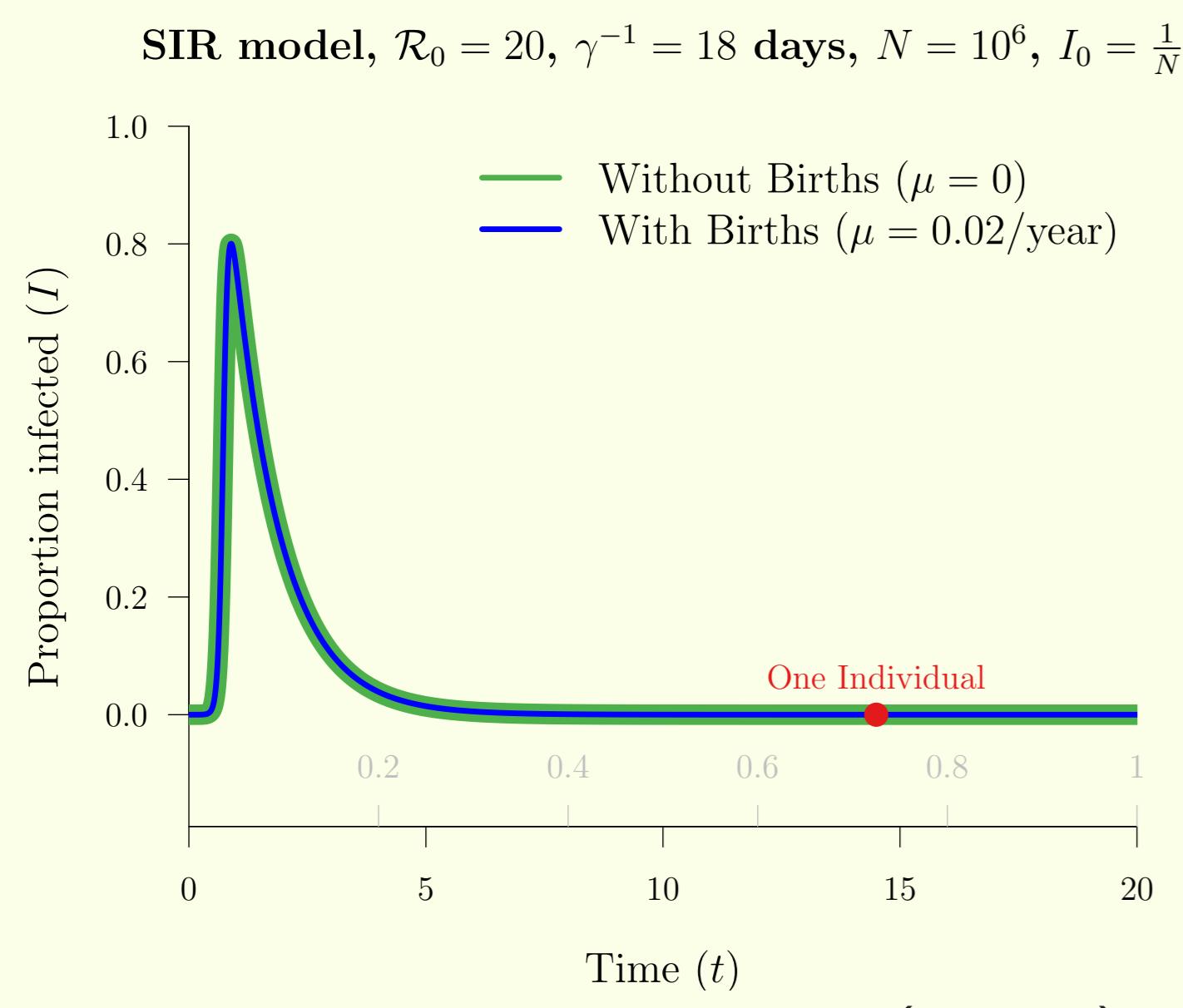




## Summary

The size of an epidemic of a newly invading pathogen increases rapidly with the basic reproduction number  $\mathcal{R}_0$ . For a disease such as measles with  $\mathcal{R}_0 \approx 20$ , the predicted proportion of the population remaining susceptible after a first epidemic is about one in a billion, and the predicted proportion is even smaller if  $\mathcal{R}_0$  is larger. Thus, the conventional wisdom is that highly transmissible diseases are unlikely to persist. This intuition is *wrong*. We show that after initial invasion, persistence is most likely if  $\mathcal{R}_0$  is very large and least likely if  $\mathcal{R}_0 \approx 3$ . We use stochastic simulations to map this counter-intuitive pattern, and show that we can match the simulations with an analytical approximation.

## The Puzzle of Persistence



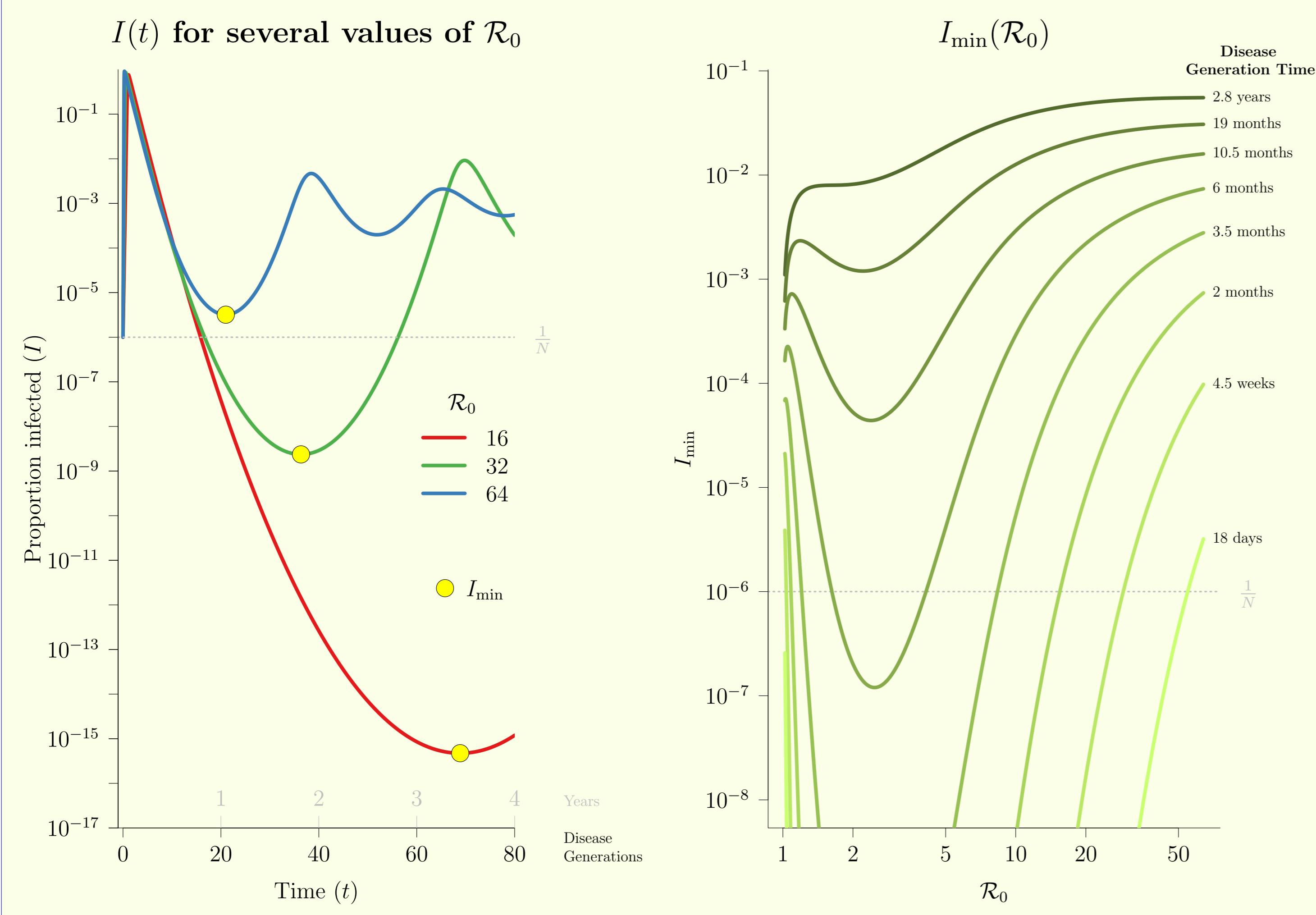
$S, I, R$  = Susceptible, Infectious, Recovered

$$\begin{aligned} \frac{dS}{dt} &= \mu N - \beta SI - \mu S \\ \frac{dI}{dt} &= \beta SI - \gamma I - \mu I \\ \frac{dR}{dt} &= \gamma I - \mu R \end{aligned}$$

$\mu$  = birth and death rates  
 $\beta$  = transmission rate  
 $\gamma$  = recovery rate  
 $\mathcal{R}_0 = \beta / (\gamma + \mu)$

- SIR model without births ( $\mu = 0$ ) accurately approximates first epidemic.
- For measles ( $\mathcal{R}_0 \approx 20$ , mean generation time  $\approx 2$  weeks), SIR model without births predicts less than one infected individual within a year  $\implies$  pathogen should not persist.
- $\mathcal{R}_0$  larger  $\implies$  faster, larger first epidemic  $\implies$  persistence *less* likely.
- How can a disease with very high  $\mathcal{R}_0$  persist after initial invasion?

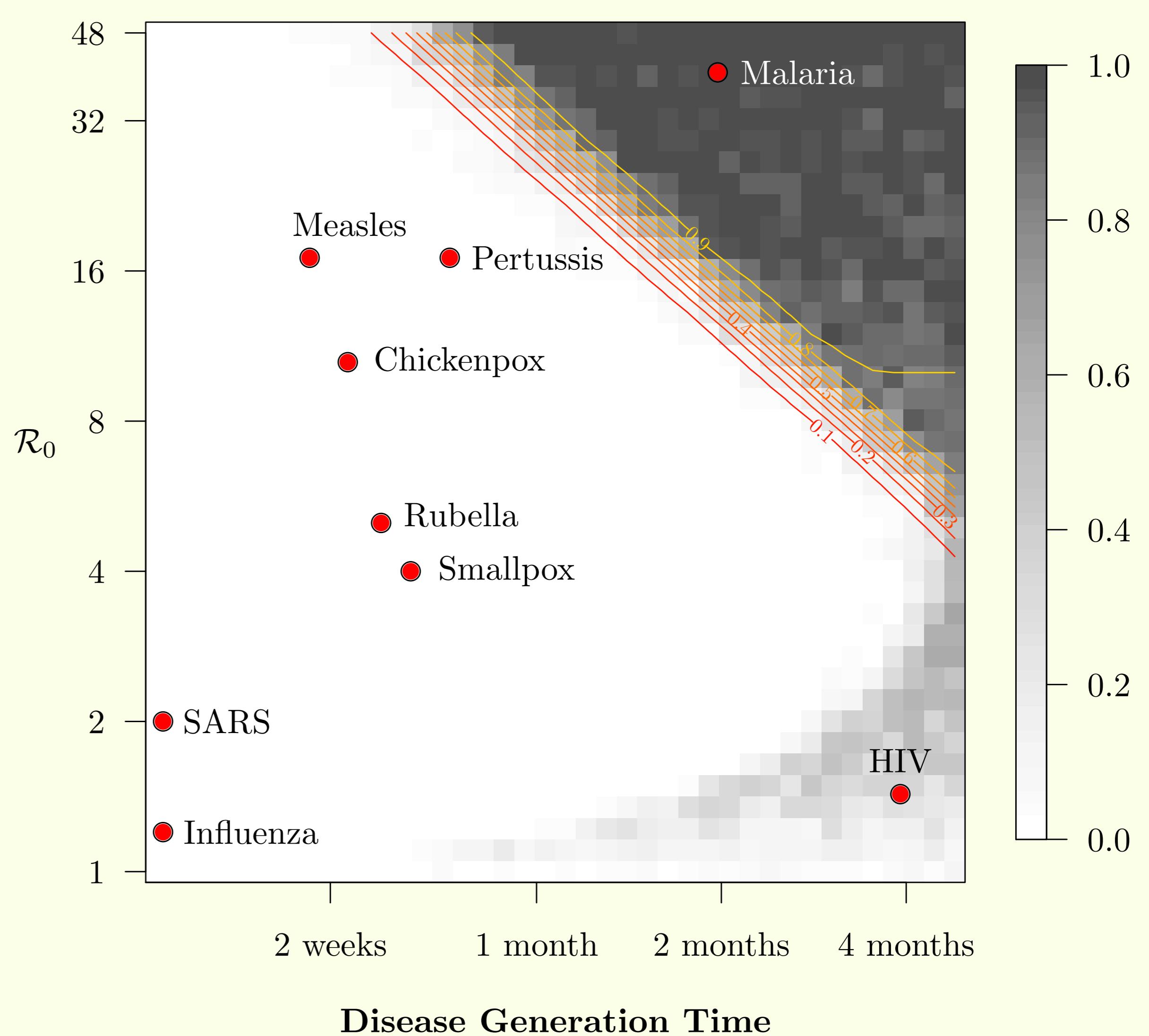
## A Mechanism for Persistence from Intrinsic Dynamics



- Error in intuition: Effect of births cannot be ignored. Must consider local minimum,  $I_{\min}$ , in prevalence  $I(t)$  (minimum occurs only with births).
- Key to persistence: Disease can persist if  $I_{\min} \gtrsim \frac{1}{N}$  (1 individual).
- Surprise: High  $\mathcal{R}_0 \implies$  High  $I_{\min} \implies$  persistence *more* likely.
- Very low  $\mathcal{R}_0$  (near 1) also yields high  $I_{\min}$  and greater persistence.
- Intermediate  $\mathcal{R}_0$  ( $\approx 3$ )  $\implies$  lowest  $I_{\min} \implies$  least likely to persist.

## Numerical and Analytical Results from Stochastic SIR Model

### Probability of Persistence



### Probabilities computed from:

- Simulations of stochastic SIR model with  $N = 10^6$  (greyscale).
- Analytical approximation valid for large  $\mathcal{R}_0$  and short disease generation time (contour lines of constant probability).

### Conclusions:

- For sufficiently long generation times:
  - ▷ Persistence almost certain for large  $\mathcal{R}_0$  (dark grey region).
  - ▷ Persistence possible for small  $\mathcal{R}_0$  (light grey region).
- Analytical approximation of probability (surprisingly!) accurate for  $\mathcal{R}_0 \gtrsim 4$ .

## Persistently Puzzling

- Persistence of measles and many other common diseases cannot be explained with this intrinsic dynamical mechanism, but other (extrinsic) persistence mechanisms have been suggested:
  - ▷ Multiple introductions into the host population [1, 2],
  - ▷ Spatial spread among cities promoting global persistence in spite of local fadeouts [3, 4],
  - ▷ Invasion with low  $\mathcal{R}_0$  followed by evolution to higher  $\mathcal{R}_0$  [5].
- An analytical approximation for the probability of post-invasion persistence remains to be found for  $\mathcal{R}_0 \lesssim 4$ .

## References

- [1] Keeling MJ, Gilligan CA. Metapopulation dynamics of bubonic plague. *Nature*. 2000;407:903–906.
- [2] Pulliam JRC, Dushoff JG, Levin SA, Dobson AP. Epidemic enhancement in partially immune populations. *PLoS ONE*. 2007;2(1):e165.
- [3] Dobson AP, Carper ER. Infectious Diseases and Human Population History. *BioScience*. 1996;46(2):115–126.
- [4] Cross PC, Johnson PLF, Lloyd-Smith JO, Getz WM. Utility of  $\mathcal{R}_0$  as a predictor of disease invasion in structured populations. *Journal of the Royal Society Interface*. 2007;4(13):315–324.
- [5] Antia R, Regoes RR, Koella JC, Bergstrom CT. The role of evolution in the emergence of infectious diseases. *Nature*. 2003;426(6967):658–661.

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