Math for Biology - An Introduction

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1 Differential Equations - An Overview

2 The Law of Mass Action

3 Enzyme Kinetics
Differential Equations - Our Goal

- We will *NOT* be solving differential equations
- The tools - Rule Bender and BioNetGen - will do that for us
- This lecture is designed to give some background about what the programs are doing
Differential Equations - An Overview

- Differential Equations contain the derivatives of (possibly) unknown functions.
- Represent how a function is changing.
- We work with first-order differential equations - only include first derivatives.
- Generally real-world differential equations are not directly solvable.
- Often we use numerical approximations to get an idea of the unknown function’s shape.
Differential Equations - Starting from the solution

- A differential equation: \( f'(x) = C \)
Differential Equations - Starting from the solution

- A differential equation: $f'(x) = C$
- A few solutions.

**Figure**: Some solutions to $f'(x) = 2$
A differential equation: $f'(x) = Cx$
Differential Equations - Starting from the solution

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- A few solutions.

**Figure:** Some solutions to $f'(x) = 2x$
Differential Equations - Initial Conditions

- How do we know which is the correct solution?
- Need to know the value for a point - the initial conditions.
- Only one necessary for these types of problems. Need an initial condition for each variable in the equation.

Exercise: Given \( f'(x) = 2x \) and \((x_0, f(x_0)) = (4, 22)\), what is the solution?

\[ f(x) = x^2 + 6. \]
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Differential Equations - A Slightly More Complex Example

- The Logistic Curve
- Models population growth
- Differential equation:
  \[ \frac{d}{dt} P(t) = P(t)(1 - P(t)) \]
- When does \( P(t) \) not change? In other words, when is the derivative equal to 0?
- Under what conditions is the derivative positive? Negative?
Differential Equations - A Slightly More Complex Example

- The Logistic Curve - Solution
- What more do we need before we find a solution?
Differential Equations - A Slightly More Complex Example

- The Logistic Curve - Solution
- What more do we need before we find a solution?
- \( P(0) = .5 \)
Differential Equations - A Slightly More Complex Example

- The Logistic Curve - Solution
- What more do we need before we find a solution?
  - $P(0) = 0.5$
  - $P(t) = \frac{1}{1 + e^{-t}}$

![Logistic Curve Graph]

- Where
  - $P(t)$ represents the population at time $t$.
  - $P(0)$ is the initial population.
  - $e^{-t}$ is the exponential decay term.

The graph illustrates the logistic growth curve, showing how the population reaches a maximum value as $t$ increases.
Differential Equations - How about this one?
Biochemical Reactions - An Application of Differential Equations

- How can we represent the concentrations of molecules in solution?
- We can represent how much the concentrations change over time as differential equations.
- A set of differential equations that closely describe how a system develops is a model of the system.
Biochemical Reactions - Terminology Review

- **Chemical Reaction** A process that changes a set of chemical species into another
- **Reactants** The initial set of chemical species
- **Products** The new set of chemical species
- **A basic synthesis reaction** $A + B \rightarrow C$
- **An equilibrium reaction** $A + B \rightleftharpoons C$
- **Conservation of Mass** The mass of the products has to equal that of the reactants (in a closed system)
Biochemical Reactions - Some Basic Questions

- How quickly does a biochemical reaction take place?
- How will different concentrations of the reactants affect the reaction rate?
- What will be the concentrations of the reactants and products at equilibrium?
The Law of Mass Action

- Describes the rate at which chemicals collide and form new compounds
- It’s a model that describes molecular interactions
- Example: $A + B \rightarrow C$
- Concentration is represented as $[A]$, $[B]$ and $[C]$. 
- The rate can be expressed as the change in the amount of compound $C$: $\frac{d[C]}{dt}$
- This rate is determined by the number of collisions between $A$ and $B$ and the probability that a collision will lead to the combination of the molecules.
The Law of Mass Action

\[ \frac{d[C]}{dt} = k[A][B] \]

- Called the Law of Mass Action

- \( k \) is the rate constant. Takes into account shapes, attraction and temperature.

- \( k \) is different for every reaction.
Equilibrium Constant

- \( A + B \xrightleftharpoons[k_-]{k_+} C \)

- \( A \) is consumed by forward reaction and produced by the reverse reaction, so

\[
\frac{d[A]}{dt} = k_- [C] - k_+ [A][B]
\]

- At equilibrium, the reactions cancel each other out and

\[
\frac{k_-}{k_+} \equiv K_{eq} = \frac{[A]_{eq}[B]_{eq}}{[C]_{eq}}
\]

- Exercise: Show that this equation follows from the previous one
Equilibrium Constant - Exercise

\[ \frac{k_-}{k_+} \equiv K_{eq} = \frac{[A]_{eq}[B]_{eq}}{[C]_{eq}} \]

- What is the relationship between the equilibrium concentrations of A, B and C if \( K_{eq} \) is greater than 1?
- Less than 1?
- Almost equal to 1?
Enzyme Basics

- Enzymes help to convert *substrates* into *products*
- Catalysts - affect the rate of the reaction but are not changed by it
- Speed up biological reactions by up to 10 million times
- Very specific - usually one enzyme catalyzes one reaction
- Regulated by feedback loops - like those found in signalling pathways
How Enzymes Work - An example
Enzyme Kinetics - A Law Breaker

- Assume a model of an enzyme catalyzed reaction:
  \[ S + E \rightarrow P + E \]
- If we increase the concentration of the substrate, what happens to the reaction rate?
Enzyme Kinetics - A Law Breaker

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Enzyme Kinetics - A Law Breaker

- Assume a model of an enzyme catalyzed reaction:
  \[ S + E \rightarrow P + E \]
- If we increase the concentration of the substrate, what happens to the reaction rate?
  - Should go up linearly
  - That’s not what happens
  - The rate only increases to a maximum value
Enzyme Kinetics - A Better Model

- $S + E \xrightleftharpoons[k_1]{k_{-1}} C \xrightarrow[k_2]{k_{-2}} P + E$

- Substrate combines with Enzyme to form Complex
- Complex breaks down into Product and Enzyme
- But the Product is mostly removed, so that reverse reaction doesn’t really occur
- Can assume that reaction doesn’t happen. The conventional form:

  - $S + E \xrightleftharpoons[k_1]{k_{-1}} C \xrightarrow[k_2]{k_{-2}} P + E$

- Called the Michaelis-Menten Model of enzyme kinetics
Enzyme Kinetics - Rates of Change

\[ S + E \xrightleftharpoons[k_{-1}]{k_1} C \xrightarrow{k_2} P + E \]

- For ease of writing, let \( s = [S] \), \( c = [C] \), \( e = [E] \), and \( p = [P] \).

- Using Law of Mass Action, can write four differential equations:

\[
\begin{align*}
\frac{ds}{dt} &= k_{-1} c - k_1 se \\
\frac{de}{dt} &= (k_{-1} + k_2)c - k_1 se \\
\frac{dc}{dt} &= k_1 se - (k_2 + k_{-1})c \\
\frac{dp}{dt} &= k_2 c
\end{align*}
\]
Enzyme Kinetics - Michaelis-Menten Equation

- Given the differential equations and some assumptions, it is possible to approximate the rate of product formation.

**Definitions:**
- \( \nu \) the rate at which the product is formed
- \( k_2 \) the rate constant for dissociation of the enzyme-product complex
- \([E]_0\) the enzyme concentration
- \([S]\) the substrate concentration
- \(K_m\) the Michaelis constant which measures the affinity of the substrate for the enzyme.

**The Michaelis-Menten equation:**

\[
\nu = k_2 [E]_0 \frac{[S]}{K_m + [S]}
\]
Enzyme Kinetics - Application to the Frog Cell Cycle

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Outline
Differential Equations - An Overview
The Law of Mass Action
Enzyme Kinetics
Enzyme Kinetics - Exercise 1

- Identify, substrate, enzyme and product
- Ignoring ATP, write the forward (phosphorylating) reaction following the Michaelis-Menten model
- What is the differential equation for the change in concentration of Wee1? Wee1-P?
- Use the Michaelis-Menten reaction to write a formula for the rate of product formation.
With the people near you, choose a reaction from the cycle

Identify, substrate, enzyme and product

Ignoring ATP, write the reaction following the Michaelis-Menten model

Use the Michaelis-Menten reaction to write a formula for the rate of product formation.

Be ready to present to the group