What is life?

Life is a pattern in space-time, rather than a material object.

Attributes of life

Reproduction

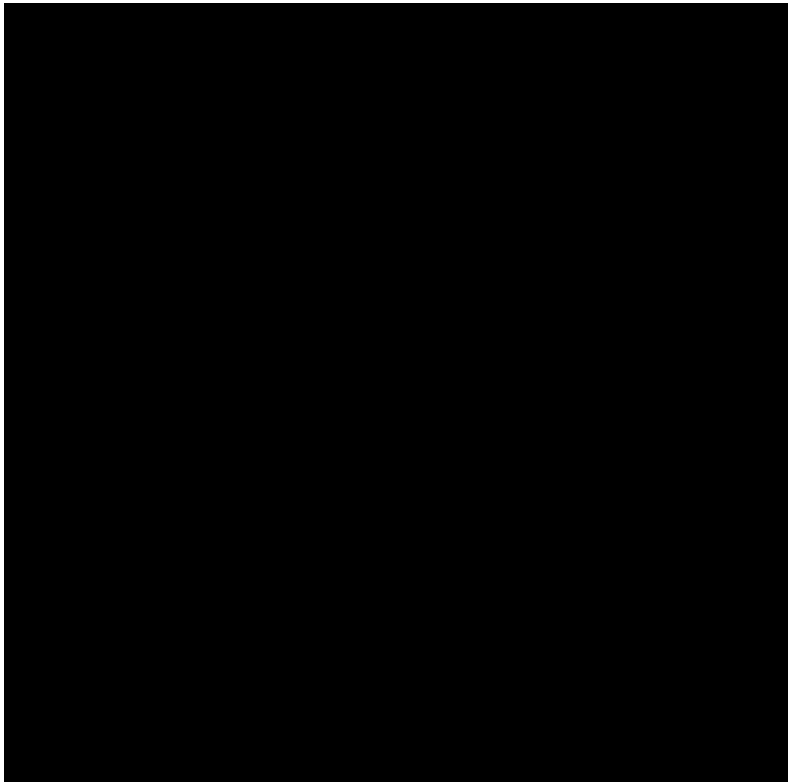
Recombining instruction sets.

Metabolism

Interacts with the environment.

Stability under perturbations

The ability to evolve.



Life requires a critical level of complexity.

Life is not a highly improbable chance event, but almost inevitable.

Stuart Kauffman

Value of this concept is that it suggests that chemical evolutionary systems may be experimentally testable.

Biological systems and physical/chemical systems are substantially different.

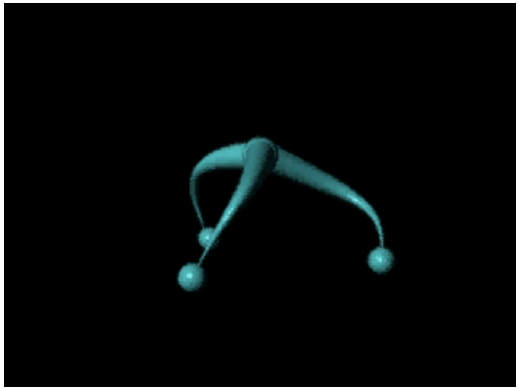
Adaptation and Evolution

Biological systems are shaped by natural selection to assure survival and maximize chances for reproduction, while physical systems are not "goal-oriented".

Self-organization

"A system in which structure appears without external pressure"

- *Results from interactions between components.*
- *Organization can evolve in time or space.*
- *May be stable or transient.*



Complexity itself triggers self-organization

(Kauffman)

How simple can life be?

Not Cells

• **Virus** = RNA or DNA wrapped in protein coat (HIV, poliomyellitis)

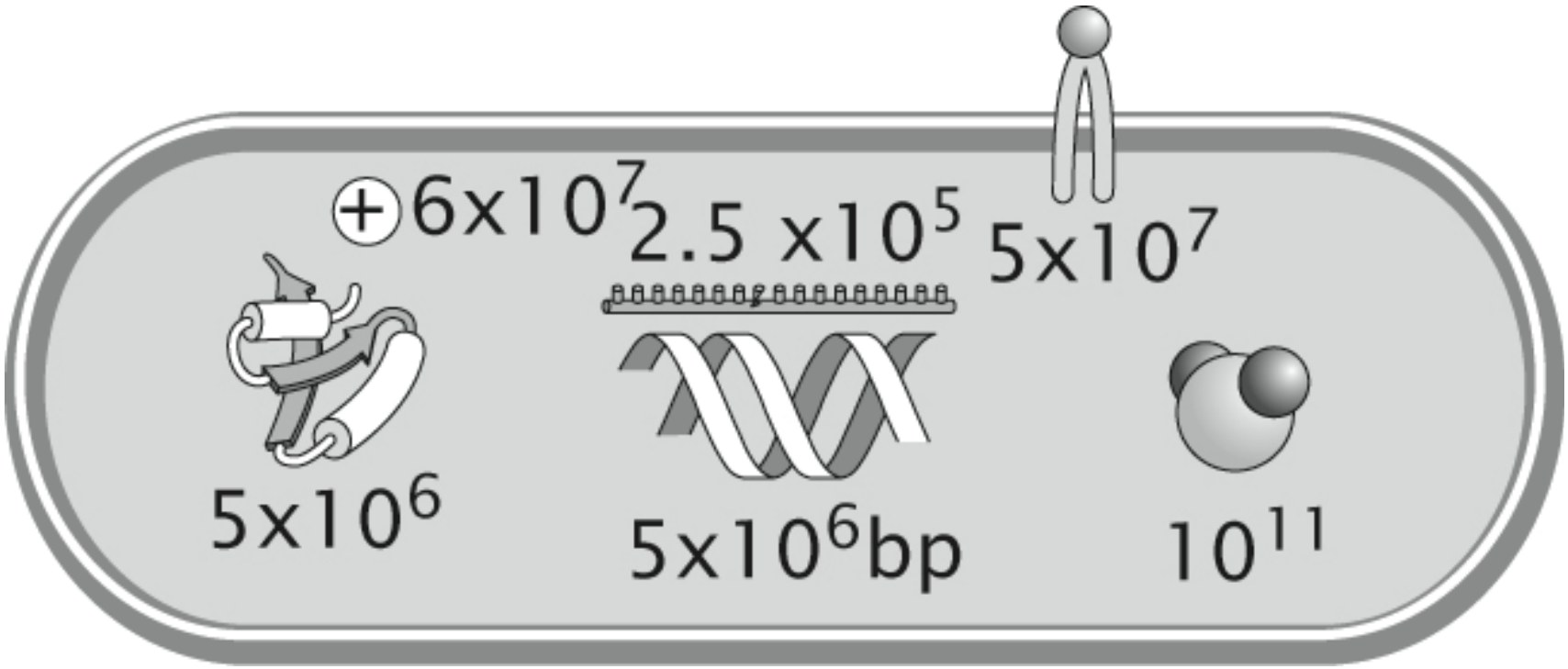
• **Viroid** = Tightly wound DNA or RNA (coconut cadang cadang, bunchy top)

• **Prions** = 1/100 to 1/1000 the size of a virus, composed of proteins (Scapies, Multiple Sclerosis, Lou Gehrig's disease)

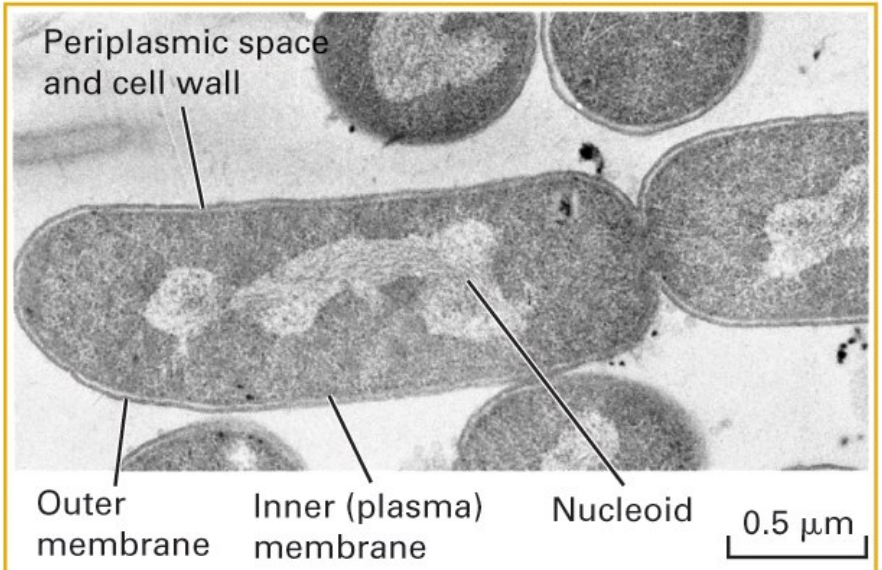
Pneumonia mycoplasma

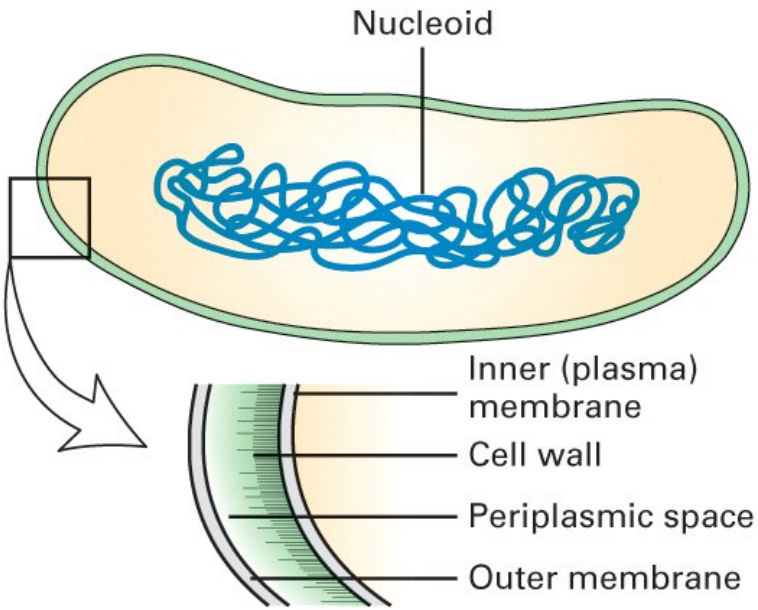
Phytoplasma and Mycoplasma = simplest cell, lack a cell wall, DNA for 200 functions (walking pneumonia)

A Single Molecule Census of the Cell

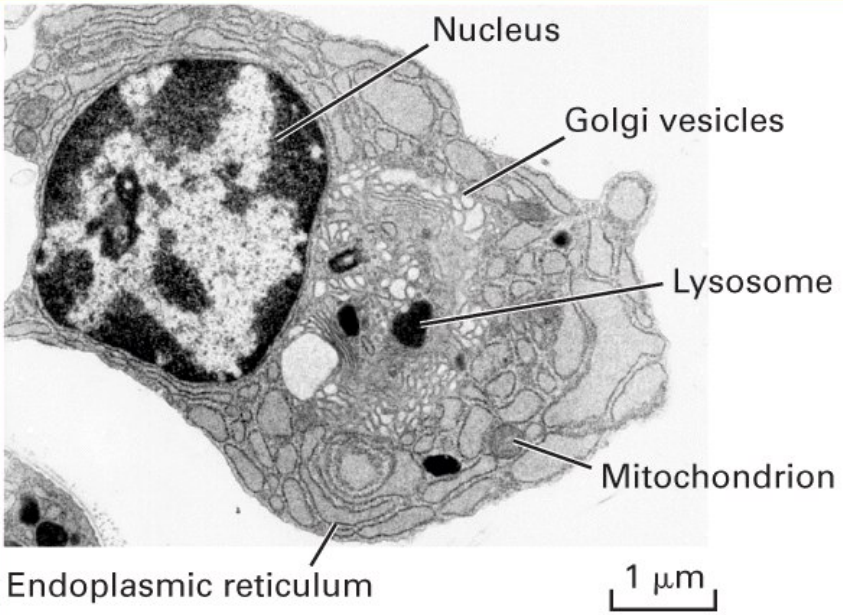


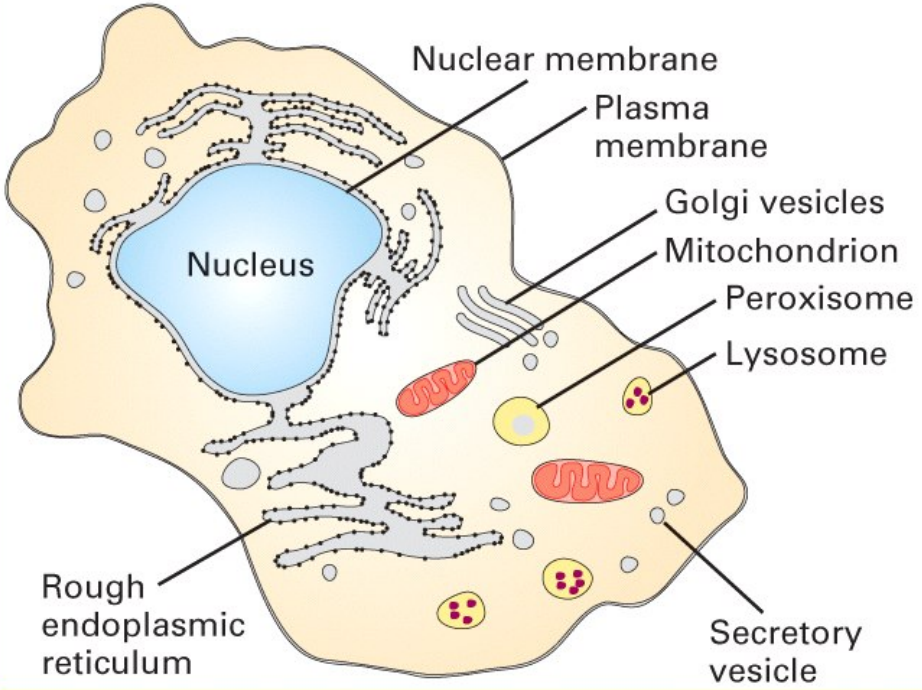
(a) Prokaryotic cell



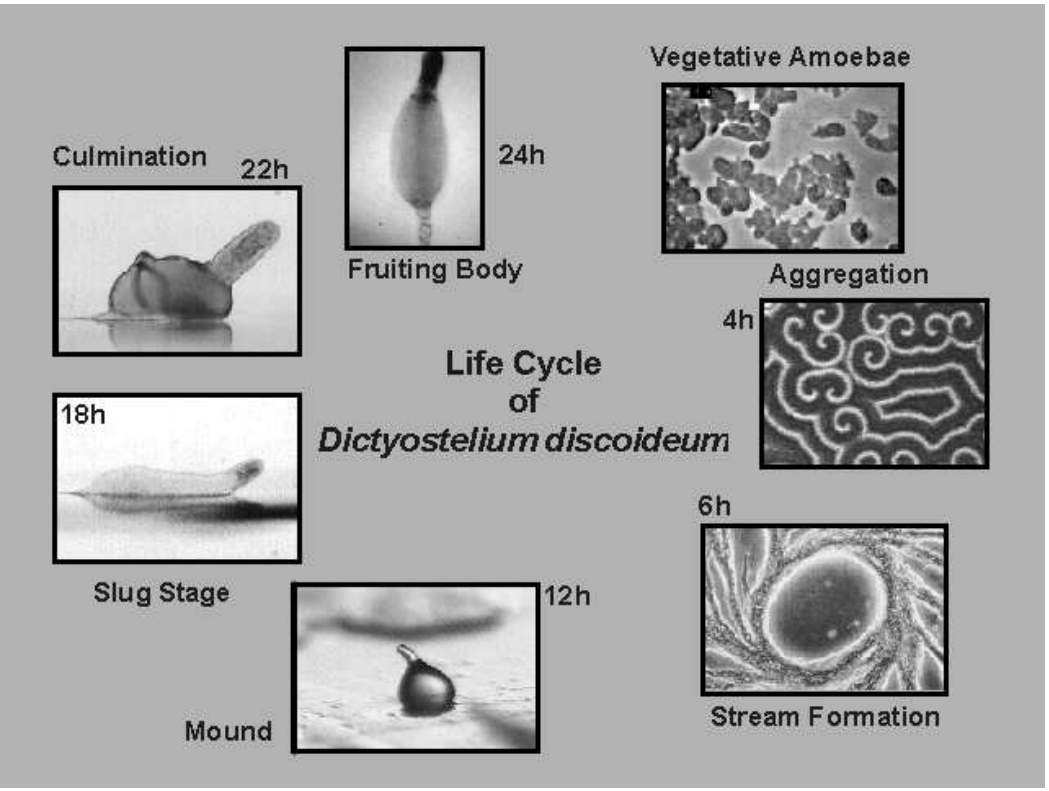


(b) Eukaryotic cell

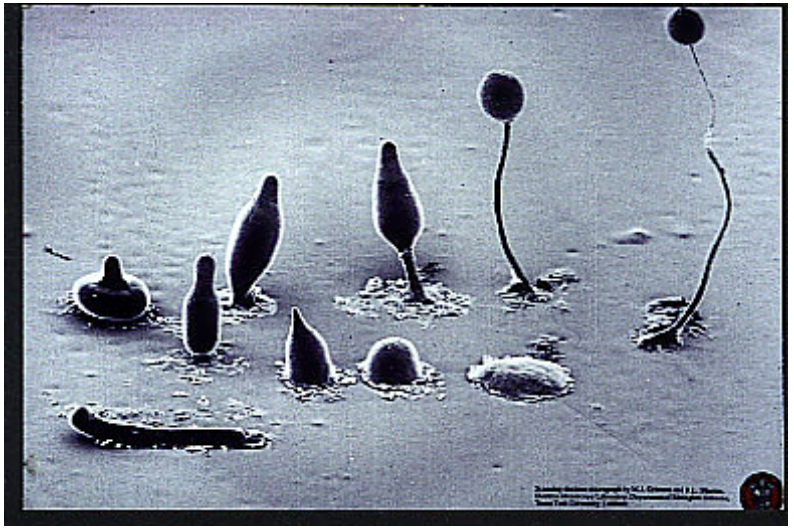




Collections of Cells - Sporulation

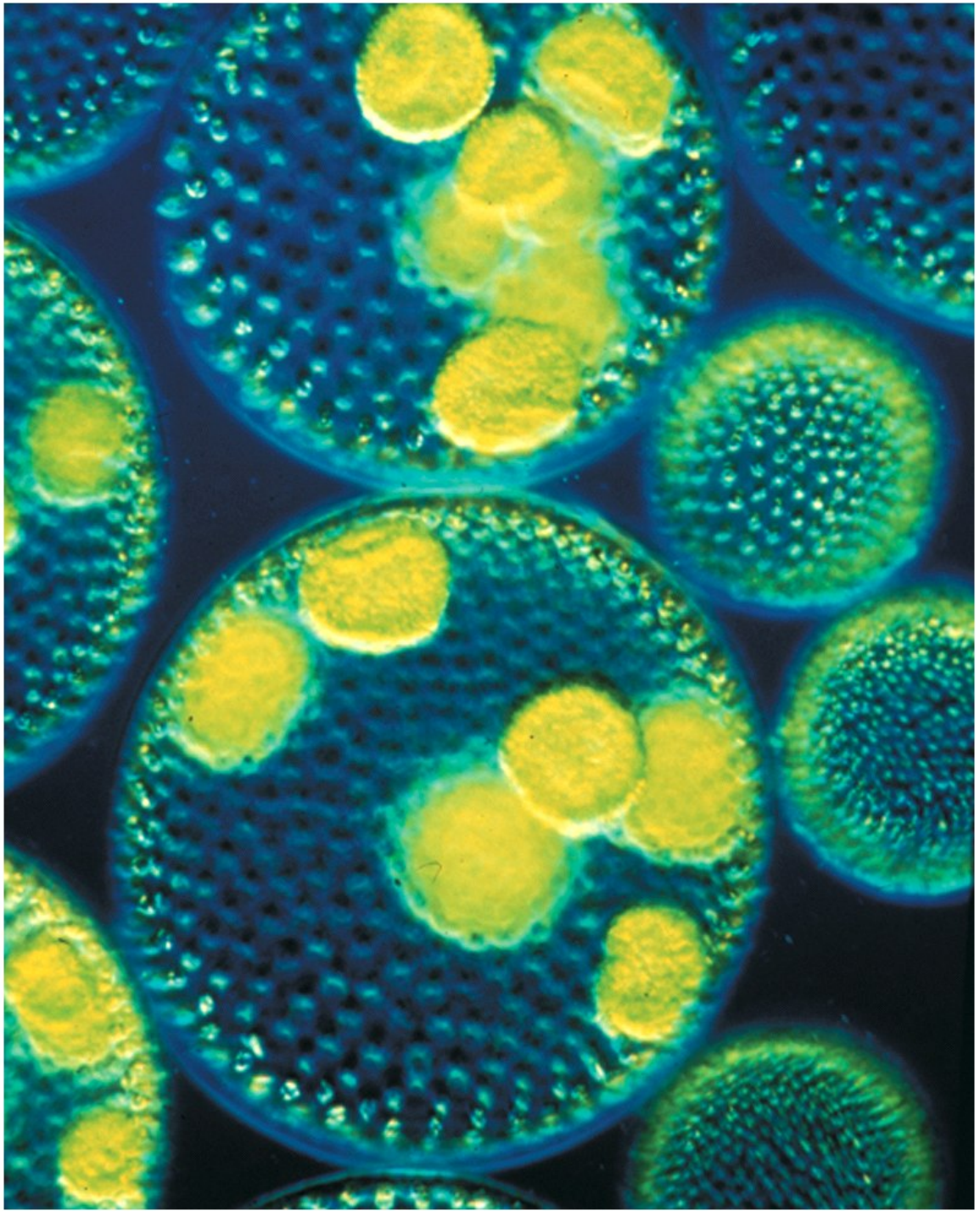


Dictyostelium discoideum

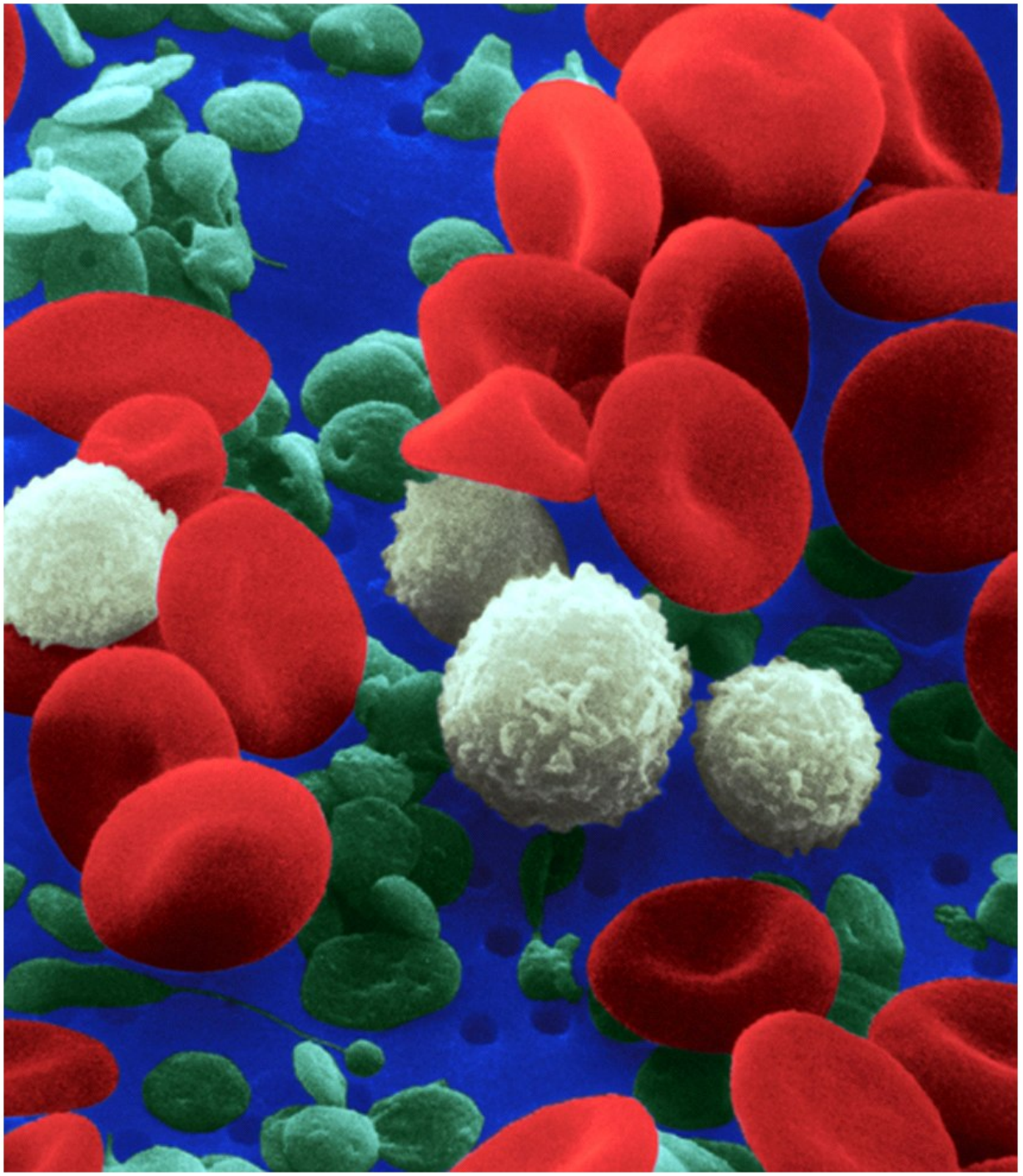


http://www.zi.biologie.uni-muenchen.de/zoologie/dicty/dicty.html

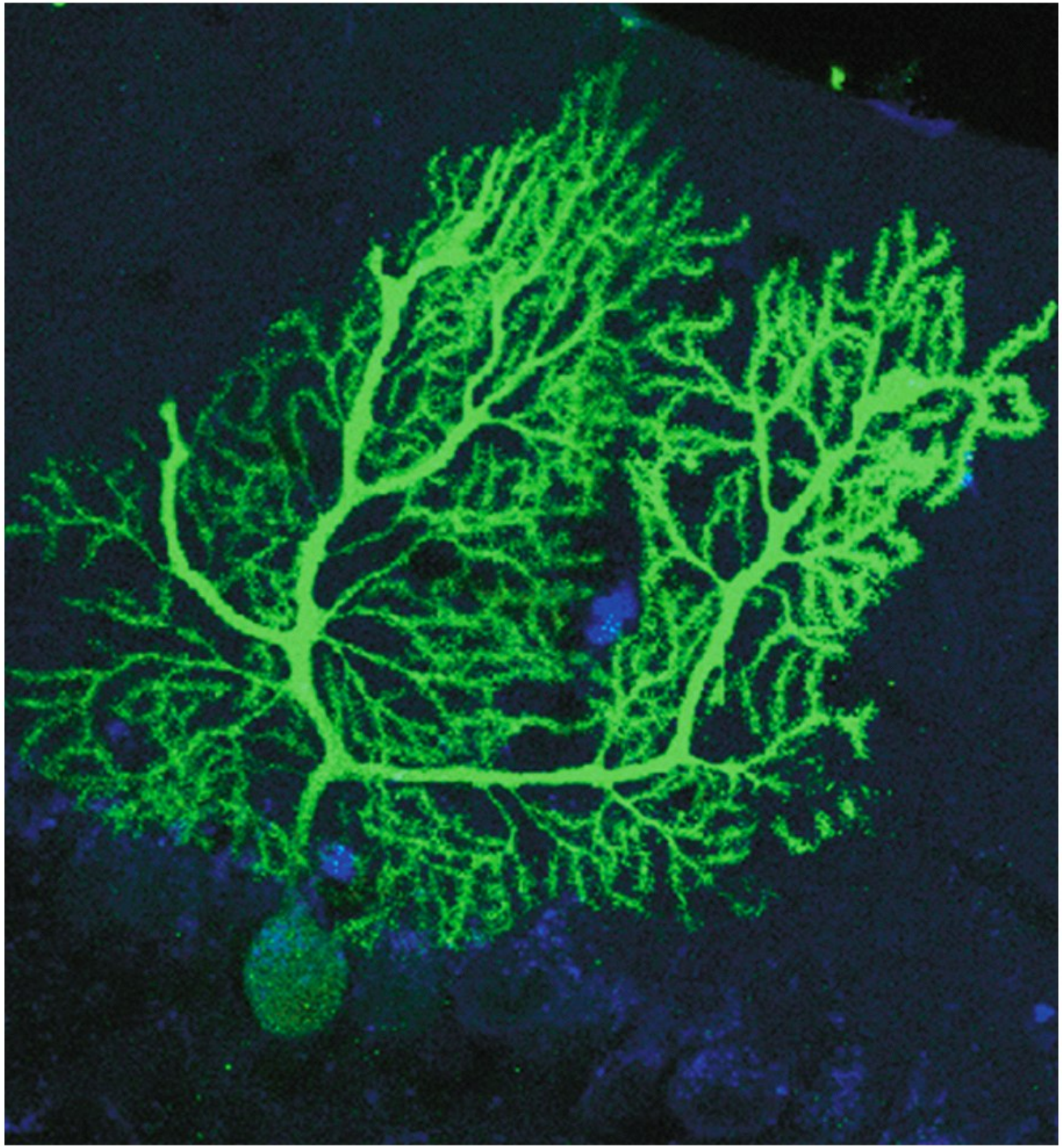
Colonies of alga



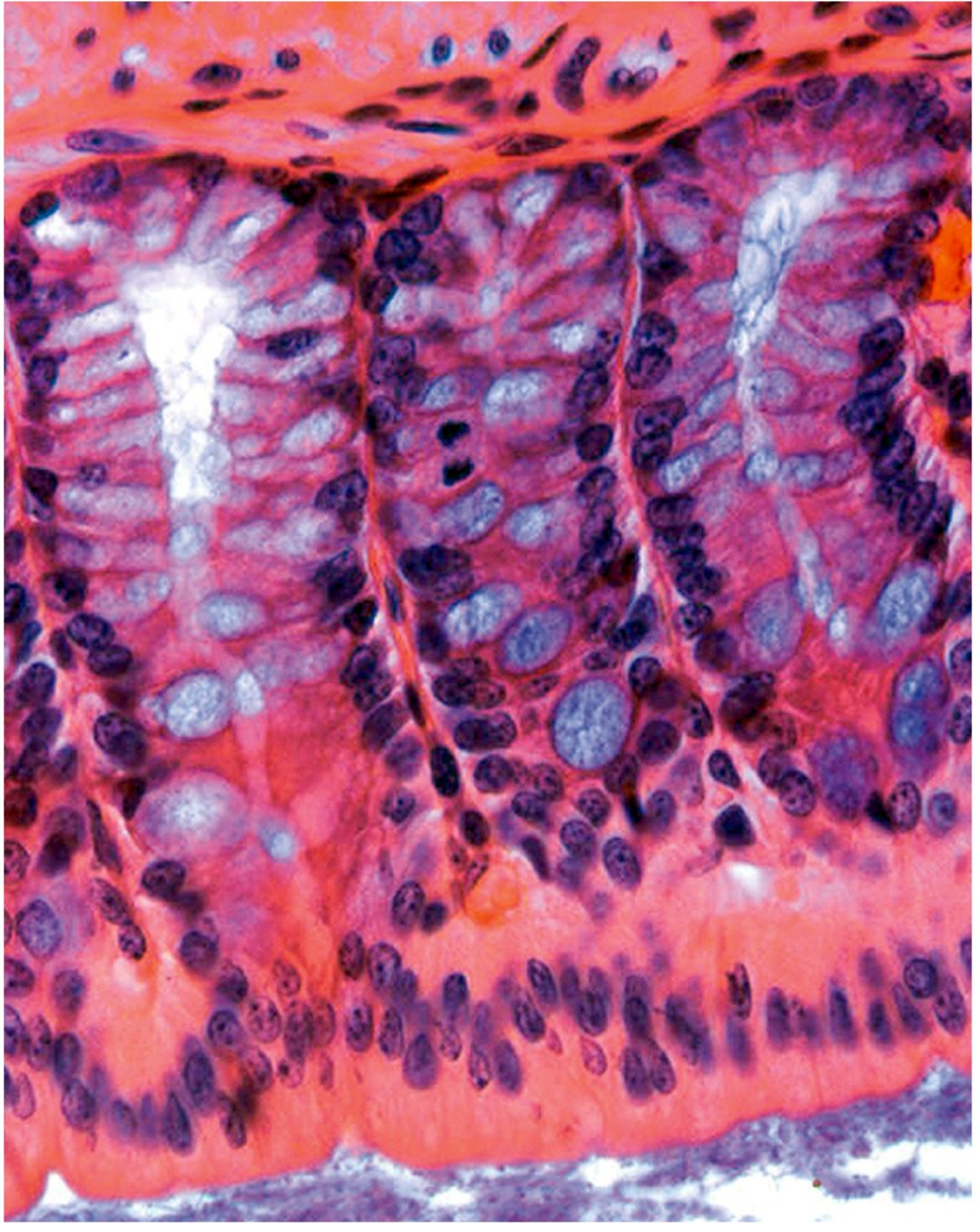
Blood cells



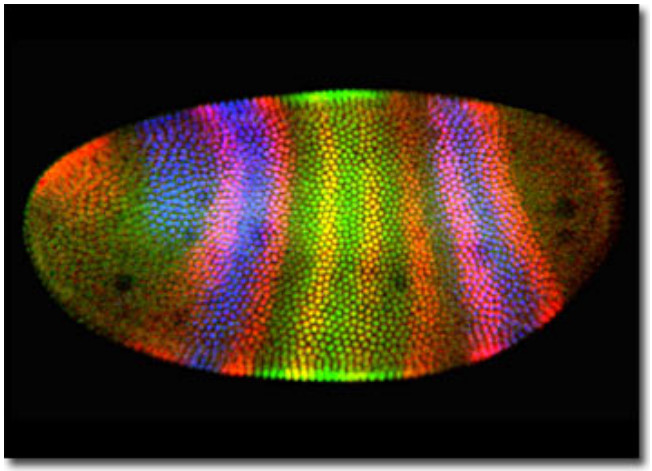
Neuron

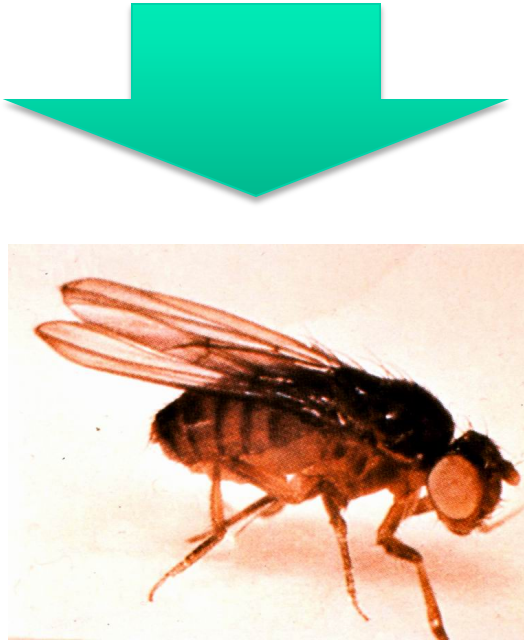


Intestinal epithelium



Collections of Cells - Organisms





Featured above is a digital image of a triple-labeled ***Drosophila*** embryo at the cellular blastoderm stage.

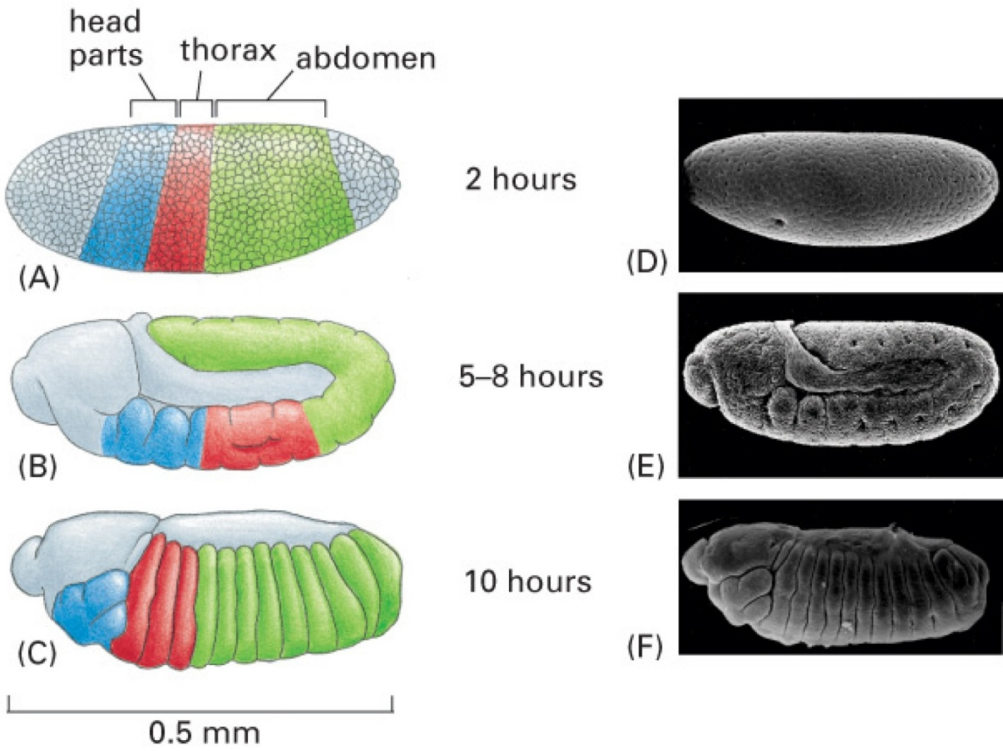


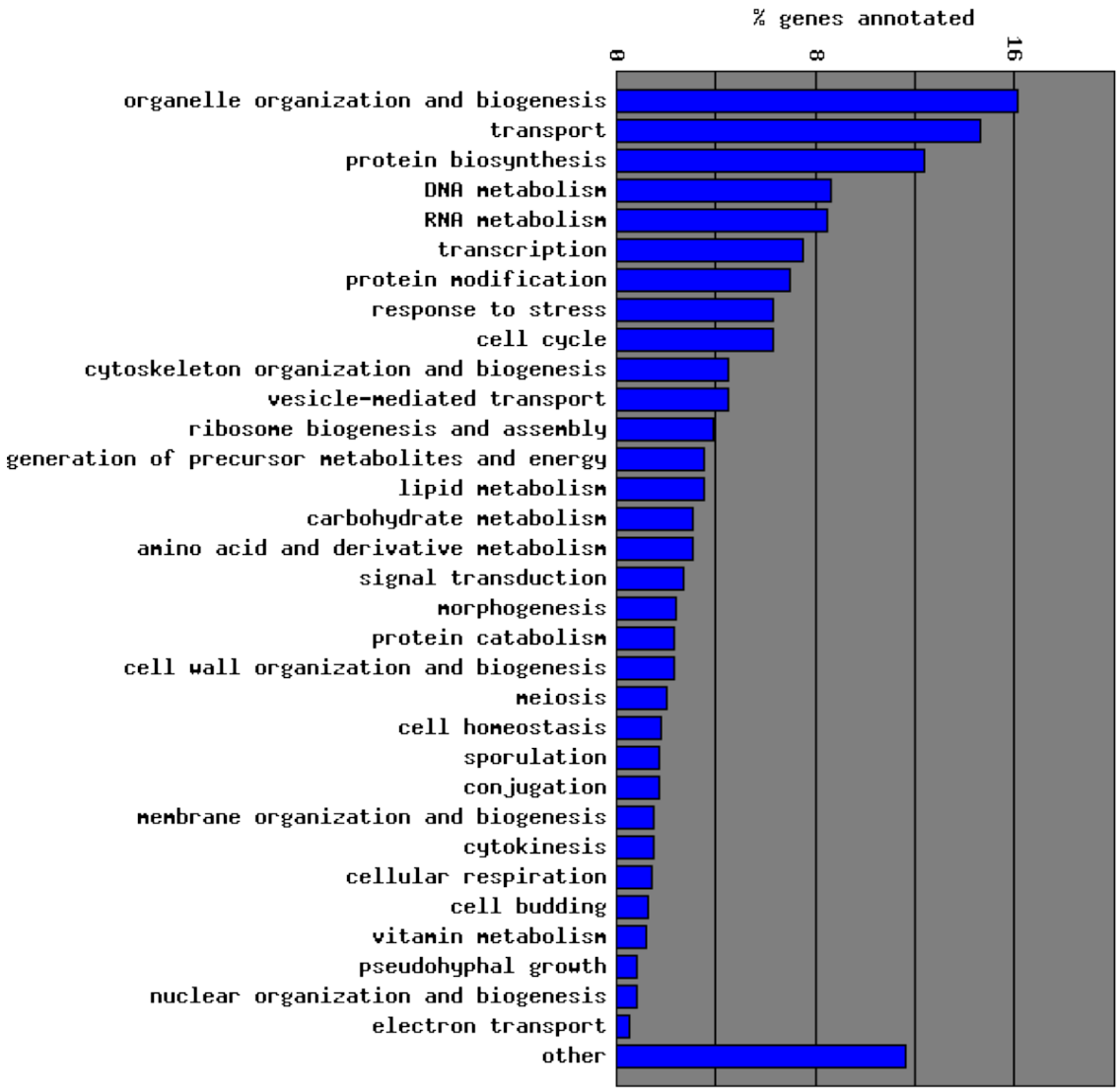
Figure 21–25. Molecular Biology of the Cell, 4th Edition.

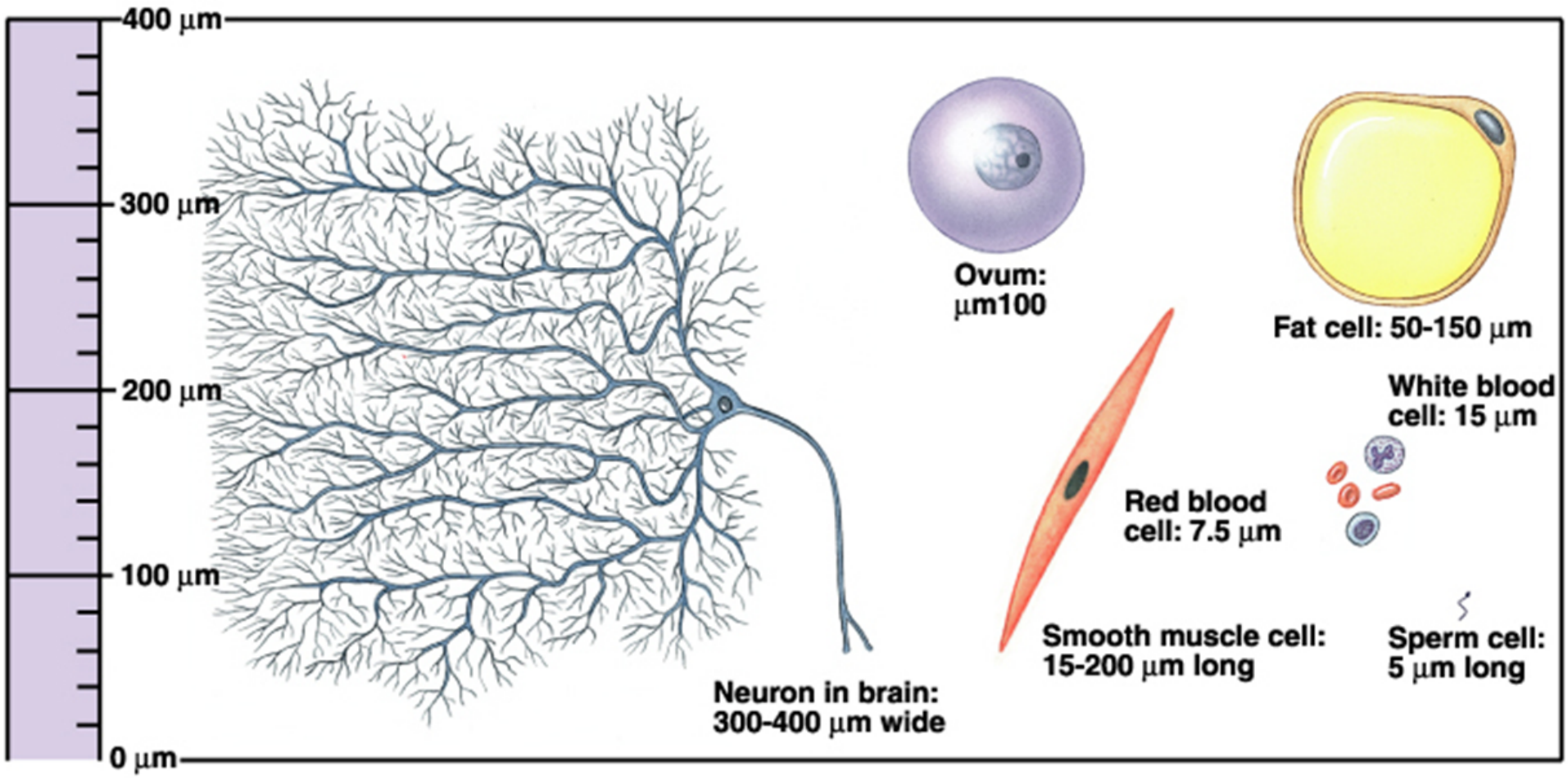
Big Picture

We have ~ 10^{20} cells .

Each has a complete instruction set (the genome).

Not all genes are expressed in a cell.





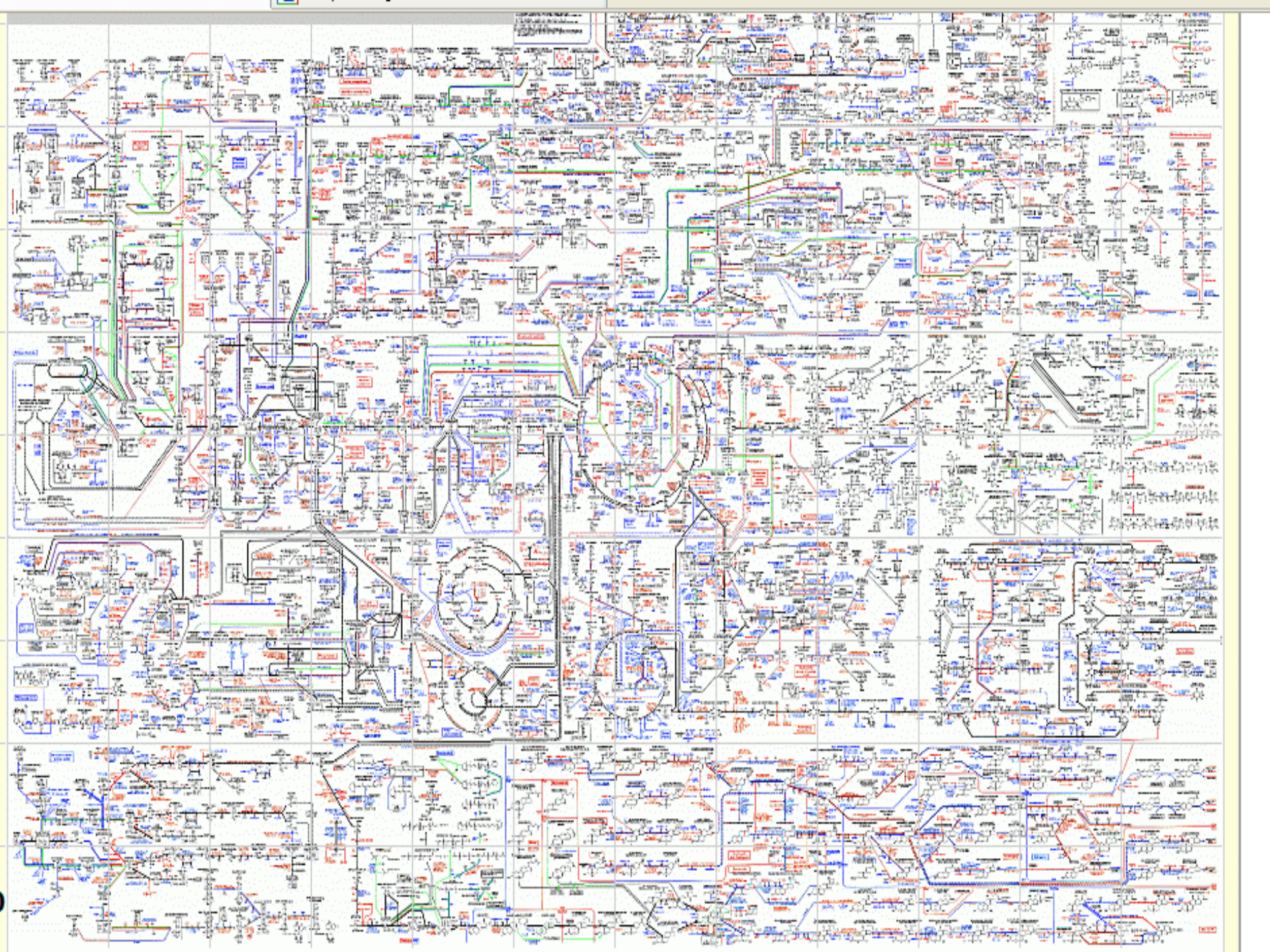
Unlike atoms and simple molecules studied in chemistry and physics, no two cells are identical.

Homeostasis

Networks of interconnecting systems that use antagonistic interplay making them stable to internal-external changes.

Selected cell parameters

Description	Units	Symbol	Value
Energy of ATP hydrolysis		ΔG_{ATP}	21 k_BT
Cytoplasmic pH*		pH_C	7.0–7.5
Cytoplasmic sodium concentration	mM	Na_c^+	15
Cytoplasmic potassium concentration	mM	K_c^+	140
Cytoplasmic chloride concentration	mM	Cl_c^-	4
Cytoplasmic ATP concentration	mM	ATP_c	5
Cytoplasmic ADP concentration	mM	ADP_c	0.1
Cytoplasmic phosphate concentration	mM	P_c	5
Cytoplasmic calcium concentration	M	Ca_c^{2+}	10^{-7}
Extracellular sodium concentration	mM	Na_e^+	145
Extracellular potassium concentration	mM	Ke^+	5
Extracellular chloride concentration	mM	Cl_e^-	110
Extracellular calcium concentration	mM	Ca_e^{2+}	2.5-5
Extracellular phosphate concentration	mM	P_e	1
Bilayer capacitance	$\mu F/cm^2$	C_0	1
Golgi complex buffering capacity	mM/pH	β_G	10, 40
ER buffering capacity	mM/pH	ER	6
Endosome buffering capacity	mM/pH	EN	50
Chloride permeability	cm/s	P_{Cl}	1.2×10^{-5}
Proton permeability	cm/s	P_p	$4.8–0.67 \times 10^{-3}$
Golgi complex volume	cm^3	V_G	6×10^{-12}
Endosome volumes	cm^3	V_{EN}	$88–0.7 \times 10^{-15}$
Golgi complex surface area	cm^2	S_G	8×10^{-6}
Endosome surface area	cm^2	S_{EN}	$1–0.06 \times 10^{-8}$

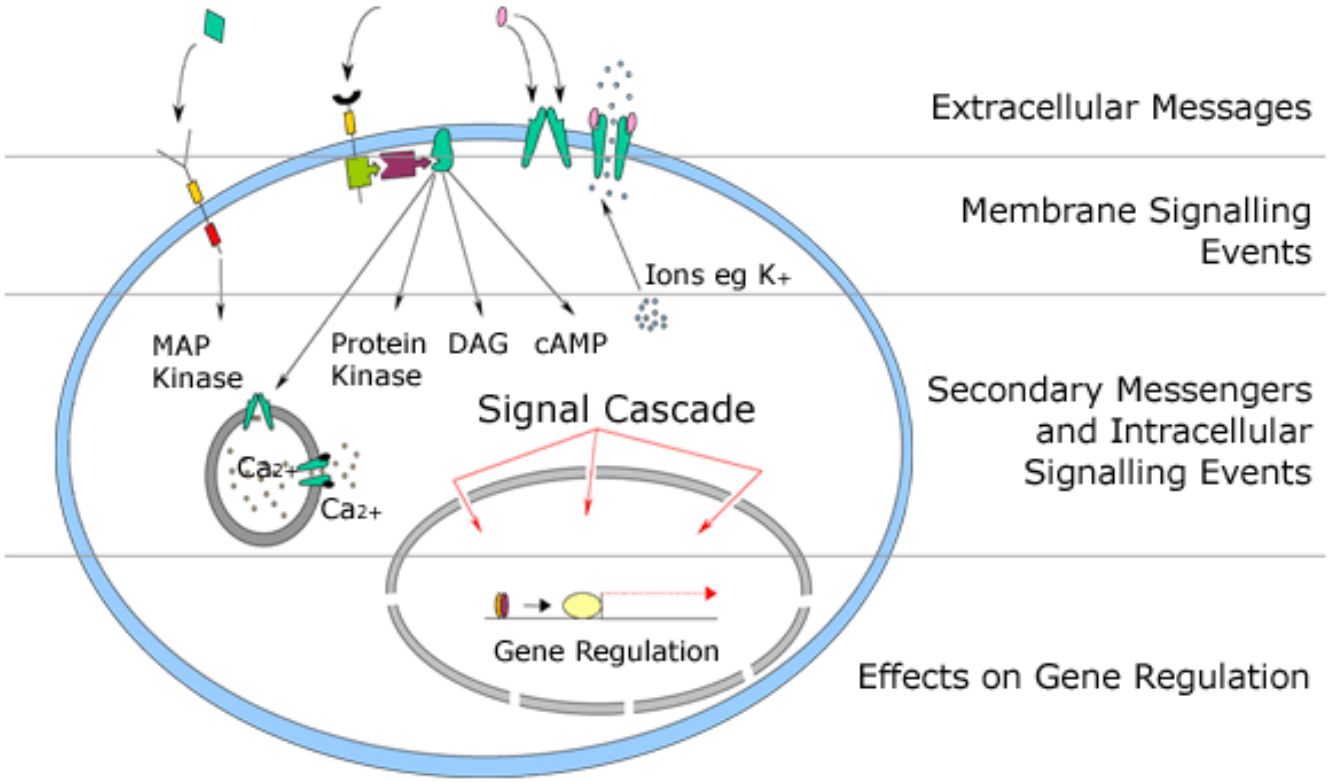


Cells as Organized Machines

Cells are computational devices.

Cells have instructions and programs too:

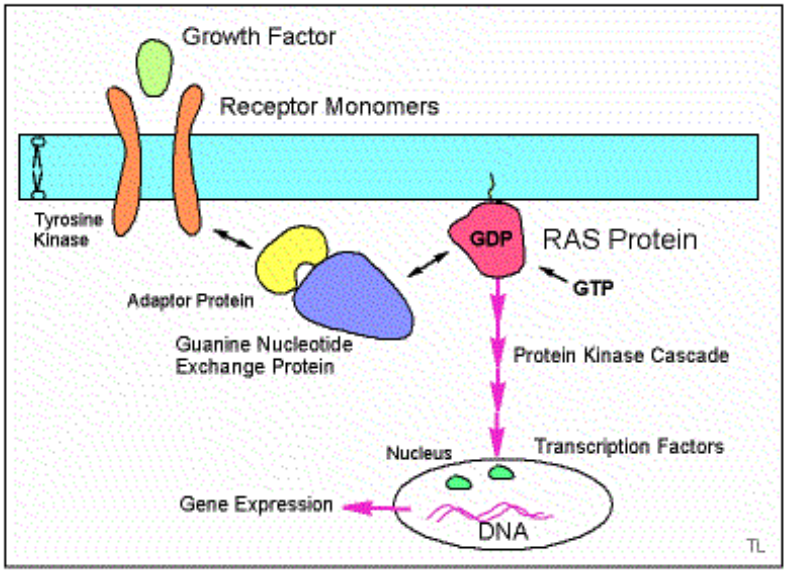
- *Genome (DNA) contains the instructions.*
- *Proteins are executables (strings of amino acids).*



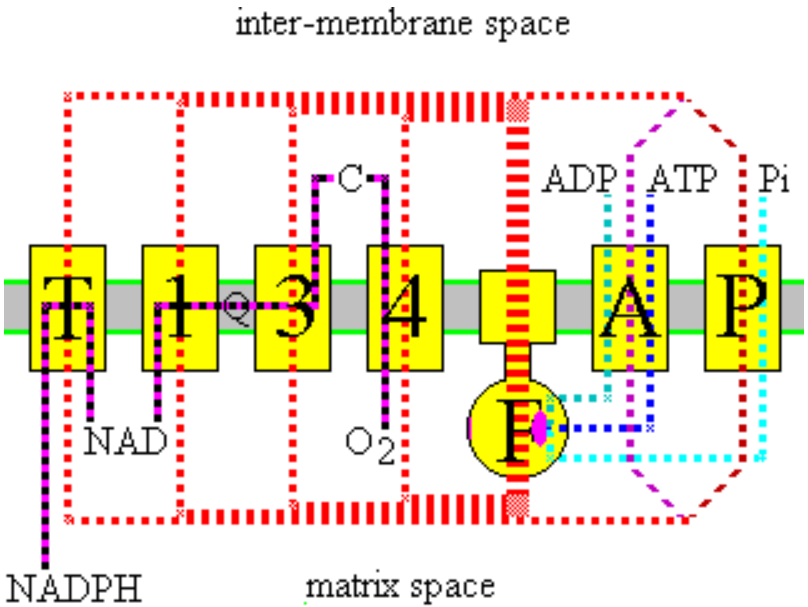
Homeostasis is maintained by directional flows

Matter

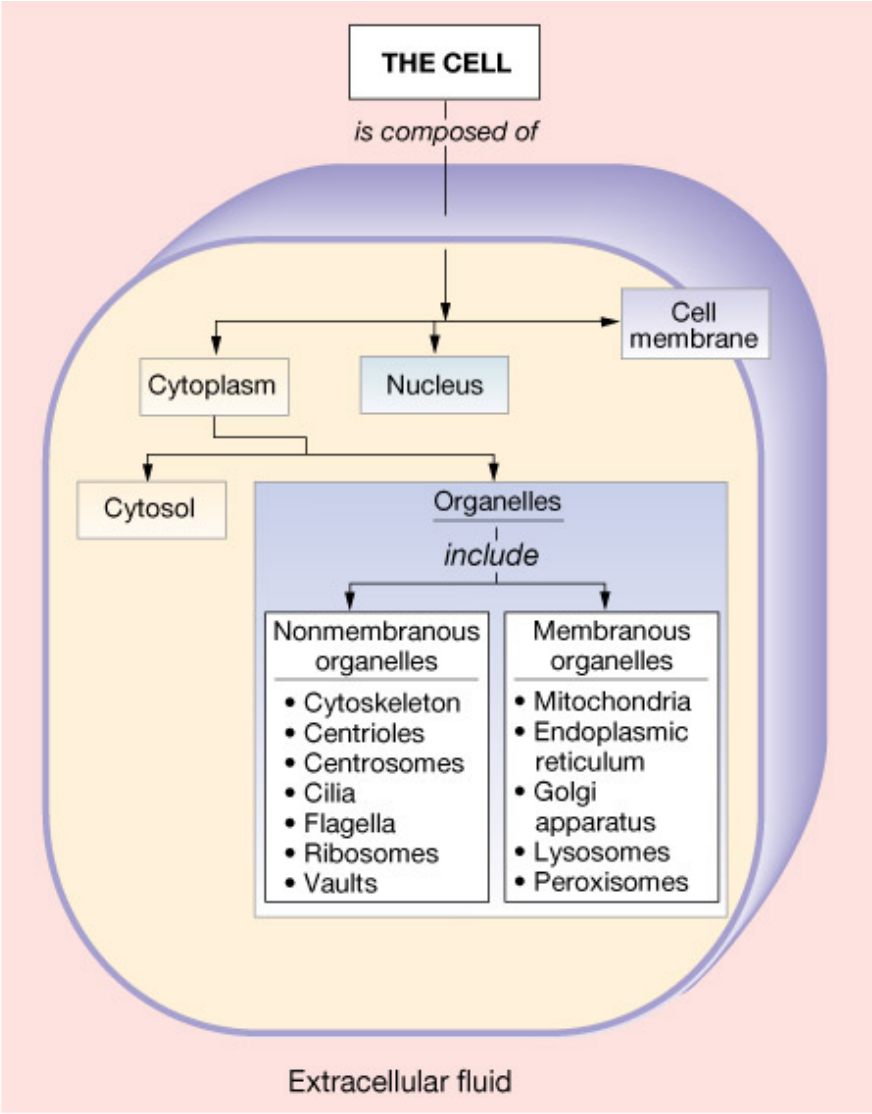
Information

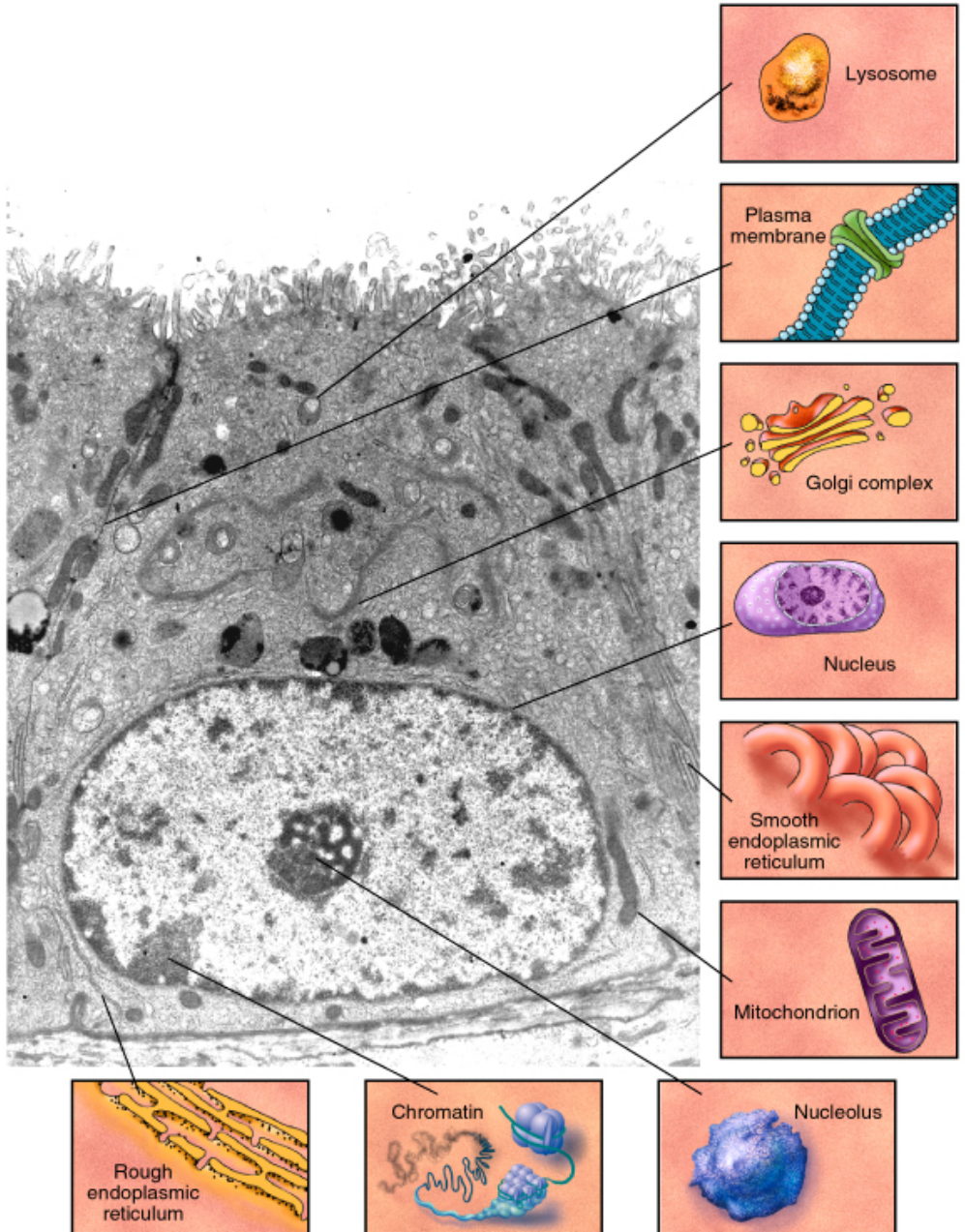


Energy

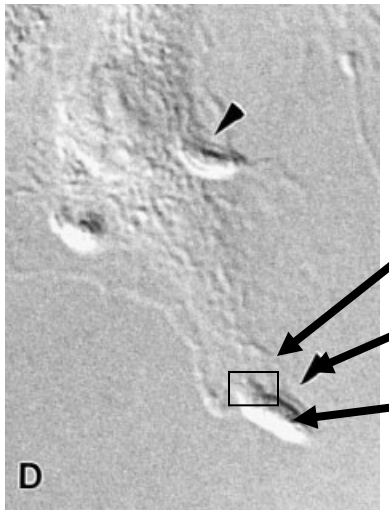


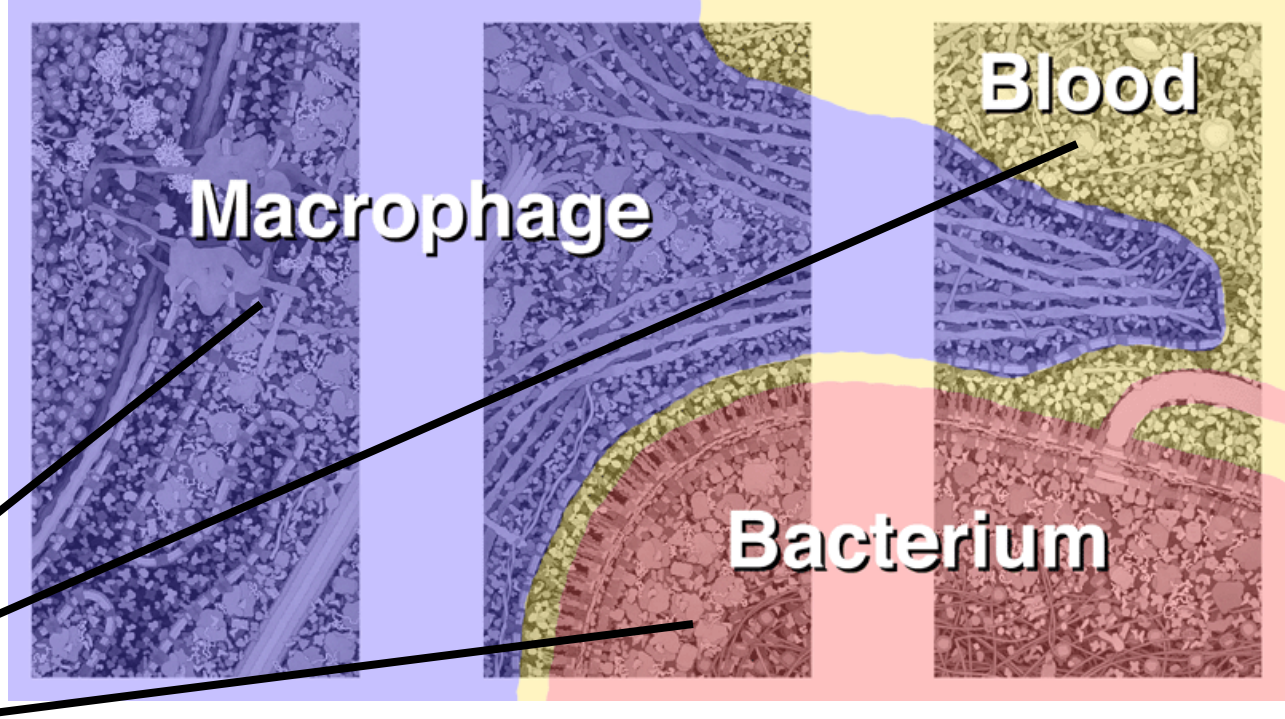
Space compartmentalization



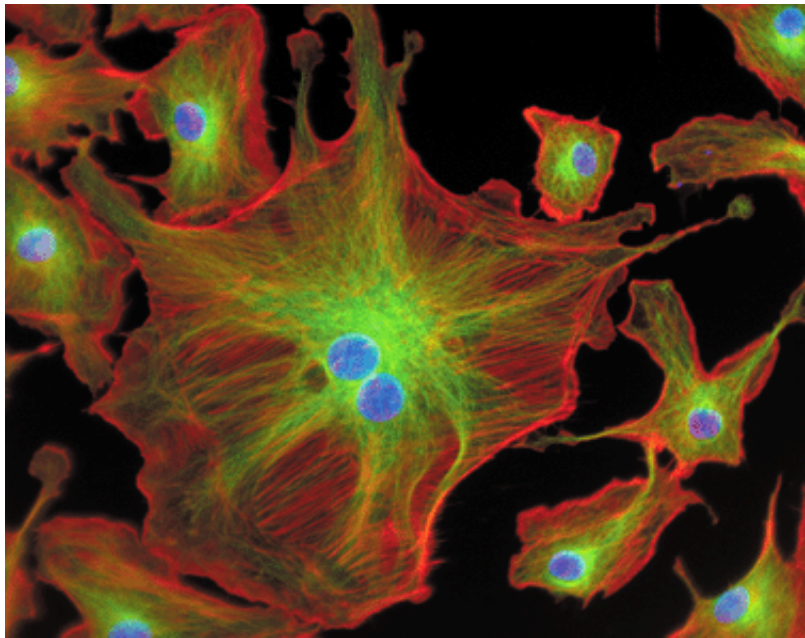


Crowding !!!!





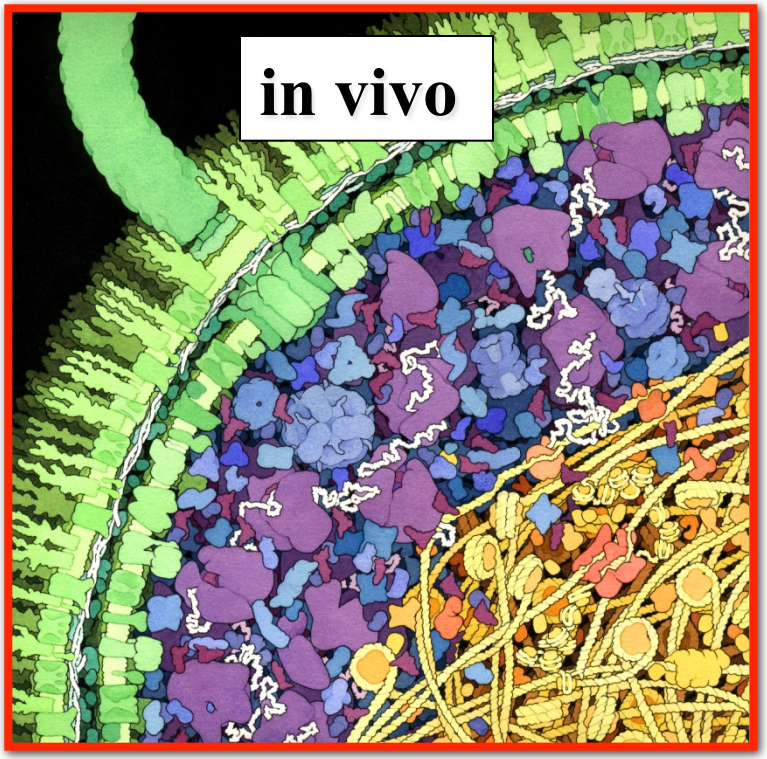
Biochemical reactions in living systems take place in media containing 50–400 mg/ml of macromolecules.

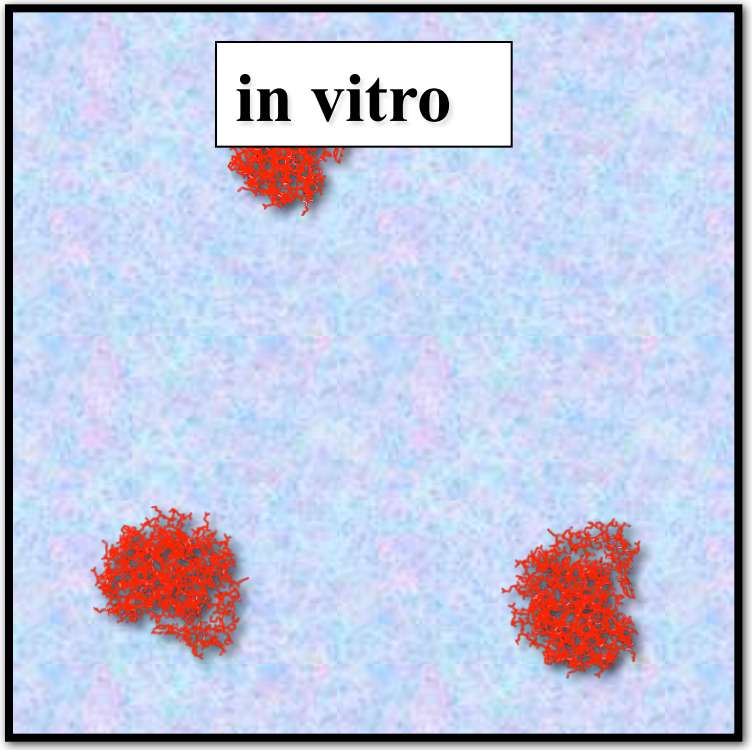


The numbers of different molecular actors in the drama matters!

Concentration might just be the most important variable in biochemistry!

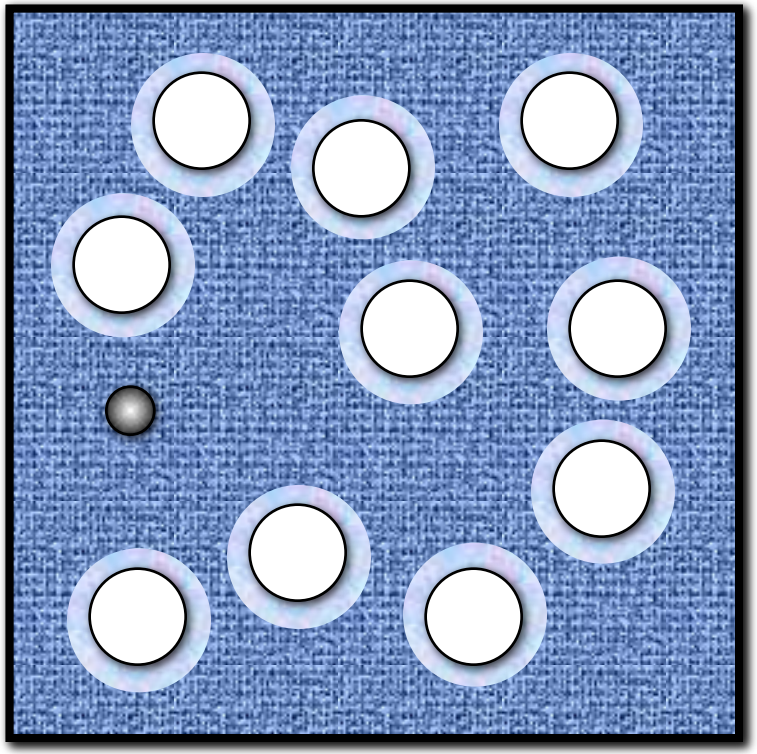
Macromolecular crowding effects



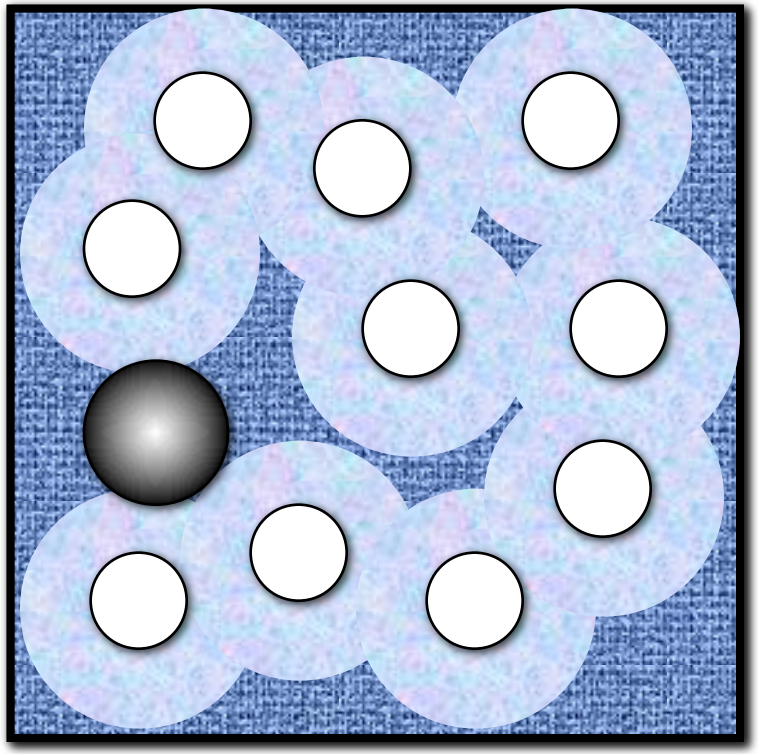


David S. Goodsell

Effect of crowding on diffusion



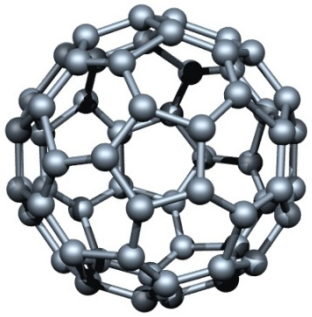
diffusion of small solute unaffected



diffusion of large solute strongly slowed down

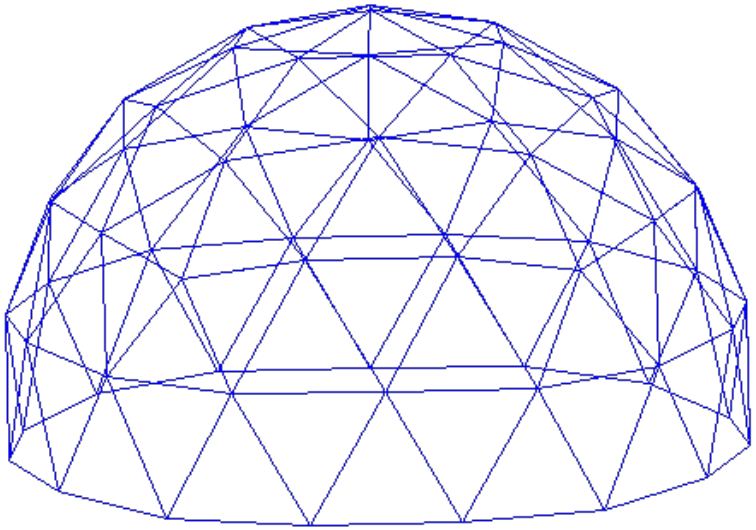
Biological Design

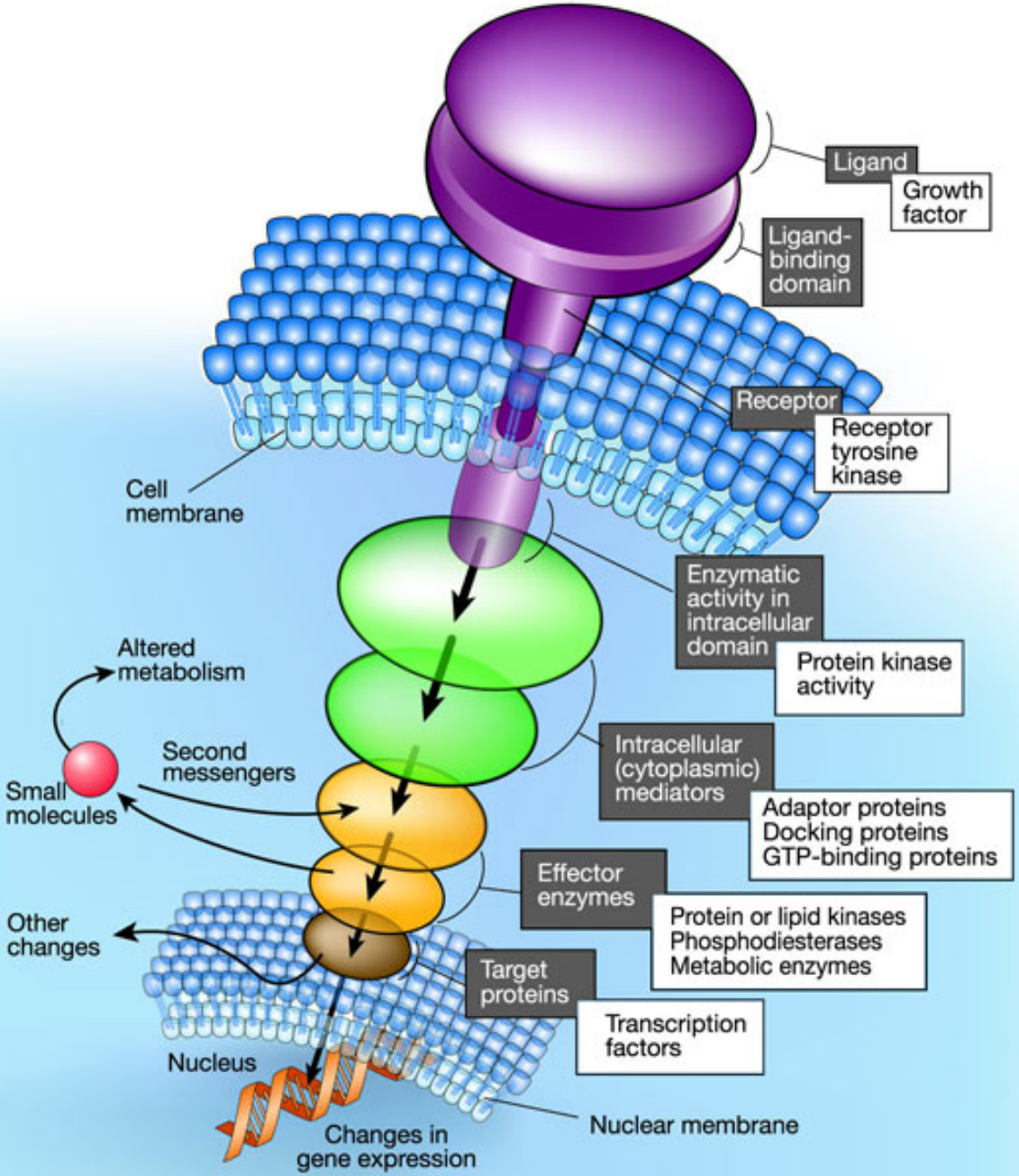
There is a recurring patterns of spirals, triangulated forms, & pentagons in everything from crystals to proteins, viruses to plankton.



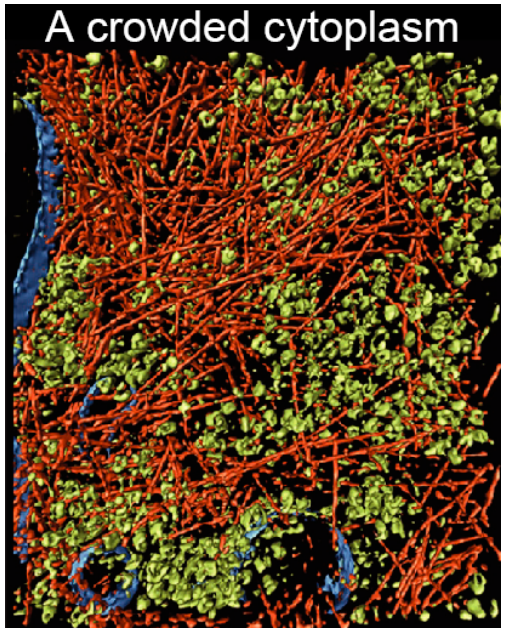
TENSEGRITY is a fundamental aspect of self-assembly - an architectural system, mechanically stable, yet dynamic, where the forces of tension and compression balance.

Tensegrity may be the most economical and efficient way to build cell structure.





Cellular information processing and passing are carried out by networks of interacting molecules.



from Downward, Nature, August (2001)

Regulatory and signaling pathways

Genetic Information Processing

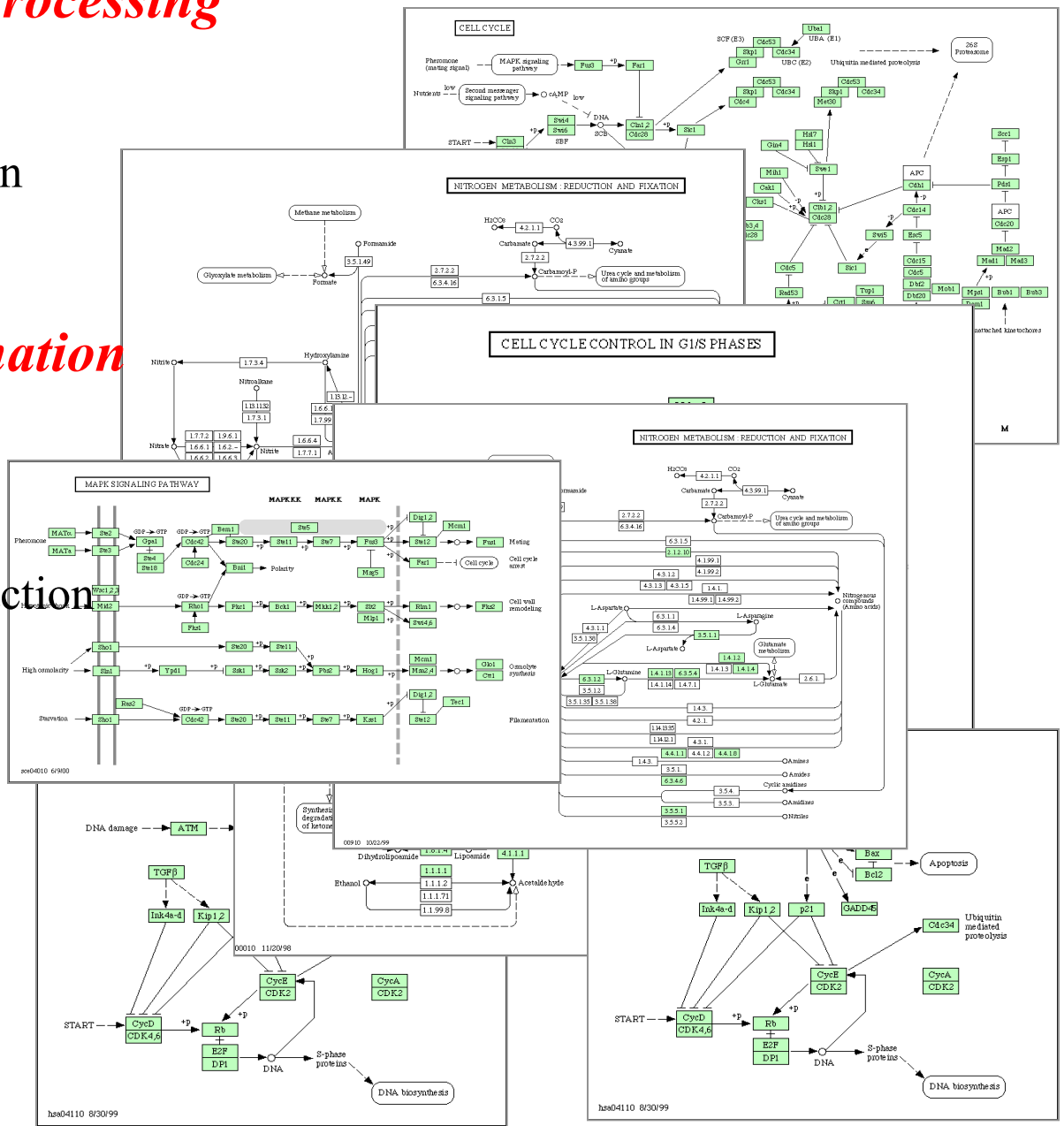
- Transcription
- Translation
- Sorting and Degradation
- Replication and Repair

Environmental Information

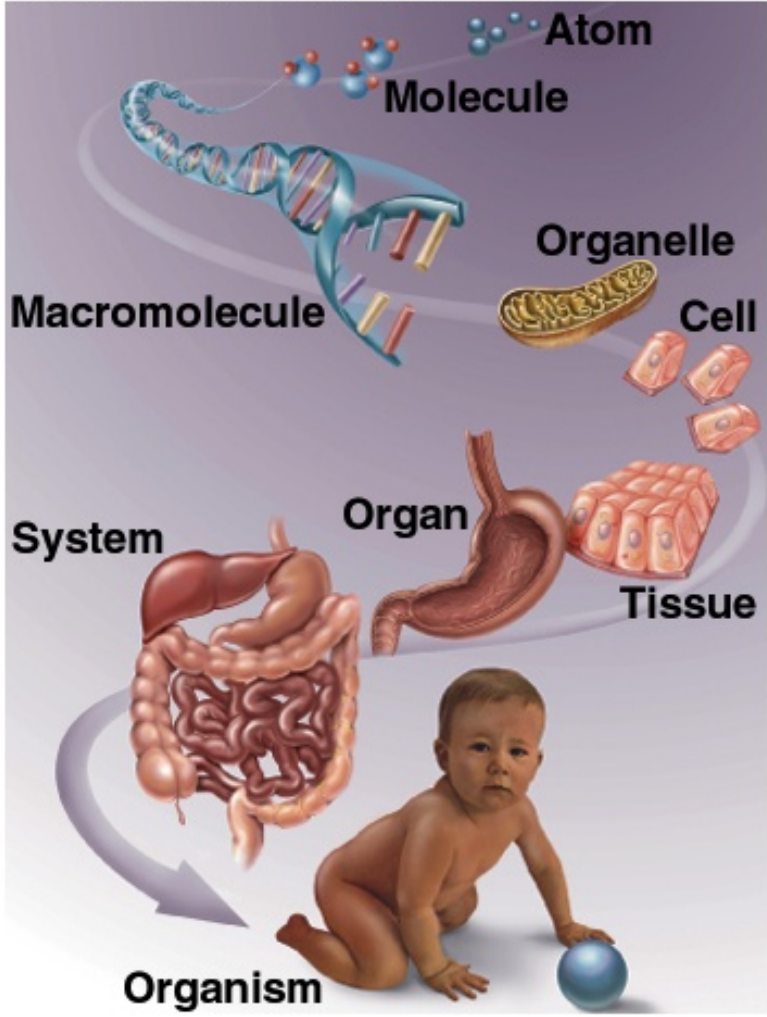
- Processing
- Membrane Transport
- Signal Transduction
- Ligand-Receptor Interaction
- Immune System

Cellular Processes

- Cell Motility
- Cell Growth and Death
- Cell Communication
- Development
- Behavior



Hierarhical organization of information – emerging properties



Genome Transcriptome Proteome Metabolome Cellome Physiome Interactome

Domain

- *Genes*
- *Promoters*
- *Gene expression*
- *Genetic networks*
- *Post-translational modifcation*
- *Protein-protein interactions*
- *Pathways*
- *Enzyme kinetics*
- *Compartments*
- *Transport*
- *Signal trans-duction*
- *Whole organ models*