An SIS Model for Two Co-Infecting diseases

Consider a model with the following compartments:

- S: Number of susceptibles
- I: Number of people infected with disease 1
- J: Number of people infected with disease 2
- B: Number of people infected with both diseases

Define some parameters as follows:

- λ , δ_X : Birth and (per-capita) death rates respectively. *X* represents one of the above compartments.
- τ_X : Transmission rate for the disease corresponding to compartment X.
- γ_X : Rate at which individuals recover from the disease corresponding to compartment X.

```
syms lambda delta_S delta_I delta_J delta_B tau_I tau_J gamma_I gamma_J delta;
params = [lambda delta_S delta_I delta_J delta_B tau_I tau_J gamma_I gamma_J];

% % Equal birth and death rates
% lambda = delta;
% params = [delta delta delta delta tau_I tau_J gamma_I gamma_J];
```

The dynamics are given by the following system:

```
• S' = \lambda - \tau_I S(I+B) - \tau_J S(J+B) + \gamma_I I + \gamma_J J - \delta_S S
```

•
$$I' = \tau_I S(I+B) - \gamma_I I - \tau_J I(J+B) + \gamma_J B - \delta_I I$$

•
$$J' = \tau_J S(J+B) - \gamma_J J - \tau_I J(I+B) + \gamma_I B - \delta_J J$$

•
$$B' = \tau_J I(J+B) + \tau_I J(I+B) - \gamma_I B - \gamma_J B - \delta_B B$$

There are some implicit assumptions in our model that should be addressed. First, our base model is SIS, where recovery from infection confers no resistance to future reinfection. Second, both infection and recovery are agnostic of what compartment an individual is in. That is, infection with disease J happens at the same rate (i.e. $\tau_J \times (J+B)$) for susceptible individuals and for those already infected with disease I. Similarly, recovery from disease J happens at the same rate for individuals with only disease J (i.e. $\gamma_J J$) as for individuals who are also infected with disease I (i.e. $\gamma_J B$). Third, the death rates differ across compartments. An additive model would set $\delta_B = \delta_I + \delta_J$.

```
syms S I J B;
```

Throughout our analysis, we will need the Jacobian, or linearized form, of our system. We present the general form of the Jacobian here, and apply it to specific cases later.

```
SIJB_Jac(S, I, J, B, params)
```

$$\begin{pmatrix} -\delta_{S} - \sigma_{1} - \tau_{J} \ (B+J) & \gamma_{I} - S \tau_{I} & \gamma_{J} - S \tau_{J} & -S \ (\tau_{I} + \tau_{J}) \\ \sigma_{1} & S \tau_{I} - \gamma_{I} - \delta_{I} - \tau_{J} \ (B+J) & I \tau_{J} & \gamma_{J} - I \tau_{J} + S \tau_{I} \\ \tau_{J} \ (B+J) & J \tau_{I} & S \tau_{J} - \gamma_{J} - \delta_{J} - \sigma_{1} & \gamma_{I} - J \tau_{I} + S \tau_{J} \\ 0 & J \tau_{I} + \tau_{J} \ (B+J) & I \tau_{J} + \sigma_{1} & I \tau_{J} - \gamma_{I} - \gamma_{J} - \delta_{B} + J \tau_{I} \end{pmatrix}$$

where

$$\sigma_1 = \tau_I (R + I)$$





Disease-Free Equilibrium

We begin our analysis by finding the critical point corresponding to the disease-free equilibrium in our model. Setting I = J = B = 0 and performing some straightforward algebra, we get $S_0 = \lambda/\delta_S$.

Next, we compute the Jacobian at this disease-free equilibrium, and find its eigenvalues.

$$\begin{pmatrix}
-\delta_S & \gamma_I - \frac{\lambda \tau_I}{\delta_S} & \gamma_J - \frac{\lambda \tau_J}{\delta_S} & -\frac{\lambda (\tau_I + \tau_J)}{\delta_S} \\
0 & \frac{\lambda \tau_I}{\delta_S} - \gamma_I - \delta_I & 0 & \gamma_J + \frac{\lambda \tau_I}{\delta_S} \\
0 & 0 & \frac{\lambda \tau_J}{\delta_S} - \gamma_J - \delta_J & \gamma_I + \frac{\lambda \tau_J}{\delta_S} \\
0 & 0 & 0 & -\delta_B - \gamma_I - \gamma_J
\end{pmatrix}$$

eig(Jac0)

ans =
$$\begin{pmatrix}
-\delta_S & \angle \\
-\delta_B - \gamma_I - \gamma_J & \bigcirc \\
\frac{\lambda \tau_I}{\delta_S} - \gamma_I - \delta_I & \bigcirc \\
\frac{\lambda \tau_J}{\delta_S} - \gamma_J - \delta_J & \bigcirc \bigcirc
\end{pmatrix}$$

The first two eigenvalues are always negative, so we focus attention on the third and fourth. Imposing the constraint that all eigenvalues be negative, we get the more informative constraints that

$$1 > \frac{\tau_I S_0}{\gamma_I + \delta_I} =: \mathcal{R}_0^I$$
, and

$$1 > \frac{\tau_J S_0}{\gamma_J + \delta_J} =: \mathcal{R}_0^J$$

Endemic Equilibrium

There are three possible endemic equilibria in our model. The first two consist of one disease having zero cases while the other disease is active (these two cases are symmetric). The third consists of both diseases being active. In the former two cases, we also set B = 0, while in the latter case $B \neq 0$.

Case 1:
$$J = B = 0$$
, $I \neq 0$

First, we cancel I in the equation I'=0 and solve for S. This gives $S_1=\frac{\gamma_I+\delta_I}{\tau_I}$. Next, we substitute this

expression for *S* into the equation S'=0 and solve for *I*. This gives $I_1=\frac{\lambda-\delta_S S_1}{\tau_I S_1-\gamma_I}=\frac{\lambda-\delta_S S_1}{\delta_I}$.

```
S1 = (gamma_I + delta_I)/tau_I;
I1 = (lambda - delta_S * S1)/delta_I;
J1 = 0;
B1 = 0;
```

Next, we evaluate the stability of this equilibrium.

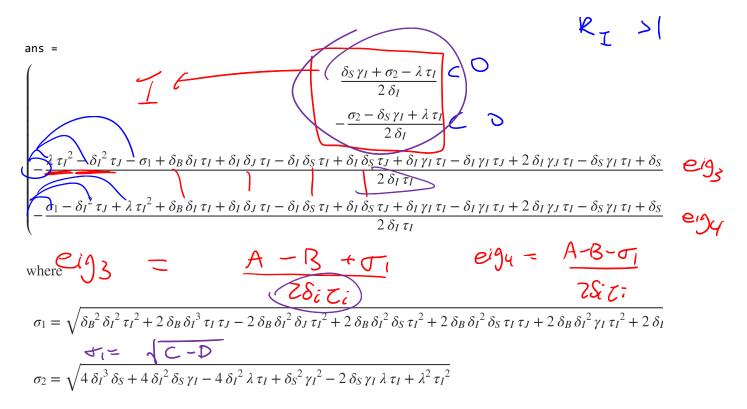
Jac1 =

$$\begin{pmatrix}
-\delta_{S} - \sigma_{2} & -\delta_{I} & \gamma_{J} - \frac{\tau_{J} (\delta_{I} + \gamma_{I})}{\tau_{I}} & -\frac{(\delta_{I} + \gamma_{I}) (\tau_{I} + \tau_{J})}{\tau_{I}} \\
\sigma_{2} & 0 & \sigma_{1} & \delta_{I} + \gamma_{I} + \gamma_{J} - \sigma_{1} \\
0 & 0 & \frac{\tau_{J} (\delta_{I} + \gamma_{I})}{\tau_{I}} - \gamma_{J} - \sigma_{2} - \delta_{J} & \gamma_{I} + \frac{\tau_{J} (\delta_{I} + \gamma_{I})}{\tau_{I}} \\
0 & 0 & \sigma_{2} + \sigma_{1} & \sigma_{1} - \gamma_{I} - \gamma_{J} - \delta_{B}
\end{pmatrix}$$

where

$$\sigma_1 = \frac{\tau_J \left(\lambda - \frac{\delta_S \left(\delta_I + \gamma_I\right)}{\tau_I}\right)}{\delta_I}$$

$$\sigma_2 = \frac{\tau_I \left(\lambda - \frac{\delta_S \left(\delta_I + \gamma_I\right)}{\tau_I}\right)}{\delta_I}$$



We cannot make much progress here. Neither the Routh-Hurwitz conditions nor the next generation matrix strategy help either. For the Routh-Hurwitz criterion, our problem is sufficiently high-dimensional that we still have some non-trivial conditions to check. Furthermore, the coefficients of our characteristic polynomial are even more complicated than the eigenvalues. For the next generation method, as far as I can tell, it is only applicable to studying stability of disease-free equilibria. It is likely possible to modify this method to study endemic equilibria, but that's beyond the scope of what I'm willing to do right now.

Restricted Case

If we assume that the death rates are all equal then we get a much more comprehensible stability analysis. We retain this assumption for all future analysis.

```
% Homogeneous death rates
params2 = [lambda delta delta delta tau_I tau_J gamma_I gamma_J];
```

The *I*-only endemic equilibrium under the reduced version of our model has $S_1 = \frac{\gamma_I + \delta}{\tau_I}$ and $I_1 = \frac{\lambda - \delta S_1}{\delta}$. Note

that we can re-write $I_1 = S_0 - S_1$. This is unsurprising because S_0 is the equilibrium population size and, at the equilibrium we are discussing, every individual is either in S or I.

```
S1_red = (gamma_I + delta)/tau_I;
I1_red = (lambda - delta * S1_red)/delta;
J1_red = 0;
B1_red = 0;
```

We now investigate the stability of the *I*-only endemic equilibrium under our reduced model.

```
Jac1_red = SIJB_Jac(S1_red, I1_red, J1_red, B1_red, params2)
```

Jac1 red =

eigs =
$$A-B+eg$$
 ZSZ_1
 ZS

Look at AB CD
$$\int J dt_1 reedul$$

 $A = 8i^2 T_1 + 8i 8s T_1 + 8i 8i T_2 + 8s 8i T_1$
 $B = M T_1i^2 + 8b 8i T_1 + 8i 8i T_2 + 8i 8i T_3 + 8i 8i T_1 + 8s$
 $C = 8i^2 8i^2 T_1i^2 + 28i 8i T_1 + 28i 8i^2 8s T_2i^2 + 28i 8i^2 8s T_1 = 428i$

$$D = 2868i \frac{1}{8i7i^2}$$

in the SIR model, whether or not there is an outbreak $(dI/dt \mid t=0 > 0)$ comes down the size of S0

Imple ABCD

$$\begin{pmatrix}
-\delta - \sigma_2 & -\delta & \gamma_J - \frac{\tau_J (\delta + \gamma_I)}{\tau_I} & -\frac{(\delta + \gamma_I) (\tau_I + \tau_J)}{\tau_I} \\
\sigma_2 & 0 & \sigma_1 & \delta + \gamma_I + \gamma_J - \sigma_1 \\
0 & 0 & \frac{\tau_J (\delta + \gamma_I)}{\tau_I} - \gamma_J - \sigma_2 - \delta & \gamma_I + \frac{\tau_J (\delta + \gamma_I)}{\tau_I} \\
0 & 0 & \sigma_2 + \sigma_1 & \sigma_1 - \gamma_I - \gamma_J - \delta
\end{pmatrix}$$

FC SCENERAL Y

where

$$\sigma_{1} = \frac{\tau_{J} \left(\lambda - \frac{\delta \left(\delta + \gamma_{I}\right)}{\tau_{I}}\right)}{\delta}$$

$$\sigma_2 = \frac{\tau_I \left(\lambda - \frac{\delta \left(\delta + \gamma_I\right)}{\tau_I}\right)}{\delta}$$

ans =

$$\begin{pmatrix} \frac{\delta^2 + \gamma_I \delta - \lambda \tau_I}{\delta} \\ -\delta \\ -\frac{\delta^2 + \gamma_J \delta - \lambda \tau_J}{\delta} \\ -\frac{\delta \gamma_J + \lambda \tau_I}{\delta} \end{pmatrix}$$

Requiring that all eigenvalues have negative real part is equivalent to requiring that $1 > \mathcal{R}_0^I$ and $1 < \mathcal{R}_0^I$. This is a very unsurprising result.

Case 2:
$$I = B = 0$$
, $J \neq 0$

This case is symmetric with the previous one.

Case 3: I, J, B All Non-Zero

Using maple, we get formulas for each compartment at this equilibrium.

```
% Copy and pasted from Maple with a bit of re-naming variables.

S3 = -delta * (tau_I * gamma_I * delta + delta * tau_J * gamma_J + lambda * tau_I * tau_J + tau_I = (delta ^ 3 * tau_I + delta ^ 2 * tau_I * gamma_I + delta ^ 2 * tau_I * gamma_J + delta ^ 3 = (delta ^ 3 * tau_J + delta ^ 2 * tau_I * gamma_I + delta ^ 2 * tau_J * gamma_I + delta ^ 3 = -(delta ^ 2 * tau_I + delta ^ 2 * tau_J + tau_I * gamma_I * delta + delta * gamma_I * tau_I * gamma_I * delta *
```

Now, we plug these formulas into the Jacobian.

Jac3 = SIJB Jac(S3, I3, J3, B3, params2)

Jac3 =

$$\begin{pmatrix}
\sigma_{2} - \delta + \sigma_{1} & \gamma_{I} - \sigma_{3} & \gamma_{J} - \sigma_{4} & -\frac{\delta (\tau_{I} + \tau_{J}) \sigma_{8}}{\tau_{I} \tau_{J} \sigma_{11}} \\
-\sigma_{2} & \sigma_{1} - \gamma_{I} - \delta + \sigma_{3} & -\frac{\sigma_{6}}{\tau_{I} \sigma_{11}} & \gamma_{J} + \frac{\sigma_{6}}{\tau_{I} \sigma_{11}} + \sigma_{3} \\
-\sigma_{1} & -\frac{\sigma_{5}}{\tau_{J} \sigma_{11}} & \sigma_{2} - \gamma_{J} - \delta + \sigma_{4} & \gamma_{I} + \frac{\sigma_{5}}{\tau_{J} \sigma_{11}} + \sigma_{4} \\
0 & -\sigma_{1} - \frac{\sigma_{5}}{\tau_{J} \sigma_{11}} & -\sigma_{2} - \frac{\sigma_{6}}{\tau_{I} \sigma_{11}} & -\delta - \gamma_{I} - \gamma_{J} - \frac{\sigma_{6}}{\tau_{I} \sigma_{11}} - \frac{\sigma_{5}}{\tau_{J} \sigma_{11}}
\end{pmatrix}$$

where

$$\sigma_1 = \tau_J \, \left(\frac{\sigma_5}{\tau_I \, \tau_J \, \sigma_{11}} - \sigma_7 \right)$$

$$\sigma_2 = \tau_I \left(\frac{\sigma_6}{\tau_I \, \tau_J \, \sigma_{11}} - \sigma_7 \right)$$

$$\sigma_3 = \frac{\delta \, \sigma_8}{\tau_J \, \sigma_{11}}$$

$$\sigma_4 = \frac{\delta \sigma_8}{\tau_L \sigma_{11}}$$

$$\sigma_5 = \delta^3 \tau_J - \delta \lambda \tau_J^2 - \gamma_I \lambda \tau_J^2 + \sigma_{10} + \delta^2 \gamma_I \tau_J + \sigma_9 + \delta \gamma_I \gamma_J \tau_I + \delta \gamma_I \gamma_J \tau_J - \gamma_I \lambda \tau_I \tau_J$$

$$\sigma_{6} = \delta^{3} \tau_{I} - \delta \lambda \tau_{I}^{2} - \gamma_{J} \lambda \tau_{I}^{2} + \sigma_{10} + \delta^{2} \gamma_{J} \tau_{I} + \sigma_{9} + \delta \gamma_{I} \gamma_{J} \tau_{I} + \delta \gamma_{I} \gamma_{J} \tau_{J} - \gamma_{J} \lambda \tau_{I} \tau_{J}$$

$$\sigma_{7} = \frac{\left(\delta^{2} + \gamma_{J} \delta - \lambda \tau_{J}\right) \left(\delta^{2} \tau_{I} + \tau_{J} \delta^{2} + \gamma_{I} \delta \tau_{I} + \gamma_{I} \tau_{J} \delta - \lambda \tau_{I}^{2} - \lambda \tau_{J} \tau_{I}\right)}{\delta \tau_{I} \tau_{J} \sigma_{11}}$$

$$\sigma_8 = \delta \gamma_I \tau_I + \delta \gamma_J \tau_J + \gamma_I \gamma_J \tau_I + \gamma_I \gamma_J \tau_J + \lambda \tau_I \tau_J$$

$$\sigma_9 = \delta^2 \gamma_J \, \tau_J$$

$$\sigma_{10} = \delta^2 \gamma_I \, \tau_I$$

$$\sigma_{11} = -\delta^2 + \lambda \, \tau_I + \lambda \, \tau_J$$

Unfortunately, Matlab takes a while to even compute the eigenvalues of the Jacobian and I don't feel like waiting. I seriously doubt that we'll get anything comprehensible out anyway.

Further Restricting the Model

Let's now try restricting the model further until we get something we can make sense of. To start, we can try setting $\lambda = \delta$. That's not enough. How about setting the transmission and recovery parameters to be the same across diseases?

```
syms tau gamma;

S3_red = -delta * (tau * gamma * delta + delta * tau * gamma + delta * tau * tau + tau * gamma I3_red = (delta ^ 3 * tau + delta ^ 2 * tau * gamma * delta + delta * gamma * tau - delta params3 = [delta delta delta delta delta tau tau gamma gamma];
```

We now substitute these (slightly) simplified expressions into the Jacobian and try to compute the eigenvalues.

```
Jac3_red = SIJB_Jac(S3_red, I3_red, J3_red, B3_red, params3)
```

$$\begin{pmatrix}
2\tau\sigma_5 - \delta & \gamma - \sigma_4 & \gamma - \sigma_4 & -\frac{2\delta\sigma_6}{\tau\sigma_8} \\
-\tau\sigma_5 & \sigma_2 & -\frac{\sigma_7}{\tau\sigma_8} & \sigma_1 \\
-\tau\sigma_5 & -\frac{\sigma_7}{\tau\sigma_8} & \sigma_2 & \sigma_1 \\
0 & \sigma_3 & \sigma_3 & -\delta - 2\gamma - \frac{2\sigma_7}{\tau\sigma_8}
\end{pmatrix}$$

where

$$\sigma_1 = \gamma + \frac{\sigma_7}{\tau \, \sigma_8} + \sigma_4$$

$$\sigma_2 = \tau \, \sigma_5 - \gamma - \delta + \sigma_4$$

$$\sigma_3 = -\tau \, \sigma_5 - \frac{\sigma_7}{\tau \, \sigma_8}$$

$$\sigma_4 = \frac{\delta \sigma_6}{\tau \sigma_8}$$

$$\sigma_5 = \frac{\sigma_7}{\tau^2 \sigma_8} - \frac{(2 \delta^2 \tau - 2 \delta \tau^2 + 2 \gamma \delta \tau) (\delta \gamma - \delta \tau + \delta^2)}{\delta \tau^2 \sigma_8}$$

$$\sigma_6 = 2 \gamma^2 \tau + 2 \delta \gamma \tau + \delta \tau^2$$

$$\sigma_7 = \delta^3 \tau + 3 \delta^2 \gamma \tau - \delta^2 \tau^2 + 2 \delta \gamma^2 \tau - 2 \delta \gamma \tau^2$$

$$\sigma_8 = 2 \delta \tau - \delta^2$$

```
% We're going to need Matlab to do more thinking for us here. Specifying
% the signs of our parameters will make this easier.
assume(delta, 'positive');
assume(tau, 'positive');
assume(gamma, 'positive');
% Compute the eigenvalues
eig(Jac3_red)
```

ans =

$$\frac{\sigma_2 + \frac{\sigma_8}{3\sigma_9} - \frac{\sigma_3}{\sigma_2}}{-\frac{\delta^2 + 5\delta\gamma + \delta\tau + 4\gamma^2 - 2\gamma\tau - 2\tau^2}{\delta - 2\tau}} - \frac{\frac{\sigma_8}{3\sigma_9} - \frac{\sigma_2}{2} + \frac{\sigma_3}{2\sigma_2} - \sigma_1}{\frac{\sigma_8}{3\sigma_9} - \frac{\sigma_2}{2} + \frac{\sigma_3}{2\sigma_2} + \sigma_1}$$

where

$$\sigma_1 = \frac{\sqrt{3} \left(\sigma_2 + \frac{\sigma_3}{\sigma_2}\right) i}{2}$$

$$\sigma_2 = \left(\sqrt{\sigma_3^3 + (\sigma_5 + \sigma_6 - \sigma_4)^2} + \sigma_5 + \sigma_6 - \sigma_4\right)^{1/3}$$

$$\sigma_3 = \frac{\sigma_7}{3 \sigma_9} - \frac{\sigma_8^2}{9 \sigma_9^2}$$

$$\sigma_4 = \frac{\sigma_8 \, \sigma_7}{6 \, \sigma_9^2}$$

$$\sigma_{5} = \frac{\delta^{5} + 17\,\delta^{4}\,\gamma + \delta^{4}\,\tau + 64\,\delta^{3}\,\gamma^{2} - 38\,\delta^{3}\,\gamma\,\tau - 14\,\delta^{3}\,\tau^{2} + 112\,\delta^{2}\,\gamma^{3} - 120\,\delta^{2}\,\gamma^{2}\,\tau + 12\,\delta^{2}\,\gamma\,\tau^{2} + 20\,\delta^{2}\,\tau^{3} + 120\,\delta^{2}\,\gamma^{3} + 120\,\delta^{2}\,\gamma^{2}\,\tau + 12\,\delta^{2}\,\gamma^{2} + 120\,\delta^{2}\,\gamma^{3} + 120\,\delta^{$$

$$\sigma_6 = \frac{\sigma_8^3}{27 \sigma_9^3}$$

$$\sigma_7 = 3 \, \delta^4 + 24 \, \delta^3 \, \gamma - 8 \, \delta^3 \, \tau + 52 \, \delta^2 \, \gamma^2 - 54 \, \delta^2 \, \gamma \, \tau + 14 \, \delta^2 \, \tau^2 + 48 \, \delta \, \gamma^3 - 72 \, \delta \, \gamma^2 \, \tau + 56 \, \delta \, \gamma \, \tau^2 - 16 \, \delta \, \tau^3 + 16 \, \delta^2 \, \gamma^2 + 16 \, \delta^2$$

$$\sigma_8 = 3 \delta^3 + 7 \delta^2 \gamma - 13 \delta^2 \tau + 4 \delta \gamma^2 - 20 \delta \gamma \tau + 20 \delta \tau^2 - 8 \gamma^2 \tau + 12 \gamma \tau^2 - 12 \tau^3$$

$$\sigma_9 = \delta^2 - 4 \delta \tau + 4 \tau^2$$

- % And their real parts (This takes a long time to run and doesn't clarify
- % things at all)
- % simplify(real(eig(Jac3_red)) < 0)</pre>

This is still too complicated. I'm going to need to come up with further simplifications for the model. Sounds like a problem for another time.

Appendix: Function Definitions

```
function Jac = SIJB_Jac(S, I, J, B, params)
   % Extract parameters
    lambda = params(1);
    delta_S = params(2);
    delta I = params(3);
    delta_J = params(4);
   delta_B = params(5);
   tau I = params(6);
   tau_J = params(7);
    gamma_I = params(8);
    gamma_J = params(9);
    J11 = -tau I*(I+B) - tau J*(J+B) - delta S;
    J12 = -tau_I*S + gamma_I;
    J13 = -tau_J*S + gamma_J;
    J14 = -(tau_I+tau_J)*S;
    J21 = tau_I*(I+B);
    J22 = tau_I*S - gamma_I - tau_J*(J+B) - delta_I;
    J23 = tau_J*I;
    J24 = tau_I*S - tau_J*I + gamma_J;
    J31 = tau_J*(J+B);
    J32 = tau_I*J;
    J33 = tau_J*S - gamma_J - tau_I*(I+B) - delta_J;
    J34 = tau_J*S - tau_I*J + gamma_I;
    J41 = 0;
    J42 = tau_J*(J+B) + tau_I*J;
    J43 = tau J*I + tau I*(I+B);
    J44 = tau_J*I + tau_I*J - gamma_I - gamma_J - delta_B;
    Jac = [J11 J12 J13 J14; J21 J22 J23 J24; J31 J32 J33 J34; J41 J42 J43 J44];
end
```