Lesson 1: Introduction to Simulation-based Inference for Epidemiological Dynamics

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Objectives for this lesson

- To understand the motivations for simulation-based inference in the study of epidemiological and ecological systems.
- To introduce the class of partially observed Markov process (POMP) models.
- To introduce the pomp `R` package.

Epidemiological and Ecological Dynamics

- Ecological systems are complex, open, nonlinear, and nonstationary.
- "Laws of Nature" are unavailable except in the most general form.
- It is useful to model them as stochastic systems.
- For any observable phenomenon, multiple competing explanations are possible.
- Central scientific goals:

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-  Which explanations are most favored by the data?
-  Which kinds of data are most informative?
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- Central applied goals:

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-  How to design ecological or epidemiological intervention?
-  How to make accurate forecasts?
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- Time series are particularly useful sources of data.

Obstacles to inference

Obstacles for *ecological* modeling and inference via nonlinear mechanistic models enumerated by Bjørnstad and Grenfell (2001)

1. Combining measurement noise and process noise.
2. Including covariates in mechanistically plausible ways.
3. Using continuous-time models.
4. Modeling and estimating interactions in coupled systems.
5. Dealing with unobserved variables.
6. Modeling spatial-temporal dynamics.

The same issues arise for *epidemiological* modeling and inference via nonlinear mechanistic models.

The *partially observed Markov process* modeling framework we focus on in this course addresses most of these problems effectively.

Course objectives

1. To show how stochastic dynamical systems models can be used as scientific instruments.
2. To teach statistically and computationally efficient approaches for performing scientific inference using POMP models.
3. To give students the ability to formulate models of their own.
4. To give students opportunities to work with such inference methods.
5. To familiarize students with the pomp package.
6. To provide documented examples for adaptation and re-use.

Questions and answers

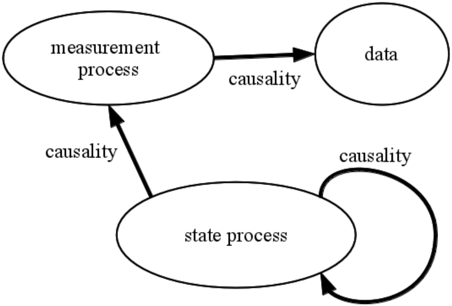
1. How does one combine various data types to quantify asymptomatic COVID-19 infections? (Subramanian, He, and Pascual 2021)
2. How effective have various non-pharmaceutical interventions been at controlling SARS-CoV-2 spread in hospitals? (Shirreff et al. 2022)
3. How does one use incidence and mobility data to infer key epidemiological parameters? (Andrade and Duggan 2022)
4. How does one make forecasts for an outbreak of an emerging infectious disease? (King et al. 2015)
5. How does one build a system for real-time surveillance of COVID-19 using epidemiological and mobility data? (Fox et al. 2022)
6. What strategies are effective at containing mumps spread on college campuses? (Shah et al. 2022)
7. What explains the resurgence of pertussis in countries with sustained high vaccine coverage? (Domenech de Cellès et al. 2018)
8. Do subclinical infections of pertussis play an important epidemiological role? (Lavine et al. 2013)

Partially observed Markov process (POMP) models

- Data $y_1^*, \dots, y_N^*$ collected at times $t_1 < \dots < t_N$ are modeled as noisy, incomplete, and indirect observations of a Markov process $\{X(t), t \geq t_0\}$.
- This is a *partially observed Markov process (POMP)* model, also known as a hidden Markov model or a state space model.
- $\{X(t)\}$ is Markov if the history of the process, $\{X(s), s \leq t\}$, is uninformative about the future of the process, $\{X(s), s \geq t\}$, given the current value of the process, $X(t)$.
- If all quantities important for the dynamics of the system are placed in the *state*, $X(t)$, then the Markov property holds by construction.
- Systems with delays can usually be rewritten as Markovian systems, at least approximately.
- An important special case: any system of differential equations $dx/dt = f(x)$ is Markovian.
- POMP models can include all the features desired by Bjørnstad and Grenfell (2001).

Schematic of the structure of a POMP

- Arrows in the following diagram show causal relations.
- A key perspective to keep in mind is that *the model is to be viewed as the process that generated the data*.
- That is: the data are viewed as one realization of the model's stochastic process.



Notation for POMP models

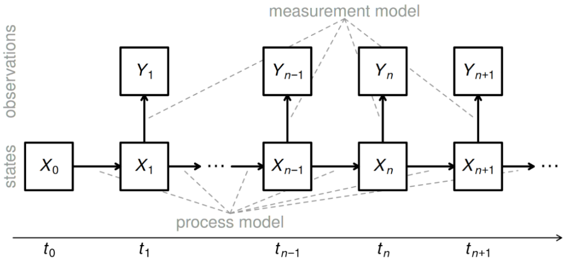
- Write $X_n = X(t_n)$ and $X_{0:N} = (X_0, \dots, X_N)$. Let Y_n be a random variable modeling the observation at time t_n.
- The one-step transition density, $f_{X_n|X_{n-1}}(x_n|x_{n-1};\theta)$, together with the measurement density, $f_{Y_n|X_n}(y_n|x_n;\theta)$ and the initial density, $f_{X_0}(x_0;\theta)$, specify the entire POMP model.
- The joint density $f_{X_{0:N},Y_{1:N}}(x_{0:N}, y_{1:N};\theta)$ can be written as

$$f_{X_0}(x_0;\theta) \prod_{n=1}^{N} f_{X_n|X_{n-1}}(x_n|x_{n-1};\theta)\, f_{Y_n|X_n}(y_n|x_n;\theta)$$

- The marginal density for $Y_{1:N}$ evaluated at the data, $y^*_{1:N}$, is

$$f_{Y_{1:N}}(y^*_{1:N};\theta) = \int f_{X_{0:N},Y_{1:N}}(x_{0:N}, y^*_{1:N};\theta)\, dx_{0:N}$$

Another POMP model schematic



- The state process, X_n, is Markovian, i.e.,

$$f_{X_n|X_{0:n-1},Y_{1:n-1}}(x_n|x_{0:n-1},y_{1:n-1}) = f_{X_n|X_{n-1}}(x_n|x_{n-1}).$$

- Moreover, Y_n, depends only on the state at that time:

$$f_{Y_n|X_{0:N},Y_{1:n-1}}(y_n|x_{0:n},y_{1:n-1}) = f_{Y_n|X_n}(y_n|x_n), \quad \text{for } n = 1,\dots,N.$$

Moving from math to algorithms for POMP models

We specify some *basic model components* which can be used within algorithms:

- `rprocess`: a draw from $f_{X_n|X_{n-1}}(x_n|x_{n-1};\theta)$
- `dprocess`: evaluation of $f_{X_n|X_{n-1}}(x_n|x_{n-1};\theta)$
- `rmeasure`: a draw from $f_{Y_n|X_n}(y_n|x_n;\theta)$
- `dmeasure`: evaluation of $f_{Y_n|X_n}(y_n|x_n;\theta)$
- `rinit`: a draw from $f_{X_0}(x_0;\theta)$

These basic model components define the specific POMP model under consideration.

What is a simulation-based method?

- Simulating random processes is often much easier than evaluating their transition probabilities.
- In other words, we may be able to write rprocess but not dprocess.
- *Simulation-based* methods require the user to specify rprocess but not dprocess.
- *Plug-and-play*, *likelihood-free* and *equation-free* are alternative terms for "simulation-based" methods.
- Much development of simulation-based statistical methodology has occurred in the past decade.

The pomp package for POMP models

- pomp is an R package for data analysis using partially observed Markov process (POMP) models (King, Nguyen, and Ionides 2016).
- Note the distinction: lower case pomp is a software package; upper case POMP is a class of models.
- pomp builds methodology for POMP models in terms of arbitrary user-specified POMP models.
- pomp provides tools, documentation, and examples to help users specify POMP models.
- pomp provides a platform for modification and sharing of models, data-analysis workflows, and methodological development.

Structure of the pomp package

It is useful to divide the pomp package functionality into different levels:

- Basic model components
- Workhorses
- Elementary POMP algorithms
- Inference algorithms

Basic model components

Basic model components are user-specified procedures that perform the elementary computations that specify a POMP model. There are nine of these:

- `rinit`: simulator for the initial-state distribution, i.e., the distribution of the latent state at time t_0.
- `rprocess` and `dprocess`: simulator and density evaluation procedure, respectively, for the process model.
- `rmeasure` and `dmeasure`: simulator and density evaluation procedure, respectively, for the measurement model.
- `rprior` and `dprior`: simulator and density evaluation procedure, respectively, for the prior distribution.
- `skeleton`: evaluation of a deterministic skeleton.
- `partrans`: parameter transformations.

The scientist must specify whichever of these basic model components are required for the algorithms that the scientist uses.

Workhorses

Workhorses are `R` functions, built into the package, that cause the basic model component procedures to be executed.

- Each basic model component has a corresponding workhorse.
- Effectively, the workhorse is a vectorized wrapper around the basic model component.
- For example, the `rprocess()` function uses code specified by the rprocess model component, constructed via the `rprocess` argument to `pomp()`.
- The rprocess model component specifies how a single trajectory evolves at a single moment of time. The `rprocess()` workhorse combines these computations for arbitrary collections of times and arbitrary numbers of replications.

Elementary POMP algorithms

These are algorithms that interrogate the model or the model/data confrontation without attempting to estimate parameters. There are currently four of these:

- `simulate` performs simulations of the POMP model, i.e., it samples from the joint distribution of latent states and observables.
- `pfilter` runs a sequential Monte Carlo (particle filter) algorithm to compute the likelihood and (optionally) estimate the prediction and filtering distributions of the latent state process.
- `probe` computes one or more uni- or multi-variate summary statistics on both actual and simulated data.
- `spect` estimates the power spectral density functions for the actual and simulated data.

POMP inference algorithms I

These are procedures that build on the elementary algorithms and are used for estimation of parameters and other inferential tasks. There are currently ten of these:

- `abc`: approximate Bayesian computation
- `bsmc2`: Liu-West algorithm for Bayesian SMC
- `pmcmc`: a particle MCMC algorithm
- `mif2`: iterated filtering (IF2)
- `enkf`, `eakf` ensemble and ensemble adjusted Kalman filters
- `traj_objfun`: trajectory matching
- `spect_objfun`: power spectrum matching
- `probe_objfun`: probe matching
- `nlf_objfun`: nonlinear forecasting

POMP inference algorithms II

Objective function methods: among the estimation algorithms just listed, four are methods that construct stateful objective functions that can be optimized using general-purpose numerical optimization algorithms such as `optim`, `subplex`, or the optimizers in the nloptr package.

References I

Andrade, Jair, and Jim Duggan. 2022. "Inferring the Effective Reproductive Number from Deterministic and Semi-Deterministic Compartmental Models Using Incidence and Mobility Data." *PLoS Comput Biol* 18 (6): e1010206. https://doi.org/10.1371/journal.pcbi.1010206.

Baracchini, Theo, Aaron A. King, Menno J. Bouma, Xavier Rodó, Enrico Bertuzzo, and Mercedes Pascual. 2017. "Seasonality in Cholera Dynamics: A Rainfall-Driven Model Explains the Wide Range of Patterns in Endemic Areas." *Adv Water Resour* 108C: 357–66. https://doi.org/10.1016/j.advwatres.2016.11.012.

Bjørnstad, O. N., and B. T. Grenfell. 2001. "Noisy Clockwork: Time Series Analysis of Population Fluctuations in Animals." *Science* 293: 638–43. https://doi.org/10.1126/science.1062226.

References II

Blake, Isobel M., Rebecca Martin, Ajay Goel, Nino Khetsuriani, Johannes Everts, Christopher Wolff, Steven Wassilak, R. Bruce Aylward, and Nicholas C. Grassly. 2014. "The Role of Older Children and Adults in Wild Poliovirus Transmission." *Proc Natl Acad Sci* 111 (29): 10604–9. https://doi.org/10.1073/pnas.1323688111.

Domenech de Cellès, Matthieu, Felicia M. G. Magpantay, Aaron A. King, and Pejman Rohani. 2018. "The Impact of Past Vaccination Coverage and Immunity on Pertussis Resurgence." *Sci Transl Med* 10 (434): eaaj1748. https://doi.org/10.1126/scitranslmed.aaj1748.

Fox, Spencer J., Michael Lachmann, Mauricio Tec, Remy Pasco, Spencer Woody, Zhanwei Du, Xutong Wang, et al. 2022. "Real-Time Pandemic Surveillance Using Hospital Admissions and Mobility Data." *Proc Natl Acad Sci* 119 (7): e2111870119. https://doi.org/10.1073/pnas.2111870119.

References III

King, Aaron A., Matthieu Domenech de Cellès, Felicia M. G. Magpantay, and Pejman Rohani. 2015. "Avoidable Errors in the Modelling of Outbreaks of Emerging Pathogens, with Special Reference to Ebola." *Proc R Soc Lond B* 282 (1806): 20150347. https://doi.org/10.1098/rspb.2015.0347.

King, Aaron A., Edward L. Ionides, Mercedes Pascual, and Menno J. Bouma. 2008. "Inapparent Infections and Cholera Dynamics." *Nature* 454 (7206): 877–80. https://doi.org/10.1038/nature07084.

King, Aaron A., Dao Nguyen, and Edward L. Ionides. 2016. "Statistical Inference for Partially Observed Markov Processes via the R Package Pomp." *J Stat Softw* 69 (12): 1–43. https://doi.org/10.18637/jss.v069.i12.

References IV

Laneri, Karina, Anindya Bhadra, Edward L. Ionides, Menno Bouma, Ramesh C. Dhiman, Rajpal S. Yadav, and Mercedes Pascual. 2010. "Forcing Versus Feedback: Epidemic Malaria and Monsoon Rains in Northwest India." *PLoS Comput Biol* 6 (9): e1000898. https://doi.org/10.1371/journal.pcbi.1000898.

Lavine, Jennie S., Aaron A. King, Viggo Andreasen, and Ottar N. Bjørnstad. 2013. "Immune Boosting Explains Regime-Shifts in Prevaccine-Era Pertussis Dynamics." *PLoS ONE* 8 (8): e72086. https://doi.org/10.1371/journal.pone.0072086.

Pons-Salort, Margarita, and Nicholas C. Grassly. 2018. "Serotype-Specific Immunity Explains the Incidence of Diseases Caused by Human Enteroviruses." *Science* 361 (6404): 800–803. https://doi.org/10.1126/science.aat6777.

References V

Romero-Severson, E. O., E. Volz, J. S. Koopman, T. Leitner, and E. L. Ionides. 2015. "Dynamic Variation in Sexual Contact Rates in a Cohort of HIV-Negative Gay Men." *Am J Epidemiol* 182 (3): 255–62. https://doi.org/10.1093/aje/kwv044.

Shah, Mirai, Gabrielle Ferra, Susan Fitzgerald, Paul J. Barreira, Pardis C. Sabeti, and Andrés Colubri. 2022. "Containing the Spread of Mumps on College Campuses." *R Soc Open Sci* 9 (1): 210948. https://doi.org/10.1098/rsos.210948.

Shirreff, George, Jean-Ralph Zahar, Simon Cauchemez, Laura Temime, and Lulla Opatowski. 2022. "Measuring Basic Reproduction Number to Assess Effects of Nonpharmaceutical Interventions on Nosocomial SARS-CoV-2 Transmission." *Emerg Infect Dis* 28 (7): 1345–54. https://doi.org/10.3201/eid2807.212339.

References VI

Subramanian, Rahul, Qixin He, and Mercedes Pascual. 2021. "Quantifying Asymptomatic Infection and Transmission of COVID-19 in New York City Using Observed Cases, Serology, and Testing Capacity." *Proc Natl Acad Sci* 118 (9): e2019716118. https://doi.org/10.1073/pnas.2019716118.

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