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

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Outline

Objectives for this lesson

- To understand the motivations for simulation-based inference in the study of epidemiological and ecological systems.

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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.

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5. To familiarize students with the **pomp** package.
6. To provide documented examples for adaptation and re-use.

Questions and answers

1. How to explain the resurgence of pertussis in countries with sustained high vaccine coverage?
2. What roles are played by asymptomatic infection and waning immunity in cholera epidemics?
3. What explains the seasonality of measles?
4. Can serotype-specific immunity explain the strain dynamics of human enteroviruses?
5. Do subclinical infections of pertussis play an important epidemiological role?

Questions and answers II

6. What is the contribution to the HIV epidemic of dynamic variation in sexual behavior of an individual over time? How does this compare to the role of heterogeneity between individuals?
7. What explains the interannual variability of malaria?
8. What will happen next in an Ebola outbreak?
9. Can hydrology explain the seasonality of cholera?
10. What is the contribution of adults to polio transmission?

Partially observed Markov process (POMP) models

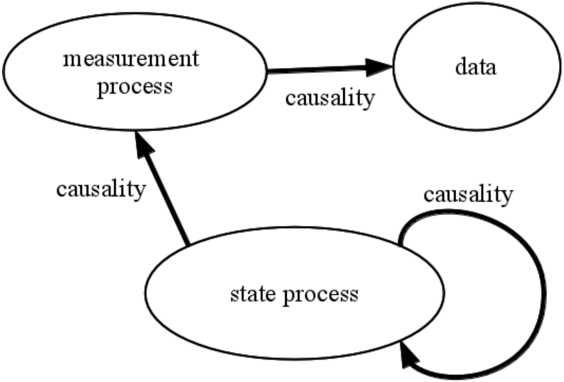
- Data $y_1^*, \dots, y_N^*$ collected at times $t_1 < \dots < t_N$ are modeled as noisy, incomplete, and indirect observations of a Markov process $\{X(t), t \geq t_0\}$.
- This is a **partially observed Markov process (POMP)** model, also known as a hidden Markov model or a state space model.
- $\{X(t)\}$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

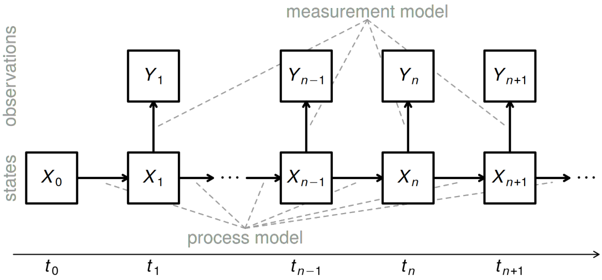
- Write $X_n = X(t_n)$ and $X_{0:N} = (X_0, \ldots, X_N)$. Let Y_n be a random variable modeling the observation at time t_n.
- The one-step transition density, $f_{X_n|X_{n-1}}(x_n|x_{n-1};\theta)$, together with the measurement density, $f_{Y_n|X_n}(y_n|x_n;\theta)$ and the initial density, $f_{X_0}(x_0;\theta)$,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

License, acknowledgments, and links

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- The materials build on previous versions of this course and related courses.
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- Produced with R version 4.0.2 and **pomp** version 3.0.2.1.

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References

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King, A. A., Nguyen, D. and Ionides, E. L. (2016). Statistical inference for partially observed Markov processes via the R package pomp, *Journal of Statistical Software* **69**(12): 1–43.