Calculus for the Life Sciences I

Lecture Notes – Other Functions and Asymptotes

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Outline

Enzyme Kinetics

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
  - β-galactosidase catalyzes the break down of lactose into glucose and galactose
  - Urease rapidly converts urea into ammonia and carbon dioxide

Enzyme Reaction

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

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

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

Reaction Model

Reaction Model

- The law of mass action applied to biochemical equations
- Differential equations are formed (Math 122)
- 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

Enzyme Production Rate

The **Michaelis-Menten reaction rate** for product

$$R([\mathrm{S}]) = \frac{k_2[\mathrm{E}_0][\mathrm{S}]}{K_m + [\mathrm{S}]} = \frac{V_{max}[\mathrm{S}]}{K_m + [\mathrm{S}]},$$

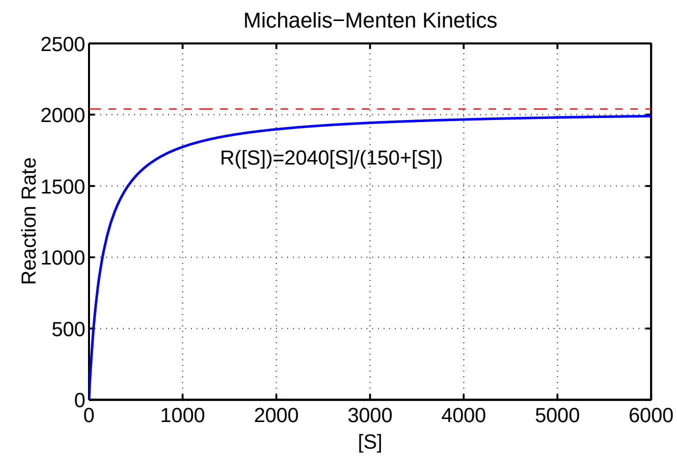
- $[S]$ is the substrate concentration
- V (or V_{max}) is called the **maximal velocity of the reaction**
- K_m is the **Michaelis constant**
- K_m is substrate concentration at which the reaction achieves half of the maximum velocity

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 filement
- 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

Binding of ATP to Myosin

Graph of the binding of ATP to Myosin



Polynomials

Polynomials

- The most **general polynomial of order n** is

$$p_n(x) = a_n x^n + a_{n-1}x^{n-1} + a_{n-2}x^{n-2} + ... + a_1 x + a_0$$

- 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

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 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

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 1

Consider the cubic polynomial given by

$$p(x) = x^3 - 3x^2 - 10x$$

Find the roots of this equation and graph this cubic polynomial

Skip Example

Solution: Factoring

$$p(x) = x^3 - 3x^2 - 10x = x(x-5)(x+2) = 0$$

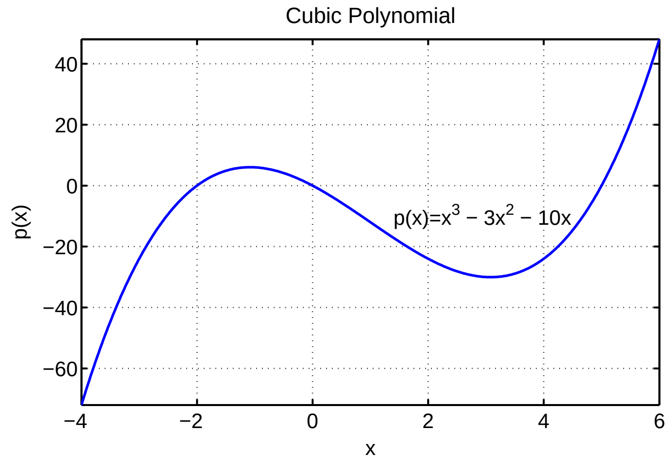
The roots of this polynomial are $x = 0, -2$, or 5

Later techniques of Calculus will find

- The high point occurring at $(-1.08, 6.04)$
- The low point occurring at $(3.08, -30.04)$

Example of Cubic Polynomial 2

Solution (cont): The graph is



Example of Quartic Polynomial

Consider the quartic polynomial given by

$$p(x) = x^4 - 5x^2 + 4$$

Find the roots of this equation

Skip Example

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

Rational Functions

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

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

- 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

Vertical Asymptote

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 $q(a) = 0$

Horizontal Asymptote

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

Horizontal Asymptotes for Rational Functions

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

Simple Hyperbola 1

The simplest rational function is

$$r(x) = \frac{1}{x}$$

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

Skip Example

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

Consider the sequence of numbers

$$x_n = \frac{1}{2}, \frac{1}{3}, \frac{1}{4}, ... \frac{1}{k} ... \qquad \text{for} \qquad n = 2, 3, 4, ..., k, ...$$

These numbers are getting closer and closer to zero

Simple Hyperbola 2

Since

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

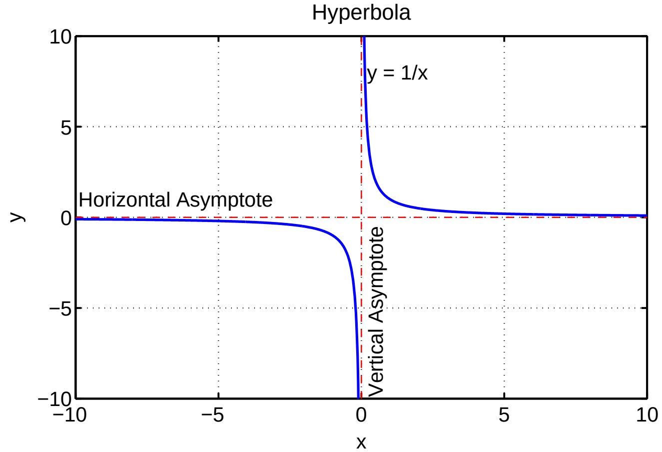
$$r(x_n) = \frac{1}{x_n} = 2, 3, 4, ..., k, ... \qquad \text{for} \qquad n = 2, 3, 4, ..., k, ...$$

which is getting larger and larger, so approaching the vertical line $x = 0$

Thus, there is a **vertical asymptote** at $x = 0$

Simple Hyperbola 3

The graph of $y = \frac{1}{x}$ is



Rational Function Example 1 1

Consider the rational function

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

Skip Example

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

Rational Function Example 1 2

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 $x = -2$

Rational Function Example 1 3

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.

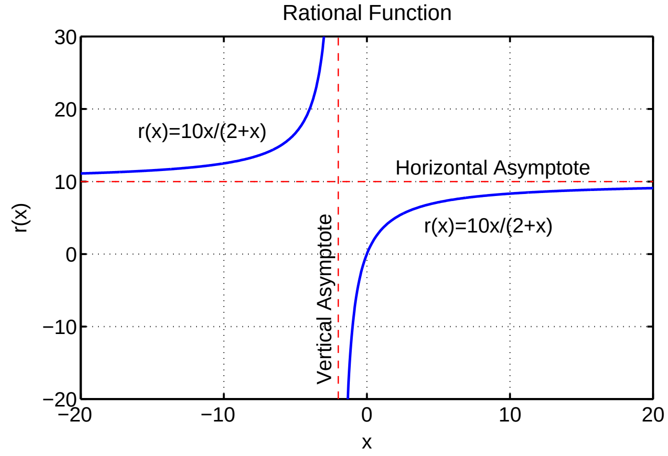
Thus, for x "large"

$$r(x) \approx \frac{10x}{x} = 10$$

Thus, a **horizontal asymptote** occurs at $y = 10$

Rational Function Example 1 4

The graph of $y = \frac{10x}{2+x}$ is



Rational Function Example 2 1

Consider the rational function

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

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

Skip Example

1. Find the domain of the function
2. Find the x and y-intercepts
3. Find vertical and horizontal asymptotes
4. Graph the function

Rational Function Example 2 2

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 $x = 3$

Rational Function Example 2 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)

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

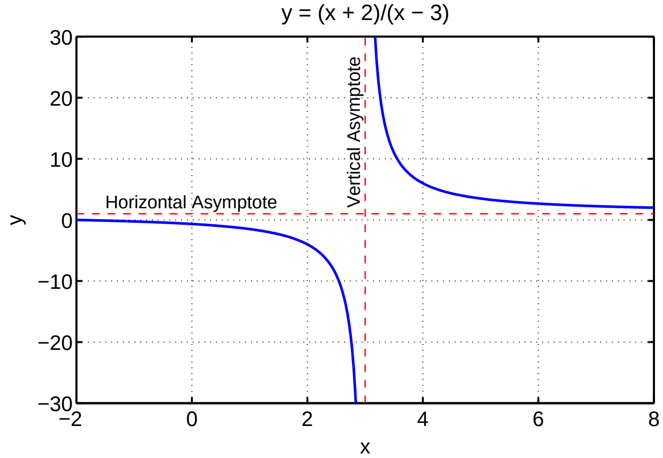
Thus, for x "large"

$$f(x) \approx \frac{x}{x} = 1$$

Thus, a **horizontal asymptote** occurs at $y = 1$

Rational Function Example 2 — 4

The graph of $y = \frac{x+2}{x-3}$ is



Rational Function Example 3 — 1

Consider the rational function

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

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

Skip Example

1. Find the domain of the function
2. Find the x and y-intercepts
3. Find vertical and horizontal asymptotes
4. Graph the function

Rational Function Example 3 — 2

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 $x = \pm 2$

Rational Function Example 3 — 3

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)

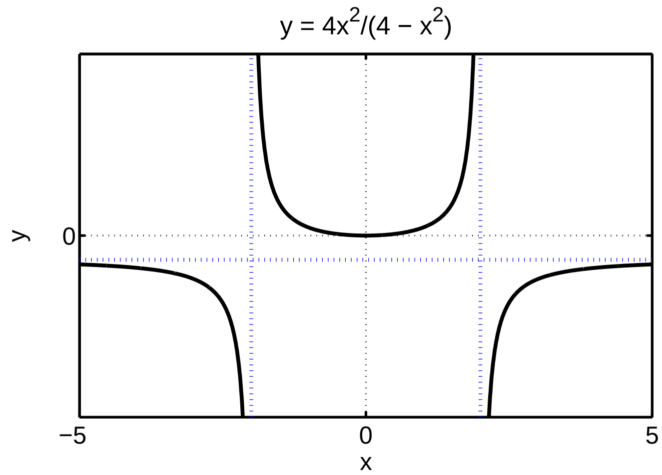
Thus, for x "large"

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

Thus, a **horizontal asymptote** occurs at $y = -4$

Rational Function Example 3

The graph of $y = \frac{4x^2}{4-x^2}$ is



Lineweaver-Burk Plot

The **Michaelis-Menten rate function** traces out a hyperbola

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

The inverse of this expression is written

$$\frac{1}{V} = \frac{K_m + [S]}{V_{max}[S]} = \frac{K_m}{V_{max}}\frac{1}{[S]} + \frac{1}{V_{max}}$$

Lineweaver-Burk Plot

The inverse expression is **linear** in $\frac{1}{[S]}$ and $\frac{1}{V}$

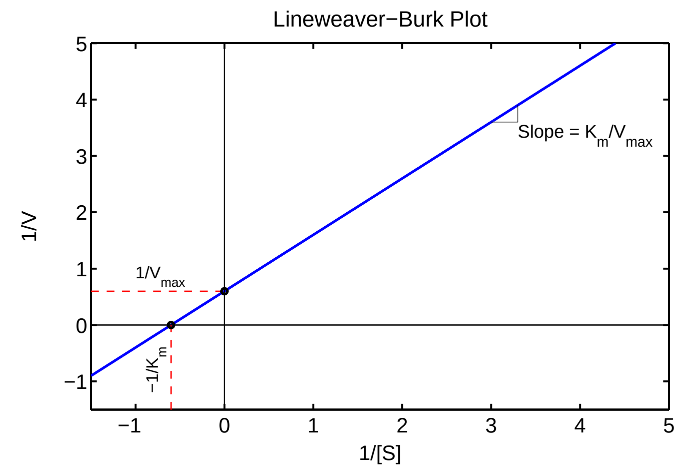
Define $y = \frac{1}{V}$ and $x = \frac{1}{[S]}$, then

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

- The slope of this line is K_m/V_{max}
- The y-intercept is $1/V_{max}$
- The x-intercept is $-1/K_m$

Lineweaver-Burk Plot

Below is the Lineweaver-Burk Plot



Lineweaver-Burk Plot 4

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

Enzyme Example 1

Suppose an enzyme satisfies the equation

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

Skip Example

- 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}

Enzyme Example 2

Solution: The graph passes through the origin with no vertical asymptotes in the domain $[S] \geq 0$

Since

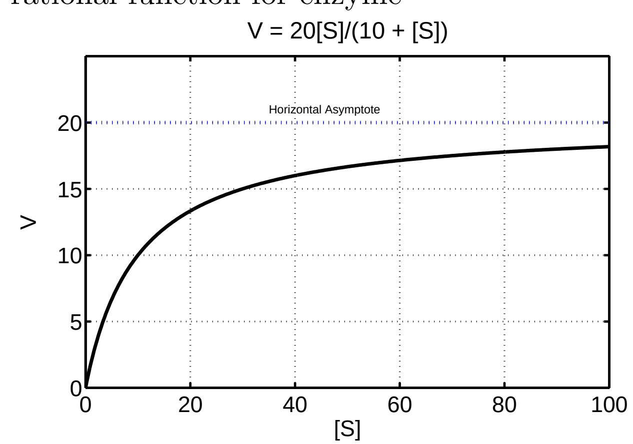
$$V = \frac{20[S]}{10 + [S]}$$

the numerator and denominator are both linear

This gives a horizontal asymptote of $V = 20$

Enzyme Example 3

Graph of rational function for enzyme



Enzyme Example 4

Solution (cont): The Lineweaver-Burk formulation looks at the inverse of the enzyme reaction formula

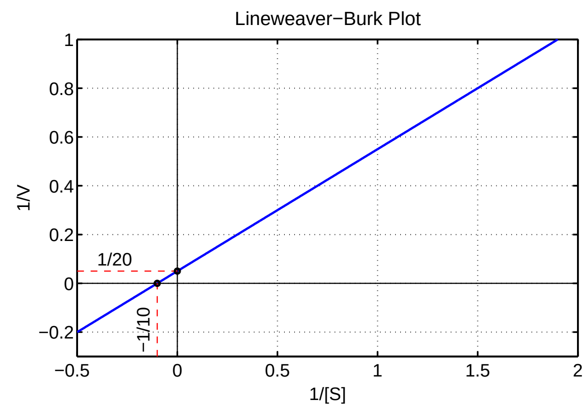
Define $x = 1/[S]$ and $y = 1/V$

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

Since the y-intercept is $1/V_{max} = \frac{1}{20}$, so $V_{max} = 20$

Enzyme Example 5

The slope is $K_m/V_{max} = \frac{1}{2}$, so $K_m = 10$



Weak Acid Chemistry

Weak Acid Chemistry

A weak acid with equilibrium constant, K_a, and normality, x, was shown to have acid concentration

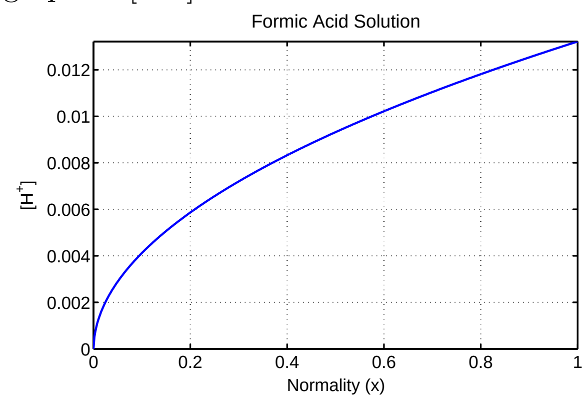
$$[H^+] = \frac{1}{2}\left(-K_a + \sqrt{K_a^2 + 4K_a x}\right)$$

The $[H^+]$ is a **square root function** of the normality, x

Formic Acid - $[H^+]$ 1

Formic Acid has an equilibrium constant, $K_a = 1.77 \times 10^{-4}$

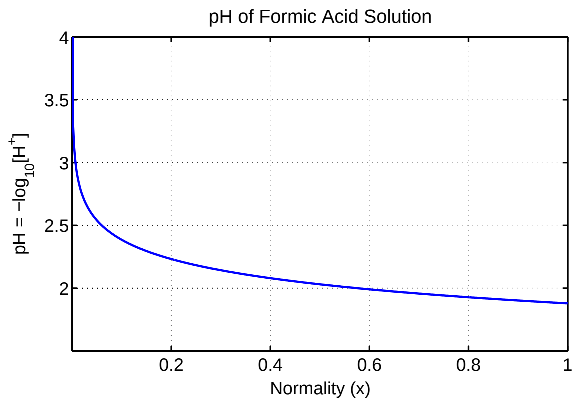
Below is a graph of $[H^+]$



Formic Acid - pH 2

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

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**

Example of Square Root Function 1

Consider the function

$$y = \sqrt{x+2}$$

Skip Example

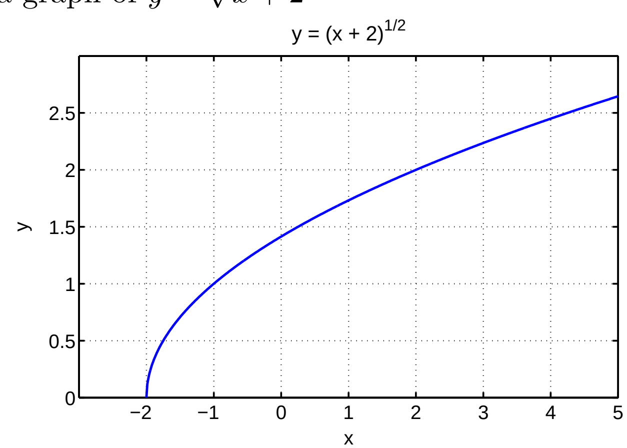
Find the domain of this function and graph the function

Solution: The domain of this function satisfies $x + 2 \geq 0$

This example has its function defined for $x \geq -2$

Example of Square Root Function 2

Below is a graph of $y = \sqrt{x+2}$



Example 2: Square Root Function 1

Consider the function

$$y = \sqrt{8 - 2x}$$

Skip Example

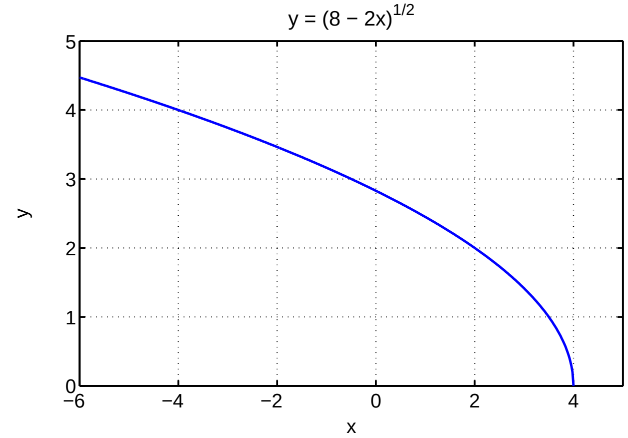
Find the domain and range of this function and graph the function

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

The range is all $y \geq 0$

Example2: Square Root Function 2

Below is a graph of $y = \sqrt{8 - 2x}$



Example 3: Square Root Function 1

Consider the function

$$y = \sqrt{8 - 2x - x^2}$$

Skip Example

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 $0 \leq y \leq 3$

Example of Square Root Function 2

Below is a graph of $y = \sqrt{8 - 2x - x^2}$