#### Lesson 8:

Case study: Panel data on dynamic variation in sexual contact rates

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#### Outline

- Panel data
- 2 Heterogeneity in sexual contact rates
- Simulation-based investigation of the fitted model
- PanelPOMP models and the panelPomp package
- 5 Likelihood-based inference for PanelPOMPs
  - Combining likelihood evaluations
  - Maximizing the likelihood

# **Objectives**

- Discuss the use of partially observed Markov process (POMP) methods for panel data, also known as longitudinal data.
- See how POMP methods can be used to understand the outcomes of a longitudinal behavioral survey on sexual contact rates.
- Introduce the R package panelPomp that extends pomp to panel data.

### Introduction to panel data

- Panel data consist of a collection of time series having no dynamic coupling.
- Each time series is called a unit
- If each unit contain insufficient information to estimate model parameters, we infer shared parameters by pooling across the whole panel.
- We may have unit-specific parameters, taking distinct values for each unit.
- The goals of developing, fitting and criticizing mechanistic models for panel data are similar to analysis of a single time series.

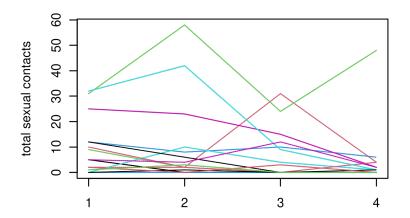
# Heterogeneities in sexual contacts

- Basic epidemiological models suppose equal contact rates for all individuals in a population.
- Sometimes these models are extended to permit rate heterogeneity between individuals.
- Rate heterogeneity within individuals, i.e., dynamic behavioral change, has rarely been considered.
- There have been some indications that rate heterogeneity plays a substantial role in the HIV epidemic.

# Data from a prospective study

- Romero-Severson *et al.* (2015) investigated whether dynamic variation in sexual contact rates are a real and measurable phenomenon.
- They analyzed a large cohort study of HIV-negative gay men in 3 cities (Vittinghoff *et al.*, 1999).
- In a simple model for HIV, with a fully mixing population of susceptible and infected individuals, the fitted variation found by Romero-Severson et al. (2015) can explain the observed prevalence history in the US despite the low per-contact infectivity of HIV.
- Here, we consider the longitudinal data from Vittinghoff et al. (1999) on total sexual contacts over four consecutive 6-month periods, for the 882 men having no missing observations.

Plotted is a sample of 15 time series from contacts.csv.



# Types of contact rate heterogeneity

We want a model that can describe all sources of variability in the data:

- Differences between individuals
- Differences within individuals over time
- Over-dispersion: variances exceeding that of a Poisson model

### A model for dynamic variation in sexual contact rates

- We use the model of Romero-Severson *et al.* (2015), with each individual making contacts at a latent rate  $X_i(t)$ .
- Each data point,  $y_{ij}$ , is the number of reported contacts for individual i between time  $t_{j-1}$  and  $t_j$ , where  $i=1,\ldots,882$  and  $j=1,\ldots,4$ .
- The unobserved process  $\{X_i(t)\}$  is connected to the data through the expected number of contacts for individual i in reporting interval j, which we write as

$$C_{ij} = \alpha^{j-1} \int_{t_{j-1}}^{t_j} X_i(t) dt,$$

where  $\alpha$  is an additional secular trend that accounts for the observed decline in reported contacts.

### Overdispersion relative to Poisson variation

- A basic stochastic model for homogeneous count data models  $y_{ij}$  as a Poisson random variable with mean and variance equal to  $C_{ij}$  (Keeling and Rohani, 2009).
- However, the variance in the data are much higher than the mean of the data (Romero-Severson *et al.*, 2012).
- Therefore, we model the data as negative binomial, a generalization of a Poisson distribution that permits variance larger than the mean:

$$y_{ij} \sim \text{NegBin} (C_{ij}, D_i),$$

with mean  $C_{ij}$  and variance  $C_{ij} + C_{ij}^2/D_i$ .

- Here,  $D_i$  is called the dispersion parameter, with the Poisson model being recovered in the limit as  $D_i$  becomes large.
- The dispersion,  $D_i$ , can model increased variance (compared to Poisson variation) for individual contacts, but cannot explain observed autocorrelation between measurements on an individual over time.

#### Autocorrelation and individual-level effects

• To model autocorrelation, we suppose that individual i has behavioral episodes within which  $X_i(t)$  is constant, but the individual enters new behavioral episodes at rate  $R_i$ . At the start of each episode,  $X_i(t)$  takes a new value drawn from a Gamma distribution with mean  $\mu_X$  and variance  $\sigma_X$ ,

$$X_i(t) \sim \mathsf{Gamma}(\mu_X, \sigma_X).$$

• To complete the model, we also assume Gamma distributions for  $D_i$  and  $R_i$ ,

$$D_i \sim \mathsf{Gamma}(\mu_D, \sigma_D),$$
  $R_i \sim \mathsf{Gamma}(\mu_R, \sigma_R).$ 

The parameters,  $\sigma_X$ ,  $\sigma_D$  and  $\sigma_R$  control individual-level differences in behavioral parameters allowing the model to encompass a wide range of sexual contact patterns.

# Parameter interpretation and identifiability

- The distinction between the effects of the rate at which new behavioral episodes begin,  $R_i$ , and the dispersion parameter,  $D_i$ , is subtle since both model within-individual variability.
- The signal in the data about distinct behavioral episodes could be overwhelmed by a high variance in number of reported contacts resulting from a low value of  $D_i$ .
- Whether the data are sufficient to identify both  $R_i$  and  $D_i$  is an empirical question.

# Consequences of dynamic behavior in an SI model for HIV

- 3 cases where contact rates are either (a) constant; (b) vary only between individuals; (c) vary both between and within individuals.
- In each case, parameterize the model by fitting the behavioral model above, and supplying per-contact infection rates from the literature.
- This simple model shows a potential role for dynamic variation.



Fig 4 of Romero-Severson et al. (2015). The median of 500 simulations are shown as lines and the  $75^{th}$  and  $25^{th}$  percentiles are shown as gray envelopes.

- 'Homogeneous' (dashed line): the epidemic was simulated where  $\mu_X$  is estimated by the sample mean (1.53  $\mathrm{month}^{-1}$ ) without any sources of between-individual or within-individual heterogeneity.
- 'Between Heterogeneity' (dotted line): the epidemic was simulated where  $\mu_X$  is estimated by the sample mean (1.53  $\mathrm{month}^{-1}$ ) and  $\sigma_X$  is estimated by the sample standard deviation (3.28  $\mathrm{month}^{-1}$ )
- 'Within+Between Heterogeneity' (solid line): the epidemic was simulated where each parameter is set to the estimated maximum likelihood estimate for total contacts.
- For all situations, the per contact probability of transmission was set to 1/120, the average length of infection was set to 10 years, and the infection-free equilibrium population size was set to 3000. The per contact probability was selected such that the basic reproduction number in the the 'Homogeneous' case was 1.53. In the 'Homogeneous', 'Between Heterogeneity', 'Within+Between Heterogeneity' cases respectively 239/500 and 172/500, 95/500 simulations died out before the 100 year mark.

#### PanelPOMP models as an extension of POMP models

- A PanelPOMP model consists of independent POMP models for a collection of units.
- The POMP models are tied together by shared parameters.
- Here, the units are individuals in the longitudinal survey.
- In general, some parameters may be unit-specific (different for each individual) whereas others are shared (common to all individuals).
- Here, we only have shared parameters. The heterogeneities between individuals are modeled as random effects with distribution determined by these shared parameters.
- Iterated filtering for POMP models was extended to PanelPOMPs by Bretó *et al.* (2019).

# Using the panelPomp R package

- The main task of panelPomp beyond pomp is to handle the additional book-keeping necessitated by the unit structure.
- PanelPOMP models also motivate methodological developments to deal with large datasets and the high dimensional parameter vectors that can result from unit-specific parameters.
- A panelPomp object for the above contact data and model is provided by contacts in panelPomp.

```
library(panelPomp)
contacts <- contacts()</pre>
```

• The implementation of the above model equations in contacts can be found in the panelPomp source code on github.

Let's start by exploring the contacts object

```
class(contacts)
[1] "panelPomp"
attr(,"package")
[1] "panelPomp"
slotNames(contacts)
[1] "unit.objects" "shared"
                                    "specific"
class(unitobjects(contacts)[[1]])
[1] "pomp"
attr(,"package")
[1] "pomp"
```

- We see that an object of class panelPomp is a list of pomp objects together with a parameter specification permitting shared and/or unit-specific parameters.
- The POMP models comprising the PanelPOMP model do not need to have the same observation times for each unit.

# Exercise 8.1. A PanelPOMP with all parameters unit-specific

Suppose a PanelPOMP model has all its parameters unit-specific. Is there anything useful to be gained from the PanelPOMP structure, or is it preferable to analyze the data as a collection of POMP models?

Worked solution

## Exercise 8.2. Methods for panelPomps

How would you find the **panelPomp** package methods available for working with a panelPomp object?

Worked solution

#### Likelihood evaluation for PanelPOMPs

- PanelPOMP models are closely related to POMPs, and particle filter methods remain applicable.
- contacts contains a parameter vector corresponding to the MLE for total contacts reported by Romero-Severson et al. (2015):

• pfilter(contacts, Np=1000) carries out a particle filter computation at this parameter vector.

# Exercise 8.3. What happens when we pfilter a panelPomp

- Describe what you think pfilter(contacts, Np=1000) should do.
- Hypothesize what might be the class of the resulting object? What slots might this object possess?
- Check your hypothesis.

#### Worked solution

## Replicated likelihood evaluations

 As usual for Monte Carlo calculations, it is useful to replicate the likelihood evaluations, both to reduce Monte Carlo uncertainty and (perhaps more importantly) to quantify it.

• This took 0.3 minutes using 24 cores.

# Combining Monte Carlo likelihood evaluations for PanelPOMPs

- We have a new consideration not found with pomp models. Each unit has its own log likelihood arising from an independent Monte Carlo computation.
- The basic pomp approach remains valid:

```
loglik1 <- sapply(pf1_results,function(x) x$logLik)
logmeanexp(loglik1,se=T)

se
-9556.0510818  0.5359242</pre>
```

• Can we do better, using the independence of units? It turns out we can (Bretó et al., 2019).

### logmeanexp versus panel\_logmeanexp

- The improvement via panel\_logmeanexp is small in this case, since the number of observation times is small.
- For longer panels, the difference becomes more important.

# Exercise 8.4. The difference between panel\_logmeanexp and logmeanexp

- The basic pomp approach averages the Monte Carlo likelihood estimates after aggregating the likelihood over units.
- The panel\_logmeanexp averages separately for each unit before combining.
- Why does the latter typically give a higher log likelihood estimate with lower Monte Carlo uncertainty?
- Either reason at a heuristic level or (optionally) develop a mathematical argument.

#### Worked solution

# Writing a PanelPOMP as a POMP

- If we can formally write a PanelPOMP as a POMP, we can use methods such as mif2 for inference.
- We could stack the panel models in different ways to make a large POMP model.
- A naive way to do inference for a PanelPOMP model as a POMP is to let an observation for the POMP be a vector of observations for all units in the PanelPOMP at that time. This gives a high-dimensional observation vector which is numerically intractable via particle filters.
- Instead, we concatenate the panels into one long time series, with dynamic breaks where the panels are glued together.

# Likelihood maximization using the PIF algorithm

- The panel iterated filtering (PIF) algorithm of Bretó et al. (2019) applies the IF2 algorithm to a POMP model constructed by concanenating the collection of panels.
- PIF is implemented in panelPomp as the mif2 method for class panelPomp.
- Comparing ?panelPomp::mif2 with ?pomp::mif2 reveals that the only difference in the arguments is that the params argument for pomp::mif2 becomes shared.start and specific.start for panelPomp::mif2.
- As an example of an iterated filtering investigation, let's carry out a local search, starting at the current estimate of the MLE.
- Following Romero-Severson *et al.* (2015) we fix  $\sigma_R = 0$ .

```
mif_results <- foreach(i=1:20) %dopar% {
  library(pomp); library(panelPomp)
  mf <- mif2(contacts.
    Nmif = if(DEBUG) 2 else 50,
    Np = if(DEBUG) 5 else 1000,
    cooling.type="geometric", # needed for panelPomp 0.10
    cooling.fraction.50=0.5,
    rw.sd=rw.sd(mu_X=0.02, sigma_X=0.02, mu_D = 0.02,
      sigma_D=0.02, mu_R=0.02, alpha=0.02)
  list(logLik=logLik(mf),params=coef(mf))
```

- This search took 16.2 minutes on 24 cores.
- We see that panelPomp iterated filtering is set up similarly to its pomp cousin.

#### Some considerations for likelihood evaluations

Similar likelihood evaluation issues arise for panelPomp as for pomp.

- The preliminary likelihood estimated as a consequence of running mif2 and extracted here by sapply(m2,logLik) does not correspond to the actual, fixed parameter, model. It is the sequential Monte Carlo estimate of the likelihood from the last filtering iteration, and therefore will have some perturbation of the parameters.
- One typically requires fewer particles for each filtering iteration than necessary to obtain a good likelihood estimate—stochastic errors can cancel out through the filtering iterations, rather than within any one iteration.
- For promising new parameter values, it is desirable to put computational effort into evaluating the likelihood sufficient to make the Monte Carlo error small compared to one log unit.

```
mif_logLik <- sapply(mif_results,function(x)x$logLik)</pre>
mif_mle <- mif_results[[which.max(mif_logLik)]]$params</pre>
pf3_loglik_matrix <- foreach(i=1:10,.combine=rbind) %dopar% {
  library(panelPomp)
  unitlogLik(pfilter(contacts,
    shared=mif_mle,Np=if(DEBUG) 50 else 10000))
```

```
panel_logmeanexp(pf3_loglik_matrix,MARGIN=2,se=T)
                        se
-9560.3145716 0.3918149
```

- This took 0.7 minutes on 24 cores.
- Here, the local search found a lower likelhood that the published MLE. Longer searches with more cooling, and/or more Monte Carlo replications, may be needed to reliably obtain accurate maximization.

#### References

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Vittinghoff E, Douglas J, Judon F, McKiman D, MacQueen K, Buchinder SP (1999). "Per-Contact Risk of Human Immunodificiency Virus Tramnsmision between Male Sexual Partners." *American Journal of Epidemiology*, **150**(3), 306–311.

# License, acknowledgments, and links

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