Human Lassa spillover rate

This code shows the analyses performed on the system of ordinary differential equations that describe the spillover of Lassa virus into humans.

■ Define model

Define the system of ODEs that describe human infection.

```
In[1]:= dsdt = b - d s - F s + λ r;
       didt = F s - (d + γ) i;
       drdt = (1 - μ) γ i - d r - λ r;
```

■ Derive relationship between seroprevalence and spillover rate

Find the equilibrium.

```
In[4]:= eq = FullSimplify[Solve[{dsdt == 0, didt == 0, drdt == 0}, {s, i, r}]]
```

$$\text{Out[4]=} \left\{\left\{s \to \frac{b\,(d+\gamma)\,(d+\lambda)}{d\,(d+F)\,(d+\gamma) + d\,(d+F+\gamma)\,\lambda + F\,\gamma\,\lambda\,\mu},\right.\right.$$
$$\left.\left. i \to \frac{b\,F\,(d+\lambda)}{d\,(d+F)\,(d+\gamma) + d\,(d+F+\gamma)\,\lambda + F\,\gamma\,\lambda\,\mu}, r \to -\frac{b\,F\,\gamma\,(-1+\mu)}{d\,(d+F)\,(d+\gamma) + d\,(d+F+\gamma)\,\lambda + F\,\gamma\,\lambda\,\mu}\right\}\right\}$$

Find seroprevalence at equilibrium (this is the data we have to work with). Note that this requires calculating the steady state population size in the presence of LASV virulence.

```
In[5]:= Pop = FullSimplify[(s + i + r) /. eq]
```

$$\text{Out[5]=} \left\{\frac{b\,(d^2 + \gamma\,\lambda + d\,(F + \gamma + \lambda) + F\,(\gamma + \lambda - \gamma\,\mu))}{d\,(d+F)\,(d+\gamma) + d\,(d+F+\gamma)\,\lambda + F\,\gamma\,\lambda\,\mu}\right\}$$

Variable [count] refers to the population size in a pixel of the population raster. Solve for the birth rate [b] for a given value of [count].

```
In[6]:= bsolve = Solve[Pop == count, b]
```

$$\text{Out[6]=} \left\{\left\{b \to \left(count\,(d^3 + d^2\,F + d^2\,\gamma + d\,F\,\gamma + d^2\,\lambda + d\,F\,\lambda + d\,\gamma\,\lambda + F\,\gamma\,\lambda\,\mu)\right) \right/ \right.$$
$$\left.\left. (d^2 + d\,F + d\,\gamma + F\,\gamma + d\,\lambda + F\,\lambda + \gamma\,\lambda - F\,\gamma\,\mu)\right\}\right\}$$

Calculate seroprevalence in terms of model parameters.

In[7]:= `Rstar = FullSimplify[r / (Pop) /. eq] // Flatten`

Out[7]= $\left\{ -\dfrac{F\,\gamma\,(-1+\mu)}{d^2 + \gamma\,\lambda + d\,(F + \gamma + \lambda) + F\,(\gamma + \lambda - \gamma\,\mu)} \right\}$

Solve for the force of infection, F, in terms of seroprevalence.

In[8]:= `foi = FullSimplify[Solve[hsero == Rstar, F]] // Flatten`

Out[8]= $\left\{ F \to -\dfrac{hsero\,(d+\gamma)\,(d+\lambda)}{d\,hsero + hsero\,\lambda + \gamma\,(-1 + hsero + \mu - hsero\,\mu)} \right\}$

Rewrite the solution for [b], defined in [bsolve], with the force of infection terms F replaced with the expression above

In[9]:= `bsolve = FullSimplify[bsolve /. foi]`

Out[9]= $\left\{ \left\{ b \to -\dfrac{count\,(d + d\,(-1 + hsero)\,\mu + hsero\,\lambda\,\mu)}{-1 + \mu} \right\} \right\}$

The rate of new infections of Lassa is F*s. Calculate this, and rewrite everything in terms of seroprevalence.

In[10]:= `NewInfRate = FullSimplify[(F /. foi) * (s /. eq /. foi) /. bsolve] // Flatten`

Out[10]= $\left\{ -\dfrac{count\,hsero\,(d+\gamma)\,(d+\lambda)}{\gamma\,(-1+\mu)} \right\}$

◼ Compare spillover rate estimates for virulence vs no virulence

Calculate the ratio of infections with, versus without, virulence.

In[11]:= ρ `= FullSimplify[(NewInfRate /. eq) / (NewInfRate /. eq /. ` $\mu \to$ `0)] // Flatten`

Out[11]= $\left\{ \dfrac{1}{1-\mu} \right\}$

In words, including virulence increases the estimated rate of LASV infections by $\rho = (1-\mu)^{-1}$.

In[12]:= ρ `/.` $\mu \to$ `0.02`

Out[12]= $\{1.02041\}$

When $\mu = 0.02$ (lower value from McCormick, Webb, 1987), increase is ~1.02, meaning roughly 2% more infections occur.

◼ Compare estimates for reinfection vs no reinfection

Calculate the ratio of infections with, versus without, reinfection.

In[13]:= `FullSimplify[(NewInfRate /. eq) / (NewInfRate /. eq /. λ → 0) ] // Flatten`

Out[13]= $\left\{ \dfrac{d + \lambda}{d} \right\}$

Reinfection multiplies the infection rate by $\frac{d+\lambda}{d}$. Calculate the effect of reinfection for a mean lifespan of 50 years, and reinfection rate λ = 0.064 / yr (from McCormick, Webb, 1987).

In[14]:= `Pars = {d → 0.02};`

Ratio of estimates of new infections with (λ = 0.064) and without (λ = 0) seroreversion is

In[15]:= `(NewInfRate /. λ → 0.064) / (NewInfRate /. λ → 0) /. Pars`

Out[15]= $\{4.2\}$

Including reinfection multiplies the infection estimates by a factor of 420%; including virulence increases estimates by 2%.

Human LASV spillover with undetectable antibody immune class

At the request of a reviewer, we also investigate the possibility that a fraction, a, of recovered individuals with immunity (R) transition into a class with undetectable immunity (C). This might be the case, for example, if immunity were caused primarily by a T-cell response in humans.

■ Define model

Define the system of ODEs that describe human infection. Note the additional class, c, and the rate term a.

In[16]:= `dsdt = b - d s - F s + λ (1 - a) r;`
`didt = F s - (d + γ) i;`
`drdt = (1 - μ) γ i - d r - λ r;`
`dcdt = a lam r - d c;`

■ Derive relationship between seroprevalence and infection rate

The remainder of this analysis is identical to what was performed above. Note that the equilibrium values of s are smaller when a > 0. Find the equilibrium.

In[20]:= `eq = FullSimplify[Solve[{dsdt == 0, didt == 0, drdt == 0, dcdt == 0}, {s, i, r, c}]]`

Out[20]= $\{\{s \rightarrow \dfrac{b\,(d+\gamma)\,(d+\lambda)}{d^3 + d\,F\,\gamma + d\,(F+\gamma)\,\lambda + d^2\,(F+\gamma+\lambda) + F\,\gamma\,\lambda\,(a+\mu-a\,\mu)}$,

$i \rightarrow \dfrac{b\,F\,(d+\lambda)}{d^3 + d\,F\,\gamma + d\,(F+\gamma)\,\lambda + d^2\,(F+\gamma+\lambda) + F\,\gamma\,\lambda\,(a+\mu-a\,\mu)}$,

$r \rightarrow -\dfrac{b\,F\,\gamma\,(-1+\mu)}{d^3 + d\,F\,\gamma + d\,(F+\gamma)\,\lambda + d^2\,(F+\gamma+\lambda) + F\,\gamma\,\lambda\,(a+\mu-a\,\mu)}$,

$c \rightarrow -\big((a\,b\,F\,\text{lam}\,\gamma\,(-1+\mu))\,/\,(d\,(d^3 + d\,F\,\gamma + d\,(F+\gamma)\,\lambda + d^2\,(F+\gamma+\lambda) + F\,\gamma\,\lambda\,(a+\mu-a\,\mu)))\big)\}\}$

Find seroprevalence at equilibrium (this is the data we have to work with). Note that this requires calculating the steady state population size in the presence of LASV virulence.

In[21]:= `Pop = FullSimplify[(s + i + r + c) /. eq]`

Out[21]= $\left\{\dfrac{b\,(d^3 + d\,\gamma\,\lambda + d^2\,(F+\gamma+\lambda) - a\,F\,\text{lam}\,\gamma\,(-1+\mu) + d\,F\,(\gamma+\lambda-\gamma\,\mu))}{d\,(d^3 + d\,F\,\gamma + d\,(F+\gamma)\,\lambda + d^2\,(F+\gamma+\lambda) + F\,\gamma\,\lambda\,(a+\mu-a\,\mu))}\right\}$

Variable [count] refers to the population size in a pixel of the population raster. Solve for the birth rate [b] for a given value of [count].

In[22]:= `bsolve = Solve[Pop == count, b]`

Out[22]= $\left\{\left\{b \rightarrow \dfrac{\text{count}\,d\,(d^3 + d^2\,F + d^2\,\gamma + d\,F\,\gamma + d^2\,\lambda + d\,F\,\lambda + d\,\gamma\,\lambda + a\,F\,\gamma\,\lambda + F\,\gamma\,\lambda\,\mu - a\,F\,\gamma\,\lambda\,\mu)}{d^3 + d^2\,F + d^2\,\gamma + d\,F\,\gamma + a\,F\,\text{lam}\,\gamma + d^2\,\lambda + d\,F\,\lambda + d\,\gamma\,\lambda - d\,F\,\gamma\,\mu - a\,F\,\text{lam}\,\gamma\,\mu}\right\}\right\}$

Calculate seroprevalence in terms of model parameters.

In[23]:= `Rstar = FullSimplify[r / (Pop) /. eq] // Flatten`

Out[23]= $\left\{-\dfrac{d\,F\,\gamma\,(-1+\mu)}{d^3 + d\,\gamma\,\lambda + d^2\,(F+\gamma+\lambda) - a\,F\,\text{lam}\,\gamma\,(-1+\mu) + d\,F\,(\gamma+\lambda-\gamma\,\mu)}\right\}$

Solve for the force of infection, F, in terms of seroprevalence. Note that the equilibrium value of foi is made larger by the parameter a.

In[24]:= `foi = FullSimplify[Solve[hsero == Rstar, F]] // Flatten`

Out[24]= $\left\{F \rightarrow -\dfrac{d\,\text{hsero}\,(d+\gamma)\,(d+\lambda)}{d^2\,\text{hsero} + d\,\text{hsero}\,\lambda - a\,\text{hsero}\,\text{lam}\,\gamma\,(-1+\mu) + d\,\gamma\,(-1+\text{hsero}+\mu-\text{hsero}\,\mu)}\right\}$

Rewrite the solution for [b], defined in [bsolve], with the force of infection terms F replaced with the expression above

In[25]:= `bsolve = FullSimplify[bsolve /. foi]`

Out[25]= $\left\{\left\{b \rightarrow -\dfrac{\text{count}\,(d + a\,\text{hsero}\,(\text{lam}-\lambda)\,(-1+\mu) + d\,(-1+\text{hsero})\,\mu + \text{hsero}\,\lambda\,\mu)}{-1+\mu}\right\}\right\}$

The rate of new infections of Lassa is F*s. Calculate this, and rewrite everything in terms of seroprevalence. The decrease in s at equilibrium that is caused by a is exactly cancelled by the increase in force of infection that is caused by a.

In[26]:= `NewInfRate = FullSimplify[(F /. foi) * (s /. eq /. foi) /. bsolve] // Flatten`

Out[26]= $\left\{ -\dfrac{\text{count hsero } (d + \gamma) \ (d + \lambda)}{\gamma \ (-1 + \mu)} \right\}$