SPATIALLY RESOLVED INFECTIOUS DISEASE MODELS FOR LOCALIZED OUTBREAK MITIGATION (AND EFFICIENT MATH. SOFTWARE)

Martin J. Kühn
joint work with many others (see slides)

Exchange at Charité

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GEFÖRDERT VOM
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HELMHOLTZ

DFG

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Federal Ministry of Research, Technology and Space

UNIVERSITÄT BONN

BONN CENTER FOR MATHEMATICAL LIFE SCIENCES

LIMES
Life & Medical Sciences Institute

DLR

Outline / Info

- Who are we?
- Motivation for spatial resolution
- Software aspects: Efficiency and performance
- Metapopulation models with epidemic control application
- Spatially resolved AI-surrogate models for on-the-fly computation
- Agent-based models with some applications
- „Off-Topic“: Basic model properties and influence on outcomes
- Concluding

→ In many places, I will only present a very brief insight into the model or the application and I am happy to discuss more details at any time.

The team

Institute of Software Technology

Department High-Performance Computing

Predictive Simulation Software

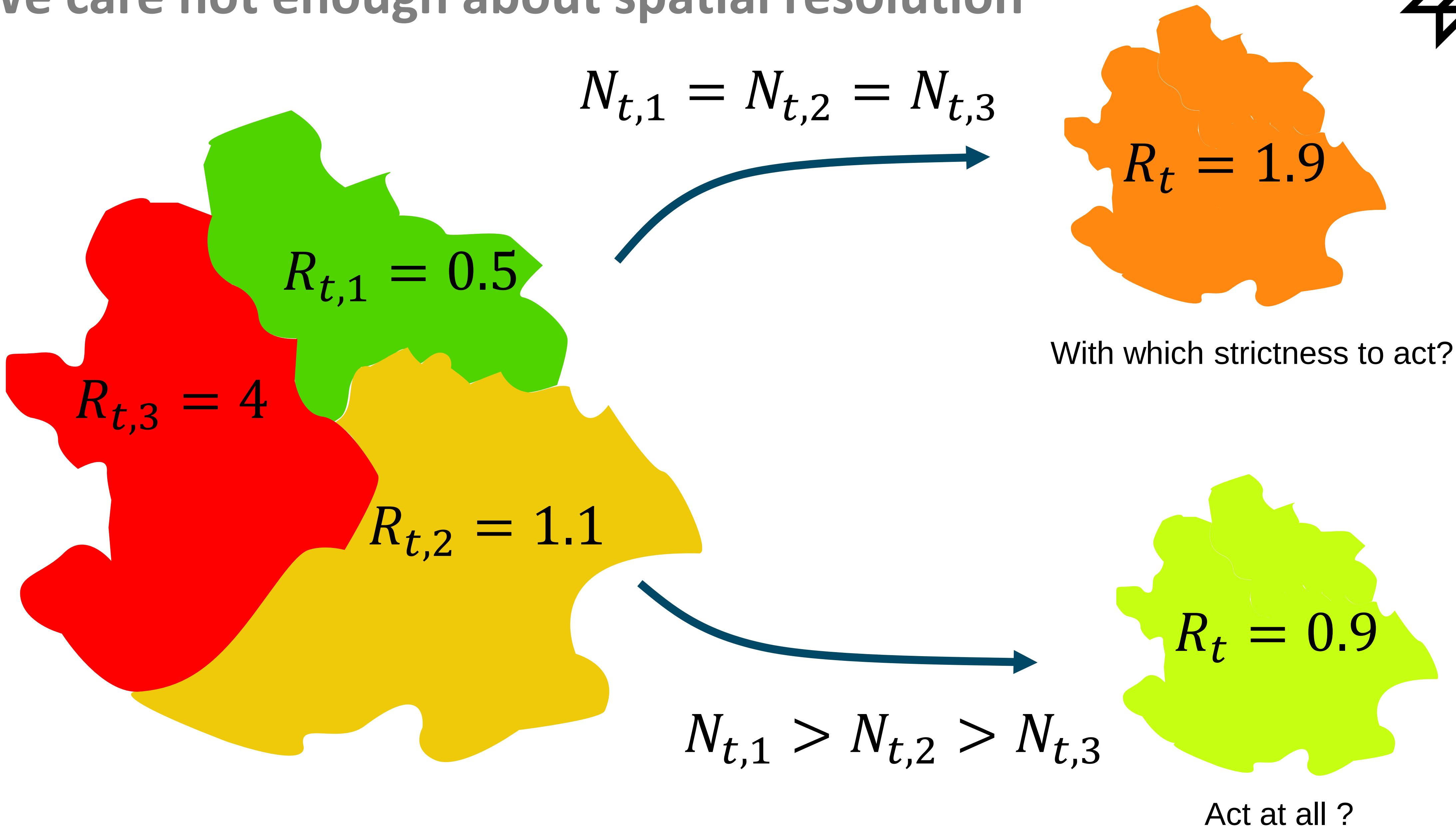
Life and Medical Sciences Institute and

Bonn Center for Mathematical Life Sciences

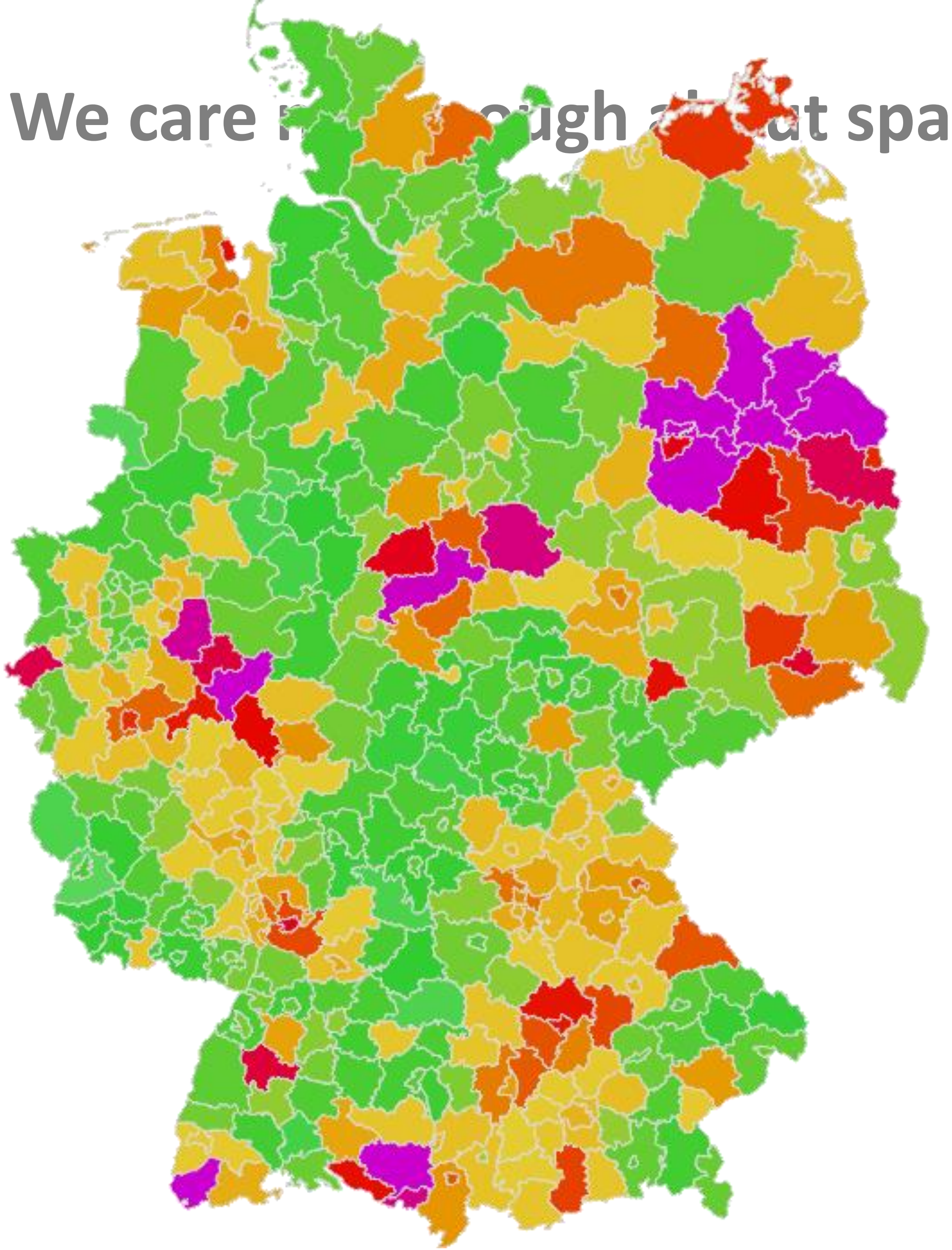
Mathematical-Epidemiological Modeling

Main backgrounds:
- ❖ Applied Mathematics
- ❖ Computer Science
- ❖ High-Performance Computing

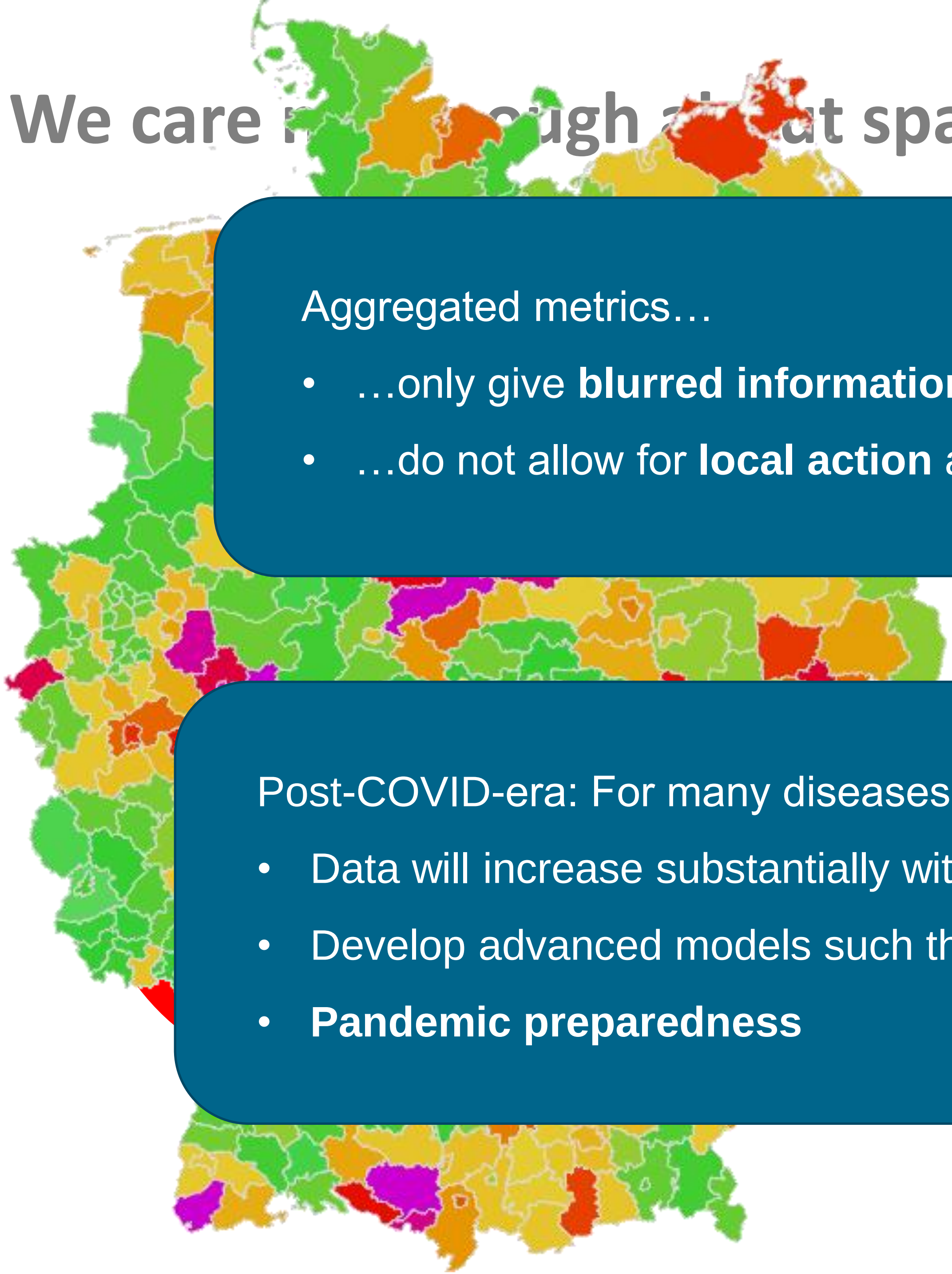
We care not enough about spatial resolution

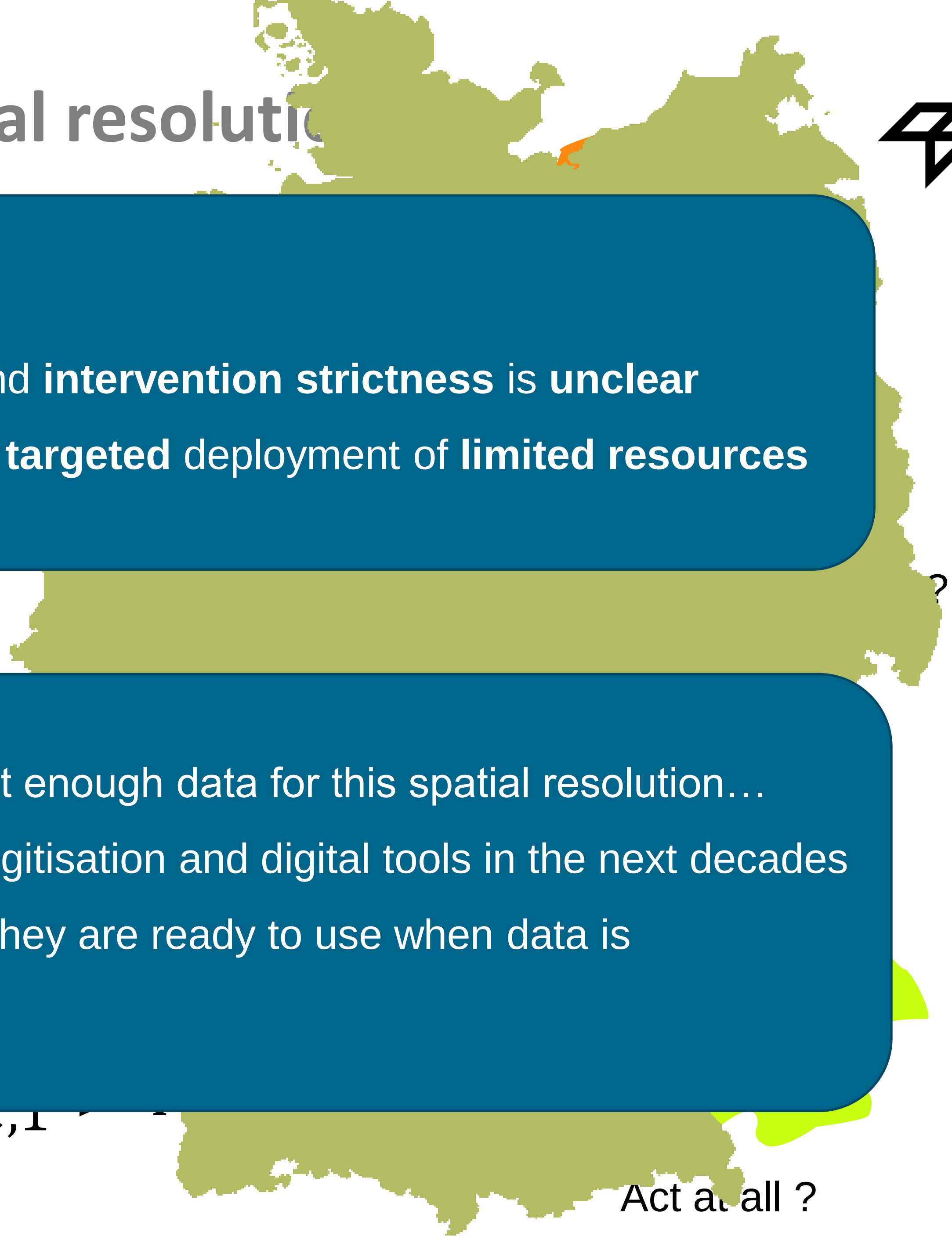


We care n… ugh a… t spatial resolutio…



We care r… ugh a… t spatial resoluti…





Aggregated metrics…

- …only give **blurred information** and **intervention strictness** is **unclear**
- …do not allow for **local action** and **targeted** deployment of **limited resources**

Post-COVID-era: For many diseases, not enough data for this spatial resolution…

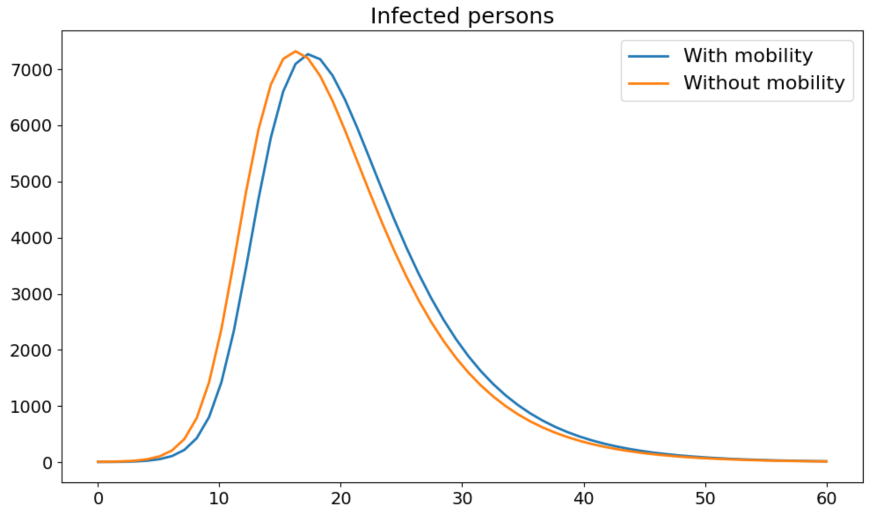
- Data will increase substantially with digitisation and digital tools in the next decades
- Develop advanced models such that they are ready to use when data is
- **Pandemic preparedness**

Act a… all ?

Missing out spatial resolution: some reasons

Aside from data availability, ODE*-SIR-type models are too easy to implement…

- „in the end, it will arrive anyway…“



→ If it looks like that, you do not use the degrees of freedom and power in spatially resolved models

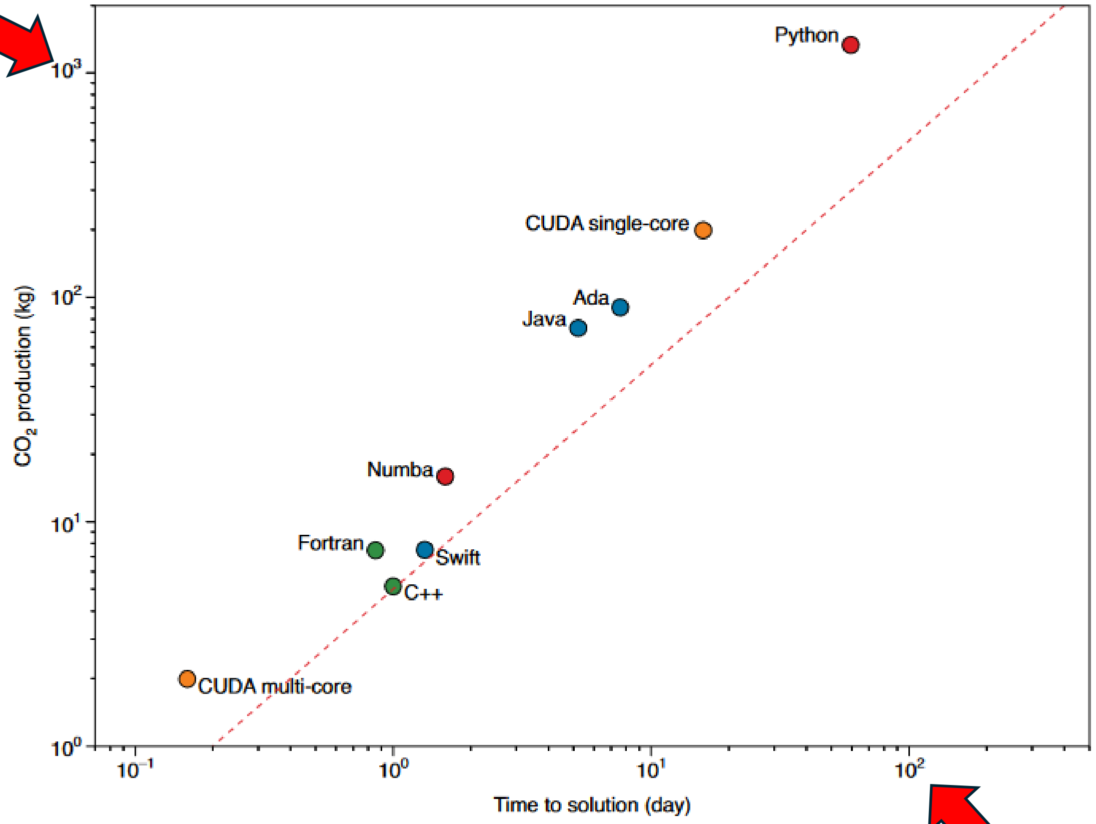
- „you cannot do metapopulation models in a small time frame“

  → well, you can…

* ODE: Ordinary differential equations

Chances of efficiency and performance

Factor 100-1000



Portegies Zwart, Nature Astronomy (2020)

Factor 100

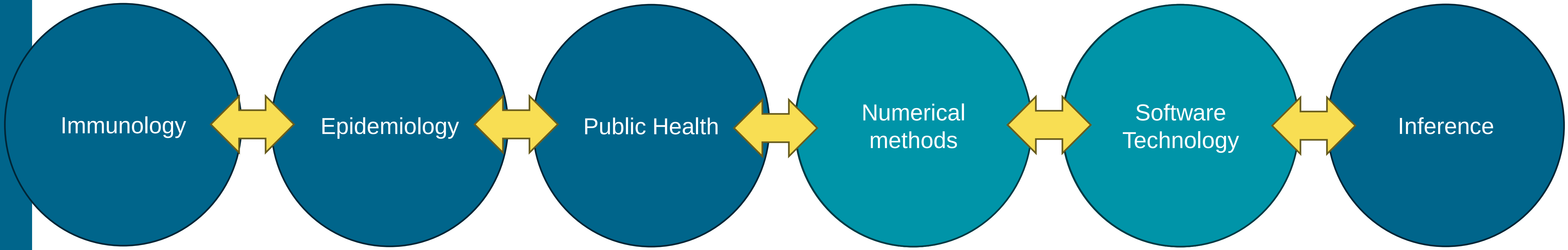
	Time
(c) C	1.00
(c) Rust	1.04
(c) C++	1.56
(c) Ada	1.85
(v) Java	1.89
(c) Chapel	2.14
(c) Go	2.83
(c) Pascal	3.02
(c) Ocaml	3.09
(v) C#	3.14
(v) Lisp	3.40
(c) Haskell	3.55
(c) Swift	4.20
(c) Fortran	4.20
(v) F#	6.30
(i) JavaScript	6.52
(i) Dart	6.67
(v) Racket	11.27
(i) Hack	26.99
(i) PHP	27.64
(v) Erlang	36.71
(i) Jruby	43.44
(i) TypeScript	46.20
(i) Ruby	59.34
(i) Perl	65.79
(i) Python	71.90
(i) Lua	82.91

Pereira et al., SLE'17 (2017)

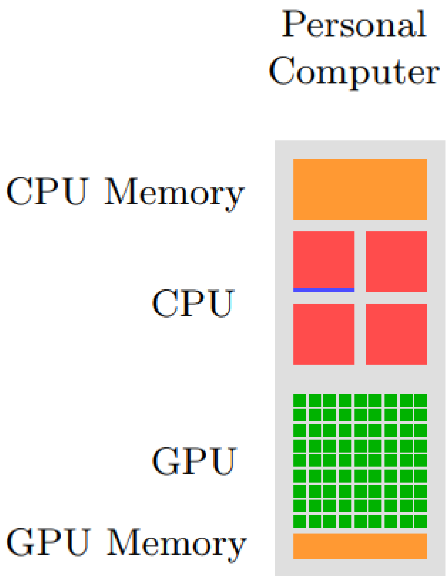
→ In hardware or other contexts: Would we build solutions for (time) critical tasks that are more than 50 times slower or use that more energy for the same task?

→ Do large-scale models in an efficient and scalable language (at least for the backend: R, python… have other use cases)

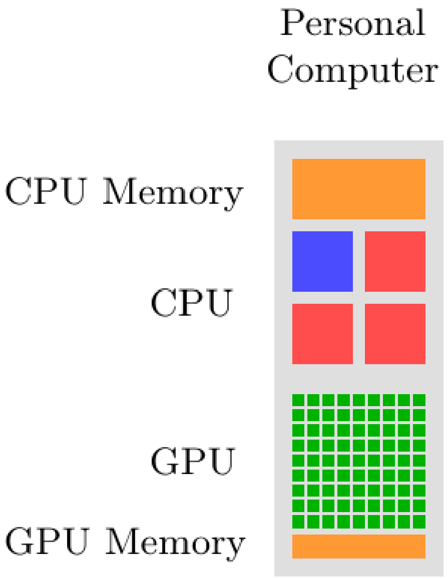
Let‘s create more interdisciplinary synergies



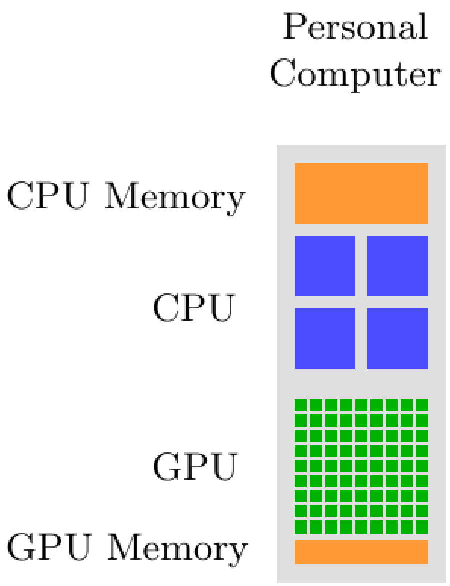
Missing out spatial resolution: Reasons and chances



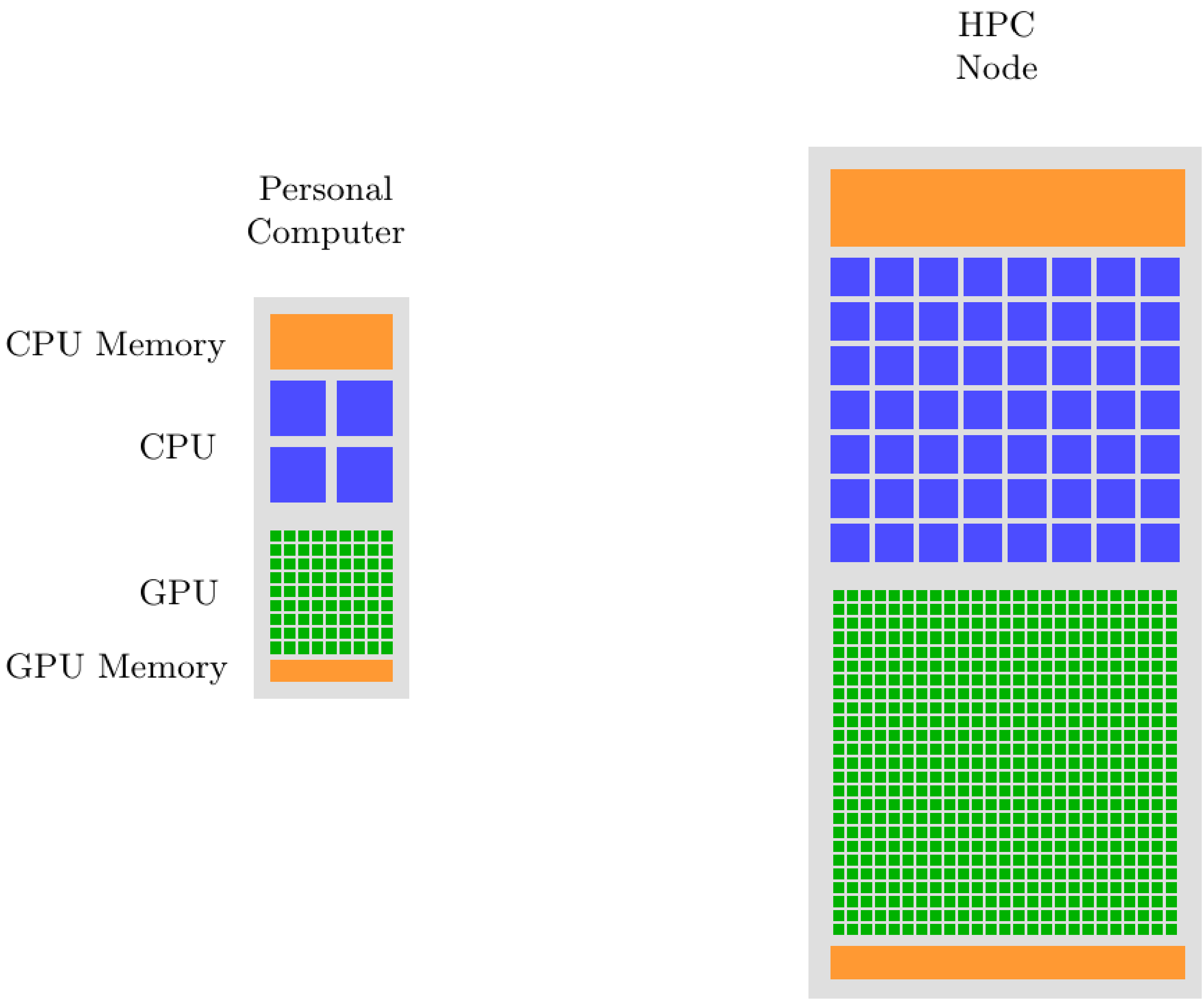
Missing out spatial resolution: Reasons and chances



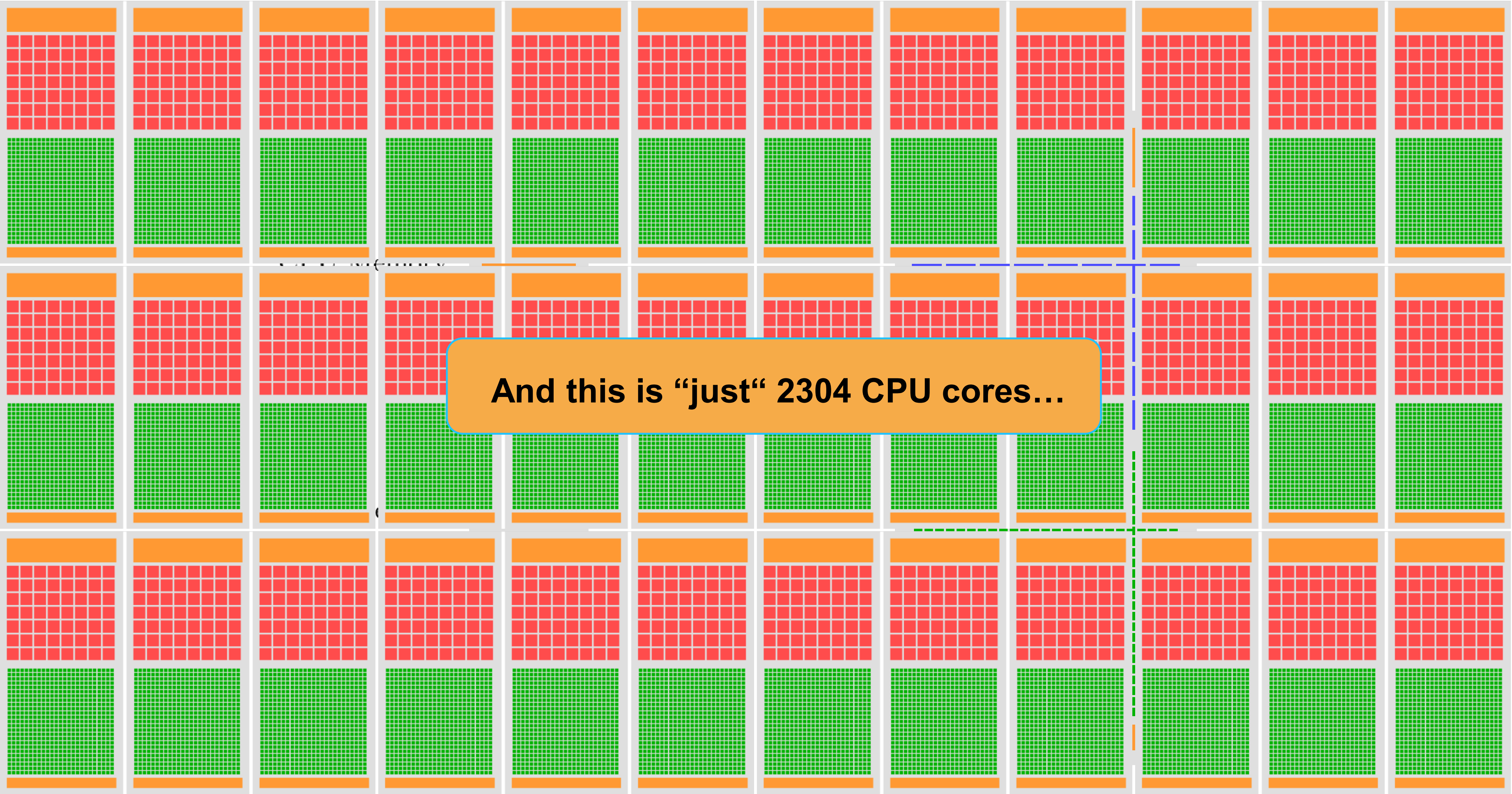
Missing out spatial resolution: Reasons and chances



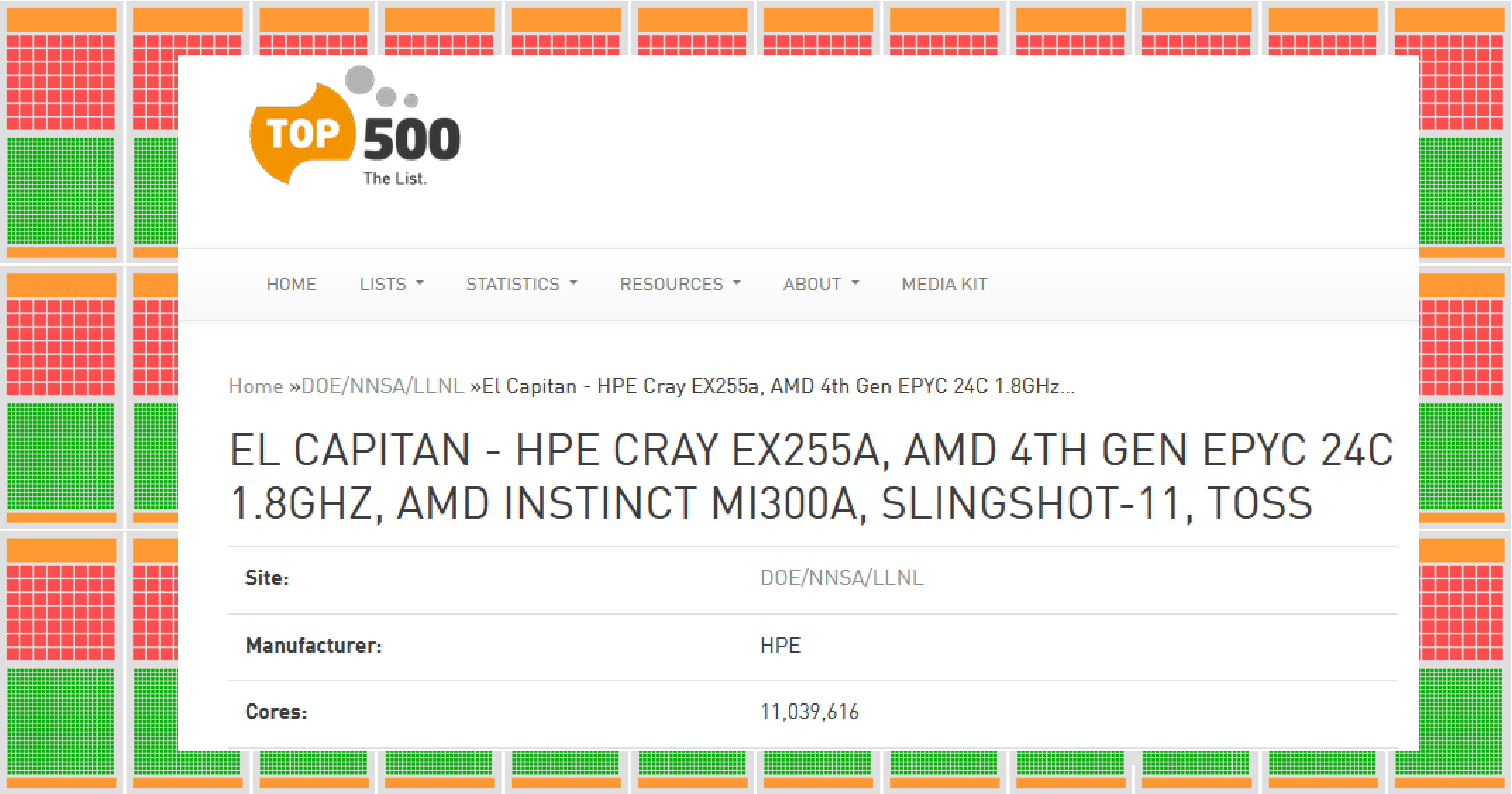
Missing out spatial resolution: Reasons and chances



Missing out spatial resolution: Reasons and chances



Missing out spatial resolution: Reasons and chances



TOP 500 The List.

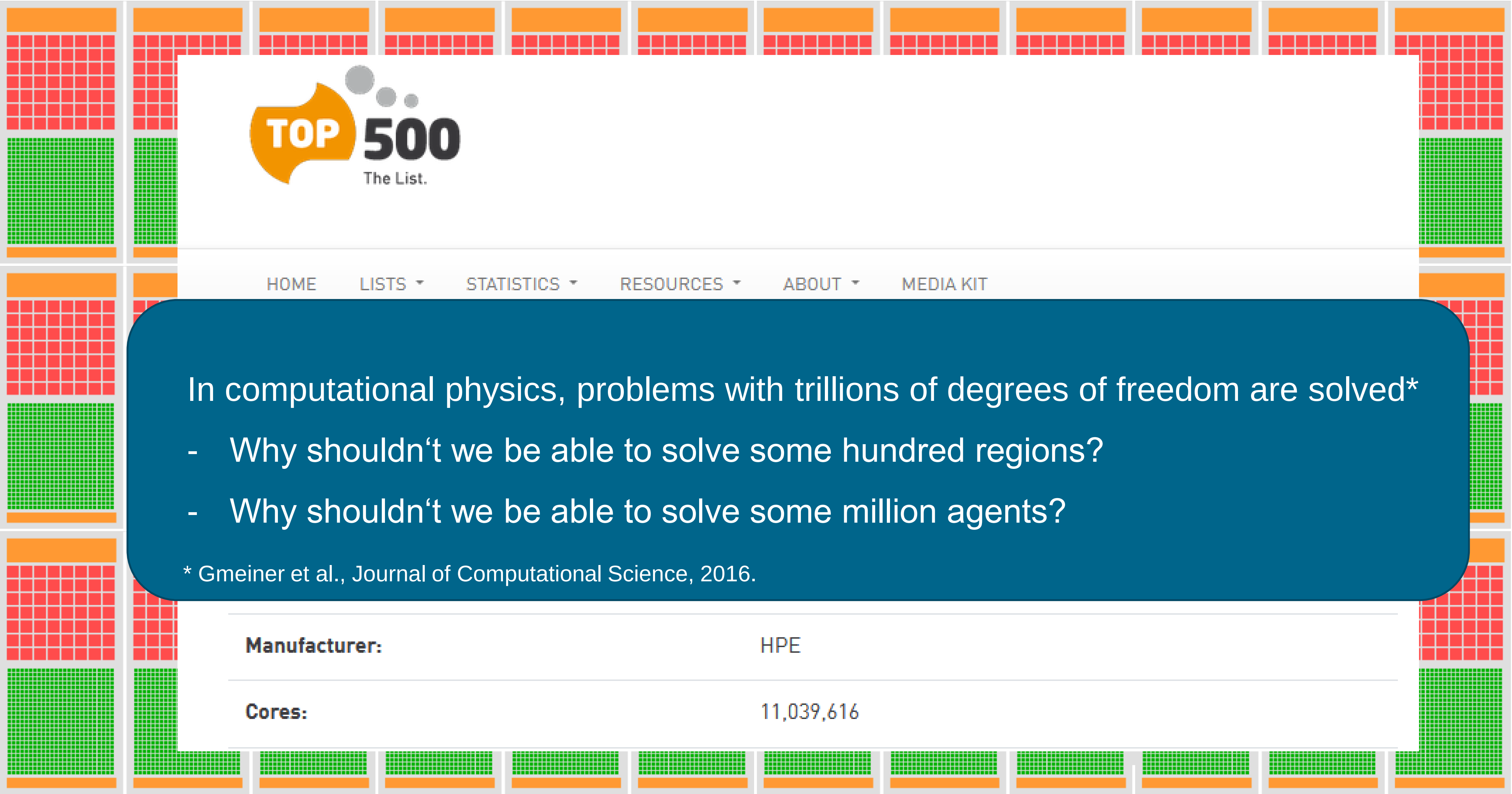
HOME LISTS STATISTICS RESOURCES ABOUT MEDIA KIT

Home »DOE/NNSA/LLNL »El Capitan - HPE Cray EX255a, AMD 4th Gen EPYC 24C 1.8GHz...

EL CAPITAN - HPE CRAY EX255A, AMD 4TH GEN EPYC 24C 1.8GHZ, AMD INSTINCT MI300A, SLINGSHOT-11, TOSS

Site:	DOE/NNSA/LLNL
Manufacturer:	HPE
Cores:	11,039,616

Missing out spatial resolution: Reasons and chances

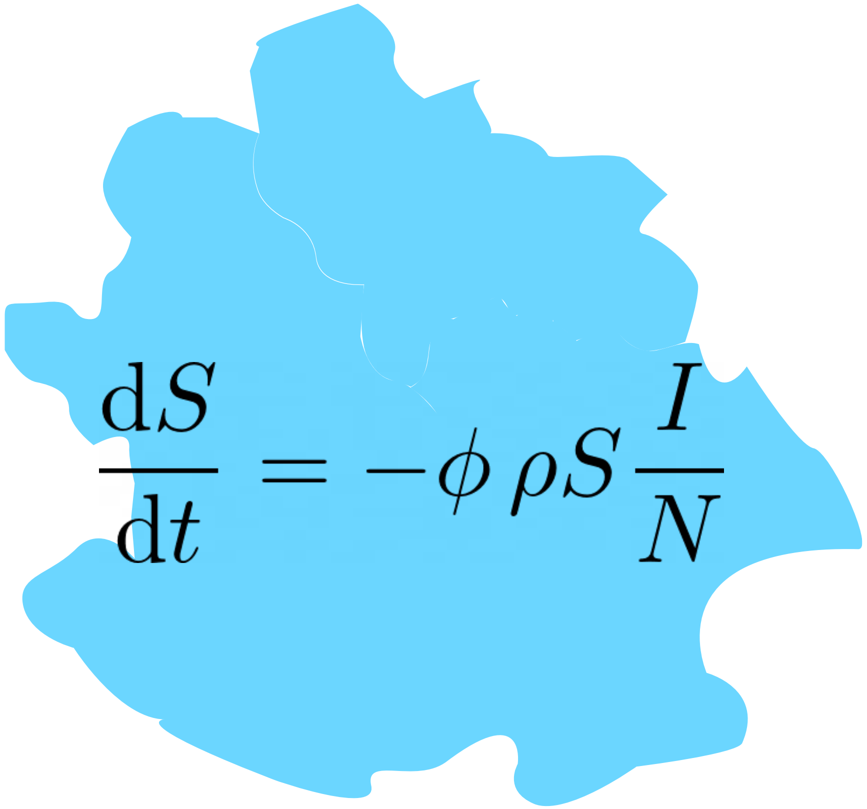


In computational physics, problems with trillions of degrees of freedom are solved*

- Why shouldn‘t we be able to solve some hundred regions?
- Why shouldn‘t we be able to solve some million agents?

* Gmeiner et al., Journal of Computational Science, 2016.

From simple ODE to metapopulation



$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\phi\,\rho S\,\frac{I}{N}$$

S : Susceptible population

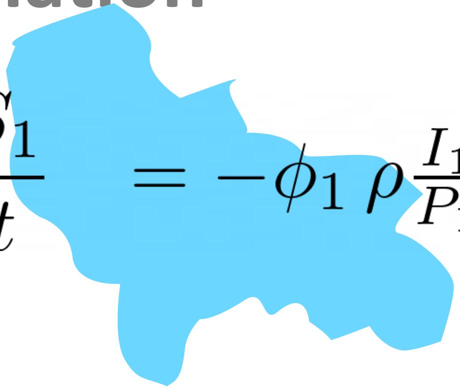
I : Infected/Infectious population

N : Total population

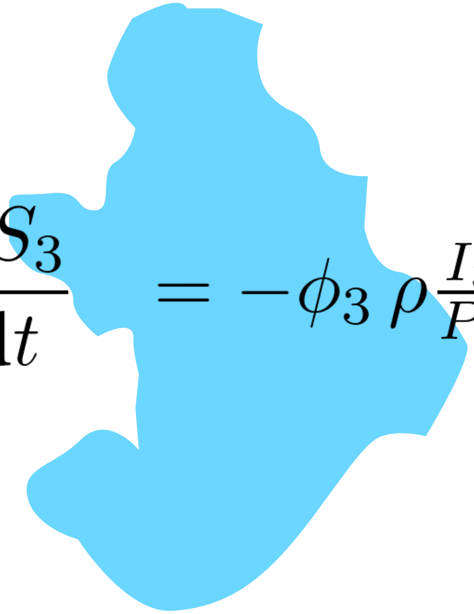
ϕ : Contact rate

ρ : Transmission probability

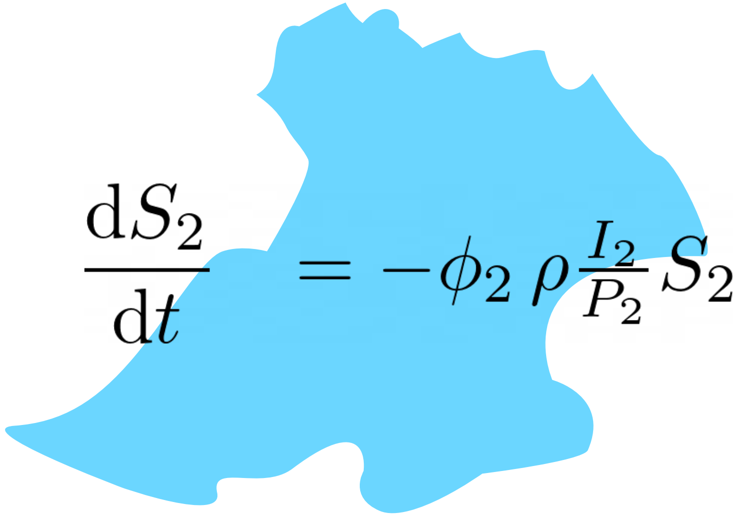
From simple ODE to metapopulation



$$\frac{\mathrm{d}S_1}{\mathrm{d}t} = -\phi_1\,\rho\frac{I_1}{P_1}S_1$$



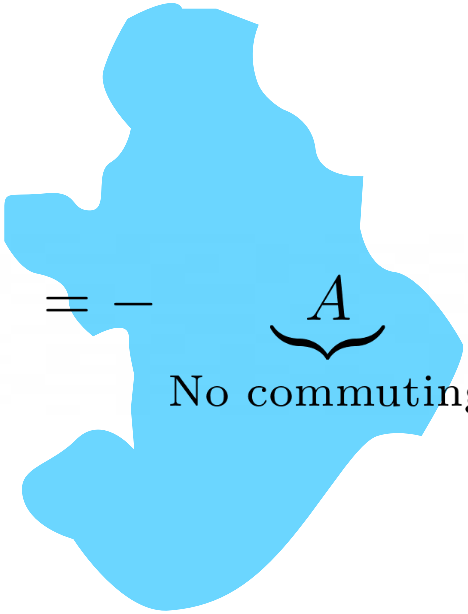
$$\frac{\mathrm{d}S_3}{\mathrm{d}t} = -\phi_3\,\rho\frac{I_3}{P_3}S_3$$



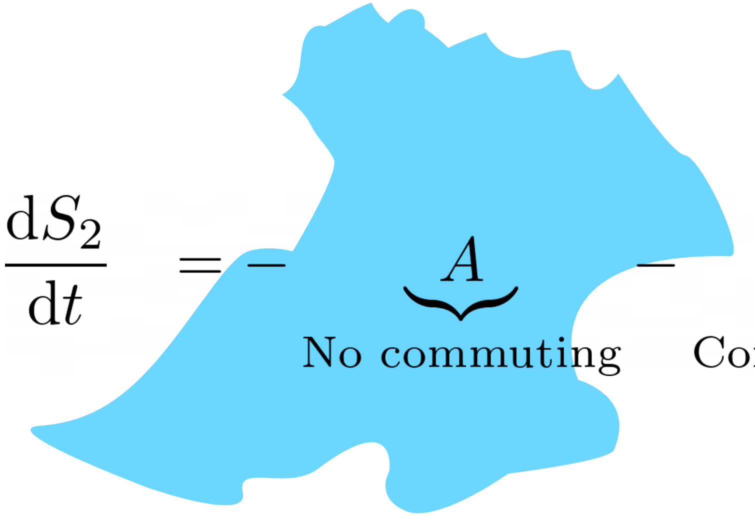
$$\frac{\mathrm{d}S_2}{\mathrm{d}t} = -\phi_2\,\rho\frac{I_2}{P_2}S_2$$

From simple ODE to metapopulation

$$\frac{\mathrm{d}S_1}{\mathrm{d}t} = -\underbrace{A}_{\text{No commuting}} - \underbrace{B}_{\text{Commuting}}$$



$$\frac{\mathrm{d}S_3}{\mathrm{d}t} = -\underbrace{A}_{\text{No commuting}} - \underbrace{B}_{\text{Commuting}}$$



$$\frac{\mathrm{d}S_2}{\mathrm{d}t} = -\underbrace{A}_{\text{No commuting}} - \underbrace{B}_{\text{Commuting}}$$

From simple ODE to metapopulation

$$\frac{\mathrm{d}S_1}{\mathrm{d}t} = -\underbrace{\frac{1}{2}\phi_1\,\rho\frac{I_1}{P_1}S_1}_{\text{No commuting phase}} - \underbrace{B}_{\text{Commuting phase}}$$

$$\frac{\mathrm{d}S_3}{\mathrm{d}t} = -\underbrace{\frac{1}{2}\phi_3\,\rho\frac{I_3}{P_3}S_3}_{\text{No commuting phase}} - \underbrace{B}_{\text{Commuting phase}}$$

h_{ij} : Commuter from region i to j

I^c : commuting infectious

I^r : remaining infectious

$$P_i = \sum_{j=1}^{n} h_{ij}$$

$$N_i = P_i - \sum_{j\neq i} h_{ij} + \sum_{j\neq i} h_{ji}$$

$$\frac{\mathrm{d}S_2}{\mathrm{d}t} = -\underbrace{\frac{1}{2}\phi_2\,\rho\frac{I_2}{P_2}S_2}_{\text{No commuting phase}} - \underbrace{B}_{\text{Commuting phase}}$$

Gerstein et al, in preparation, 2025

From simple ODE to metapopulation

$$\frac{\mathrm{d}S_1}{\mathrm{d}t} = -\underbrace{\frac{1}{2}\phi_1\,\rho\frac{I_1}{P_1}S_1}_{\text{No commuting phase}} - \underbrace{\frac{1}{2}\left(\phi_1\,\rho\frac{I_1^r}{N_1}S_1^r + \phi_1\,\rho\frac{I_1^c}{N_1}S_1^r + \rho S_1\sum_{j\neq 1}\phi_j\,\frac{h_{1j}}{P_1}\frac{I_j^r + I_j^c}{N_j}\right)}_{\text{Commuting phase}}$$

$$\frac{\mathrm{d}S_3}{\mathrm{d}t} = -\underbrace{\frac{1}{2}\phi_3\,\rho\frac{I_3}{P_3}S_3}_{\text{No commuting phase}} - \underbrace{B}_{\text{Commuting phase}}$$

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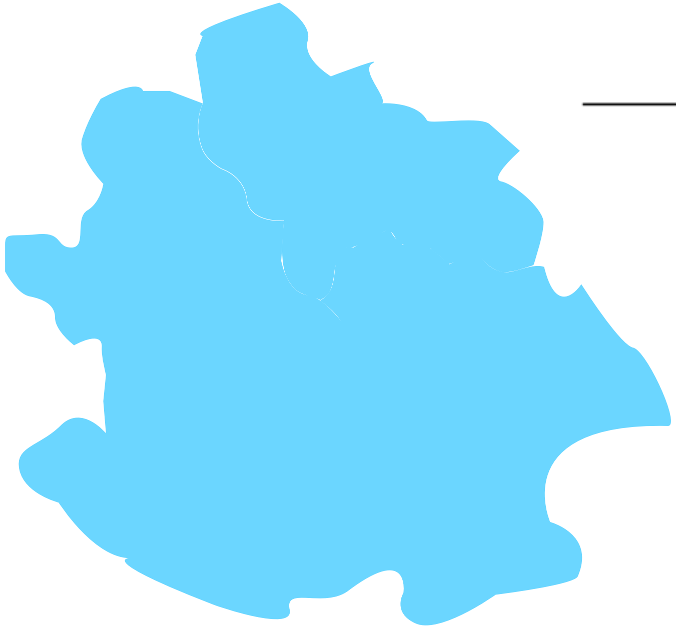
Gerstein et al, in preparation, 2025

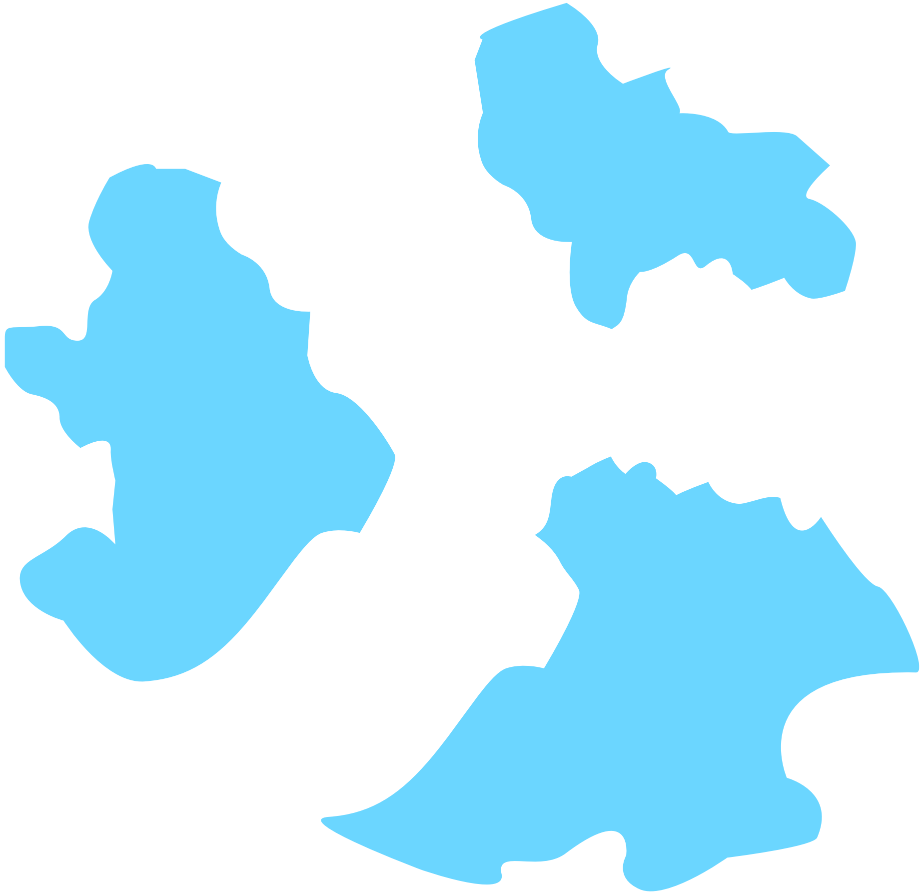
From simple ODE to metapopulation

→ For uniformly distributed cases, the models should return the same output

Basic reproduction numbers for different numbers of regions.

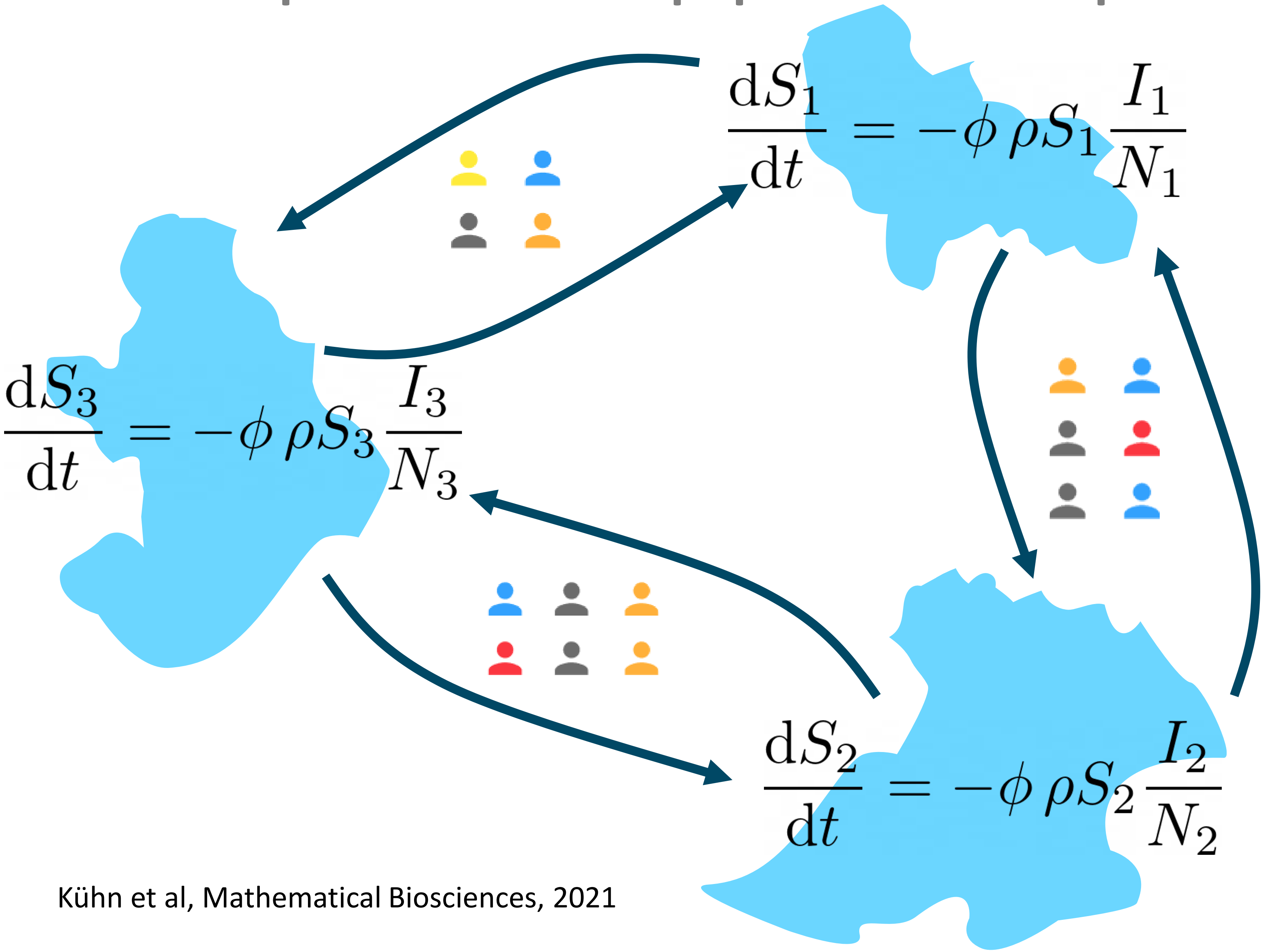
Number of Regions	Model A	Model B	Model C
1	4.48161	4.48161	4.48161
2	4.48161	[illegible].6021[illegible]	4.48161
5	4.48161	6.2[illegible]43	4.48161
10	4.48161	6.[illegible]54	4.48161
20	4.48161	[illegible].6105[illegible]	4.48161
50	4.48161	6.67782	4.48161





Gerstein et al, in preparation, 2025

From simple ODE to metapopulation: A Graph-ODE alternative



$$\frac{\mathrm{d}S_1}{\mathrm{d}t} = -\phi\,\rho S_1 \frac{I_1}{N_1}$$

$$\frac{\mathrm{d}S_3}{\mathrm{d}t} = -\phi\,\rho S_3 \frac{I_3}{N_3}$$

$$\frac{\mathrm{d}S_2}{\mathrm{d}t} = -\phi\,\rho S_2 \frac{I_2}{N_2}$$

- Use a graph with regions as nodes
- One edge per, e.g., pair (infection state, age group)
- Advance nodes in parallel from t to t+0.5 and from t+0.5 to t+1

Advantage:
- Parallelism

Disadvantage:
- Returning commuters need to be approximated
- Theory more complex

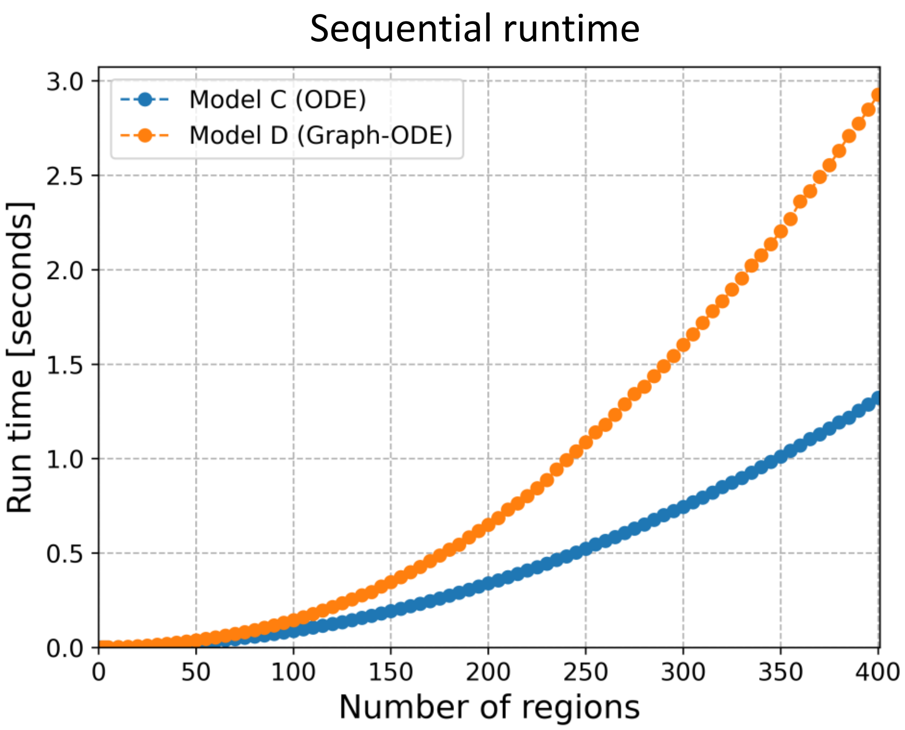
Kühn et al, Mathematical Biosciences, 2021

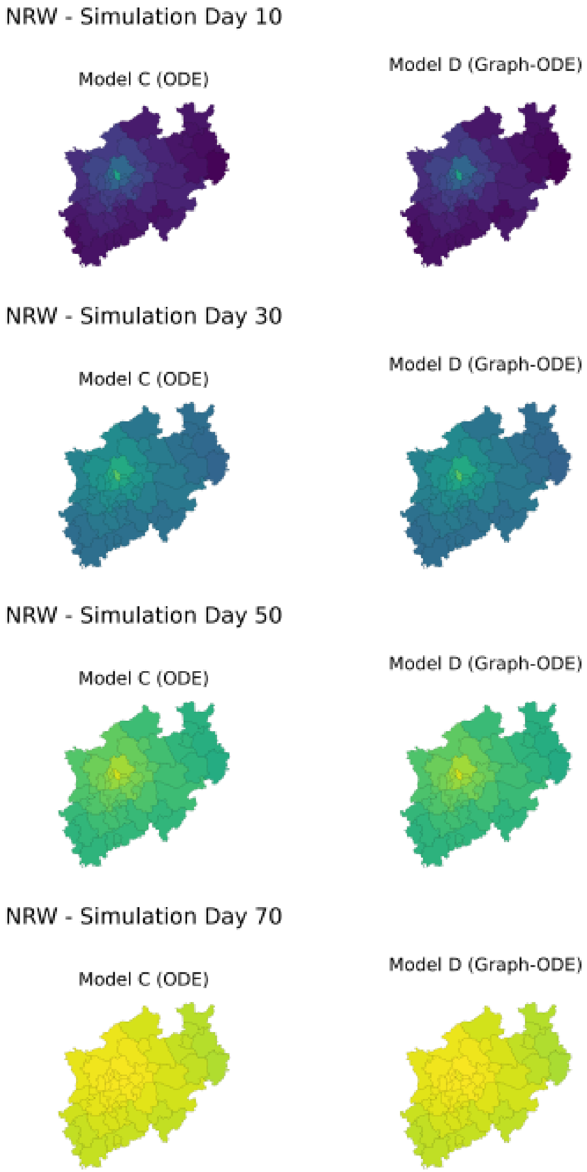
ODE vs. Graph-ODE metapopulation

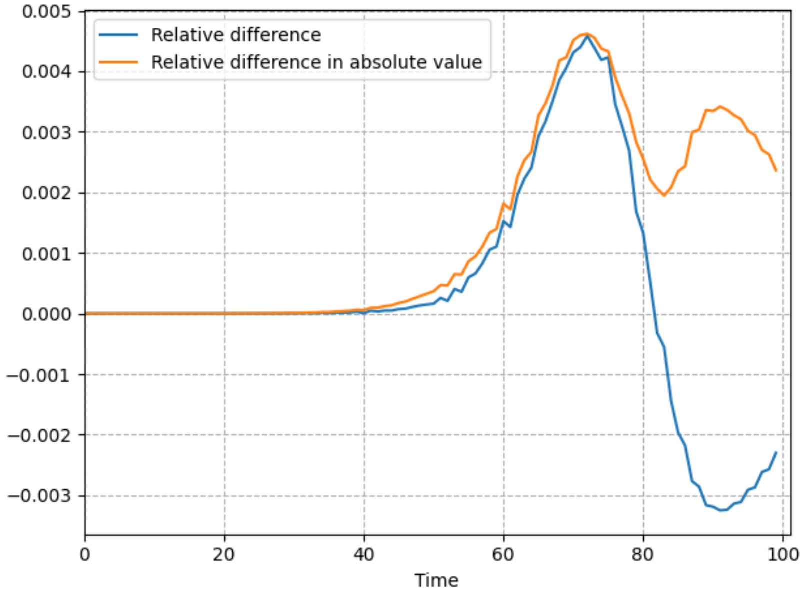
Carlotta Gerstein

Henrik Zunker

DLR



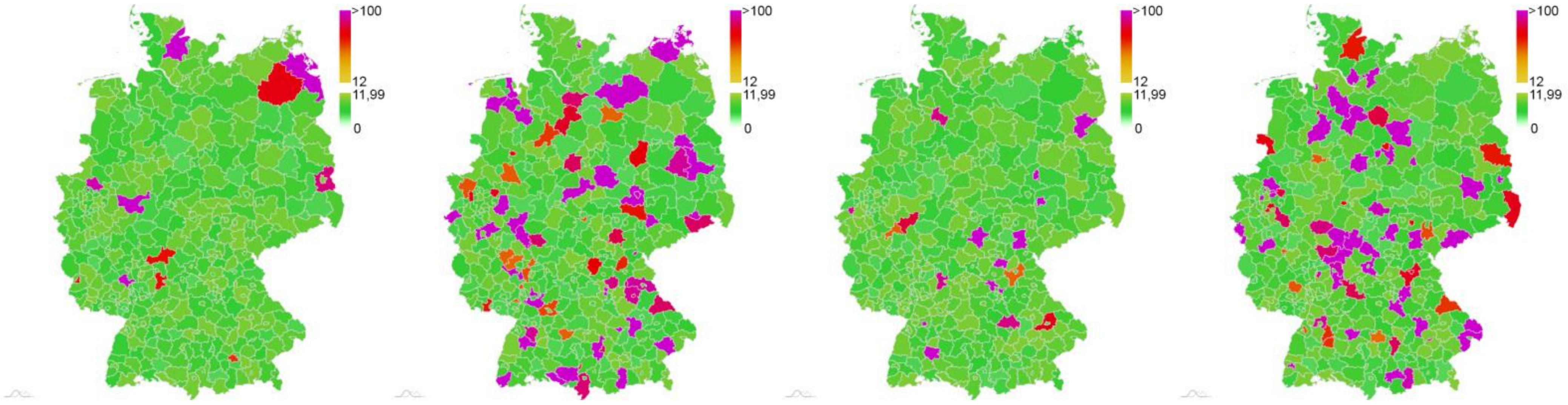




Gerstein et al, in preparation, 2025/26
Zunker et al, in preparation, 2025/26

Application: Numerical assessment of the “NoCovid” control strategy

- “NoCovid” is not “ZeroCovid”
- NoCovid: “Controlling the Covid-19 pandemic through Green Zones”

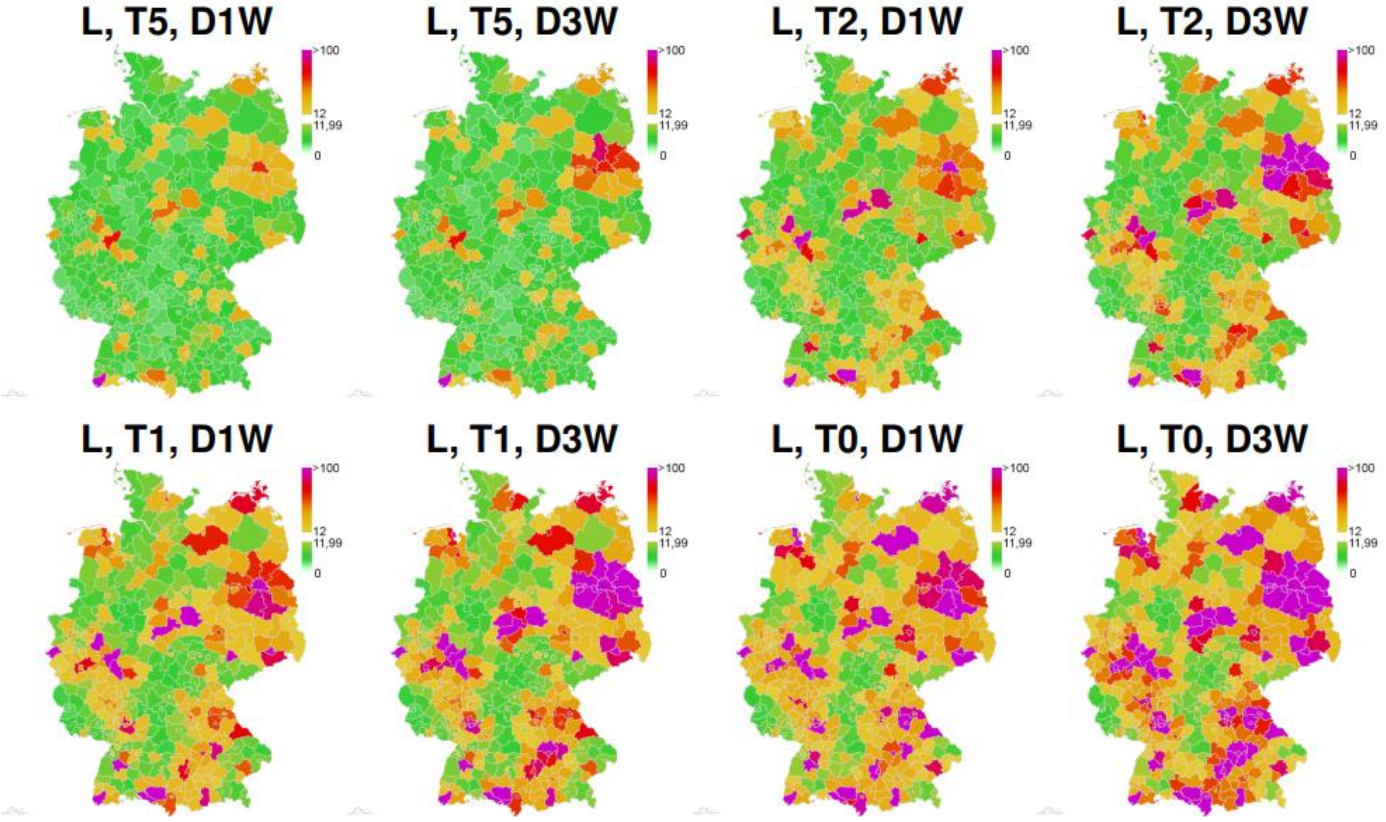


Four different initial scenarios. Random initial incidence (weekly cases per 100 000 individuals) of 75-150 for 2-20% of the counties and incidence below 10 otherwise

- 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, ...)

Application: Numerical assessment of the “NoCovid” control strategy

- T0, T1, T2, T5: No testing, testing once, twice or five times per week
- L: Lockdown
- D1W, D3W: Implementations of interventions with one or three weeks delay

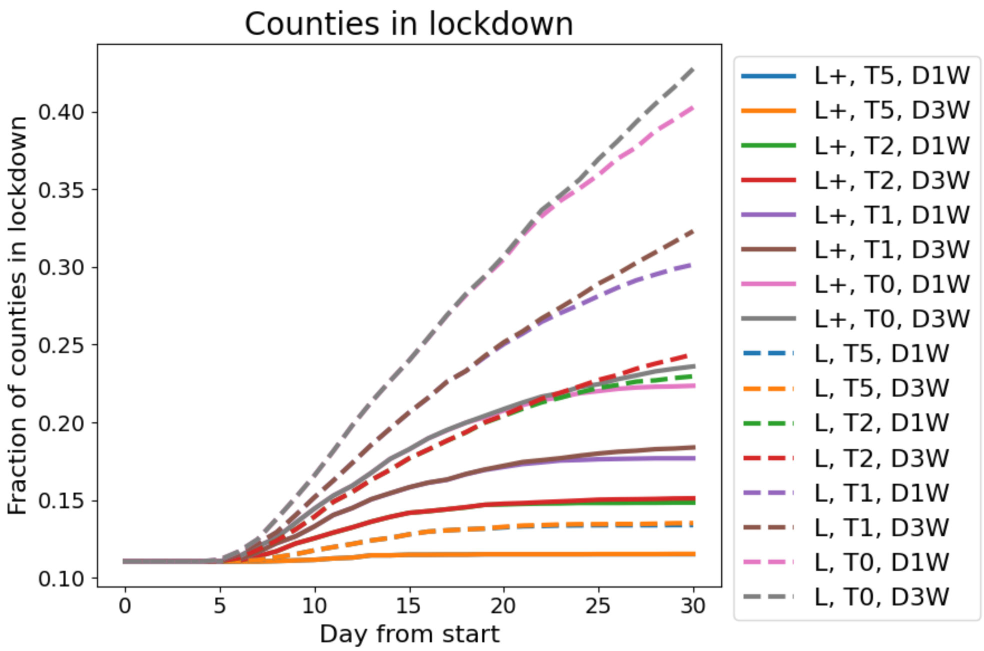


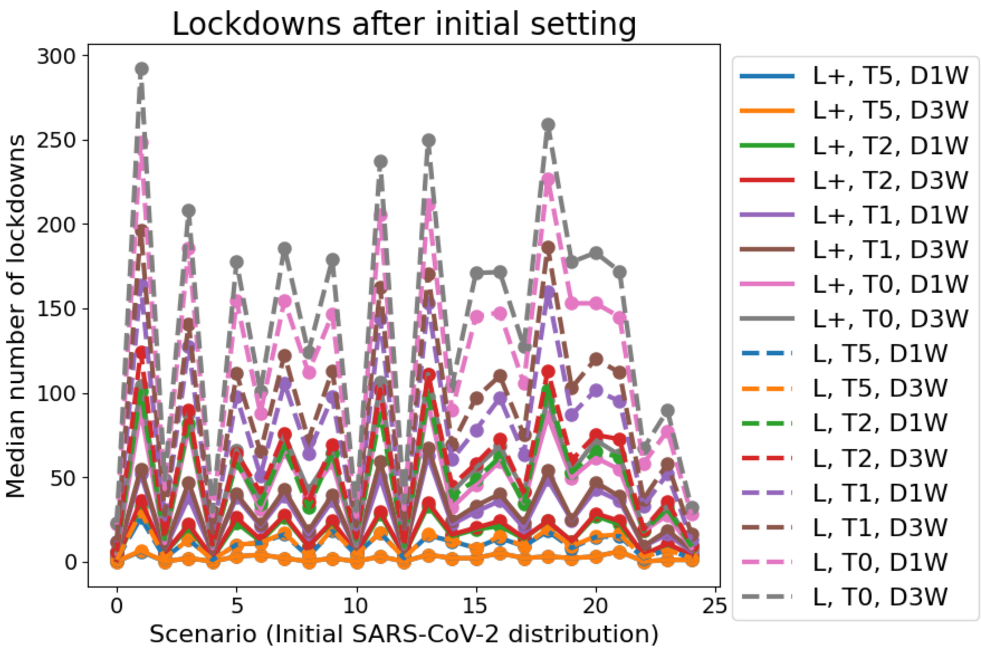
Simulated spread of SARS-CoV-2 cases for one initial scenario of about 18 % red zones and 8 different strategies. Median result after 30 days of simulation time.

Kühn et al., BMC Infectious Diseases (2022)
https://doi.org/10.1186/s12879-022-07302-9

Control (2022)

Application: Numerical assessment of the “NoCovid” control strategy





- T0, T1, T2, T5: No testing, testing once, twice or five times per week
- L, L+: Lockdown or strict lockdown
- D1W, D3W: Implementations of interventions with one or three weeks delay

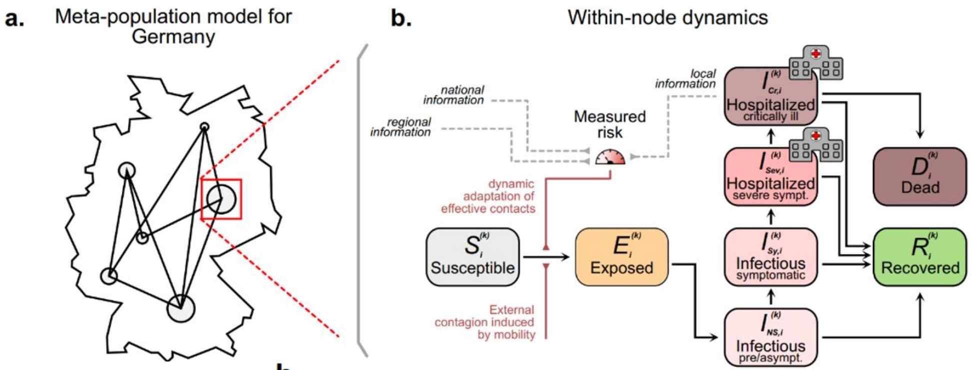
Control (2022)

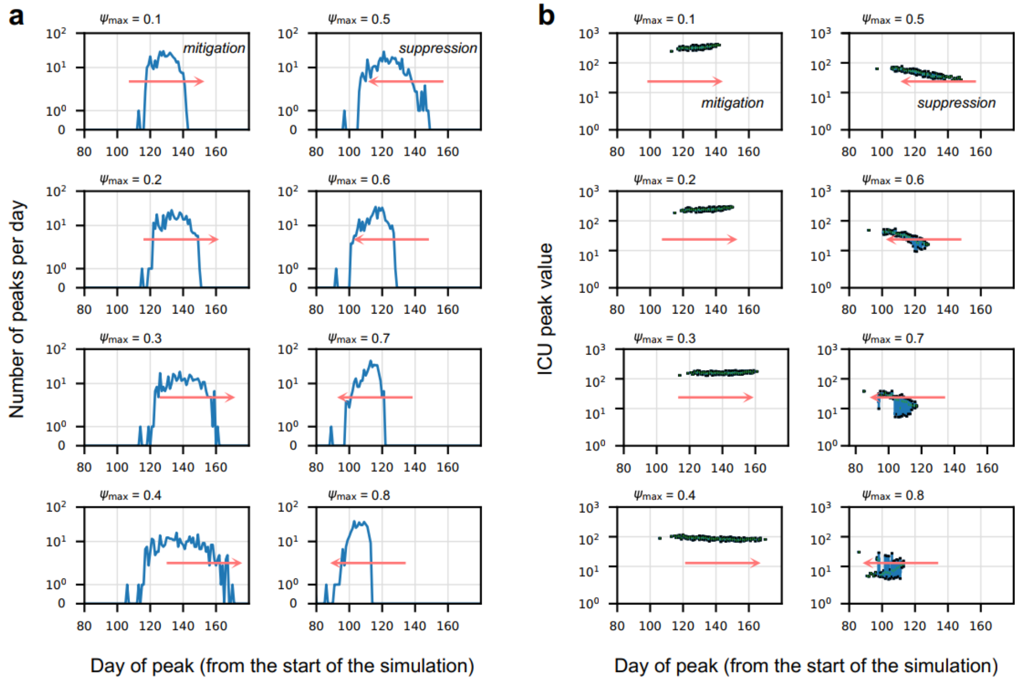
Kühn et al., BMC Infectious Diseases (2022)
https://doi.org/10.1186/s12879-022-07302-9

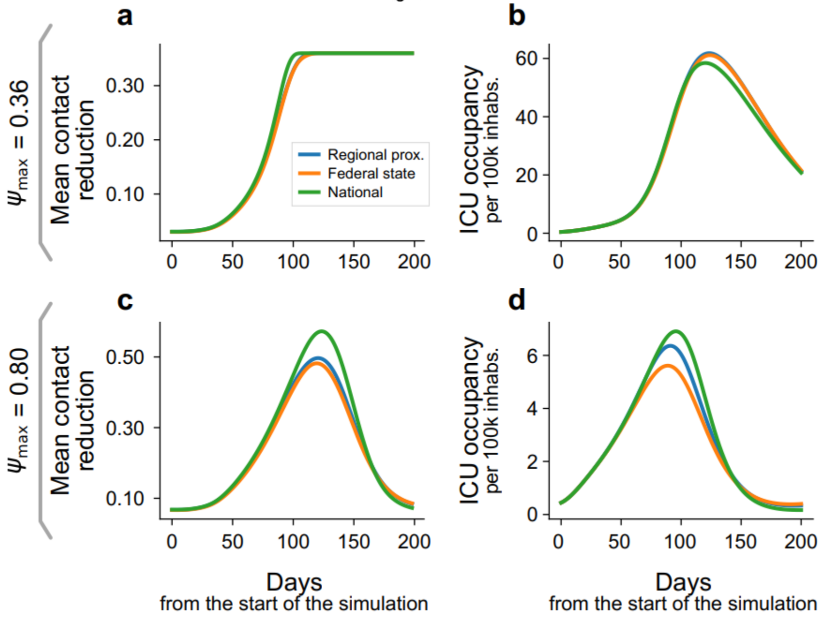
ODE-based metapopulation with feedback mechanism

Henrik Zunker

- Integration of spatially resolved human behavior
- Feedback loop based on perceived risk with memory kernel
- Nominal ICU capacity as threshold for regulation measures
- Regulation updates the effective contact rate





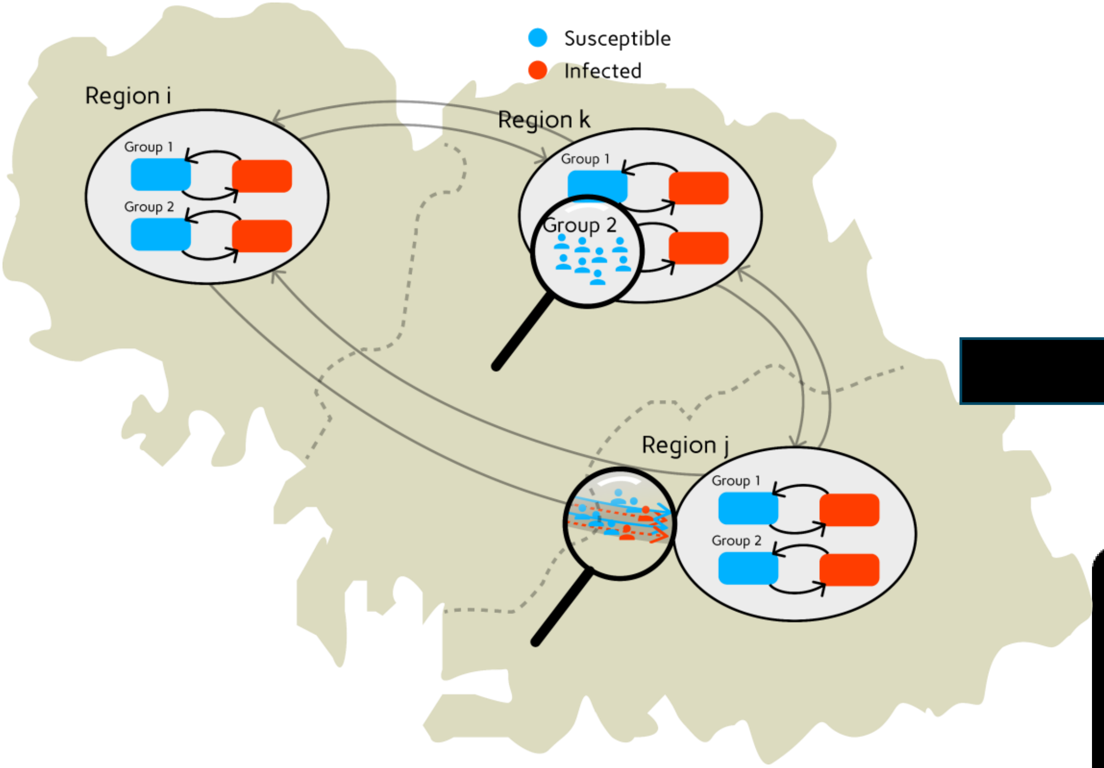


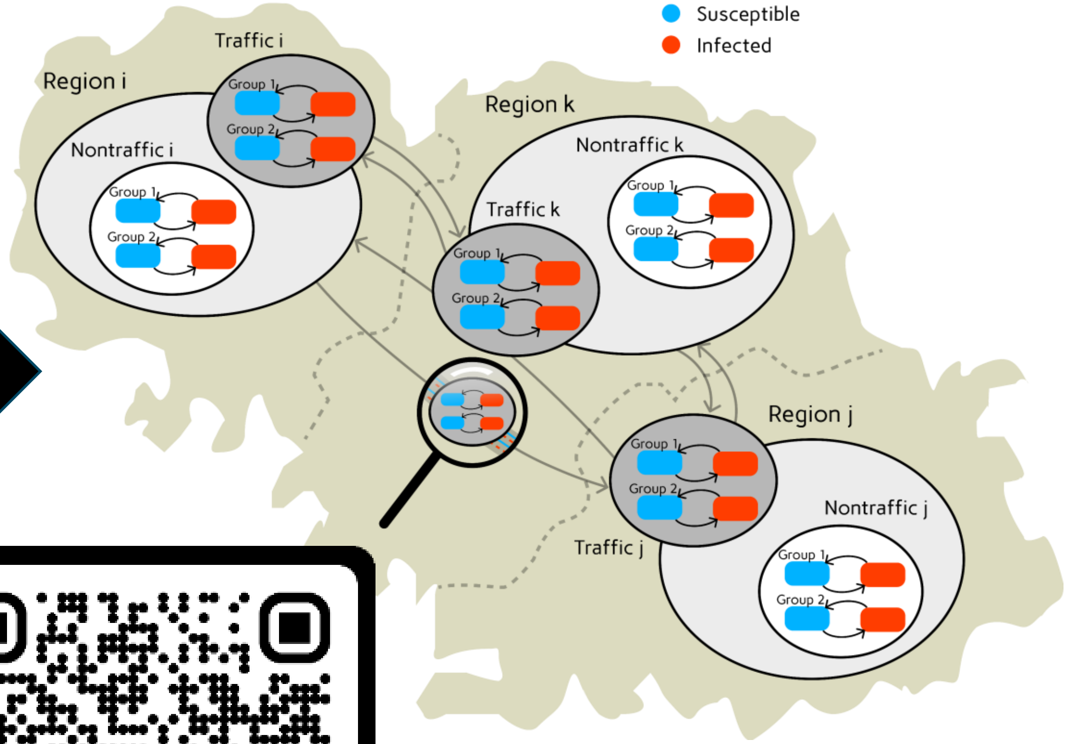
https://doi.org/10.1016/j.chaos.2025.116782
Zunker et al., Chaos, Solitons & Fractals (2025)

Extension to travel-time aware Graph-ODE metapopulation

Henrik Zunker

DLR





Metapop (2024)

Zunker et al., PLOS Comp Bio (2024)
https://doi.org/10.1371/journal.pcbi.1012630

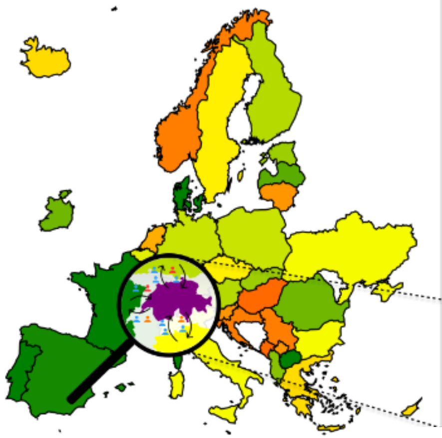
AI-based on-the-fly computation for web applications

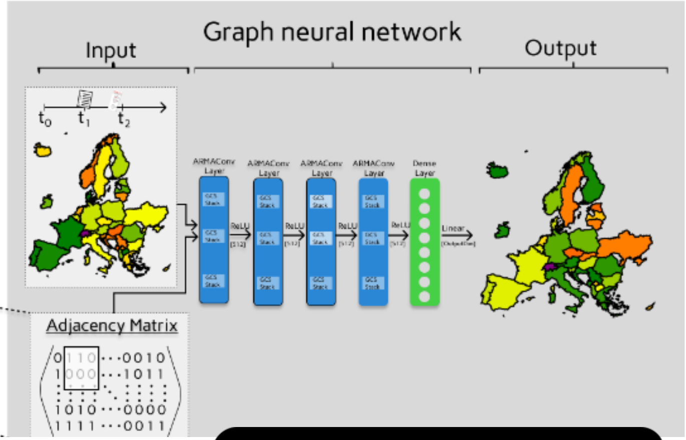

Agatha Schmidt Henrik Zunker

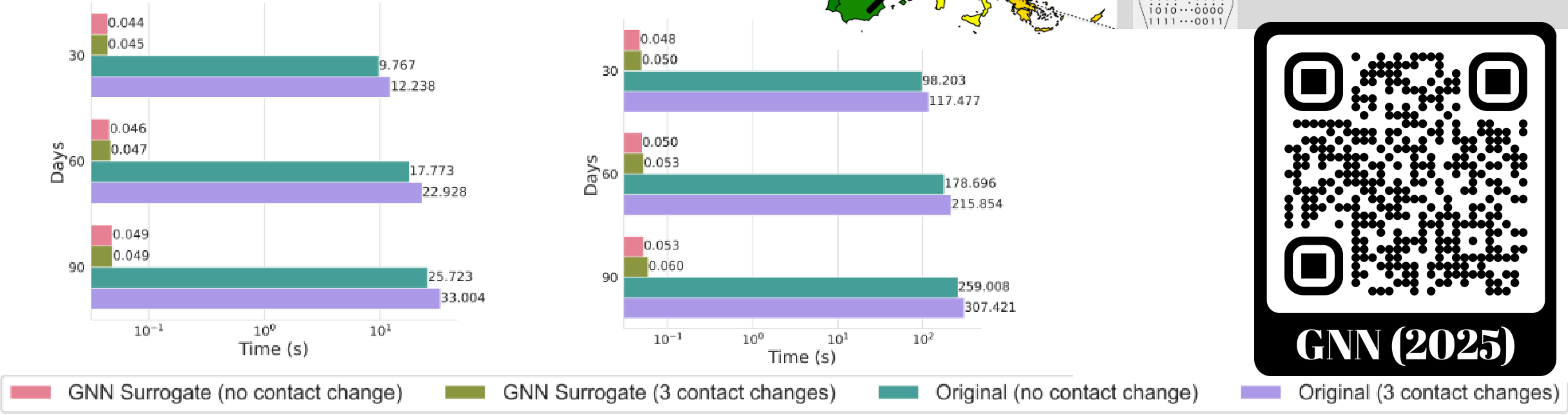
- Simulate spatially resolved expert models
- Train spatially resolved AI surrogates (Graph Neural Networks) on expert model‘ outcomes

→ **Enables low-barrier web access for decision makers**

→ **Timely reaction for pandemic mitigation**







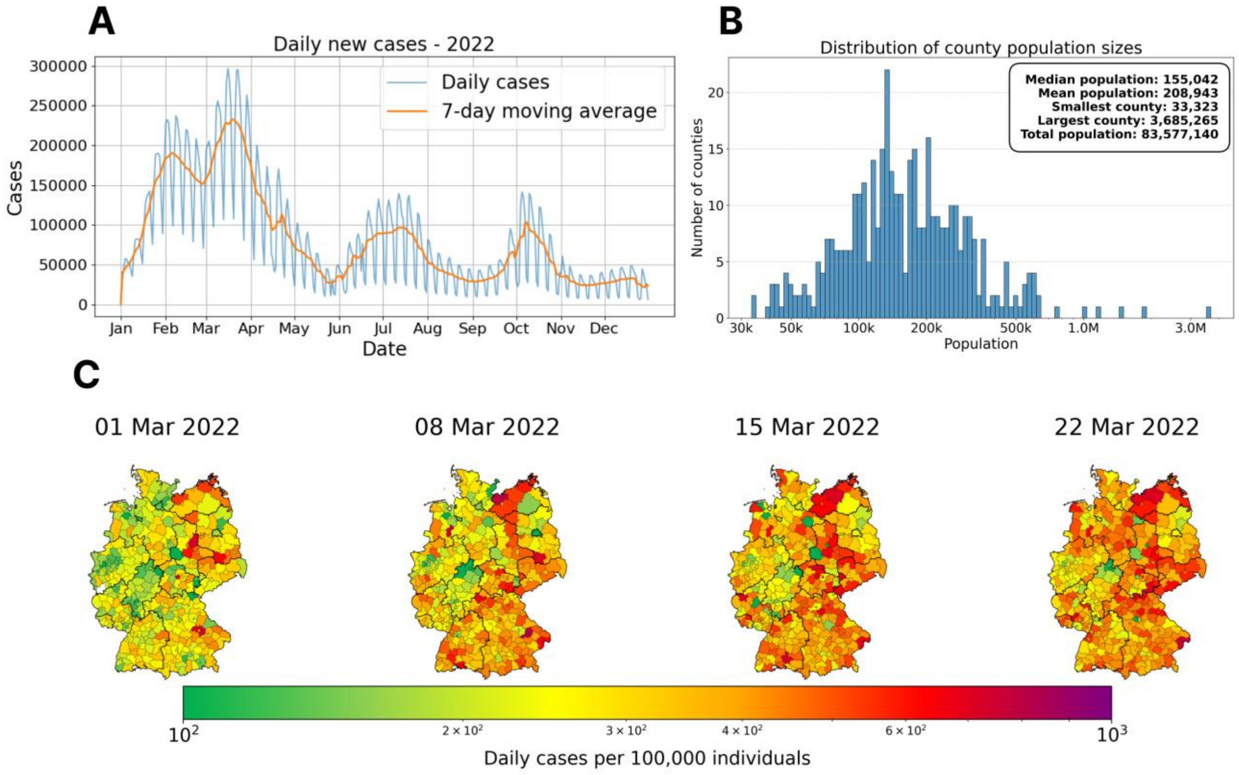
GNN (2025)

Schmidt et al., Submitted (2025) https://arxiv.org/abs/2411.06500

Federated learning with differential privacy

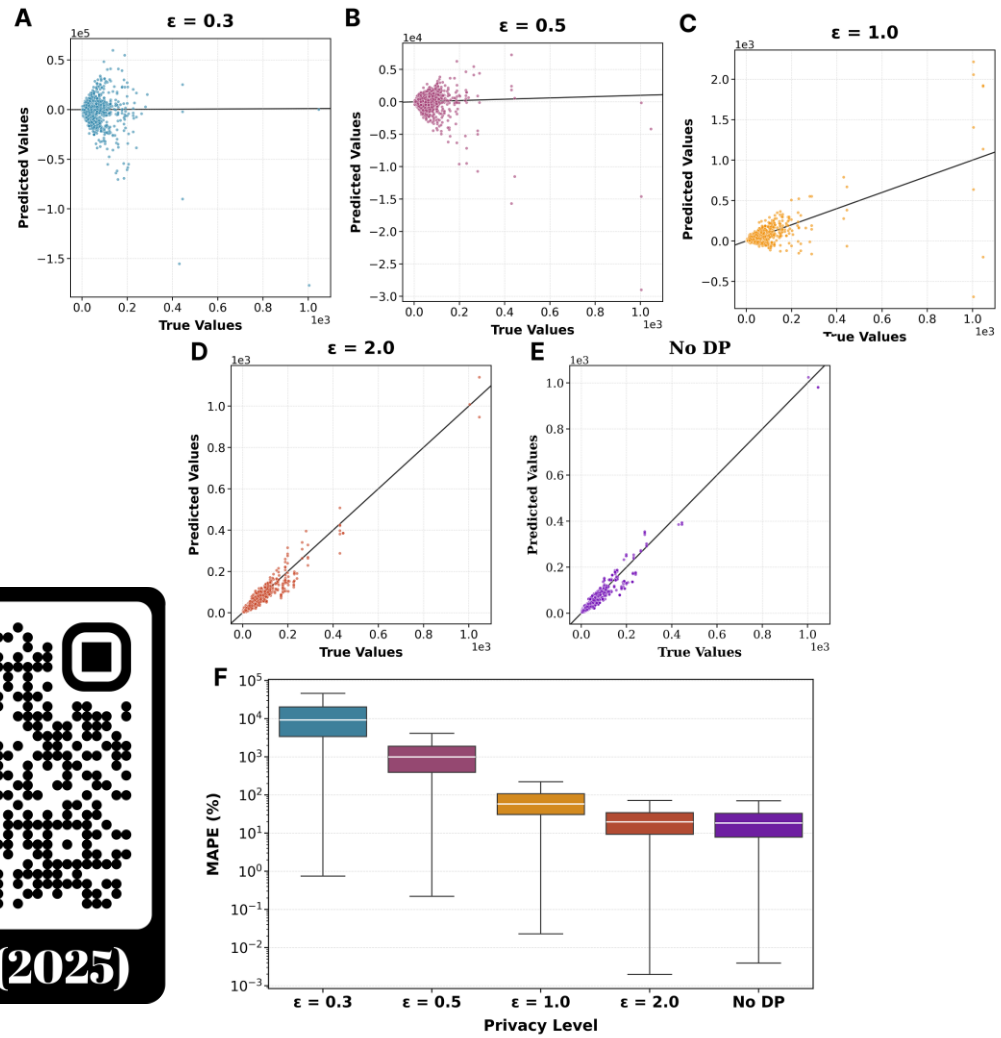
Henrik Zunker

- Centralizing data challenging due to high sensitivity and privacy constraints
- Federated learning train a shared model without centralizing raw data
- Differential privacy ensures protection of private and sensitive data



Kerkouche, Zunker et al., Submitted (2025)
https://arxiv.org/abs/2509.14024

FL-DP (2025)



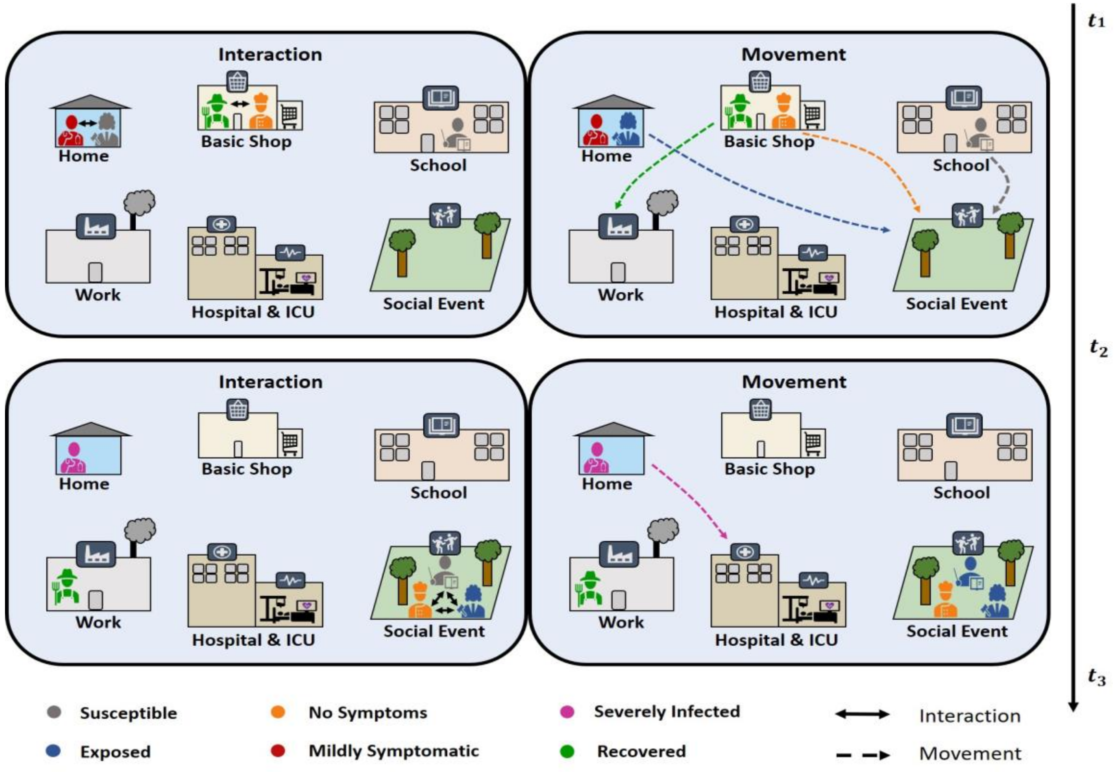
Agent-based modeling







- Model individuals (or households) as individual agents
- Computational cost scales (super)linearly with number of agents
- Study and answer research questions on a “microscopic“ level (e.g. individual decisions, test strategies, viral load…)

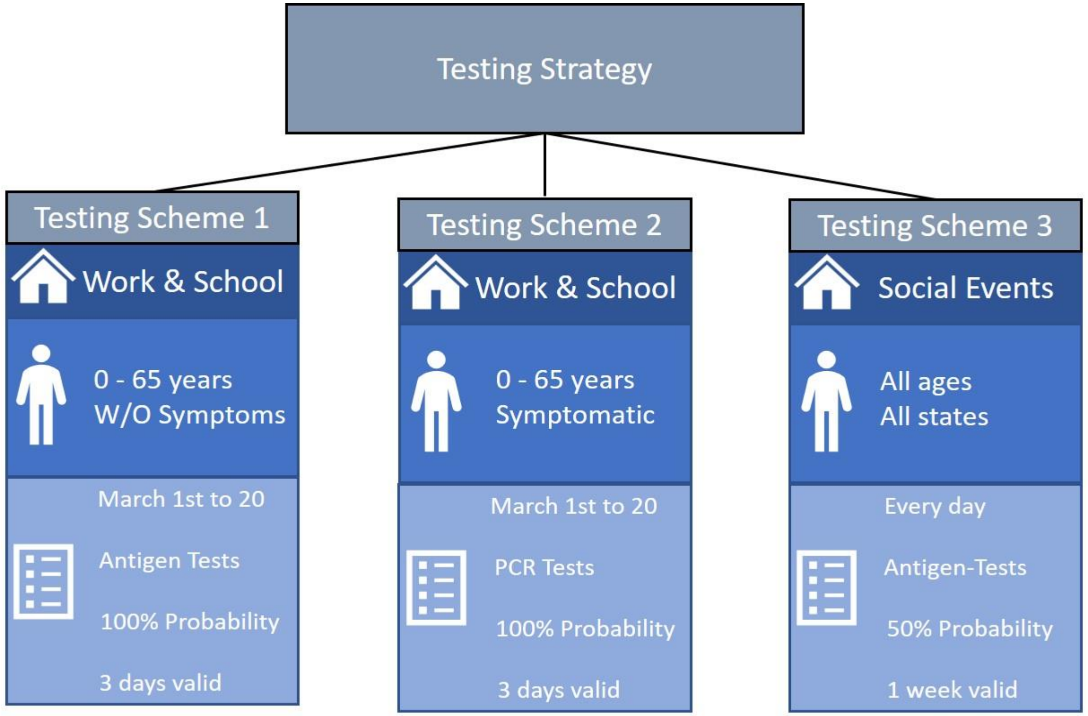


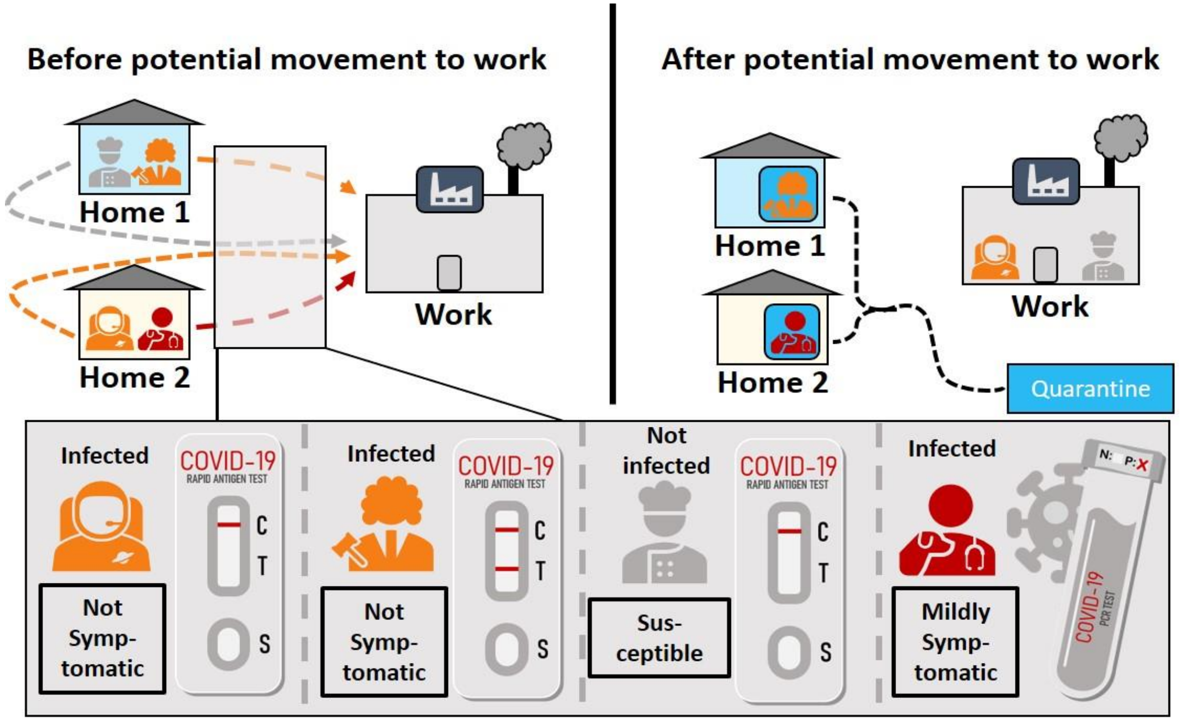
Algorithm 1: Trip-based agent-based simulation

$t \leftarrow t_0 \in \mathbb{R}$
while $t \leq t_{\max}$ **do**
  for *each location* **do**
    Execute agents’ interactions
  for *each agent* **do**
    Perform individual movement
  $t \leftarrow t + \Delta t$

Agent-based modeling: Testing strategies


Sascha Korf

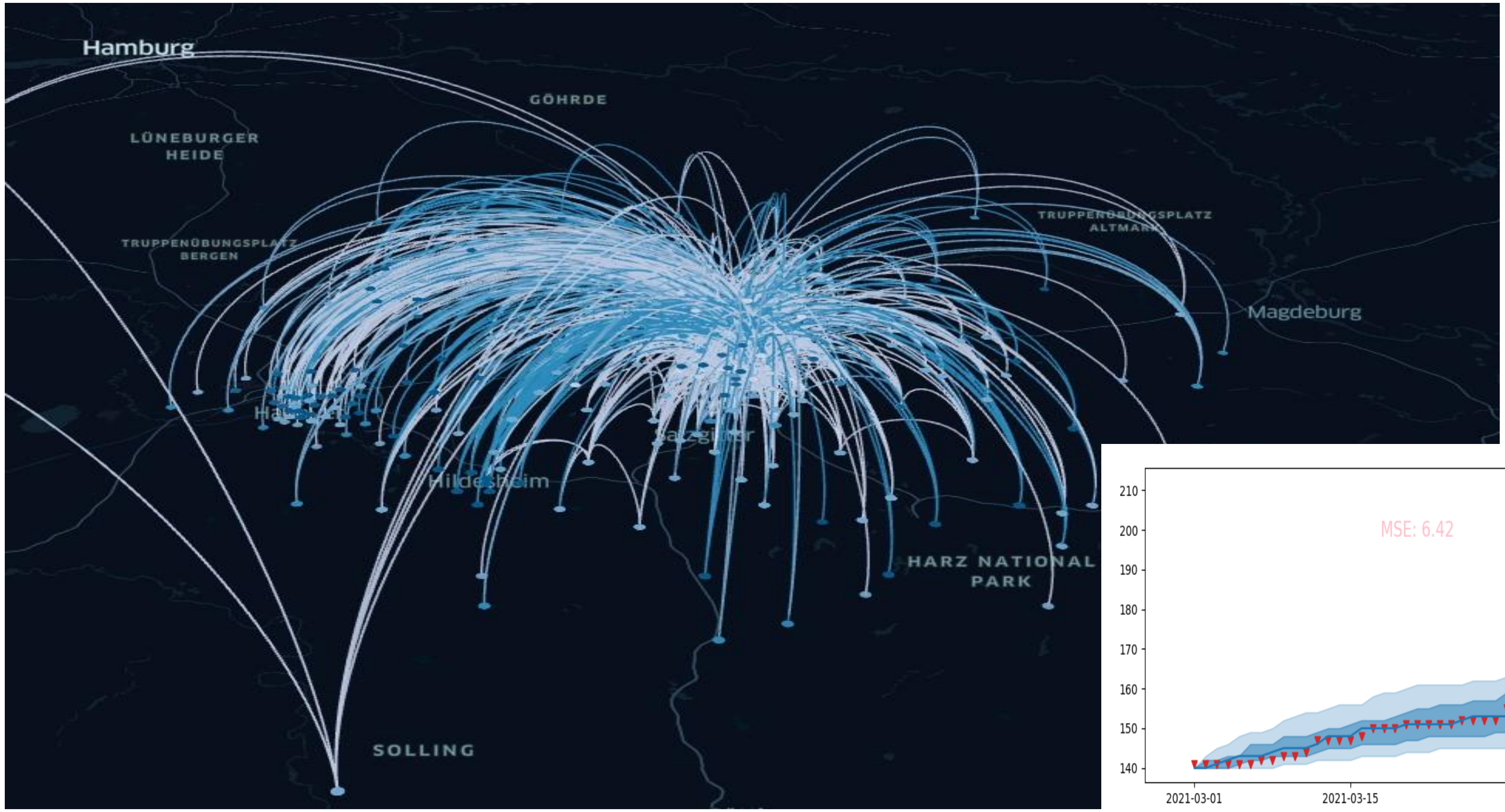




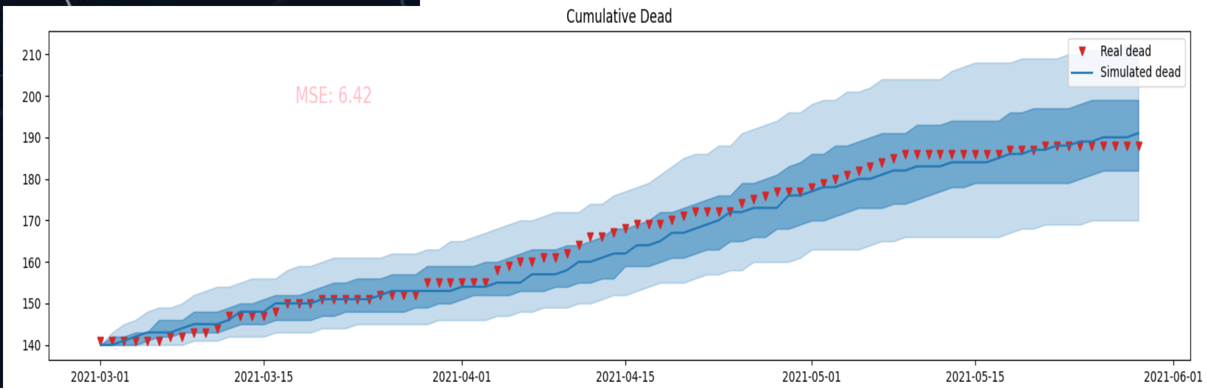
Sascha Korf

ABM: Application to city-scale

- Approximately 370.000 persons from Brunswick and the surrounding area
- Over 1.3 million trips per day



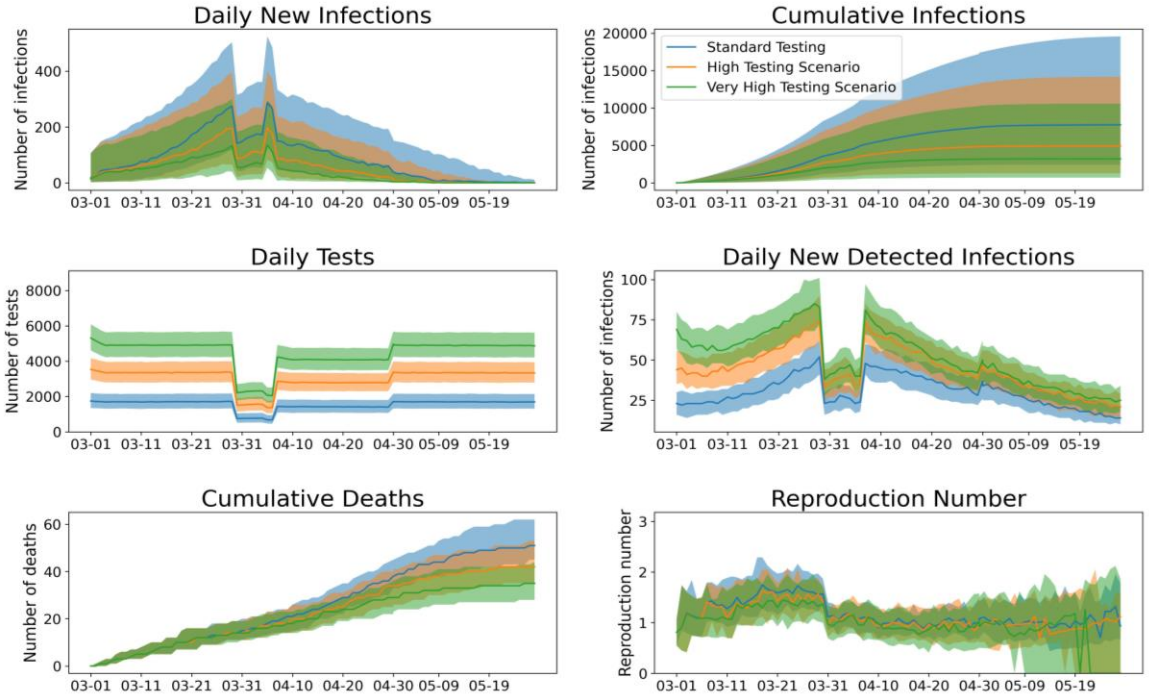
ABM (2025)



ABM: Advanced testing strategies

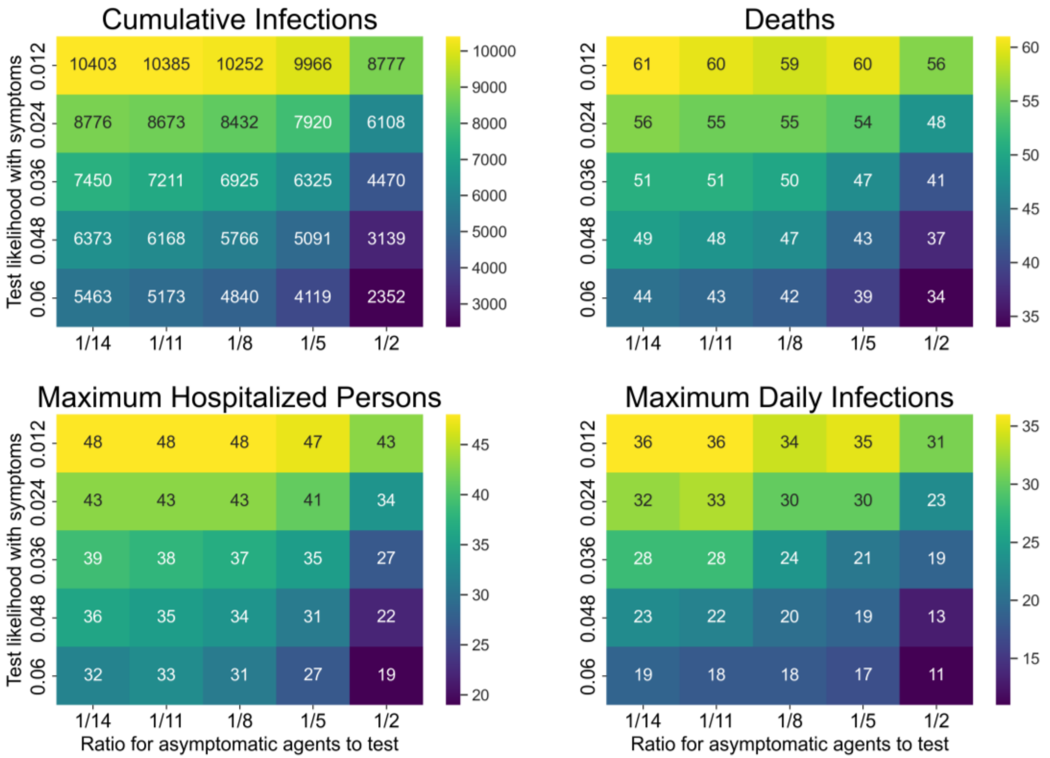

Sascha Korf

- Scenario analysis



- Symptomatic vs. general testing

More symptomatic testing



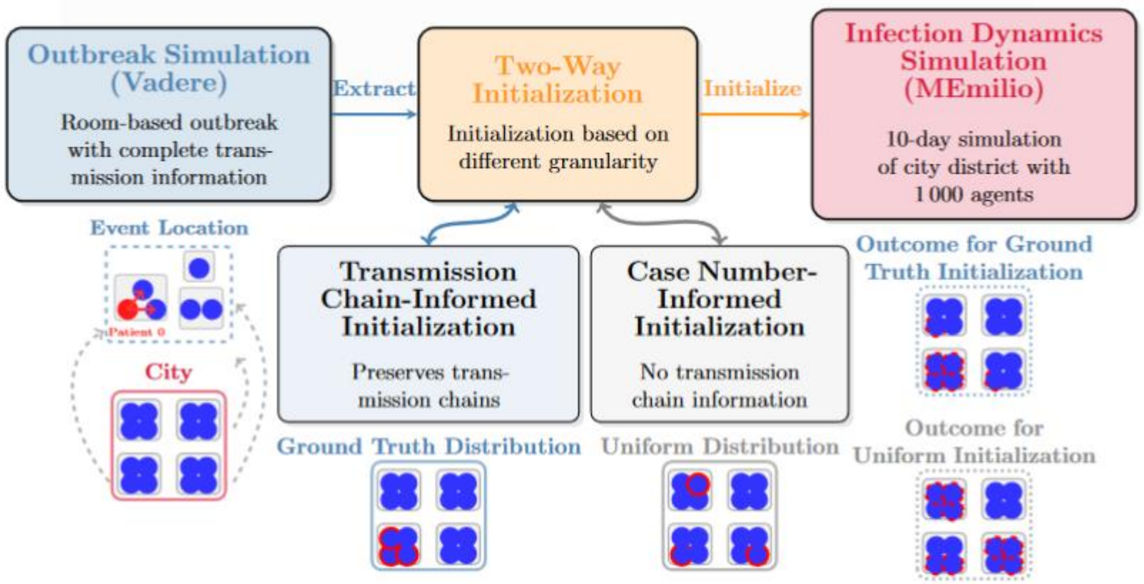
More symptom-independent testing

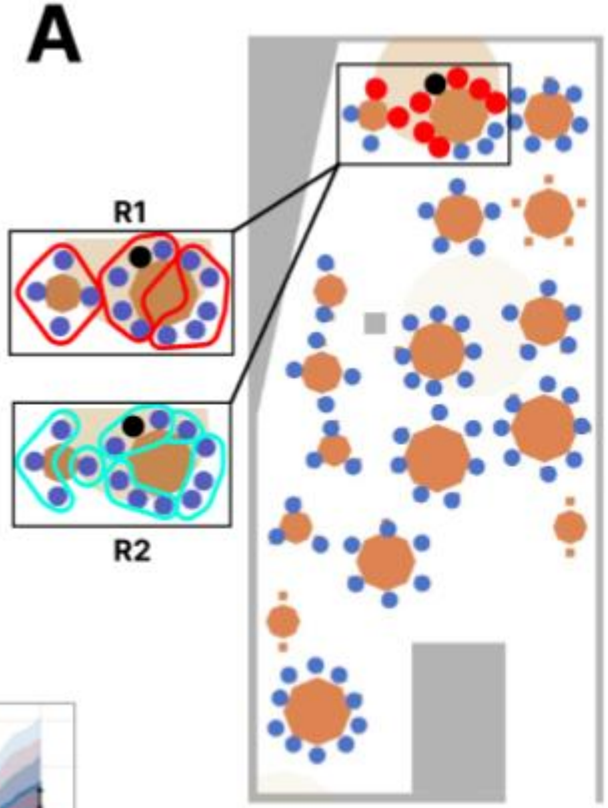
Kerkmann, Korf et al., Computers in Biology and Medicine (2025)
https://doi.org/10.1016/j.compbiomed.2025.110269

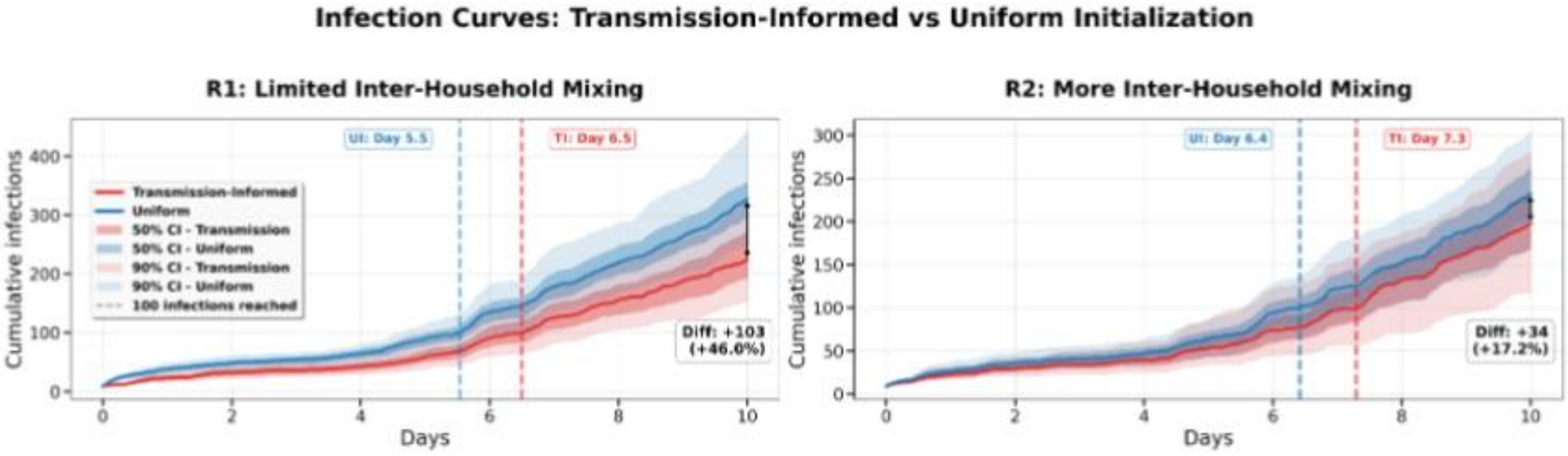
ABM (2025)

ABM: Effects of missing transmission chains

Sascha Korf







-- Link to come --

Korf et al., Submitted (2025)

ABM: Joint ABM-Wastewater model

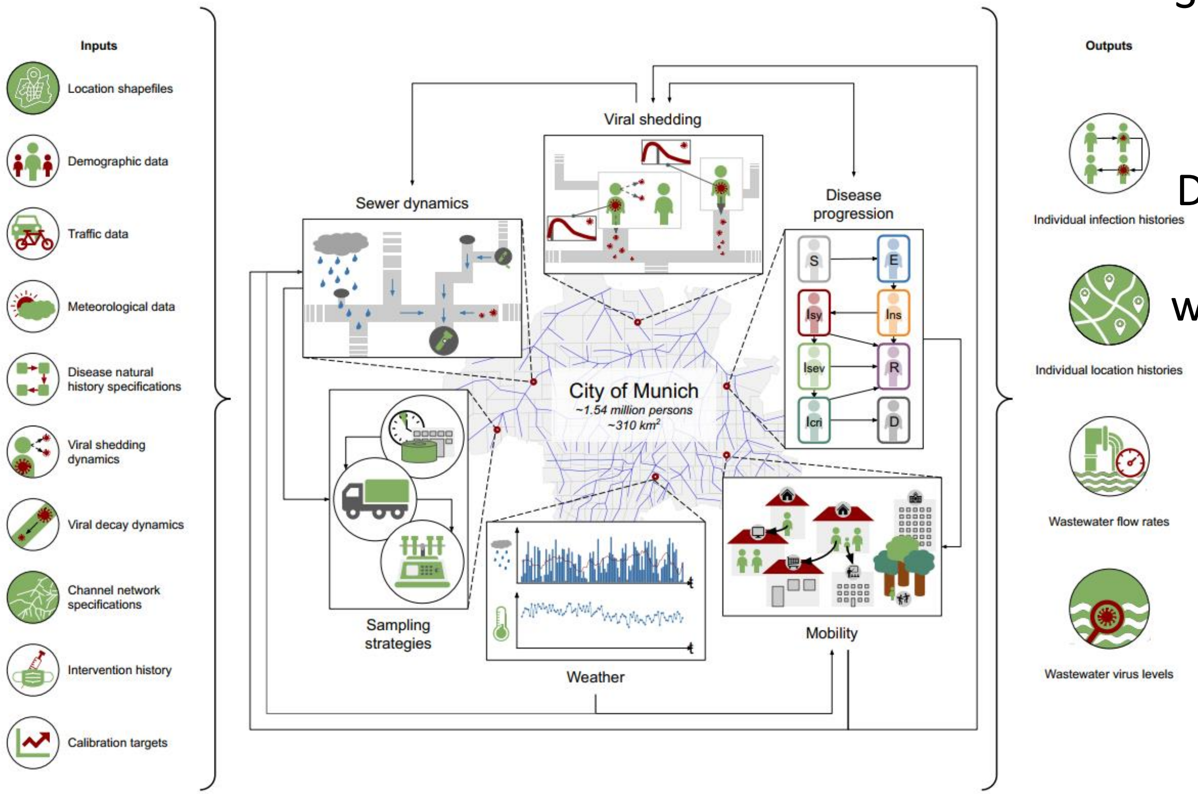
INSIDe

Munich (2025)

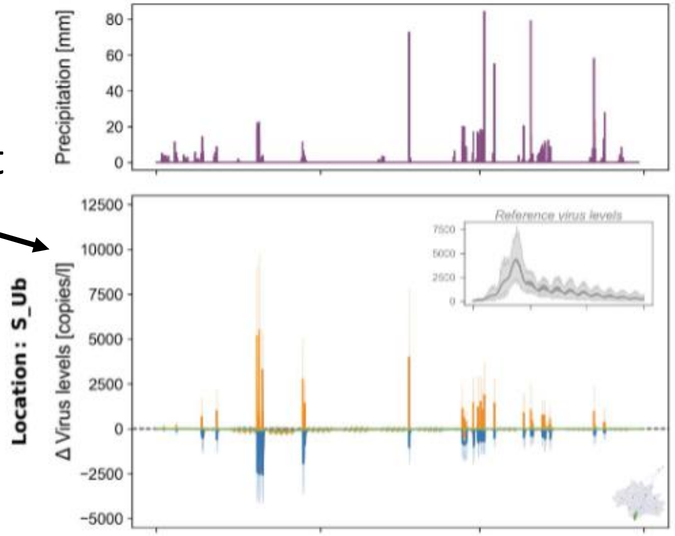
Julia Bicker

DLR

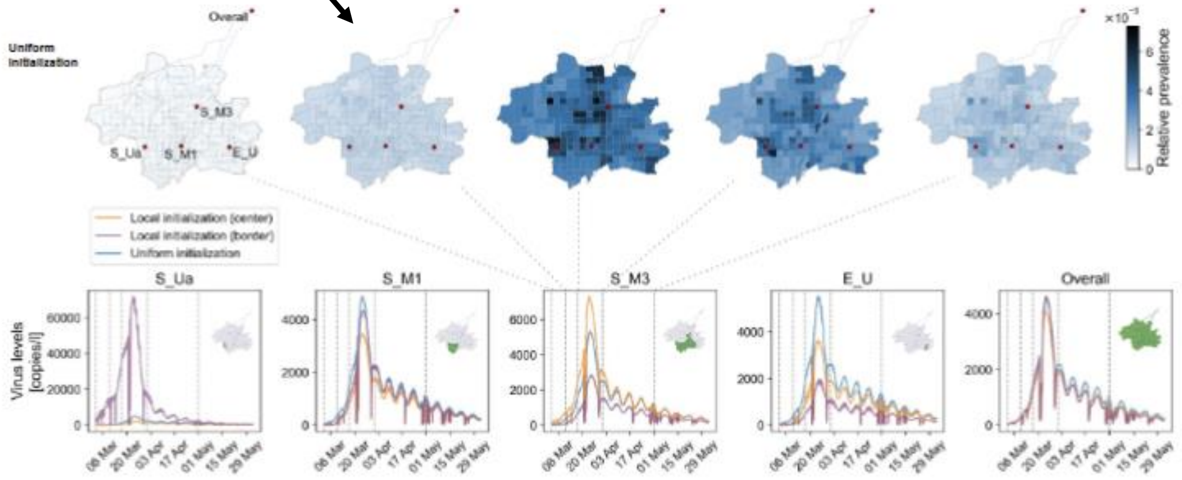
"How does can testing-based detection be improved by combination with wastewater?"



Studying the effect of different normalization strategies for rain events



Detailed insights into population and wastewater dynamics



Bicker, Tomza, Wallrafen et al., Submitted (2025)

https://doi.org/10.1101/2025.09.25.25336633

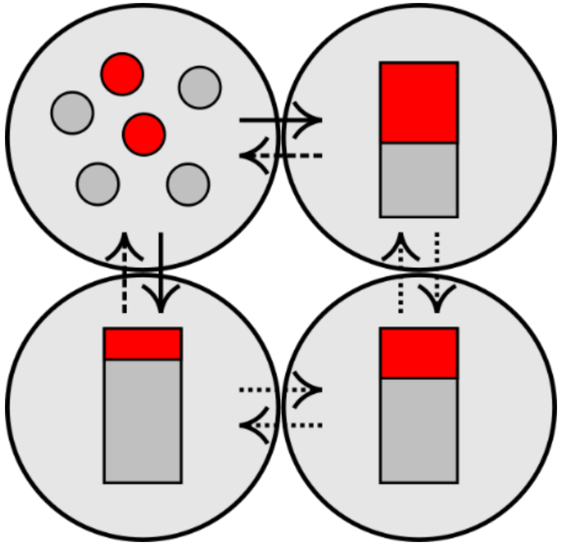
Hybrid agent-metapopulation: Spatial hybrid


Julia Bicker


René Schmieding

- Idea:
  - Interest in infection spread in particular region
  - Exclusive availability of data in specific region (or computational resources limited)
- Concept:
  - Agent-based model in region of interest (focus region)
  - ODE-based models for connected regions

→ **Detailed results** in focus region while considering **influence of connected regions** in **runtime efficient** manner



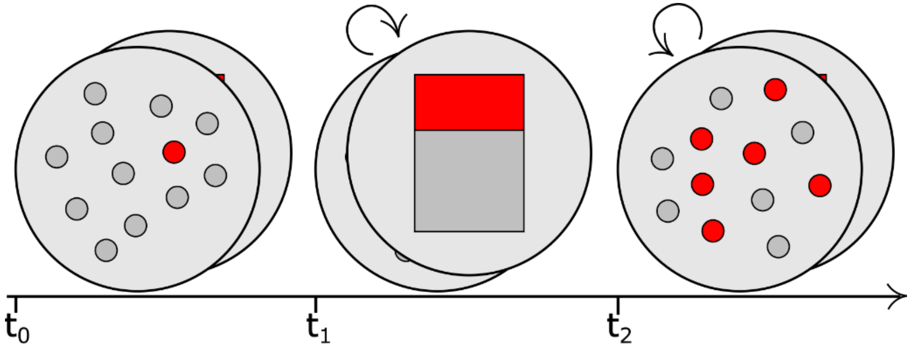
Bicker, Schmieding et al., Infectious Disease Modelling (2025)
https://doi.org/10.1016/j.idm.2024.12.015

Hybrid agent-metapopulation: Temporal hybrid

Julia Bicker

René Schmieding

- Idea:
  - Low case numbers:
    High stochasticity and individual behavior is important
  - High case numbers:
    Individual behavior is less influential and single simulation outcomes are close to averaged results



- Concept:

  Switch between agent-based and ODE-based model during the simulation according to a threshold value

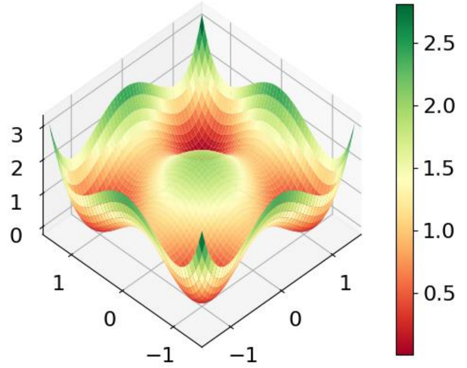
  → Capture stochasticity and individual behavior when necessary for **accurate outcomes** while using **runtime advantage** when possible

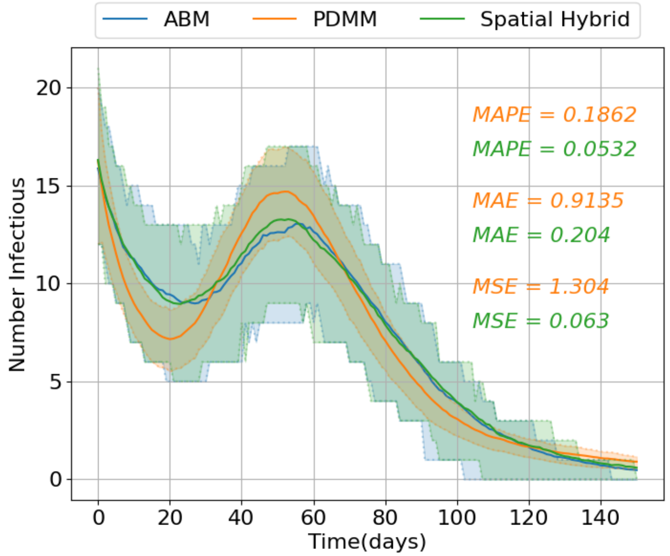
Bicker, Schmieding et al., Infectious Disease Modelling (2025)
https://doi.org/10.1016/j.idm.2024.12.015

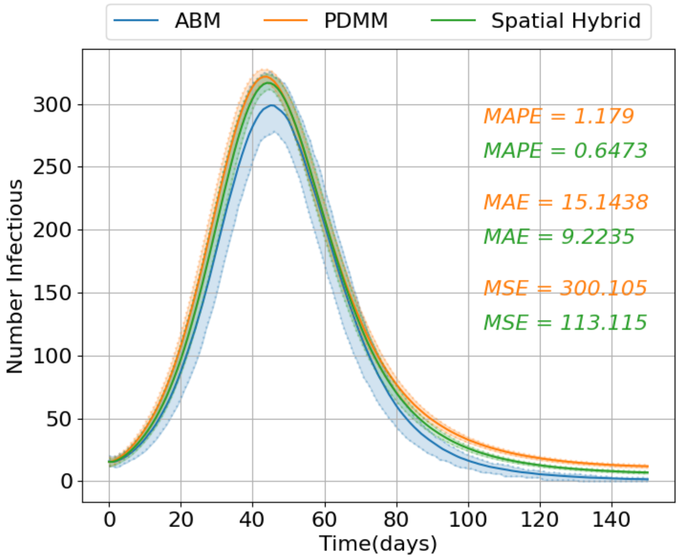
Proof-of-concept spatial hybrid model

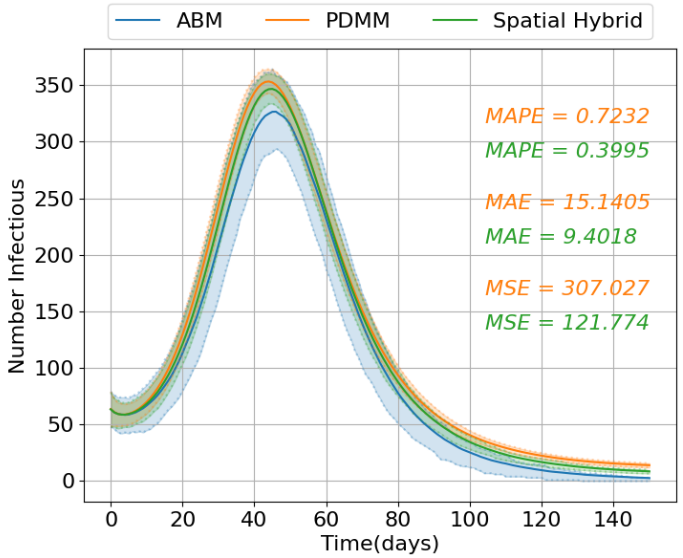

Julia Bicker René Schmieding

- Setup: 8000 agents, 1% of population initially infected
- Focus region: $\Omega_1 = (-\infty, 0) \times (0, \infty)$
- Transmission rate in $\Omega_2 = (0, \infty) \times (0, \infty)$ corresponding to $R_0 = 2.4$
- Transmission rate in other regions corresponding to $R_0 = 0.8$









Bicker, Schmieding et al., Infectious Disease Modelling (2025)
https://doi.org/10.1016/j.idm.2024.12.015

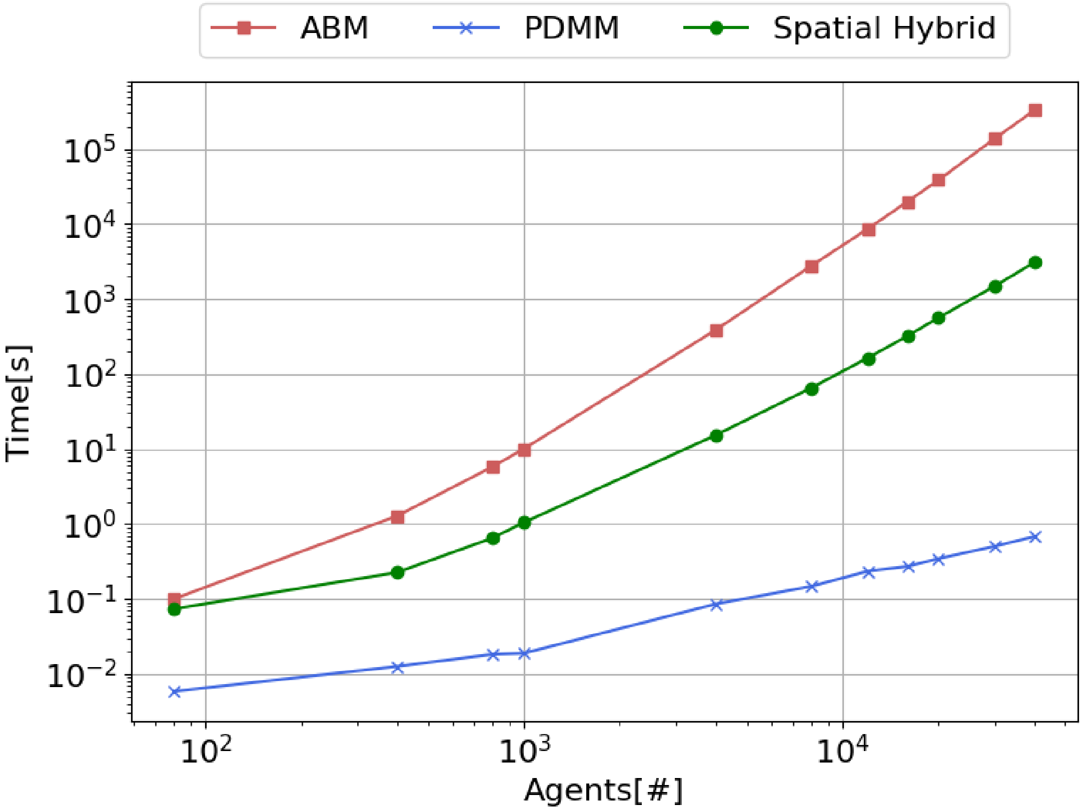
Julia Bicker

René Schmieding

Proof-of-concept spatial hybrid model

- Spatial-hybrid has same scaling behavior like ABM
- For **400 agents**: Runtime of spatial-hybrid **1 order of magnitude** lower than for ABM
- For **40,000 agents**: Spatial-hybrid reduces runtime by **98%**

Hybrid (2025)



Bicker, Schmieding et al., Infectious Disease Modelling (2025)
https://doi.org/10.1016/j.idm.2024.12.015

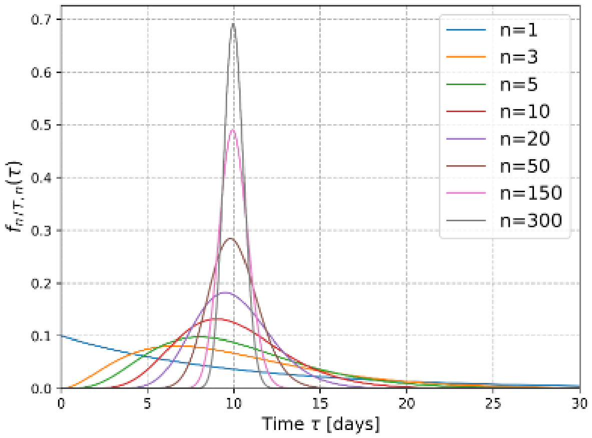
Basic model properties
(without spatial resolution for now)

Impact of distributions on epidemic peaks

Lena Plötzke

Anna Wendler

- Distributions have impact on epidemic peaks and timings
- Literature sometimes mentions over- / underestimation by exponential distribution
- Situation is highly complex and no general rule



Different Erlang/Gamma distributions

LCT (2025)

https://doi.org/10.1016/j.matcom.2025.07.045

Plötzke et al., Mathematics and Computers in Simulation (2025)

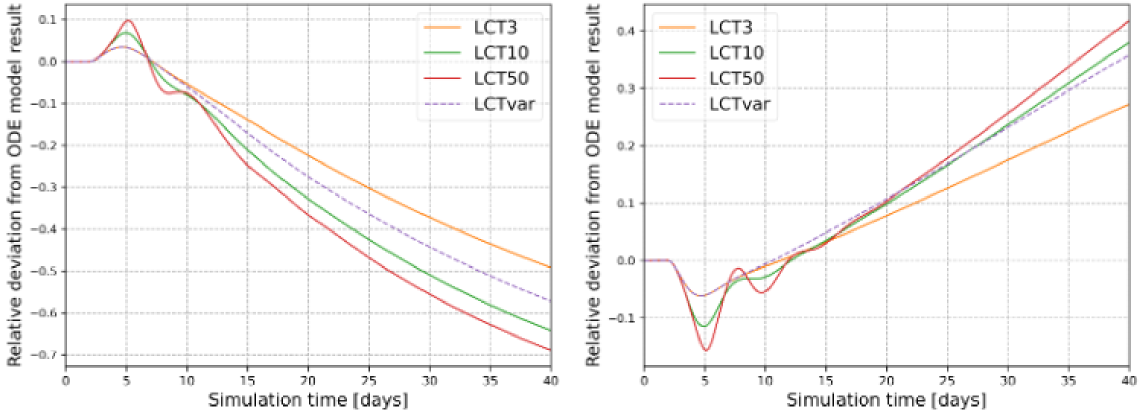


Figure 7: Relative difference in daily new transmissions around change points. Relative comparison of the daily new transmissions of different LCT models compared to a simple ODE model around change points. The contact rate $\phi(t)$ is halved (left) or doubled (right) after the second simulation day. Further notation as in Fig. 3.

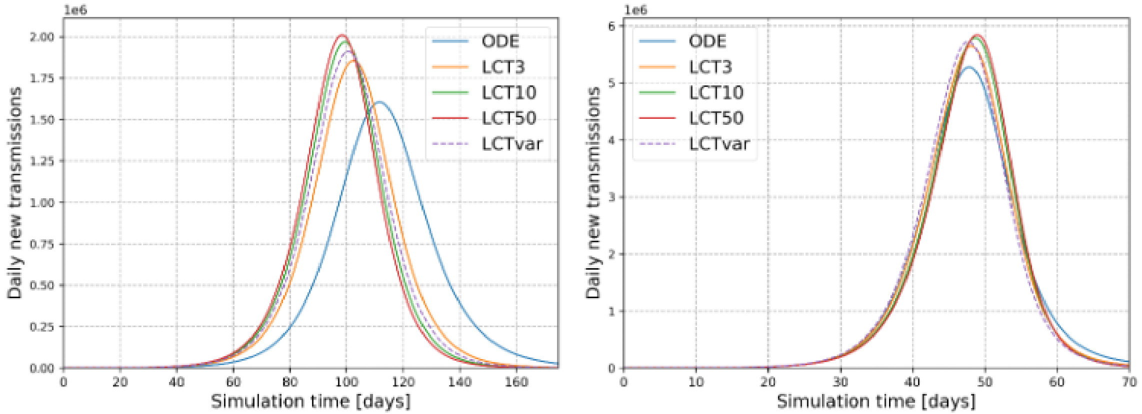


Figure 8: Daily new transmissions to compare the predicted epidemic peaks. Illustration of the predicted peaks of the daily new transmissions of LCT models with different numbers of subcompartments against a simple ODE model. The contact rate is set such that $\mathcal{R}_{\text{eff}}(0) \approx 2$ (left) or $\mathcal{R}_{\text{eff}}(0) \approx 4$ (right). Further notation as in Fig. 3.

Integro-differential equation-based (IDE) model

Anna Wendler

- Simple ODE models are restricted to exponential stay time distributions
  → not realistic according to literature
- First generalization: Use of Linear Chain Trick allows Erlang distributed stay times
- Full flexibility: Models based on integro-differential equations (IDEs) allow **arbitrary stay time distribution**

Advantages:

- Possibility to capture **more realistic modeling assumptions** than ODE models
- Parameters can be made dependent on **time since infection**, e.g. mean infectivity
- Can include **history of disease dynamics** when initializing

Disadvantages:

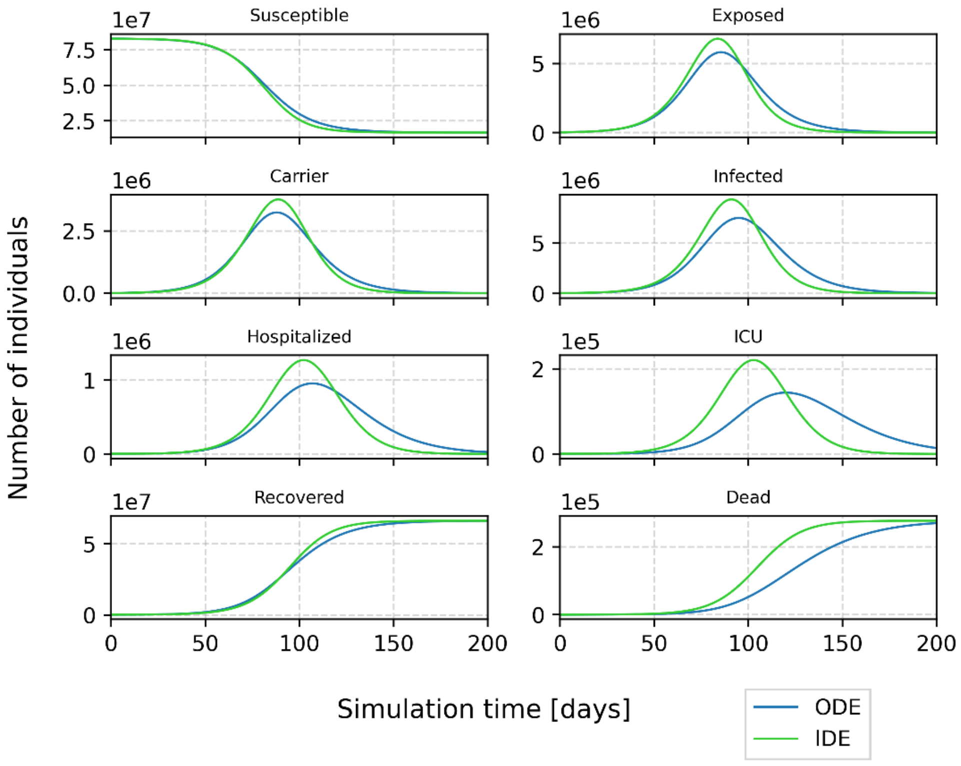
- Only few numerical solvers available; **not as efficient as ODE solvers**
- Data on distributions not widely available
- Assumption of (to some extent) **homogenous and well-mixed population**

IDE application

- Lognormal distributions according to data on COVID-19 in IDE model
- Corresponding exponential distributions in ODE model
- Epidemic peaks differ with respect to size and timing

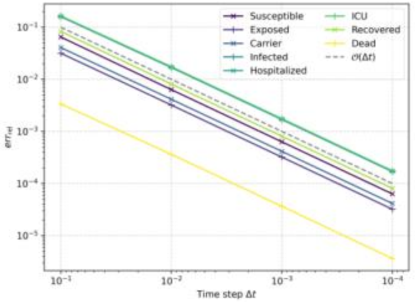
→ Distribution assumption has impact on simulation results and thus on basis for mitigation action

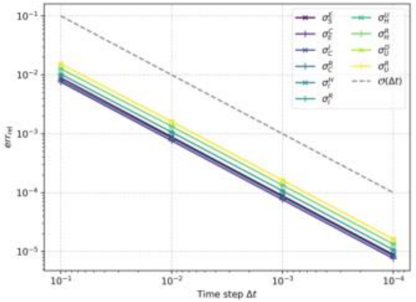
- Numerical scheme preserves biological properties and converges linearly



Anna Wendler

https://doi.org/10.1016/j.amc.2025.129636
Wendler et al., Applied Mathematics and Computation (2025)



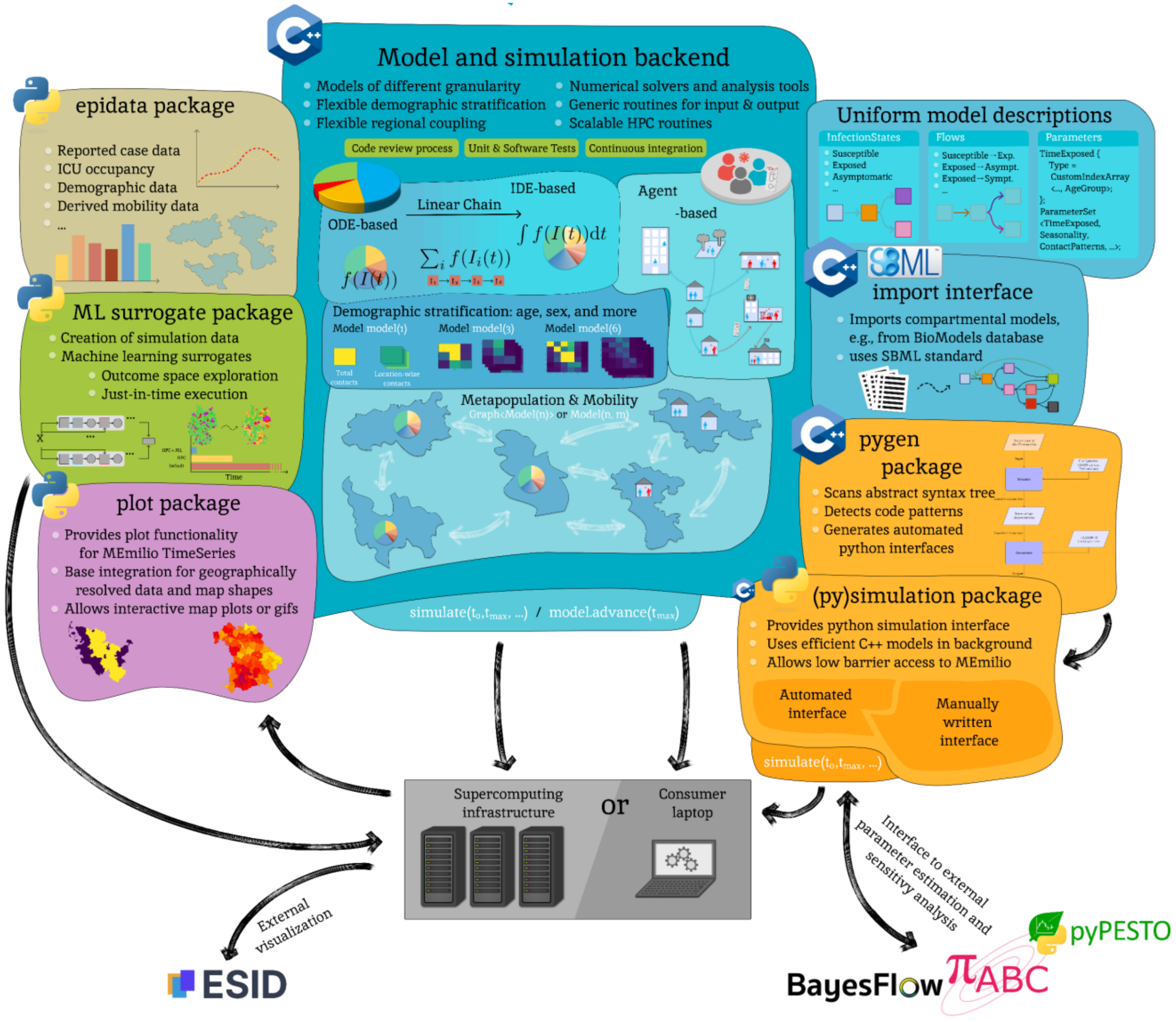


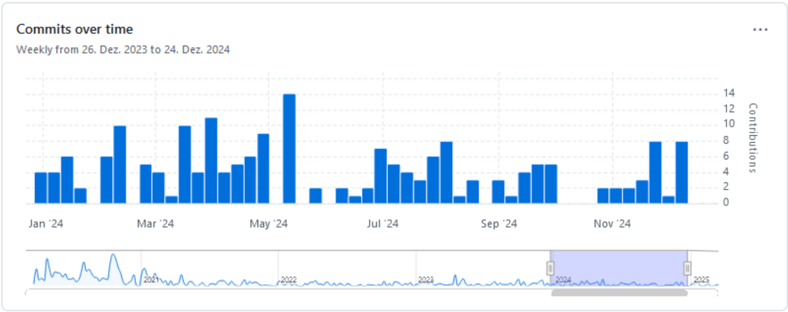
IDE (2025)

MEmilio

A high performance Modular EpideMIcs simuLatIOn software

DLR





Contributors

- 2024: 20
- Overall: 41

Activity (on main) August 2025

- 20 active pull requests (12 merged)
- 31 active issues (22 closed)
- 18 active authors

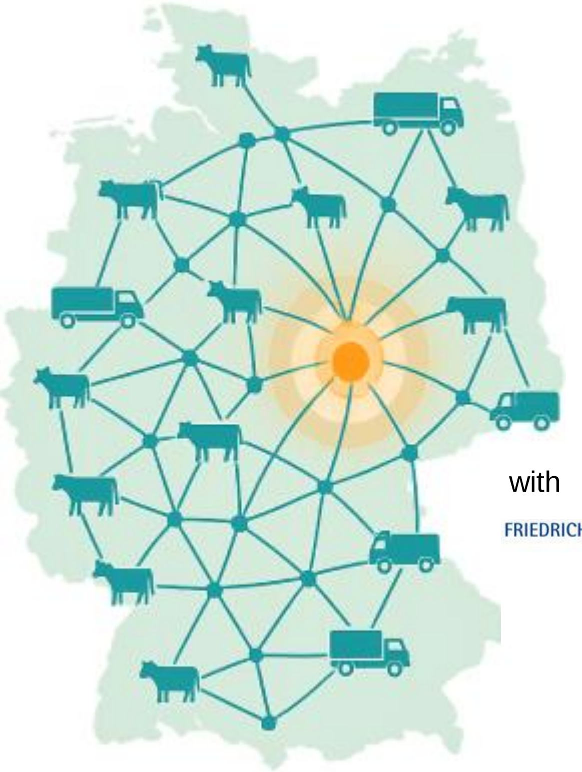
Software & Unit Tests

CI passing · codecov 97%

- C++: ca. 650 (2023: ca. 300)
- Python: ca. 230 (2023: ca. 200)

What applications are next (and new)?

- To some extent: RSV, Influenza, highly pathogenic avian influenza (HPAI)
- Post-acute infection syndromes (PAIS), in particular Long Covid/PCC
- Aerosol modeling and transmission chains
- Extension of AI surrogate models
- Model the spread of a foot-and-mouth disease outbreaks
  - affected animals: cattle, sheep, pigs
  - Test out different interventions measures with respect to financial and workforce constraints
  - Use a graph for the transport network and stochastic models for each herd (180.000 nodes)
  - Use spatial information to represent disease spread along other transmission paths



Kilian Volmer

with

FRIEDRICH-LOEFFLER-INSTITUT
FLI
Bundesforschungsinstitut für Tiergesundheit
Federal Research Institute for Animal Health

Workshop:
Multiscale Infectious Disease Modeling

March 18-20, 2026

https://www.bcml.uni-bonn.de/bcmls2

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Thanks to our funders! / Thank you for your attention!

Questions / Exchange ? → **Martin.Kuehn@DLR.de**