Lecture 6: Nonlinear Systems Analysis

Today we learn methods of analyzing how the behavior of a nonlinear system is affected by parameter values. We will discuss nondimensional analysis, which allows us to reduce the number of parameters in a system to a small number of essential nondimensional parameters, which can be used to identify important relationships in a system. This simplifies our job of understanding how to characterize how the system responds to changes in these parameters, using bifurcation and sensitivity analysis. We will learn common bifurcation diagrams for system with one nondimensional parameter, which helps us categorize system dynamics.

Nondimensional analysis:

Nondimensional analysis is a tool we can apply to both linear and nonlinear models. After we build a model (that is, once we have mathematical equations), it is usually possible to simplify the model by nondimensionalization. The nondimensional form usually has fewer parameters, and allows us to understand the relationships between parameters, so is more amenable to analysis. Also, the characteristic time constants we calculate are very helpful for making sure we run a simulation for the right amount of time (eg 5X the longest time constant). While we learned to identify time constants in linear ODEs, we can't use those methods for nonlinear ODEs or PDEs.

SPICE Procedure for nondimensionalizing a model.

1. Define the unknown **S**caling **P**arameter that relates each dependent and independent variable to a new nondimensional variable (τ, i in this example): $\tau = \frac{t}{c_t},\ i = I/c_I$. ($c_t$ will be the characteristic time constant). The scaling parameters have the same units as the original variables, making the newly defined variables unitless, or nondimensional.
2. **I**nsert these nondimensional variables into the original equation and simplify.
3. Set the **C**oefficients of each term to one to solve for the new scaling parameters (c_t, c_I). If this is not possible for all the coefficients, you will set one or more of the coefficients to a new nondimensional parameter.
4. **R**ewrite the **E**quations new model succinctly, with its relationship to the original variables and parameters. Now you should have a new equation in which all variables and parameters are nondimensional (have no units.)

Example: recall the electric circuit from Lecture 2:

$$\frac{dI_2}{dt} = \frac{V_a(t)}{CR_2R_1} - \frac{R_1 + R_2}{CR_2R_1} I_2(t)$$

Now we want to nondimensionalize it.

1) Nondimensional variables definitions:

   $\tau = \frac{t}{c_t}$, $u = I_2/c_I$, which means $t = \tau c_t$, $I_2 = c_I u$, and $dt = d\tau c_t$, $dI_2 = c_I du$

2) Insert these into the original model:

$$\frac{c_I}{c_t}\frac{du}{d\tau} = \frac{V_a(t)}{CR_2R_1} - \frac{R_1 + R_2}{CR_2R_1} c_I u$$

   simplify to

$$\frac{du}{d\tau} = \frac{c_t V_a(t)}{c_I CR_2R_1} - \frac{c_t(R_1 + R_2)}{CR_2R_1} u$$

3) Set coefficients to one to solve for the scaling parameters.

   $\frac{c_t(R_1+R_2)}{CR_2R_1} = 1$, or $c_t = \frac{CR_1R_2}{R_1+R_2}$. You can confirm that this has units of time.

   $\frac{c_t V_a(t)}{c_I CR_2R_1} = 1$ or $c_I = \frac{c_t V_a(t)}{CR_2R_1} = \frac{V_a(t)}{R_1+R_2}$.

   However, we need this to be constant, so we need to pick something like max(Va(t)) if the input is not constant. You can confirm that this has units of current.

4) Rewrite the new equation and a set of equations that relate it to the original:

$$\frac{du}{d\tau} = f(t) - u$$

$$f(t) = \frac{V_a(t)}{Max\big(V_a(t)\big)}$$

$$u = \frac{(R_1 + R_2)}{\max\big(V_a(t)\big)} I_2$$

$$\tau = \frac{(R_1 + R_2)}{CR_1R_2} t$$

Note that in the case of constant, $V_a(t) = \max\big(V_a(t)\big)$, so $f(t) = 1$, and the equation simplified to $\frac{du}{d\tau} = 1 - u$. The original model had 4 parameters; R1, R2, C, and Va. The new model has no parameters. **This tells us that this system will behave essentially the same for all parameters, except that the magnitude of I2 and the time scale will depend on the scaling parameters** $c_I = \frac{V_a(t)}{R_1+R_2}$ and $c_t = \frac{CR_1R_2}{R_1+R_2}$.

Example 2: In lecture 2, we derived the PK model (here we use $k_3 = P_3/V_B$, but doesn't matter.)

$$\frac{dC_B}{dt} = \frac{D(t)}{V_B} - \left(\frac{P}{V_B} + k_3\right) C_B + \frac{P}{V_B} C_I$$

$$\frac{dC_I}{dt} = \frac{P}{V_I} C_B - \frac{P}{V_I} C_I$$

1) define nondimensional variables:

   $\tau = t/c_t$ and $\gamma = C/c_c$ are unitless times and concentrations.

2) Insert into model

$$\frac{c_c d\,\gamma_B}{c_t dt} = \frac{D(t)}{V_B} - \left(\frac{P}{V_B} + k_3\right) \mathrm{c_c}\gamma_B + \frac{P}{V_B}\, \mathrm{c_c}\gamma_I$$

$$\frac{c_c d\gamma_I}{c_t dt} = c_c \frac{P}{V_I}\gamma_B - c_c \frac{P}{V_I}\gamma_I$$

   and simplify

$$\frac{d\,\gamma_B}{dt} = \frac{c_t D(t)}{\mathrm{c_c} V_B} - \left(\frac{P}{V_B} + k_3\right) c_t\gamma_B + \frac{P}{V_B} c_t\, \gamma_I$$

$$\frac{d\gamma_I}{dt} = c_t \frac{P}{V_I}\gamma_B - c_t \frac{P}{V_I}\gamma_I$$

3) Set coefficients to one and solve

   $\left(\frac{P}{V_B} + k_3\right) c_t = 1, \quad \frac{P}{V_B} c_t = 1, \quad \frac{c_t D(t)}{\mathrm{c_c} V_B} = 1, \quad c_t \frac{P}{V_I} = 1$

   - We will pick the second equation $\frac{P}{V_B} c_t = 1$ because it shows up in some form twice. Thus, $c_t = V_B/P$ is our characteristic time constant. So $\tau = tP/V_B$
   - Now we are ready to solve for $\mathrm{c_c}$ using the 3rd equation. $\mathrm{c_c} = \frac{c_t D(t)}{V_B} = \frac{V_B D(t)}{P V_B} = \frac{D(t)}{P}$. This only makes sense for a constant input: $D(t) = D^0$, so $\mathrm{c_c} = \frac{D^0}{P}$, and $\gamma_B = C_B P/D^0$, and $\gamma_I = C_I P/D^0$ If D(t) is an instantaneous (impulse) dose of d0, in mg, then we can set $\mathrm{c_c} = \mathrm{d0/V_B}$.
   - We will define the remaining coefficients as new nondimensional parameters: We get: $\alpha = c_t \frac{P}{V_I} = \frac{V_B P}{P V_I} = V_B/V_I$. Thus, $\alpha = V_B/V_I$ is the ratio of volumes. The last coefficient is: $\left(\frac{P}{V_B} + k_3\right) c_t = \left(\frac{P}{V_B} + k_3\right)\frac{V_B}{P} = 1 + \frac{k_3 V_B}{P}$. For convenience, we may want to set $\beta = \frac{k_3 V_B}{P}$. Then, $\beta \ll 1$ if $k_3 \ll P/V_B$, while $\beta \ll 1 \gg 1$ if $k_3 \gg P/V_B$. That is, β is the ratio of clearance versus transfer between compartments.

4) Rewrite to get nondimensional ODE (with definitions of the nondimensional variables and parameters highlighted above)

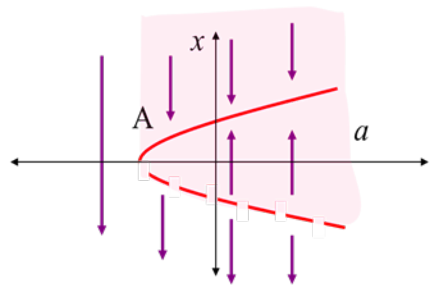
$$\frac{d\gamma_B}{dt} = 1 - (1 + \beta)\,\gamma_B + \gamma_I$$

$$\frac{d\gamma_I}{dt} = \alpha(\gamma_B - \gamma_I)$$

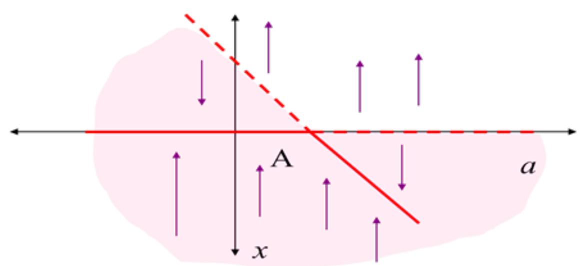
Bifurcation Analysis

Effect of parameters. The types of solutions possible for a system may depend on the parameter values in addition to the system structure. The parameter value at which a system changes behavior is called a *bifurcation*. For example, in a simple bifurcation (below), the system bifurcates when the parameter a = A. On one side of this bifurcation point, there are no equilibrium points, while on the other there are two, one stable and one unstable. A *bifurcation diagram* illustrates the system behavior by plotting the values of one of the variables (x) at all equilibrium points for each value of a parameter (a). The stable equilibrium points are shown as solid curves, and unstable equilibrium points as dashed curves. A stable limit cycle is illustrated as a dotted line at the two extreme values of the variable Bifurcation diagrams can also use arrows to show the direction the system moves when not at equilibrium, although this can be inferred from the stability.

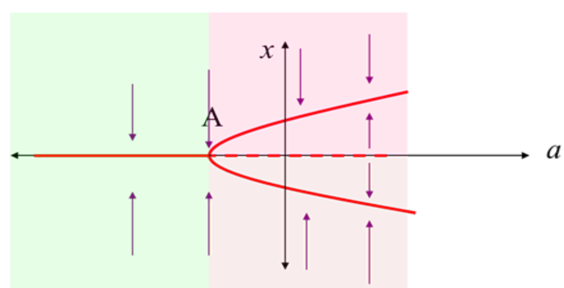
A *simple bifurcation, also called a fold bifurcation, a saddle-node bifurcation, or a turning-point bifurcation,* has no equilibrium points on one side of a critical parameter value (in this diagram, a < A), and two equilibrium points (one stable and one unstable) on the other side of the critical parameter value. The 'fold' and 'turning-point' names reflect the fact that the single equilibrium point line turns or folds over on itself.



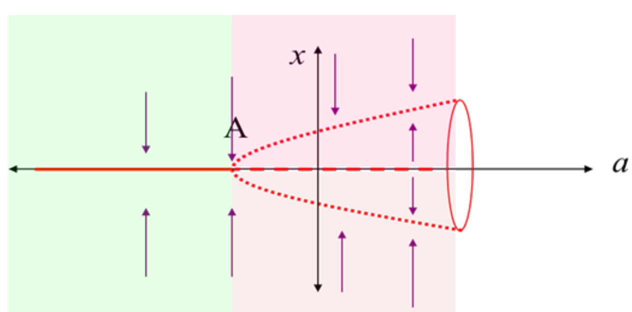
A *transcritical bifurcation* shows the intersection of two bifurcation curves, where both switch stability at the intersection. For all values of a, there are thus two equilibrium points, one of which is stable, so that some initial conditions flow into the stable equilibrium point, while others diverge infinitely. The only importance of whether $a < A$ or $a > A$ is to determine which of the two equations defines the stable equilibrium point.



A *pitchfork bifurcation* has two lines. One of which folds on itself, while the other switches stability where they cross. On one side of the critical parameter value, there is only a single equilibrium point (here, $a < A$ gives a single stable equilibrium point), while the remaining parameter values give three equilibrium points. When the curved equilibrium point line is the stable equilibrium point (as shown for this illustration), the system exhibits a bistable switch, since there are two stable and one unstable equilibrium points.



A *hopf bifurcation* includes a limit cycle with a central unstable equilibrium point, but only above on one side of a critical parameter value. On the other side of this value, the system collapses into a single stable equilibrium point, so the cycling behavior is lost. Note that the hopf bifurcation and the pitchfork bifurcation look very similar except that the hopf bifurcation cycles.



Example 1: Lotka-Volterra Model

If you can obtain an analytic solution for the equilibrium points, you can determine how the number of equilibrium points depends on the parameter values. The Jacobian can then be used to characterize the type of each parameter value. This information can be used to plot a bifurcation diagram. (However, the stable limit cycles cannot be calculated this way).

For the Lotka Volterra example, we have four parameter values. To ask how the different parameter values determine the equilibrium and steady state conditions, we need to return to the equations for these. Recall that we identified two equilibrium points, $(H, P) = (0,0)$ and $(H, P) = \left(\frac{m}{b}, \frac{r}{a}\right)$, with no assumptions made about the parameter values. However, when we calculated the eigenvalues, we simply plugged in the numeric values of the parameters, so we did make some assumptions. To know how the stability depends on the parameters, we need to obtain the analytic solution for the eigenvalues, or do a lot of numeric testing. Since we have four parameters to consider, the analytic is easier. Recall that the eigenvalues are the solutions to: $\det(J - \lambda I) = 0$, and that for a 2D matrix, $\det\begin{bmatrix} a & b \\ c & d \end{bmatrix} = ad - bc$. Thus, we need to solve:

$$\det(J - \lambda I) = \begin{bmatrix} r - aP - \lambda & -aH \\ bP & bH - m - \lambda \end{bmatrix} = (r - aP - \lambda)(bH - m - \lambda) + aHbP = 0$$

For (0,0), This simplifies to:

$$(r - \lambda)(-m - \lambda) = \lambda^2 + (m - r)\lambda - mr = 0$$

This is in the form: $A\lambda^2 + B\lambda + C = 0$ with $A = 1, B = m - r, C = -mr$ so we solve this with the quadratic equation to get

$$\lambda = \frac{\left(-B \pm \sqrt{B^2 - 4AC}\right)}{2A} = \frac{\left(r - m \pm \sqrt{(m - r)^2 + 4mr}\right)}{2} = \frac{(r - m \pm (m + r)}{2}$$

So $\lambda_1 = \frac{2r}{2} = r$, and $\lambda_2 = \frac{-2m}{2} = -m$. Thus, as long as m and r are positive values, (0,0) is a saddle point.

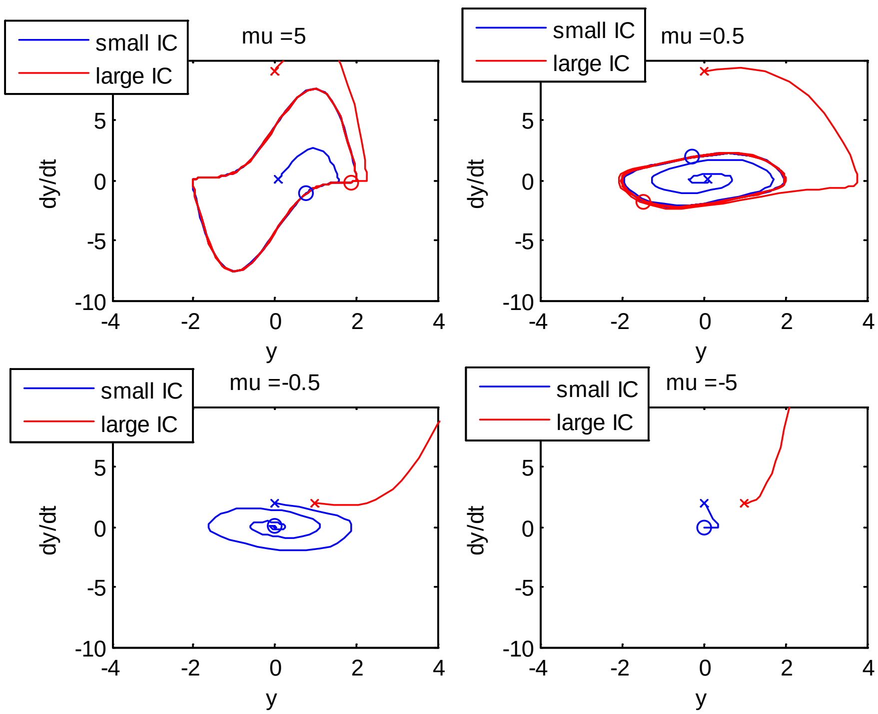
For $\left(\frac{m}{b}, \frac{r}{a}\right)$, this simplifies to: $(-\lambda)(-\lambda) + \frac{am}{b} * \frac{br}{a} = \lambda^2 + mr = 0$, or $\lambda = 0 \pm i\sqrt{mr}$. Thus, as long as m and r are positive, this is a neutrally stable focus.

If we are not constrained by positive values for r (meaning Hares die off on their own instead of reproduce), then we would find that (0,0) is a stable point, which makes sense. And, there would be a saddle point at (m/b, r/a), since $\lambda = \pm\sqrt{-mr}$. (but, this saddle point has negative Predator value, which makes no sense.) Since we did not consider neutrally stable equilibrium points in the bifurcation diagrams, this system does not fit into one of those even if we wanted to consider the full nonphysiological range of parameters.

Example 2: Van der Pol.

Recall that the Van der Pol model has only equilibrium point, (0,0), this gives $J = \begin{bmatrix} 0 & 1 \\ -1 & \mu \end{bmatrix}$. This seems simple enough to do the analytic calculation, so the eigenvalues of this system are the solution to $\det\left(\begin{bmatrix} 0 - \lambda & 1 \\ -1 & \mu - \lambda \end{bmatrix}\right) = -\lambda(\mu - \lambda) + 1 = 0$. This is again a quadratic equation: $\lambda^2 - \lambda\mu + 1 = 0$ with solutions $\lambda = \left(\mu \pm \sqrt{\mu^2 - 4}\right)/2$. If $\mu > 2$, then the value in the square root is positive, but is less than μ^2, so the square root term can never overcome the μ term, and all lambda values are positive real numbers. In this case, (0,0) is an unstable node, and the solution shoots away from (0,0). If $0 < \mu < 2$, then the roots are complex, with real positive components, and (0,0) is an unstable focus, so solutions will oscillate away from this point. If $-2 < \mu < 0$, then the eigenvalues are all complex with negative real components, so the solution oscillates into (0,0). If $\mu < -2$, then the eigenvalues are negative real numbers and the solution approaches the origin without oscillations.

However, this does not give us complete information. In either case, the solution may expand infinitely, or may reach a limit cycle. To find out which, we simply have to plot some solutions. In the plots below, the 'x' indicates the initial condition and the 'o' the value when the simulation stopped, (which is not necessarily an equilibrium point.)

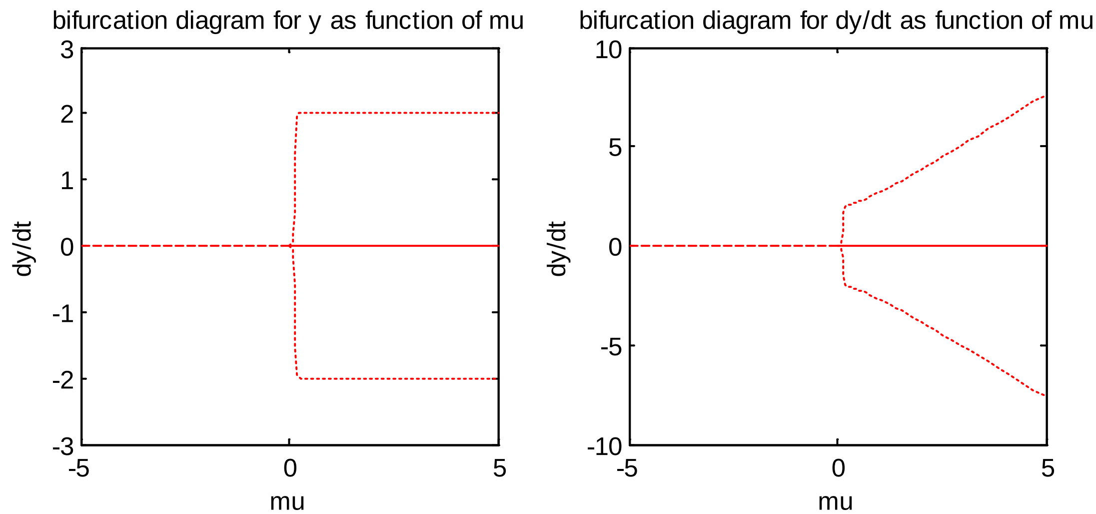


With the small initial conditions (if the initial conditions are close enough to the equilibrium point) we see that the solution indeed leaves (0,0) for positive values of mu but approaches for negative values. This verifies our analytic calculations about this equilibrium point.

However, we also see a stable limit cycle for positive mu, which we may have suspected from the analytic, but is best seen from the numerical solutions. We know this is a stable limit cycle because we see the same cycle for very different initial conditions.

Note that large initial conditions (not close to the equilibrium point) expand infinitely for negative mu, so there is some difficult-to-identify separatrix that distinguishes which points decay to 0 versus expand infinitely.

This system is a Hopf bifurcation, since there is one stable equilibrium point for mu < 0, and an unstable one plus a stable limit cycle for mu > 0. However, note that the hopf bifurcation diagram does not indicate that some initial y-values will expand infinitely (for mu < 0), nor indicates the location of the separatrix. The hopf diagram can be plotted by calculating the max and min values of the limit cycle and combining this with the analytic information obtained above about the stability of the equilibrium point. Since there are two variable values, it is helpful to do a bifurcation plot for each one:



The code to obtain this was:

```
I = 100;
x = linspace(-1,1,I);
mu = 5*x.^3;
for i = 1:I
   [t,Y] = ode23(@vdpODE, [0 100], [0.001,0.001], [], mu(i));
   start = floor(size(Y,1)/2);
   ymin(i) = min(Y(start:end,1)); ymax(i) = max(Y(start:end,1));
   dymin(i) = min(Y(start:end,2)); dymax(i) = max(Y(start:end,2));
end
figure(2);
subplot(1,2,1)
plot(mu(I/2+1:I),ymin(I/2+1:I),'r:'); hold on;
plot(mu(I/2+1:I),ymax(I/2+1:I),'r:');
plot(mu(I/2+1:I),0*mu(I/2+1:I),'r');
plot(mu(1:I/2),0*mu(1:I/2),'r--');
xlabel('mu')
ylabel('dy/dt')
title('bifurcation diagram for y as function of mu')
subplot(1,2,2)
plot(mu(I/2+1:I),dymin(I/2+1:I),'r:'); hold on;
plot(mu(I/2+1:I),dymax(I/2+1:I),'r:');
plot(mu(I/2+1:I),0*mu(I/2+1:I),'r');
plot(mu(1:I/2),0*mu(1:I/2),'r--');
xlabel('mu')
ylabel('dy/dt')
title('bifurcation diagram for dy/dt as function of mu')
```

Summary

1. To simplify systems analysis by reducing the number of variables, we nondimensionalize a system using the SPICE procedure: Define the **S**caling **P**arameters, **I**nsert the nondimensional variables into the ODE, set the **C**oefficients to one, and rewrite the **E**quations that define the system succinctly.
2. Most systems will have more coefficients than scaling parameters, so that you cannot set all to one, and instead replace the complicated coefficient with a nondimensional parameter, that will determine the qualitative behavior of the system.
3. Bifurcation analysis determines how the number and type of equilibrium points change with parameter values, and is most easily performed on the simplified nondimensional system.
4. A bifurcation diagram shows the values of a variable at the equilibrium points for each value of a parameter. Stable points are indicated by solid lines, unstable points by dashed lines, and stabile limit cycles by dotted lines.
5. Many systems with one variable can be described as having one of four common bifurcations: simple/fold bifurcation (zero vs one stable equilibrium point), transcritical bifurcation (one stable and one unstable equilibrium point), pitchfork bifurcation (one vs two stable equilibrium points) hopf bifurcation (one stable equilibrium point vs a limit cycle).