

Mathematical Challenges in managing Covid19 pandemics

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- Covid19 pandemics introduction
- ICU load simulator
- Is the standard modelling approach for infection dynamics sufficient?
- Summary

What do we see in Germany data?



- Observations (Germany) are affected by multiple, heterogeneous interventions
 Hard / weak lockdowns
 - → Local / country-wide measures
 - → NPI / vaccination



Explicit control actions



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- mission



- The Covid19 ICU load Simulator (DIVI-Prognosemodell) has been developed to
 - Identify upcoming risks to exceed German ICU capacities for Covid19 treatment
 - **1.** In time to initialise NPI's appropriate to avoid critical situations
 - 2. Predict **setpoints** to be achieved by NPI's
 - 2. Evaluate scenarios combining spreading dynamics, vaccination and mutants with respect to risk for critical situations for ICU capacities
 - 3. Monitoring of infection/ hospitalization data for **rapid identification of trend switches**
 - 4. learning efficiency of NPI's in specific spreading scenarios from model-based **retrospective analysis**

- technical todo's



→ Simulation of daily time course of ICU loads

- » on Germany / federal state level
- » Multiple scenarios representing the impact of
 - Spreading dynamics within NPI setpoints
 - Mutants
 - Vaccination strategies
 - Saisonal effects

on ICU load

- » > 4 weeks prognosis horizon within scenarios with +-10% confidence
- » Uncertainty quantification
- Model assisted monitoring of infection dynamics wrt phase transitions





- mechanisms to be simulated
 - Risk for severe course of disease towards admission to ICU strongly depends on age
 - Infection dynamics depends of
 - » Social contact network (SCN)
 - » NPI's affecting SCN topology
 - » NPI's affecting infection rates on contacts (e.g. masks)
 - » Non-stochastic
 - Vaccination affects both spreading and risk for severe course of disease

- challenges: data



Data sources

→ Infection dynamics: RKI Dashboard data (age-group stratified)

- » Time lag due to reporting delays
- » Very high daily variability due to reporting, almost periodic
- \rightarrow Vaccination rates, age stratified

→ ICU loads: DIVI Intensivregister

- » Daily reporting with low noise level
- » age-related information
- » ICU admission rates

→ Publications....

Modelling hospital load: DIVI Covid19 ICU Simulator



- conceptual design





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- ICU modul
 - ICU modul computes the time course of ICU loads
 - → by means of convolution of the age-stratified time courses of infection rates x(t) with
 - » risk profile for severe course of disease
 - » age stratified distribution of length of stay in ICU
 - both assessed from independent data from sentinel hospitals
 - » time delay ICU admission vs. infection
 - » quantified risk of ICU admission
 - derived from x(t) and ICU load data
 - ICU modul structure:
 - $\rightarrow ICU_{load}(t) = \sum_{i} \int_{0}^{t} B(t t', i) * x_{i}(t') dt'$
 - $\Rightarrow B(t t', i) = R(i) * \int S(t_{adm} t') * B'(t_{LoS}, i) dt'$
 - Special features:
 - Robustness: convolution is compact mapping
 - \rightarrow Hölder inequality guarantees upper bounds & error bounds



- scenario module: mean field models SEIR models
- Mean field models decompose the population into compartments
 - Within each compartment, contacts between individuals are assumed tight and homogeneous
 - Between compartments, contacts between individuals are assumed sparse and homogeneous
 - Population within each compartment is characterized by specific features resulting in specific dynamic parameters

\rightarrow Within each compartment k, infection status is characterized by the state variables

- » Sk: number of susceptible individuals in compartment k
- » Ek: number of exposed, but not infectous individuals in compartment k
- » Ik: number of exposed and infectous individuals in compartment k
- » Rk: number of recovered (removed) individuals in compartment k



- most used: mean field models SEIR models
- Dynamics in mean field models is quantified by ODE system:

$$\begin{split} \vec{E}_{k} &= \sum_{k} r_{kk}, S_{k}I_{k}, - \kappa E_{k} \\ \vec{I}_{k} &= \kappa E_{k} - \lambda_{k}I_{k} \\ \vec{S}_{k} &= -\sum_{k} r_{kk}, S_{k}I_{k}, & \longleftarrow \\ \vec{R}_{k} &= \lambda_{k}I_{k} \end{split}$$
That's what RKI reports as incidence

- Why are mean-field SEIR-models popular?
 - → With increasing #compartments, SEIR-models approximate network-based models
 - \rightarrow Easy to set up, established numerics
 - \rightarrow # of parameters to be fit can be limited

- Predicting ICU loads 2nd wave
- 2nd wave monitoring



<figure>



10.1.2021







- assessment of scenarios for 3rd wave

Model predictions unchanged since April 15



7.5.21

15



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Model fit to reality: Mean field models suggest exponential dynamics – is that right?



A network-based explanation of why most COVID-19 infection curves are linear

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Edited by Nils C. Stenseth, University of Oslo, Oslo, Norway, and approved July 23, 2020 (received for review May 22, 2020)



Fig. 1. Cumulative numbers of positively tested cases normalized to the last day (8 May 2020). Countries, even though many followed radically different strategies in response to the pandemic, seem to belong to one of three groups: (A) countries with a remarkably extended linear increase of the cumulated number of positively tested cases, including the United States, the United Kingdom, and Sweden, and (8) countries with an extended linear increase that tends to level off and enter a regime with a smaller slope. *B*, *Inset* shows an extended regime after the peak (cases per population size).



updates

Fig. 2. Schematic demonstration of the model. Nodes are connected in a Poissonian small-world network. Locally close neighbors resemble the family contacts, and long links to different regions represent contacts to others, such as people at work. (A) Initially, a subset of nodes is infected folue), and most are susceptible (green). (B) At every timestery, infected nodes spread the disease to any of their neighbors with probability r. Ather d days infected nodes turn into "recovered" and no longer spread the disease. (C) The dynamics end when no more nodes can be infected and all are recovered. (D) Infection ource P(t) (blue dots) for the model on a dense Poissonian small-world network, D = 8. The daily cases (red) first increase and then decrease. For comparison, we show the recovered case, R(t), of the corresponding SIR model with $\gamma = 1/d$, and $\beta = nD/N$ (green). The mean-field conditions are obviously justified to a large extent. (E) Situation for the same parameters except for a lower average degree, D = 3. The first increases and not to the SIR model or volviously isotal to not the nearly constant for a long time. The dynamics reach a hat at about 17% infected. The discrepancy to the SIR model orgen by volvious is used to the SIR model or volvious.

Towards a hybrid modelling framework for pandemic spreading dynamics - what do we see in Germany data?



Analysis of 2nd wave throughout Germany reveals convolution of exponential and linear growth dynamics affecting efficiency of lockdown measures



Towards a framework for pandemic spreading dynamics - what do we see in Germany data?



- SEIR-models represent dynamics in terms of "homogeneous" compartments → How to define a compartment?
- Data: daily infection incidences
 - \rightarrow 16 federals states (+ Germany overall)
 - \rightarrow 5 age groups
 - \rightarrow 85-dimensional state vector x(t) ε R⁸⁵ representing the dynamics
 - » crosstalk-matrix r_{kk} has 3570 elements to be estimated from data
 - How about the dimensionality of the dynamics?

Towards a framework for pandemic spreading dynamics - what do we see in Germany data?



Correlation pattern of state-age stratified incidences reveals existence of few modes of spreading dynamics across Germany: r(t,t') = corr(x(t),x(t'))





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Towards a framework for pandemic spreading dynamics[®] – Summary



- Dimensionality of compartimentalisation of mean field models can be significantly reduced by integration of apparent coherent dynamic spreading modes
- Fluctuation analysis around coherent spreading dynamics may reveal insight into driving mechanisms of initialisation of infection waves
- Adequate modelling of pandemic spreading needs a network-based dynamic approach, where the network topology has to be identified from data (?)

Acknowledgements



Institute for Computational Biomedicine

BMBF – SMITH

- → G. Marx (OIM)
- → J. Bickenbach (OIM)
- \rightarrow S. Fritsch (OIM)

DIVI

- \rightarrow C. Karagiannidis (U Witten-Herdecke)
- \rightarrow S. Weber-Carstens (Charite Berlin)

