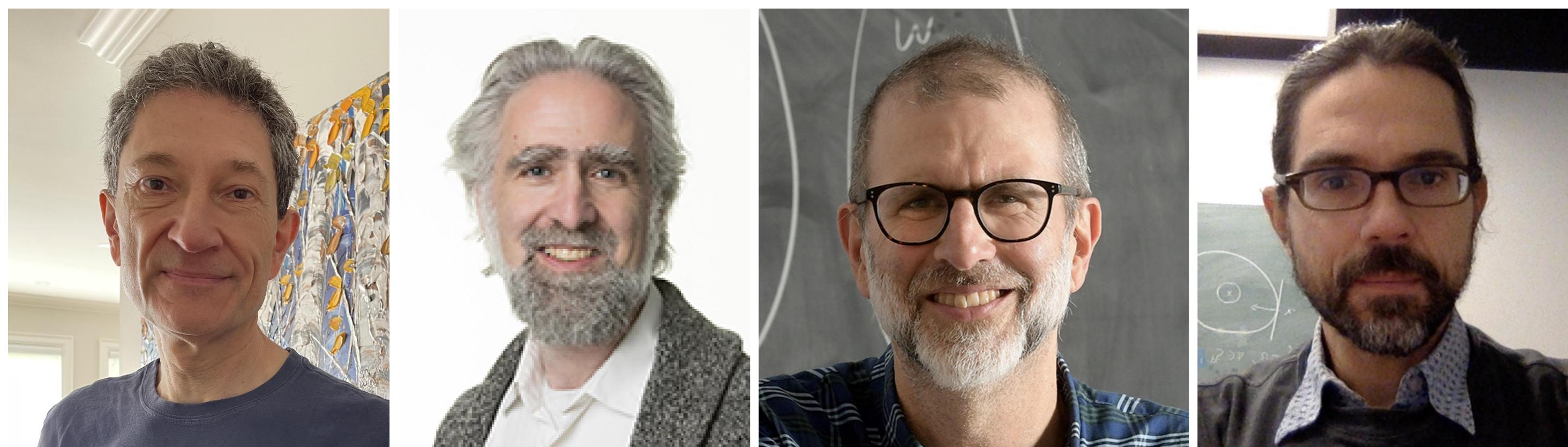




The probability that an emerging infectious disease will burn out

David Earn¹, Ben Bolker¹, Jonathan Dushoff¹, Todd Parsons²

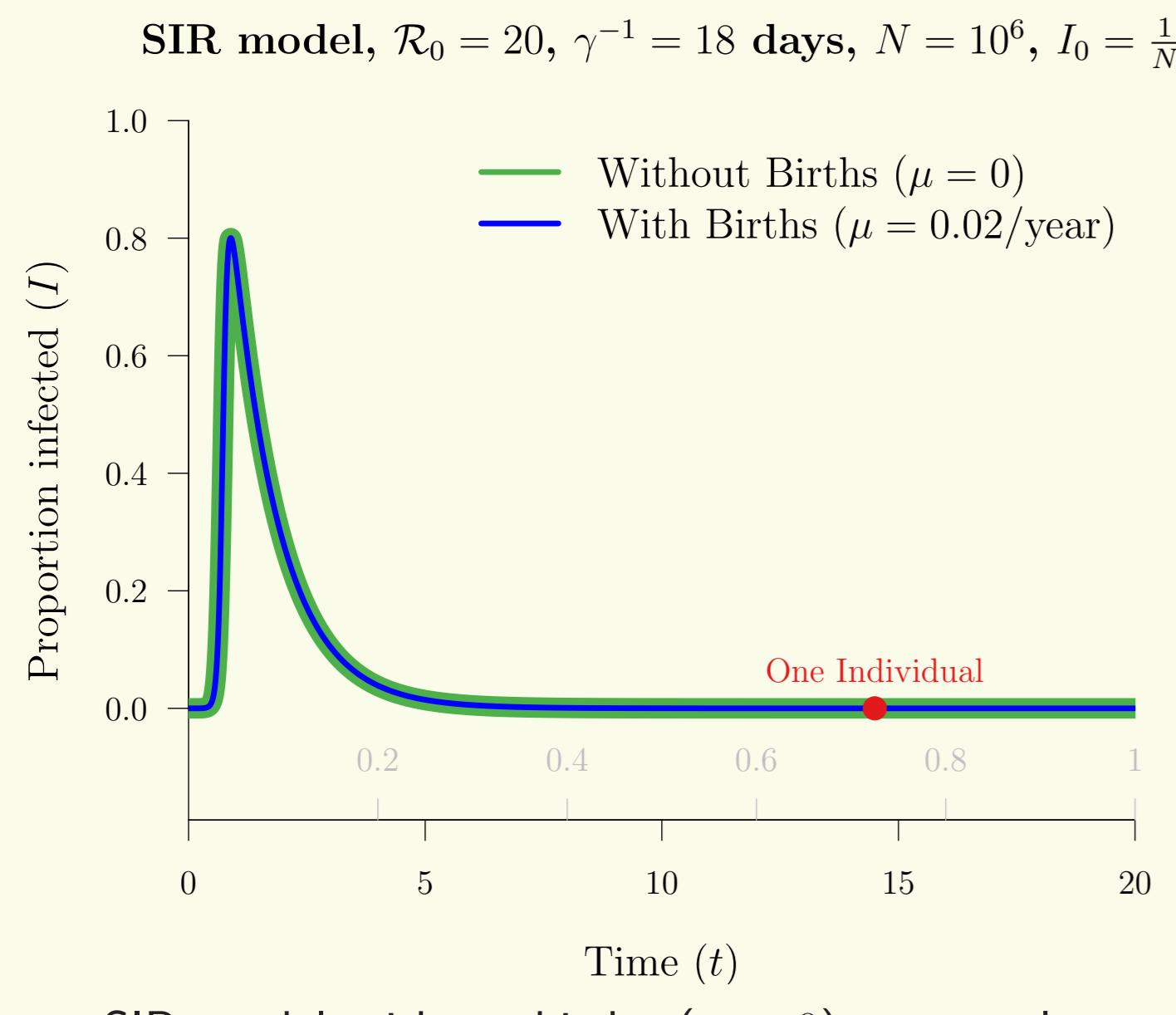
¹McMaster University, Hamilton, Ontario, Canada; ²LPSM, CNRS, Paris, France



Summary

If a new pathogen causes a large epidemic, it might “burn out” before causing a second epidemic. The burnout probability can be estimated from large numbers of computationally intensive simulations, but an easily computable formula for the burnout probability has never been found. In a poster at EEID 2014 [1], we argued, primarily based on simulations, that persistence after a major epidemic is puzzling for most infectious diseases. Using a conceptually simple approach, we have now derived [2] an accurate and easily computable formula for the burnout probability for the stochastic SIR epidemic model with vital dynamics (host births and deaths), and for the stochastic SIRS model (which includes decay of immunity). Our analysis shows that the burnout probability is always smaller for diseases with longer infectious periods or shorter durations of immunity, but is bimodal with respect to transmissibility (\mathcal{R}_0) unless infectious periods are atypically long. Our SIRS results imply that failing to prevent SARS-CoV-2 from taking off initially made it almost certain that it would persist. Persistence of other common, human infectious diseases cannot be explained by susceptible recruitment alone.

The Puzzle of Persistence



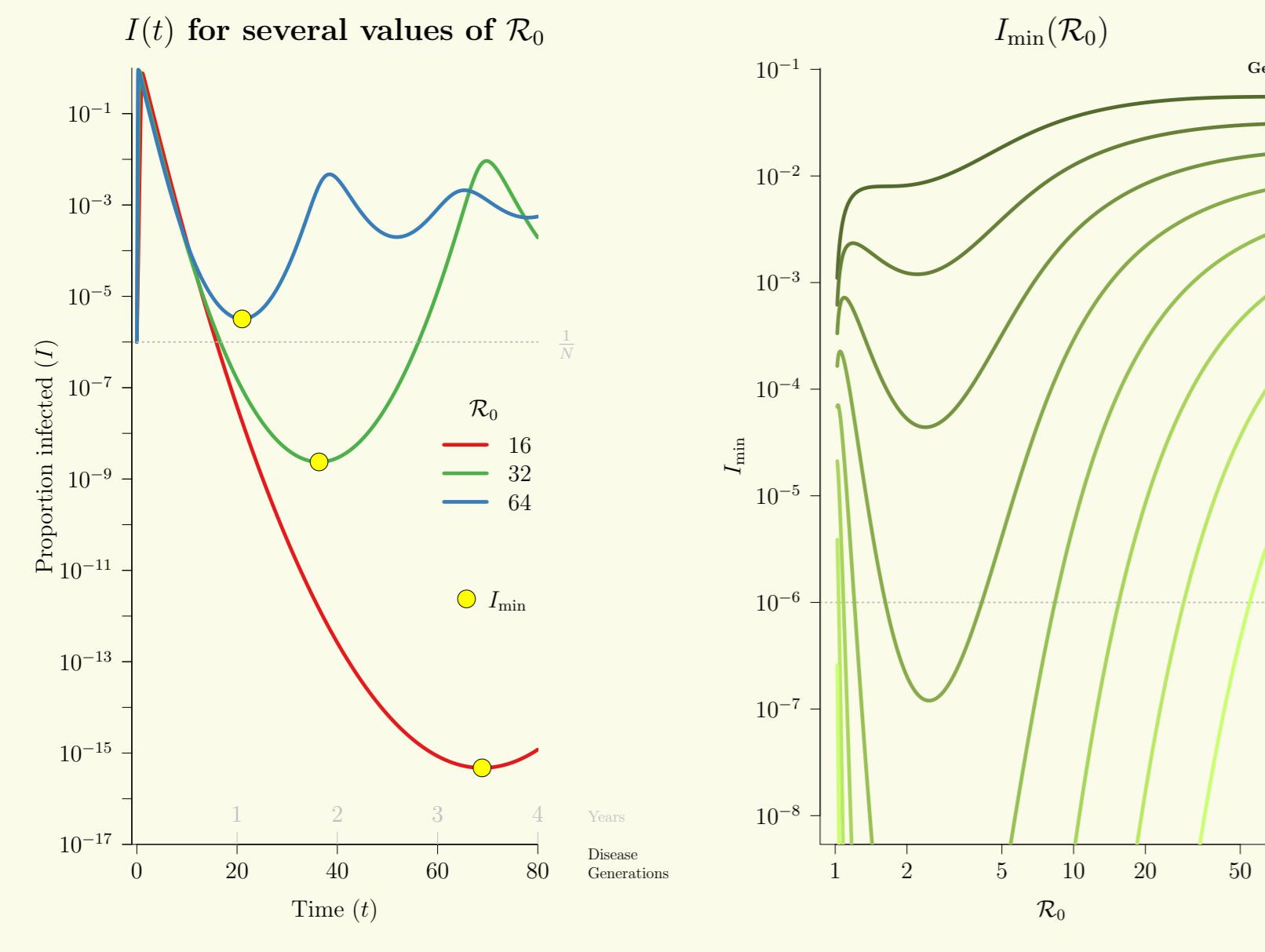
$S, I, R = \text{Susceptible, Infectious, Recovered}$

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

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

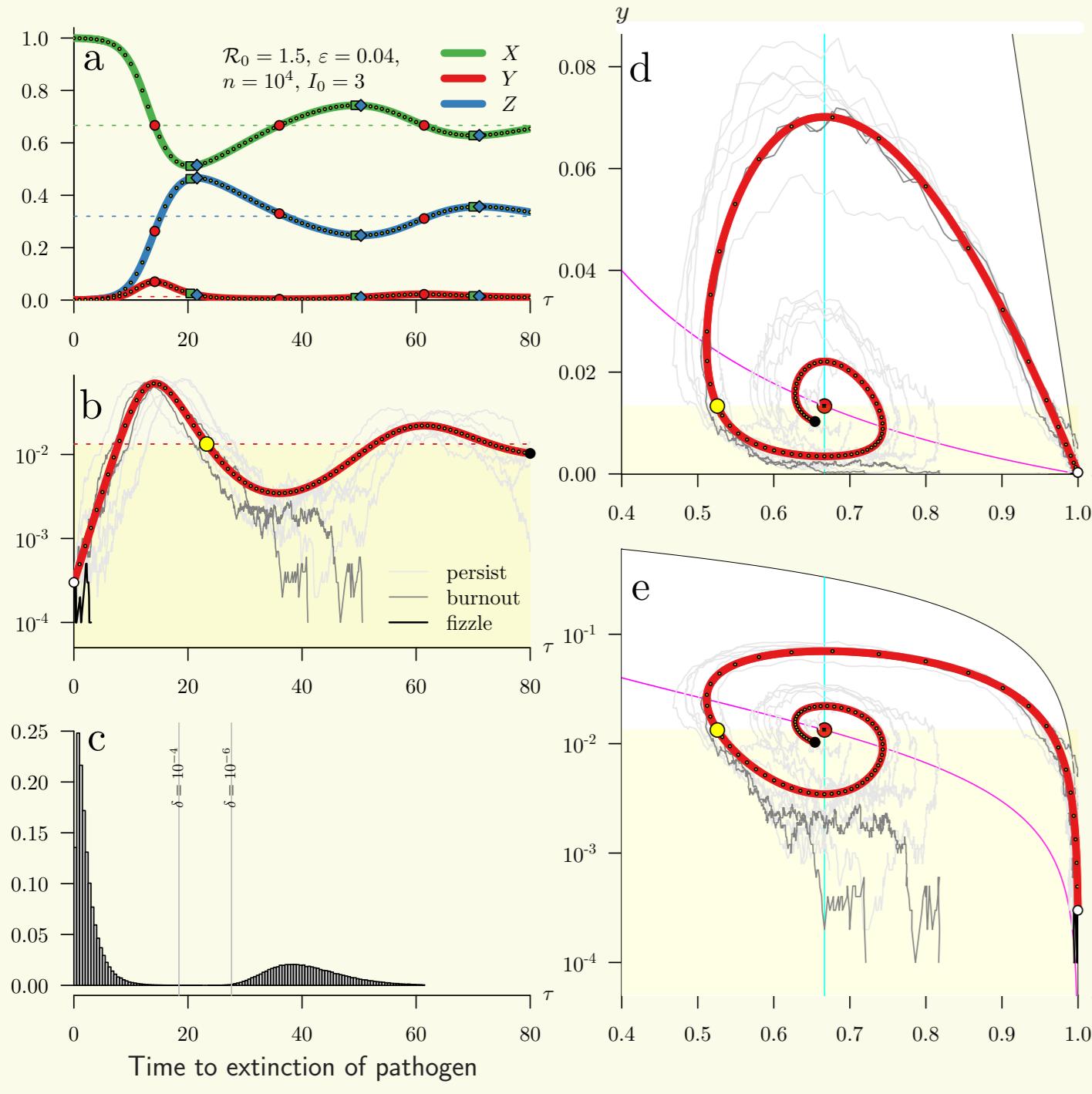
- SIR model without births ($\mu = 0$) accurately approximates first epidemic.
- For measles ($\mathcal{R}_0 \approx 20$, mean generation time ≈ 2 weeks), SIR model without births predicts less than one infected individual within a year \implies pathogen should not persist.
- \mathcal{R}_0 larger \implies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

Susceptible recruitment cannot be ignored



- Deterministic model approaches equilibrium (\hat{S}, \hat{I}) via damped oscillations, but stochastic model can go extinct at any time.
- Disease can persist if $I_{\min} \gtrsim \frac{1}{N}$ (1 individual).
- High $\mathcal{R}_0 \implies$ High $I_{\min} \implies$ persistence *more* likely.
- Very low \mathcal{R}_0 (near 1) also yields high I_{\min} .
- Persistence probability minimized for $2 \lesssim \mathcal{R}_0 \lesssim 2.57$ (depends on infectious period) [2].

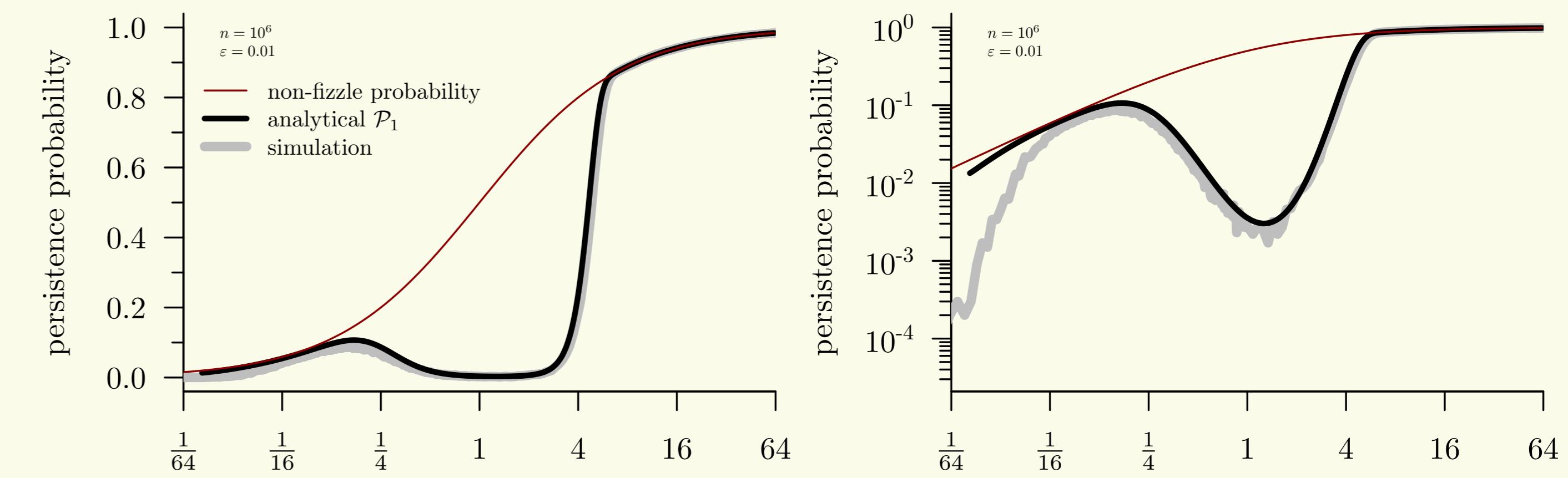
Burnout probability: hybrid deterministic-stochastic analysis



- Fizzle with probability $(\frac{1}{\mathcal{R}_0})^k$ if $I_0 = k$ infectives introduced (homogeneous branching process).
 - If spread did *not* fizzle, use deterministic trajectory $I(t)$ (via matched asymptotic approximation [3]) to find post-outbreak susceptible proportion (S_{in}) at entry (yellow dot) into boundary layer ($I < \hat{I}$).
 - Within boundary layer, approximate $I(t)$ as inhomogeneous branching process [4] to derive burnout probability [2],
- $$g \approx \left(1 + 1/\sqrt{\varepsilon(\mathcal{R}_0 - 1)} \left(\frac{a}{z}\right)^a e^{z-a}\right)^{-1}$$
- $$\varepsilon = \frac{\text{mean infectious period}}{\text{mean lifetime}}, \quad z = \frac{\mathcal{R}_0}{\varepsilon}(1 - S_{in}), \quad a = \frac{\mathcal{R}_0}{\varepsilon}(1 - \hat{S}).$$
- Repeat for any number of cycles (but persistence is almost certain if burnout did not occur after the first outbreak).

SIR persistence probability formula agrees with simulations

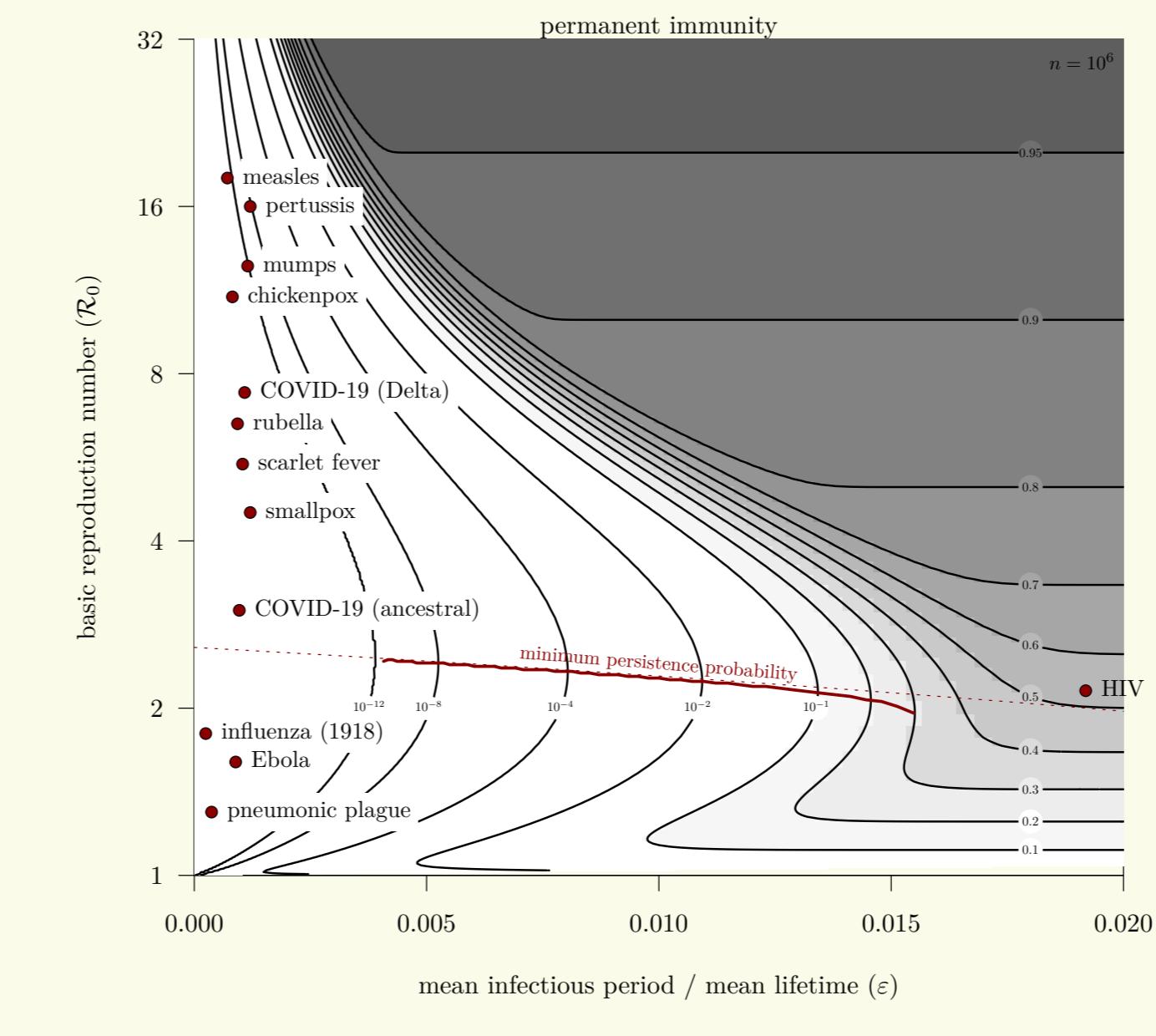
SIR persistence probability as a function of $\mathcal{R}_0 - 1$



- Probability of *not* fizzling after k infectives introduced: $p_k = 1 - (\frac{1}{\mathcal{R}_0})^k$.
- Probability of *not* burning out after *not* fizzling: $\mathcal{P}_1(\mathcal{R}_0, \varepsilon, n, k) = p_k(1 - q^{n\hat{I}})$.
- Estimates of \mathcal{P}_1 via computationally demanding simulations of the stochastic SIR model (grey) agree closely with our fully analytical approximation (black) [2]. Discrepancies are apparent only on the log scale (right panel), and only in the limit $\mathcal{R}_0 \rightarrow 1$ (where the approximation is not valid). The plot above exaggerates this difference, because we chose $\varepsilon = 0.01$, which is atypically large (see next plot).

SIR vs SIRS: effect of decay of immunity on persistence

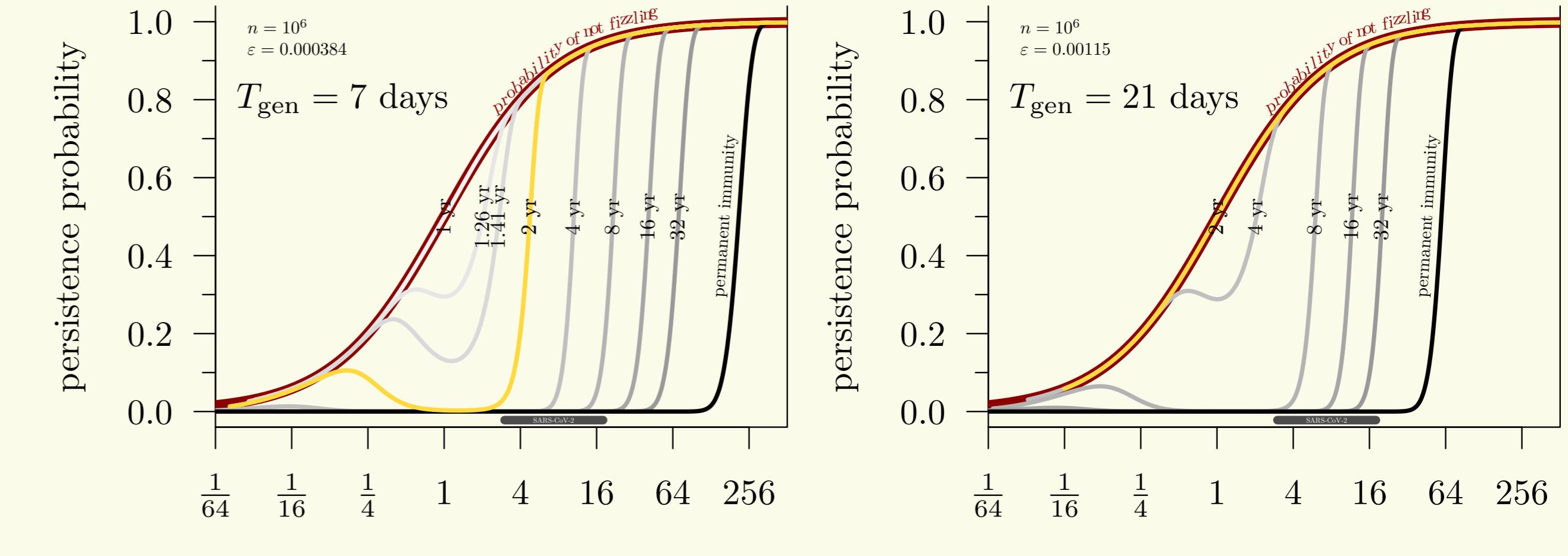
contours of persistence probability: SIR model



- If immunity is permanent (left panel) the SIR model predicts most diseases should have burnt out.
- If immunity lasts only a few years (right panel) the SIRS model predicts persistence.

SARS-CoV-2 was destined to persist after invasion

SIRS persistence probability as a function of $\mathcal{R}_0 - 1$



- Given that SARS-CoV-2 did *not* fizzle, and the mean immune period is short, the probability that it would have burnt out if allowed to spread without control was negligible.

Persistently Puzzling

- Persistence of measles and many other infectious diseases with permanent or near-permanent immunity cannot be explained by the SIR or SIRS models. Mechanisms other than homogeneous mixing and decay of immunity must play a role. Perhaps:
 - Multiple introductions into the host population [5],
 - Spatial spread among cities promoting global persistence in spite of local fadeouts [6],
 - Invasion with low \mathcal{R}_0 followed by evolution to higher \mathcal{R}_0 [7].

References

- Earn DJD, Champredon D, de Jonge MS, Drohan SE, Hempel K, Molina C, Papst I, Rosati DP, Bolker BM, Dushoff J. The Puzzling Persistence of Invading Pathogens. Poster presentation at the 2014 Ecology and Evolution of Infectious Diseases Conference "Multi-Scale Mechanisms of Disease Emergence and Control", Colorado State University. 2014.
- Parsons TL, Bolker BM, Dushoff J, Earn DJD. The probability of epidemic burnout in the stochastic SIR model with vital dynamics. PNAS. 2024;121(5):e2313708120. Available from: <https://www.pnas.org/doi/10.1073/pnas.2313708120>.
- Parsons TL, Earn DJD. Uniform asymptotic approximations for the phase plane trajectories of the SIR model with vital dynamics. SIAM Journal on Applied Mathematics. 2024; in press.
- Kendall DG. On the Generalized "Birth-and-Death" Process. Ann Math Stat. 1948;19(1):1-15.
- Pulliam JRC, Dushoff JG, Levin SA, Dobson AP. Epidemic enhancement in partially immune populations. PLoS ONE. 2007;2(1):e165.
- 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):315-24.
- Antia R, Regoes RR, Koella JC, Bergstrom CT. The role of evolution in the emergence of infectious diseases. Nature. 2003;426(6967):658-61.

Acknowledgements

We were supported by NSERC Discovery grants and a CNRS International Emerging Actions grant.