LECTURES IN BIOPHYSICS

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Physics contributes to biology by instrumentation and basic concepts

Outline of the lectures

10.1	The biological cell, its molecular elements and physical principles Single molecule force measurements	3h	U
17.1	Molecular motors: fundamentals, experiments and theory	3h	U&D
24.1	Origin of life	2h	D
31.1	Overstretching DNA and RNA double helices	1h	U
7.2	Cycle kinetics	2h	D
14.2	DNA hybridization	1h	U
28.2	Biosensors and DNA-based nanotechnology	1h	U
6.3	Regulatory networks and cellular noise	2h	U&D
13.3	Regulation of shape and size of the biological cell Single molecule FRET as molecular ruler	2h	D&T

Seminars (27.3 et 3.4) 6h

Deepen the knowledge in selected topics and grade the students

The biological cell

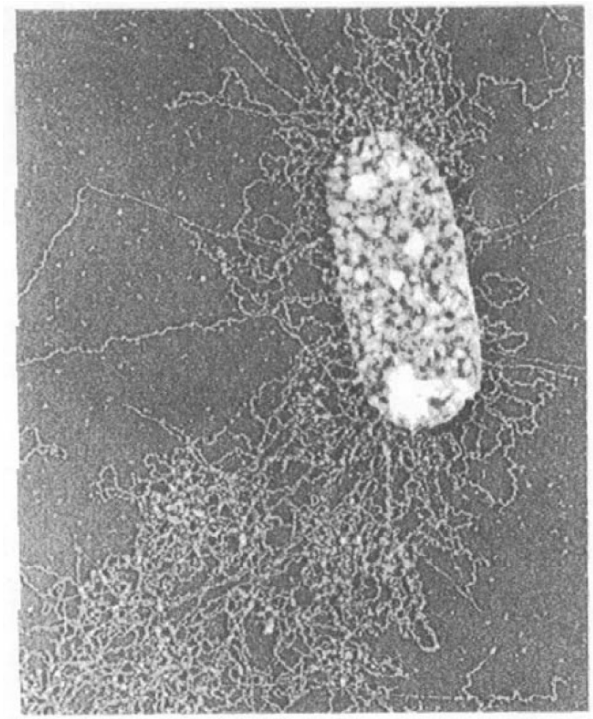
(1) Every living organism is composed of one or severall cells.

(2) The cell is the structural basis of life.

(3) A cell can only emerge from a division of a preexisting cell.

A disrupted *Eschericha coli* cell (détergents).
We observe the outcoming DNA.

Keeton, Gould Biological Sciences 5th Editon,
Norton Company NY



1 μm

The biological cell: molecular elements and physical principles

1 Description of the biological cell

2 Molecular elements

3 Energy and entropy

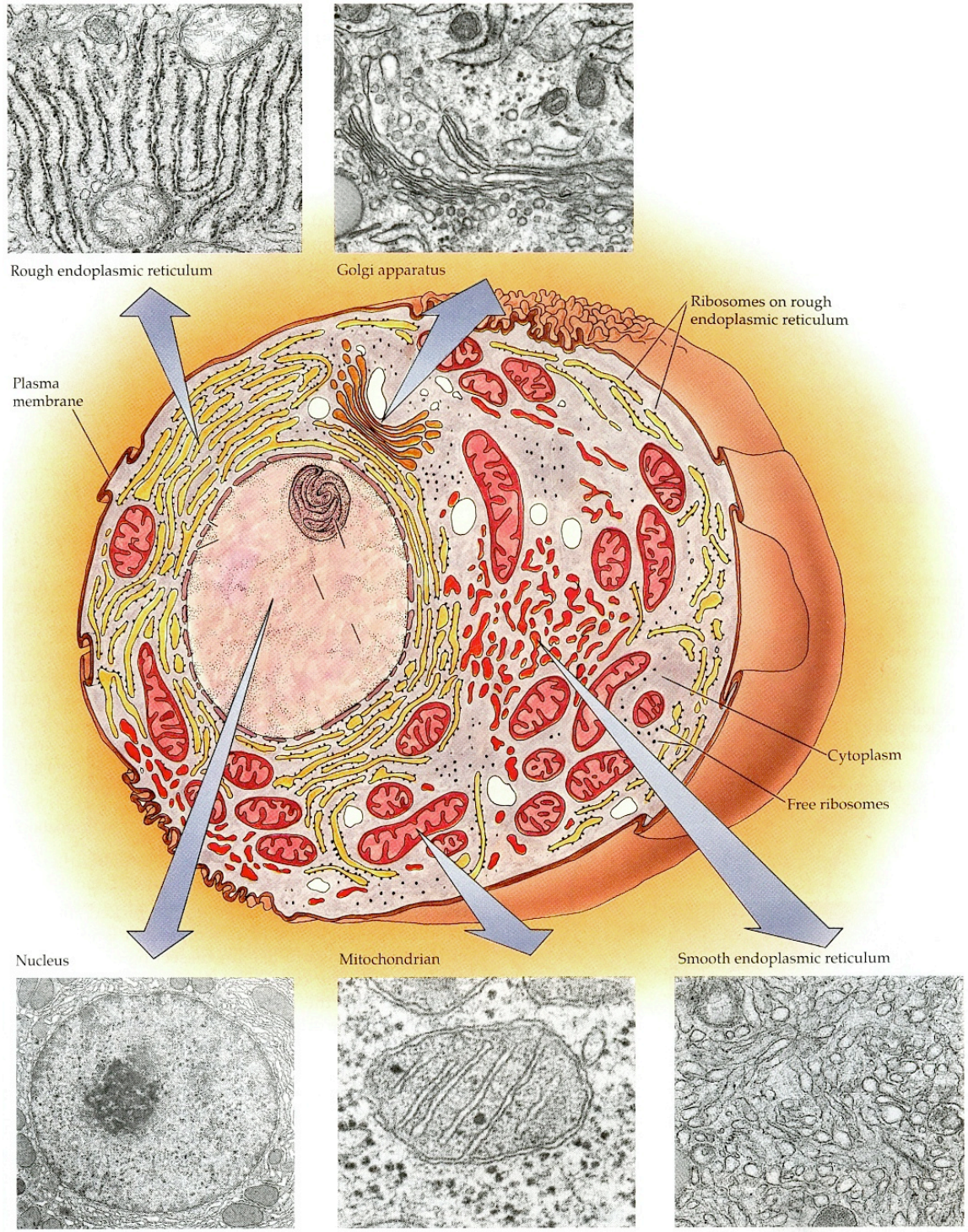
4 Enzymatic catalysis

5 Some enzymatic processes

1
Description of the biological cell

1) Compartments
2) Genetic program
3) Reproduction
4) Energy consumption
5) Chemical reactions
6) Mechanical activities
7) External stimulations
8) Auto-regulation

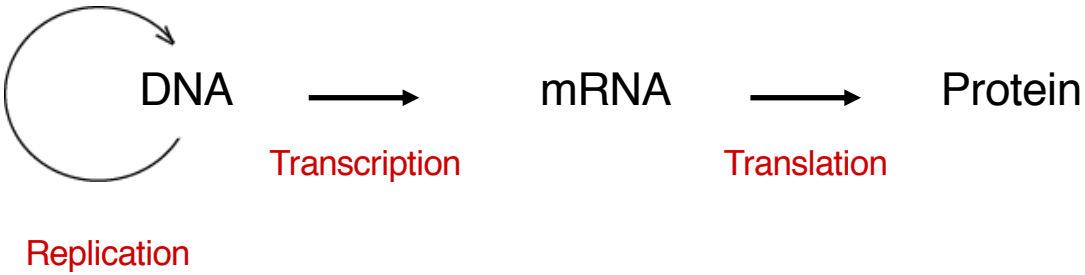
70% H_2O



2 Molecular elements

- DNA
- RNA
- Proteins
- Phospholipids

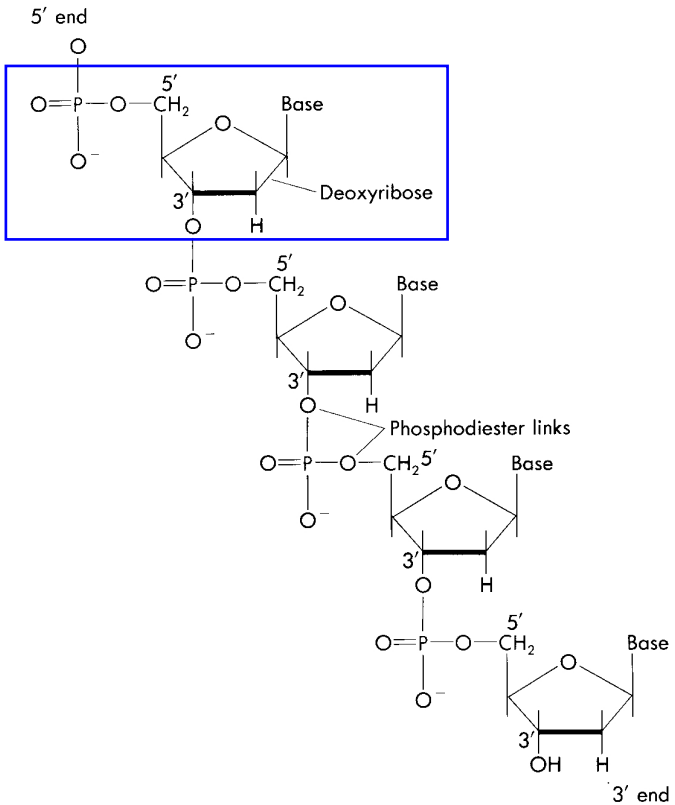
Central dogma of molecular biology



The whole is dynamic, with constantly creation and annihilation.

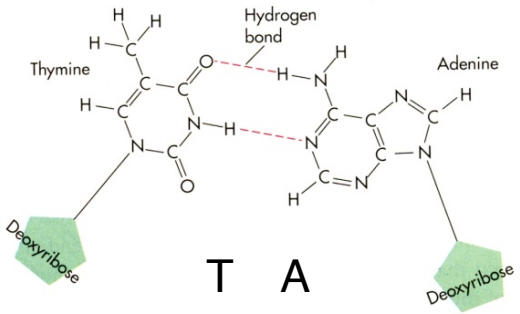
	DNA	RNA
Phosphat		
Sugar	Desoxyribose	Ribose
Base	T A C G	U A C G

Polymerisation by phosphodiester links

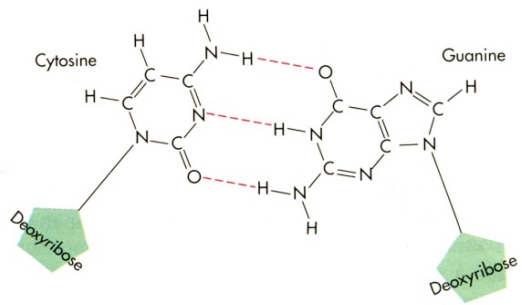


Hydrogen binding between bases

Pyrimidine - Purine

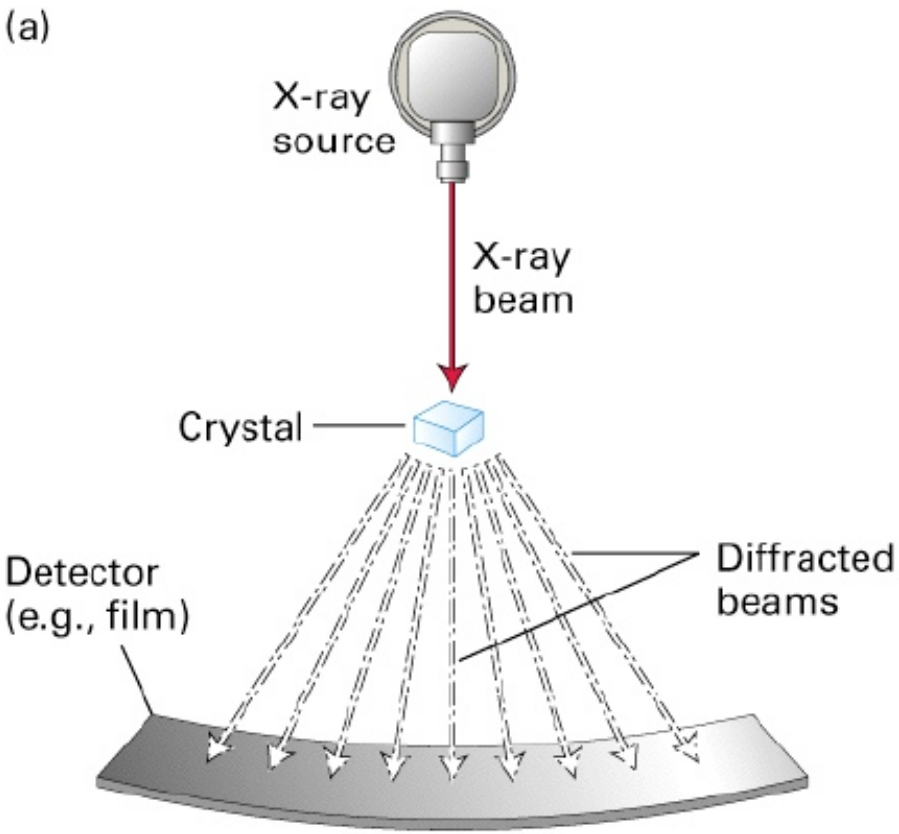


T A

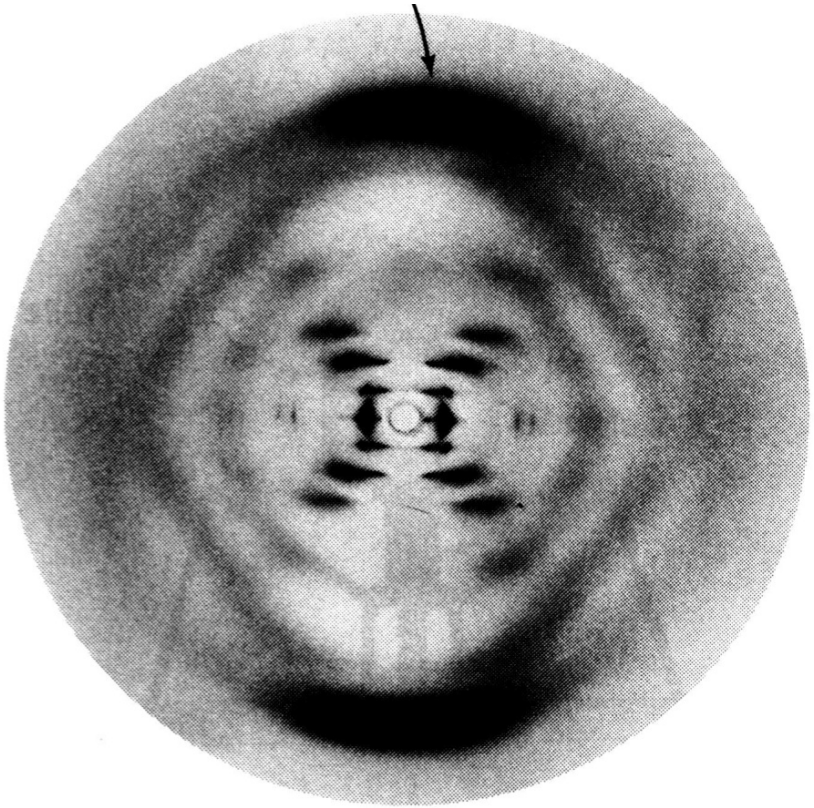


C G

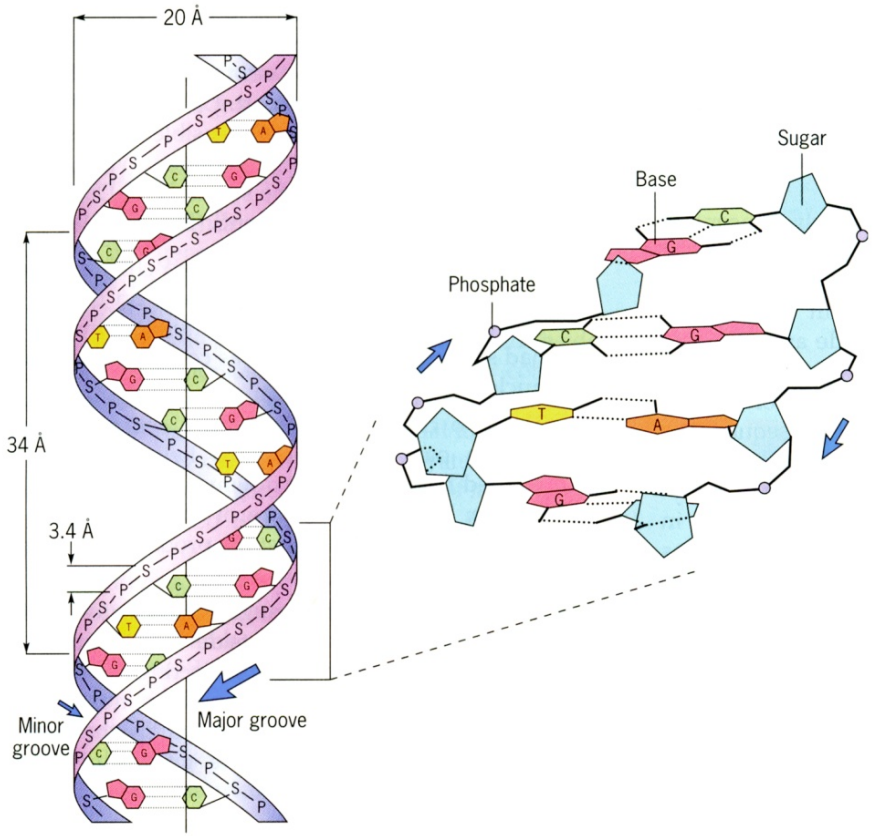
Structure determination by
x-ray scattering



Diffraction pattern of the
DNA double helix



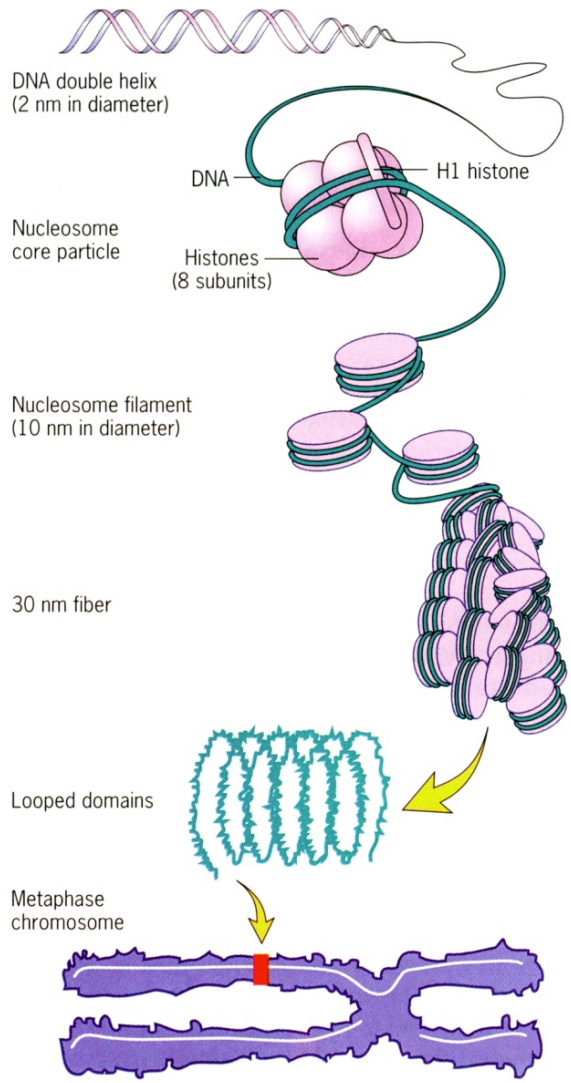
DNA double helix



Genetic information: …GTCAGTAAC…

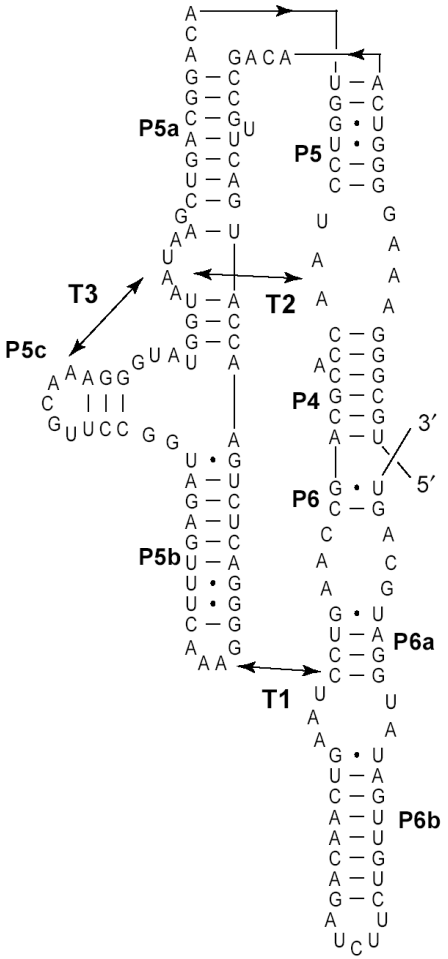
	# bases	length
Bacteriophage λ :	48 kb	16 μm
E-coli :	4 Mb	1.3 mm
Human :	3 Gb	1 m

Hierarchical organisation of the chromatin

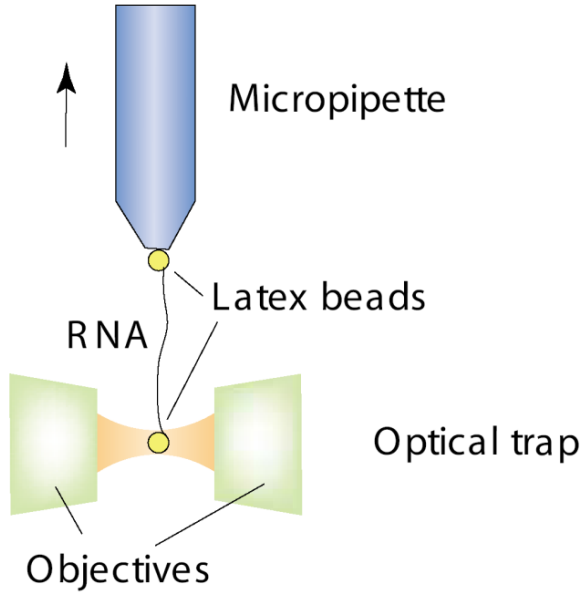


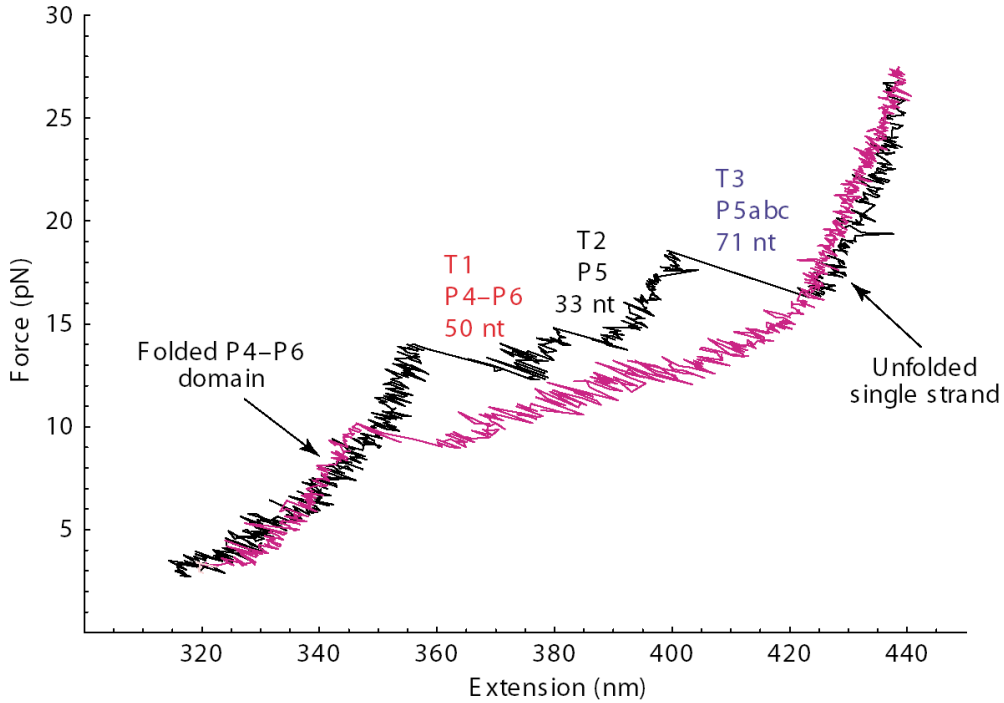
1 μm chromosome ~ 1 cm DNA ~ 7.5 Mbyte

RNA folding



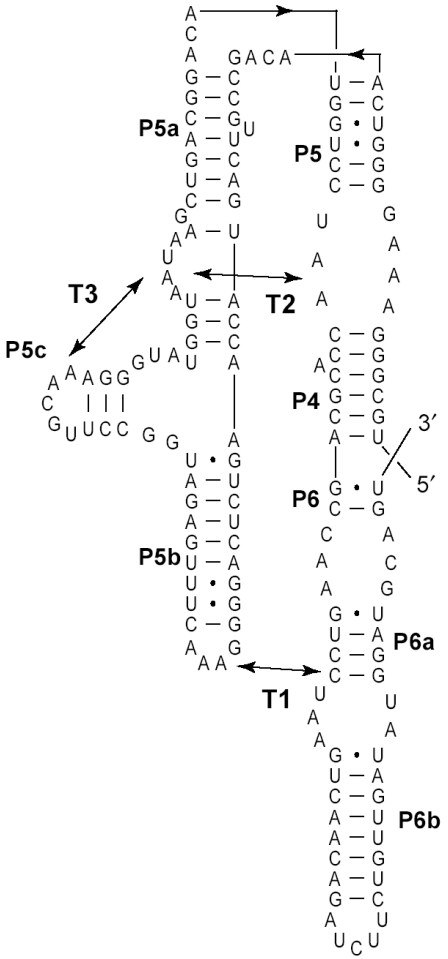
kT_{300K} = 25 meV = 4 pN nm





Onoa et al, Science 299, 1892 (2003)

RNA folding



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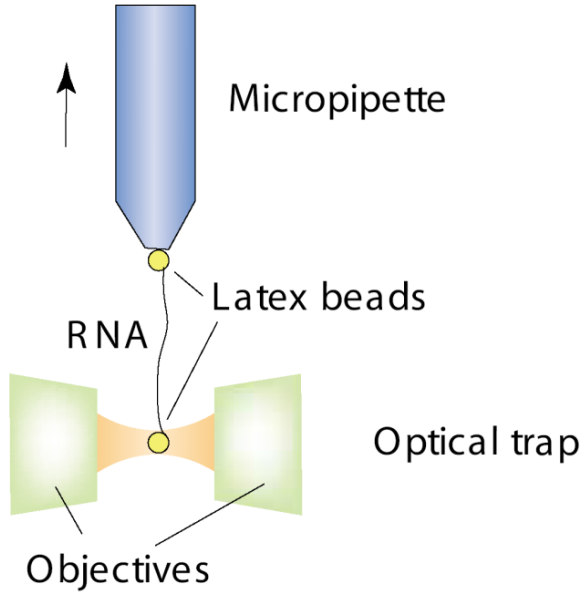
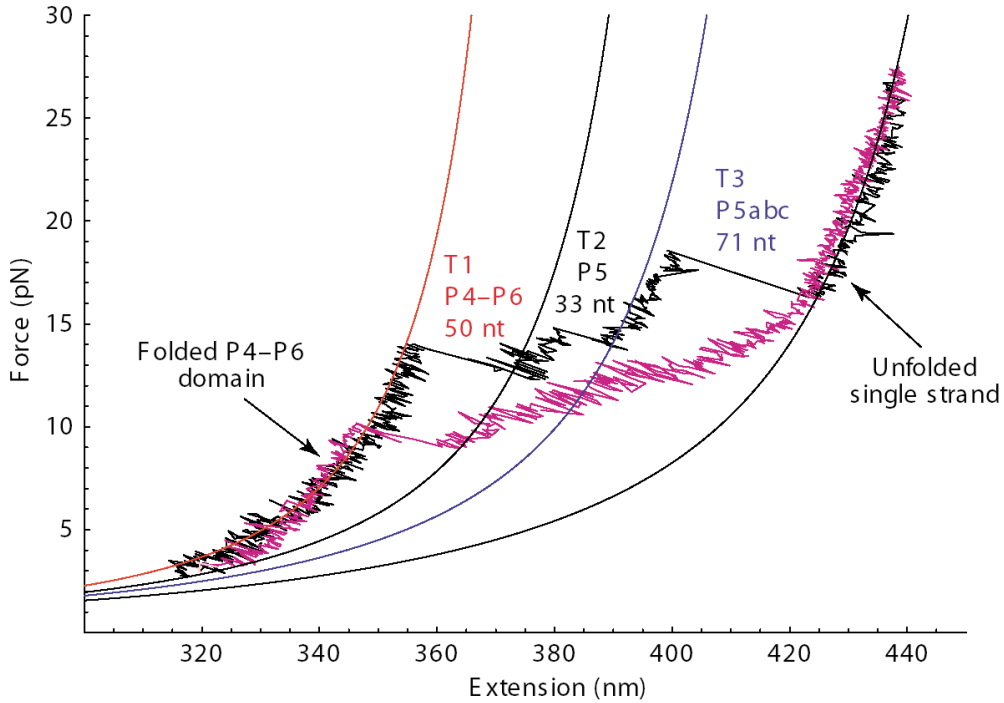
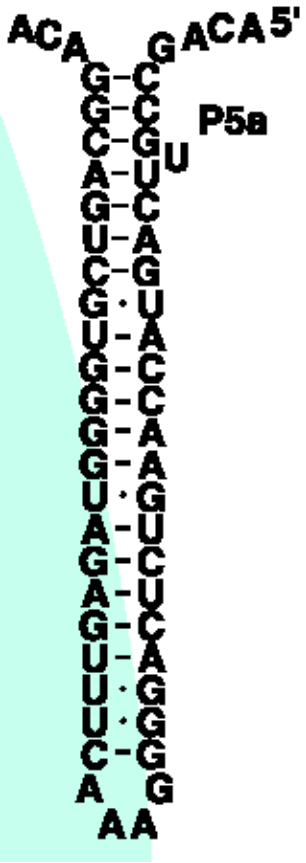
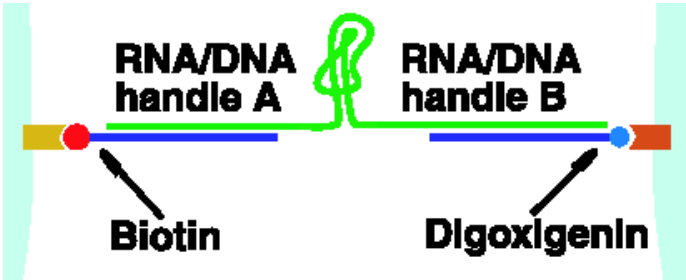


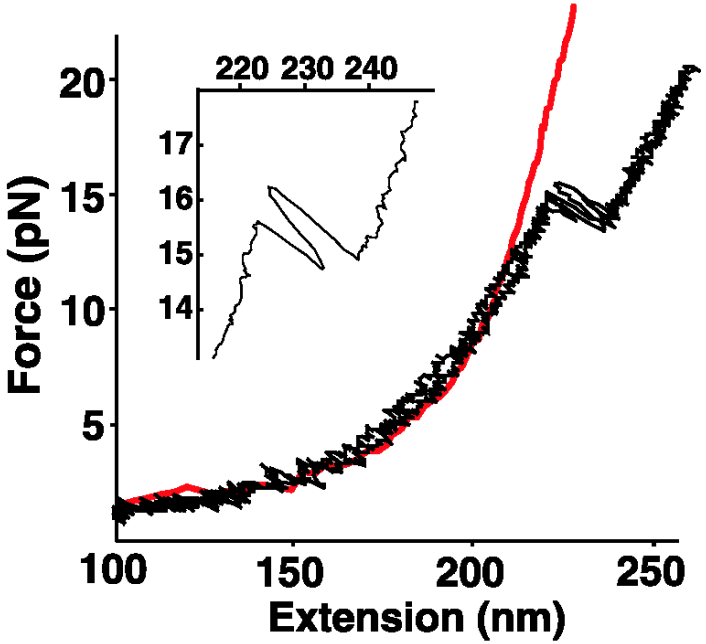


Onoa et al, Science 299, 1892 (2003)

An elementary RNA structure: the RNA hairpin

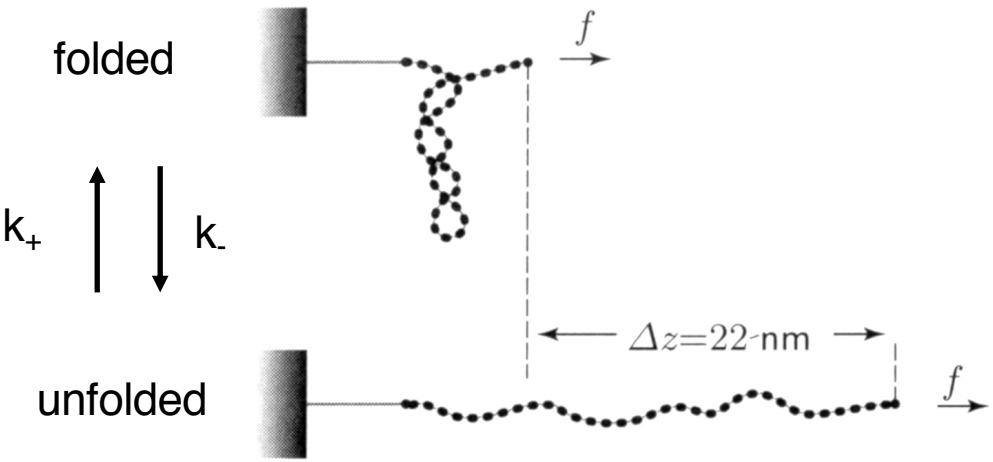


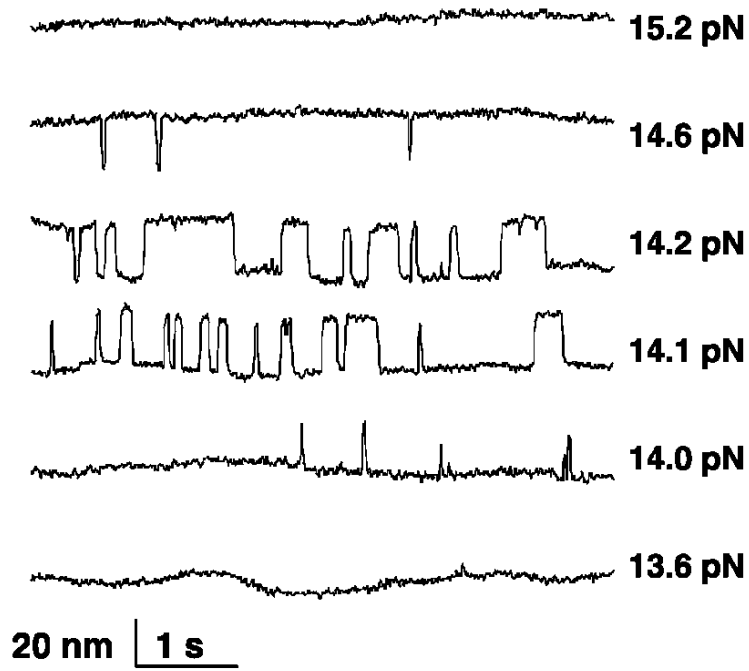


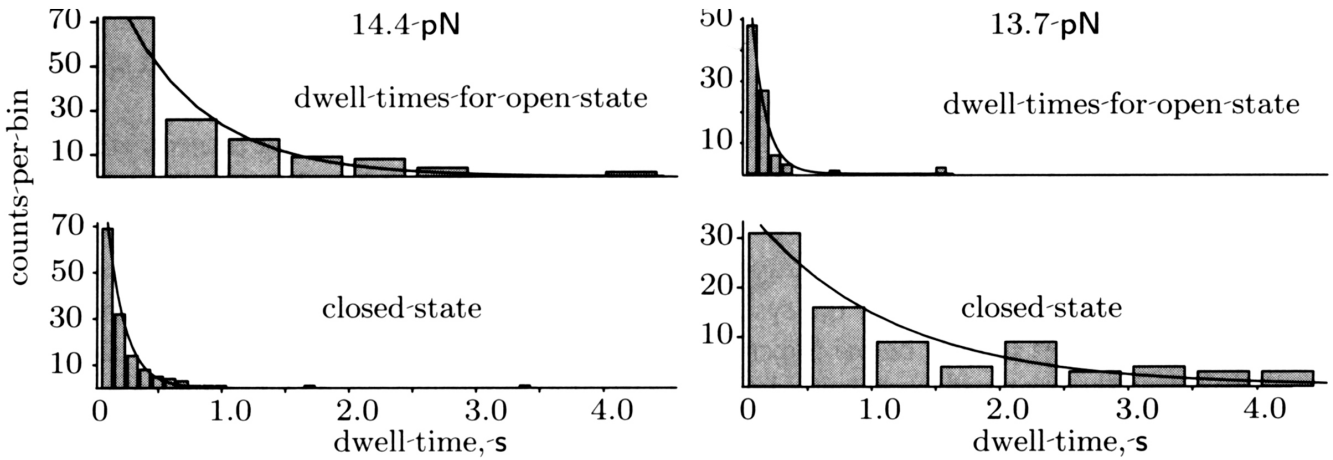


Liphardt et al, Science 292, 733 (2001)

Transitions between folded and unfolded states







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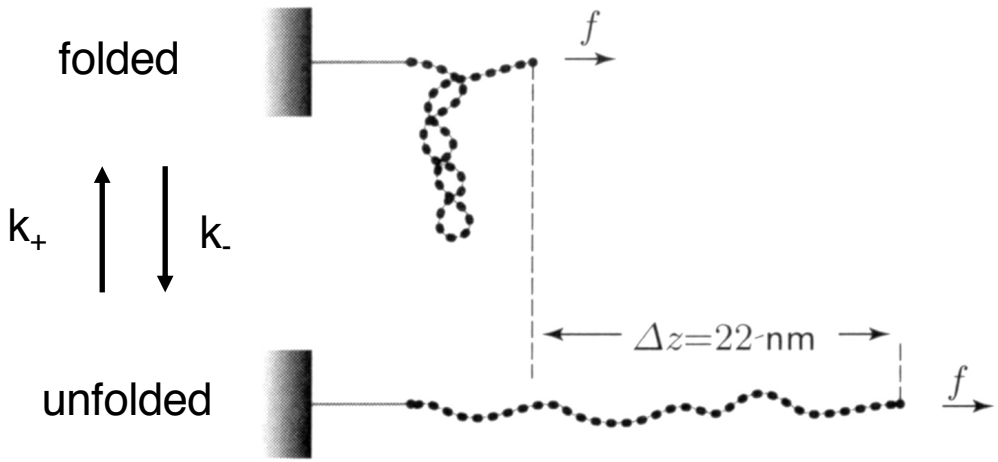
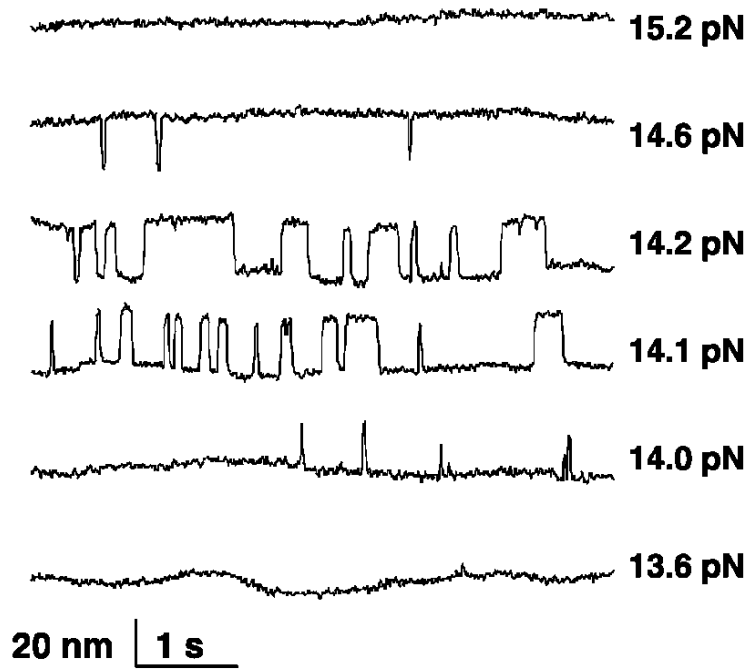
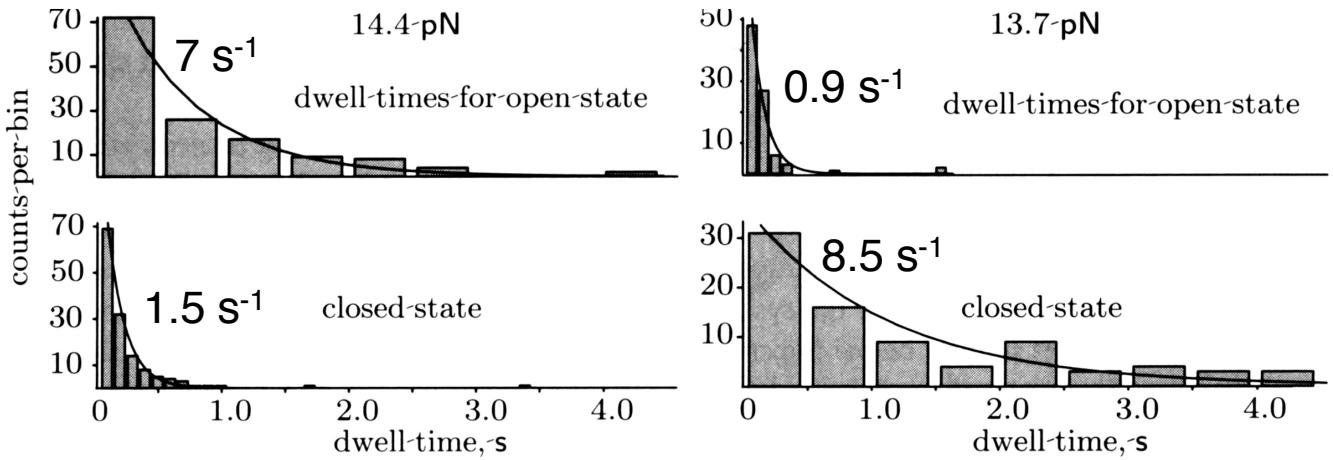




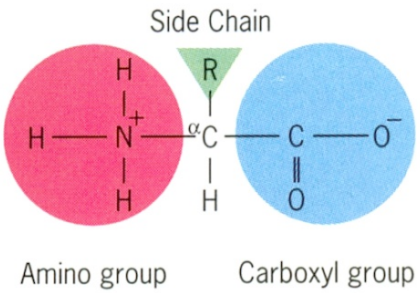


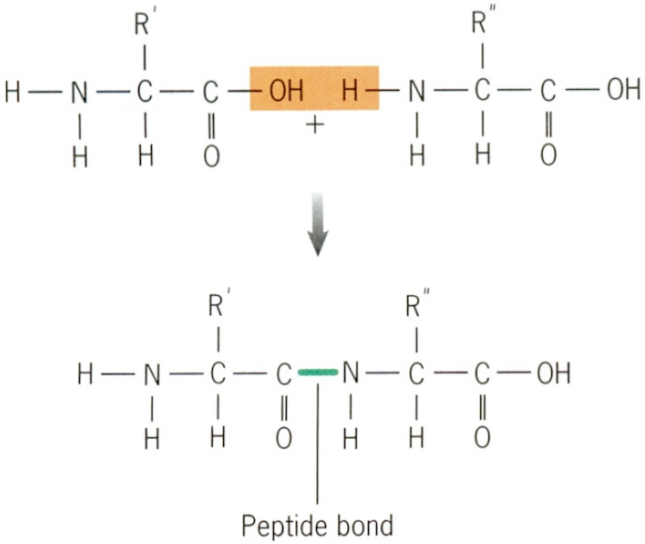
$k_+ \exp(-k_+ t)$

$k_- \exp(-k_- t)$

Proteins

Polymerisation of amino acids





The successive nucleotides of the mRNA code for one amino acid

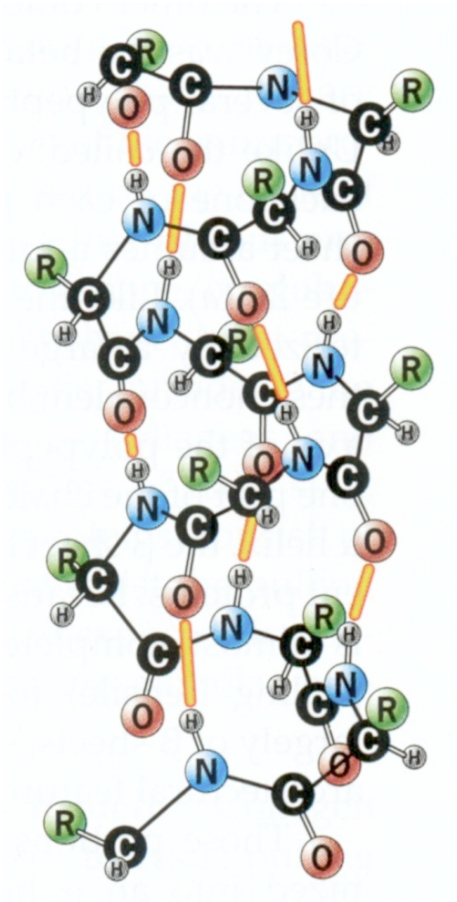
ex: UGC code la cystéine
CAC code la histidine

Genetic code

FIRST POSITION (5′ END)	SECOND POSITION U	SECOND POSITION C	SECOND POSITION A	SECOND POSITION G	THIRD POSITION (3′ END)
U	Phe	Ser	Tyr	Cys	U
	Phe	Ser	Tyr	Cys	C
	Leu	Ser	Stop	Stop	A
	Leu	Ser	Stop	Trp	G
C	Leu	Pro	His	Arg	U
	Leu	Pro	His	Arg	C
	Leu	Pro	Gln	Arg	A
	Leu	Pro	Gln	Arg	G
A	Ile	Thr	Asn	Ser	U
	Ile	Thr	Asn	Ser	C
	Ile	Thr	Lys	Arg	A
	Met	Thr	Lys	Arg	G
G	Val	Ala	Asp	Gly	U
	Val	Ala	Asp	Gly	C
	Val	Ala	Glu	Gly	A
	Val	Ala	Glu	Gly	G

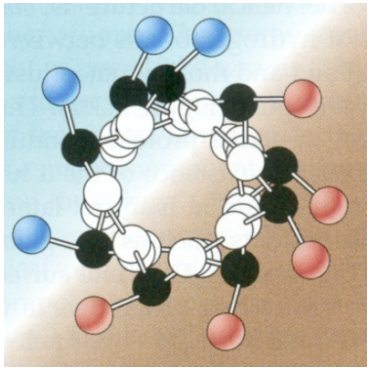
Protein secondary structure

α helix



0.56 nm

watetr

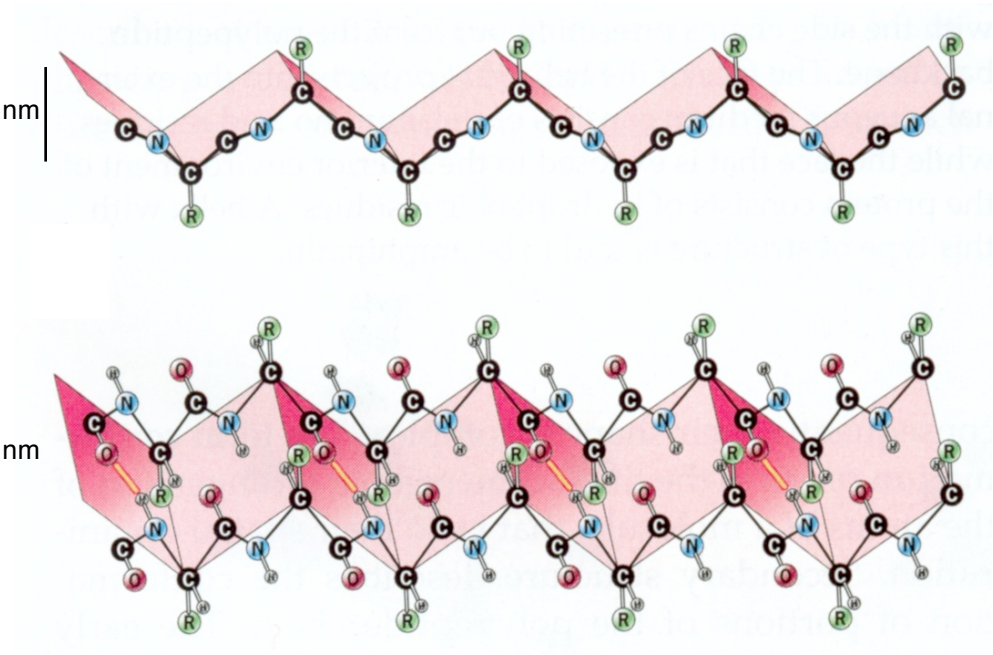


protein

0.5 nm

β sheet

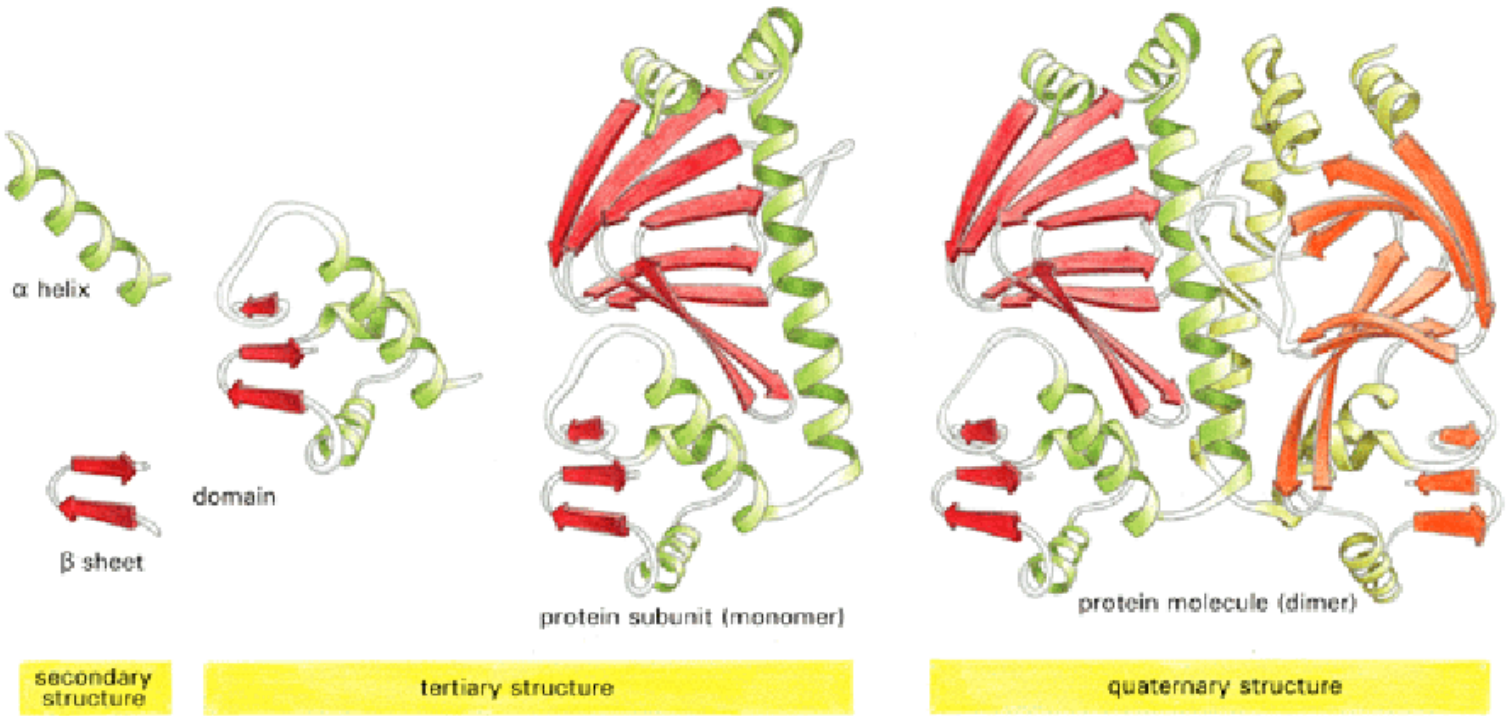
0.5 nm



0.5 nm

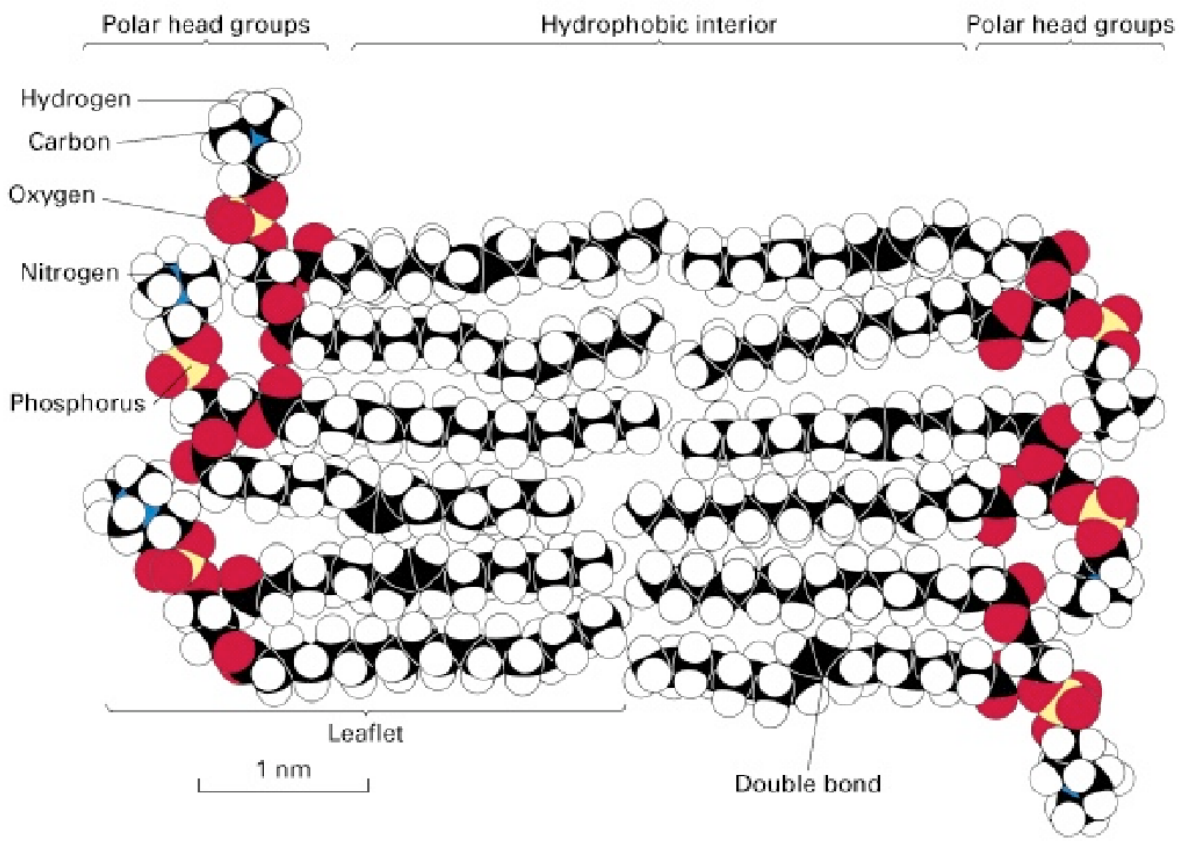
0.7 nm

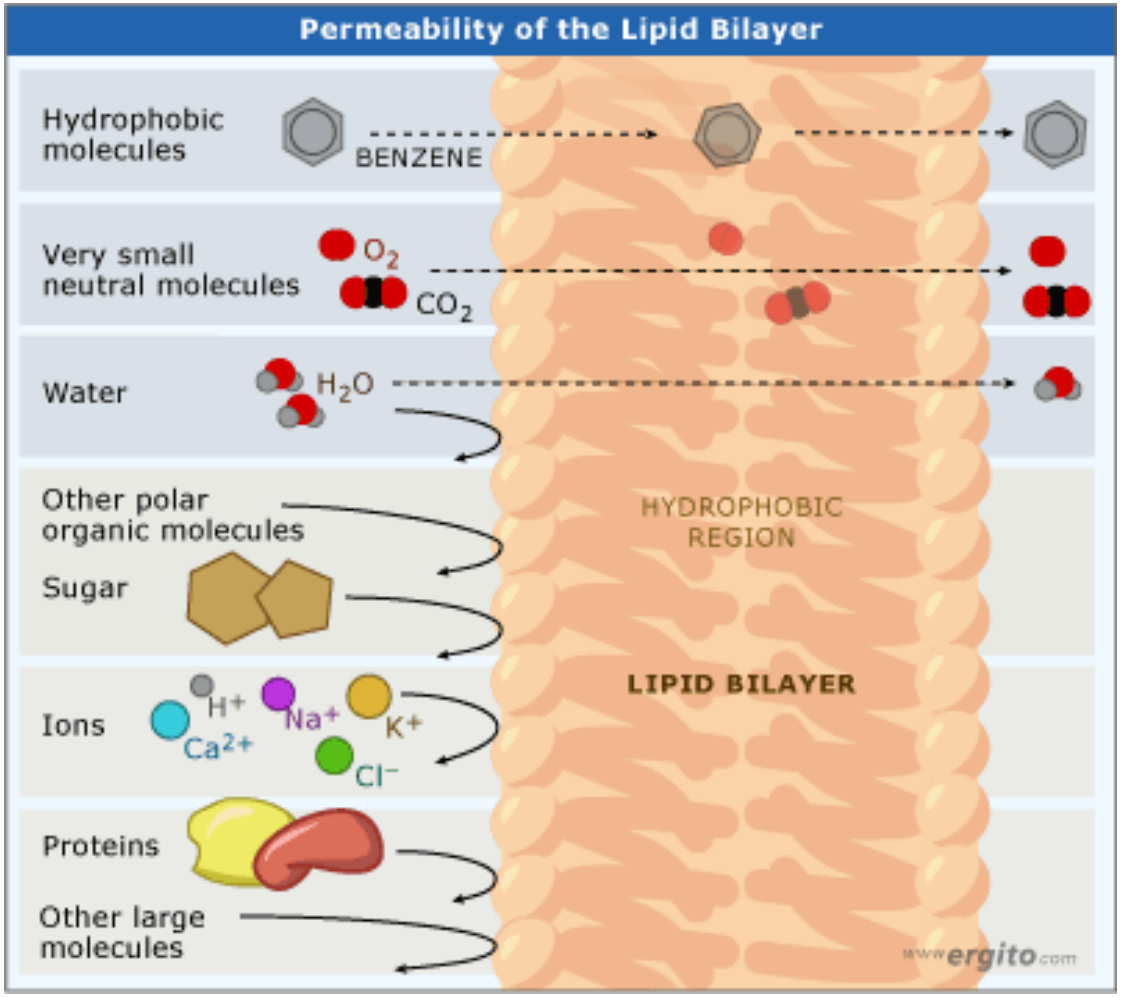
Three levels of organisations for a protein



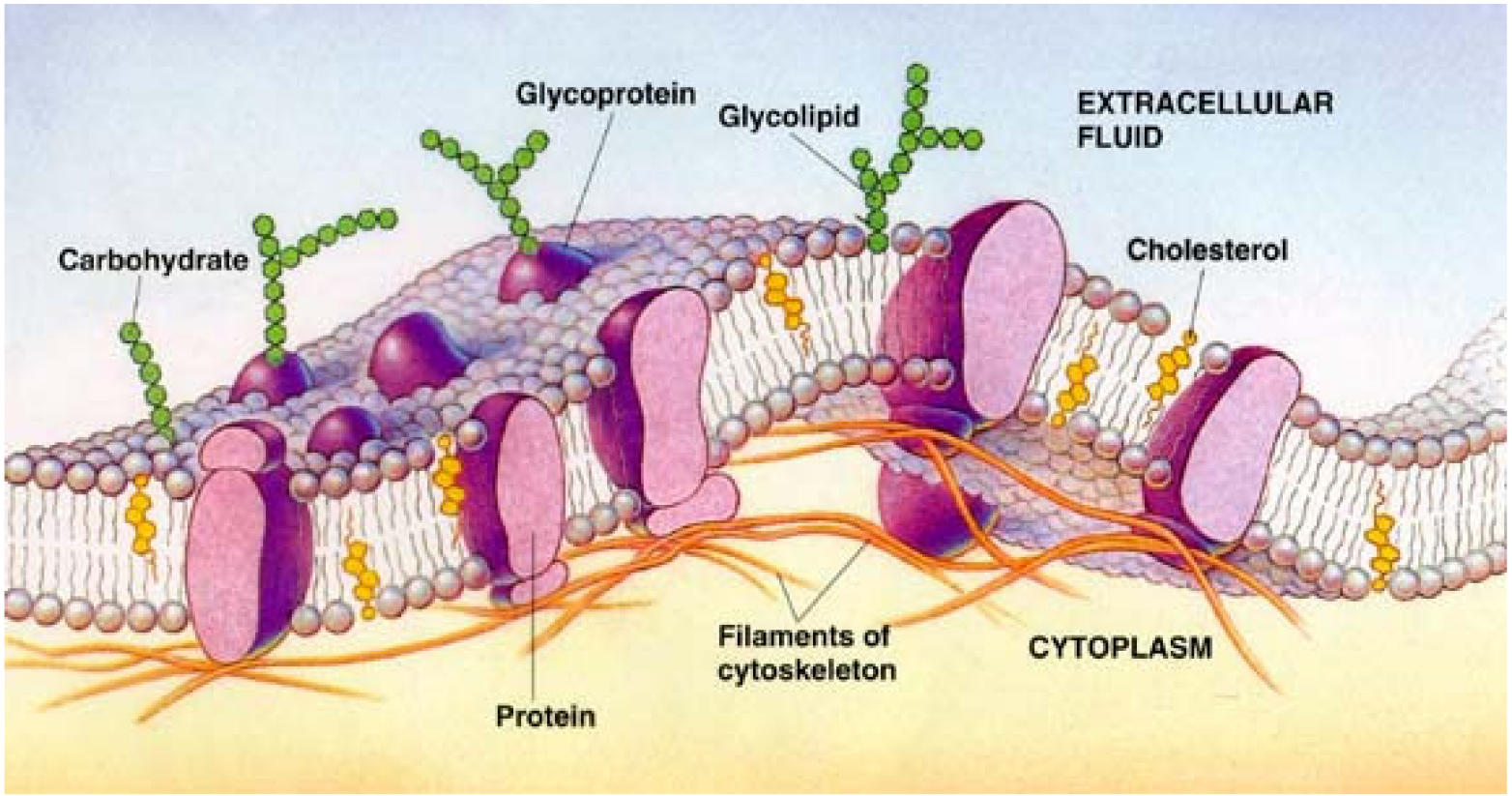
Phospholipids as elementary building blocks of biological membranes

These molecules spontaneously form bilayers, because of their amphiphilic character




Permeability of the Lipid Bilayer
Hydrophobic molecules
BENZENE
Very small neutral molecules
O_2
CO_2
Water
H_2O
Other polar organic molecules
Sugar
Ions
H^+
Na^+
K^+
Ca^{2+}
Cl^-
Proteins
Other large molecules
HYDROPHOBIC REGION
LIPID BILAYER
www.ergito.com

Membrans: 2D liquids as a matrix for functional units

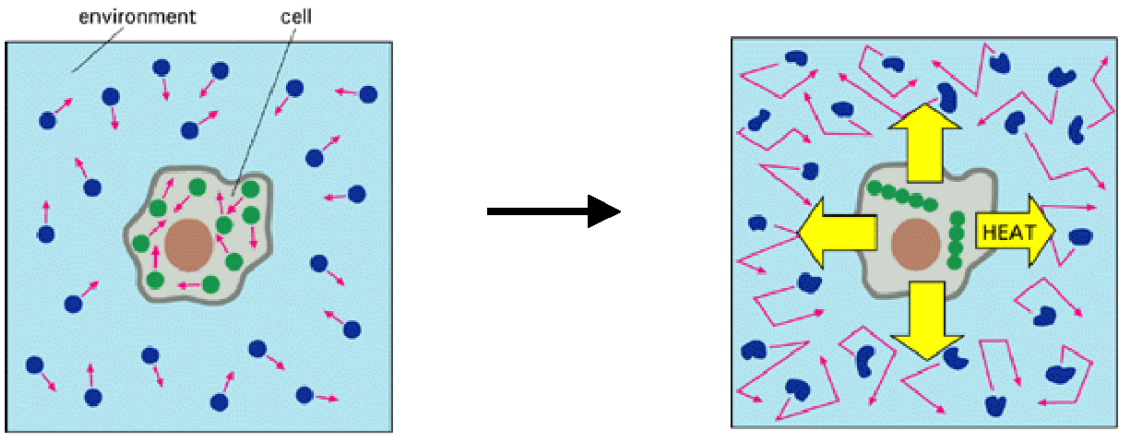


3 Creation and maintenance of structures: energy and entropy

La cellule biologique obéit-elle à la seconde loi de la thermodynamique?

Ensemble microcanonique
S -> max

Ensemble canonique
F=E-TS -> min



Dans la cellule: $\Delta F<0$ et $\Delta S<0$.

-> Cellule donne de l'entropie au bain, donc émets de la chaleur $T\Delta S$

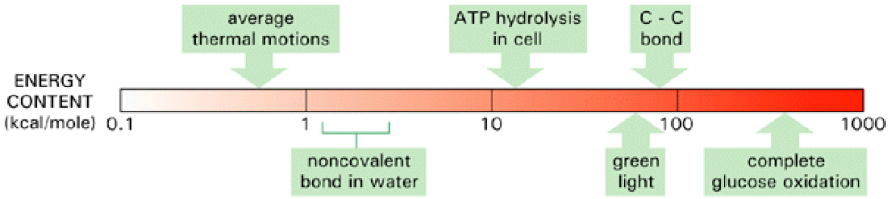
F=E-TS -> Cellule importe de l'énergie et vit dans un régime hors-équlibre.

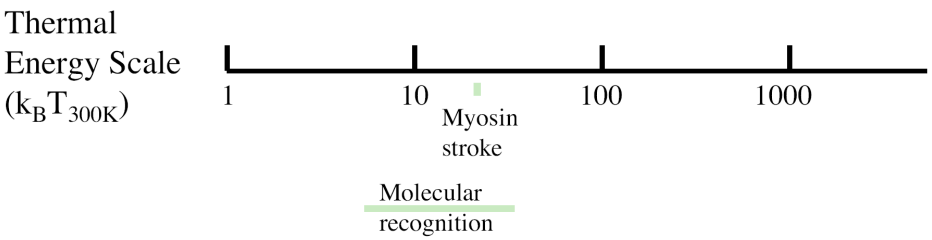
Importation d'énergie sous formes de molécules et/ou photons.

Dans la cellule la molécule d'ATP sert comme porteur d'énergie.

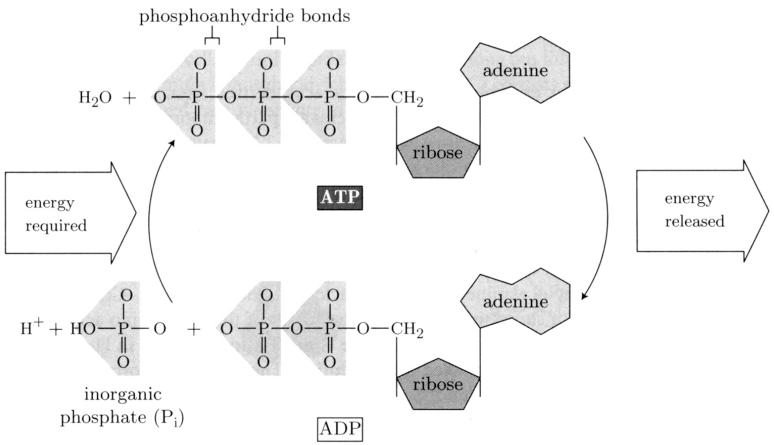
Ordres de grandeurs d'énergie de la cellule

$1k_BT_{300K} = 25\ meV = 4\ pNnm = 0.6\ kcal/Mol = 2.5\ kJ/Mol$

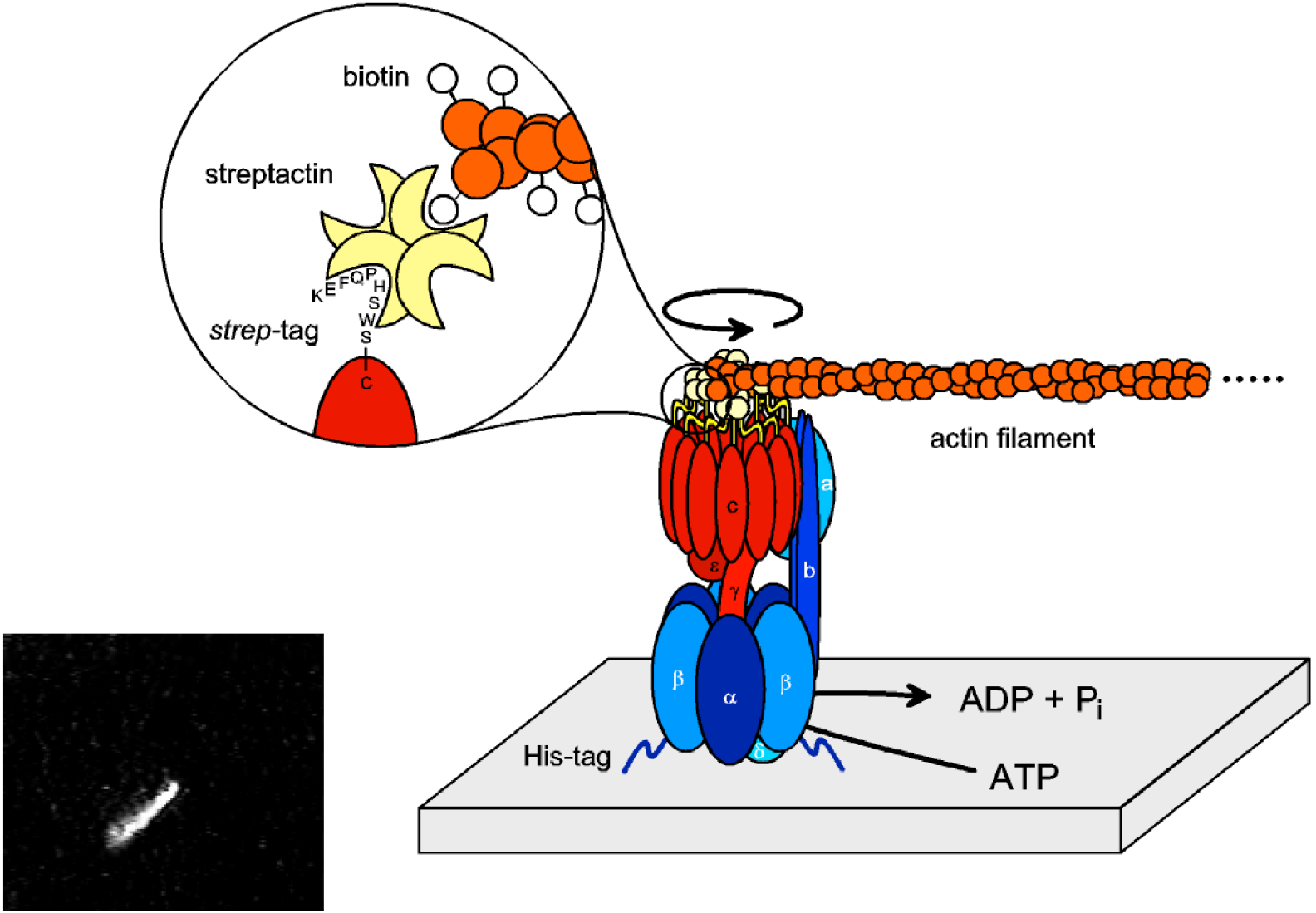




Hydrolyse de l'ATP:
source d'énergie pour de nombreux réactions biochimiques dans la cellule



F0/F1 ATPase: conversion d'un gradient de proton en ATP ou l'inverse



4 The enzymatic catalysis

Example: decomposition of hydrogen peroxid:

$$H_2O_2 \longrightarrow H_2O + \frac{1}{2} O_2 \qquad \Delta G^0 = -40kT \text{ exothermal}$$

Sample of 1M H_2O_2 à 25° C

Without enzyme: 10^{-8} M/s, 1% in 2 weeks
with 1mM catalase: 10^{4} M/s, 1% in 1 μs

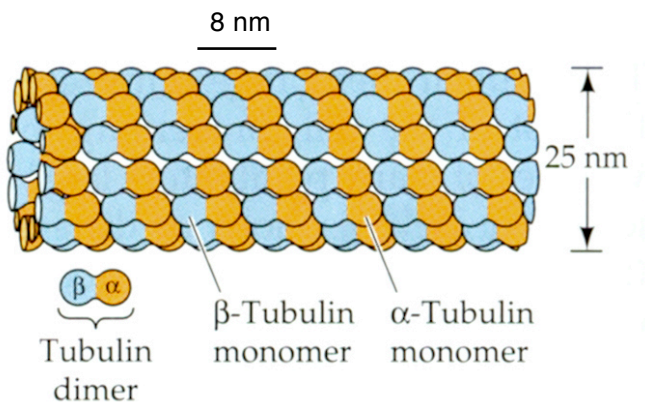
Saturating kinetics
$\nu_{max}=10^4$ M/s -> One molecule of catalase decomposes up to $\nu_{max}/c_E = 10^7$ molecules/s

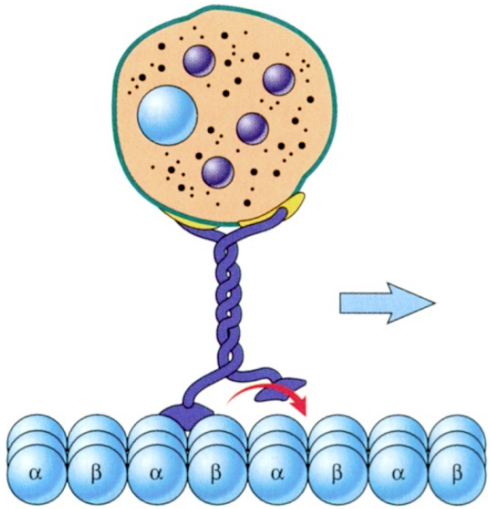
10^2-10^3 moleculs/s is a typical rate for the activity of an enzypm.

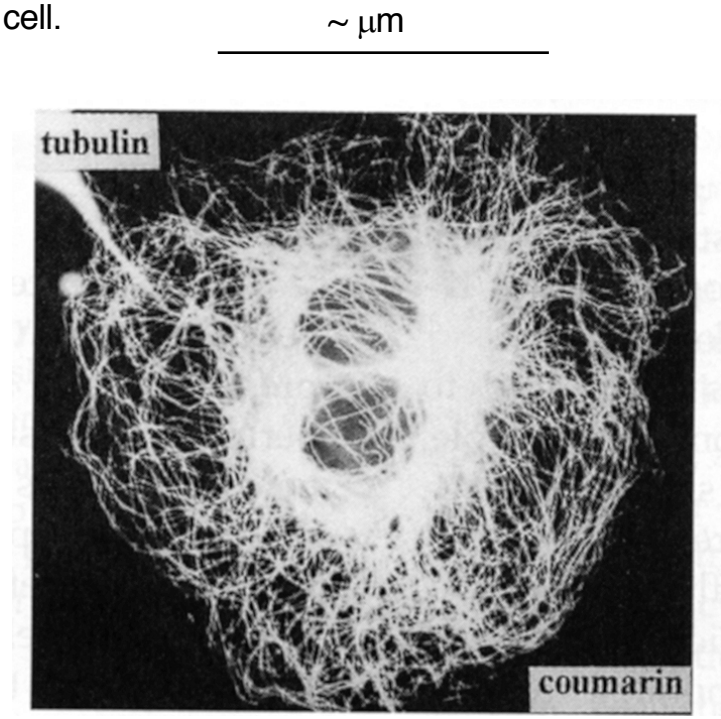
5 Some enzymatic processes

Kinesin: a molecular motor that consumes ATP

Microtubules mechanically stabilize the cell.
Are the most rigid of the three types of filaments that occur in the cell.





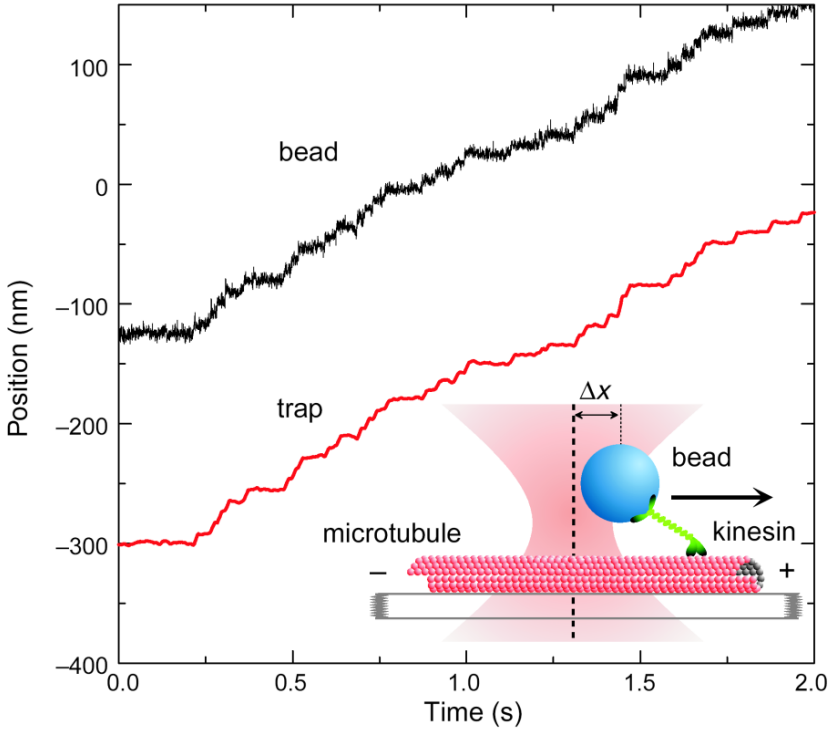


Fluorescence image of the microtubules in a biological cell.

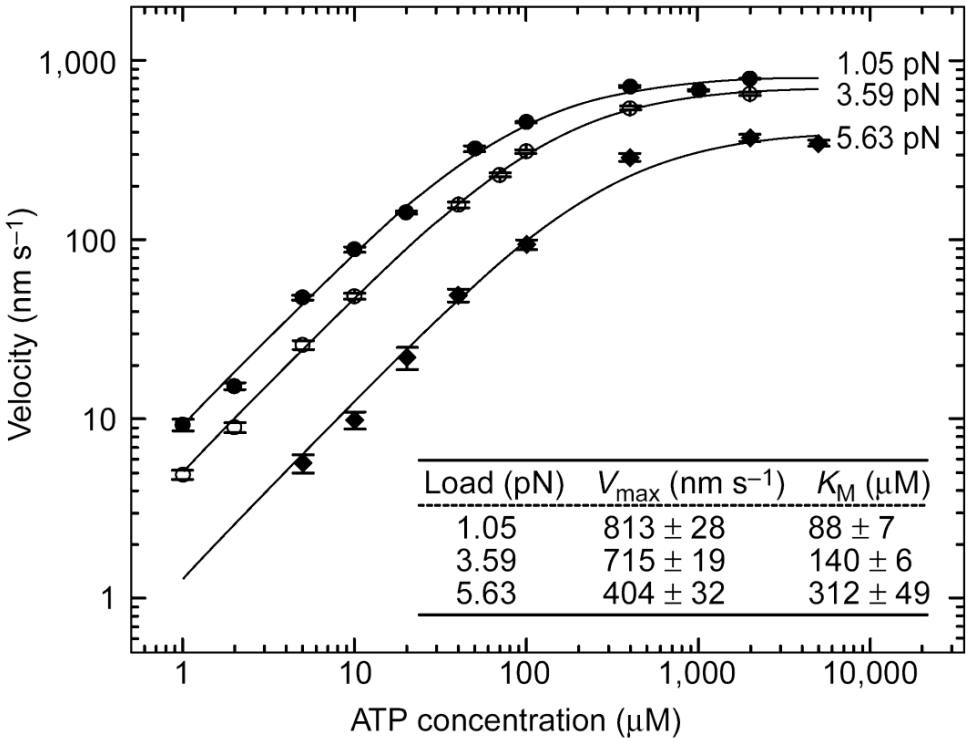
Kinesin advances by 8nm steps along the microtubule and consumes 1 ATP/step.

Enzymology at the single-molecule scale

Mesurement of the steps with an optical trap



Michaelis-Menten kinetics, in the presence of a force acting against the motion.



$$v = v_{max} \frac{[ATP]}{K_m + [ATP]}$$

Visscher et al, Nature 400, 184 (1999)