Chart, scatter chart

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Figure 1

Diagram, schematic

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Figure 2: (A) Infection duration is determined by the dynamics of the immune-parasite interaction, which are driven by negative and positive feedback loops. Some of these loops act to promote chronic infections, whereas others act to promote clearance. (B) If negative feedbacks dominate the system dynamics, then infection duration will vary smoothly across an environmental gradient, and variation in dose with a single environment will have little effect on infection duration. (C) If positive feedbacks dominate, however, then infection duration will exhibit tipping point behavior, where duration changes as a tipping point is crossed. Moreover, variation in dose can tip the system between short- and long-duration infections.

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Figure 3. (A) Nullclines for the interaction between the clearance-promoting Th2 response and parasite biomass. Intersections of the nullclines labeled with filled circles are stable. There are two simultaneously stable equilibria for the system, representing a chronic infection (P > 0) and an acute infection (P = 0). (B) Nullclines for the interaction between the clearance-promoting Th2 response and the chronicity-promoting Th1 response. Again, filled circles represent stable equilibria. Here there are four stable equilibria, representing a naïve T-cell population (low Th1 and Th2), a high co-activation equilibrium, and two polarized response equilibria. (C-D) Variation in dose and the initial state of the immune system can reveal which feedbacks are the critical drivers of infection outcome. If clearance-promoting feedback loops are stronger than chronicity-promoting loops and the immune system is initially Th1-biased, then low dose will lead to a chronic infection but high doses will be cleared (C1); if the immune system is initially Th2-biased, then parasites are cleared, regardless of dose (D1). If chronicity-promoting feedback loops are stronger than clearance-promoting loops and the immune system is initially Th1-biased, then chronic infections occur regardless of dose (C2); if the immune system is initially Th2-biased, then low-dose infections are cleared and high-dose infections will lead to a chronic infection (D2).