Biophysics

Prof. dr hab. Inż Marek Langner
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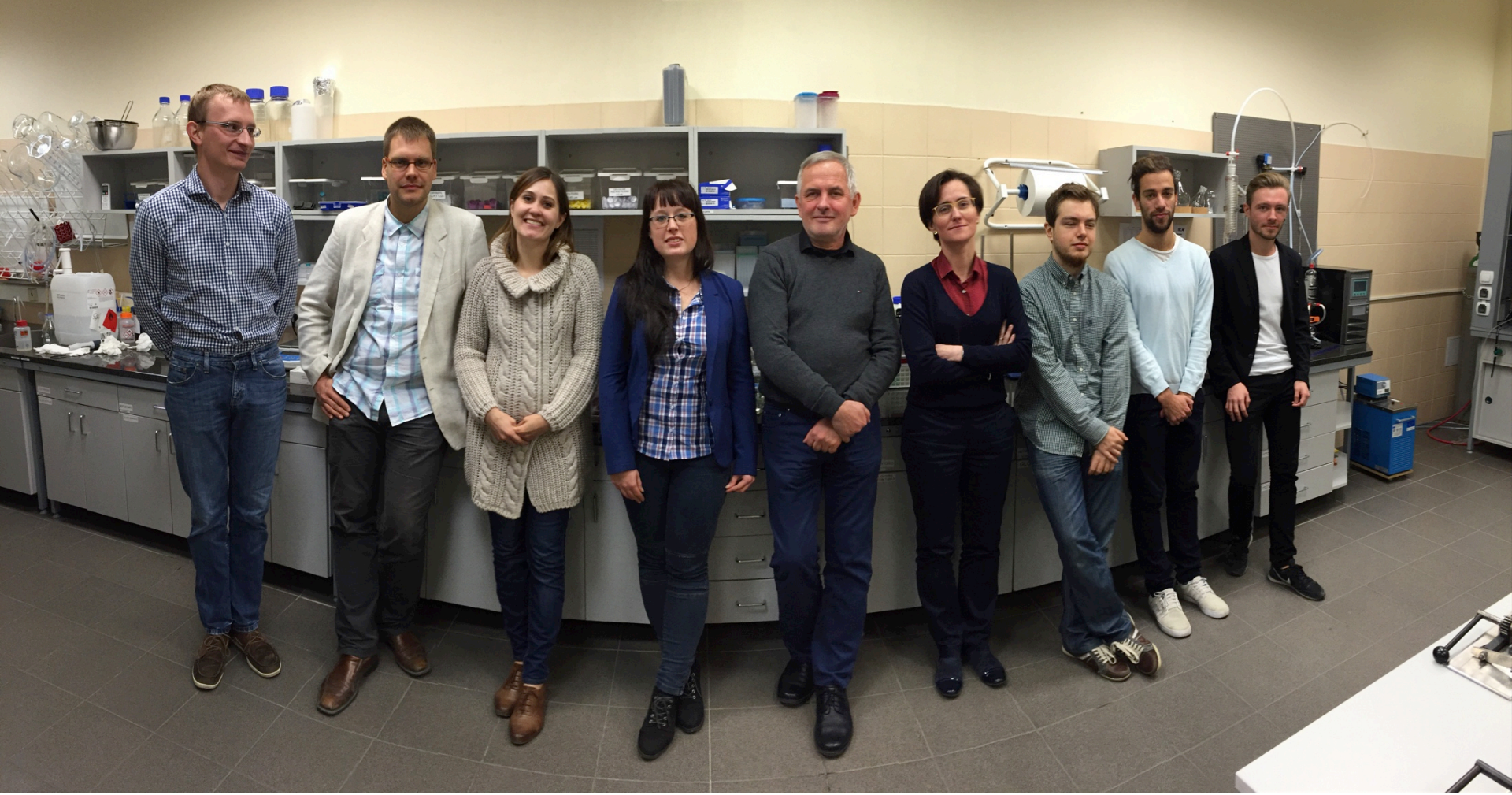
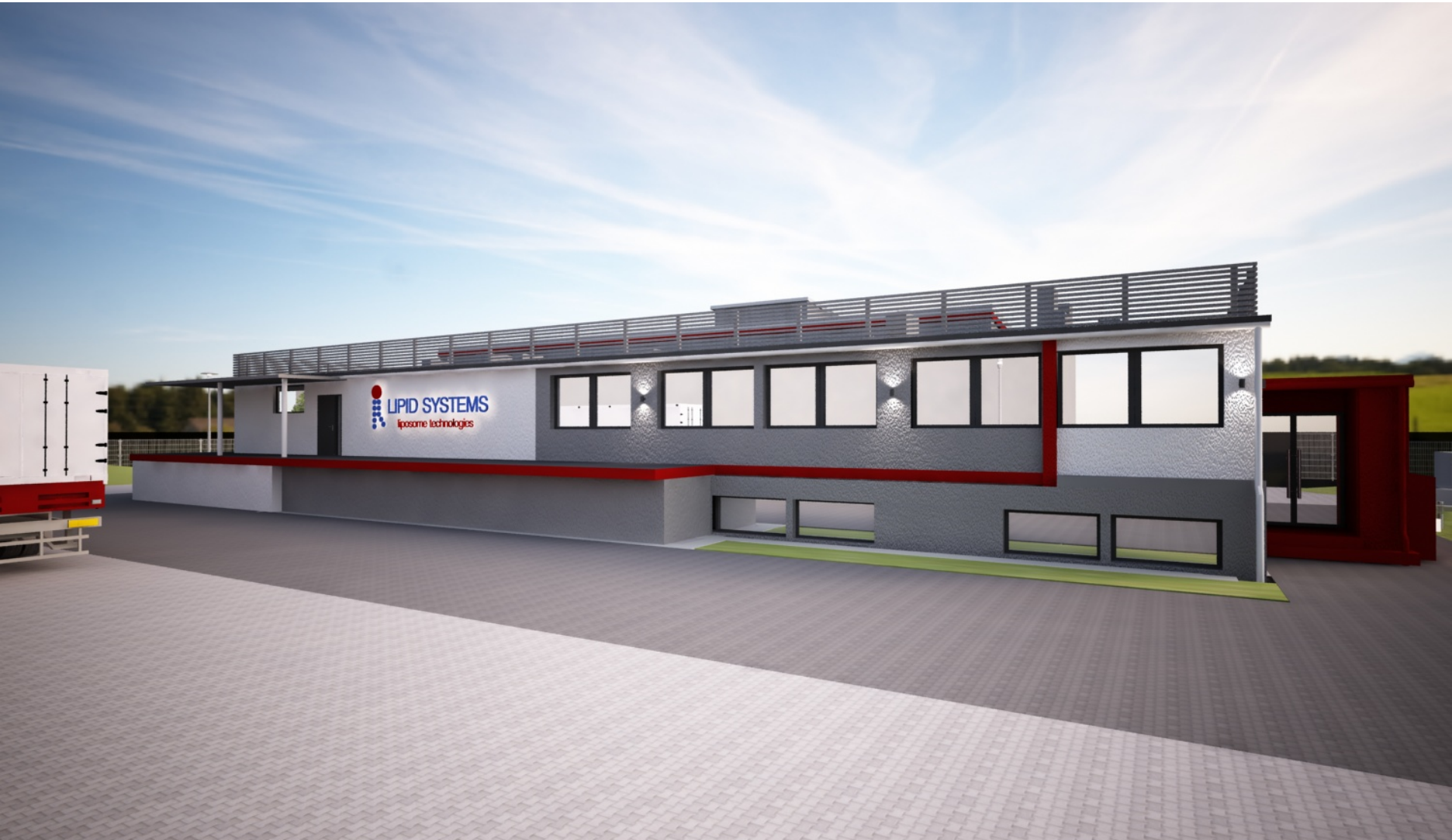
D-1, room: 8A



Laboratory for Biophysics of Macromolecular Aggregates

We are doing science in the field of biophysics of lipids and transfer acquired knowledge into practice (application of lipid aggregates in pharmacology).

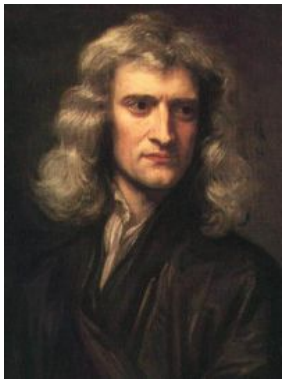


KONSULTACJE

Poniedziałek 15:00 – 17:00
Środa 13:00 – 15:00

Physics is about laws

Newton's 3 Laws (Mechanics)

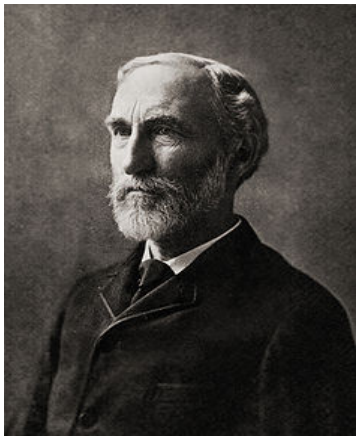


Isaac Newton
1642-1727

(Electricity & Magnetism)
Maxwell's 4 Equations

James Clerk Maxwell
1831-1879

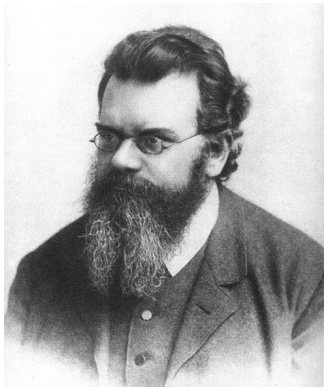
(Thermodynamics)
Gibb's Free Energy



J. Willard Gibbs
1839-1903

(Quantum Mechanics)
Schrodinger's Eq'n

Erwin Schrödinger
1887-1961



Ludwig Boltzmann 1844-1906

(Stat. Mechanics
of Entropy)

$$S = k \cdot \log W$$

Does Biology have any great theories/laws?

Charles Darwin, Age 51, 1860, On the Origin of Species

Evolution

Life evolved from simpler forms

One of the best tested scientific theories

Evolution is a series of tricks/random events

Build complex beings from simpler parts

Often many ways of doing things

Our life form is just one.

Laws of physics can explain all biological phenomena.

Problem: The phenomena are very complex

Two general approaches:

"wholistic" – entire organism or organ systems – includes sensory organs = eye, ear, taste; heart, kidney, etc, imaging methods

"component/synthesis" – structure/function of purified parts and re-assembly of complex – includes

macromolecules – protein, DNA, RNA, lipids, viruses

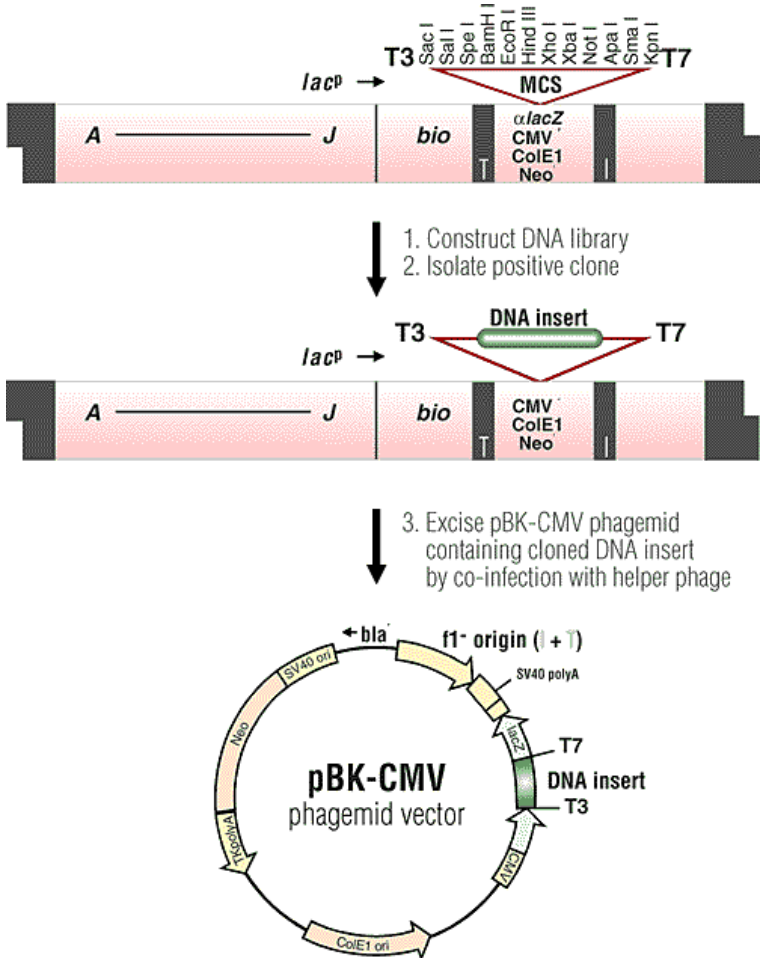
subcellular – membranes, organelles

cellular – specialized cells = muscle, nerve; motility; development; communication

Tranfsormation of biological sciences

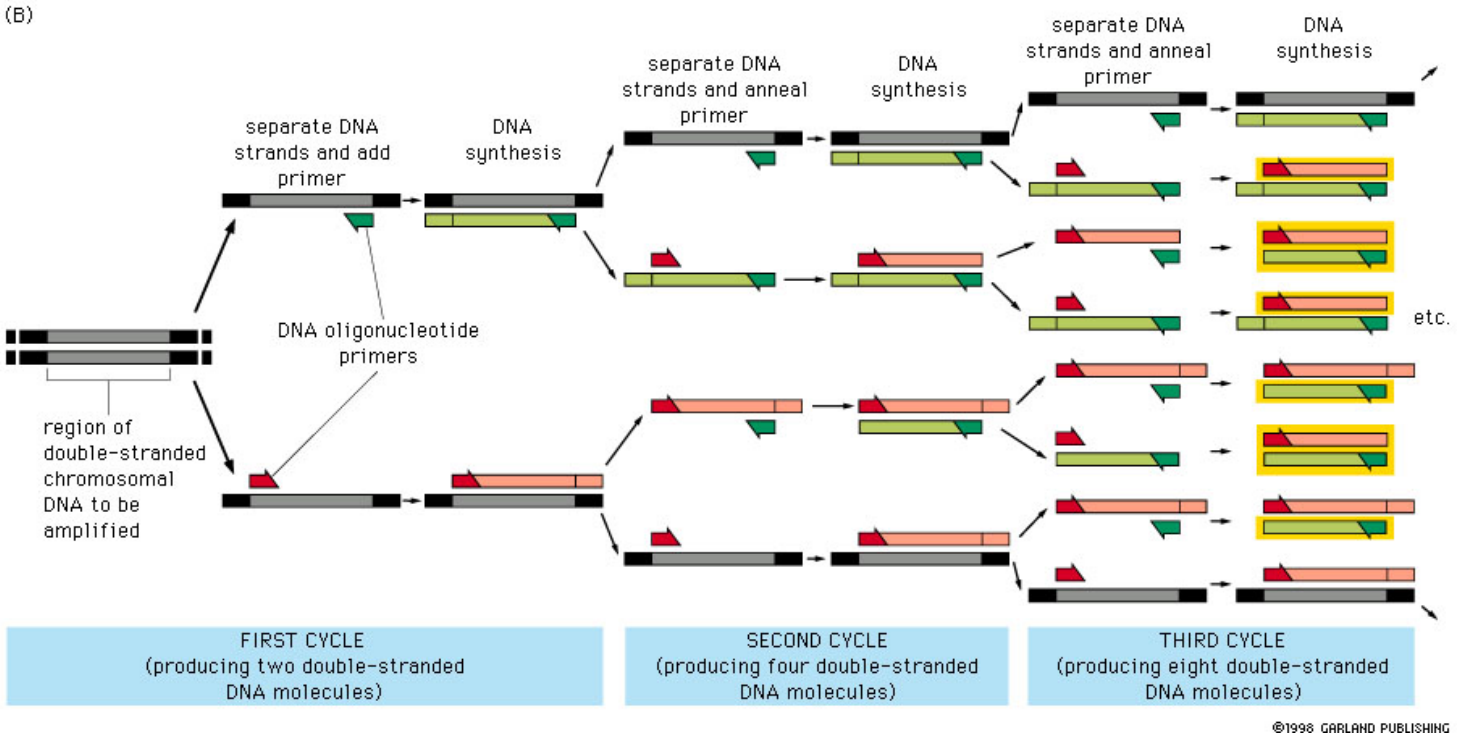
Experimental Transformation of Biology: Cutting, Inserting and Ligating

- *The Key Point: molecular manipulation of DNA both out of and in cells.*
- *The consequence: can find out how much RNA and DNA is in cells, can force cells to express genes of interest at will.*

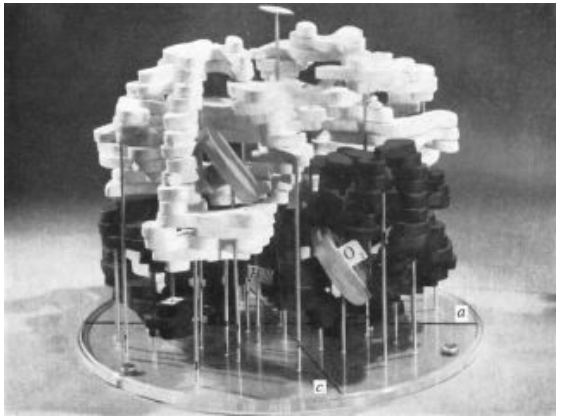


www.stratagene.com

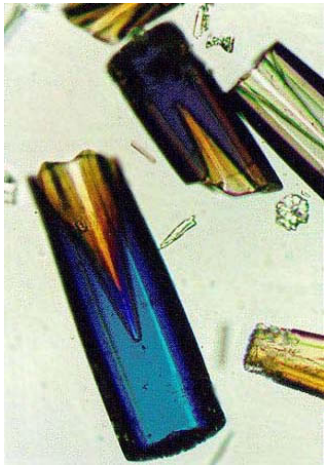
Experimental Transformation of Biology: Polymerase Chain Reaction



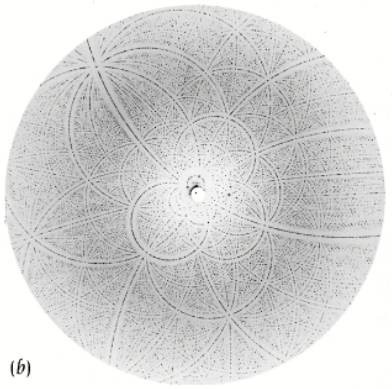
The Experimental Transformation of Biology: Molecular Structures



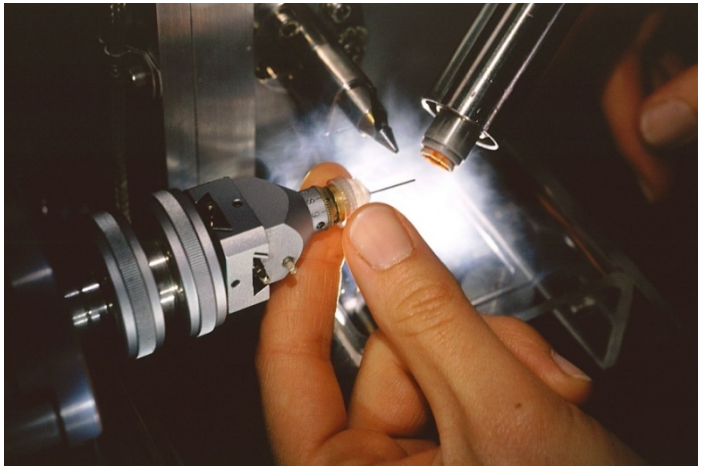
Experimental Transformation of Biology: X-Ray Crystallography of Proteins



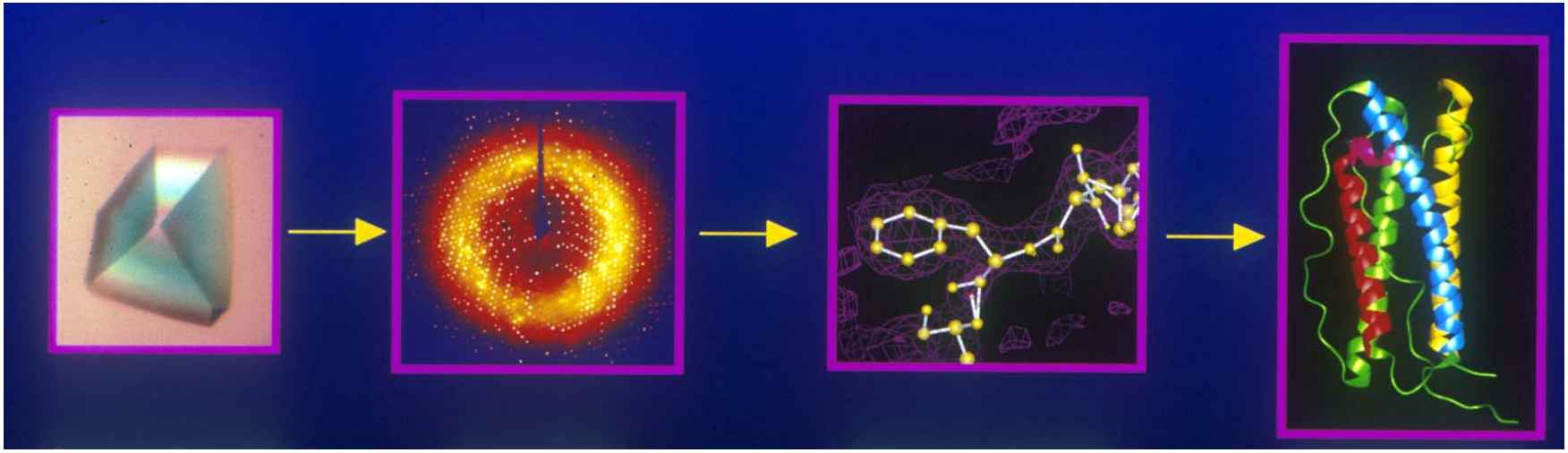
(*a*)



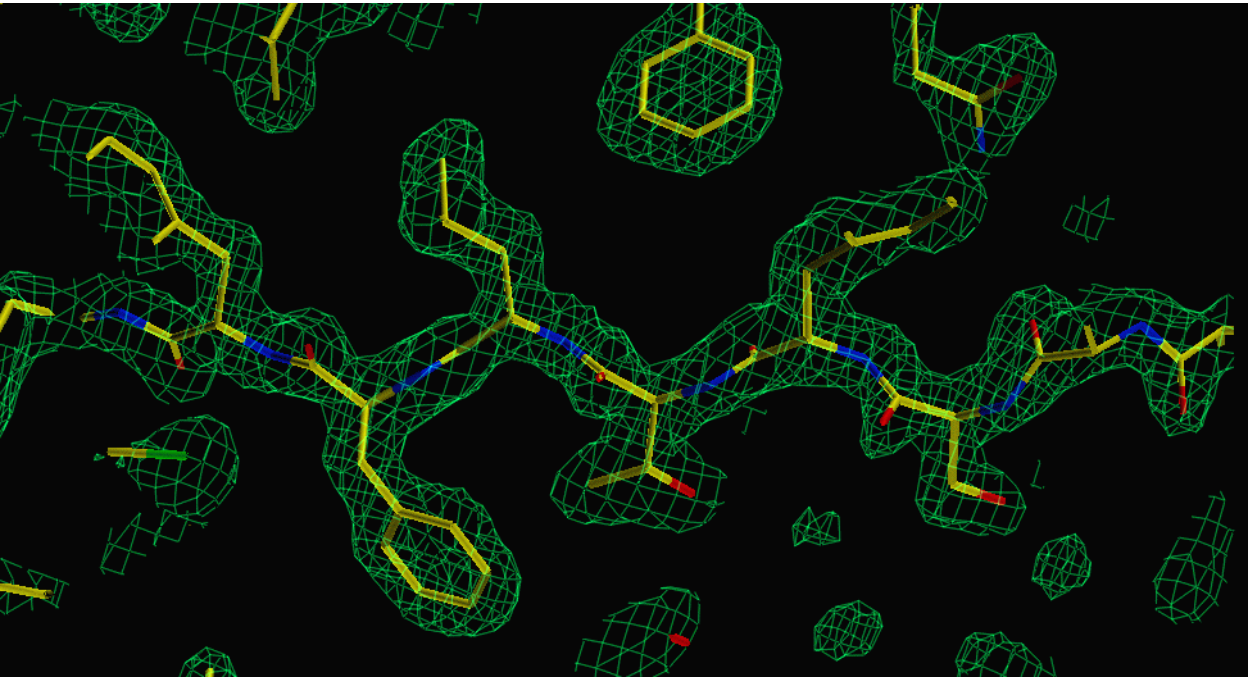
(*b*)



X-ray Crystallography

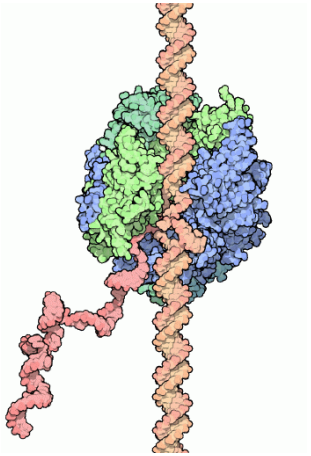


Crystal Growth | *X-ray Data* | *Electron Density* | *Protein Model*

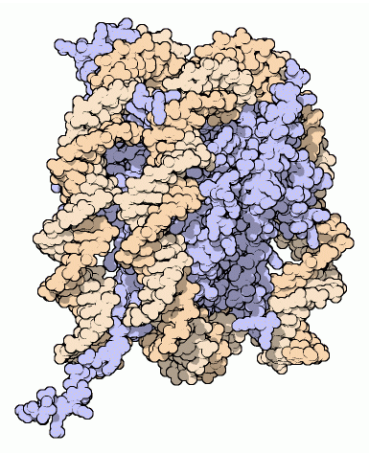


PDB Structures and PDB Files

- *Protein Data Base – the outcome from structural biology.*
- *http://www.rcsb.org/pdb/*

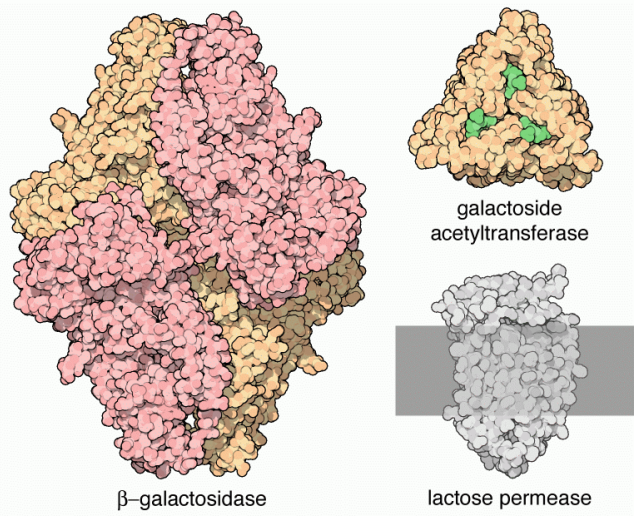


RNA polymerase



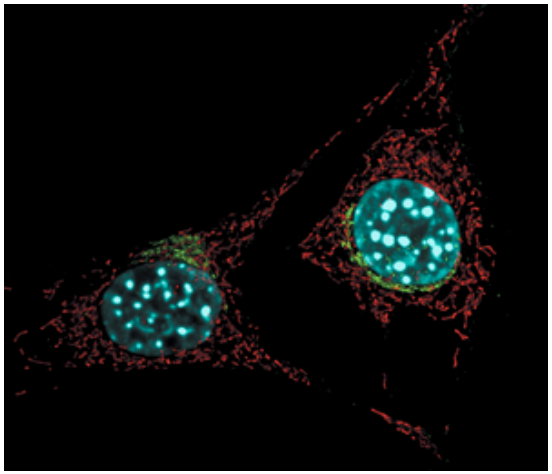
Nucleosome

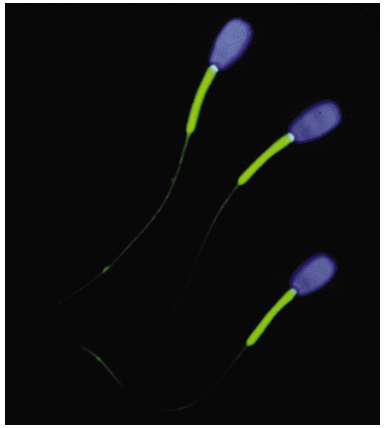
All cartoons due to David Goodsell, Scripps

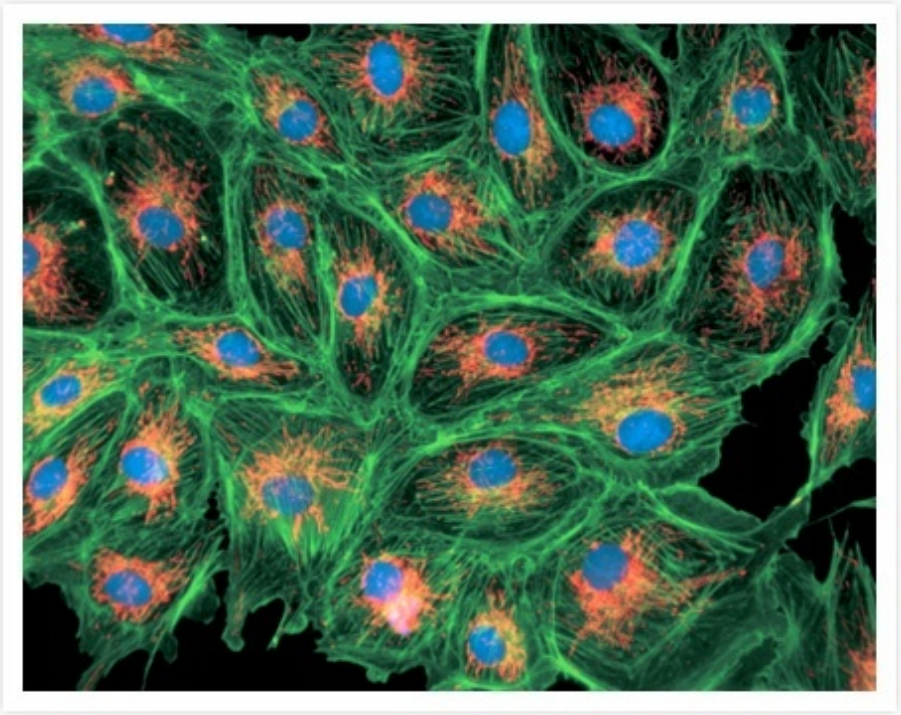


Experimental Transformation of Biology: Imaging Proteins in Live Cells

- *All figures taken from Molecular Probes gallery.*

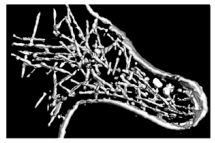




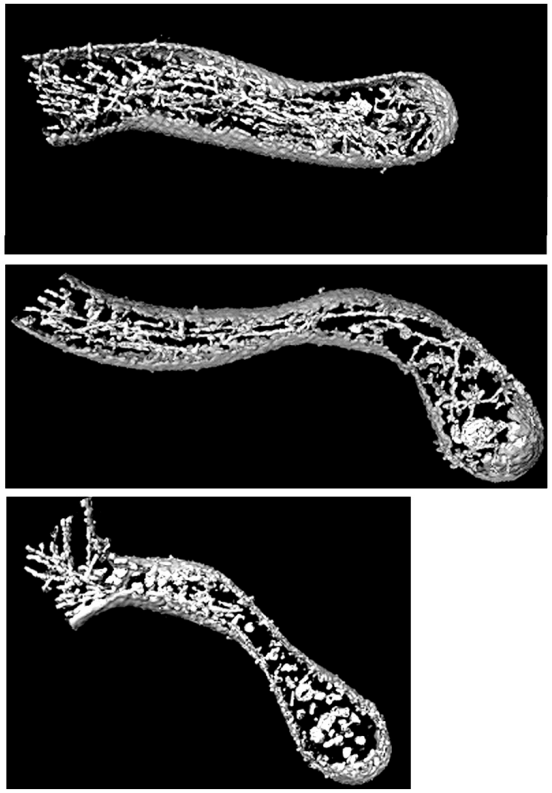


Experimental Transformation of Biology: Structures from Cryo EM

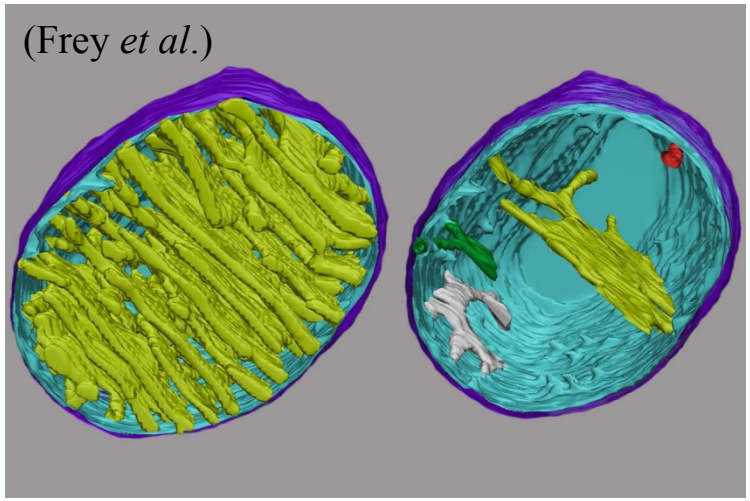
Filopodia in motile cells



(Medalia *et al*.)

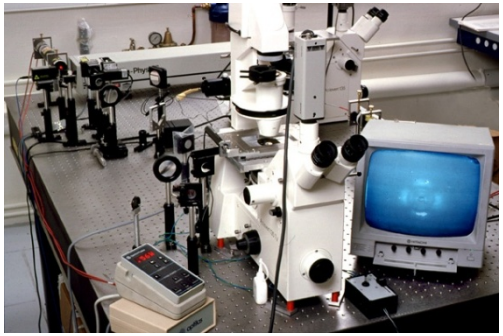


Mitochondria

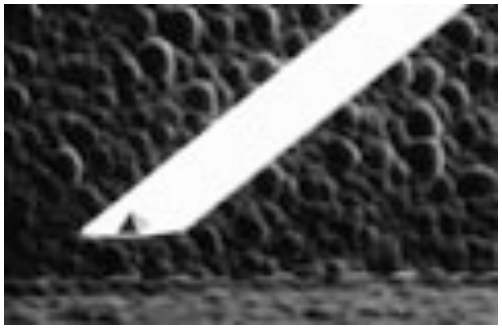


Experimental Transformation of Biology: Single Molecule Biophysics

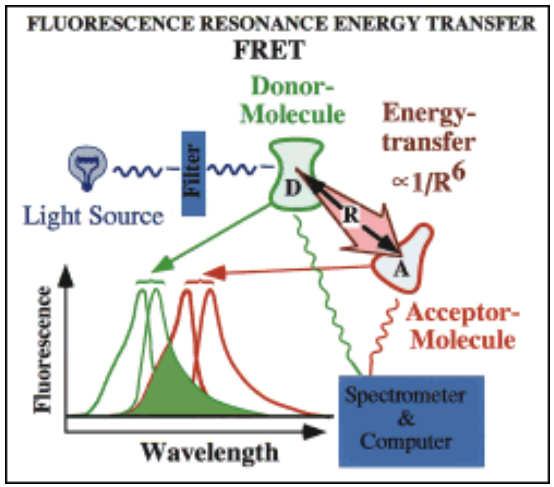
Optical Tweezers



AFM



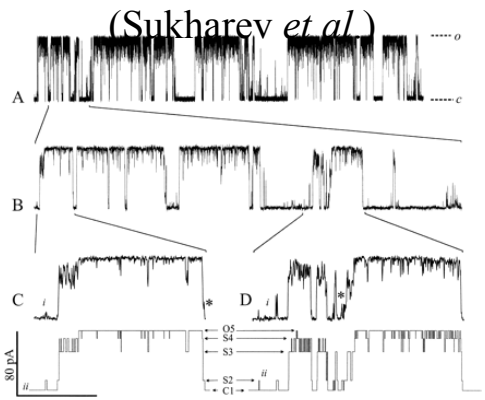
FRET



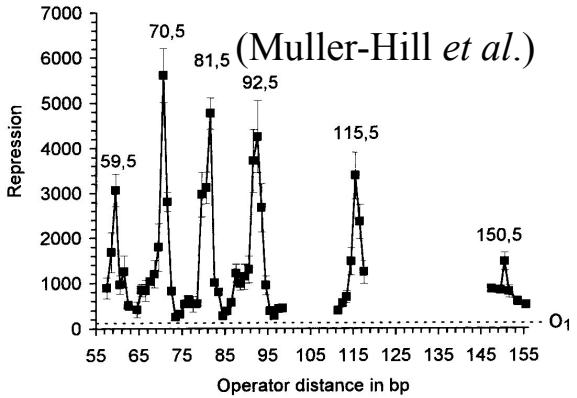
The Quantitative Outcome

Quantitative data demands quantitative models and quantitative models demand quantitative experimentation

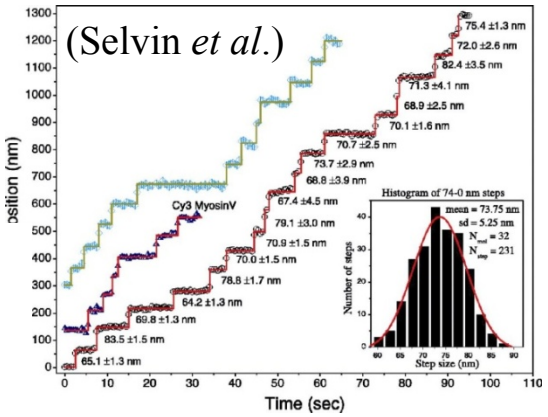
- ***Cartoon-level models deprive us of the full understanding lurking in the data.***
- ***New mode of thinking – precise understanding followed by control and synthesis.***



Ion channel dynamics



Gene regulation



Motor dynamics

Biophysics

Advanced interdisciplinary science involving: physics, biology, chemistry, mathematics.

1892: Karl Pearson (missing link between biology and physics => name biophysics),
1943: Erwin Schrodinger (Nobel Prize, 1933) lecture series: What is Life
1946: Biophysics Research Unit, King's College, London, hire physicists to work on questions of biological significance; Maurice Wilkins, Rosalind Franklin: X-ray diffraction of DNA
1953: Francis Crick (particle physicist turned into biophysicist at Cambridge) and James Watson (biologist): double helix structure of DNA
1957: The Biophysical Society founded

What is the goal of biophysics?

(1) Create simplified models of biological systems

(2) Make quantitative predictions

(3) Experimentally test quantitative predictions

Biophysical topics based on relative size of the subject:

- molecular and subcellular biophysics
- physiological and anatomical biophysics
- environmental biophysics

Molecular and Subcellular Biophysics

- The Structure and Conformation of Biological Molecules
- Structure Function Relationships
- Conformational Transitions
- Ligand Binding and Intermolecular Binding
- Diffusion and Molecular Transport
- Membrane Biophysics
- DNA and Nucleic Acid Biophysics
- Protein Biophysics
- Energy Flow and Bioenergetics
- Thermodynamics
- Statistical Mechanics
- Kinetics
- Molecular Machines
- Allosterics – molecular crowding

Molecular and Subcellular Biophysics

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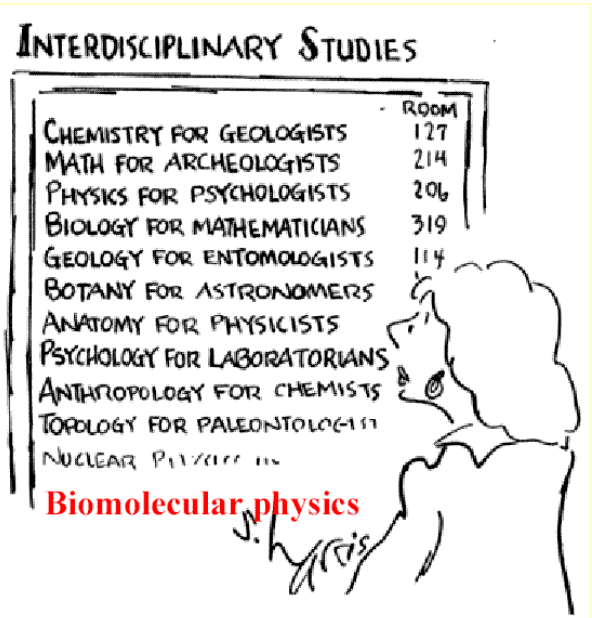


Suggested reading

Podstawy Biologii Komórki

Bruce **Alberts**, Dennis Bray, Karen Hopkin, Alexander Johnson, Julian Lewis , Martin Raff, Keith Roberts, Peter Walter PWN 2009.

The Chemistry of Life

Steven Rose. Penguin, London 1999.

Physical Chemistry

(5th edition). P.W. Atkins. Oxford University Press, 1994.

Biofizyka - Podręcznik dla studentów

(2002) pod red. F.Jaroszyka, Wydawnictwo PZWL

Molecular Cell Biology

by Lodish et al. (6th or 5th Edition) Freeman & Co., 2007 or 2004

Physical Biology of the Cell

by *Rob Phillips, Jane Kondev and Julie Theriot*. Garland Science 2008

Biological Physics. Energy, Information, Life

by Philip Nelson Freeman & Co., 2004

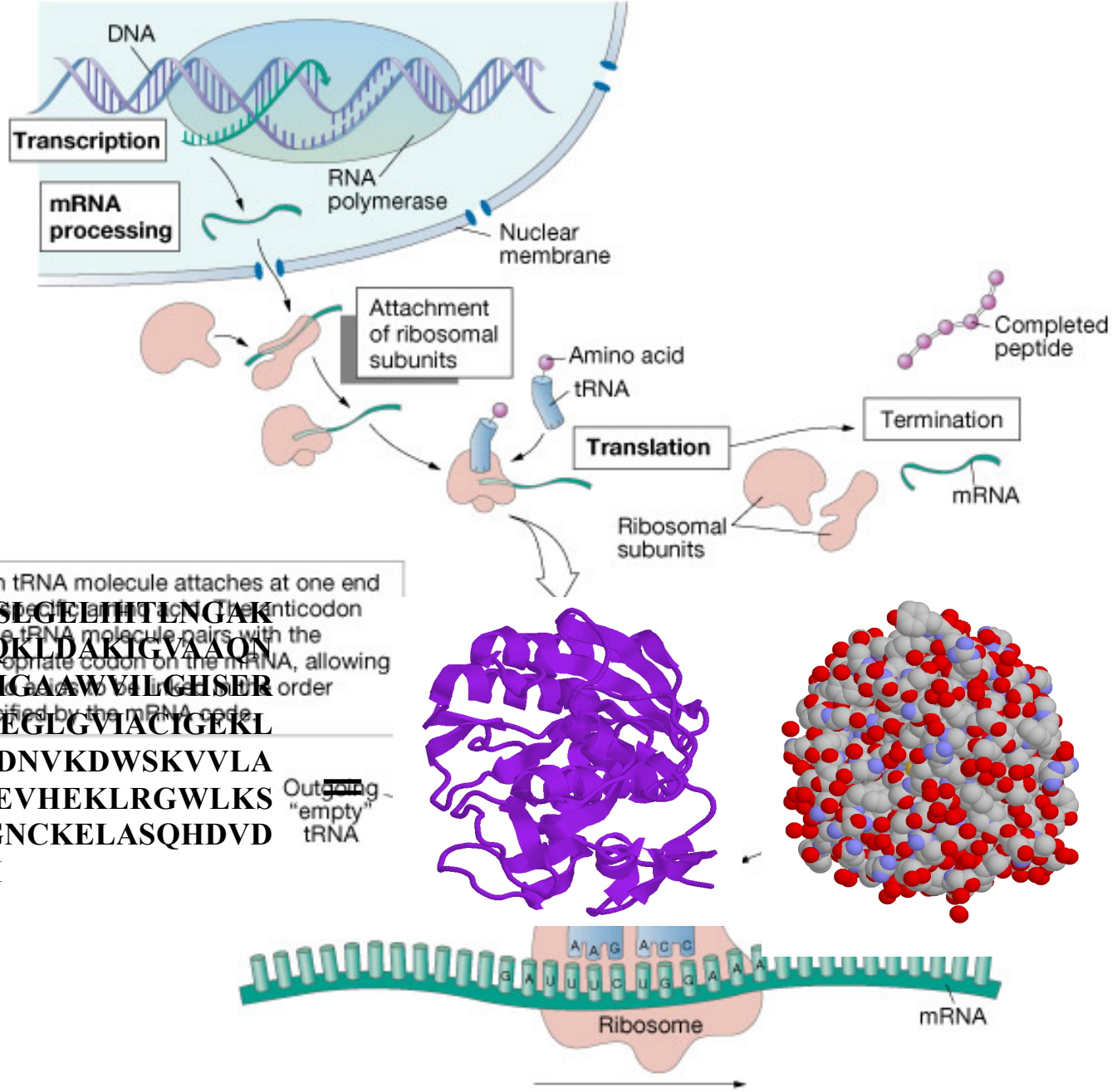
Molecular and Cellular Biophysics

by Meyer Jackson Cambridge University Press, 2006

Mechanics of Motor Proteins and Cytoskeleton

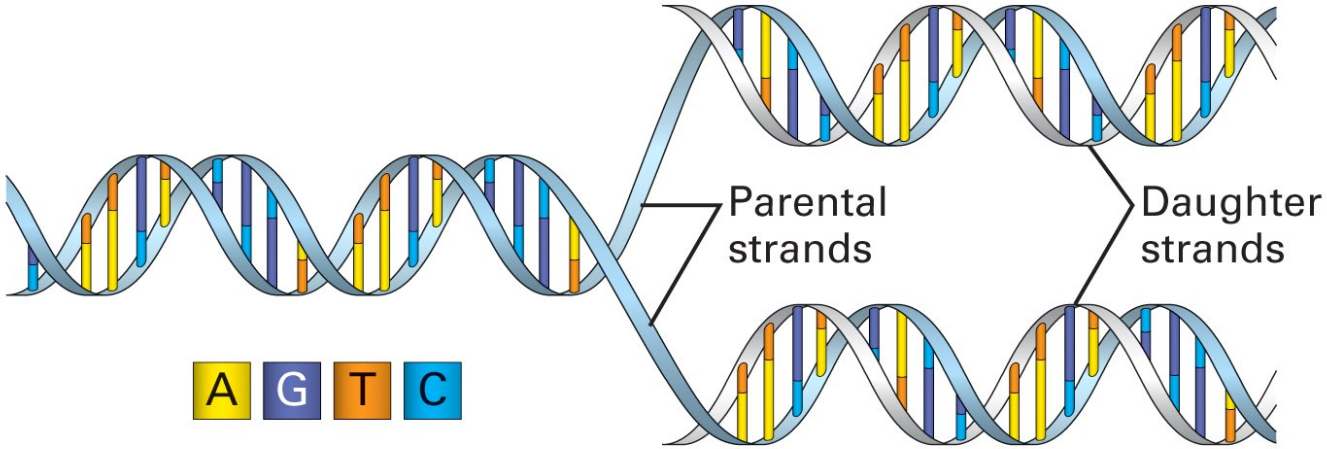
by Jonathan Howard Sinauer, 2001

The main dogma of biology

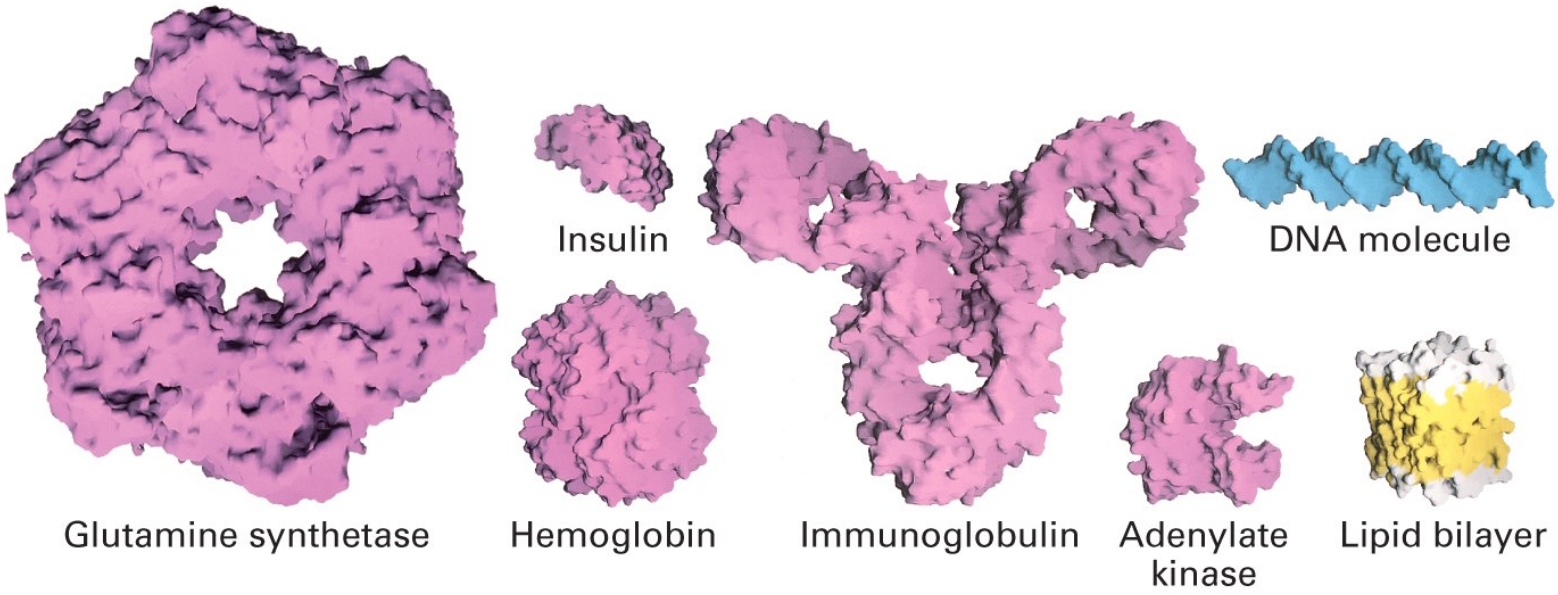


APRKFFVGGNWKMNGDKKSLGELIHTLNGAK
LSADTEVVCGAPSIYLDFARQKLDAKIGVAAQN
CYKVPKGAFTGEISPAMIKDIGAAWVILGHSER
RHVFGESDELIGQKVAHALAEGLGVIACIGEKL
DEREAGITEKVVFEQTKAIADNVKDWSKVVLA
YEPVWAIGTGKTATPQQAQEVHEKLRGWLKS
HVSDAVAQSTRIIYGGSVTGGNCKELASQHDVD
GFLVGGASLKPEFVDIINAKH

DNA: Legislative Branch



Proteins: Executive Branch



Length scales

Electron orbital ~0.1 Å
Covalent bond ~1Å
Hydrogen bond ~ 3.5Å

MEMS – Micro Electro Mechanical devices 10 – 100 μm

10^{-11} 10^{-10} 10^{-9} 10^{-8} 10^{-7} 10^{-6} 10^{-5} 10^{-4} 10^{-3} 10^{-2} 10^{-1} 1 10m

"nano" world

The scale of things

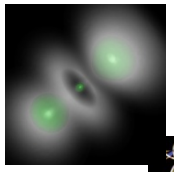
Radiation:

soft X-ray

UV

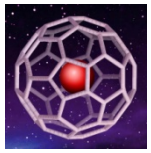
infrared

microwave

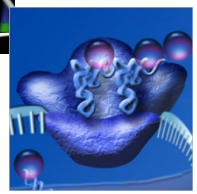


H ~1Å

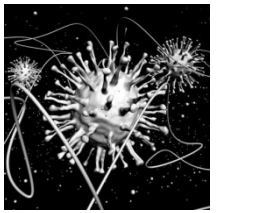
DNA (d~2 nm)



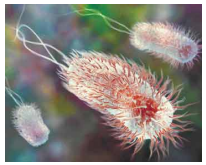
carbon buckyball (d~1 nm)



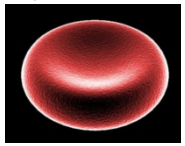
ribosome (~20x30 nm)



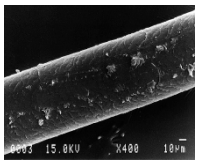
large virus (~100 nm)



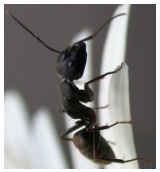
E. coli (~2 μm)



Red blood cell (~2-5 μm)



hair (~0.1 mm)



ant (~5 mm)

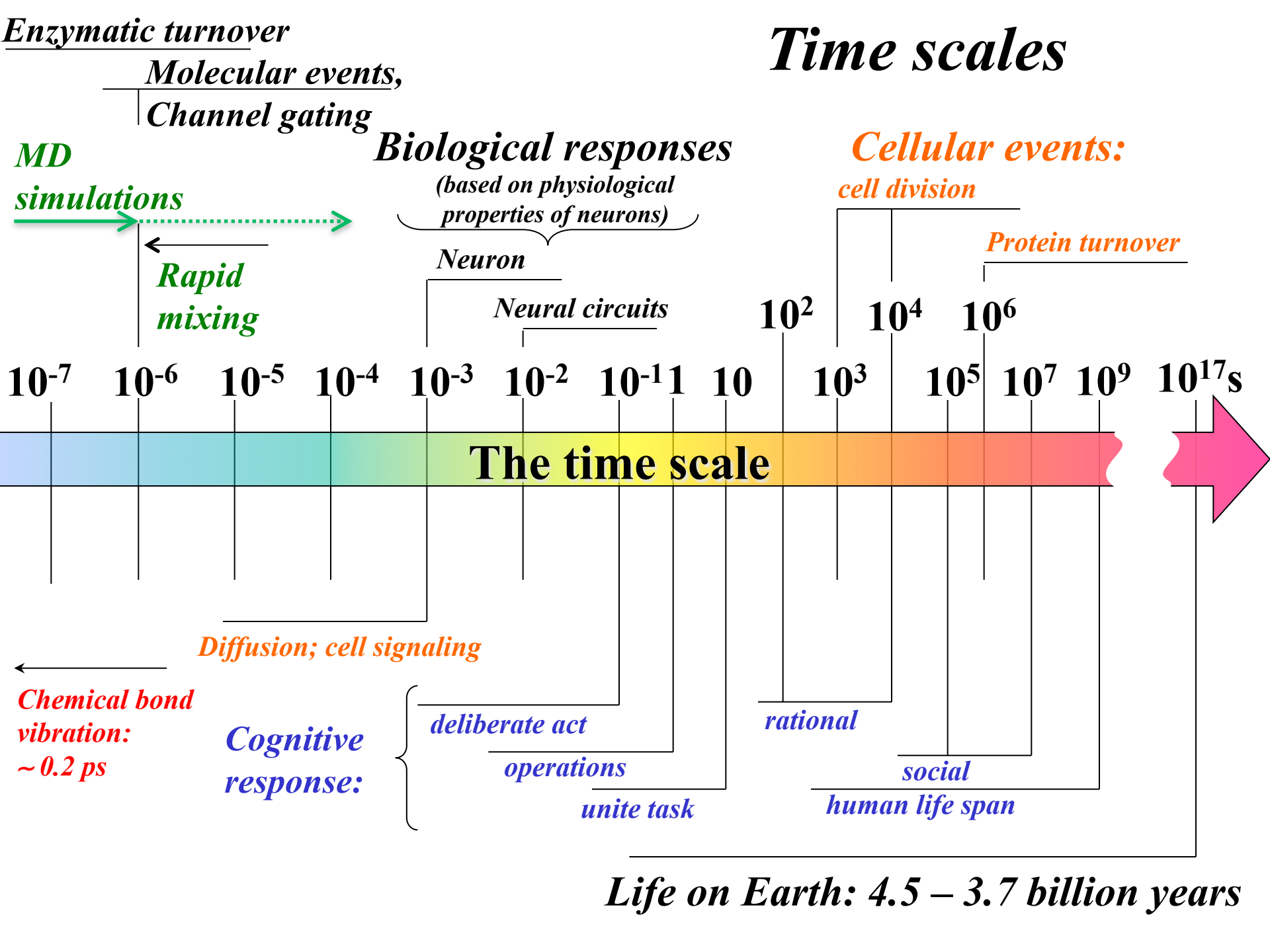
human (~1.5 – 2m)

Electron microscopy

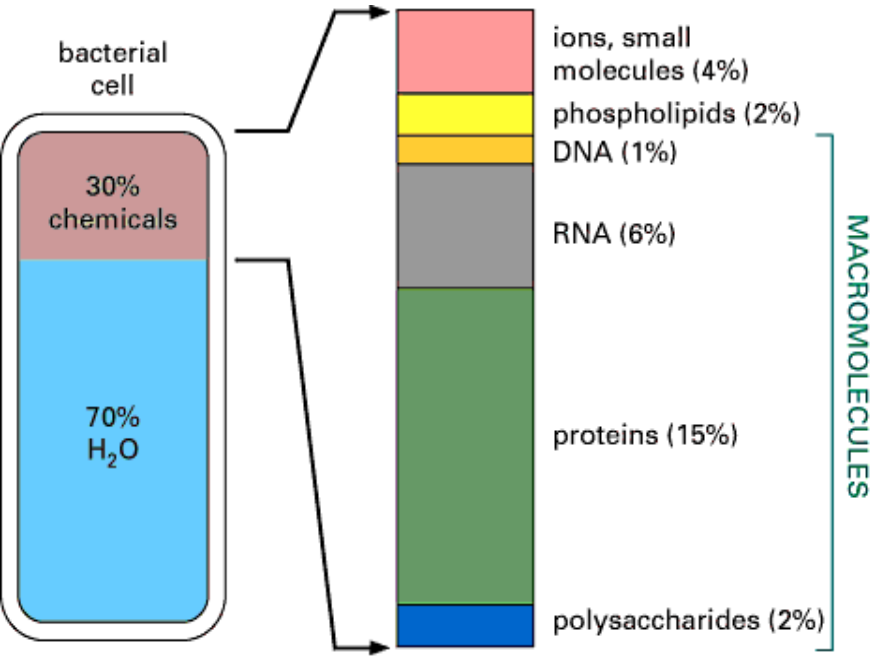
CryoEM

light microscopy

Time scales


Enzymatic turnover
Molecular events,
Channel gating
MD simulations
Rapid mixing
Biological responses
(based on physiological properties of neurons)
Neuron
Neural circuits
Cellular events:
cell division
Protein turnover
10^2
10^4
10^6
10^-7
10^-6
10^-5
10^-4
10^-3
10^-2
10^-1
1
10
10^3
10^5
10^7
10^9
10^17s
The time scale
Diffusion; cell signaling
Chemical bond vibration: ~0.2 ps
Cognitive response:
deliberate act
operations
unite task
rational
social
human life span
Life on Earth: 4.5 – 3.7 billion years

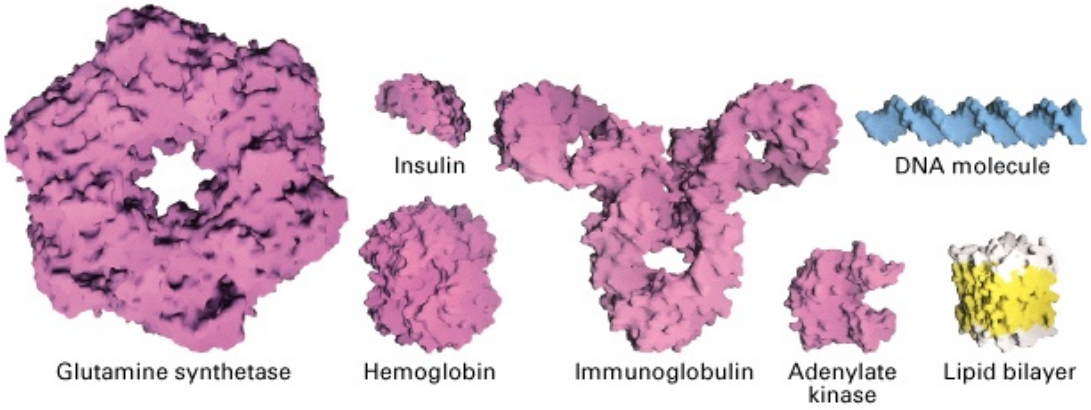
Molecular Composition of Cells

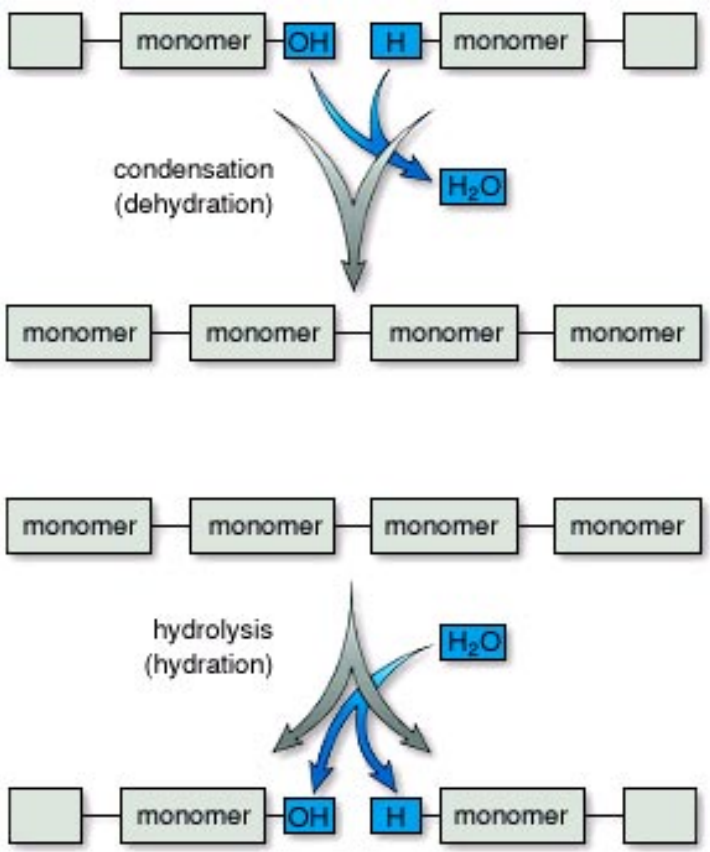


Molecular Components of an *E. coli* Cell

	Percentage of total weight of cell	Approximate number of different molecular species
Water	70	1
Proteins	15	3,000
Nucleic acids		
DNA	1	1
RNA	6	>3,000
Polysaccharides	3	5
Lipids	2	20
Monomeric subunits and intermediates	2	500
Inorganic ions	1	20

Biochemical Toolkits





building blocks of the cell	larger units of the cell
SUGARS	POLYSACCHARIDES
FATTY ACIDS	FATS/LIPIDS/MEMBRANES
AMINO ACIDS	PROTEINS
NUCLEOTIDES	NUCLEIC ACIDS

Nucleic acids

Coding information.

Proteins

The main and most evolutionary stable property of a protein is not the exact sequence of amino acids that make it up, nor the exact folding process, but its collection of surface features that determine its function.

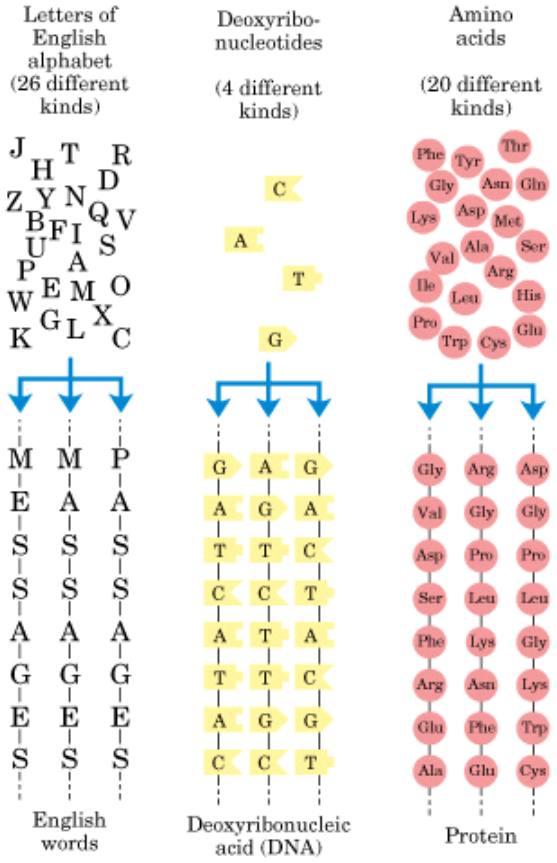
Lipids

Membranes are containers, but with an active surface that acts as an interface to its contents.

Carbohydrates

They form unique surface structures that are subject to recognition.

For a segment of 8 subunits, the number of different sequences possible =



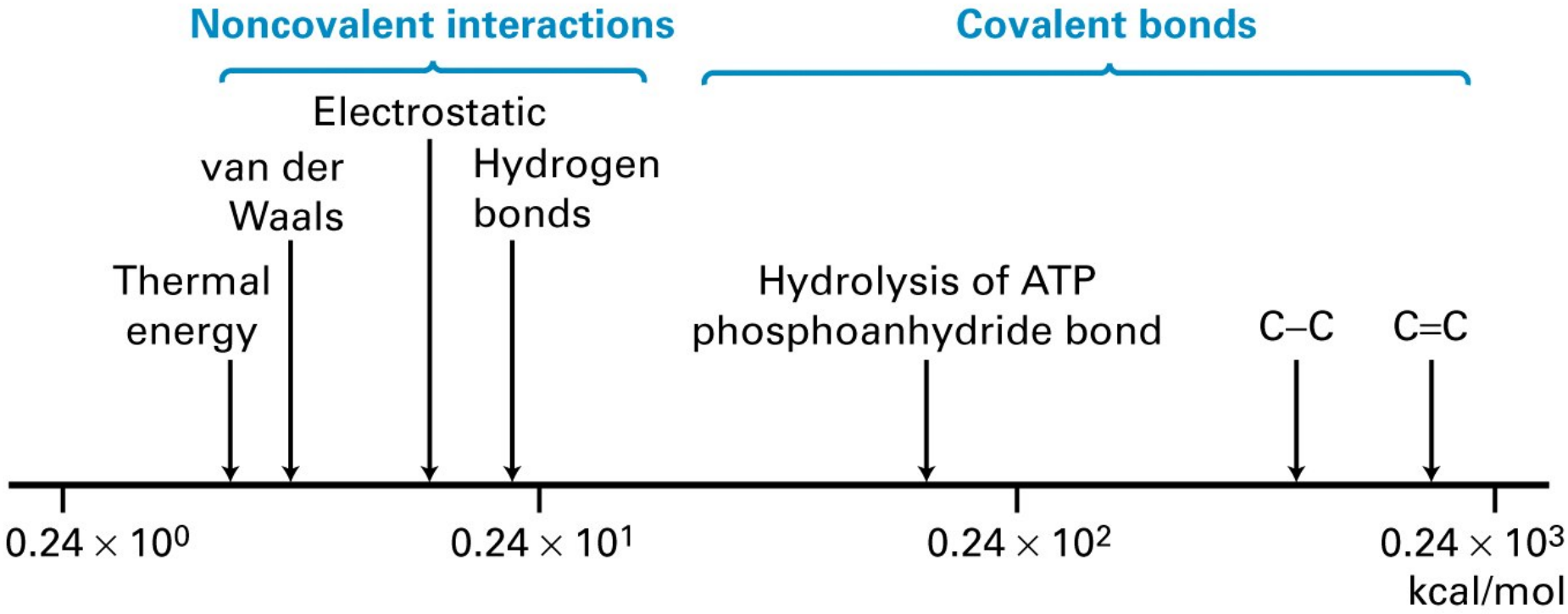
$26^8 = 2.1 \times 10^{11}$

$4^8 = 6.6 \times 10^4$

$20^8 = 2.56 \times 10^{10}$

Energy

Conformational changes	***1-10 kT***
Protein Folding	***6 - 30 kT***
Biotin-Avidin bond	***35 kT***



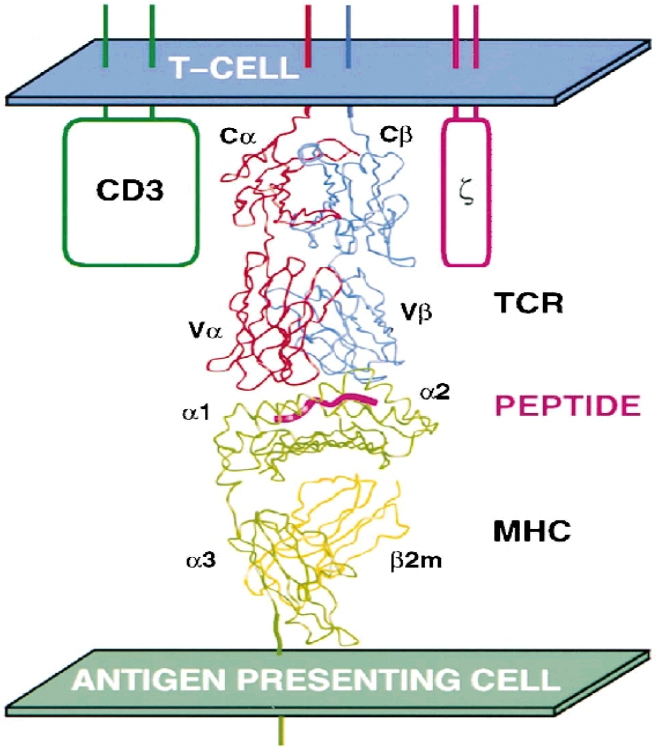
Biomolecular structure is determined by a combination of covalent and noncovalent bonds.

*Covalent bonds are static entities which are little effected by environment – **stability**.*

*Noncovalent bonds exist in a dynamic equilibrium - **flexibility**.*

Strengths of Bonds Common in Biomolecules

Type of bond	Bond dissociation energy* (kJ/mol)	Type of bond	Bond dissociation energy (kJ/mol)
Single bonds		**Double bonds**	
O—H	461	C═O	712
H—H	435	C═N	615
P—O	419	C═C	611
C—H	414	P═O	502
N—H	389		
C—O	352	**Triple bonds**	
C—C	348	C≡C	816
S—H	339	N≡N	930
C—N	293		
C—S	260		
N—O	222		
S—S	214		



Hierarhical organization of information in a cell

Sequence: Sequence of DNA and Proteins

Structure: 3D Structure of Proteins and other biomolecules and molecular complexes

Interactions: How molecules interact