Within-host dynamics

Understanding within-host host-parasite interactions (focus on dynamics)

Lots of molecular biology, genetics (*recognition* mechanisms and *effector* mechanisms), won't deal with that now.

Interaction between different components of the immune system (modeled at different levels of detail/realism), parasite populations (maybe in multiple compartments?)

Longitudinal data (relatively rare), distributional data.

HIV dynamics under (ineffective) treatment

Bonhoeffer, Coffin, and Nowak (1997)

- Early HIV antivirals: relatively ineffective due to rapid mutation
- Large decline in virus loads (up to 300-fold decline in viral RNA in some patients)
- but no clearance
- **within-host** $R_0 \approx 50$

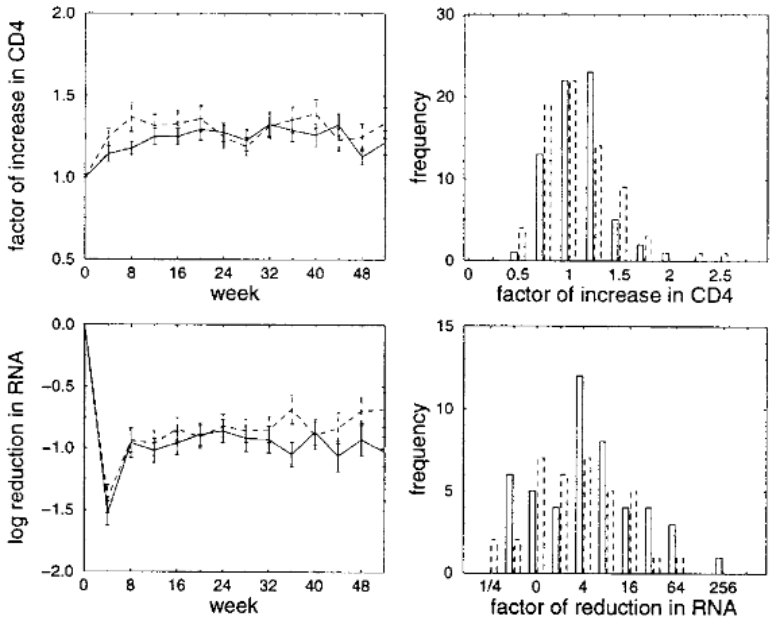
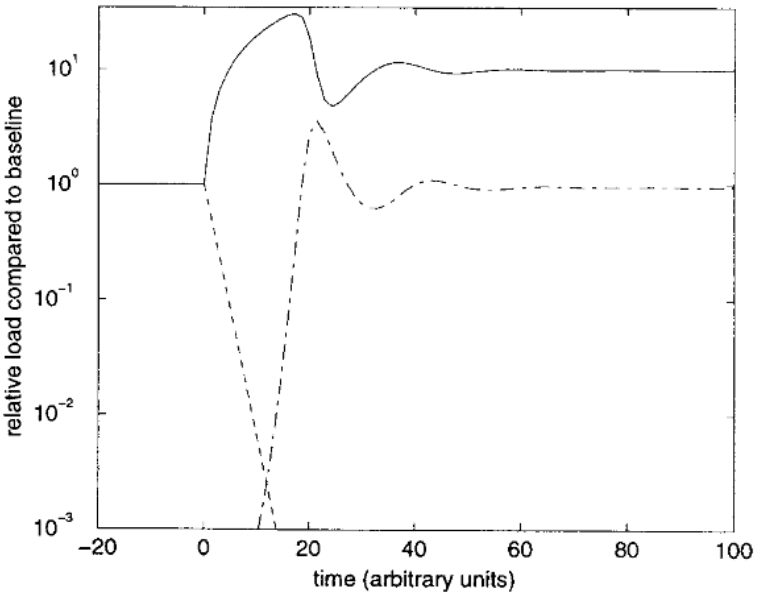


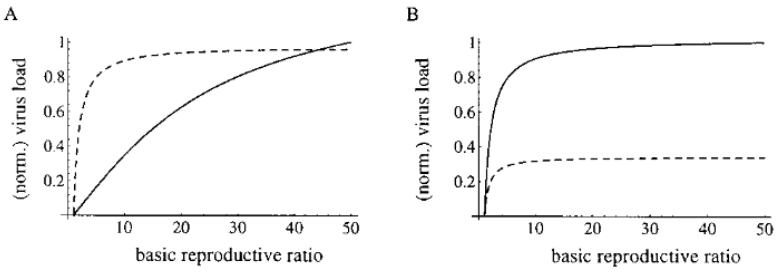
FIG. 1. Mean change in CD4 cell count and log mean change of HIV-1 RNA load compared to baseline in patients treated with a low-dose (dashed line) and high-dose (solid line) combination of lamivudine and zidovudine. In each treat-



- "virus load paradox": if R_0 is initially 50, we would have to reduce it to slightly above 1 but never **below** 1 to see these results.

$$\frac{dC}{dt} = \lambda - \mu C - \beta CV$$
$$\frac{dV}{dt} = \beta CV - aV$$

- add a drug-resistant type to the model
- add mutation (and back-mutation) to the model
- add immune responses ($dz/dt = kV - \gamma z$)
- homeostasis of infectible cells (logistic growth)
- virus-induced killing of uninfected cells (e.g. gp120 shedding)
- differential effects of drug on different types
- distribution of infectibility

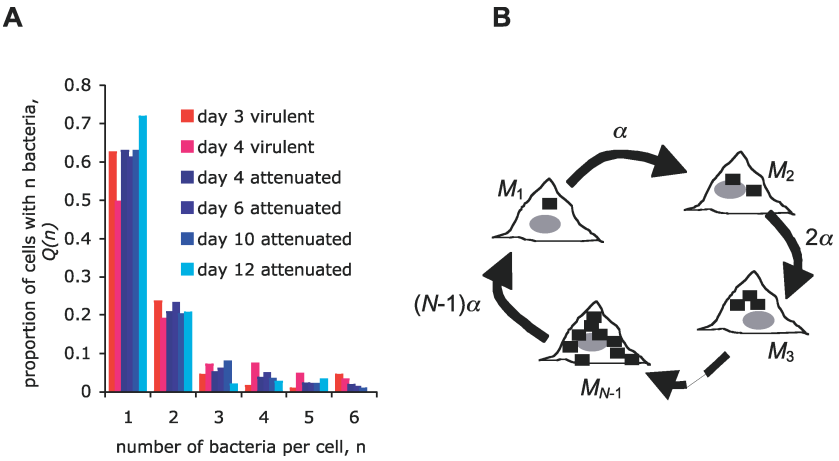


Within-host (and within-cell) dynamics of salmonella

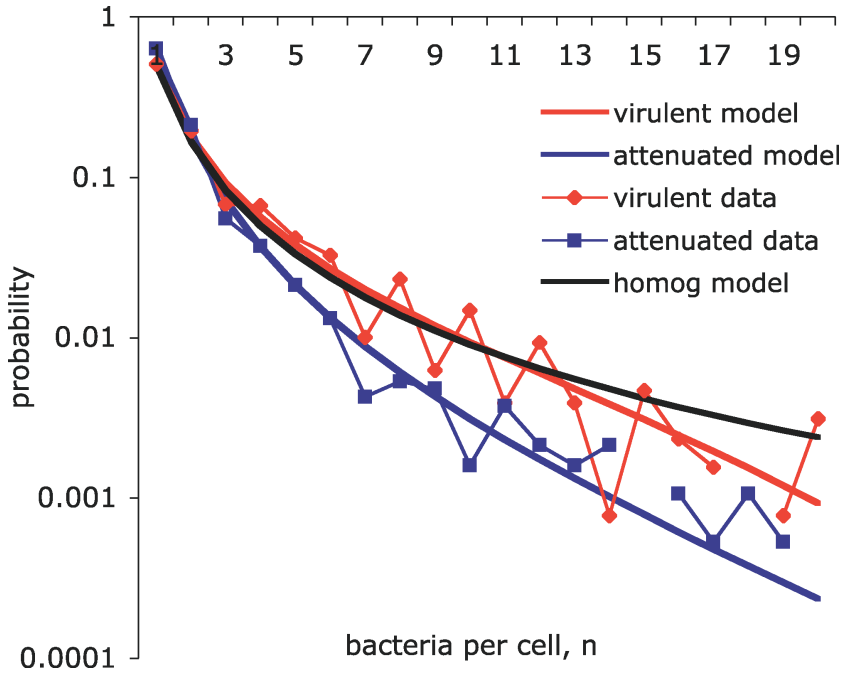
- intracellular bacterium

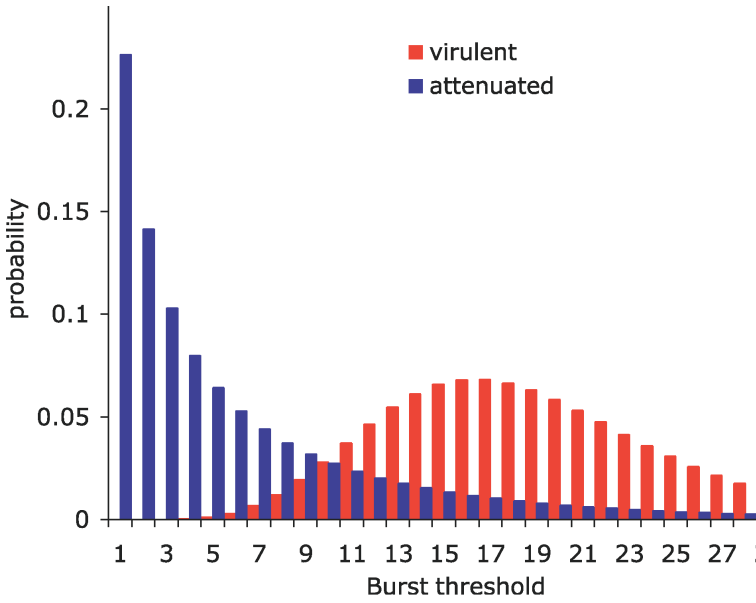
  Brown et al. (2006)

- model:



- assume that host cells are always available (infinite S)





- distribution: two categories, or a range of **burst sizes** ?
- "constitutive" vs "stochastic" models
- density-dependence in growth and/or burst probability?
- extracellular killing (bactericidal) vs slowing/preventing intracellular growth (bacteriostatic)

  > our analysis predicts that the efficacy of common extracellular antibiotics can be enhanced by supplementation with antibiotics slowing intracellular bacterial division [bacteriostatic drugs]. This implies that both bacteriostatic and bactericidal drugs can potentiate the therapeutic efficacy of extracellular antibiotics.

References

Bonhoeffer, S, J M Coffin, and M A Nowak. 1997. "Human Immunodeficiency Virus Drug Therapy and Virus Load." *Journal of Virology* 71 (4): 3275–8. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC191463/.

Brown, Sam P, Stephen J Cornell, Mark Sheppard, Andrew J Grant, Duncan J Maskell, Bryan T Grenfell, and Pietro Mastroeni. 2006. "Intracellular Demography and the Dynamics of Salmonella Enterica Infections." *PLoS Biol* 4 (11): e349. https://doi.org/10.1371/journal.pbio.0040349.

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