HIV virulence evolution in structured epidemic models

Ben Bolker and Sang Woo Park
McMaster University, Hamilton, Ontario, Canada

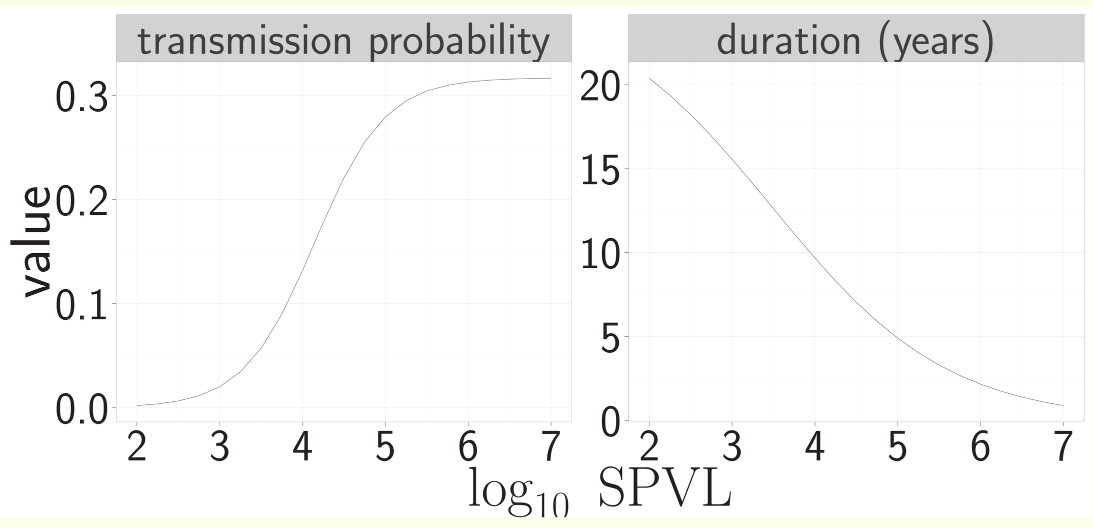
McMaster University

Michael G. DeGroote INSTITUTE FOR INFECTIOUS DISEASE RESEARCH

Summary

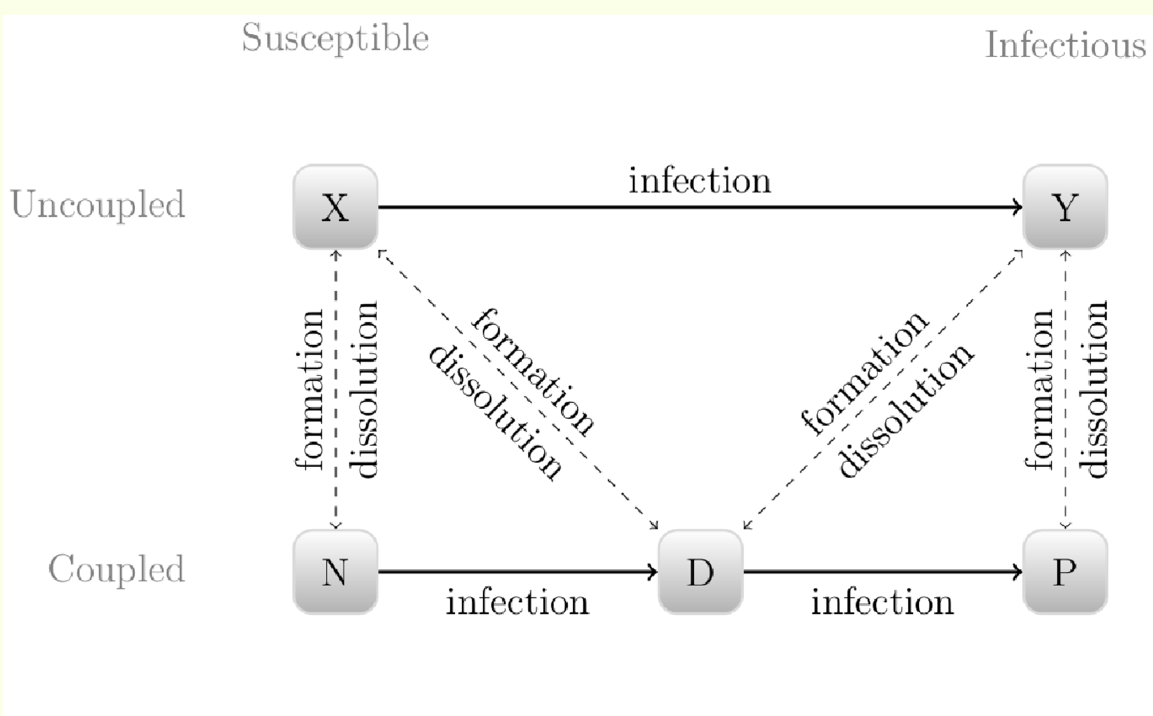
Pathogens can evolve rapidly in response to changing conditions (e.g., epidemic stage or public health interventions). Models of **eco-evolutionary dynamics** often neglect important epidemiological processes, such as the dynamics of sexual partnerships. We compared **models with a range of complexity** of partnership dynamics and extra-partnership contact.

Tradeoff theory



- **tradeoff theory**: virulence evolution mediated by transmission-vs-clearance tradeoff
- still debated [1, 2]
- HIV [3]: **set-point viral load** correlated with transmission probability, rate of progression to AIDS (data from Rakai, Uganda)
- eco-evolutionary virulence dynamics: [4]

Epidemiological structure



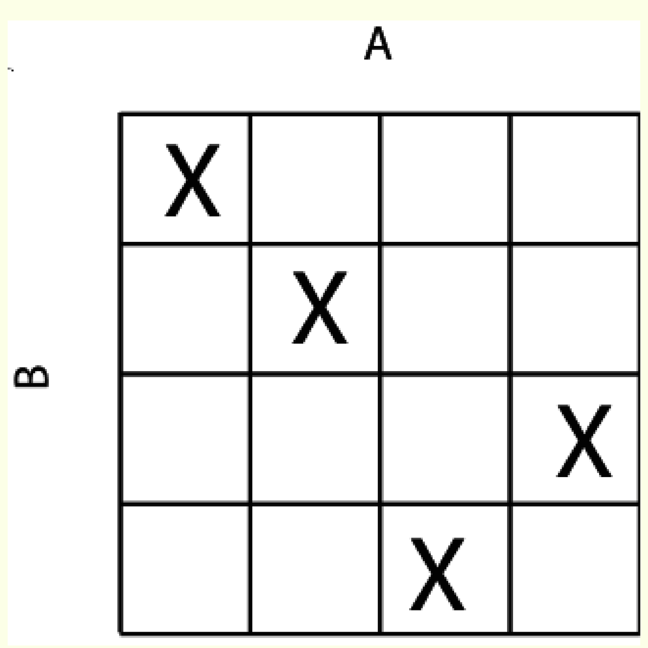
Champredon *et al.* 2013 [5]

Spectrum of model complexity:

- **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

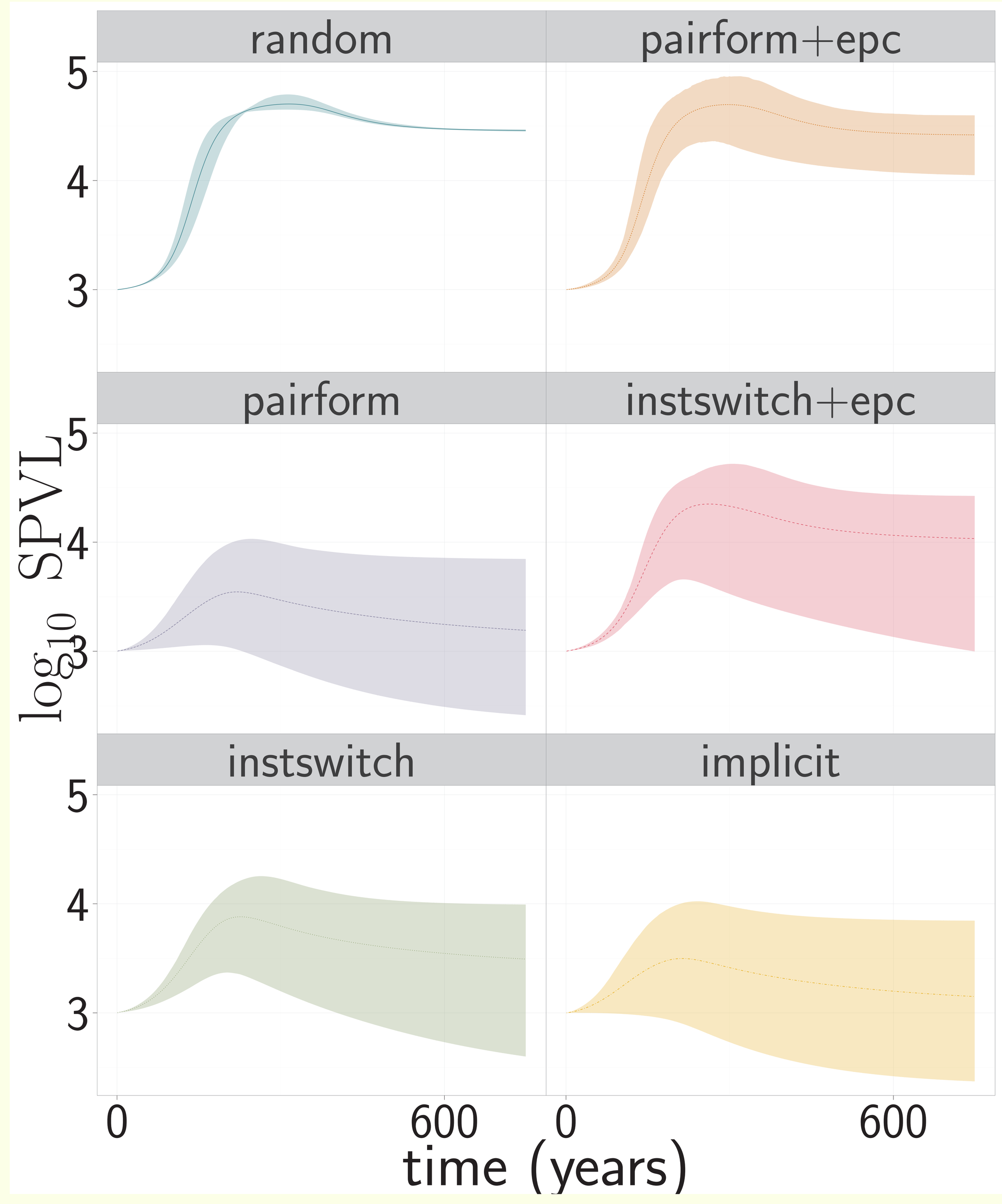
Simplified disease model (single stage only)

Sampling strategy



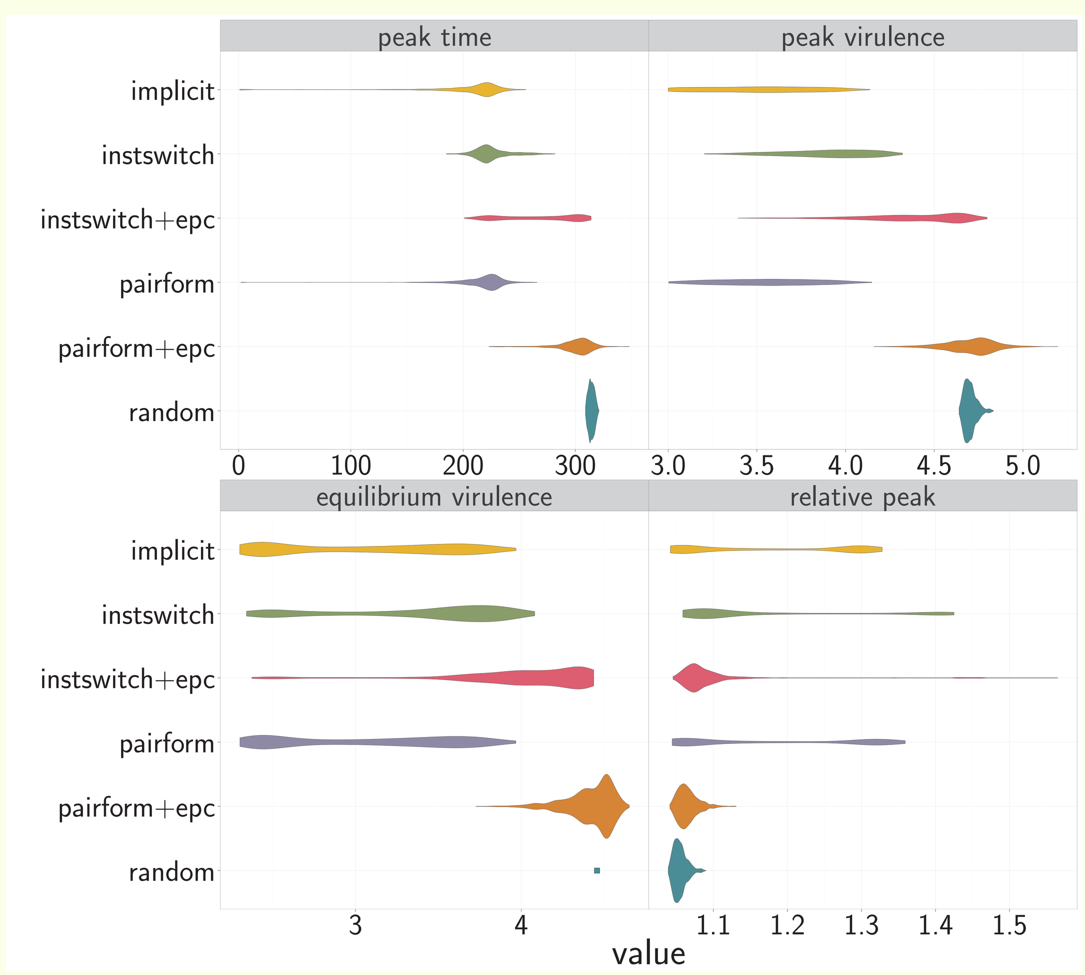
- Latin hypercube sampling: parameters from [5]
- parameters calibrated across models to the same **initial epidemic growth rate** (r)

Basic eco-evolutionary dynamics

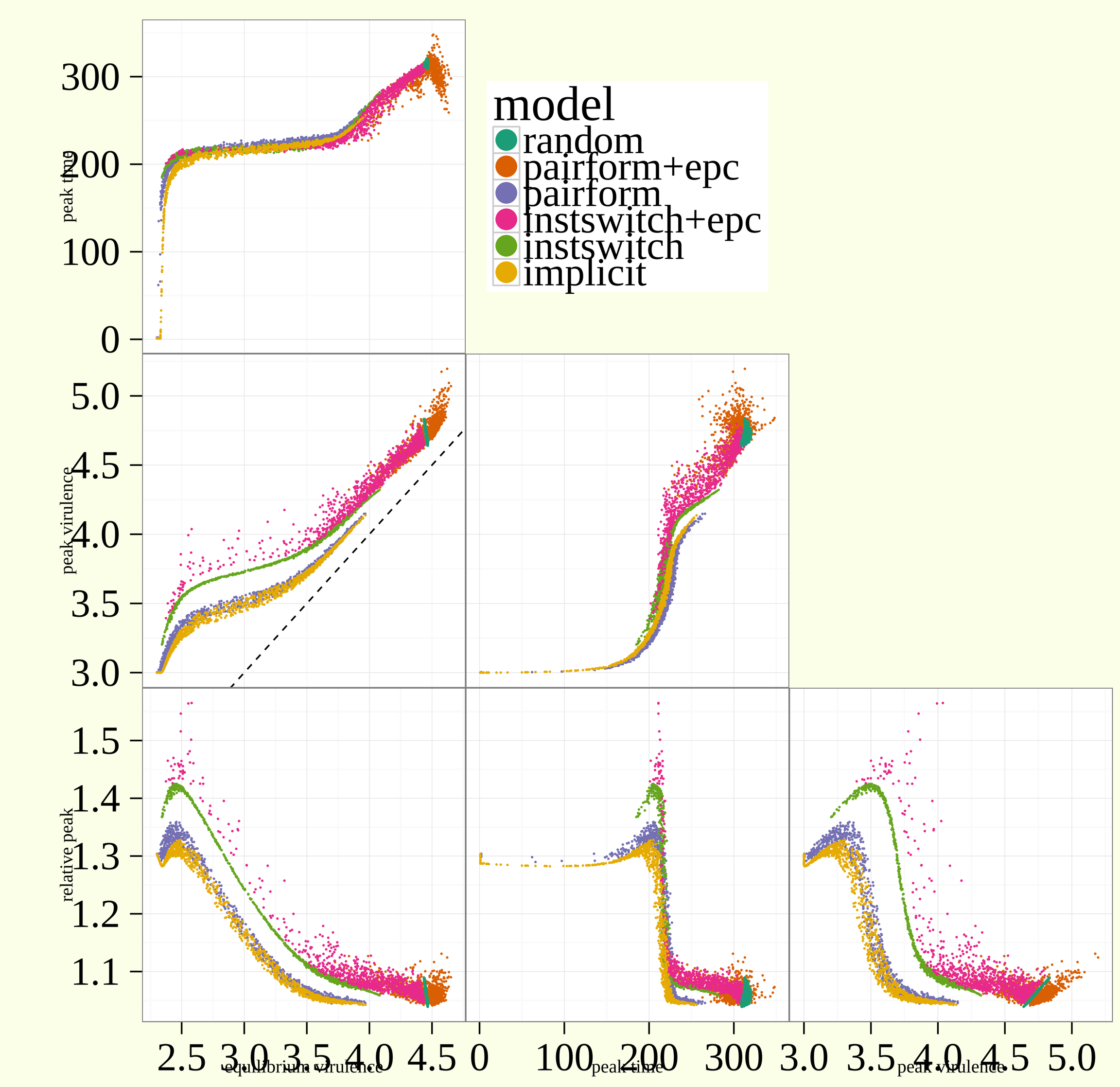


- significant variation across model structures
- least (random) and most (pairform+epc) models **most similar**: single individuals and extra-pair contact wash out effects of structure
- implicit model is **most different**
- random-mixing model underestimates (?) variability

Univariate summary



Bivariate summary



Conclusions and open questions

- Random-mixing models gave the closest match to the most realistic models; extra-pair contact washed out the effects of epidemiological structure
- Variation among models (model structure) ≈ variation within models (parameter uncertainty)
- Large differences in evolutionary dynamics among different epidemiological models suggest caution in predicting evolutionary responses

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. Available from: http://www.cell.com/article/S016953471500049X/abstract.

[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. Available from: http://www.sciencemag.org/content/343/6177/1243727.

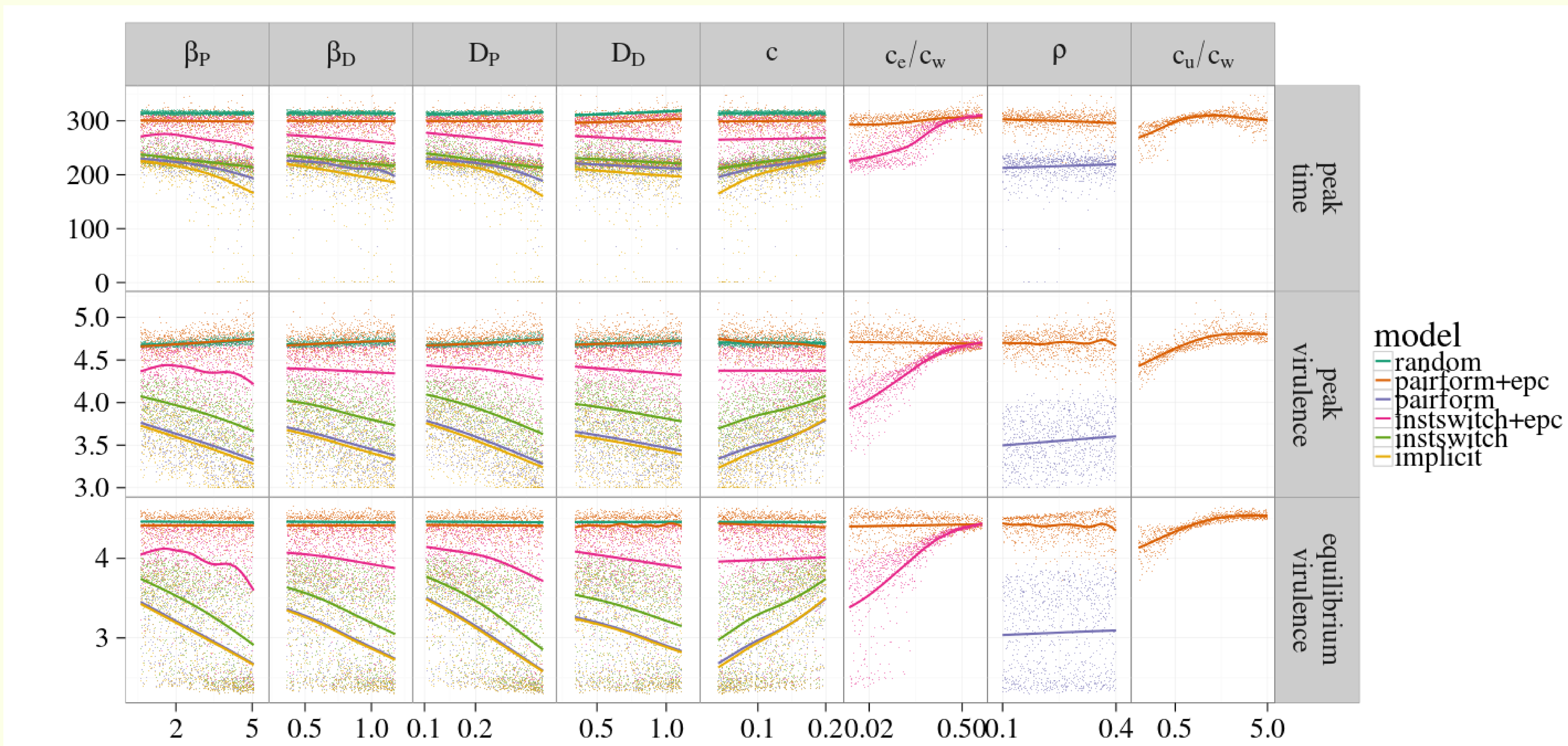
[4] Shirreff G, Pellis L, Laeyendecker O, Fraser C. Transmission Selects for HIV-1 Strains of Intermediate Virulence: A Modelling Approach. PLoS Computational Biology. 2011 Oct;7(10):e1002185. WOS:000297262700019.

[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

We thank Christophe Fraser for providing access to code, and the Natural Sciences and Engineering Research Council of Canada (NSERC) for funding.

Sensitivity



http://www.math.mcmaster.ca/bolker/
bolker@mcmaster.ca