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Anna Wendler

Shared work with Lena Plötzke, Hannah Tritzschak and Martin J. Kühn

An extension of age-of-infection models: A SECIR model based on integro-differential equations for epidemic outbreaks

3RD (INTER-) NATIONAL CONFERENCE ON INFECTIOUS DISEASE MODELING

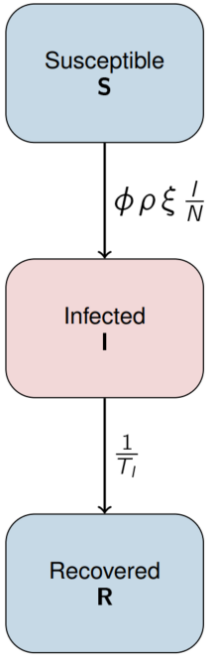
26 - 28 FEBRUARY 2025 IN BERLIN

Ordinary-differential equation (ODE) based model

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

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

$$R'(t) = \frac{1}{T_I}\,I(t)$$



$\phi(t)$	Number of contacts at time t
$\rho(t)$	Transmission probability at time t
$\xi(t)$	Proportion of infected individuals that are not isolated at time t
T_I	Mean stay time in compartment I

Motivation for age-of-infection model

- Simple ODE models are restricted to exponentially distributed stay times in compartments
  - But: unrealistic assumption[1,2]
- Choice of transition distributions impacts disease dynamics; in particular at change points

➢ Need for **flexible** choice of transition distributions

➢ Use model based on **integro-differential equations** (IDE)

[1] Wearing et al., Appropriate Models for the Management of Infectious Diseases, 2005. https://doi.org/10.1371/journal.pmed.0020174
[2] d'Onofrio, Mixed pulse vaccination strategy in epidemic model with realistically distributed infectious and latent times, 2004. https://doi.org/10.1016/S0096-3003(03)00331-X

IDE-SIR model

$$S'(t) = -\frac{S(t)}{N}\,\phi(t)\,\rho(t)\int_{-\infty}^{t} \underbrace{\xi(t, t-x)\,\underbrace{\gamma_I^R(t-x)\,\overbrace{\sigma_S^I(x)}^{\text{New infections at time } x}}_{\text{Individuals that are still infected at time } t}}_{\text{Individuals that are still infected and not isolated at time } t}\,\mathrm{d}x$$

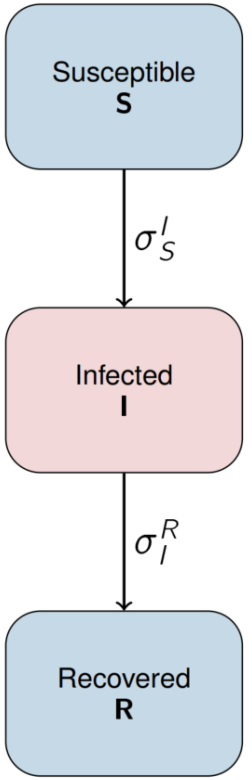
$\sigma_S^I(\mathrm{x})$	Number of individuals transitioning from S to I at time x
$\gamma_I^R(\tau)$	Mean proportion of individuals that are still infected at infection age τ
$\xi(t,\tau)$	Proportion of infected individuals that are not isolated at time t and infection age τ
$\rho(t)$	Transmission probability at time t
$\phi(t)$	Number of contacts at time t

IDE-SIR model

$$S'(t) = -\frac{S(t)}{N}\,\phi(t)\,\rho(t)\int_{-\infty}^{t}\xi(t,t-x)\,\gamma_I^R(t-x)\,\sigma_S^I(x)\,dx$$

$$I(t) = \int_{-\infty}^{t}\gamma_I^R(t-x)\,\sigma_S^I(x)\,dx$$

$$R(t) = \int_{-\infty}^{t}\left(1-\gamma_I^R(t-x)\right)\sigma_S^I(x)\,dx$$



IDE-SIR model

$$S'(t) = -\frac{S(t)}{N}\,\phi(t)\,\rho(t)\int_{-\infty}^{t}\xi(t,t-x)\,\gamma_I^R(t-x)\,\sigma_S^I(x)\,dx$$

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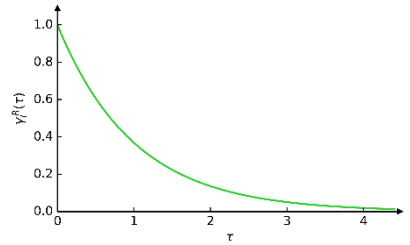
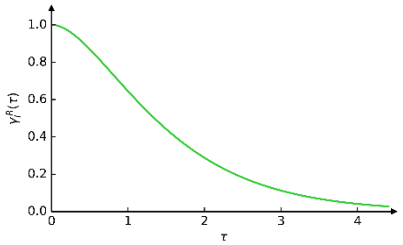
Flexible choice of transition distributions:

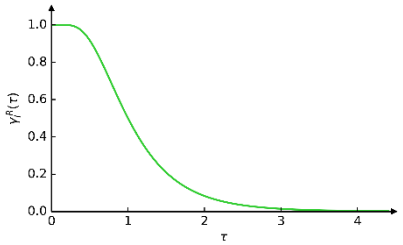
Exponential



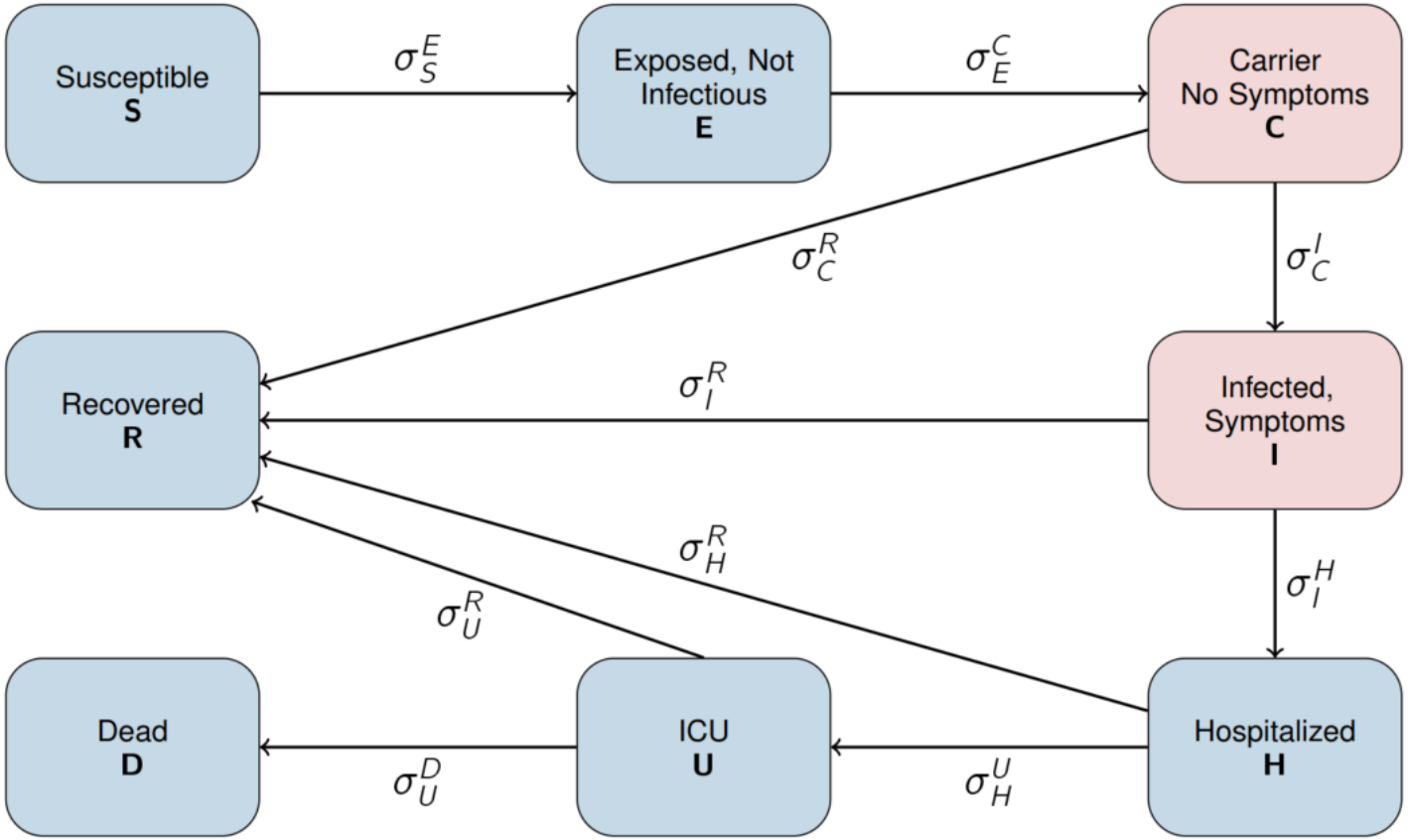
Gamma



Lognormal



Extension to IDE-SECIR model



Numerical scheme preserves biological properties

- Extension of nonstandard numerical scheme[3] that preserves important biological properties:
  - Scheme is mass conserving

$$\hat{S}(t_n) + \hat{E}(t_n) + \hat{C}(t_n) + \hat{I}(t_n) + \hat{H}(t_n) + \hat{U}(t_n) + \hat{R}(t_n) + \hat{D}(t_n) = \mathrm{N}.$$

  - Susceptible compartment is monotonically decreasing and converges to some final size

$$\lim_{n\to\infty} \hat{S}(t_n) = \hat{S}_\infty(\Delta t).$$

  - Recovered and Dead compartments are monotonically increasing and converge

$$\lim_{n\to\infty} \hat{R}(t_n) = \hat{R}_\infty(\Delta t), \qquad \lim_{n\to\infty} \hat{D}(t_n) = \hat{D}_\infty(\Delta t).$$

  - Flows converge to 0

$$\lim_{n\to\infty} \hat{\sigma}_{z_1}^{z_2}(t_n) = 0.$$

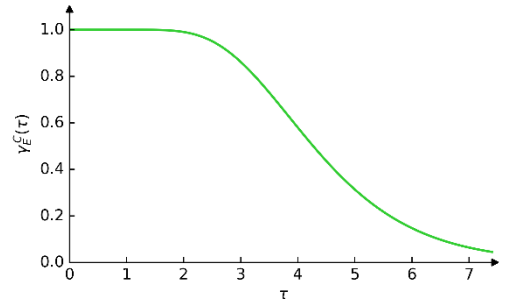
[3] Messina et al., A non-standard numerical scheme for an age-of-infection epidemic model, 2022. https://doi.org/10.3934/jcd.2021029

Numerical comparison of IDE and ODE models

Assess impact of distribution by comparing IDE-SECIR model with a corresponding ODE model:

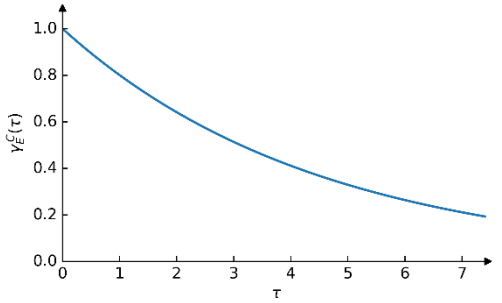
IDE model:

- Use **lognormal distributions** according to data on COVID-19[4]



ODE model:

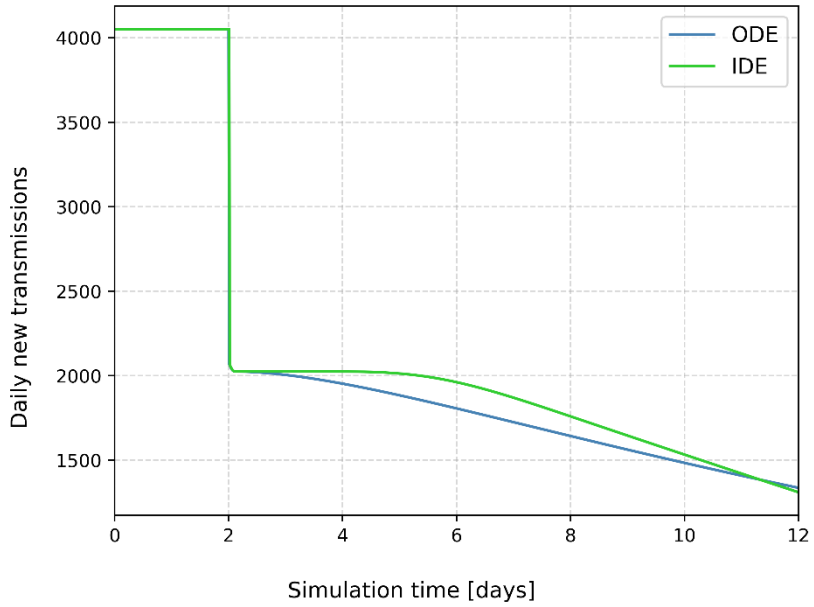
- Use **exponential distributions** with corresponding mean stay times

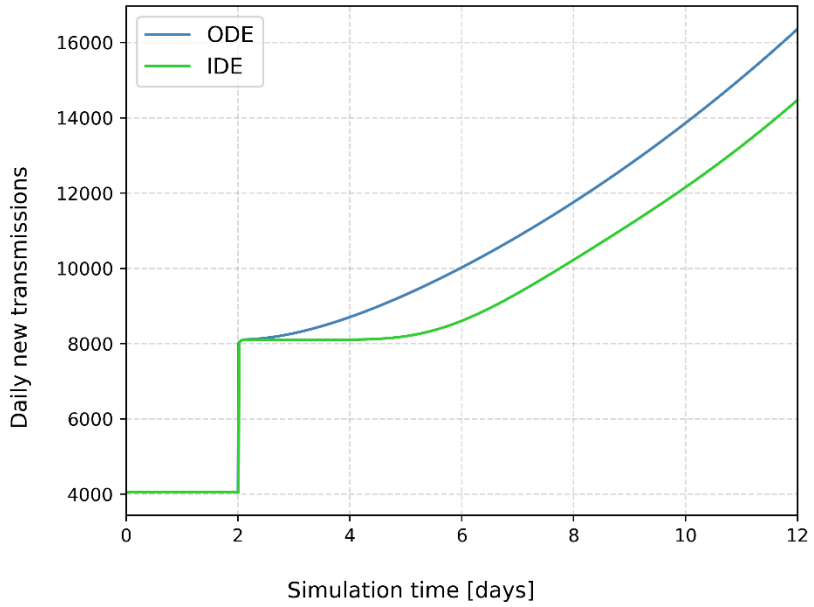


[4] Kerr et al., Covasim: An agent-based model of COVID-19 dynamics and interventions, 2021. https://doi.org/10.1371/journal.pcbi.1009149

Behavior at change points

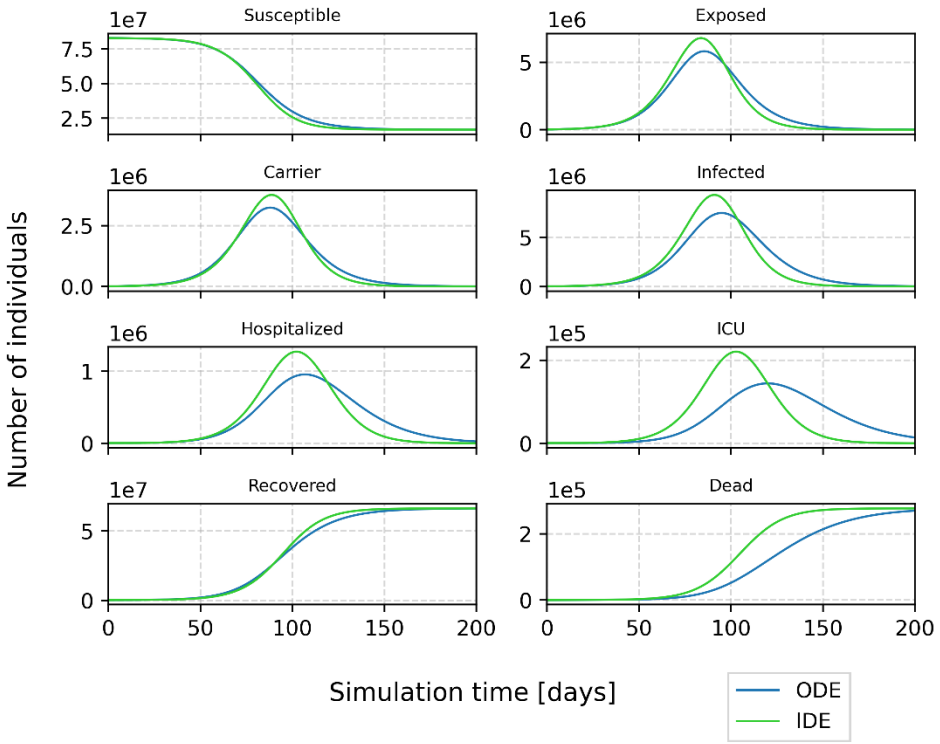
IDE model reacts slower to change in contact rate than ODE model, agreeing with literature [5,6]





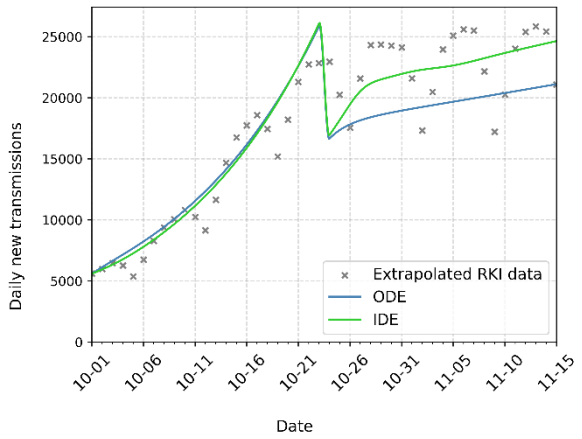
[5] Dey et al., Lag time between state-level policy interventions and change points in COVID-19 outcomes in the United States, 2021. https://doi.org/10.1016/j.patter.2021.100306
[6] Guglielmi et al., Identification of time delays in COVID-19 data, 2023. https://doi.org/10.1515/em-2022-0117

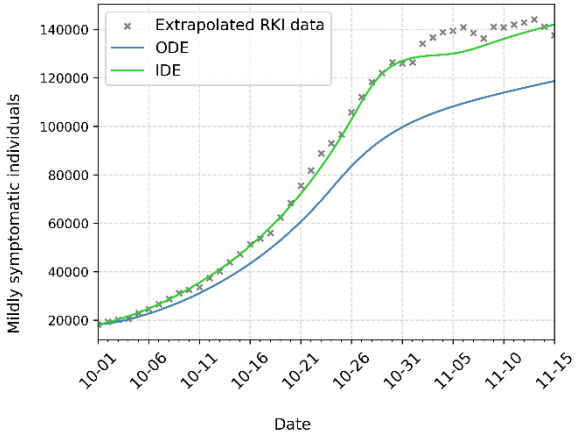
Epidemic peak behavior

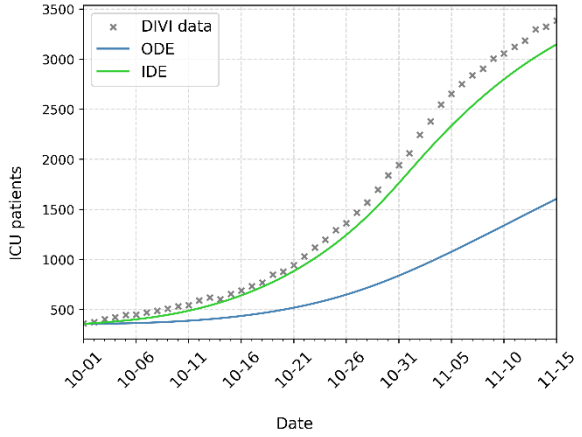


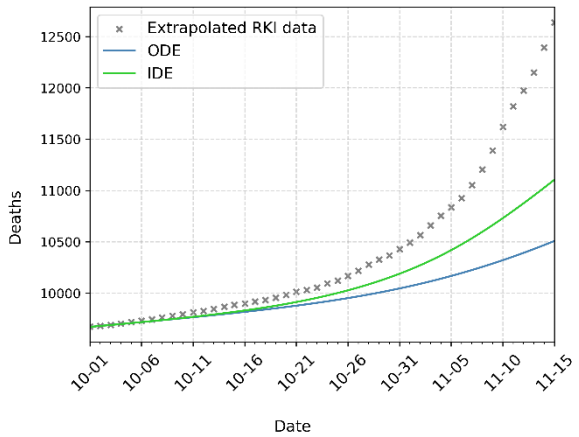
- Higher epidemic peak in IDE model
- Different timings of peak
- Same final size for both models

COVID-19 inspired scenario









Conclusion

- Using IDE model allows flexible choice of transition distributions
- Extended solver that preserves important biological properties
- Choice of distributions has significant impact on disease dynamics

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aufgrund eines Beschlusses des Deutschen Bundestages

Paper

IDE (2024)

Software MEmilio

MEmilio

THANK YOU FOR YOUR ATTENTION!

MODELING NETWORK for Severe Infectious Diseases