HE70A Winter 2004
Professor Bob Goldberg

Lecture #2 What are Genes?

THEMES / CONCEPTS

1. Review Last lecture – What is Genetic Engineering?
2. Go over Survey Results
3. Review How Genes Function
4. How is Science CARRIED out?
5. What was KNOWN About Genes ~ 1940?
6. Does the nucleus contain Genetic Material?
7. Properties of Genes
8. Griffith / Avery Experiments → DNA Genetic Material
9. Bacteria + Bacterial Genomes
10. Molecules in cell
11. TRANSFORMATION is a General Phenomenon -- Other Bacterial Traits / Animals / PLANTS

STOP 1/13/04 — to pg 34

12. Structure of DNA
13. Genes, DNA, + Chromosomes
14. Anatomy of a Gene
15. Yo! It's in the Switches → Development
16. Engineering Body FORM

STOP 1/15/04

2 Class Lectures but with Loss of Discussion

NO X FILES – Cutting + Splicing DNA

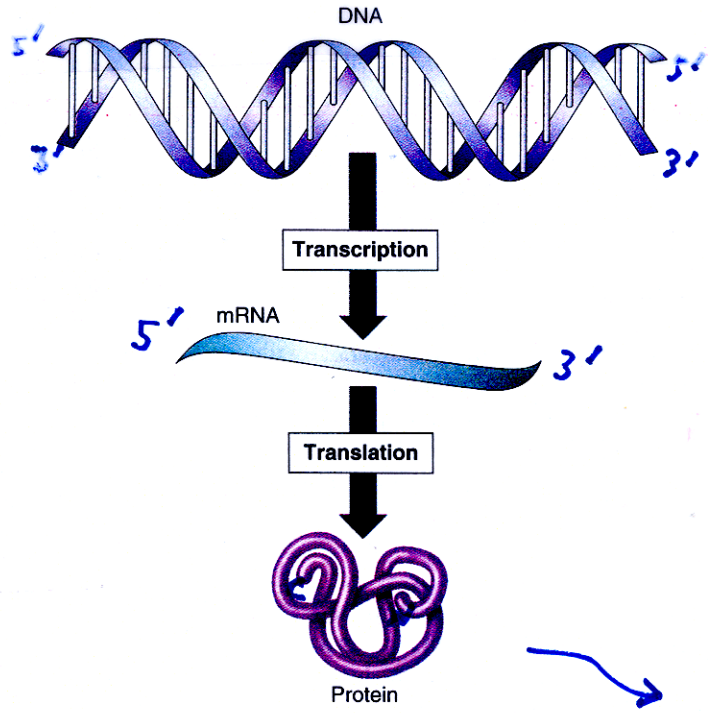
clips – Goldfish Again, Insect R Plants
DNA Structure, Interviews

What Are the Functions of A Gene?

collection of Genes

Genotype

Gene



Replication

Gene Action

Phenotype

Cell Function

FIGURE 15.5
The Central Dogma of gene expression. DNA is transcribed to make mRNA, which is translated to make a protein.

GENETIC Engineering Alters Cell Function By Changing Genotype

Gene Action Leads to Specific Traits

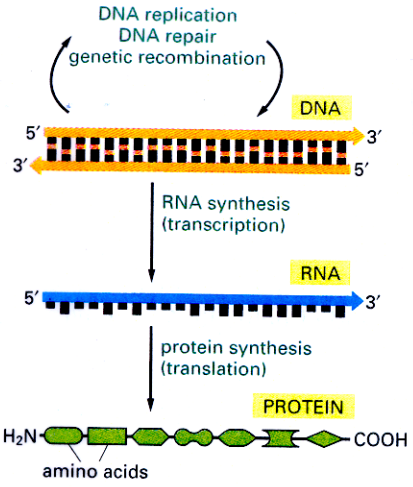
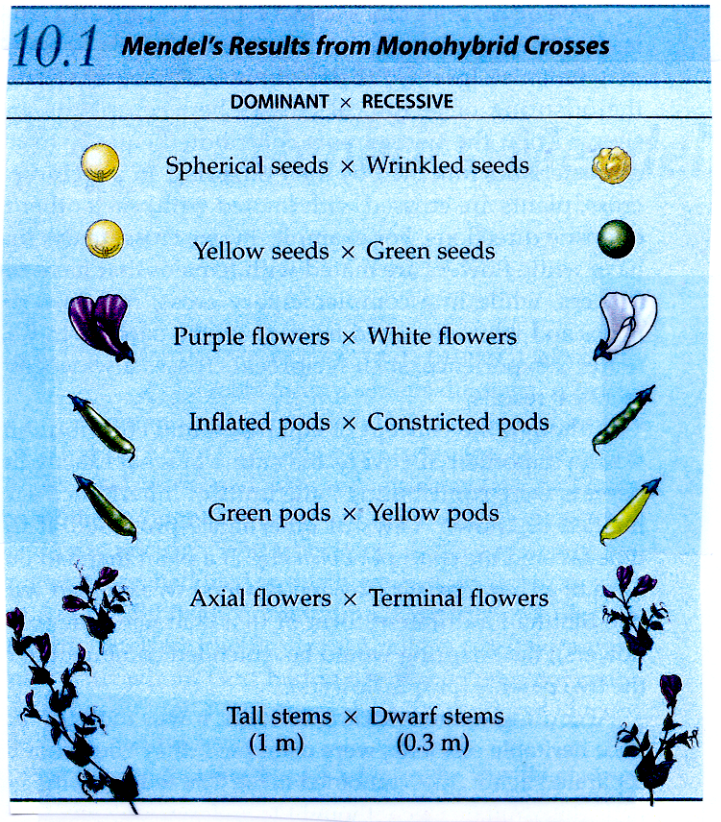


Figure 6–2 The pathway from DNA to protein. The flow of genetic information from DNA to RNA (transcription) and from RNA to protein (translation) occurs in all living cells.



Altering Genes By Mutation Leads to Genetic Variability - Different Forms of Same Gene

Genetic Engineering Can Create Amounts of New Gene Variability Not Found in "Nature"!!

How is science carried out?

Observation → Hypothesis → Predictions (if...then)

↓

Experimentation
(Testing Hypothesis)

↓

Results & Analysis of Data
(New Observations)

↓

Conclusions

↙ Verify Hypothesis

↓ Reject Hypothesis

↘ Modify Hypothesis

→ New Predictions

↓

New Experiments & Results

↓

New Conclusions

Scientists look for "what did I miss" & analyze results critically. Hypotheses are rejected - never proved

One question always leads to another

What Was Known About Genes Prior to 1940s?

1. On Chromosomes
2. At Specific Location on Chromosomes
3. Directed Formation of Specific Traits
4. Could Mutate - Mutations Stable
5. Followed Mendel's Laws of Heredity
6. Probably either protein or Nucleic Acid (DNA or RNA)

HAMMERLING'S GRAFTING EXPERIMENT SHOWING THE NUCLEUS CONTAINS GENETIC MATERIAL

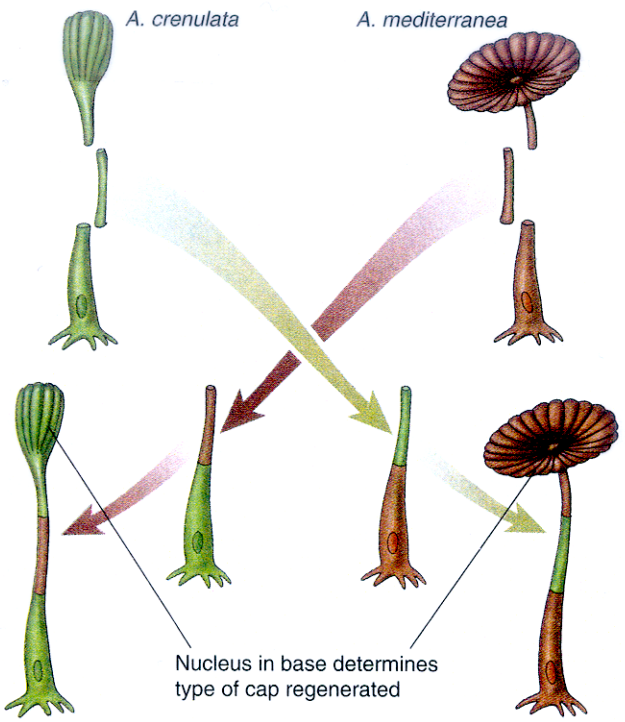


FIGURE 14.2
Hammerling's *Acetabularia* reciprocal graft experiment. Hammerling grafted a stalk of each species of *Acetabularia* onto the foot of the other species. In each case, the cap that eventually developed was dictated by the nucleus-containing foot rather than by the stalk.

1930's

Hypothesis?
Predictions?

Hypothesis to Explain CAP at TOP FROM NUCLEUS at Bottom?

But what Molecule/Substance in the nucleus is Responsible for the Phenotype?

FROG CLONING EXPERIMENT SHOWS THAT THE NUCLEUS contains the Genetic Material TO PROGRAM all of DEVELOPMENT

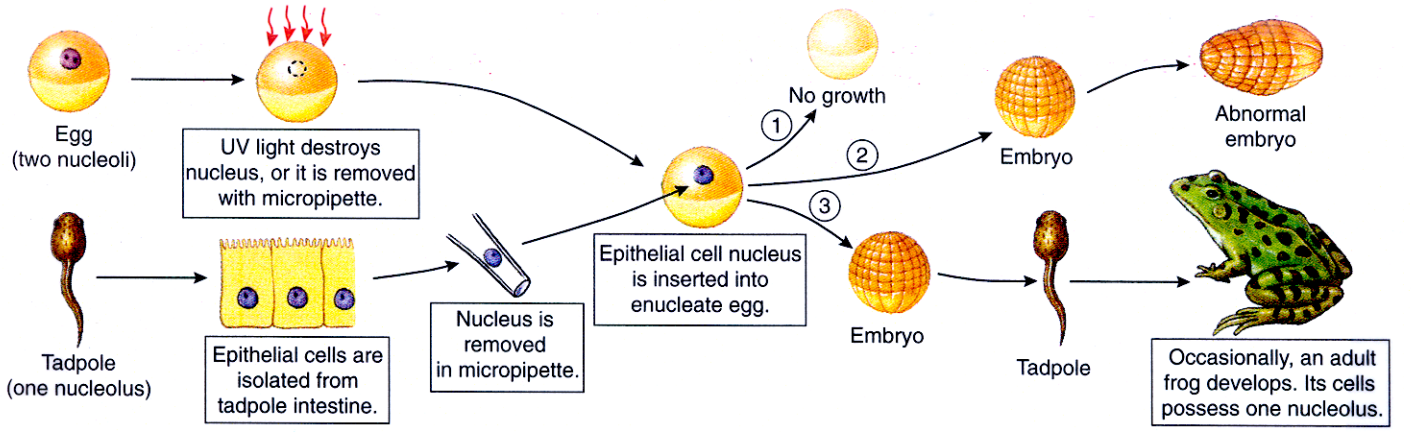


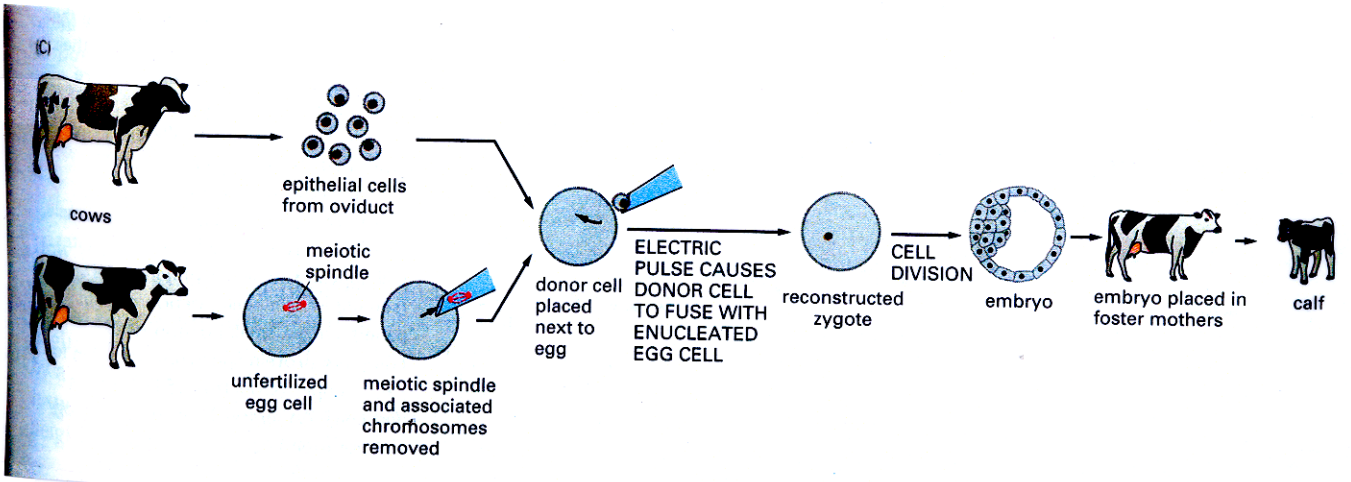
FIGURE 14.3
Briggs and King's nuclear transplant experiment. Two strains of frogs were used that differed from each other in the number of nucleoli their cells possessed. The nucleus was removed from an egg of one strain, either by sucking the egg nucleus into a micropipette or, more simply, by destroying it with ultraviolet light. A nucleus obtained from a differentiated cell of the other strain was then injected into this enucleate egg. The hybrid egg was allowed to develop. One of three results was obtained in individual experiments: (*1*) no growth occurred, perhaps reflecting damage to the egg cell during the nuclear transplant operation; (*2*) normal growth and development occurred up to an early embryo stage, but subsequent development was not normal and the embryo did not survive; and (*3*) normal growth and development occurred, eventually leading to the development of an adult frog. That frog was of the strain that contributed the nucleus and not of the strain that contributed the egg. Only a few experiments gave this third result, but they serve to clearly establish that the nucleus directs frog development.

First Cloning Experiment – 1952

Briggs & King

Hypothesis? Predictions?

FROG CLONING Experiment of the 1950's lead to CLONING of MAMMALS TODAY



SHOWS THAT THE NUCLEUS CONTAINS ALL GENES NEEDED TO PROGRAM ALL OF MAMMAL DEVELOPMENT

But.... how was it shown that genes are made of DNA?

What About Human Cloning?

WIRED

[EXCLUSIVE]

THE MAKING OF A HUMAN CLONE

7 DAYS INSIDE A MAVERICK EMBRYO LAB

Embryos? Adult Human Beings?

Genetically Engineer Cloned Human Embryos.

Is a "Clone" human?

ORGANISMS THAT HAVE BEEN CLONED

1. Plants
2. Frogs
3. Mice
4. Rats
5. Sheep (Dolly)
6. Goats
7. Mules
8. Cattle
9. Horses
10. Pigs
11. Cats (cc - copy cat)
12. Monkeys (ANDi - inserted DNA)
13. Humans ?!

Leading to Ethical Issues & new opportunities (e.g., curing human disorders, saving endangered species, etc.)

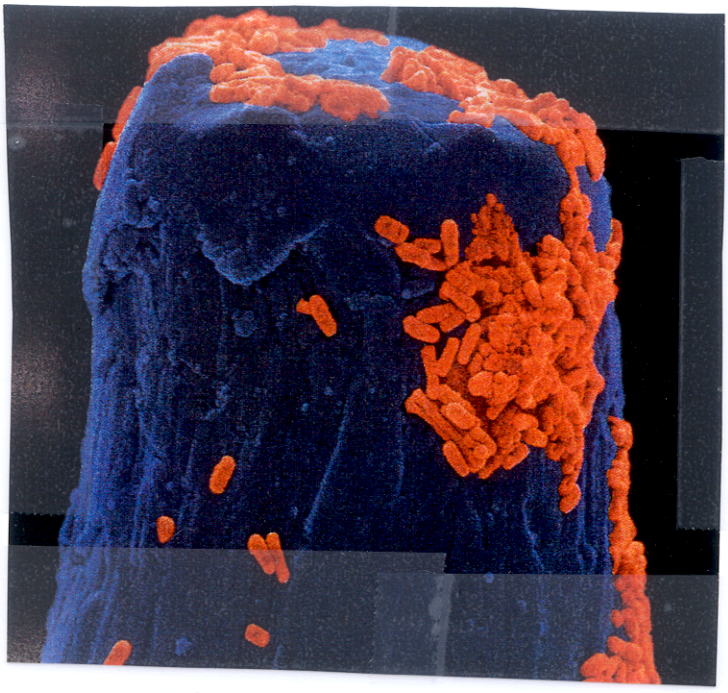
What ARE THE PROPERTIES OF A Gene?

1. Replication
2. Stability (Mutations)
3. Universality
   (a) all cells
   (b) all organisms
4. Direct cell function/Phenotype

HOW SHOW THAT DNA IS The Genetic Material?

How Can these Properties Be Tested Experimentally?
What Predictions Follow FROM These Properties

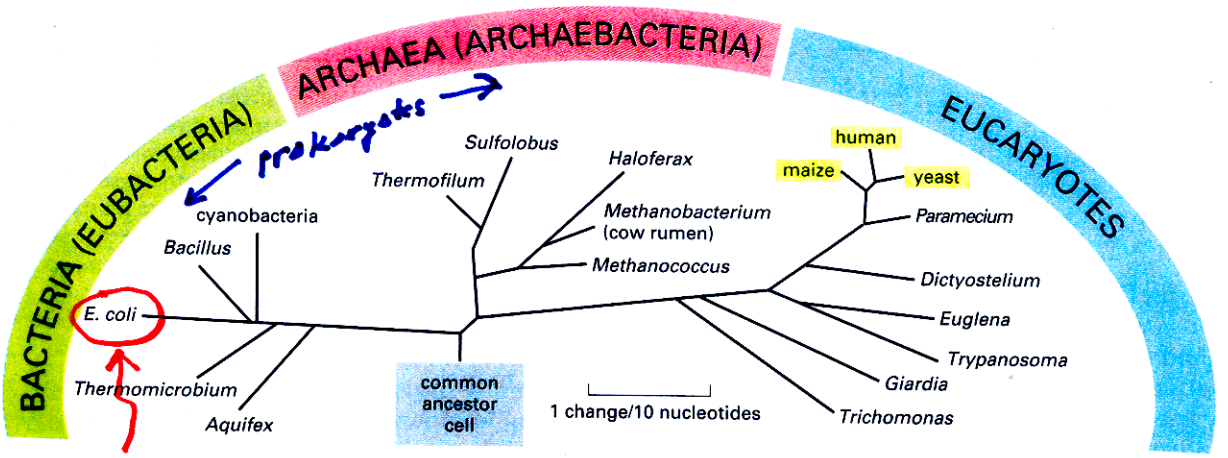
GRIFFITH'S Experiment with
PNEUMONIA BACTERIA
1927



Bacteria on a pinhead!

The First Genetic Engineering Experiment - Except That WAS Not Understood For Another 50 years!

BACTERIA ARE PROKARYOTIC SINGLE CELL ORGANISMS

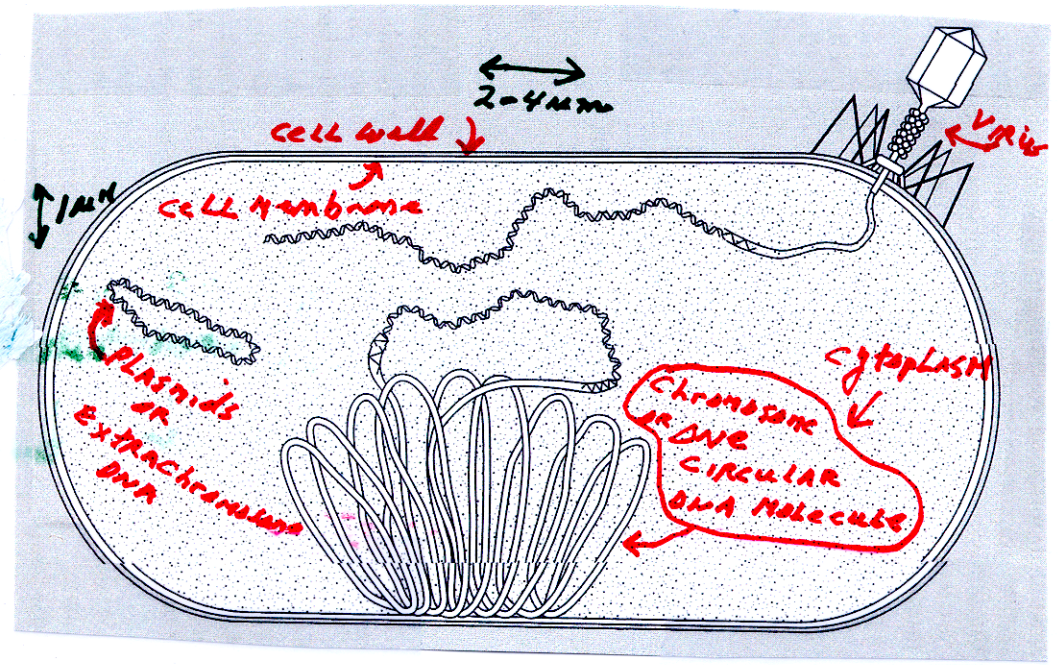


genetic engineering factories
(colon bacteria)

Figure 1–21 The three major divisions (domains) of the living world. Note that traditionally the word *bacteria* has been used to refer to procaryotes in general, but more recently has been redefined to refer to eubacteria specifically. Where there might be ambiguity, we use the term *eubacteria* when the narrow meaning is intended. The tree is based on comparisons of the nucleotide sequence of a ribosomal RNA subunit in the different species. The lengths of the lines represent the numbers of evolutionary changes that have occurred in this molecule in each lineage (see Figure 1–22).

How show that these creatures are related? Predictions?

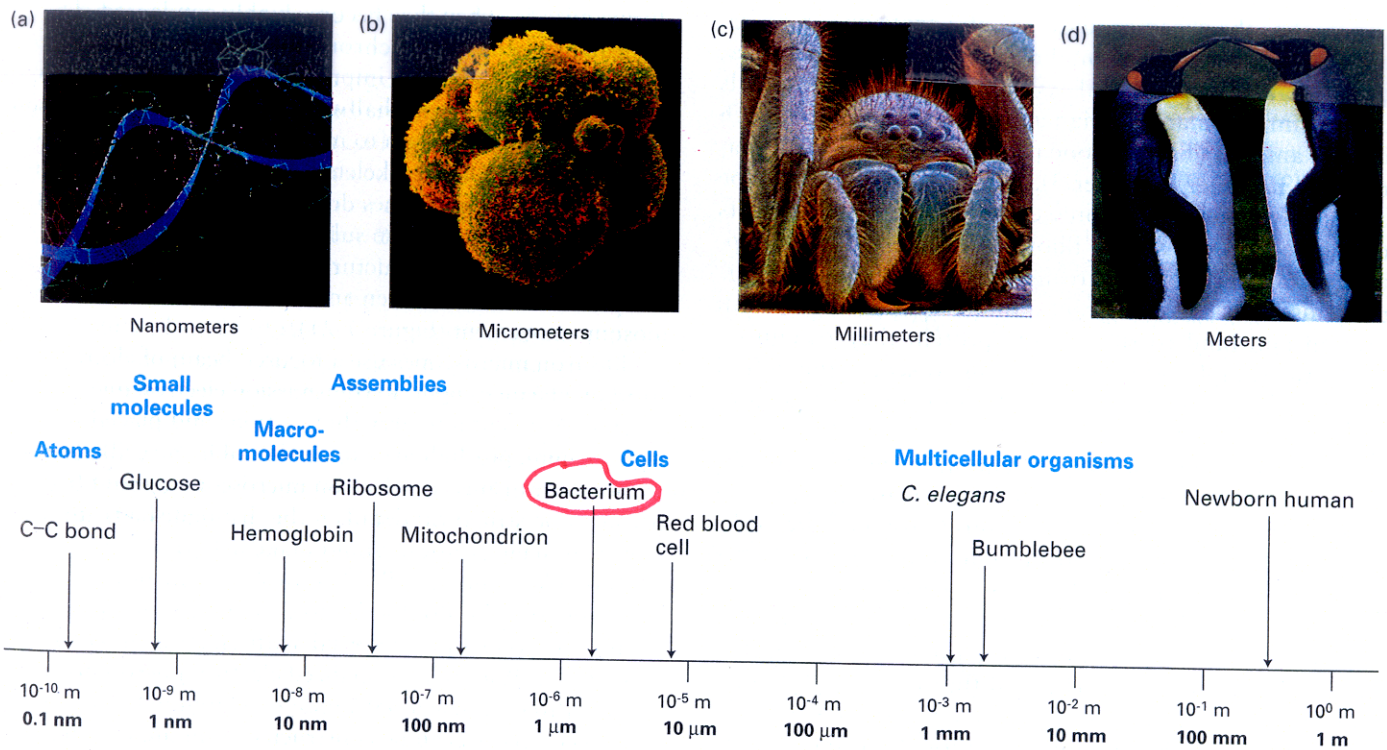
A "Typical" Bacterial Cell



Plasmids – 2,000 – 150,000 bp (1 – 100 genes)
Chromosome – 500,000 – 5,000,000 bp (500 – 4500 genes)

E. coli DNA = ~ 1.4 mm (10^{-3} m) in circumference
Small plasmid DNA = 1.4 μm (10^{-6} m) in circumference
→ antibiotic^R genes – "vectors" for genetic engineering

Size Relationships Between Atoms, Molecules, Cells, & Organisms



▲ **FIGURE 1-20 Biologists are interested in objects ranging in size from small molecules to the tallest trees.** A sampling of biological objects aligned on a logarithmic scale. (a) The DNA double helix has a diameter of about 2 nm. (b) Eight-cell-stage human embryo three days after fertilization, about 200 μm across. (c) A wolf spider, about 15 mm across. (d) Emperor penguins are about 1 m tall. [Part (a) Will and Deni McIntyre. Part (b) Yorgas Nikas/Photo Researchers, Inc. Part (c) Gary Gaugler/Visuals Unlimited, Inc. Part (d) Hugh S. Rose/Visuals Unlimited, Inc.]

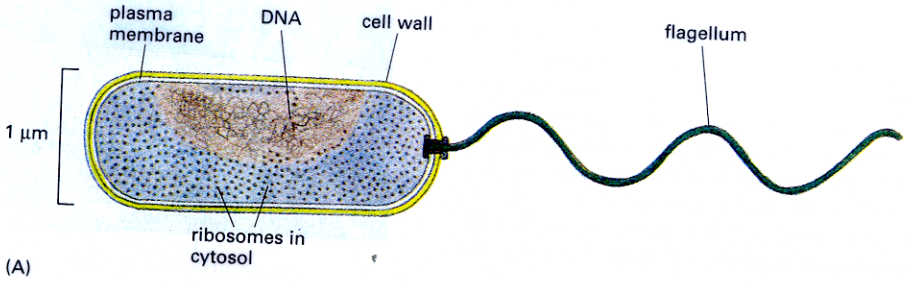
$1\,\mu m = 10^{-6}\,m$

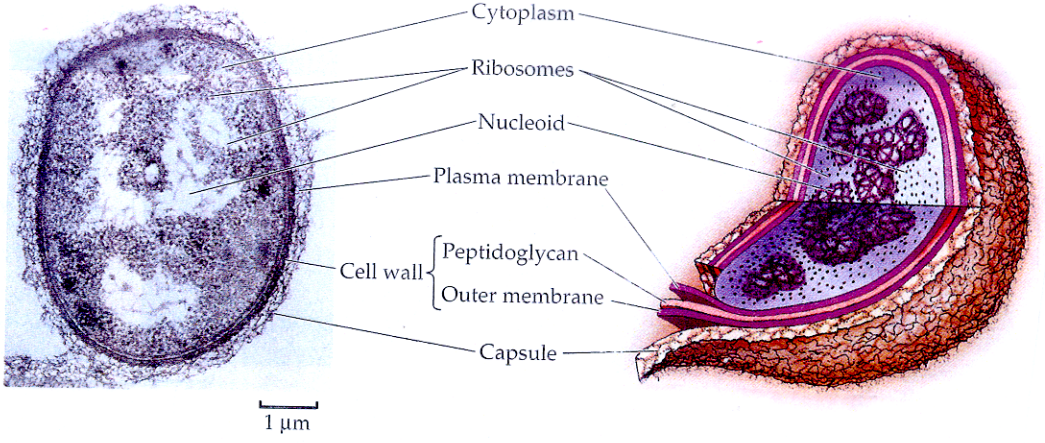
$1\,Å = 10^{-10}\,m$

$10\,Å = 1\,nm = 1 \times 10^{-9}\,m$

Bacteria = 2-5 μ

BACTERIA CELL STRUCTURE





4.4 A Prokaryotic Cell
The bacterium *Pseudomonas aeruginosa* illustrates typical prokaryotic cell structures. The electron micrograph on the left is magnified about 80,000 times. Note the existence of several protective structures external to the plasma membrane.

BACTERIA HAVE MUCH LESS DNA & FEWER GENES THAN HIGHER ORGANISMS

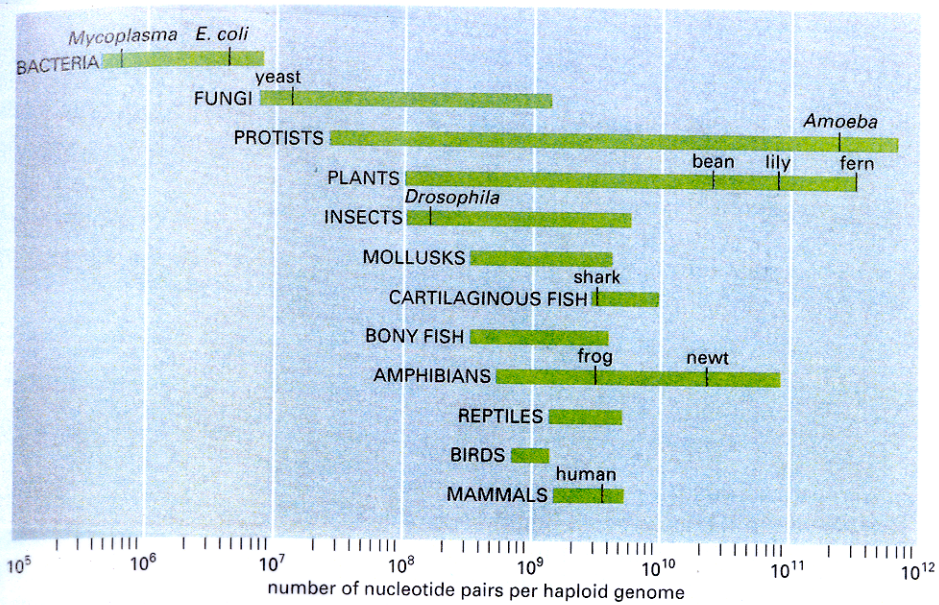


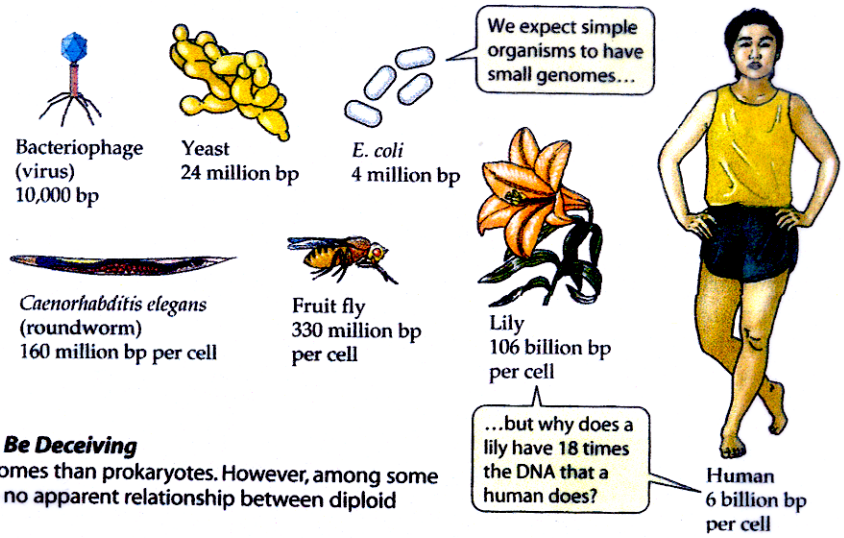
Figure 1–38 Genome sizes compared. Genome size is measured in nucleotide pairs of DNA per haploid genome, that is, per single copy of the genome. (The cells of sexually reproducing organisms such as ourselves are generally diploid: they contain two copies of the genome, one inherited from the mother, the other from the father.) Closely related organisms can vary widely in the quantity of DNA in their genomes, even though they contain similar numbers of functionally distinct genes. (Data from W.-H. Li, Molecular Evolution, pp. 380–383. Sunderland, MA: Sinauer, 1997.)

E. coli	4,600,000 bp	4300 genes
HUMANS	3,200,000,000 bp	35,000 genes

Note: HUMAN Genome ~ 1000x Larger than E. coli but only ~ 10x larger # genes !! Hypothesis?

Genome size & Gene Number Don't ALWAYS Correlate

Genome size



14.1 Amounts of Genomic DNA Can Be Deceiving
Eukaryotes have more DNA in their genomes than prokaryotes. However, among some eukaryotes—especially plants—there is no apparent relationship between diploid genome size and organism complexity.

Gene # from sequencing Projects

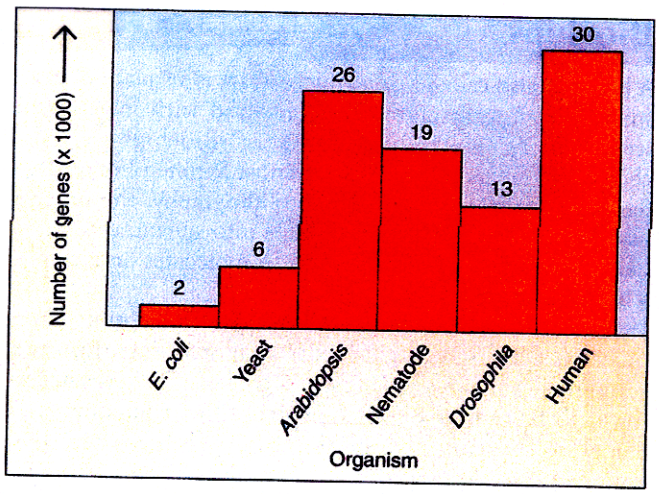


FIGURE 19.15
What the human genome is like. The human genome has an unexpectedly small number of genes, some 30,000. This is not many more than the plant *Arabidopsis*, and only a third more than nematode worms.

MANY, MANY BACTERIAL GENOMES HAVE BEEN SEQUENCED

TABLE 1–1 Some Genomes That Have Been Completely Sequenced

SEQUENCING POSSIBLE BECAUSE OF GENETIC ENGINEERING

SPECIES	SPECIAL FEATURES	HABITAT	GENOME SIZE (1000s OF NUCLEOTIDE PAIRS PER HAPLOID GENOME)	NUMBER OF GENES (PROTEINS)
EUBACTERIA				
Mycoplasma genitalium	smallest genome of any known cell	human genital tract	580	468
Synechocystis sp.	photosynthetic, oxygen-generating (cyanobacterium)	lakes and streams	3573	3168
Escherichia coli	laboratory favorite	human gut	4639	4289
Helicobacter pylori	causes stomach ulcers and predisposes to stomach cancer	human stomach	1667	1590
Bacillus subtilis	bacterium	soil	4214	4099
Aquifex aeolicus	lithotrophic; lives at high temperatures	hydrothermal vents	1551	1544
Mycobacterium tuberculosis	causes tuberculosis	human tissues	4447	4402
Treponema pallidum	spirochaete; causes syphilis	human tissues	1138	1041
Rickettsia prowazekii	bacterium most closely related to mitochondria; causes typhus	lice and humans (intracellular parasite)	1111	834
Thermotoga maritima	organotrophic; lives at high temperatures	hydrothermal vents	1860	1877
ARCHAEA				
Methanococcus jannaschii	lithotrophic, anaerobic, methane-producing	hydrothermal vents	1664	1750
Archaeoglobus fulgidus	lithotrophic or organotrophic, anaerobic, sulfate-reducing	hydrothermal vents	2178	2493
Aeropyrum pernix	aerobic, organotrophic hot-steam vents	coastal volcanic	669	2620
EUCARYOTES				
Saccharomyces cerevisiae (budding yeast)	minimal model eucaryote	grape skins, beer	12,069	~6300
Arabidopsis thaliana (wall cress)	model organism for flowering plants	soil and air	~142,000	~26,000
Caenorhabditis elegans (nematode worm)	simple animal with perfectly predictable development	soil	~97,000	~19,000
Drosophila melanogaster (fruit fly)	key to the genetics of animal development	rotting fruit	~137,000	~14,000
Homo sapiens (human)	most intensively studied mammal	houses	~3,200,000	~30,000

(+) Anthrax, Cholera, Diptheria, Pneumonia, Plague, Leprosy, Lyme Disease, Syphilis, etc.

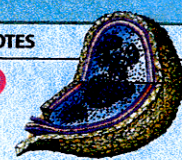
143 as of TODAY!

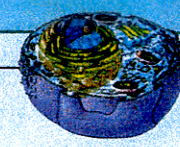
ONE OF THE MOST EXCITING AREAS OF BIOLOGY TODAY!

Bacterial Genes & Genomes Differ from Those of Higher organisms

14.1 A Comparison of Prokaryotic and Eukaryotic Genes and Genomes

CHARACTERISTIC	PROKARYOTES	EUKARYOTES
Genome size (base pairs)	10^4–10^7	10^8–10^{11}
Repeated sequences	Few	Many
Noncoding DNA within coding sequences	Rare	Common
Transcription and translation separated in cell	No	Yes
DNA segregated within a nucleus	No	Yes
DNA bound to proteins	Some	Extensive
Promoter	Yes	Yes
Enhancer/silencer	Rare	Common
Capping and tailing of mRNA	No	Yes
RNA splicing required	Rare	Common
Number of chromosomes in genome	One	Many





Only in Details - Not overall Chemical/DNA Features

BACTERIA ARE HIGHLY DIVERSE CREATURES

Table 34.1 Bacteria

Major Group	Typical Examples		Key Characteristics
			ARCHAEBACTERIA
Archaebacteria	Methanogens, thermophiles, halophiles		Bacteria that are not members of the kingdom Eubacteria. Mostly anaerobic with unusual cell walls. Some produce methane. Others reduce sulfur.
			EUBACTERIA
Actinomycetes	*Streptomyces*, *Actinomyces*		Gram-positive bacteria. Form branching filaments and produce spores; often mistaken for fungi. Produce many commonly used antibiotics, including streptomycin and tetracycline. One of the most common types of soil bacteria; also common in dental plaque.
Chemoautotrophs	Sulfur bacteria, *Nitrobacter*, *Nitrosomonas*		Bacteria able to obtain their energy from inorganic chemicals. Most extract chemical energy from reduced gases such as H_2S (hydrogen sulfide), NH_3 (ammonia), and CH_4 (methane). Play a key role in the nitrogen cycle.
Cyanobacteria	*Anabaena*, *Nostoc*		A form of photosynthetic bacteria common in both marine and freshwater environments. Deeply pigmented; often responsible for "blooms" in polluted waters.
Enterobacteria	*Escherichia coli*, *Salmonella*, *Vibrio*		Gram-negative, rod-shaped bacteria. Do not form spores; usually aerobic heterotrophs; cause many important diseases, including bubonic plague and cholera.
Gliding and budding bacteria	Myxobacteria, *Chondromyces*		Gram-negative bacteria. Exhibit gliding motility by secreting slimy polysaccharides over which masses of cells glide; some groups form upright multicellular structures carrying spores called fruiting bodies.
Pseudomonads	*Pseudomonas*		Gram-negative heterotrophic rods with polar flagella. Very common form of soil bacteria; also contain many important plant pathogens.
Rickettsias and chlamydias	*Rickettsia*, *Chlamydia*		Small, gram-negative intracellular parasites. *Rickettsia* life cycle involves both mammals and arthropods such as fleas and ticks; *Rickettsia* are responsible for many fatal human diseases, including typhus (*Rickettsia prowazekii*) and Rocky Mountain spotted fever. Chlamydial infections are one of the most common sexually transmitted diseases.
Spirochaetes	*Treponema*		Long, coil-shaped cells. Common in aquatic environments; a parasitic form is responsible for the disease syphilis.

FACTORIES FOR Genetic Engineering

Bacteria are among the most lethal organisms on the Earth!

Table 34.2 Important Human Bacterial Diseases

Disease	Pathogen	Vector/Reservoir	Epidemiology
Anthrax	*Bacillus anthracis*	Animals, including processed skins	Bacterial infection that can be transmitted through contact or ingested. Rare except in sporadic outbreaks. May be fatal.
Botulism	*Clostridium botulinum*	Improperly prepared food	Contracted through ingestion or contact with wound. Produces acute toxic poison; can be fatal.
Chlamydia	*Chlamydia trachomatis*	Humans, STD	Urogenital infections with possible spread to eyes and respiratory tract. Occurs worldwide; increasingly common over past 20 years.
Cholera	*Vibrio cholerae*	Human feces, plankton	Causes severe diarrhea that can lead to death by dehydration; 50% peak mortality if the disease goes untreated. A major killer in times of crowding and poor sanitation; over 100,000 died in Rwanda in 1994 during a cholera outbreak.
Dental caries	*Streptococcus*	Humans	A dense collection of this bacteria on the surface of teeth leads to secretion of acids that destroy minerals in tooth enamel—sugar alone will not cause caries.
Diphtheria	*Corynebacterium diphtheriae*	Humans	Acute inflammation and lesions of mucous membranes. Spread through contact with infected individual. Vaccine available.
Gonorrhea	*Neisseria gonorrhoeae*	Humans only	STD, on the increase worldwide. Usually not fatal.
Hansen's disease (leprosy)	*Mycobacterium leprae*	Humans, feral armadillos	Chronic infection of the skin; worldwide incidence about 10–12 million, especially in Southeast Asia. Spread through contact with infected individuals.
Lyme disease	*Borrelia bergdorferi*	Ticks, deer, small rodents	Spread through bite of infected tick. Lesion followed by malaise, fever, fatigue, pain, stiff neck, and headache.
Peptic ulcers	*Helicobacter pylori*	Humans	Originally thought to be caused by stress or diet, most peptic ulcers now appear to be caused by this bacterium; good news for ulcer sufferers as it can be treated with antibiotics.
Plague	*Yersinia pestis*	Fleas of wild rodents: rats and squirrels	Killed ¼ of the population of Europe in the 14th century; endemic in wild rodent populations of the western U.S. today.
Pneumonia	*Streptococcus, Mycoplasma, Chlamydia*	Humans	Acute infection of the lungs, often fatal without treatment
Tuberculosis	*Mycobacterium tuberculosis*	Humans	An acute bacterial infection of the lungs, lymph, and meninges. Its incidence is on the rise, complicated by the development of new strains of the bacteria that are resistant to antibiotics.
Typhoid fever	*Salmonella typhi*	Humans	A systemic bacterial disease of worldwide incidence. Less than 500 cases a year are reported in the U.S. The disease is spread through contaminated water or foods (such as improperly washed fruits and vegetables). Vaccines are available for travelers.
Typhus	*Rickettsia typhi*	Lice, rat fleas, humans	Historically a major killer in times of crowding and poor sanitation; transmitted from human to human through the bite of infected lice and fleas. Typhus has a peak untreated mortality rate of 70%.

HOW WAS DNA DEMONSTATED TO BE THE GENE?

Genetic Engineering Begins!

FIGURE 15.1
The unraveled chromosome of an *E. coli* bacterium. This complex tangle of DNA represents the full set of assembly instructions for the living organism *E. coli*.

IT'S ALL IN THE DNA!