Mathematical Biology Notes

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1 One-Dimensional Systems

- This class of biological systems can be modelled as an ODE of the form

$$\frac{dx}{dt} = f(x), \quad x(0) = x_0$$

where $x(t)$ is a real-valued function of time t and $f(x)$ is a real-valued function of x.

1.1 Existence and Uniqueness Theorem

- It turns out a unique solution exists if $f(x)$ is sufficiently smooth.

- If $f(x)$ and $f'(x)$ are continuous on an open interval R and $x_0 \in R$, then the initial value problem has a unique solution $x(t)$ on some time interval $(-\tau, \tau)$ about $t = 0$.

- The solution only applies over the interval $(-\tau, \tau)$ and not necessarily for all time.

1.2 Fixed Points and Their Stability

1.2.1 Fixed Points

- **Fixed points** are values of x for which $\dot{x} = f(x) = 0$.

- If points near a fixed point x move towards it, then x is **stable**. If points move away from it, then x is **unstable**. If in one direction points move towards it and on the other points move away from it, then it is **half-stable**.

- We can construct a phase portrait depicting the space $(x, f(x))$ and check the flow of trajectories based on the fixed points. The flow moves to the right when $f(x) > 0$ and to the left when $f(x) < 0$.

1.2.2 Linear Stability Analysis

- If we expand the Taylor series for $f(x)$ around a fixed point x^*, ignore the higher order terms, and denote $\eta := x - x^*$ as the perturbation around x^*, we get

$$\frac{d\eta}{dt} = f'(x^*)\eta$$

- If $f'(x^*) > 0$, then x^* is an **unstable fixed point**. That is since η grows over time.

- If $f'(x^*) < 0$, then x^* is a **stable fixed point**. That is since η decays over time.

- When $f'(x^*) = 0$, stability cannot be determined without examining the higher order terms of the Taylor series, and so this tool is not suitable.

1.3 Bifurcations

- Often we have parameters in $f(x)$ that allow us to control the system.

- If a change in some parameter changes the number or behaviour of fixed points, we say a **bifurcation** has occurred.

- The parameter value at which a bifurcation occurs is called the **bifurcation point**.

- In 1D systems, only <u>three</u> types of bifurcations can occur. They can be described using their **normal forms**.

- If a system can be expressed in terms of these normal forms, then we can say such a bifurcation exists.

- A bifurcation diagram is a plot on the (r, x) space where r is the control parameter responsible for the bifurcation.

1.3.1 Saddle-node bifurcation

- Here, a pair of fixed points, one stable and one unstable, are either created or destroyed.

- It is given by the normal form

$$\frac{dx}{dt} = r \pm x^2$$

- The bifurcation diagram is a parabola when $r \leq 0$ and none when $r > 0$.

1.3.2 Transcritical bifurcation

- Here, a pair of fixed points, one stable and one unstable, exchange stability.

- It is given by the normal form

$$\frac{dx}{dt} = rx - x^2$$

- The bifurcation diagram involves the x-axis and a line exchanging stability at $(0, 0)$.

1.3.3 Pitchfork bifurcation

- This bifurcations comes in two flavors: **supercritical** and **subcritical**.

- In the supercritical case, one stable fixed point turns into two stable and one unstable fixed points. It is given by the normal form

$$\frac{dx}{dt} = rx - x^3$$

- The bifurcation diagram is given by a right-facing pitchfork with the middle fork as unstable.

- In the subcritical case, one unstable fixed point turns into two unstable and one stable fixed points. It is given by the normal form

$$\frac{dx}{dt} = rx + x^3$$

- The bifurcation diagram is given by a left-facing pitchfork with the middle fork as stable.

1.4 One dimensional systems in biology

1.4.1 Logistic growth

- A primitive formulation for population size is modelling under **exponential growth**, taking into account the per capita birth and death rates b and μ. Deriving the ODE yields

$$\frac{dx}{dt} = rx, \quad x(0) = x_0$$

where $r = b - \mu$ is the **net growth rate**. The corresponding solution is given by

$$x(t) = x_0 e^{rt}$$

- Here, the population either decays to zero or grows without bound. To fix this, we consider a parameter K which refers to the maximum size the population can reach.

- We can encode the growth through a $(1 - x/K)$ term which is zero when $x = K$ and arrive at the **logistic equation**

$$\frac{dx}{dt} = rx \left(1 - \frac{x}{K}\right)$$

where r is the **intrinsic growth rate** and K is the **carrying capacity**. The corresponding solution is given by

$$x(t) = \frac{Kx_0}{x_0 + (K - x_0)e^{-rt}}$$

- K can be interpreted as the maximum population size that can be maintained by the available resources.

- Its fixed points are given by an unstable $x^* = 0$ and a stable $x^* = K$.

1.4.2 SIS model

- We model the spread of diseases on a susceptible population S, and an infective population I, where $N = S + I$ is fixed. The dynamics can be expressed as

$$\frac{dS}{dt} = -\underbrace{\lambda SI/N}_{\text{get infected}} + \underbrace{\gamma I}_{\text{recovery}} + \underbrace{\delta N}_{\text{birth}} - \underbrace{\delta S}_{\text{death}},$$

$$\frac{dI}{dt} = \underbrace{\lambda SI/N}_{\text{get infected}} - \underbrace{\gamma I}_{\text{recovery}} - \underbrace{\delta I}_{\text{death}}$$

where $\lambda I/N$ is the infection rate per susceptible, γ is the recovery rate per infective, and δ is the birth/death rate per-capita,

- Substituting $S = N - I$, we can rearrange the terms in the second equation as

$$\frac{dI}{dt} = (\lambda - \gamma - \delta)I \left(1 - \frac{\lambda}{N(\lambda - \gamma - \delta)}I\right)$$

which is essentially a logistic equation with parameters $r = \lambda - \gamma - \delta$ and $K = \frac{N(\lambda - \gamma = \delta)}{\lambda}$

1.4.3 Logistic growth with harvesting

- Previously, we assume our system is closed, we can modify the logistic equation to get

$$\frac{dx}{dt} = rx \left(1 - \frac{x}{K}\right) - H$$

where H is the **harvesting rate**.

- There is a saddle-node bifurcation at $H = rK/4$. When $H > rK/4$, the roots are complex and there are no fixed points. When $H \leq rK/4$, then there is one stable and one unstable fixed point.

1.4.4 The spruce budworm

- We model the population of budworms N with the equation

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right) - p(N)$$

where $p(N)$ is the rate of change in the budworm population.

- The predation can be dsescribed by the function

$$p(N) = \frac{BN^2}{A^2 + N^2}$$

where $B > 0$ is the **predation rate** as $N \to \infty$ and $A > 0$ is a measure of the **threshold population size** where predation suddenly increases. This leaves us with

$$\frac{dN}{dt} = rN\left(1 - \frac{N}{K}\right) - \frac{BN^2}{A^2 + N^2}$$

- By setting $N = Ax$, $\tau = \frac{A}{B}t$, $R = \frac{rA}{B}$, and $k = \frac{K}{A}$, we get the non-dimensionalised form

$$\frac{dx}{d\tau} = Rx\left(1 - \frac{x}{k}\right) - \frac{x^2}{1 + x^2}$$

- Clearly, $x^* = 0$ is a fixed point. Other fixed points are governed by

$$R\left(1 - \frac{x}{k}\right) = \frac{x}{1 + x^2}$$

which produces three additional fixed points $a < b < c$.

- If R is decreased, a and b combine and vanish, leading to a saddle-node bifurcation.

- If R is increased, b and c combine and vanish, leading to a saddle-node bifurcation as well.

- The model exhibits **hysterisis**. That is, suppose the system is at a fixed point x_a^*. We vary our parameters, causing a bifurcation and the system to be at x_c^* instead. If we modify the parameters back, we observe the system does not go back to its original fixed point.

- The model also exhibits **bistability**. That is, the presence of two stable fixed points.

1.4.5 Chemical kinetics

- Suppose we have two molecules A and B that react to form another molecule C at rate k_1. We express this symbollically as

$$A + B \xrightarrow{k_1} C$$
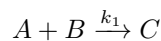
- Writing the concentration of the molecules as $a = [A], b = [B], c = [C]$, the **law of mass action** states that the reaction rate is proportional to the product of the concentration of the reactants. Thus the rates are given by

$$\frac{dc}{dt} = k_1 ab$$
$$\frac{da}{dt} = -k_1 ab$$
$$\frac{db}{dt} = -K - 1ab$$

- More generally, suppose there are n molecules $X_1, \ldots, X_n$ with concentrations $x_1, \ldots, x_n$ respectively, and the molecules can undergo r reactions, each of which may be expressed as

$$s_{1j}^R X_1 + s_{2j}^R X_2 + \cdots + s_{nj}^R X_n \xrightarrow{k_j} s_{1j}^P X_1 + s_{2j}^P X_2 + \cdots + s_{nj}^P X_n$$
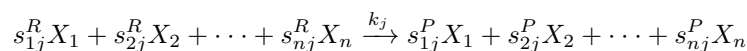
for $j = 1, \ldots, r$, where s_{ij}^R and s_{ij}^P are the stoichiometric coefficients on the reactant and product sides for species i and reaction j. Writing $s_{ij} = s_{ij}^P - s_{ij}^R$, the law of mass action gives

$$\frac{dx_i}{dt} = \sum_{j=1}^{r} s_{ij} k_j \prod_{l=1}^{n} x_l^{s_{lj}^R}$$

1.4.6 Michaelis-Menten model

- The most basic model for enzymatic reactions is the process proposed by Michaelis and Menten involving substrate S, enzyme E, a complex SE, and a product P. The reaction is described by

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} SE \overset{k_2}{\longrightarrow} P + E$$
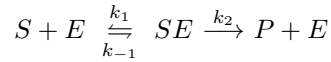
- Denoting $c = [SE]$ as the concentration of the complex, we have the differential equations

$$\frac{dc}{dt} = k_1 se - (k_{-1} + k_2)c,$$

$$\frac{de}{dt} = -k_1 se + (k_{-1} + k_2)c,$$

$$\frac{ds}{dt} = -k_1 se + k_{-1}c,$$

$$\frac{dp}{dt} = k_2 c$$

- Since $d(c + e)/dt = 0$, then $c + e = e_0$ and, as p only depends on c, then we only need to consider the two coupled differential equations

$$\frac{dc}{dt} = k_1 e_0 s - (k_1 s + k_{-1} + k_2)c,$$

$$\frac{ds}{dt} = -k_1 e_0 s + (k_1 s + k_{-1})c$$

with initial condition $s(0) = s_0$ and recall $c(0) = 0$.

- This can be non-dimensionalised into

$$\epsilon \frac{dv}{d\tau} = u - (u + K)v,$$

$$\frac{du}{d\tau} = -u + (u + K - \lambda)v$$

with initial conditions $u(0) = 1$ and $v(0) = 0$.

- We can use a **quasi-steady approximation** by assuming that $\epsilon \ll 1$ and so the above reaction occurs extremely quick compared to the bottom. We can then assume it is already in a steady state and thus

$$0 = u - (u + K)v$$

leading to a 1D system

$$\frac{du}{d\tau} = -\lambda \frac{u}{u + K}$$

- For $u > 0$, the RHS $-\lambda u/(u + K) < 0$ and thus u decreases monotonically with $u = 0$ as an asymptotically stable fixed point.

- Whereas, considering a non-dimensionalised version of the product $p = s_0 w$,

$$\frac{dw}{d\tau} = \lambda \frac{u}{u + K}$$

tells us the product increases monotonically in time with a rate that decreases as the substrate u is depleted.

2   Multi-dimensional Systems

- This class of models are concerned with n-dimensional systems expressed as

$$\frac{dx_i}{dt} = f_i(x_1, \dots, x_n)$$

for $i = 1, \dots, n$, which in vector form becomes

$$\frac{d\mathbf{x}}{dt} = \mathbf{f}(\mathbf{x})$$

where $\mathbf{x} = (x_1, \dots, x_n)^T$ and $\mathbf{f} = (f_1(\mathbf{x}), \dots, f_n(\mathbf{x}))^T$.

2.1 Existence and Uniqueness Theorem

- If the functions $f_i(\mathbf{x})$ and their first derivative $\partial f_i/\partial x_j$ are continuous for $-\infty < x_k < \infty$, then for any initial condition

$$\mathbf{x}(0) = \mathbf{x}_0$$

  there exists a unique solution for a small time interval $-\delta < t < \delta$. In particular, if $\mathbf{f}$ is bounded linearly, i.e.

$$\|\mathbf{f}(\mathbf{x})\| \leq c_1 \|\mathbf{x}\| + c_2$$

  for some positive constants c_1, c_2, then the solutions can be uniquely extended to all $-\infty < t < \infty$.

2.2 Fixed points and their stability

- A fixed point is said to be **stable** if $\forall \delta_1$, $\exists \delta_2$ such that if $\|\mathbf{x}(0) - \mathbf{x}^*\| < \delta_2$, then the solution exists for all $t > 0$ and $\|\mathbf{x}(t) - \mathbf{x}^*\| < \delta_1$ for all $t > 0$.

- A stable fixed point is **asymptotically stable** if any solution $\mathbf{x}(t)$ with $\mathbf{x}(0)$ near $\mathbf{x}^*$ converges to $\mathbf{x}^*$ ast $t \to \infty$.

- A fixed point is **unstable** if it is not stable.

2.2.1 Stability

- We can linearise $\mathbf{f}$ about $\mathbf{x}^*$ such that

$$\mathbf{f}(x) = A(\mathbf{x} - \mathbf{x}_0) + \text{h.o.t.}$$

  where A is the Jacobian matrix whose elements are given by

$$a_{ij} = \frac{\partial f_i}{\partial x_j}(\mathbf{x}^*)$$

- (**Stability theorem**) Let $\mathbf{x}^*$ be a fixed point and linearise $\mathbf{f}(\mathbf{x})$ as above. If all the eigenvalues of the Jacobian matrix A have negative real parts, then $\mathbf{x}^*$ is asymptotically stable, and $\|\mathbf{x}(t) - \mathbf{x}^*\| \leq ce^{-\mu t}$ for all $t > 0$ if $\|\mathbf{x}(0) - \mathbf{x}^*\|$ is sufficiently small.

  - If at least one of the eigenvalues has a positive real part, then $\mathbf{x}^*$ is unstable.

- Solving for $\tau = \text{trace}(A)$ and $\Delta = \det(A)$, we find that

  - In the real case, i.e. $\tau^2 - 4\Delta > 0$, we have
    1. **stable node** if $\lambda_1, \lambda_2 < 0$
    2. **unstable node** if $\lambda_1 > 0, \lambda_2 > 0$
    3. **saddle point** if $\lambda_! > 0, \lambda_2 < 0$
  - In the degenerate case, i.e. $\tau^2 - 4\Delta = 0$, we have
    1. **stable star** if $\lambda_1 = \lambda_2 < 0$
    2. **unstable star** if $\lambda_1 = \lambda_2 > 0$
  - In the complex case, i.e. $\tau^2 - 4\Delta > 0$, we have
    1. **stable spiral** if $\Re(\lambda_1) = \Re(\lambda_2) < 0$
    2. **unstable spiral** if $\Re(\lambda_1) = \Re(\lambda_2) > 0$
    3. **centre** if $\Re(\lambda_1) = \Re(\lambda_2) = 0$.

2.2.2 Phase portraits

- In two dimensions, the phase portrait typically includes fixed points, closed orbits, indication of fixed point stability.

- The **nullclines** are curves where either $dx_1/dt = 0$ or $dx_2/dt = 0$. As they act as the boundary between when $dx_1/dt < 0$ and $dx_1/dt > 0$, the flow of trajectories can be established.

2.3 Multidimensional models of biological processes

2.3.1 SIS model for two interacting populations

- We adapt the SIS model to include a distinction between male and female populations in the case of venereal disease transmission.

$$\frac{dS}{dt} = -rSI^* + aI$$

$$\frac{dS^*}{dt} = -r^*S^*I + a^*I^*$$

$$\frac{dI}{dt} = rSI^* - aI$$

$$\frac{dI^*}{dt} = r^*S^*I - a^*I^*$$

- Similarly before, since $S = N - I$ and $S^* = N^* - I^*$, then we can simplify

$$\frac{dI}{dt} = rI^*(N - I) - aI$$

$$\frac{dI^*}{dt} = r^*I(N^* - I^*) - a^*I^*$$

- Non-dimensionalising, we get

$$\frac{du}{d\tau} = Rv(1 - u) - u = f_1(u, v) \qquad \frac{dv}{d\tau} = R^*u(1 - v) - A^*v = f_2(u, v)$$

- This yields the nullclines

$$v = \frac{u}{R(1 - u)}, \quad u = \frac{A^*v}{R^*(1 - v)}$$

- Solving for the fixed points, we find fixed points

$$(u^*, v^*) = (0, 0), \quad \left(\frac{R - A^*}{R^*(R + 1)}, \frac{R^* - A^*}{R(R^* + A^*)} \right)$$

where the latter fixed point only exists when $R^*R - A^* > 0$, known as a threshold condition. Evaluating the Jacobian at the above fixed points and solving for their eigenvalues, we find that the trivial fixed point is unstable and the non-trivial fixed point is stable.

- Expressing the threshold as $(rN/a)(r^*N^*/a^*) > 1$, we can interpret this as: an epidemic can be avoided if the product of the maximum number of males that are infected for each infective female rN/a and r^*N^*/a^* is less than one.

2.3.2 Genetic control system

- We can model the protein concentration p with respect to the mRNA concentration m, and their degrading rates k_{1p} and k_{2m}. We also assume that mRNA presence leads to the creation of a protein with rate k_{3m}. The resulting ODE is then

$$\frac{dp}{dt} = k_3m - k_1p$$

$$\frac{dm}{dt} = h_1\frac{p^2}{H^2 + p^2} - k_2m$$

- Non-dimensionalising, we get

$$\frac{du}{d\tau} = av - bu$$

$$\frac{dv}{d\tau} = \frac{u^2}{1 + u^2} - v$$

- This yields the nullclines

$$v = \frac{b}{a}u, \quad v = \frac{u^2}{1 + u^2}$$

- Setting $\alpha = b/a$ and solving for the fixed points, we find three solutions

$$(u^*, v^*) = (0, 0), \left(\frac{1 \pm \sqrt{1 - 4\alpha^2}}{2\alpha}, \frac{1 \pm \sqrt{1 - 4\alpha^2}}{2} \right)$$

- Finding the Jacobian, and evaluating at $(0, 0)$, we find that it is stable. Solving for the eigenvalues of the other two fixed points, we find one is stable and the other is unstable.

- We find that bistability indicates that some initial concentration of protein and mRNA can see to it that the protein production to goes to zero or sustains itself at a level. This allows the gene to have a switching mechanism.

2.3.3 Competition between populations

- We model two populations of species competing for the same resource. We assume that in isolation each species evolves according to logistic growth and that when the other species is present, the death rate is proportional to the population size of the other. We thus have

$$\frac{dN_1}{dt} = r_1 N_1 \left(1 - \frac{N_1}{K_1} - b_{12} \frac{N_2}{K_1} \right)$$
$$\frac{dN_2}{dt} = r_2 N_2 \left(1 - \frac{N_2}{K_2} - b_{21} \frac{N_1}{K_2} \right)$$

- Non-dimensionalising, we get

$$\frac{du_1}{d\tau} = u_1(1 - u_1 - a_{12}u_2)$$
$$\frac{du_2}{d\tau} = \rho u_2(1 - u_2 - a_{21}u_1)$$

- This yields the nullclines

$$u_1(1 - u_1 - a_{12}u_2) = 0, \quad \rho u_2(1 - u_2 - a_{21}u_1) = 0$$

- We find that based on the values of a_{12} and a_{21}, the nullclines may either intersect or not. In fact, there are two cases when they do and two when they don't. There are four possible fixed points

$$(u^a st, v^*) = (0, 0), (0, 1), (1, 0), \left(\frac{1 - a_{12}}{1 - a_{12}a_{21}}, \frac{1 - a_{21}}{1 - a_{12}a_{21}} \right)$$

- In three of the four cases, one of the species goes extinct. This competition-induced extinction is known as the **principle of competitive exclusion**. We find that this depends on the competition coefficients and carrying capacities.

2.3.4 Predator-Prey systems (Lotka-Volterra)

- We aim to model populations of preys N and predators P that interact with each other. This can be written as

$$\frac{dN}{dt} = aN - bNP$$
$$\frac{dP}{dt} = -dP + cNP$$

where a, b, c, d are positive constants. The prey population grows with birth rate aN, while the predator population dies with rate $-dP$. Interactions between two populations allows the predator population to grow at rate cNP and the prey population to decrease with rate $-bNP$.

- Non-dimensionalising, we get

$$\frac{du}{d\tau} = u(1 - v)$$
$$\frac{dv}{d\tau} = \alpha v(u - 1)$$

- We find the fixed points

$$(u^*, v^*) = (0, 0), (1, 1)$$

- Solving for the Jacobian evaluated on the fixed points, we find that $(0, 0)$ is unstable but that $(1, 1)$ is a centre (of which linear analysis alone is insufficient).

- The solutions to the above equations show oscillatory behaviour occurring close to the fixed point of which persists even from far away. In fact, changing the initial condition defines each of these orbits.

- From this we can say that there is no natural oscillation in the population levels as different initial population sizes yield different oscillations. We also find that lowering the initial predator population results in larger peaks in their population size.

3 Oscillations and bifurcations

3.1 Existence of closed orbits (Poincaré-Bendixson Theorem)

- Suppose that

    1. R is a closed, bounded subset of the plane
    2. $d\mathbf{x}/dt = \mathbf{f}(\mathbf{x})$ is a continuously differentiable vector field on an open set containing R
    3. R does not contain any fixed points
    4. There exists a trajectory C confined in R (it starts and remains in R forever)

    Then either C is a closed orbit, or it spirals towards a closed orbit at $t \to \infty$.

- Typically, the fourth condition can be shown by choosing an R for which it is a **trapping set**, meaning that the flow points inward along the boundary ∂R, i.e. $\mathbf{f}(\mathbf{x}) \cdot \mathbf{n}(\mathbf{x}) < 0$ for all $x \in \partial R$.

3.1.1 More-realistic predator-prey system

- To fix the biologically unrealistic and mathematically undesirable properties of the Lotka-Volterra system, we can incorporate logistic growth and a nonlinear predation term

$$\frac{dN}{dt} = N\left(r\left(1 - \frac{N}{K}\right) - k\frac{P}{N + D}\right)$$
$$\frac{dP}{dt} = sP\left(1 - h\frac{P}{N}\right)$$

where r, K, k, D, s, h are positive constants.

- Here, the predation term is similar to spruce-budworm in that for low N, predation increases as the prey population increases but for large N predation is largely independent of N. Whereas, the predator population follows a logistic-like equation where the carrying capacity is proportional to the size of the prey population.

- Non-dimensionalising, we get

$$\frac{du}{d\tau} = u(1 - u) - \frac{auv}{u + d}$$
$$\frac{dv}{d\tau} = bv\left(1 - \frac{v}{u}\right)$$

- We find the nullclines

$$u = 0, \quad v = \frac{(1-u)(u+d)}{a}, \quad v = u, \quad v = 0$$

- We may construct a closed region R as a rectangle with endpoints $(0,0), (0.99, 0), (0, 1), (0.99, 1)$. Solving for the change in u and v on the boundaries, we find that the flow moves inwards.

- However, this set contains a fixed point. To account for this, we puncture the set by introducing an infinitesimally small circle around it and show that the flow still moves inwards. For this to occur, the point must be an unstable fixed point (saddle does not work). Looking at the Jacobian, we can find conditions for when this happens.

- A supercritical **Hopf bifurcation** occurs as we turn from getting a stable fixed point into an unstable node and a stable limit cycle.

3.2 Relaxation oscillators

- The Poincaré-Bendixson theorem could only suggest where a limit cycle exists but does not tell us anything about the radius, shape, nor period of the orbit.

- To do so, we consider a one-dimensional system

$$\frac{du}{dt} = f_1(u; v)$$

that exhibits bistability for a range of parameter v. We turn this into another variable and consider the system

$$\frac{du}{dt} = f_1(u, v)$$
$$\frac{dv}{dt} = \epsilon f_2(u, v)$$

- When $0 < \epsilon \ll 1$, then we can consider a quasi-steady approximation and so the solution will follow the nullcline $f_1(u, v) = 0$ until it reaches some point where it leaves the nullcline. Since v is a slow variable, the trajectory keeps a constant v and leaps to the other end of the nullcline moving in the opposite direction. Once again it flows and leaps back, forming a **relaxation oscillator limit cycle**.

3.3 Fitzhugh-Nagumo model

- The dimensionless version of which is given by

$$\frac{dv}{dt} = f(v) - w + I_a$$
$$\frac{dw}{dt} = bv - \gamma w$$

where $f(v) = v(a - v)(v - 1)$ and v and w represent the membrane potential and the ion conductance respectively.

- Here, v is the fast variable, whereas w is the slow variable. This exactly produces a relaxation oscillator whose orbit changes shape as parameters are modified.

- To approximate the period of the orbit, we only consider places where w is changing as the jumps between nullclines are near instantaneous.

  1. First, we determine the local minima and maxima of the nullcine by considering $df/dv = 0$, say (v_-, w_-) and (v_+, w_+)

  2. Next, we draw (horizontal as v is fast) lines from (v_-, w_-) and see where they intersect with the other nullcline, say (v_*, w_-). Similarly, say we end up at $(v_+ - 1 + a/2, w_+)$ from (v_+, w_+).

3. We compute the time T_1 it takes for the solution to move from v_* to v_+ and time T_2 for the solution to move from 1 to v_- along the nullclines. We do so by separating and integrating the differential equation for the slow variable, i.e.

$$\int_{w(v_*)}^{w(v_+)} \frac{dw}{v-w} = \int_0^{T_1} \gamma \, dt$$

then performing a substitution for dv and solving for T_1.

4. The total period is then given by $T = T_1 + T_2$.

3.4 Bifurcations

- We extend our idea of bifurcations to higher dimensions, particularly in the 2D case.

3.4.1 Saddle-node, transcritical and pitchfork bifurcations

- The three types of bifurcations found in one-dimensional systems can be extended to two dimensions with the addition of the equation

$$\frac{dy}{dt} = -y$$

This requires the flow to approach the x-axis for which the behaviour is similar to the one-dimensional case.

3.4.2 Hopf Bifurcations

- This bifurcation comes in two flavours: supercritical and subcritical.

  ○ The **supercritical** Hopf bifurcation involves a stable spiral becoming unstable simultaneously as a limit cycle emerges from it.

  ○ The **subcritical** Hopf bifurcation involves a stable spiral surrounded by an unstable cycle becoming unstable when the cycle collapses in on the fixed point.

- By performing a weakly nonlinear analysis of the system, i.e. expanding $\mathbf{f}(\mathbf{x}; \mu)$ to cubic order, solving for the eigenvectors of the Jacobian to derive the Stuart-Landau equation, and working in polar coordinates, we find that the Hopf bifurcation can be viewed as a pitchfork bifurcation for the radius of the limit cycle.

- Finding the fixed point corresponding to the radius, we find an approximate radius for the stable limit cycle.

3.4.3 Hopf bifurcation in the FItzhugh-Nagumo model

- Given the set of equations

$$\frac{dv}{dt} = f(v) - w + I_a$$
$$\frac{dw}{dt} = \gamma(v - w)$$

where $f(v) = v(a - v)(v - 1)$.

- Finding the Jacobian and its eigenvalues, we derive an expression for which the real roots are zero and we can solve for the frequency given by

$$\omega^2 = \gamma(1 - \gamma)$$

- When a Hopf bifurcation occurs, the fixed point will change from a stable spiral to an unstable spiral. Thus, at the bifurcation, we must have $\Re(\lambda_\pm) = 0$, and we write $\lambda_\pm = \pm i\omega$ where ω is the frequency.

- We can obtain a very good approximation of the period through $T = 2\pi/\omega$.

4 Spatial dynamics

- We attempt to introduce spatial variables into our models to efficiently capture spatial constraints involved in practice.

4.1 Reaction-diffusion equations

- We develop the theory first for $\mathbf{x} \in \mathbb{R}^3$ and then reduce it to cases of $x \in \mathbb{R}$ and $\mathbf{x} \in \mathbb{R}^2$.

- Consider an arbitrary region in space $\Omega \subset \mathbb{R}^3$ with outward-facing unit normal $\hat{\mathbf{n}}(\mathbf{x})$ of the boundary $\partial\Omega$. The total amount of chemicals in Ω at time t is given by

$$\int_\Omega u(\mathbf{x}, t) d^3\mathbf{x}$$

- This quantity changes in two ways: by evolving under some function $f(u, \mathbf{x}, t)$ within Ω or entering and leaving Ω through its boundary with motion given by the vector field $mathbf{J}(\mathbf{x}, t)$. Thus

$$\frac{d}{dt} \int_\Omega u(\mathbf{x}, t) d^3\mathbf{x} = \int_\Omega f(u, \mathbf{x}, t) d^3\mathbf{x} - \int_{\partial\Omega} \mathbf{J}(\mathbf{x}, t) \cdot \hat{\mathbf{n}}(\mathbf{x}) dS$$

where the latter integrand is the flux into Ω.

- Simplifying this by pushing the time-derivative inwards (since Ω does not change in time) in the LHS, using the divergence theorem to rewrite the second integral, and vanishing the integrand, we arrive at

$$\frac{\partial u}{\partial t} = f - \boldsymbol{\nabla} \cdot \mathbf{J}$$

- We consider the case when $\mathbf{J}$ describes the tendency for u to move from regions with higher values to lower values, i.e. in the direction opposite its gradient

$$\mathbf{J} = -D\boldsymbol{\nabla}u$$

where D is a positive constant called the **diffusion coefficient**. We thus arrive at

$$\frac{\partial u}{\partial t} = f + D\boldsymbol{\nabla}^2 u$$

4.2 Fisher-Kolmogorov (FK) Equation

- We model the spread of an advantageous gene mutation in a population. Here, we have

$$f(u) = ku(1 - u)$$

which is logistic growth with unit carrying capacity where u is the percentage of the population carrying the advantageous gene.

- We also consider the case of one spatial dimension so that $\nabla^2 \to \partial^2/\partial x^2$ yielding

$$\frac{\partial u}{\partial t} = ku(1 - u) + D\frac{\partial^2 u}{\partial x^2}$$

- Non-dimensionalising, we get

$$\frac{\partial u}{\partial \tau} = u(1 - u) + \frac{\partial^2 u}{\partial X^2}$$

4.2.1 Travelling waves

- Since $u = 0$ and $u = 1$ are fixed points of the logistic equation

$$\frac{du}{d\tau} = u(1 - u)$$

we say that these are **homogeneous steady solutions** of the spatially extended system

- We consider the FK equation with the conditions that

$$u \to 1 \text{ as } X \to -\infty, \quad u \to 0 \text{ as } X \to \infty$$

which requires the solution to transition from $u = 1$ to $u = 0$ over some region of space.

- Expecting that the transition region will move to the right, we search for a **travelling wave solution** which has the form

$$u(X, \tau) = U(\xi), \ \xi = X - c\tau$$

where the constant $c \geq 0$ is the wave speed, which is yet to be determined. This solution can be viewed as having a fixed shape shifted to the right by amount $c\tau$ at time τ.

- We have from this ansatz,

$$\frac{\partial u}{\partial \tau} = -c\frac{dU}{d\xi}, \quad \frac{\partial^2 u}{\partial X^2} = \frac{d^2 U}{d\xi^2}$$

which turns the FK equation into the second-order ODE

$$\frac{d^2 U}{d\xi^2} = -U(1 - U) - c\frac{dU}{d\xi}$$

that can be expressed as a system of first-order ODEs with $V = dU/d\xi$

$$\frac{dU}{d\xi} = V$$
$$\frac{dV}{d\xi} = -U(1 - U) - cV$$

- Performing linear stability analysis and only considering ranges for constants that make sense biologically, we find that $(0, 0)$ is a stable node and $(1, 0)$ is a saddle.

- Thus the FK equation can support travelling wave solutions with admissible wave speeds of $c \geq 2$.

4.2.2 Wave speed

- The above, however, does not give information regarding for which initial conditions $u(X, 0)$ will cause travelling waves to emerge nor the specific values of c that waves might have.

- Kolmogorov showed that if the initial condition satisfies

$$u(X, 0) = u_0(X) \geq 0, \quad u_0(X) = \begin{cases} 1 & \text{if } X \leq X_1 \\ 0 & \text{if } X \geq X_2 \end{cases}$$

with $X_1 < X_2$ and $u_0(X)$ is a continuous function of X in the interval (X_1, X_2), then the solution eventually evolves into the travelling wave solution with $U(\xi)$ with $c = 2$.

4.3 Spatial dynamics of predator-prey system

- Instead of describing spatial dynamics of an isolated popualtion, we examine how reaction-diffusion equations can be coupled to model interacting populations.

- Interactions are included by considering a system of PDEs, expressed as

$$\frac{\partial \mathbf{u}}{\partial t} = \mathbf{f} + \mathcal{D}\nabla^2 \mathbf{u}$$

where $\mathbf{u}(\mathbf{x}, t)$ and $\mathbf{f}(\mathbf{u}, \mathbf{x}, t)$ are vectors and now $\mathcal{D}$ is the diffusion matrix which is assumed to be diagonal, where $\mathcal{D}_{ii} = D_i$ the diffusion coefficient of a species i.

- Consider the system

$$\frac{\partial N}{\partial t} = rN\left(1 - \frac{N}{K}\right) - aNP + D_1 \frac{\partial^2 N}{\partial x^2}$$

$$\frac{\partial P}{\partial t} = bNP - cP + D_2 \frac{\partial^2 P}{\partial x^2}$$

as previously with the predator prey system but with the addition of diffusion for the populations to spread.

- Non-dimensionalising, we get

$$\frac{\partial u}{\partial \tau} = u\left(1 - u - v\right) + D\frac{\partial^2 u}{\partial X^2}$$

$$\frac{\partial v}{\partial \tau} = \alpha v(u - \beta) + \frac{\partial^2 v}{\partial X^2}$$

- We consider when $D = 0$ and thus have

$$\frac{\partial u}{\partial \tau} = u\left(1 - u - v\right)$$

$$\frac{\partial v}{\partial \tau} = \alpha v(u - \beta) + \frac{\partial^2 v}{\partial X^2}$$

In doing so, we set a constraint that preys are unable to move.

- First, we remove the diffusive term and simply consider the system of ODEs

$$\frac{du}{d\tau} = u\left(1 - u - v\right)$$

$$\frac{dv}{d\tau} = \alpha v(u - \beta)$$

- Though linear stability analysis, we find that the fixed points $(0,0)$ and $(1,0)$ are unstable, whereas $(\beta, 1-\beta)$ is a stable node when $4\alpha < \beta/(1-\beta)$ and a stable spiral for $4\alpha > \beta(1-\beta)$.

- Looking for travelling wave solutions of the form

$$u(X, \tau) = U(\xi), \quad v(X, \tau) = V(\xi)$$

with $\xi = X - c\tau$. Based on the fixed points of the ODE system, we impose

$$U \to 1, \ V \to 0, \ \text{as } \xi \to \infty, \quad U \to \beta \text{ and } V \to 1 - \beta, \ \text{as } \xi \to -\infty$$

- Substituting the travelling wave ansatz, we obtain

$$-c\frac{dU}{d\xi} = U(1 - U - V)$$

$$-c\frac{dV}{d\xi} = \alpha V(U - \beta) + \frac{d^2 V}{d\xi^2}$$

and setting $W = dV/d\xi$, we arrive at the three dimensional system

$$\frac{dU}{d\xi} = \frac{U}{c}(U + V - 1)$$

$$\frac{dV}{d\xi} = W$$

$$\frac{dW}{d\xi} = \alpha V(\beta - U) - cW$$

- When performing linear stabiliity analysis on the constrained fixed points $(1, 0, 0)$ and $(\beta, 1 - \beta, 0)$, we find the characteristic equation is not easily handled. However, we can solve for the local maxima and minima when α is zero and observe that the cubic is shifted upwards with positive α.

- We find that α reaches a critical value α_c for which one of the eigenvalues has multiplicity two. When $\alpha > \alpha_c$, we have one real and two complex unstable eigenvalues which causes oscillatory behaviour. When $\alpha \leq \alpha_c$, the unstable eigenvalue is real and so, as ξ increases, we move from $(U, V) = (\beta, 1 - \beta)$ to $(1, 0)$.

- Here, the wave speed is given by the minimum possible value

$$c^2 = 4\alpha(1 - \beta)$$

4.4 Spatial spread of epidemics

- We extend the SIS model to consider spatial dynamics with the following set of equations

$$\frac{\partial S}{\partial t} = -rSI + aI + D\frac{\partial^2 S}{\partial x^2}$$
$$\frac{\partial I}{\partial t} = rSI - aI + D\frac{\partial^2 I}{\partial x^2}$$

where the susceptibles and the infectives have the same diffusion coefficient. As we assume $N = S + I$ is constant, we thus have

$$\frac{\partial I}{\partial t} = rI(N - I) - aI + D\frac{\partial^2 I}{\partial x^2}$$

which can be rearranged to

$$\frac{\partial I}{\partial t} = kI\left(1 - \frac{I}{K}\right) + D\frac{\partial^2 I}{\partial x^2}$$

which, when writing $u = I/K$, yields the FK equation.

- Finding a travelling wave solution, we find that $c^2 < 4KD$ admits oscillatory solutions near $I = 0$ which would lead to a negative population size. Hence we have $c^2 \geq 4KD$ and the wave speed is $c = 2\sqrt{KD} = 2\sqrt{(rN - a)D}$.

- We can interpret this as: the spatial spread of the disease can be slowed by reducing the diffusion coefficient, by increasing the recovery rate, or by reducing the transmission contact.

4.4.1 Spread of rabies in a fox population

- We now consider a susceptible population that does not diffuse and an infective population that does not recover, but instead die. This describes the spread of rabies in a fox population

$$\frac{\partial S}{\partial t} = -rSI$$
$$\frac{\partial I}{\partial t} = rSI - aI + D\frac{\partial^2 I}{\partial x^2}$$

- Non-dimensionalising, we get

$$\frac{\partial s}{\partial tau} = -sh$$
$$\frac{\partial h}{\partial \tau} = sh - \alpha h + \frac{\partial^2 h}{\partial X^2}$$

- Removing the diffusive term and solving the ODE, we find that provided $h = 0$, the population size does not change.

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- We assume the infective population is spatially lcoalised, i.e.
$$h \to 0 \text{ as } x \to \pm\infty$$

- We thus have the boundary conditions
$$\frac{ds}{dz} \to 0 \text{ as } x \to -\infty, \quad s \to 1 \text{ as } x \to \infty$$

- Assuming the population are travelling waves and rearranging the terms, we arrive at the system
$$\frac{d\Sigma}{d\xi} = \frac{\Sigma H}{c}$$
$$\frac{dH}{d\xi} = P$$
$$\frac{dP}{d\xi} = -cP + \alpha H - \Sigma H$$

- We know we have a fixed point $(1, 0, 0)$. Examining its stability through the Jacobian, we find the eigenvalues
$$\lambda = 0, \ \lambda = \frac{1}{2}\left(-c \pm \sqrt{c^2 + 4(\alpha - 1)}\right)$$

- To avoid oscillatory solutions that produce negative population sizes, the wave speed must satisfy
$$c^2 \geq 4(1 - \alpha)$$

- This condition means $(1, 0, 0)$ is stable, which makes sense as the solution should tend to $(1, 0, 0)$ as $\xi \to \infty$.

4.5 Pattern formation

4.5.1 Turing instability

- Consider the general system of reaction diffusion equations
$$\frac{\partial u}{\partial t} = f(u, v) + D_1 \nabla^2 u$$
$$\frac{\partial v}{\partial t} = g(u, v) + D_2 \nabla^2 v$$

for morphogen concentrations u and v in a region of space $\Omega \subset \mathbb{R}^3$. We assume no morphogens enter Ω through $\partial\Omega$ and impose no-flux boundary conditions
$$\hat{\mathbf{n}} \cdot \nabla u = 0 \text{ and } \hat{\mathbf{n}} \cdot \nabla v = 0$$

for $\mathbf{x} \in \partial\Omega$. We are interested in what conditions must be met for the system to emit patterns.

- First, consider the system of ODEs
$$\frac{du}{dt} = f(u, v)$$
$$\frac{dv}{dt} = g(u, v)$$

  ○ For patterns to emerge, this system must have a stable fixed point (u^*, v^*) and so we must have
  $$\tau = trace(\mathbf{J}) < 0, \quad \Delta = det(J) > 0$$

- Now, we consider the stability of the homogeneous steady solutions, i.e. by adding perturbations ϵ as in
$$u(\mathbf{x}, t) = u^* + \epsilon U(\mathbf{x}, t)$$
$$v(\mathbf{x}, t) = v^* + \epsilon V(\mathbf{x}, t)$$

where $0 < \epsilon \ll 1$ and see if the perturbations $U(\mathbf{x}, t), V(\mathbf{x}, t)$ grow or decay with time.

- For an ODE system, they clearly decay as (u^*, v^*) is stable. However, this is not necessarily the case for a PDE system.
- In fact, for patterns to emerge, the homogeneous solution must be unstable from their spatial dependencies.

- Substituting back into the original equation and Taylor expanding f and g about the perturbations for $e \ll 1$, we get

$$\frac{\partial \mathbf{W}}{\partial t} = \mathbf{J}\mathbf{W} + \mathcal{D}\nabla^2 \mathbf{W}$$

where $\mathbf{W} = (U, V)^T$ and $\mathcal{D}$ is the diagonal diffusion matrix.

- Using ansatz,

$$\mathbf{W}(\mathbf{x}, t) = \boldsymbol{\zeta} F(t)\phi(\mathbf{x})$$

where ζ is a constant vector, $F(t)$ is a function of time, and $\phi(\mathbf{x})$ is a function of space. Substituting and rearranging, we get

$$\frac{\boldsymbol{\zeta}}{F}\frac{dF}{dt} = \mathbf{J}\boldsymbol{\zeta} + \frac{\mathcal{D}\boldsymbol{\zeta}}{\phi}\nabla^2\phi$$

- Since $\mathbf{J}\boldsymbol{\zeta}$ is independent of both t and $\mathbf{x}$, we have the following eigen value problems

$$\frac{dF}{dt} = \lambda F$$

with solution $F = e^{\lambda t}$ and

$$\nabla^2\phi + k^2\phi = 0, \ \mathbf{x} \in \Omega$$
$$\hat{\mathbf{n}} \cdot \nabla\phi = 0, \ \mathbf{x} \in \partial\Omega$$

which leads to the third eigenvalue problem

$$(\mathbf{J} - k^2\mathcal{D})\boldsymbol{\zeta} = \lambda\boldsymbol{\zeta}$$

- Hence we find a solution

$$\mathbf{W} = \boldsymbol{\zeta}\phi(\mathbf{x})e^{\lambda t}$$

where $\lambda(k^2)$ satisfies

$$\det(\lambda I - \mathbf{J} + k^2\mathcal{D}) = 0$$

- Thus if $\Re(\lambda) > 0$ then perturbations with spatial dependence will grow, leading to pattern formation. Otherwise, it decays.

4.5.2 Conditions for pattern formation

- In order for $\Re(\lambda) > 0$, the matrix $\mathbf{M} = \mathbf{J} - k^2\mathcal{D}$ must either have

$$trace(\mathbf{M}) = J_{11} + J_{22} - k^2(D_1 + D_2) > 0$$

or, alternatively,

$$det(\mathbf{M}) = (J_{11} - k^2D_1)(J_22 - k^2D_2) - J_{21}J_{12} < 0$$

- However, $J_{11} + J_{22} = trace(J) < 0$ as the ODE fixed point is stable, and since $k^2.D_1, D_2 > 0$, then $trace(\mathbf{M}) < 0$.

- Hence we need $det(\mathbf{M}) < 0$ to get $\Re(\lambda) > 0$. Solving for the critical values $k_\pm^2$ which make $det(\mathbf{M}) = 0$, we get

$$k_\pm^2 = \frac{(D_2J_{11} + D_1J_{22}) \pm \sqrt{(D_2J_{11} + D_1J_{22})^2 - 4D_1D_2det(\mathbf{J})}}{2D_1D_2}.$$

- For $k_\pm^2$ to be real and positive, we must have

$$D_2 J_{11} + D_1 J_{22} > 0$$
$$(D_2 J_{11} + D_1 J_{22})^2 - 4 D_1 D_2 det(\mathbf{J}) > 0$$

We then find that $D_2 > D_1$ is a necessity and $k_+^2 = k_-^2$ corresponds to the bifurcation point for when the spatially homogeneous solution becomes unstable. Hence we have the critical value of k^2

$$k_c^2 = \sqrt{\frac{det(\mathbf{J})}{D_1 D_2}}$$

4.6 Pattern formation in one and two-dimensions

- Consider the dimensionless reaction-diffusion system

$$\frac{\partial u}{\partial t} = a - u + u^2 v + \nabla^2 u$$
$$\frac{\partial v}{\partial t} = b - u^2 v + d \nabla^2 u$$

where a, b, d are positive.

- Solving for the ODE case, we find that

$$J(u^*, v^*) = \begin{bmatrix} \frac{b-a}{a+b} & (a+b)^2 \\ -\frac{2b}{a+b} & -(a+b)^2 \end{bmatrix}.$$

- As we want stability of fixed points, we must have

$$trace(J(u^*, v^*)) = J_{11} + J_{22} < 0$$
$$det(J(u^*, v^*)) = J_{11} J_{22} - J_{21} J_{12} > 0$$

the latter of which is satisfied as $det(J) = (a+b)^2$, whereas the first yields the condition

$$b - a < (a+b)^3$$

- As we want $\Re(\lambda) > 0$, we must have

$$D_1 J_{22} + D_2 J_{11} > 0$$
$$(D_2 J_{11} + D_1 J_{22})^2 - 4 D_1 D_2 det(J) > 0$$

the first of which yields the conditions

$$d > (a+b)^3/(b-a), \quad b > a$$

and the second resulting in

$$(d(b-a) - (a+b)^3)^2 > 4d(a+b)^4$$

4.6.1 In one-dimension

- In the one-dimensional case, we have the system

$$\frac{\partial u}{\partial t} = a - u + u^2 v + \frac{\partial^2 u}{\partial x^2}$$
$$\frac{\partial v}{\partial t} = b - u^2 v + d\frac{\partial^2 v}{\partial x^2}$$

for $x \in \Omega = (0, L)$. The no-flux boundary conditions are

$$\frac{\partial u}{\partial x}(0) = \frac{\partial u}{\partial x}(L) = \frac{\partial v}{\partial x}(0) = \frac{\partial v}{\partial x}(L) = 0$$

- Linearising about the homogeneous steady-state solution, we get

$$\frac{\partial \mathbf{W}}{\partial t} = \mathbf{J}\mathbf{W} + \mathcal{D}\frac{\partial^2 \mathbf{W}}{\partial x^2}$$

  subject to the constraints

$$\frac{\partial \mathbf{W}}{\partial x}(0) = \frac{\partial \mathbf{W}}{\partial x}(L) = 0$$

- With the ansatz $\mathbf{W} = \boldsymbol{\zeta} F(t)\phi(x)$, we yield two eigen value problems

$$\frac{dF}{dt} = \lambda F$$

  and

$$\frac{\partial^2 \phi}{\partial x^2} + k^2 \phi = 0$$

$$\frac{\partial \phi}{\partial x}(0) = \frac{\partial \phi}{\partial x}(L) = 0$$

- Solving for ϕ that satisfies the boundary conditions and the differential equation, we find

$$\phi(x) = \cos\left(\frac{n\pi x}{L}\right)$$

- And, so the most general form of the perturbation is

$$\mathbf{W}(x,t) = \sum_n a_n \boldsymbol{\zeta}_n \mathrm{e}^{\lambda(n\pi/L)t} \cos\left(\frac{n\pi x}{L}\right)$$

- To make $det(\mathbf{M}) = 0$ where $\mathbf{M} = \mathbf{J} - k^2\mathcal{D}$, we can solve a range for k that establishes patterns.

4.6.2   In two dimensions

- Now consider the two dimensional case where we have

$$\frac{\partial u}{\partial t} = a - u + u^2 v + \frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2}$$

$$\frac{\partial v}{\partial t} = b - u^2 v + d\left(\frac{\partial^2 v}{\partial x^2} + \frac{\partial^2 v}{\partial y^2}\right)$$

  with a domain $\Omega = (0, L) \times (0, H)$.

- The no-flux boundary conditions are

$$\frac{\partial u}{\partial x}(0, y) = \frac{\partial u}{\partial x}(L, y) = \frac{\partial v}{\partial x}(0, y) = \frac{\partial v}{\partial x}(L, y) = 0$$

$$\frac{\partial u}{\partial y}(x, 0) = \frac{\partial u}{\partial y}(x, H) = \frac{\partial v}{\partial y}(x, 0) = \frac{\partial v}{\partial y}(x, H) = 0$$

- The fixed points, J, and conditions for pattern formation and range of k^2 are the same as above. However, the realised vlues of k will now make use of a ϕ which is a solution to

$$\frac{\partial^2 \phi}{\partial x^2} + \frac{\partial^2 \phi}{\partial y^2} + k^2 \phi = 0$$

$$\frac{\partial \phi}{\partial x}(0, y) = \frac{\partial \phi}{\partial x}(L, y) = \frac{\partial \phi}{\partial x}(x, 0) = \frac{\partial \phi}{\partial x}(x, H) = 0$$

- Using separation of variables, we find that

$$\phi_{n,m}(x, y) = \cos\left(\frac{n\pi x}{L}\right)\cos\left(\frac{m\pi y}{H}\right)$$

where n, m are positive integers. Solving for the eigenvalue k^2, as above, we find

$$k_{n,m}^2 = \left(\frac{n\pi}{L}\right)^2 + \left(\frac{m\pi}{H}\right)^2$$

and so the general solution is

$$\mathbf{W}(x, y, t) = \sum_n \sum_m a_{n,m} \boldsymbol{\zeta}_{n,m} e^{\lambda(k_{n,m}^2)t} \cos\left(\frac{n\pi x}{L}\right) \cos\left(\frac{m\pi y}{H}\right).$$

- Stripes arise when $H \ll L$ whereas spots occur when $H \approx L$.

5 Stochastic processes

- We attempt to introduce stochasticity into our models rather than simply consider the deterministic cases.

5.1 Continuous-Time Markov Chains (CTMC)

- We consider a random variable $X(t)$ that depends on time t and takes values in the natural numbers (i.e. $0, 1, \ldots$).

5.1.1 Transition probabilities

- We define the transition probabilities as

$$p_{ji}(t - s) = P(X(t) = j \mid X(s) = i)$$

for $s < t$. The matrix $P(t) = (p_{ji}(t))$ is called the transition matrix.

- These transition probabilities satisfy the Chapman-Kolmogorov equations

$$p_{ji}(t + s) = \sum_{k=0}^{\infty} p_{jk}(t) p_{ki}(s)$$

which in matrix form is $\mathbf{P}(t + s) = \mathbf{P}(t)\mathbf{P}(s)$. We also have

$$\sum_{j=0}^{\infty} p_{ji}(t) = 1, \ t \geq 0$$

- A **Poisson process** $(X_t)_{t \geq 0}$ is defined by

  1. At $t = 0$, $X(0) = 0$.
  2. For small Δt, the transition probabilities are given by

  $$p_{i+1,i}(\Delta t) = \lambda \Delta t + o(\Delta t)$$
  $$p_{i,i}(\Delta t) = 1 - \lambda \Delta t + o(\Delta t)$$
  $$p_{j,i}(\Delta t) = o(\Delta t)$$

  where $j \geq i + 2$. If $j < i$, then $p_{j,i}(\Delta t) = 0$.

- We say $f(\Delta t) = o(\Delta t)$ if

$$\lim_{\Delta t \to 0} \frac{f(\Delta t)}{\Delta t} = 0$$

5.1.2 Generator matrix

- We assume that $\mathbf{P}(0) = I$. Then the entries of the generator matrix q_{ji} are defined as

$$q_{ji} = \lim_{\Delta t \to 0^+} \frac{p_{ji}(\Delta t) - p_{ji}(0)}{\Delta t} = \lim_{\Delta t \to 0^+} \frac{p_{ji}(\Delta t)}{\Delta t}$$

for $i \neq j$, and

$$q_{ii} = \lim_{\Delta t \to 0^+} \frac{p_{ii}(\Delta t) - p_{ii}(0)}{\Delta t} = \lim_{\Delta t \to 0^+} \frac{p_{ii}(\Delta t) - 1}{\Delta t}$$

Since $\sum_{j=0}^{\infty} p_{ji}(\Delta t) = 1$, then $1 - p_{ii}(\Delta t) = \sum_{j \neq i} p_{ji}(\Delta t)$ and so

$$q_{ii} = -\sum_{j \neq i} q_{ji}$$

- We have

$$Q = \lim_{\Delta t \to 0^+} \frac{P(\Delta t) - I}{\Delta t}$$

and so for sufficiently small Δt, we can say

$$p_{ji}(\Delta t) = \delta_{ji} + q_{ji}\Delta t + o(\Delta t)$$

5.1.3 Generator matrix for the Poisson process

- The matrix is one whose entries are given by

$$q_{ii} = -\lambda, \quad q_{i+1,i} = \lambda$$

5.2 Kolmogorov differential equations

- First consider the Chapman-Kolmogorov equation

$$p_{ji}(t + \Delta t) = \sum_{k=0}^{\infty} p_{jk}(\Delta t)p_{ki}(t)$$

substituting the expression for small Δt,

$$p_{ji}(t + \Delta t) = \sum_{k=0}^{\infty} [\delta + jk + q_{jk}\Delta t + o(\Delta t)]p_{ki}(t)$$

as row sums are one and we have a kronecker delta, we rearrange to get

$$\frac{p_{ji}(t + \Delta t) - p_{ji}(t)}{\Delta t} = \sum_{k=0}^{\infty} q_{jk}p_{ki}(t) + \frac{o(\Delta t)}{\Delta t}$$

and taking the limit we arrive at

$$\frac{dp_{ji}}{dt} = \sum_{k=0}^{\infty} q_{jk}p_{ki}(t)$$

which in matrix form is

$$\frac{d\mathbf{P}}{dt} = Q\mathbf{P}$$

This is known as the **forward Kolmogorov equation**.

- In component form, we have

$$\frac{dp_i}{dt} = \sum_{k=0}^{\infty} q_{ik}p_k(t) = \sum_{k=0}^{\infty}\sum_{i=0}^{\infty} q_{ik}p_k z^i$$

5.2.1 Forward Kolmogorov equation for the Poisson process

- By definition of the Poisson process, we have $p_i(t) = p_{i0}(t)$ and so

$$\frac{dp_0}{dt} = -\lambda p_0$$

$$\frac{dp_i}{dt} = -\lambda p_{i-1} - \lambda p_i, \quad \text{for } i \geq 1$$

- The initial condition $X(0) = 0$ yields

$$p_0(t) = e^{-\lambda t}$$

- Substituting onto the forward equation and solving for $p_1(t)$, we have

$$p_1(t) = \lambda t e^{-\lambda t}$$

and, in fact, we find the general rule

$$p_i(t) = \frac{(\lambda t)^i}{i!} e^{-\lambda t}$$

- Computing the mean and variance

$$m(t) = \sum_{i=0}^{\infty} i \frac{(\lambda t)^i}{i!} e^{-\lambda t} = \lambda t$$

$$\sigma^2(t) = \sum_{i=0}^{\infty} i^2 \frac{(\lambda t)^i}{i!} e^{-\lambda t} - (\lambda t)^2 = \lambda t$$

shows that $p_i(t)$ is indeed Poisson distributed with rate λt.

- Alternatively, we can solve for the **generating function** given by

$$\mathcal{P}(z, t) = \sum_{i=0}^{\infty} p_i(t) z^i$$

- With this, we can solve for the exact values and moments

$$p_i(t) = \frac{1}{i!} \left. \frac{\partial^i \mathcal{P}}{\partial z^i} \right|_{z=0}$$

$$m(t) = \left. \frac{\partial \mathcal{P}}{\partial z} \right|_{z=1}$$

$$\sigma^2(t) = \left. \frac{\partial^2 \mathcal{P}}{\partial z^2} \right|_{z=1} + \left. \frac{\partial \mathcal{P}}{\partial z} \right|_{z=1} - \left(\left. \frac{\partial \mathcal{P}}{\partial z} \right|_{z=1} \right)^2.$$

- We can derive a PDE for $\mathcal{P}(z, t)$ using the forward Kolmogorov equation

$$\frac{\partial \mathcal{P}}{\partial t} = \sum_{i=0}^{\infty} \frac{dp_i}{dt} z^i$$

  ○ For a Poisson process, note that we have

$$\frac{dp_0}{dt} = -\lambda p_0$$

$$\frac{dp_i}{dt} = -\lambda p_i + \lambda p_{i-1}, \quad \text{for } i > 0$$

  ○ And so substituting onto the PDE,

$$\frac{\partial P}{\partial t} = -\lambda \sum_{i=0}^{\infty} p_i(t) z^i + \lambda \sum_{i=1}^{\infty} p_{i-1}(t) z^i.$$

reindexing terms, we find

$$\frac{\partial \mathcal{P}}{\partial t} = \lambda (z - 1) \mathcal{P}$$

of which with initial condition $\mathcal{P}(z, 0) = 1$, we get the solution

$$\mathcal{P}(z, t) = e^{\lambda(z-1)t}$$

5.3 Simple birth process

- We consider the simple birth process governed by the infinitesimal transition probabilities

$$p_{i+j,i}(\Delta t) = \begin{cases} \lambda i \Delta t + o(\Delta t), & j = 1 \\ 1 - \lambda i \Delta t + o(\Delta t), & j = 0 \\ o(\Delta t), & j \geq 2 \\ 0, & j < 0 \end{cases}$$

- Here λ is the birth rate per capita.

5.3.1 Mean and variance

- We find that the non-zero entries of the generator matrix are given by

$$q_{ii} = -\lambda i, \quad q_{i+1,i} = \lambda i$$

and thus the forward Kolmogorov equation is

$$\frac{dp_{Nj}}{dt} = -\lambda N p_{Nj}$$

$$\frac{dp_{ji}}{dt} = \lambda(j-1)p_{j-1,i} - \lambda j p_{ji}, \quad \text{for } i \geq N+1$$

- The probability generating function is given by

$$\mathcal{P}(z,t) = \frac{z^N e^{-N\lambda t}}{[1 - z(1 - e^{-\lambda t})]^N}$$

- Solving for the mean and variance, we find

$$m(t) = Ne^{\lambda t}, \quad \sigma^2(t) = Ne^{2\lambda t}(1 - e^{-\lambda t})$$

5.4 Simple birth and death process

- We consider the simple birth and death process governed by the infinitesimal transition probabilities

$$p_{i+j,i}(\Delta t) = \begin{cases} \lambda i \Delta t + o(\Delta t), & j = 1 \\ 1 - (\lambda + \mu)i \Delta t + o(\Delta t), & j = 0 \\ \mu i \Delta t + o(\Delta t), & j = -1 \\ o(\Delta t), & j \neq -1, 0, 1 \end{cases}$$

- Here, μ is the death rate per capita.

5.4.1 Mean and Variance

- We find that the non-zero entries of the generator matrix are

$$q_{ii} = -(\lambda + \mu)i, \quad q_{i+1,i} = \lambda i, \quad q_{i-1,i} = \mu i$$

- The probability generating function is given by

$$\mathcal{P}(z,t) = \left(\frac{e^{(\mu-\lambda)t}(\lambda z - \mu) - \mu(z-1)}{e^{(\mu-\lambda)t}(\lambda z - \mu) - \lambda(z-1)} \right)^N, \lambda \neq \mu.$$

- Solving for the mean and variance, we find

$$m(t) = Ne^{(\lambda-\mu)t}, \quad \sigma^2(t) = N\frac{\lambda+\mu}{\lambda-\mu}e^{(\lambda-\mu)t}\left(e^{(\lambda-\mu)t} - 1\right)$$

- We also can calculate

$$p_0(t) = \left(\frac{\mu - \mu e^{(\mu-\lambda)t}}{\lambda - \mu e^{(\mu-\lambda)t}} \right)^N$$

and see that, by letting $t \to \infty$,

$$p_0(\infty) = \begin{cases} 1, & \text{if } \lambda \leq \mu \\ \left(\frac{\mu}{\lambda}\right)^N, & \text{if } \lambda > \mu \end{cases}$$

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5.4.2 Stationary probability distribution for a birth and death process

- Note that the generator matrix is given by

$$
Q = \begin{bmatrix}
-\lambda_0 & \mu_1 & & & \\
\lambda_0 & -(\mu_1 + \lambda_1) & \mu_2 & & \\
& \lambda_1 & -(\mu_2 + \lambda_2) & \mu_3 & \\
& & \ddots & & \ddots
\end{bmatrix}.
$$

- Note that the stationary probability distribution is given by $Q\pi = 0$ with $\sum_{i=0}^{\infty} \pi_i = 1$ and $\pi_i \geq 0$. Evaluating $Q\pi = 0$, we get

$$
0 = -\lambda_0 \pi_0 + \mu_1 \pi_1
$$
$$
0 = \lambda_{i-1}\pi_{i-1} - (\lambda_i + \mu_i)\pi_i + \mu_{i+1}\pi_{i+1}
$$

- We can show by induction or solve recursively then that

$$
\pi_i = \frac{\lambda_0 \lambda_1 \cdots \lambda_{i-1}}{\mu_1 \mu_2 \cdots \mu_i} \pi_0
$$

where we have that

$$
\pi_0 = \left(1 + \sum_{i=1}^{\infty} \frac{\lambda_0 \lambda_1 \cdots \lambda_{i-1}}{\mu_1 \mu_2 \cdots \mu_i} \right)^{-1}
$$

5.5 Logistic growth process

- Consider the original logistic equation

$$
\frac{dn}{dt} = rn\left(1 - \frac{n}{K}\right)
$$

- Treating the RHS as the difference between thebirth and death rates, i.e.

$$
\lambda_n - \mu_n = rn - \frac{r}{K}n^2
$$

we can non-dimensionalise the rates to be

$$
\lambda_i = b_1 i + b_2 i^2 > 0
$$
$$
\mu_i = d_1 i + d_2 i^2 > 0
$$

where b_1, b_2, d_1, d_2 are positive constants

- We proceed with the same calculations as before and get

$$
\frac{dp_i}{dt} = -(\lambda_i + \mu_i)p_i(t) + \lambda_{i-1}p_{i-1}(t) + \mu_{i+1}p_{i+1}(t).
$$

- We can obtain the mean by multiplying above by i and summing by i to get

$$
\frac{dm}{dt} = -\sum_i i(\lambda_i + \mu_i)p_i(t) + \sum_i i\lambda_{i-1}p_{i-1}(t) + \sum_i i\mu_{i+1}p_{i+1}(t).
$$

which when re-indexed, yields

$$
\frac{dm}{dt} = \sum_i \left((b_1 - d_1)i - (d_2 - b_2)i^2 \right) p_i(t),
$$

- Since $\sigma^2(t) = \sum_i i^2 p_i(t) - m^2(t)$, we finally get

$$
\frac{dm}{dt} = rm\left(1 - \frac{m}{K}\right) - r\frac{\sigma^2(t)}{K}
$$

where $r = (b_1 - d_1)$ and $K = (b_1 - d_1)/(d_2 - b_2)$

- The above equation models the mean as having a logistic growth but with an extra term capturing the nonlinear dependence of the birth and death rates on the population size.

5.6 Stochastic SIS model

- Consider the original SIS model

$$\frac{dS}{dt} = -\frac{\beta}{N}SI + \gamma I$$
$$\frac{dI}{dt} = \frac{\beta}{N}SI - \gamma I$$

Using $S = N - I$, we have then

$$\frac{dI}{dt} = \frac{\beta}{N}I(N - I) - \gamma I$$

- We can ascertain from above: the birth and death rates

$$\lambda_i = \begin{cases} \frac{\beta}{N}i(N - i) & \text{for } i = 0, 1, \ldots, N \\ 0 & i > N \end{cases}$$

and

$$\mu_i = \gamma i$$

5.7 Quasistationary probability distribution

- As with all the models before, we observe that $\lim_{t \to \infty} p_0(t) = 1$ as $X = 0$ is an absorbing state.

- To avoid this effect, we remove the $X = 0$ state by having $\mu_1 = 0$ and so the altered generator matrix $\tilde{Q}$ becomes the same as before but with the first row and column removed.

- The quasistationary probability distribution is then given by $\tilde{Q}\tilde{\pi} = 0$ with $\sum_{i=1}^{\infty} \tilde{\pi}_i = 1$. Solving yields

$$\tilde{\pi}_i = \frac{\lambda_1 \lambda_2 \cdots \lambda_{i-1}}{\mu_2 \mu_3 \cdots \mu_i}\tilde{\pi}_1$$