Mathematical Epidemiology

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Outline

Questions are very welcomed at any point.

Chapters:

1. Mathematical background
2. Intro to epidemic models
3. More epidemic models
4. Bonus section

1. Mathematical Background

What is differentiation?

- Mathematical way of determining **how quickly a function changes as** the independent variable (here it will be **time**) **changes**
- Often process can be phrased in terms of how quickly things change
- Allows us to **find equilibrium** (/stationary) **points** of functions

$$\boxed{\frac{dy(t)}{dt} = \dot{y}(t) = \lim_{\delta t \to 0}\left(\frac{y(t+\delta t)-y(t)}{\delta t}\right)}$$

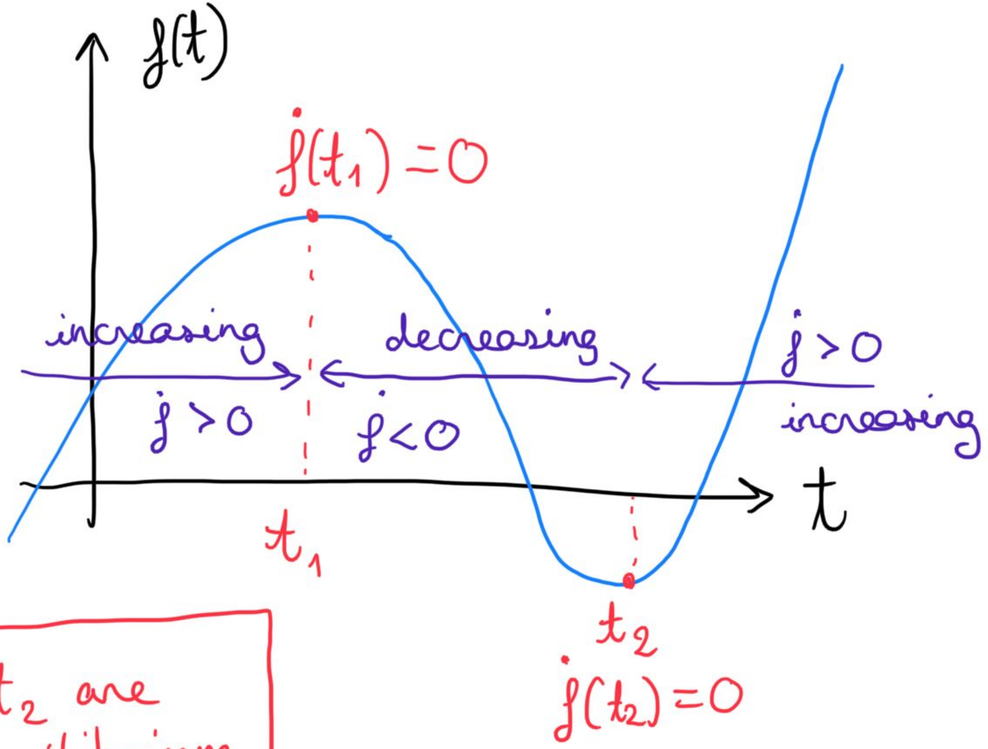
Egs, velocity = derivative of the spatial position, acceleration = derivative of velocity

The sign of a derivative

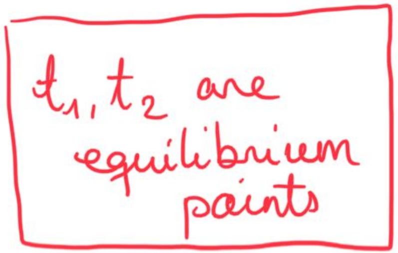
$$\dot{f} > 0 : \text{increasing}$$

$$\dot{f} = 0 : \text{equilibrium}$$

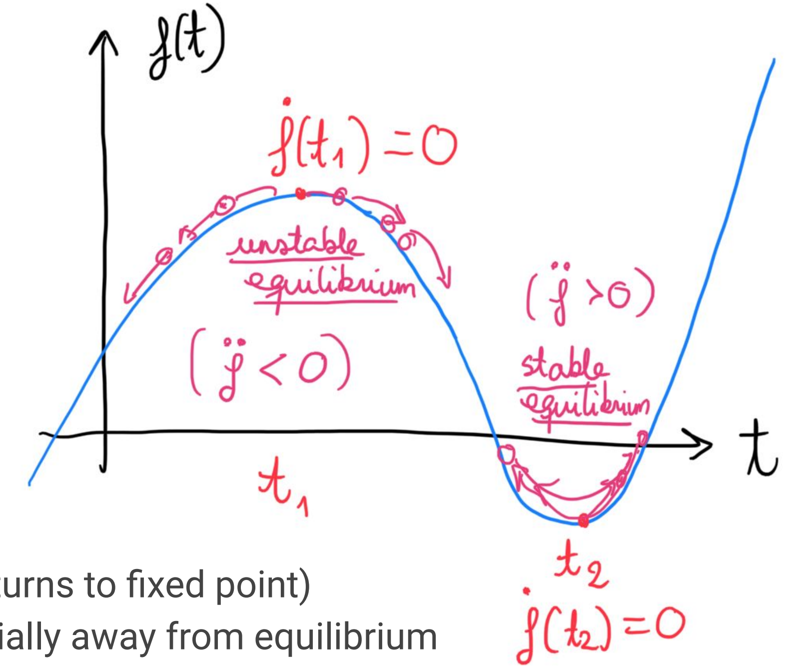
$$\dot{f} < 0 : \text{decreasing}$$



Equilibrium points = fixed points
System doesn't change



Stability Analysis



- If function tends to a **constant value**, that value must be a **fixed point**
- Usually fixed points control **long-term Behaviour**
- Fixed points can be:
    - **Stable**: small perturbations decay (system returns to fixed point)
    - **Unstable:** small perturbations grow exponentially away from equilibrium
- **Stability determined by** looking at second derivative or directly to the behaviour of a **small perturbation**

Differential Equations

Equation relating an (unknown) **function** to its derivatives

$$0 = F(t, Y(t), \dot{Y}(t), \ddot{Y}(t), \ldots)$$

Here we want to **solve for the function Y**
(in normal equations we solve for the independent variable ‘x’ or ‘t’)

Examples: $\dot{Y} = \beta Y \Rightarrow Y(t) = Ae^{\beta t}$

$$m\ddot{x}(t) = -\beta\dot{x}(t) - kx(t)$$

$$\ddot{y} + \dot{y} = \cos\omega t$$

System of Differential Equations

Systems of equations: (solve for x, y numbers)	Systems of differential equations (solve for x(t), y(t) functions)
$x + y = 2$ $x - 2y = 1$	$\dot{y} = x + y$ $\dot{x} = x - y$
$xy = 1$ $x + y^2 = 4$	$\dot{y} = xy^2$ $\dot{x} = y + \sin \omega t$

2. Intro to Epidemic Models

Basic Reproduction Ratio

Expected number of secondary cases generated per primary case in a largely susceptible population.

$$R_0 = \frac{\beta N}{\gamma}$$

transmission rate → β

total population size → N

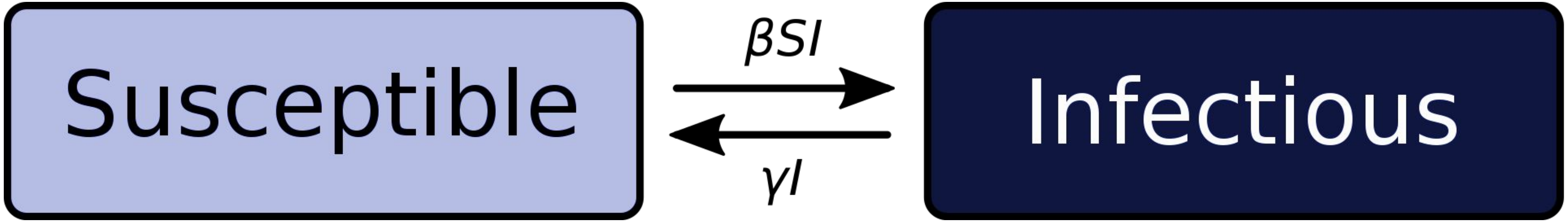
recovery rate → γ

Some Estimated Basic Reproductive Ratios.

Infectious Disease	*Host*	*Estimated R_0*
FIV	Domestic Cats	1.1–1.5
Rabies	Dogs (Kenya)	2.44
Phocine Distemper	Seals	2–3
Tuberculosis	Cattle	2.6
Influenza	Humans	3–4
Foot-and-Mouth Disease	Livestock farms (UK)	3.5–4.5
Smallpox	Humans	3.5–6
Rubella	Humans (UK)	6–7
Chickenpox	Humans (UK)	10–12
Measles	Humans (UK)	16–18
Whooping Cough	Humans (UK)	16–18

Keeling, M.J. and Rohani, P. (2007) *Modeling Infectious Diseases in Humans and Animals*. Princeton University Press.

SIS model



$$\dot{S} = -\beta S I + \gamma I$$

$$\dot{I} = +\beta S I - \gamma I$$

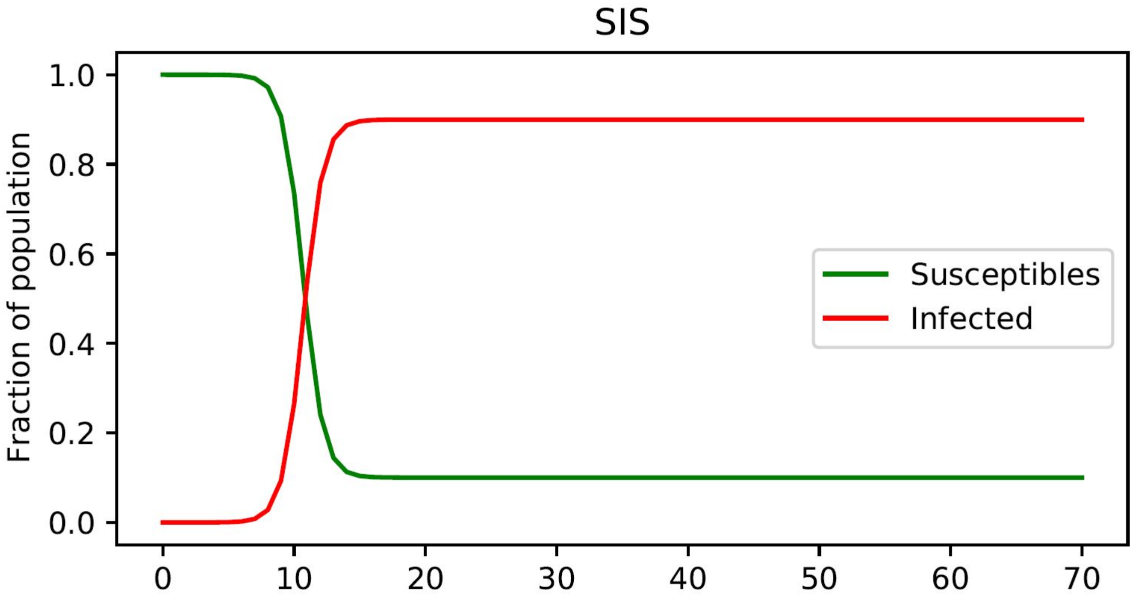
$$S + I = N$$

Individuals do **not gain immunity** to the infection after surviving it.

Common model for **flus**, and most **STIs**.

Exact solution to SIS

$$\dot{I} = +\beta I(N - I) - \gamma I = I(\gamma[R_0 - 1] - \beta I)$$



$$I(t) = \frac{\gamma(R_0 - 1)}{A \exp\left[-\gamma(R_0 - 1)t\right] + \beta}$$

SIR model

$$\dot{S} = -\beta IS$$
$$\dot{I} = +\beta IS - \gamma I$$
$$\dot{R} = +\gamma I$$

$$S + I + R = N \text{ (fixed)}$$

Individuals either:

- **recover** -> **immunity**
- **die**

(both go into the recovered compartment)

Stability analysis

Disease-Free Equilibrium $S^* = N, I^* = 0, R^* = 0$

Small perturbation away from the equilibrium: $S(0) \approx N$

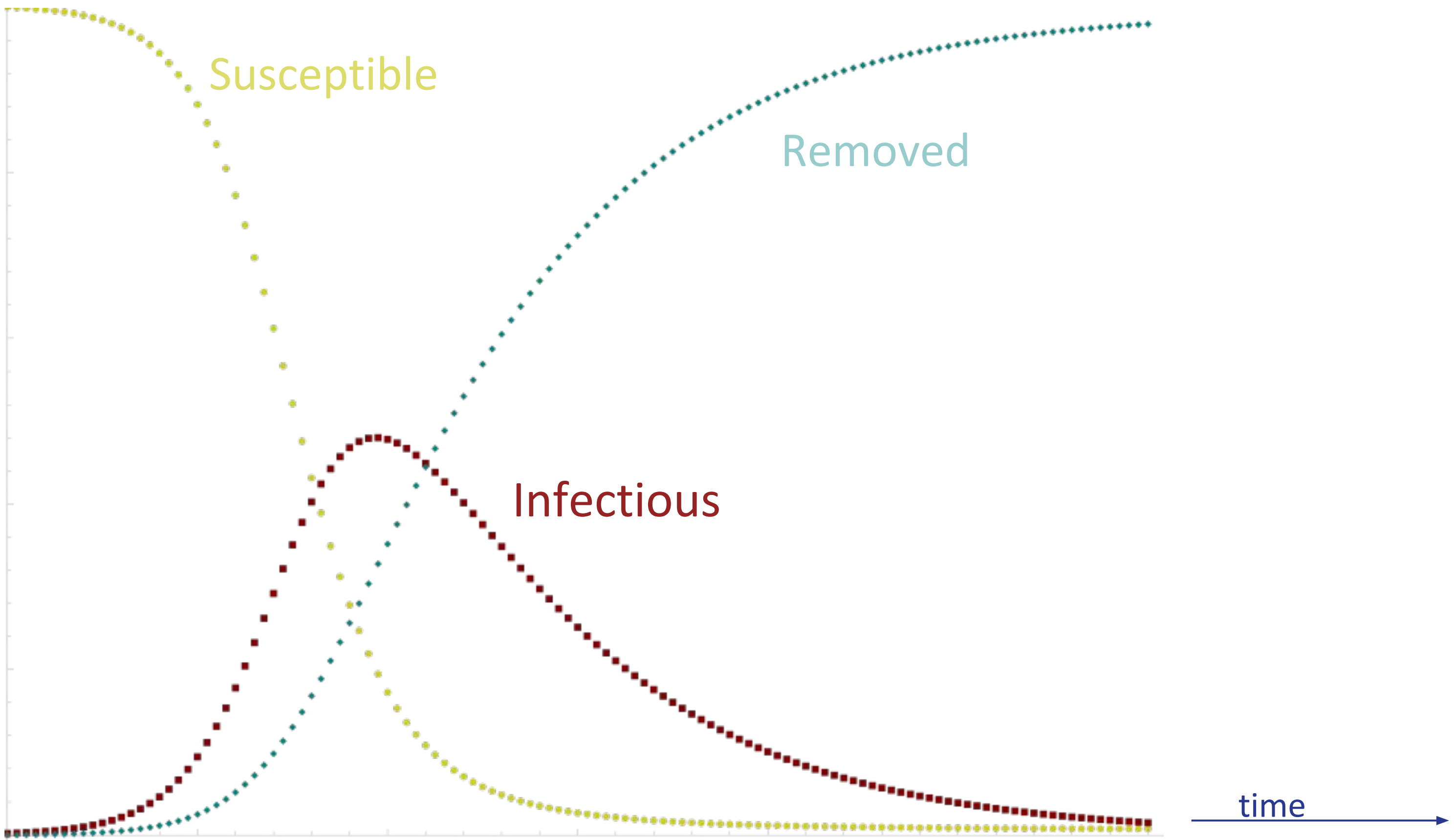
At the early stages of an epidemic:

$$\dot{I}(t) \approx (\beta N - \gamma) I(t) = \gamma (R_0 - 1) I(t)$$

$$R_0 < 1 \Rightarrow \dot{I}(0) < 0 \Rightarrow \text{cases decrease}$$

$$R_0 > 1 \Rightarrow \dot{I}(0) > 0 \Rightarrow \text{cases increase}$$

The epidemic "curve" (for R0>1)



Vaccination (a simple model)

p: proportion of the population that is vaccinated

Modify the standard equations for SIR:

$$\dot{S} = -\beta(1-p)SI$$

$$\dot{I} = +\beta(1-p)SI - \gamma I$$

$$\dot{R} = \gamma I$$

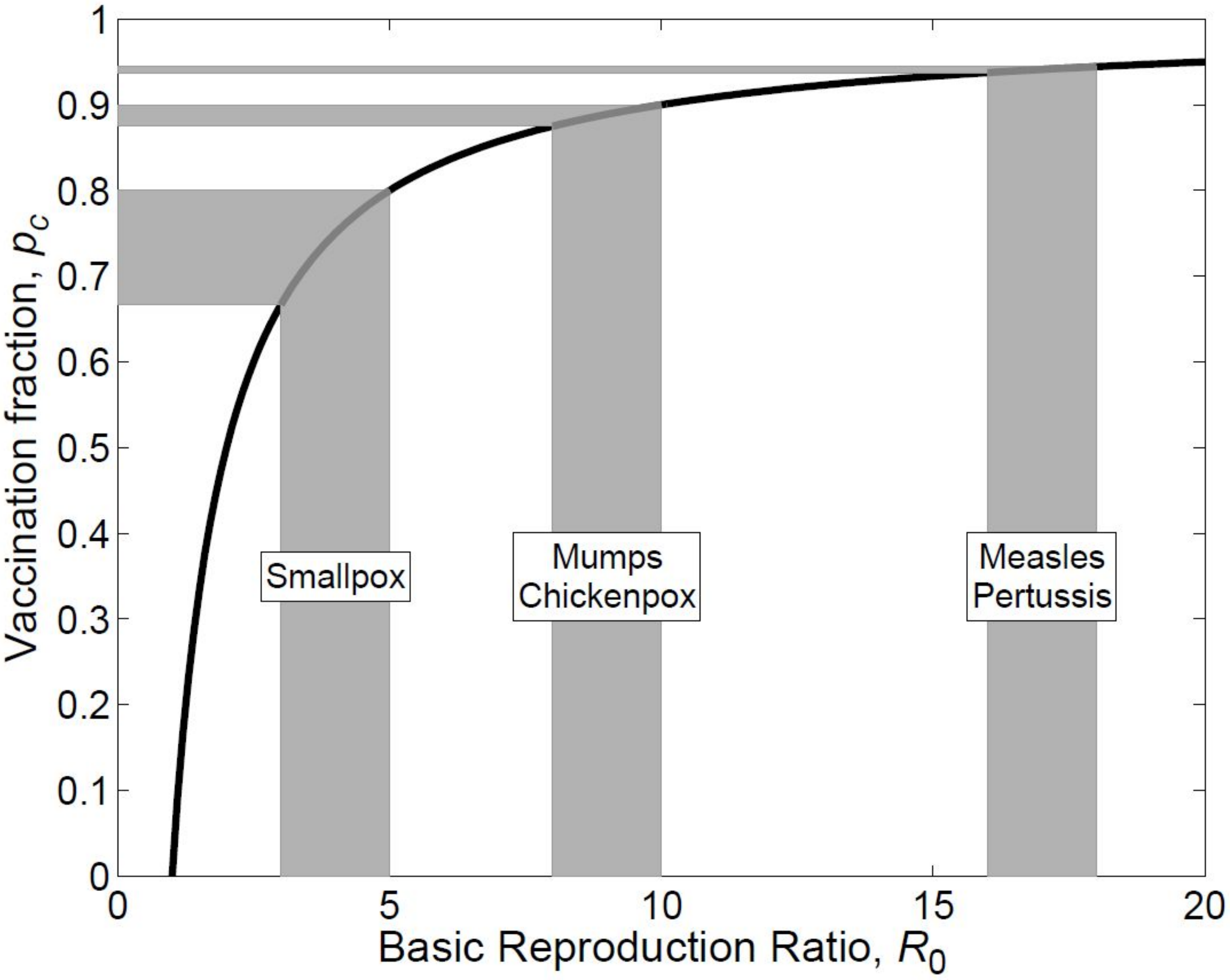
$$S + I + R = N$$

Condition for **no epidemic**:

No vaccination | vaccination

$\beta N < \gamma$ --> $\beta(1-p)N < \gamma$

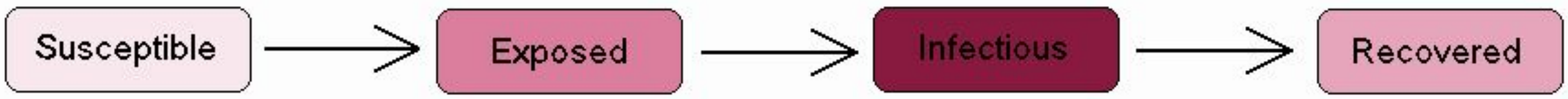
$$\boxed{p > 1 - 1/R_0}$$


Smallpox
Mumps
Chickenpox
Measles
Pertussis
Vaccination fraction, p_c
Basic Reproduction Ratio, R_0
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1
0
5
10
15
20

Break!

3. More Epidemic Models

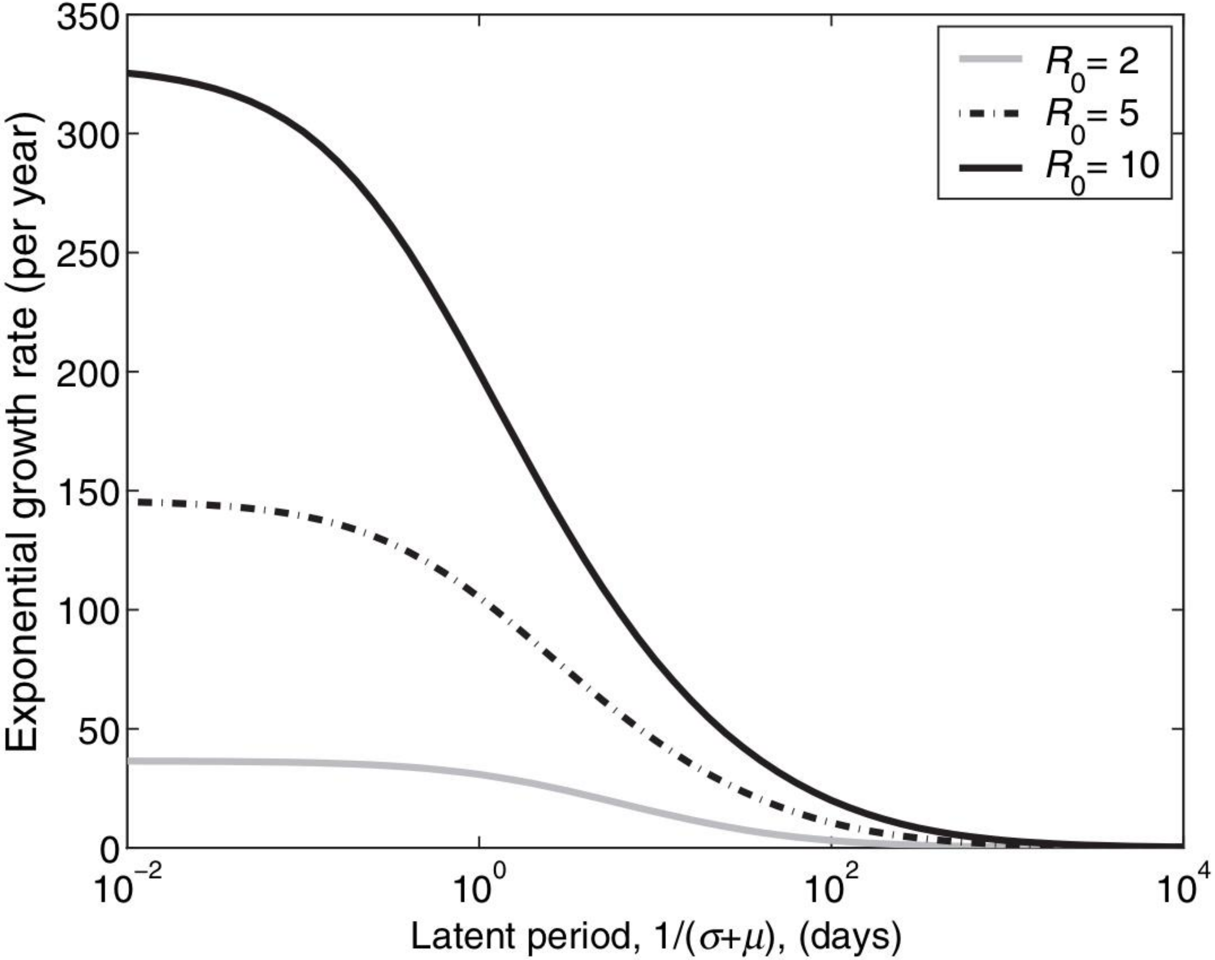
SEIR model



Latent period: after a very small initial inoculation (a few bacterial cells or virions), the pathogen reproduces within the host (but abundance is too low for transmission to other hosts)

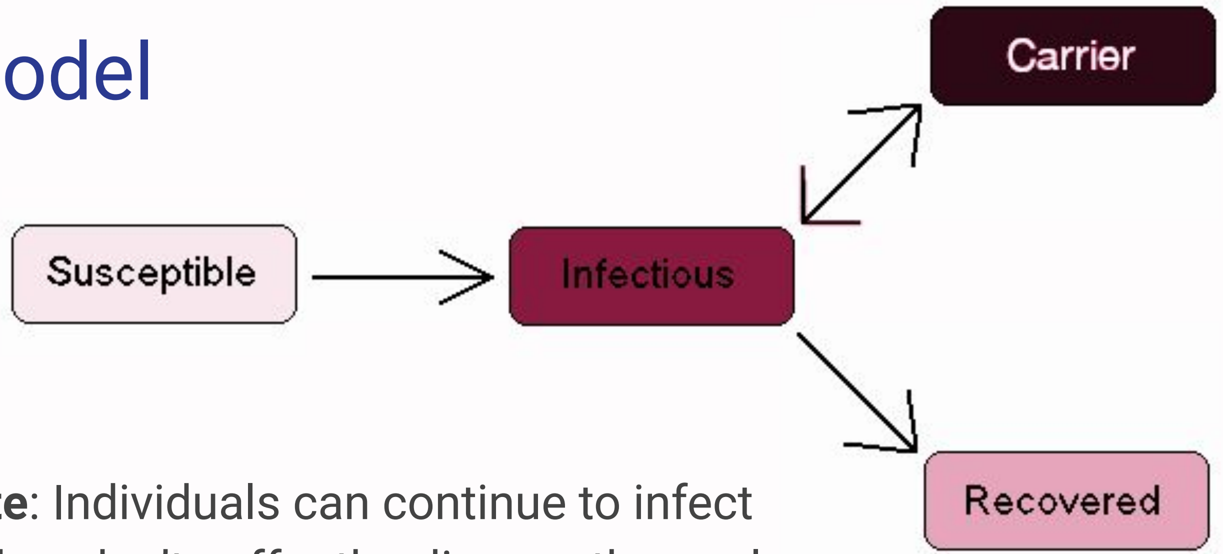
-Eg, smallpox

Slower growth rate than SIR model after pathogen invasion.



350
300
250
200
150
100
50
0
Exponential growth rate (per year)
10^{-2}
10^{0}
10^{2}
10^{4}
Latent period, $1/(\sigma+\mu)$, (days)
$R_0 = 2$
$R_0 = 5$
$R_0 = 10$

SICR model

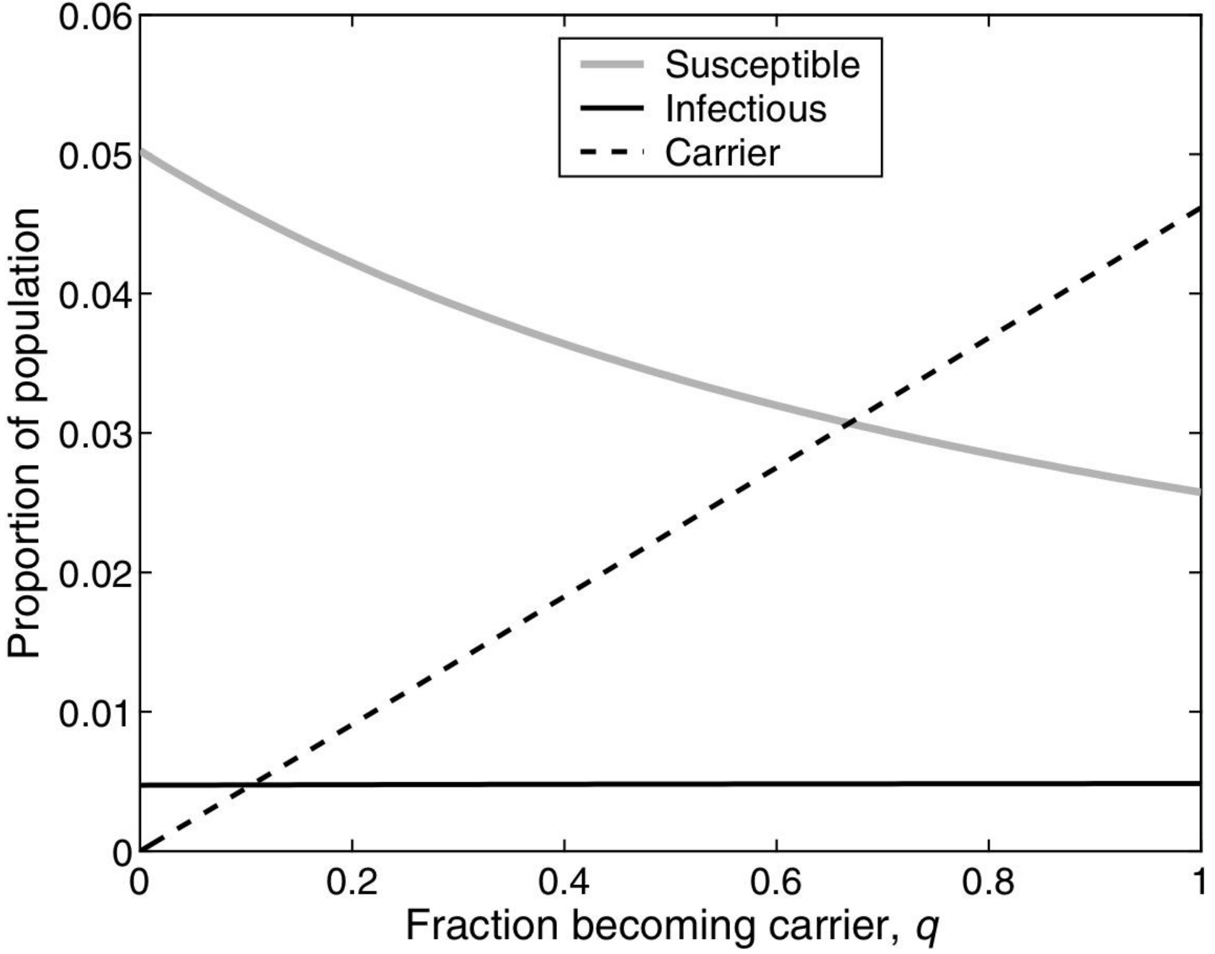


-**Carrier State**: Individuals can continue to infect others, but they don't suffer the disease themselves.

Hepatitis B, herpes.

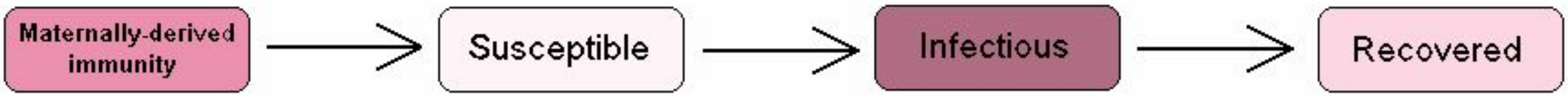
-Could also go back to infectious compartment:

Tuberculosis, typhoid fever



Susceptible
Infectious
Carrier
Proportion of population
Fraction becoming carrier, q
0.06
0.05
0.04
0.03
0.02
0.01
0
0
0.2
0.4
0.6
0.8
1

More compartmental models

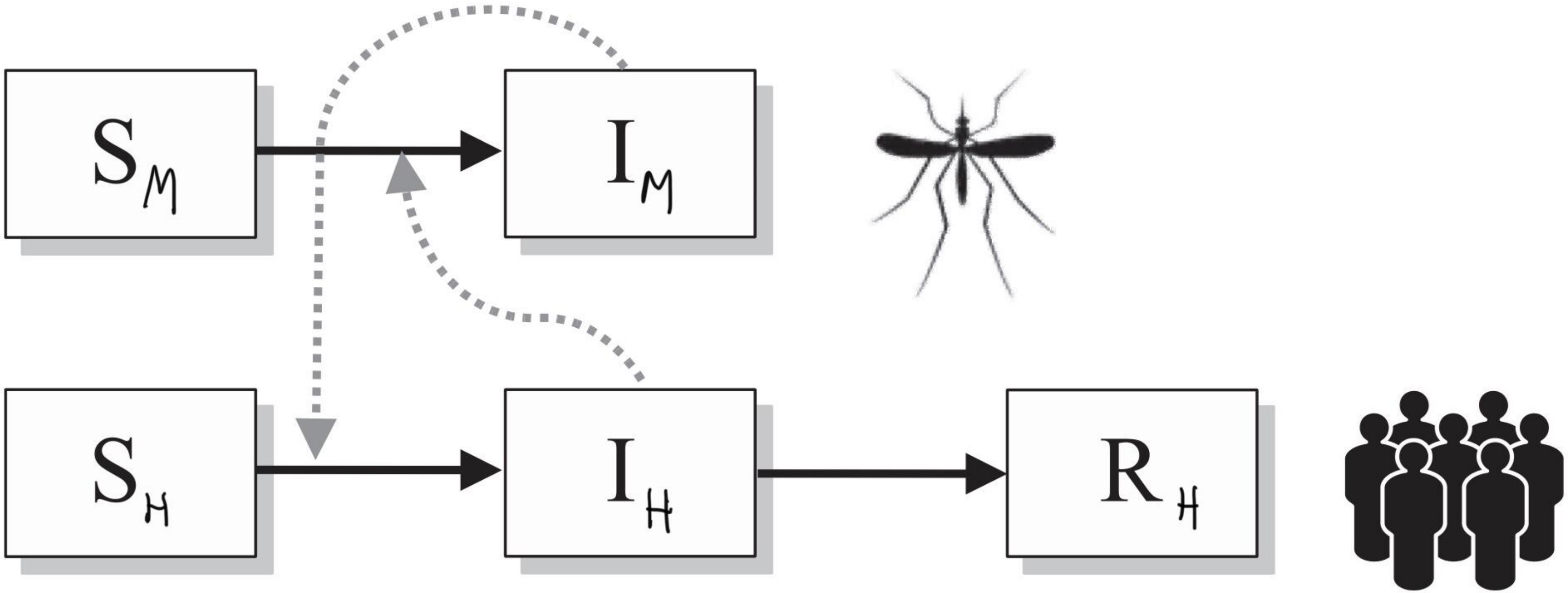


- **MSIR:** passive immunity - babies born immune for the first few months of life due to protection from maternal antibodies. (eg measles)
- **SIRS:** temporal (waning) immunity (eg mumps)
- **SI:** no recovery (eg HIV, BSE, Leishmaniasis, H5N1)

More compartments:

- “A” for asymptomatics
- “Q” for quarantined

Mosquito vectored transmission



Malaria. Dengue fever

Equations

rate at which a particular human is bitten by a mosquito

mosquito bite rate

$$r = \frac{b}{N_H}$$

total number of humans

$$\dot{S}_H = -rT_{HM}I_M S_H$$

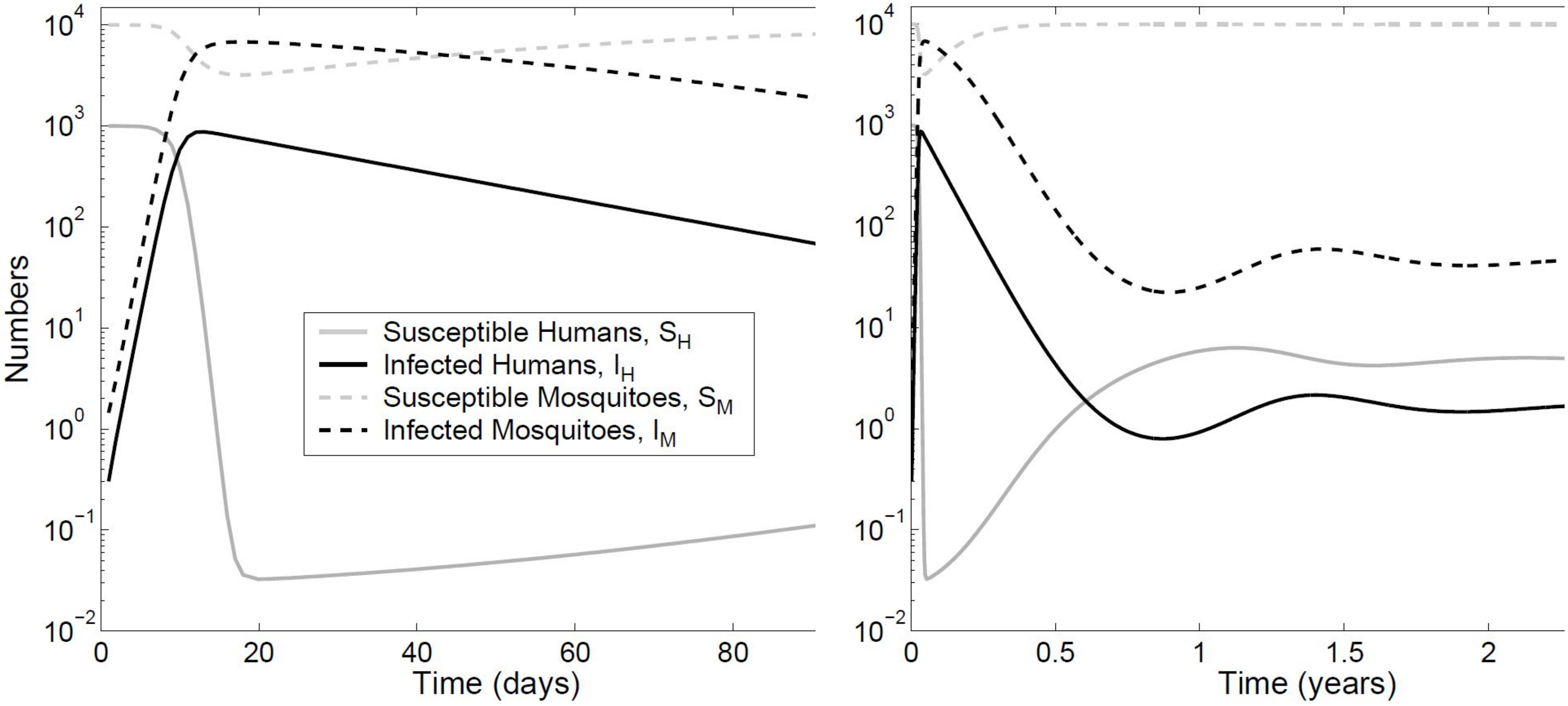
$$\dot{I}_H = rT_{HM}I_M S_H - \gamma_H I_H$$

$$\dot{S}_M = -rT_{MH}I_H S_M$$

$$\dot{I}_M = rT_{MH}S_H I_M$$

T_{HM} : transmission probability mosquito → human

T_{MH} : transmission probability human → mosquito



Numbers
Time (days)
Time (years)
Susceptible Humans, S_H
Infected Humans, I_H
Susceptible Mosquitoes, S_M
Infected Mosquitoes, I_M
10^{-2}
10^{-1}
10^{0}
10^{1}
10^{2}
10^{3}
10^{4}
0
20
40
60
80
0.5
1
1.5
2

4. Bonus: Jacobians and SIR with natural dynamics

Small perturbations in systems of DEs

Linear system

$$\left.\begin{aligned}\dot{x} &= ax + by \\ \dot{y} &= cx + dy\end{aligned}\right\} \underset{\text{rewrite}}{\Longrightarrow} \begin{pmatrix}\dot{x} \\ \dot{y}\end{pmatrix} = \underbrace{\begin{pmatrix}a & b \\ c & d\end{pmatrix}}_{\text{Jacobian matrix}} \begin{pmatrix}x \\ y\end{pmatrix}$$

$$J = \begin{pmatrix}a & b \\ c & d\end{pmatrix} \doteq \text{Jacobian}$$

"trace" $= \text{tr}\, J = a + d$

"determinant" $= \det J = ad - cb$

If $\text{tr}\, J < 0$ and $\det J \geq 0$, the fixed point is stable

SIR with natural dynamics

μ: per capita rate of births and natural deaths

$$\begin{cases} \dot{S} = \underbrace{\mu N}_{\text{births}} - \beta S I - \mu S \\ \dot{I} = +\beta S I - \gamma I - \mu I \\ \dot{R} = +\gamma I - \mu R \end{cases}$$

natural deaths

Endemic equilibrium:

$$(S^*, I^*, R^*) = \left(\frac{\gamma + \mu}{\beta}, \frac{\mu}{\beta} \left(\frac{\beta N}{\mu + \gamma} - 1 \right), N - I^* - S^* \right)$$

Requires $\frac{\beta N}{\gamma + \mu} = R_0 > 1$

Stability of Endemic Equilibrium

Near endemic equilibrium, small perturbations $\delta S, \delta I$ are given to linear order by

$$\begin{pmatrix} \dot{\delta S} \\ \dot{\delta I} \end{pmatrix} = J \begin{pmatrix} \delta S \\ \delta I \end{pmatrix} \quad \text{where} \quad J = \begin{pmatrix} -\mu - \beta I^* & -\beta S^* \\ \beta I^* & \underbrace{-\gamma - \mu + \beta S^*}_{=0} \end{pmatrix}$$

$$\Rightarrow \begin{cases} \operatorname{tr} J = -(\mu + \beta I^*) < 0 \\ \det J = \beta^2 I^* S^* > 0 \end{cases}$$

$\Rightarrow$ **Endemic equilibrium is stable**

Conclusion

For a given infection:
Can you write down a diagram for a compartmental model?
Can you write down the system of differential equations it?

Do you believe that maths can be a very useful tool in biology/medicine?

Questions?

FEEDBACK FORM + RESOURCES PAGE

Feedback Form: https://forms.gle/nSh91uxifm8hynUJ6

Resources Page:
www.mariaalegriagutierrez.wordpress.com/epi-talk-bio

Contact: mag84@cam.ac.uk

THANK YOU

Thank You