AN OVERVIEW ON MOBILITY-AWARE MODELS FOR INFECTIOUS DISEASE DYNAMICS

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Outline

- Introduction
- Mathematical modeling process
- From simple ODE-SIR to Hybrid-Graph-ODE
- Why should we care about mobility and spatial resoltion?
- Numerical assessment of the NoCovid strategy
- Generalizations by Integro-differential equations
- Agent-based models
- Hybrid epidemiological models
- Digression: Data Science

Introduction

Some recent epi- and pandemics

- 2019: SARS-CoV-2 (2020-2021: 14.9m excess deaths; 336.8 million years of life lost[1])
- 2012: MERS-CoV (≈1k deaths[2])
- 2009: Influenza A (150-575k deaths[2])
- 2002: SARS-CoV (≈1k deaths[2])
- 1968: Influenza A (≈1m deaths[2])

[1] WHO World Health Statistics 2023, [2] Abdelrahman et al., Front. Immunol. (2021).

IPBES Workshop Report on Biodiversity and Pandemics

Daszak et al. (2020), doi:10.5281/zenodo.4147317

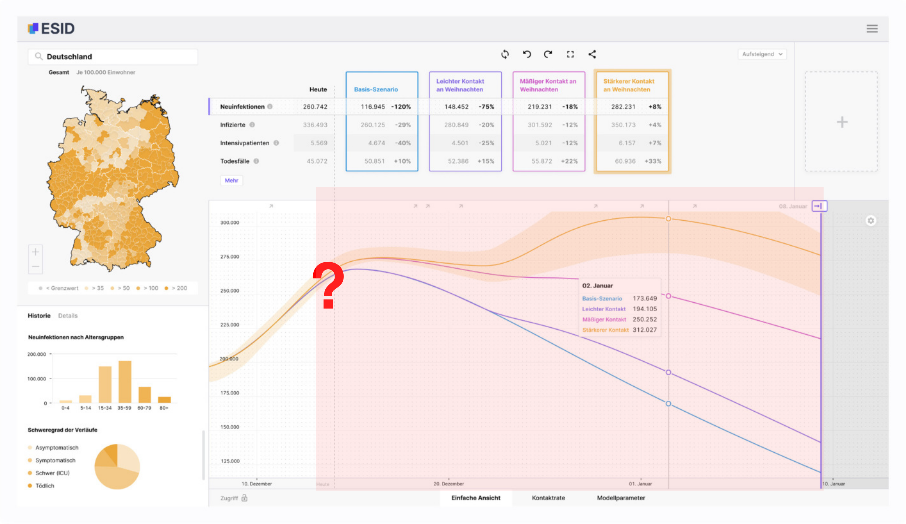
- “Without predictive and preventative strategies, pandemics will emerge more often, spread more rapidly, kill more people [...] with more devastating impact than ever”
- Estimation: More than 600 000 “undiscovered viruses” in “mammal and avian hosts [...] could have the ability to infect humans”
- The costs for prevention of pandemics are “trivial in comparison to the trillions of dollars of impact due to COVID-19, let alone the rising tide of future diseases.”
- “Reducing pandemic risks [...] would cost 1-2 orders of magnitude less than estimates of the economic damages caused by global pandemics”

Motivation for infectious disease research

- Epidemics and pandemics are **no** “once in every 100 years” event
- The frequency of epidemics and pandemics could increase
- Endemic infectious diseases can still cause a large number of deaths and people suffering from the disease (with or without dying from it)
  - HIV, Malaria, and Tuberculosis account for 9k deaths eachs day[3]

[3] Brauer, Castillo-Chavez, Feng (2019)

Motivation for infectious disease modeling

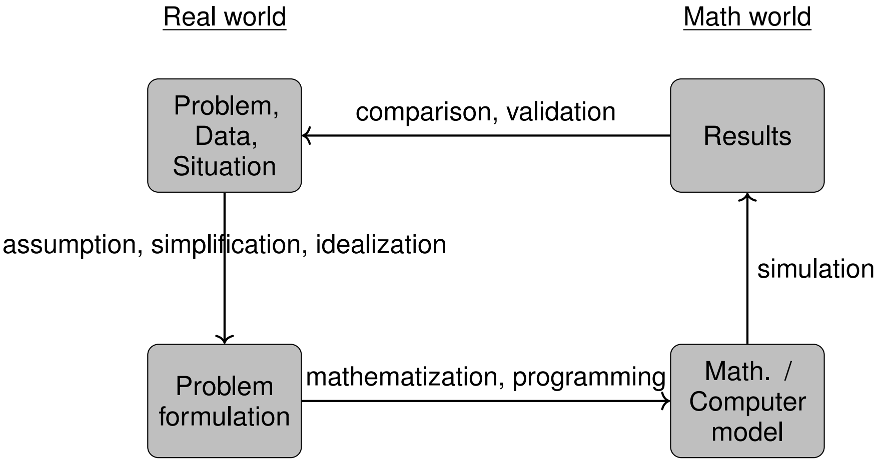


Infectious disease dynamics: Approaches

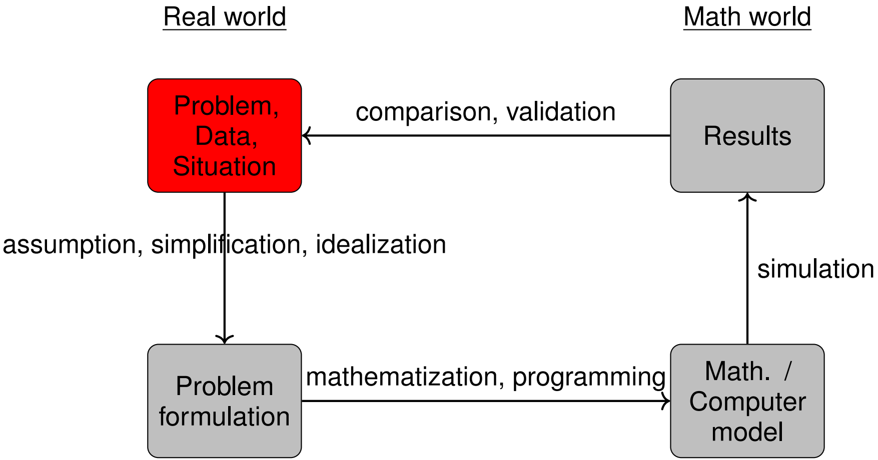
- Real life experiments not feasible
- Knowledge from other situations might be difficult to transfer directly
- Theoretical or mathematical models can help to gain insight
- Use of modern computers allows to consider detailed models and a lot of scenarios, e.g.,
  - home-office ratio of 10 %,
  - vs home-office ratio of 30 %,
  - closure of X,
  - vs closure of Y,
  - ...

The mathematical modeling process on an example

Schematic view of mathematical modeling process



Schematic view of modeling process: Problem, Data, Situation



Examples of Problem, Data, Situation

Sars-CoV-2 in Europe in beginning of 2020:

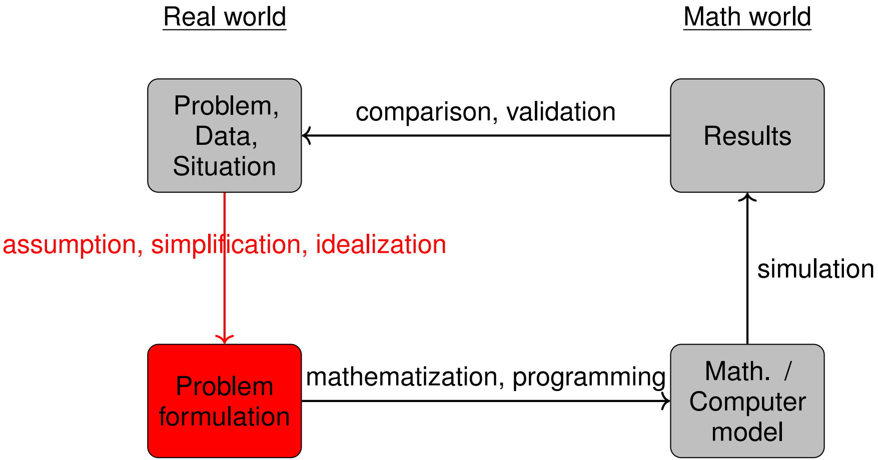
- A new pathogen appeared on scene

- Some confirmed cases in some regions

ID_County	County	Gender	Date	Confirmed	Deaths	Recovered
1001	SK Flensburg	female	2020-01-13	1	0	1
			2020-03-10	1	0	1
			2020-03-11	1	0	1
			2020-03-12	1	0	1
			2020-03-14	2	0	2
			2020-03-15	1	0	1
			2020-03-17	2	0	2
			2020-03-19	1	0	1
			2020-03-20	1	0	1
			2020-03-21	1	0	1
			2020-03-22	1	0	1
			2020-03-26	2	0	2
			2020-03-31	1	0	1
			2020-05-17	1	0	1
			2020-05-21	3	0	3
			2020-05-22	1	0	1
			2020-05-28	1	0	1
			2020-06-04	1	0	1
			2020-06-06	1	0	1

- Some knowledge about the transmission as they appeared

Schematic view of modeling process: Problem formulation



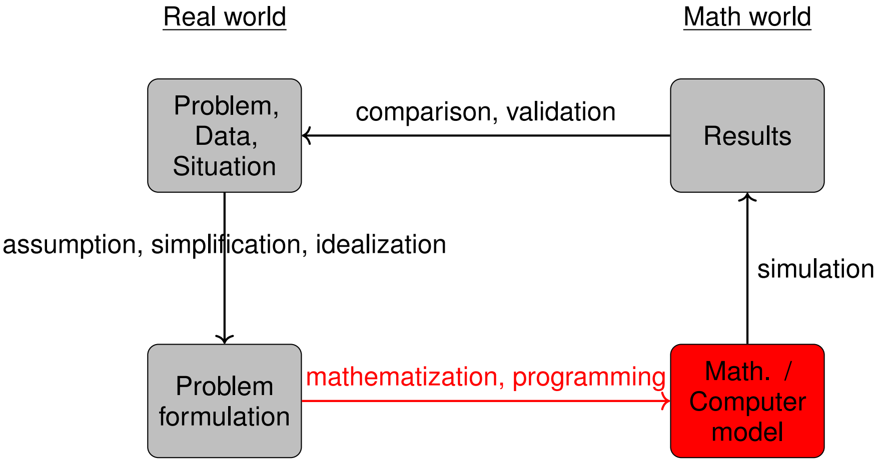
Problem formulation and examples of assumption and simplification

- A "contact" leads to transmission with some probability ρ
  $\rightarrow$ Needs a definition (simple physical, exposure through air, sexual, waterborne, ...)

- all people are equally susceptible
  $\rightarrow$ neglect that (cross-)immunity could reduce risk

- ...

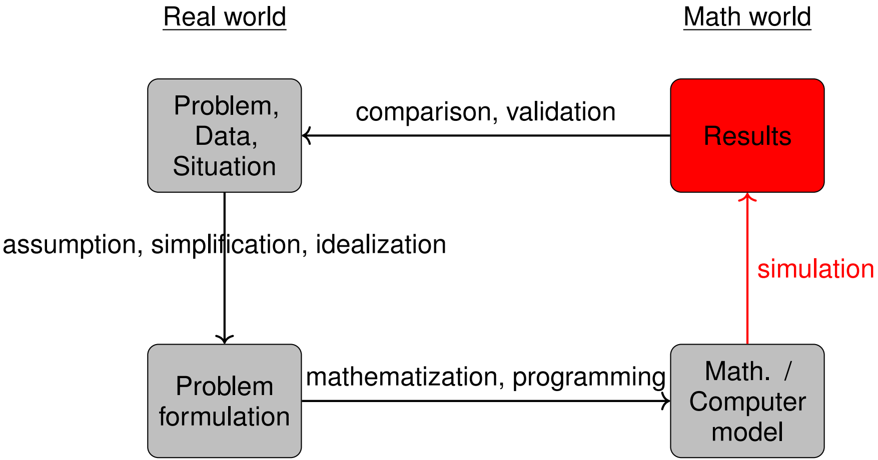
Schematic view of modeling process: Math. / Computer model



Mathematical model and examples of mathematization, programming

- A person is described as an *agent*
  - It has features such as age or infection state
  - We can set and ask if the person is in quarantine
  - ...
- For every infection state, we need to estimate the time a person is in this state and translate this into a parameter
- Let $X \sim \mathcal{U}[0,1]$ be uniformly distributed. For every contact of a person P with an infected person, we draw a sample x_i from X. If $x_i \leq \rho$, the virus gets transmitted.
- ...

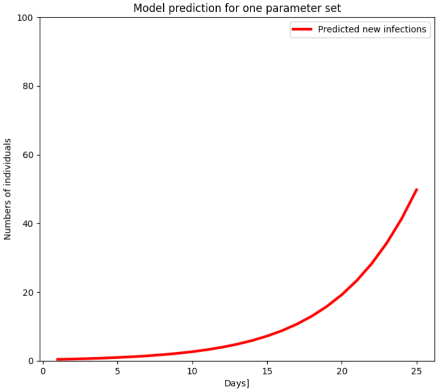
Schematic view of mathematical modeling process: Results

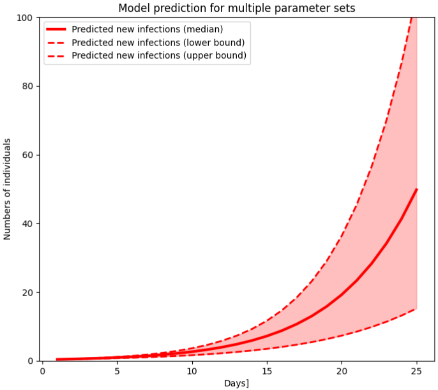


Results and examples of simulation

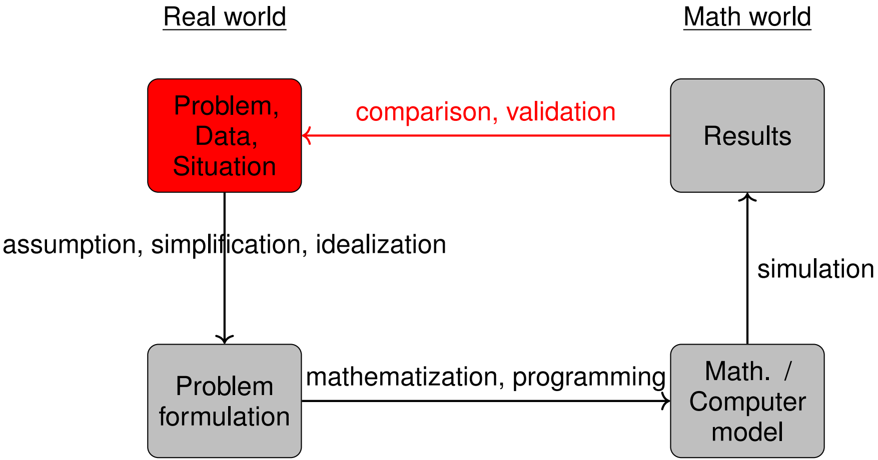
- Given a set of parameters, one can compute the outcome of the model
- Outcomes are often computed as approximations using a computer and not by an analytical solution (which may be difficult or impossible to obtain)
- Input parameters are uncertain and uncertainty in the input leads to uncertainty in the output (although often with different quantification)
- Simulations with multiple sets of parameters can assess uncertainty in the prediction

Results and examples of simulation



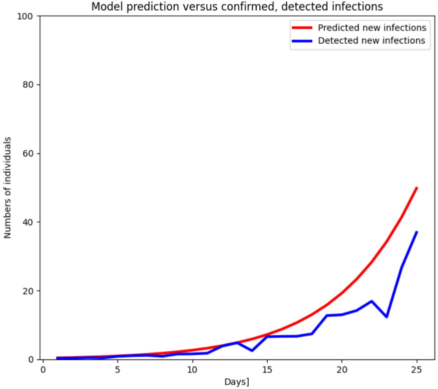


Schematic view of mathematical modeling process: Validation

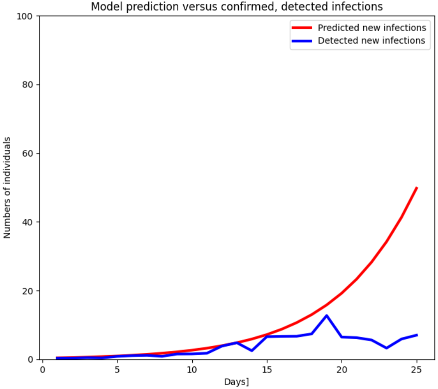


Examples of comparison, validation

Scenario A:



Scenario B:



Examples of comparison, validation

- Problems of underdetection, delayed reporting, week-end effects etc. in real data
- Changed real world behavior has to be reflected in model runs
- ...

$\rightarrow$ start anew and adapt simplifications, assumptions, model, parameters, ...

From simple ODE-SIR to Hybrid-Graph-ODE

A simple ODE-SIR model

- S (*Susceptible*): Persons that are susceptible to get the virus if they ”get in contact”
- I (*Infected (Infectious)*): Persons that have the virus and can transmit it to susceptibles
- R (*Removed*): Persons that had the virus and cannot infect again
- ϕ (contact rate): the number of contacts per day
- ρ: the transmission risk when ”having a contact“ with an infectious person
- T_I: The time a person is on average in infected state

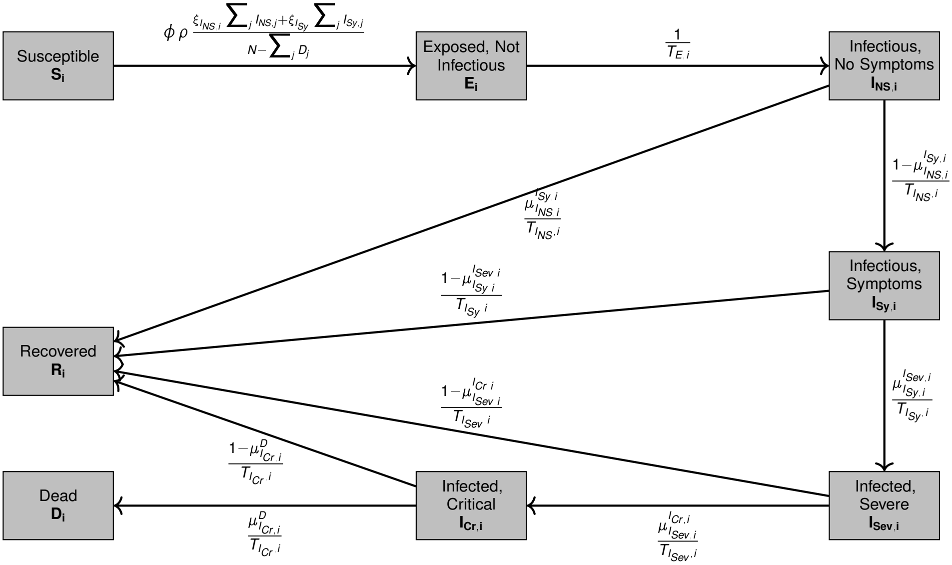
A simple ODE-SIR model

- We consider the deterministic system

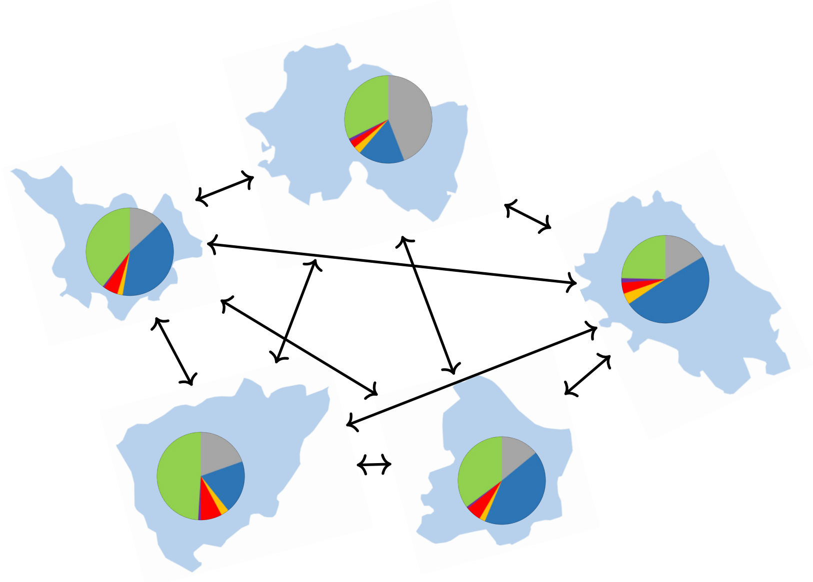
$$
\begin{aligned}
S'(t) &= -\rho\phi\frac{I(t)}{N}S(t),\\
I'(t) &= \rho\phi\frac{I(t)}{N}S(t) - \frac{1}{T_I}I(t),\\
R'(t) &= \frac{1}{T_I}I(t).
\end{aligned}
\tag{1}
$$

- We present the system (1) by the following flow chart:

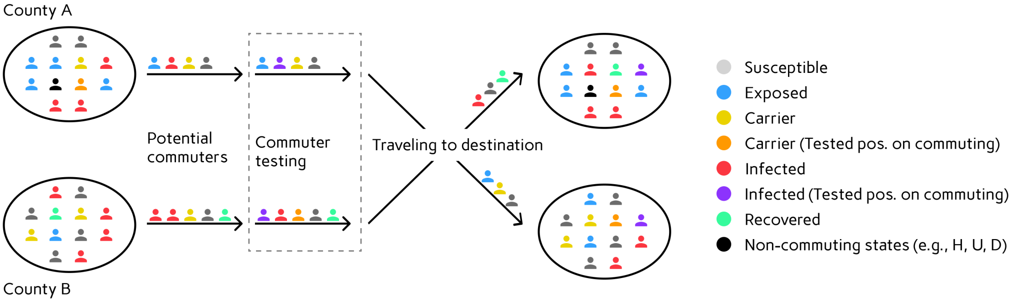
An age-resolved ODE-SECIR-type model



Spatial resolution for EBMs: Hybrid Graph-ODE model



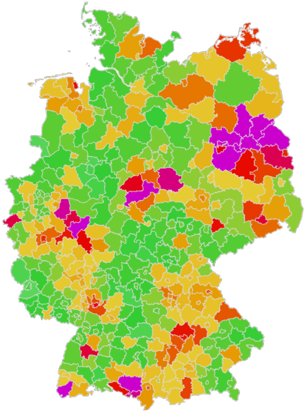
Commuter testing in hybrid graph-ODE model



Why should we care about spatial resolution?

Why should we care about spatial resolution?

What the situation is:

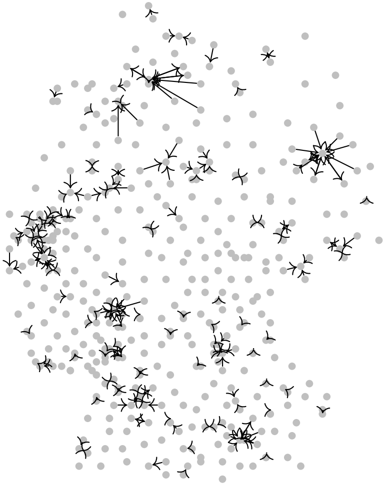


What a simple Germany-SIR model sees:

Why should we care about mobility?

Why should we care about mobility?

Official home and work locations: Connections of more than 10k persons



Source: Federal Agency of Work, 2020.

“In the end, it will arrive anyway...”

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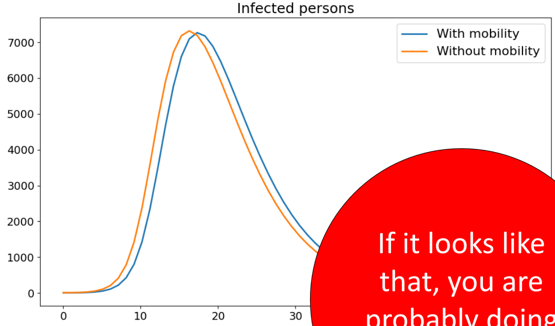
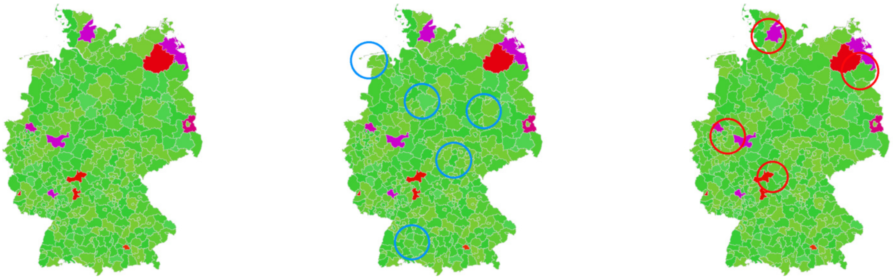


If it looks like that, you are probably doing it wrong...

Well... This is the curve, only unity directly...

Limited ressources is an argument, not an obstacle

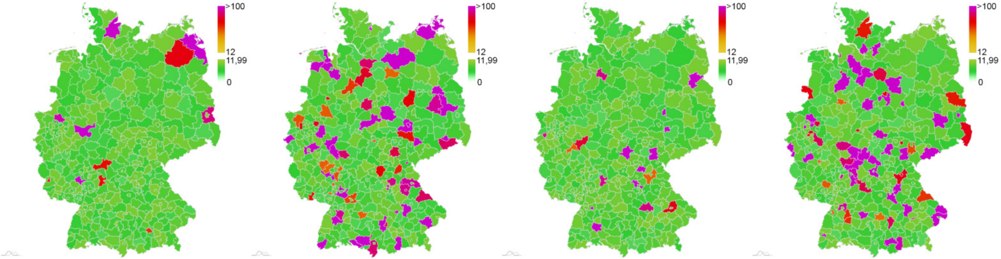


- Ressources are always limited
- Preparation is better than reaction
- Swift reaction can save lives

Numerical assessment of the NoCovid strategy

Numerical assessment of the NoCovid strategy

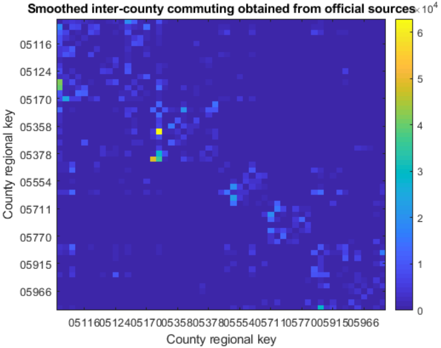
- NoCovid $\neq$ ZeroCovid, NoCovid $\neq$ Chinese strategy
- NoCovid: “Controlling the Covid-19 pandemic through Green Zones”

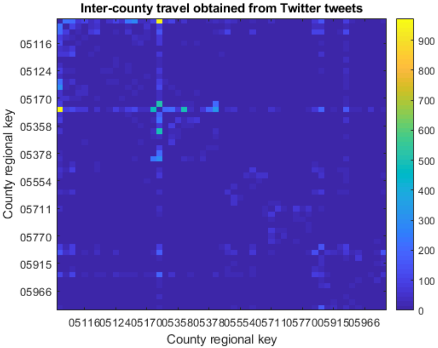


Four different initial scenarios. Random initial incidence (weekly cases per 100 000 individuals) of 75-150 for 2-20% of the counties and incidence below 10 otherwise (top).

Inter-regional contacts: Official sources and social network

E.g., North Rhine-Westfalia:



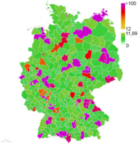


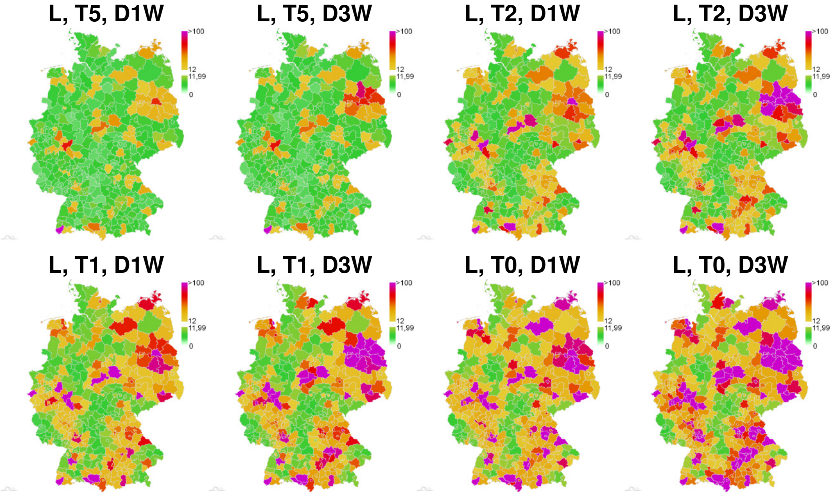
Vorläufige bundesweite Verkehrsströme (PANDEMOS Output):

`https://mobilithek.info/offers/573360269906817024`

Numerical assessment of the NoCovid strategy

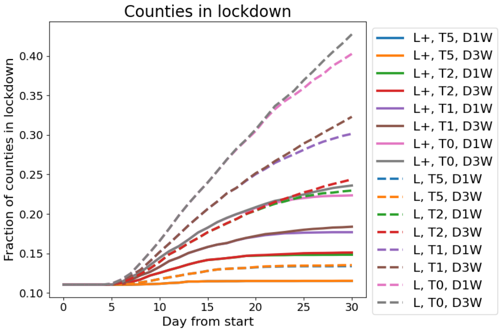
- Test of commuters coming from red zones
- 75 % detection ratio (averaged value for mix of massive deployment of antigen tests plus PCR, RTD-PCR and pool tests)
- Considering different frequencies (daily, twice per week, ...)

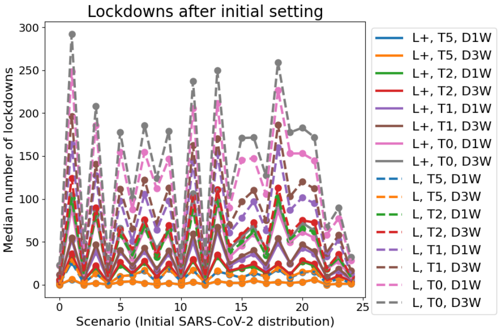




Simulated spread of SARS-CoV-2 cases for one initial scenario of about 18 % red zones and 8 different strategies. Median result after 30 days of simulation time.

Numerical assessment of the NoCovid strategy





Generalizations of ODE-based models by Integro-differential equations

IDE-based models as generalization of ODE-based models: Part I

- $\gamma_I^R(\tau)$ is the fraction of infected individuals that will still recover from infection after time τ (i.e., that is still infected at time τ).
- We need

$$\begin{aligned} \gamma_I^R(0) = 1, \quad \gamma_I^R(\tau) \geq 0 \quad \text{for all } \tau \geq 0, \\ \gamma_I^R(x) \text{ monotonously decreasing}, \quad \int_0^\infty \gamma_I^R(\tau) \mathrm{d}\tau < \infty. \end{aligned} \tag{2}$$

- Theorem 1 shows that our ODE-SIR model implicitly assumed that compartment stays were exponential.

Theorem 1

Consider the system of integro-differential equations

$$S'(t) = \rho\,\phi(t)\,\frac{S(t)}{N}\int_{t_0}^{t}\gamma_I^R(t-x)\,S'(x)\,\mathrm{d}x,$$
$$I(t) = -\int_{t_0}^{t}\gamma_I^R(t-x)\,S'(x)\,\mathrm{d}x, \qquad (3)$$
$$R(t) = -\int_{t_0}^{t}\left(1-\gamma_I^R(t-x)\right)S'(x)\,\mathrm{d}x.$$

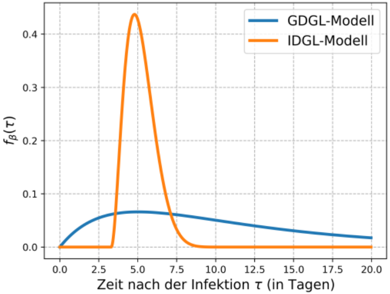
Let $\gamma_I^R(\tau) = \exp(-\frac{\tau}{T_I})$. *Then* (3) *reduces to*

$$S'(t) = -\rho\,\phi(t)\,I(t)\,\frac{S(t)}{N}$$
$$I'(t) = \rho\,\phi(t)\,I(t)\,\frac{S(t)}{N} - \frac{1}{T_I}I(t)$$
$$R'(t) = \frac{1}{T_I}I(t)$$

IDE-based models as generalization of ODE-based models: Part II

- Infectiousness depends on age of infection: $\rho \to \rho(\tau)$
- Contacts depend on age of infection: $\phi(t) \to \phi(t,\tau)$

"Infectiousness" over time



More details: Keimer/Pflug (2020), Plötzke (2020).

IDE-based models as generalization of ODE-based models II

Theorem 2

Consider the system of integro-differential equations

$$\begin{aligned}
S'(t) &= \frac{S(t)}{N} \int_{t_0}^{t} \phi(t, t-x)\rho(t-x)\, \gamma_I^R(t-x)\, S'(x)\, \mathrm{d}x, \\
I(t) &= -\int_{t_0}^{t} \gamma_I^R(t-x)\, S'(x)\, \mathrm{d}x, \\
R(t) &= -\int_{t_0}^{t} \left(1 - \gamma_I^R(t-x)\right) S'(x)\, \mathrm{d}x.
\end{aligned} \tag{4}$$

Let $\gamma_I^R(\tau) = \exp(-\frac{\tau}{T_I})$, $\rho(\tau) = \rho$, *and* $\phi(t,\tau) = \phi(t)$.*Then* (4) *reduces to:*

$$\begin{aligned}
S'(t) &= -\rho\, \phi(t)\, I(t)\, \frac{S(t)}{N} \\
I'(t) &= \rho\, \phi(t)\, I(t)\, \frac{S(t)}{N} - \frac{1}{T_I} I(t) \\
R'(t) &= \frac{1}{T_I} I(t)
\end{aligned}$$

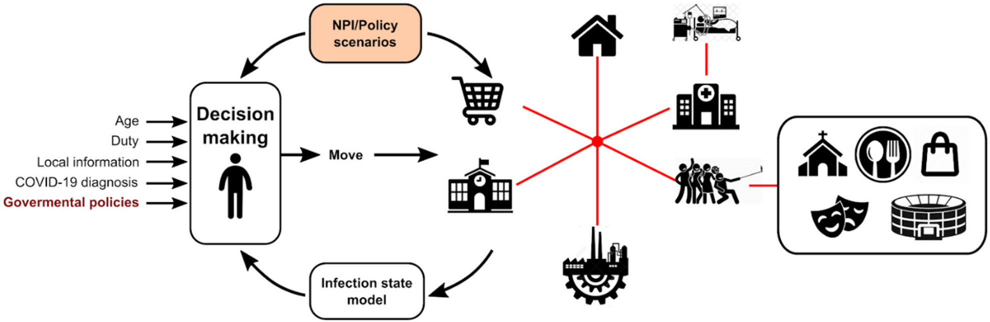
Agent-based models (ABM)

Agent-based modeling

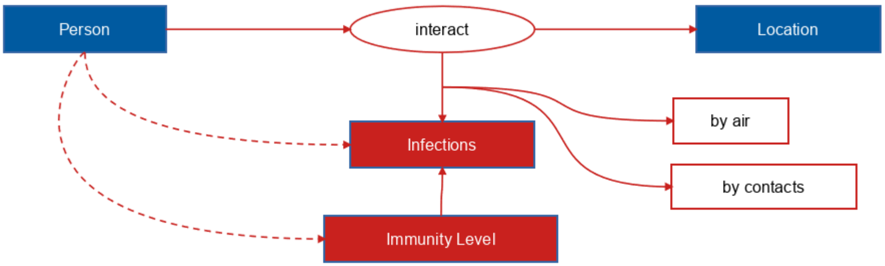
- **Agents**
  Object which holds information, e.g., infection status, current location or age
- **Locations**
  Multiple locations which can be visited, e.g., individual homes, schools, workplaces
- **Rules / Interactions**
  Interactions of different Agents at a current location, or rules for traveling between locations

$\rightarrow$ micro granularity & stochastic effects !

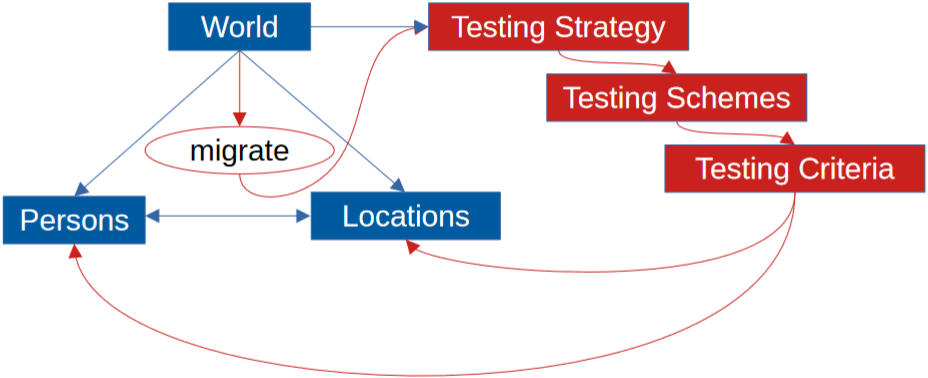
Agent-based modeling



Agent-based modeling: Infection Model



Agent-based modeling: Testing Scheme

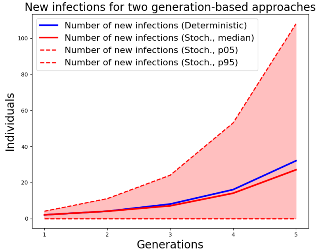


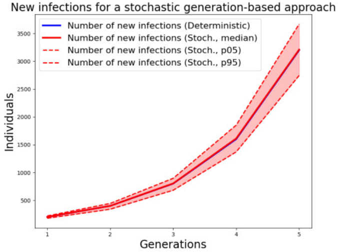
Further reading: D. Kerkmann, S. Korf, K. Nguyen, ..., M. J. Kühn. Evaluating Test, Isolate and Self-Protection Strategies for Infectious Diseases using an Agent-based Model (In preparation, 2024)

Hybrid epidemiological models

Hybrid epidemiological models

- Gain fine-scaled insights to, e.g., households with limited resources
- Spatial hybridization can focus compute ressource to area of interest
- Motivation for temporal hybridization



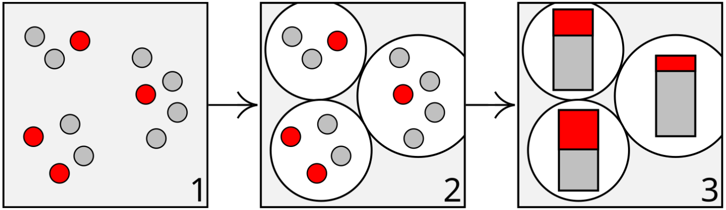


Hybrid epidemiological models

Hybrid models require (nontrivial) population exchange

- Fine $\rightarrow$ ... $\rightarrow$ coarse : By projection
- Coarse $\rightarrow$ ... $\rightarrow$ fine : (Re-)generate data necessary

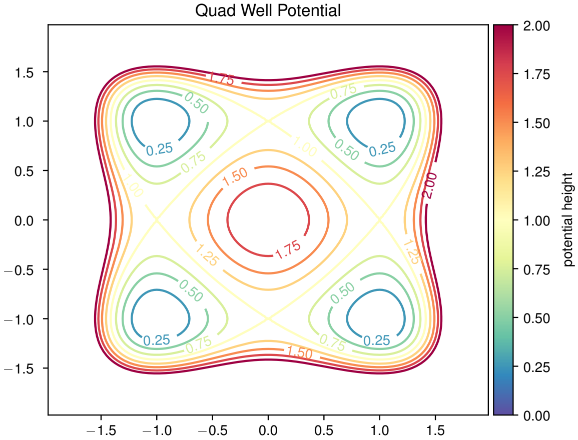
Multiscale Model

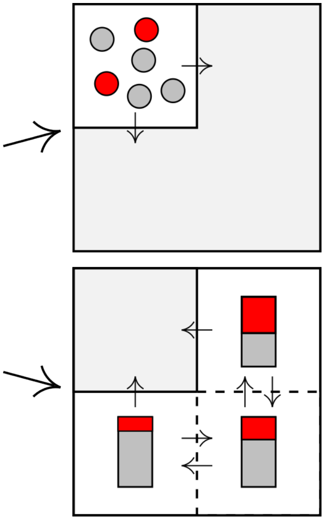


1. Agent Based Model (ABM)
2. Stochastic Metapopulation Model (SMM)
3. Piecewise Deterministic Metapopulation Model (PDMM)

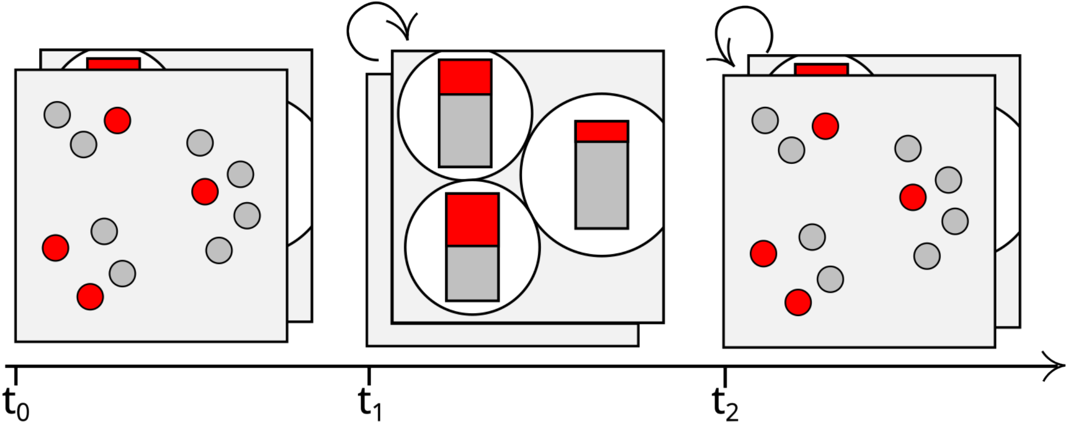
Winkelmann et al. Mathematical modeling of spatio-temporal population dynamics and application to epidemic spreading, Mathematical Biosciences, 2021.

Hybridization - Spatial Approach

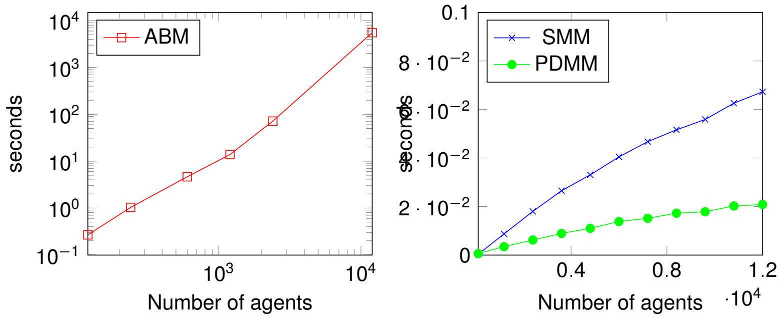




Hybridization - Temporal Approach

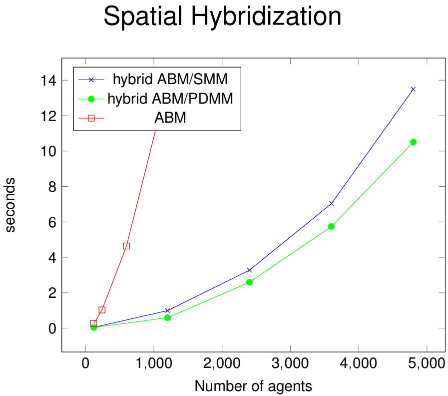


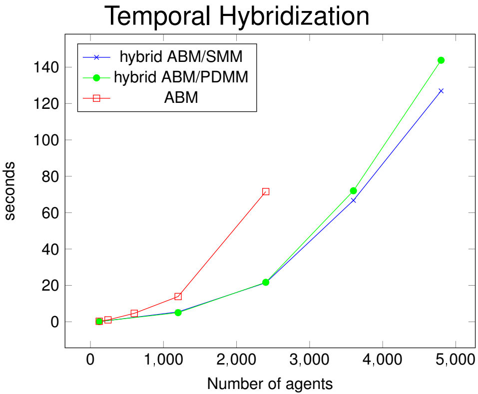
Results - Computational Costs



- Runtime in seconds for 120 up to 12000 agents
- at 12000 agents: $\approx$ 1.5 hours (ABM) vs. $<$ 0.1 second (SMM/PDMM)

Results - Computational Costs

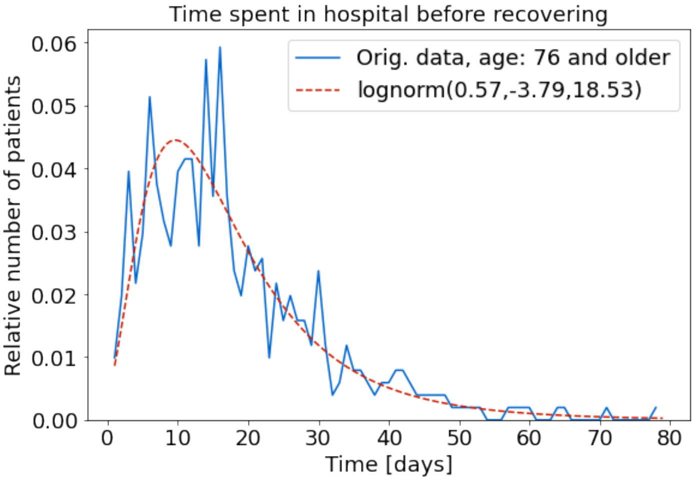




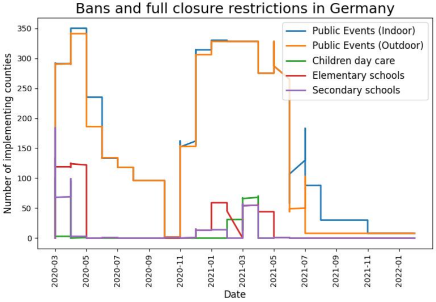
Further reading: J. Bicker, R. Schmieding, M. J. Kühn. Hybrid epidemiological models for compute- and energy-efficient insights on disease dynamics on individual and country-wide scale (Working title, in preparation, 2023)

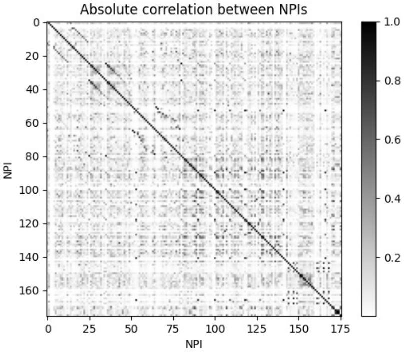
Digression: Data science

Data science is essential part of the process



Data science is essential part of the process



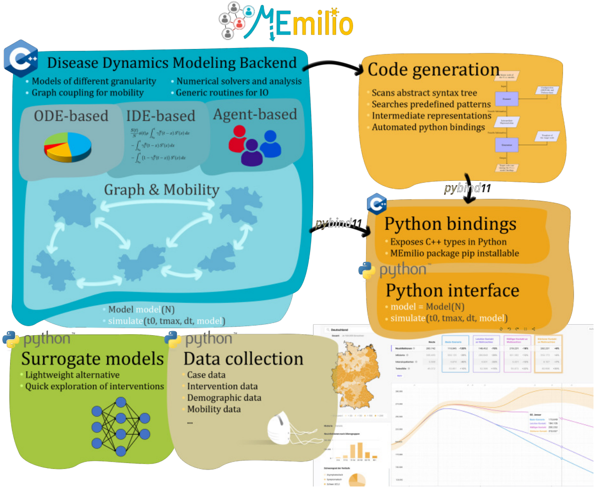


Further reading: A. Wendler, P. Lenz, M. J. Kühn. Inferring the effectiveness of nonpharmaceutical interventions against COVID-19 in Germany and Neural Network Predictors (Working title, in preparation, 2024)

Summary

- Mobility and spatial resolution are important ingredients
- Simple-ODE-based models can be extended
  - By Integro-differential equations for more realistic state transitions
  - By graphs for more realistic spatial distribution of the pathogen
- Agent-based models provide insights on individual or house hold level...
- ...but are computationally expensive.
- Hybrid models try to combine the “best out of two worlds”
- Data science is essential part of the process

MEmilio: A high performance Modular EpideMIcs simuLatIOn software



Further reading

All models and techniques available open source:

A high performance Modular EpideMIcs simuLatIOn software
https://github.com/SciCompMod/memilio

Further reading:

- W. Koslow, M. J. Kühn, S. Binder et al. Appropriate relaxation of non-pharmaceutical interventions minimizes the risk of a resurgence in SARS-CoV-2 infections in spite of the Delta variant (2022). PLoS Comput Biol 18(5): e1010054.

- M. J. Kühn, D. Abele, S. Binder et al. Regional opening strategies with commuter testing and containment of new SARS-CoV-2 variants (2022). BMC Infectious Diseases 22:333

- ...Several papers to be submitted in 2023...

Thank you

Joint work with:
D. Abele, D. Kerkmann, S. Korf, H. Zunker, A. Wendler, J. Bicker, K. Nguyen, M. Klitz, W. Koslow, M. Siggel, J. Kleinert, K. Rack, S. Binder, L. Plötzke, R. Schmieding, P. Lenz, M. Betz, C. Gerstein, A. Schmidt, M. Meyer-Hermann, A. Basermann, ...

"Predictive Simulation Software" at Institute for Software Technology:
We are highly interested in future collaborations in
Mathematics / Computer Science + Epidemiology / Life Science !

Thank you for your kind attention!