BMS 1901 Calculus for Life Sciences

Week9

10/26/2021

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Study objectives

To understand the Area Problem in Biology

Able to solve a definite integral using Riemann sum

Able to find indefinite integrals

To understand the fundamental theorem of calculus

References:

Biocalculus by Stewart and Day

Chp5.1 Areas, Distances, and Pathogenesis

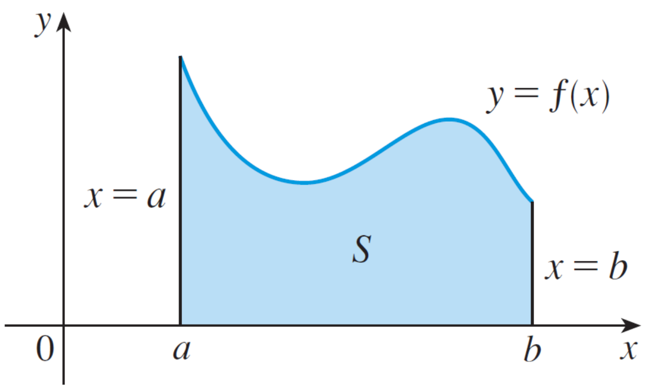
Chp5.2 The Definite Integral

Chp

The Area Problem

We begin by attempting to solve the *area problem*: Find the area of the region S that lies under the curve $y = f(x)$ from a to b.

This means that S, illustrated in Figure 1, is bounded by the graph of a continuous function f [where $f(x) \geq 0$], the vertical lines $x = a$ and $x = b$, and the x-axis.



$$S = \{(x, y) \mid a \leqslant x \leqslant b,\ 0 \leqslant y \leqslant f(x)\}$$

Figure 1

The Area Problem

For a rectangle, the area is defined as the product of the length and the width. The area of a triangle is half the base times the height. The area of a polygon is found by dividing it into triangles (as in Figure 2) and adding the areas of the triangles.

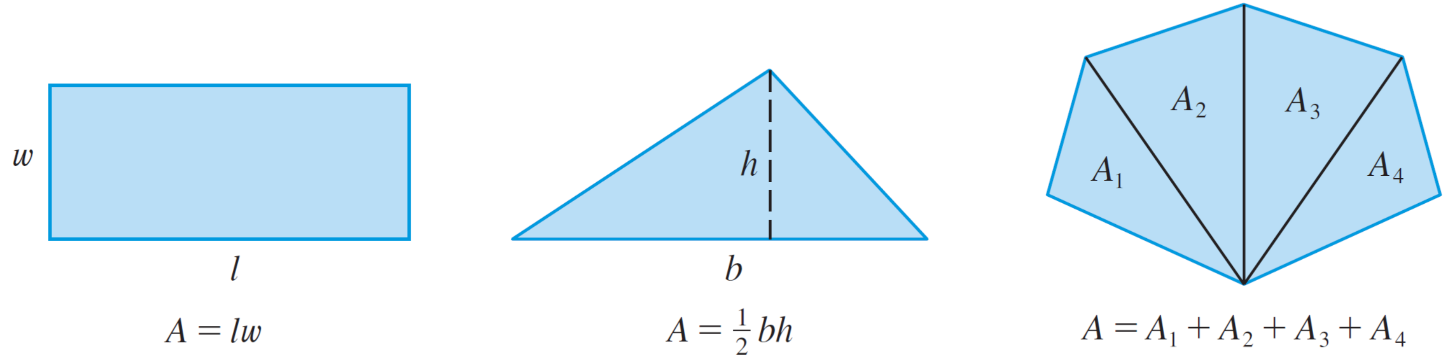


Figure 2

The Area Problem

However, it isn't so easy to find the area of a region with curved sides.

We first approximate the region *S* by rectangles and then we take the limit of the areas of these rectangles as we increase the number of rectangles. The next example illustrates the procedure.

Example 1

Use rectangles to estimate the area under the parabola $y = x^2$ from 0 to 1 (the parabolic region S illustrated in Figure 3).

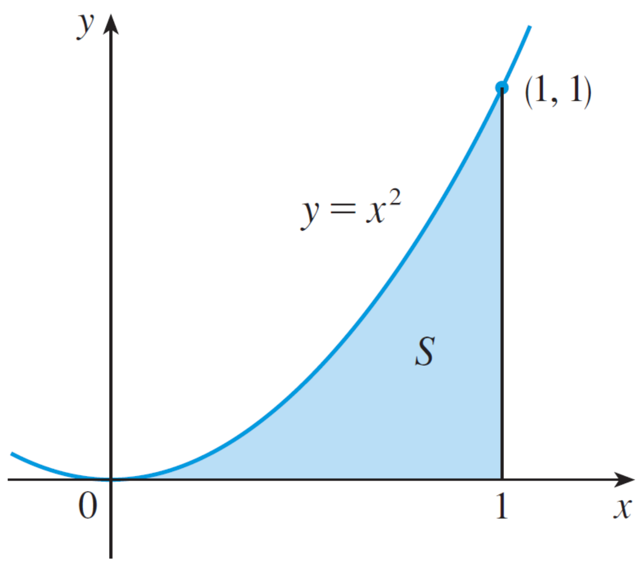


Figure 3

Example 1 – *Solution*

Suppose we divide S into four strips S_1, S_2, S_3, and S_4 by drawing the vertical lines $x = \frac{1}{4}$, $x = \frac{1}{2}$, and $x = \frac{3}{4}$ as in Figure 4(a).

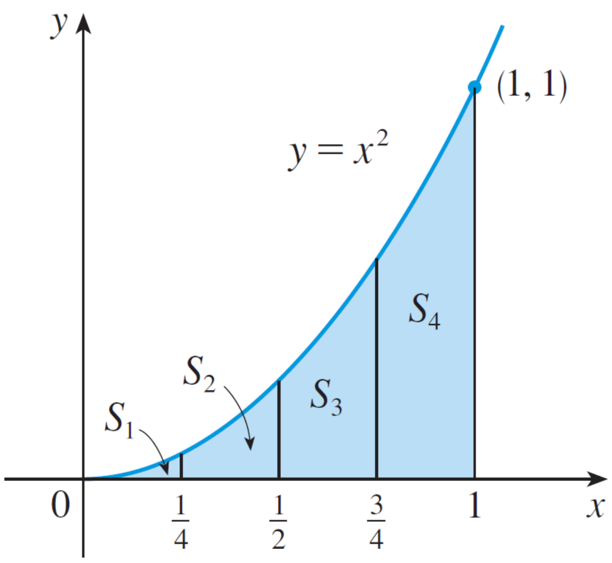


Figure 4(a)

Example 1 – *Solution*

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We can approximate each strip by a rectangle that has the same base as the strip and whose height is the same as the right edge of the strip [see Figure 4(b)].

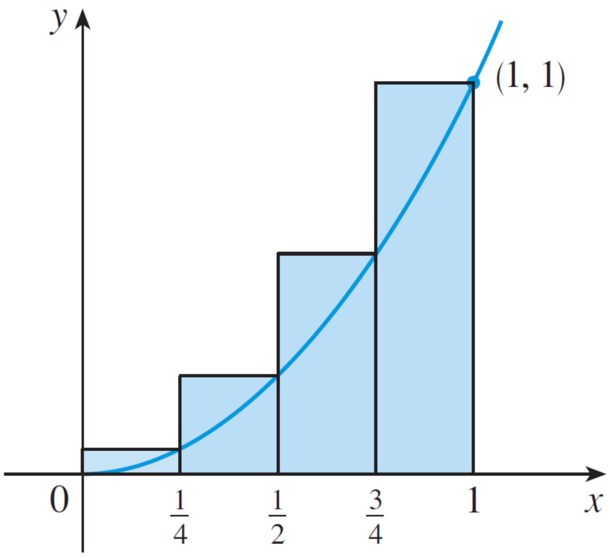


Figure 4(b)

Example 1 – *Solution*

cont'd

In other words, the heights of these rectangles are the values of the function $f(x) = x^2$, at the right end-points of the subintervals

$$\left[0, \tfrac{1}{4}\right], \left[\tfrac{1}{4}, \tfrac{1}{2}\right], \left[\tfrac{1}{2}, \tfrac{3}{4}\right], \text{ and } \left[\tfrac{3}{4}, 1\right].$$

Each rectangle has width $\frac{1}{4}$ and the heights are $\left(\frac{1}{4}\right)^2, \left(\frac{1}{2}\right)^2, \left(\frac{3}{4}\right)^2,$ and 1^2. If we let R_4 be the sum of the areas of these approximating rectangles, we get

$$R_4 = \frac{1}{4} \cdot \left(\frac{1}{4}\right)^2 + \frac{1}{4} \cdot \left(\frac{1}{2}\right)^2 + \frac{1}{4} \cdot \left(\frac{3}{4}\right)^2 + \frac{1}{4} \cdot 1^2 = \frac{15}{32} = 0.46875$$

From Figure 4(b) we see that the area *A* of *S* is less than R_4, so

$$A < 0.46875$$

Example 1 – *Solution*

cont'd

Instead of using the rectangles in Figure 4(b) we could use the smaller rectangles in Figure 5 whose heights are the values of $f(x)$ at the *left* endpoints of the subintervals. (The leftmost rectangle has collapsed because its height is 0.)

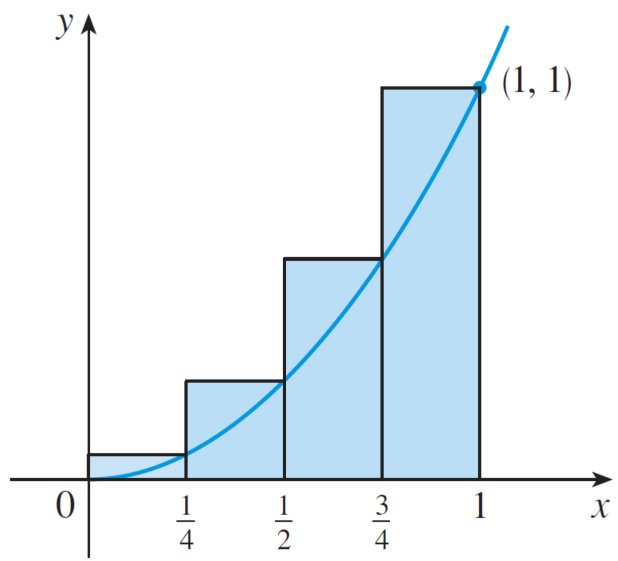


Figure 4(b)

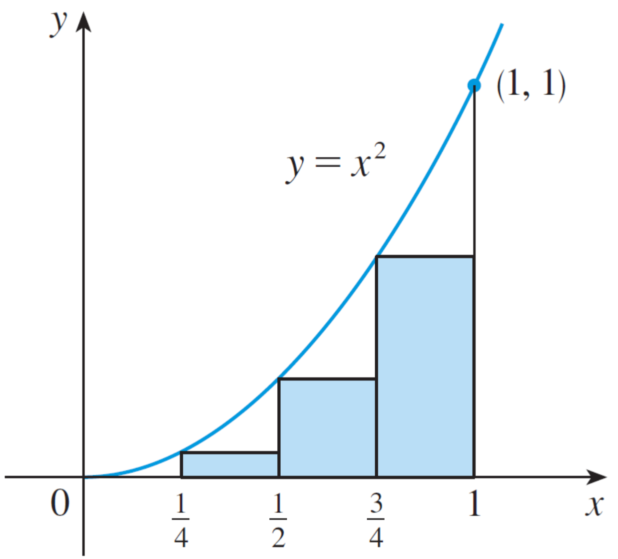


Figure 5

Example 1 – *Solution*

cont'd

The sum of the areas of these approximating rectangles is

$$L_4 = \frac{1}{4} \cdot 0^2 + \frac{1}{4} \cdot \left(\frac{1}{4}\right)^2 + \frac{1}{4} \cdot \left(\frac{1}{2}\right)^2 + \frac{1}{4} \cdot \left(\frac{3}{4}\right)^2 = \frac{7}{32} = 0.21875$$

We see that the area of S is larger than L_4, so we have lower and upper estimates for A:

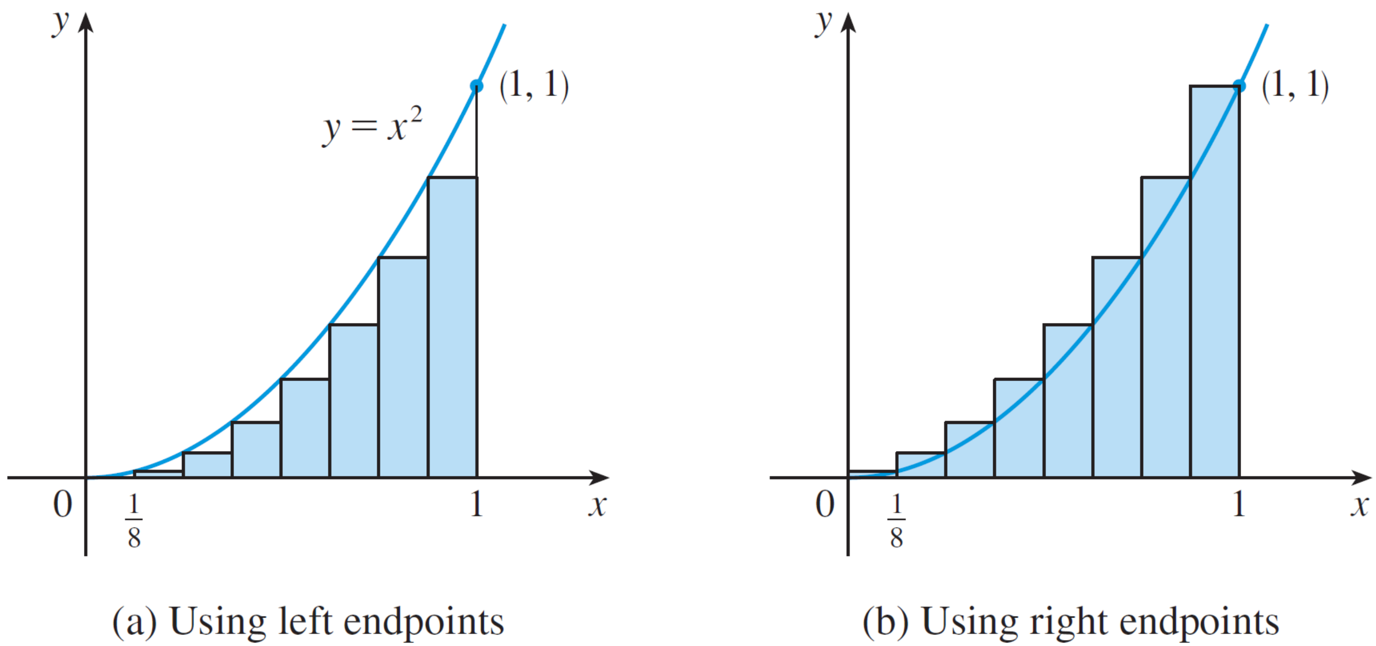
$$0.21875 < A < 0.46875$$

We can repeat this procedure with a larger number of strips.

Example 1 – *Solution*

cont'd

Figure 6 shows what happens when we divide the region *S* into eight strips of equal width.



Approximating *S* with eight rectangles

Figure 6

Example 1 – *Solution*

cont'd

By computing the sum of the areas of the smaller rectangles (L_8) and the sum of the areas of the larger rectangles (R_8), we obtain better lower and upper estimates for A:

$$0.2734375 > A > 0.3984375$$

So one possible answer to the question is to say that the true area of S lies somewhere between 0.2734375 and 0.3984375.

We could obtain better estimates by increasing the number of strips.

Example 1 – *Solution*

cont'd

The table below shows the results of similar calculations (with a computer) using n rectangles whose heights are found with left endpoints (L_n) or right endpoints (R_n).

n	L_n	R_n
10	0.2850000	0.3850000
20	0.3087500	0.3587500
30	0.3168519	0.3501852
50	0.3234000	0.3434000
100	0.3283500	0.3383500
1000	0.3328335	0.3338335

In particular, we see by using 50 strips that the area lies between 0.3234 and 0.3434.

Example 1 – *Solution*

cont'd

With 1000 strips we narrow it down even more: A lies between 0.3328335 and 0.3338335.

A good estimate is obtained by averaging these numbers: $A \approx 0.3333335$.

The Area Problem

As n increases, both L_n and R_n become better and better approximations to the area of S.

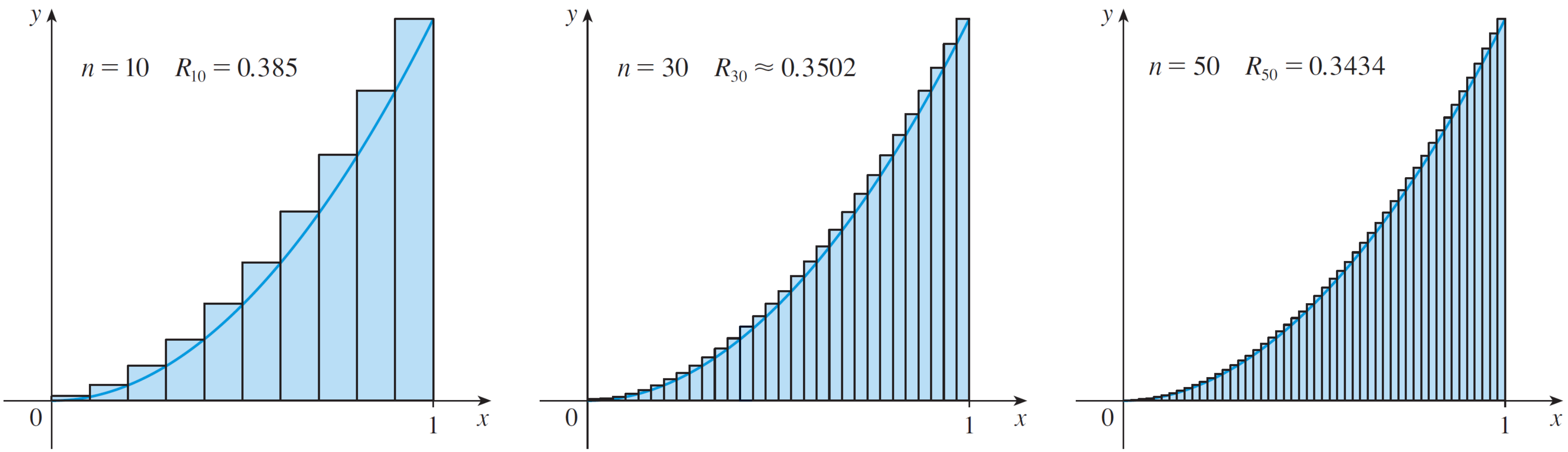
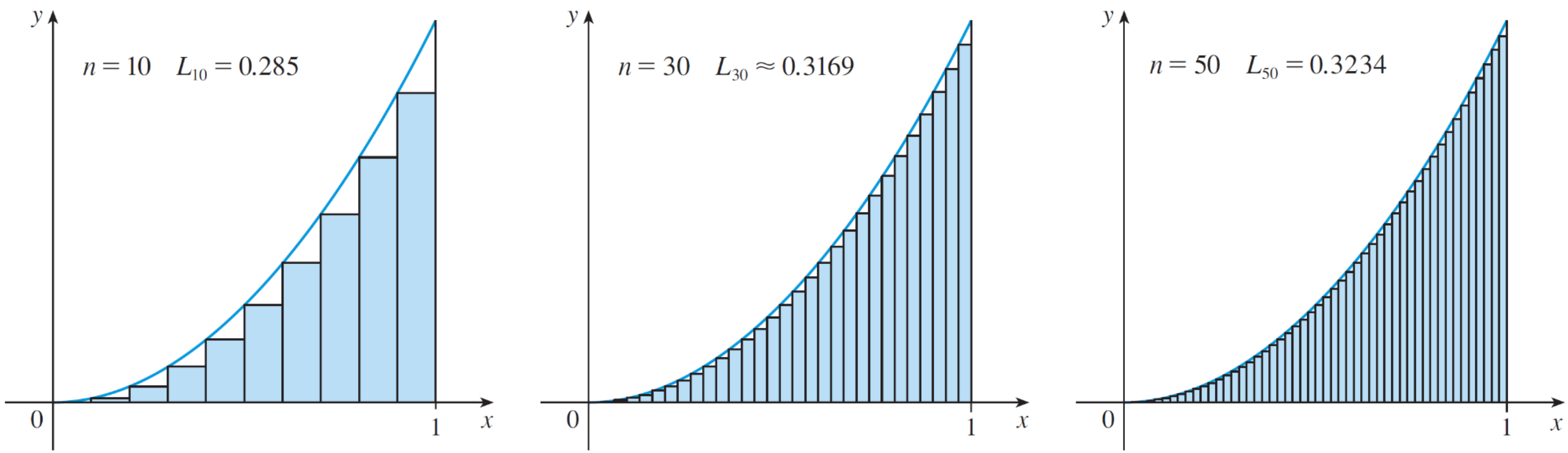


Figure 8

The Area Problem



The area is the number that is smaller than all upper sums and larger than all lower sums.

Figure 9

Therefore we *define* the area *A* to be the limit of the sums of the areas of the approximating rectangles, that is,

$$A = \lim_{n \to \infty} R_n = \lim_{n \to \infty} L_n = \frac{1}{3}$$

The Area Problem

Let's divide the region S into n strips $S_1, S_2, \ldots, S_n$ of equal width as in Figure 10.

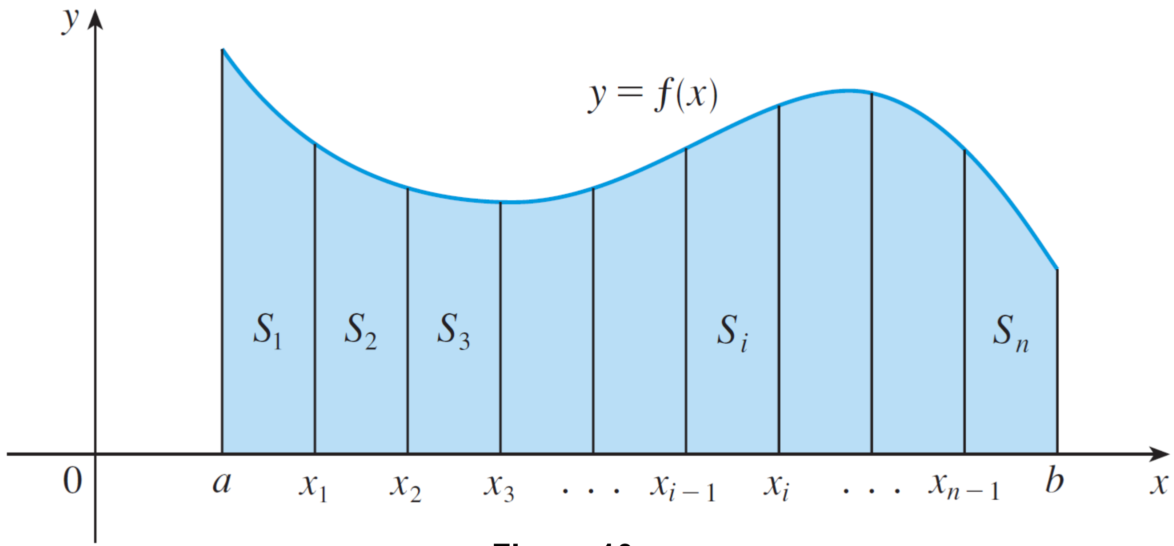


Figure 10

The width of the interval $[a, b]$ is $b - a$, so the width of each of the n strips is

$$\Delta x = \frac{b - a}{n}$$

The Area Problem

Let's approximate the ith strip S_i by a rectangle with width Δx and height $f(x_i)$, which is the value of f at the right endpoint (see Figure 11).

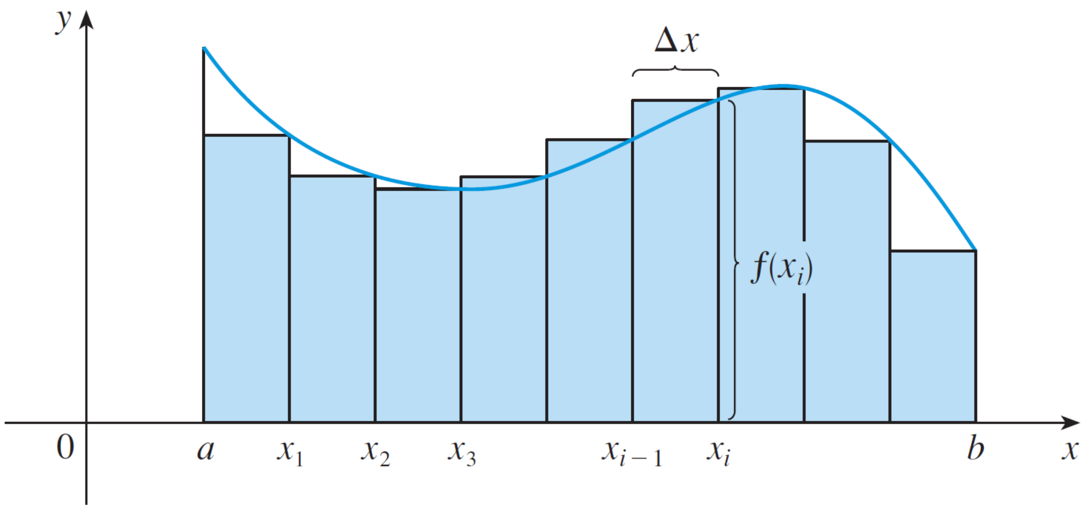


Figure 11

Then the area of the ith rectangle is $f(x_i)\,\Delta x$.

The Area Problem

The area of *S* is approximated by the sum of the areas of these rectangles, which is

$$R_n = f(x_1)\,\Delta x + f(x_2)\,\Delta x + \cdots + f(x_n)\,\Delta x$$

(2) Definition The **area** A of the region S that lies under the graph of the continuous function f is the limit of the sum of the areas of approximating rectangles:

$$A = \lim_{n \to \infty} R_n = \lim_{n \to \infty} [f(x_1)\,\Delta x + f(x_2)\,\Delta x + \cdots + f(x_n)\,\Delta x]$$

We get the same value if we use left endpoints:

(3) $$A = \lim_{n \to \infty} L_n = \lim_{n \to \infty} [f(x_0)\,\Delta x + f(x_1)\,\Delta x + \cdots + f(x_{n-1})\,\Delta x]$$

Example: Pathogenesis

Pathogenesis

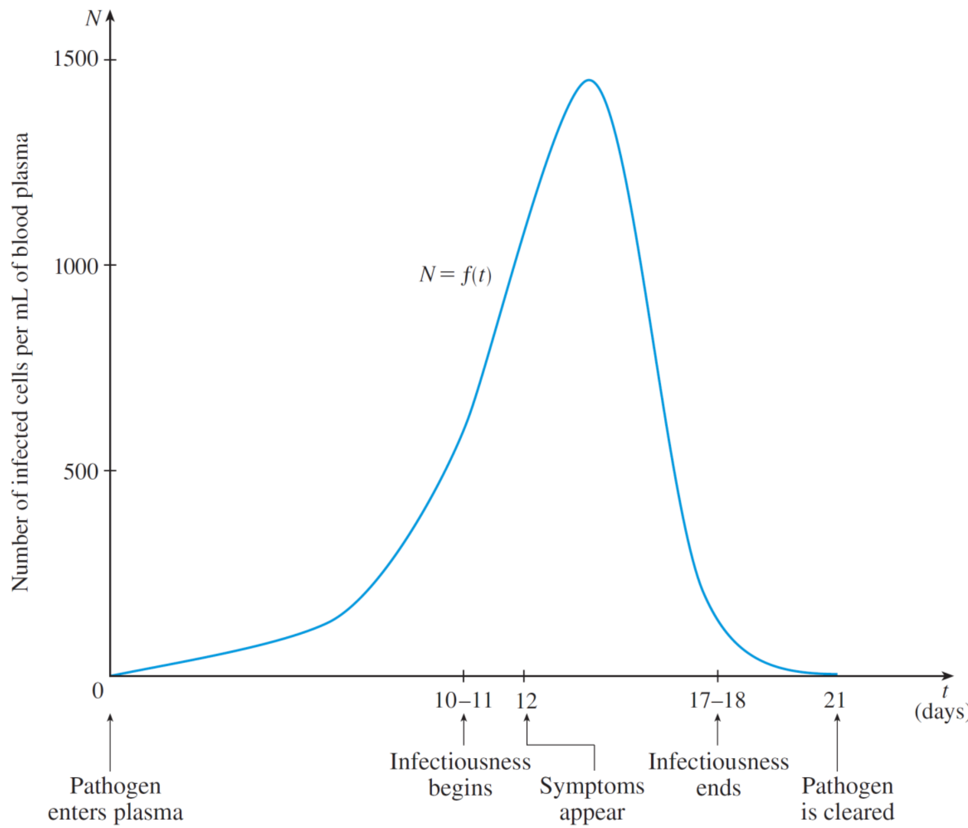
In general, the term *pathogenesis* refers to the way a disease originates and develops over time. In the case of measles, the virus enters through the respiratory tract and replicates there before spreading into the bloodstream and then the skin.

In a person with no immunity to measles the characteristic rash usually appears about 12 days after infection. The virus reaches a peak density in the blood at about 14 days.

The virus level then decreases fairly rapidly over the next few days as a result of the immune response.

Pathogenesis

This progression is reflected in the pathogenesis curve in Figure 17.



Measles pathogenesis curve

Figure 17

Pathogenesis

Notice that the vertical axis is measured in units of number of infected cells per mL of blood plasma.

Let's denote by f the measles pathogenesis function in Figure 17. Therefore $f(t)$ gives the number of infected cells per mL of plasma on day t.

Measles symptoms are thought to develop only after the immune system has been exposed to a **threshold** "amount of infection."

The amount of infection is determined by both the **number of infected cells** per mL and by the **duration** over which these cells are exposed to the immune system.

Pathogenesis

If the density of infected cells were constant during infection, then the total **amount of infection** would be measured as

$$\text{amount of infection} = \text{density of infected cells} \times \text{time}$$

with the units being (number of cells per mL) × days.

Of course the density is not constant, but we can break the duration of infection into shorter time intervals over which the density changes very little.

Pathogenesis

If each of these shorter time intervals has width Δt, we could add the areas $f(t_i)\,\Delta t$ of the rectangles in Figure 18 and get an approximation to the amount of infection over the first 12 days.

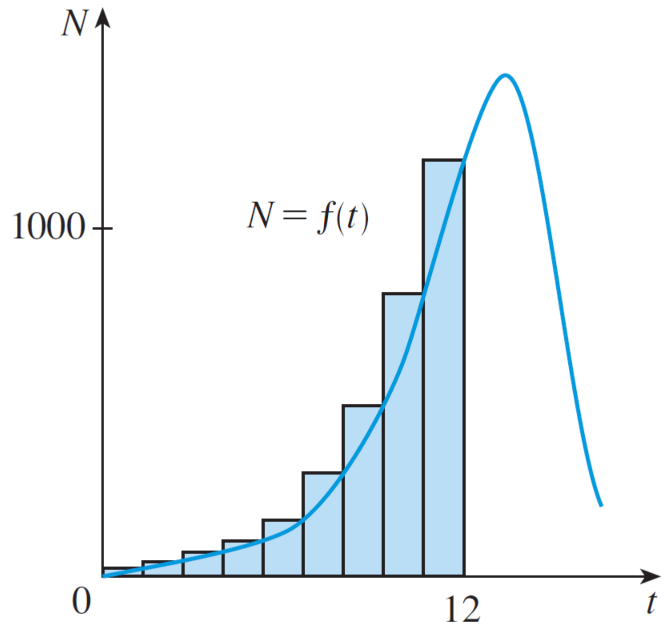


Figure 18

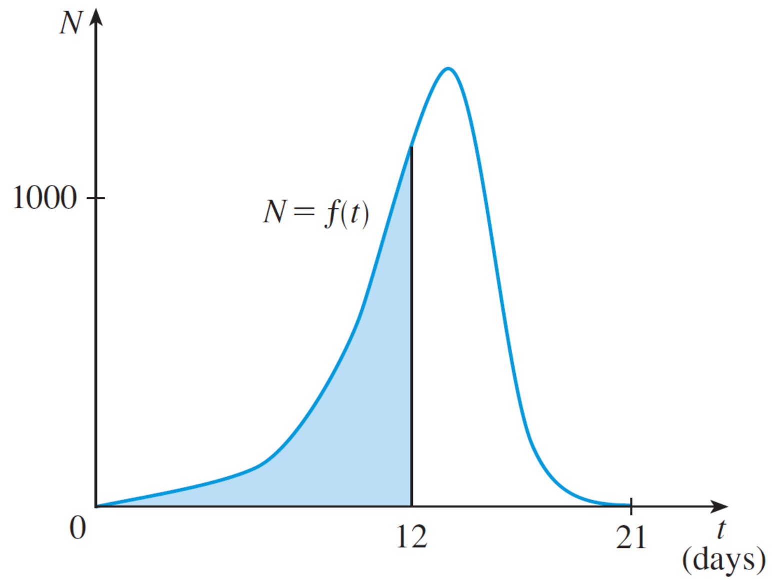
Pathogenesis

Then we take the limit as $\Delta t \to 0$ and the number of rectangles becomes large.

We conclude that the amount of infection needed to stimulate the appearance of symptoms is as follows.

> The area under the pathogenesis curve $N = f(t)$ from $t = 0$ to $t = 12$ (shaded in Figure 19) is equal to the total amount of infection needed to develop symptoms.

Pathogenesis



Area under pathogenesis curve up to 12 days is the amount of infection needed for symptoms.

Figure 19

The measles pathogenesis curve has been modeled by the polynomial

$$f(t) = -t(t - 21)(t + 1)$$

Matlab codes for estimating the area

```
% define independent variable and function
syms x
f(x)= 3-(3/4)*(x^2)

% display the chart
figure;
fplot(f)

% adjust limits and place legend
xlim([0 2]); ylim([0 3]); legend('f(x)')
bins = 5;
width = 2/bins;
for i = 1:bins
   xval = i*width;           % select a value of x
   height = double(f(xval));  % calculate the corresponding value of f(x)

   % plot a rectangle in red
   rectangle('Position',[xval 0 width height],'EdgeColor','r');
end
% add label and title
xlabel('x');title('Area under a curve, rough approximation');
```

You can play with the value of bins

The Definite Integral

The Definite Integral

We know a limit of the form

(1) $$\lim_{n\to\infty} \sum_{i=1}^{n} f(x_i^*)\,\Delta x = \lim_{n\to\infty} [f(x_1^*)\,\Delta x + f(x_2^*)\,\Delta x + \cdots + f(x_n^*)\,\Delta x]$$

We therefore give this type of limit a special name and notation.

(2) Definition of a Definite Integral If f is a function defined for $a \leqslant x \leqslant b$, we divide the interval $[a, b]$ into n subintervals of equal width $\Delta x = (b - a)/n$. We let $x_0\ (= a), x_1, x_2, \ldots, x_n\ (= b)$ be the endpoints of these subintervals and we let $x_1^*, x_2^*, \ldots, x_n^*$ be any **sample points** in these subintervals, so x_i^* lies in the ith subinterval $[x_{i-1}, x_i]$. Then the **definite integral of f from a to b** is

$$\int_a^b f(x)\,dx = \lim_{n\to\infty} \sum_{i=1}^{n} f(x_i^*)\,\Delta x$$

provided that this limit exists. If it does exist, we say that f is **integrable** on $[a, b]$.

The Definite Integral

Note 1
The symbol $\int$ was introduced by Leibniz and is called an **integral sign**. It is an elongated *S* and was chosen because an integral is a limit of sums.

In the notation $\int_a^b f(x)\,dx$, $f(x)$ is called the **integrand** and *a* and *b* are called the **limits of integration**; *a* is the **lower limit** and *b* is the **upper limit**.

For now, the symbol *dx* has no meaning by itself; $\int_a^b f(x)\,dx$ is all one symbol. The *dx* simply indicates that the independent variable is *x*. The procedure of calculating an integral is called **integration**.

The Definite Integral

Note 2
The definite integral $\int_a^b f(x)\,dx$ is a **number**; it does not depend on *x*. In fact, we could use any letter in place of *x* without changing the value of the integral:

$$\int_a^b f(x)\,dx = \int_a^b f(t)\,dt = \int_a^b f(r)\,dr$$

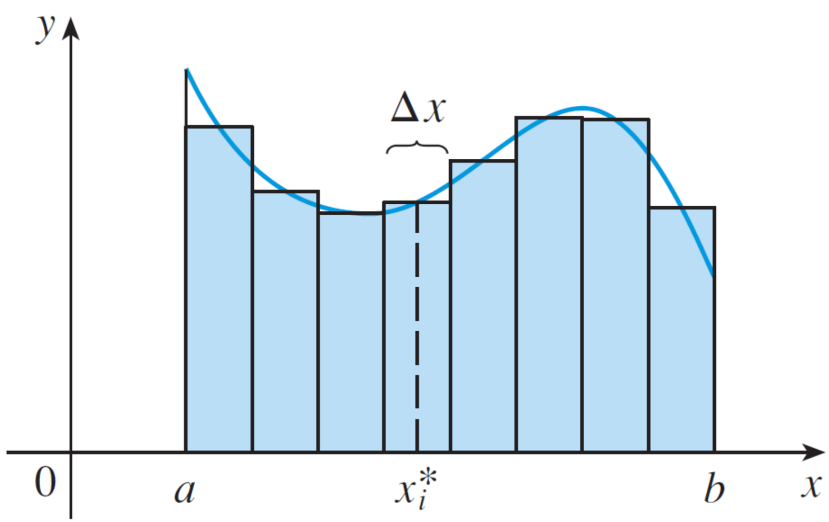
Note 3
The sum

$$\sum_{i=1}^{n} f(x_i^*)\,\Delta x$$

is called a **Riemann sum**.

The Definite Integral

We know that if *f* happens to be positive, then the Riemann sum can be interpreted as a sum of areas of approximating rectangles (see Figure 1).

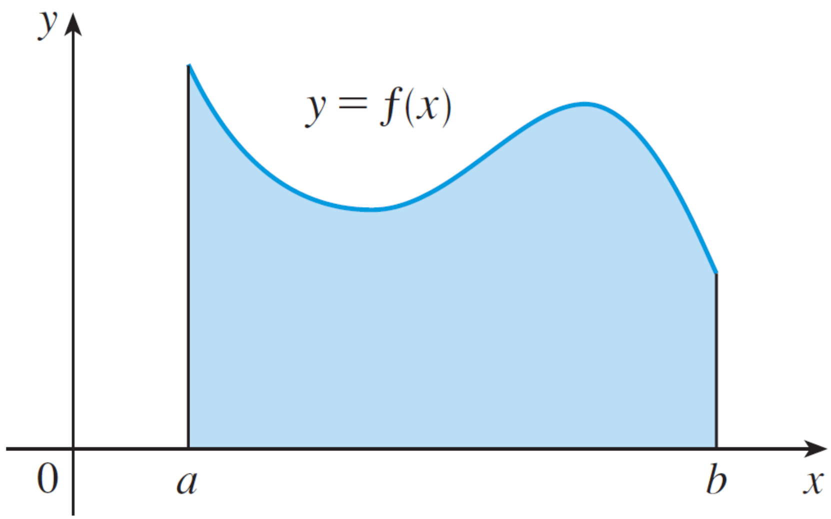


If $f(x) \geq 0$, the Riemann sum $\Sigma f(x_i^*)\,\Delta x$ is the sum of areas of rectangles.

Figure 1

The Definite Integral

The definite integral $\int_a^b f(x)\,dx$ can be interpreted as the area under the curve $y = f(x)$ from a to b. (See Figure 2.)

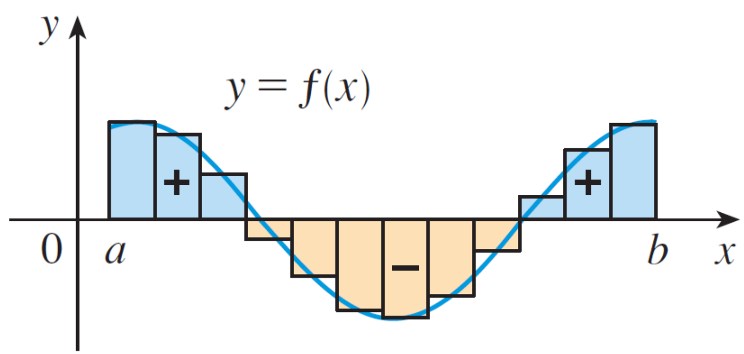


If $f(x) \geq 0$, the integral $\int_a^b f(x)\,dx$ is the area under the curve $y = f(x)$ from a to b.

Figure 2

The Definite Integral

If *f* takes on both positive and negative values, as in Figure 3, then the Riemann sum is the sum of the areas of the rectangles that lie above the *x*-axis and the *negatives* of the areas of the rectangles that lie below the *x*-axis (the areas of the blue rectangles *minus* the areas of the gold rectangles).

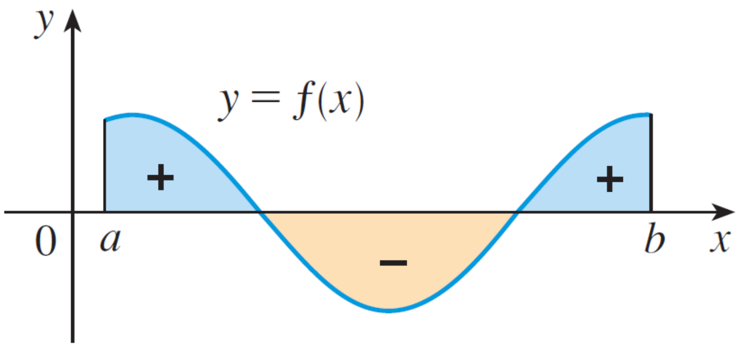


$\sum f(x_i^*)\,\Delta x$ is an approximation to the net area.

Figure 3

The Definite Integral

When we take the limit of such Riemann sums, we get the situation illustrated in Figure 4.



$\int_a^b f(x)\,dx$ is the net area.

Figure 4

The Definite Integral

A definite integral can be interpreted as a **net area,** that is, a difference of areas:

$$\int_a^b f(x)\,dx = A_1 - A_2$$

where A_1 is the area of the region above the *x*-axis and below the graph of *f*, and A_2 is the area of the region below the *x*-axis and above the graph of *f*.

Indefinite Integrals

Indefinite Integrals

Because of the relation given by the Evaluation Theorem between antiderivatives and integrals, the notation $\int f(x)\,dx$ is traditionally used for an antiderivative of f and is called an **indefinite integral**. Thus

$$\boxed{\int f(x)\,dx = F(x) \qquad \text{means} \qquad F'(x) = f(x)}$$

A definite integral $\int_a^b f(x)\,dx$ is a *number*, whereas an indefinite integral $\int f(x)\,dx$ is a *function* (or family of functions).

Indefinite Integrals

The connection between them is given by the Evaluation Theorem: If *f* is continuous on [*a*, *b*], then

$$\int_a^b f(x)\,dx = \int f(x)\,dx \Big]_a^b$$

Any formula can be verified by differentiating the function on the right side and obtaining the integrand. For instance,

$$\int \sec^2 x\,dx = \tan x + C \qquad \text{because} \qquad \frac{d}{dx}(\tan x + C) = \sec^2 x$$

Indefinite Integrals

(1) Table of Indefinite Integrals

$$\int [f(x) + g(x)]\,dx = \int f(x)\,dx + \int g(x)\,dx$$

$$\int cf(x)\,dx = c\int f(x)\,dx$$

$$\int x^n\,dx = \frac{x^{n+1}}{n+1} + C \quad (n \neq -1)$$

$$\int \frac{1}{x}\,dx = \ln|x| + C$$

$$\int e^x\,dx = e^x + C$$

$$\int e^{kx}\,dx = \frac{1}{k}e^{kx} + C$$

$$\int a^x\,dx = \frac{a^x}{\ln a} + C$$

$$\int \sin x\,dx = -\cos x + C$$

$$\int \cos x\,dx = \sin x + C$$

$$\int \sec^2 x\,dx = \tan x + C$$

$$\int \csc^2 x\,dx = -\cot x + C$$

$$\int \sec x \tan x\,dx = \sec x + C$$

$$\int \csc x \cot x\,dx = -\csc x + C$$

$$\int \frac{1}{x^2+1}\,dx = \tan^{-1} x + C$$

Example 3

Find the general indefinite integral

$$\int (10x^4 - 2\sec^2 x)\, dx$$

Solution:

Using our convention and Table 1 and properties of integrals, we have

$$\begin{aligned} \int (10x^4 - 2\sec^2 x)\, dx &= 10\int x^4\, dx - 2\int \sec^2 x\, dx \\ &= 10\,\frac{x^5}{5} - 2\tan x + C \\ &= 2x^5 - 2\tan x + C \end{aligned}$$

You should check this answer by differentiating it.

The Net Change Theorem

The Net Change Theorem

Net Change Theorem The integral of a rate of change is the net change:

$$\int_a^b F'(x)\,dx = F(b) - F(a)$$

Example 7 – *Integrating rate of growth*

If $N(t)$ is the size of a population at time t, explain the biological meaning of

$$\int_{t_1}^{t_2} \frac{dN}{dt}\, dt$$

Solution:

The derivative dN/dt is the **rate of growth of the population**. According to the Net Change Theorem, we have

$$\int_{t_1}^{t_2} \frac{dN}{dt}\, dt = N(t_2) - N(t_1)$$

This is the net change in population during the time period from t_1 to t_2. The population increases when births happen and decreases when deaths occur.

The Fundamental Theorem

The Fundamental Theorem

The first part of the Fundamental Theorem deals with functions defined by an equation of the form

(2) $$g(x) = \int_a^x f(t)\, dt$$

where *f* is a continuous function on [*a*, *b*] and *x* varies between *a* and *b*. Observe that *g* depends only on *x*, which appears as the variable upper limit in the integral.

If *x* is a fixed number, then the integral $\int_a^x f(t)\, dt$ is a definite number. If we then let *x* vary, the number $\int_a^x f(t)\, dt$ also varies and defines a function of *x* denoted by *g*(*x*).

The Fundamental Theorem

If f happens to be a positive function, then $g(x)$ can be interpreted as the area under the graph of f from a to x, where x can vary from a to b.

(Think of g as the "area so far" function; see Figure 4.)

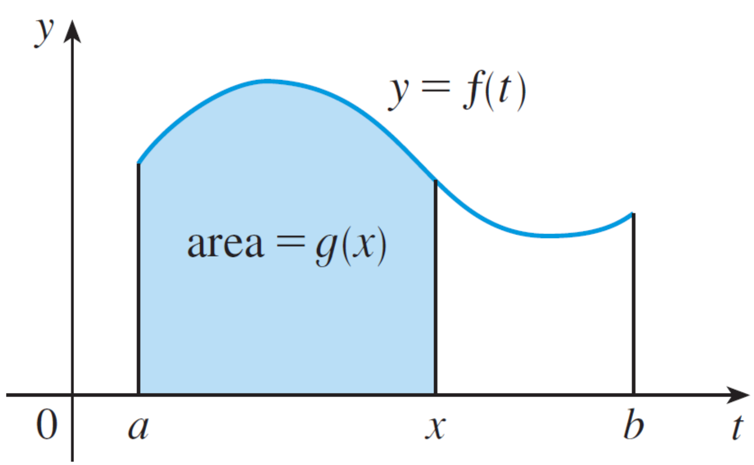


Figure 4

Example 9

If $g(x) = \int_a^x f(t)\,dt$ where $a = 1$ and $f(t) = t^2$, find a formula for $g(x)$ and calculate $g'(x)$.

Solution:

In this case we can compute $g(x)$ explicitly using the Evaluation Theorem:

$$g(x) = \int_1^x t^2\,dt = \frac{t^3}{3}\Big]_1^x = \frac{x^3 - 1}{3}$$

Then

$$g'(x) = \frac{d}{dx}\left(\tfrac{1}{3}x^3 - \tfrac{1}{3}\right)$$

$$= x^2$$

The Fundamental Theorem

The Fundamental Theorem of Calculus, Part 1 If f is continuous on $[a, b]$, then the function g defined by

$$g(x) = \int_a^x f(t)\,dt \qquad a \leqslant x \leqslant b$$

is an antiderivative of f, that is, $g'(x) = f(x)$ for $a < x < b$.

Using Leibniz notation for derivatives, we can write this theorem as

$$\frac{d}{dx}\int_a^x f(t)\,dt = f(x)$$

when *f* is continuous.

Evaluating Definite Integrals

Evaluation Theorem If f is continuous on the interval $[a, b]$, then

$$\int_a^b f(x)\,dx = F(b) - F(a)$$

where F is any antiderivative of f, that is, $F' = f$.

When applying the Evaluation Theorem we use the notation

$$F(x)\Big]_a^b = F(b) - F(a)$$

and so we can write

$$\int_a^b f(x)\,dx = F(x)\Big]_a^b \qquad \text{where} \qquad F' = f$$

Other common notations are $F(x)\,\big|_a^b$ and $[F(x)]_a^b$.

Example 1

Evaluate $\int_1^3 e^x \, dx$.

Solution:

An antiderivative of $f(x) = e^x$ is $F(x) = e^x$, so we use the Evaluation Theorem as follows:

$$\int_1^3 e^x \, dx = e^x \Big]_1^3 = e^3 - e$$

Differentiation and Integration as Inverse Processes

The Fundamental Theorem of Calculus Suppose f is continuous on $[a, b]$.

1. If $g(x) = \int_a^x f(t)\,dt$, then $g'(x) = f(x)$.

2. $\int_a^b f(x)\,dx = F(b) - F(a)$, where F is any antiderivative of f, that is, $F' = f$.

Appendix: Systems of Two Autonomous Differential Equations

Systems of Two Autonomous Differential Equations

The **predator-prey equations** is an example of two *coupled* differential equations that incorporates these assumptions is as follows:

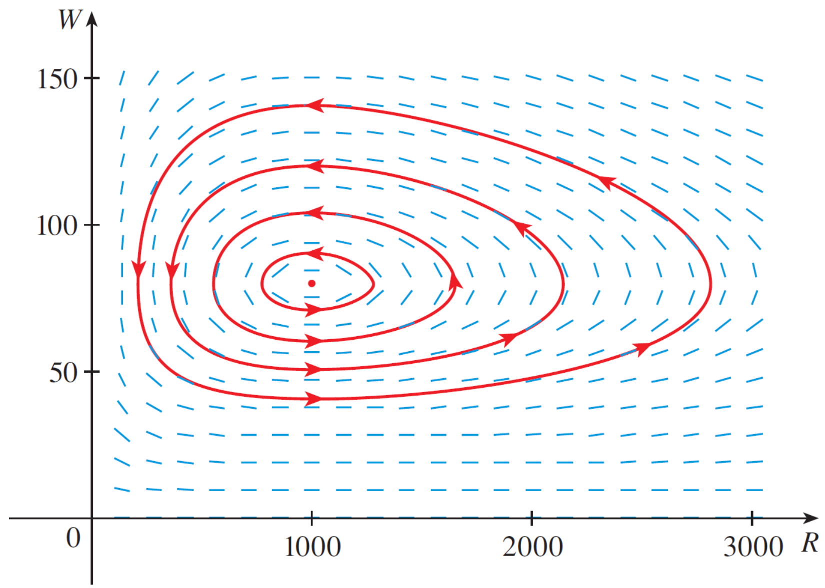
(1) $$\frac{dR}{dt} = rR - aRW \qquad \frac{dW}{dt} = -kW + bRW$$

where *k*, *r*, *a*, and *b* are positive constants.

Notice that the term $-aRW$ decreases the growth rate of the prey and the term bRW increases the growth rate of the predators.

Systems of Two Autonomous Differential Equations

This direction field is always tangent to the parametric curves representing solutions to Equations 1, as shown in Figure 4.



Phase portrait of the system

Terminology

A two-dimensional **system of linear differential equations** has the form

$$\frac{dx_1}{dt} = a_{11}(t)x_1 + a_{12}(t)x_2 + g_1(t)$$

$$\frac{dx_2}{dt} = a_{21}(t)x_1 + a_{22}(t)x_2 + g_2(t)$$

where $x_1(t)$ and $x_2(t)$ are unknown functions, $a_{ij}(t)$ are coefficients, and $g_i(t)$ are functions of time (sometimes called forcing, or input, functions).

Terminology

Equation 1 is a system of linear *first-order nonautonomous* differential equations.

If A and $\mathbf{g}$ are independent of time, then Equation 1 is a system of linear first-order *autonomous* differential equations.

Terminology

The autonomous system of equations for which **g = 0** is called a **homogeneous** system. Any autonomous system of equations for which **g ≠ 0** (which is called a **nonhomogeneous** system) can be reduced to a homogeneous system in which **g** = **0** through a change of variables.

Thus we consider systems of the form

$$\frac{dx_1}{dt} = a_{11}x_1 + a_{12}x_2$$

$$\frac{dx_2}{dt} = a_{21}x_1 + a_{22}x_2$$

or, in matrix notation,

$$\frac{d\mathbf{x}}{dt} = A\mathbf{x} \qquad (2)$$

Example 1 – *Radioimmunotherapy*

Radioimmunotherapy is a cancer treatment in which radioactive atoms are attached to tumor-specific antibody molecules and then injected into the bloodstream.

The antibody molecules then attach only to tumor cells, where they deliver the cell-killing radioactivity. Mathematical models have been used to optimize this treatment.

Let's use $x_1(t)$ and $x_2(t)$ to denote the amount of antibody (in μg) in the blood and the tumor, respectively, at time t (in minutes after the start of treatment).

Example 1 – *Radioimmunotherapy* cont'd

If a denotes the per unit rate of clearance from the blood, b the per unit rate of movement from the blood into the tumor, and c the per unit rate of clearance from the tumor, a simple model is

$$\frac{dx_1}{dt} = -ax_1 - bx_1$$

$$\frac{dx_2}{dt} = bx_1 - cx_2$$

Terminology

Definition The x_1-nullcline of differential equation (2) is the set of points in the x_1x_2-plane satisfying the equation $dx_1/dt = 0$. From Equation 2, this is the line defined by the equation $a_{11}x_1 + a_{12}x_2 = 0$. The x_2-nullcline of differential equation (2) is the set of points in the x_1x_2-plane satisfying the equation $dx_2/dt = 0$. From Equation 2, this is the line defined by the equation $a_{21}x_1 + a_{22}x_2 = 0$.

Thus a system of two linear differential equations has two nullclines, one for each variable.

Both nullclines are straight lines and they intersect at the origin because both $dx_1/dt = 0$ and $dx_2/dt = 0$ at the point $(x_1, x_2) = (0, 0)$. (See Figure 1.)

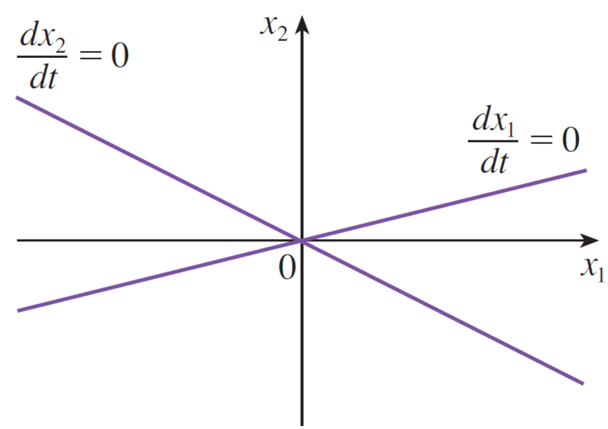


Figure 1

The Area Problem