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A Delay Differential Equation approach to model the COVID-19 pandemic

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Motivation and Aim: SEIR (Susceptible – Exposed – Infected – Recovered) approach is a classic modeling method that has frequently been applied to the study of infectious disease epidemiology. However, in the vast majority of SEIR models and models derived from them transitions from one population group to another are described using the mass-action law which assumes population homogeneity. That causes some methodological limitations or even drawbacks, particularly inability to reproduce observable dynamics of key characteristics of an infection such as, for example, the incubation period and progression of the disease's symptoms which require considering different time scales as well as probabilities of different disease trajectories.
Methods and Algorithms: In this study, we propose an alternative approach to simulate the epidemic dynamics that is based on two concepts:
1. System of differential equations with time delays in the next form (e.g. for incubation period):

$$\frac{dI}{dt} = \frac{-dE}{dt}(t) = \sum_{i=1}^{n} k_i \cdot E(t - \Delta_i),$$

where n, $\Delta_1,\ldots,\Delta_n,k_1,\ldots k_n$- parameters estimated to precisely reproduce a duration of a certain transition like incubation period, recovery period, etc.
2. Instant transitions to replicate correct fractions of patients with particular symptoms. For example, some of patients with mild symptoms will progress to worse symptoms, while the second part of patients will recover. Both these transitions will then be performed with different speed. The issue arises from the state when larger subgroup of patients should undergo slower transition with smaller derivative. Proposed solution is that patients with mild symptoms are instantly divided into two subgroups: “mild symptoms who will recover” and “mild symptoms who will get worse”.
Results: The suggested modeling approach is fundamental and can be applied to the study of many infectious diseases epidemiology. We used it to create SEIR-like model in BioUML platform [1] with instant and delayed transitions. The Stringency index [2] was used as a generalized characteristic of the non-pharmaceutical government interventions implemented in corresponding countries to contain the virus spread. The model also includes: availability of intensive care units for critically ill, testing regime, vaccination, loosing of immunity through time and appearance of new strains. The

overall scheme of the model is presented on Fig. 1. The model was calibrated and adapted to COVID-19 pandemic in Germany and France.

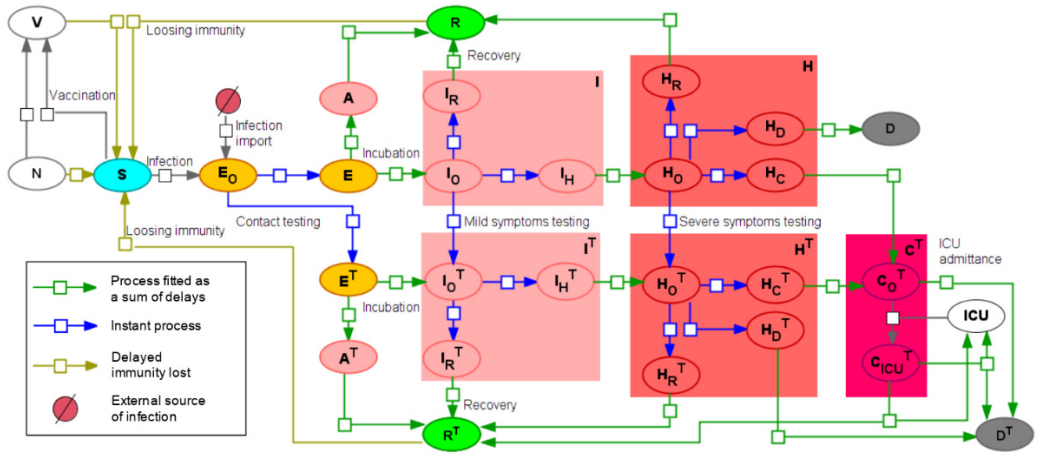

Fig. 1. Overall SEIR-like model with instant and delayed processes. Colored boxes represent compartments divided into subgroups with different disease paths

Conclusion: The developed approach allows for accurate modeling of transitions in the model (e.g. incubation period), while the transition parameters may be estimated separately of the rest of the model. Thus, the number of model parameters is decreased and their epidemiological interpretation becomes more clear (i.e. "fraction of patients with serious symptoms"). The developed models are available through the web interface of BioUML software at https://gitlab.sirius-web.org/covid-19/dde-epidemiology-model. Models are available both through visual representation in the platform and in Jupyter notebooks which enable users to reproduce simulation results and figures presented in this study.

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References

1. Kolpakov F., Akberdin I., Kashapov T., Kiselev L., Kolmykov S., Kondrakhin Y., Kutumova E., Mandrik N., Pintus S., Ryabova A., Sharipov R. BioUML: an integrated environment for systems biology and collaborative analysis of biomedical data. *Nucleic Acids Res*. 2019;47(W1):W225-W233.
2. Hale T., Angrist N., Goldszmidt R., Kira B., Petherick A., Phillips T., Webster S., Cameron-Blake E., Hallas L., Majumdar S., Tatlow H. A global panel database of pandemic policies (Oxford COVID-19 Government Response Tracker). *Nat Hum Behav*. 2021;5(4):529-538.