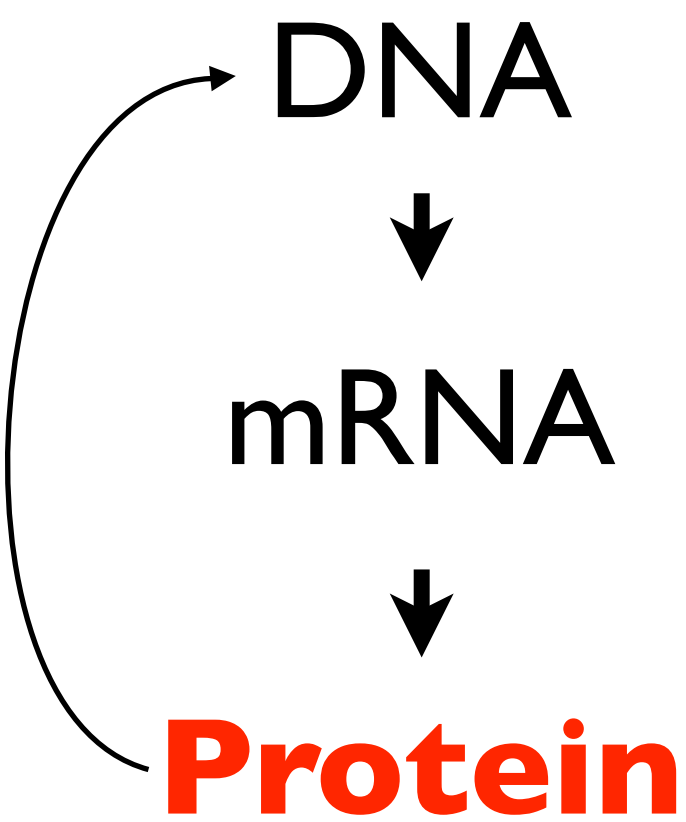
Nucleic Acids
Why do I care?

Proteins do everything, right?

revolutions at the turn of the century

opportunities for the 21st century

In the beginning…

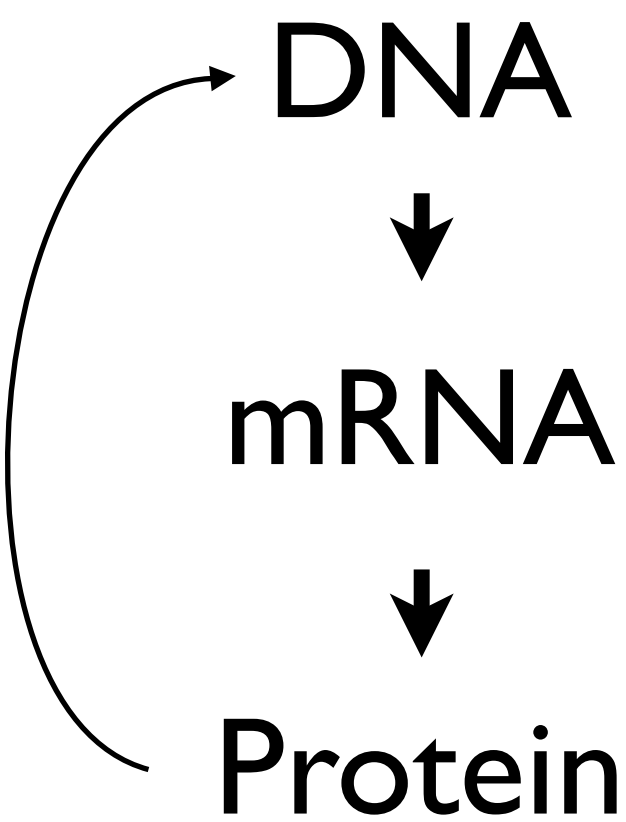


Archival information storage

Transient information storage

Catalysis, structure, regulation, et al.

Chicken & Egg?

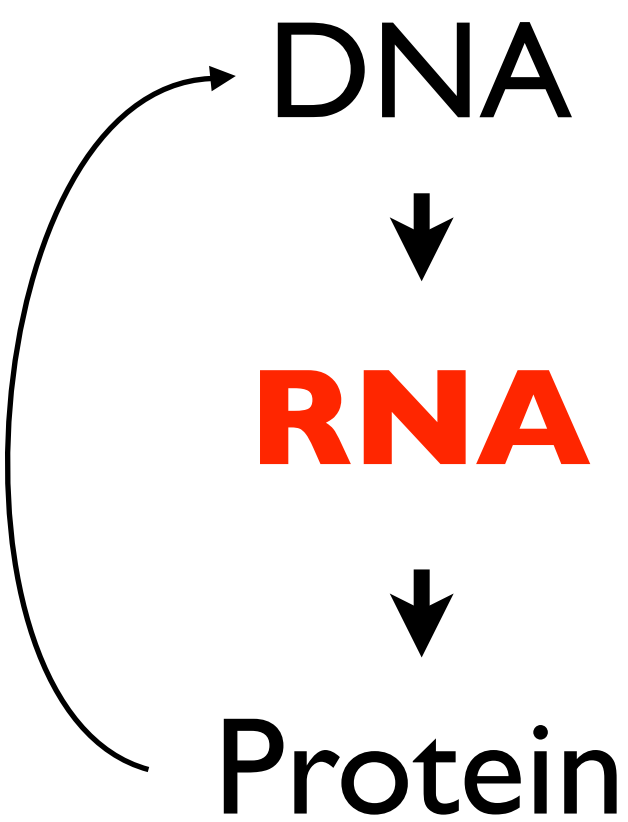


Archival information storage

Transient information storage

Catalysis, structure, regulation, et al.

RNA can do everything



Archival information storage

Transient information storage
Catalysis!

1980-2000

Catalysis, structure, regulation, et al.

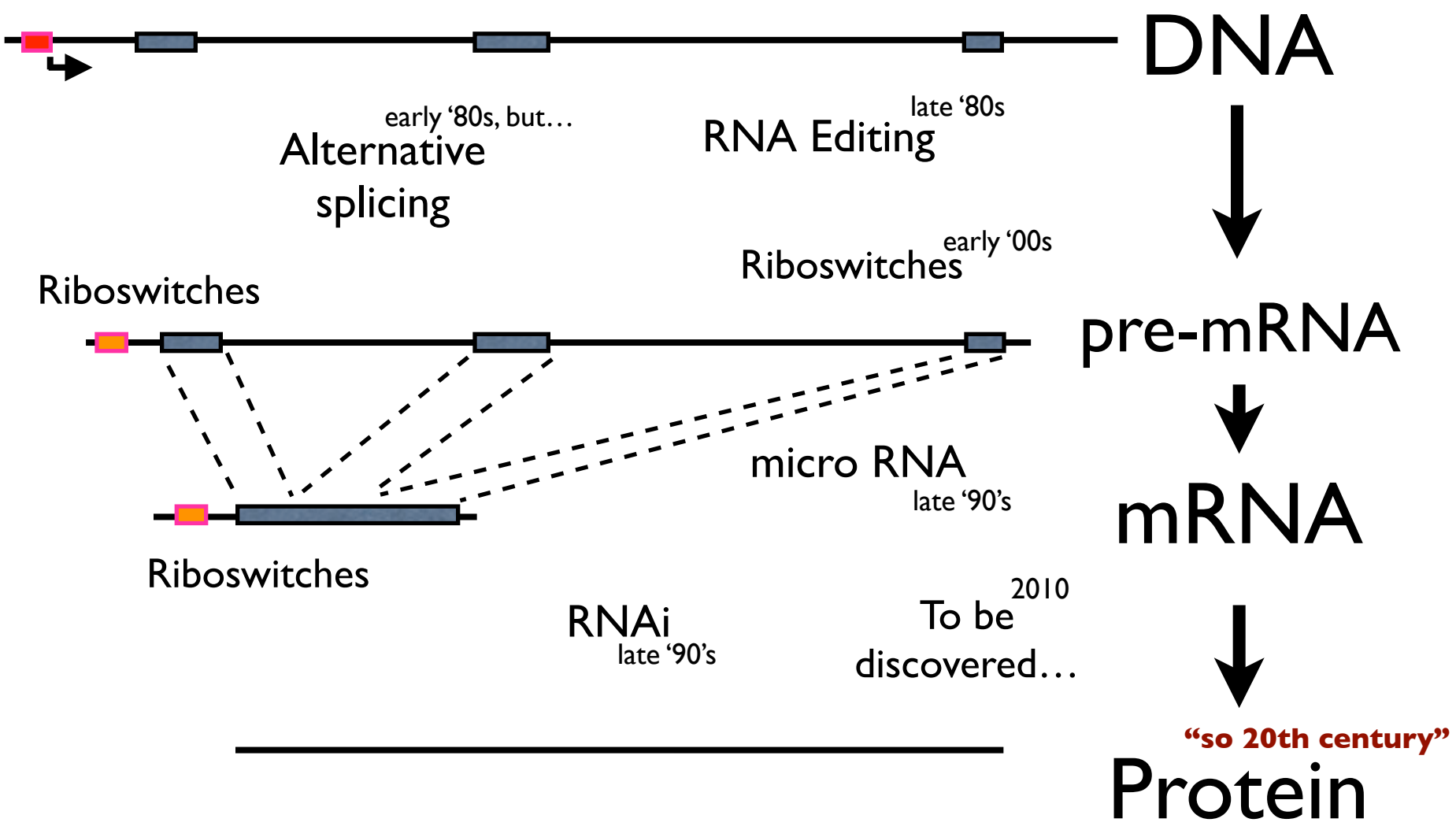
Project Encode (2007)

(More) rewriting of textbooks

June 2007, published in Nature

- Some regions of DNA far from protein-coding genes (extreme "junk?") are nevertheless highly conserved
- Most of both strands of the DNA is transcribed (far beyond that required for protein-coding genes)

21st Century Opportunities



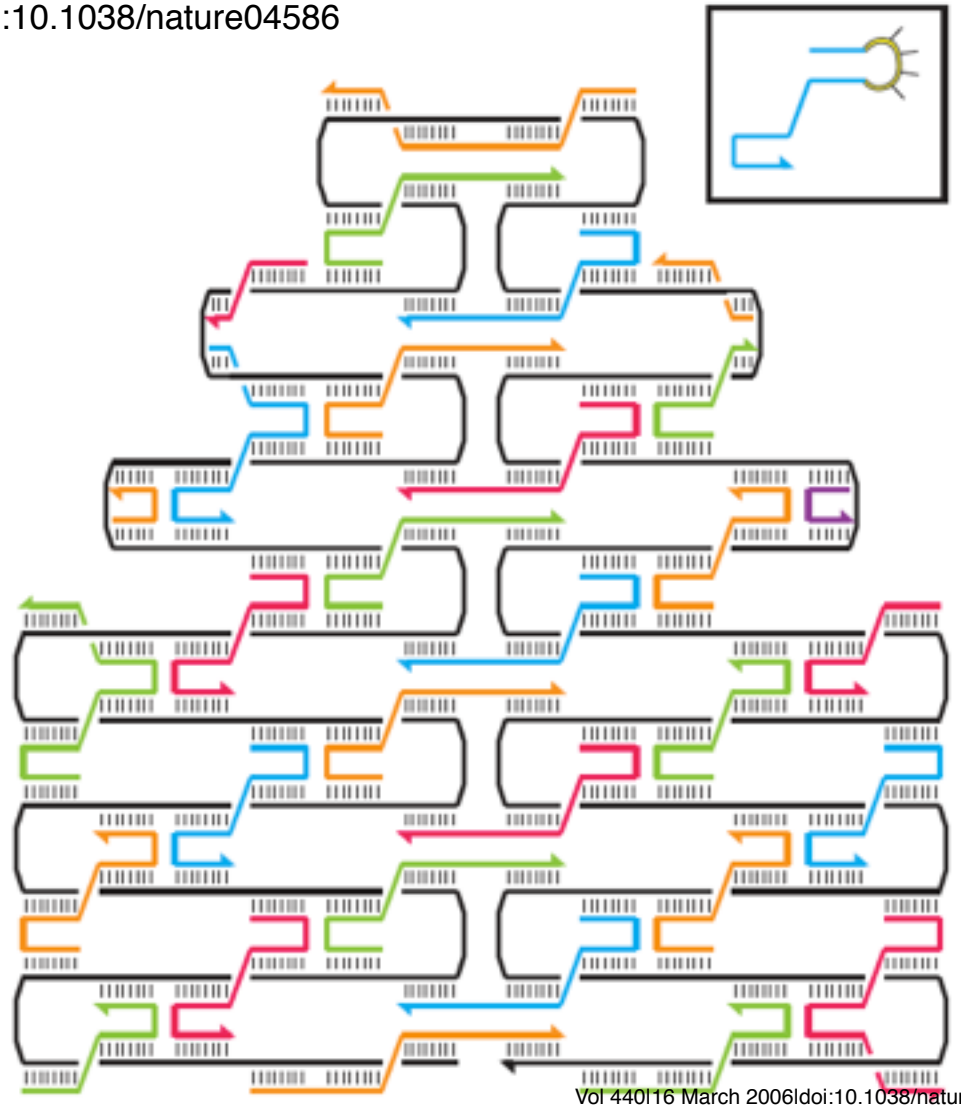
DNA(RNA) Nanotechnology

Folding DNA to create nanoscale shapes & patterns

Paul W. K. Rothemund Nature Vol 440l16 March 2006ldoi:10.1038/nature04586

Start with long single stranded DNA (black line)

Then add a large number of carefully designed short, complementary oligos (staples) to "stitch" the DNA into a more compact (and well-defined) structure



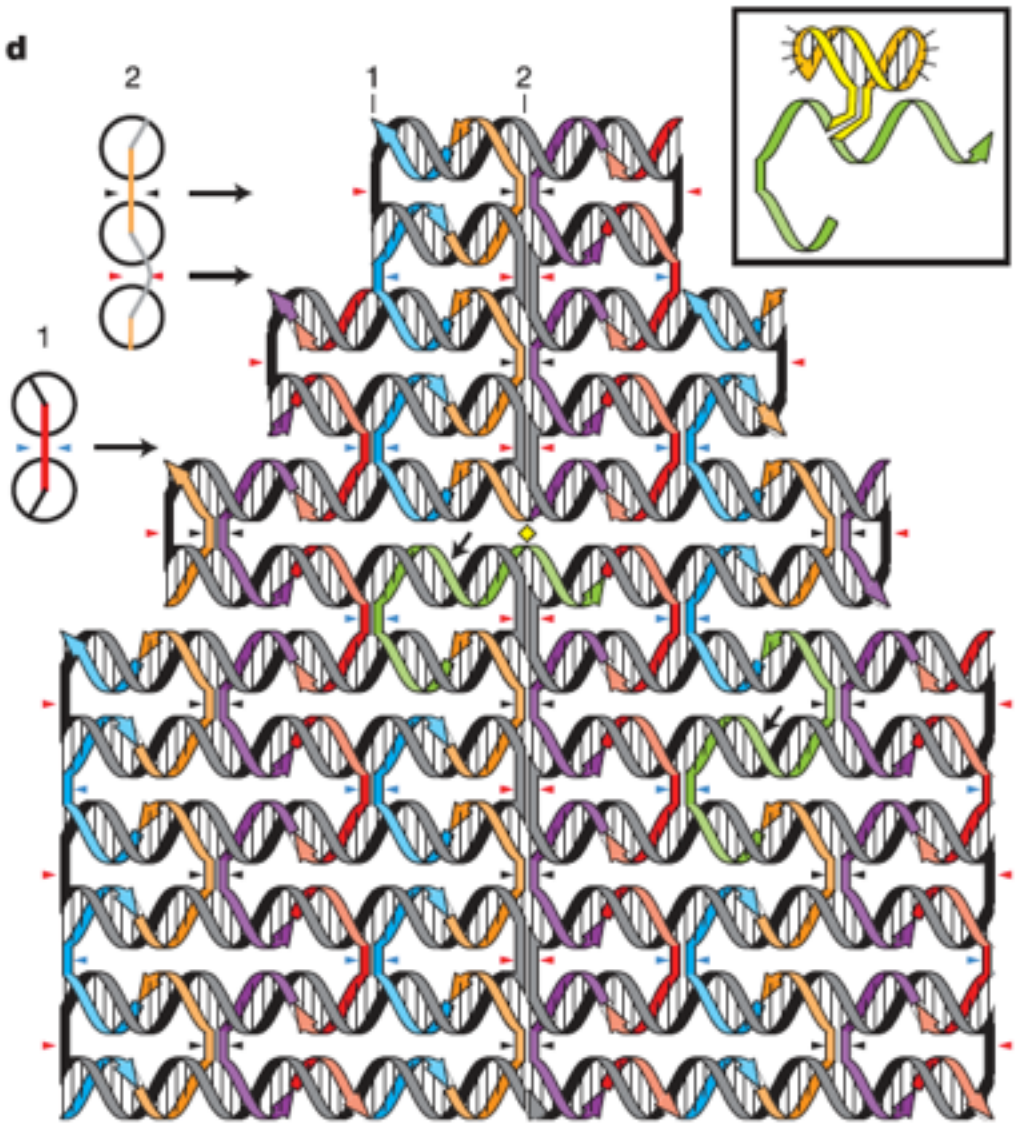
Vol 440l16 March 2006ldoi:10.1038/nature04

DNA(RNA) Nanotechnology

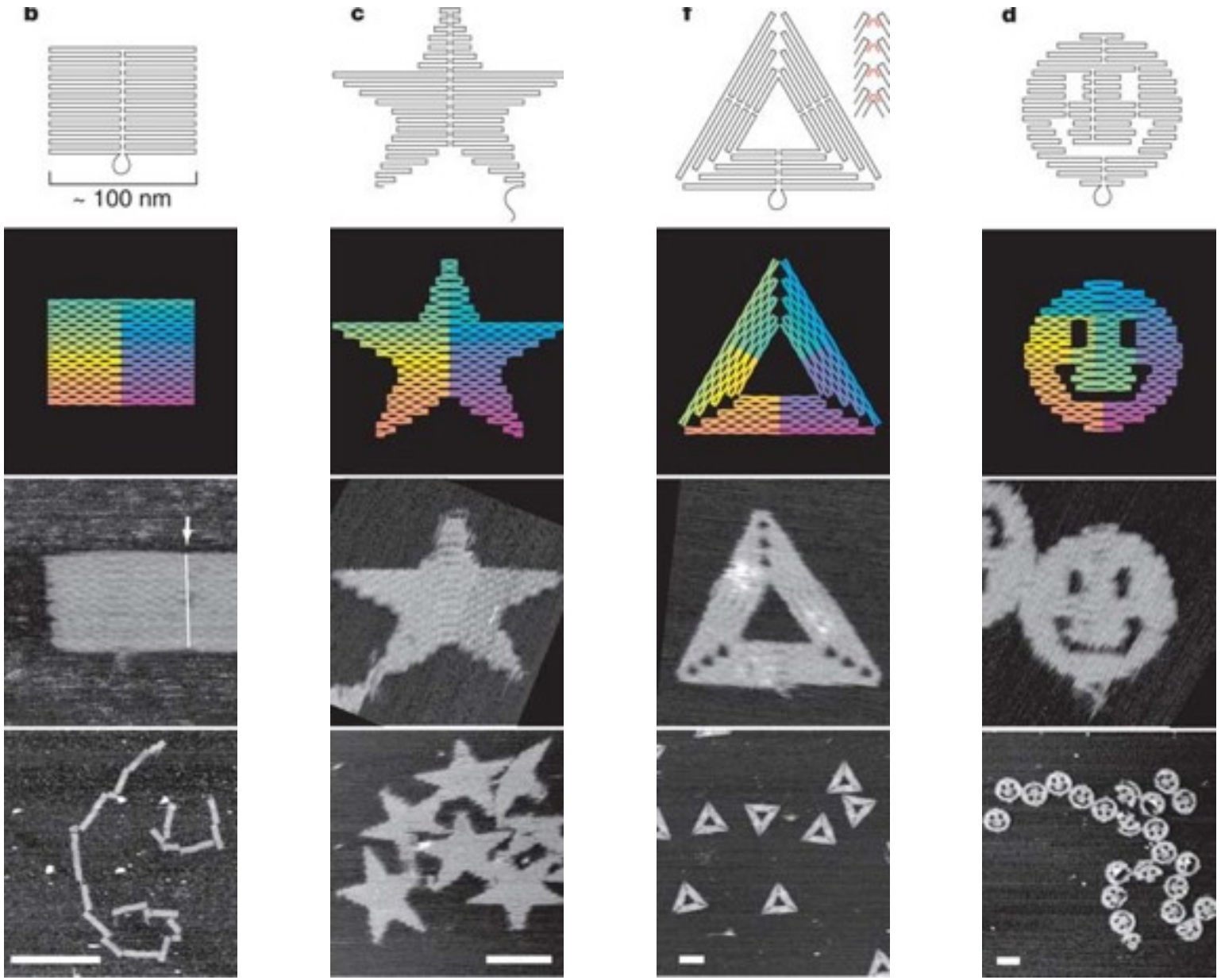
Start with long single stranded DNA (black line)

Then add a large number of carefully designed short, complementary oligos (staples) to "stitch" the DNA into a more compact (and well-defined) structure

Pay careful attention to the DNA helical phasing



DNA(RNA) Nanotechnology



DNA(RNA) Nanotechnology

NANO LETTERS

Letter

pubs.acs.org/NanoLett

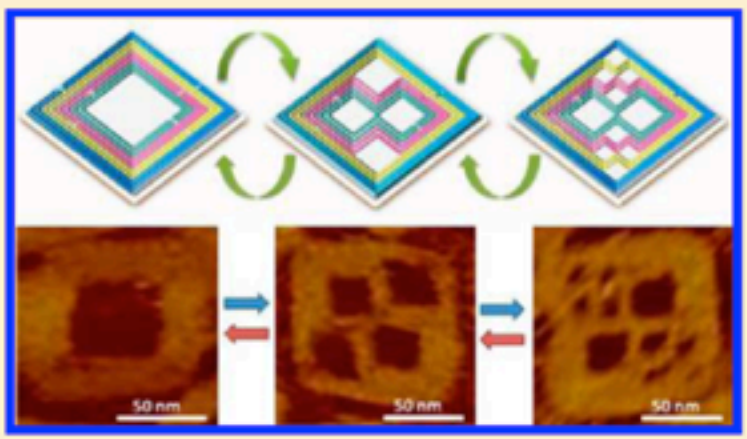
Reconfigurable DNA Origami to Generate Quasifractal Patterns

Fei Zhang,[†] Jeanette Nangreave,[†] Yan Liu,*[,‡] and Hao Yan*[,†]

[†]Department of Chemistry and Biochemistry and [‡]The Biodesign Institute, Arizona State University, Tempe, Arizona 85287, United States

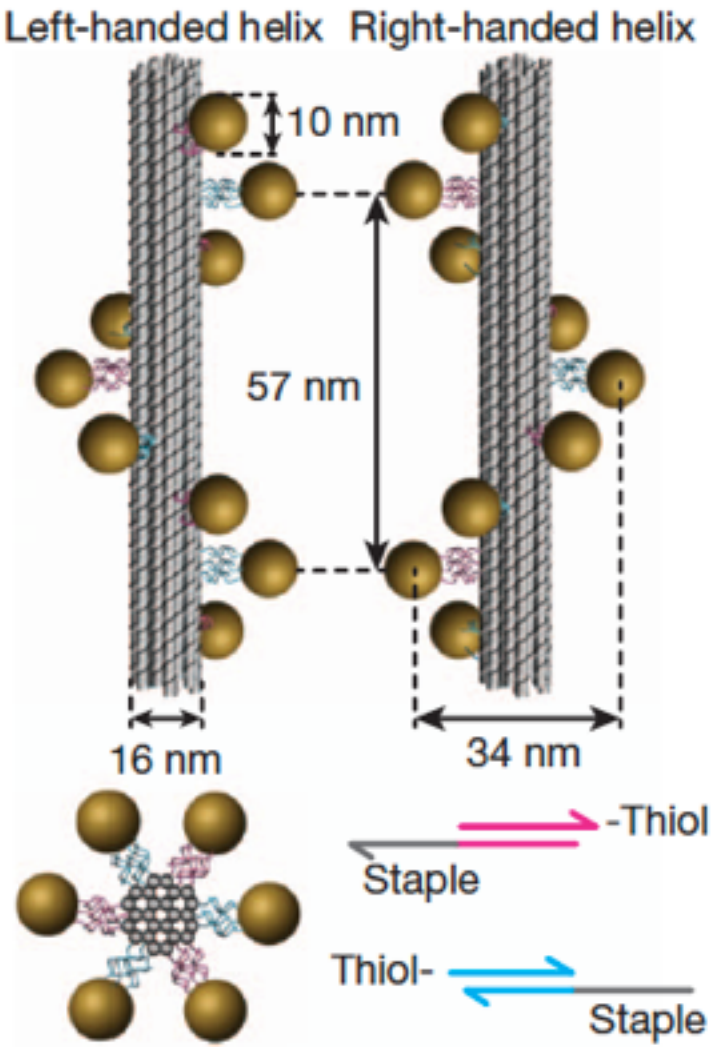
Supporting Information

ABSTRACT: The specificity of Watson–Crick base pairing, unique mechanical properties of DNA, and intrinsic stability of DNA double helices makes DNA an ideal material for the construction of dynamic nanodevices. Rationally designed strand displacement reactions can be used to produce dynamic reconfiguration of DNA nanostructures postassembly. Here we describe a 'fold–release–fold' strategy of multiple strand displacement and hybridization reactions to reconfigure a simple DNA origami structure into a complex, quasifractal pattern, demonstrating a complex transformation of DNA nanoarchitectures.



KEYWORDS: *Dynamic DNA nanotechnology, strand displacement, reconfiguration, fractal*

DNA(RNA) Nanotechnology

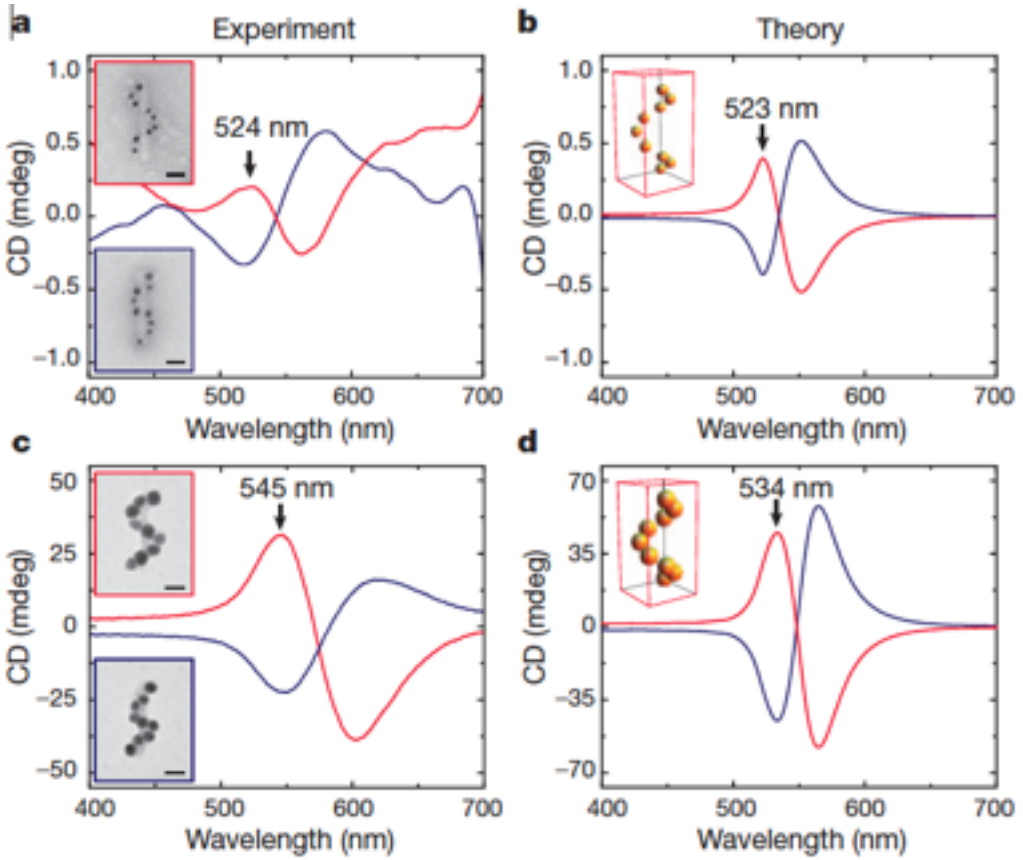


LETTER

doi:10.1038/nature10889

DNA-based self-assembly of chiral plasmonic nanostructures with tailored optical response

Anton Kuzyk[1]*†, Robert Schreiber[2]*, Zhiyuan Fan[3], Günther Pardatscher[1], Eva-Maria Roller[2], Alexander Högele[2], Friedrich C. Simmel[1], Alexander O. Govorov[3] & Tim Liedl[2]



DNA(RNA) Nanotechnology

nature Vol 465|13 May 2010|doi:10.1038/nature09012

LETTERS

Molecular robots guided by prescriptive landscapes

Kyle Lund[1,2], Anthony J. Manzo[3], Nadine Dabby[4], Nicole Michelotti[3,5], Alexander Johnson-Buck[3], Jeanette Nangreave[1,2], Steven Taylor[6], Renjun Pei[6], Milan N. Stojanovic[6,7], Nils G. Walter[3], Erik Winfree[4,8,9] & Hao Yan[1,2]

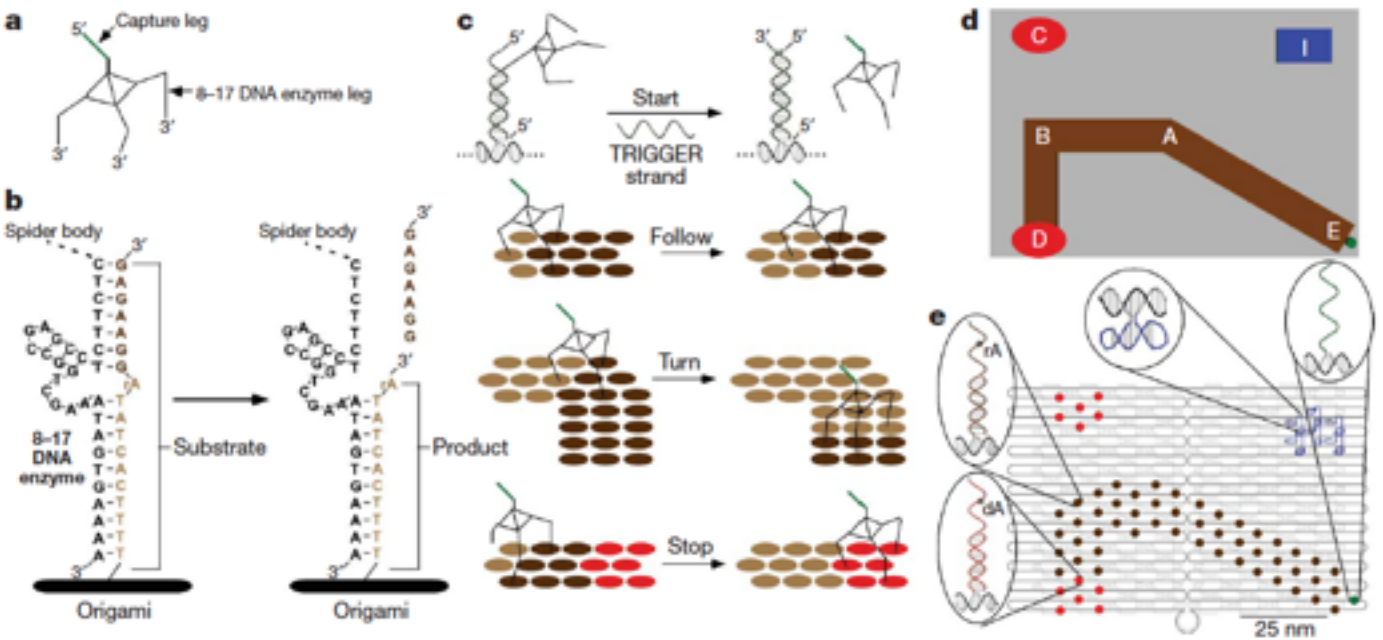
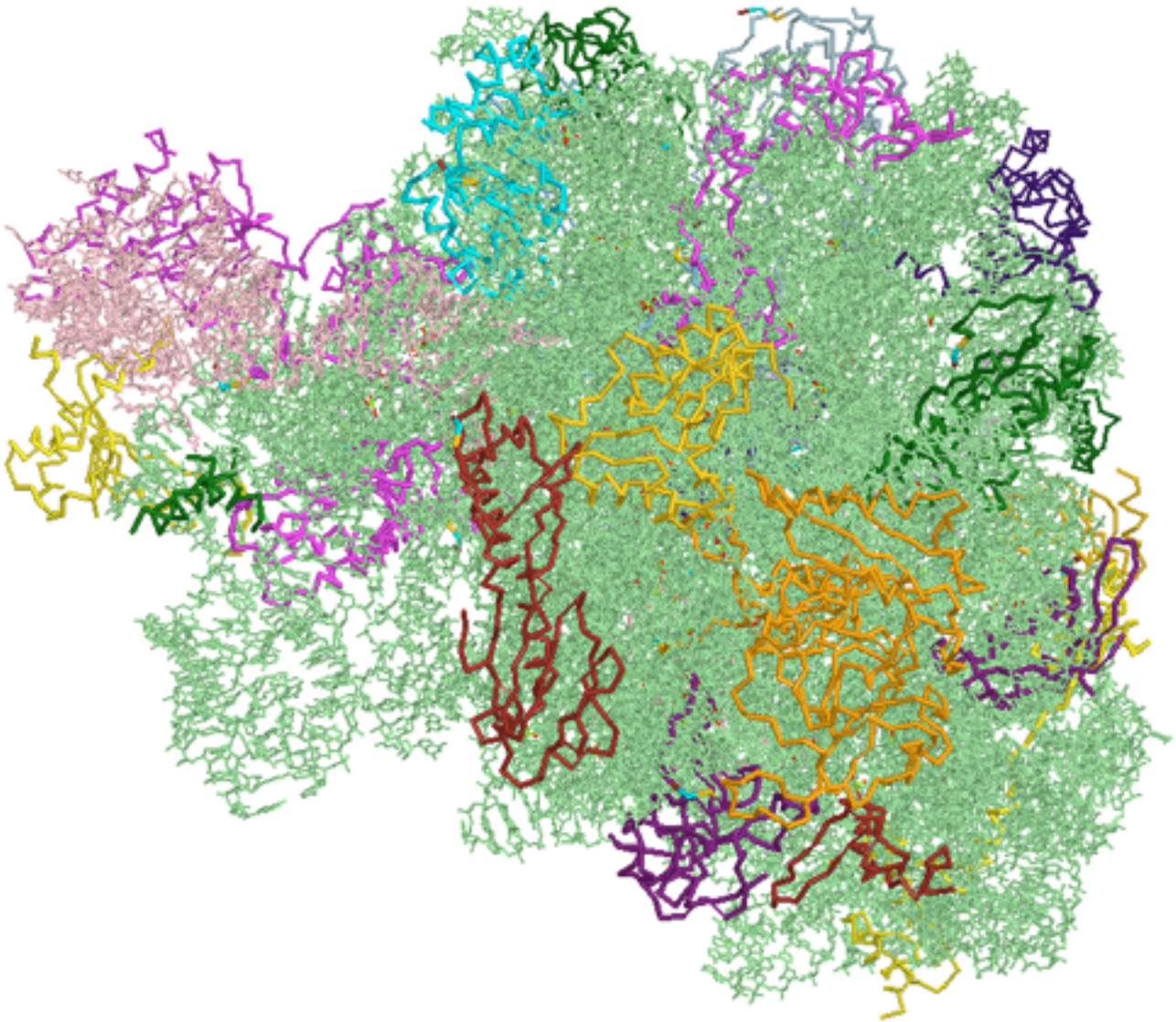


Figure 1 | Deoxyribozyme-based molecular walker and origami prescriptive landscape. **a**, The NICK3.4A$_{3+1}$ spider consists of a substrate track, turns and continues to a STOP site (red). **d**, Schematic of the DNA origami landscape with positions A–E labelled; track EABD is shown

DNA(RNA) Nanobiotechnology

Ribosome

An RNA machine with protein cofactors



What stabilizes protein structures?

What *directs* protein structures?

The DNA Duplex

What stabilizes the duplex?

What *directs* duplex structure?

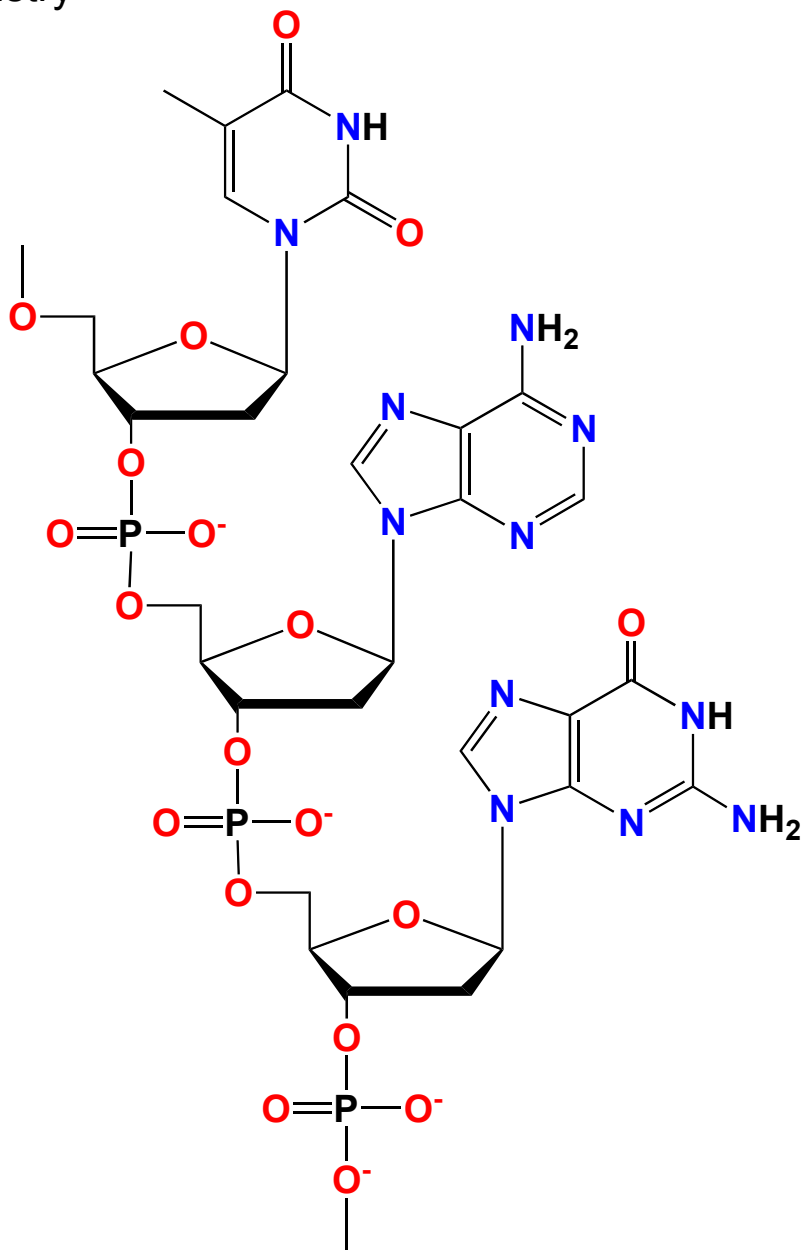
Which is most stable?

```
5′-ACCGCCGACGT-3′
3′-TGGCGGCTGCA-5′
```

```
5′-ACCGCCGACGT-3′
3′-AGGCGGCTGCC-5′
```

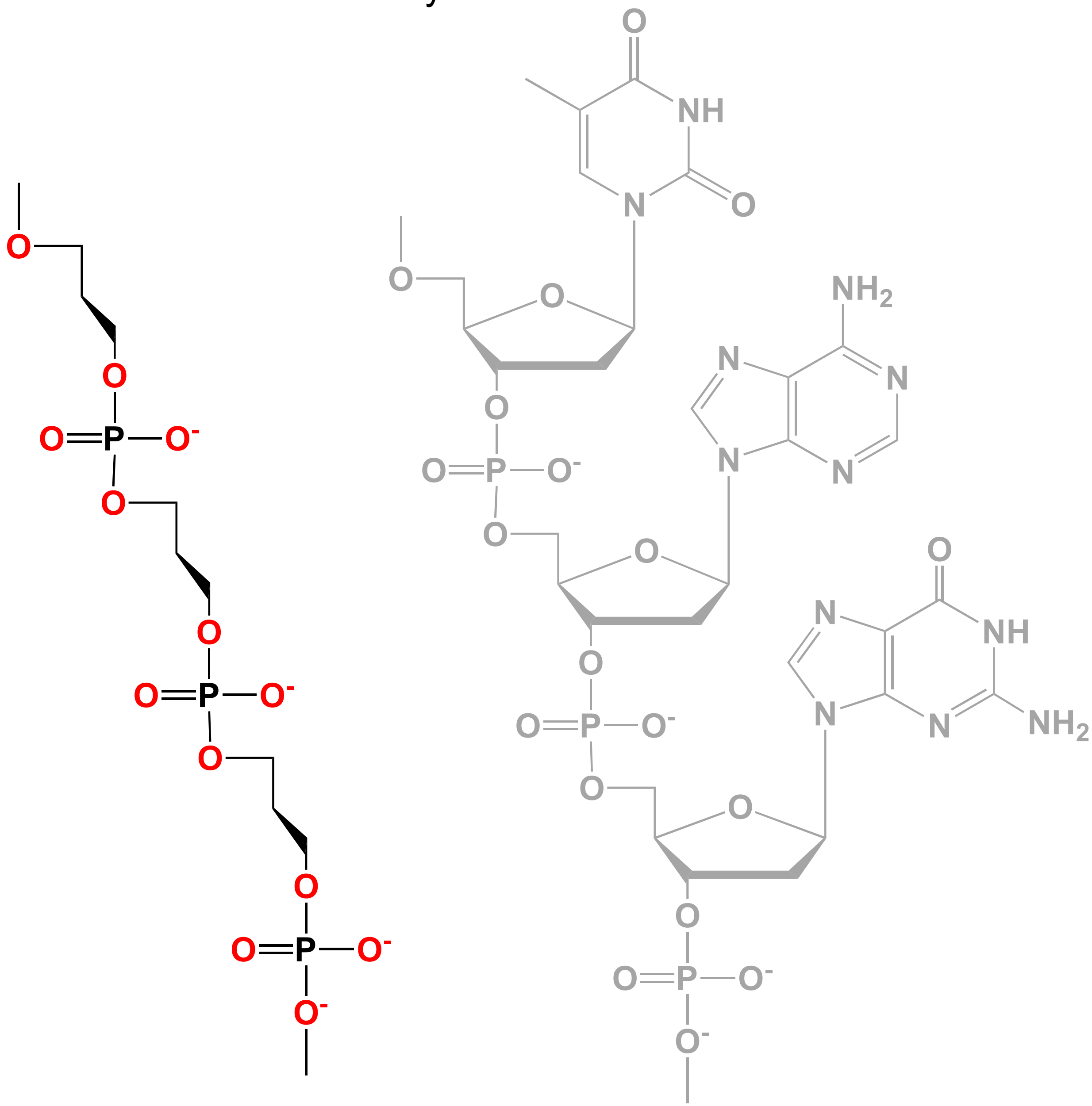
DNA

A look at the Chemistry



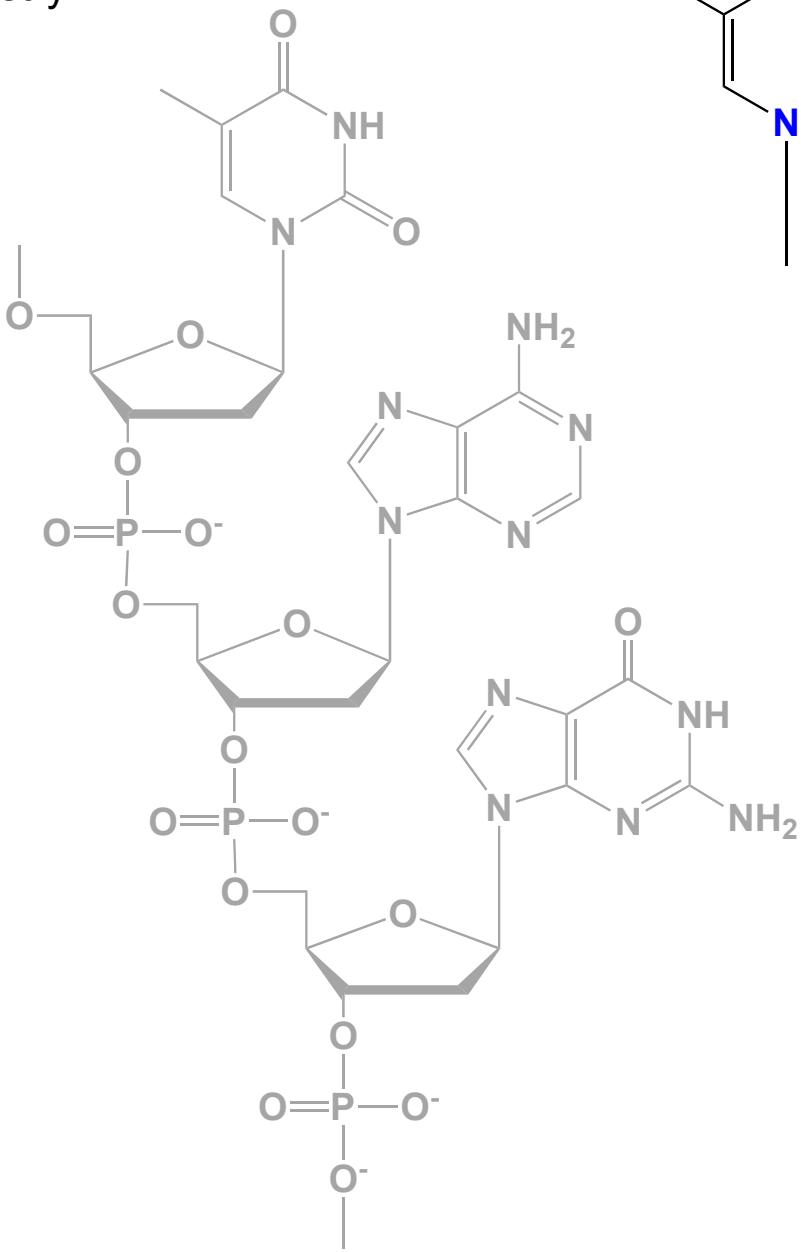
DNA

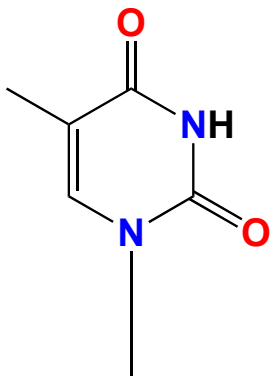
A look at the Chemistry

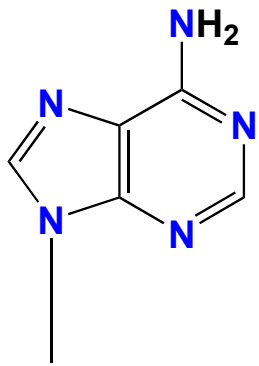


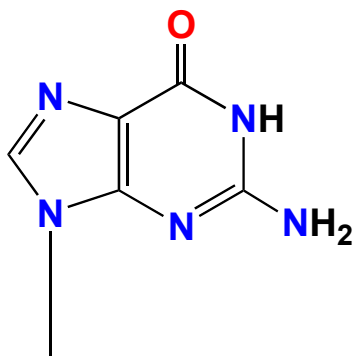
DNA

A look at the Chemistry



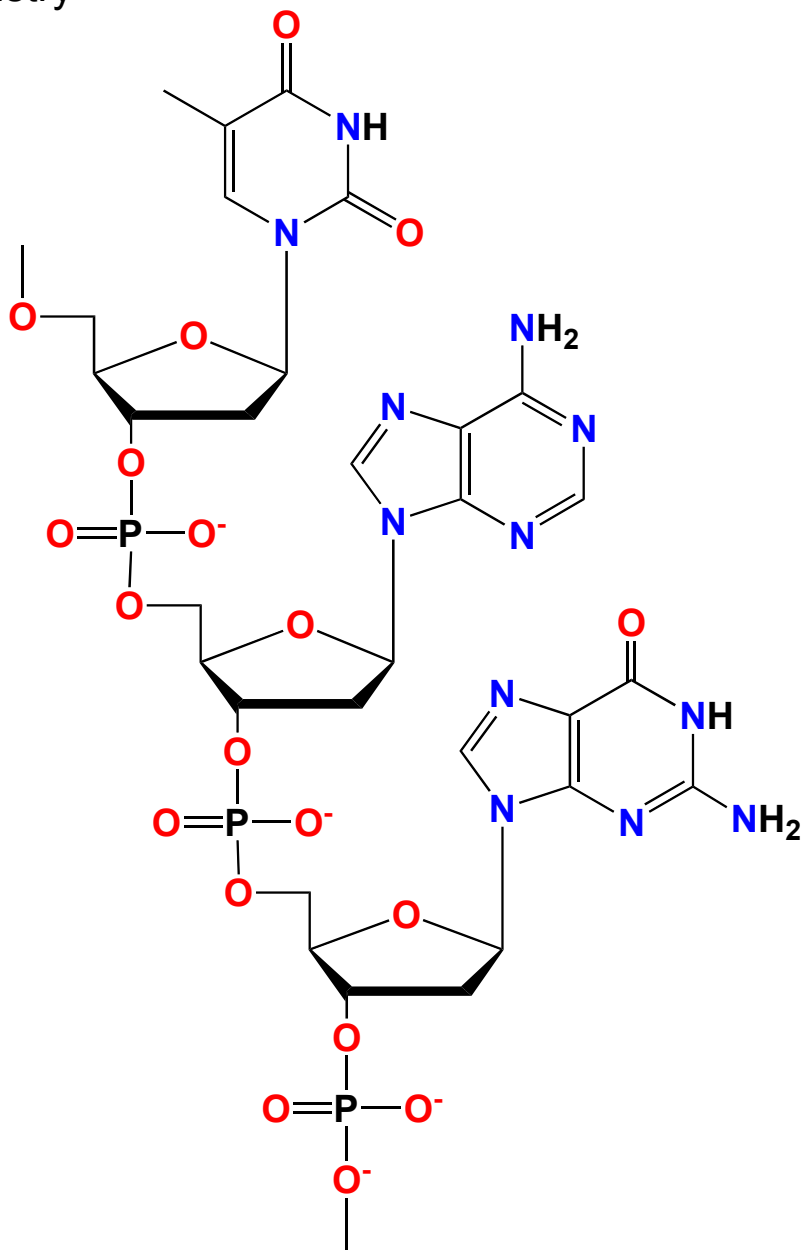






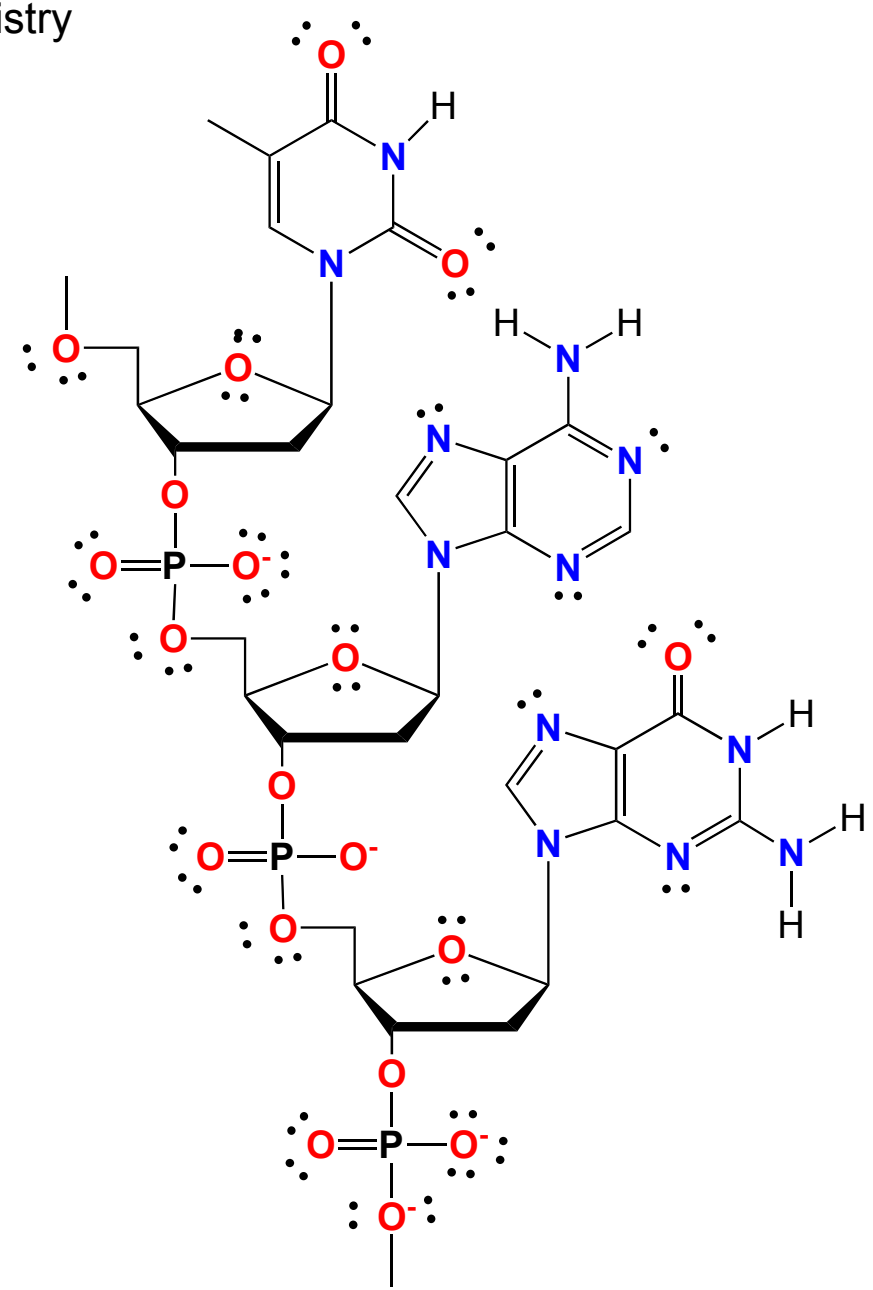
DNA

A look at the Chemistry



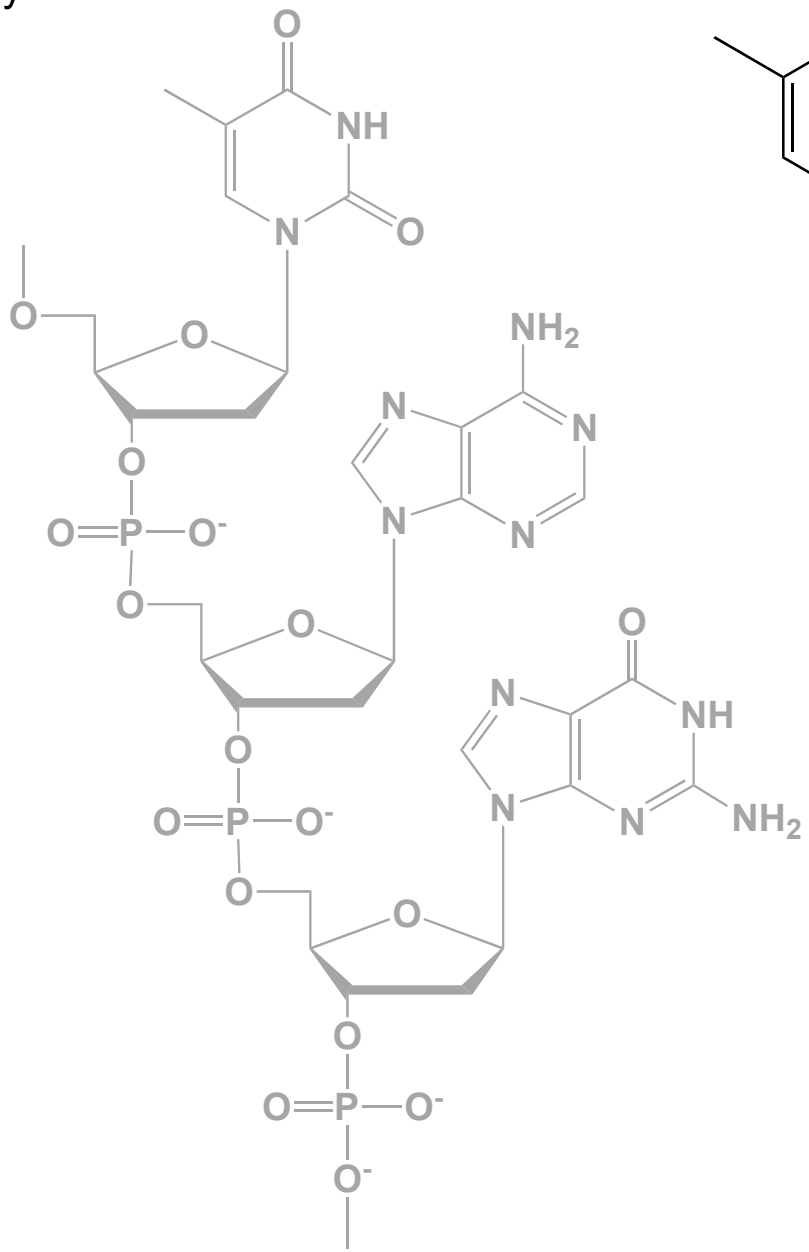
DNA

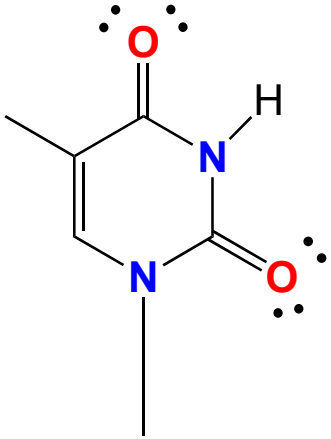
A look at the Chemistry

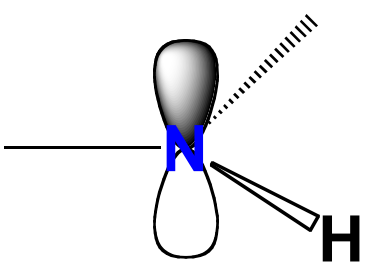


DNA

A look at the Chemistry

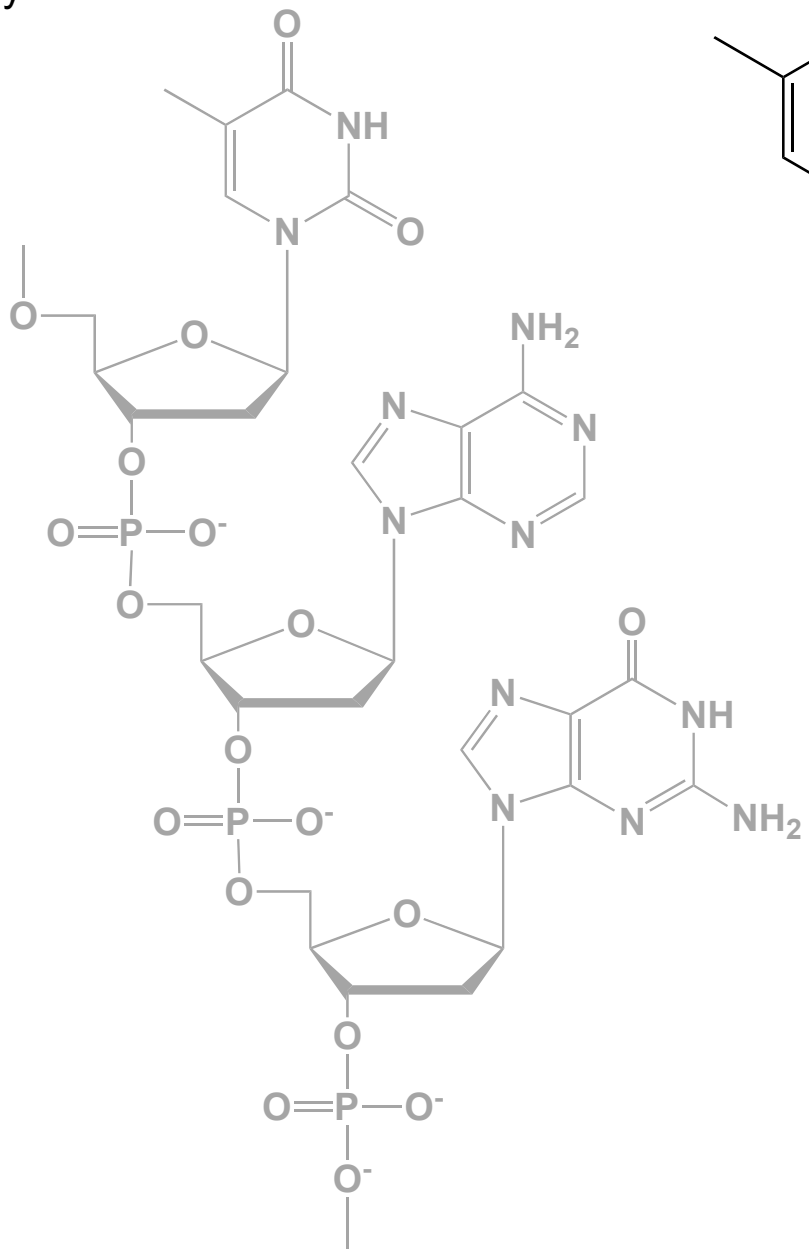


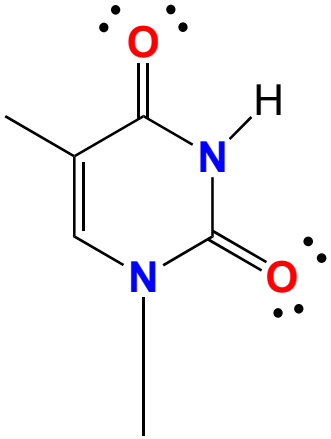


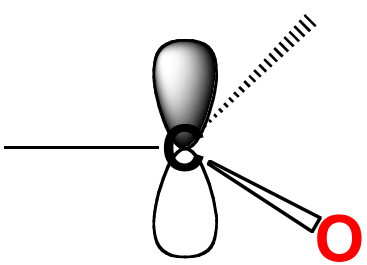


DNA

A look at the Chemistry

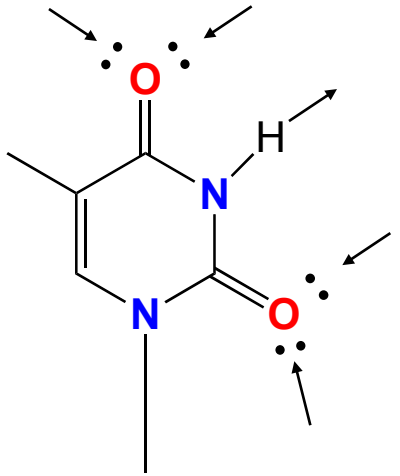


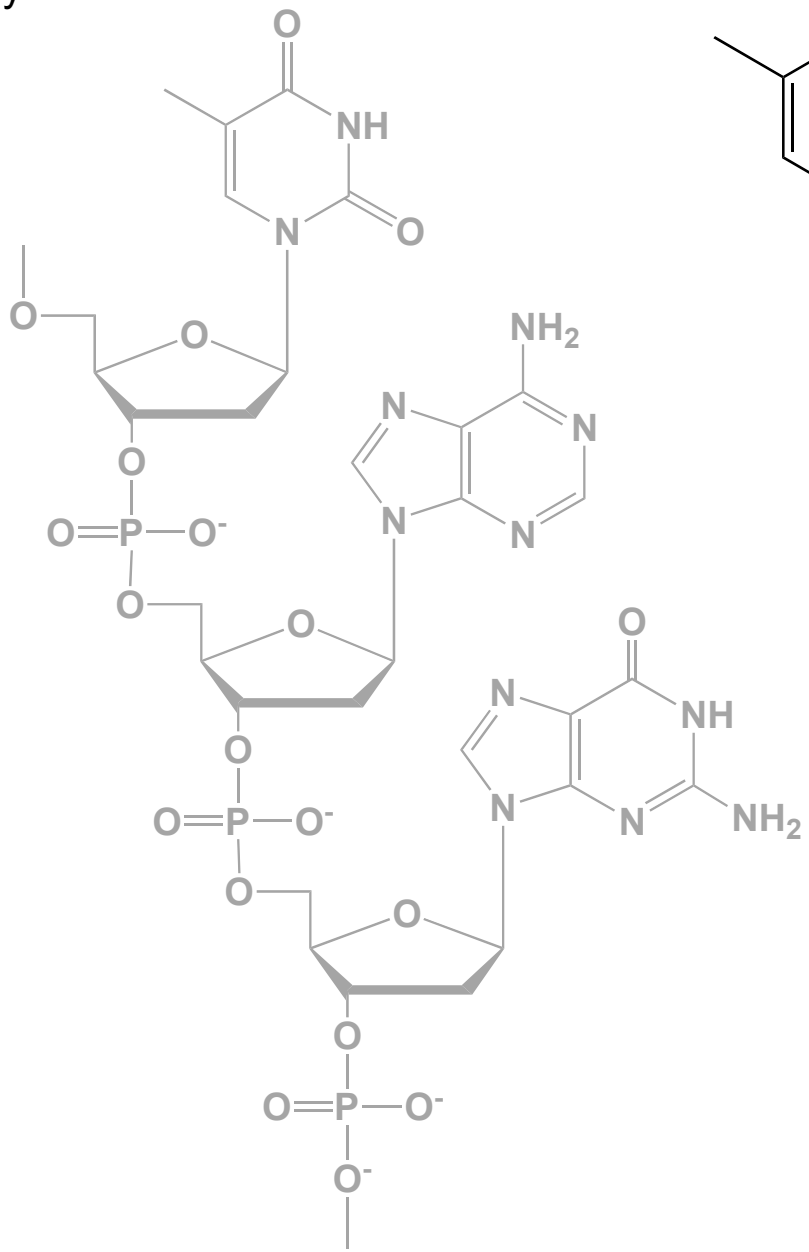




DNA

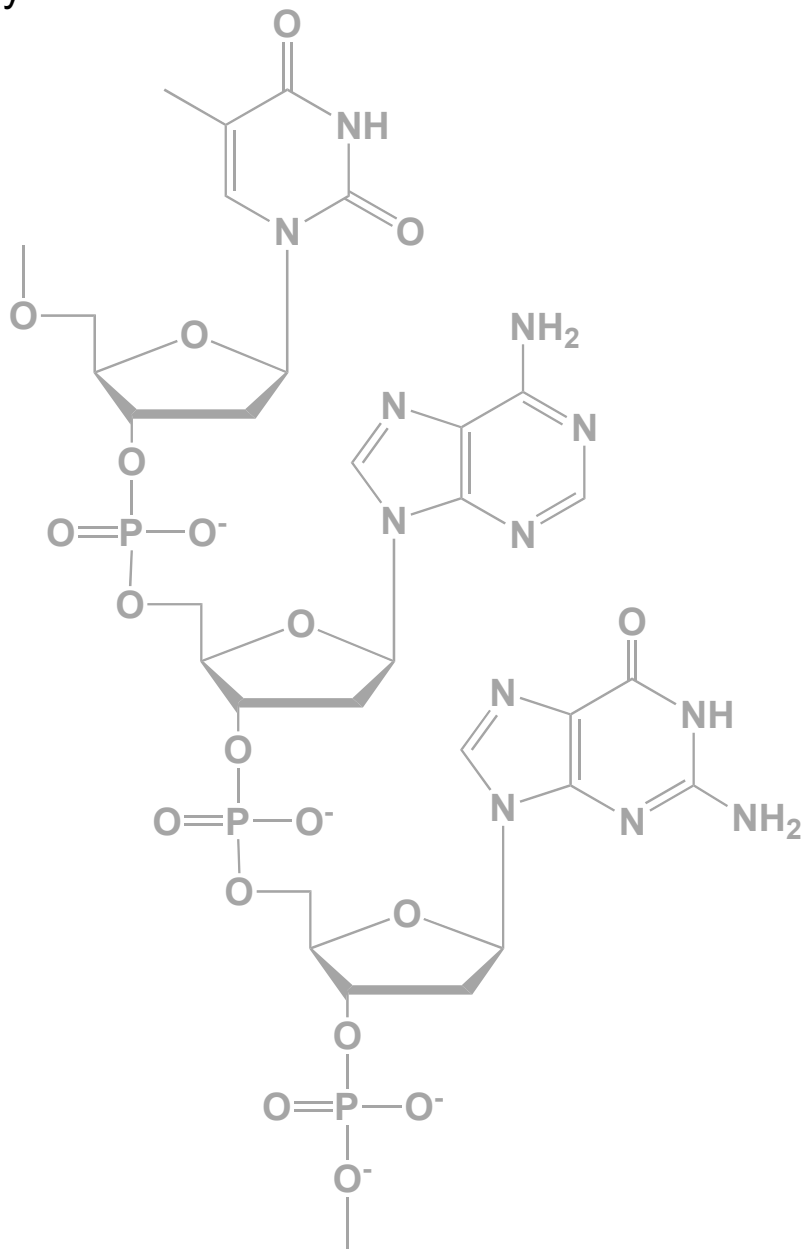
A look at the Chemistry

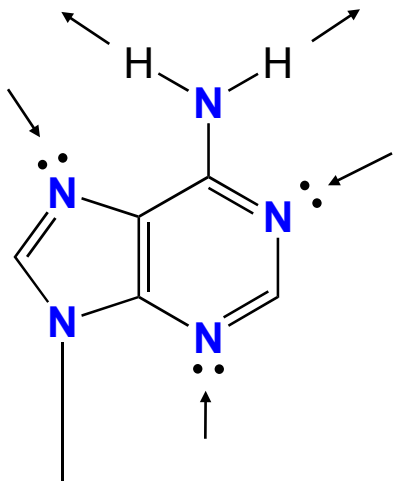




DNA

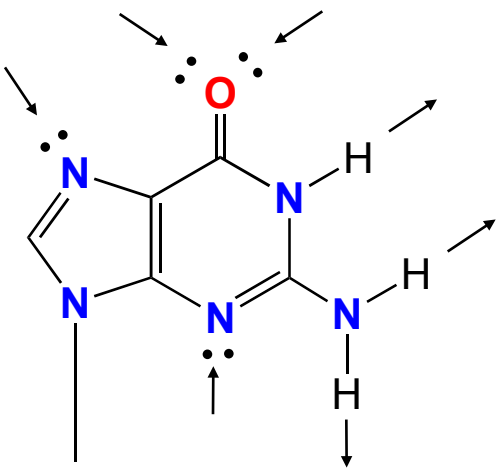
A look at the Chemistry

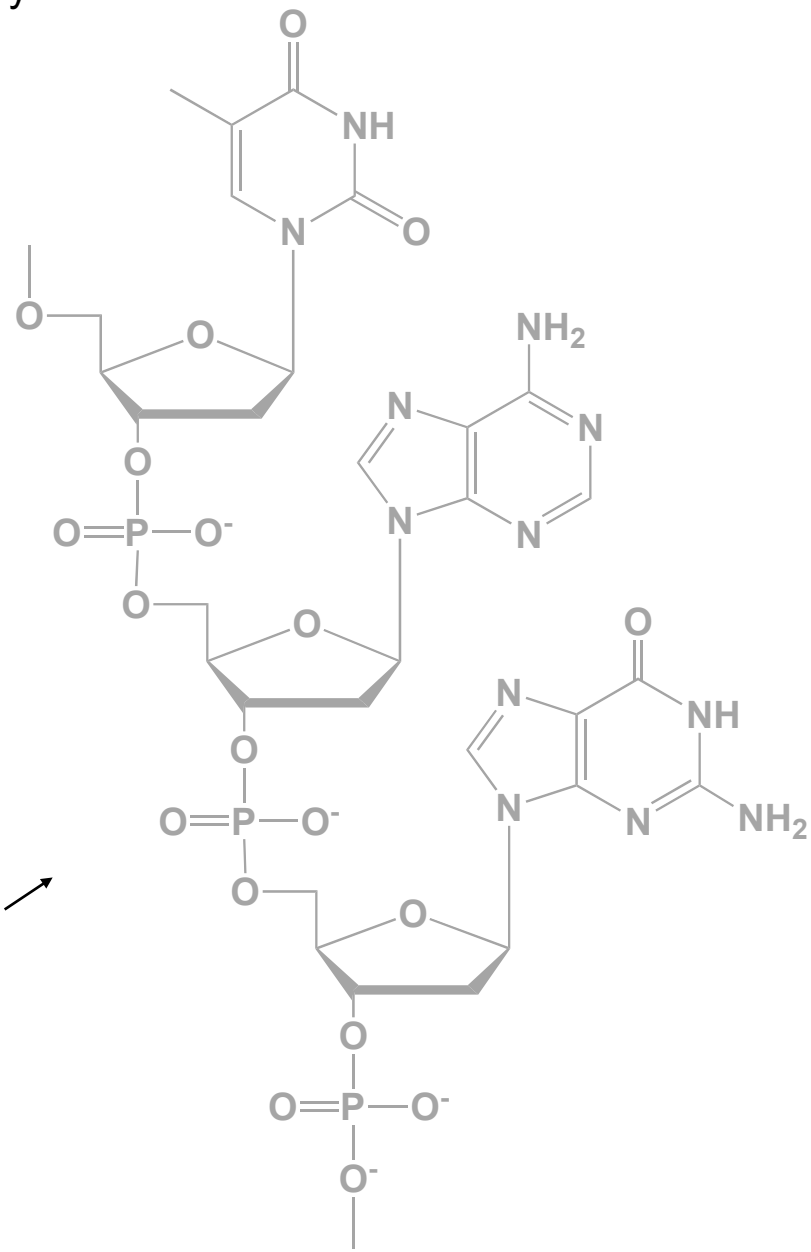




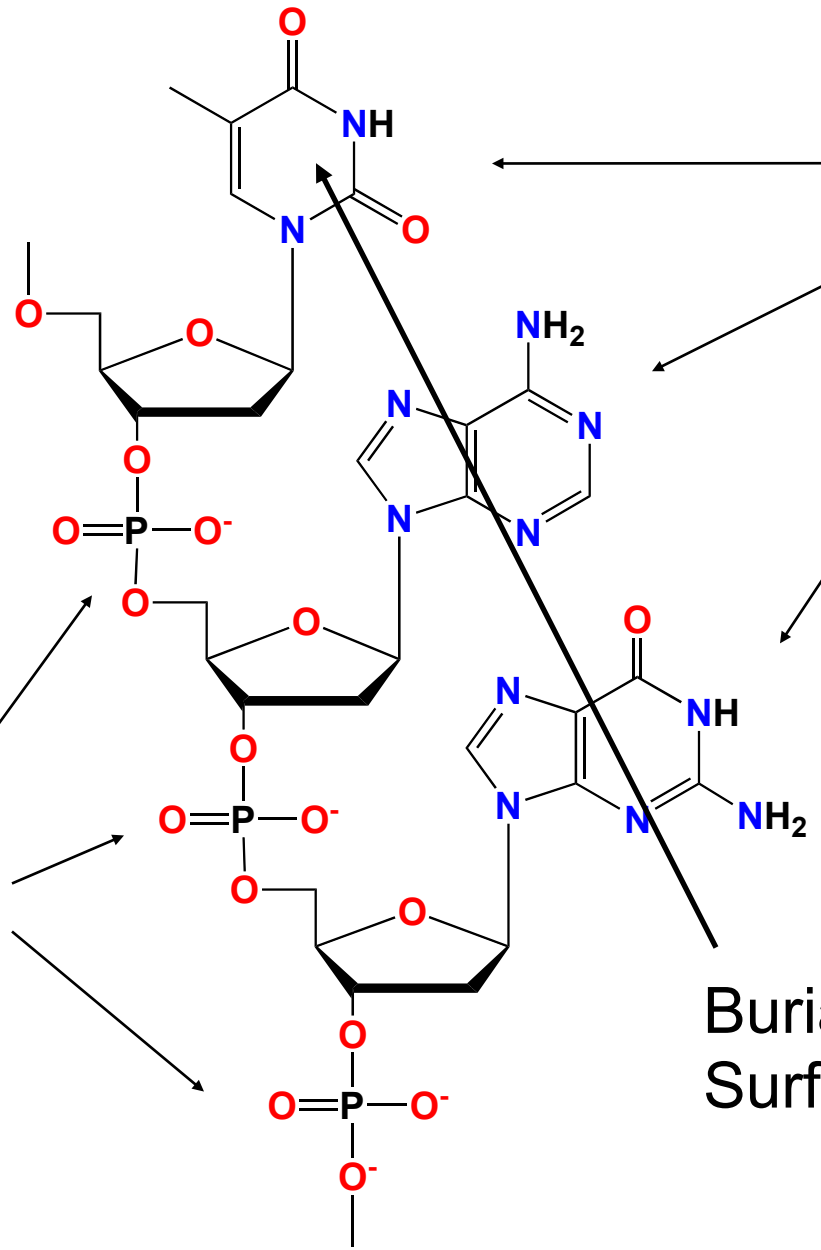
DNA

A look at the Chemistry





What forces are important?



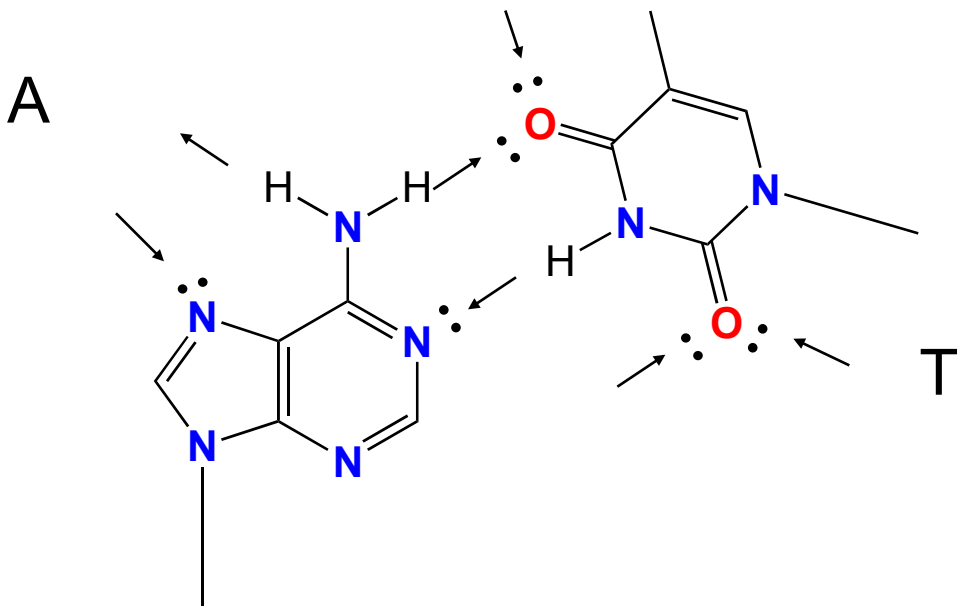
Hydrogen Bonding

Electrostatics

Burial of Hydrophobic Surface & Stacking

Base Pairing

(Donors matched to Acceptors)

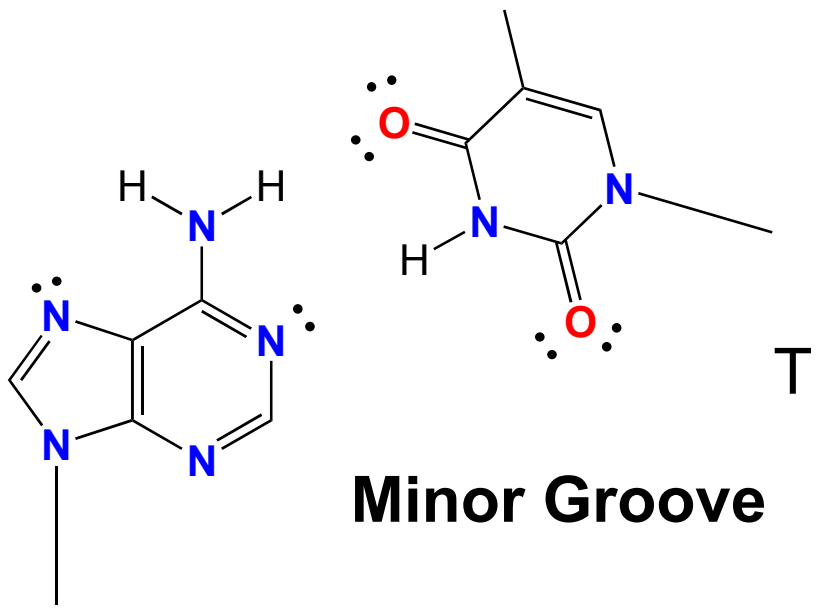


Base Pairing

(Donors matched to Acceptors)

Major Groove

A

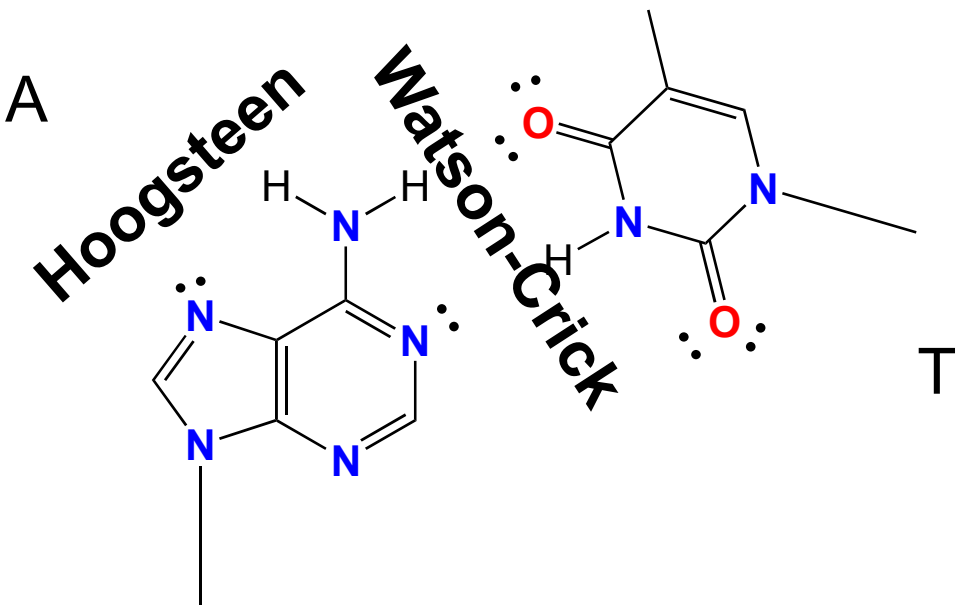


T

Minor Groove

Base Pairing

(Donors matched to Acceptors)



Base Pairing

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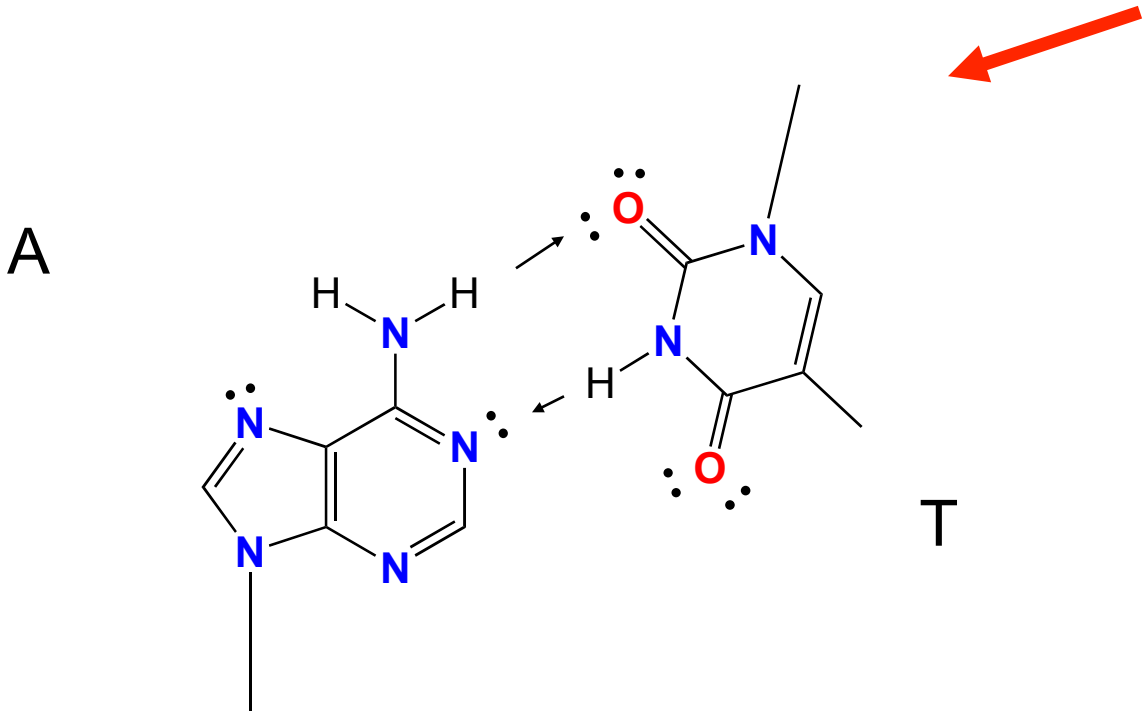
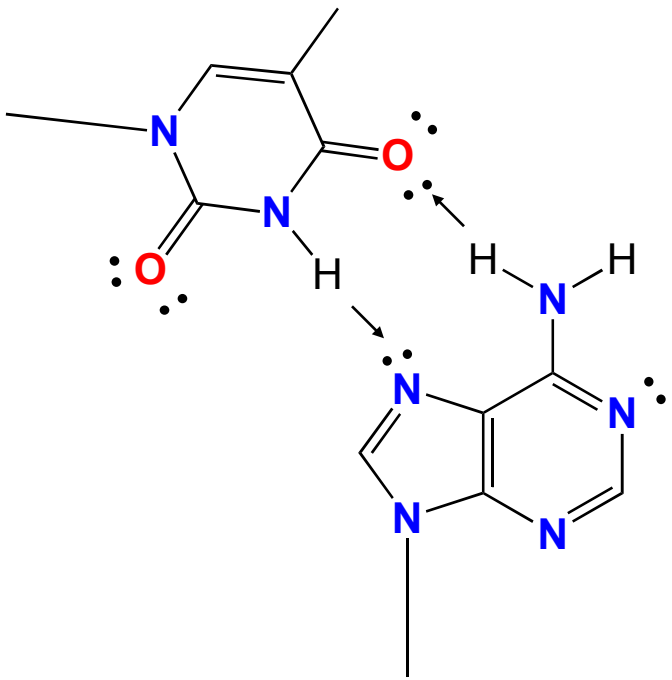


Good base pairing
Watson-Crick facing
but *Anti-Watson-Crick* orientation

Base Pairing

(Donors matched to Acceptors)

T

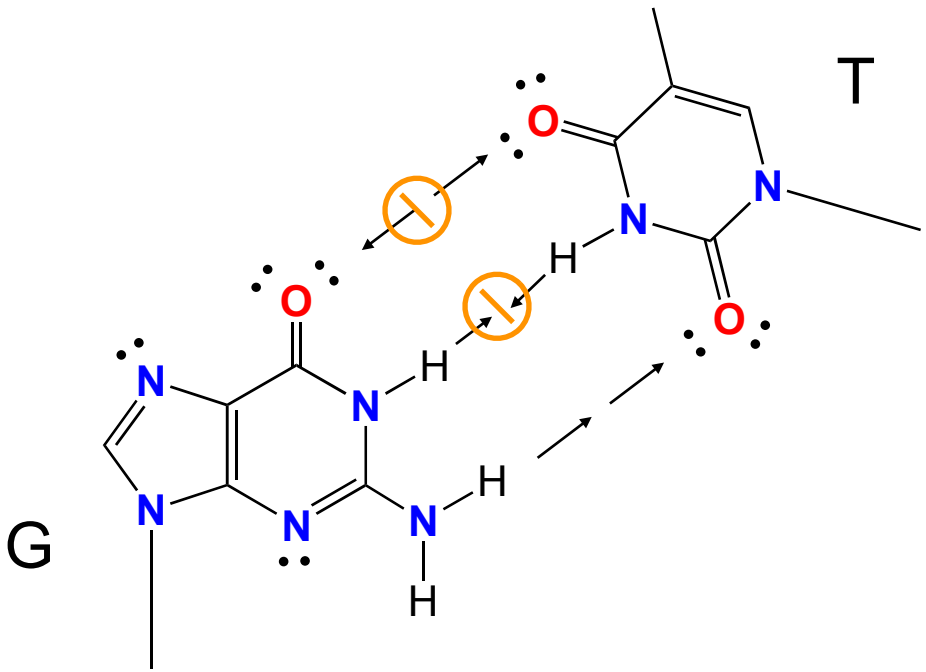


A

Good base pairing
WC-Hoogsteen facing

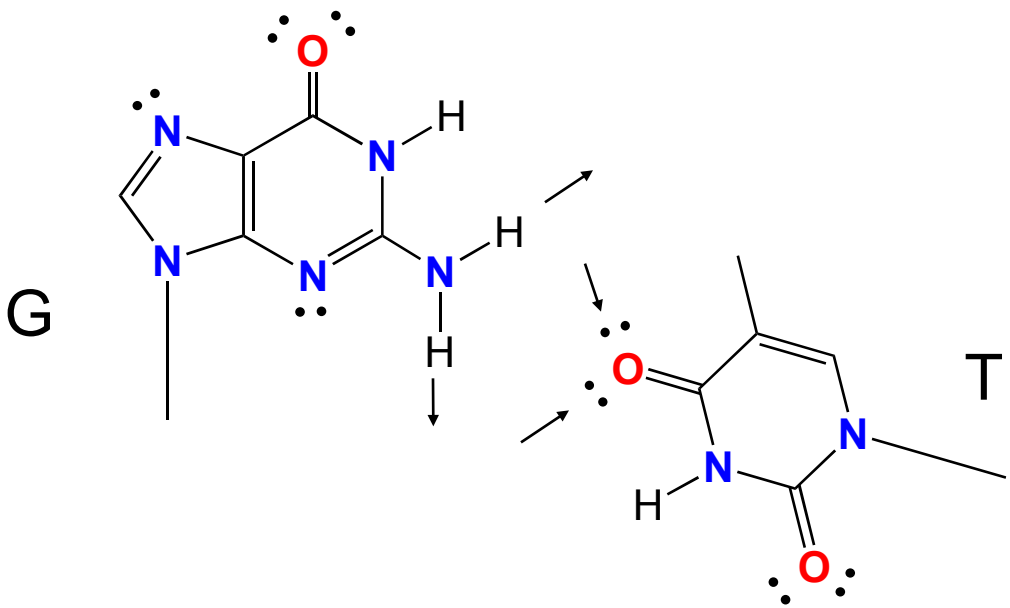
Bad Base Pairing

(Donors ***not*** matched to Acceptors)

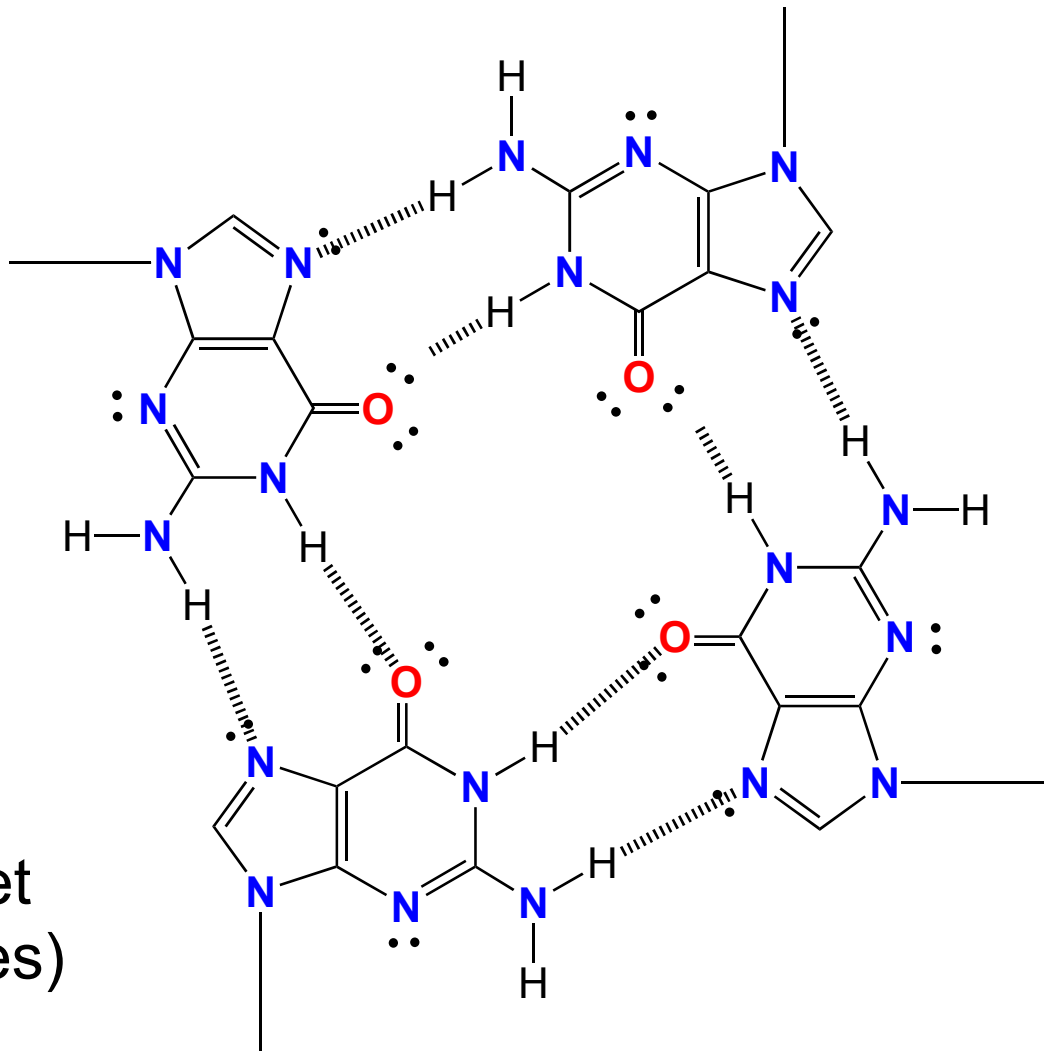


Bad Base Pairing

(Donors to Acceptors with ***terrible angles***)

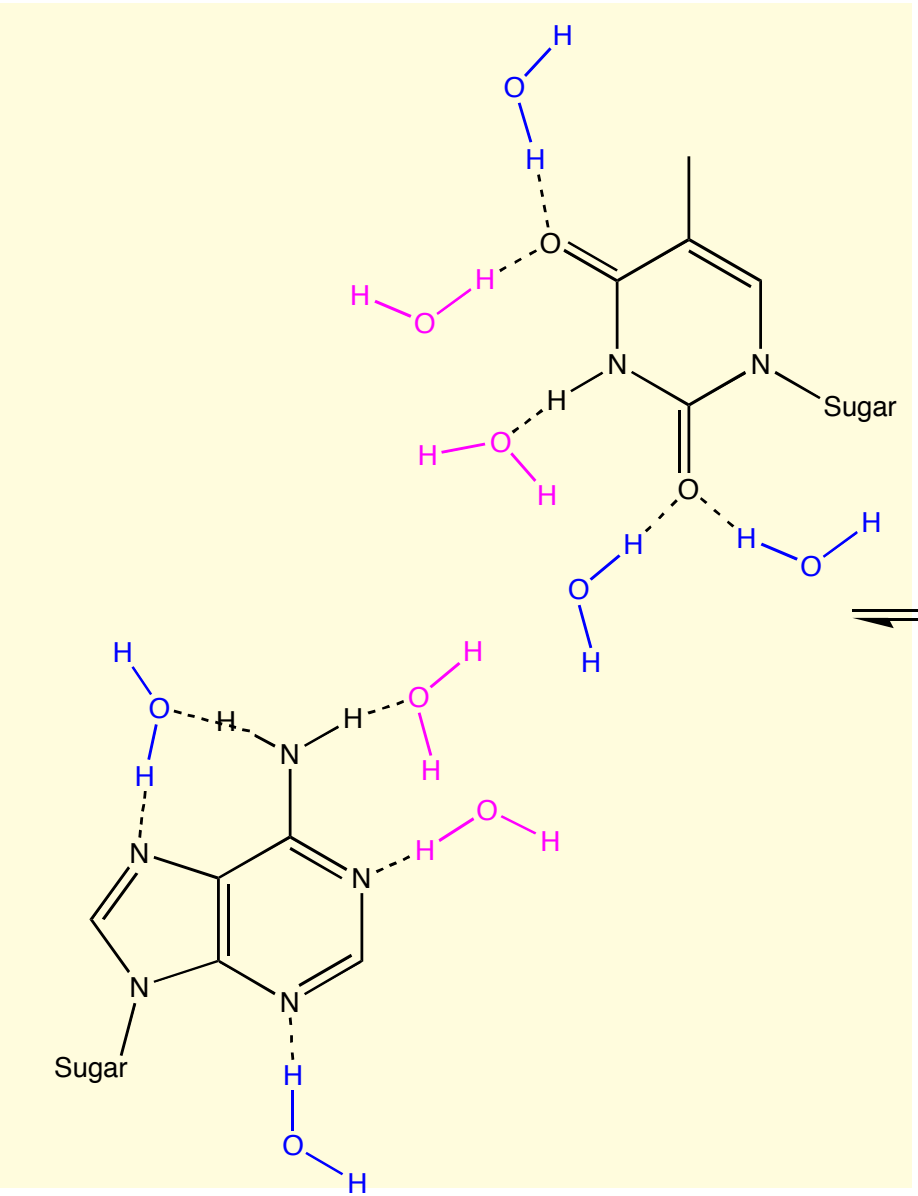


Wild (but good) Base Pairing

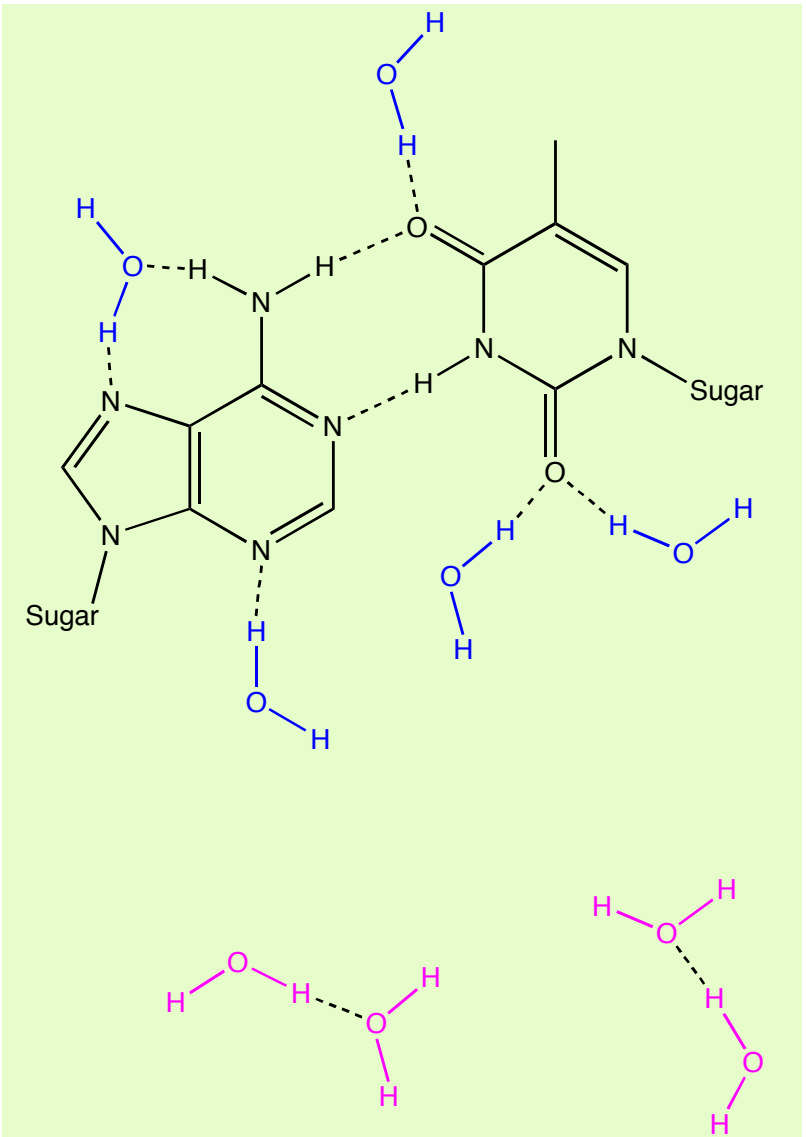


G-quartet
(Telomeres)

AT Base Pair

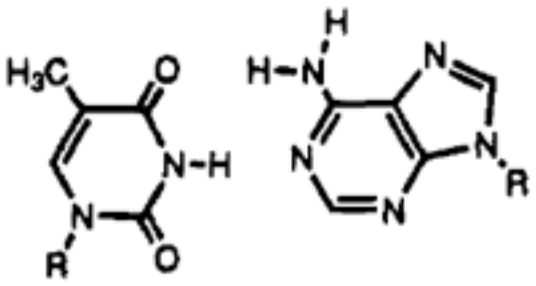


Ten H-Bonds

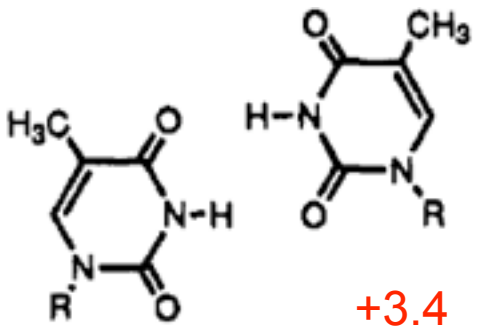


Ten H-Bonds

How important are H-bonds in DNA?

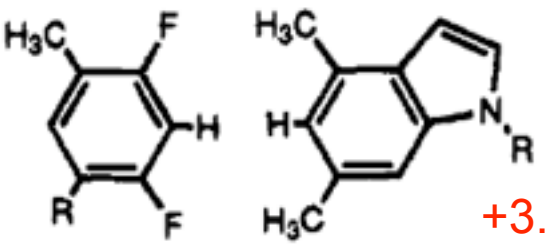


T - A



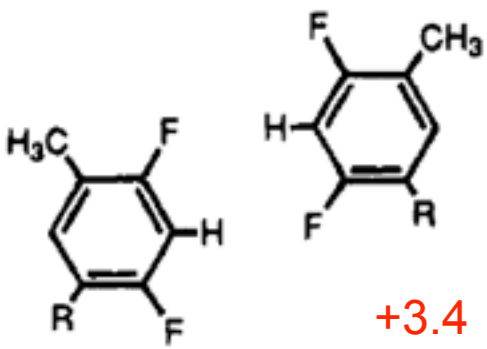
+3.4

T - T



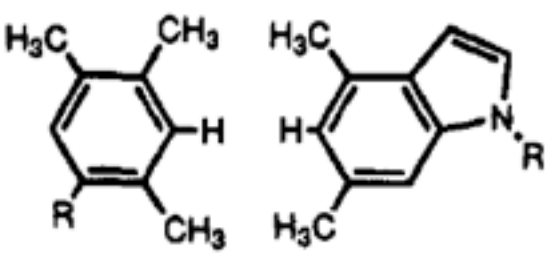
+3.7

F - D



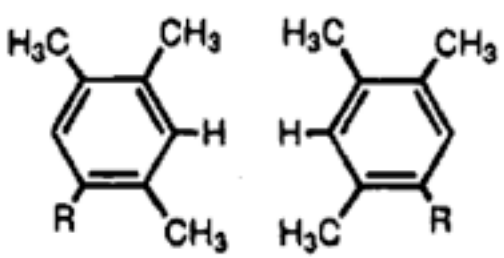
+3.4

F - F



+3.5

B - D



+3.0

B - B

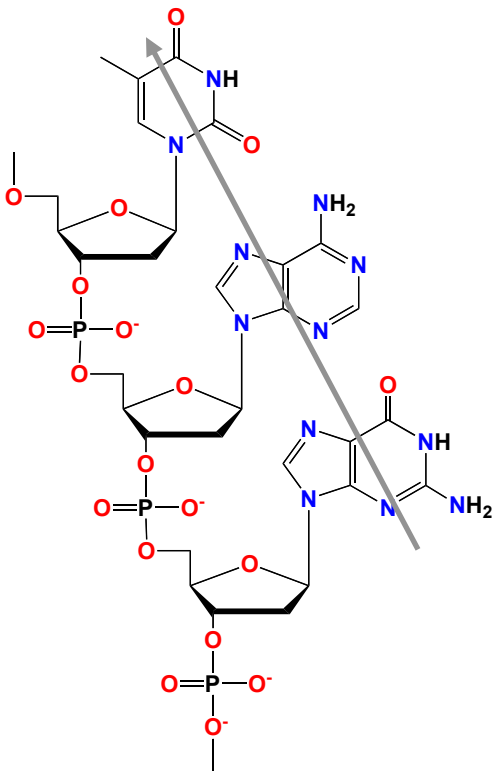
J. Am. Chem. Soc., Vol. 117, No. 7, 1995 1867

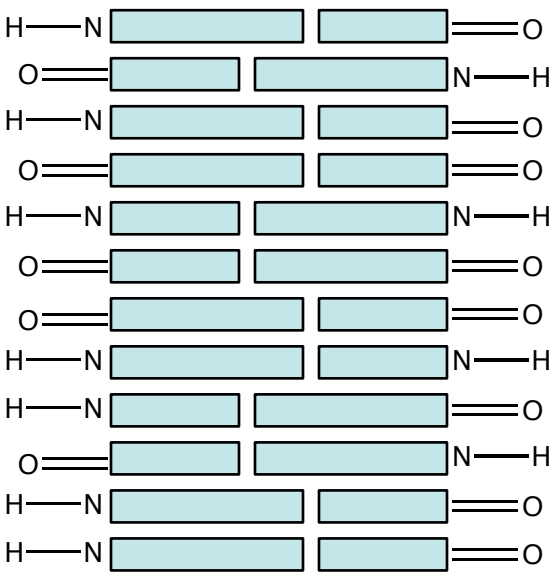
Table 1. Free Energies and Melting Temperatures for Dodecamer Duplexes Containing a Variable T−X, F−X, B−X, or D−X Base Pair (X = A, T, C, G)

duplex	T_m (°C) [a]	$-\Delta G°_{25}$ (kcal)
5′-CTTTTGTTTCTT 3′-GAAAACAAAGAA	39.4	12.3
5′-CTTTTGTTTCTT 3′-GAAAACGAAGAA	26.4	8.7
5′-CTTTTGTTTCTT 3′-GAAAACGAAGAA	30.7	9.3
5′-CTTTTGTTTCTT 3′-GAAAACTAAGAA	27.1	8.9
5′-CTTTTGFTTCTT 3′-GAAAACAAAGAA	21.4	7.4
5′-CTTTTGFTTCTT 3′-GAAAACGAAGAA	25.0	8.2
5′-CTTTTGFTTCTT 3′-GAAAACGAAGAA	23.0	8.0
5′-CTTTTGFTTCTT 3′-GAAAACTAAGAA	20.2	7.3
5′-CTTTTGBTTCTT 3′-GAAAACAAAGAA	21.0	7.5
5′-CTTTTGBTTCTT 3′-GAAAACGAAGAA	22.9	7.8
5′-CTTTTGBTTCTT 3′-GAAAACGAAGAA	20.1	7.6
5′-CTTTTGBTTCTT 3′-GAAAACTAAGAA	20.3	6.7
5′-CTTTTGDTTCTT 3′-GAAAACAAAGAA	20.8	7.4
5′-CTTTTGDTTCTT 3′-GAAAACGAAGAA	22.2	7.6
5′-CTTTTGDTTCTT 3′-GAAAACGAAGAA	19.7	7.4
5′-CTTTTGDTTCTT 3′-GAAAACTAAGAA	17.6	6.9

[a] Conditions: 100 mM NaCl, 10 mM $MgCl_2$, 10 mM Na·PIPES, pH 7.0, 1.6 μM each strand.

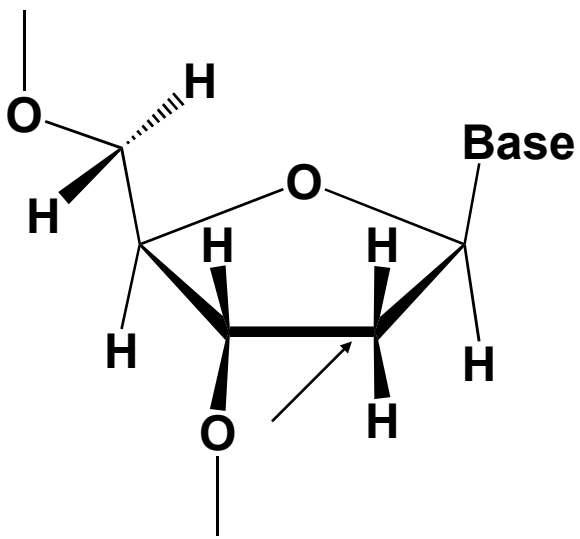
Burial of hydrophobic surface drives helix formation (hydrophobic core / stacking interactions)

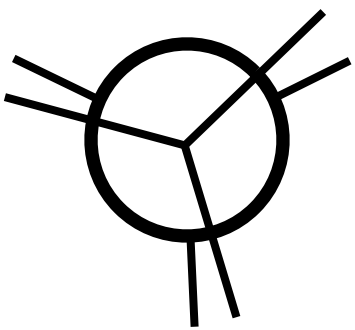


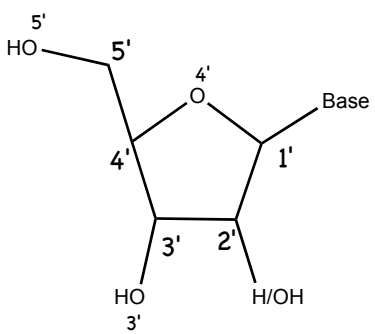


Flat faces are nonpolar
Edges are very polar (can H-bond)

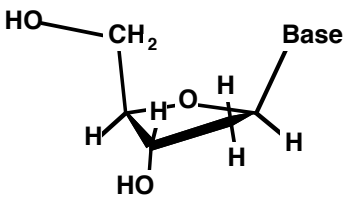
Furanose Sugar Ring



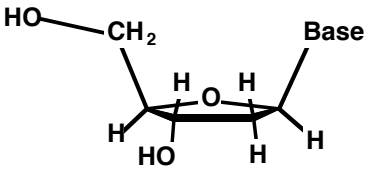




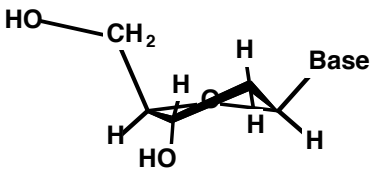
Furanose Sugar Ring



C3' exo



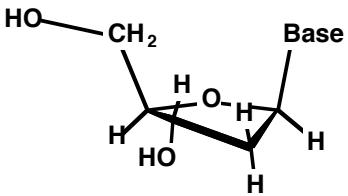
Unpuckered



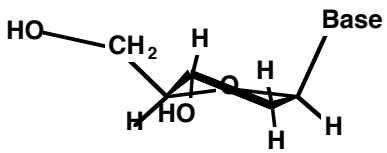
C2' endo

endo

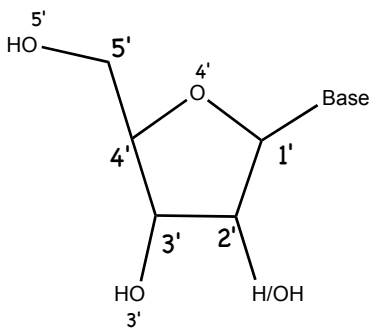
exo

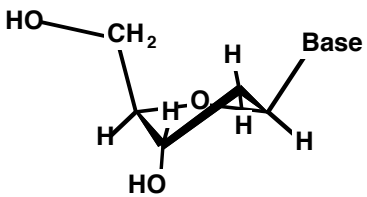


C2' exo

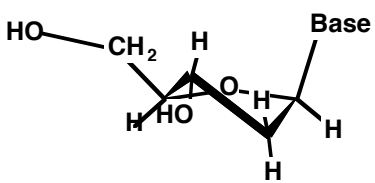


C3' endo

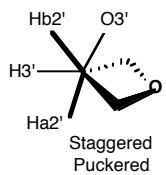




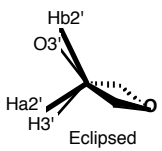
C2' endo - C3' exo



C2' exo - C3' endo

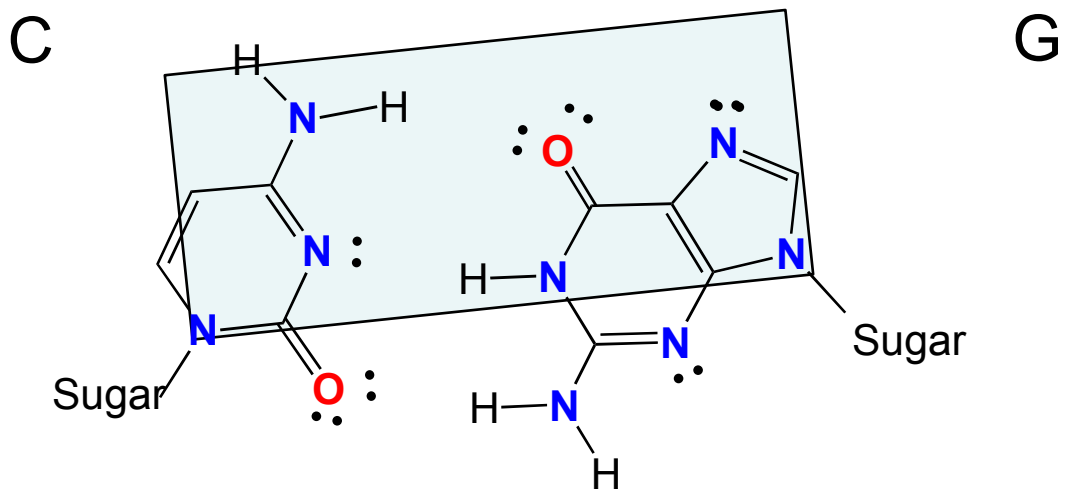


Staggered
Puckered



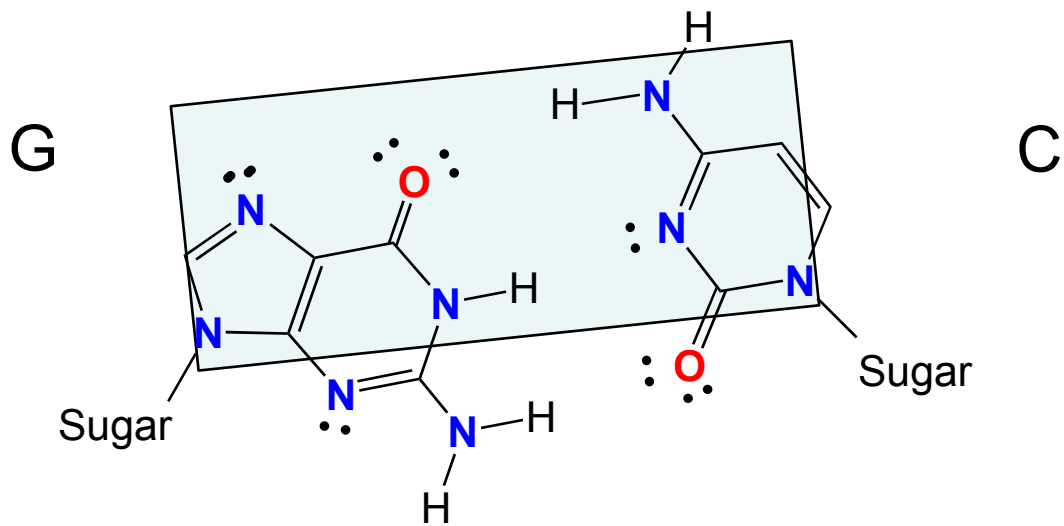
Eclipsed
Planar

Why is Watson-Crick so good?



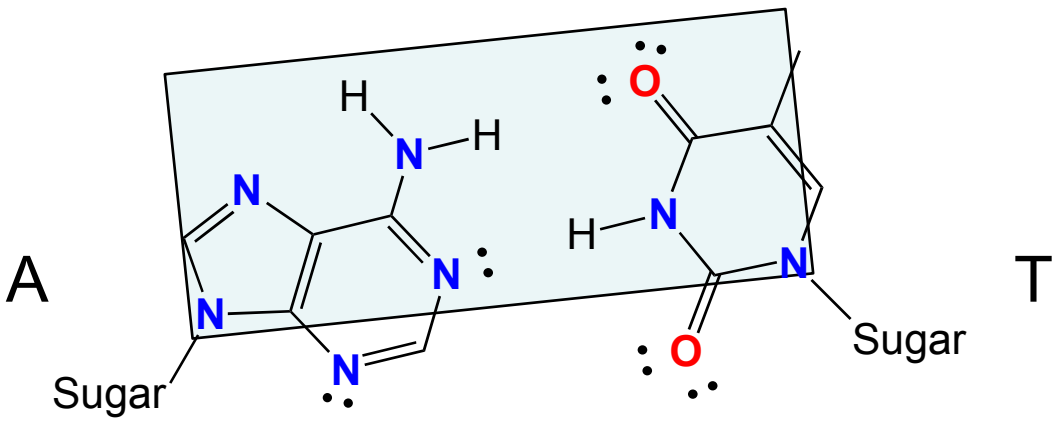
All four WC base pairs
are
isosteric

Why is Watson-Crick so good?



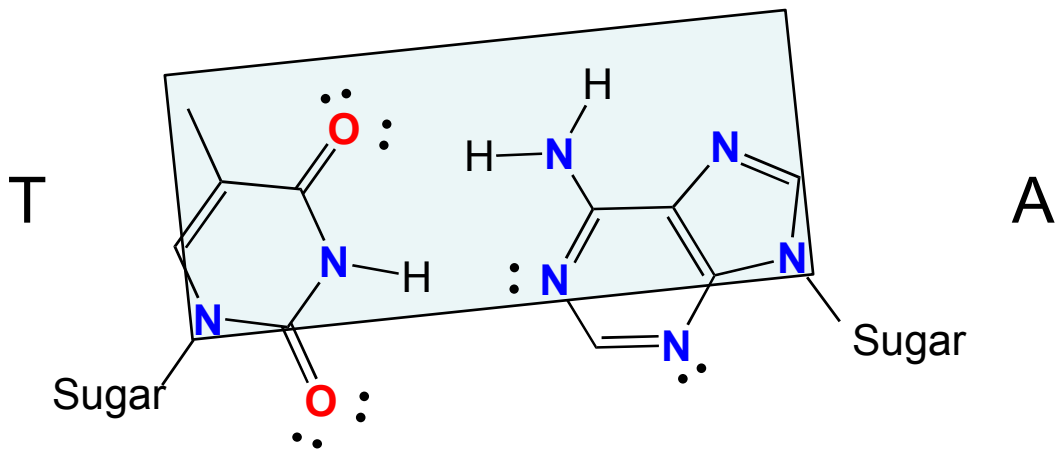
All four WC base pairs
are
isosteric

Why is Watson-Crick so good?



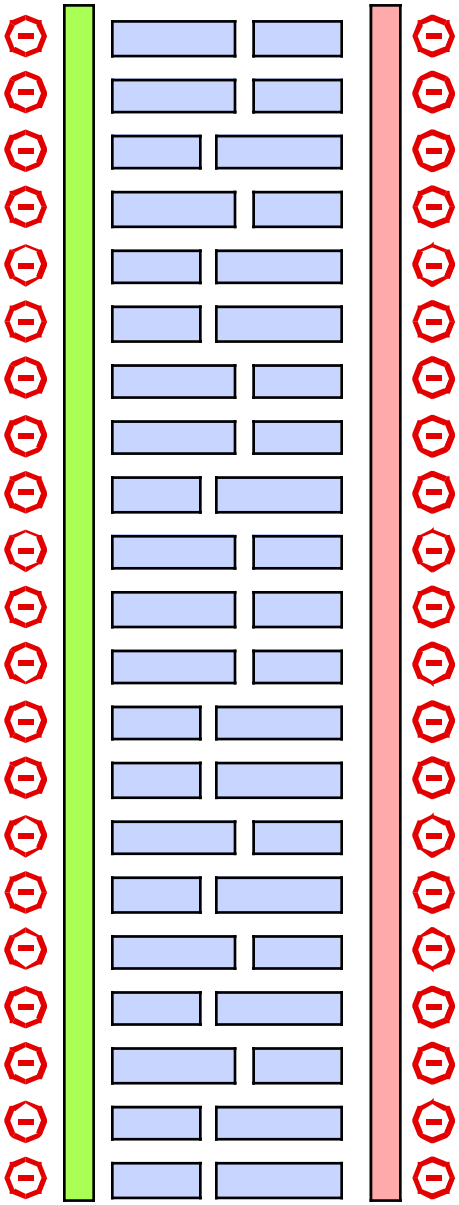
All four WC base pairs
are
isosteric

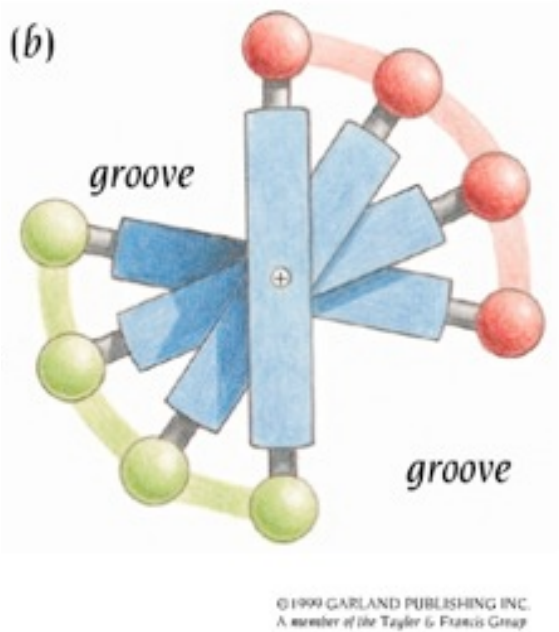
Why is Watson-Crick so good?

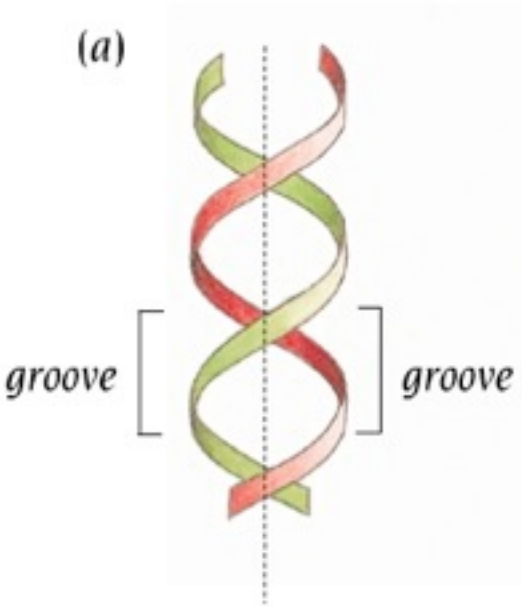


All four WC base pairs
are
isosteric

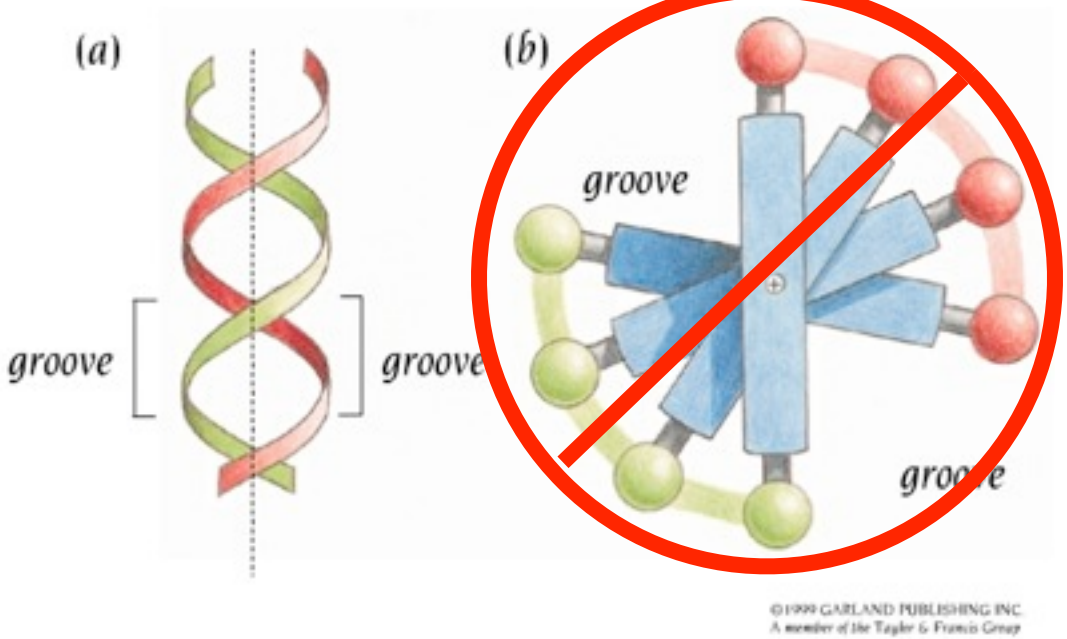
Why ***a helix***?

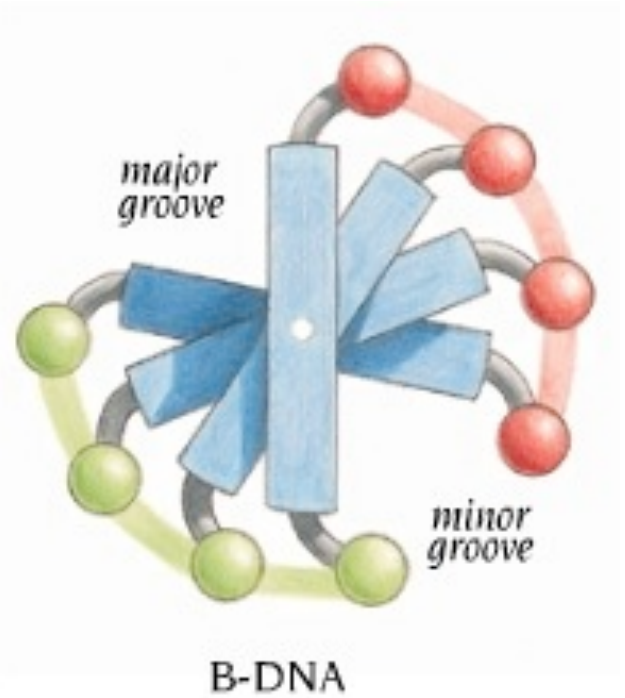


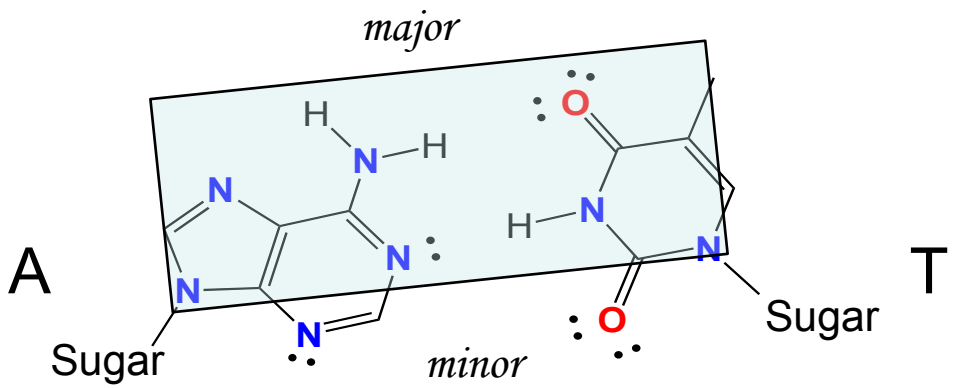




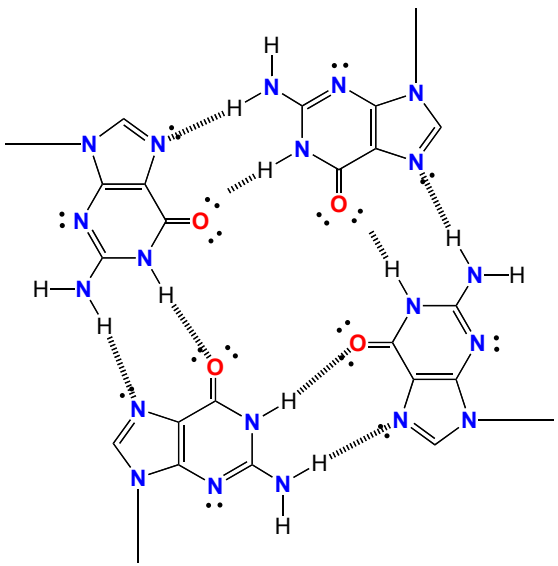
Why ***major*** and ***minor*** grooves?

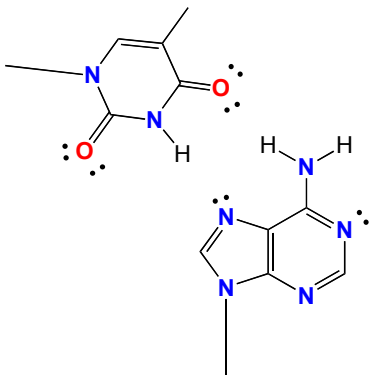


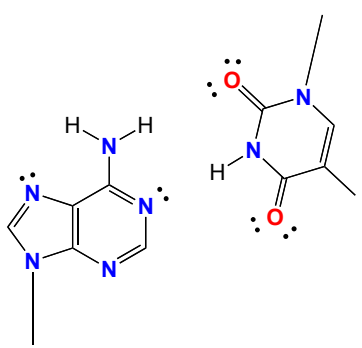


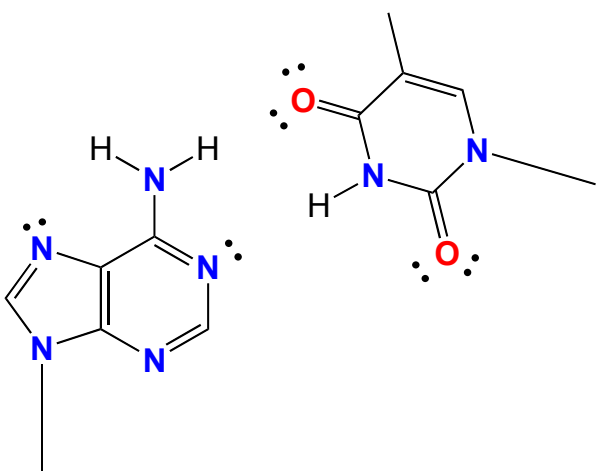


Nucleic Acid - Nucleic Acid Recognition





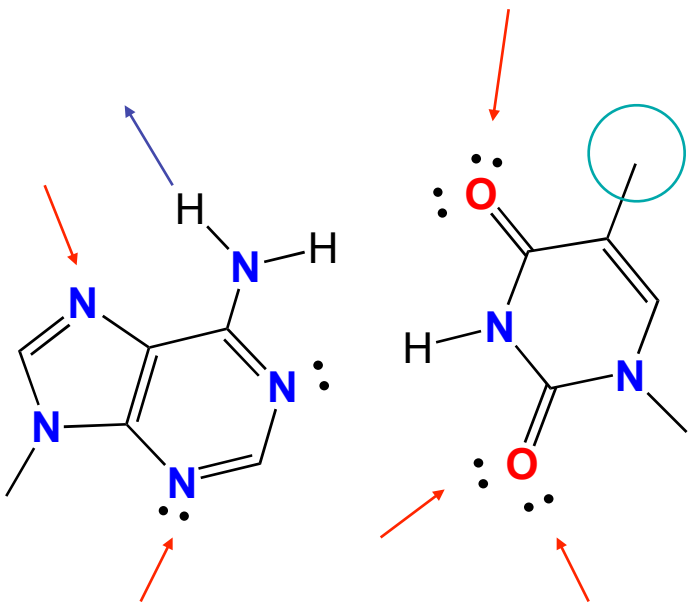




Why is the major groove so good?

Major Groove

A



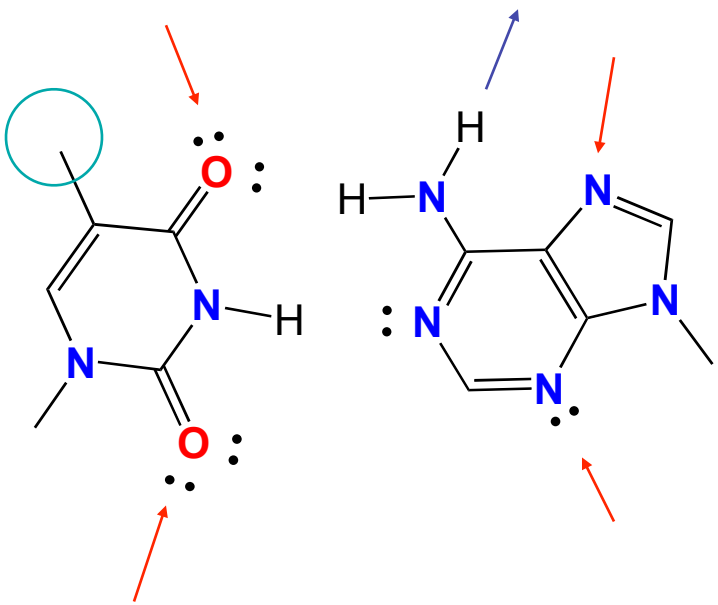
T

Minor Groove

Why is the major groove so good?

Major Groove

T



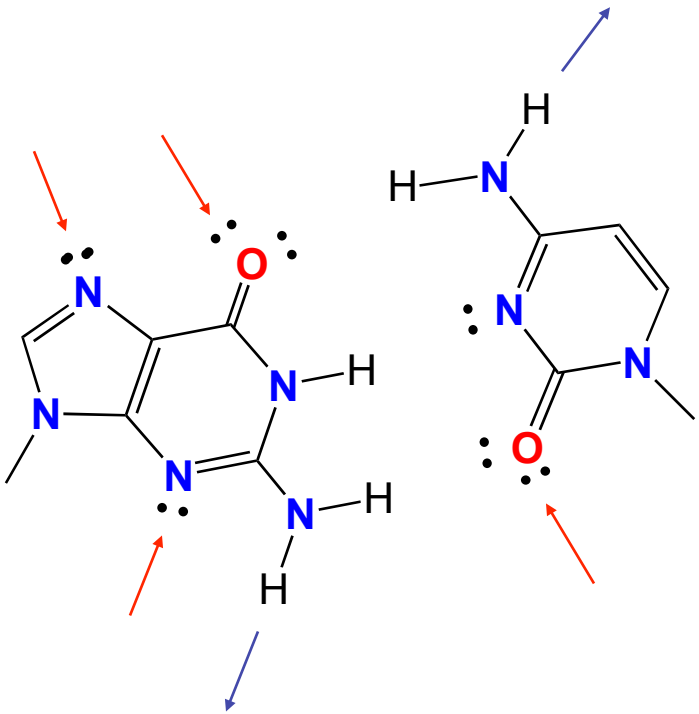
A

Minor Groove

Why is the major groove so good?

Major Groove

G



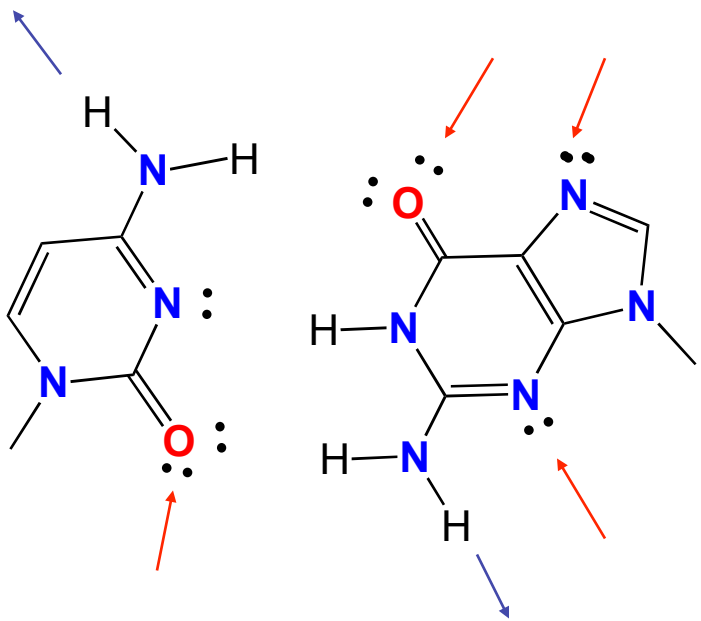
C

Minor Groove

Why is the major groove so good?

Major Groove

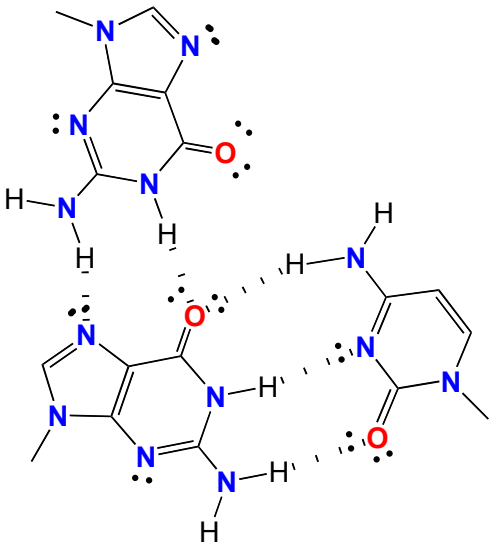
C

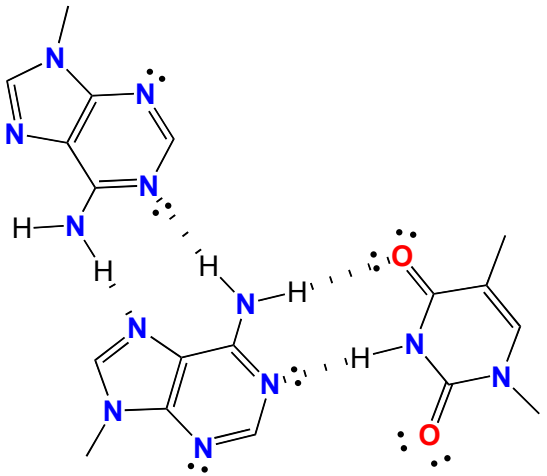


G

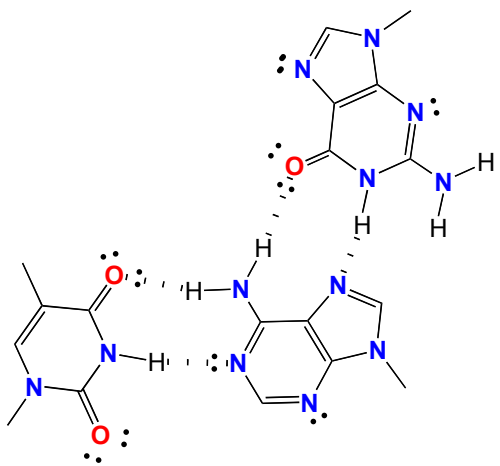
Minor Groove

Nucleic Acid “Triples / Platforms”





Major Groove Interactions

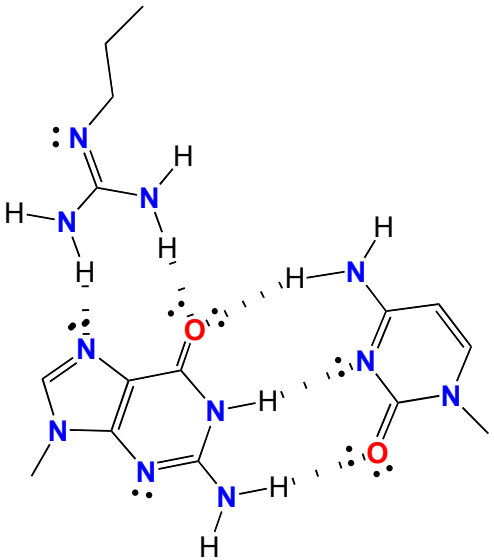


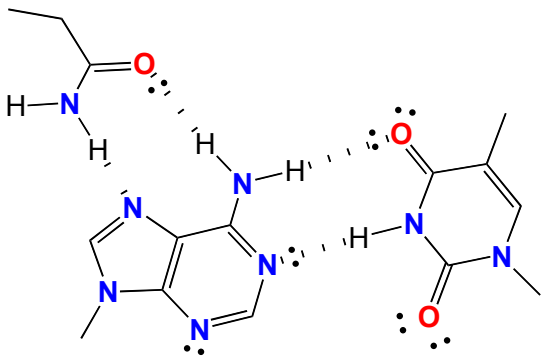
Protein - Nucleic Acid Interactions

Gln

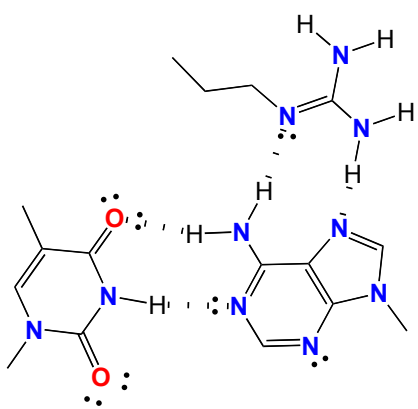
Asn

Arg





Major Groove Interactions



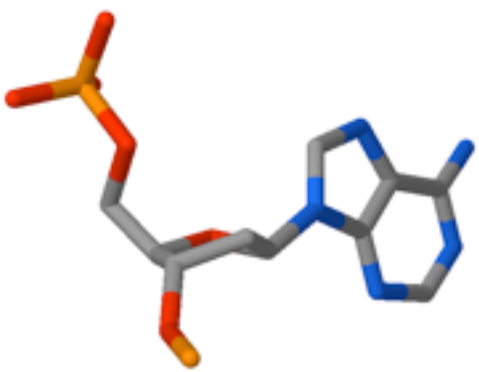
B-form DNA

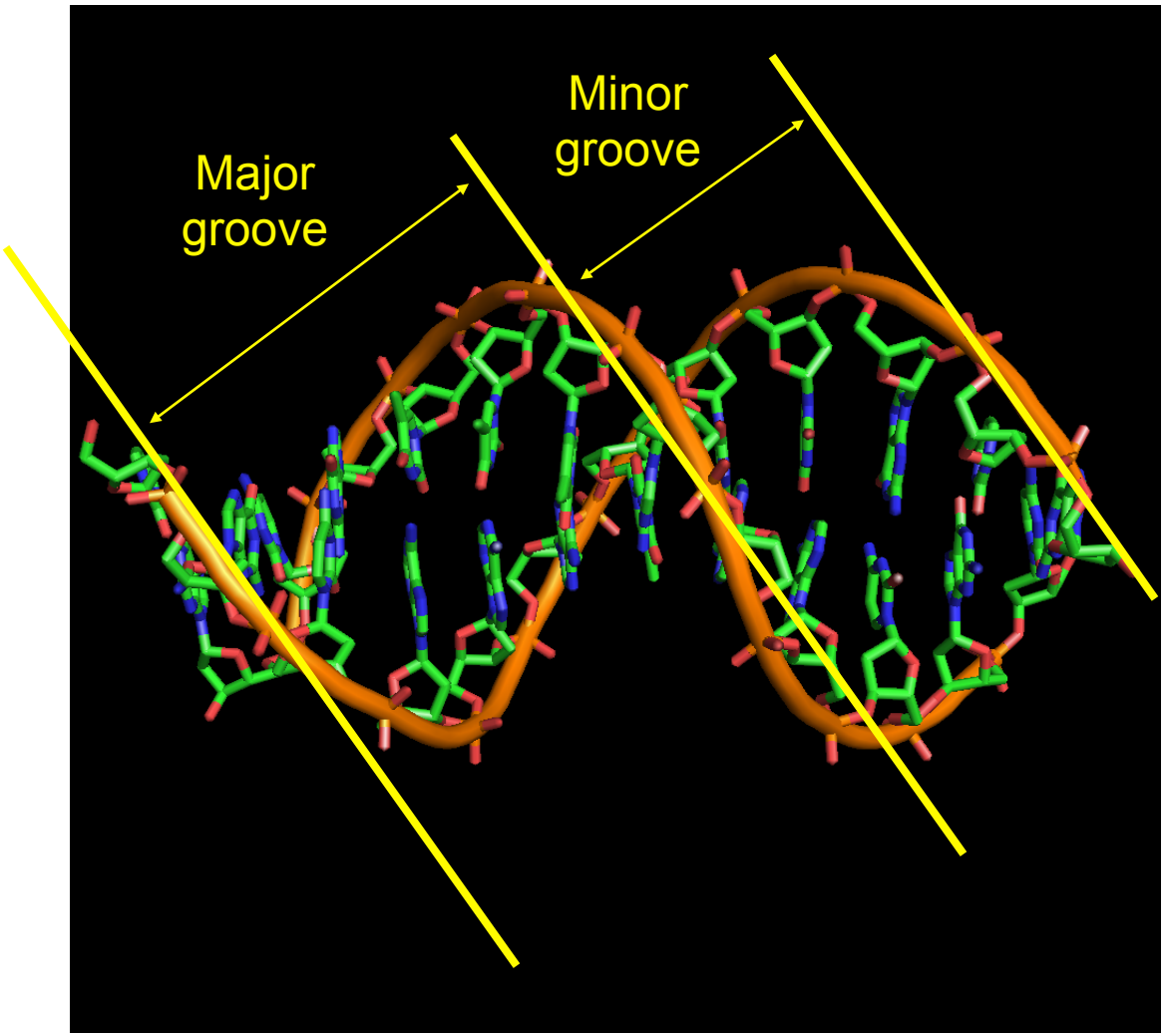
B-form

Residues per turn =10
Twist per base pair = 36°
Rise per pair = 3.4Å
c2'-endo

Minor groove width = 5.7Å
Major groove width = 11.7Å

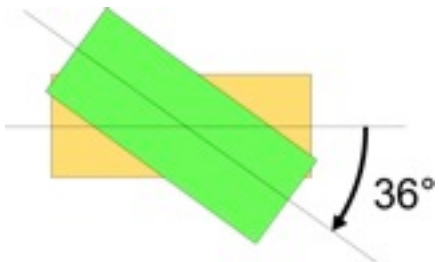
Minor groove depth = 7.5Å
Major groove depth = 8.8Å





B-form DNA

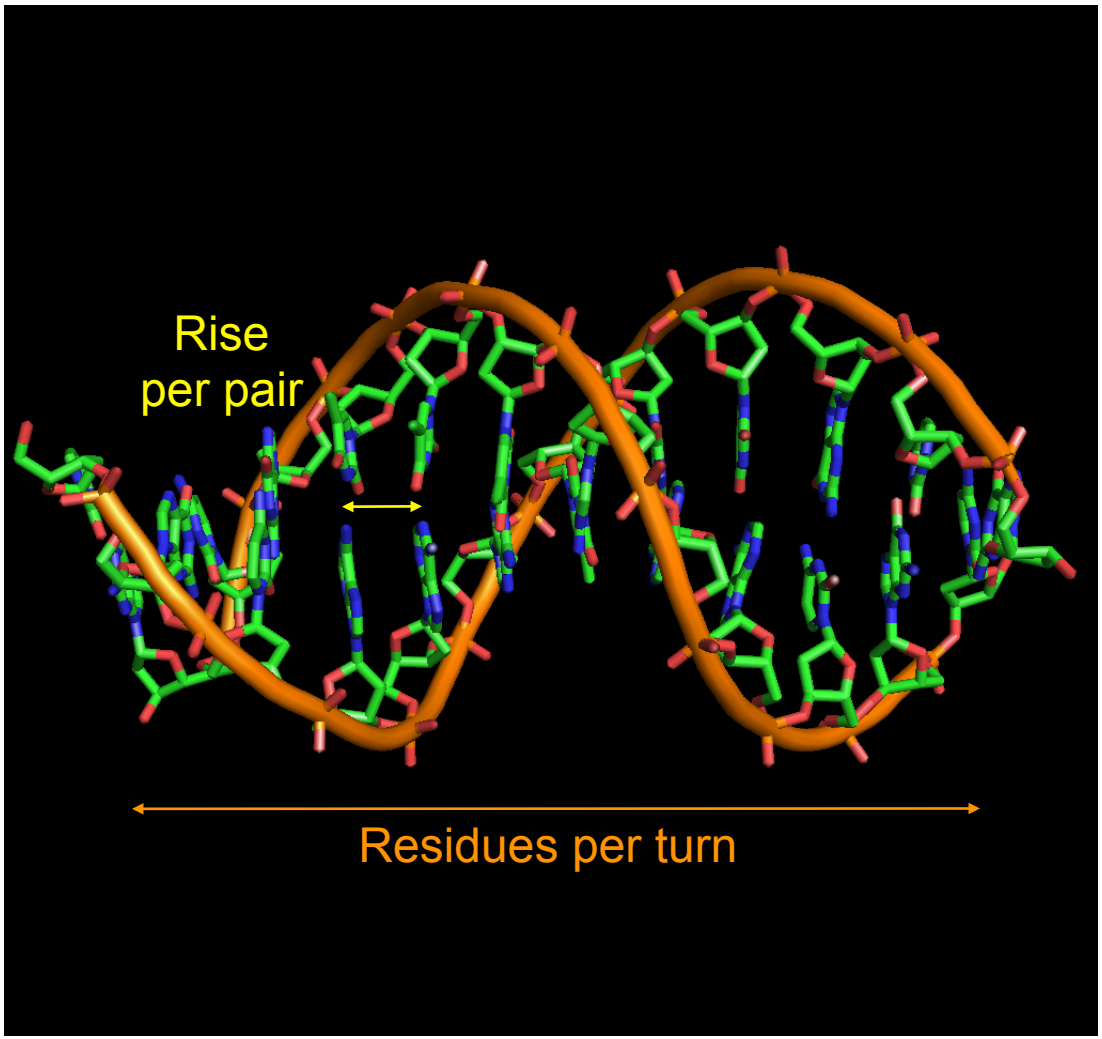
Residues per turn =10
Twist per base pair = 36°



Rise per pair = 3.4Å
c2'-endo

Minor groove width = 5.7Å
Major groove width = 11.7Å

Minor groove depth = 7.5Å
Major groove depth = 8.8Å

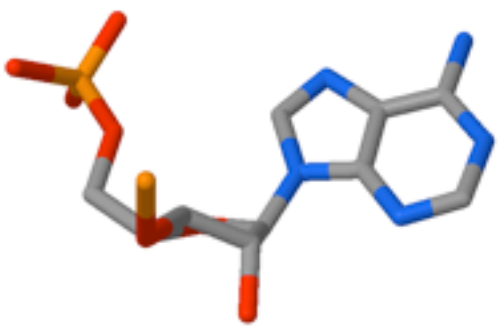


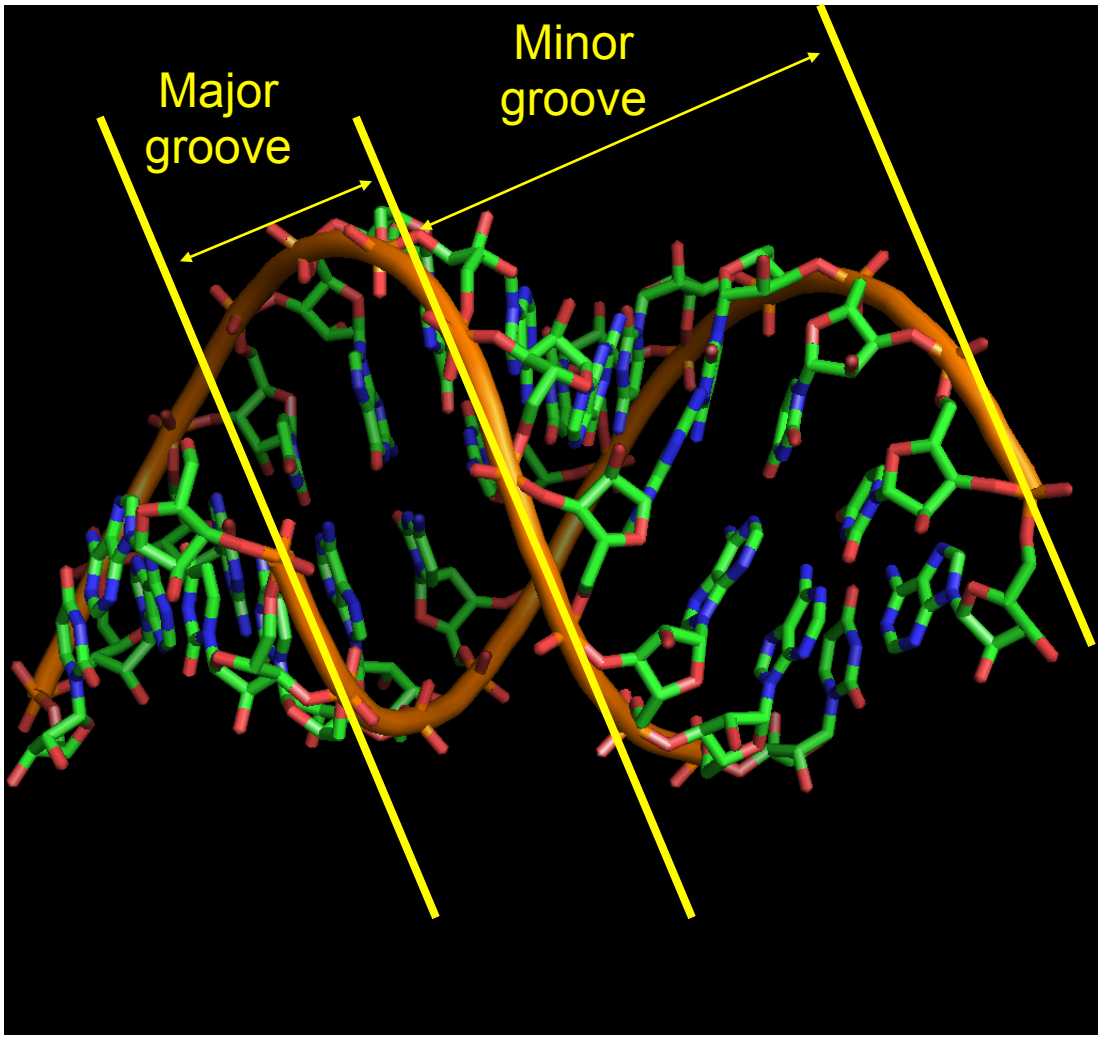
A-form RNA

Residues per turn =11
Twist per base pair = 33°
Rise per pair = 2.9Å
c3'-endo

Minor groove width = 11Å
Major groove width = 2.7Å

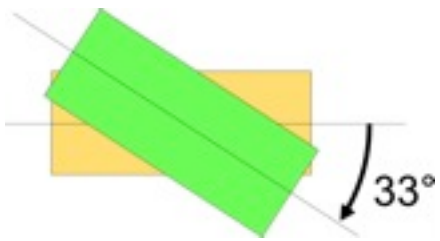
Minor groove depth = 2.8Å
Major groove depth = 13.5Å





A-form RNA

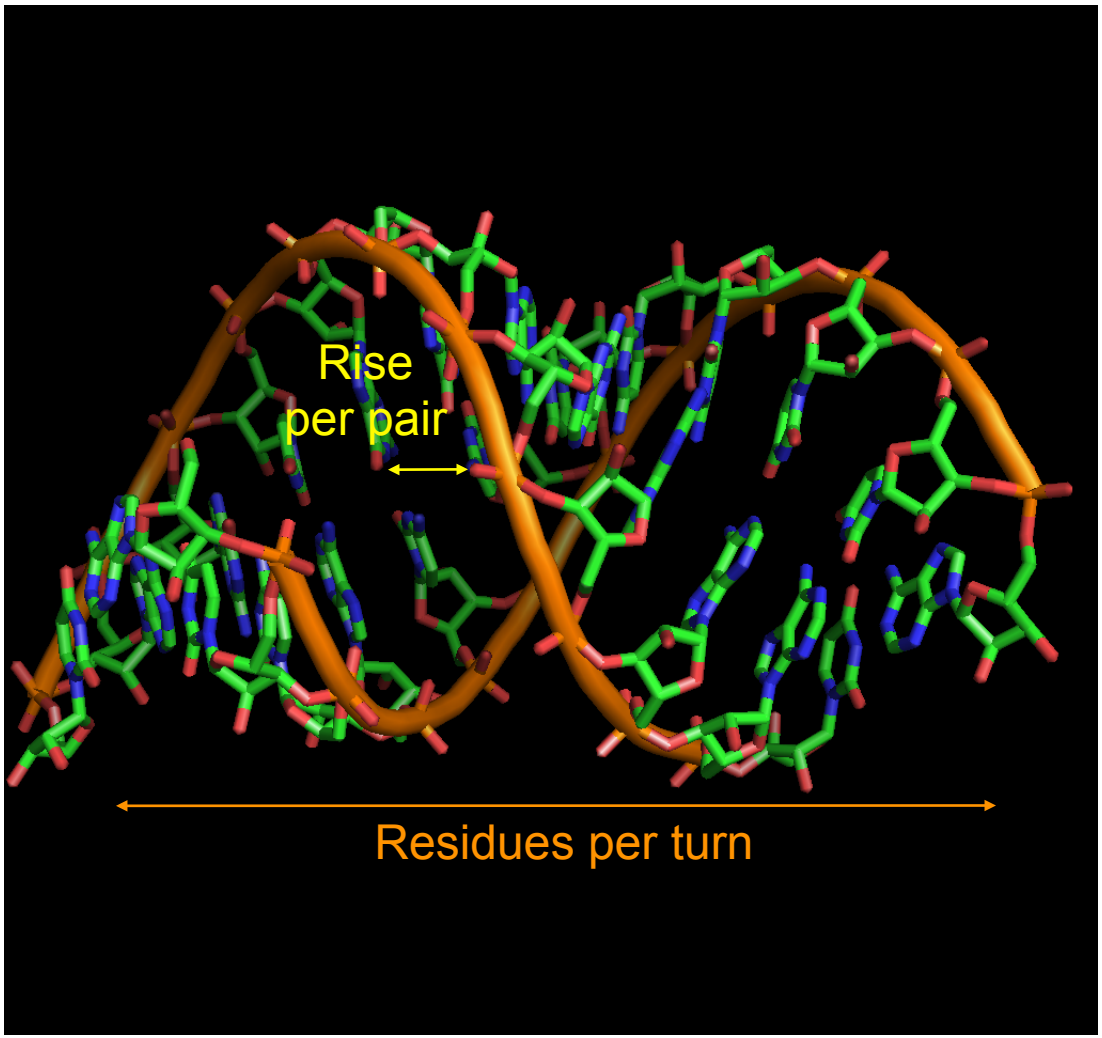
Residues per turn =11
Twist per base pair = 33°



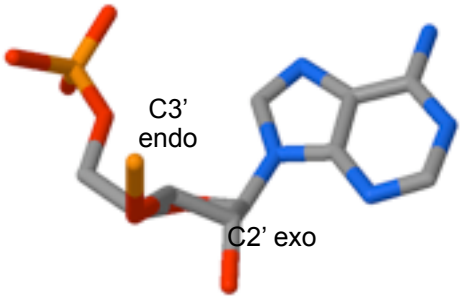
Rise per pair = 2.9Å
c3'-endo

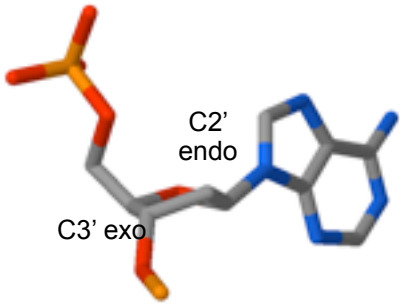
Minor groove width = 11Å
Major groove width = 2.7Å

Minor groove depth = 2.8Å
Major groove depth = 13.5Å



Compare





A-form (RNA)

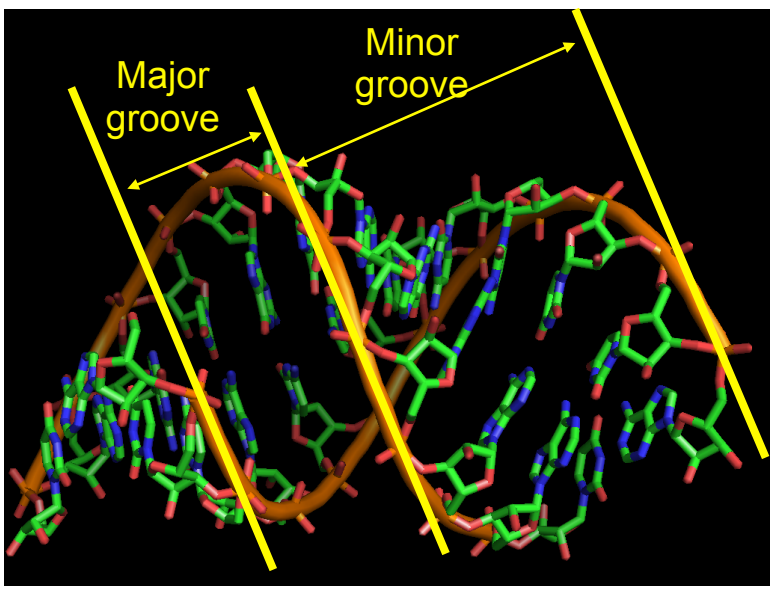
Minor groove width = 11Å
Major groove width = 2.7Å

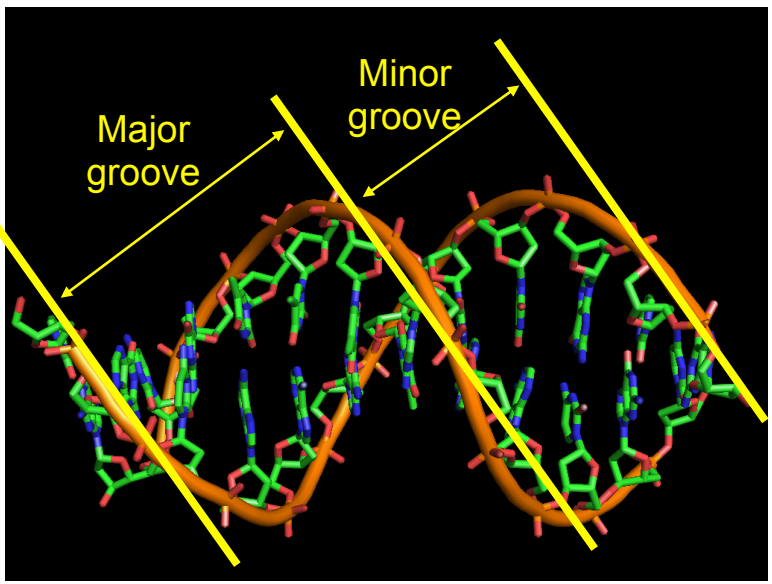
Minor groove depth = 2.8Å
Major groove depth = 13.5Å

B-form (DNA)

Minor groove width = 5.7Å
Major groove width = 11.7Å

Minor groove depth = 7.5Å
Major groove depth = 8.8Å





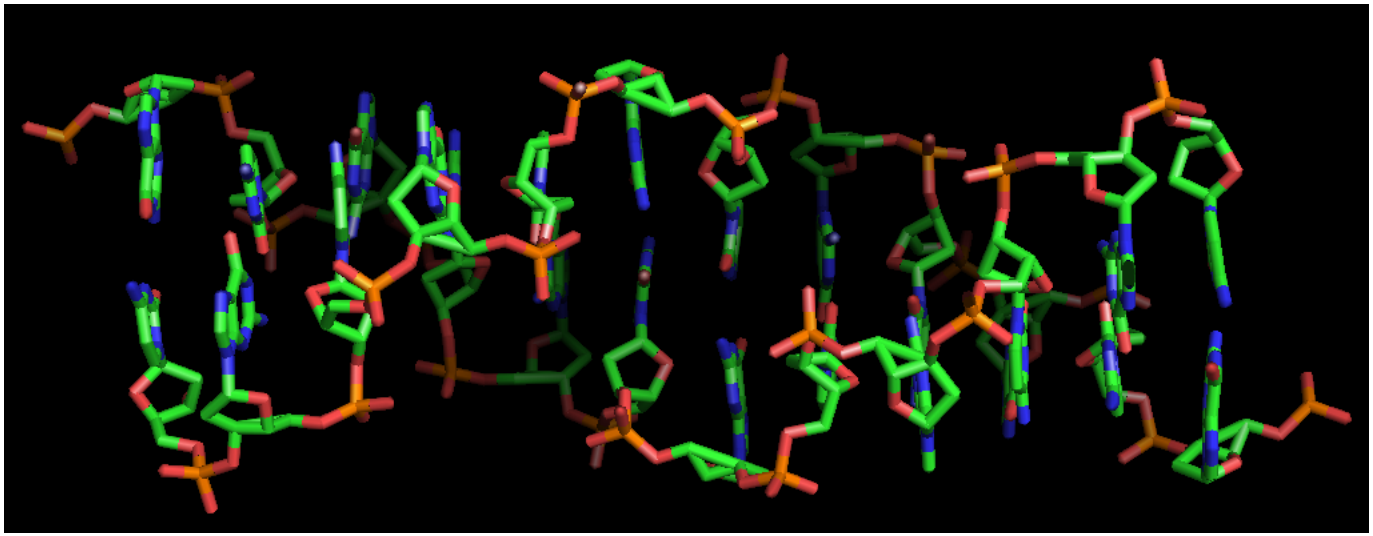
Z-DNA

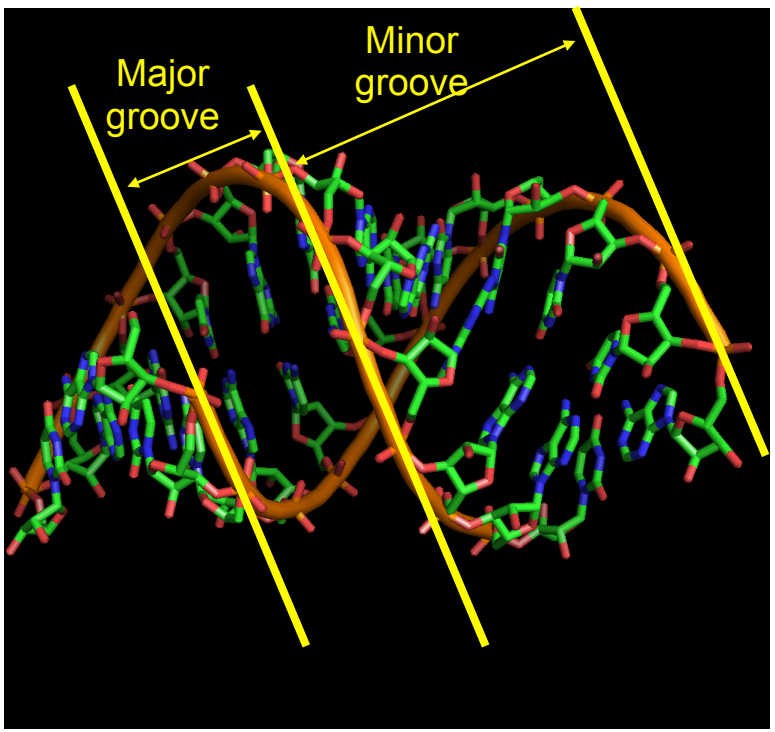
Residues per turn =12
Twist per base pair = -9 / -51°

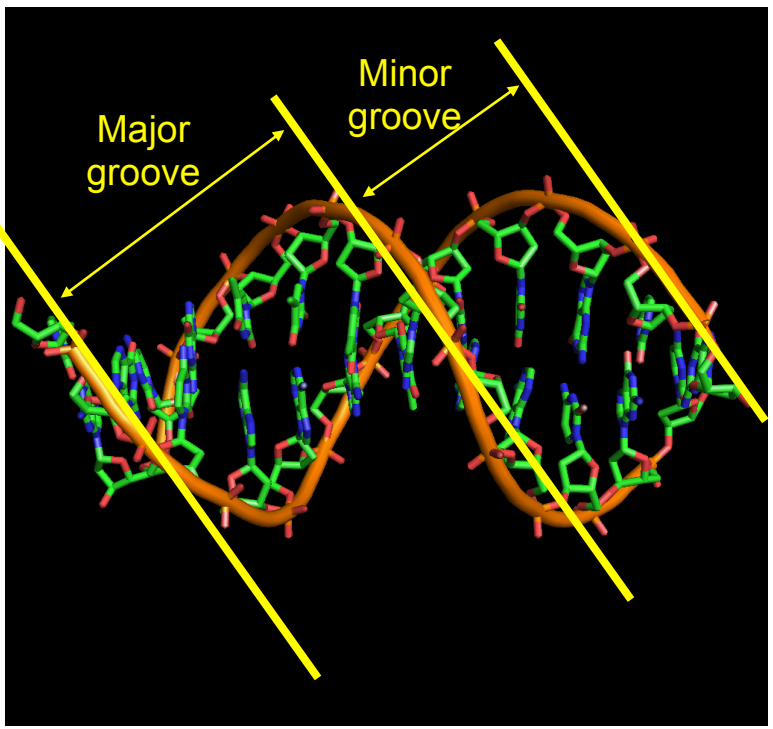
Rise per pair = 3.7Å
c3'-endo(syn) / c2'-endo

Minor groove width = 2.0Å
Major groove width = 8.8Å

Minor groove depth = 13.8Å
Major groove depth = 3.7Å

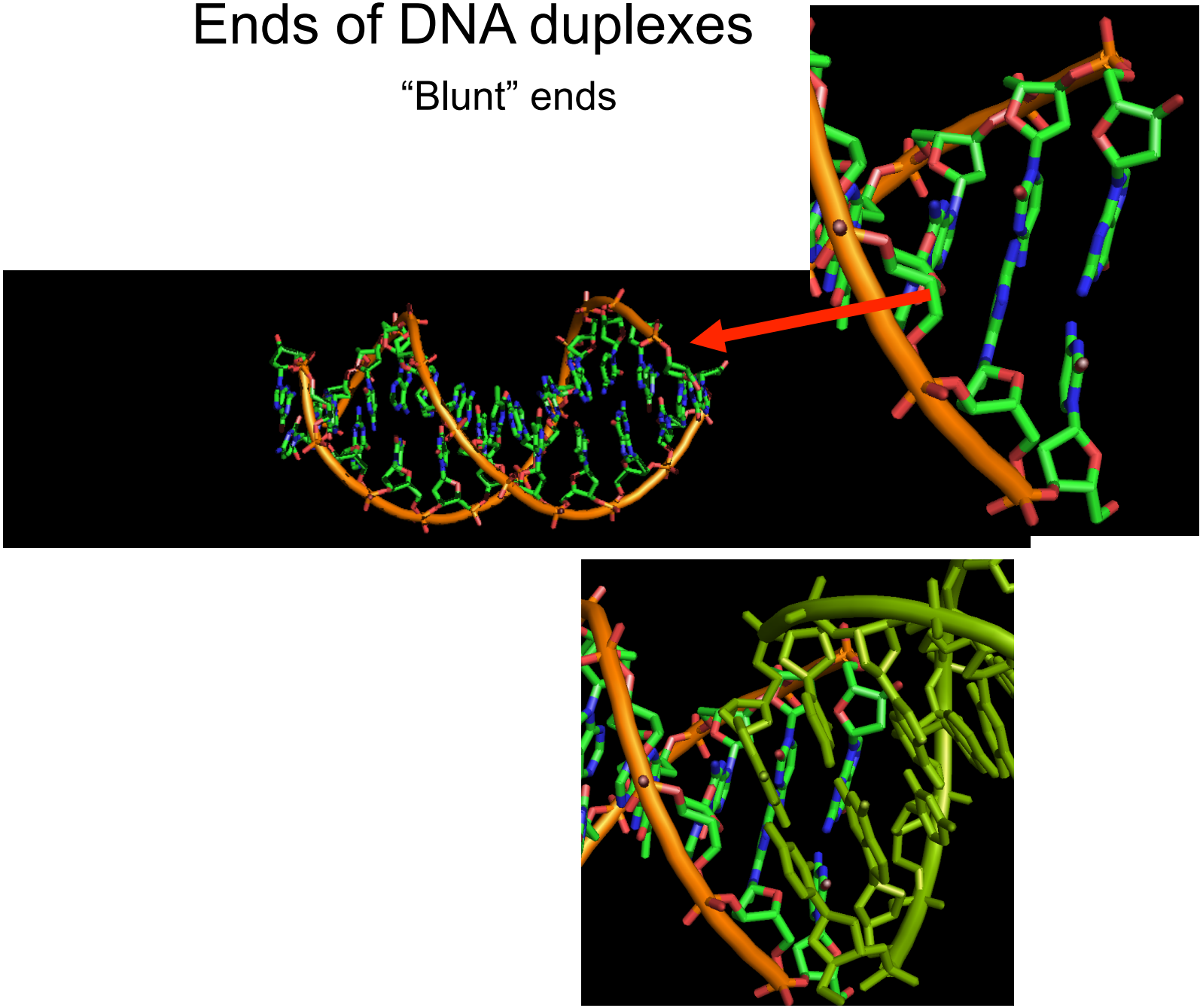






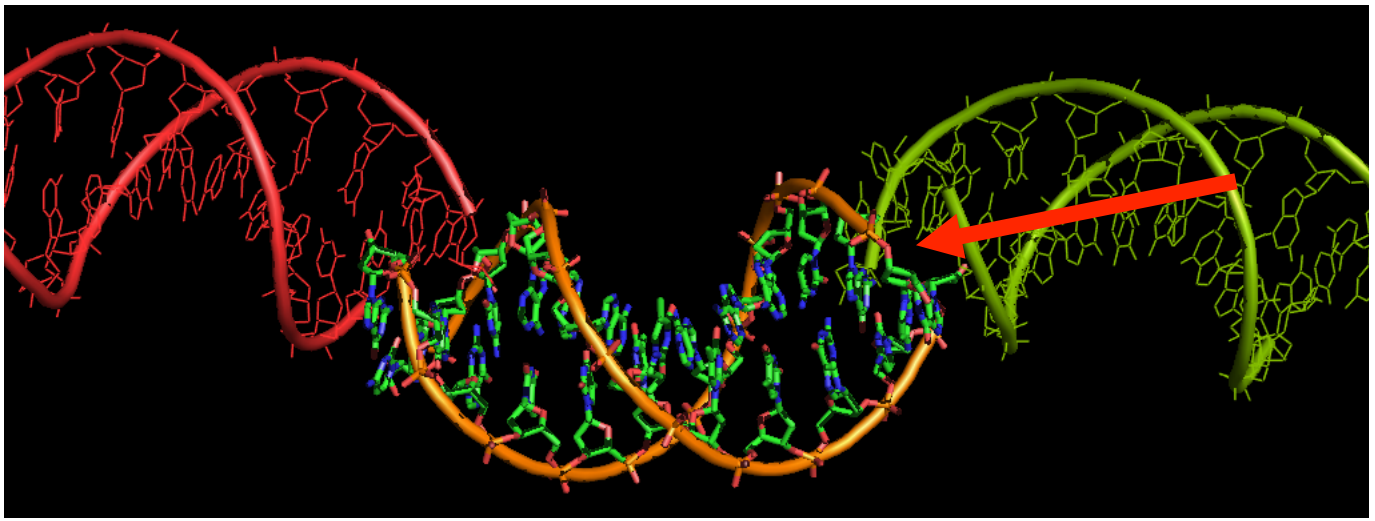
Ends of DNA duplexes

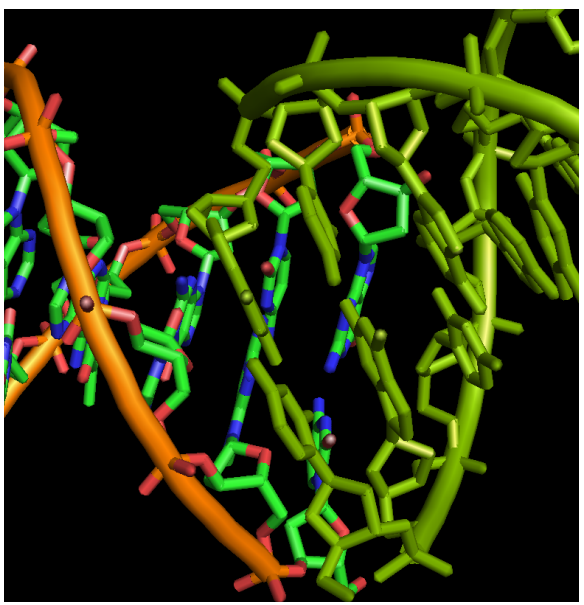
"Blunt" ends



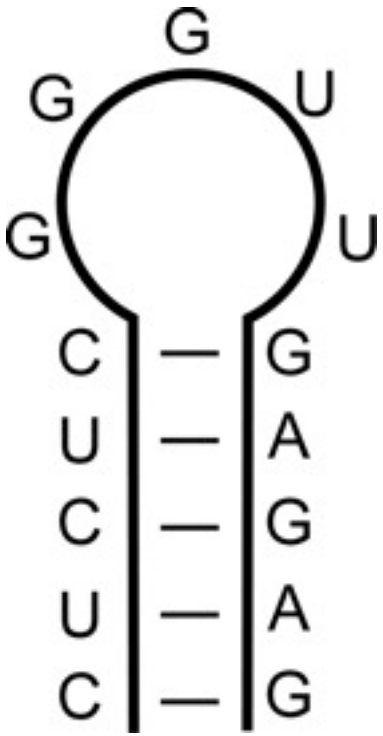
Ends of DNA duplexes

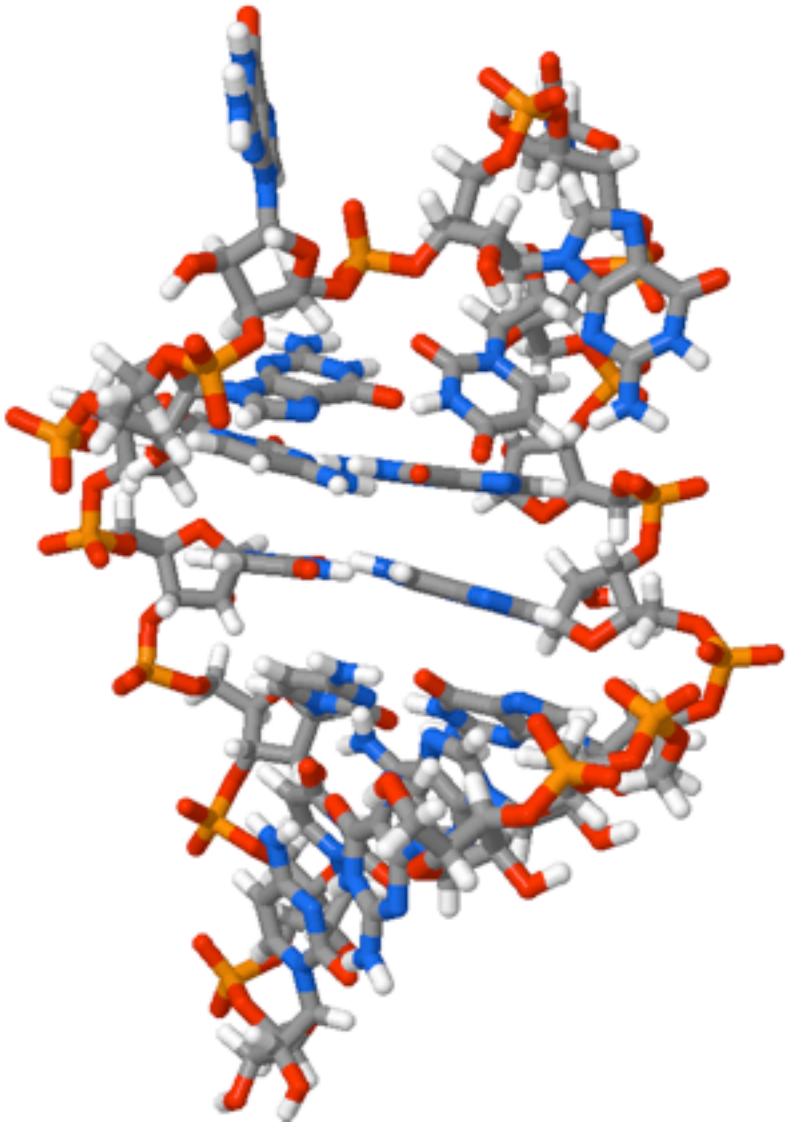
"Blunt" ends



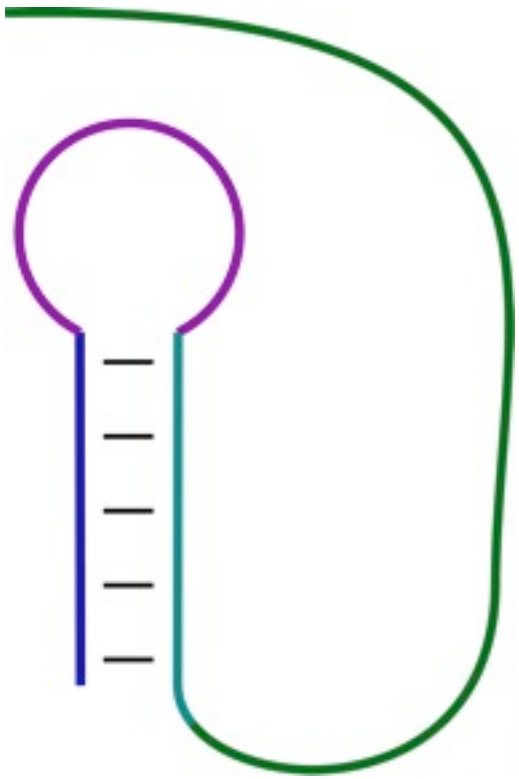


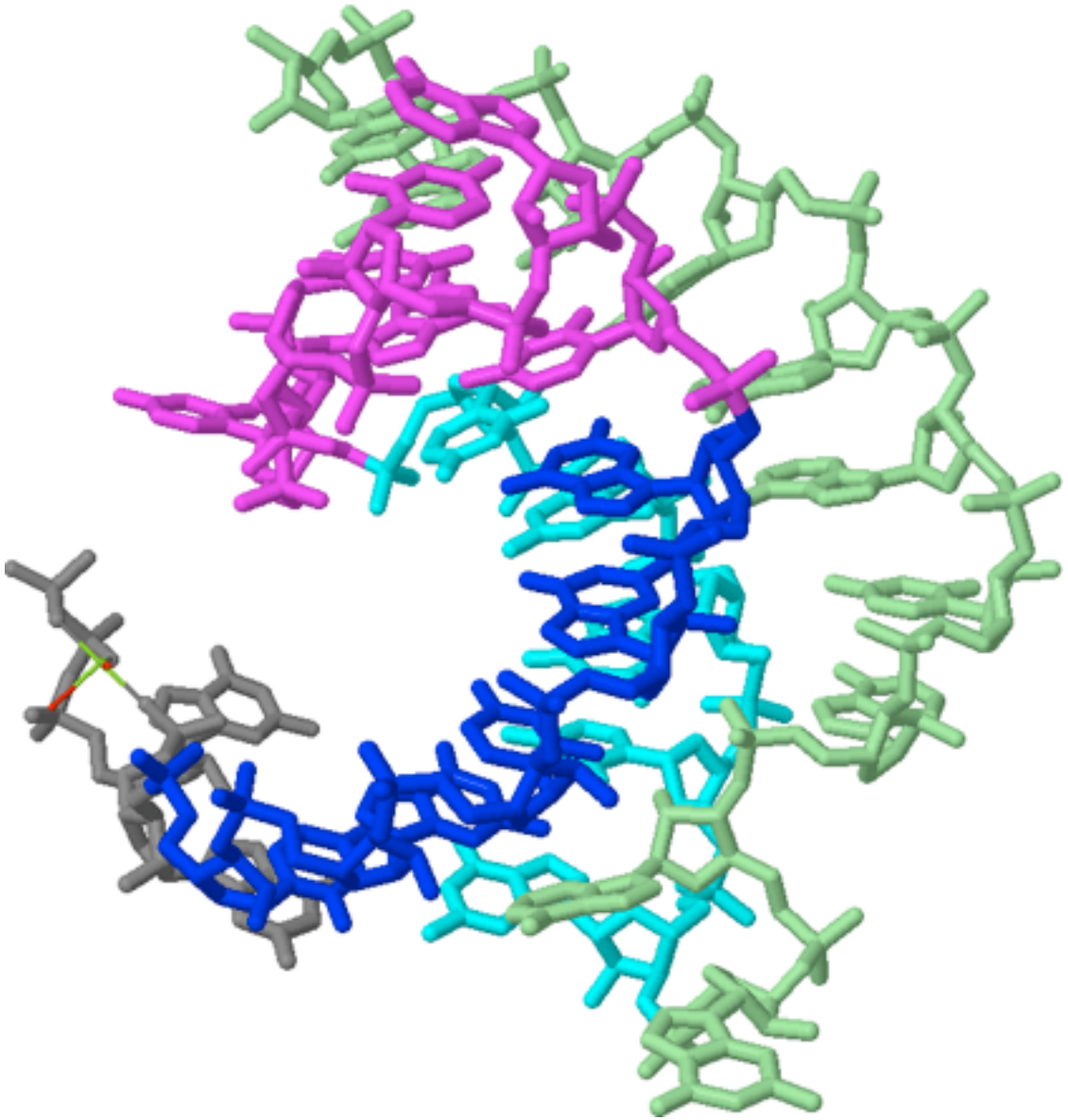
Simple Structure - Hairpin



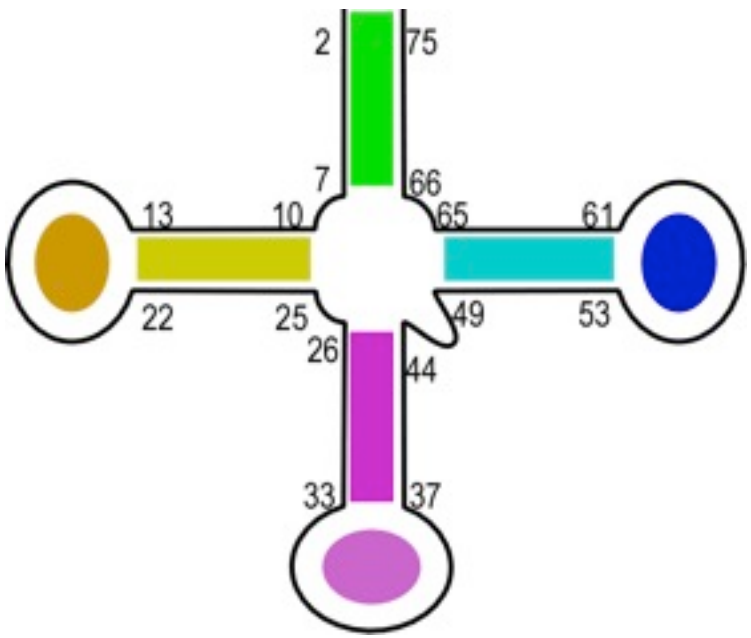


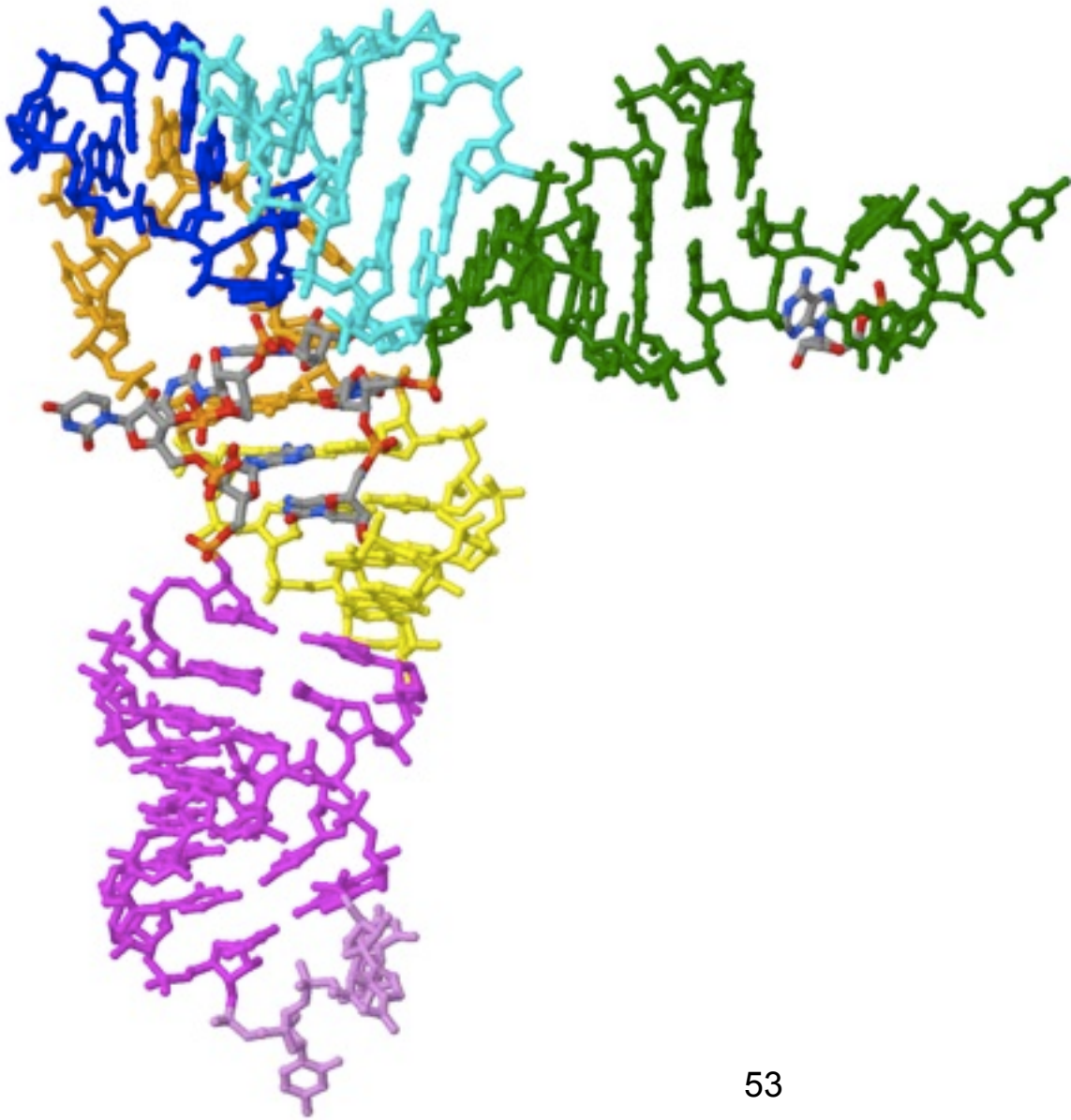
Classic Structure - Pseudoknot



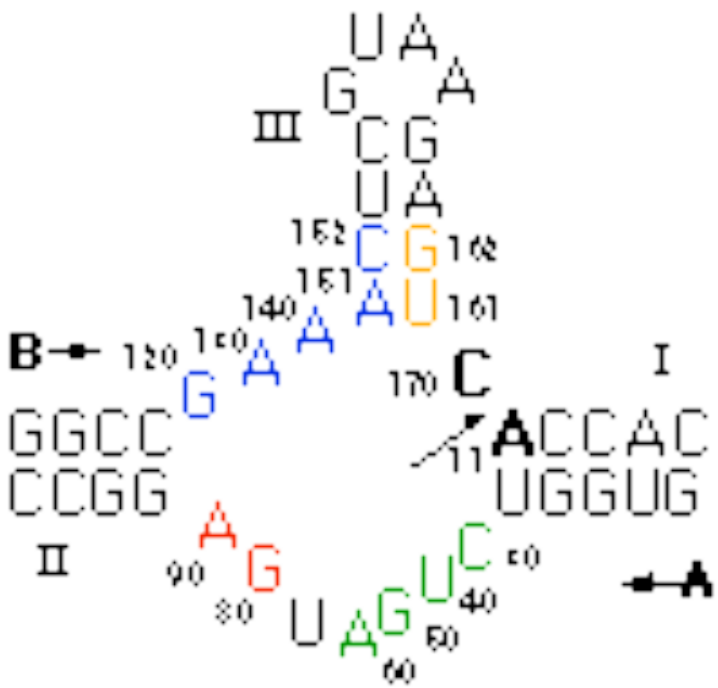


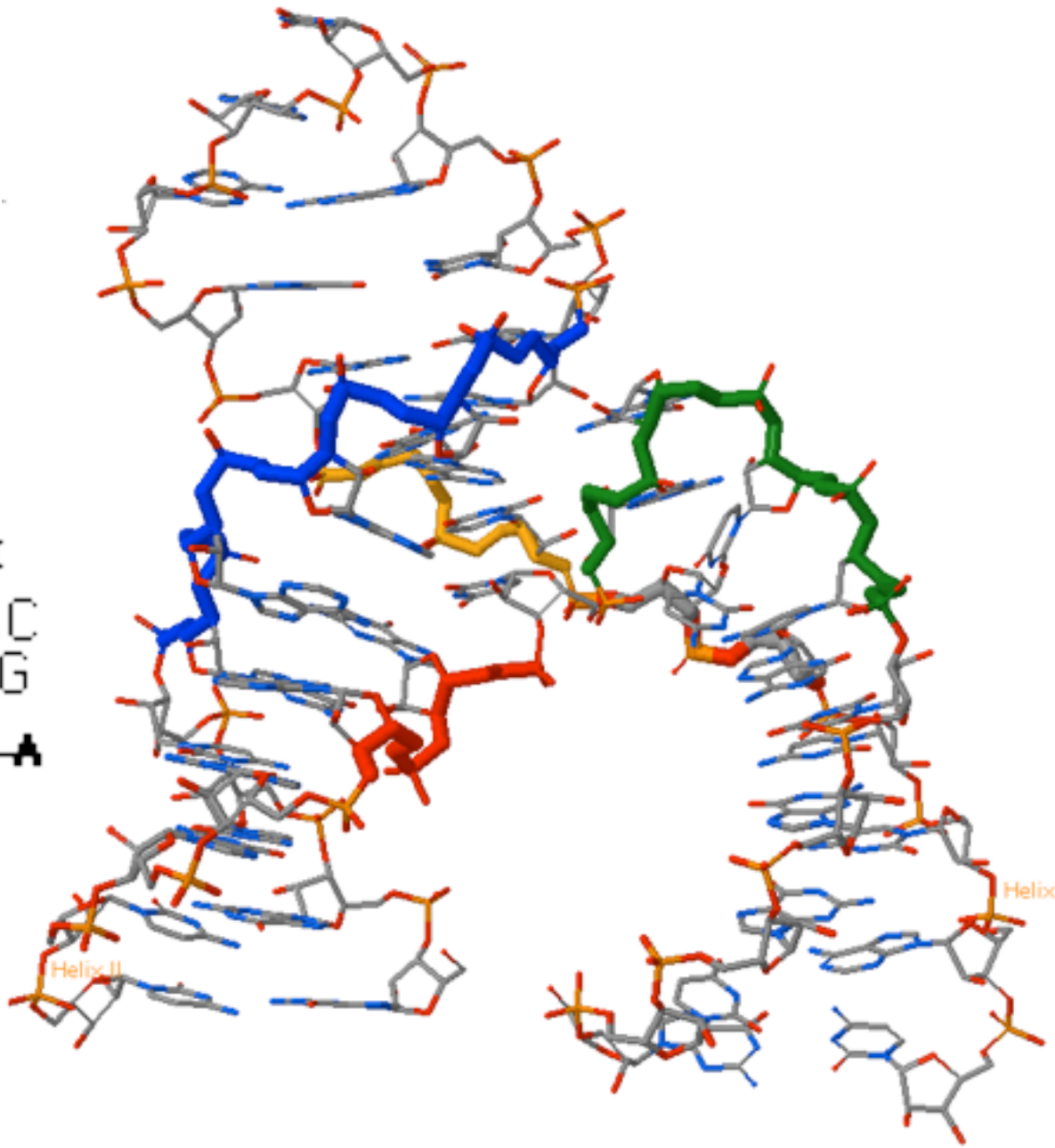
tRNA



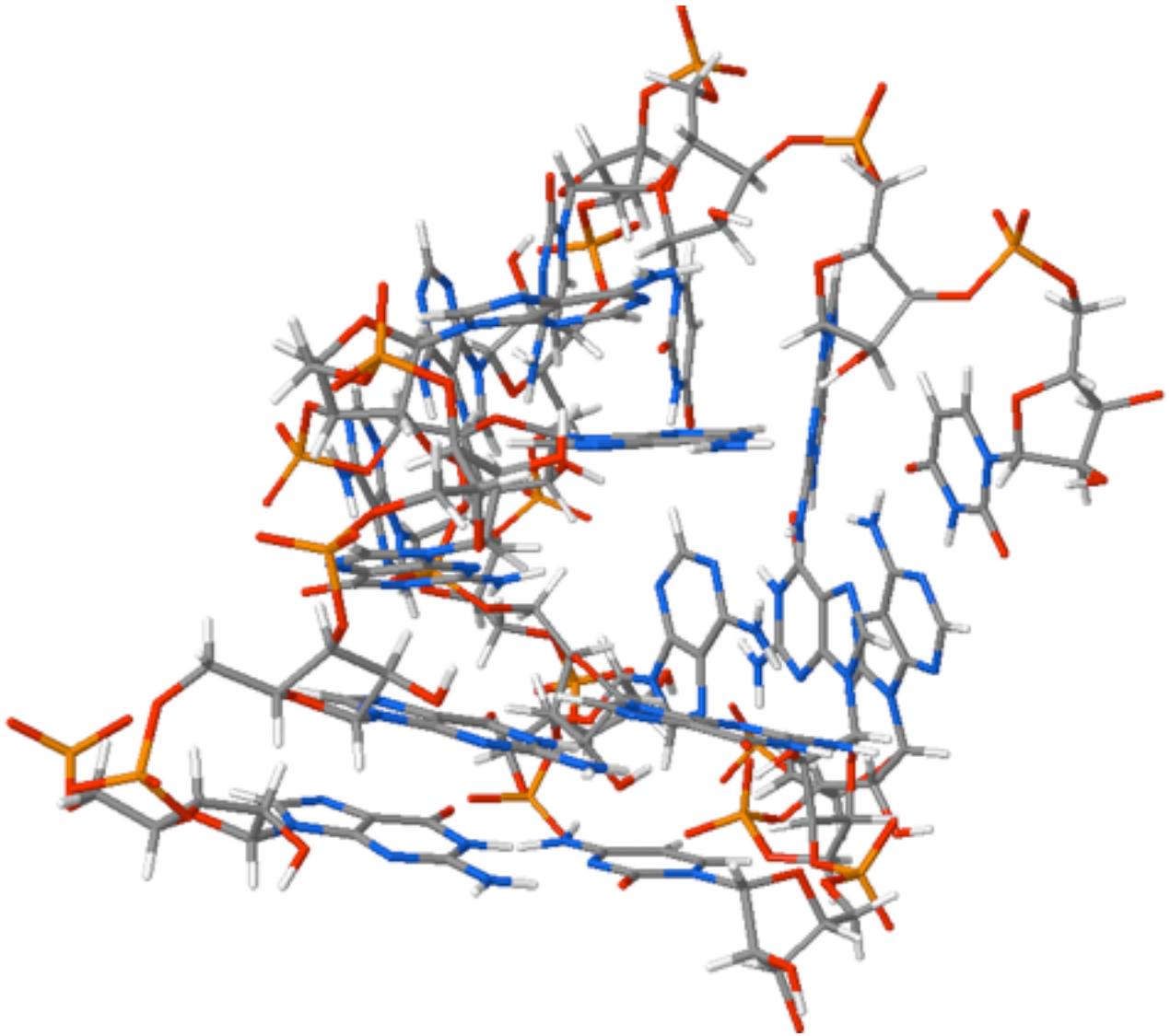


Hammerhead Ribozyme

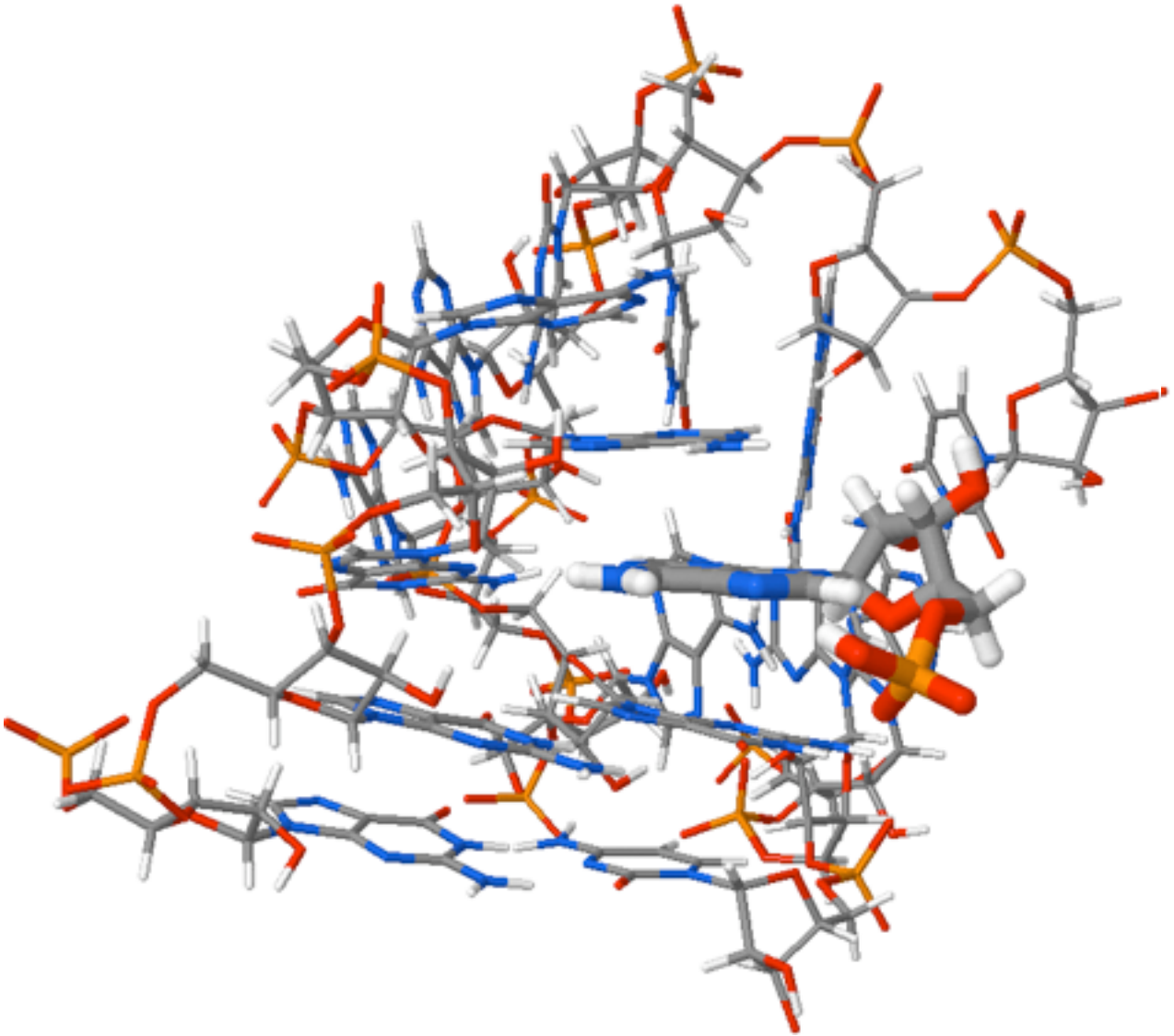




AMP Aptamer

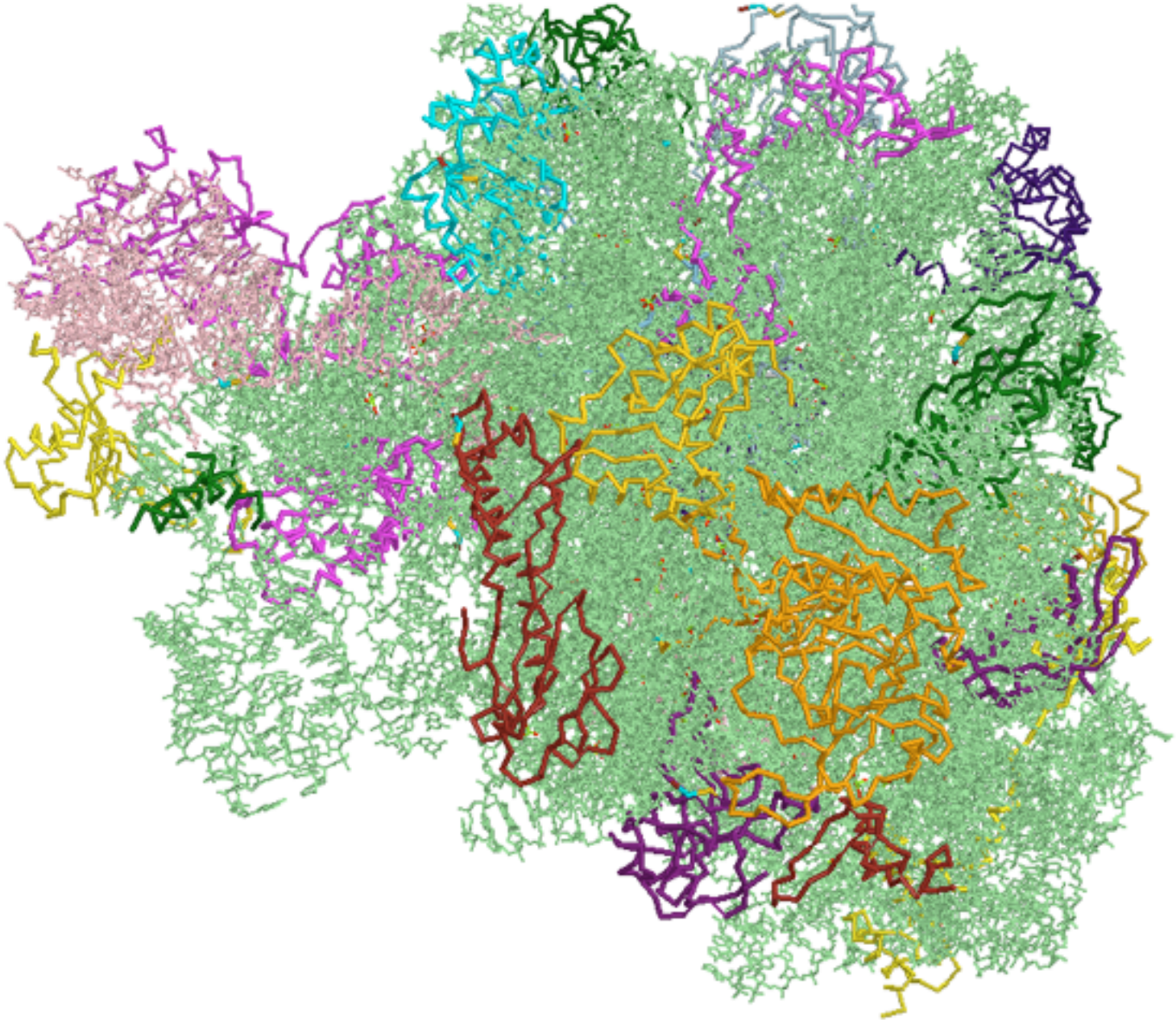


AMP Aptamer



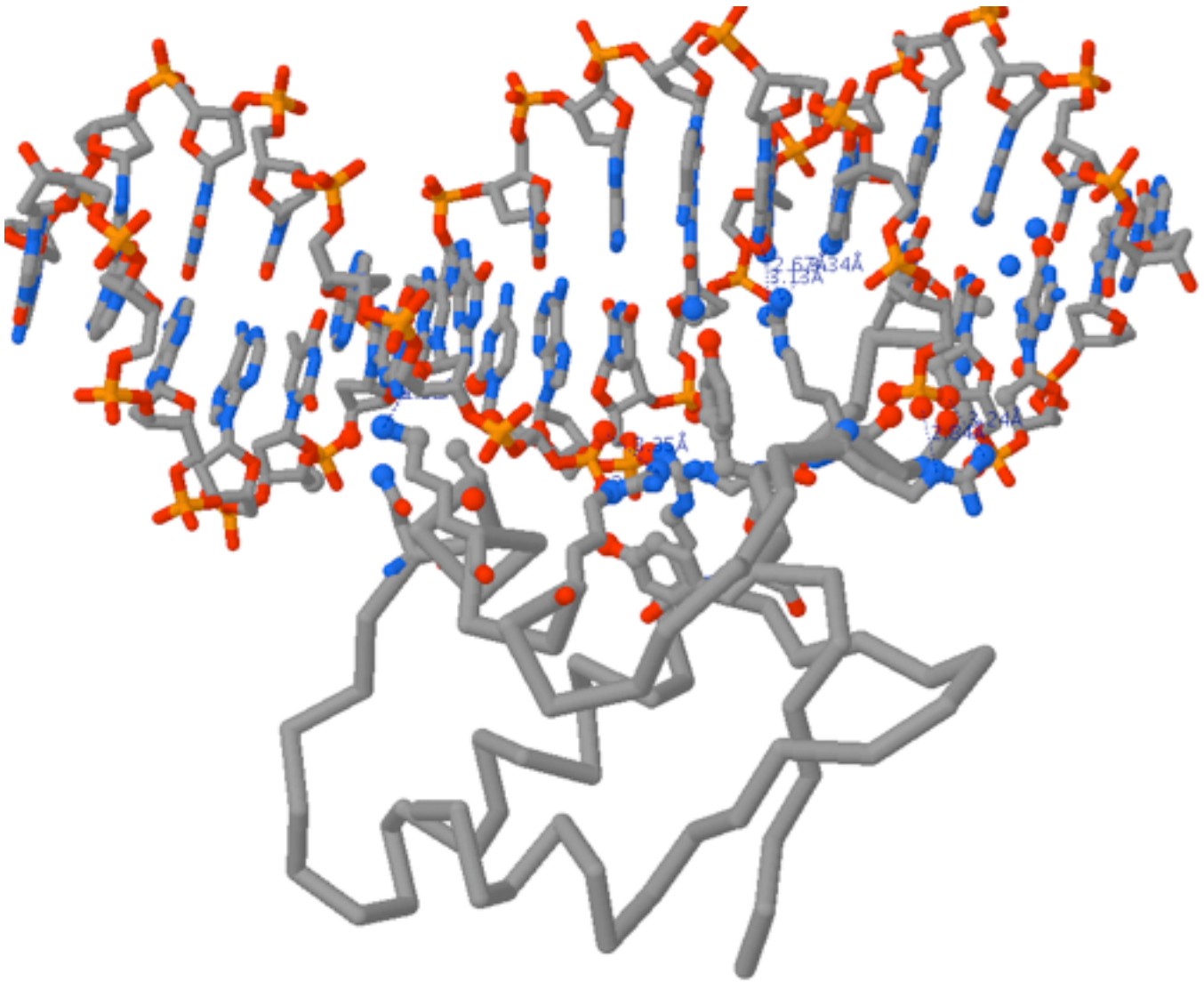
Ribosome

An RNA machine with protein cofactors



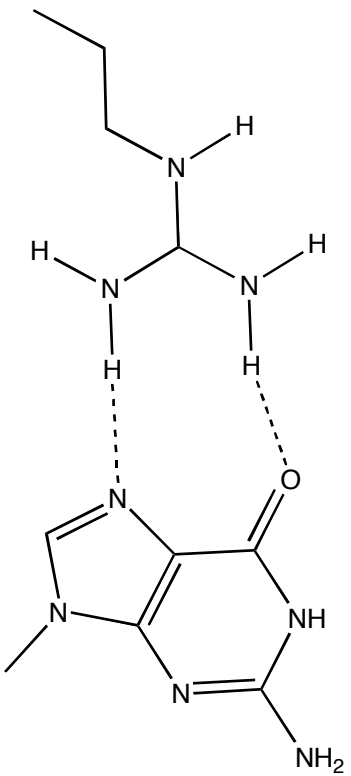
Winged Helix DNA Binding Domain

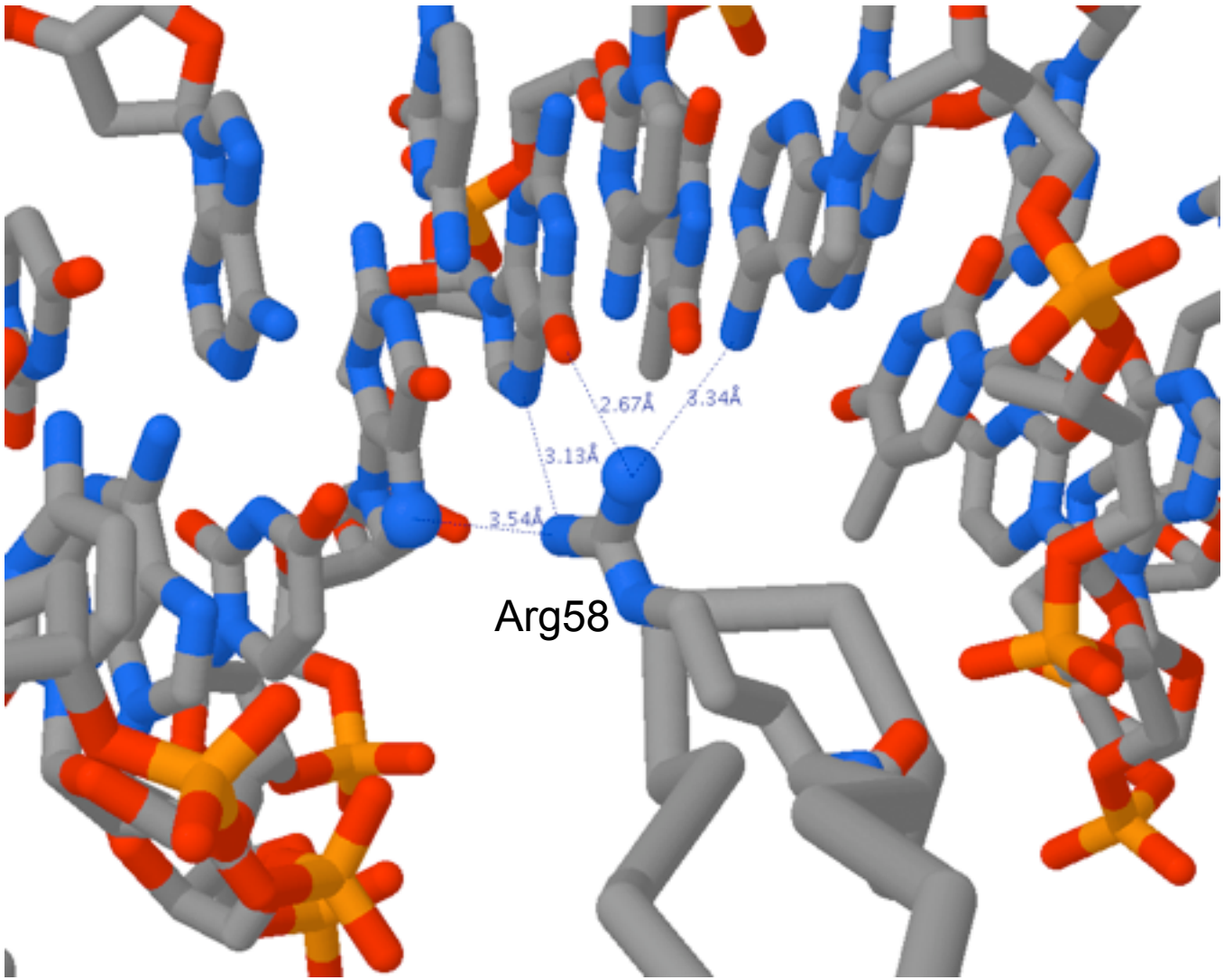
Classic helix-turn-helix



Winged Helix DNA Binding Domain

Classic helix-turn-helix





Hrfx1 bound to its X-box binding site