

Within-host dynamics

Understanding within-host host-parasite interactions (dynamically)

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 (rare), distributional data.

Bonhoeffer, Coffin, and Nowak (1997)

300-fold decline in viral RNA in some patients, but not clearance

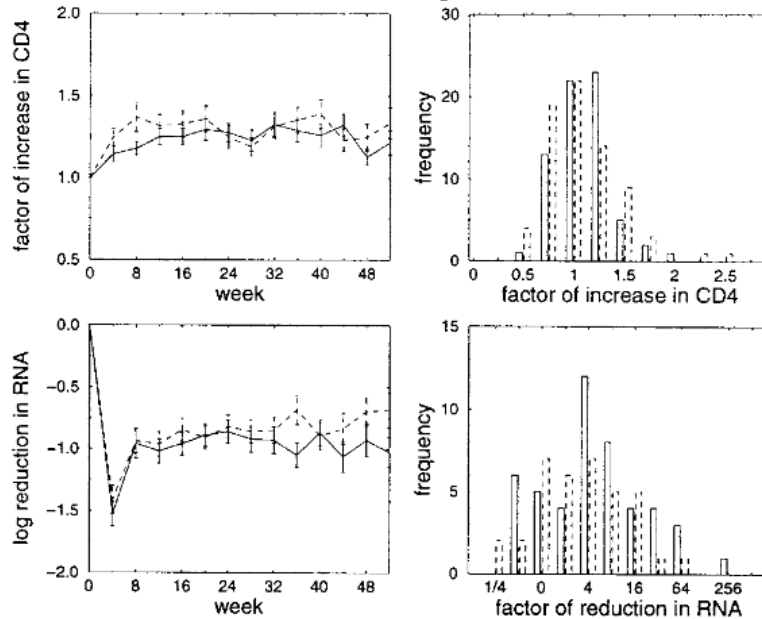
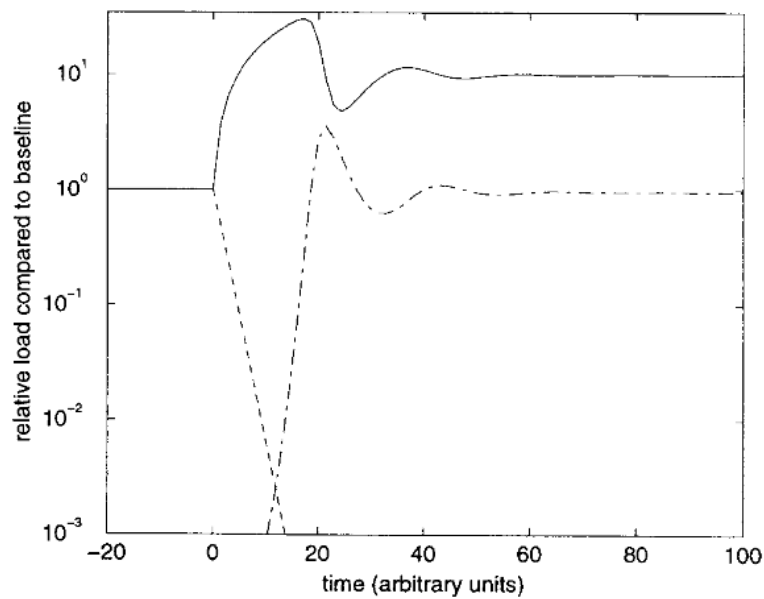


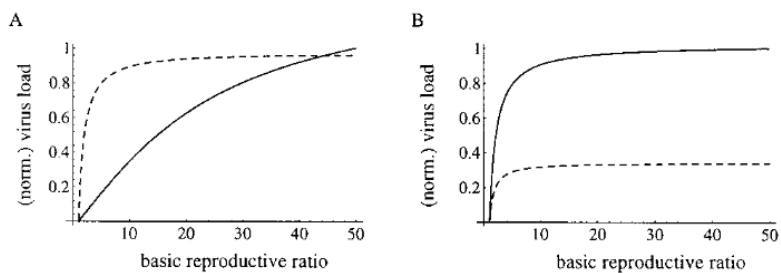
FIG. 1. Mean change in CD4 cell count and log mean change of HIV-1 RNA load compared to baseline in patients treated with a low-dose (dashed line) and high-dose (solid line) combination of lamivudine and zidovudine. In each treat-



“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.

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

- add a drug-resistant type
- add mutation
- 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



Brown et al. (2006)

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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