concentration of S exceeds a certain threshold. Let $g(t)$ denote the concentration of the gene product, and assume that the concentration s_0 of S is fixed. The model is

$$\dot{g} = k_1 s_0 - k_2 g + \frac{k_3 g^2}{k_4^2 + g^2}$$

where the k's are positive constants. The production of g is stimulated by s_0 at a rate k_1, and by an *autocatalytic* or positive feedback process (the nonlinear term). There is also a linear degradation of g at a rate k_2.

a) Show that the system can be put in the dimensionless form

$$\frac{dx}{d\tau} = s - rx + \frac{x^2}{1+x^2}$$

where $r > 0$ and $s \geq 0$ are dimensionless groups.

b) Show that if $s = 0$, there are two positive fixed points x^* if $r < r_c$, where r_c is to be determined.

c) Assume that initially there is no gene product, i.e., $g(0) = 0$, and suppose s is slowly increased from zero (the activating signal is turned on); what happens to $g(t)$? What happens if s then goes back to zero? Does the gene turn off again?

d) Find parametric equations for the bifurcation curves in (r,s) space, and classify the bifurcations that occur.

e) Use the computer to give a quantitatively accurate plot of the stability diagram in (r,s) space.

For further discussion of this model, see Lewis et al. (1977); Edelstein–Keshet (1988), Section 7.5; or Murray (2002), Chapter 6.

3.7.6 (Model of an epidemic) In pioneering work in epidemiology, Kermack and McKendrick (1927) proposed the following simple model for the evolution of an epidemic. Suppose that the population can be divided into three classes: $x(t)$ = number of healthy people; $y(t)$ = number of sick people; $z(t)$ = number of dead people. Assume that the total population remains constant in size, except for deaths due to the epidemic. (That is, the epidemic evolves so rapidly that we can ignore the slower changes in the populations due to births, emigration, or deaths by other causes.)

Then the model is

$$\begin{aligned}\dot{x} &= -kxy \\ \dot{y} &= kxy - ly \\ \dot{z} &= ly\end{aligned}$$

where k and l are positive constants. The equations are based on two assumptions:

(i) Healthy people get sick at a rate proportional to the product of x and y. This would be true if healthy and sick people encounter each other at a rate proportional to their numbers, and if there were a constant probability that each such encounter would lead to transmission of the disease.

(ii) Sick people die at a constant rate l.

The goal of this exercise is to reduce the model, which is a *third-order system*, to a first-order system that can analyzed by our methods. (In Chapter 6 we will see a simpler analysis.)

a) Show that $x + y + z = N$, where N is constant.

b) Use the $\dot{x}$ and $\dot{z}$ equation to show that $x(t) = x_0 \exp(-kz(t)/l)$, where $x_0 = x(0)$.

c) Show that z satisfies the first-order equation $\dot{z} = l[N - z - x_0 \exp(-kz/l)]$.

d) Show that this equation can be nondimensionalized to

$$\frac{du}{d\tau} = a - bu - e^{-u}$$

by an appropriate rescaling.

e) Show that $a \geq 1$ and $b > 0$.

f) Determine the number of fixed points u^* and classify their stability.

g) Show that the maximum of $\dot{u}(t)$ occurs at the same time as the maximum of both $\dot{z}(t)$ and $y(t)$. (This time is called the ***peak*** of the epidemic, denoted t_{peak}. At this time, there are more sick people and a higher daily death rate than at any other time.)

h) Show that if $b < 1$, then $\dot{u}(t)$ is increasing at $t = 0$ and reaches its maximum at some time $t_{\text{peak}} > 0$. Thus things get worse before they get better. (The term ***epidemic*** is reserved for this case.) Show that $\dot{u}(t)$ eventually decreases to 0.

i) On the other hand, show that $t_{\text{peak}} = 0$ if $b > 1$. (Hence no epidemic occurs if $b > 1$.)

j) The condition $b = 1$ is the *threshold* condition for an epidemic to occur. Can you give a biological interpretation of this condition?

k) Kermack and McKendrick showed that their model gave a good fit to data from the Bombay plague of 1906. How would you improve the model to make it more appropriate for AIDS? Which assumptions need revising?

For an introduction to models of epidemics, see Murray (2002), Chapter 10, or Edelstein–Keshet (1988). Models of AIDS are discussed by Murray (2002) and May and Anderson (1987). An excellent review and commentary on the Kermack–McKendrick papers is given by Anderson (1991).

c) Find an equation for the homoclinic orbit that separates closed and nonclosed trajectories.

6.5.3 Find a conserved quantity for the system $\ddot{x} = a - e^x$, and sketch the phase portrait for $a < 0$, $a = 0$, and $a > 0$.

6.5.4 Sketch the phase portrait for the system $\ddot{x} = ax - x^2$ for $a < 0$, $a = 0$, and $a > 0$.

6.5.5 Investigate the stability of the equilibrium points of the system $\ddot{x} = (x - a)(x^2 - a)$ for all real values of the parameter a. (Hints: It might help to graph the right-hand side. An alternative is to rewrite the equation as $\ddot{x} = -V'(x)$ for a suitable potential energy function V and then use your intuition about particles moving in potentials.)

6.5.6 (Epidemic model revisited) In Exercise 3.7.6, you analyzed the Kermack–McKendrick model of an epidemic by reducing it to a certain first-order system. In this problem you'll see how much easier the analysis becomes in the phase plane. As before, let $x(t) \geq 0$ denote the size of the healthy population and $y(t) \geq 0$ denote the size of the sick population. Then the model is

$$\dot{x} = -kxy, \qquad \dot{y} = kxy - ly$$

where $k, \ell > 0$. (The equation for $z(t)$, the number of deaths, plays no role in the x, y dynamics so we omit it.)

a) Find and classify all the fixed points.
b) Sketch the nullclines and the vector field.
c) Find a conserved quantity for the system. (Hint: Form a differential equation for dy/dx. Separate the variables and integrate both sides.)
d) Plot the phase portrait. What happens as $t \to \infty$?
e) Let (x_0, y_0) be the initial condition. An *epidemic* is said to occur if $y(t)$ increases initially. Under what condition does an epidemic occur?

6.5.7 (General relativity and planetary orbits) The relativistic equation for the orbit of a planet around the sun is

$$\frac{d^2u}{d\theta^2} + u = \alpha + \varepsilon u^2$$

where $u = 1/r$ and r, θ are the polar coordinates of the planet in its plane of motion. The parameter α is positive and can be found explicitly from classical Newtonian mechanics; the term εu^2 is Einstein's correction. Here ε is a very small positive parameter.

a) Rewrite the equation as a system in the (u, v) phase plane, where $v = du/d\theta$.
b) Find all the equilibrium points of the system.