Modelling in Biology
2007 Examination Answers

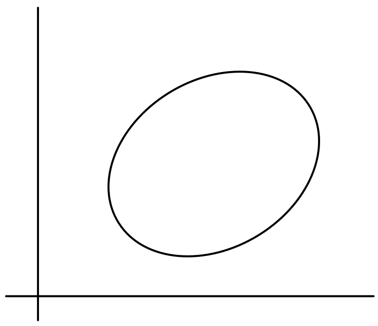
Question 1

A fractal object is a geometric shape that can be subdivided into parts, each of which is a reduced copy of the whole. One mathematical example of a fractal is the cantor set where has an infinite number of points but zero length. Such a cantor set is the ternary cantor set generated by continually removing the middle third of a set of line segments. What is left is an infinite number of small points but with zero length. A biological example of fractals can be found in plants such as ferns and broccoli as well as snowflakes.

If the dynamics of a system are chaotic and the system is bounded in three dimensional space, then the attractor of the system must be a fractal. For example, the Lorentz system is a bounded system whose trajectories must continue forever but never cross each other. For this to occur, the trajectories must organize itself such that it takes up zero volume, the main characteristic of a fractal geometry. There is no other possible method to enclose an infinite extending line within a bounded space. The fractal geometry of the Lorentz system can be easily visualized by considering the Poincaré section of the 3D trajectory phase portrait. The points at which the trajectory intersect the plane for a fractal.

Question 2

A limit cycle is an attracting periodic solution and is represented in the phase plane by a closed line as shown in the figure below. A limit cycle can only occur in systems of more than one dimension.



Considering the system $\ddot{x} + kx = 0$, this cannot have a limit cycle as there is no attractor in the solution. It can be shown that the fixed point at (0,0) when plot on the $\dot{x}$ vs $\dot{y}$ phase plane is a center. However, with every initial condition, this would produce another center and a different radius, so there is no overall attractor of the system. Hence, the system does not have a limit cycle even though there are periodic solutions.

Question 3

Part a)

Consider the following system:

$$\dot{x} = -\frac{r}{2} - \frac{1}{4} + (1+r)x - x^2$$

Finding the fixed points, we set $\dot{x} = 0$ and solve for x^*.

$$x^* = \frac{(1+r) \pm \sqrt{(1+r)^2 - 4\left(\frac{r}{2} + \frac{1}{4}\right)}}{2}$$

$$x^* = \frac{(1+r) \pm \sqrt{1 + 2r + r^2 - 2r - 1}}{2}$$

$$x^* = \frac{(1+r) \pm r}{2} = \frac{1}{2}, \frac{1+2r}{2}$$

Stability of the fixed points can be found by differentiating the equation and substituting our fixed points. Let $\dot{x} = f(x) = -\frac{r}{2} - \frac{1}{4} + (1+r)x - x^2$

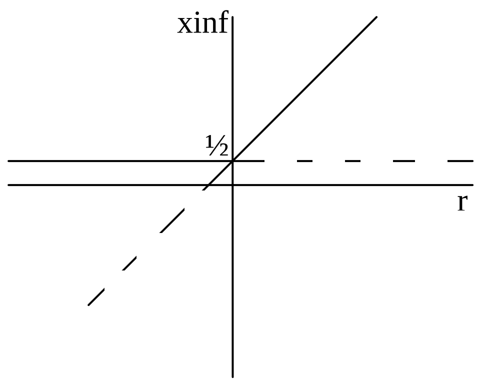
$$f'(x) = (1+r) - 2x$$

$$f'(\frac{1}{2}) = r$$

$$f'(\frac{1+2r}{2}) = -r$$

We can see from the above that the bifurcation occurs when *r* = 0 and that the fixed point at ½ becomes unstable when *r* is positive and vice versa for the other fixed point.

The bifurcation diagram is shown below. This is a transcritical bifurcation where the two fixed points collide and exchange stabilities.

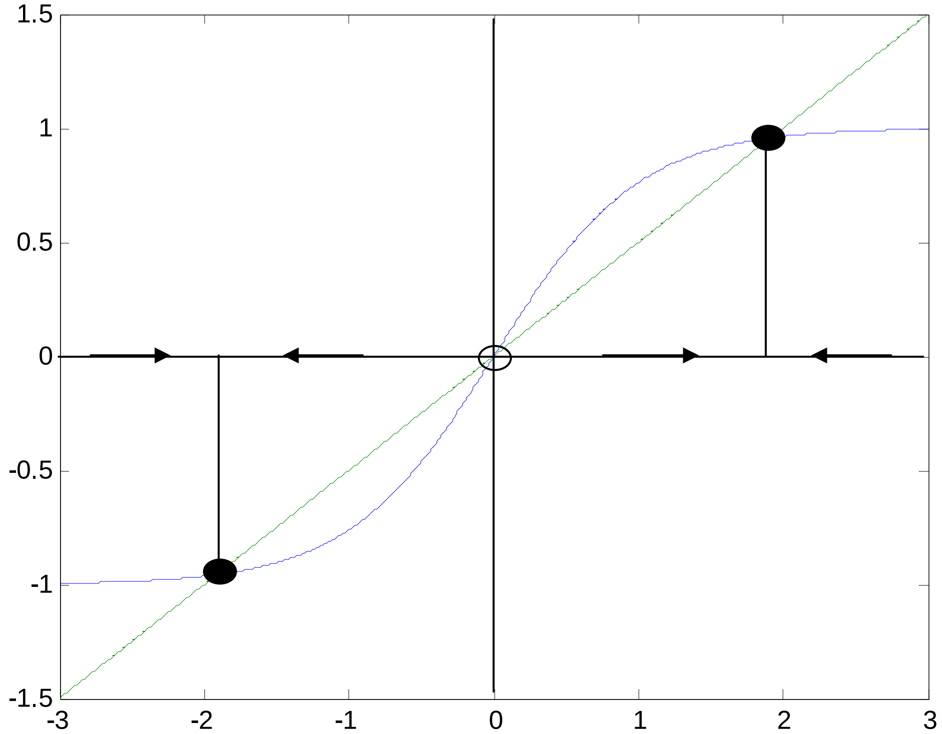


Part b)

Consider the system

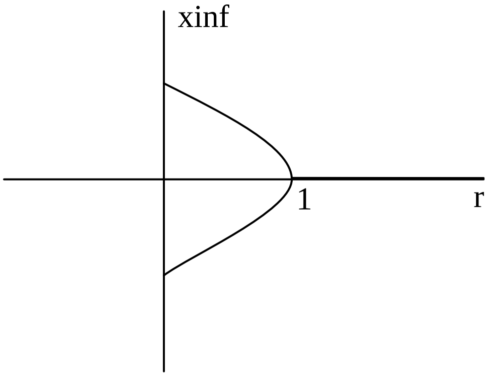
$\dot{x} = \tanh(x) - rx$

Since this is a one-dimensional system, we can plot the two parts separately and come up with the flows of the problem



We know that at 0, the slope of tanh(x) = 1, so the bifurcation occurs when r = 1. Any r value below that will only have 1 fixed point and any r value above that will have three fixed points.

The bifurcation diagram is shown below. Below 0, only the 0 fixed point is present and will be unstable. This is a pitchfork bifurcation.



Question 4

A monte carlo method is a stochastic algorithm which incorporate a degree of uncertainty into the differential equation. A model incorporating a monte carlo simulation will usually contain a deterministic portion and a stochastic portion which includes the generation of a random number that is attenuated by the mean and standard deviation of the noise that needs to be modeled. These are usually used to model real world examples such as variability in the stock market as well as kinetic reactions involving only a few molecules and cannot be accurately described by continuum models.

In the code, three variables are defined and random numbers assigned to them. To see this more simply, we'll define them as follows:

x = pp(1)
y = pp(2)
z = pp(3)

From the code we can also see that we are using the rand() function which can only take values from 0 to 1. Hence, our variables are also bounded: $0 < x < 1$, $0 < y < 2$, and $0 < z < 1$. The total volume of our box is hence 1 x 2 x 1 = 2.

The conditional statement implements the following:

If $x^2 + \frac{1}{4}y^2 + z^2 \leq 1$, then Q is incremented by 2. If not, then Q is not incremented.
The code in effect performs a volume integration of the function. By setting each variable to 0 in turn, we can see that the shape of the graph is an ellipsoid. However, due to our constraints, we will only be taking half of the volume. We can do this integration by the disc method by ignoring the variable z for the moment.

$$x = \sqrt{1 - \frac{1}{4}y^2}$$

$$Volume = \pi \int x^2 dy = \pi \int_0^2 1 - \frac{1}{4}x^2\ dy$$

$$Volume = \frac{4\pi}{3}$$

However, we notice that the final value P is actual the proportion of points that hit inside the volume and not the actual volume of the half-ellipsoid. The volume which we are "throwing darts at" is actually 2 x (1 x 2 x 1) = 4, so the value of P as Nfinal approach infinity is:

$$\lim_{Nfinal \to \infty} = \frac{\pi}{3}$$

Question 5

Consider the following system:

$$\dot{x} = 1 - (b+1)x + ax^2y$$
$$\dot{y} = bx - ax^2y$$

Find all the fixed points in the system and classify their stability as a function of the parameters a and b.

The fixed points in the system are given by $\dot{x} = \dot{y} = 0$.

$$0 = 1 - (b+1)x + ax^2y$$
$$0 = bx - ax^2y$$

Adding the two equations:

$$0 = 1 - (b+1)x + bx$$
$$1 - x = 0$$
$$x = 1$$

$$0 = b(1) - a(1)y$$
$$y = \frac{b}{a}$$

Hence, only one fixed point at $(1, \frac{b}{a})$.

To evaluate the stability, we turn to the Jacobian

$$Jac = \begin{pmatrix} -(b+1) + 2ay & ax^2 \\ b - 2ay & -ax^2 \end{pmatrix}$$

Evaluated at the fixed point

$$Jac = \begin{pmatrix} b-1 & a \\ -b & -a \end{pmatrix}$$

To obtain stability, we look at the tau and delta values

$$\tau = b - 1 - a$$
$$\Delta = -a(b-1) + ab = a$$

Since $a > 0$, then delta will always be positive, ruling out a saddle node. Whether the fixed point is stable or unstable depends on the value of tau. Where it changes stability is when tau = 0, or when $b = 1 + a$. Hence, if $b > 1 + a$, tau is greater than zero, and hence the fixed point is unstable. Likewise, if $b < 1 + a$, then tau is less than zero, and hence the fixed point is stable.

The Hopf bifurcation occurs when there is a change in behavior of the fixed point such that it goes from a stable fixed point to an unstable fixed point with the emergence of a limit cycle.

This value, as calculated above by setting tau = 0, is when $b = 1 + a$. Here, we must assume that with the emergence of the unstable fixed point, that the system has a limit cycle attractor and does not just go to infinity. As the value of *b* increases, we still remain in the unstable region and the limit cycle continues to increase. If *b* continues to increase such that $\tau^2 > 4\Delta$, then the fixed point becomes an unstable node. This does not exclude the function from not having a limit cycle, it's only that local stability analysis around the fixed point is such that it looks like an unstable node. Global stability analysis would be required to determine the presence of a limit cycle as *b* continues to increase.

Proving the existence of the limit cycle depends on us first finding a boundary region such that it contains no fixed points, that $\dot{x}$ and $\dot{y}$ are continuously differentiable everywhere in the region, and that all trajectories enter the bounded region and do not exit (Poincaré-Bendixson Theorem). If these all hold true, then there must be a limit cycle within the bounded region. How does the amplitude and shape of the limit cycle change as *b* becomes larger? To answer this question, we can look at the eigenvalues of the system when the limit cycle first appears. The eigenvalues are calculated from the Jacobian matrix evaluated at the fixed point such that:

$$\begin{vmatrix} b-1-\lambda & a \\ -b & -a-\lambda \end{vmatrix} = 0$$

$$0 = (b-1-\lambda)(-a-\lambda) + ab$$
$$0 = \lambda^2 + (a-b+1)\lambda + a$$

$$\lambda = \frac{-(a+1-b) \pm \sqrt{(a-b+1)^2 - 4a}}{2}$$

At the Hopf bifurcation, b = a + 1 and our eigenvalues reduce to:

$$\lambda = \frac{\pm\sqrt{-4a}}{2} = \pm i\sqrt{a} = \pm i\sqrt{b-1}$$

We can clearly see here that for the existence of a limit cycle, $b > 1$. The size of the limit cycle depends upon the magnitude of the imaginary part of the eigenvalue, and from the above equation, we can see that the size scales with $\sqrt{b-1}$. When *b* is close to the Hopf bifurcation, the limit cycle is circular in shape. As we increase *b* further, we can no longer look at the local stability analysis we have just performed and we can no longer justify whether or not the limit cycle is circular in shape or not. More likely than not, the limit cycle will being to deform as *b* increases since it is bounded by the *a* and *b* axes on the phase plane.

Question 6

The biophysical explanation of the variables:

C_m = the membrane capacitance generated by the buildup of ions on both sides of the plasma membrane

V_m = membrane potential, the potential difference between the inside of the cell and the outside bulk fluid

G_{Na} = conductance of the sodium ions which is dependent upon voltage-gated ion channels (which is hence dependent upon the voltage)

G_K = conductance of the potassium ions which is also dependent upon voltage-gated ion channels

E_{Na}, E_K = membrane potentials generated by the barrier membrane for each ion

G_L = conductance to take into account the leaky membrane. This does not depend on the voltage and is modelled as a fixed value resistor and not a potentiometer

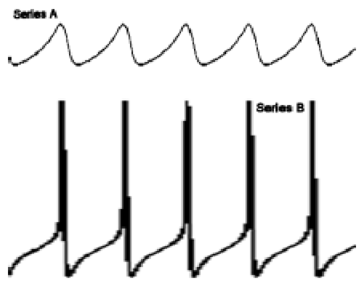
E_L = the leaky voltage, generated by the movement of ions by diffusion across the membrane

$I_{Na,K,L}$ = the current that flow through the membrane due to all the phenomenon listed above

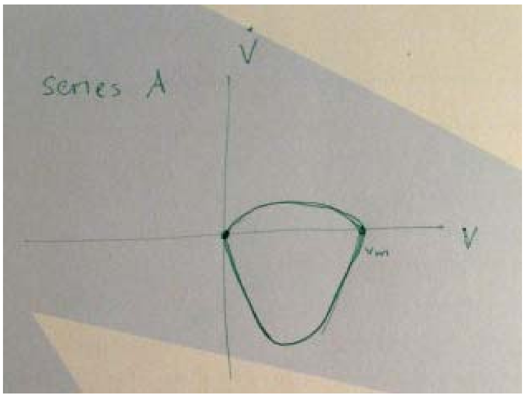
The total equation for the circuit is shown below:

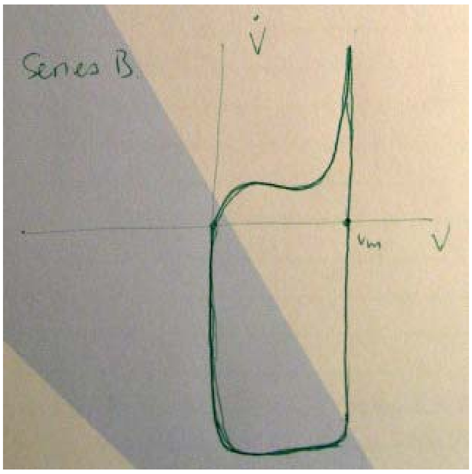
$$C_m \frac{dV_m}{dt} = G_{Na}(V - E_{Na}) + G_K(V - E_K) + G_L(V - E_L)$$

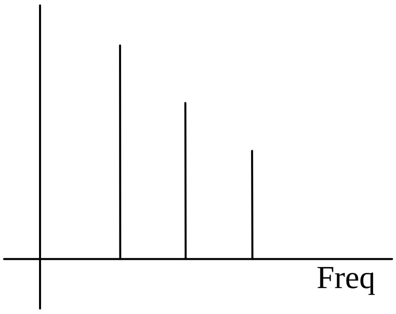
The variables *m*, *n*, and *h* are non-measurable voltage dependent parameters that were included to fit the observed data. These are internal variables that cannot be modified but are needed to explain the behaviour of the system. Although these three variables were initially shown to be "good fits" for the observed data, they were subsequently explained by the voltage gated ion channel phenomena.

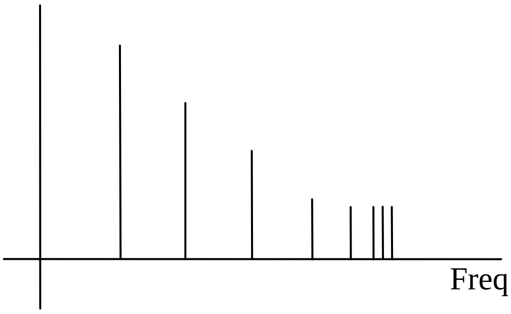


What do the phase portraits of these two series look like?









We notice that in series A, the limit cycle is more gentle since the gradient is not very large relative to series B. In series B, we notice that the gradient becomes almost infinity and then reverts to almost negative infinity very quickly leading to what looks like the asymptote. Also, we notice that right after the gradient turns, series B quickly return back to the zero value with little change in the gradient, explaining the flat bottom section in the phase plane.

With respect to the power spectrum, both spectra will have a similar large peak at the dominant frequency seen in both series. However, it is the presence of higher frequencies that sets series B apart from series A. These frequencies are there because of the spikes. In effect, the power spectra looks at the fourier transform of the function. Recall that for a delta function, the fourier transform is a uniform distribution of all frequencies. We can relate series B to almost being a delta function, and hence, we'll see the presence of higher frequencies than series A.