What is... epidemic modeling?

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29.4.2022

General modeling challenges

Reality

Model

General modeling challenges

- Real world problems are complex and every model is a simplification of reality! ("All models are wrong, but some are useful.")
- Realistic models have usually (too) many parameters, no analytical solution and high simulation effort.
- A model that is an over-simplification does not describe the problem accurately enough to be useful.

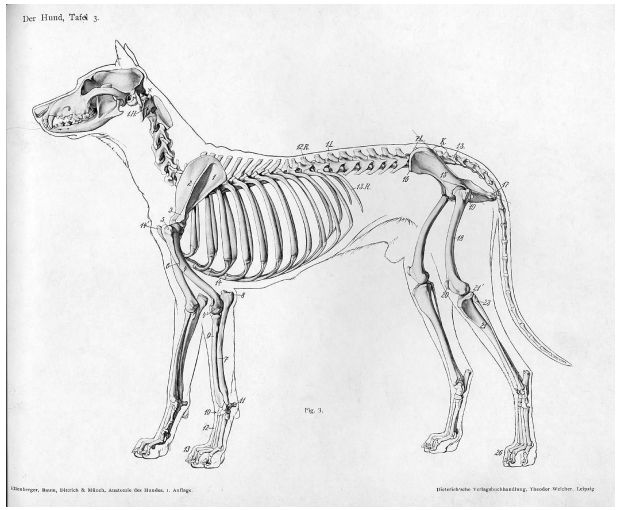


Figure: Useful model

- We want to find a compromise between the two extremes of too complicated and too simple models.
- In general it is a good strategy to first start with a simple model that captures the most important features and then expand it to make it more realistic.

Problem: epidemic spreading

- Spreading of infectious diseases is a very complex problem. Some aspects that each are already complex problems on their own are:
  - virus-host interactions on a cellular level
  - physical dynamics of transmission processes (e.g. aerosols, droplets with viral load)
  - general behavior and **mobility** of people inside societies

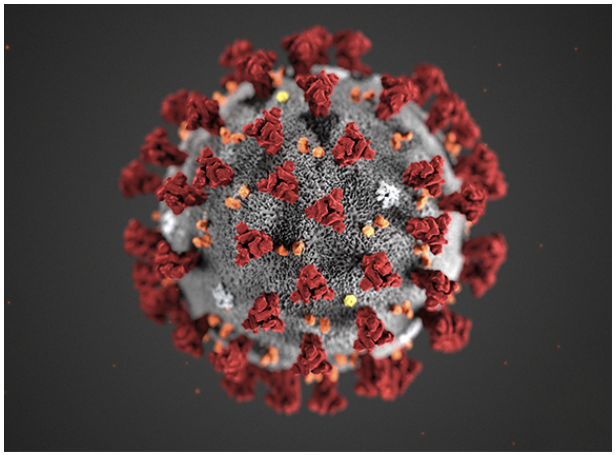


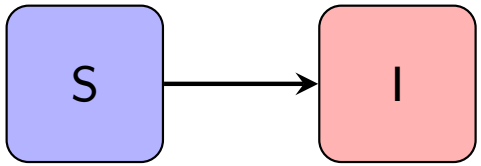
Figure: Coronavirus

- The first challenge is to find the right model scale for our problem.
  - We are interested in the epidemic spreading on the population scale and will thus make very strong simplifications for the course of the disease in individuals and transmission dynamics. Also our model for societal dynamics and mobility will be simple.
  - We start with the simplest model and then see which extensions are useful.

Compartmental models for epidemic spreading

Model assumptions:

- We assume a constant population of N individuals.
- We divide the population in different **compartments** depending on the epidemiological **status**. In the simplest version an individual can be either
  - **susceptible** to the virus
  - **infectious** and able to transmit the virus



Flow diagram of SI model

- We denote the number of susceptible individuals at time t with $S(t)$ and the number of infectious individuals with $I(t)$ and it holds that $N = S(t) + I(t)$ for all times t
- We assume that each contact between susceptible and infected individuals leads to a transmission of the virus with a constant **infection rate** $\gamma_{SI} > 0$.
- We assume a **sufficiently large** population that is **well-mixed**, such that each possible contact between susceptible and infectious individuals has the same probability.

Formulation as a jump process:

- We denote the system state by $X(t) := (S(t), I(t))$ and start in the state $X(0) = (S(0), I(0))$
- Each susceptible individual has the probability rate $\gamma_{SI} \frac{I}{N}$ for a status transition from S to I associated with the state change vector $e_{SI} := (-1, 1)$
- The evolution of the system can be written as the jump process

$$X(t) = X(0) + \mathcal{P}\left(\int_0^t \gamma_{SI} \frac{S(s)I(s)}{N} ds\right) e_{SI}$$

with $\mathcal{P}$ being a unit rate Poisson process.

- Since we assumed a sufficiently large population we can approximate the jump process with a system of ordinary differential equations.

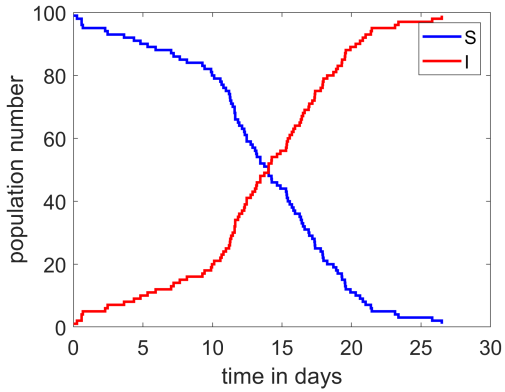


Figure: Jump SI model (low population)

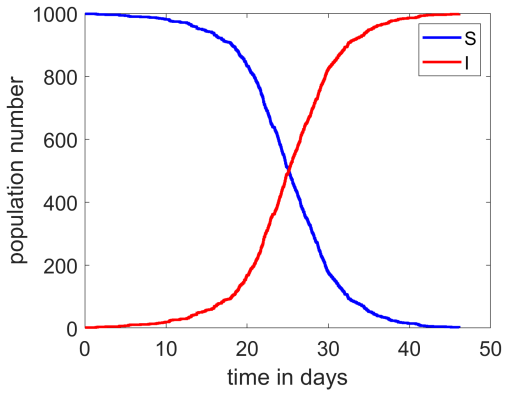


Figure: Jump SI model (high population)

Formulation as an ODE system:

- The evolution of the system is given by

$$\frac{dS(t)}{dt} = -\gamma_{SI}\frac{S(t)I(t)}{N}$$
$$\frac{dI(t)}{dt} = \gamma_{SI}\frac{S(t)I(t)}{N}$$

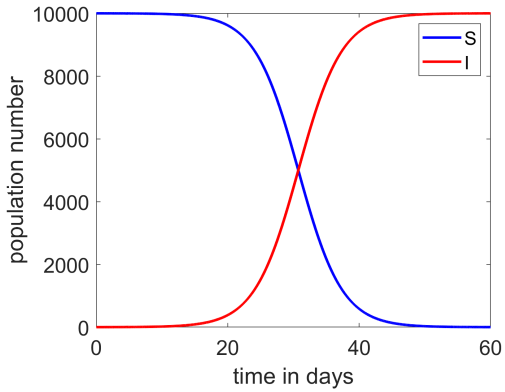


Figure: ODE SI model

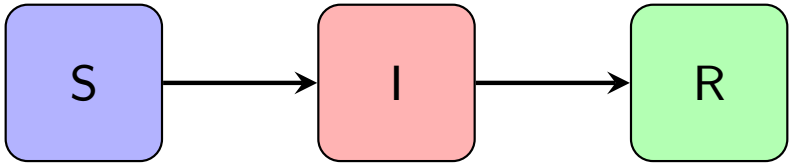
- We can substitute $S(t) = N - I(t)$ to obtain the ODE

$$\frac{dI(t)}{dt} = \frac{\gamma_{SI}}{N}I(t)(N - I(t))$$

for which an analytical solution is given by the **logistic growth** function

$$I(t) = N\left(1 + e^{-\gamma_{SI}t}\left(\frac{N}{I(0)} - 1\right)\right)^{-1}$$

Expansion to SIR model



- We introduce an additional compartment for individuals that are **removed** from the infection dynamics. This compartment refers normally mainly to *recovered* individuals but can also include e.g. quarantined or deceased individuals.
- The number of removed individuals at time t is given by $R(t)$ and the system state is expanded to $X(t) := (S(t), I(t), R(t))$.
- The status transition from S to I is as before but now associated with the vector $e_{SI} := (-1, 1, 0)$
- The status transition from I to R happens with a constant rate γ_{IR} and requires no interaction. The associated state change vector is $e_{IR} := (0, -1, 1)$.
- We distinguish between two types of status transitions (**adoptions**):
  1. *first order* adoptions that require no interaction (e.g. $I \to R$)
  2. *second order* adoptions that require pairwise interaction (e.g. $S + I \to 2I$)

Expansion to SIR model

- The evolution of the system is given by

$$\frac{dS(t)}{dt} = -\gamma_{SI}\frac{S(t)I(t)}{N}$$
$$\frac{dI(t)}{dt} = \gamma_{SI}\frac{S(t)I(t)}{N} - \gamma_{IR}I(t)$$
$$\frac{dR(t)}{dt} = \gamma_{IR}I(t)$$

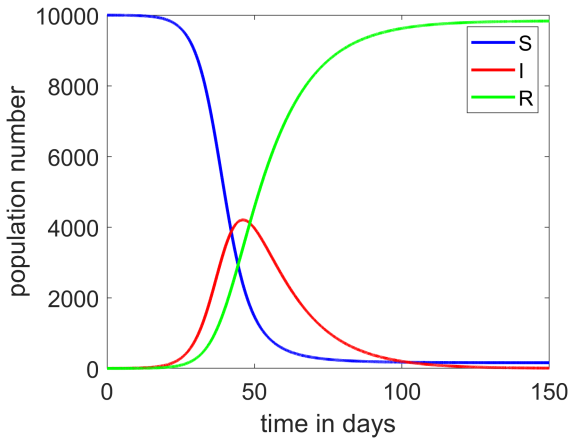
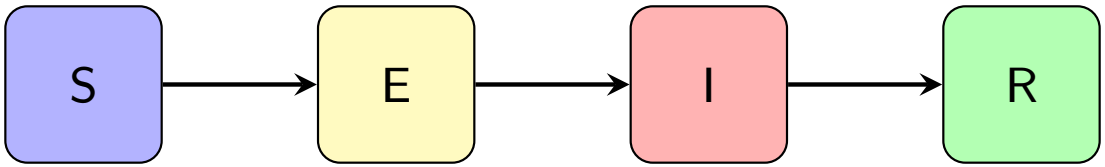


Figure: SIR model

- We cannot give an explicit solution to the system and need to solve it with numeric integration. This is also the case for further model expansions.
- The basic reproduction number is given by $R_0 := \frac{\gamma_{SI}}{\gamma_{IR}}$. We only have an outbreak of the disease if $R_0 S(0) > N$
- Instead of only two steady states in the SI model now an infinite number of steady states, i.e. any system state with 0 infected individuals.

Expansion to SEIR



- We introduce an additional compartment for individuals that have been **exposed** to the virus but are not yet infectious. The number of removed individuals at time t is given by $E(t)$ and the system state is expanded to $X(t) := (S(t), E(t), I(t), R(t))$.
- We have a second order adoption $S + I \to E + I$ for transitions from S to E with infection rate γ_{SE} and state change vector $e_{SE} := (-1, 1, 0, 0)$
- We have two first order adoptions:
  1. $E \to I$ with **manifestation** rate γ_{EI} and state change vector
  $$e_{EI} := (0, -1, 1, 0)$$
  2. $I \to R$ with removal rate γ_{IR} and state change vector
  $$e_{IR} := (0, 0, -1, 1)$$

Expansion to SEIR

- The evolution of the system is given by

$$\frac{dS(t)}{dt} = -\gamma_{SE}\frac{S(t)I(t)}{N}$$
$$\frac{dE(t)}{dt} = \gamma_{SE}\frac{S(t)I(t)}{N} - \gamma_{EI}E(t)$$
$$\frac{dI(t)}{dt} = \gamma_{EI}E(t) - \gamma_{IR}I(t)$$
$$\frac{dR(t)}{dt} = \gamma_{IR}I(t)$$

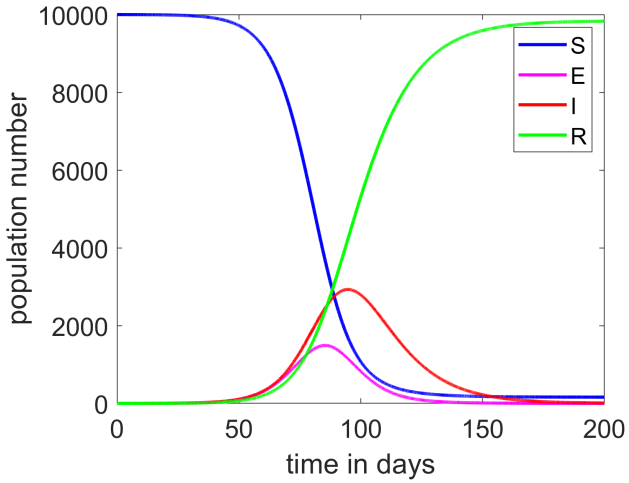


Figure: SEIR model

- As an alternative to an E compartment there exist also SIR models with delay differential equations to model an incubation period.
- Depending on the exact definition of E and I compartments there are also SEIR models with transmissions between S-E contacts.

SEIR Model parameters

Infection rate

- The infection rate captures the transmission probability for each contact as well as the frequency of contacts within the population.
- Measures that reduce the transmission probability (e.g. wearing masks) and measures that reduce the amount of contacts (e.g. lockdown) both can be realized by lowering the infection rate of the model.

Manifestation rate

- The manifestation rate is an intrinsic property of the virus.

Removal rate

- The removal rate captures all events that lead to a removal from the infection dynamics most prominently recovery from the disease.
- Examples for measures that can be modeled with an increased removal rate are contact tracing, quarantine, isolation etc.

Further model expansions

Expansions within compartmental ODE models:

- Additional compartments:
  - D: **deceased** individuals
  - V: **vaccinated** individuals
  - Q: **quarantined** individuals
- Loss of immunity after some time (SIS,SIRS, SEIRS etc.)
- Time dependent rates, e.g. for modeling seasonality or measures

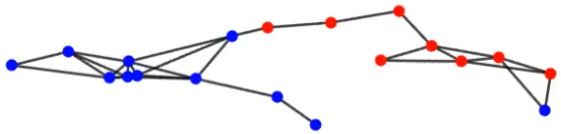
Expansions to other model types:

- Compartmental ODE models are on the macroscopic scale.
- The well-mixed population assumption is a strong simplification of mobility and social interactions. For many research questions we want to consider a finer (spatial) resolution.
- **Microscale**: **agent-based** models (ABM), **network** models
- **Mesoscale**: **metapopulation** models

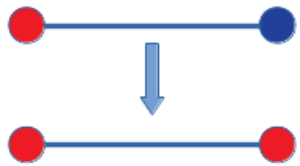
Epidemic network models

- We consider a set of n nodes $\mathcal{N}$ that represent individuals and an edge set $\mathcal{E}$ encoding contacts between the individuals.
- Each node is assigned an epidemic status as and the compartments refer to sets of nodes. The system state is a vector $X(t)$ of length n with entry $X^{(k)}(t)$ referring to the status of node k at time t.
- For each node k and each status transition $i \to j$ we have a state change vector $e_{ij}^{(k)}$.

Contact network



Transmission along an edge



  - We define the adjacency matrix $A_{SI}(X)$ for S-I contacts of system state X with entries

$$A_{SI}^{(ij)}(X) := \begin{cases} 1, & \text{if } i \in S, j \in I, (i,j) \in \mathcal{E} \\ 0 & \text{else} \end{cases}$$

Jump process for SEIR network model

- We define adoption rate functions for each possible event:
  - $f_{SE}^{(k)}(X) := \gamma_{SE} \sum_{l=1}^{N} A_{SI}^{(kl)}(X)$
  - $f_{EI}^{(k)}(X) := \begin{cases} \gamma_{EI}, & \text{if } k \in E \\ 0 & \text{else} \end{cases}$
  - $f_{IR}^{(k)}(X) := \begin{cases} \gamma_{IR}, & \text{if } k \in I \\ 0 & \text{else} \end{cases}$
- The development of the system is given by the jump process

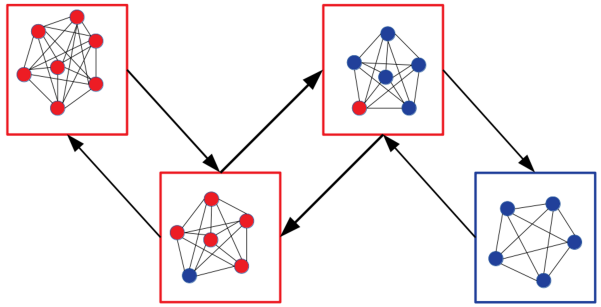
$$\begin{aligned} X(t) = X(0) + \sum_{k=1}^{N} & \mathcal{P}_1^{(k)} \left(\int_0^t f_{SE}^{(k)}(X(s))ds \right) e_{SE}^{(k)} \\ & + \mathcal{P}_2^{(k)} \left(\int_0^t f_{EI}^{(k)}(X(s))ds \right) e_{EI}^{(k)} \\ & + \mathcal{P}_3^{(k)} \left(\int_0^t f_{IR}^{(k)}(X(s))ds \right) e_{IR}^{(k)} \end{aligned}$$

with $\mathcal{P}_i^{(k)}, i = 1, ..., 3$ being independent unit rate Poisson processes.

Metapopulation models

- We consider a network of m subpopulations with $N^{(1)}, ..., N^{(m)}$ members.
- For each subpopulation k we define c compartments $N_1^{(k)}, ..., N_c^{(k)}$, one for each possible status.
- The system state is encoded by the population matrix N

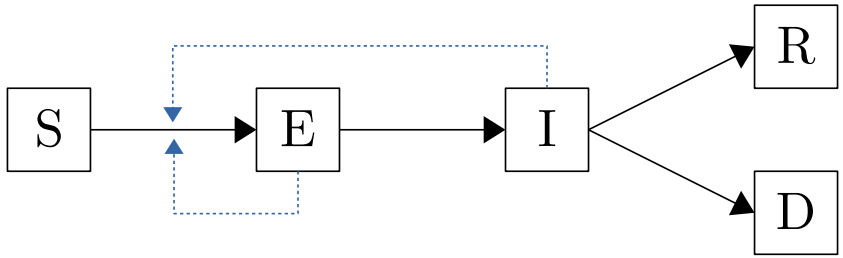
Network of subpopulations



  - We consider two general types of possible events:
    1. **adoption** events from status i to status j within a subpopulation k associated with the state change $E_j^{(k)} - E_i^{(k)}$ and the rate $\gamma_{ij}^{(k)}$
    2. **transition** events from subpopulation k to subpopulation l involving an individual of status i associated with the state change $E_i^{(l)} - E_i^{(k)}$ and the rate λ_i^{kl}
  - We model the adoption dynamics within subpopulations deterministically and the transitions between subpopulations with jumps. Such a process is called piecewise-deterministic Markov process (PDMP).

PDMP metapopulation example

Flow diagram of the infection dynamics within subpopulations



- We consider five compartments (S,E,I,R,D) and assume that transmissions between exposed and susceptible individuals are possible.
- The internal dynamics are given by the ODE system

$$
\begin{aligned}
\frac{d}{dt}\boldsymbol{N}_S^{(k)} &= -\left(\gamma_{SE}^{(k)}\boldsymbol{N}_E^{(k)} + \gamma_{SI}^{(k)}\boldsymbol{N}_I^{(k)}\right)\boldsymbol{N}_S^{(k)} \\
\frac{d}{dt}\boldsymbol{N}_E^{(k)} &= \left(\gamma_{SE}^{(k)}\boldsymbol{N}_E^{(k)} + \gamma_{SI}^{(k)}\boldsymbol{N}_I^{(k)}\right)\boldsymbol{N}_S^{(k)} - \gamma_{EI}^{(k)}\boldsymbol{N}_E^{(k)} \\
\frac{d}{dt}\boldsymbol{N}_I^{(k)} &= \gamma_{EI}^{(k)}\boldsymbol{N}_E^{(k)} - \left(\gamma_{IR}^{(k)} + \gamma_{ID}^{(k)}\right)\boldsymbol{N}_I^{(k)} \\
\frac{d}{dt}\boldsymbol{N}_R^{(k)} &= \gamma_{IR}^{(k)}\boldsymbol{N}_I^{(k)} \\
\frac{d}{dt}\boldsymbol{N}_D^{(k)} &= \gamma_{ID}^{(k)}\boldsymbol{N}_I^{(k)}
\end{aligned}
$$

PDMP metapopulation example

- The jump process for the transitions between subpopulations is given by

$$\sum_{k,l=1,k\neq l}^{m} \sum_{i=1}^{n_s} \mathcal{P}_i^{(kl)} \left(\int_0^t \lambda_i^{(kl)} \boldsymbol{N}_i^{(k)}(s) ds \right) (E_i^{(l)} - E_i^{(k)})$$

- The PDMP for the combined development is given by the sum of the jump process for transitions and the solution of the ODE system for adoptions.
- Instead of physical transitions between subpopulations one can alternatively define adoption rate functions for rare in-between interactions. This is more fitting if the subpopulations are not defined in a spatial but rather in a social sense (e.g. different age groups).

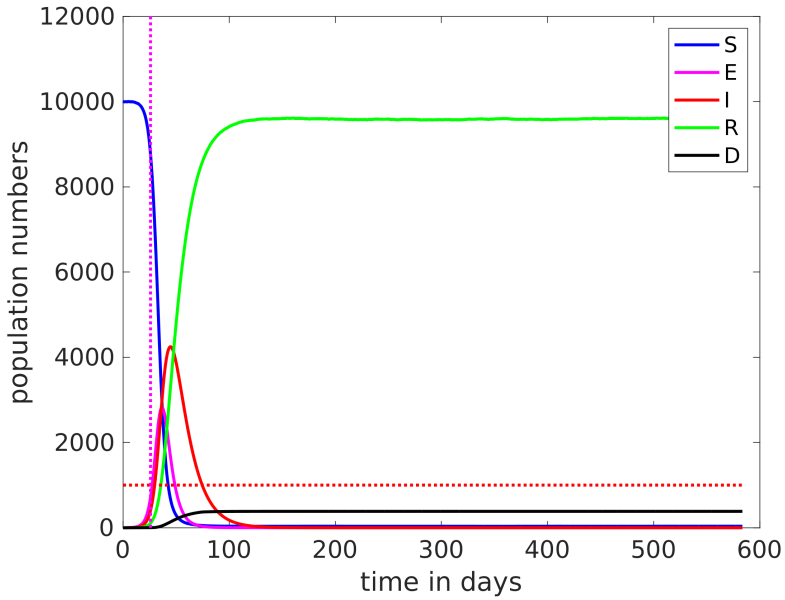
PDMP metapopulation simulation example

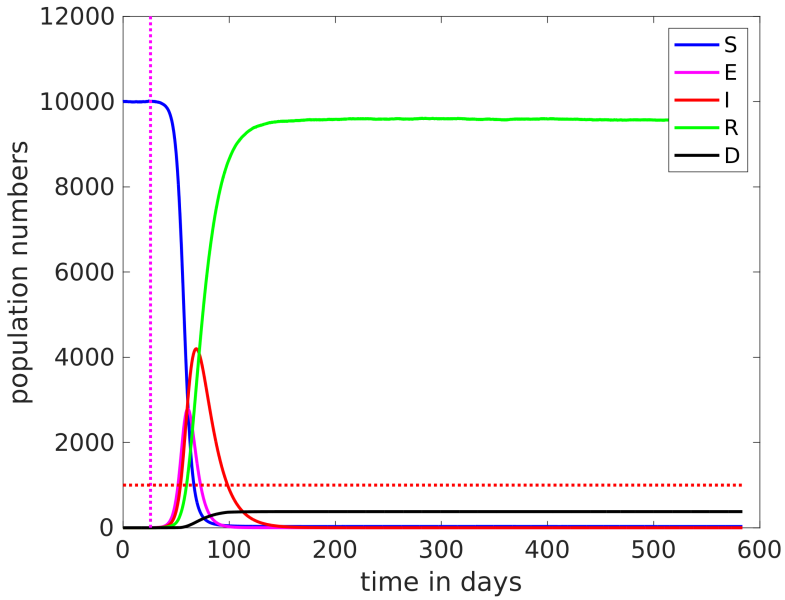
:

- For the following simulation example we consider two subpopulations whith the disease starting in subpopulation 1.
- We consider changing infection rates to model a phase of strict and a phase of moderate internal measures once the number of infected individuals is above a threshold.
- We consider changing transition rates to model travel restrictions between the subpopulations.
- We consider an increased death rate if the number of infections is higher than a threshold for the capacity of the health care system.
- We have chosen 3 simulation scenarios:
  1. No measures
  2. Only internal measures
  3. Internal measures and travel restrictions

PDMP metapopulation simulation example

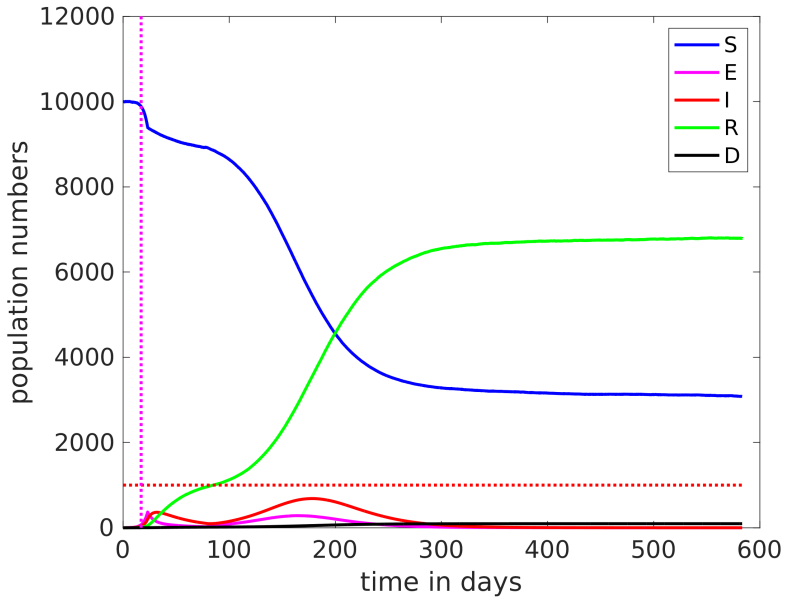
Example simulation for Scenario 1

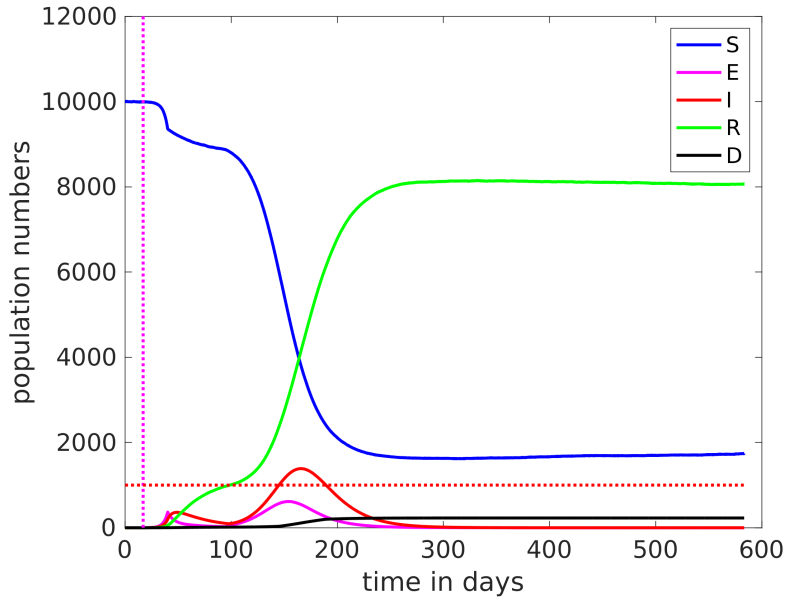




PDMP metapopulation simulation example

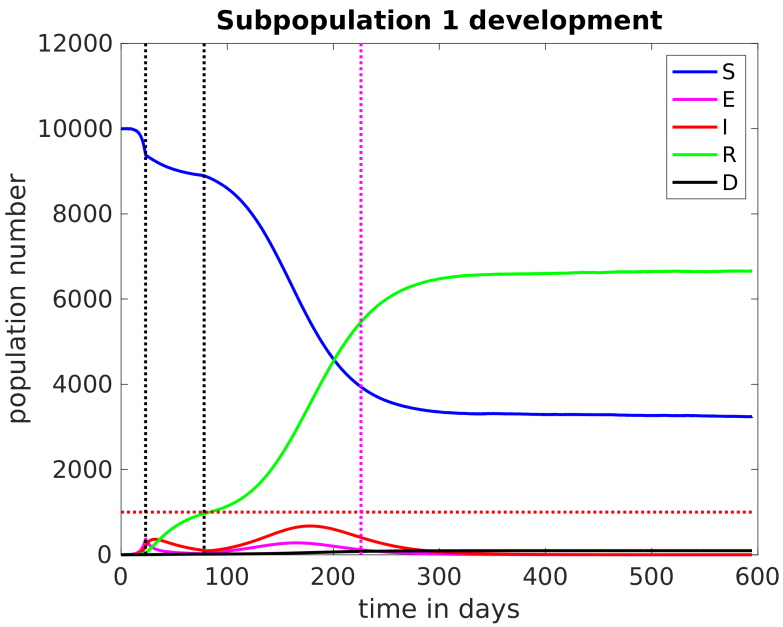
Example simulation for Scenario 2

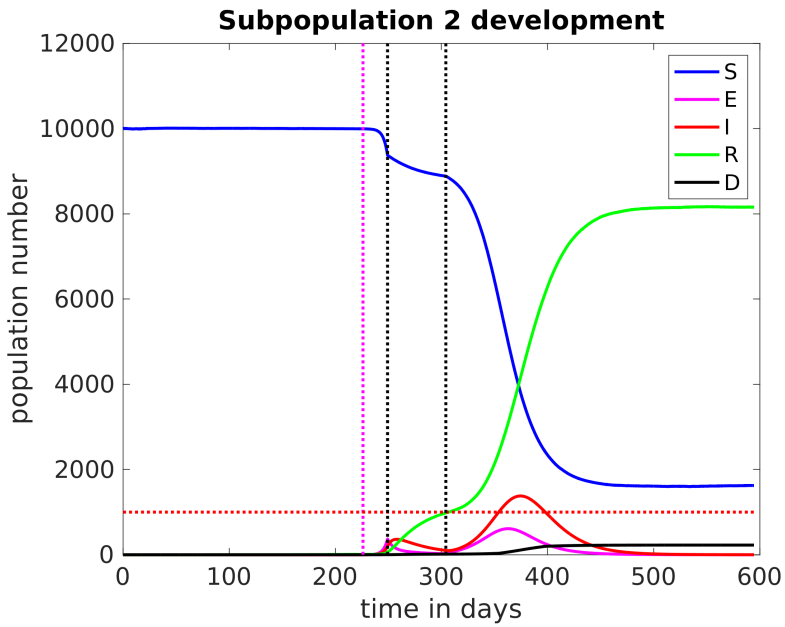




PDMP metapopulation simulation example

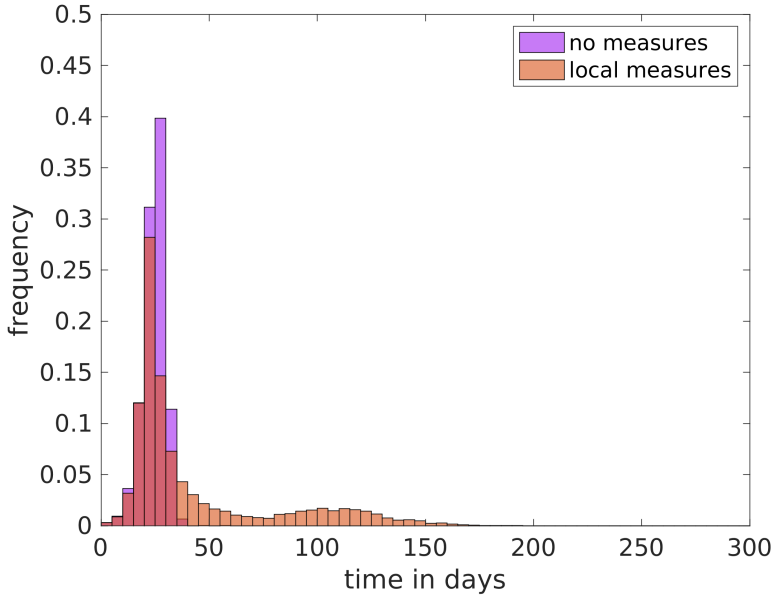
Example simulation for Scenario 3

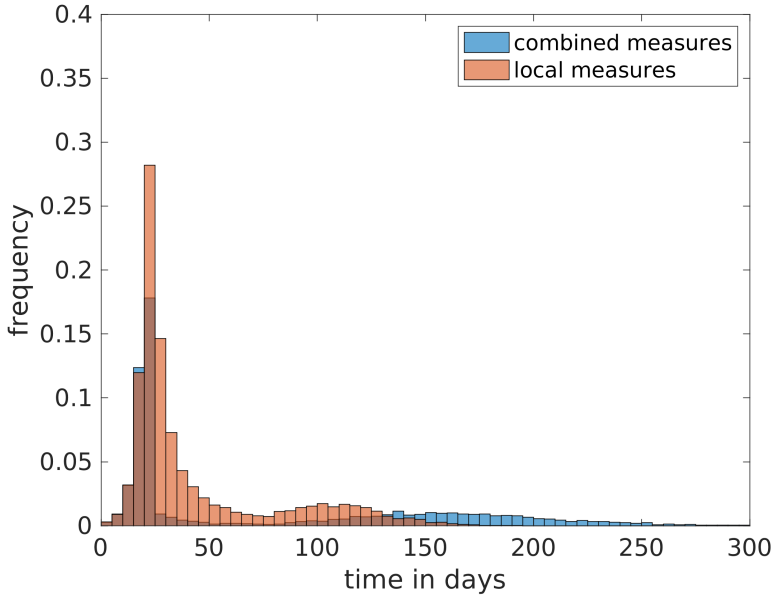




PDMP metapopulation simulation example

First infection time distribution for subpopulation 2





Agent-based models

- Microscale model on individual level
- Possibility for realistic data-based mobility model combined with spreading dynamics
- Dynamics are given by a jump process for discrete or a jump diffusion process for continuous movements
- Most detailed but also computationally expensive model type
- Challenge: calibration/estimation of model parameters

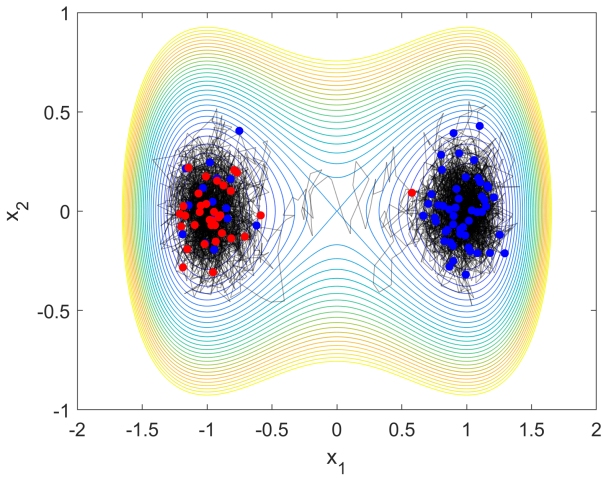
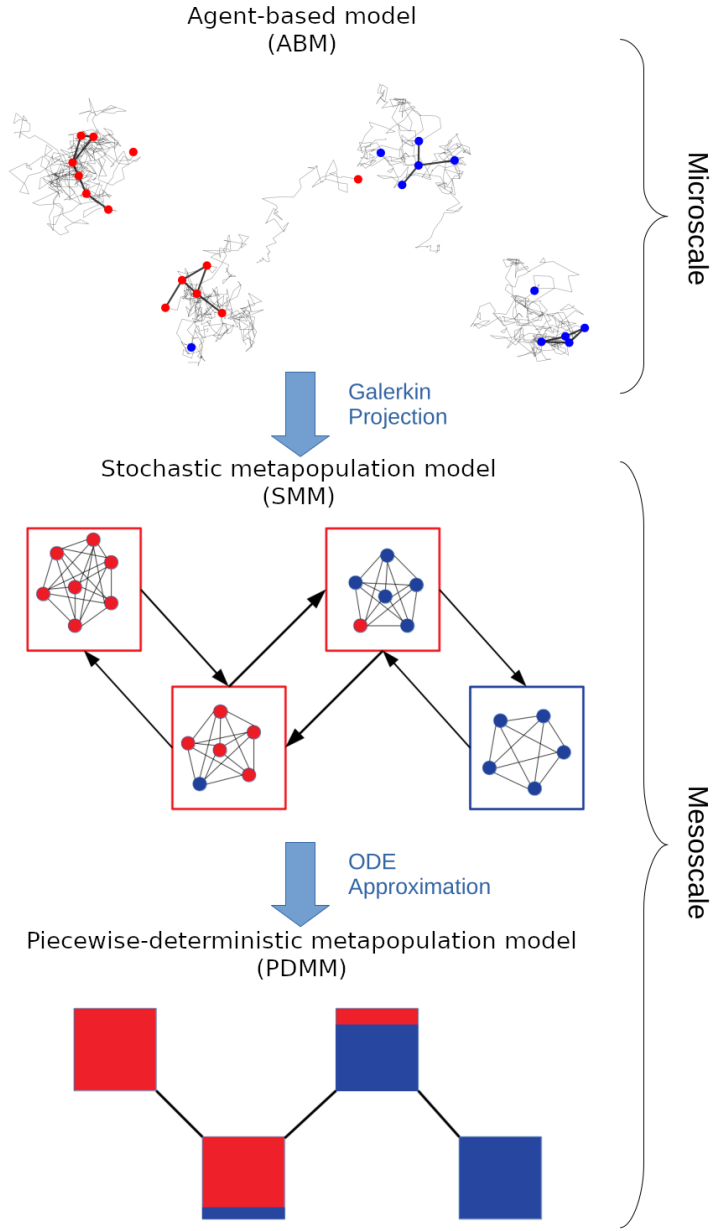


Figure: Snapshot of an ABM simulation

Further information (and shameless advertising)

Epidemic modeling papers of the computational humanities group (ZIB):

- Winkelmann, S., Zonker, J., Schütte, C., and Conrad, N. D. (2021). Mathematical modeling of spatio-temporal population dynamics and application to epidemic spreading. *Mathematical biosciences, 336, 108619.*
- Wulkow, H., Conrad, T. O., Djurdjevac Conrad, N., Müller, S. A., Nagel, K., and Schütte, C. (2021). Prediction of Covid-19 spreading and optimal coordination of counter-measures: From microscopic to macroscopic models to Pareto fronts. *Plos one, 16(4), e0249676.*



Final Slide

Thank you for your attention!