CORE126

Moderní technologie pro studium života

Karel Kubíček: Základní stavební prvky buňky

Composition of the Earth's Crust, Seawater, and the Human Body*

Earth's Crust		Seawater		Human Body†	
Element	%	Compound	m*M*	Element	%
O	47	Cl^-	548	H	63
Si	28	Na^+	470	O	25.5
Al	7.9	Mg^{2+}	54	C	9.5
Fe	4.5	SO_4^{2-}	28	N	1.4
Ca	3.5	Ca^{2+}	10	Ca	0.31
Na	2.5	K^+	10	P	0.22
K	2.5	HCO_3^-	2.3	Cl	0.08
Mg	2.2	NO_3^-	0.01	K	0.06
Ti	0.46	HPO_4^{2-}	<0.001	S	0.05
H	0.22			Na	0.03
C	0.19			Mg	0.01

*Figures for the earth's crust and the human body are presented as percentages of the total number of atoms; seawater data are millimoles per liter. Figures for the earth's crust do *not* include water, whereas figures for the human body do.

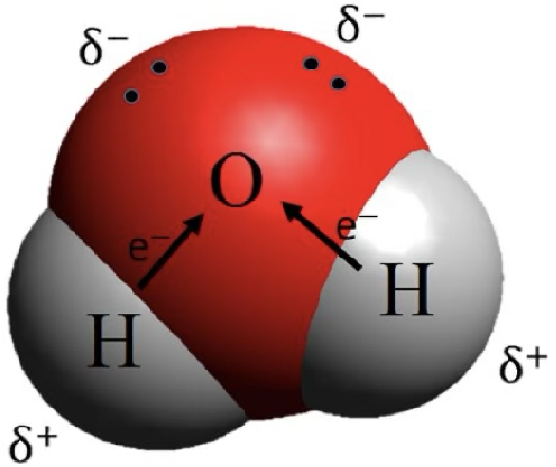
†Trace elements found in the human body serving essential biological functions include Mn, Fe, Co, Cu, Zn, Mo, I, Ni, and Se.

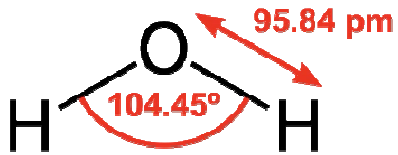
Chemické složení lidského těla

a. (65 %) Voda
b. (20 %) Proteiny
c. (12 %) Lipidy (tuky)
d. (1.1 %) Nukleové kyseliny
e. Ionty (Na^+, K^+, Cl^-, PO_4^{3-} ...)
f. Plyny (O_2, CO_2, …), karbohydráty (glukóza), hydroxyapatit (forma vápníku a fosfátu – zuby, kosti), volné radikály, etc.

Voda

je nezbytná pro existenci života jak jej známe





Credit to prof. Robert Vácha

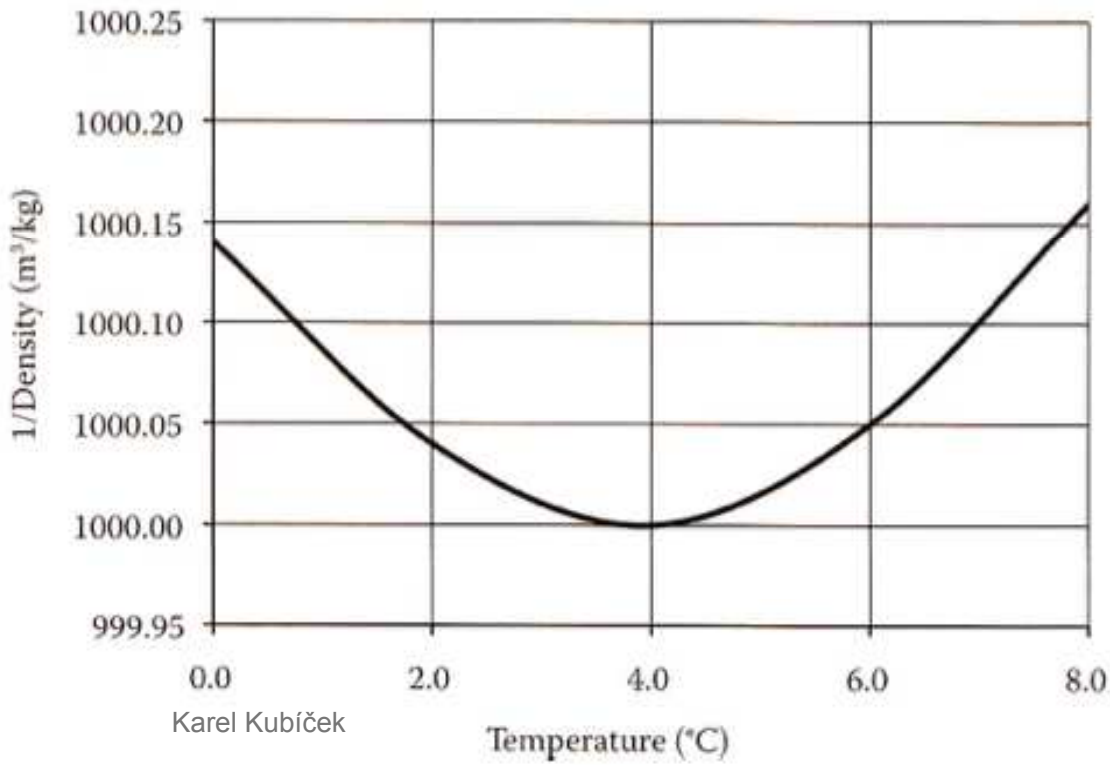
74 anomalií vody

http://www1.lsbu.ac.uk/water/water_anomalies.html

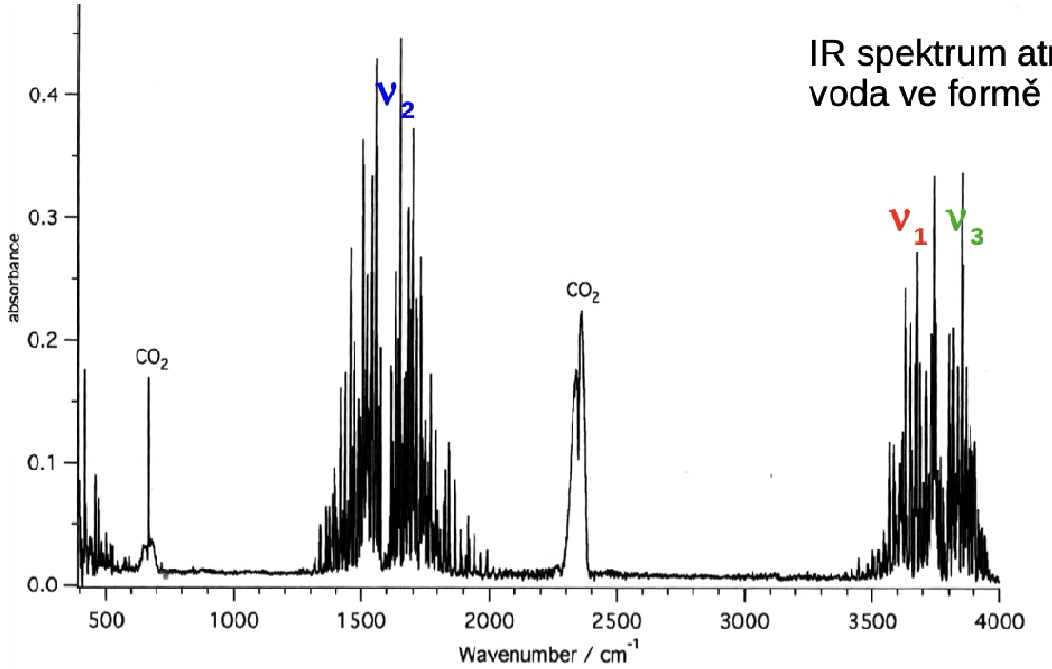
- Phase anomalies P1-P13
- Density anomalies D1-D22
- Material anomalies M1-M18
- Thermodynamic anomalies T1-T11
- Physical anomalies F1-F10

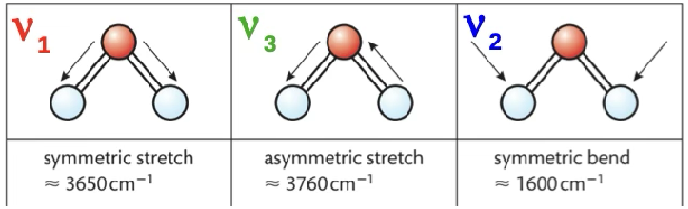
Hustota vody

- charakteristická vlastnost vody
- významná pro existenci života na Zemi
- hustotní maximum při 4 °C → led má menší hustotu než kapalná voda, a proto plave na hladině



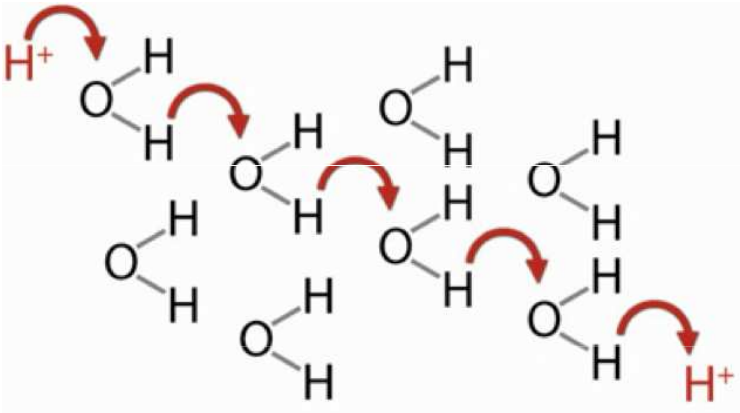
Vibrace molekuly vody



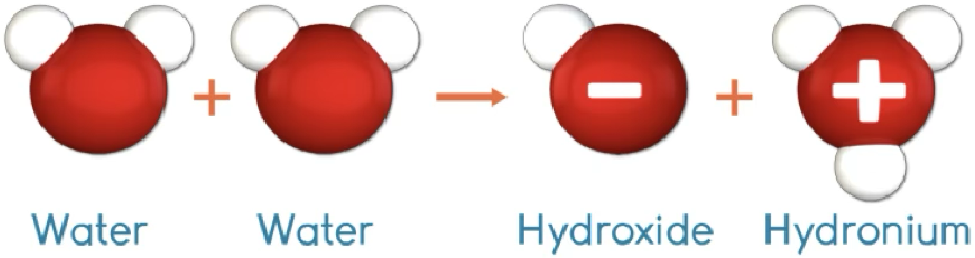


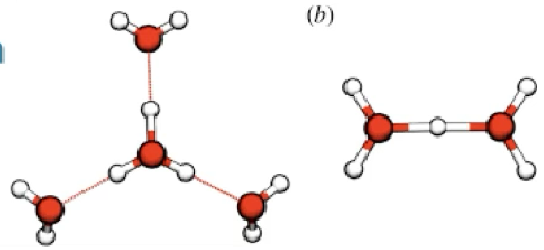
Kapalná voda x led

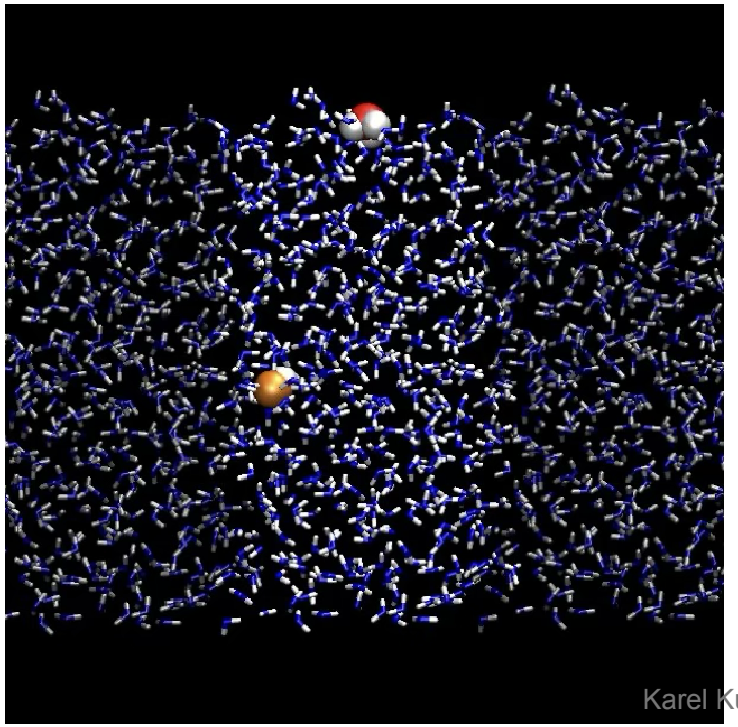
- počet sousedů je v kapalné vodě **5**, v ledu **4**
- průměrný počet vodíkových vazeb na molekulu je v kapalině ~3.5 v ledu 4
- úhel H-O-H je **v kapalině 104.5°** ⇒ menší než **v ledu 109.5°**
- molekuly vody mohou vyplňovat mezery přítomné ve struktuře ledu
- v ledu je vyšší protonová vodivost a mobilita (protony přeskakují podél sítě vodíkových vazeb – Grotthussův mechanismus)



Autoionizační vlastnost vody

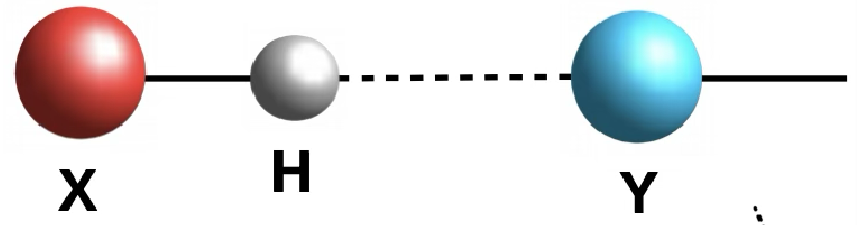




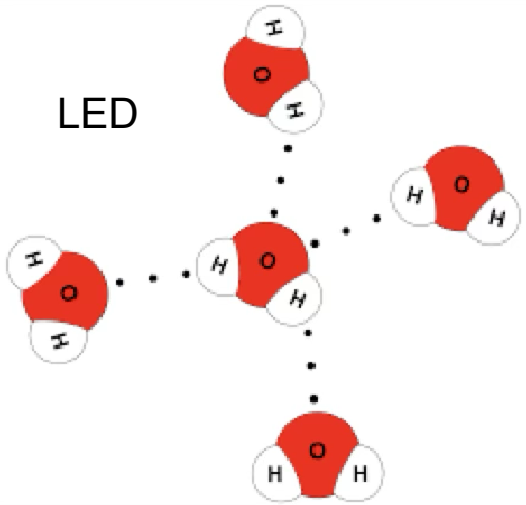


Vodíková vazba

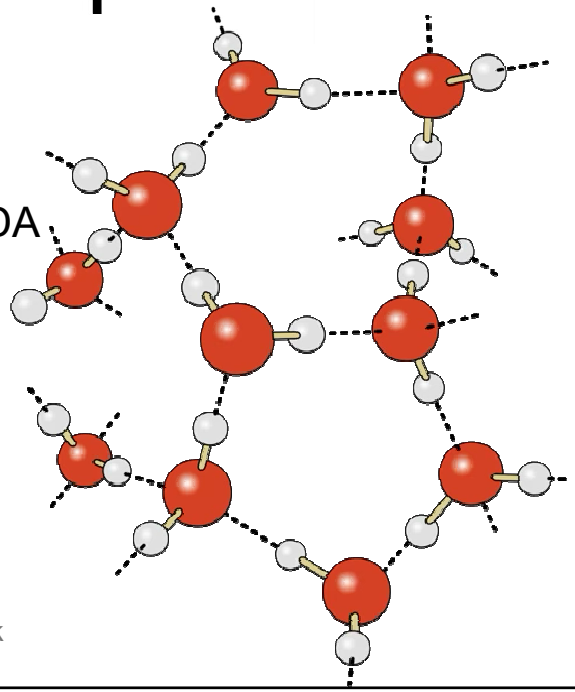
IUPAC: The hydrogen bond is an attractive interaction between a hydrogen atom from a molecule or a molecular fragment X-H in which X is more electronegative than H, and an atom or a group of atoms in the same or a different molecule, in which there is evidence of bond formation.



LED



VODA

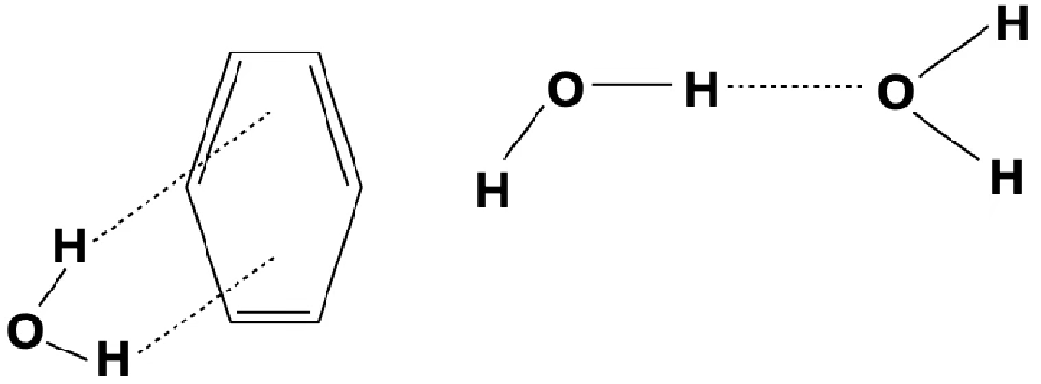


Vodíková vazba

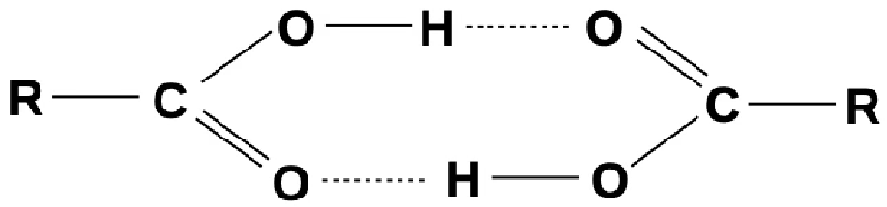
- interakce v důsledku přenosu náboje mezi donorem a akceptorem
- atomy X a H jsou spojeny kovalentní vazbou, která je polarizovaná – s rostoucí elektronegativitou X roste i síla vazby H...Y
- vodíková vazba je obvykle planární – čím více se úhel blíží 180°, tím je vodíková vazba silnější a vzdálenost H...Y menší
- při vzniku vodíkové vazby obvykle dochází k nárůstu délky vazby X-H, což se v IR spektroskopii projeví červeným posunem, ale existují i vodíkové vazby, které způsobují modrý nebo žádný posun vibračních frekvencí v IR
- vodíková vazba vykazuje charakteristické signatury v NMR spektroskopii
- kritérium, že délka vodíkové vazby je menší než součet van der Waalsových poloměrů, neplatí obecně, platí pouze pro silné vodíkové vazby

Příklady vodíkové vazby

slabé

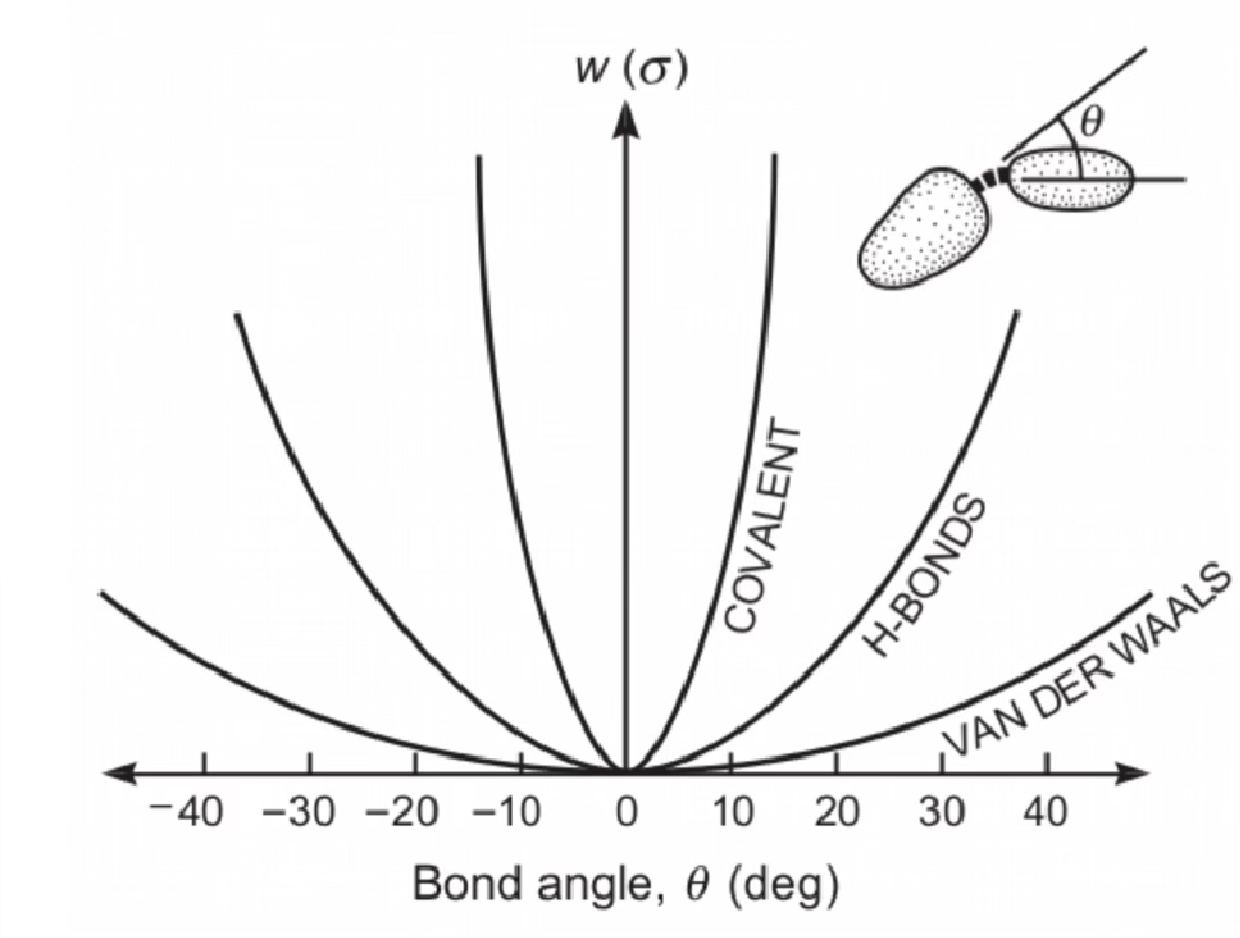


střední

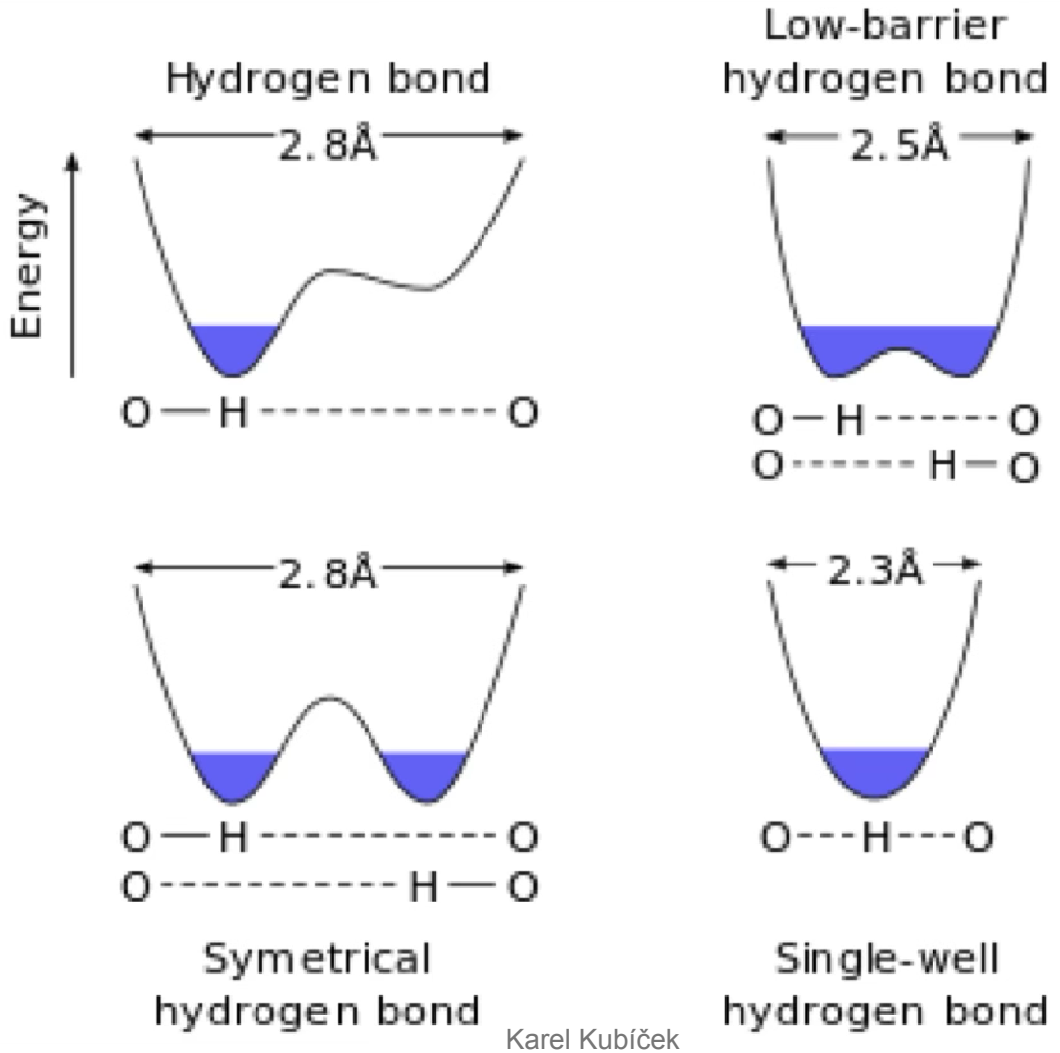


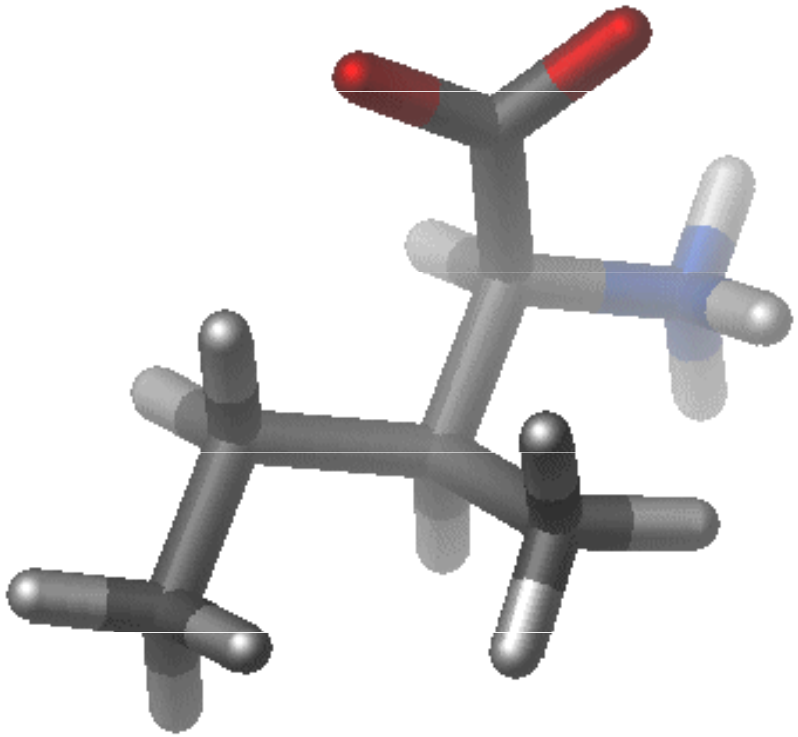
silné

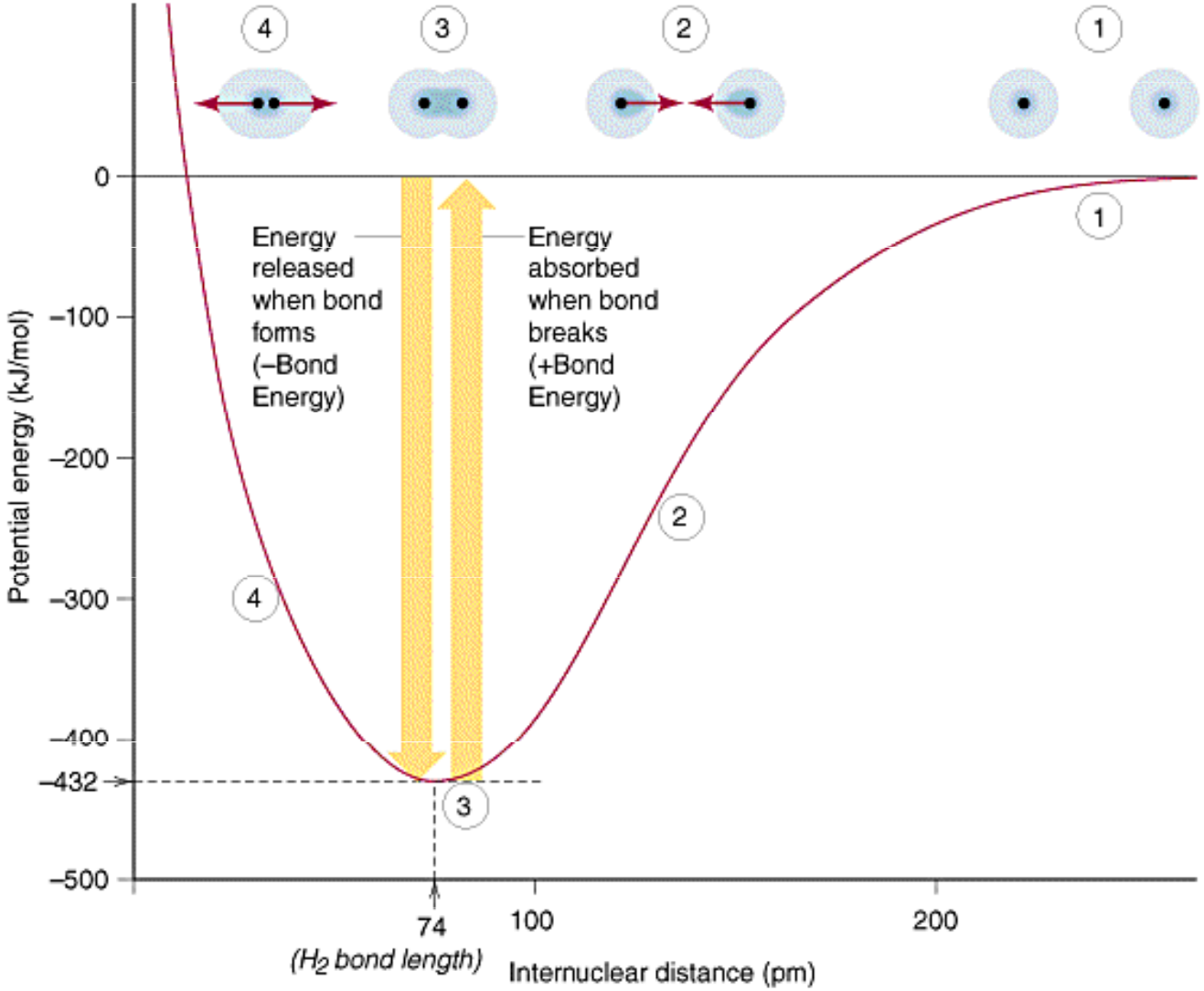
Směrovost vodíkové vazby



Potenciální energie vodíkové vazby

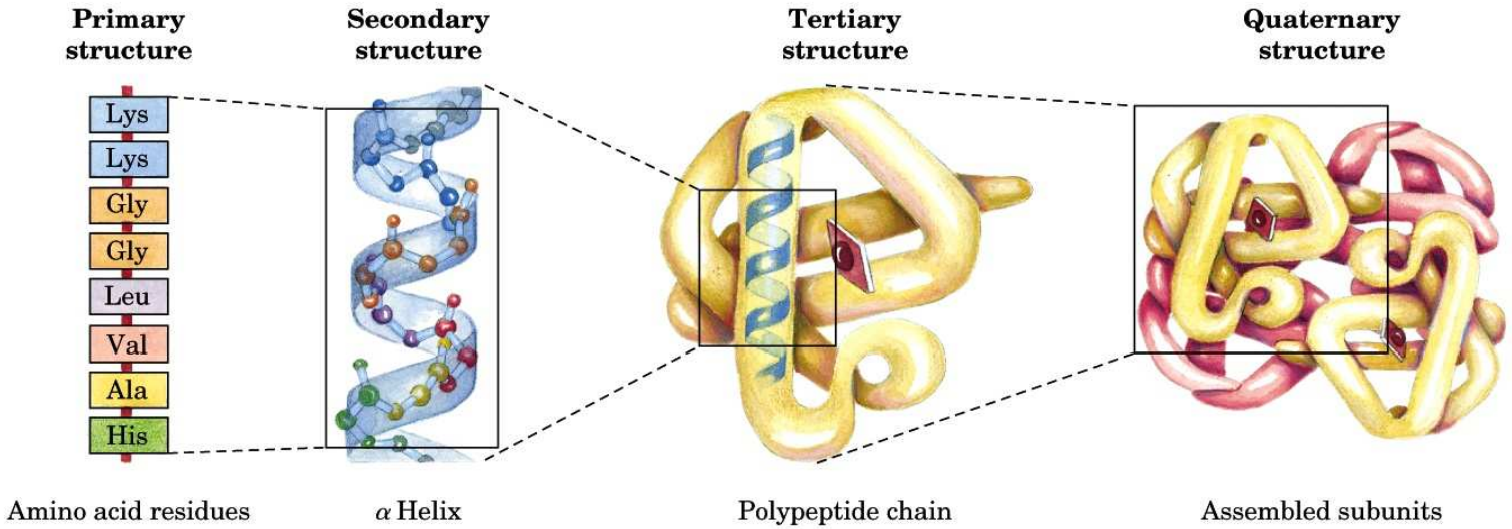





4
3
2
1
0
−100
−200
−300
−400
−432
−500
Potential energy (kJ/mol)
Energy released when bond forms (−Bond Energy)
Energy absorbed when bond breaks (+Bond Energy)
1
2
3
4
74
(H2 bond length)
100
200
Internuclear distance (pm)

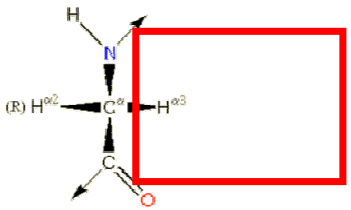
Proteiny

Levels of Protein Structure

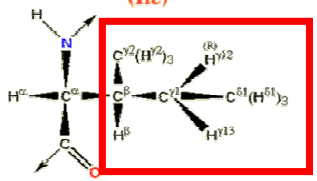


6) Aminokyseliny s alifatickým postranním řetězcem

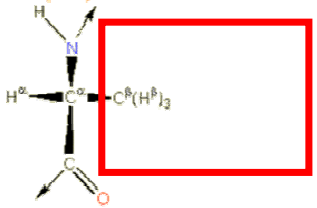
Glycine (Gly)



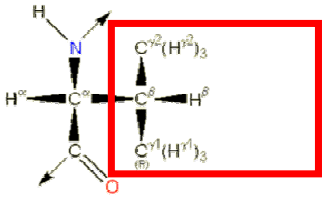
L-Isoleucine (Ile)



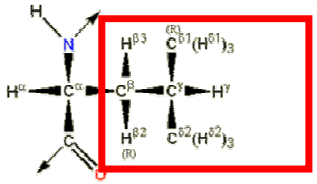
L-Alanine (Ala)



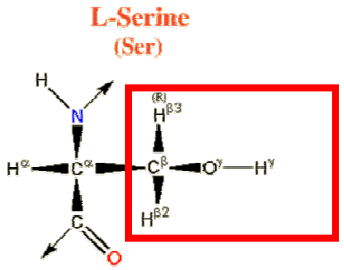
L-Valine (Val)

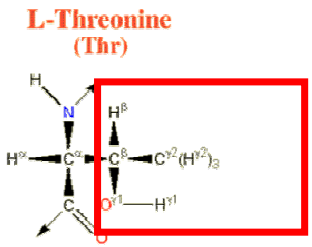


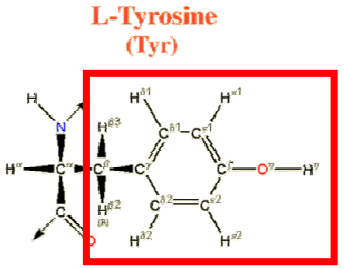
L-Leucine (Leu)



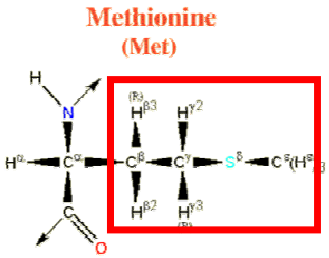
7) Aminokyseliny s hydroxylovou (OH) skupinou

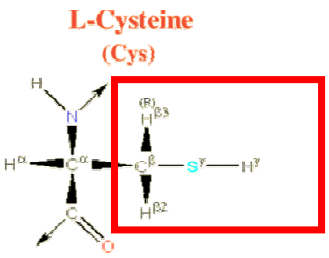






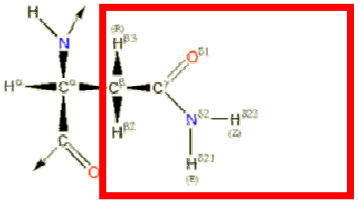
8) Aminokyseliny s atomem síry



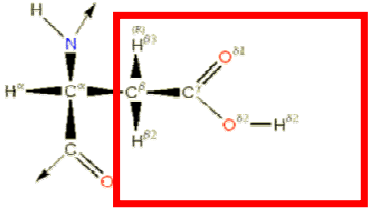


9) Aminokyseliny s acidickými skupinami nebo jejich amidy

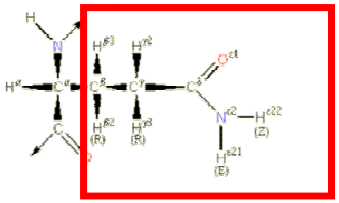
L-Aspargine
(Asn)



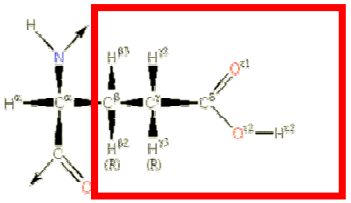
L-Aspartic Acid
(Asp)



L-Glutamine
(Gln)

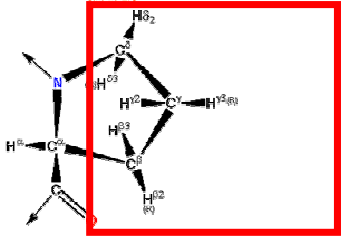


L-Glutamic Acid
(Glu)



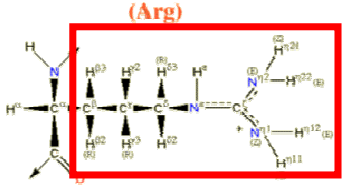
10) Imino kyselina

L-Proline
(Pro)

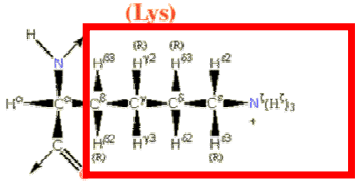


11) Aminokyseliny s basickými skupinami

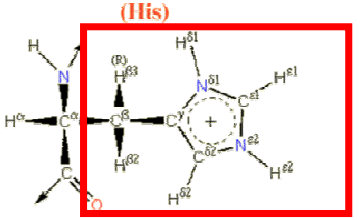
L-Arginine
(Arg)



L-Lysine
(Lys)

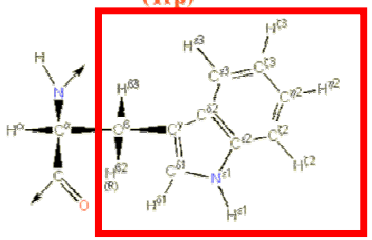


L-Histidine
(His)

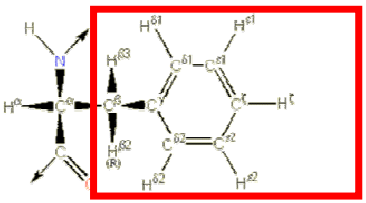


12) Aminokyseliny s aromatickými kruhy

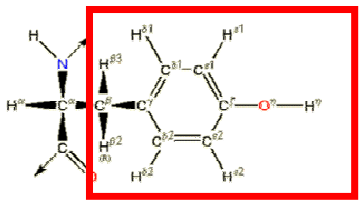
L-Tryptophan
(Trp)



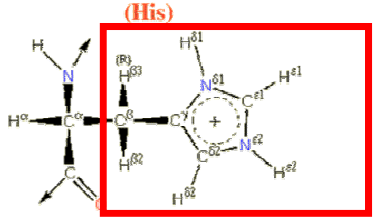
L-Phenylalanine
(Phe)

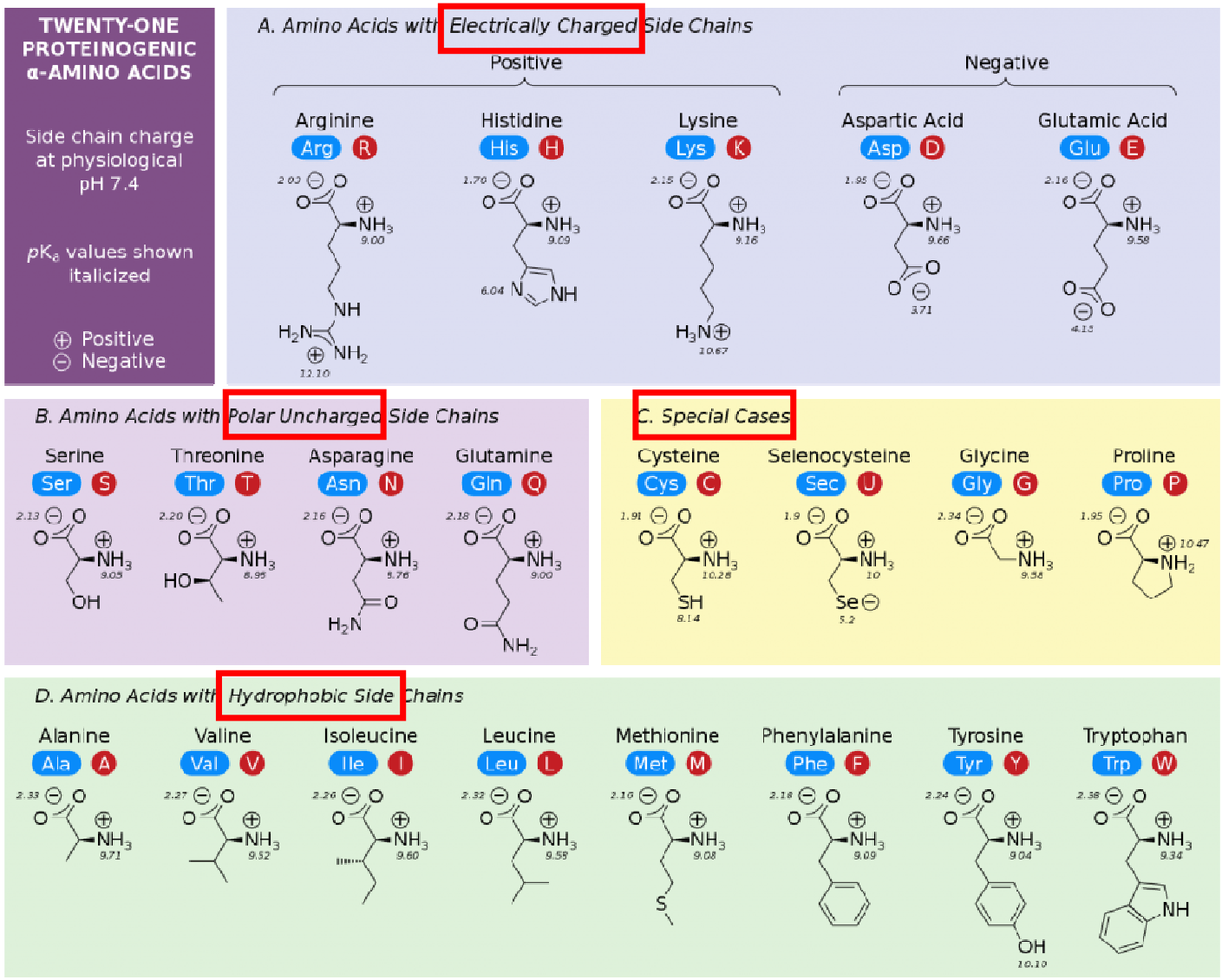


L-Tyrosine
(Tyr)



L-Histidine
(His)





https://chemistrytalk.org/wp-content/uploads/2023/03/ProteinogenicAminoAcids.svg-1024x819-1.png

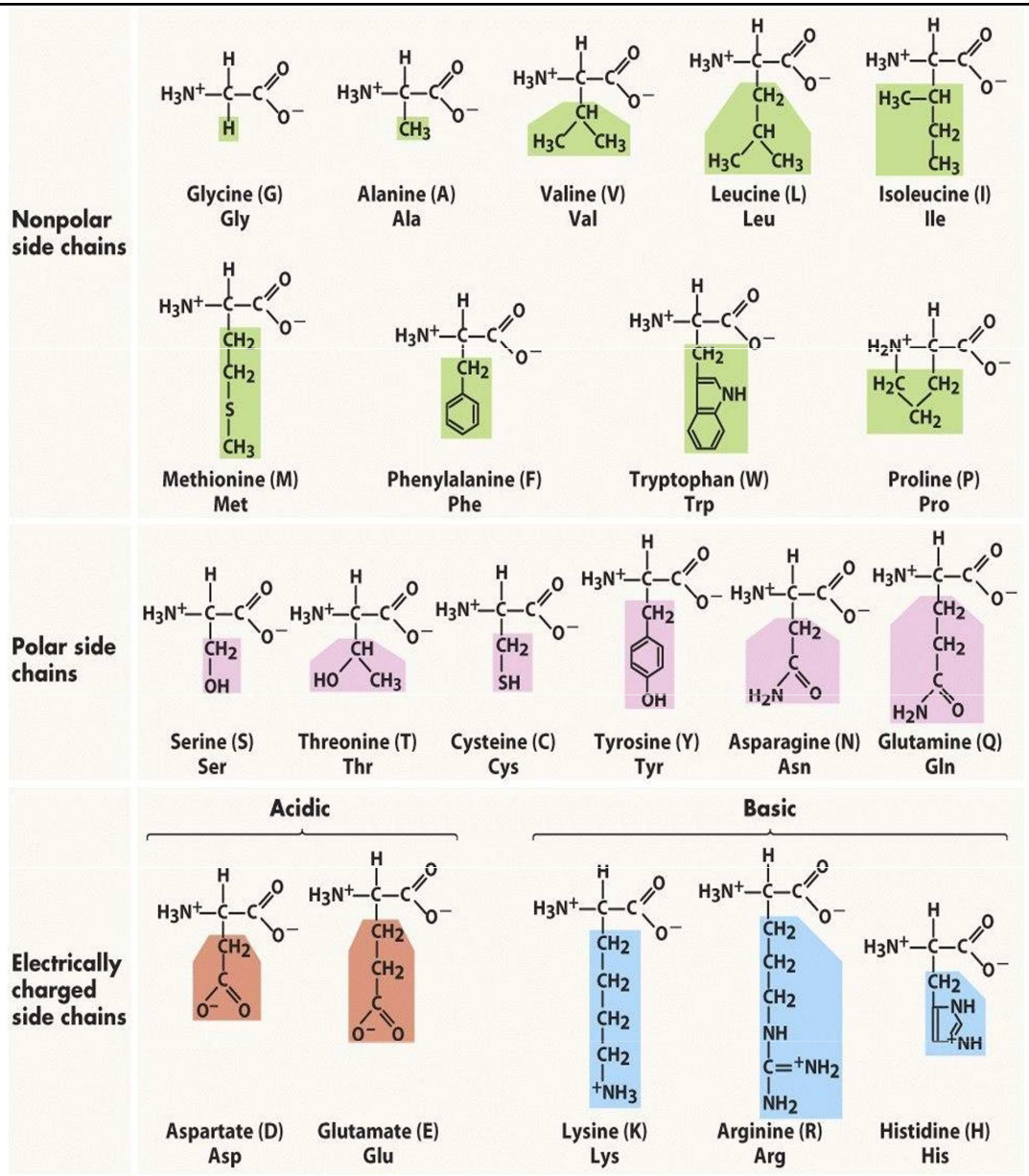
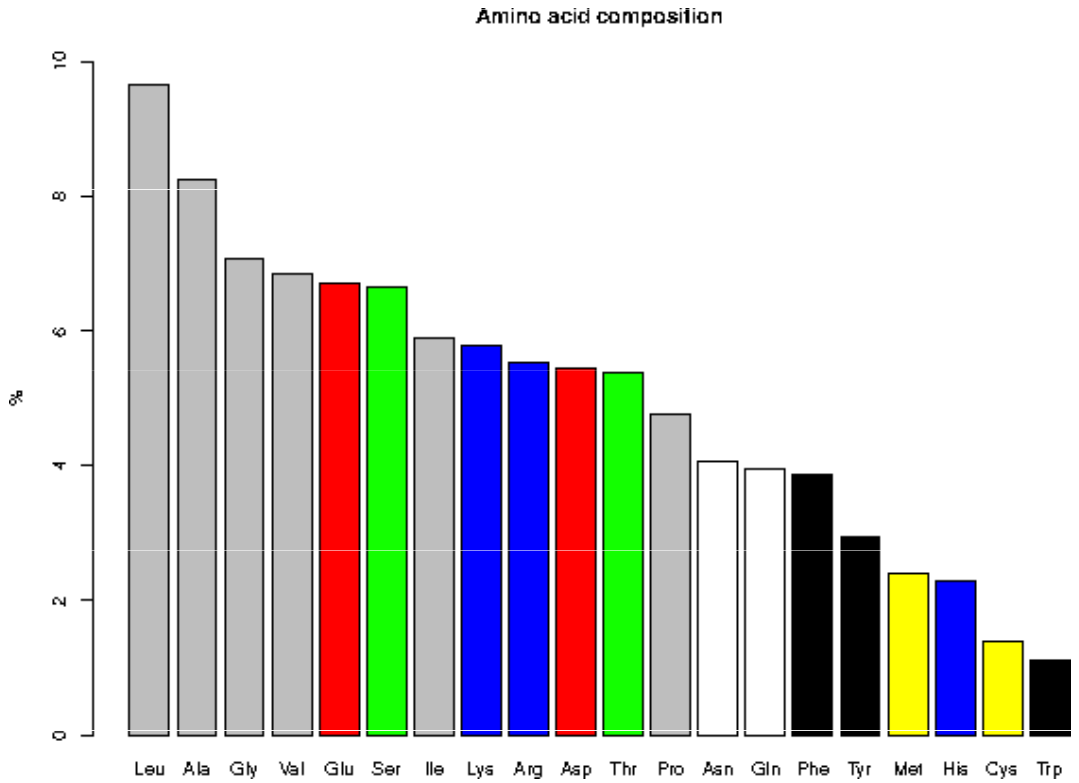


Figure 3-5 Biological Science, 2/e

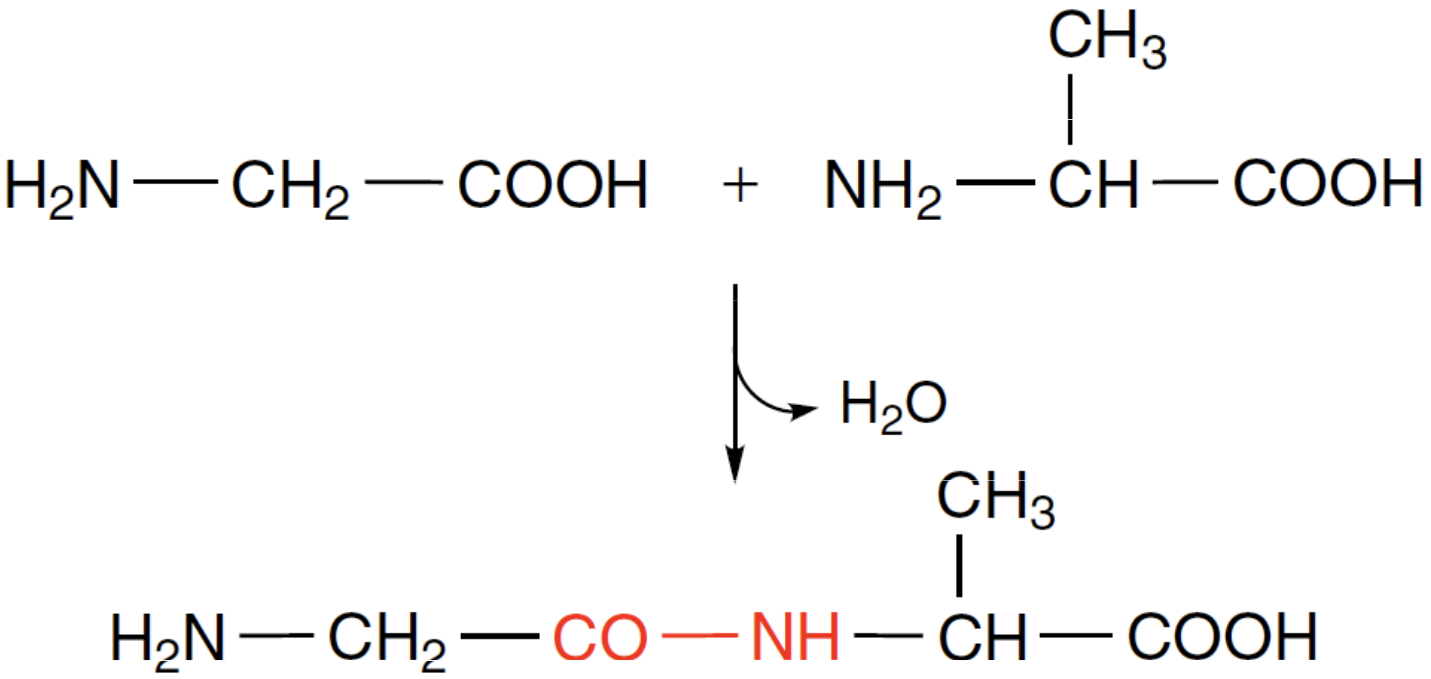
Composition in percent for the complete database



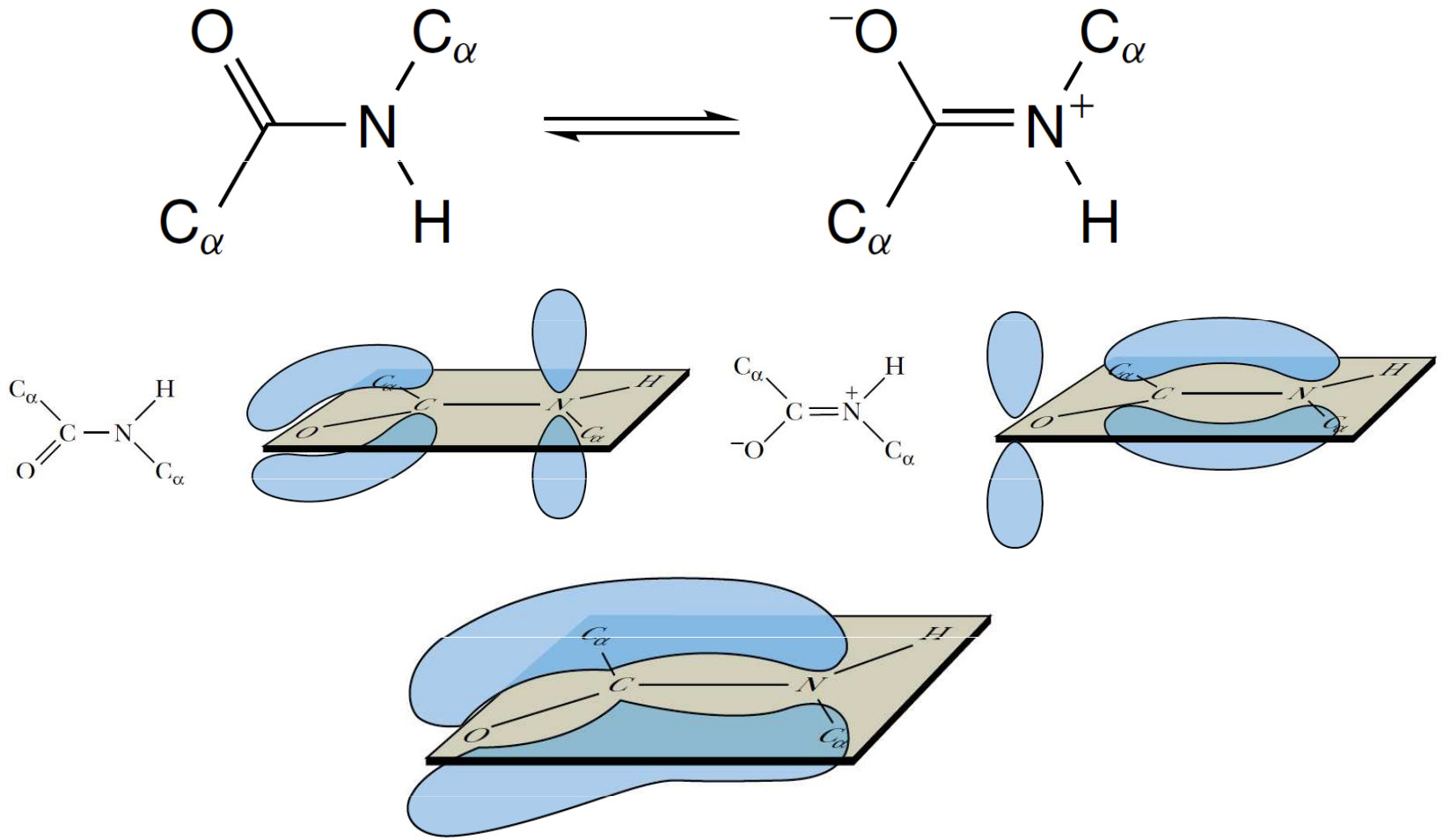
Legend: gray = aliphatic, red = acidic, green = small hydroxy, blue = basic, black = aromatic, white = amide, yellow = sulfur

https://web.expasy.org/docs/relnotes/relstat.html

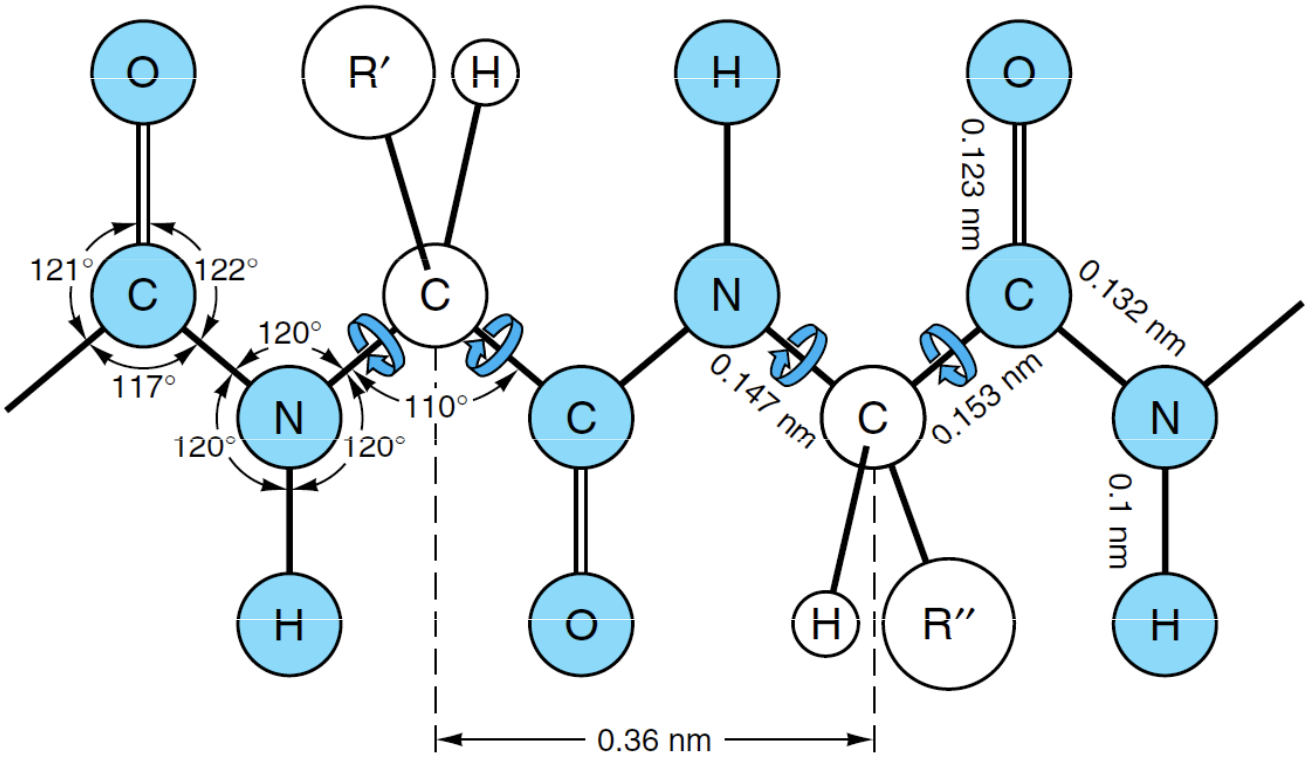
III] Peptidy, proteiny – vznik polymerů polymerizační reakcí



IV] Peptidová vazba – pseudo dvojitá vazba => amidová rovina



V] Proteinová páteř, primární struktura, číslování od **N**-konce (terminu) směrem k **C**-konci



Informace o 3D (proteinové) struktuře jsou zapsány v kartézských souřadnicích
Nejrozšířenější formát PDB (ProteinDataBank, www.pdb.org)

```
ATOM    128  N   HIS O  18      20.321   6.124  17.761  1.00 11.40
ATOM    129  CA  HIS O  18      21.097   5.169  18.563  1.00 13.62
ATOM    130  C   HIS O  18      22.581   5.413  18.454  1.00 17.00
ATOM    131  O   HIS O  18      23.031   5.592  17.321  1.00 15.45
ATOM    132  CB  HIS O  18      20.883   3.747  18.034  1.00 16.68
ATOM    133  CG  HIS O  18      19.557   3.103  18.437  1.00 11.72
ATOM    134  ND1 HIS O  18      19.252   2.806  19.725  1.00 11.66
ATOM    135  CD2 HIS O  18      18.479   2.751  17.657  1.00 16.32
ATOM    136  CE1 HIS O  18      18.021   2.238  19.730  1.00 14.91
ATOM    137  NE2 HIS O  18      17.552   2.185  18.473  1.00 17.58

HETATM 1633  NC  HEM O 104      15.182   3.191  16.831  1.00 21.22
HETATM 1634  C1C HEM O 104      15.433   3.334  15.488  1.00 17.49
HETATM 1635  C2C HEM O 104      15.046   4.605  15.145  1.00 31.21
HETATM 1636  C3C HEM O 104      14.623   5.242  16.323  1.00 14.38
HETATM 1637  C4C HEM O 104      14.661   4.346  17.360  1.00 14.50
HETATM 1638  CMC HEM O 104      15.299   5.349  13.850  1.00 15.54
HETATM 1639  CAC HEM O 104      14.314   6.707  16.409  1.00 31.67
HETATM 1640  CBC HEM O 104      13.170   7.262  15.615  1.00 10.23

HETATM 1609 FE   HEM O 104      15.801   1.483  17.954  1.00  9.37
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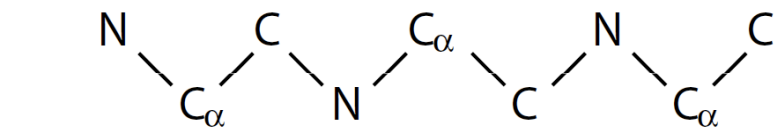
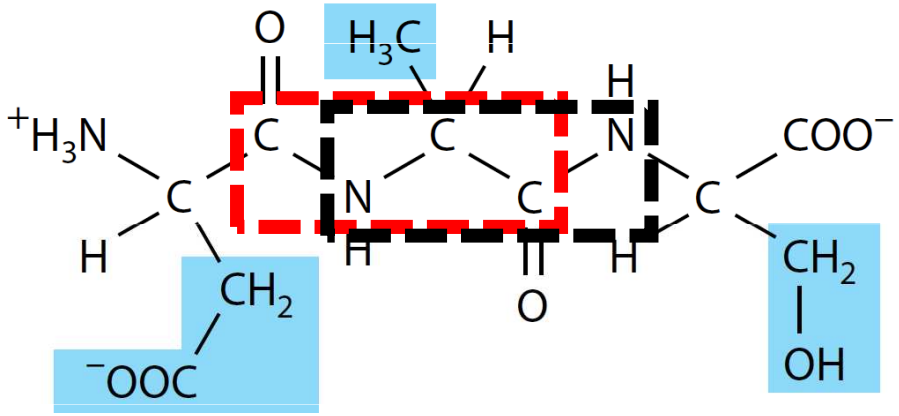
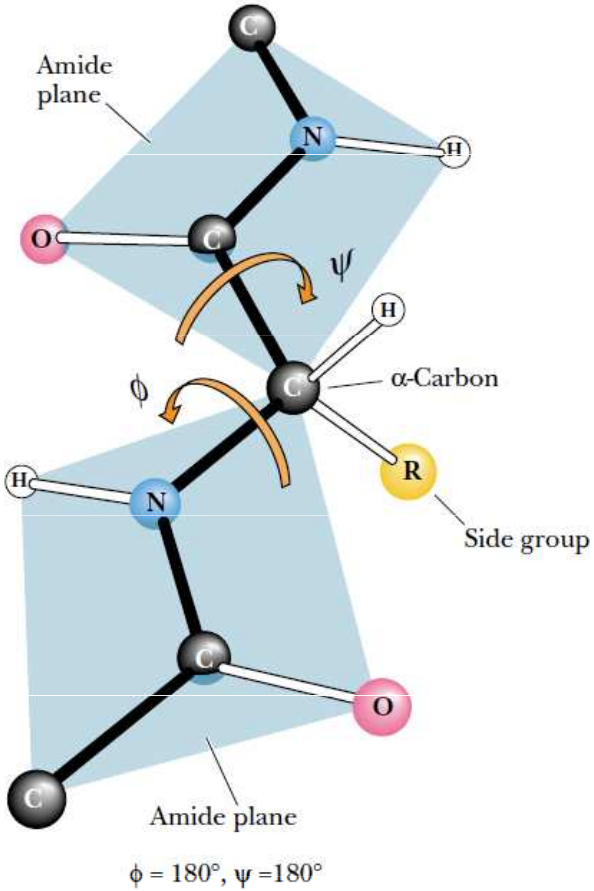






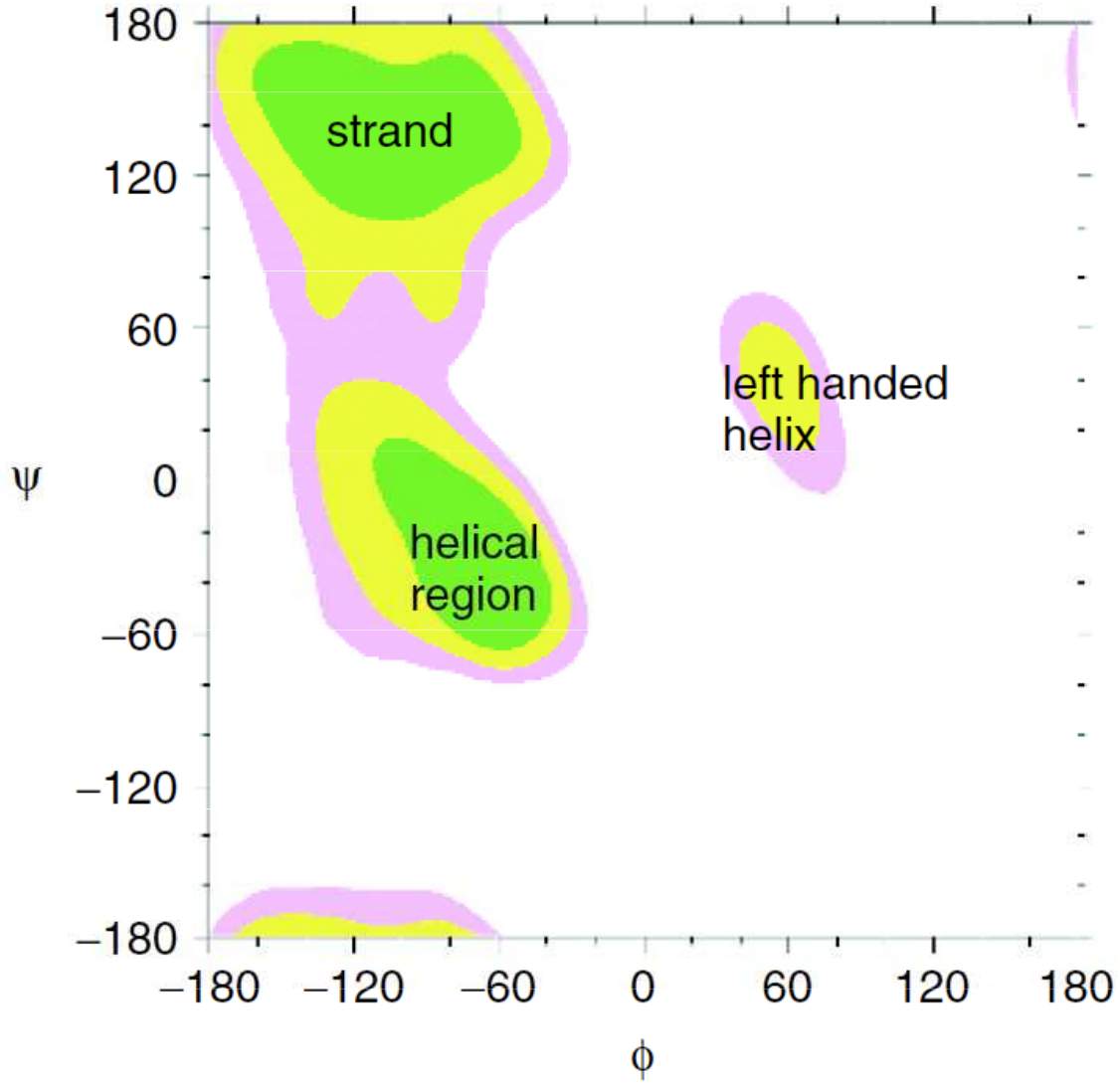
ϕ – **CO, N, C_α, CO** (CO někdy značeno C')
ψ – **N, C_α, CO, N**

Structural parameters for protein secondary structures

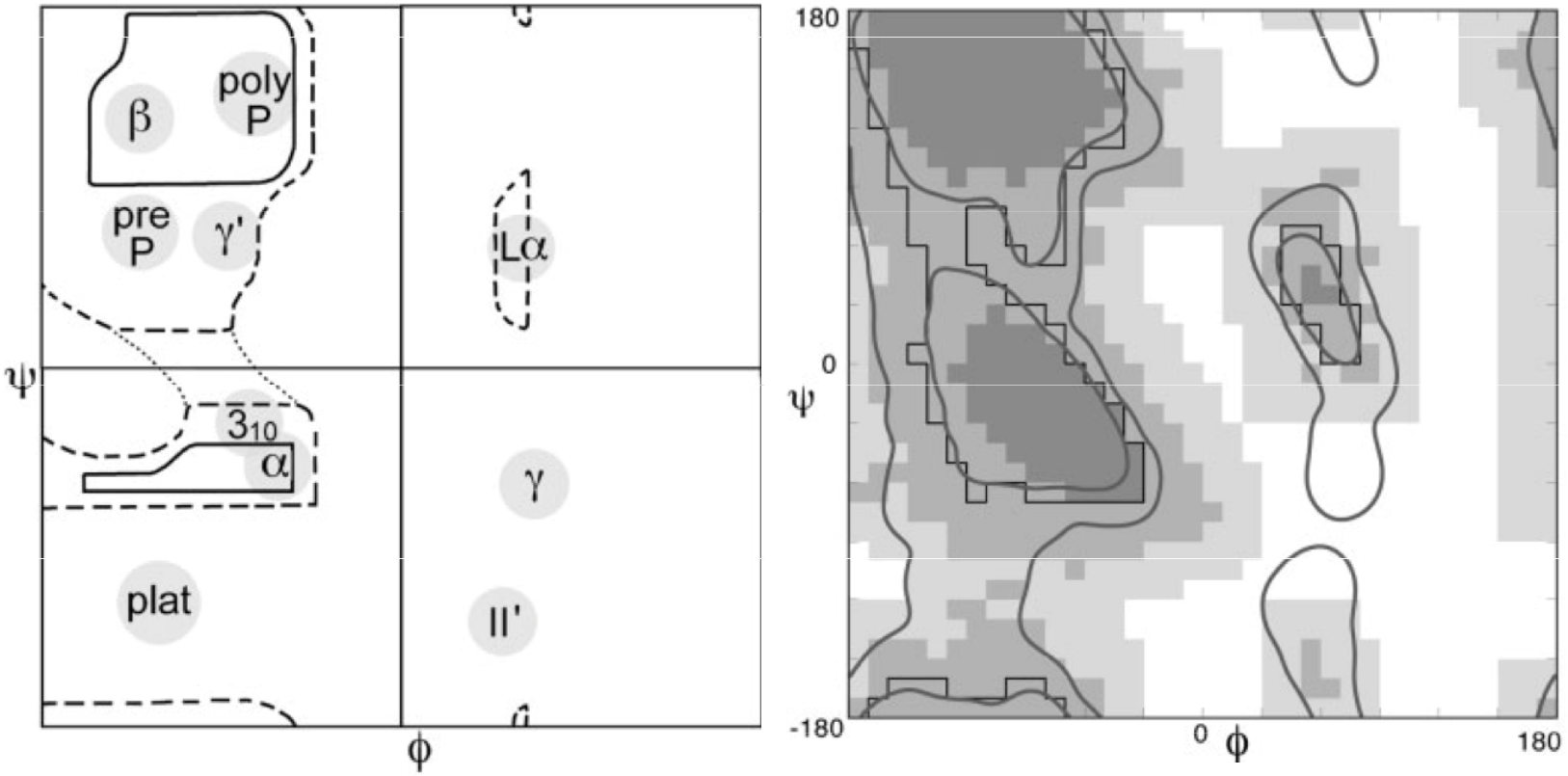
Structural element	ϕ	ψ	*n*	*d*	*p*
α-helix	-57	-47	3.6	1.5	5.5
3_{10}-helix	-49	-26	3.0	2.0	6.0
β-helix	-57	-70	4.4	1.1	5.0
Polyproline II helix	-79	+149	3.0	3.1	9.4
Parallel β-strand	-119	+113	2.0	3.2	6.4
Antiparallel β-strand	-139	+135	2.0	3.4	6.8

ϕ and ψ are the conformational angles of the mainchain, with ω ~180°(trans conformation)
n = number of residues per turn
d = displacement between successive residues along the helix/strand axis
p = the pitch of helix/strand, the distance along the helix/strand axis of a complete sec. struct. element. Note that *p*=*n* x *d* (equation is exact, error is in rounding of *n* and *d*)

VI] Ramachandranův diagram



Ramachandranův diagram – komplet



https://proteopedia.org/wiki/index.php/Tutorial:Ramachandran_principle_and_phi_psi_angles

Tutorial:Ramachandran principle and phi psi angles

The Ramachandran Principle
Phi (ϕ) and Psi (ψ) Angles in Proteins

The Ramachandran Principle says that alpha helices, beta strands, and turns are the most likely conformations for a polypeptide chain to adopt, because most other conformations are impossible due to steric collisions between atoms.

This interactive tutorial is also available as an Animated Slideshow or YouTube Video, and there is a Quiz.

At right is a fragment of a polypeptide chain. In the center is a single complete alanine residue. Check **Alanine** to identify its atoms[1]. The other atoms are fragments of adjacent amino acids[2]. *Drag with your mouse to rotate the model.*

The Alanine is covalently bonded to other amino acids through peptide bonds. Check Peptide Bonds to locate them.

The double bonds between main chain (backbone) C and O delocalize, making th peptide bonds also have partial double bonds (*half-dotted bonds*). This prevents th peptide bond from rotating.

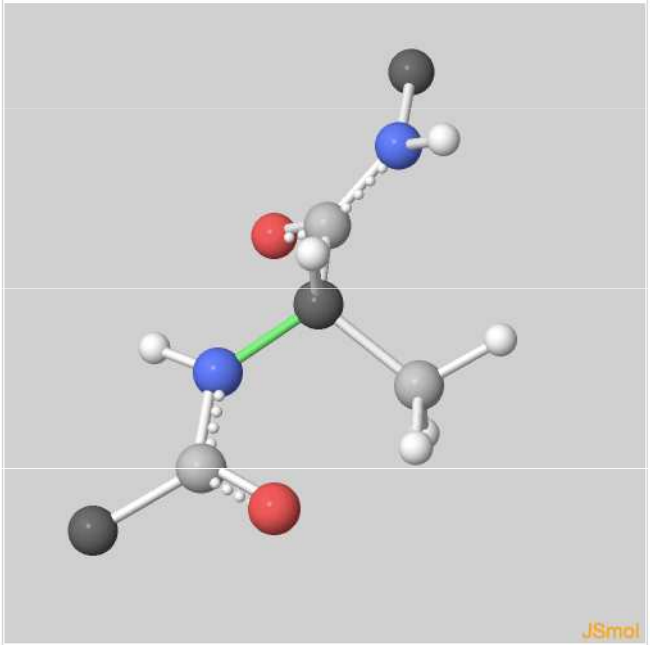
Each peptide bond holds six atoms in a plane. Check **Planes** to see them.

The alpha carbon (Cα) in the center of each amino acid is held in the main chain by two rotatable bonds. The dihedral (torsion) angles of these bonds are called[3] Phi and Psi (in Greek letters, ϕ and ψ). *Use the radio buttons (top of right panel) to identify the rotatable main-chain bonds, and click the -20° and +20° buttons to see them rotate.*

Click the **Reset** button.

The balls shown are much smaller than the atoms they represent. Check **van der Waals** to see the real sizes of the atoms[4]. In fact, most Phi and Psi angle combinations are impossible because two atoms cannot occupy the same space.

Check **Show Clashes** to see where non-bonded atoms are overlapping, and thus in physically impossible positions. (This model simulation allows two atoms to overlap, unlike real atoms.)



Cα C H N O

Phi ϕ Psi ψ
165° 165°
-20° +20°

Alanine
Peptide Bonds
Planes

van der Waals[4]
Show Clashes

Reset

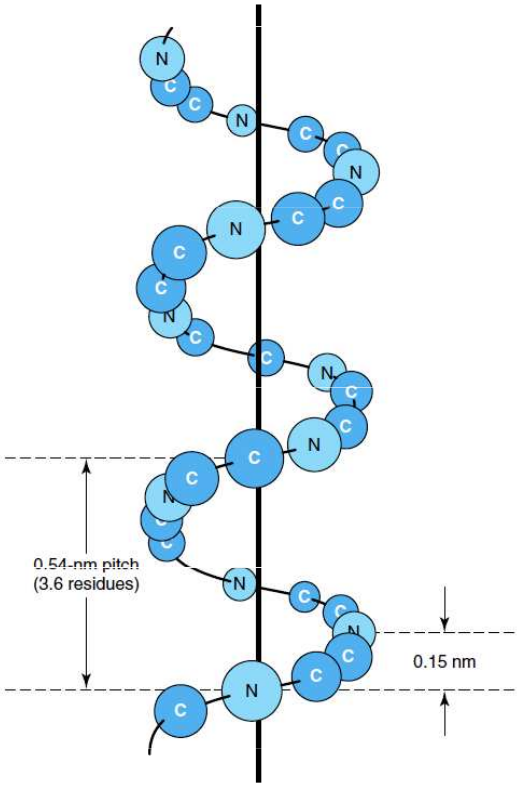
Figure 7.1. Sir John Kendrew with the model of insulin, one of the first protein structures to be determined by X-ray crystallography. Components of the actual model are just visible through the forest of vertical support rods.

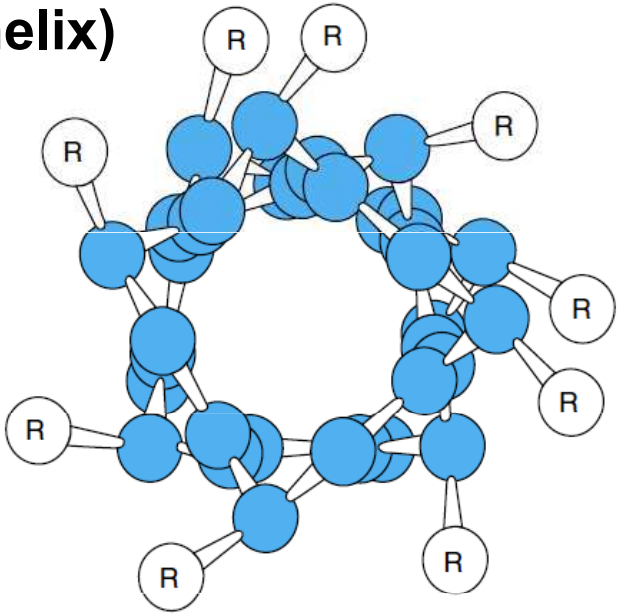
VII] Sekundární struktura

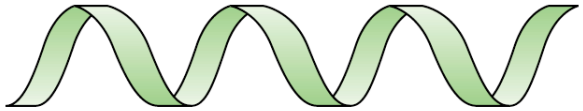
1) α-šroubovice (α-helix)

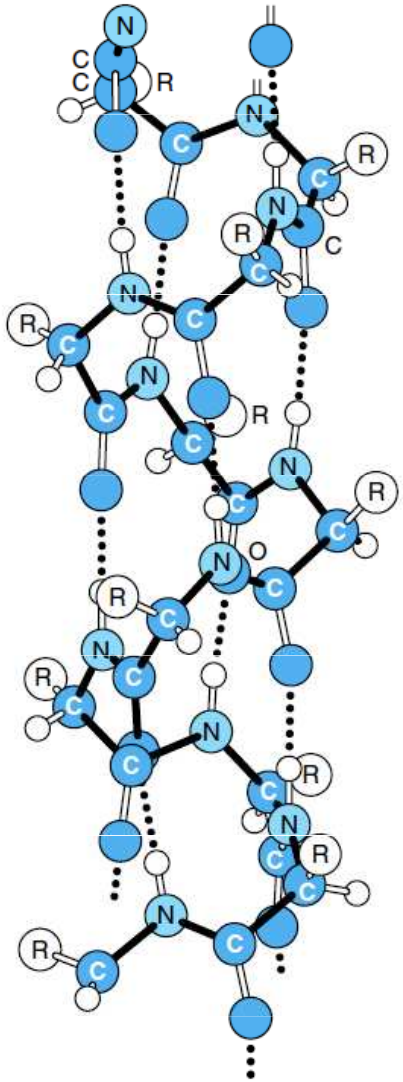
2) β-skládaný list (β-sheet)

3) Ohyb, smyčka (loop/turn)

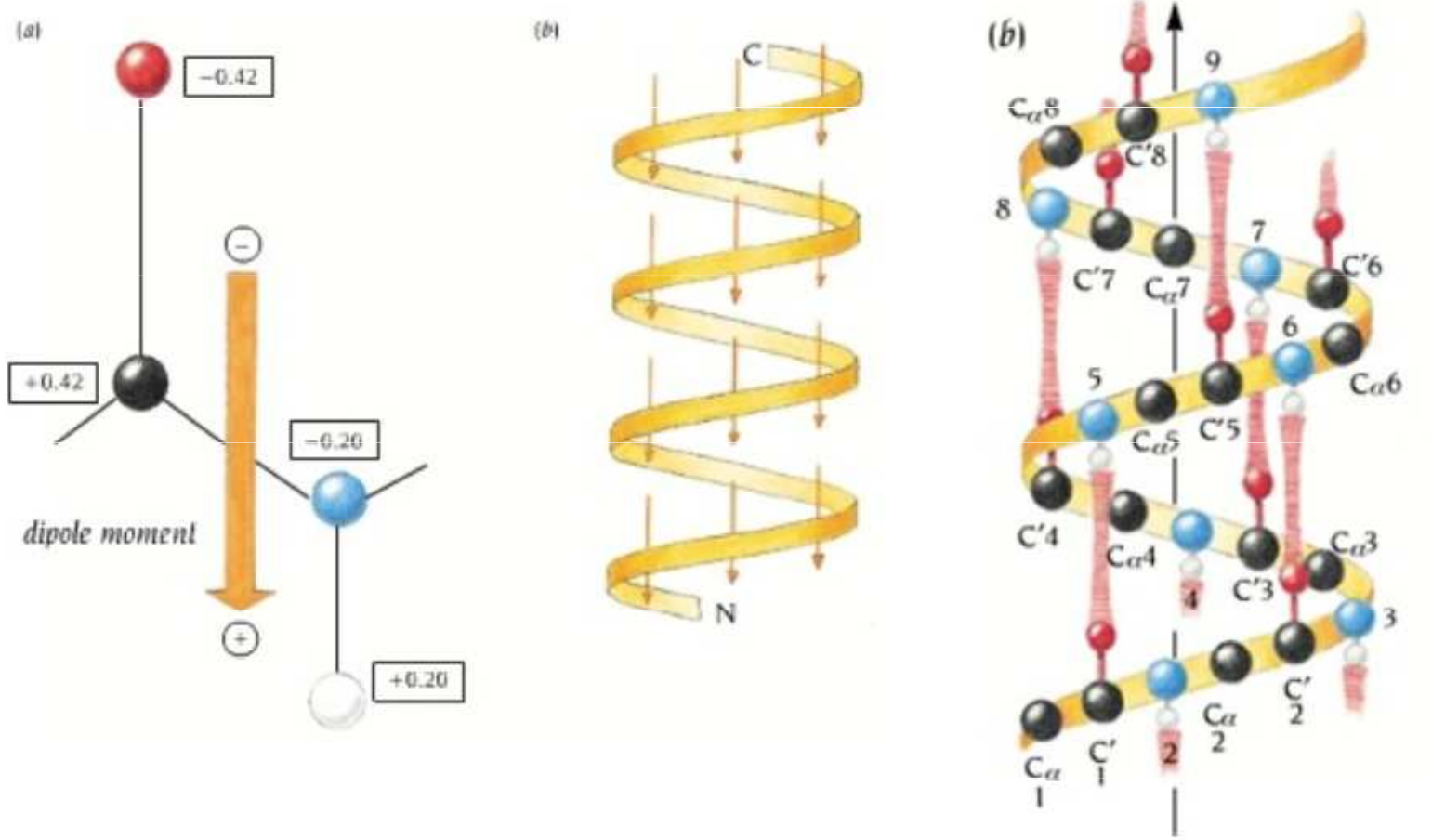






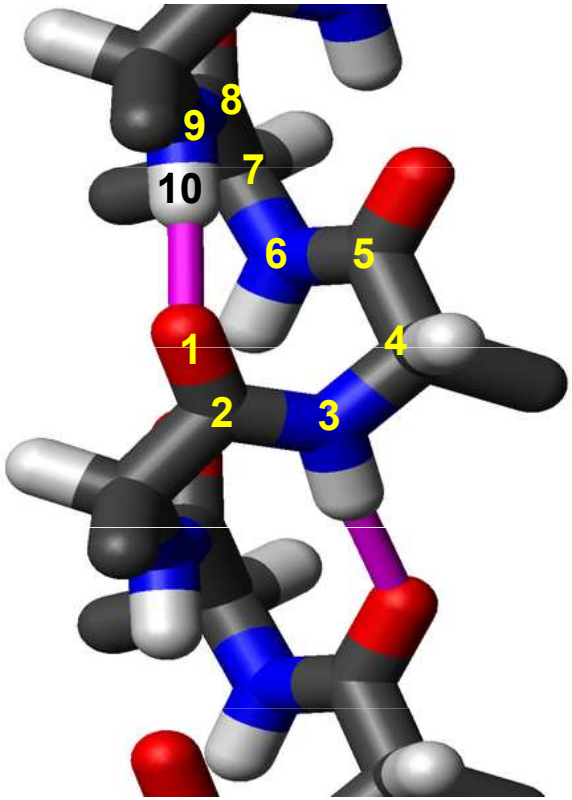


The α helix has a dipole moment



Ostatní motivy sekundární struktury :

1. polyprolinová šroubovice I & II – levotočivá, 3.3 nebo 3 (PPI, PPII, v uvedeném pořadí) aminokyseliny/otočku
2. šroubovice 3_{10} (srovnej s 3.6_{13})– pravotočivá, 3 aminokyseliny/otáčku, 10 atomů vytváří kruh uzavřený vodíkovou vazbou, např. poly-Ala
3. π-šroubovice – pravotočivá, 4.1 aminokyseliny/otáčku
4. β-šroubovice – vzniká uspořádáním β-skládaných listů do pravo- i levotočivé šroubovice.



3_{10}helix, α helix, π helix

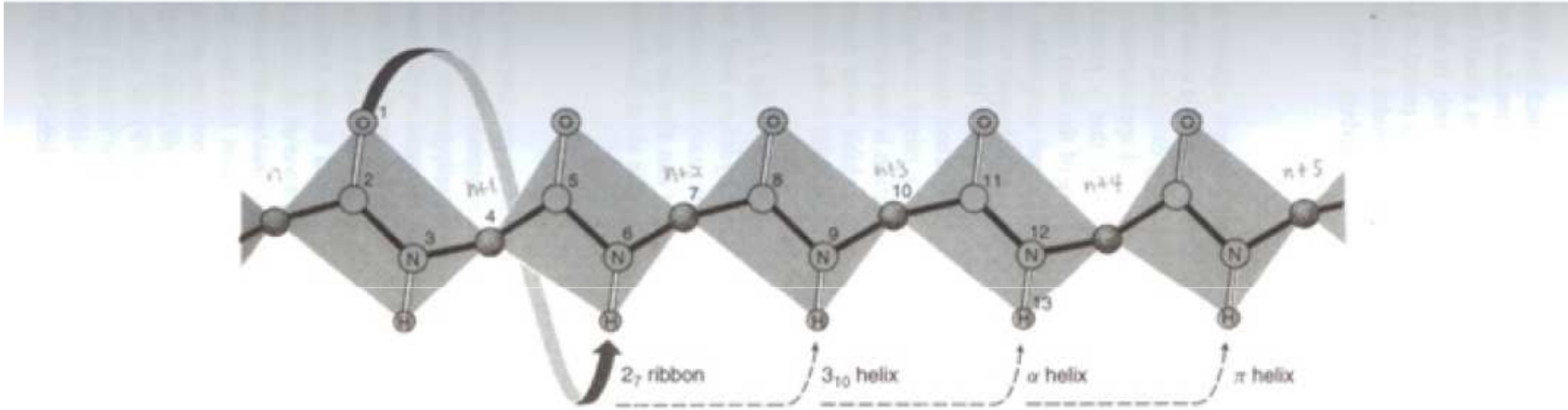
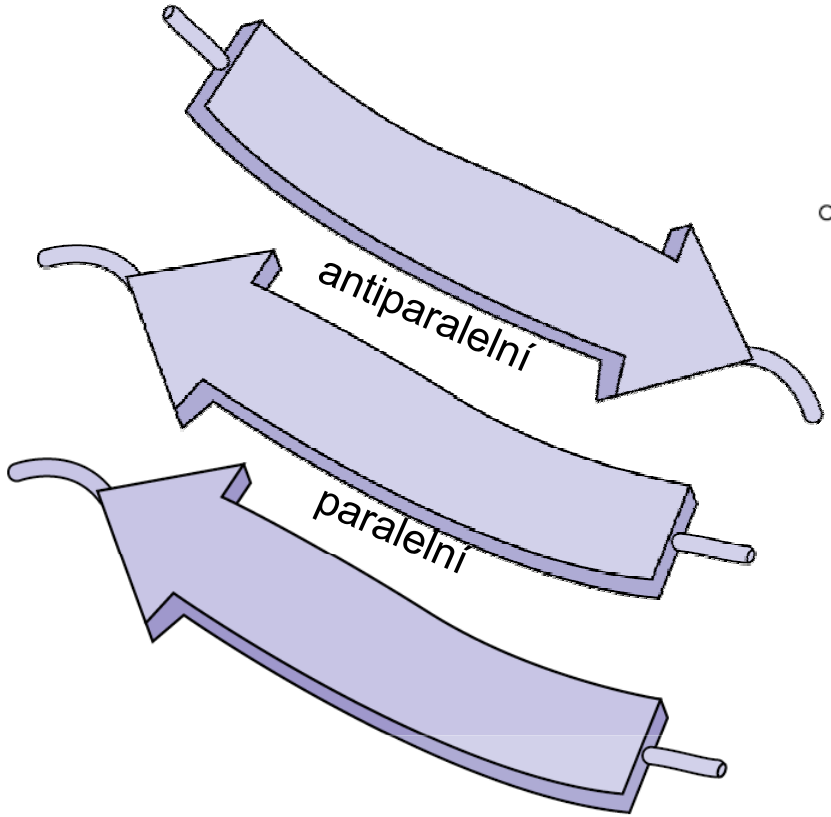


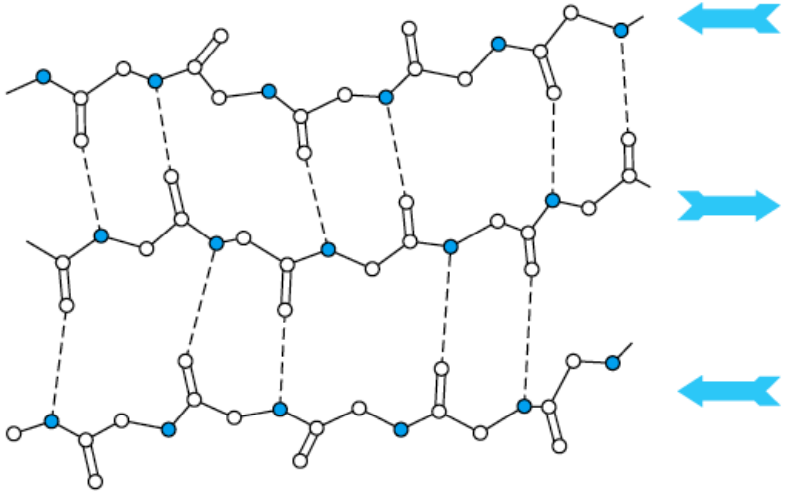
Figure 2.8. The hydrogen bonding patterns of different helical secondary structures. The peptide backbone is shown in an extended conformation, with an arrow denoting the hydrogen bonding pairings that would occur in each type of helix. The common α helix, depicted in Figure 2.7, forms hydrogen bonds between the carbonyl oxygen of each residue and the amide proton of the residue 4 residues ahead in the helix. The 3_{10} helix forms hydrogen bonds between the carbonyl oxygen of each residue and the amide proton of the residue 3 residues ahead, forming a more narrow and elongated helix. The π helix forms hydrogen bonds between the carbonyl oxygen of each residue and the amide proton of the residue five residues ahead, forming a wider helix. The 2_7 ribbon is not a regular secondary structure, but is shown here to demonstrate all possible hydrogen bond pairings. *From R. E. Dickerson and I. Geis. The Structure and Action of Proteins. New York: Harper & Row, 1969. Used with permission from Geis Archives.*

VII] Sekundární struktura

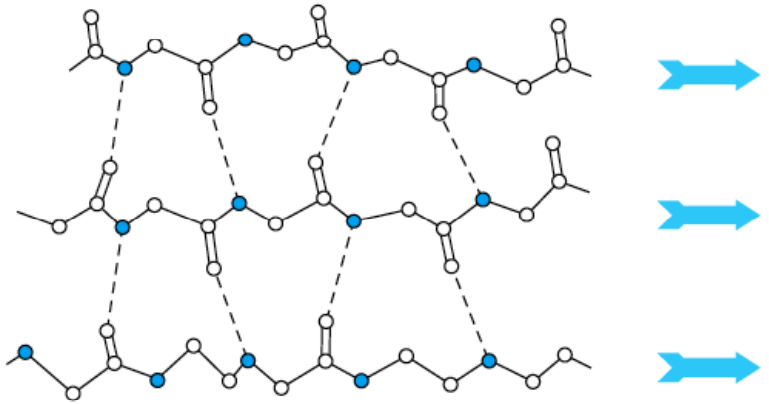
1) α-šroubovice (α-helix)
2) **β-skládaný list (β-sheet)**
3) Ohyb, smyčka (loop/turn)



antiparalelní uspořádání



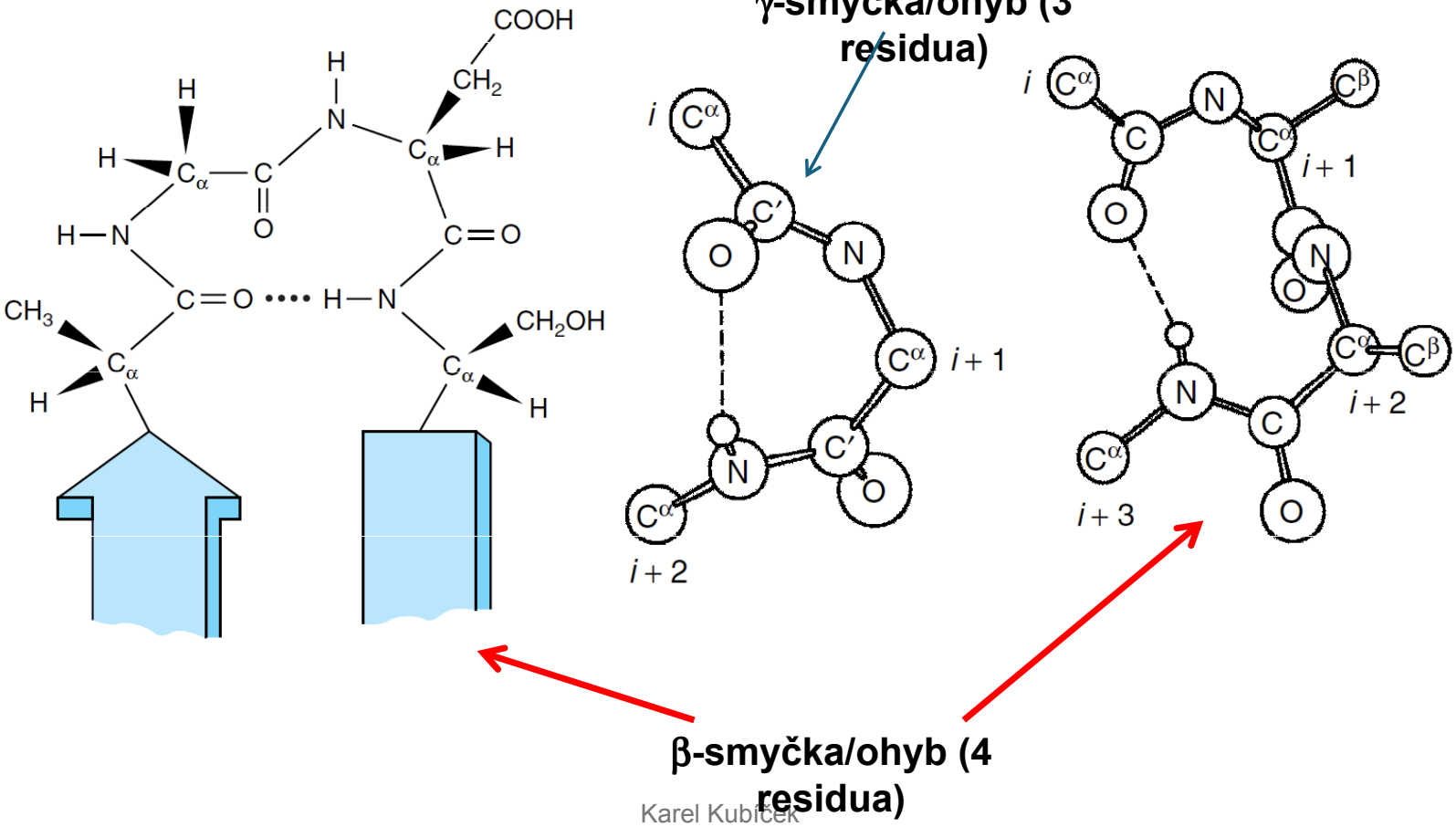
paralelní uspořádání



VII] Sekundární struktura

1) α-šroubovice (α-helix)
2) β-skládaný list (β-sheet)

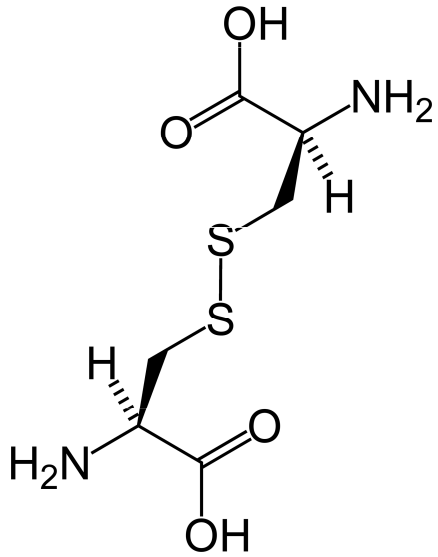
3) Ohyb, smyčka (loop/turn)



Disulfide bonds

Created through **oxidation** of sulfhydryl groups

$$2\ RSH \rightarrow RS\text{-}SR + 2\ H^+ + 2\ e^-$$



This process of oxidation can produce:

1) stable protein dimers,
2) polymers,
3) complexes, in which the sulfide bonds can help in protein folding.

Disulfide bonds

i) intramolecularly – within a polypeptide chain, usually responsible for stabilizing **tertiary** structures of proteins

ii) Intermolecularly – between polypeptide chains, are attributed to stabilizing **quaternary** protein structures

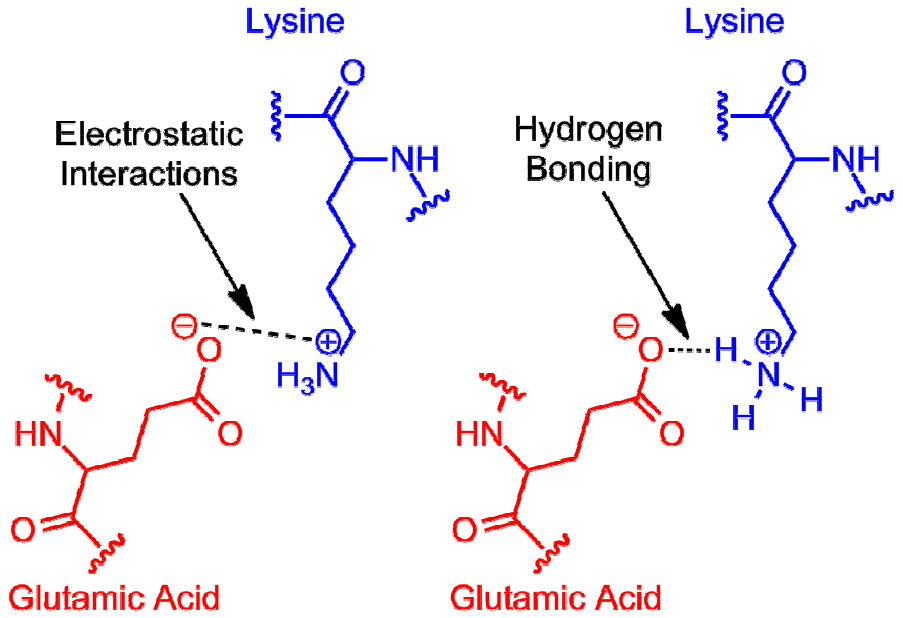
https://en.wikibooks.org/wiki/Structural_Biochemistry/Chemical_Bonding/_Disulfide_bonds

Salt bridge

combination of two non-covalent interactions:

i) hydrogen bonding

ii) ionic bonding



a) most often arises from the anionic carboxylate ($RCOO^-$) of either **aspartic** or **glutamic acid** and the cationic ammonium (RNH_3^+) from **lysine** or the guanidinium ($RNHC(NH_2)_2^+$) of **arginine**

b) other residues with ionizable side chains such as histidine, tyrosine, and serine can also participate

c) The **N-O** distance required is less than 4 Å. Greater than this distance apart do not qualify as forming a salt bridge.

https://en.wikipedia.org/wiki/Salt_bridge_(protein_and_supramolecular)

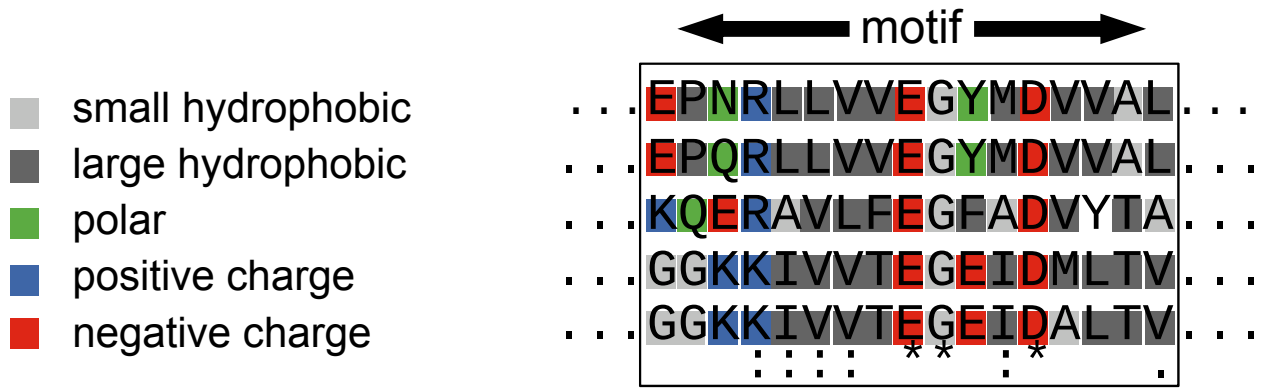
Primary sequence reveals important clues about a protein

One sequence keeps silent about its three-dimensional structure
Two aligned sequences whisper
But tables of many aligned sequences shout out loud

Primary sequence reveals important clues about a protein

• Evolution conserves amino acids that are important to protein structure and function across species. Sequence comparison of multiple “homologs” of a particular protein reveals highly conserved regions that are important for function.

• Clusters of conserved residues are called “motifs” -- motifs carry out a particular function or form a particular structure that is important for the conserved protein.



Some motifs in protein sequences

Structure of function identified	Motif
Nucleotide-binding site	**G*G**G**
N-glycosylation site	**N*S** or **N*T**
Nuclear protein transit sequence	**KKKRKV**
Factor IX proteinase cleavage site	**IEGR**
Serine proteinase active site	**GDSGG**
Acid proteinase active site	**FDTGS**
Fibronectin cell adhesion sequence	**RGDS**
Copper binding site	**H***H…H** or **H****H…H**

* = any single amino acid (AA)
*** = several AAs
... = any number of AAs

Protein folding

The **Levinthal paradox** states that if an averaged sized protein would sample all possible conformations before finding the one with the lowest energy, the whole **process would take billions of years**.

Proteins **typically** fold within **0.1 and 1000 seconds**, therefore the protein folding process must be directed some way through a specific folding pathway.

Protein folding

Anfinsen's Classic Experiment: The "Protein Folding Problem" asks a very simple question:

"How does the primary structure of a protein determine its 2– and 3– structure?".

We have known for many decades that proteins fold into their correct 3-D structures inside the cell. But correct folding during synthesis on the ribosome or later with assistance from unknown cellular factors could explain the *in vivo* results.

In the 1960's, Anfinsen and his coworkers performed a series of seminal experiments *in vitro* that answered a key part of the problem. The original work led Anfinsen to propose his "Thermodynamic Hypothesis", which states that the native conformation of a protein is adopted spontaneously. In other words, there is sufficient information contained in the protein sequence to guarantee correct folding from any of a large number of unfolded states. A schematic diagram of Anfinsen's experiment is shown below in two parts:

Proceedings of the

NATIONAL ACADEMY OF SCIENCES

Volume 47 · Number 9 · September 15, 1961

THE KINETICS OF FORMATION OF NATIVE RIBONUCLEASE DURING OXIDATION OF THE REDUCED POLYPEPTIDE CHAIN

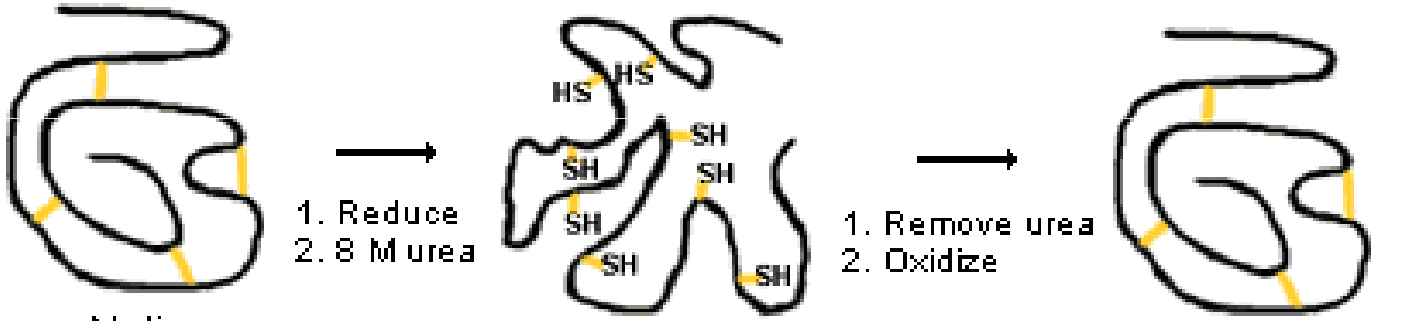
BY C. B. ANFINSEN, E. HABER,* M. SELA,† AND F. H. WHITE, JR.

LABORATORY OF CELLULAR PHYSIOLOGY AND METABOLISM, NATIONAL HEART INSTITUTE, NATIONAL INSTITUTES OF HEALTH

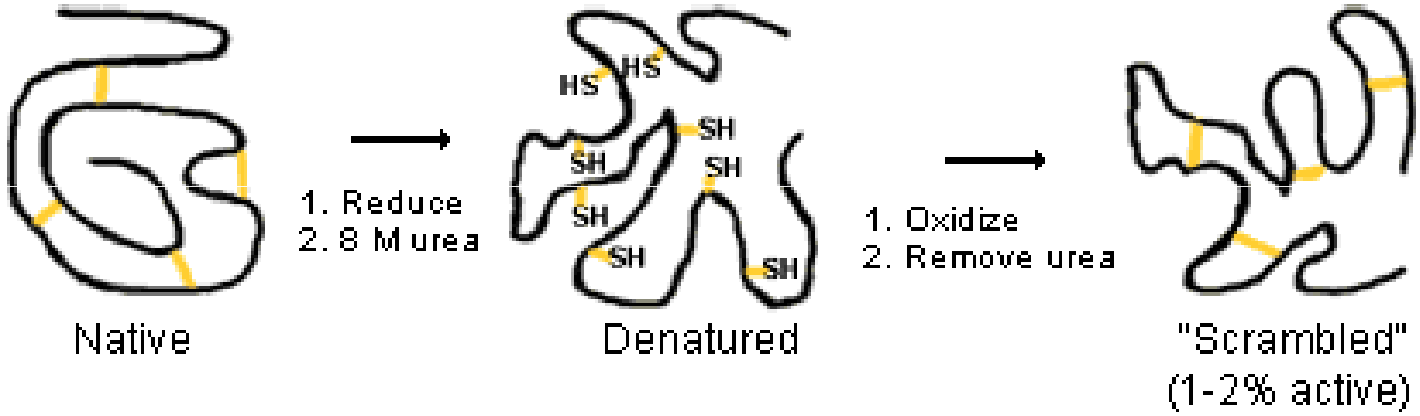
Communicated by John T. Edsall, July 31, 1961

Bovine pancreatic ribonuclease is completely reduced by treatment with mercaptoethanol in 8 *M* urea to yield a randomly coiled polypeptide chain containing eight cysteine residues.[1–3] Under optimal conditions of polypeptide concentration and pH, essentially complete reformation of the disulfide bonds of the native enzyme occurs in the presence of molecular oxygen.[2, 3] From chemical and physical studies of the reformed enzyme, it may be concluded that the information for the correct pairing of half-cystine residues in disulfide linkage, and for the assumption of the native secondary and tertiary structures, is contained in the amino acid sequence itself.

The Observation:



The Control:



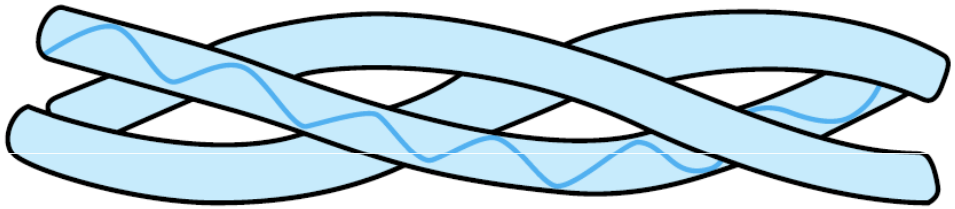
VII] Terciární struktura proteinů

1) Kolagen

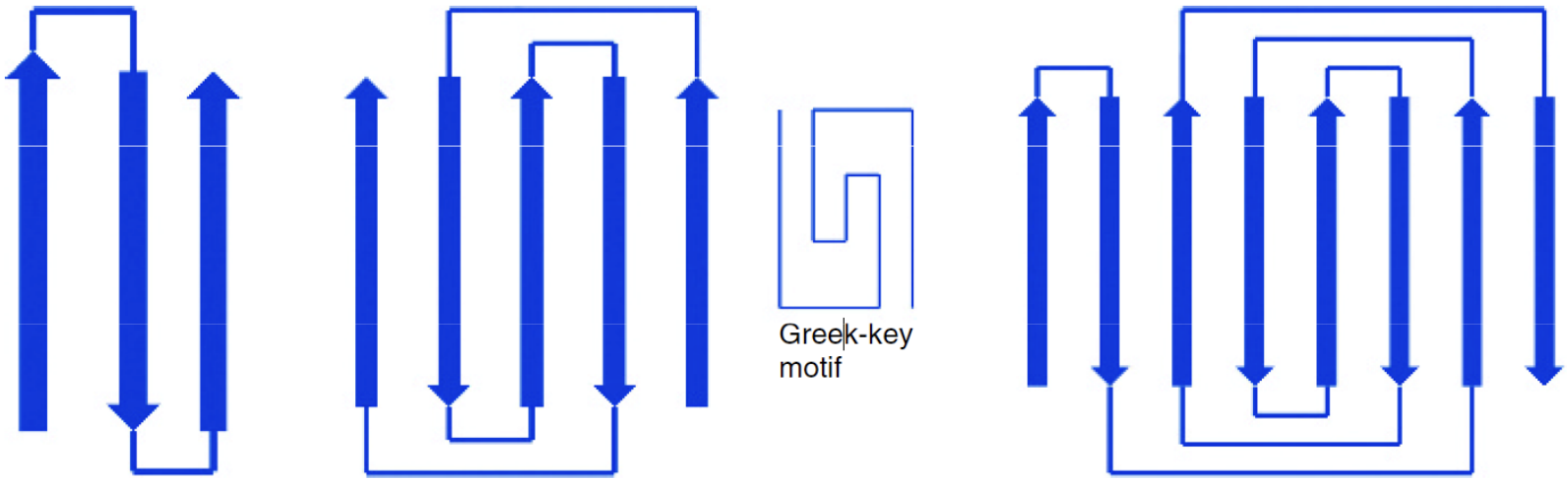
Primární struktura: – Gly – X – Y – Gly – X – Y – Gly – X – Y –

Sekundární struktura:

Terciární struktura:



3) Strukturní motivy v proteinech

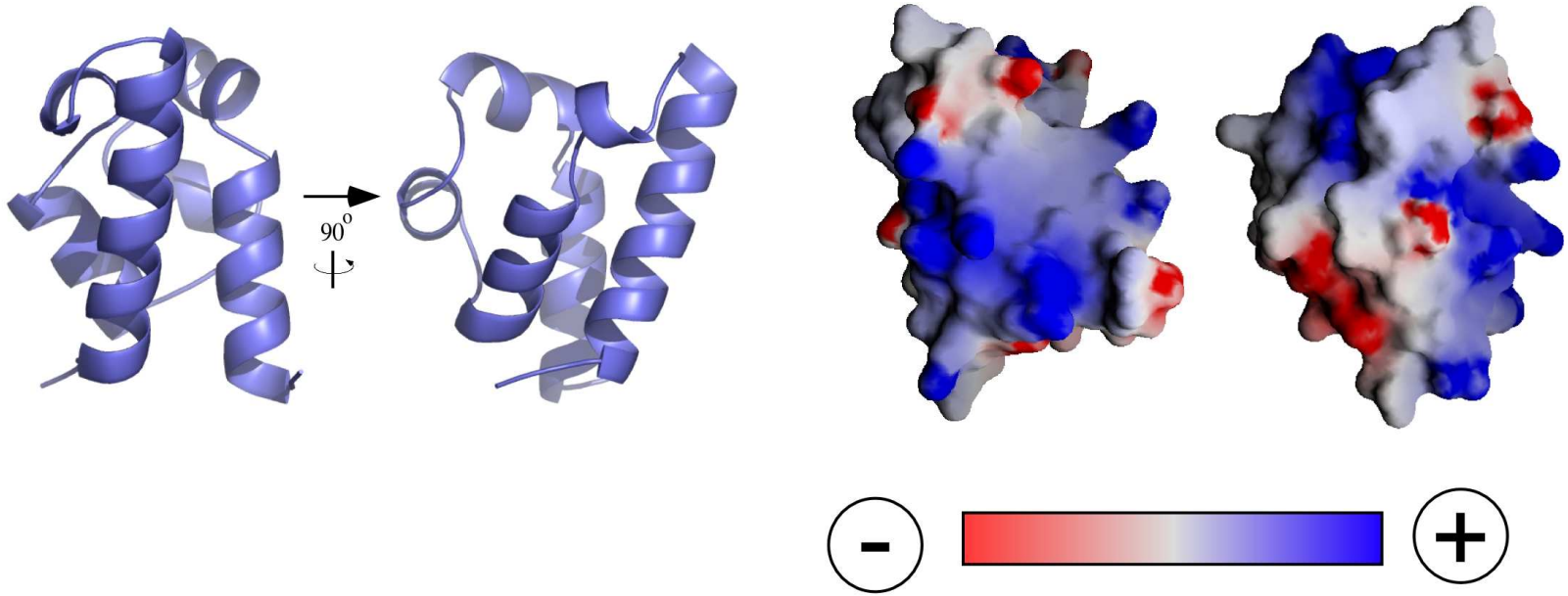


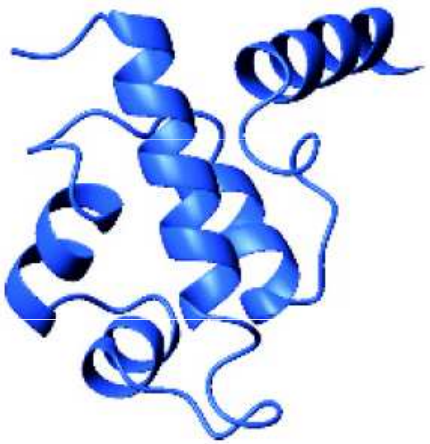
β-meandr

Řecký klíč

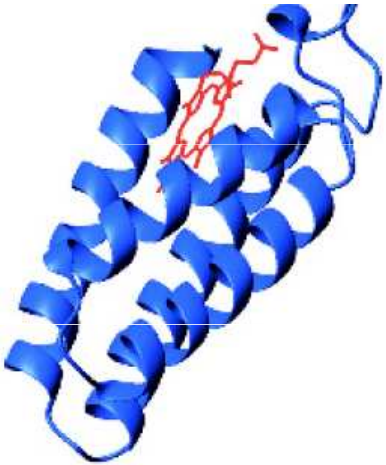
Swiss/Jelly roll

Charged and polar R-groups tend to map to protein surfaces

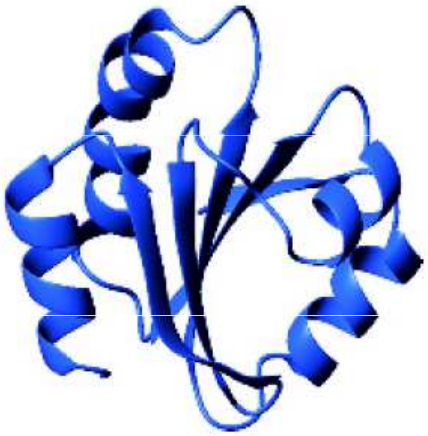




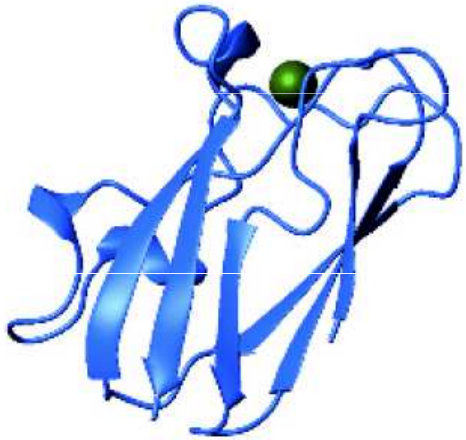
λ repressor



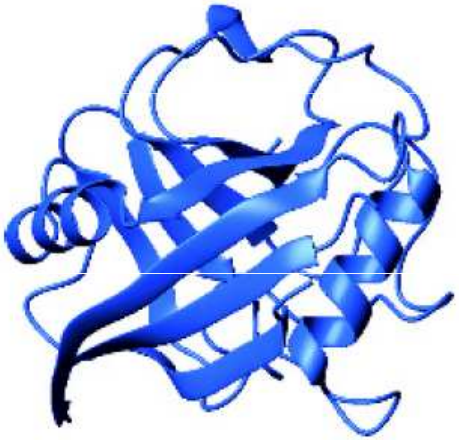
Cytochrome b_{562}



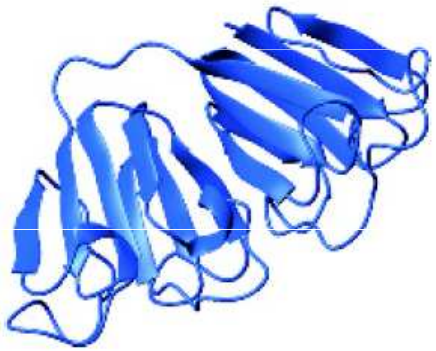
Thioredoxin



Plastocyanin



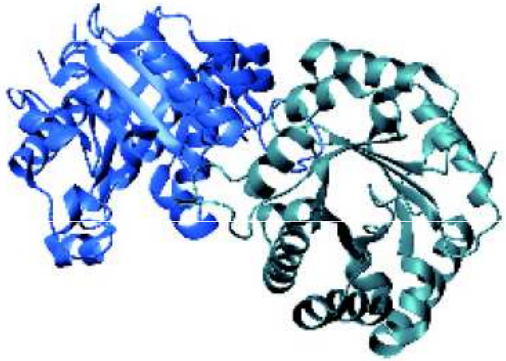
cis-trans proline isomerase



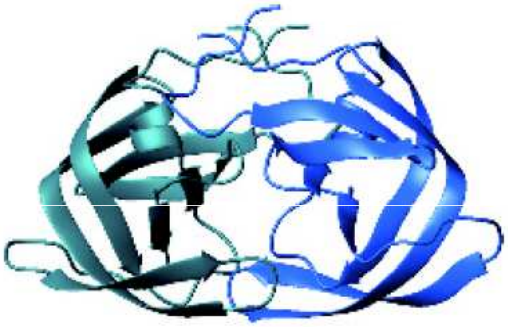
γ-crystallin

VIII] Kvartérní struktura proteinů

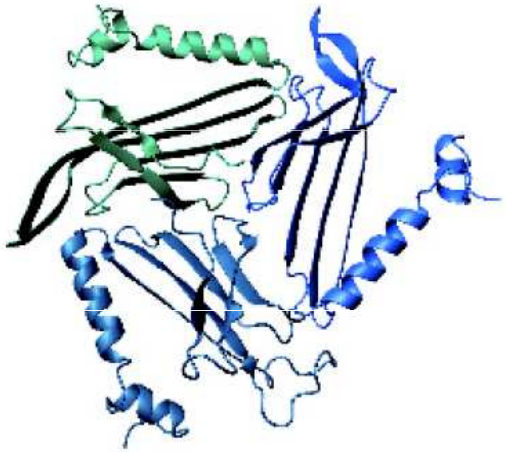
1) **Multimery**
2) **Homo-/hetero-mery**



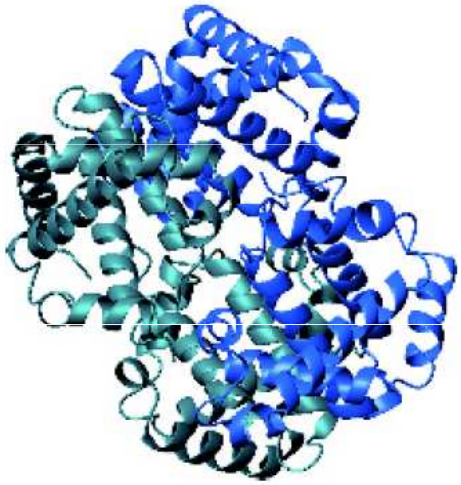
Triose phosphate isomerase (TIM)



HIV protease



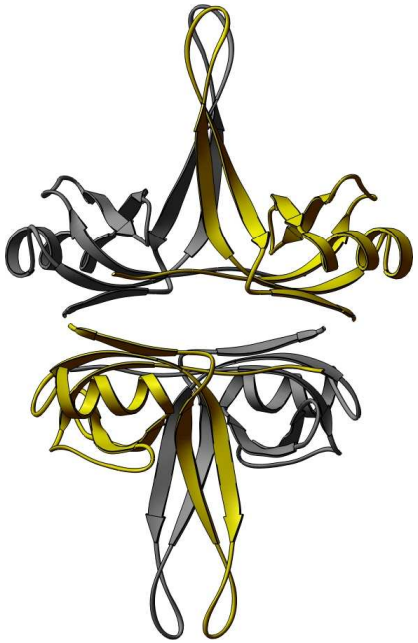
MS2 viral capsid protein



Haemoglobin

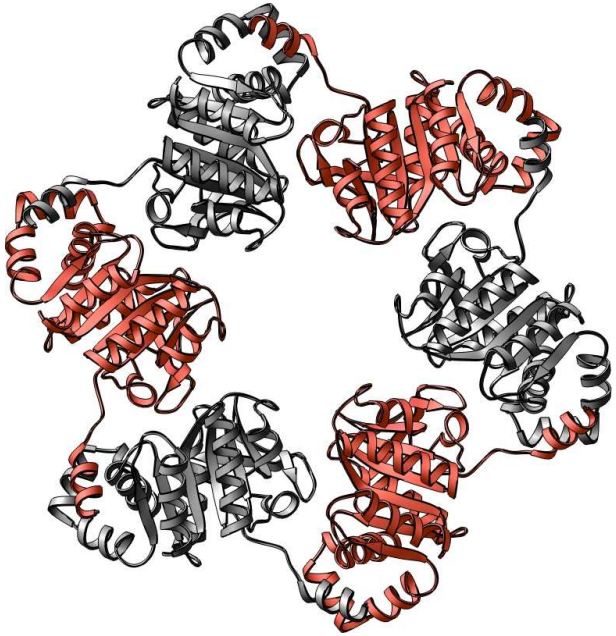
Examples of other quaternary structures

Tetramer



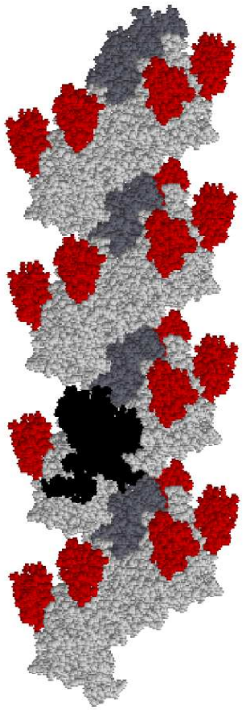
SSB
Allows coordinated DNA binding

Hexamer



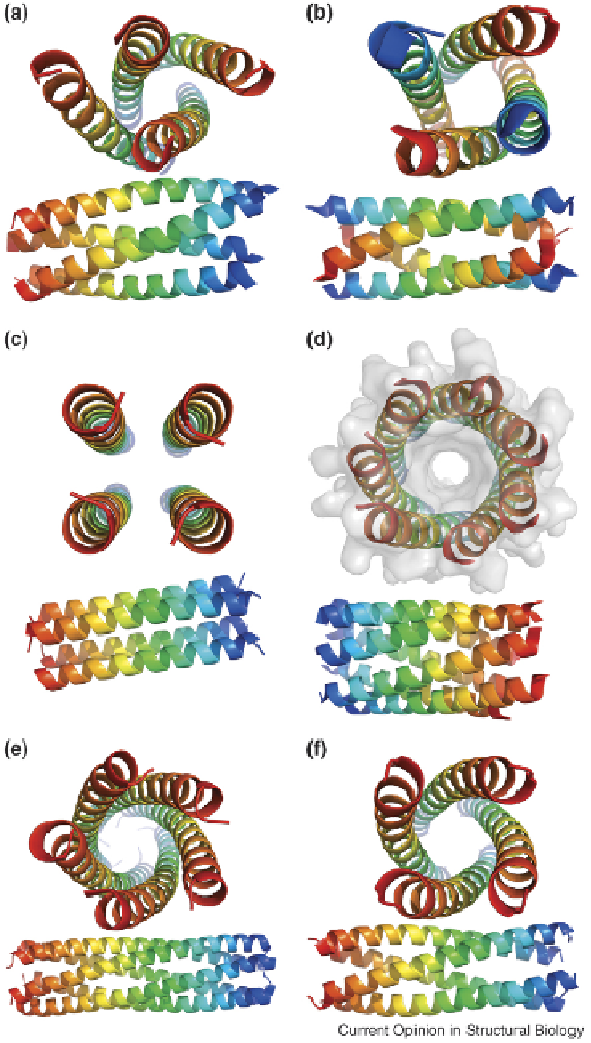
DNA helicase
Allows coordinated DNA binding and ATP hydrolysis

Filament



Recombinase
Allows complete coverage of an extended molecule

Coiled coils



Grigoryan and Keating, 2008

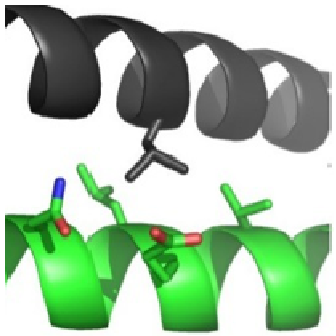
Coiled coils

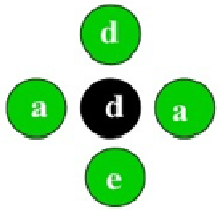
- bundle of α-helices
- usually 2,3,4 helices
- parallel or antiparallel
- oligomers: homo- or hetero-

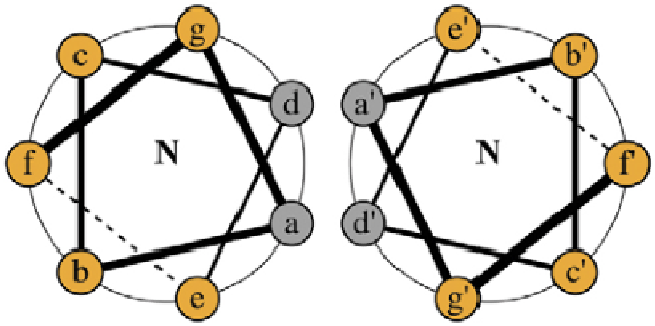
- 3.5 amino acids / turn
- 7 amino acid register
- inner residues - **hydrophobic**
- outer residues - **hydrophilic**

- **knobs-into-holes**:
  a residue from one helix (**knob**) packs into a space surrounded by **4** side-chains of the facing helix (**hole**)

[abcdefg]n







Lupas, A.N., and Gruber, M. (2005).
The Structure of α-Helical Coiled Coils.

Useful software

- **COILS** (prediction of coiled coil regions)
  http://embnet.vital-it.ch/software/COILS_form.html
- **MARCOIL** (prediction of coiled coil regions)
  http://bcf.isb-sib.ch/webmarcoil/webmarcoilINFOC1.html
- **MULTICOIL** (prediction of coiled coil regions, oligomeric state)
- **LOGICOIL** (oligomeric state probabilities)
  http://coiledcoils.chm.bris.ac.uk/LOGICOIL/
- **DrawCoil 1.0** (heptade diagrams)
  http://www.grigoryanlab.org/drawcoil/
- **CCBuilder** (building CC from the sequence)
  http://coiledcoils.chm.bris.ac.uk/app/cc_builder/
- **SOCKET** (locate knobs-into-holes packing between alpha-helices in PDB structures)
  http://coiledcoils.chm.bris.ac.uk/socket/index.html
- **CCCP** (Coiled-coil Crick Parameterization)
  http://www.grigoryanlab.org/cccp/

Confidence in structural features of proteins determined by X-ray crystallography

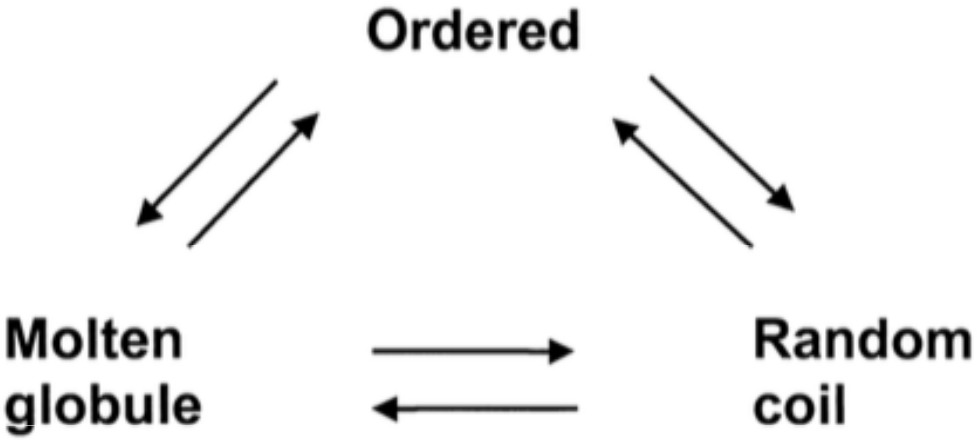
(estimates are very rough and strongly depend on the quality of the data)

Structural feature			Resolution		
	5 Å	3 Å	2.5 Å	2 Å	1.5 Å
Chain tracing	-	Fair	Good	Good	Good
Secondary structure	Helices fair	Fair	Good	Good	Good
Sidechain conformations	-	-	Fair	Good	Good
Orientation of peptide planes	-	-	Fair	Good	Good
Protein hydrogen atoms visible	-	-	-	-	Good

XII] Metody pro určování třídimenzionální struktury (bio)molekul na atomární úrovni

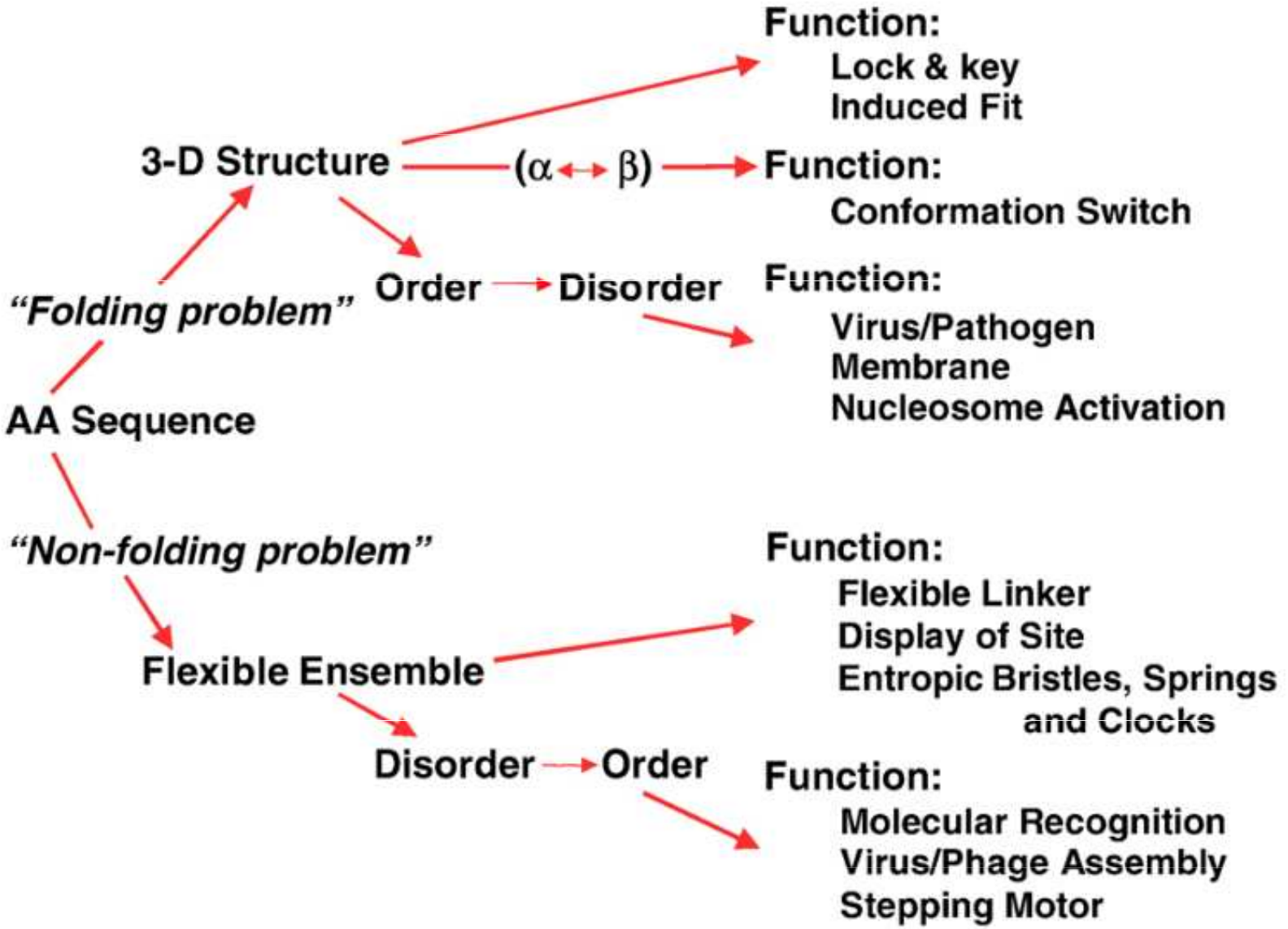
1) NMR – nukleární (=jaderná) magnetická rezonance – měření (také) v kapalném prostředí
2) Rentgenová krystalografie - (měření především v krystalu)
3) Kryo-elektronová mikroskopie

THE PROTEIN TRINITY



Proposal: Function can arise from any of the three protein forms and transitions between them.

J Mol Graph Model 19, 2001,



BiochimBiophysActa 1804, 2010, 1231-64

IX] Funkce proteinů:

1) Enzymy – katalyzátory biologických reakcí
2) Transportní proteiny (hemoglobin)
3) Regulační proteiny (např. hormon insulin)
4) Skladovací (storage) – např. ovalbumin – zdroj dusíku pro vyvíjející se ptačí embryo
5) “Pohybové” proteiny – actin, myosin, tubulin, dynein, kinesin
6) Strukturní proteiny – zajišťujicí vytvoření a udržení biologické struktury – α-keratin, kolagen, elastin, fibroin etc.
7) Ochranné – imunoglobuliny, fibrinogen, thrombin

X] Proteinová databáze – PDB

WWW.RCSB.ORG

XI] Vizualizační programy

1) ChimeraX
2) Chimera
3) PyMol
4) VMD

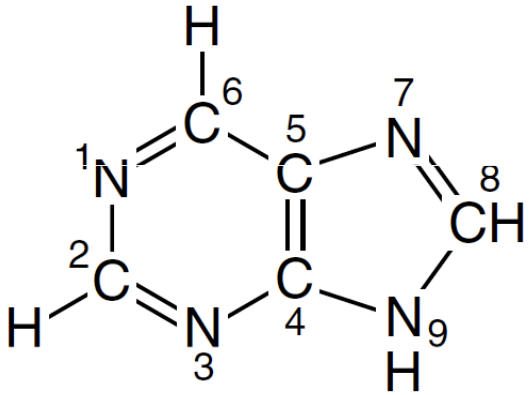
Nukleové kyseliny

Základní stavební kameny nukleových kyselin:

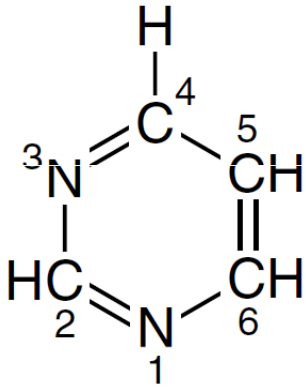
1) Báze
   i) Purinové – menší, číslování arom. kruhu protisměru hod. r., **adenin (A)**, **guanin (G)**, obecně **R**
   ii) Pyrimidinové – větší, číslování ve směru hod. r., **cytosin (C)**, **uracil (U)**, **thymin (T)**, obecně **Y**
2) Cukr – 2'-deoxyribóza (**DNA**), ribóza (**RNA**)
3) Fosfát

Báze:

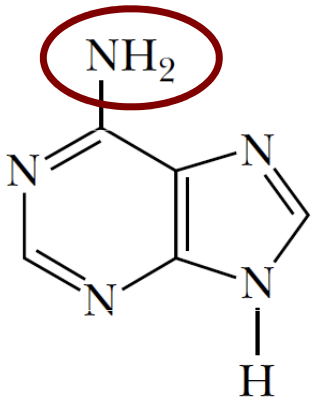
1) Standardní
2) Modifikované: N6-methyl-dA, 5-methyl-dC, xanthin, hypoxanthin, uric acid, 7-methylguanine, dimetylaminoadenin



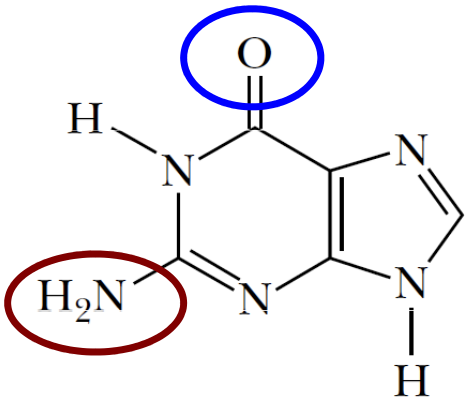
Purin (R)



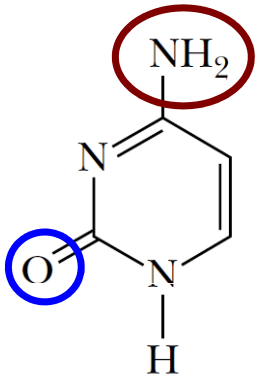
Pyrimidin (Y)



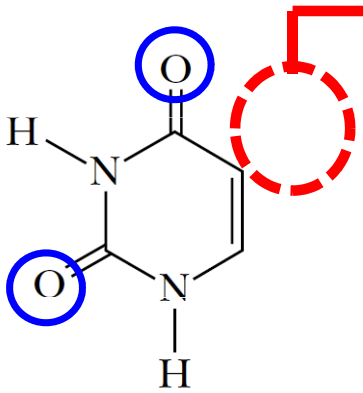
Adenine
(6-amino purine)



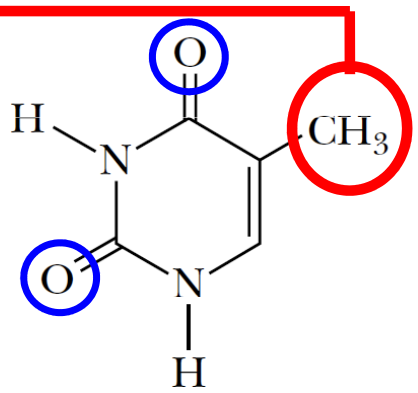
Guanine
(2-amino-6-oxy purine)



Cytosine
(2-oxy-4-amino pyrimidine)

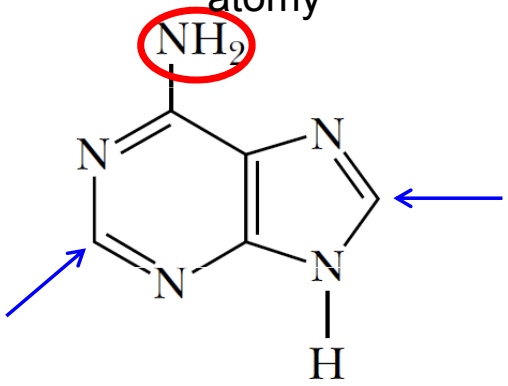


Uracil
(2-oxy-4-oxy pyrimidine)

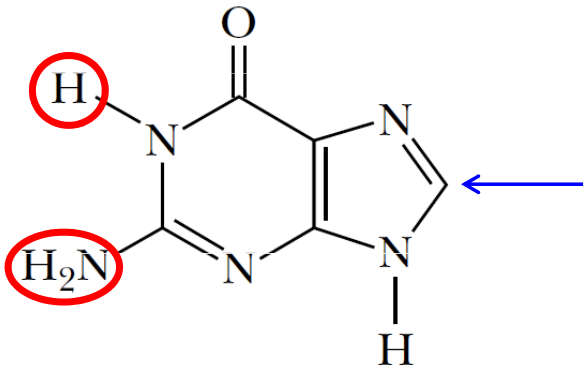


Thymine
(2-oxy-4-oxy 5-methyl pyrimidine)

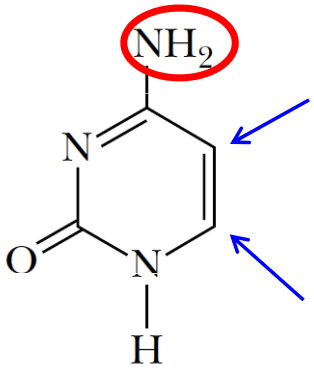
Vyměnitelné a **aromatické** vodíkové atomy



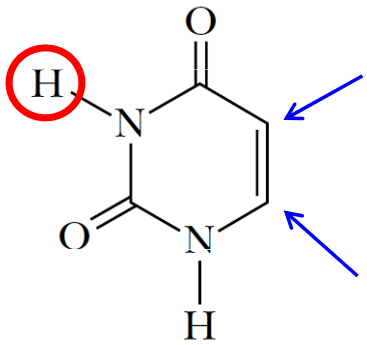
Adenine
(6-amino purine)



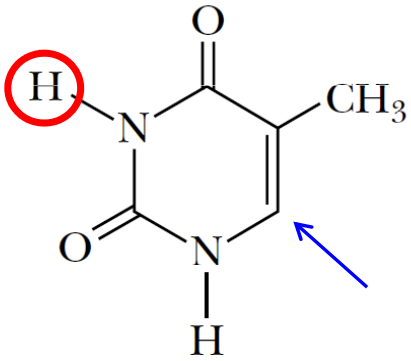
Guanine
(2-amino-6-oxy purine)



Cytosine
(2-oxy-4-amino pyrimidine)

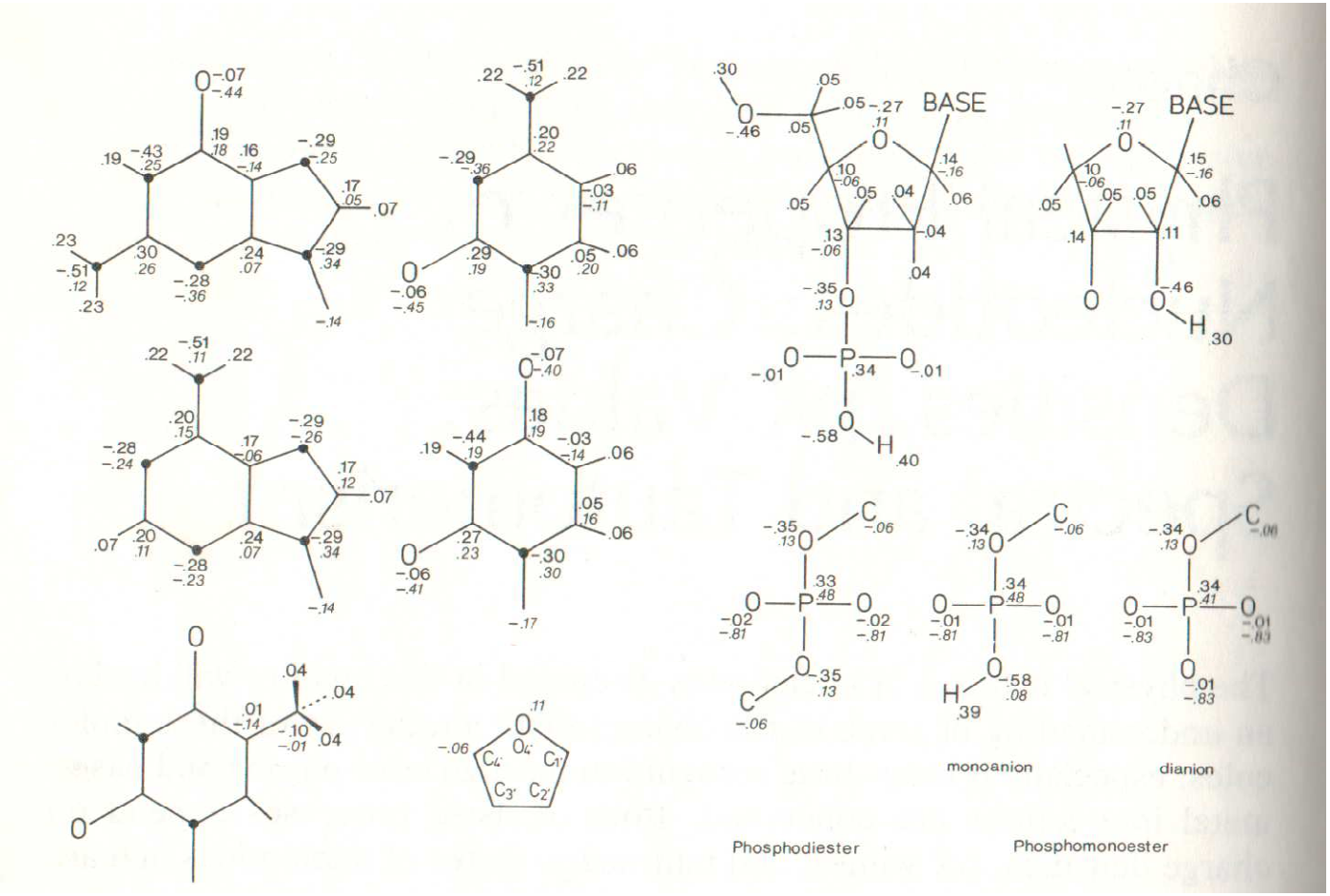


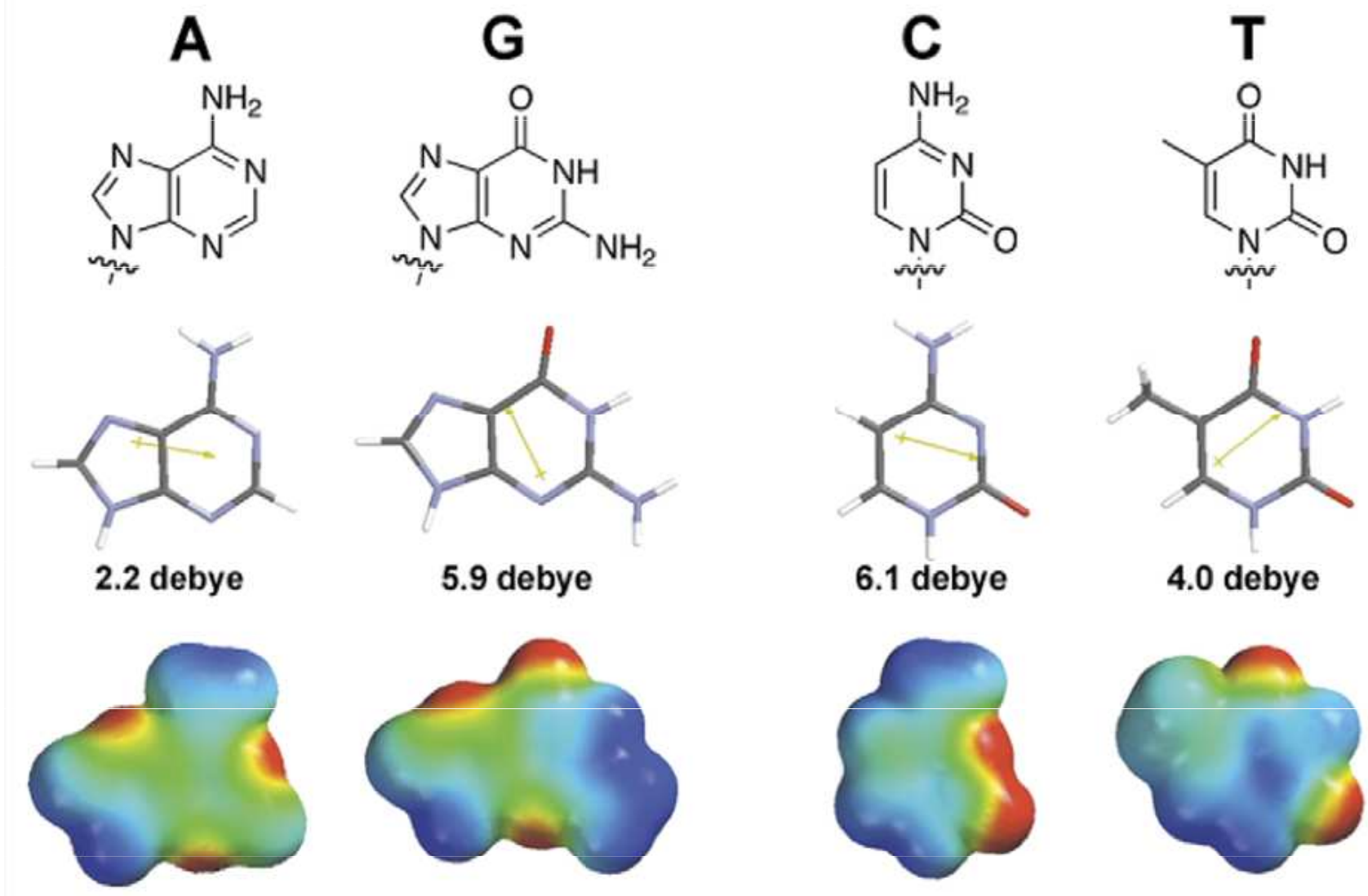
Uracil
(2-oxy-4-oxy pyrimidine)



Thymine
(2-oxy-4-oxy 5-methyl pyrimidine)

Hustoty nábojů v nukleotidech rozdělené podle **Del Re**ho σ nábojů (Roman) a **Hückel**ových π nábojů (kurzíva)

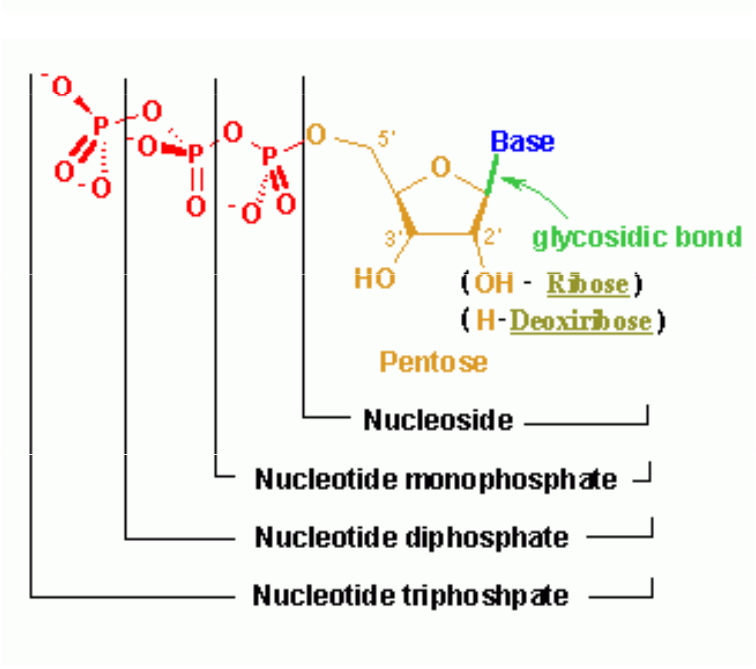


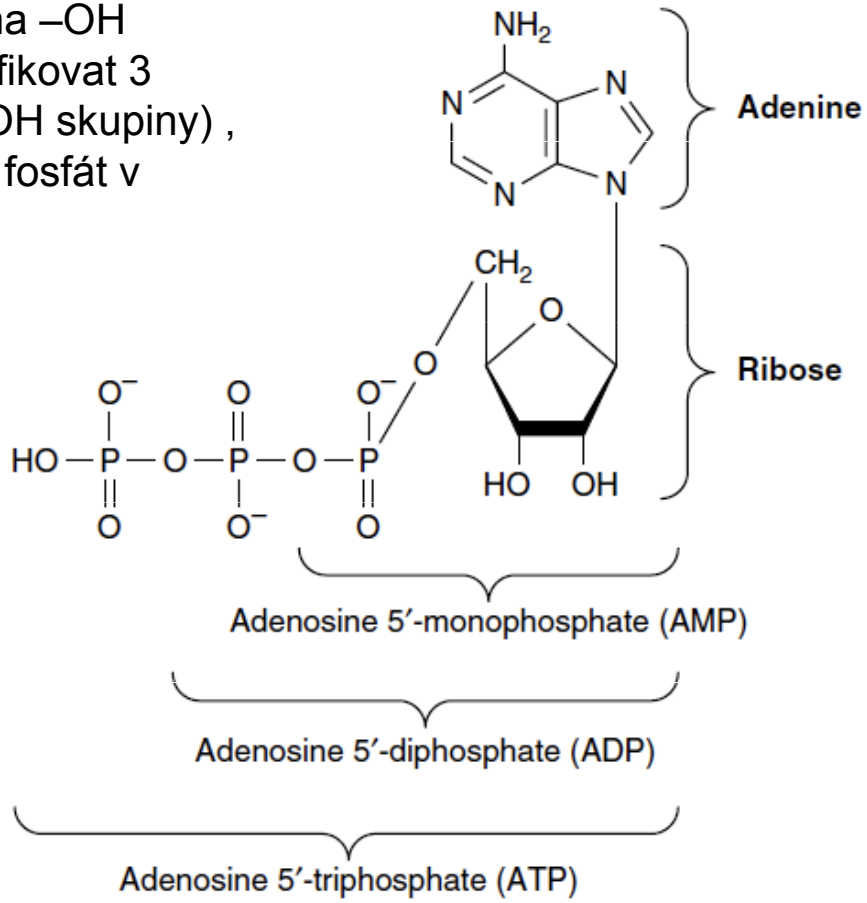

A
G
C
T
NH2
O
NH
N
2.2 debye
5.9 debye
6.1 debye
4.0 debye

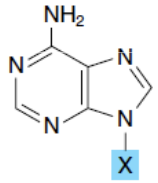
Tautomerie amino (amin<->imin**) a keto (**keto<->enol forma**) skupin purinů a pyrimidinů, fyziologické podmínky favorizují amino a keto formy**

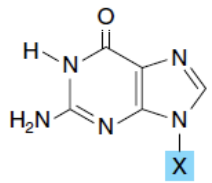
Nukleosidy a nukleotidy

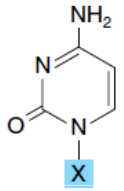
Nukleo**tid** vzniká esterifikací fosforylu na –OH skupinu nukleo**sid**u. V riboze lze esterifikovat 3 skupiny (ve 2'-deoxy-riboze pouze 2 –OH skupiny) , přesto má drtivá většina ribonukleotidů fosfát v poloze 5'

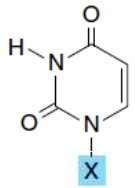


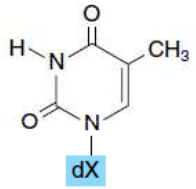




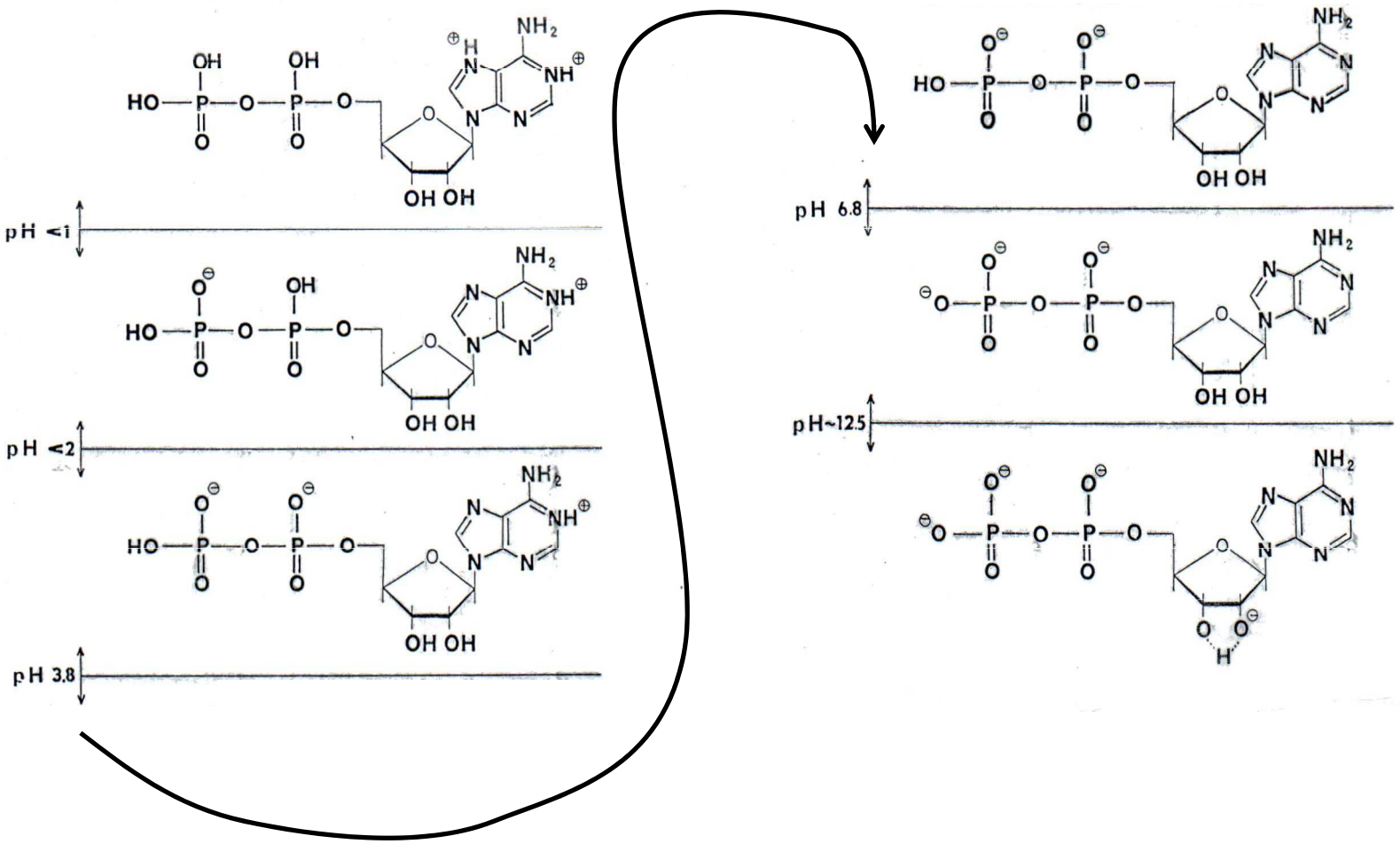




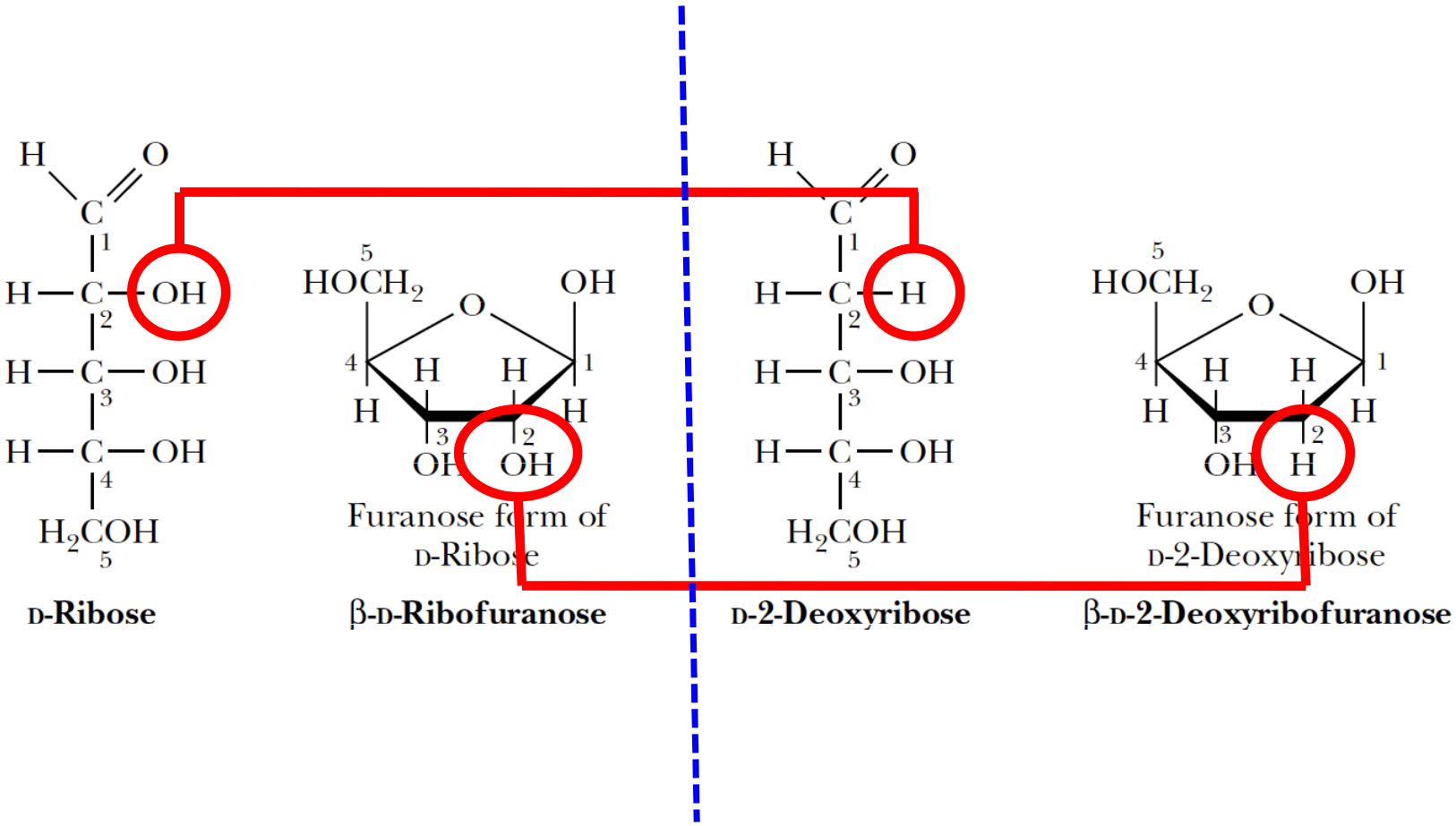


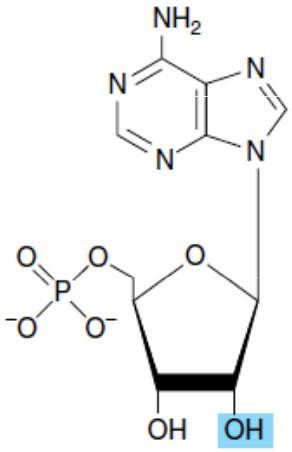


Název báze, **X=H**	Nukleosid, **X=(deoxy)ribóza**	Nukleotid, **X= fosfo.ribóza**
Adenin	Adenosin	Adenosinmonofosfát **AMP**
Guanin	Guanosin	Guanosinmonofosfát **GMP**
Cytosin	Cytidin	Cytidinmonofosfát **CMP**
Uracil	Uridin	Uridinmonofosfát **UMP**
Thymin	Thymidin	Thymidinmonofosfát **TMP**

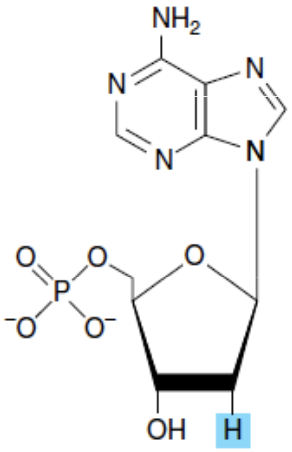

pH <1
pH <2
pH 3.8
pH 6.8
pH ~12.5

Cukr

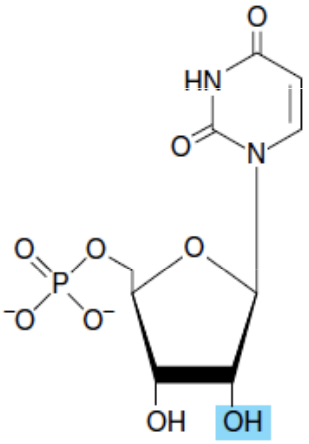

D-Ribose
β-D-Ribofuranose
D-2-Deoxyribose
β-D-2-Deoxyribofuranose
Furanose form of
D-Ribose
Furanose form of
D-2-Deoxyribose



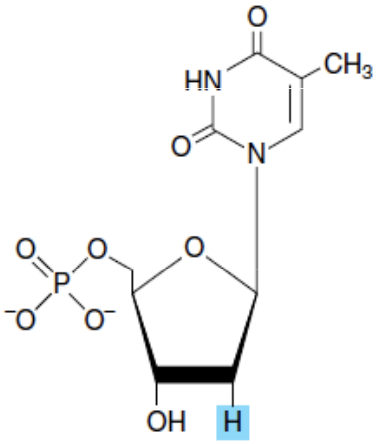
AMP



dAMP

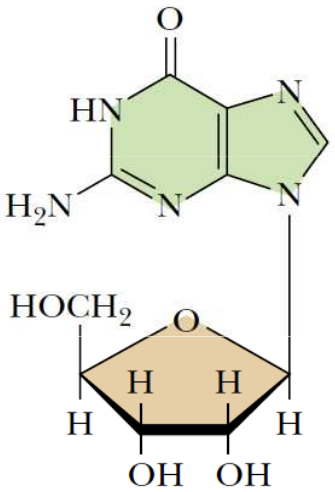


UMP

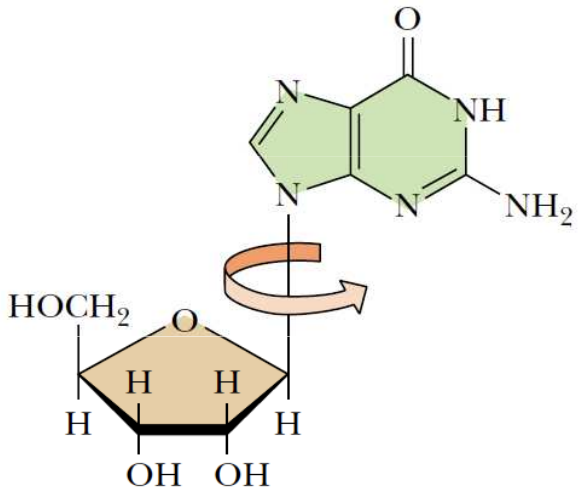


dTMP

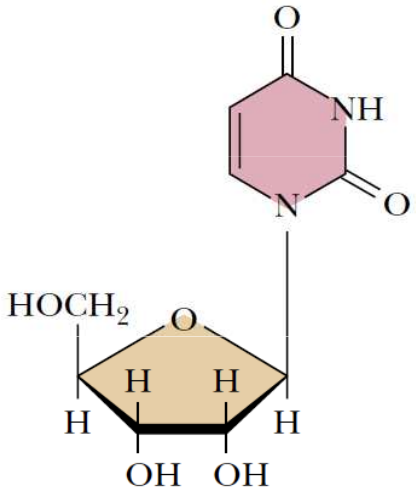
Vlivem stérického bránění báze se vyskytují dvě konformační uspořádání báze-cukr: ***syn***/***anti***
Oba způsoby uspořádání se vyskytují v přírodě, přičemž **ANTI** převažuje



syn **Guanosine**

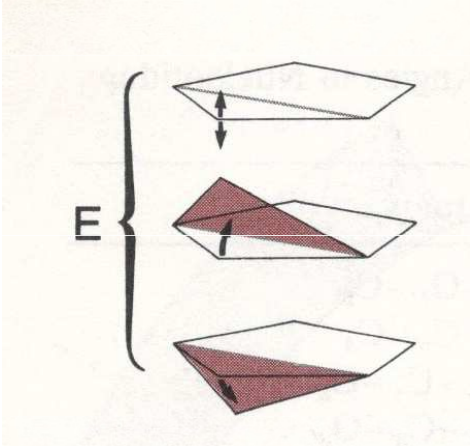


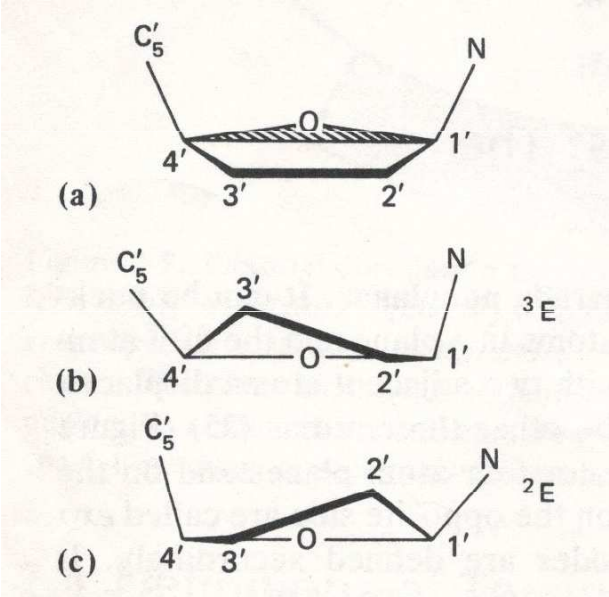
anti **Guanosine**

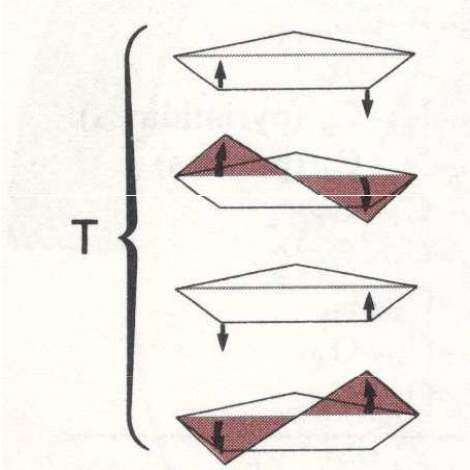


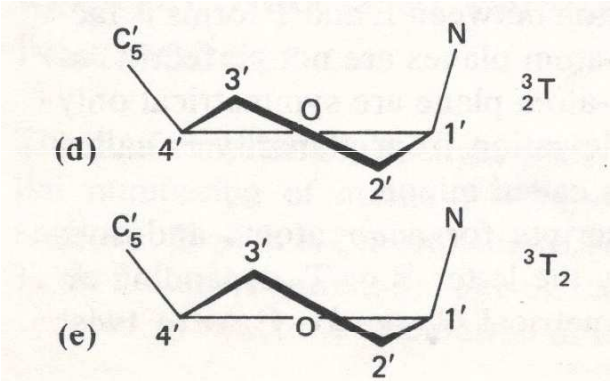
anti **Uridine**

Konformace cukru - Sugar pucker

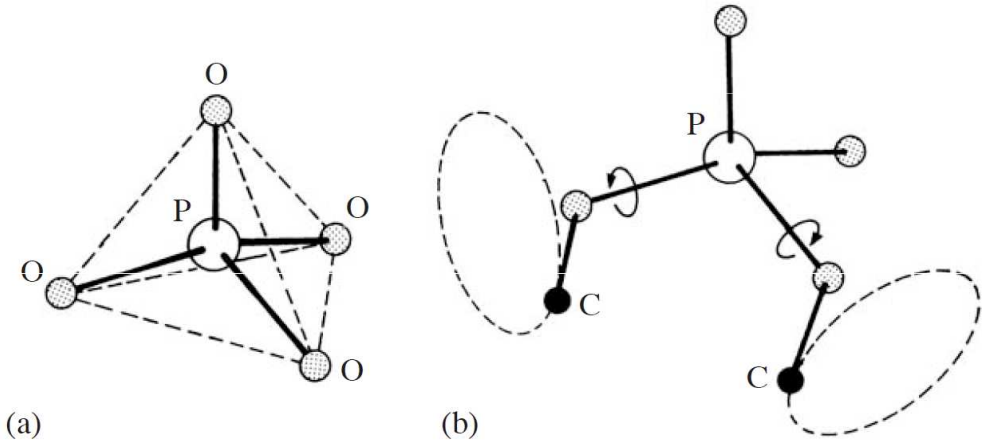




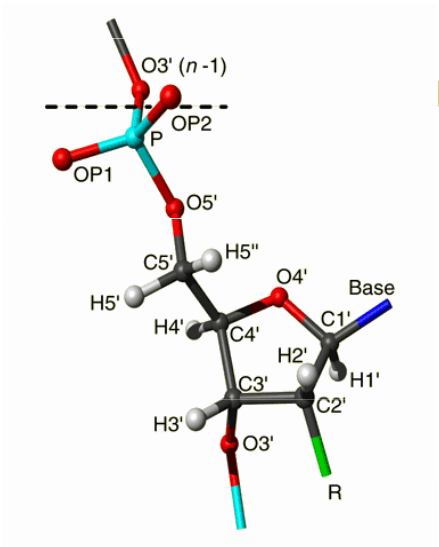


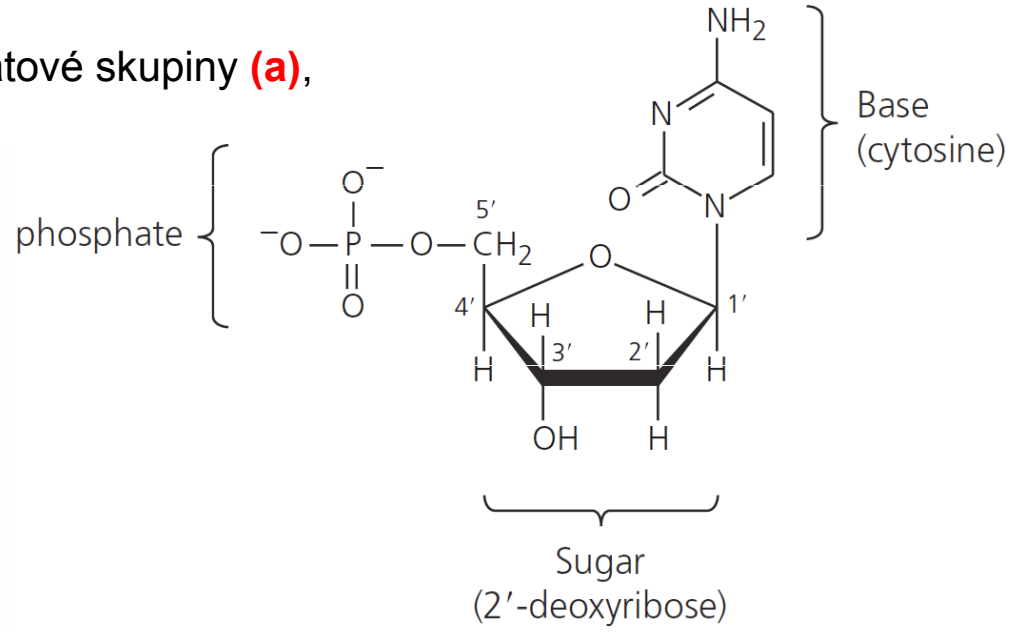


Fosfát; páteř nukleové kyseliny



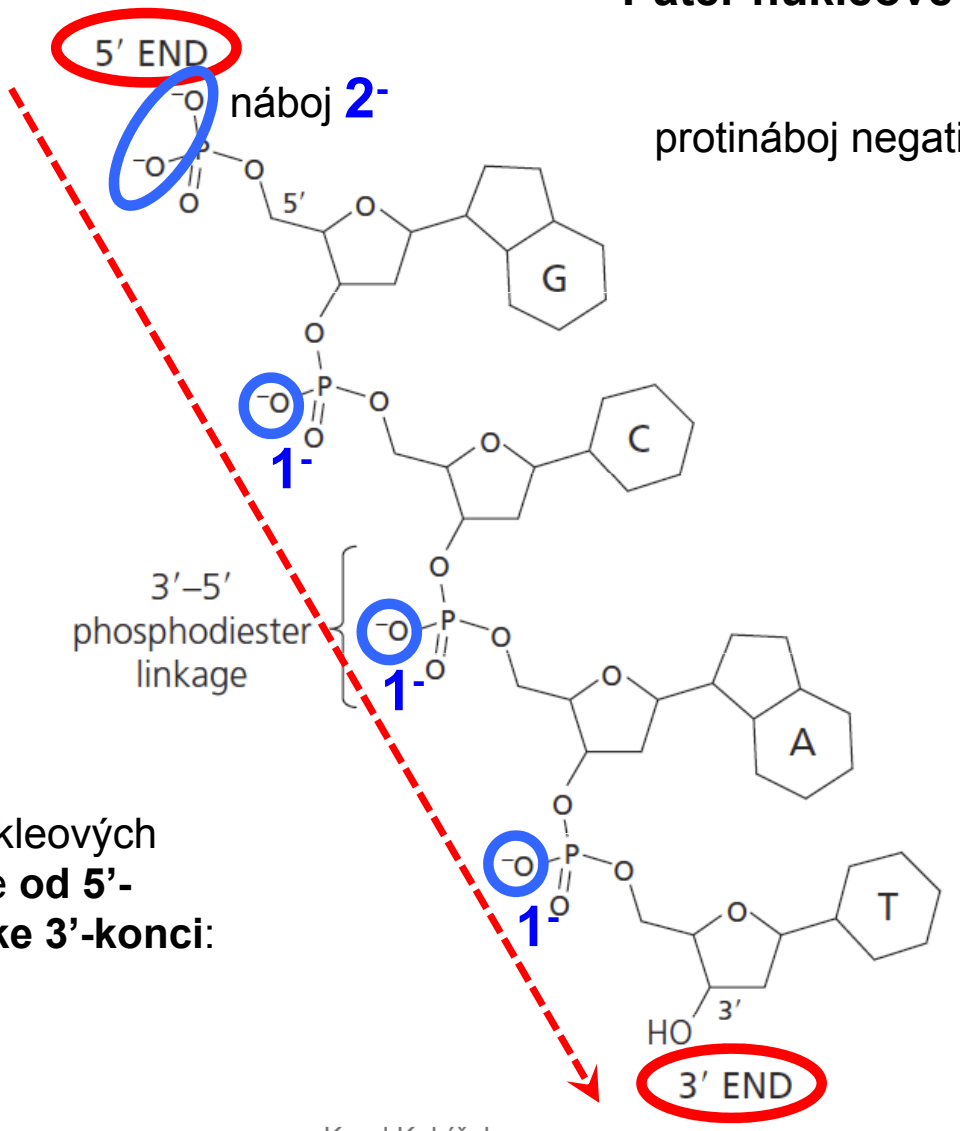
Tetrahedrální uspořádání fosfátové skupiny **(a)**, volnost rotace **(b)**





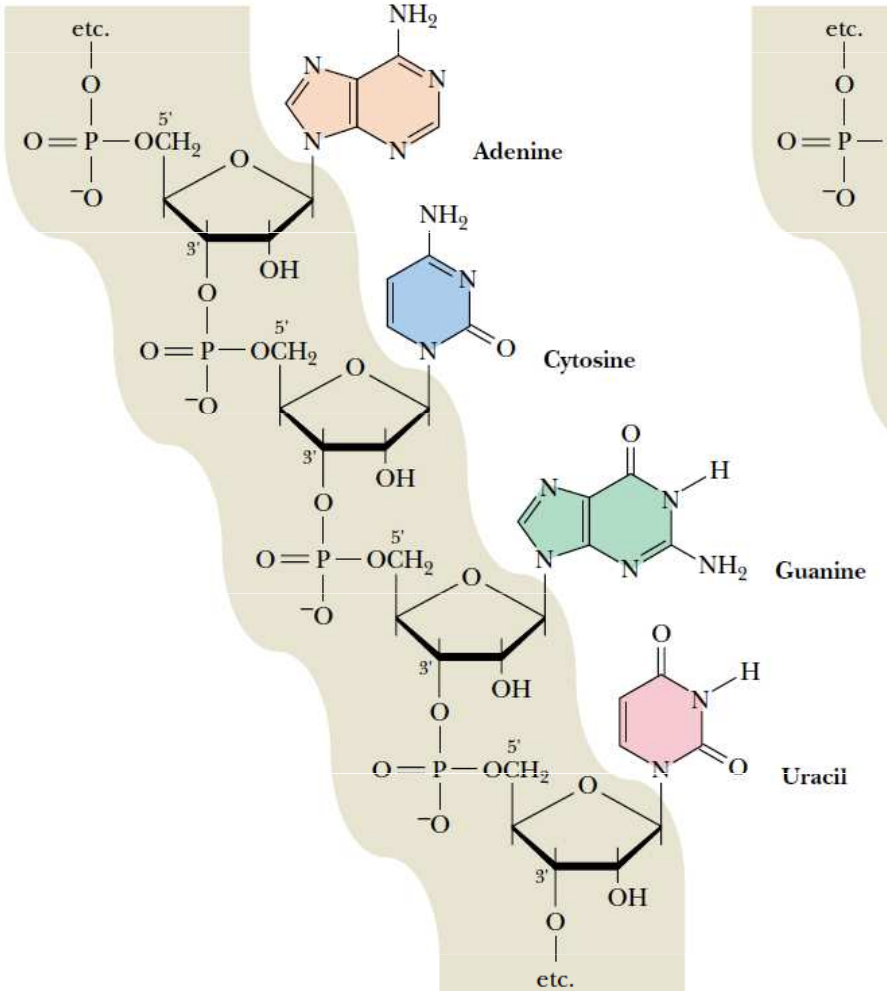
Páteř nukleové kyseliny

protináboj negativně nabité páteři: Na^+, K^+

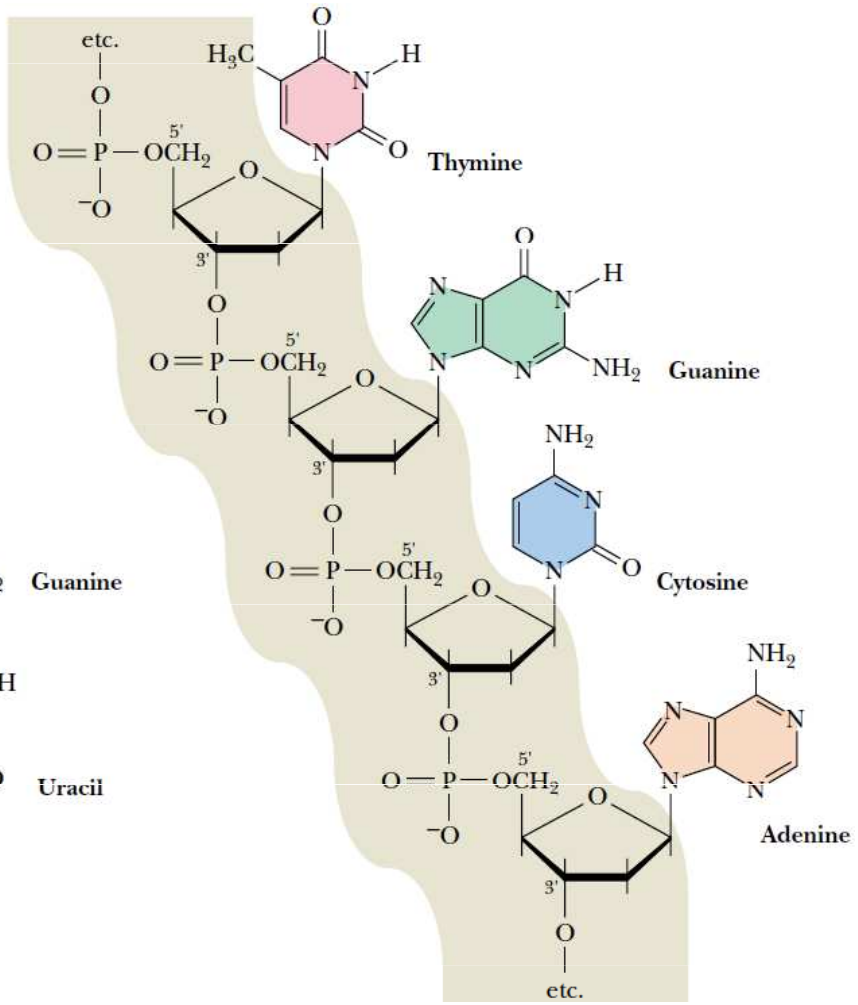


Báze v páteři nukleových kyselin číslujeme **od 5'-konce** směrem **ke 3'-konci**:
5'-GCAT-3'

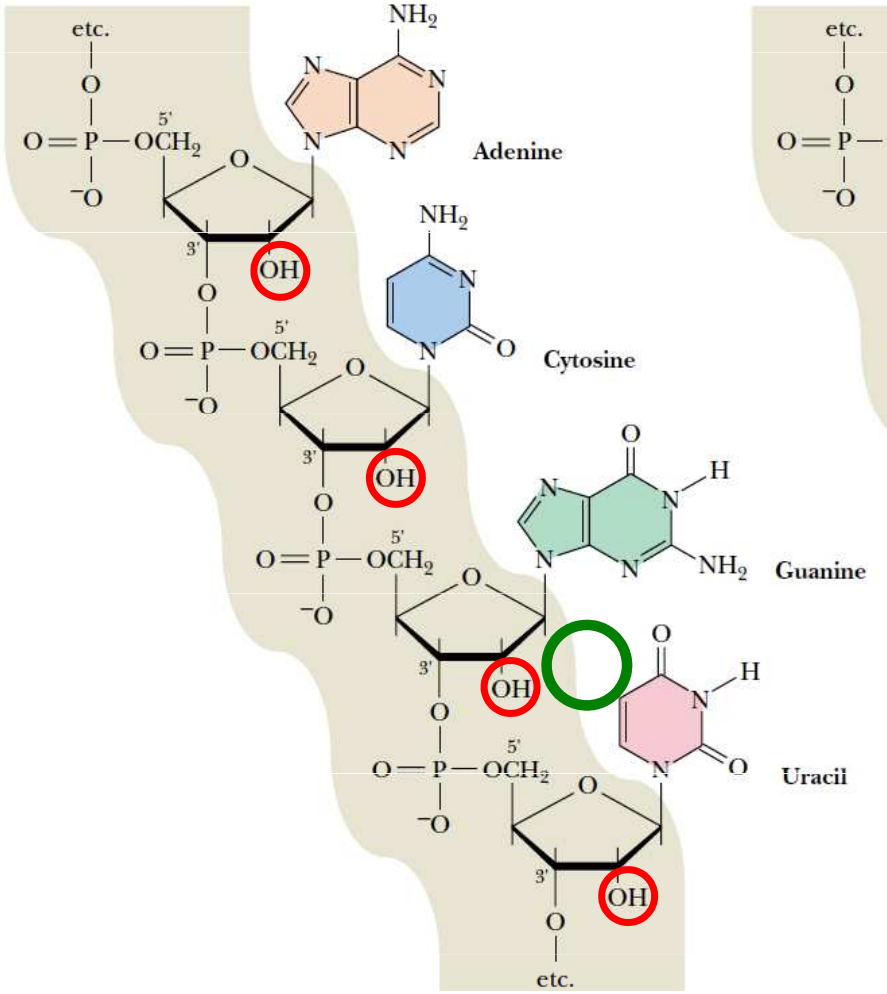
RNA


etc.
Adenine
Cytosine
Guanine
Uracil
etc.

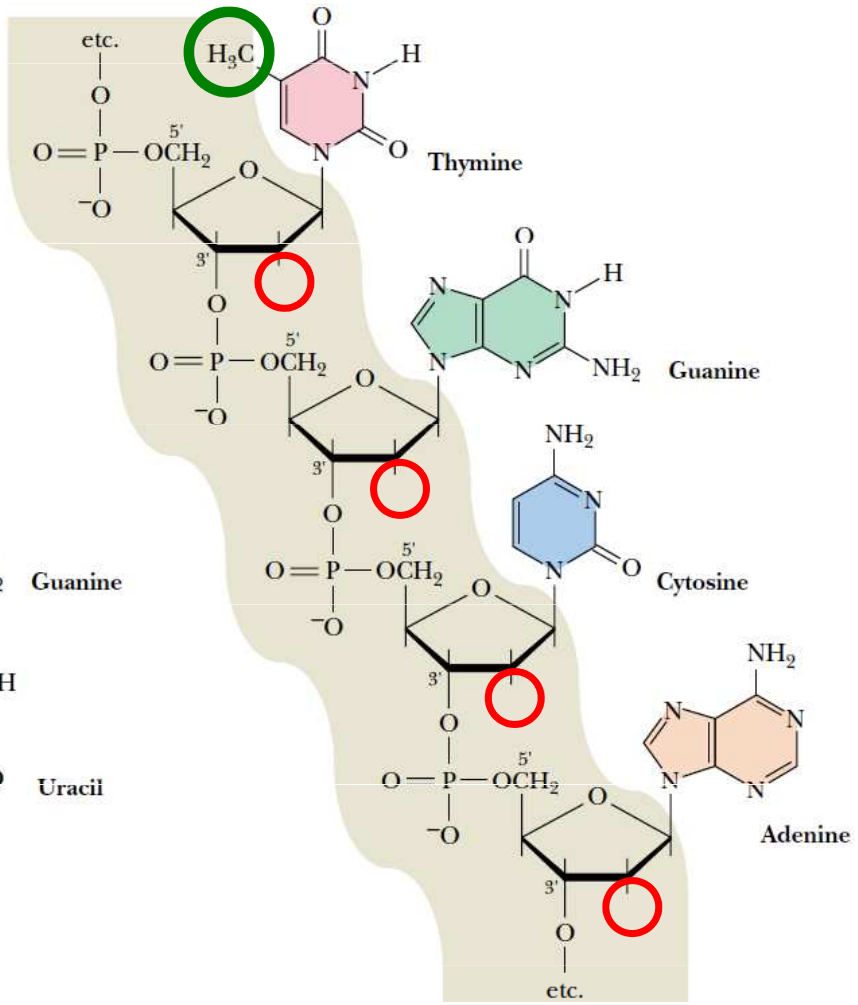
DNA


etc.
Thymine
Guanine
Cytosine
Adenine
etc.

RNA


etc.
Adenine
Cytosine
Guanine
Uracil
etc.

DNA


etc.
Thymine
Guanine
Cytosine
Adenine
etc.

A PROPOSED STRUCTURE FOR THE NUCLEIC ACIDS

By Linus Pauling and Robert B. Corey

Gates and Crellin Laboratories of Chemistry,* California Institute of Technology

Communicated December 31, 1952

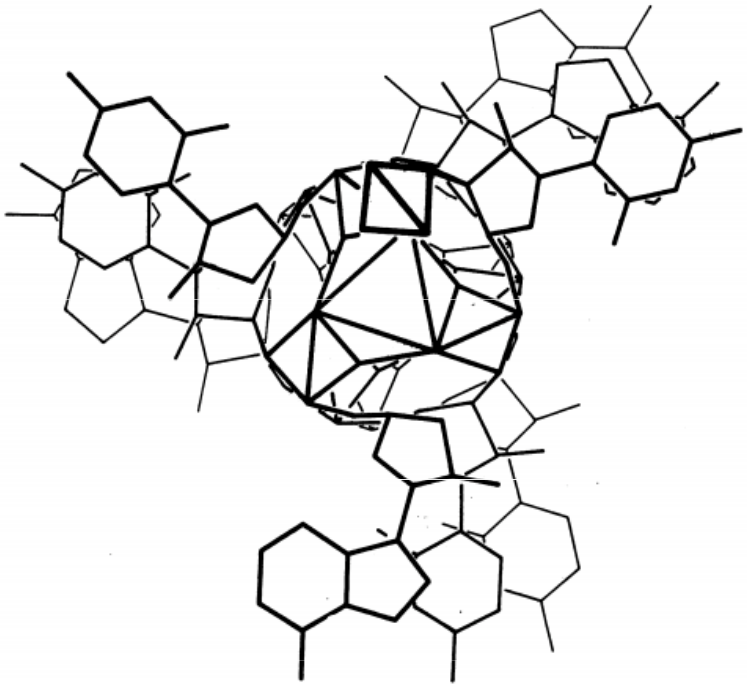
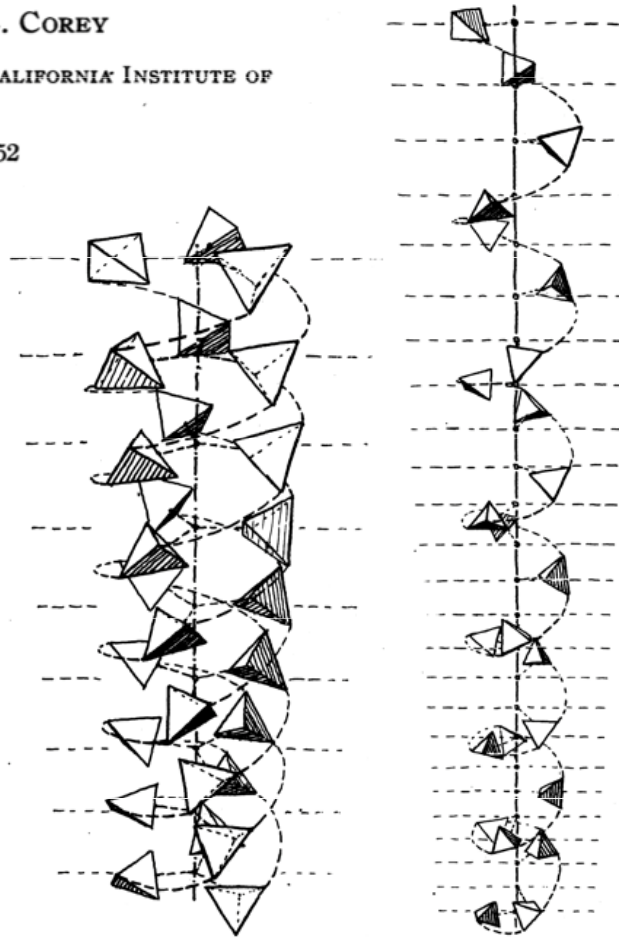
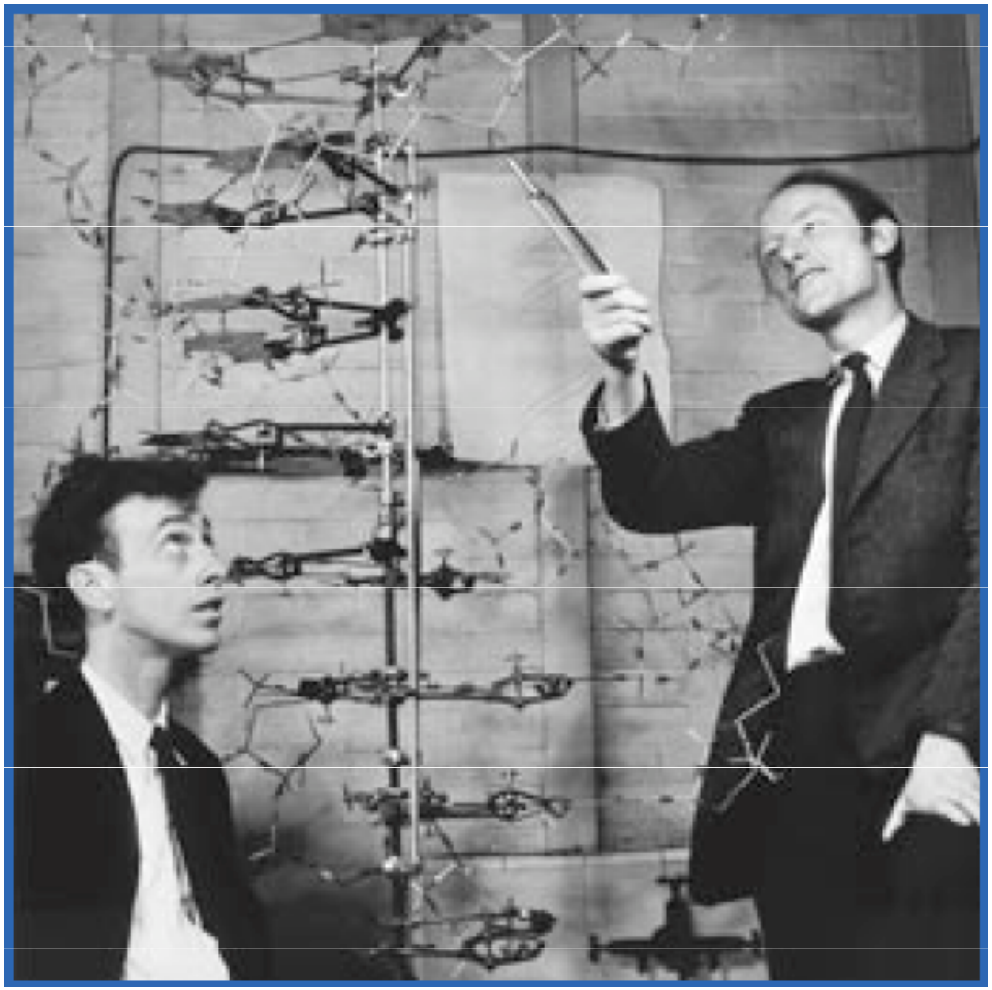


FIGURE 6

Plan of the nucleic acid structure, showing several nucleotide residues.

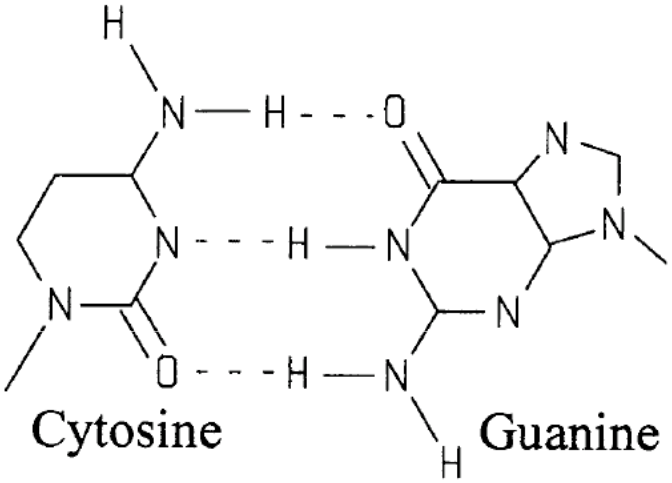


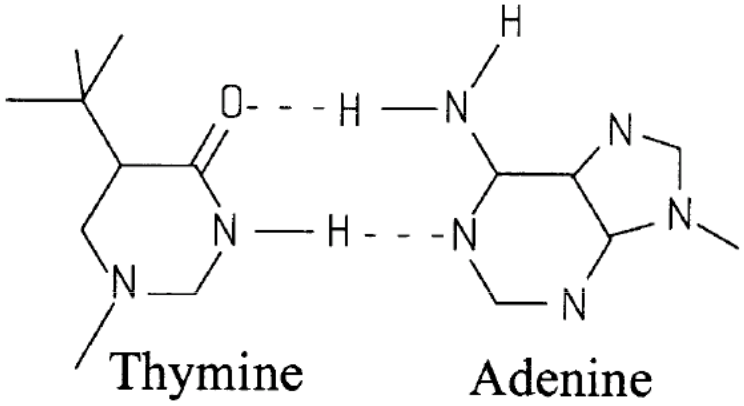
Párování bází NK: Watson-Crick, NC za medicínu a fyziologii 1962 [Watson(***1928**)]



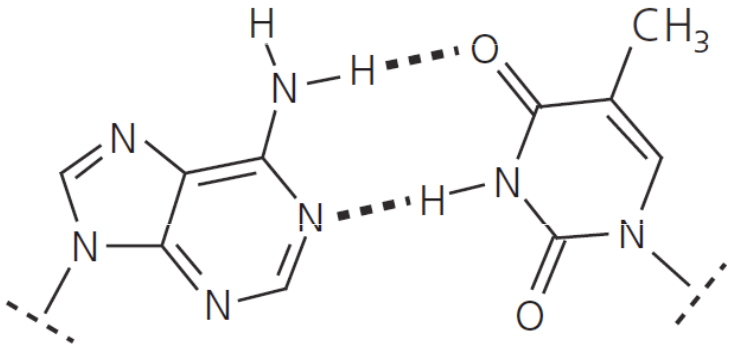
Vodíkové vazby

Jednotlivé řetězce dvojité šroubovice drží díky complementárními vazbami **N•••H-N** a **=O•••H-N**, které vznikají mezi **C**ytosinem a **G**uaninem a **T**hyminem a **A**deninem.

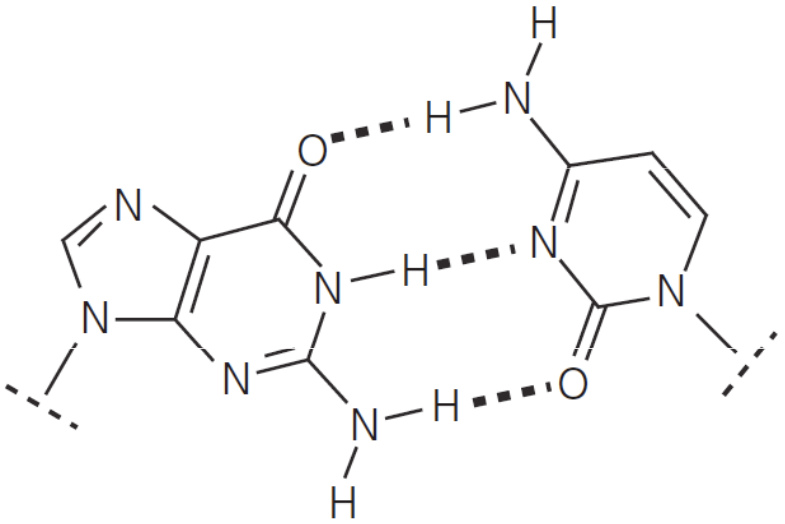




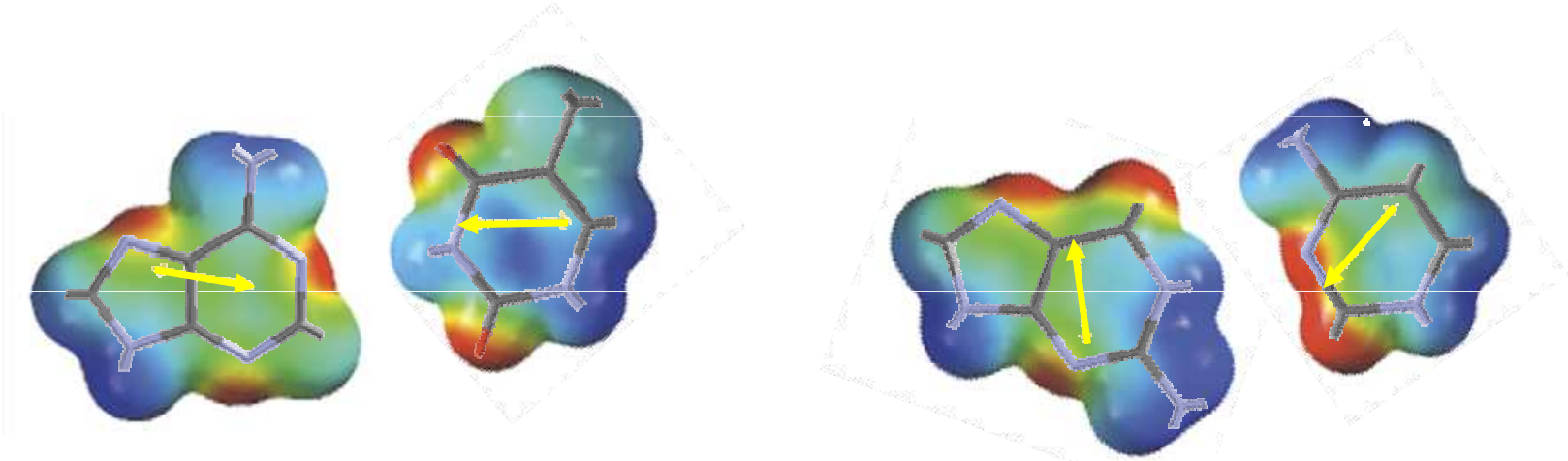
Každá vodíková vazba přispívá cca **20 kJ/mol** ke stabilizaci dvojšroubovice



adenine : thymine

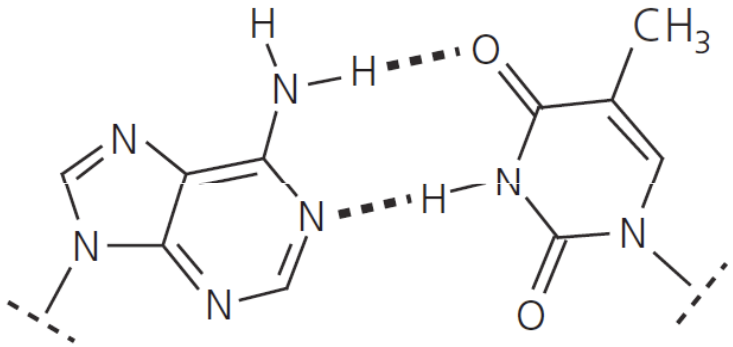


guanine : cytosine

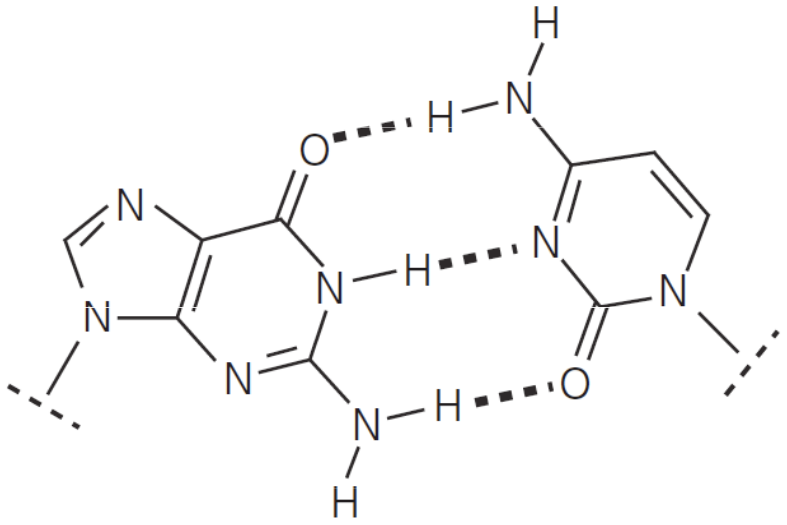


rozložení náboje v nukleobázích **+** **0** **-**, šipky označují dipólový moment

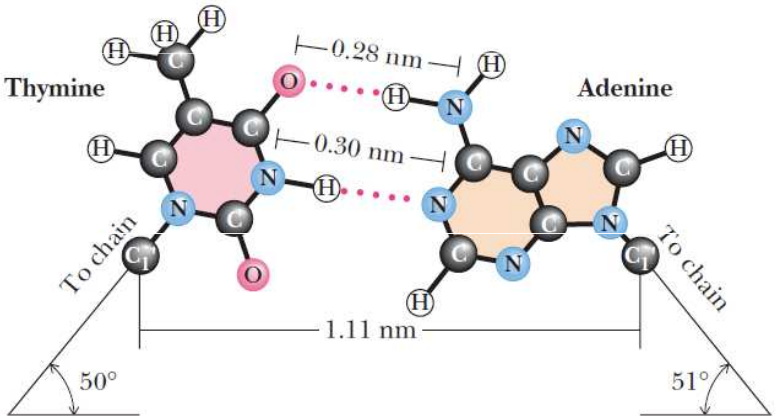
Watson-Crickovské párování bazí

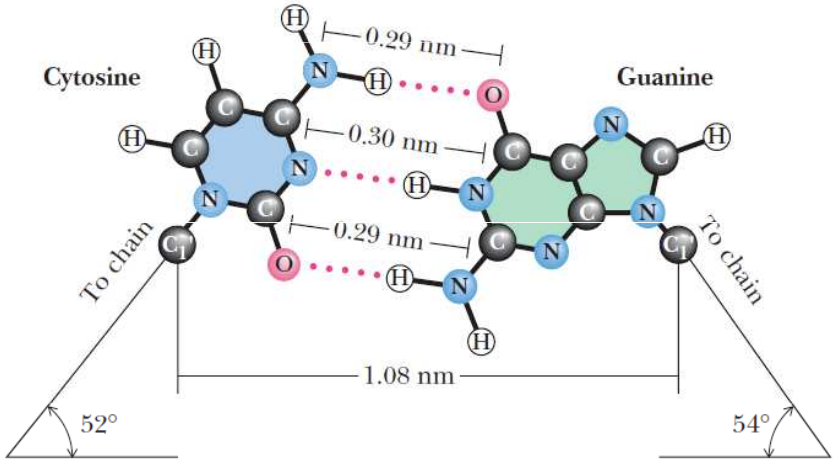


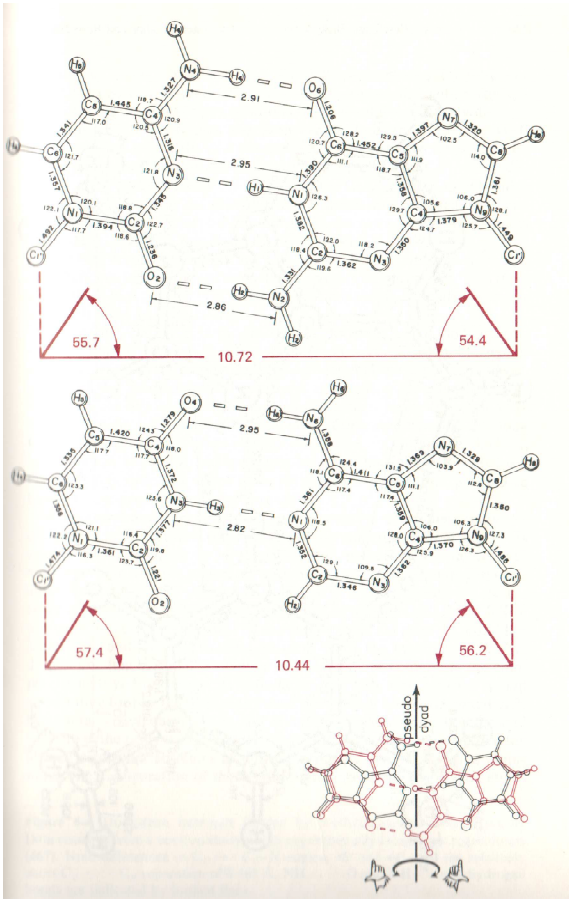
adenine : thymine

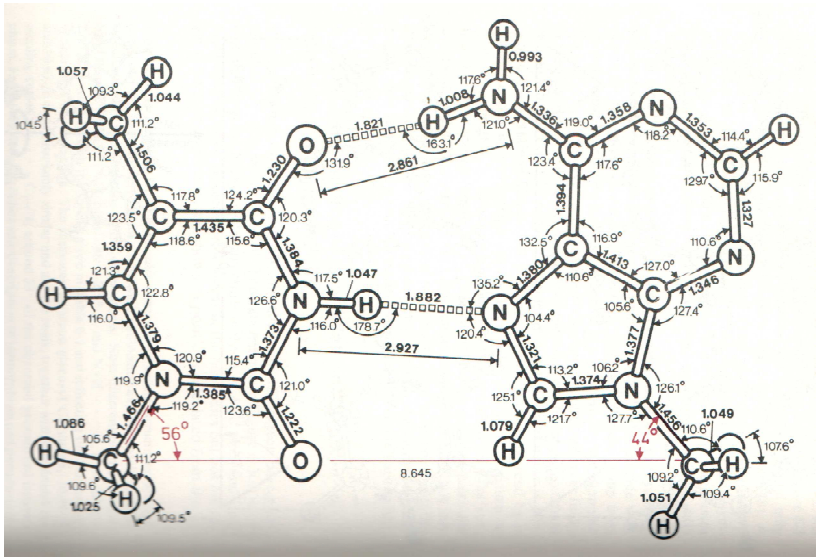


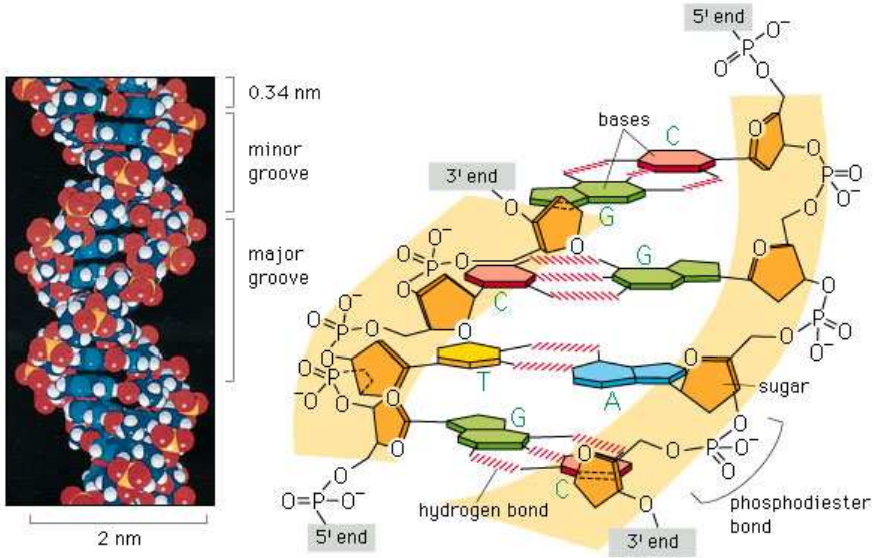
guanine : cytosine

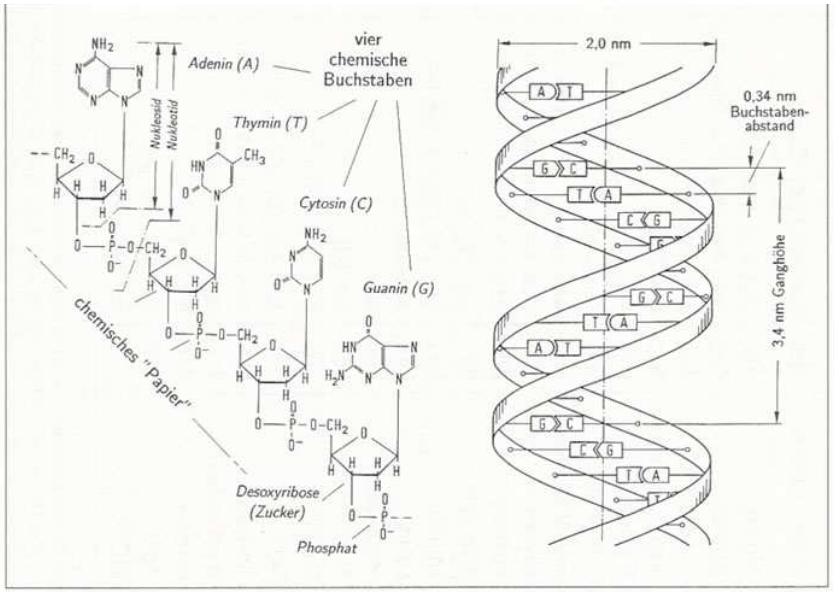


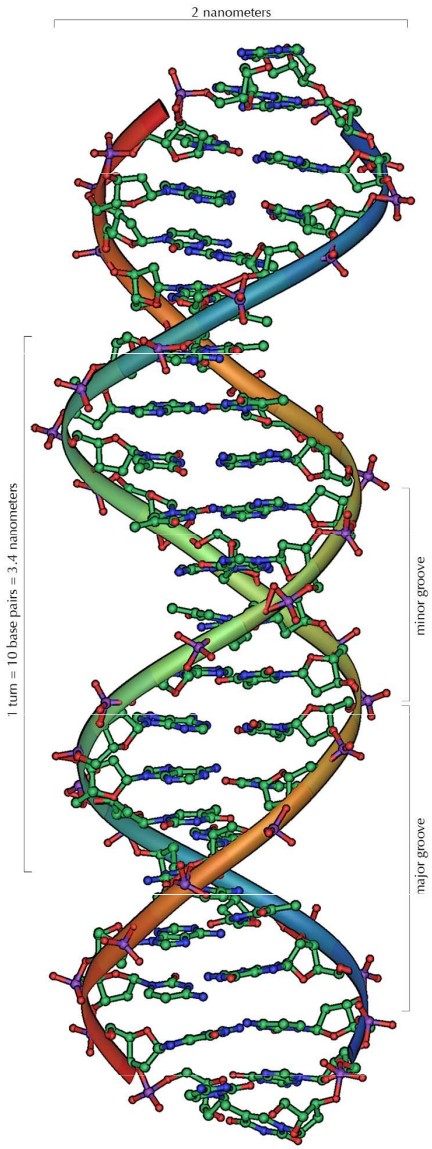


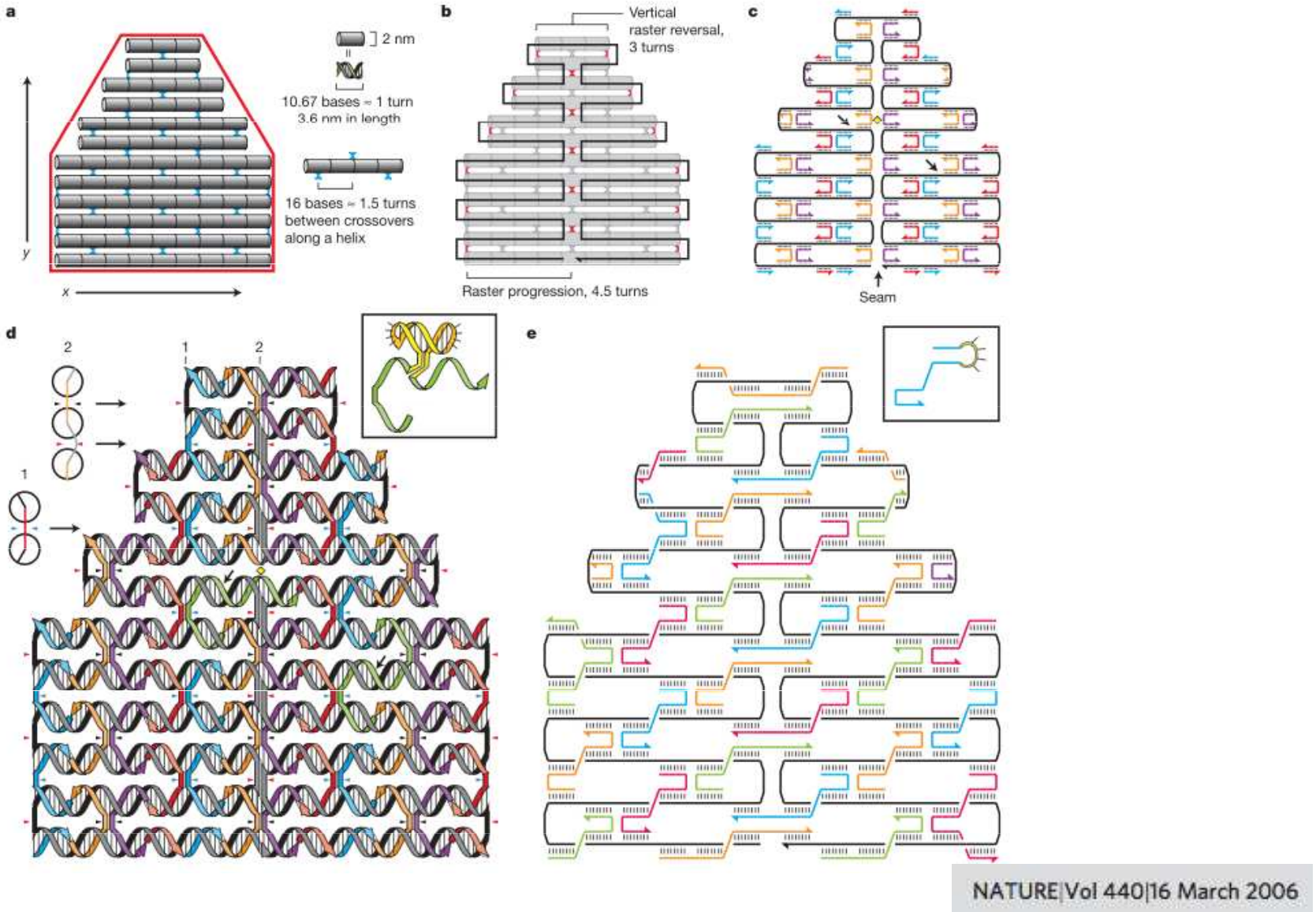

55.7
10.72
54.4
57.4
10.44
56.2
pseudo
cyod

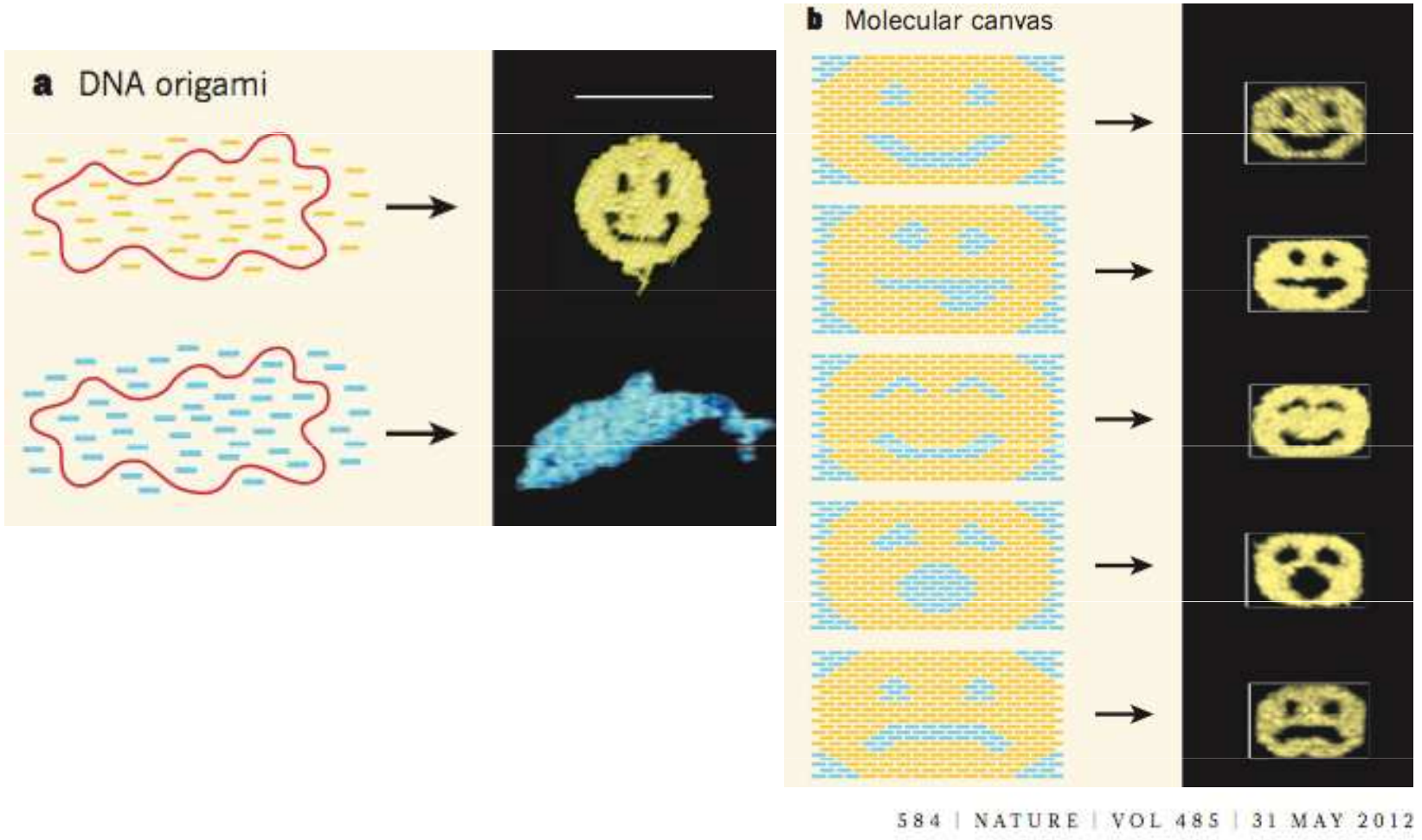

56°
44°
8.645


0.34 nm
minor groove
major groove
2 nm
5' end
bases
3' end
sugar
hydrogen bond
phosphodiester bond
5' end
3' end


vier chemische Buchstaben
Adenin (A)
Thymin (T)
Cytosin (C)
Guanin (G)
Nukleosid
Nukleotid
chemisches "Papier"
Desoxyribose (Zucker)
Phosphat
2,0 nm
0,34 nm Buchstaben-abstand
3,4 nm Ganghöhe


2 nanometers
1 turn = 10 base pairs = 3.4 nanometers
minor groove
major groove


a
2 nm
10.67 bases ≈ 1 turn
3.6 nm in length
16 bases ≈ 1.5 turns
between crossovers
along a helix
y
x
b
Vertical
raster reversal,
3 turns
Raster progression, 4.5 turns
c
Seam
d
2
1
2
1
e
NATURE|Vol 440|16 March 2006



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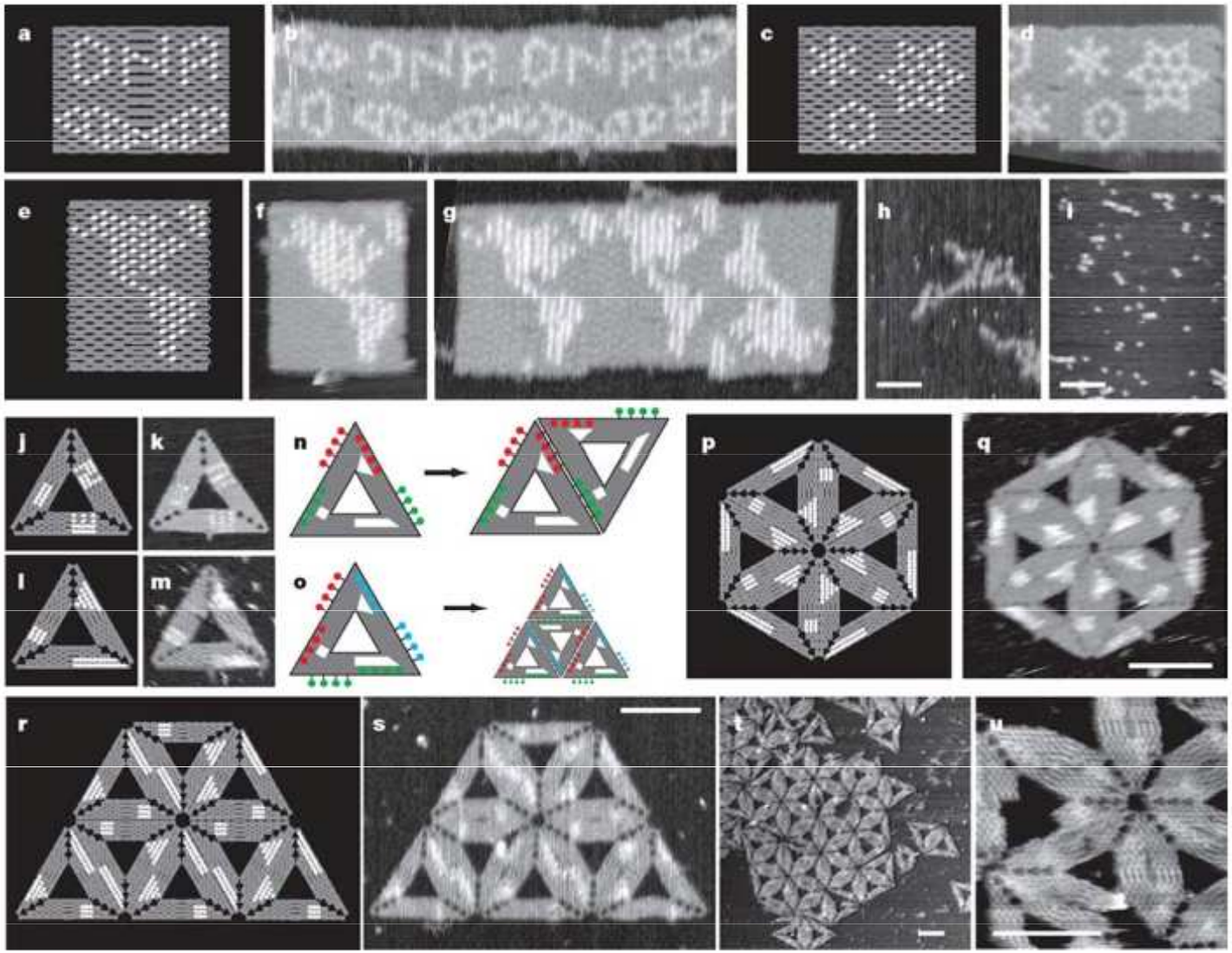
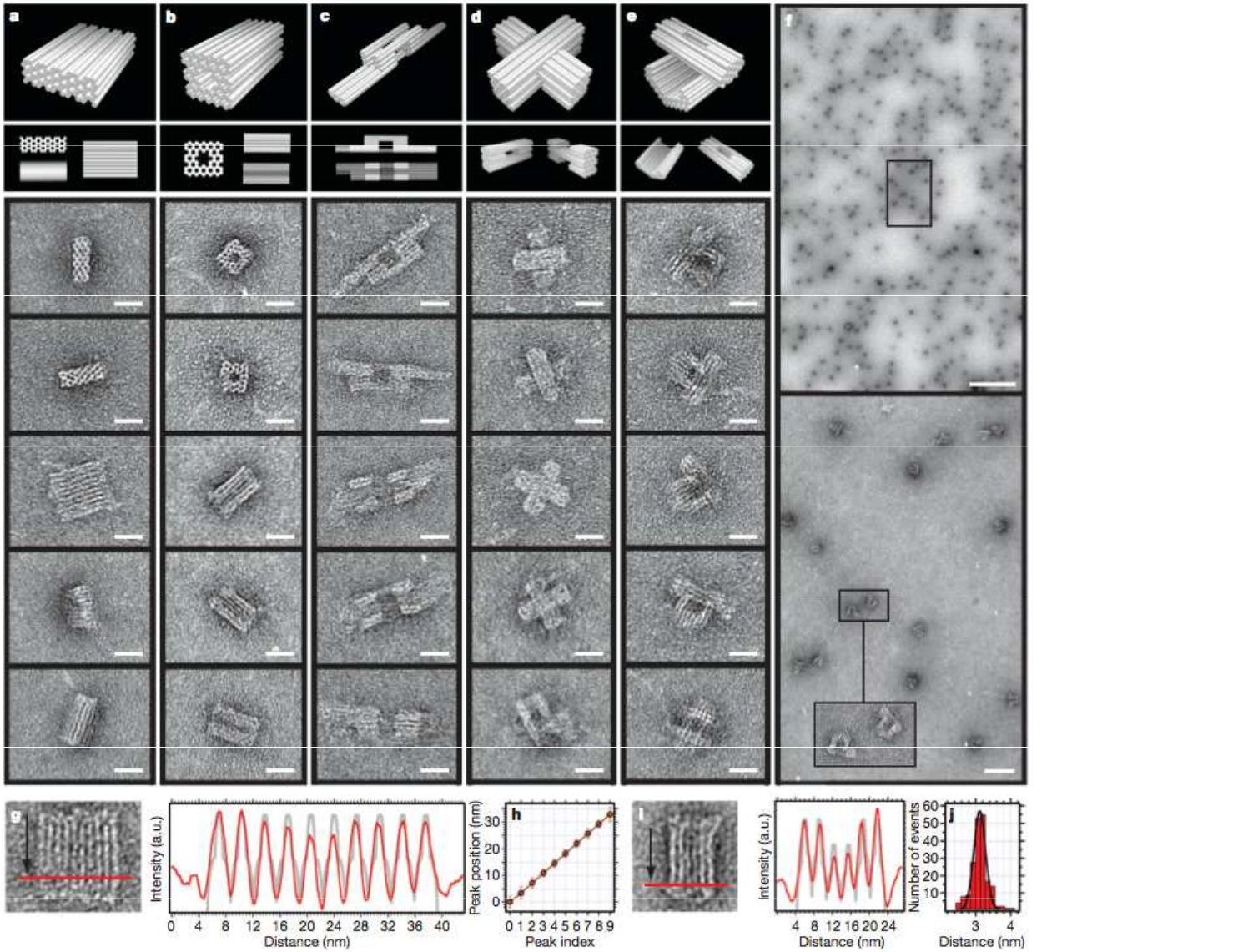
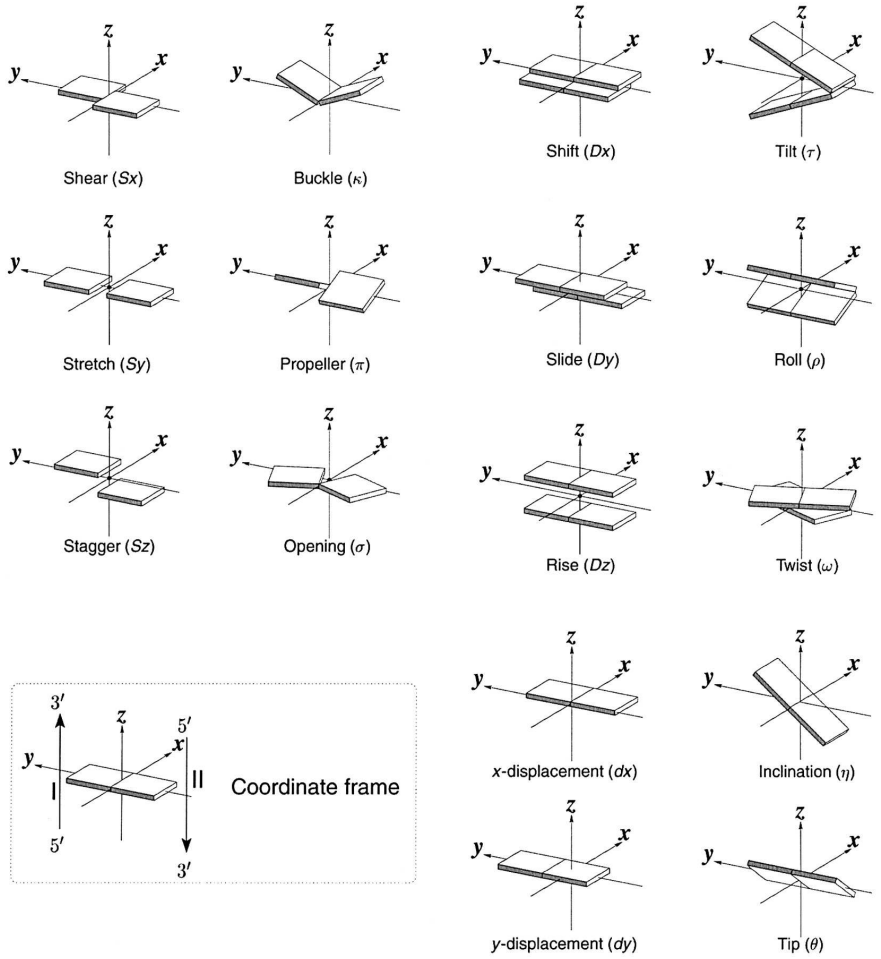


NATURE|Vol 440|16 March 2006



Vol 459 | 21 May 2009 | doi:10.1038/nature08016

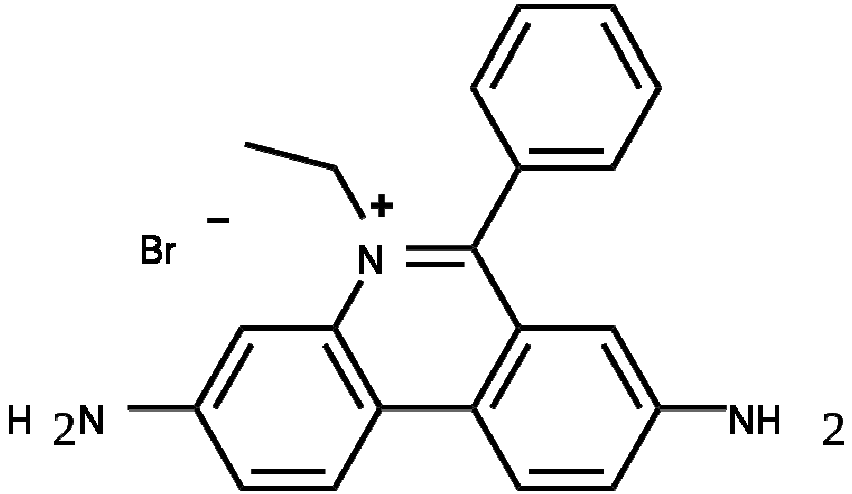
Geometrie páru bazí



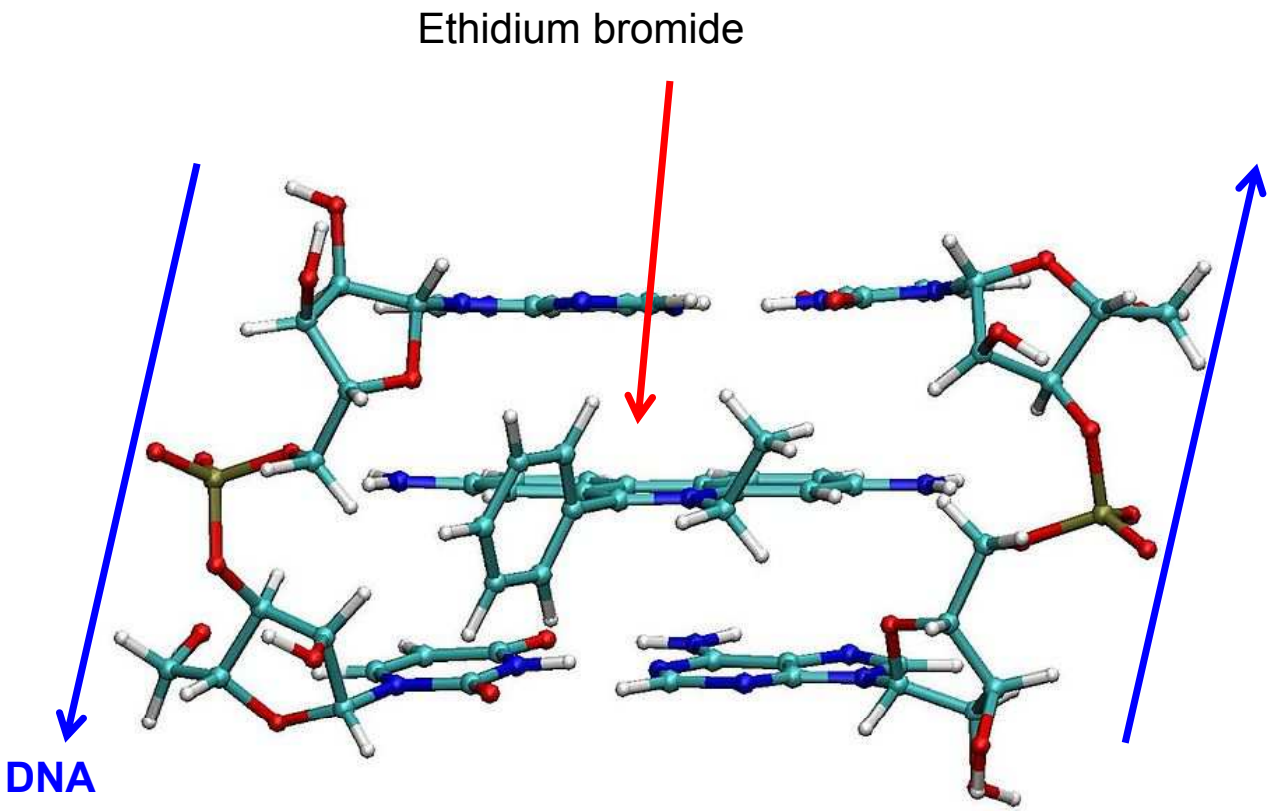
http://nar.oxfordjournals.org/content/31/17/5108/F1.large.jpg

Interkalace – vmezeření

1) Planární molekuly (nejčastěji organické polycyklické aromatické kruhy) mohou interagovat s molekulami nukleových kyselin interkalací, tzn. vmezeřením se mezi dvě po sobě jdoucí báze n. páry bazí
2) Důsledkem je změna strukturních parametrů dvoušroubovice => narušení např. replikace DNA
3) Chemoterapie, značení nukleových kyseliny (ethidium bromid) atp.

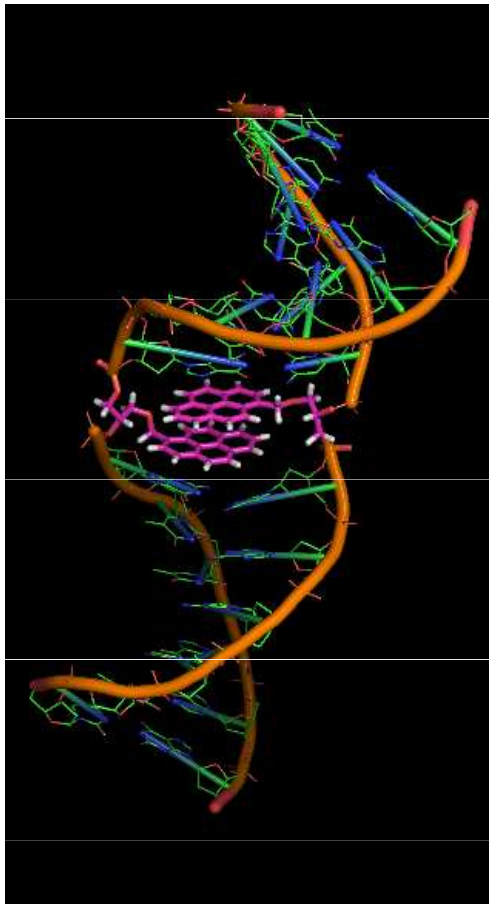


Ethidium bromide
!!! Mutagenní !!!

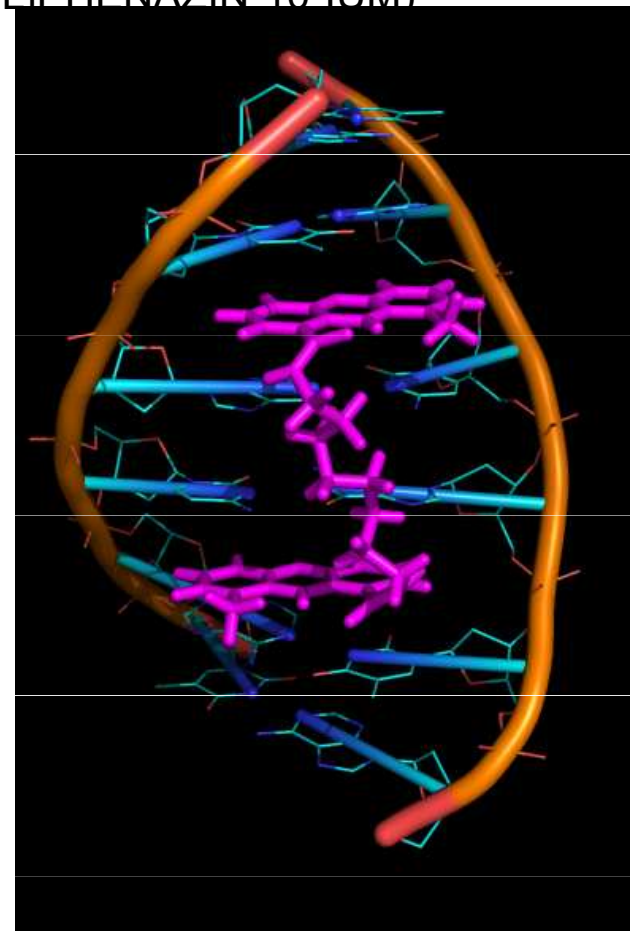

Ethidium bromide
DNA

Decamer DNA šroubovice interkalovaný dvěma

2-HYDROXY-3-(PYREN-1-YLMETHOXY)PROPYL DIHYDROGEN fosfátovými bázemi (PDB ID: 1S88)

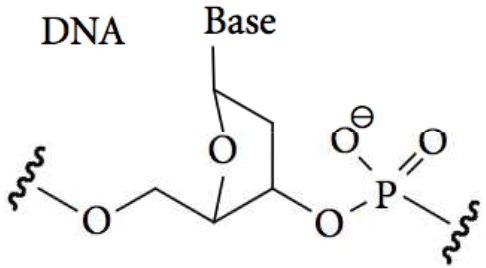


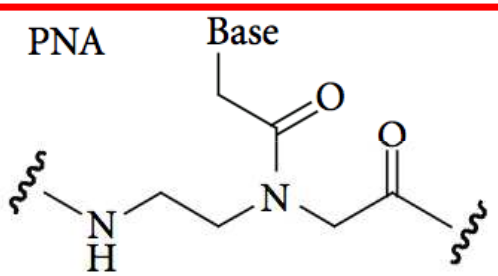
Hexamer DNA šroubovice interkalovaný bispphenazinem – protinádorovým léčivem (1-METHYL-9-[12-(9-METHYLPHENAZIN-10-IUM-1-YL)-12-OXO-2,11-DIAZA-5,8-DIAZONIADODEC-1-ANOYL]PHENAZIN-10-IUM)
PDB ID: 1X95

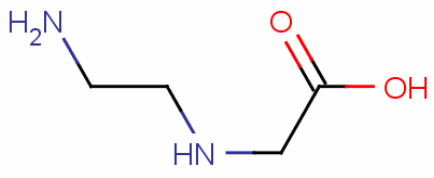


Peptidová nukleové kyseliny (PNA)

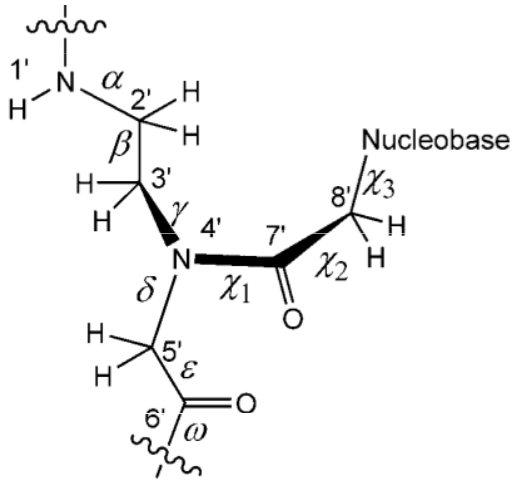
- Nejsou kyselinami!!!
- Jsou syntetické, nicméně se předpoládá(lo), že mohli figurovat jako vývojový stupeň v počátcích vzniku života (naproti tomu stojí “RNA svět”)
- Nemají v páteři negativně nabitý fosfát => silnější vazba mezi bázemi



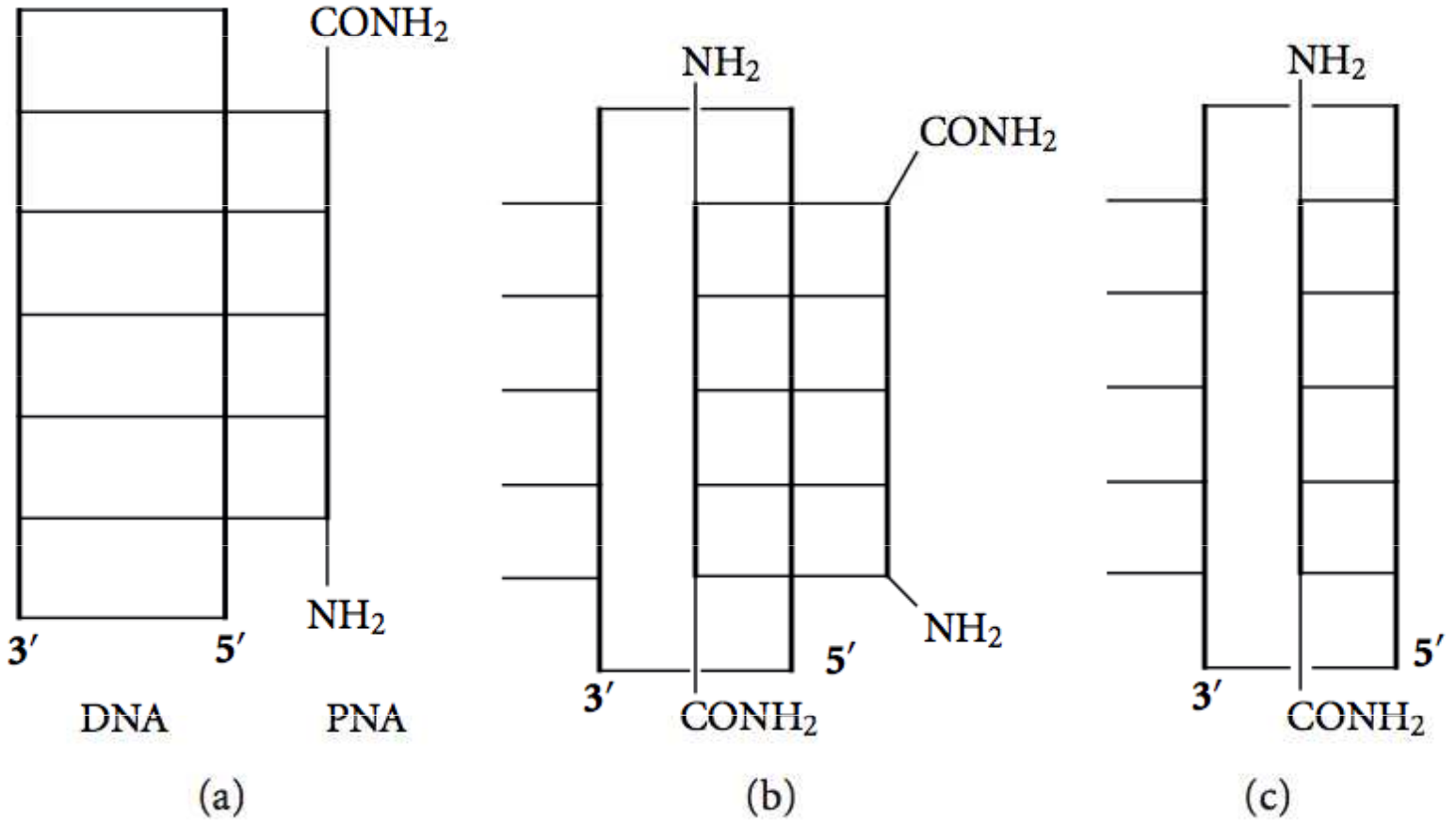




N-aminoethyl glycin



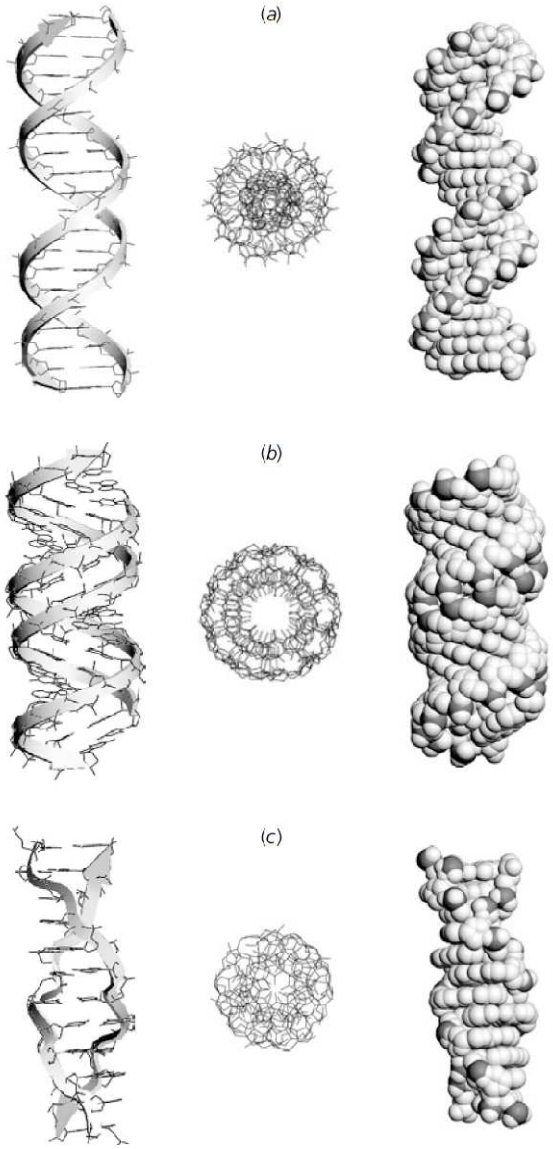
Interakce mezi PNA a DNA dvoušroubovicí



a - triplexová struktura, **b** – triplexová struktura nahrazením jednoho DNA řetězce, **c** – duplexová struktura nahrazením jednoho DNA řetězce

Nejběžnější typy DNA: **B**-DNA (a), **A**-DNA (b), **Z**-DNA (c)

DNA konformace	B	A	Z
Směr vinutí	pravotočivá	pravotočivá	levotočivá
Počet parů bazí na otáčku	10.5	11.0	12.0
Průměr šroubovice	~2.0 nm	~2.6 nm	~1.8 nm
Konformace cukru	C2'-*endo*	C3'-*endo*	C2'-*endo* (pyr) C3'-*endo* (pur)
Velký žlábek *Major groove*	široký, hluboký	úzký, hluboký	plochý
Malý žlábek *Minor groove*	úzký, hluboký	široký, mělký	úzký, hluboký



Definice dihedrálních a torzních úhlů

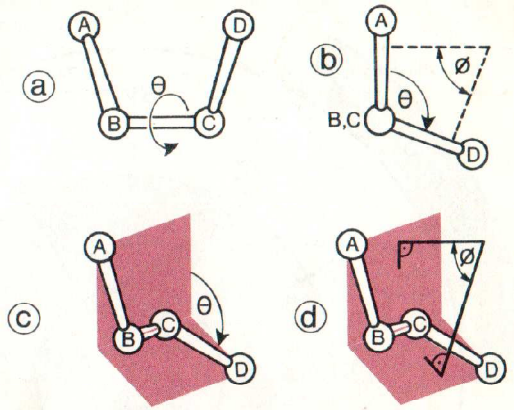


Figure 2-4. Definition of *torsion* and *dihedral angles*. (a) *Torsion angle* θ (A–B–C–D) describing orientations of bonds A–B and C–D with respect to the central bond B–C. (b) View along B→C. θ is the torsion angle between the projected bonds A–B and C–D; the complement ϕ is called the *dihedral angle*. If A–B and C–D are *cis*-planar (coinciding in projection), angles θ and ϕ are 0°; they are counted positive if the far bond C–D rotates clockwise with respect to the near bond A–B. (c) θ is defined as the angle between planes A–B–C and B–C–D. (d) The *dihedral angle* ϕ represents the angle between normals to these planes.

Table 2-2. Definition of Torsion Angles in Nucleotides [From (16).][a]

Torsion angle	Atoms involved
α	${}_{(n-1)}O_{3'}-P-O_{5'}-C_{5'}$
β	$P-O_{5'}-C_{5'}-C_{4'}$
γ	$O_{5'}-C_{5'}-C_{4'}-C_{3'}$
δ	$C_{5'}-C_{4'}-C_{3'}-O_{3'}$
ϵ	$C_{4'}-C_{3'}-O_{3'}-P$
ζ	$C_{3'}-O_{3'}-P-O_{5'(n+1)}$
χ	$O_{4'}-C_{1'}-N_1-C_2$ (pyrimidines) $O_{4'}-C_{1'}-N_9-C_4$ (purines)
ν_0	$C_{4'}-O_{4'}-C_{1'}-C_{2'}$
ν_1	$O_{4'}-C_{1'}-C_{2'}-C_{3'}$
ν_2	$C_{1'}-C_{2'}-C_{3'}-C_{4'}$
ν_3	$C_{2'}-C_{3'}-C_{4'}-O_{4'}$
ν_4	$C_{3'}-C_{4'}-O_{4'}-C_{1'}$

[a] Atoms designated $(n-1)$ and $(n+1)$ belong to adjacent units.

Description	*N*	Clustered torsions										Cluster number
		γ	δ	ε	ζ	$\alpha+1$	$\beta+1$	$\gamma+1$	$\delta+1$	χ	$\chi+1$	
'Canonical' A-form, labeled AI	**192**	**54**	**82**	**205**	**285**	**294**	**172**	**55**	**83**	**201**	**202**	**8**
AII, A-form with an $\alpha + 1/\gamma + 1$ switch	44	52	82	195	291	149	194	182	87	204	188	19
A with δ, $\delta + 1$ close to O4′-endo	9	44	101	192	281	297	182	44	99	210	211	25
AI–BI, with δ C3′-, $\delta + 1$ C2′-endo	32	54	86	194	281	301	179	55	142	214	251	41
AI–BI, with δ O4′-, $\delta + 1$ C2′-endo	34	54	99	186	274	297	178	51	141	235	264	47
BI–AI, with $\delta 1$ O4′-endo	100	51	130	183	267	297	171	51	106	250	239	32
BII–AI, with an $\alpha + 1/\gamma + 1$ switch, high $\beta + 1$	9	49	146	257	186	60	224	196	90	260	200	110
BI variation in complexes	412	45	137	178	255	304	187	45	139	252	256	58
'Canonical' B-form, labeled BI	**1,531**	**47**	**136**	**184**	**262**	**302**	**179**	**45**	**138**	**251**	**260**	**54**
BII variation in complexes	269	43	140	201	216	314	156	46	140	261	253	86
BII-form	**340**	**46**	**143**	**245**	**172**	**297**	**142**	**46**	**141**	**269**	**259**	**96**
BI, with an $\alpha + 1/\gamma + 1$ switch	109	46	139	195	245	32	196	296	150	252	253	116
BI, 3′-mismatches with an $\chi + 1$ syn, $\alpha + 1/\gamma + 1$ switch	8	50	137	196	225	33	187	295	145	257	70	122
AI–BI, 3′-mismatches with $\chi + 1$ syn	14	58	91	214	280	295	176	56	139	238	67	121
Z-form, Y–R step	21	54	147	264	76	66	186	179	95	205	61	123
ZI-form, R–Y step	40	177	96	242	292	210	233	54	144	63	205	124
ZII-form, R–Y step	18	179	95	187	63	169	162	44	144	58	213	126

'Description' is a short annotation of the conformation, '*N*' is the number of dinucleotides which define the conformation, 'Clustered Torsions' are the arithmetic means calculated for the torsions used in the clustering process, with the torsions being defined in Figure 1. Bold font is used merely to indicate the three most important DNA forms.

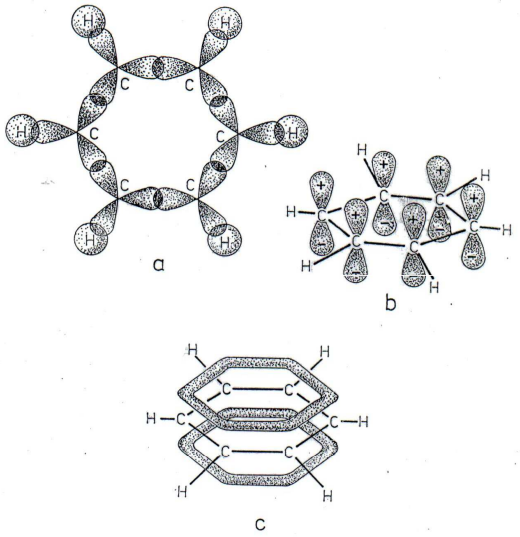
Nucleic Acids Research, 2008, Vol. 36, No. 11, 3690–3706

Stabilita DNA dvojšroubovice:

1) Vodíkové můstky
2) Londonovy disperzní síly (LDF), dipól-dipólové interakce

Nukleopár	Vodíkové vazby	LDF	Celková E
A:T	-26	+1.0	-25.0
G:C	-40	-16.3	-56.3

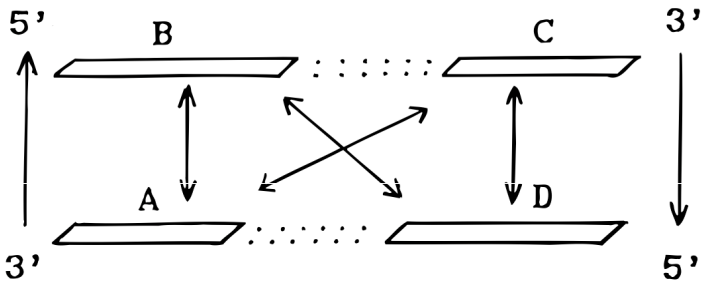
Energie v kJ/mol



A:T – opačné dipóly, G:C – působí atraktivně

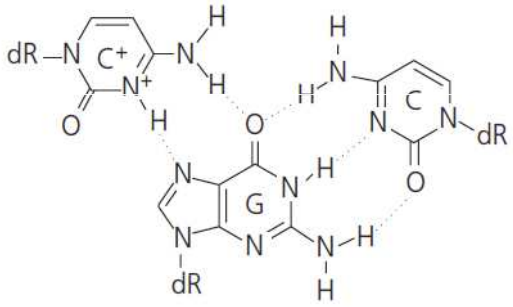
3) Patrové interakce – stacking

Působí mezi jednotlivými patry nukleopárů, stabi-lizují dvojšoubovici díky ***elektronovým korelacím, van der Waals***ovým a ***Coulomb***ickým ***interakcím***

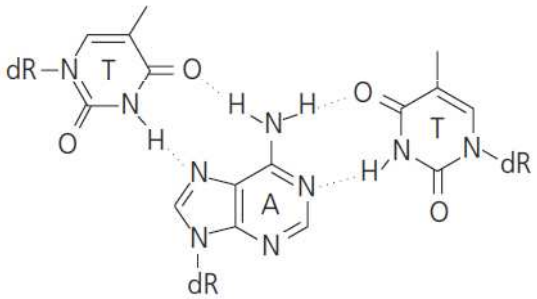


Non-Watson-Crickovské (Hoogsteenovo – Karsten Hoogsteen) párování bazí

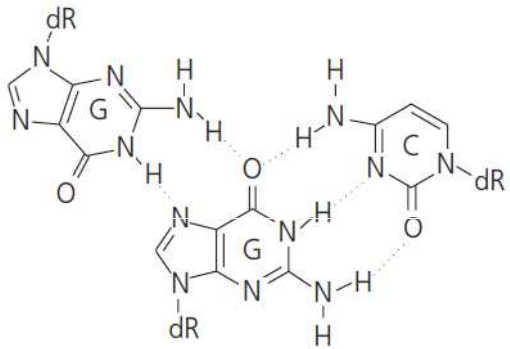
Triplexové struktury



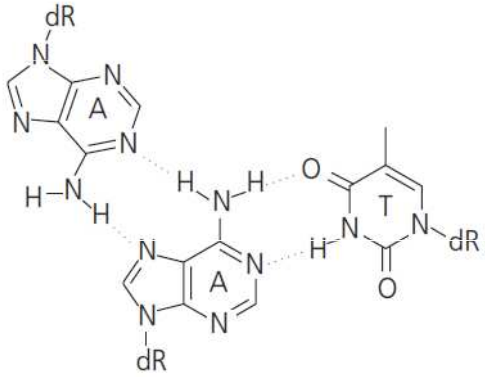
C+·GC



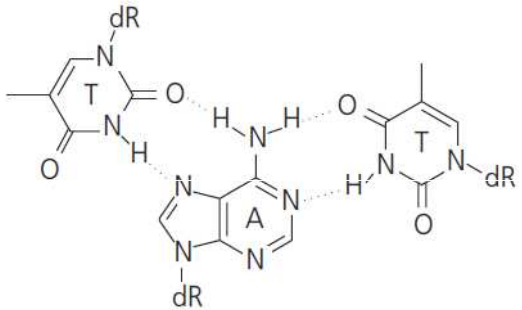
T·AT



G·GC

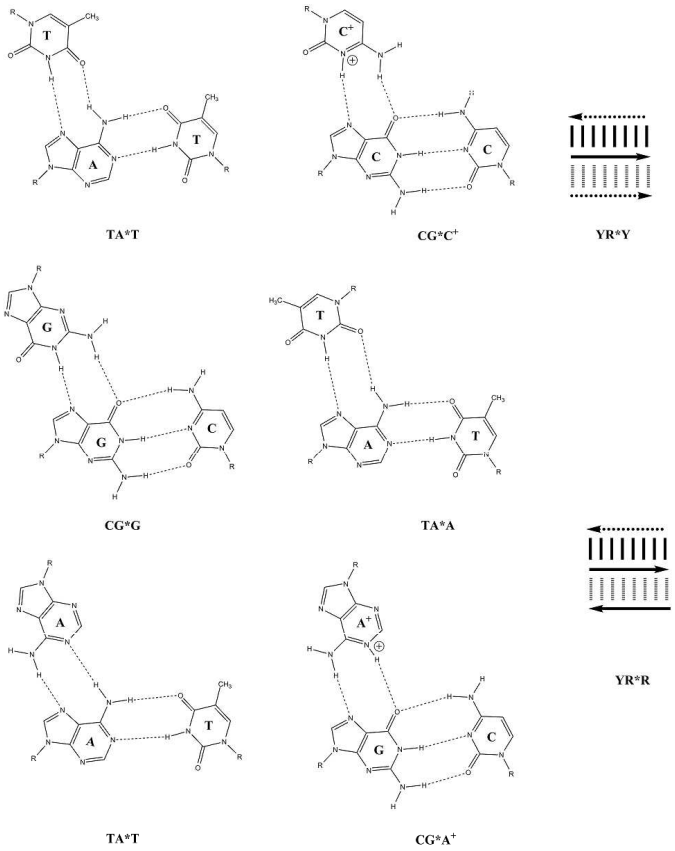


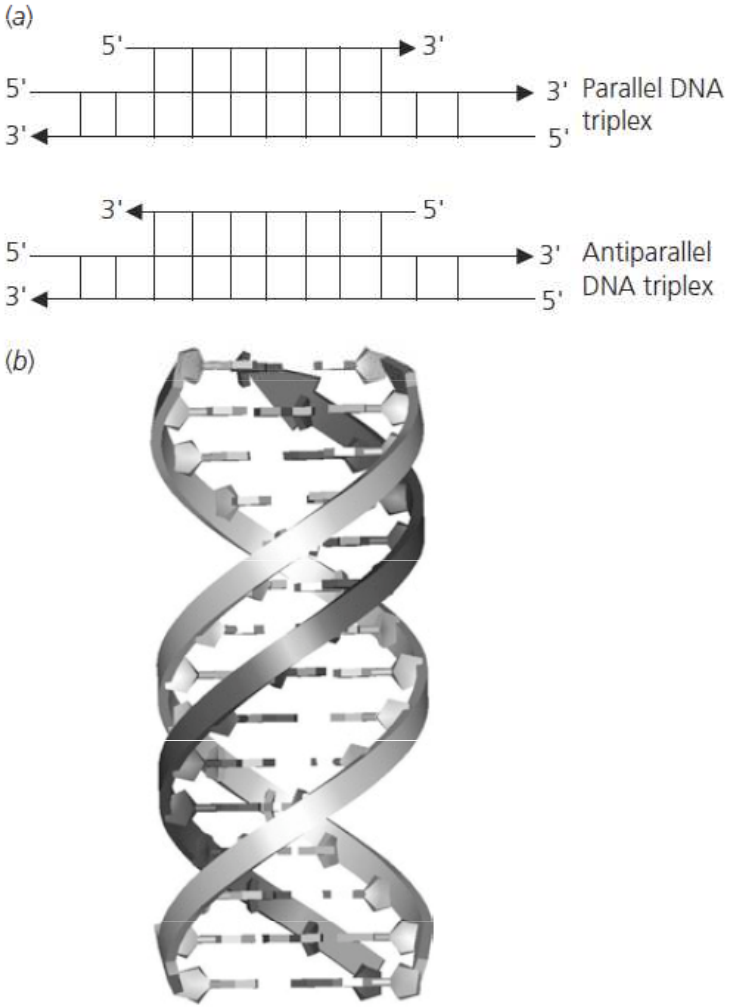
A·AT



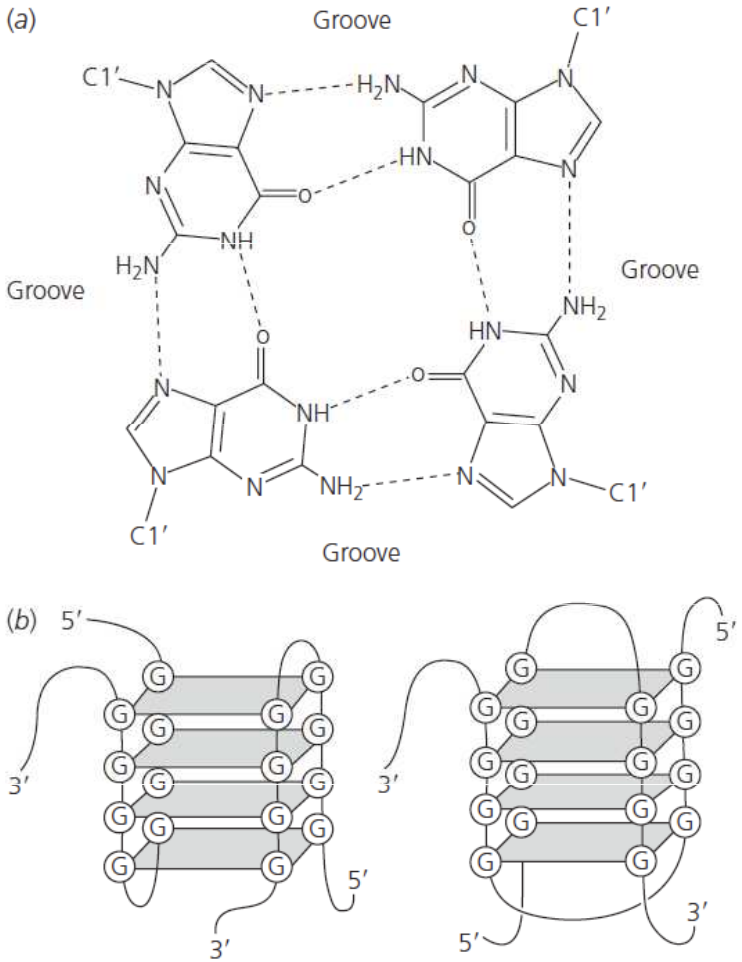
T·AT

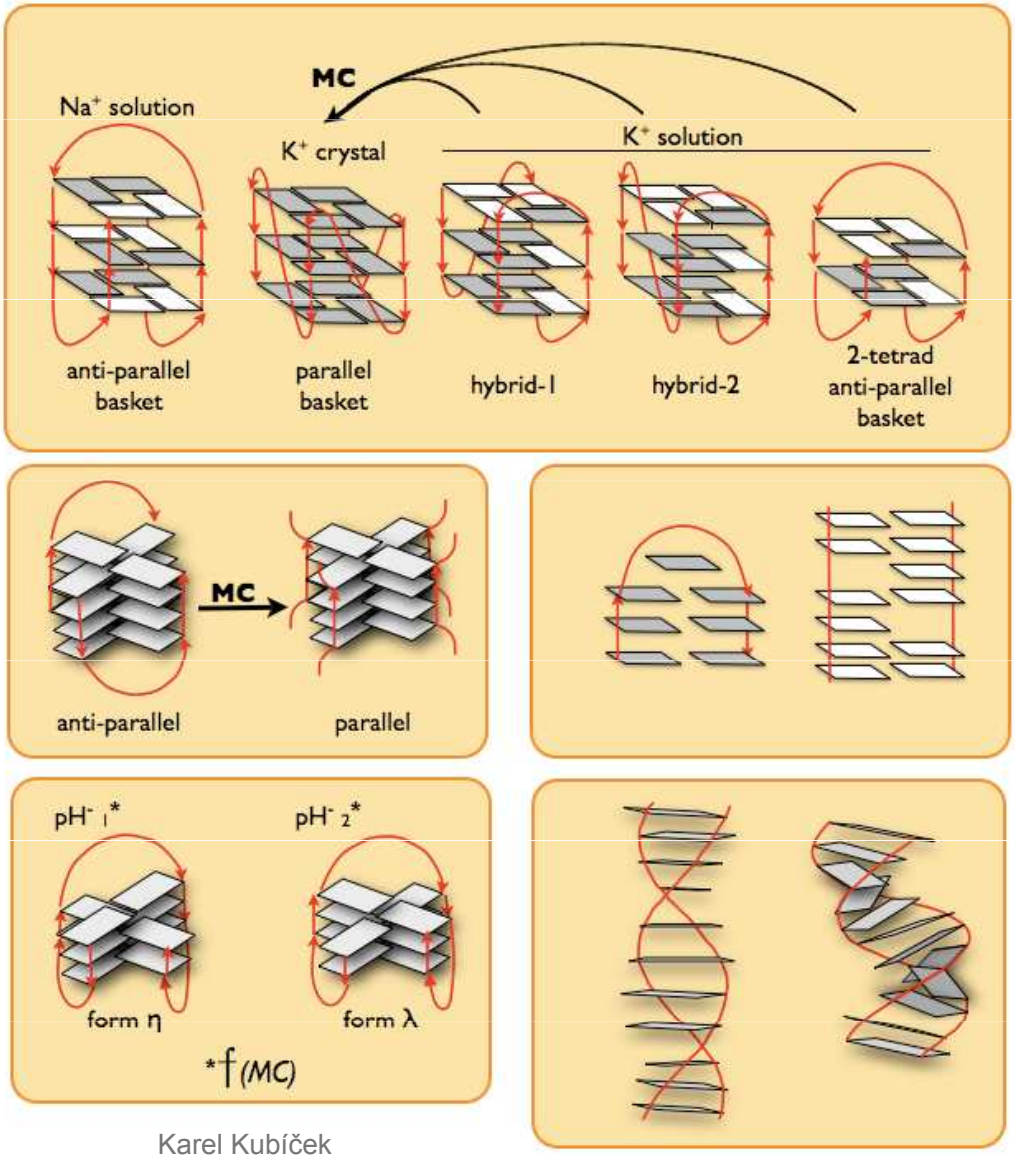
Triplexové struktury





Quadruplexové struktury



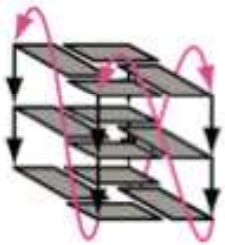

MC
Na+ solution
K+ crystal
K+ solution
anti-parallel basket
parallel basket
hybrid-1
hybrid-2
2-tetrad anti-parallel basket
MC
anti-parallel
parallel
pH- 1*
pH- 2*
form η
form λ
*f (MC)

Polymorfie telomerických opakování *in vitro*

NMR

NMR X-ray ---------- **Sekvenčně závislé**

Na^+ K^+ K^+ K^+ K^+ K^+/PEG



parallel propeller

Wang et al. Structure (1993)

Parkinson et al. Nature (2002)

Ambrus et al. Nucleic Acids Res. (2006)

Dai et al. Nucleic Acids Res. (2007)

Lim et al. J Am Chem Soc. (2009)

Heddi et al. J Am Chem Soc. (2011)

Polymorfie telomerických opakování *in vivo*

In-cell NMR

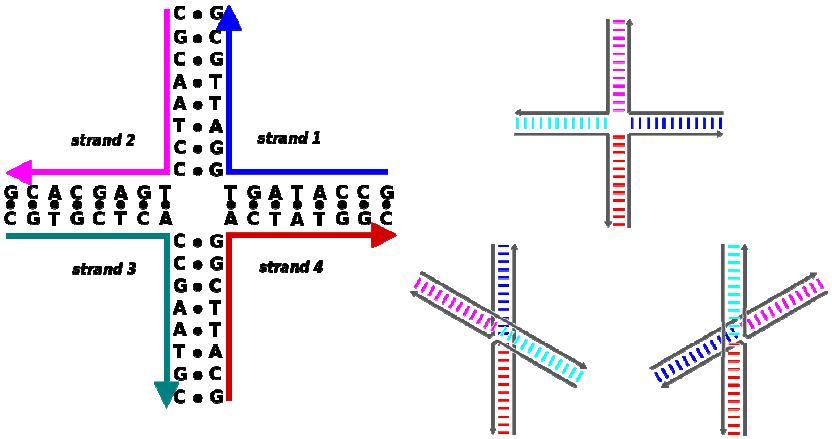
Sekvenčně závislé

? X

Hansel et al. Nucl Acids Res (2011)

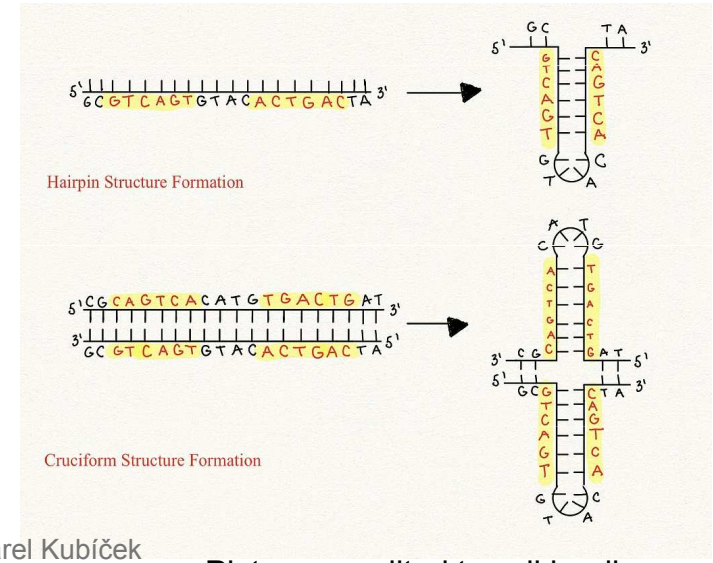
Další významné formy DNA:

1) Hollidayův spoj (**Holliday** junction) klíčový meziprodukt v mnoha typech genetické rekombinace a také při opravě dvouřetězcových zlomů.



2) displacement loop (**D-loop,** D-smyčka)
3) **R-loop** (**R**-smyčka)

4) Křížová struktura DNA (**cruciform**)



5) **i-motif DNA**

6) DNA nanotechnologie – DNA origami

Pictures credited to: wikipedia.org

Další významné formy DNA:

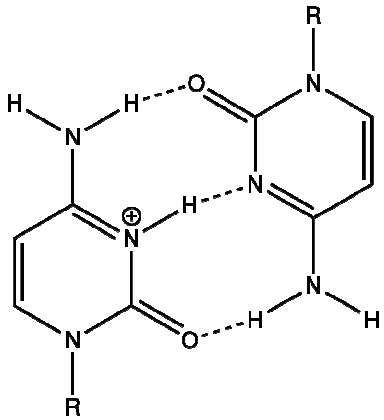
1) Hollidayův spoj (**Holliday** junction) klíčový meziprodukt v mnoha typech genetické rekombinace a také při opravě dvouřetězcových zlomů.

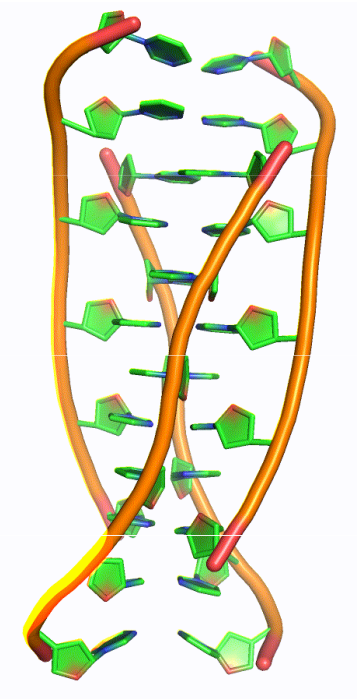
2) displacement loop (**D-loop,** D-smyčka)
3) **R-loop** (**R**-smyčka)

4) Křížová struktura DNA (**cruciform**)

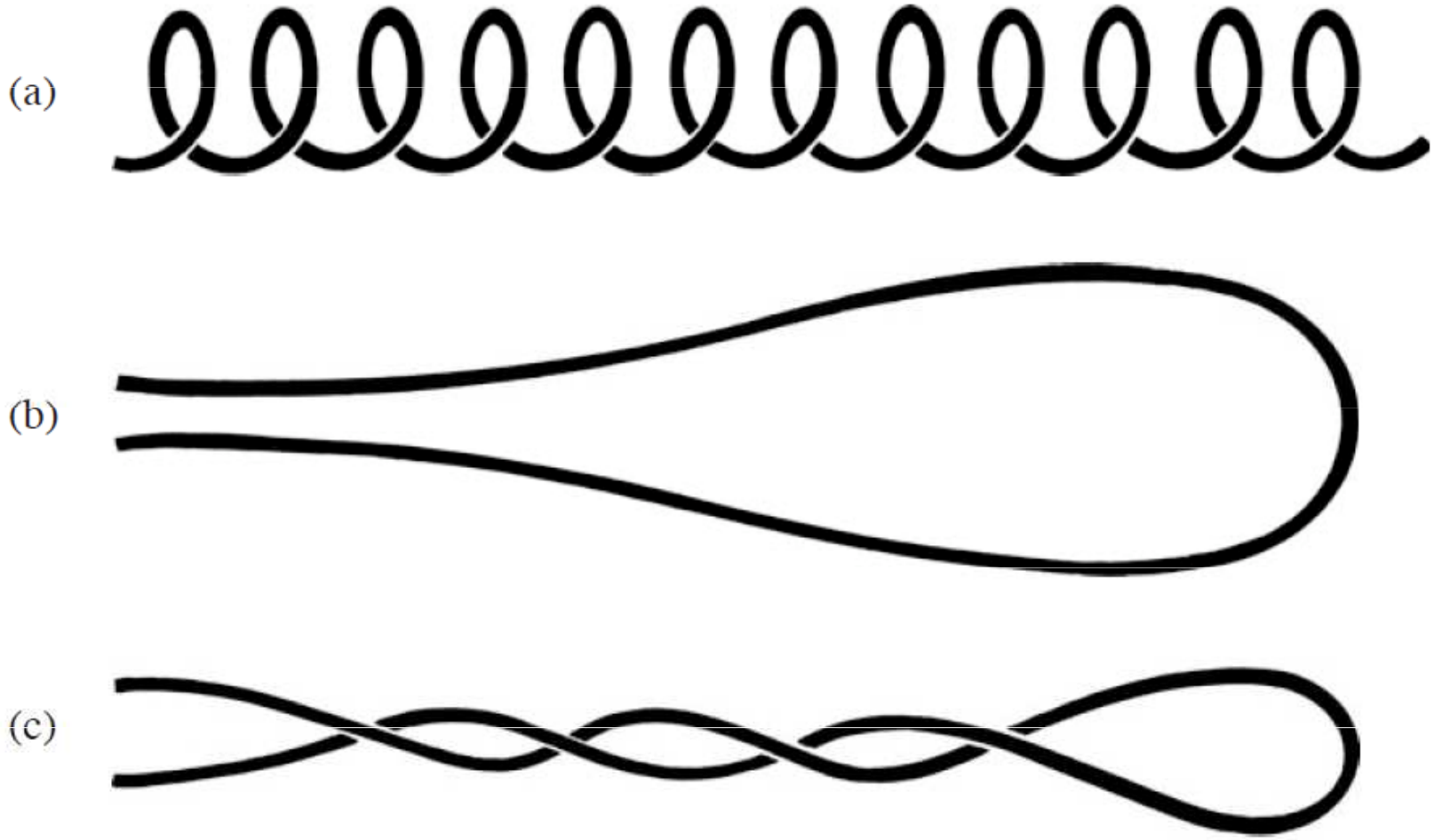
5) i-motif DNA / i-motif RNA

6) DNA nanotechnologie – DNA origami





Pictures credited to: wikipedia.org


(a)
(b)
(c)

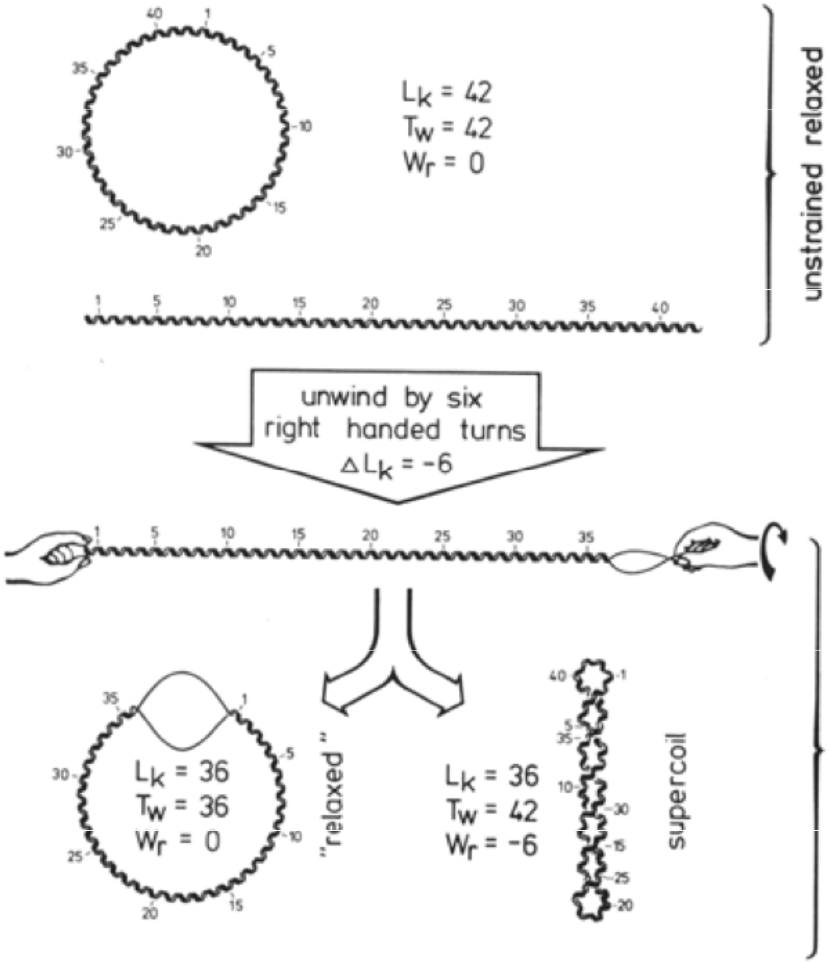
Superhelikální cirkulární DNA

$$L_k = W_r + T_w$$

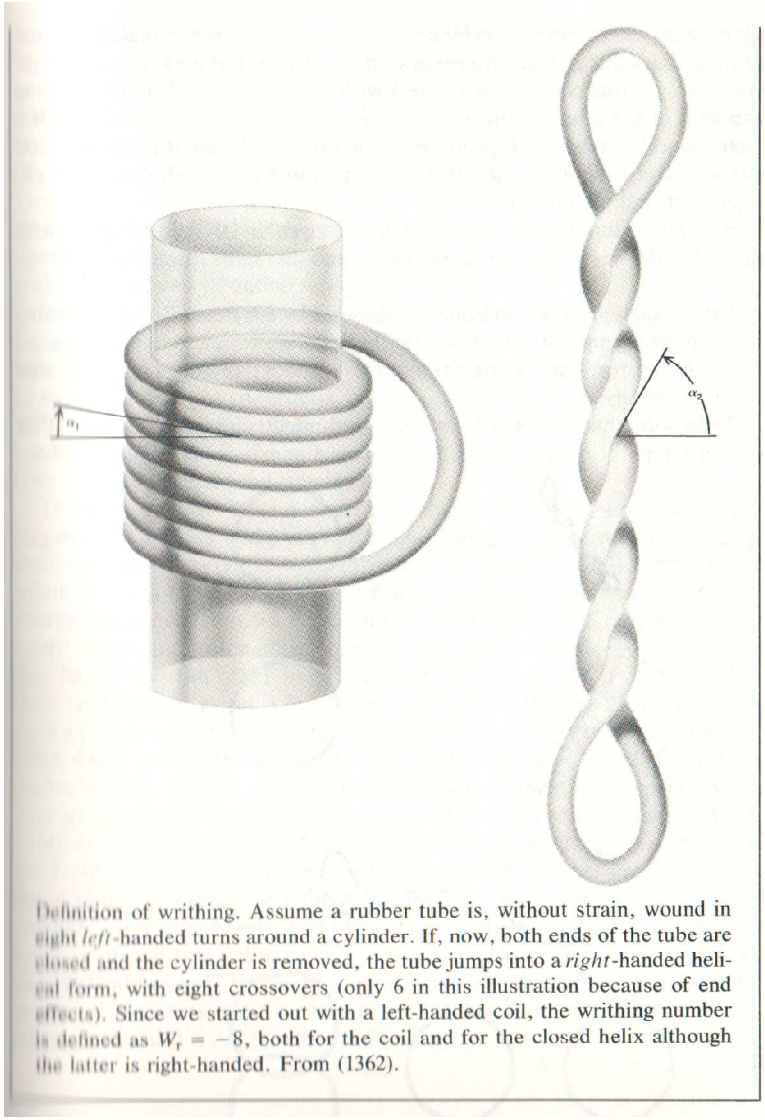
Lk - *linking* () – topologická vlastnost cirkulární DNA, udává, kolikrát je jeden řetězec DNA obtočen kolem druhého v pravotočivém směru (vzhledem k tomu, že referenční je B-DNA). **L**k zůstává pro danou cirkulární DNA konstantní (neboť "konce" jsou zafixované a nemůže docházet k rozvinutí). **L**k nabývá vždy celočíselných hodnot (konce DNA dvoušroubovice na sebe musí "pasovat", aby došlo k uzavření kruhu).

Tw - *twisting* (otočení) – v relaxovaném stavu se Tw=**L**k. **T**w udává počet 360° otoček, které jsou na dvojšroubovici podél celé kružnice. Vzhledem k tomu, že pro B-DNA připadá cca 10 párů bazí na jednu otočku, **T**w je přibližně rovno počtu párů bazí / 10. Pro pravotočivé otáčky je **T**w kladné.

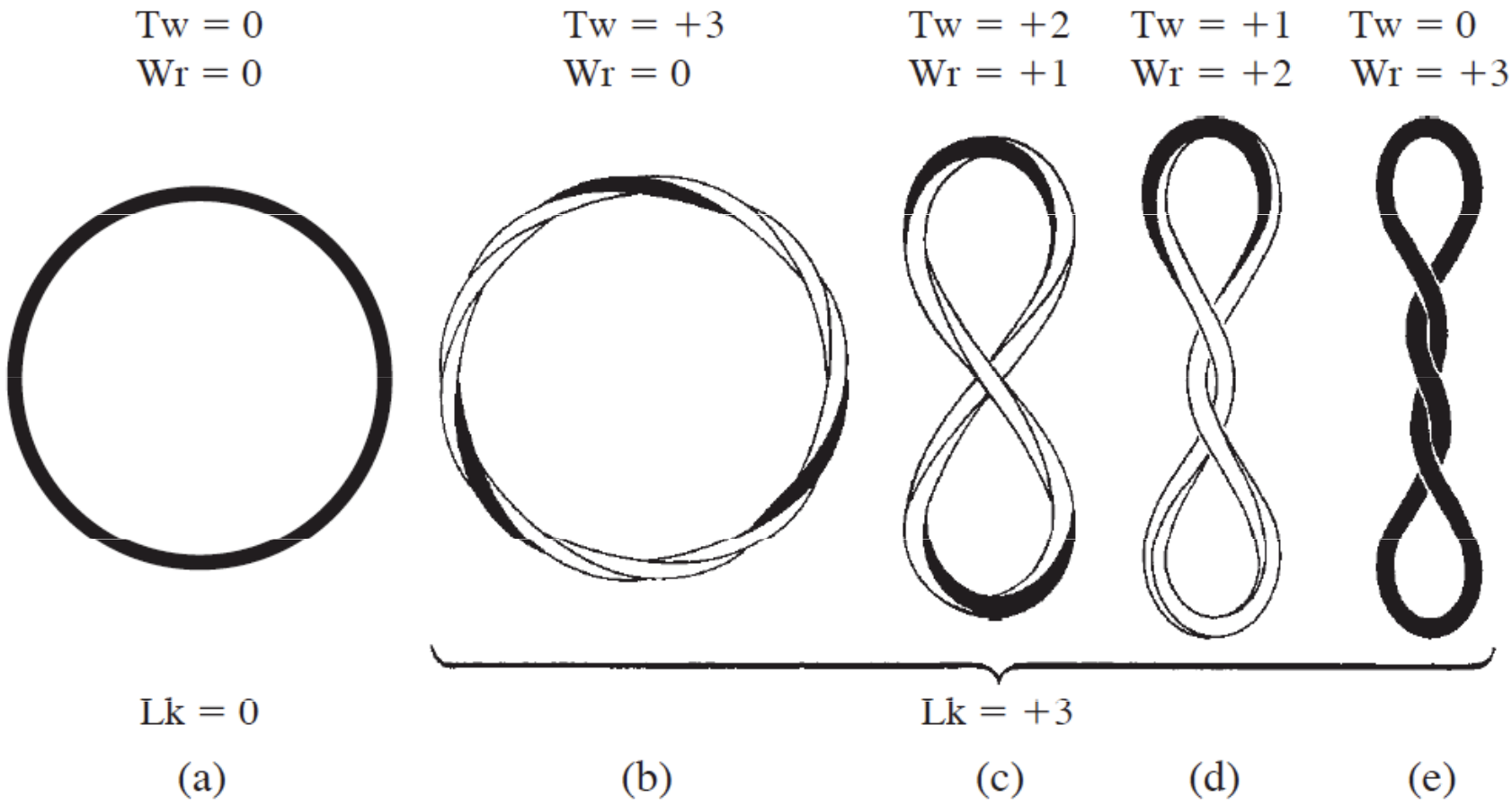
Wr - *writhing* (skřížení) – z důvodu strukturních "potřeb" DNA různé hodnoty **L**k kružnice mohou způsobit nikoliv změnu v otáčkách (**T**w), ale vznik superhelixu (superšroubovice). Vznik superhelixu je definován číslem **W**r. Pro pravotočivé superšroubovice je **W**r záporné!!!

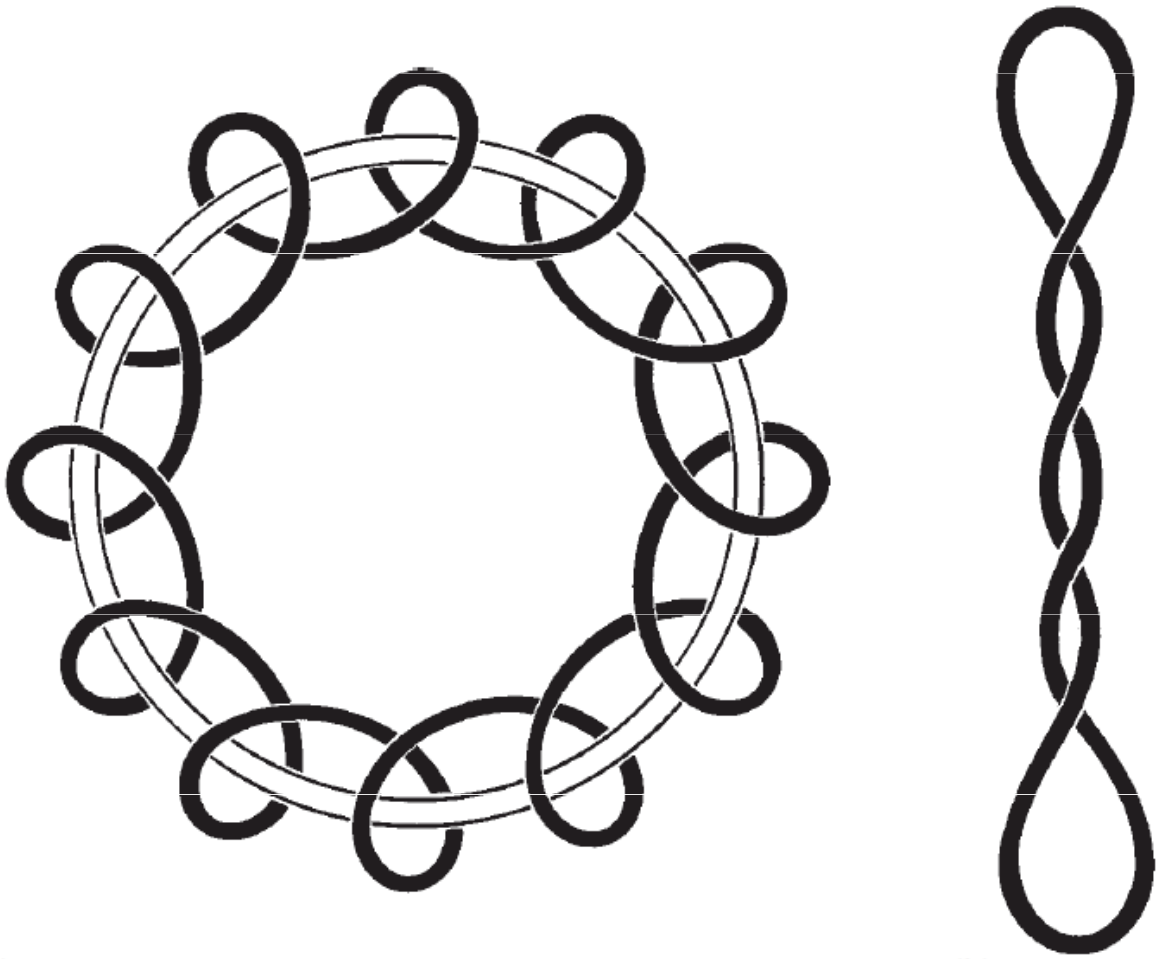


Vzhledem k tomu, že má DNA tendenci udržet B-DNA topologii, Tw se zvýší zpět na 42. Lk je ovšem topologické číslo, které **MUSÍ** zůstat konstantní, tedy 36 a k zachování rovnice *Lk=Wr+Tw* Wr musí nabýt hodnoty **Wr=-6**.



Definition of writhing. Assume a rubber tube is, without strain, wound in eight *left*-handed turns around a cylinder. If, now, both ends of the tube are closed and the cylinder is removed, the tube jumps into a *right*-handed helical form, with eight crossovers (only 6 in this illustration because of end effects). Since we started out with a left-handed coil, the writhing number is defined as $W_r = -8$, both for the coil and for the closed helix although the latter is right-handed. From (1362).

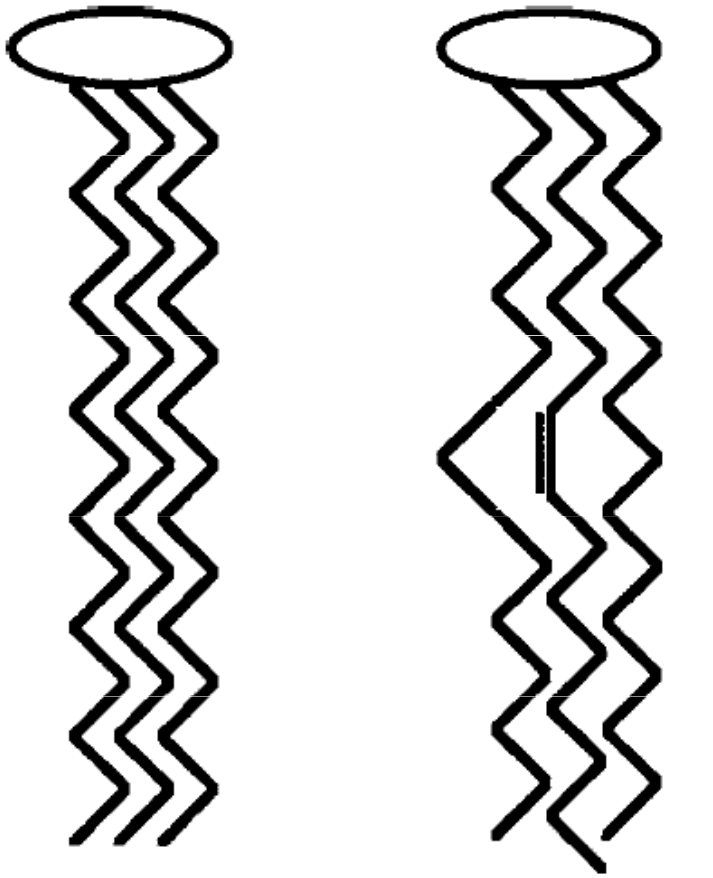

Tw = 0
Wr = 0
Tw = +3
Wr = 0
Tw = +2
Wr = +1
Tw = +1
Wr = +2
Tw = 0
Wr = +3
Lk = 0
Lk = +3
(a)
(b)
(c)
(d)
(e)



Lipidy

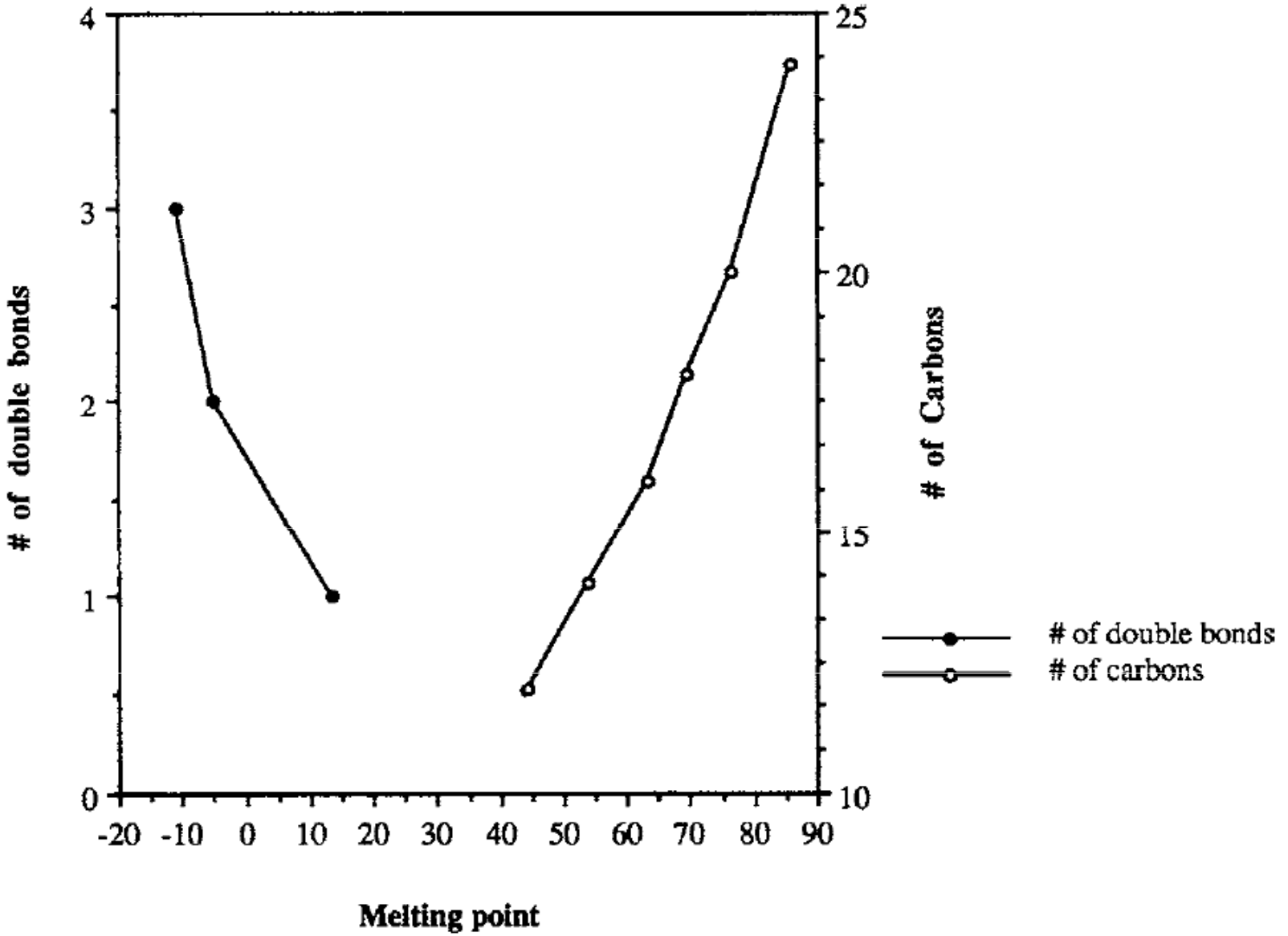
Lipidy
-**Hydrofobní** (nerozpustné ve vodě; obsahující pouze nepolární skupinu) nebo **amfifilní** (obsahují jak polární, tak nepolární skupinu)
-Zásobarny metabolické energie

Mastné kyseliny
-Dlouhý, nepolární $-CH_2-$ konec
-Polární karboxylová skupina
-**Nasycené** (stearová, plamitová, arašídová)
-**Nenasycené** - **mono**- (jedna dvojitá vazba; olejová)/**poly**-(více dvojitých vazeb) nenasycené



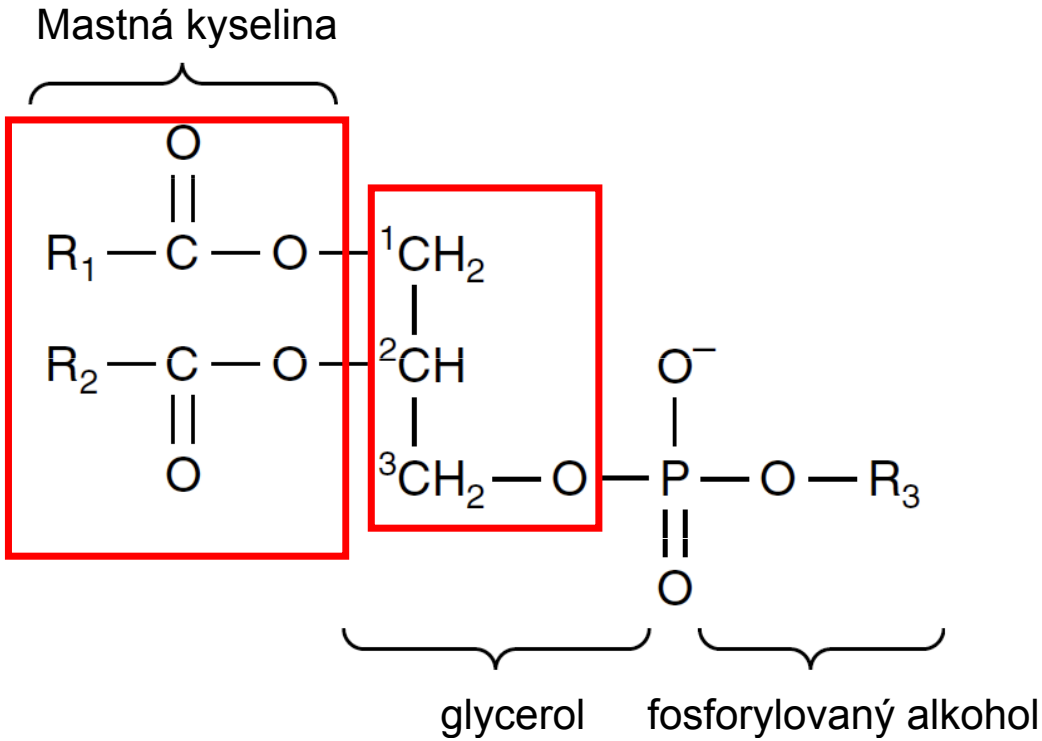
Saturated fatty acids

Unsaturated fatty acids

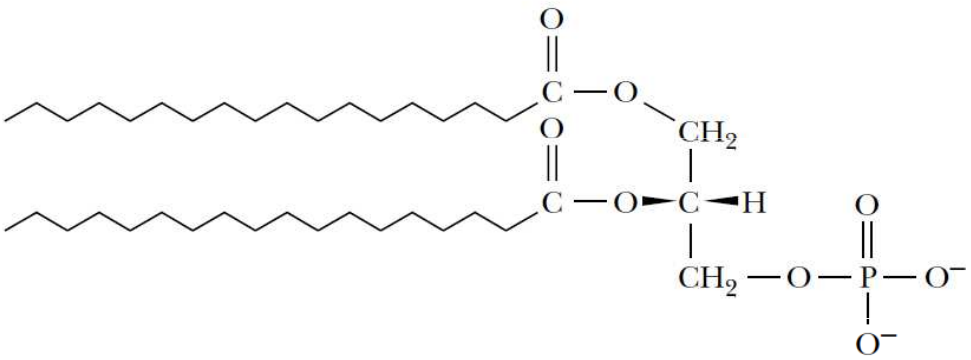

4
3
2
1
0
25
20
15
10
-20 -10 0 10 20 30 40 50 60 70 80 90
# of double bonds
# of Carbons
Melting point
# of double bonds
# of carbons

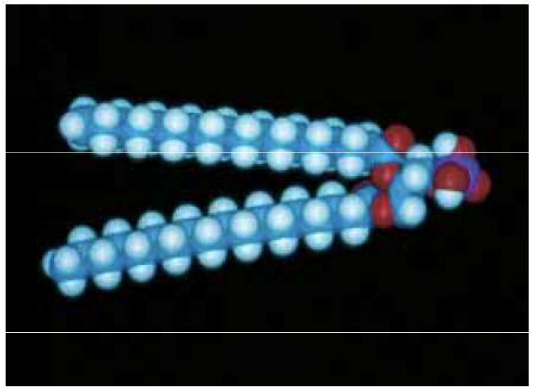
Fosfolipidy

- Esenciální prvek biologických membrán

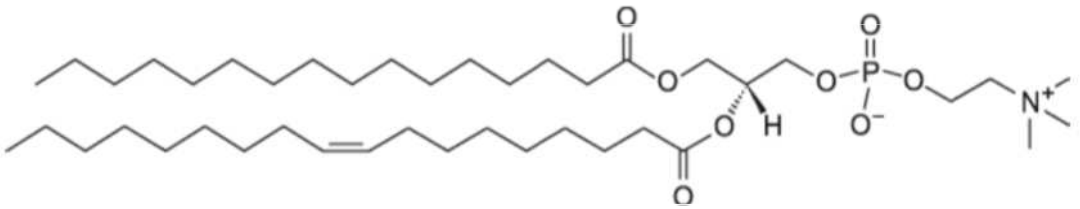


Kyselina fosfatidová –základní sloučenina fosfolipidů

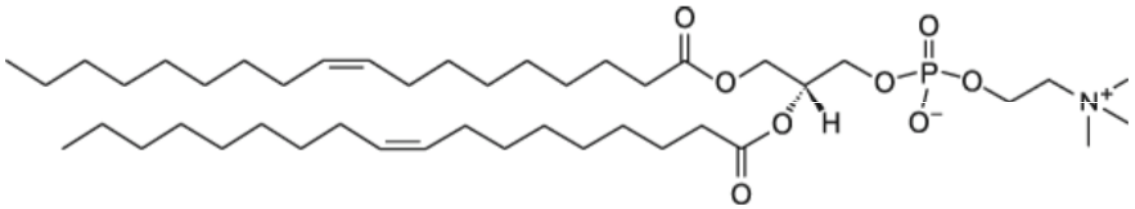




Zkratky

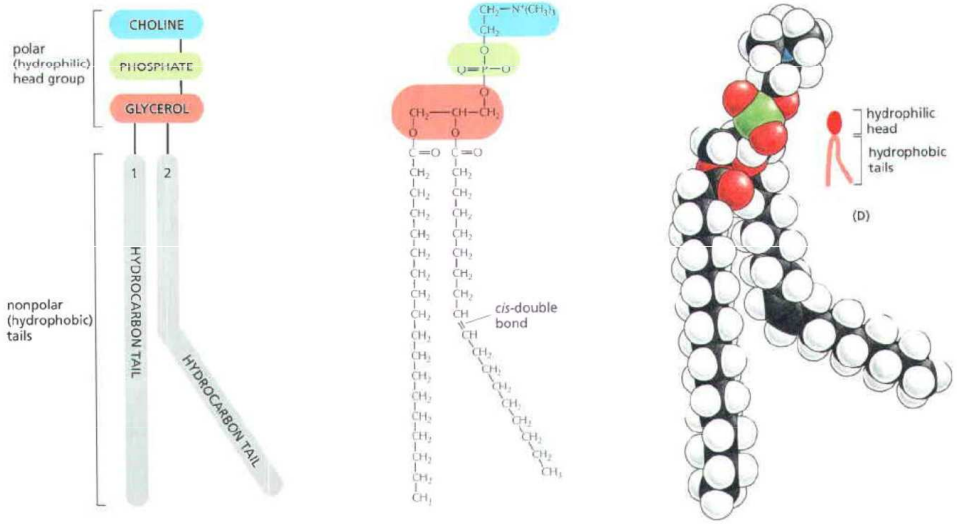


POPC 1-palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine

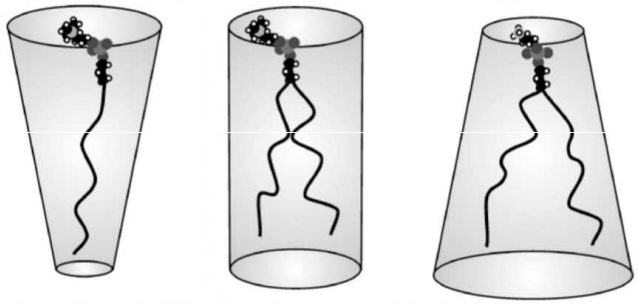


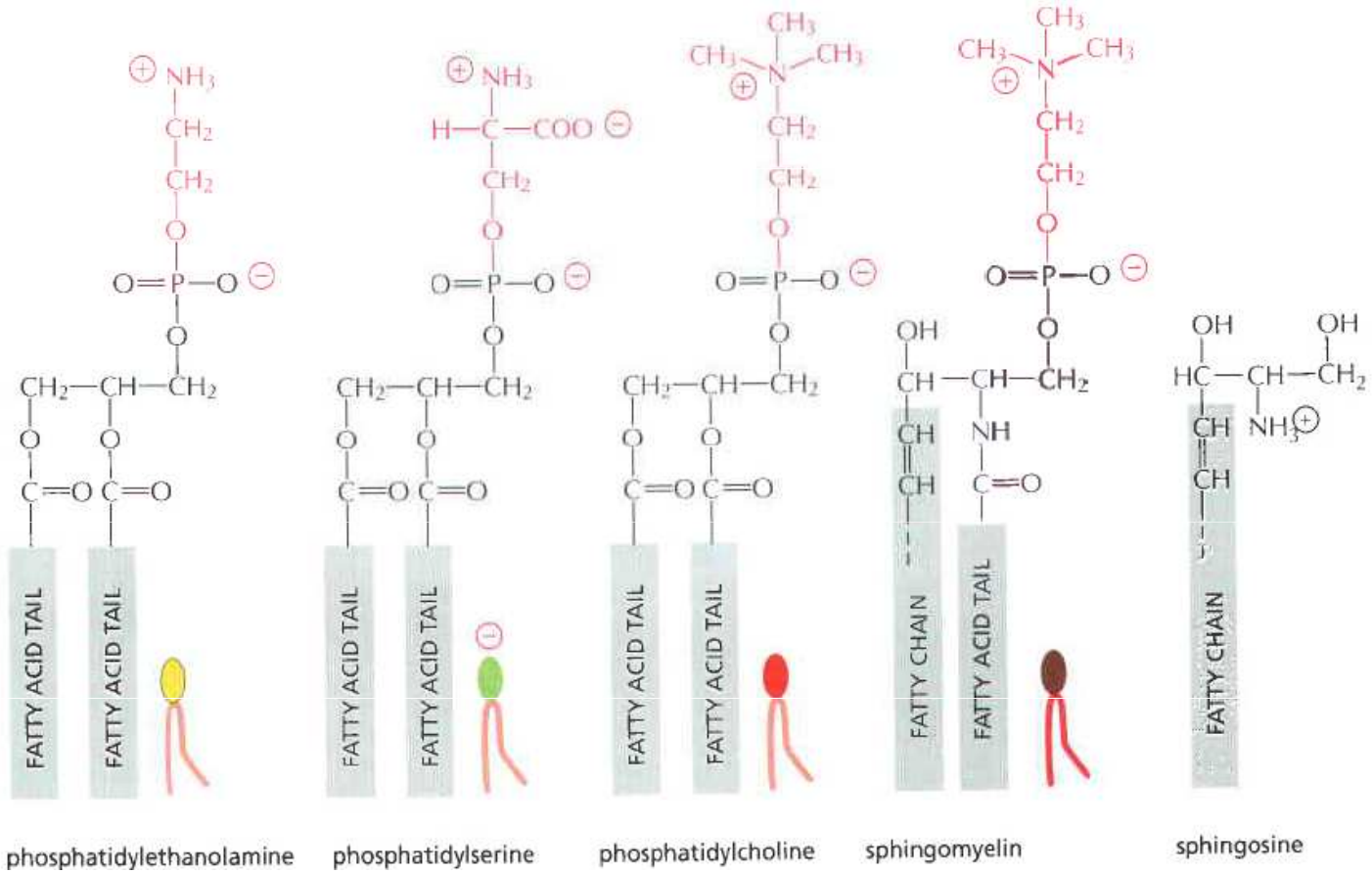
DOPC 1,2-dioleoyl-sn-glycero-3-phosphocholine

Fosfolipidy

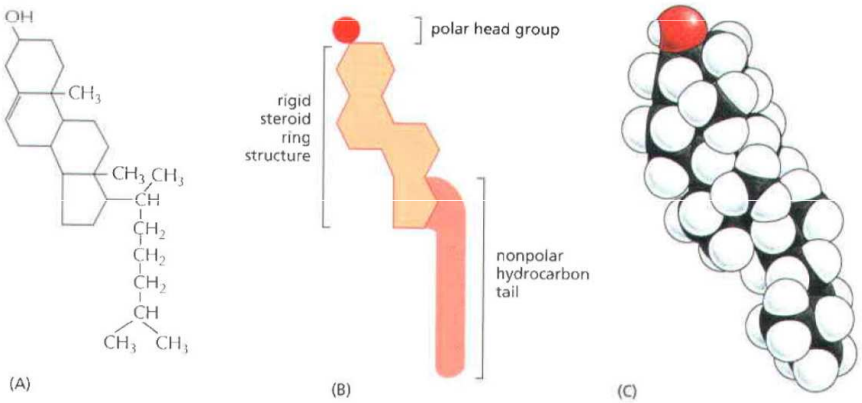


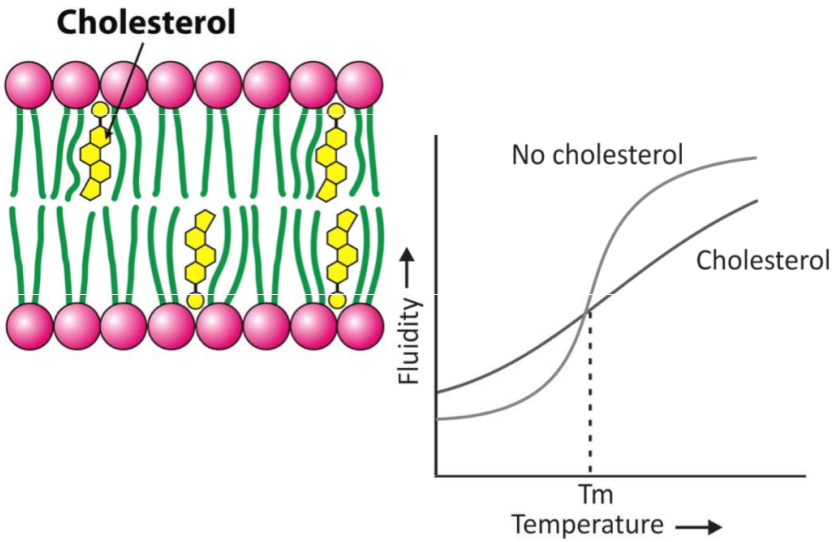
Tvar lipidů

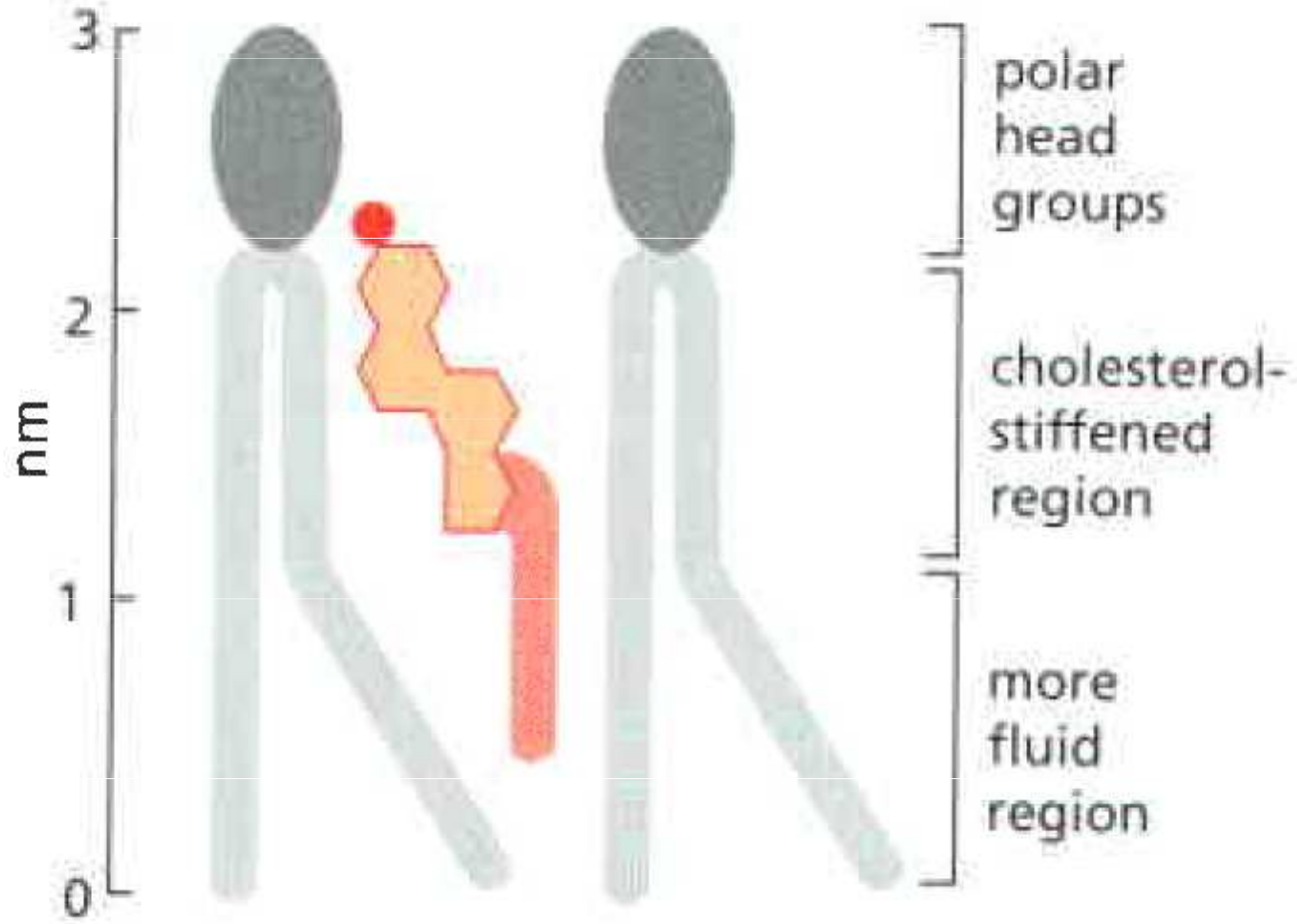



FATTY ACID TAIL
FATTY ACID TAIL
FATTY ACID TAIL
FATTY ACID TAIL
FATTY ACID TAIL
FATTY ACID TAIL
FATTY CHAIN
FATTY ACID TAIL
FATTY CHAIN
phosphatidylethanolamine
phosphatidylserine
phosphatidylcholine
sphingomyelin
sphingosine

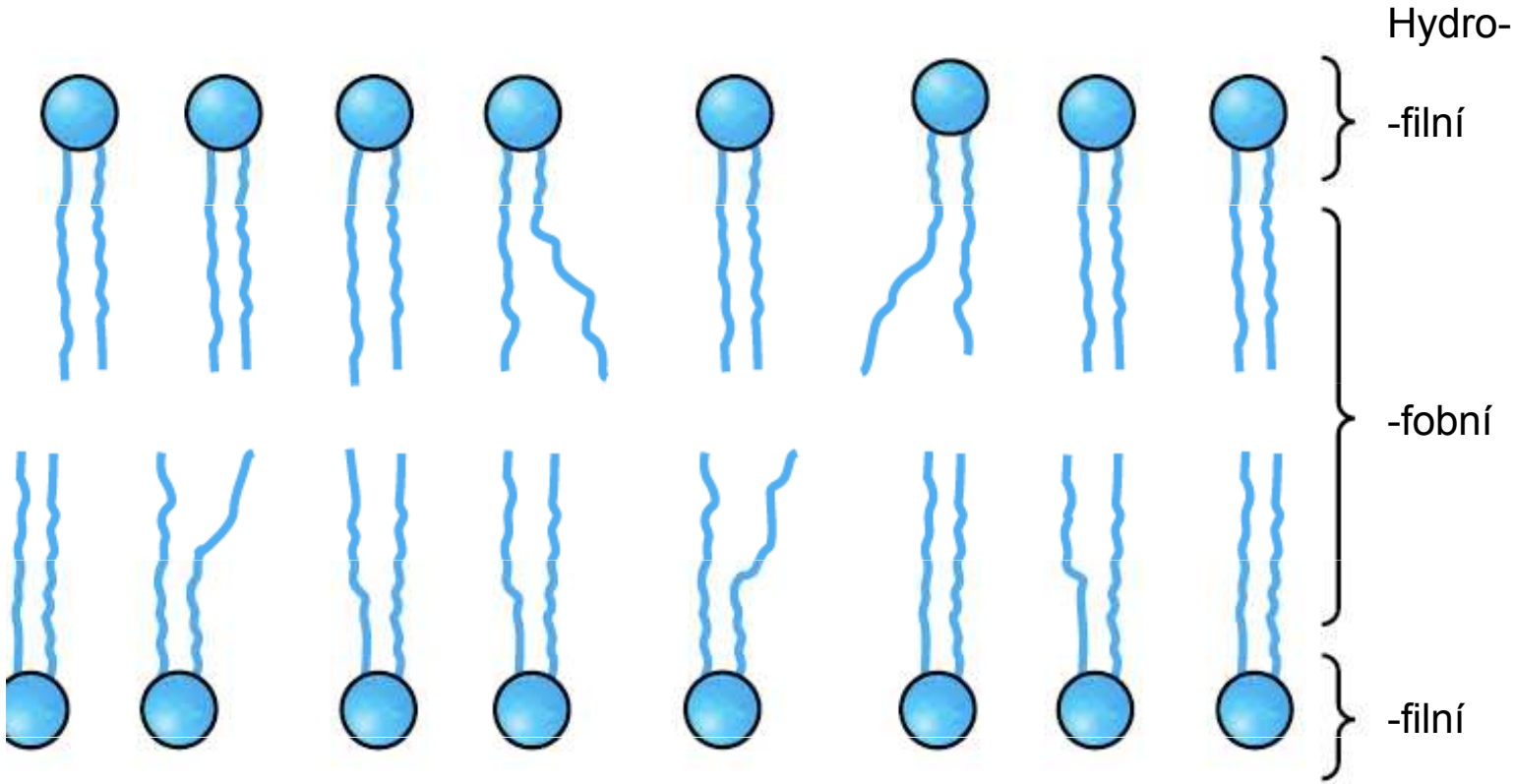
Cholesterol

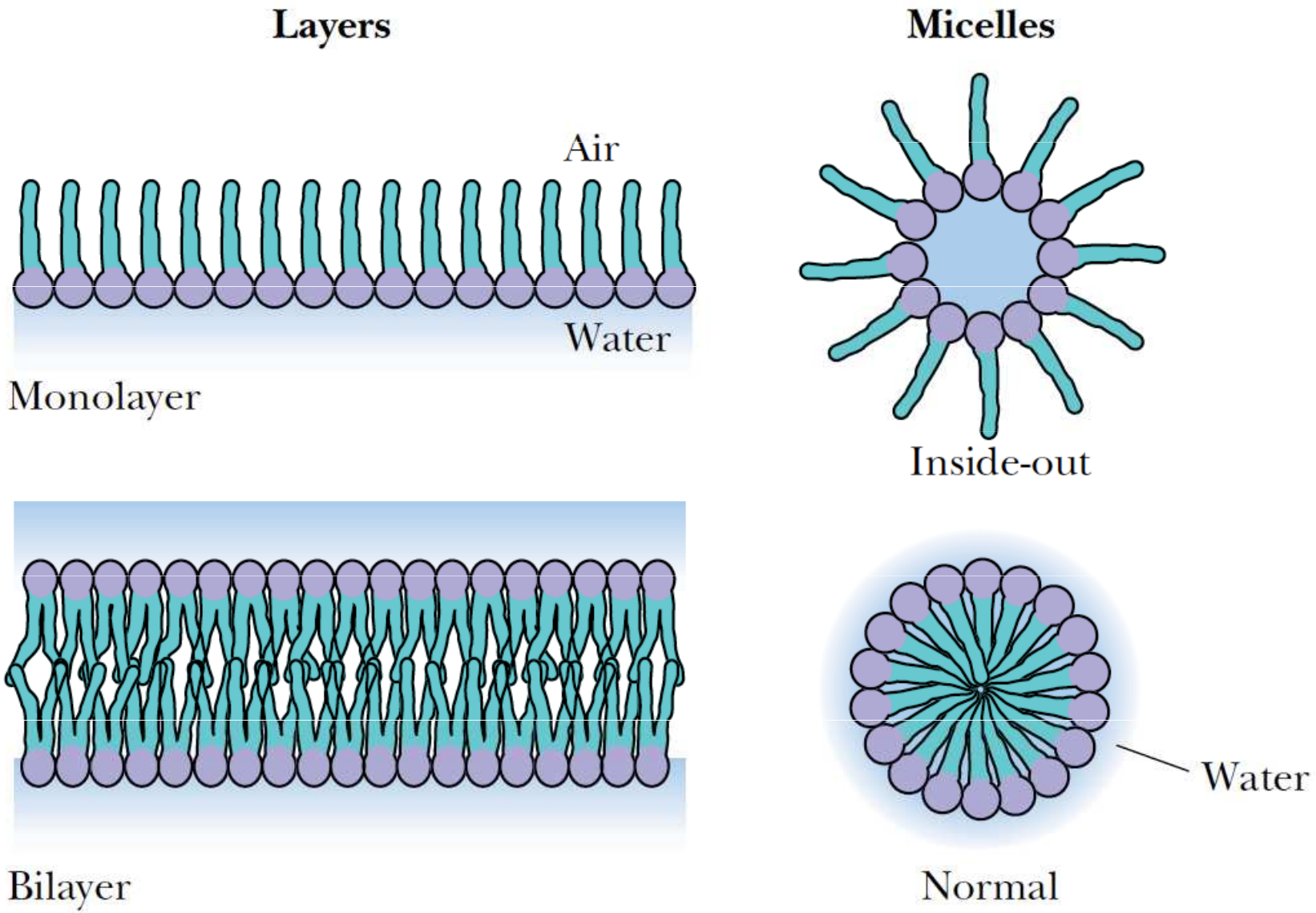




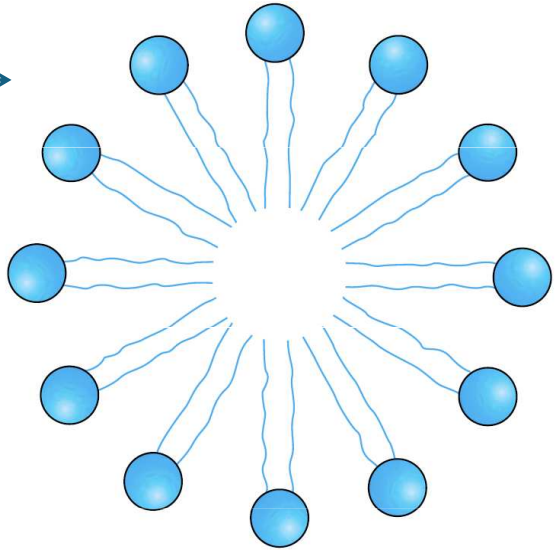

3
2
1
0
nm
polar
head
groups
cholesterol-
stiffened
region
more
fluid
region

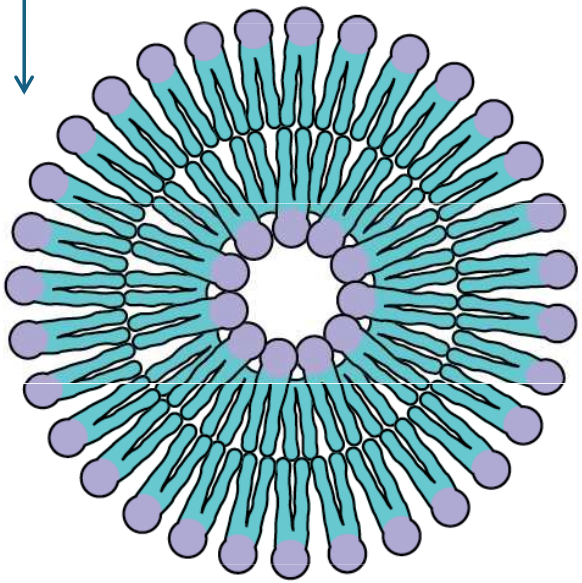
Lipidová dvojvrstva

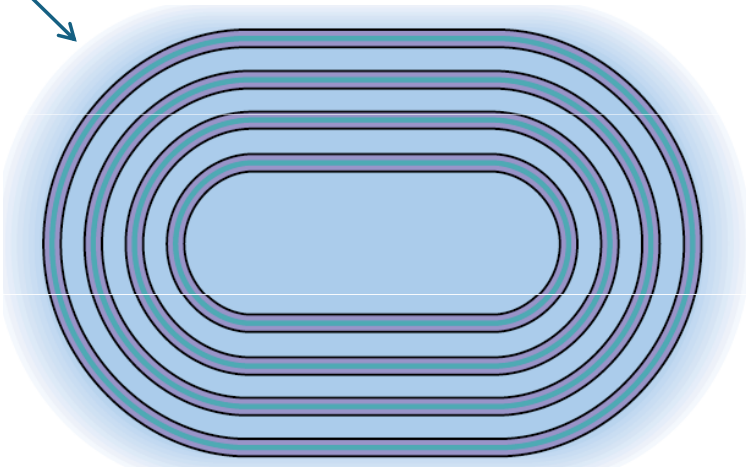


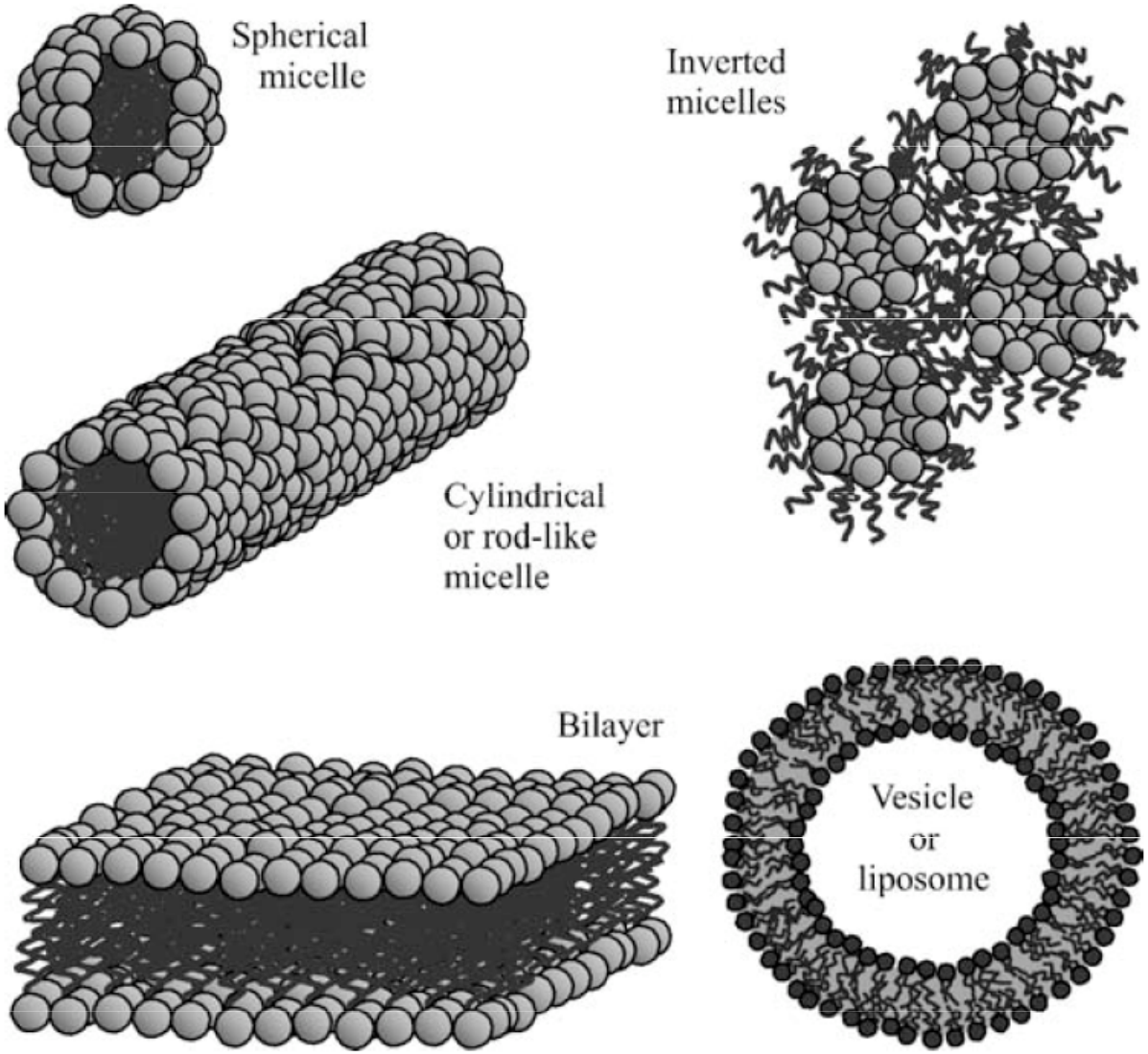

Layers
Micelles
Air
Water
Monolayer
Inside-out
Bilayer
Water
Normal

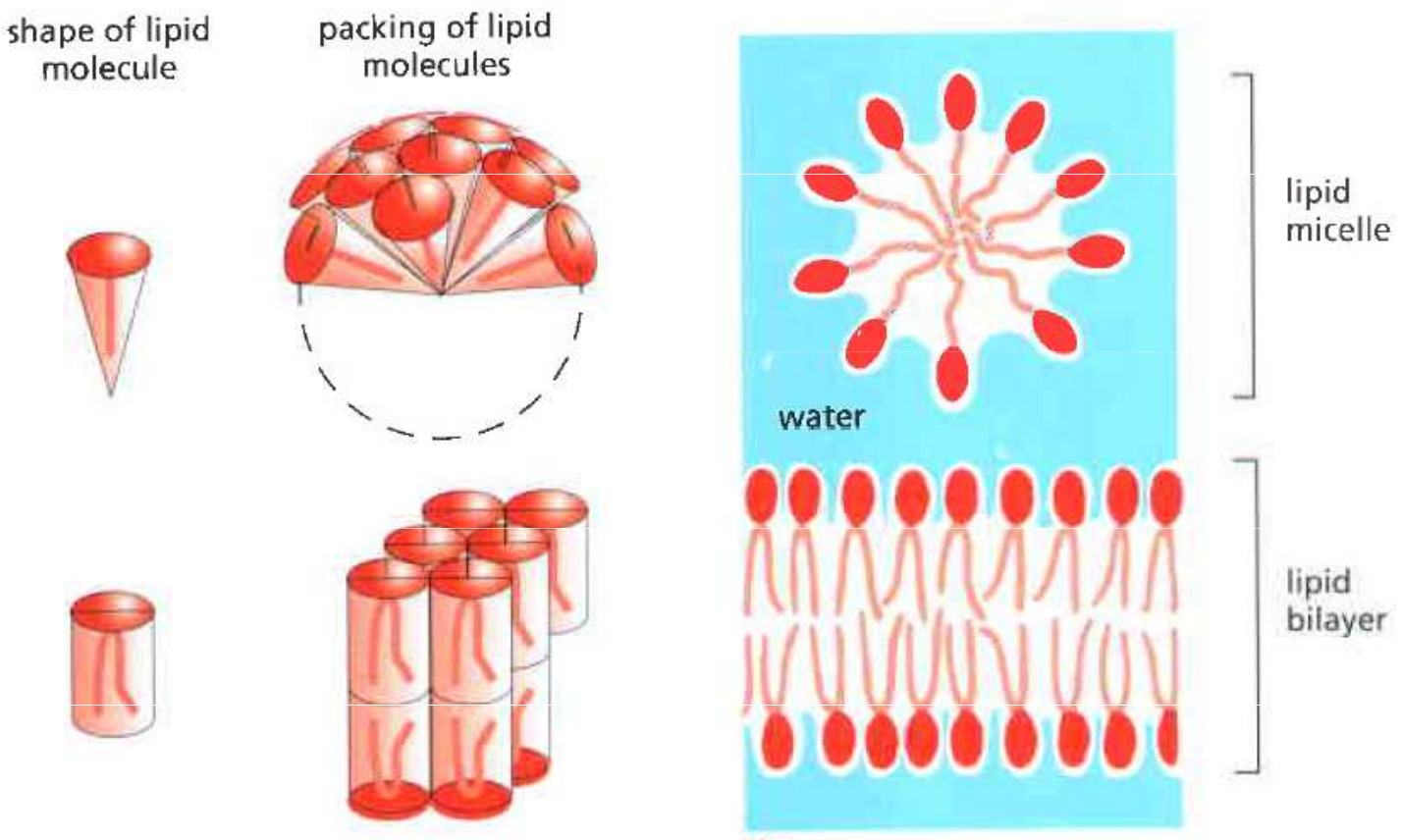
Micela
Unilamelární vesikula
Multilamelární vesikula

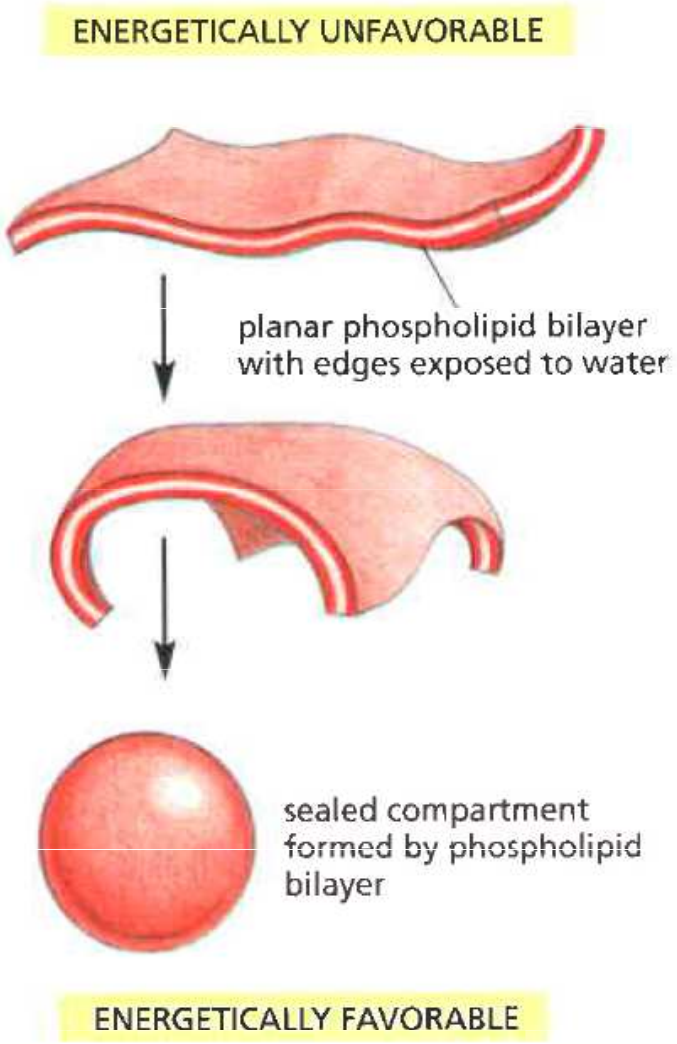


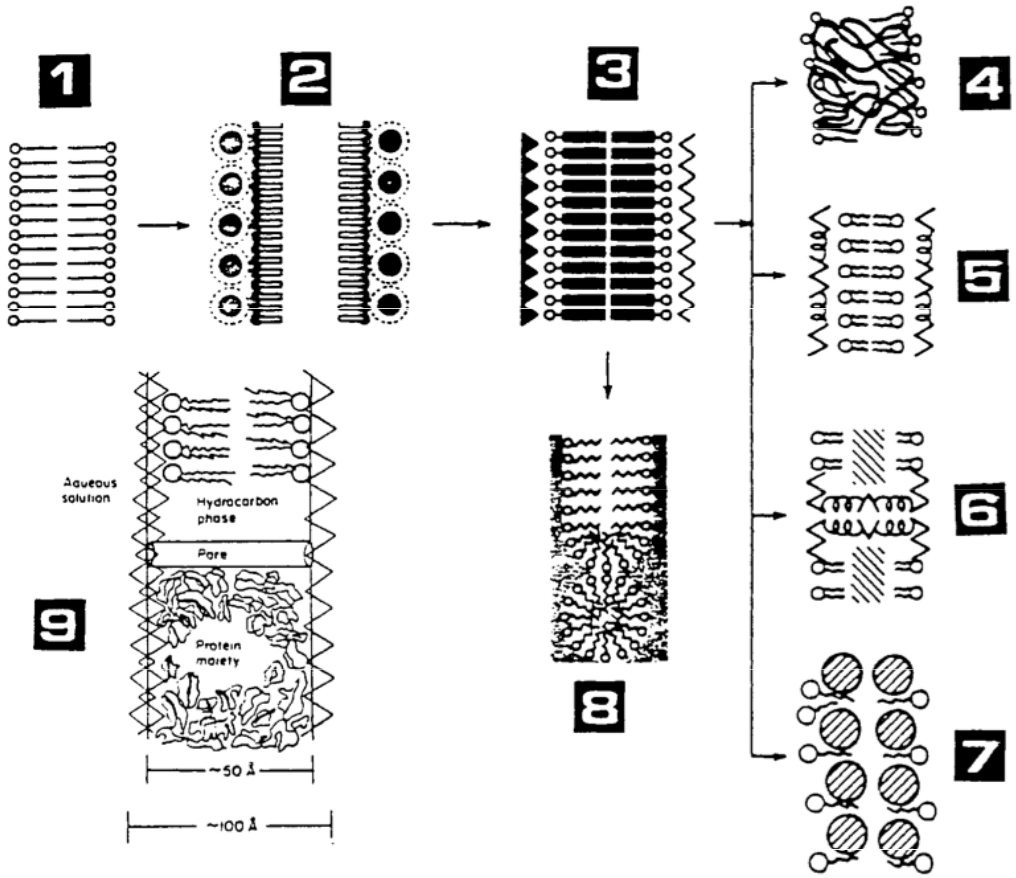





Spherical micelle
Inverted micelles
Cylindrical or rod-like micelle
Bilayer
Vesicle or liposome


shape of lipid molecule
packing of lipid molecules
water
lipid micelle
lipid bilayer

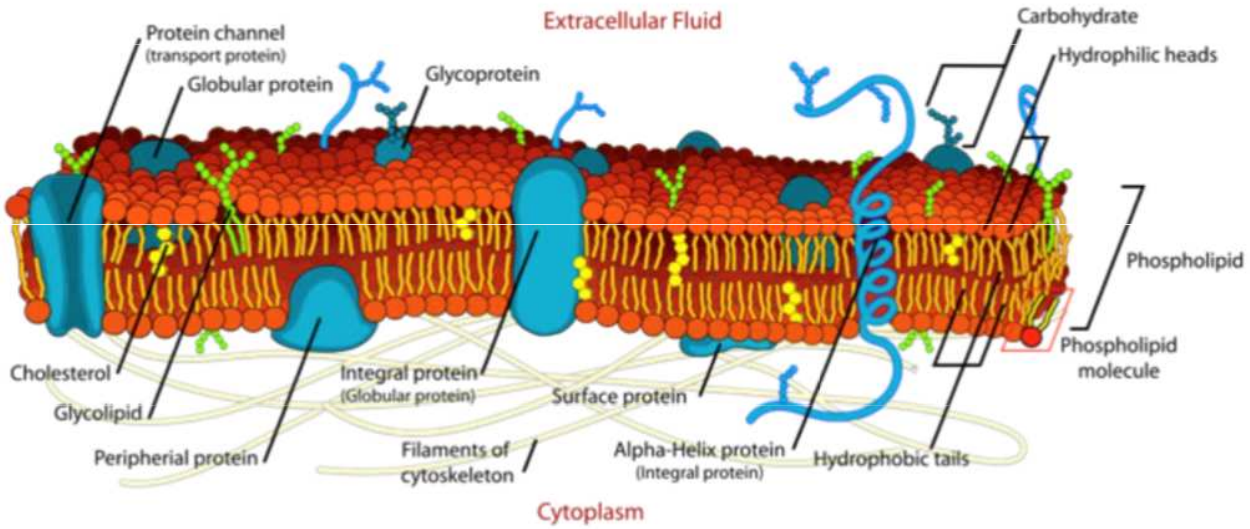

ENERGETICALLY UNFAVORABLE
planar phospholipid bilayer
with edges exposed to water
sealed compartment
formed by phospholipid
bilayer
ENERGETICALLY FAVORABLE



1) Gorter & Grendel
2) Harvey, Danielli, Davson
3) Robertson (X-ray diffraction)
4) Benson
5) Singer & Nicolson
6) --------”----------
7) Green
8) Sjostrand & Lucy
9) Brown (**1971**)

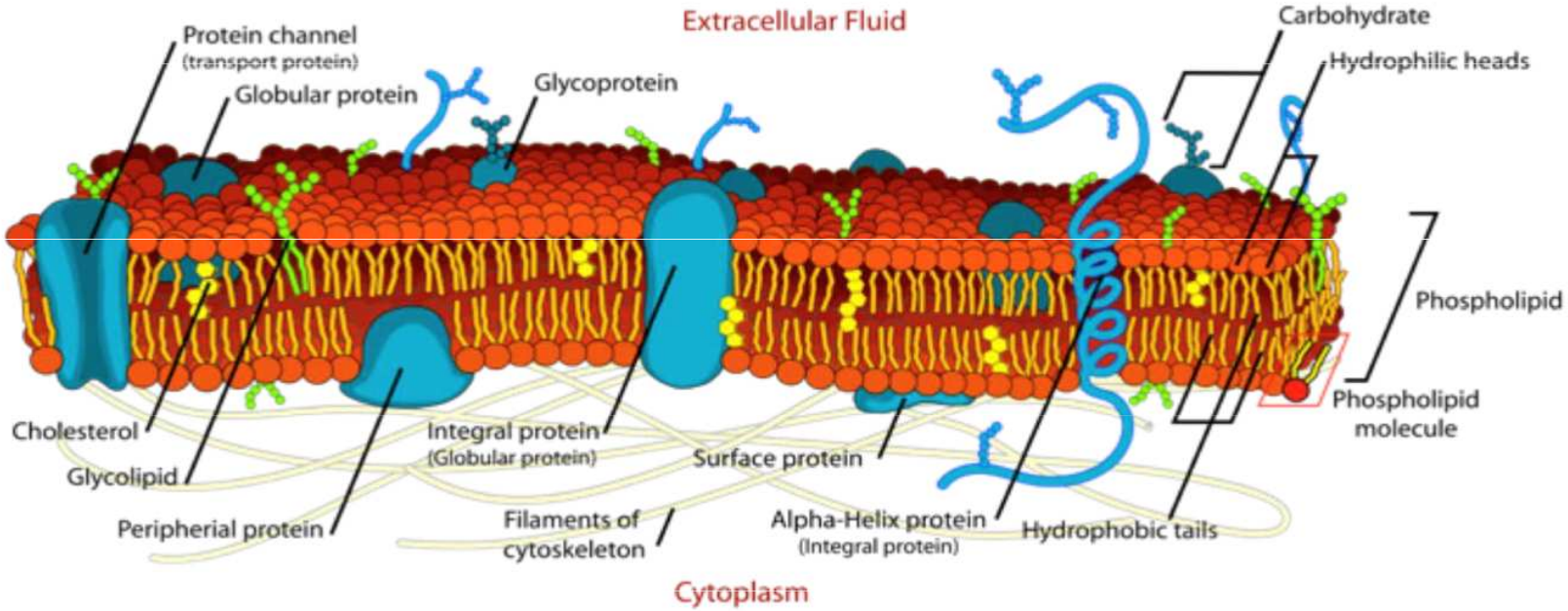
Složení

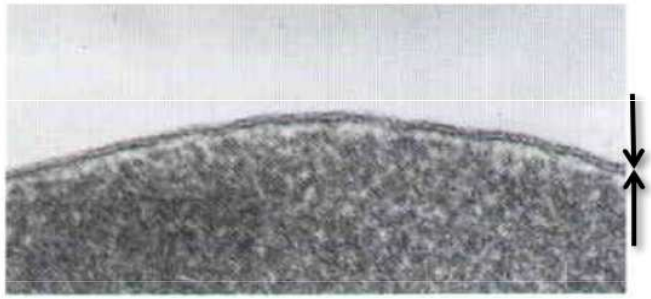
- lipidy
- cukry
- proteiny



1) Lipoprotein: lipid + protein, který je většinou rozpustný v H_2O
2) Proteolipid: protein + lipid, ---------”------- v organice (e.g. 2:1 = $CHCl_3$: CH_3OH)
3) Glycolipid: lipid + carbohydrate. Cukry glycolipidů jsou na vnějším povrchu a velmi pravděpodobně se účastní mezibuněčných komunikací
4) Glycoprotein: carbohydrate + protein. Podobně jako glycolipidy, cukerné zbytky glycoproteinů jsou připojeny na ne-cytoplasmické straně membrány.

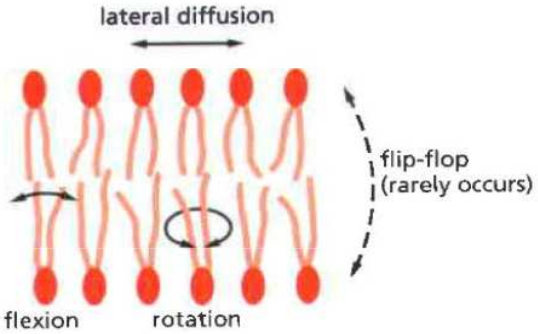
Současný model membrány





3-5 nm

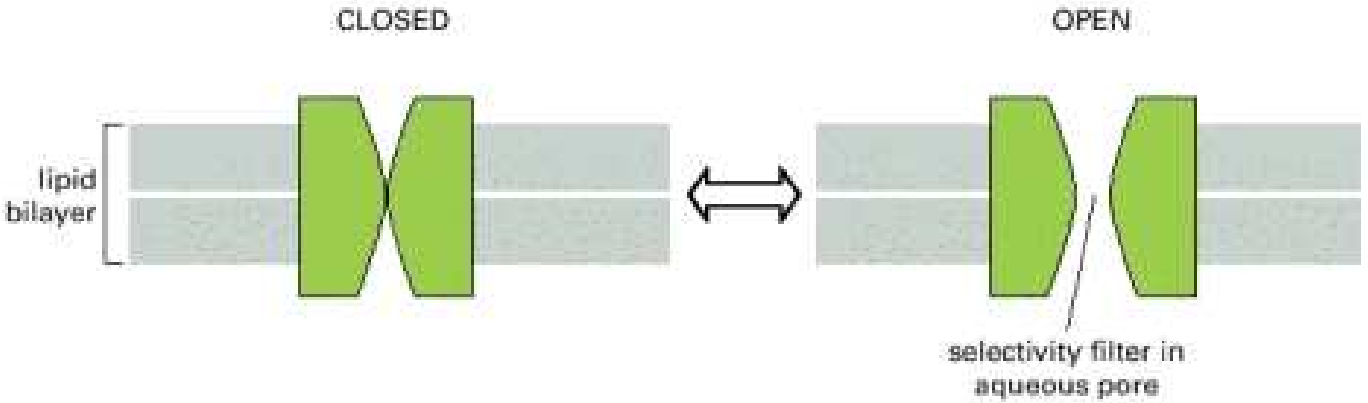
fluid mosaic model – 2d tekutá vrstva



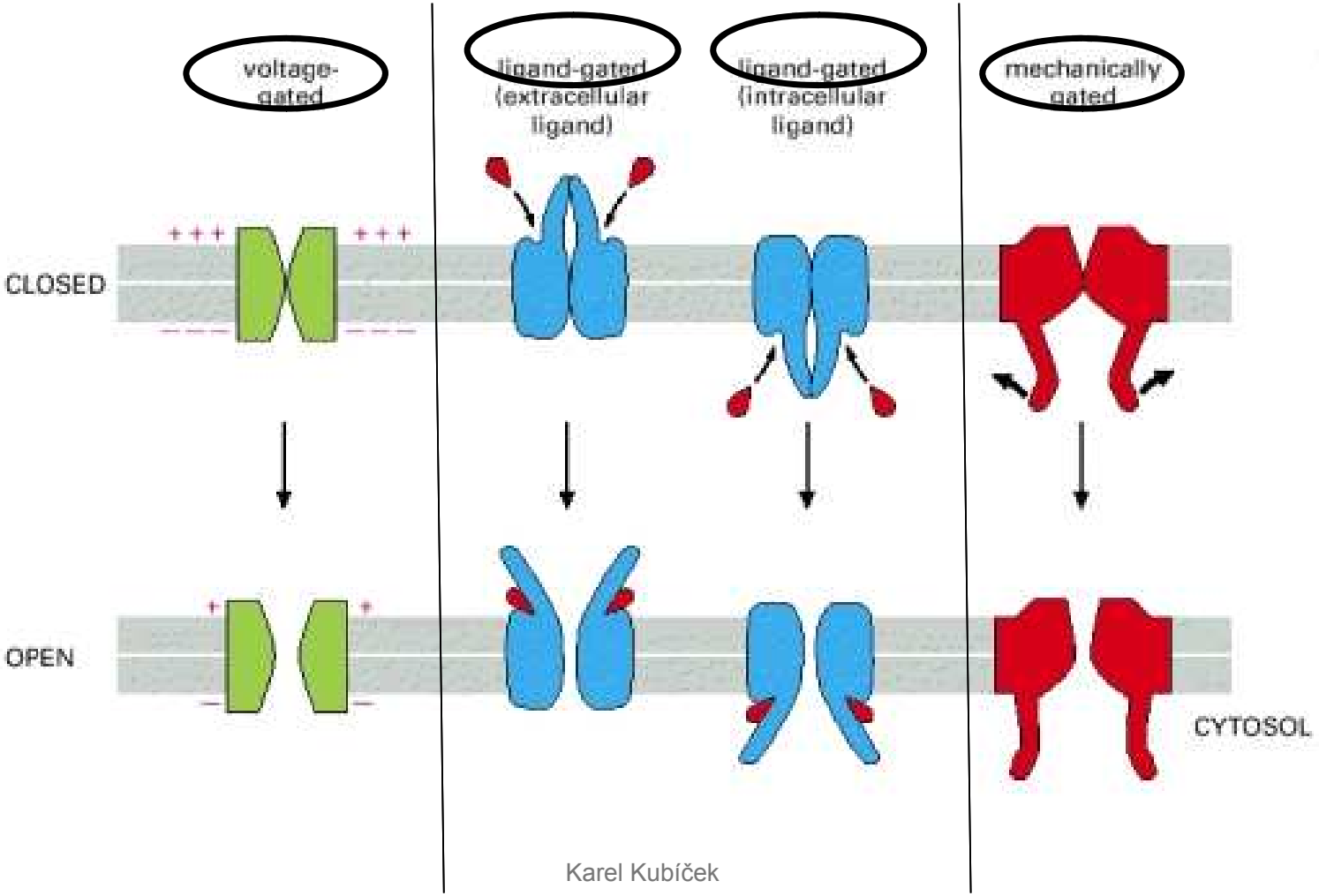
Membránové kanály

Výměna iontů **mezi vnitřním** a **vnějším** prostředím **buňky** je **uskutečňována membránovými kanály**.
Kanály se liší od přenašečů mají pevná vazebná místa pro ionty a v membráně **vytvářejí póry propustné pro vodu**.
Otevírání/uzavírání těchto **pórů**/kanálů (vrátkování/gating) se může dít několika mechanismy. Vedle **elektrického** je **vrátkování** některých kanálů ovládáno jinými podněty (**chemickou vazbou látek**, **mechanickým napětím** aj.).
Průchod iontů celým kanálem **nelze považovat za volnou difuzi**. Většina kanálů je totiž charakterizována větší či menší mírou selektivity v propustnosti iontů. V tomto smyslu hovoříme o sodíkových, draslíkových, vápníkových nebo chloridových kanálech.
Transport iontů kanály nevyžaduje dodání energie.

Otevírání/zavírání kanálů (gating/vrátkování)



Otevírání/zavírání kanálů (gating/vrátkování)



Buňky

Tvary a velikosti vybraných bakterií

spherical cells
e.g., *Streptococcus*

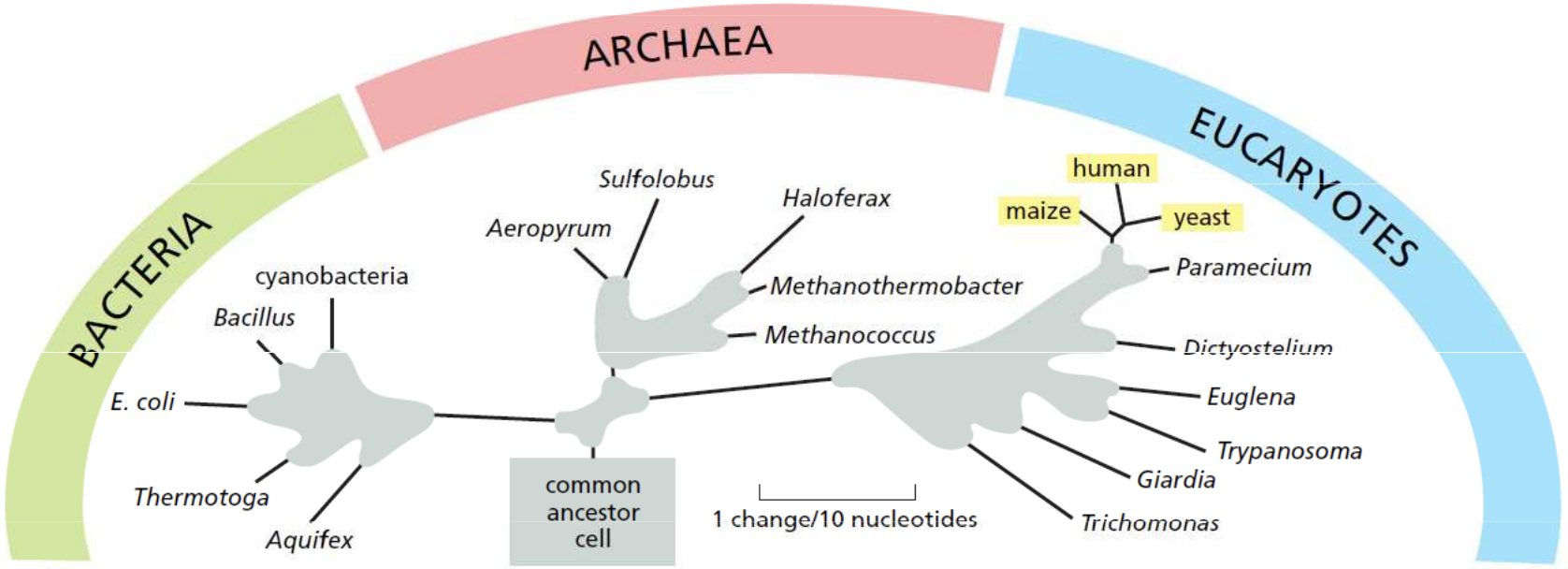
rod-shaped cells
e.g., *Escherichia coli, Vibrio cholerae*

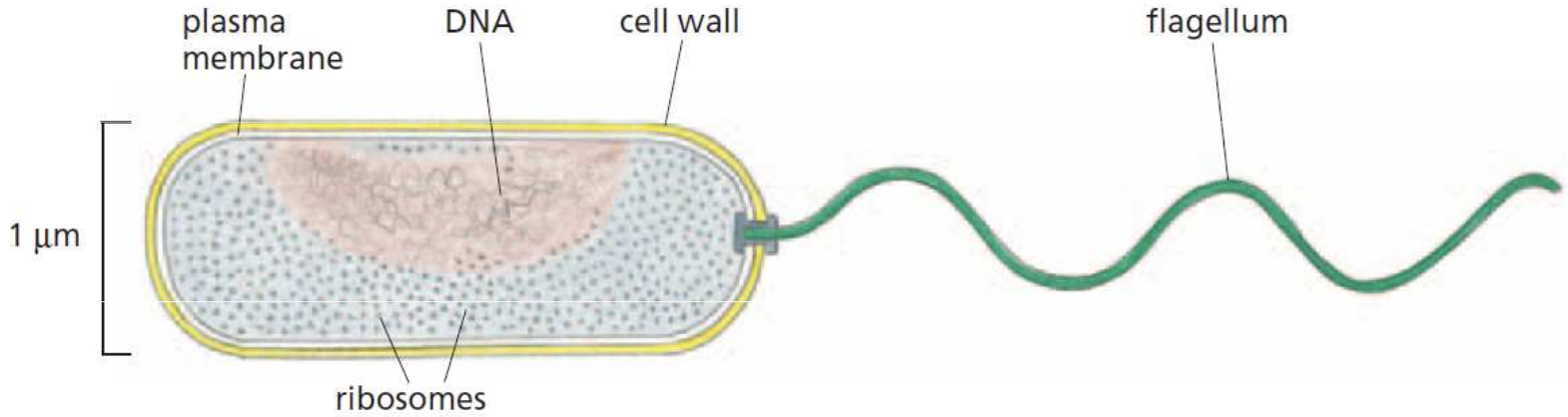
the smallest cells
e.g., *Mycoplasma, Spiroplasma*

spiral cells
e.g., *Treponema pallidum*

Základní rozdělení živého světa

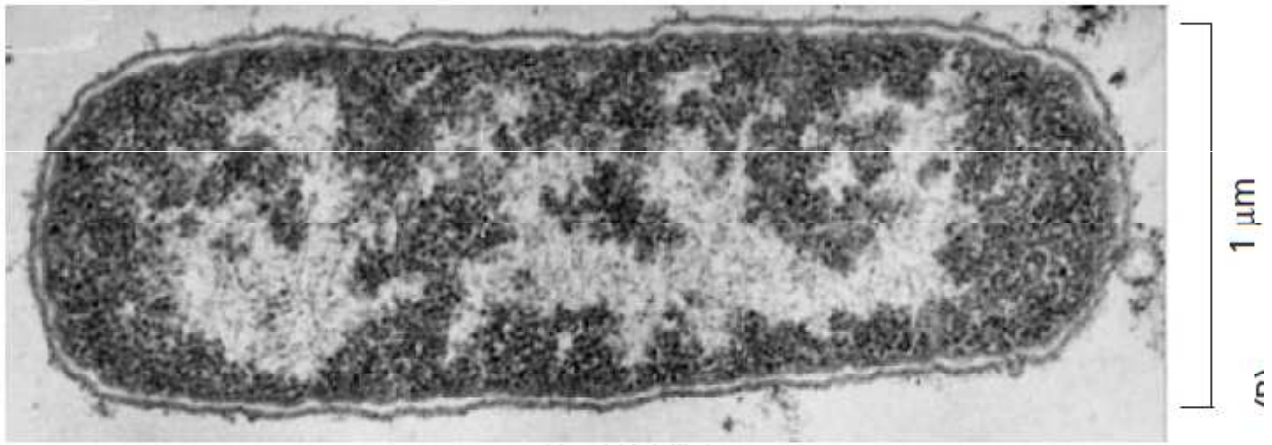
1) Prokaryoty
2) Eukaryoty



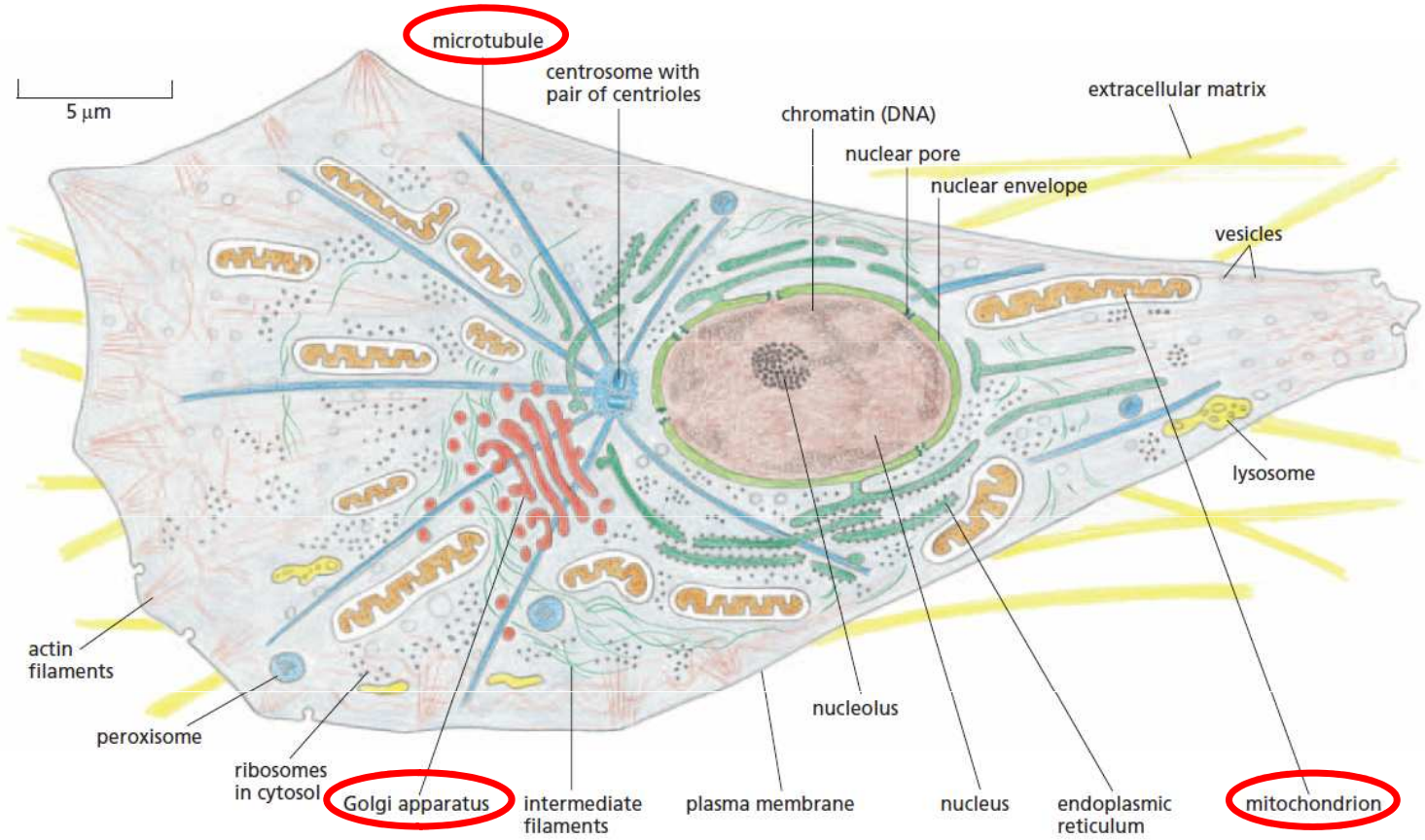


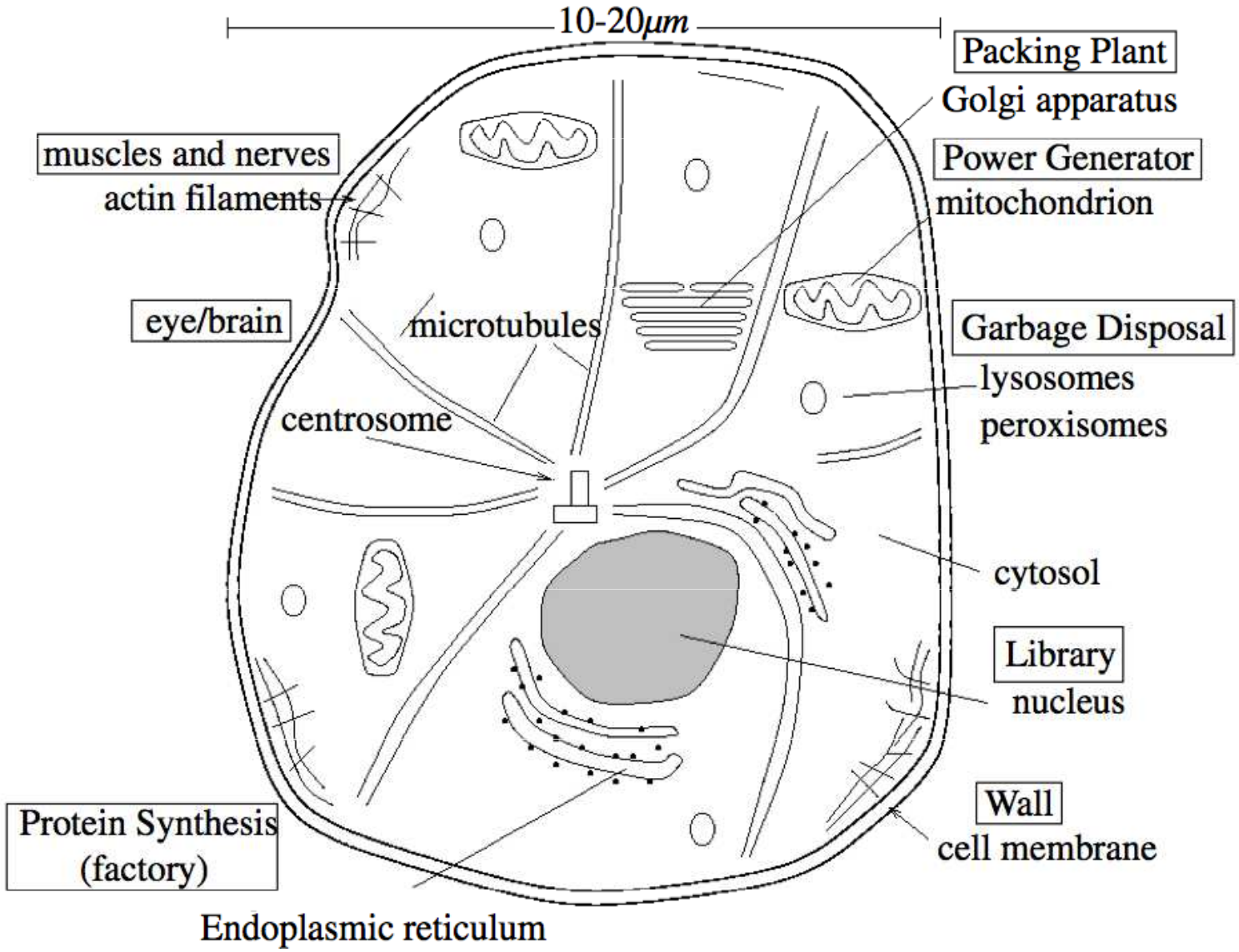
Vibrio cholerae

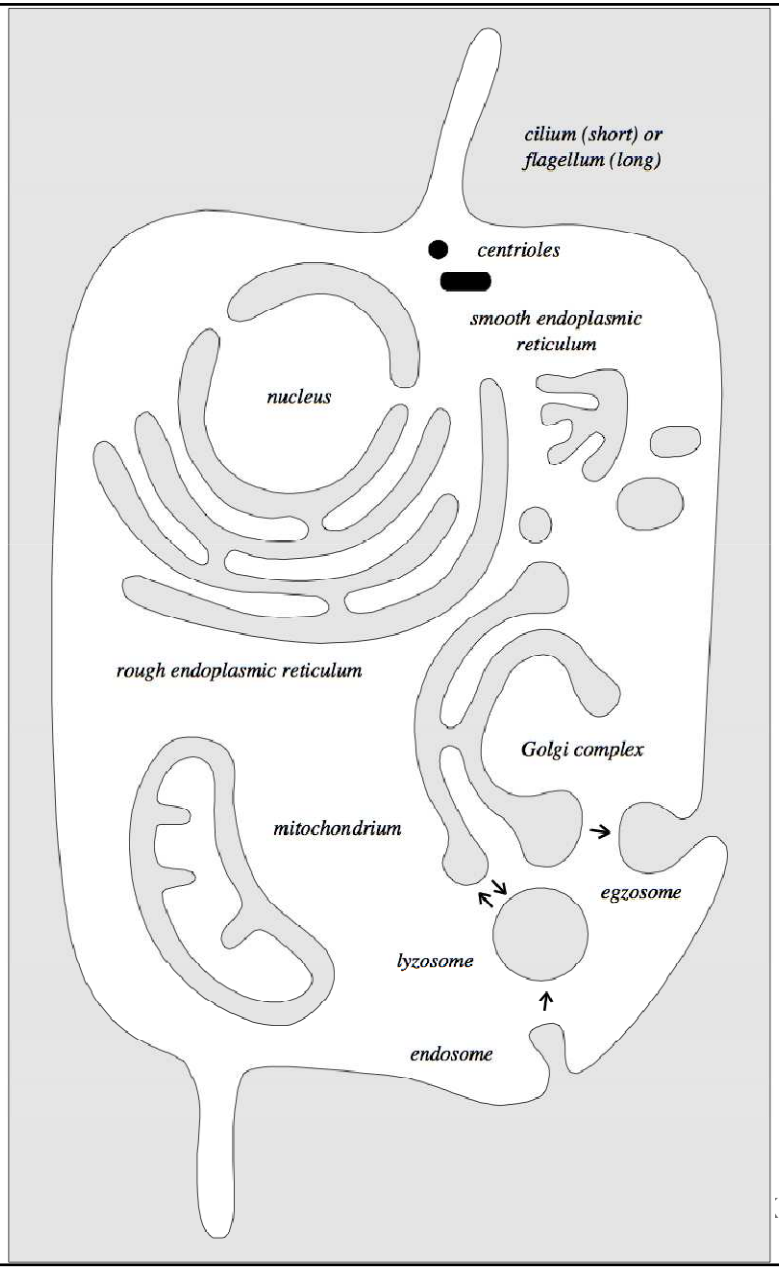
Escherischia coli (E.coli)

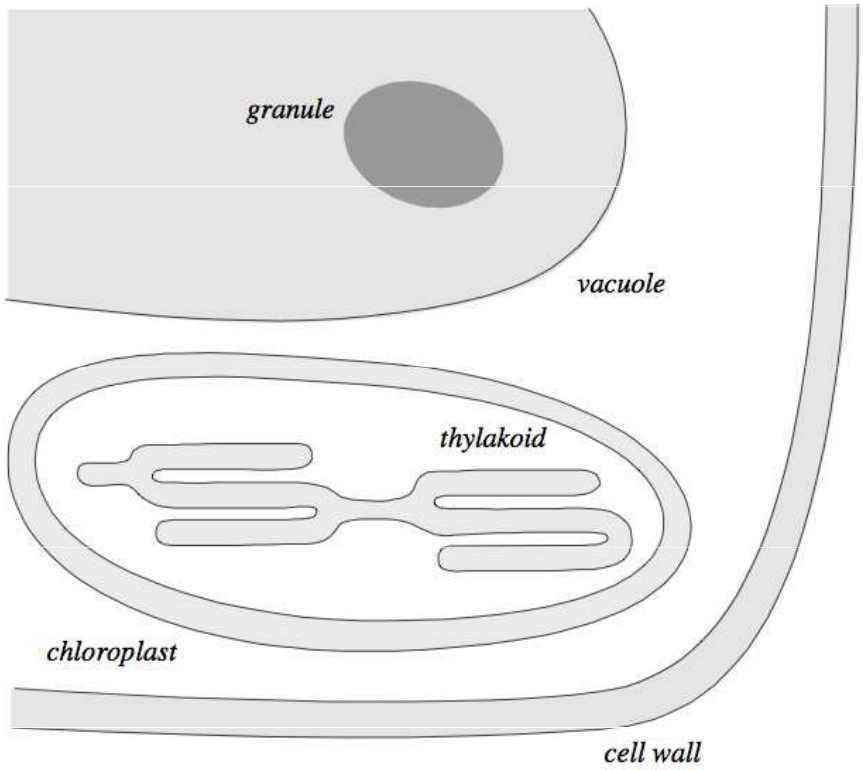


Eukaryotická buňka

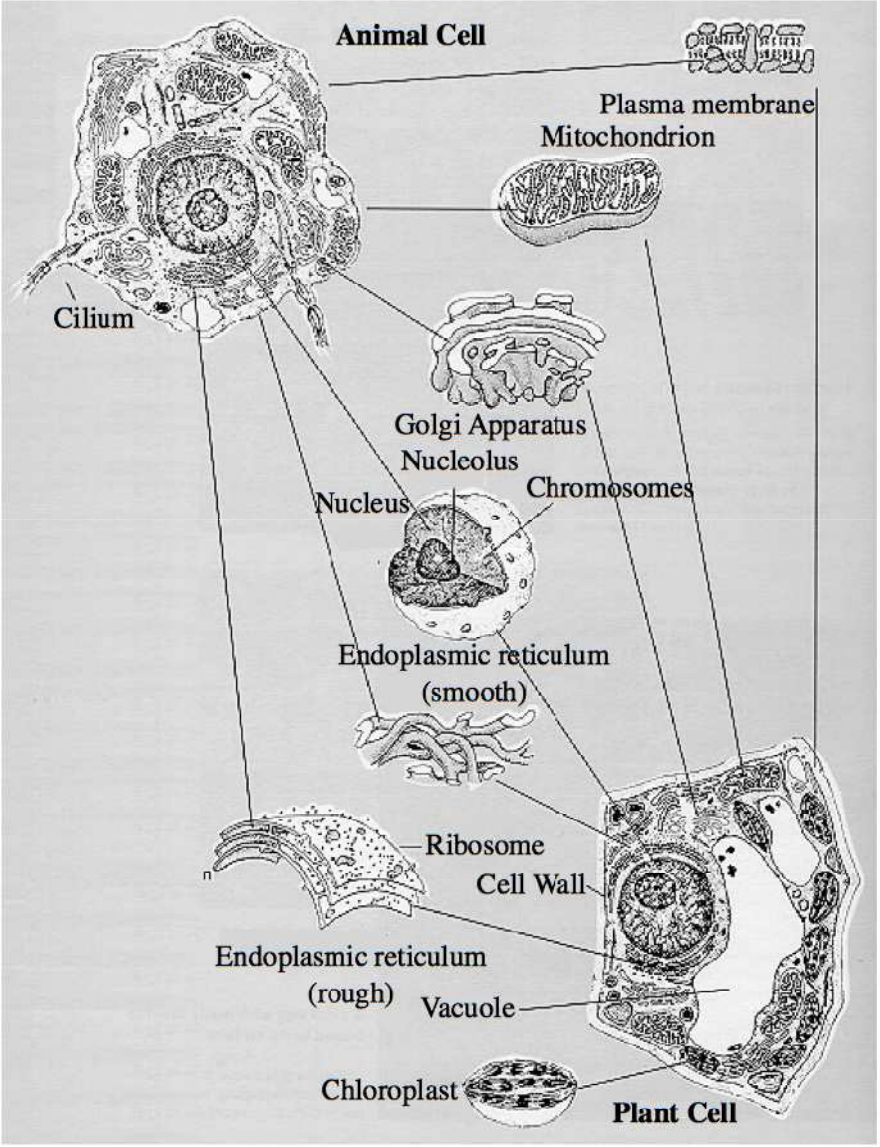



10-20μm
Packing Plant
Golgi apparatus
muscles and nerves
actin filaments
Power Generator
mitochondrion
eye/brain
microtubules
Garbage Disposal
lysosomes
peroxisomes
centrosome
cytosol
Library
nucleus
Wall
cell membrane
Protein Synthesis
(factory)
Endoplasmic reticulum





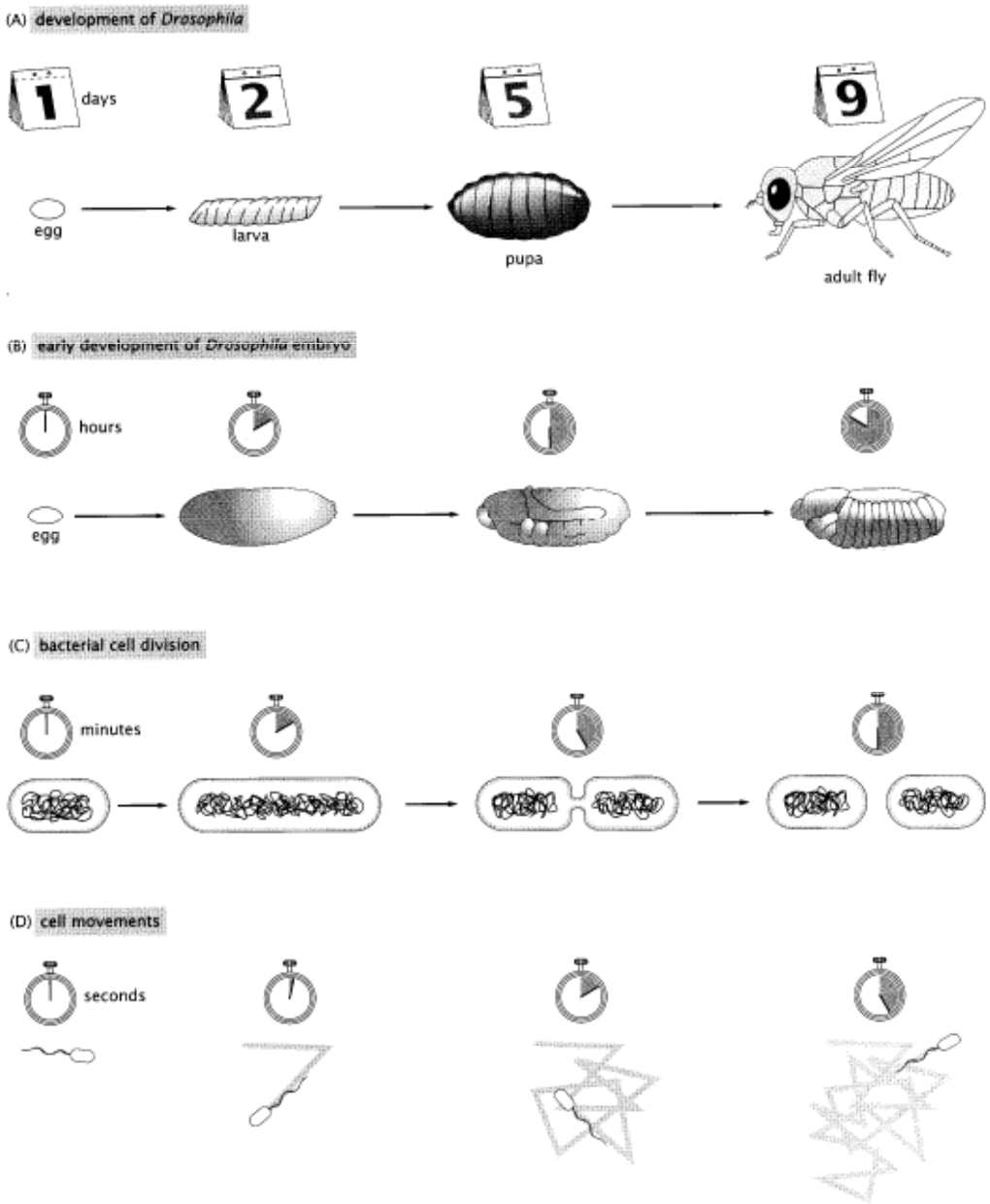
Další organely v rostlinné buňce

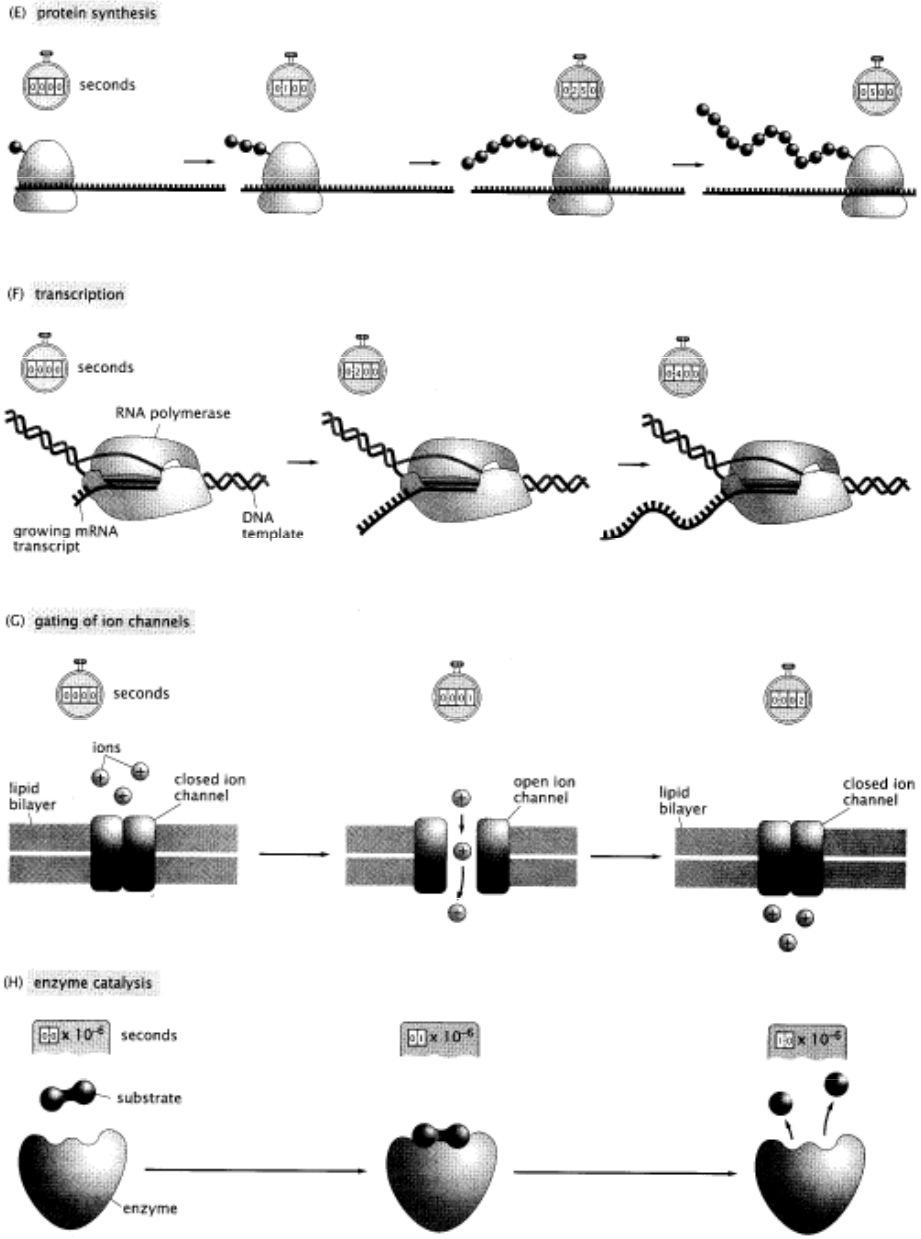

Animal Cell
Plasma membrane
Mitochondrion
Cilium
Golgi Apparatus
Nucleolus
Chromosomes
Nucleus
Endoplasmic reticulum
(smooth)
Ribosome
Cell Wall
Endoplasmic reticulum
(rough)
Vacuole
Chloroplast
Plant Cell

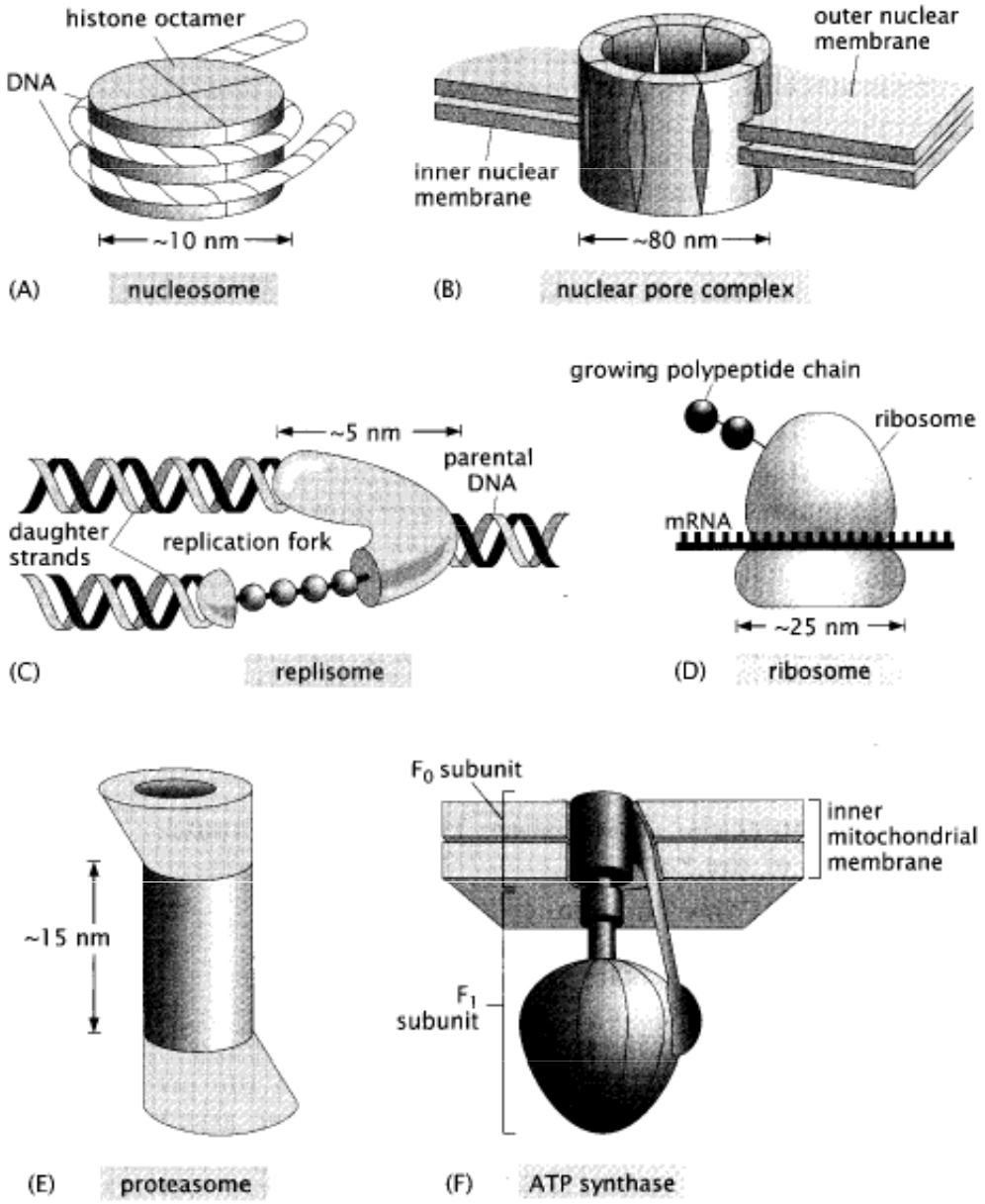
Makromolekulární konsenzus v buňce ***E. coli***

Substance	% of total dry weight	Number of molecules
Macromolecule		
Protein	55.0	2.4×10^6
RNA	20.4	
23S RNA	10.6	19,000
16S RNA	5.5	19,000
5S RNA	0.4	19,000
Transfer RNA (4S)	2.9	200,000
Messenger RNA	0.8	1,400
Phospholipid	9.1	22×10^6
Lipopolysaccharide	3.4	1.2×10^6
DNA	3.1	2
Murein	2.5	1
Glycogen	2.5	4,360
Total macromolecules	**96.1**	
Small molecules		
Metabolites, building blocks, etc.	2.9	
Inorganic ions	1.0	
Total small molecules	**3.9**	

E. coli	Cell volume	$V_{E.\ coli}$	$\approx 1\,\mu m^3$
	Cell mass	$m_{E.\ coli}$	≈ 1 pg
	Cell cycle time	$t_{E.\ coli}$	≈ 3000 s
	Cell surface area	$A_{E.\ coli}$	$\approx 6\,\mu m^2$
	Genome length	$N_{bp}^{E.\ coli}$	$\approx 5 \times 10^6$ bp
	Swimming speed	$v_{E.\ coli}$	$\approx 20\,\mu m/s$
Yeast	Volume of cell	V_{yeast}	$\approx 60\,\mu m^3$
	Mass of cell	m_{yeast}	≈ 60 pg
	Diameter of cell	d_{yeast}	$\approx 5\,\mu m$
	Cell cycle time	t_{yeast}	≈ 200 min
	Genome length	N_{bp}^{yeast}	$\approx 10^7$ bp
Organelles	Diameter of nucleus	$d_{nucleus}$	$\approx 5\,\mu m$
	Length of mitochondrion	l_{mito}	$\approx 2\,\mu m$
	Diameter of transport vesicles	$d_{vesicle}$	≈ 50 nm
Water	Volume of molecule	V_{H_2O}	$\approx 10^{-2}$ nm^3
	Density of water	ρ	1 g/cm^3
	Viscosity of water	η	≈ 1 centipoise (10^{-2} g/(cm s))
	Hydrophobic embedding energy	$\approx E_{hydr}$	25 cal/(mol Å^2)
DNA	Length per base pair	l_{bp}	$\approx 1/3$ nm
	Volume per base pair	V_{bp}	≈ 1 nm^3
	Charge density	λ_{DNA}	2 e/0.34 nm
	Persistence length	ξ_P	50 nm
Amino acids and proteins	Radius of "average" protein	$r_{protein}$	≈ 2 nm
	Volume of "average" protein	$V_{protein}$	≈ 25 nm^3
	Mass of "average" amino acid	M_{aa}	≈ 100 Da
	Mass of "average" protein	$M_{protein}$	$\approx 30{,}000$ Da
	Protein concentration in cytoplasm	$c_{protein}$	≈ 300 mg/mL
	Characteristic force of protein motor	F_{motor}	≈ 5 pN
	Characteristic speed of protein motor	v_{motor}	≈ 200 nm/s
	Diffusion constant of "average" protein	$D_{protein}$	$\approx 100\,\mu m^2/s$
Lipid bilayers	Thickness of lipid bilayer	d	≈ 5 nm
	Area per molecule	A_{lipid}	$\approx \frac{1}{2}$ nm^2
	Mass of lipid molecule	m_{lipid}	≈ 800 Da


(A) development of *Drosophila*
1 days
2
5
9
egg
larva
pupa
adult fly
(B) early development of *Drosophila* embryo
hours
egg
(C) bacterial cell division
minutes
(D) cell movements
seconds

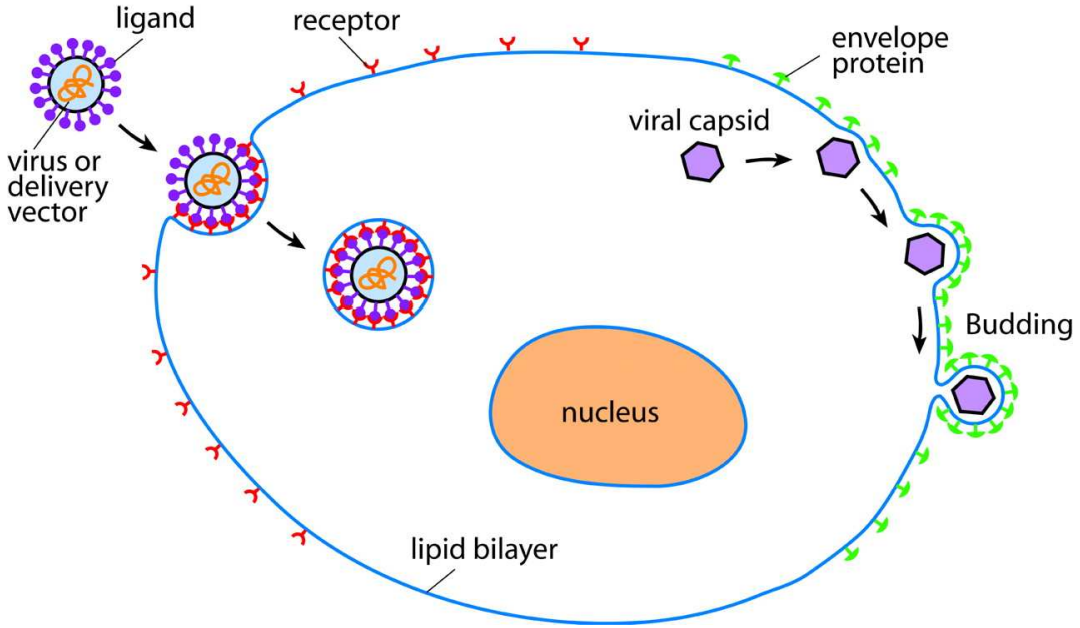

(E) protein synthesis
seconds
(F) transcription
seconds
RNA polymerase
growing mRNA transcript
DNA template
(G) gating of ion channels
seconds
ions
lipid bilayer
closed ion channel
open ion channel
lipid bilayer
closed ion channel
(H) enzyme catalysis
seconds
substrate
enzyme


histone octamer
DNA
~10 nm
(A) nucleosome
outer nuclear membrane
inner nuclear membrane
~80 nm
(B) nuclear pore complex
~5 nm
parental DNA
daughter strands
replication fork
(C) replisome
growing polypeptide chain
ribosome
mRNA
~25 nm
(D) ribosome
~15 nm
(E) proteasome
F_0 subunit
inner mitochondrial membrane
F_1 subunit
(F) ATP synthase

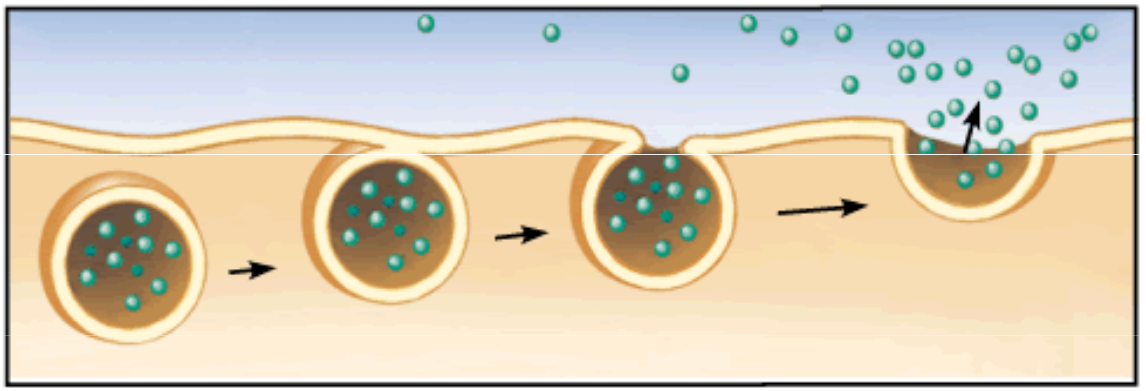
ENDO-

-

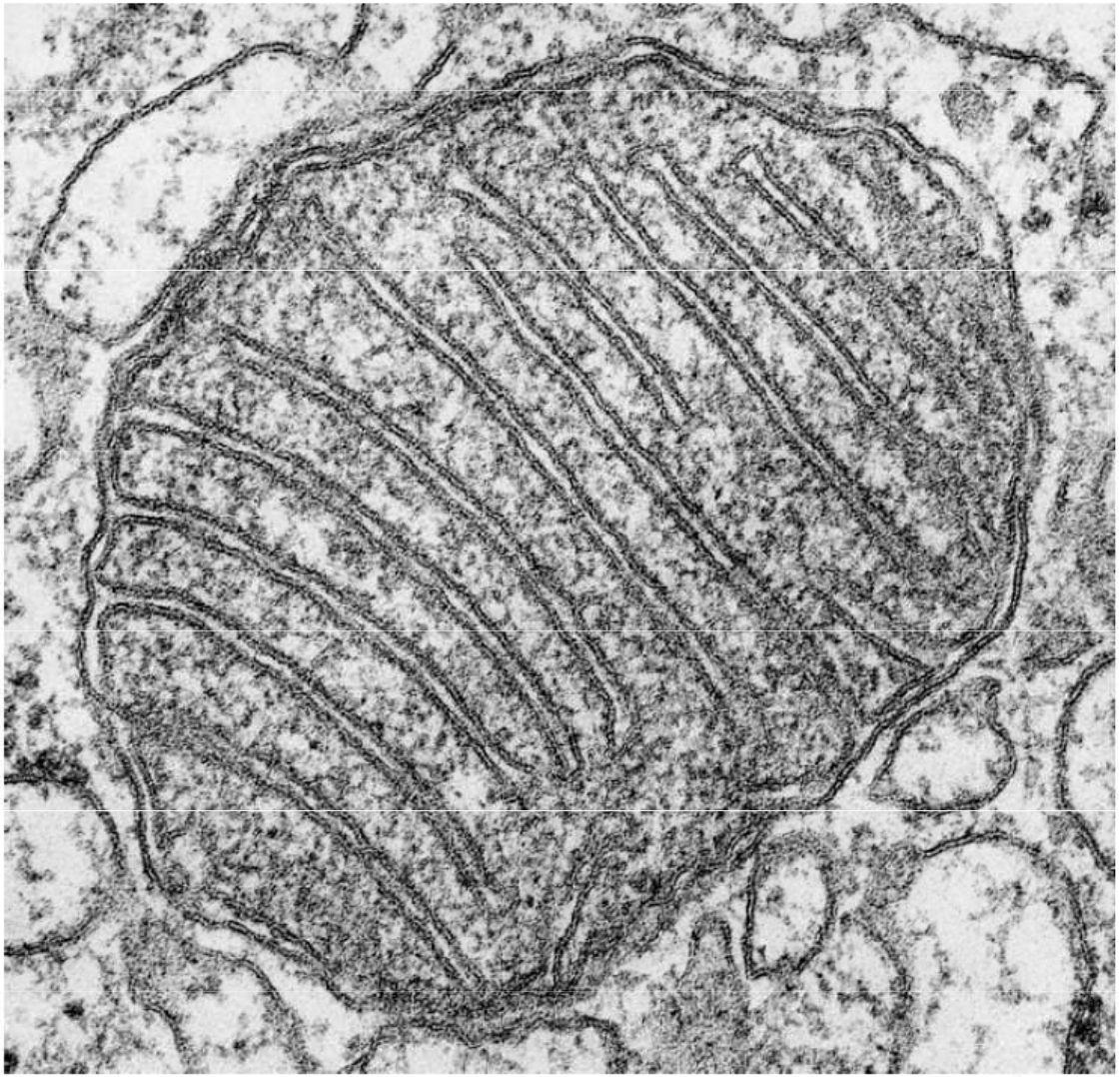
CYTOSIS

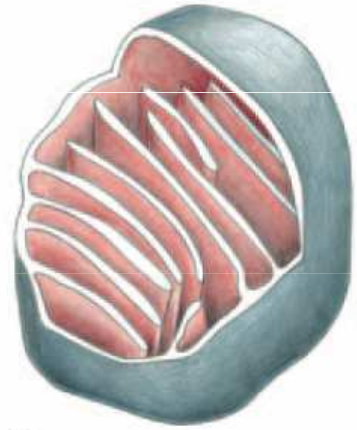


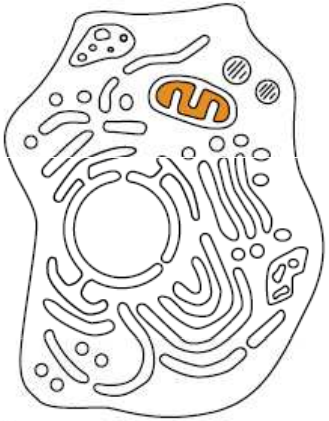
EXO-



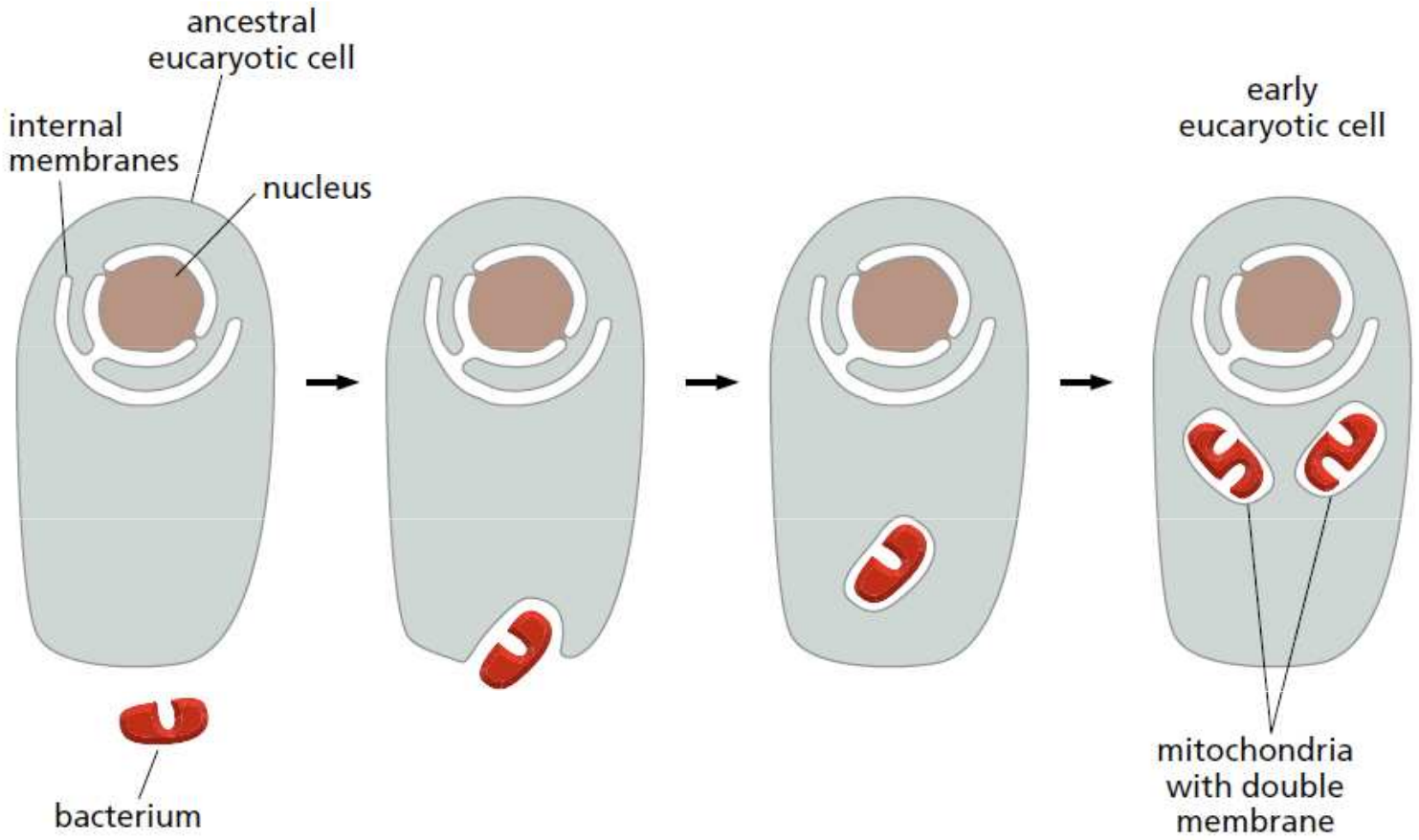
Mitochondrie



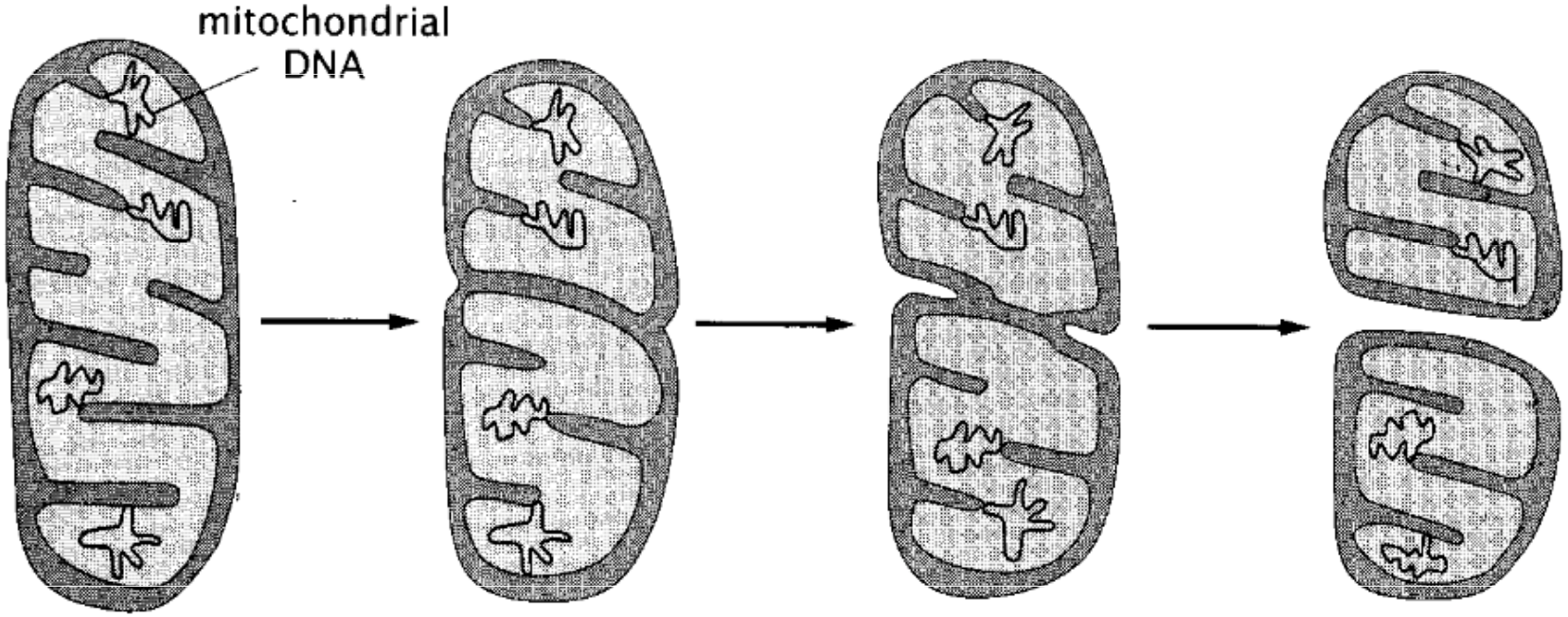




Vznik mitochondrie



Fission – dělení mitochondrie



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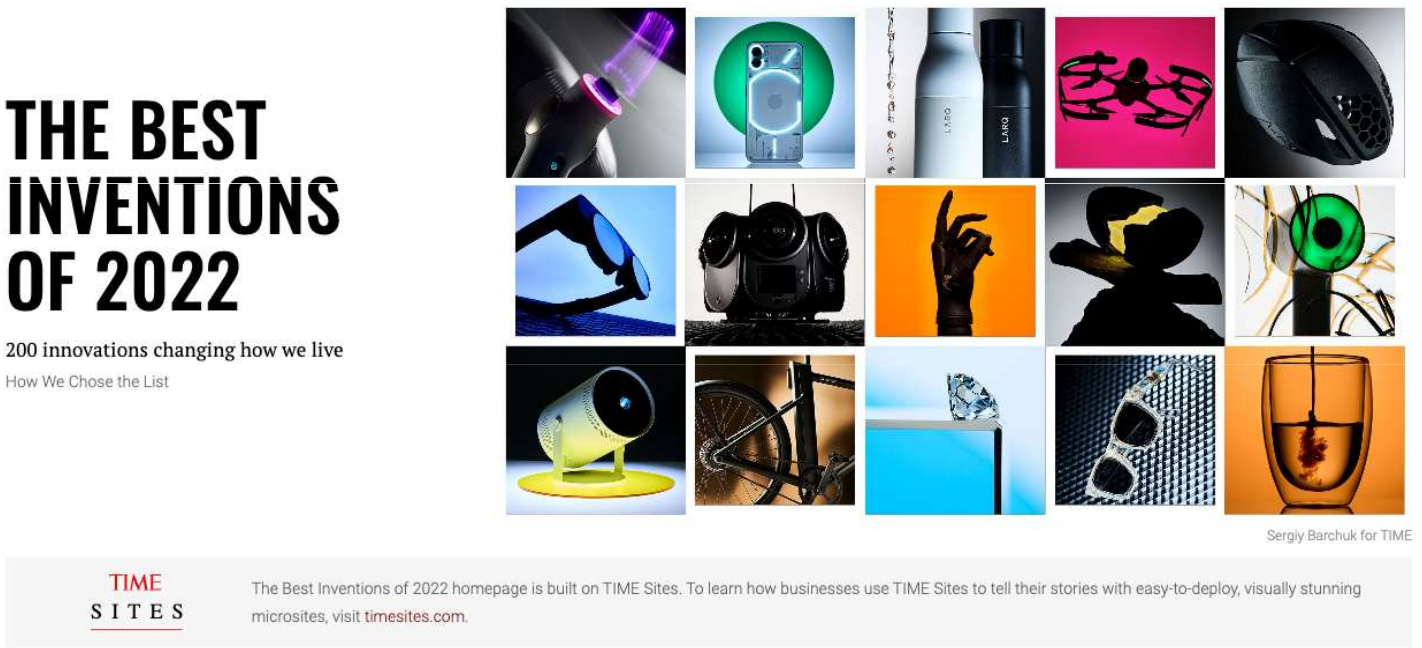
https://www.biorxiv.org/

Mosalaganti, Obarska-Kosinska, Siggel et al

Title: Artificial intelligence reveals nuclear pore complexity

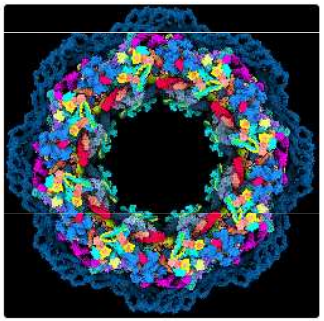
Authors:

Shyamal Mosalaganti[1,2,3†], Agnieszka Obarska-Kosinska[1,4†], Marc Siggel[4,5,6†], Beata Turonova[1,2], Christian E. Zimmerli[1,2], Katarzyna Buczak[2‡] , Florian H. Schmidt[2§], Erica Margiotta[1,2], Marie-Therese Mackmull[2¶], Wim Hagen[2], Gerhard Hummer[5,7*], Martin Beck[1,2*], Jan Kosinski[2,4,6*]



https://time.com/collection/best-inventions-2022/6229912/deepmind-alphafold/

AI



MAPPING LIFE'S BUILDING BLOCKS

DEEPMIND ALPHAFOLD

DETECTING DESTRUCTION OF WAR

SCALE AI AUTOMATED DAMAGE IDENTIFICATION

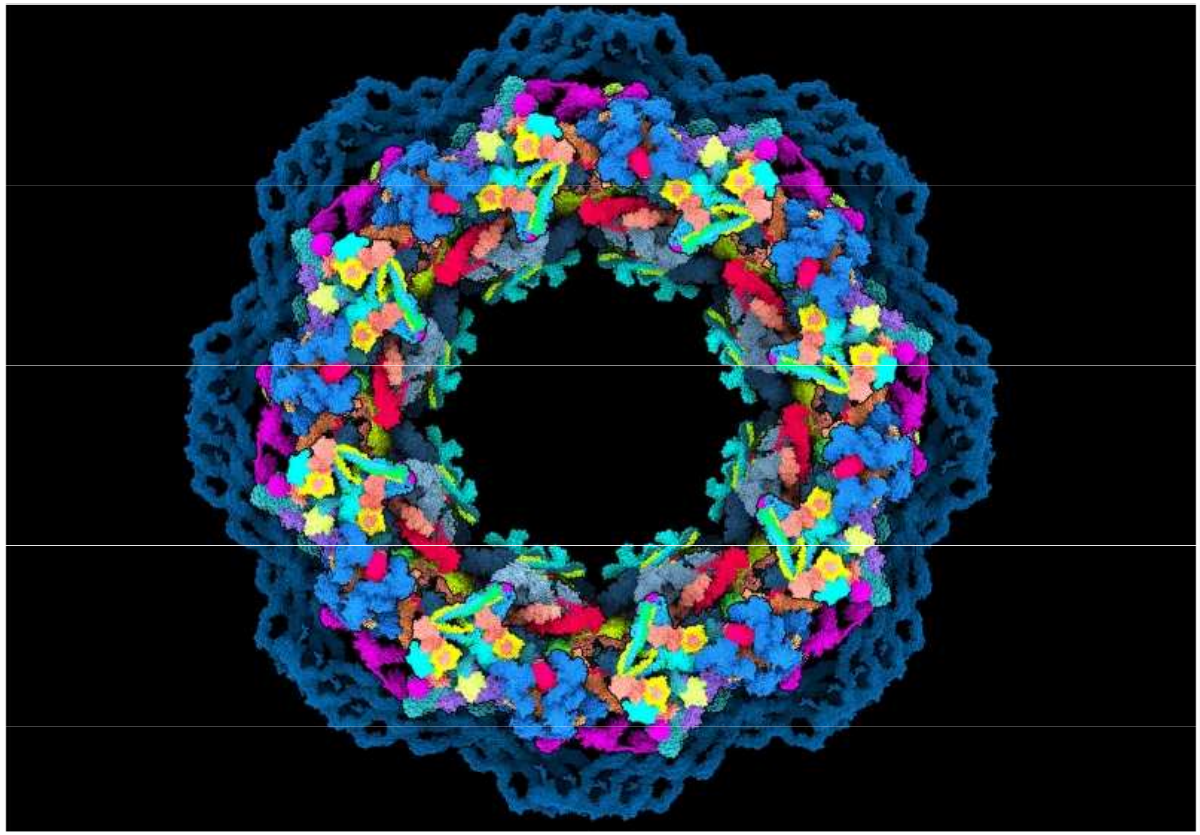
ARTIFICIAL IMAGINATION

OPENAI DALL-E 2

← THE BEST INVENTIONS OF 2022

Mapping Life

DeepMind AlphaFold

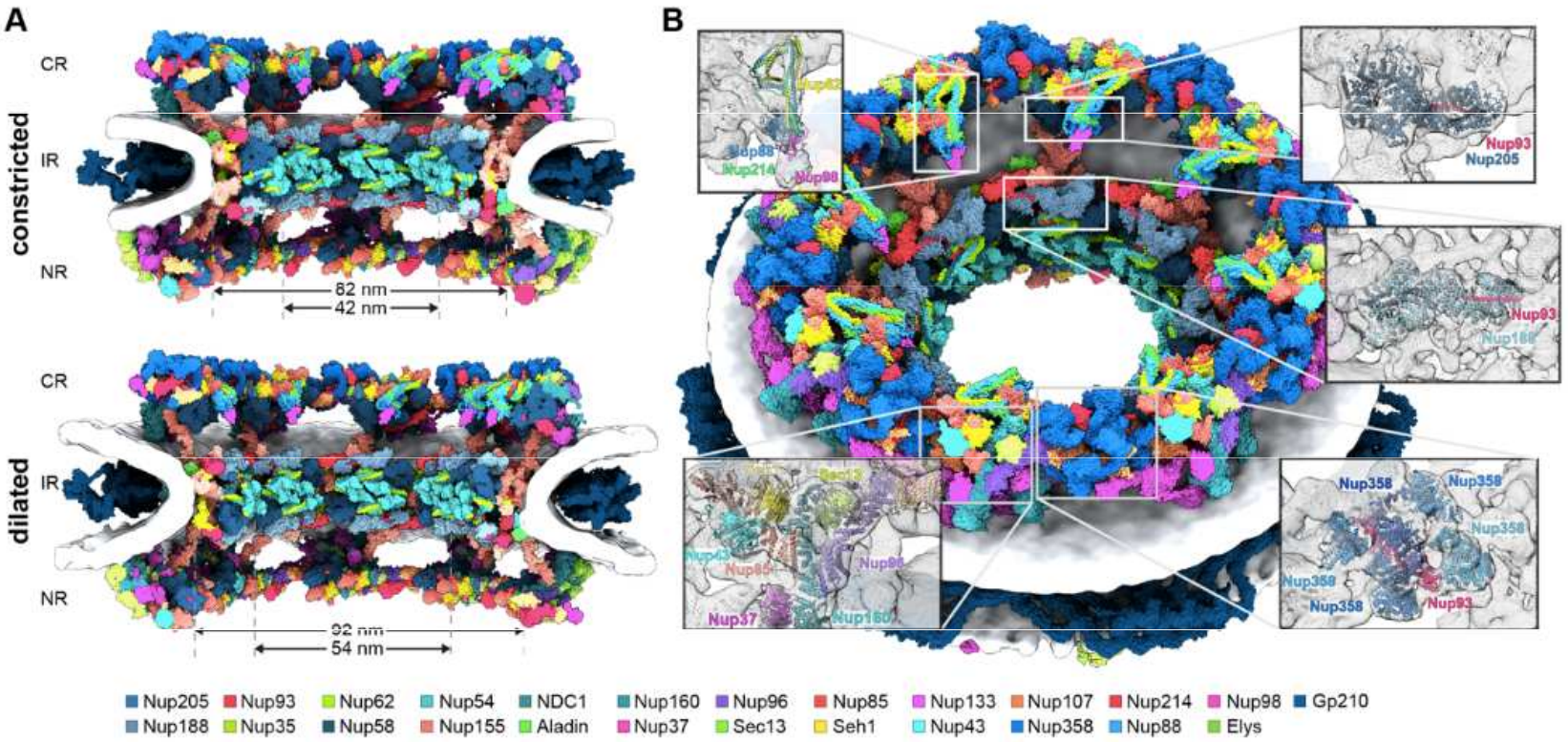


BY BILLY PERRIGO

BY **BILLY PERRIGO**

NOVEMBER 10, 2022 6:20 AM EST

In the recent past, discerning the exact 3D structure of a single protein took around five years. Today the same task is possible in seconds thanks to the machine learning program AlphaFold, developed by Alphabet subsidiary DeepMind. In July, the company announced that AlphaFold had predicted the structures of 200 million proteins—nearly all known to humankind. And in what CEO Demis Hassabis described as a "gift to humanity," DeepMind made the structures, along with AlphaFold's underlying code, freely available to all. That will likely accelerate the work of scientists around the world trying to solve humanity's toughest problems. The company says AlphaFold is now being used in efforts as diverse as fighting antibiotic resistance and Parkinson's disease, and tackling plastic pollution.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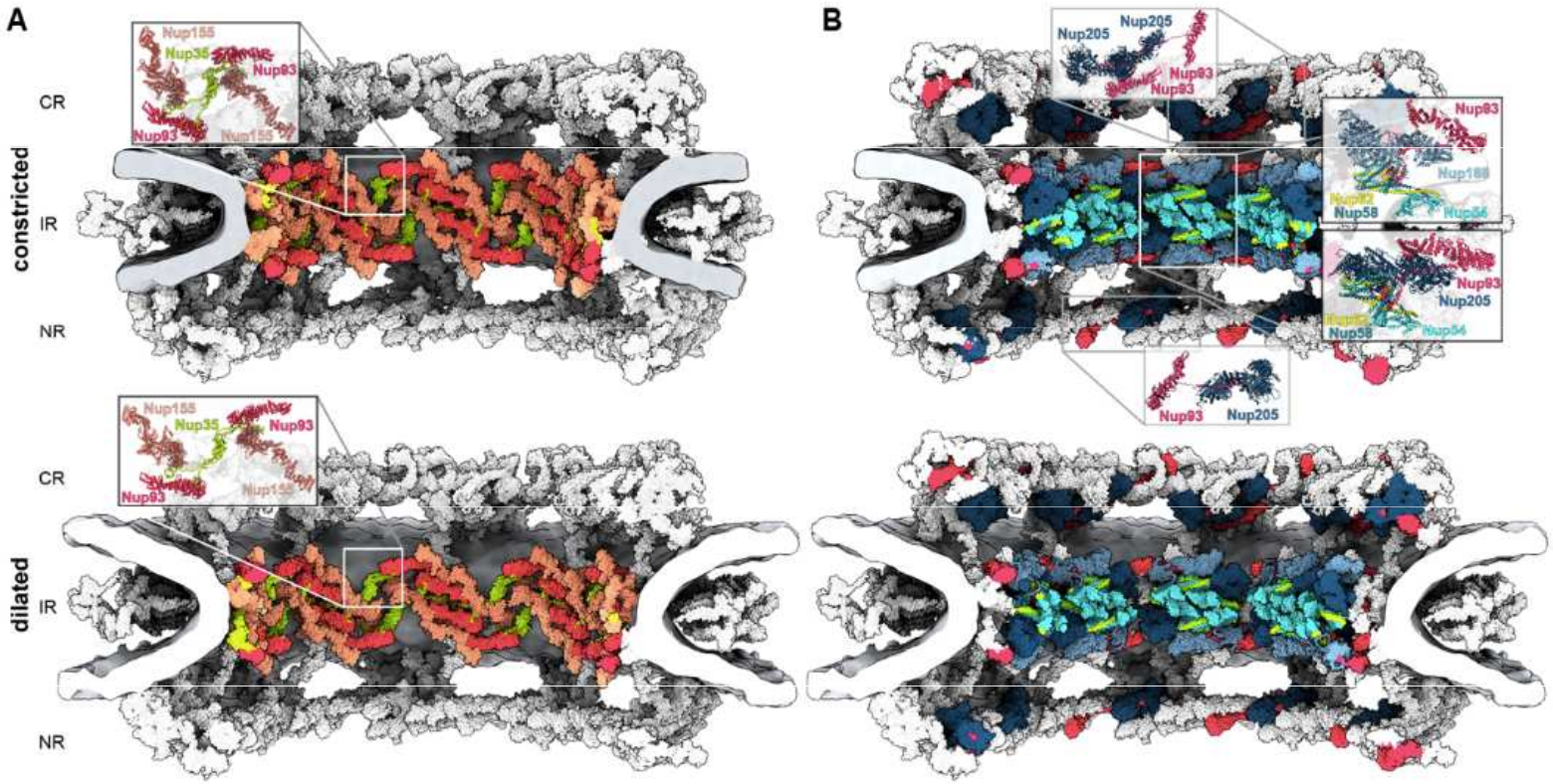
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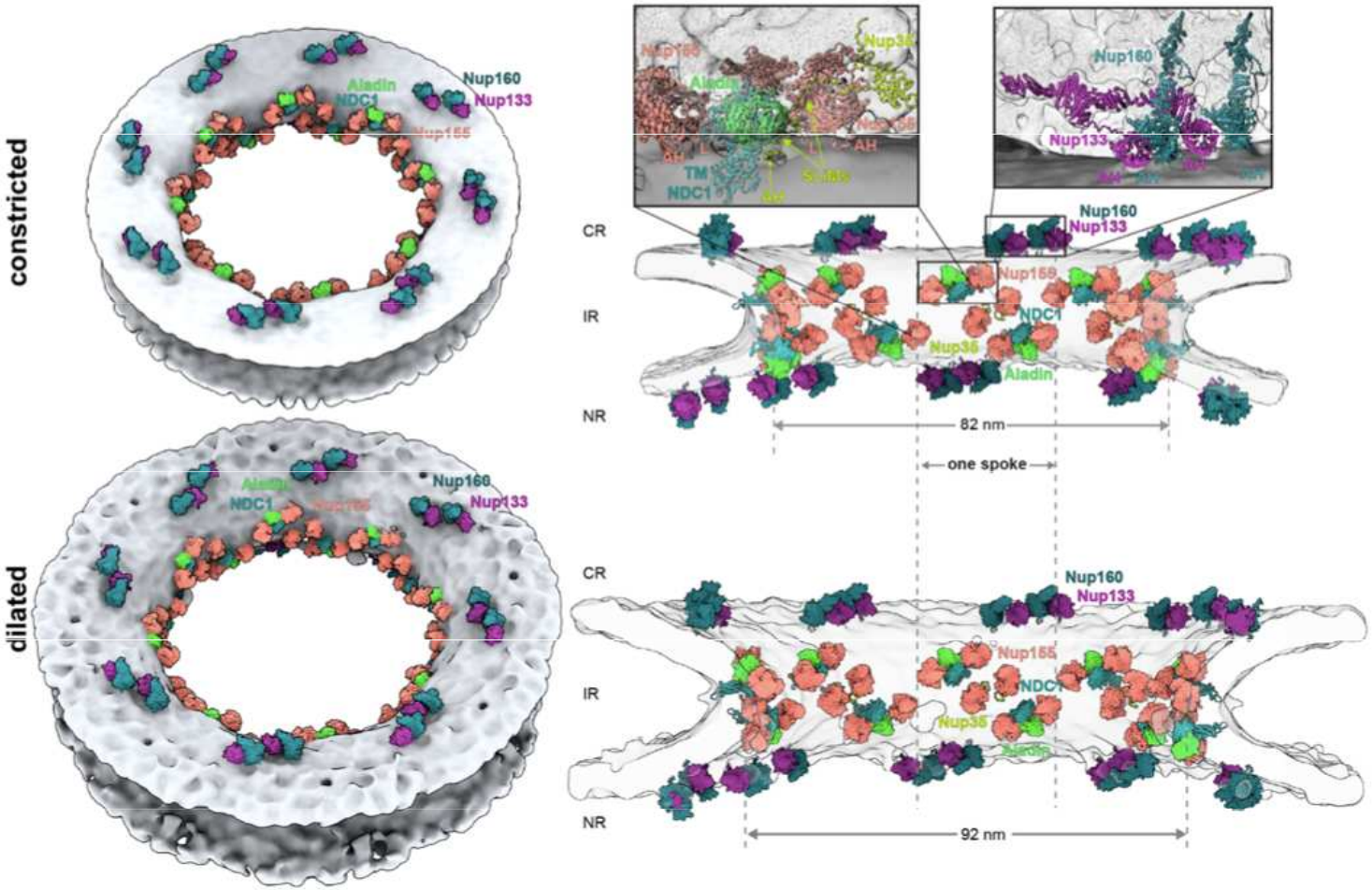
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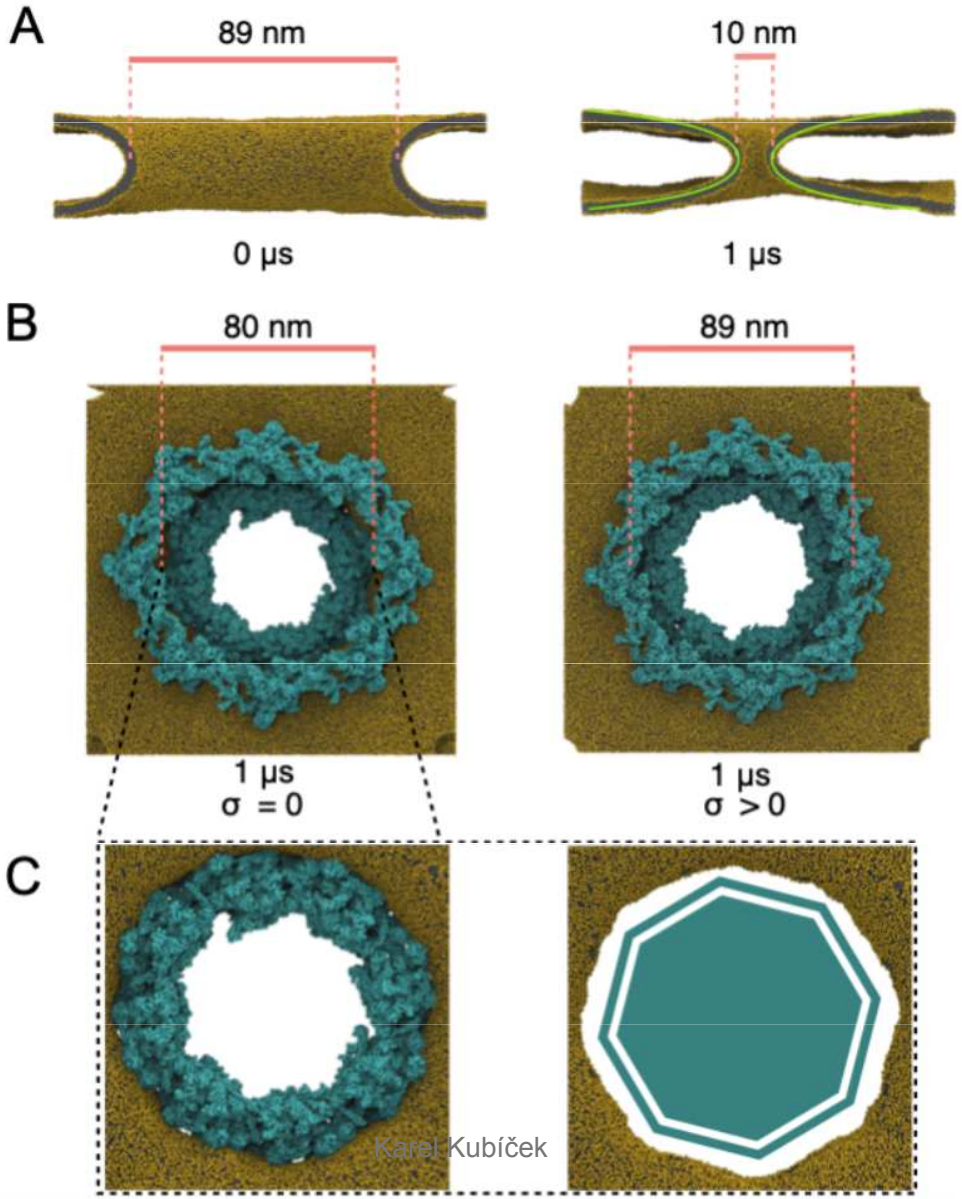
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