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 $n >> 1$ we may model it with continuous equations.

Example. (2) $n \to \partial_t P(n,t) = W \cdot P(n,t)$, Markov processes. Here $P(n,t)$ is a probablity(?), 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': $\partial_t n(x,t) = f(n(x,t)) + D\nabla^2(x,t)$ 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 $t \to \infty$ we have $n(t) \to 1$. Now we can investigate if the population size is stable, and if it has any fixed points.

Let's now define $\mathbf{n} = (n_1, ..., n_p)$, 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.

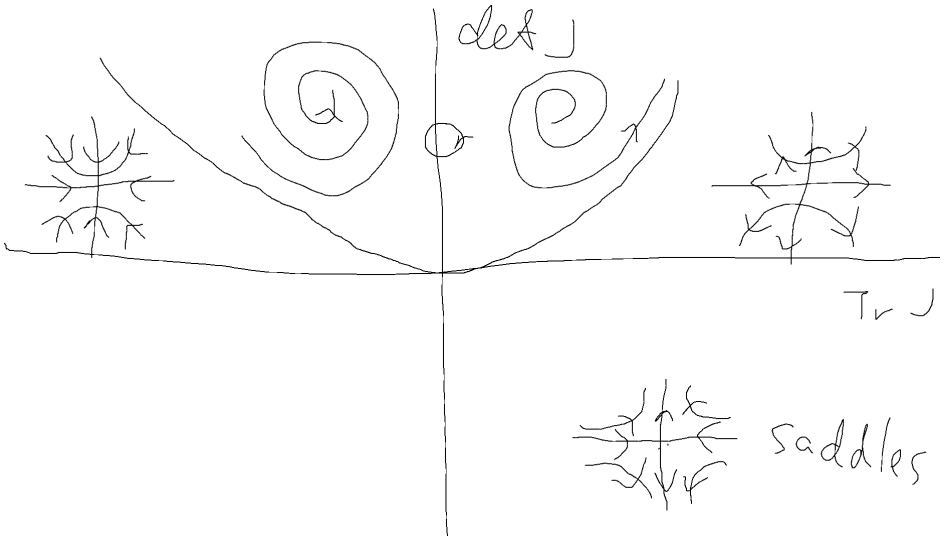
$$\begin{aligned} \frac{d}{dt}\delta\mathbf{n} &= \mathbf{f}(\mathbf{n}^* + \delta\mathbf{n}) \\ a &= \mathbf{f}(\mathbf{n}^*) + \frac{\partial f_i}{\partial n_j}\delta_{nj} + \frac{1}{2}\frac{\partial^2 f_i}{\partial n_j \partial n_k}\delta_{n_j}\delta_{n_k} \end{aligned}$$

So $\frac{d}{dt}\delta\mathbf{n} = J \cdot \partial\mathbf{n}$, so $\delta n(t) = e^{Jt} \cdot \delta n(0)$. If λ_i's are the eigenvalues of J, we consider the real part of λ_i: if $Re(\lambda_i) < 0$, 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

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

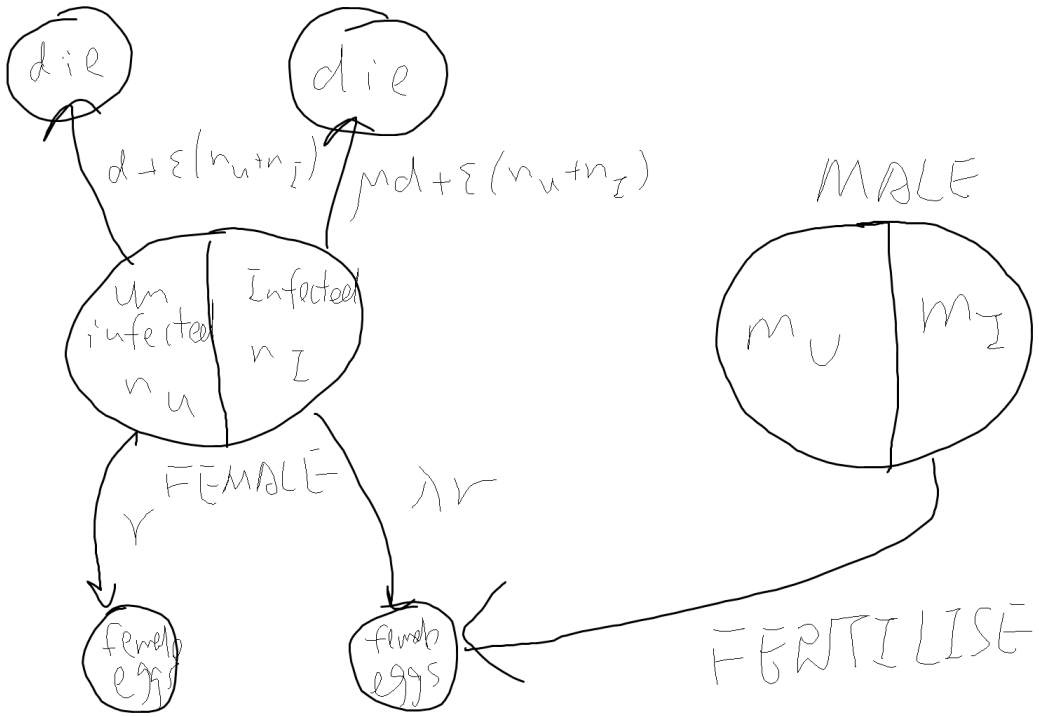
Where the matrix is J. Now we have $\lambda_1\lambda_2 = \det J$ and $\lambda_1 + \lambda_2 = \operatorname{tr} J$. Determined by the signs of those two, we have different possible behaviours:



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 $t \to \infty$?



F	M	frequency	rate	Outcome
U	U	$n_U \cdot m_U$	r	U
U	I	$n_U \cdot m_I$		X
I	U	$n_I \cdot m_U$	λr	I
I	I	$n_I \cdot m_I$	λr	I

$$m_U = \frac{n_U}{n_U + n_I}$$

$$m_I = \frac{n_I}{n_U + n_I}$$

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)

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

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 $t \to rt$, and rescaling the population as $n \to \frac{\varepsilon}{r}n$, we get (?)

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

and the second equation becomes (???)

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

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

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

so that our differential equations become

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

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

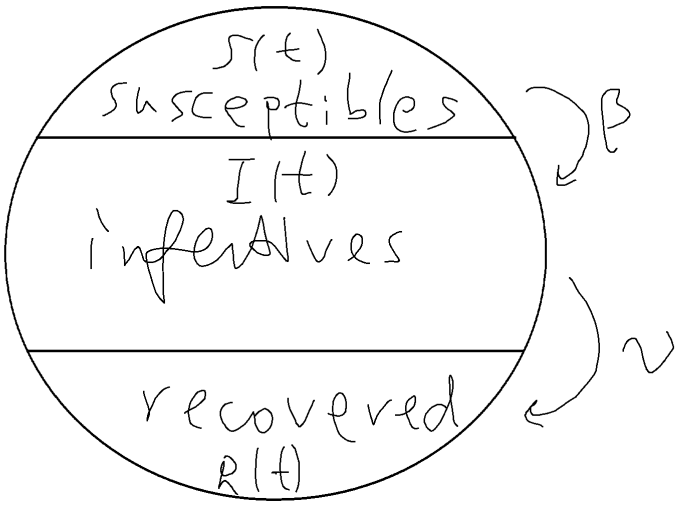
$$\frac{d}{dt}\begin{pmatrix}n_U\\n_I\end{pmatrix} = \begin{pmatrix}f_U(n_U,n_I)\\f_I(n_U,n_I)\end{pmatrix}$$

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 $(n_I^*, 0)$).

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

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

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,

$$\frac{dS}{dt} = -\beta SI$$
$$\frac{dI}{dt} = \beta SI - \nu I$$

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".

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

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

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 $t \to \infty$, $S(t) = \sigma N$ ($\sigma < 1$, $I(t) \to 0$. So

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