Non-Linear Models: Ex 5.6 Infectious Diseases

Example: Infectious Diseases

Can be classified into 2 broad categories:

1. those caused by viruses & bacteria (microparasitic diseases e.g. smallpox, measles),
2. those due to ‘vectors’ (macroparasitic diseases such as malaria).

Main distinction btw them:

1. former reproduce in-host & are transmitted directly from one host to another,
2. latter need a means of transmission (i.e. insect etc.).

We focus on microparasitic diseases.

Virus & host organism are not a predator-prey system, for a number of reasons:

1. Virus numbers in individual host vary greatly, thus model can’t say how many are infected.
2. Key question is disease spread in population, difficult to model with Predator-prey.
3. Predator-prey model does not have any stable equilibria.

To model diseases, pop’n divided into 3 groups:

1. susceptibles (i.e. those not immune to disease),
2. infectives (those who can infect non-immunes),
3. removed (dead or in quarantine or immune).

Symbols $S, I, R$ denote these resp groups at time $t$. 

Notes
Following assumptions are made:

1. rate of change of infectives $\propto$ no. of contacts btw $I$ & $S$ (or each $I$ infects a constant fraction $\beta$ of $S$ per unit time)
2. no. of $I$ who become $R$ is proportional to $I$

Equations are thus:

\[
\begin{align*}
\dot{S} &= -\beta IS \\
\dot{I} &= \beta IS - \nu I \\
\dot{R} &= \nu I
\end{align*}
\]  \hspace{1cm} (5.30)

$\beta, \nu$ are infection & removal rates, $\dot{S} = \frac{dS}{dt}$ etc.

$\beta$ governs speed of disease spread
$\nu$ governs rate infected hosts die/otherwise removed.

By adding 3 equations, can see that

\[
\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI}{dt} + \frac{dR}{dt} = 0, \text{i.e. } S + I + R = N \text{ for const } N
\]

Rest of the initial conditions are

$S(0) = S_0 > 0$, $I(0) = I_0 > 0$, $R(0) = 0.0$

Given these initial conditions from Eqn.(5.30b) get:

\[
\left. \frac{dI}{dt} \right|_{t=0} = I_0 (\beta S_0 - \nu) \begin{cases} < 0, & \text{if } S_0 < \nu/\beta \\ > 0, & \text{if } S_0 > \nu/\beta \end{cases}
\]  \hspace{1cm} (5.31)
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- Ratio $\rho = \nu/\beta$, known as relative removal rate.
- From Eqn.(5.30a), $\frac{dS}{dt} < 0$
- So $S(t) \leq S_0$ & (if $S_0 < \rho$) so $S(t) < \rho$ for all $t$.
- Corresponding to different values of $\rho$, two distinct cases:
  1. From Eqn.(5.30b), if $S < \rho$
     - Then $\frac{dI}{dt} < 0$ meaning infectives never grow.
     - So as $t \to \infty$, infection will die out.
  2. If $S_0 > \rho$,
     - In same way $\frac{dI}{dt} > 0$ for all $t$ such that $S(t) > \rho$.
     - Implies for some time $t \in [0, t_0)$, must have $I(t) > I_0$.
     - Say this is an epidemic situation.

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- A plot of $S$, $I$ and $R$ is shown in Fig 5.6.

**Figure 5.6**: SIR Model for $\rho = 100$: Susceptible, Infected, Removed
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- To further analyse the model, see \((S, I)\) phase-plane in Fig. 5.7.
- Can express Eqn.s(5.30a,b) as

\[
\frac{dI}{dt} = \frac{I(\beta S - \nu)}{-\beta IS} = -1 + \frac{\rho}{S}, \quad (5.32)
\]

provided \(I \neq 0\). Can derive:

\[
I(t) = I_0 - S(t) + \rho \ln S(t) + S_0 - \rho \ln S_0 \quad (5.33)
\]

- See from Eqn.(5.33), Fig. 5.7 that \(I_{\text{max}}\) when \(S = \rho\).
- Show trajectories various \((S_0, I_0)\) & as per predator-prey, all move anti-clockwise.
- A trajectory starts on line \(I + S = N\) (as \(R(0) = 0\)) & \(S\) decreases with time.
- If \((S_0, I_0)\) is in epidemic region of Fig. 5.7, \(I \uparrow\) until \(S = \rho\).

Notes

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![Figure 5.7: SIR Model Phase-Plane Plot for \(\rho = 4\)](image-url)

Notes
How does disease eventually die out with SIR model?
From Eqn.s(5.30a,c):
\[
\frac{dS}{dR} = -\frac{\beta IS}{\nu I} = -\frac{S}{\rho}, \tag{5.34}
\]

thus \(S = S_0 e^{-R/\rho}\).

But, \(\forall t \geq 0, R \leq N\) means \(S(t) \geq S_0 e^{-N/\rho}\), i.e. as \(t \to \infty\), \(S > 0\).

But, from Eqn.(5.30c) \(\frac{dR}{dt} > 0 \ \forall t \geq 0\) \(\forall t \geq 0\), so, if need to keep \(R \leq N\), then need \(\frac{dR}{dt} \to 0\), as \(t \to \infty\).

From Eqn.(5.30c), this can only happen if \(I(\infty) = 0\).

\[\Rightarrow\] Disease wiped out from lack of infectives & not susceptibles.

More general model than SIR (more applicable), is one with only partial immunity.
Called SIRS model & permits previously infected (i.e. removed) individuals to return to susceptible pop’n
Do so at a rate proportional to the number removed.
Mathematically SIRS can be expressed as:
\[
\begin{align*}
\frac{dS}{dt} &= -\beta IS + \gamma R \\
\frac{dI}{dt} &= \beta IS - \nu I \tag{5.35} \\
\frac{dR}{dt} &= \nu I - \gamma R
\end{align*}
\]

Again the total population, \(S + I + R = N\), is constant.
SIRS can be analysed using standard methods, equilibrium states found to be:

\[
\begin{align*}
\dot{S} &= 0 \Rightarrow \frac{\beta IS}{\gamma} = R \\
\dot{I} &= 0 \Rightarrow \frac{\beta IS}{\gamma} = \nu I \\
\dot{R} &= 0 \Rightarrow \frac{\nu I}{\gamma} = R
\end{align*}
\]  

(5.36)

- These yield 2 equilibrium points:
  - \( \bar{S}_1 = N, \bar{I}_1 = 0, \bar{R}_1 = 0 \),
  - This (trivial) equilibrium point can be shown to be stable.
  - Here, pop’n all healthy but susceptible & disease eradicated.

A further equilibrium point can be found:

- Put \( S = \nu / \beta \) (from Eqn.(5.36b)) & \( R = \nu I / \gamma \) (from Eqn.(5.36c)) into \( S + I + R = N \) to give:

\[
\begin{align*}
\bar{S}_2 &= \frac{\nu}{\beta}, \quad \bar{I}_2 = \frac{\gamma \beta N - \nu}{\beta \gamma + \nu}, \quad \bar{R}_2 = \frac{\nu \beta N - \nu}{\beta \gamma + \nu}
\end{align*}
\]  

(5.37)

- \( (\bar{S}_2, \bar{I}_2, \bar{R}_2) \) is only meaningful if all values are +ive.
- i.e. \( \frac{\beta}{\nu} N > 1 \) (i.e. +ive numerators for \( \bar{I}_2, \bar{R}_2 \)).
- This is a threshold point
- It is minimum pop’n for a disease to become endemic.
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- Have seen $\rho = \nu / \beta$ (relative removal rate) above;

- Now define its reciprocal $\beta / \nu$ as follows:
  - As removal rate from infectives is $\nu$ (units 1/time), so average infectivity period is $1/\nu$.
  - $\beta$ is fraction of contacts (btw $I$ & $S$) resulting in infections,
  => $\beta \times 1/\nu$ is pop’n fraction in contact with $I$’s in infectious period.

- Hence $\sigma = \beta N / \nu$ is disease’s infectious contact number\(^{18}\)

- So, from above, and usefully enough, the disease will become endemic in the population if $\sigma > 1$.

\(^{18}\)Also known as the intrinsic reproductive rate sometimes denoted $R_0$.  

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- Can see this effect quite clearly in phase-plane.

- By using $R = N - S - I$, can write Eqn.s(5.35a,b) as:

\[
\begin{align*}
\dot{S} &= -\beta IS + \gamma (N - S - I) \\
\dot{I} &= \beta IS - \nu I
\end{align*}
\]  

(5.38)

- In Fig 8(a) pop’n cannot sustain disease & it dies out;

- In Fig 8(b), get steady-state

\[
\begin{align*}
\bar{S}_2 &= \frac{\nu}{\beta}, & \bar{I}_2 &= \frac{\gamma N - \nu}{\beta \gamma + \nu}.
\end{align*}
\]

- Jacobian corresponding to Eqn.(5.38) at $(\bar{S}_2, \bar{I}_2)$ is:

\[
A(\bar{S}_2, \bar{I}_2) = \begin{pmatrix}
-\gamma & -(\beta \bar{I}_2 + \gamma) \\
\beta \bar{I}_2 & \beta \bar{S}_2 - \nu
\end{pmatrix}
\]  

(5.39)
Recall, for stability: $\text{Tr}(A) < 0$ & $\text{Tr}(A) > 0$.
Can show $(\bar{S}_2, \bar{I}_2)$ is stable when $\sigma > 1$ is satisfied.

The SIS Model:
- A special case of SIR where infection doesn’t give lasting immunity.
- Such infections\(^{19}\) have no recovered state & individuals become susceptible again after infection.
- The equations are thus:

$$\frac{dS}{dt} = -\beta IS + \nu I$$
$$\frac{dI}{dt} = \beta IS - \nu I$$

\(^{19}\text{e.g. tuberculosis, meningitis, & infections leading to the common cold}\)
So for total population, $N$, it holds that:

$$\frac{dN}{dt} = \frac{dS}{dt} + \frac{dI}{dt} = 0$$

i.e. $S + I = N$ for constant (initial) population $N$.

Expressing $I$ in terms of $S$ in eqn.(5.40), can be seen that:

$$\frac{dI}{dt} = (\beta N - \nu)I - \beta I^2$$

A logistic growth form with $r = \beta N - \nu$, $K = N - \frac{\nu}{\beta}$ so 2 cases:

1. for $\frac{\nu}{\beta} N > 1$, $\lim_{t \to \infty} I(t) = \frac{\beta N - \nu}{\beta}$ & disease will spread,
2. for $\frac{\nu}{\beta} N \leq 1$, $\lim_{t \to \infty} I(t) = 0$ & disease will die out.

A plot of the former SIS model case is shown in Fig 5.9.

**Figure 5.9:** SIS Model for $\rho = 100$: Susceptible, Infected
Eradication & Control for the Models above:

- For SIR model, for eqn(5.37) $S_0 \approx N$, the total pop’n.
  
  - So, from eqn(5.37) & eqns(5.40,5.37) for SIS & SIRS models, respectively infectious contact number, $\sigma$ or $R_0 = \beta N/\nu$ is important.
  
  - It is pop’n fraction in contact with an infective in infectious period.
  
  - Equates to mean number of secondary cases one infected case causes without interventions to control the infection.
  
  - It helps model spread of an infectious disease thro a pop’n.

From $\beta N/\nu$ can reduce infectious disease spread by:

- $\uparrow \nu$, removal rate of infectives.
- $\beta \downarrow$, infection rate btw S & I. e.g. Disinfection, movement controls in Foot-and-Mouth.
- Reduce effective number $N$ which has the effect of $\downarrow S$.
- Again for the Foot-and-Mouth example:
  
  - Slaughter potential contacts surrounding infected farms
  
  - This was employed but politically controversial.
  
  - Vaccination of susceptibles for an epidemic.
Immunizing a pop'n from a disease is impractical due to cost

Logistics of administering vaccine to millions is difficult.

Also costs:
- Direct costs of producing & administering the dosage and
- Indirect costs of public info campaigns
- Indirect costs of bureaucracy to ensure all have been vaccinated.

Thus would like to be able to provide safety from disease at the lowest possible cost.

Actually only have to immunize a fraction of pop'n to give herd immunity.
- Specifically must reduce effective value of $N$ to kill disease.
- From SIR model must move enough people such that (from eqn(5.31)), $\beta S_0 - \nu < 0$ so that $\dot{I} < 0$.
- i.e. need to lower epidemic threshold below one.
- Or fraction of pop'n to be immunized is such that $S_0 < \nu / \beta$
- i.e. $100 \times (1 - \nu / \beta)$ % of susceptibles must be immunized.
This makes sense as for small $\nu$, takes longer to recover from infection

- So an infective has more time to infect people.
- Thus as $\nu \downarrow$, $1 - \nu/\beta \uparrow$; need to inoculate a larger pop'n fraction.
- As $\beta \uparrow$, each infected person contacts more people in a given period and $1 - \nu/\beta \uparrow$.
- Thus again need to inoculate a larger fraction of pop'n.

$R_0$ & $1 - 1/R_0$ shown in % Table 5.2 for common diseases.

<table>
<thead>
<tr>
<th>Disease</th>
<th>Transmission</th>
<th>$R_0$</th>
<th>$1 - 1/R_0$ %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Measles</td>
<td>Airborne</td>
<td>12 to 18</td>
<td>92 to 94.5</td>
</tr>
<tr>
<td>Pertussis</td>
<td>Airborne droplet</td>
<td>12 to 17</td>
<td>92 to 94</td>
</tr>
<tr>
<td>Diphtheria</td>
<td>Saliva</td>
<td>6 to 7</td>
<td>84</td>
</tr>
<tr>
<td>Smallpox</td>
<td>Social contact</td>
<td>5 to 7</td>
<td>80 to 85</td>
</tr>
<tr>
<td>Polio</td>
<td>Fecal-oral route</td>
<td>5 to 7</td>
<td>80 to 85</td>
</tr>
<tr>
<td>Rubella</td>
<td>Airborne droplet</td>
<td>5 to 7</td>
<td>80 to 85</td>
</tr>
<tr>
<td>HIV/AIDS</td>
<td>Bodily Fluids</td>
<td>2 to 5</td>
<td>50 to 80</td>
</tr>
<tr>
<td>SARS</td>
<td>Airborne droplet</td>
<td>2 to 5</td>
<td>50 to 80</td>
</tr>
<tr>
<td>Influenza (1918)</td>
<td>Airborne droplet</td>
<td>2 to 3</td>
<td>50 to 80</td>
</tr>
<tr>
<td>Cholera</td>
<td>Fecal-oral route</td>
<td>2.9</td>
<td>65.5</td>
</tr>
</tbody>
</table>

**Table 5.2:** Values for $R_0$ for Several Common Infectious Diseases
Non-Linear Models: The Chemostat Revisited

The Chemostat Revisited

- Back to chemostat above, can look at phase-plane plot.
- Derived the equations:

\[
\frac{dn}{d\tau} = f(n, c) = \alpha_1 \left( \frac{nc}{1 + c} \right) - n \quad (5.41)
\]

\[
\frac{dc}{d\tau} = g(n, c) = -\left( \frac{nc}{1 + c} \right) - c + \alpha_2 \quad (5.42)
\]

with (dimensionless) parameters:

\[
\alpha_1 = \frac{VK_{max}}{F} \quad \text{and} \quad \alpha_2 = \frac{C_0}{K_n}
\]

The phase-plane plot for \( n, c \) is shown in Fig 5.10.
- shows, when \( \alpha_1 = 3, \alpha_2 = 1 \), two equilibrium points:

\[
(\tilde{n}_1, \tilde{c}_1) = \left[ \alpha_1 \left( \frac{1}{\alpha_1 - 1} \right), \frac{1}{\alpha_1 - 1} \right] = \left( \frac{3}{2}, \frac{1}{2} \right)
\]

and

\[
(\tilde{n}_2, \tilde{c}_2) = (0, \alpha_2) = (0, 1)
\]

as predicted.

Eqns(5.41, 5.42) also contain dimensionless time, bacterial population & nutrient concentrations respectively:

\[
\tau = \frac{tF}{V}, \quad n = \frac{NaVK_{max}}{FK_n}, \quad c = \frac{C}{K_n}
\]

Notes
FIGURE 5.10: Chemostat Phase-Plane Plot, $\alpha_1 = 3, \alpha_2 = 1$