A Model incorporating exposure to the disease

- When a susceptible individual is infected, one may assume that the infected susceptible goes through a latent period before becoming infectious.
- For this reason, we introduce a of exposed individuals
- Diseases such as TB, HIV etc have this characteristic

- The variables in this model are

$S(t)$	Susceptible population
$E(t)$	Individuals Exposed to the disease
$I(t)$	Individuals infected with the disease
$R(t)$	$Removed individuals$

- A model which includes the exposed class is given by

$$
\begin{aligned}
\frac{dS}{dt} &= bN - dS - \lambda IS/N \\
\frac{dE}{dt} &= \lambda IS/N - (\epsilon + d)E \\
\frac{dI}{dt} &= \epsilon E - (\gamma + \alpha d)I \\
\frac{dR}{dt} &= \gamma I - dR
\end{aligned}
$$

- The total population is given by $N(t)S(t) + E(t) + I(t) + R(t)$
- Adding the model equations we obtain

$$\frac{dN}{dt} = (b - d)N - \alpha I$$

- In order to work with state variables that add up to one, we introduce the following variables

$$s = S/N, \;\; e = E/N, \;\; i = I/N, \;\; r = R/N$$

- Now

$$s + e + i + r = 1.$$

- The model equations become

$$
\begin{aligned}
\frac{ds}{dt} &= b - bs - \lambda is + \alpha is \\
\frac{de}{dt} &= \lambda is - (\epsilon + b)e + \alpha ie \\
\frac{di}{dt} &= \epsilon e - (\gamma + \alpha + b)i + \alpha i^2 \\
\frac{dr}{dt} &= \gamma i - br + \alpha ir
\end{aligned}
$$

- Note that r does not appear in the first three equations. This allows us to omit the equation for r
- We study the subsystem

$$\begin{aligned}
\frac{ds}{dt} &= b - bs - \lambda is + \alpha is \\
\frac{de}{dt} &= \lambda is - (\epsilon + b)e + \alpha ie \\
\frac{di}{dt} &= \epsilon e - (\gamma + \alpha + b)i + \alpha i^2
\end{aligned}$$

$$\epsilon + b$$

- From biological considerations, we can study this disease in the closed set

$$\Gamma = \left\{(s, e, i) \in \mathbf{R}_{+}^{3} | \mathbf{0} \leq \mathbf{s} + \mathbf{e} + \mathbf{i} \leq \mathbf{1}\right\}$$

- We can show that Γ is positively invariant with respect to the reduced model
- The reduced model has a disease free equilibrium at $P_0 = (1,\ 0,\ 0)$
- First, we find the reproduction number of the reduced matrix

$$(\gamma + \alpha + b)(\epsilon + b)$$

- The Jacobian matrix of the reduced matrix at P_0 is

$$J(P_0) = \begin{pmatrix} -(\epsilon + b) & \lambda \\ \epsilon & -(\gamma + \alpha + b) \end{pmatrix}$$

- The Eigenvalues of this matrix are obtained from

$$\sigma^2 + ((\gamma+\alpha+b)+(\epsilon+b))\sigma + (\gamma+\alpha+b)(\epsilon+b) - \epsilon\lambda = 0$$

- The Eigenvalues are

$$\begin{aligned}
\sigma &= -(\lambda + \alpha\epsilon + 2b) \\
&\pm \; sqt(\lambda + \alpha\epsilon + 2b) - 4\left((\gamma + \alpha + b)(\epsilon + b) - \epsilon\lambda\right) \\
&= -(\lambda + \alpha\epsilon + 2b) \\
&\pm \; sqt(\lambda + \alpha\epsilon + 2b) - 4(\gamma + \alpha + b)(\epsilon + b)\left(1 - R_0\right) \\
&> 0 \qquad\qquad \text{for} \quad R_0 < 1.
\end{aligned}$$

- The disease free equilibrium point P_0 is locally stable for $R_0 < 1$.

- We can use the Lyapunov function L to prove global stability where

$$L = \epsilon e + (\epsilon + b)i$$

- Global stability of P_0 in Γ when $R_0 < 1$ precludes the existence of equilibria other than P_0.
- The study of endemic equilibria is restricted to the case $\sigma > 1$.
- We cannot determine the coordinates of the endemic equilibrium point. One can use compound matrices to prove the local stability of this point.

- The Jacobian matrix at the point $P = (s, e, i)$ is

$$J(P) = \begin{pmatrix} -b - \lambda i + \alpha i & 0 & -\lambda s + \alpha s \\ \lambda i & -(\epsilon + b) + \alpha i & \lambda s + \alpha s \\ 0 & \epsilon & M \end{pmatrix}$$

$$M = -(\gamma + \alpha + b) + 2\alpha i$$

- We shall prove the following result
- Lemma: Let A be an $m \times m$ matrix with real entries. For A to be stable, it is necessary and sufficient that
  1. The second compound matrix $A^{[2]}$ is stable
  2. $(-1)^m det(A) > 0$

- We want to prove that the endemic equilibrium point is asymptotically stable if $R_0 > 1$
- Let $A = (a_{ij})$ for $m = 3$ the second compound matrix is given by

$$\begin{pmatrix} a_{11} + a_{22} & a_{23} & -a_{13} \\ a_{32} & a_{11} + a_{33} & a_{12} \\ -a_{31} & a_{21} & a_{22} + a_{33} \end{pmatrix}$$

- The Jacobian matrix $J^{[2]}(P)$ is

$$J(P) = \begin{pmatrix} -2b - \lambda i + 2\alpha i & \lambda s + \alpha e & N1 \\ \epsilon & N2 & 0 \\ 0 & \lambda i & N3 \end{pmatrix}$$

$$N1 = \lambda s - \alpha s$$

$$N2 = -2b - \lambda i - \gamma - \alpha + 3\alpha i$$

$$N3 = -2b - \epsilon - \gamma - \alpha + 3\alpha i$$

- For $P^* = (s^*, e^*, i^*)$ and the diagonal matrix $D = diag(i^*, e^*, s^*)$, the matrix $J^{[2]}(P^*)$ is similar to $DJ^{[2]}(P^*)D^{-1}$

$$\begin{pmatrix} -2b - \lambda i^* - \epsilon + 2\alpha i^* & M2 & \lambda i^* - \alpha i^* \\ \frac{\epsilon e^*}{i^*} & M3 & 0 \\ 0 & \frac{\lambda i^* s^*}{e^*} & M4 \end{pmatrix}$$

$$M2 = \frac{\lambda i^* s^*}{e^*} + \alpha i^*$$

$$M3 = -2b - \lambda i^* - \alpha - \gamma + 3\alpha i^*$$

$$M4 = -2b - \epsilon - \gamma - \alpha + 3\alpha i^*$$

- The matrix $J^{[2]}(P)$ is stable if and only if $DJ^{[2]}(P^*)D^{-1}$ is stable
- Since the diagonal elements of the matrix $DJ^{[2]}(P^*)D^{-1}$ are negative, we can use the argument that the matrix $DJ^{[2]}(P^*)D^{-1}$ if it is diagonally dominant.
- The diagonal sums are given by

$$\begin{aligned} g_1 &= -2b - \epsilon + 2\alpha i^* + 2\frac{\lambda i^* s^*}{e^*} \\ g_2 &= -2b - \lambda i^* - \gamma - \alpha + 3\alpha i^* + \frac{\epsilon e^*}{i^*} \\ g_3 &= -2b - \epsilon - \gamma - \alpha + 3\alpha I^* + \frac{\lambda i^* s^*}{e^*} \end{aligned}$$

- From the left hand side of the reduced model (at the DFE) we have the following relations

$$\begin{aligned}
\frac{b}{s^*} &= b + \lambda i^* - \alpha i^* \\
\frac{\lambda i^* s^*}{e^*} &= (\epsilon + b) - \alpha i^* \\
\frac{\lambda i^* s^*}{e^*} & \\
\frac{\epsilon e^*}{i^*} &= \lambda + \alpha + b - \alpha i^*
\end{aligned}$$

- Substituting these relations we obtain

$$\mu = max{-b + \alpha i^*,\ -b - \lambda i^* + 2\alpha i^*,\ -b - \gamma - \alpha + 2\alpha i^*}$$

- Using the relation $\lambda < \alpha$ we have $\mu < 0$ which implies the diagonal dominance as claimed.
- It is easy to show that

$$\begin{aligned} \det(J(P^*)) &= -\lambda b\epsilon(1-s^*) + \lambda b i^* \left(\frac{\alpha i^*}{e^*}\right) + \left(\frac{b\alpha\epsilon e^*}{s^*}\right) \\ &= -\lambda b\epsilon(1-s^*) + \lambda b i^* \left(\frac{\alpha i^*}{e^*}\right) + \lambda b\epsilon e^* \left(\frac{\alpha}{\lambda s^*}\right) \\ &\leq -\lambda b\epsilon(1-s^*-i^*-e^*) < 0. \end{aligned}$$

- We shall use the following variables to describe the dynamics of a simple HIV/AIDS model

$$
\begin{aligned}
S(t) &= \text{Susceptible individuals} \\
I(t) &= \text{Infected individuals} \\
A(t) &= \text{Individuals who have developed AIDS}
\end{aligned}
$$

- We want to use this technique to determine the stability of the following simple HIV/AIDS model

$$\begin{aligned}\frac{dS}{dt} &= \Pi - \mu S - \beta_1 SI - \beta_2 SA\\ \frac{dI}{dt} &= \beta_1 SI + \beta_2 SA - (\alpha + \mu)I\\ \frac{dA}{d}t &= \alpha I - (d + \mu)A\end{aligned}$$

- Include treatment for AIDS patients and repeat the analysis.
- Modify the model to include (i) differential susceptibility (ii) differential infectivity