10.555 Bioinformatics

Principles, Method, Applications

Inorganic vs Organic Compounds

INORGANIC COMPOUNDS	ORGANIC COMPOUNDS
thermostable	low melting points
mostly ionic	molecular (bigger) mostly made of C, H, N, O
few	many (essentially due to C's ability to form compounds with other substances and itself)
	isomers
	polymers

Chemical Bonds

Metallic (electrons are free-flowing in the crystal of metals)

Metals: characterized by thermal/electric conductivity, the ability to be "squeezed" and "pulled," release electrons when heated or when hit by light of appropriate frequency

Covalent bonds

Non-Covalent bonds

Covalent Bonds

Covalent (electrons are shared)

between non-metals / some times between non-metal and metal

Non-polar

participating atoms have approximately the same atomic number

Polar

participating atoms have different atomic number

Characteristics of compounds built of covalent bonds:

gas, liquid, solid

Non-Covalent Bonds

Ionic (electrons are donated/accepted)
  between metal and non-metal (or group of non-metals)

Characteristics of compounds built of ionic bonds:
- solid in room T
- high melting points
- when melted they can be electrolyzed (proving ionic nature)

Non-Covalent Bonds

Hydrogen bonds: relatively weak bonds, formed between H (participating in a dipolar covalent bond) and a more electronegative element (F, O, N)

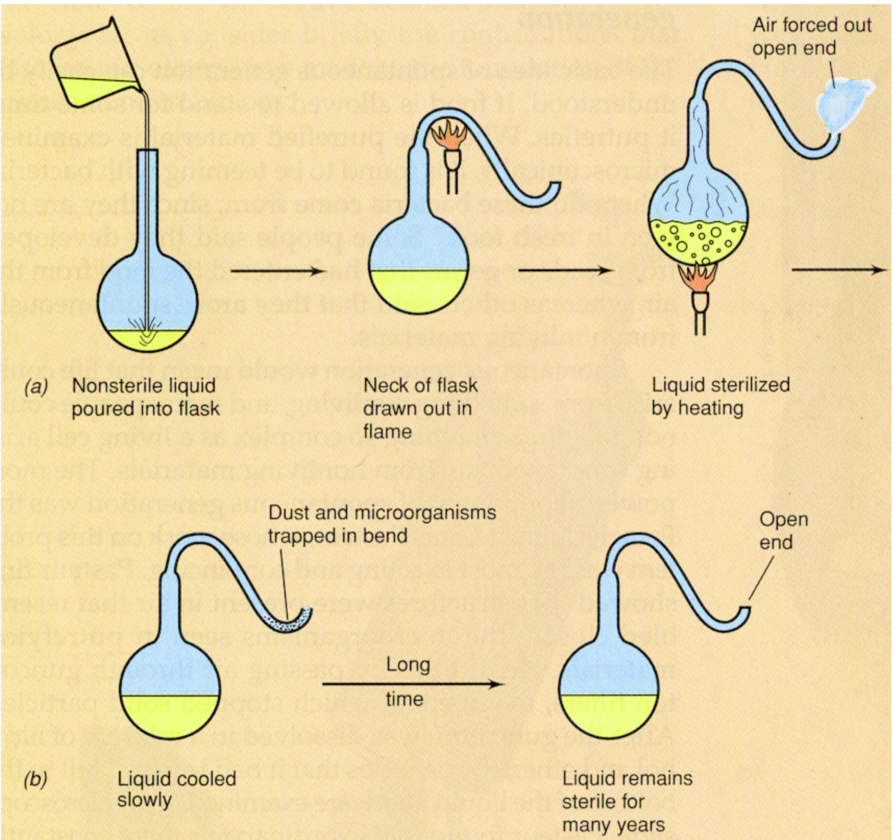
the strongest are those where D-H-A are in a straight line

van der Waals interactions: bonds between the transient dipoles caused by momentary random fluctuations in the electron distribution of the participating atoms (covalent bonds are shorter than "van der Waals bonds")

Water As A Solvent

- the water molecule is polar
- polar molecules are water soluble
- opposite is true of non-polar
- hydrogen bonding makes for highly-cohesive water and results in
  - high surface tension
  - high specific heat
  - high boiling point
- highly polar water is beneficial for the cell by forcing non-polar substances to aggregate and remain together (e.g. non-polar lipids that are contained in the membranes)

Pasteur's Experiment



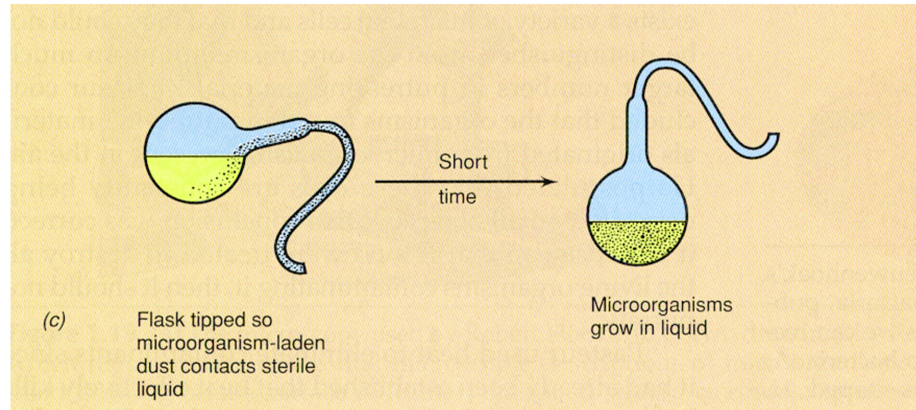


Figure 1.21 Pasteur's experiment with the swan-necked flask. (a) Sterilizing the contents of the flask. (b) If the flask remains upright, no microbial growth occurs. (c) If microorganisms trapped in the neck reach the sterile liquid, they grow rapidly.

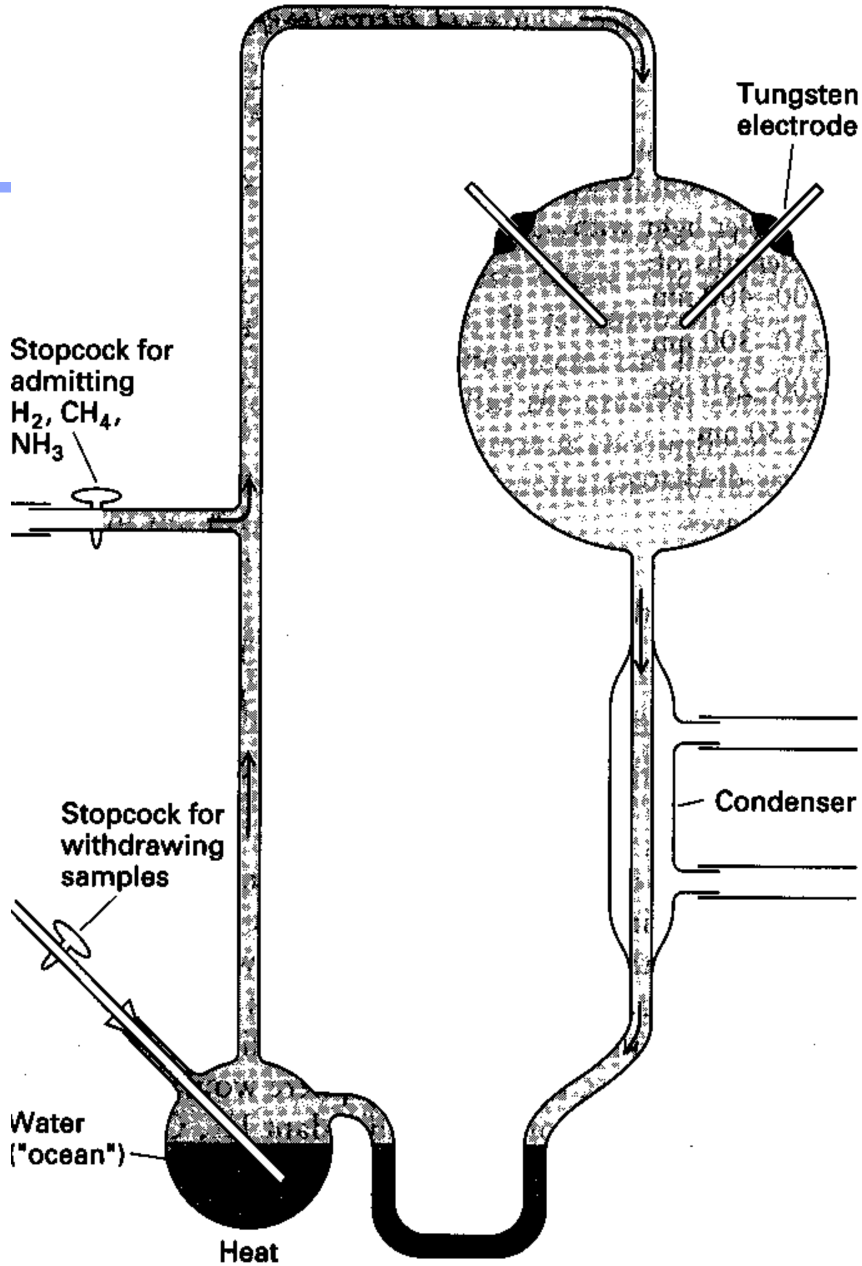
Figure from: Brock Biology of Microorganisms
Madigan/Martinko/Parker pp22

The Hallmarks Of A Cell

- self feeding
- self replicating / growing
- able to differentiate
- able to send/receive signals through chemical mechanisms
- evolves

The First Cell?

- Oparin/Haldane ideas (CH_4, H_2O, NH_3, H_2) - 1920
- Stan Miller's Experiment (1953)



▲ **Figure 26-2** The apparatus used by Stanley Miller to simulate prebiotic organic synthesis. [See S. L. Miller, 1988, *Cold Spring Harbor Symp. Quant. Biol.* 52:17.]

Figure from: Molecular Cell Biology 2nd edition
Darnell/LodishBaltimore pp1052

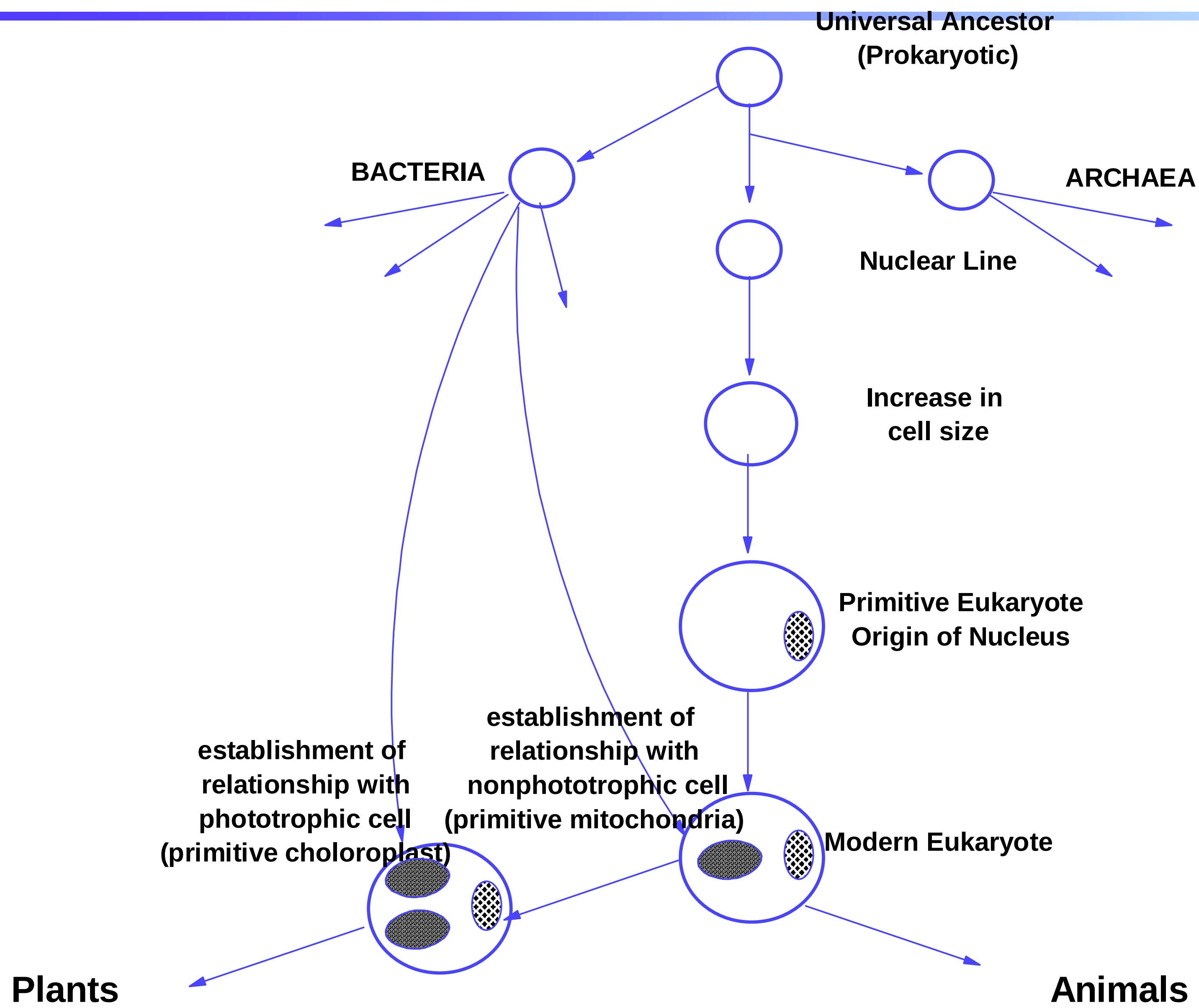
- aggregates / organization / feedings

- solar energy

  +

  $6\ CO_2 + 12\ H_2O \quad \text{---->} \quad C_6H_6(OH)_6 + 6\ H_2O + 6\ O_2$

Endosymbiotic Theory



Darwin's Ideas About Evolutions

- organisms have the tendency to multiply from one generation to the next
- although the members of a species tend to multiply their number remains fairly constant from one generation to the next
- organisms compete among themselves to maintain their numbers
- within a species there is variations; variations are external but also pertain to the organism's survival abilities
- within a species some organisms are favored over other and survive
- beneficial characteristics of some organisms accumulate over time eventually leading to the creation of new species different from the original

Modern Ideas About Evolutions

- mutation: the enabling agent
- natural selection
- genetic isolation (population dynamics)
  - geography
  - ecology
  - reproductive incompatibility

Milestone Experiments

- Griffith's experiment (1928)
  - 3 serotypes for *S. pneumoniae*: I, II and III
  - 2 forms: S (smooth/virulent) R (rough/harmless)
  - IS -> IR

mouse infected by IS -> dead
mouse infected by IIR -> alive
mouse infected by 'heat killed IS' -> alive
BUT
mouse infected by IIR <u>and</u> 'heat killed IS' -> <u>**dead**</u>

- the "transforming principle"

Milestone Experiments (cont.)

- Avery's experiment (1944)
  - used 'heat killed IS'

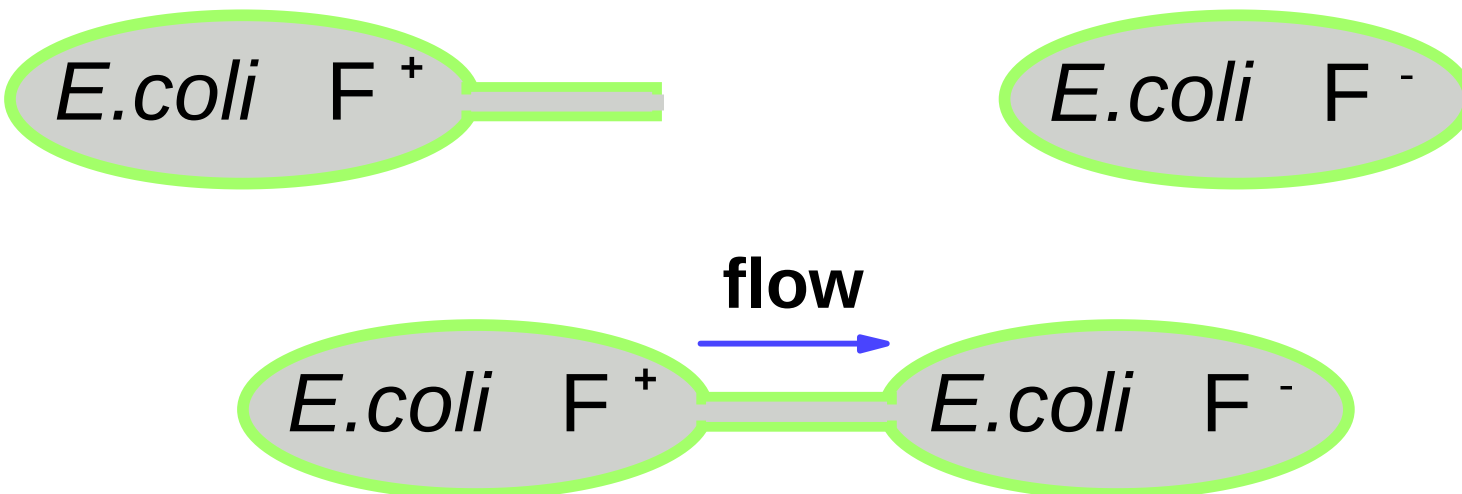
    BUT after processing

    - with *PROTEase* -> mouse dead
    - with *RNAase* -> mouse dead
    - with *DNAase* -> mouse ALIVE!

- so the "transforming principle" is DNA!

Milestone Experiments (cont.)

- Lederberg/Tatum experiments (1946)
- Cavalli-Sforza, Jacob, and others



- culprit was shown to be the 95Kb "***F*** plasmid" that codes for 30 genes

Milestone Experiments (cont.)

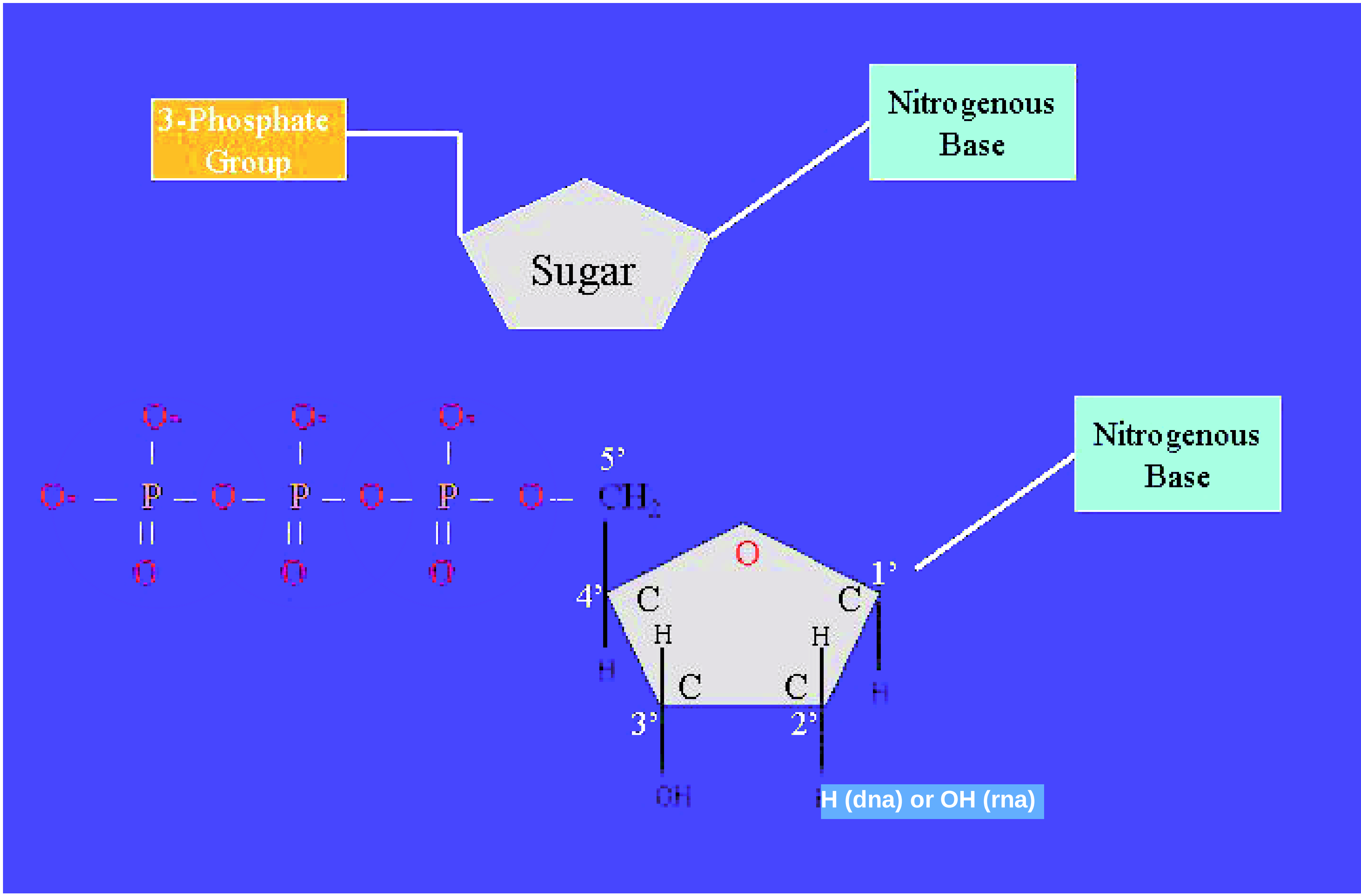
- Chargaff's base ratios (1945-50)
  - used different tissues
  - used different organisms

- in all cases:

A = T   and G = C

(which means that A+G = T+C)

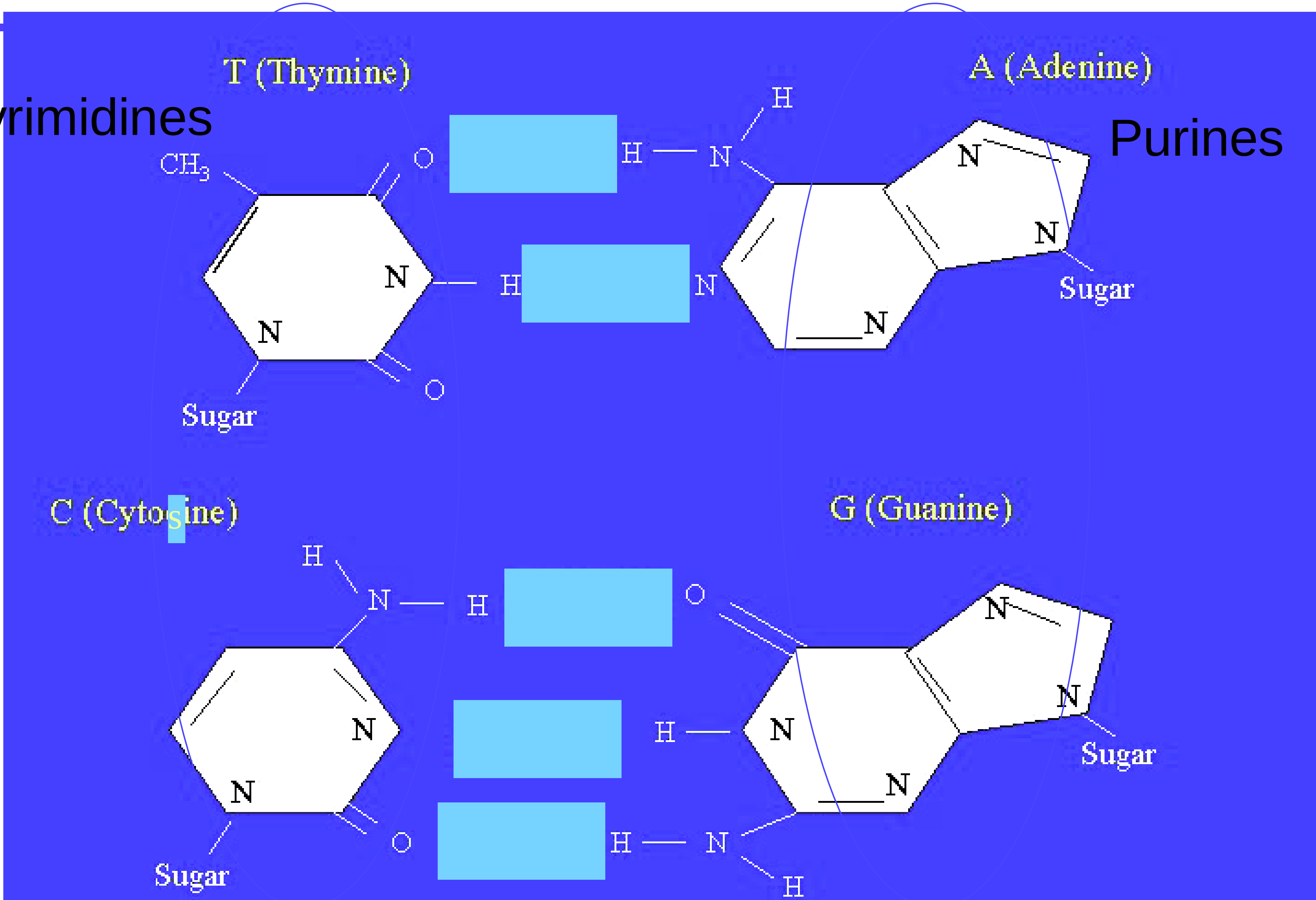
Nucleic Acids



Bases

Pyrimidines

Purines



Polymerization

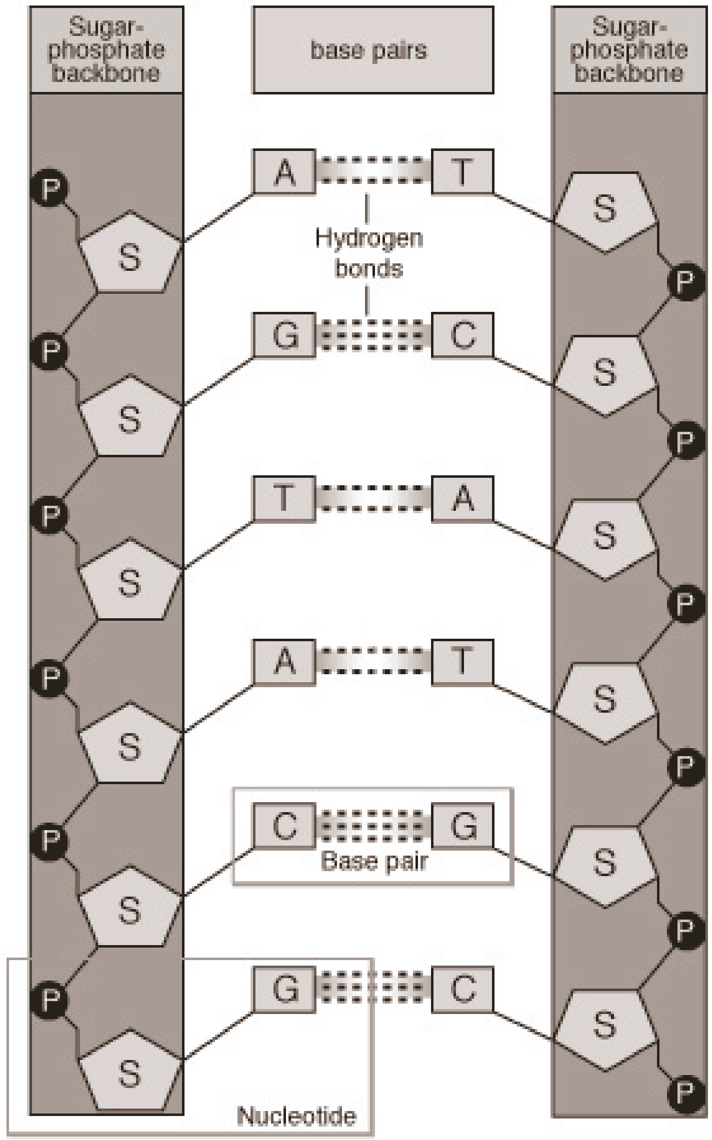
```
            BASE                O                 BASE
              |                 ||                  |
          (sugar)    +   HO  -  P  -  O  -(sugar)         ------->
          |                     |          |
          OH                    O-        OH


            BASE      O                BASE
              |       ||                 |
(5' end)  (sugar)- O - P - O -(sugar)  + H2O          (3' end)
                       |       |
                       O-     OH
```

phospho-diester bond

and pairing...

The End Result



10 bases
34 Angstroms

From: http://www.accessexcellence.org//GG/dna2.html
Artist: Darryl Leja

"The results suggest a helical structure... containing probably 2, 3, or 4 co-axial nucleic acid chains per helical unit, and having the phosphate group on the outside."

From a report written by Rosalind Franklin in February 1952, a year before Watson and Crick proposed the double helix structure.

"Rosalind Franklin and DNA" by A. Sayre

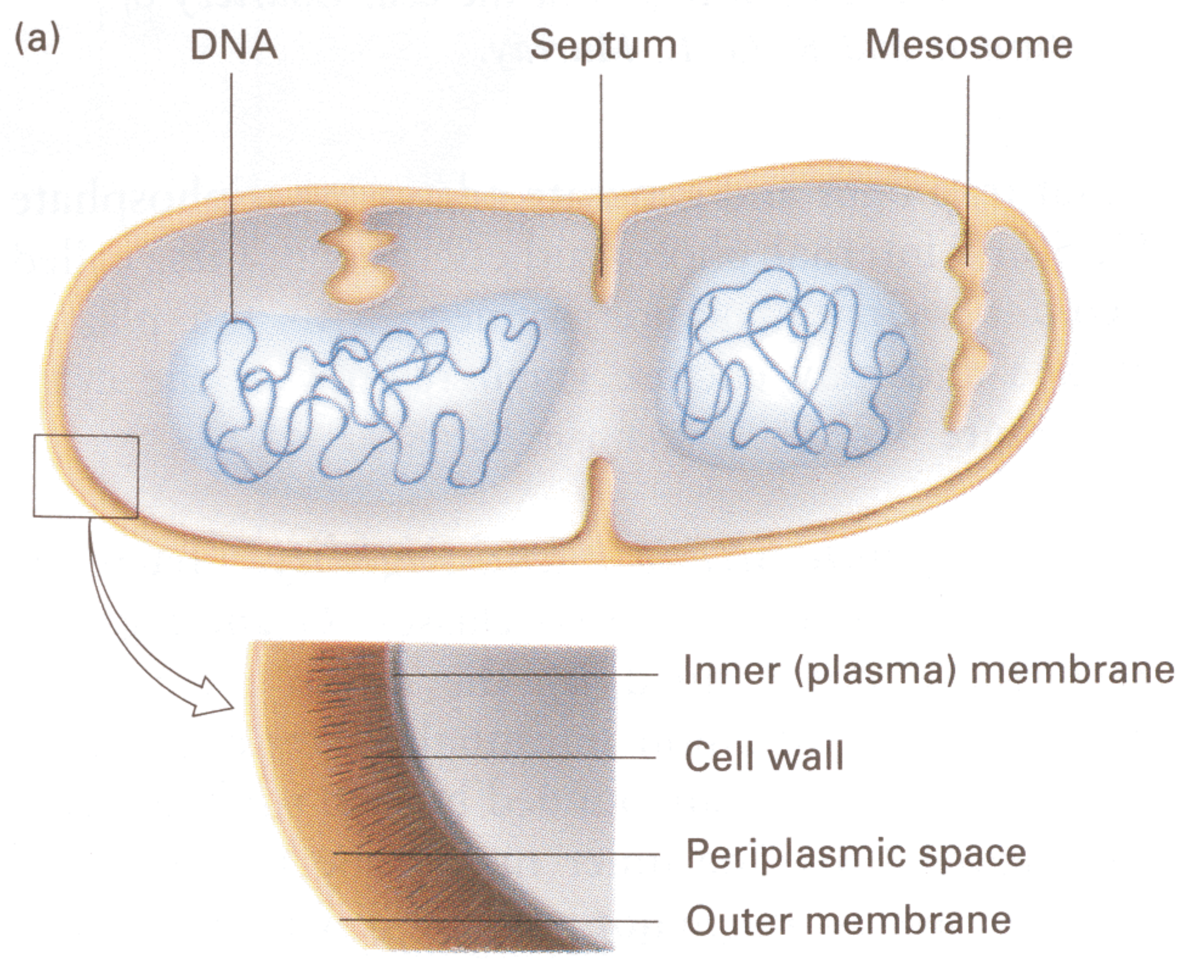
How Big Is Big?

Species	Size	Domain
E. Coli		bacteria
S.cerevisiae		eukaryotes
Wheat		eukaryotes
Insects		eukaryotes
D. melanogaster		eukaryotes
M. janaschii		archaea
Fern		eukaryotes
Fish		eukaryotes
Moluscs		eukaryotes
H. sapiens		eukaryotes
Maize		eukaryotes
Salamander		eukaryotes
Mammals		eukaryotes
Nematodes		eukaryotes
Flowering Plants		eukaryotes
Fungi		eukaryotes

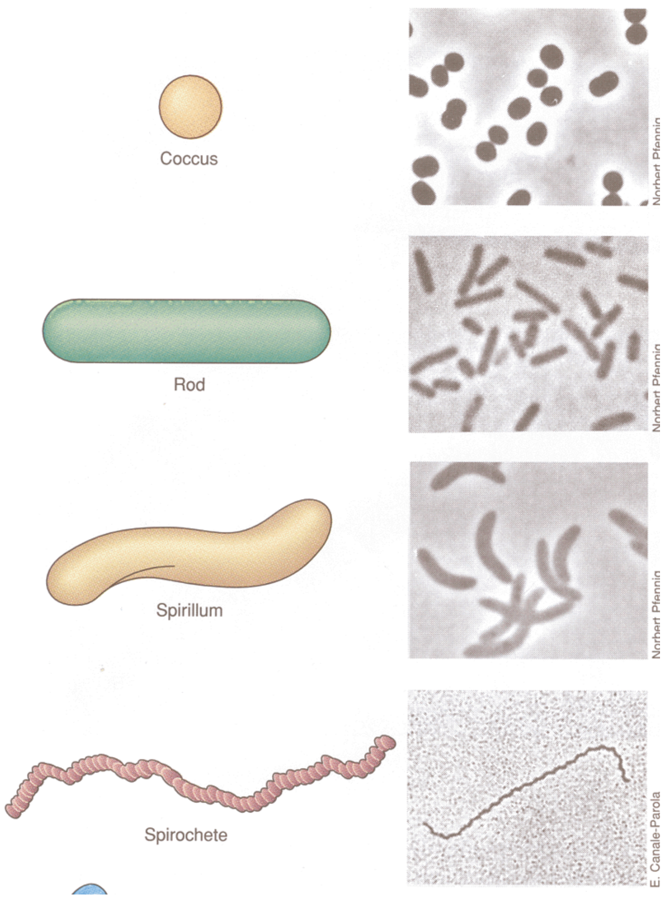
How Big Is Big? (cont.)

Species	Size			Domain
M. janaschii			1,700,000	archaea
E. Coli			4,000,000	bacteria
Yeast			20,000,000	eukaryotes
Fruit fly			165,000,000	eukaryotes
Fungi	9,400,000	to	175,000,000	eukaryotes
Nematodes	75,000,000	to	620,000,000	eukaryotes
H. sapiens			3,000,000,000	eukaryotes
Fern	600,000,000	to	4,050,000,000	eukaryotes
Moluscs	375,000,000	to	5,100,000,000	eukaryotes
Mammals	2,350,000,000	to	5,550,000,000	eukaryotes
Fish	650,000,000	to	6,950,000,000	eukaryotes
Insects	47,000,000	to	12,000,000,000	eukaryotes
Maize			15,000,000,000	eukaryotes
Wheat			18,000,000,000	eukaryotes
Salamander			90,000,000,000	eukaryotes
Flower Plants	5,000,000	to	120,000,000,000	eukaryotes

Example Prokaryotic Cell



Prokaryotic Cell Shape



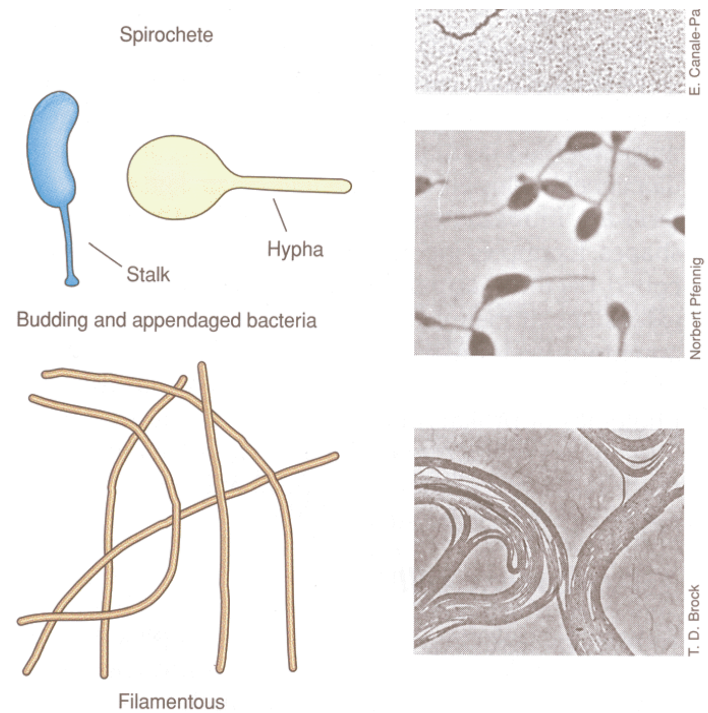


Figure 3.9 Representative cell shapes (morphology) in prokaryotes. Next to each drawing is a phase photomicrograph showing an example of that morphology. Organisms are coccus, *Thiocapsa roseopersicina* (diameter of a single cell = 1.5 µm); rod, *Desulfuromonas acetoxidans* (diameter = 1 µm); spirillum, *Rhodospirillum rubrum* (diameter = 1 µm); spirochete, *Spirochaeta stenostrepta* (diameter = 0.25 µm); budding and appendaged, *Rhodomicrobium vannielii* (diameter = 1.2 µm); filamentous, *Chloroflexus aurantiacus* (diameter = 0.8 µm)

All Sorts Of Variations

Organism	Linear Chromosome	Circular Chromosome	Linear Plasmid	Circular Plasmid
Agrobacterium tumefaciens C58	1	1		2
Bacillus cereus F0836 76		1		1
Brucelia melitensis		2		
Leptospira interrogans		1		1
Rhizobium meliloti		1		2
Rhodobacter sphaeroides		2		
Rhodococcus facians	1		1	
Streptomyces ambofaciens	1			
Streptomyces lividans 66	1		>1	
S. cerevisiae	16			
D. melanogaster	4			
H. Sapiens	23			
Maize	10			
Salamander	12			