BioMath - 1-D dynamics- August 31, 2015

1. **Brobdingnag**. Suppose that the birth rate in the country Brobdingnag is proportional to the current population, with some fixed proportionality constant b (in units of year^{-1}). And suppose that the death rate is also proportional to the current population, with constant d.

   • Write down the differential equation for the overall rate of change of the population $p(t)$, i.e., what is $\dot{p}(t)$?

   • What are the conditions (i.e., relative values of b and d) under which a population of zero individuals would be a stable point for Brobdingnag? What are the conditions under which zero individuals is an unstable point?

   • If $b = 0.2$ and $d = 0.1$, how long does it take for the population to double?

   It turns out that Brobdingnagians are choosing to have very few children these days, with the result that although d remains at $d = 0.1$, the value of b has fallen to $b = 0.05$. In response, the Brodingnaginian king has started encouraging immigration, which comes in at a constant rate of m people per year.

   • What is the differential equation for $p(t)$ now? What is the value of m such that the Brobdingnagian population would stabilize at 20 million people?

   • Use Euler integration (namely, $p(t + \delta t) \approx p(t) + \dot{p}(t)\delta t$) in Matlab to numerically obtain the growth in population for $b = 0.05, d = 0.1, m = 2$ million, starting from $p(0) = 1$ million. Solve the same equation analytically, and plot the two solutions together. Start with a timestep size $\delta t = 0.1$ years. Now change the step size. What happens when $\delta t > 20$ years? How about $\delta t > 40$ years?

2. **Bistable membrane potential.**

   As the neuroscientists amongst you either know or will soon learn, NMDA channels are transmembrane proteins that are glutamate receptors (their extracellular part can bind to he neurotransmitter glutamate), and in addition they have the particular charm of being also voltage-dependent. That is, the electrical resistance of these channels depends not only on how much glutamate is bound, but also on the transmembrane voltage itseld. This is because NMDA channels are blocked by extracellular magnesium ions; when the intracellular voltage becomes depolarized (i.e., positive) enough, this pushes the positively charged magnesium ions away from the channel, and allows the NMDA channel to open, and thus reduces its electrical resistance. The net effect is that the current that the NMDA channel lets in when glutamate is bound to it can be described by the nonlinear voltage-dependent function:

$$I_{NMDA} = g_{NMDA} \frac{1}{1 + 0.15e^{-0.08V}} (E_{NMDA} - V)$$

where V is the neuron's membrane potential, measured in millivolts, and $E_{NMDA} \approx 0$ mV. You're studying a neuron that –like all neurons– also has a constitutive leak current (formed by other channels in the membrane), such that

$$I_{leak} = g_{leak}(E_{leak} - V)$$

The voltage equation is

$$C_m \frac{dV}{dt} = I_{NMDA} + I_{leak}$$

Use $E_{leak} = -80$ and, for simplicity, let's use units where $C_m = 1, g_{NMDA} = 1,$ and $g_{leak} = 0.2$.

• Plot $\frac{dV}{dt}$ as a function of V. Identify the fixed points. Which are stable and which are unstable? Comment on the biological implications of what you found.

Some authors have suggested that these properties of NMDA channels may be related to short-term memory (e.g., Lisman, Fellous, and Wang, 1998).

3. **The perils of Euler integration**

   Consider the equation $\dot{x} = -2x$.

   • Consider the iteration rule $x(t + \Delta t) = (1 - k\Delta t)x(t)$, where k is a positive constant. What happens to x as a function of time if $k\Delta t < 1$? What happens if $1 < k\Delta < 2$? What happens if $2 < k\Delta t$? (Feel free to use Matlab to simulate the integration rule and see the results for yourself, but at the end of it, the goal is to understand the results you got, not simply observe them in Matlab.)

   • Use Euler integration ($x(t + \Delta t) = x(t) + \Delta t\dot{x}(t)$) to plot $x(t)$ for t running from 0 to 5, starting at $x(t = 0) = 5$. Use a variety of values of Δt. What do you observe? Is there a value of Δt at which the behavior qualitatively changes? Can you relate what you find here to what you found in the previous bullet point?

4. **Oscillations**

   Consider the equation

$$\dot{x} = \lambda x \tag{1}$$

• Plot x as a function of time for complex λ, for the following cases: (1) λ is purely imaginary, its real component is zero. (2) λ has positive real component, and negative imaginary component. (3) λ has positive real component, and positive imaginary component. (4) λ has negative real component, and negative imaginary component. (5) λ has negative real component, and positive imaginary component.

5. **Diagonal multi-dimensional dynamics**

   Suppose you have a set of one-dimensional differential equations, $\dot{x}_i = \lambda_i x$. Write the set of λ_i into a diagonal matrix,

   $$D = \begin{pmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & ... \end{pmatrix}$$

   You can then think of your set of independent differential equations as a single vector differential equation,

   $$\dot{\mathbf{x}} = D\mathbf{x} \tag{2}$$

   • Thinking in these mutlidimenstional terms, what are the conditions under which the multi-dimensional origin, $\mathbf{x} = 0$, is a stable point? What happens if some λ_i are less than zero and others are greater than zero?

   • Suppose you were using Euler integration to numerically solve equation (2), and let's say one of the λs is negative: $\lambda_i < 0$. What happens when $-2 < \lambda_i \Delta t < -1$? What happens when $\lambda_i \Delta t < -2$? How does this relate to the "perils of Euler integration" question above?

6. **Bistable membrane potential continued**

   Let's investigate the NMDA current, from problem 2 above, but now using Matlab.

   • Write a program that uses Euler integration (namely, $V(t + \delta t) = V(t) + \delta t \frac{dV}{dt}$) to solve

   $$\frac{dV}{dt} = I_{NMDA} + I_{leak} + \eta$$

   where η is a random number, drawn independently from a Gaussian (i.e., normal) distribution with mean 0 and standard deviation $\sigma\sqrt{\delta t}$, where δt is your integration timestep and σ is a parameter that controls the magnitude of the noise.

   • Display the results of your program with an animation: plot $\frac{dV}{dt}$ vs V, and on that plot putting a big blue dot that indicates the current value of V (and consequently the current value of $\frac{dV}{dt}$, as goven by equation (1)). To plot the dot, you can use the command

```
handle = line(V, Vdot, 'b.'); drawnow
```

And then after each timestep of your program you can update the position of the dot by using

```
set(handle, 'XData', newV, 'YData', newVdot); drawnow
```

(The `drawnow` command tells Matlab "go ahead and display everything you haven't displayed yet; that is, flush your display commands buffer."). We use the `set` command as above to make the animation will be smoother. It'll have less flicker than if you cleared your axes and replotted everything. Finally, if the animation moves too fast to properly see it, you might want to use the `pause` command to slow it down.

• Run your program over a few simulated seconds for different values of σ, each time starting from $V(0) = -75$. For each of the values of σ, plot a histogram of the values of V that you got over the simulation. Can you find a value of σ for which this histogram has two peaks? Where are the two peaks? Comment on what you observe.

• Write a function that, given $V(0)$ and the magnitude of an injected current, I_{inj}, computes what the value of $V(20)$ is. Plot two lines: $V(20)$ as a function of I_{inj} for $V(0) = -75$, and $V(20)$ as a function of I_{inj} for $V(0) = +5$. What is the significance fo the two lines being separate? What you've plotted is what is known as a classic hysteresis curve.