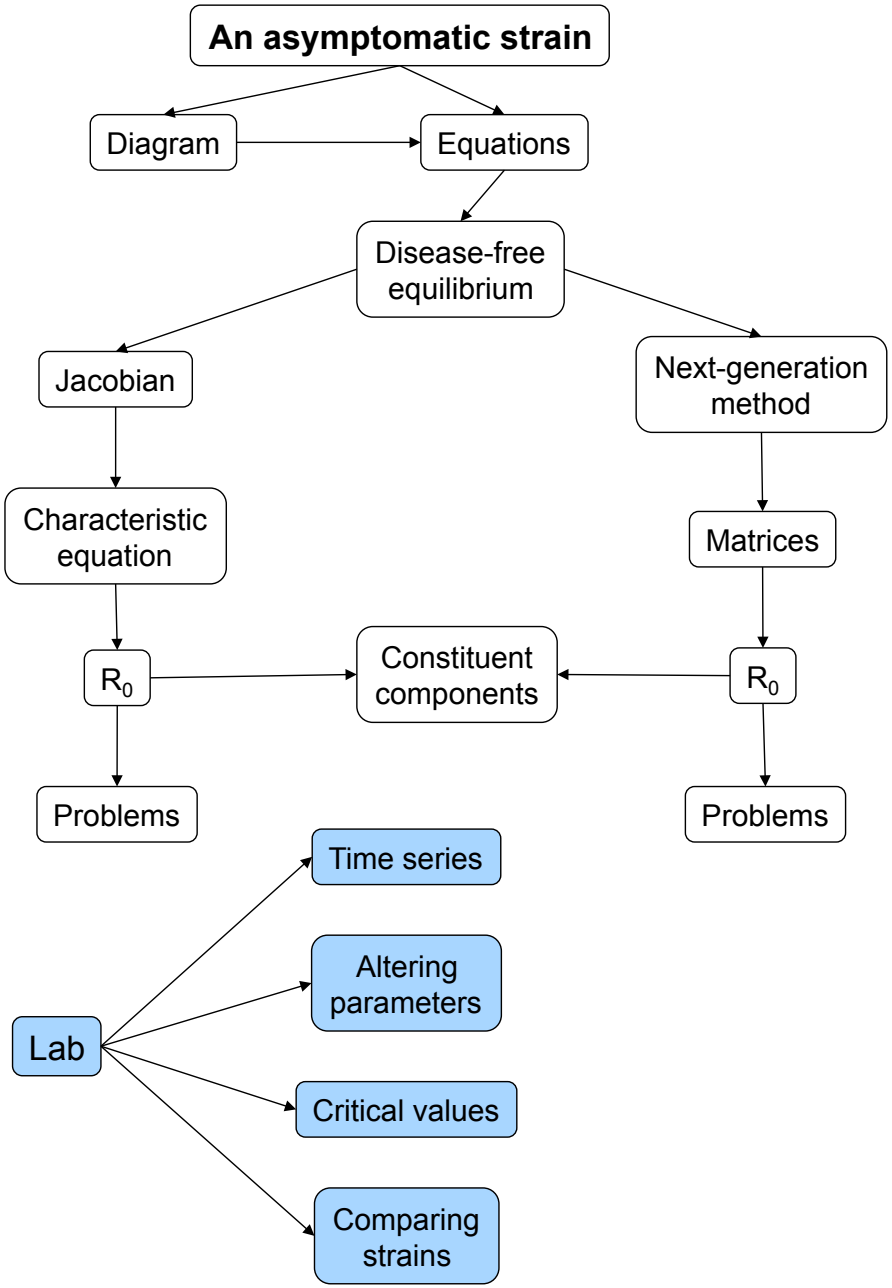
A disease with an asymptomatic class

- Infection may split into a symptomatic class and an asymptomatic one
- Eg COVID-19
- Asymptomatic individuals may not know they're infected
- Hence they may not seek treatment and will socially distance less
- However, they may transmit the virus at a lower rate, since they have a lower viral load
- They may also recover faster (or not, depending)
- Immunity may not be permanent.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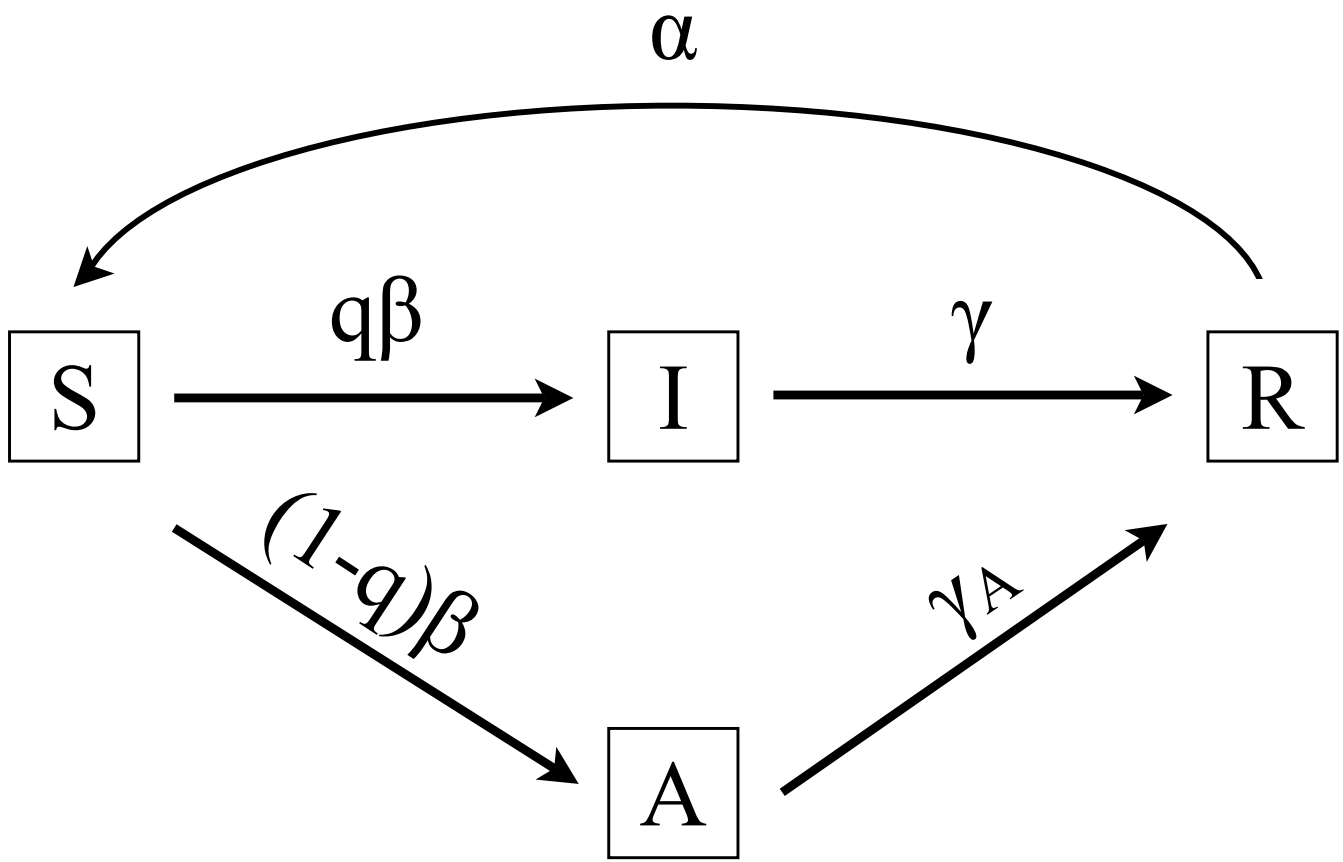
Asymptomatic infection

Many diseases do not confer permanent immunity, but rather provide only temporary immunity.
Influenza is one such disease, because the virus mutates each year.
Previously, we used delay differential equations to describe this effect, but they're not essential.
So here we'll move from susceptible to infected to recovered and then have the ability to return to the susceptible class.

A tweak we can add is to suppose that some proportion of infected individuals are asymptomatic.
That is, they are still infected (and infectious), but they may have different transmission and recovery rates.
We're not explicitly modelling symptoms per se, so the effect is to split the infectious class in two.
One thing to be careful of: the word "proportion".
Upon infection, a fraction of individuals q will move to the regular infected class, while the remainder $(1 - q)$ will move to the asymptomatic class.


α
qβ
γ
S
I
R
(1-q)β
γA
A

Note that susceptibles can be infected by either symptomatic or asymptomatic individuals.
So there are *four* infection terms floating around, characterised by $q\beta$, $(1-q)\beta$, $q\beta_A$ and $(1-q)\beta_A$.
The differential equations are given by

$$
\begin{aligned}
S' &= \lambda - \beta SI - \beta_A SA + \alpha R - \mu S \\
I' &= q\beta SI + q\beta_A SA - \mu I - \gamma I \\
A' &= (1-q)\beta SI + (1-q)\beta_A SA - \mu A - \gamma_A A \\
R' &= \gamma I + \gamma_A A - \alpha R - \mu R.
\end{aligned}
$$

The disease-free equilibrium is given by

$$(\bar{S}, \bar{I}, \bar{A}, \bar{R}) = \left(\frac{\lambda}{\mu}, 0, 0, 0\right).$$

Next, we'd like to find the reproduction number.
We're going to do this in two ways, to illustrate some of the issues that may arise.
So we'll outline the key steps for each.

Using the characteristic polynomial

Here are the steps we need to take:

1. Find the Jacobian matrix.
2. Evaluate the Jacobian at the disease-free equilibrium
3. Determine the characteristic equation.
4. Use information about the coefficients to develop an R_0.
5. Identify any problems that arise.

Differentiating, the Jacobian is

$$J = \begin{bmatrix} -\beta I - \beta_A A - \mu & -\beta S & -\beta_A S & \alpha \\ q\beta I + q\beta_A A & q\beta S - \mu - \gamma & q\beta_A S & 0 \\ (1-q)\beta I + (1-q)\beta_A A & (1-q)\beta S & (1-q)\beta_A S - \mu - \gamma_A & 0 \\ 0 & \gamma & \gamma_A & -\alpha - \mu \end{bmatrix}$$

$$J\Big|_{\text{DFE}} = \begin{bmatrix} -\mu & -\beta\bar{S} & -\beta_A\bar{S} & \alpha \\ 0 & q\beta\bar{S} - \mu - \gamma & q\beta_A\bar{S} & 0 \\ 0 & (1-q)\beta\bar{S} & (1-q)\beta_A\bar{S} - \mu - \gamma_A & 0 \\ 0 & \gamma & \gamma_A & -\alpha - \mu \end{bmatrix}.$$

The characteristic equation is then

$$\det\left(J\Big|_{\text{DFE}} - \Lambda I\right) = (-\mu - \Lambda)(-\alpha - \mu - \Lambda)\det M,$$

where

$$M = \begin{bmatrix} q\beta\bar{S} - \mu - \gamma - \Lambda & q\beta_A\bar{S} \\ (1-q)\beta\bar{S} & (1-q)\beta_A\bar{S} - \mu - \gamma_A - \Lambda \end{bmatrix}.$$

The first two eigenvalues are always negative, while the characteristic equation for M is

$$\begin{aligned}0 &= (q\beta\bar{S} - \mu - \gamma - \Lambda)((1-q)\beta_A\bar{S} - \mu - \gamma_A - \Lambda) - q(1-q)\beta\beta_A\bar{S}^2 \\ &= \Lambda^2 + \Lambda\left[\mu + \gamma - q\beta\bar{S} + \mu + \gamma_A - (1-q)\beta_A\bar{S}\right] \\ &\quad + (\mu+\gamma)(\mu+\gamma_A) - q\beta\bar{S}(\mu+\gamma_A) - (\mu+\gamma)(1-q)\beta_A\bar{S}.\end{aligned}$$

Rearranging the constant term of the characteristic equation, we have

$$(\mu+\gamma)(\mu+\gamma_A) = q\beta\bar{S}(\mu+\gamma_A) + (\mu+\gamma)(1-q)\beta_A\bar{S}$$

$$R_0 = \frac{q\beta\bar{S}}{\mu+\gamma} + \frac{(1-q)\beta_A\bar{S}}{\mu+\gamma_A}.$$

What problems arise here?
Answer: we didn't consider the coefficient of the linear term in the characteristic equation.
Consider

$$b = \mu + \gamma - q\beta\bar{S} + \mu + \gamma_A - (1-q)\beta_A\bar{S}.$$

If $b > 0$, then the largest eigenvalue will be negative if $R_0 < 1$ and will be positive if $R_0 > 1$.
What happens if $b < 0$?
It's certainly possible that it might be, as there are negative terms in it.
If $b < 0$, then the largest eigenvalue will be positive, regardless of the constant term.
So even if $R_0 < 1$, the disease-free equilibrium will be unstable.

Evaluating b at the threshold

There's one more thing we can do, however, which is evaluate b at the threshold $R_0 = 1$.
At the threshold, the constant term is zero, so if the other eigenvalue is negative, then small changes in the constant term won't change the negativity of the other eigenvalue.
That is, if $b < 0$ when $R_0 = 1$, we will have local stability.
Using the condition $R_0 = 1$ gives us a further constraint that can allow some of the negative terms to be cancelled.

Substituting

$$\mu + \gamma = q\beta\bar{S} + \frac{\mu + \gamma}{\mu + \gamma_A}(1 - q)\beta_A\bar{S}$$

gives

$$\begin{aligned} b\Big|_{R_0=1} &= \cancel{q\beta\bar{S}} + \frac{\mu + \gamma}{\mu + \gamma_A}(1 - q)\beta_A\bar{S} - \cancel{q\beta\bar{S}} + \mu + \gamma_A - (1 - q)\beta_A\bar{S} \\ &= \frac{\mu + \gamma - (\mu + \gamma_A)}{\mu + \gamma_A}(1 - q)\beta_A\bar{S} + \mu + \gamma_A \\ &= \frac{\gamma - \gamma_A}{\mu + \gamma_A}(1 - q)\beta_A\bar{S} + \mu + \gamma_A \end{aligned}$$

This will be positive if $\gamma \geq \gamma_A$;
i.e., if recovery from symptomatic infection is faster than asymptomatic infection.
So if asymptomatic infection lasts longer, then R_0 is a threshold.
However, this is unlikely to be true for most diseases, because the viral load for asymptomatic infection is lower, so recovery should be quicker.
This condition isn't sharp though.
So we could have $\gamma < \gamma_A$ and still have $b\big|_{R_0=1} > 0$.
We'll explore this case in the lab.

Splitting R_0 into its constituent components

Suppose $q = 1$, so that nobody is asymptomatic.
Then, from the model, the asymptomatic equation becomes

$$A' = -\mu A - \gamma_A A,$$

so $A \to 0$ as $t \to \infty$.
So we might as well set $A = 0$.
(More formally, if $A(0) = 0$, then $A \equiv 0$.)

Then the infected equation becomes

$$\begin{aligned} I' &= \beta SI - \mu I - \gamma I \\ &= (\beta S - \mu - \gamma)I, \end{aligned}$$

so we can set

$$R_0^I = \frac{\beta \bar{S}}{\mu + \gamma}.$$

This is the reproduction number for a single infected individual in a wholly susceptible population.
In particular, if $R_0^I < 1$, then $I' < 0$, whereas if $R_0^I > 1$, then $I' > 0$.

Next suppose that $q = 0$, so that everybody is asymptomatic.
The infected equation becomes

$$I' = -\mu I - \gamma I,$$

so we can set $I = 0$.
The asymptomatic equation becomes

$$\begin{aligned} A' &= \beta_A SA - \mu A - \gamma_A A \\ &= (\beta_A S - \mu - \gamma_A)A. \end{aligned}$$

We can then define

$$R_0^A = \frac{\beta_A \bar{S}}{\mu + \gamma_A}.$$

This is the reproduction number for a single asymptomatic individual in a population of susceptibles.

We can thus write

$$\begin{aligned} R_0 &= \frac{q\beta\bar{S}}{\mu+\gamma} + \frac{(1-q)\beta_A\bar{S}}{\mu+\gamma_A} \\ &= qR_0^I + (1-q)R_0^A. \end{aligned}$$

That is, R_0 can be split into a linear combination of the individual reproduction numbers for each of the two substrains of the virus.

Using the next-generation method

Here are the steps we need to take using this method:

1. Identify the infected classes.
2. Determine the matrix of new infections and the matrix of transfer terms.
3. Find the largest eigenvalue to calculate R_0.
4. Identify any problems that arise.

First, let's note that the only infected classes are the I and A classes.
So this will reduce our problem to a two-dimensional one.
The vector of new infections is

$$\mathcal{F} = \begin{bmatrix} q\beta SI + q\beta_A SA \\ (1-q)\beta SI + (1-q)\beta_A SA \end{bmatrix}.$$

We are expressing the middle two equations in the form $\mathcal{F} - \mathcal{V}$, so the vector of transfer terms is

$$\mathcal{V} = \begin{bmatrix} \mu I + \gamma I \\ \mu A + \gamma_A A \end{bmatrix}.$$

Differentiating, we have the matrices

$$F = \begin{bmatrix} q\beta S & q\beta_A S \\ (1-q)\beta S & (1-q)\beta_A S \end{bmatrix} \qquad V = \begin{bmatrix} \mu+\gamma & 0 \\ 0 & \mu+\gamma_A \end{bmatrix}$$

The reproduction number is the largest eigenvalue of FV^{-1}, so (using Appendix C) we have

$$FV^{-1}\Big|_{\text{DFE}} = \begin{bmatrix} q\beta\bar{S} & q\beta_A\bar{S} \\ (1-q)\beta\bar{S} & (1-q)\beta_A\bar{S} \end{bmatrix} \begin{bmatrix} \dfrac{1}{\mu+\gamma} & 0 \\ 0 & \dfrac{1}{\mu+\gamma_A} \end{bmatrix}$$

$$= \begin{bmatrix} \dfrac{q\beta\bar{S}}{\mu+\gamma} & \dfrac{q\beta_A\bar{S}}{\mu+\gamma_A} \\ \dfrac{(1-q)\beta\bar{S}}{\mu+\gamma} & \dfrac{(1-q)\beta_A\bar{S}}{\mu+\gamma_A} \end{bmatrix}.$$

Next we need to find the largest eigenvalue, so (using Appendix C again) we have

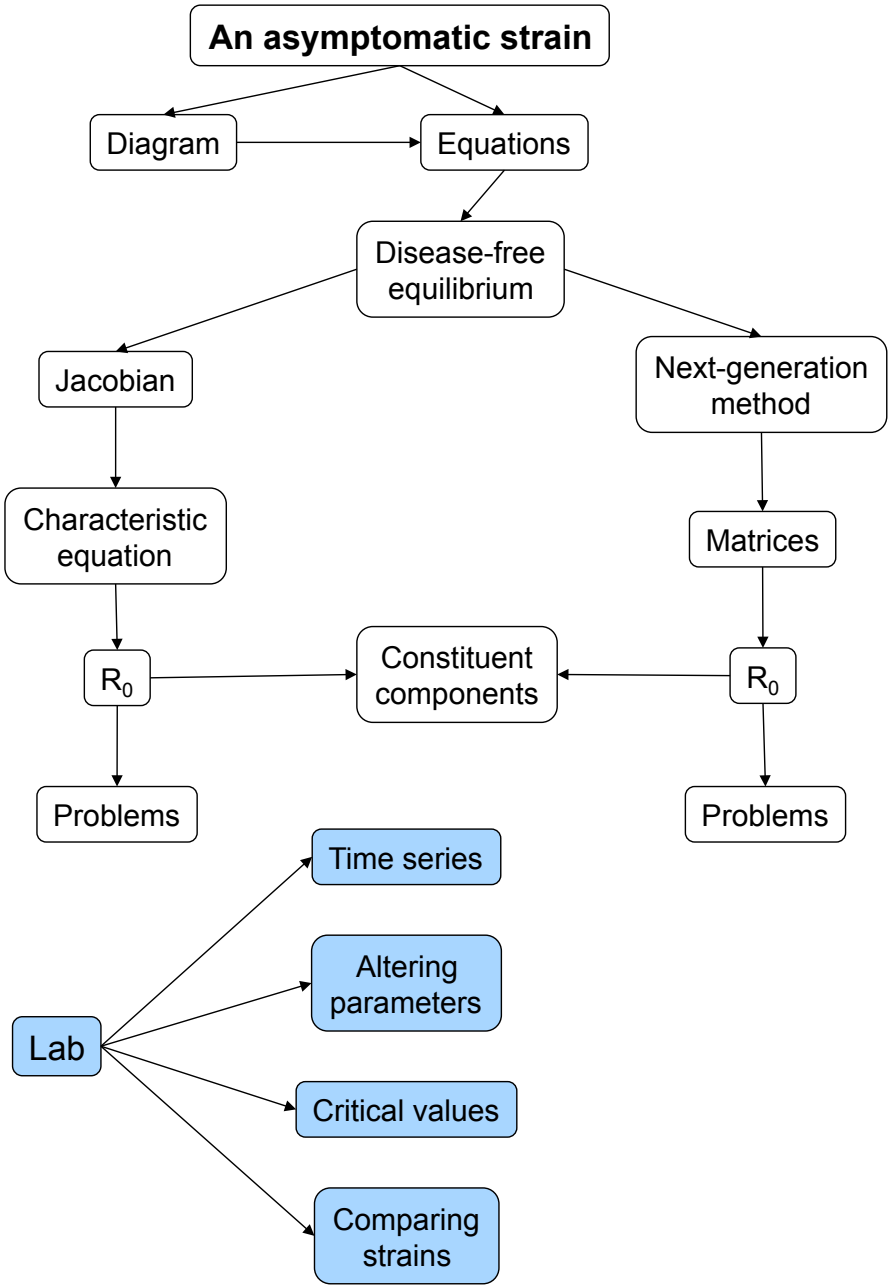
$$\begin{aligned}
\det(FV^{-1} - \Lambda I) &= \det \begin{bmatrix} \dfrac{q\beta\bar{S}}{\mu+\gamma} - \Lambda & \dfrac{q\beta_A\bar{S}}{\mu+\gamma_A} \\ \dfrac{(1-q)\beta\bar{S}}{\mu+\gamma} & \dfrac{(1-q)\beta_A\bar{S}}{\mu+\gamma_A} - \Lambda \end{bmatrix} \\
&= \Lambda^2 - \Lambda\left(\frac{q\beta\bar{S}}{\mu+\gamma} + \frac{(1-q)\beta_A\bar{S}}{\mu+\gamma_A}\right) + \frac{q\beta\bar{S}}{\mu+\gamma}\frac{(1-q)\beta_A\bar{S}}{\mu+\gamma_A} \\
&\quad - \frac{q\beta_A\bar{S}}{\mu+\gamma_A}\frac{(1-q)\beta\bar{S}}{\mu+\gamma} \\
&= \Lambda\left(\Lambda - \frac{q\beta\bar{S}}{\mu+\gamma} - \frac{(1-q)\beta_A\bar{S}}{\mu+\gamma_A}\right).
\end{aligned}$$

The smaller eigenvalue is 0, while the larger one is

$$\begin{aligned}
R_0 &= \frac{q\beta\bar{S}}{\mu+\gamma} + \frac{(1-q)\beta_A\bar{S}}{\mu+\gamma_A} \\
&= qR_0^I + (1-q)R_0^A.
\end{aligned}$$

Note that R_0 is the largest eigenvalue from the next-generation method...
...but it is NOT the largest eigenvalue from the Jacobian or characteristic equation methods.
Instead, it's a *rearrangement* of the largest eigenvalue from the Jacobian or characteristic equation methods.
(Yes, it's confusing.)

What problems arise now?
Well, we got the same R_0 as with the previous method, but without the constraint of $b > 0$.
So does that constraint matter?
We'd never know it existed if we only used the next-generation method.
We'll explore that in the lab.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