Primary Infection by HIV
Phillips (1996) Science 271:497-499

"The model is defined by four equations describing the interrelated changes over time in the number of activated, uninfected CD4 lymphocytes (R), latently infected cells (L), actively infected cells (E), and free virions (V)."

"These equations can be explained as follows."

"Activated, uninfected CD4 lymphocytes (R) arise at a constant rate Γ tauτ, where Γ is the rate at which new, uninfected CD4 lymphocytes arise and τ is the proportion that are activated, and they are removed by HIV-independent cell death at rate μ or by infection at rate βV"

```
dR[t]/dt == Γ τ - μ R[t] - β R[t] V[t]
```

"Upon infection, a proportion p of cells become latently infected (L), and these are removed by either HIV-independent cell death or by activation at rate α"

```
dL[t]/dt == p β R[t] V[t] - μ L[t] - α L[t]
```

"Actively infected cells are generated immediately after infection or from the activation of latently infected cells before they die at rate δ"

```
dE[t]/dt == (1-p) β R[t] V[t] + α L[t] - δ E[t]
```

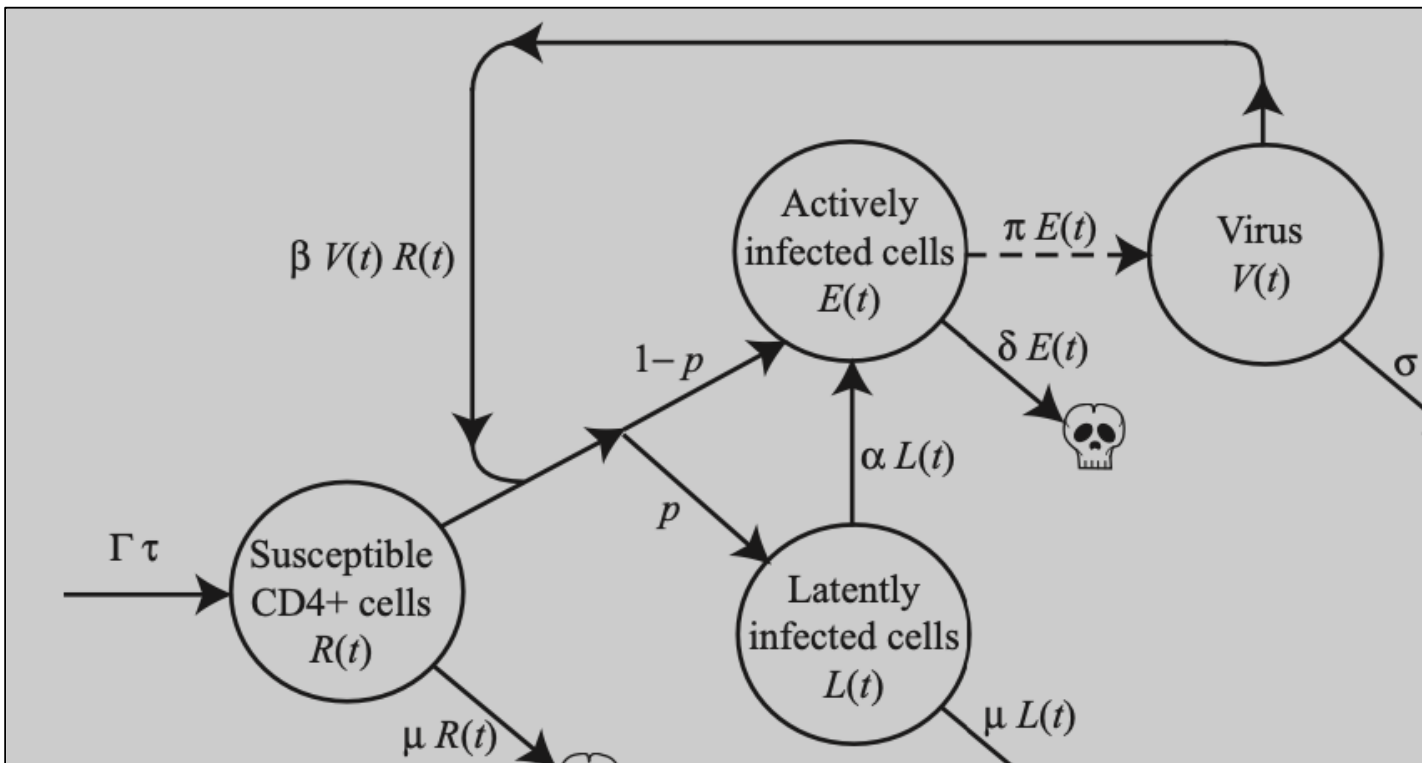
"Free virions are produced at rate π by actively infected cells and removed at rate σ"

```
dV[t]/dt == π E[t] - σ V[t]
```

→ **S**;

Hint: Type "Esc" then spell out a greek letter like "mu" then "Esc" to format a greek letter.

Figure 1:



1 Equations

Type the set of equations:
Hint: Use command-1 to insert a comment.

(%i1)
```
eqns: [
  dRdt : Γ·τ – μ·R– β·R·V,
  dLdt : p·β·R·V – μ·L – α·L,
  dEdt :  (1–p)·β·R·V + α·L – δ·E,
  dVdt : π·E – σ·V];
```

eqns $$\left[\Gamma\,\tau - R\,\mu - R\,V\,\beta, -(L\,\mu) + R\,V\,p\,\beta - L\,\alpha, -(E\,\delta) + R\,V\,(1-p)\,\beta + L\,\alpha, \pi\,E - V\,\sigma\right]$$

Variables:

(%i2)
```
vars : [R, L, E, V];
```

vars $$[R, L, E, V]$$

Maxima knows many of the rules of algebra and calculus and allows us to focus on the insights that matt
 For example, we could
calculate the derivative of an equation with respect to a variable

(%i3)
```
eqns[1];
```

(%o3) $$\Gamma\,\tau - R\,\mu - R\,V\,\beta$$

(%i4)
```
diff(eqns[1],V);
```

(%o4) $$-(R\,\beta)$$

2 Calculating an equilibrium

As we'll learn later in class, an equilibrium is a point where the system does not change over time.

Maxima can be used to solve systems of equations like these for when nothing changes:

(%i5)
```
equil:solve([ 0= Γ·τ – μ·R– β·R·V,
  0=p·β·R·V – μ·L – α·L,
  0=  (1–p)·β·R·V + α·L – δ·E,
  0= π·E – σ·V],vars);
```

equil $$\left[\left[R=\frac{\Gamma\,\tau}{\mu}, L=0, E=0, V=0\right], \left[R=-\left(\frac{(\delta\,\mu+\alpha\,\delta)\,\sigma}{(\pi\,p-\pi)\,\beta\,\mu-\pi\,\alpha\,\beta}\right), L=\right.\right.$$
$$\frac{((\pi\,p^2-\pi\,p)\,\Gamma\,\beta\,\mu-\pi\,p\,\Gamma\,\alpha\,\beta)\,\tau+(p\,\delta\,\mu^2+p\,\alpha\,\delta\,\mu)\,\sigma}{(\pi\,p-\pi)\,\beta\,\mu^2+(\pi\,p-2\,\pi)\,\alpha\,\beta\,\mu-\pi\,\alpha^2\,\beta}, E=-\left(\frac{((\pi\,p-\pi)\,\Gamma\,\beta\,\mu-\pi\,\Gamma\,\alpha\,\beta)\,\tau+(\delta\,\mu^2+\alpha\,\delta\,\mu)\,\sigma}{\pi\,\beta\,\delta\,\mu+\pi\,\alpha\,\beta\,\delta}\right), V=-$$
$$\left.\left.\left(\frac{((\pi\,p-\pi)\,\Gamma\,\beta\,\mu-\pi\,\Gamma\,\alpha\,\beta)\,\tau+(\delta\,\mu^2+\alpha\,\delta\,\mu)\,\sigma}{(\beta\,\delta\,\mu+\alpha\,\beta\,\delta)\,\sigma}\right)\right]\right]$$

The above shows two equilibria - how do they differ?

Let's look at how the equilibrium density of viruses changes with increasing infectivity β:

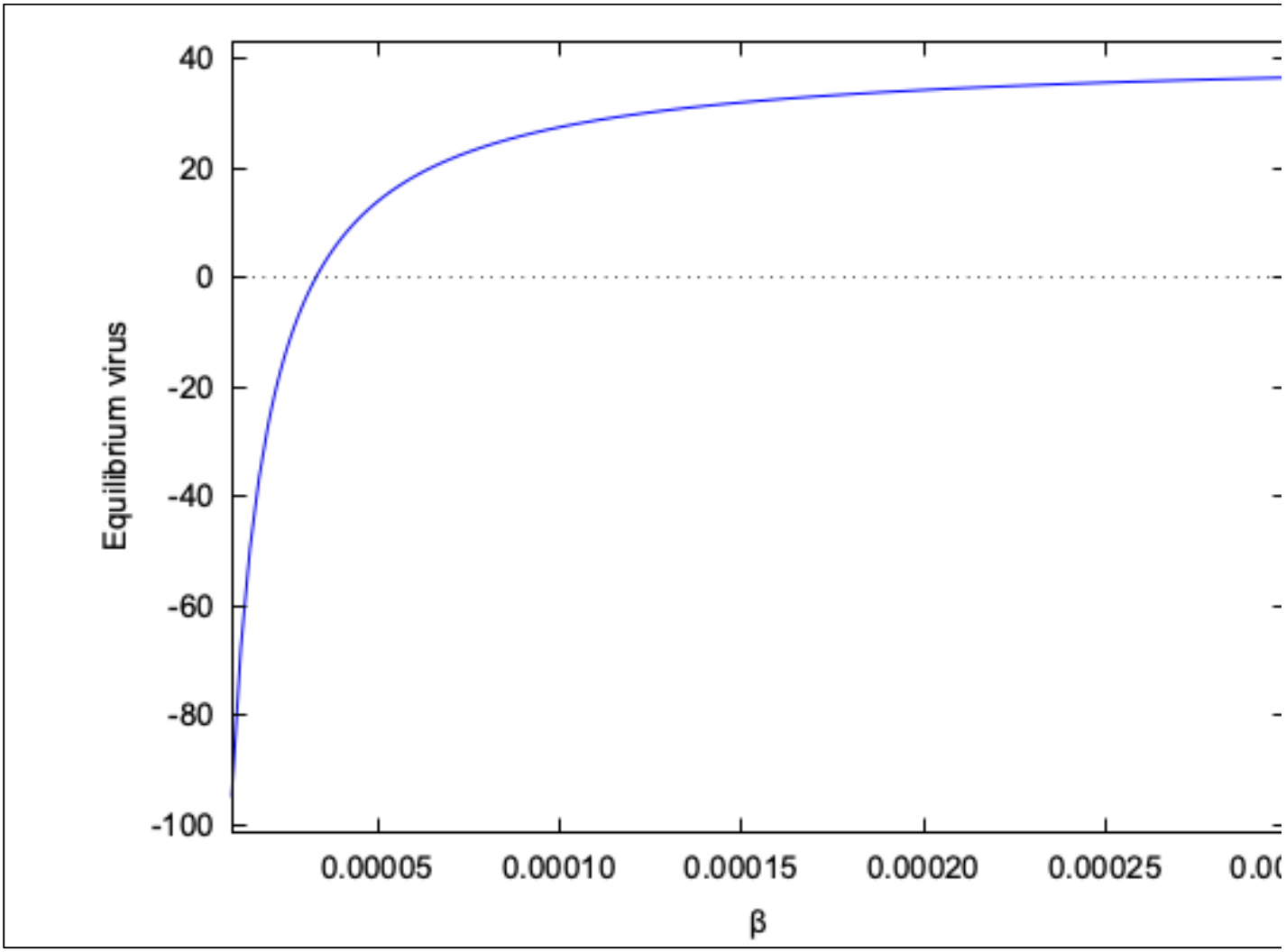
(%i6)
```
part(equil,2,4,2);
```

(%o6) $$-\left(\frac{((\pi\,p-\pi)\,\Gamma\,\beta\,\mu-\pi\,\Gamma\,\alpha\,\beta)\,\tau+(\delta\,\mu^2+\alpha\,\delta\,\mu)\,\sigma}{(\beta\,\delta\,\mu+\alpha\,\beta\,\delta)\,\sigma}\right)$$

(%i7)
```
toplot(β):=subst([Γ = 1.36, μ =1.36·10^(–3),τ = 0.2, p = 0.1, α= 3.6·10^(–2),
    σ= 2, δ= 0.33, π = 100], part(equil,2,4,2))$
```

(%i8)
```
wxplot2d([toplot(β)], [β, 0.00001, 0.00030],[ylabel,"Equilibrium virus"]);
```

(%t8)



(%o8)

3 Example plot

Here we susbtitute in some parameter values into the equations: ... + 0 hidden lines

(%i9)
```
example:subst([Γ = 1.36, μ =1.36·10^(−3),τ = 0.2,β = 0.00027, p = 0.1, α= 3.6·10^(−2),
    σ= 2, δ= 0.33, π = 100], eqns);
```

example $[-(2.7\ 10^{-4}\ R\ V)-0.00136\ R+0.272, 2.7000000000000002\ 10^{-5}\ R\ V-0.037360000000000004\ L, 2.43\ 10^{-4}\ R\ V+0.036000000000000004\ L-0.33\ E, 100\ E-2\ V]$

Here we give an initial starting point for the set of variables (in the order defined by vars):

(%i10)
```
plotstart : [200, 0, 0, 4·10^(−7)];
```

plotstart $\left[200, 0, 0, \frac{1}{2500000}\right]$

Then we plug the equations, the variables, and the starting point into numerical solver of differential (rkf45):

(%i12)
```
load(rkf45);

sol:rkf45(example,vars,plotstart,[t,0,100],
      report=true,absolute_tolerance=1e-8)$
```

(%o11)
```
/opt/homebrew/Cellar/maxima/5.47.0_13/share/maxima/5.47.0/share/contrib/rkf45/rkf45.mac
----------------------------------------------------
Info: rkf45:
  Integration points selected: 2435
   Total number of iterations: 2438
       Bad steps corrected: 4
    Minimum estimated error: 1.1944957732972676 10^-11
```

Maximum estimated error: 9.509779974666209 10^{-9}
Minimum integration step taken: 0.004050002389230092
Maximum integration step taken: 1.1832890887028396

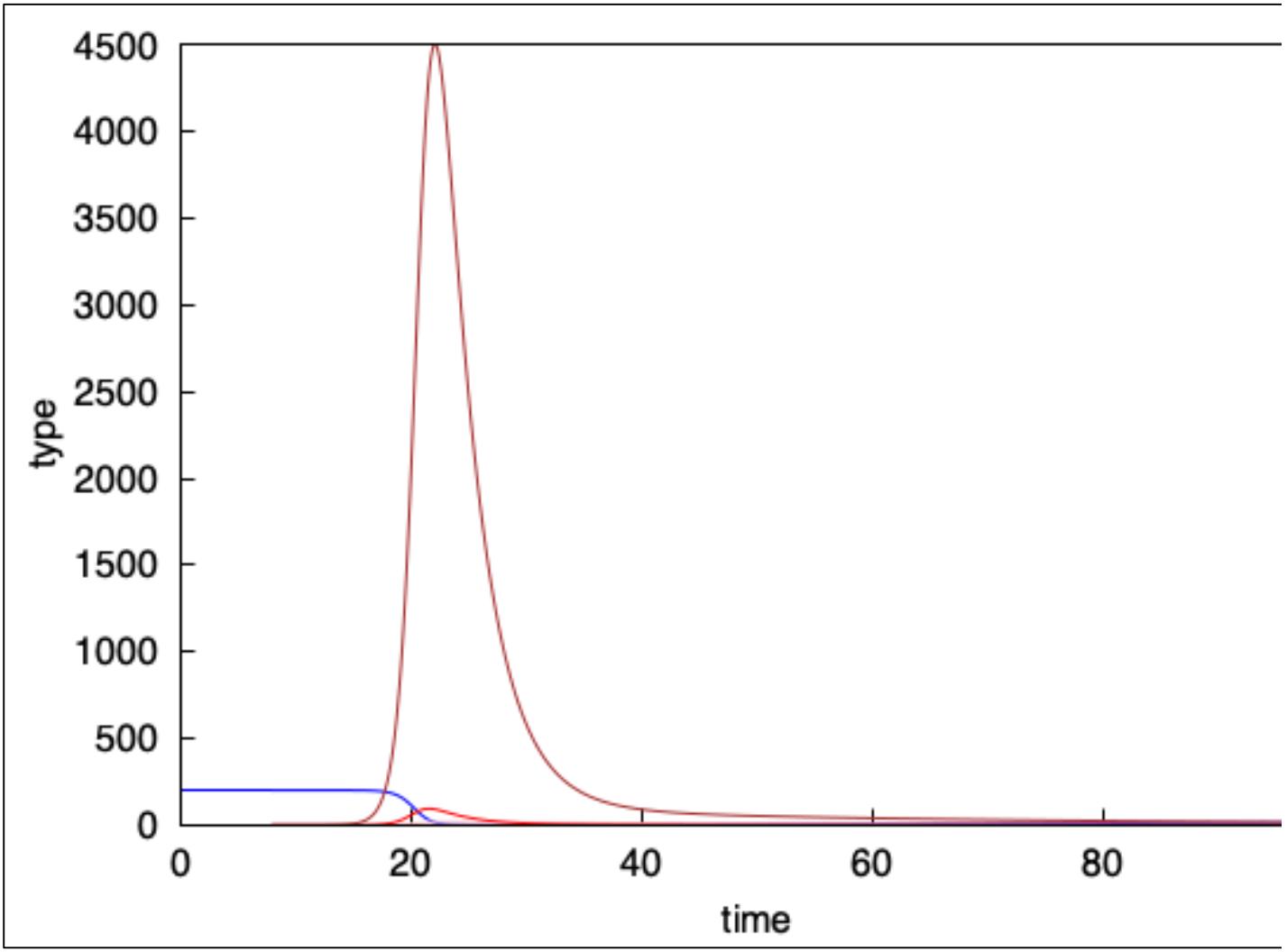
Here we pull out the list from the solution for each variable ("first" is time, then each of the variab
list, starting with
susceptibles):

(%i17)
```
time:makelist(part(sol,t,1),t,1,length(sol))$
susceptibles: makelist(part(sol,t,2),t,1,length(sol))$
active: makelist(part(sol,t,3),t,1,length(sol))$
latent: makelist(part(sol,t,4),t,1,length(sol))$
virus: makelist(part(sol,t,5),t,1,length(sol))$
```

Plotting the curves, coloured according to the flow diagram (blue for susceptibles, pink for exposed, r
presymptomatic, brown for
infected, and orange for asymptomatic):

(%i18)
```
wxdraw2d(point_type=-1,points_joined=true,color=blue,points(time,susceptibles),
  color=pink,points(time,active),color=red,points(time,latent),
  color=brown,points(time,virus),
  xlabel="time",ylabel="type");
```

(%t18)

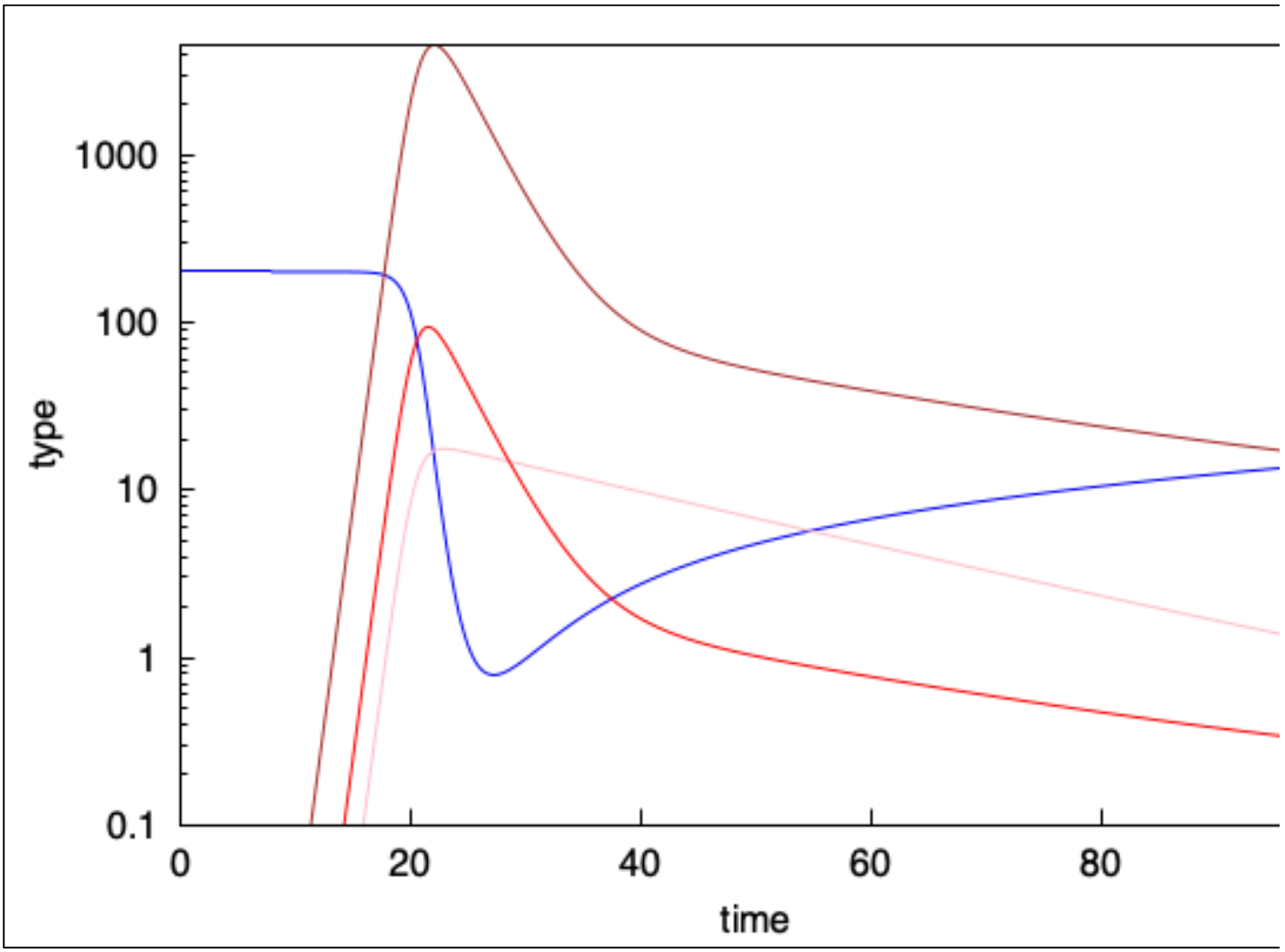


(%o18)

Alternatively, we could plot this on a log-scale along the y-axis (as did Philips):

(%i19)
```
wxdraw2d(logy=true,point_type=-1,points_joined=true,color=blue,points(time,susceptibles),
  color=pink,points(time,active),color=red,points(time,latent),
  color=brown,points(time,virus),
  xlabel="time",ylabel="type");
```

(%t19)



(%o19)