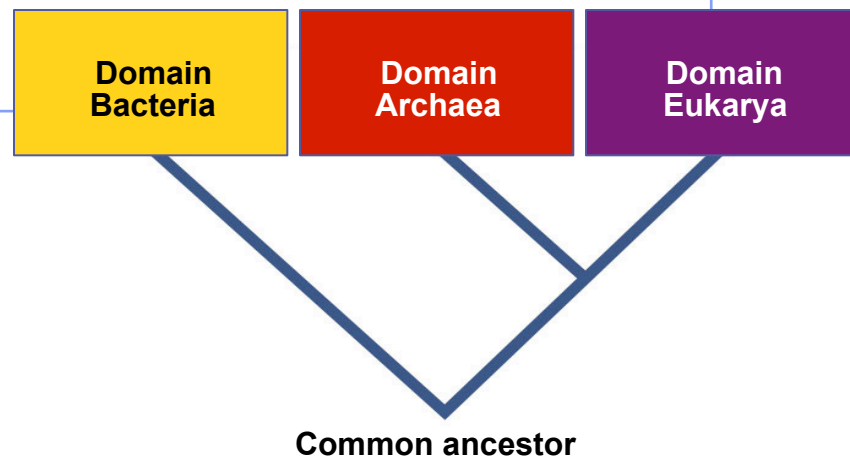
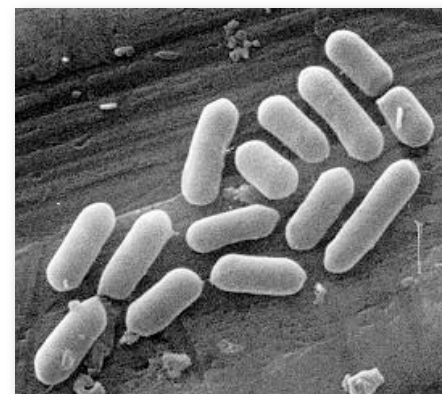




# Prokaryotes

Domain Bacteria

Domain Archaeobacteria



# Prokaryotic Phylogeny

Prokaryotes, bacteria and archaea, were originally placed in the Kingdom Monera.

Recent molecular analysis of nucleotide sequences have shown that these two groups are distinctly different and diverge from one another very early in the history of life.

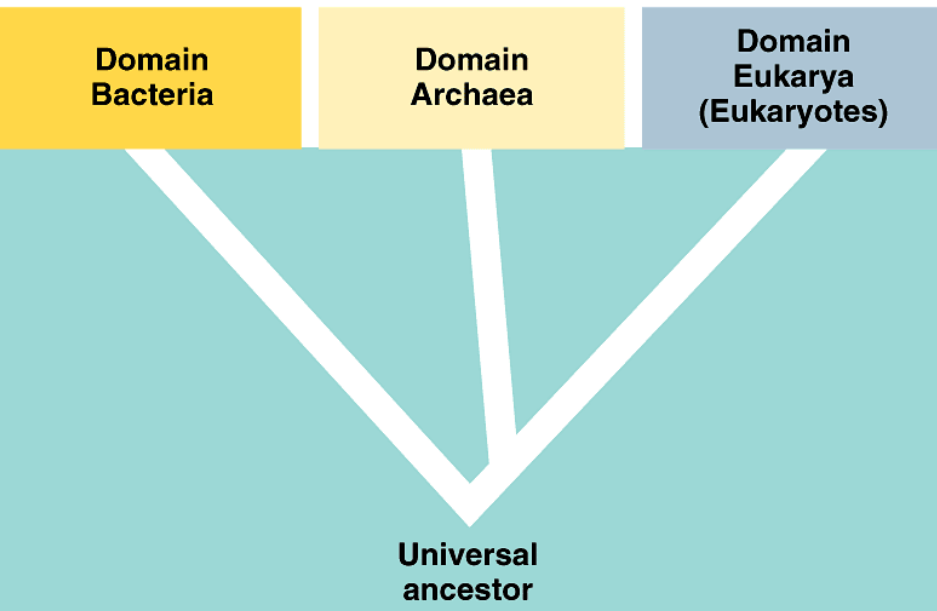


Table 27.2 A Comparison of the Three Domains of Life

CHARACTERISTIC	DOMAIN		
	Bacteria	Archaea	Eukarya
Nuclear envelope	Absent	Absent	Present
Membrane-enclosed organelles	Absent	Absent	Present
Peptidoglycan in cell wall	Present	Absent	Absent
Membrane lipids	Unbranched hydrocarbons	Some branched hydrocarbons	Unbranched hydrocarbons
RNA polymerase	One kind	Several kinds	Several kinds
Initiator amino acid for start of protein synthesis	Formyl-methionine	Methionine	Methionine
Introns (noncoding parts of genes)	Absent	Present in some genes	Present
Response to the antibiotics streptomycin and chloramphenicol	Growth inhibited	Growth not inhibited	Growth not inhibited
Histones associated with DNA	Absent	Present	Present
Circular chromosome	Present	Present	Absent
Ability to grow at temperatures >100°C	No	Some species	No

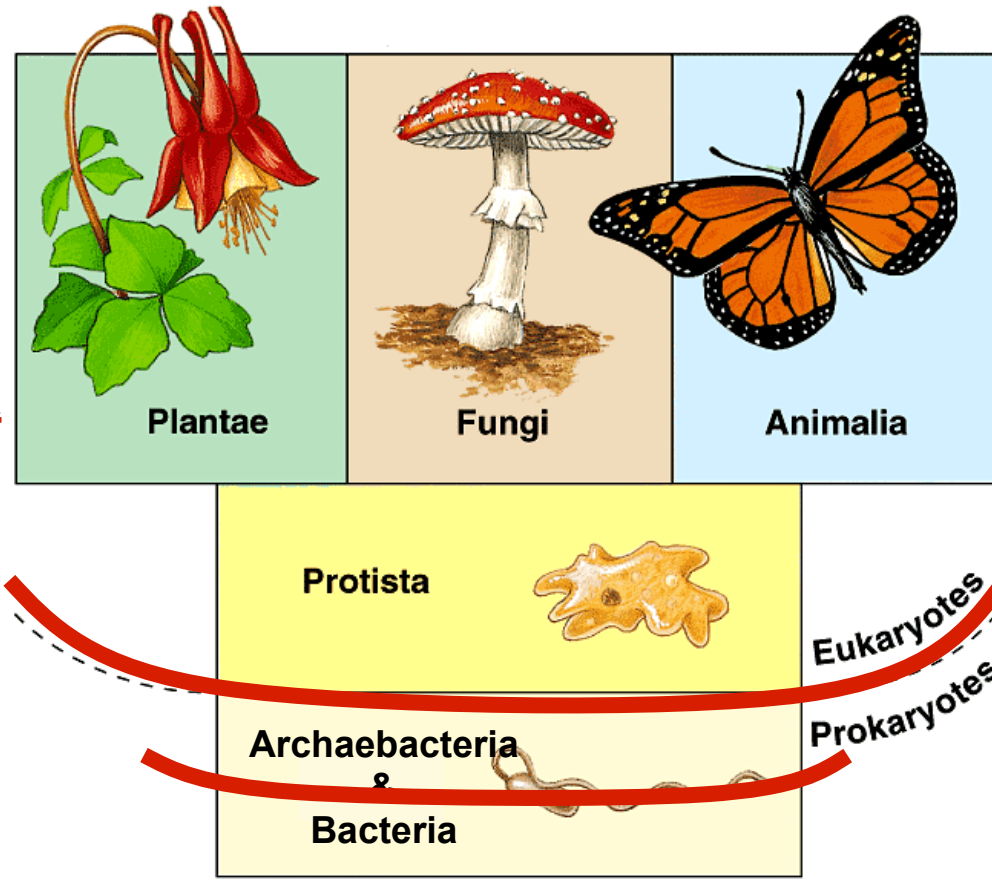
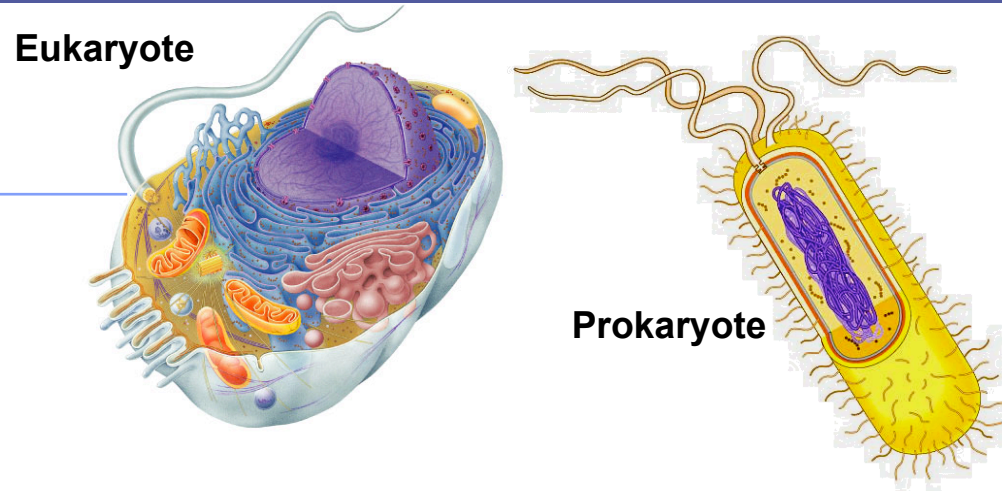
# Classification

## Old 5 Kingdom system

- Monera, Protists, Plants, Fungi, Animals

## New 3 Domain system

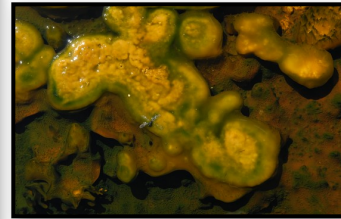
- ◆ reflects a greater understanding of evolution & molecular evidence
  - Prokaryote: Bacteria
  - Prokaryote: Archaeobacteria
  - Eukaryotes
    - ◆ Protists
    - ◆ Plants
    - ◆ Fungi
    - ◆ Animals



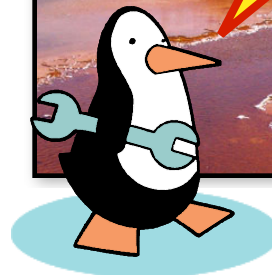
# Bacteria live *EVERYWHERE!*

- Bacteria live in all ecosystems

- ◆ on plants & animals
- ◆ in plants & animals
- ◆ in the soil
- ◆ in depths of the oceans
- ◆ in extreme cold
- ◆ in extreme hot
- ◆ in extreme salt
- ◆ on the living
- ◆ on the dead



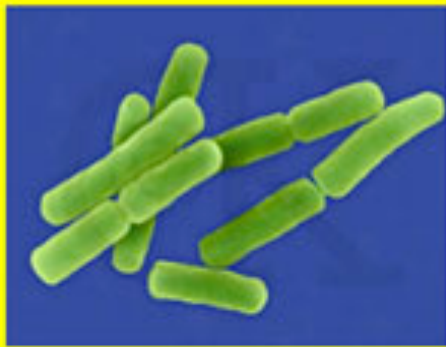
Microbes always find a way to make a living!



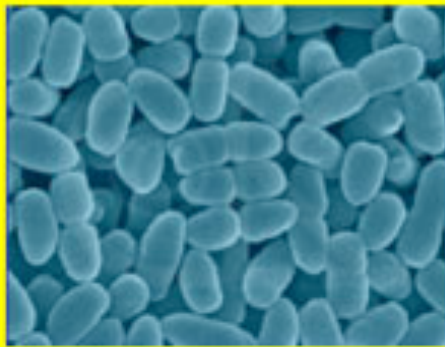
# Bacterial shapes

Rods and spheres and spirals... Oh My!  
*(bacillus and coccus and spirilus)*

*Bacillus*



*Bordetella*



*Clostridium*



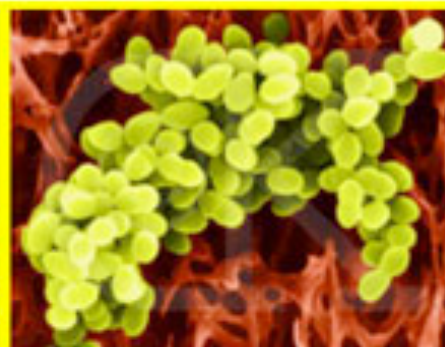
*Escherichia*



*Spirulina*



*Staphylococcus*



*Streptococcus*



*Salmonella*

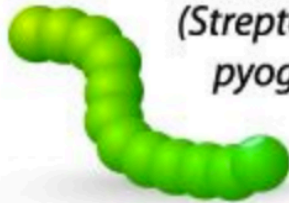


# BACTERIA SHAPES

## SPHERES (COCCI)



**Diplococci**  
(*Streptococcus pneumoniae*)

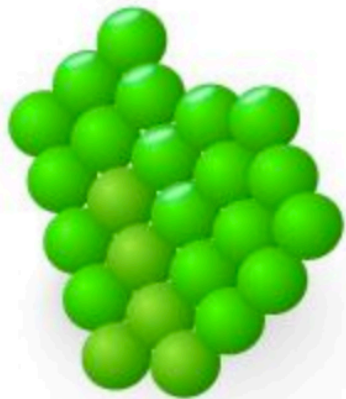


**Streptococci**  
(*Streptococcus pyogenes*)

### Tetrad



**Sarcina**  
(*Sarcina ventriculi*)

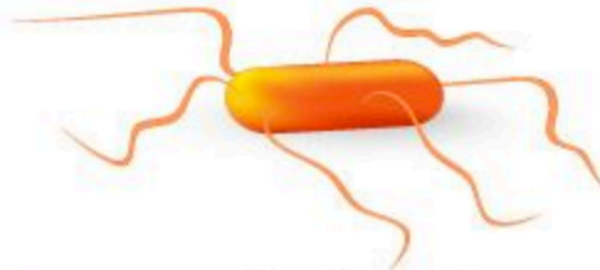


**Staphylococci**  
(*Staphylococcus aureus*)

## RODS (BACILLI)



**Chain of bacilli**  
(*Bacillus anthracis*)



**Flagellate rods**  
(*Salmonella typhi*)



**Spore-former**  
(*Clostridium botulinum*)

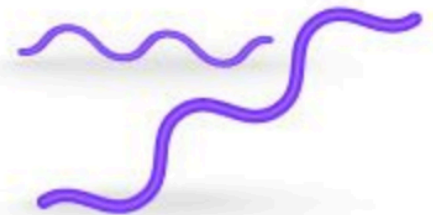
## SPIRALS



**Vibrios**  
(*Vibrio cholerae*)



**Spirilla**  
(*Helicobacter pylori*)

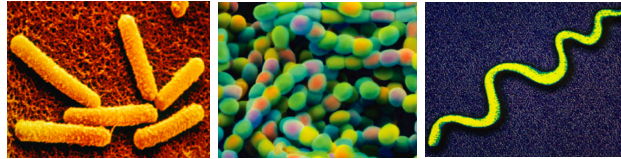


**Spirochaetes**  
(*Treponema pallidum*)

# Bacterial Structure

- **Unicellular**

- ◆ **bacilli, cocci, spirilli**

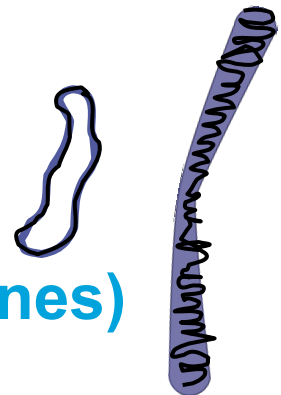
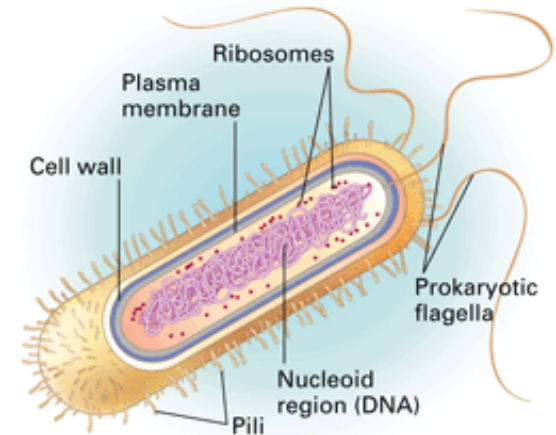
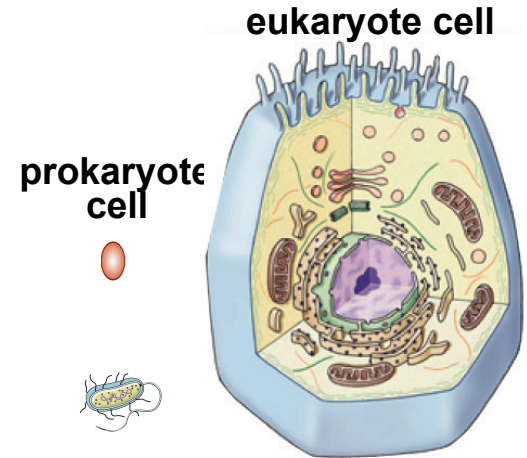


- **Size**

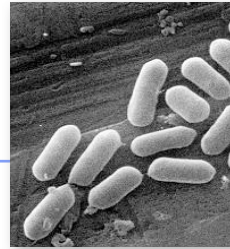
- ◆ **1/10 size of eukaryote cell**
  - 1 micron (1 $\mu$ m)

- **Internal structure**

- ◆ **no internal compartments**
  - no membrane-bound organelles
  - only ribosomes
- ◆ **circular chromosome, naked DNA**
  - not wrapped around proteins (no histones)

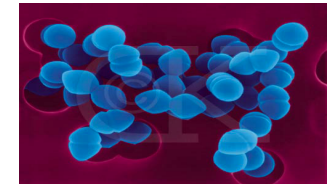
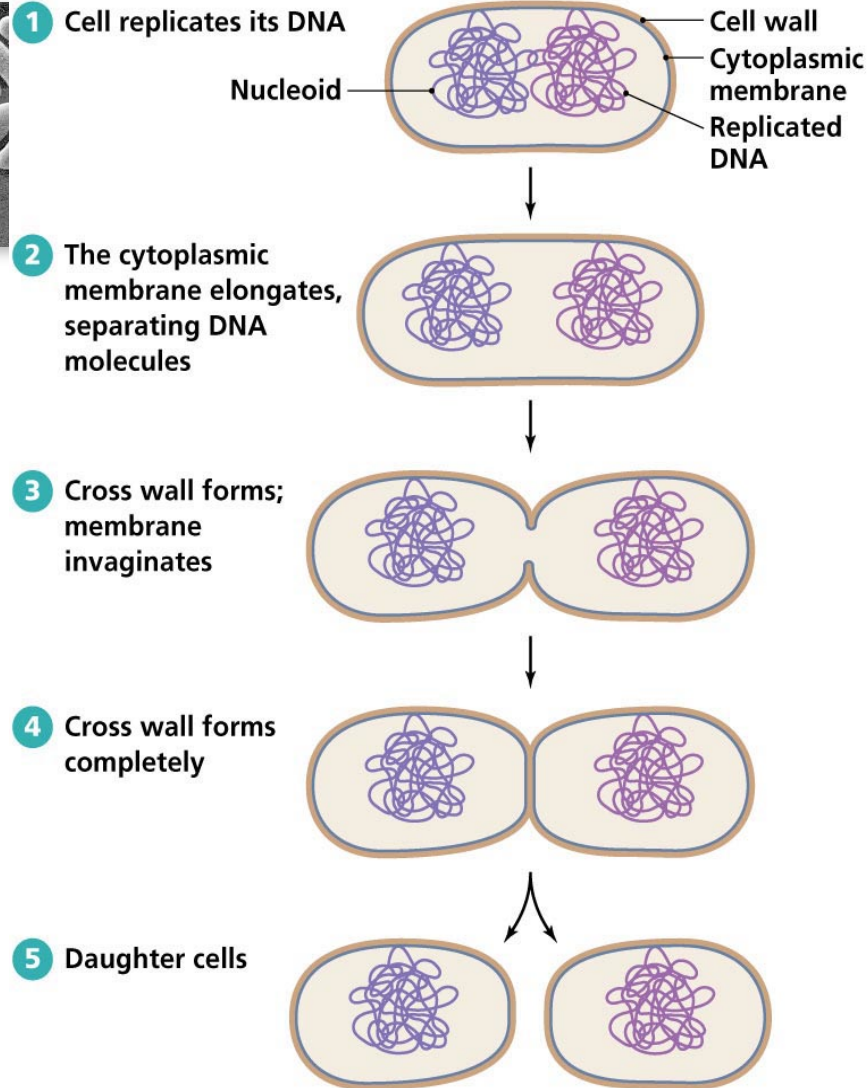
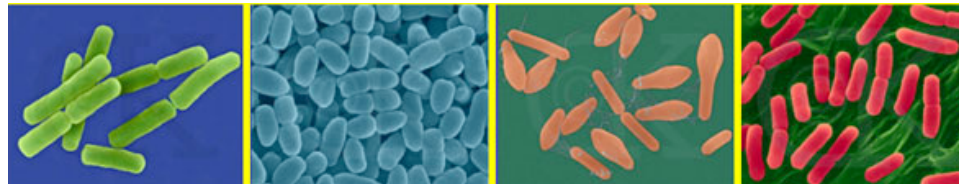
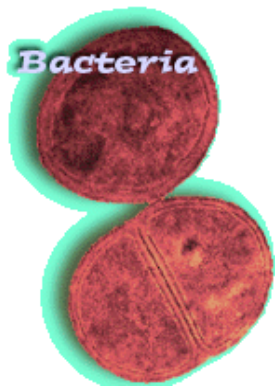


# Bacteria



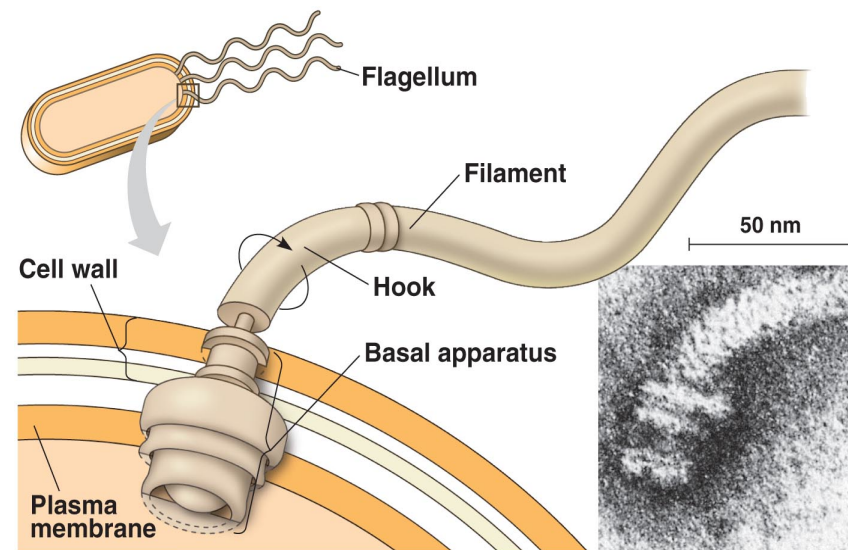
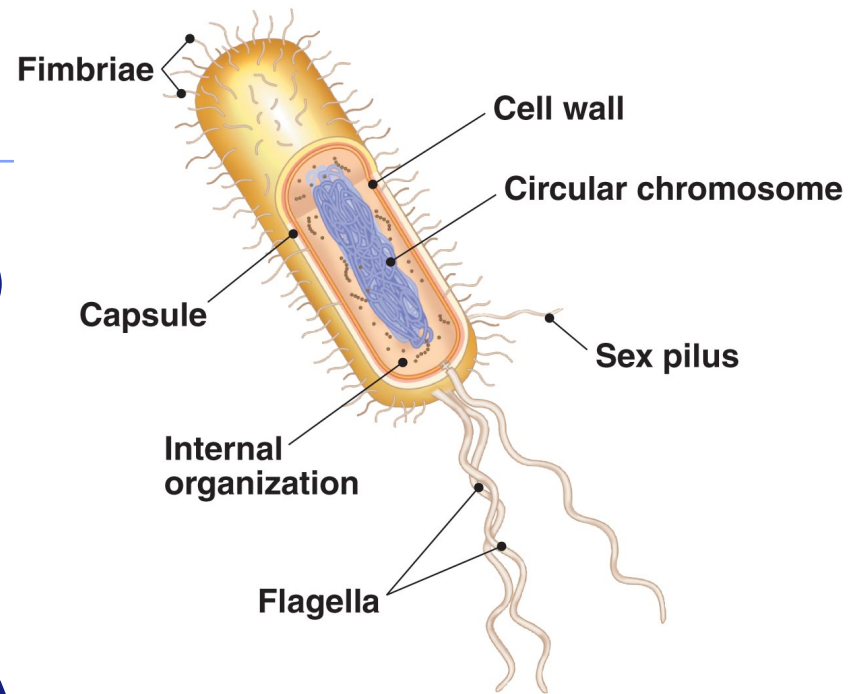
## ■ Bacteria review

- ◆ one-celled prokaryotes
- ◆ Do not reproduce by mitosis
  - Divides by **binary fission**
- ◆ rapid growth
  - New generation every. ~20 minutes
  - $10^8$  (100 million) colony overnight!
  - ◆ dominant form of life on Earth
  - ◆ incredibly diverse



# Bacterial Structure

- Some prokaryotes have **fimbriae** (a.k.a. **attachment pili**)
  - allows them to stick to their substrate or other individuals in a colony
- **Sex pili** are longer than fimbriae and allow prokaryotes to exchange DNA
- The most common method of locomotion in bacteria is the **flagellum** allowing for **taxis**.
  - The ability of mobile cells move in a desired direction away from stimuli
    - **PHOTOTAXIS, CHEMOTAXIS, MAGNETOTAXIS**



# Bacterial genome

## ■ Single circular chromosome

- ◆ Haploid (1n)
- ◆ No introns or exons
- ◆ Naked DNA
  - no histone proteins
- ◆ ~4 million base pairs
  - ~4300 genes
  - 1/1000 DNA in eukaryote

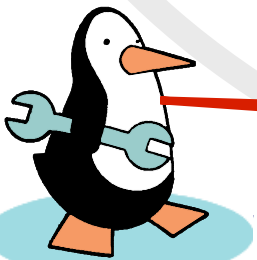
## ◆ Bacteria do not form gametes

- How then do they increase their

- ◆ Genetic transfer is the mechanism by which DNA is transferred from a donor to a recipient.
1. Mutations
  2. Transformation
  3. Conjugation
  4. Transduction

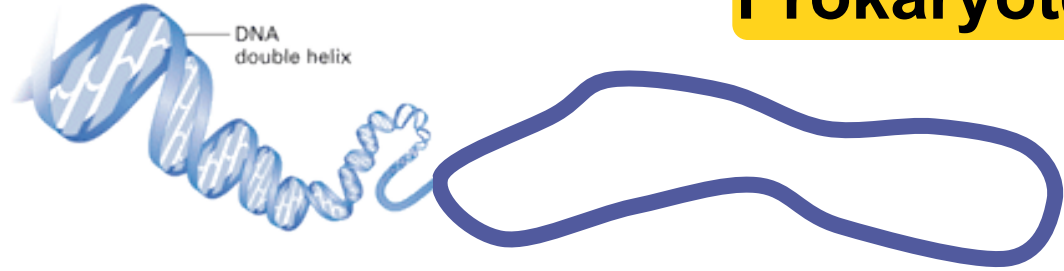
nor have sex  
genetic diversity?

How have these little guys gotten to be so diverse??

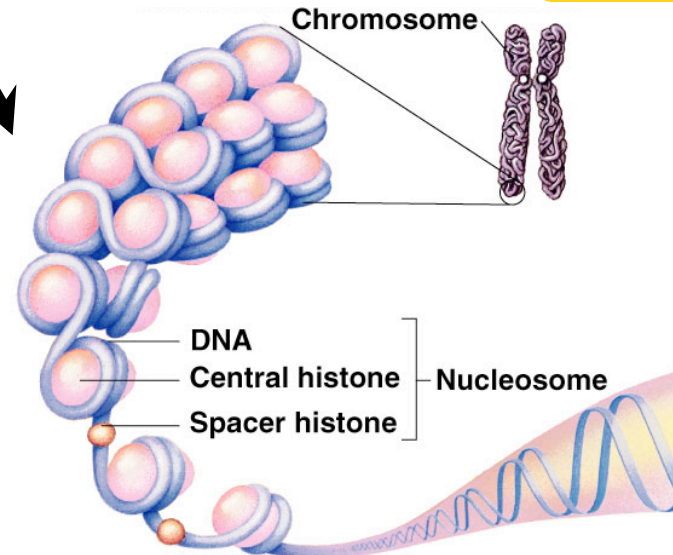


# Prokaryote vs. Eukaryote Chromosome

**Prokaryote**



**Eukaryote**



**double helix**

# Variations in Cell Interior Exist in Bacteria

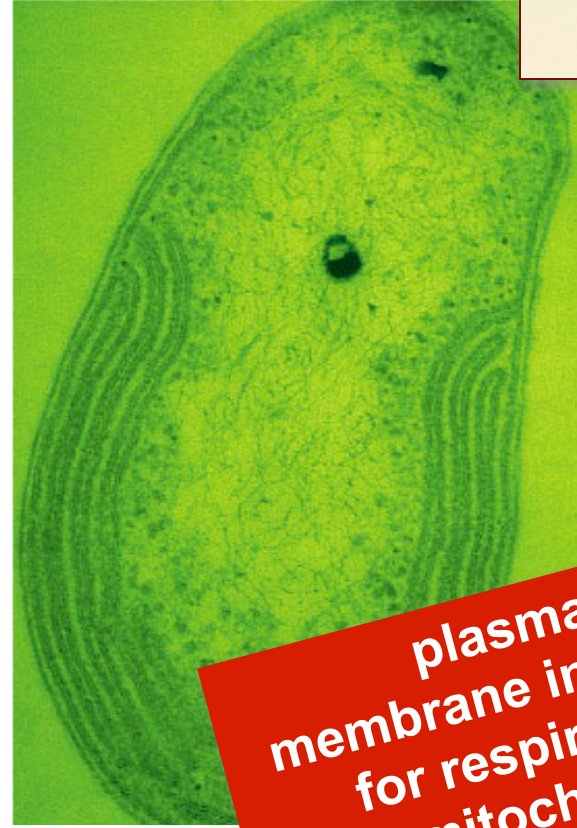
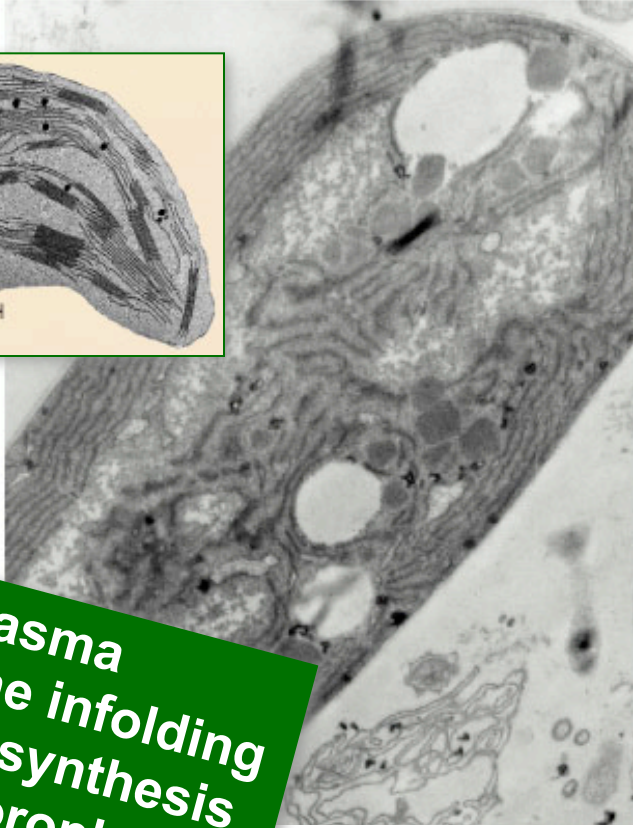
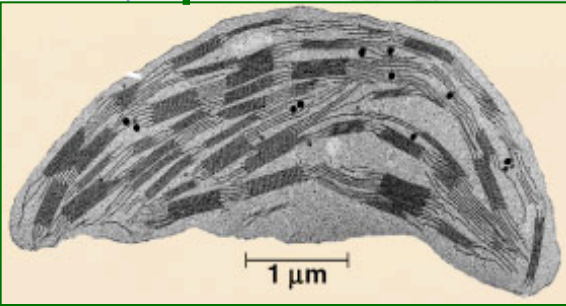
mitochondria

**cyanobacterium  
(photosynthetic) bacterium**

**aerobic bacterium**



**chloroplast**

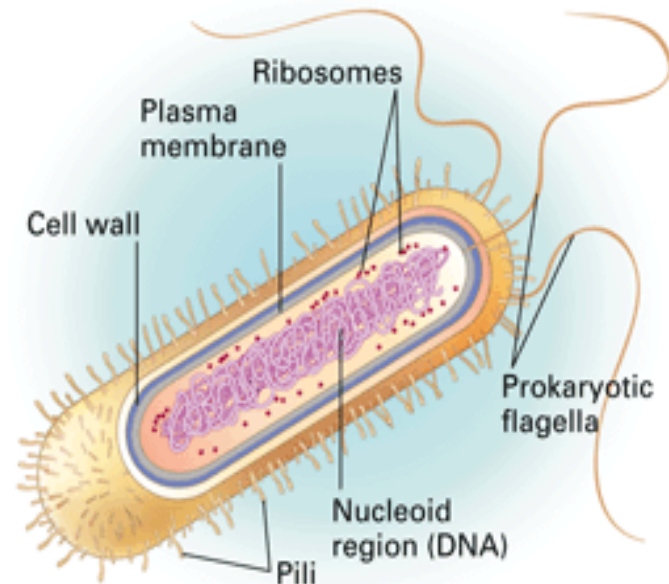


plasma membrane infolding for photosynthesis like a chloroplast's **thylakoids**

plasma membrane infolding for respiration like a mitochondrion's **cristae**

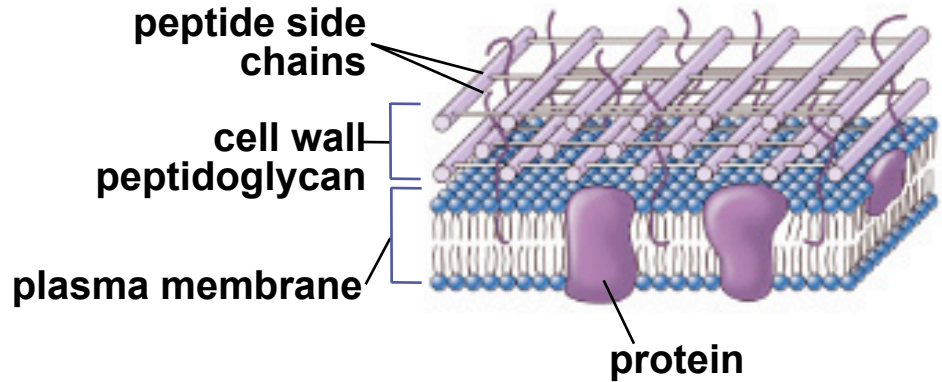
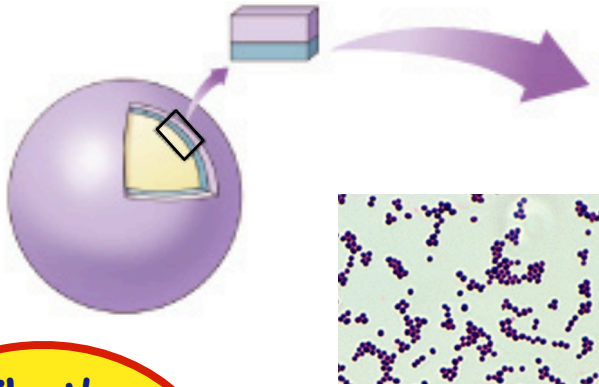
# Cell-Surface Structures

- An important feature of nearly all prokaryotic cells is their cell wall, which maintains cell shape, provides physical protection, and prevents the cell from bursting in a hypotonic environment
  - Eukaryote cell walls are made of cellulose or chitin
  - Bacterial cell walls contain peptidoglycan, a network of sugar polymers cross-linked polypeptides
    - Many antibiotics target peptidoglycan bacterial cell walls while bacterial ribosome
  - A polysaccharide or protein layer called a capsule covers many prokaryotes



# Eubacterial Cell Wall Structure

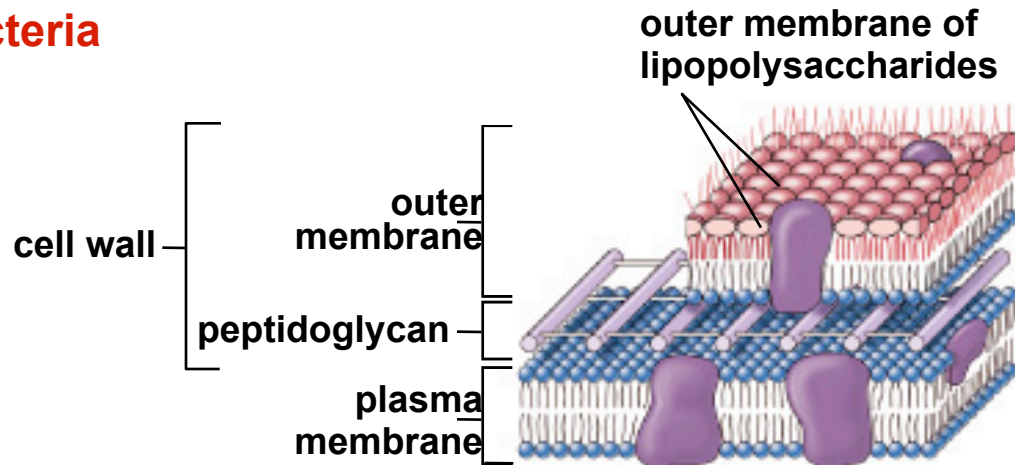
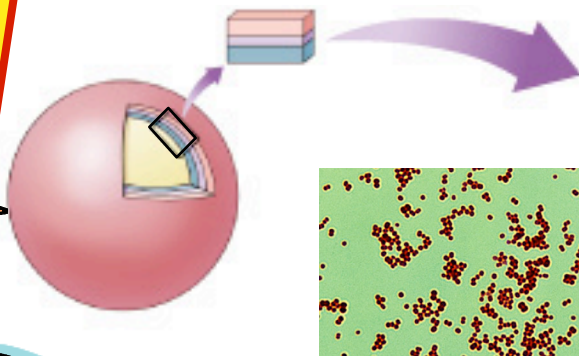
## Gram-positive bacteria



That's important for your doctor to know!

peptidoglycan = polysaccharides + amino acid chains  
lipopolysaccharides = lipids + polysaccharides

## Gram-negative bacteria



peptidoglycan = polysaccharides + amino acid chains  
lipopolysaccharides = lipids + polysaccharides

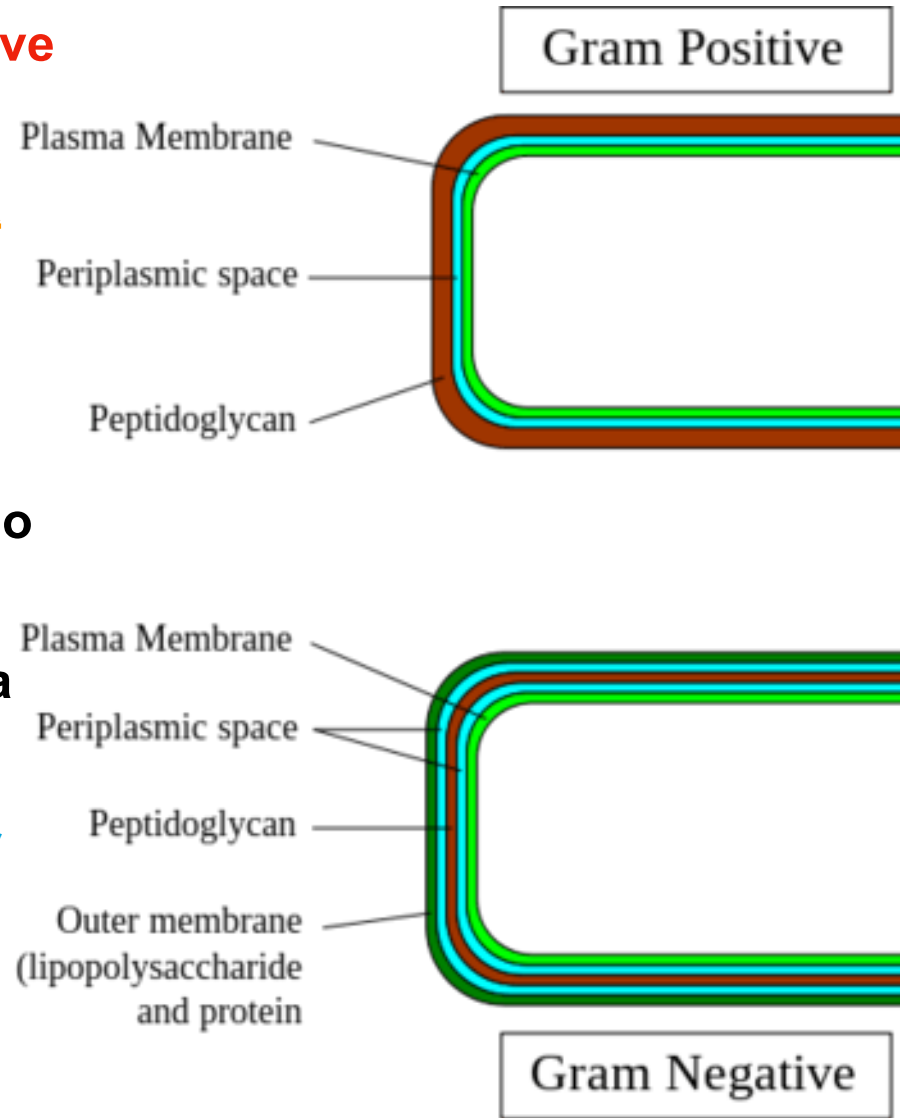
# Eubacterial Cell Wall Structure

Both gram-positive and gram-negative bacteria can be pathogenic

Six gram-positive genera of bacteria are known to cause disease in humans: Streptococcus, Staphylococcus, Corynebacterium, Listeria, Bacillus and Clostridium.

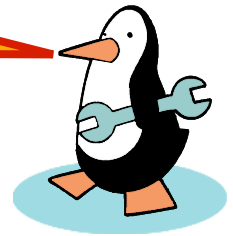
Many gram-negative bacteria are also pathogenic e.g., Pseudomonas aeruginosa, Neisseria gonorrhoeae, Chlamydia trachomatis, and Yersinia pestis.

*Gram-negative bacteria are also more resistant to antibiotics and their outer membrane comprises a complex lipopolysaccharide (LPS) whose lipid portion acts as an endotoxin.*



# Transformation

Let's increase genotypic diversity.



## ■ Many bacteria are opportunists

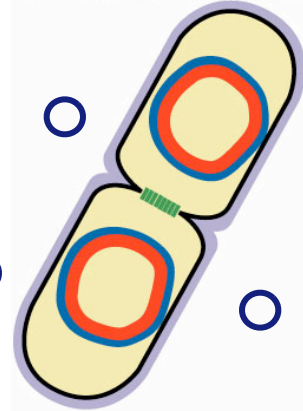
- ◆ pick up small pieces of naked foreign DNA wherever it may be hanging out
  - have surface transport proteins that are specialized for the uptake of naked DNA
    - ◆ While *E. coli* lacks this specialized mechanism, it can be induced to take up small pieces of DNA if cultured in a medium with a relatively high concentration of calcium ions.
      - In biotechnology, this technique has been used to foreign DNA into *E. coli*.
- ◆ import bits of chromosomes from other bacteria
- ◆ incorporate the DNA bits into their own chromosome
  - express new genes
    - ◆ Process of internalizing foreign DNA = **TRANSFORMATION**
      - The genetically transformed cell is called a **recombinant cell** because it has a different genetic makeup than the donor and the recipient
      - Give rise to genetic diversity in the population = diversity in the population.
  - form of 'recombination'

## Remember Griffith?

mix heat-killed **pathogenic** & **non-pathogenic** bacteria



# Generating Genetic variation in bacteria



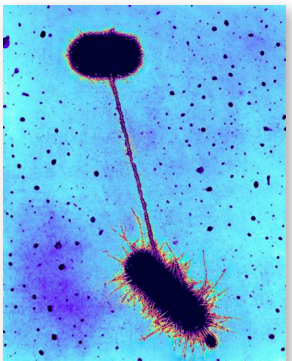
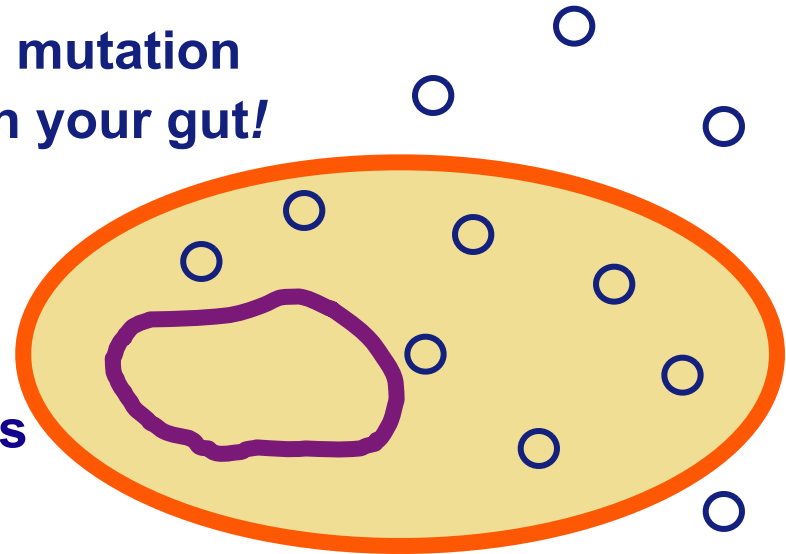
## ■ Mutations

- ◆ **bacteria can reproduce every 20 minutes**
  - binary fission
- ◆ **error rate in copying DNA is higher in prokaryotes than eukaryotes** (*prokaryotic DNA polymerase lacks proofreading ability that*)
  - 1 in every 200 bacteria has a mutation
  - you have billions of *E. coli* in your gut!
    - ◆ *lots of mutation potential!*

## ■ Genetic recombination

### **bacteria share genes**

- **plasmids contain extra genes**
  - ◆ **small supplemental circles of DNA**
- **conjugation = the process by which bacteria can share a copy of their plasmid or genes with neighboring bacteria**
  - ◆ **direct transfer of DNA “horizontally”**



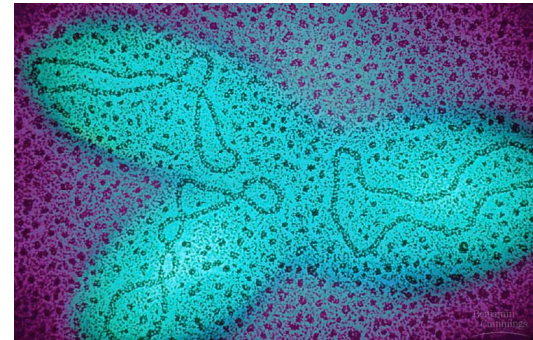
**conjugation**

# Extrachromosomal DNA exists inside prokaryotes

## ■ Plasmids

### ◆ Small supplemental circles of DNA

- 5000 - 20,000 base pairs
- self-replicating
  - ◆ Replicate separately from chromosome



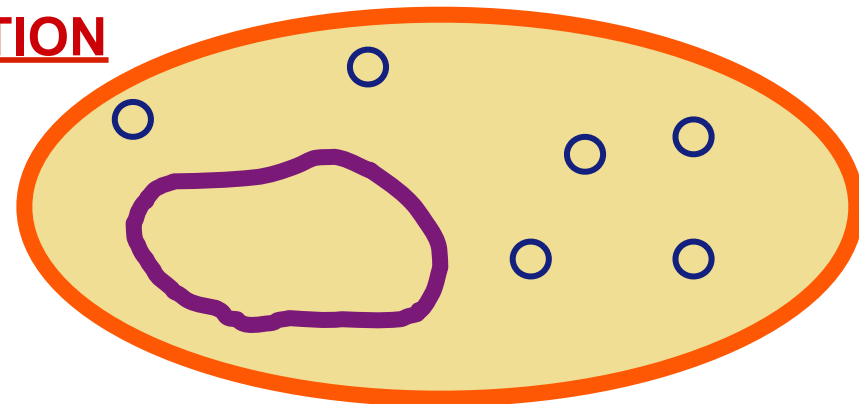
### ◆ carry extra genes

- 2-30 genes
  - ◆ Often also genes for antibiotic resistance

### ◆ Plasmids can be exchanged between bacteria

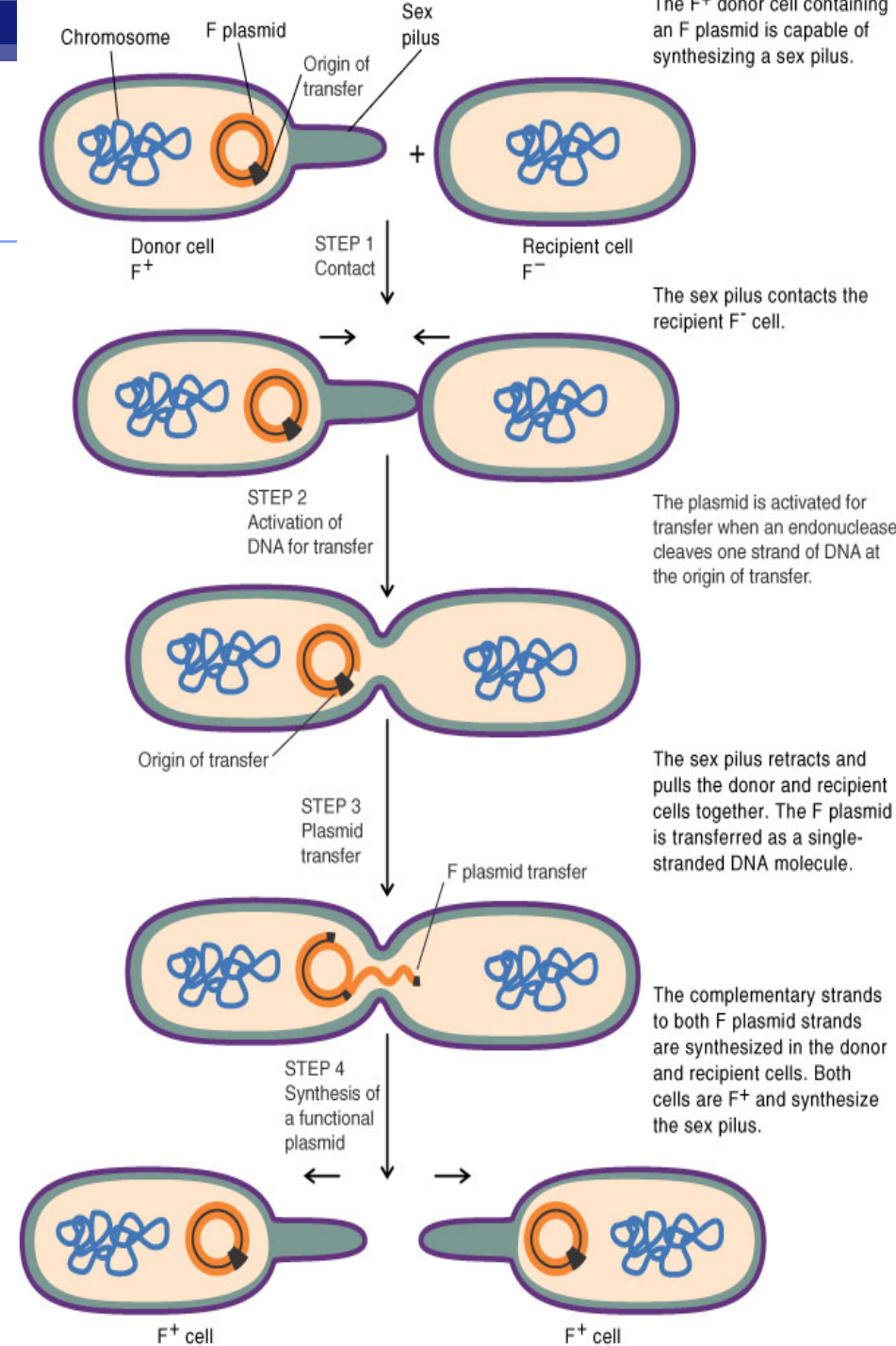
- bacterial “sex” = CONJUGATION
- can lead to rapid evolution!!!

### ◆ can be imported from environment



# Conjugation

- A special plasmid is needed for conjugation
  - ◆ The **F plasmid** (fertility plasmid) facilitates conjugation.
    - This can give a bacterium new genes that may help it survive in a changing environment.
  - ◆ Some plasmids can integrate reversibly into the bacterial chromosome.
    - An integrated plasmid is called an **episome**.
      - ◆ Bacteria that have a F plasmid are referred to as **F<sup>+</sup>** or male.
      - ◆ Those that do not have an F plasmid are **F<sup>-</sup>** or female.



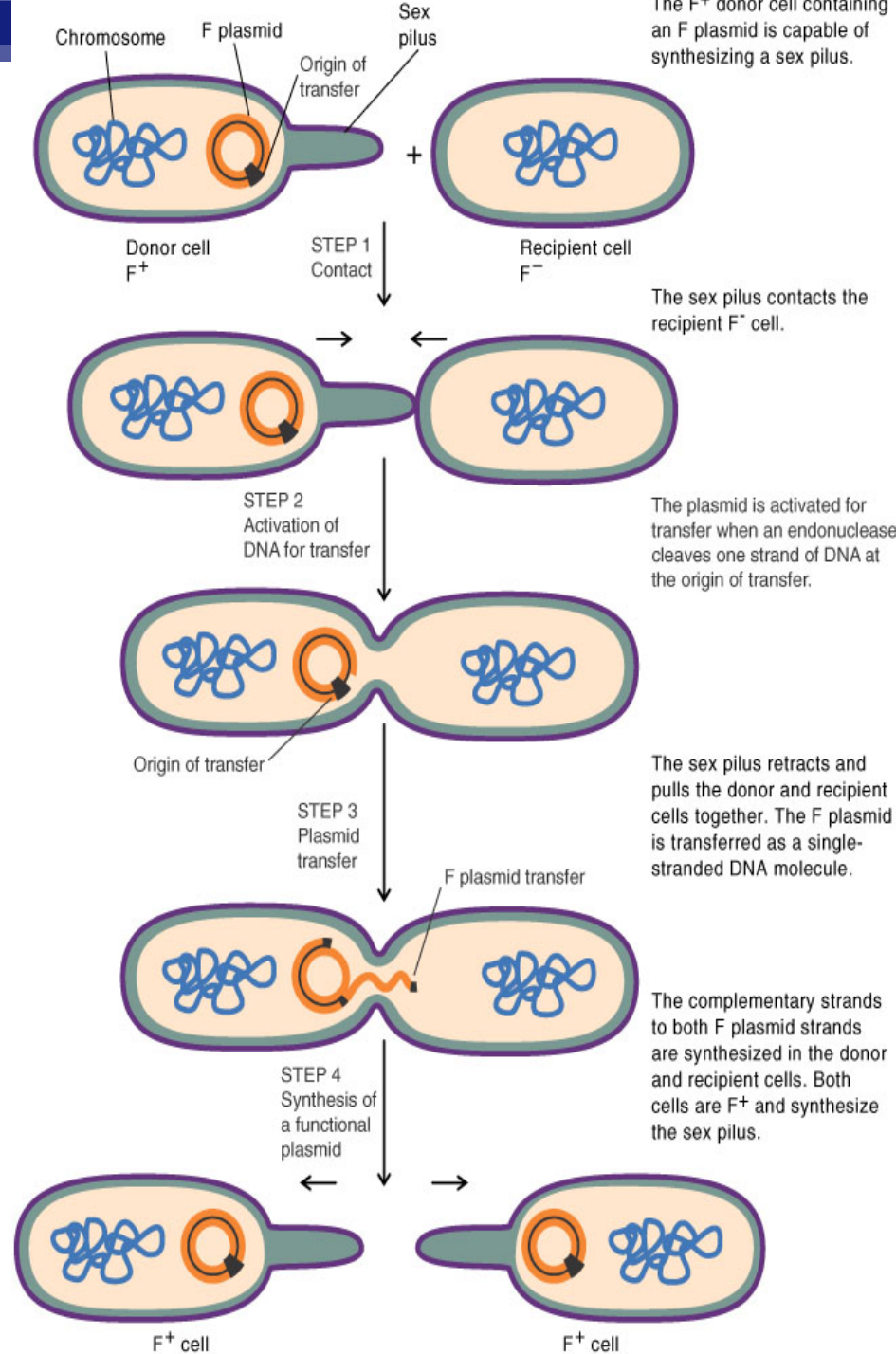
# Conjugation

- The F plasmid consists of 25 genes that mostly code for production of sex pili.

- ◆ A conjugation event occurs when the male cell extends his sex pili and one attaches to the “female” (F- bacteria)

- This attached pilus is a temporary cytoplasmic bridge through which a replicating F plasmid is transferred from the male to the female.

- ◆ When transfer is complete, the result is two “male” cells.

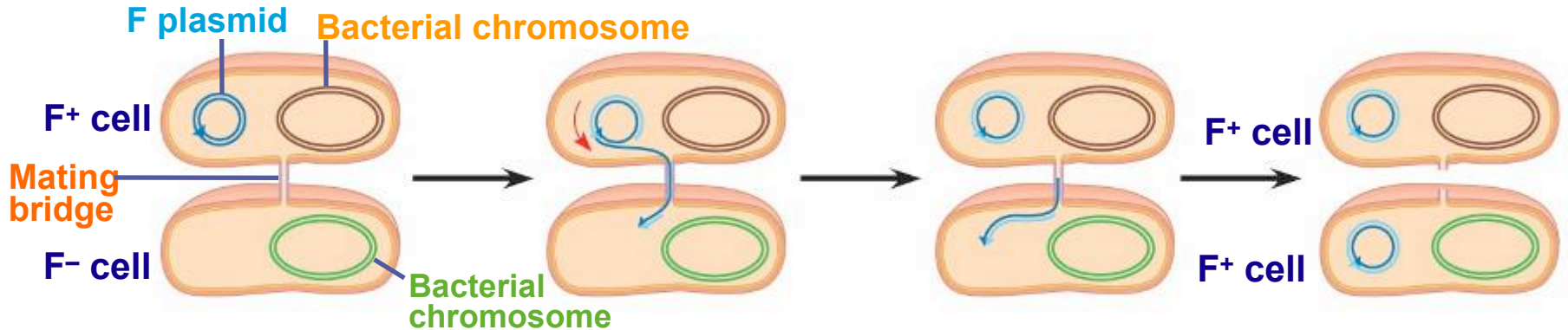


# Conjugation

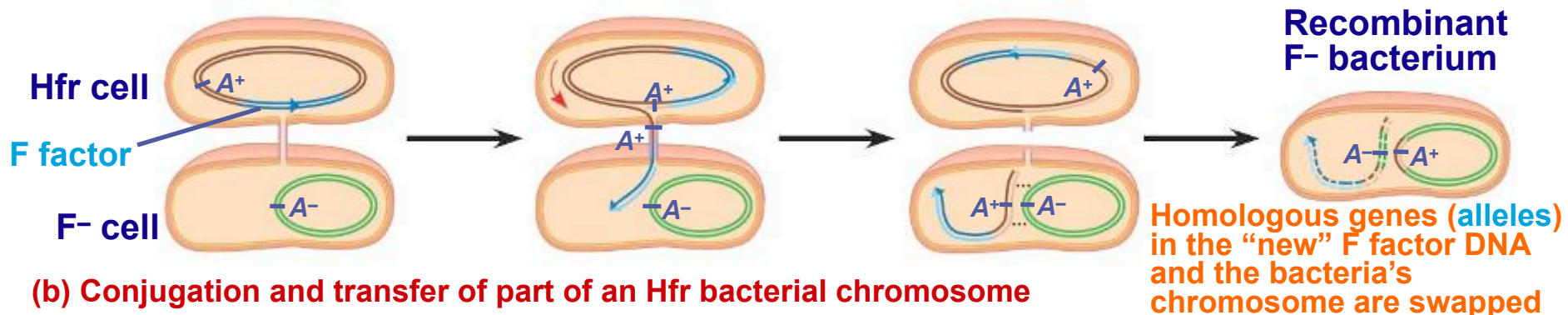


◆ The F plasmid can behave as an episome.

- When the F+ plasmid is integrated within the bacterial chromosome, the cell is called an Hfr cell (high frequency of recombination cell).
  - Hfr cell still behaves as a F+ cell, transferring F genes to a F-cell, but now some of the bacterial chromosome is moves along with the episome to the new bacterial cell

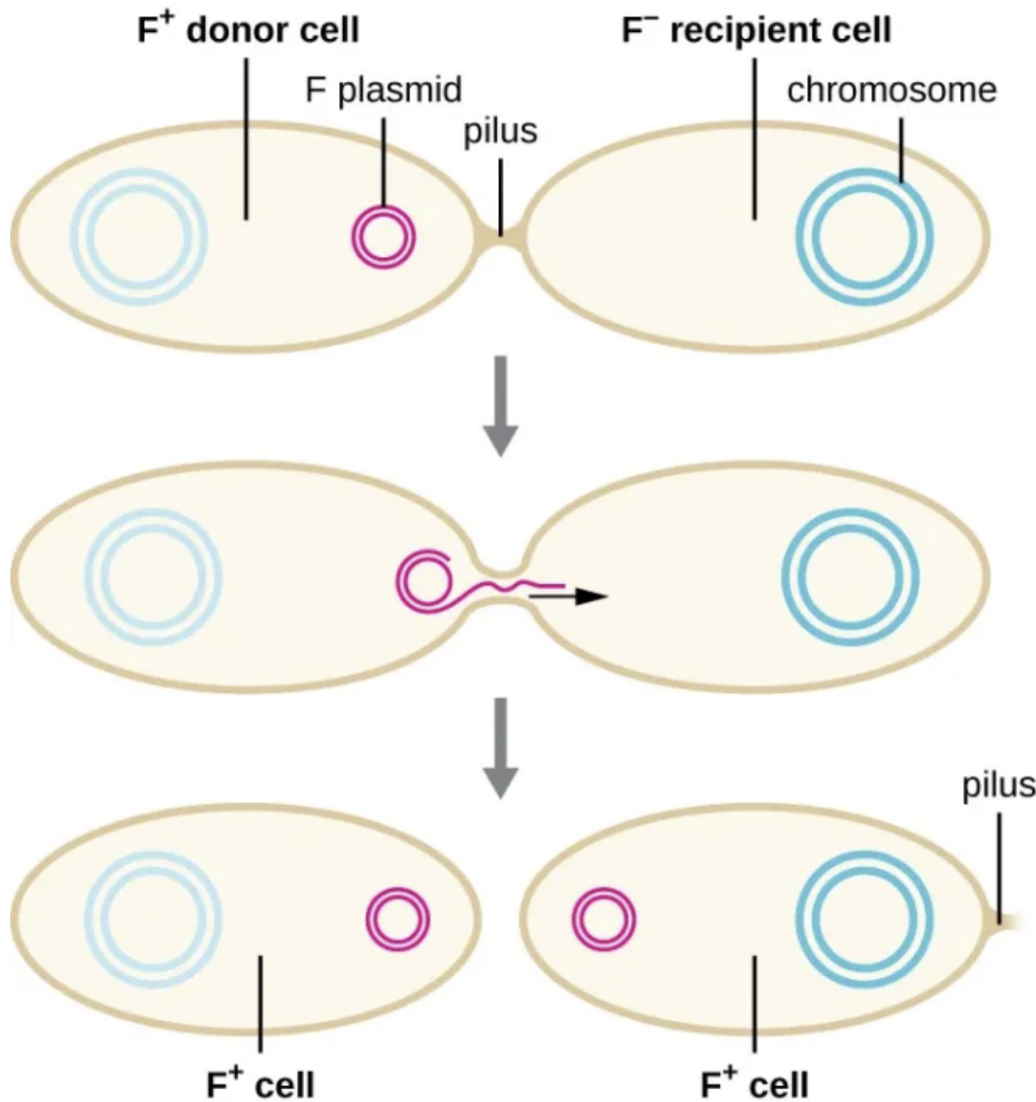


(a) Conjugation and transfer of an F plasmid



(b) Conjugation and transfer of part of an Hfr bacterial chromosome

# Conjugation Initiated by F<sup>+</sup> Bacteria



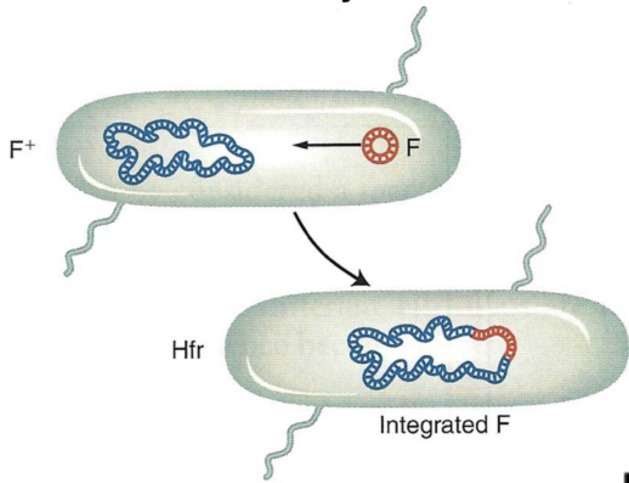
1 Pilus of donor cell attaches to recipient cell. Pilus contracts, drawing cells together to make contact with one another.

2 One strand of F plasmid DNA transfers from donor cell to recipient cell.

3 Donor synthesizes complementary strand to restore plasmid. Recipient synthesizes complementary strand to become F<sup>+</sup> cell with pilus.

Conjugation between F<sup>+</sup> and F<sup>-</sup> cells, turns the F<sup>-</sup> cell into an F<sup>+</sup> cell as the recipient cell gains the F plasmid that allows it to now build its own sex pilus in order to share its new F plasmid (and any additional genes the plasmid may contain) with a new neighbor.

F<sup>+</sup> becomes Hfr by recombination

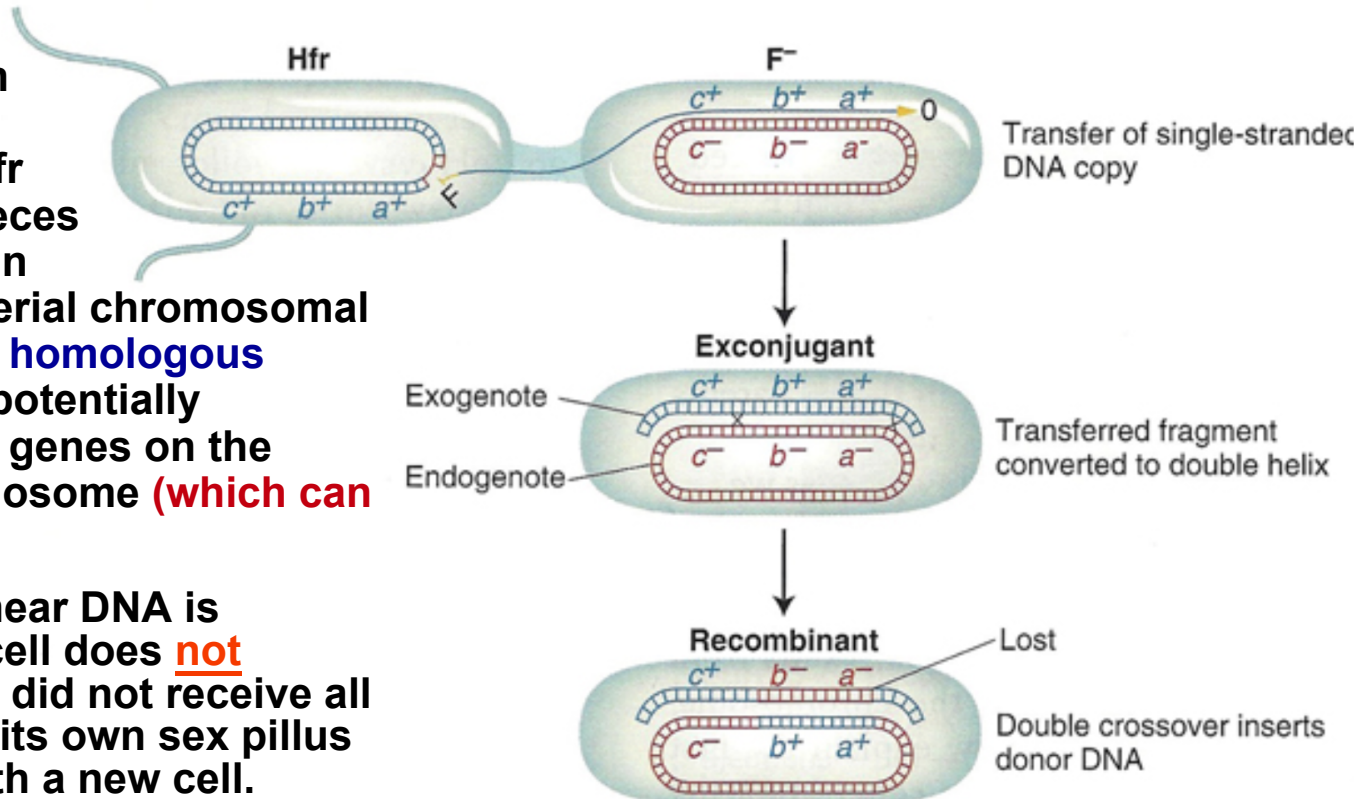


# Conjugation Initiated by Hfr Bacteria

Hfr strains transfer chromosome to F<sup>-</sup>

Conjugation between an Hfr cell and a non-Hfr cell transfers some genes from the Hfr cell's bacterial chromosome to the non-Hfr cell where homologous pieces of DNA on the linear foreign piece of DNA and the bacterial chromosomal DNA are swapped through **homologous recombination**, therefore, potentially changing the alleles of the genes on the recipient's bacterial chromosome (**which can alter phenotype**).

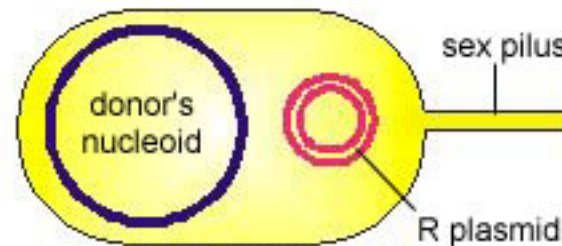
After recombination the linear DNA is destroyed. The Recipient cell does **not** become an Hfr cell since it did not receive all the genes needed to build its own sex pilus and thus mating bridge with a new cell.



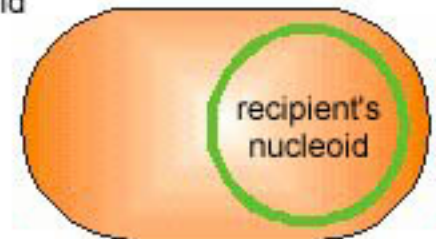
# R Plasmids and Antibiotic Resistance

- **R plasmids** carry genes for antibiotic resistance
  - Antibiotics select for bacteria with genes that are resistant to the antibiotics
    - Antibiotic resistant strains of bacteria are becoming more common

The bacterium with an R-plasmid is multiple antibiotic resistant and can produce a sex pilus (serve as a genetic donor).



Bacterium with R plasmid: multiple antibiotic resistant and male (donor).

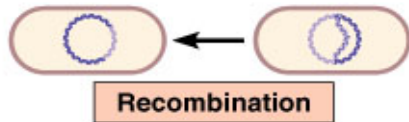


Bacterium without R plasmid: antibiotic sensitive and female (recipient).

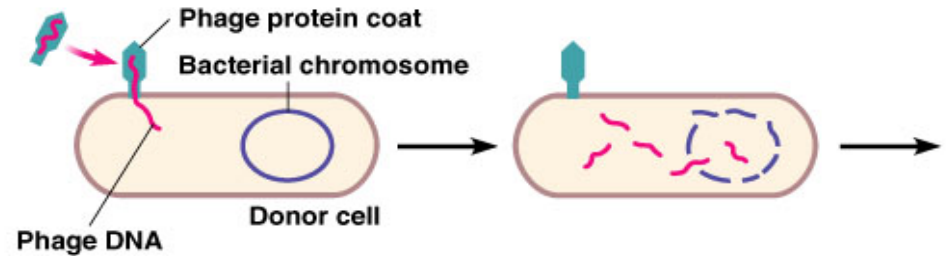
# Mutations are a big source of genetic diversity

- But together with transformation, conjugation, and finally transduction, genetic information gets shared.

- ◆ **Transduction** - when viruses inadvertently carry genetic information from one bacterial cell to another

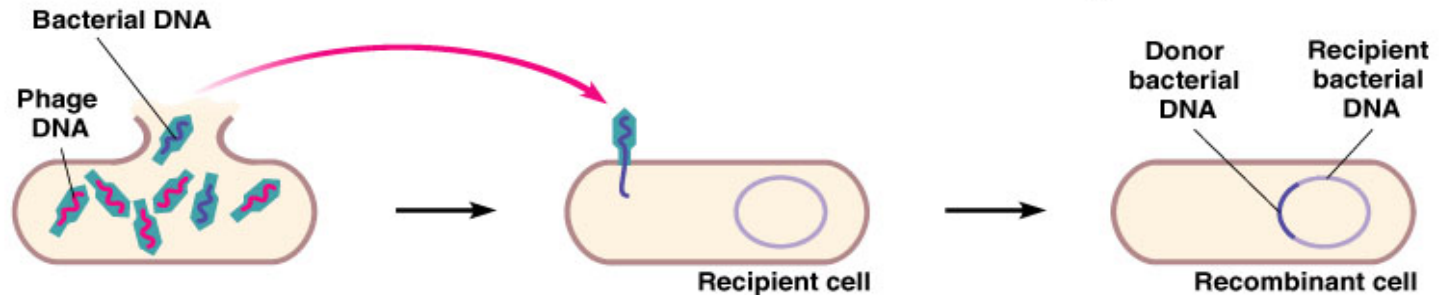


**Bacteriophages or Phages (bacterial viruses) are obligatory intracellular parasites and must invade a host cell in order to reproduce.**



1 A phage infects the donor bacterial cell.

2 Phage DNA and proteins are made, and the bacterial chromosome is broken down into pieces.



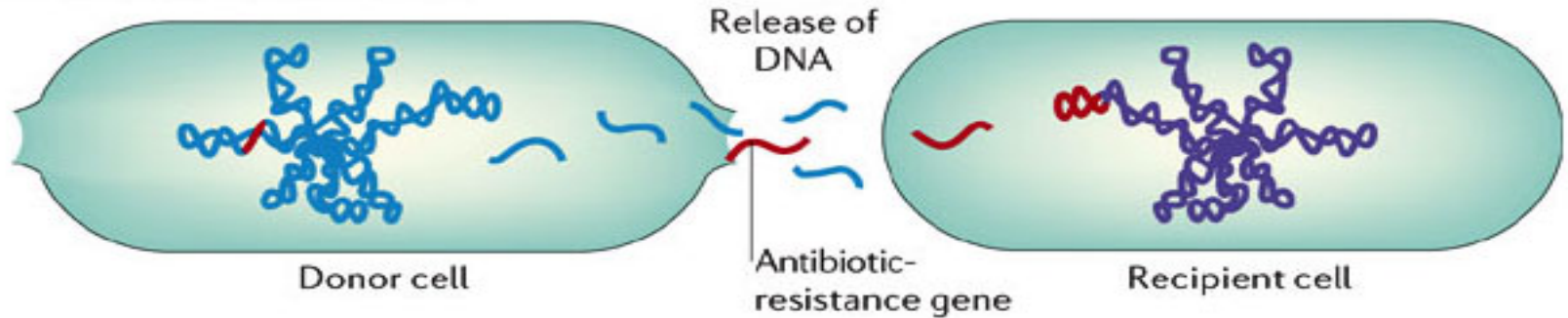
3 Occasionally during phage assembly, pieces of bacterial DNA are packaged in a phage capsid. Then the donor cell lyses and releases phage particles containing bacterial DNA.

4 A phage carrying bacterial DNA infects a new host cell, the recipient cell.

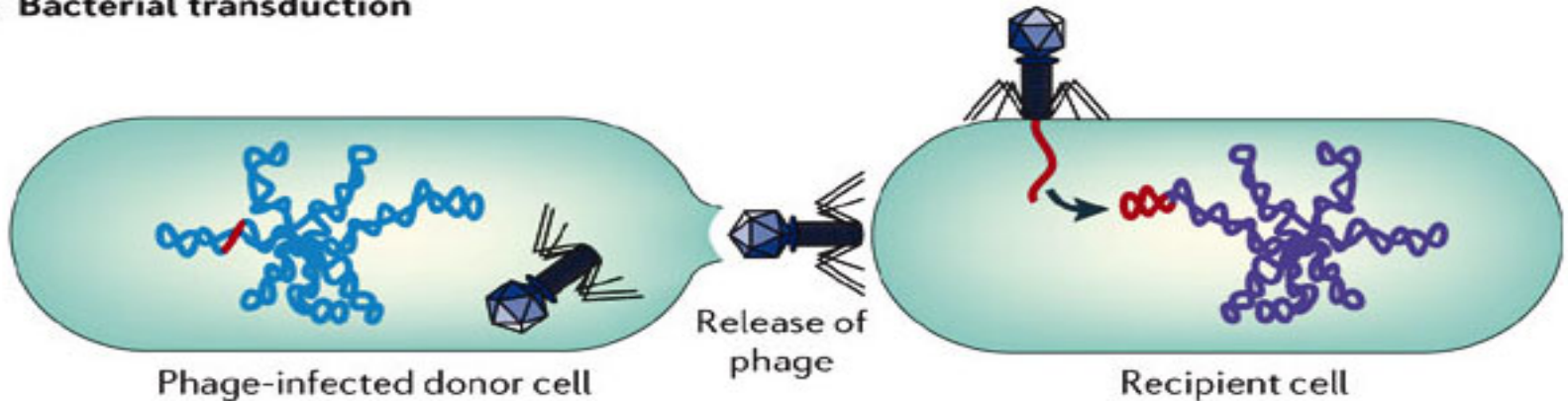
5 Recombination can occur, producing a recombinant cell with a genotype different from both the donor and recipient cells.

# Bacteria make recombinant DNA = increase their genetic diversity

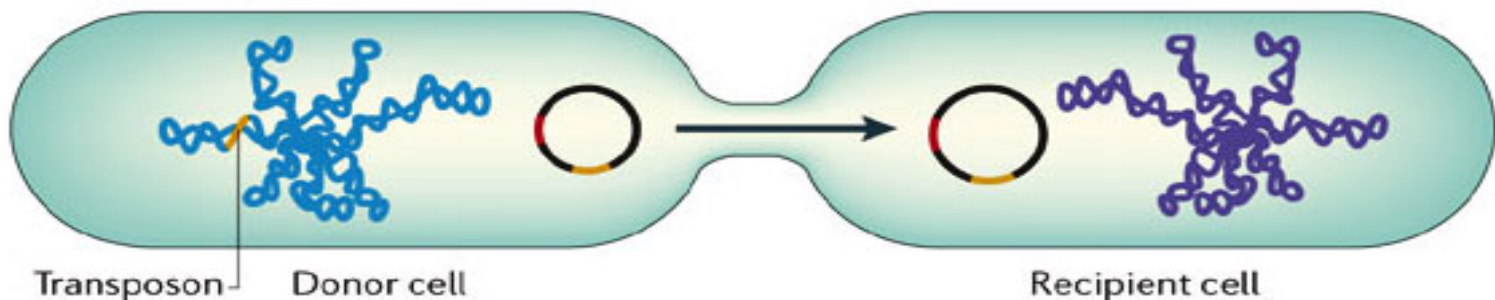
## a Bacterial transformation



## b Bacterial transduction

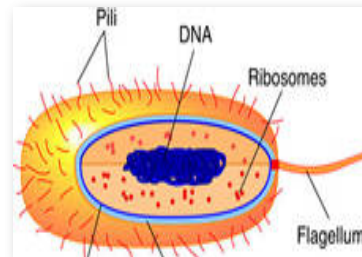
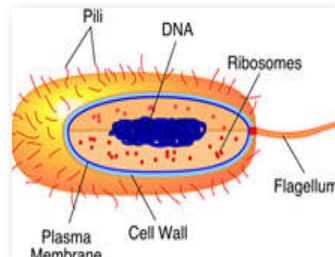
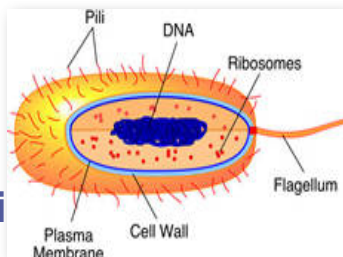
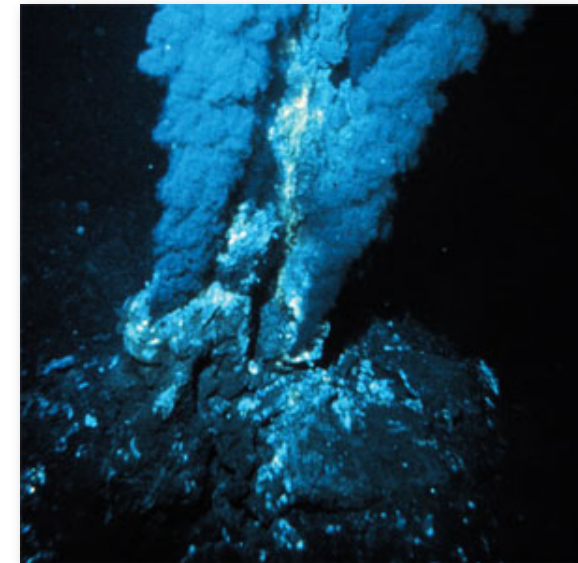
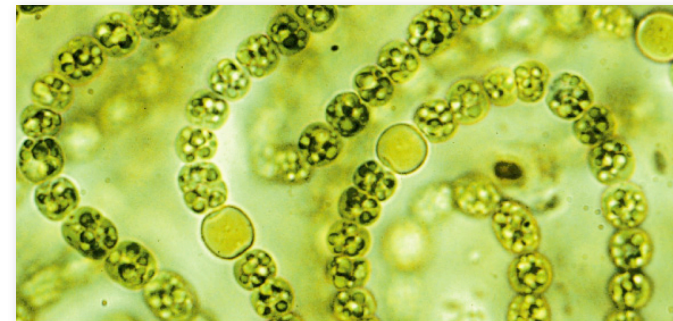


## c Bacterial conjugation



# Prokaryotic metabolism

- **How do bacteria acquire their energy & nutrients?**
  - ◆ **Where does it get C from for making organic compounds....**
    - **Auto** = C from CO<sub>2</sub>
    - **Hetero** = C from organic compounds
  - ◆ **Where is energy harvested from**
    - **Photo** = energy from sunlight
    - **Chemo** = energy from chemical bonds
- **photoautotrophs**
  - ◆ photosynthetic bacteria
- **chemoautotrophs**
  - ◆ oxidize inorganic compounds
    - nitrogen, sulfur, hydrogen...
- **chemoheterotrophs**
  - ◆ live on plant & animal matter
  - ◆ decomposers & pathogens

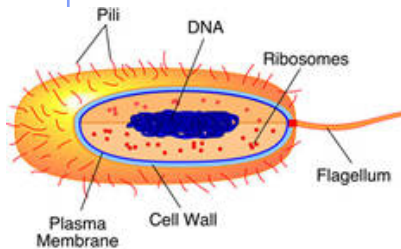


**Table 27.1 Major Nutritional Modes**

<b>Mode of Nutrition</b>	<b>Energy Source</b>	<b>Carbon Source</b>	<b>Types of Organisms</b>
<b>Autotroph</b>			
Photo-autotroph	Light	CO <sub>2</sub>	Photosynthetic prokaryotes, including cyanobacteria; plants; certain protists (algae)
Chemo-autotroph	Inorganic chemicals	CO <sub>2</sub>	Certain prokaryotes (for example, <i>Sulfolobus</i> )
<b>Heterotroph</b>			
Photo-heterotroph	Light	Organic compounds	Certain prokaryotes
Chemo-heterotroph	Organic compounds	Organic compounds	Many prokaryotes and protists; fungi; animals; some parasitic plants

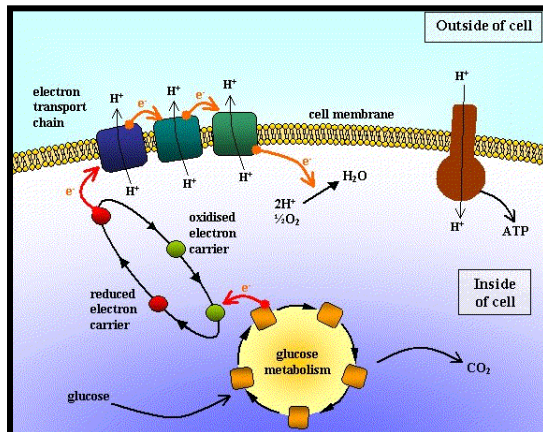
# The Role of Oxygen in Metabolism

- **Prokaryotic metabolism varies with respect to  $O_2$ :**
  - **Obligate aerobes require  $O_2$  for cellular respiration**
    - Use their plasma membrane instead of mitochondria for their **Electron Transport Chain**, pumping  $H^+$  out of the cell and allowing diffusing back into the cell to make ATP



In prokaryotes the enzymes and intermediates of the Krebs cycle are distributed throughout the cytoplasm.

The pyruvate-dehydrogenase complex (catalyzes the conversion of pyruvate to acetyl CoA) and electron transport system are associated with the plasma membrane.



Some bacteria do not use organic molecules as the source of electrons.

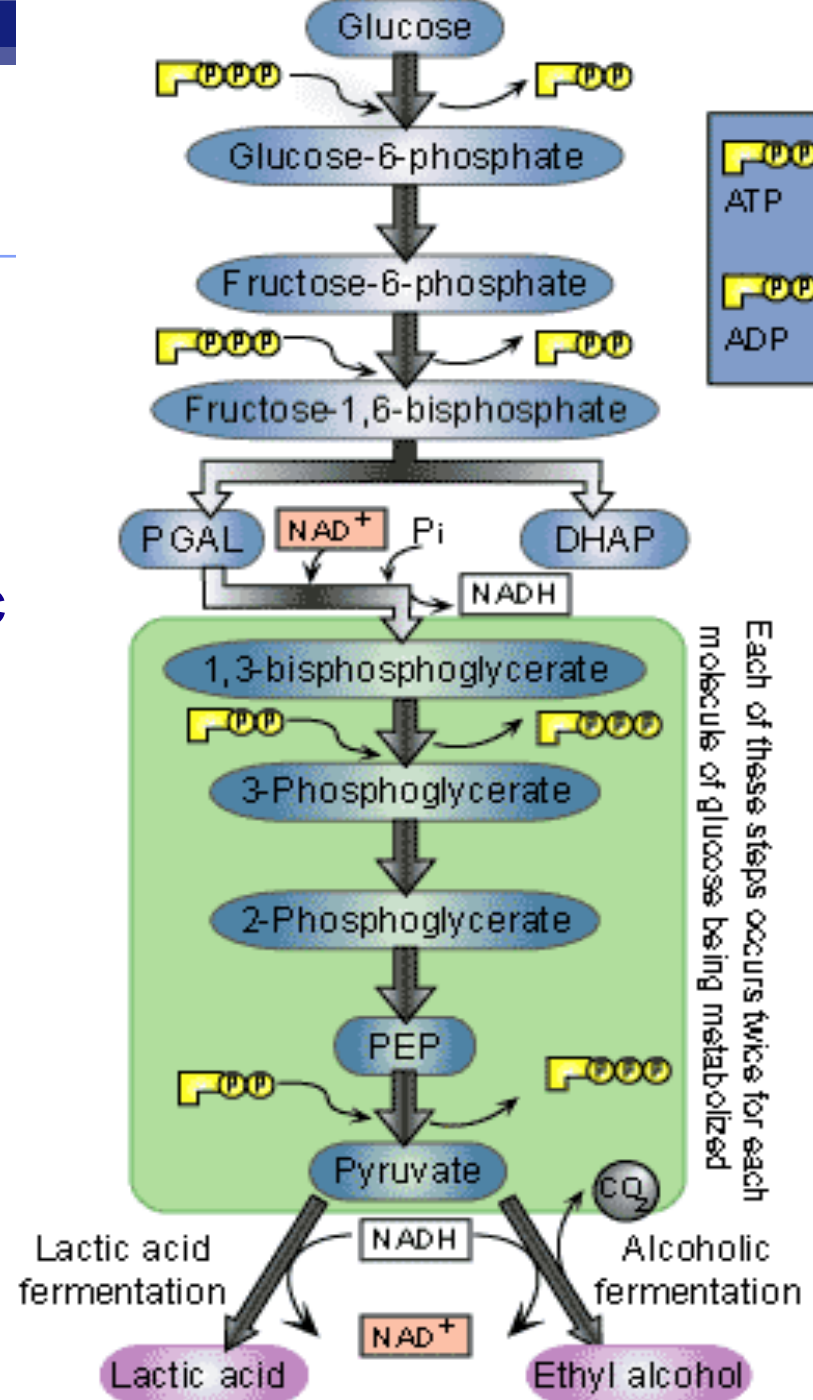
These bacteria can strip electrons directly from inorganic substances (such as  $H_2S$ ,  $H_2$ , or  $Fe^{++}$ )

Aerobic species of prokaryotes use  $O_2$  as the final acceptor of electrons.

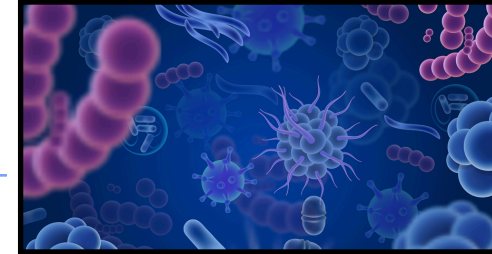
# The Role of Oxygen in Metabolism

**Prokaryotic metabolism varies with respect to O<sub>2</sub>:**

1. **Obligate anaerobes are poisoned by O<sub>2</sub> and use fermentation or anaerobic respiration**
2. **Facultative anaerobes can survive with or without O<sub>2</sub>**

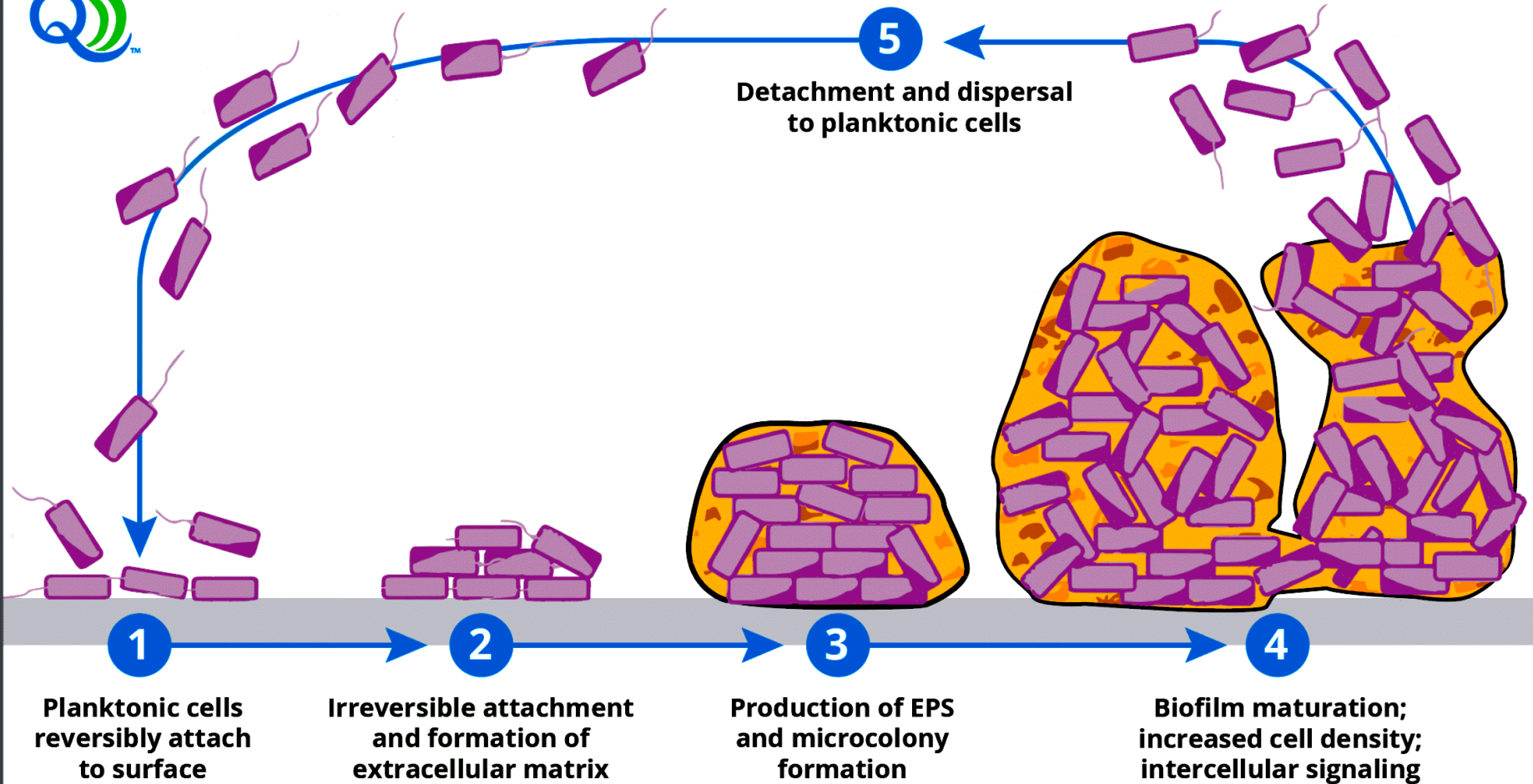


# Bacterial Biofilms



- A **biofilm** is a highly organized, structured, multicellular community of structured **communities** of microorganisms (usually bacteria) attached to a surface and enclosed in a **self-produced** matrix of **secreted** extracellular polymeric substances (EPS), **essentially a protective "slime" made of polysaccharides, proteins, and DNA.**
  - ◆ **Formation Steps:** Bacteria first adhere to a surface, then produce and secrete EPS, mature into a 3D structure, and eventually disperse, releasing cells to colonize new areas to do the same, rowing the biofilm and the colony or community.
  - ◆ **Communication:** Bacteria within biofilms communicate through **quorum sensing**, a signaling mechanism that regulates behavior and enhances resistance (Review: Ch.11)
    - Bacteria secrete signaling molecules (**autoinducers**) into the environment. As the population density increases, the concentration of these molecules hits a critical threshold. This triggers a signal transduction pathway that changes gene expression across the entire population simultaneously so biofilm matrix production begins by the bacteria in the colony or community.

# Biofilm Formation by Bacteria



# Examples of Biofilms

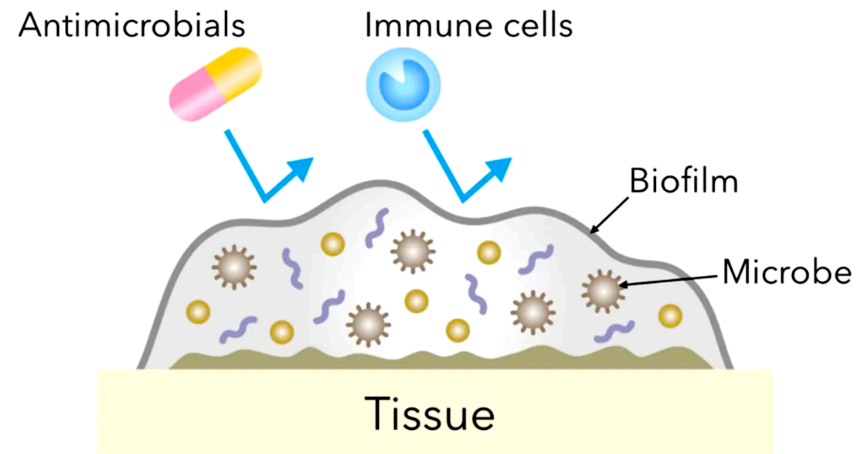


- Biofilms form on implants and medical devices (ex: heart valves, catheters) and cause chronic infections like Cystic Fibrosis in the lungs.
- Biofilms can corrode pipes and contaminate food processing surfaces.
- That orange or pink ring that develops around your drain or shower curtain is usually a biofilm. Simply rinsing the shower doesn't remove it. You have to scrub it. This is because the EPS matrix acts like a biological glue, resisting the shear force of running water, preventing bacteria from getting washed away.
- Dental Plaque is a biofilm that can result in tooth decay and cavities.
  - ◆ Salivary proteins adhere to the enamel, providing a surface for certain bacteria to attach. Some of these bacteria are anaerobic (*surviving where less oxygen penetrates into the deepest layers of the biofilm next to the tooth enamel*) and so ferment sugars, producing lactic acid as a byproduct. The biofilm matrix traps this acid against your tooth, dissolving the enamel and causing cavities.
    - **Not all are bad!** Biofilms in the gut microbiome of animals help with digestion of ingested nutrients and protect against pathogens by outcompeting harmful bacterial, making it so they cannot proliferate in the area occupied by the beneficial bacterial (*an example of Competitive Exclusion*).

# Bacterial Biofilm's Evolutionary Advantage

## ■ Beneficial / Adaptive Properties of Biofilms

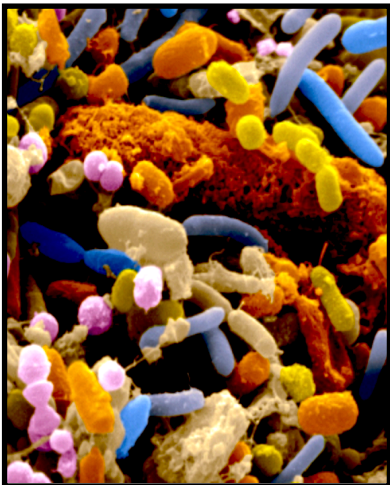
- ◆ **Protection:** The EPS matrix acts as a physical shield that protects bacteria against UV light, desiccation (dehydration), and antibiotics from host immune systems, harsh environments, and other external threats.
  - Biofilm bacteria can be up to 100 to 1000 times more resistant to antibiotics (protected from antibiotics) than free-floating (planktonic) bacteria.
- ◆ **Adhesion:** By allowing bacteria to adhere through the matrix to a surface, they allow bacteria to remain in a nutrient-rich environment rather than being washed away by fluid flow.



# Bacterial Community Dynamics Inside Biofilms

## ■ Cooperation vs Mutualism vs Competition


- ◆ Biofilms are not just "piles of bacteria."
  - Biofilms are functional ecosystems.
- ◆ **Cooperation:** Different species often live together in a single biofilm. One species' metabolic waste might be another's primary food source. One species might have evolved to help another species if this **cooperation** or **mutualism** increases the biological fitness and survival of both species.

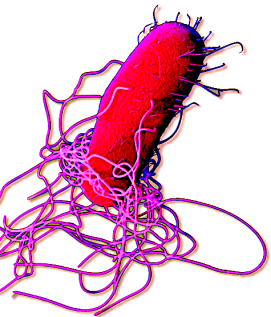




- ◆ **Mutualism** is a type of **longer-term symbiotic interaction** where different species may have evolved to depend on each other for each other's survival, benefiting both.
- ◆ **Cooperation**, by contrast, is a broader term often referring to beneficial interactions (**including shorter-term interactions**) between members of the same species (**intra-specific cooperative behavior**) or non-obligatory interactions between species (**interspecific cooperation**) where species work together in a beneficial manner to both, but can survive apart.

# Bacterial Community Dynamics Inside Biofilms

## ■ Cooperation vs Mutualism vs Competition

- 
- ◆ **Horizontal Gene Transfer (HGT):** The close proximity of cells and the increased density of cells in a biofilm significantly increases the rate of gene sharing, allowing for the **more rapid spread of beneficial genes** like antibiotic-resistance genes or genes for cooperative behavior.

- 
- **Conjugation:** Direct cell-to-cell contact through pili, which is very frequent in the dense structure of biofilms.
  - **Transformation:** Uptake of free extracellular DNA (eDNA) released within the matrix.
  - **Transduction:** Transfer of DNA between bacteria mediated by bacteriophages.

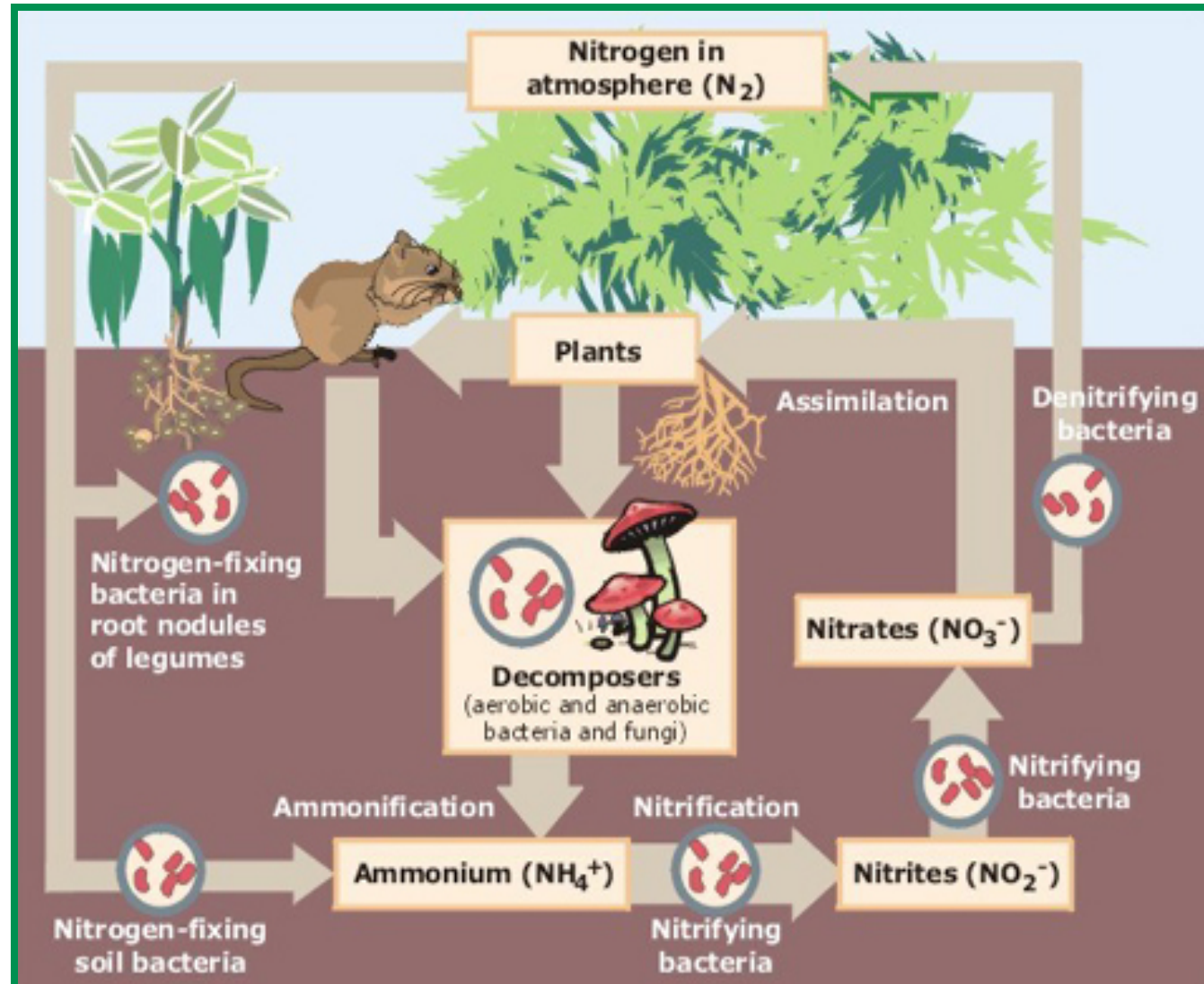
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- 
- ◆ **Competition:** Bacteria competing for **resources** (nutrients, space) may also secrete **toxins** (bacteriocins) within the biofilm to kill off competing strains of other bacteria, ensuring their own lineage dominates the space and increases its survival rates and thus biological fitness.

# Nitrogen Metabolism & the Nitrogen Cycle

- Prokaryotes can metabolize nitrogen in a variety of ways

- In nitrogen fixation, some chemoheterotrophic prokaryotes convert atmospheric nitrogen ( $N_2$ ) to ammonia ( $NH_3$ )

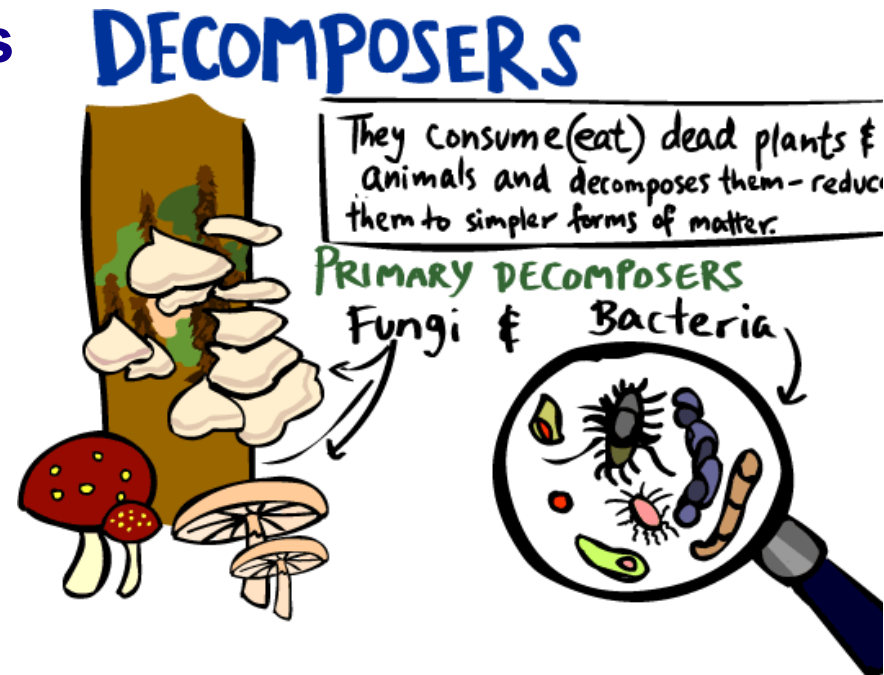
- Other prokaryotes then convert  $NH_3$ ,  $NO_2^-$  and  $NO_3^-$ , the chief way plants get their nitrogen!!!



# Chemical Cycling

- Prokaryotes play a major role in the recycling of chemical elements between the living and nonliving components of ecosystems

- Chemoheterotrophic prokaryotes function as decomposers, breaking down corpses, dead vegetation, and waste products



- ♦ These bacteria convert organic molecules back into organic ions in the soil - the minerals photosynthetic organisms like plants will later absorb to make their organic molecules out of, which are then passed through the ecosystem when consumers consume producers.

# Bacteria as pathogens

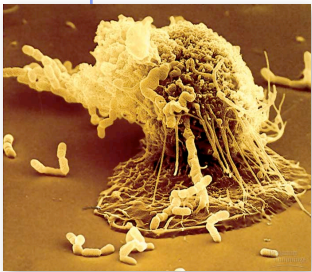
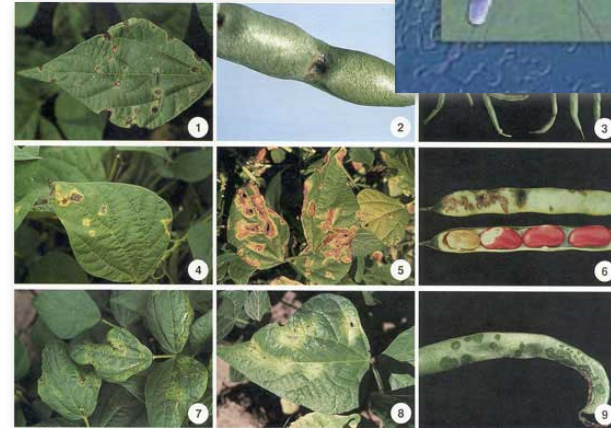
## ■ Disease-causing microbes

### ◆ plant diseases

- wilts, fruit rot, blights

### ◆ animal diseases

- tooth decay, ulcers
- anthrax, botulism
- plague, leprosy, “flesh-eating” disease
- STDs: gonorrhea, chlamydia
- typhoid, cholera
- TB, pneumonia
- lyme disease



# Bacteria also include beneficial & necessary organisms

- Life on Earth is dependent on bacteria
- Prokaryotes are so important to the biosphere that if they were to disappear the prospects for any other life surviving would be dim

- ◆ decomposers

- recycling of nutrients from dead to living

- ◆ nitrogen fixation

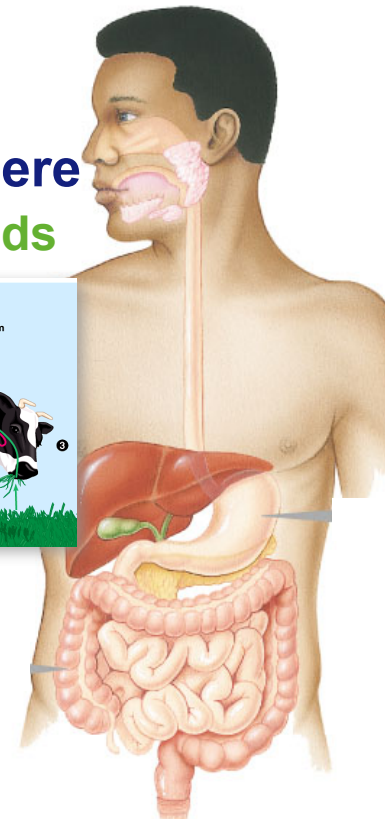
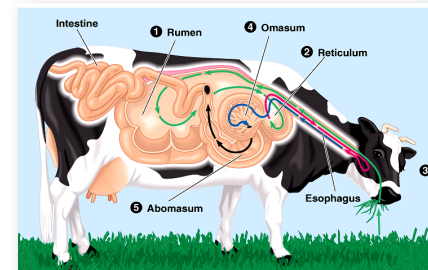
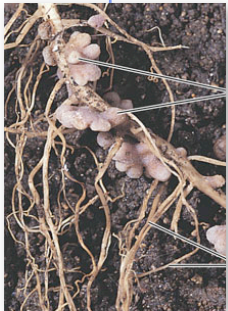
- ONLY organisms that can fix N from atmosphere
  - ◆ needed for synthesis of proteins & nucleic acids
  - ◆ Live in plant root nodules

- ◆ help in digestion (E. coli)

- digest cellulose for herbivores
  - ◆ Can make cellulase enzyme
- produce vitamins K & B<sub>12</sub> for humans

- ◆ produce foods & medicines

- from yogurt to insulin



**Got any  
Questions??  
Ask da' Boss!**



illustration: Don Smith