FYTN12

Systems Biology
– Models and Computations

Population models
Single species: Logistic growth

\[ \frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right) \]
Single species: Logistic growth

\[
\frac{dN}{dt} = rN \left(1 - \frac{N}{K}\right) \quad \rightarrow \quad N(t) = \frac{K P_0 e^{rt}}{K + P_0(e^{rt} - 1)}
\]
Two species: Lotka-Volterra

\[
\frac{dx}{dt} = \alpha x - \beta xy
\]
\[
\frac{dy}{dt} = \delta xy - \gamma y
\]

Predator-prey system that you've simulated.

- Unlimited food for prey (x)
- Predators limited only by prey
- Predators have unlimited appetite
- Individuals are ageless
Two species: Lotka-Volterra

\[
\frac{dx}{dt} = \alpha x - \beta xy \\
\frac{dy}{dt} = \delta xy - \gamma y
\]

What’s the population here?
Stochastic population models

- Spatial structure
  - Well-mixed
  - Discrete locations (graph)
  - Continuous / fine grid
- Individuals with properties?
  - Age, sex, health...
  - Track individuals?
  - Or compartments: sick/healthy, male/female?
  - Discretize e.g. age?
Example: SIR model

- Epidemiological model describing a disease outbreak
- Individuals are Susceptible, Infectious or Recovered

\[
\begin{align*}
\frac{dS}{dt} &= -\beta \frac{IS}{N} \\
\frac{dI}{dt} &= \beta \frac{IS}{N} - \gamma I \\
\frac{dR}{dt} &= \gamma I
\end{align*}
\]
Hand-in problem: Rabbits and foxes

- Imagine the world as a big grassy field with animals.
- Foxes eat rabbits, rabbits eat grass, grass needs to regrow.
- Grass can regrow only if there is no animal sitting on it.
- Animals starve if they eat too seldom.
- Animals die of other causes too.
- Animals have limited feeding capacity.
- Animals divide in proportion to their food surplus (their intake between the minimum and the maximum)

Write down equations for this system of three variables.
Call the amount of tall grass $G$, number of rabbits $R$, foxes $F$.
Size of the world $N$. Make up names for other parameters, e.g. $d_R$ and $d_F$ for the “spontaneous” death rates. Can you suggest sensible ranges for the parameters?
Simpson's paradox

● Among the 9th graders at a school, the grade point average in 2013 was 13.45 for girls and 12.72 for boys. The total average was 13.16.

● In 2014, the averages among the school's 9th graders had improved to 13.57 for girls and 12.81 for boys but the total had fallen to 13.11.

● Why?

● 13.45 * 0.6 + 12.72 * 0.4 = 13.158

● 13.57 * 0.4 + 12.81 * 0.6 = 13.114
Simpson's Paradox: In a heterogeneous population, trends may come out the wrong way around.

Example: Treatments against large/small kidney stones.

<table>
<thead>
<tr>
<th>size</th>
<th>treatment A</th>
<th>treatment B</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$\frac{81}{87} = 93%$</td>
<td>$\frac{234}{270} = 87%$</td>
</tr>
<tr>
<td>large</td>
<td>$\frac{192}{263} = 73%$</td>
<td>$\frac{55}{80} = 69%$</td>
</tr>
<tr>
<td>all</td>
<td>$\frac{273}{350} = 78%$</td>
<td>$\frac{289}{350} = 83%$</td>
</tr>
</tbody>
</table>

Reason for the problem: choice of treatment is not independent of kidney stone size.
Common good producer / non-producer interaction:

• Substance X is required/helpful for survival/growth
• Producing X costs precious resources
• Some individuals produce X, others don't.
• The non-producers grow more quickly

• Can the producers beat the non-producers?
  • Perhaps if populations without producers go extinct?
  • Even if no disasters occur?
Simpson's Paradox in a Synthetic Microbial System

JS Chuang, O Rivoire and S Leibler,
Science 323, 272-275 (2009)

General ideas:

• The fraction of producers ($p$) affects the growth rate of both producers and non-producers. Different initial $p$ gives different $p'$ at some later time, with $p' \leq p$.

• Pooling cultures with different $p$ can nonetheless make the overall $p'$ higher.

• Splitting a population into sub-populations with different $p$ requires very low numbers of cells.
Project 4 A: Simpson's paradox

• Implement deterministic model of the system.
• Predict growth and $p'$ as functions of $p$ (fig 2A).
• Do you observe Simpson's paradox as in fig 2B?
• Randomly partition/dilute population as in fig 3 (with deterministic model); reproduce $\Delta p$ as a function of $\lambda$.
• Can repeated rounds of partitioning/dilution lead to a fixed value of $p$ different from 0 or 1?
• What if the growth is simulated stochastically – does it make a difference?
Project 4 A, variants

• Idea I: Simulate the spread of the bacteria among puddles of food (berries?) to investigate how robust the 'paradox' is.

• Idea II: Implement the system spatially. For inspiration, see e.g.

A cell-based model for quorum sensing in heterogeneous bacterial colonies
P. Melke, P. Sahlin, A. Levchenko, and H. Jönsson
Project 4 B: Rabbits and foxes

• Start from your equations for the hand-in problem.
• Find parameters that give coexistence of species in deterministic simulations.
• Simulate stochastically and compare.
• Idea I: Implement spatially, with Gillespie and “diffusion” of animals.
• Idea II: Implement spatially with one randomly walking animal per lattice point, making rules to match the equations.
• Idea III: Examine interactions if more species are added.
Presentations and schedule

• Hand-in problem and slides due 08:30 as before.
• Choose 4 A or 4 B.
• Work on these projects individually, but don't hesitate to ask each other and/or teachers.
• We need to split presentations into two groups. Both on Wednesday 4/3 or some on Monday or Tuesday?
• Strictly enforced time limit: 9 minutes, or 12 minutes if you did not present on Project 1.
A note on grading

• We grade presentations, looking at aspects like ambition level, implementation, results, slides/presentation quality, participation (asking and answering questions).

• The final grade is only U / G / VG so there is little point in talking about specific percentages etc.

• Presentations and hand-in problem will account for a large minority (say 30-45%) of the final grade.

• All projects must be presented unless otherwise agreed. We'll schedule a session for missed presentations at the end of the course.