Mathematical modeling of infectious diseases: An introduction

Mathematical Colloquium @ Heinrich Heine University Düsseldorf

Martin J. Kühn

based on joint work with

Daniel Abele, Wadim Koslow, Margrit Klitz, Kathrin Rack, Martin Siggel, Luca Spataro, Jonas Gilg, Jan Kleinert, Matthias Häberle, Lena Plötzke, Achim Basermann, Sebastian Binder, Michael Meyer-Hermann

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Motivation

Most recent epi- and pandemics:

- 2019: SARS-CoV-2 (≈5m deaths [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])

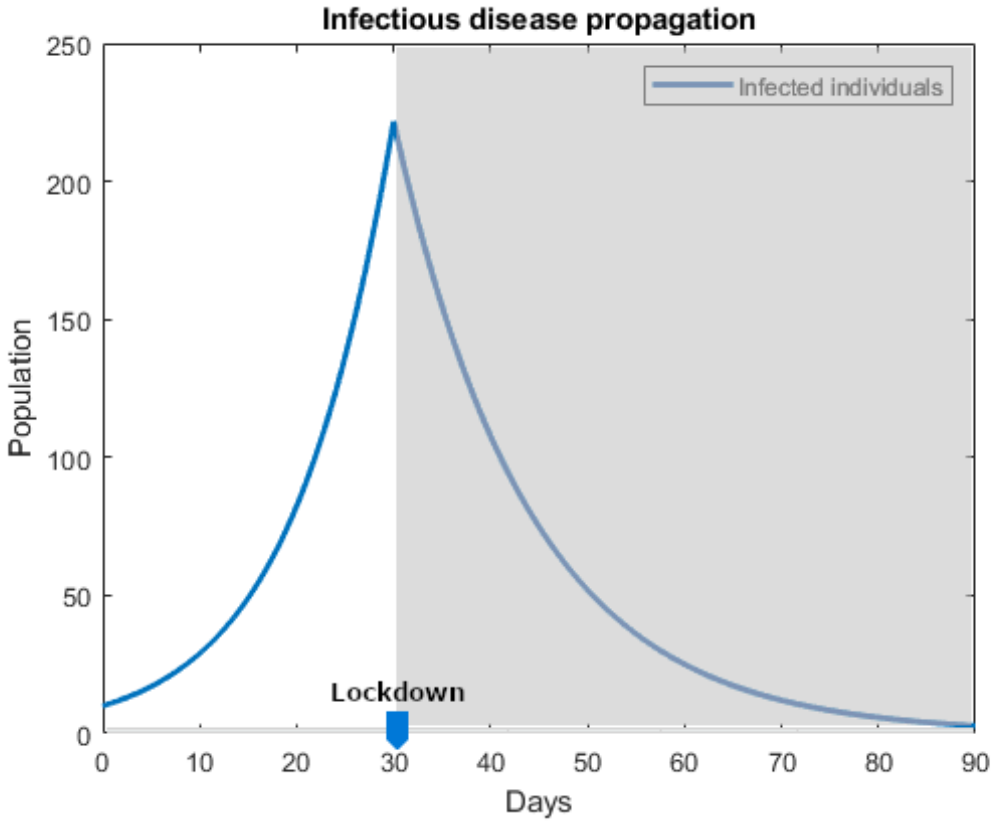
cf. [1] Johns Hopkins University (JHU), [2] Abdelrahman et al., Front. Immunol. (2021).

UNESCO/IPBES report:

- "future pandemics will emerge more often, spread more rapidly, do more damage to the world economy"
- "experts estimate that the cost of risk reduction to prevent pandemics is 100 times less than the cost of responding to such pandemics"

Motivation

Educational tools available:

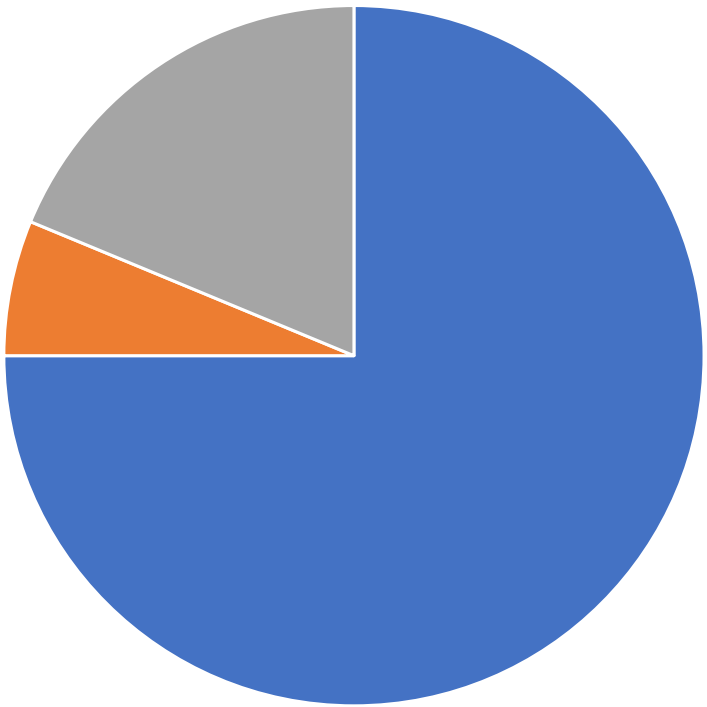


...but not suited for informed decision!

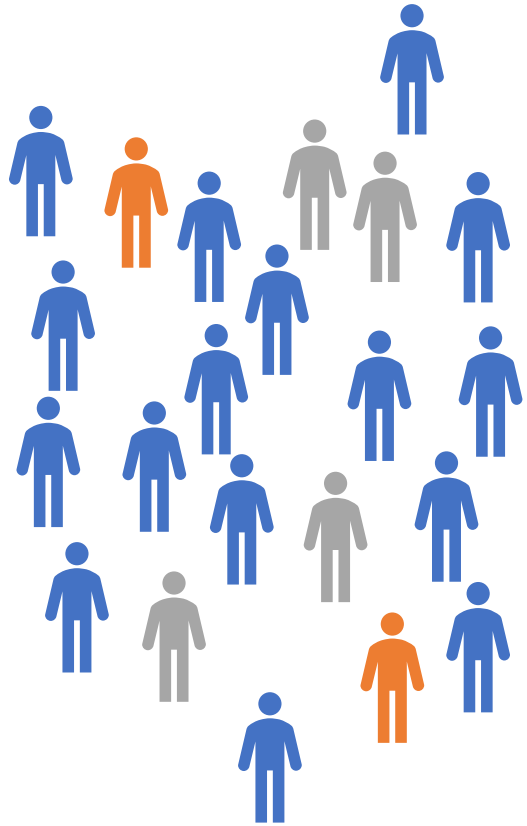
Outline

- Approaches to model the spread of infectious diseases
- Ideas and limitations of simple ODE-models
- From ODE-models to Integro-Differential equation-models
- Hybrid graph-ODE-SIR-type/metapopulation models
- Some comments and perspective

Modeling of infectious diseases: One classification approach



- Differential equations
- Delay-differential equations
- Integro-differential equations



Agent-based modeling

Simple ODE- or Agent-based modeling

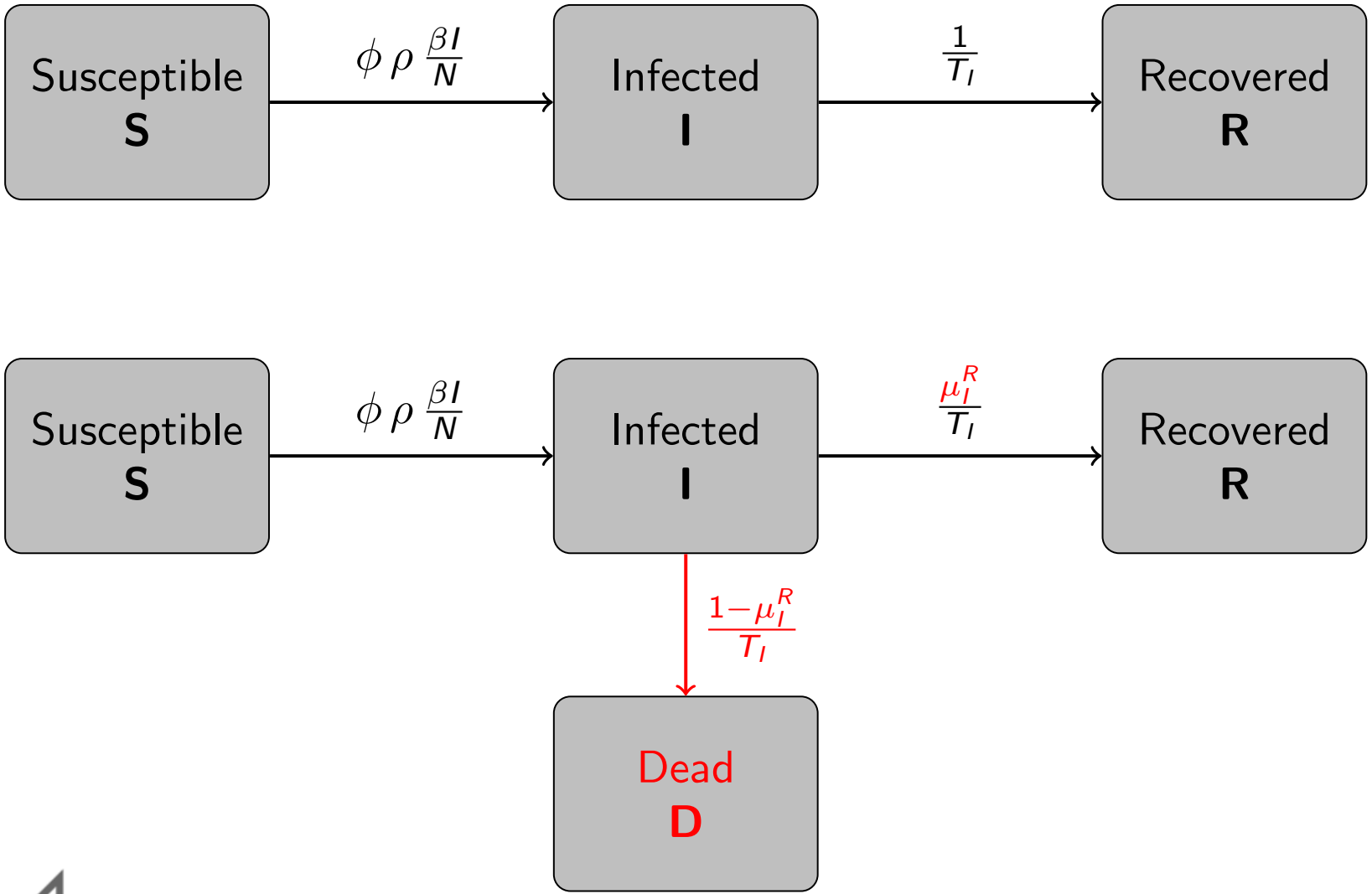
- *Compartments* (in ODE-models) or *(infection) states* (in ABMs) define different infection states of a disease, e.g.
  - **S**: Susceptible
  - **I**: Infected
  - **R**: Recovered
  - $N = S + I + R$: Total population
- Compartments contain proportions of the population, i.e., subpopulations
- Often *SIR-model* is used equivalently with *ODE-SIR model* but ABM-SIR or IDE-SIR could be meant as well!

Simple ODE-based modeling

- ρ: transmission risk
- ϕ: daily number of contacts
- T_{C_1}: time in a compartment C_1
- $\mu_{C_1}^{C_2}$: transition probability to get from C_1 to C_2

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

Simple ODE-based modeling of infectious diseases: SIR/SIRD/SIR-type



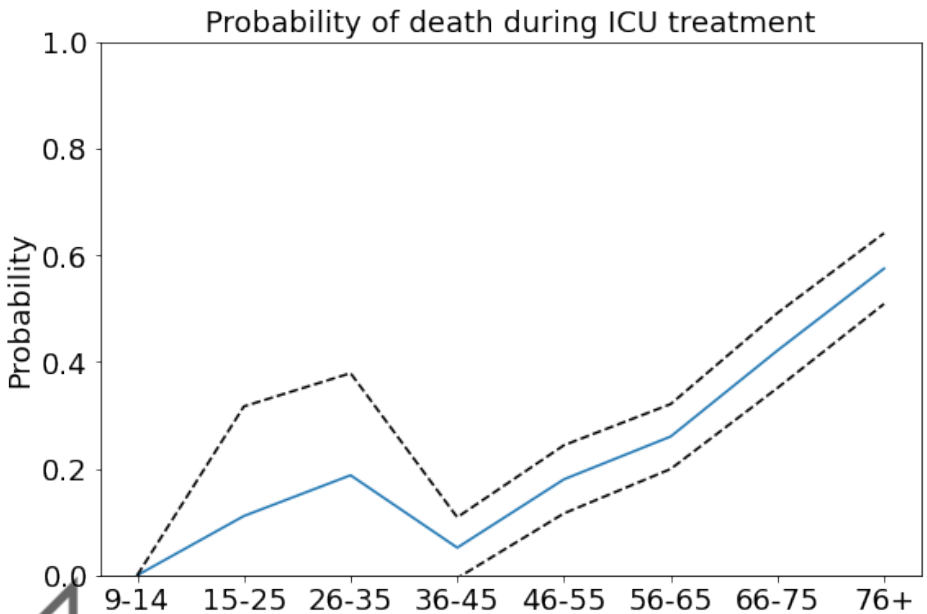
ODE-based modeling: Advantages and limitations

- cheap to compute
- well established methods to analyze for, e.g., equilibria
- homogeneous mixing assumption may be wrong
  → introducing age-resolution (ODE)
  → introducing different subpopulations (ODE)
  → introducing spatial heterogeneity (hybrid)
- compartment stays are exponential and, e.g., viral load constant
  → considering integral terms (Integro-DE)
- stochastic effects not reflected
  → ... (SDE/ABM)

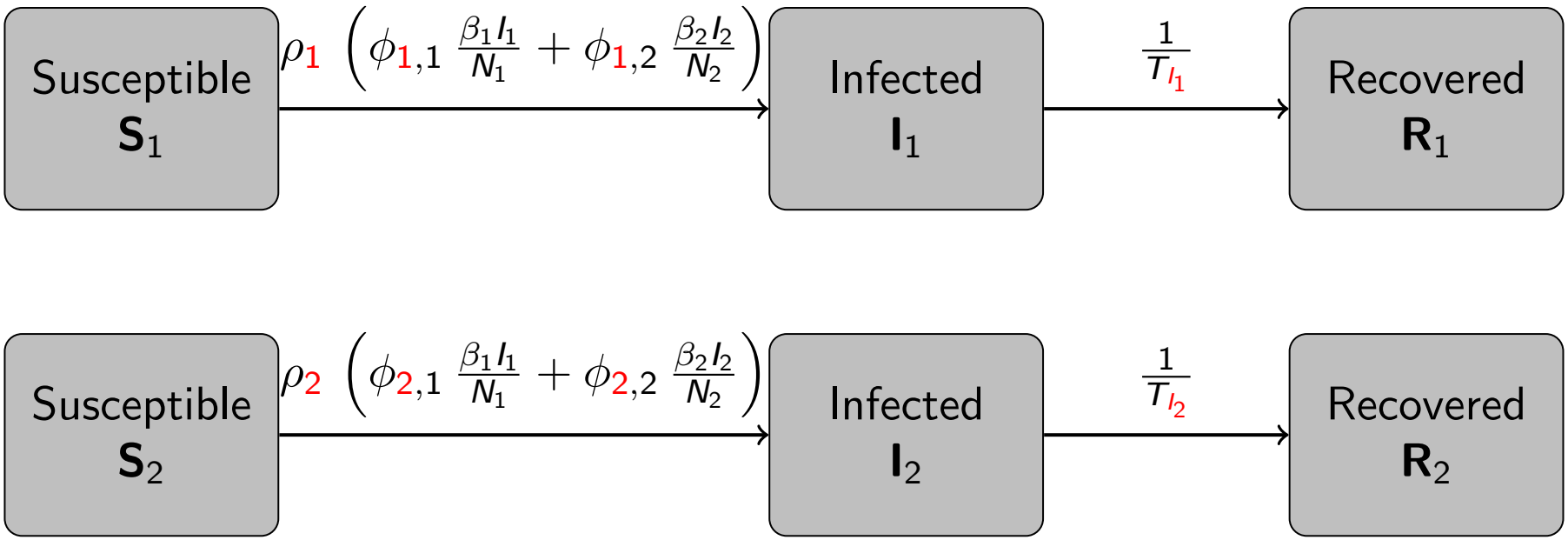
Motivation for age-resolved models

"...age structure is one of the most important aspects of heterogeneity in disease modeling." (Brauer et al. Mathematical models in epidemiology, (2019))

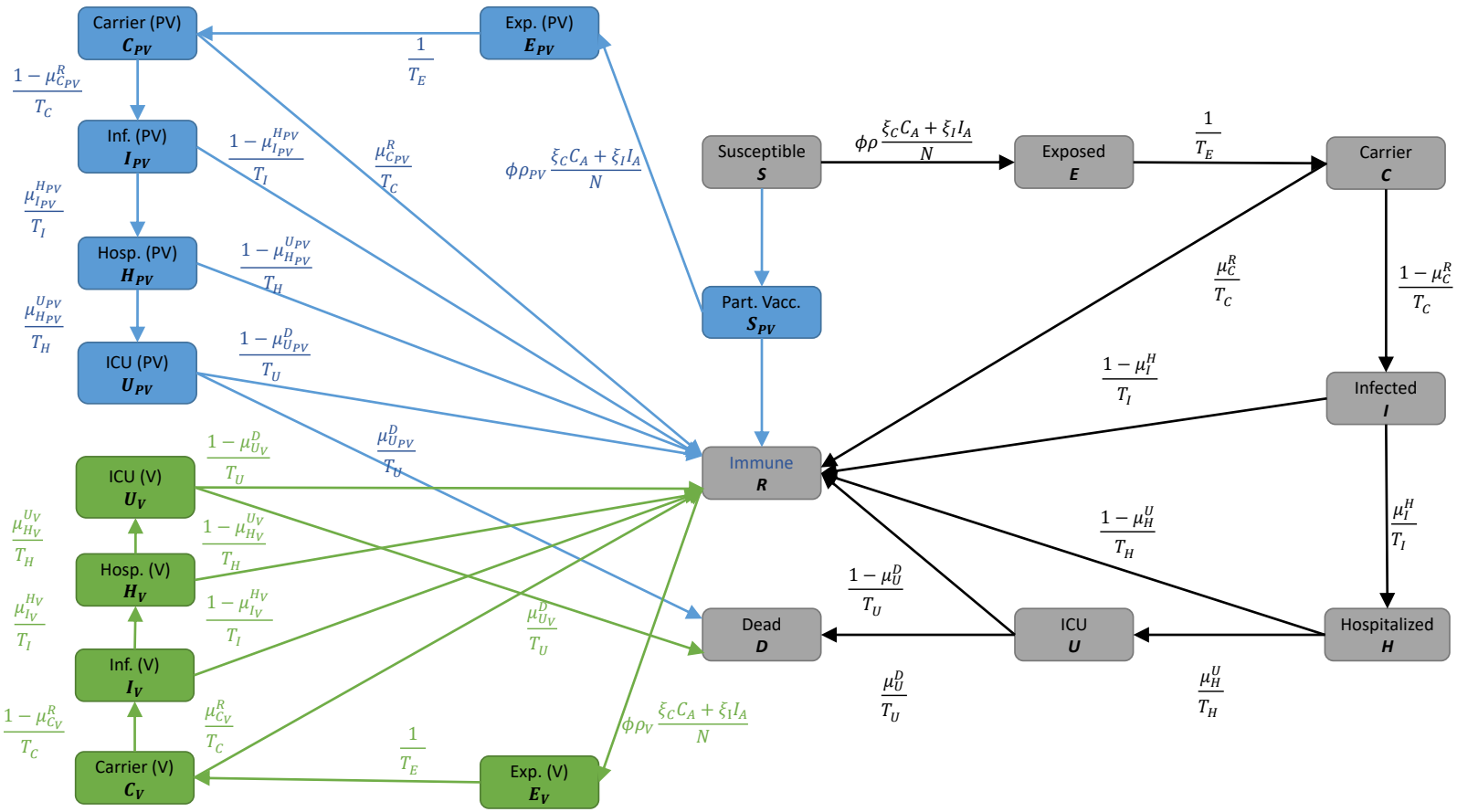
- Nonpharmaceutical interventions focus different age-groups, e.g.,
  - School closures
  - Remote working
  - Senior protection
- Disease parameters are highly age-dependent



Simple example of age-resolved models for two age groups



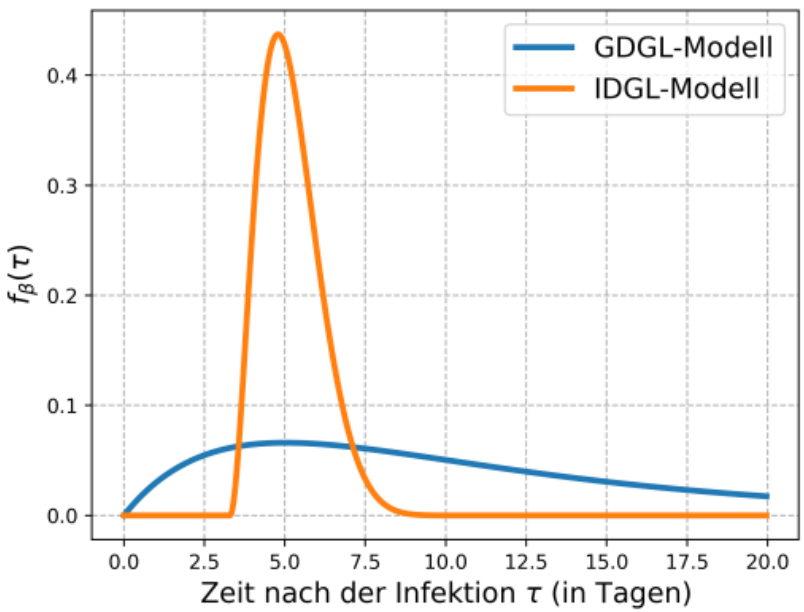
An ODE-SIR-type model with vaccination paths and hospitalization surveillance



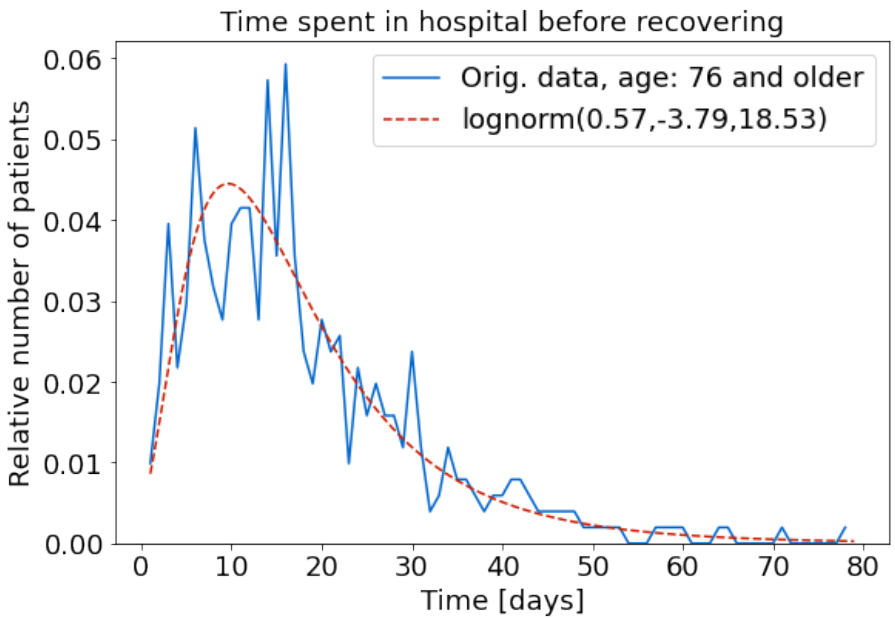
More details: Koslow et al., "Appropriate relaxation of non-pharmaceutical interventions minimizes the risk of a resurgence..." (2021).

Digression on parameter distributions

"Infectiousness" over time



Analysis of LEOSS data set



More details: Kühn et al., Math. Biosciences (2021), Keimer/Pflug (2020), Plötzke (2020).

Generalization to Integro-Differential equations (age of infection models)

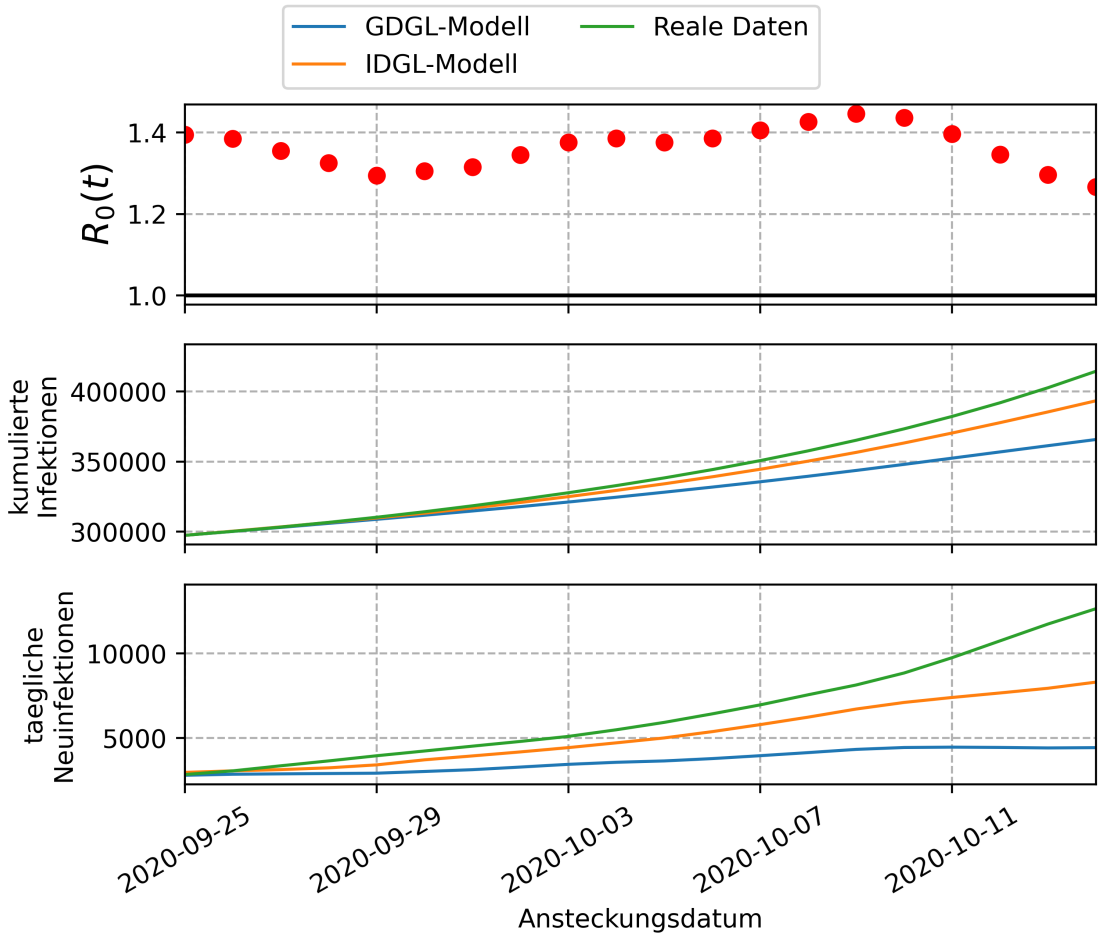
$$
\begin{aligned}
S'(t) &= \frac{S(t)}{N} \int_{\hat{T}}^{t} \phi(t, t-x)\rho(t, t-x)\, t_I^R(t-x)\, S'(x)\,\mathrm{d}x \\
I(t) &= -\int_{\hat{T}}^{t} t_I^R(t-x)\, S'(x)\,\mathrm{d}x \qquad (2) \\
R(t) &= -\int_{\hat{T}}^{t} \left(1 - t_I^R(t-x)\right) S'(x)\,\mathrm{d}x.
\end{aligned}
$$

Theorem

Let $t_I^R(\tau) = \exp(-\frac{\tau}{T_I})$, $\rho(t,\tau) = \rho(t)$, *and* $\phi(t,\tau) = \phi(t)$. *Then* (2) *reduces to:*

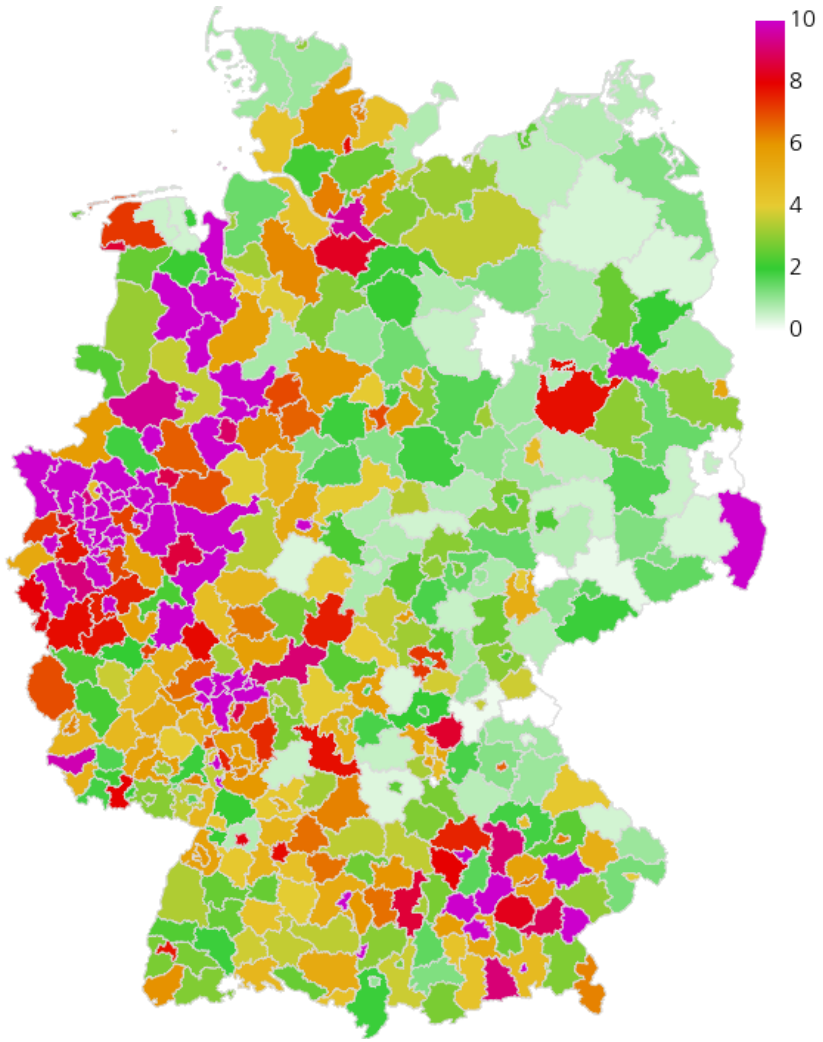
$$
\begin{aligned}
S'(t) &= -\phi(t)\,\rho(t)\,I(t)\,\frac{S(t)}{N} \\
I'(t) &= \phi(t)\,\rho(t)\,I(t)\,\frac{S(t)}{N} - \frac{1}{T_I} I(t) \\
R'(t) &= \frac{1}{T_I} I(t)
\end{aligned}
$$

Some simple comparison

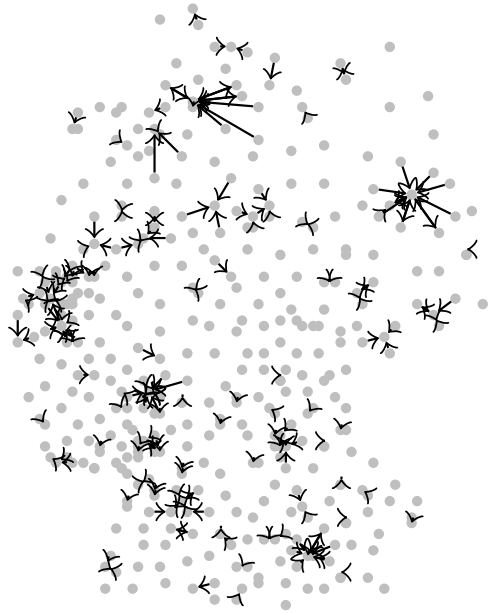


More details: Plötzke (2020).

A motivation for spatial heterogeneity



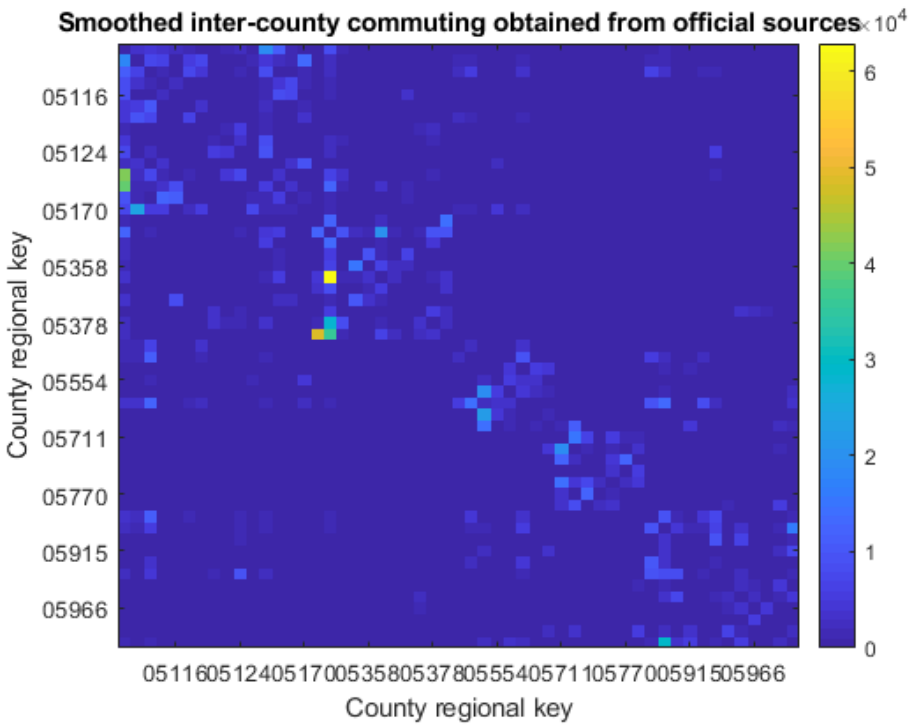
Spatial resolution and metapopulation models

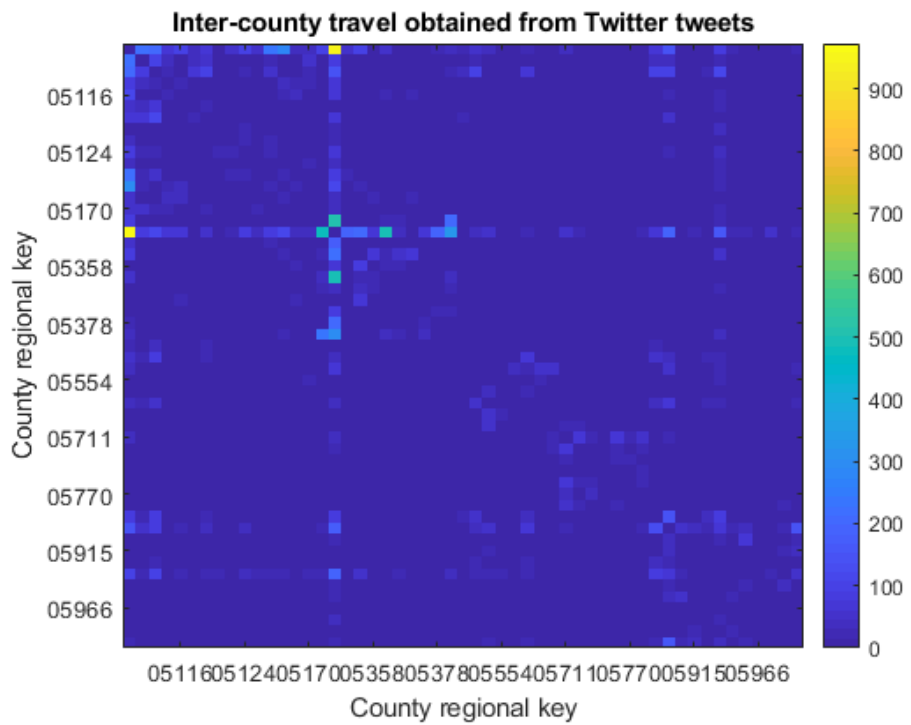


- Disease propagation differs in regions
  $\rightarrow$ "Coupled"-local models
- Dense mobility to neighbors, sparse mobility for long-distance
- Different approaches
  - No explicit movement: modify force of infection $\phi\rho I$
  - Explicit travel by modeling N_{ij}
  - Explicit travel travel with residence times
  - Explicit travel with residence time and explicit travel time

Digression on inter-regional contact classification

North Rhine-Westfalia:





Numerical study of the NoCovid strategy

- NoCovid ≠ ZeroCovid
- NoCovid: "Controlling the Covid-19 pandemic through Green Zones"

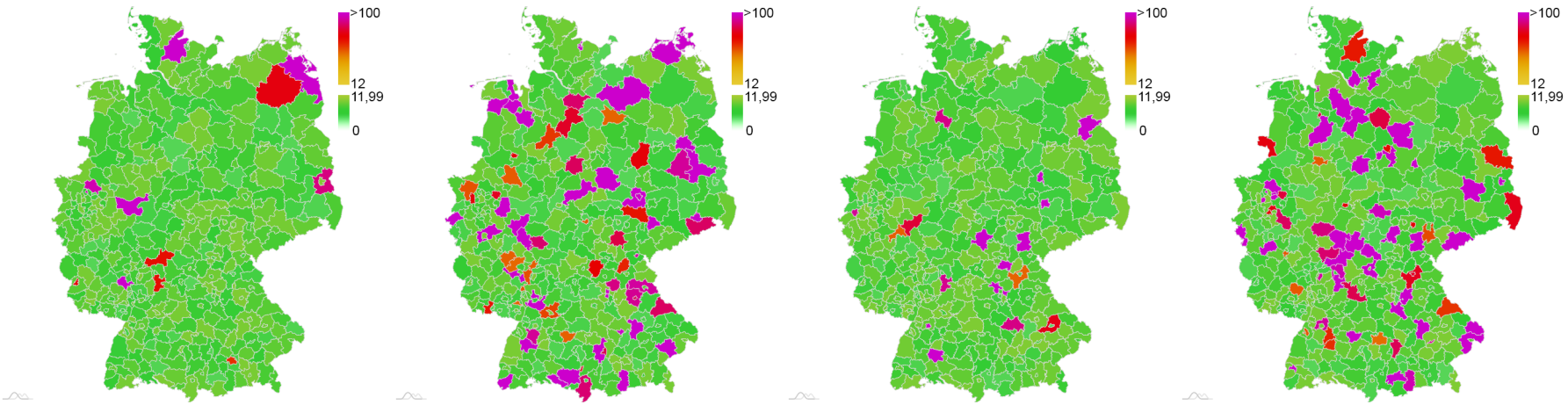
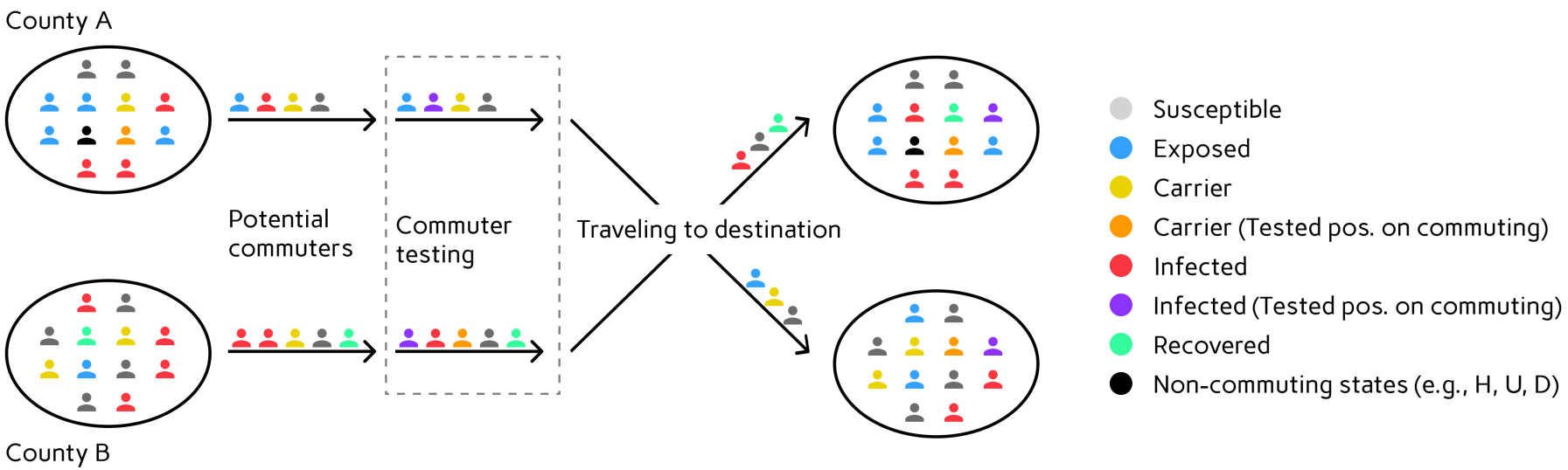


Figure: Four different initial scenarios. Random initial incidence (weekly cases per 100 000 individuals) of 75-150 for 2-20% of the counties and incidence below 10 otherwise (top).

Numerical study 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, ...)



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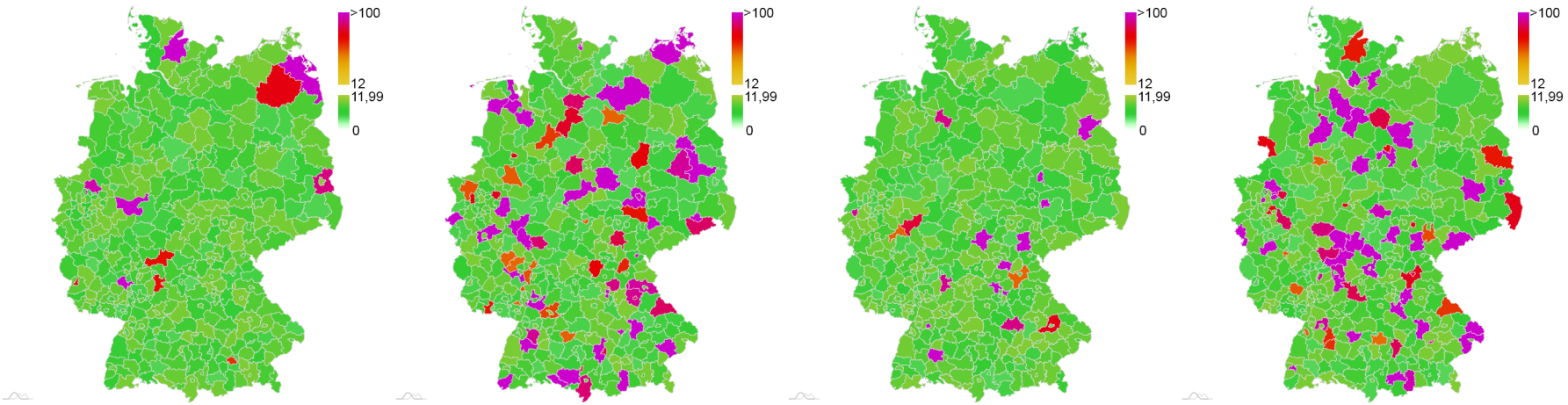

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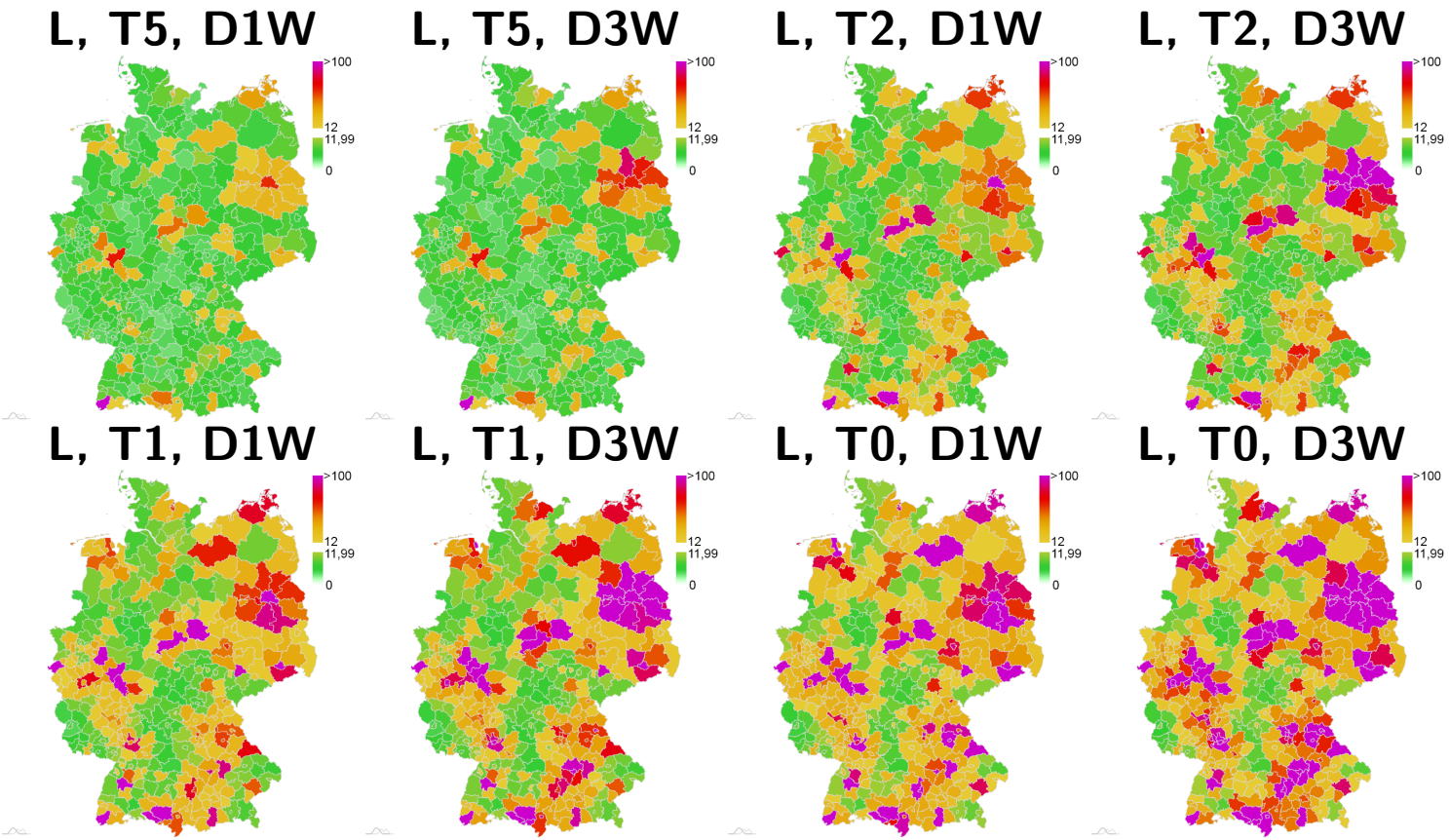
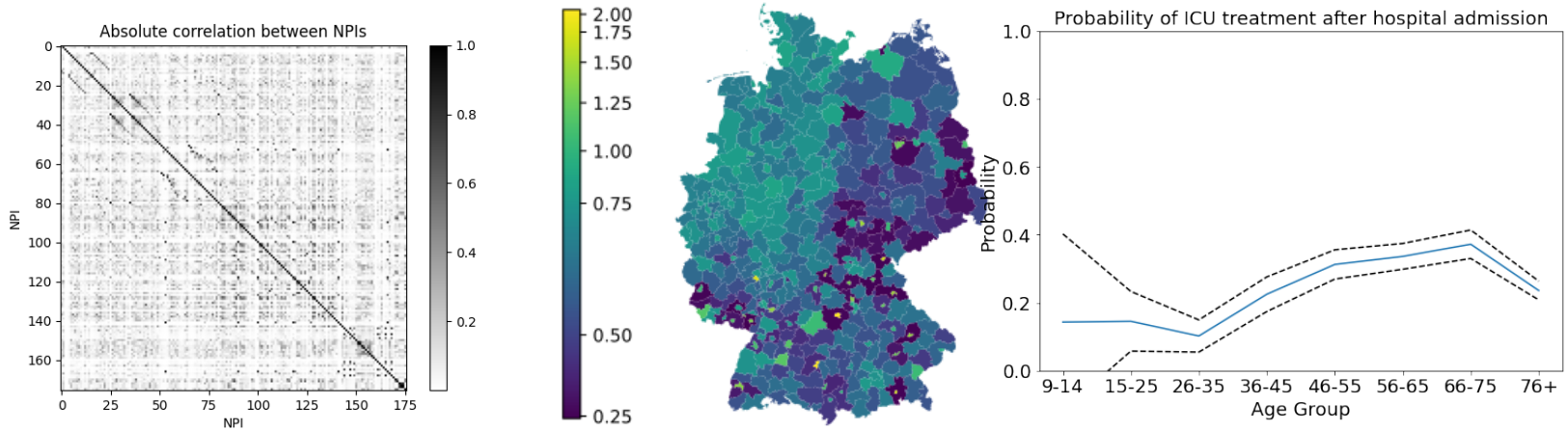


Figure: Simulated spread of SARS-CoV-2 cases for one initial scenario of about 18 % red zones and 8 different strategies. Median result after 30 days of simulation time.

See also: Prof. Dr. Michael Meyer-Hermann at the "2nd Global Summit of the World Health Network" (or "Ernst-Abbe-Kolloquium")

Some comments and perspective

- So far, we have seen epidemic disease models
- endemic disease models need birth rates and disease-independent death rates
- Vector-borne diseases need modeling of vectors (e.g., mosquitos, flies)
- Data is another challenge



- Stochasticity or ABMs not mentioned here
  → preliminary ABM in `https://github.com/DLR-SC/memilio`
  → PhD project "Data-driven Agent-based modeling for infectious diseases"

Further reading:

- Kühn et al. **Assessment of effective mitigation and prediction of the spread of SARS-CoV-2 in Germany using demographic information and spatial resolution**. Mathematical Biosciences 339, 108648 (2021).
- Kühn et al. **Regional opening strategies with commuter testing and containment of new SARS-CoV-2 variants**. medrxiv https://doi.org/10.1101/2021.04.23.21255995 (2021).
- Koslow 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**. medrxiv https://doi.org/10.1101/2021.07.09.21260257 (2021).

Thank you for your kind attention!

DLR