Calculus for the Life Sciences
Lecture Notes – Other Functions and Asymptotes

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Outline

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   - ATP and Myosin

2. Polynomials
   - Applications of Polynomials

3. Rational Functions
   - Vertical Asymptote
   - Horizontal Asymptote
   - Lineweaver-Burk Plot

4. Square Root Functions
   - Weak Acid Chemistry
Proteins

- Life forms are characterized by their distinct molecular composition, especially proteins
- Proteins are the primary building blocks of life
- Enzymes are proteins that facilitate reactions inside the cell
- Enzymes are noted for their specificity and speed under a narrow range of conditions
  - $\beta$-galactosidase catalyzes the break down of lactose into glucose and galactose
  - Urease rapidly converts urea into ammonia and carbon dioxide
**Michaelis-Menten Enzyme Reaction**

- Substrate, $S$, combines reversibly to the enzyme $E$ to form a enzyme-substrate complex $ES$
- The complex decomposes irreversibly to form a product $P$

$$E+S \overset{k_1}{\underset{k_{-1}}{\rightleftharpoons}} ES \overset{k_2}{\rightarrow} E+P.$$ 

- The law of mass action is applied to these biochemical equations
Reaction Model

- The law of mass action applied to biochemical equations
- Differential equations are formed (later in the course)
- Simplifications for basic reactions
  - The enzyme-substrate complex forms extremely rapidly, creating a **quasi-steady state**
  - The forward reaction or **turnover number**, \( k_2 \), occurs on a slower time scale
The **Michaelis-Menten reaction rate** for product

\[ R ([S]) = \frac{k_2[E_0][S]}{K_m + [S]} = \frac{V_{max}[S]}{K_m + [S]}, \]

- \([S]\) is the substrate concentration
- \(V\) (or \(V_{max}\)) is called the **maximal velocity of the reaction**
- \(K_m\) is the **Michaelis constant**
- \(K_m\) is substrate concentration at which the reaction achieves half of the maximum velocity
Binding of ATP to Myosin

- Binding of ATP to myosin in forming cross-link bridges to actin for the power stroke of striated muscle tissue satisfies a Michaelis-Menten kinetics.
- The reaction velocity is an actual velocity of motion, where the chemical energy of ATP is transformed into mechanical energy by movement of the actin filament.
- For rabbit psoas muscle tissue, experimental measurements give $V_{max} = 2040$ nm/sec and $K_m = 150$ mM.
- The initial rise in the reaction velocity is almost linear.
- As the concentration increases, there are diminishing returns with the eventual saturation of the reaction at some maximal rate.
Graph of the binding of ATP to Myosin

\[ R([S]) = \frac{2040[S]}{150+[S]} \]
Polynomials

- The most **general polynomial of order** \( n \) is

\[
p_n(x) = a_n x^n + a_{n-1} x^{n-1} + a_{n-2} x^{n-2} + \ldots + a_1 x + a_0
\]

- Coefficients \( a_i \) are constants and \( n \) is a positive integer
- \( a_n \neq 0 \)
- **Degree of a polynomial** is the same as the **order of the polynomial**
- Linear functions are first order polynomials
- Quadratic functions are second order polynomials
Applications of Polynomials

- Polynomials can fit complicated data, providing a simple model
- Excellent routines exist for finding the best least squares fit of a polynomial to data
- Polynomials are defined for all values of $x$ and form very smooth curves
- It is easy to use polynomials for interpreting data
  - Finding where minimum and maximum values occur
  - Computing the area under the curve
- These phenomena are topics that Calculus covers
Properties of Polynomials

- Polynomials are considered nice functions because of their well-behaved properties.
- Difficult to find the roots of an equation (setting $p_n(x) = 0$) for a polynomial with $n > 2$, and rarely even possible for $n > 4$.
- Easy to use in approximations or numerical methods.
Example of Cubic Polynomial

Consider the cubic polynomial given by

\[ p(x) = x^3 - 3x^2 - 10x \]

Find the roots of this equation and graph this cubic polynomial

Solution: Factoring

\[ p(x) = x^3 - 3x^2 - 10x = x(x - 5)(x + 2) = 0 \]

The roots of this polynomial are \( x = 0, -2, \) or \( 5 \)

Later techniques of Calculus will find

- The high point occurring at \((-1.08, 6.04)\)
- The low point occurring at \((3.08, -30.04)\)
Solution (cont): The graph is

\[ p(x) = x^3 - 3x^2 - 10x \]
Consider the quartic polynomial given by

\[ p(x) = x^4 - 5x^2 + 4 \]

Find the roots of this equation

**Solution: Factoring**

\[ p(x) = (x^2 - 1)(x^2 - 4) = (x - 1)(x + 1)(x - 2)(x + 2) = 0 \]

The roots of this polynomial are \( x = -2, -1, 1, 2 \)
Rational Functions

**Definition:** A function $r(x)$ is a **rational function** if $p(x)$ and $q(x)$ are polynomials and

$$r(x) = \frac{p(x)}{q(x)} \quad \text{for} \quad q(x) \neq 0$$

- The domain of the rational function, $r(x)$, is all $x$ such that $q(x) \neq 0$
- The roots of the polynomial $q(x)$ are candidates for **vertical asymptotes** of $r(x)$
- When the order of the polynomial in the numerator of a rational function is less than or equal to the order of the polynomial of the denominator, then a **horizontal asymptote** occurs
Definition: When the graph of a function \( f(x) \) approaches a vertical line, \( x = a \), as \( x \) approaches \( a \), then that line is called a **vertical asymptote**

- A function cannot continuously cross a vertical asymptote
- Most of the time a rational function, \( r(x) = \frac{p(x)}{q(x)} \) has a vertical asymptote at \( x = a \) when \( q(a) = 0 \)
**Definition:** When the graph of a function $f(x)$ approaches a horizontal line, $y = c$, as $x$ becomes very large and positive ($x \to \infty$), or $x$ becomes very large and negative ($x \to -\infty$), then the line, $y = c$, is called a **horizontal asymptote**

Note that a function can cross a horizontal asymptote for “small” values of $x$
Horizontal Asymptotes for Rational Functions

Let \( r(x) \) be a rational function with polynomial \( p(x) = a_n x^n + \ldots + a_0 \) of degree \( n \) in the numerator and polynomial \( q(x) = b_m x^m + \ldots + b_0 \) of degree \( m \) in the denominator.

1. If \( n < m \), then \( r(x) \) has a horizontal asymptote of \( y = 0 \).
2. If \( n > m \), then \( r(x) \) becomes unbounded for large values of \( x \) (positive or negative).
3. If \( n = m \), then \( r(x) \) has a horizontal asymptote of \( y = a_n / b_n \).
The simplest rational function is

\[ r(x) = \frac{1}{x} \]

where \( p(x) = 1 \) and \( q(x) = x \)

This function is defined for all \( x \neq 0 \) (domain)

Consider the sequence of numbers

\[ x_n = \frac{1}{2}, \frac{1}{3}, \frac{1}{4}, ..., \frac{1}{k}, ... \]

for \( n = 2, 3, 4, ..., k, ... \)

These numbers are getting closer and closer to zero
Since

\[ r(x_n) = \frac{1}{x_n} = \frac{1}{1/n} = n \]

\[ r(x_n) = \frac{1}{x_n} = 2, 3, 4, \ldots, k, \ldots \quad \text{for} \quad n = 2, 3, 4, \ldots, k, \ldots \]

which is getting larger and larger, so approaching the vertical line \( x = 0 \)

Thus, there is a **vertical asymptote** at \( x = 0 \)
The graph of \( y = \frac{1}{x} \) is
Consider the rational function

\[ r(x) = \frac{10x}{2 + x} \]

This function is typical of a function from Michaelis-Menten enzyme kinetics.

1. Find the domain of the function
2. Find the \( x \) and \( y \)-intercepts
3. Find vertical and horizontal asymptotes
4. Graph the function
Solution: The denominator is zero when \( x = -2 \) so the domain is

\[ x \neq -2 \]

The function passes through the origin, \( x \) and \( y \)-intercepts are zero.

The edge of the domain is \( x = -2 \), so we see there is a **vertical asymptote** at \( x = -2 \).
Solution (cont): The rational function is

\[ r(x) = \frac{10x}{2 + x} \]

The numerator and denominator are linear functions (degree of polynomials are the same)

\[ p(x) = 10x \quad \text{and} \quad q(x) = x + 2 \]

Alternately, we can see that as \( x \) get “large,” then the 2 in \( q(x) \) becomes insignificant.

Thus, for \( x \) “large”

\[ r(x) \approx \frac{10x}{x} = 10 \]

Thus, a horizontal asymptote occurs at \( y = 10 \)
The graph of \( y = \frac{10x}{2+x} \) is

\[
\begin{array}{c|c}
\text{r(x)} & 10/2+1 \\
\hline
-20 & -10 \\
0 & 0 \\
10 & 10 \\
20 & 20 \\
30 & 30 \\
\end{array}
\]
Consider the rational function

\[ f(x) = \frac{x + 2}{x - 3} \]

where \( p(x) = x + 2 \) and \( q(x) = x - 3 \)

1. Find the domain of the function
2. Find the \( x \) and \( y \)-intercepts
3. Find vertical and horizontal asymptotes
4. Graph the function
Solution: The denominator is zero when \( x = 3 \) so the domain is

\[ x \neq 3 \]

The \( x \)-intercept is found when the numerator is zero, so \( x = -2 \)

The \( y \)-intercept is \( f(0) = -\frac{2}{3} \)

The edge of the domain is \( x = 3 \), so we see there is a **vertical asymptote** at \( x = 3 \)
Solution (cont): The rational function is

\[ f(x) = \frac{x + 2}{x - 3} \]

The numerator and denominator are linear functions (degree of polynomials are the same)

\[ p(x) = x + 2 \quad \text{and} \quad q(x) = x - 3 \]

Thus, for \( x \) “large”

\[ f(x) \approx \frac{x}{x} = 1 \]

Thus, a **horizontal asymptote** occurs at \( y = 1 \)
The graph of \( y = \frac{x+2}{x-3} \) is
Consider the rational function

\[ f(x) = \frac{4x^2}{4 - x^2} \]

where \( p(x) = 4x^2 \) and \( q(x) = 4 - x^2 \)

1. Find the domain of the function
2. Find the \( x \) and \( y \)-intercepts
3. Find vertical and horizontal asymptotes
4. Graph the function
Solution: The denominator is zero when \( x = \pm 2 \) so the domain is

\[
x \neq \pm 2
\]

This function clearly passes through the origin, so the \( x \) and \( y \)-intercept is \( (x, y) = (0, 0) \)

Note that this function is an even function

The edge of the domain is \( x = \pm 2 \), so we see there are vertical asymptotes at \( x = \pm 2 \)
Solution (cont): The rational function is

\[ f(x) = \frac{4x^2}{4 - x^2} \]

The numerator and denominator are quadratic functions (degree of polynomials are the same)

Thus, for \( x \) “large”

\[ f(x) \approx \frac{4x^2}{-x^2} = -4 \]

Thus, a horizontal asymptote occurs at \( y = -4 \)
The graph of $y = \frac{4x^2}{4-x^2}$ is
The Michaelis-Menten rate function traces out a hyperbola

\[ V = \frac{V_{\text{max}} [S]}{K_m + [S]} \]

The inverse of this expression is written

\[ \frac{1}{V} = \frac{K_m + [S]}{V_{\text{max}}[S]} = \frac{K_m}{V_{\text{max}}[S]} + \frac{1}{V_{\text{max}}} \]
The inverse expression is **linear** in \( \frac{1}{[S]} \) and \( \frac{1}{V} \)

Define \( y = \frac{1}{V} \) and \( x = \frac{1}{[S]} \), then

\[
y = \frac{K_m}{V_{max}} x + \frac{1}{V_{max}}.
\]

- The slope of this line is \( K_m/V_{max} \)
- The \( y \)-intercept is \( 1/V_{max} \)
- The \( x \)-intercept is \( -1/K_m \)
Below is the Lineweaver-Burk Plot

![Lineweaver-Burk Plot](image)

The graph shows a linear relationship between $1/V$ and $1/[S]$. The slope of the line is equal to $K_m/V_{max}$. The intercepts are:

- $1/V_{max}$ when $1/[S] = 0$
- $-1/K_m$ when $1/[S] = 0$

The equation of the line is:

$$\frac{1}{V} = \frac{1}{V_{max}} + \left(2 \cdot \frac{K_m}{V_{max}}\right) \cdot \frac{1}{[S]}$$
The **Lineweaver-Burk Plot** provides a valuable method for experimentally measuring the characteristics of an enzyme.

Experimentally, one measures the rate (velocity) of a reaction $V$ as a function of the substrate concentration $[S]$.

Find the best least squares linear fit to the inverse of the data.

The intercepts and slope give the constants $V_{max}$ and $K_m$.

If the data aren’t linear, then the enzyme is not Michaelis-Menten type.
Suppose an enzyme satisfies the equation

\[ V = \frac{20[S]}{10 + [S]} \]

- Create a graph for \([S] \geq 0\), showing any asymptotes
- Find the Lineweaver-Burk plot for this enzyme
- Find the enzyme’s characteristic parameters, \(K_m\) and \(V_{max}\)
**Solution:** The graph passes through the origin with no vertical asymptotes in the domain \([S] \geq 0\)

Since

\[
V = \frac{20[S]}{10 + [S]}
\]

the numerator and denominator are both linear

This gives a horizontal asymptote of \(V = 20\)
Graph of rational function for enzyme

\[ V = \frac{20[S]}{10 + [S]} \]
Solution (cont): The Lineweaver-Burk formulation looks at the inverse of the enzyme reaction formula.

Define $x = 1/[S]$ and $y = 1/V$

\[
y = \frac{10 + 1/x}{20/x} = \frac{10x + 1}{20} = \frac{1}{2}x + \frac{1}{20}
\]

Since the $y$-intercept is $1/V_{\max} = \frac{1}{20}$, so $V_{\max} = 20$
The slope is $K_m/V_{max} = \frac{1}{2}$, so $K_m = 10$
A weak acid with equilibrium constant, $K_a$, and normality, $x$, was shown to have acid concentration

$$[H^+] = \frac{1}{2} \left( -K_a + \sqrt{K_a^2 + 4K_a x} \right)$$

The $[H^+]$ is a square root function of the normality, $x$
Formic Acid has an equilibrium constant, $K_a = 1.77 \times 10^{-4}$.

Below is a graph of $[H^+]$.

![Graph of Formic Acid Solution](image)
The concentration of \([H^+]\) for **Formic Acid** was graphed above. The pH of the solution is \(-\log_{10}([H^+])\).

Below is a graph of the pH.
Square Root Function

- The square root function is the inverse of the quadratic function
- The square root function is only defined for positive quantities under the radical
- The domain of a square root function is found by solving the inequality for the function under the radical being greater than zero
Consider the function

\[ y = \sqrt{x + 2} \]

Find the domain of this function and graph the function

**Solution:** The domain of this function satisfies \( x + 2 \geq 0 \)

This example has its function defined for \( x \geq -2 \)
Below is a graph of $y = \sqrt{x + 2}$

$y = (x + 2)^{1/2}$
Consider the function

\[ y = \sqrt{8 - 2x} \]

**Solution:** The domain of this function satisfies \(8 - 2x \geq 0\) or \(x \leq 4\)

The range is all \(y \geq 0\)
Example 2: Square Root Function

Below is a graph of \( y = \sqrt{8 - 2x} \)
Example 3: Square Root Function

Consider the function

\[ y = \sqrt{8 - 2x - x^2} \]

Find the domain and range of this function and graph the function.

**Solution:** The domain of this function satisfies

\[ 8 - 2x - x^2 = (4 + x)(2 - x) \geq 0 \]

This example has its function defined for \(-4 \leq x \leq 2\).

Since the maximum occurs at \(x = -1\) (with \(y(-1) = \sqrt{9}\))

The range is \(0 \leq y \leq 3\).
Below is a graph of $y = \sqrt{8 - 2x - x^2}$

$y = (8 - 2x - x^2)^{1/2}$