Basic methods for setting up models: Differential Equations

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LSHTM

Objectives

- By the end of this lecture you should
  - understand how models of the transmission dynamics of an infection are set up using *differential* equations
  - be able to write down *differential* equations to describe the transmission dynamics of an infection
  - understand the relationship between difference and differential equations
  - understand the key input parameters which go into differential equations

Difference equation model of measles

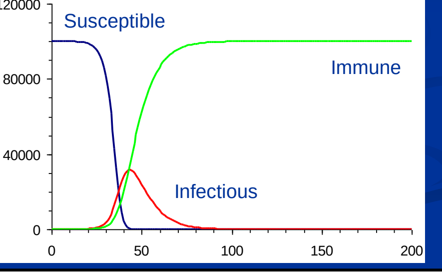
Susceptible S_t $\xrightarrow{\lambda_t}$ *Pre infEctious E_t* $\xrightarrow{f}$ *Infectious I_t* $\xrightarrow{r}$ *Recovered R_t*

$$S_{t+1} = S_t - \lambda_t * S_t$$
$$E_{t+1} = E_t + \lambda_t * S_t - f * E_t$$
$$I_{t+1} = I_t + f * E_t - r * I_t$$
$$R_{t+1} = R_t + r * I_t$$

Where $\lambda_t = \beta * I_t$

This enabled us to make predictions for the evolution of the epidemic over time

Difference equation model of measles

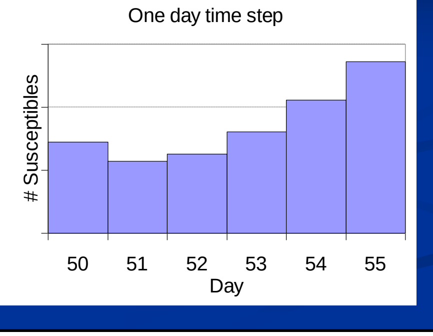


Model prediction using a <u>one</u> day timestep

Day	Number of individuals who are:		
	Susceptible	Infectious	Newly infected by the end of the current time step ($\beta \times S_t \times I_t$)
50	9.45	24044	4.22
51	9.14	22381	3.80
52	9.26	20735	3.56
53	9.61	19131	3.41
54	10.11	17586	3.30
55	10.72	16114	3.21

$\beta = 1.86 \times 10^{-5}$ *per day*

Model prediction using a <u>one</u> day timestep

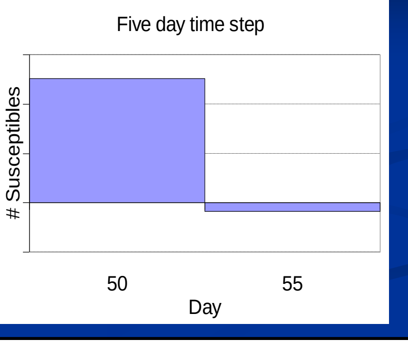


Model prediction using a five day timestep

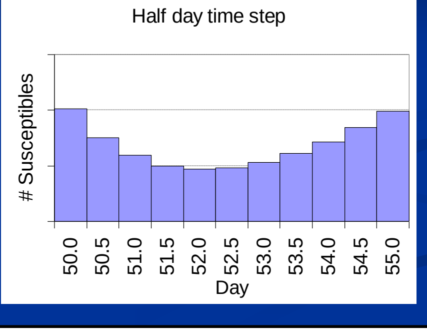
Day	Number of individuals who are:		
	Susceptible	Infectious	Newly infected by the end of the current time step ($\beta \times S_t \times I_t$)
50	50387	11530	53948
55	-3551	24265	-8002

$\beta = 9.29 \times 10^{-5}$ per 5 days

Model prediction using a five day timestep



Model prediction using a half day timestep



Conclusion

- The highest precision is obtained when we use time steps that are as small as possible
- i.e. we update our model *continuously*, rather at set intervals (eg. every day)
- We can do this using *differential* equations

Differential equations

- *Differential* equations are very similar to the *difference* equations you have seen
- *Difference* equations described the total number of individuals in each category at time *t*
- *Differential* equations describe the *rate of change of the number* of individuals in each category at time *t*

... equations

The *number* of susceptibles at time (assumed constant between t and t+1)

't' in brackets (t) to show we assume time flows continuously

...ential equati...

The *rate of change in the number* of susceptibles at time t

Difference	Differential
$S_{t+1} = S_t - \lambda_t S_t$	$\frac{dS(t)}{dt} = -\lambda(t)S(t)$
$E_{t+1} = E_t + \lambda_t S_t - fE_t$	$\frac{dE(t)}{dt} = \lambda(t)S(t) - fE(t)$
$I_{t+1} = I_t + f E$ ... I_t	$\frac{dI(t)}{dt} = fE(t)$ ...
	$\frac{dR(t)}{dt} =$ ...

The *risk* of susceptibles becoming pre-infectious between t and t+1

The *rate* at which susceptibles become pre-infectious per unit time, at time t

(1) Intuitive explanation of differential equations

- *Rate of change* in the number of individuals in a given category over time is given by:

  The number who ***enter*** the category per unit time

  - the number who ***exit*** the category per unit time

The *rate of change* in the number of susceptible individuals over time

$\lambda(t)$ f r

S(t) → E(t) → I(t) → R(t)

$\frac{dS(t)}{dt}$ = 0 - the number of susceptible individuals who become pre-infectious per unit time

= - the force of infection $\lambda(t)$ times the number of susceptible individuals $S(t)$

$$\frac{dS(t)}{dt} = -\lambda(t) * S(t)$$

The *rate of change* in the number of pre-infectious individuals over time

$\lambda(t)$ f r

S(t) → E(t) → I(t) → R(t)

$\frac{dE(t)}{dt}$ = + the number of susceptible individuals who become pre-infectious per unit time

- the number of pre-infectious individuals who become infectious per unit time

$$\frac{dE(t)}{dt} = \lambda(t) * S(t) \; - f * E(t)$$

Differential equations for our measles model

$\lambda(t)$ f r

S(t) → E(t) → I(t) → R(t)

The same can be done for the rate of change in the number infectious dI(t)/dt, and the number immune dR(t)/dt

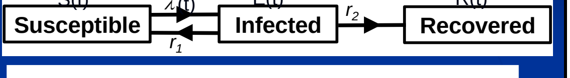
$$\frac{dS(t)}{dt} = -\lambda(t)S(t)$$

$$\frac{dE(t)}{dt} = \lambda(t)S(t) - fE(t)$$

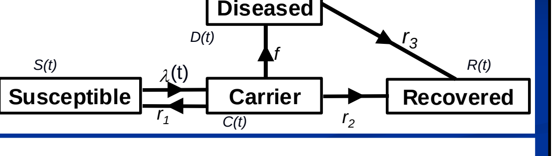
$$\frac{dI(t)}{dt} = fE(t) - rI(t)$$

$$\frac{dR(t)}{dt} = rI(t)$$

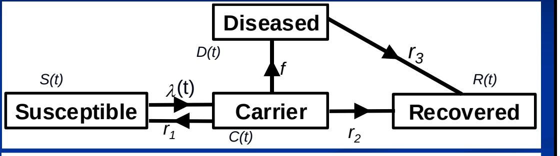
Differential equations for Hookworm



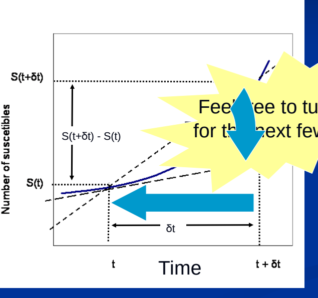
Differential equations for Haemophilus Influenza type B (HiB)



Differential equations for Haemophilus Influenza type B

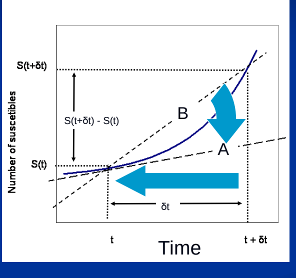


(2) More mathematical explanation of differential equations



- The *rate of change* in the number of ceptibles at time t is dient of line A
- equal to the gradient of line B as the size of the time step (δt) becomes very small
- IE as the gradient of line B tends to the gradient of line A

More mathematical explanation of differential equations

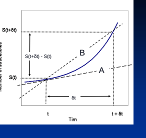


This can be written down as

$$\frac{dS(t)}{dt} = \frac{S(t+\delta t) - S(t)}{\delta t} \qquad (1)$$

as $\delta t \rightarrow 0$

More mathematical explanation of differential equations



$$\frac{dS(t)}{dt} = \frac{S(t+\delta t) - S(t)}{\delta t} \quad \text{as } \delta t \rightarrow 0$$

- But we need an equation that predicts dS(t)/dt in terms of other parameters that we can estimate such as *λ(t)* (incidence), not by measuring the change in the number of susceptibles directly
- This can be derived using a similar logic to that used to derive the difference equations

More mathematical explanation of differential equations

- The number of susceptibles at time t+δt is

S(t+δt) = the number of susceptibles at time t, S(t) (2)
- the number infected between time t and t+ δt

- When the size of the time step is sufficiently small, the number of susceptible individuals who are infected between *t* and *t+δt* is the number infected per unit time multiplied by the size of the time step ie

$$S(t+\delta t) = S(t) - \lambda(t)S(t)\delta t$$

More mathematical explanation of differential equations

$$S(t+\delta t) = S(t) - \lambda(t)S(t)\delta t$$

- If we subtract S(t) from both sides, we get

$$S(t+\delta t) - S(t) = -\lambda(t)S(t)\delta t$$

- Dividing both sides of the equation by *δt*, we have

$$\frac{S(t+\delta t) - S(t)}{\delta t} = -\lambda(t)S(t) \qquad (3)$$

More mathematical explanation of differential equations

$$\frac{S(t+\delta t) - S(t)}{\delta t} = -\lambda(t)S(t) \qquad (3)$$

- Equation (1) told us that if δt is taken to be infinitesimally small, then :

$$\frac{dS(t)}{dt} = \frac{S(t+\delta t) - S(t)}{\delta t} \quad \text{as } \delta t \to 0 \qquad (1)$$

- We can see that

$$\frac{dS(t)}{dt} = \frac{S(t+\delta t) - S(t)}{\delta t} = -\lambda(t)S(t)$$

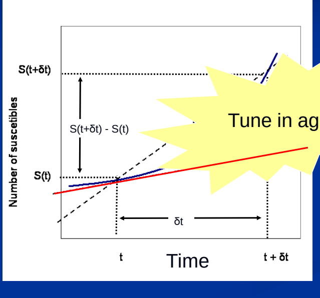
More mathematical explanation of differential equations

$$\frac{dS(t)}{dt} = \frac{S(t+\delta t) - S(t)}{\delta t} = -\lambda(t)S(t)$$

- Therefore, the *rate of change in the number of susceptibles* at time t is

$$\frac{dS(t)}{dt} = -\lambda(t)S(t)$$

More mathematical explanation of differential equations



To summarise:

•The *rate of change* in ...mber of ...ibles at time t is ...dient of line A

Tune in again

•And that is equal to

$$\frac{dS(t)}{dt} = -\lambda(t)S(t)$$

What model structure is described by these equations?

$$\frac{dS(t)}{dt} = -\lambda(t)S(t) + rI(t)$$
$$\frac{dI(t)}{dt} = +\lambda(t)S(t) - rI(t)$$

And again

$$\frac{dS(t)}{dt} = -\lambda(t)S(t)$$
$$\frac{dI(t)}{dt} = +\lambda(t)S(t) - rI(t)$$
$$\frac{dR(t)}{dt} = +rI(t)$$

And finally…

$$\frac{dS(t)}{dt} = -\lambda(t)S(t) + aR(t)$$
$$\frac{dI(t)}{dt} = +\lambda(t)S(t) - rI(t)$$
$$\frac{dR(t)}{dt} = +rI(t) - aR(t)$$

Solving differential equations

- We can do the same for dE/dt, dI/dt and dR/dt
- Which gives us a set of differential equations which describe the *rate of change* over time:

$$\frac{dS(t)}{dt} = -\lambda(t)S(t)$$
$$\frac{dE(t)}{dt} = \lambda(t)S(t) - fE(t)$$
$$\frac{dI(t)}{dt} = fE(t) - rI(t)$$
$$\frac{dR(t)}{dt} = rI(t)$$

But this is often not what we want

We want to predict the *number* of susceptibles (etc) at time t ie:
S(t) = … , E(t) =…, etc

- As for difference equations, we need to solve these equations.
- In this case this means integrating them

Solving differential equations

- There are only a few, simple cases where we can write down the solution to these equations
  - This is called solving the equations *analytically*
- For the rest we solve them *numerically* using a computer package
  - To solve the equations, the computer package converts the differential equations back into difference equations, but then adjusts the results to correct of the errors
- This is what we will do now in the practical using a software package called Berkeley Madonna

Summary

- You should now
  - understand how models of the transmission dynamics of an infection are set up using *differential* equations
  - be able to write down *differential* equations to describe the transmission dynamics of an infection
  - understand the relationship between difference and differential equations

If you only take one thing away

$$S(t) \xrightarrow{\lambda(t)} E(t) \xrightarrow{f} I(t) \xrightarrow{r} R(t)$$

$$\frac{dS(t)}{dt} = -\lambda(t)S(t)$$
$$\frac{dE(t)}{dt} = \lambda(t)S(t) - fE(t)$$
$$\frac{dI(t)}{dt} = fE(t) - rI(t)$$
$$\frac{dR(t)}{dt} = rI(t)$$

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