Computational and Systems Biology Course 186—Modeling of Biological Systems by Connecting Biological Knowledge and Intuition with Mathematics and Computing

Instructor: Van Savage
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Monday and Wednesday, 2-3:50 pm
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Joke

When Galileo dropped objects from the tower of Pisa, what if he’d been a stamp-collector scientist?

Tension between finding right general, simple, useful idea and being exact and specific for every case.
Fun Problem

You travel one mile at 30 miles per hour, how fast do you need to travel the second mile, so that your average speed over the two miles is 60 miles per hour?
Equation for change: one discrete step

Translate idea/picture/process to equations

\[ x(t + 1) = 2x(t) \]

\[ x(t + 1) = r_d x(t) \]

\( r_d \) is an average that ignores individual variation.

\[ x(t + 1) = r_d x(t) + f(t) + \text{const} \]

Simple case in terms of biology and math but will see that several subtleties already arise.
What about for real units of time or space? How to convert this to differences and derivatives?

$$x(t) = x(0)e^{rt}$$

continuous solution

$$x(N) = x(0)e^{\ln(r_d)N} = x(0)e^{\left[\frac{\ln(r_d)}{\Delta t}\right](N\Delta t)}$$

match to discrete solution?

Note we used $N$, number of steps, not $t$ for time (how we started) for discrete solution because that is what we really mean. Need to multiply and divide by $\Delta t$ within exponential.

Check for consistency at setup and solution. Doesn’t match. Is $r$ related to $r_d-1$ or $\ln(r_d)$?
What about taking logarithm of ratios at earlier stage? Becomes difference of log’s.

\[
\ln\left[\frac{x(t+1)}{x(t)}\right] = \ln[x(t+1)] - \ln[x(t)] = \ln[r_d]
\]

\[
\frac{d \ln x}{dt} = \frac{\ln(r_d)}{\Delta t}
\]

Now continuous eqn and solution are both same form as discrete solution. Why is this derivation more consistent?

Growth is exponential so log space is more natural space in which to think about change. That is linear “steps” and “differences” happen in ln space, not linear space. IMPLICIT CHOICE OF FUNCTIONAL SPACE IS ESSENTIAL AND REQUIRES THOUGHT!

Can matter for computational choices and algorithms as well!
What about for real units of time or space? How to convert this to differences and derivatives for arbitrary or small step sizes? Don’t implicitly assume step size must be 1.

\[
x(t + 1) - x(t) = (r_d - 1)x(t)
\]

\[
\lim_{\Delta t \to 0} \frac{x(t + \Delta t) - x(t)}{\Delta t} = \frac{(r_d - 1)}{\Delta t} x(t)
\]

\[
\frac{dx}{dt} = rx(t)
\]

\(r_d\) is number and \(r\) is rate. Keep units straight!
Also, what about small $\Delta t$ without limit all the way to 0? What can we learn from this?

$$x(t + \Delta t) = x(t) + \frac{dx}{dt} \bigg| _{t} \Delta t + \frac{d^2x}{dt^2} \bigg| _{t} \Delta t + \frac{(t + \Delta t - t)^2}{2!} + \frac{d^3x}{dt^3} \bigg| _{t} \Delta t + \frac{(t + \Delta t - t)^3}{3!} + \cdots$$

$$= x(t) + \frac{dx}{dt} \bigg| _{t} \Delta t + \frac{d^2x}{dt^2} \bigg| _{t} \Delta t + \frac{\Delta t^2}{2!} + \frac{d^3x}{dt^3} \bigg| _{t} \Delta t + \frac{\Delta t^3}{3!} + \cdots$$

We were effectively just using first two terms on right side for all derivations so far, which are only terms that exist in limit to zero, but for any non-zero value of $\Delta t$ (all computational methods), the second derivative term and higher orders matter and choices about space and lack of linearity (i.e., curvature) matter. We were implicitly ignoring higher-order terms for linear space derivation before. For this case log space is where finite steps in $\Delta t$ do not enter less because higher-order derivatives are all zero because function is just linear. These exact considerations are the core of numerical/computational algorithms we will consider later.
Exponential is linear in logarithmic space

If $\Delta t$ is not zero, these differences eventually matter. Log transform changes exponential into linear space. Since solution is exponential, this means it changes our equation into linear space. Maybe hard to guess this first time so need **multiple iterations of thinking** to get it correct!
How to model

• Draw picture and create notation in intuitive space

• Usually trying to describe change with time or space or some other dimension/variable or fixed points or response to some perturbation

• Use Math to change to different space in which problem is much easier to solve, even if less obvious to formulate

• Complexity-Stability debate: basic biological question

• Network of connections

• Linear Algebra—eigenvalues, eigenvectors, determinants, etc.

• Translating between biology and math must be careful at all steps and use and gain intuition!
Complexity and Stability—protein interaction network
Complexity and Stability—protein interaction network
Complexity and Stability—epistasis and gene interactions
Complexity and Stability—
cell types and physiology
Complexity and Stability—C elegans neurons
Complexity and Stability—
general drug interactions (applicable here?)
Complexity and Stability—predator-prey food web

Little Rock Lake Food Web

92 species, 997 links, 11 links/species
“True stability results when presumed order and presumed disorder are balanced. A truly stable system expects the unexpected, is prepared to be disrupted, waits to be transformed.”

-Tom Robbins

Read more at: https://www.brainyquote.com/quotes/keywords/stability.html
"A diverse ecosystem will also be resilient, because it contains many species with overlapping ecological functions that can partially replace one another. When a particular species is destroyed by a severe disturbance so that a link in the network is broken, a diverse community will be able to survive and reorganize itself... In other words, the more complex the network is, the more complex its pattern of interconnections, the more resilient it will be."

- Fritjof Capra
"Biological diversity is being lost at a rate unequalled since the appearance of modern ecosystems more than 40 million years ago. A quarter of all mammals are threatened with extinction; and nearly 70% of the world’s fish stocks are fully exploited, overexploited or depleted."

- Royal Society

Not just true for ecology, where these ideas were first formulated, but for all the networks we’ve shown if we want to understand, predict, and manipulate them.
How can we build off last lecture to get dynamical equations at each node?

For species $i$ with no interactions, we have

$$\frac{dx_i}{dt} = \dot{x}_i(t) = r_i x_i(t) \left( 1 - \frac{x_i(t)}{K_i} \right)$$
Joke

What do you get when you cross a mosquito with a mountain climber?

Nothing. You can't cross a vector and a scalar.
Convert linear ODEs to matrix form

In matrix form

\[
\dot{X}(t) = \left( I - \text{diag}(X(t)) \right) \text{diag}(K^{-1}) \text{diag}(R) X(t)
\]

where

\[
\dot{X}(t) = \begin{bmatrix}
\dot{x}_1(t) \\
\dot{x}_2(t) \\
\vdots \\
\dot{x}_n(t)
\end{bmatrix}, \quad X(t) = \begin{bmatrix}
x_1(t) \\
x_2(t) \\
\vdots \\
x_n(t)
\end{bmatrix}
\]
Convert linear ODEs to matrix form

\[
\text{diag}(R) = \begin{pmatrix}
  r_1 & 0 & 0 \\
  0 & r_2 & 0 \\
  0 & 0 & r_3
\end{pmatrix}
\]

\[
\text{diag}(R)X(t) = \begin{pmatrix}
  r_1 x_1 \\
  r_2 x_2 \\
  r_3 x_3
\end{pmatrix}
\]
Convert linear ODEs to matrix form

In matrix form

\[
\dot{X}(t) = \left( I - \text{diag}(X(t))\text{diag}(K^{-1}) \right)\text{diag}(R)X(t)
\]

where

\[
I_3 = \begin{pmatrix}
1 & 0 & 0 \\
0 & 1 & 0 \\
0 & 0 & 1
\end{pmatrix}
\]

\[
\text{diag}(K^{-1}) = \begin{pmatrix}
1/K_1 & 0 & 0 \\
0 & 1/K_2 & 0 \\
0 & 0 & 1/K_3
\end{pmatrix}
\]

For 3 species case
Add interactions

In matrix form

$$\dot{X}(t) = \left( \text{diag}(R) + \text{diag}(X(t)) A \right) X(t)$$

where for 3 species

$$A = \begin{pmatrix}
    -r_1 / K_1 & A_{12} & A_{13} \\
    A_{21} & -r_2 / K_2 & A_{23} \\
    A_{31} & A_{32} & -r_3 / K_3
\end{pmatrix}$$

And no interactions means $$A_{ij} = 0$$
Interaction matrix to network

\[ A = \begin{pmatrix}
-r_1 / K_1 & 0 & A_{13} \\
0 & -r_2 / K_2 & A_{23} \\
A_{31} & A_{32} & -r_3 / K_3
\end{pmatrix} \]
Multiply this out into equations

$$\text{diag}(X(t))A = \begin{pmatrix} -\frac{x_1 r_1}{K_1} & x_1 A_{12} & x_1 A_{13} \\ x_2 A_{21} & -\frac{x_2 r_2}{K_2} & x_2 A_{23} \\ x_3 A_{31} & x_3 A_{32} & -\frac{x_3 r_3}{K_3} \end{pmatrix}$$
Multiply this out into equations

$$
\text{diag}(X(t))AX(t) = \begin{bmatrix}
-x_1 \left( \frac{r_1}{K_1} \right)x_1 + x_1 A_{12} x_2 + x_1 A_{13} x_3 \\
x_2 A_{21} x_1 - x_2 \left( \frac{r_2}{K_2} \right)x_2 + x_2 A_{23} x_3 \\
x_3 A_{31} x_1 + x_3 A_{32} x_2 - x_3 \left( \frac{r_3}{K_3} \right)x_3
\end{bmatrix}
$$

Can see here that the $A_{ij}$ terms couple together species $i$ and $j$ in the differential equations, representing interactions. Sometime called transfer function, but more generally any type of interaction.
Alternative notation

For species $i$ with interactions, we have

$$\frac{dx_i}{dt} = \dot{x}_i(t) = r_i x_i(t) - \sum_{j=1}^{n} x_i(t) A_{ij} x_j(t)$$
Add interactions

In matrix form

\[ \dot{X}(t) = \left( \text{diag}(R) + \text{diag}(X(t))A \right)X(t) \]

No interactions means \( A_{ij} = 0 \)

Positive (increases growth) interactions means \( A_{ij} > 0 \)

Negative (decreases growth) interactions means \( A_{ij} < 0 \)
Why is this form useful?

Because of many couple equations, because linear algebra provides standard methods for changing to different, easier space and for doing stability analysis.
What larger lessons are we learning?

1. You can already wade into deep and sophisticated debates with knowledge you have of math and biology and curiosity

2. There are always subtle choices to make in approaching and calculating a problem. Standard methods are generic (good) but not always best suited to your problem (bad). Finding best-suited method makes everything easier, both analytically and numerically, and sometimes makes the impossible become possible.

3. Same methods show up again and again. Fixed points, dynamical space, Taylor series, logistic equation
Dynamical systems flow relative to equilibrium/fixed points

What is functional form as fixed point is approached? This describes region and dynamics that are relevant for many scientific questions.
What is the equilibrium or fixed point?

\[ 0 = \dot{X}(t) = g(X^*) \]

because assumes things are no longer changing, meaning fixed
Most generic method to find dynamical, functional form—linearization through Taylor series

\[
\dot{X} = g(X) \sim g(X^*) + (X - X^*) \left[ \frac{dg_{ij}(X)}{dx_i} \right]_{X=X^*} + \frac{1}{2} (X - X^*)^2 \left[ \frac{d^2 g_{ij}(X)}{dx_i^2} \right]_{X=X^*} + \ldots
\]

\[
\sim (X - X^*) \left[ \frac{dg_{ij}(X)}{dx_i} \right]_{X=X^*} \equiv (\delta X) \left[ \frac{dg_{ij}(X)}{dx_i} \right]_{X=X^*}
\]

\(\delta X\) measures deviations from equilibrium assumed to start small as perturbation

\[
\text{assumes } \frac{1}{2} (\delta X) \left[ \frac{d^2 g_{ij}(X)}{dx_i^2} \right]_{X=X^*} \gg \left[ \frac{dg_{ij}(X)}{dx_i} \right]_{X=X^*}
\]
Recall linear algebra

\[ \left| \frac{dg_{ij}(X)}{dx_i} \right|_{X=X^*} \equiv J(X^*) \]

is the Jacobian so

\[ \dot{X}(t) = J(X^*)(\delta X) \]

and

\[ \frac{d(\delta X)}{dt} = \frac{d}{dt}(X-X^*) = \frac{dX}{dt} = \dot{X}(t) \]
Recall linear algebra

Matrices are diagonalizable in terms of eigenvalues and eigenvectors. In eigenspace, Jacobian can be written as

\[ J_3(x^*) = \text{diag}(\lambda_i) = \begin{bmatrix} \lambda_1 & 0 & 0 \\ 0 & \lambda_2 & 0 \\ 0 & 0 & \lambda_3 \end{bmatrix} \]

CHANGE/CHOOSE the space of problem to make math easy. Like choosing log instead of linear space in last class or choosing the correct coordinate system.
Recall linear algebra

So can use eigenvectors to change matrix equation to eigenspace to become

\[
\frac{d(\delta X)}{dt} = J(X^*)\delta X \Rightarrow \frac{d(\delta Z)}{dt} = \text{diag}(\lambda_i)\delta Z
\]

where \(\delta Z\) times eigenvectors is in original space, so row by row equations

\[
\frac{d(\delta z_i)}{dt} = \lambda_i \delta z_i
\]

which is simplest linear ODE with solution

\[
\delta z_i(t) = c_i e^{\lambda_i t}
\]
Recall linear algebra

Eigenvectors form a basis, so any vector can be written as a linear combination of eigenvectors. When transforming back to original space using eigenvectors, we just get linear combination of solutions in eigenspace, so

$$\delta x_i(t) = \sum_{j=1}^{n} a_j \delta z_j(t) = \sum_{j=1}^{n} b_j e^{\lambda_j t}$$

If all eigenvalues have negative real part, all terms in sum will decay exponentially to 0, so the deviation from our fixed point will always decay to 0, meaning we return to our fixed point and are always stable. In contrast, if the real part of any eigenvalue is positive, that will lead to exponential growth and perturbed state will diverge from fixed point. Any solution with component in direction of that eigenvector will be unstable.
Recall linear algebra

Or can also reason that if solutions return to original state (i.e., are stable) in the eigenspace, and there is a constant transformation (using the eigenvalues) back to the original space, then the original space must also return to the exact same state and be stable. Thus, we can directly look at

\[ \delta z_i(t) = c_i e^{\lambda_i t} \]

If all eigenvalues have negative real part, solutions for each state will decay exponentially to 0, so the deviation from our fixed point will always decay to 0, meaning we return to our fixed point and are always stable. In contrast, if the real part of any eigenvalue is positive, that will lead to exponential growth and perturbed state will diverge from fixed point for at least one species, probably multiple species that are mixed with or affected by that eigenstate.
Flow near fixed point after perturbation

As time, \( t \), gets large (goes to infinity), the real part of the eigenvalue determines the stability and behavior:

1. \( \text{Re}[\lambda] < 0 \) : the system returns to equilibrium (\( \delta x \rightarrow 0 \)) (stable)
2. \( \text{Re}[\lambda] > 0 \) : the system diverges from equilibrium (unstable)
3. \( \text{Re}[\lambda] = 0 \) : the system oscillates around equilibrium
4. \( \lambda = 0 \) : the system stays at new point
Still need to find $J(x^*)$ and diagonalize

$$J_{ij}(x^*) = \frac{d}{dx_i} \left[ \left( \text{diag}(R) + \text{diag}(X(t))A \right) X(t) \right]_{ij} \bigg|_{x=x^*}$$

$$\Rightarrow J(x^*) = \text{diag}(R) + 2 \text{diag}(X^*(t))A$$

Will talk in a bit about finding eigenvalues, but interesting thing here is that this depends on $X^*$ itself and $R$ and not just interactions that constrain equilibrium point of dynamics. Is this correct?
How else could we do this?

Especially given what we learned last time.

\[ 0 = \dot{X}(t) = f(X)X \]

and if \( X \) does not equal 0 (uninteresting trivial solution) then

\[ 0 = f(X^*) \]
Most generic method to find dynamical, functional form—linearization through Taylor series

\[ \dot{X} = f(X)X \sim X \left[ f(X^*) + (X - X^*) \left( \frac{df_{ij}(X)}{dx_i} \right)_{X=X^*} + \frac{1}{2} (X - X^*)^2 \left( \frac{d^2 f_{ij}(X)}{dx^2_j} \right)_{X=X^*} + \ldots \right]. \]

\[ \sim X(X - X^*) \left( \frac{df_{ij}(X)}{dx_i} \right)_{X=X^*} \equiv X(X - X^*) \left( \frac{df_{ij}(X)}{dx_i} \right)_{X=X^*} \]

assumes \[ \frac{1}{2} (\delta X) \left( \frac{d^2 f_{ij}(X)}{dx^2_i} \right)_{X=X^*} \gg \left( \frac{df_{ij}(X)}{dx_i} \right)_{X=X^*} \]
Recall linear algebra

\[ \begin{bmatrix} \frac{df_{ij}(X)}{dx_j} \end{bmatrix}_{X=X^*} \equiv \tilde{J}(X^*) \]

is the Jacobian so

\[ \dot{X}(t) = \text{diag}(X(t)-X^*)\tilde{J}(X^*)X(t) \]
Recall linear algebra

Matrices are diagonalizable in terms of eigenvalues and eigenvectors, so in eigenspace

\[
\tilde{J}_3(X^*) = \text{diag}(\tilde{\lambda}_i) = \begin{bmatrix}
\tilde{\lambda}_1 & 0 & 0 \\
0 & \tilde{\lambda}_2 & 0 \\
0 & 0 & \tilde{\lambda}_3
\end{bmatrix}
\]

CHANGE/CHOOSE the space of problem to make math easy. Like choosing log instead of linear space in last class or choosing the correct coordinate system.
Recall linear algebra

So matrix equation in eigenspace becomes

\[
\frac{dX}{dt} = \text{diag}(X(t)-X^*)J(X^*)X(t)
\]

\[
\Rightarrow \frac{dZ}{dt} = \text{diag}(Z(t)-Z^*)\text{diag}(\lambda_i)Z(t)
\]

so row by row equations become

\[
\frac{dz_i}{dt} = z_i \tilde{\lambda}_i (z_i - z_i^*)
\]

which we can solve with partial fractions as before \((x_i^*, z_i^*>0)\)

\[
Z_i(t) = \frac{c_i Z_i}{1 - \left(1 - \frac{z_i^*}{z_i(0)}\right)e^{\tilde{\lambda}_i z_i^* t}}
\]
Recall linear algebra

Eigenvectors form a basis, so any vector can be written as a linear combination of eigenvectors. When transforming back to original space using eigenvectors, we just get linear combination of solutions in eigenspace, so

$$z_i(t) = \frac{c_i z_i^*}{1 - (1 - \frac{z_i^*}{z_i(0)}) e^{\tilde{\lambda}_i z_i^* t}}$$

If all $z_i$ return to $z_i^*$, then all $x_i$ return to $x_i^*$ because if solutions are stable in one space, they are stable everywhere. If all eigenvalues have real negative part, we return to fixed points and are always stable. In contrast, if the real part of any eigenvalue is positive, that will lead to exponential growth and perturbed state will go to 0 and diverge from nontrivial fixed point and be unstable.
As time, $t$, gets large (goes to infinity), the real part of the eigenvalue determines the stability and behavior:

1. $\text{Re}[\lambda] < 0$: the system returns to equilibrium ($x_i \rightarrow x_i^*$) (stable)
2. $\text{Re}[\lambda] > 0$: the system diverges from equilibrium (unstable)
3. $\text{Re}[\lambda] = 0$: the system oscillates around equilibrium
4. $\lambda = 0$: the system stays at new point
Still need to find $J(x^*)$ and diagonalize

$$\tilde{J}_{ij}(x^*) = \frac{d}{dx_i} \left[ \text{diag}(R) + \text{diag}(X(t))A \right]_{ij} \bigg|_{X=X^*} \Rightarrow \tilde{J}(x^*) = A$$

Dependence on $X^*$ is totally gone now. Only interaction matrix matters now, as it should.
Finding eigenvalues

Equation for an eigenvector/eigenbasis where multiplying by matrix is like multiplying by a specific eigenvalue, constant factor.

\[(A - \lambda I)x_i = 0\]

For non-trivial (non-zero) \(x_i\), term in parentheses must cause zero, so that means we cannot divide by it (cannot divide by zero), so that in matrix thinking, this means it is not invertible. Do you recall condition for invertibility?

\[\det(A - \lambda I) = 0\]

This condition means matrix in parentheses form is not invertible
Finding eigenvalues

This condition leads to nth-order polynomial equation equal to zero, so solving roots of equation gives eigenvalues. Let’s do generic 2x2 matrix as example.

\[
A = \begin{bmatrix}
    a & b \\
    c & d
\end{bmatrix}
\]

Polynomial equation becomes

\[
\lambda^2 - TrA \lambda + \text{det } A = 0
\]

So solutions are

\[
\lambda_\pm = \frac{TrA}{2} \left[ 1 \pm \sqrt{1 - \frac{4 \text{det } A}{(TrA)^2}} \right]
\]
More linear algebra with eigenvalues

Diagonal version of matrix is

$$A = \begin{pmatrix} \lambda_+ & 0 \\ 0 & \lambda_- \end{pmatrix}$$

and

$$TrA = \lambda_+ + \lambda_-$$

$$\text{det } A = \lambda_+ \lambda_-$$

also straightforward to calculate eigenvalues
Finding eigenvalues

Often assumed that $a=d=-|a|$ (meaning negative number), so

$$\lambda_\pm = -|a| \left[ 1 \pm \sqrt{\frac{bc}{|a|^2}} \right] = -|a| \pm \sqrt{bc}$$

Condition for negative eigenvalues is therefore

$$bc < |a|^2$$

Translates into inter-specific (between species) competition being less than intra-specific (within species) competition. Compete more fiercely against self because fill same niche.
Return to complexity-stability debate

Lord Bob May model

n—number of proteins or genes or species
determines size of nxn matrix

\[ C = \frac{\text{number of links}}{\text{number of pairs}} \] [How many pairs?]
realized connectance among parts and related to complexity
determines number of non-zero entries in interaction matrix A

\[ \sigma = \text{standard deviation/width of normal distribution from which interactions are randomly sampled. Related to strength of interaction.} \]
Return to complexity-stability debate

Allow $n$ to be large and non-diagonal entries into matrix are random, so seems difficult to calculate eigenvalues, but powerful theorem that shows eigenvalues all fall in circle like the below.

Karl Nyman thesis
Circle centered at -1 but has diameter that grows as $\sqrt{nC\sigma}$.

At some point, the right side will cross 0, and then the system will become unstable. So, large complex systems are unstable?

Karl Nyman thesis
Why ecological networks?

1950's Paradigm:

*Complex communities MORE stable than simple communities*

1970's Challenge:

*Complex communities LESS stable than simple communities*

Current & Future Research:

“Devious strategies” that promote stability and species coexistence
Seems counter to what we see in nature from genes to proteins to ecosystems. What gives?

**Several problems with assumptions**

1. Interaction matrices are NOT random. The is structure/hierarchy/modularity through all of these, and this is where a lot of the interesting biological knowledge and reasoning and more and more math in current research is coming in!

2. Most models assume r and K are constants, but they vary in systematic and important ways.

3. Assumes all else is constant, but environment (meaning body, climate, diseases, etc.) can and does change over relevant time scales and that could be very important and essential.

But what can we say generically to deal with these?
That is **current research** and what we’re learning and is exciting!!
Empirical regularities \(\rightarrow\) modeling opportunities

**Simple, stochastic, single-dimensional models of food-web structure**

Explain "the phenomenology of observed food web structure, using a minimum of hypotheses"

1) Two Parameters: \(S\) (species richness) and \(C\) (connectance)
2) Assign each species \(i\) a uniform random "niche value" \(n_i\) of 0 to 1
3) Simple rules distribute links from consumers to resources

\[
\begin{array}{c}
\downarrow & \downarrow & \downarrow & \downarrow & \blacktriangle & \blacktriangle & \blacktriangle & \downarrow \\
0 & & & & n_i & & & 1
\end{array}
\]
1) *Cascade Model*
2) *Niche Model*
3) *Nested Hierarchy Model*
4) *Generalized Cascade Model*
5) *Relaxed Niche Models*
6) *Random Models*
Connectance affects robustness to invasion

1. Most successful invasions do not lead to extinctions
2. Extinction cascades occur more often than single extinctions
3. High $C$ webs more robust to invasions
4. When high $C$ webs experience extinctions, they are of higher magnitude
5. Empirical test with rock pool mesocosms in process.
Empirical Body-Size Ratios

Model: Persistence as $f$ (Body-Size Ratios)

Brose et al. 2006 Ecology Letters
Modeling species interactions, \( S > 2 \)

1) **Community Matrices**: Species interaction coefficients describe the impact of species \( i \) on growth of species \( j \) at equilibrium population densities.  
LOCAL STABILITY

2) **Food-Web Modules**: Population dynamics of \( S = 3-9 \) interacting species via numerical integration of linked ordinary differential equations.  
POPULATION STABILITY

3) **Complex Food Webs**: Population dynamics of \( S \geq 10 \) interacting species.  
POPULATION STABILITY, SPECIES PERSISTENCE, etc.

- **Population Dynamics + Structure**: run population dynamics on complex networks
- **Population + Evolutionary Dynamics**: evolve complex webs from a few species
- **EcoPath with EcoSim**: a black-box software package based on static, linear, steady-state, mass-balance snapshots of specific systems + dynamic projections
- **Individual-based models**: build systems up from simple agents governed by simple rules
Complexity that works is built up out of modules that work perfectly, layered one over the other.
Kevin Kelly

Read more at: https://www.brainyquote.com/quotes/keywords/complexity.html
How do these ideas translate to other biological systems?