Mathematical Epidemiology for the People, Part Two - towards the equilibrium

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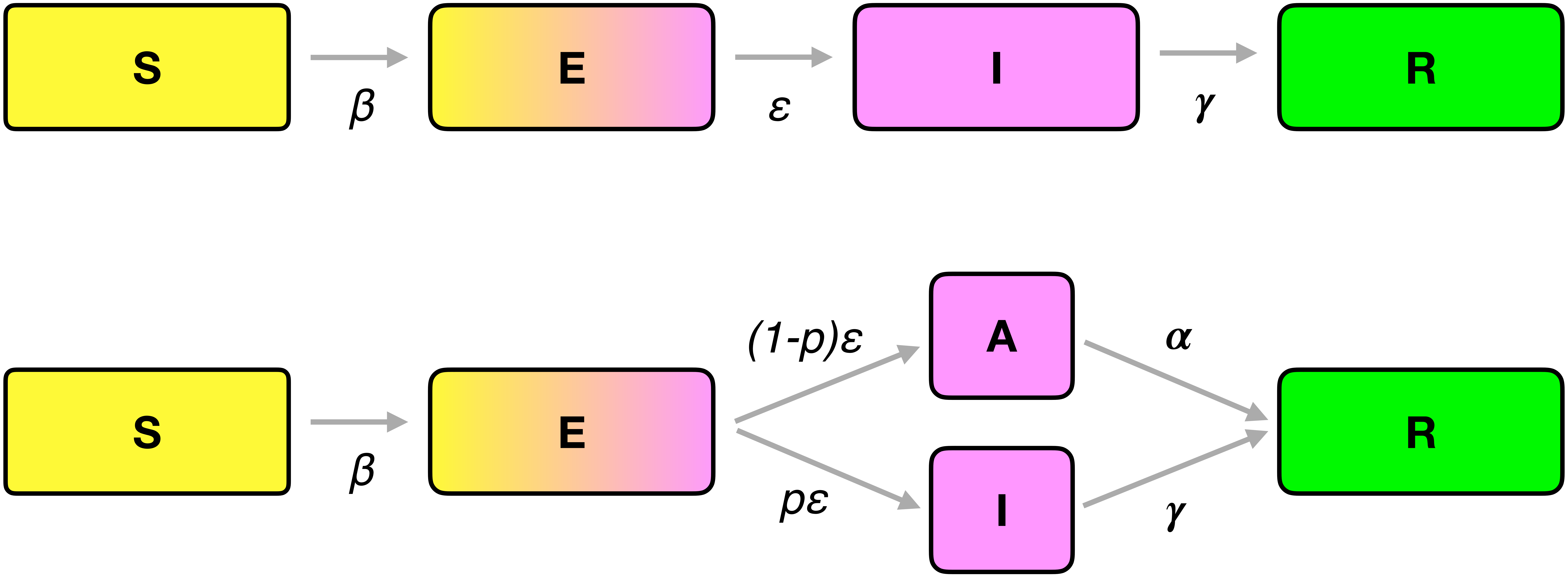
Brief Refresh

SIR Compartmental Epidemic Model
- based on Kermack-McKendrick theory since 1927

Towards COVID-19 Realities



SIR Compartmental Epidemic Model
- based on Kermack-McKendrick theory since 1927

$$\frac{dS(t)}{dt} = -\frac{\beta}{N} I(t)S(t) \qquad \frac{dI(t)}{dt} = \frac{\beta}{N} I(t)S(t) - \gamma I(t) \qquad \frac{dR(t)}{dt} = \gamma I(t)$$

$$\mathcal{R}_0 = \frac{\beta}{\gamma},\ \mathcal{R}_e(t) = \mathcal{R}_0 \frac{S(t)}{N}$$

$$S(0) + I(0) + R(0) = N$$

$$S'(t) + I'(t) + R'(0) = 0$$

Going Dimensionless

$$s(t) = {}^{S(t)}\!/_{N} \qquad i(t) = {}^{I(t)}\!/_{N} \qquad r(t) = {}^{R(t)}\!/_{N}$$

$$\frac{ds(t)}{dt} = -\beta i(t)s(t) \qquad \frac{di(t)}{dt} = \beta i(t)s(t) - \gamma i(t) \qquad \frac{dr(t)}{dt} = \gamma i(t)$$

$$\mathcal{R}_0 = \frac{\beta}{\gamma},\ \mathcal{R}_e(t) = \mathcal{R}_0 s(t)$$

$$s(0) + i(0) + r(0) = 1$$

$$s'(t) + i'(t) + r'(0) = 0$$

All Those “***R***”s

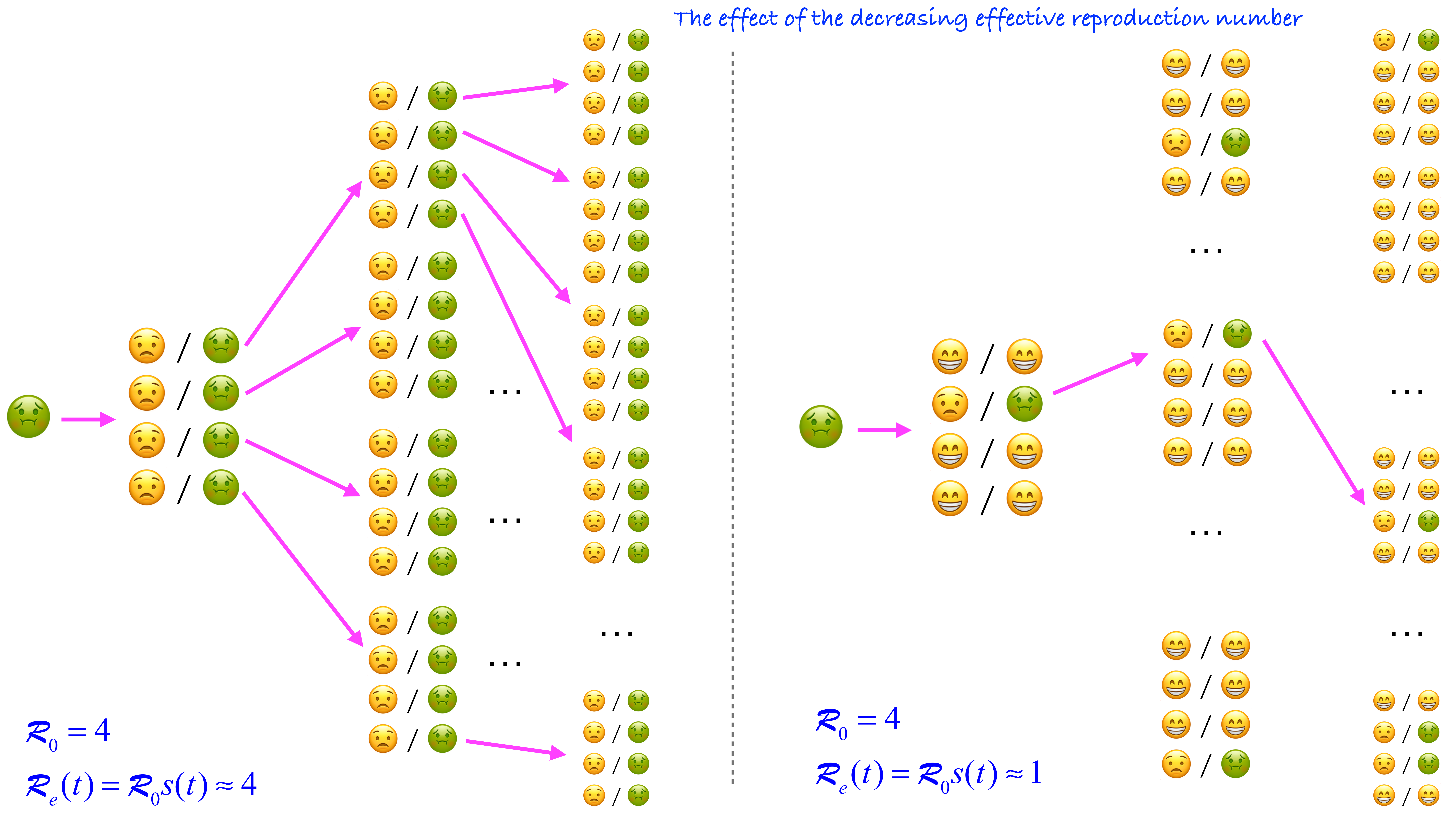
$$\mathcal{R}_0 = \frac{\beta}{\gamma}$$

$$\mathcal{R}_e(t) = \mathcal{R}_0 \frac{S(t)}{N} = \mathcal{R}_0 s(t)$$

$$controlled - \mathcal{R}_0 = \frac{\beta_t}{\gamma_t}$$

*) In this particular model

- Basic reproduction number $\boldsymbol{R}_0$
  - inherent model constant, describes important qualitative aspects, e.g. equilibria and their stability
- Effective reproduction number $\boldsymbol{R}_e(t)$
  - what we observe in daily experience
- Controlled reproduction number $\boldsymbol{R}_{0,t}$
  - what we aim for with our interventions


The effect of the decreasing effective reproduction number
$\mathcal{R}_0 = 4$
$\mathcal{R}_e(t) = \mathcal{R}_0 s(t) \approx 4$
$\mathcal{R}_0 = 4$
$\mathcal{R}_e(t) = \mathcal{R}_0 s(t) \approx 1$

Partial Optimisation Criteria (SIR-based)

Susceptible $\xrightarrow{\beta}$ **Infected** $\xrightarrow{\gamma}$ **Removed**

$s(t) = {}^{S(t)}/_{N}$ $\quad i(t) = {}^{I(t)}/_{N}$ $\quad r(t) = {}^{R(t)}/_{N}$

$$\frac{ds(t)}{dt} = -\beta i(t) s(t) \qquad \frac{di(t)}{dt} = \beta i(t) s(t) - \gamma i(t) \qquad \frac{dr(t)}{dt} = \gamma i(t)$$

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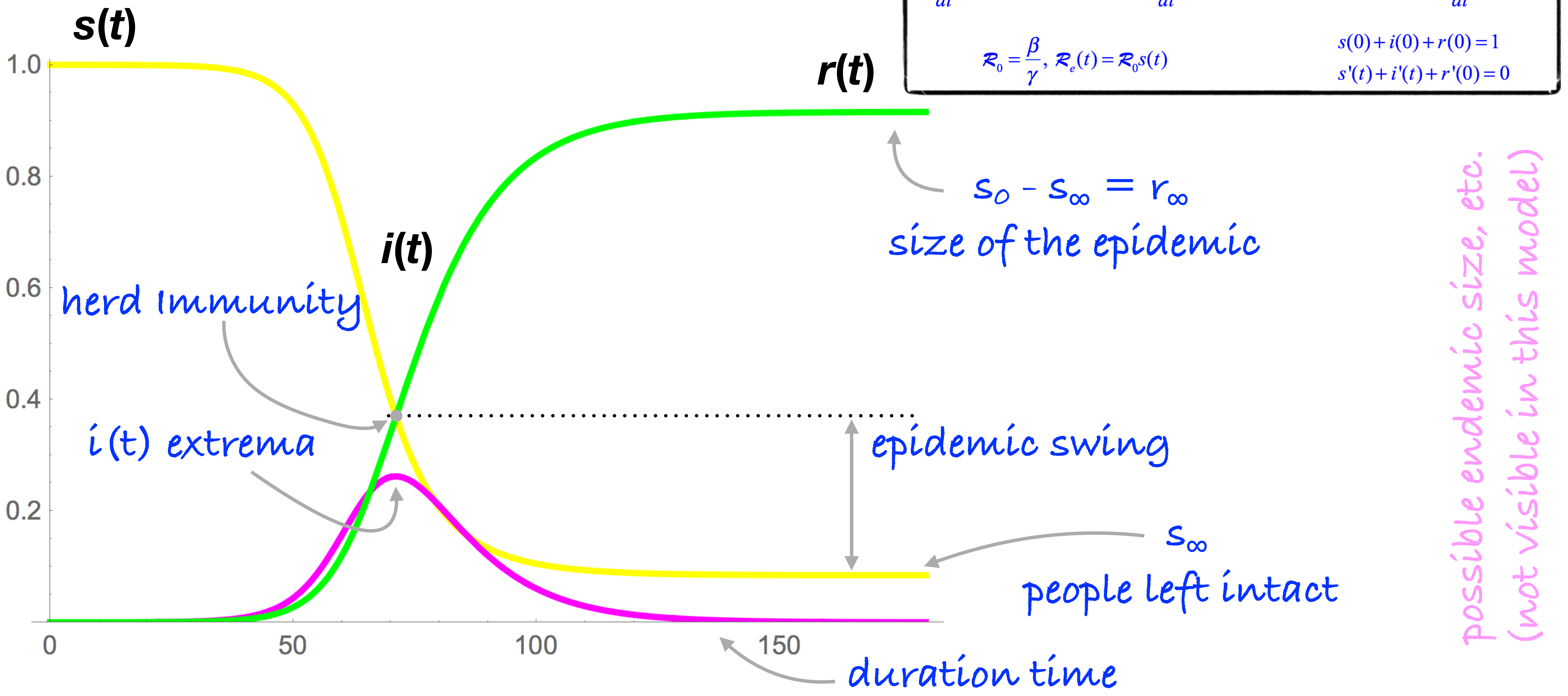
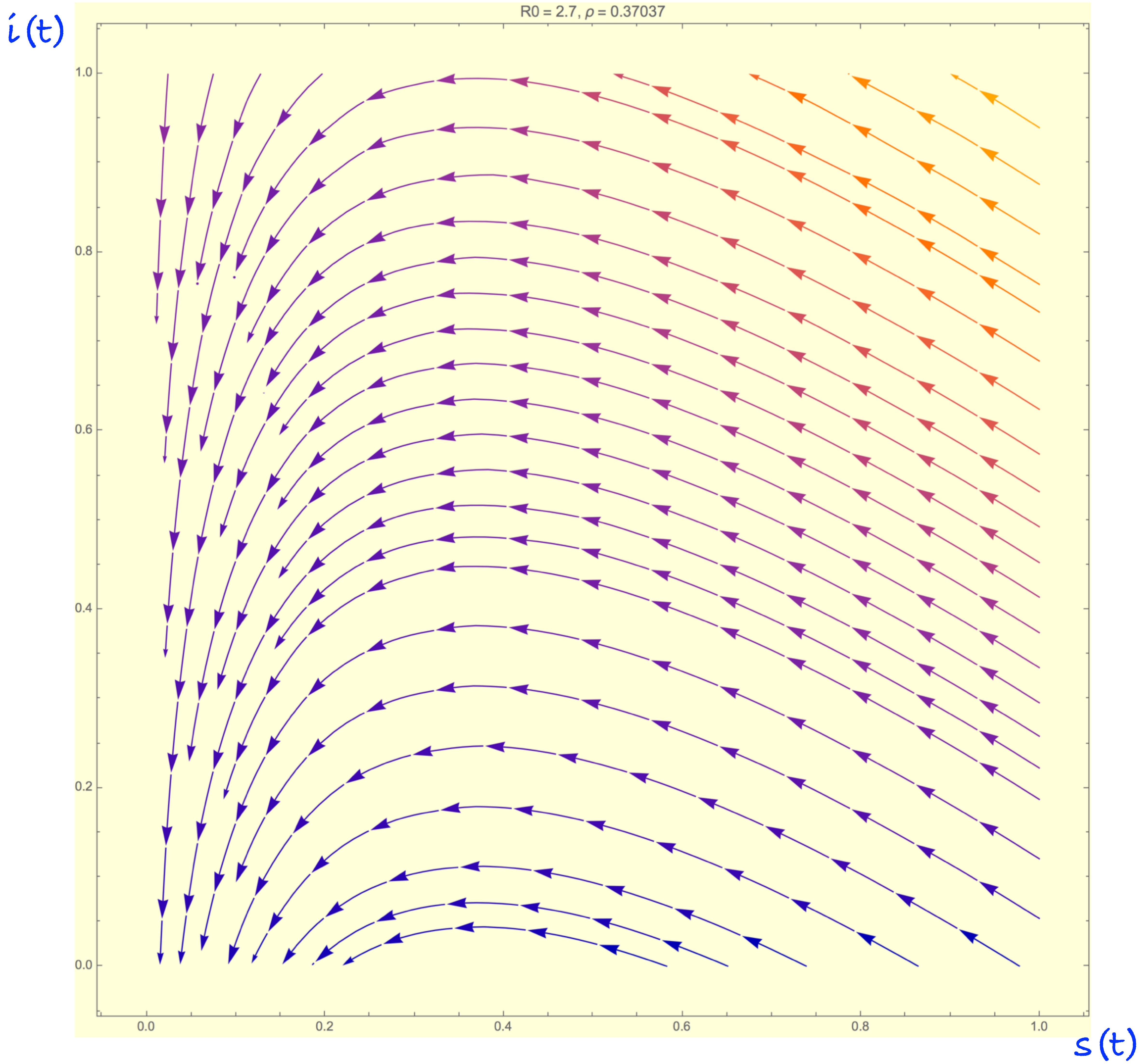
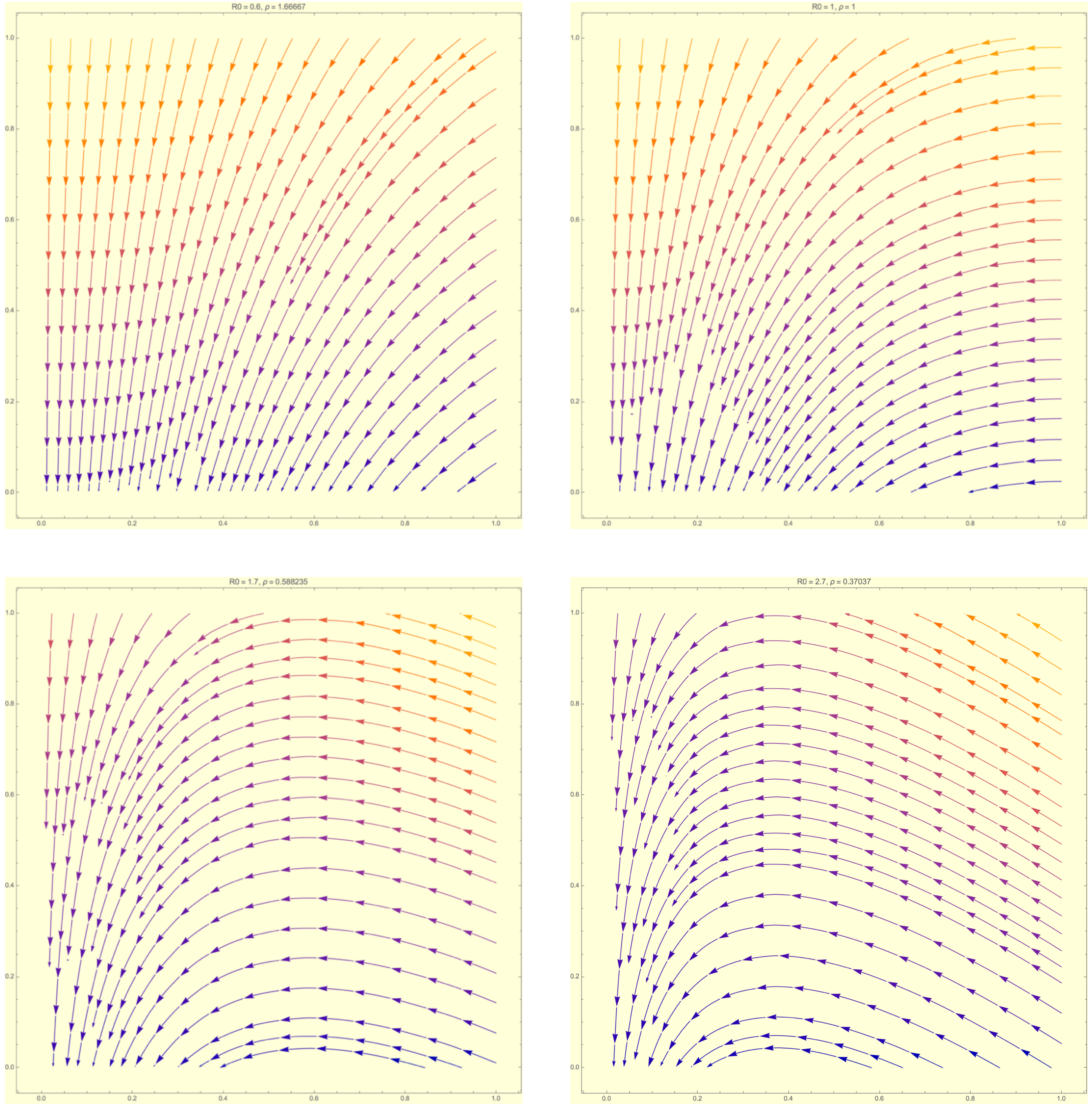


From Epidemic to Endemic

Epidemic Phase Portrait (yet, another viewpoint on the epidemic)



$\boldsymbol{R}_0$ Dependency and Consequences

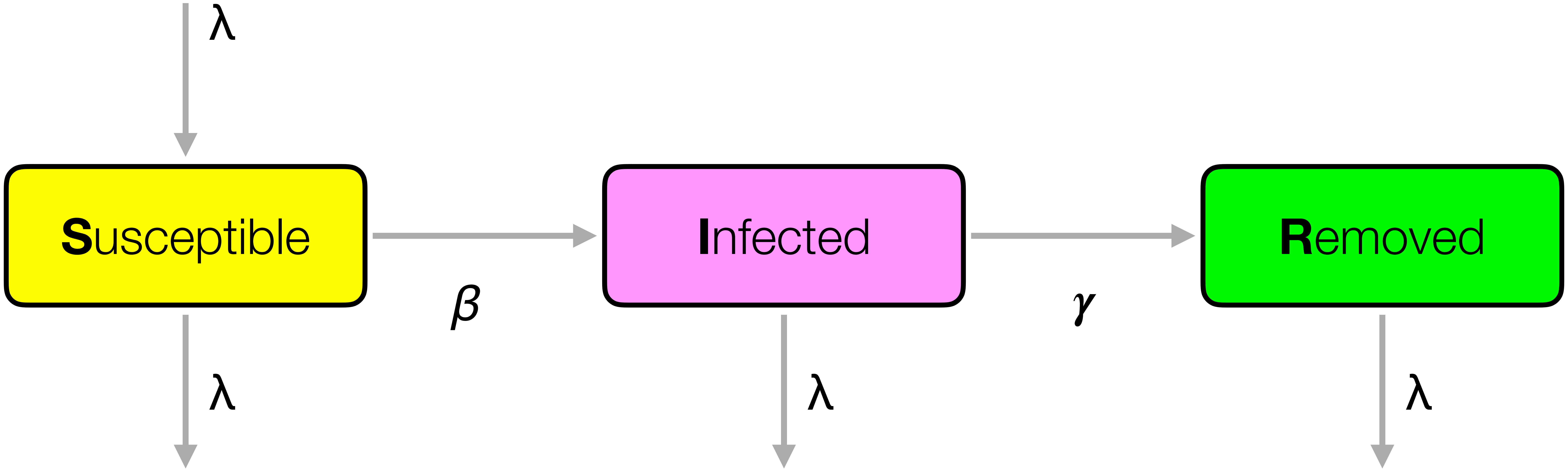


- phase field together with the herd immunity threshold ρ is fully determined by the (possibly controlled) basic reproduction number ($\rho = 1/R_0$)

- lockdowns primarily control **basic *R***, this is actually swapping one field for another one (back-and-forth)

- vaccination addresses the **effective *R***, this is actually a wormhole in the unchanged field

SIR Compartmental Epidemic Model
- including simple demography, now



- we set λ very high (with respect to a pure demography) here to illustrate endemic equilibrium in general
- on the other hand, in reality, demography is not the only reason for endemic states anyway

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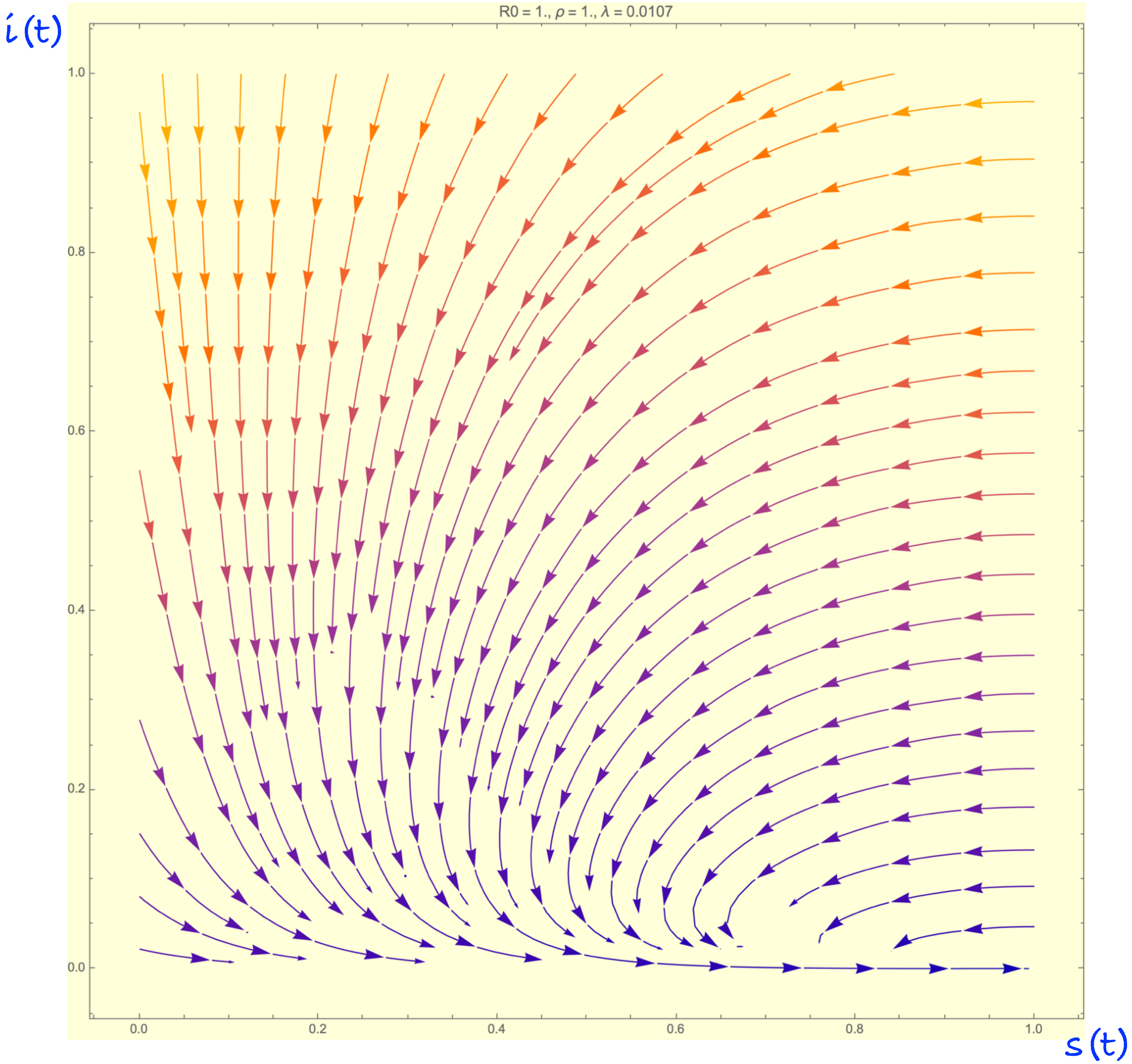
Perceiving Demography in the Phase Portrait



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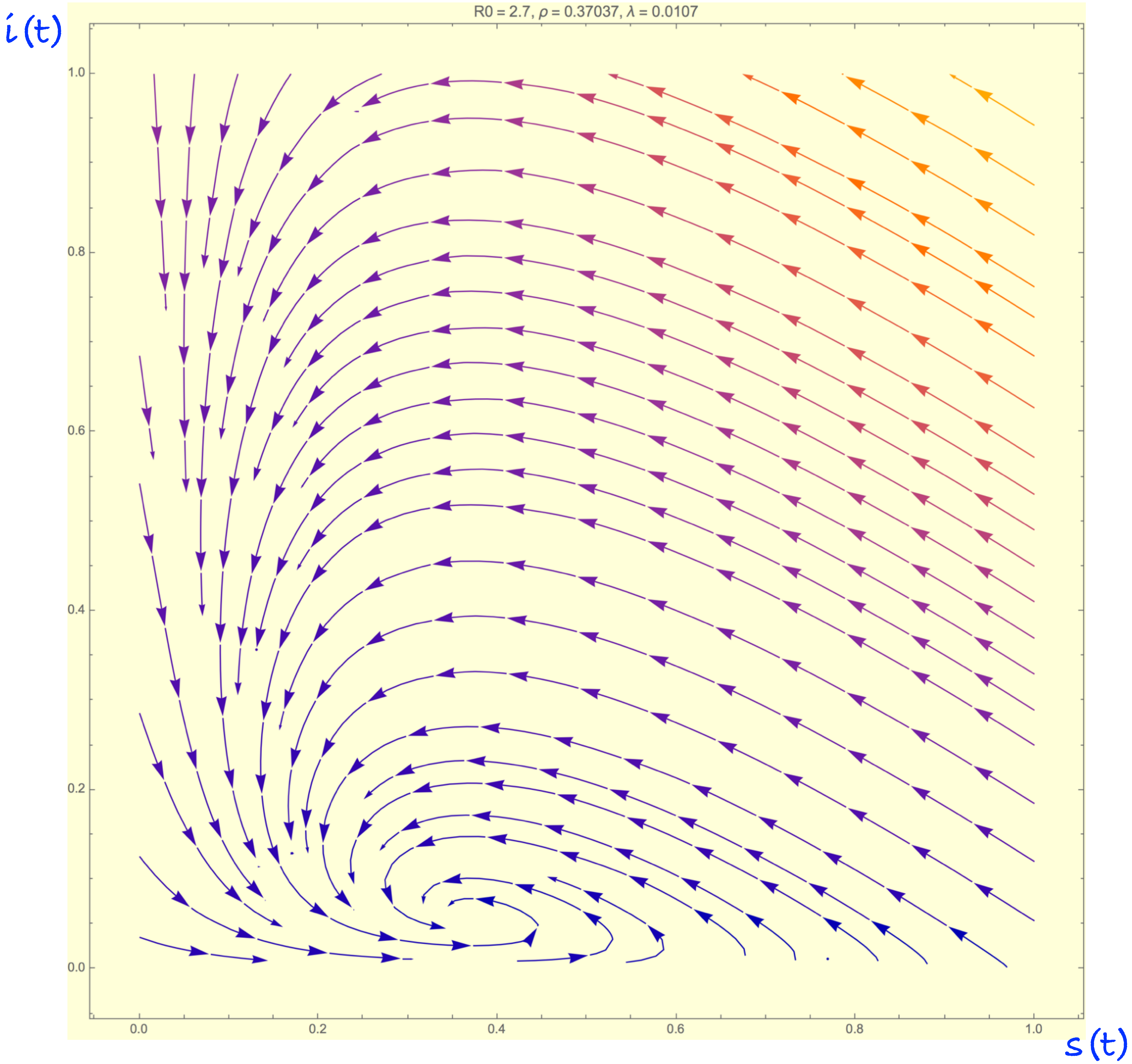
Endemic Equilibrium



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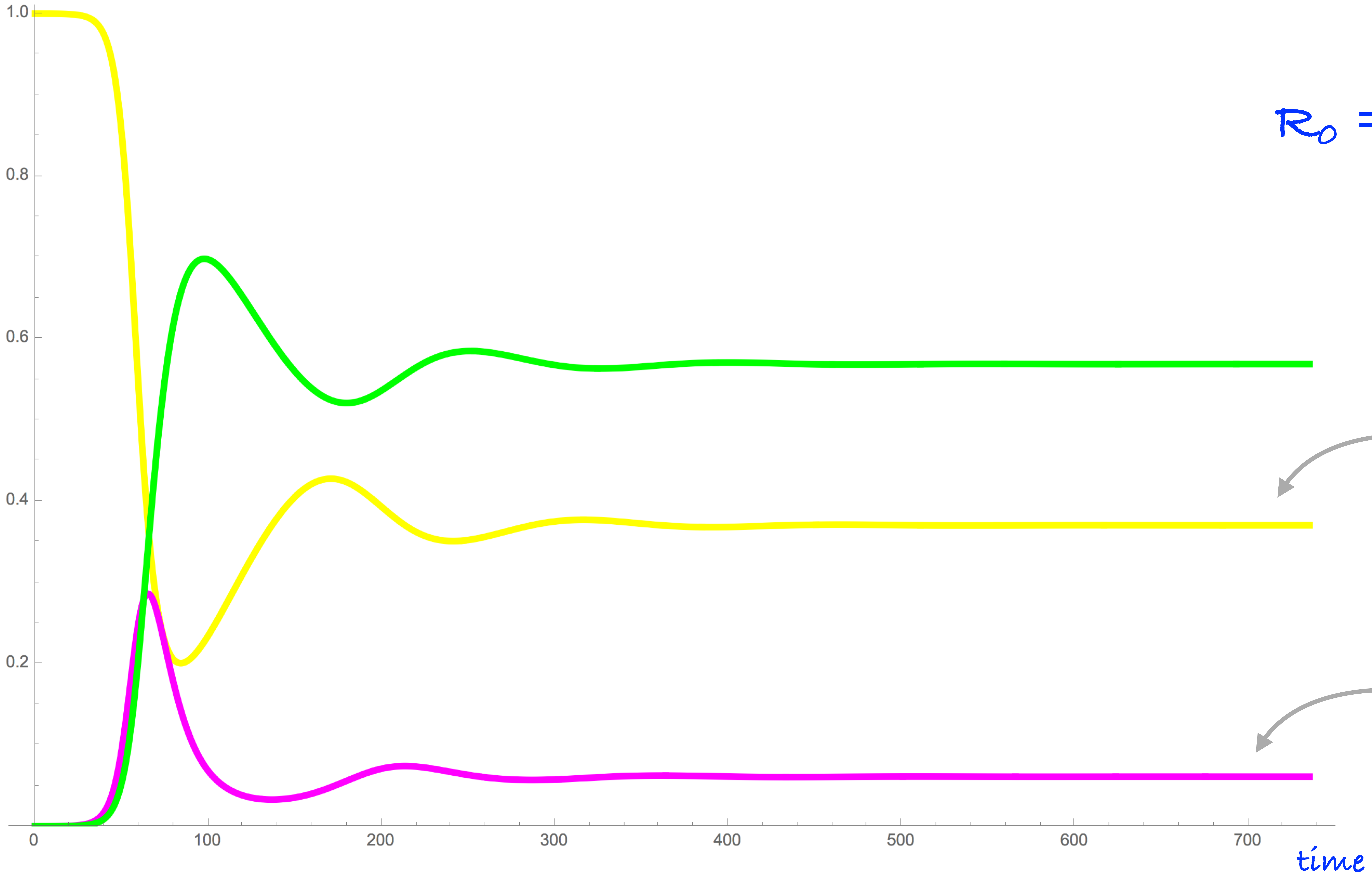
Endemic Equilibrium is Asymptotically Stable for $\boldsymbol{R}_0 > 1$



$R_0 = \beta / (\lambda + \gamma) \cong 2.7$

$s^* = 1/R_0 \cong 0.37$

$i^* \cong 0.06$

Qualitative Realities

Trust the mathematics,
not so the mathematicians.

Prevalence Decrease Roadmap - Reality versus Mighty Wish

- also relevant for the important viral load estimates

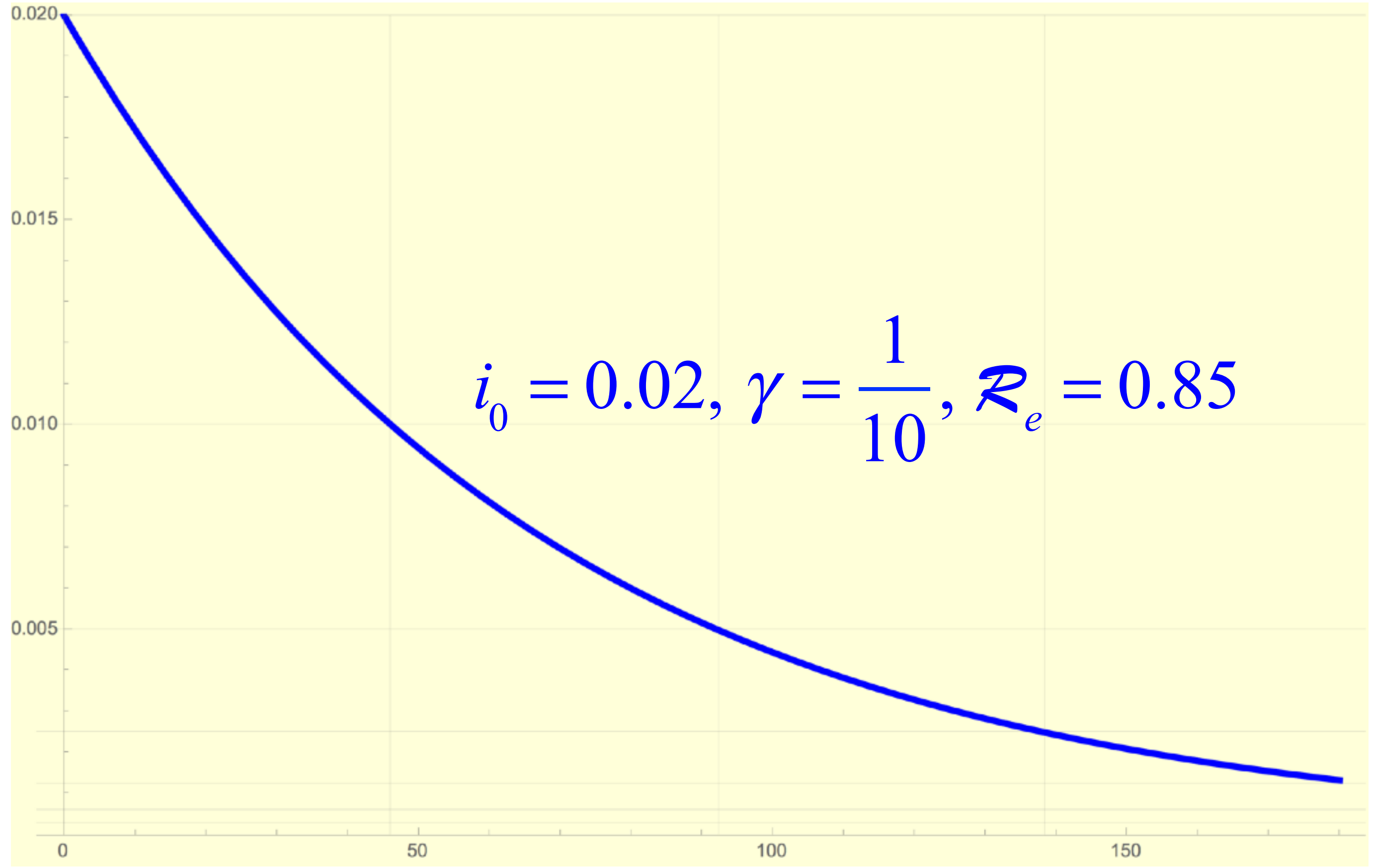
$$\frac{di(t)}{dt} = \beta i(t)s(t) - \gamma i(t)$$

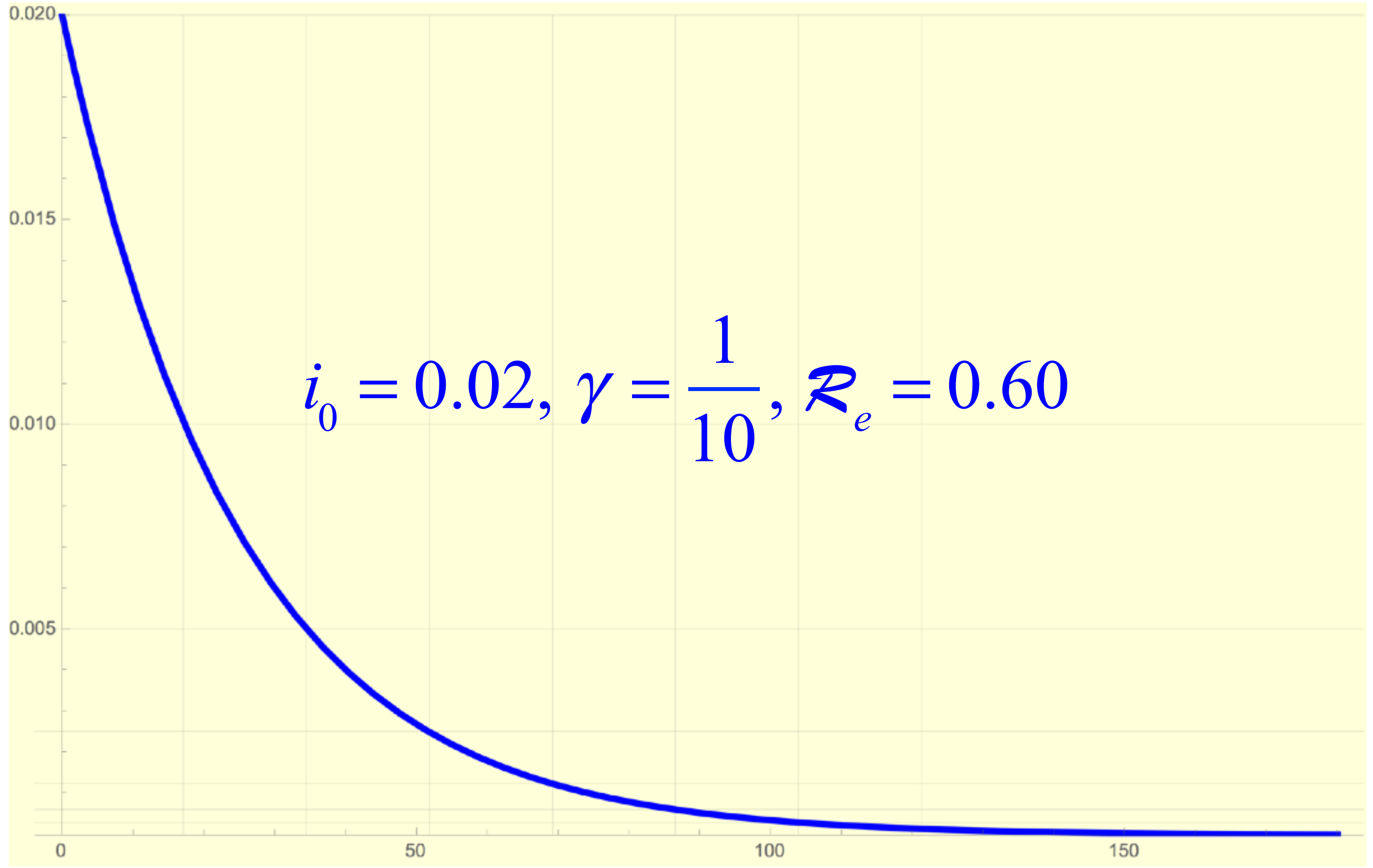
$$= -\gamma i(t)(1 - \frac{\beta}{\gamma} s(t)) = -\gamma i(t)(1 - \mathcal{R}_e(t))$$

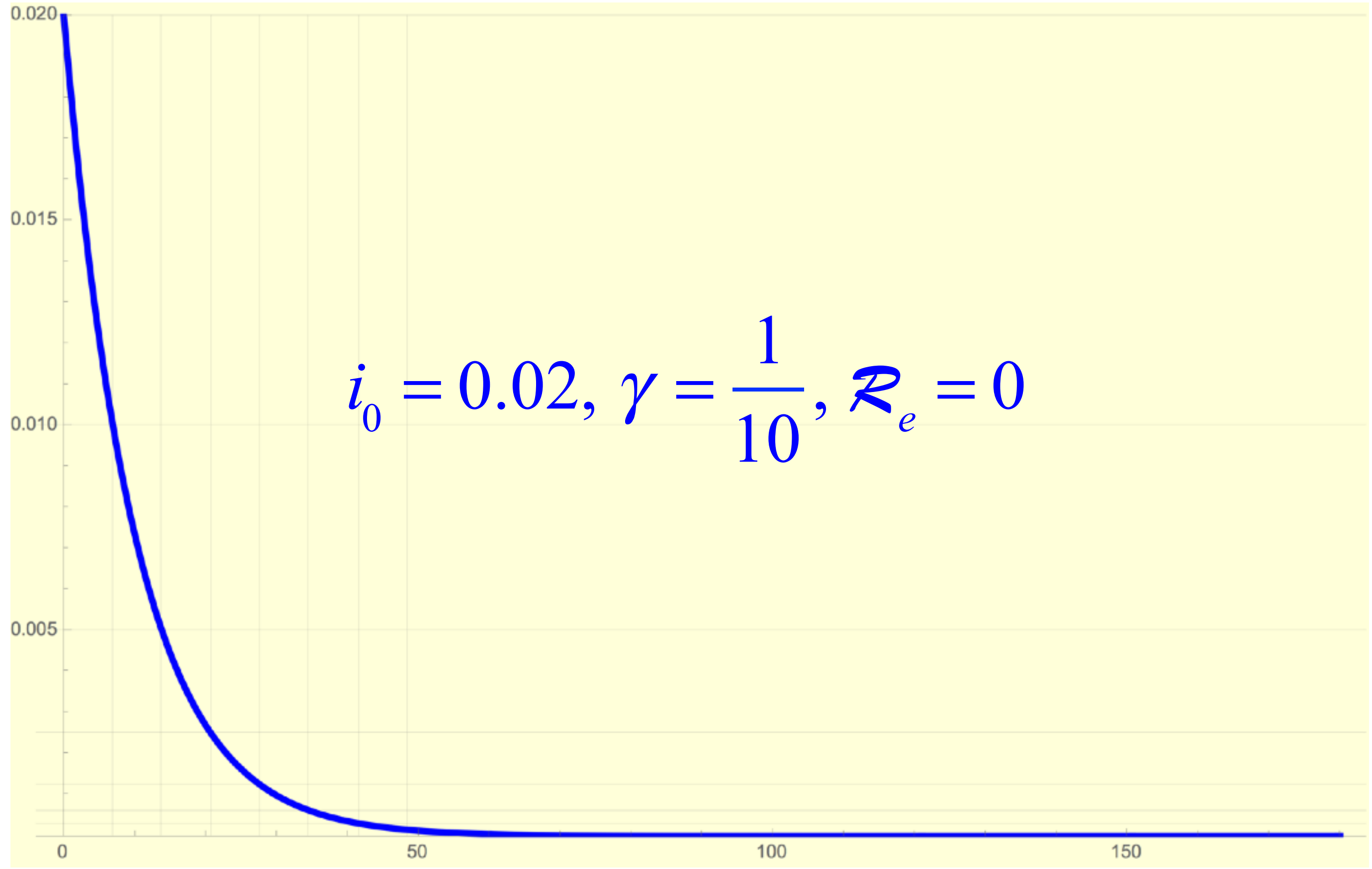
$$\text{stationary } \mathcal{R}_e : \; i(t) = i_0 e^{-\gamma(1-\mathcal{R}_e)t}$$

$$t_{1/2} = \frac{\ln 2}{\gamma}(1 - \mathcal{R}_e)^{-1}$$

- discloses the mechanics behind expectable prevalence decrease trajectory
- *stationary* effective reproduction number assumption is plausible enough for the qualitative assessment
- for the incidence viewpoint note then $ds(t)/dt = -\gamma \boldsymbol{R}_e(t) i(t)$
- asymptotically stable equilibrium 0 for $\boldsymbol{R}_e < 1$







Decrease Half-Time Sensitivity Overview (KNM-D2)

R_e	$t_{1/2}$ [d]		
	$\gamma^{-1} = 10$	$\gamma^{-1} = 14$	$\gamma^{-1} = 21$
0	7	10	15
0.6	17	24	36
0.65	20	28	42
0.7	23	32	49
0.75	28	39	58
0.8	35	49	73
0.85	46	65	97
0.9	69	97	146
0.95	139	194	291
> 1	N/A	N/A	N/A

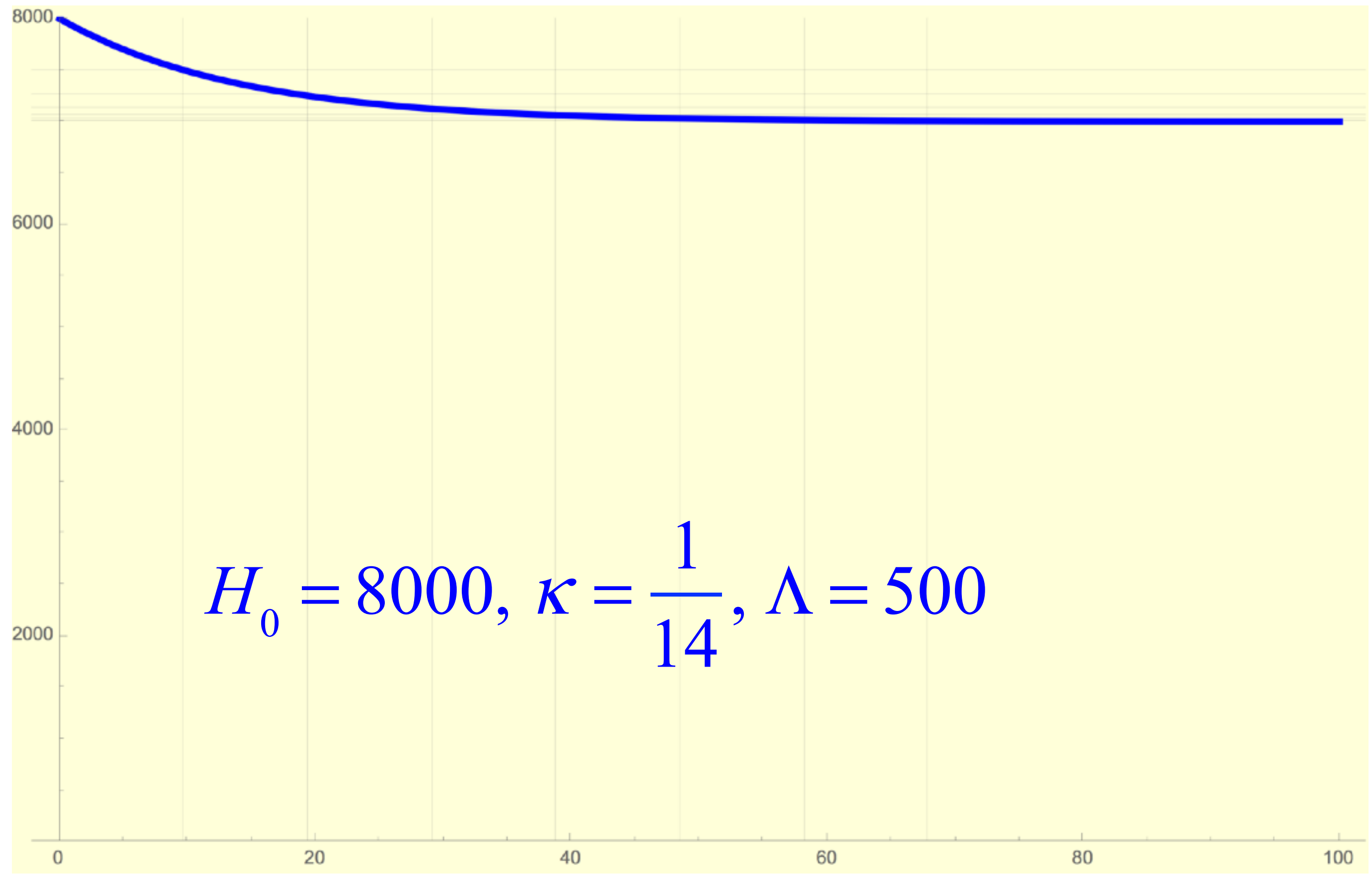
Consider a “Constant In, Fraction Out” Mechanism

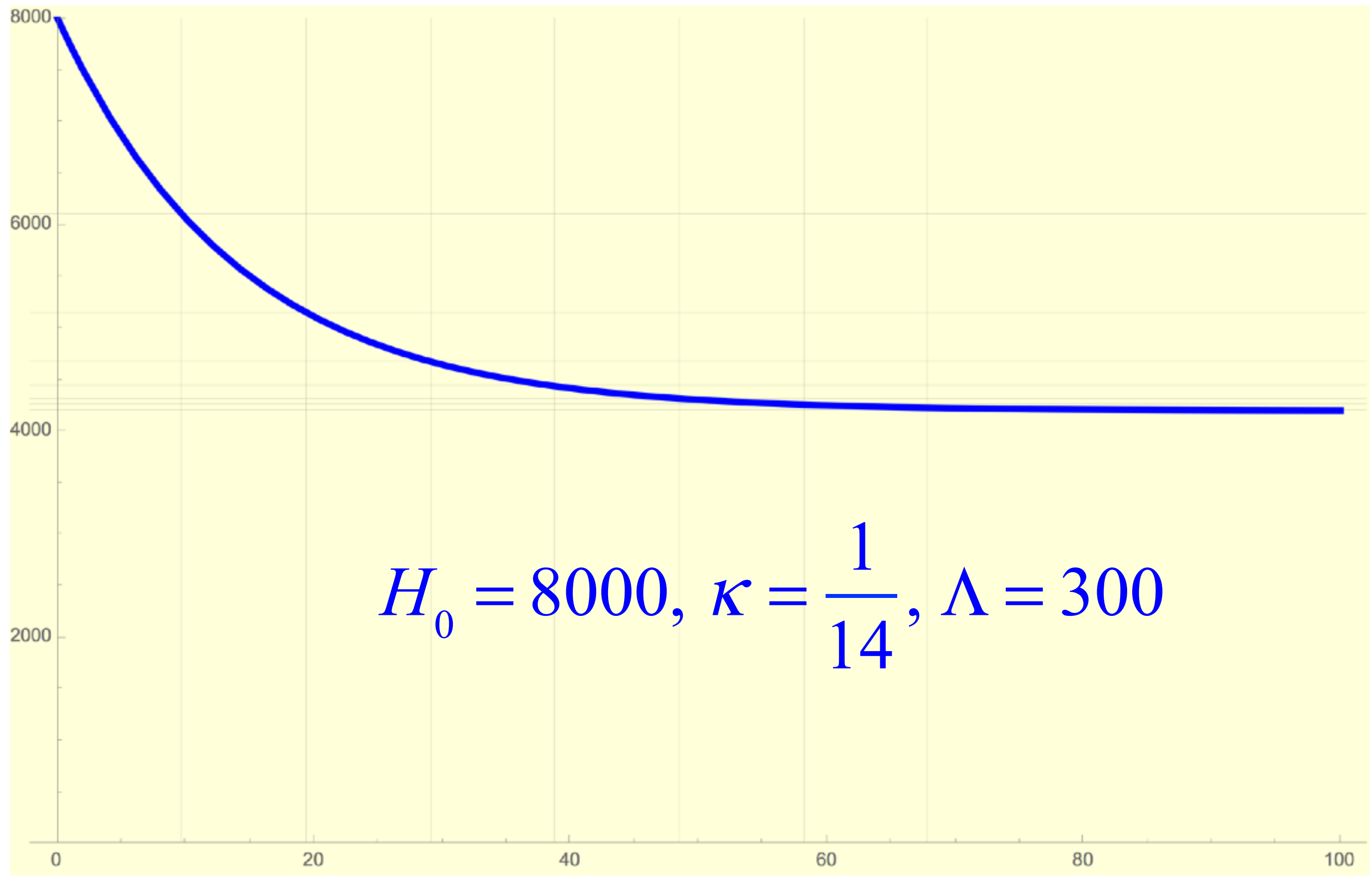
$$\frac{dH(t)}{dt} = \Lambda - \kappa H(t)$$

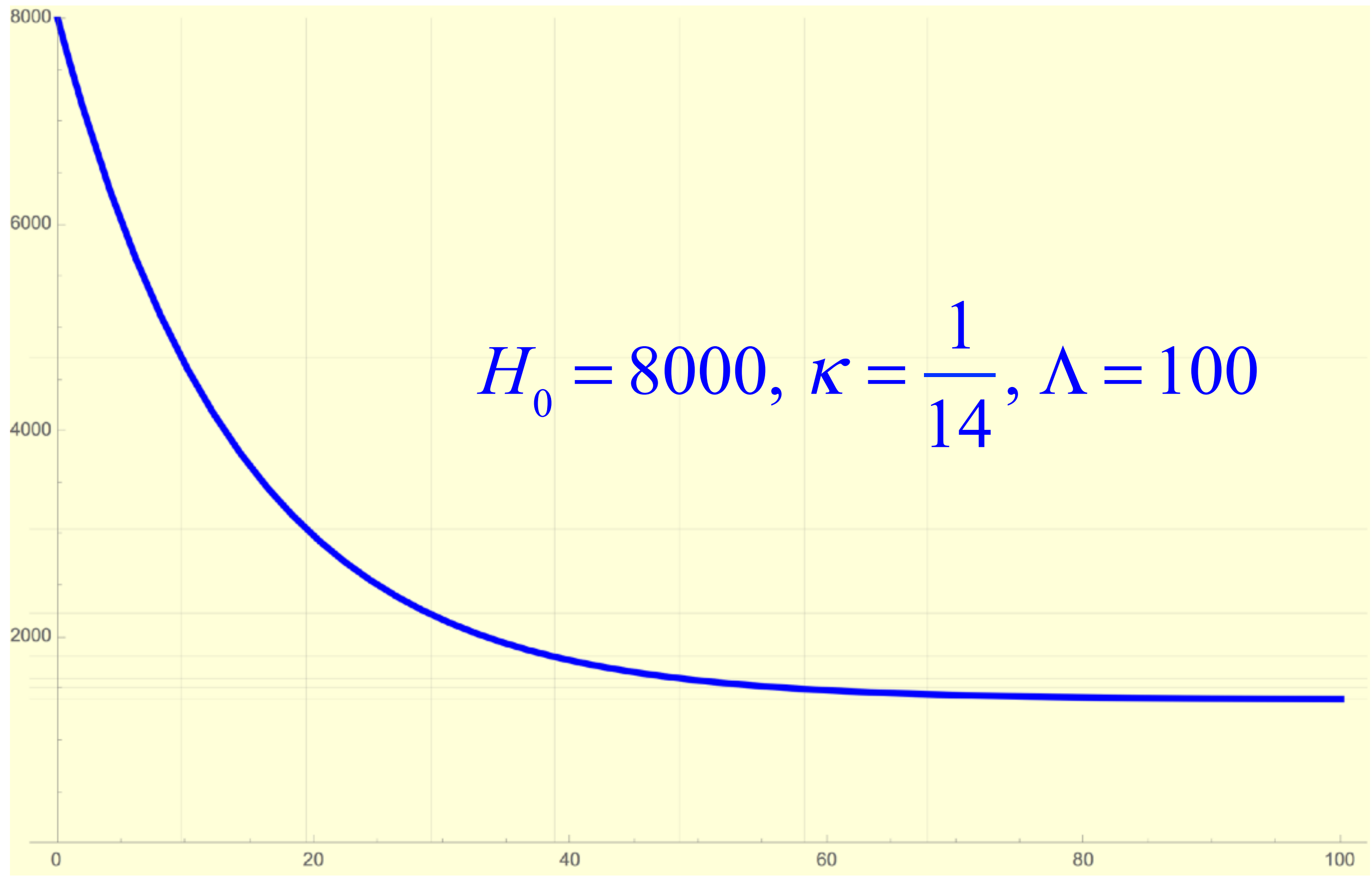
$$H(t) = H_0 e^{-\kappa t} + \frac{\Lambda}{\kappa}(1 - e^{-\kappa t})$$

$$t_{1/2} = \frac{\ln 2}{\kappa}$$

- simplified mechanics of hospital occupancy under stationary incidence levels
- illustrates expectable behaviour under (quasi)endemic conditions
- asymptotically stable equilibrium Λ/κ

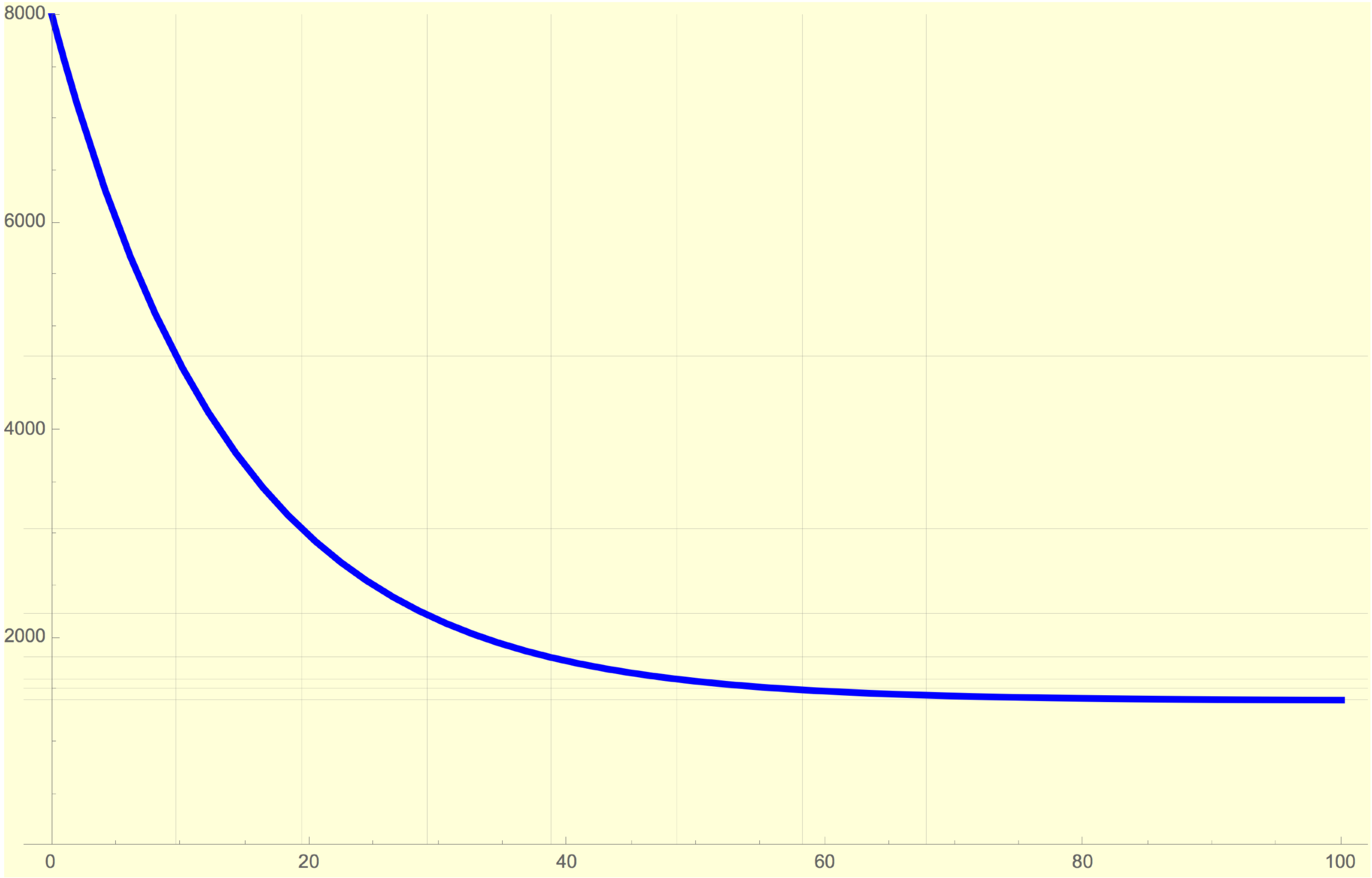




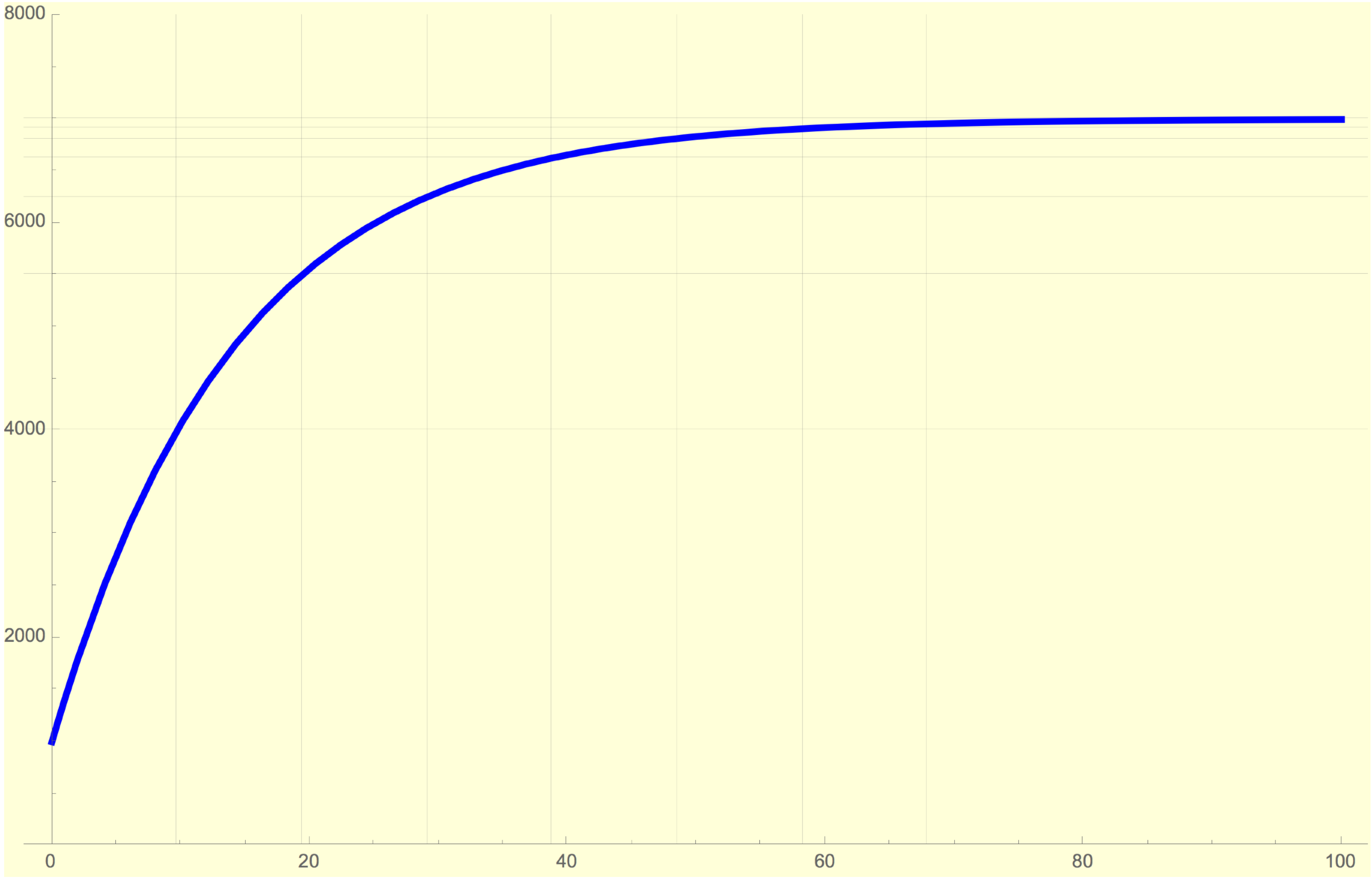


KNM-D1

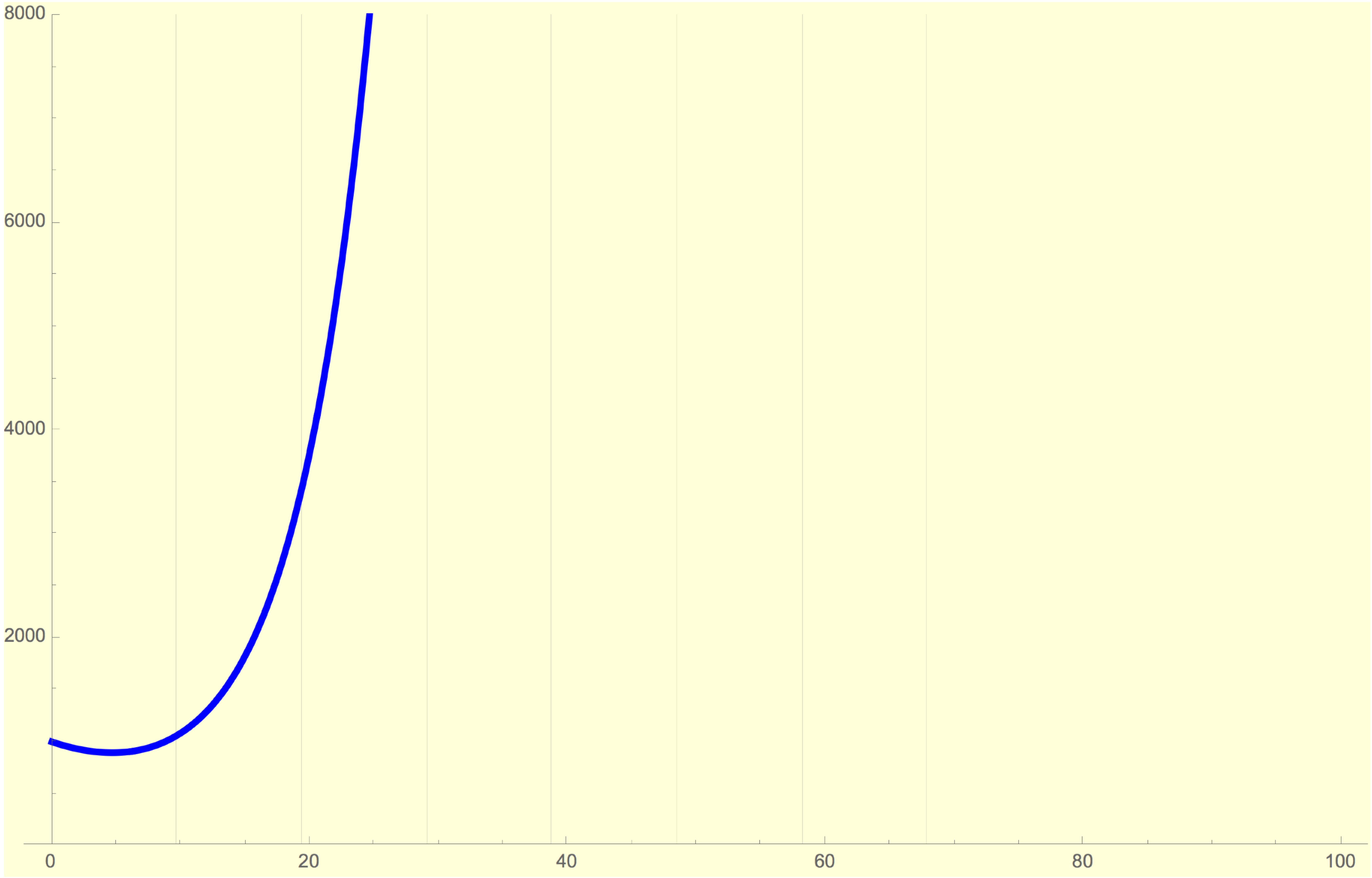
Qualitative Assessment: The Good



Qualitative Assessment: The Ugly



Qualitative Assessment: The Bad



Basic Vaccination Inequalities

$$\mathcal{R}_e(t) = \mathcal{R}_0 s(t) = \mathcal{R}_0(s_0 - p(t))$$

$$\approx \mathcal{R}_0(1 - p(t)) \text{ for } s_0 \approx 1$$

$$\mathcal{R}_e(t) < 1 \Leftrightarrow p(t) > 1 - \frac{1}{\mathcal{R}_0}$$

$$\text{resp. } p_\varepsilon(t) > \frac{1}{\varepsilon}\left(1 - \frac{1}{\mathcal{R}_0}\right)$$

For instance, AZD 1222 with 63.09% efficacy [WHO] eliminates $\mathbf{R}_0 < 2.7$.

- Assumptions:
  - vaccine distributed *uniformly among yet-susceptible* people
  - vaccine efficacy ε
  - immunity does not vanish in near time (circa one year, at least)
- Recovered people fraction bearing natural immunity then sums up with the vaccinated fraction
  - not shown here for clarity

Conclusion

- Mathematical modelling is the key part to create a platform where many experts from different areas can *share and dispute* their ideas
  - since mathematics is the ultimate language of this universe
- The more important decisions are to be made, the more we shall talk about the security and safety of our models
  - simply put **trust, but test**
  - mechanistic models do offer incredible opportunities to verify vital components of other models, here e.g. the reproduction number and risk index estimates as well as countermeasures effect

Revision History

- 2021/04/09: release version 1
- 2021/04/10: clarification notes on endemic illustrations added
- 2021/04/22: epidemic swing noted to support Kermack-McKendrick theorem formulation using the herd immunity overshoot
- 2021/04/22: herd immunity threshold noted as yet another optimisation criteria; makes sense (what is the “normal” behaviour?)