

Systems biology

Epidemiological modeling in StochSS Live!

Richard Jiang^{1,†}, Bruno Jacob^{2,†}, Matthew Geiger³, Sean Matthew³, Bryan Rumsey³, Prashant Singh⁴, Fredrik Wrede⁴, Tau-Mu Yi⁵, Brian Drawert ^{6,‡,*}, Andreas Hellander^{4,‡} and Linda Petzold^{1,2,‡}

¹Department of Computer Science, University of California-Santa Barbara, Santa Barbara, CA 93117, USA, ²Department of Mechanical Engineering, University of California-Santa Barbara, Santa Barbara, CA 93106, USA, ³National Environmental Modeling and Analysis Center (NEMAC), University of North Carolina at Asheville, Asheville, NC 28804, USA, ⁴Department of Information Technology, Uppsala University, Uppsala 751 05, Sweden, ⁵Department of Molecular, Cellular and Developmental Biology, University of California-Santa Barbara, Santa Barbara, CA 93106, USA and ⁶Department of Computer Science, University of North Carolina at Asheville, Asheville, NC 28804, USA

*To whom correspondence should be addressed.

†The authors wish it to be known that, in their opinion, the first two authors should be regarded as Co-First Authors.

‡The authors wish it to be known that, in their opinion, the last three authors should be regarded as Joint Senior Authors.

Associate Editor: Teresa Przytycka

Received on September 22, 2020; revised on January 20, 2021; editorial decision on January 24, 2021; accepted on January 26, 2021

Abstract

Summary: We present StochSS Live!, a web-based service for modeling, simulation and analysis of a wide range of mathematical, biological and biochemical systems. Using an epidemiological model of COVID-19, we demonstrate the power of StochSS Live! to enable researchers to quickly develop a deterministic or a discrete stochastic model, infer its parameters and analyze the results.

Availability and implementation: StochSS Live! is freely available at <https://live.stochss.org/>

Contact: bdrawert@unca.edu

Supplementary information: [Supplementary data](#) are available at Bioinformatics online.

1 Introduction

Epidemiological models are essential tools to assist public health authorities in the planning of policy responses to pandemic prevention and control (Thompson, 2020). In general, these models are classified into different categories (deterministic/stochastic), treatment of the populations (continuous/discrete) or spatial dependence and distribution of the population (homogeneous/heterogeneous) (Garner and Hamilton, 2011).

An example of a recent application of epidemiological modeling is the study of early transmission dynamics and effectiveness of control measures in individuals infected by the novel coronavirus disease (COVID-19). As of September 7, 2020, COVID-19 has been responsible for over 27 million reported cases and 900,000 deaths worldwide (World Health Organization, 2020). Given the global impact of the virus, several software tools have been developed, mostly focused on either deterministic (Flaxman et al., 2020) or stochastic (Sanyi et al., 2020) models. These tools typically require some level of technical expertise.

On the mathematical level, most epidemiological models are structurally identical to models of chemical kinetics widely used in systems biology (Hoops et al., 2006; Lopez et al., 2013). In the systems biology community, there has been a large focus the last decade on increasingly efficient stochastic simulation algorithms and on

tools to improve usability for modelers. We have in previous work developed a wide range of model development and simulation tools for such models in the StochSS Suite of Software. We believe that there is great urgency and potential for a software environment that makes epidemiological modeling easily accessible to a wide audience, and that bridges the notation gap needed to effectively reuse simulation tools from systems biology for epidemiological models. To accomplish this we present StochSS Live!, a powerful web-based tool that enables users to create models, perform simulations, infer parameters and visualize the results through simple and intuitive workflows, and have developed a stochastic COVID-19 epidemiological model accessible via StochSS Live!

StochSS Live! enables easy access to the powerful feature set of the simulation and model analysis toolkits in the StochSS Suite of Software (Abel et al., 2016; Singh et al., 2020). StochSS Live! builds on and extends the model development UI from (Drawert et al., 2016) in several ways: Through a set of clear, user-friendly interfaces used directly from a web browser (hence requiring no installation), a researcher can explicitly define their model, simulate it using deterministic or stochastic solvers, analyze and explore the parameter space using either traditional parameter sweeps or workflows guided by unsupervised machine learning. Users can also calibrate the model to observed data using highly scalable likelihood-free

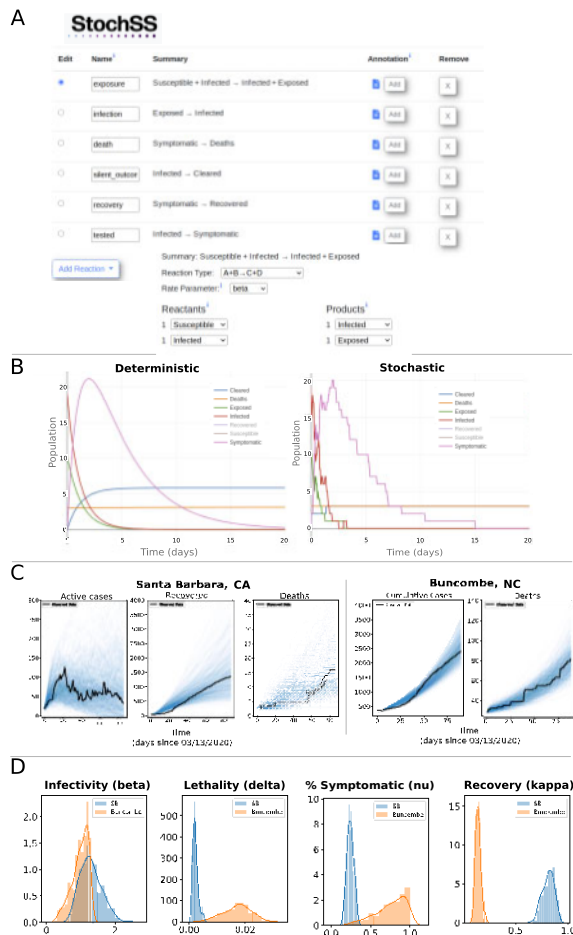


Fig. 1. Snapshot of the StochSS Live! web interface. (A) The user can explicitly define populations, parameters and reactions. (B) The preview window settings allow the user to preview simulation results for both deterministic and stochastic models. (C) Example of parameter sweep inference in StochSS Live! The blue lines are computed realizations obtained by the stochastic solver and the black lines correspond to the official data. Notice that, regardless of the fact that data from Buncombe and Santa Barbara counties have different scales and different levels of stochasticity, StochSS Live! is capable of modeling both cases. (D) Comparison of posteriors from Santa Barbara and Buncombe counties

parameter inference. Specifically, StochSS Live! utilizes the Approximate Bayesian Computation (Sisson et al., 2018) algorithms implemented in Sciope (Singh et al., 2020) to provide an easy interface for parameter estimation given a parameterized model and observed data. Other libraries for model calibration such as PyBioFitNet (Mitra et al., 2019), DEAP (Félix-Antoine et al., 2012) or PyDREAM (Shockley et al., 2018) can also be implemented by the user through the Jupyter notebooks generated for each model. For analysis needs that goes beyond the capability of the UI, StochSS Live! will automatically generate templated Jupyter notebooks that can be shared and extended. This automated dual representation of models and computational workflows via a UI and as code is a defining feature of StochSS Live! and greatly simplifies collaboration between domain and computational experts.

2 Epidemiological model

To demonstrate the use of StochSS Live! for epidemiological modeling, we consider the infection dynamics of COVID-19 in two US counties: Santa Barbara, CA and Buncombe, NC. The data were gathered from Santa Barbara's Health Department and Dong et al. (2020), between March 13 and August 31, 2020. We construct an extended SEIRD model with symptomatic and asymptomatic compartments using the StochSS Live! model builder, as shown in

Figure 1A. We divide the population into seven groups: susceptible, exposed, infected, symptomatic, recovered, deceased and cleared individuals. Transition events between these groups are shown in Figure 1A. The user can immediately preview sample trajectories from either deterministic or stochastic versions of the system simply by selecting the respective option (Fig. 1B).

Figure 1C and D shows the results of parameter inference for a discrete stochastic version of the model. Inference is performed using Approximate Bayesian Computation, allowing for uncertainty quantification of parameters and predictions. In Figure 1C, each realization (blue lines) corresponds to a simulation using a parameter sample from the posterior distribution, which are contrasted with the data (black lines). Figure 1D shows the posteriors for parameters for both counties. While infectivity rates between the two counties are roughly the same, the estimated lethality rate is a bit higher in Buncombe county, although there is substantial uncertainty. We do note that this particular model does not seem to sufficiently capture the data as evidenced in Figure 1C and would need to be further iterated upon before any strong conclusions can be drawn. For a complete description of the model as well as replicating notebooks, we refer the reader to the Supplementary Information.

3 Conclusion

Our model of COVID-19 demonstrates epidemiological capabilities of StochSS Live!, a freely available, user-friendly web-based service for the development, simulation and analysis of a wide range of models. To make these capabilities as widely accessible as possible, we provide StochSS Live! In addition, the StochSS Suite of Software provides the individual tools, if you wish to integrate them into your own software.

Funding

We acknowledge funding from NIBIB Award 2-R01-EB014877-04A1. No official position or official endorsement should be inferred.

Conflict of Interest: none declared.

References

- Abel, J.H. et al. (2016) GillesPy: a python package for stochastic model building and simulation. *IEEE Life Sci. Lett.*, 2, 35–38.
- Dong, E. et al. (2020) An interactive web-based dashboard to track covid-19 in real time. *Lancet Infect. Dis.*, 20, 533–534.
- Drawert, B. et al. (2016) Stochastic simulation service: bridging the gap between the computational expert and the biologist. *PLoS Comput. Biol.*, 12, e1005220.
- Flaxman, S. et al. (2020) Estimating the effects of non-pharmaceutical interventions on COVID-19 in Europe. *Nature*, 584, 257–261.
- Garner, M.G. and Hamilton, S.A. (2011) Principles of epidemiological modelling. *Rev. Sci. Tech. OIE*, 30, 407–416.
- Hoops, S. et al. (2006) COPASI—a complex pathway simulator. *Bioinformatics*, 22, 3067–3074.
- Lopez, C.F. et al. (2013) Programming biological models in python using PySB. *Mol. Syst. Biol.*, 9, 646.
- Mitra, E.D. et al. (2019) PyBioNetFit and the biological property specification language. *IScience*, 19, 1012–1036.
- Sanyi, T. et al. (2020) Stochastic discrete epidemic modeling of COVID-19 transmission in the province of Shaanxi incorporating public health intervention and case importation. <https://www.medrxiv.org/content/10.1101/2020.02.25.20027615v1>.
- Shockley, E.M. et al. (2018) PyDREAM: high-dimensional parameter inference for biological models in python. *Bioinformatics*, 34, 695–697.
- Singh, P. et al. (2020) Scalable machine learning-assisted model exploration and inference using Sciope. *Bioinformatics*. <https://academic.oup.com/bioinformatics/advance-article/doi/10.1093/bioinformatics/btaa673/5876021>.
- Sisson, S.A. et al. (2018) Handbook of Approximate Bayesian Computation. Boca Raton, FL: CRC Press.
- Thompson, R.N. (2020) Epidemiological models are important tools for guiding COVID-19 interventions. *BMC Med.*, 18, 1–4.
- World Health Organization (2020) Coronavirus disease (COVID-19) weekly epidemiological update.