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

Aaron A. King and Edward L. Ionides
Translated to pypomp by Kunyang He

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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 `pypomp` Python package.
- An R-`pomp` version of this course is available.
- `pypomp` supports graphical processing unit (GPU) hardware and automatic differentiation.

Why is epidemiological and ecological inference hard?

- **Complex, open, nonlinear, and non-stationary systems:**
  Precise “laws of nature” are unavailable.
  It is useful to model them as stochastic processes.
  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* (POMP) 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 `pypomp` package.
6. To provide documented examples for adaptation and re-use.

Questions and answers I

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)
6. What strategies are effective at containing mumps spread on college campuses? (Shah et al., 2022)

Questions and answers II

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)
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)

Questions and answers III

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

A **POMP model** consists of data $y_1^*, \dots, y_N^*$ collected at times $t_1 < \dots < t_N$, modeled as noisy, incomplete, and indirect observations of a Markov process $\{X(t), t \geq t_0\}$. This is 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.

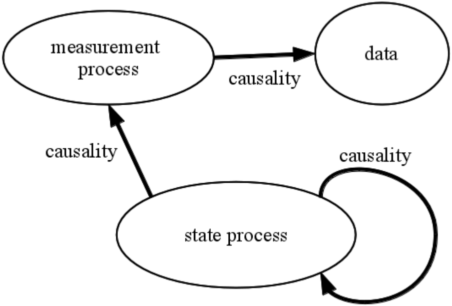


Figure 1: Schematic of the structure of a POMP

Notation for POMP models

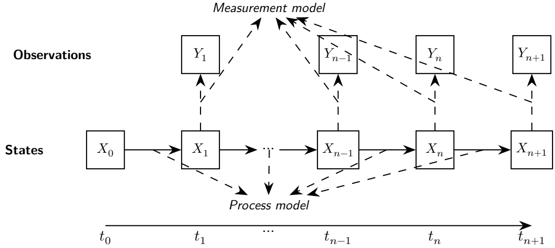
- Write $X_n = X(t_n)$ and $X_{0:N} = (X_0, \dots, X_N)$. Let Y_n be a random variable modeling the observation at time t_n.
- The one-step transition density, $f_{X_n|X_{n-1}}(x_n|x_{n-1};\theta)$, together with the measurement density, $f_{Y_n|X_n}(y_n|x_n;\theta)$ and the initial density, $f_{X_0}(x_0;\theta)$,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

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

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*.
- Much development of simulation-based statistical methodology has occurred in the past decade.

The pypomp package

- `pypomp` is a Python framework for building, simulating and fitting partially observed Markov process (POMP) models et al (2025).
- `pypomp` builds methodology for POMP models in terms of arbitrary user-specified POMP models.
- `pypomp` provides tools, documentation, and examples to help users specify POMP models.
- `pypomp` provides a platform for modification and sharing of models, data-analysis workflows, and methodological development.
- `pypomp` is built on JAX for just-in-time compilation, automatic differentiation (AD) and CPU/GPU/TPU execution.

Structure of the pypomp package

We conventionally denote the `pypomp` package by `pp`:

```
import pypomp as pp
from pypomp.pomp_class import Pomp
```

Suppose `mod` is a pypomp representation of a POMP model, so `mod` has class `Pomp`.

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

- Basic model components: building `mod` to specify the desired POMP model
- Elementary POMP algorithms: investigating `mod` at a fixed set of parameters
- Inference algorithms: parameter estimation, model selection and diagnostics

Basic model components

Basic model components are user-specified methods belonging to `mod` that perform the elementary computations that specify a POMP model. There are five of these:

`rinit`: simulator for the initial-state distribution, i.e., the distribution of the latent state at time t_0.

`rproc`: simulator for the process model.

`rmeas` and **`dmeas`**: simulator and density evaluation procedure, respectively, for the measurement model.

`par_trans`: parameter transformations.

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

Classes for basic model components

`mod.rinit` has class `RInit`

`mod.dmeas` has class `DMeas`

`mod.rmeas` has class `RMeas`

`mod.rproc` has class `RProc`

`mod.par_trans` has class `ParTrans`

These methods are not vectorized, i.e., they evaluate the model properties for a single realization of the model.

They are designed to be vectorized via a call to JAX `vmap`, and this happens internally in pypomp methods.

Elementary POMP algorithms

These are methods for `mod` that use the basic components or the data to interrogate the confrontation without attempting to estimate parameters. There are currently two 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.

POMP inference algorithms

These are methods for `Pomp` models that call the elementary algorithms and are used for estimation of parameters and other inferential tasks. There are currently three of these:

`mif`: Likelihood maximization via the IF2 iterated filtering algorithm.

`mop`: An automatically differentiatble “measurement off-parameter” particle filter.

`train`: Likelihood maximization based on `mop` or related strategies.

Examples of POMP models in pypomp

Four example constructor functions returning `Pomp` objects.

`pp.dacca`: The historical Dacca cholera data with the model of King et al. (2008)

`pp.LG`: A linear Gaussian example for validating Monte Carlo methods against exact Kalman filter calculations

`pp.measles.measlesPomp.UKMeasles`: Pre-vaccination meases in England and Wales with the model of He et al. (2010)

`pp.spx`: A stochastic volatility model for the S&P 500 stock market index.

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