

Mathematical Biology

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0 Miscellaneous

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Moodle page: Handwritten notes by lecture; Matlab/Python programming examples; solved exercises.

This course involves 3 models: Deterministic temporal models (11 lectures), Stochastic temporal models (5 lectures), Deterministic spatio-temporal models (8 lectures).

The focus of this course is biochemical reactions and population processes.

(some introductory speech)

Example. (1, Transient population) If we use $n(t)$ to denote the size of a population, we may want to model $\frac{dn}{dt} = f(n)$ by an ODE, or maybe if we have several components $\mathbf{n}(t)$ then we may want to model $\frac{d\mathbf{n}}{dt} = \mathbf{f}(\mathbf{n})$ which is a system of ODEs.

Note that although n should be an integer (discrete), when $n \gg 1$ we may model it with continuous equations.

Example. (2) $n \rightarrow \partial_t P(n, t) = W \cdot P(n, t)$, Markov processes. Here $P(n, t)$ is a probability(?), n being a state, and W being the transition matrix.

Example. (3)

If we include spatial aspect, we may have $n(t)$ becoming $n(x, t)$. Now there might be 'diffusion': $\partial_t n(x, t) = f(n(x, t)) + D \nabla^2 n(x, t)$ where $\nabla^2 = \frac{\partial^2}{\partial x^2}$; this is the reaction-diffusion equation.

1 Birth-death models

The general idea is that we have a population of size $n(t)$; per capita per unit time, we have births of rate b and deaths of rate d . Then we can write

$$n(t + \Delta t) = n(t) + bn\Delta t - dn\Delta t$$

So we have an ODE

$$\frac{dn}{dt} = (b - d)n = rn$$

where $r = b - d$. This has an easy solution $n(t) = n_0 e^{rt}$, assuming r is a constant. We see that if r is positive then the population grows exponentially, and if r is negative then the population decreases to 0 asymptotically.

Now probably b and d are related to n by $b(n) = bn$ and $d(n) = dn^2$ due to competition. Then we have

$$\frac{dn}{dt} = bn - dn^2$$

which we can definitely rewrite as

$$\frac{dn}{dt} = \alpha n(1 - n)$$

by some change of variable on n . Now

$$\begin{aligned} \frac{dn}{n(1-n)} &= \alpha dt \\ \implies \frac{dn}{n} + \frac{dn}{1-n} &= \alpha dt \\ \implies \ln n - \ln(1-n) &= \alpha t + c \\ \implies n &= \frac{n_0 e^{\alpha t}}{(1-n_0) + n_0 e^{\alpha t}} \end{aligned}$$

where we are given that $t = 0$, $n = n_0$. If $t \gg \frac{1}{\alpha}$, when $t \rightarrow \infty$ we have $n(t) \rightarrow 1$. Now we can investigate if the population size is stable, and if it has any fixed points.

Let's now define $\mathbf{n} = (n_1, \dots, n_p)$, i.e. p populations, and $\frac{d\mathbf{n}}{dt} = \mathbf{f}(\mathbf{n})$. If $\mathbf{n} = \mathbf{n}^*$ is a fixed point, then $\frac{d\mathbf{n}}{dt} = 0$, i.e. $\mathbf{f}(\mathbf{n}) = 0$. Now if we apply a small perturbation $\mathbf{n} = \delta\mathbf{n}^* + \delta\mathbf{n}$, i.e.

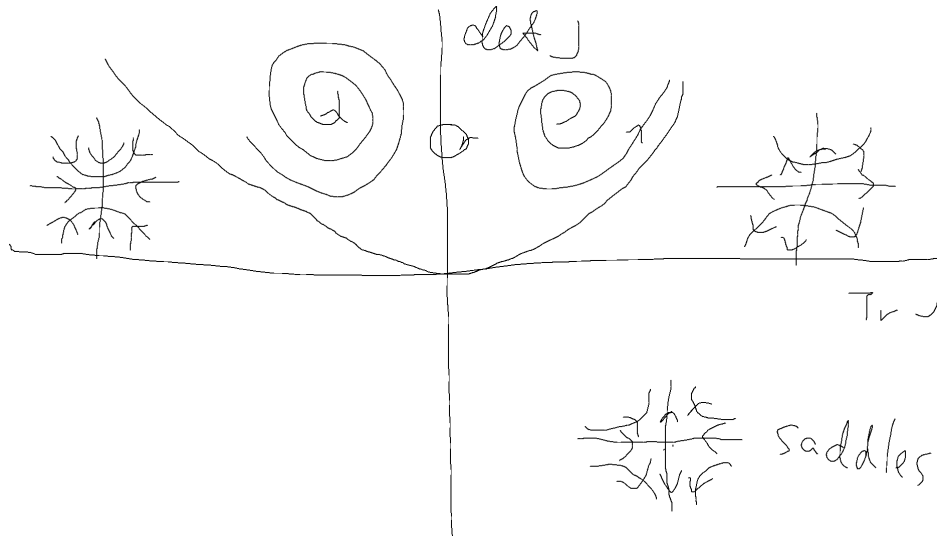
$$\begin{aligned} \frac{d}{dt}\delta\mathbf{n} &= \mathbf{f}(\mathbf{n}^* + \delta\mathbf{n}) \\ a &= \mathbf{f}(\mathbf{n}^*) + \frac{\partial f_i}{\partial n_j} \delta n_j + \frac{1}{2} \frac{\partial^2 f_i}{\partial n_j \partial n_k} \delta n_j \delta n_k \end{aligned}$$

So $\frac{d}{dt}\delta\mathbf{n} = J \cdot \delta\mathbf{n}$, so $\delta\mathbf{n}(t) = e^{Jt} \cdot \delta\mathbf{n}(0)$. If λ_i 's are the eigenvalues of J , we consider the real part of λ_i : if $\text{Re}(\lambda_i) < 0$, then if $p \geq 5$ we only have numerical solutions, if $3 \leq p \leq 5$ we have analytic solutions, and $p = 2$ is an easy case (recall p is the number of populations):

- If $p = 2$, $\mathbf{n} = (n_1, n_2)$, then

$$\frac{d}{dt} \begin{pmatrix} \delta_{n_1} \\ \delta_{n_2} \end{pmatrix} = \begin{pmatrix} \frac{\partial f_1}{\partial n_1} & \frac{\partial f_1}{\partial n_2} \\ \frac{\partial f_2}{\partial n_1} & \frac{\partial f_2}{\partial n_2} \end{pmatrix} \cdot \begin{pmatrix} \delta_{n_1} \\ \delta_{n_2} \end{pmatrix}$$

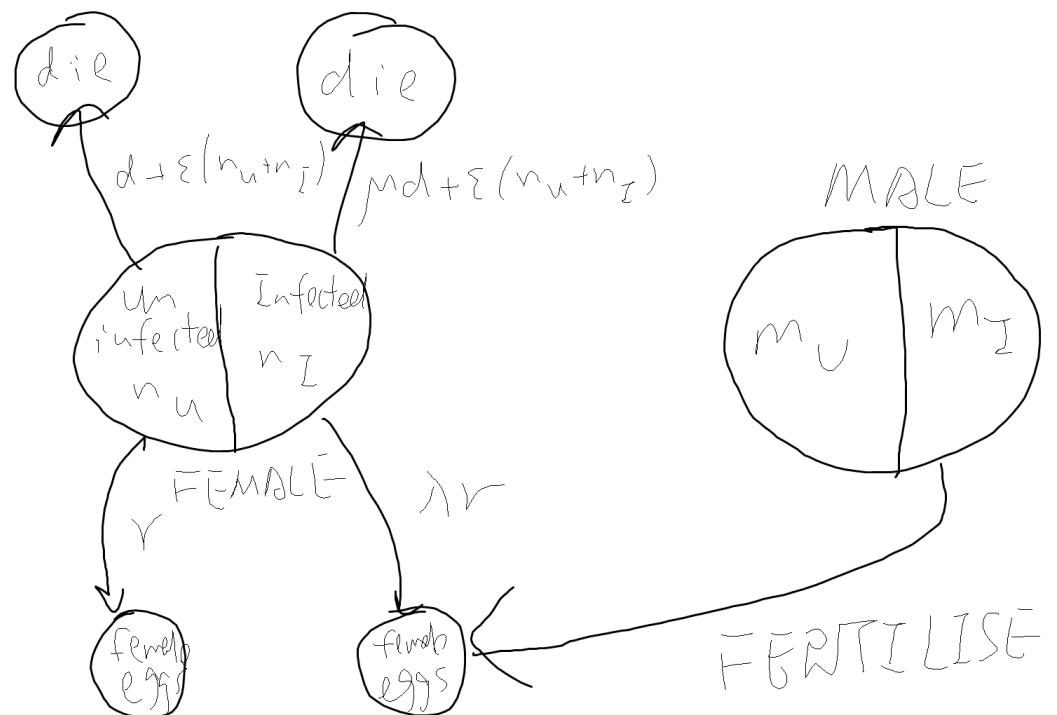
Where the matrix is J . Now we have $\lambda_1 \lambda_2 = \det J$ and $\lambda_1 + \lambda_2 = \text{tr } J$. Determined by the signs of those two, we have different possible behaviours:



Now let's consider the spread of Dengue. There are several processes going on at the same time:

- (1) Mosquitos carry dengue;
- (2) Wolbachia infect mosquitos;
- (3) Infected mosquitos do not transmit dengue;
- (4) Wolbachia transmission only across generations.

Question: will an intially infected population of mosquitos eventually spread over the entire population as $t \rightarrow \infty$?



F	M	frequency	rate	outcome	
U	U	$n_u \cdot m_u$	r	U	$m_u =$
U	I	$n_u \cdot m_i$		X	$\frac{n_u}{n_u + n_i}$
I	U	$n_i \cdot m_u$	λr	I	$m_i =$
I	I	$n_i \cdot m_i$	λr	I	$\frac{n_i}{n_u + n_i}$

We always assume that there are enough males to fertilise the female eggs.

Now consider $\frac{d}{dt}$ of n_U and n_I (uninfected and infected females). From the above tables we should be able to get (hopefully)

$$\begin{aligned}\frac{d}{dt}n_U &= rn_U \frac{n_U}{n_U + n_I} - dn_U - \varepsilon(n_U + n_I)n_U \\ \frac{d}{dt}n_I &= \lambda rn_I \frac{n_U}{n_U + n_I} + \lambda rn_I \frac{n_I}{n_U + n_I} - \mu dn_I - \varepsilon(n_U + n_I)n_I \quad (*)\end{aligned}$$

This is our model when $p = 2$. The term with ε is the death rate associated with competition.

We'll try to simplify these equations. By rescaling the time as $t \rightarrow rt$, and rescaling the population as $n \rightarrow \frac{\varepsilon}{r}n$, we get (?)

$$\begin{aligned}\frac{d}{dt}n_U &= n_U \frac{n_U}{n_U + n_I} - \frac{d}{r}n_U - (n_U + n_I)n_U \\ &= n_U \left[\frac{n_U}{n_U + n_I} - \frac{d}{r} - (n_U + n_I) \right] \quad (1)\end{aligned}$$

and the second equation becomes (???)

$$\frac{d}{dt}n_I = n_I \left[\lambda - \mu \frac{d}{r} - (n_U + n_I) \right] \quad (2)$$

We'd like to see that the model has at least the fixed points $\mathbf{n}^* = (n_U^*, 0)$ and $(0, n_I^*)$. The lecture then somehow defines

$$\begin{aligned}n_I^* &= \lambda - \mu \frac{d}{r} \\ n_U^* &= 1 - \frac{d}{r}\end{aligned}$$

so that our differential equations become

$$\begin{aligned}\frac{d}{dt}n_U &= n_U \left[n_U^* - \frac{n_I}{n_U + n_I} - (n_U + n_I) \right] \\ \frac{d}{dt}n_I &= n_I [n_-^* (n_U + n_I)]\end{aligned}$$

which has fixed points $(0, 0)$, $(n_U^*, 0)$, $(0, n_I^*)$, $(n_I^*(1 - n_I^* - n_U^*), n_I^*(n_U^* - n_I^*))$. The first is unstable, the second two are stable and the last fixed point is a saddle. This is disappointing because we want a small infection to be spread out to the whole population, but in that case the second fixed point needs to be unstable.

Global analysis:

We can plot the flow of the ode system

$$\frac{d}{dt} \begin{pmatrix} n_U \\ n_I \end{pmatrix} = \begin{pmatrix} f_U(n_U, n_I) \\ f_I(n_U, n_I) \end{pmatrix}$$

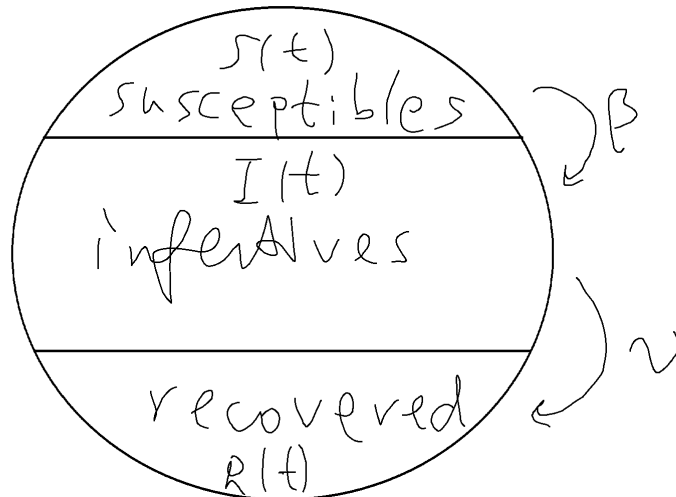
This is usually done by programming. We'll try to sketch the flow of this model:



Qualitative behaviour: we need a finite (large) $n_I(0)$ (in order to converge to $(n_u^*, 0)$).

For quantitative part we can only do numerical integrations.

Now we consider an epidemic model, where each individual may pass through three phases: susceptibles, infectives, recovered (compartment models – same individual for different phases). We use $S(t), I(t), R(t)$ to denote the population of each of them.



Now we want to know what is the rate of their change. We use biological datum, from which we know there is a per capita infection rate β , a recovery rate ν , so

in conclusion we have

$$\begin{aligned}\frac{d}{dt}S &= -\beta SI \\ \frac{d}{dt}I &= \beta SI - \nu I \\ \frac{d}{dt}R &= \nu\end{aligned}$$

Also we expect the population to be closed, i.e. the total population should not change over time (unlike the previous model), so

$$\frac{d}{dt}(S + I + R) = 0$$

Which is true. So it's sufficient to look at just two equations,

$$\begin{aligned}\frac{dS}{dt} &= -\beta SI \\ \frac{dI}{dt} &= \beta SI - \nu I\end{aligned}$$

What are the questions we want to ask? We may want to know:

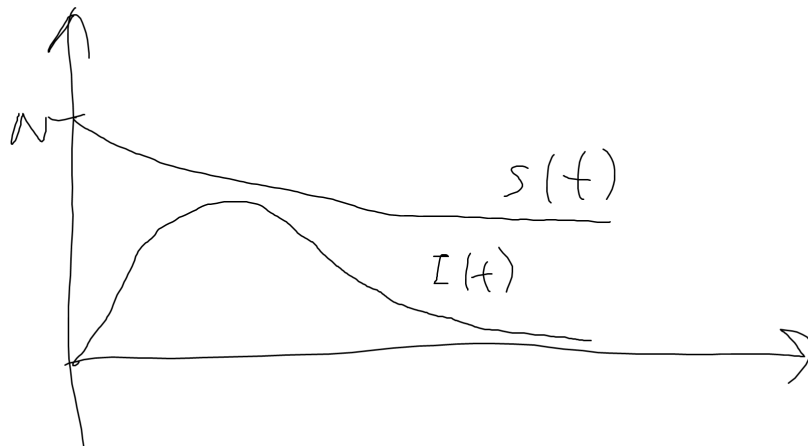
- When can you have an *outbreak*, i.e. $\frac{dI}{dt} > 0$;
- What is the final size of the outbreak?
- What vaccination strategy would work best?
- Endemic $\implies I^* > 0$, finite number of I in steady state.

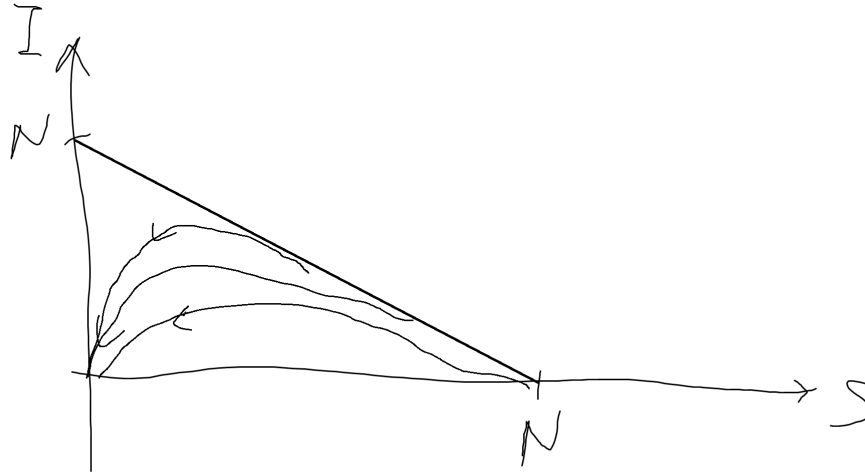
For obvious reason we call this the "SIR model".

(Q1)

at $t = 0$, $\frac{d}{dt}I = [\beta S(0) - \nu] \cdot I(0)$, so $\frac{\beta}{\nu}S(0) > 1 \implies \frac{\beta N}{\nu} > 1 = \mathcal{R}_0$, the reproduction ratio, or the mean number of susceptibles infected per infective.

(Q2)





We had $dS = -\beta SI dt$, $dI = (\beta SI - \nu I) dt$, so

$$\begin{aligned} \frac{dI}{dS} &= \frac{(\beta SI - \nu I)}{-\beta SI} = -1 + \frac{\nu}{\beta} \cdot \frac{1}{S} \\ &= \frac{N}{\mathcal{R}_0} \cdot \frac{1}{S} - 1 \end{aligned}$$

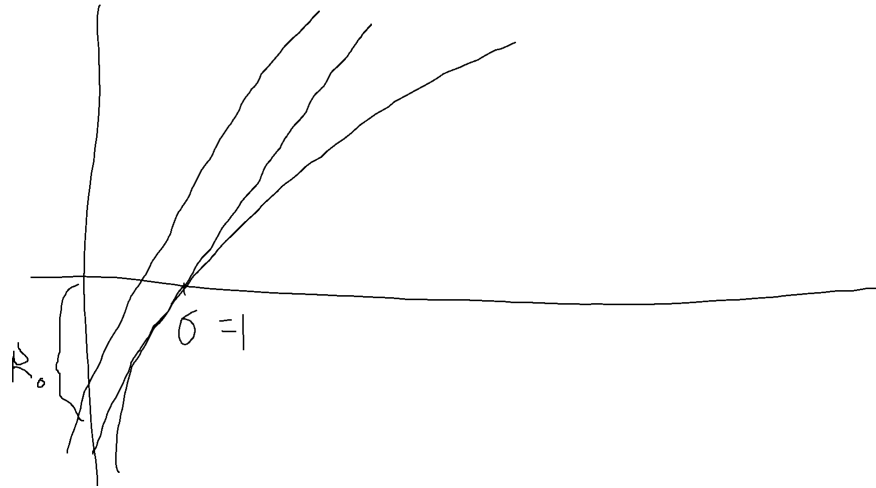
So

$$I = \frac{N}{\mathcal{R}_0} \ln S - S + \text{const}$$

Now $I(t) - I(0) = \frac{N}{\mathcal{R}_0} \ln \frac{S(t)}{S(0)} - (S(t) - S(0))$. As $t \rightarrow \infty$, $S(t) = \sigma N$ ($\sigma < 1$), $I(t) \rightarrow 0$. So

$$\begin{aligned} 0 &= \frac{N}{\mathcal{R}_0} \ln \sigma - (\sigma N - N) \\ \sigma - \frac{1}{\mathcal{R}_0} \ln \sigma &= 1 \end{aligned}$$

We can rewrite the second equation as $\mathcal{R}_0(\sigma - 1) = \ln \sigma$. Clear $\sigma = 1$ is a solution, but we are not interested in that. For $\mathcal{R}_0 \gg 1$, $\sigma \approx e^{-\mathcal{R}_0}$. (by sketching curves be-



low and analyze intersections?)

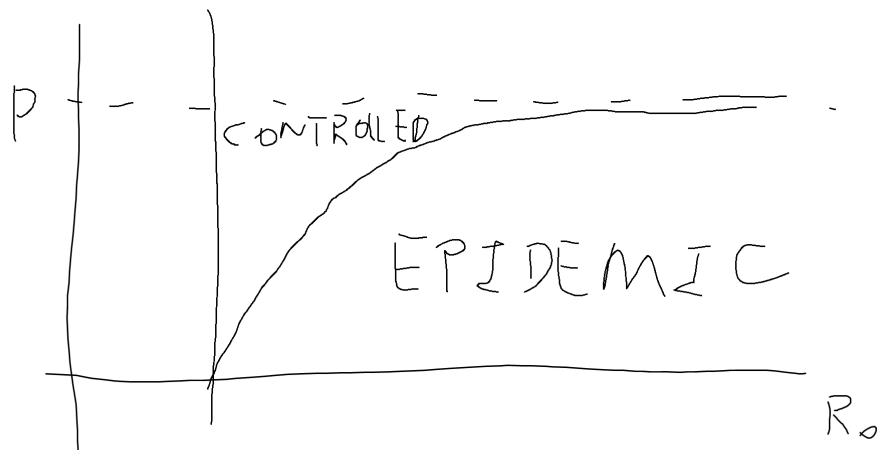
Insight: in any epidemic, only a fraction of the population is infected. Size of the epidemic $= (1 - \sigma)N$.

(Q3)

Vaccination? We can use pre-vaccination, i.e. vaccinate in anticipation of an outbreak. Let p be the fraction of the population being vaccinated. At $t = 0$ we have

$$S(0) \approx (1 - p)N$$

$$\frac{\beta}{\nu} S(0) > 1 \implies \frac{\beta}{\nu} (1 - p)N = (1 - p)\mathcal{R}_0 > 1$$



so $p > 1 - \frac{1}{\mathcal{R}_0}$.

(Q4)

Endemic: $I(t) \rightarrow I^* > 0$ as $t \rightarrow \infty$.

Biological datum: suppose we have a finite rate of birth of S , and of death of

S, I, R . Now

$$\frac{d}{dt}S = -\beta SI - \mu S + \mu N$$

$$\frac{d}{dt}I = \beta SI - \nu I - \mu I$$

$$\frac{d}{dt}R = \nu I - \mu R$$

at $t = 0$, $\mathcal{R} = \frac{\beta}{\nu + \mu}N(??)$. So

$$S^* = \frac{\mu + \nu}{\beta} = \frac{N}{\mathcal{R}_0}$$

$$I^* = \frac{\mu(N - S^*)}{\beta S^*} = \frac{\mu}{\beta}(\mathcal{R}_0 - 1)$$

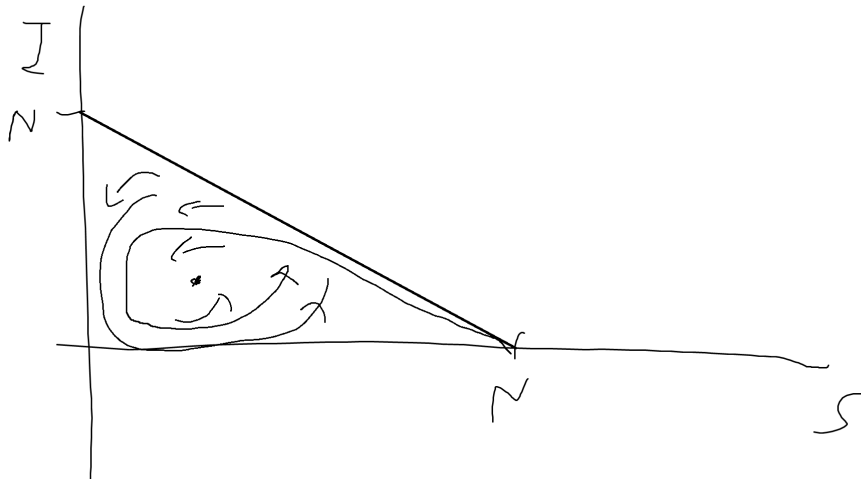
We had a Jacobian (?)

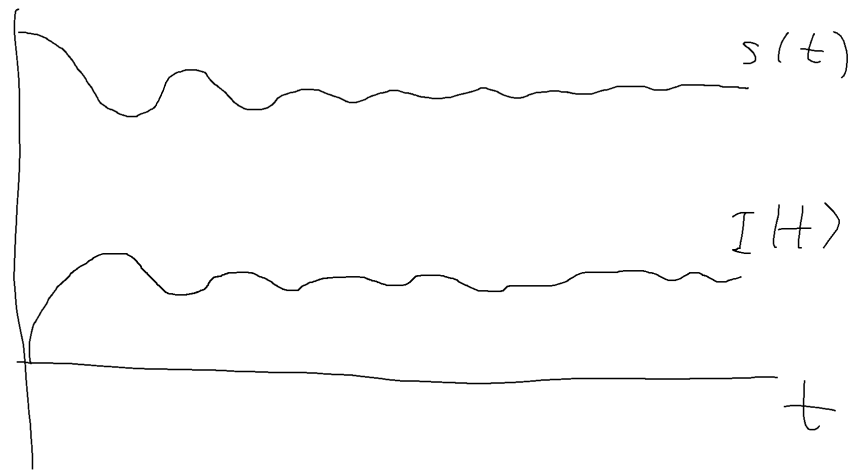
$$J = \begin{pmatrix} -\beta I - \mu & -\beta S \\ \beta I & \beta S - \nu - \mu \end{pmatrix}$$

so

$$J^* = \begin{pmatrix} -\mu \mathcal{R}_0 & -(\mu + \nu) \\ \beta(\mathcal{R}_0 - 1) & 0 \end{pmatrix}$$

$\lambda = -\frac{1}{2}\mu \mathcal{R}_0 \pm i\sqrt{\mu\nu(\mathcal{R}_0 - 1)}$ (?). If we assume $\nu \gg \mu$, then rate of recovery \gg rate of death, so we get a short lived disease.





Time period is $T = \frac{2\pi}{\omega} = \frac{2\pi}{\sqrt{\mu\nu(R_0-1)}}$

If $\mu \gg \nu$, for example, for Measles we have $\mu \sim \frac{1}{70}$ years, $\nu \sim \frac{1}{10}$ days, $R_0 \sim 20$, so the period of oscillation $T \approx 2.18$ years. Then we have the following pattern.

