Mathematical physiology

Problem sheet 0

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

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

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

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

Sketch the trajectories in the positive quadrant of the phase plane.

2. For the system

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

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

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

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

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

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

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

where

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

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,

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

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

Show that

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

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

$$S + E \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} C \overset{k_2}{\to} E + P,$$

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, $j = 0, 1, \ldots, n$, where $C_0 = E$, satisfying the reactions

$$S + C_{i-1} \underset{k_{-i}}{\overset{k_i}{\rightleftharpoons}} C_i \overset{k_i^+}{\to} C_{i-1} + P.$$

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 $k_1 \to 0$ 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 $a \to \infty$?

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?