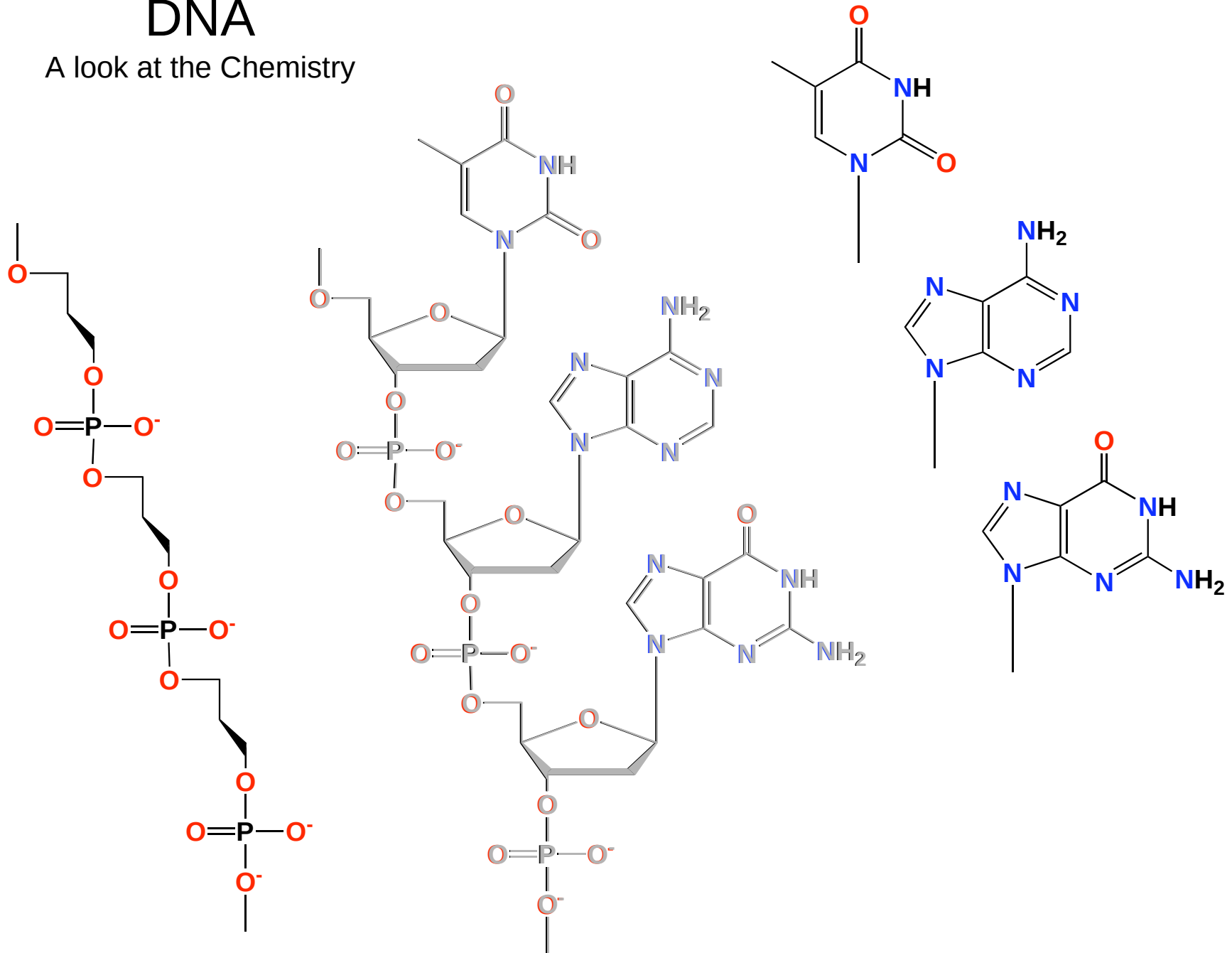


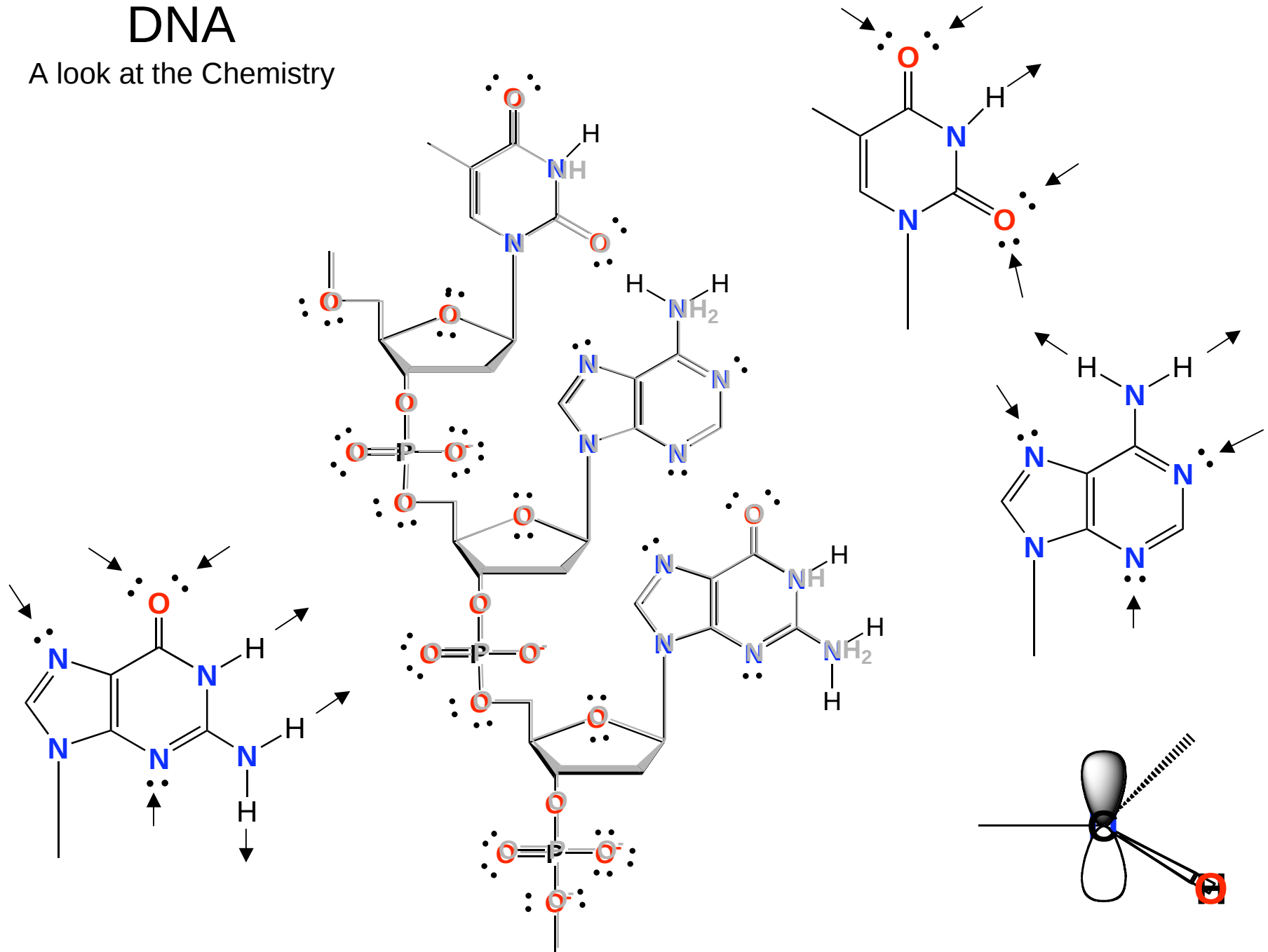
DNA

A look at the Chemistry

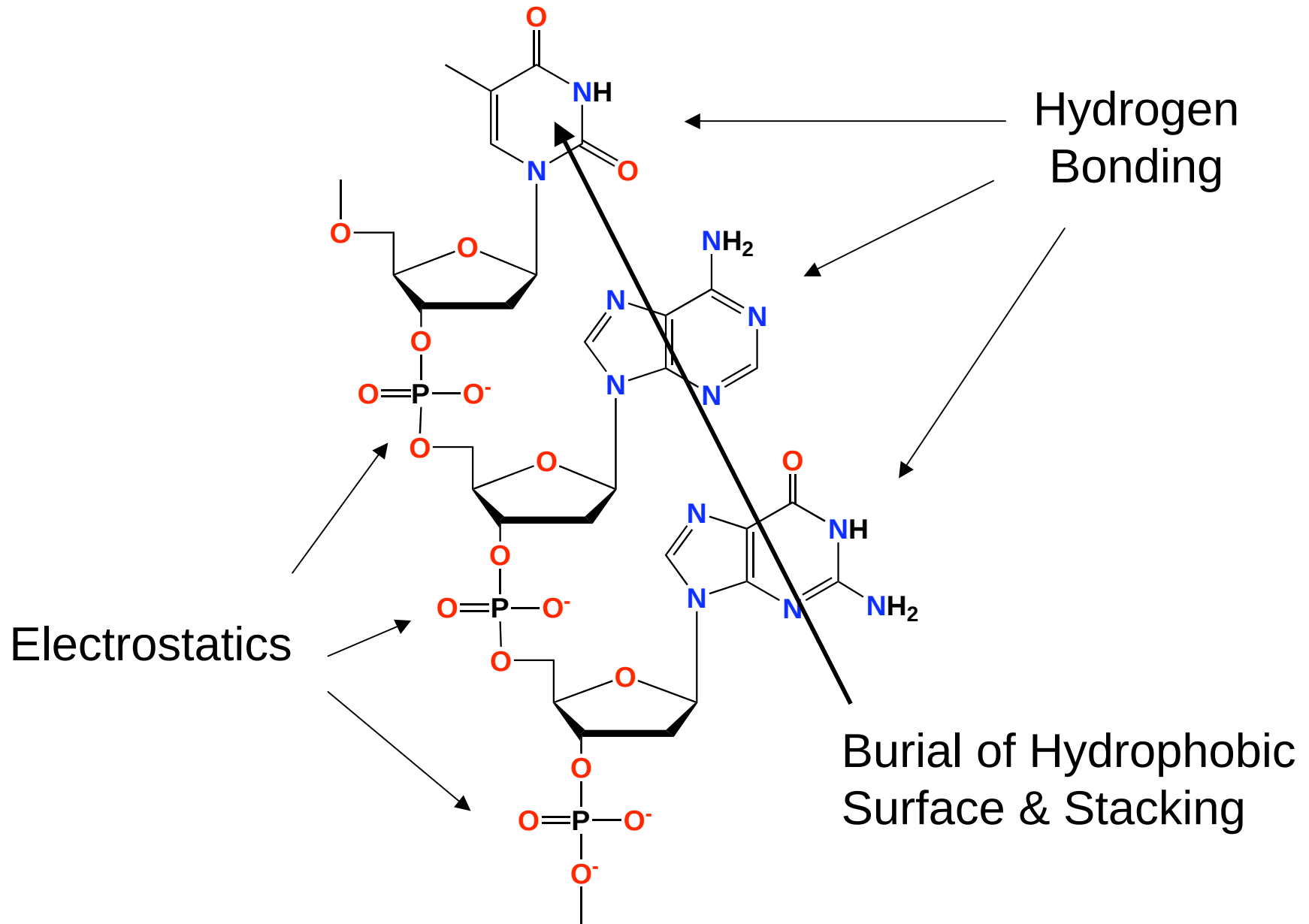


DNA

A look at the Chemistry

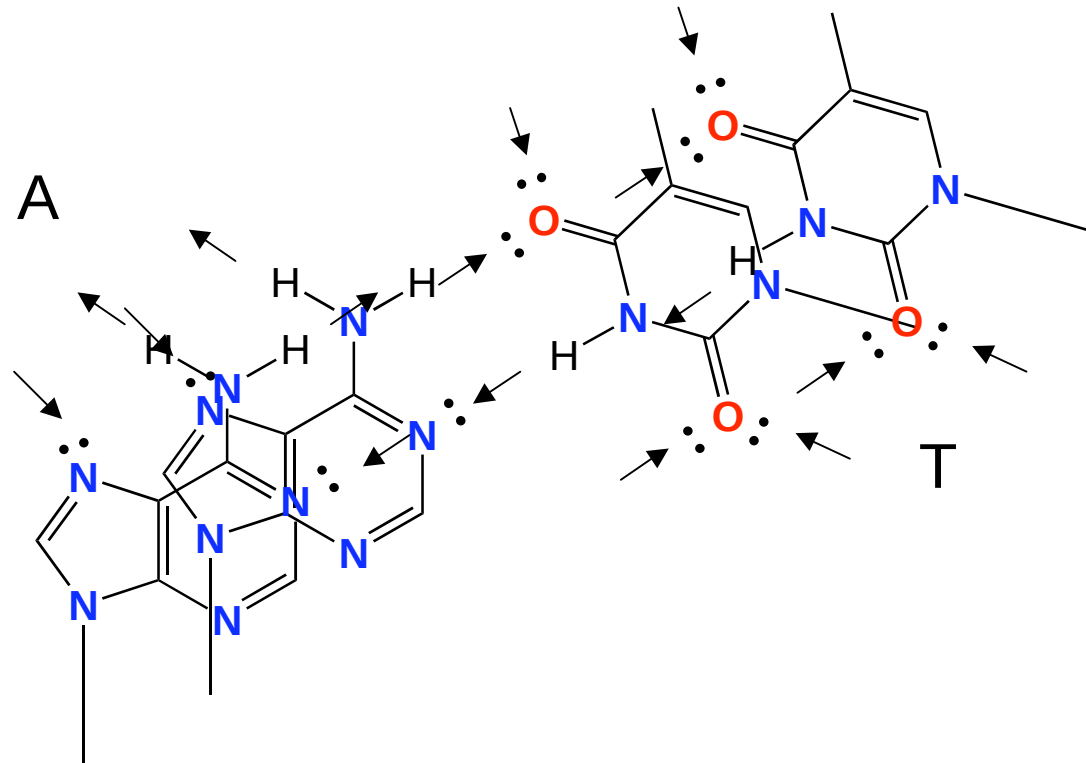


What forces are important?



Base Pairing

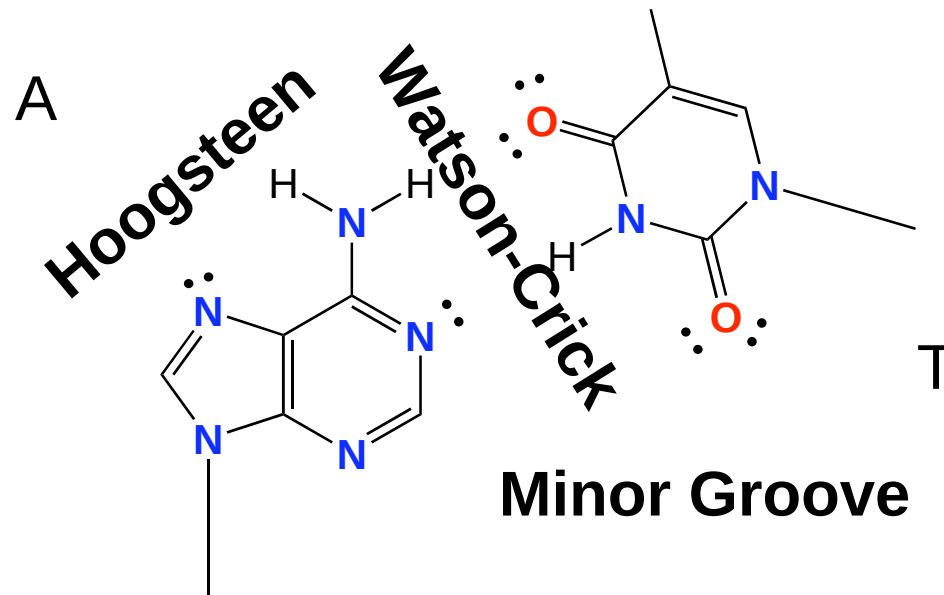
(Donors matched to Acceptors)



Base Pairing

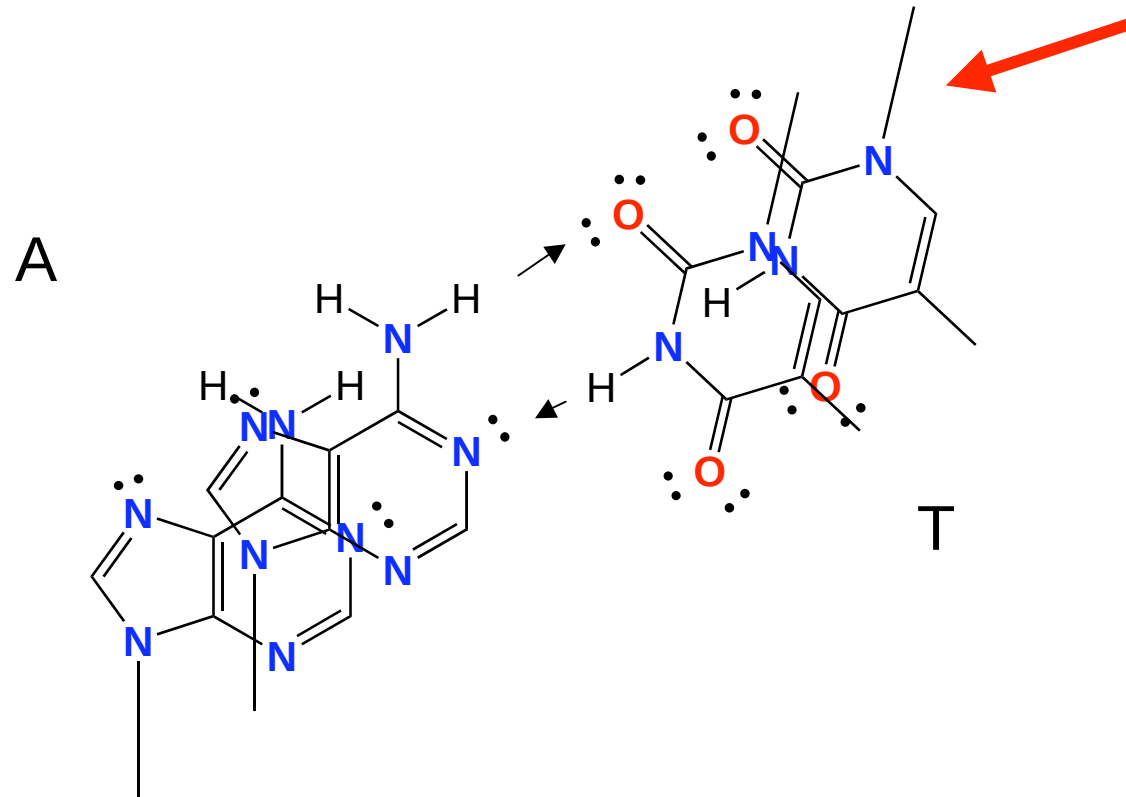
(Donors matched to Acceptors)

Major Groove



Base Pairing

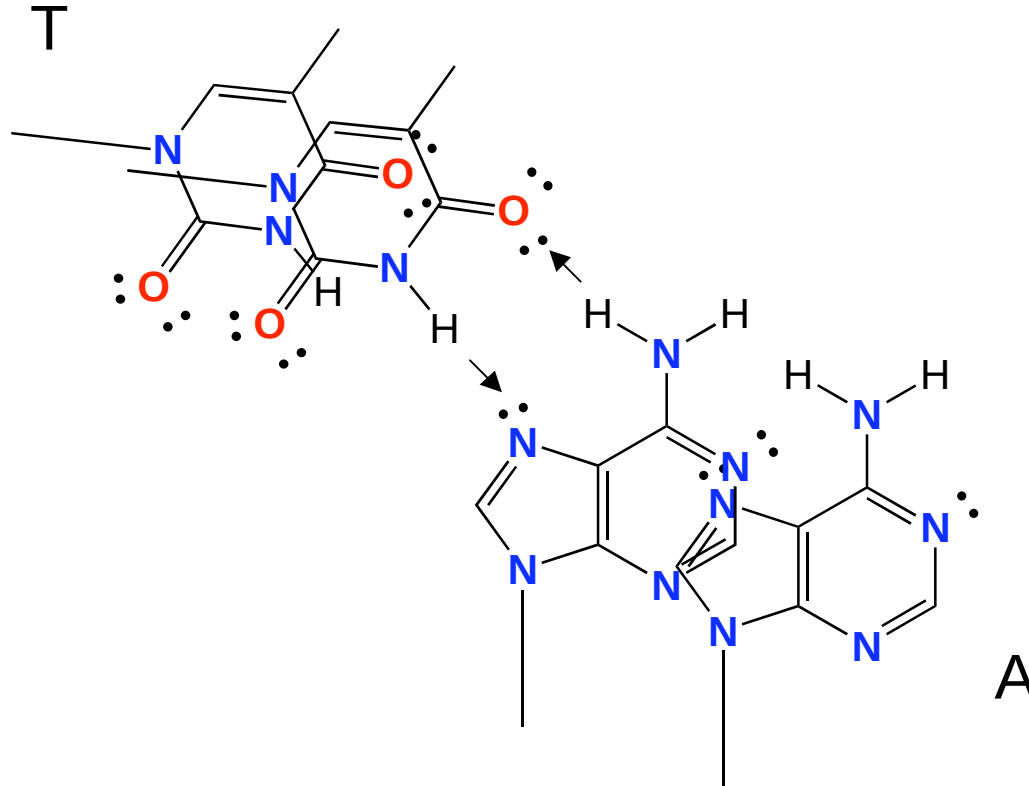
(Donors matched to Acceptors)



Good base pairing
Watson-Crick facing
but *Anti-Watson-Crick* orientation

Base Pairing

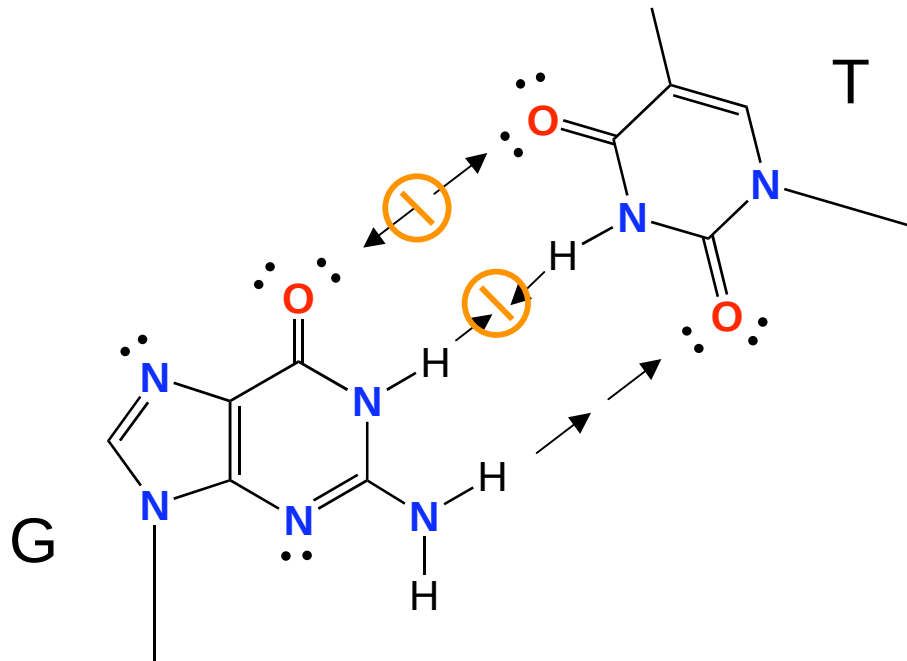
(Donors matched to Acceptors)



Good base pairing
WC-Hoogsteen facing

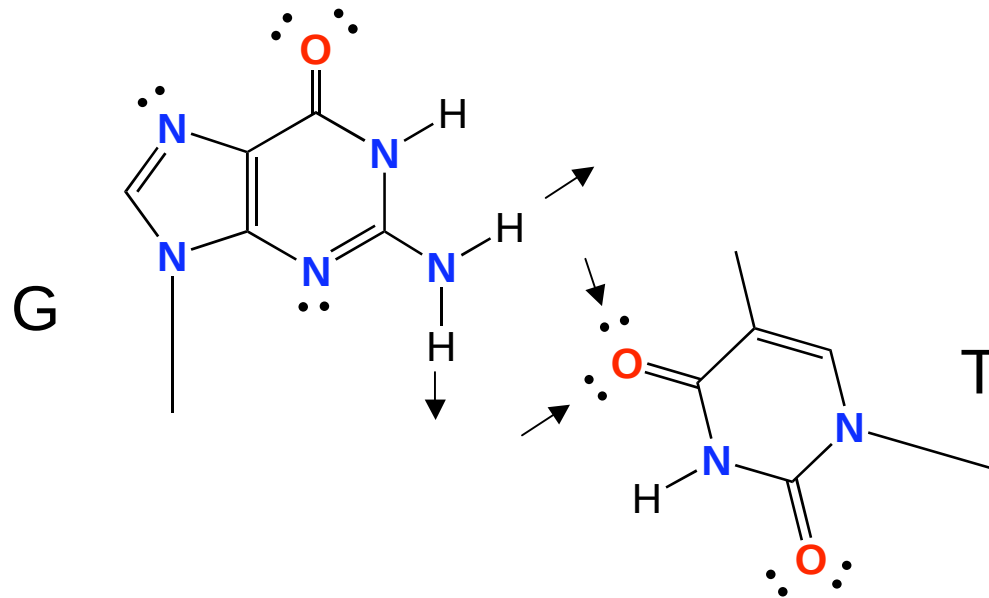
Bad Base Pairing

(Donors **not** matched to Acceptors)

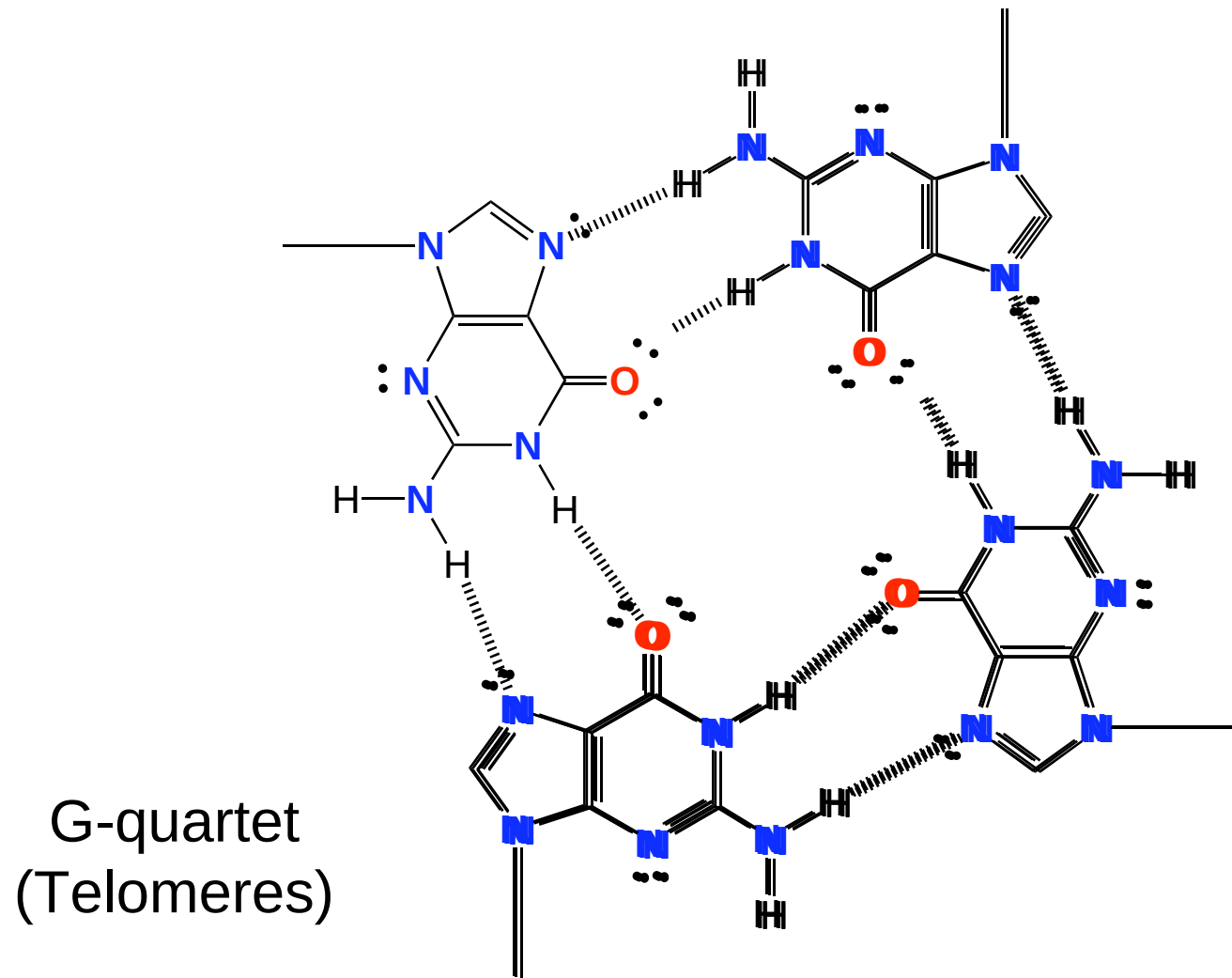


Bad Base Pairing

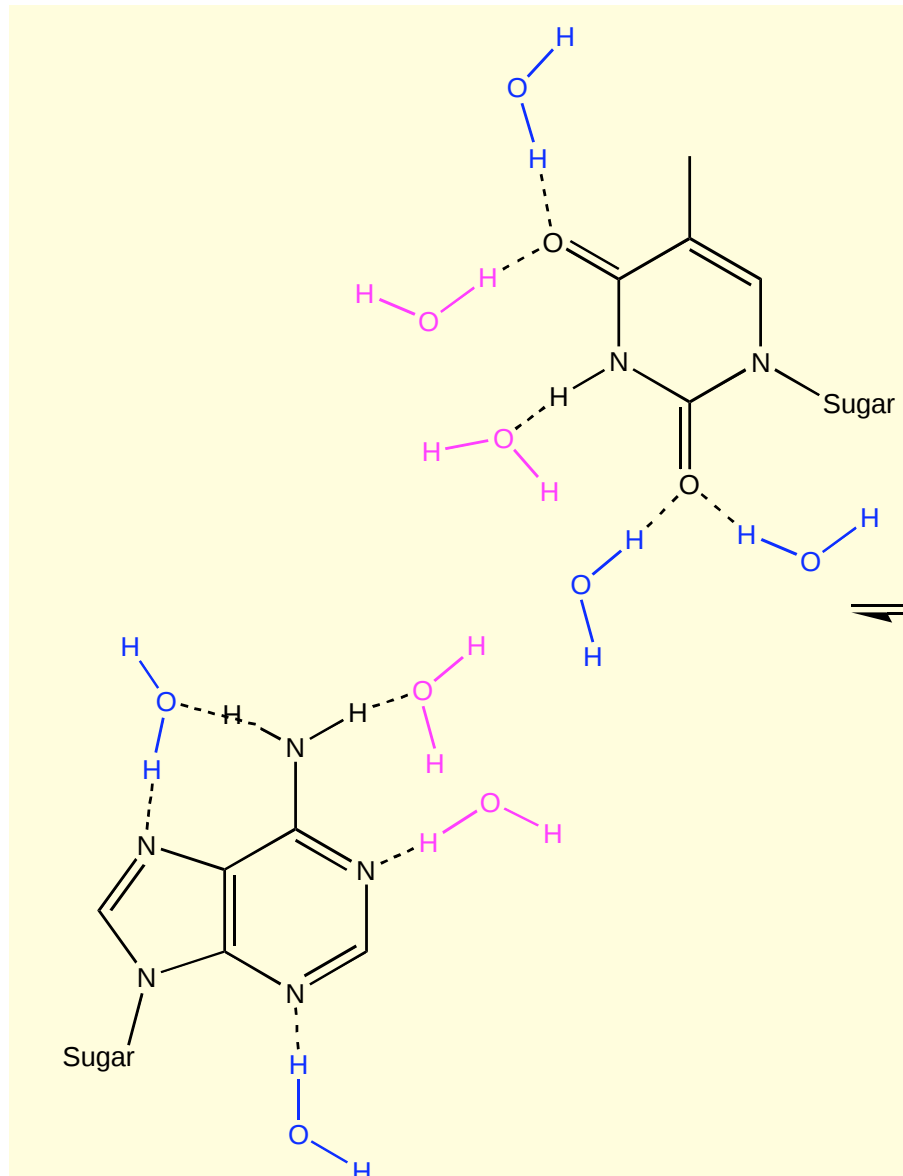
(Donors to Acceptors with *terrible angles*)



Wild (but good) Base Pairing

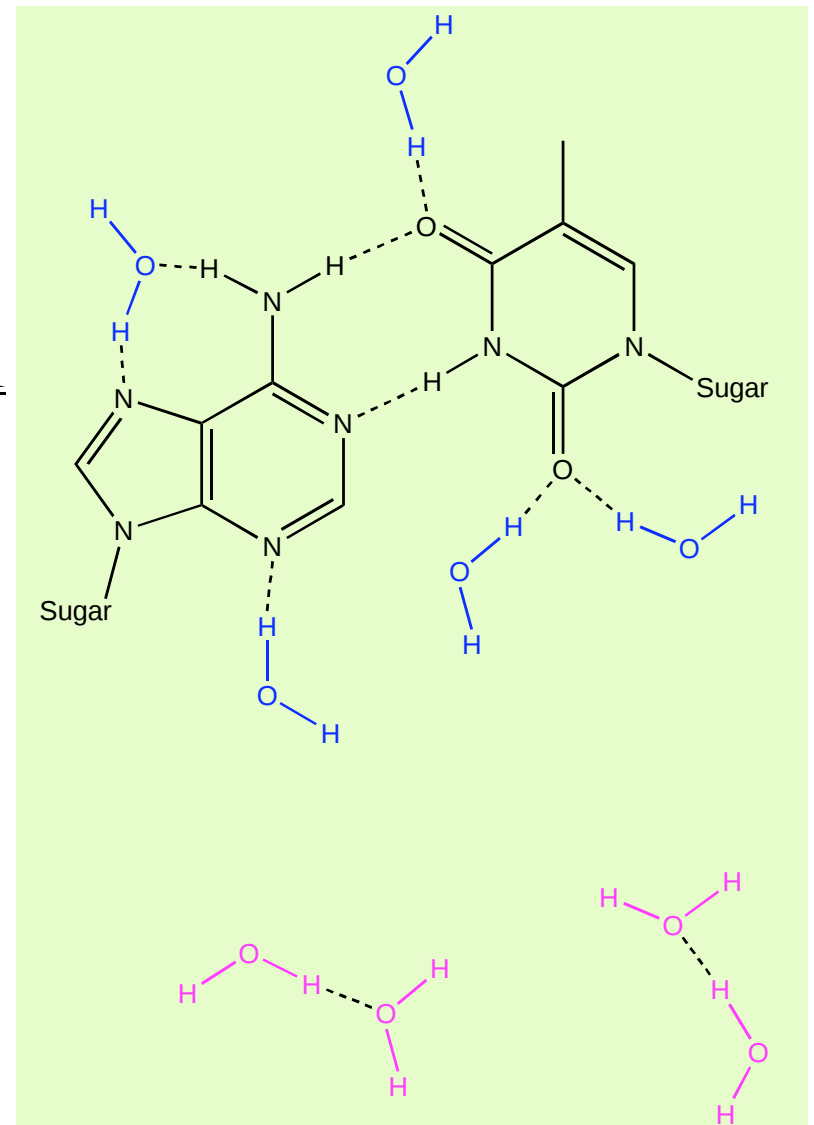


AT Base Pair

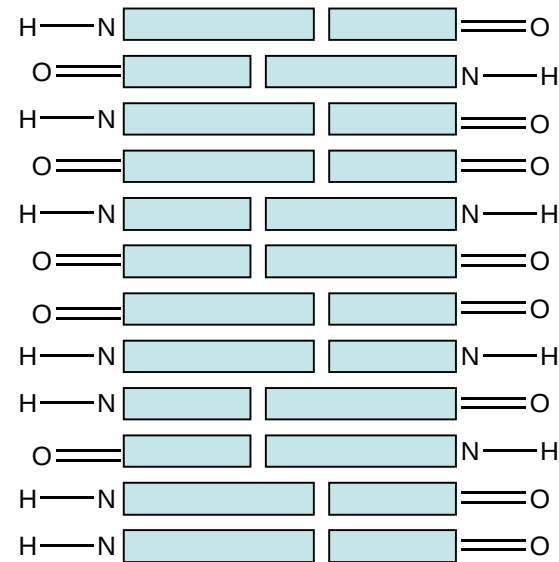
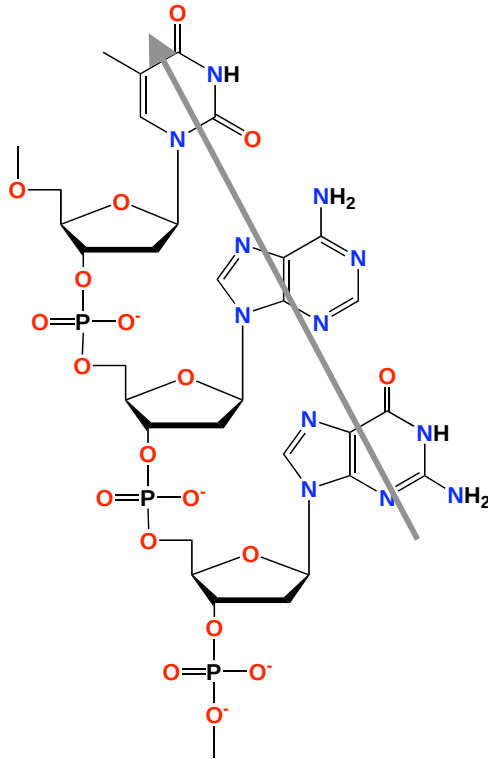


Ten H-Bonds

Ten H-Bonds



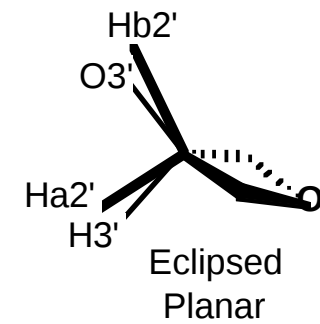
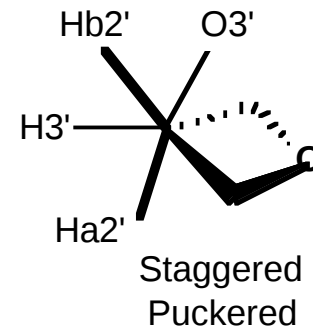
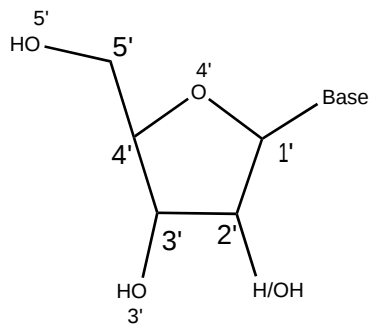
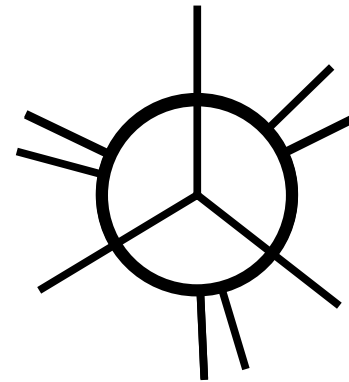
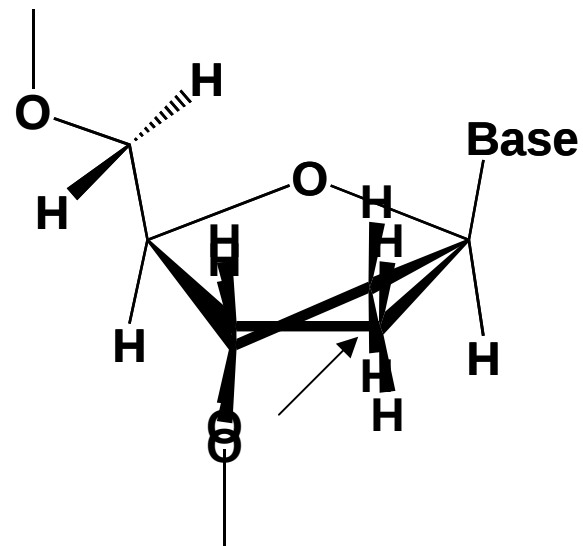
Burial of hydrophobic surface drives helix formation (hydrophobic core / stacking interactions)



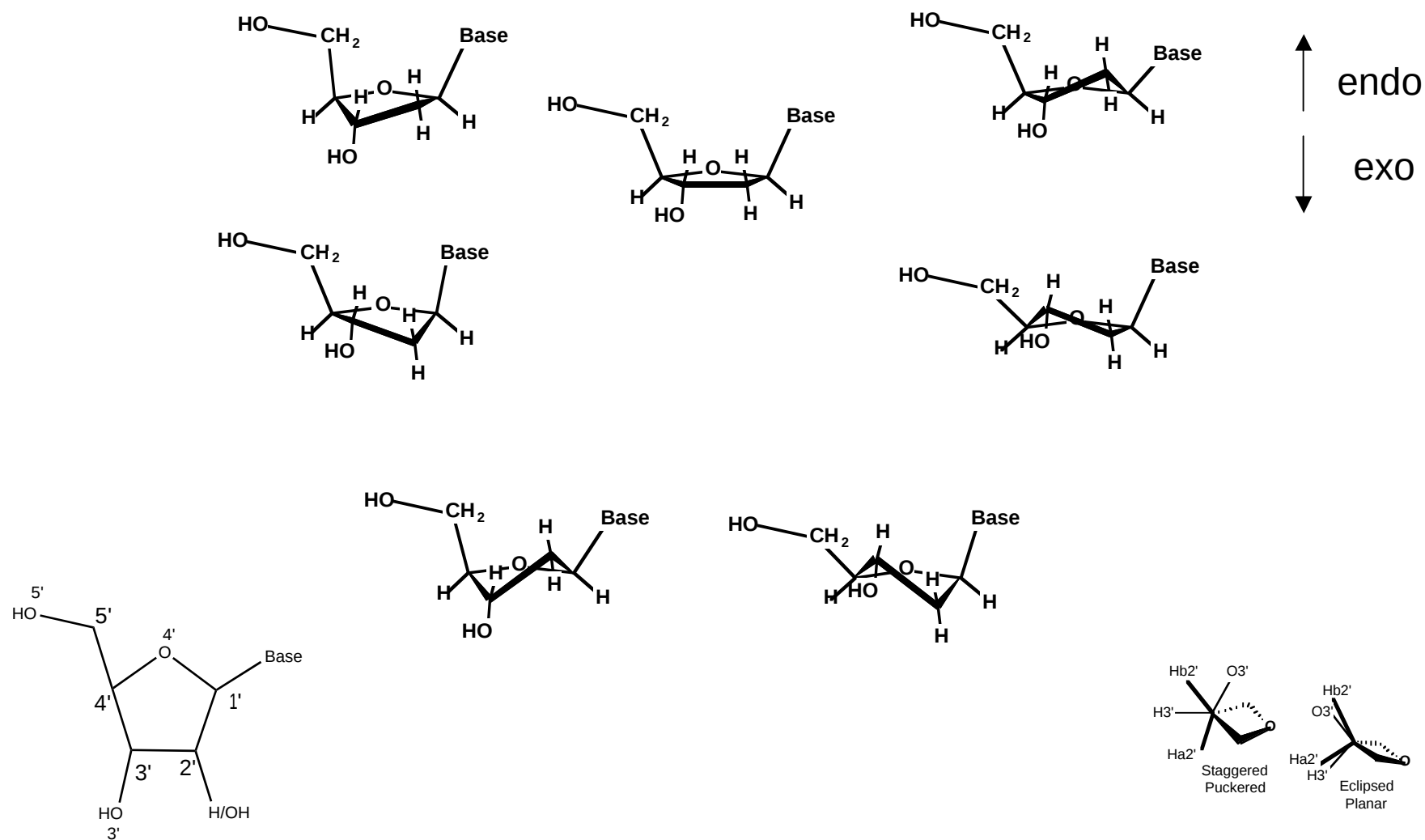
Flat faces are nonpolar
Edges are very polar (can H-bond)

Other chemical constraints

Furanose Sugar Ring



Furanose Sugar Ring



Letters to Nature

Nature **430**, 377-380 (15 July 2004) | doi: 10.1038/nature02692

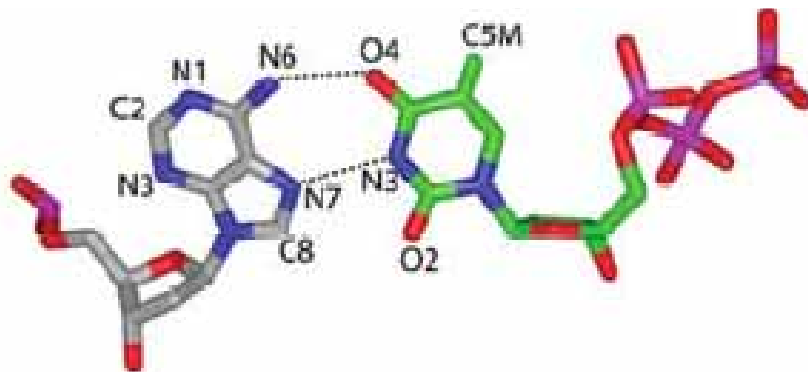
Replication by human DNA polymerase- ϵ occurs by Hoogsteen base-pairing

Deepak T. Nair¹, Robert E. Johnson², Satya Prakash², Louise Prakash²
and Aneel K. Aggarwal¹

A crystal structure from July 2004 shows that an error correcting (and error-prone) DNA polymerase uses Hoogsteen-WC base pairing to recognize the incoming substrate dNTP.

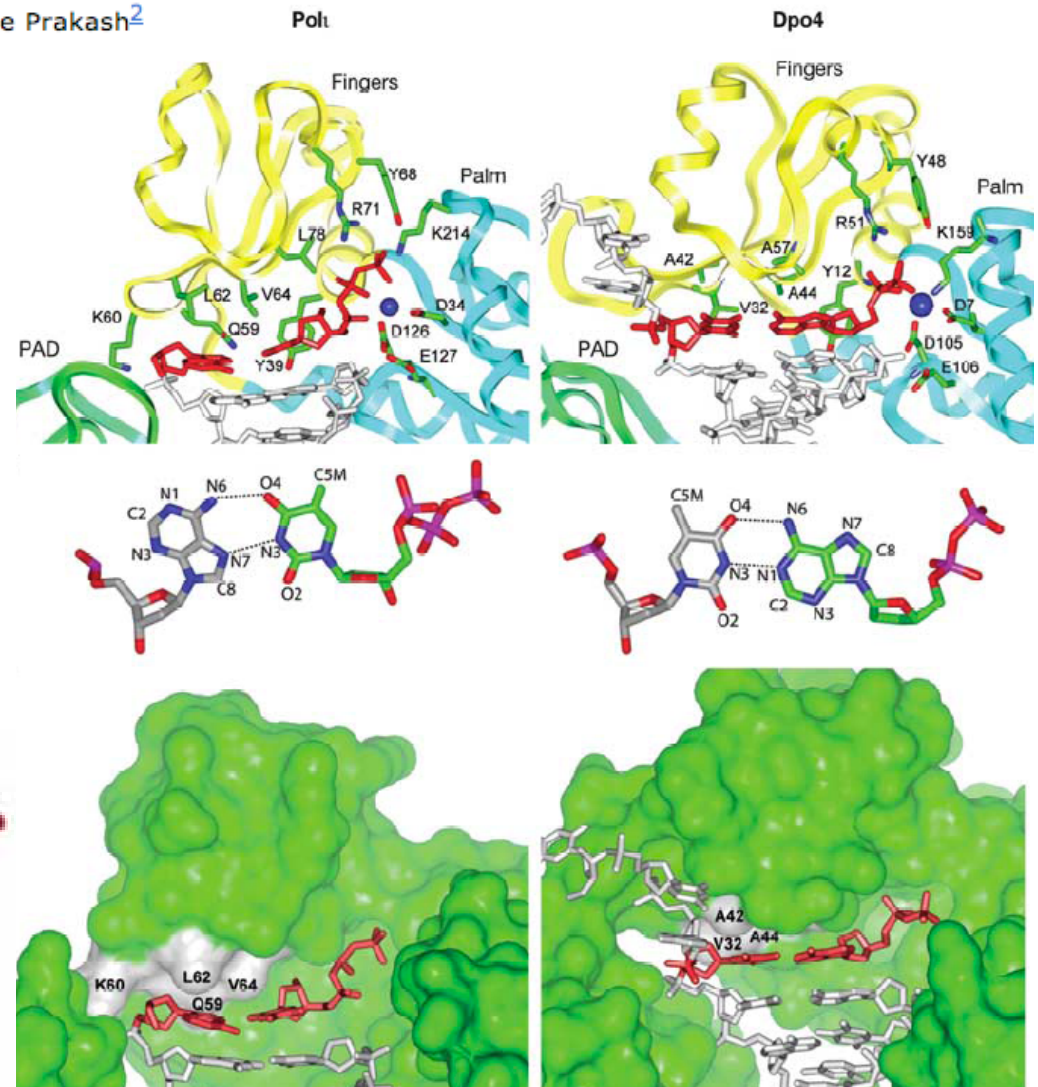
This supports biochemical studies that had been suggesting such a pairing.

This polymerase is good at bypassing lesions in the DNA (eg, damaged Watson-Crick face of G).

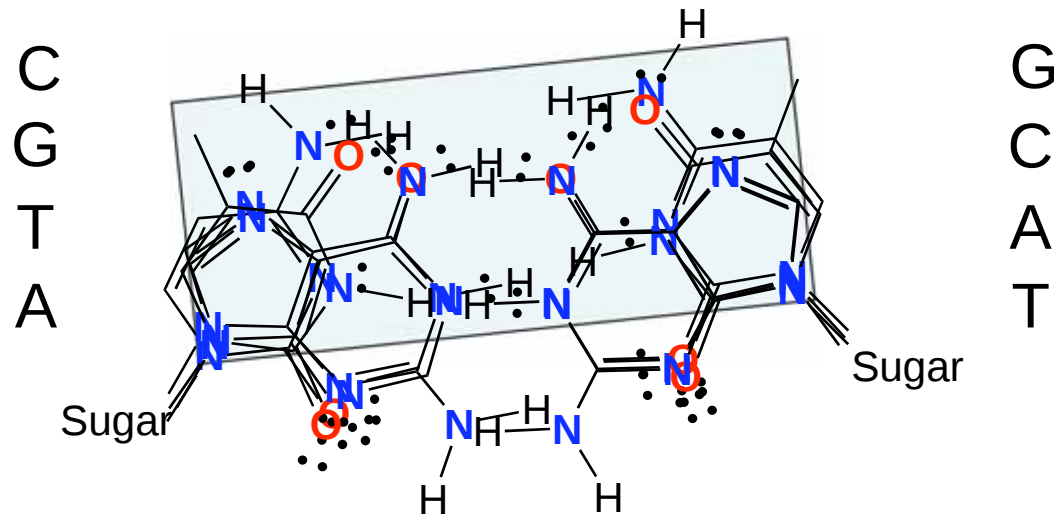


Hoogsteen vindicated

But... perhaps not...

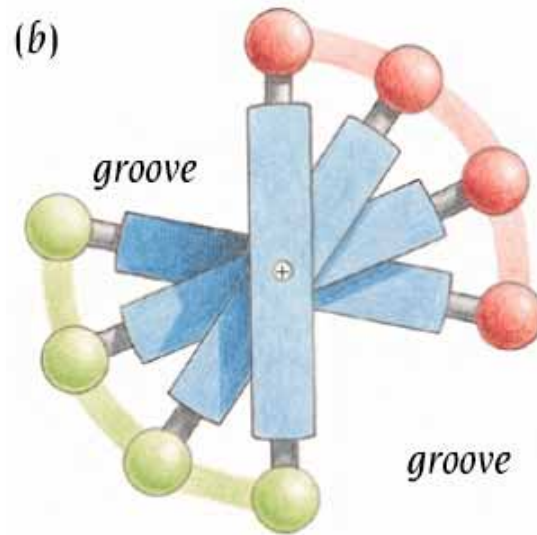
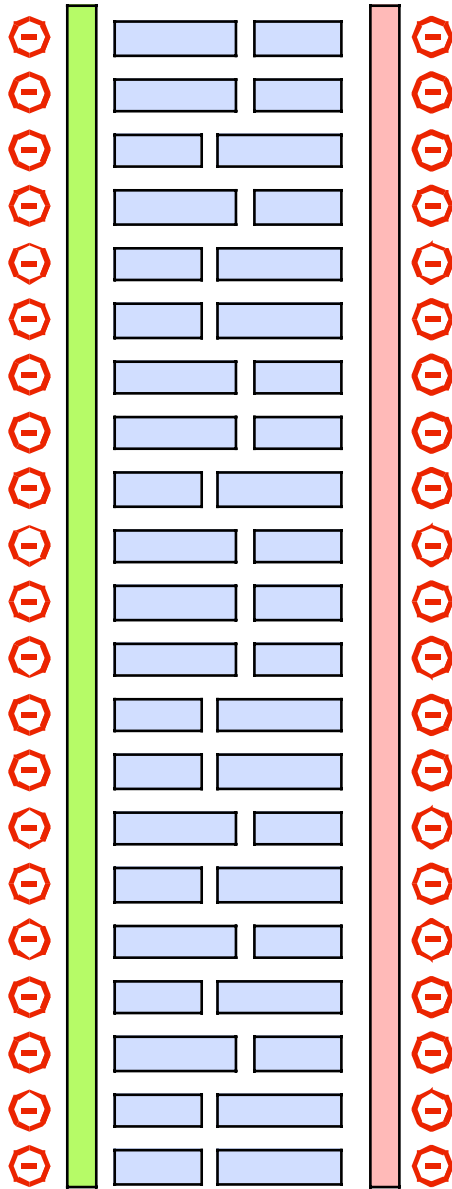


Why is Watson-Crick so good?

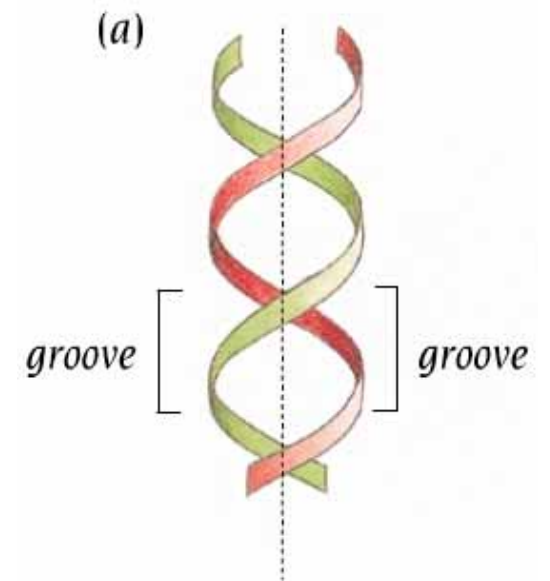


All four WC base pairs
are
isosteric

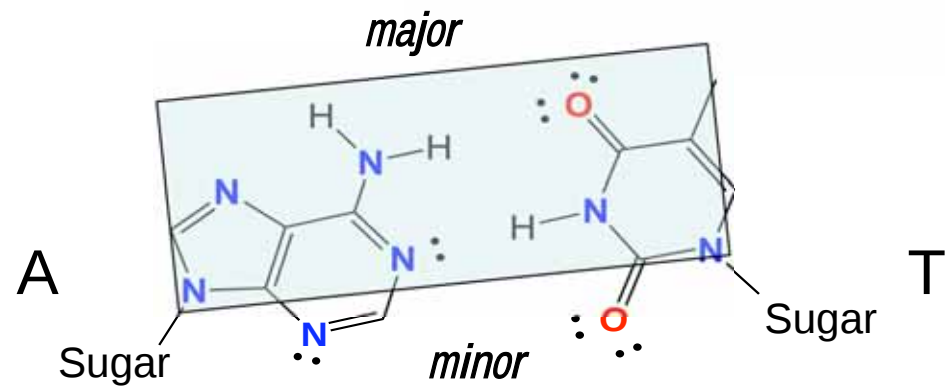
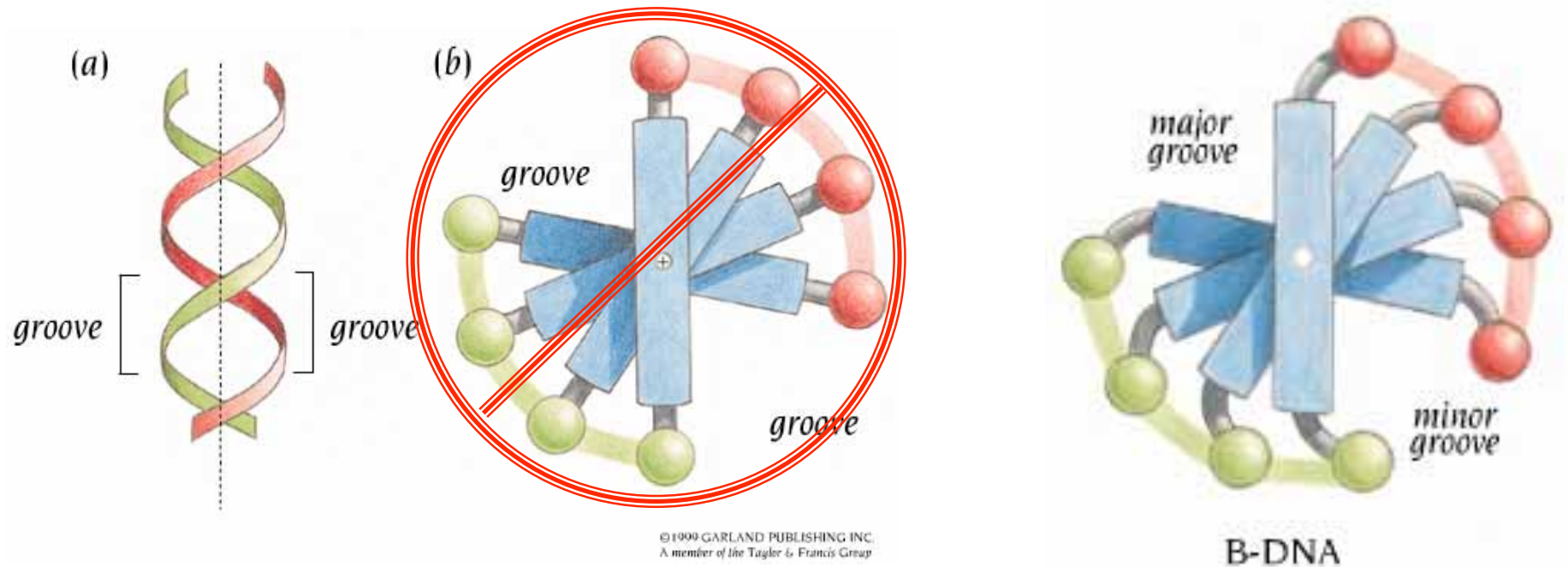
Why a *helix*?



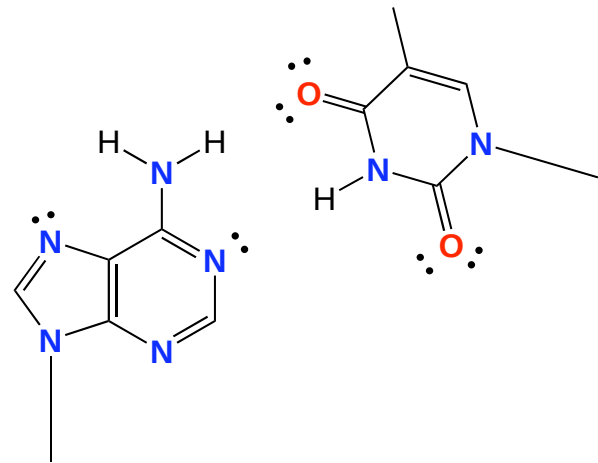
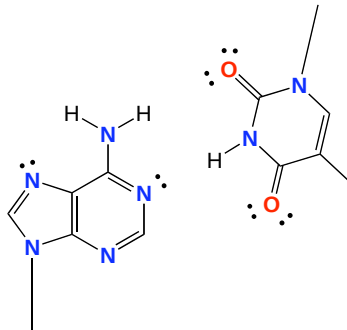
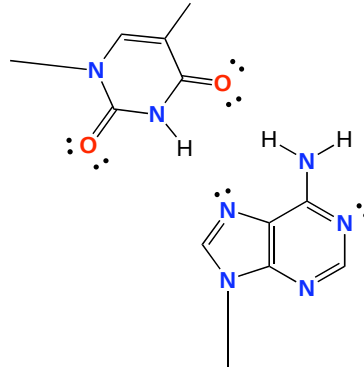
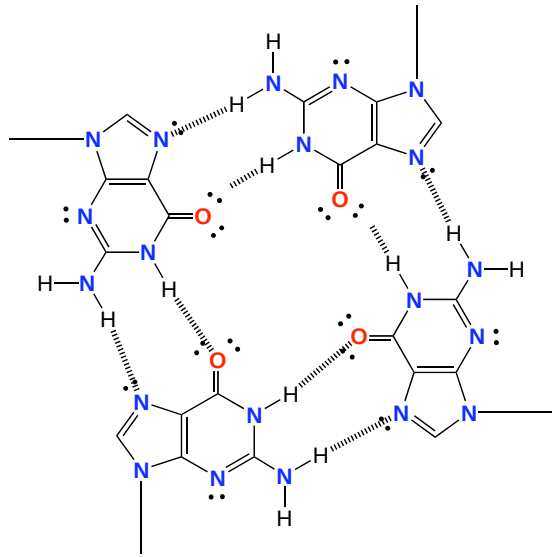
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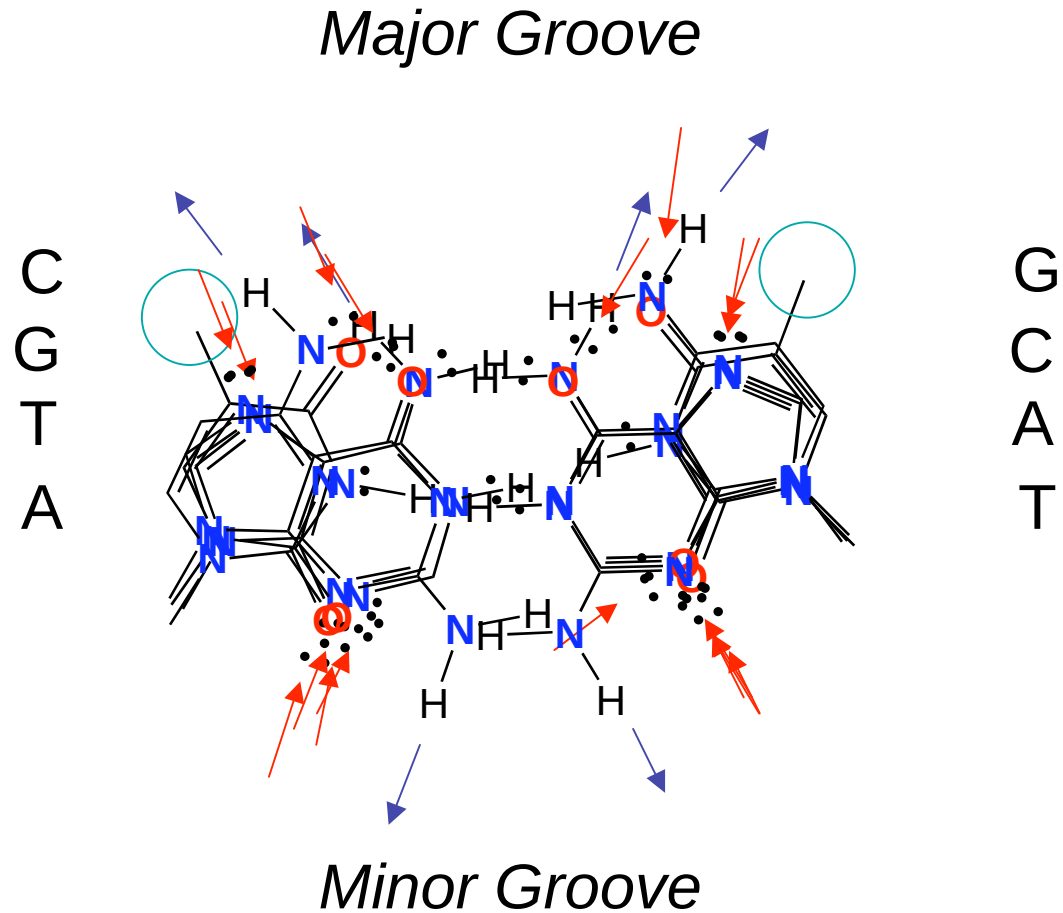
Why *major* and *minor* grooves?



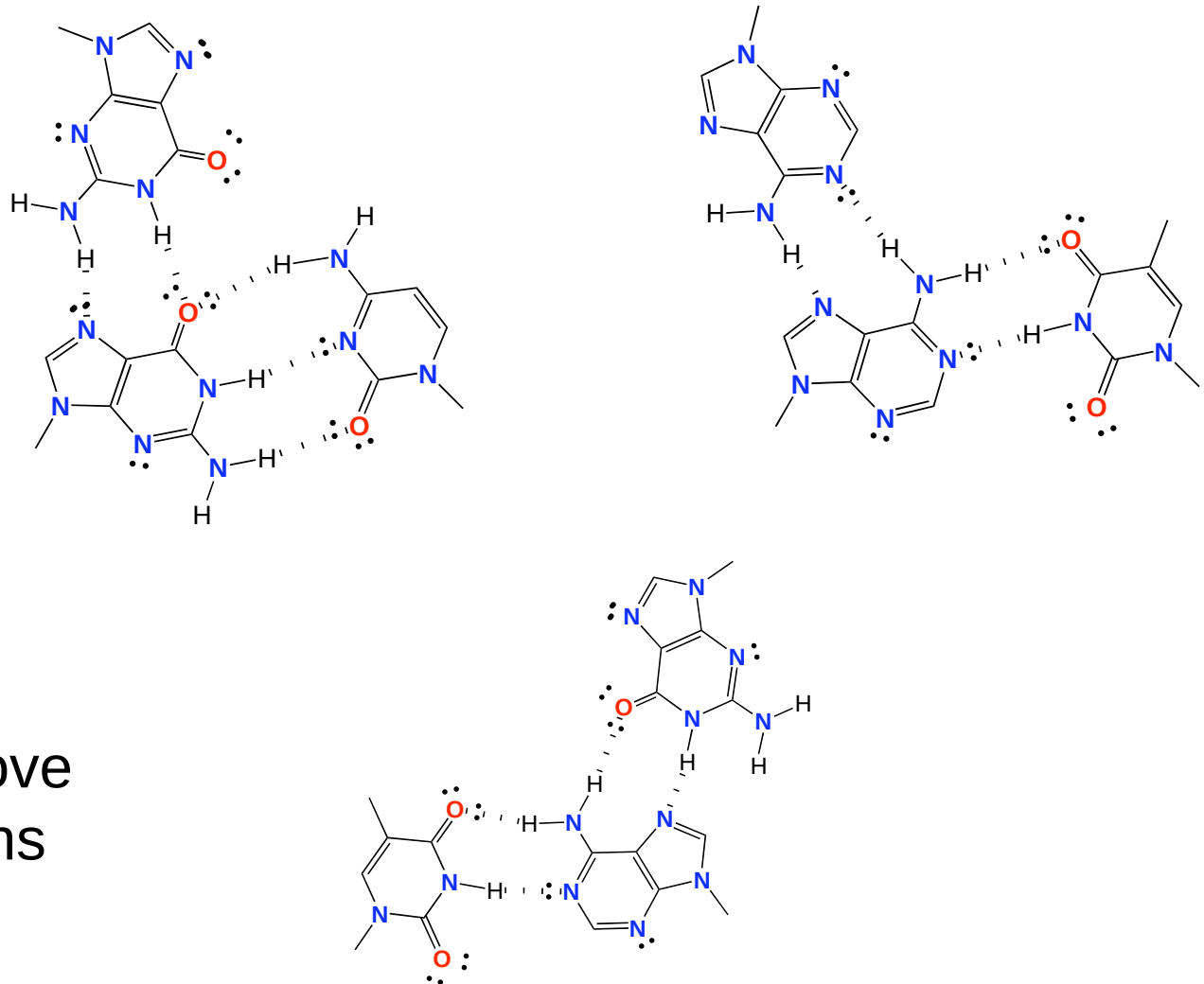
Nucleic Acid - Nucleic Acid Recognition



Why is the major groove so good?



Nucleic Acid “Triples / Platforms”



Major Groove
Interactions

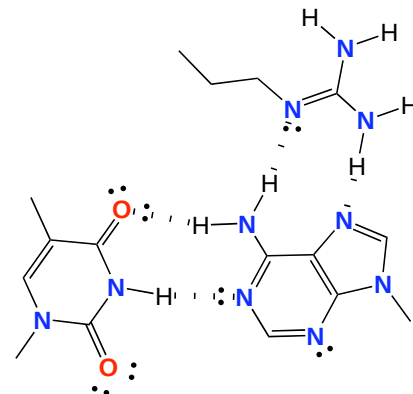
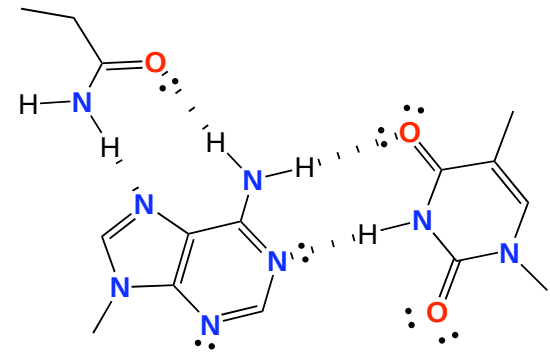
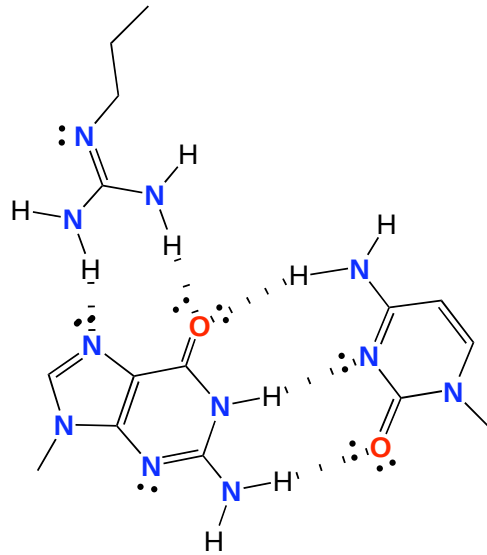
Protein - Nucleic Acid Interactions

Gln

Asn

Arg

Major Groove
Interactions



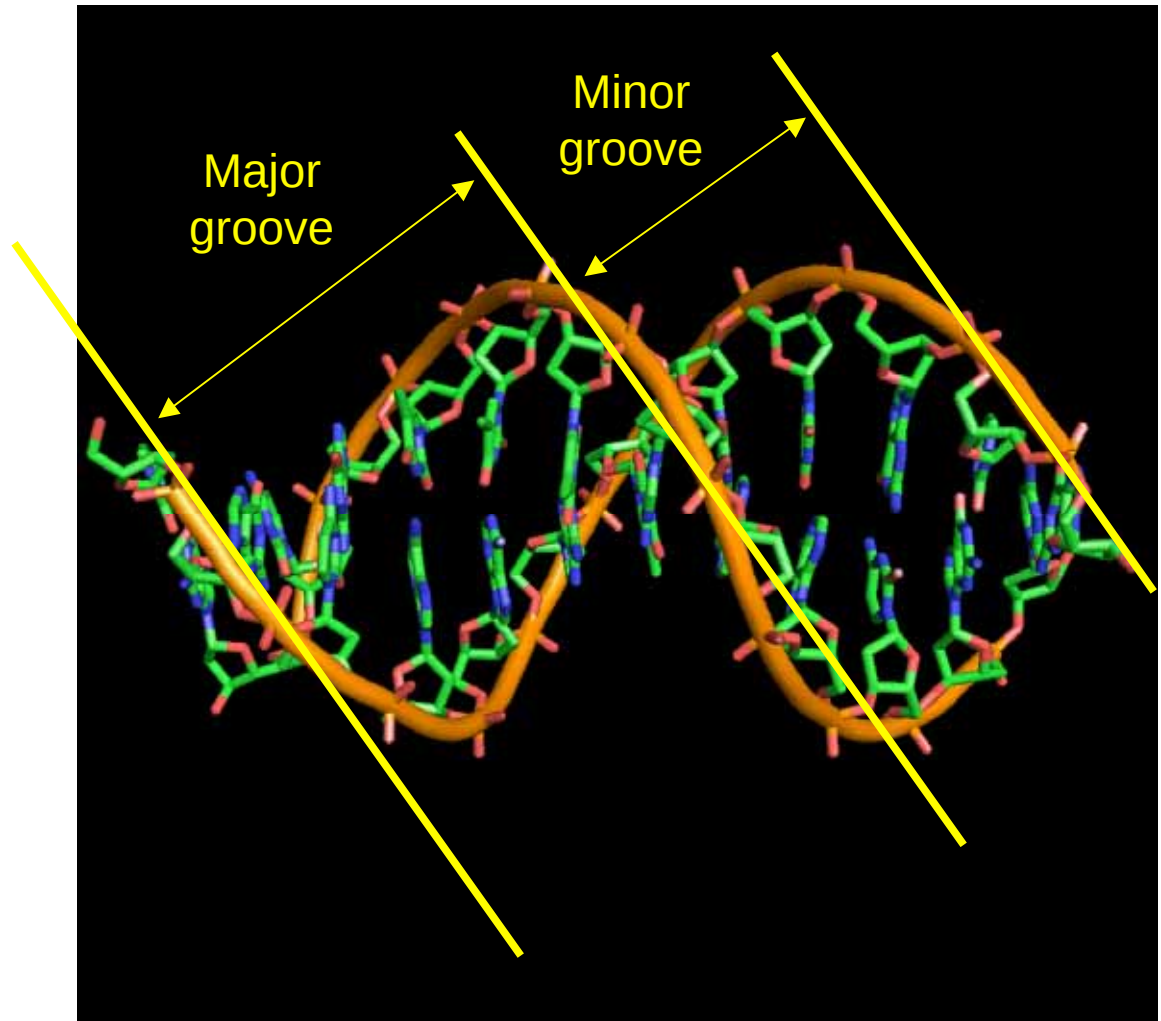
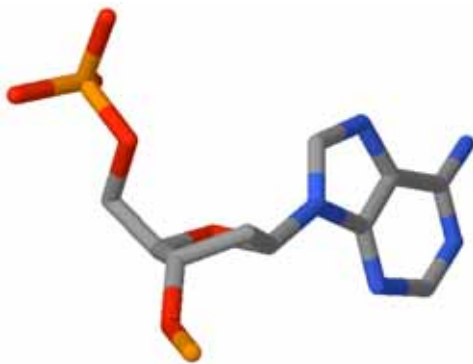
B-form DNA

B-form

Residues per turn = 10
Twist per base pair = 36°
Rise per pair = $3.4\text{\AA}$
c2'-endo

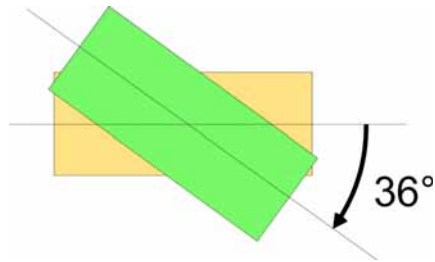
Minor groove width = $5.7\text{\AA}$
Major groove width = $11.7\text{\AA}$

Minor groove depth = $7.5\text{\AA}$
Major groove depth = $8.8\text{\AA}$



B-form DNA

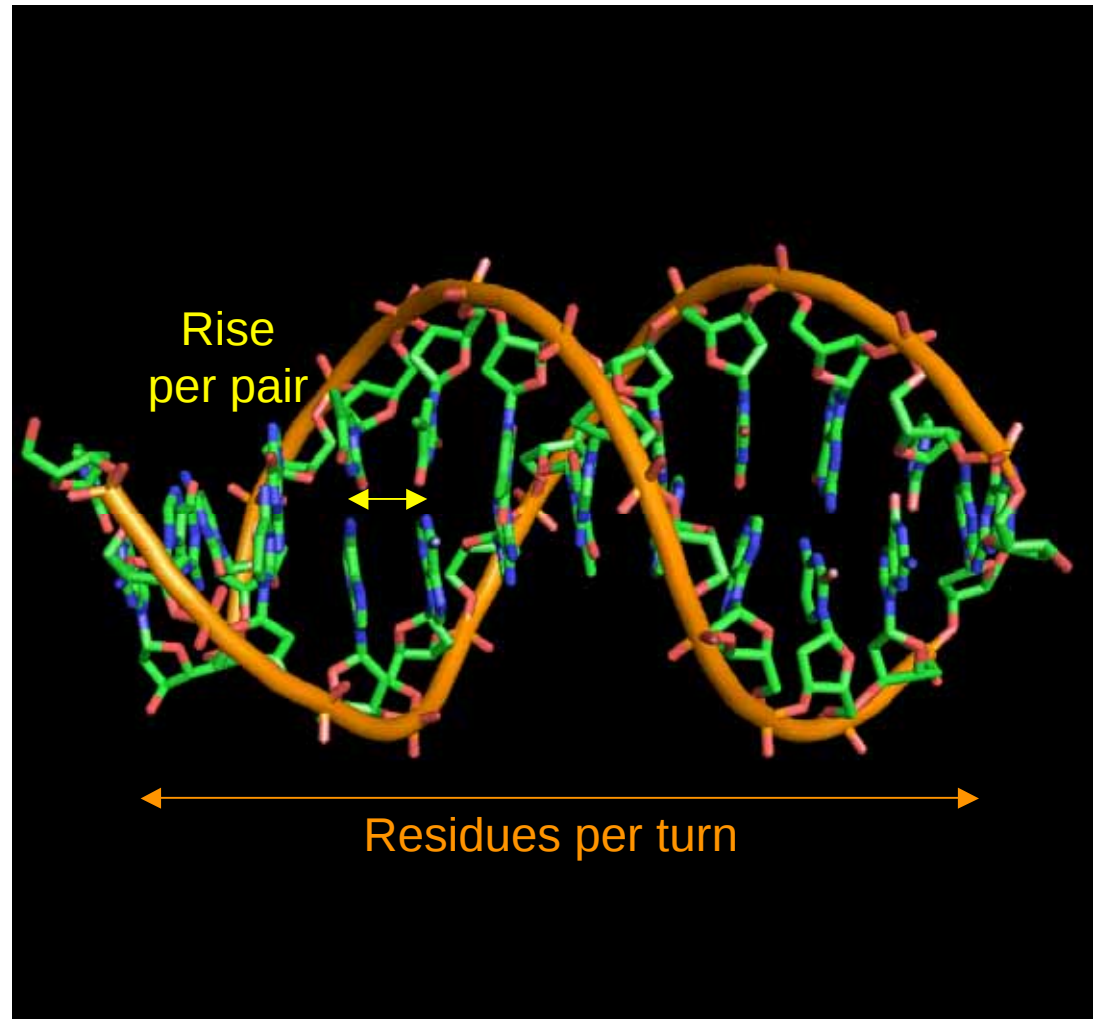
Residues per turn = 10
Twist per base pair = 36°



Rise per pair = $3.4\text{\AA}$
c2'-endo

Minor groove width = $5.7\text{\AA}$
Major groove width = $11.7\text{\AA}$

Minor groove depth = $7.5\text{\AA}$
Major groove depth = $8.8\text{\AA}$

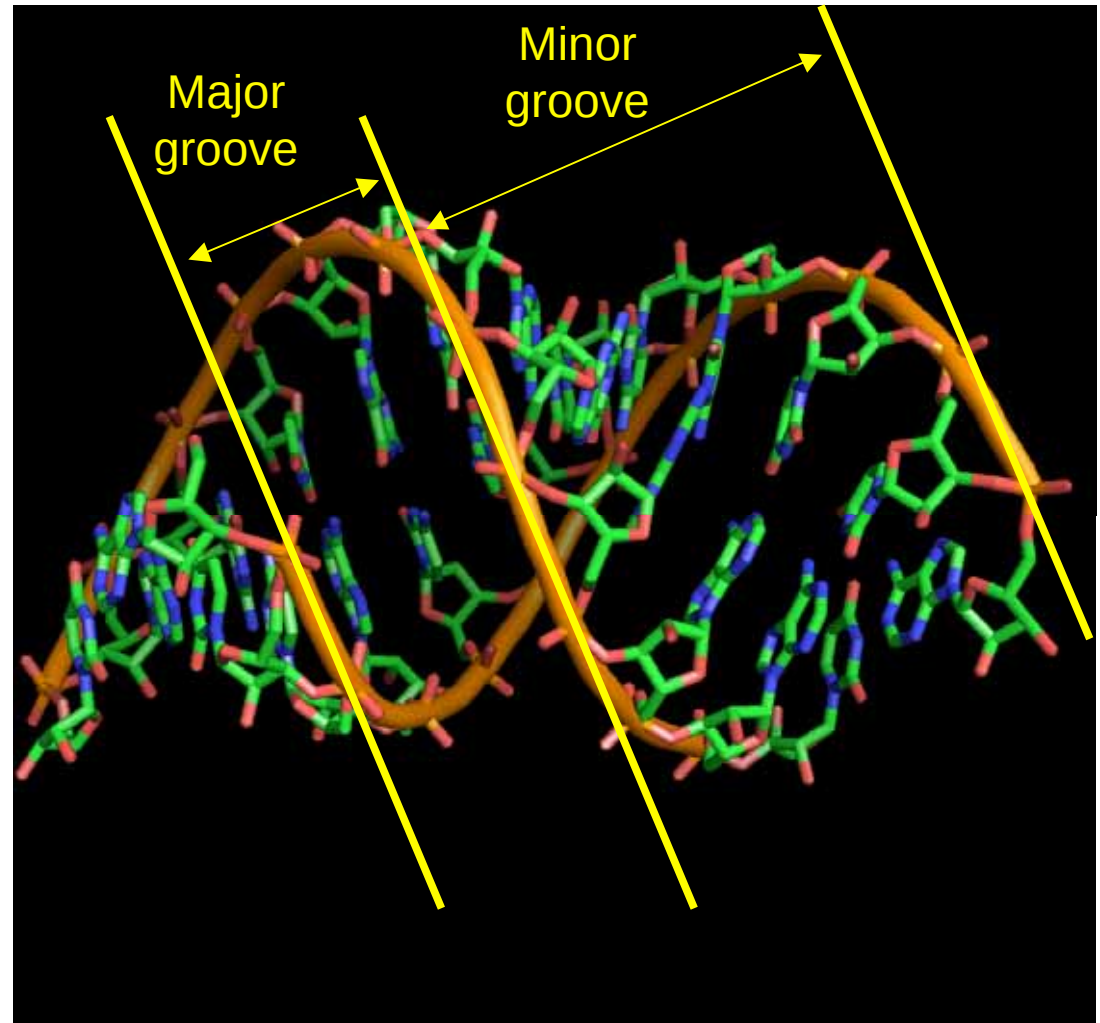
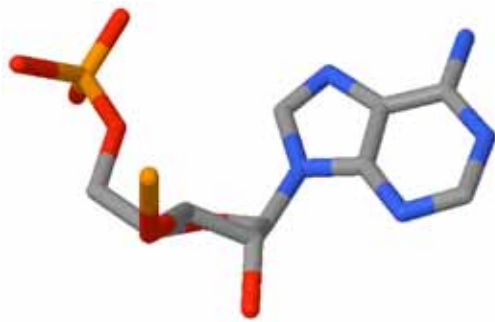


A-form RNA

Residues per turn = 11
Twist per base pair = 33°
Rise per pair = $2.9\text{\AA}$
c3'-endo

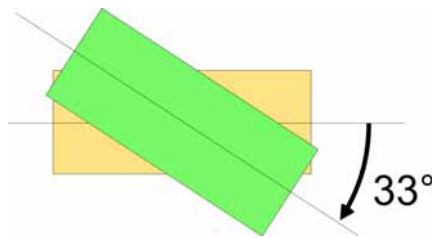
Minor groove width = $11\text{\AA}$
Major groove width = $2.7\text{\AA}$

Minor groove depth = $2.8\text{\AA}$
Major groove depth = $13.5\text{\AA}$



A-form RNA

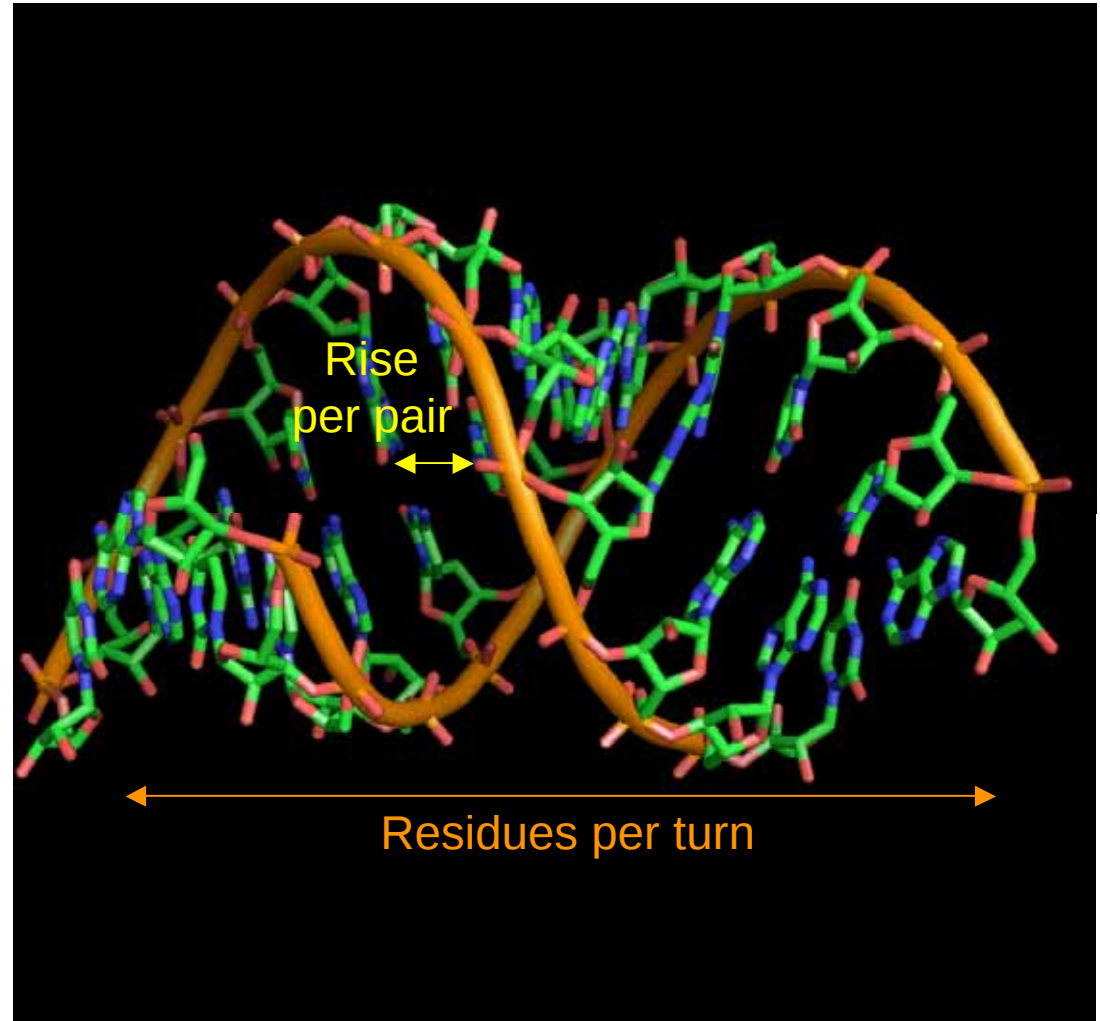
Residues per turn = 11
Twist per base pair = 33°



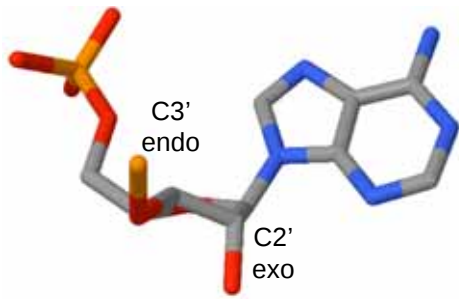
Rise per pair = $2.9\text{\AA}$
c3'-endo

Minor groove width = $11\text{\AA}$
Major groove width = $2.7\text{\AA}$

Minor groove depth = $2.8\text{\AA}$
Major groove depth = $13.5\text{\AA}$



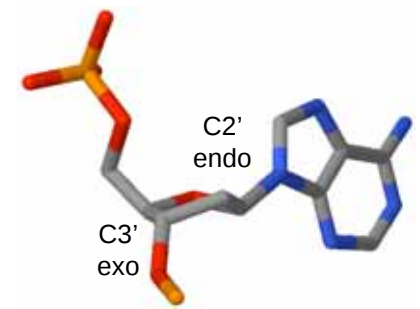
Compare



A-form (RNA)

Minor groove width = $11\text{\AA}$
Major groove width = $2.7\text{\AA}$

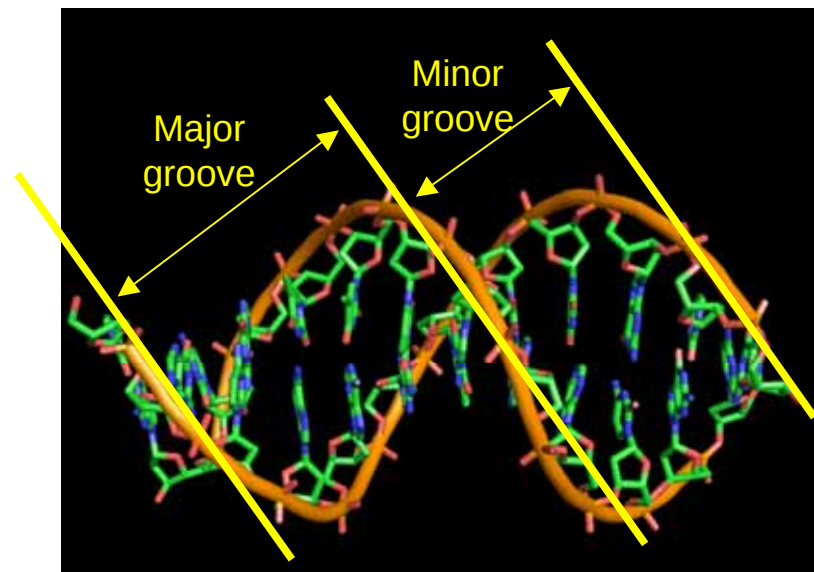
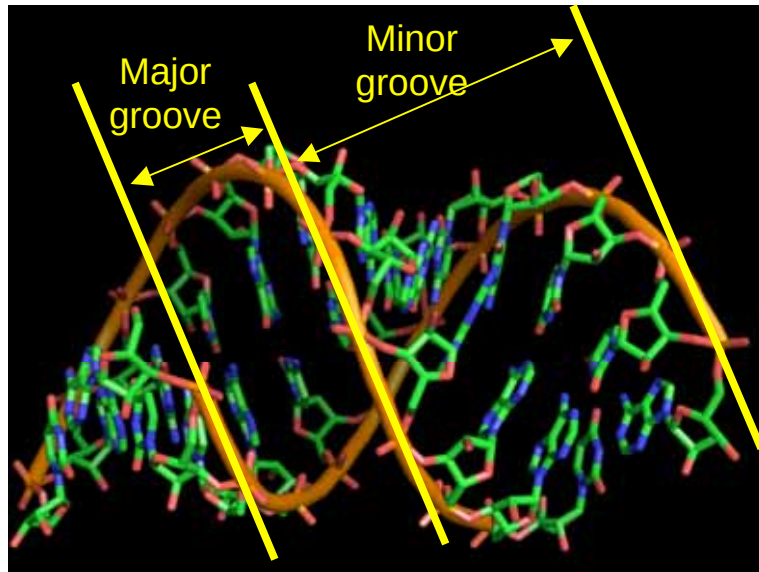
Minor groove depth = $2.8\text{\AA}$
Major groove depth = $13.5\text{\AA}$



B-form (DNA)

Minor groove width = $5.7\text{\AA}$
Major groove width = $11.7\text{\AA}$

Minor groove depth = $7.5\text{\AA}$
Major groove depth = $8.8\text{\AA}$



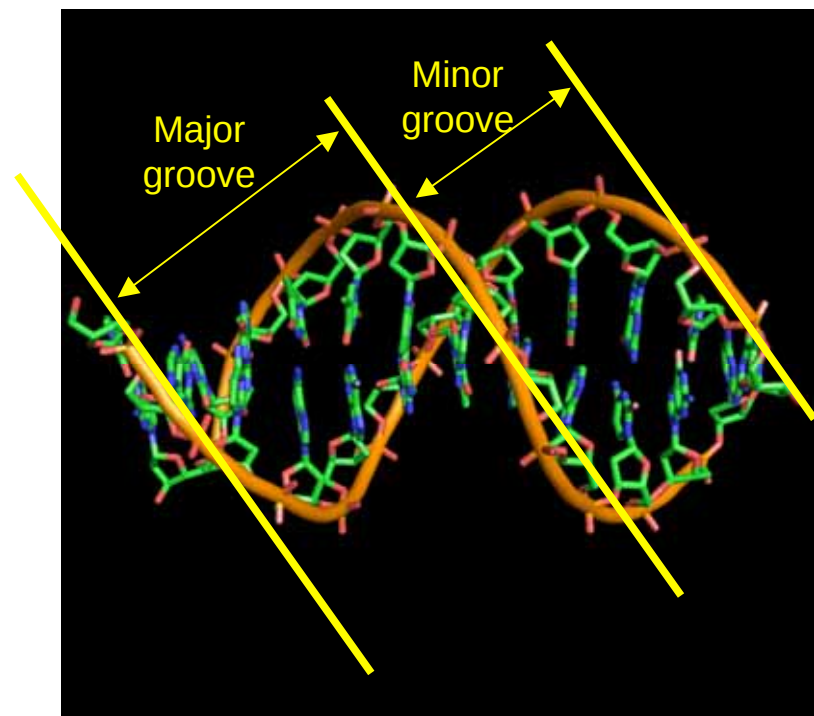
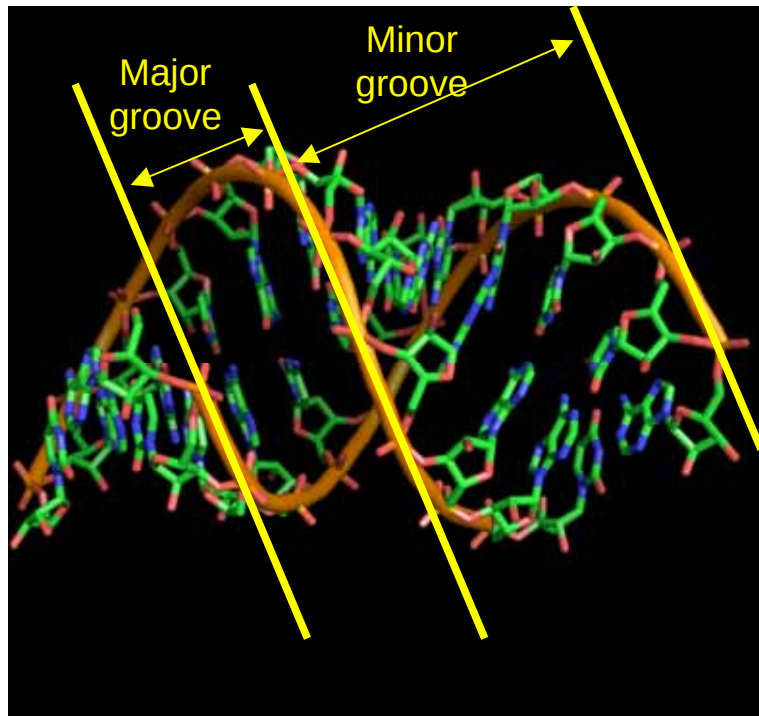
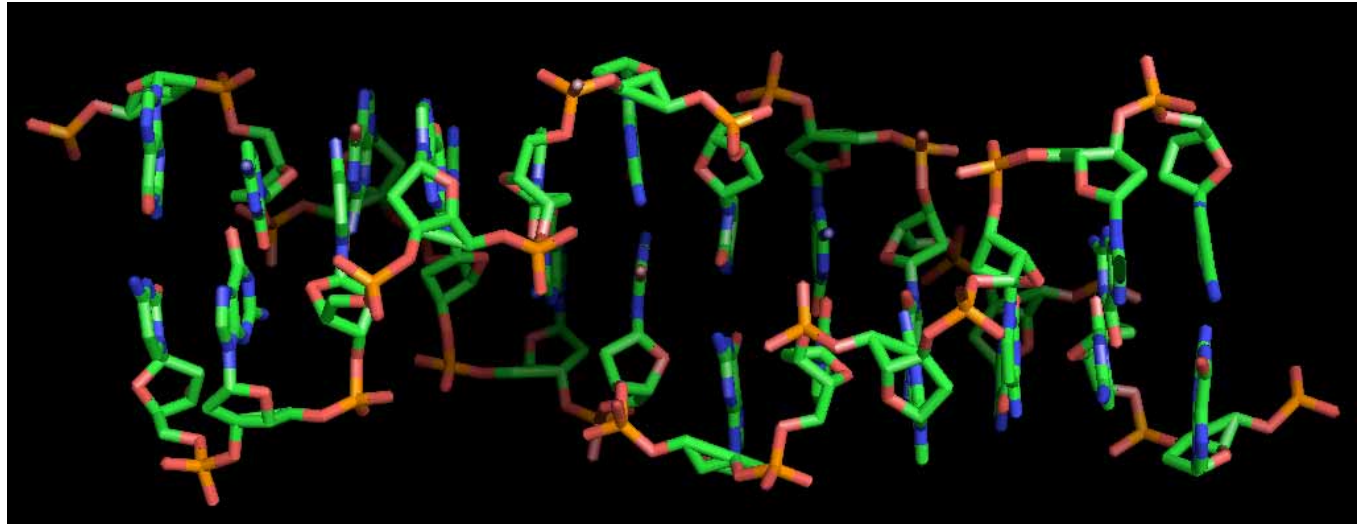
Z-DNA

Residues per turn = 12
Twist per base pair = -9° / -51°

Rise per pair = $3.7\text{\AA}$
c3'-endo(syn) / c2'-endo

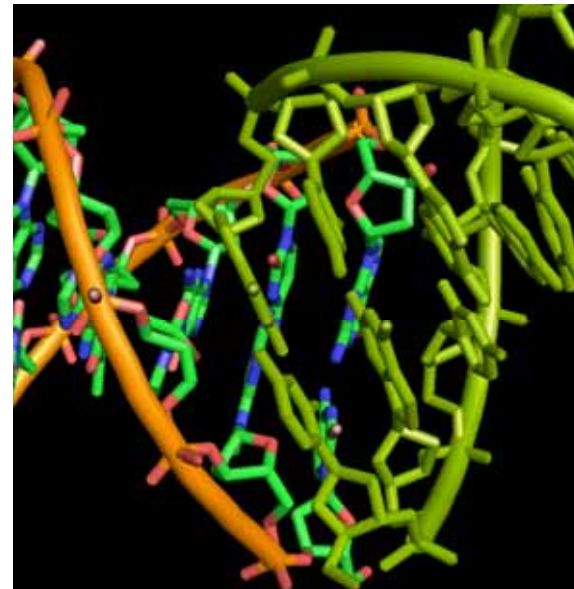
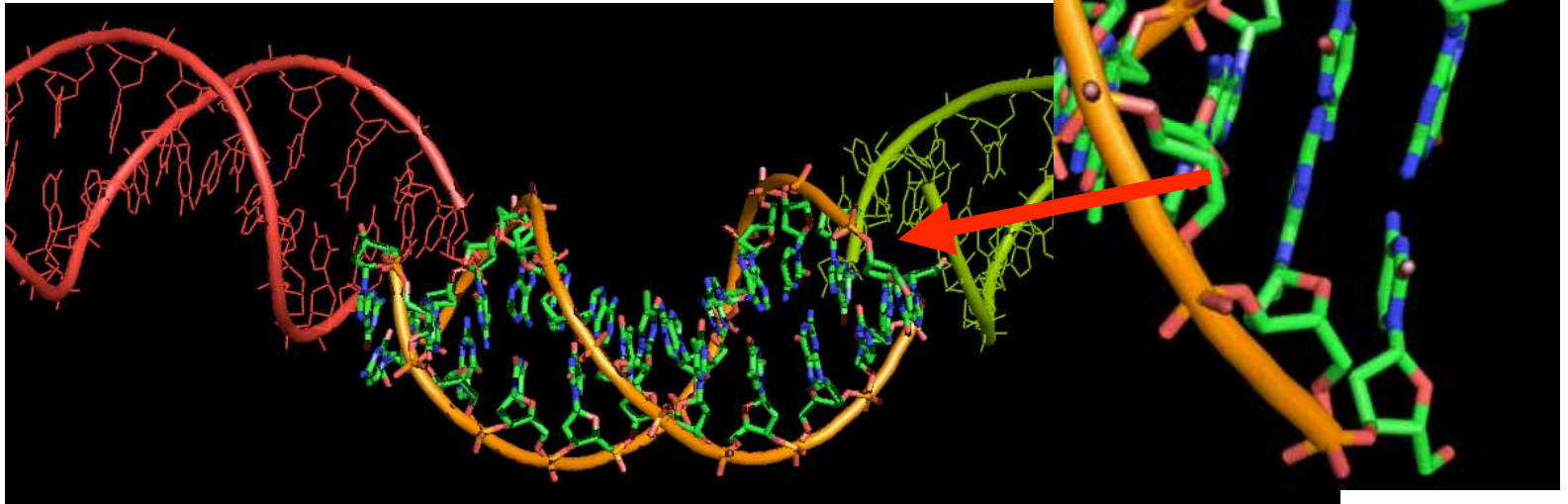
Minor groove width = $2.0\text{\AA}$
Major groove width = $8.8\text{\AA}$

Minor groove depth = $13.8\text{\AA}$
Major groove depth = $3.7\text{\AA}$

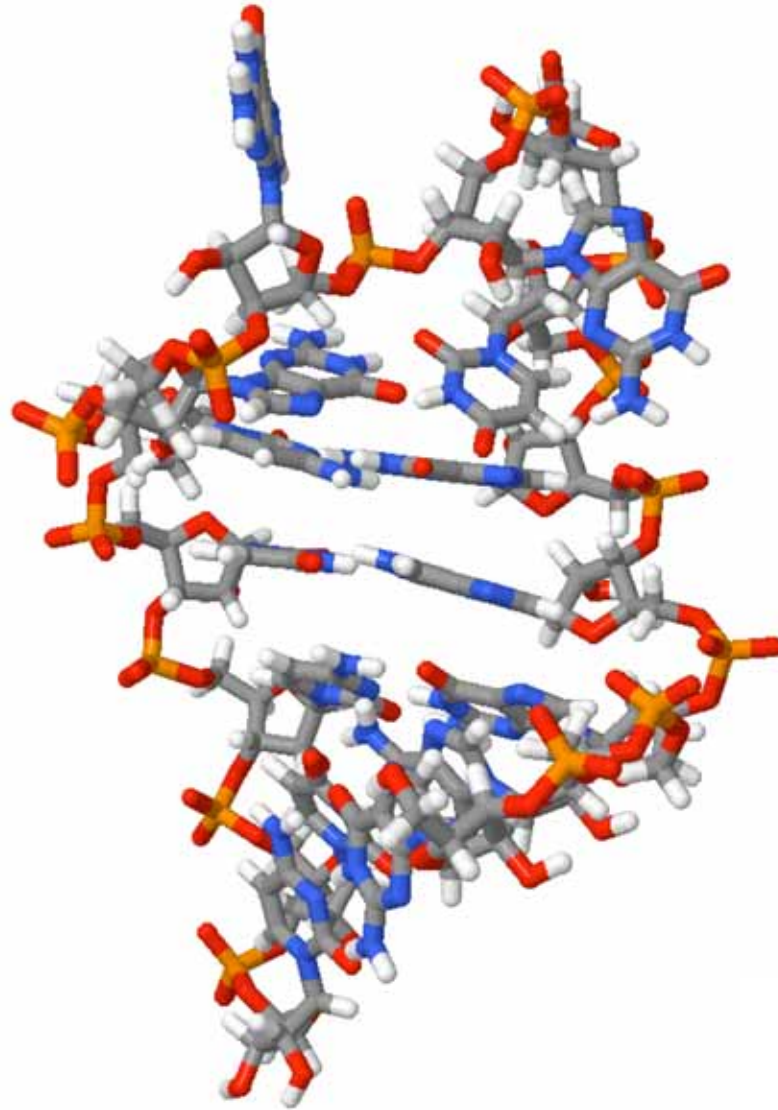
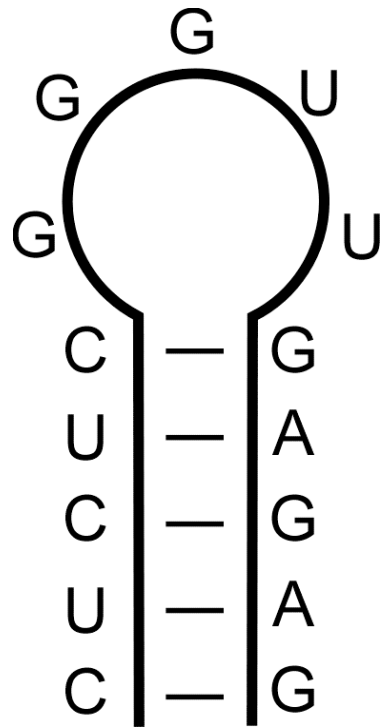


Ends of DNA duplexes

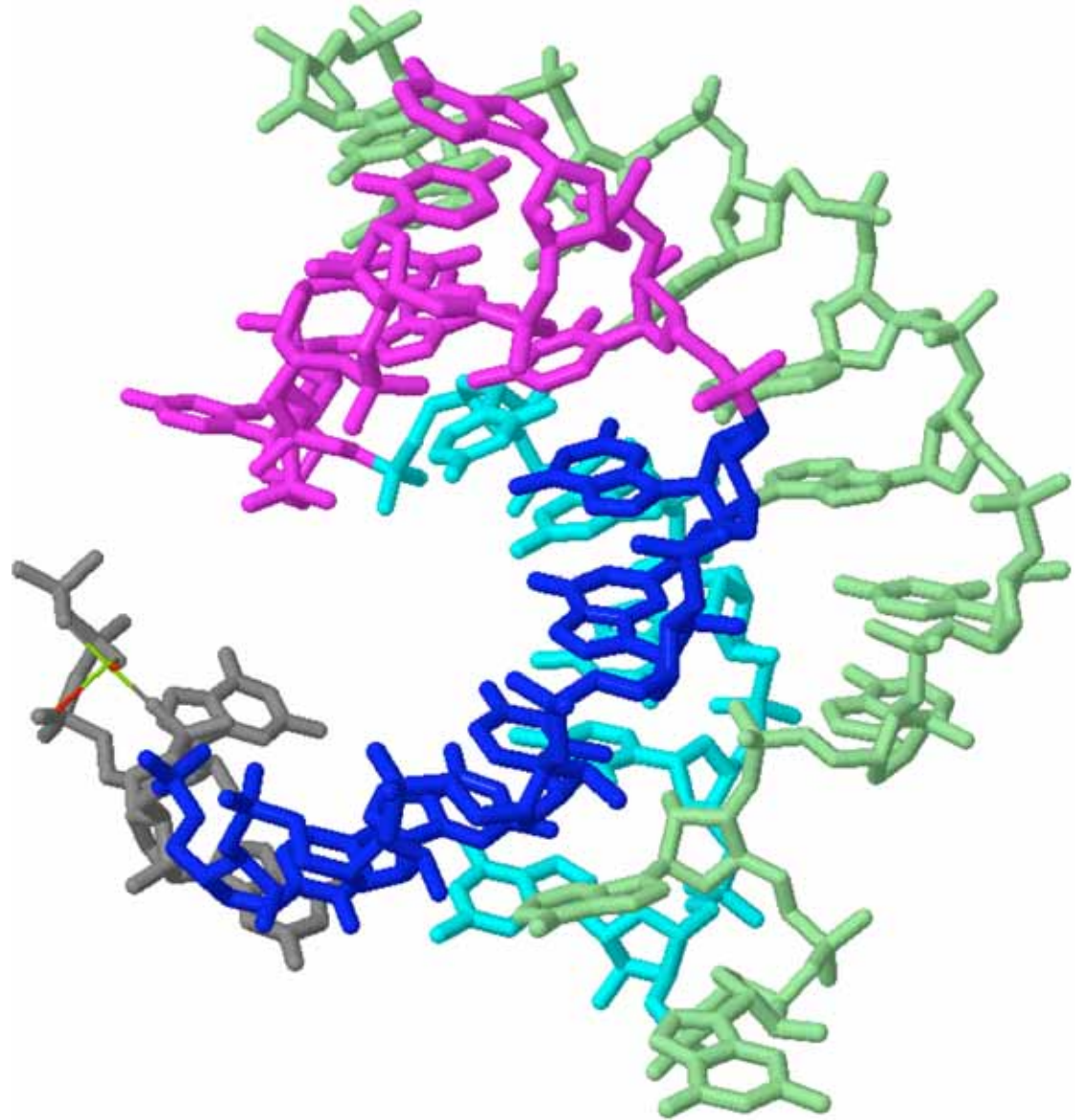
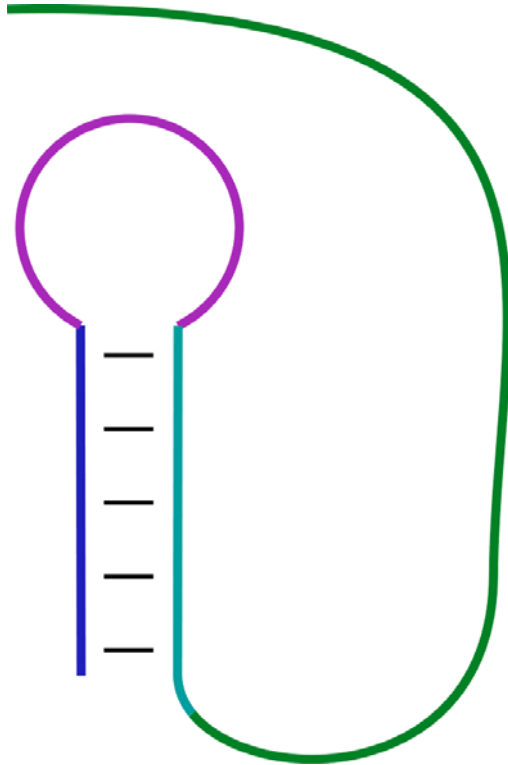
“Blunt” ends



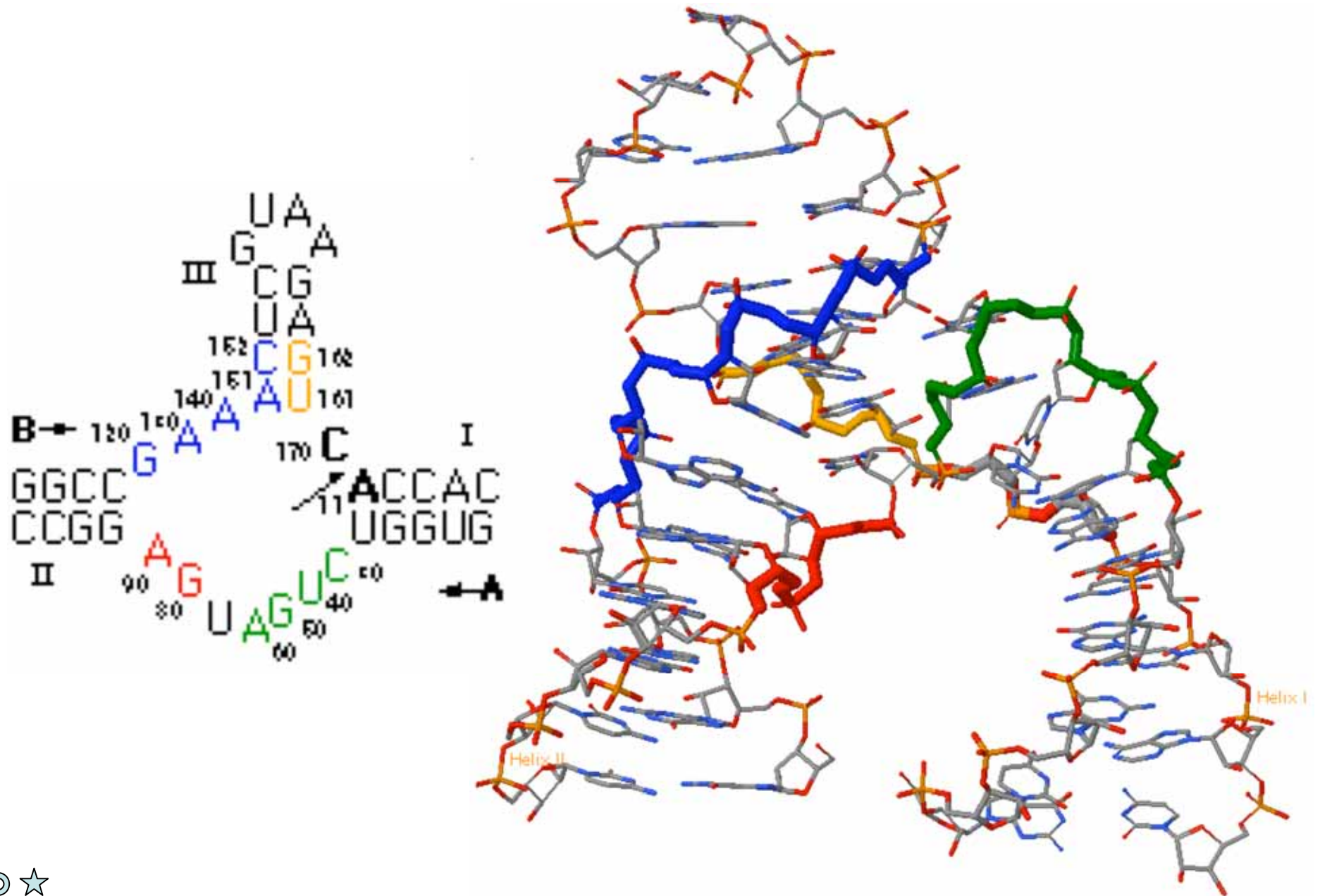
Simple Structure - Hairpin



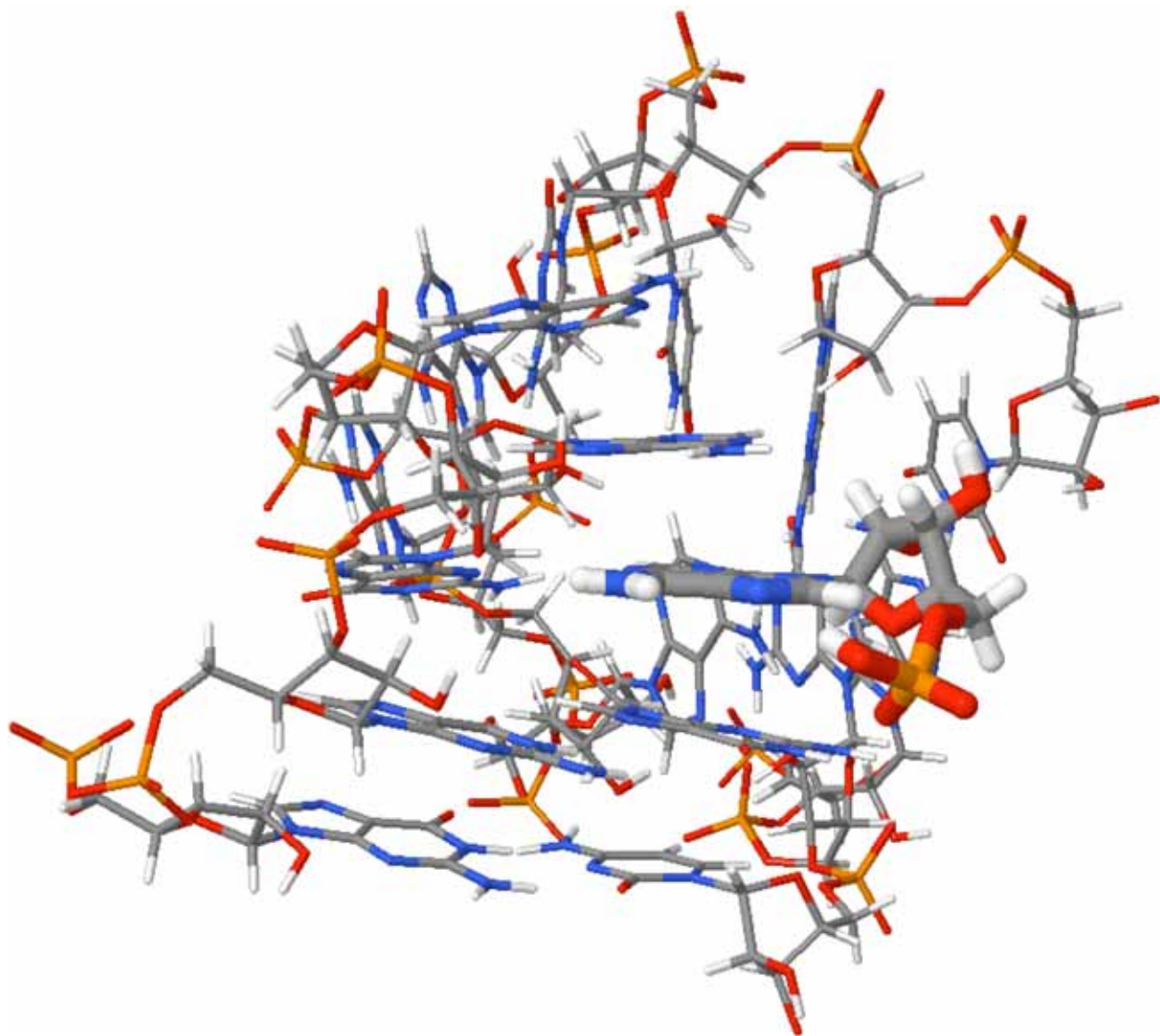
Classic Structure - Pseudoknot



Hammerhead Ribozyme

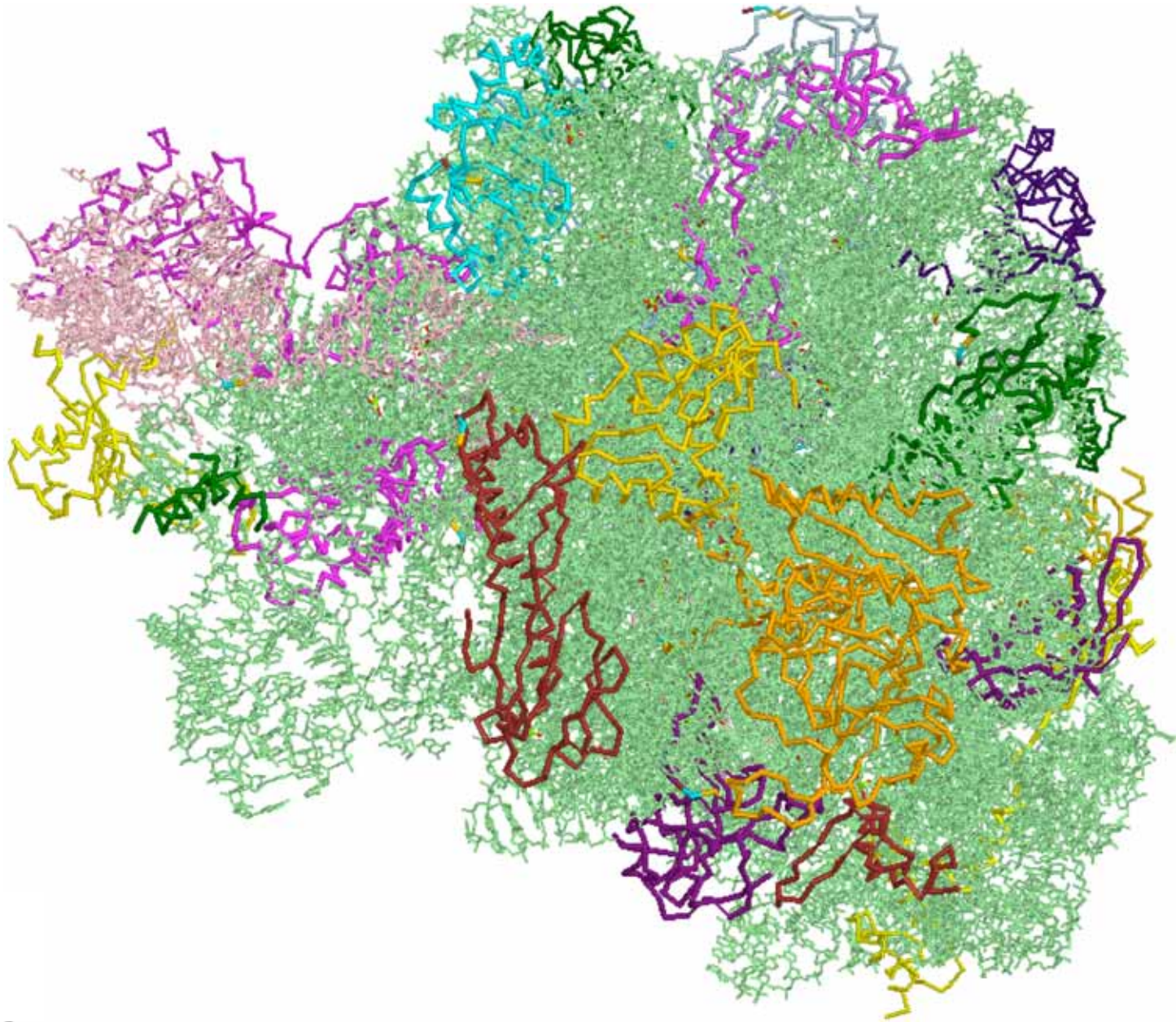


AMP Aptamer



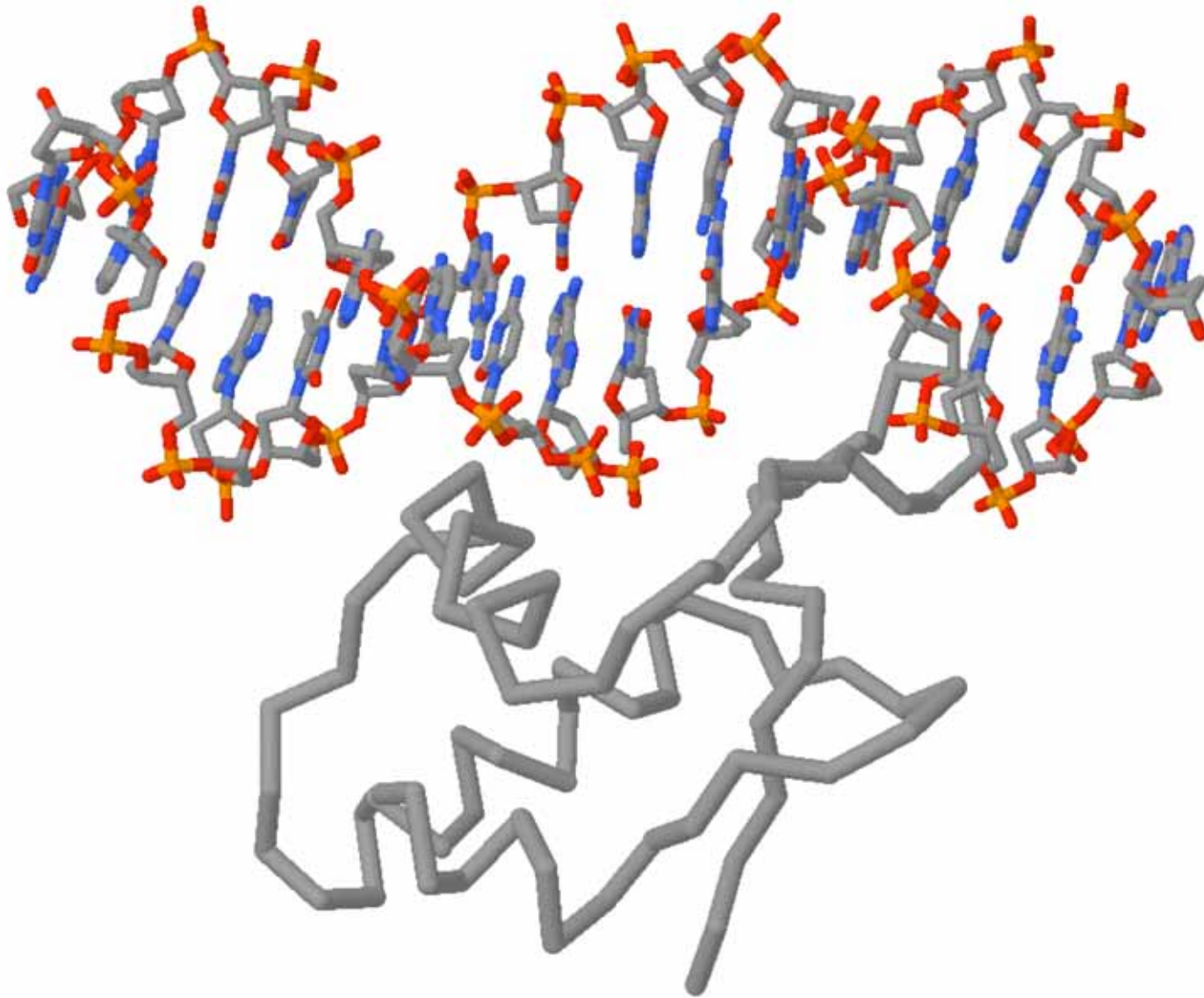
Ribosome

An RNA machine with protein cofactors



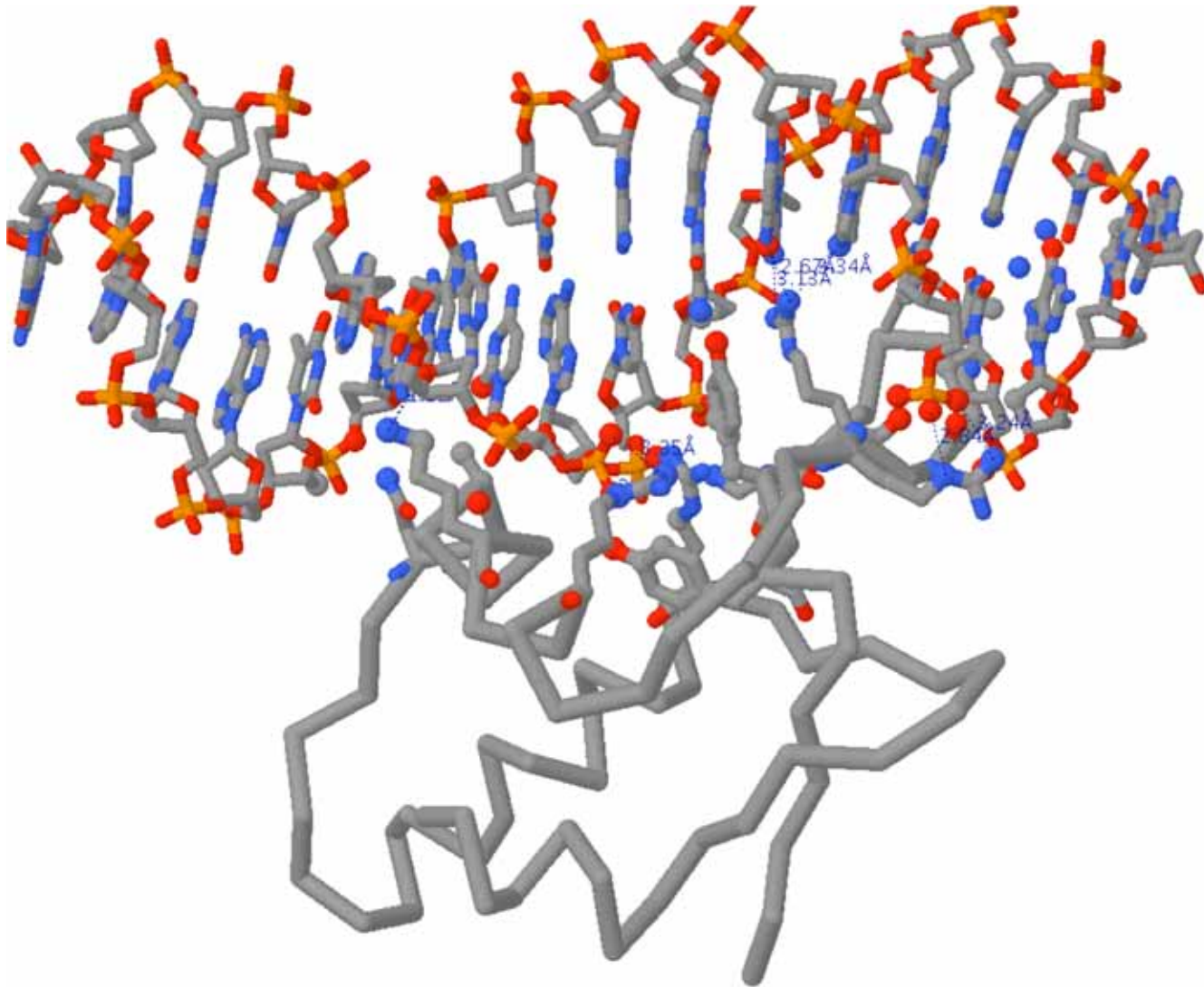
Winged Helix DNA Binding Domain

Classic helix-turn-helix



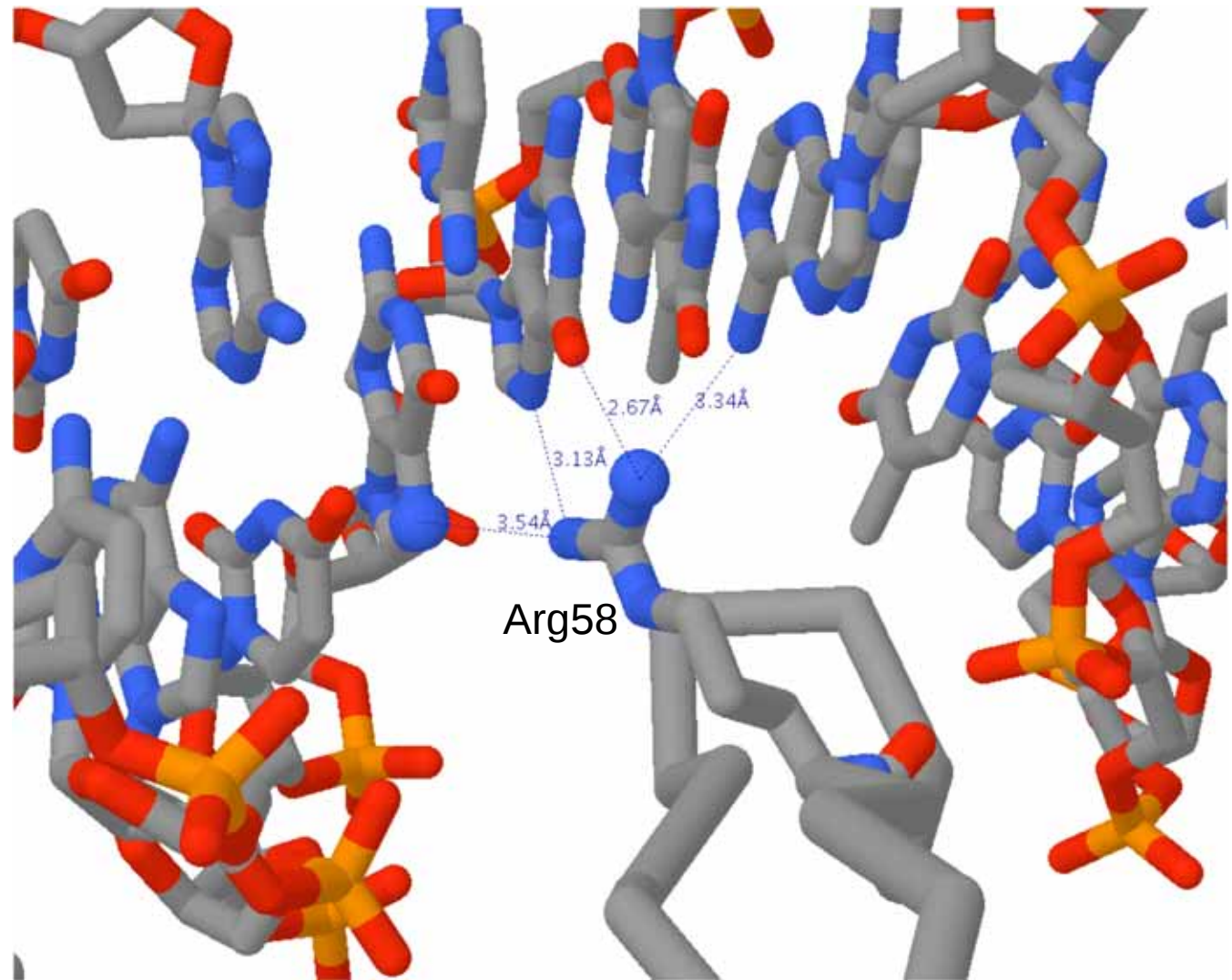
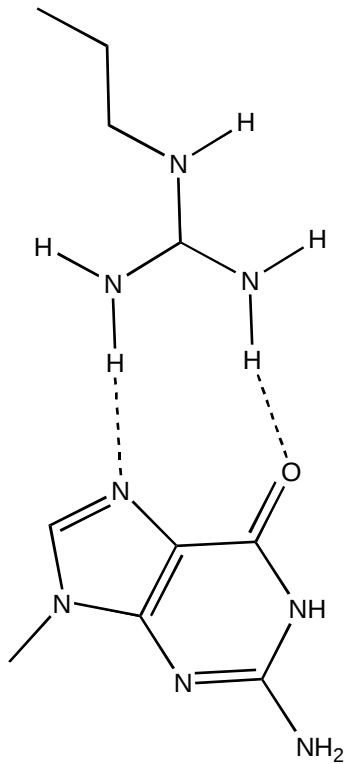
Winged Helix DNA Binding Domain

Classic helix-turn-helix



Winged Helix DNA Binding Domain

Classic helix-turn-helix



Hrfx1 bound to its X-box binding site