

Introduction to Simulation-based Inference for Epidemiological Dynamics

Aaron A. King and Edward L. Ionides

Outline

- 1 Introduction
 - What makes epidemiological inference hard?
 - Course overview
- 2 Partially observed Markov processes
 - Mathematical definitions
 - From math to algorithms
- 3 The **pomp** package

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:
 - Which explanations are most favored by the data?
 - Which kinds of data are most informative?
- Central applied goals:
 - How to design ecological or epidemiological intervention?
 - How to make accurate forecasts?
- 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 *et al.*, 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)

Questions and answers II

- 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)
- ⑨ Can serotype-specific immunity explain the strain dynamics of human enteroviruses? (Pons-Salort and Grassly, 2018)
- ⑩ How does dynamic variation in individual sexual behavior contribute to the HIV epidemic? How does this compare to the role of heterogeneity between individuals? (Romero-Severson *et al.*, 2015)

Questions and answers III

- 11 What is the contribution of adults to polio transmission? (Blake *et al.*, 2014)
- 12 What explains the interannual variability of malaria? (Laneri *et al.*, 2010)
- 13 Can hydrology explain the seasonality of cholera? (Baracchini *et al.*, 2017)
- 14 What roles are played by asymptomatic infection and waning immunity in cholera epidemics? (King *et al.*, 2008)

Partially observed Markov process (POMP) models

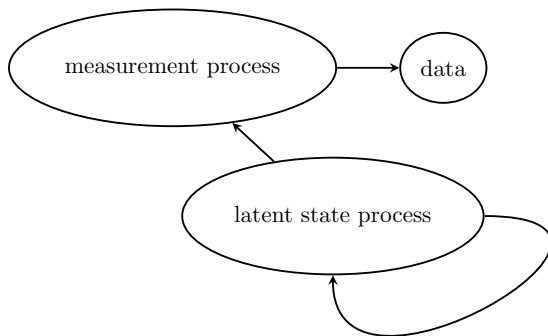
- Data y_1^*, \dots, y_N^* collected at times $t_1 < \dots < t_N$ are modeled as noisy, incomplete, and indirect observations of a Markov process $\{X(t), t \geq t_0\}$.
- This is a **partially observed Markov process (POMP)** model, also known as a hidden Markov model or a state space model.
- $\{X(t)\}$ 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.

Partially observed Markov process (POMP) models II

- 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 POMDP

- 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

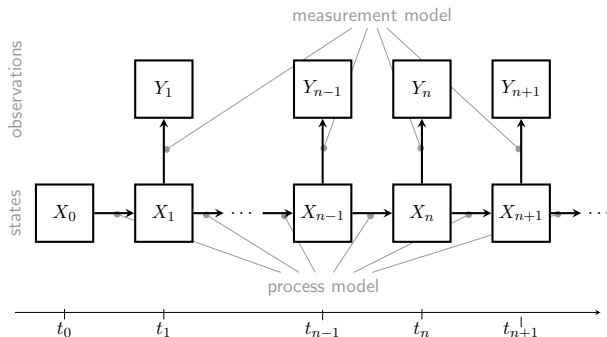
- Write $X_n = X(t_n)$ and $X_{0:N} = (X_0, \dots, X_N)$. Let Y_n be a random variable modeling the observation at time t_n .
- The one-step transition density, $f_{X_n|X_{n-1}}(x_n|x_{n-1}; \theta)$, together with the measurement density, $f_{Y_n|X_n}(y_n|x_n; \theta)$ and the initial density, $f_{X_0}(x_0; \theta)$, 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 *et al.*, 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 multivariate summary statistics on both actual and simulated data.
- `spect` estimates the power spectral density functions for the actual and simulated data.

POMP inference algorithms

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

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

- Andrade J, Duggan J (2022). “Inferring the effective reproductive number from deterministic and semi-deterministic compartmental models using incidence and mobility data.” *PLoS Comput Biol*, **18**(6), e1010206.
[doi: 10.1371/journal.pcbi.1010206](https://doi.org/10.1371/journal.pcbi.1010206).
- Baracchini T, King AA, Bouma MJ, Rodó X, Bertuzzo E, Pascual M (2017). “Seasonality in cholera dynamics: a rainfall-driven model explains the wide range of patterns in endemic areas.” *Adv Water Resour*, **108C**, 357–366. [doi: 10.1016/j.advwatres.2016.11.012](https://doi.org/10.1016/j.advwatres.2016.11.012).
- Bjørnstad ON, Grenfell BT (2001). “Noisy clockwork: Time series analysis of population fluctuations in animals.” *Science*, **293**, 638–643.
[doi: 10.1126/science.1062226](https://doi.org/10.1126/science.1062226).

References II

- Blake IM, Martin R, Goel A, Khetsuriani N, Everts J, Wolff C, Wassilak S, Aylward RB, Grassly NC (2014). “The role of older children and adults in wild poliovirus transmission.” *Proc Natl Acad Sci*, **111**(29), 10604–10609. doi: [10.1073/pnas.1323688111](https://doi.org/10.1073/pnas.1323688111).
- Domenech de Cellès M, Magpantay FMG, King AA, Rohani P (2018). “The impact of past vaccination coverage and immunity on pertussis resurgence.” *Sci Transl Med*, **10**(434), eaaj1748. doi: [10.1126/scitranslmed.aaj1748](https://doi.org/10.1126/scitranslmed.aaj1748).

References III

- Fox SJ, Lachmann M, Tec M, Pasco R, Woody S, Du Z, Wang X, Ingle TA, Javan E, Dahan M, Gaither K, Escott ME, Adler SI, Johnston SC, Scott JG, Meyers LA (2022). “Real-time pandemic surveillance using hospital admissions and mobility data.” *Proc Natl Acad Sci*, **119**(7), e2111870119. doi: [10.1073/pnas.2111870119](https://doi.org/10.1073/pnas.2111870119).
- King AA, Domenech de Cellès M, Magpantay FMG, Rohani P (2015). “Avoidable errors in the modelling of outbreaks of emerging pathogens, with special reference to Ebola.” *Proc R Soc Lond B*, **282**(1806), 20150347. doi: [10.1098/rspb.2015.0347](https://doi.org/10.1098/rspb.2015.0347).

References IV

- King AA, Ionides EL, Pascual M, Bouma MJ (2008). “Inapparent infections and cholera dynamics.” *Nature*, **454**(7206), 877–880. doi: [10.1038/nature07084](https://doi.org/10.1038/nature07084).
- King AA, Nguyen D, Ionides EL (2016). “Statistical inference for partially observed Markov processes via the R package pomp.” *J Stat Softw*, **69**(12), 1–43. doi: [10.18637/jss.v069.i12](https://doi.org/10.18637/jss.v069.i12).
- Laneri K, Bhadra A, Ionides EL, Bouma M, Dhiman RC, Yadav RS, Pascual M (2010). “Forcing versus feedback: epidemic malaria and monsoon rains in northwest India.” *PLoS Comput Biol*, **6**(9), e1000898. doi: [10.1371/journal.pcbi.1000898](https://doi.org/10.1371/journal.pcbi.1000898).

References V

- Lavine JS, King AA, Andreasen V, Bjørnstad ON (2013). “Immune boosting explains regime-shifts in prevaccine-era pertussis dynamics.” *PLoS ONE*, **8**(8), e72086. doi: [10.1371/journal.pone.0072086](https://doi.org/10.1371/journal.pone.0072086).
- Pons-Salort M, Grassly NC (2018). “Serotype-specific immunity explains the incidence of diseases caused by human enteroviruses.” *Science*, **361**(6404), 800–803. doi: [10.1126/science.aat6777](https://doi.org/10.1126/science.aat6777).
- Romero-Severson EO, Volz E, Koopman JS, Leitner T, Ionides EL (2015). “Dynamic variation in sexual contact rates in a cohort of HIV-negative gay men.” *Am J Epidemiol*, **182**(3), 255–262. doi: [10.1093/aje/kwv044](https://doi.org/10.1093/aje/kwv044).


References VI

- Shah M, Ferra G, Fitzgerald S, Barreira PJ, Sabeti PC, Colubri A (2022).
“Containing the spread of mumps on college campuses.” *R Soc Open Sci*, **9**(1), 210948. doi: [10.1098/rsos.210948](https://doi.org/10.1098/rsos.210948).
- Shirreff G, Zahar JR, Cauchemez S, Temime L, Opatowski L (2022).
“Measuring basic reproduction number to assess effects of nonpharmaceutical interventions on nosocomial SARS-CoV-2 transmission.” *Emerg Infect Dis*, **28**(7), 1345–1354.
doi: [10.3201/eid2807.212339](https://doi.org/10.3201/eid2807.212339).

References VII

Subramanian R, He Q, Pascual M (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. doi: [10.1073/pnas.2019716118](https://doi.org/10.1073/pnas.2019716118).

License, acknowledgments, and links

- The materials build on [previous versions of this course and related courses](#).
- Licensed under the [Creative Commons Attribution-NonCommercial license](#). Please share and remix non-commercially, mentioning its origin. 
- Produced with R version 4.3.2 and **pomp** version 5.6.
- Compiled on February 26, 2024.

[Back to Lesson](#)

[pomp homepage](#)