Analysis of an SEIR model with Non-Constant Population

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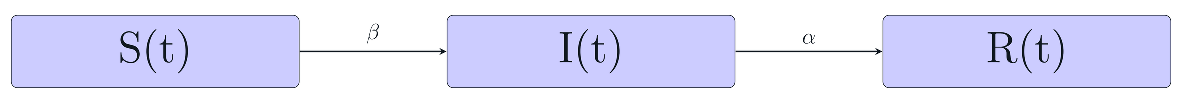
Introduction

- Epidemiology: a subject that studies the patterns of diseases and health related factors among the human population.
- We are particularly focused on the spread of infectious diseases.
- Mathematical modeling: a description of a system using mathematical tools and language.
- Mathematical models can be used to better understand the behavior of a disease and to study the relationships among its components.
- Reproduction number ($\mathcal{R}_0$): the number of secondary cases one infectious individual will produce in a population consisting only of susceptible individuals during its infectious period [1]

Basic SIR Model

- The SIR epidemic model created by Kermack and McKendrick serves as a good introduction to epidemic modeling[1].
- In this model, the total population N(t) is described as the sum of three non-intersecting classes: the susceptible class: S(t), the infected class: I(t), and the recovered class: R(t).

$$N(t) = S(t) + I(t) + R(t)$$



Incidence

- It is common to assume that the rate of infection is proportional to the product of the number of susceptible people and the number of infectious people.
- We define incidence as the number of individuals becoming infected per unit time.
- We can then describe incidence as βSI, where β is a transmission rate constant.
- As individuals become infected, they move out of the susceptible class and into the infected class.
- Therefore,

$$S'(t) = -\text{incidence} = -\beta SI$$

Adding Recovery Rate

- Using a similar approach, we define α as the rate of individuals who are recovering per unit time.
- Therefore, the number of people in the infectious class is changing by $+\beta SI$ and $-\alpha I$.

$$I'(t) = \beta SI - \alpha I$$

- The recovered class is changing by $+\alpha$I

$$R'(t) = \alpha I$$

We can then define a basic differential model.

$$\begin{aligned} S'(t) &= -\beta IS, \\ I'(t) &= \beta IS - \alpha I, \\ R'(t) &= \alpha I \end{aligned}$$

Adding the equations above, we get:

$$N'(t) = S'(t) + I'(t) + R'(t) = 0$$

Notice $N(t)$ is constant.

SEIR Model

- We chose to work with an SEIR model. This model incorporates another variable, the exposed class.

$$N(t) = S(t) + E(t) + I(t) + R(t)$$

- The exposed class allows us to account for individuals who come into contact with infected people, but they themselves may not be infected.

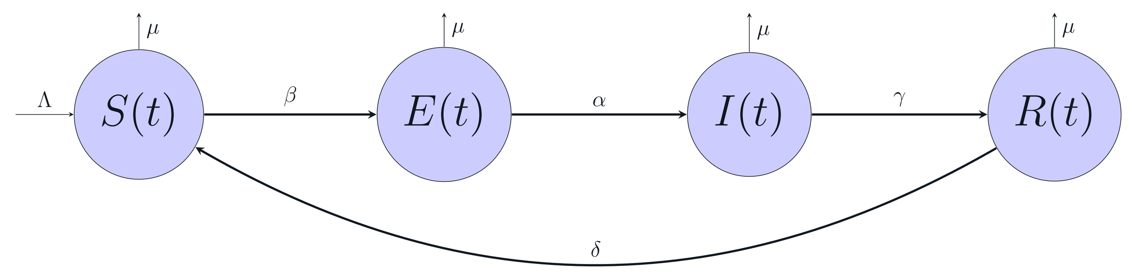
State variables:

- $S(t)$: Number of susceptible individuals at time t
- $E(t)$: Number of exposed individuals at time t
- $I(t)$: Number of infectious individuals at time t
- $R(t)$: Number of recovered individuals at time t

Parameters:

- Λ: Birth rate
- β: Exposure rate
- γ: Recovery rate
- μ: Natural death rate
- δ: Re-susceptibility rate

Our Model Flowchart



Differential Equation Model [2]

$$\begin{cases} S'(t) &= \Lambda - \beta SI - \mu S + \delta R \\ E'(t) &= \beta SI - \alpha E - \mu E \\ I'(t) &= \alpha E - \gamma I - \mu I \\ R'(t) &= \gamma I - \mu R - \delta R \end{cases} \tag{1}$$

Adding the equations, we get:

$$N'(t) = \Lambda - \mu N$$

Note: unlike the SIR model from before, in this SEIR model, $N(t)$ is not constant.

Equilibrium

- The time-independent solutions to a differential equation model with constant coefficients are called equilibrium points.
- These can be determined by setting $S'(t) = E'(t) = I'(t) = R'(t) = 0$. Thus, our equilibrium model is

$$\begin{cases} \Lambda - \beta S^* I^* - \mu S^* + \delta R^* &= 0 \\ \beta S^* I^* - \alpha E^* - \mu E^* &= 0 \\ \alpha E^* - \gamma I^* - \mu I^* &= 0 \\ \gamma I^* - \mu R^* - \delta R^* &= 0 \end{cases} \tag{2}$$

- The system will have two solutions when $I^* = 0$ or $I^* \neq 0$.
- Where $I^* = 0$ the equilibrium is disease free, and it occurs when the disease is not present within the population.
- Where $I^* \neq 0$ the equilibrium is endemic, and it occurs when the disease is present.

Equilibrium of our Model

- We now want to determine the equilibrium of our model.
- For Disease Free Equilibrium (DFE), we let $I^* = 0$, which gives: $E^* = 0$, $R^* = 0$, and $S^* = \frac{\Lambda}{\mu}$. Thus, DFE for our model is $\mathcal{E}^* = (S^*, E^*, I^*, R^*) = (\frac{\Lambda}{\mu}, 0, 0, 0)$
- For Endemic Equilibrium (EE) we let $I^* \neq 0$. Hence, EE for the model is: $\mathcal{E}^* = (S^*, E^*, I^*, R^*)$ where:

$$S^* = \frac{\Lambda\mu + \Lambda\delta + \delta\gamma I^*}{\mu^2 + \beta I^* \mu + \delta\beta I^* + \delta\mu},$$

$$E^* = \frac{\beta I^* (\Lambda\mu + \Lambda\delta + \delta\gamma I^*)}{(\alpha + \mu)(\mu^2 + \beta I^* \mu + \delta\beta I^* + \delta\mu)},$$

$$R^* = \frac{\delta I^*}{\mu + \delta}$$

Linearization

- Stability of a nonlinear system can often be inferred from the stability of a corresponding linear system obtained through the process of linearization.
- We consider a point close to our equilibrium point (S^*, E^*, I^*, R^*) with small perturbations $a(t), b(t), c(t)$, and $d(t)$

$$a(t) = S(t) - S^*$$
$$b(t) = E(t) - E^*$$
$$c(t) = I(t) - I^*$$
$$d(t) = R(t) - R^*$$

Plugging in (1):

$$\begin{aligned} a'(t) &= \Lambda - \beta(a + S^*)(c + I^*) - \mu(a + S^*) + \delta(d + R^*) \\ b'(t) &= \beta(a + S^*)(c + I^*) - \alpha(b + E^*) - \mu(b + E^*) \\ c'(t) &= \alpha(b + E^*) - \gamma(c + I^*) - \mu(c + I^*) \\ d'(t) &= \gamma(c + I^*) - \mu(d + R^*) - \delta(d + R^*) \end{aligned}$$

Simplifying:

$$\begin{aligned} a'(t) &= -\beta a I^* - \beta S^* c - \mu a + \delta d \\ b'(t) &= \beta a I^* + \beta S^* c - \alpha b - \mu b \\ c'(t) &= \alpha b - \gamma c - \mu c \\ d'(t) &= \gamma c - \mu d - \delta d \end{aligned}$$

The solutions to the previous system are of the form:

$$a(t) = \overline{a} e^{\lambda t},\ b(t) = \overline{b} e^{\lambda t},\ c(t) = \overline{c} e^{\lambda t},\ d(t) = \overline{d} e^{\lambda t}$$

Where λ is our eigenvalue.

Plugging these in:

$$\begin{aligned} \overline{a}\lambda e^{\lambda t} &= -\beta \overline{a} e^{\lambda t} I^* - \beta S^* \overline{c} e^{\lambda t} - \mu \overline{a} e^{\lambda t} + \delta \overline{d} \\ \overline{b}\lambda e^{\lambda t} &= \beta \overline{a} e^{\lambda t} I^* + \beta S^* \overline{c} e^{\lambda t} - \alpha \overline{b} e^{\lambda t} - \mu \overline{b} e^{\lambda t} \\ \overline{c}\lambda e^{\lambda t} &= \alpha \overline{b} e^{\lambda t} - \gamma \overline{c} e^{\lambda t} - \mu \overline{c} e^{\lambda t} \\ \overline{d}\lambda e^{\lambda t} &= \gamma \overline{c} e^{\lambda t} - \mu \overline{d} e^{\lambda t} - \delta \overline{d} e^{\lambda t} \end{aligned}$$

Canceling $e^{\lambda t}$:

$$\begin{aligned} \overline{a}\lambda &= -\beta \overline{a} I^* - \beta S^* \overline{c} - \mu \overline{a} + \delta \overline{d} \\ \overline{b}\lambda &= \beta \overline{a} I^* + \beta S^* \overline{c} - \alpha \overline{b} - \mu \overline{b} \\ \overline{c}\lambda &= \alpha \overline{b} - \gamma \overline{c} - \mu \overline{c} \\ \overline{d}\lambda &= \gamma \overline{c} - \mu \overline{d} - \delta \overline{d} \end{aligned}$$

Rearranging:

$$\begin{cases} (\lambda + \beta I^* + \mu)\overline{a} + (\beta S^*)\overline{c} - (\delta)\overline{d} &= 0 \\ (\lambda + \alpha + \mu)\overline{b} - (\beta I^*)\overline{a} - (\beta S^*)\overline{c} &= 0 \\ (-\alpha)\overline{b} + (\lambda + \gamma + \mu)\overline{c} &= 0 \\ (-\gamma)\overline{c} + (\lambda + \mu + \delta)\overline{d} &= 0 \end{cases} \tag{3}$$

Plugging in Disease Free Equilibrium

- We substititute $S^* = \frac{\Lambda}{\mu}$, $E^* = 0$, $I^* = 0$, $R^* = 0$ into system (3):

$$\begin{cases} (\lambda + \mu)\overline{a} - (\frac{\beta\Lambda}{\mu})\overline{c} - (\delta)\overline{d} &= 0 \\ (\lambda + \alpha + \mu)\overline{b} - (\frac{\beta\Lambda}{\mu})\overline{c} &= 0 \\ (-\alpha)\overline{b} + (\lambda + \gamma + \mu)\overline{c} &= 0 \\ (-\gamma)\overline{c} + (\lambda + \mu + \delta)\overline{d} &= 0 \end{cases} \tag{4}$$

In order for system (4) to have a non-zero solution, we need the following:

$$\begin{vmatrix} (\lambda + \mu) & 0 & -\frac{\beta\Lambda}{\mu} & -\delta \\ 0 & (\lambda + \alpha + \mu) & \frac{-\beta\Lambda}{\mu} & 0 \\ 0 & -\alpha & (\lambda + \gamma + \mu) & 0 \\ 0 & 0 & -\gamma & (\lambda + \mu + \delta) \end{vmatrix} = 0$$

$$(\lambda + \mu)(\lambda + \mu + \delta)[\lambda^2 + \lambda(\gamma + \alpha + 2\mu) + (\alpha + \mu)(\gamma + \mu) - \frac{\beta\Lambda\alpha}{\mu}] = 0 \tag{5}$$

Equation (5) is the characteristic equation.

Theorem 1 ([2]). *A necessary and sufficient condition for an equilibrium to be locally asymptotically stable is that all eigenvalues of the Jacobian have negative real part.*

So for our disease-free equilibrium to be stable we must have all $\lambda < 0$:

We solve the first two terms for λ in (5):

$$\lambda = -\mu$$
$$\lambda = -\mu - \delta$$

Solving the quadratic term:

$$\lambda^2 + \lambda(\gamma + \alpha + 2\mu) + (\alpha + \mu)(\gamma + \mu) - \frac{\beta\Lambda\alpha}{\mu} = 0$$

Using the quadratic formula:

$$\lambda = \frac{-(\gamma + \alpha + 2\mu) \pm \sqrt{(\gamma + \alpha + 2\mu)^2 - 4[(\mu + \alpha)(\gamma + \mu) - \frac{\beta\Lambda\alpha}{\mu}]}}{2}$$

Case 1: taking negative sign

$$\lambda = \frac{-(\gamma + \alpha + 2\mu) - \sqrt{(\gamma + \alpha + 2\mu)^2 - 4[(\mu + \alpha)(\lambda + \mu) - \frac{\beta\Lambda\alpha}{\mu}]}}{2}$$

We can clearly see that in this case λ will be negative.

Case 2: taking positive sign

$$\lambda = \frac{-(\gamma + \alpha + 2\mu) + \sqrt{(\gamma + \alpha + 2\mu)^2 - 4[(\mu + \alpha)(\gamma + \mu) - \frac{\beta\Lambda\alpha}{\mu}]}}{2}$$

We can see, if $(\mu + \alpha)(\gamma + \mu) - \frac{\beta\Lambda\alpha}{\mu} > 0$, then lambda will be negative.

Using this condition, we rearrange:

$$(\mu + \alpha)(\gamma + \mu) - \frac{\beta\Lambda\alpha}{\mu} > 0 \Leftrightarrow (\mu + \alpha)(\gamma + \mu) > \frac{\beta\Lambda\alpha}{\mu} \Leftrightarrow 1 > \frac{\beta\Lambda\alpha}{\mu(\mu + \alpha)(\mu + \gamma)}$$

We denote $\frac{\beta\Lambda\alpha}{\mu(\mu+\alpha)(\mu+\gamma)}$ by $\mathcal{R}_0$

Reproduction Number

Theorem 2. *The disease-free equilibrium for the model is stable if and only if $\mathcal{R}_0 < 1$. It is unstable whenever $\mathcal{R}_0 > 1$*

Our $\mathcal{R}_0$: $\frac{\beta\Lambda\alpha}{\mu(\mu+\alpha)(\mu+\gamma)}$

Application and Future Work

- In the future, we plan to work on analyzing the stability of endemic equilibrium.
- We want to consider a more complex model to account for greater intricacies.
- We want to try fitting real-world data to our model to analyze its accuracy for different diseases.

References

References

[1] W.O. Kermack and A.G. McKendrick, A contribution to mathematical theory of epidemics, *Proc. Roy. Soc. Lond. A*, **115** (1927), 700-721

[2] Maia Martcheva An Introduction to Mathematical Epidemiology, *Texts in Applied Mathematics* , **61**(2015),50-64