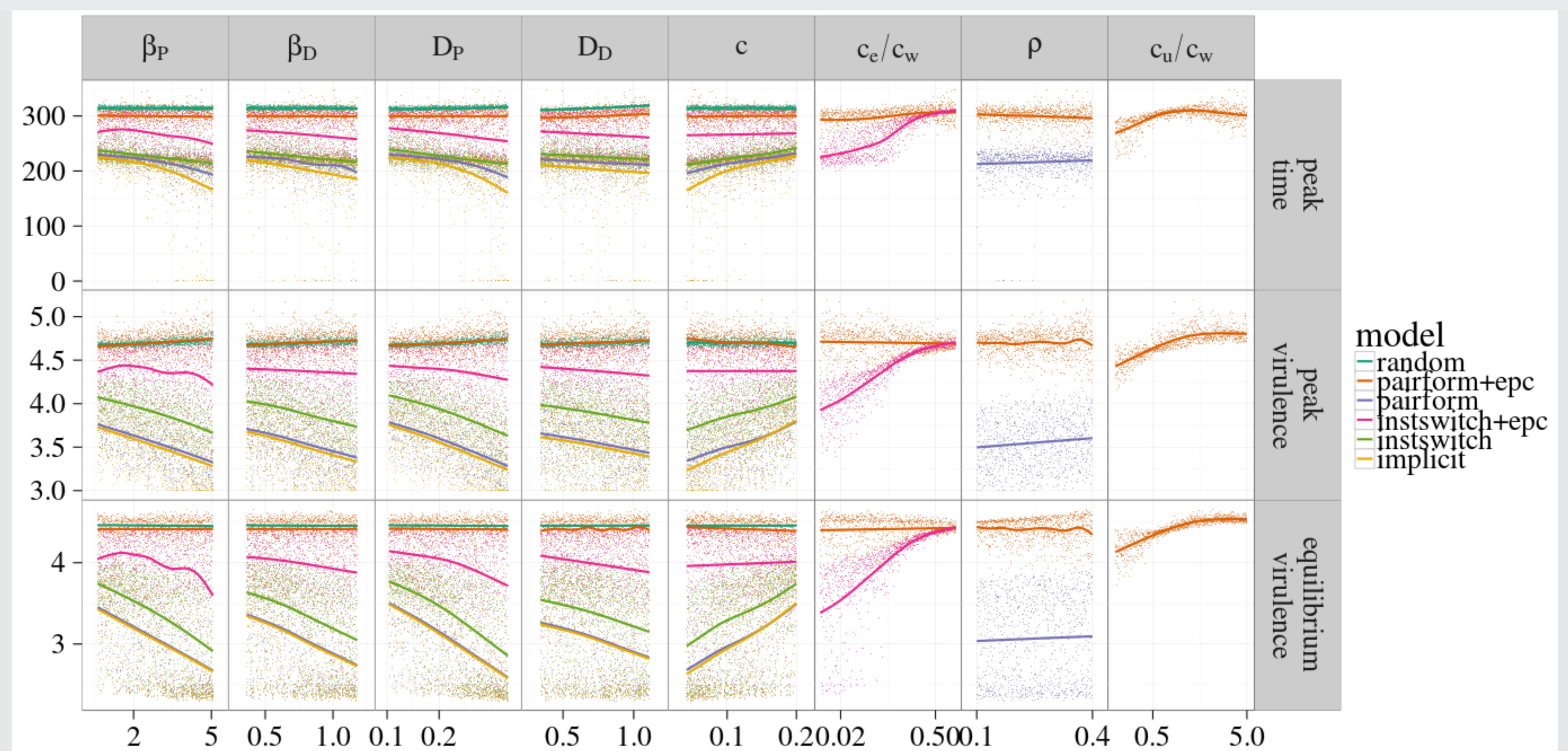

- **80% of total variability** in peak SPVL is among- vs. within-model
- least (random) and most (pairform+epc) models **most similar**: single individuals and extra-pair contact wash out effects of structure
- implicit model is **most different**
- random-mixing model underestimates variability

Sensitivity

- $\beta_{P,D}$: early/late-stage transmission probability; $D_{P,D}$: early/late-stage duration; c: partnership dissolution rate; c_e/c_w: extra- vs within-pair contact ratio; ρ: partnership formation rate; c_u/c_w: uncoupled contact rate ratio

Conclusions and open questions

- Random-mixing models best matched the most realistic models; extra-pair and uncoupled individuals washed out the effects of epidemiological structure
- Implicit models did worst
- Variation among models (model structure) $\gtrsim$ variation within models (parameter uncertainty)
- Large differences in evolutionary dynamics among different epidemiological models $\rightarrow$ caution in predicting evolutionary responses
- **neglected:** disease life history details, sex workers, age-structured mixing ... agent-based models?

Univariate summaries

- peak timing: epc > finite pair-formation effects
- equilibrium virulence: interaction
- low-equilibrium outcomes for intermediate-complexity models

References

[1] Ebert D, Bull JJ. Challenging the trade-off model for the evolution of virulence: is virulence management feasible? Trends Microbiol. 2003;11(1):15–20.

[2] Alizon S, Michalakis Y. Adaptive virulence evolution: the good old fitness-based approach. Trends in Ecology & Evolution. 2015 Jan;30(5):248–254.

[3] Fraser C, Lythgoe K, Leventhal GE, Shirreff G, Hollingsworth TD, Alizon S, et al. Virulence and Pathogenesis of HIV-1 Infection: An Evolutionary Perspective. Science. 2014 Mar;343(6177):1243727.

[4] Shirreff G, Pellis L, Laeyendecker O, Fraser C. Transmission Selects for HIV-1 Strains of Intermediate Virulence: A Modelling Approach. PLoS Computational Biology. 2011 Oct;7(10):e1002185. WOS:000297262700019.

[5] Champredon D, Bellan S, Dushoff J. HIV Sexual Transmission Is Predominantly Driven by Single Individuals Rather than Discordant Couples: A Model-Based Approach. PLoS ONE. 2013 12;8(12):e82906.

Acknowledgements

https://github.com/bbolker/HIV_LHS/

bolker@mcmaster.ca