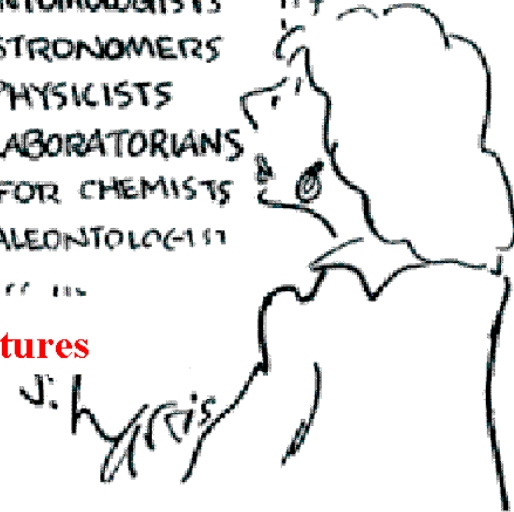


prof.. Marek Langner,  
Wrocław University of Technology  
and Sciences,  
Tel. 320-23-84  
D-1, room: 219/2 or 8A

## INTERDISCIPLINARY STUDIES

	ROOM
CHEMISTRY FOR GEOLOGISTS	127
MATH FOR ARCHEOLOGISTS	214
PHYSICS FOR PSYCHOLOGISTS	206
BIOLOGY FOR MATHEMATICIANS	319
GEOLOGY FOR ENTOMOLOGISTS	114
BOTANY FOR ASTRONOMERS	
ANATOMY FOR PHYSICISTS	
PSYCHOLOGY FOR LABORATORIANS	
ANTHROPOLOGY FOR CHEMISTS	
TOPOLOGY FOR PALEONTOLOGISTS	
NUCLEAR PHYSICS	

**Bionanostructures**



E-mail: [marek.langner@pwr.edu.pl](mailto:marek.langner@pwr.edu.pl)

# *Bio-nano-structures*

# *Nanoscience - Studying INDIVIDUAL nanometer scale things*

- From NNI (**National Nanotechnology Initiative**) The Initiative and its Implementation Plan :
- The essence of nanotechnology is the ability to work at the molecular level, atom by atom, to create large structures with fundamentally new molecular organization. Compared to the behavior of isolated molecules of about 1 nm ( $10^{-9}$  m) or of bulk materials, behavior of structural features in the range of about  $10^{-9}$  to  $10^{-7}$  m (**1 to 100 nm** - a typical dimension of 10 nm is 1,000 times smaller than the diameter of a human hair) exhibit important changes. Nanotechnology is concerned with materials and systems whose structures and components exhibit novel and significantly improved physical, chemical, and biological properties, phenomena, and processes due to their nanoscale size.

# *National technology for the 21<sup>st</sup> century: Leading to a new industrial revolution*

## Initiatives:

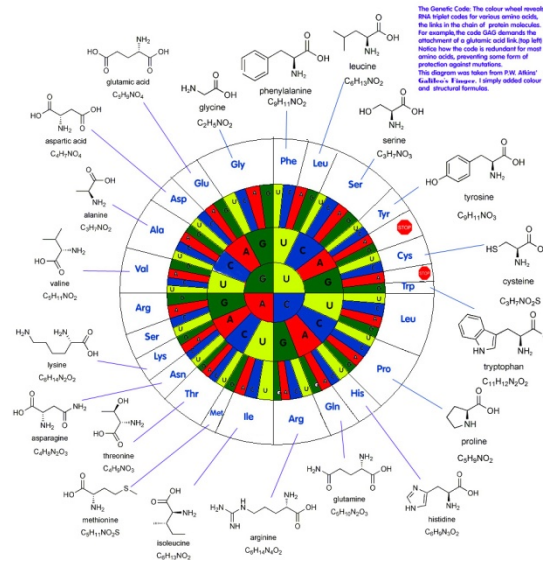
1. Research on fundamental understanding and discoveries.
2. Design of nanostructured materials.
3. Nanodevices: information, bio, medical.
4. Applications of nanomaterials and devices to energy, health, environment, and security.
5. Education of a new generation of skilled workers.

# The “Great Ideas of Old Biology”



## Cell Theory

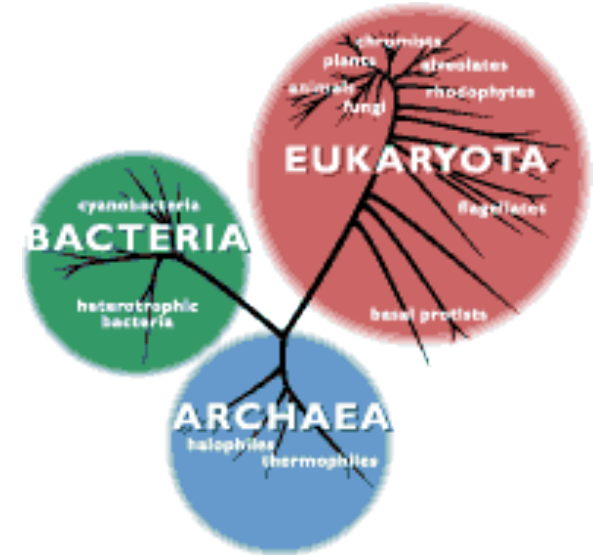
- Living organisms made of cells - not always obvious.
- Cellular diversity.
- The great domains of life.



The Genetic Code: The colour wheel reveals that triplet codes for amino acids exist, the links in the chain of protein molecules. For example, the code GAG demands the attachment of a glutamic acid link (top left). Notice how the code is redundant for most amino acids, preventing some form of protection against mutation. This diagram was taken from P.M. Adder, 'Genetics', 1980. I simply added colour and structural formulae.

## Biochemical Unity

- Universality of the genetic code.
- Metabolic similarities and differences.



## The Theory of Evolution

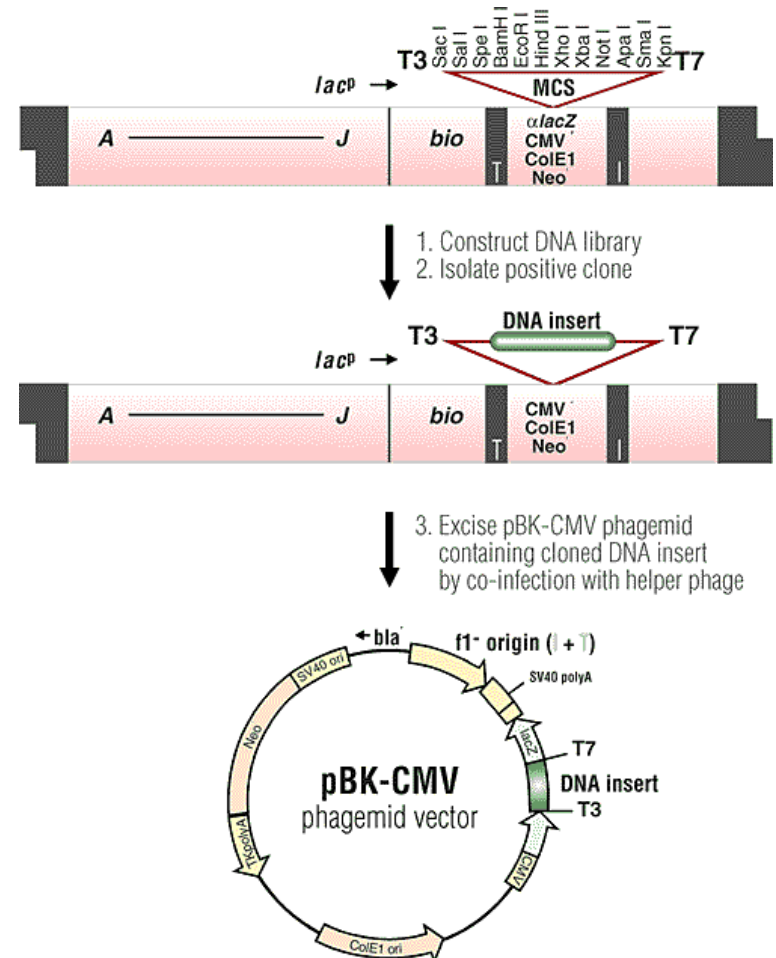
- The ingredients of evolution: variation and selection.
- “Nothing in biology makes sense except in the light of evolution.” -Dobzhansky



# Experimental Transformation of Biology: Cutting, Inserting and Ligating

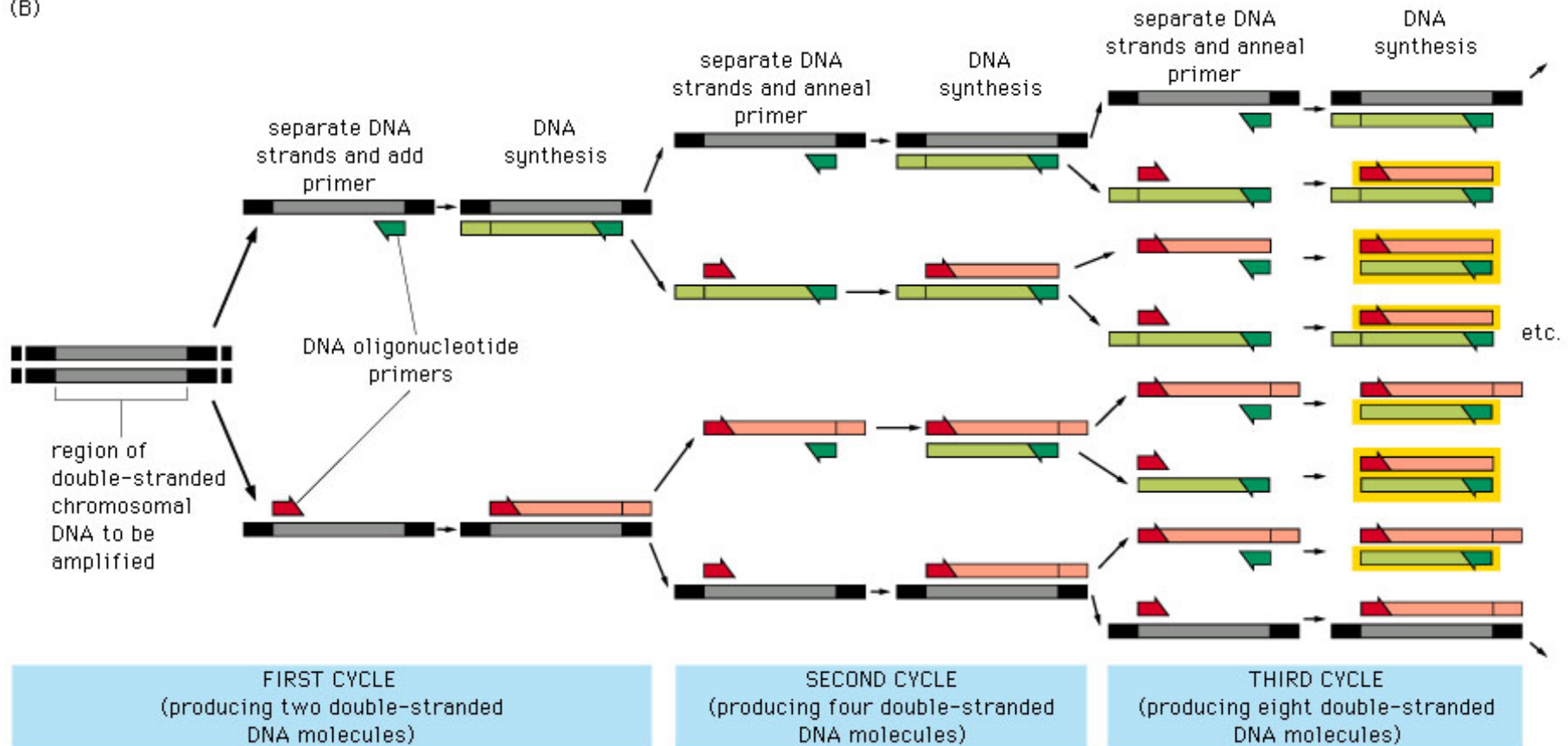
*The Key Point: molecular manipulation of DNA both out of and in cells.*

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

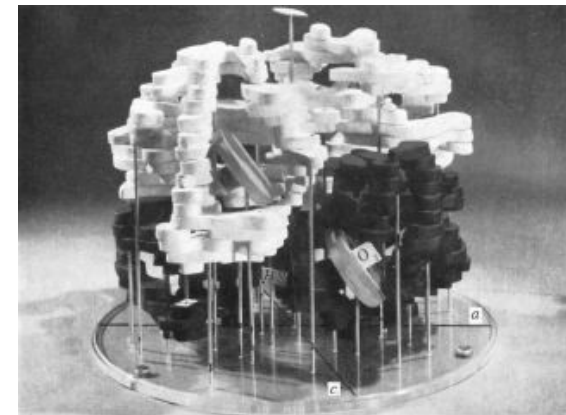
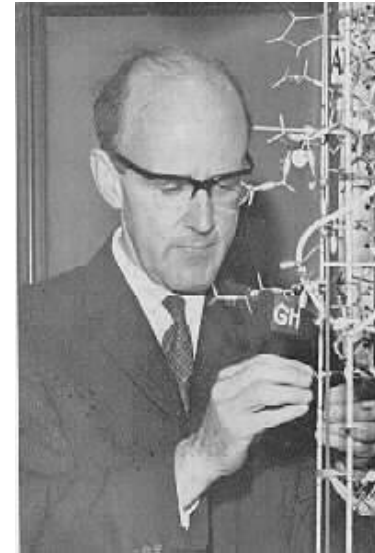
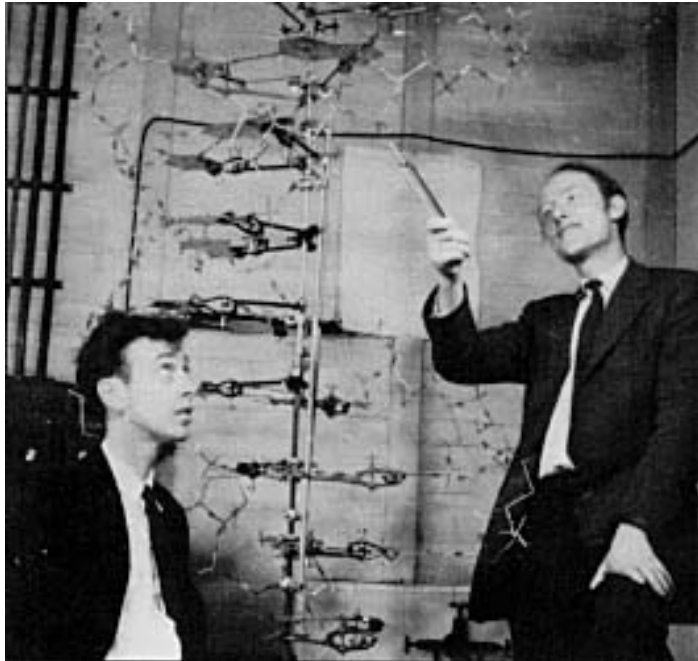


# Experimental Transformation of Biology: Polymerase Chain Reaction

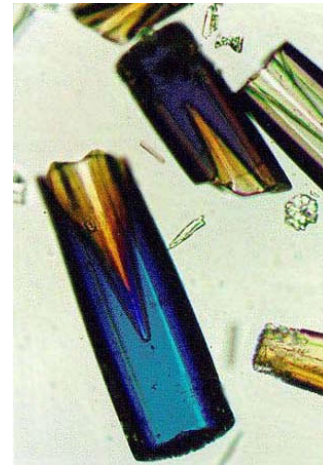
(B)



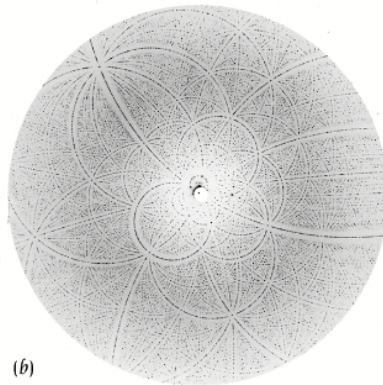
# The Experimental Transformation of Biology: Structure of Molecules



# Experimental Transformation of Biology: X-Ray Crystallography of Proteins



(a)



(b)

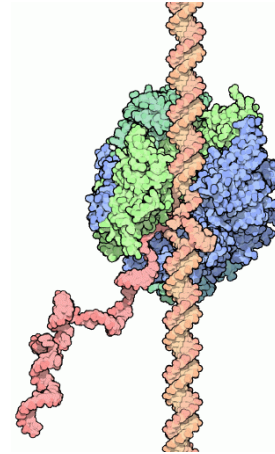
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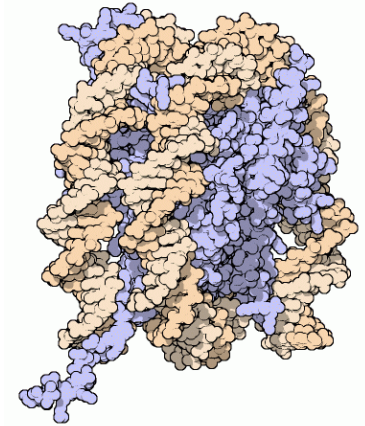
# PDB – Proteins Data Base

*The Outcome from Structural Biology: Boat loads of atomic coordinates.*

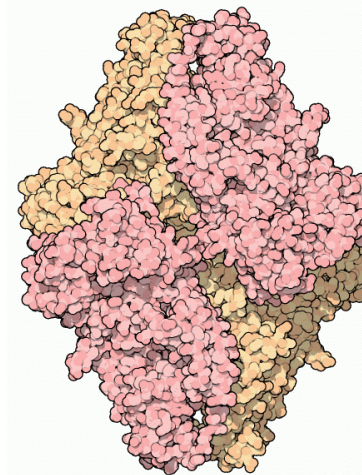
*“A science is built up of facts as a house is built up of bricks, but a mere accumulation of facts is no more a science than a pile of bricks is a house.” – Poincare*



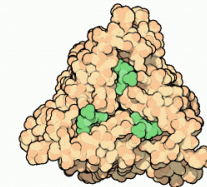
*RNA polymerase*



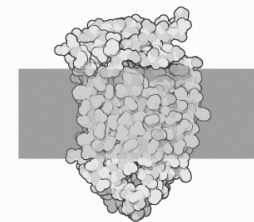
*Nucleosome*



*β-galactosidase*



*galactoside  
acetyltransferase*

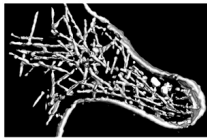


*lactose permease*

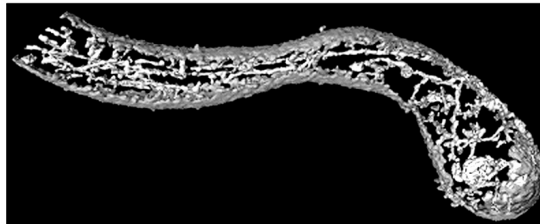


# Experimental Transformation of Biology: Structures from Cryo EM

## *Filopodia in motile cells*

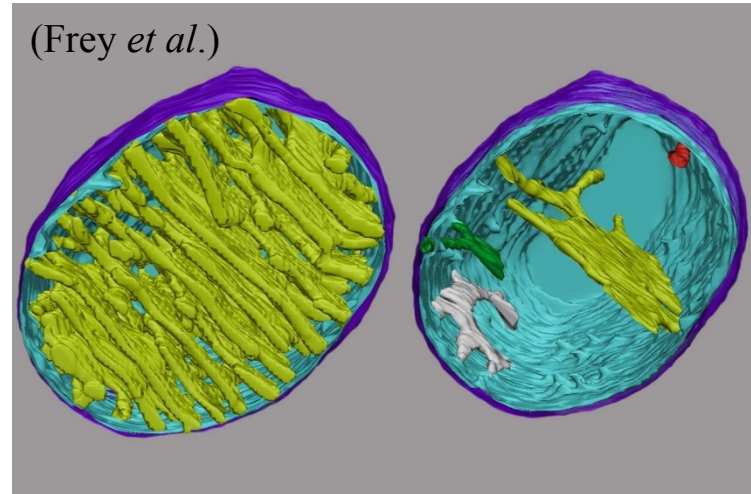


(Medalia *et al.*)



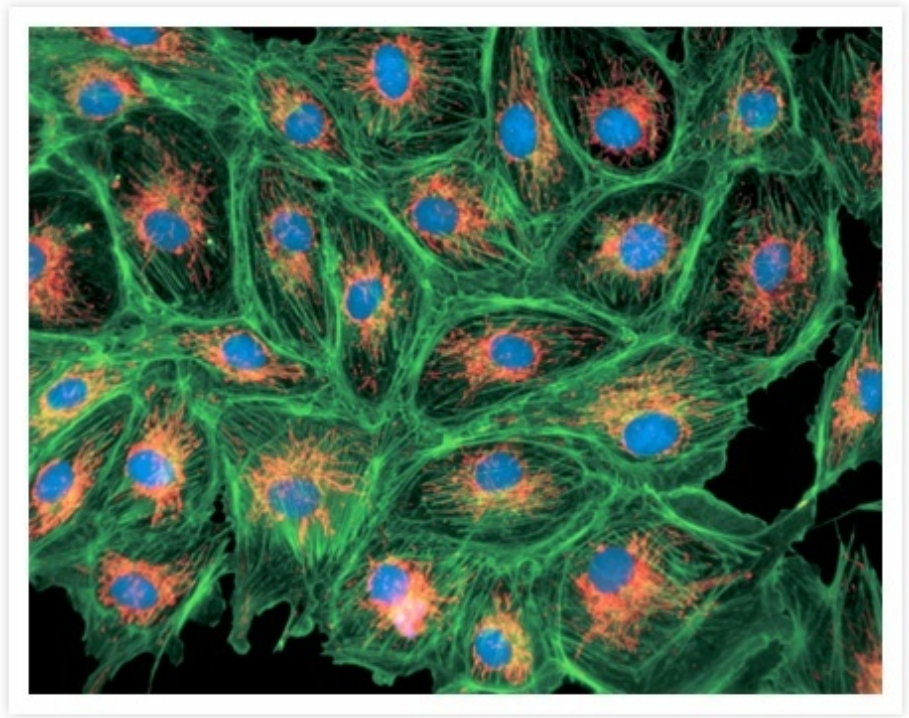
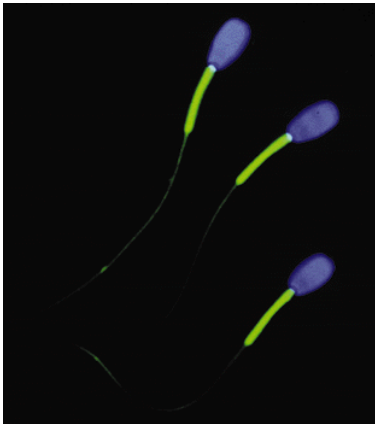
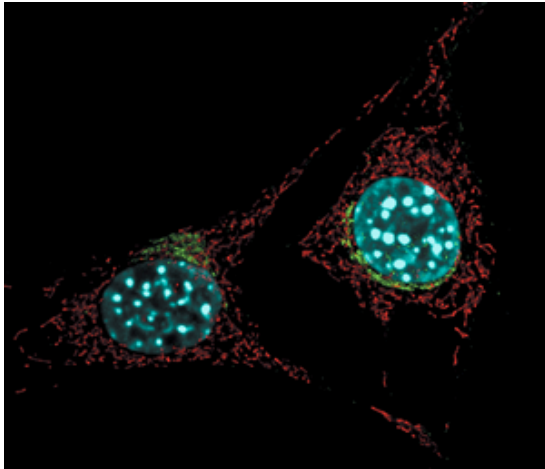
## *Mitochondria*

(Frey *et al.*)



# Experimental Transformation of Biology: Imaging Proteins in Live Cells

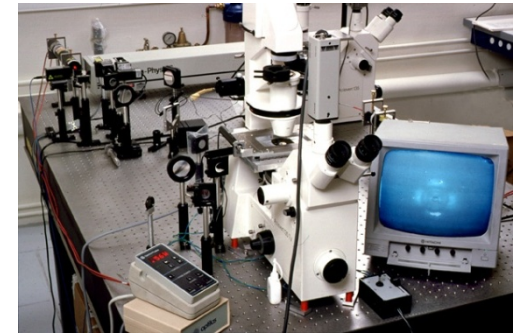
*All figures taken from Molecular Probes gallery.*



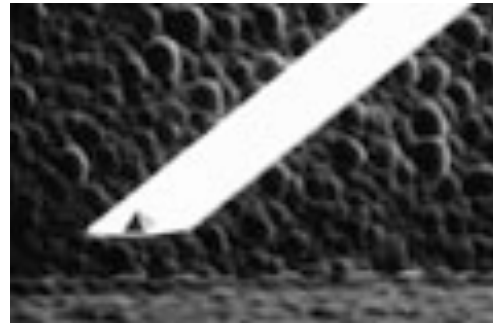


# Experimental Transformation of Biology: Single Molecule Biophysics

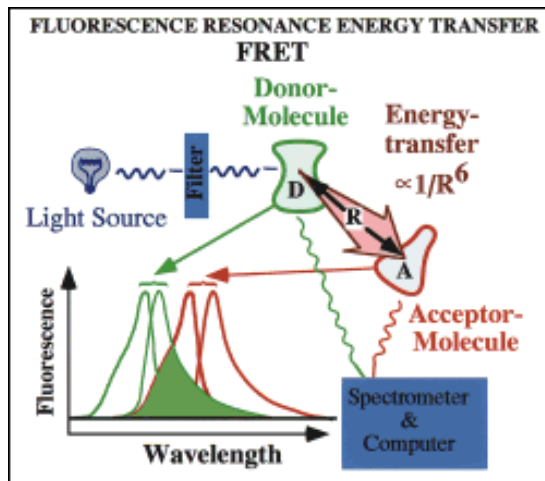
## *Optical Tweezers*



## *AFM*



## *FRET*

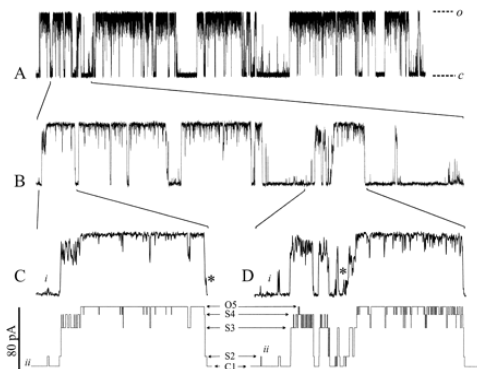


# The Quantitative Outcome

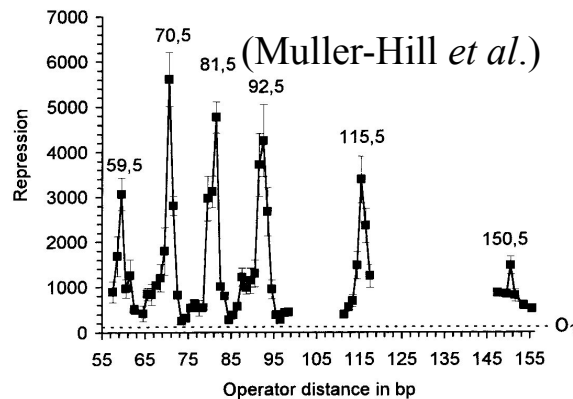
*Quantitative Data Demands Quantitative Models and  
Quantitative Models Demand Quantitative Experimentation*

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

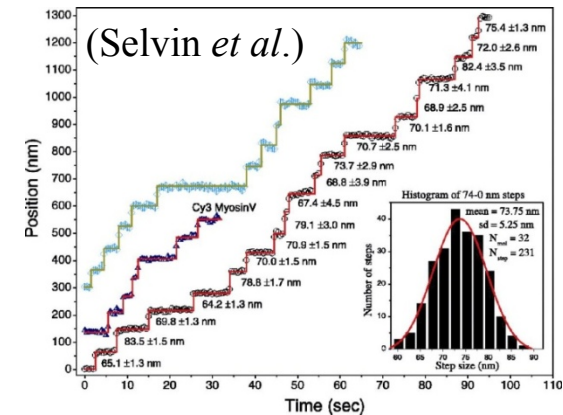
(Sukharev *et al.*)



***Ion channel dynamics***



***Gene regulation***



***Motor dynamics***

# *Change on Philosophical level.*

*Life requires a critical level of complexity.*

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

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

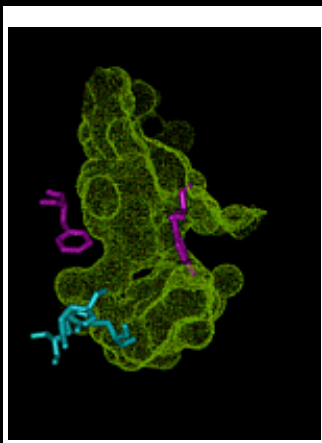


Stuart Kauffman

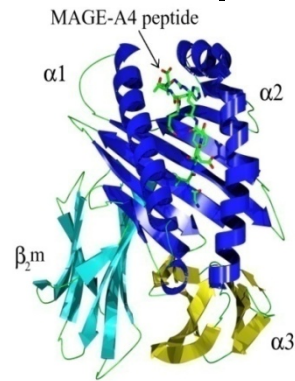
*The numbers of different  
molecular actors in the drama  
matters!*

*Concentration might just be the  
most important variable in  
biochemistry!*

# Attributes of soft matter

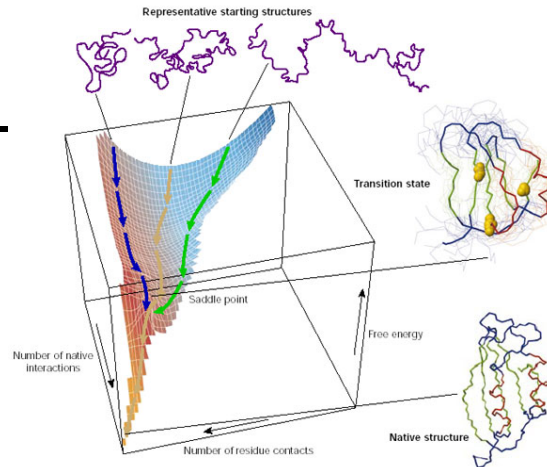


*Dynamics  
and  
flexibility*

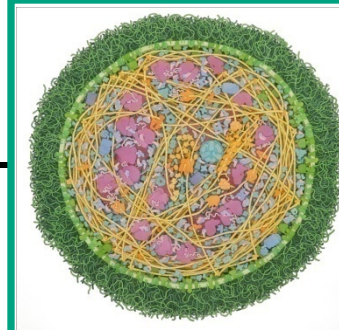
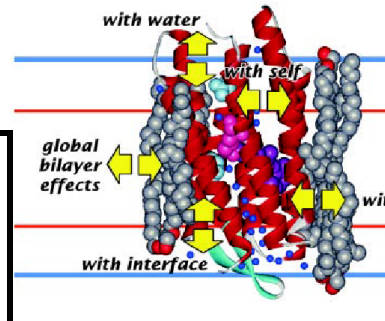


*Specificity*

*Selforganization*



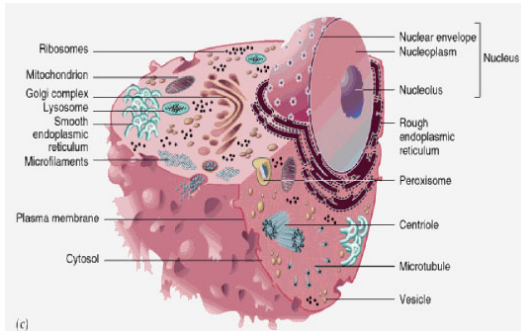
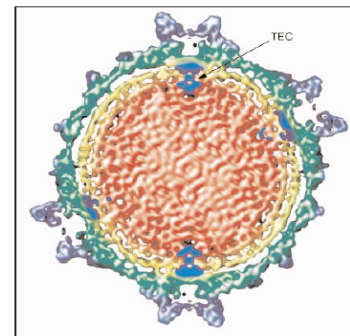
*Tensegrity*



*Crowding*

*Evolution !*

*Emergent properties*

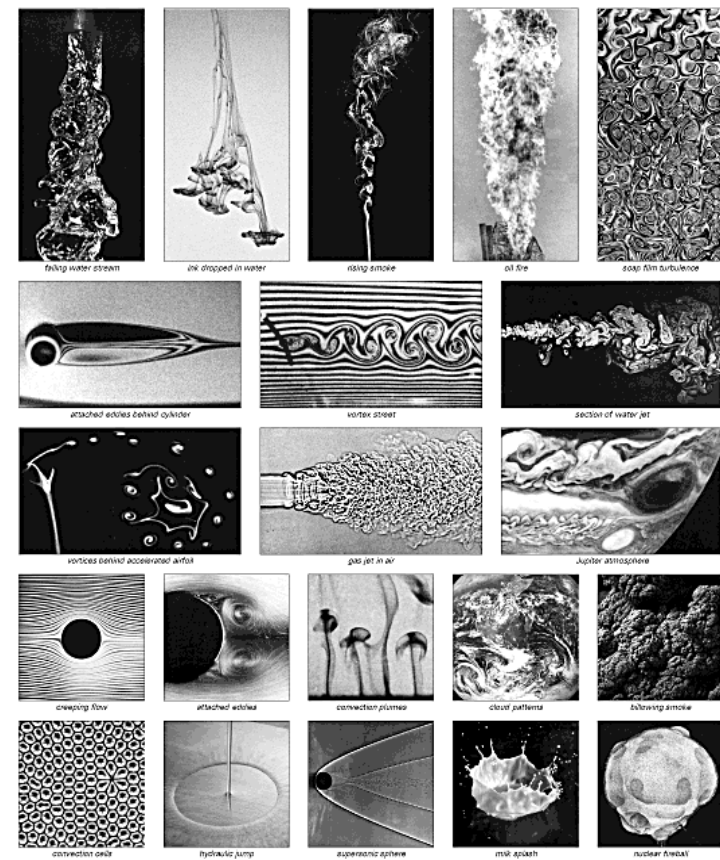


*Modularity & Homeostasis*



# *Simple systems*

Simple systems are ones in which global properties are inherent in the properties of their component parts.



Examples of typical patterns generated in various kinds of fluid flow. Note the frequent occurrence of seemingly random turbulence.

*Simple systems are additive, and scale with increasing numbers of components.*

*Predictable, can be studied top-down or bottom up by traditional reductional science.*

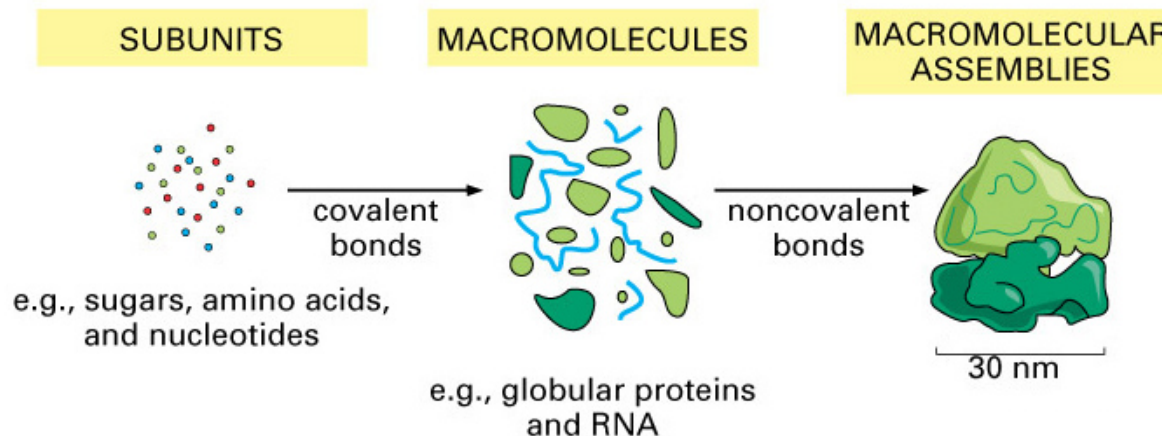
# Complex System

It can be defined by what they are not:

- Complex systems are not simple ones.
- The fundamental characteristic of a complex system is that it exhibits emergent properties

Defn: Emergent properties are ones that arise due to the interactions in a system, and are not inherent in the individual components.

***Complicated  $\neq$  Complex***





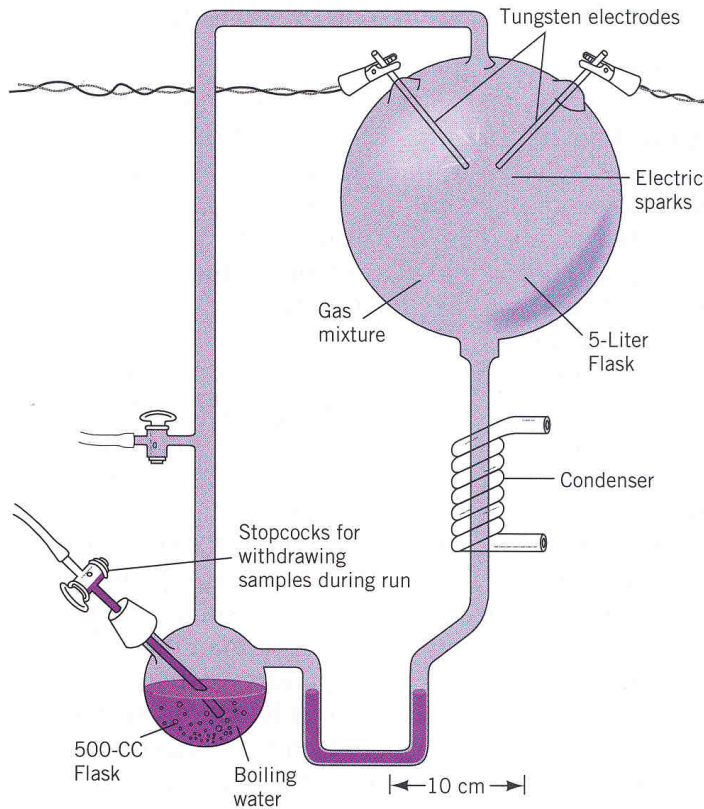
# *New perception of evolution*

## *Emergent Steps*

---

- 1. Emergence of biomolecules*
- 2. Emergence of organized molecular systems*
- 3. Emergence of self-replicating molecular systems*
- 4. Emergence of natural selection*

# *The Miller-Urey Experiment*



**Table 3–8** Some of the products shown to form under prebiotic conditions

## *Amino acids*

Glycine  
 Alanine  
 $\alpha$ -Aminobutyric acid  
 Valine  
 Leucine  
 Isoleucine  
 Proline  
 Aspartic acid  
 Glutamic acid  
 Serine  
 Threonine

## *Carboxylic acids*

Formic acid  
 Acetic acid  
 Propionic acid  
 Straight and branched fatty acids ( $C_4$ – $C_{10}$ )  
 Glycolic acid  
 Lactic acid  
 Succinic acid

## *Nucleic acid bases*

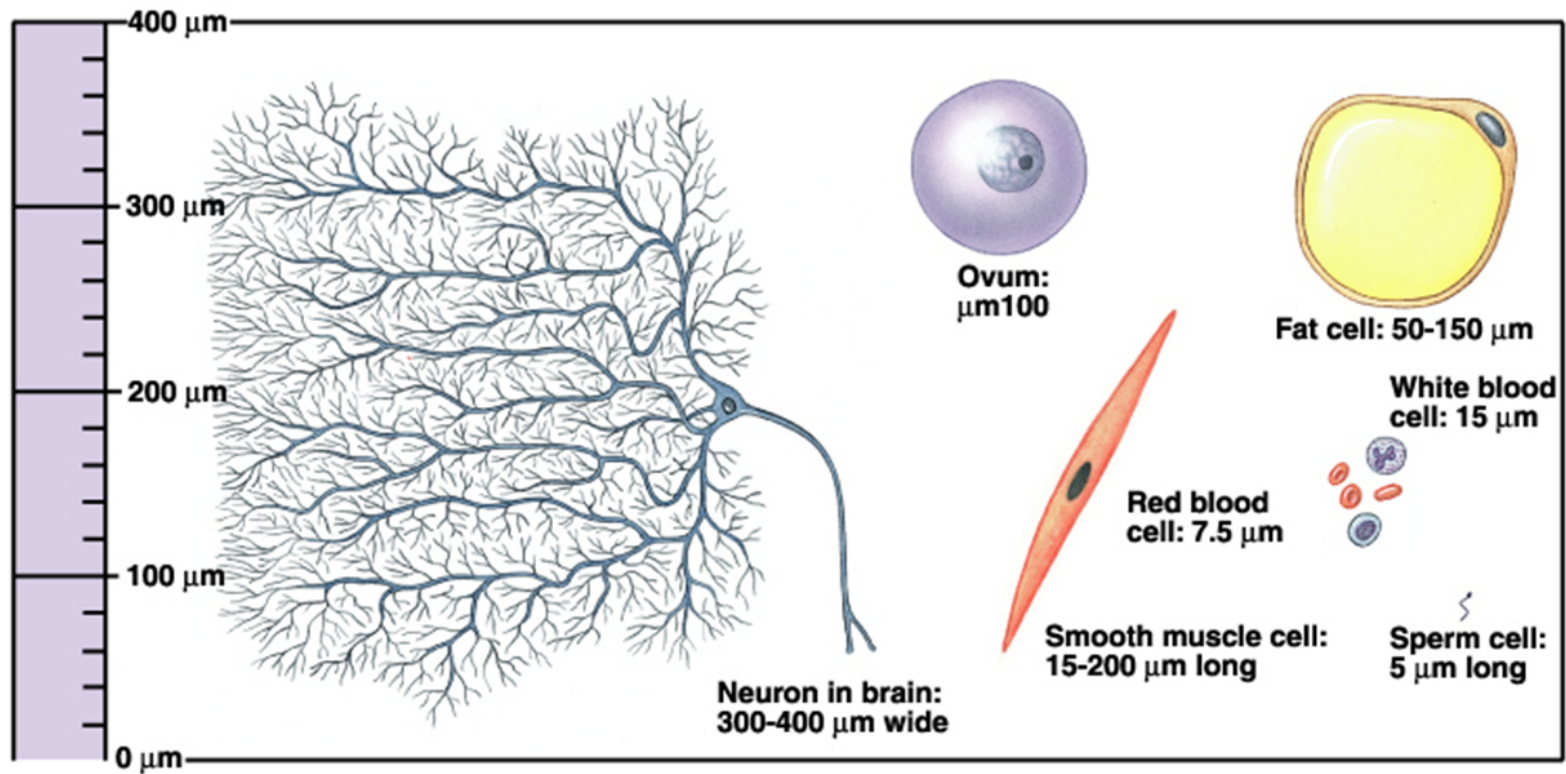
Adenine  
 Guanine  
 Xanthine  
 Hypoxanthine  
 Cytosine  
 Uracil

## *Sugars*

Straight and branched pentoses and hexoses

*Organic synthesis near the ocean-atmosphere interface.*

# *The basic unit of life - Cell*



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



# 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.*

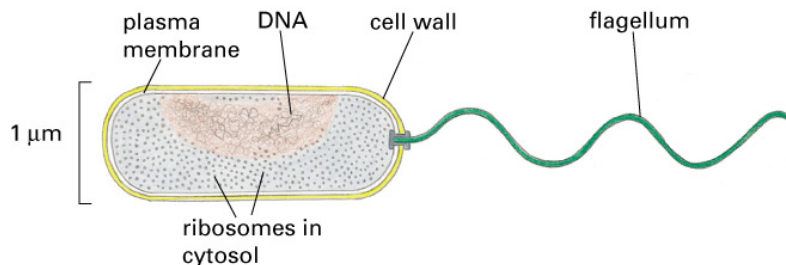


Figure 1–18 part 1 of 2. Molecular Biology of the Cell, 4th Edition.

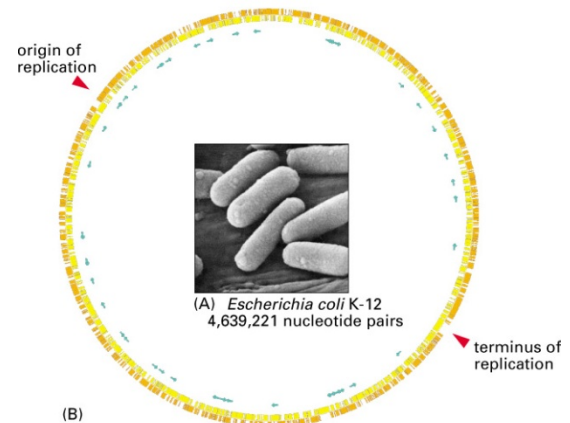
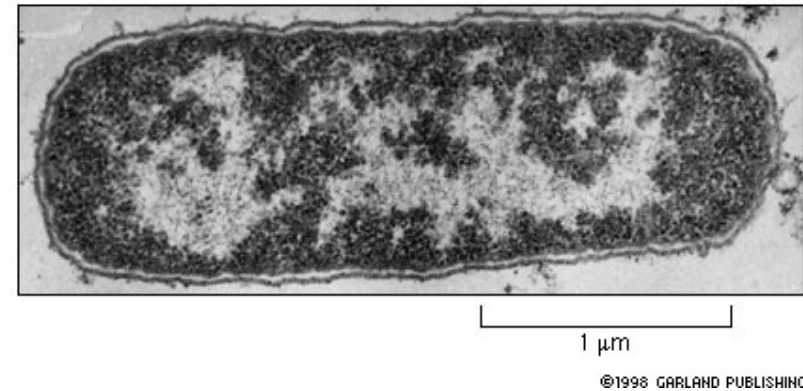
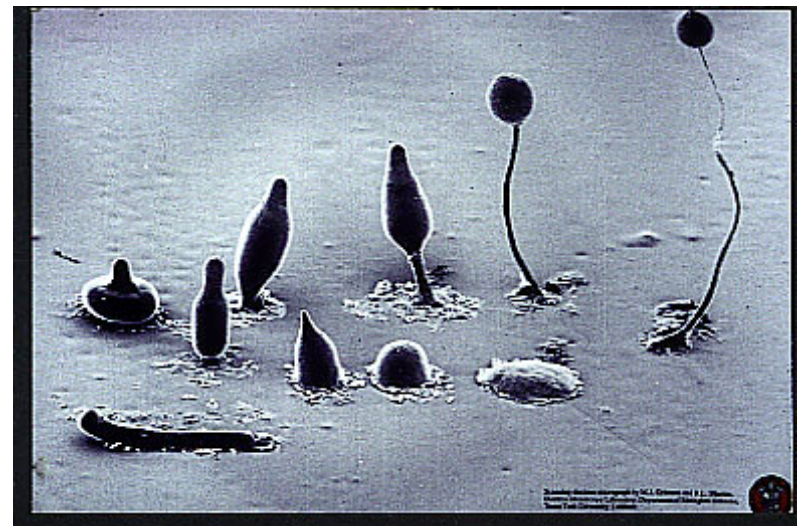
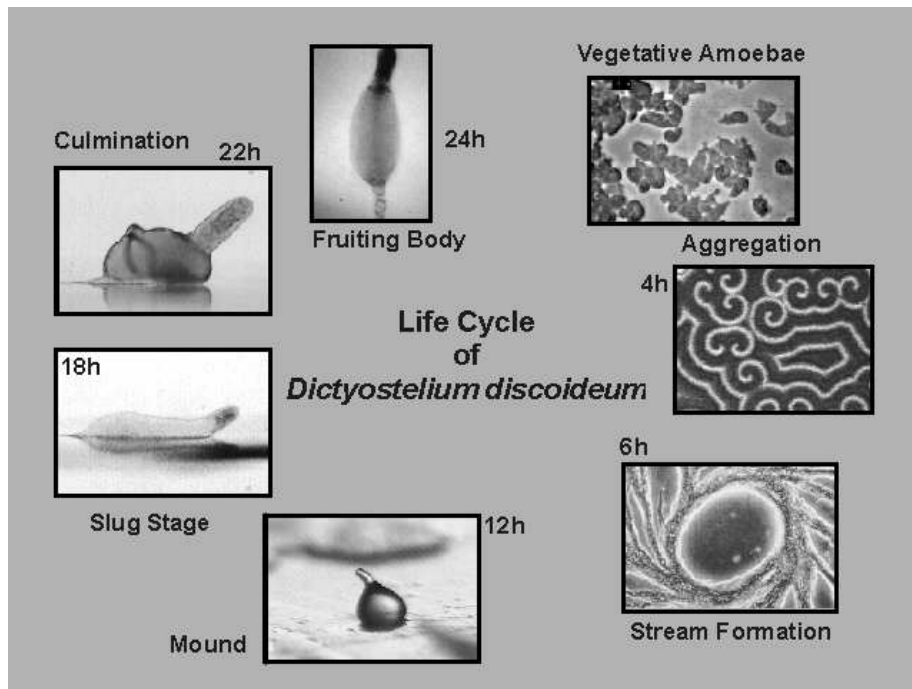


Figure 1–30. Molecular Biology of the Cell, 4th Edition.

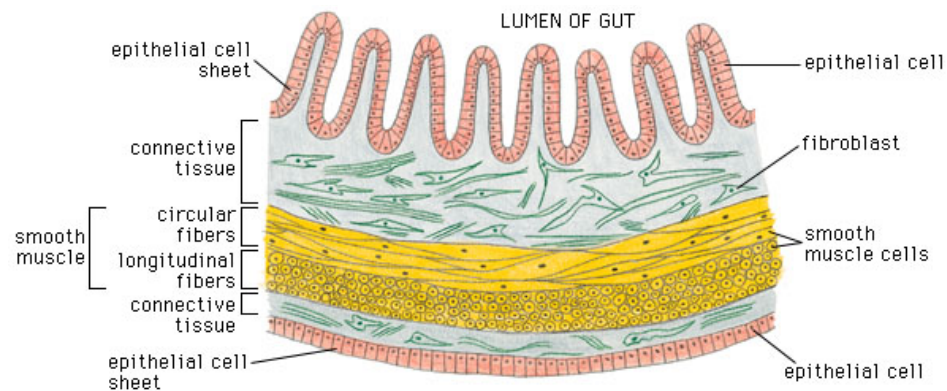
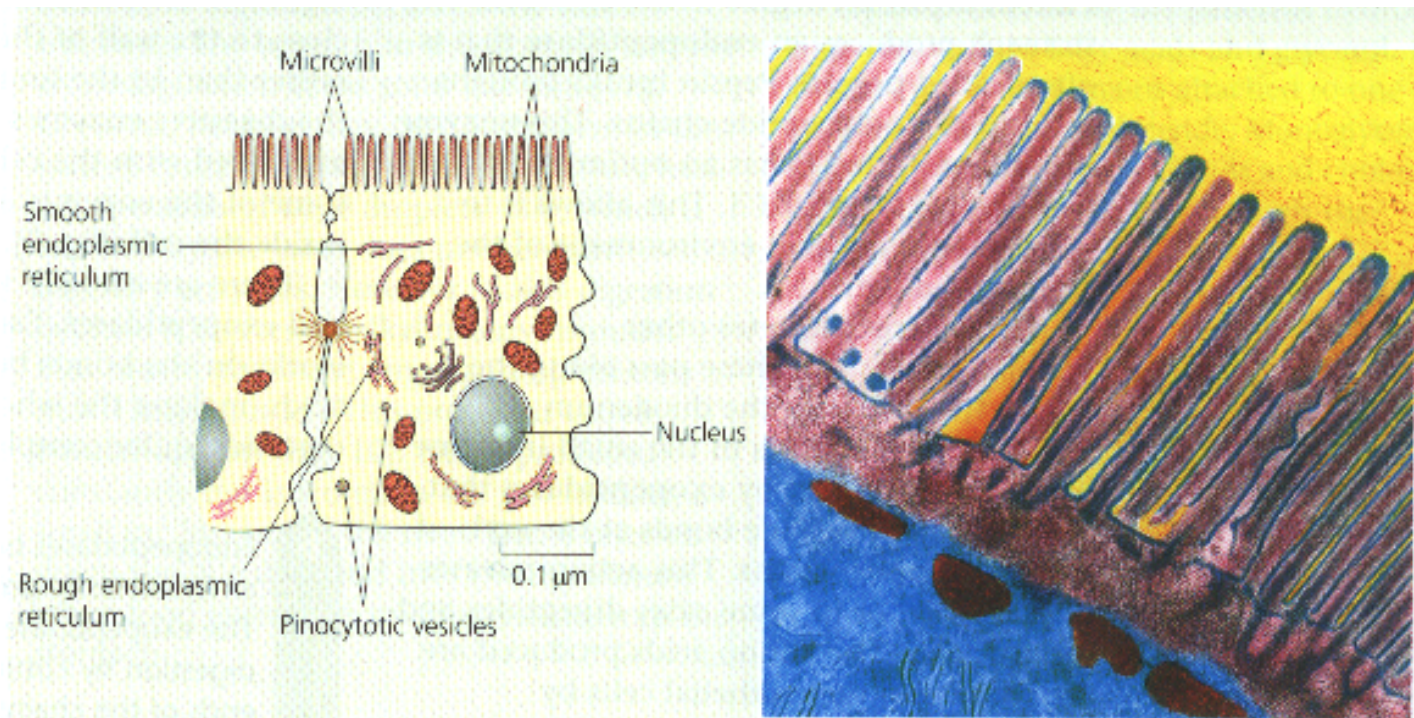
# Collections of Cells – Sporulation

## *The road to higher level organization*



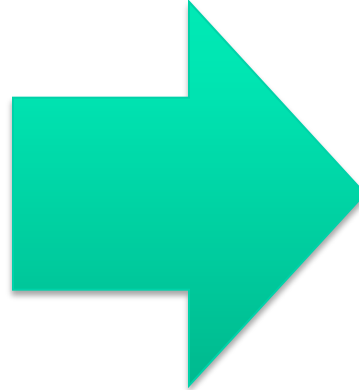
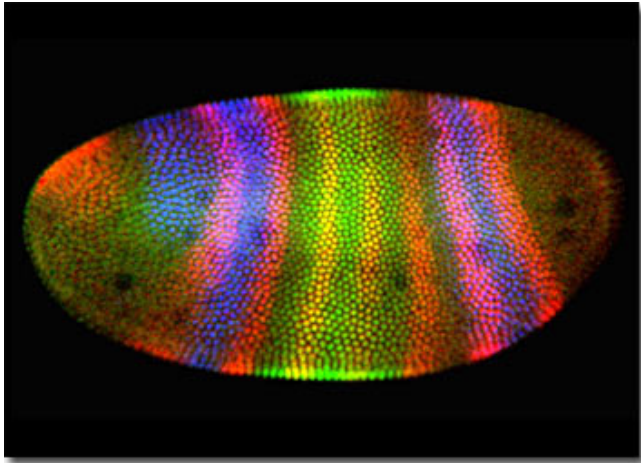
<http://www.zi.biologie.uni-muenchen.de/zoologie/dicty/dicty.html>

# Collections of Cells - Tissues





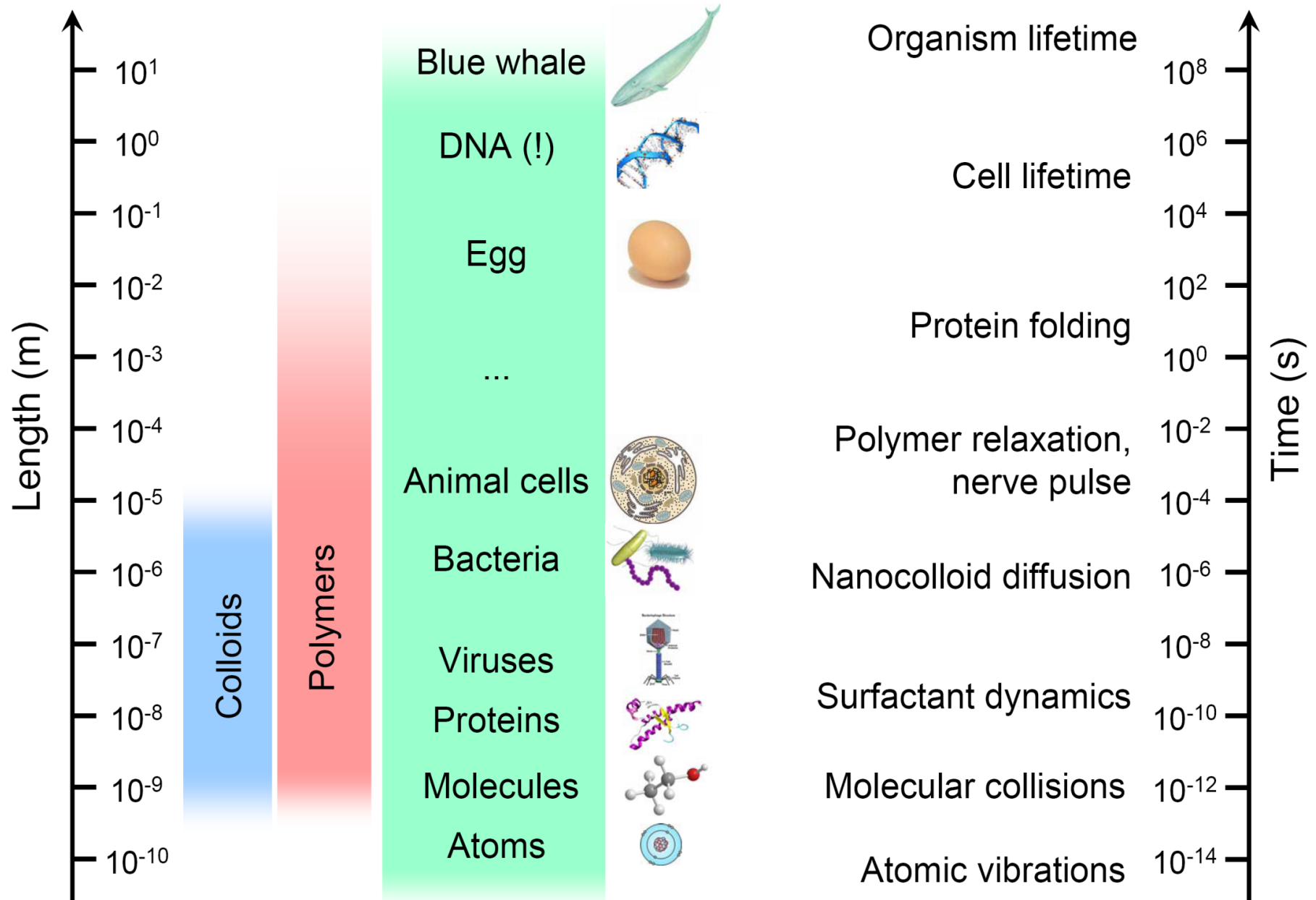
# Collections of Cells - Organisms



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 image won the *BioTechniques* cover of the year award in 1993.

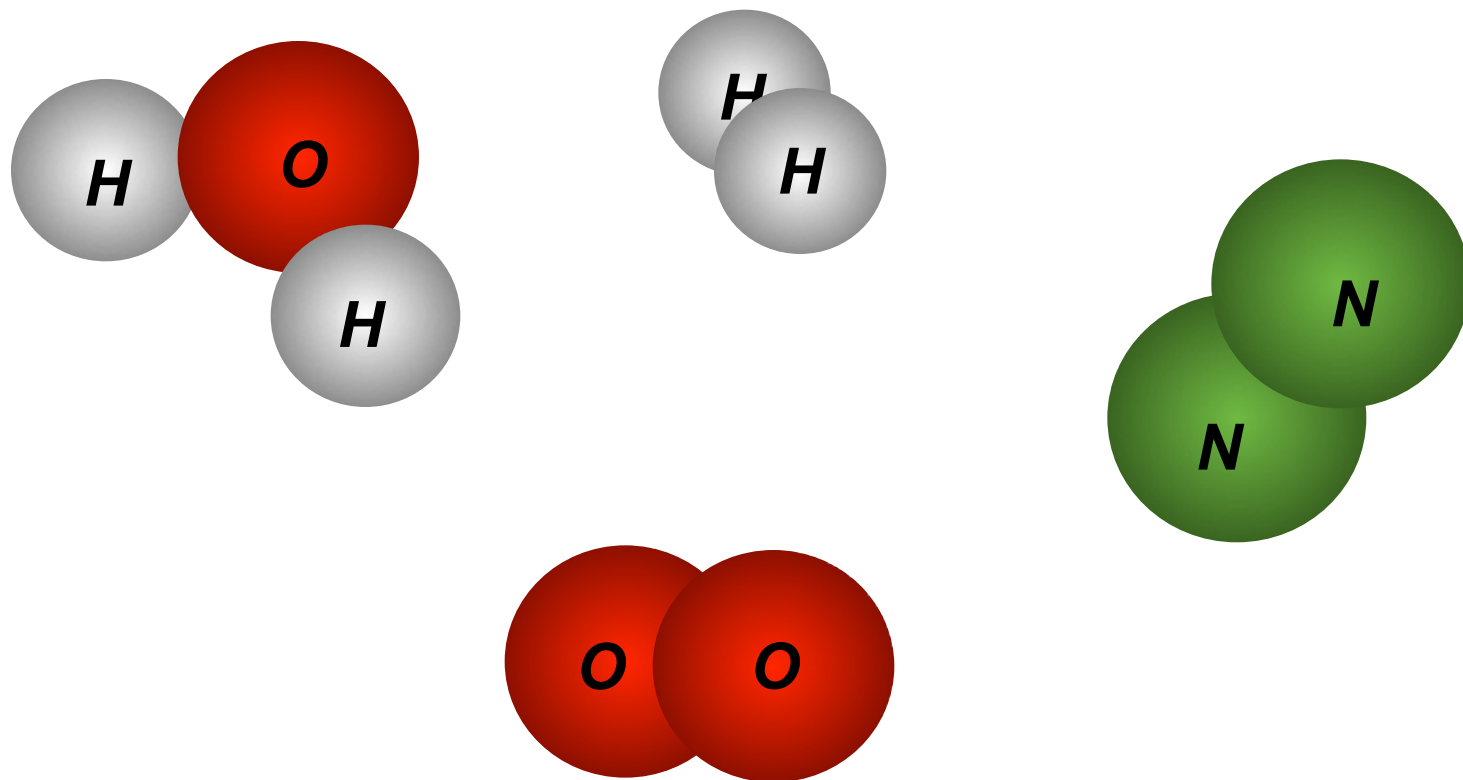


# *Time and length scales*

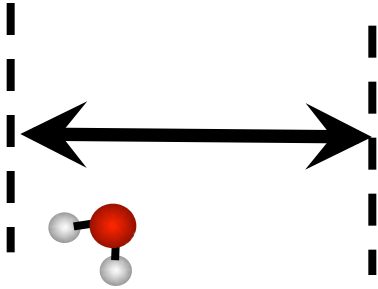


***Nanoscale = molecular scale***

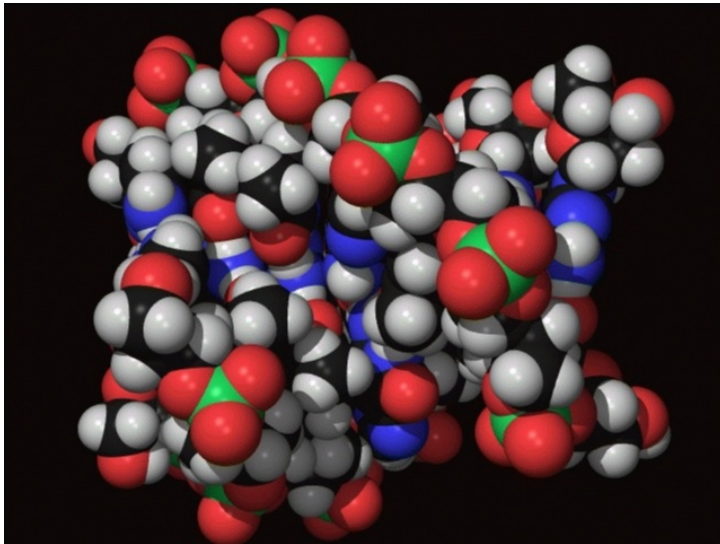
One Nanometer



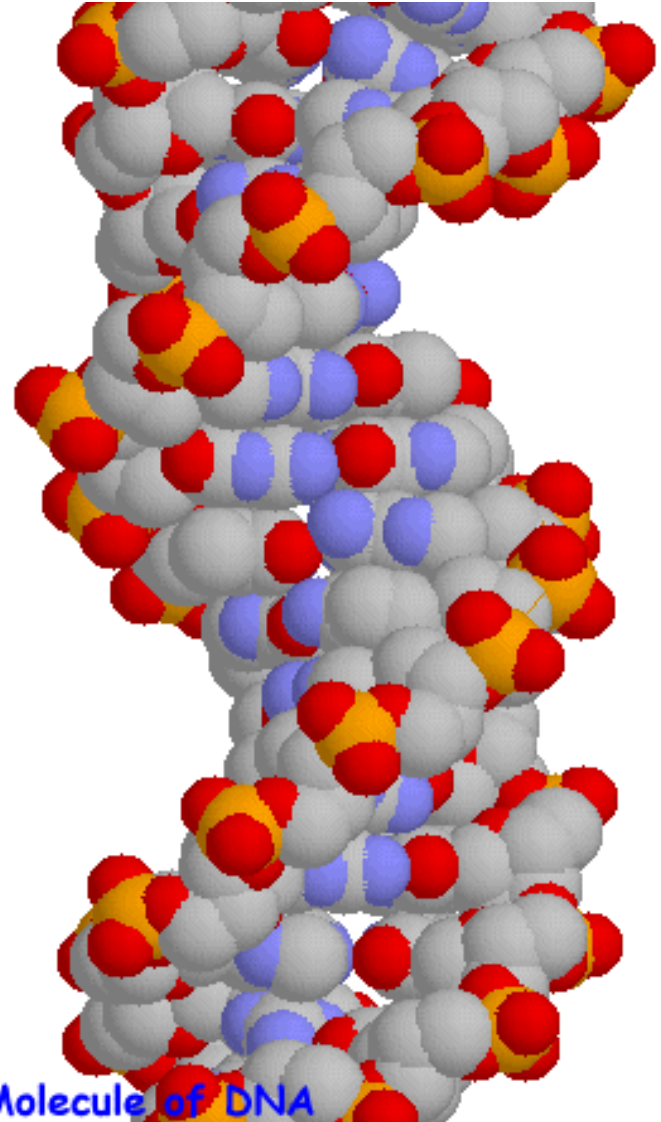
# One Nanometer



*Water (H<sub>2</sub>O)*



*Small Protein*



*Molecule of DNA*

# Nanoscopic Dimensions

Atomic

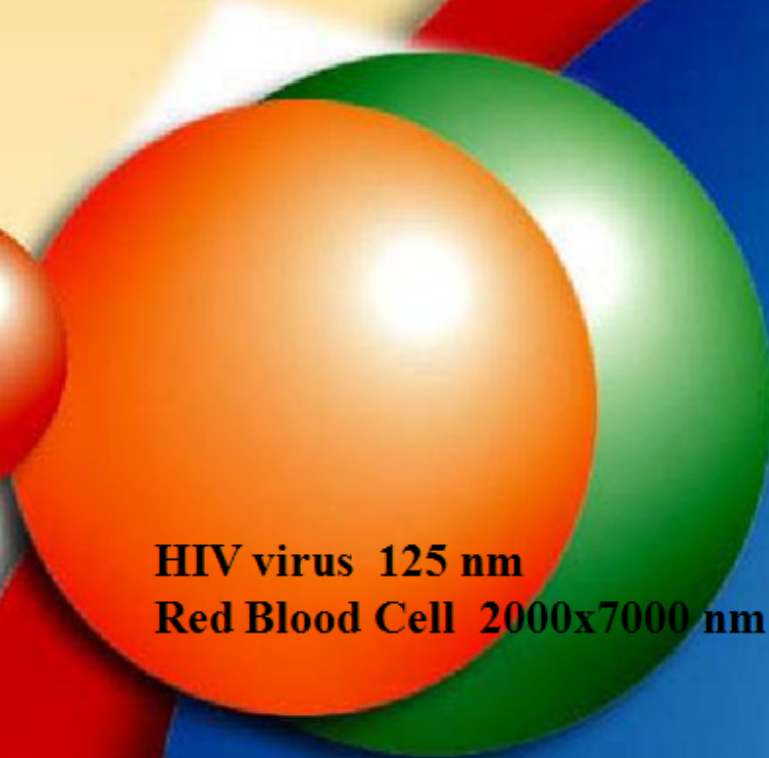
Molecular

Nanoscopic

Viral

Microbial

Cellular



Argon 0.3 nm

CH<sub>4</sub> 0.4 nm

H<sub>2</sub>O 0.3 nm

~1 nm ~100 nm

Albumin 6.5 nm

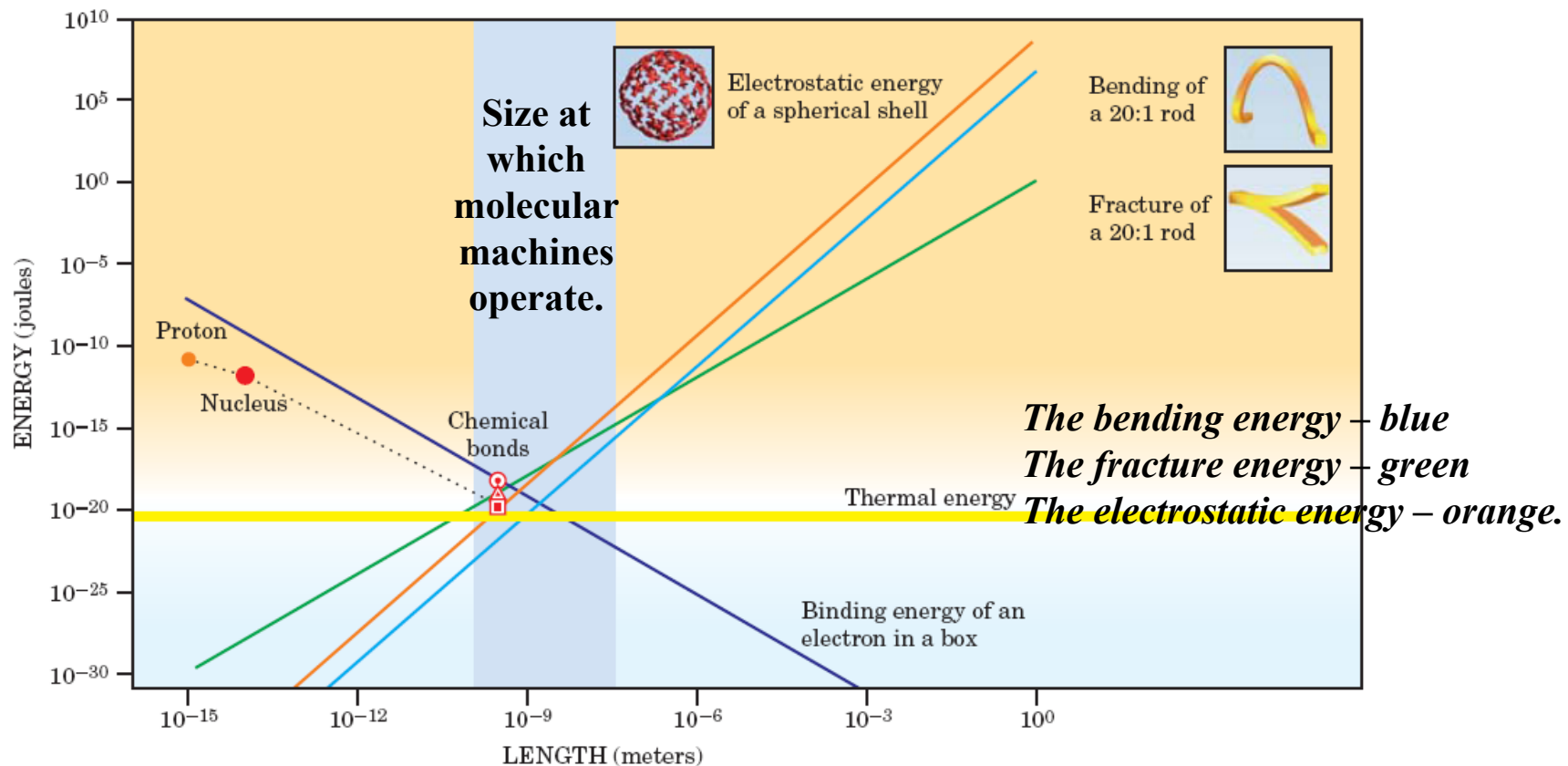
Ribosome 25 nm

HIV virus 125 nm

Red Blood Cell 2000x7000 nm

# *The energy scale*

*thermal, chemical, mechanical, and electrostatic energies are associated with an object scale.*



# *Physical model and the nano-scale of life*

*Cosmic scale*

$$F = \frac{m_0}{\sqrt{1 - \frac{v^2}{c^2}}} a$$

*Macroscale*

$$F = ma$$

*Bio-nano-scale*

$$\xi \frac{dx}{dt} = -\frac{\partial \varphi(x, t)}{\partial t} + f_B(t)$$

*Quantum Mechanics*

$$i\hbar \frac{\partial}{\partial t} \Psi = \hat{H} \Psi$$

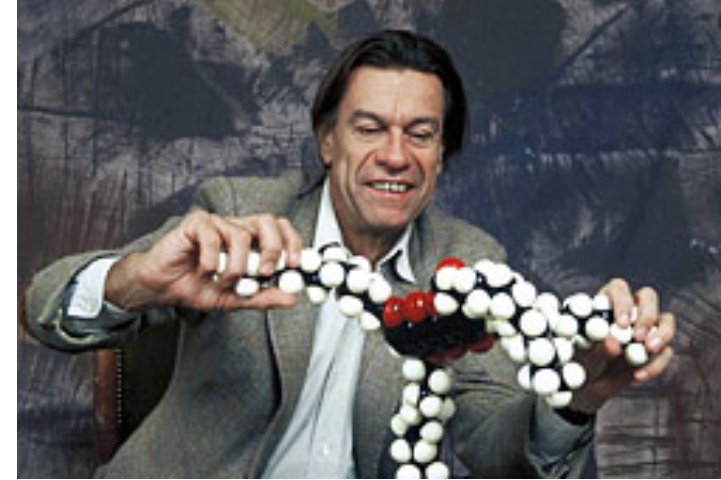


**Time-dependent Schrödinger equation (*general*)**



# *Soft Matter – the material*

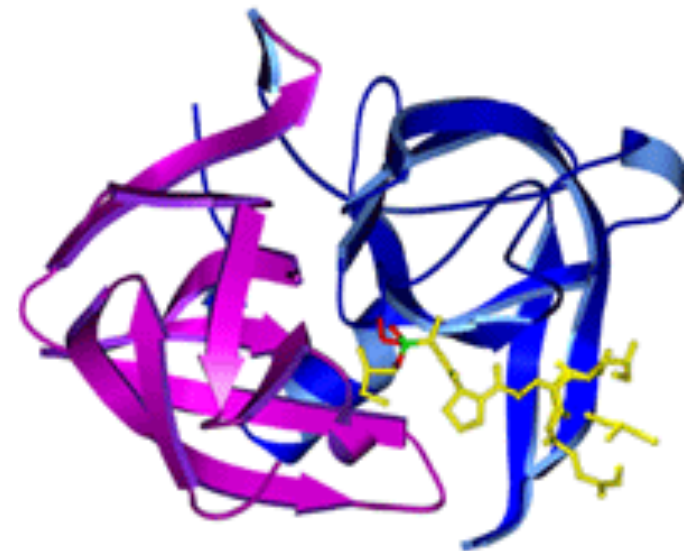
*Pierre-Gilles de Gennes received the 1991 Physics Nobel Prize for bringing order into soft matter, particularly liquid crystals and polymers.*



*Biomolecular structure is determined by a combination of covalent and non-covalent bonds.*

*Covalent bonds are static entities which are not effected by environment – **stability**.*

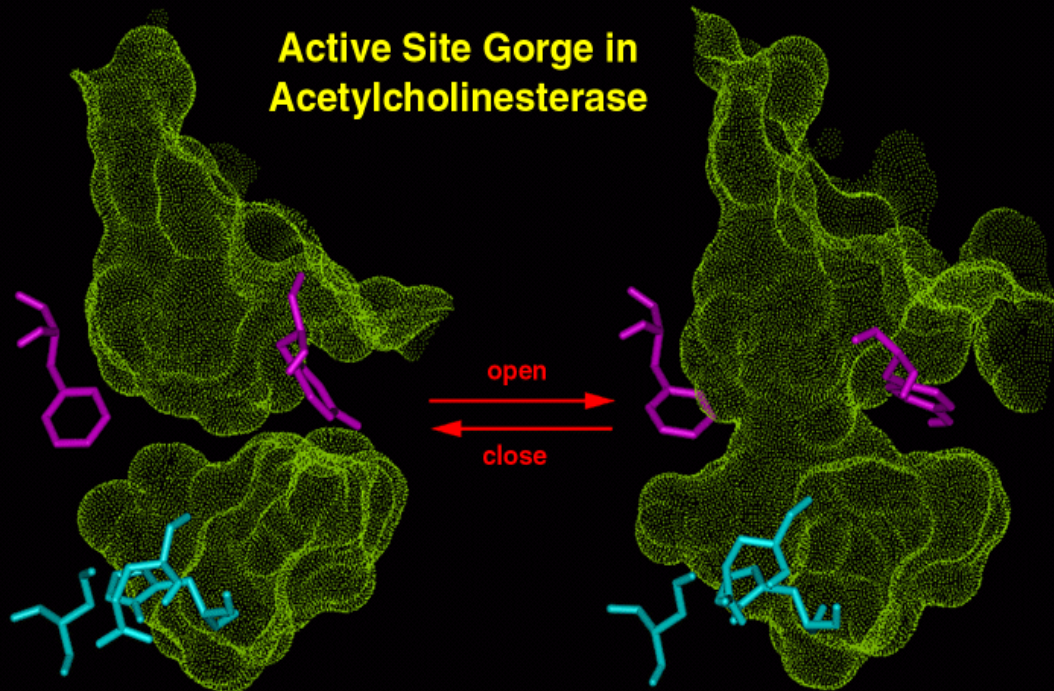
*Non-covalent bonds exist in a dynamic equilibrium - **flexibility**.*



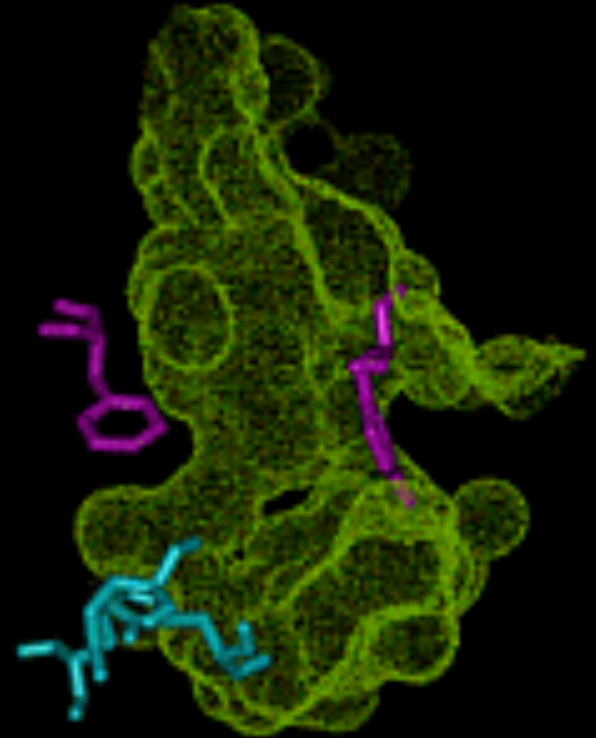
# *Biology works within $kT$*

$1kT = 0.62 \text{ kcal/mole}$  (at  $T=300\text{K}$ )

$$\text{Probability} \propto e^{-\frac{\Delta G}{kT}}$$

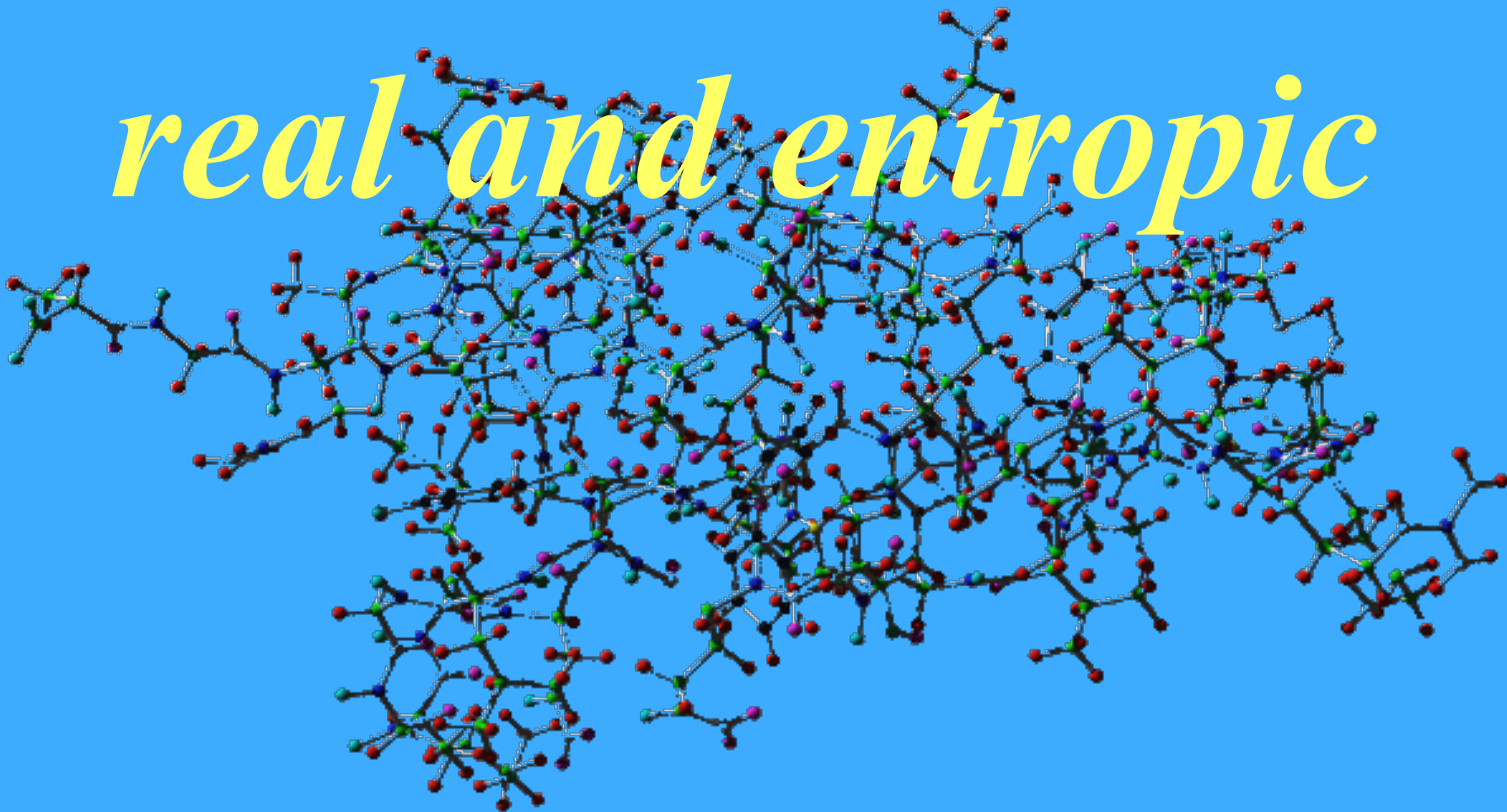


McCammon Group - UCSD



*Acetylcholinesterase*

# *Interactions real and entropic*



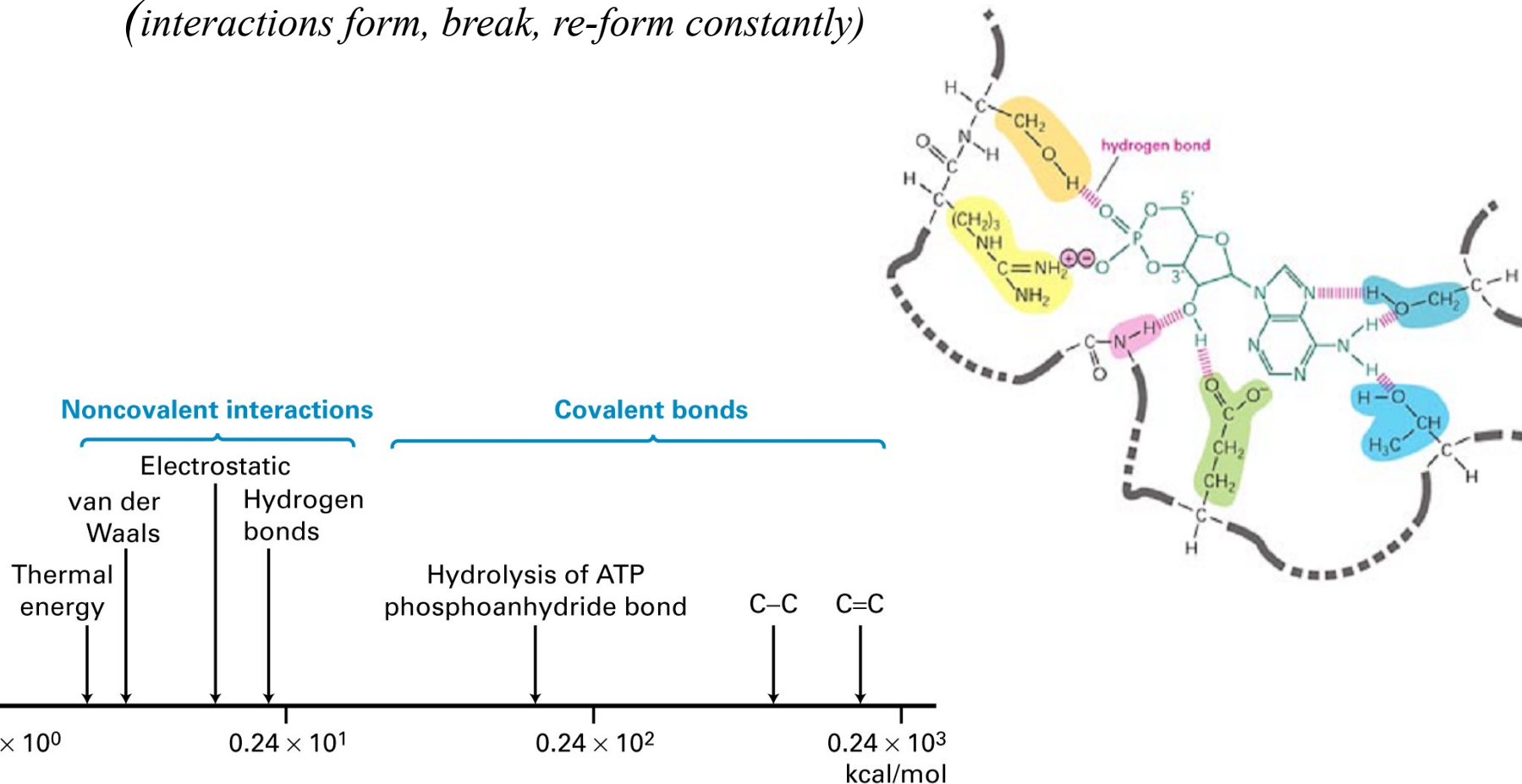
$$\Delta G = \Delta H - T\Delta S$$

# *Intra- and Inter-molecular interactions is what biology is all about.*

*Weak Interactions are additive*

*Weak interactions are dynamic*

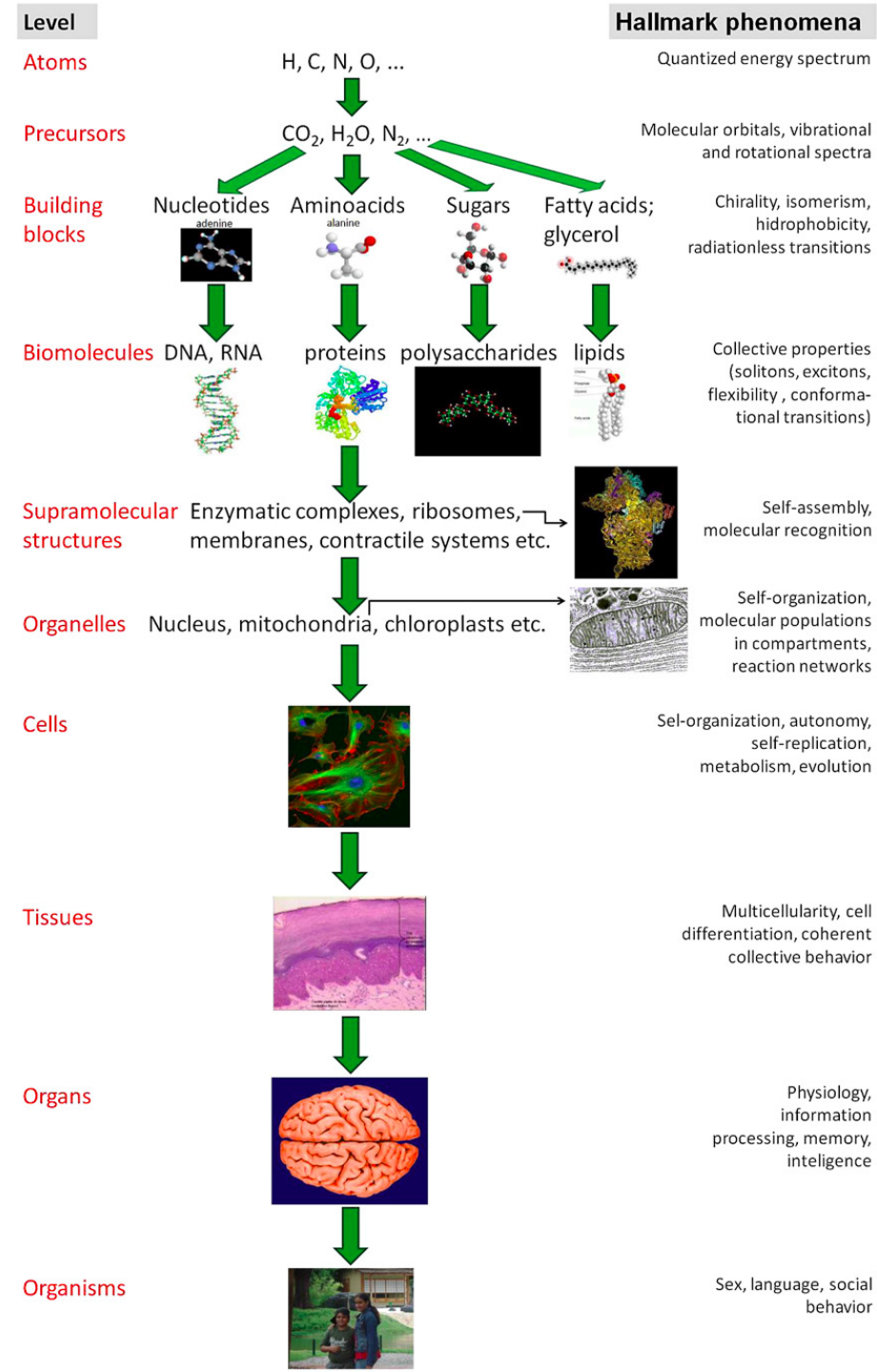
*(interactions form, break, re-form constantly)*





# *The hierarchy of life from atoms to living organisms.*

- New phenomena emerge at each upper level that cannot be seen at lower ones.
- Information flows both up and down these scales.





# *Homeostasis*

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

*Quantitated by a set of critical parameters*

*[pH, I(composition),  $\Pi$ , c(glucose)...]*

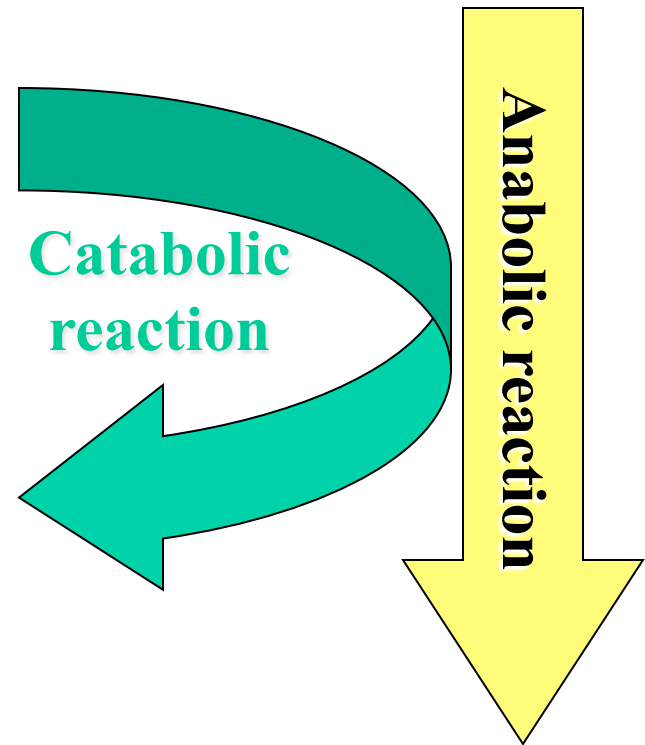
*$M_i(a_i.....)$*

# *Design of Metabolism*

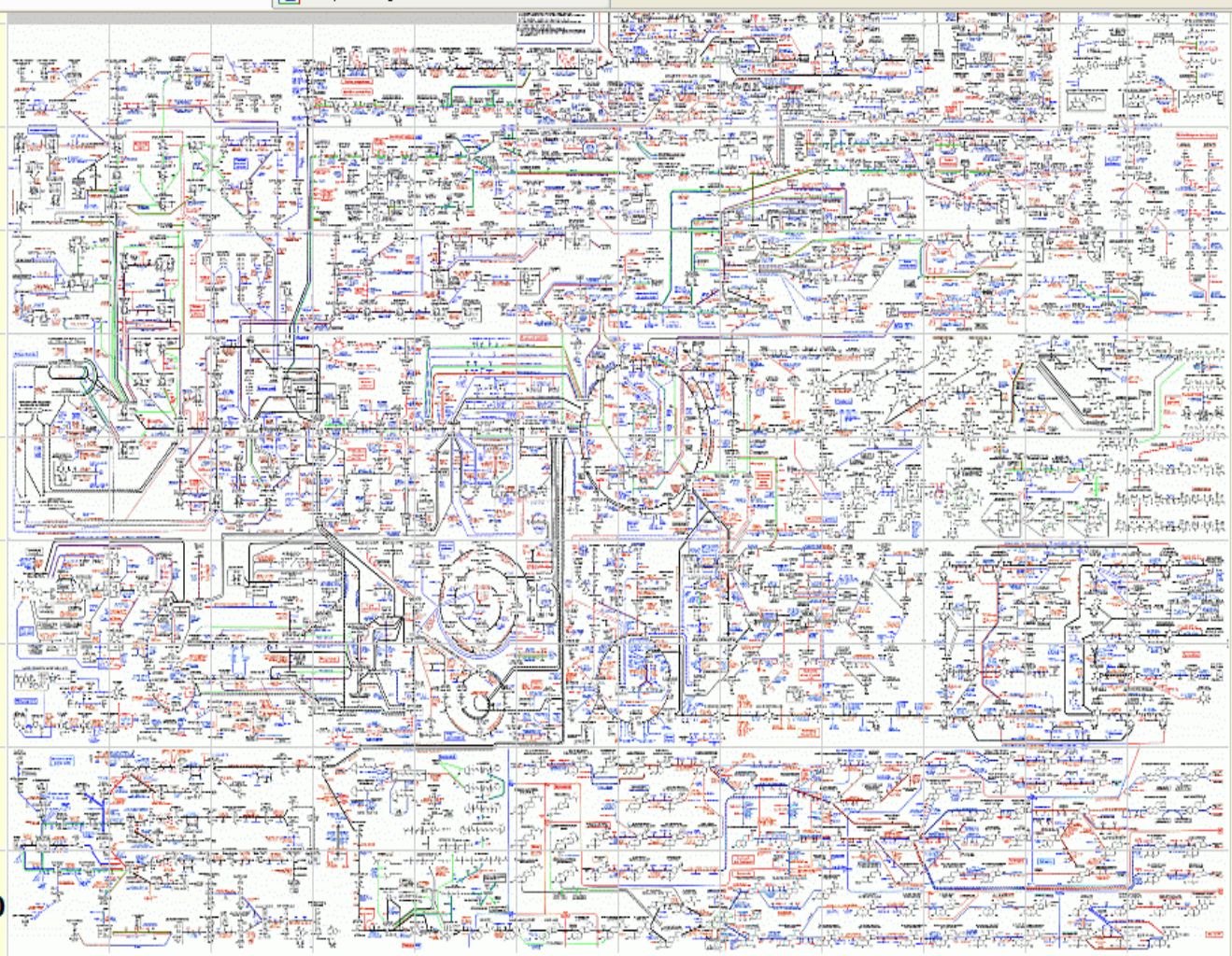
*Anabolic reaction - biosynthesis*

*Catabolic reaction - oxidation (removal) of  $e^-$ 's from foodstuffs*

*Coupling reactions that are energetically unfavorable with reactions that are energetically favored.*



*Metabolic reactions – are events inside cells, controlled by coordinated **molecular machines**.*



**Robustness** – important tasks of a cell can be completed even as genetic and environmental conditions vary – metabolic compensation.

# *Definition of allostasis*

The process by which a state of internal, physiological equilibrium is maintained by an organism in response to actual or perceived environmental and psychological stressors.

Therefore, *allostasis* is the process that keeps the organism alive and functioning, i.e. maintaining homeostasis or “maintaining stability through change” and promoting adaptation and coping, at least in the short run. — Bruce S. McEwen, *Neurobiology of Aging*, 2000

*Process, which can be evaluated by dynamics of metabolome.*

# *Allostasis*

*The concept of allostasis refers to maintenance of stability through change.*

The concept of allostasis was introduced by Sterling and Eyre to describe the adaptive mechanisms that allow maintenance of normality at the expense of robust, energy-costing adaptive mechanisms.

*Whereas the concept of homeostasis refers to mechanisms that prevent change and ensure the maintenance of the ideal steady state of a function (e.g. pH, dissolved oxygen), allostasis refers to the changes that are required in response to severe challenges and are aimed at restoring the homeostasis of the system.*



# *The organization – the other perspective*

## *Cellular homeostasis*

***Micro homeostasis*** – tissue level – cell physiology

*Micro homeostasis depends physical constraints within organ (local allostasis) - physiology.*

***Macro homeostasis*** – organism level

*Macro homeostasis is a sum of micro homeostasis and is regulated by global allostasis – the medicine.*

The space – spatially organizing autonomous structures (cell and/or organs) in aqueous phase (body fluids).

***Body fluids serve as a allostatic medium, which can be quantitated by the global metabolome.***

**Metabolomics** is the "systematic study of the unique chemical fingerprints of cellular (physiological) processes".

The metabolome represents the collection of all metabolites in a biological cell, tissue, organ or organism, **which are the end products of cellular processes.**

# *Perception of a biological system – human body*

## *Structure*

- compartments
- mechanical integrity and stability – tensrigity,
- self-organization – hydrophobic effect

## *Dynamics*

- electrochemical gradients,
- mechanical balnce
- temporal system perturbations (mechanical, chemical, electrical) – communication.

## *Homeostasis and Allostasis*

## *Action*

- molecular devices
- flux and availability of energy

## *Memory*

- genes
- text files – epitopes - specificity

*Transformation of  
information*

Digital files -  
genes

Text files -  
proteins

Molecular  
machine

*Transformation  
of energy*

Electromotive  
force

Proton-motive  
force

ATP

*Transformation  
of structure*

Hydrophobic-  
hydrophilic  
balance

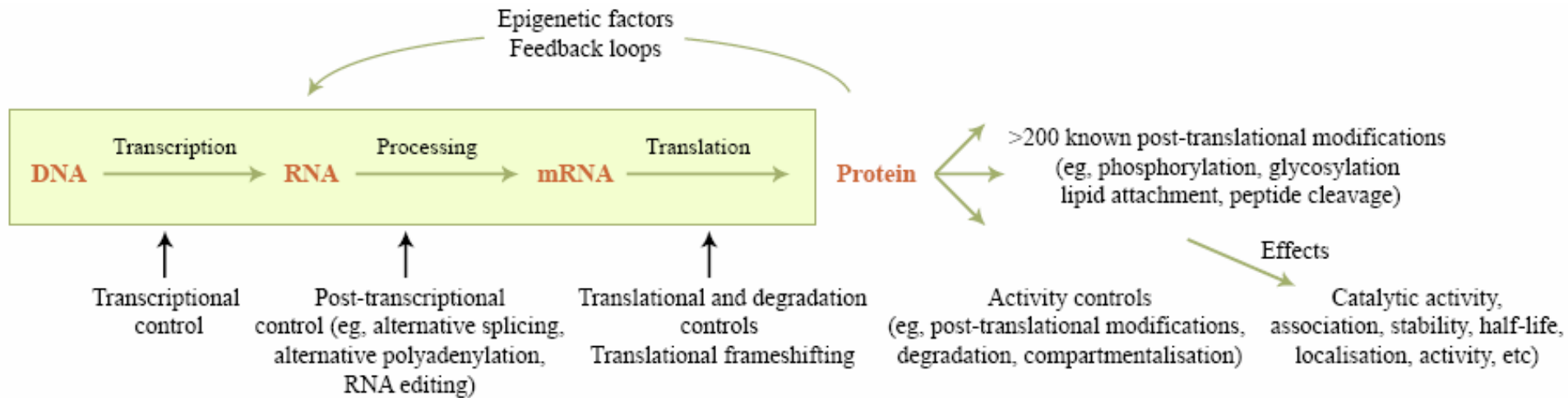
Aggregation

Spacio/temporal  
organization

Homeostasis

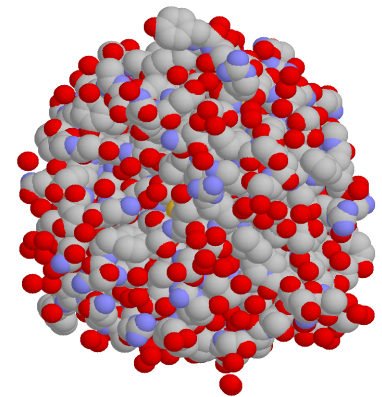
# *Transformation of information*

## *Central dogma of biology*



APRKFFVGGNWKMNGDKKSLGELIHTL  
NGAKLSADTEVVCGAPSIYLDFAHQKLD  
AKIGVAAQNCYKVPKGAFTGEISPAMIKD  
IGAAWVILGHSERRHVFGESEDELIGQKVA  
HALAEGLGVIACIGEKLDEREAGITEKVV  
FEQTKAIADNVKDWSKVVLAYEPVWAIG  
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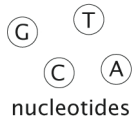
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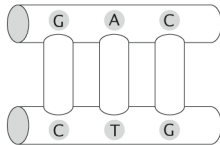


# Crick's great "polymer" languages

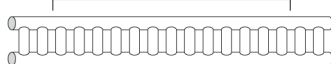
## NUCLEIC ACIDS



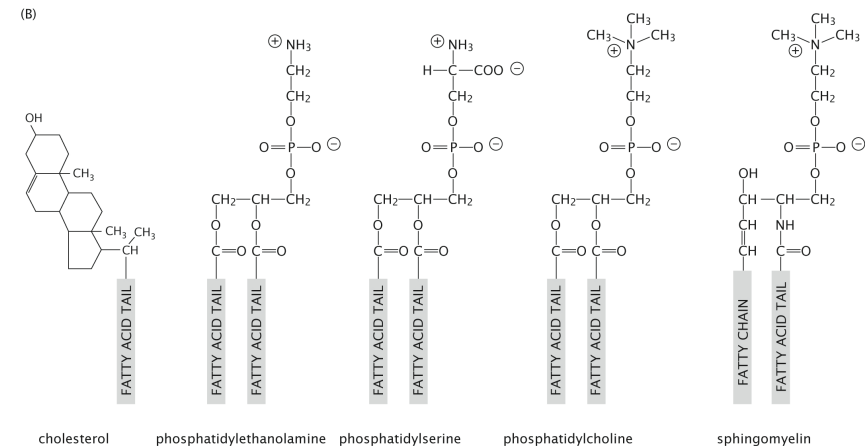
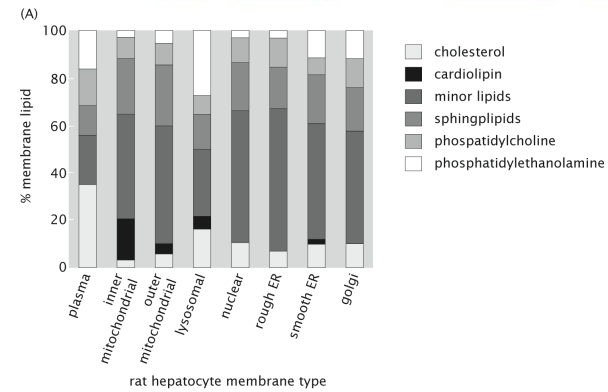
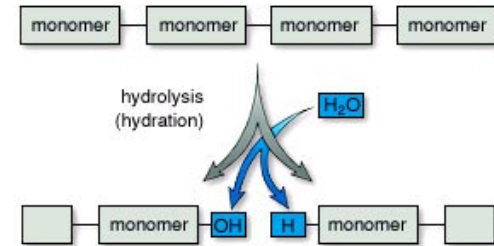
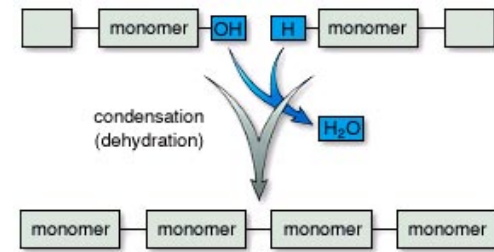
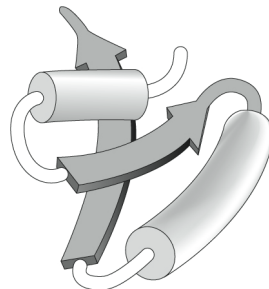
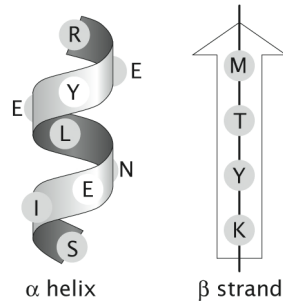
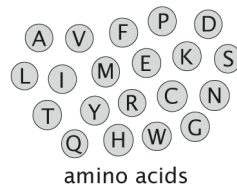
### codon



### gene

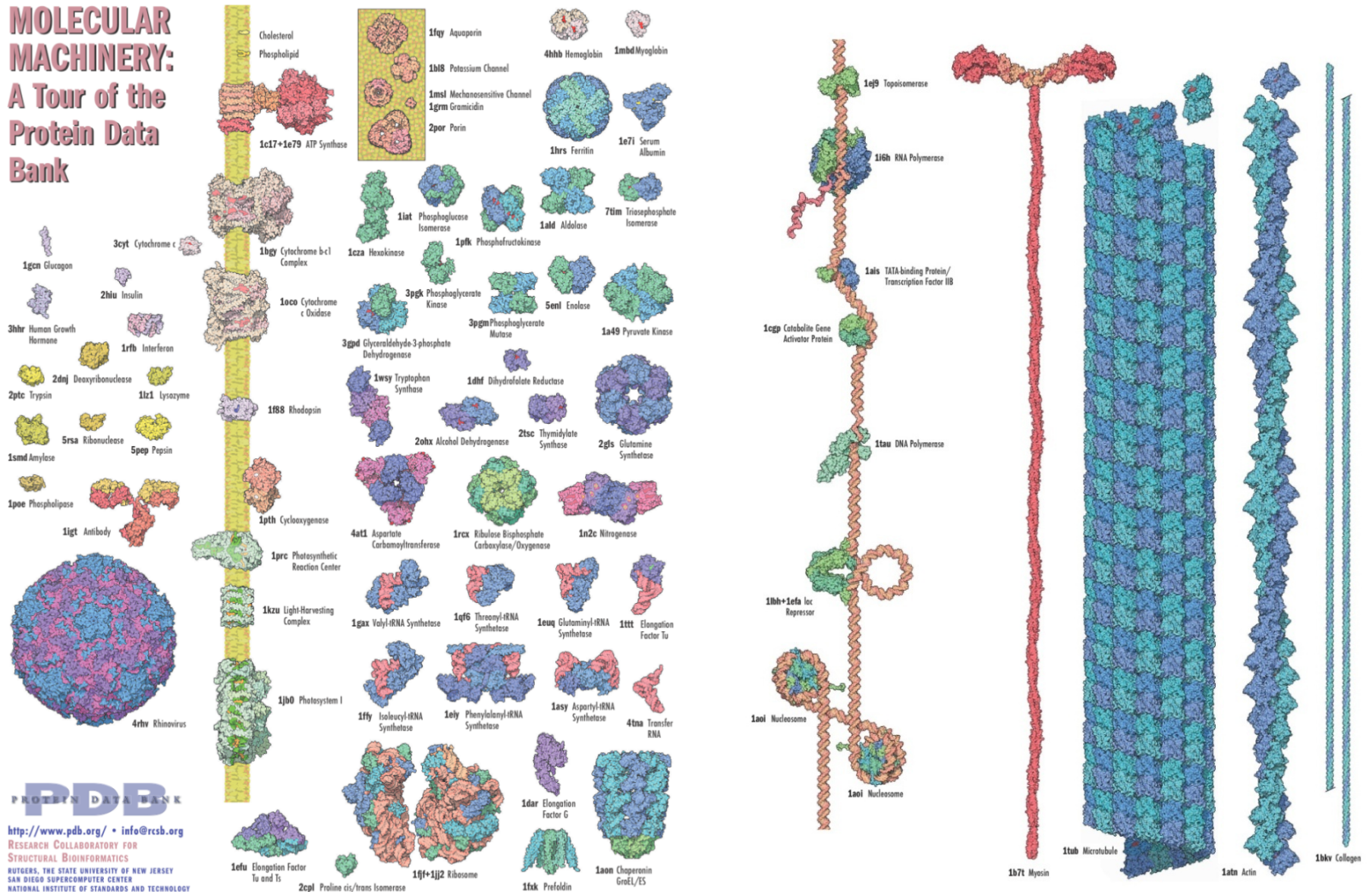


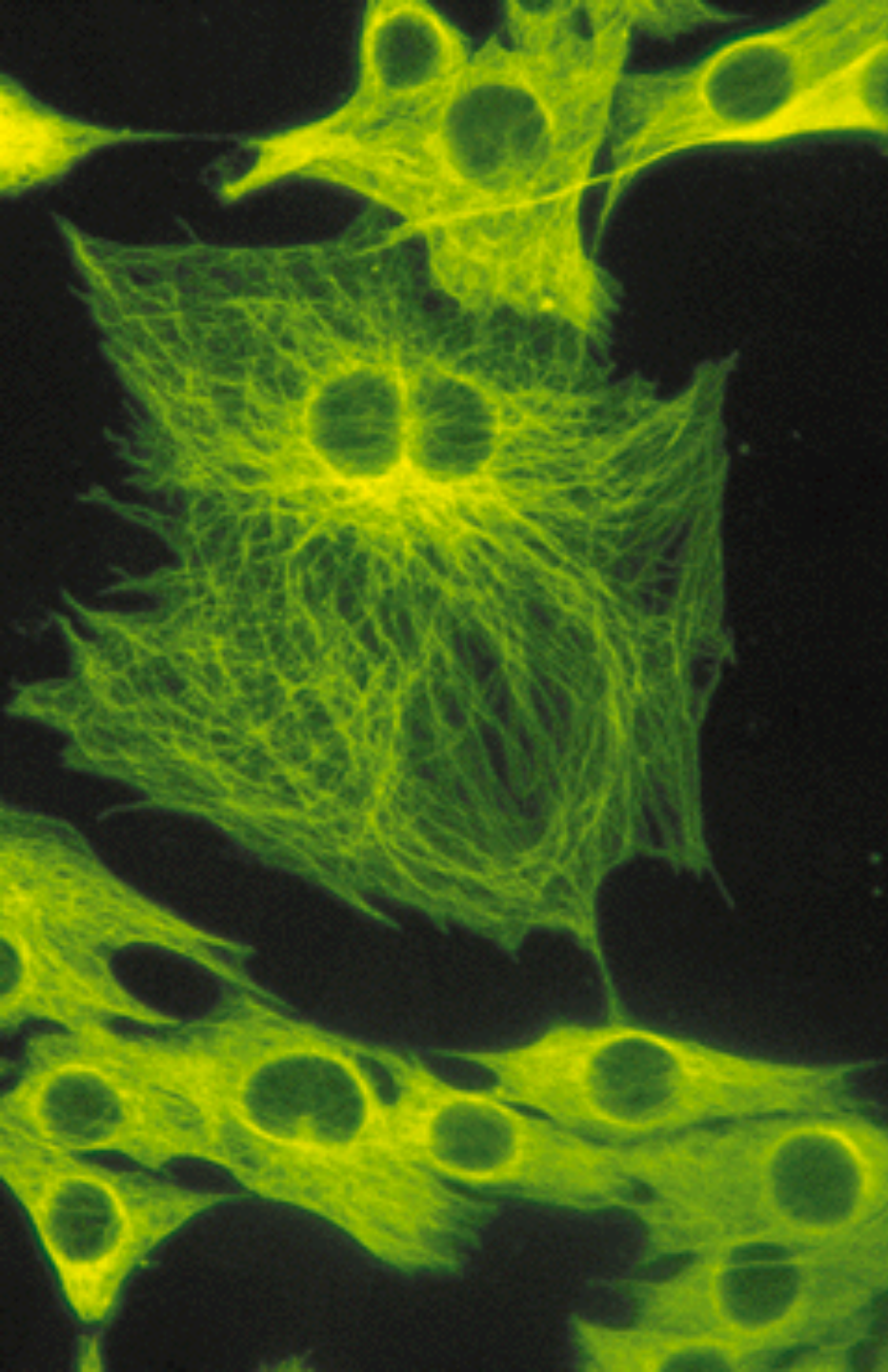
## PROTEINS



# Proteins are encoding text files

## MOLECULAR MACHINERY: A Tour of the Protein Data Bank

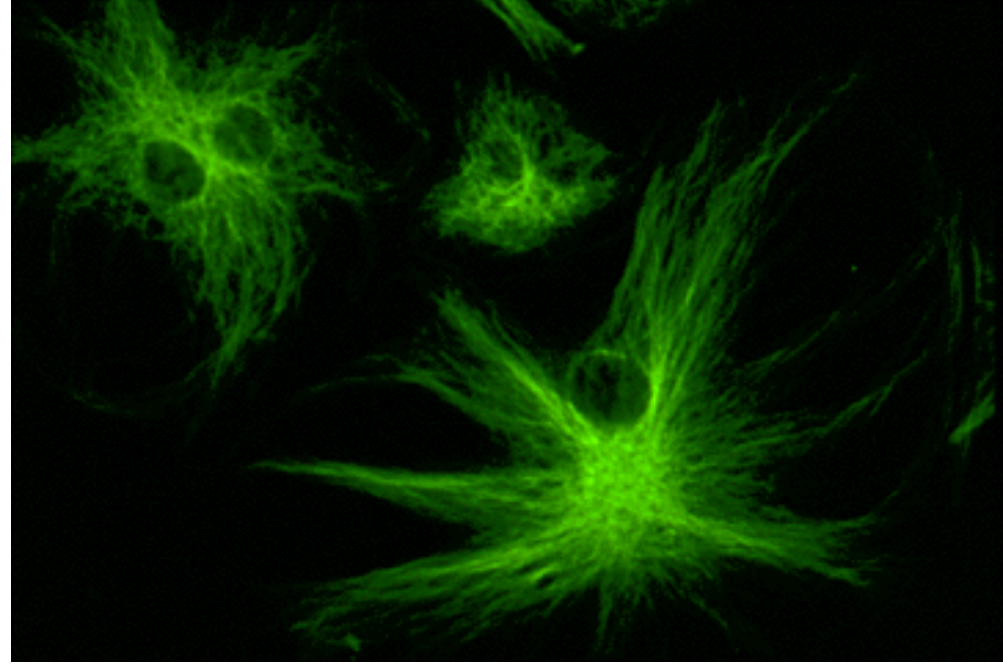
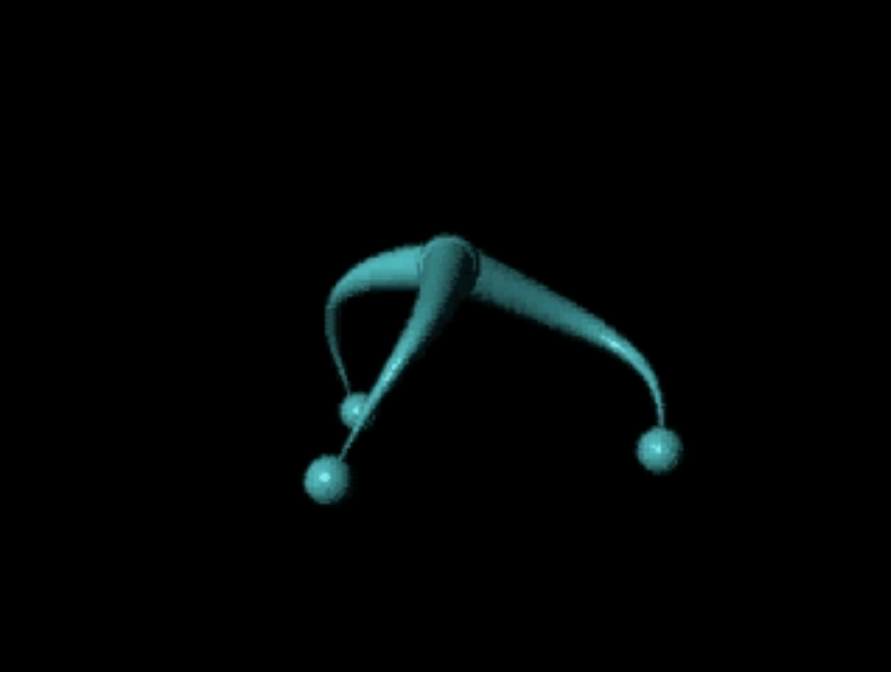




*The molecules and cells that form our tissues are continually removed and replaced*

*It is the maintenance of pattern and architecture that we call life.*

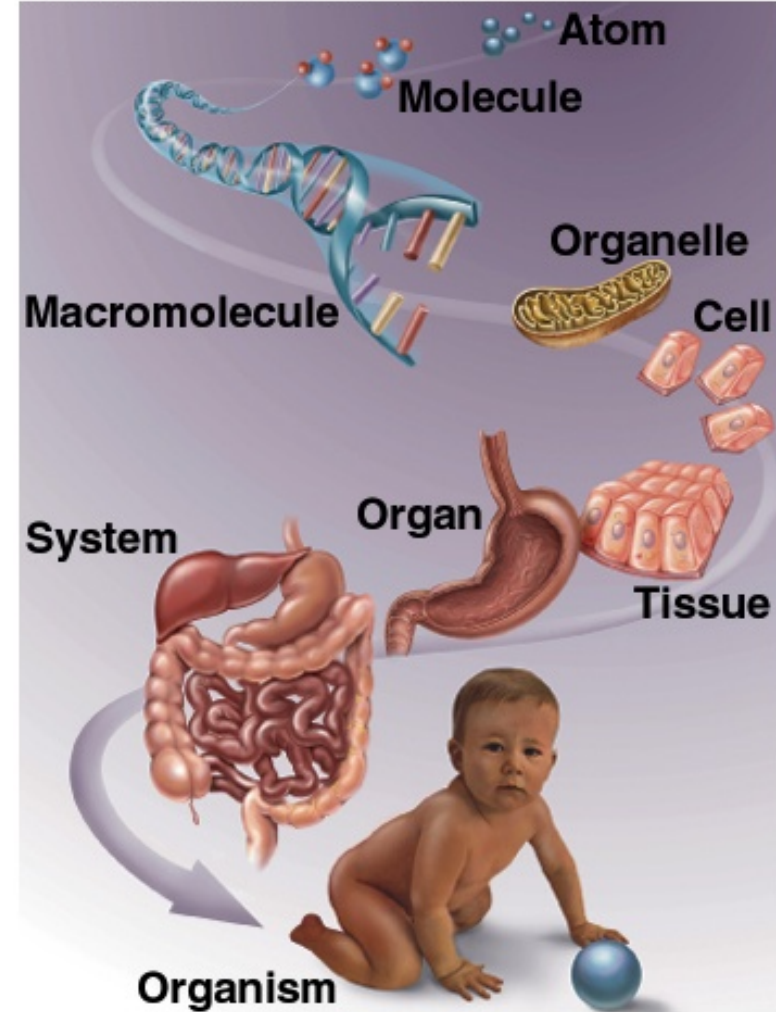




*A self-organised system* continuously consumes and dissipates energy to maintain itself.

*Self-assembling system* releases free energy during their organization leading to static structures in which no energy flows.

# *Hierarchical organization of information – emerging properties*



*Genome Transcriptome Proteome Metabolome Cellome Physiome Interactome*

<i>Domain</i>	•Genes	•Gene expression	•Post-translational modification	•Pathways	•Compartments	•Whole organ models
	•Promoters	•Genetic networks	•Protein-protein interactions	•Enzyme kinetics	•Transport •Signal transduction	



# ***Bio-Nano Manufacturing:***

Where Bottom-up Chemistry Meets Top-Down Engineering

