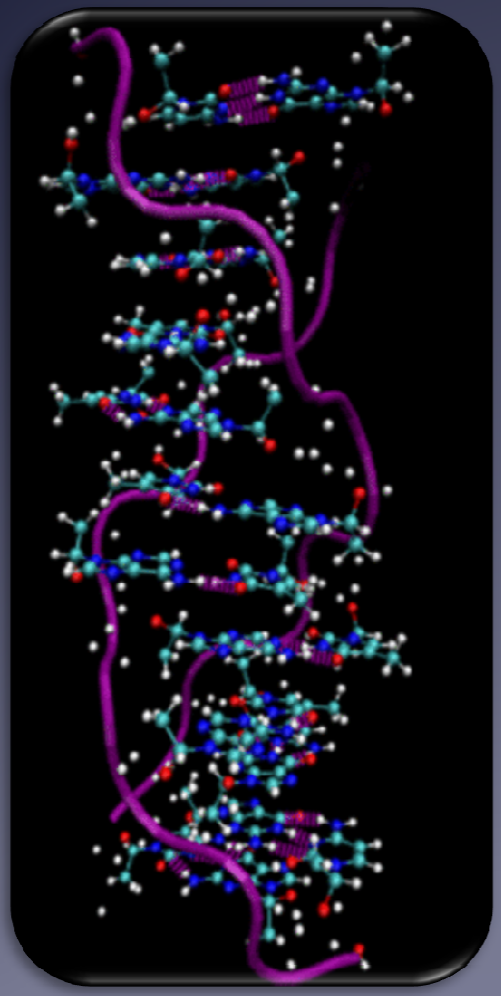


DNA structure

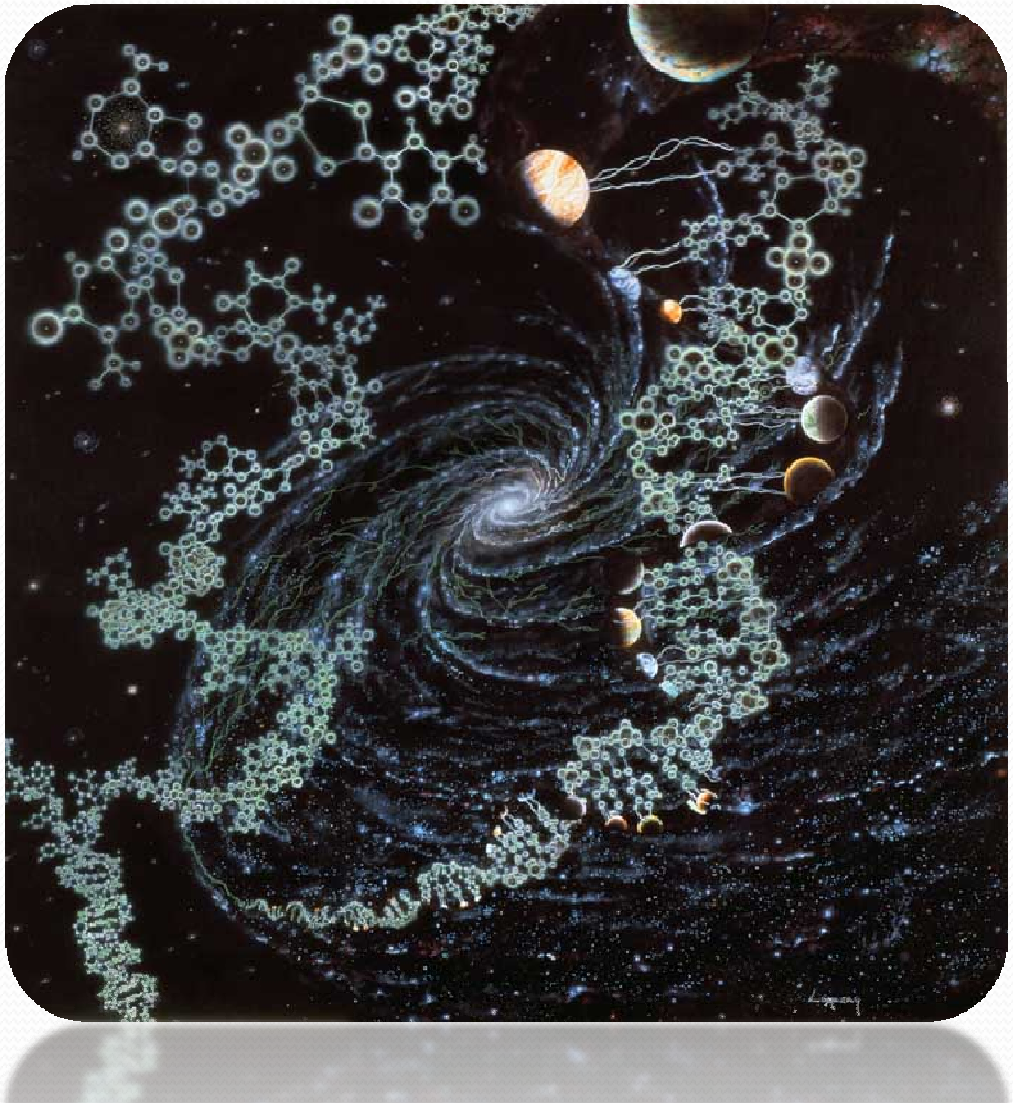
Laura Carol
Elisabet Freixas
Alba Romaguera

Structural Biology – UPF

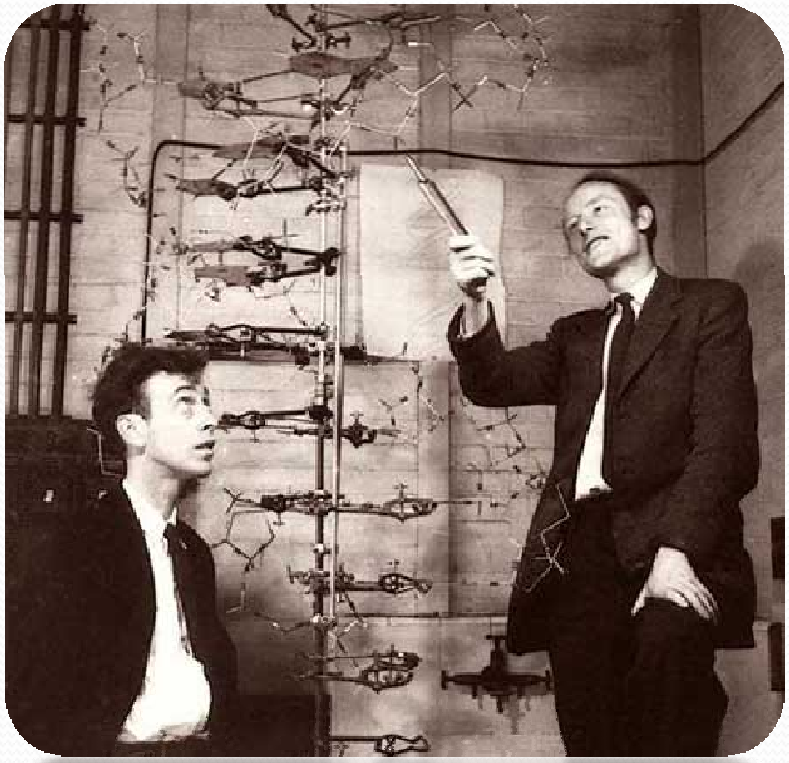
Introduction

- **DNA**

store and transmit genetic information



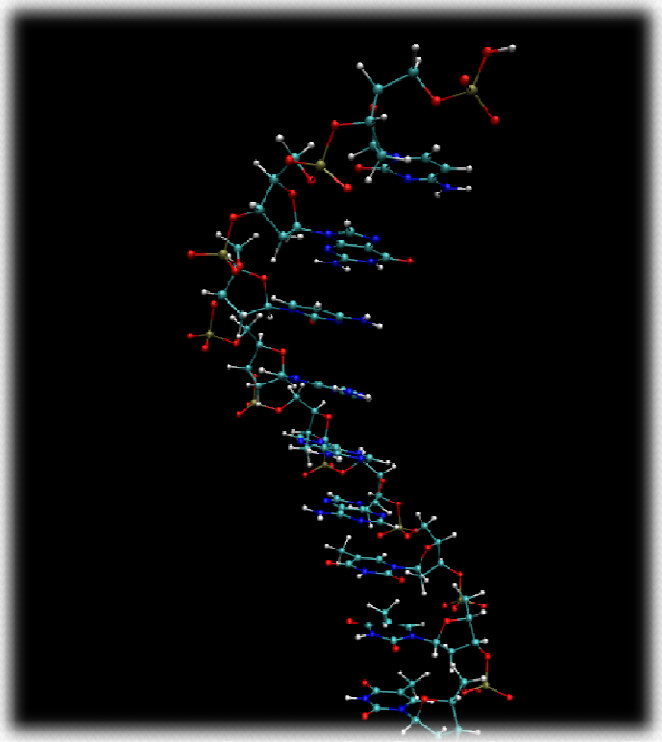
A little bit of history



- End of s. XIX, **Friedrich Miescher** isolates for first time DNA in salmon sperm
- 1944 **Avery, MacLeod & McC**arty discovered DNA could transfect from a pathogenic bacteria strain to another no pathogenic.
- Experiment of transfection of E.Coli by Bacteriophage T2. **Hershey & Chase**
- 1953 **Watson & Crick** proposed a structure for DNA after observing a X-ray diffraction image of DNA taken by **R. Franklin** (1952)

DNA

Composition



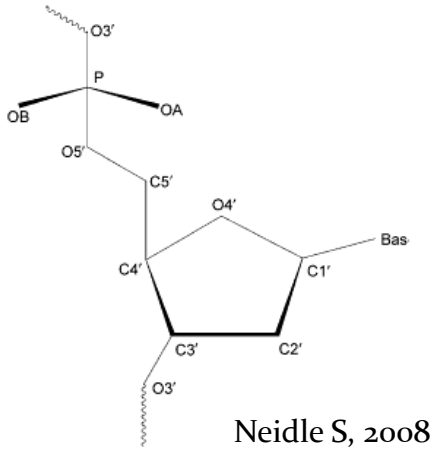
DNA (deoxyribonucleic acid): macromolecule composed by a repetition of:

- Backbone
  - Phosphate group
  - Sugar: 2'-deoxyribose

  } phosphodiester bond

  glycosidic bond

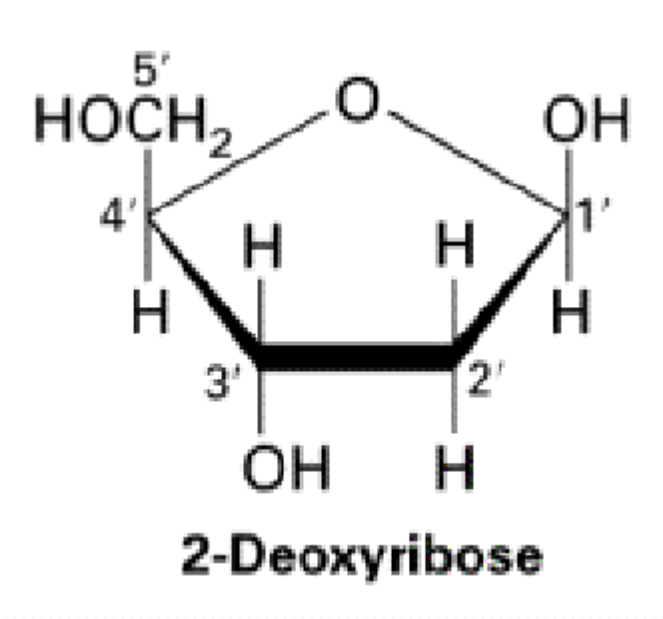
- Nitrogenous base

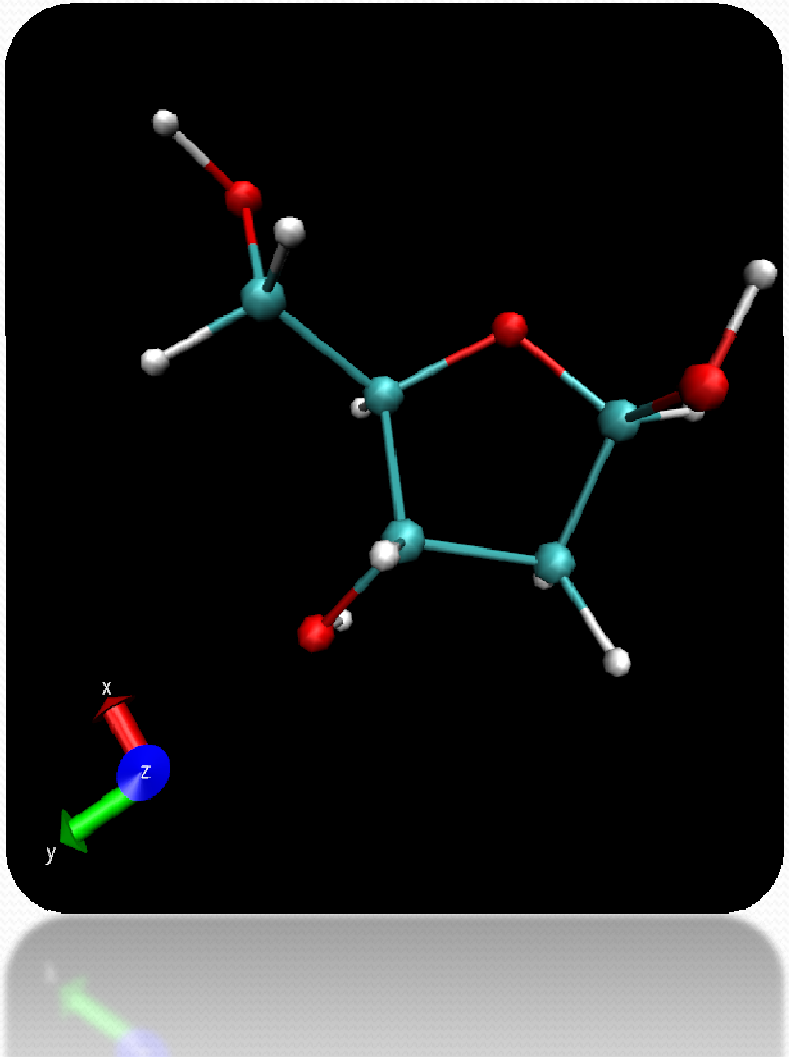


Neidle S, 2008

Backbone

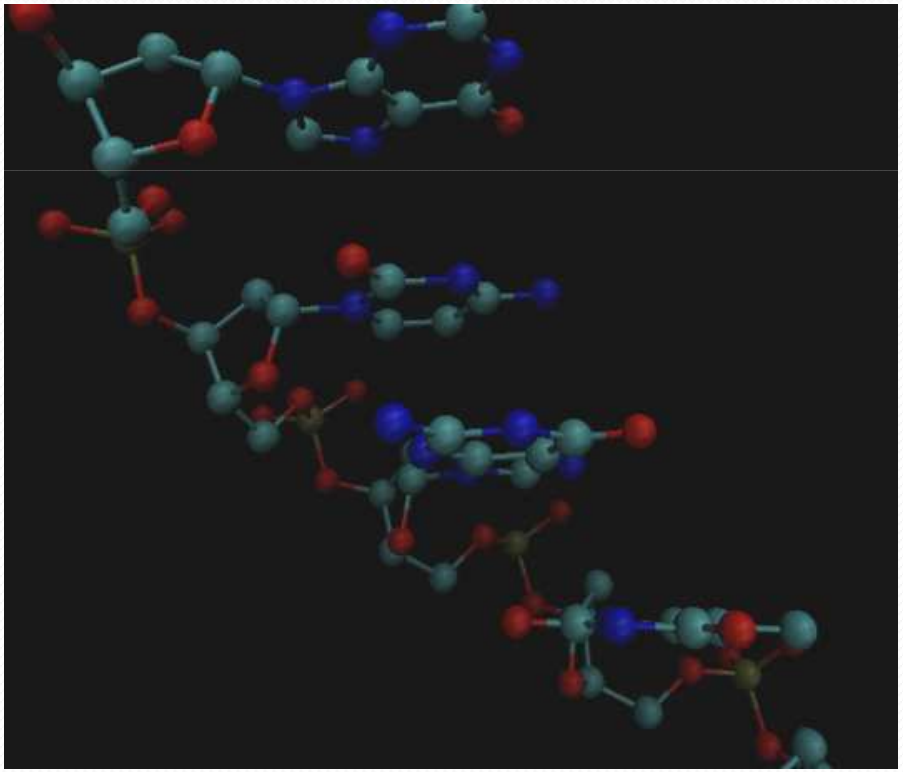
- **β-D-2-deoxyribose**

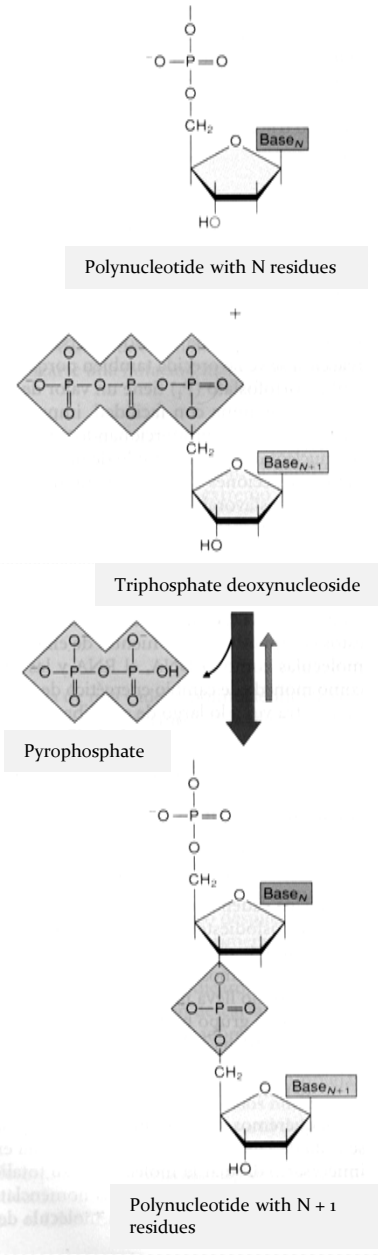




Backbone

- Phosphate group - Phosphodiester bond

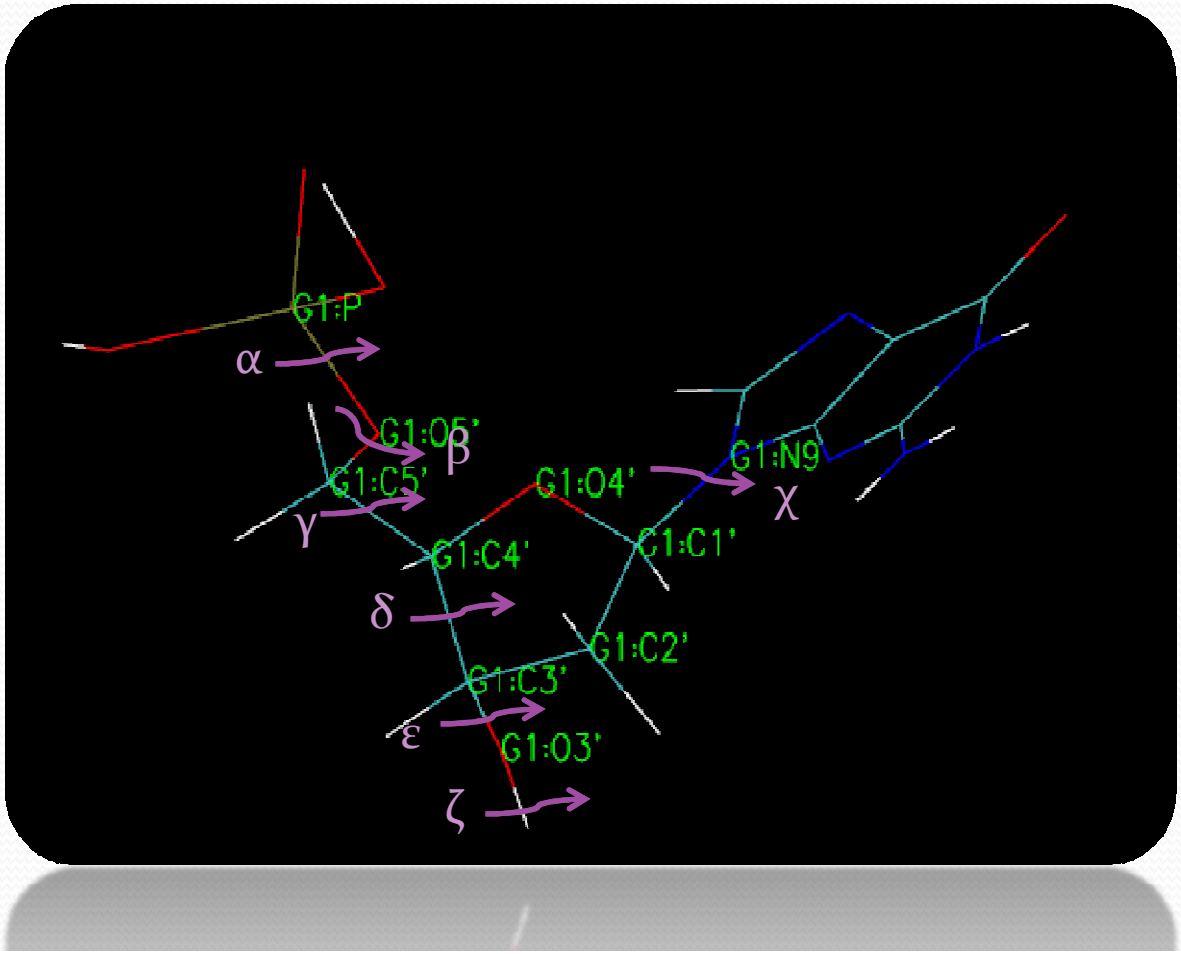




Mathews CK, 2002

Backbone

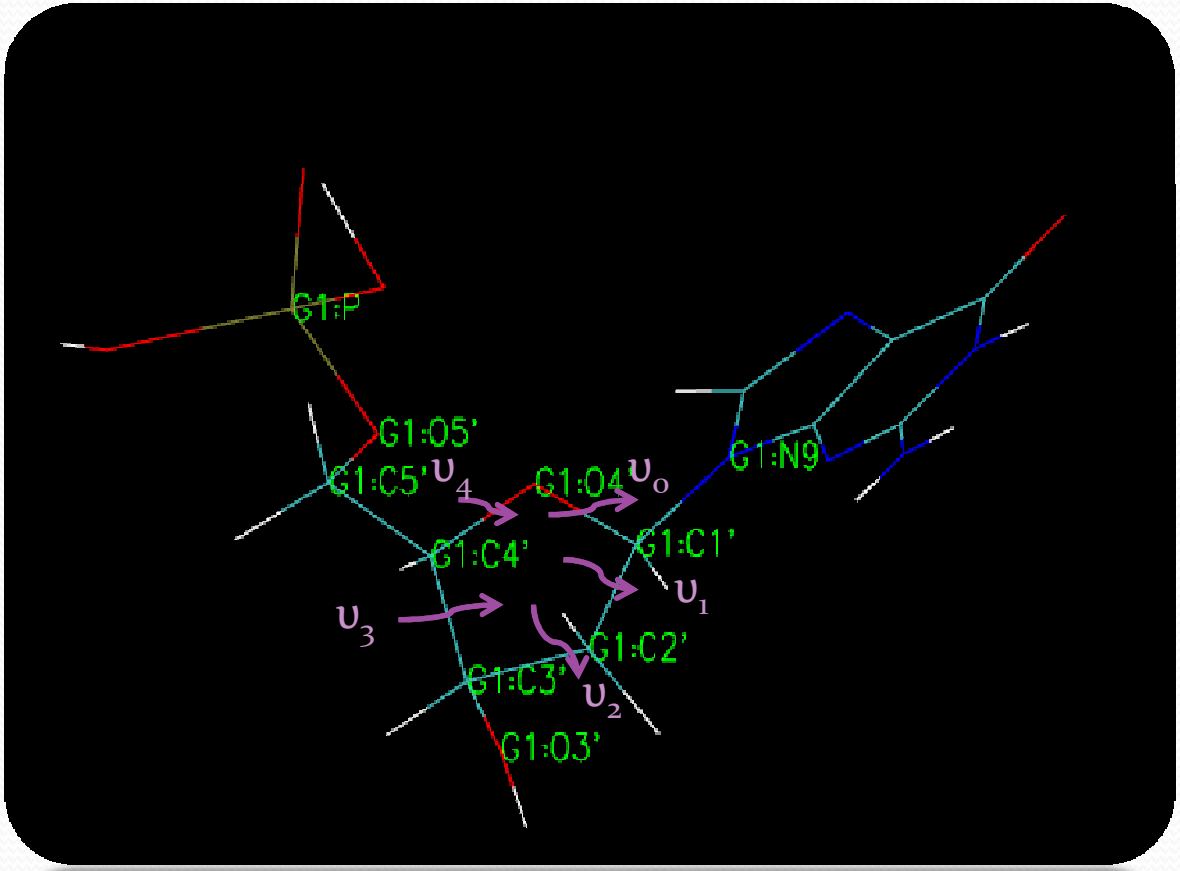
- Rotation



α O3'-P-O5'-C5'
β P-O5'-C5'-C4'
γ O5'-C5'-C4'-C3'
δ C5'-C4'-C3'-O3'
ε C4'-C3'-O3'-P
ζ C3'-O3'-P-O5'
χ O4'-C1'-N9/N1-C4/C2

Backbone

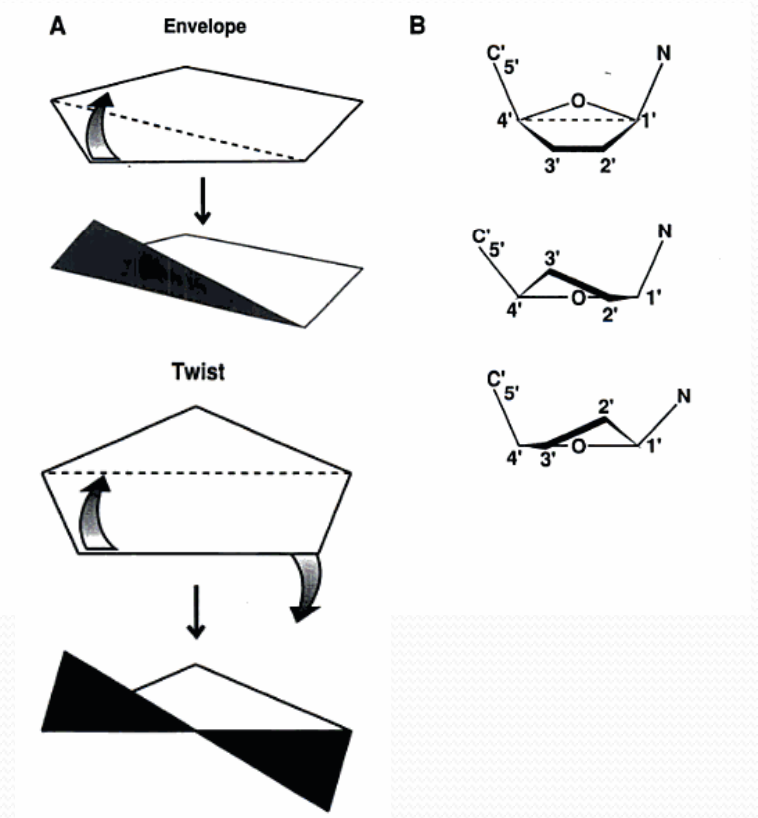
- desoxyribose angles

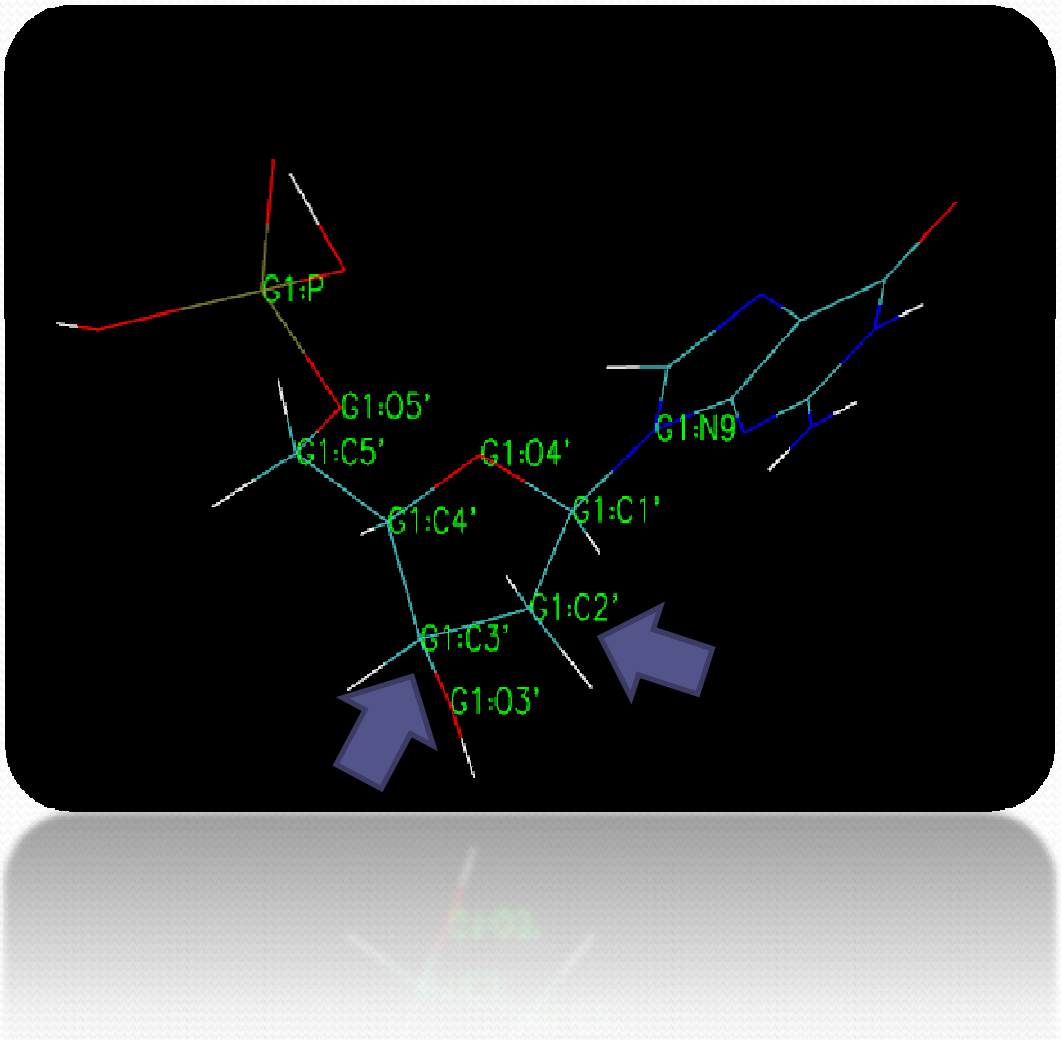


v0: C4'-O4'-C1'-C2'
v1: O4'-C1'-C2'-C3'
v2: C1'-C2'-C3'-C4'
v3: C2'-C3'-C4'-O4'
v4: C3'-C4'-O4'-C1'

Backbone

Deoxyribose conformations

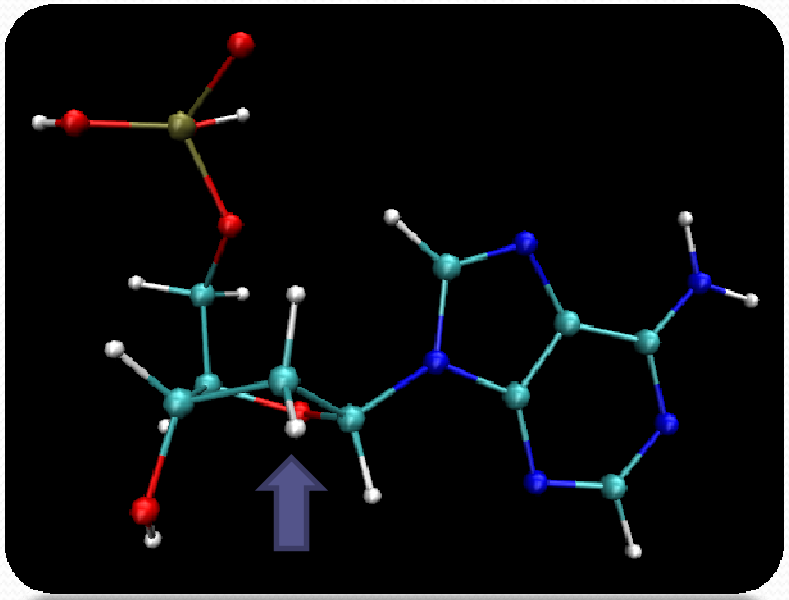


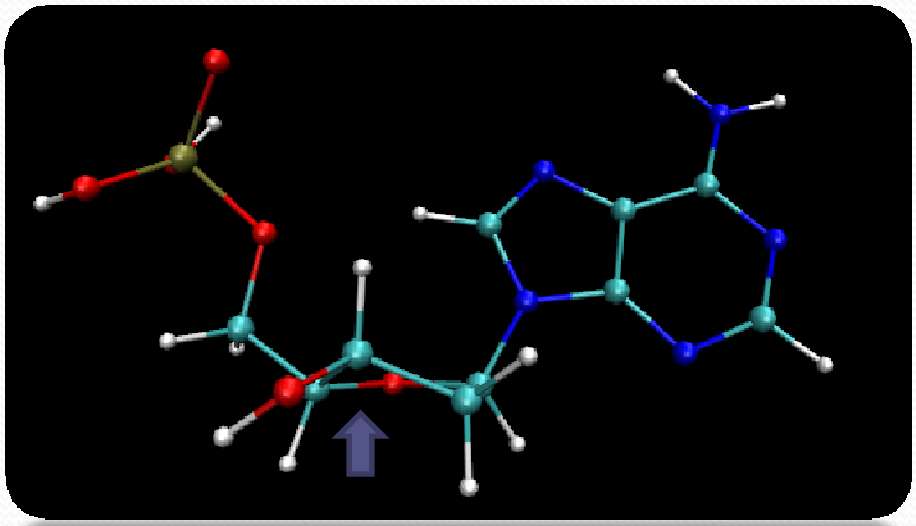


Backbone

- Ring pucker

C2'endo (**B-DNA**/Z-DNA C/T) – C3'endo (**A-DNA**/ Z-DNA A/G)

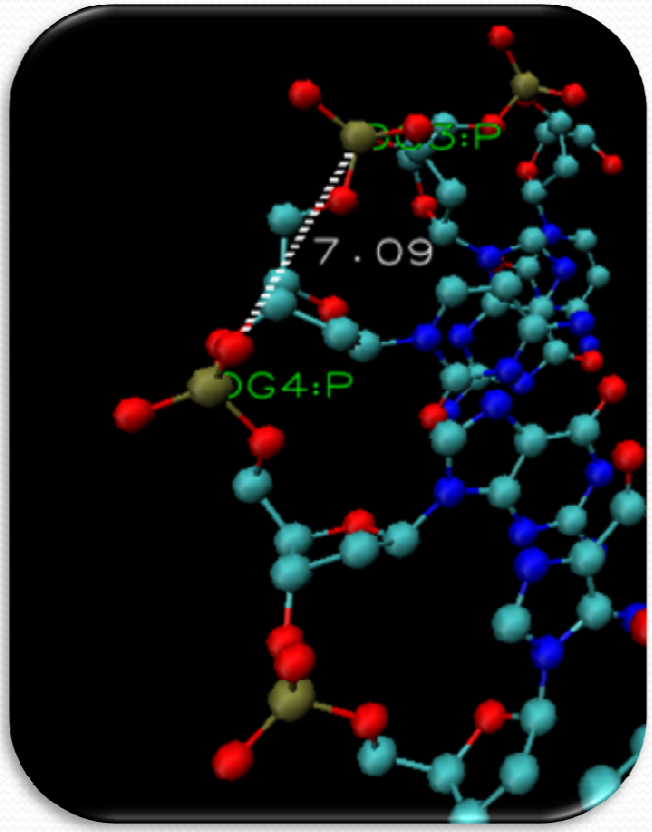


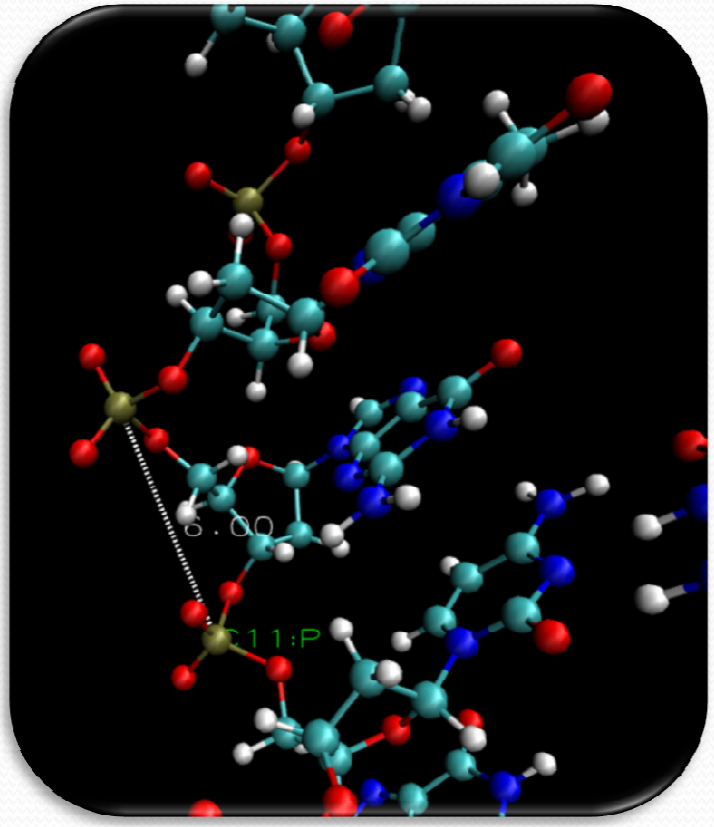


Backbone

- Ring Pucker - distance between P

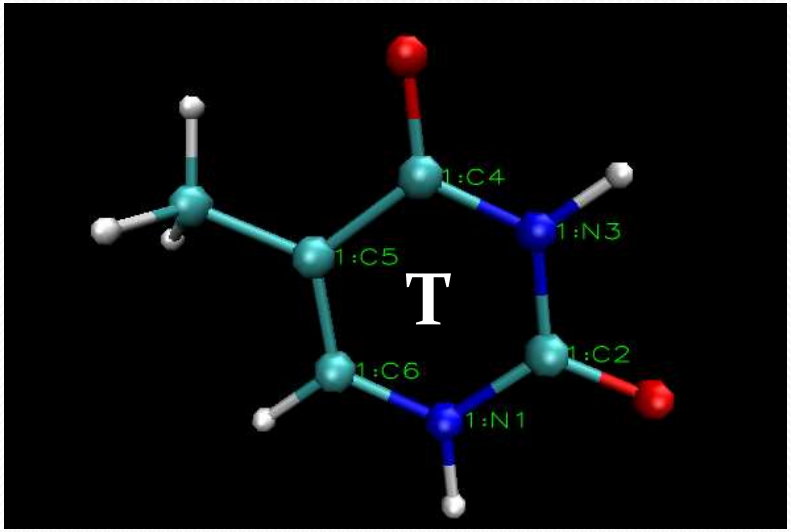
  C2'endo (**B-DNA** / Z-DNA C/T) – C3'endo (A-DNA / **Z-DNA** A/**G**)

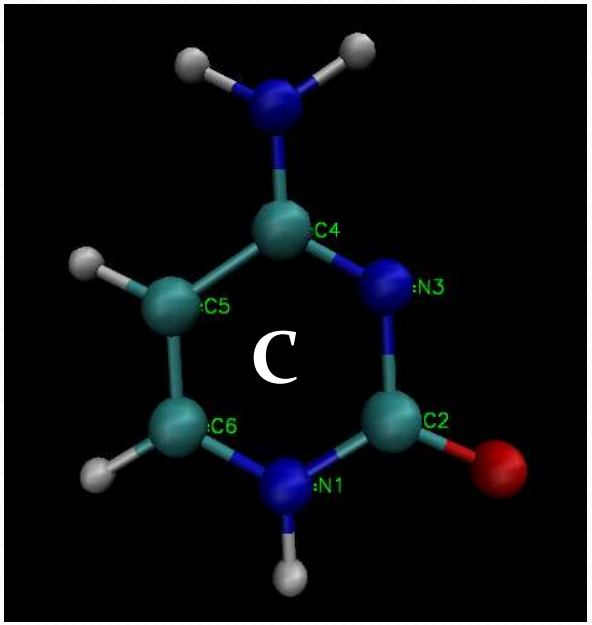




Nitrogenous bases

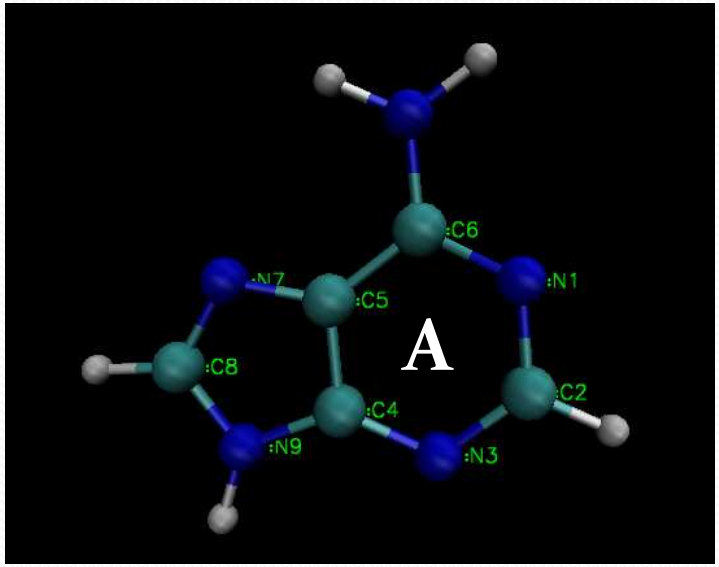
- Four nitrogenous bases: G C T A
  - Pyrimidine (Y)
    - Thymine (T)
    - Cytosine (C)

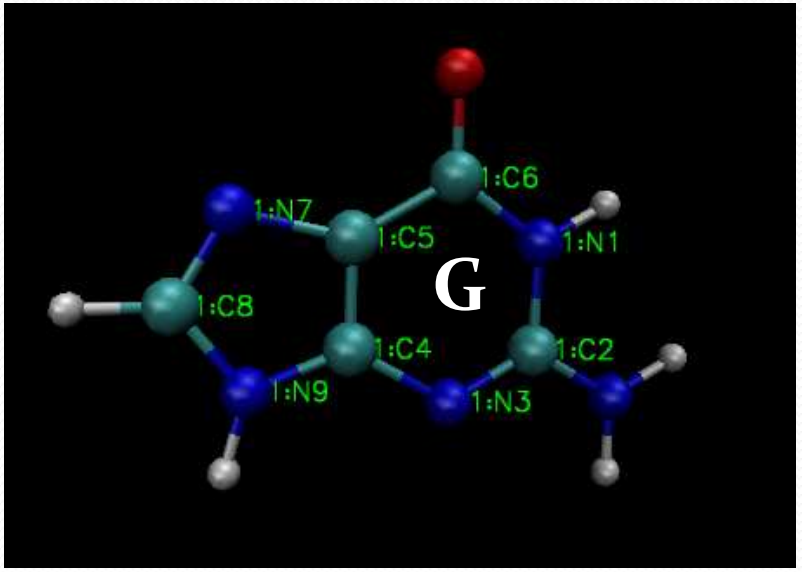




Nitrogenous bases

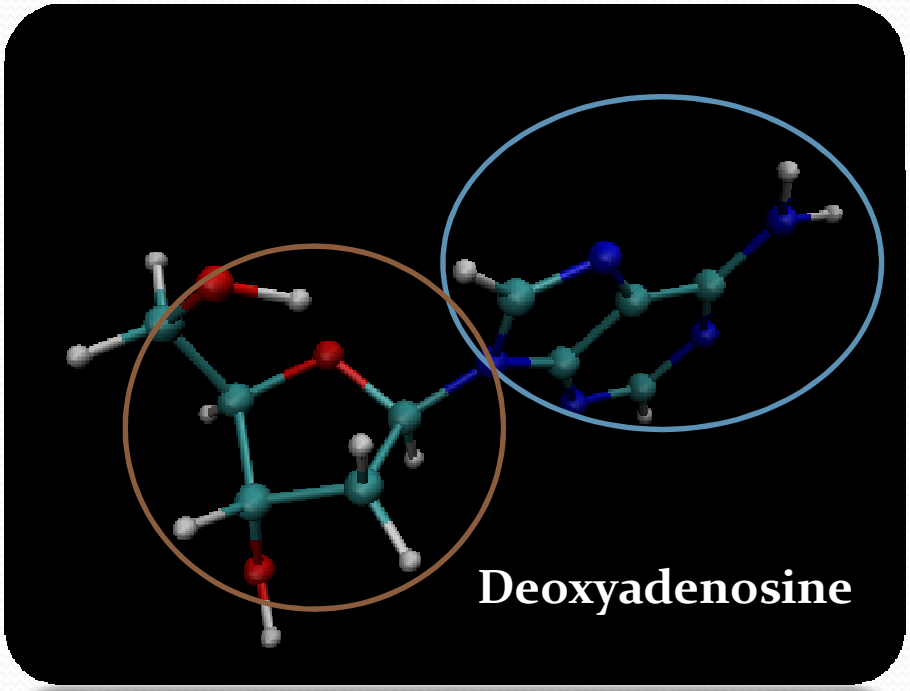
- Four nitrogenous bases: G C T A
  - Purines (R)
    - Adenine (A)
    - Guanine (G)

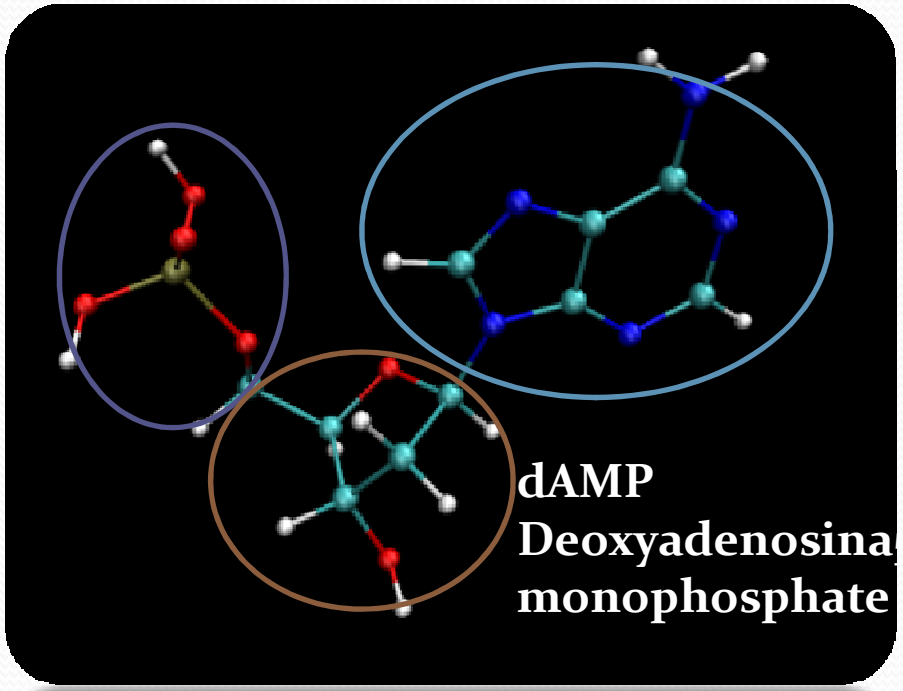




Nitrogenous bases

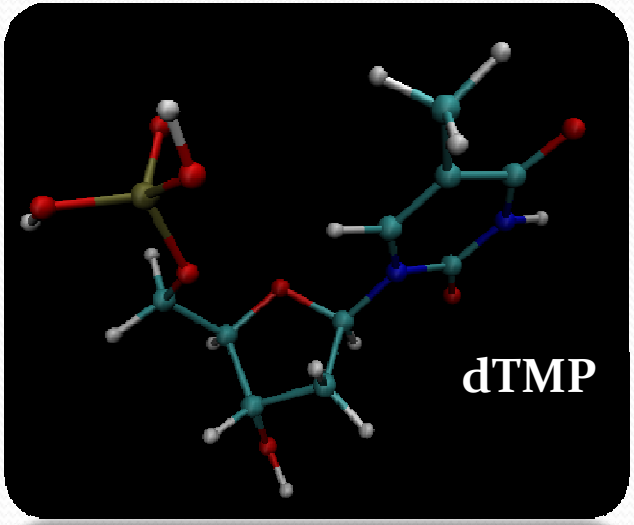
- Deoxynucleoside – deoxynucleotide

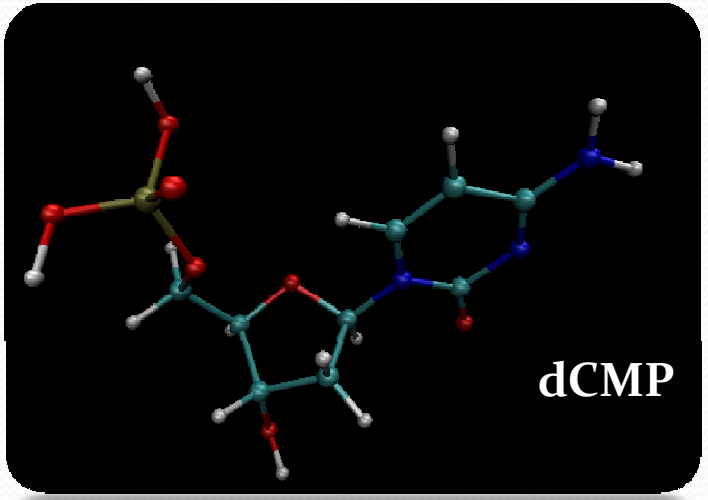


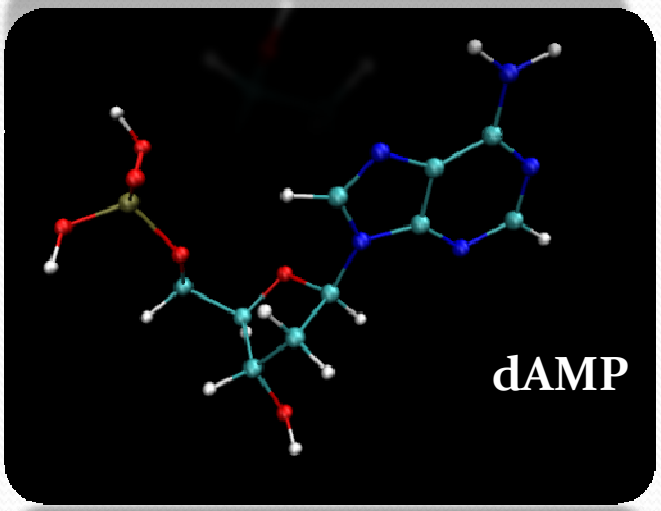


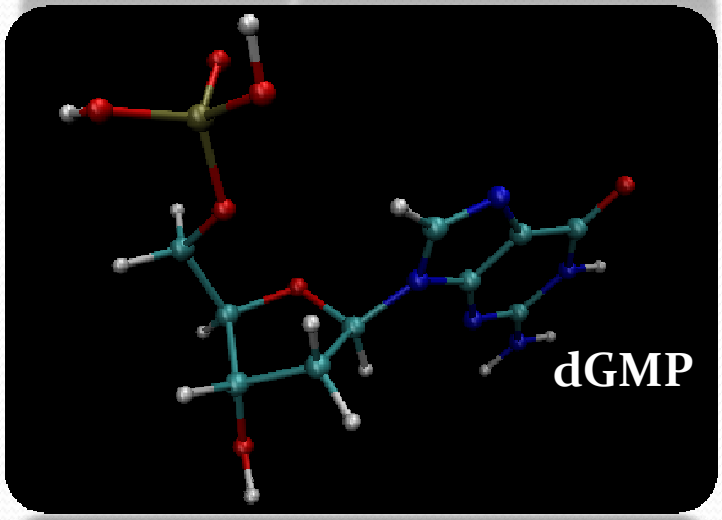
Nitrogenous bases

Deoxynucleotides









Nitrogenous bases

- Properties

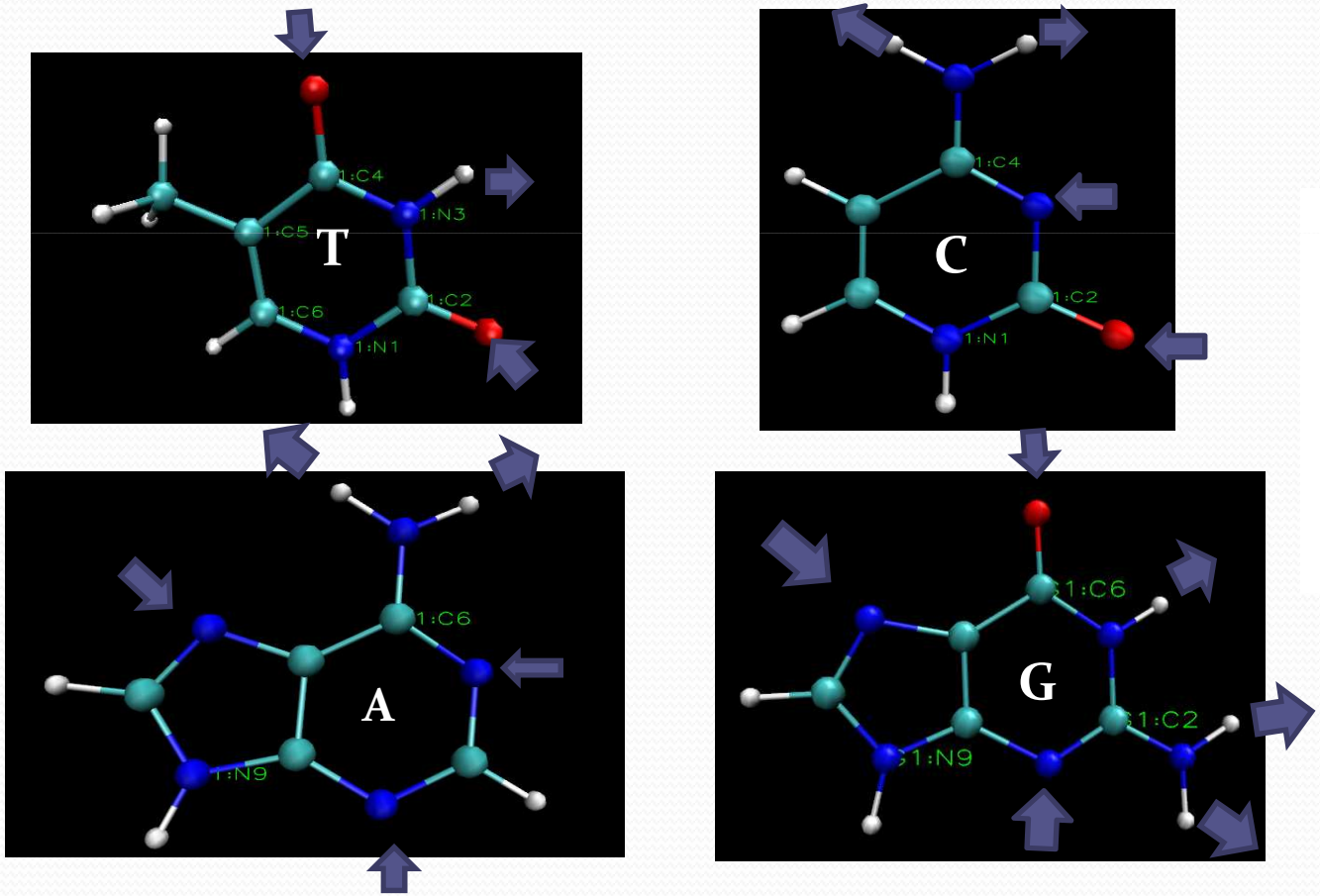


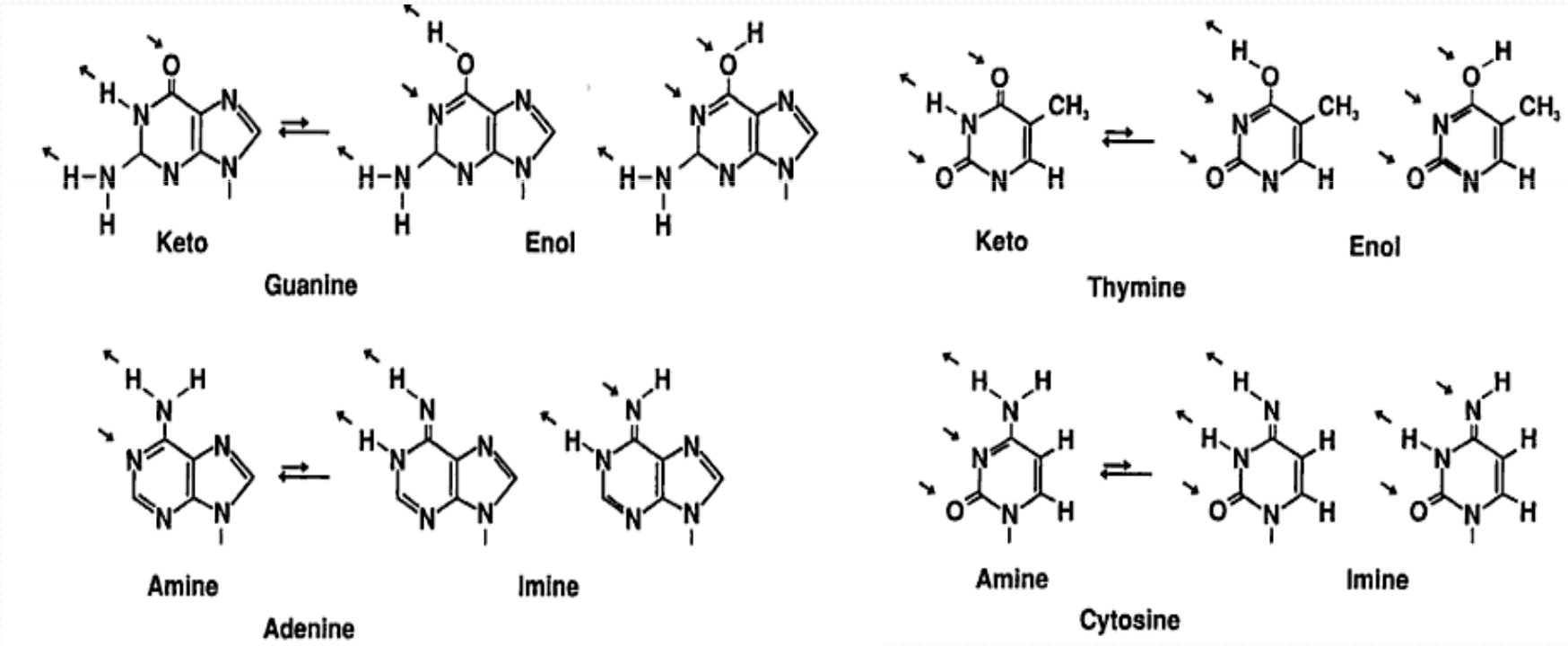
Table 2.1 *pK_a values for bases in nucleosid*

Bases (site of protonation)	*Nucleoside*
Adenine (N-1)	3.63
Cytosine (N-3)	4.11
Guanine (N-7)	2.20
Guanine (N-1)	9.50
Thymine (N-3)	9.80
Uracil (N-3)	9.25

Blackburn GM, 2006

Nitrogenous bases

- Tautomers

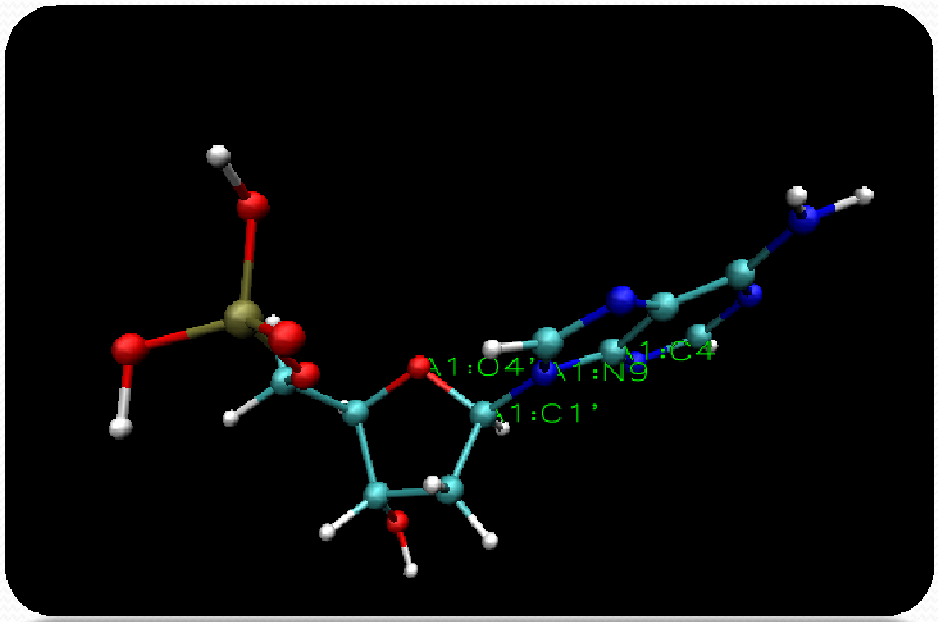


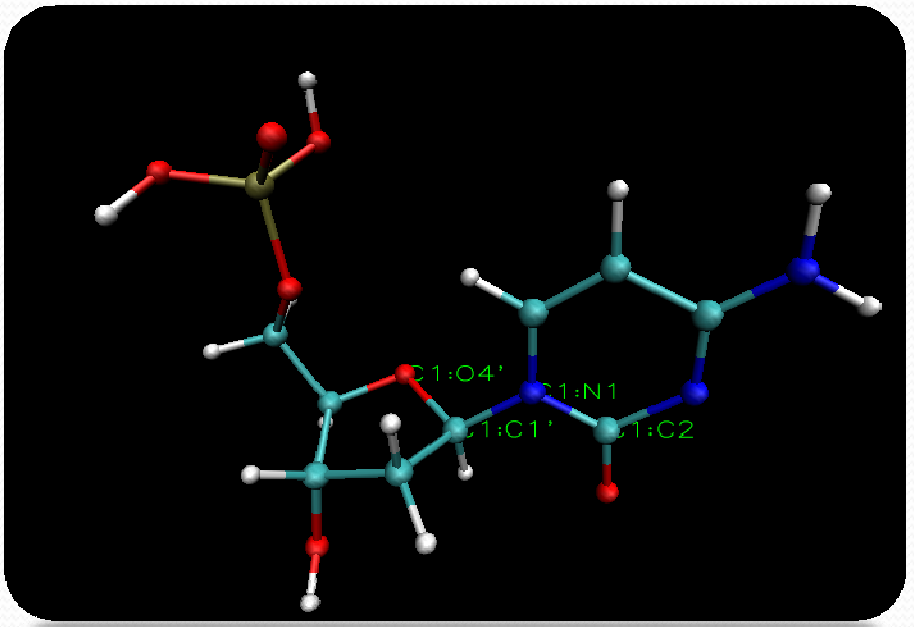
Sinden RR, 1994

Nitrogenous bases

- β Glycosidic bond

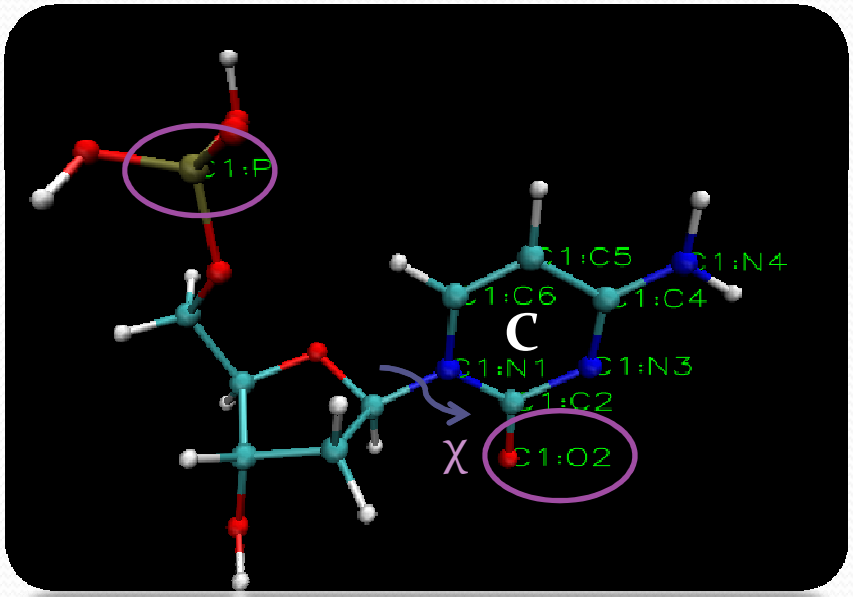
Purines: O4'-C1'-N9-C4 Pyrimidines O4'-C1'-N1-C2

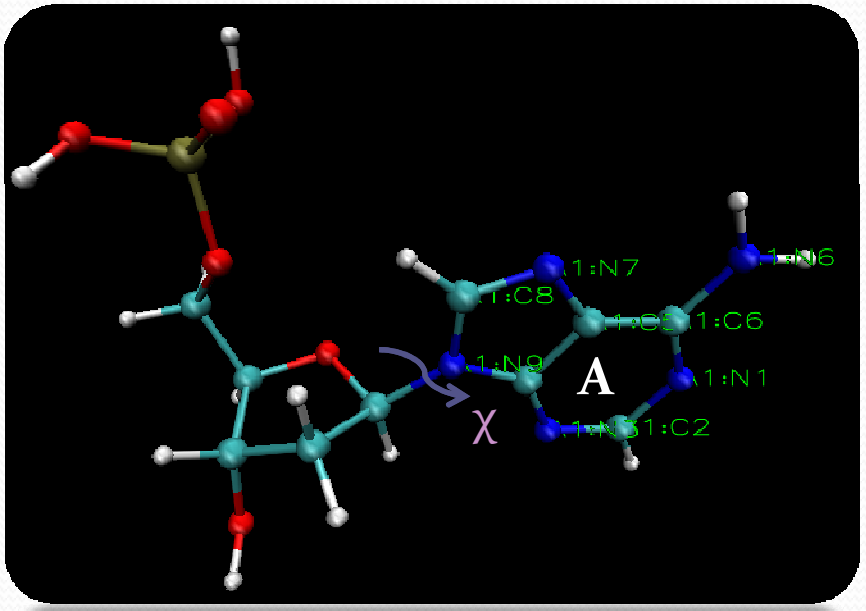




Nitrogenous bases

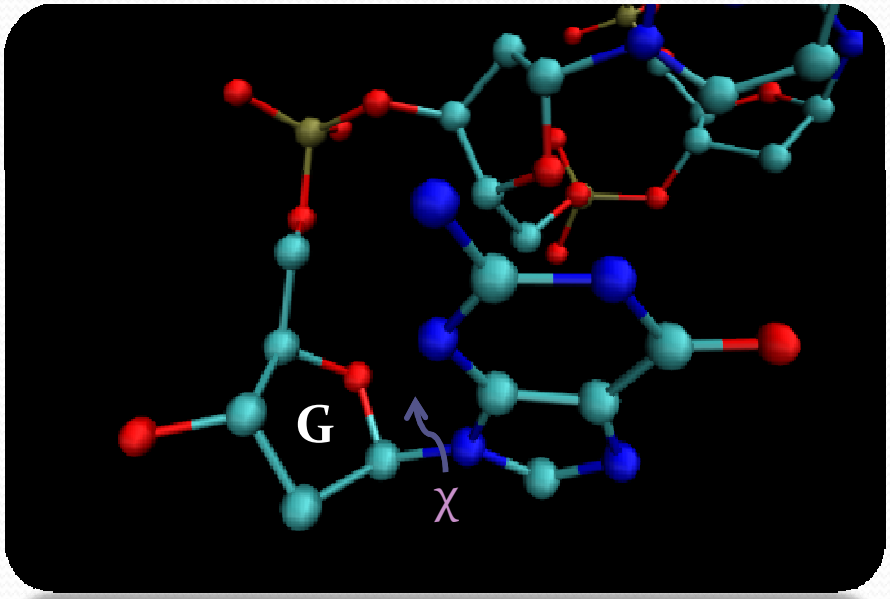
- Anti (B-DNA/A-DNA/Z-DNA pyrimidine) $-120^{o} > \chi > 180^{o}$





Nitrogenous bases

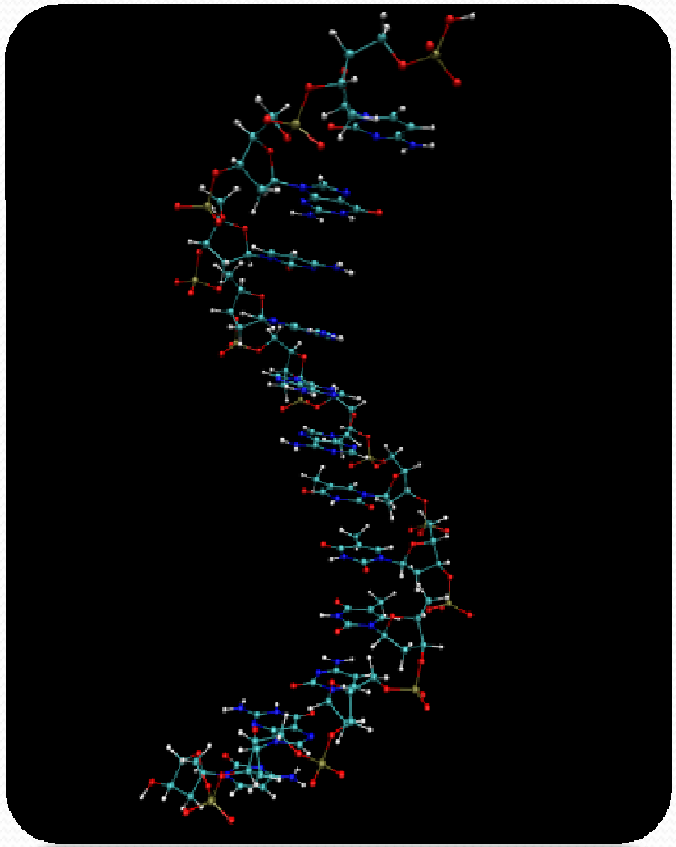
- Syn conformation (Z-DNA purine) $0^{\circ} < \chi < 90^{\circ}$

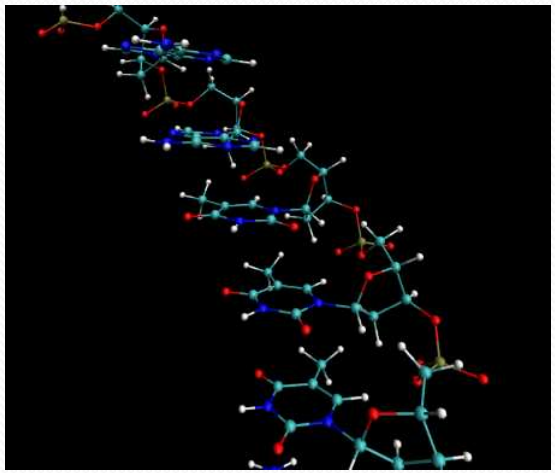


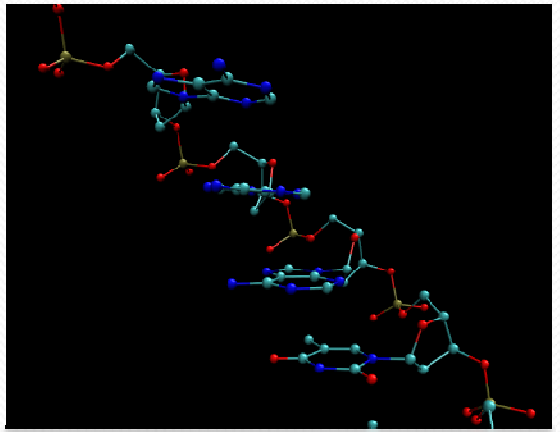
PRIMARY STRUCTURE

Primary structure

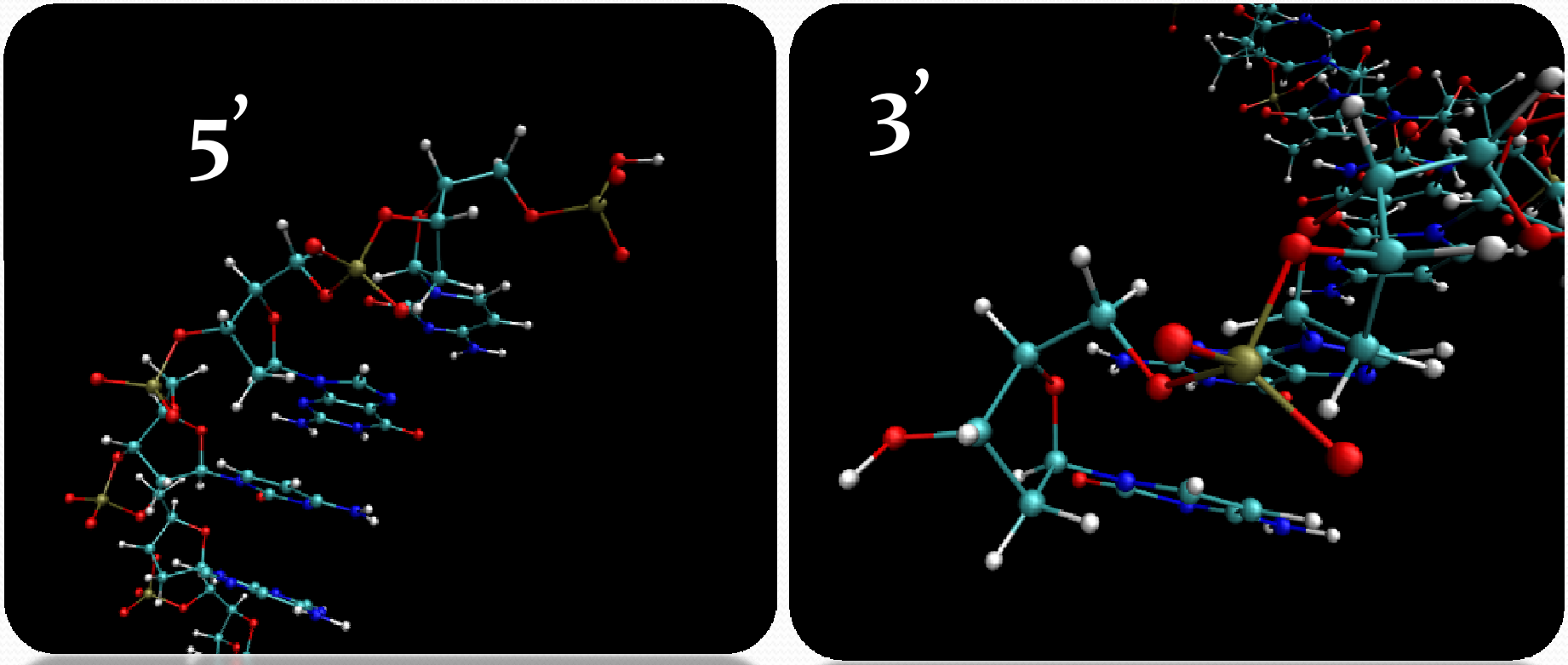
Single strand







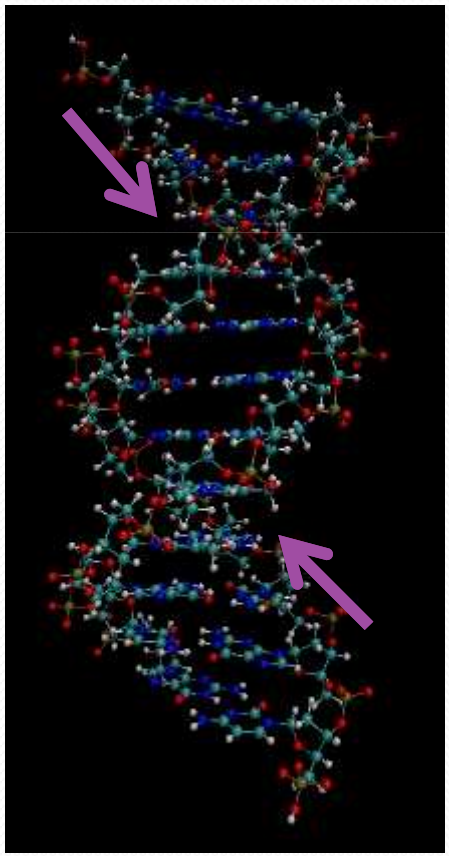
Primary structure

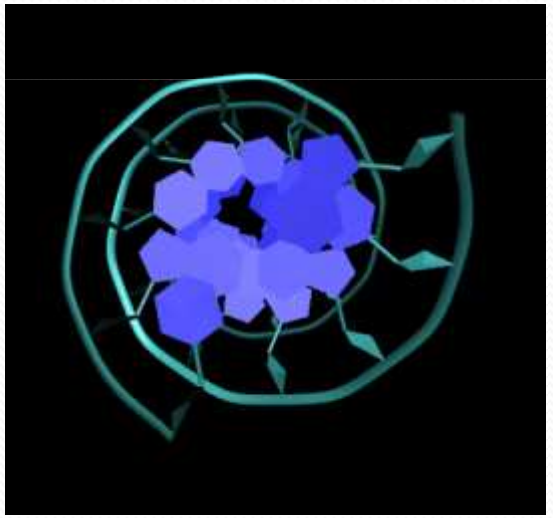


SECONDARY STRUCTURE

Secondary structure

- Watson and Crick double helix model

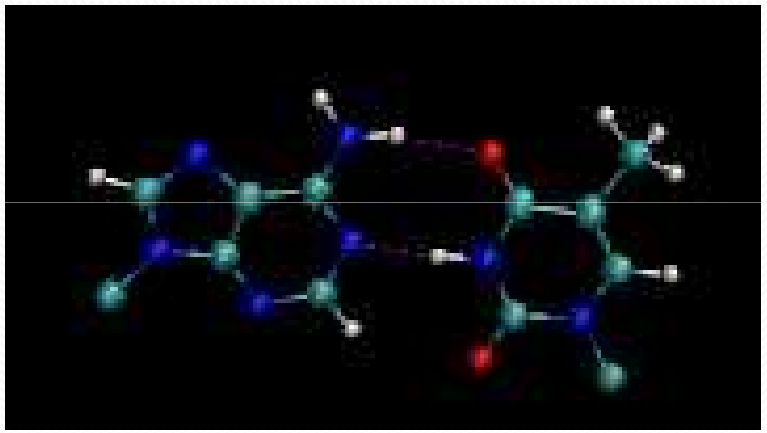


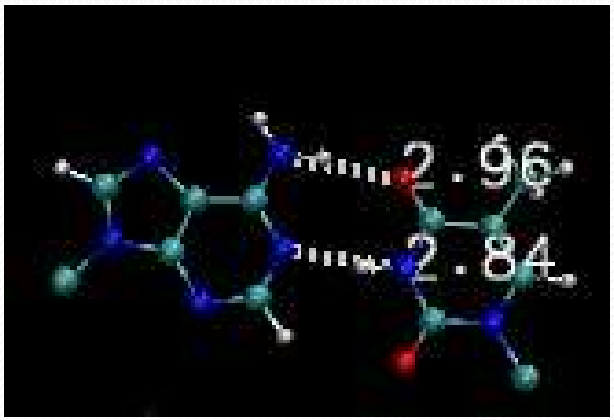


Secondary structure

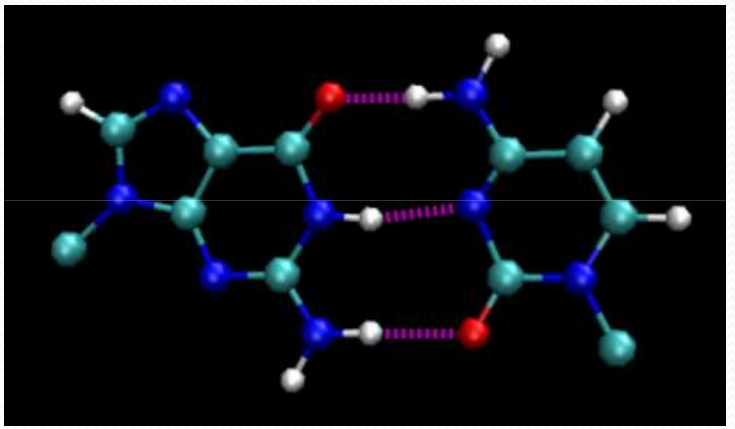
Base Pairing Watson & Crick

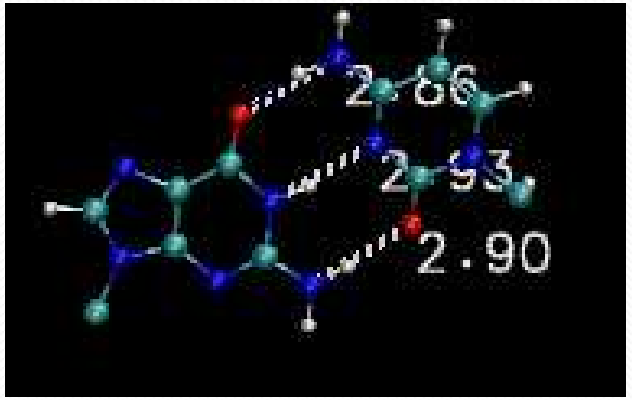
A·T





G·C

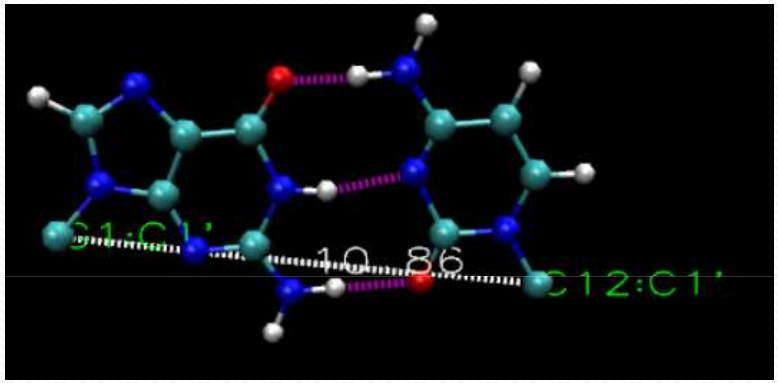


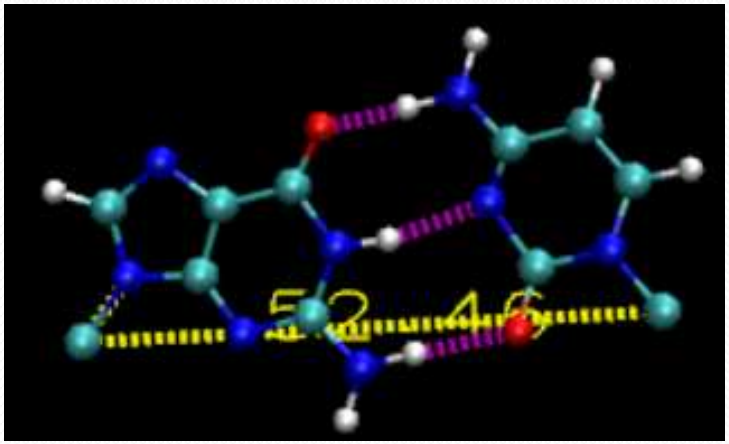


Secondary structure

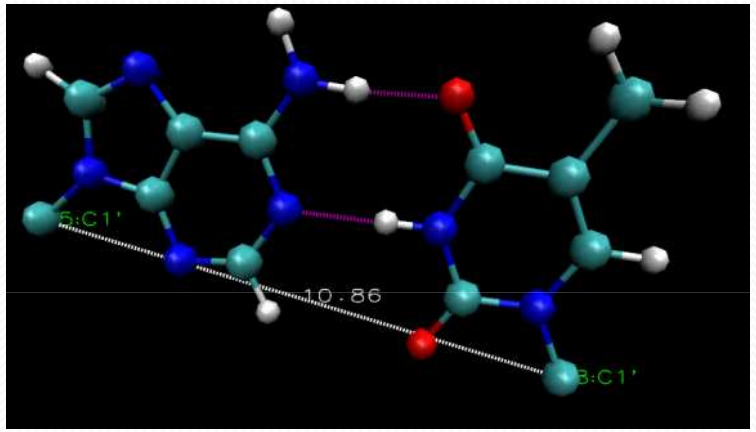
Base Pairing Watson & Crick

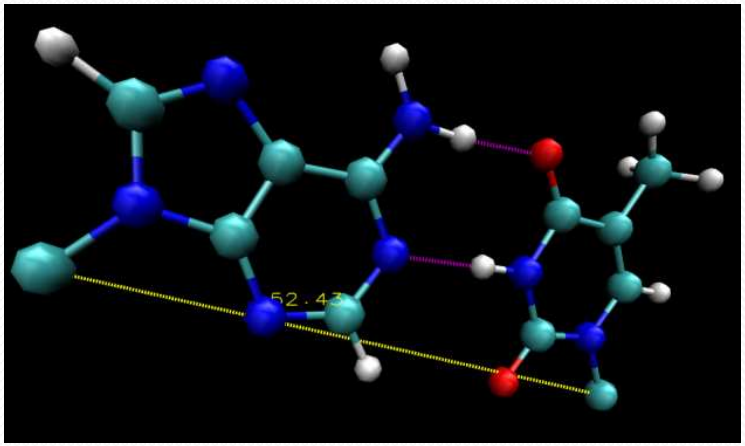
G·C





A·T



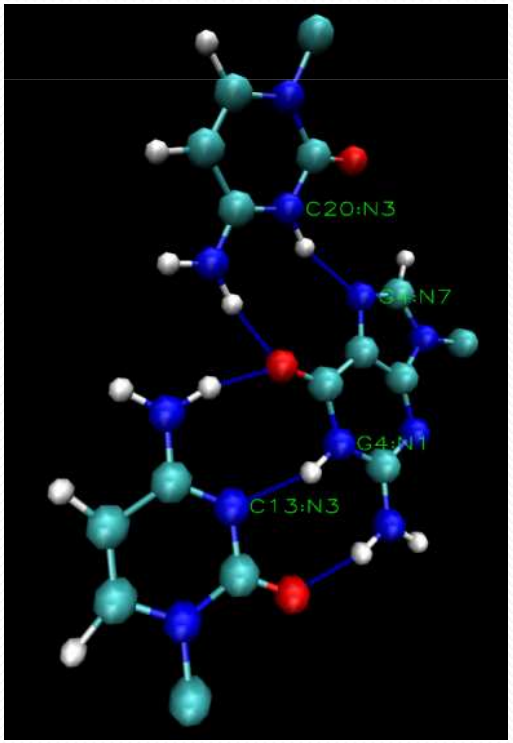


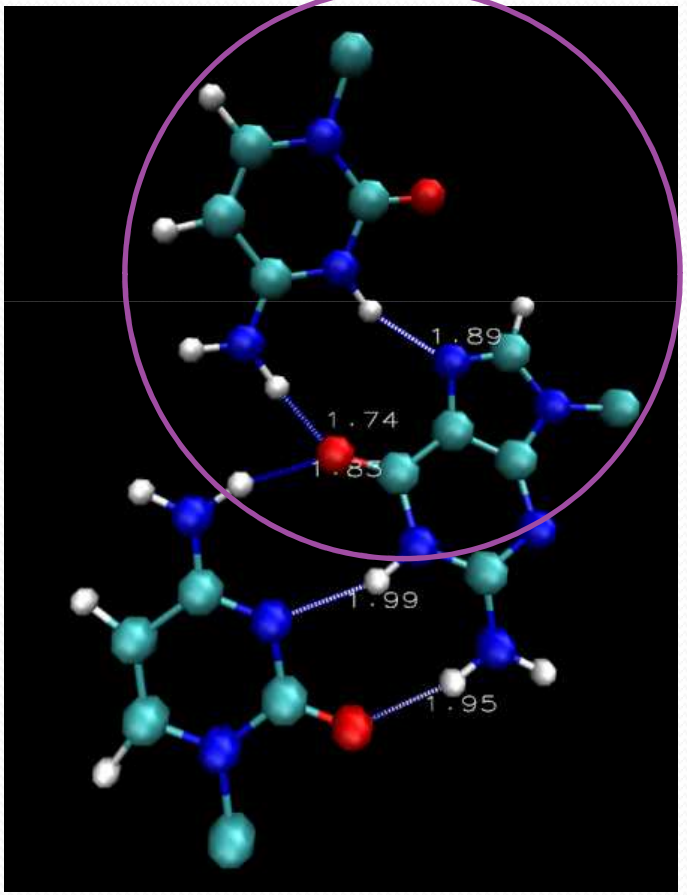
Secondary structure

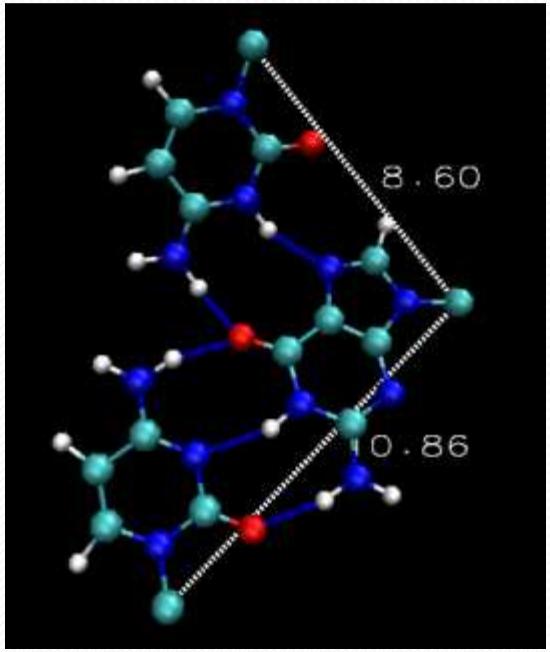
Hoogsteen base pairing

- C+*G·C

Triple helix





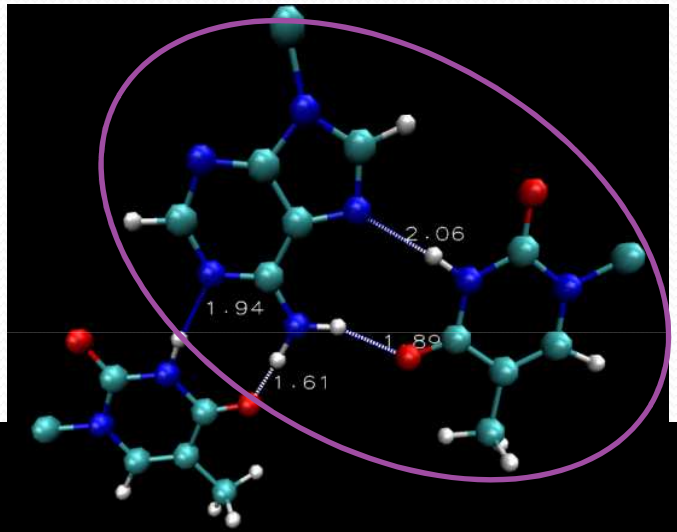


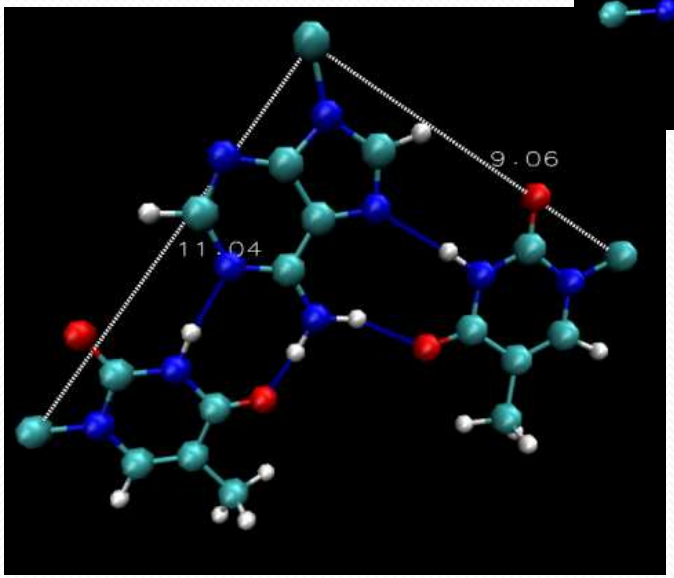
Secondary structure

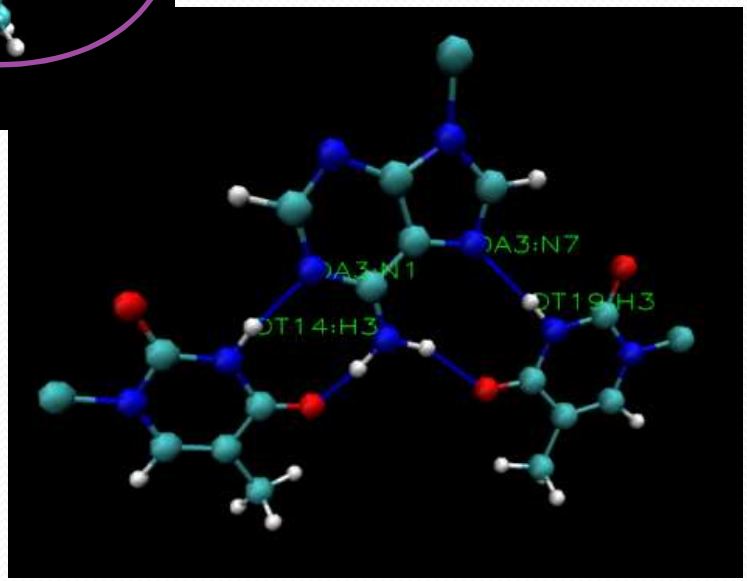
Hoogsteen base pairing

- **T·A*T**

Triple helix

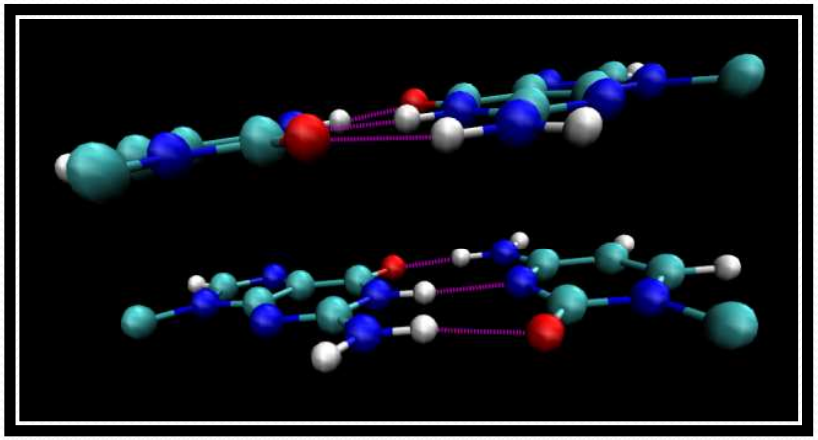






Secondary structure

- Base pair stacking



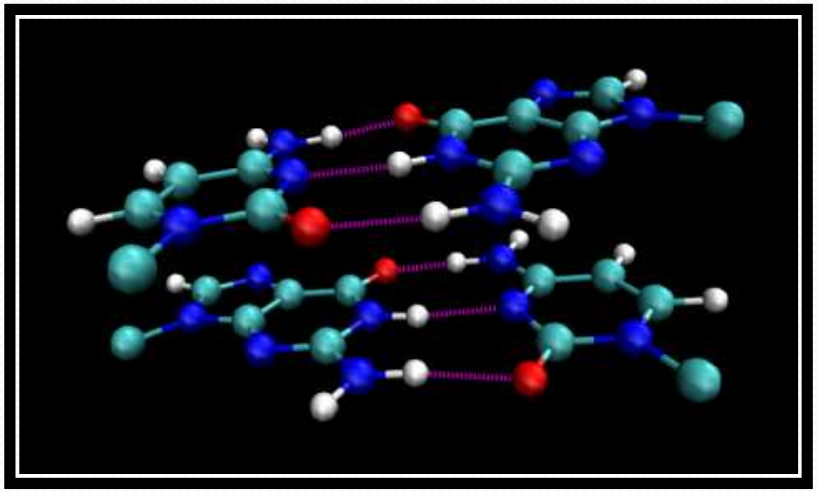


Table 1.2
Base Pair Stacking Energies

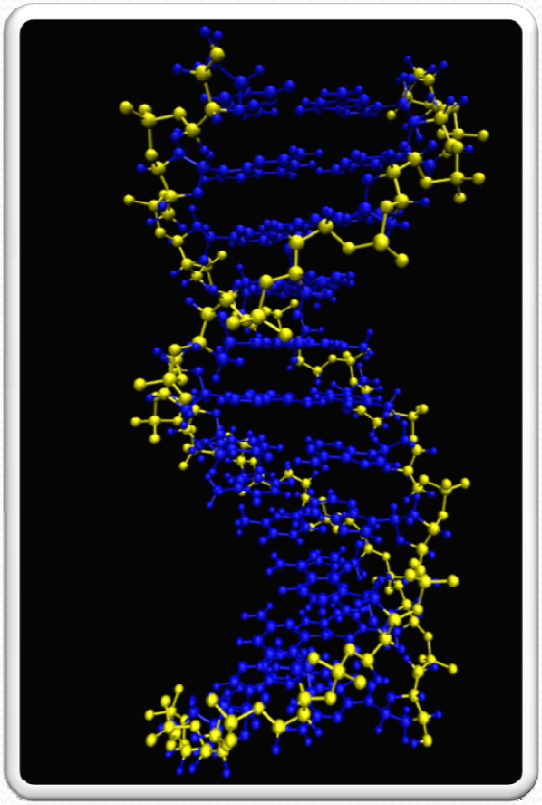
Dinucleotide base pairs	Stacking energies (kcal/mol/stacked pair)[a]
(GC) · (GC)	−14.59
(AC) · (GT)	−10.51
(TC) · (GA)	− 9.81
(CG) · (CG)	− 9.69
(GG) · (CC)	− 8.26
(AT) · (AT)	− 6.57
(TG) · (CA)	− 6.57
(AG) · (CT)	− 6.78
(AA) · (TT)	− 5.37
(TA) · (TA)	− 3.82

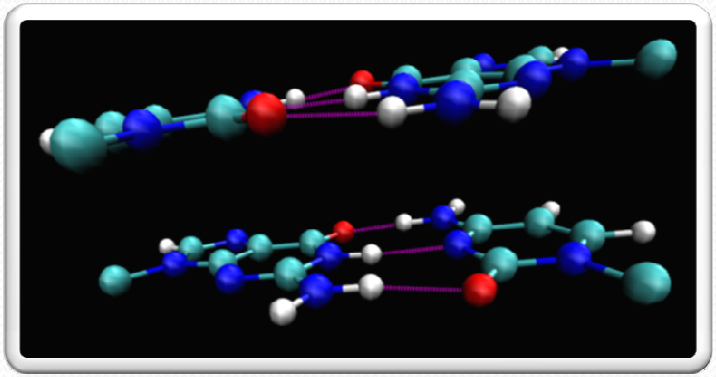
[a]Data from Ornstein *et al.* (1978).

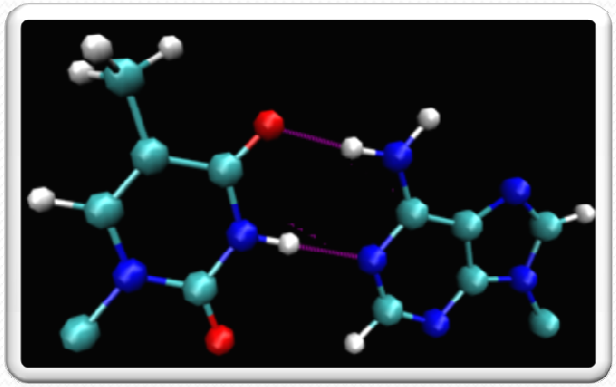
Sinden RR, 1994

Secondary structure

- Stability
  - Hydrogen bonds between bases
  - Base pair stacking



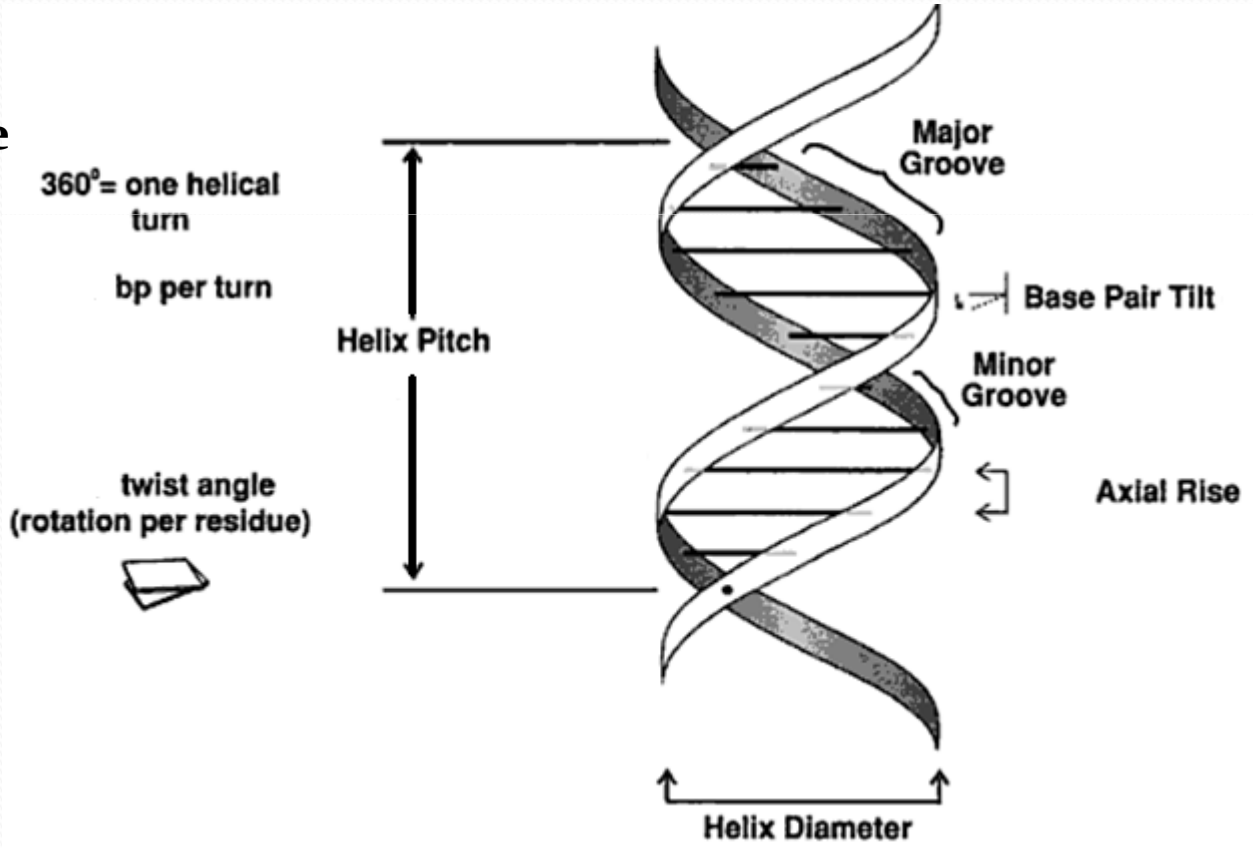




Secondary structure

- Conformational Parameters

•Major/minor groove
• Helix sense
• Residues per turn
• Axial rise
• Helix pitch
• Helix diameter
•Base pair tilt



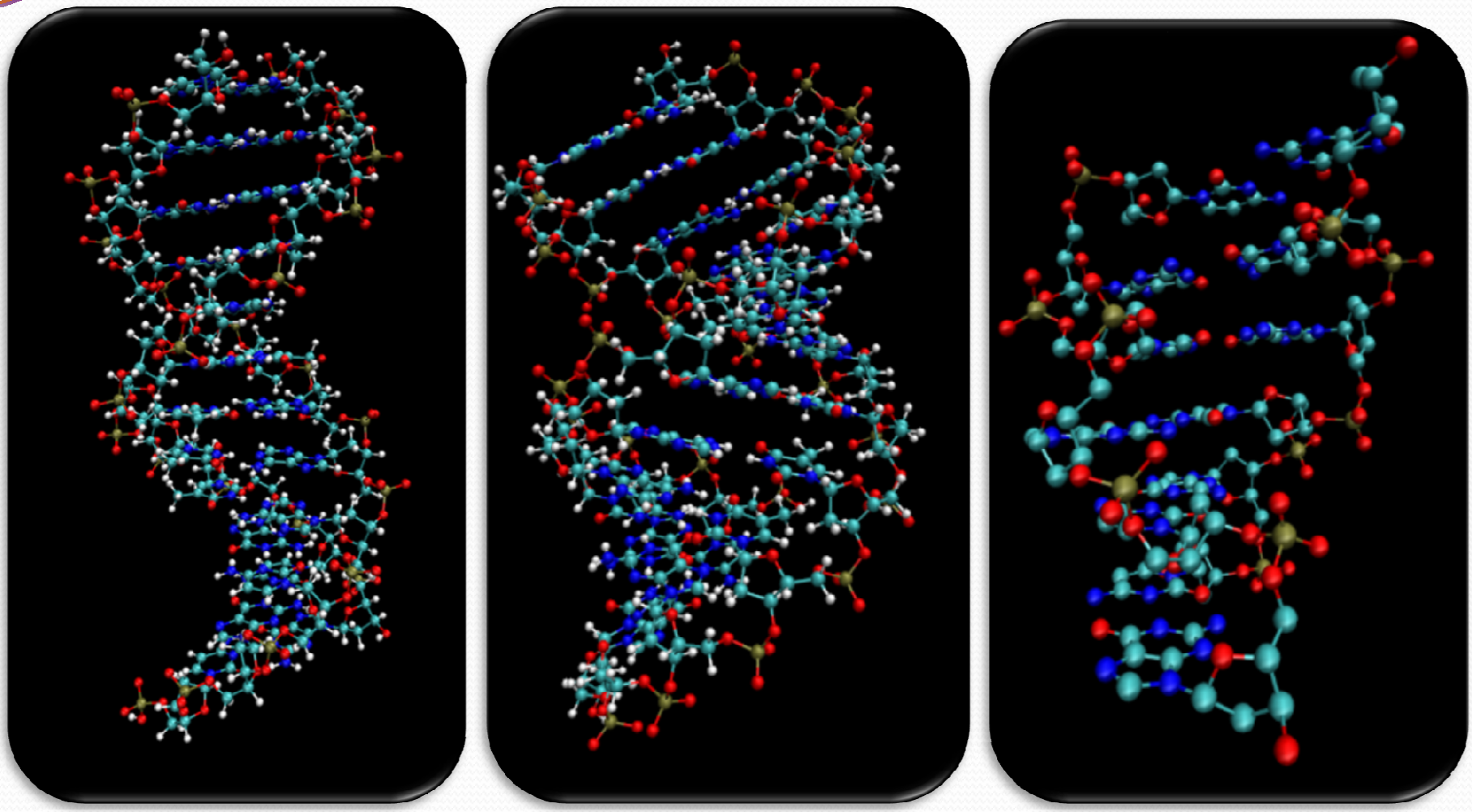
DNA FORMS

- **Canonical forms:**

  DNA duplexes:

  - **A-DNA**
  - **B-DNA**
  - **Z-DNA**

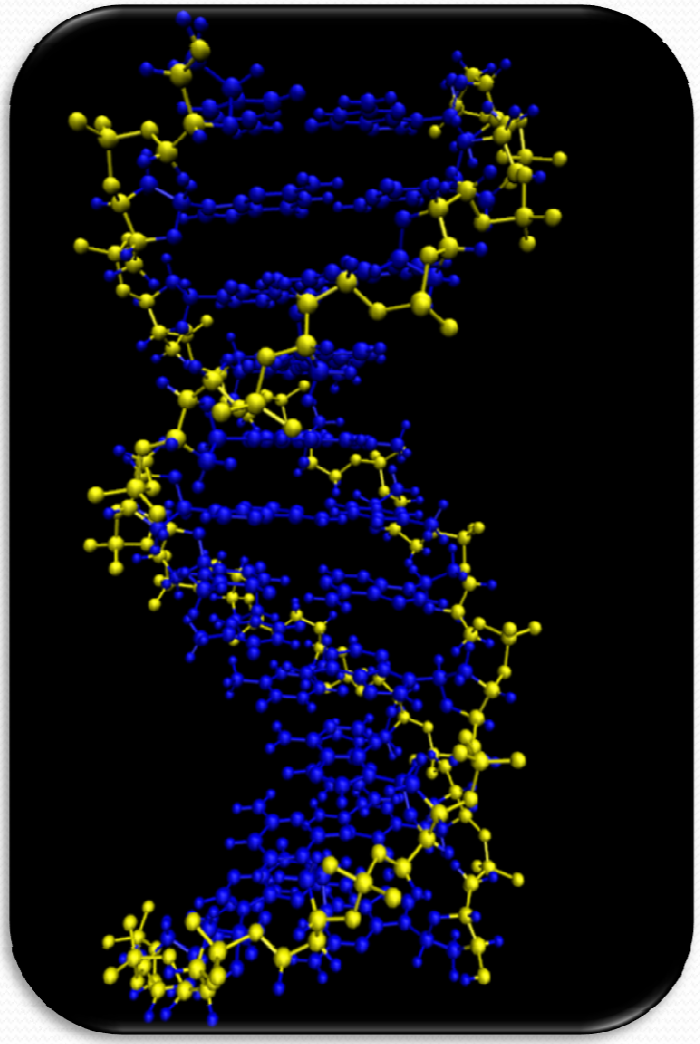
- Non-canonical forms:
  - Triplexes
  - Quadruplexes

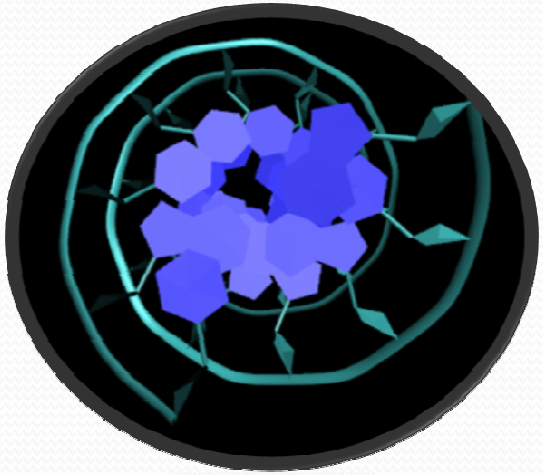


Canonical forms

Structural parameter	A-DNA	B-DNA	Z-DNA
Helical sense	Right-handed	Right-handed	Left-handed
Major groove	Narrow and deep	Wide and deep	Flattened
Minor groove	Wide and shallow	Narrow and deep	Narrow and deep
Helical diameter (Å)	23	20	18
Sugar pucker	C3'-endo	C2'-endo	C2'-endo at C C3'-endo at G
Glycosidic bond	anti	anti	Anti at C, syn at G
Helical pitch (Å)	28,2	34	45
Base pairs/ turn (n)	11	10,4	12 (6 dímers)
Axial rise(Å)	2,9	3,3	3,7
Tilt (º)	19	-6	-9
Rotation per residue (=360º/n)	33^{o}	36^{0}	60^{o} per dimmer 30^{0} per residue
Repeat unit (base pairs)	1	1	2
Phosphate conformation (α/ζ)(°)	-88/-44	-40/-98	-146/80 at C 60/-58 at G

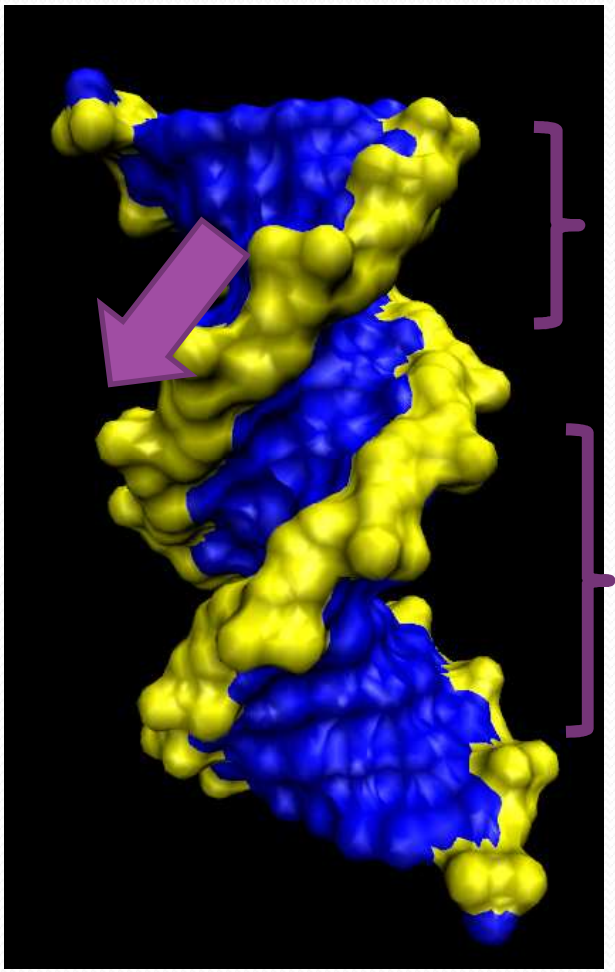
B-DNA





B-DNA

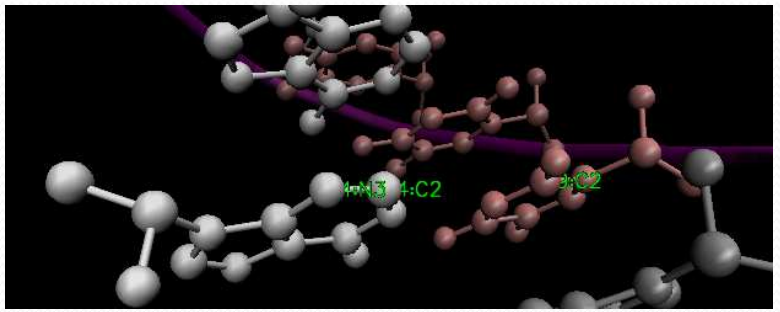
Structural parameter	B-DNA
Helical sense	Right-handed
Major groove	Wide and deep
Minor groove	Narrow and deep
Helical diameter (Å)	20
Sugar pucker	C2’-endo
Glycosidic bond	anti
Helical pitch (Å)	34
Base pairs/ turn (n)	10,4
Axial rise(Å)	3,3
Tilt (º)	-6



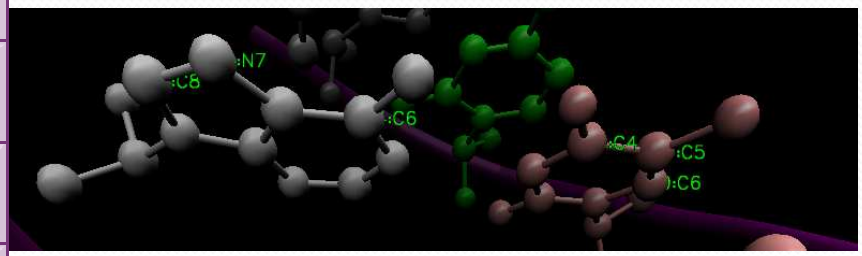
PDB: 2HKB

B-DNA

Structural parameter	B-DNA
Helical sense	Right-handed
Major groove	Wide and deep
Minor groove	Narrow and deep
Helical diameter (Å)	20
Sugar pucker	C2'-endo
Glycosidic bond	anti
Helical pitch (Å)	34
Base pairs/ turn (n)	10,4
Axial rise(Å)	3,3
Tilt (º)	-6



Minor groove

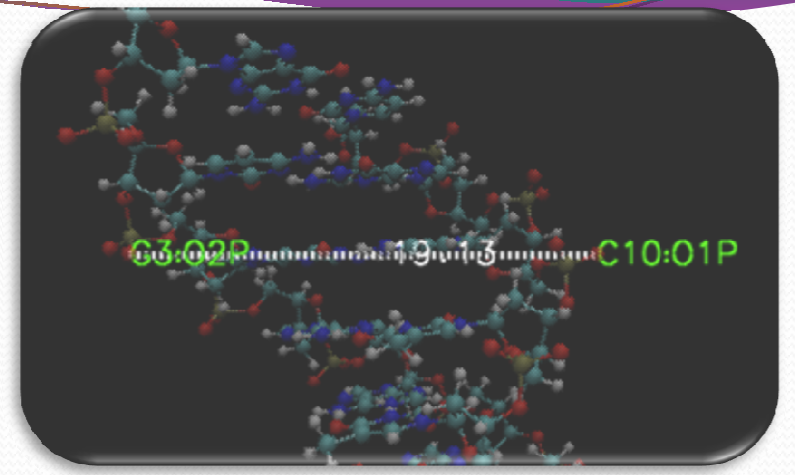


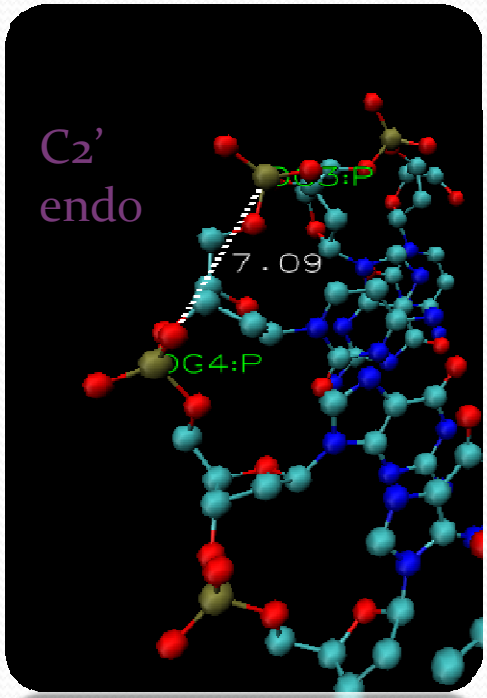
Major groove

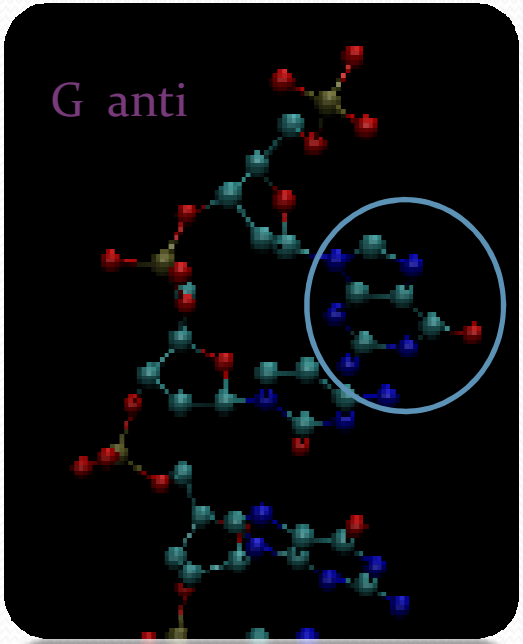
PDB: 2HKB

B-DNA

Structural parameter	B-DNA
Helical sense	Right-handed
Major groove	Wide and deep
Minor groove	Narrow and deep
Helical diameter (Å)	**20**
Sugar pucker	**C2'-endo**
Glycosidic bond	**anti**
Helical pitch (Å)	34
Base pairs/ turn (n)	10,4
Axial rise(Å)	3,3
Tilt (º)	-6



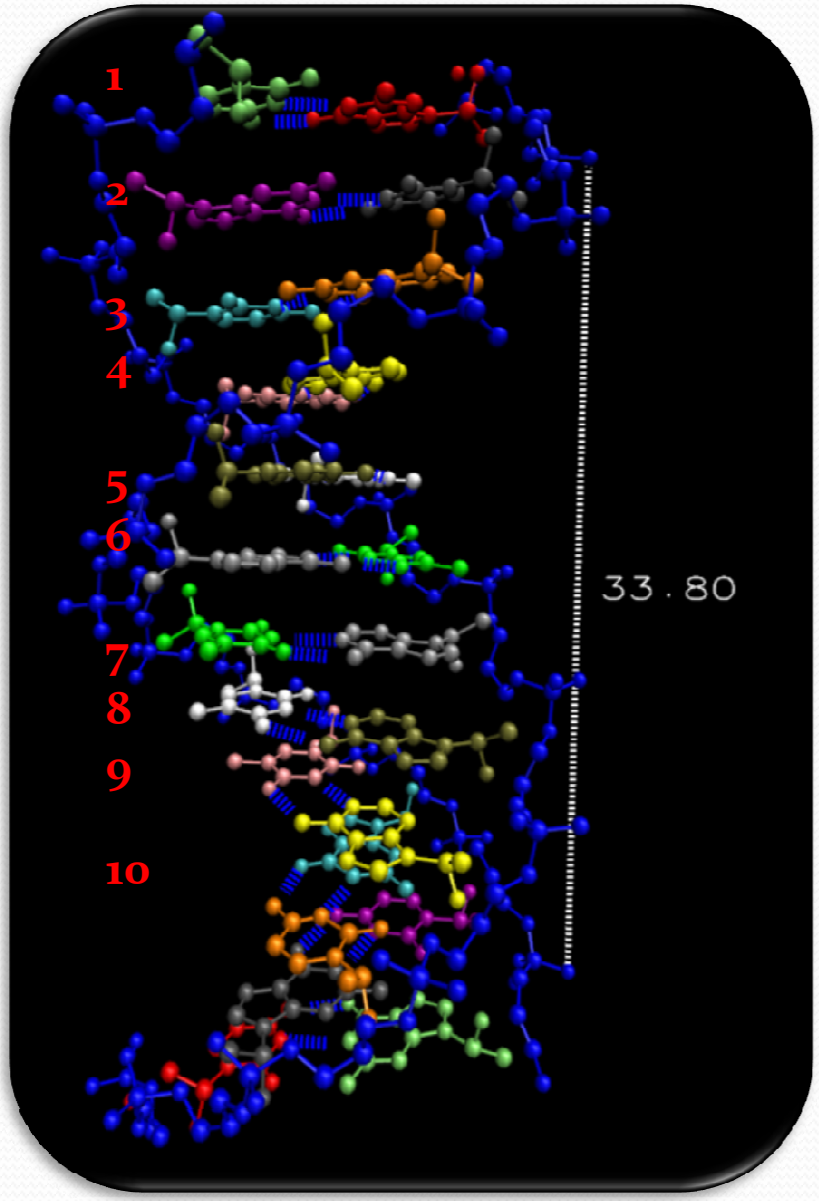




PDB: 2HKB

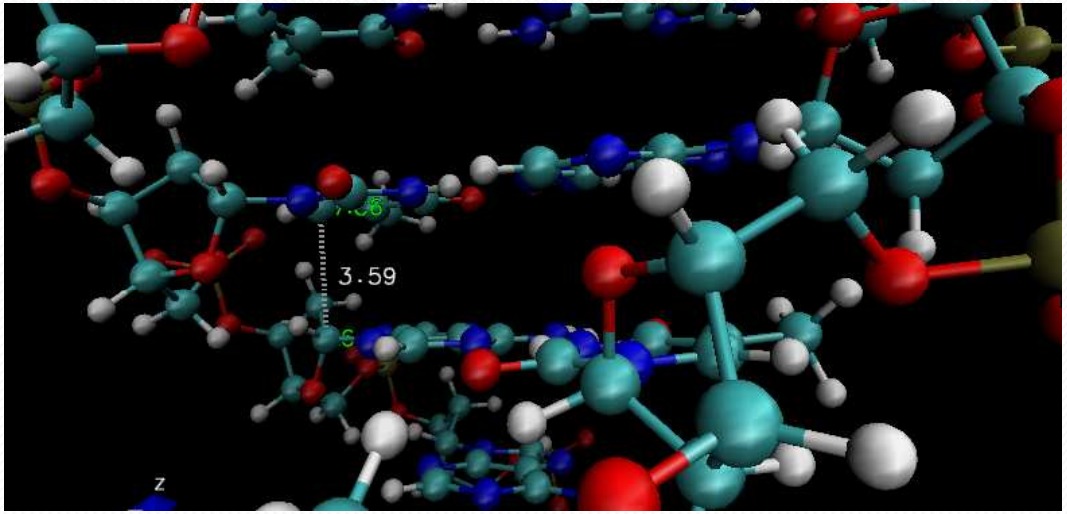
B-DNA

Structural parameter	B-DNA
Helical sense	Right-handed
Major groove	Wide and deep
Minor groove	Narrow and deep
Helical diameter (Å)	20
Sugar pucker	C2’-endo
Glycosidic bond	anti
Helical pitch (Å)	**34**
Base pairs/ turn (n)	**10,4**
Axial rise(Å)	3,3
Tilt (º)	-6



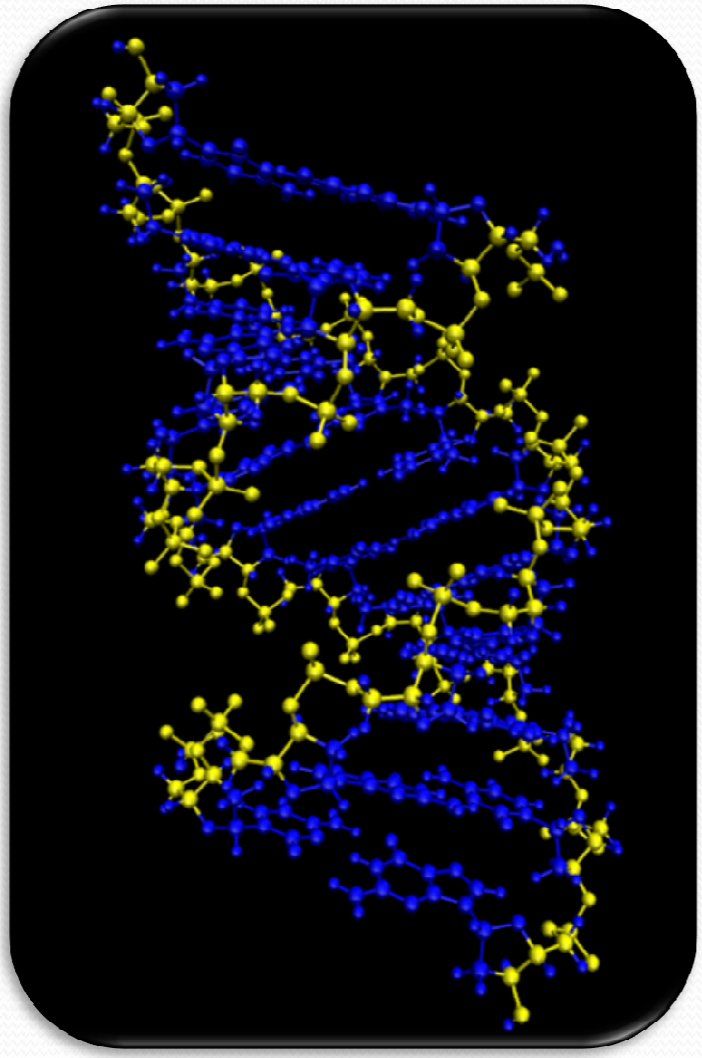
B-DNA

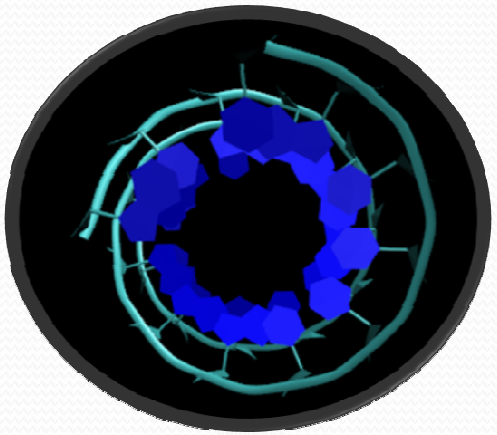
Structural parameter	B-DNA
Helical sense	Right-handed
Major groove	Wide and deep
Minor groove	Narrow and deep
Helical diameter (Å)	20
Sugar pucker	C2'-endo
Glycosidic bond	anti
Helical pitch (Å)	34
Base pairs/ turn (n)	10,4
Axial rise(Å)	**3,3**
Tilt (º)	-6



PDB: 2HKB

A-DNA

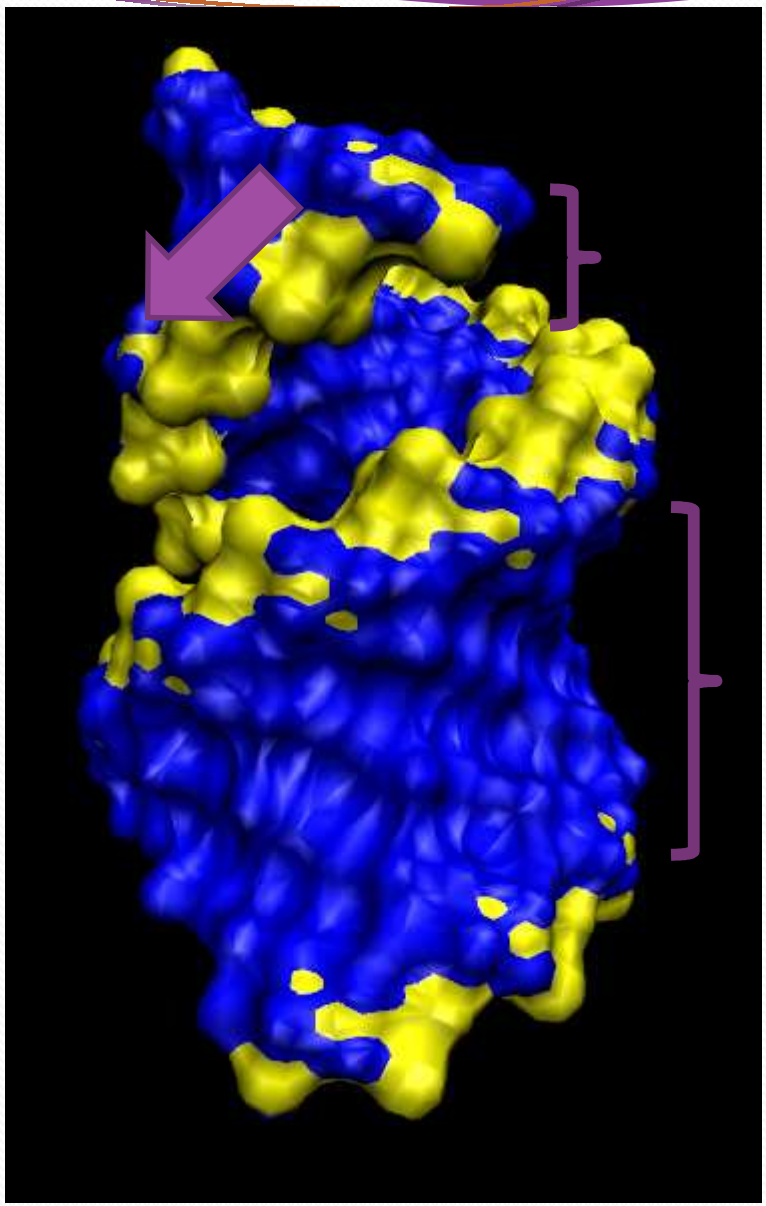




PDB: 115D

A-DNA

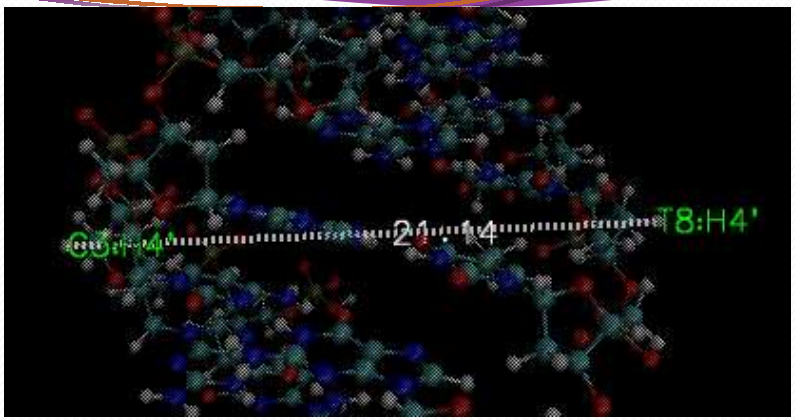
Structural parameter	A-DNA
Helical sense	Right-handed
Major groove	Narrow and deep
Minor groove	Wide and shallow
Helical diameter (Å)	23
Sugar pucker	C3’-endo
Glycosidic bond	anti
Helical pitch (Å)	28,2
Base pairs/ turn (n)	11
Axial rise(Å)	2,9
Tilt (º)	19

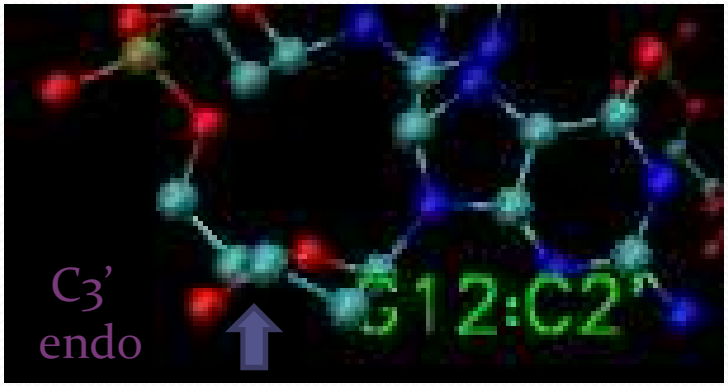


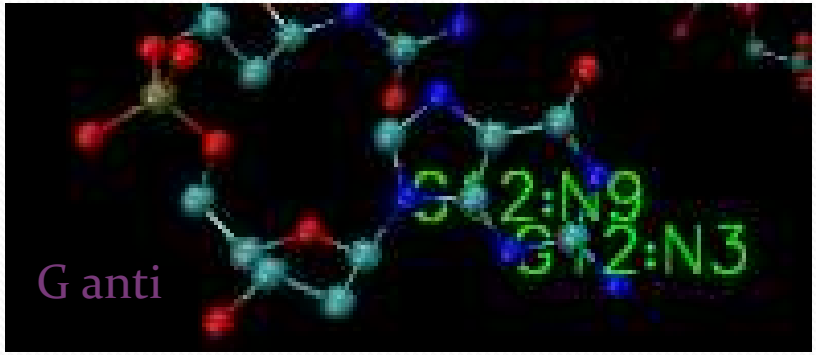
PDB: 115D

A-DNA

Structural parameter	A-DNA
Helical sense	Right-handed
Major groove	Narrow and deep
Minor groove	Wide and shallow
Helical diameter (Å)	**23**
Sugar pucker	**C3'-endo**
Glycosidic bond	**anti**
Helical pitch (Å)	28,2
Base pairs/ turn (n)	11
Axial rise(Å)	2,9
Tilt (º)	19



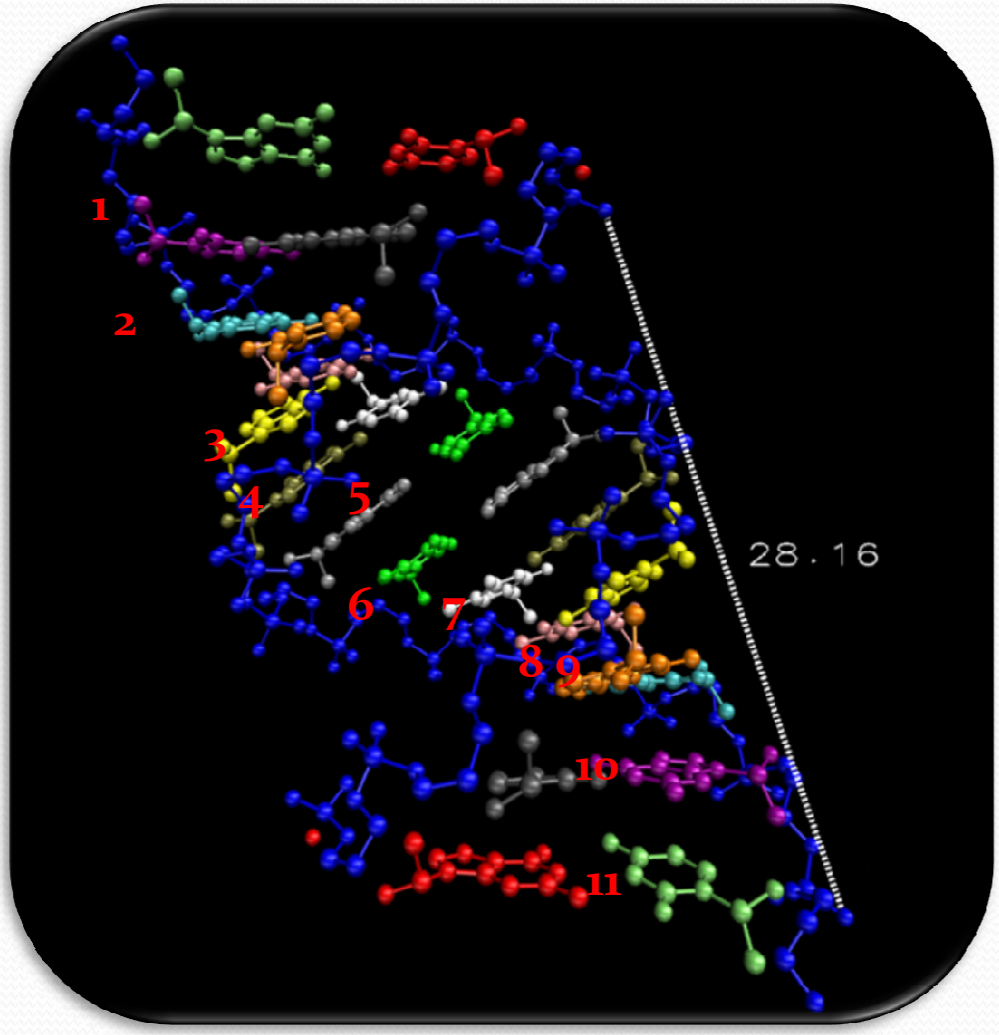




PDB: 115D

A-DNA

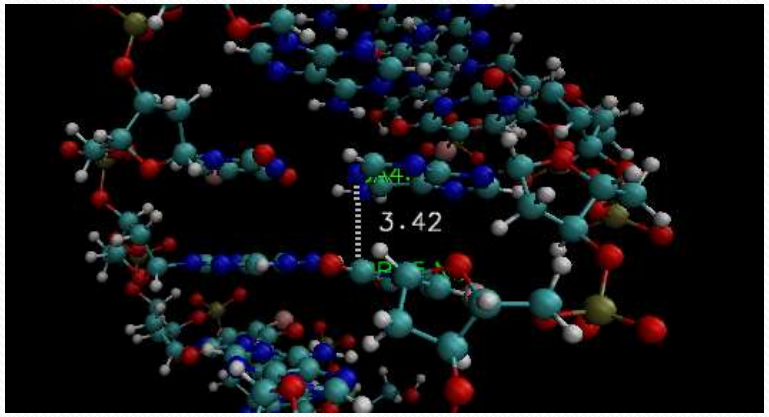
Structural parameter	A-DNA
Helical sense	Right-handed
Major groove	Narrow and deep
Minor groove	Wide and shallow
Helical diameter (Å)	23
Sugar pucker	C3'-endo
Glycosidic bond	anti
Helical pitch (Å)	**28,2**
Base pairs/ turn (n)	**11**
Axial rise(Å)	2,9
Tilt (º)	19

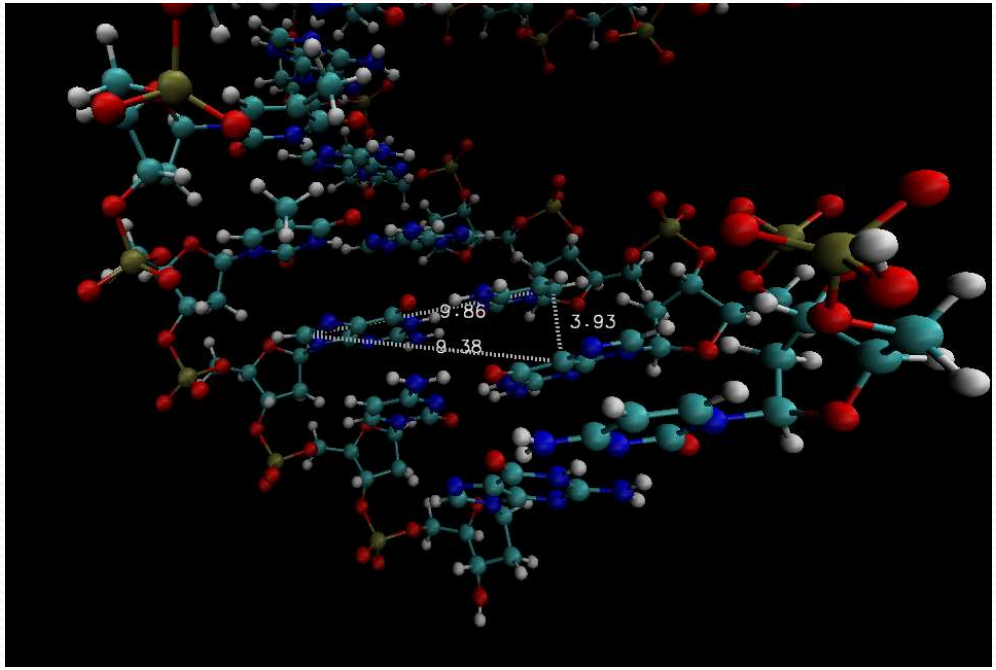


PDB: 115D

A-DNA

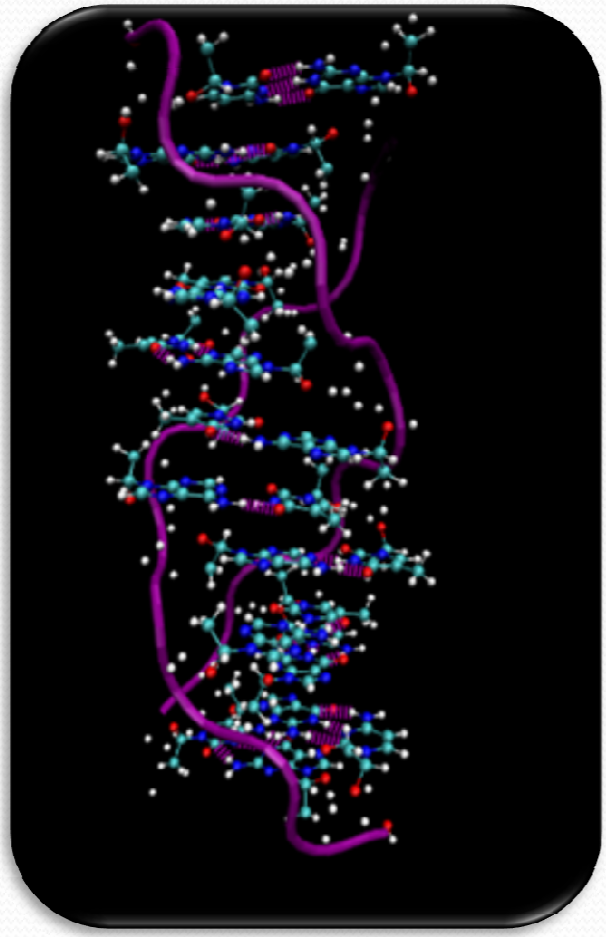
Structural parameter	A-DNA
Helical sense	Right-handed
Major groove	Narrow and deep
Minor groove	Wide and shallow
Helical diameter (Å)	23
Sugar pucker	C3’-endo
Glycosidic bond	anti
Helical pitch (Å)	28,2
Base pairs/ turn (n)	11
Axial rise(Å)	**2,9**
Tilt (º)	**19**

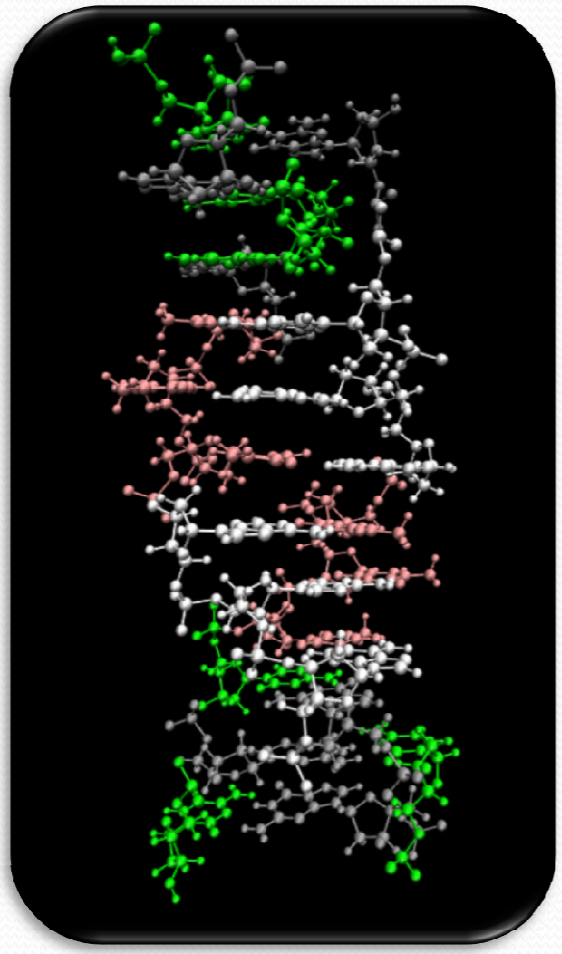




PDB: 115D

Z-DNA

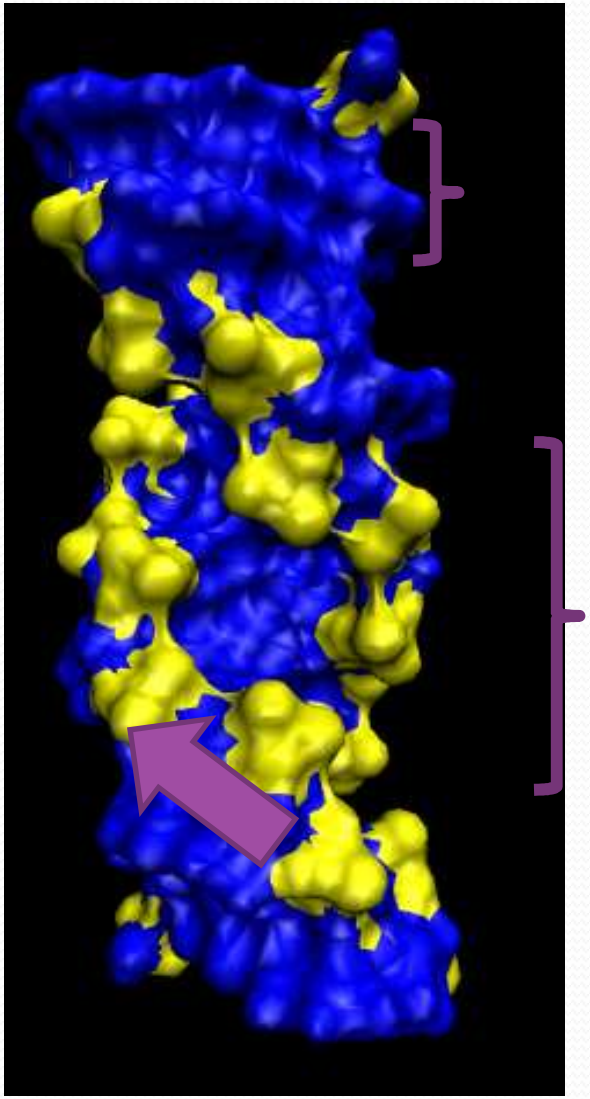




PDB: 1DCG

Z-DNA

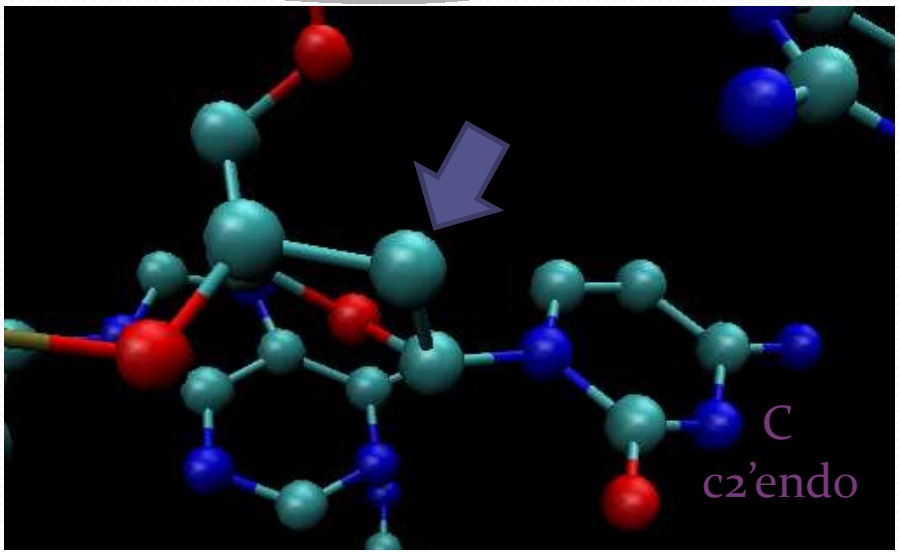
Structural parameter	Z-DNA
Helical sense	Left-handed
Major groove	Flattened
Minor groove	Narrow and deep
Helical diameter (Å)	18
Sugar pucker	C2'-endo at C C3'-endo at G
Glycosidic bond	Anti at C, syn at G
Helical pitch (Å)	45
Base pairs/ turn (n)	12 (6 dímers)
Axial rise(Å)	3,7
Tilt (º)	-9

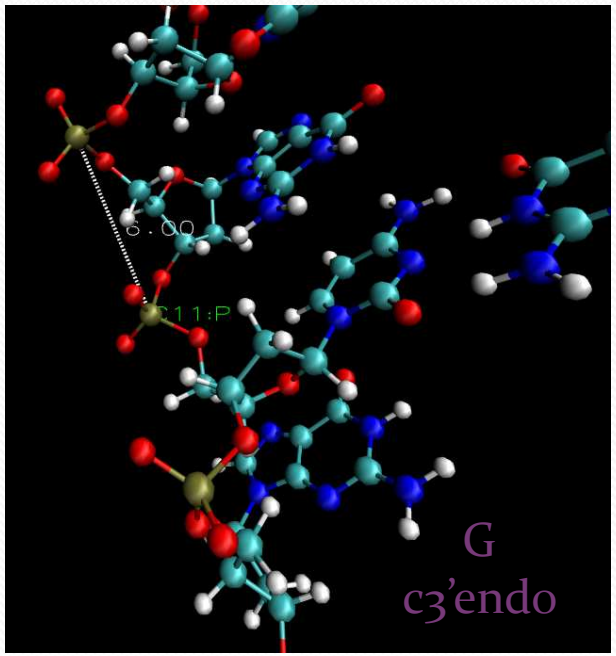


PDB: 1DCG

Z-DNA

Structural parameter	Z-DNA
Helical sense	Left-handed
Major groove	Flattened
Minor groove	Narrow and deep
Helical diameter (Å)	18
Sugar pucker	**C2'-endo at C** **C3'-endo at G**
Glycosidic bond	Anti at C, syn at G
Helical pitch (Å)	45
Base pairs/ turn (n)	12 (6 dímers)
Axial rise(Å)	3,7
Tilt (º)	-9





PDB: 1DCG

Z-DNA

Structural parameter	Z-DNA
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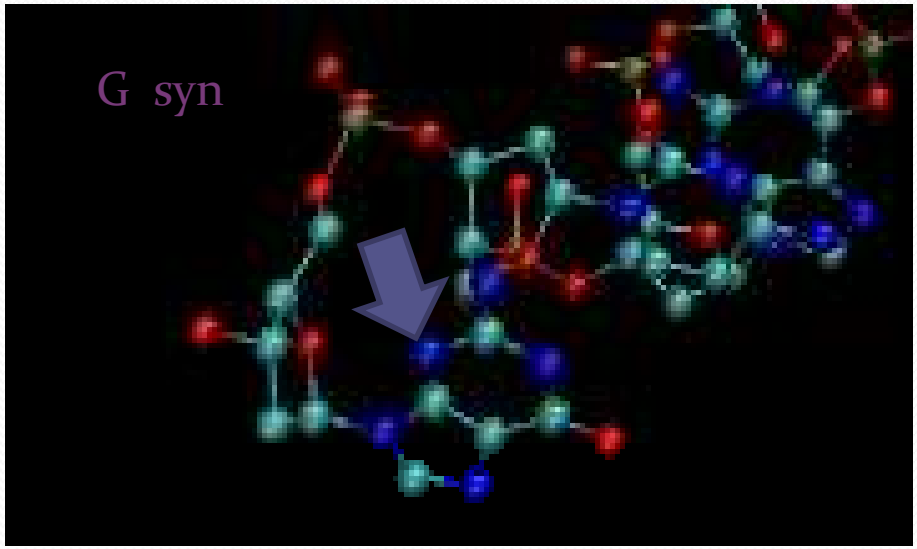
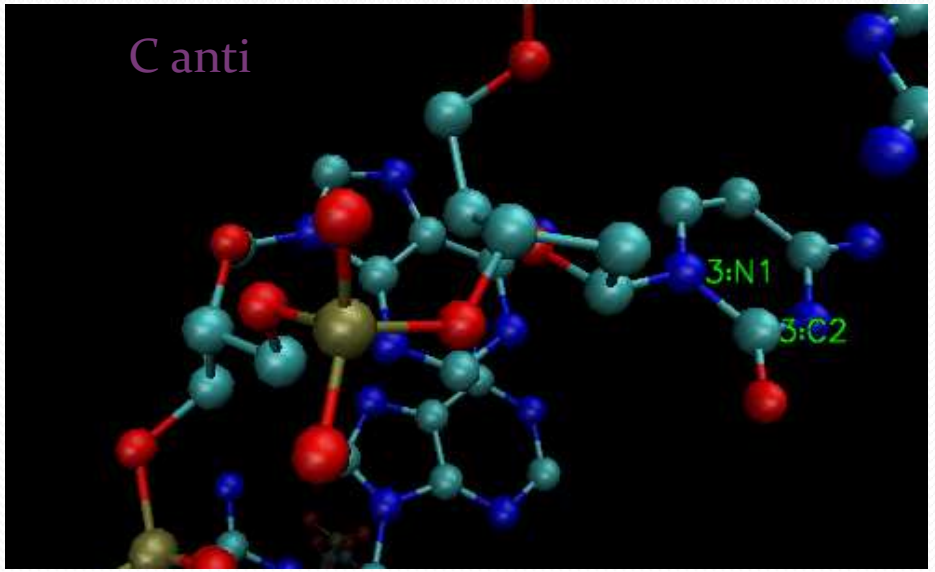
Tilt (º)	-9

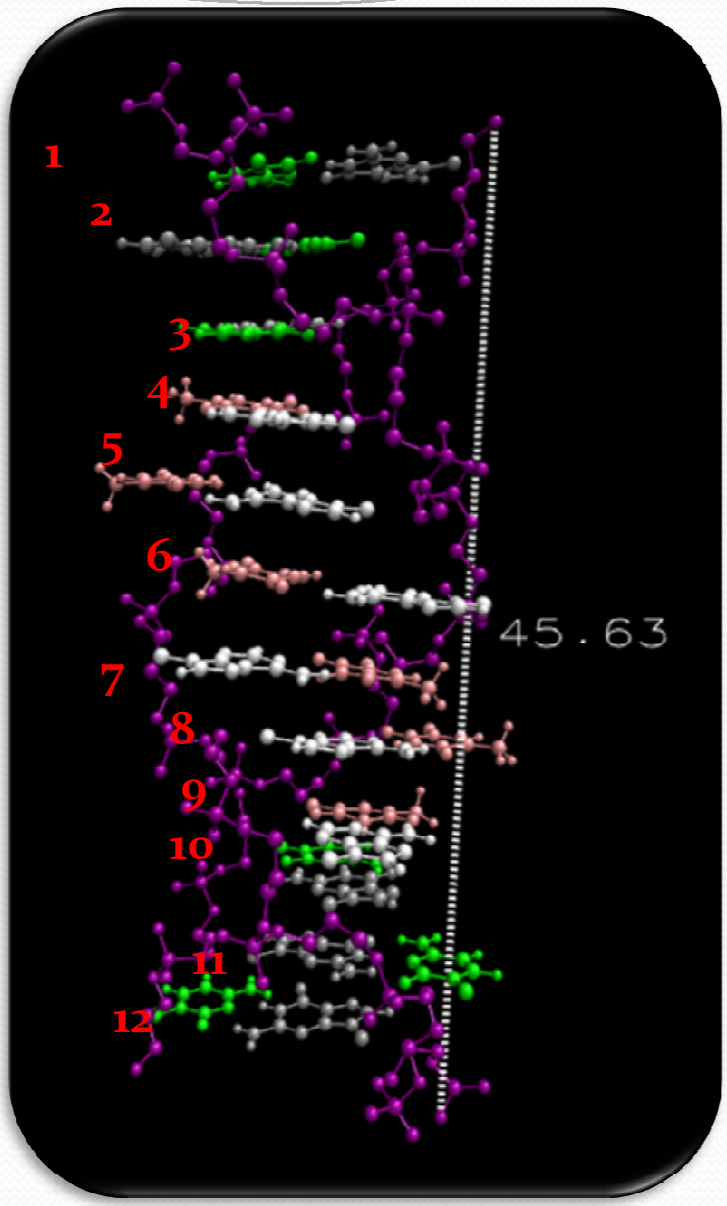




PDB: 1DCG

Z-DNA

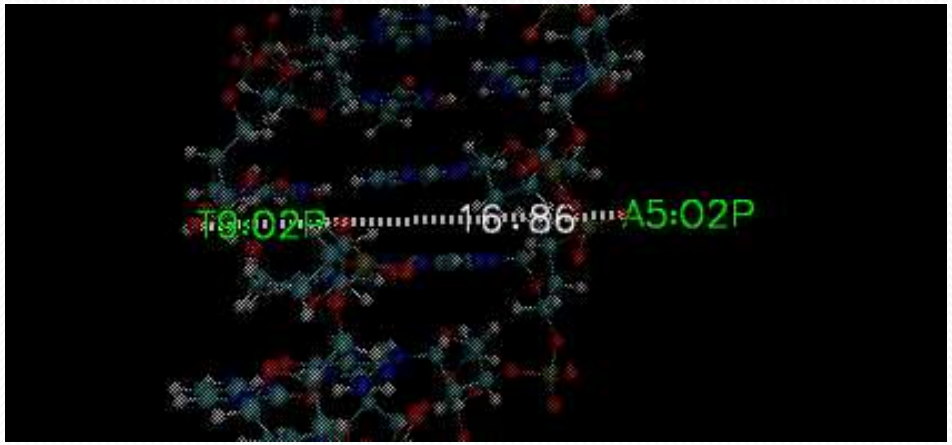
Structural parameter	Z-DNA
Helical sense	Left-handed
Major groove	Flattened
Minor groove	Narrow and deep
Helical diameter (Å)	18
Sugar pucker	C2'-endo at C C3'-endo at G
Glycosidic bond	Anti at C, syn at G
Helical pitch (Å)	**45**
Base pairs/ turn (n)	**12 (6 dímers)**
Axial rise(Å)	3,7
Tilt (º)	-9

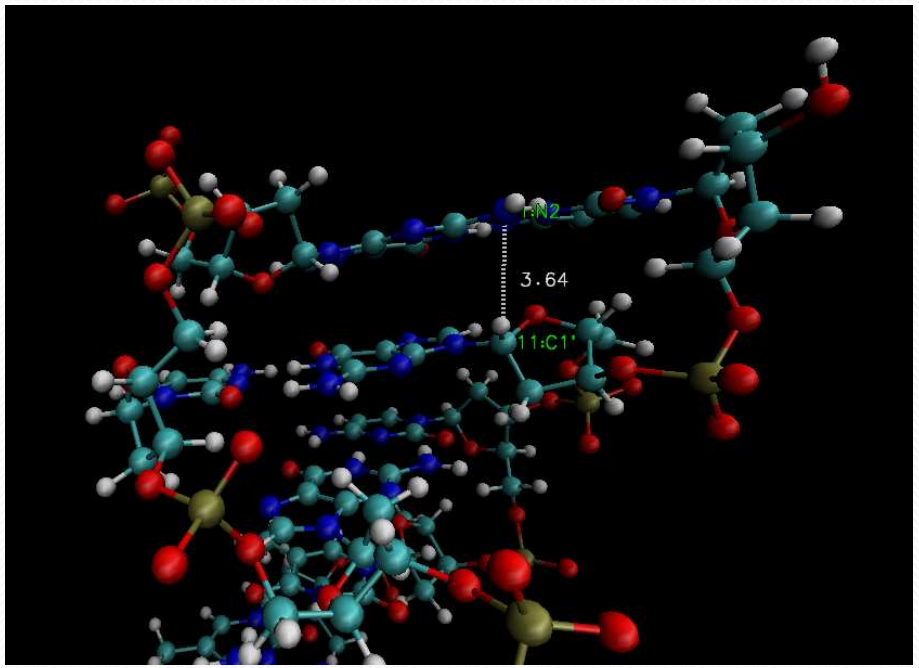


PDB: 1DCG

Z-DNA

Structural parameter	Z-DNA
Helical sense	Left-handed
Major groove	Flattened
Minor groove	Narrow and deep
Helical diameter (Å)	**18**
Sugar pucker	C2'-endo at C C3'-endo at G
Glycosidic bond	Anti at C, syn at G
Helical pitch (Å)	45
Base pairs/ turn (n)	12 (6 dímers)
Axial rise(Å)	**3,7**
Tilt (º)	-9





PDB: 1DCG

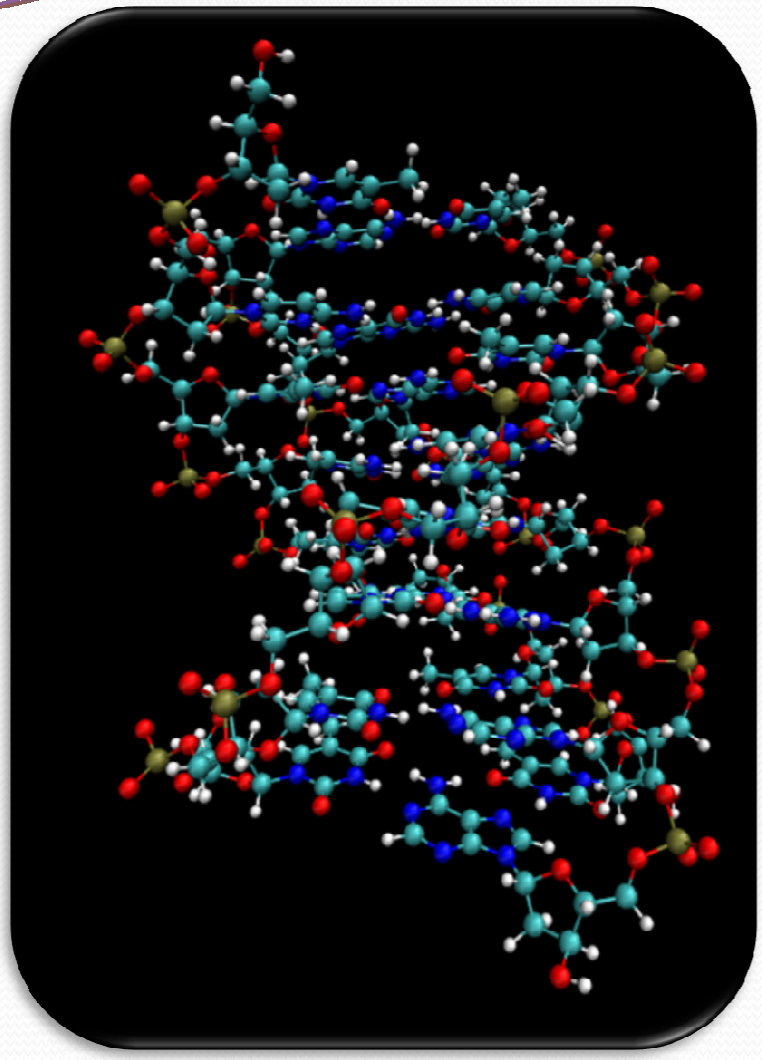
- ✓ Canonical forms:

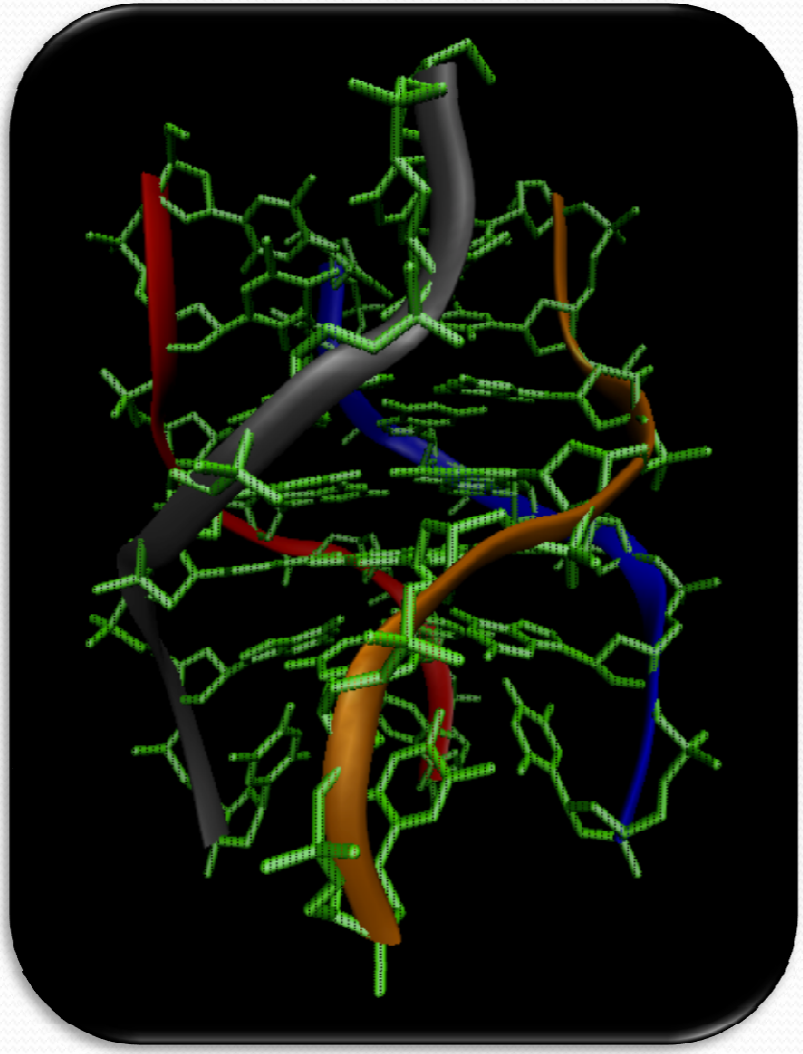
  DNA duplexes:

  - A-DNA
  - B-DNA
  - Z-DNA

- ✓ **Non-canonical forms:**

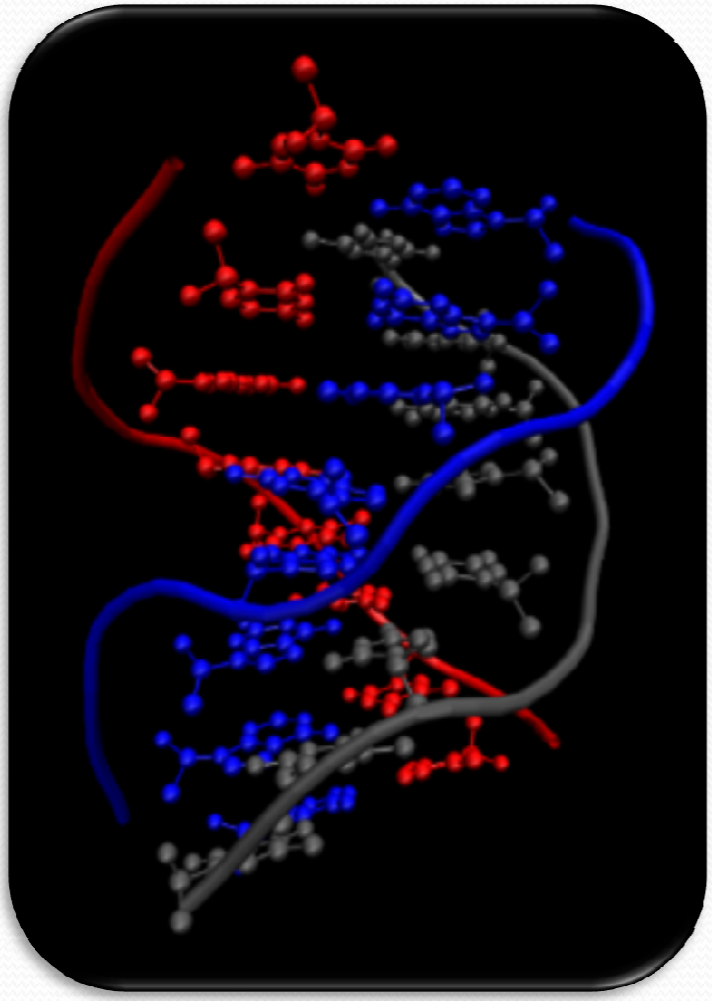
  - **Triplexes**
  - **Quadruplexes**

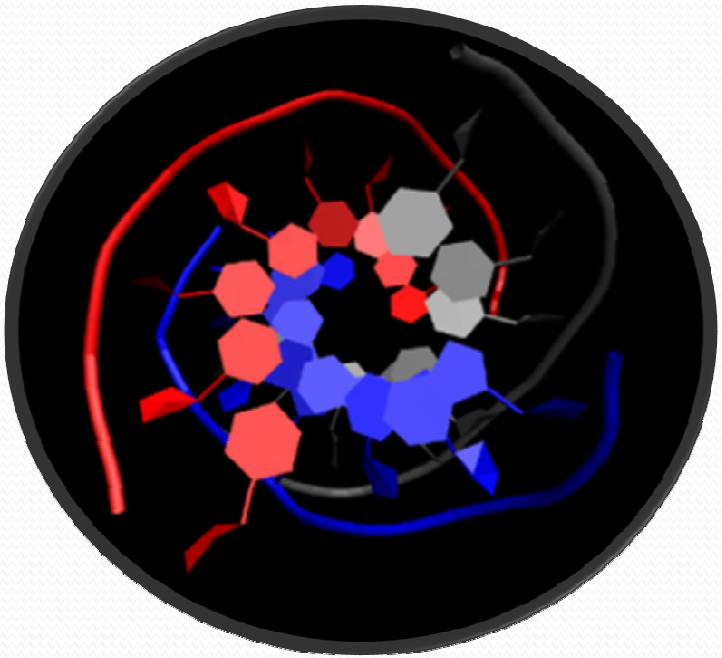




Non-canonical forms

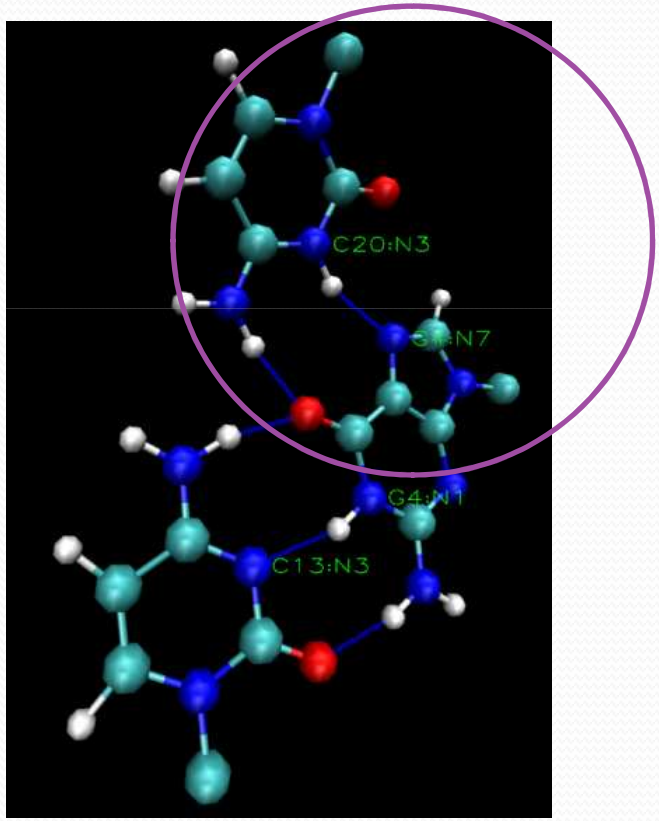
Triplexes

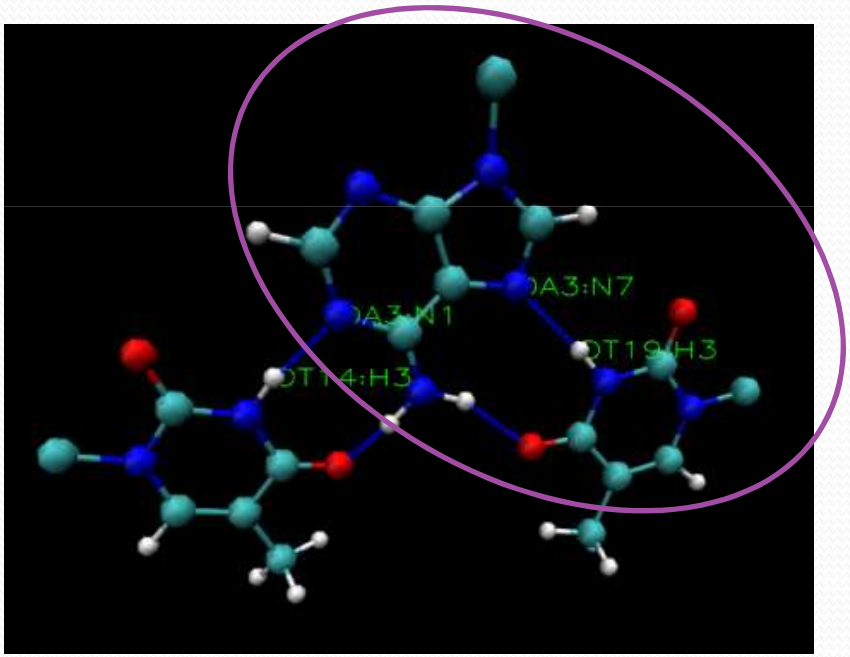




PDB: 1D3X

Triplexes – Hoogsteen base pair

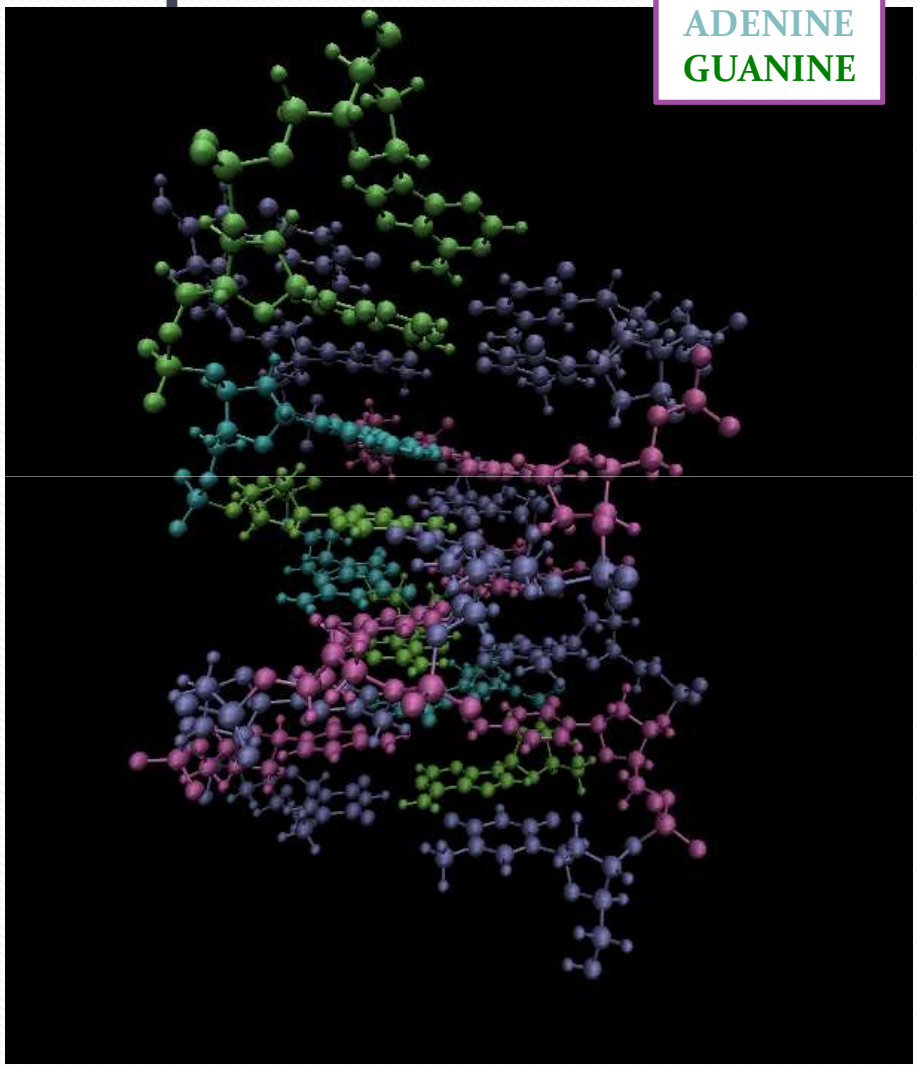




PDB: 1D3X

Classification of triplexes

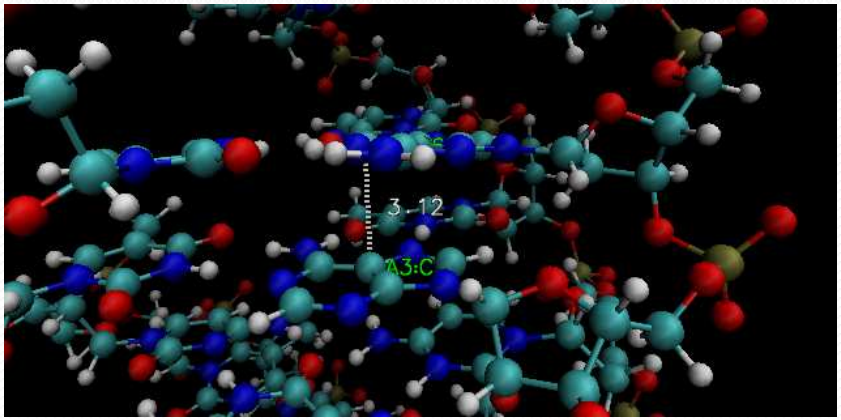
- YR*Y or YR*R
- Built from DNA, RNA or both.
- Intramolecular or intermolecular.
- Orientation

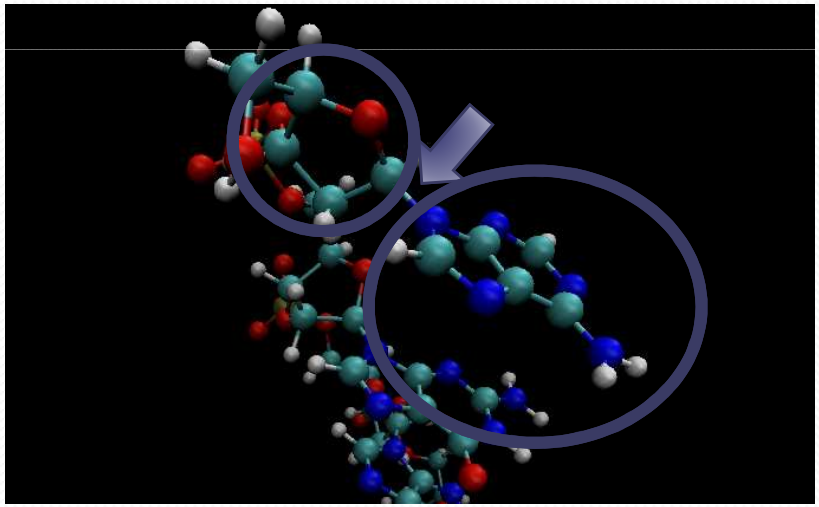


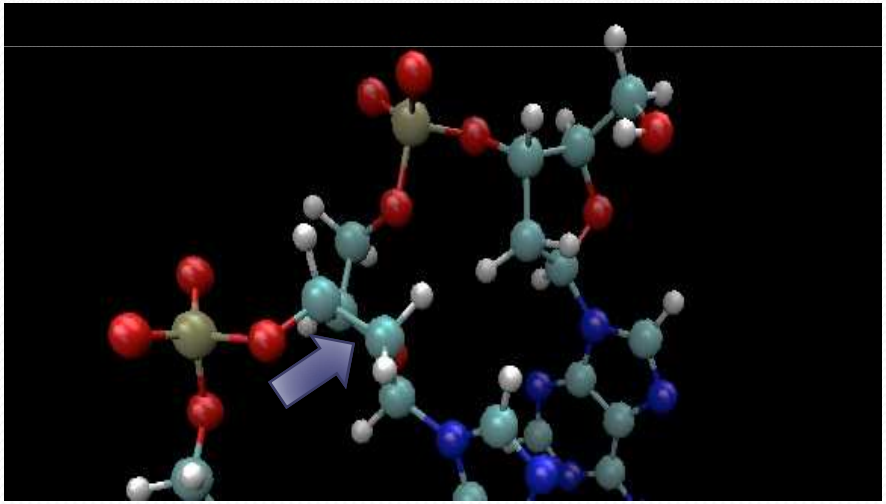
PDB: 1D3X

Triplexes

Axial Rise	3,4 nm
Glycosidic bond	Anti
Sugar pucker	C2' endo



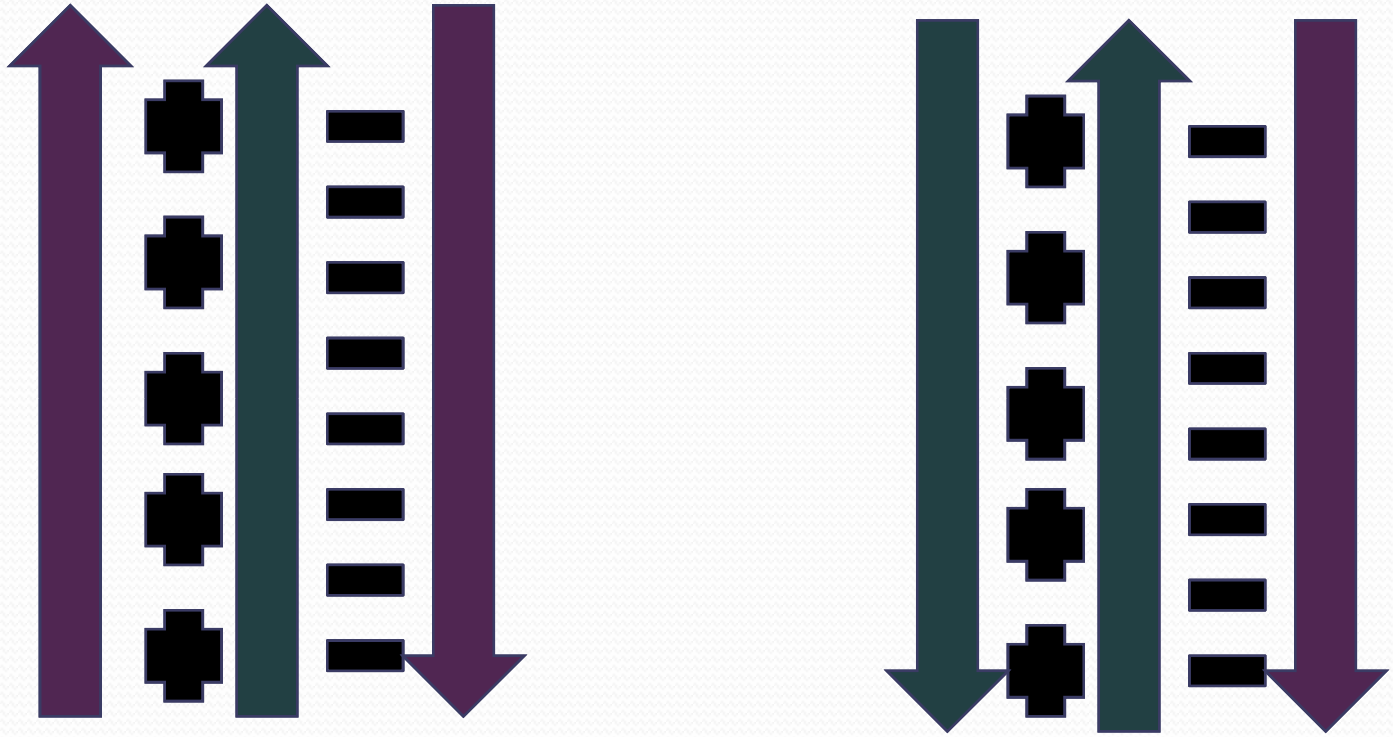




PDB: 1D3X

PARALLEL MOTIF

ANTIPARALLEL MOTIF



Hogsteen

Watson-Crick

Homopyrimidine strand (T+C)

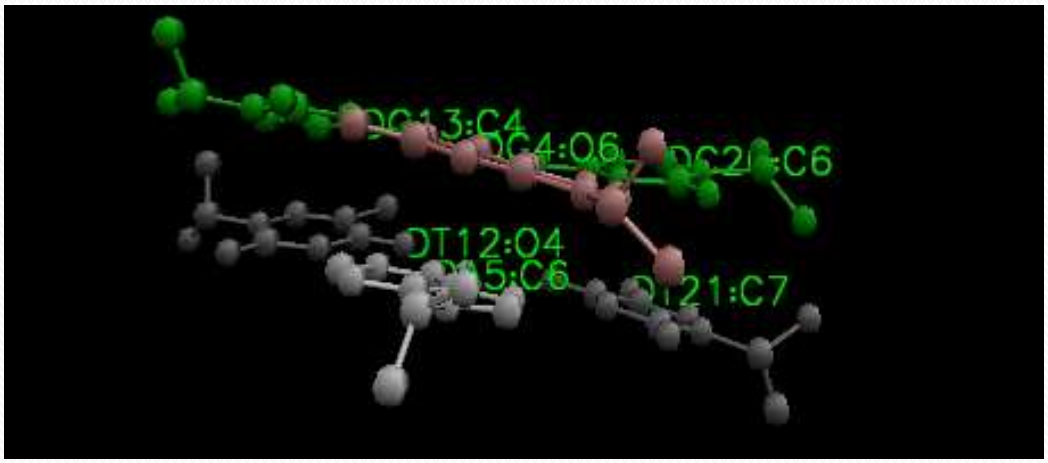
Homopurine strand (A+G)

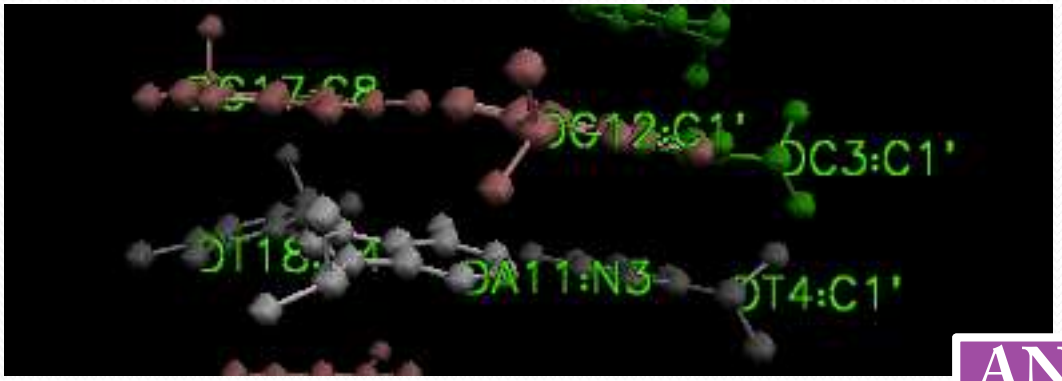
PARALLEL TRIPLEX (YR*Y)

Pyrimidine

Purine

PDB: 1D3X



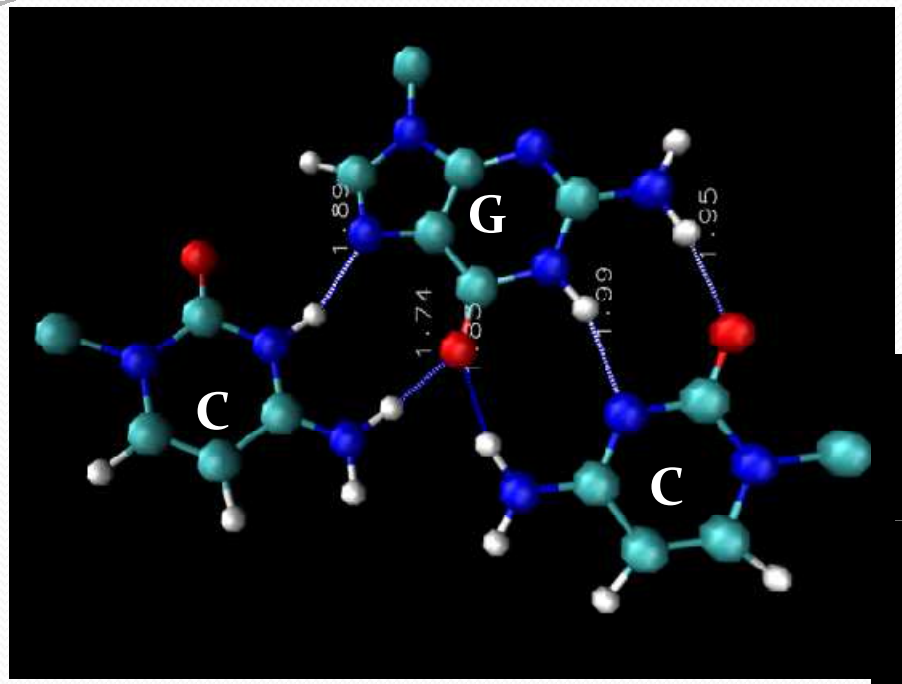


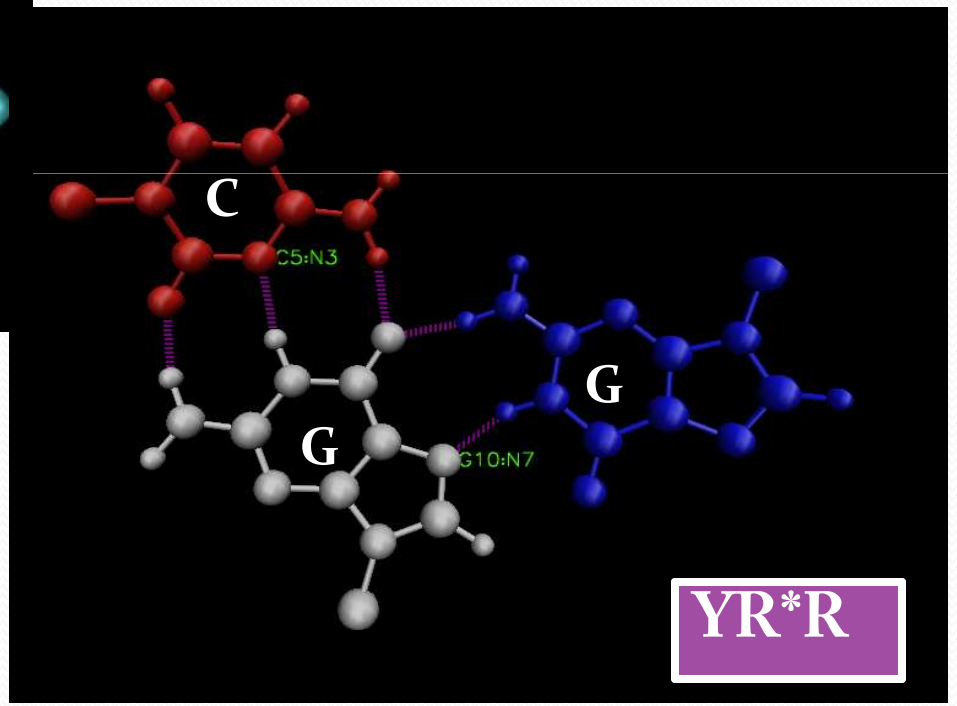
ANTI-PARALLEL TRIPLEX (YR*R)

PDB: 134D

YR*Y

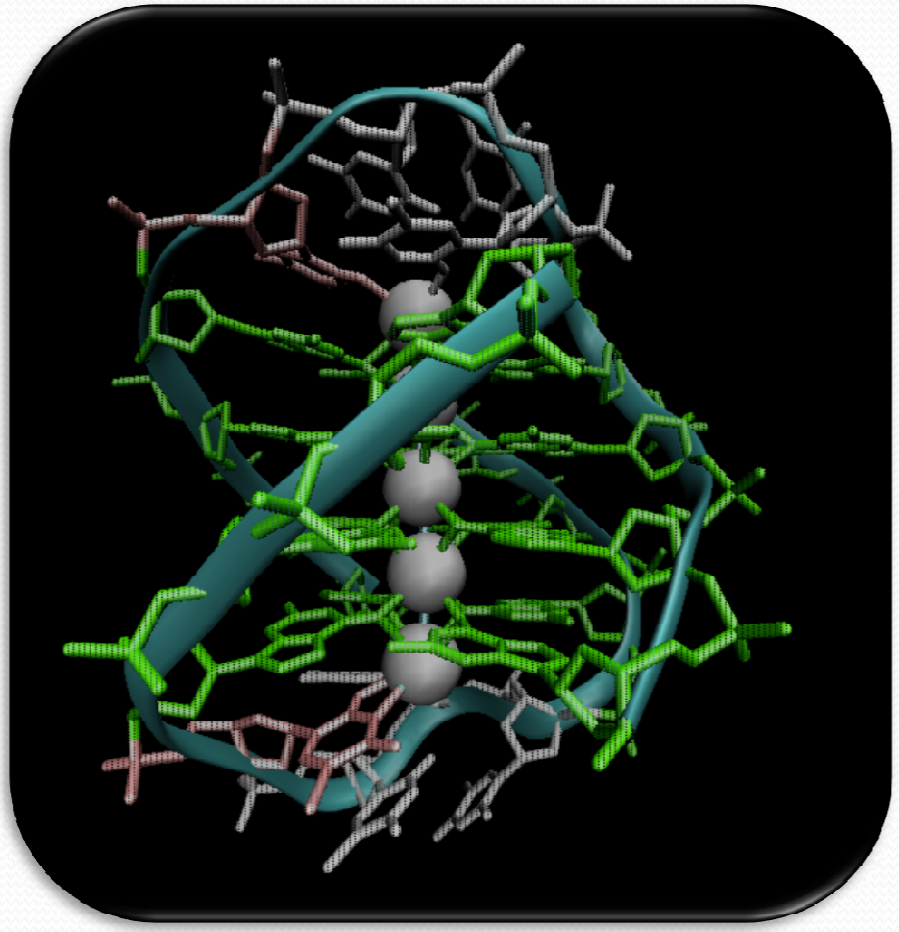
PDB: 1D3X





PDB: 134D

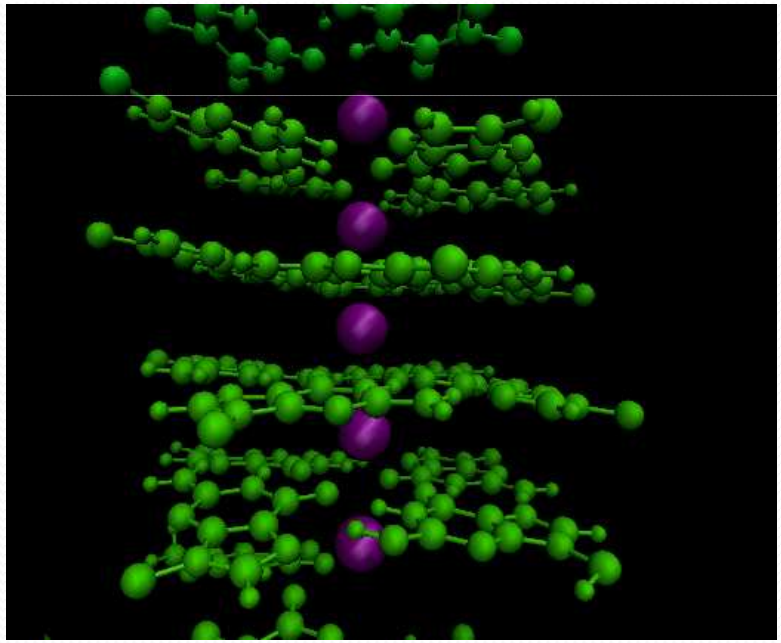
Quadruplexes



PDB: 1JPQ

G-QUADRUPLEX STRUCTURES

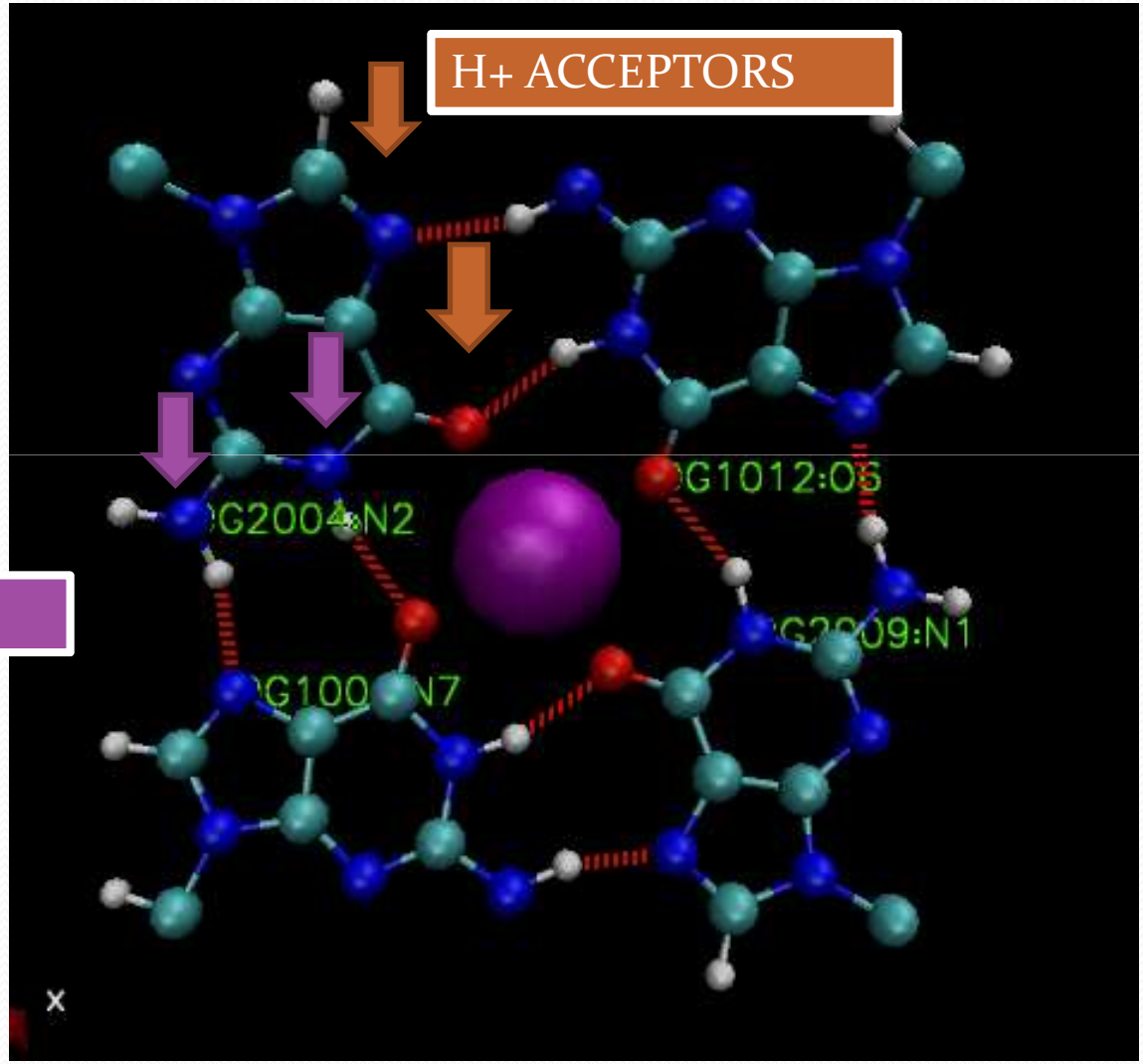
- A G-quadruplex is a DNA secondary structure that consists of multiple vertically stacked guanine tetrads.
- Identified in:
  - Eukaryotic telomeres
  - Non-telomeric genomic regions
    - Gene promoters
    - Recombination sites
    - DNA tandem repeats



PDB: 1JPQ

G-TETRADE:

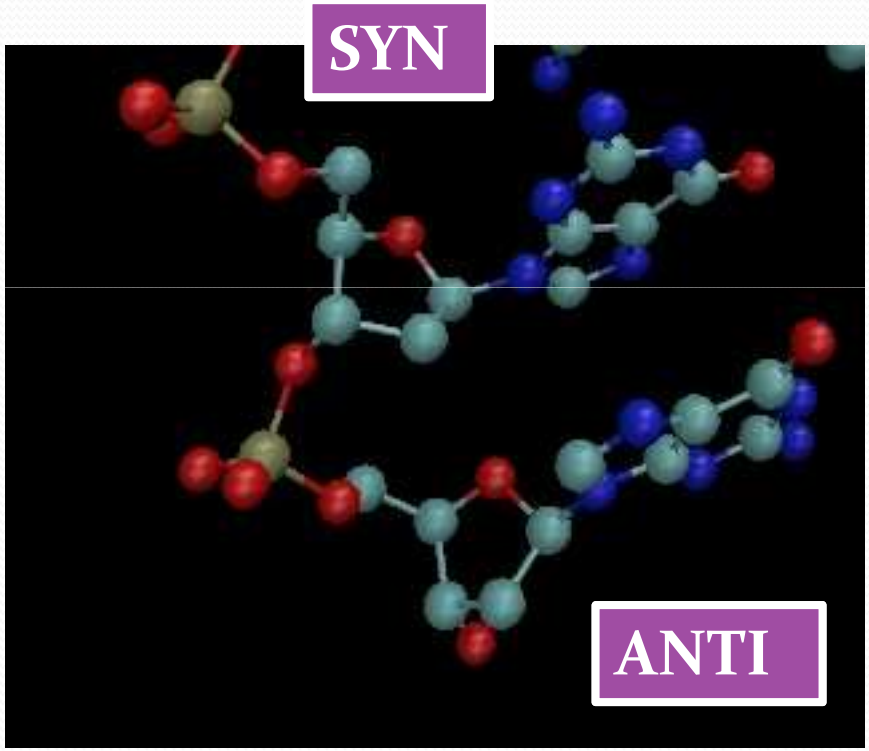
- 4 guanines
- monovalent cation



PDB: 1JPQ

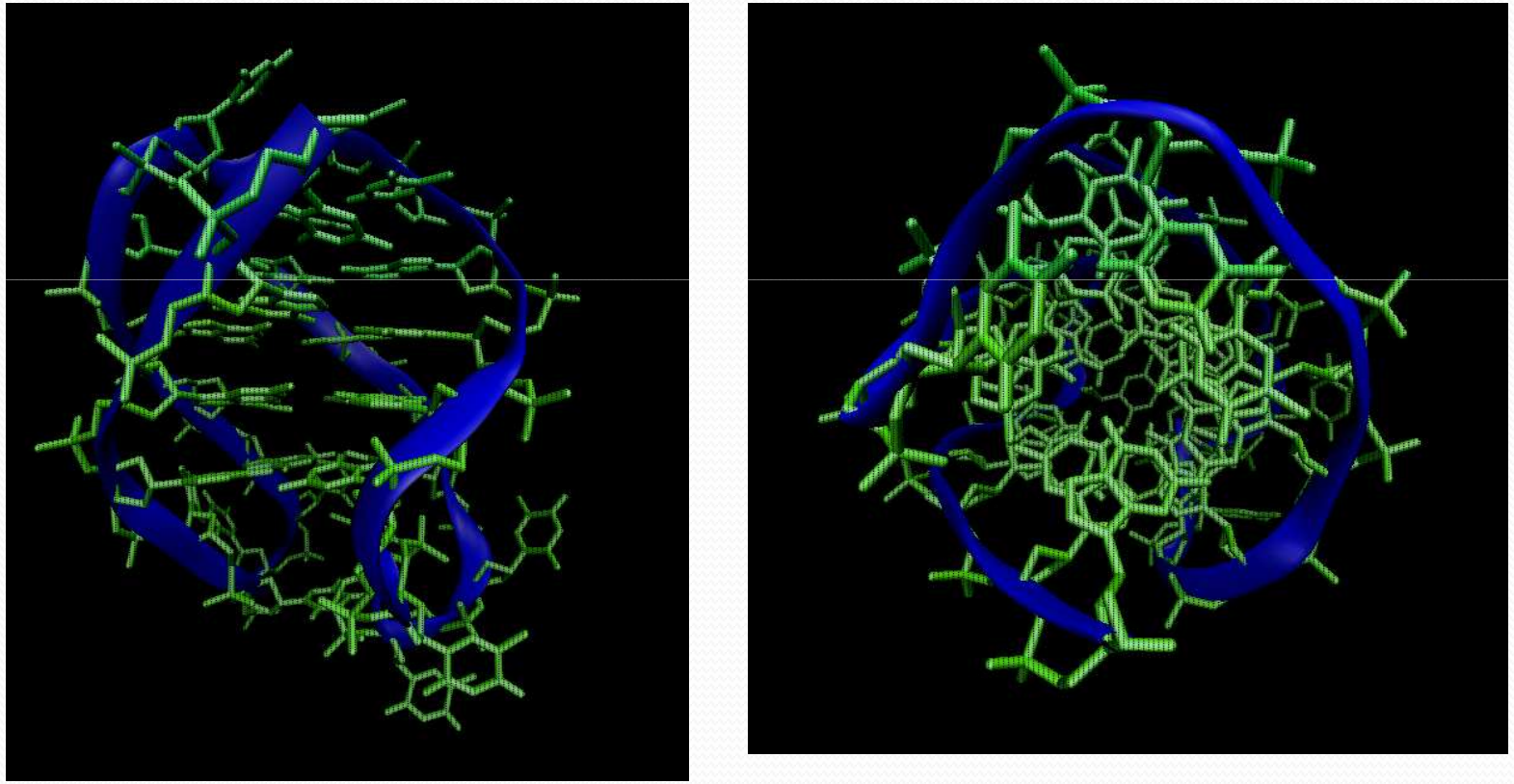
G-quadruplexes classification

- Number of strands
- Orientation
- Conformation
- Loop



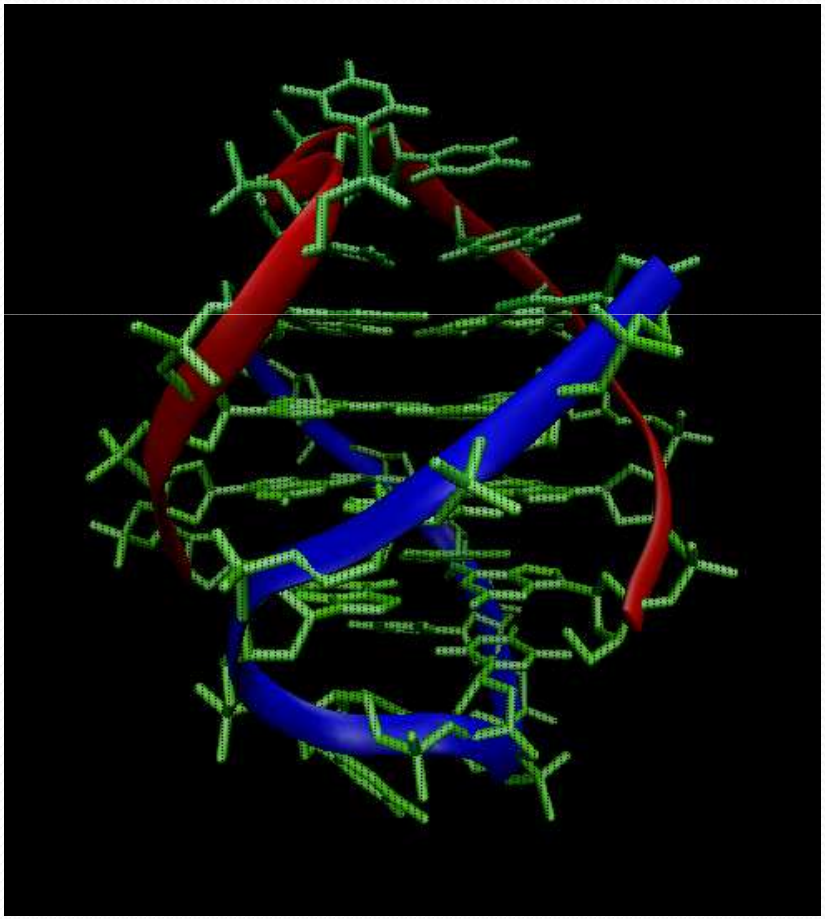
PDB: 1JPQ

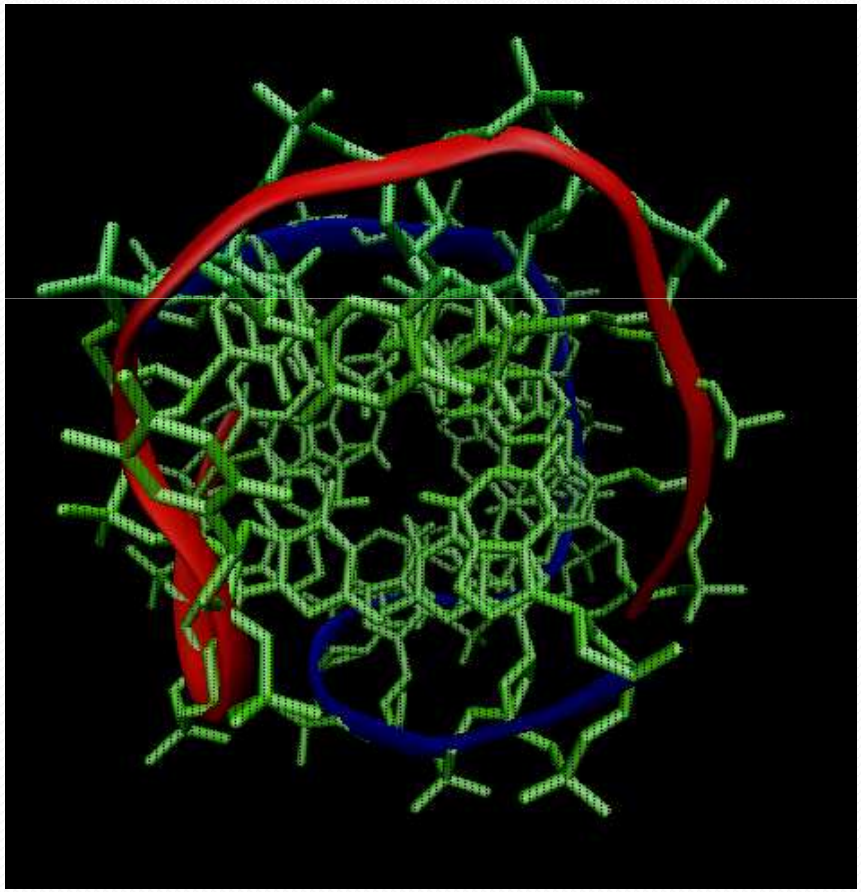
Unimolecular quadruplex structure



PDB: 201d

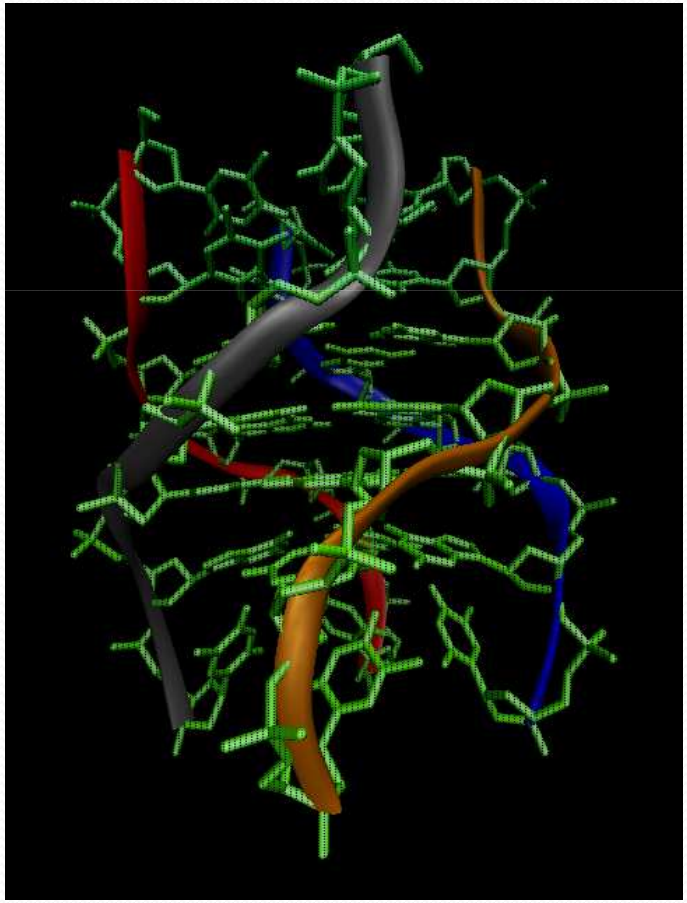
Bimolecular quadruplex structure

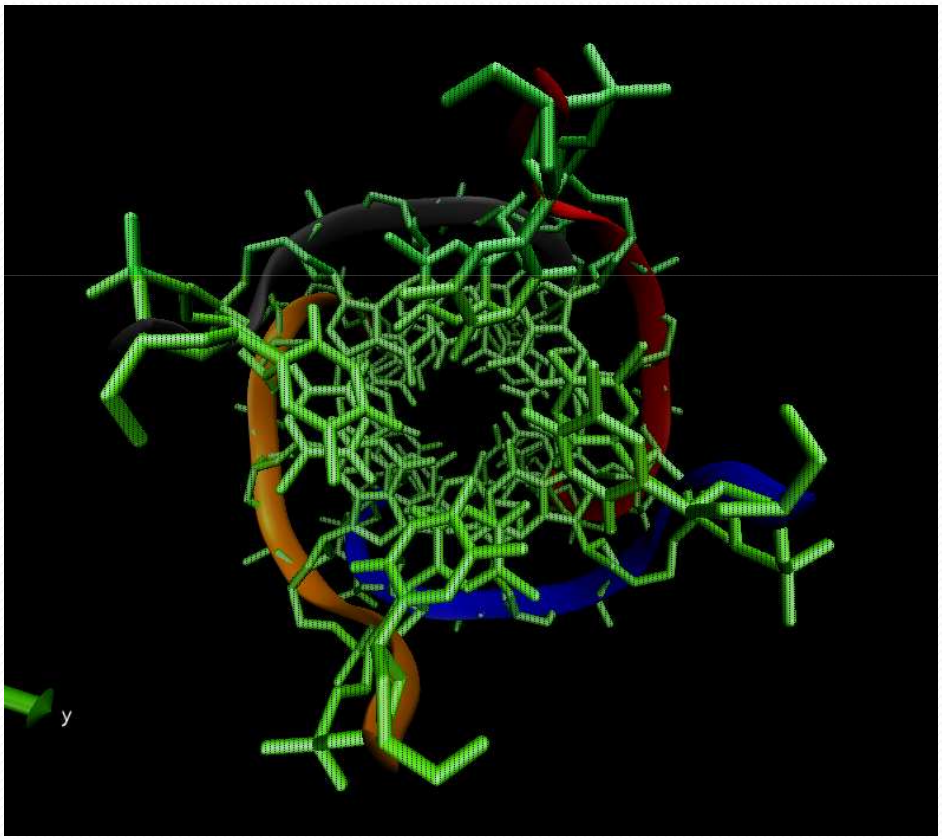




PDB: 1JPQ

Tetramolecular quadruplex structure





PDB: 139B

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Thank you for your attention