

Mathematical physiology

PROBLEM SHEET 0. [2018]

1. The Lotka–Volterra system is given by

$$\dot{x} = x(1 - y),$$

$$\dot{y} = \mu y(x - 1).$$

Write the equations in terms of $X = x - 1$ and $Y = y - 1$, and show that there is a first integral of the equation of the form

$$\mu w(X) + w(Y) = E, \quad (*)$$

where E is constant. If the minimum value of $E = 0$, give the definition of $w(X)$, and draw its graph.

We now wish to show that the trajectories satisfying $(*)$ form closed loops in the (X, Y) plane. To show this, define a function $r(\xi)$ by

$$\xi = +\sqrt{w(r)} \quad \text{if } r > 0,$$

$$\xi = -\sqrt{w(r)} \quad \text{if } r < 0,$$

and show that $r(\xi)$ is a smooth, monotonically increasing function, give its behaviour as $\xi \rightarrow \pm\infty$, and draw its graph.

Now consider the transformation from (X, Y) to (ξ, η) space given by $X = r(\xi)$, $Y = r(\eta)$. Show that the trajectories in (X, Y) space are mapped to the curves

$$\mu\xi^2 + \eta^2 = E,$$

and deduce that these form closed loops in (ξ, η) space and hence also (X, Y) space.

2. For the system

$$\dot{x} = \frac{x}{1+x} [F(x) - y],$$

$$\dot{y} = \beta[G(x) - y],$$

where

$$F(x) = (k - x)(1 + x), \quad G(x) = \frac{bx}{1 + x},$$

where $k > 1$, $b > k^2$ and $\beta > 0$, show that there is at least one fixed point (x_0, y_0) in the first quadrant. Assuming that $F'(x_0) > 0$, that this fixed point is unique, and that it is oscillatorily unstable, draw the nullclines of the system, and draw the trajectories in the phase plane.

Construct a bounding box for the trajectories, and show using the Poincaré–Bendixson theorem that the system has at least one stable limit cycle.

[*Hint: you can assume there is a small circle C surrounding the fixed point on which all trajectories are directed outwards; the bounding box then consists of an inner curve C , and an outer curve which consists of straight (horizontal or vertical) lines, together with a curve A in the part of the quadrant where $\dot{x} < 0$, $\dot{y} < 0$. Show that in this region, when x is small,*

$$\frac{dy}{dx} \approx \frac{\beta y}{x(y-k)} > \frac{\beta k}{x(y-k)},$$

and use this information to construct a suitable curve A to complete the construction of B .]

3. For a cubic nonlinearity, the travelling wave solutions of the nonlinear diffusion equation

$$u_t = f(u) + u_{xx}$$

satisfy the phase plane equations

$$U' = -V,$$

$$V' = f(U) - V,$$

where $U' = \frac{dU}{d\xi}$, $V' = \frac{dV}{d\xi}$, and

$$(U, V) \rightarrow (1, 0) \quad \text{as } \xi \rightarrow -\infty,$$

$$(U, V) \rightarrow (0, 0) \quad \text{as } \xi \rightarrow \infty,$$

where we take

$$f(U) = 2U(U-1)(a-U),$$

with $0 < a < 1$.

Carry out a phase plane analysis in the case $a < \frac{1}{2}$, assuming that $c > 0$ and that a connecting trajectory exists, and draw the phase plane trajectories.

[*Harder.*] In order to prove that there is a unique connecting trajectory, we can use a monotonicity argument.

Show that the separatrix arriving at $(0, 0)$ is determined by

$$\frac{dV}{dU} = c - \frac{f(U)}{V}, \quad V \approx \lambda_0 U \quad \text{as } U \rightarrow 0, \quad (*)$$

where

$$\lambda_0 = \frac{1}{2}[c + \{c^2 - 4f'(0)\}^{1/2}].$$

Show that λ_0 is a monotonically increasing function of c . Deduce that if two solutions of (*) are denoted V_1 and V_2 , corresponding to two values $c_1 < c_2$, then for small U , $V_1 < V_2$.

Show that if $V_1 = V_2$ at some $U > 0$, then necessarily $V_1' \geq V_2'$ at that point. Using (*), show that this contradicts the assumption that $c_1 < c_2$. Hence deduce that $V(U; c)$ is a monotonically increasing function of $c > 0$.

Show that for large c , $V \approx cU$, so that in particular $V(1, c) > 0$ and the arriving separatrix at the origin is above the leaving separatrix at $(1, 0)$ for large c .

Show that for small c ,

$$\frac{1}{2}V^2 + \int_0^U f(U) dU \approx 0,$$

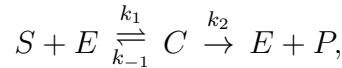
and deduce that the separatrix arriving at $(0, 0)$ passes through $(U_0, 0)$ where U_0 is the minimum positive value such that $\int_0^{U_0} f(U) dU = 0$. Deduce that if $U_0 < 1$, the arriving separatrix is below the leaving separatrix for small c .

Show that

$$U_0 = \frac{2}{3}(a+1) - \frac{2}{3} \left[\left(\frac{1}{2} - a \right) (2-a) \right]^{1/2},$$

and deduce that U_0 exists and is < 1 iff $a < \frac{1}{2}$. Hence show that there is a unique connecting trajectory between $(1, 0)$ and $(0, 0)$ with $c > 0$ if $a < \frac{1}{2}$, but no such trajectory exists for any $c > 0$ if $a > \frac{1}{2}$.

4. Derive a suitably scaled form of the Michaelis-Menten model for the reaction

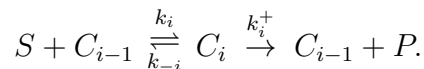


and show that it depends on the parameters

$$K = \frac{k_{-1} + k_2}{k_1 S_0}, \quad \lambda = \frac{k_2}{k_1 S_0}, \quad \varepsilon = \frac{E_0}{S_0},$$

where S_0 and E_0 are the initial values of S and E . If $\varepsilon \ll 1$, show that the solution consists of an outer layer in which $t = O(1)$, and an inner layer in which $t = O(\varepsilon)$, and find explicit approximations for these. Hence show that S decreases linearly initially, but exponentially at large times.

5. An enzyme has n binding sites for a substrate S . If the enzyme complexes with j bound sites are denoted as C_j , write down the rate equations for the concentrations of S , P and C_j , $j = 0, 1, \dots, n$, where $C_0 = E$, satisfying the reactions



Deduce that

$$C_0 = E_0 - \sum_1^n C_i,$$

where E_0 is the initial enzyme present. Use the quasi-steady state assumption to show that $R_i = 0$, $i = 1, \dots, n$, where

$$R_i = k_i S C_{i-1} - (k_{-i} + k_i^+) C_i,$$

and deduce that the reaction rate $r = dP/dt$ is given approximately by

$$r = \frac{E_0 \sum_{r=1}^n k_r^+ \phi_r S^r}{1 + \sum_{j=1}^n \phi_j S^j},$$

where

$$\phi_j = \prod_{i=1}^j \frac{1}{K_i}, \quad K_i = \frac{k_{-i} + k_i^+}{k_i}.$$

Deduce that if $k_1 \rightarrow 0$ with $k_1 k_n$ finite, the reaction rate is approximated by the Hill equation

$$r = \frac{k_n^+ E_0 S^n}{\prod_{i=1}^n K_i + S^n}.$$

6. Suppose a population has a size distribution $\phi(a, t)$, where a is age and t is time: $\phi \delta a$ is the number of individuals with ages between a and $a + \delta a$. The birth rate $b(a)$ depends on age, as does the mortality rate $m(a)$. Show that

$$\phi_t + \phi_a = -m\phi,$$

and explain why the birth rate appears in the boundary condition

$$\phi(0, t) = \int_0^\infty b(a) \phi(a, t) da.$$

What is assumed about ϕ as $a \rightarrow \infty$?

Show that the steady size distribution with age of a population is given by the solution of the linear integral equation

$$\phi(a) = \int_0^\infty G(a, \xi) \phi(\xi) d\xi,$$

where $G(a, \xi)$ should be specified.

Use the method of characteristics to show that for $t > a$, the solution for ϕ is

$$\phi = \int_0^\infty b(\xi) \phi(\xi, t - a) d\xi \exp \left[- \int_0^a m(\eta) d\eta \right].$$

Deduce an approximate equation for ϕ if $b(\xi) = 0$ for $\xi < t_m$, $b = B$ (constant) for $t_m < \xi < t_m + t_b$, $b = 0$ for $\xi > t_m + t_b$, where t_b is small, and hence show that if $x(t) = \phi(t_m, t)$, then

$$x(t) \approx \Lambda x(t - t_m),$$

where $\Lambda = B t_b \exp \left[- \int_0^{t_m} m(\eta) d\eta \right]$. Why is this obvious?