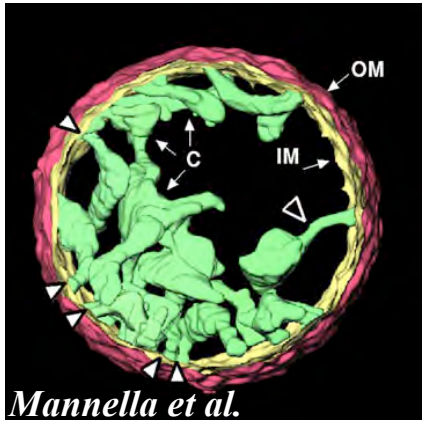
Lecture 1: The Size of Things - A Feelin For the Numbers

Quantitative Models of Biological Function

Sizing up Cells

Structure and Function of Organ



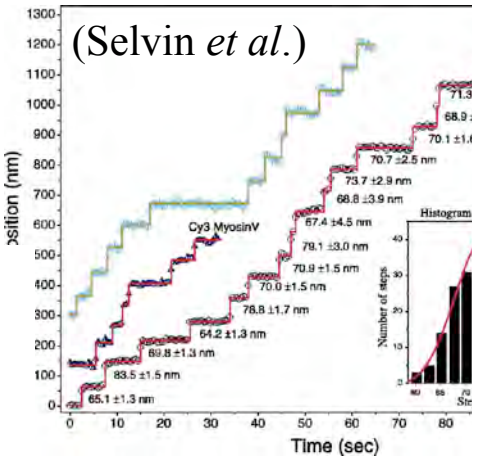
APh/BE161: Physical Biology of the Cell

The Quantitative Imperative

Quantitative Data Demands Quantitative Models and Quantitative Models Demand Quantitative Experimentation

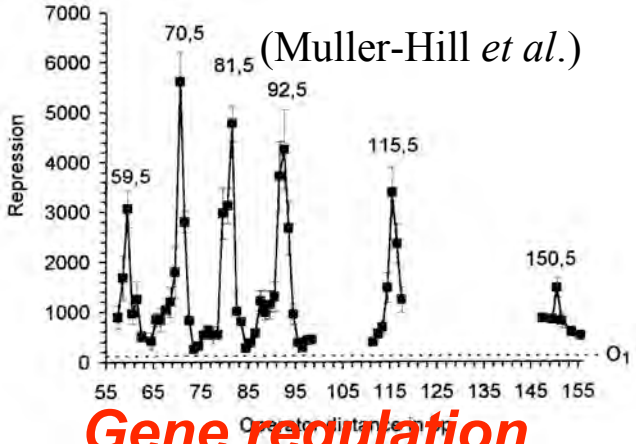
"I often say that when you can measure what you are speaking about, and express it in numbers, you know something about it; but when you cannot express it in numbers, your knowledge is of a meagre and unsatisfactory kind; it may be the beginning of knowledge, but you have scarcely, in your thoughts, advanced to the stage of Science, whatever the matter may be."
Lord Kelvin

(Selvin *et al.*)



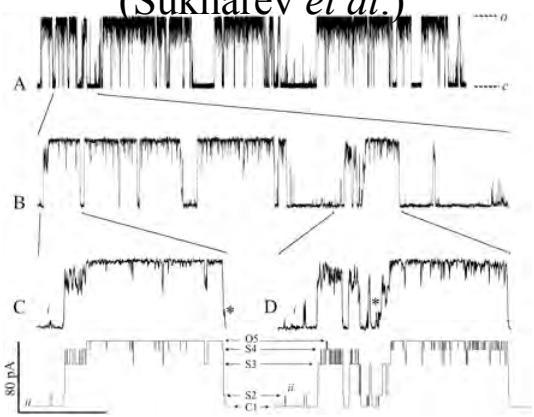
Motor dynam

(Muller-Hill *et al.*)



Gene regulation

(Sukharev *et al.*)



Ion channel dynamics

Prokaryotes and Eukaryotes

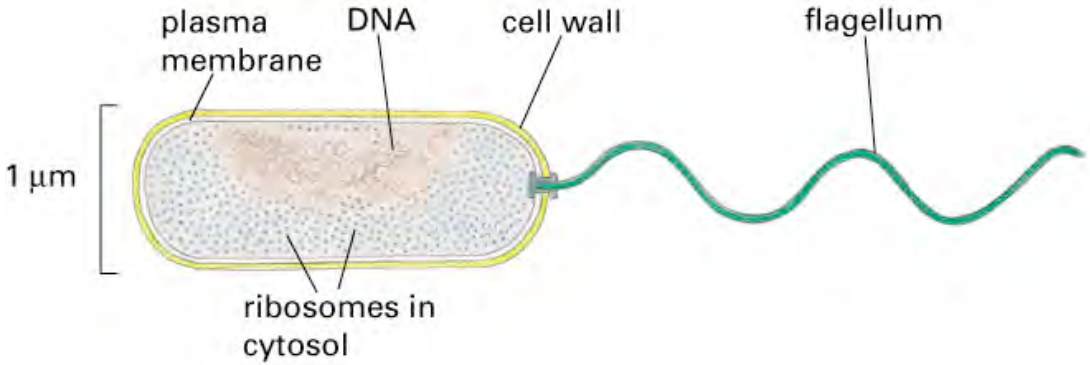
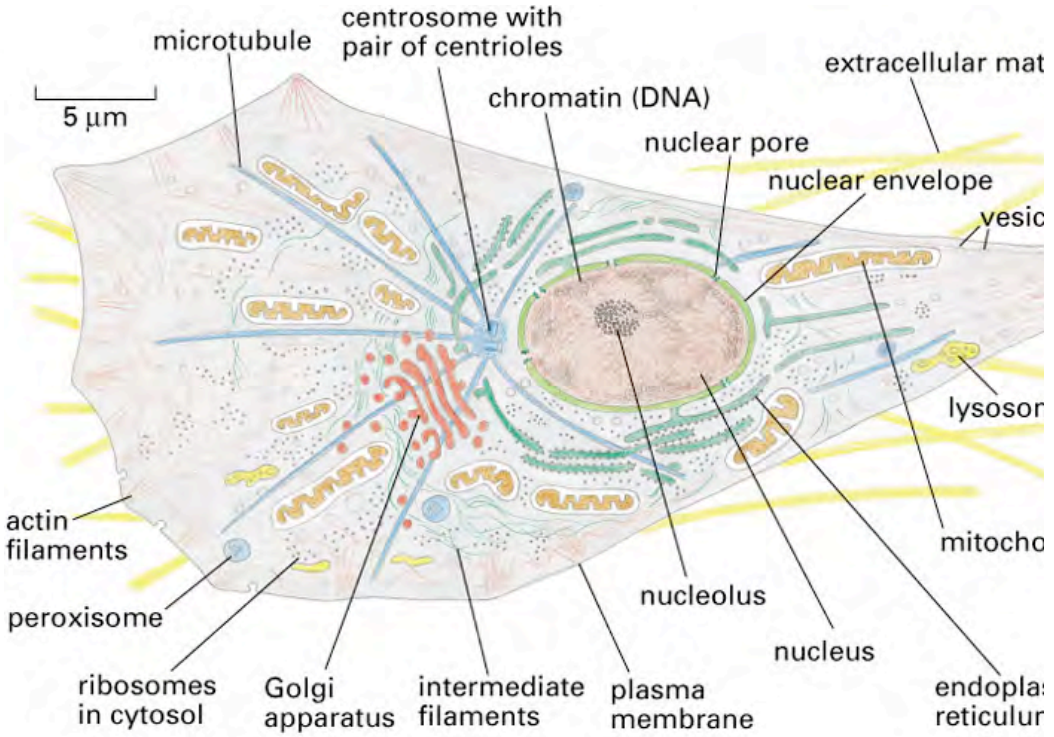


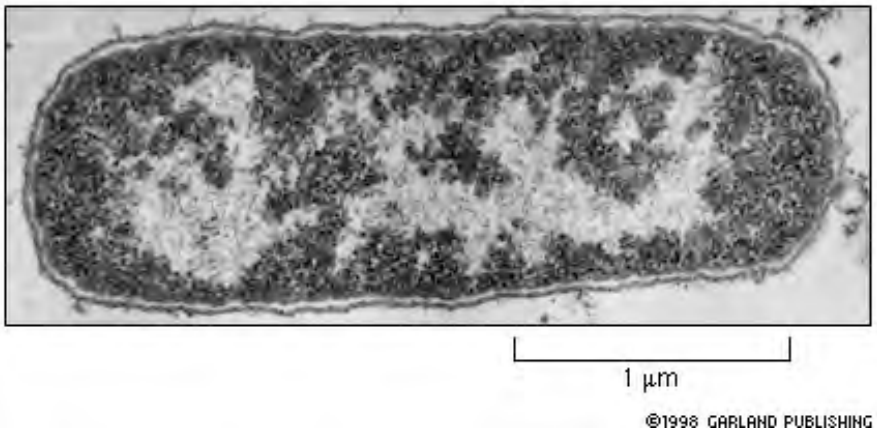
Figure 1–18 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

Shapes, sizes and contents of different types of cells.



The Standard Ruler: E. Coli

- ***The Standard Cell:*** ***"Not everyone is mindful of it, but cell biologists have two cells of interest; the one they are studying and Escherichia coli." – Schaechter et al.***
- ***Cells: There is nothing smaller that is alive, nothing bigger is more alive – paraphrasing J. Theriot.***



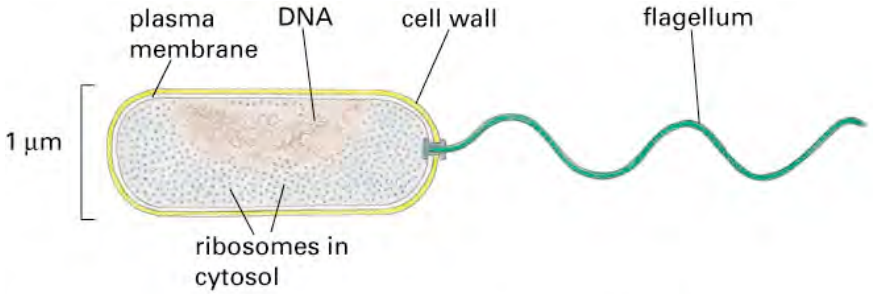


Figure 1–18 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

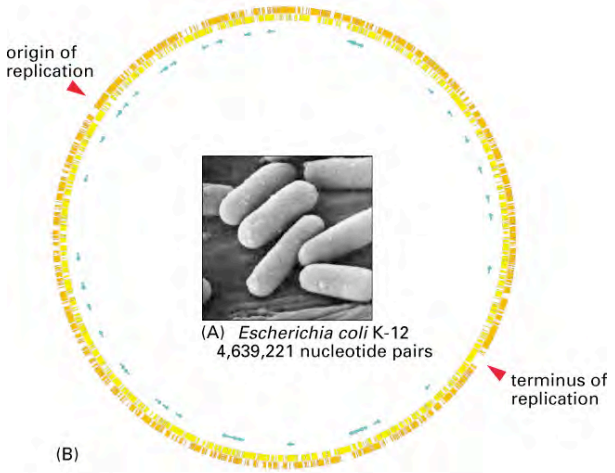


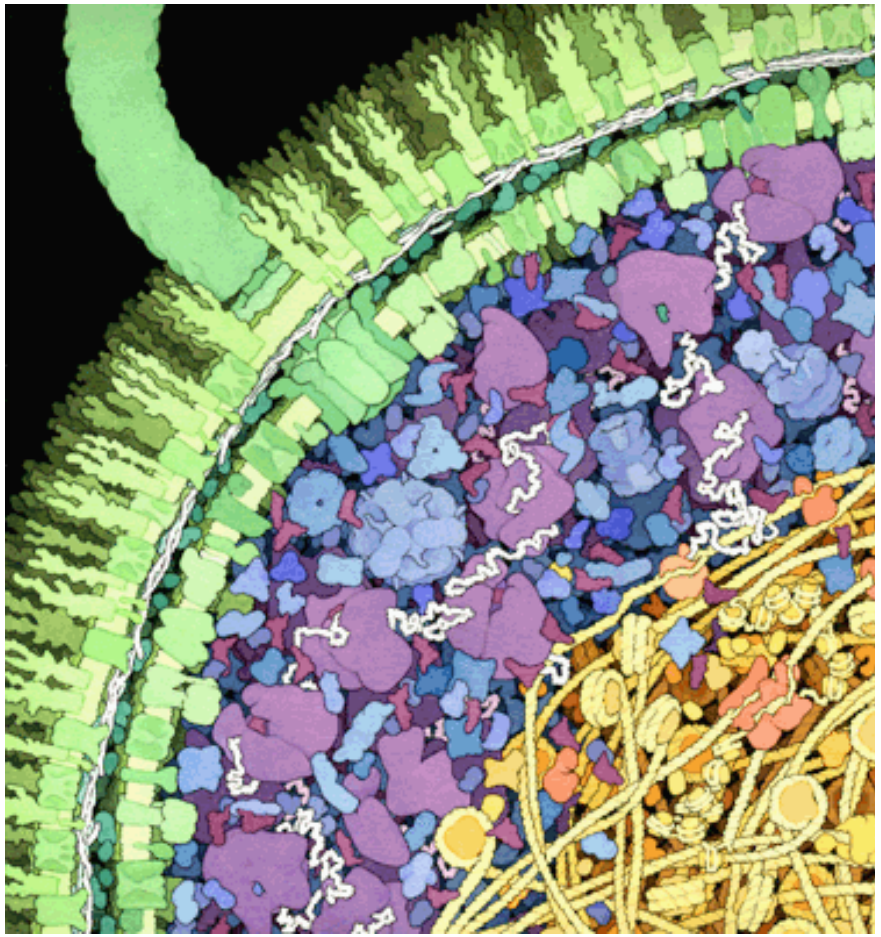
Figure 1–30. Molecular Biology of the Cell, 4th Edition.

What's Inside of a Cell?

Main macromolecular constituents of *E. coli* and HeLa cells

Component	Amount per HeLa cell	Amount per *E. coli* cell
Total dry weight	400 pg	0.4 pg
Total DNA	15 pg	0.017 pg
Total RNA	30 pg	0.10 pg
Total protein	300 pg	0.2 pg
Cytoplasmic ribosomes	4×10^6	3×10^4
Cytoplasmic tRNAs	6×10^7	4×10^5
Cytoplasmic mRNAs	7×10^5	4×10^3

source: Lodish et al., Molecular Cell Biology 3rd ed.

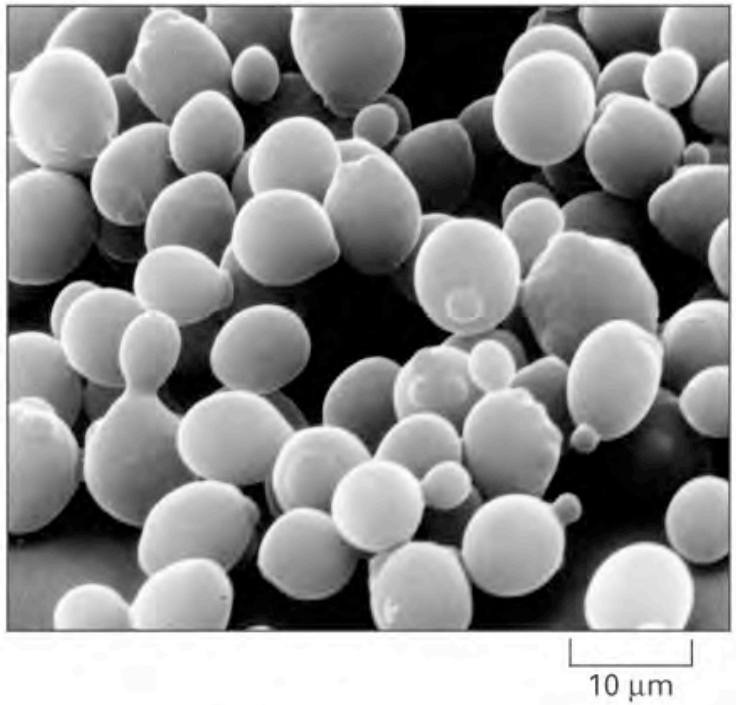


Composition of an *E. coli* cell

Component	Molecules per cell	Kinds of molecules
Protein	2,360,000	1050
RNA		
r R N A	56,100	3
tRNA	205,000	60
mRNA	1,380	400
Lipid	22,000,000	4 major
Lipopolysaccharide	1,200,000	1
Metabolites, cofactors, ions	> 400,000,000	800+

source: Moran et al., Biochemistry 2nd ed.

The Standard Eukaryote: S. cerevisiae



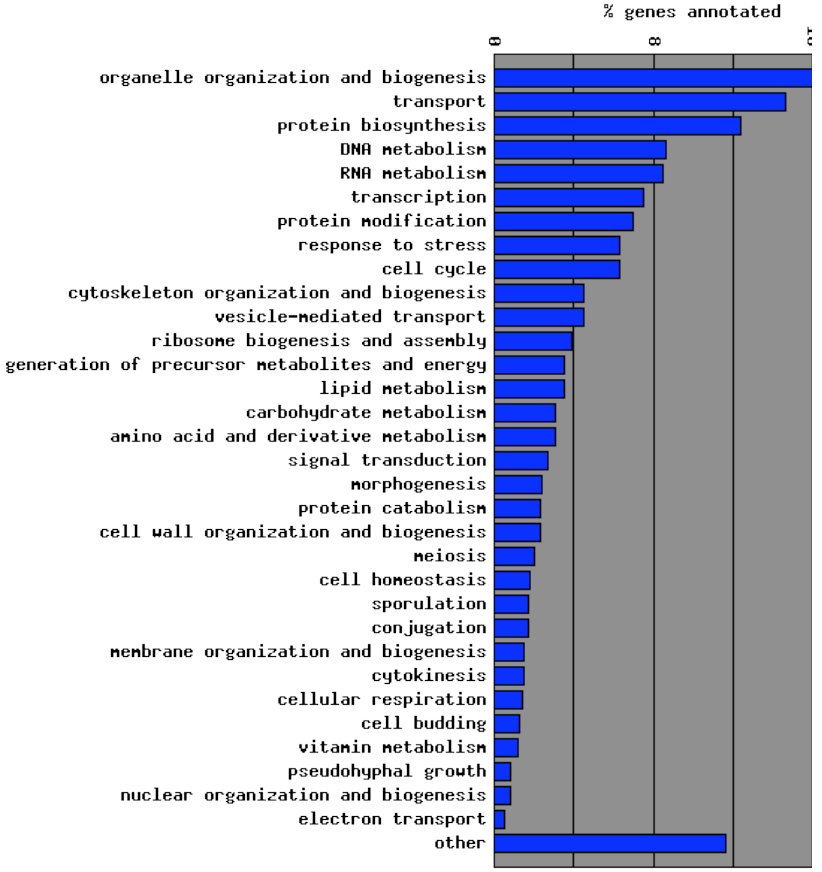
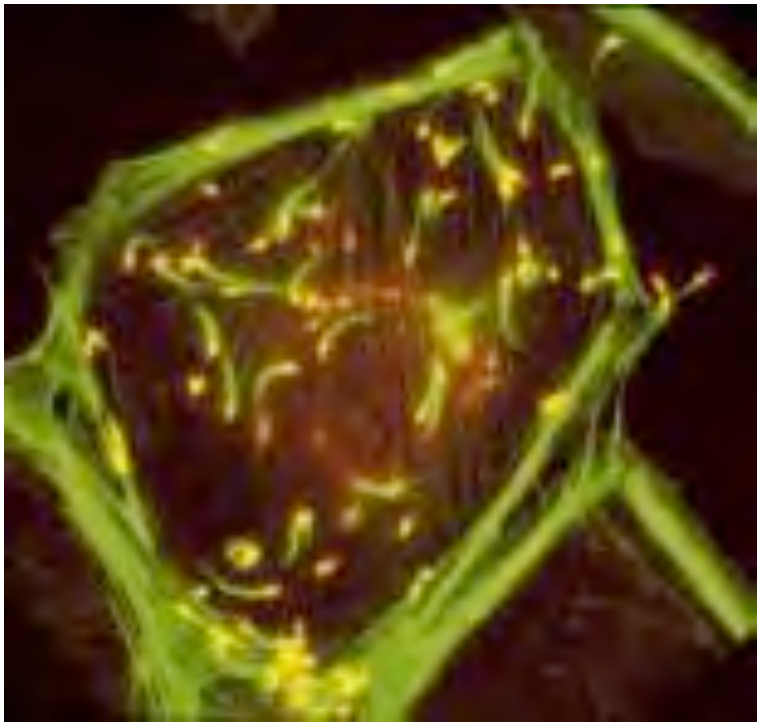


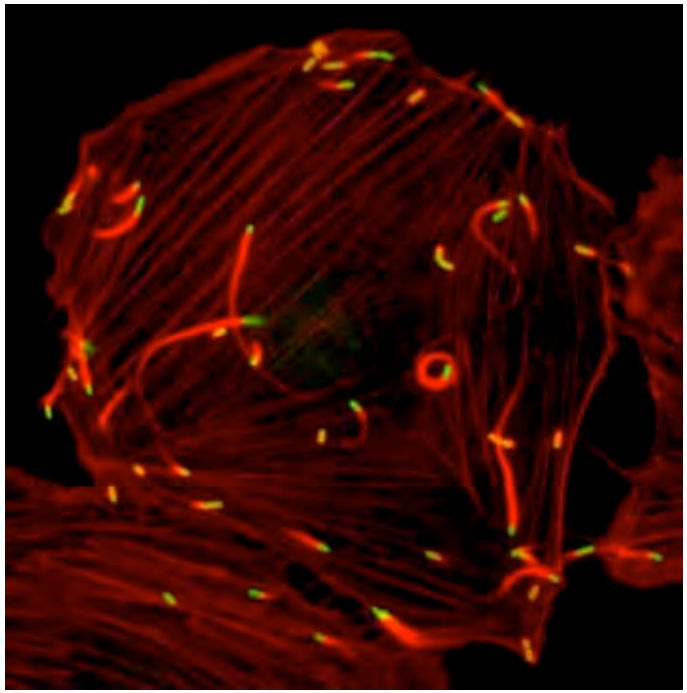
Figure 1-32 Essential Cell Biology, 2/e. (© 2004 Garland Science)

Other Hall of Fame Cells: Prokaryotes

http://www.molbio.princeton.edu/labs/newton/A.gif

Other Hall of Fame Cells: Prokaryote - Listeria monocytogenes



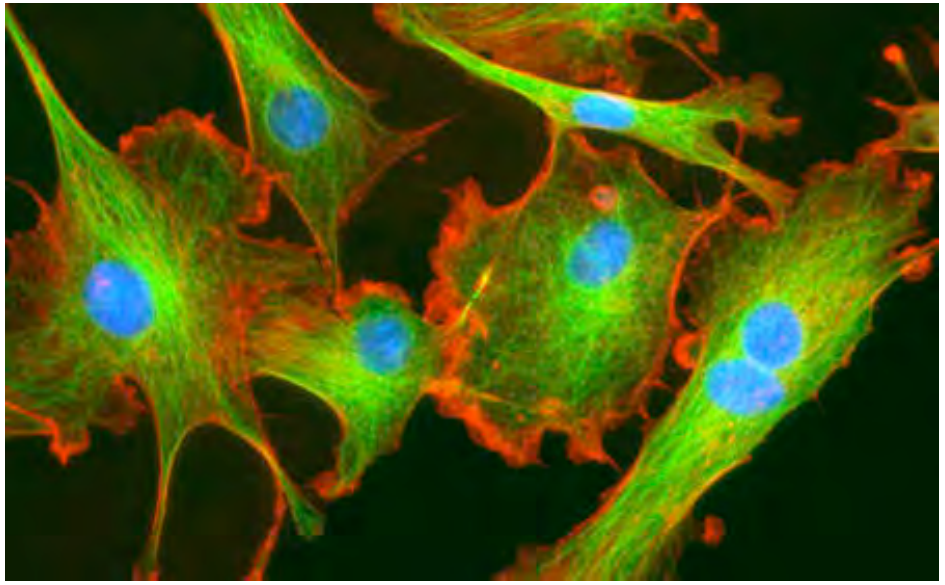


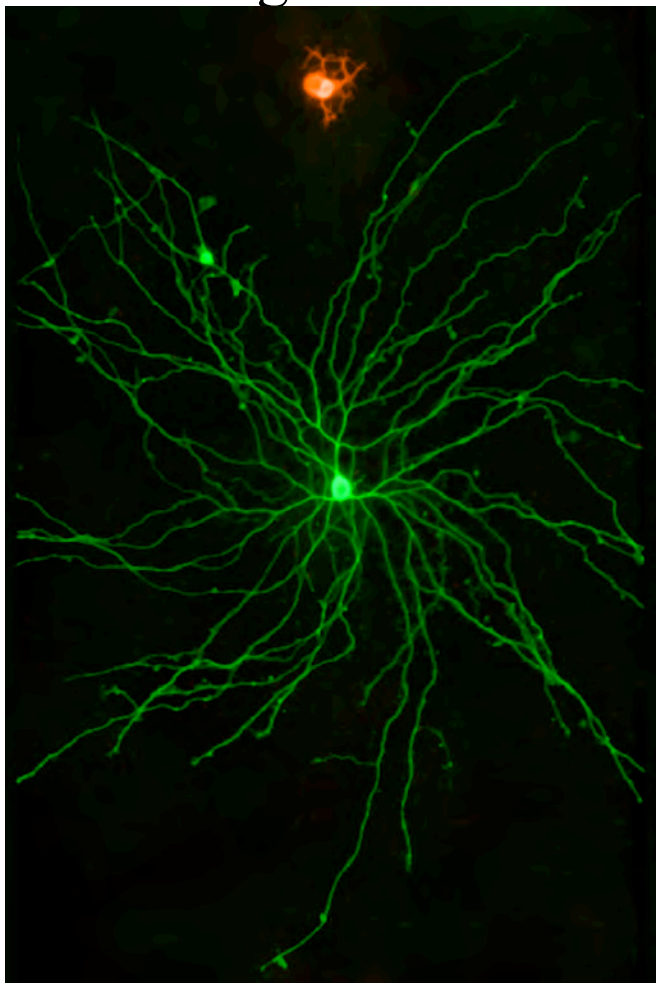
Theriot Lab - Stanford University, see their amazing movies

Other Hall of Fame Cells: Eukaryotes

http://www.utah.edu/unews/news_images/070101_nerv

Structure and function intimately related



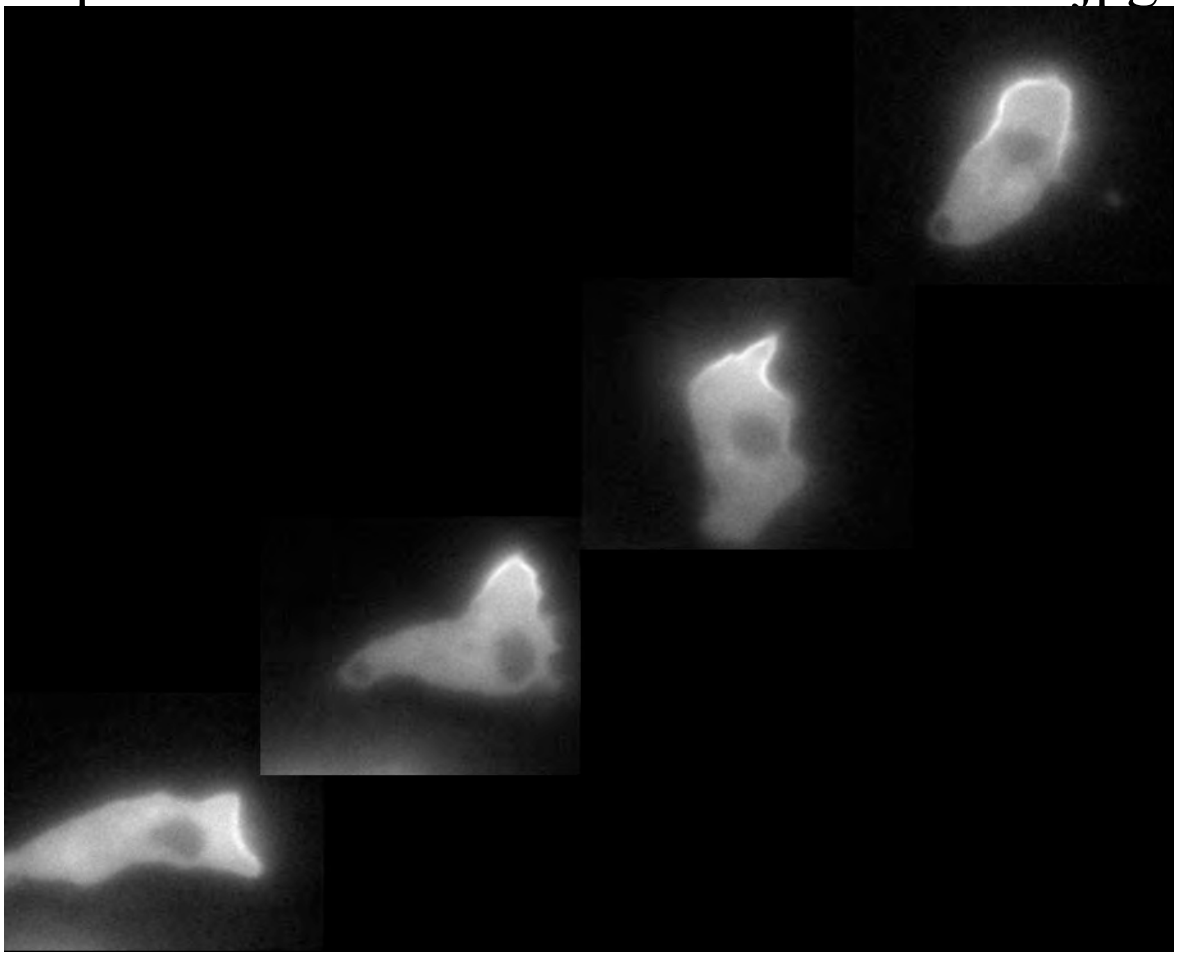


Annoying feature: no scale bars!

http://www.cimaging.net/Examples/D1_Cells/FAC1_Protein/Fibroblast/fibroblast.html

Other Hall of Fame Cells: Eukaryotes

http://web.mit.edu/azadeh/www/Picture5.jpg

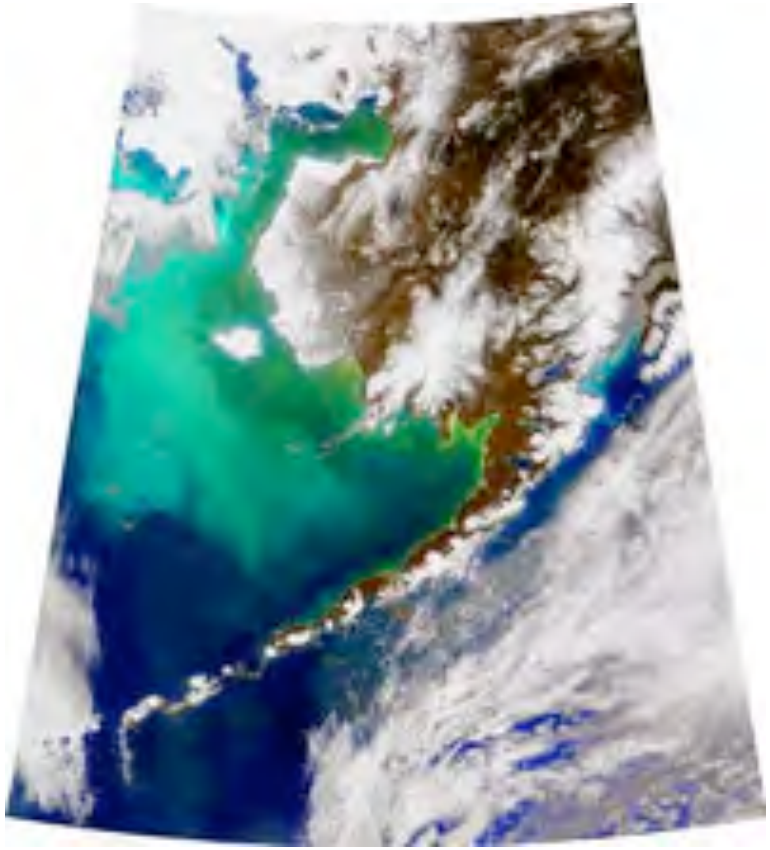


Annoying feature: no scale bars!

Dictyostelium discoideum - amoeba with cool lifesty

Other Hall of Fame Cells: Eukaryotes

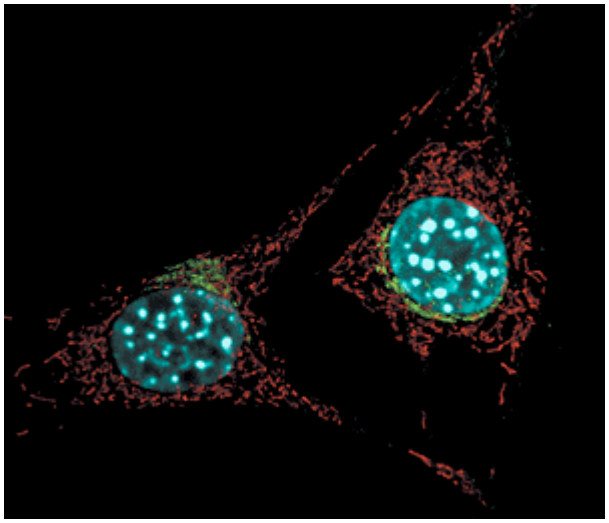
http://www.exn.ca/Stories/1998/09/21/58.asphttp://www.exn.ca/Stories/1998/09/21/58.asp

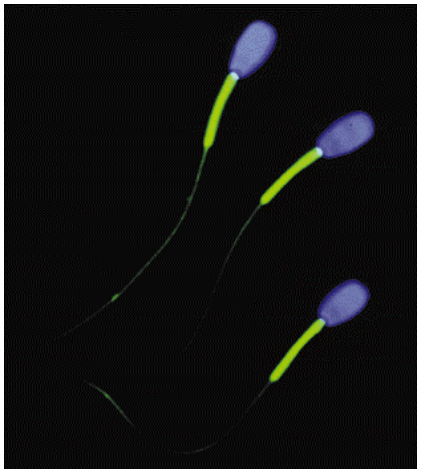


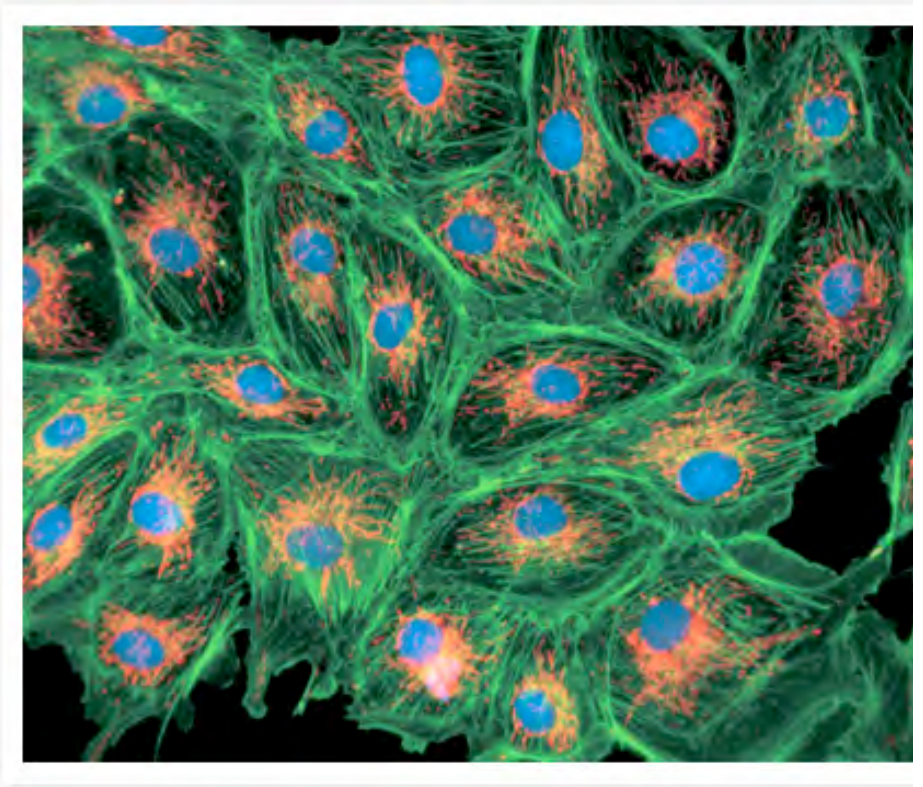
Emiliana huxleyi - coccolithophore

Experimental Transformation of Biology: Imaging Proteins in Live Cells

- *All figures taken from Molecular Probes gallery.*

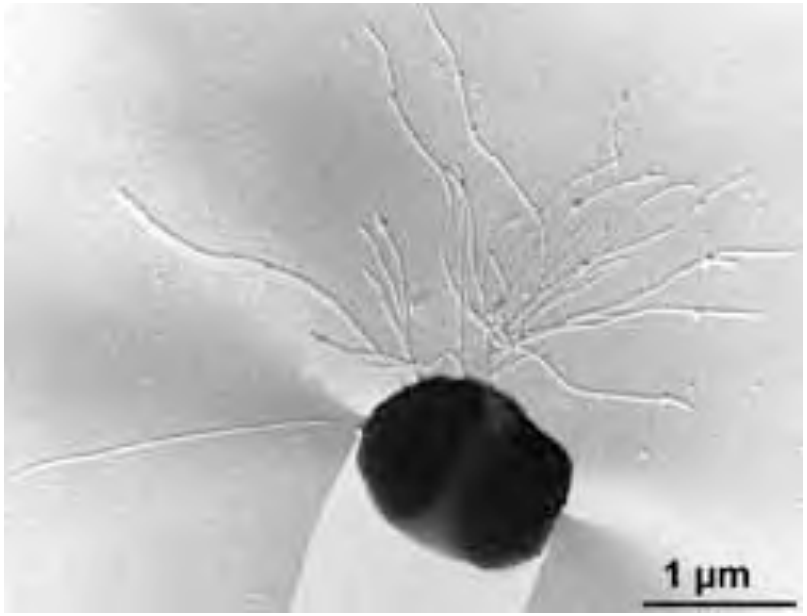


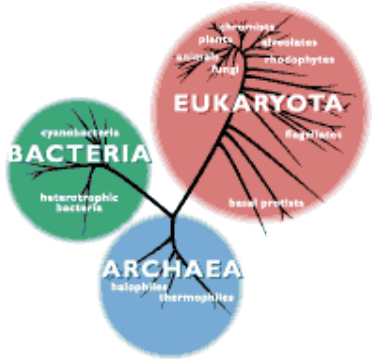




Annoying feature: no scale bars!

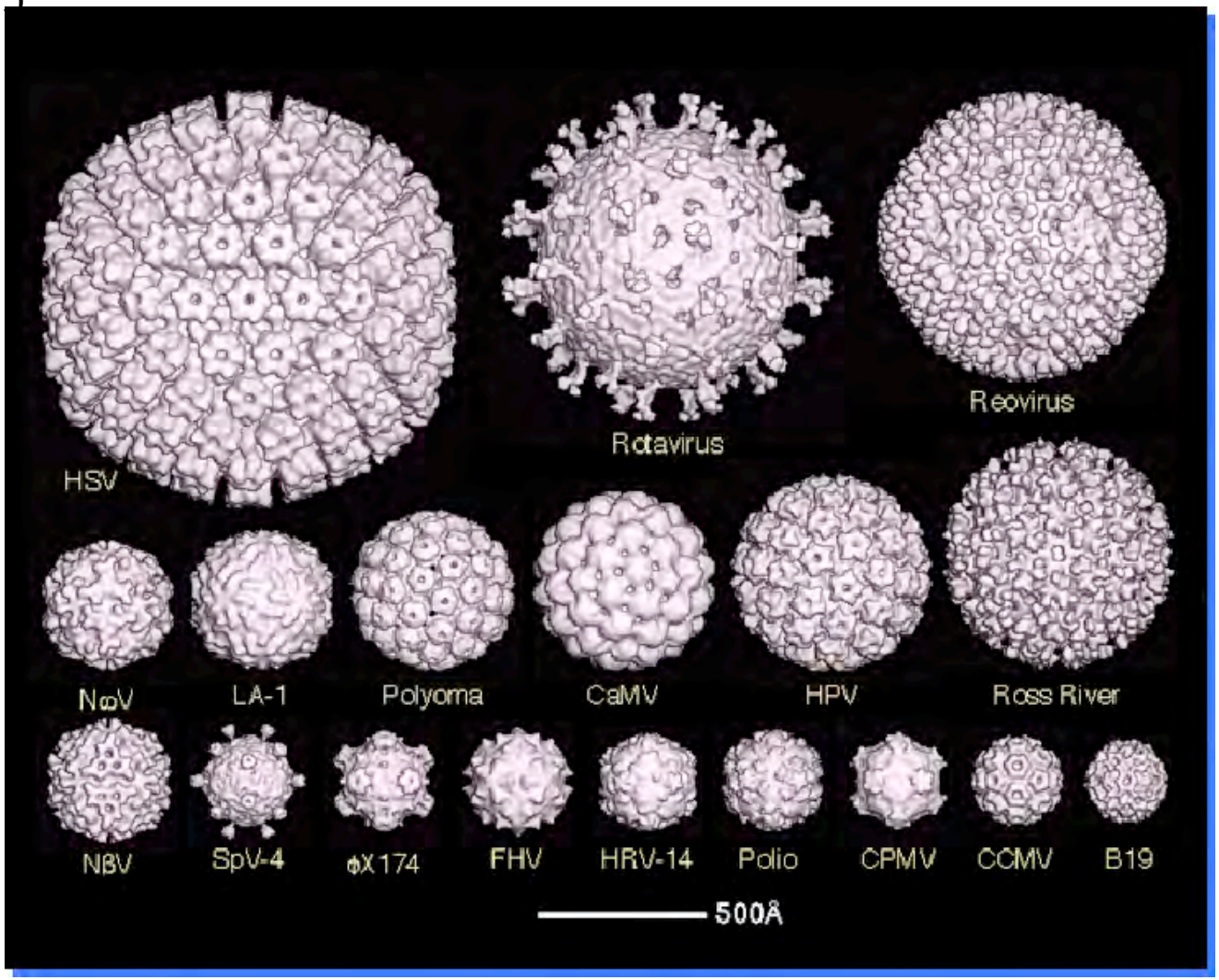
Other Hall of Fame Cells: Archaea





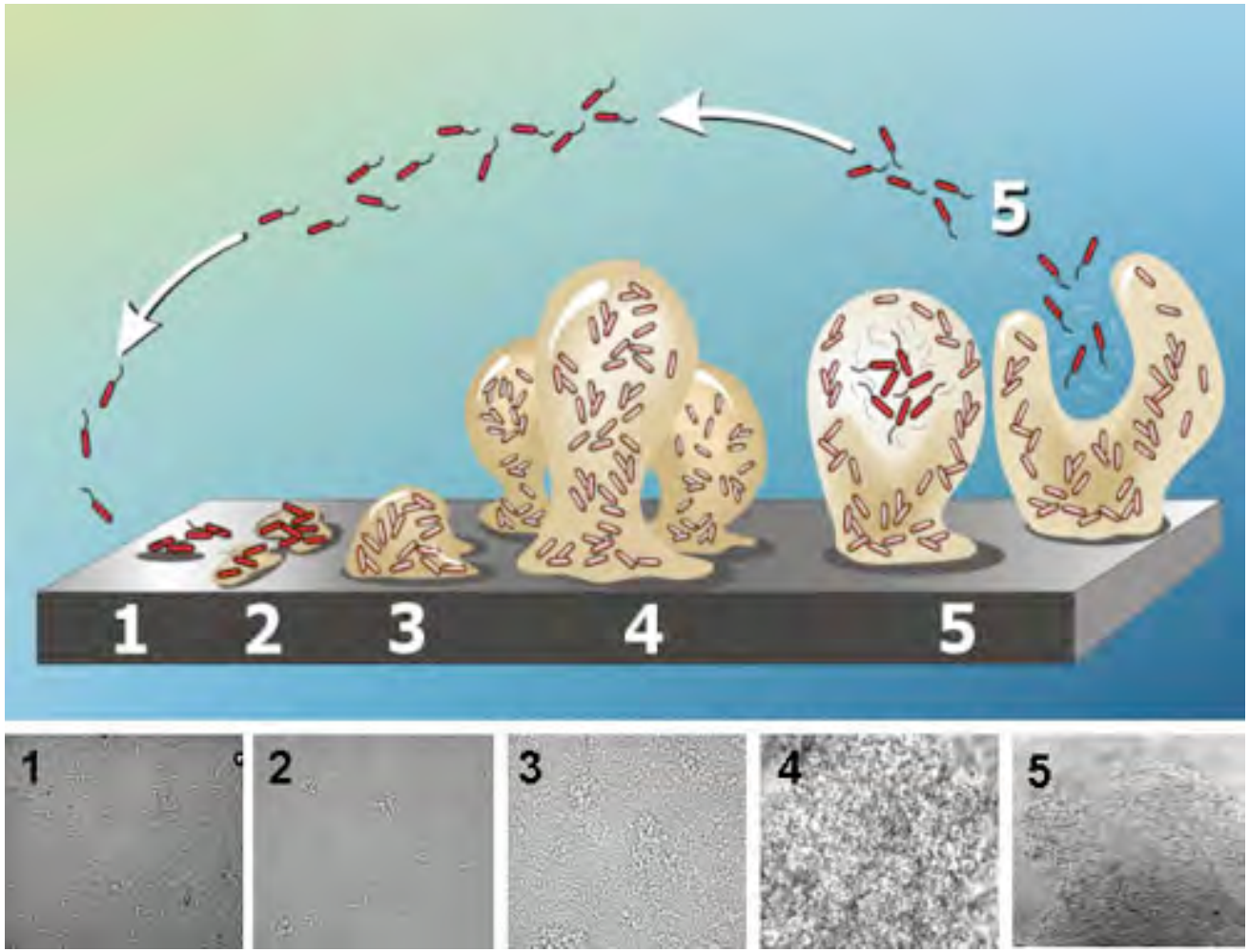
Structure of Viruses

(Baker *et al.*)

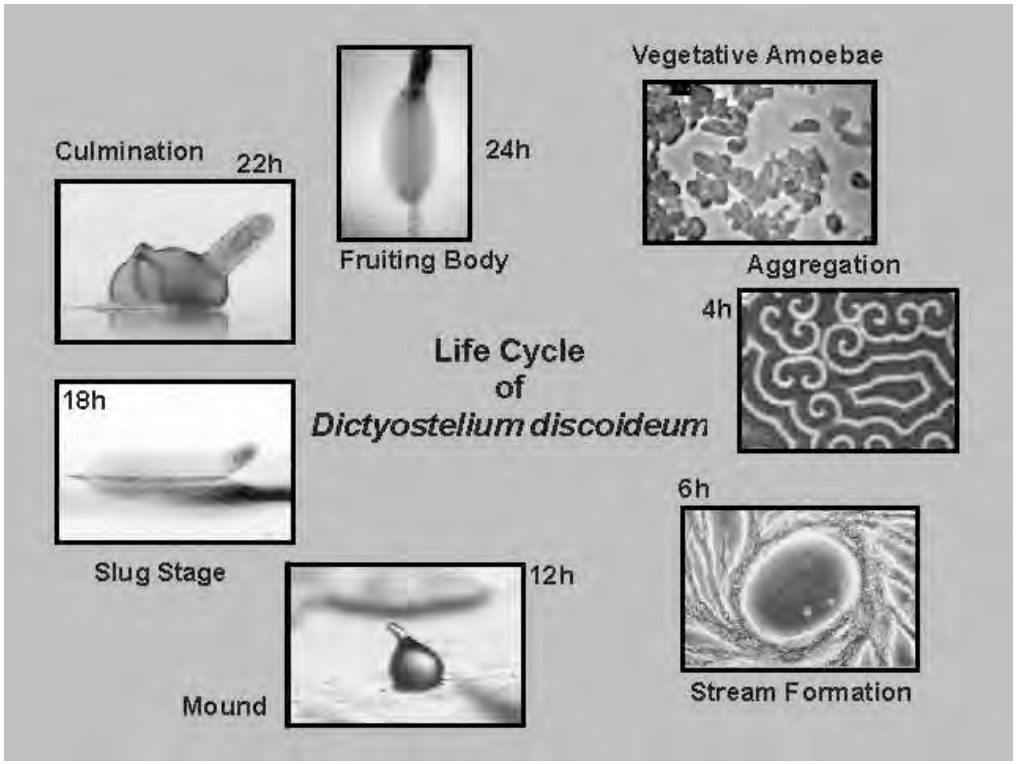


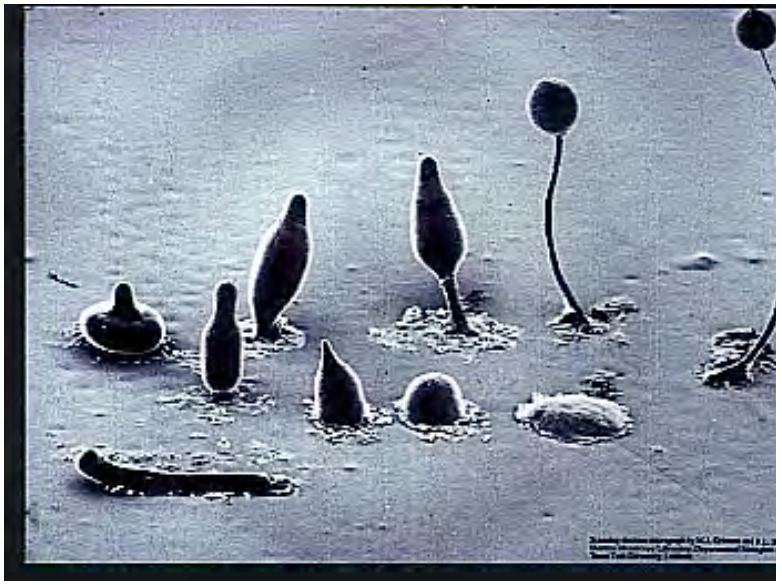
Collections of Cells - Biofilms

http://biology.binghamton.edu/davies/images/biofilm.jpg



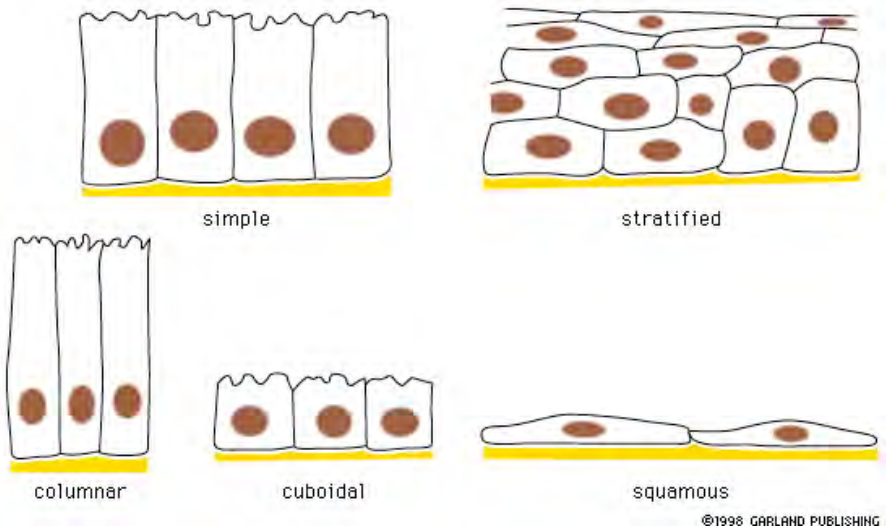
Collections of Cells - Sporulation

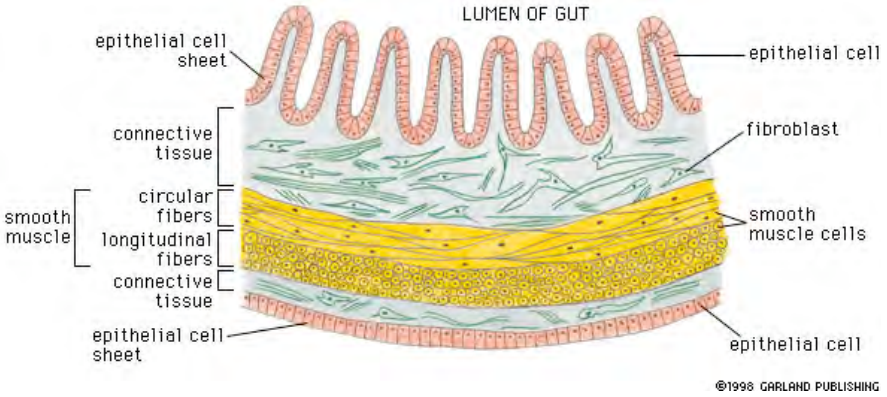


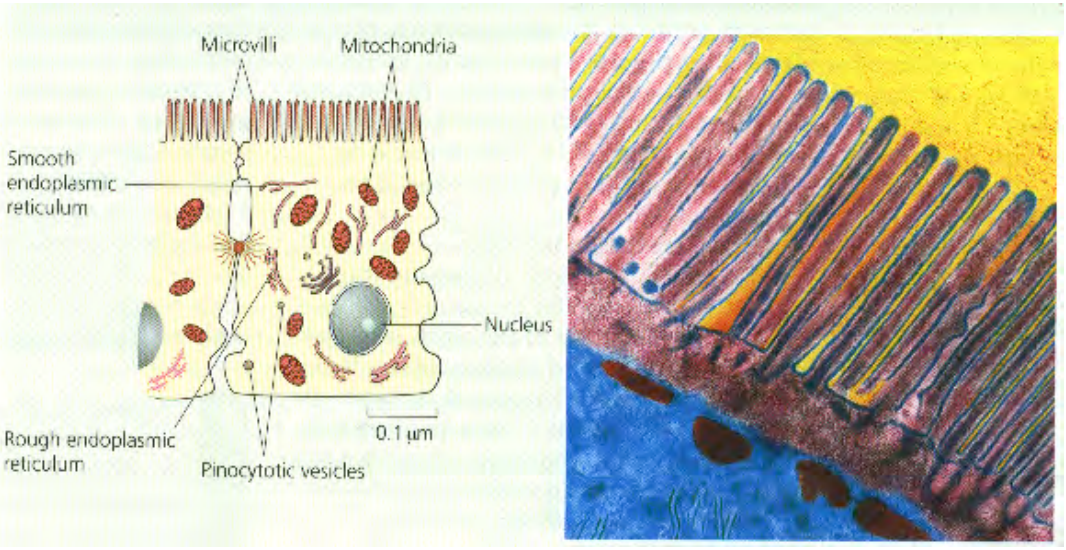


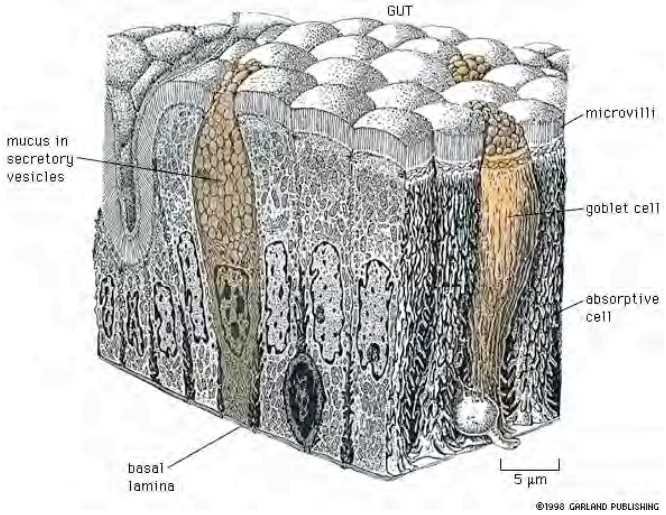
http://www.zi.biologie.uni-muenchen.de/zoologie/dicty/dicty.html

Collections of Cells - Tissues









C Elegans – a worm with 959 cells

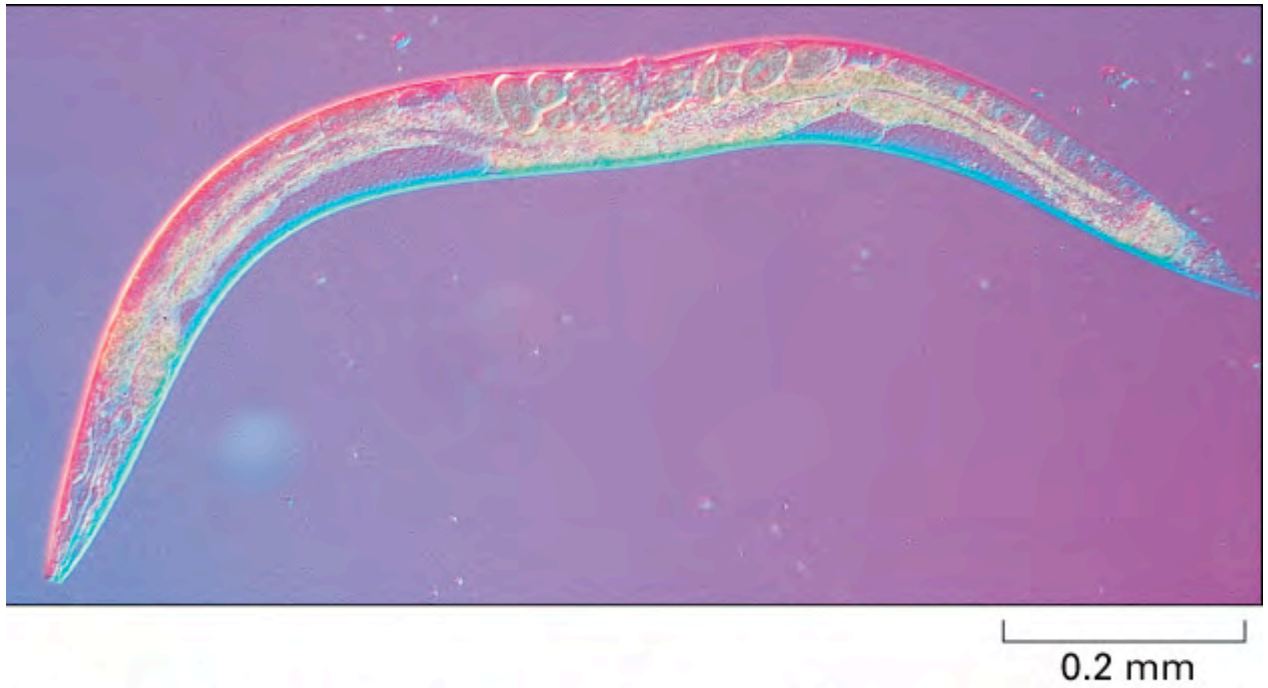
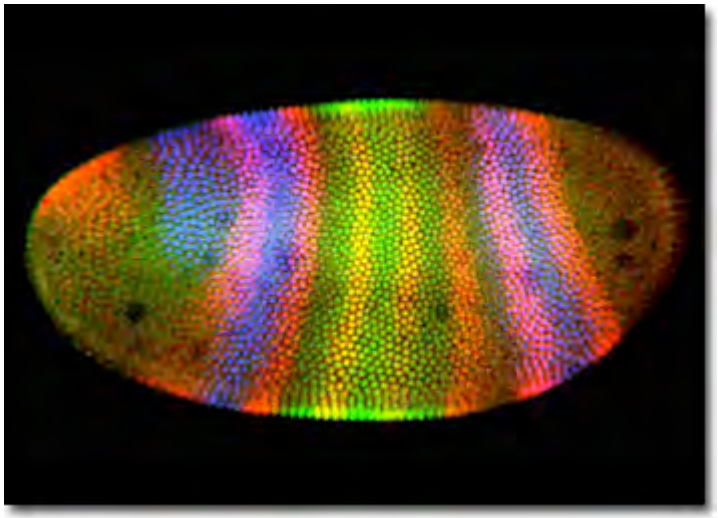


Figure 1–47. Molecular Biology of the Cell, 4th Edition.

Collections of Cells - Organisms



Featured above is a digital image of a triple-labeled ***Drosophila*** embryo at the cellular blastoderm stage. The specimen was immunofluorescently labeled with antibodies to the hairy protein in red, Kruppel in green, and giant in blue. This amazing image won the ***BioTechniques*** cover of the year award in 1993. From Stephen Paddock.

What's Inside of a Cell?

Main macromolecular constituents of *E. coli* and HeLa cells

Component	Amount per HeLa cell	Amount per *E. coli* cell
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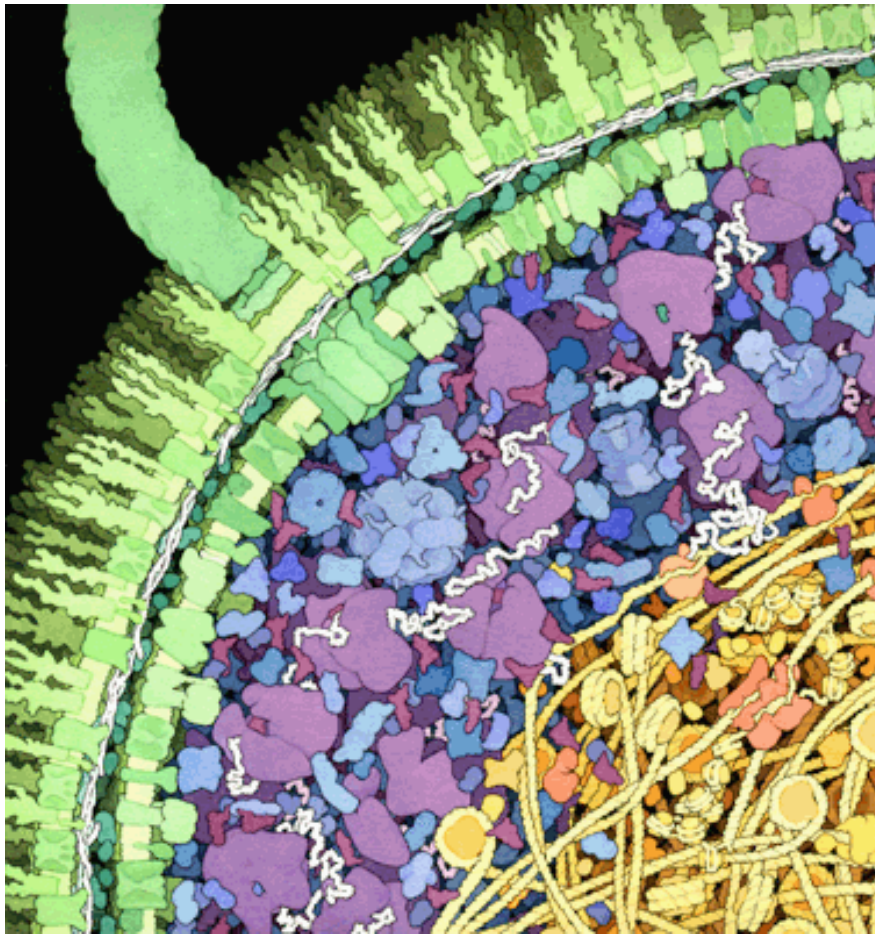
source: Lodish et al., Molecular Cell Biology 3rd ed.



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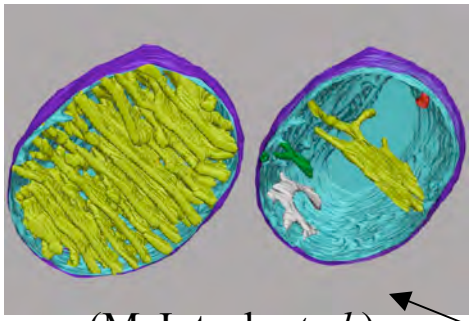
RNA		
r R N A	56,100	3
tRNA	205,000	60
mRNA	1,380	400
Lipid	22,000,000	4 major
Lipopolysaccharide	1,200,000	1
Metabolites, cofactors, ions	> 400,000,000	800+

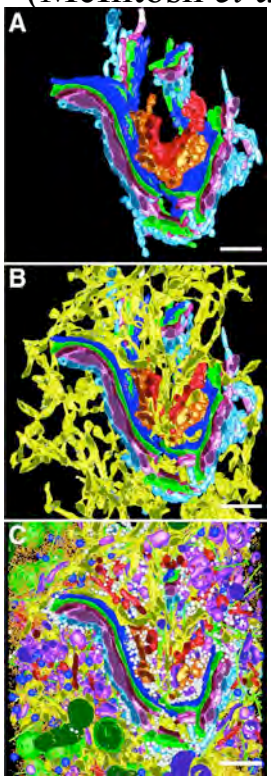
source: Moran et al., Biochemistry 2nd ed.

What Are Cells Made Of?

(Frey *et al.*)



(McIntosh *et al.*)



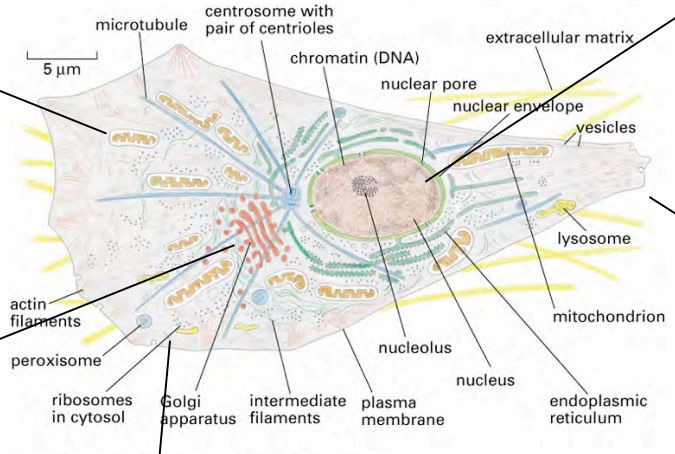
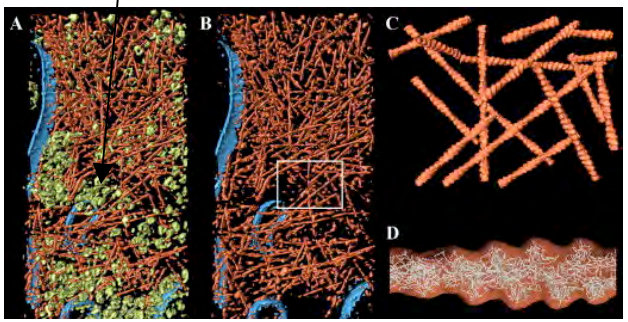
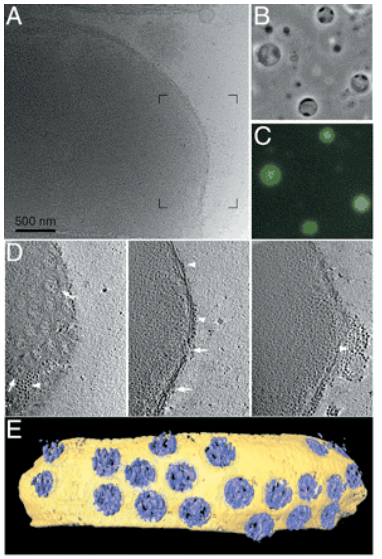
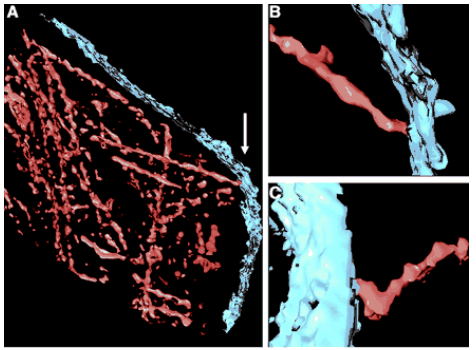


Figure 1–31. Molecular Biology of the Cell, 4th Edition.





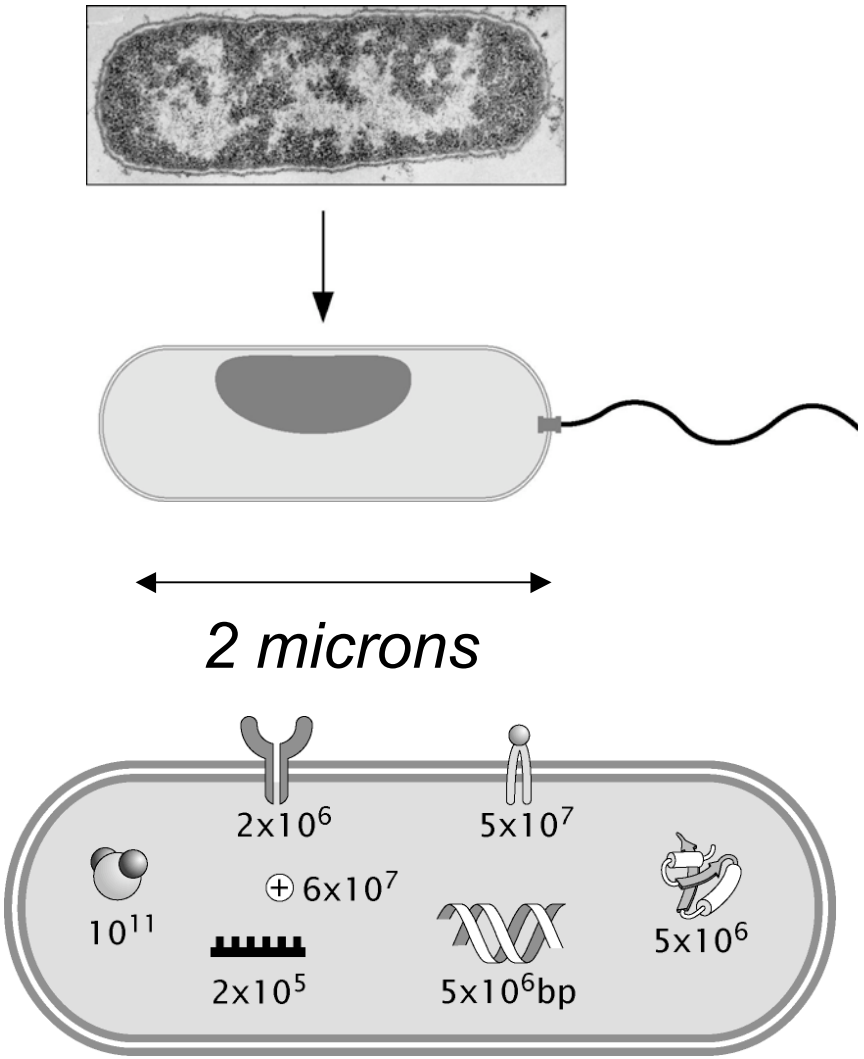
(Medalia *et al.*)



A Single Molecule Census of the Cell

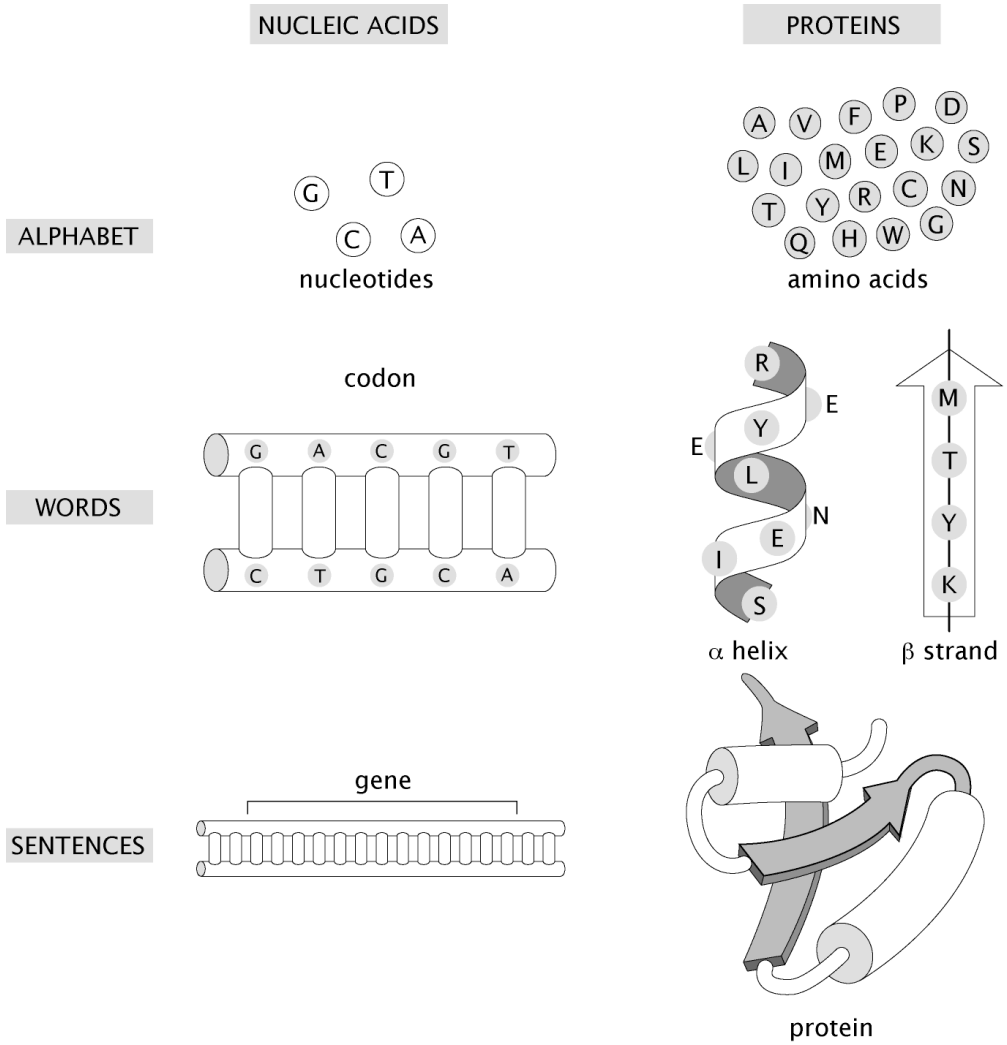
- ***The Standard Cell:*** ***"Not everyone is mindful of it, but cell biologists have two cells of interest; the one they are studying and Escherichia coli." – Schaechter et al.***
- ***20-40% of the protein stockpile consists of integral membrane proteins. An estimate: roughly 500 copies each of 1000 different membrane proteins. ½ of the cell surface area is dedicated to these proteins.***

Not a full census: ignored lipopolysaccharides, peptidoglycan, etc.. – that is fun too!

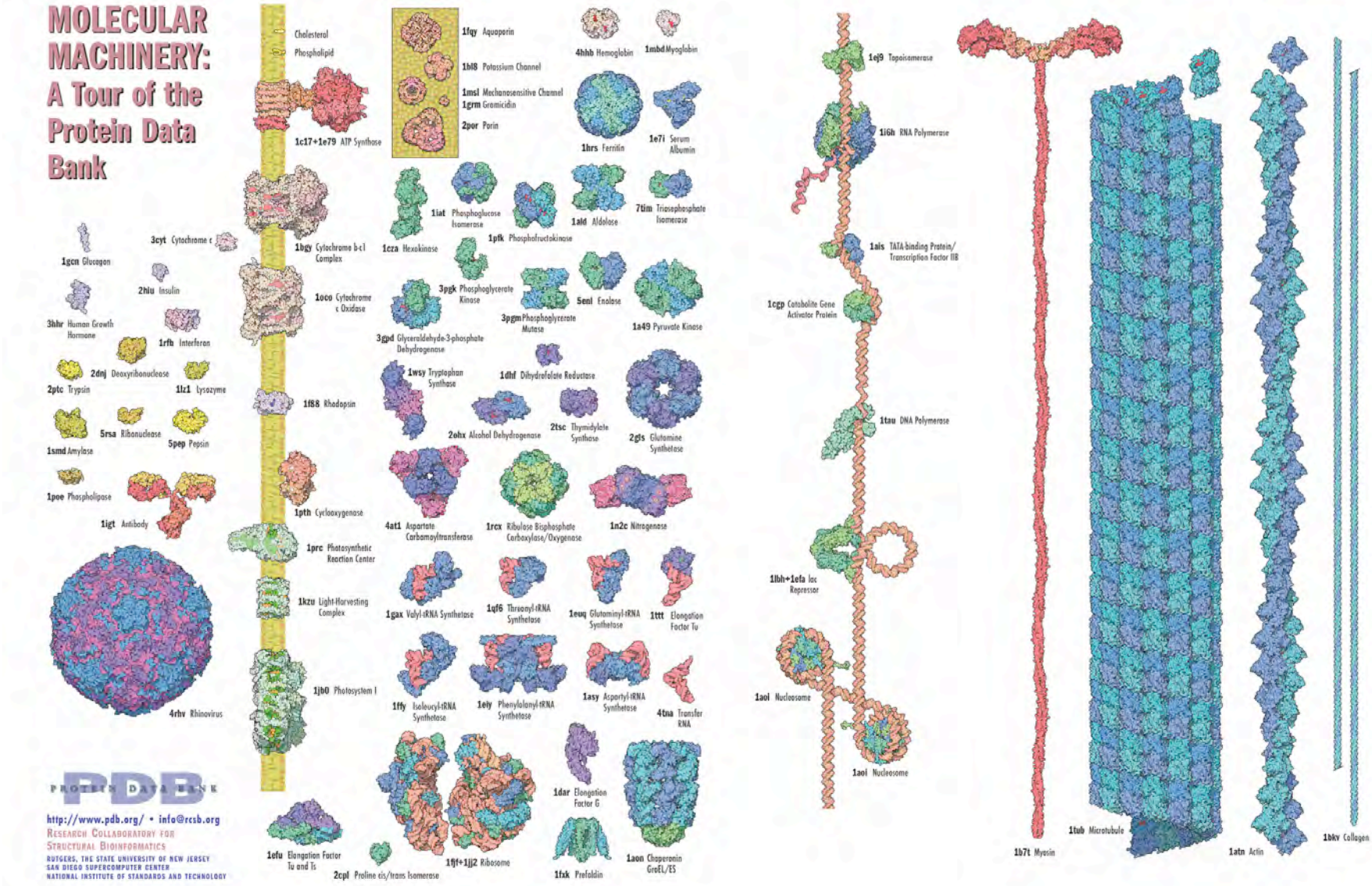


A Single Molecule Census of the Cell: The Parts List - Crick's Great Polymer Languages

Two great classes of biological polymers of the Central Dogma.



A Tour of Some of the Macromolecules of Life: Goodsell's Cartoons



A Single Molecule Census of the Cell: The Parts List

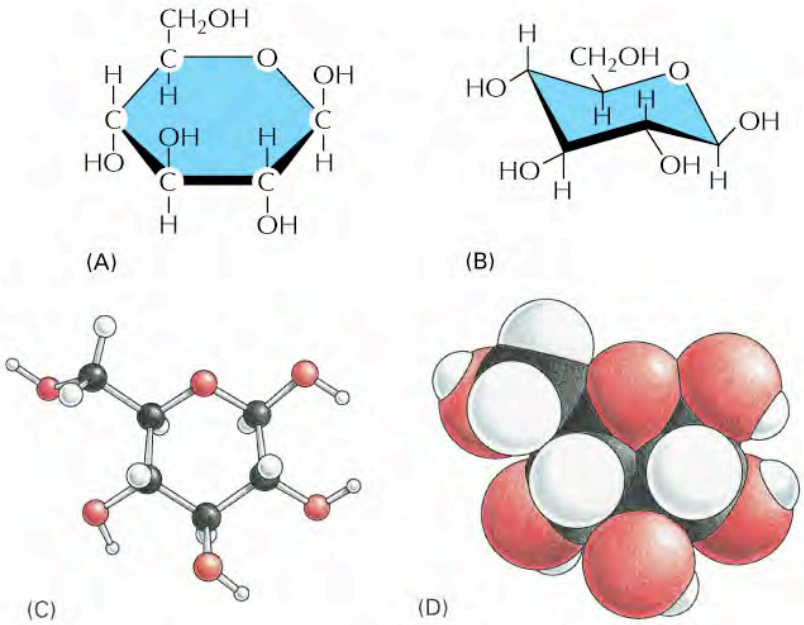


Figure 2.16 Essential Cell Biology, 2/e. (© 2004 Garland Science)

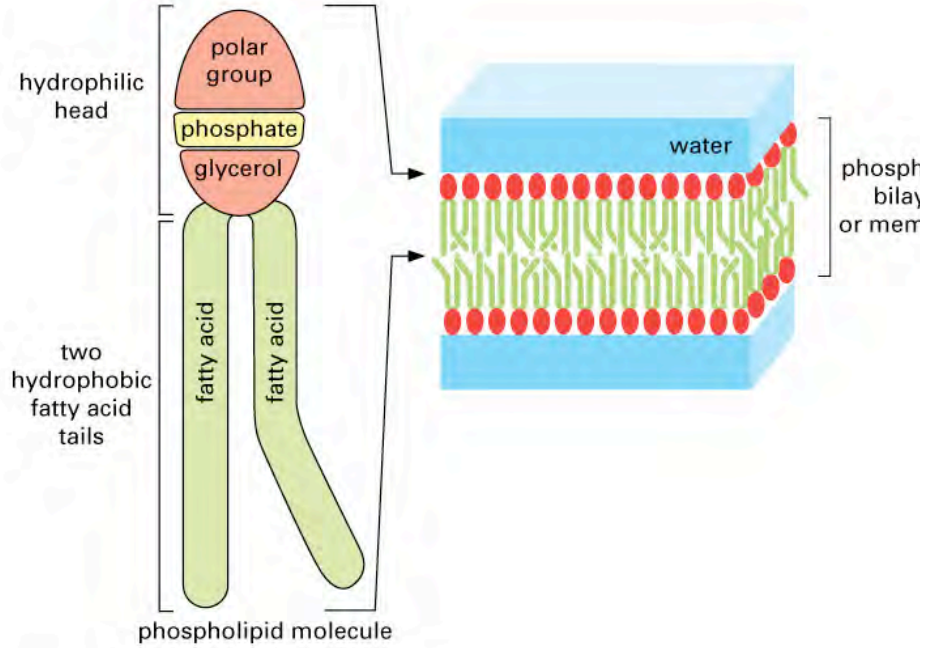
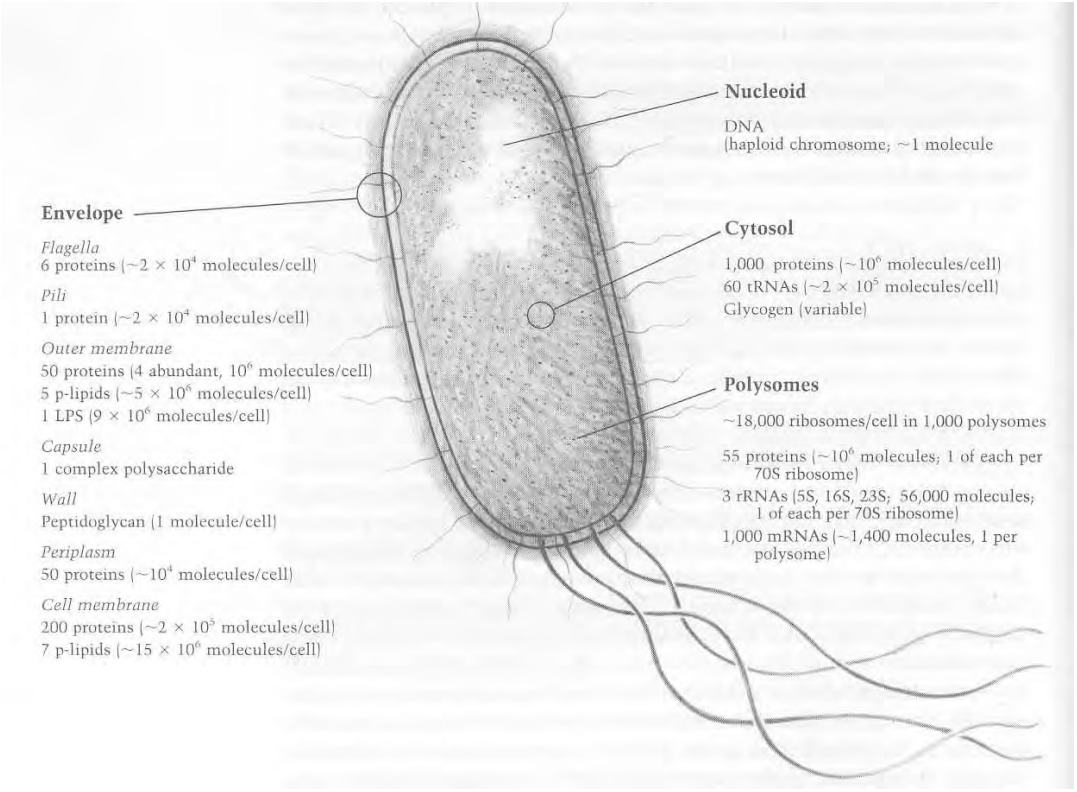
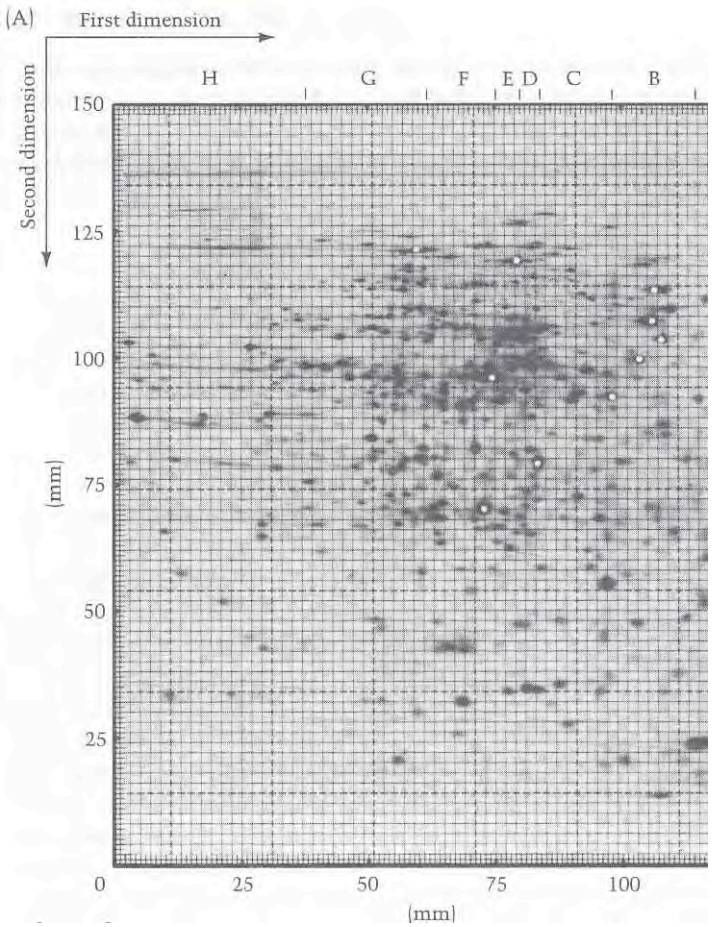


Figure 2-20 Essential Cell Biology, 2/e. (© 2004 Garland Science)

A Single Molecule Census of the Cell





A Single Molecule Census of the Cell: Part 2

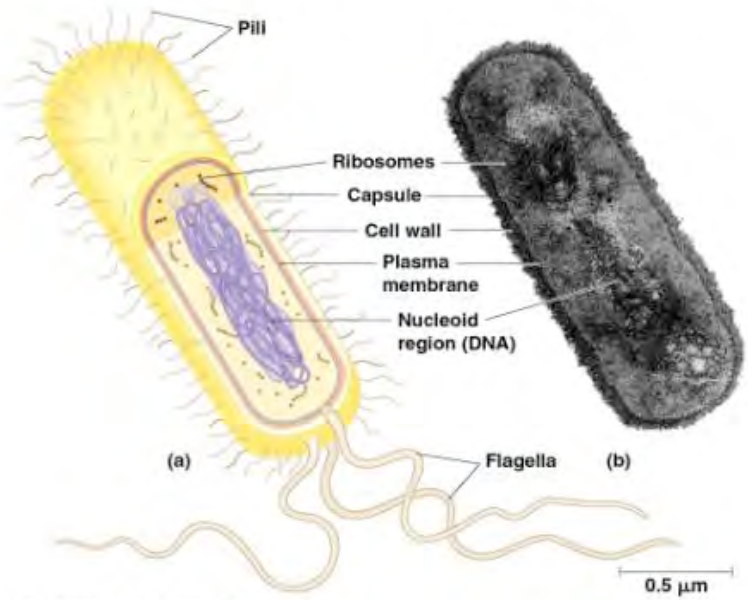


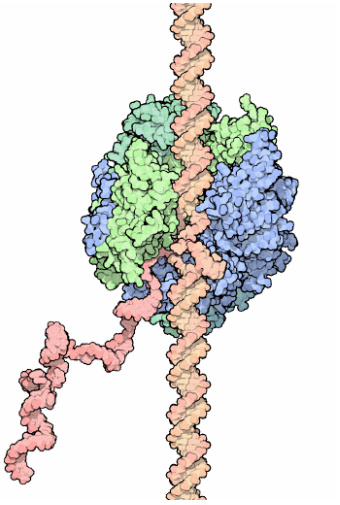
Table 1. Overall macromolecular composition of an average *E. coli* B/r cell[a]

Macromolecule	Percentage of total dry weight	Weight per cell (10^{15} × weight, grams)		Molecular weight	Number of molecules per cell	D ki m
Protein	55.0	155.0		4.0×10^4	2,360,000	1,
RNA	20.5	59.0				
23S rRNA			31.0	1.0×10^6	18,700	
16S rRNA			16.0	5.0×10^5	18,700	
5S rRNA			1.0	3.9×10^4	18,700	
transfer			8.6	2.5×10^4	205,000	
messenger			2.4	1.0×10^6	1,380	
DNA	3.1	9.0		2.5×10^9	2.13	
Lipid	9.1	26.0		705	22,000,000	
Lipopolysaccharide	3.4	10.0		4346	1,200,000	
Murein	2.5	7.0		$(904)_n$	1	
Glycogen	2.5	7.0		1.0×10^6	4,360	
Total macromolecules	96.1	273.0				
Soluble pool	2.9	8.0				
building blocks			7.0			
metabolites, vitamins			1.0			
Inorganic ions	1.0	3.0				
Total dry weight	100.0	284.0				
Total dry weight/cell		2.8×10^{-13}g				
Water (at 70% of cell)		6.7×10^{-13}g				
Total weight of one cell		9.5×10^{-13}g				

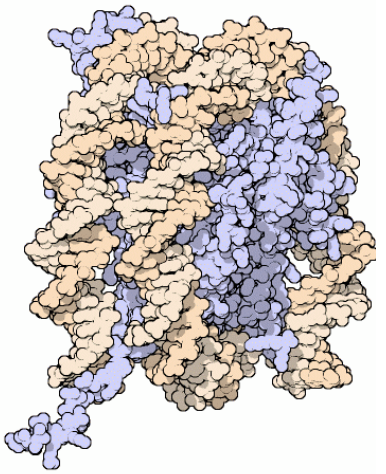
[a]In balanced growth at 37°C in glucose minimal medium, mass doubling time, *g*, of 40 minutes. The assembled from Dennis and Bremer (1974), Maaløe (1979), F. C. Neidhardt (unpublished), Roberts et a and Umbarger (1977).
[b]There are four classes of phospholipids, each of which exists in many varieties as a result of variable f residues.

PDB Structures and PDB Files

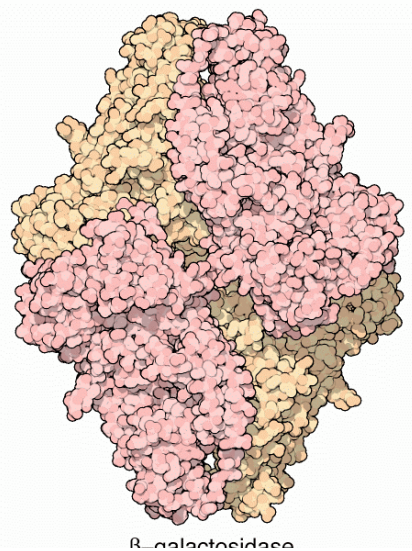
- *The Outcome from Structural Biology: Boat loads of atomic coordinates.*
- *"A science is built up of facts as a house is built up of bricks, but a mere accumulation of facts is no more a science than a pile of bricks is a house." – Poincare*
- *See http://www.rcsb.org/pdb/*
- *All cartoons due to David Goodsell, Scripps*

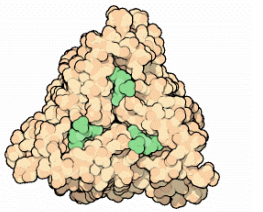


RNA polymerase

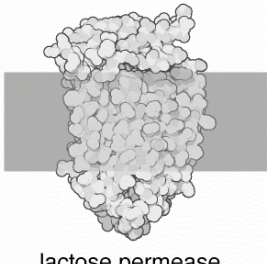


Nucleosome





galactoside acetyltransferase



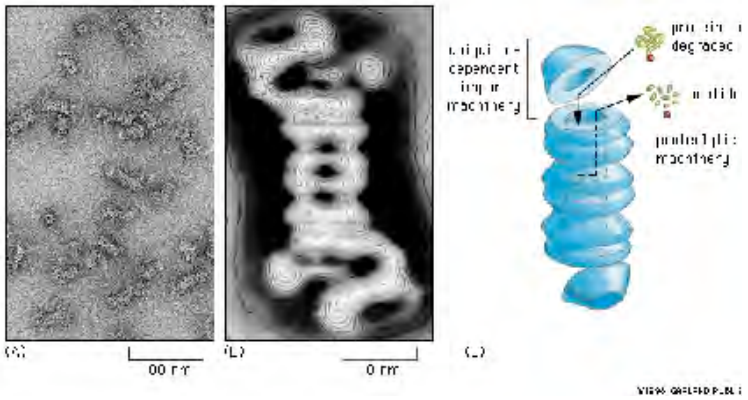
β-galactosidase

lactose permease

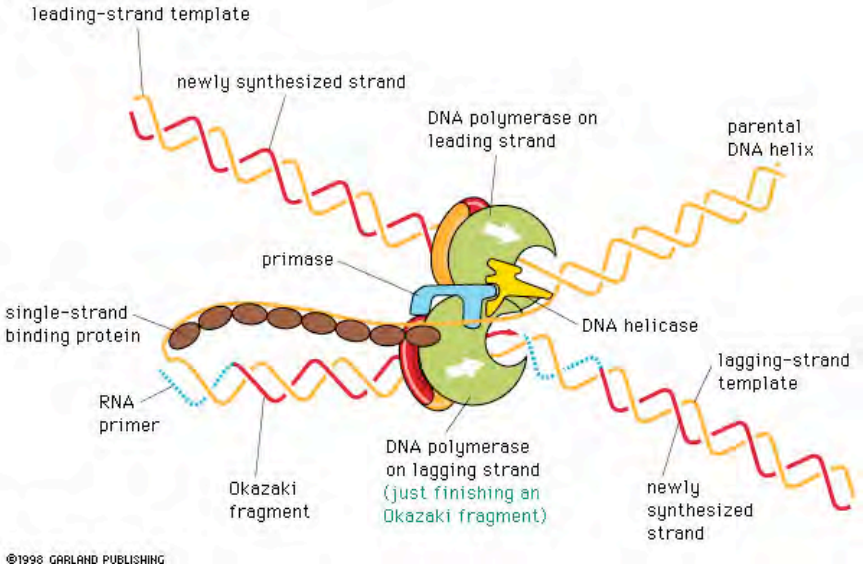
Somes: The Biologists Ons Macromolecular Assemblies

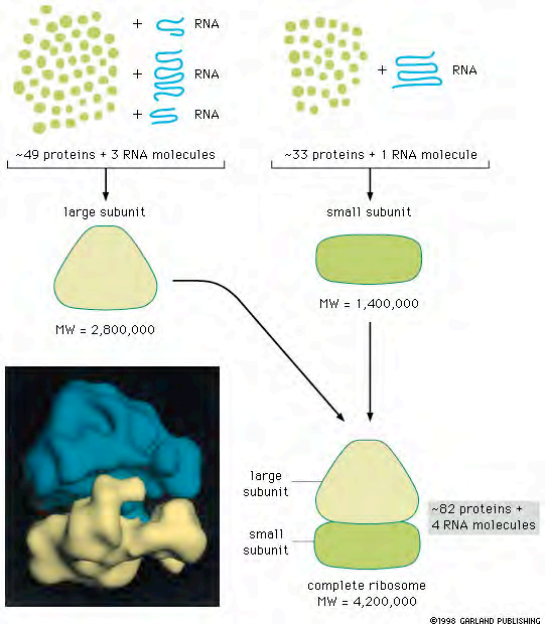
- *Physicists characterize collective excitations as ONS (phonons, magnons, excitons, etc…)*
- *Biologists also consider collective phenomena in the form of interacting macromolecular complexes.*

Proteosome



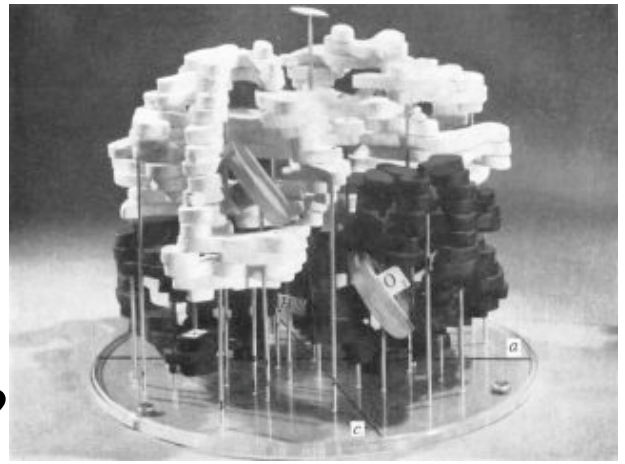
Replisome





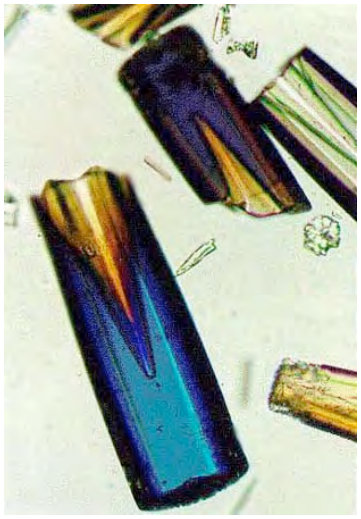
Ribosome

The Experimental Transformation of Biology: Molecular Structures

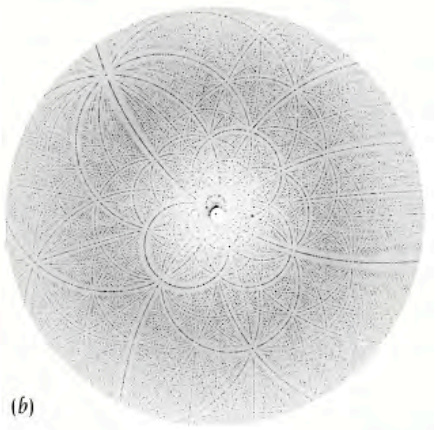


How do we know what we know about structures?

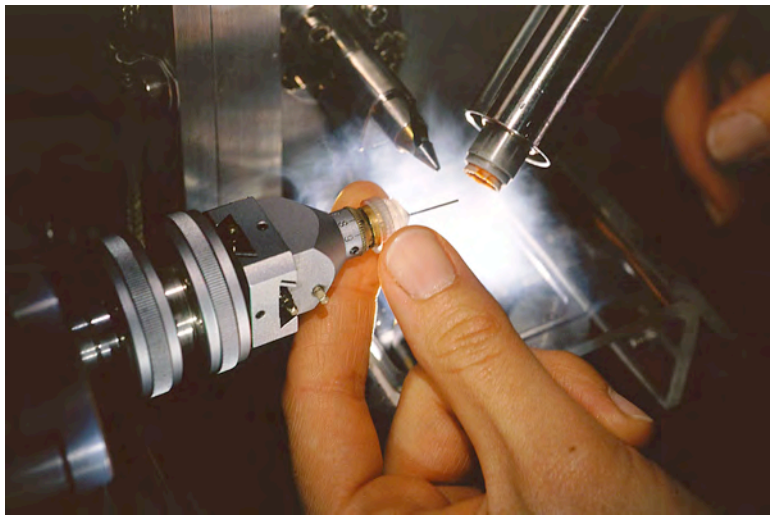
Experimental Transformation of Biology: X-Ray Crystallography of Proteins



(a)

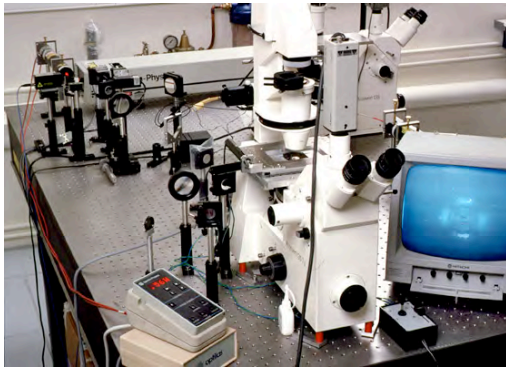


(b)



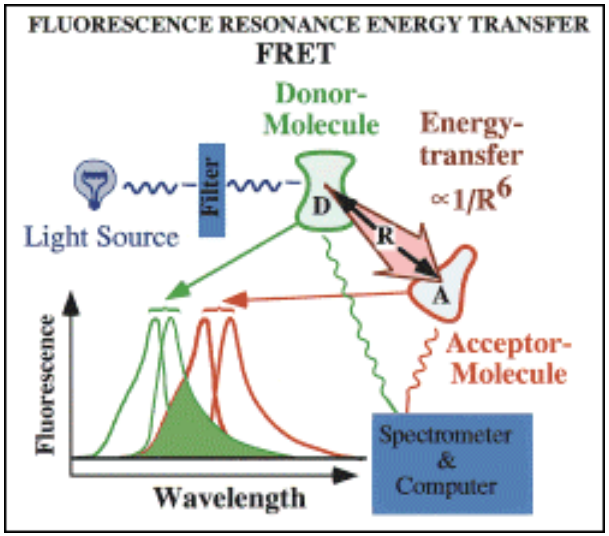
Experimental Transformation of Biology: Single Molecule Biophysics

Optical Tweezers

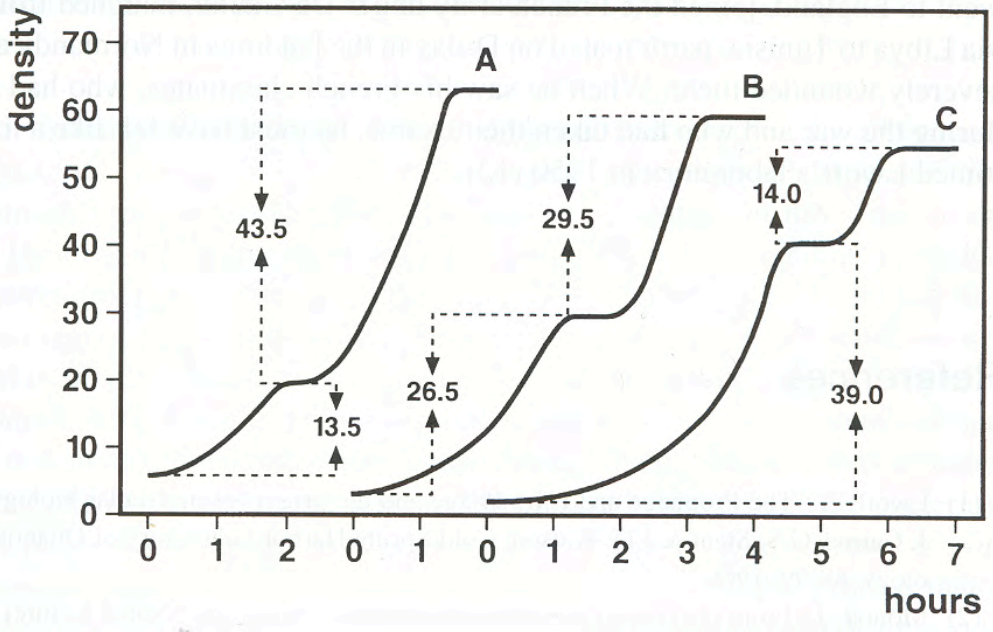


AFM

FRET



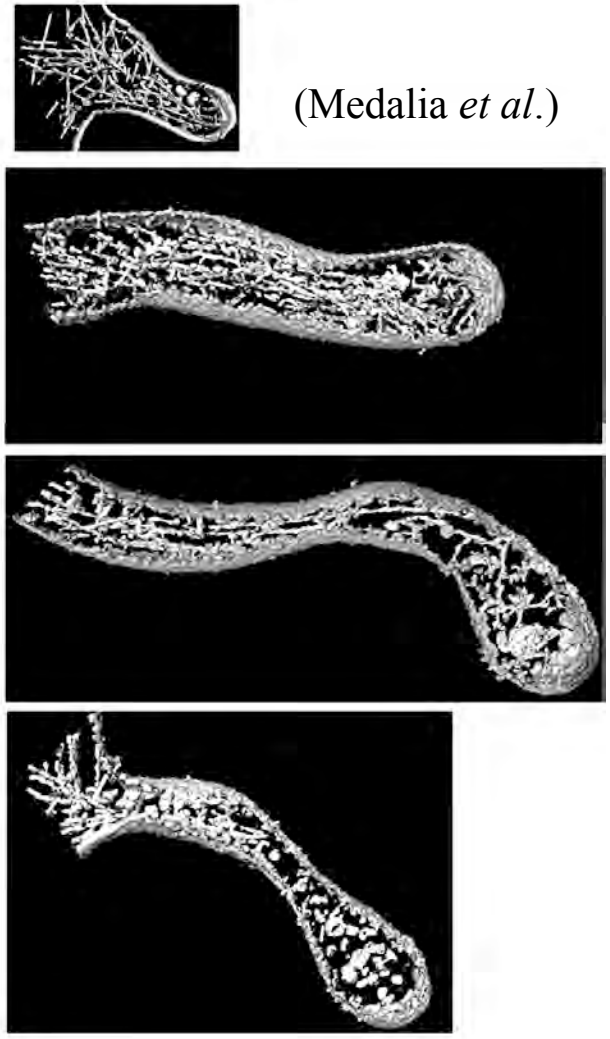
The Lac Operon: The Hydrogen Atom of Gene Regulation



"Tout ce qui est vrai pour le Colibacille est vrai pour l'élépl

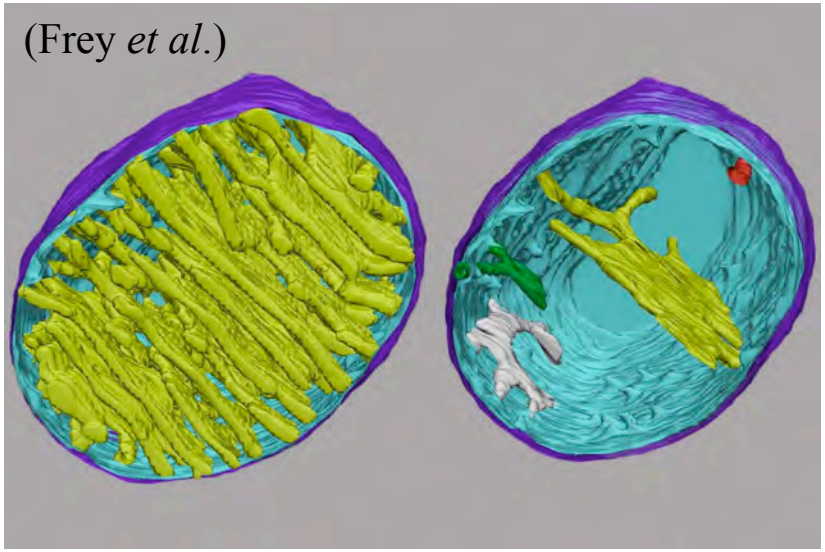
Experimental Transformation of Biology: Structures from Cryo EM

Filopodia in motile cells



(Medalia *et al*.)

Mitochondria



(Frey *et al*.)