Why differential equations fail to describe the dynamics of epidemics

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Z. Fodor, S.D. Katz, T.G. Kovacs, arXiv:2004.07208

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Outline

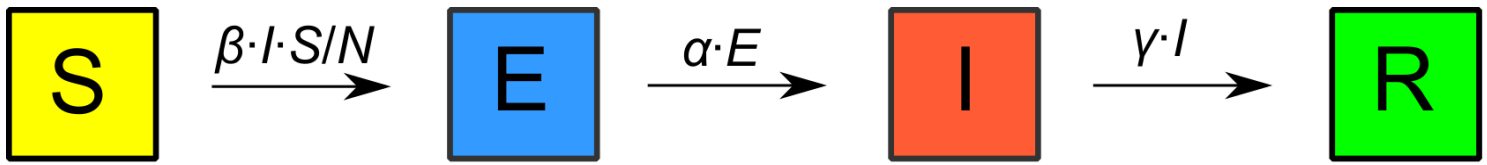
Introduction

- compartmental epidemiological models divide the population into pools such as
  Susceptible, Exposed, Infectious, Quarantined, Recovered, etc.
- the dynamics is often described by ordinary differential equations
- the variables of these models are the number of people in these pools ($S(t), E(t)$, etc.)
- at any time the change of these variables depend on themselves at the same time (no memory).
- The parameters of the models (transition rates between the pools) may depend on time

Notations & definitions

- We compare different models in a highly simplified scenario
- incubation period: the period of time between exposure and when symptoms begin
- t_e : "exposed" part of incubation period when a person is not yet infectious
- t_i : "infectious" part of incubation period when a person is still asymptomatic
- $t_{\text{incubation}} = t_e + t_i$ out of which a person infects others for t_i days
- we assume that everyone gets quarantined (and reported) when symptoms begin.
- R_0 : basic reproduction number: average number of new infections caused by a single person

The SEIR model



- Four compartments for a population of size $N = S + E + I + R$

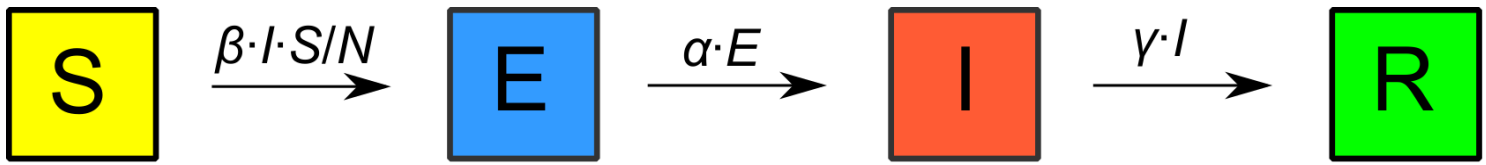
$$\frac{dS}{dt} = -\beta \frac{I}{N} S, \quad \frac{dE}{dt} = \beta \frac{I}{N} S - \alpha E, \quad \frac{dI}{dt} = \alpha E - \gamma I, \quad \frac{dR}{dt} = \gamma I,$$

- For the initial phase $S \approx N$, two coupled equations for E & I:

$$\frac{d}{dt}\begin{pmatrix} E \\ I \end{pmatrix} = \begin{pmatrix} -1/t_e & R_0/t_i \\ 1/t_e & -1/t_i \end{pmatrix} \begin{pmatrix} E \\ I \end{pmatrix} \quad \text{with} \quad t_e = \frac{1}{\alpha}, \quad t_i = \frac{1}{\gamma}, \quad R_0 = \beta t_i$$

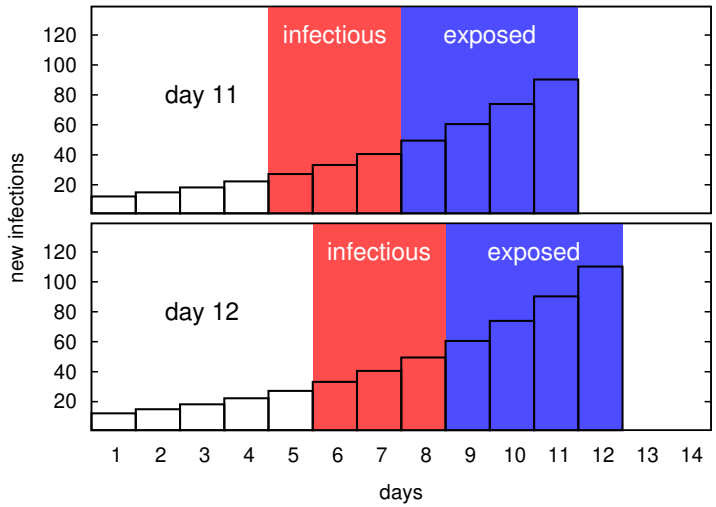
- We use this simple case to demonstrate SEIR's flaws (extension to the full model is trival)

The SEIR model II



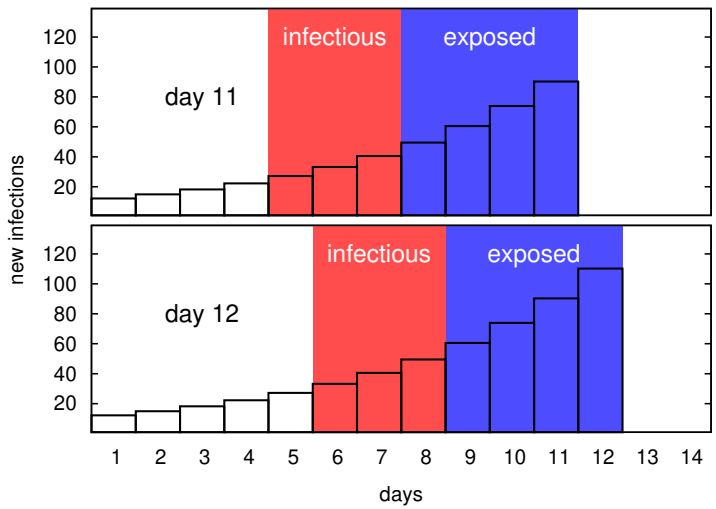
- transition rates are assumed to be proportional to the number of people in the pools
- on average people spend t_e and t_i days in E and I
- everyone leaves the pools with the same probability, irrespective of how much time they actually spent there
- any change in $\beta(R_0)$ immediately changes the $I \to R$ rate (no delay)

How to do it correctly



- a single function can describe the full history and all the pools
- $\rho(t)$ is the number of new infections on day t
- EXPOSED: everyone who was infected less than t_e days ago
- INFECTIOUS: everyone who was infected less than $t_e + t_i$ and more than t_e days ago

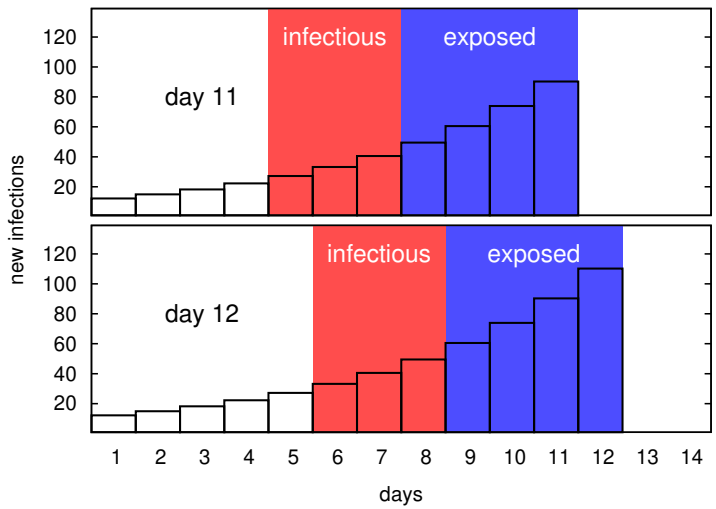
How to do it correctly



- as time passes people automatically switch categories
- the only non-trivial ingredient which determines the dynamics is the rate of new infections

$$\rho(t+1) = \beta \sum_{\tau=t-t_i-t_e+1}^{t-t_e} \rho(\tau), \qquad \beta = \frac{R_0}{t_i}$$

How to do it correctly



- continuous case:
  $\rho(t)dt$ is the number of new infections between t and $t + dt$
- dynamics is described by an integral equation:

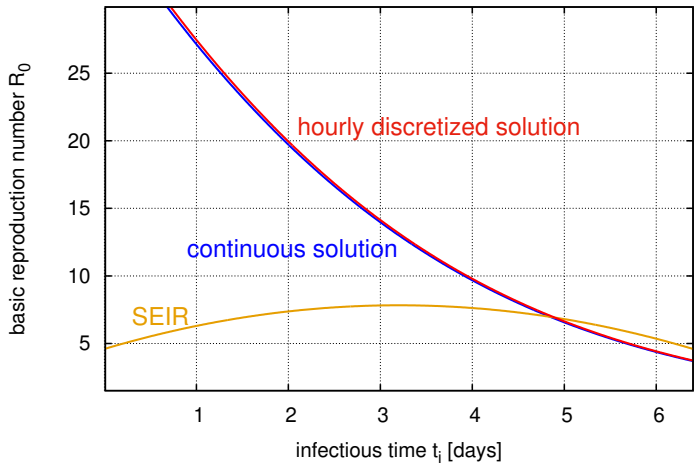
$$\rho(t) = \beta \int_{t-t_i-t_e}^{t-t_e} \rho(\tau)\, d\tau, \qquad \beta = \frac{R_0}{t_i}.$$

- known since 1920's but not widely used

Determination of R_0

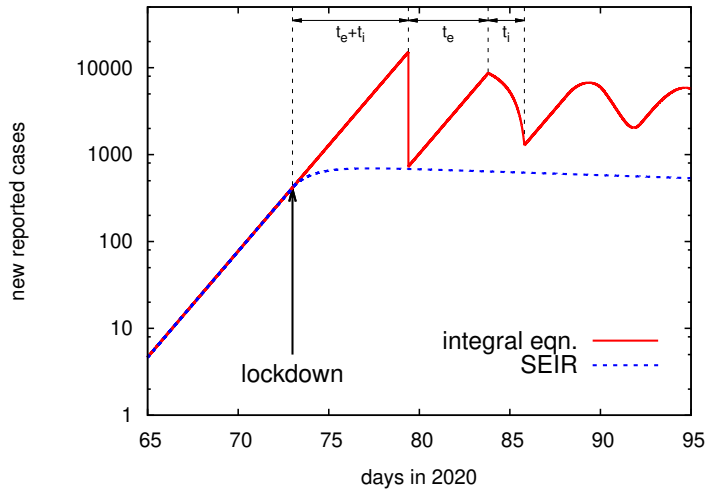
- exponential growth solves both the *SEIR*- and the integral equations: $E(t), I(t), \rho(t) \propto \exp(\lambda t)$
- $R_0^{(\mathrm{SEIR})} = 1 + \lambda(t_e + t_i) + \lambda^2 \cdot t_e t_i$ and $R_0^{(\mathrm{integral})} = \frac{t_i \lambda}{e^{-\lambda t_e} - e^{-\lambda(t_e + t_i)}}$
- a discretization of the integral method with Δt yields
  $R_0^{(\mathrm{discretized})} = (e^{\lambda \Delta t} - 1)/(\lambda \Delta t) \cdot R_0^{(\mathrm{integral})}$
- for small $\lambda t_e, \lambda t_i$ an expansion gives
  $R_0^{(\mathrm{integral})} = 1 + \lambda(t_e + \frac{t_i}{2}) + \lambda^2(\frac{t_e^2}{2} + \frac{t_e t_i}{2} + \frac{t_i^2}{12}) + \mathcal{O}(\lambda^3)$
- $R_0^{(\mathrm{integral})} \neq R_0^{(\mathrm{SEIR})} \rightarrow$ SEIR is never a good approximation!

Determination of R_0



- parameters consistent with the initial exponential phase in NYC
- $1/\lambda = 1.78$ days, $t_e + t_i = 6.4$ days [Backer,Klinkenberg, Wallinga, 2020]
- SEIR is symmetric for $t_e \leftrightarrow t_i$ exchange, weak dependence on t_i
- integral equation solution depends strongly on t_i
- hourly discretization is sufficient
- intial R_0 in NYC could have been as high as 20 (vs. 7-8 from SEIR)

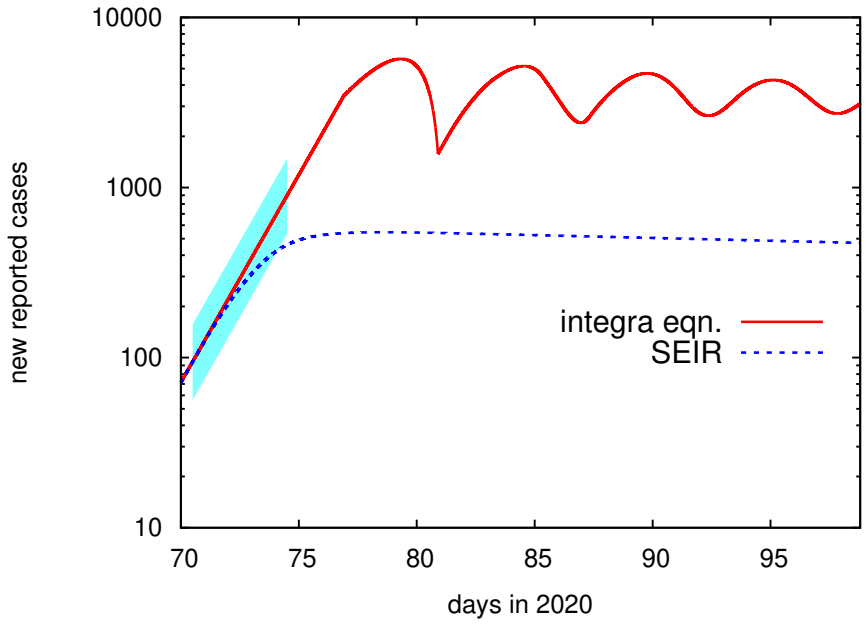
Changing R_0, delay & oscillation



- reported cases:
  people leaving I, i.e. dR/dt for SEIR, $\rho(t - t_e - t_i)$ for int. eqn.
- What if R_0 is suddenly decreased (e.g. to 0.95 on day 73)?
- SEIR prediction changes immediately
- integral eqn. provides a delay and an oscillation with t_e, t_i scales

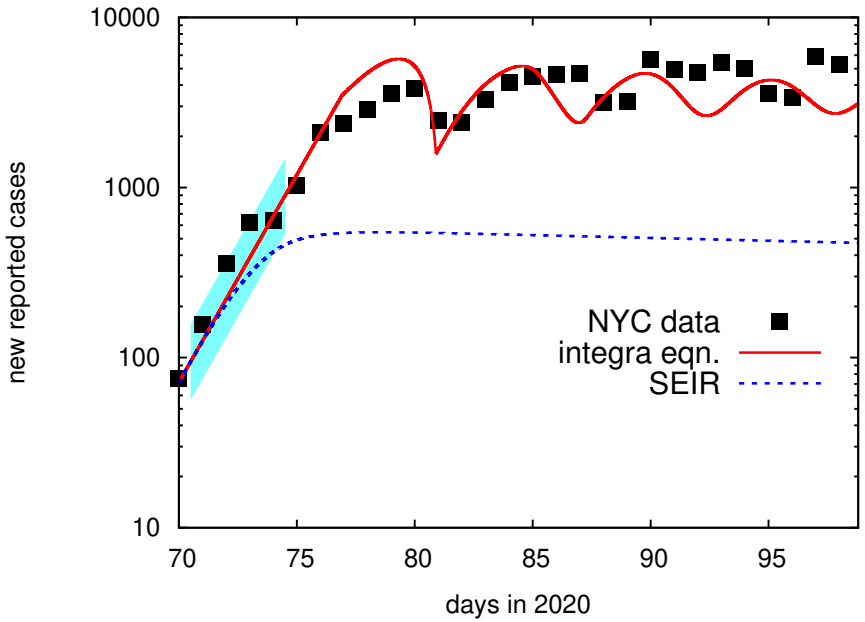
The integral equation at work

Smoothening the change



- decreasing R_0 gradually to 0.95 during days 71–74
- delay and oscillation still present but with smaller amplitude
- comparing with actual data one may read off t_e, t_i

Smoothening the change



- decreasing R_0 gradually to 0.95 during days 71–74
- delay and oscillation still present but with smaller amplitude
- Data from NYC, Italy, Spain, Germany, the Netherlands gives $t_e + t_i \approx 7.4$ days

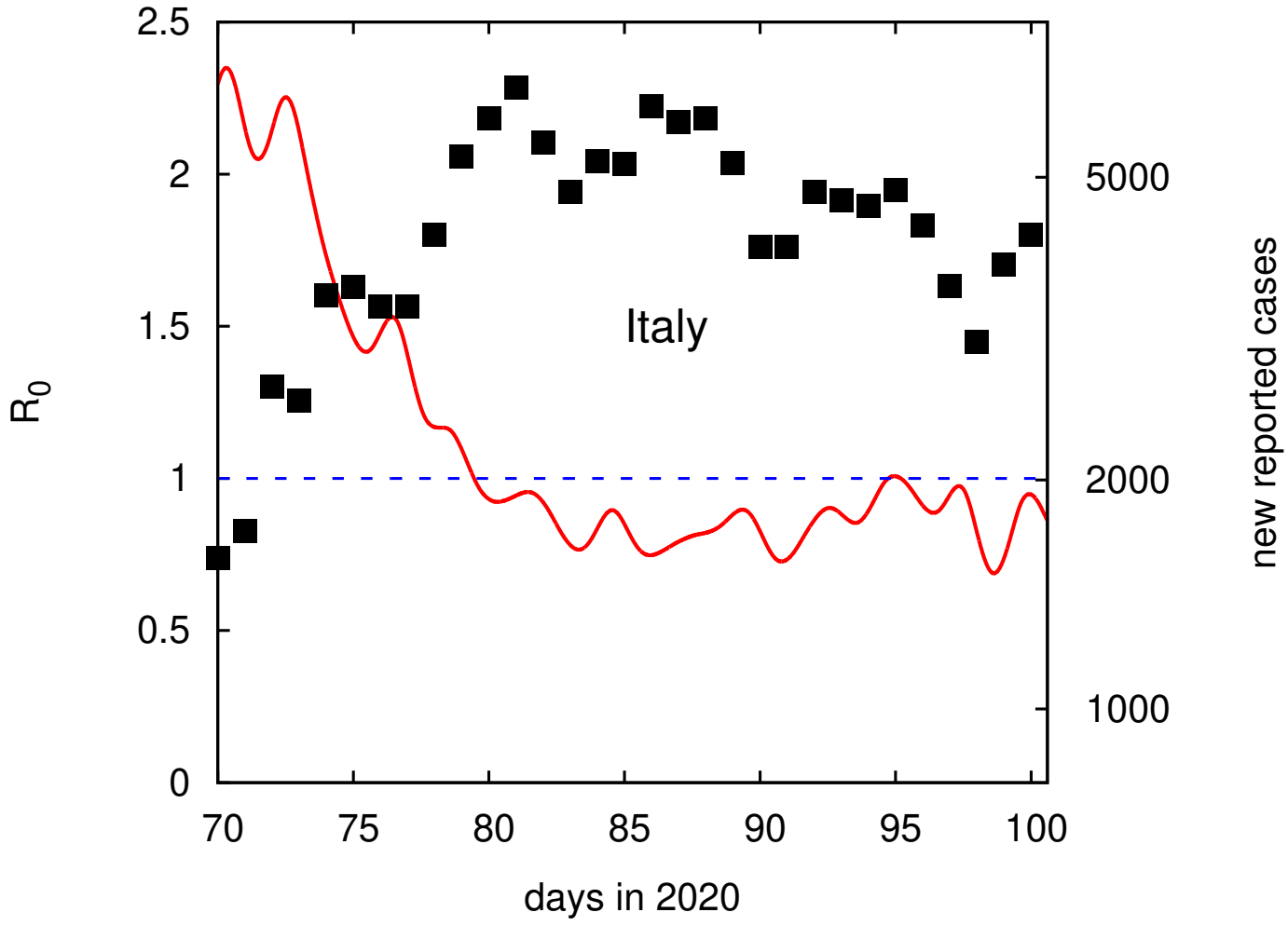
Time dependence of R_0

- Once t_e and t_i are known, one can solve the integral eqn. for R_0

$$R_0(t) = \frac{t_i \rho(t)}{\int_{t-t_i-t_e}^{t-t_e} \rho(\tau)\, d\tau}$$

- we assume that the measured data represents $\rho(t - t_e - t_i)$
- we interpolate the data using a cubic spline
- as an illustration we apply this with $t_e = 6$ days and $t_i = 1.4$ days for several regions

Time dependence of R_0



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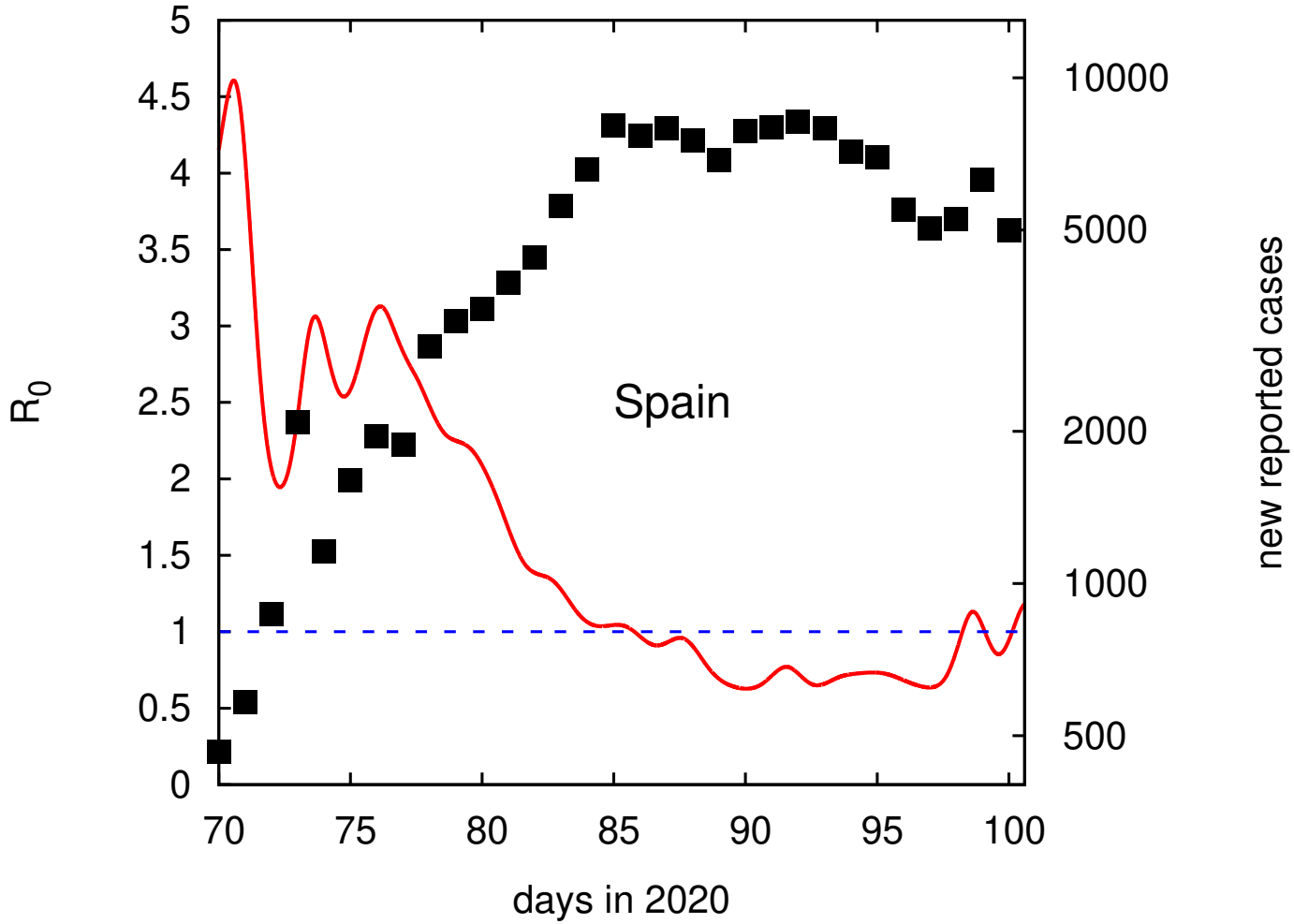

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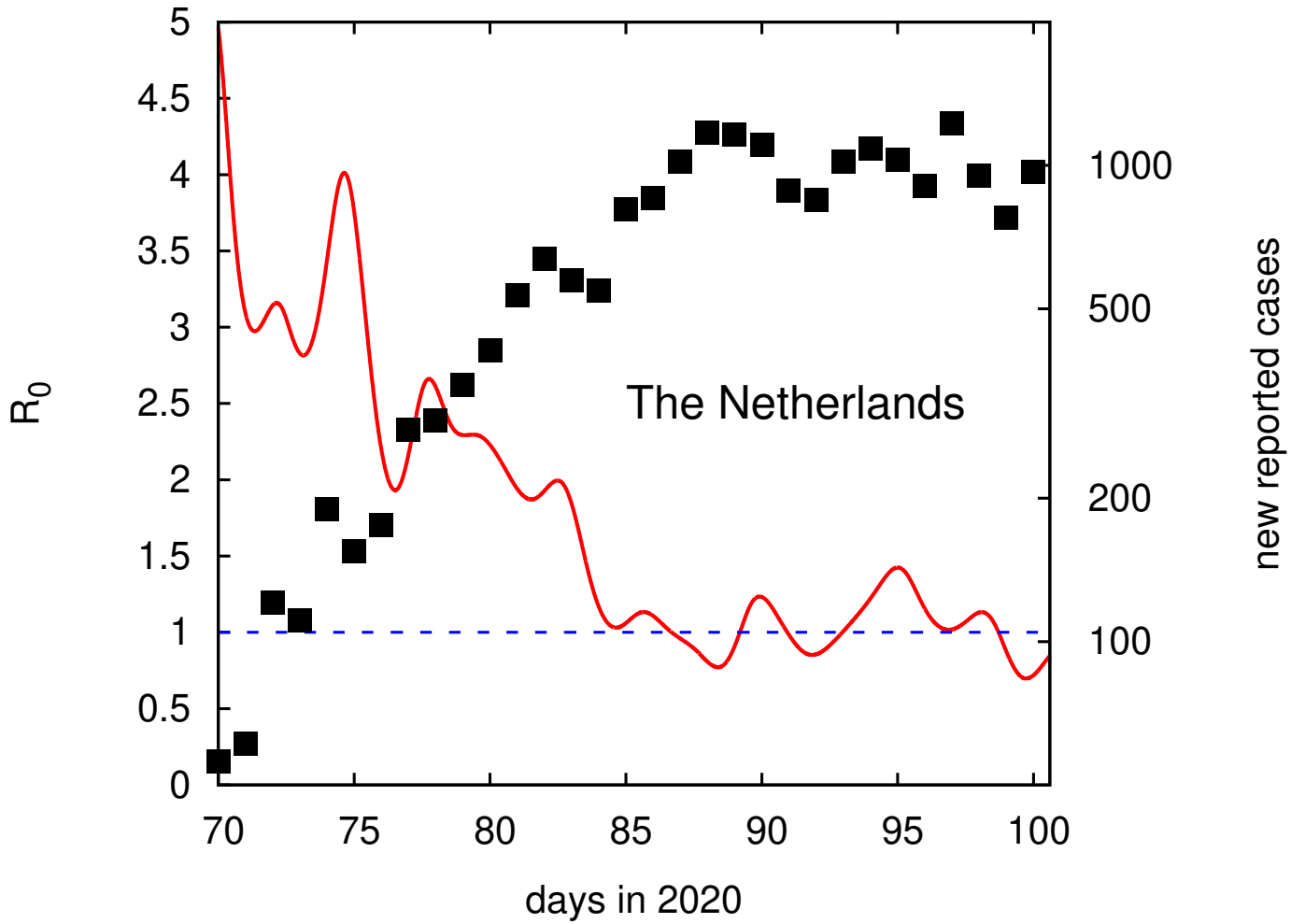
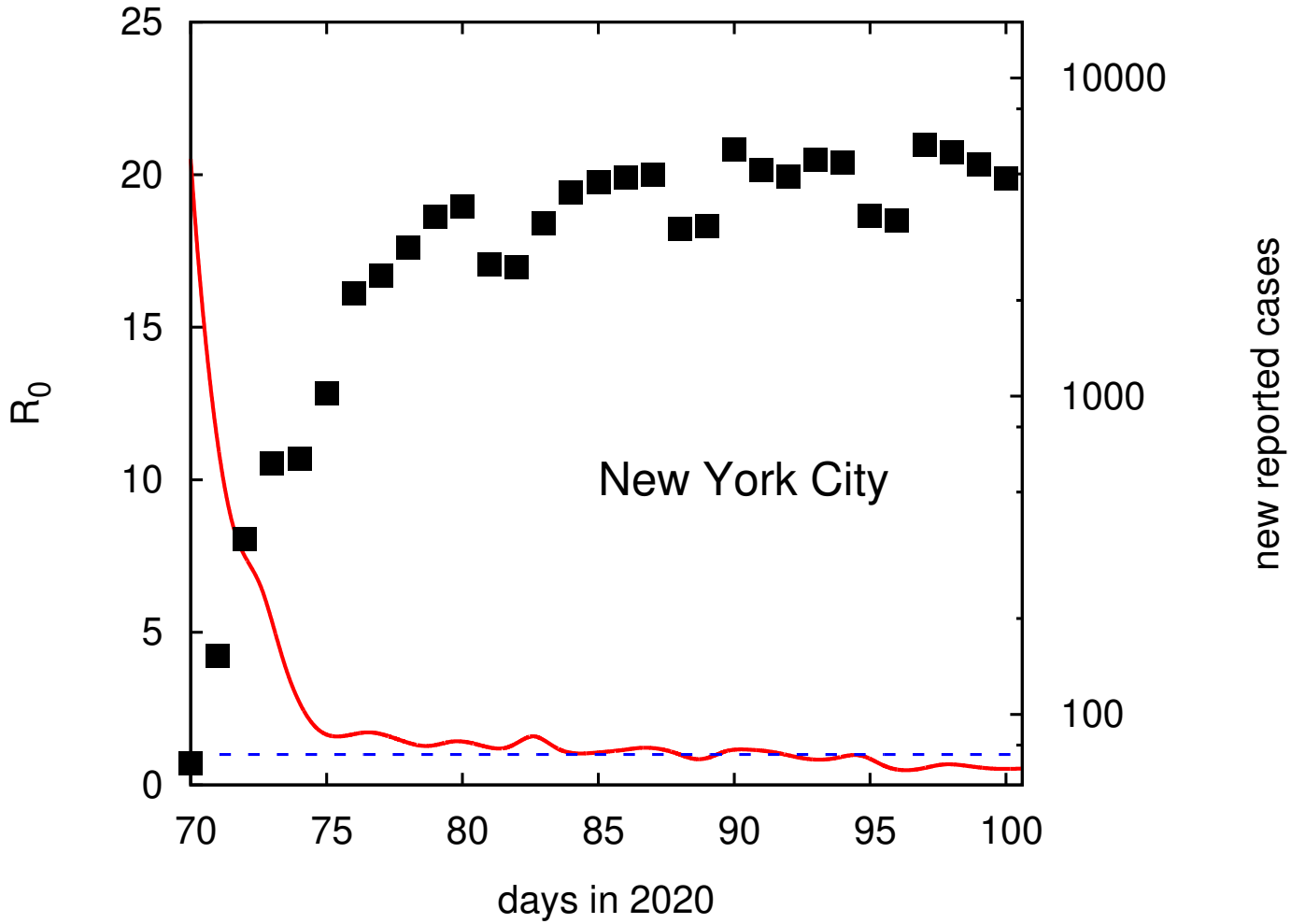
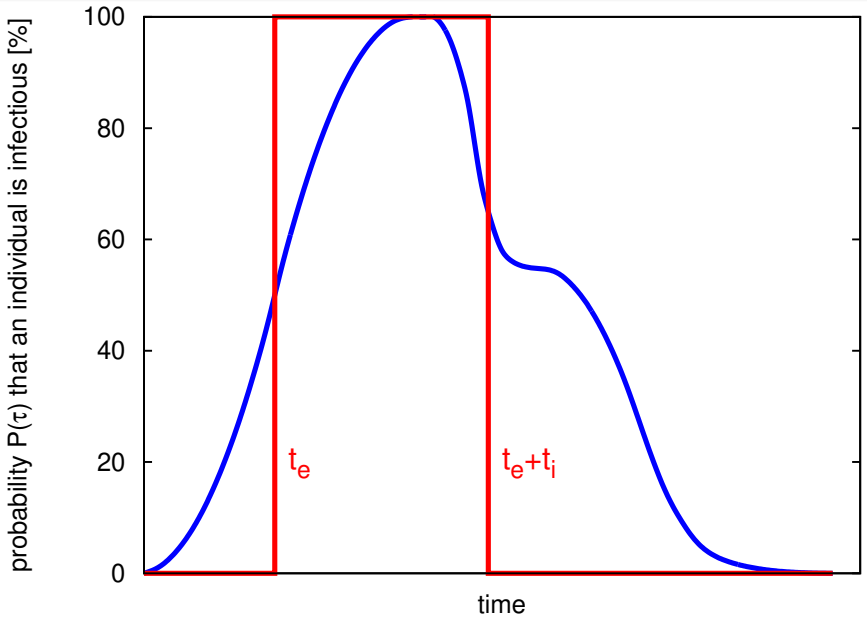


Time dependence of R_0



Generalizations



- In reality t_e and t_i are described by probability distributions
- dynamics is governed by $P(\tau)$:
  the probability that a person at time τ after exposure is infectious

$$\rho(t) = \beta \int_0^\infty \rho(t-\tau)P(\tau)d\tau, \qquad R_0 = \beta \int_0^\infty P(\tau)d\tau$$

Extensions

- inclusion of S is trivial

$$\rho(t) = \beta \frac{S(t)}{N} \int_0^\infty \rho(t-\tau) P(\tau) d\tau, \qquad S(t) = N - \int_{-\infty}^t \rho(\tau) d\tau$$

- one can have multiple sub-compartments described by $\rho_i(t)$ and cross-infection rates β_{ij}
(age groups, location, showing/not showing symptoms, etc.)

$$\rho_i(t) = \frac{S_i(t)}{N_i} \sum_j \beta_{ij} \int_0^\infty \rho_j(t-\tau) P_j(\tau) d\tau, \quad S_i(t) = N_i - \int_{-\infty}^t \rho_i(\tau) d\tau$$

Conclusions

- SEIR-like differential equations fail to correctly describe the dynamics of epidemics
  - R_0 is incorrect (even for small incubation period)
  - the delay after change of R_0 is not explained
  - the oscillation after change of R_0 is not explained
- the integral equation formalism corrects all these shortcomings
- change of R_0 after interventions can be monitored
- any extension of SEIR can also be included in the integral formalism
- Future decisions should be based on the integral equation formalism