Estimating contact matrices from seroprevalence data, or susceptible reconstruction, using WAIFW tensors

Ben Bolker

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1 Introduction

Some thoughts about using susceptible reconstruction (etc.) to estimate contact rates in structured population models. This combines ideas of Fine and Clarkson (1982) "susceptible reconstruction" with the basic principle of Anderson & May's WAIFW matrix reconstruction of age-structured contact rates. This extends an idea I had a long time ago (dig out Mathematica worksheet?) about using tensor products with WAIFW matrices.

2 Estimating force of infection / susceptibles

2.1 From age-structured seroprevalence data

Anderson and May derived the age-specific force of infection, $\lambda(a)$, from age-structured serological data (making an equilibrium assumption so that $\partial S(a)/\partial a = -\lambda(a)S(a)$), and then solved the equations for the components of $\boldsymbol{\beta}$. Useful references are Grenfell and Anderson (1985); Anderson and May (1985, 1992), although the only one I have handy is Anderson and May (1992) (Appendix D), which doesn't give an enormous amount of detail.

If we have a cross-sectional (or longitudinal) survey of seroprevalence, and we're willing to assume temporal homogeneity ...

2.2 From equilibrium multi-species seroprevalence

Consider a multi-compartment SIR model (with mass-action transmission, vital dynamics with balanced births and deaths, exponentially distributed infectious periods, etc.: several of these assumptions can probably be relaxed a bit):

$$S_i' = +\mu_i N_i + S_i(-\sum \beta_{ij} I_j - \mu_i) \quad (1)$$

$$I_i' = +S_i \cdot \sum \beta_{ij} I_j - I_i(\mu_i + \gamma_i) \quad (2)$$

$$R_i' = +\gamma_i I_i - \mu_i R_i \quad (3)$$

If we have seroprevalence data and are willing to assume the epidemic is at equilibrium, we know S^*, the number of non-exposed individuals (assuming that antibody response is instantaneous, or at least on a short time scale,

and permanent). (In general I will write scalars with subscripts; vectors as variables without subscripts; and matrices and tensors in bold. Element-by-element multiplication is denoted by $A \cdot B$, division by A/B.)

Suppose we know N (constant population size), μ (birth/death rate) and γ (recovery rate) for each species, from field observations or lab experiments. At equilibrium we also know

$$R^* = I^* \cdot (\gamma/\mu)$$

and

$$I^* = (N - S^*)/(1 + \gamma/\mu)$$

Then we know everything in the middle equation except $\beta_{ij} = \boldsymbol{\beta}$.

2.3 From case reporting data/susceptible reconstruction

If we have case reporting data and birth rate data (or are willing to assume homogeneous birth rates etc.), and can make an assumption that the reporting period is equal to the generation time of the epidemic (although we can relax this: cite Olga Krylova; also cite Mollison and ud Din?, Bobashev?), then we can follow (Fine and Clarkson, 1982) in assuming that the reported cases are equal to the incidence, and also to the removal rate from susceptibles:

$$\begin{aligned} S_{t+1} &= S_t - I_t + b_t \\ I_{t+1} &= \Lambda_t S_t = I_t \boldsymbol{\beta} S_t \end{aligned} \tag{4}$$

There are lots of things we have to assume/be careful about — doing the accounting for timing (i.e., how the times are matched up between I and S), measurement, error, etc.. The Bjørnstadt/Finkenstädt/Grenfell TSIR model attempts to handle some of these issues.

3 Estimating $\boldsymbol{\beta}$

3.1 General principles

We'd like to solve for $\boldsymbol{\beta}$, but we don't have enough information, since we only have n data to estimate n^2 quantities (allowing for asymmetric transmission between species, which Anderson and May dismiss in the age-structured case but which is perhaps more plausible in the more general multi-compartmental/multi-species case). The Anderson and May "WAIFW matrix" approach, developed for age-structured problems, assumes we can structure the matrix to reduce the number of free parameters. What is new here, as far as I know, is (1) the idea of using a tensor to describe the structure of the WAIFW matrix and its relationship with the reduced parameter vector b; (2) applying the technique to (non-age-structured) situations — multi-species or spatial

In particular, there is a "WAIFW tensor" $\boldsymbol{T}$ that constructs an $n \times n$ WAIFW matrix from an n-parameter vector of contact components (don't know what to call these). We say $\boldsymbol{\beta} = b\boldsymbol{T}$. Then

$$\boldsymbol{\beta} I^* = (b\boldsymbol{T}) I^* = b(\boldsymbol{T} I^*) \tag{5}$$

and we should be able to solve for b in the equations above.

3.2 General (simple) example

OK, so how does this work? Let's say I want to work with a WAIFW matrix that looks like this:

$$\begin{pmatrix} b_1 & b_1 & b_3 \\ b_1 & b_1+b_2 & b_3 \\ b_3 & b_3 & b_3 \end{pmatrix}; \tag{6}$$

i.e., group 1 mixes with itself and group 2 at the same rate; group 2 mixes within itself at a higher rate; and group 3 mixes with itself and everyone else at a different (lower?) rate. (This is a typical WAIFW matrix from the age-structured case — it's a simplified version of "WAIFW 1" from Anderson and May (1992) p. 177; it might not make a lot of sense in the cross-species case, but I'm using it because it's familiar. Everything should generalize to arbitrary matrices, I think.)

(As R defines matrices and arrays, columns are the first dimension, rows the second, and "tables" the third)

```
library(tensor)
T <- array(
  c(1,1,0,   ## b1 elements by column
    1,1,0,
    0,0,0,
#
    0,0,0,   ## b2 elements by column
    0,1,0,
    0,0,0,
#
    0,0,1,   ## b3 elements by column
    0,0,1,
    1,1,1),
  dim=c(3,3,3))
```

The first "table" corresponds to the b_1 component, the second to the b_2 component, and the third to the b_3 component: our $\boldsymbol{\beta}$ matrix is just $\sum T_{ijk} b_k$ (i.e., we're right- rather than left-multiplying; if we want to left-multiply, it would be good to figure out the general rules for transposition matching the matrix rule $(AB)^T = B^T A^T$: which dimensions do we transpose, and how do we specify that in R?).

Pick some reasonable (and distinguishable) values for b, and make b into a $3 \times 1 \times 1$ tensor for compatibility:

```
(b <- array(c(0.1, 0.8, 0.01), dim = c(3, 1, 1)))
## , , 1
##
##      [,1]
## [1,] 0.10
## [2,] 0.80
## [3,] 0.01
```

Now multiply, summing the third slice of $\mathbf{T}$ times the first slice of b

```
beta <- drop(tensor(T, b, 3, 1))
beta
##      [,1] [,2] [,3]
## [1,] 0.10 0.10 0.01
## [2,] 0.10 0.90 0.01
## [3,] 0.01 0.01 0.01
```

(`drop()` just gets rid of unwanted dimensions — e.g. the tensor product returns a $3 \times 3 \times 1 \times 1$ result, `drop()` turns it into a 3×3 matrix.)

Now all I have to do is figure out how to multiply by I^* instead. Suppose $I^* = \{100, 200, 50\}$. Then $\boldsymbol{\beta} I^*$ is:

```
I <- c(100, 200, 50)
drop(beta %*% I)
## [1]  30.5 190.5   3.5
```

To combine with I^* first: our overall expression is

$$\sum_j \left(\sum_k T_{ijk} b_k \right) I_j^* = \sum_k \left(\sum_j T_{ijk} I_j^* \right) b_k =$$

The only (!?) confusing part is that columns are represented by the *first* index of an R matrix or tensor, not the second: as the expression above shows, we will want to right-multiply by b after we have multiplied by S_j^* and dropped the j index.

```
I.arr <- array(I, dim = c(3, 1, 1))
drop(drop(tensor(T, I.arr, 1, 1)) %*% drop(b))
## [1]  30.5 190.5   3.5
```

4 Example #2

It's a bit silly, but I can illustrate this with a longer example: (Actually it's not silly at all. I had the previous equations badly wrong the first time around!)

Load the ODE-solver package and define a function to calculate the gradient; use parameters $\mu = \{0.01, 0.01, 0.01\}$; $\gamma = \{0.01, 0.02, 0.01\}$; and β as defined above (Figure 1).

Now try to reconstruct. Suppose we know μ, γ, N, and S^*, and are hence able to reconstruct (see above) I^* and R^*. Then

$$\begin{aligned} 0 &= S^* \cdot (\boldsymbol{\beta} I^*) - I^* \cdot (\mu + \gamma) \\ (\boldsymbol{\beta} I^*) &= I^* \cdot (\mu + \gamma) / S^* \\ (\boldsymbol{T} I^*) b &= I^* \cdot (\mu + \gamma) / S^* \\ b &= (\boldsymbol{T} I^*)^{-1} (I^* \cdot (\mu + \gamma) / S^*) \end{aligned} \tag{7}$$

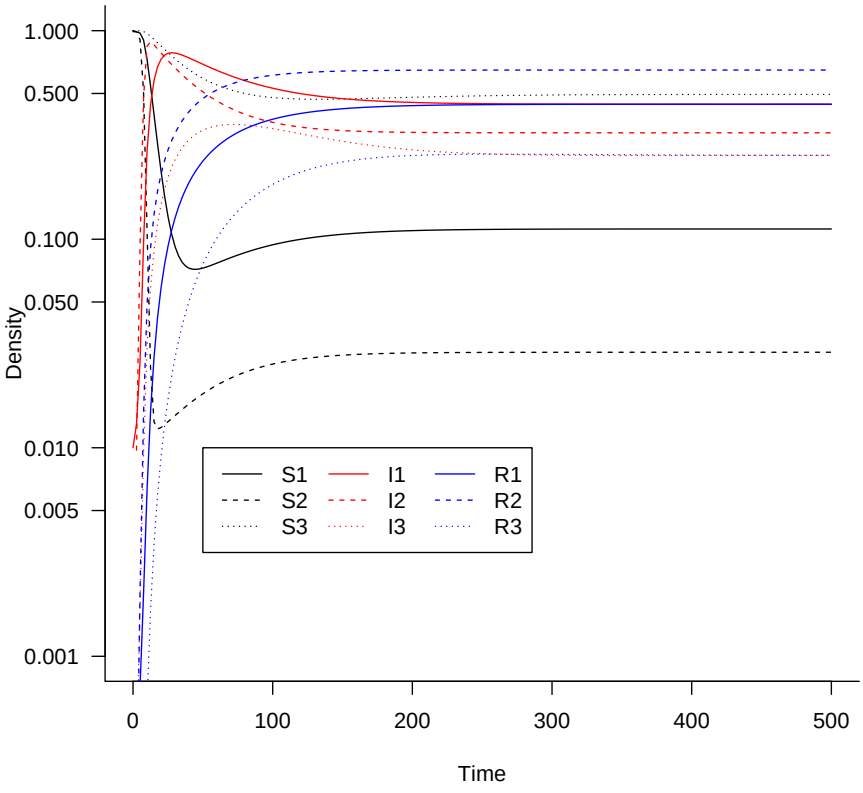

Figure 1: Results of multi-species ODE model

Final S^* values:

```
S.end <- L1[200, 2:4]
S.end
##       1       2       3
## 0.11198 0.02871 0.49497
```

Reconstruct I^*, R^*:

```
I.end <- (N - S.end)/(1 + gamma/mu)
R.end <- I.end * gamma/mu
```

Multiply the WAIFW tensor by I^*, invert, and apply it to the other side of the equation:

```
TI <- drop(tensor(T, array(I.end, dim = c(3, 1, 1)), 1, 1))
drop(solve(TI) %*% (I.end * (mu + gamma)/S.end))
## [1] 0.10 0.80 0.01
```

It works (this is very close to the original b vector of $\{0.1, 0.8, 0.01\}$ — in this ridiculously simplified case ...

5 Extensions

A more reasonable WAIFW matrix for a multi-species model might be

$$\begin{pmatrix} b_1 & b_3 & b_3 \\ b_3 & b_2 & b_3 \\ b_3 & b_3 & b_2 \end{pmatrix}, \tag{8}$$

representing a reservoir host (species 1, with strong within-species mixing b_1); two non-reservoir hosts (with weak within-species mixing b_2); and spillover at rate b_3. Then $\mathbf{T}$ is as follows:

```
## , , 1
##
##      [,1] [,2] [,3]
## [1,]    1    0    0
## [2,]    0    0    0
## [3,]    0    0    0
##
## , , 2
##
##      [,1] [,2] [,3]
## [1,]    0    0    0
## [2,]    0    1    0
## [3,]    0    0    1
##
## , , 3
##
```

```
##      [,1] [,2] [,3]
## [1,]    0    1    1
## [2,]    1    0    1
## [3,]    1    1    0
```

(If each parameter is specified separately as here, then the sum of slices is exactly 1 for each element; sometimes as above it may be more interesting to parameterize the matrix in terms of *contrasts*.)

```
range(apply(T, c(1, 2), sum))
## [1] 1 1
```

5.1 Spatial examples

Need to work out how this goes for a spatial example: it should look more or less identical to the previous case, except that (1) we want to work with susceptible-reconstruction information rather than equilibria, (2) the WAIFW matrix can just be a within-vs-between matrix (to start).

The appropriate WAIFW tensor for a 4-city example is just

```
## , , within
##
##      [,1] [,2] [,3] [,4]
## [1,]    1    0    0    0
## [2,]    0    1    0    0
## [3,]    0    0    1    0
## [4,]    0    0    0    1
##
## , , between
##
##      [,1] [,2] [,3] [,4]
## [1,]    0    1    1    1
## [2,]    1    0    1    1
## [3,]    1    1    0    1
## [4,]    1    1    1    0
```

although we could also consider parameterizing it additively, i.e. $\{\beta_w = b_1 + b_2, \beta_b = b_2\}$ rather than $\{\beta_w = b_1, \beta_b = b_2\}$ as above.

5.2 Least-squares solutions

What if we're willing to *underspecify* the problem, i.e. specify fewer than n elements of b? Thus $\mathbf{T}$ would be $n \times n \times m$, with $m < n$; for example, if we only wanted to specify different within- and between-species contact rates, or in the case above we had more than two non-reservoir hosts with (assumed) equal within-species contact rates. Then I wonder if we could set this up as a least-squares problem? We would then be trying to find b so that the sum of squared differences between the observed seroprevalences and the predicted seroprevalences was minimized ... (of course if we were serious about statistics

it would be nice to have m considerably less than n, so that we had more than a few degrees of freedom to describe the fit ... this could probably only happen with a data set with a large number of groups — although if the groups were patches ...)

I'm now pretty sure that we can indeed do this: if we want the least-squares solution, i.e.

$$\arg\min_b (Y - \boldsymbol{X}b)^T (Y - \boldsymbol{X}b) \tag{9}$$

with an appropriate choice of Y and $\boldsymbol{X}$, we can reduce to the previously solved problem of linear least-squares fitting; in particular we can use `lm.fit` in R, which takes a response vector and a model matrix (we might even be able to use this model matrix in a GLM fit, e.g. a Poisson distribution — we would need an identity link in order to avoid screwing up the theoretical relationships).

For example, in the second reconstruction above, we have $Y = I^* \cdot (\mu+\gamma)/S^*$, $\boldsymbol{X} = \boldsymbol{T}I^*$.

References

Anderson, R. M. and R. M. May (1985). Age-related changes in the rate of disease transmission: implications for the design of vaccination programmes. *Journal of Hygiene (Cambridge) 94*, 365–436.

Anderson, R. M. and R. M. May (1992). *Infectious Diseases of Humans: Dynamics and Control*. Oxford University Press.

Fine, P. E. M. and J. A. Clarkson (1982). Measles in England and Wales-I: an analysis of factors underlying seasonal patterns. *International Journal of Epidemiology 11*, 5–15.

Grenfell, B. T. and R. M. Anderson (1985). The estimation of age-related rates of infection from case notifications and serological data. *Journal of Hygiene (Cambridge) 95*, 419–436.