

Doc. Mgr. Karel Kubíček, Ph.D.

F1190: Nukleové kyseliny

Nukleové kyseliny

Doporučená literatura:

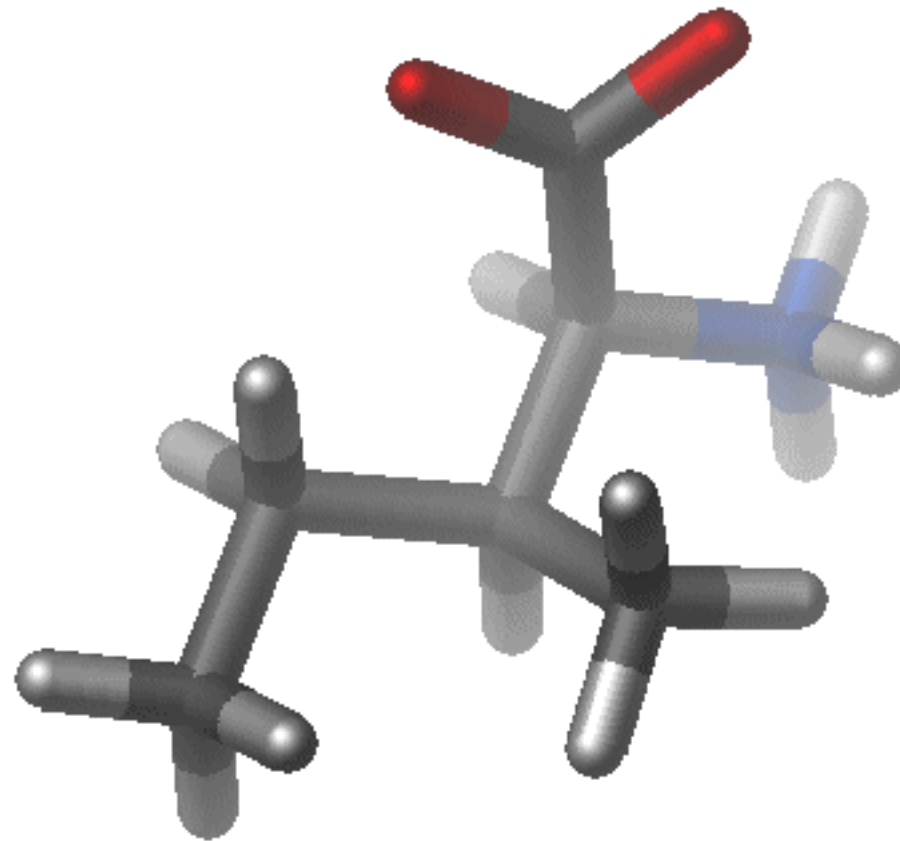
- 1) Neidle, S.: Principles of Nucleic Acid Structure, Elsevier, AP, 2008
- 2) Calladine, C.R., Drew, H.R., Luisi, B.F., Travers, A.A.: Understanding DNA – The Molecule and How It Works, 3rd Ed., Elsevier Academic Press, 2004
- 3) Bates, A.D., Maxwell, A.: DNA Topology, Oxford Bioscience, 2005
- 4) Cotterill, R.: Biophysics: An Introduction, John Wiley & Sons, Ltd. 2002
- 5) Voet, D, and Voetová, J.G.: Biochemie, Victoria Publishing
- 6) Murray, R.K., Granner, D. K., Mayes, P., A., Rodwell, V., W.: Harper's Illustrated Biochemistry, Lange Medical Books, 2003
- 7) Schuenemann, V.: Biophysik: Eine Einfuehrung, Springer, 2005
- 8) Garrett, R.H., Grisham, C.M.: Biochemistry, 2nd ed., 1999
- 9) Bergethon, P.R., The Physical Basis of Biochemistry: The Foundations of Molecular Biophysics, 2nd ed., Springer, 2010

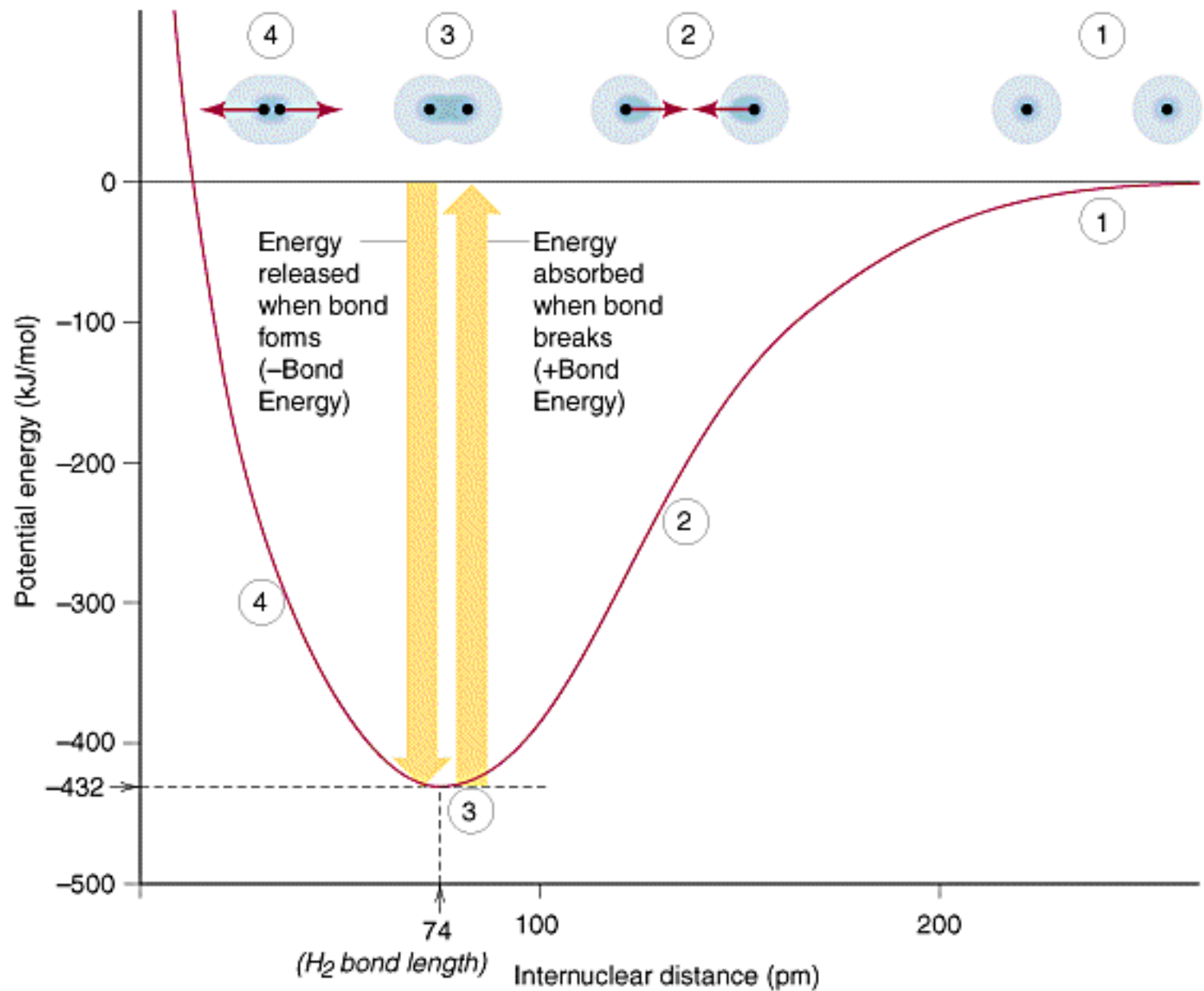
Nukleové kyseliny

-DNA

-RNA

-PNA





Bond stretching

- Morse potential

$$V_{bond} = D_e \{1 - \exp[-a(l - l_0)]\}^2$$

D_e = Depth of potential energy minimum

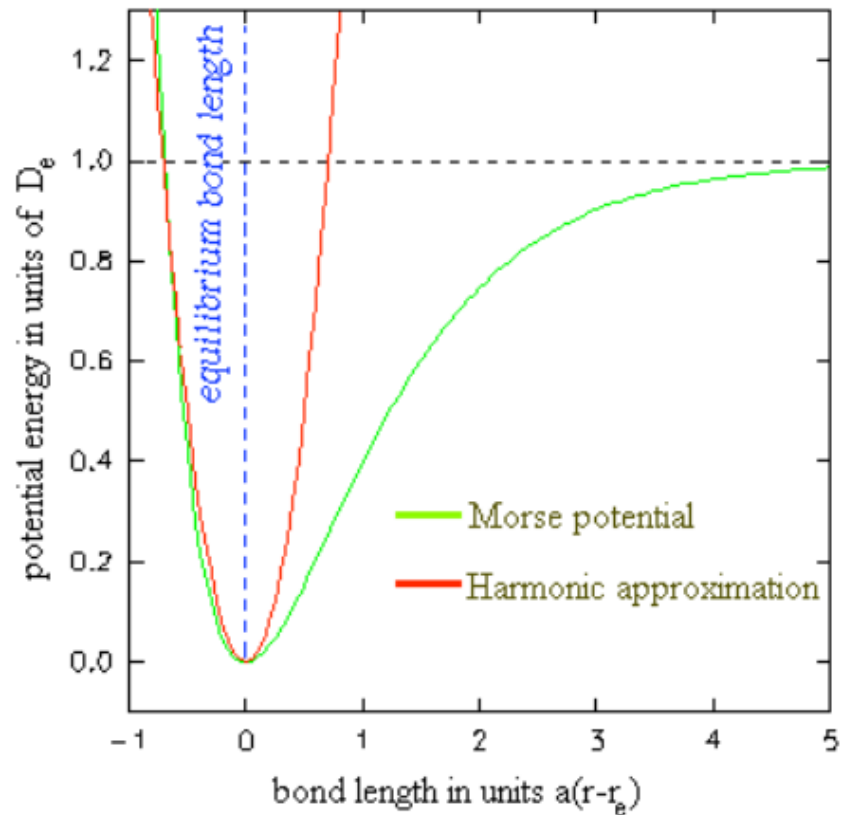
a = Width of the potential well

l_0 = Reference bond length

- Hooke's law

$$V_{bond} = \sum_{bonds} \frac{k_R}{2} (l_i - l_{i,0})^2$$

- (Does not allow bond breaking/ forming therefore cannot handle chemical reactions; need to use other method e.g. QM/MM, Morse potential)



© O. S. Smart, 1995

MM calculations typically do not go far from reference value

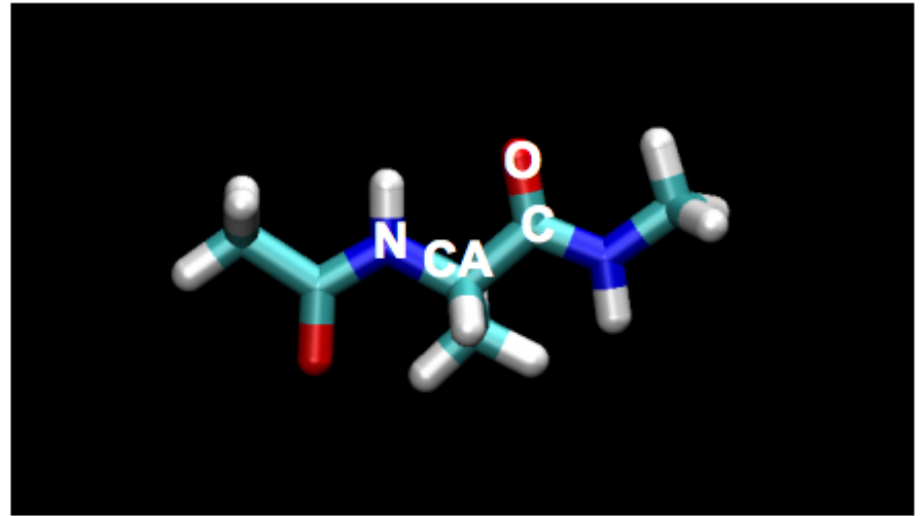
Bond stretching parameters

$$V_{bond} = \sum_{bonds} \frac{k_R}{2} (l_i - l_{i,0})^2$$

- k_R = obtained from vibrational spectra
- l_0 = obtained from X-ray crystallography
- Hard degree of freedom

If $dl = .2\text{\AA}$ for carbonyl

$V_{bond} = 11.4 \text{ kcal/mol} !!!$



Type	k_R (kcal/mol/ \AA^2)	L_0 (\AA)
CA-N	337	1.44
C=O	570	1.22

ΔThe disulfide (-**S-S**-) bond is strong, with a typical bond dissociation energy of 60 kcal/mole (251 kJ mol⁻¹). However, being about 40% weaker than C-C and C-H bonds, length ~205pm (cca 50pm longer than -C-C-).

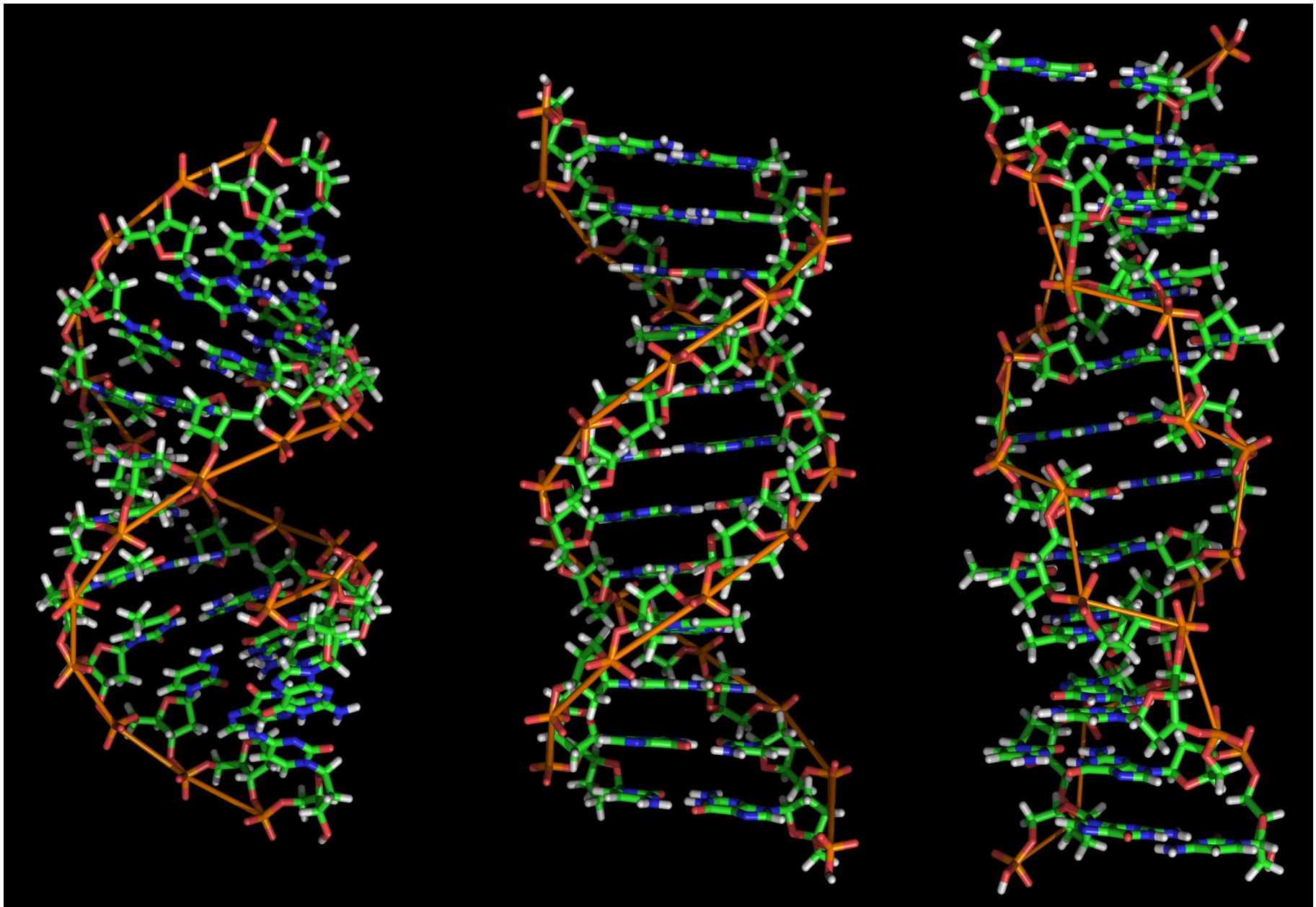
Bond	Length (pm)	E(kJ/mol)
H-H	74	436
H-C	109	413
H-N	101	391
H-O	96	366
H-F	92	568
C-C	154	348
C=C	134	614
C-N	147	308
C-O	143	360
C-S	182	272
C-F	135	488
N-N	145	170
O-O	148	145
O=O	121	498

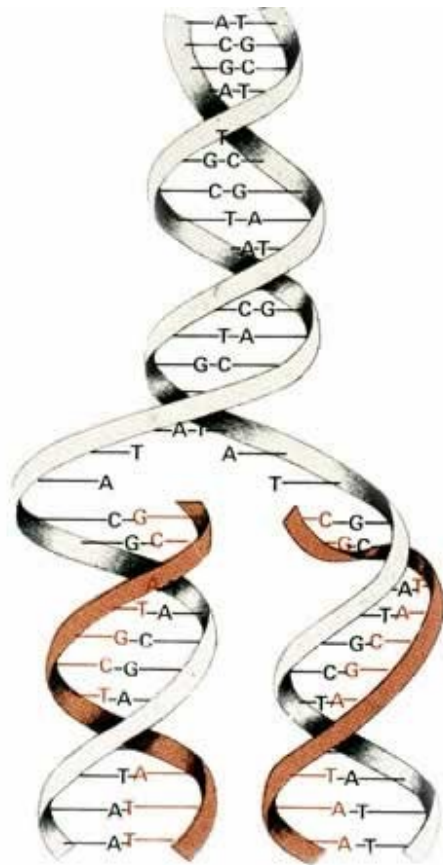
$$1\text{kcal}=4.184\text{kJ}; \quad \text{pm}=1.10^{-12}\text{m}$$

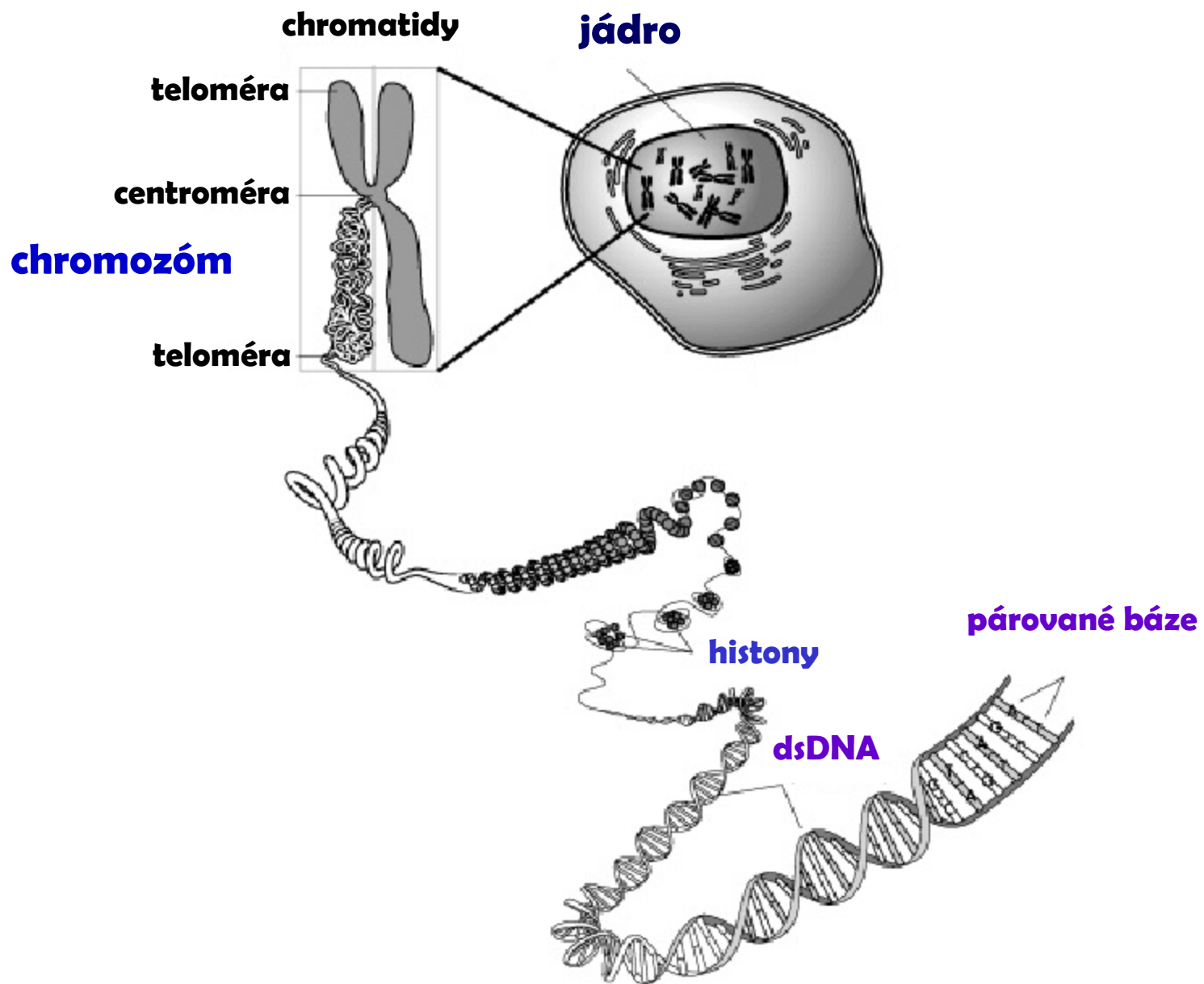
F–H... : F (161.5 kJ/mol or 38.6 kcal/mol)
 O–H... : N (29 kJ/mol or 6.9 kcal/mol)
 O–H... : O (21 kJ/mol or 5.0 kcal/mol)
 N–H... : N (13 kJ/mol or 3.1 kcal/mol)
 N–H... : O (8 kJ/mol or 1.9 kcal/mol)
 HO–H... : OH⁺₃ (18 kJ/mol[10] or 4.3 kcal/mol; data obtained using molecular dynamics as detailed in the reference and should be compared to 7.9 kJ/mol for bulk water, obtained using the same molecular dynamics.)

Table 1. General characteristics of the three major types of H-bonds. The numerical information shows the comparative trends only [13]

H-bond parameters	Strong	Moderate	Weak
Interaction type	Strongly covalent	Mostly electrostatic	Electrostatic/dispersed
Bond lengths (H...Y[Å])	1.2–1.5	1.5–2.2	>2.2
Lengthening of X–H (Å)	0.08–0.25	0.02–0.08	<0.02
X–H Vs. H...Y	X–H ≈ H...Y	X–H < H...Y	X–H << H...Y
H-bond length (X·Y [Å])	2.2–2.5	2.5–3.2	>3.2
Directionality	Strong	Moderate	Weak
H-bond angles (°)	170–180	>130	>90
H-bond strength (kcal/mol)	15–40	4–15	<4
Relative Infrared shift (cm ⁻¹)	25%	10–25%	<10%







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**

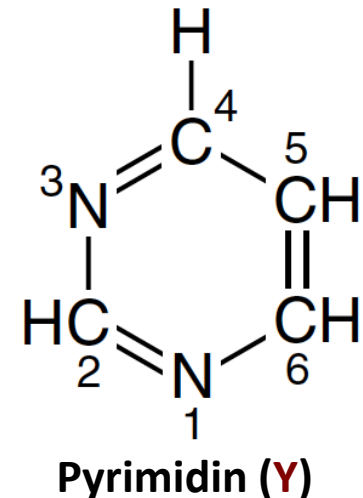
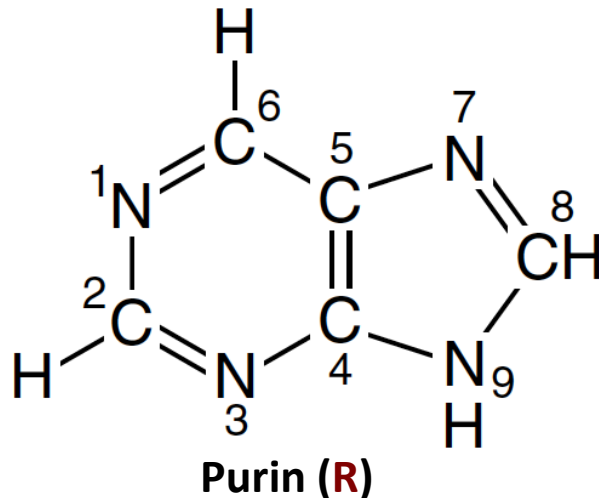
2) Cukr – 2'-deoxyribóza (**DNA**), ribóza (**RNA**)

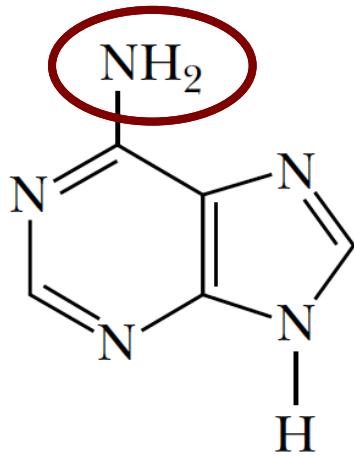
3) Fosfát

Báze:

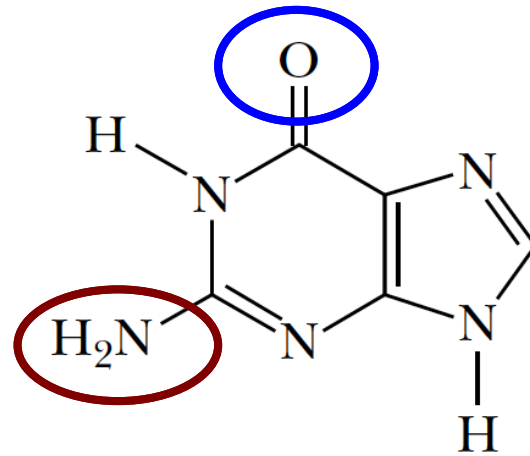
1) Standardní

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

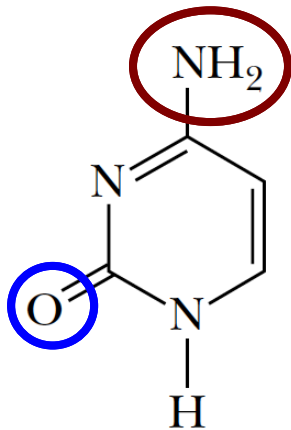




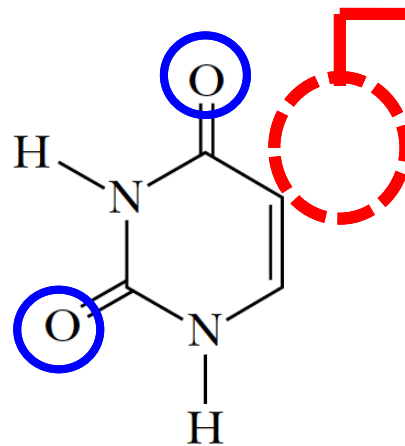
Adenine
(6-amino purine)



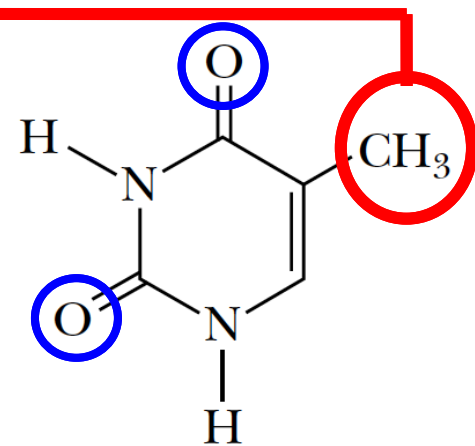
Guanine
(2-amino-6-oxy purine)



Cytosine
(2-oxy-4-amino
pyrimidine)

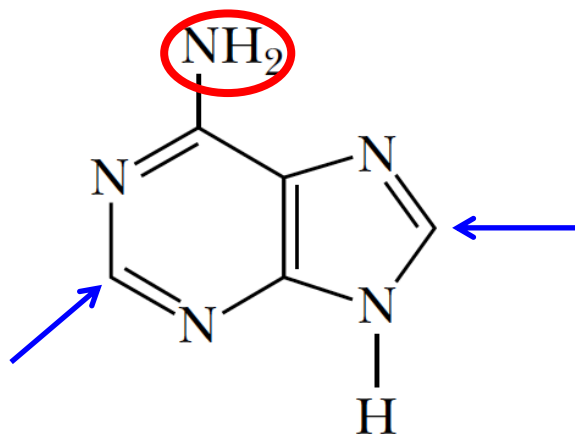


Uracil
(2-oxy-4-oxy
pyrimidine)

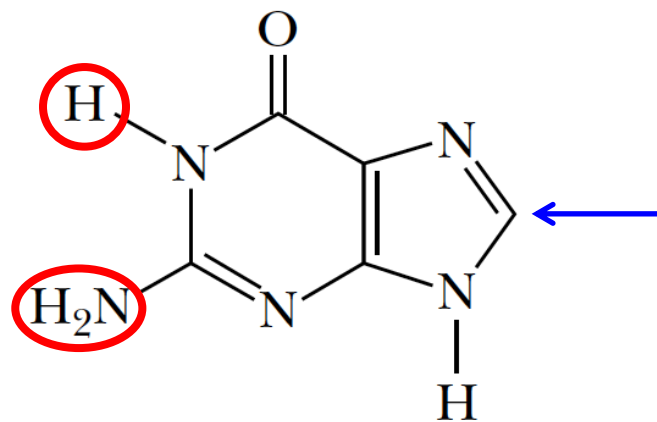


Thymine
(2-oxy-4-oxy
5-methyl pyrimidine)

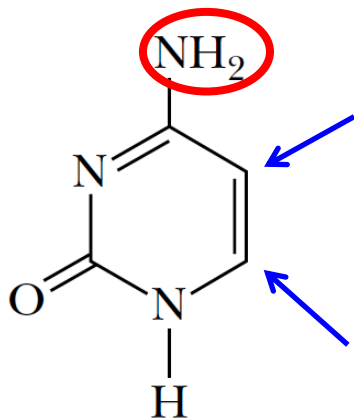
Vyměnitelné a aromatické vodíkové atomy



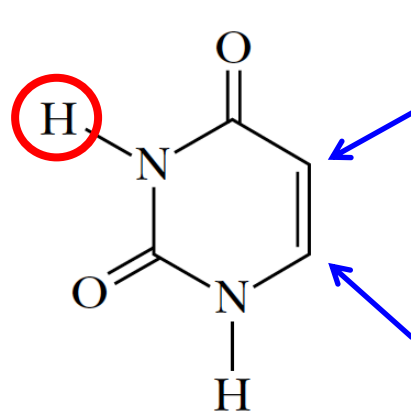
Adenine
(6-amino purine)



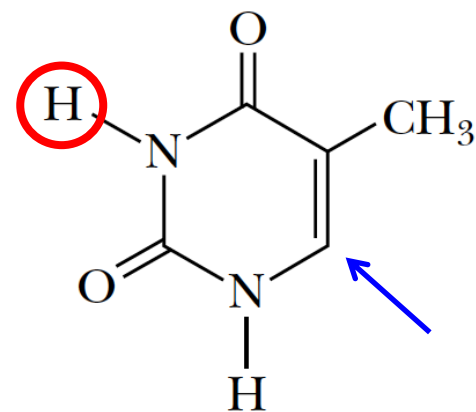
Guanine
(2-amino-6-oxo purine)



Cytosine
(2-oxo-4-amino pyrimidine)

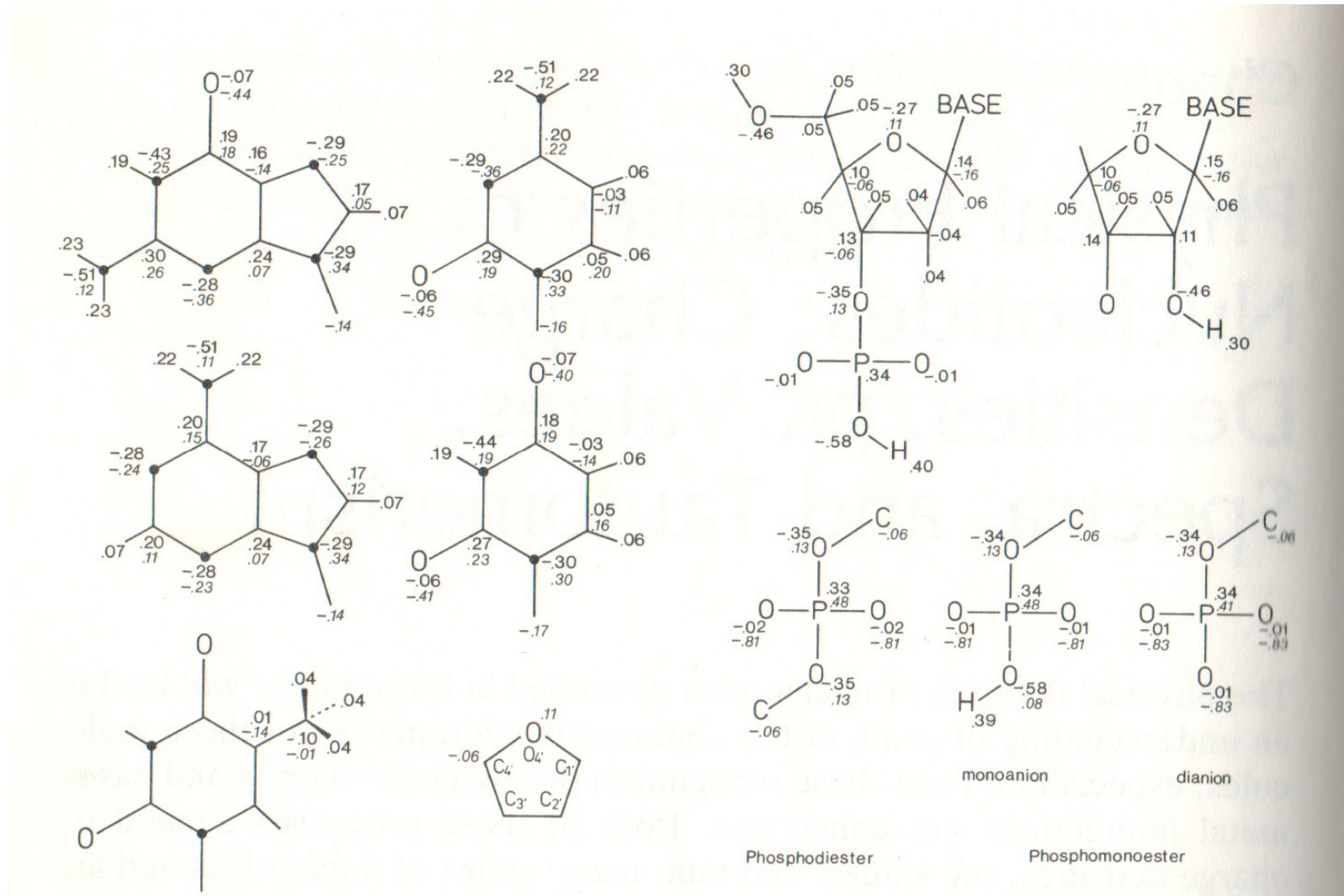


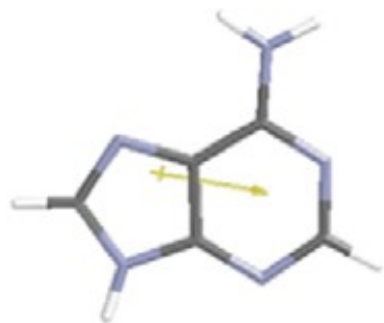
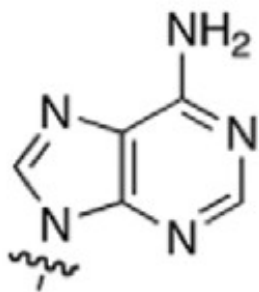
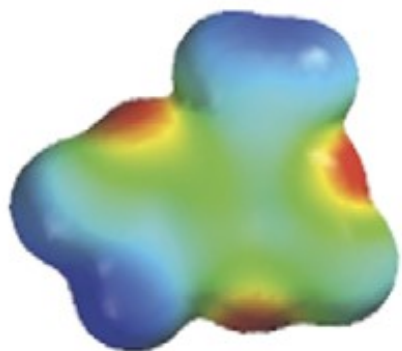
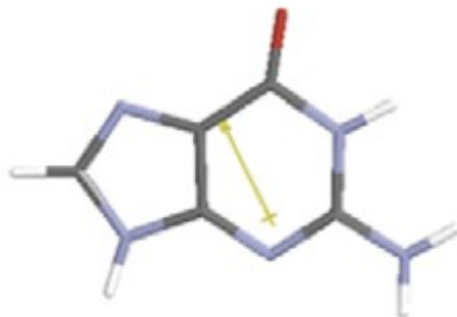
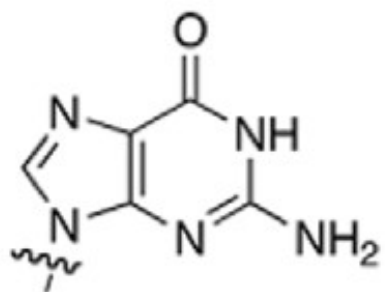
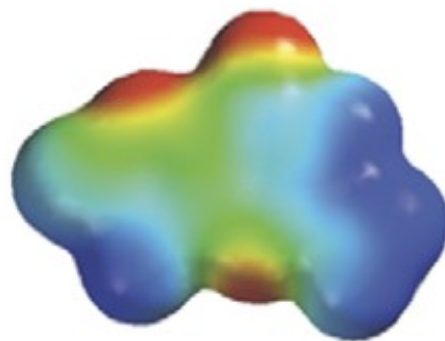
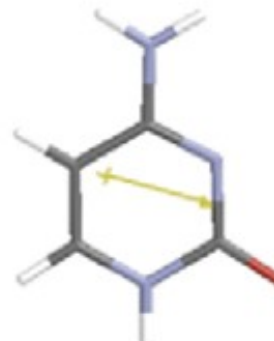
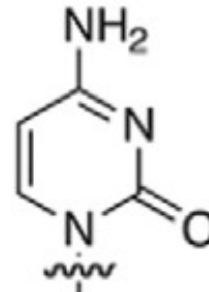
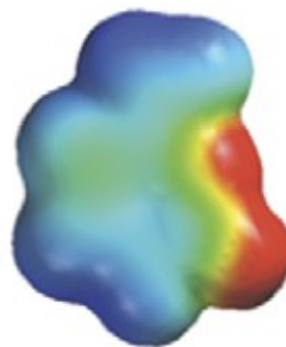
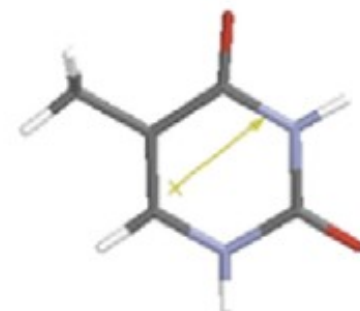
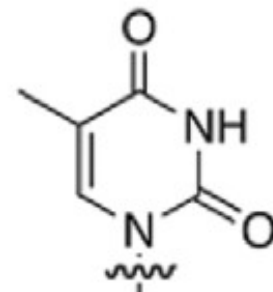
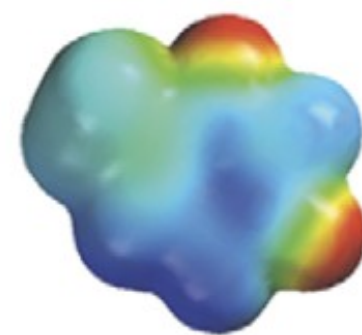
Uracil
(2-oxo-4-oxo pyrimidine)



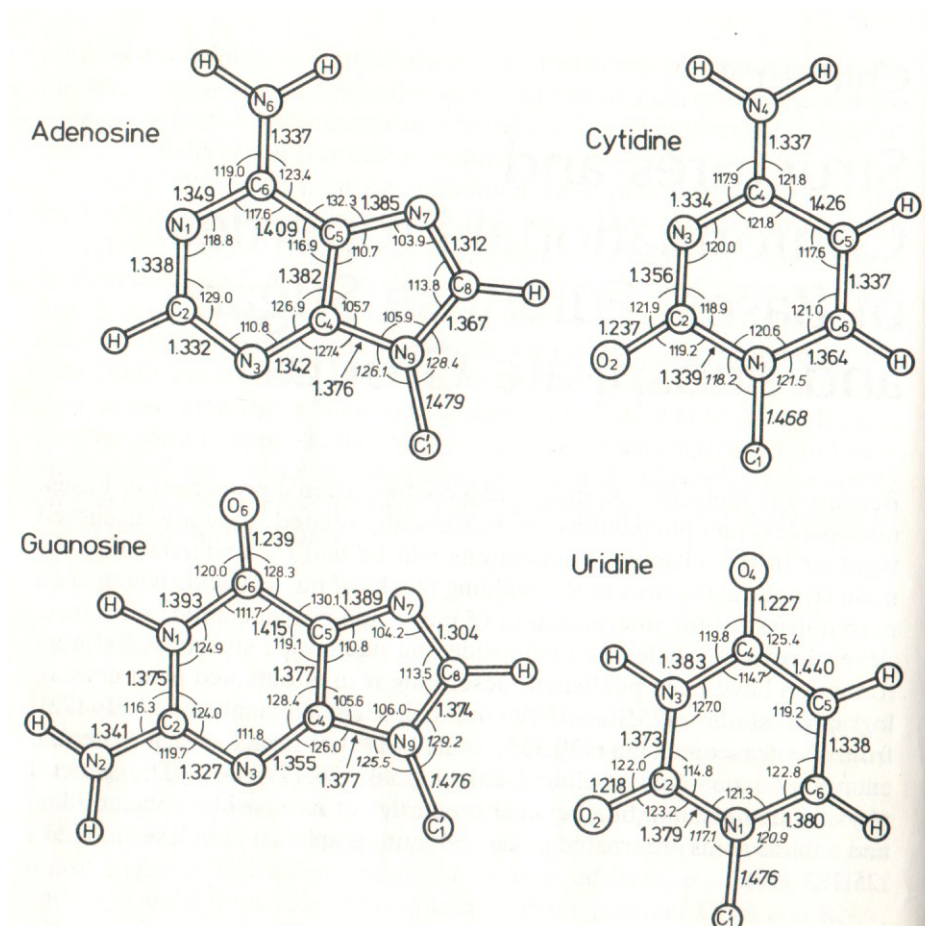
Thymine
(2-oxo-4-oxo 5-methyl pyrimidine)

Hustoty nábojů v nukleotidech rozdělené podle Del Reho σ nábojů (Roman) a Hückelových π nábojů (kurzíva)

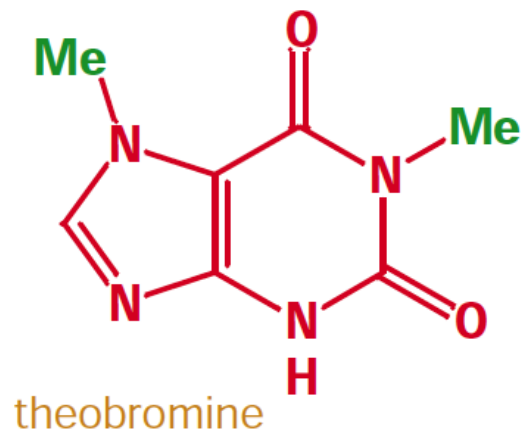
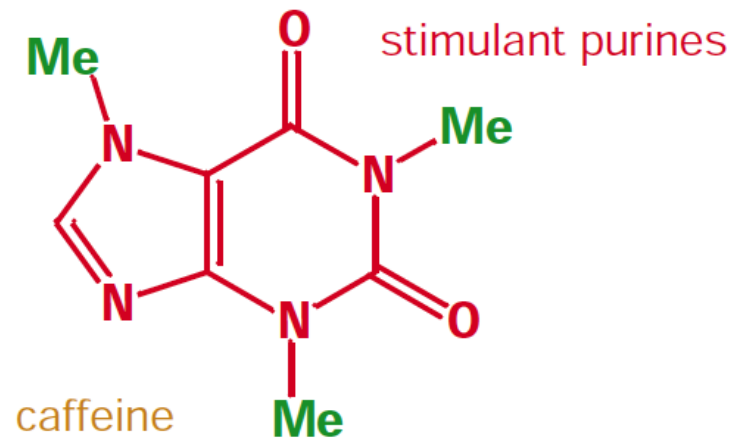
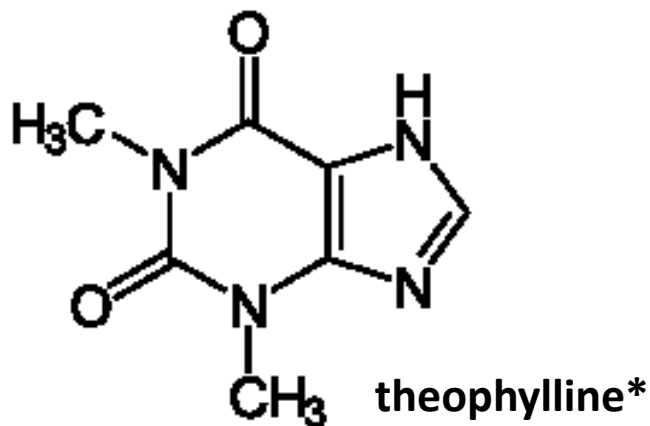


A**2.2 debye****G****5.9 debye****C****6.1 debye****T****4.0 debye**

Vazebné parametry bází nukleových kyselin



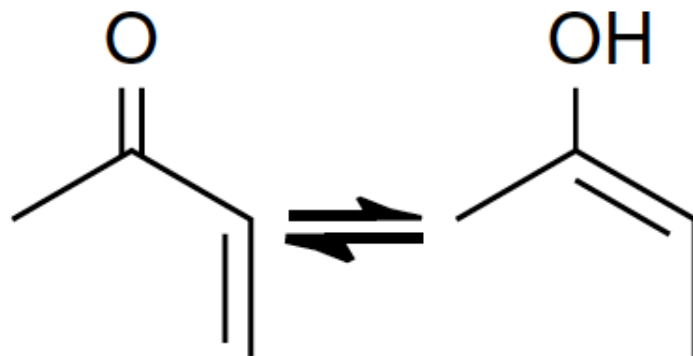
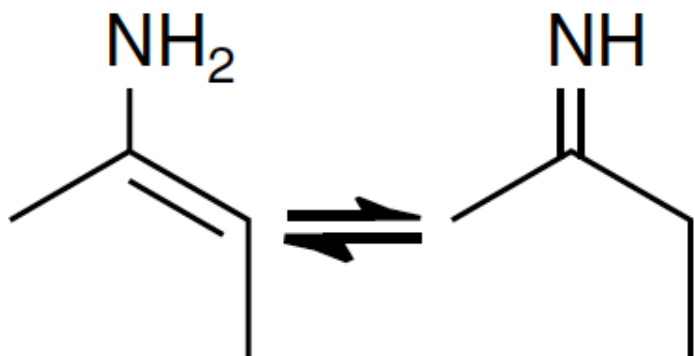
Stimulanty obsažené v kávě , čaji a čokoládě jsou metylované puriny



Me=CH₃

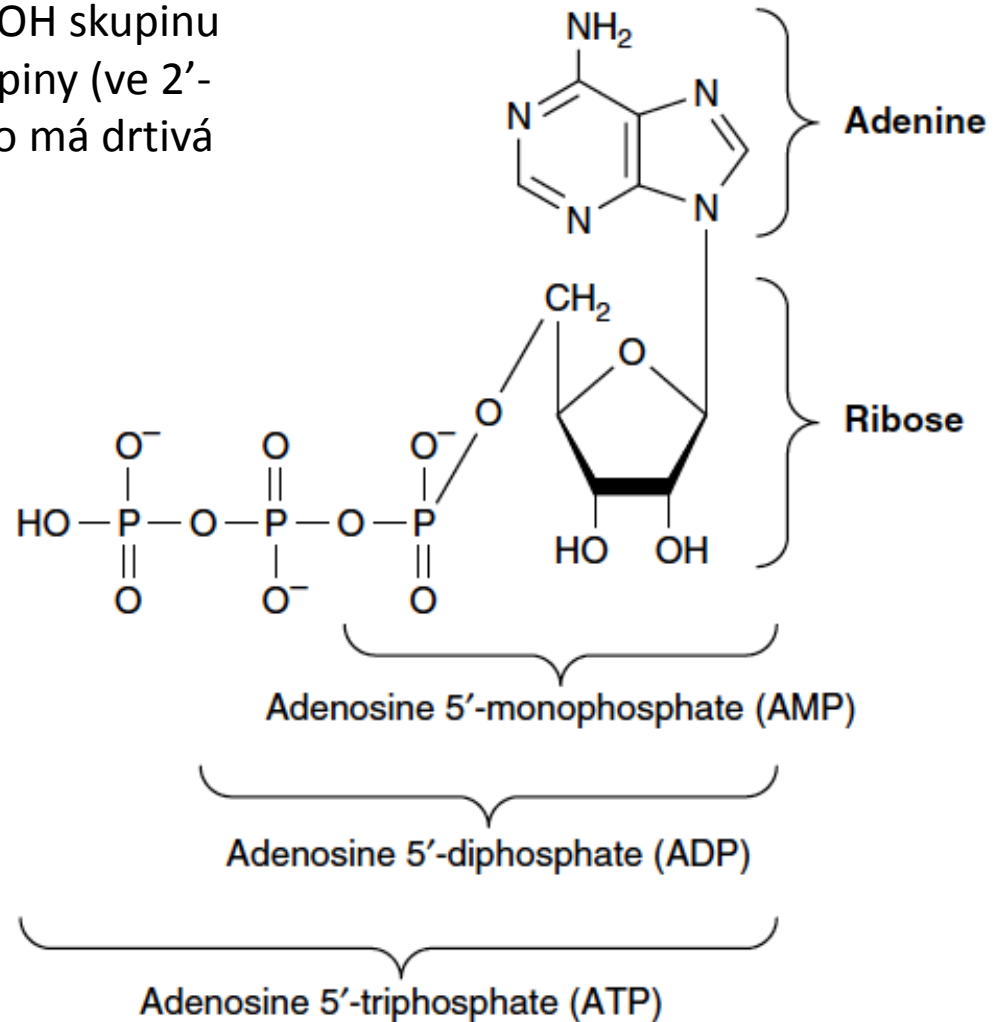
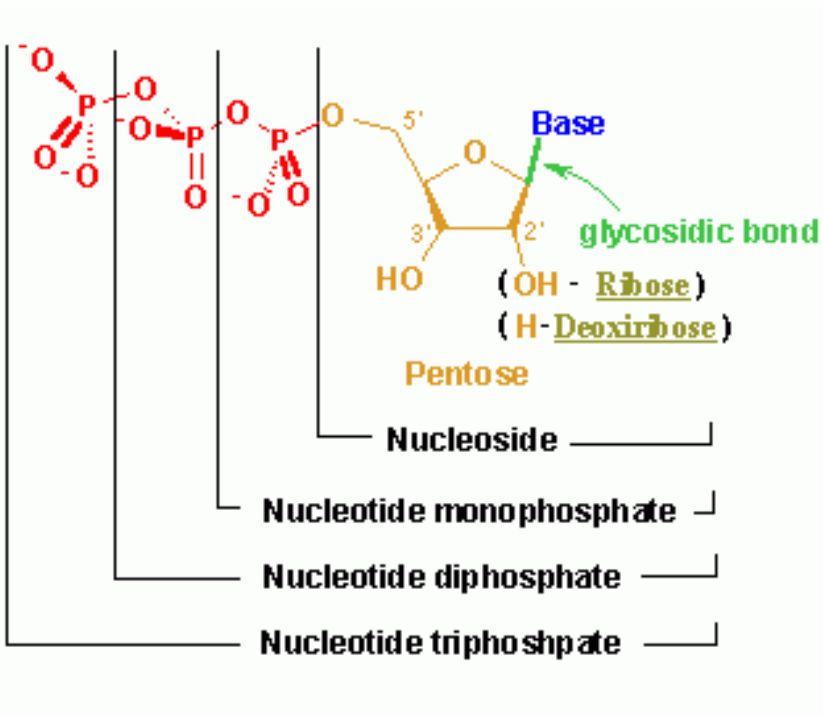
* Obsažen v čaji, ale není stimulantem

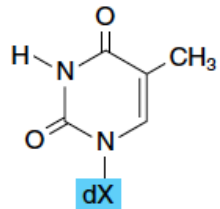
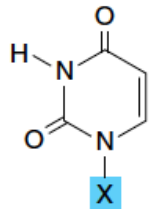
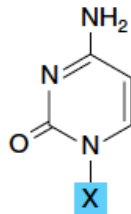
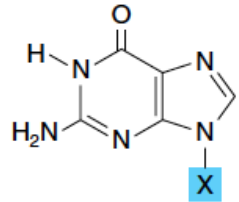
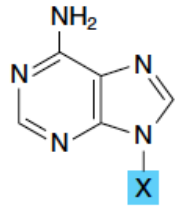
Tautomerie amino (amin \leftrightarrow imin) a keto (keto \leftrightarrow enol forma) skupin purinů a pyrimidinů, fyziologické podmínky favorizují amino a keto formy



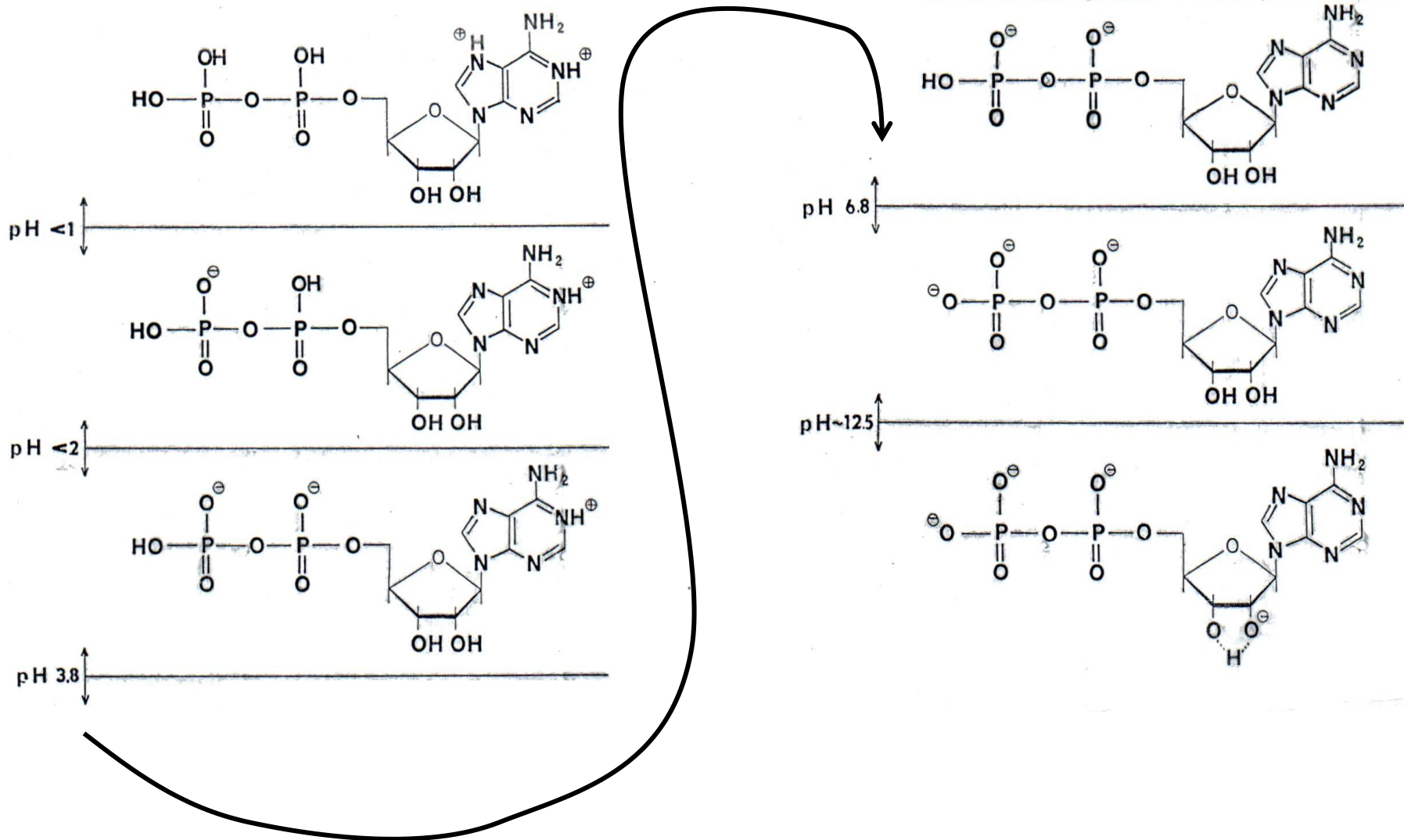
Nukleosidy a nukleotidy

Nukleotid vzniká esterifikací fosforýlu na –OH skupinu nukleosidu. V riboze lze esterifikovat 3 skupiny (ve 2'-deoxy-riboze pouze 2 –OH skupiny) , přesto má drtivá většina ribonukleotidů fosfát v poloze 5'.

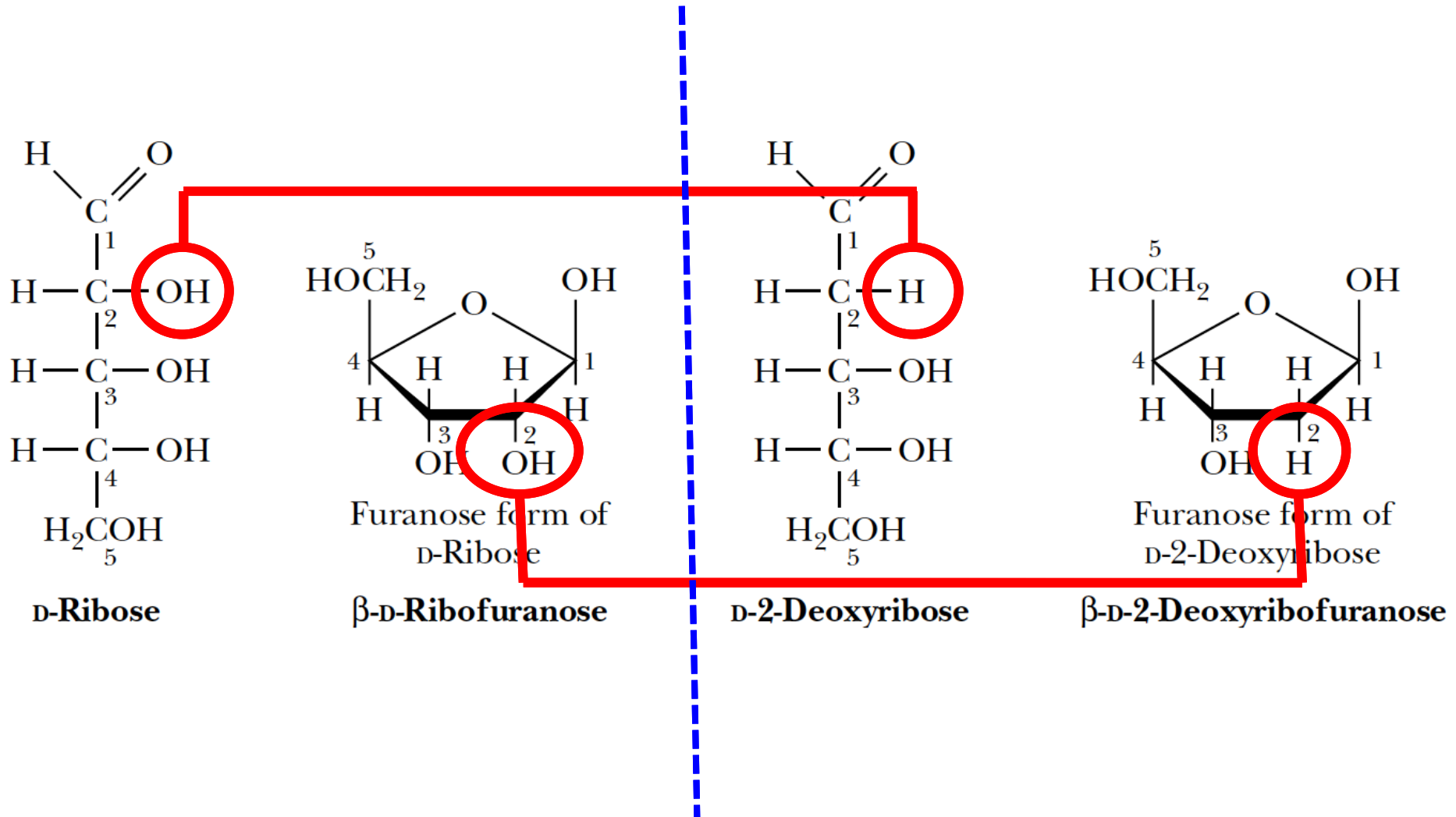


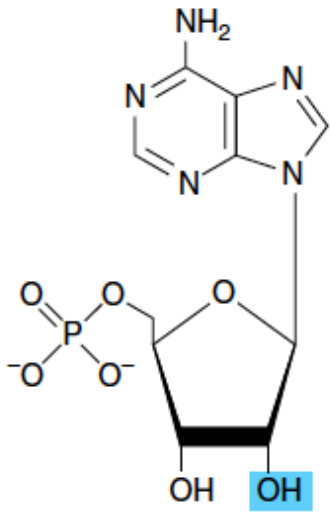


Název báze, X=H	Nukleosid, X=(deoxy)ribóza	Nukleotid, X= fosfo.ribóza
Adenin	Adenosin	Adenosinmonofosfát AMP
Guanin	Guanosin	Guanosinmonofosfát GMP
Cytosin	Cytidin	Cytidinmonofosfát CMP
Uracil	Uridin	Uridinmonofosfát UMP
Thymin	Thymidin	Thymidinmonofosfát TMP

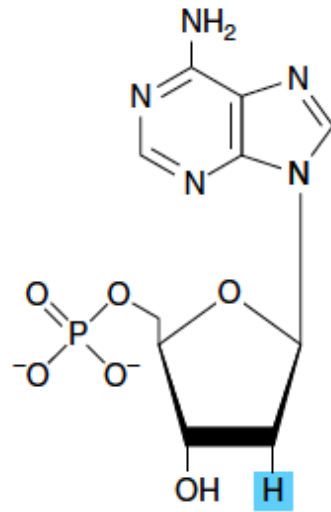


Cukr

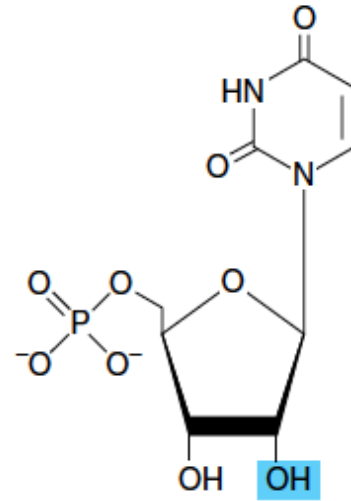




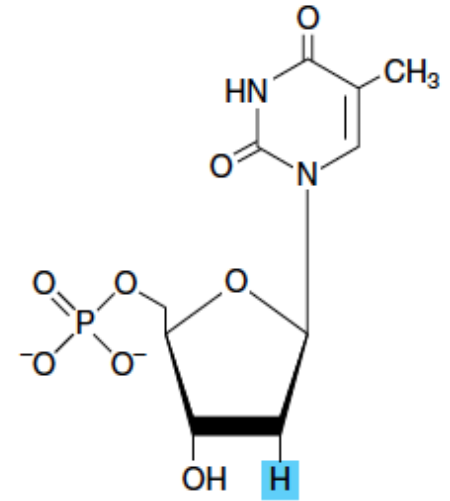
AMP



dAMP

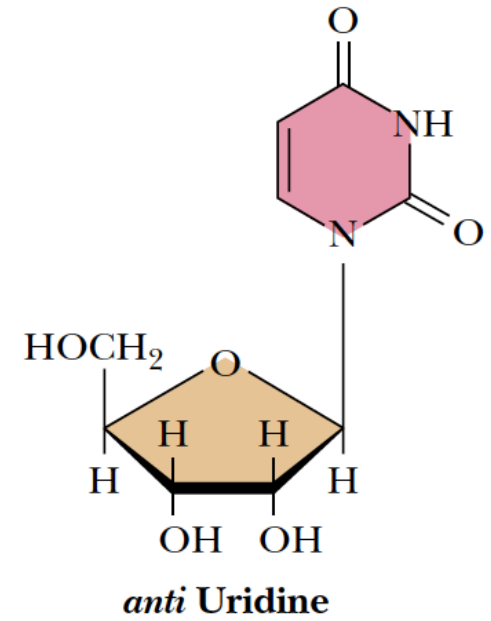
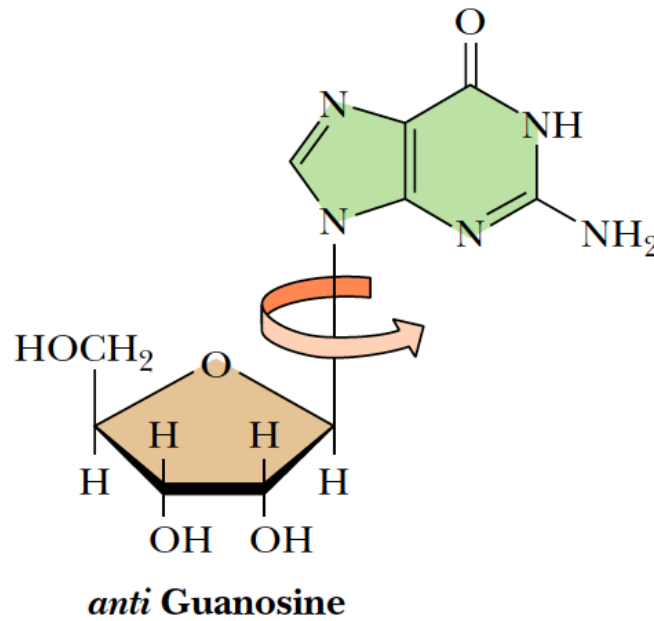
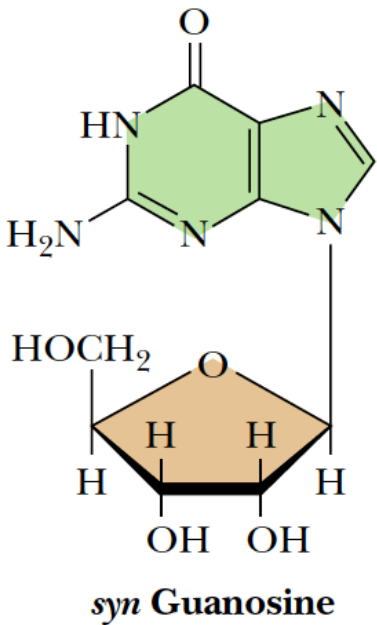


UMP

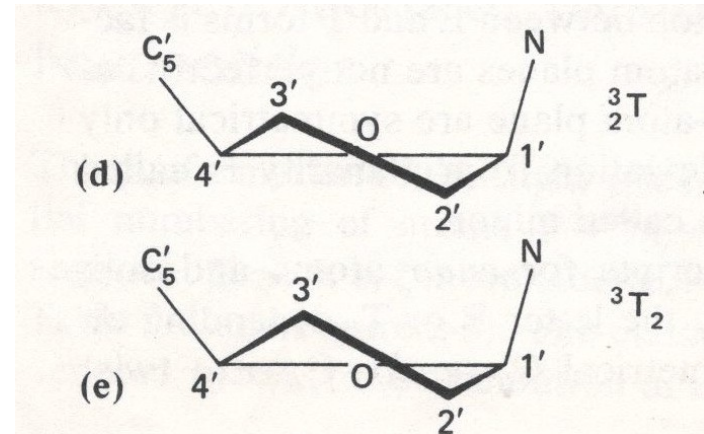
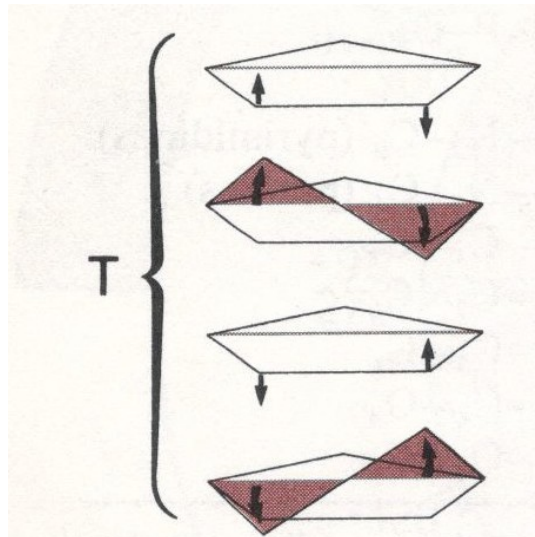
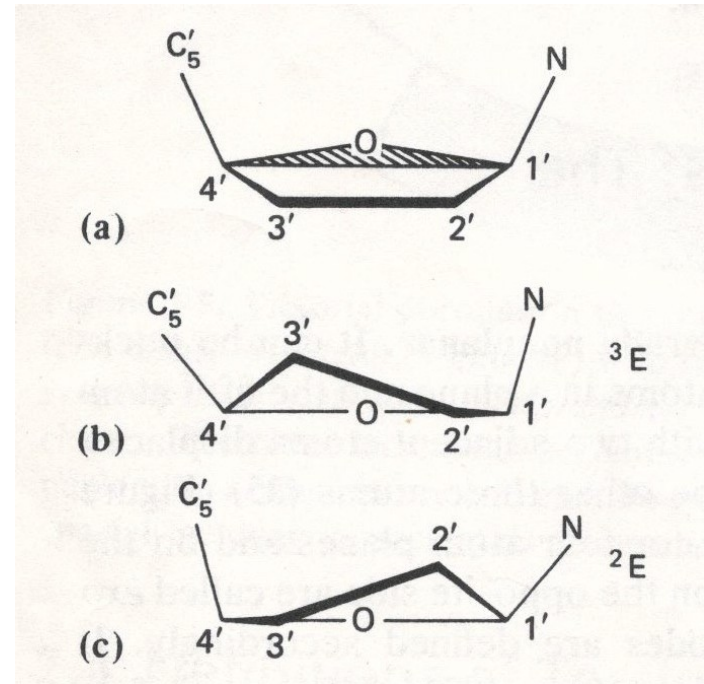
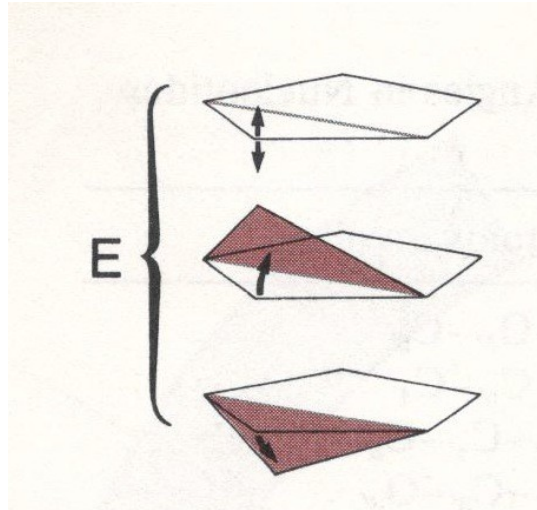


dTMP

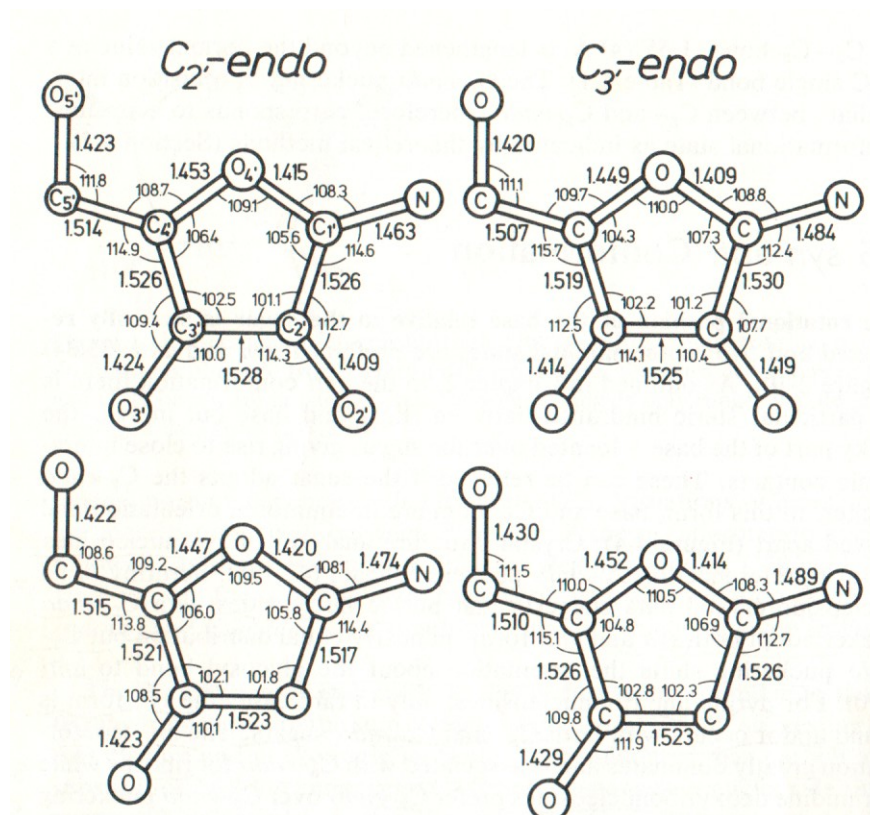
Vlivem stérického bránění báze se vyskytují dvě konformační uspořádání báze-cukr: *syn/anti*
Oba způsoby uspořádání se vyskytují v přírodě, přičemž **ANTI** převažuje



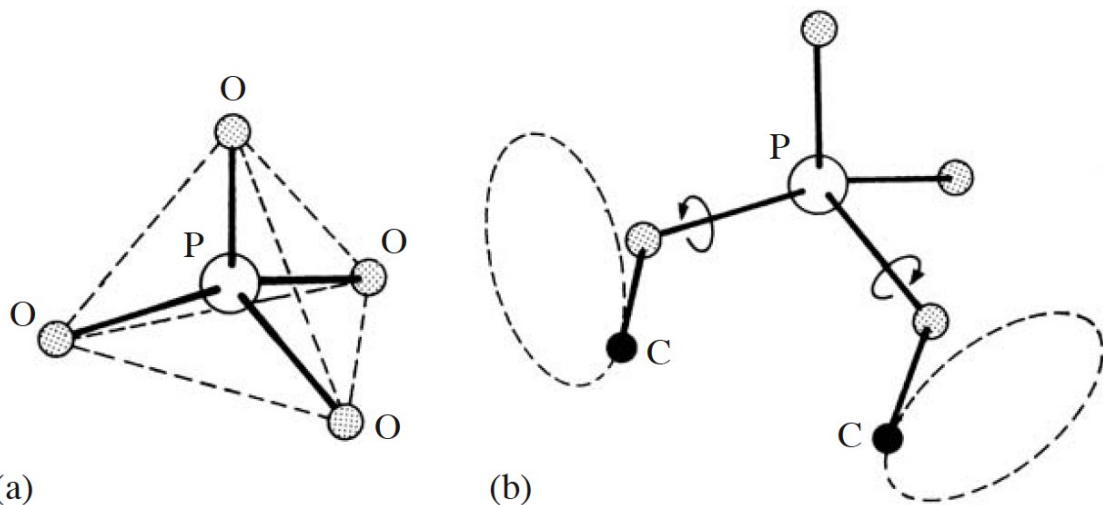
Konformace cukru - Sugar pucker



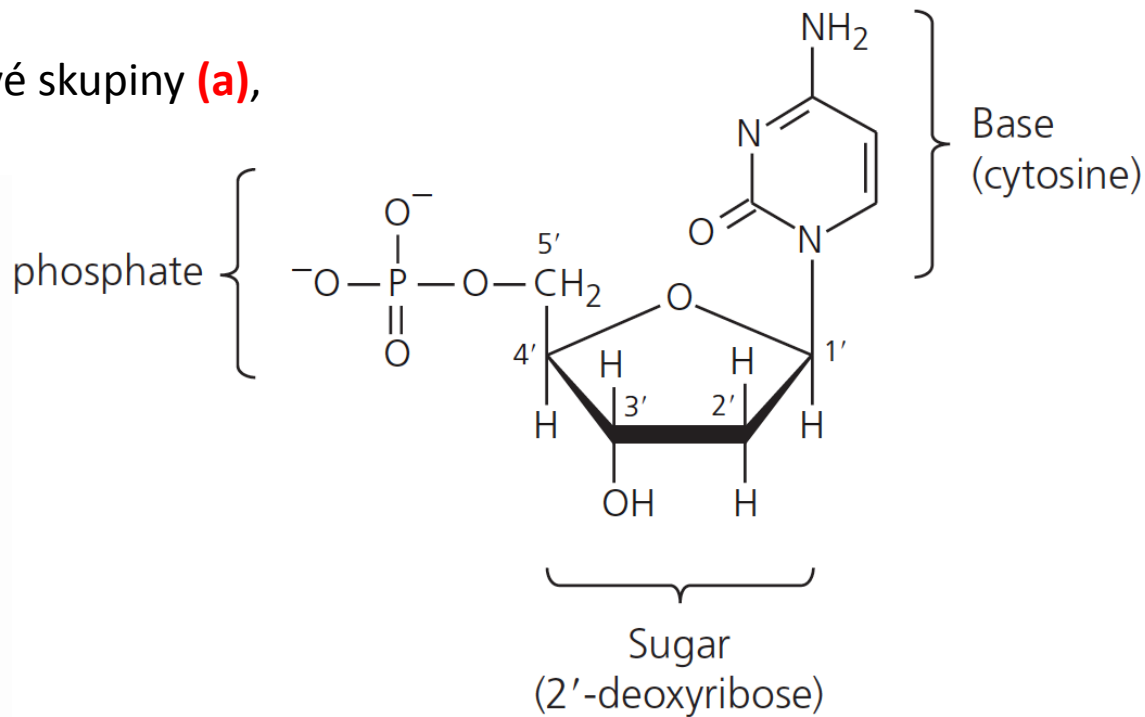
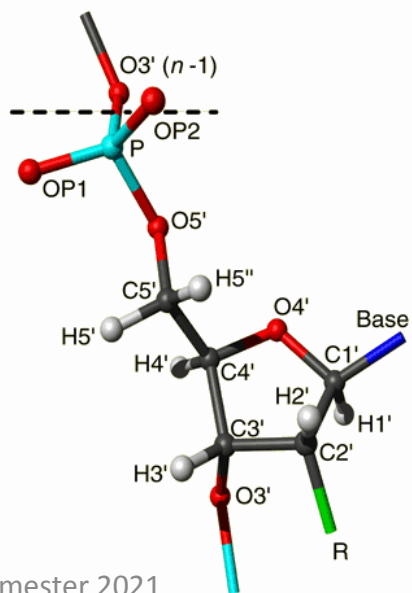
Vazebné parametry cukerných zbytků nukleových kyselin



Fosfát; páteř nukleové kyseliny

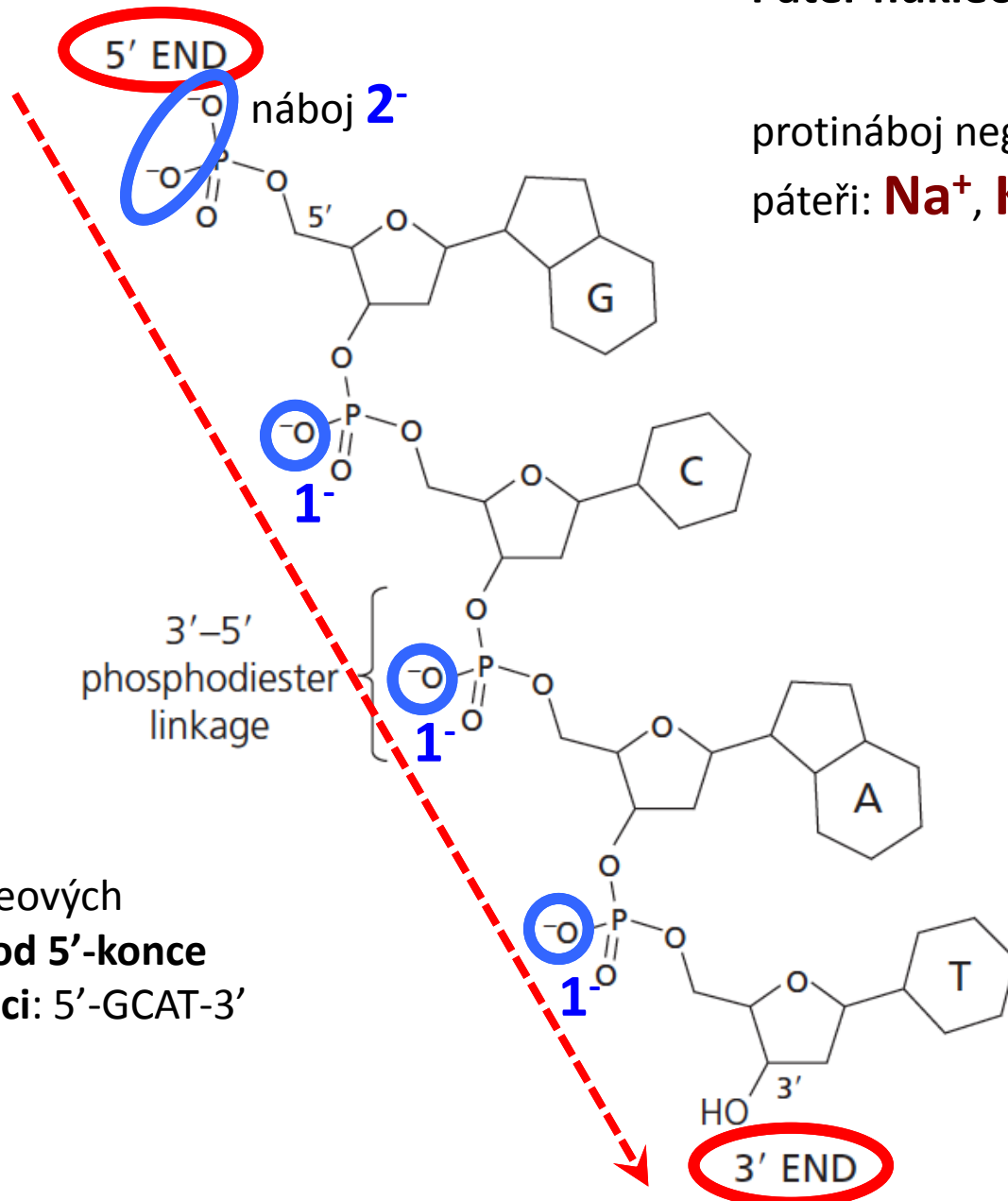


Tetraedrání uspořádání fosfátové skupiny **(a)**,
volnost rotace **(b)**



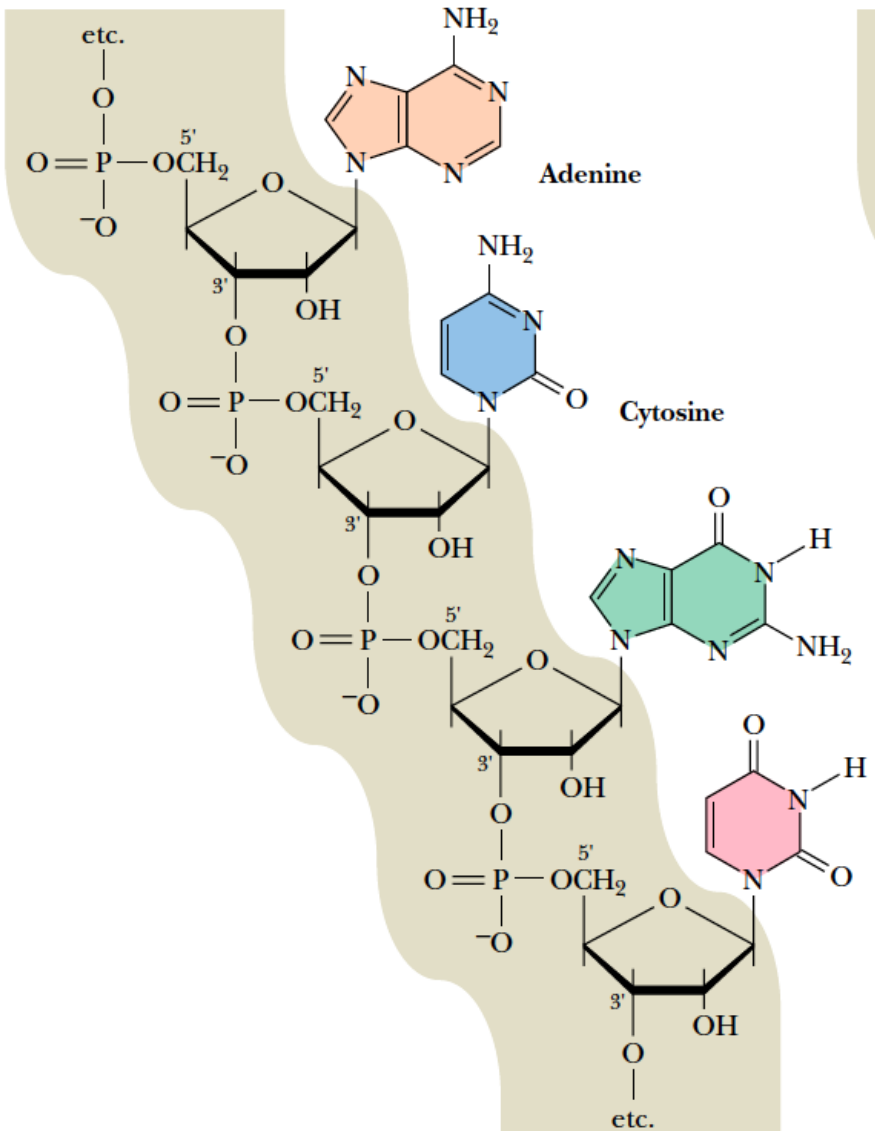
Páteř nukleové kyseliny

protináboj negativně nabitě
páteři: **Na⁺**, **K⁺**

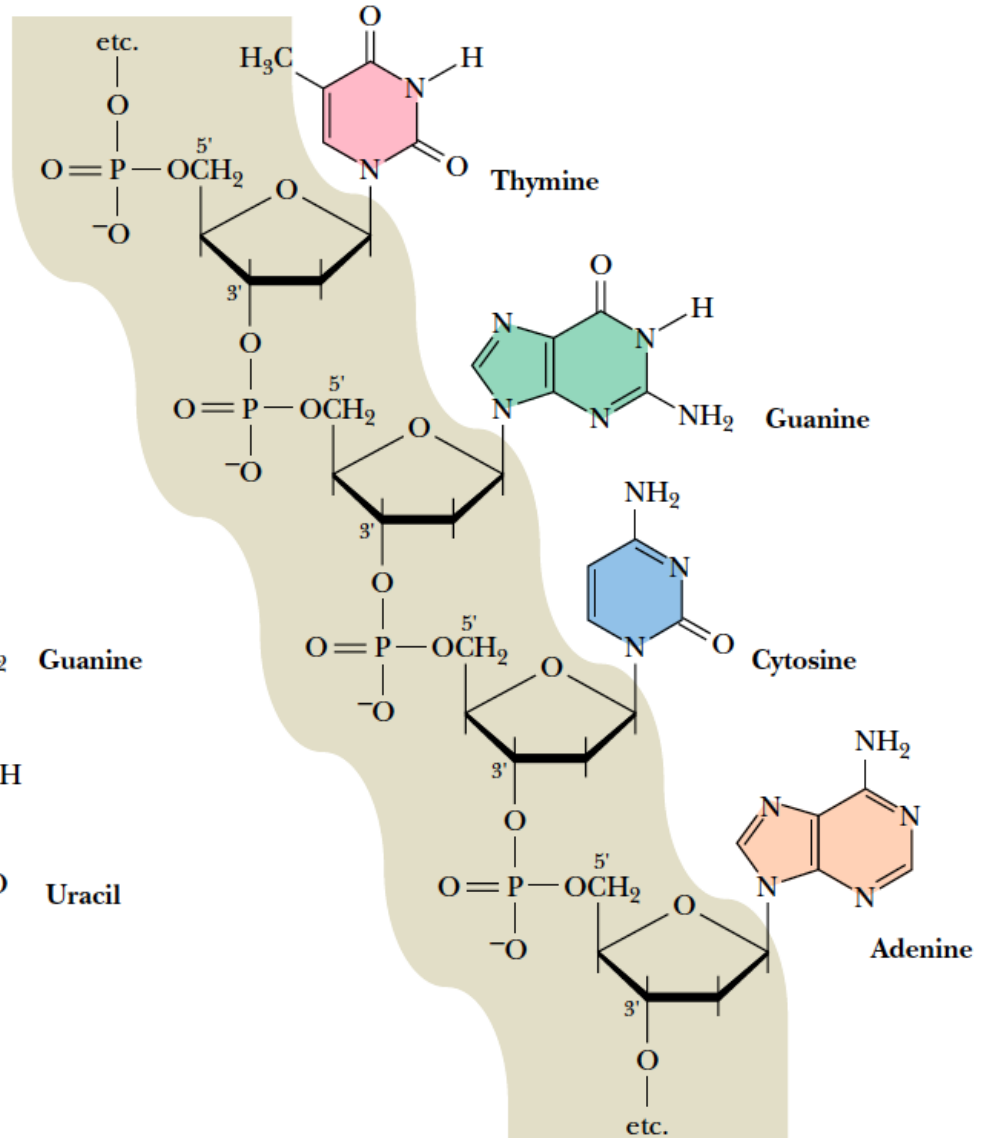


Báze v páteři nukleových
kyselin číslujeme **od 5'-konce**
směrem **ke 3'-konci**: 5'-GCAT-3'

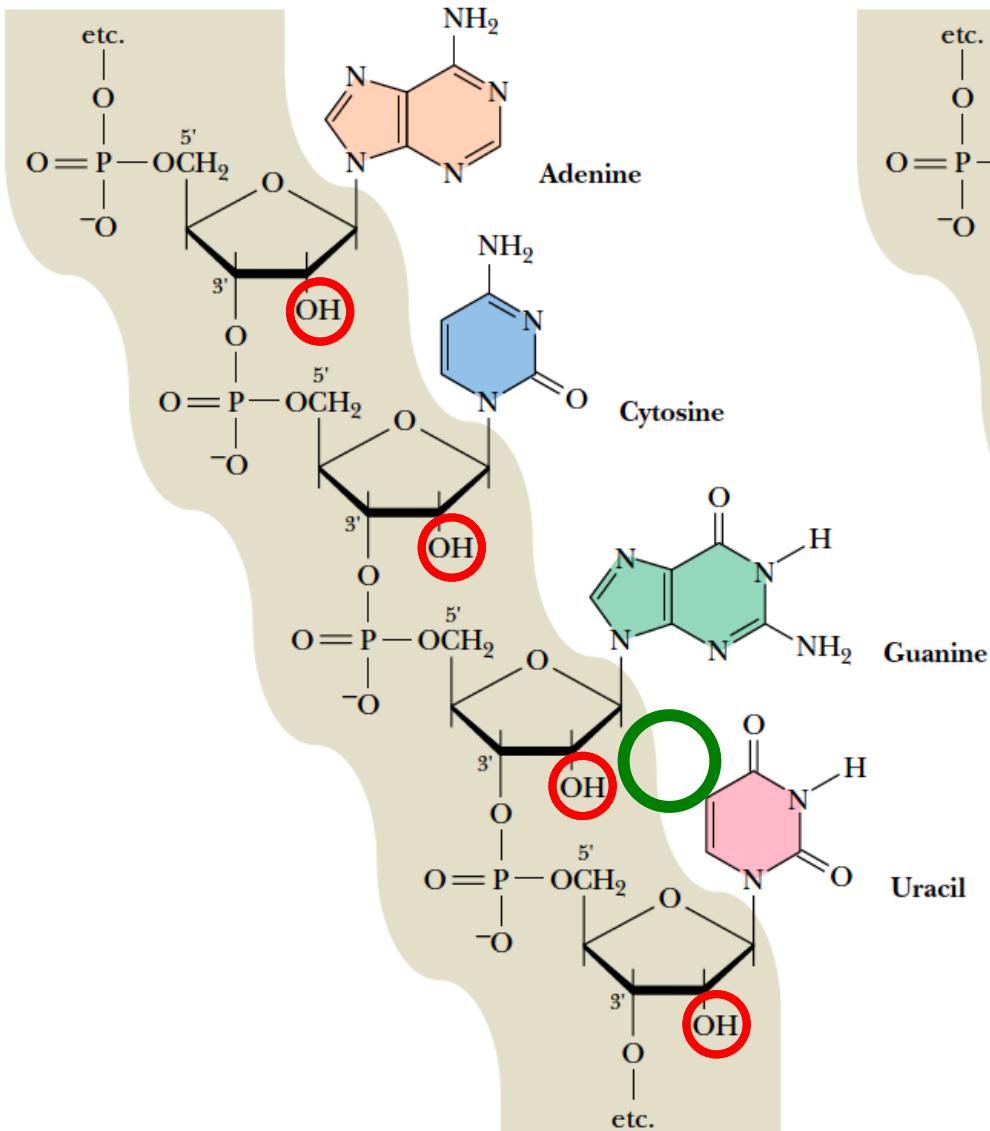
RNA



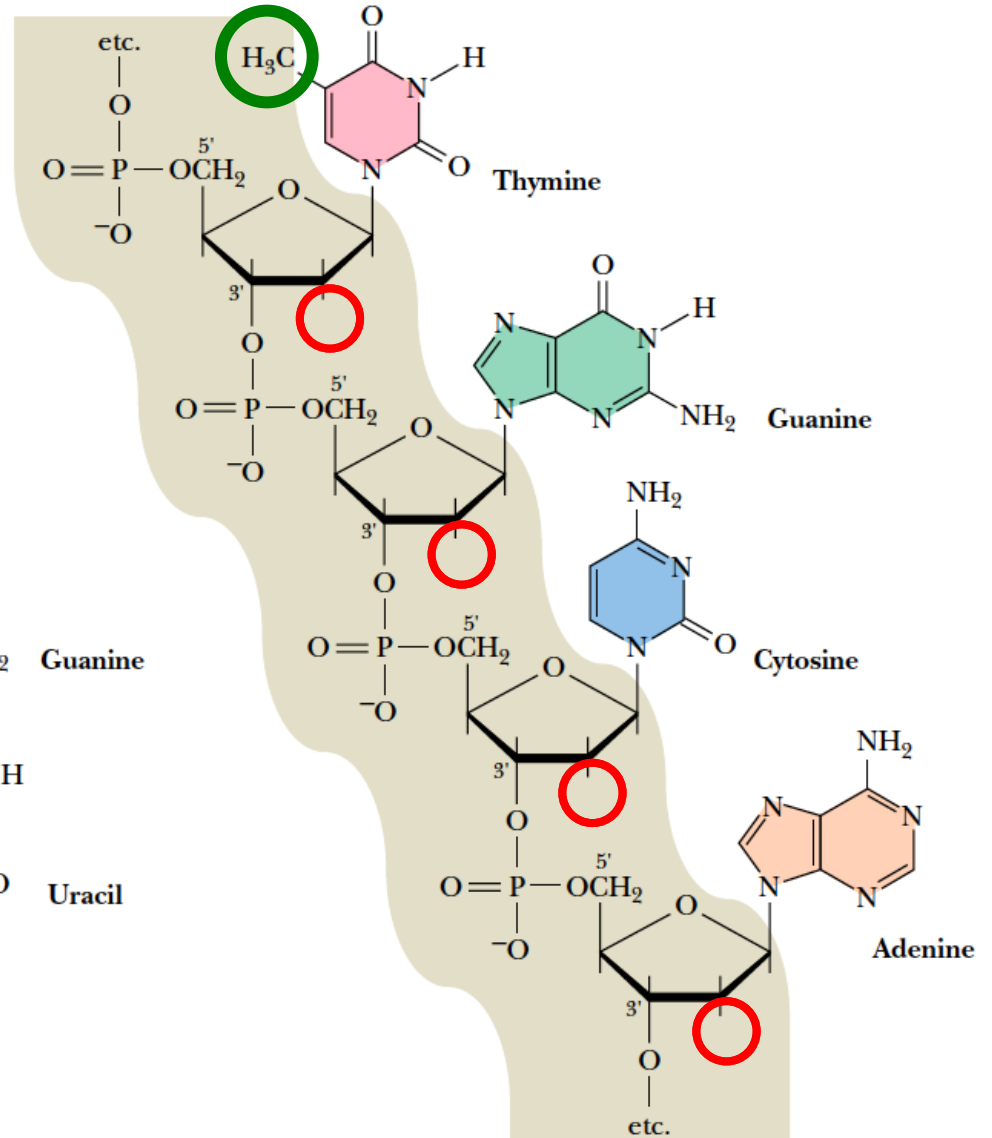
DNA



RNA



DNA



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

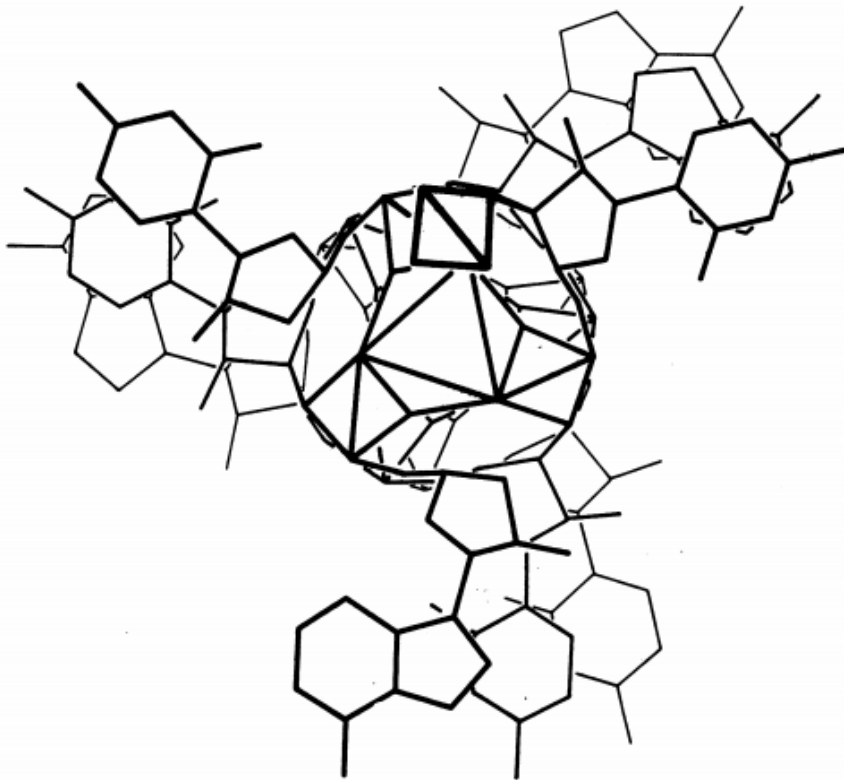
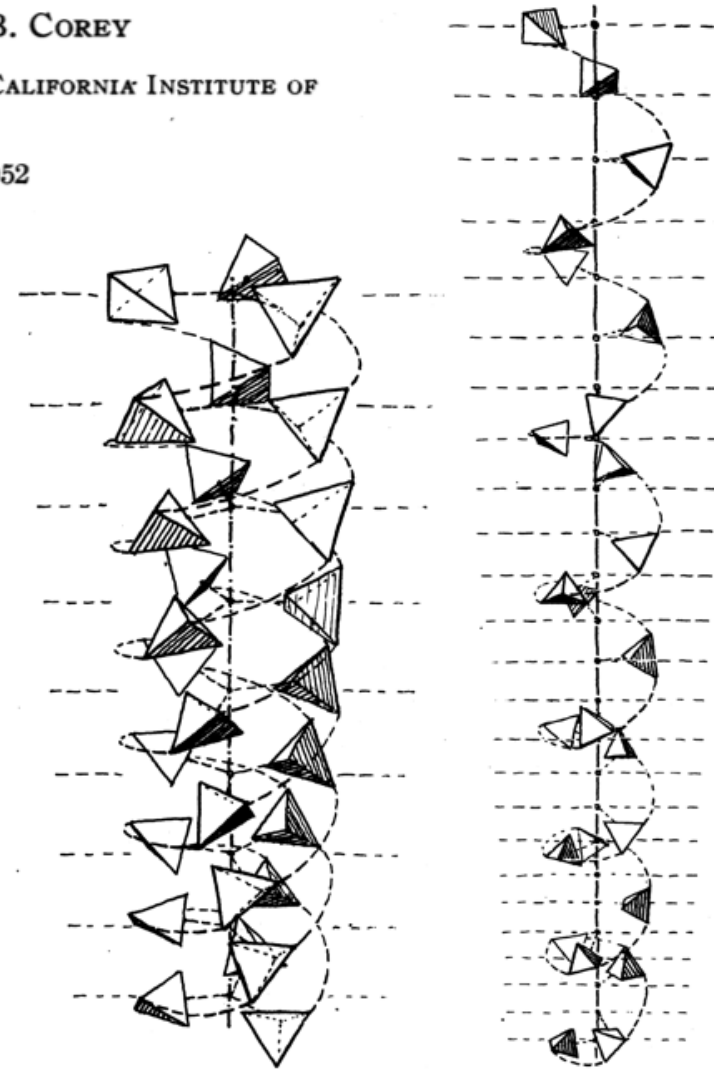


FIGURE 6

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

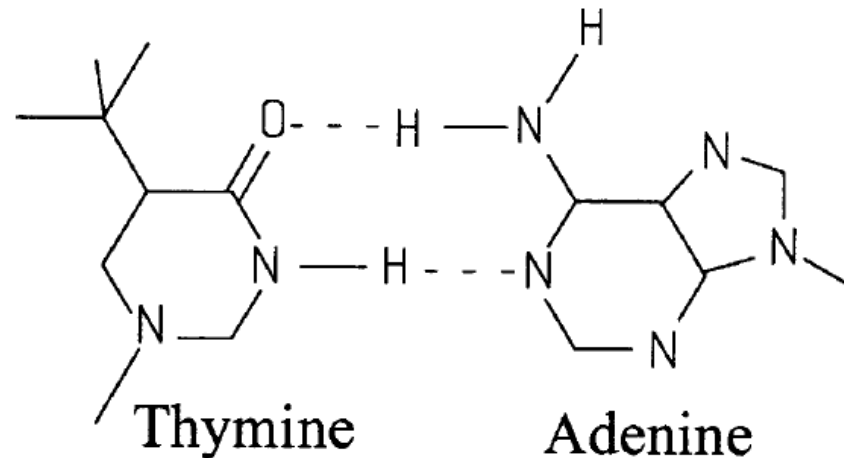
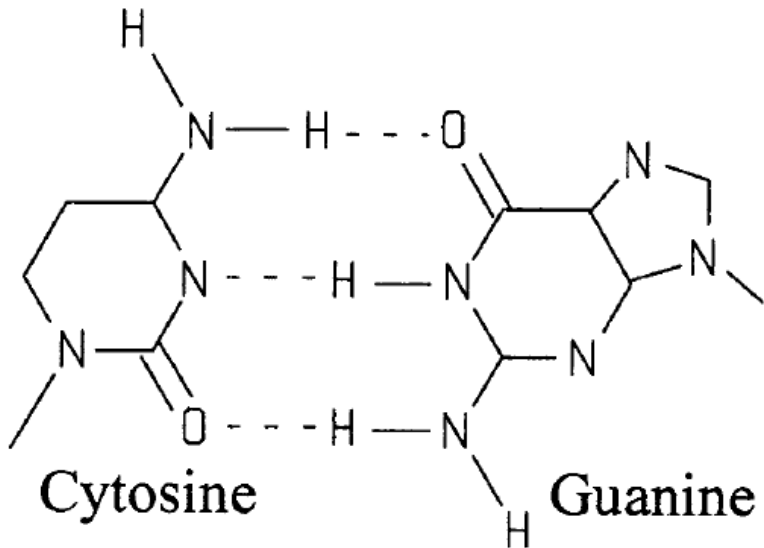


Párování bází NK: Watson-Crick, NC za medicínu a fyziologii 1962 [Watson(*1928)]

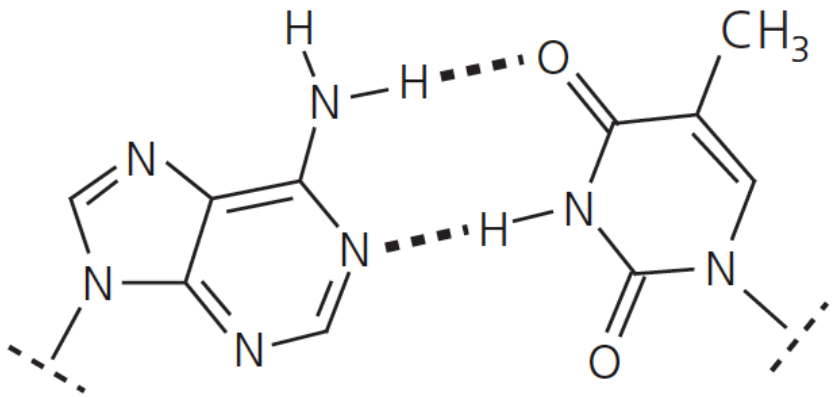


Vodíkové vazby

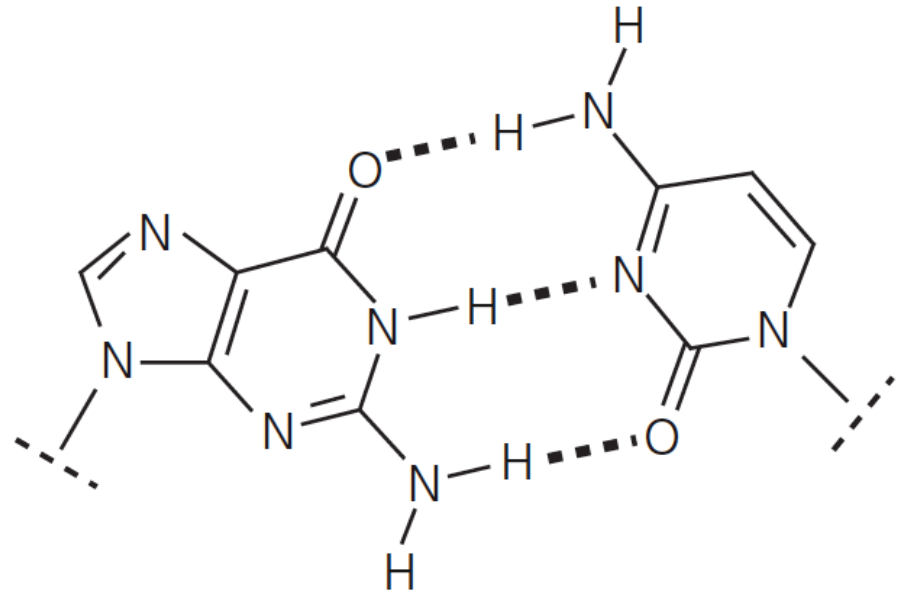
Jednotlivé řetězce dvojité šroubovice drží díky complementárními vazbami **N•••H-N** a **=O•••H-N**, které vznikají mezi **Cytosinem** a **Guaninem** a **Thyminem** a **Adeninem**.



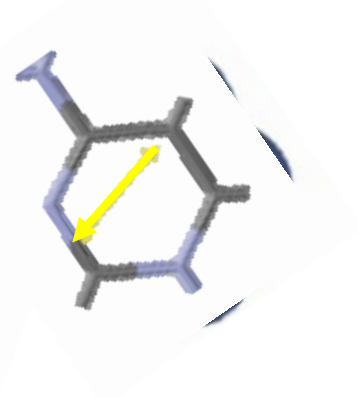
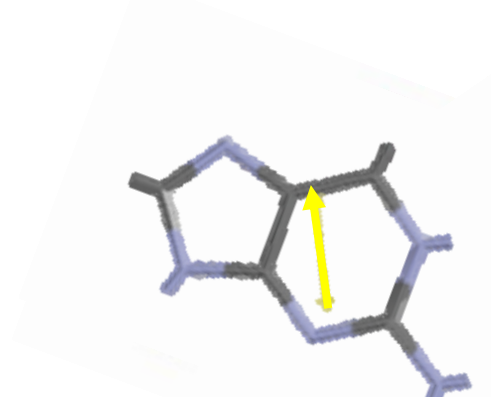
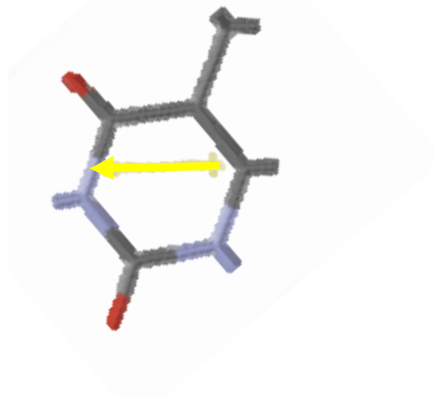
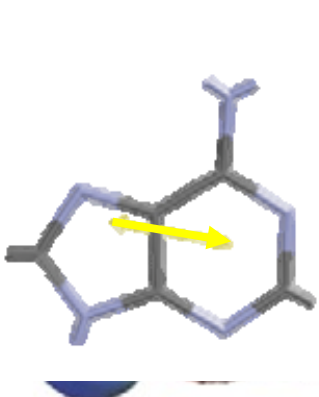
Každá vodíková vazba přispívá cca **20 kJ/mol** ke stabilizaci dvojšroubovice



adenine : thymine

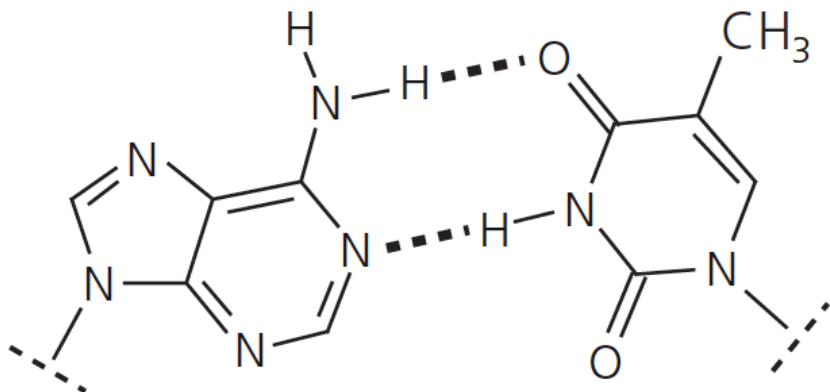


guanane : cytosine

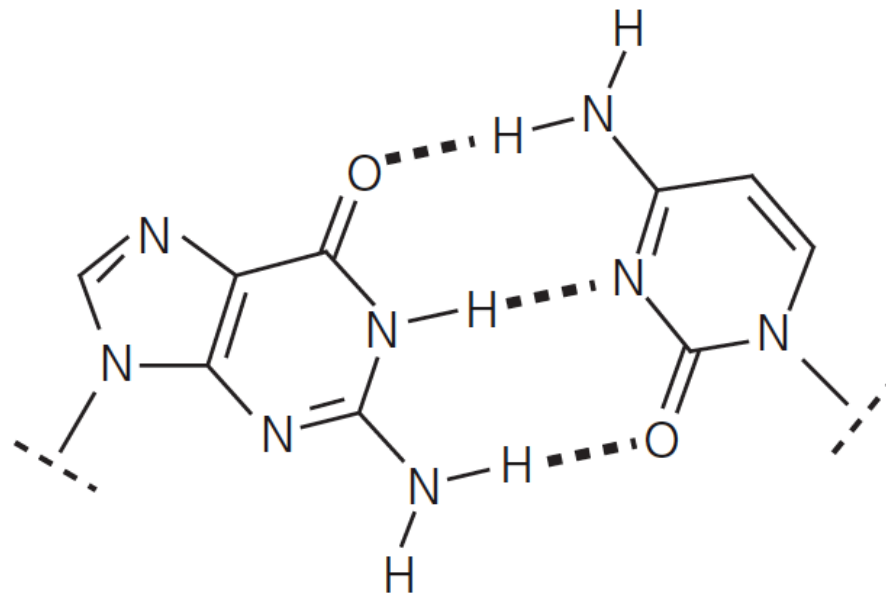


rozložení náboje v nukleobázích + 0 -, šipky označují dipólový moment

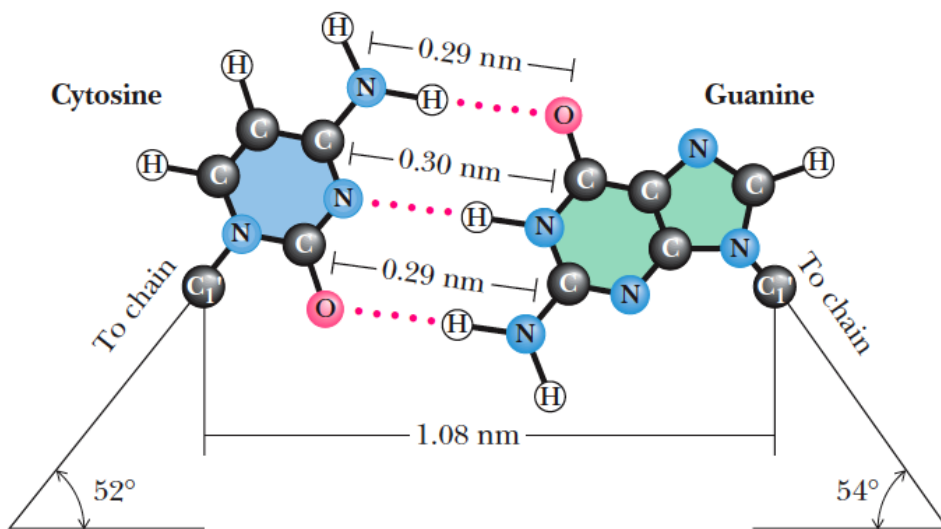
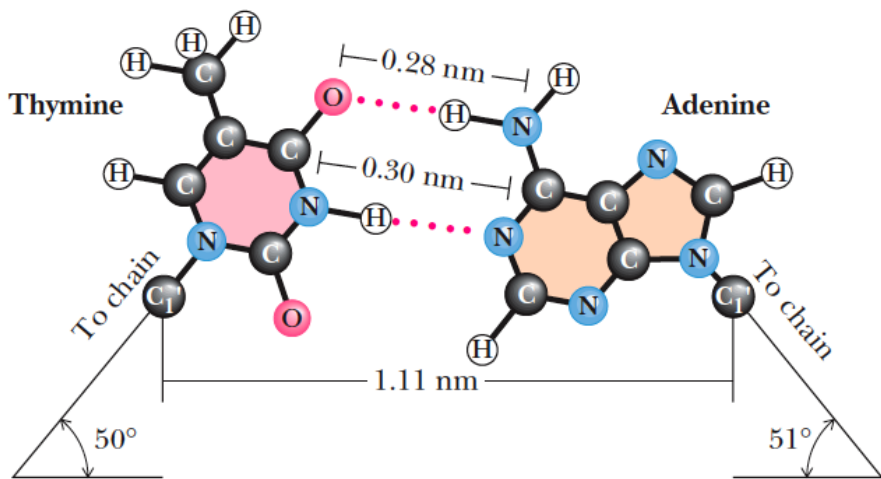
Watson-Crickovské párování bází

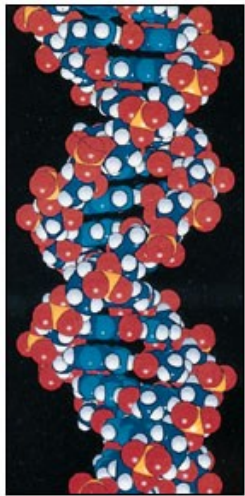


adenine : thymine



guanine : cytosine



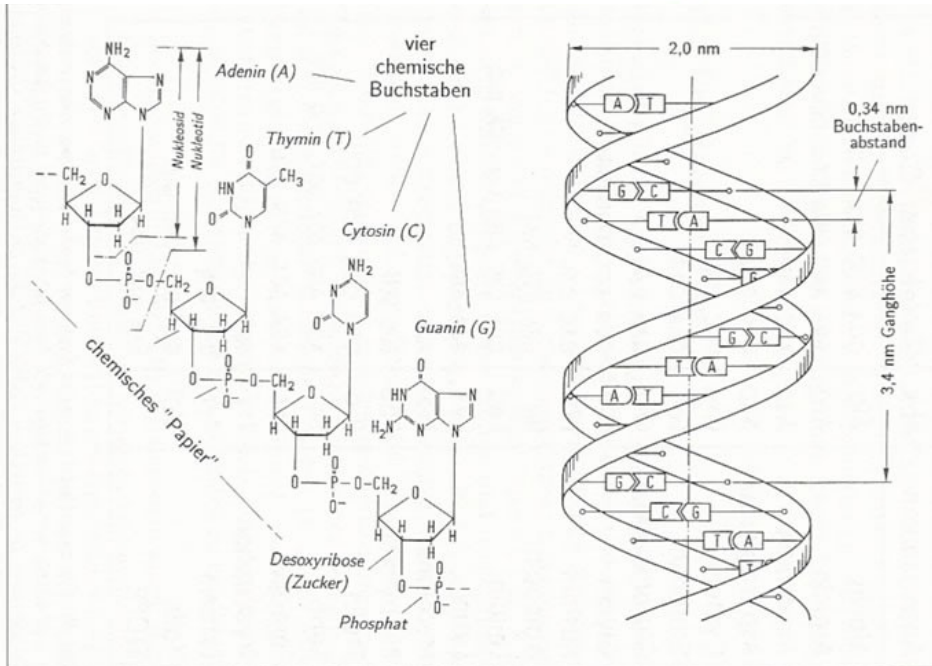
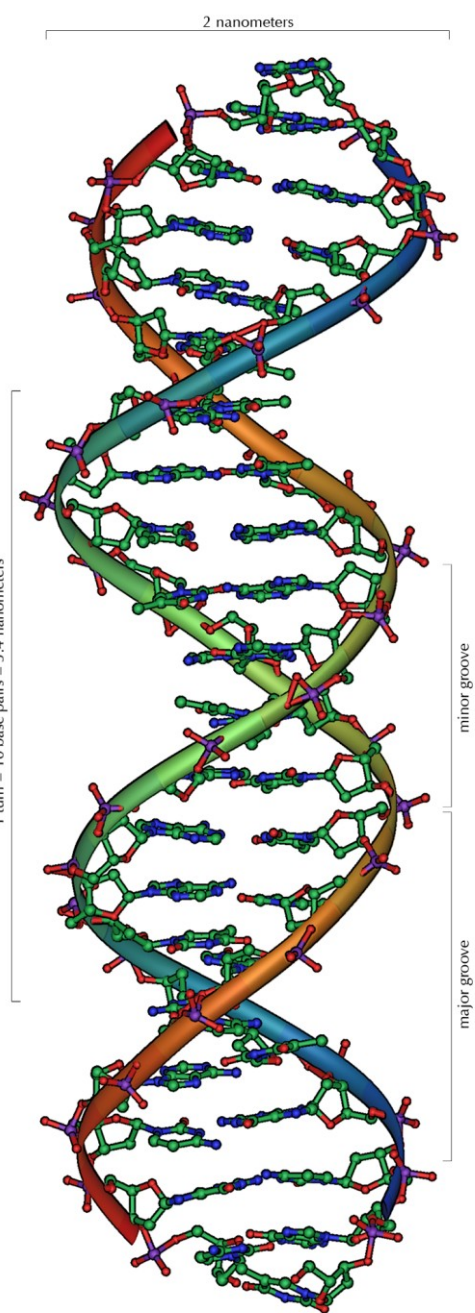
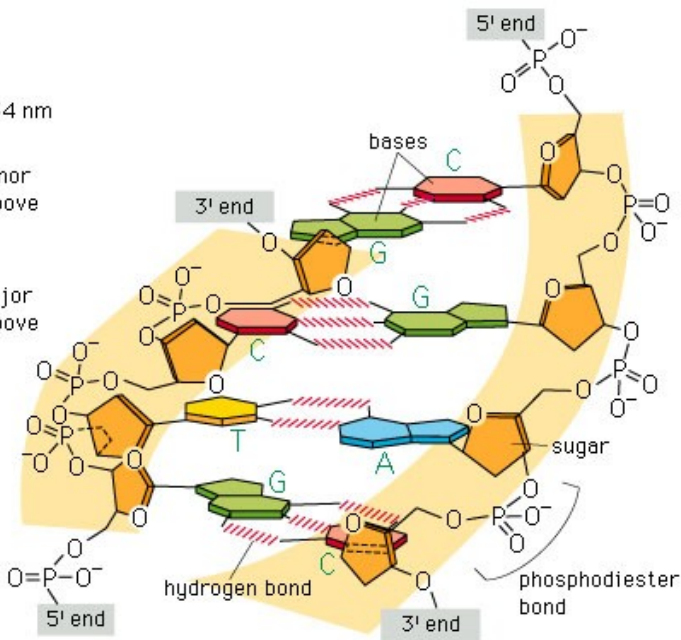


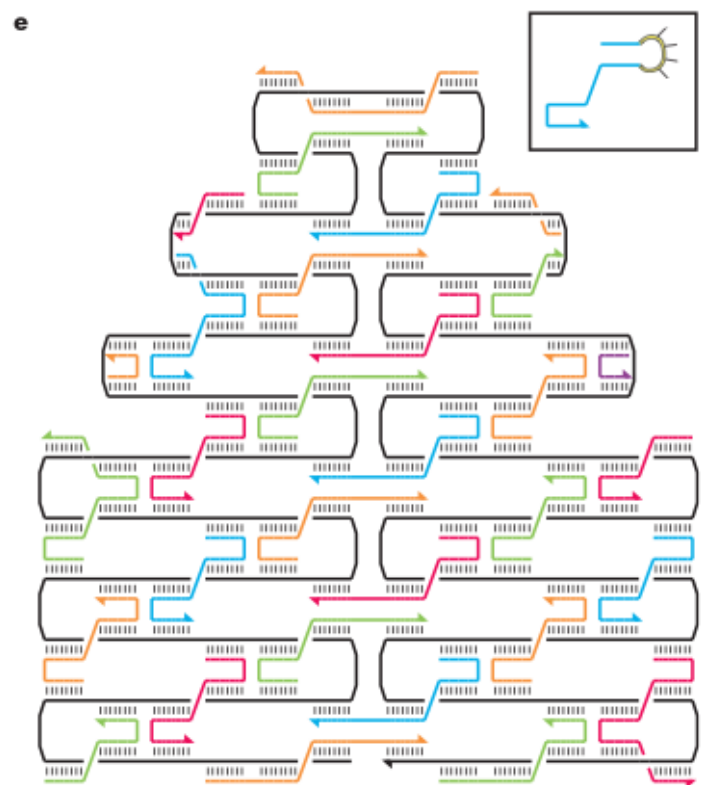
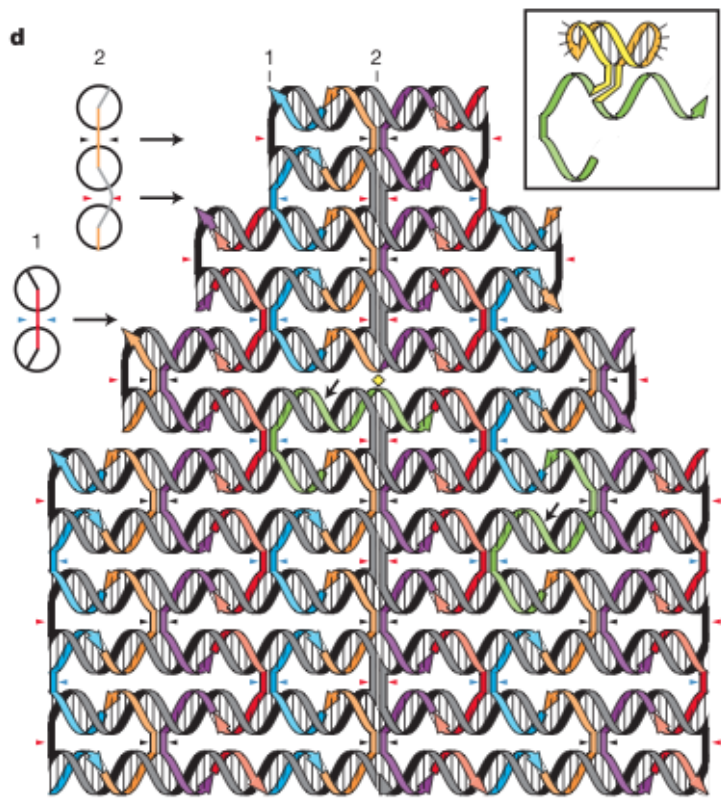
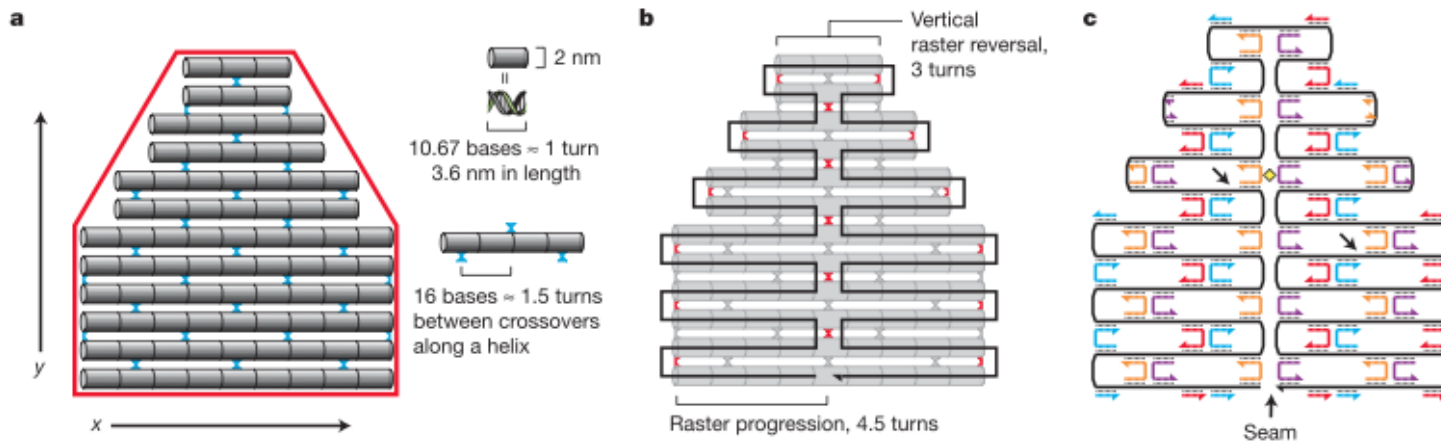
2 nm

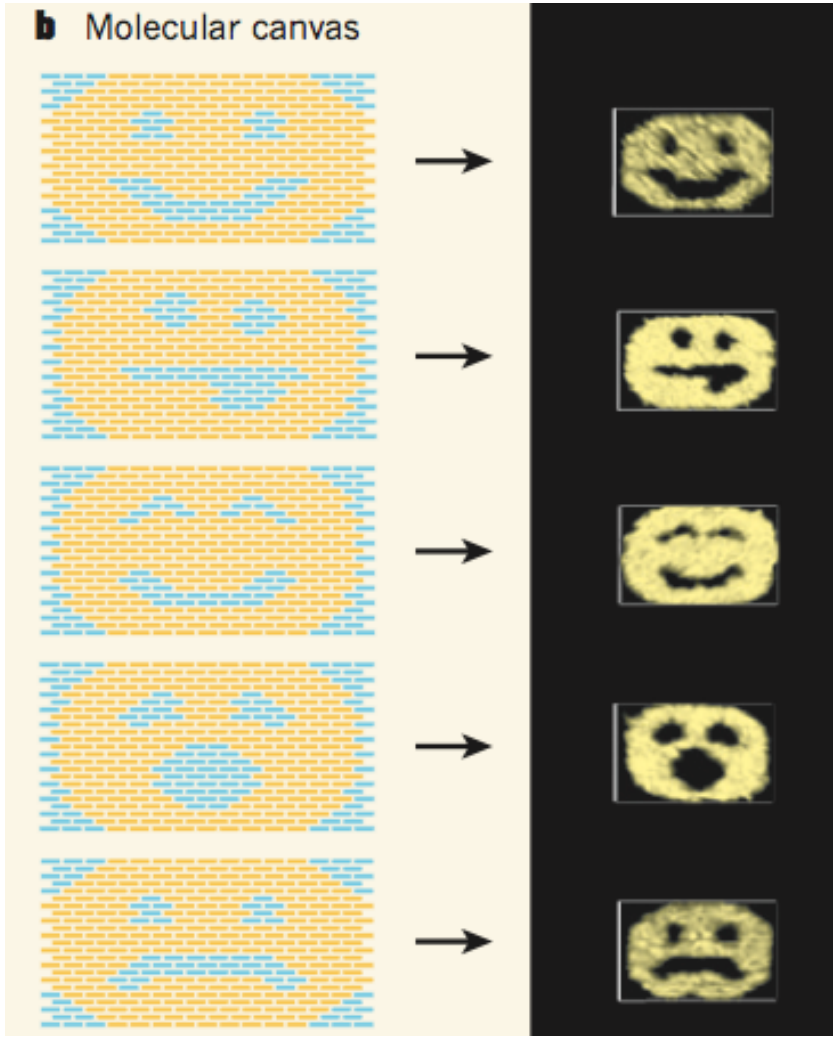
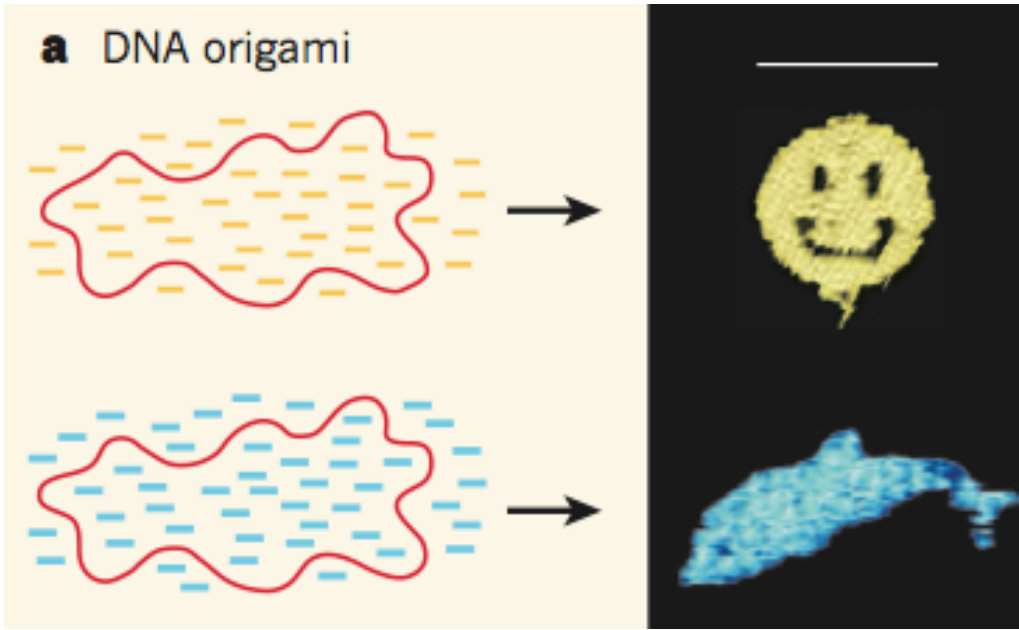
0.34 nm

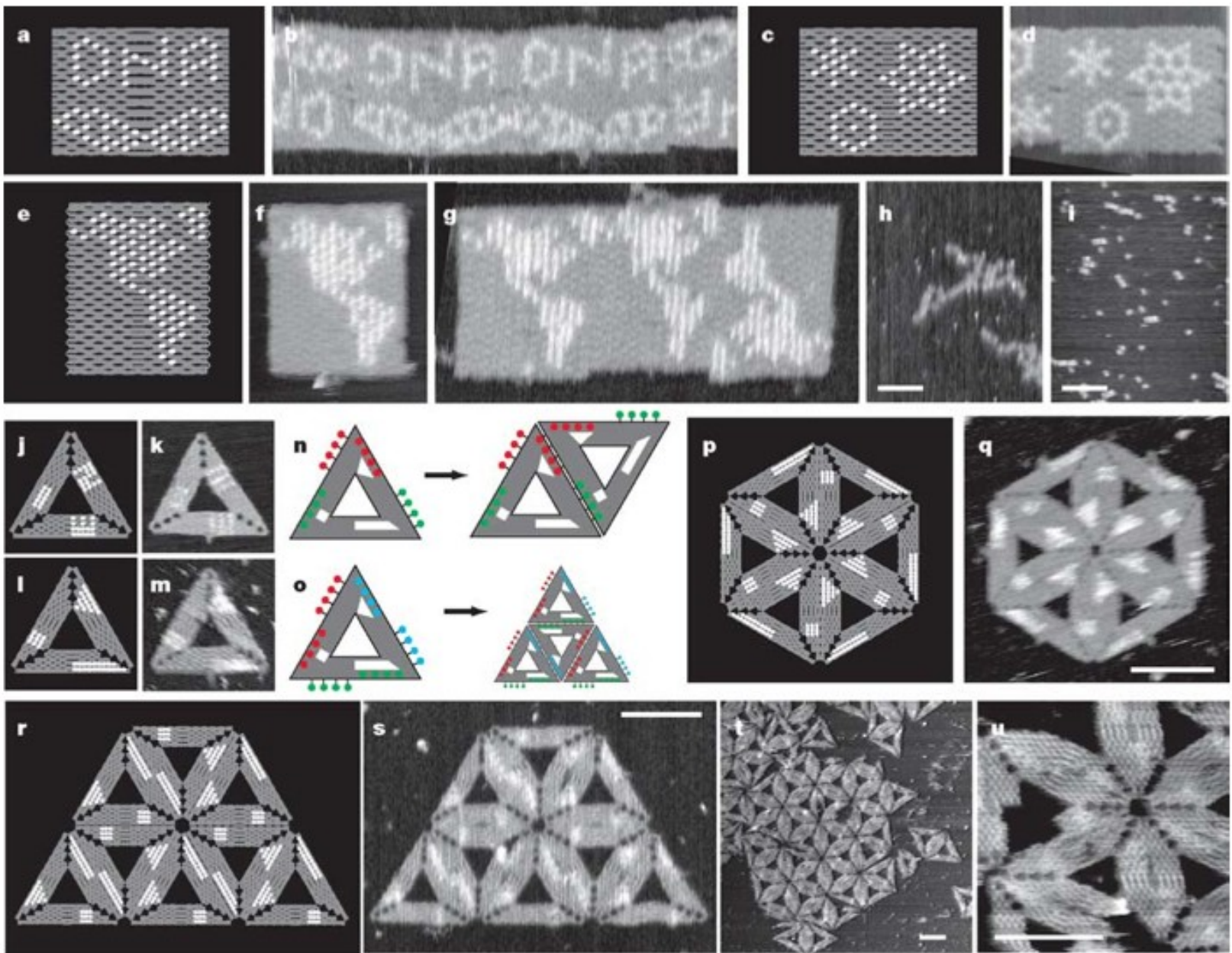
minor groove

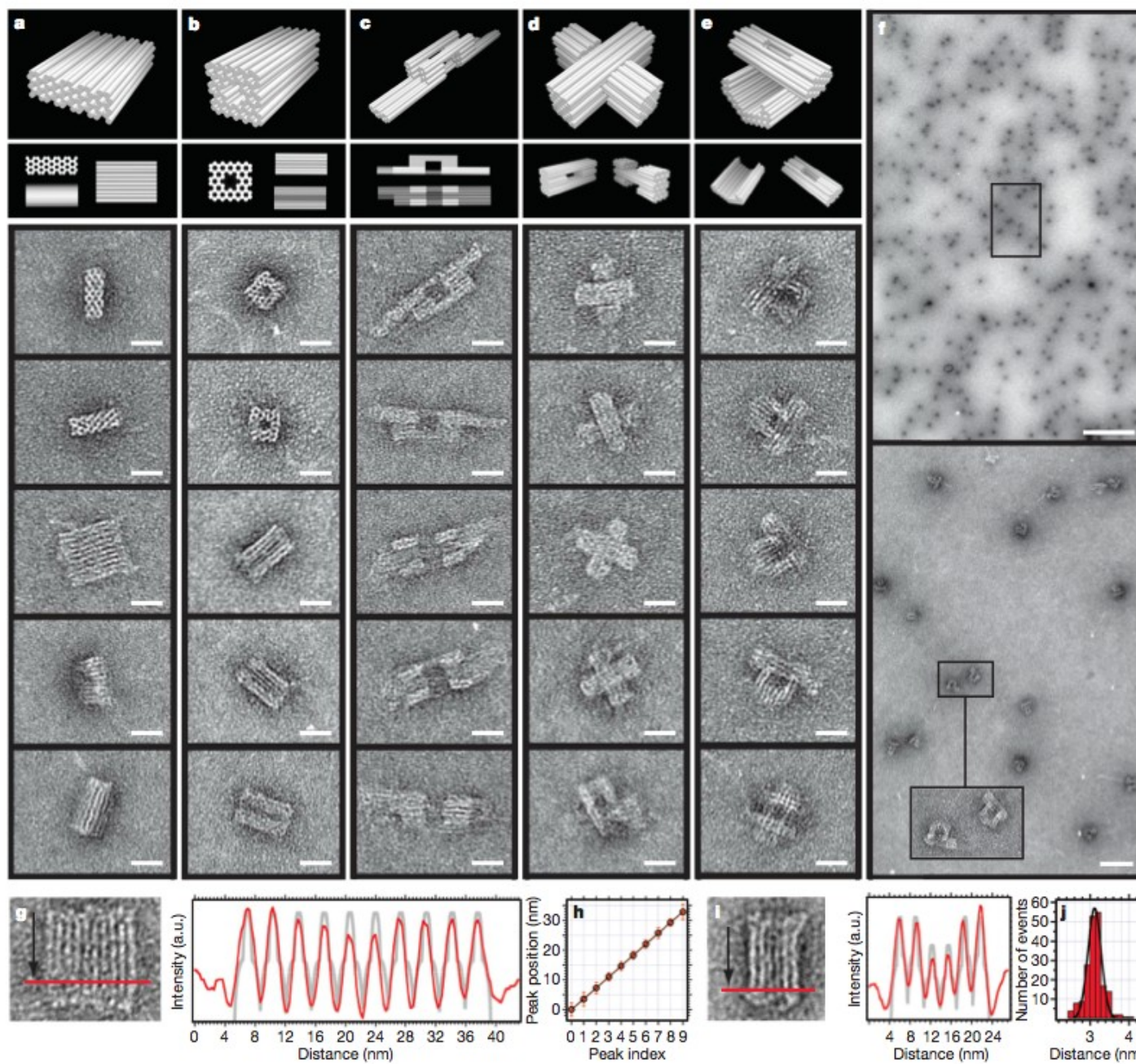
major groove



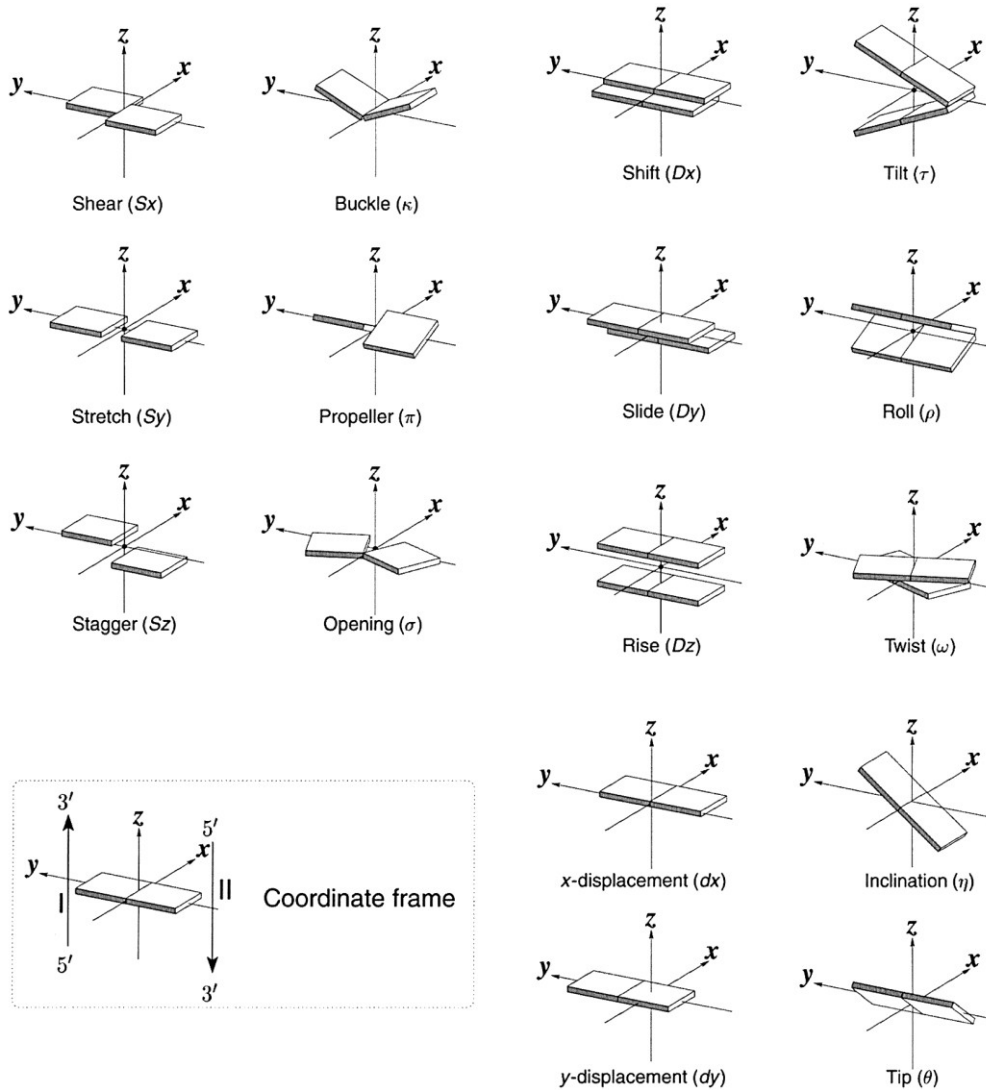






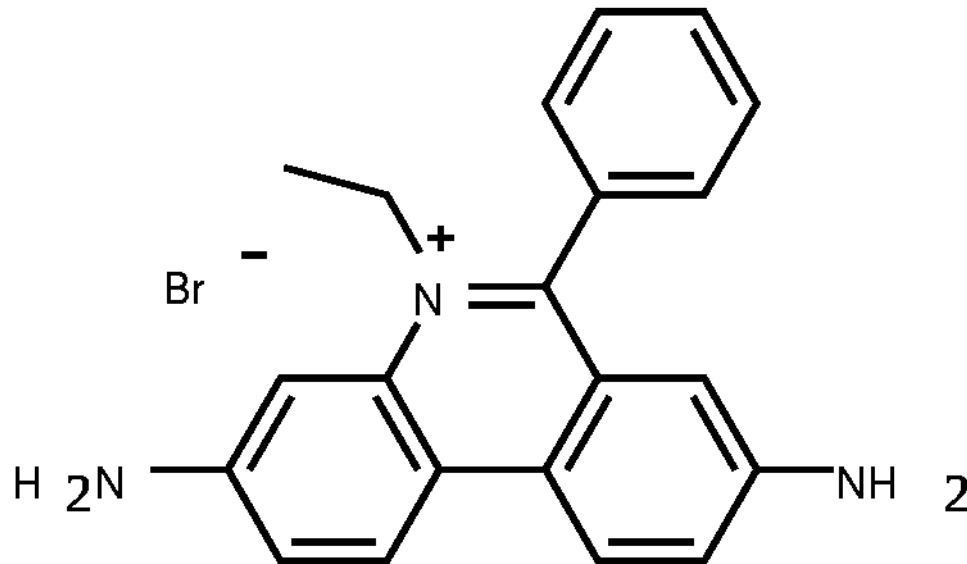


Geometrie páru bazí



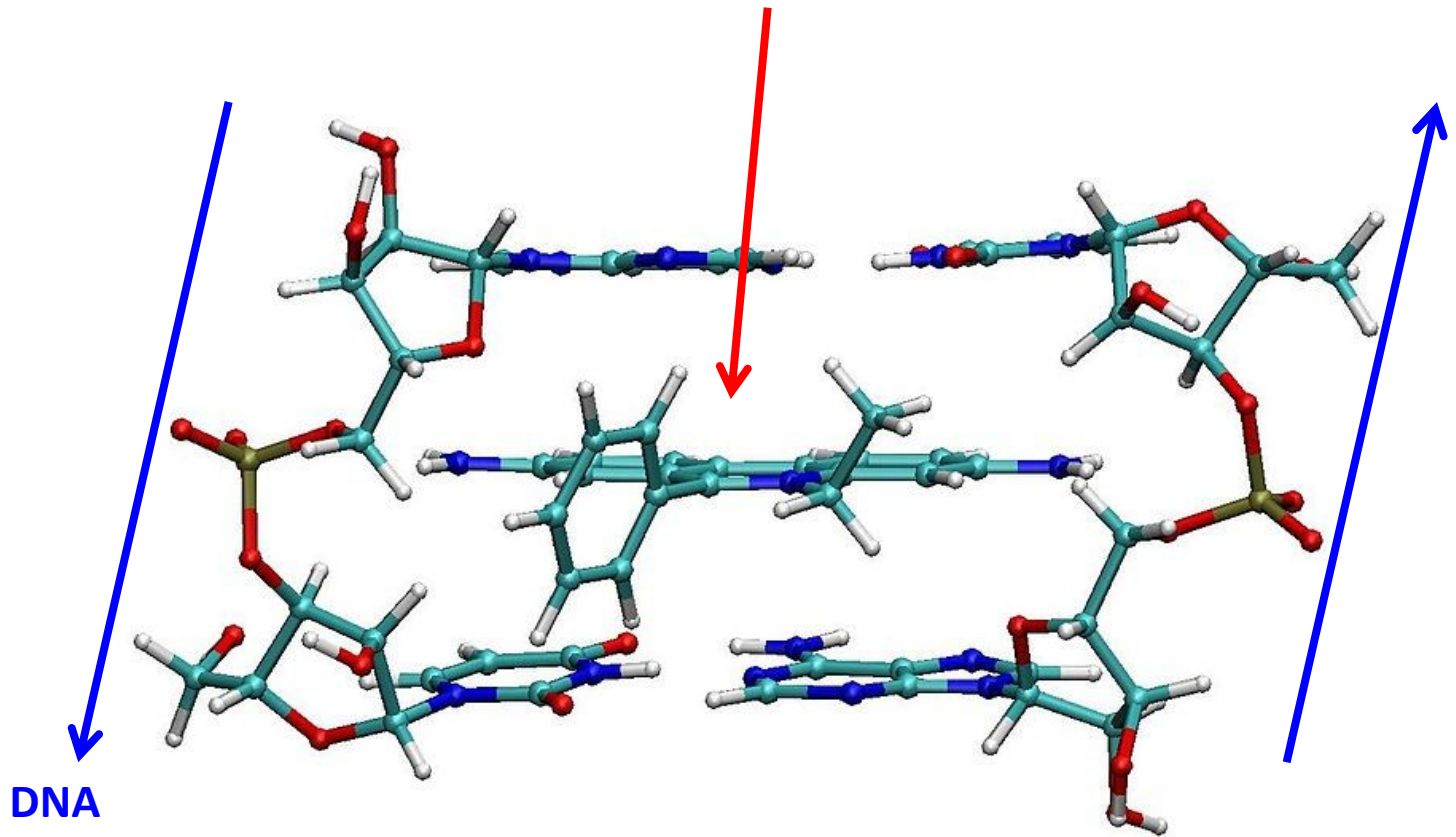
Interkalace – vmezeření

- 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.



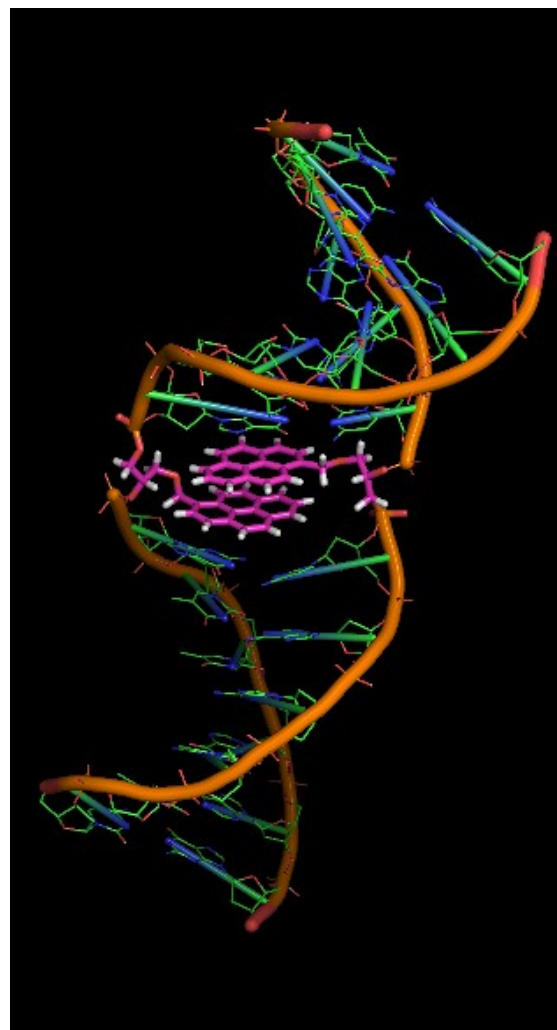
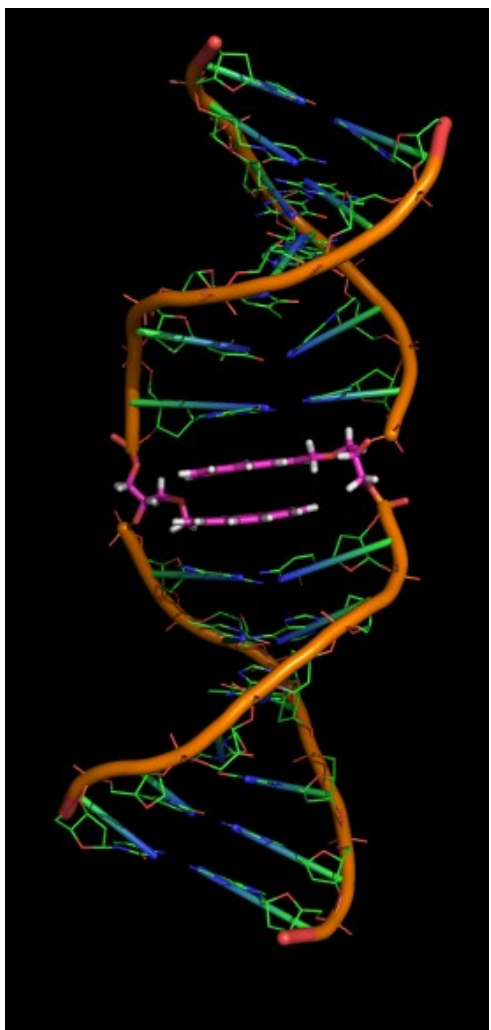
Ethidium bromide
!!! Mutagenní !!!

Ethidium bromide

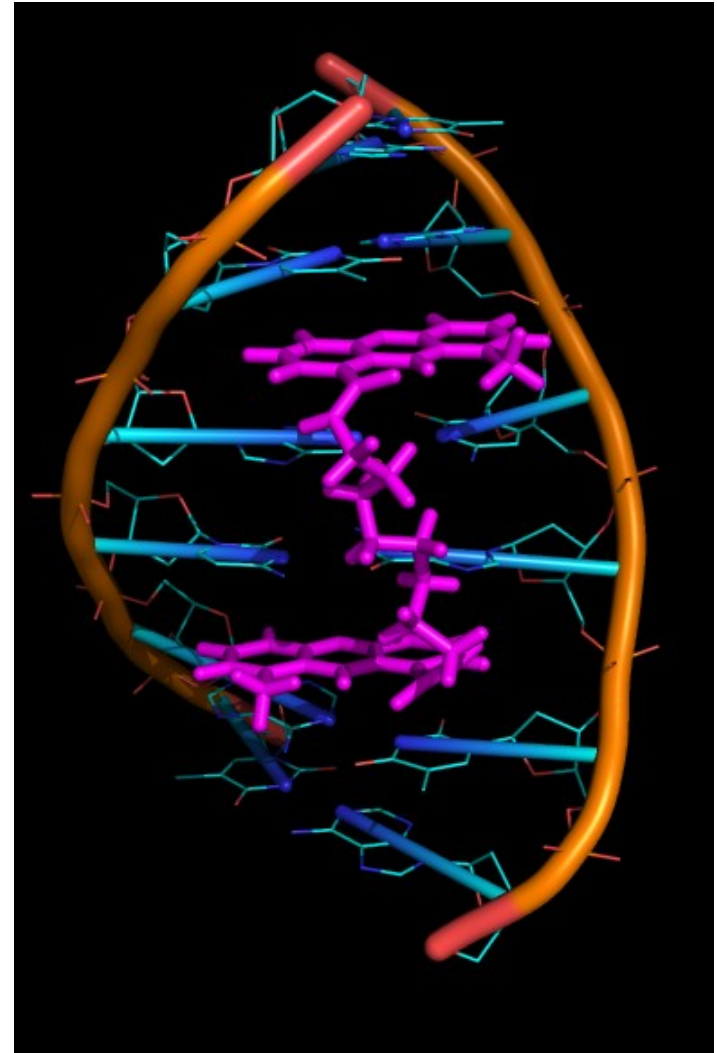


Decamer DNA šroubovice interkalovaný dvěma

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

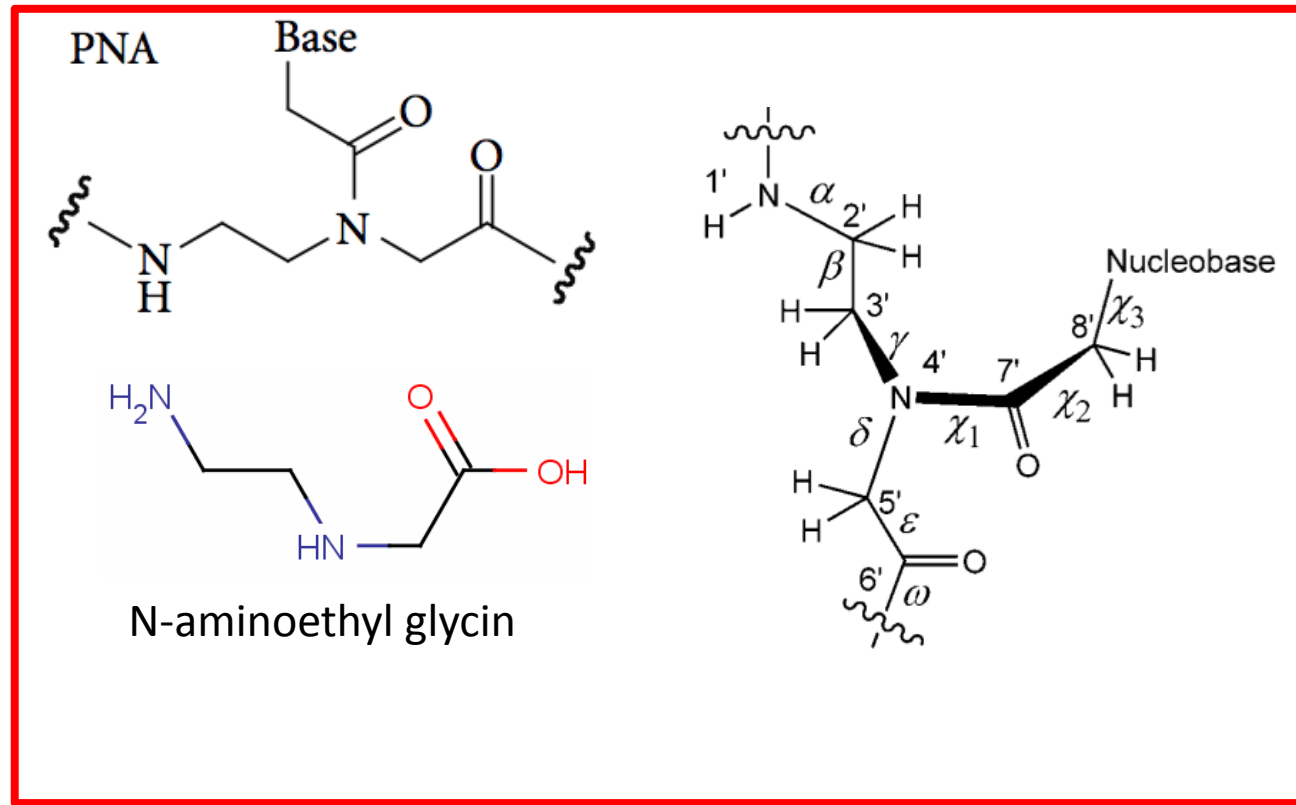
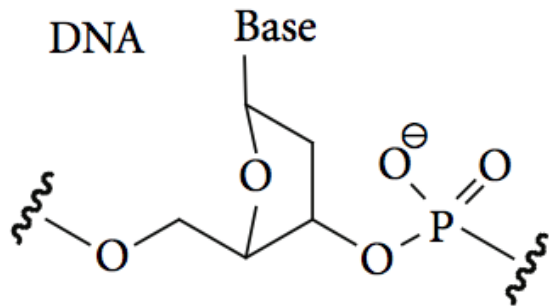


Hexamer DNA šroubovice interkalovaný bisphenazinem – protinádorovým léčivem
(1-METHYL-9-[12-(9-METHYLPHENAZIN-10-IUM-1-YL)-12-OXO-2,11-DIAZA-5,8-DIAZONIADODEC-1-ANOYL]PHENAZIN-10-IUM)
PDB ID: 1X95

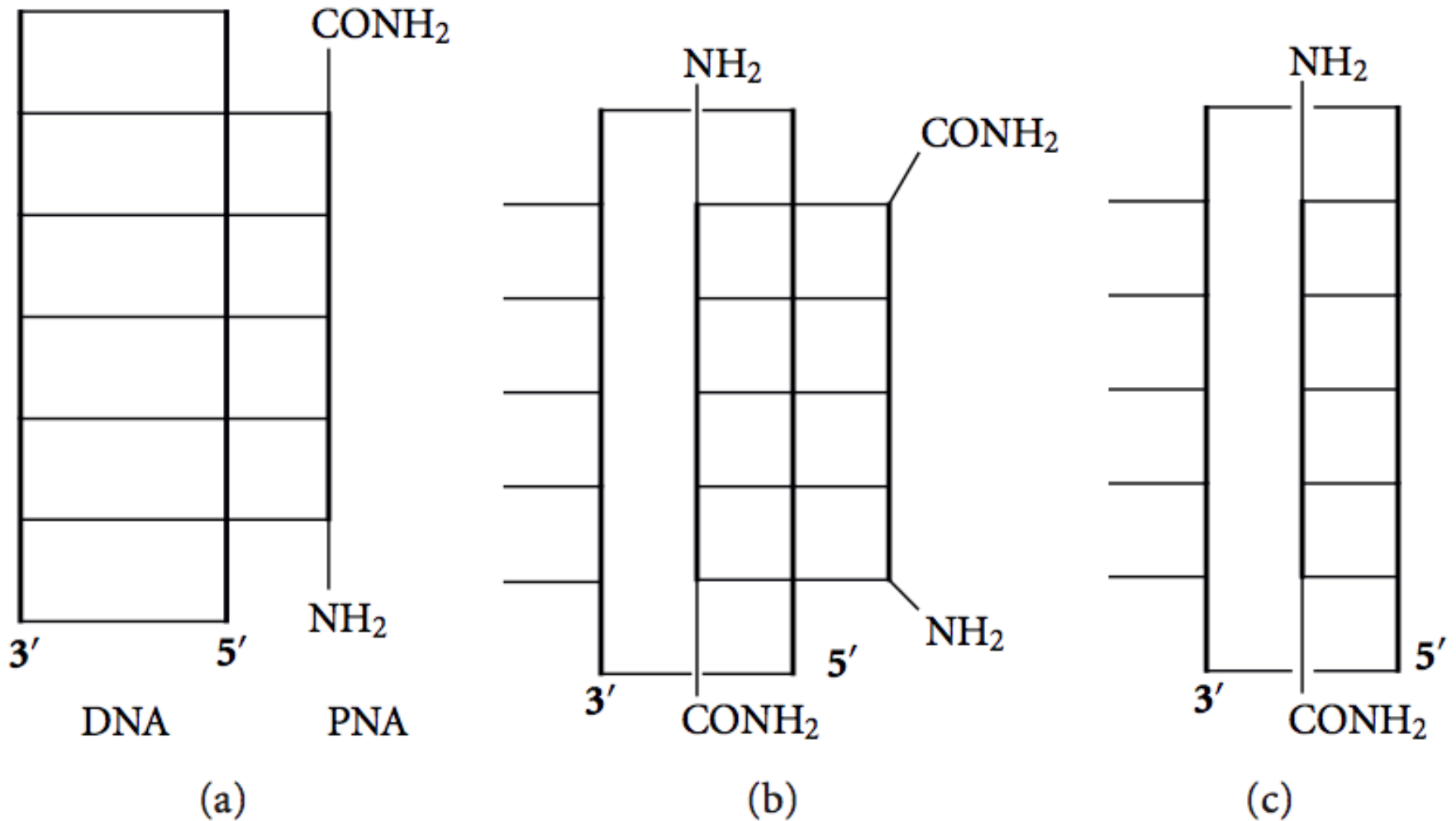


Peptidová nukleové kyseliny (PNA)

- Nejsou kyselinami!!!
- Jsou syntetické, nicméně se předpokládá(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



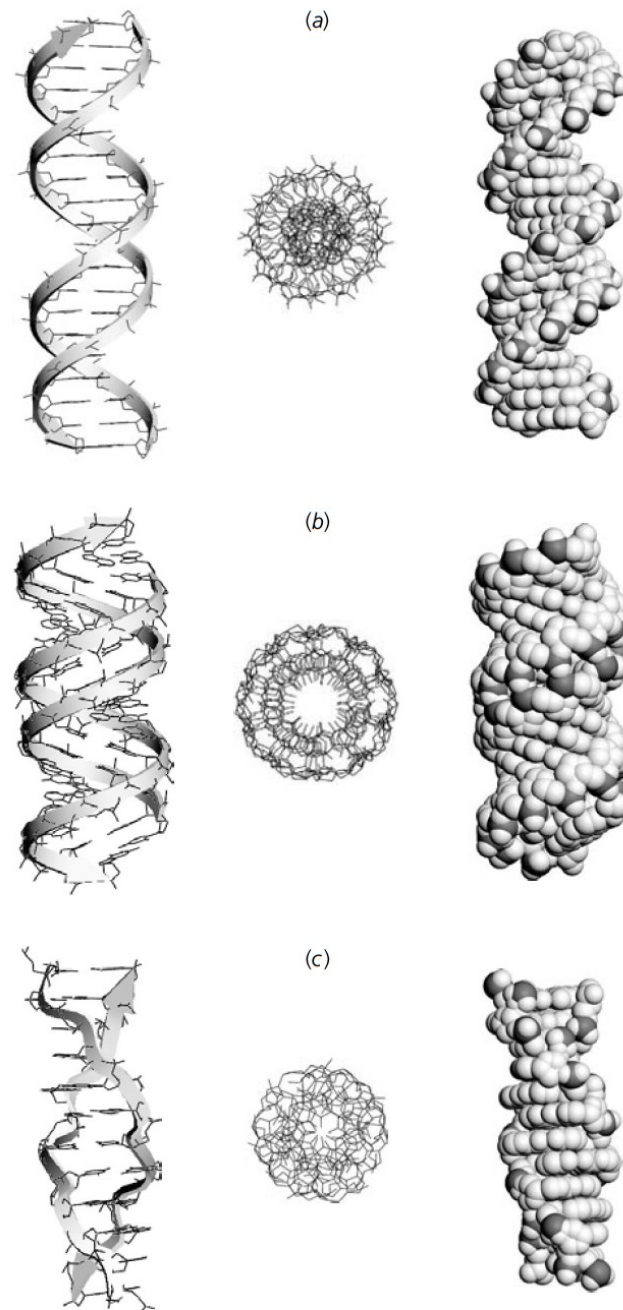
Interakce mezi PNA a DNA dvoušroubovicí



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'- <i>endo</i>	C3'- <i>endo</i>	C2'- <i>endo</i> (pyr) C3'- <i>endo</i> (pur)
Velký žlábek <i>Major groove</i>	široký, hluboký	úzký, hluboký	plochý
Malý žlábek <i>Minor groove</i>	úzký, hluboký	široký, mělký	úzký, hluboký



Definice dihedrálních a torzních úhlů

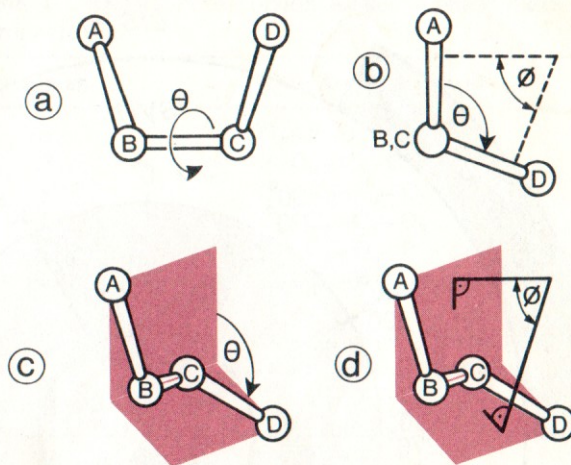


Figure 2-4. Definition of *torsion* and *dihedral* angles. (a) *Torsion angle* θ (A–B–C–D) describing orientations of bonds A–B and C–D with respect to the central bond B–C. (b) View along B→C. θ is the torsion angle between the projected bonds A–B and C–D; the complement ϕ is called the *dihedral angle*. 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	${}^{(n-1)}\text{O}_{3'}-\text{P}-\text{O}_{5'}-\text{C}_{5'}$
β	$\text{P}-\text{O}_{5'}-\text{C}_{5'}-\text{C}_{4'}$
γ	$\text{O}_{5'}-\text{C}_{5'}-\text{C}_{4'}-\text{C}_{3'}$
δ	$\text{C}_{5'}-\text{C}_{4'}-\text{C}_{3'}-\text{O}_{3'}$
ϵ	$\text{C}_{4'}-\text{C}_{3'}-\text{O}_{3'}-\text{P}$
ζ	$\text{C}_{3'}-\text{O}_{3'}-\text{P}-\text{O}_{5'{}^{(n+1)}}$
χ	$\text{O}_{4'}-\text{C}_{1'}-\text{N}_1-\text{C}_2$ (pyrimidines) $\text{O}_{4'}-\text{C}_{1'}-\text{N}_9-\text{C}_4$ (purines)
ν_0	$\text{C}_{4'}-\text{O}_{4'}-\text{C}_{1'}-\text{C}_{2'}$
ν_1	$\text{O}_{4'}-\text{C}_{1'}-\text{C}_{2'}-\text{C}_{3'}$
ν_2	$\text{C}_{1'}-\text{C}_{2'}-\text{C}_{3'}-\text{C}_{4'}$
ν_3	$\text{C}_{2'}-\text{C}_{3'}-\text{C}_{4'}-\text{O}_{4'}$
ν_4	$\text{C}_{3'}-\text{C}_{4'}-\text{O}_{4'}-\text{C}_{1'}$

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

Description	<i>N</i>	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 δ 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

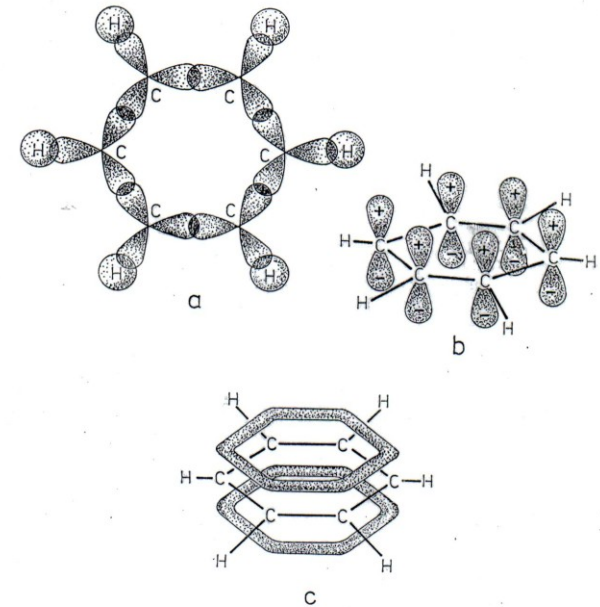
'Description' is a short annotation of the conformation, '*N*' is the number of dinucleotides which define the conformation, 'Clustered Torsions' are the arithmetic means calculated for the torsions used in the clustering process, with the torsions being defined in Figure 1. Bold font is used merely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

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

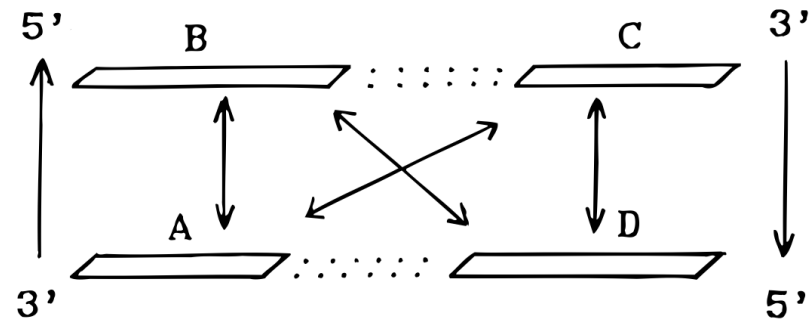
Energie v kJ/mol



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

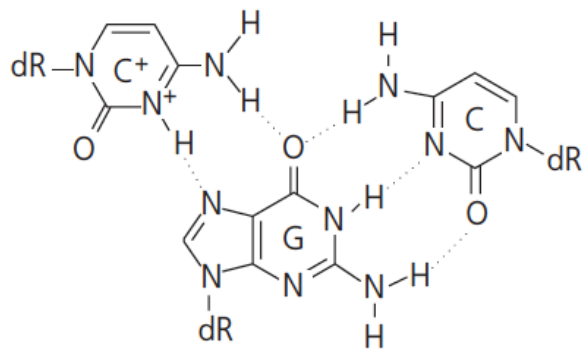
3) Patrové interakce – stacking

Působí mezi jednotlivými patry nukleopárů, stabilizují dvojšroubovici díky **elektronovým korelacím**, **van der Waalsovým** a **Coulombickým interakcím**

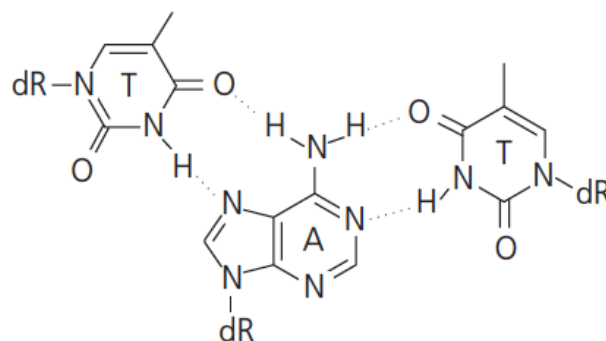


Non-Watson-Crickové (Hoogsteenovo – Karsten Hoogsteen) párování bází

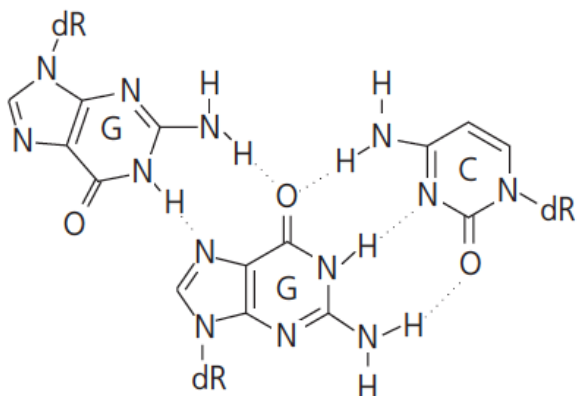
Triplexové struktury



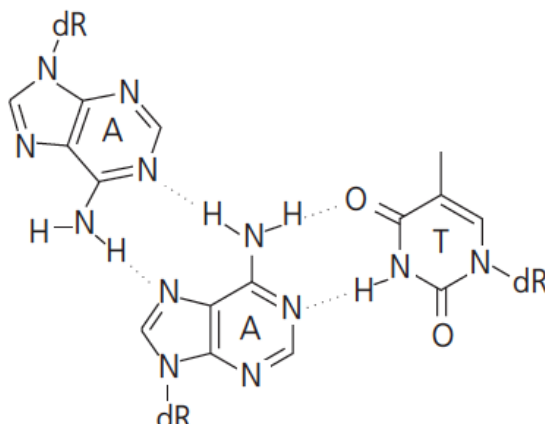
C⁺·GC



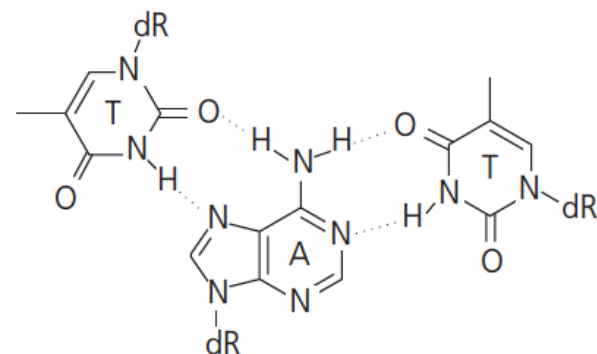
T·AT



G·GC

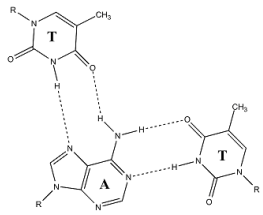


A·AT

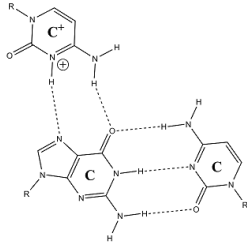


T·AT

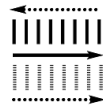
Triplexové struktury



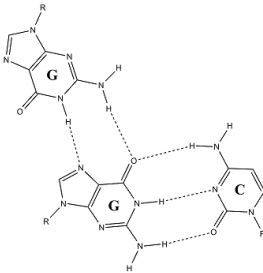
TA*T



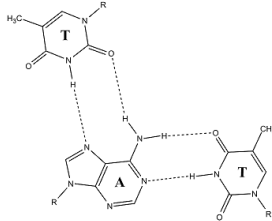
CG*C+



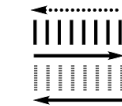
YR*Y



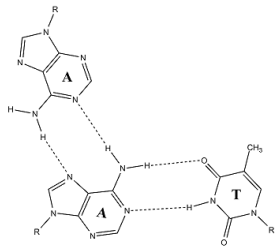
CG*G



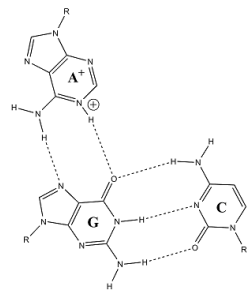
TA*A



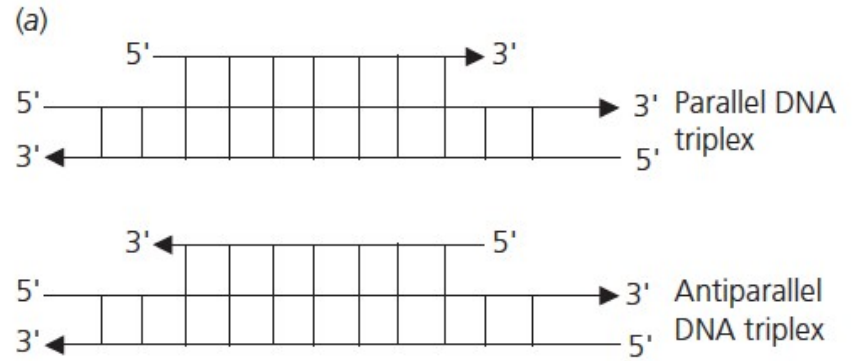
YR*R



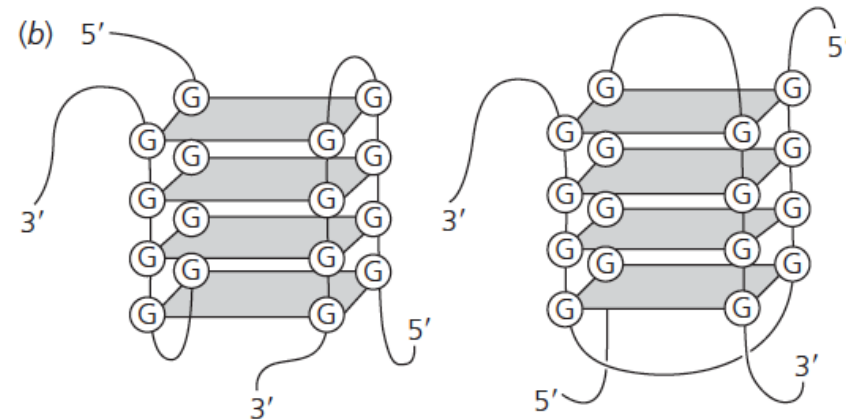
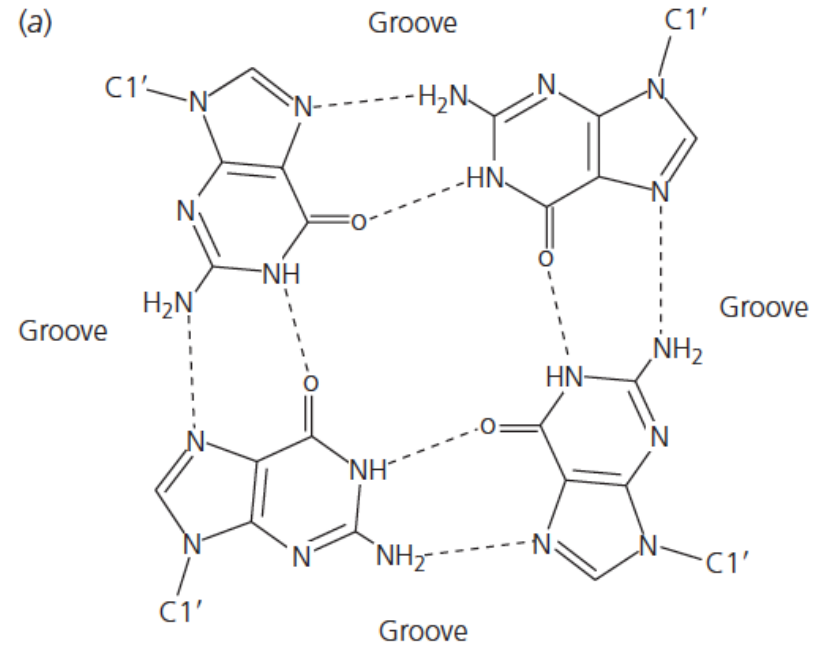
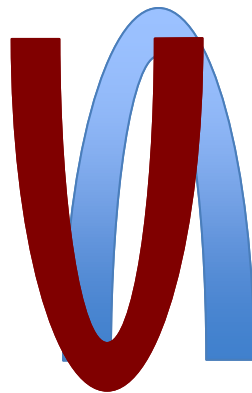
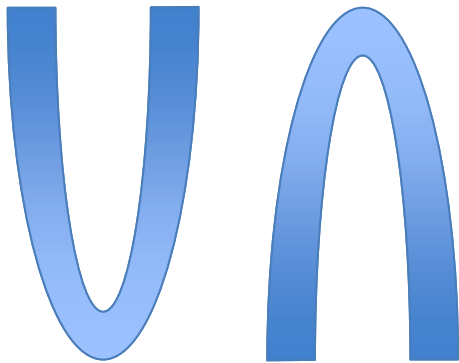
TA*T

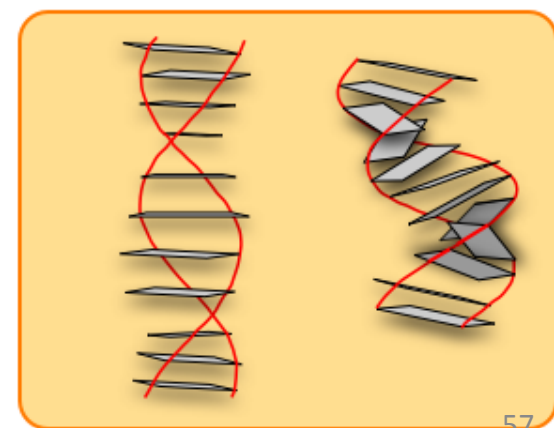
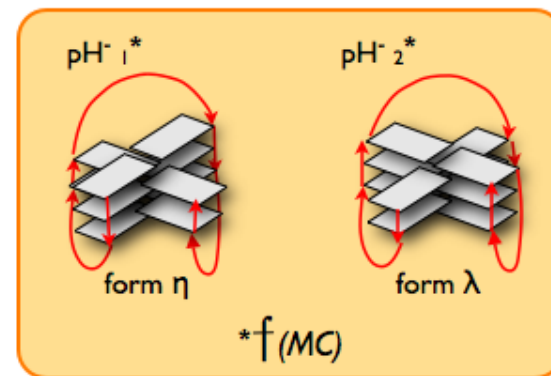
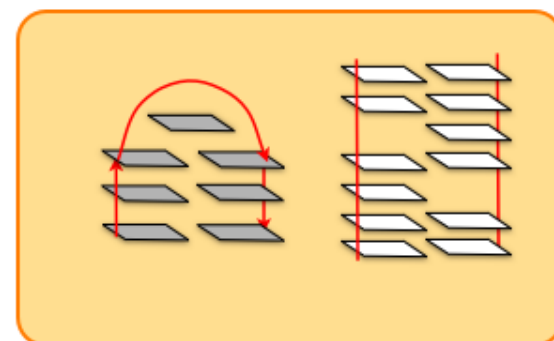
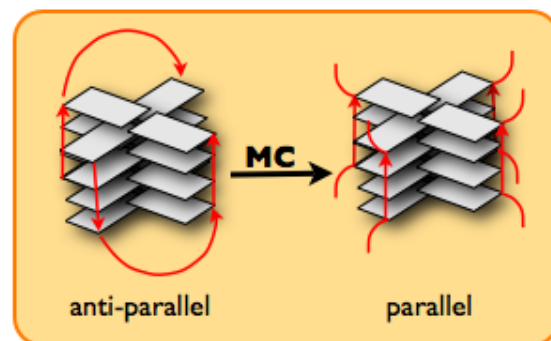
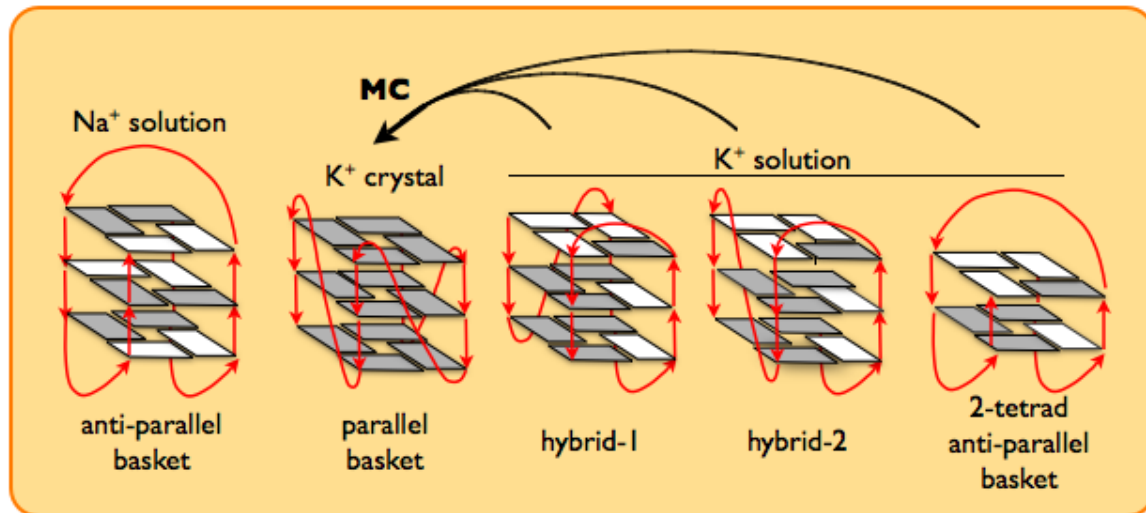


CG*A+



Quadruplexové struktury





Polymorfie telomerických opakování *in vitro*

NMR

NMR

X-ray

Sekvenčně závislé

Na⁺

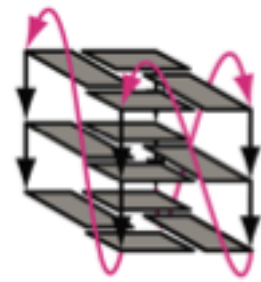
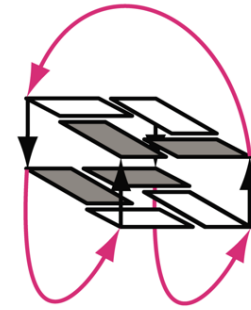
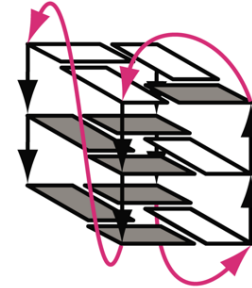
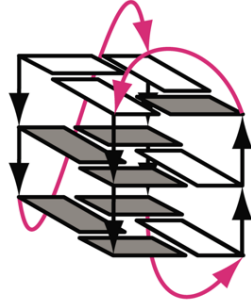
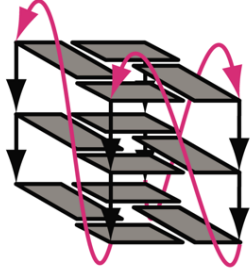
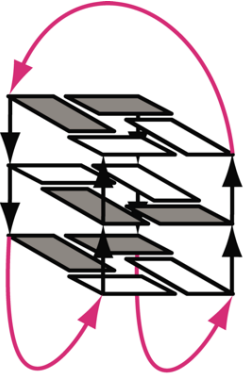
K⁺

K⁺

K⁺

K⁺

K⁺/PEG



**antiparallel
basket**

**parallel
propeller**

hybrid-1

hybrid-2

**2-tetrad
antiparallel
basket**

**parallel
propeller**

Wang et al. Structure (1993)

Parkinson et al. Nature (2002)

Amrus et al. Nucleic Acids Res. (2006)

Dai et al. Nucleic Acids Res. (2007)

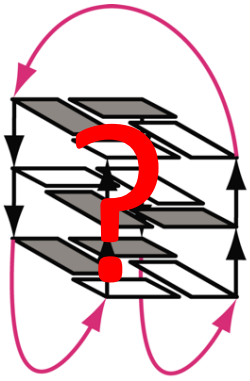
Lim et al. J Am Chem Soc. (2009)

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

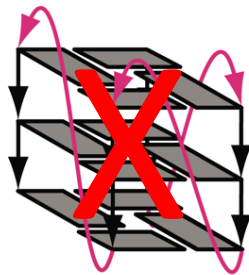
Polymorfie telomerických opakování *in vivo*

In-cell NMR

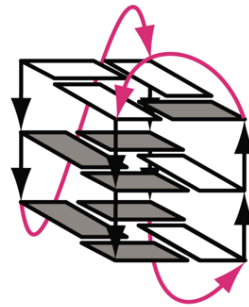
Sekvenčně závislé



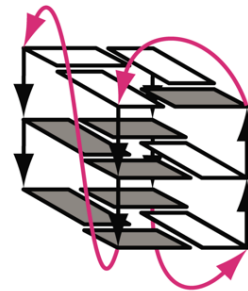
**antiparallel
basket**



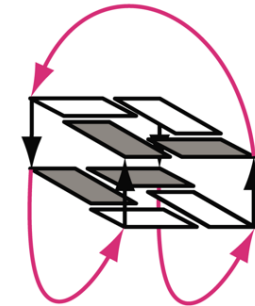
**parallel
propeller**



hybrid-1



hybrid-2



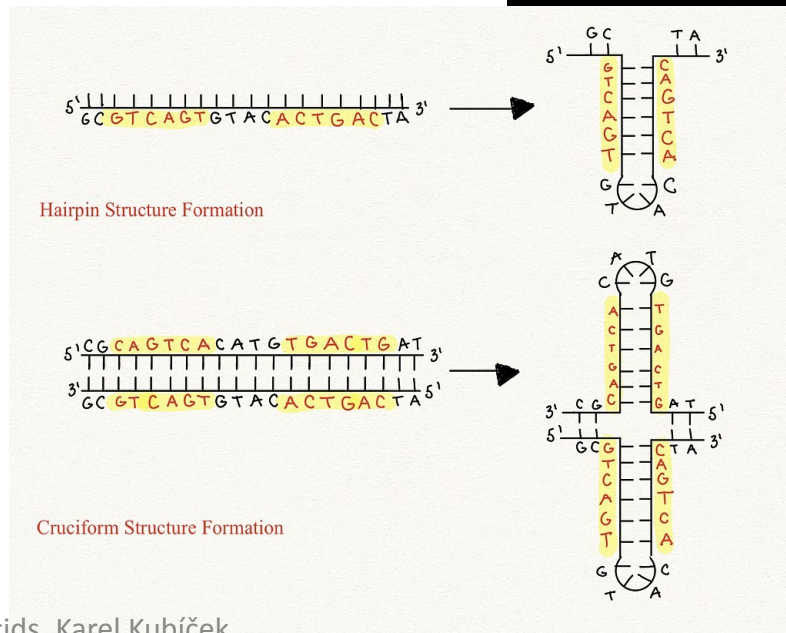
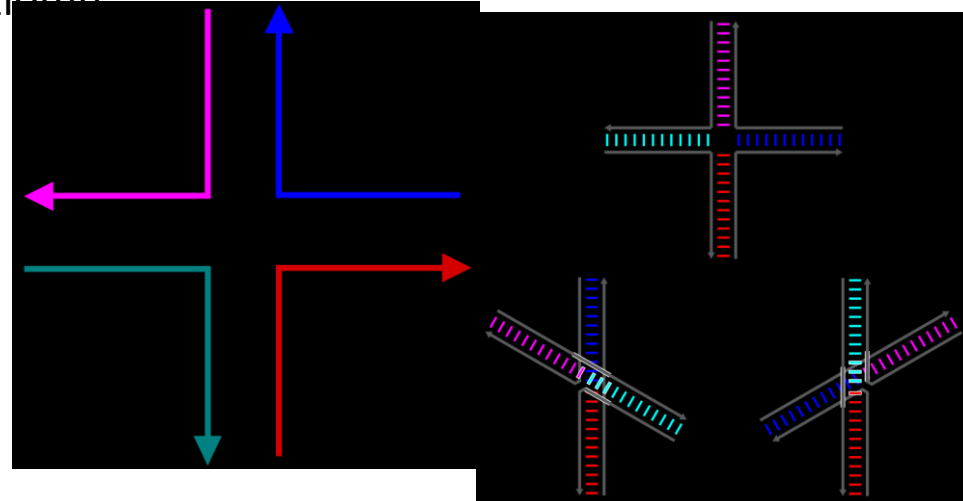
**2-tetrad
antiparallel
basket**

Hansel et al. Nucl Acids Res (2011)

Další významné formy DNA:

- 1) Hollidayův spoj (**Holliday junction**)
- 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

klíčový meziprodukt v mnoha typech genetické rekombinace a také při opravě dvouřetězcových zlomů



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1) Hollidayův spoj (**Holliday junction**)

klíčový meziprodukt v mnoha typech genetické rekombinace a také při opravě dvouřetězcových zlomů.

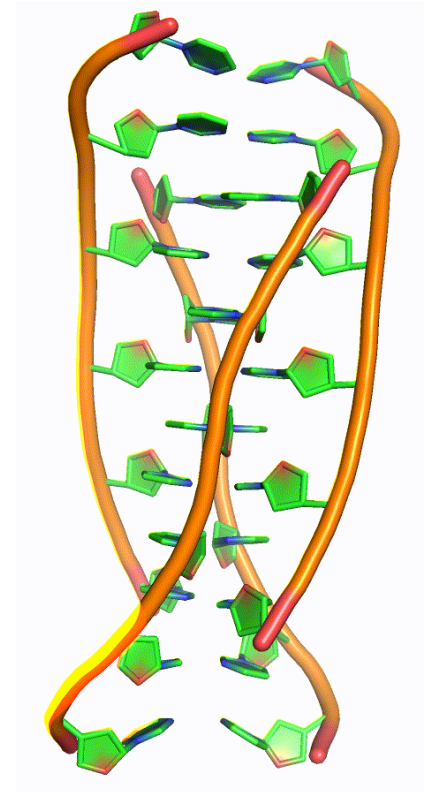
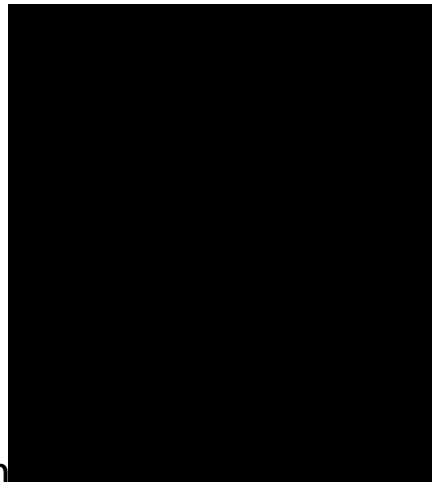
2) displacement loop (**D-loop**, D-smyčka)

3) **R-loop** (R-smyčka)

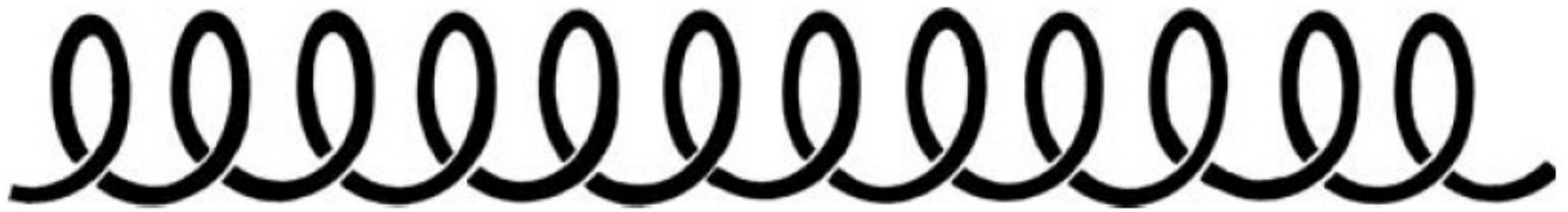
4) Křížová struktura DNA (**cruciform**)

5) **i-motif DNA / i-motif RNA**

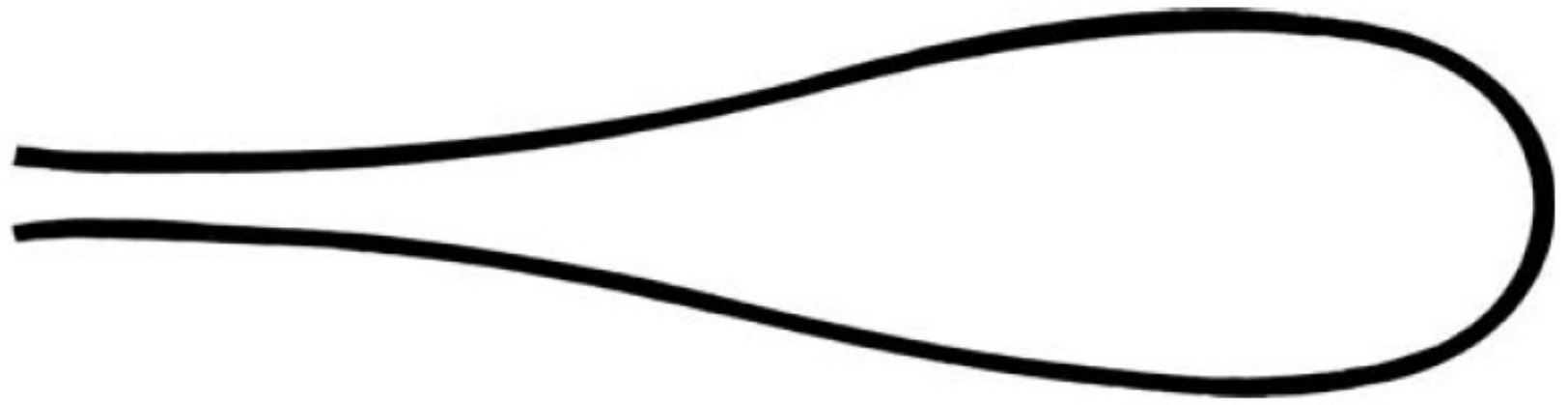
6) DNA nanotechnologie – DNA origami



(a)



(b)



(c)



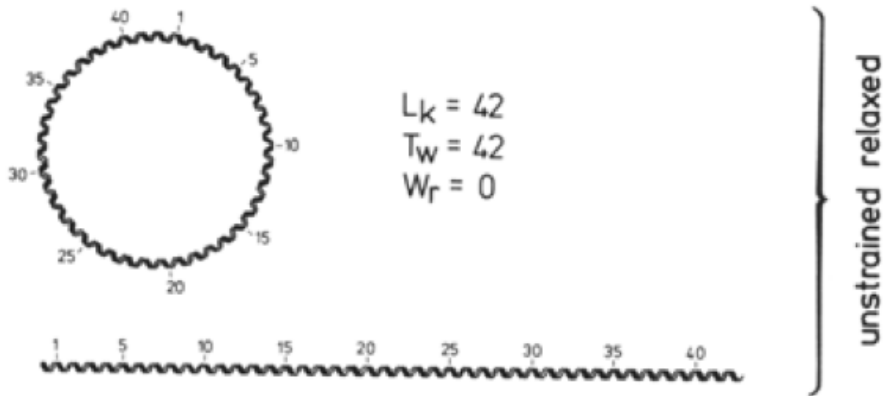
Superhelikální cirkulární DNA

$$L_k = W_r + T_w$$

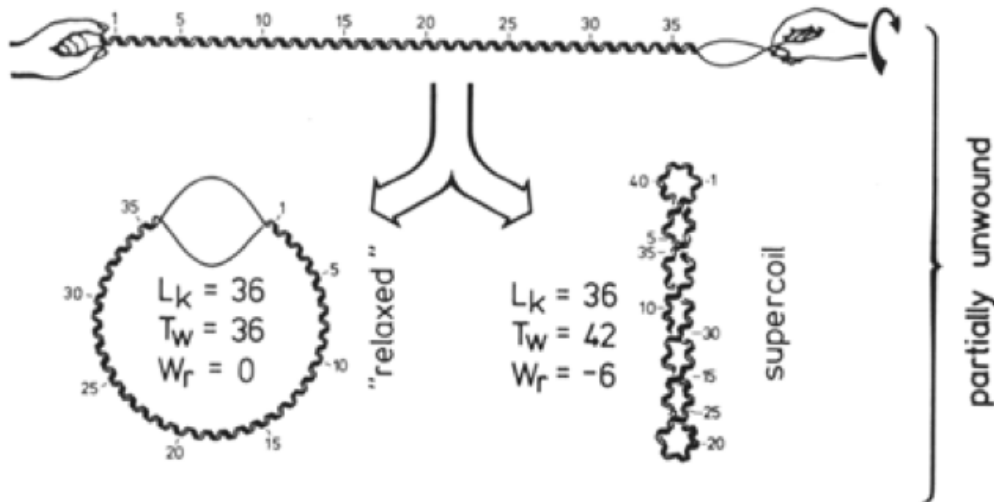
L_k - *linking* () – topologická vlastnost cirkulární DNA, udává, kolikrát je jeden řetězec DNA obtočen kolem druhého v pravotočivém směru (vzhledem k tomu, že referenční je B-DNA). **L_k** zůstává pro danou cirkulární DNA konstantní (neboť “konce” jsou zafixované a nemůže docházet k rozvinutí). **L_k**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

T_w - *twisting* (otočení) – v relaxovaném stavu se **T_w**=**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.

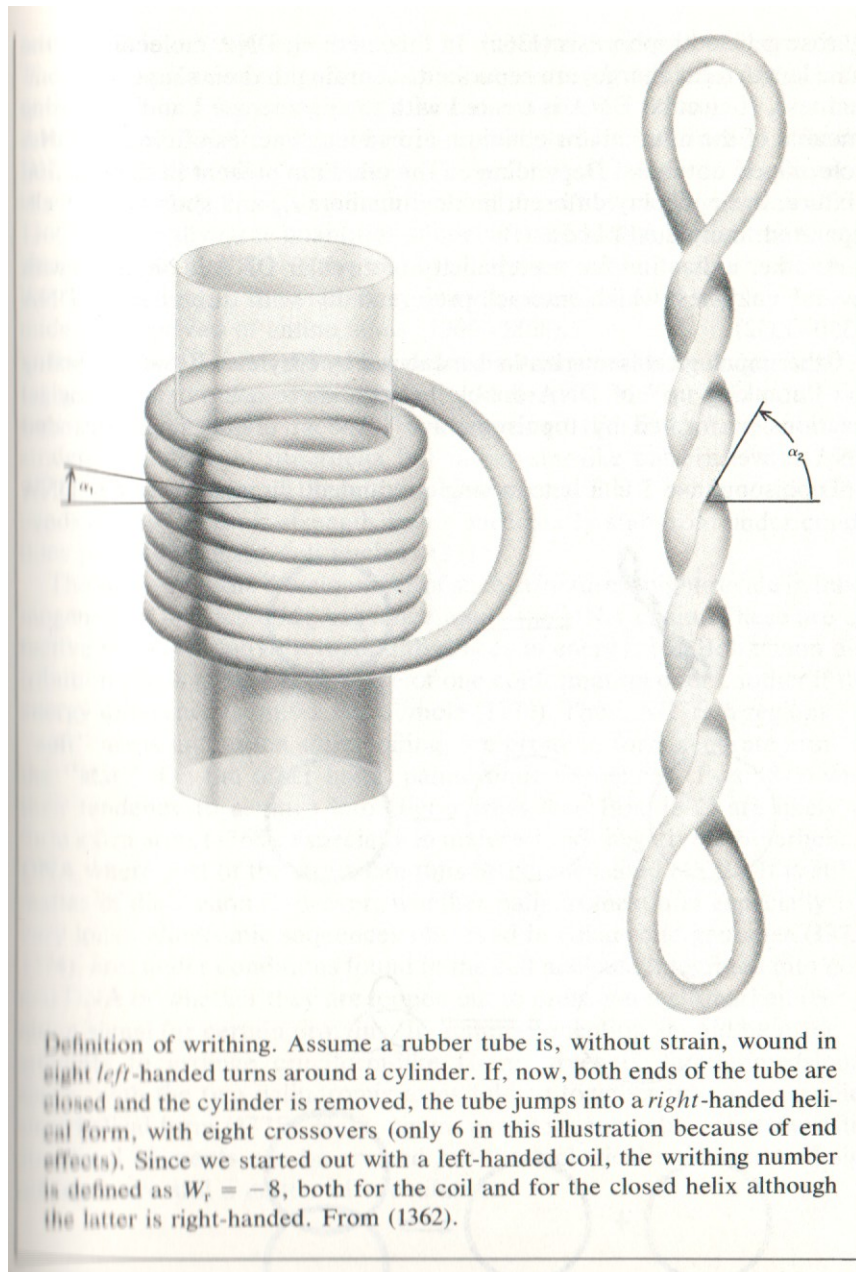
W_r - *writhing* (skřížení) – z důvodu strukturních “potřeb” DNA různé hodnoty **L_k** kružnice mohou způsobit nikoliv změnu v otáčkách (**T_w**), ale vznik superhelixu (superšroubovice). Vznik superhelixu je definován číslem **W_r**. Pro pravotočivé superšroubovice je **W_r** záporné!!!



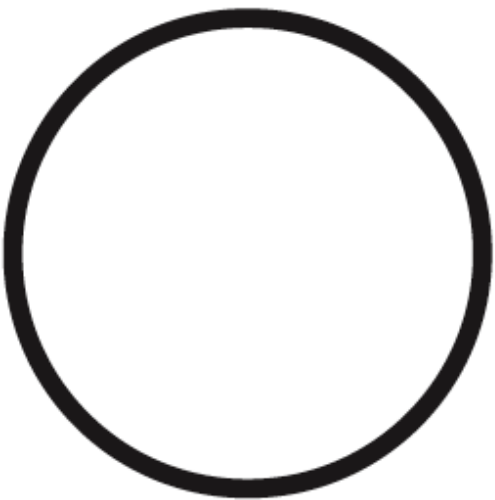
unwind by six
right handed turns
 $\Delta L_k = -6$



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



$$\text{Tw} = 0$$
$$\text{Wr} = 0$$



$$\text{Lk} = 0$$

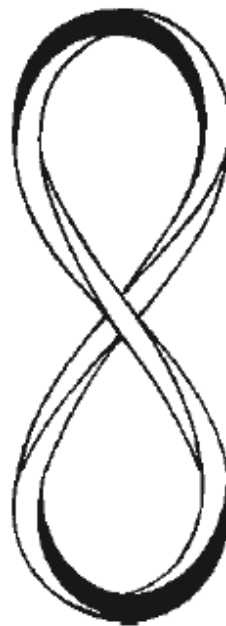
(a)

$$\text{Tw} = +3$$
$$\text{Wr} = 0$$



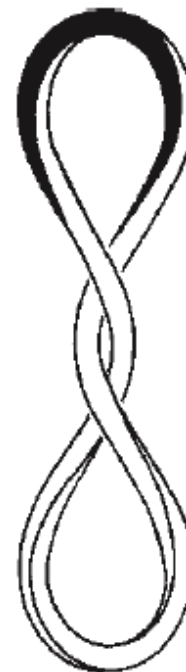
(b)

$$\text{Tw} = +2$$
$$\text{Wr} = +1$$



(c)

$$\text{Tw} = +1$$
$$\text{Wr} = +2$$



(d)

$$\text{Tw} = 0$$
$$\text{Wr} = +3$$



(e)



$$\text{Lk} = +3$$

