Modeling the COVID-19 epidemic in Germany

with emphasis on case detection and compliance with NPIs

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Outline

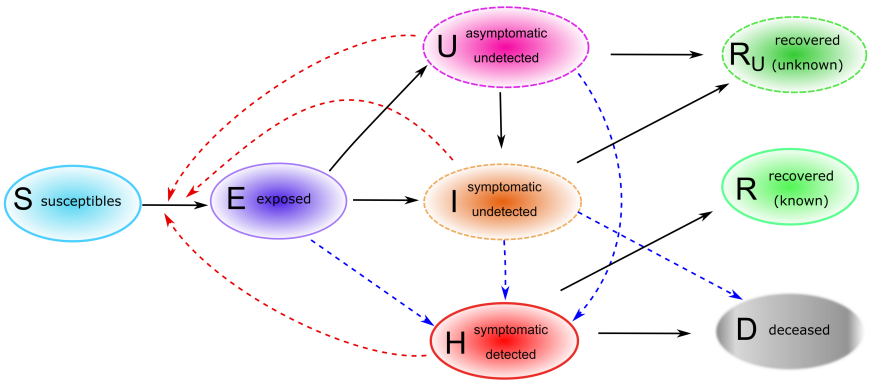
1. Basic modeling assumptions
2. Under ascertainment and testing capacity
3. (Non)compliance with non pharmaceutical interventions
4. Rebounding incidence after NPIs

Outline

SEIR type ODE models

- start with basic SEIR model
- split I by symptoms and detection status

Susceptibles
Exposed (not yet infectious)
Undetected infectious (asympt.)
Infectious (symptomatic, undetected)
H detected infectiuous
Recovered (from known infection)
R_U unknown recovered
Deceased



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\begin{aligned}
\dot{S} &= -\lambda S \\
\dot{E} &= \lambda S - \alpha E \\
\dot{U} &= (1-\varrho_0)\alpha E - \gamma_U U \\
\dot{I} &= (1-\eta_0)\varrho_0 \alpha E - \gamma_I I \\
\dot{H} &= \eta_0 \rho_0 \alpha E + \hat{\eta}_1 \gamma_U U \\
&\quad + \eta_1 \gamma_I I - \gamma_H H \\
\dot{R} &= (1-\delta_H)\gamma_H H \\
\dot{R}_U &= (1-\hat{\eta}_1)\gamma_U U \\
&\quad + (1-\eta_1)(1-\delta_I)\gamma_I I \\
\dot{D} &= \eta_1 \delta_I \gamma_I I + \delta_H \gamma_H H
\end{aligned}
$$

$$
\lambda = \beta_I I + \beta_U U + \beta_H H
$$

PARAMETRIZATION OF THE MODEL

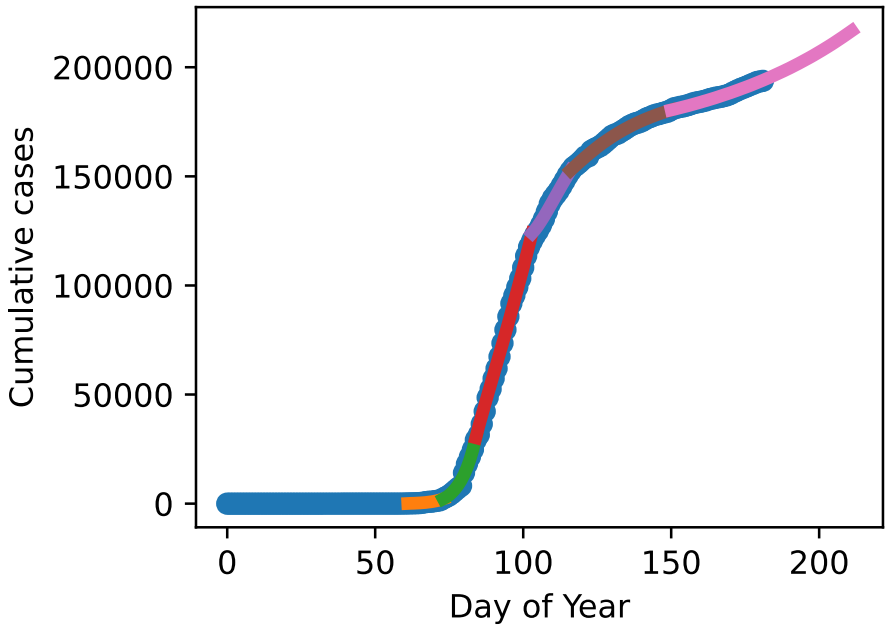
“FIXED” VALUES

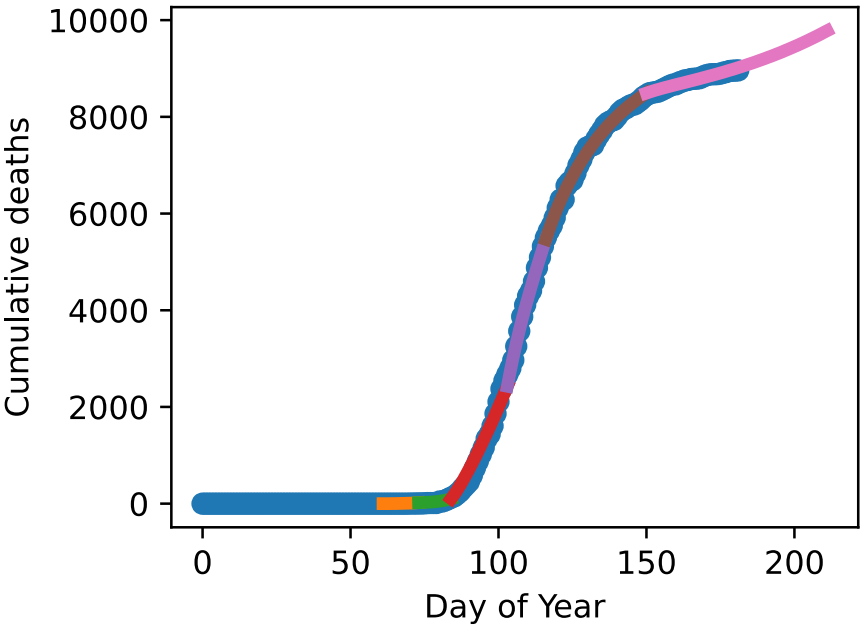
Variable	Description	Value
$1/\gamma_E$	Mean incubation period	5.5 d
$1/\gamma_I$, $1/\gamma_H$	Mean duration of symptomatic infection	7 d
$1/\gamma_U$	Mean duration of asymptomatic incection	6 d
ρ_0	Probability of developing symptoms	0.67
$\hat{\eta}_1$	Probability of early detection	0.067

FITTING FREE PARAMETERS

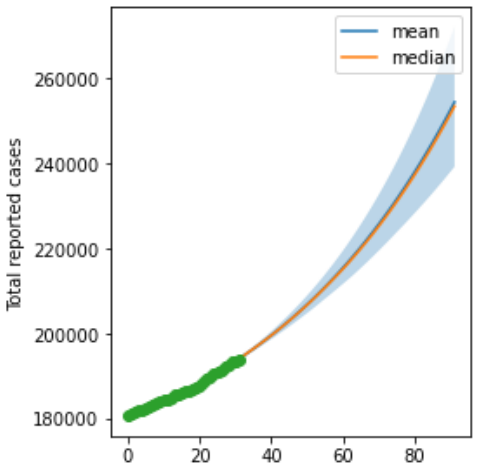
Variable	Description	Value
η_0	Probability of early detection	[0, 1]
η_1	Probability of detection	[0, 1]
β_U	Transmission rate (asymp. undetected)	open
β_I	Transmission rate (symp. undetected)	0.8 β_U
β_H	Transmission rate (detected)	0.1 β_U

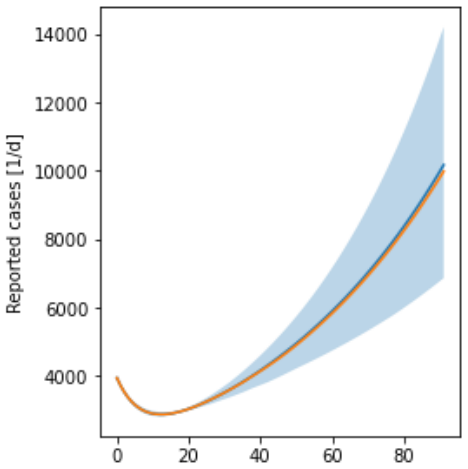
FIT FOR CUMULATIVE CASES AND DEATH

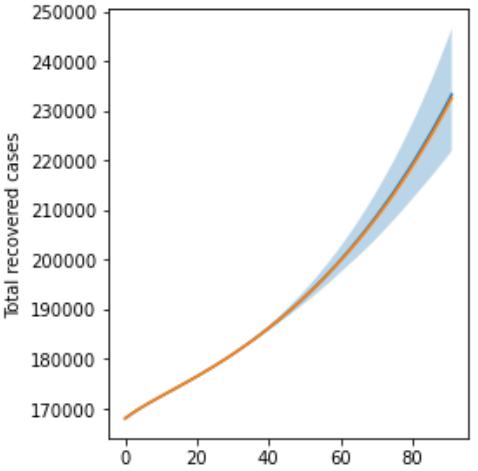


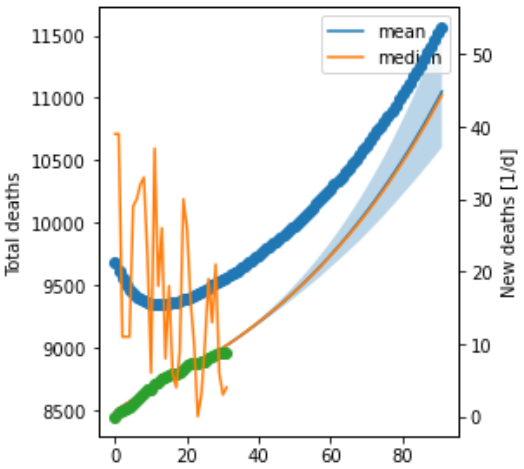


ESTIMATING UNCERTAINTIES

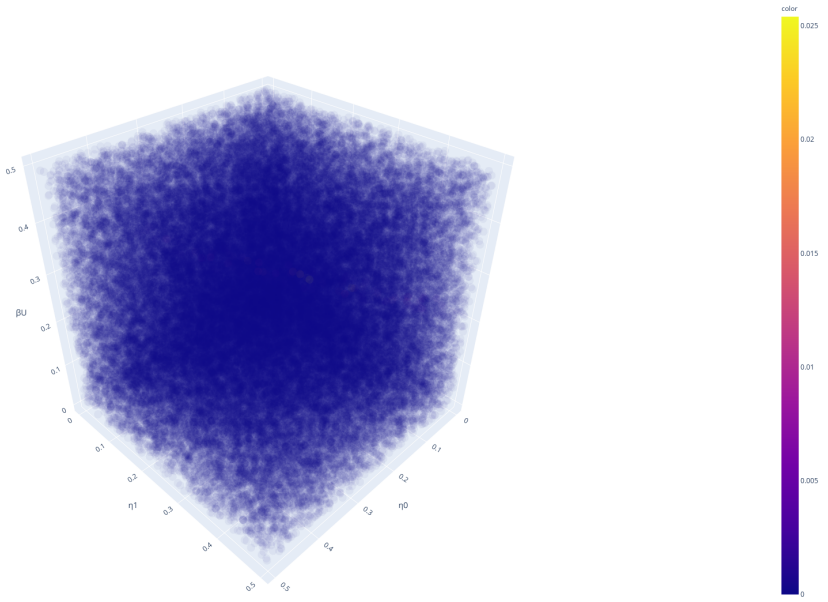








SAMPLING



AKAIKE CRITERION

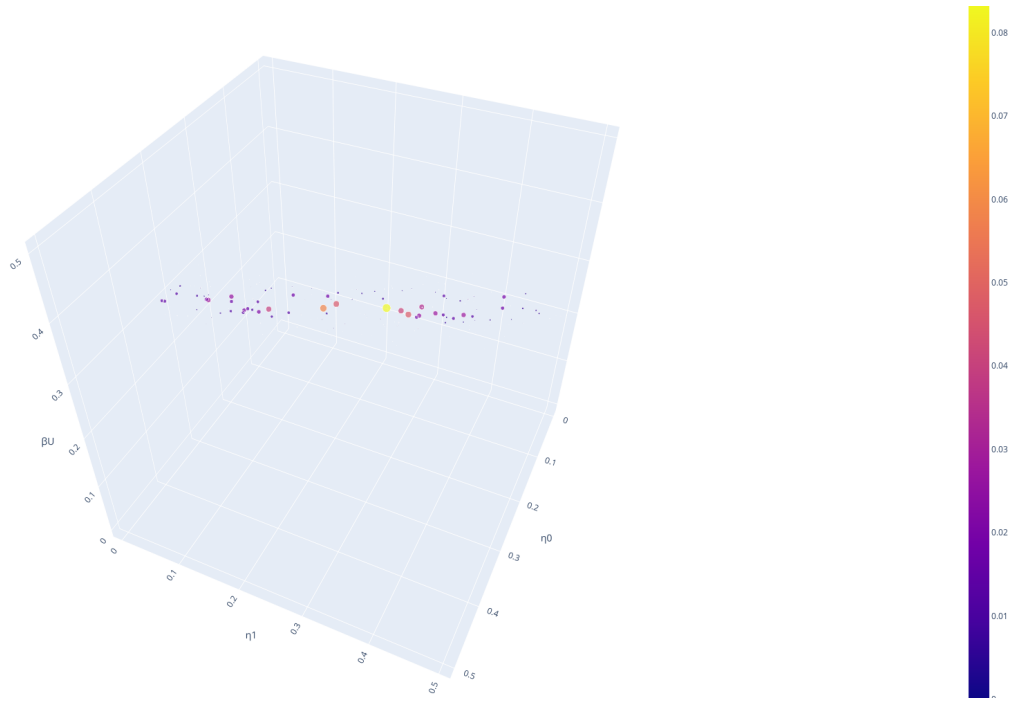
$$AICc = n\left[\ln\left(\frac{SSE}{n}\right)\right] + 2k + \frac{2k(k+1)}{(n-k-1)}$$

$$w_i = \frac{e^{-\Delta_i/2}}{\sum_{j=1}^{J} e^{-\Delta_j/2}}$$

SSE: Sum of errors
n: number of data points
k: number of degrees of freedom

$$\Delta_i = AICc_i - AICc_{min}$$

SAMPLING WITH WEIGHTS



JÜLICH
Forschungszentrum

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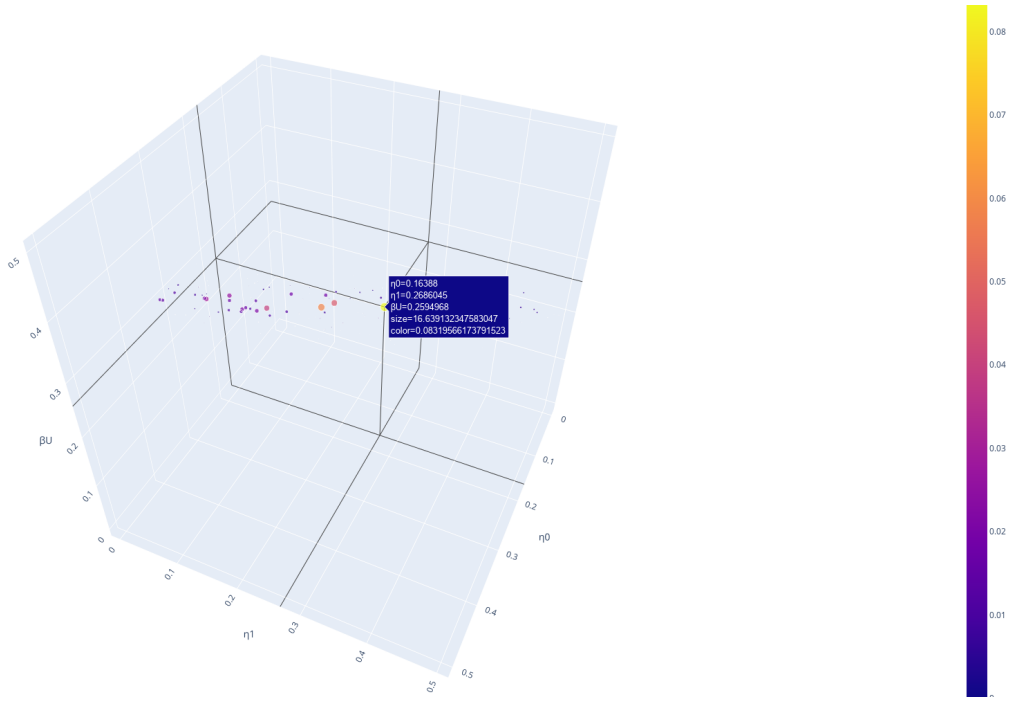

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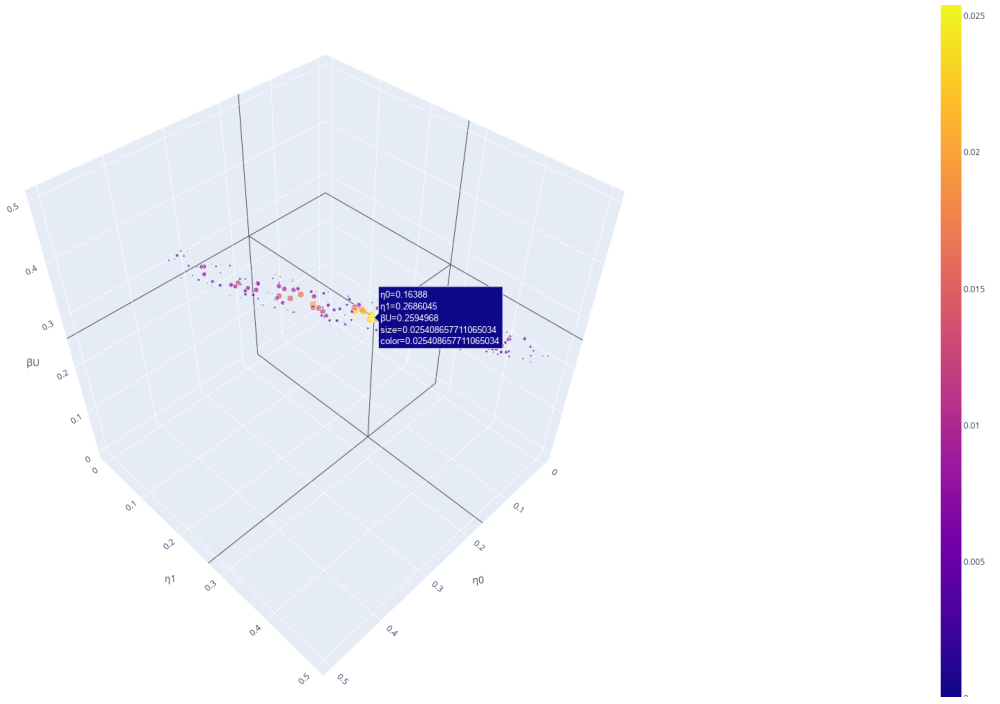
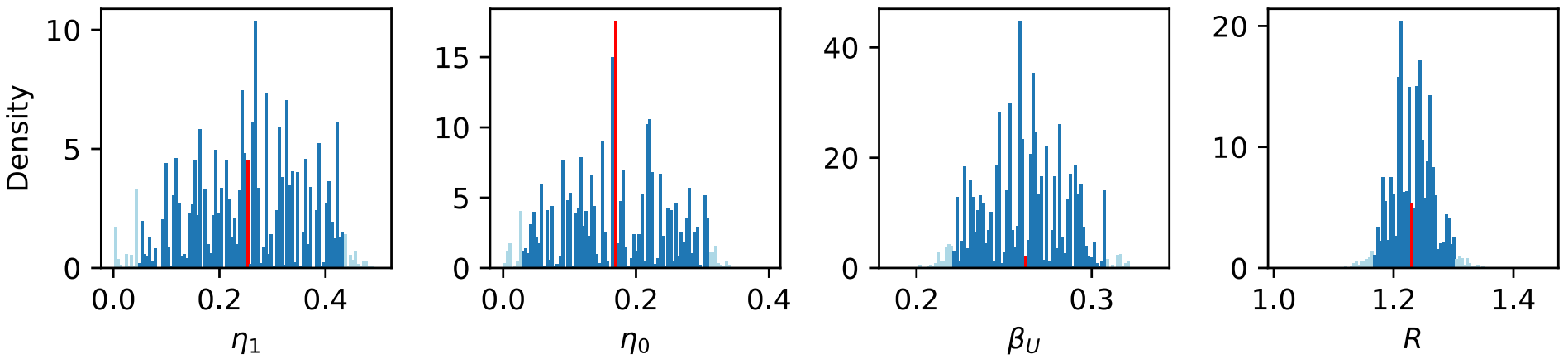
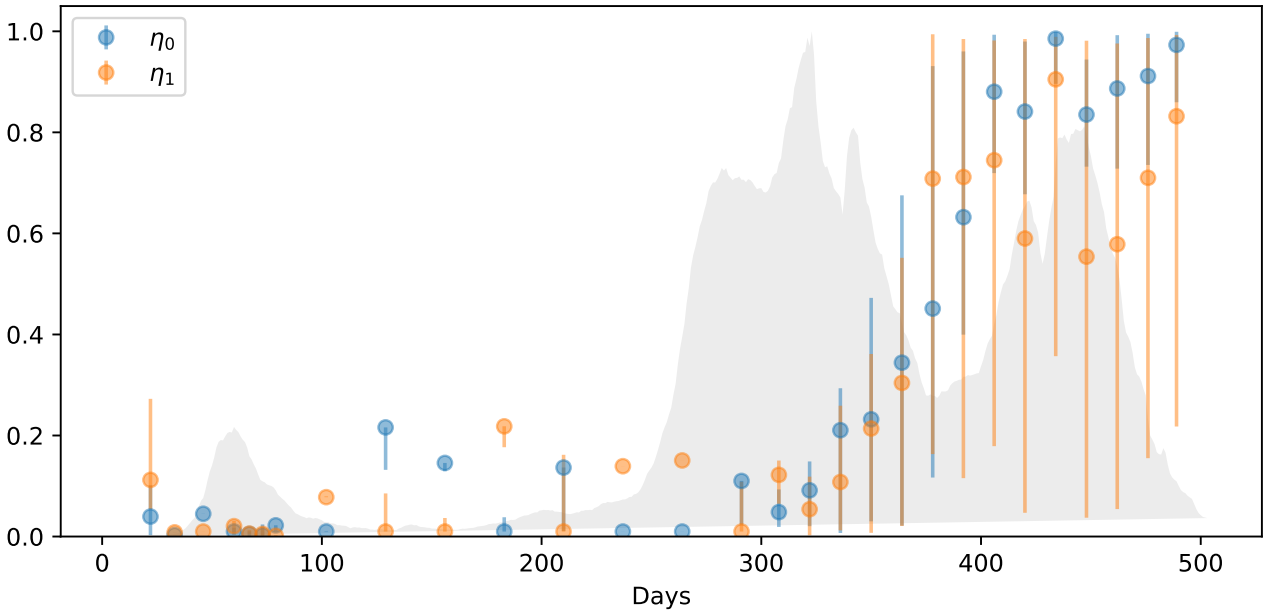


WEIGHTED HISTOGRAMS

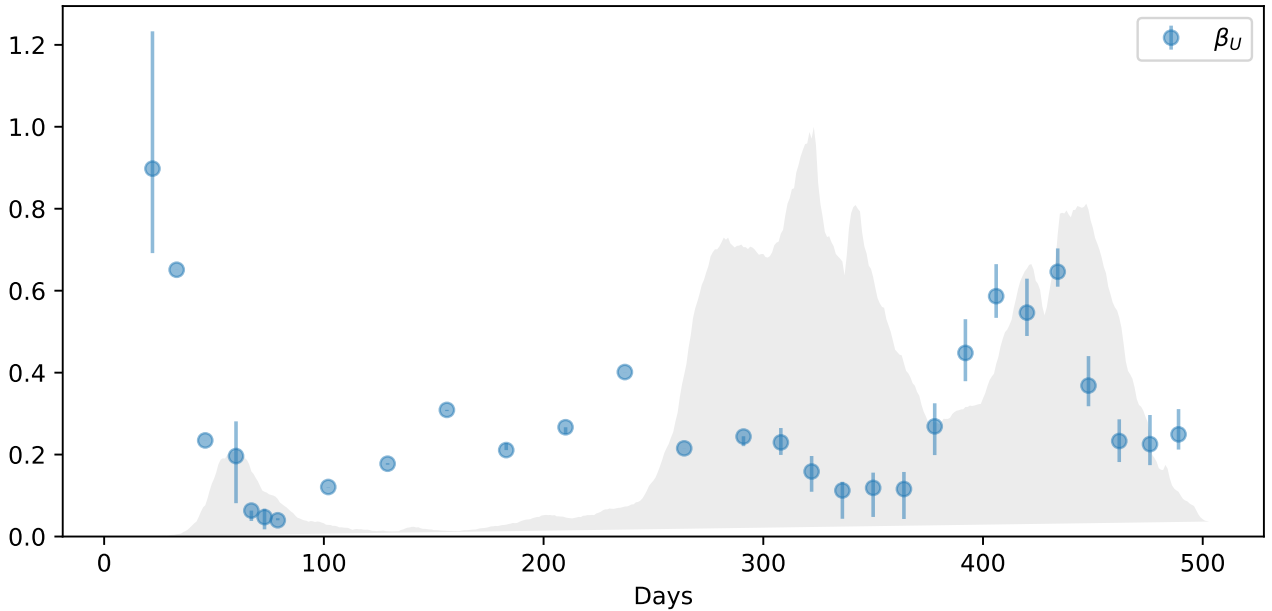


R0 1.23255756174012 1.2354879763906725 1.166431095900522 1.3025629948769604
Weight lost: 1.0981928365770746e-06.
Found mean: 1.228265190421039 3

ETAS OVER TIME



B_U OVER TIME



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possible extensions:

- further distinguish infectious individuals: hospitalized, on ICU
- vaccinations, waning immunity ...

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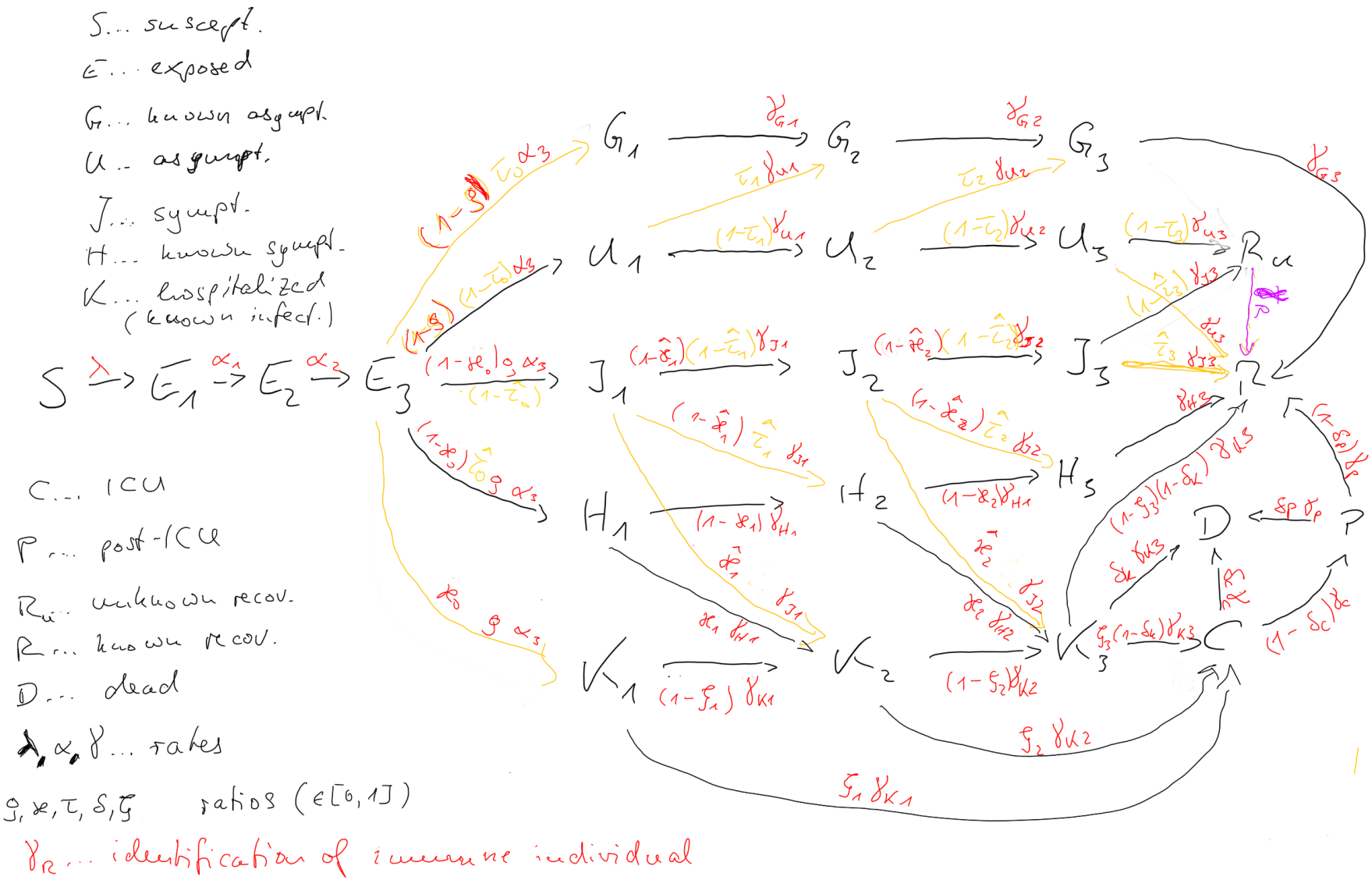
Illustration of possible extensions



Outline

Limited testing capacity

SEUIR model (I = detected cases, no distinction of asympt. infections):

$$
\begin{aligned}
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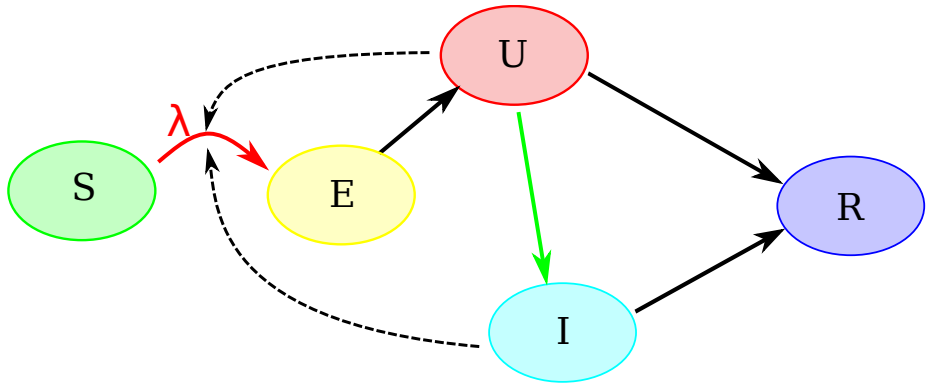
$$

Tests are a fast variable: σ, τ, ρ are large to ensure that testing capacity cannot be "stored": $\dot{T} \approx 0$, i.e.,

$$T \approx \frac{\sigma}{\tau + \langle \rho, X \rangle}$$

model structure:



only $U \to I$ contributes to "daily new cases"

Unrealistic: constant detection ratio $\frac{\eta_U}{\eta_U + \gamma_U}$ independent of prevalence

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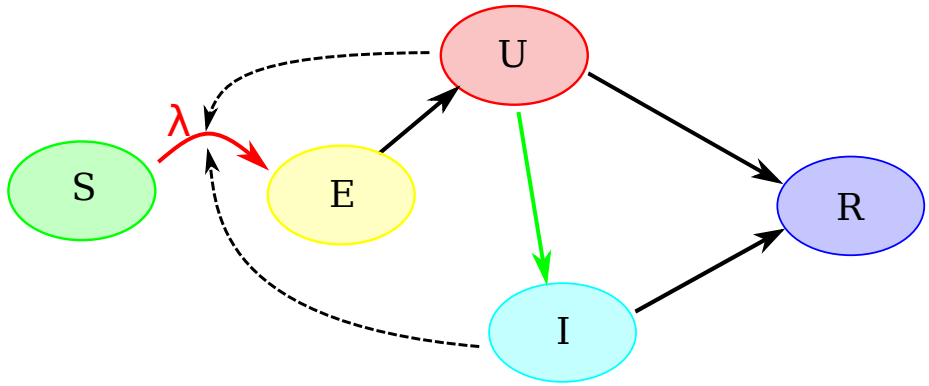

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\dot{I} &= \rho_U T U - \gamma_I I \\
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\end{aligned}$$

add Test "population":

$$\dot{T} = \sigma - \tau T - \langle \rho, X \rangle T$$

$\rho = (\rho_S, \rho_E, \rho_U, \rho_I, \rho_R)$,
$X = (S, E, U, I, R)$

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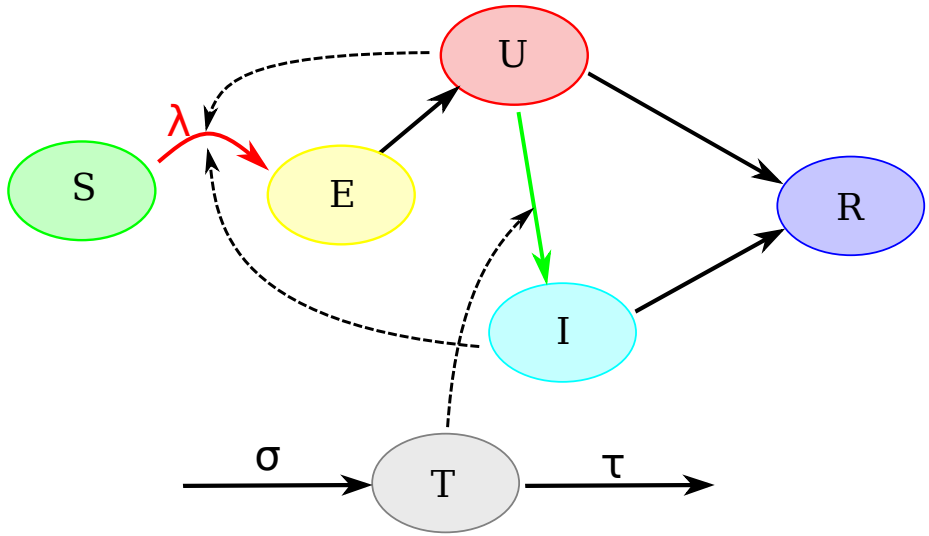

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now:

$$\eta_U = \rho_U T$$

varies depending on tests

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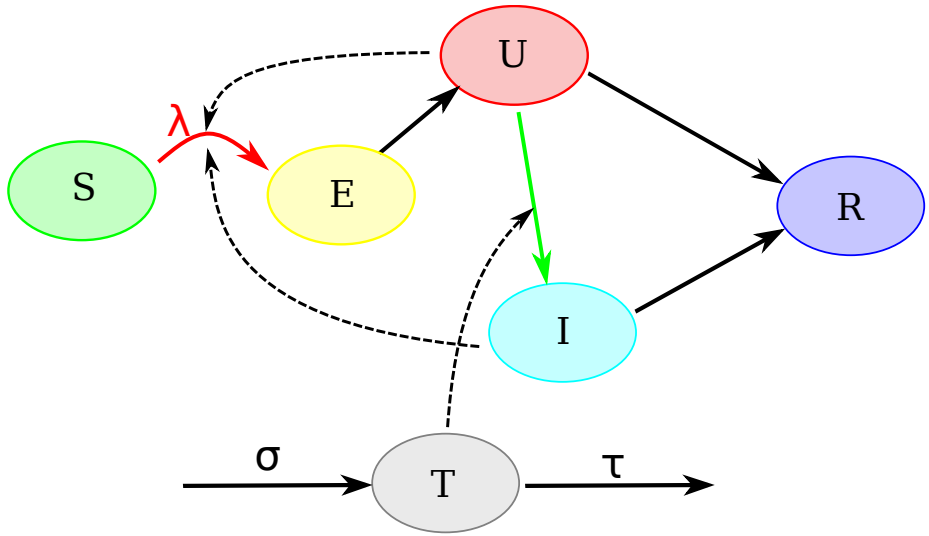

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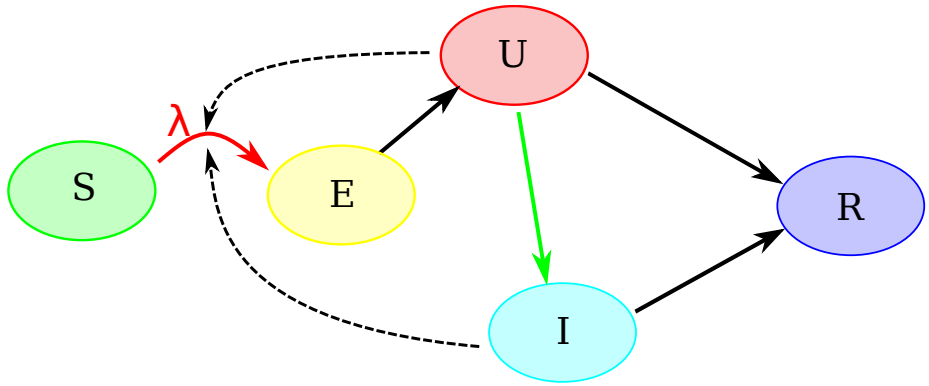

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now:

$$\eta_U = \rho_U T \approx \frac{\sigma\rho_U}{\tau + \langle \rho, X\rangle}$$

Illustration of state dependent detection

compare 4 models for detection:

- *tests as population:* keep test population T
- *testing rate dep. on X:* calculate $\eta_U = \frac{\sigma\rho_U}{\tau+\langle\rho,X\rangle}$
- *testing rate dep. on U:* approximate $\tau + \rho_S S + \rho_E E + \rho_I I + \rho_R R$ by constant K
  $\eta_U = \frac{\sigma\rho_U}{K+\rho_U U}$
- *constant testing rate:* $\eta_U =$ const., independent of state

N.B.:

$$\mathcal{R}_0 = \frac{\beta_U}{\eta_U|_{DFE} + \gamma_U} + \frac{\beta_I}{\gamma_I}\,\frac{\eta_U|_{DFE}}{\eta|_{DFE} + \gamma_U}$$

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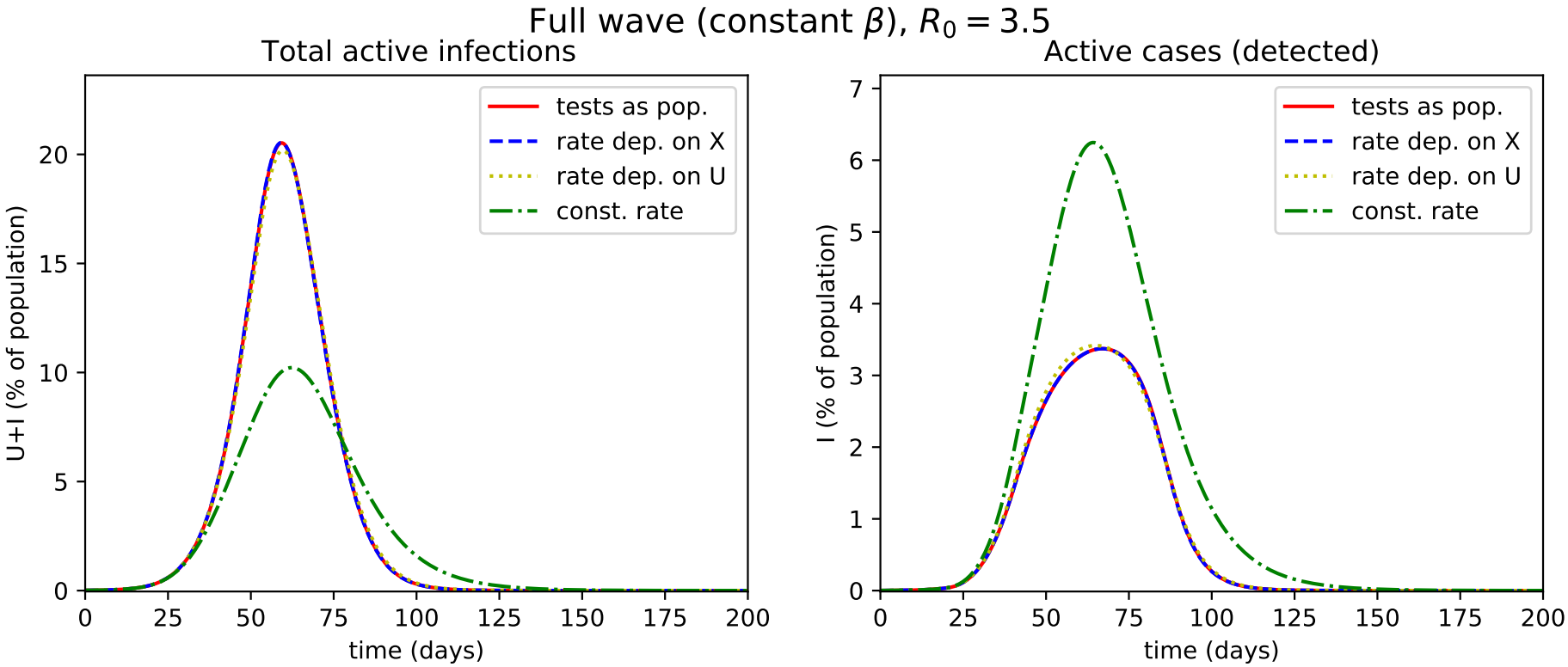
consider 2 scenarios:

- full epidemic wave: epidemic runs through population unrestrictedly
- with panic factor: transmission decreased at high *known* prevalence, e.g.:

$$\beta = \beta_0 \left(\alpha + (1-\alpha)\exp(-\theta I^2)\right)$$

Illustration of state dependent detection

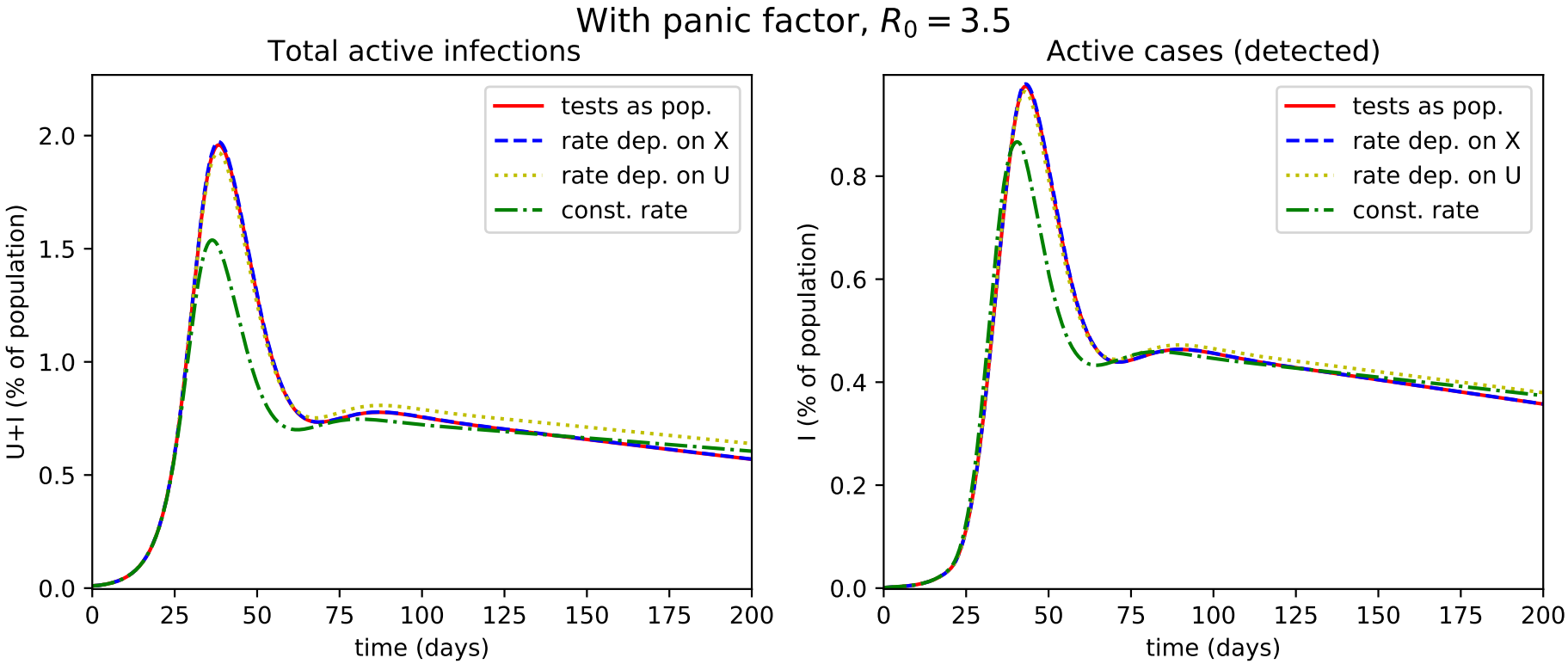


no panic factor, high peak prevalence

max. detection ratio $\approx 30\%$

for constant detection ratio: overly optimistic peak height

Illustration of state dependent detection



with panic factor: curve significantly flattened

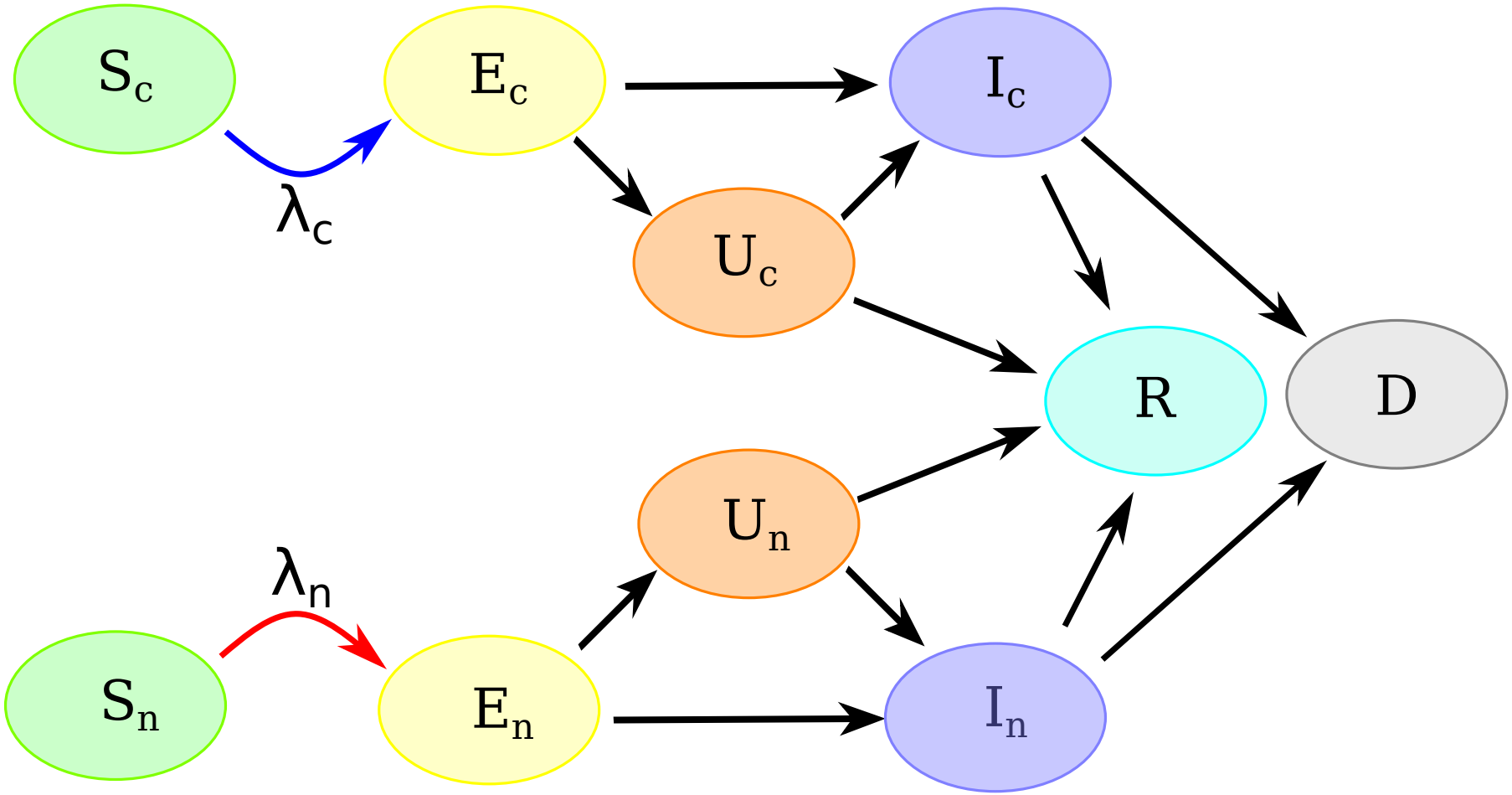
max. detection ratio $\approx 30\%$ (and fairly constant)

for constant detection ratio: panic sets in faster $\implies$ lower peak

Outline

Noncompliance with NPIs

two subpopulations ("**c**ompliant", "**n**oncompliant") – for $m = c, n$:



three stages for E, last one already infectious

Noncompliance with NPIs

two subpopulations ("**c**ompliant", "**n**oncompliant") – for $m = c, n$:

$$
\begin{aligned}
\dot{S}_m &= -\lambda_m(t) S_m \\
\dot{E}_{1,m} &= \lambda_m(t) S_m - \gamma_E E_{1,m} \\
\dot{E}_{2,m} &= \gamma_E E_{1,m} - \gamma_E E_{1,m} \\
\dot{E}_{3,m} &= \gamma_E E_{2,m} - (\gamma_E + \tau_m) E_{3,m} \\
\dot{U}_m &= \gamma_E E_{3,m} - (\gamma_U + \eta_m) U_m \\
\dot{I}_m &= \tau_m E_{3,m} + \eta_m U_m - \gamma_I I_m \\
\dot{R} &= (1-\delta)\gamma_I (I_c + I_n) + \gamma_U (U_c + U_n) \\
\dot{D} &= \delta \gamma_I (I_c + I_n)
\end{aligned}
$$

where

$$
\lambda_m = \sum_{k=c,n} (\beta_{km,E} E_{3,k} + \beta_{km,U} U_k + \beta_{km,I} I_k)
$$

$$
\beta_{km,X} = \beta_0 \mu_X a_k s_m
$$

$t < t_0$: $a_c = a_n = s_c = s_n = 1$ (no difference); $\mathcal{R}_0 \approx 1.5$
$t \geq t_0$: $a_c, s_c < 1$, $a_n = s_n = 1$; $\mathcal{R}_c < \mathcal{R}_0$

Incidence with noncompliance

quick increase to 20,000 new cases per day, then reduce $a_c s_c$ to $\frac{1}{2}$

detected cases for different compliance levels

source: https://cosimo.fz-juelich.de/

control reproduction number:

$$\mathcal{R}_c = (r\rho + 1 - \rho)\mathcal{R}_0 = (1 - (1 - r)\rho)\mathcal{R}_0$$

with $r = a_c s_c$ and compliance level ρ

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quick increase to 20,000 new cases per day, then reduce $a_c s_c$ to $\frac{1}{2}$

total infections for different compliance levels

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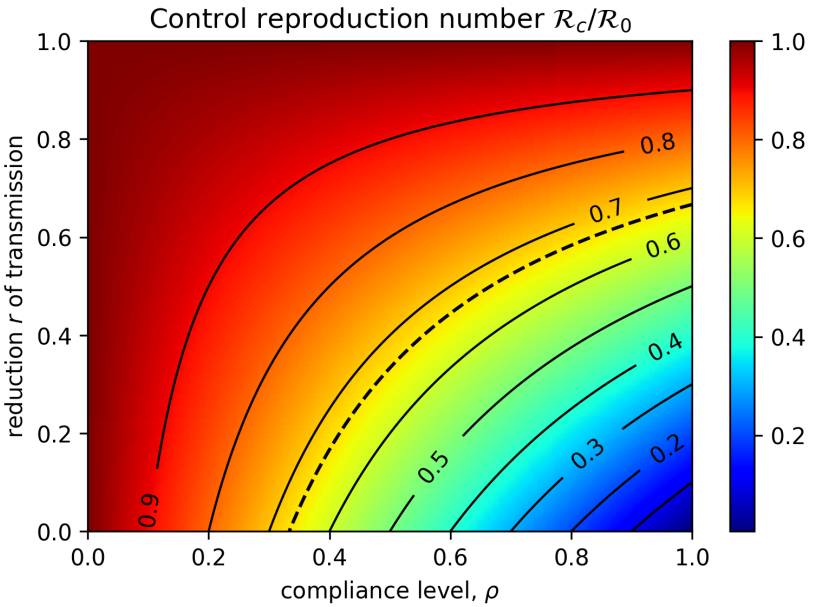
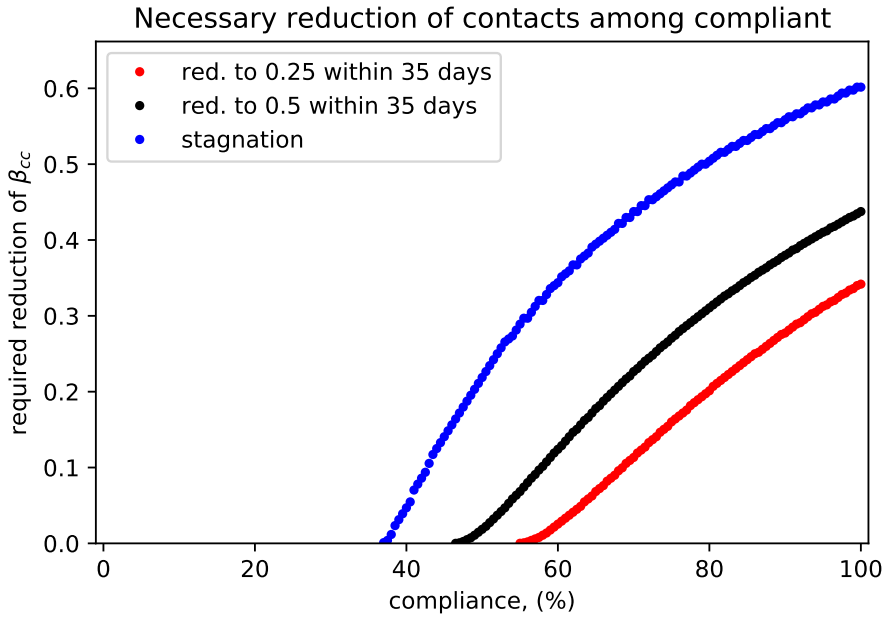
$\mathcal{R}_c$ vs. R_t

$$\mathcal{R}_c = (r\rho + 1 - \rho)\mathcal{R}_0 = (1 - (1 - r)\rho)\mathcal{R}_0$$



theoretical control reproduction number depending on r, ρ

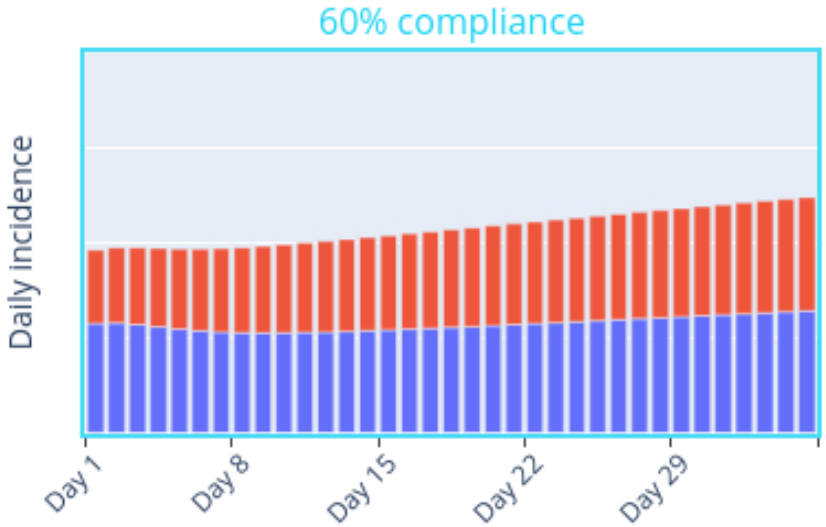


(ρ, r) combinations required for different incidence goals

As long as $S \approx N$ and the prevalence is small, $\mathcal{R}_c$ is a good approximation for R_t

Outline

Rebound effect: motivation



brief stagnation of incidence after intervention

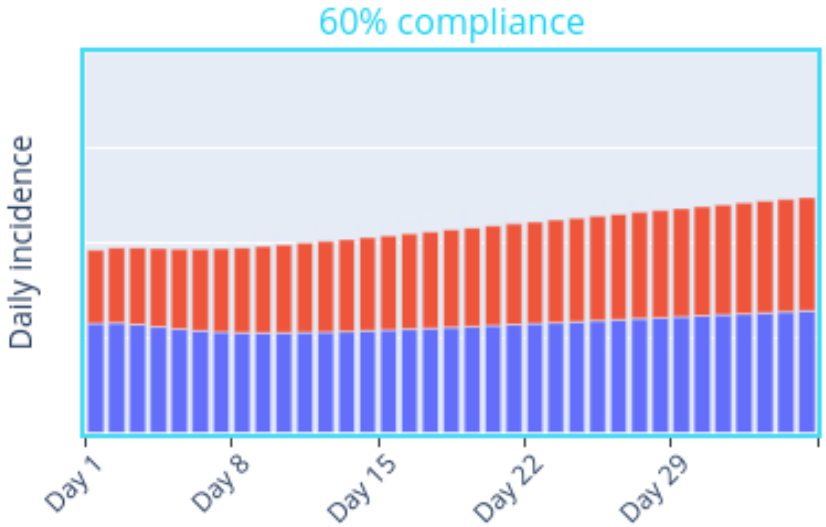
then: incidence rises again

Are people becoming complacent once an intervention shows an effect?

Not necessarily: transient drops of incidence despite $\mathcal{R}_c > 1$ are possible:

1. instantaneous drop of new infections
2. rotation in phase space

Rebound effect: motivation



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Are people becoming complacent once an intervention shows an effect?

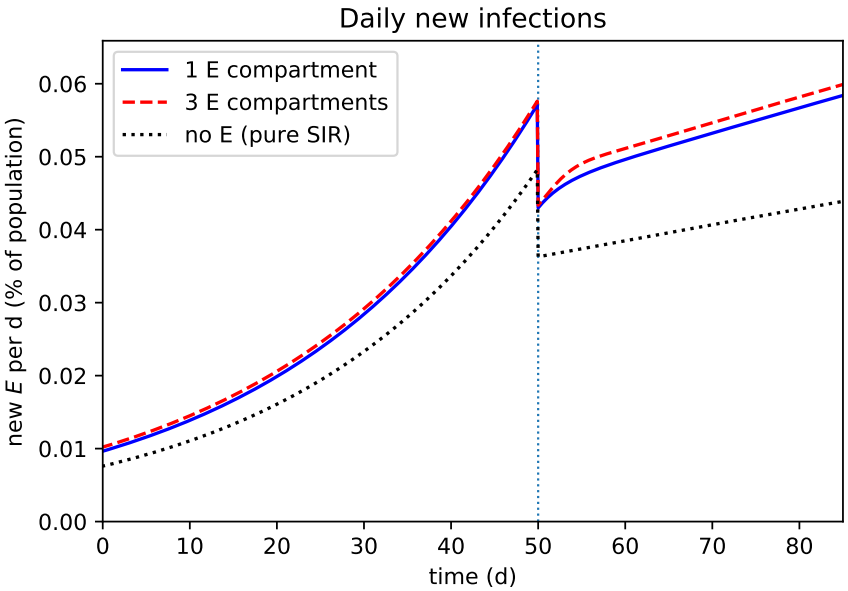
Not necessarily: transient drops of incidence despite $\mathcal{R}_c > 1$ are possible:

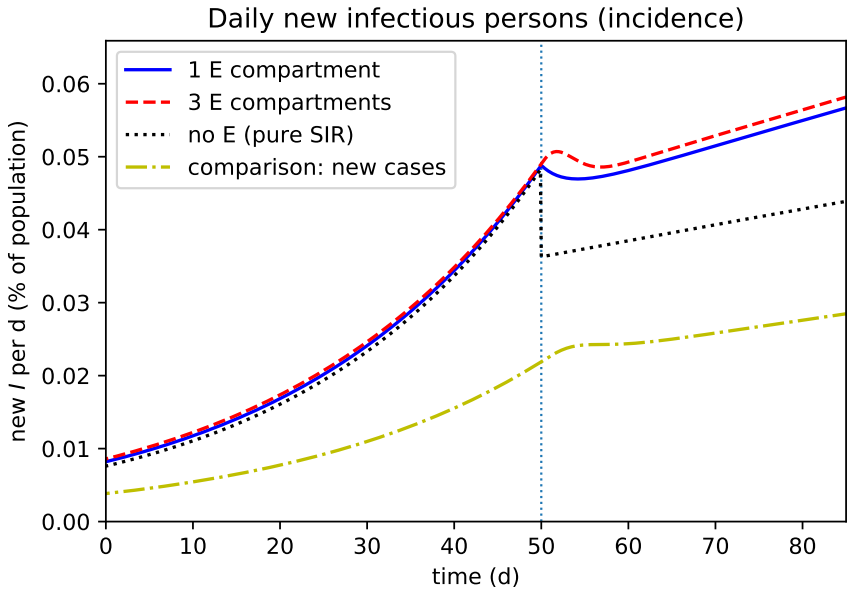
1. instantaneous drop of new infections
2. rotation in phase space

Rebound effect: explanation 1

following actual new infections

- consider simple model with uniform compliance
- observe difference between new infections, new infectious individuals, and new cases





$\mathcal{R}_0 \approx 1.5$ (for 50 days)
intervention on day 50: decrease β by 25% $\implies$ $\mathcal{R}_c \approx 1.125$

Rebound effect: explanation 2

for heterogeneous population: rotation in phase space

- before intervention: compliant fraction among infected individuals equals ρ
- after intervention: noncompliant fraction among infected individuals rises

illustration at simple SIR model with compliance:

$$\dot{S}_m = -(\beta_{cm} I_c + \beta_{nm} I_n) S_m, \qquad \dot{I}_m = (\beta_{cm} I_c + \beta_{nm} I_n) S_m - \gamma I_m$$

linearization about DFE $(\rho N, (1-\rho)N, 0, 0)$:

$$\beta_0 N \begin{pmatrix} -a_c s_c I_c - a_n s_c I_n & 0 & -a_c s_c \rho & -a_n s_c \rho \\ 0 & -a_c s_n I_c - a_n s_n I_n & -a_c s_n (1-\rho) & -a_n s_n (1-\rho) \\ a_c s_c I_c + a_n s_c I_n & 0 & a_c s_c \rho - \frac{\gamma}{\beta_0 N} & a_n s_c \rho \\ 0 & a_c s_n I_c + a_n s_n I_n & a_c s_n (1-\rho) & a_n s_n (1-\rho) - \frac{\gamma}{\beta_0 N} \end{pmatrix}$$

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consider (with $\beta = \beta_0 N$):

$$\begin{pmatrix} \beta a_c s_c \rho - \gamma & \beta s_c \rho \\ \beta a_c (1-\rho) & \beta(1-\rho) - \gamma \end{pmatrix}, \qquad \text{EVal}: \quad \begin{array}{c} \lambda_1 = \beta(a_c s_c \rho + (1-\rho)) - \gamma \\ \lambda_2 = -\gamma < 0 \end{array}$$

$$\mathcal{R}_c = (a_c s_c \rho + (1-\rho)) \tfrac{\beta}{\gamma} > 1 \iff \lambda_1 > 0 \qquad \text{(NGM approach)}$$

eigenvector for λ_1 in I_c-I_n plane: $(s_c \rho, 1-\rho)^T$

Rebound effect: explanation 2

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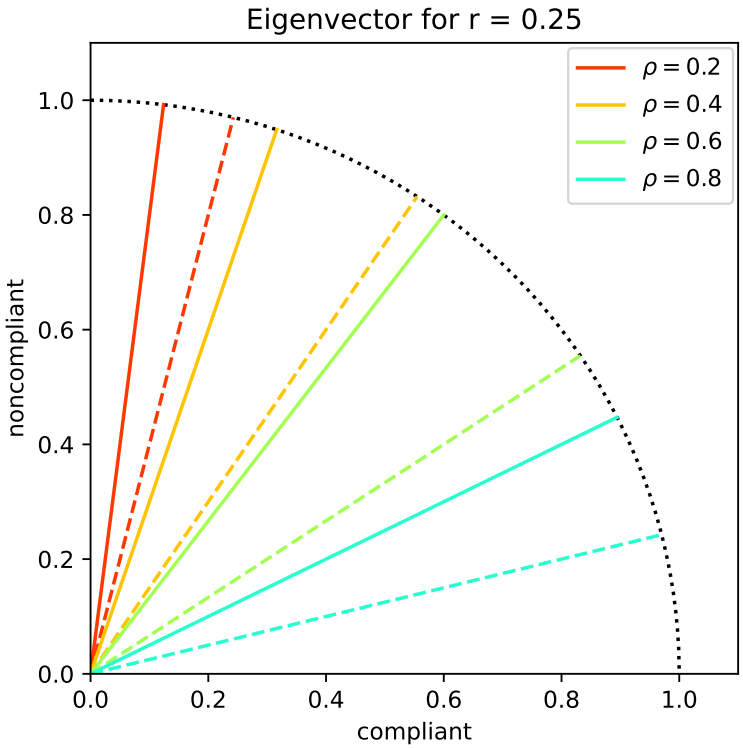

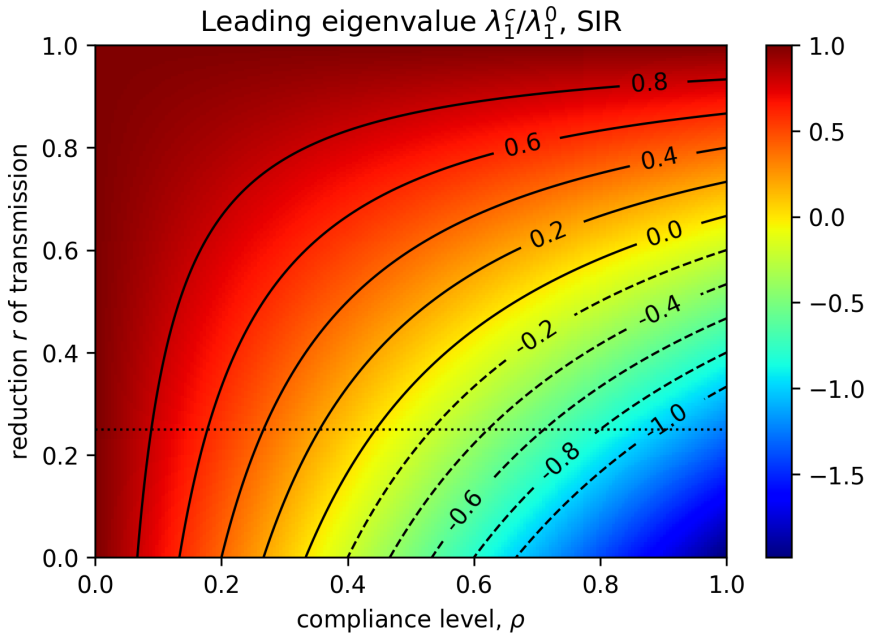

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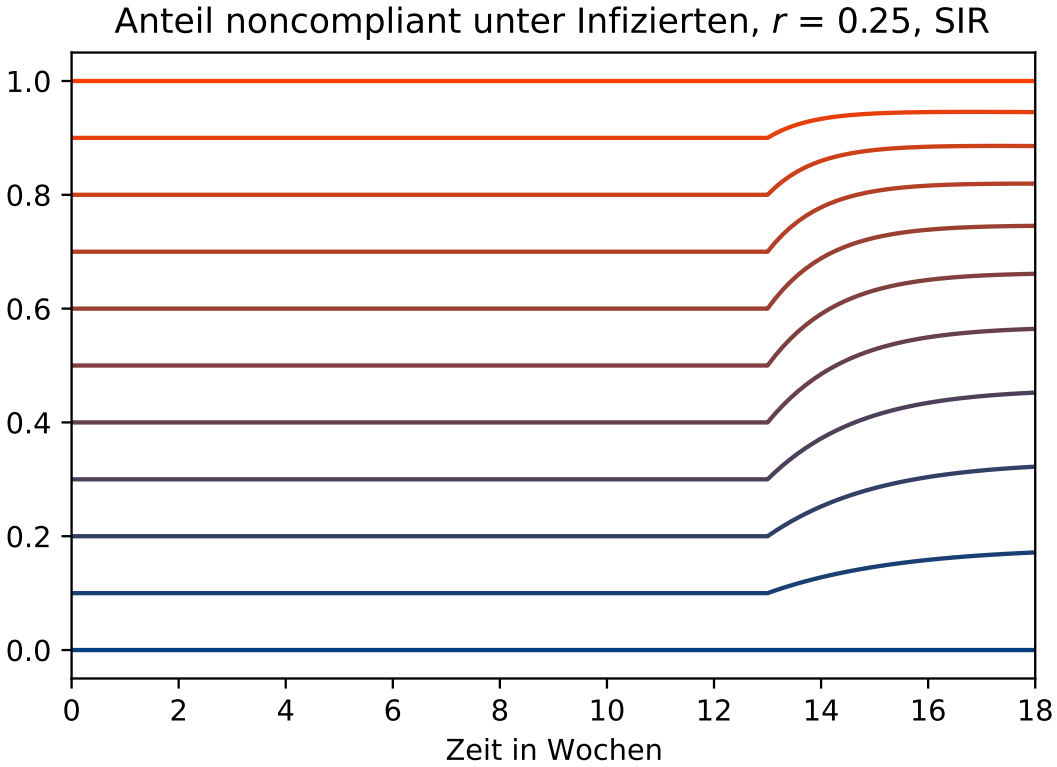

rotation of solution vector towards eigenvector for λ_1

plotted:

$$\frac{I_n}{I_n + I_c}$$

N.B.: can occur even with $\mathcal{R}_c = \mathcal{R}_0$ [24]

Thanks to
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and

to you

for your attention