Mathematical Epidemiology - Compartmental Models Essentials

Lecture series at Faculty of Mathematics and Physics, CUNI in Prague

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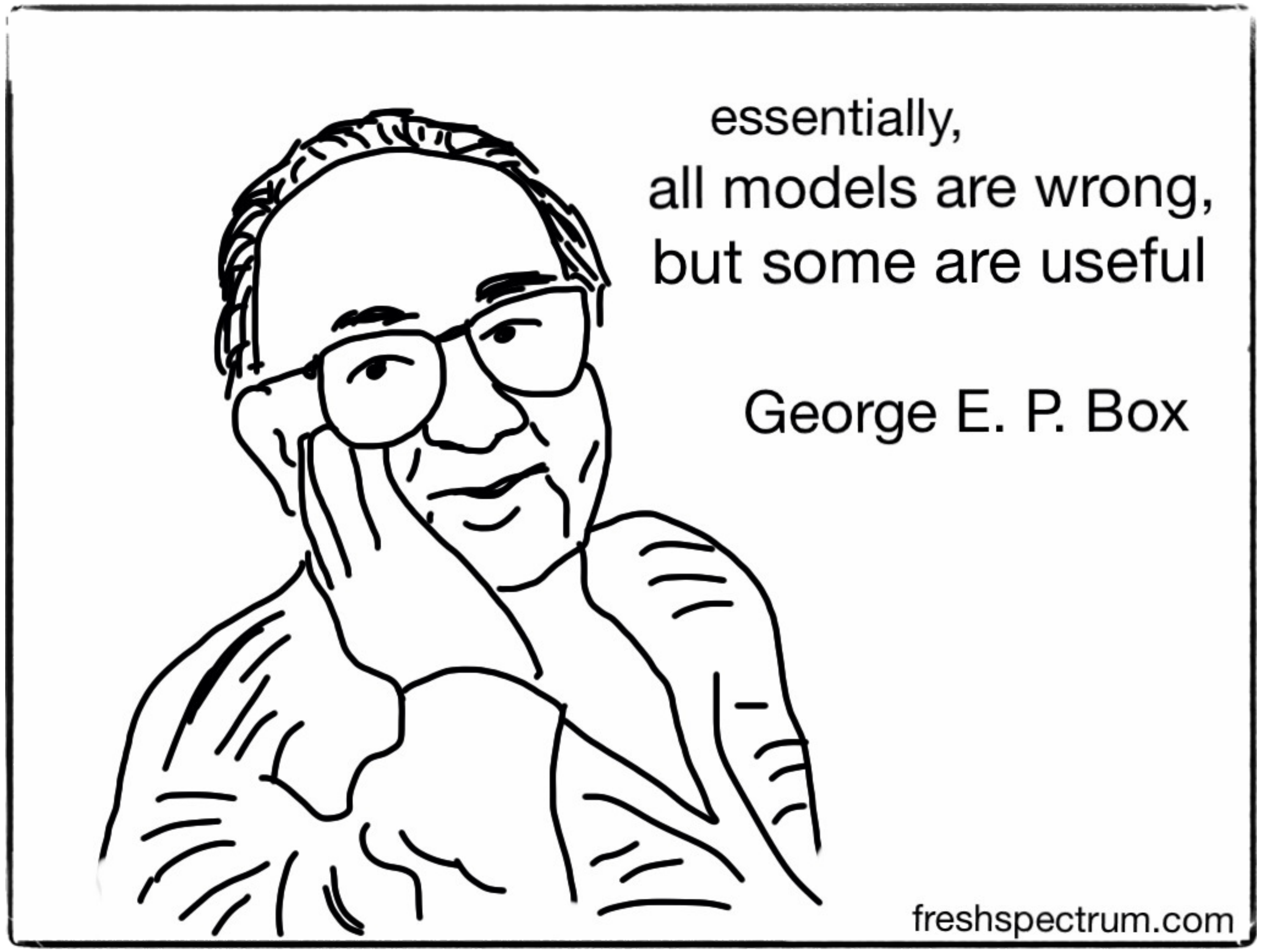
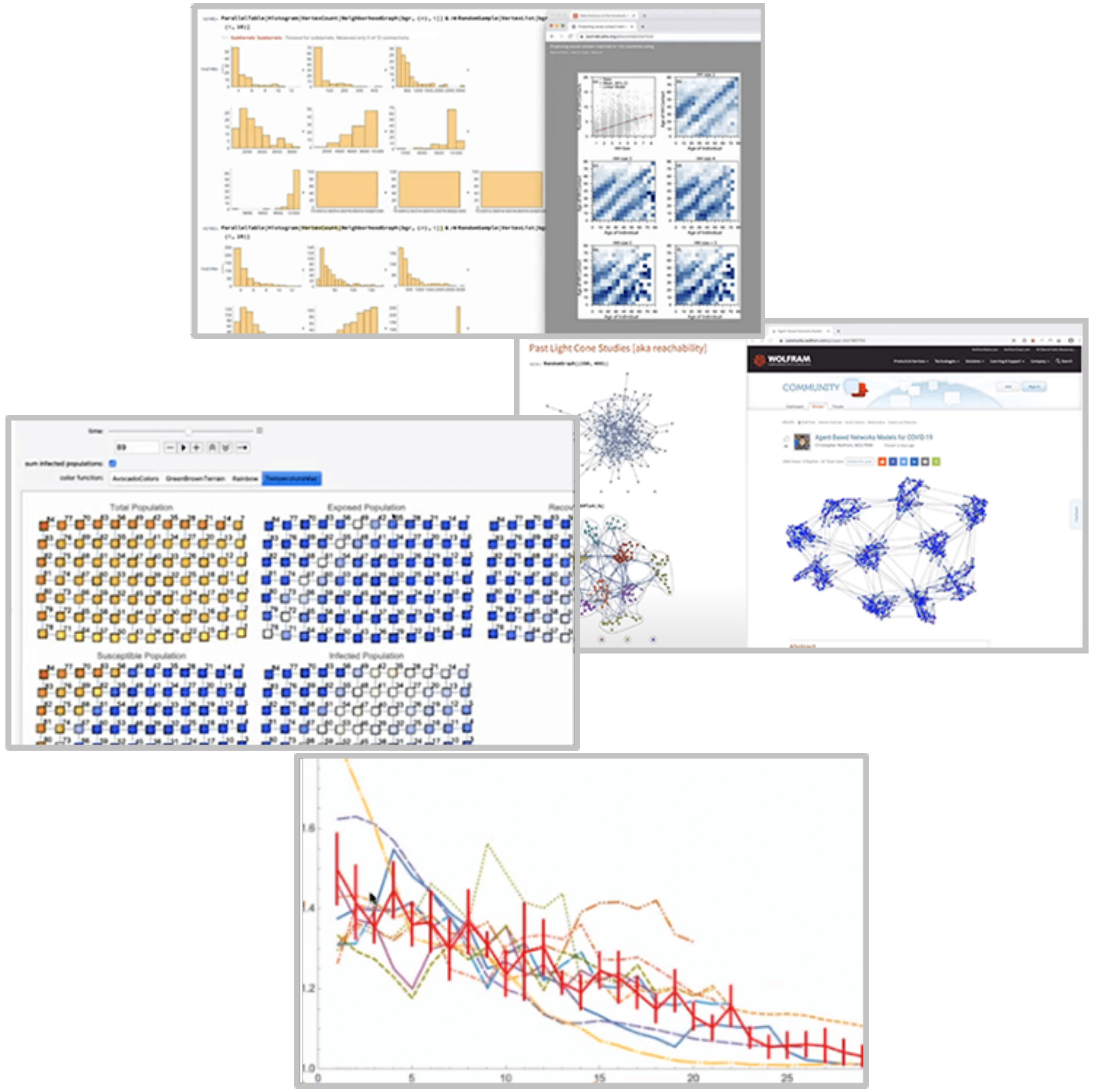
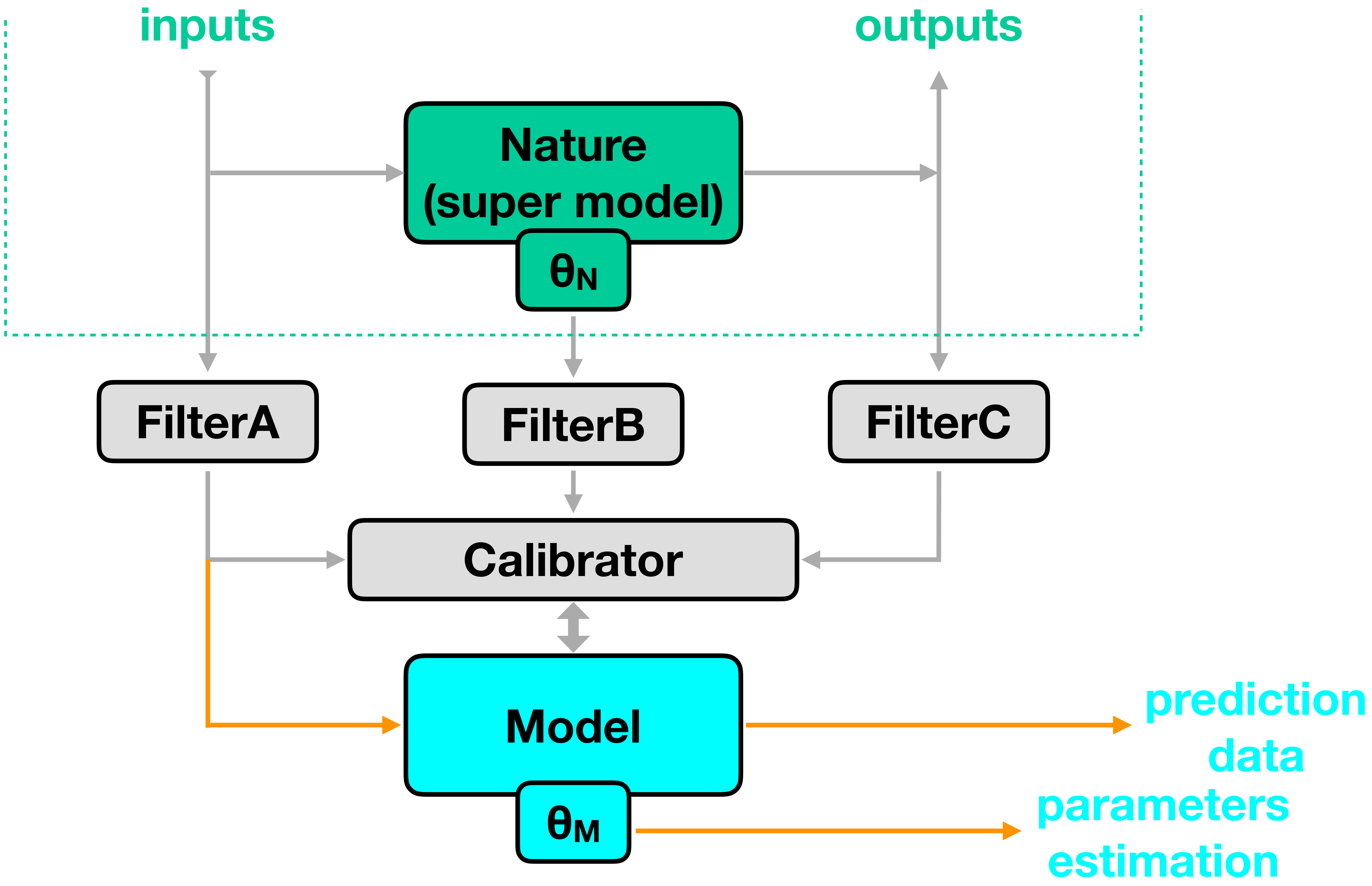
Have you said "modelling"?

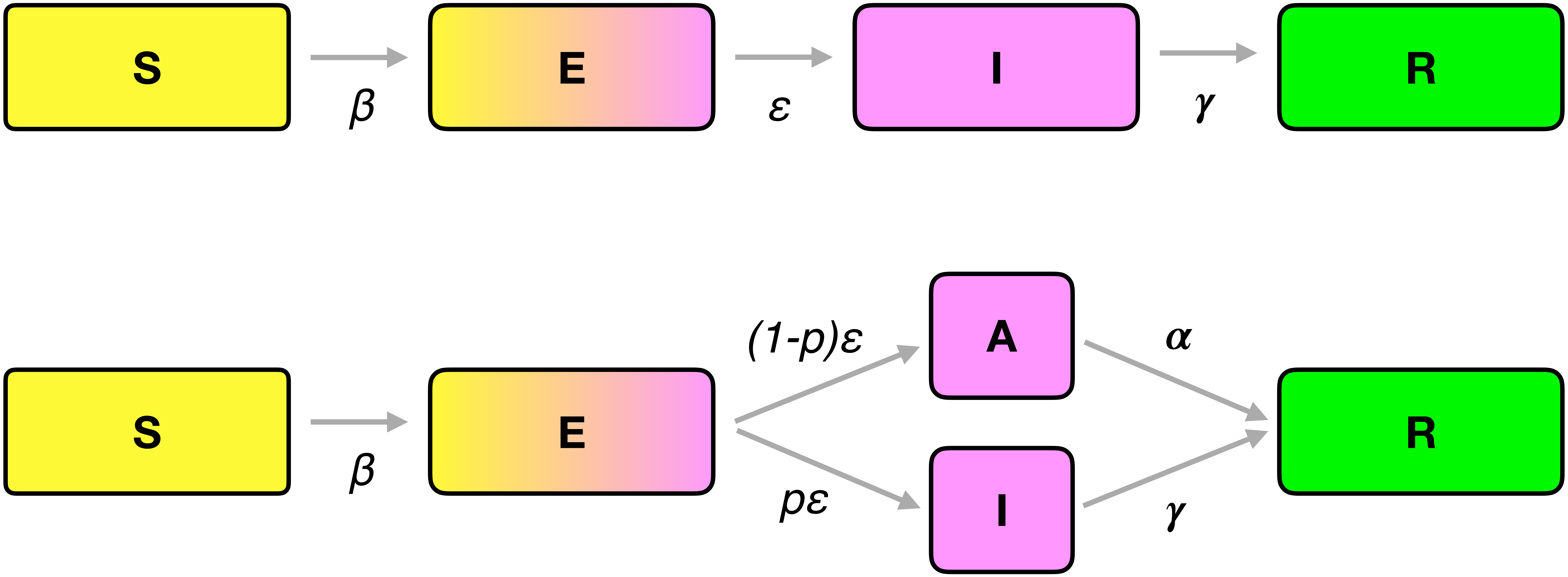




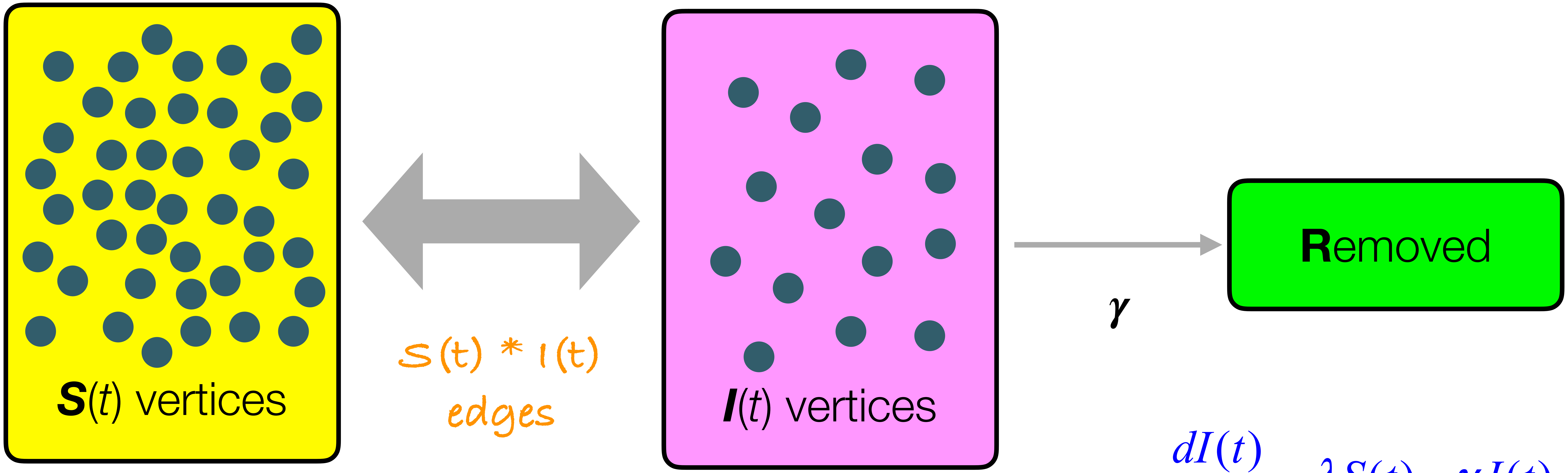

inputs
outputs
Nature
(super model)
θ_N
FilterA
FilterB
FilterC
Calibrator
Model
θ_M
prediction
data
parameters
estimation

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

Towards COVID-19 *Quantitative* Realities - SEIR and SEAIR



SIR Compartmental Epidemic Model
- zooming on the mass action mechanism



$$\lambda = \frac{\beta}{N} I(t)$$

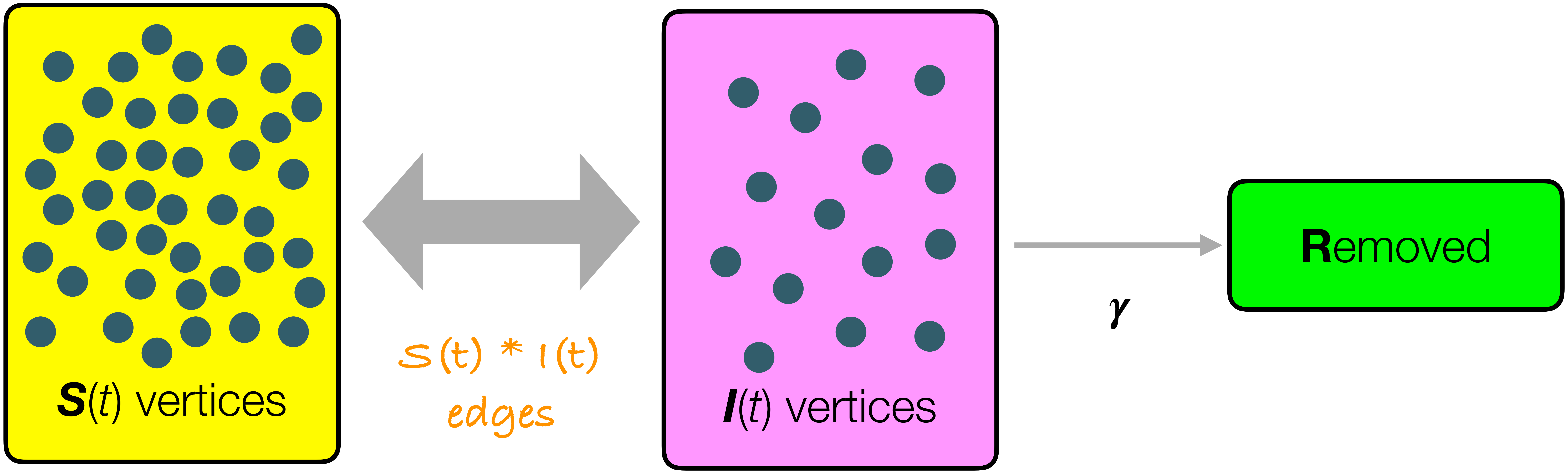
infection force

$$\frac{dS(t)}{dt} = -\frac{\beta}{N} I(t)S(t) = -\lambda S(t)$$

$$\frac{dI(t)}{dt} = \lambda S(t) - \gamma I(t)$$

$$\frac{dR(t)}{dt} = \gamma I(t)$$

SIR Compartmental Epidemic Model
- zooming on the mass action mechanism



$$\frac{dS(t)}{dt} = -\frac{\gamma \cdot \mathcal{R}_0 \cdot season(t) \cdot control(t)}{N} S(t)I(t) = -\gamma R_e(t) I(t)$$

$$\frac{dI(t)}{dt} = \gamma \left(\frac{\mathcal{R}_0 \cdot season(t) \cdot control(t)}{N} S(t) - 1 \right) I(t) = \gamma (R_e(t) - 1) I(t)$$

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

$R_e(t)$ stands for the effective reproduction number

All Those "***R***"s

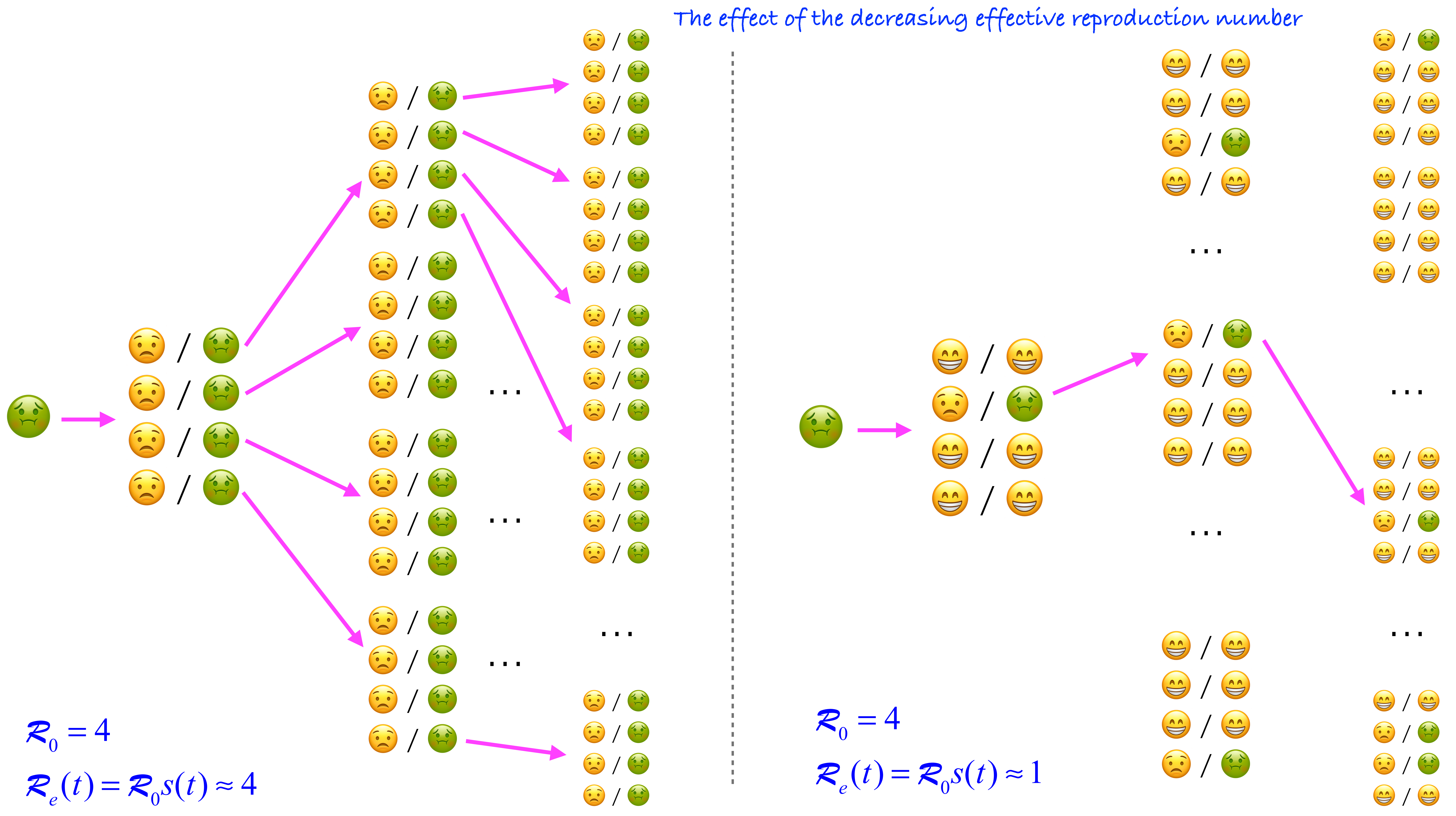
$$\mathcal{R}_0 = \frac{\beta}{\gamma}$$

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

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

*) in this particular model

- *In general, the average number of people one infectious individual infects under particular circumstances.*
- 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
$\mathcal{R}_0 = 4$
$\mathcal{R}_e(t) = \mathcal{R}_0 s(t) \approx 4$
$\mathcal{R}_0 = 4$
$\mathcal{R}_e(t) = \mathcal{R}_0 s(t) \approx 1$

Ordinary Differential Equations - What do they say here?

$$X(t+\Delta t) = X(t) + [\Lambda + \alpha X(t) + \beta X(t)Y(t)]\Delta t$$

$$\frac{X(t+\Delta t) - X(t)}{\Delta t} = \Lambda + \alpha X(t) + \beta X(t)Y(t)$$

$$\lim_{\Delta t \to 0} \frac{X(t+\Delta t) - X(t)}{\Delta t} = \frac{dX(t)}{dt}$$

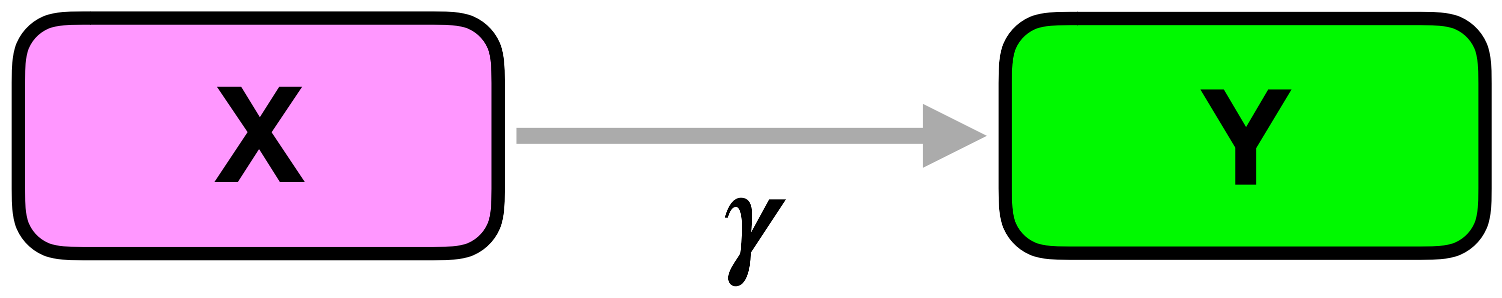
$$\frac{dX(t)}{dt} = \Lambda + \alpha X(t) + \beta X(t)Y(t)$$

- General form of ODE as used in many deterministic models of biological processes
  - incorporates various kinds of growth/decrease action and handles the infinitesimal time steps correctly
  - Λ is an *instantaneous **absolute** rate of change* of a "degree-zero" growth/decrease process
  - α is an *instantaneous **relative** rate of change* of a "degree-one" growth/decrease process
  - β analogous to α, this time for a **mass action** ("degree-two") growth/decrease process

Understanding (Isolated) Spontaneous Flow

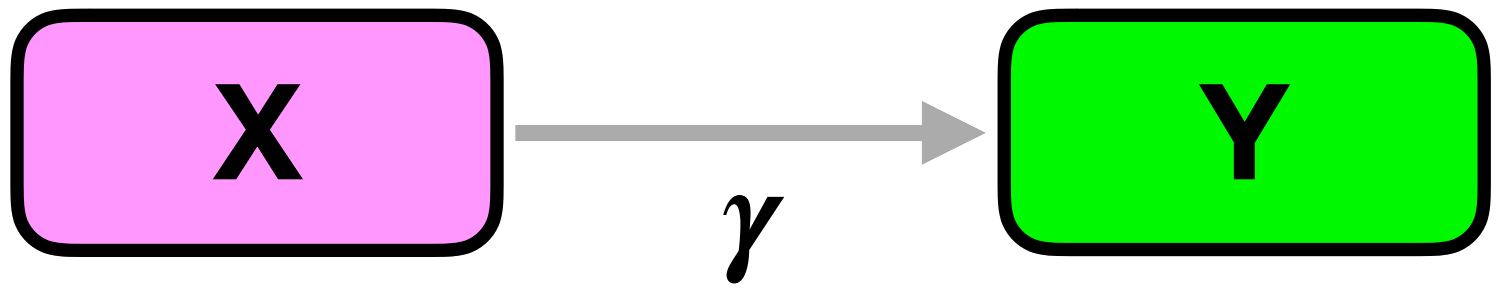
For an illustration, let us have

$$\frac{dX(t)}{dt} = -\gamma X(t) \text{ and } \frac{dY(t)}{dt} = \gamma X(t)$$



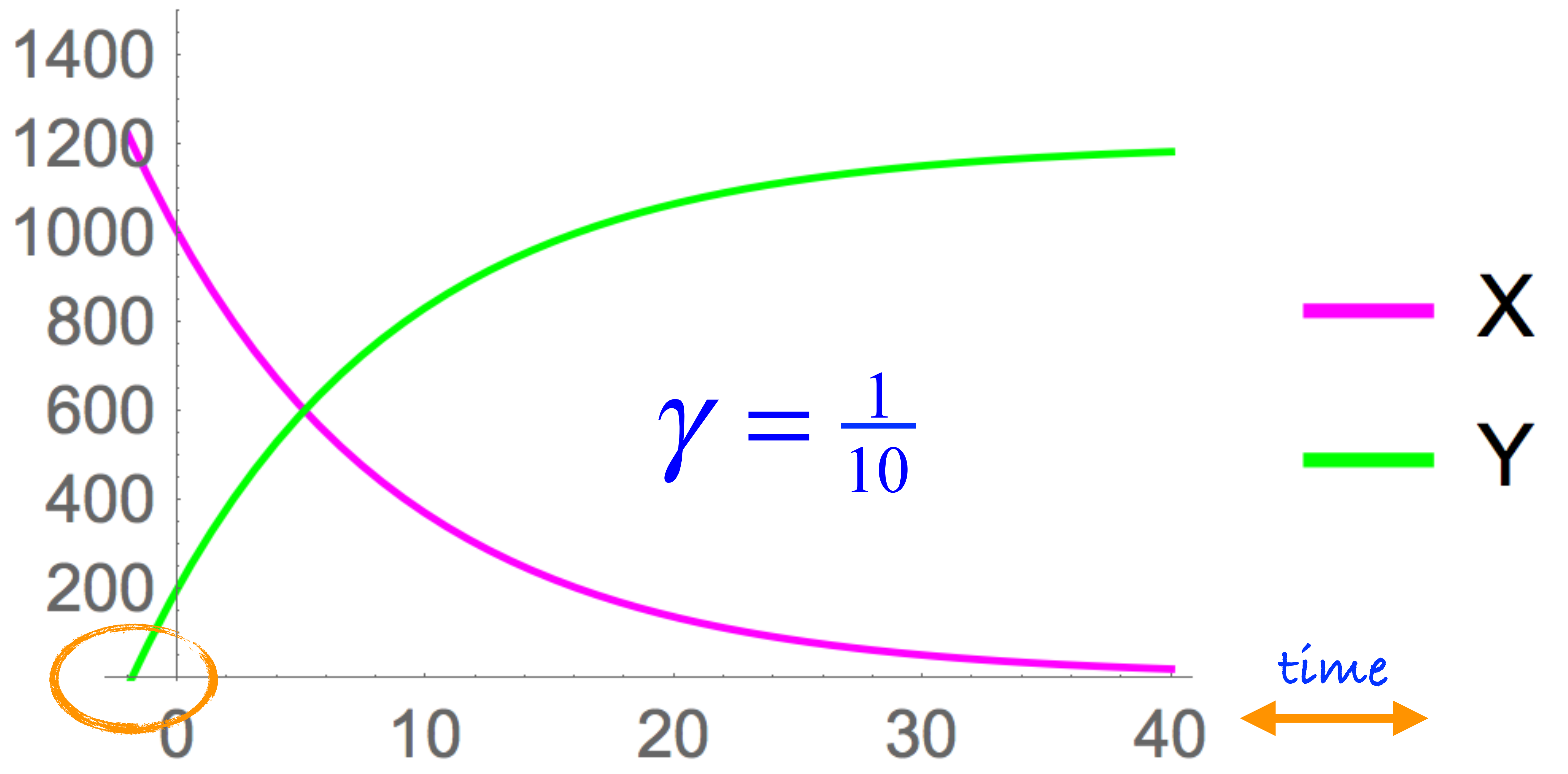
- We have two connected population decrease/growth sub-models
    - the solution is easy to find analytically
- Be careful the constant relative rate assumption is helpful, but it is just an approximation
    - this is in turn equivalent to the exponential waiting time distribution, as noted below

Analytical Solution of (Isolated) Spontaneous Flow



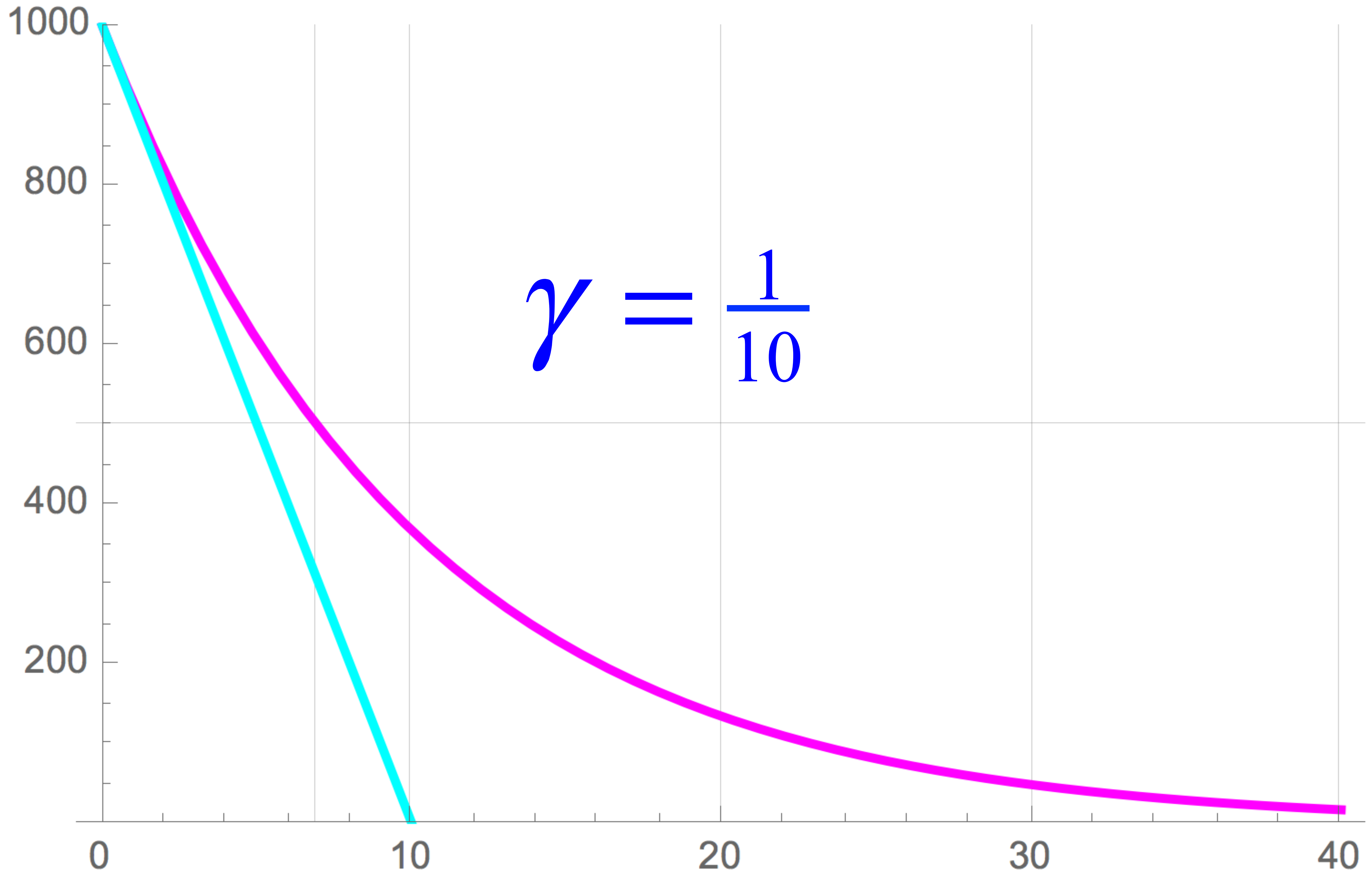
$$X(t) = X_0 e^{-\gamma t}$$

$$Y(t) = X_0 (1 - e^{-\gamma t}) + Y_0$$



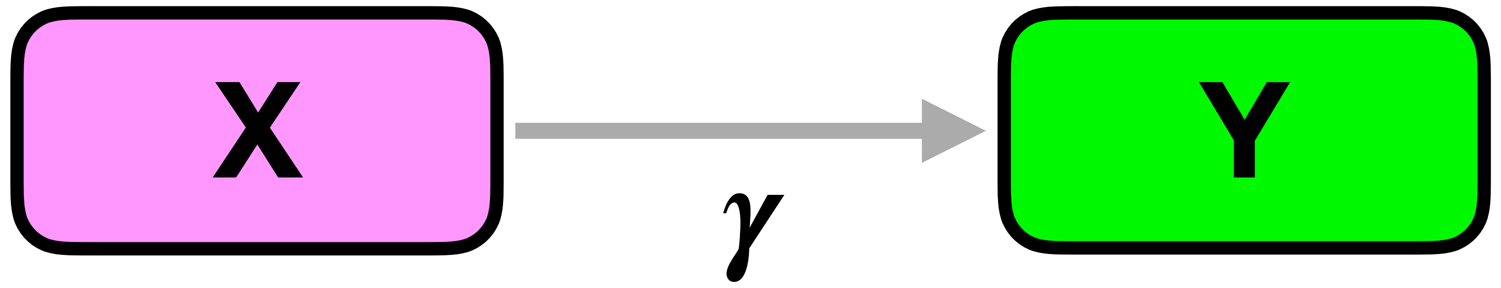
- Having fitted the initial conditions (X_0, Y_0) and γ, we can **run the model back and forth**
  - the initial conditions can be further given for any time instant, not just in $t = 0$
- This is an example of deterministic models reversibility which is in turn very interesting in itself
  - sure, be careful about the interpretation of the results, e.g. What would $y(t) < 0$ remind us?

Cautionary Note: Exponential vs Linear Decrease
- exponential decrease speed also decreases exponentially



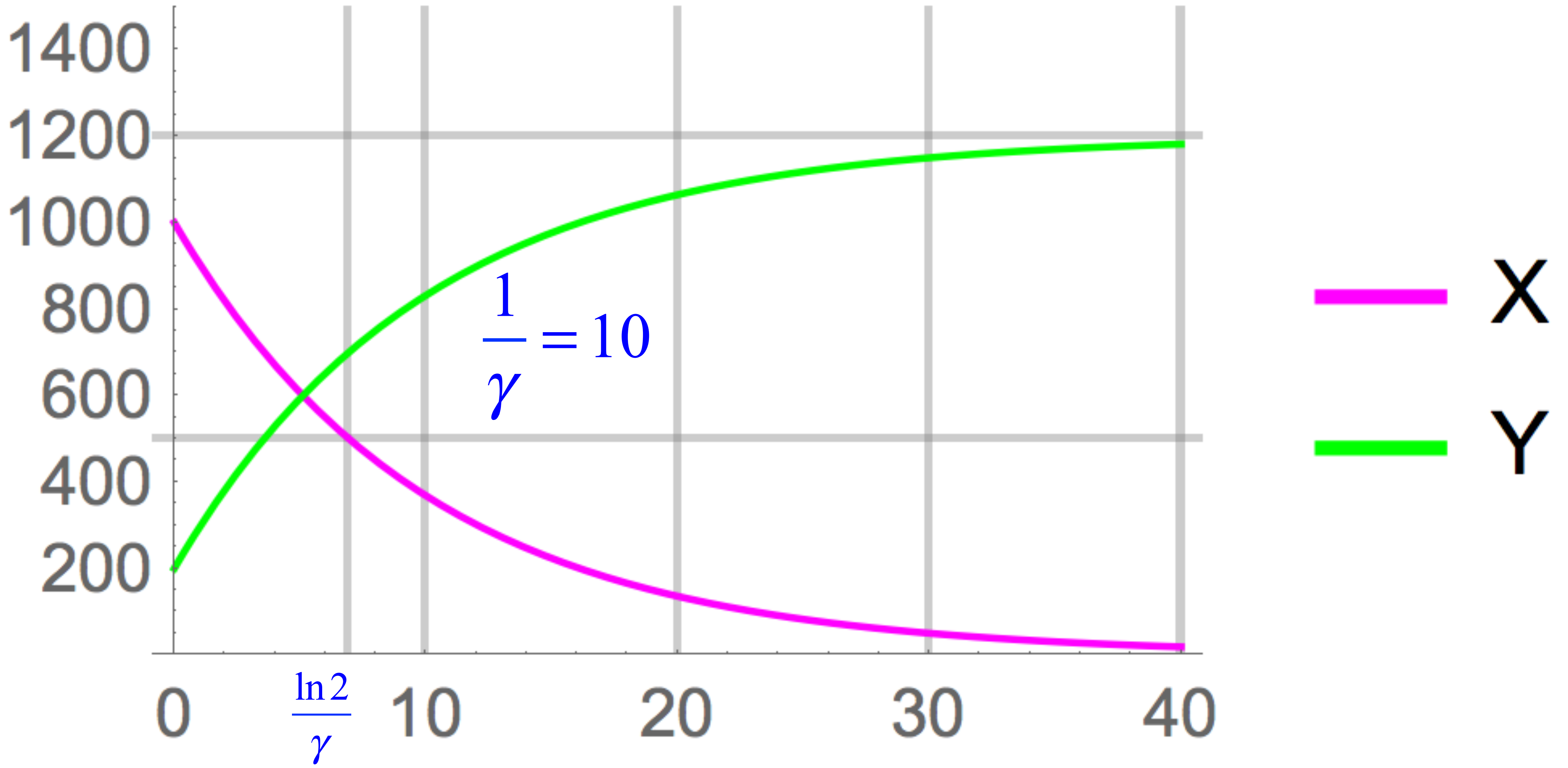
time	exp	lin
0	1000	1000
1	905	900
2	819	800
3	741	700
4	670	600
5	607	500
6	549	400
7	497	300
8	450	200
9	407	100
10	368	0

Fitting the γ Rate



$$\frac{X(t)}{X_0} = e^{-\gamma t}$$

$$F_W(t) = 1 - \frac{X(t)}{X_0} = 1 - e^{-\gamma t}$$

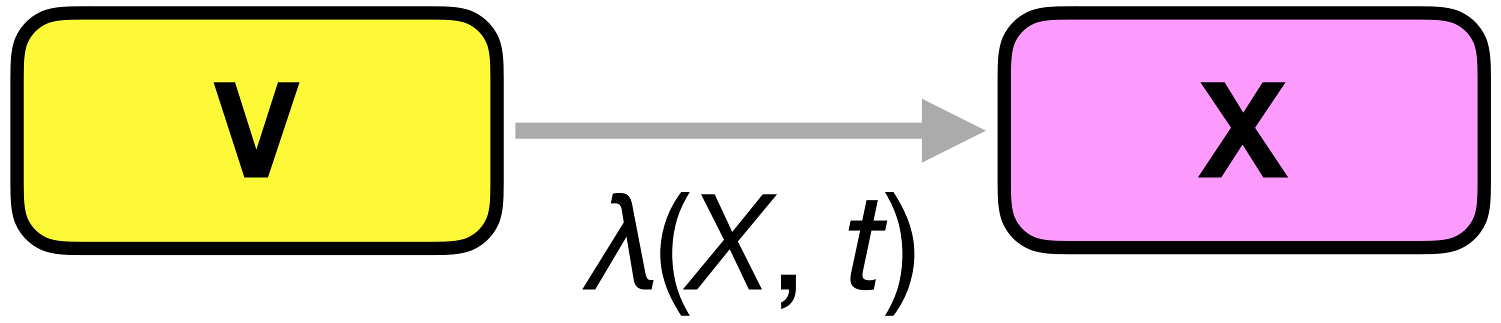


- $F_W(t)$ is then the cumulative distribution function of a random variable *W* denoting the waiting time until a randomly chosen member of *X* leaves this compartment
  - this is the exponential distribution with **E**[*W*] = $1/\gamma$ and median m[*W*] = $(\ln 2)/\gamma$
- **So, we can fit the rate γ as the reciprocal of the (estimated) mean time of staying in the compartment *X***

Understanding (Isolated) Induced Flow

$$\frac{dV(t)}{dt} = -\lambda(X,t)V(t) = -\frac{\beta}{N}X(t)V(t)$$

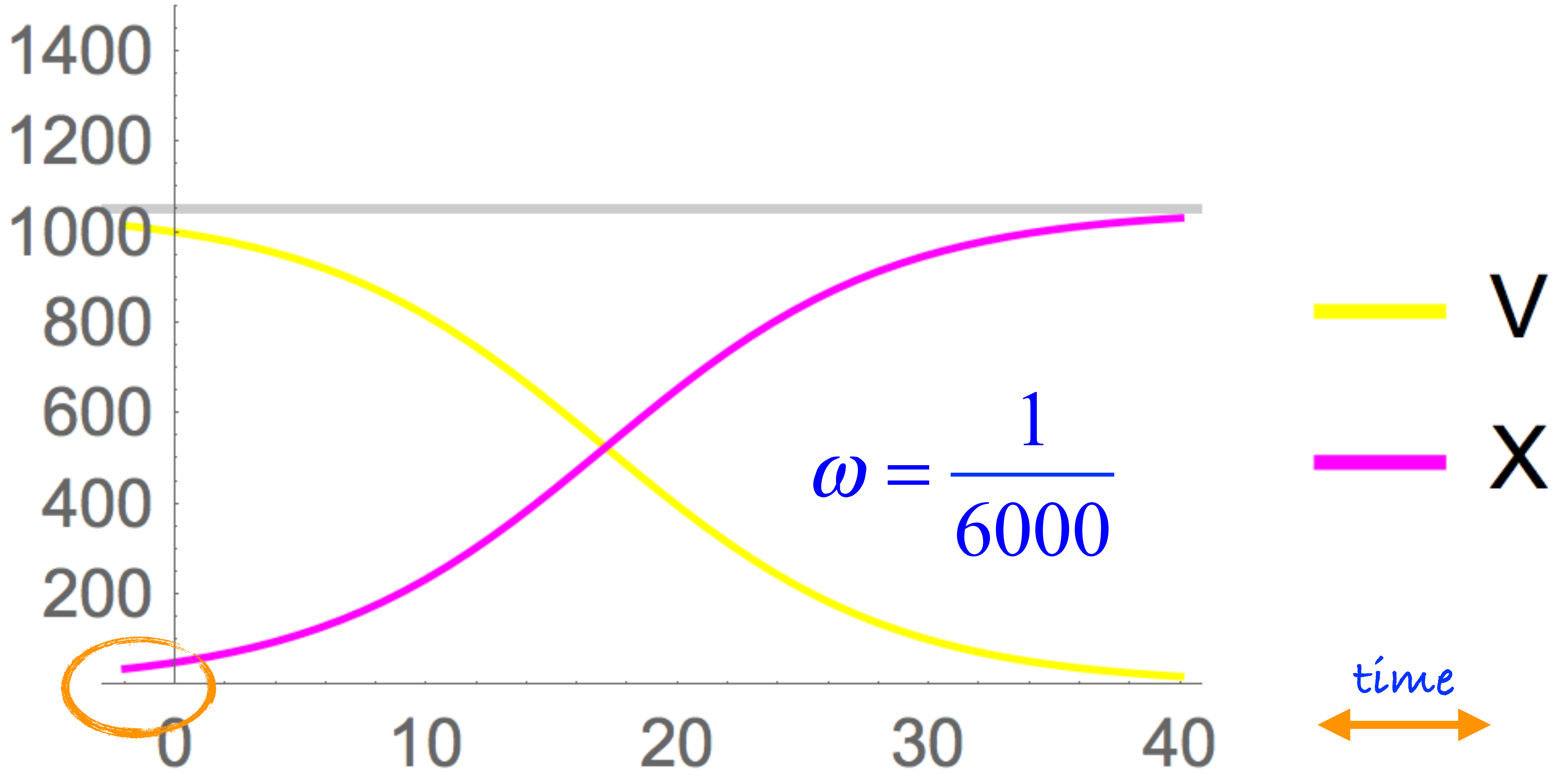
$$\frac{dX(t)}{dt} = \lambda(X,t)V(t) = \frac{\beta}{N}X(t)V(t)$$



- In epidemiology, $\lambda(X, t)$ is also called ***infection force***
  - it brings a nonlinear term invoking *the law of mass action* mechanism
- Note $X(t)V(t)$ is corresponds to the number of possibly infective edges in the *complete bipartite contact graph* (assuming ideal mixing) $K_{S(t),I(t)}$ of the population network in the given time instant
  - β / N is the *probabilistic* instantaneous relative rate of the infection spreading through these edges

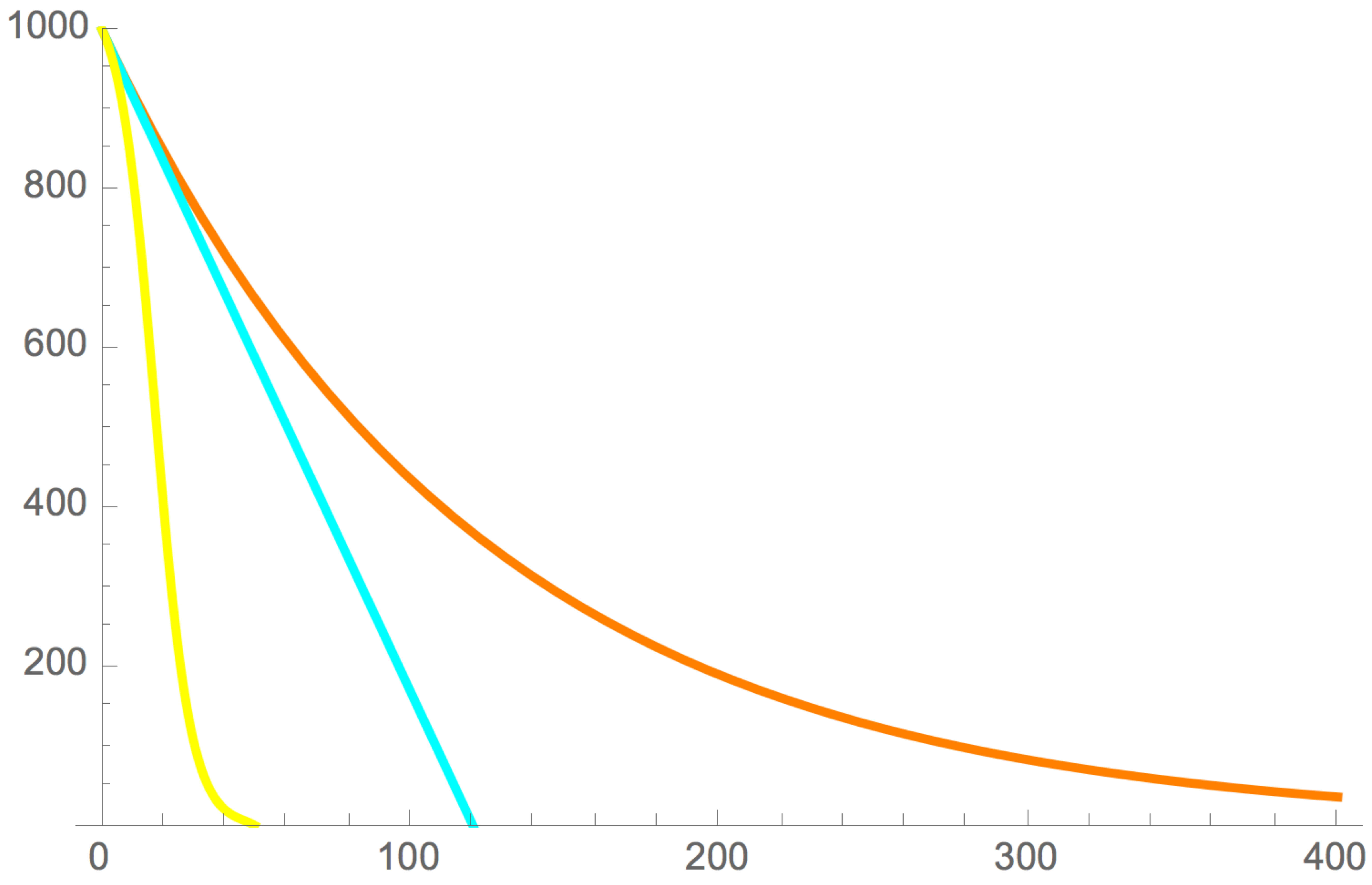
Isolated Mass Action Solution Example

$$\lambda(X, t) = \omega X(t)$$



- Solution found numerically, though this particular one can still be found analytically, noting $X(t) = N - V(t)$
  - leading to the *logistic equation / curve*
  - contains not so surprising (almost) exponential episodes followed by somewhat relaxed regions

Exponential, Linear, and Mass Action Slopes Comparison



Finalising the Picture and Going Dimensionless

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

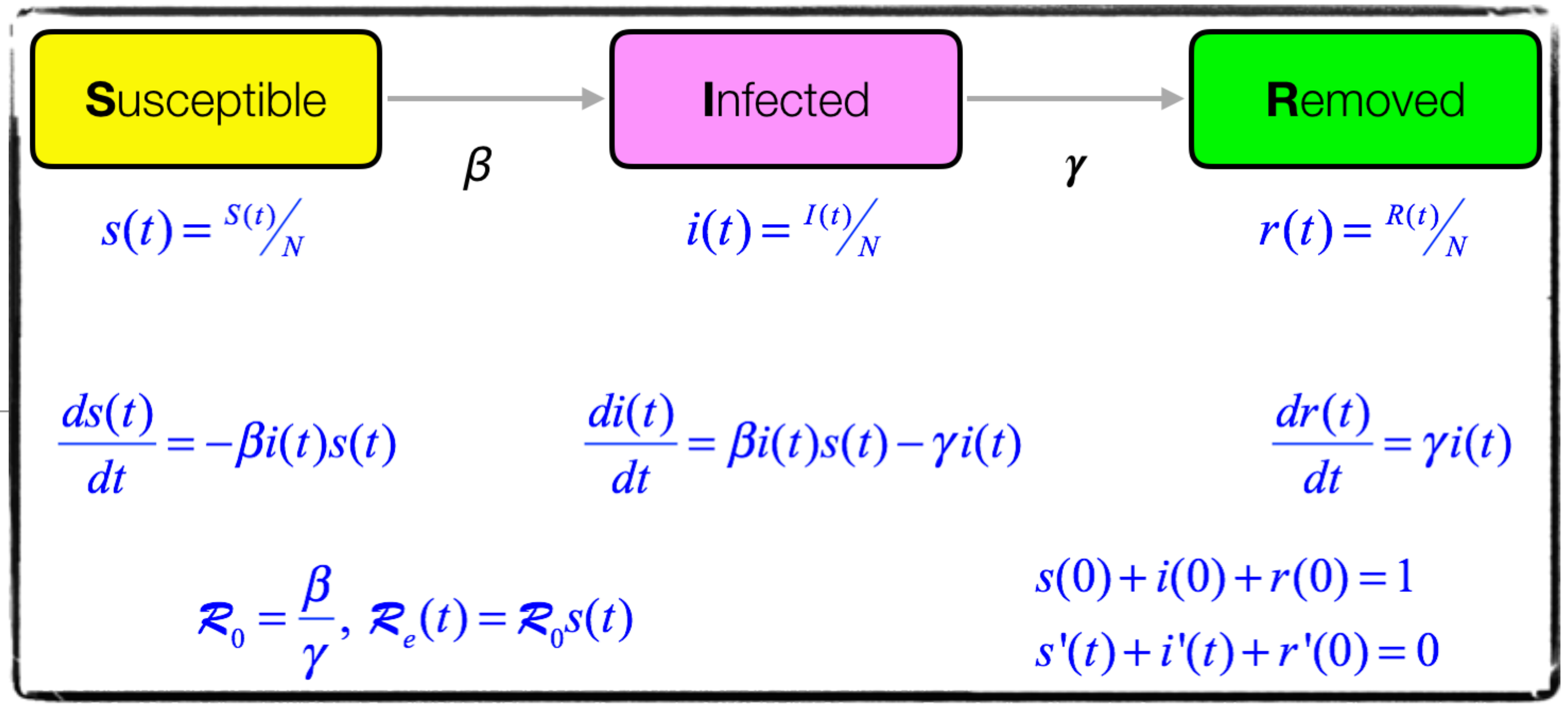
$$\frac{ds(t)}{dt} = -\beta i(t)s(t) \qquad \frac{di(t)}{dt} = \beta i(t)s(t) - \gamma i(t) \qquad \frac{dr(t)}{dt} = \gamma i(t)$$

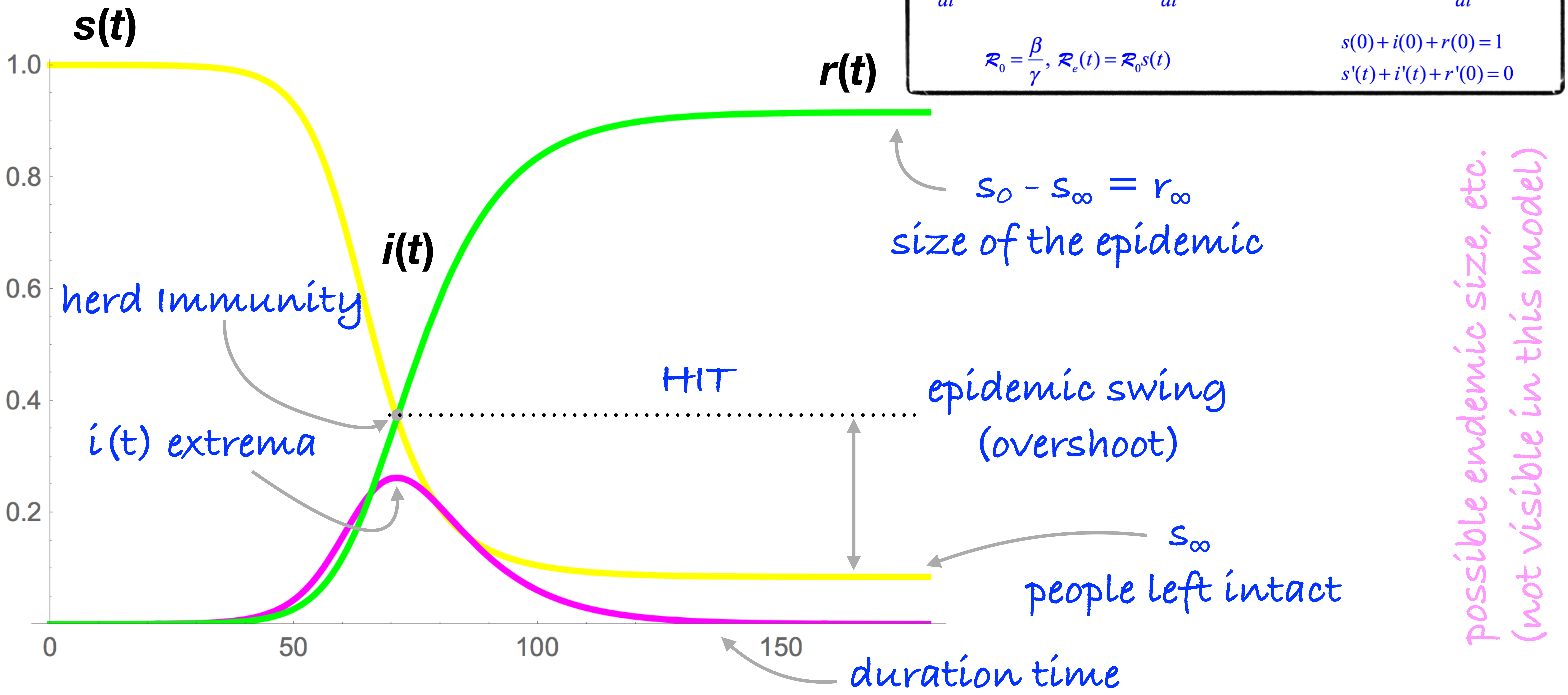
$$\mathcal{R}_0 = \frac{\beta}{\gamma}, \; \mathcal{R}_e(t) = \mathcal{R}_0 s(t)$$

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

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

Partial Optimisation Criteria (SIR-based)





Anti-Epidemic Interventions

transmission rate intervention ⬇

- moderating contact rate
- decreasing infection probability

removal rate intervention ⬆

- broad testing
- contact tracing
- vaccination

β ⬇ $\quad$ γ ⬆

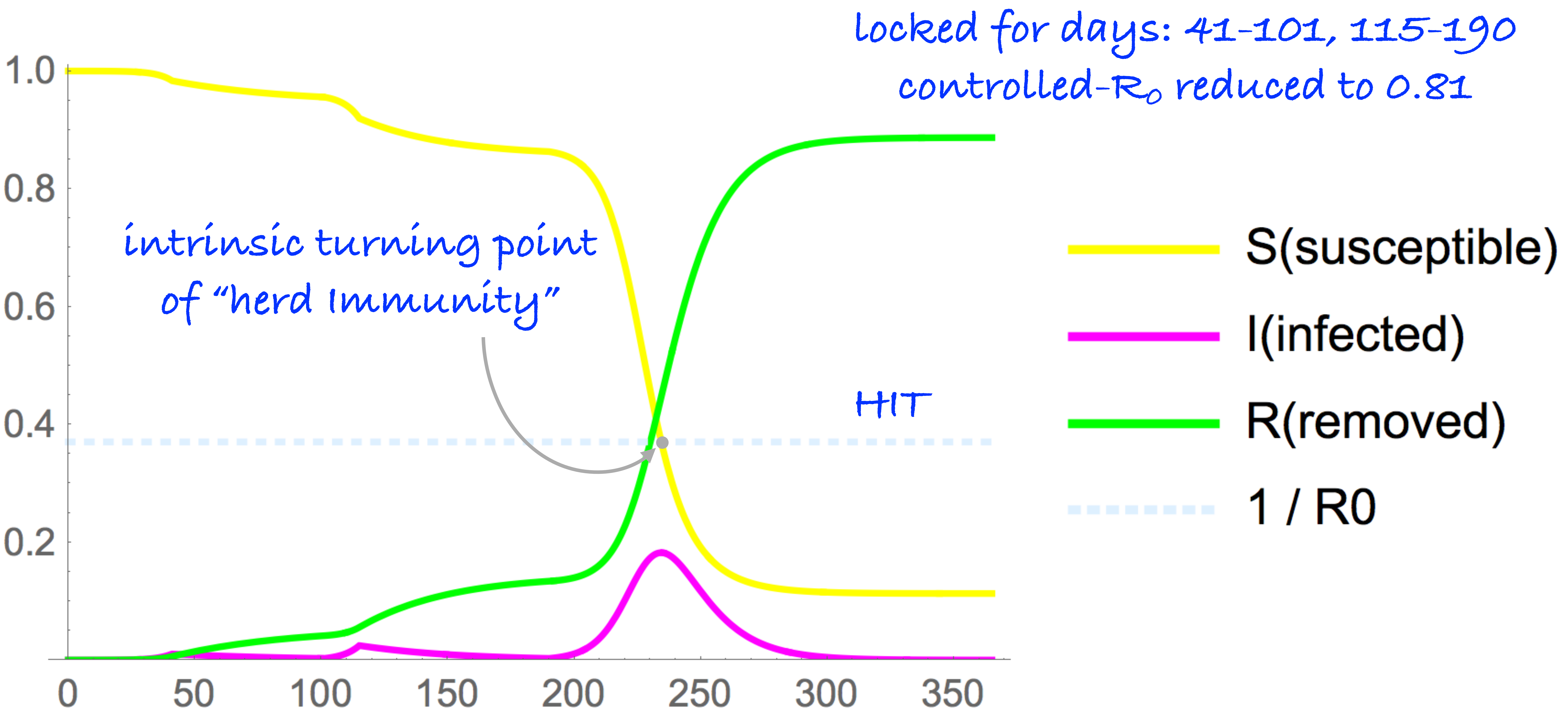
$s(t) = S(t)/N \qquad i(t) = I(t)/N \qquad r(t) = R(t)/N$

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

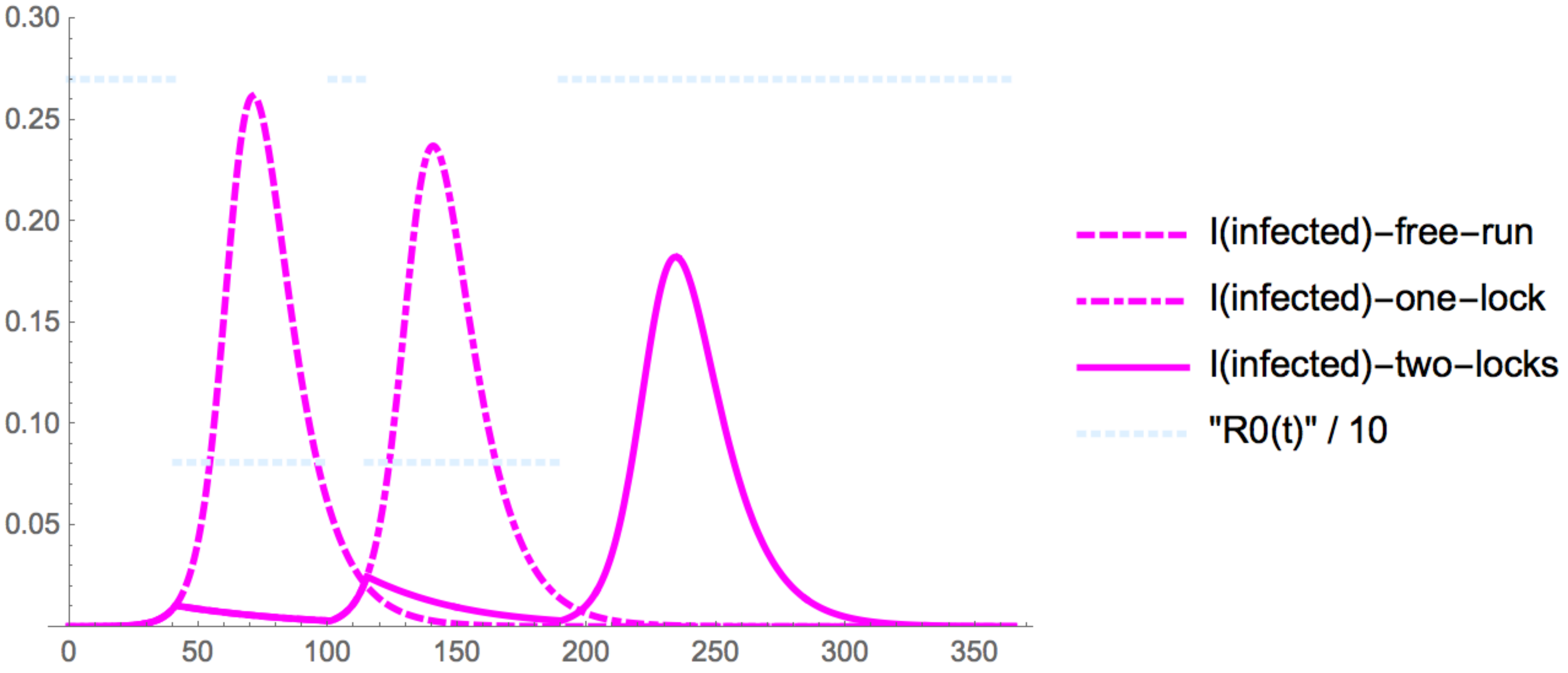
$$\mathcal{R}_0 = \frac{\beta}{\gamma}, \ \mathcal{R}_e(t) = \mathcal{R}_0 s(t)$$

$$s(0) + i(0) + r(0) = 1$$
$$s'(t) + i'(t) + r'(t) = 0$$

Example: Qualitative Study of Two Ideal Consecutive Lockdowns



Example: Infectious Compartment Comparative Close-Up



Real-World Lockdown *Serious Modelling Example* (UK)

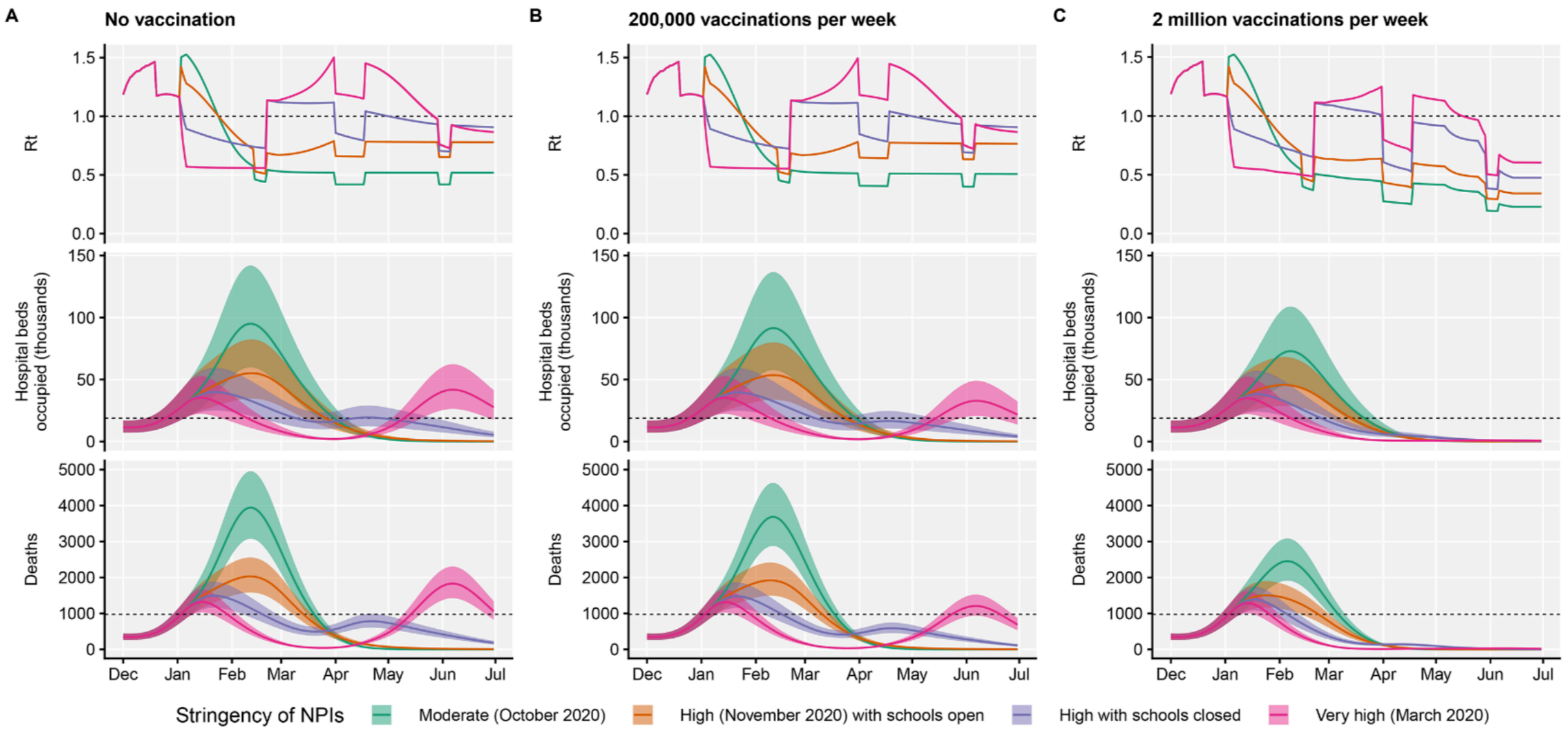
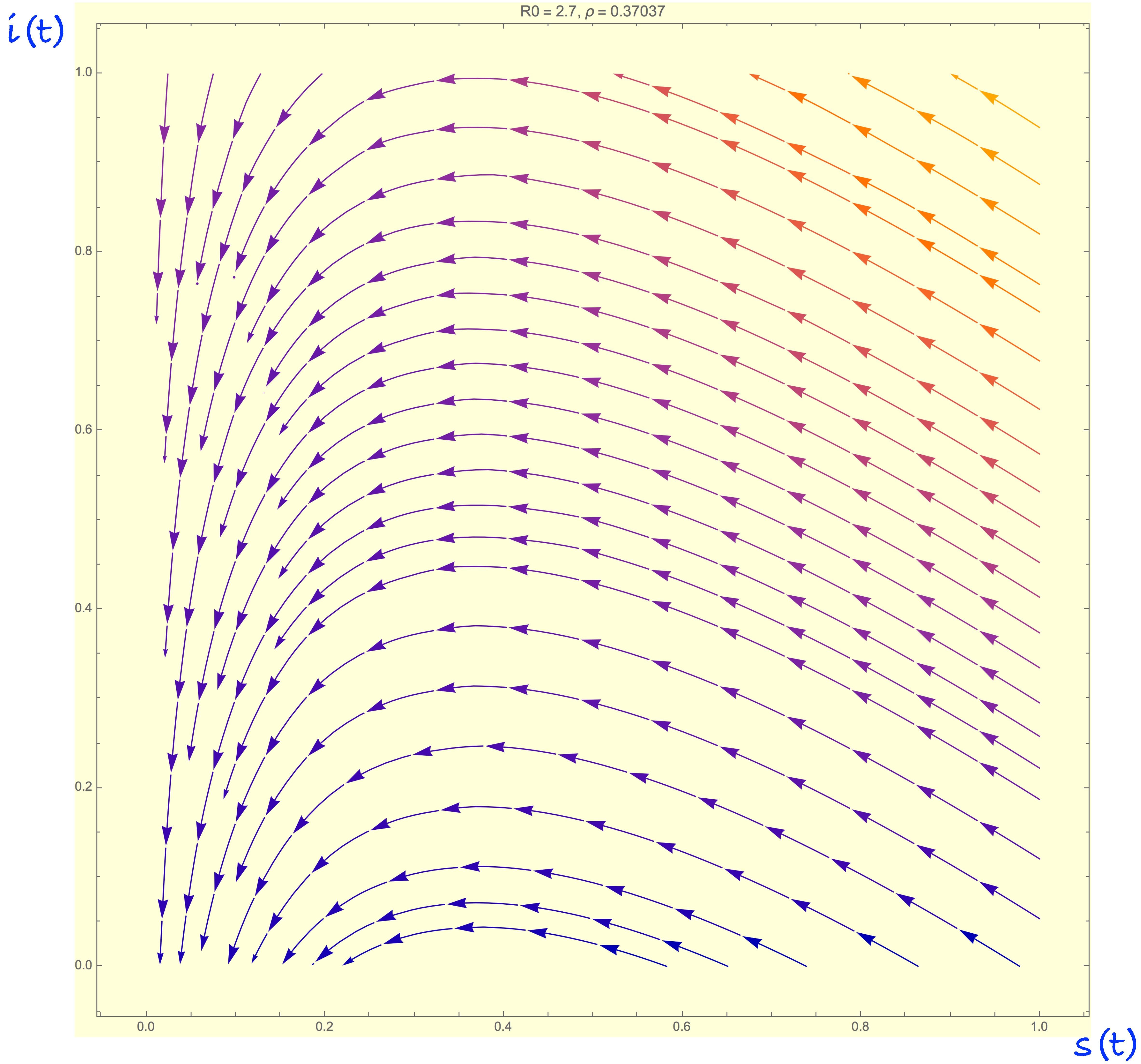


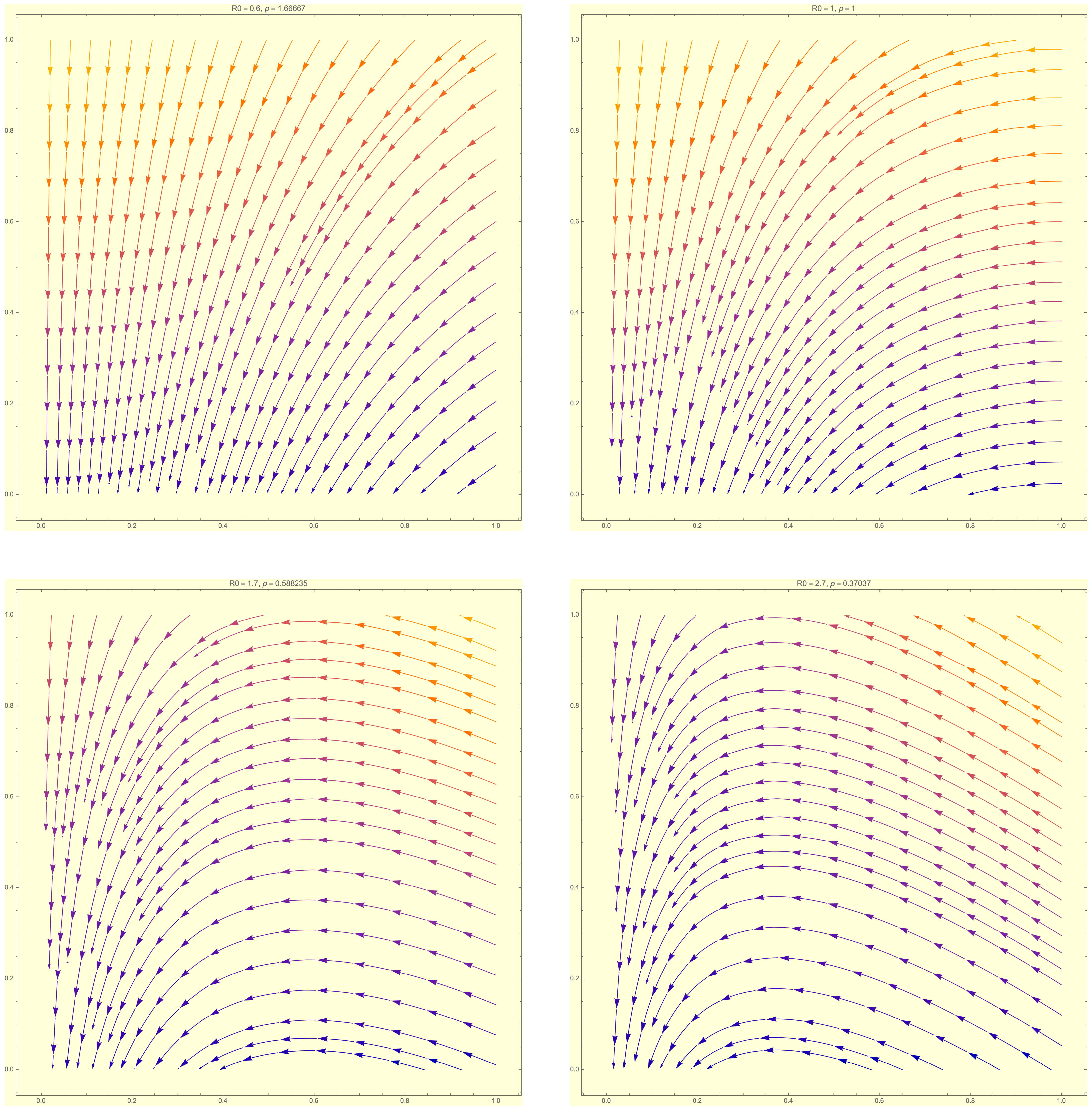
Fig. 4. Projections of epidemic dynamics under different control measures. We compare four alternative scenarios for non-pharmaceutical interventions from 1 January 2021: (i) mobility returning to levels observed during relatively moderate restrictions in early October 2020; (ii) mobility as observed during the second lockdown in England in November 2020, then gradually returning to October 2020 levels from 1 March to 1 April 2021, with schools open; (iii) as (ii), but with school

[https://science.sciencemag.org/content/early/2021/03/03/science.abg3055]

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



R_0 Dependency and Consequences

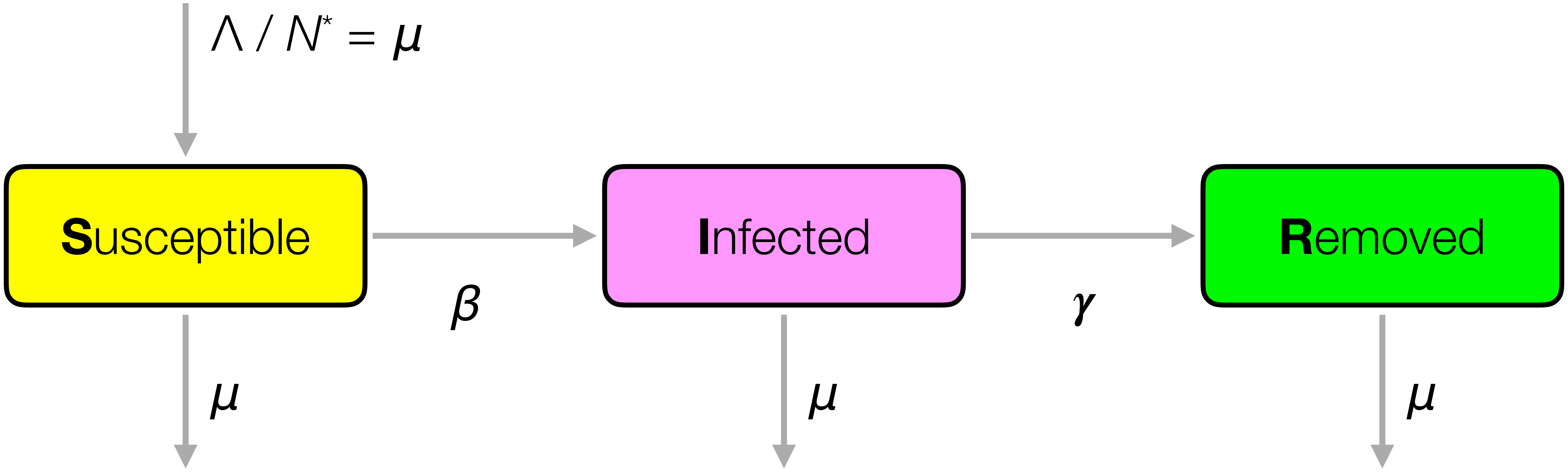


- phase field together with the herd immunity threshold ρ is fully determined by the (possibly controlled) basic reproduction number ($\rho = 1/R_0$)

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

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

SIR Compartmental Epidemic Model
- including simple demography, now



- we set μ 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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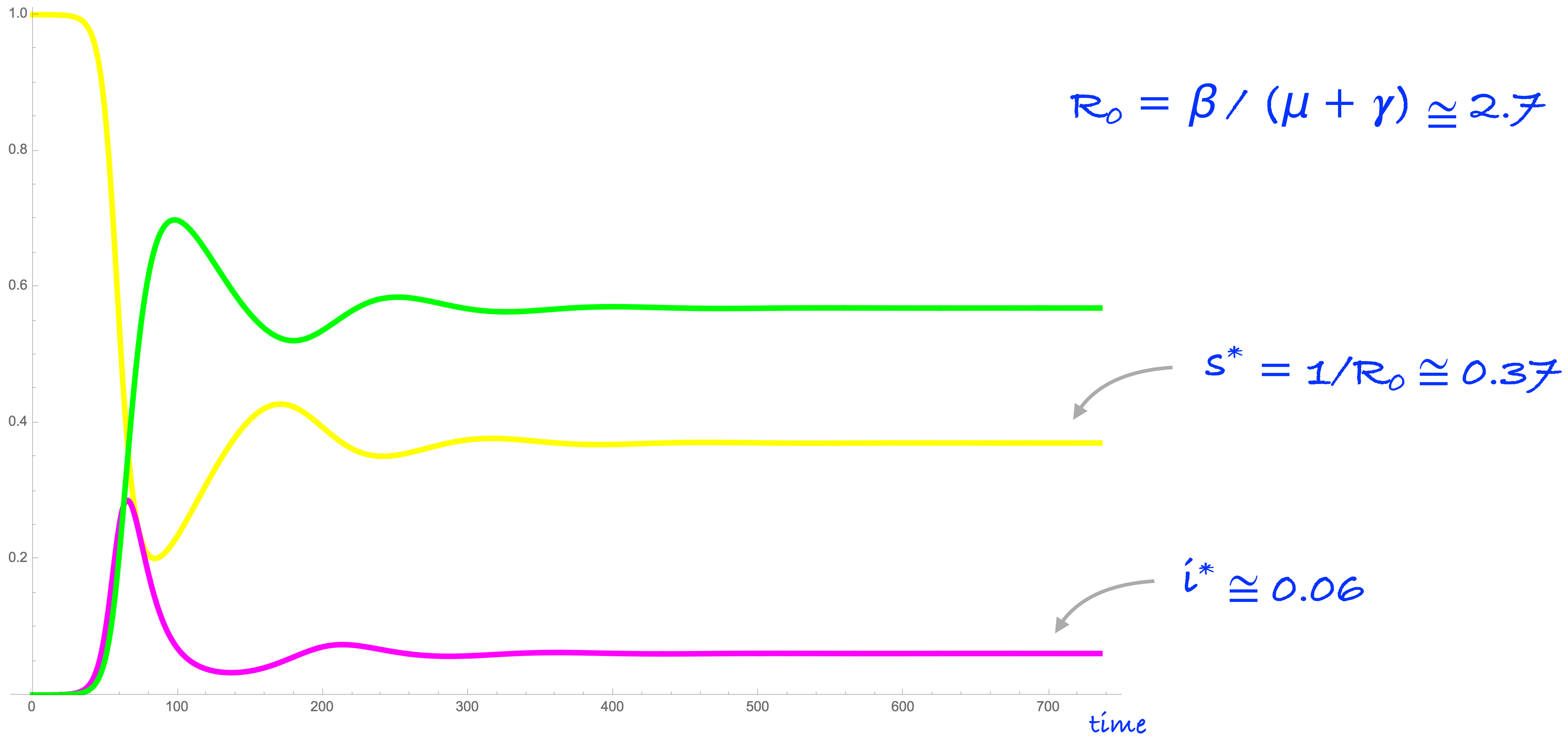
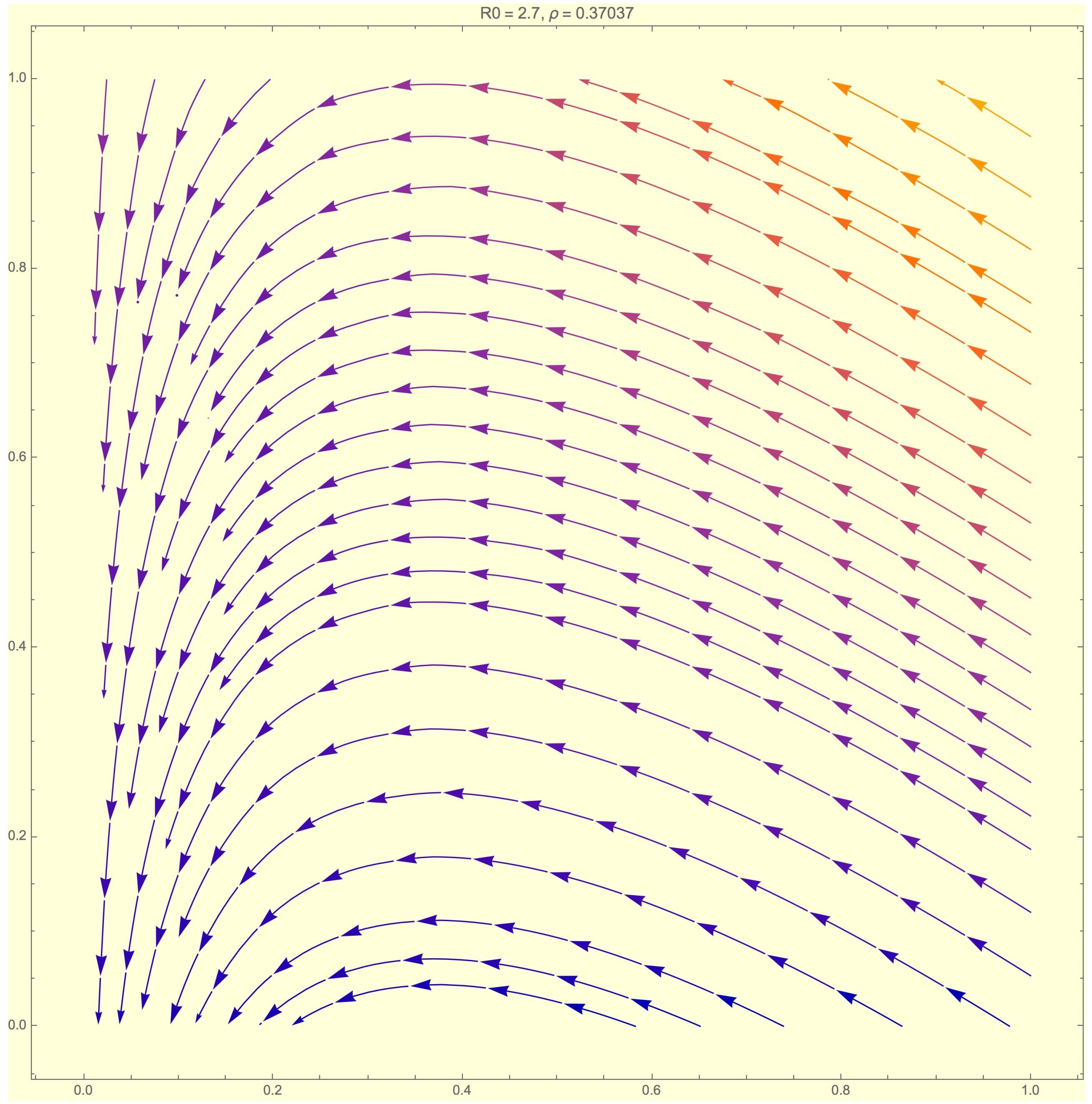
- on the other hand, in reality, demography is not the only reason for endemic states anyway

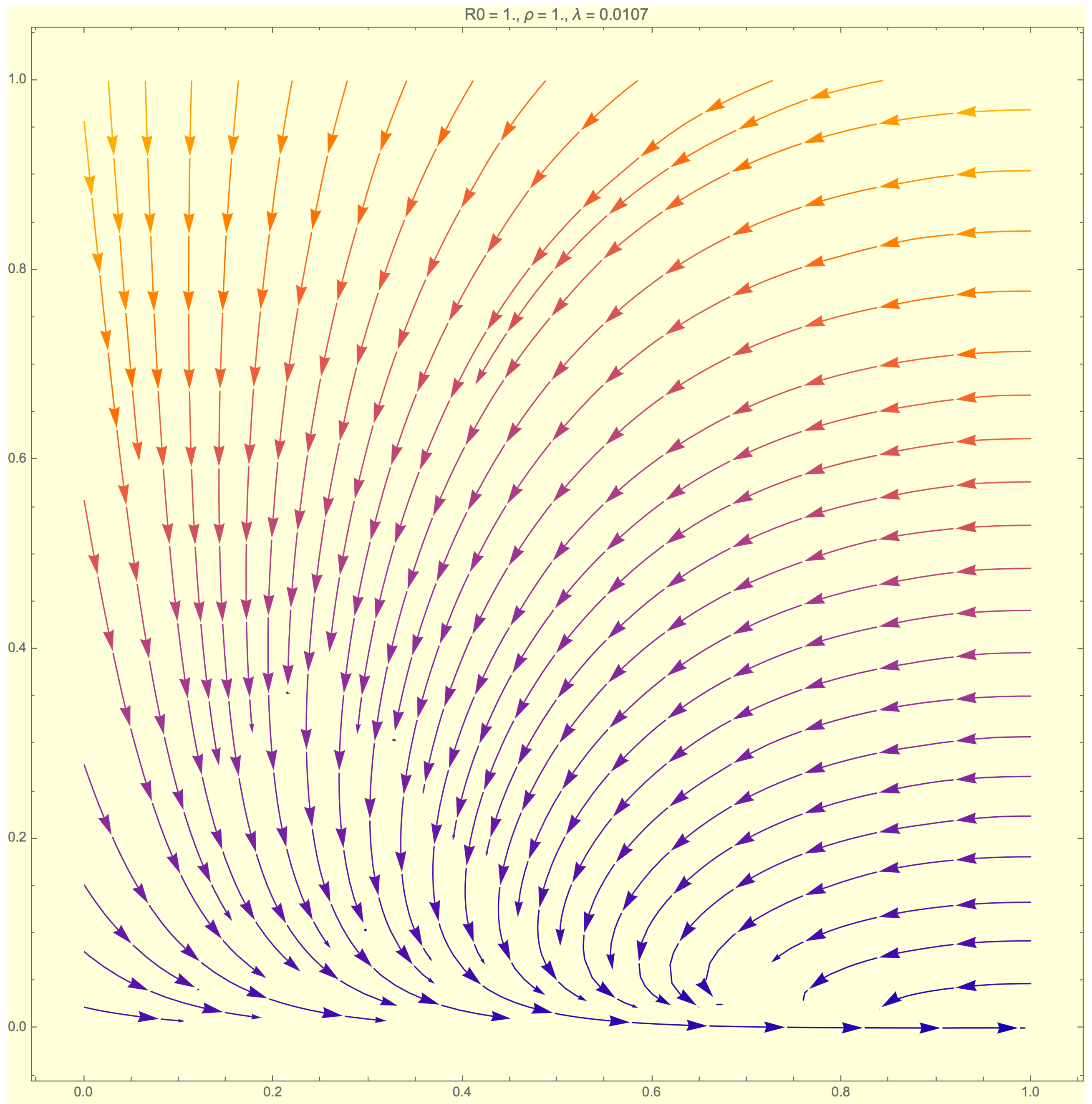
Endemic Equilibrium is Asymptotically Stable for $\boldsymbol{R}_0 > 1$



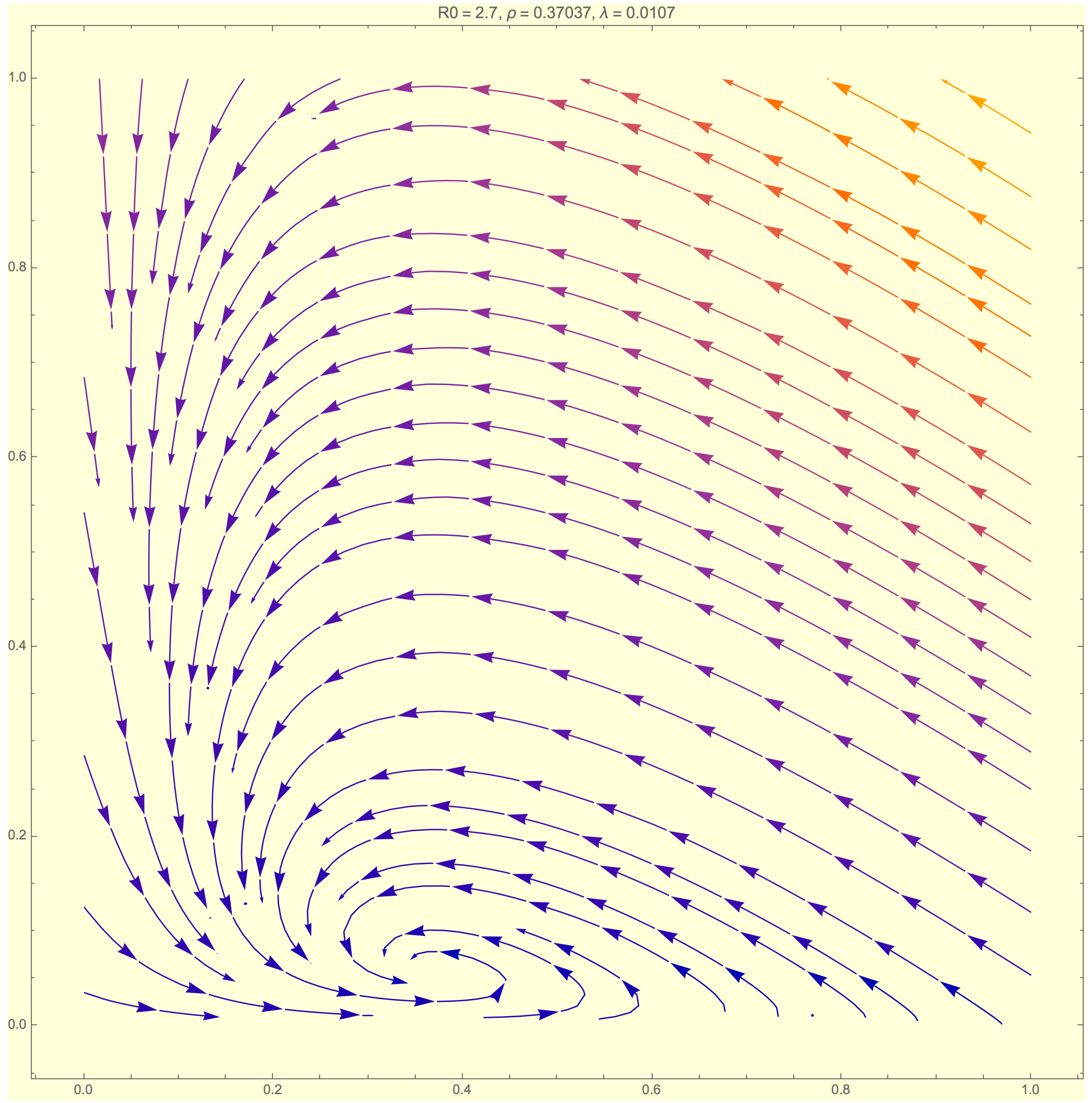
Direction field of the model* equations brings yet-another viewpoint



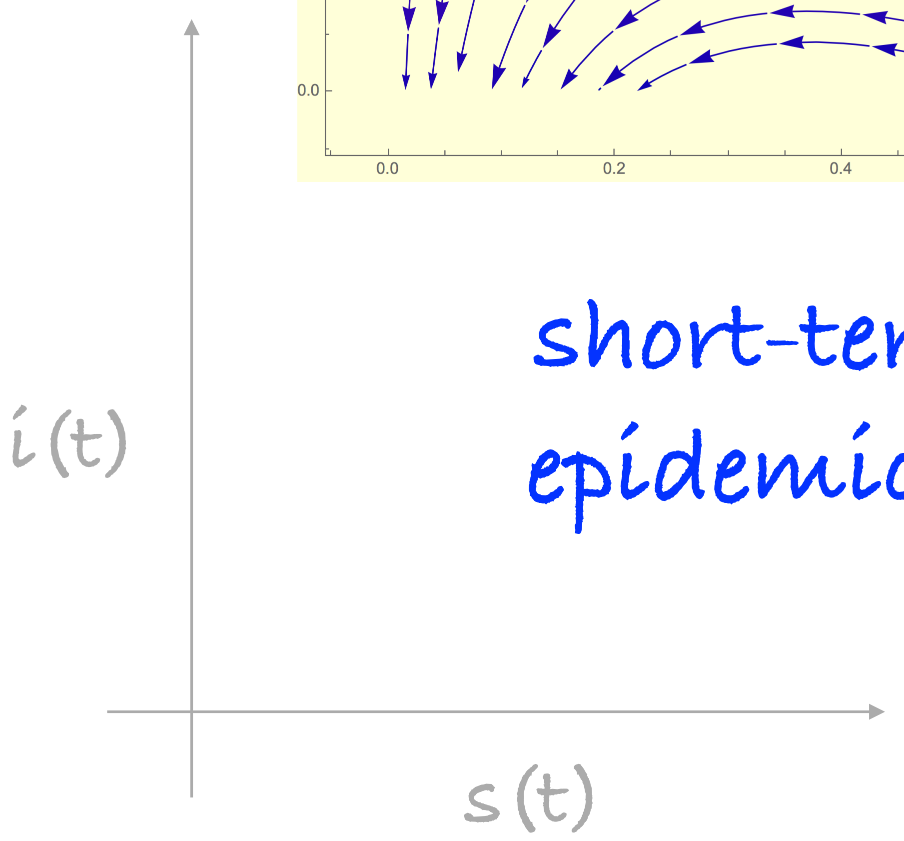
short-term simple
epidemic outbreak



long-term equilibrium
disease-free
$R_0 < 1$

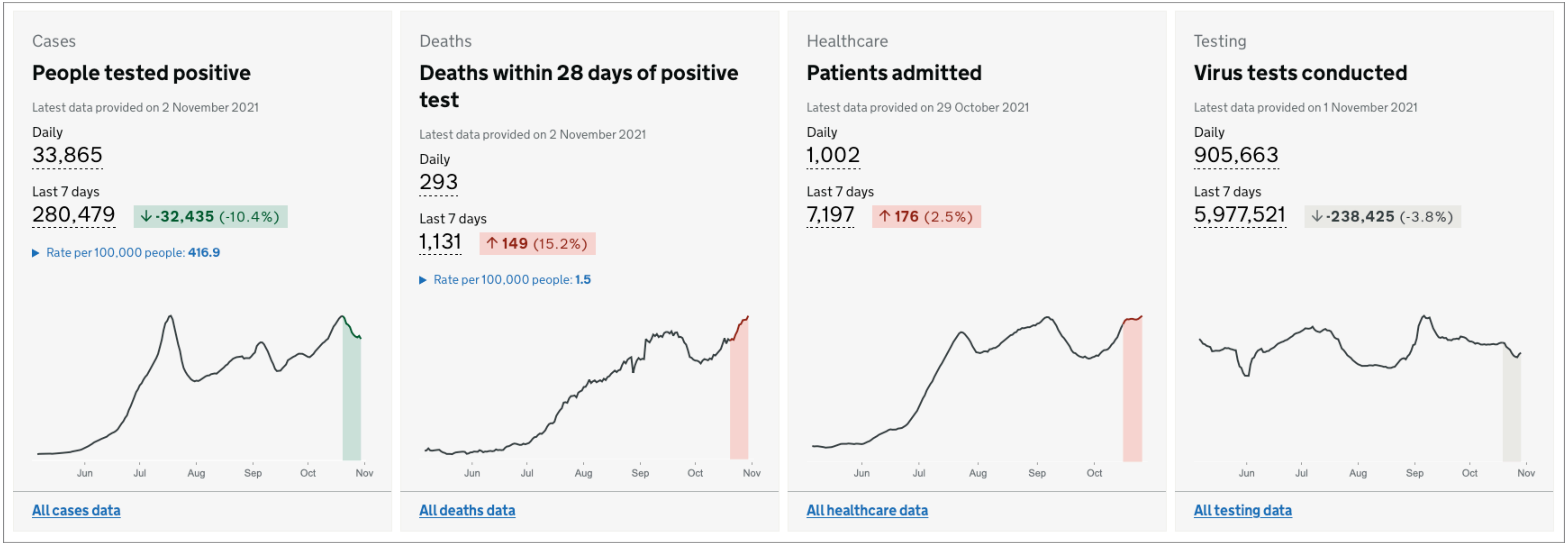


long-term equilibrium
endemic
$R_0 > 1$



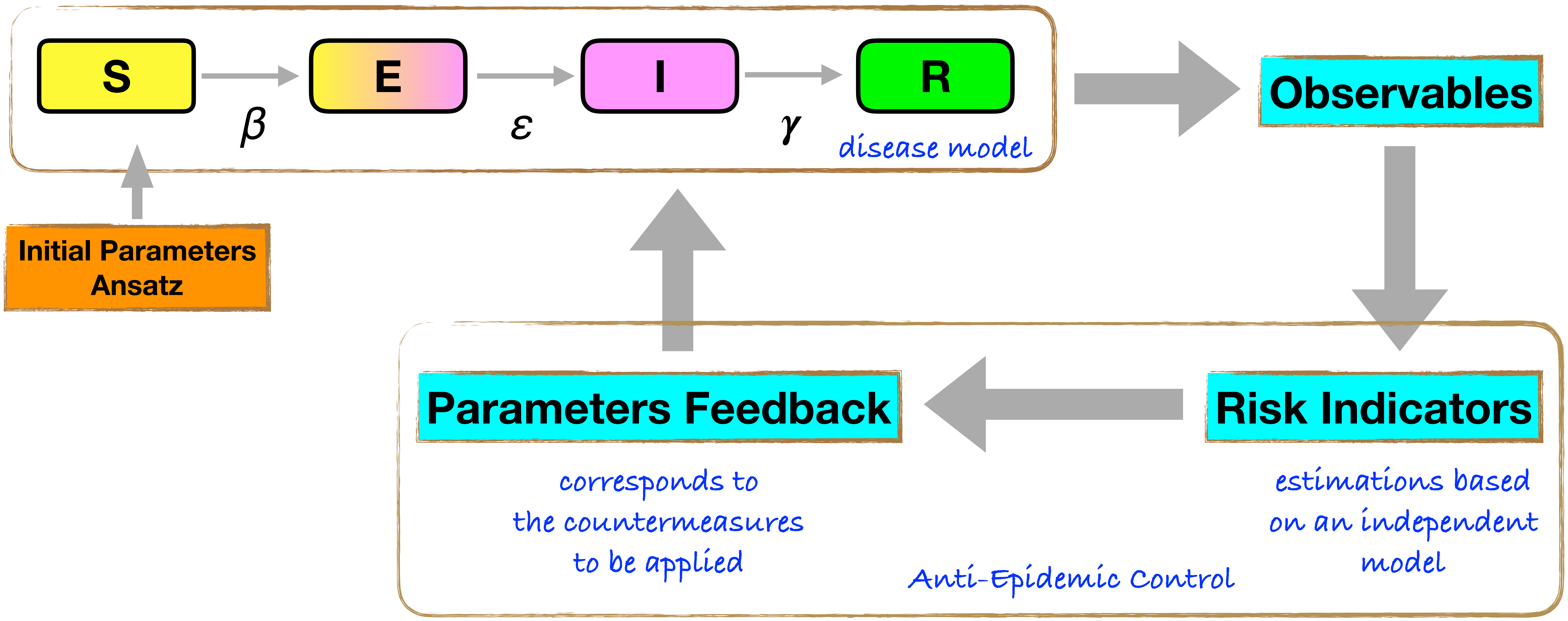
*) SIR and SIR with demography

UK-Style Equilibrium and One More Thing to Add



[https://coronavirus.data.gov.uk]

Anti-Epidemic Controls Simulation (for whatever purpose)



*) Note the SEIR model is just an example

Consider This Control Chain

epidemic code → the pandemic → the government → the economics

How Much Can We Trust the Models?

- Not much when a *deliberate manipulation* is under question

- There are two principal vulnerabilities allowing for "***anti-epidemic take over***"

  - invertibility, we can find a calibration for any physically plausible epidemic forecast

  - reversibility, we can track this calibration back in time to see how to manipulate contemporary statistical data to get the desired forecast

- Assuming we can predict the governmental reaction on the forecast, we could control the state this way

References and Further Reading

(1) Bjornstad, O.-N.: *Epidemics - Models and Data Using R*, Springer, 2018

(2) Brauer, F., Castillo-Chavez, C., and Feng, Z.: *Mathematical Models in Epidemiology*, Texts in Applied Mathematics, Vol. 69, Springer, 2019

(3) Kiss, I.-Z., Miller, J.-C., and Simon, P.-L.: *Mathematics of Epidemics on Networks – From Exact to Approximate Models*, Interdisciplinary Applied Mathematics, Vol. 46, Springer, 2017

(4) Li, M.-Y.: *An Introduction to Mathematical Modelling of Infectious Diseases*, Springer, 2018

(5) Martcheva, M.: *An Introduction to Mathematical Epidemiology*, Texts in Applied Mathematics, Vol. 61, Springer, 2015

(6) Vynnycky, E. and White, R.-G.: *An Introduction to Infectious Disease Modelling*, Oxford University Press, 2010

Revision History

- 2021/11/03: release version 1
- 2021/11/25: demographic parameters clarification, references updated