

Mathematical modelling for determining COVID-19 incidence from testing data

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- Different approaches to COVID-19 mitigation throughout the world

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- ▶ Different approaches to COVID-19 mitigation throughout the world
- ▶ To compare mitigation-strategies, the impact of differences in data-collection must be understood.

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- ▶ Different approaches to COVID-19 mitigation throughout the world
- ▶ To compare mitigation-strategies, the impact of differences in data-collection must be understood.
- ▶ The role of testing: Confirmation of symptoms, required for various activities or entirely voluntary?

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- ▶ To compare mitigation-strategies, the impact of differences in data-collection must be understood.
- ▶ The role of testing: Confirmation of symptoms, required for various activities or entirely voluntary?
- ▶ **How do we compare case-counts between periods and places where testing activity was different?**

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- ▶ In particular: For each reported case of COVID-19, how many unidentified cases?

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Let's look at some data...

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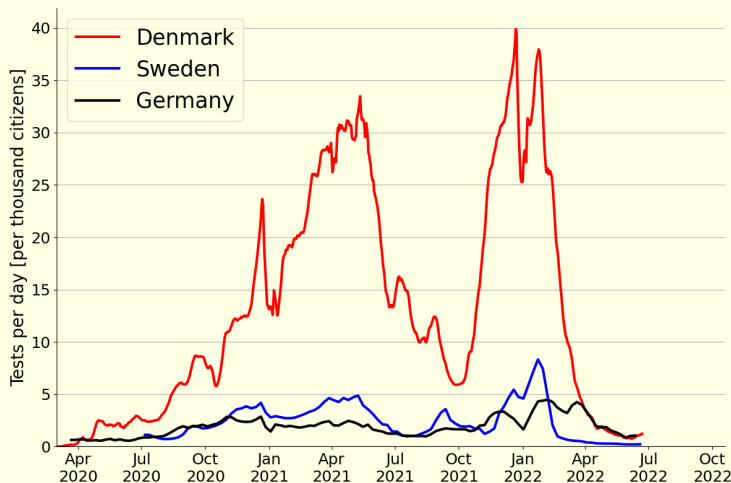
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- We aim to determine the assertion ratio between observed cases and the total number of COVID-19 cases.

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- ▶ We aim to determine the assertion ratio between observed cases and the total number of COVID-19 cases.
- ▶ This ratio can be used as a correction-factor for observed data.

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- ▶ We aim to determine the assertion ratio between observed cases and the total number of COVID-19 cases.
- ▶ This ratio can be used as a correction-factor for observed data.
- ▶ We extend the classic SIR-model to include voluntary testing that identifies pre- and asymptomatic cases.

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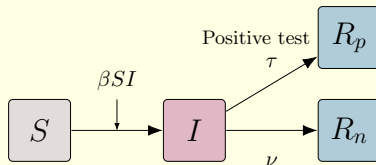
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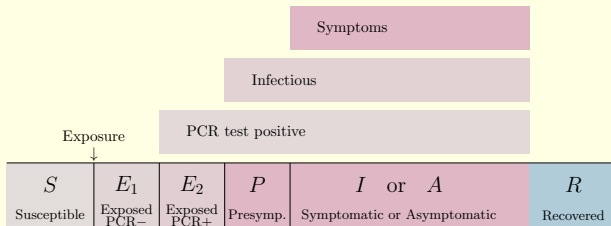
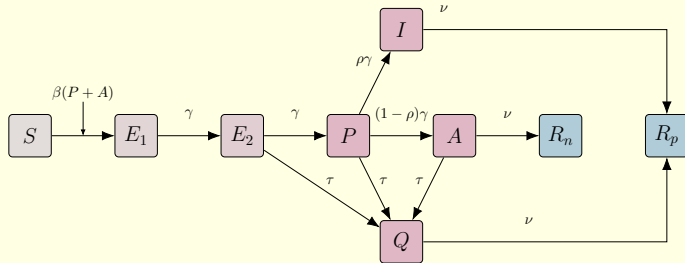
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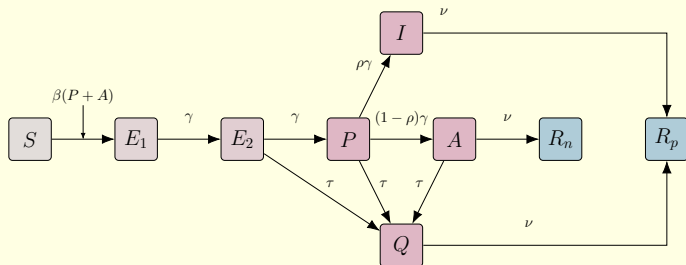
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$$\dot{S} = -\beta S(P + A)$$

$$\dot{E}_1 = \beta S(P + A) - \gamma E_1$$

$$\dot{E}_2 = \gamma E_1 - (\gamma + \tau) E_2$$

$$\dot{P} = \gamma E_2 - (\gamma + \tau) P$$

$$\dot{I} = \gamma \rho P - \nu I$$

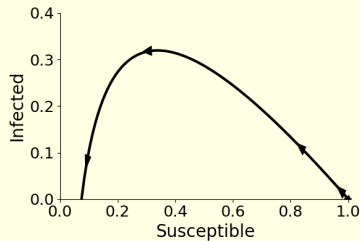
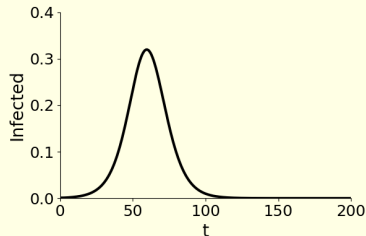
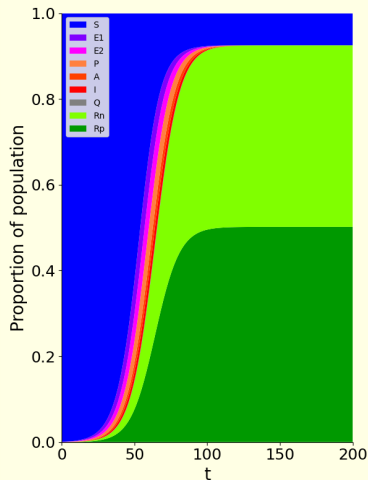
$$\dot{A} = \gamma(1 - \rho)P - (\nu + \tau)A$$

$$\dot{Q} = \tau(E_2 + P + A) - \nu Q$$

$$\dot{R}_p = \nu Q + \nu I$$

$$\dot{R}_n = \nu A$$

General dynamics like classic SIR-model.



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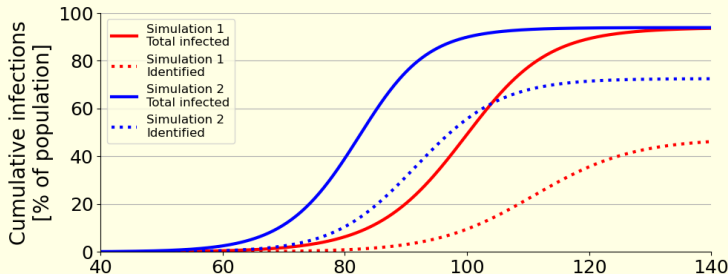
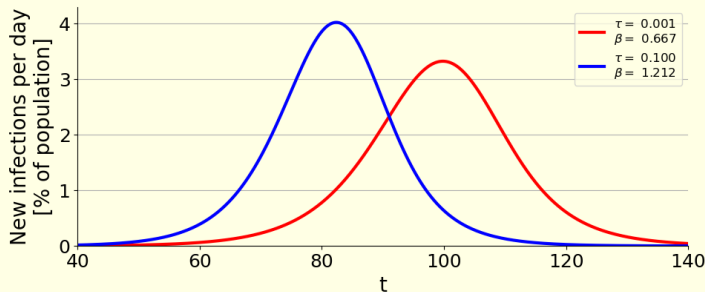
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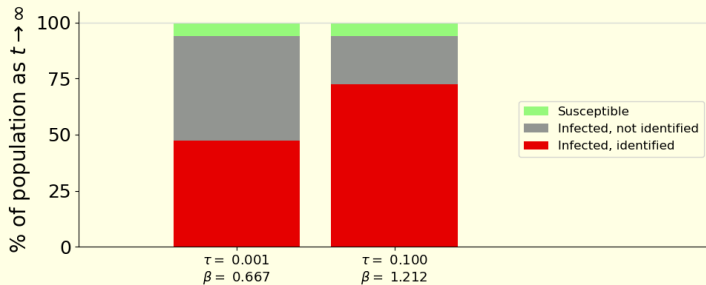
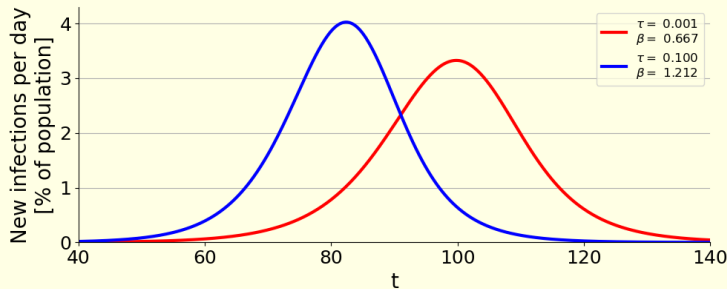
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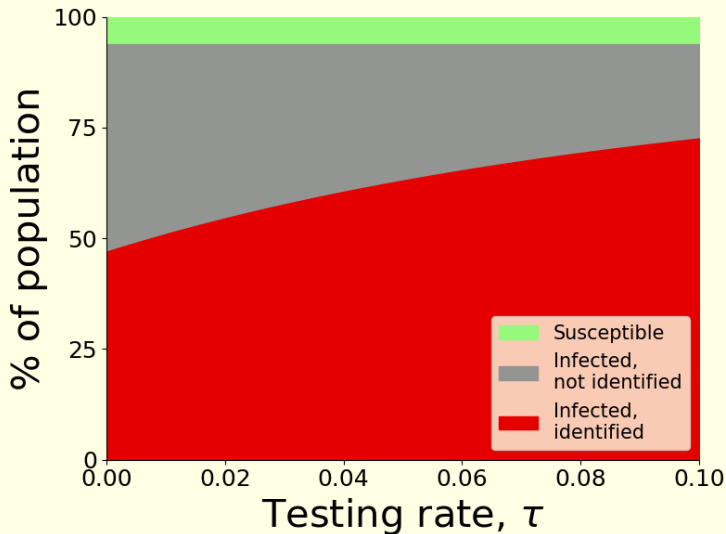
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(β chosen such that final size is fixed)

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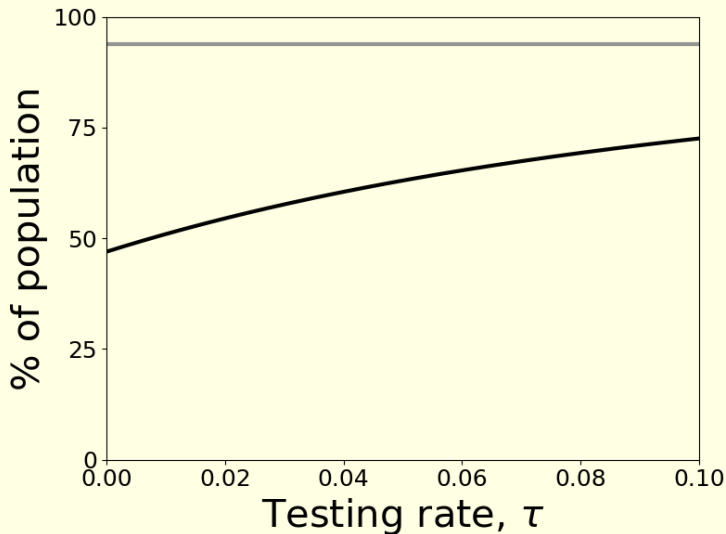
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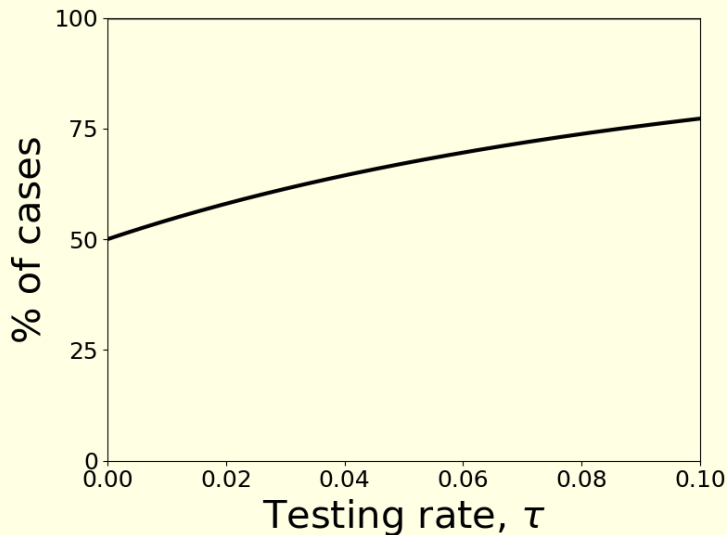
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Fixed final size and (τ, β)



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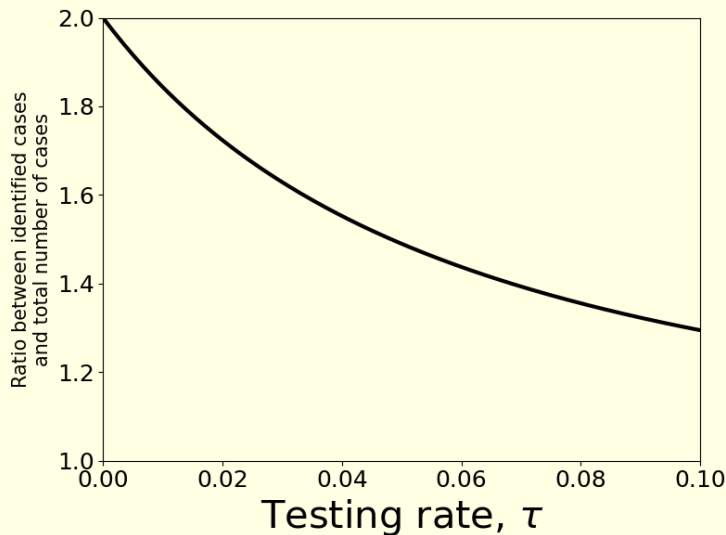
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We consider the assertion ratio as the fraction of cases identified:

$$K = \frac{R_p(t)}{(R_n(t) + R_p(t))} \quad (1)$$

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We consider the assertion ratio as the fraction of cases identified:

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The correction-factor is K^{-1} .

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The correction-factor is K^{-1} .

Inspired by previous work on epidemic final size (Andreasen, 2018),

$$K = 1 - \left(1 - \frac{\tau}{\gamma + \tau}\right) \left(1 - \frac{\gamma\rho + \tau}{\gamma + \tau}\right) \left(\frac{\nu}{\nu + \tau}\right) \quad (2)$$

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Note that K is independent of β .

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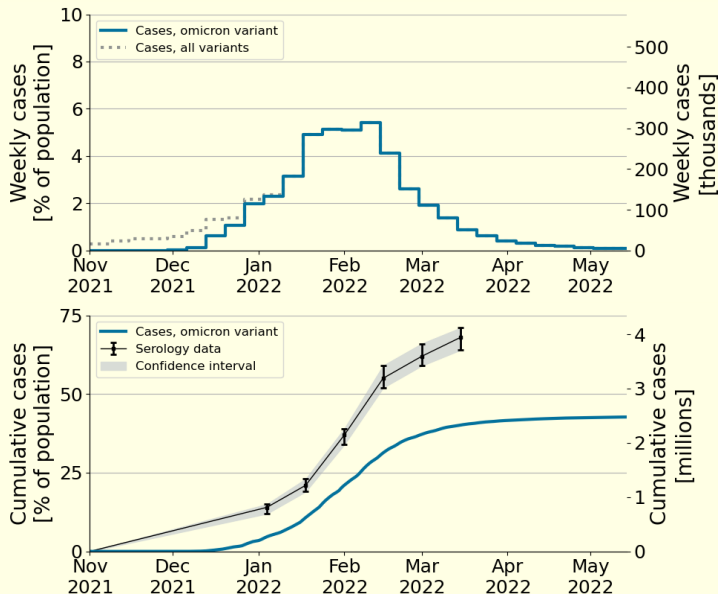
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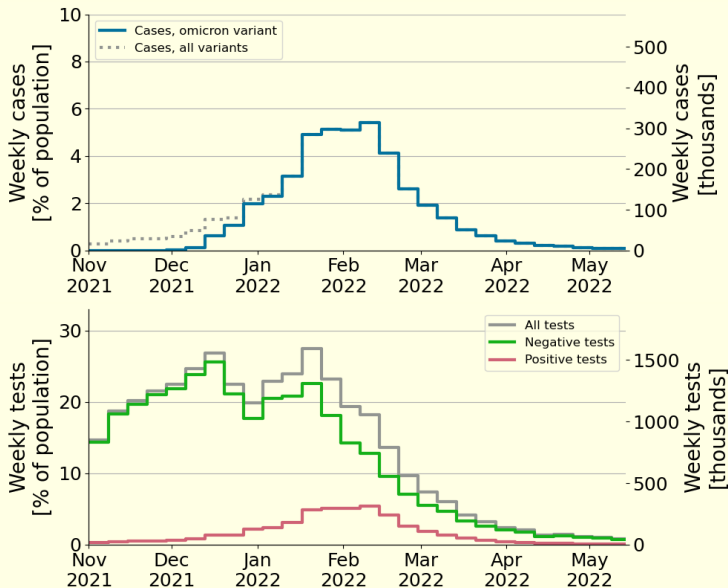
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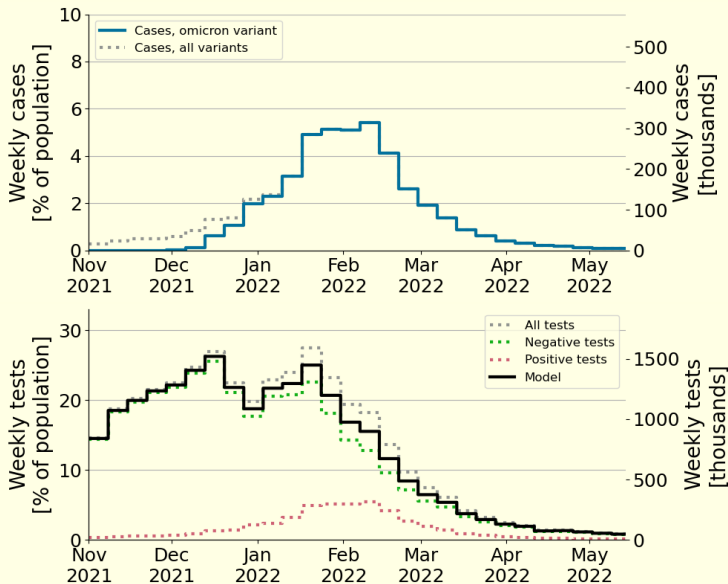
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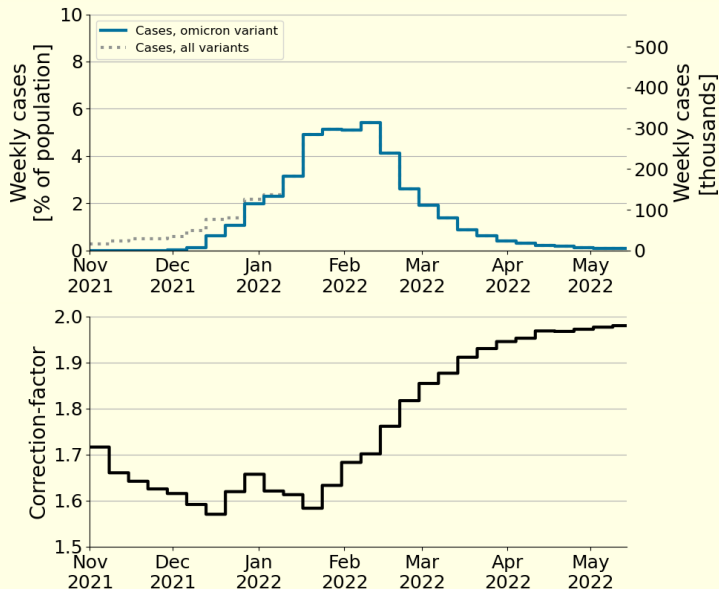
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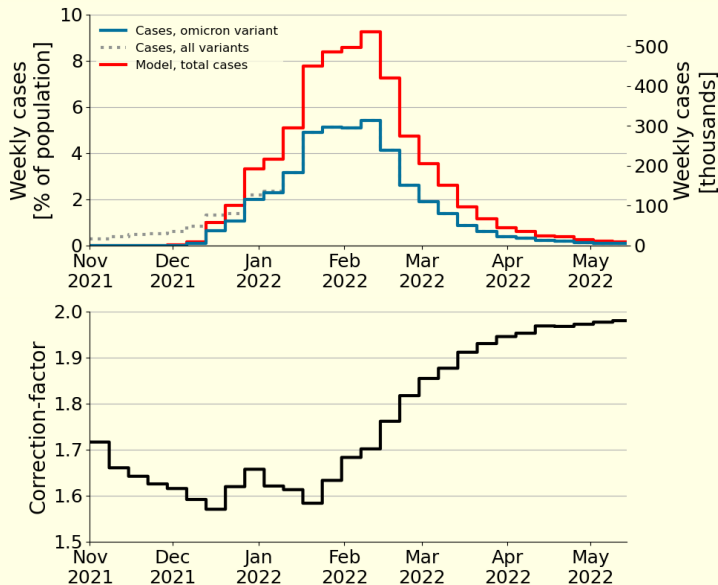
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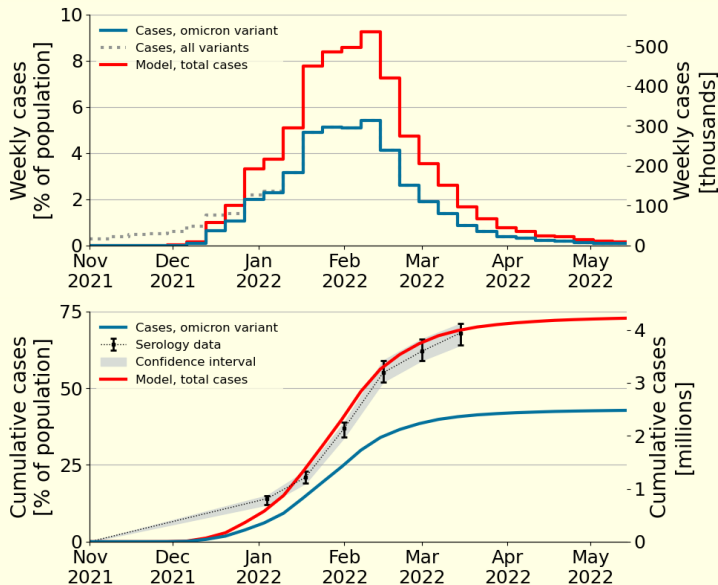
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A.3 Final Size Calculations

As $t \rightarrow \infty$, the model system approaches a steady state without any active cases. In this section, we derive an analytic expression for the value that the fraction of cases identified, $K(t)$, approaches as $t \rightarrow \infty$.

To obtain an expression for K_F , we follow the methodology previously considered by 7.

For notational purposes, we define for each variable x , the integral over the full epidemic as $T_x \equiv \int_0^\infty x dt$.

From the system of differential equations given in equations (1), we write up the following quantities:

$$\dot{S}/S = -\beta(P+A) \quad (3a)$$

$$\dot{S} + E_1 + E_2 = -(\gamma + \tau)E_2 \quad (3b)$$

$$\dot{S} + E_1 + E_2 + P = -(\gamma + \tau)P - \tau E_2 \quad (3c)$$

$$\dot{S} + E_1 + E_2 + P + A = -(\nu + \tau)A - (\gamma\rho + \tau)P - \tau E_2 \quad (3d)$$

As t approaches infinity, the stability of the systems implies that all variables apart from S , R_p and R_n are zero. We denote that final size of these variables as $S(t) \xrightarrow{t \rightarrow \infty} \sigma$, $R_p(t) \xrightarrow{t \rightarrow \infty} r_p$ and $R_n(t) \xrightarrow{t \rightarrow \infty} r_n$.

Integrating equations (3) from $t = 0$ to $t = \infty$ yields:

$$\log \sigma = -\beta(T_P - T_A) \quad (4a)$$

$$\sigma - S_0 - E_{1,0} - E_{2,0} = -(\gamma + \tau)T_{E_2} \quad (4b)$$

$$\sigma - S_0 - E_{1,0} - E_{2,0} + P_0 = -(\gamma + \tau)T_P - \tau T_{E_2} \quad (4c)$$

$$\sigma - S_0 - E_{1,0} - E_{2,0} - P_0 - A_0 = -(\nu + \tau)T_A - (\gamma\rho + \tau)T_P - \tau T_{E_2} \quad (4d)$$

Where X_0 denote the initial condition for variable X .

Furthermore, observe that the equations for R_n and R_p , equations (2) and (3) respectively, when integrated from $t = 0$ to $t = \infty$ yields:

$$r_p - R_{p,0} = \nu T_Q + \nu T_I \quad (5)$$

$$r_n - R_{n,0} = \nu T_A \quad (6)$$

In general, we consider initial conditions such that the vast majority of the population is initially susceptible, $S_0 \approx 1$, and the initial number of cases is low, $0 < E_{1,0} \ll 1$. In the limit where $S_0 \rightarrow 1$, with $E_{1,0} \rightarrow 0$, $E_{2,0} \rightarrow 0$, $P_0 \rightarrow 0$ and $A_0 \rightarrow 0$, equations (4) become:

$$\log \sigma = -\beta(T_P - T_A) \quad (7a)$$

$$\sigma = 1 - (\gamma + \tau)T_{E_2} \quad (7b)$$

$$\sigma = 1 - (\gamma + \tau)T_P - \tau T_{E_2} \quad (7c)$$

$$\sigma = 1 - (\nu + \tau)T_A - (\gamma\rho + \tau)T_P - \tau T_{E_2} \quad (7d)$$

Assuming $T_P + T_A \neq 0$, this can be written as:

$$\beta = \frac{-\log \sigma}{T_P + T_A} \quad (8a)$$

$$T_{E_2} = \frac{1}{\gamma + \tau}(1 - \sigma) \quad (8b)$$

$$T_P = \frac{1}{\gamma + \tau}(1 - \sigma - \tau T_{E_2}) \quad (8c)$$

$$T_A = \frac{1}{\nu + \tau}(1 - \sigma - (\gamma\rho + \tau)T_P - \tau T_{E_2}) \quad (8d)$$

We define $K_F = \frac{r_p}{r_p + r_n}$ and note that at steady state $\sigma = 1 - r_p - r_n$ must hold. This implies that $K_F = \frac{1}{1 - \sigma}$. Combining equations (5) with equations (5) and (6) under the assumptions $R_{p,0} = 0$ and $R_{n,0} = 0$ and simplifying yields:

$$K_F = \frac{r_p}{r_p + r_n} = \frac{r_p + r_n - r_n}{r_p + r_n} = 1 - \frac{r_n}{r_p + r_n} = 1 - \frac{r_n}{1 - \sigma} = 1 - \frac{\nu}{1 - \sigma} T_A \quad (9)$$

$$K_F = 1 - \left(\frac{\nu}{\gamma + \tau} \right) \left(1 - \frac{\sigma}{\gamma + \tau} \right) \left(1 - \frac{\gamma\rho + \tau}{\gamma + \tau} \right) \quad (10)$$

For initial conditions sufficiently close to the case where $S_0 = 1$ and all other variables are zero, K_F is an approximation of the final size of $K(t)$ as $t \rightarrow \infty$.

Note that the expression for K_F , equation (10) is independent of σ and β .

Furthermore, in the absence of tests, i.e. for $\tau = 0$, we have $K_F = 1 - (1 - \beta)(1 - \rho) = \rho$. This is expected, as only the symptomatic cases, I , are found in the situation where $\tau = 0$, and the symptomatic cases make up exactly ρ of all cases.

In the situation where all cases are symptomatic, $\rho = 1$, we obtain $K_F = 1$, that is, all cases are identified.

We note that equation (10) describes a relation between β and σ . Since T_P and T_A are described in terms of γ , τ , ρ and σ , it is possible to use equation (10) to determine a value of β that yields a particular σ .

$$\frac{R_p}{R_n + R_p} = 1 - \left(1 - \frac{\tau}{\gamma + \tau} \right) \left(1 - \frac{\gamma\rho + \tau}{\gamma + \tau} \right) \left(\frac{\nu}{\nu + \tau} \right)$$

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$$\frac{R_p}{R_n + R_p} = 1 - \left(1 - \frac{\tau}{\gamma + \tau}\right) \left(1 - \frac{\gamma\rho + \tau}{\gamma + \tau}\right) \left(\frac{\nu}{\nu + \tau}\right)$$

can be rewritten as:

$$1 - \frac{R_p}{R_n + R_p} =$$
$$\frac{R_n}{R_n + R_p} = \left(\frac{\gamma}{\gamma + \tau}\right) \left(\frac{(1 - \rho)\gamma}{\gamma + \tau}\right) \left(\frac{\nu}{\nu + \tau}\right)$$

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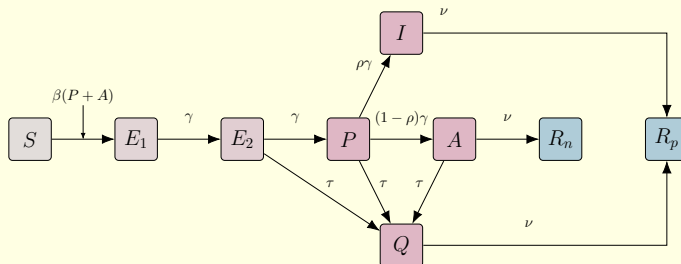
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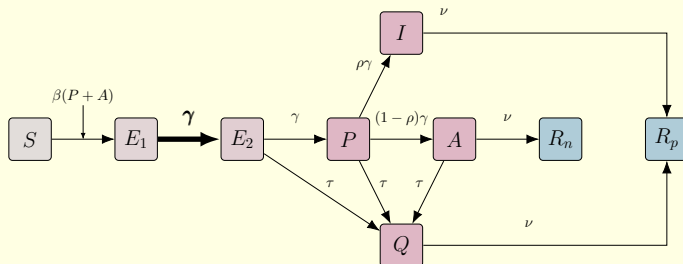
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$$\left(\frac{\gamma}{\gamma} \right)$$

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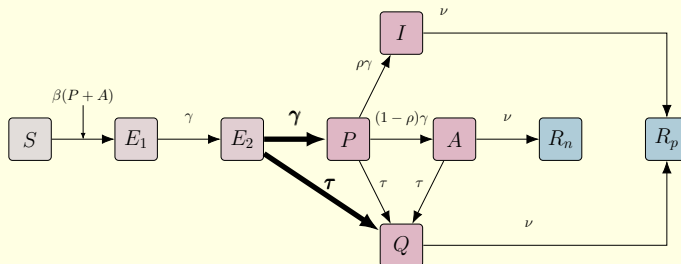
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$$\left(\frac{\gamma}{\gamma} \right) \left(\frac{\gamma}{\gamma + \tau} \right)$$

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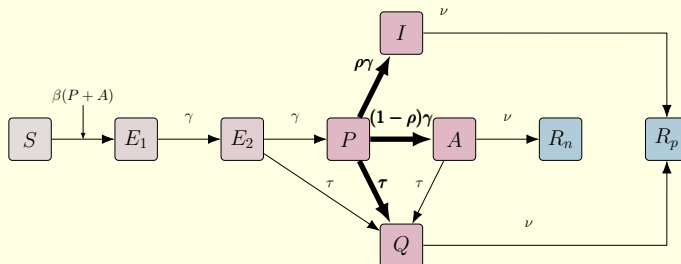
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$$\left(\frac{\gamma}{\gamma}\right) \left(\frac{\gamma}{\gamma + \tau}\right) \left(\frac{(1 - \rho)\gamma}{\gamma + \tau}\right)$$

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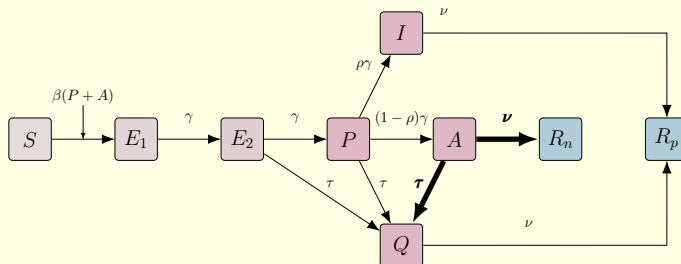
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$$\left(\frac{\gamma}{\gamma}\right) \left(\frac{\gamma}{\gamma + \tau}\right) \left(\frac{(1 - \rho)\gamma}{\gamma + \tau}\right) \left(\frac{\nu}{\nu + \tau}\right)$$

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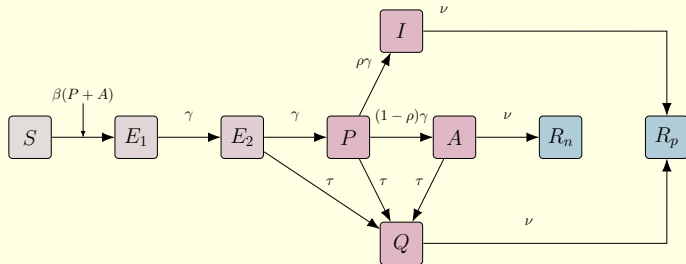
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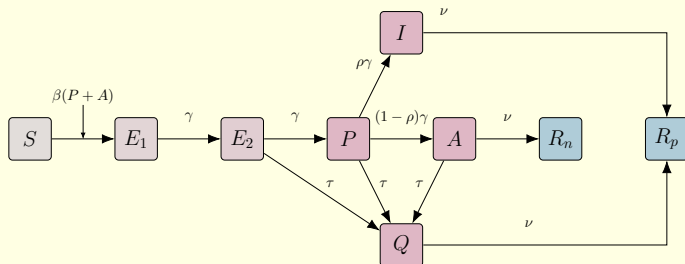


$$\frac{R_n}{R_n + R_p} = \left(\frac{\gamma}{\gamma + \tau} \right) \left(\frac{\gamma(1 - \rho)}{\gamma + \tau} \right) \left(\frac{\nu}{\nu + \tau} \right)$$

Simplified method, Matrix-form

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In the work of van den Driache and Watmough (2002), a matrix V is defined for a general family of SIR-type models, describing flows in the “infected sub-system”.

Considering sub-system $x = (E_1, E_2, P, I, A)$ and determining the matrix V , we describe inputs $\alpha = (1, 0, 0, 0, 0)$ and outputs $\omega = (0, 0, 0, 0, \nu)$, and observe that:

$$\frac{R_n}{R_n + R_p} = \omega V^{-1} \alpha^T$$

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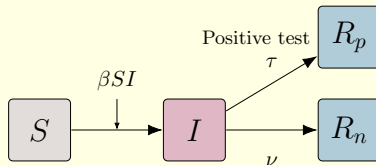
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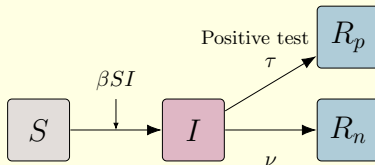
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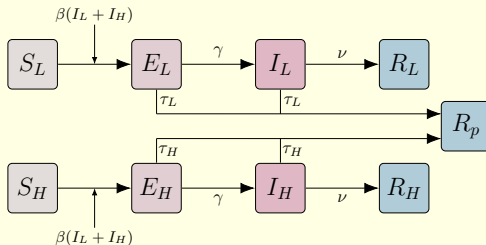
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Flow-considerations:
$$\frac{R_n}{R_n + R_p} = \frac{\nu}{\nu + \tau}$$

Extension to other models, example 2



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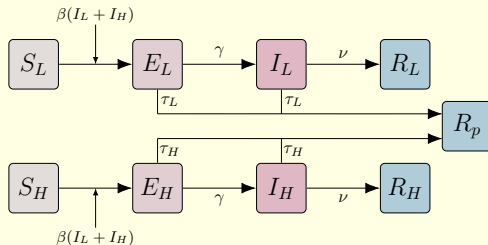
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$$x = (E_H, E_L, I_H, I_L), \quad V = \begin{pmatrix} \gamma + \tau_H & 0 & 0 & 0 \\ 0 & \gamma + \tau_L & 0 & 0 \\ \gamma & 0 & \nu + \tau_H & 0 \\ 0 & \gamma & 0 & \nu + \tau_L \end{pmatrix}$$

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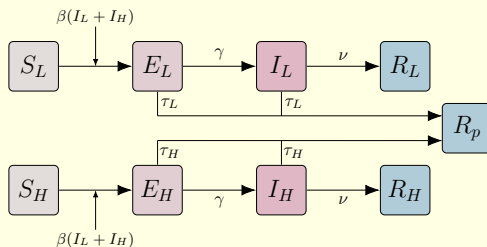
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$$\alpha = \left(\frac{S_H}{S_H + S_L}, \frac{S_L}{S_H + S_L}, 0, 0 \right) \text{ and } \omega = (0, 0, \nu, \nu)$$

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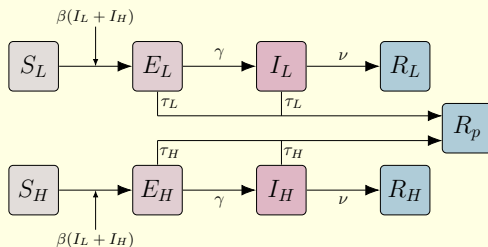
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$$x = (E_H, E_L, I_H, I_L), \quad V = \begin{pmatrix} \gamma + \tau_H & 0 & 0 & 0 \\ 0 & \gamma + \tau_L & 0 & 0 \\ \gamma & 0 & \nu + \tau_H & 0 \\ 0 & \gamma & 0 & \nu + \tau_L \end{pmatrix}$$

$$\alpha = \left(\frac{S_H}{S_H + S_L}, \frac{S_L}{S_H + S_L}, 0, 0 \right) \text{ and } \omega = (0, 0, \nu, \nu)$$

$$\text{Hence: } \omega V^{-1} \alpha^T = \frac{\nu \gamma}{S_H + S_L} \left(\frac{S_H}{(\nu + \tau_H)(\gamma + \tau_H)} + \frac{S_L}{(\nu + \tau_L)(\gamma + \tau_L)} \right)$$

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- We determine a relation between observed COVID-19 cases and total new cases, as a function of testing-rate.

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- ▶ *What I learned:* When considering the dynamic flow in SIR-type models, a number of results may follow trivially from the model-formulation...
- ▶ and that some time-consuming calculations may be replaced by a more careful description of the problem you're trying to solve.

Thank you for your attention.



Feel free to also contact me
with questions or comments

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