1. Within-host Dynamics

Here is the within-host model. Solve for the endemic virus equilibrium:

In[∘]:=
```
Solve[{r*V - c*V*L == 0,  g0 + g*r*V - m*L == 0}, {V, L}]
```

Out[∘]=
$$\left\{\left\{V \to -\frac{c\,g0 - m\,r}{c\,g\,r},\ L \to \frac{r}{c}\right\},\ \left\{V \to 0,\ L \to \frac{g0}{m}\right\}\right\}$$

$$\text{Vstar} = \frac{m*r - c*g0}{g*c*r};$$

$$\text{Lstar} = \frac{r}{c};$$

Now, take those endemic, within-host equilibria and embed them in the virulence and transmission terms for the population model -- this gives some biological significance to r. w is motivated as host vulnerability to immunopathology (i.e. inflammation), so hosts with higher values for w are most susceptible to disease. We can try scaling this as the inverse of host lifespan corrected for body size (so values are higher for the shortest-lived hosts):

2. **First, both complete tolerance:**

In[∘]:=
```
BetaT = zeta*Vstar;
alphaT = ((v - Tv) * r * Vstar) + ((w - Tw) * g * r * Vstar);
BetaT
```

Out[∘]=
$$\frac{(-c\,g0 + m\,r)\,zeta}{c\,g\,r}$$

In[∘]:=
```
alphaT
```

Out[∘]=
$$\frac{(-c\,g0 + m\,r)\,(-Tv + v)}{c\,g} + \frac{(-c\,g0 + m\,r)\,(-Tw + w)}{c}$$

Now, embed these transmission and virulence terms in the invasion fitness for a population-level S-I model:

In[∘]:=
```
InvasionFit = BetaT / (mu + alphaT);
FullSimplify[InvasionFit]
```

Out[∘]=
$$\frac{(c\,g0 - m\,r)\,zeta}{r\,(m\,r\,(Tv + g\,Tw - v - g\,w) - c\,(g0\,(Tv - v) + g\,(mu + g0\,Tw - g0\,w)))}$$

2. Selection gradient on r

And now, differentiate with respect to r to get this for dInvasion Fit/dr:

In[∘]:=
```
partialD = FullSimplify[D[InvasionFit, r]];
partialD
```

Out[∘]=
$$\Big(\big(m^2\,r^2\,(Tv + g\,Tw - v - g\,w) + 2\,c\,g0\,m\,r\,(-Tv - g\,Tw + v + g\,w) + c^2\,g0\,(g0\,(Tv - v) + g\,(mu + g0\,Tw - g0\,w))\big)\,zeta\Big) \Big/ \Big(r^2\,(c\,g0\,(Tv - v) + c\,g\,(mu + g0\,(Tw - w)) + m\,r\,(-Tv + v + g\,(-Tw + w)))^2\Big)$$

And then set equal to 0 and solve for r*

In[∘]:= `FullSimplify[Solve[{partialD == 0}, {r}]]`

Out[∘]= $$\left\{\left\{r \to \frac{c\ g0\left(1+\frac{c\ g\ m\ mu}{\sqrt{c^2\ g\ g0\ m^2\ mu\ (-Tv-g\ Tw+v+g\ w)}}\right)}{m}\right\},\left\{r \to \frac{c\ g0\left(1-\frac{c\ g\ m\ mu}{\sqrt{c^2\ g\ g0\ m^2\ mu\ (-Tv-g\ Tw+v+g\ w)}}\right)}{m}\right\}\right\}$$

$$\mathbf{rstar} = \frac{c\ g0\left(1+\frac{c\ g\ m\ mu}{\sqrt{c^2\ g\ g0\ m^2\ mu\ (-Tv-g\ Tw+v+g\ w)}}\right)}{m};$$

3. Checking stability

We can check if rstar is convergence stable and therefore an ESS by taking the second derivative of the invasion fitness with respect to r and evaluating at r* : is it negative?

In[∘]:= `secondDr = FullSimplify[D[partialD , r]];`
`secondDr`

Out[∘]= $$\Big(\big(-6\ c\ g0\ m^2\ r^2\ (Tv+g\ Tw-v-g\ w)^2+2\ m^3\ r^3\ (Tv+g\ Tw-v-g\ w)^2+6\ c^2\ g0\ m\ r\ (Tv+g\ Tw-v-g\ w)\ (g0\ (Tv-v)+g\ (mu+g0\ Tw-g0\ w))-2\ c^3\ g0\ (g0\ (Tv-v)+g\ (mu+g0\ Tw-g0\ w))^2\big)\ zeta\Big)\Big/\Big(r^3\ (c\ g0\ (Tv-v)+c\ g\ (mu+g0\ (Tw-w))+m\ r\ (-Tv+v+g\ (-Tw+w)))^3\Big)$$

In[∘]:= `r = rstar;`
`FullSimplify[secondDr]`

Out[∘]= $$-\Big(\Big(2\ c^2\ g\ g0\ m^8\ mu\ (Tv-v+g\ (Tw-w))^3\ \Big(-2\ \sqrt{c^2\ g\ g0\ m^2\ mu\ (-Tv-g\ Tw+v+g\ w)}-c\ m\ (g0\ (-Tv+v)+g\ (mu-g0\ Tw+g0\ w))\Big)\ zeta\Big)\Big/\Big(\Big(c\ g\ m\ mu+\sqrt{c^2\ g\ g0\ m^2\ mu\ (-Tv-g\ Tw+v+g\ w)}\Big)^3\ \Big(c\ g0\ m\ (-Tv-g\ Tw+v+g\ w)+\sqrt{c^2\ g\ g0\ m^2\ mu\ (-Tv-g\ Tw+v+g\ w)}\Big)^3\Big)\Big)$$

This expression is clearly negative (also supported by the PIP), meaning that rstar is an ESS.

4. Virulence at optimal r* for the reservoir host

We can also use the expression for r* to calculate an expression for alpha*, the virulence experienced by the reservoir host infected with a virus evolved to r*. To do this, we simply plug the within-host parameters into our expression for alpha, assuming r=r*.

This yields the following expression:

In[∘]:= `FullSimplify[alphaT]`

Out[∘]= $$\frac{\sqrt{c^2\ g\ g0\ m^2\ mu\ (-Tv+v+g\ (-Tw+w))}}{c\ g\ m}$$

$$\text{alpha*} = \frac{\sqrt{c^2\ g\ g0\ m^2\ mu\ (-Tv+v+g\ (-Tw+w))}}{c\ g\ m}$$