A SECIR MODEL BASED ON INTEGRO-DIFFERENTIAL EQUATIONS FOR EPIDEMIC OUTBREAKS

An extension of age-of-infection models

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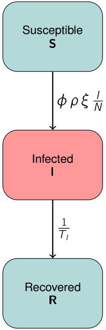
Joint work with *Lena Plötzke* and *Martin J. Kühn*

SIR model based on ordinary differential equations (ODE)

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

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

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



$\phi(t)$: 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 IDE model

- Simple ODE models are restricted to exponentially distributed stay times in compartments

  $\Rightarrow$ Unrealistic assumption[1]

- Choice of transition distribution impacts disease dynamics, in particular at change points

$\Rightarrow$ Need for flexible choice of transition distributions

$\Rightarrow$ Use model based on integro-differential equations (IDE)

[1] Wearing et al., PLOS Medicine (2005), https://doi.org/10.1371/journal.pmed.0020174.

IDE-SIR model

$$S'(t) = -\frac{S(t)}{N}\,\phi(t)\,\rho(t)\int_{-\infty}^{t} \xi(t, t-x)\; \underbrace{\gamma_I^R(t-x)\; \underbrace{\sigma_S^I(x)}_{\text{New infections at time } x}}_{\text{Number of individuals that are still infected at time } t}\; dx$$

$\sigma_S^I(x)$: 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

$\phi(t)$: Number of contacts at time t

$\rho(t)$: Transmission probability at time t

$\xi(t, \tau)$: Proportion of infected individuals that are not isolated at time t and infection age τ

IDE-SIR model

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

$$= -S(t)\,\varphi(t)$$

$\sigma_S^I(x)$: 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

$\phi(t)$: Number of contacts at time t

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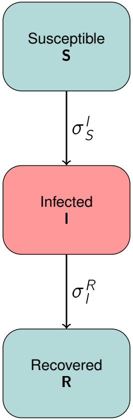
IDE-SIR model

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

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

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



IDE-SIR model

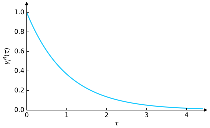
$$S'(t) = -\frac{S(t)}{N}\,\phi(t)\,\rho(t)\int_{-\infty}^{t} \xi(t,t-x)\,\gamma_I^R(t-x)\,\sigma_S^I(x)\,dx$$

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

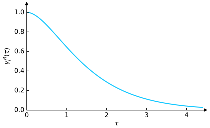
$$R(t) = \int_{-\infty}^{t} \left(1-\gamma_I^R(t-x)\right)\sigma_S^I(x)\,dx$$

Flexible choice of transition distributions:

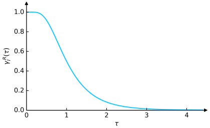
Exponential



Gamma



Log-normal



IDE-SIR model

$$\sigma_S^I(x) = -S'(x) = S(x)\,\varphi(x)$$

$$\begin{aligned}\sigma_I^R(x) &= \frac{d}{dx}\left(\int_{\infty}^{x}(1-\gamma_I^R(x-u))\,\sigma_S^I(u)\,du\right)\\ &= -\int_{\infty}^{x}\gamma_I^{R\prime}(x-u)\,\sigma_S^I(u)\,du\end{aligned}$$

Discretization

$$S'(t) = -S(t)\,\varphi(t)$$

$$= -\frac{S(t)}{N}\,\phi(t)\,\rho(t)\int_{-\infty}^{t} \xi(t, t-x)\,\gamma_I^R(t-x)\,\sigma_S^I(x)\,dx$$

Non-standard finite difference scheme[1]:

$$\widehat{S}'(t_{n+1}) = -\widehat{\sigma}_S^I(t_{n+1}) = -\widehat{S}(t_{n+1})\,\widehat{\varphi}(t_n)$$

[1] Messina et al., Journal of Computational Dynamics (2022), http://dx.doi.org/10.3934/jcd.2021029.

Discretization

Backwards difference scheme for $\widehat{S}'$:

$$\frac{\widehat{S}(t_{n+1}) - \widehat{S}(t_n)}{\Delta t} = -\widehat{S}(t_{n+1})\,\widehat{\varphi}(t_n)$$

$$\Longleftrightarrow \qquad \widehat{S}(t_{n+1}) = \frac{\widehat{S}(t_n)}{1 + \Delta t\,\widehat{\varphi}(t_n)}$$

Non-standard rectangular rule to approximate integral:

$$\widehat{\varphi}(t_{n+1}) = \frac{1}{N}\phi(t_{n+1})\,\rho(t_{n+1})\,\Delta t \sum_{i=a}^{n} \xi(t_{n+1}, t_{n+1-i})\,\gamma_I^R(t_{n+1-i})\,\widehat{\sigma}_S^I(t_{i+1})$$

Discretization

Flows:

$$\widehat{\sigma}_S^I(t_{n+1}) = \widehat{S}(t_{n+1})\,\widehat{\varphi}(t_n)$$

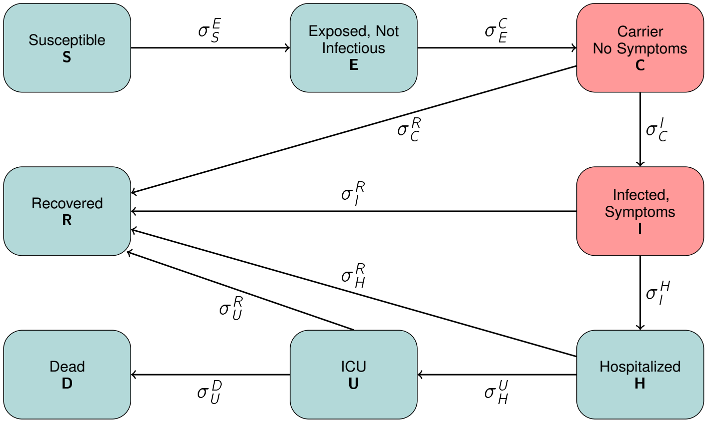
$$\widehat{\sigma}_I^R(t_{n+1}) = -\Delta t \sum_{i=a}^{n} \gamma_I^{R\prime}(t_{n+1-i})\,\widehat{\sigma}_S^I(t_{i+1})$$

Remaining compartments:

$$\widehat{I}(t_{n+1}) = \widehat{I}(t_n) + \Delta t\,\widehat{\sigma}_S^I(t_{n+1}) - \Delta t\,\widehat{\sigma}_I^R(t_{n+1})$$

$$\widehat{R}(t_{n+1}) = \widehat{R}(t_n) + \Delta t\,\widehat{\sigma}_I^R(t_{n+1})$$

Extension to IDE-SECIR model[1,2]



[1] Kühn et al., Mathematical Biosciences (2021), `https://doi.org/10.1016/j.mbs.2021.108648`.
[2] Wendler et al., in preparation.

Theoretical properties of discretization scheme

Theorem[1]

Let $\Delta t > 0$ be arbitrary but fixed. Let $\frac{d}{d\tau}\gamma_{z_1}^{z_2}(\tau)$ be approximated using a backwards difference scheme and let there hold

$$\widehat{S}(t_0) + \widehat{E}(t_0) + \widehat{C}(t_0) + \widehat{I}(t_0) + \widehat{H}(t_0) + \widehat{U}(t_0) + \widehat{R}(t_0) + \widehat{D}(t_0) = N.$$

Then the following holds.

- *For all $n \in \mathbb{N}$ there holds*

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

- *The sequence $(\widehat{S}(t_n))_{n\in\mathbb{N}_0}$ is monotonically decreasing and*

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

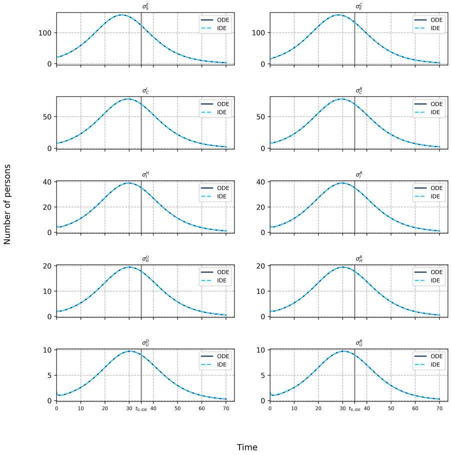
- *The sequences $(\widehat{\sigma}_{z_1}^{z_2}(t_n))_{n\in\mathbb{N}_0}$ are bounded and*

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

[1] Wendler et al., in preparation.

Comparison of IDE and ODE model

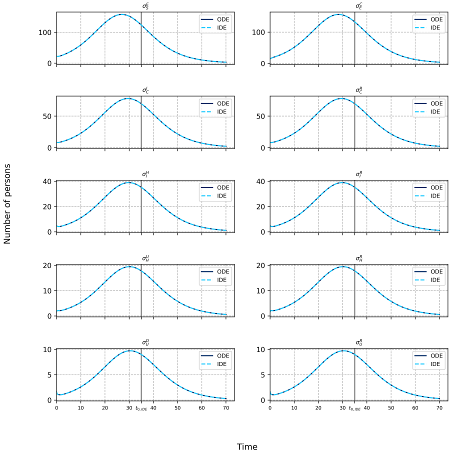
- With appropriate choice of parameters: IDE model reduces to ODE model

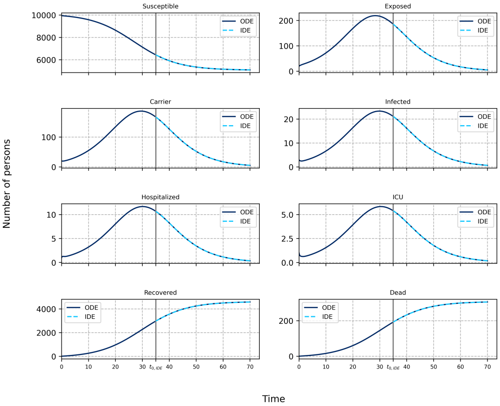


- To validate our discretization:
  - Solve ODE model with Runge-Kutta using small time step

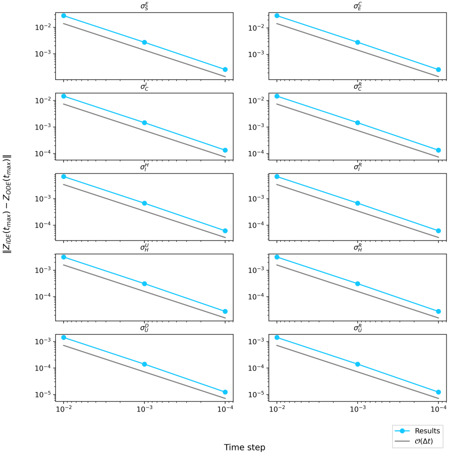
    $\Rightarrow$ Define this as ground truth
  - Compute initial flows for IDE model until $t_{0,\text{IDE}}$ based on ODE results
  - Simulate IDE model and compare with ODE results

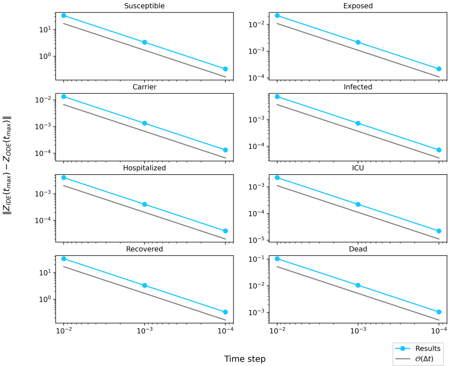
Comparison of IDE and ODE model





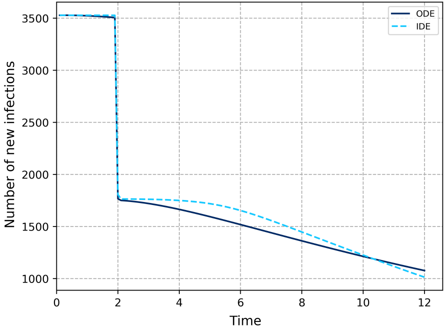
Convergence of IDE model

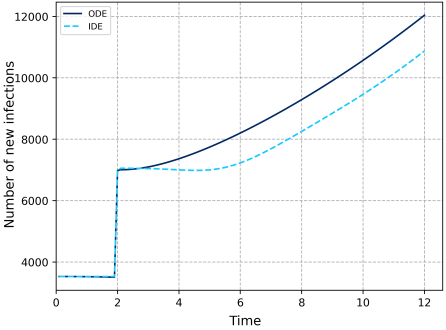




Behavior at change points

- In IDE model: Log-normally distributed stay times[1]
- Change contact rate to model implementation and cancelation of NPIs

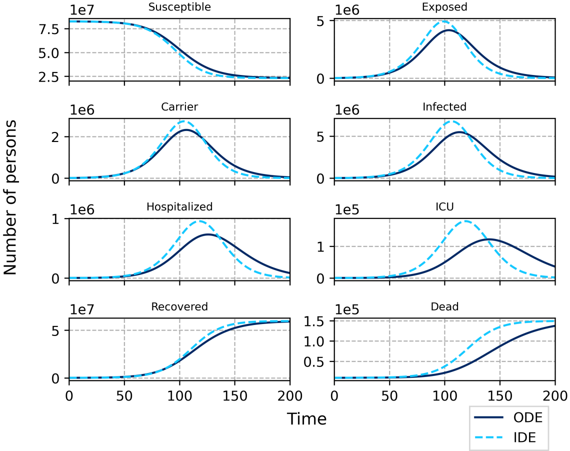




- IDE model reacts slower to change in contact rate than ODE model

[1] Kerr et al., PLOS Computational Biology (2021), https://doi.org/10.1371/journal.pcbi.1009149.

Epidemic peak behavior for compartments



- Higher maximum in Hospitalized and ICU compartments when using IDE model

Conclusion

- Using IDE model allows flexible choice of transition distributions
- Application of non-standard numerical scheme
  - Conserves important properties of disease dynamics
  - Converges linearly
- Choice of distributions has significant impact on disease dynamics

Thank you for your attention!

GitHub repository: `https://github.com/SciCompMod/memilio`

IDE-SECIR model

$$S'(t) = -\frac{S(t)}{N - D(t)}\, \phi(t)\, \rho(t)$$
$$\int_{-\infty}^{t} \xi_C(t, t-x) \left(\mu_C^I \, \gamma_C^I(t-x) + \left(1 - \mu_C^I\right) \gamma_C^R(t-x)\right) \sigma_E^C(x)$$
$$+ \xi_I(t, t-x) \left(\mu_I^H \, \gamma_I^H(t-x) + \left(1 - \mu_I^H\right) \gamma_I^R(t-x)\right) \sigma_C^I(x) \; dx$$

IDE-SECIR model

$$E(t) = \int_{-\infty}^{t} \gamma_E^C(t-x)\,\sigma_S^E(x)\,dx$$

$$C(t) = \int_{-\infty}^{t} \left(\mu_C^I\,\gamma_C^I(t-x) + \left(1-\mu_C^I\right)\gamma_C^R(t-x)\right)\sigma_E^C(x)\,dx$$

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

$$H(t) = \int_{-\infty}^{t} \left(\mu_H^U\,\gamma_H^U(t-x) + \left(1-\mu_H^U\right)\gamma_H^R(t-x)\right)\sigma_I^H(x)\,dx$$

$$U(t) = \int_{-\infty}^{t} \left(\mu_U^D\,\gamma_U^D(t-x) + \left(1-\mu_U^D\right)\gamma_U^R(t-x)\right)\sigma_H^U(x)\,dx$$

$$R(t) = \int_{-\infty}^{t} \sigma_C^R(x) + \sigma_I^R(x) + \sigma_H^R(x) + \sigma_U^R(x)\,dx$$

$$D(t) = \int_{-\infty}^{t} \sigma_U^D(x)\,dx.$$

IDE-SECIR model

$$\sigma_S^E(t) = -S'(t) = S(t)\,\varphi(t)$$

$$\sigma_C^I(t) = -\int_{-\infty}^{t} {\gamma_C^I}'(t-x)\,\mu_C^I\,\sigma_E^C(x)\,dx$$

$$\sigma_I^H(t) = -\int_{-\infty}^{t} {\gamma_I^H}'(t-x)\,\mu_I^H\,\sigma_C^I(x)\,dx$$

$$\sigma_H^U(t) = -\int_{-\infty}^{t} {\gamma_H^U}'(t-x)\,\mu_H^U\,\sigma_I^H(x)\,dx$$

$$\sigma_U^D(t) = -\int_{-\infty}^{t} {\gamma_U^D}'(t-x)\,\mu_U^D\,\sigma_H^U(x)\,dx$$

$$\sigma_E^C(t) = -\int_{-\infty}^{t} {\gamma_E^C}'(t-x)\,\sigma_S^E(x)\,dx$$

$$\sigma_C^R(t) = -\int_{-\infty}^{t} {\gamma_C^R}'(t-x)\,\left(1-\mu_C^I\right)\sigma_E^C(x)\,dx$$

$$\sigma_I^R(t) = -\int_{-\infty}^{t} {\gamma_I^R}'(t-x)\,\left(1-\mu_I^H\right)\sigma_C^I(x)\,dx$$

$$\sigma_H^R(t) = -\int_{-\infty}^{t} {\gamma_H^R}'(t-x)\,\left(1-\mu_H^U\right)\sigma_I^H(x)\,dx$$

$$\sigma_U^R(t) = -\int_{-\infty}^{t} {\gamma_U^R}'(t-x)\,\left(1-\mu_U^D\right)\sigma_H^U(x)\,dx$$