

# LIVING IN A microbial world

second edition

**Bruce V. Hofkin**

This document overviews the media resources available for instructors and students who use *Living in a Microbial World*, Second Edition. It contains the complete table-of-contents for the resources on the Garland Science Learning System, as well as the text of the voice-over narration for all the movies.

## MEDIA RESOURCE LOCATIONS

The media resources for *Living In A Microbial World*, Second Edition are available in two locations. Resources intended solely for instructors are available on the Garland Science Website. Resources for students and instructors are available on the Garland Science Learning System (GSLs).

## INSTRUCTOR RESOURCES ON THE GARLAND SCIENCE WEBSITE

The following resources are available for instructors only on the Garland Science Website:

<http://instructors.garlandscience.com>

If you already have an approved instructor account, login using your email and password. If you are new to Garland Science, select “Instructor Registration” and complete the form. Once you are verified as an instructor, you will be able to access the resources.

### Figures

The images from the book are available in two convenient formats, PowerPoint® and JPEG. Figures are searchable by figure number, figure name, or by keywords used in the legends.

### Instructor Test Bank

Over 200 questions in a variety of formats: multiple-choice, matching, fill-in-the-blank, true/false, depth-of-understanding. Answers to all questions are supplied. Questions and answers are supplied as a Microsoft Word® file and can be used in homework, examinations, and personal response systems (clickers).

### Movies

The 24 movies include both animations that explain processes in detail and videos of biological processes. Each movie has a voice-over narration, and the text of the narration is located in the last section of this document, as well as on the website. Movies are provided in Windows® and Macintosh®-compatible formats for easy import into PowerPoint. The movies are available to students in the GSLs modules (see below).

### Media Guide

This document, which you are currently reading, overviews the multimedia package available for students and instructors. It contains the complete table-of-contents for the resources on the Garland Science Learning System, as well as the text of the voice-over narration for all the movies.

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Macintosh is a trademark of Apple, Inc.

## STUDENT AND INSTRUCTOR RESOURCES ON THE GARLAND SCIENCE LEARNING SYSTEM (GSL)

*Living In A Microbial World*, Second Edition comes with a redemption code that gives students free access to original tutorials with assessments, quizzes, 24 movies designed to complement the book, vocabulary review, and hints to the end-of-chapter questions, all on the Garland Science Learning System (GSL). For students to receive a redemption code with free access to the GSL, you must use the following ISBN when placing the book order: **9780815346012**.

The Garland Science Learning System allows instructors to:

- Use the modules to stimulate class discussion and enhance student participation.
- Assign tutorials to track student understanding of microbiology concepts.
- Use the quizzes to gauge comprehension of textbook topics.
- Engage students' imaginations with 24 movies that bring microbiology to life.
- Customize content to match your course and suit your students' needs.

Accessing the GSL modules is simple, just ...

1. Go to <http://garlandscience.rocketmix.com> and register. Select "Instructor Access" from the main menu and submit the form.
2. After registration is confirmed, you may access your course. At the top of the Instructor Dashboard you will see an "Enrolment Link," which is a URL address unique to your course that you provide students
3. The link will take students to the registration portal for your course, and once they sign up, everyone will be ready to go!
4. The system is free to instructors. Students may access the system free of charge by using the redemption code on their textbook. If they have not purchased a new textbook with a code, they can access the GSL by paying a fee.

The complete set of resources available on the GSL is listed below.

## GARLAND SCIENCE LEARNING SYSTEM CONTENTS

### Chapter 1

- Tutorial: The Scientific Method (discover how to prove you're right scientifically and why a scientific theory isn't merely theoretical)
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

### Chapter 2

- Tutorial: Protein Structure and Denaturation (discover why a fried egg doesn't look like a raw egg and why it's important that proteins fold like socks in a clothes dryer)
- Movie: Glucose Molecule
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

### Chapter 3

- Tutorial: Structure and Clinical Significance of Endospores (discover why anthrax is an ideal biological weapon)
- Movie: Bacterial Flagellum Action
- Movie: Fluidity of the Lipid Bilayer
- Movie: Structure of Lipids and the Lipid Bilayer
- Movie: Phagocytosis
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

### Chapter 4

- Tutorial: Naming Organisms Scientifically (discover the scientist's answer to Juliet's question: What's in a name?)
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

### Chapter 5

- Tutorial: Viral Biosynthesis (investigate viral factories and their assembly lines)
- Movie: DNA Virus Replication
- Movie: RNA virus (+ strand) Replication
- Movie: RNA virus (- strand) Replication
- Movie: HIV Infection
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

### Chapter 6

- Tutorial: Koch's Postulates (discover how self-experimentation and a peptic ulcer won the Nobel Prize for Medicine)
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

### Chapter 7

- Tutorial: Regulation of Gene Expression (discover how bacteria turn genes on and off)
- Movie: DNA Molecule
- Movie: DNA Replication
- Movie: Translation
- Movie: Conjugation
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

### Chapter 8

- Tutorial: Selective and Differential Culture Media (discover how you can tell if a bacterium is a vampire)
- Movie: ATP Molecule
- Movie: Glycolysis
- Movie: ATP Synthase
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

### Chapter 9

- Tutorial: Natural Selection (discover why the outbreak of cholera was worse in Chile than in Ecuador)
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

### Chapter 10

- Tutorial: Microbes in the Environment (discover what microbes have done for you)
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

### Chapter 11

- Tutorial: Exotoxins and Endotoxins (investigate bacterial weapons and discover how horseshoe crabs prevent hospital infections)
- Movie: Cholera Exotoxin Mechanism
- Movie: Intracellular *Listeria* infection
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

**Chapter 12**

- Tutorial: Adaptive Immune Response (meet the superheroes of the immune system)
- Movie: Neutrophils Moving Towards an Attractant
- Movie: Neutrophil Chasing a Bacterium
- Movie: Lymphocytes Moving to a Site of Injury
- Movie: Immunoglobulins
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary review

**Chapter 13**

- Tutorial: Antibiotic Targets (learn how magic bullets work)
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

**Chapter 14**

- Tutorial: Antigenic Shift and the Flu (discover why flu is a problem year after year after year)
- Movie: Antigenic Drift
- Movie: Antigenic Shift
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

**Chapter 15**

- Tutorial: Metagenomics (discover how you know bacteria are there if you can't see them and can't grow them)
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

**Chapter 16**

- Tutorial: Fermentation and Food (discover why a lack of oxygen can be a good thing, especially if you like beer, wine, yogurt, cheese, or bread)
- Quiz with Feedback
- Hints for End-of-Chapter Concept Questions
- Vocabulary Review

**Chapter 17**

- Tutorial: Microbial Biopesticides (discover how to grow crops with added pesticides built in)
- Quiz with Feedback
- Help Answering the Concept Questions
- Vocabulary Review

## MOVIES AND SCRIPTS

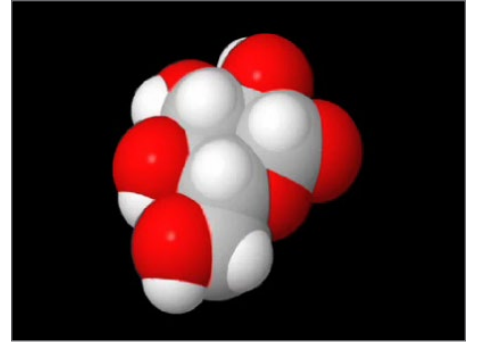
- 2.1 Glucose
- 3.1 Bacterial Flagellum
- 3.2 Fluidity of the Lipid Bilayer
- 3.3 Phospholipids and Lipid Bilayer
- 3.4 Phagocytosis
- 3.5 DNA Virus Replication
- 5.1 RNA Virus (+ strand) Replication
- 5.2 RNA Virus (- strand) Replication
- 5.3 HIV Infection
- 7.1 DNA Structure
- 7.2 Replication
- 7.3 Translation
- 7.4 Conjugation
- 8.1 ATP
- 8.2 Glycolysis
- 8.3 ATP Synthase: A Molecular Turbine
- 11.1 Cholera Exotoxin
- 11.2 Intracellular *Listeria* Infection
- 12.1 Chemotaxis of Neutrophils
- 12.2 Neutrophil Chase
- 12.3 Lymphocyte Homing
- 12.4 Antibody Structure
- 14.1 Antigenic Drift
- 14.2 Antigenic Shift

## 2.1 Glucose

A glucose molecule is a six-carbon sugar, consisting of a total of 24 atoms.

It is very polar due to its hydroxyl groups to which water molecules can hydrogen bond.

By convention, carbon atoms are shown in gray, oxygen in red and hydrogen in white.



## 3.1 Bacterial Flagellum

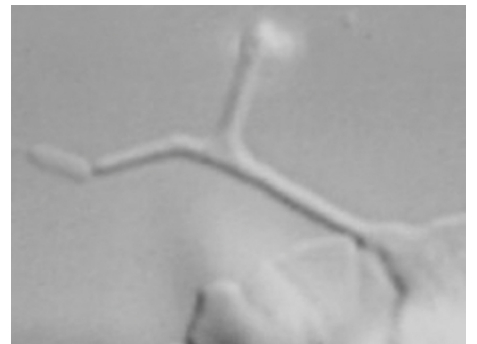
Many species of bacteria propel themselves through their environment by spinning helical motorized flagella. *Rhodobacter* cells have one flagellum each, whereas *E. coli* cells have multiple flagella that rotate in bundles. Each flagellum consists of a helical filament that is 20 nanometers wide and up to 15 microns long and spins on the order of 100 times per second.



Video: Howard C. Berg, Harvard University.

## 3.2 Fluidity of the Lipid Bilayer

To demonstrate the fluidity of the lipid bilayer, a piece of the plasma membrane of this neuronal cell is pulled out with laser tweezers. Remarkably, moving this membrane tubule rapidly back and forth does not rupture the plasma membrane, which flows quickly to adapt to the mechanical distortion.



Video: Steven M. Block, Stanford University.

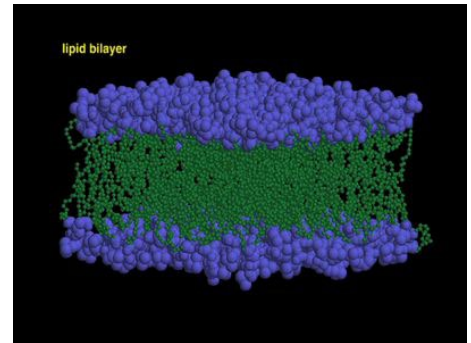
### 3.3 Phospholipids and Lipid Bilayer

Phospholipids contain a head group, choline in this case, that is attached via a phosphate group to a 3-carbon glycerol backbone. Two fatty acid tails are attached to the remaining two carbons of the glycerol.

The head groups and the phosphate are polar, that is, they prefer to be in an aqueous environment.

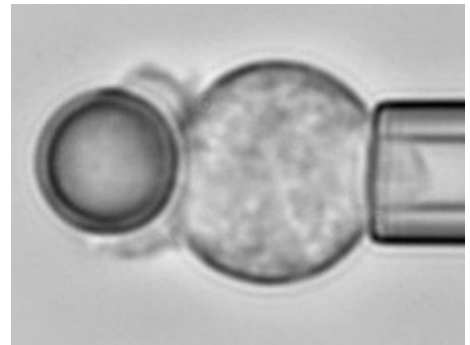
In contrast the fatty acid tails are hydrophobic, that is, they are repelled from water. The fatty acid tails on phospholipids can be saturated, with no double bonds, or unsaturated, with one or more double bonds. The double bonds are usually in the *cis*-configuration, which introduces sharp kinks. When forming a bilayer, unsaturated fatty acid tails pack loosely, which allows the bilayer to remain fluid. If there were no double bonds, bilayers would solidify to a consistency resembling bacon grease.

In a lipid bilayer, lipids arrange themselves so that their polar head groups are exposed to water and their hydrophobic tails are sandwiched in the middle.



### 3.4 Phagocytosis

In this experiment, a bead coated with antibodies, on the left, is presented to a neutrophil held by a pipette on the right. The neutrophil quickly engulfs the bead by phagocytosis. In a similar experiment, a particle made of a chemoattractant found on the surface of fungi, like yeast, is presented to a neutrophil. Note how the neutrophil extends its pseudopods before it surrounds the particle and completely engulfs it. Here the particle is presented to the neutrophil and moved around. As the particle moves, the neutrophil senses the chemoattractant. Pseudopods retract and then protrude towards the new position of the chemoattractant. When the neutrophil finally contacts its target, it engulfs it by phagocytosis.

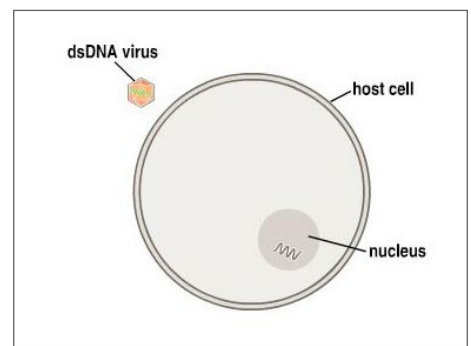


**Video I:** Marc Herant and Micah Dembo, Boston University, and Volkmar Heinrich, University of California at Davis. **Video II and III:** Volkmar Heinrich and Cheng-Yuk Lee, University of California at Davis.

### 3.5 DNA Virus Replication

The biosynthesis of double-stranded DNA viruses takes place in the nucleus of the host cell and uses the host cell's machinery. After entering the host cell, the virion uncoats in the cytoplasm, releasing the double-stranded DNA. The double-stranded DNA then moves into the nucleus, where transcription begins. RNA polymerase uses one strand of the viral DNA to transcribe some of the viral genes (the early genes) into messenger RNA, which leaves the nucleus and is translated into viral proteins, known as early proteins.

These early proteins move into the nucleus and interact with the host-cell machinery and viral DNA. The host cell's DNA polymerase replicates the double-stranded viral DNA, producing multiple copies of the original genome. After replication of the viral genome, additional genes of the viral DNA are transcribed (the late genes). This mRNA enters the cytoplasm where it is translated into the capsomere proteins used to assemble new viral capsids. After replication, the newly synthesized double-stranded DNA viral genomes migrate to the cytoplasm, where they are moved into the new capsids, forming complete, intact virions.



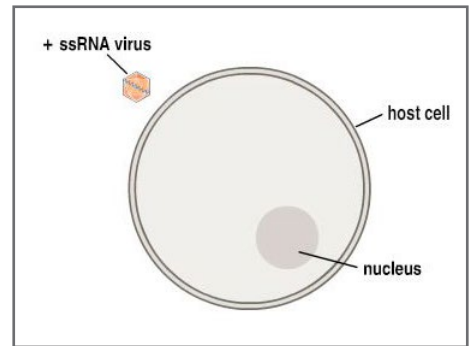


## 5.1 RNA Virus (+ strand) Replication

Single-stranded RNA viruses contain either a negative RNA strand or a positive RNA strand. In this animation, we will look at the biosynthesis of a positive RNA strand.

After entering the host cell, the virion uncoats in the cytoplasm, releasing the positive, single-stranded RNA. Since the positive RNA strand is already in the form of messenger RNA, it can be translated immediately into capsomere proteins used to assemble new viral capsids. The viral messenger RNA is also translated into an RNA-dependent RNA polymerase that is used to replicate the viral genome. The virus must make its own enzyme to replicate its genome since host cell RNA polymerases cannot use RNA as a template.

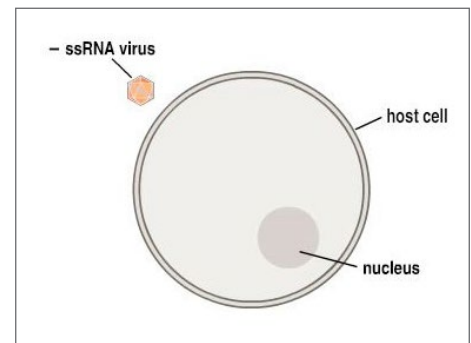
Replication of the positive RNA strand is accomplished in two steps. First, the viral RNA polymerase uses the positive strand as a template to synthesize a complementary negative strand. Second, this newly synthesized negative strand acts as a template to make many positive RNA genomes. The newly made positive strands combine with the new capsids to make new virions.



## 5.2 RNA Virus (- strand) Replication

Single-stranded RNA viruses contain either a positive RNA strand or a negative RNA strand. In this animation, we will look at the biosynthesis of a negative RNA strand.

After entering the host cell, the virion uncoats in the cytoplasm, releasing the negative, single-stranded RNA and a viral RNA polymerase. Unlike positive, single-stranded RNA, the negative stranded RNA is not in the form of messenger RNA. So the viral RNA polymerase must first make positive RNA strands. These positive RNA strands are in the form of messenger RNA and can be translated into capsomere proteins used to assemble new viral capsids and other viral proteins. The positive RNA strand is also used as a template to produce new negative RNA strand genomes. The newly made negative RNA strands combine with the capsids and viral RNA polymerase to make new virions.



## 5.3 HIV Infection

HIV is an important example of a retrovirus. The infection cycle begins when HIV binds receptors on the host cell.

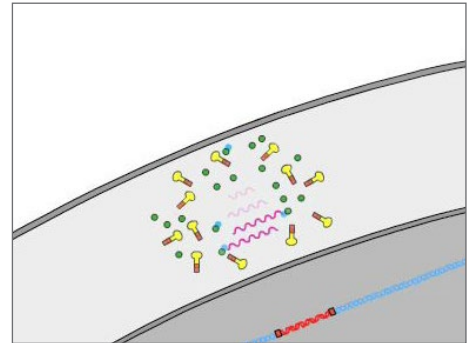
Interactions of the virus with these membrane receptors allow viral uncoating and the entry of the nucleocapsid, containing the viral genome, into the cell.

The viral reverse transcriptase, which is an integral part of the viral particle, copies the RNA genome of HIV into double-stranded DNA. The viral genome then integrates into the DNA of the host cell.

In this state the virus is latent; that is, it can persist in the cell in an inactive state.

Reactivation of the virus occurs when the host cell becomes activated and viral transcription is initiated. This results in the accumulation of viral proteins as well as genome-length RNA transcripts of the virus.

Viral proteins assemble at the cell membrane with copies of the RNA genome, and bud off to create a new viral particle



## 7.1 DNA Structure

Two DNA strands intertwine to form a double helix. Each strand has a backbone composed of phosphates and sugars to which the bases are attached. The bases form the core of the double helix, while the sugar-phosphate backbones are on the outside.

The DNA backbone is assembled from repeating deoxyribose sugar units that are linked through phosphate groups. Each phosphate carries a negative charge, making the entire DNA backbone highly charged and polar.

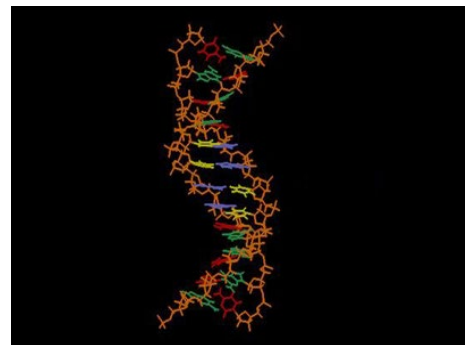
A cyclic base is attached to each sugar. The bases are planar and extend out perpendicular to the path of the backbone. Pyrimidine bases are composed of one ring and purine bases of two rings. Adjacent bases are aligned so that their planar rings stack on top of one another. Base stacking contributes significantly to the stability of the double helix.

In a double helix, each base on one strand is paired to a base on the other strand that lies in the same plane. In these base pairing interactions, guanine always pairs with cytosine, and thymine with adenine.

A GC pair is stabilized by three hydrogen bonds formed between amino and carbonyl groups that project from the bases.

In contrast, an AT pair is stabilized by two hydrogen bonds.

The specificity of base pairing—that is, C always pairing with G, and A always pairing with T—ensures that the two strands are complementary. This is important for DNA replication and transcription.



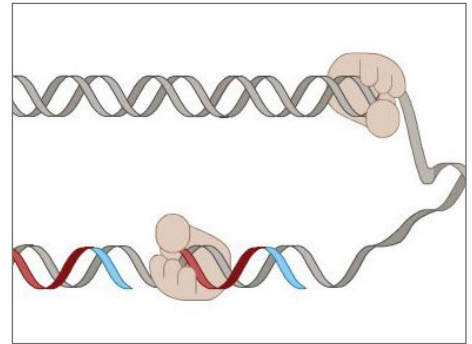
## 7.2 Replication

Replication begins when enzymes uncoil the double-stranded DNA molecule and separate the strands. These strands serve as templates for synthesizing new DNA molecules. The area where the strands separate is called the replication fork.

The two template strands are anti-parallel; that is, they are oriented in opposite directions. One strand is oriented in the 3' to 5' direction, and called the leading strand template; the other strand is oriented in the 5' to 3' direction, and called the lagging strand template.

On the leading strand template, DNA polymerase attaches at an area where a small piece of RNA, called a primer, has been attached to the DNA. As the DNA polymerase moves down the leading strand in the 3' to 5' direction, it synthesizes a complementary strand. This synthesis of a new DNA strand, called replication, proceeds continuously toward the opening replication fork.

Replication of the lagging strand is more complicated because DNA polymerase only works in the 5' to 3' direction. Thus, the lagging strand must be completed in segments using a backstitching mechanism. The DNA polymerase begins replicating at an RNA primer attached to the DNA and continues until it reaches the end of the fragment. Each segment of DNA replicated on the lagging strand is called an Okazaki fragment. As the lagging strand is being made, the enzyme RNAase H degrades the RNA primer, and then a DNA polymerase molecule fills in the gap with nucleotides. Once the gap is filled, the ends of the separate DNA pieces are linked together by the enzyme DNA ligase. Though the leading strand is made continuously and the lagging strand is made in Okazaki fragments, the process is simultaneous and continuous and replication of each strand keeps up with the uncoiling of the parental DNA at the replication fork.



## 7.3 Translation

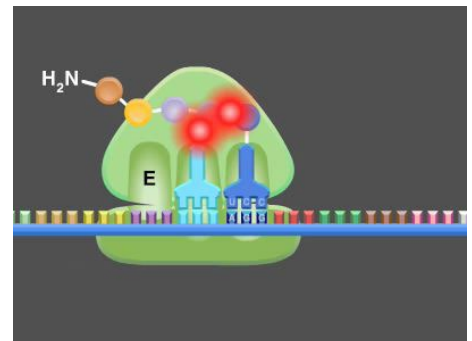
To extend a growing polypeptide chain, the ribosome must select the correct amino acids that are specified by the messenger RNA.

A tRNA amino acid complex enters the free site on the ribosome. If the anticodon of the charged tRNA does not match the codon in the messenger RNA, the tRNA is rejected.

The process of trial and error repeats until the correct tRNA is identified.

If the tRNA is correctly matched and remains bound for a long enough time, it is committed to be used in protein synthesis.

The ribosome catalyzes the formation of the new peptide bond and undergoes a dramatic conformational change. This switches the ribosome back to the state in which it can accept the next incoming tRNA.



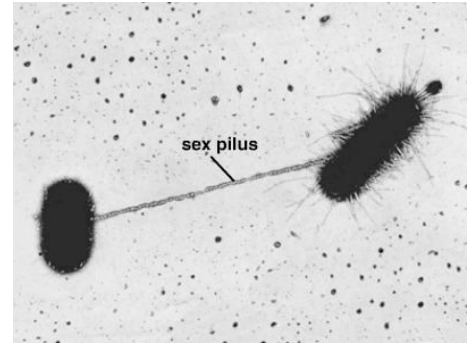
## 7.4 Conjugation

In this electron micrograph, one bacterium has contacted another by a long protein tube known as a sex pilus. Such contact initiates a type of bacterial mating in which one bacterium—the donor with the sex pili—transfers DNA to a recipient, which lacks sex pili.

The donor cell contains a circular piece of DNA, called an F plasmid, that is transferred to the recipient cell. Only one strand of the double-stranded F plasmid is transferred. The complementary strand is synthesized by the recipient cell.

Because the F plasmid contains all the genes required for making sex pili and for transferring the DNA, both bacteria are now potential DNA donors.

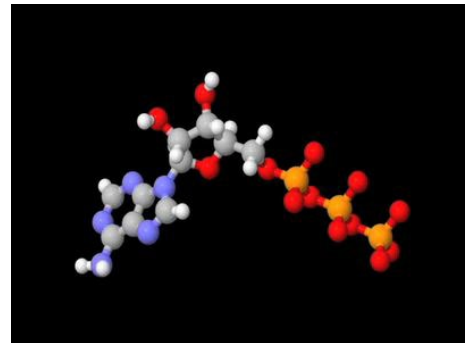
The F plasmid can also bring along other genes from the donor's chromosome, thereby allowing even more extensive genetic transfer between the two cells.



Electron micrograph: Charles C. Brinton, Jr and Judith Carnahan.

## 8.1 ATP

ATP molecules store and supply energy for cellular processes. An ATP molecule contains three building blocks: the flat purine ring system containing multiple nitrogen atoms shown in blue, the ribose sugar in the middle, and the three phosphate groups with the phosphorus atoms shown in yellow.

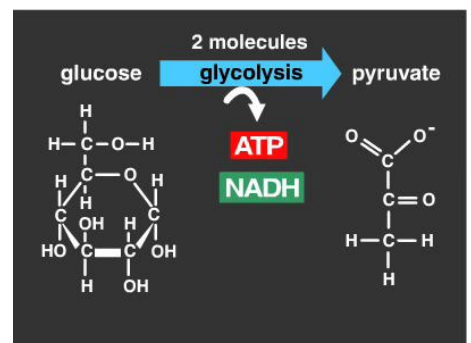


## 8.2 Glycolysis

Cells break down food molecules, such as glucose, through multi-step pathways. In the process of glycolysis, the breakdown of one glucose molecule into two three-carbon molecules produces a net gain of energy that is captured by the molecules ATP and NADH. The breakdown product, pyruvate, next enters the Krebs Cycle, where it can be used to generate more energy.

Glycolysis involves a sequence of 10 steps. In the first three steps, energy in the form of ATP is invested to be recouped later. In the fourth and fifth steps, this energy allows glucose to be split into two smaller molecules from which energy can be harnessed efficiently. And in the last five steps, energy is released step-wise as ATP and NADH. The elegant chemistry that evolved to catalyze these reactions ensures that energy is released in small portions that can be efficiently captured. Less controlled combustion reactions would release most of the energy as heat.

The chemistry of glycolysis is conserved all the way from bacteria to animal cells.

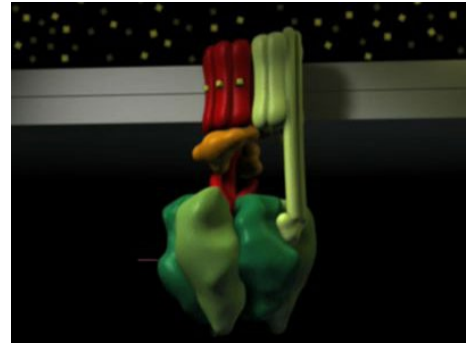


## 8.3 ATP Synthase

ATP synthase is a molecular machine that works like a turbine to convert the energy stored in a proton gradient into chemical energy stored in the bond energy of ATP.

The flow of protons down their electrochemical gradient drives a rotor that lies in the membrane. It is thought that protons flow through an entry open to one side of the membrane and bind to rotor subunits. Only protonated subunits can then rotate into the membrane, away from the static channel assembly. Once the protonated subunits have completed an almost full circle, and have returned to the static subunits, an exit channel allows them to leave to the other side of the membrane. In this way, the energy stored in the proton gradient is converted into mechanical, rotational energy.

The rotational energy is transmitted via a shaft attached to the rotor that penetrates deep into the center of the characteristic lollipop head, the F1 ATPase, which catalyzes the formation of ATP.

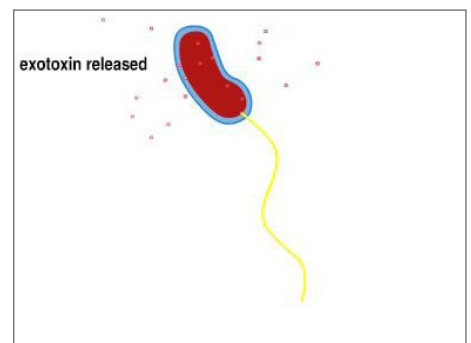


## 11.1 Cholera Exotoxin

*Vibrio Cholerae* is a Gram-negative bacterium that produces a powerful exotoxin. Once in the host's intestine, the bacteria secrete the exotoxin into the surrounding environment.

Each exotoxin molecule consists of two parts: an A subunit and a B subunit. The A subunit is made of two parts: A1 and A2. The B subunit allows the exotoxin to bind to membrane proteins on intestinal epithelial cells. Binding of the B subunit stimulates the host cell to engulf the exotoxin by endocytosis.

The vesicle containing the exotoxin fuses with the Golgi apparatus and is transported to the endoplasmic reticulum (the, ER). Inside the ER, the active part of the A subunit (A1) is released into the cytoplasm, while the B and A2 subunits return to the cell membrane where they are released by exocytosis. The A1 subunit activates a host protein, which opens a channel in the cell membrane, causing water and electrolytes to leave the cell, and enter the intestine. This results in severe diarrhea, which is the primary symptom of a cholera infection.

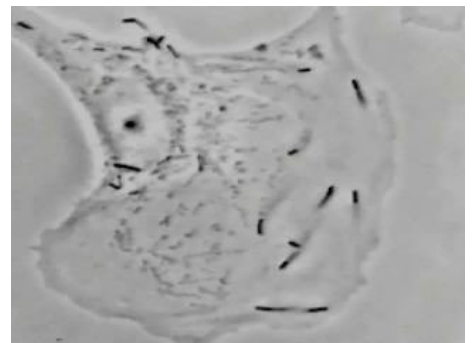


TEM: Eye of Science/Photo Researchers Inc.

## 11.2 Intracellular *Listeria* Infection

In this video, we see a mammalian cell infected with *Listeria monocytogenes*. The bacteria are the small, darkly stained organisms seen moving rapidly within the larger animal cell. This Gram-positive bacterial species is able to grow at low temperatures and humans often become infected after consuming contaminated moist, refrigerated food such as soft cheeses. Most infections are asymptomatic, but occasionally *Listeria* can invade the central nervous system where it can cause meningitis.

*Listeria* can infect new cells when an uninfected cell phagocytoses a bacterium from an infected cell. Once inside a new cell, the bacterium is able to replicate. Because *Listeria* transfer directly from cell-to-cell, they also avoid immune detection and attack.

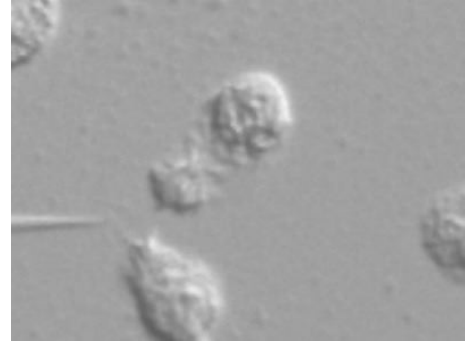


Video I: Julie A. Theriot, Stanford University School of Medicine; Daniel A. Portnoy, University of California at Berkeley. Video II: Julie A. Theriot, Stanford University School of Medicine; Frederick S. Soo, Stanford University.

## 12.1 Chemotaxis of Neutrophils

These human neutrophils, taken from the blood of a graduate student, are mobile cells that will quickly migrate to sites of injury to help fight infection. They are attracted there by chemical signals that are released by other cells of the immune system or by invading microbes.

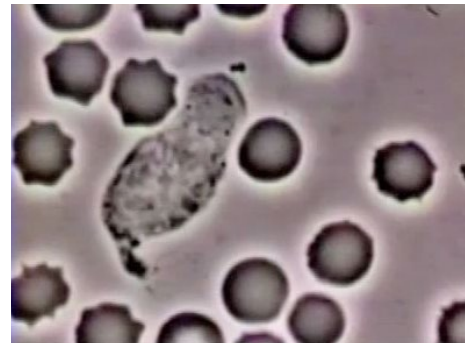
In this experiment tiny amounts of chemoattractant are released from a micropipette. When neutrophils sense these compounds they polarize and move towards the source. When the source of the chemoattractant is moved, the neutrophil immediately sends out a new protrusion, and its cell body reorients towards the new location.



**Video:** Henry Bourne and John Sedat, University of California at San Francisco; Orion Weiner, Harvard Medical School.

## 12.2 Neutrophil Chase

Neutrophils are white blood cells that hunt and kill bacteria. In this spread, a neutrophil is seen in the midst of red blood cells. *Staphylococcus aureus* bacteria have been added. The small clump of bacteria release a chemoattractant that is sensed by the neutrophil. The neutrophil becomes polarized, and starts chasing the bacteria. The bacteria, bounced around by thermal energy, move in a random path, seeming to avoid their predator. Eventually, the neutrophil catches up with the bacteria and engulfs them by phagocytosis.



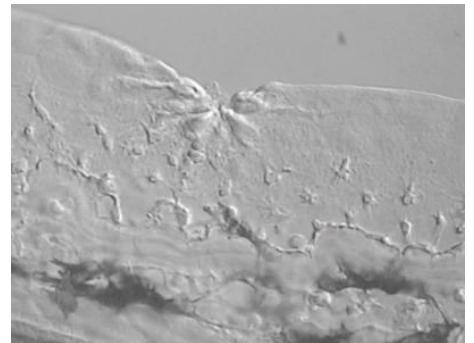
**Video:** David Roger, Vanderbilt University. **Digital capture:** Tom Stossel, Brigham and Women's Hospital, Harvard Medical School.

## 12.3 Lymphocyte Homing

To visualize lymphocyte homing to a site of injury, a zebrafish larva was anaesthetized and its fin pierced with a needle to introduce a small wound. A vein is seen at the bottom of the frame.

Because the fin is very thin and transparent, we can watch directly as lymphocytes crawl out of the blood vessel and migrate towards the wound. They are attracted there by chemicals released from damaged cells, invading bacteria, and other lymphocytes.

In a zoomed out view we can appreciate that lymphocyte invasion is restricted to the wounded area. The static cells that are dispersed in the connective tissue are fibroblasts. In these movies, 60 minutes of real time are compressed into 15 seconds.

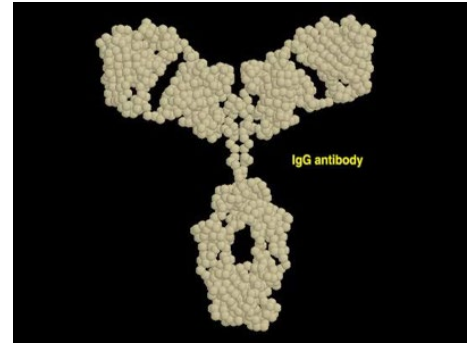


**Video:** Michael Redd and Paul Martin, University College London.

## 12.4 Antibody Structure

Antibodies of the immunoglobulin G class are Y-shaped glycoproteins that circulate in the blood stream. They bind to and inactivate foreign molecules—the antigens—and mark them for destruction. Each IgG molecule consists of two light chains and two heavy chains. The heavy chains have carbohydrates attached. The regions of the antibody that bind to antigens are located at the very tips of the two arms.

Antigens bind to the tip of each antibody arm, generally two molecules per antibody. In the example shown here, the antigen binds to the antibody via a large contact surface, providing a tight and highly specific association.



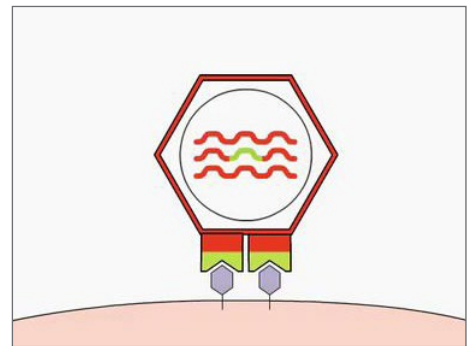
## 14.1 Antigenic Drift

Pathogens, such as the influenza virus, have receptors that enable them to bind to host cell surfaces.

Antibodies to these viral receptors prevent the virus from binding to and infecting cells. These are neutralizing antibodies, since they neutralize the ability of the virus to infect the cell.

However, some viruses will have mutations that alter the receptor in ways that prevent the binding of neutralizing antibodies while leaving the virus able to bind to, and infect, host cells.

In this way the pattern of antigens expressed by a virus can change over time. This process of accumulation of small changes is called antigenic drift, and contributes to our susceptibility to influenza infections year after year.



## 14.2 Antigenic Shift

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Antibodies to these viral receptors prevent the virus from binding to and infecting cells. These are neutralizing antibodies, since they neutralize the ability of the virus to infect the cell.

In some cases, viruses arise that are able to escape the effects of neutralizing antibodies. This can happen when two different strains of influenza virus are able to infect the same host cell.

The progeny viruses produced from such doubly-infected cells can contain segments of genome from either of the two original viruses.

Some viruses will acquire a segment of genome from the other strain encoding the receptor for host cell surfaces.

Neutralizing antibodies that block the binding of the original virus will be unable to recognize the receptor from the second strain and will be unable to prevent the virus binding to and infecting host cells. This process, in which large changes in the antigenicity of the virus occur, is known as antigenic shift. These large changes can mean that much of the immunity against the original virus is ineffective, and such antigenic shift mutations are often associated with large-scale virus epidemics.

