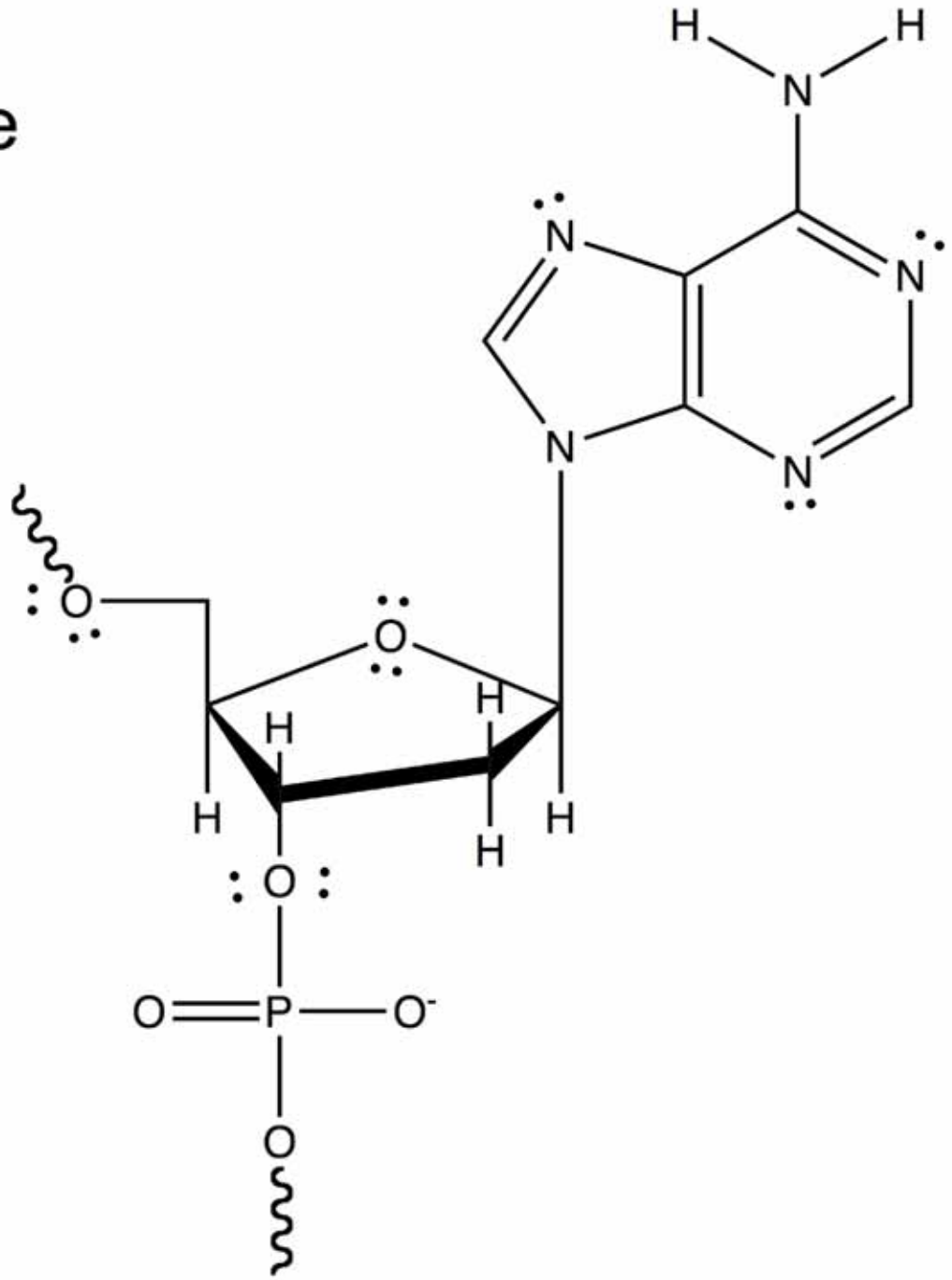
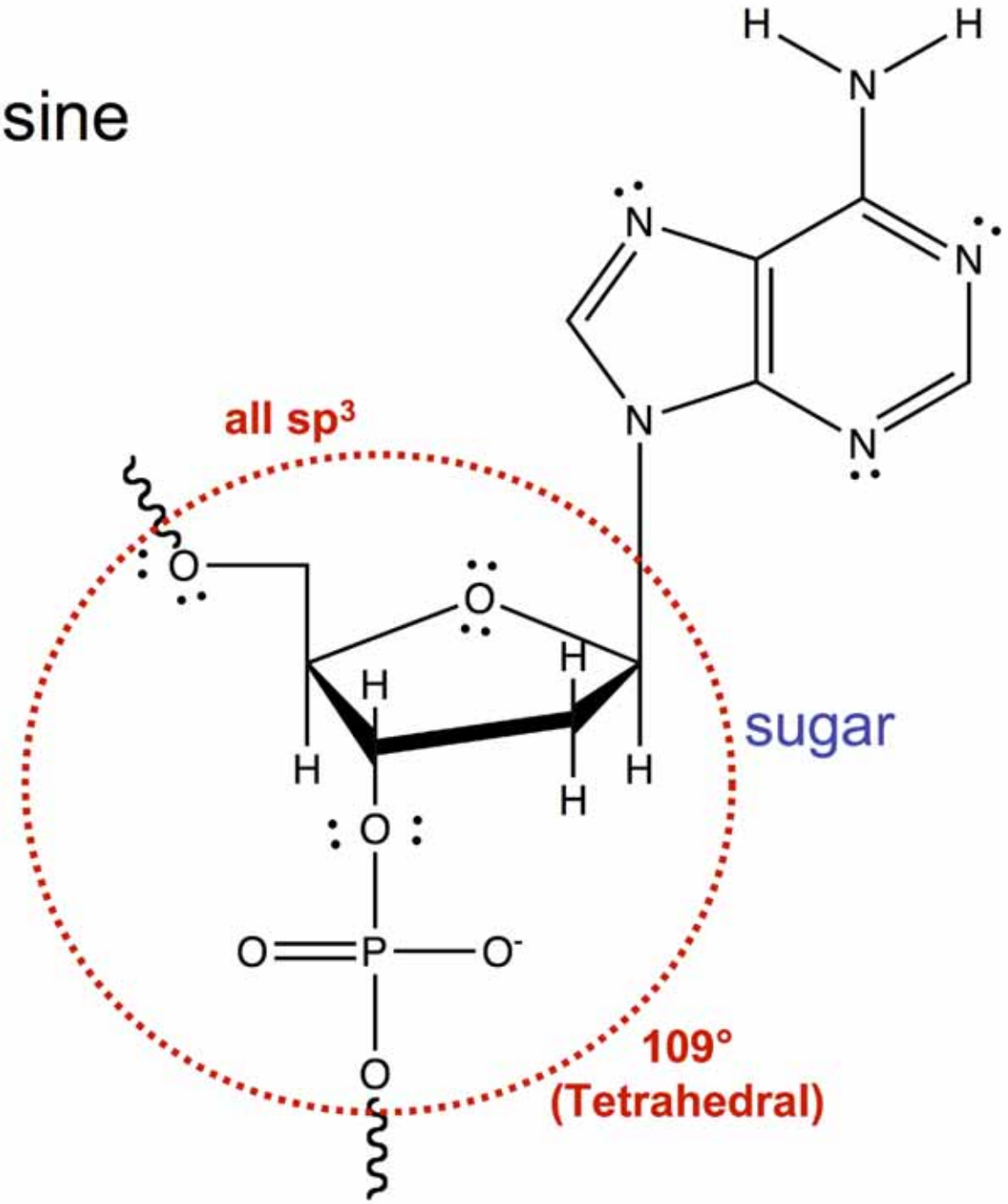
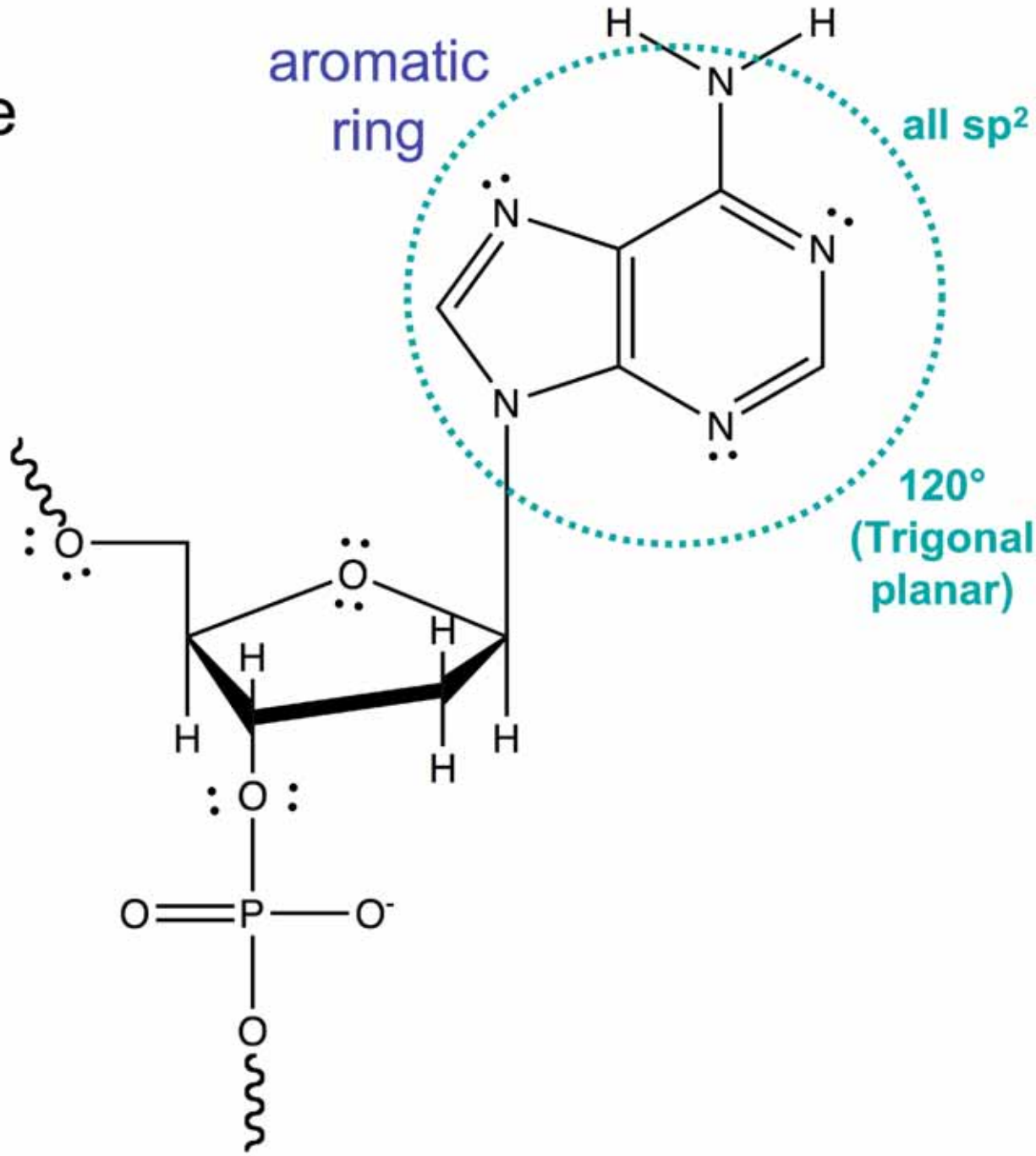
Adenosine



Adenosine

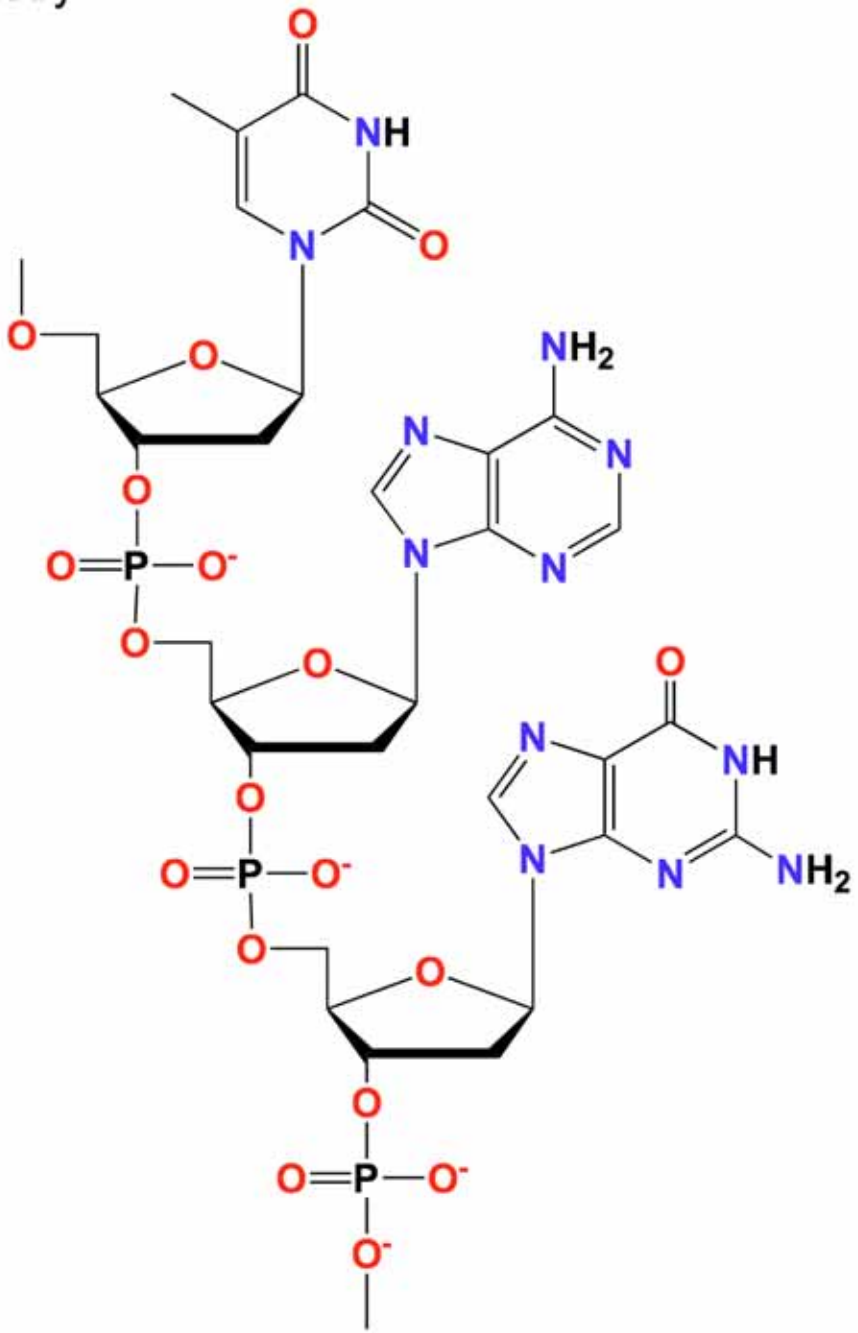


Adenosine


aromatic ring
all sp²
120° (Trigonal planar)
H
H
N
N
N
N
N
O
O
H
H
H
H
H
O
O
P
O
O
O

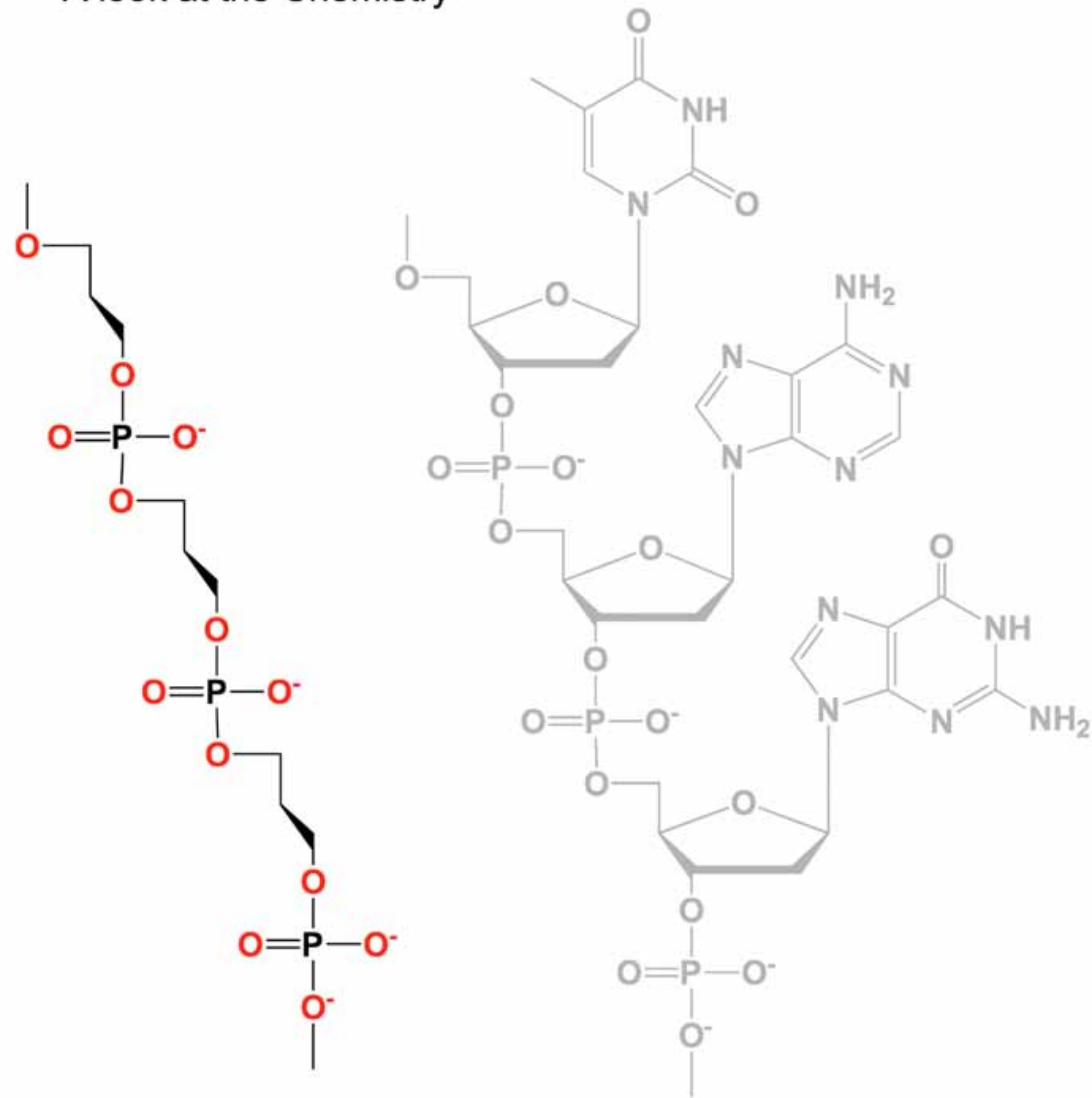
DNA

A look at the Chemistry



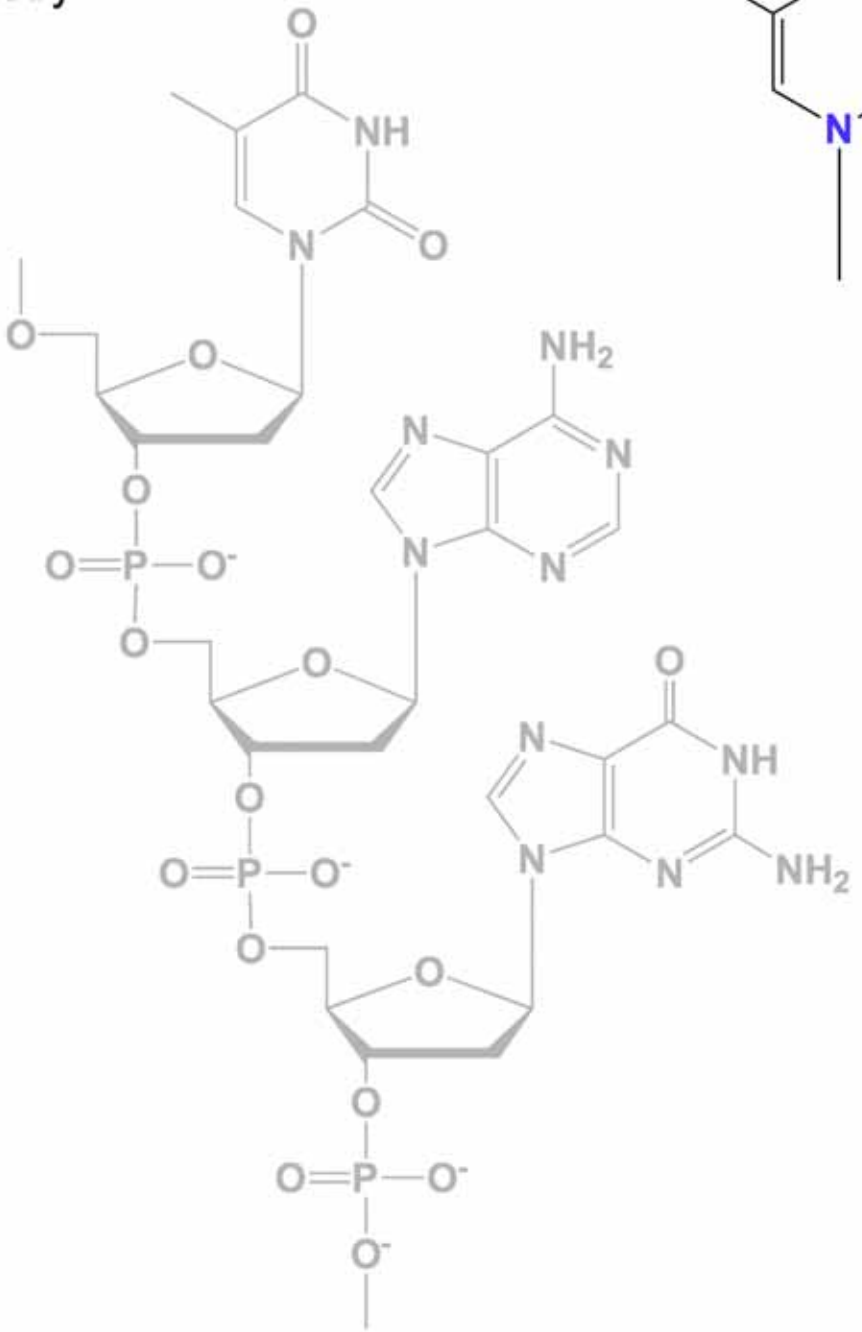
DNA

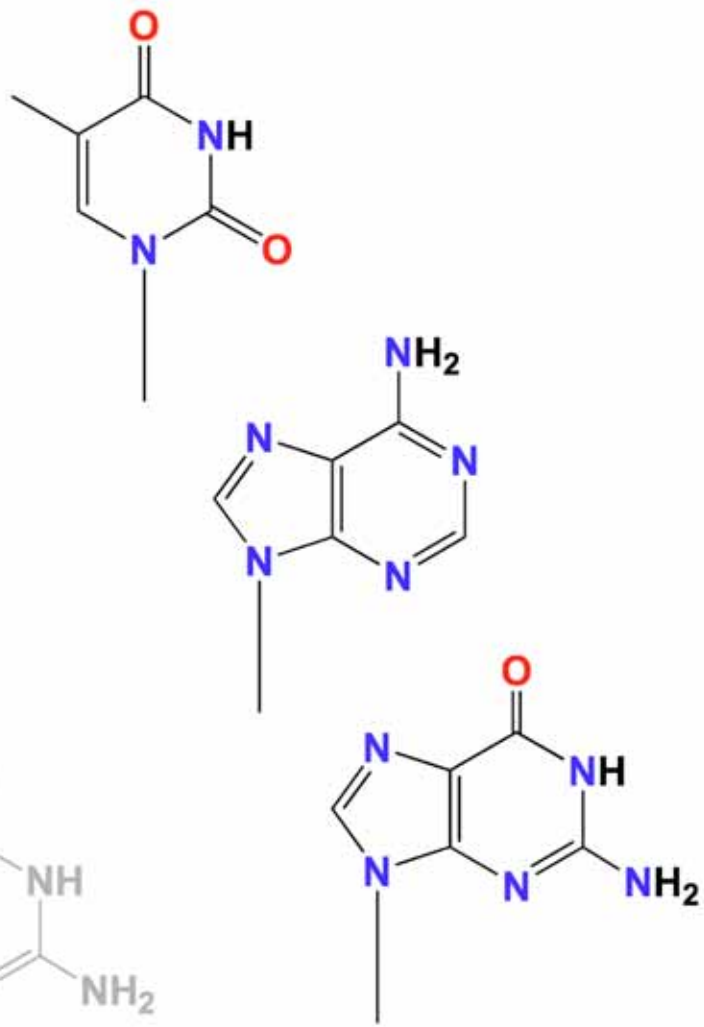
A look at the Chemistry



DNA

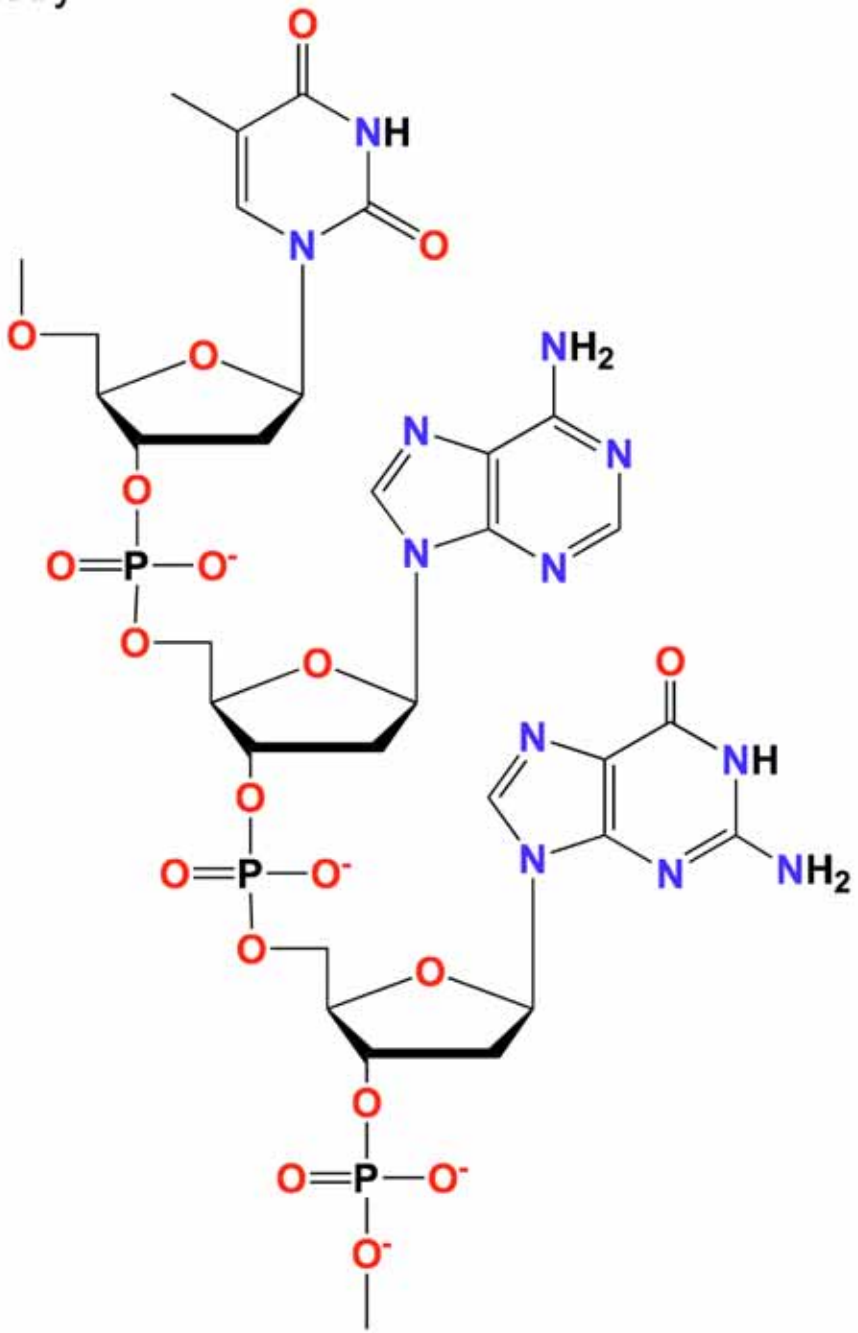
A look at the Chemistry





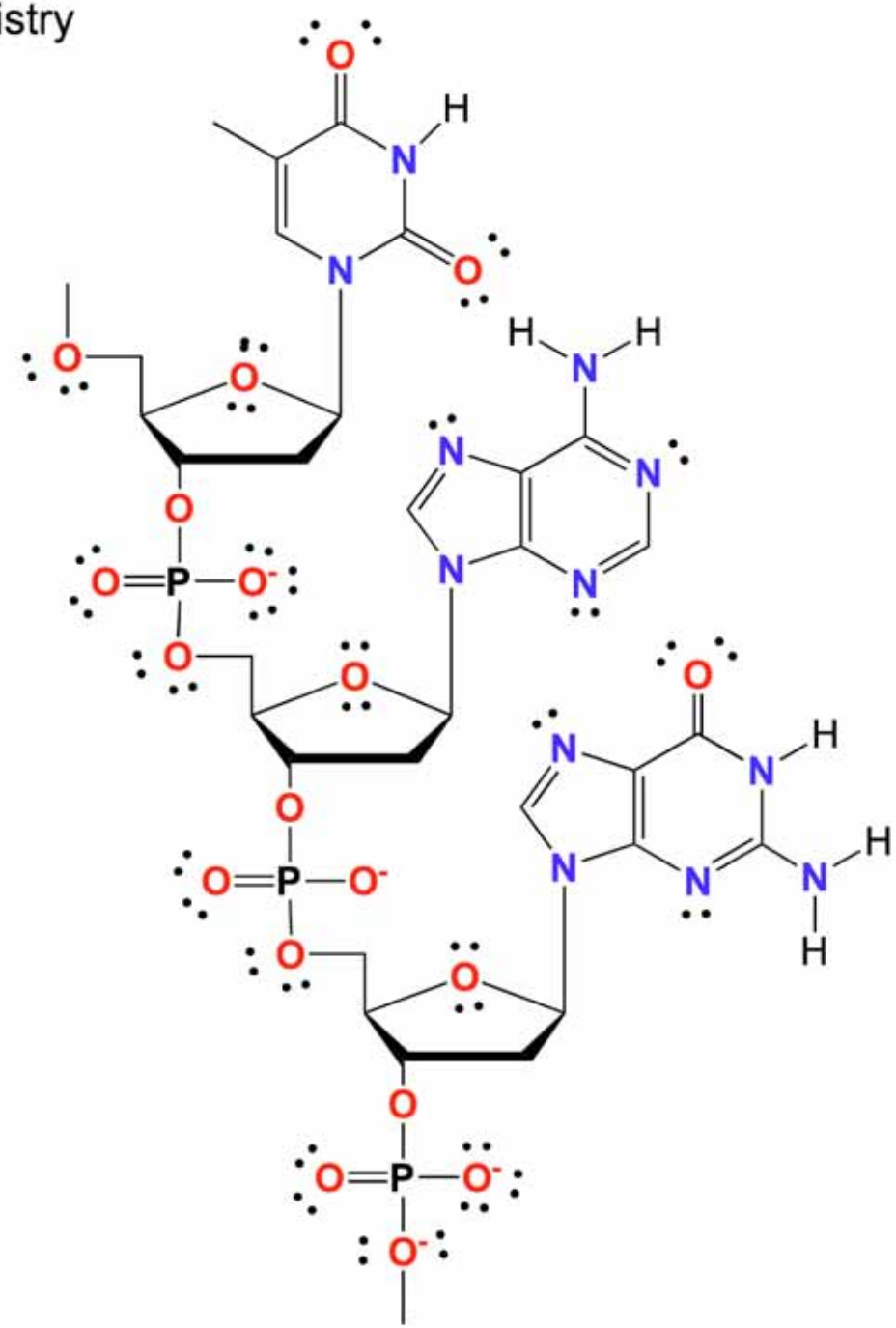
DNA

A look at the Chemistry



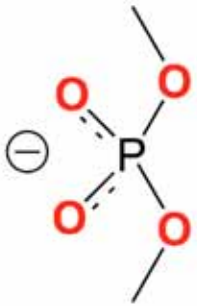
DNA

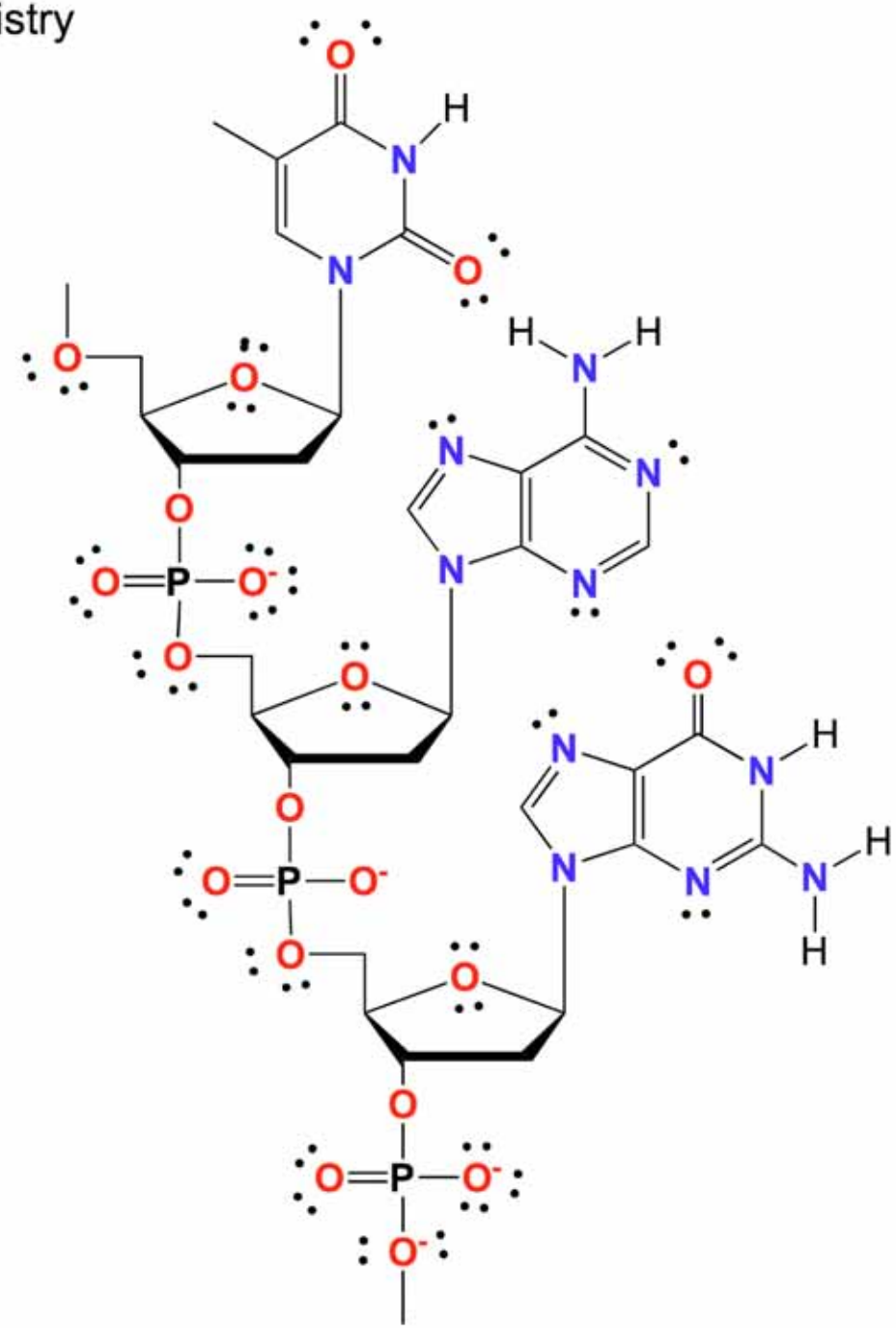
A look at the Chemistry



DNA

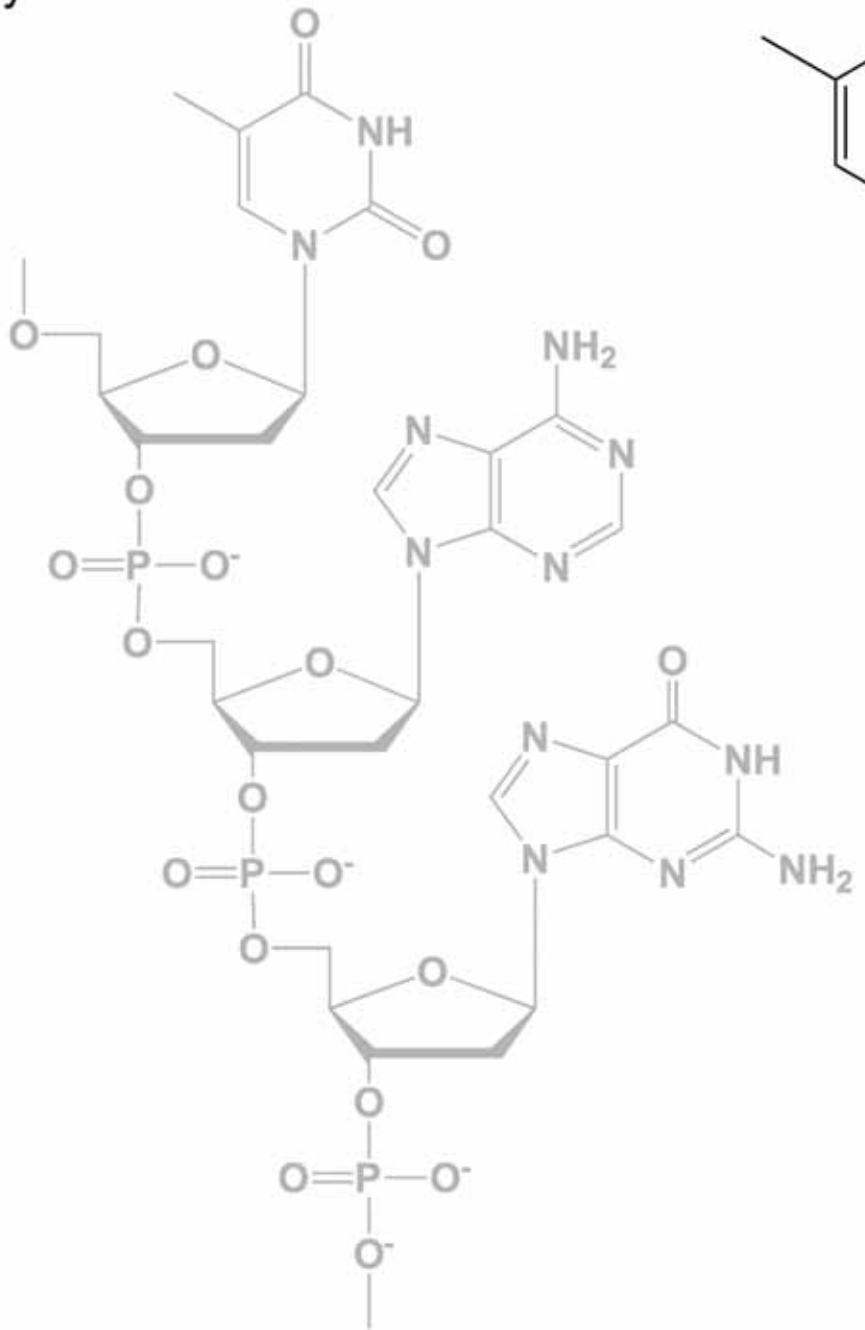
A look at the Chemistry

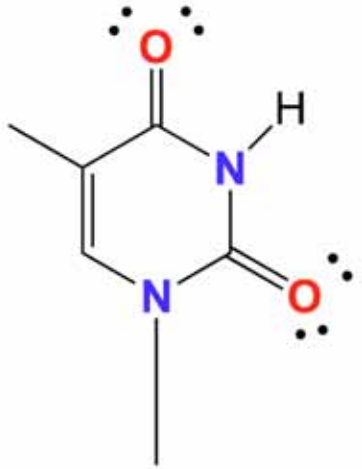




DNA

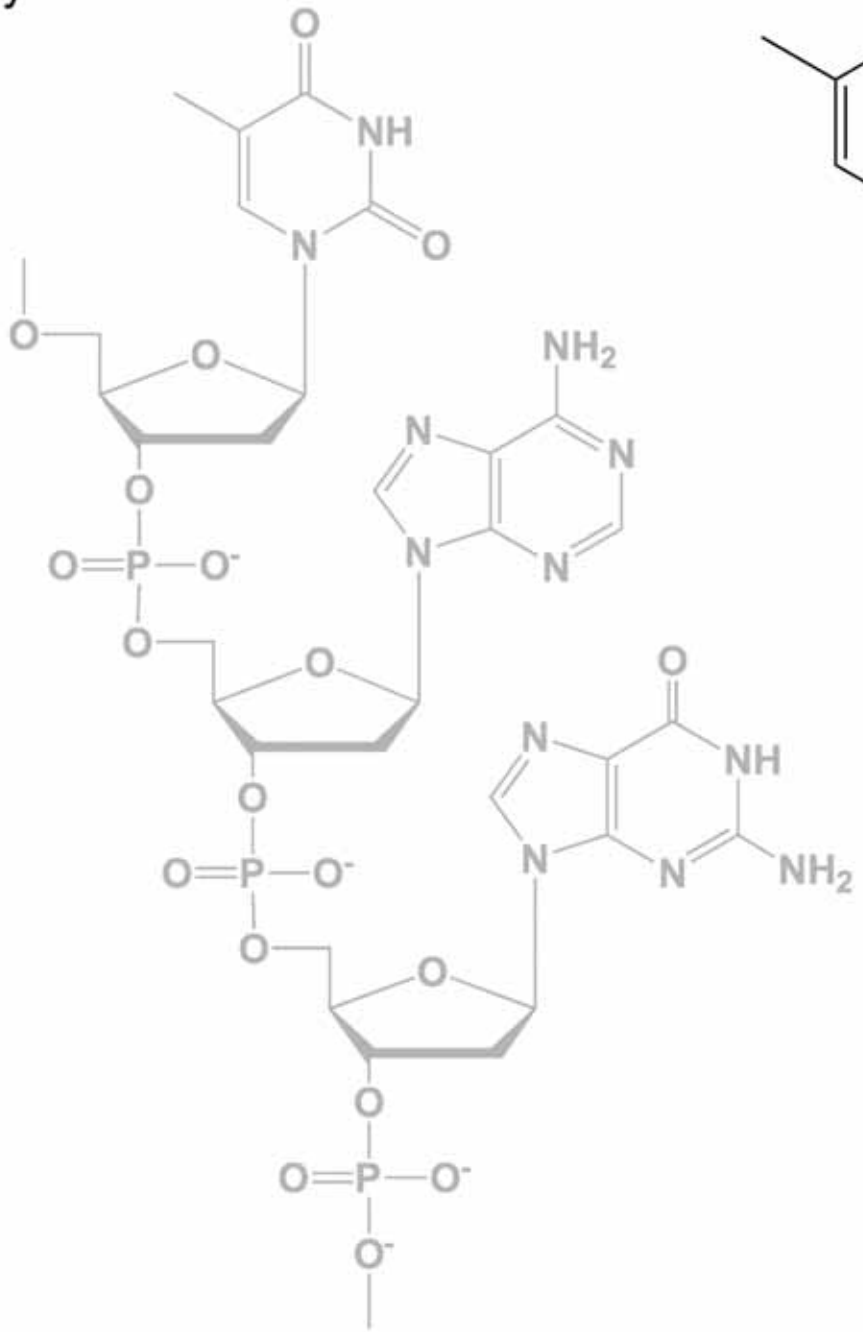
A look at the Chemistry

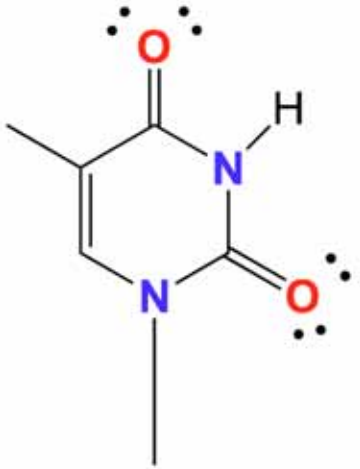


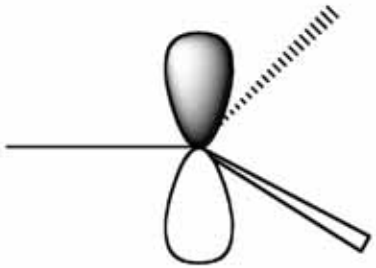


DNA

A look at the Chemistry

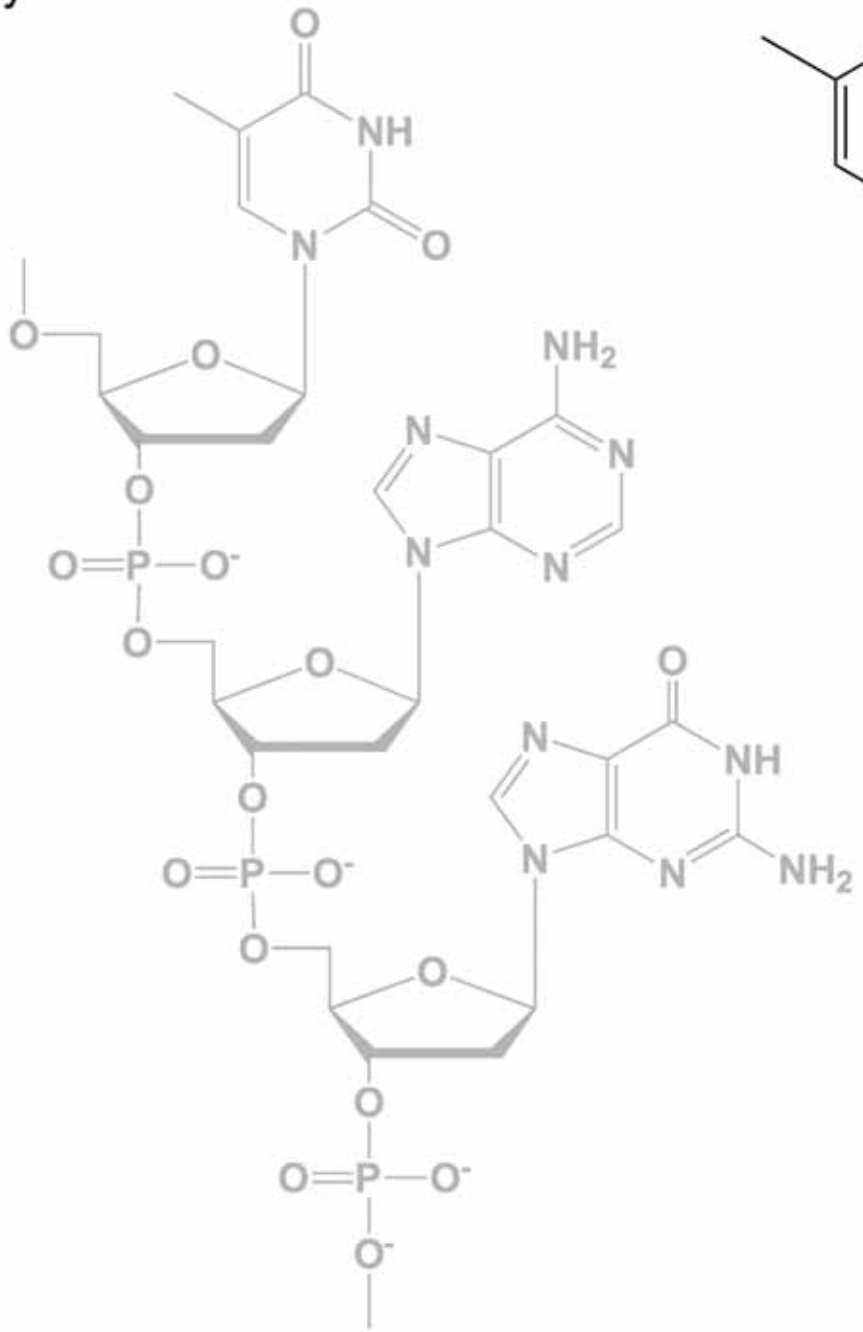


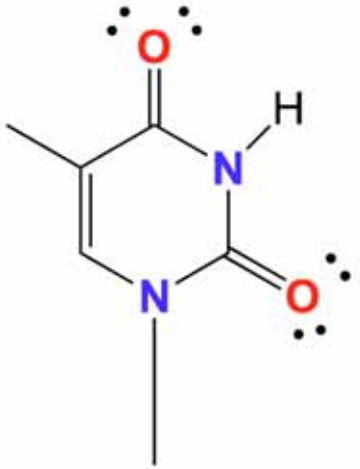


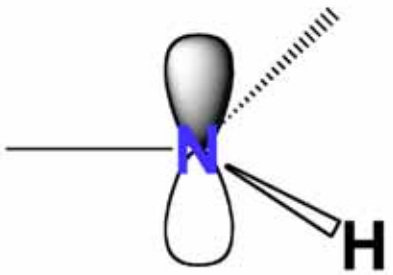


DNA

A look at the Chemistry

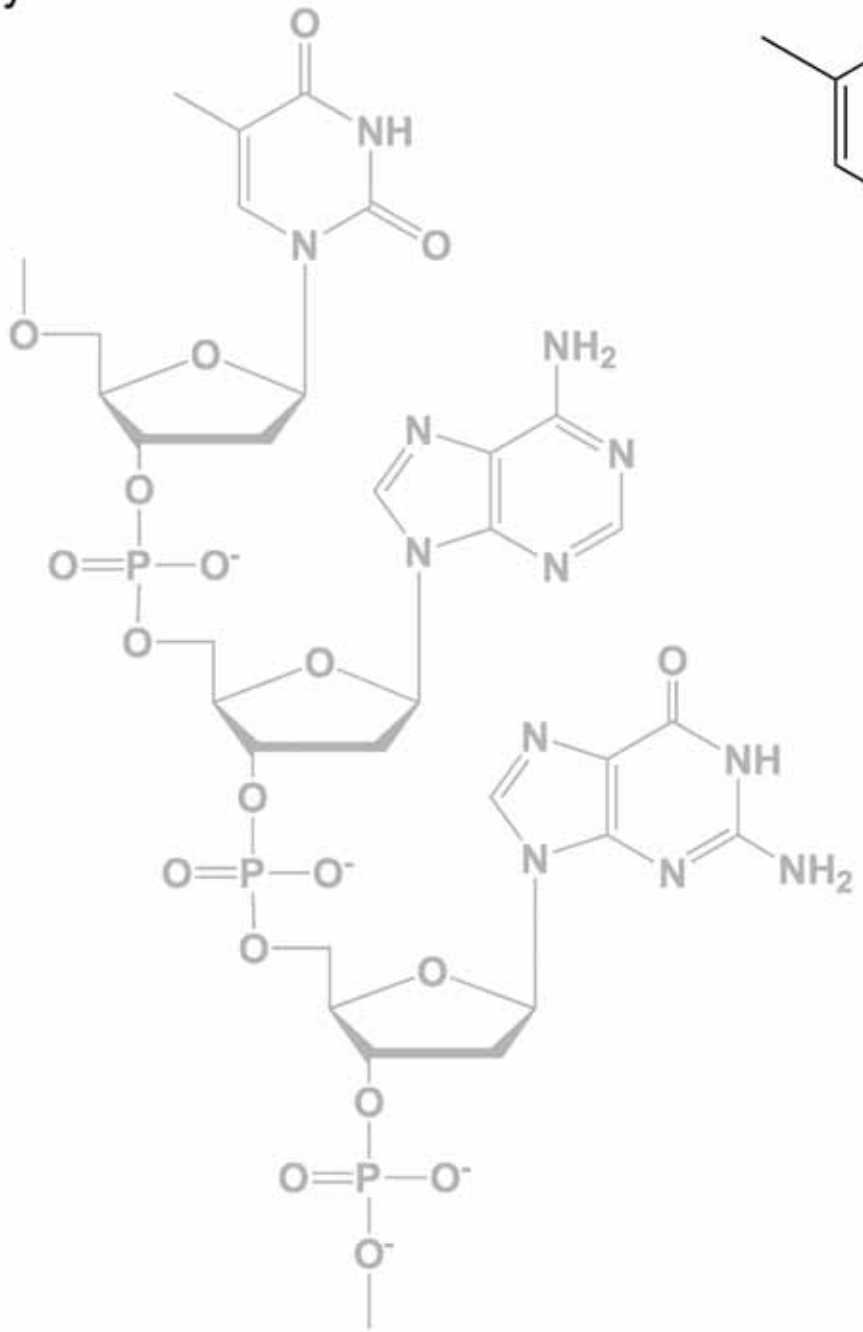


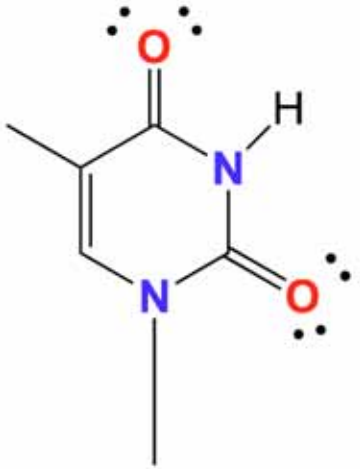


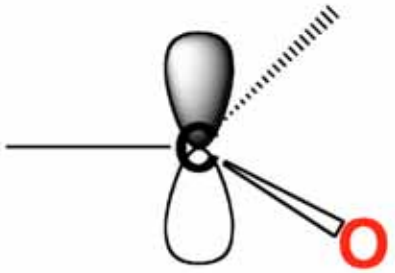


DNA

A look at the Chemistry

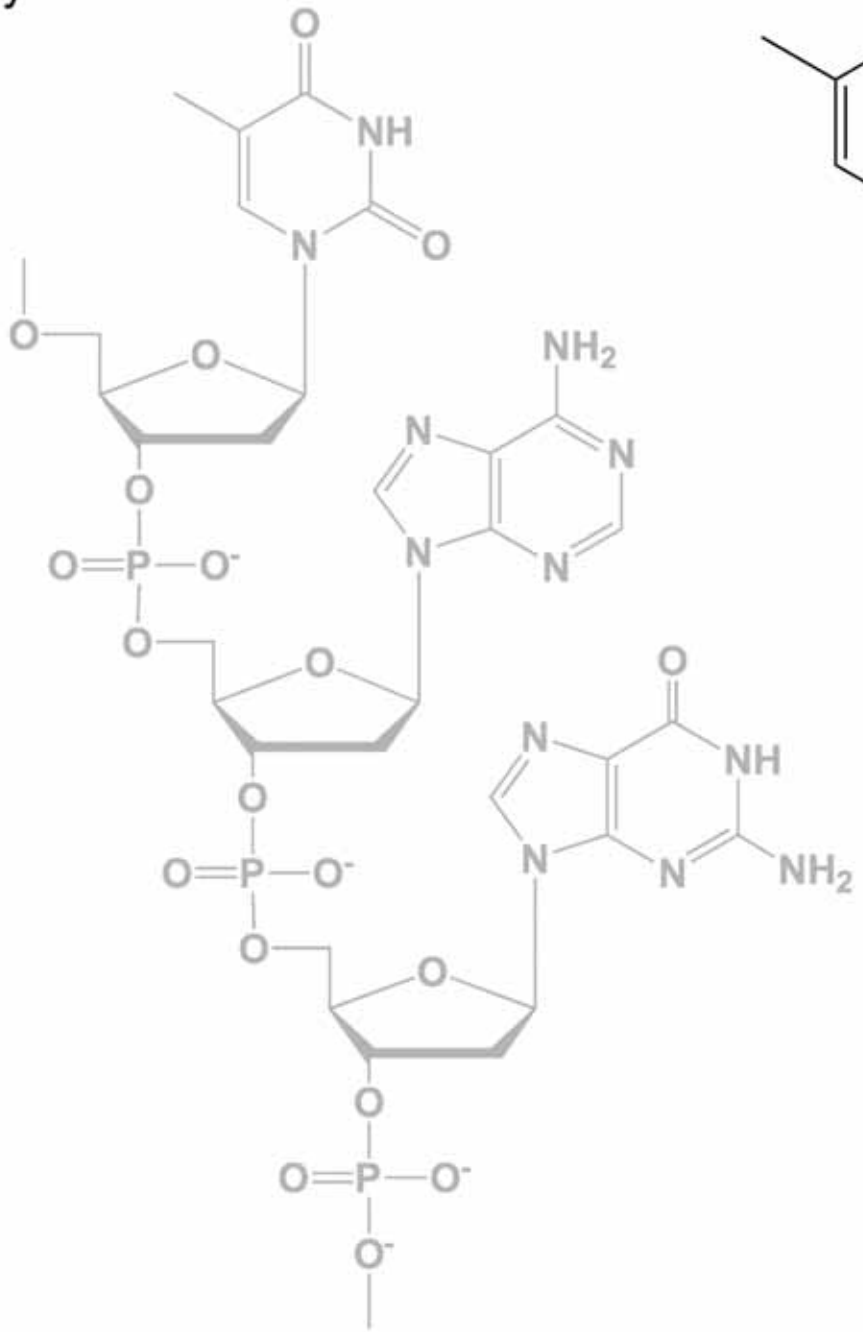


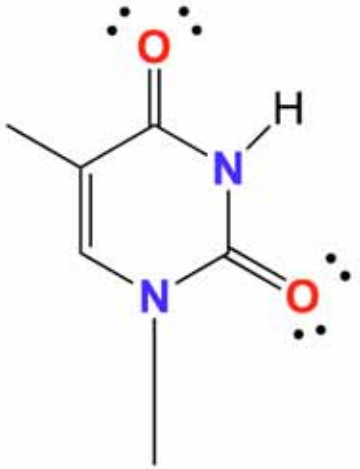


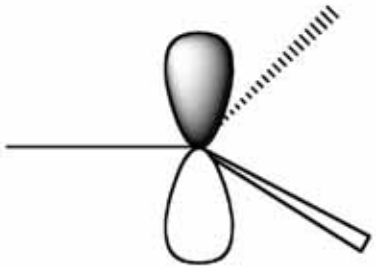


DNA

A look at the Chemistry

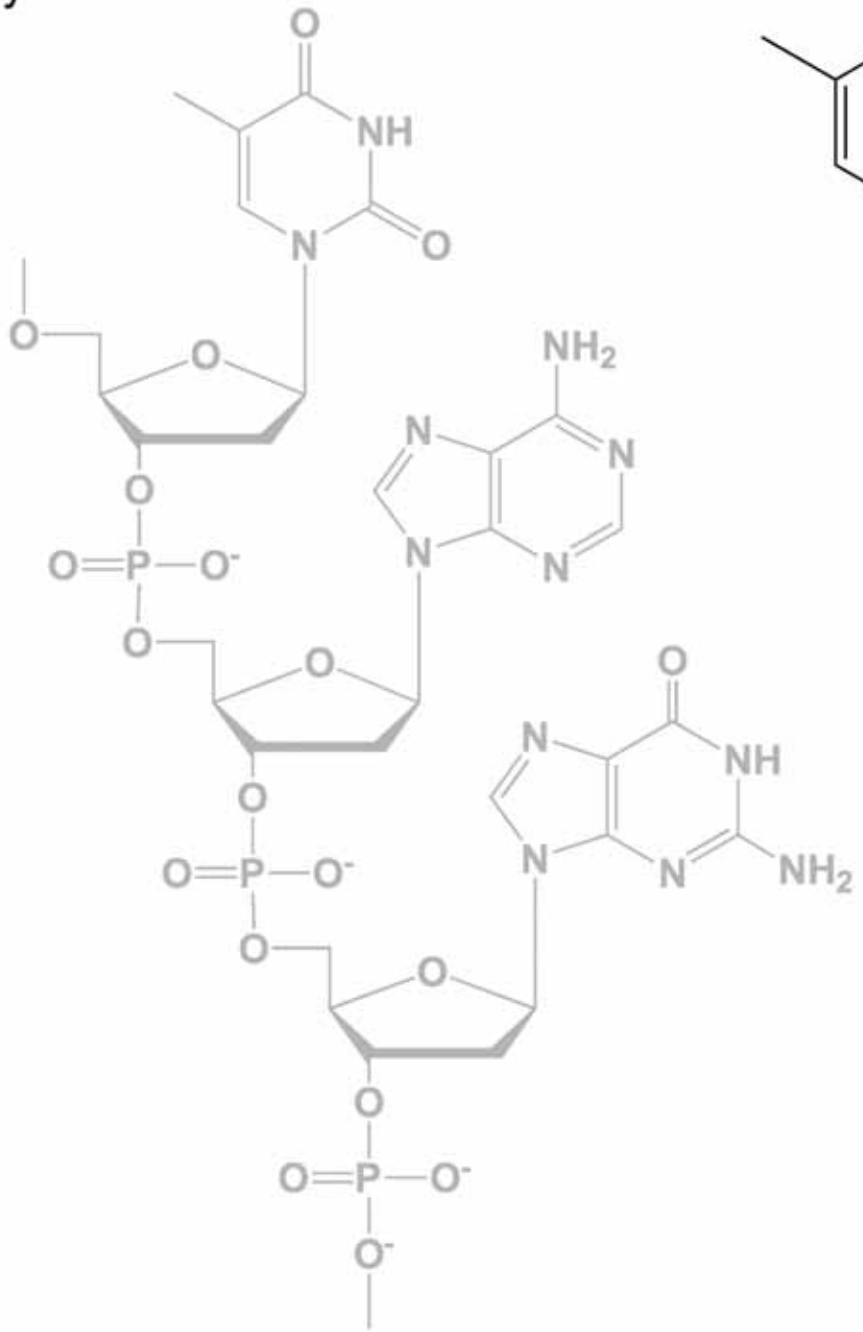


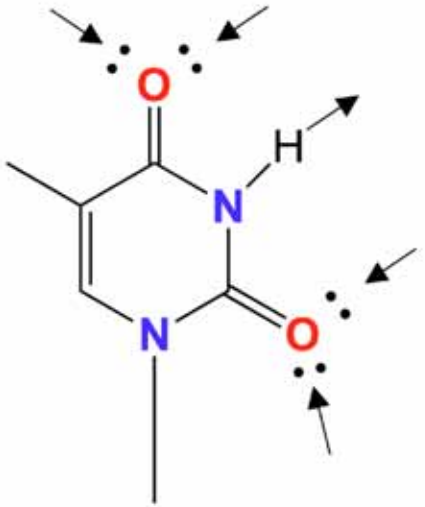


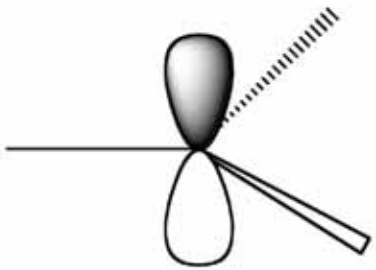


DNA

A look at the Chemistry

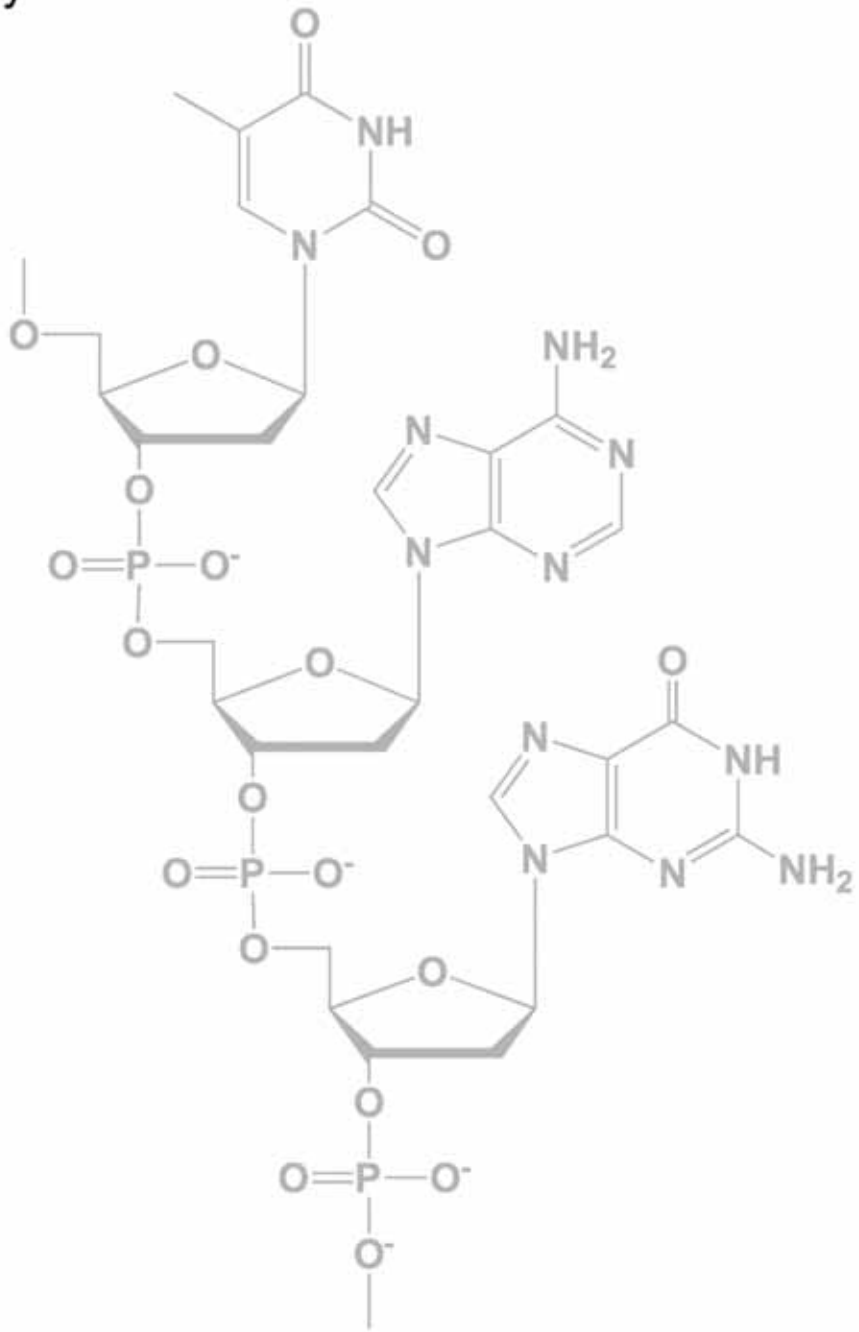


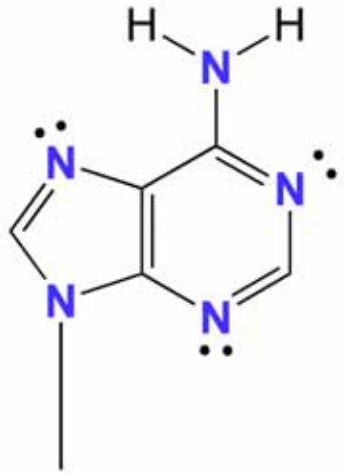


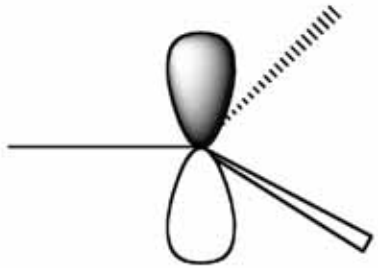


DNA

A look at the Chemistry

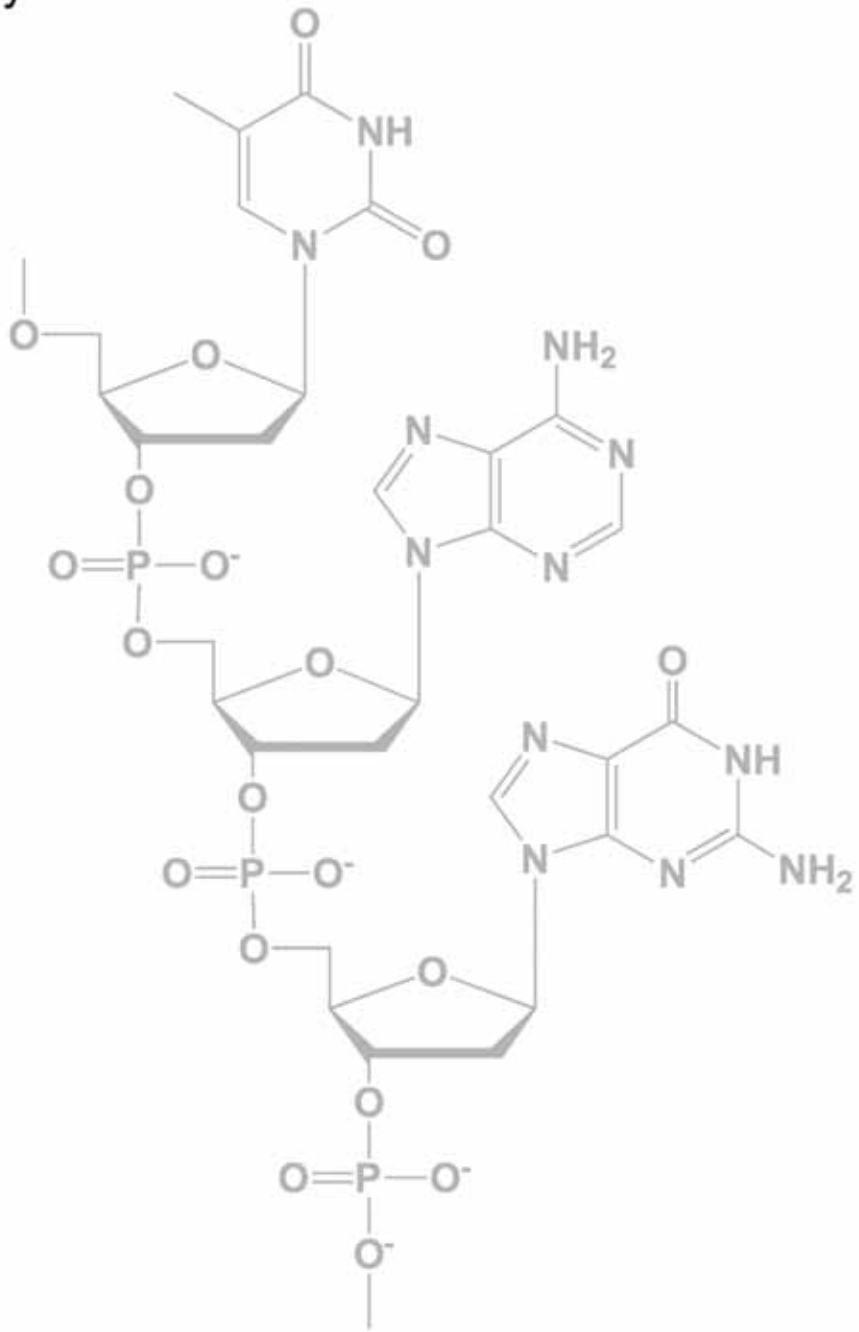


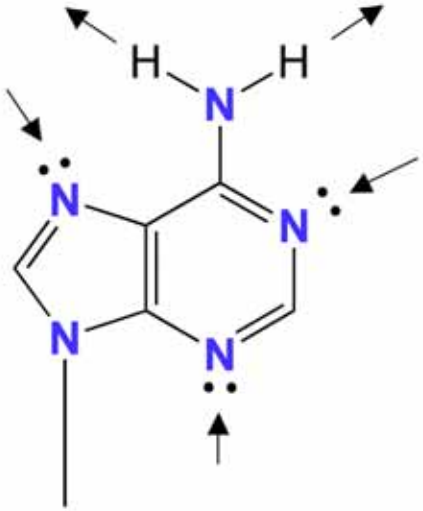


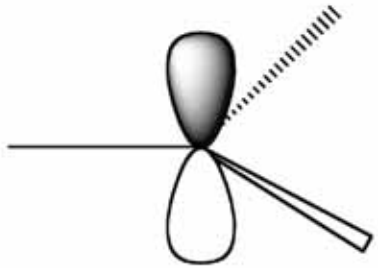


DNA

A look at the Chemistry

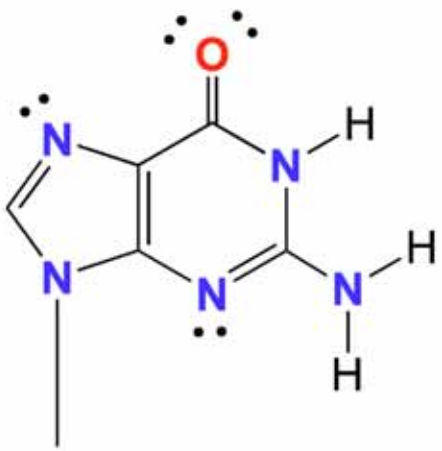


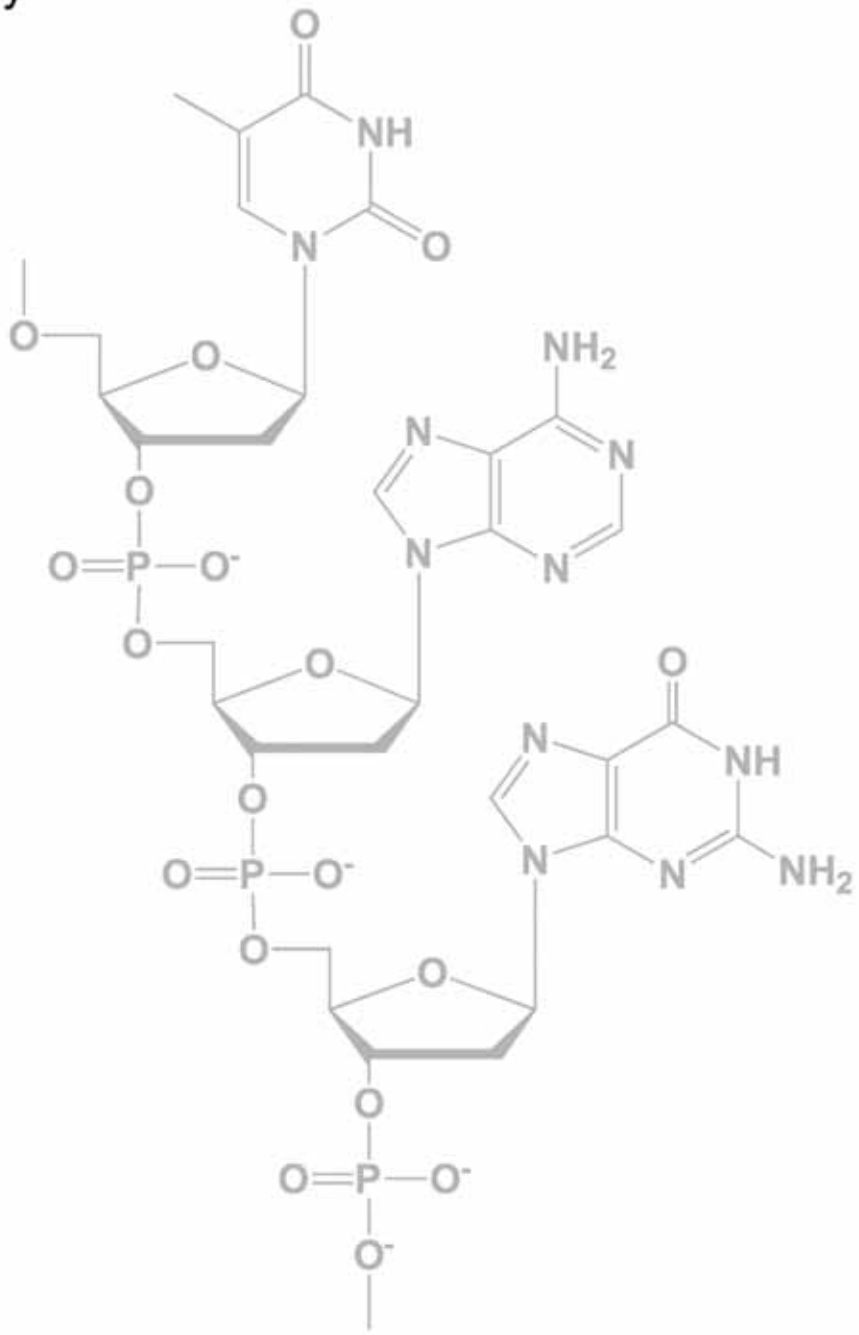


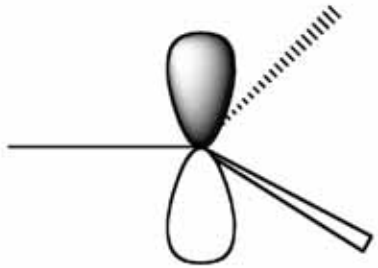


DNA

A look at the Chemistry

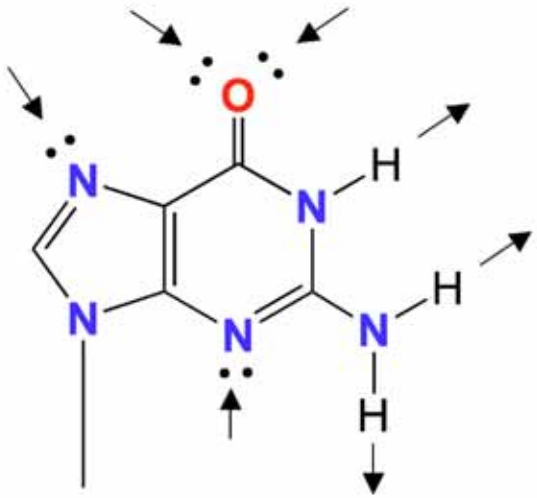


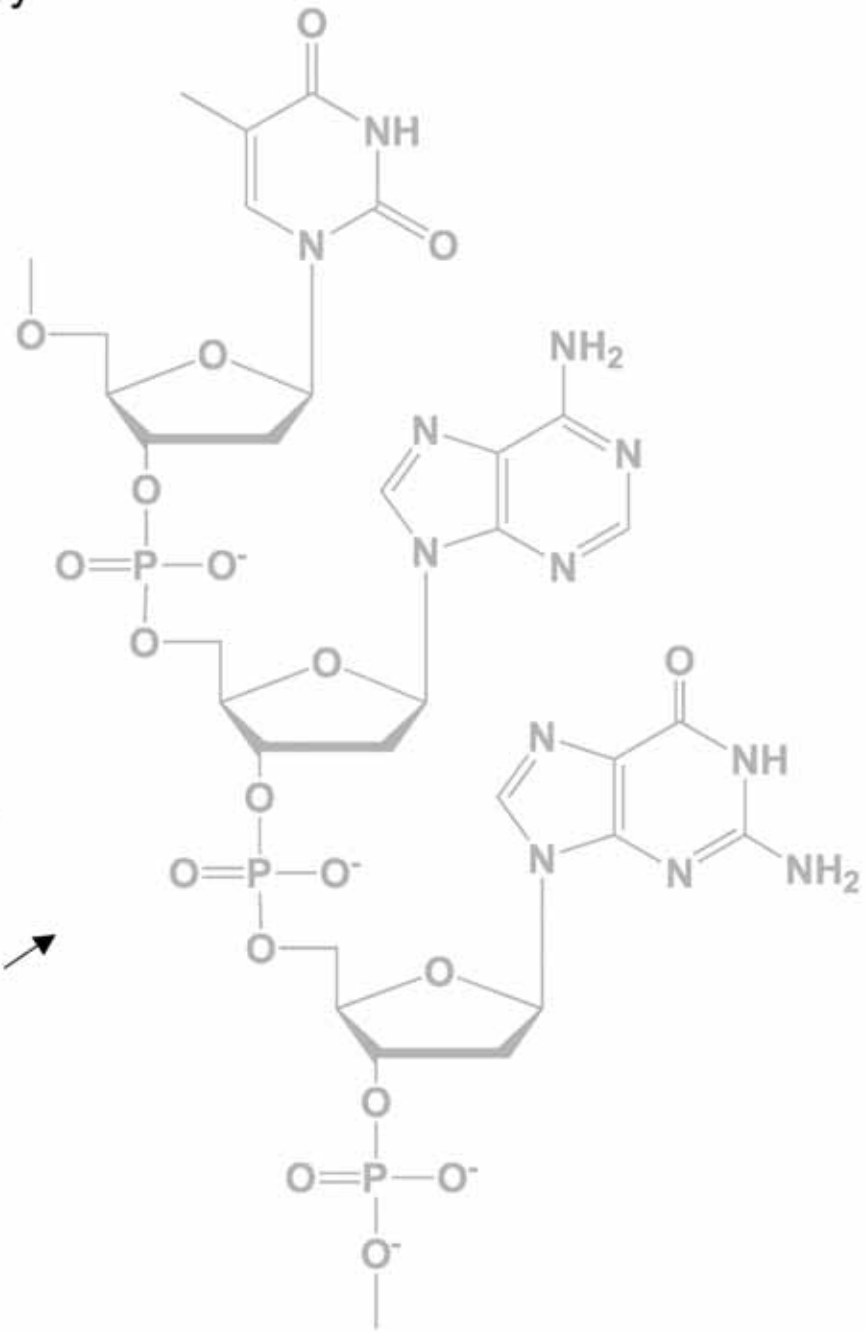


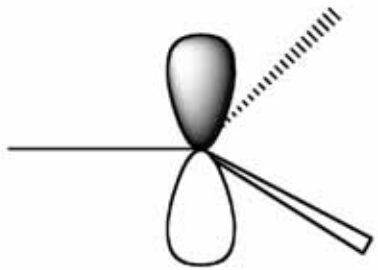


DNA

A look at the Chemistry



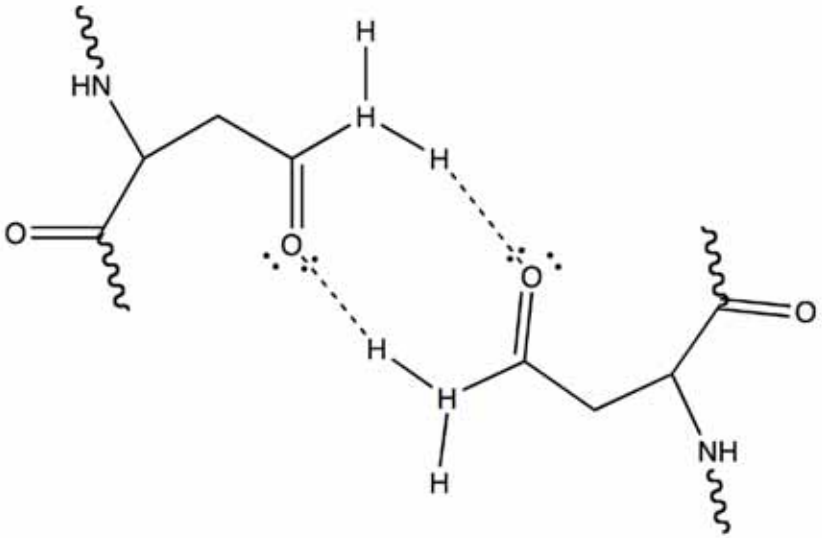


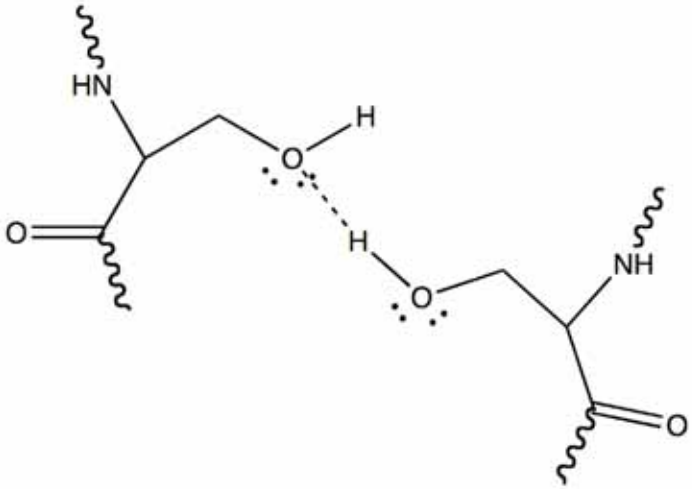


The "Two-Fer" Principle

For hydrogen-bonding in biology, whenever possible,
try to get "two for the price of one"

This is ***more* than twice** as good as this





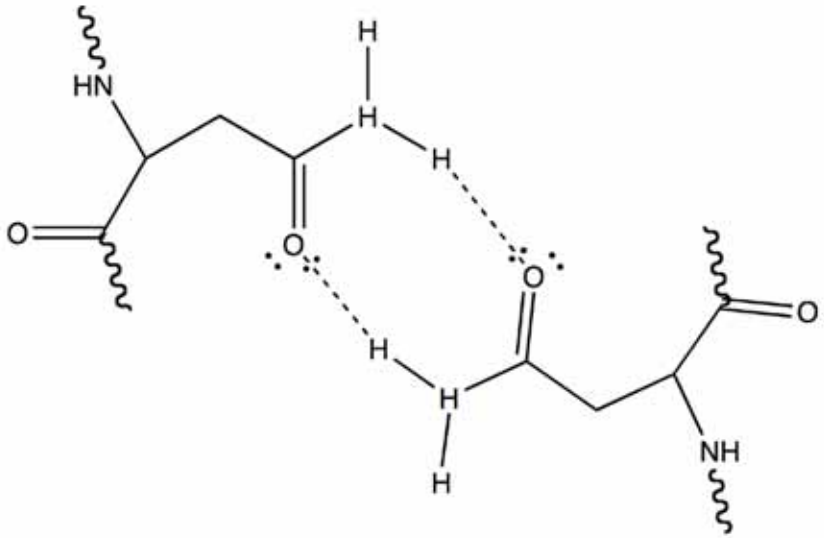
Bringing the two side chains together requires an entropic price

Forming the second H-bond in an already restricted pair does not require paying the entropy price a second time

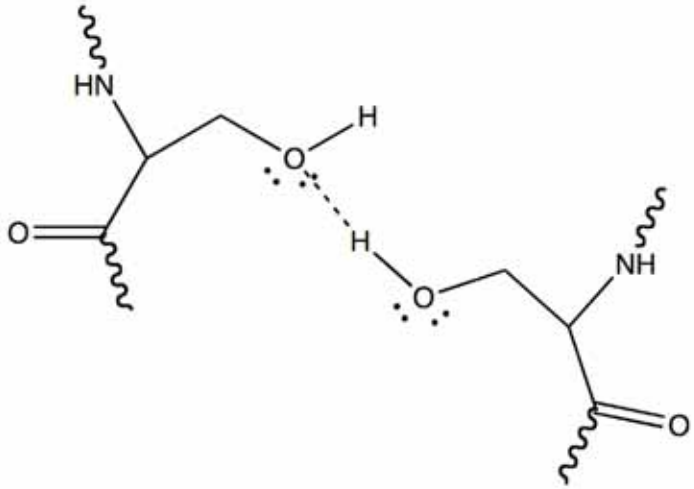
The "Two-Fer" Principle

For hydrogen-bonding in biology, whenever possible,
try to get "two for the price of one"

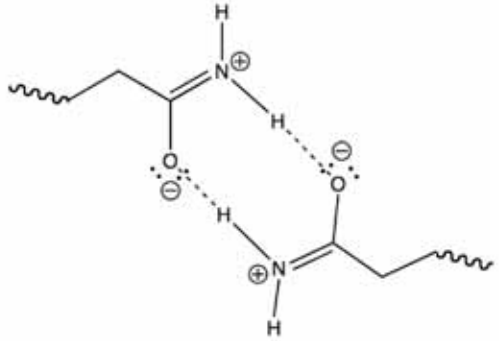
This is ***more* than twice** as good



as this

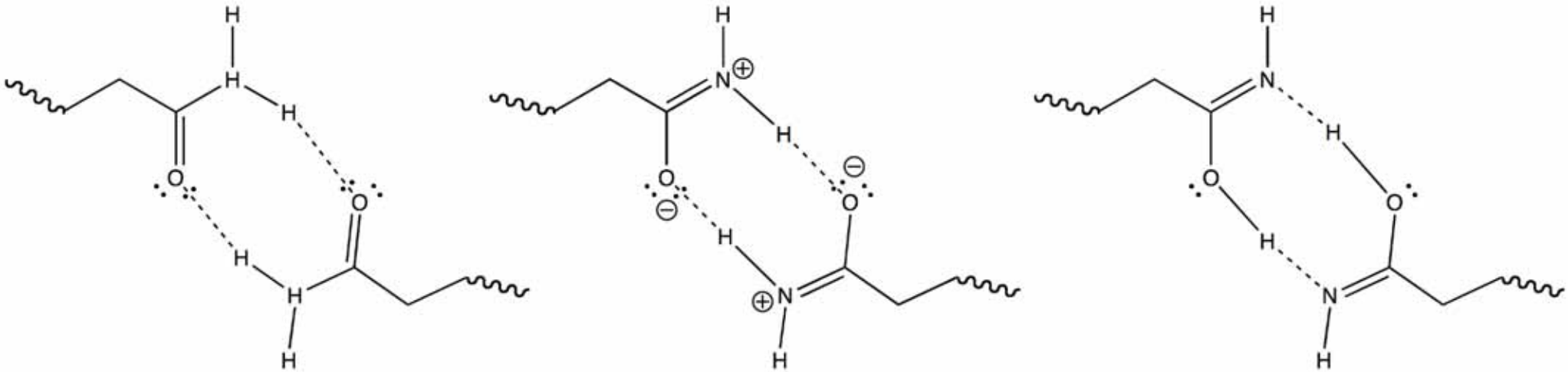


There is also an electronic argument

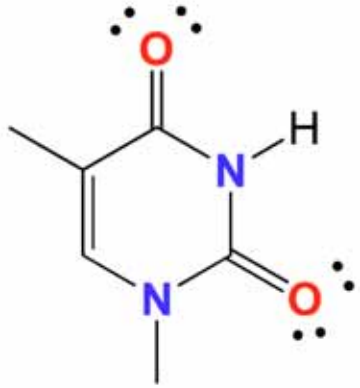


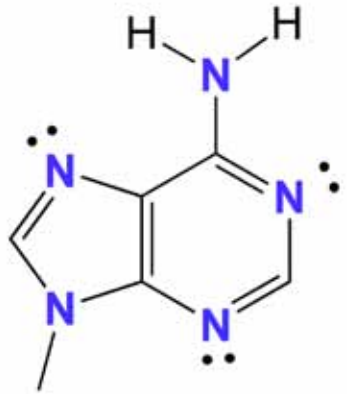
Think about alternate resonance
forms for the amido group

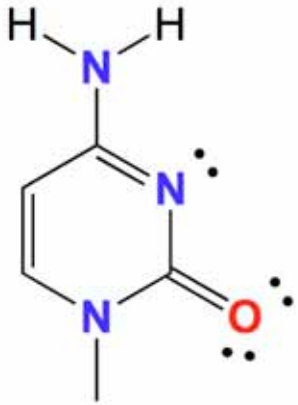
Resonance Forms

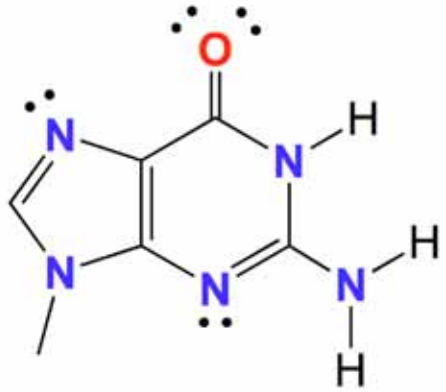


Hydrogen Bonding in Nucleic Acid Bases

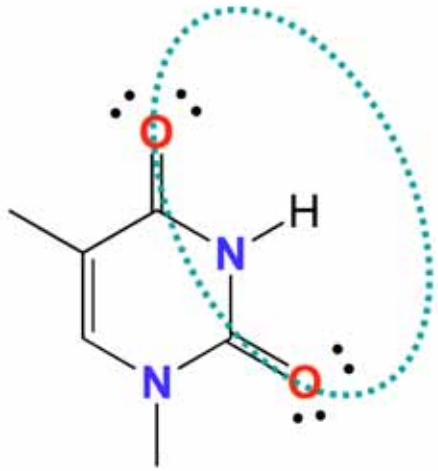


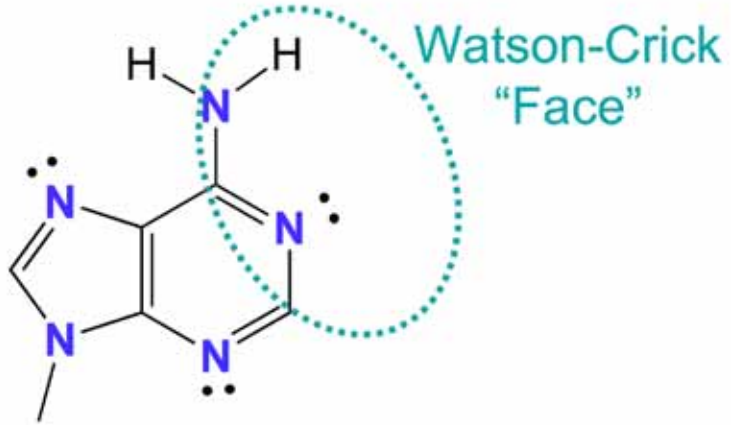


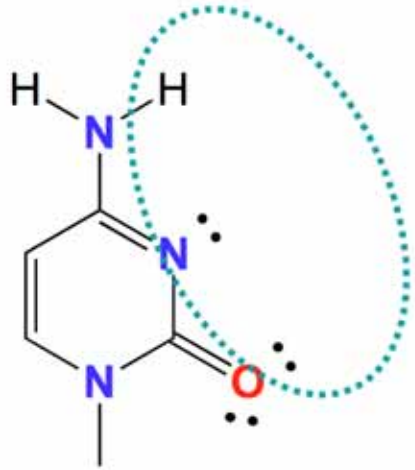


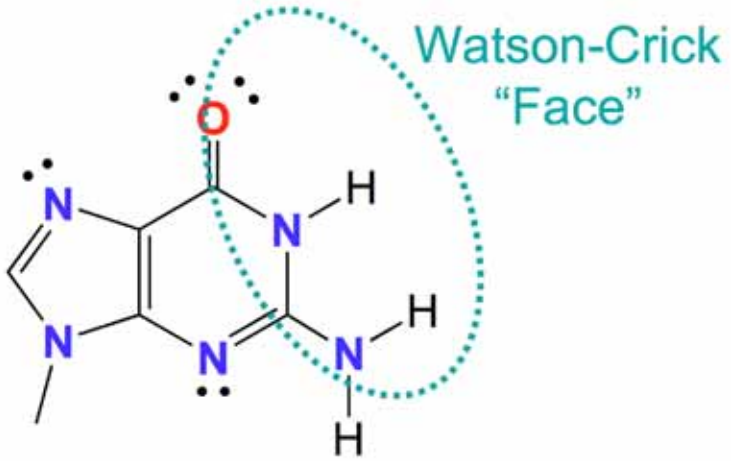


Hydrogen Bonding in Nucleic Acid Bases

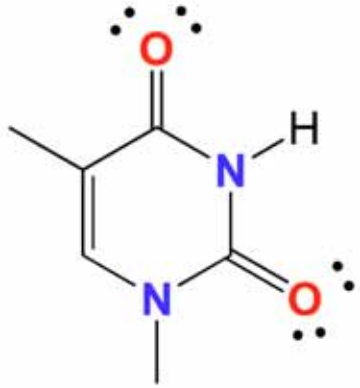




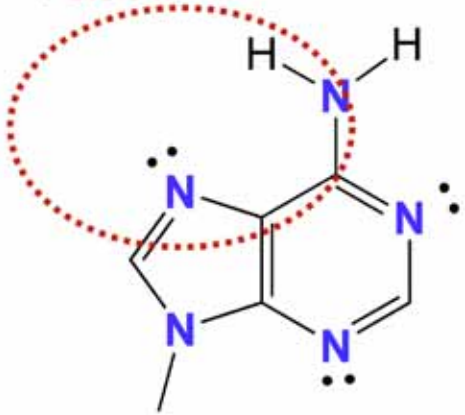


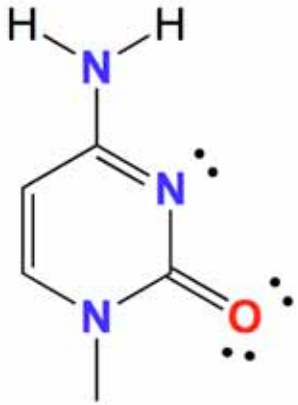


Hydrogen Bonding in Nucleic Acid Bases

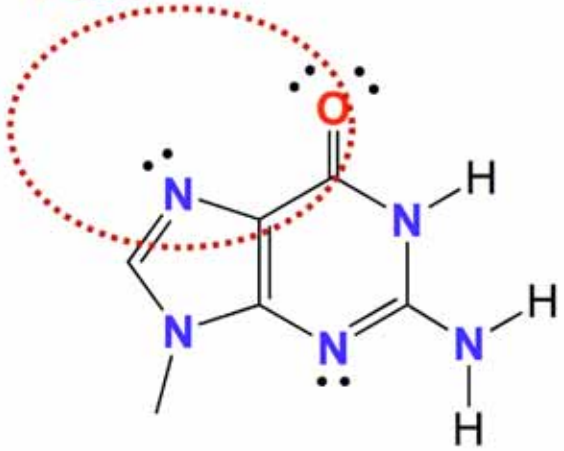


Hoogsteen
"Face"

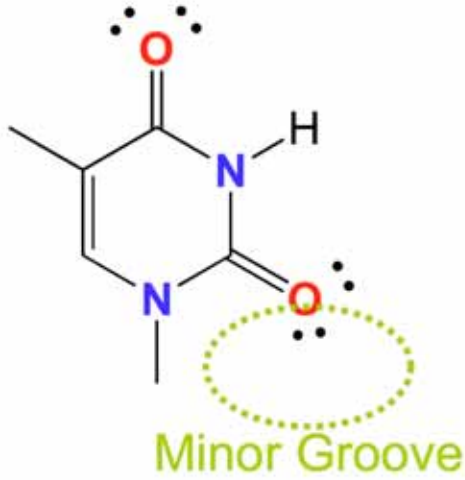


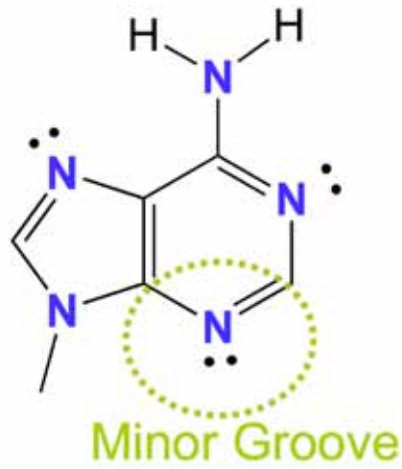


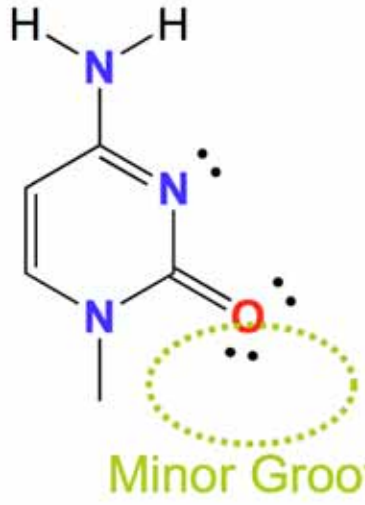
Hoogsteen
"Face"



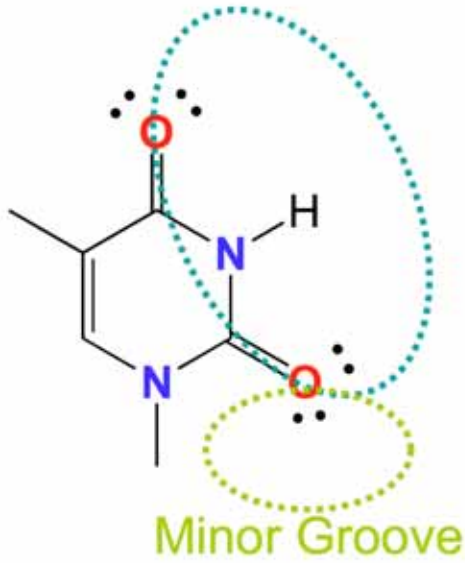
Hydrogen Bonding in Nucleic Acid Bases

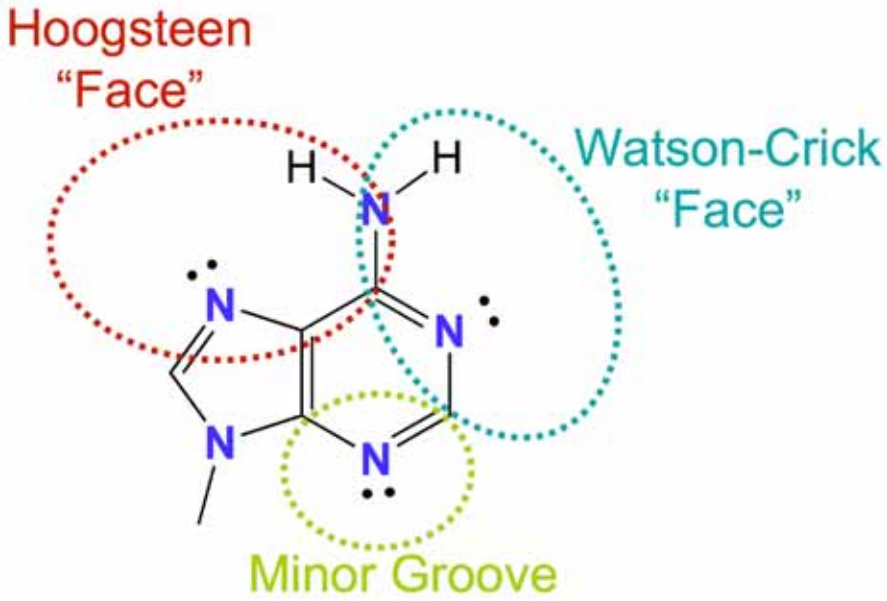


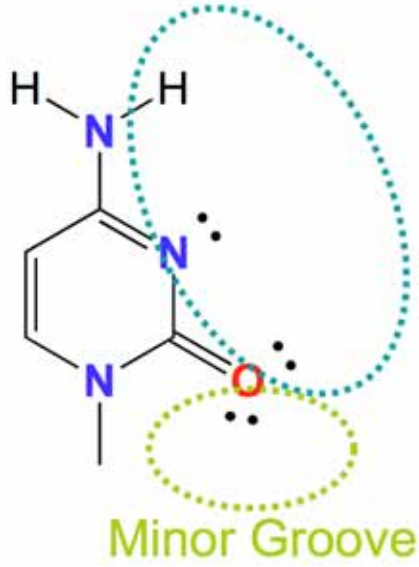


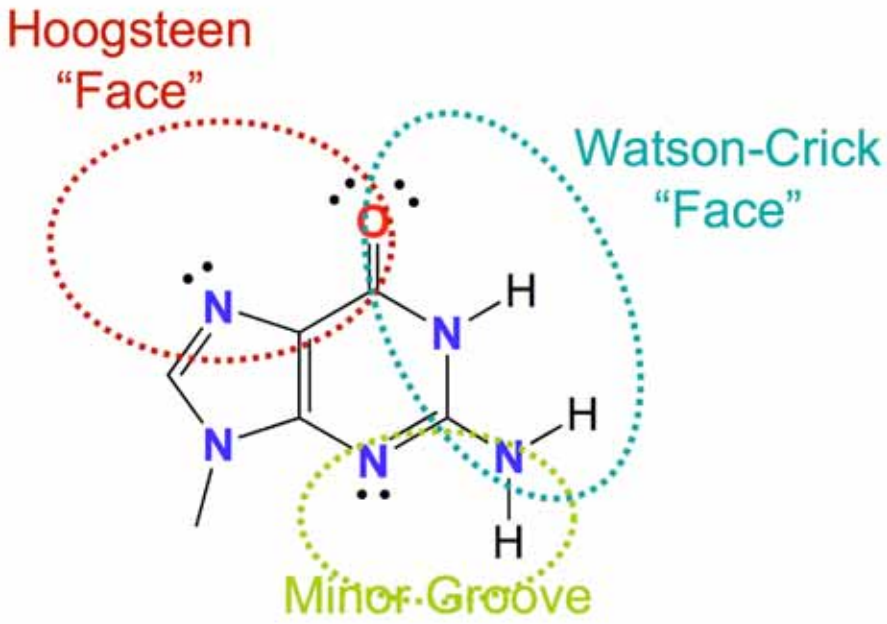


Hydrogen Bonding in Nucleic Acid Bases

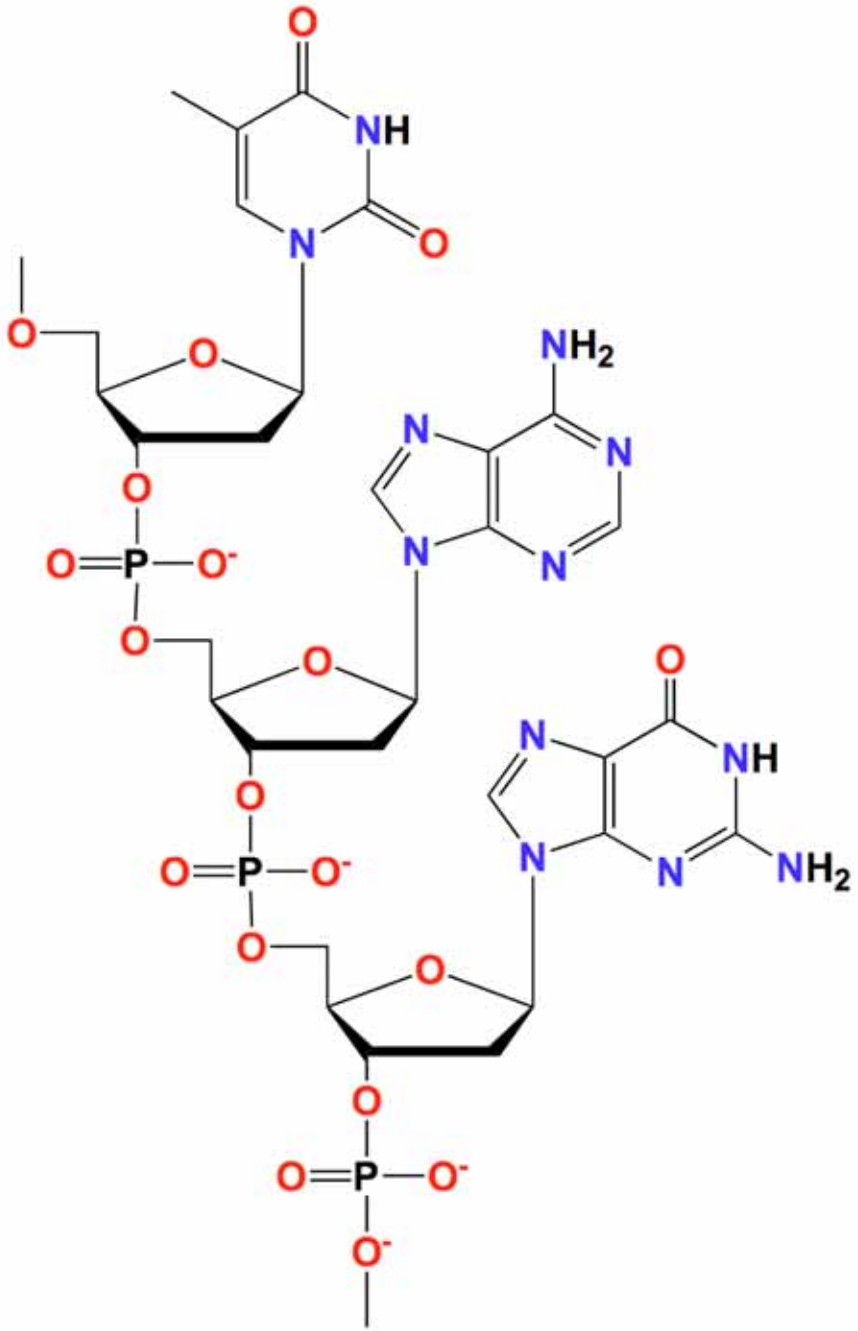




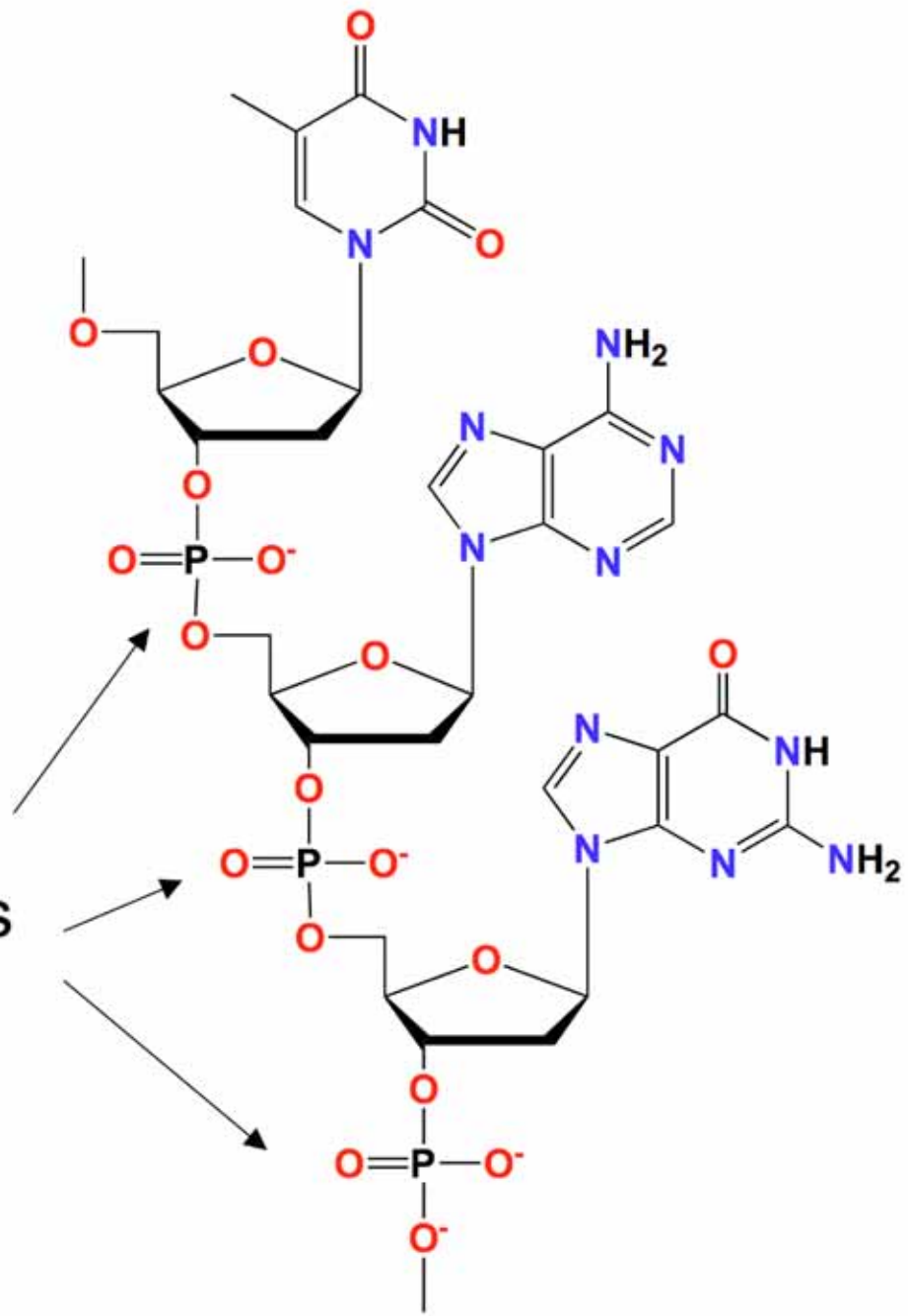




What forces are important?

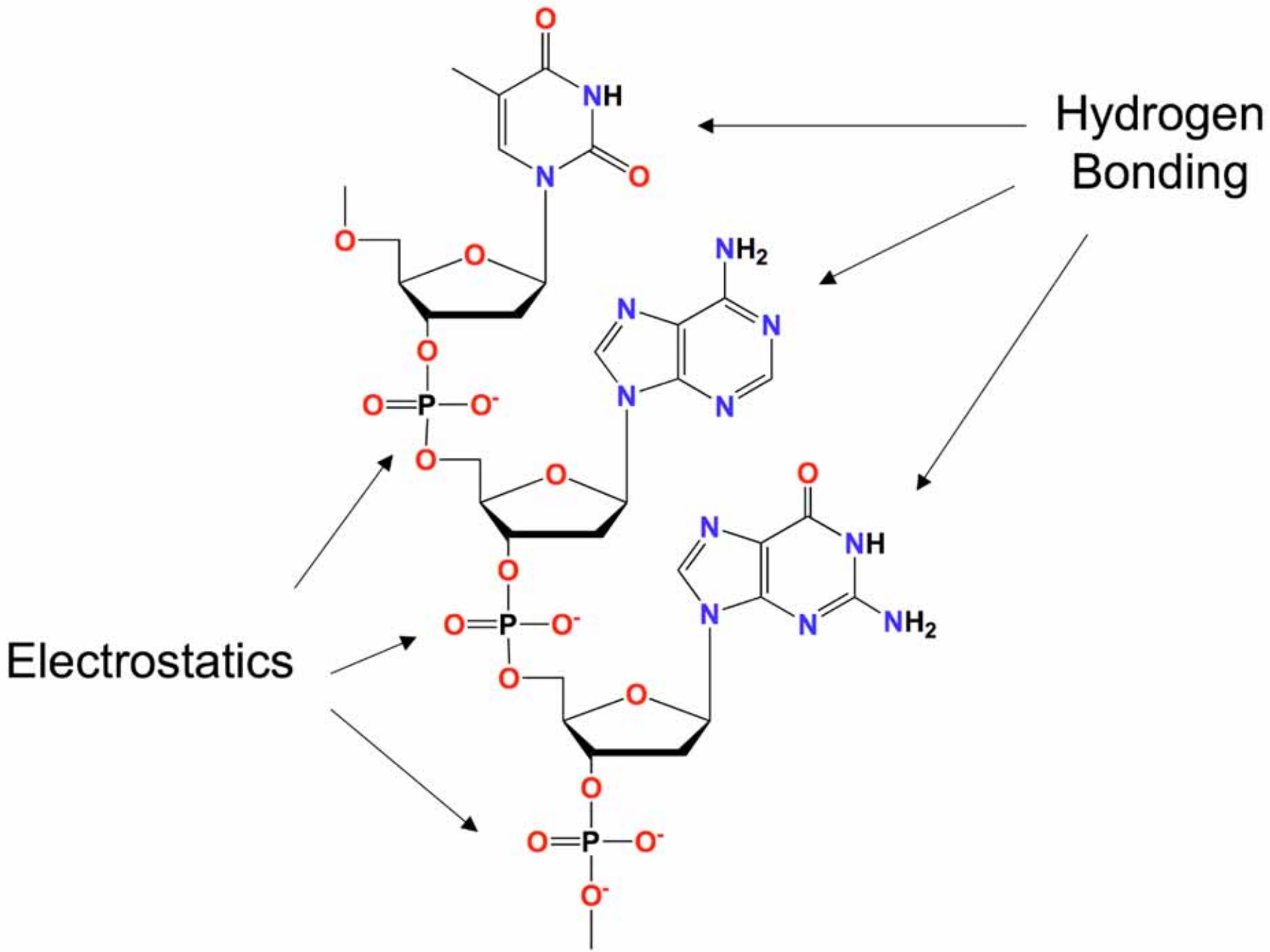


What forces are important?

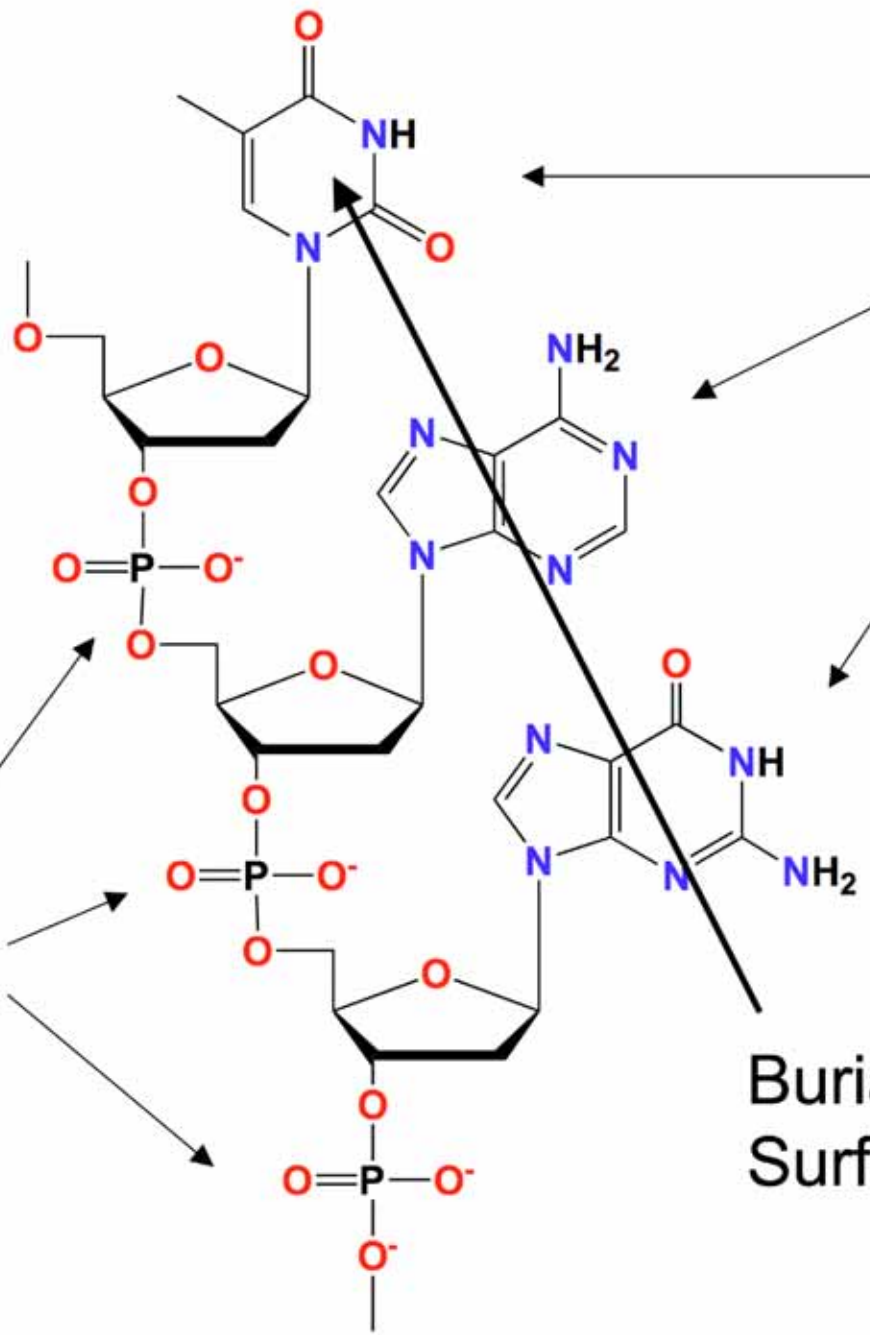


Electrostatics

What forces are important?



What forces are important?



Hydrogen Bonding

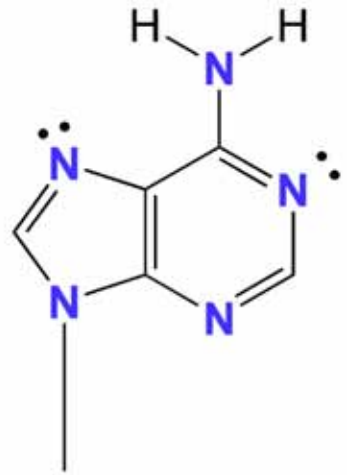
Electrostatics

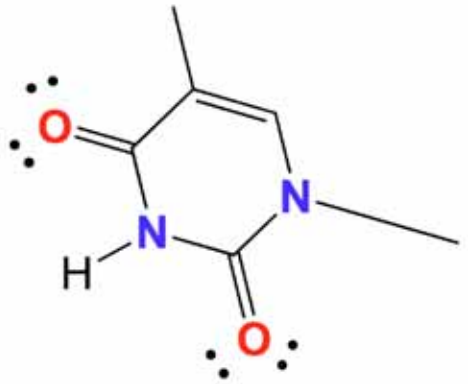
Burial of Hydrophobic Surface & Stacking

Base Pairing

(Donors matched to Acceptors)

A

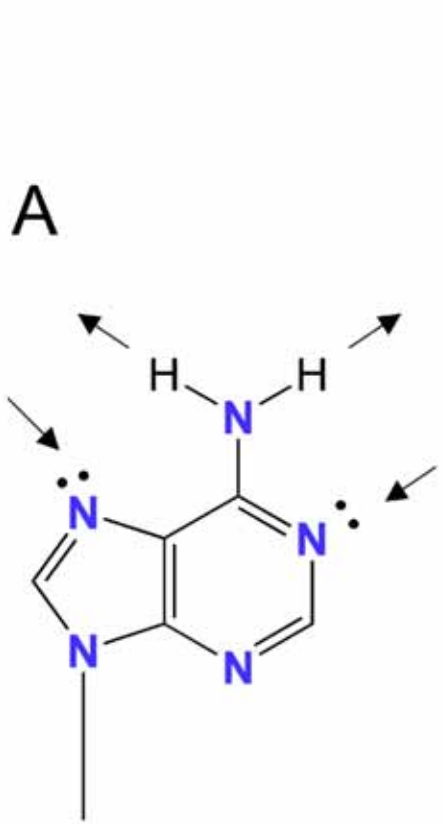


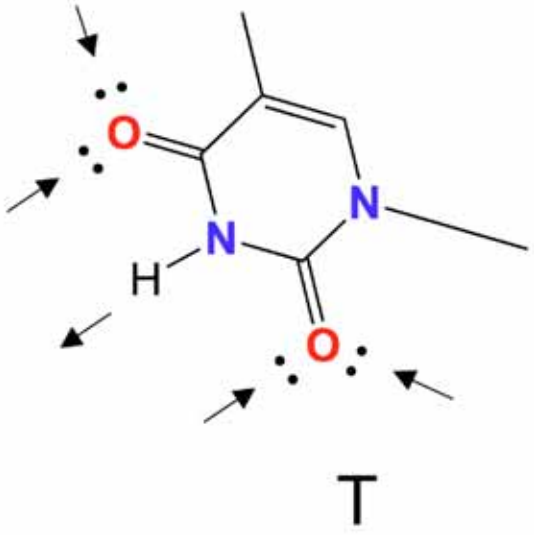


T

Base Pairing

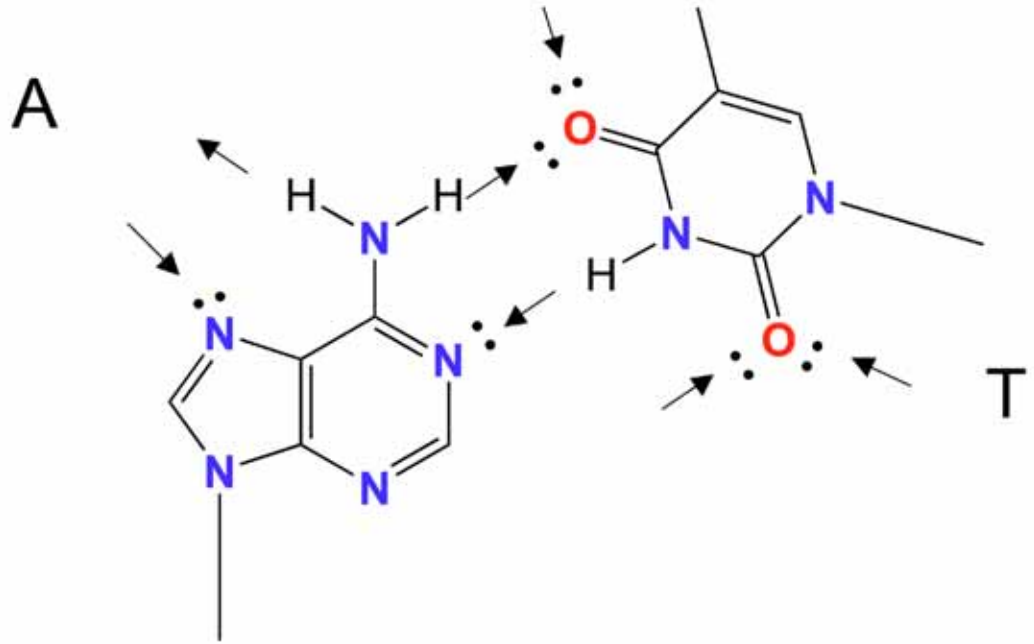
(Donors matched to Acceptors)





Base Pairing

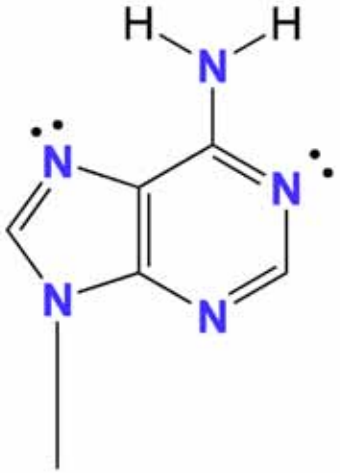
(Donors matched to Acceptors)

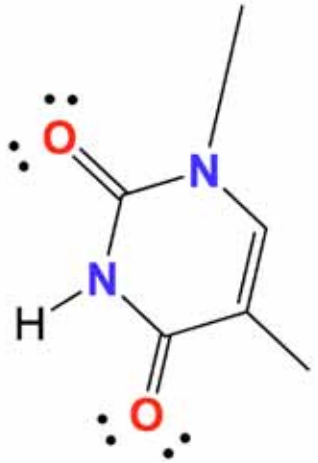


Base Pairing

(Donors matched to Acceptors)

A



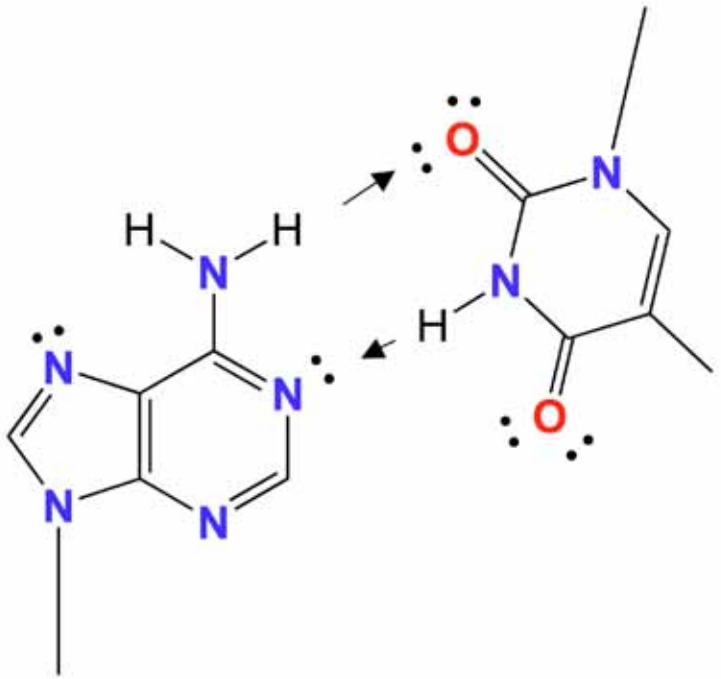


T

Base Pairing

(Donors matched to Acceptors)

A

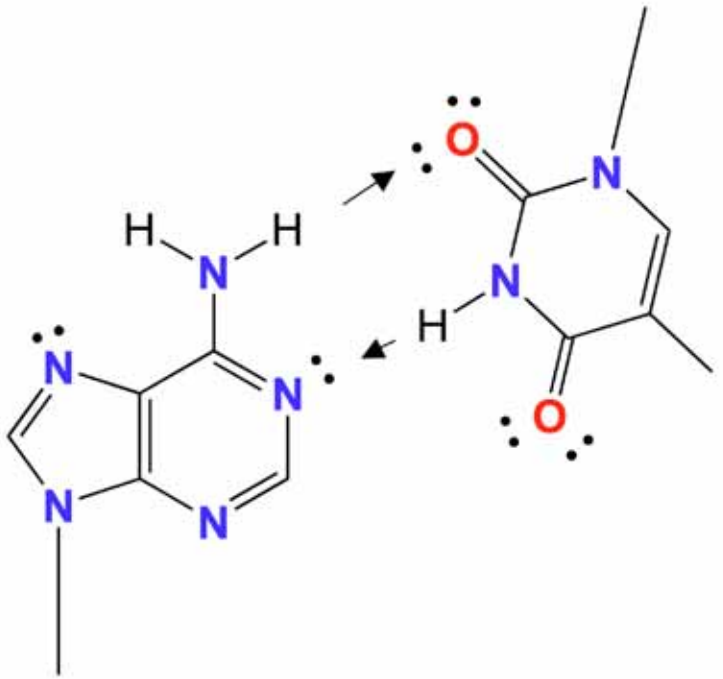


T

Base Pairing

(Donors matched to Acceptors)

A



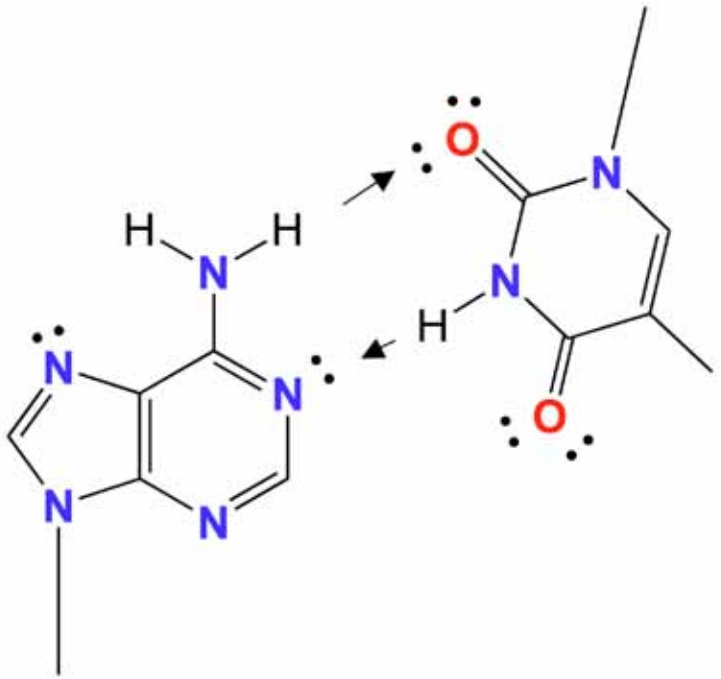
T

Good base pairing

Base Pairing

(Donors matched to Acceptors)

A



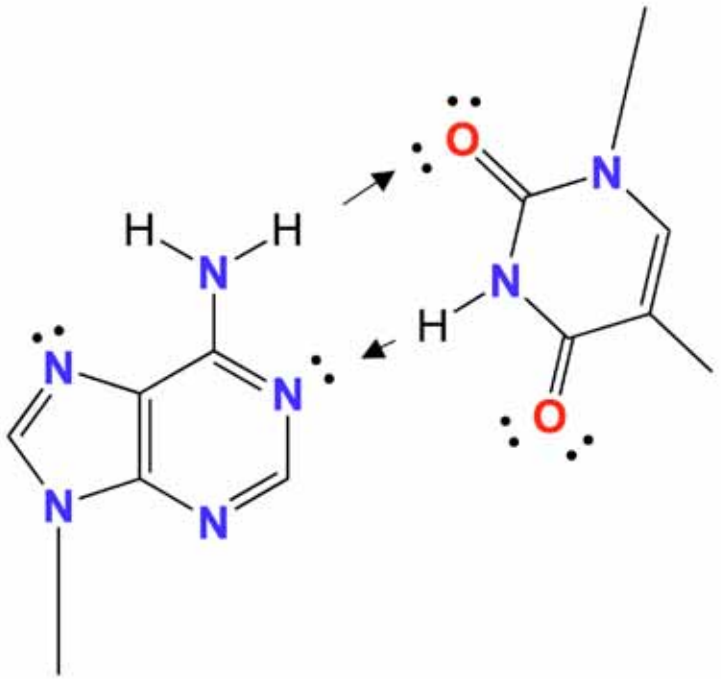
T

Good base pairing
Watson-Crick facing

Base Pairing

(Donors matched to Acceptors)

A



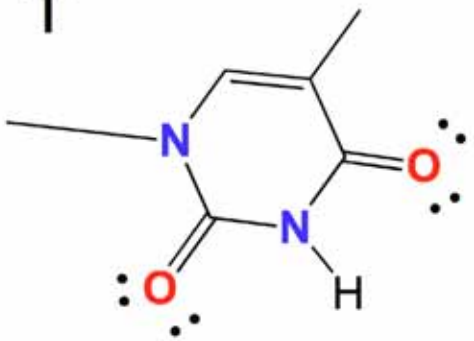
T

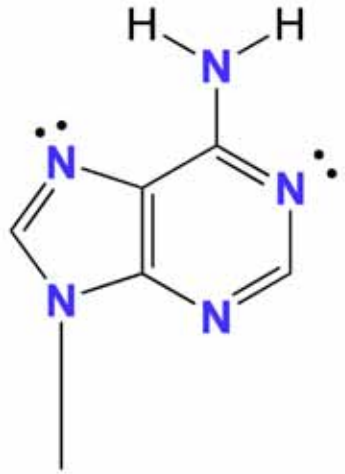
Good base pairing
Watson-Crick facing
but *Anti-Watson-Crick* orientation

Base Pairing

(Donors matched to Acceptors)

T



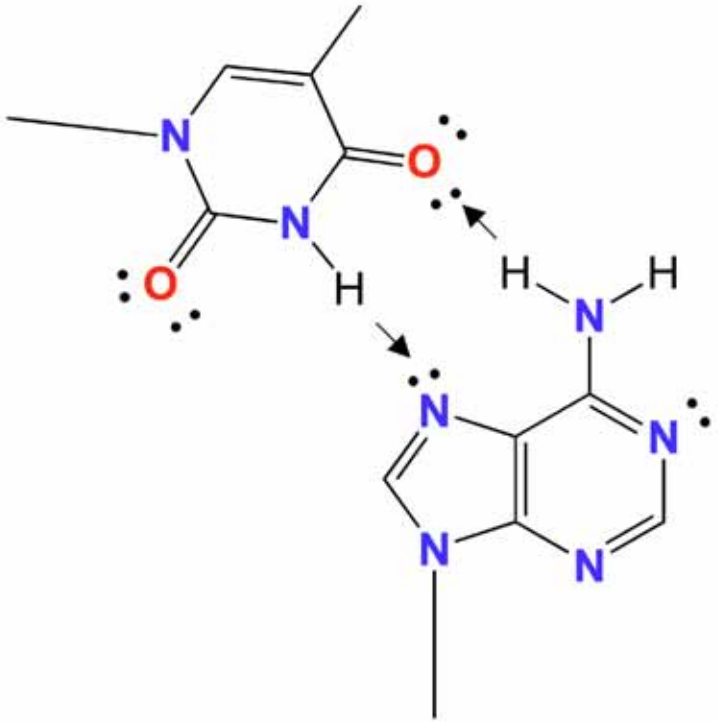


A

Base Pairing

(Donors matched to Acceptors)

T

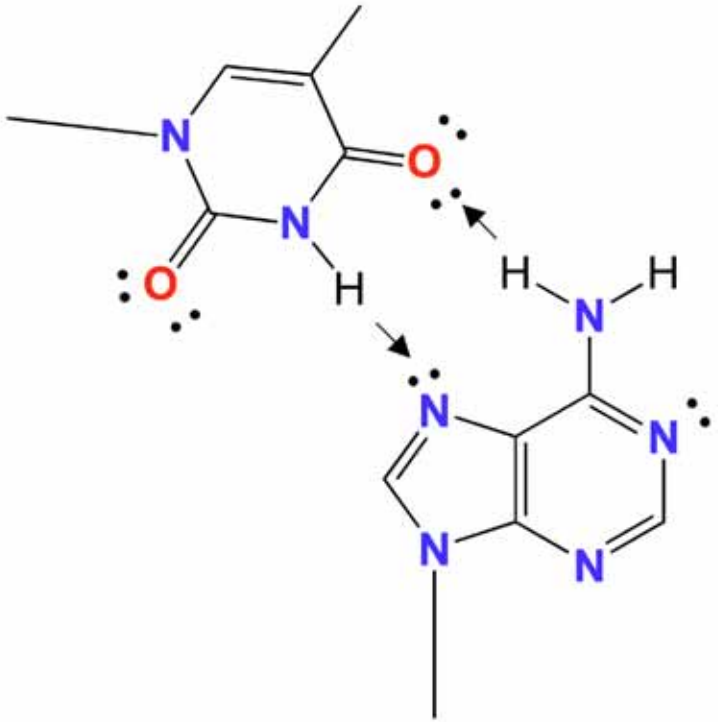


A

Base Pairing

(Donors matched to Acceptors)

T



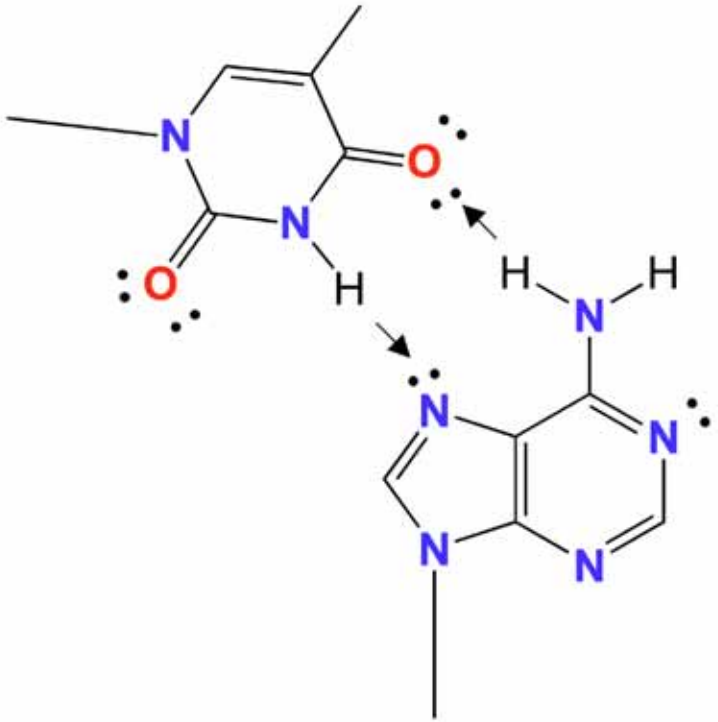
A

Good base pairing

Base Pairing

(Donors matched to Acceptors)

T



A

Good base pairing
WC-Hoogsteen facing

G

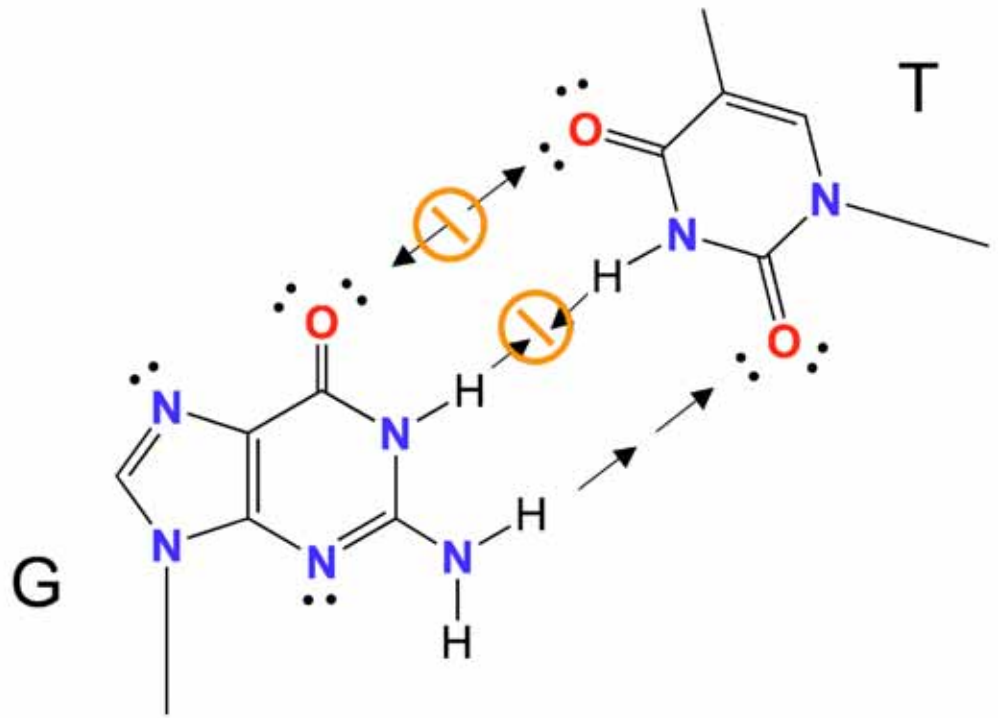
T

G
T

G
T

Bad Base Pairing

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



G

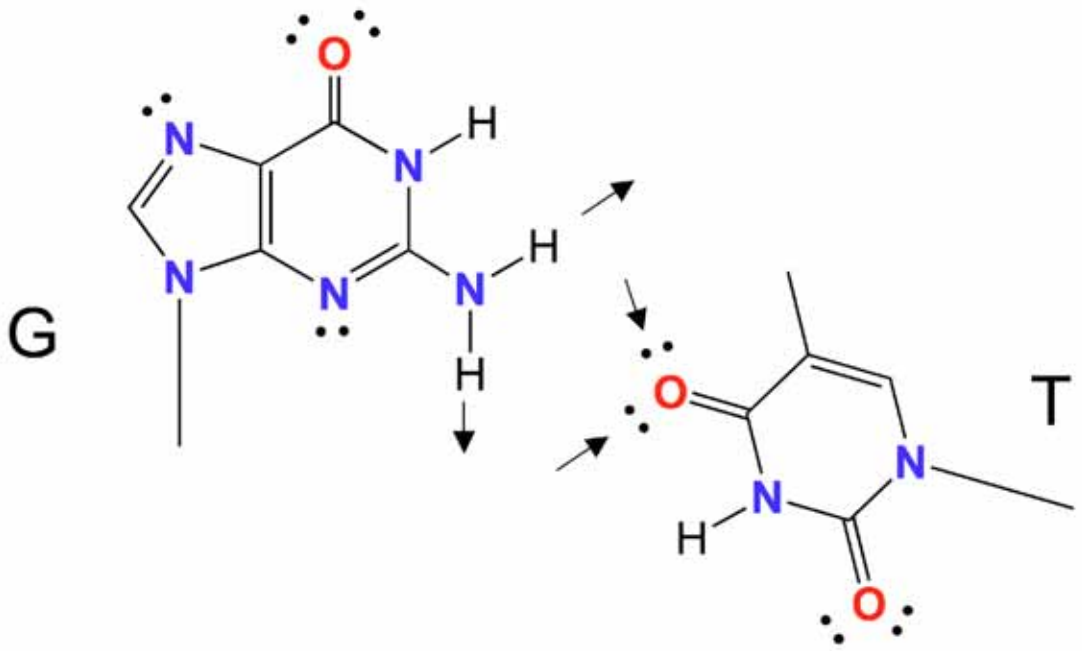
T

G

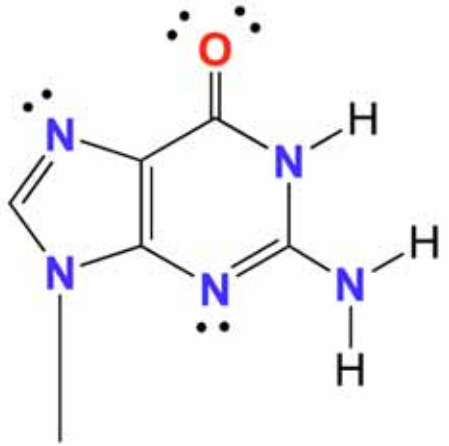
T

Bad Base Pairing

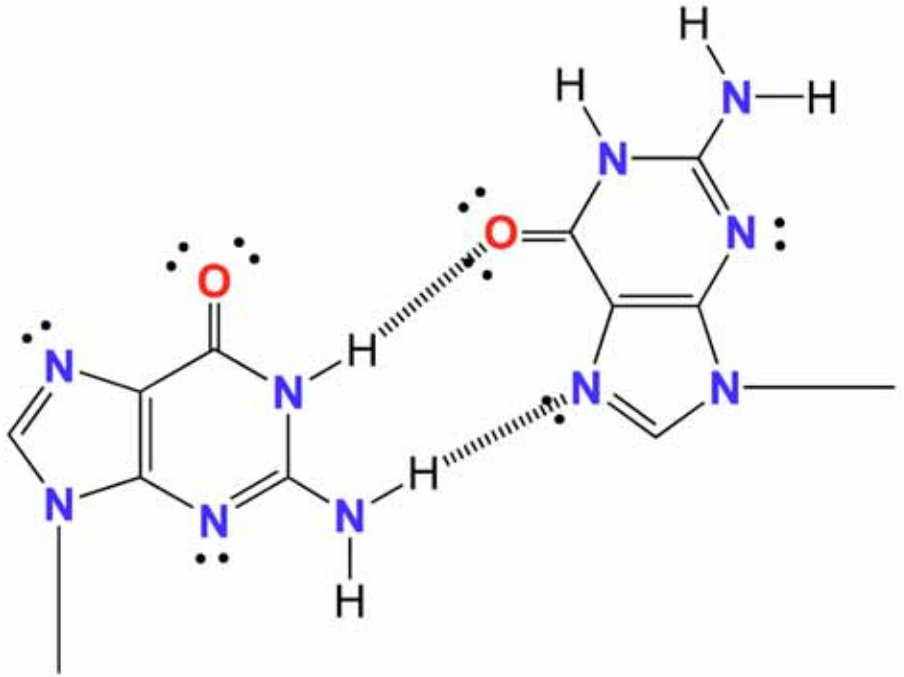
(Donors to Acceptors with ***terrible angles***)



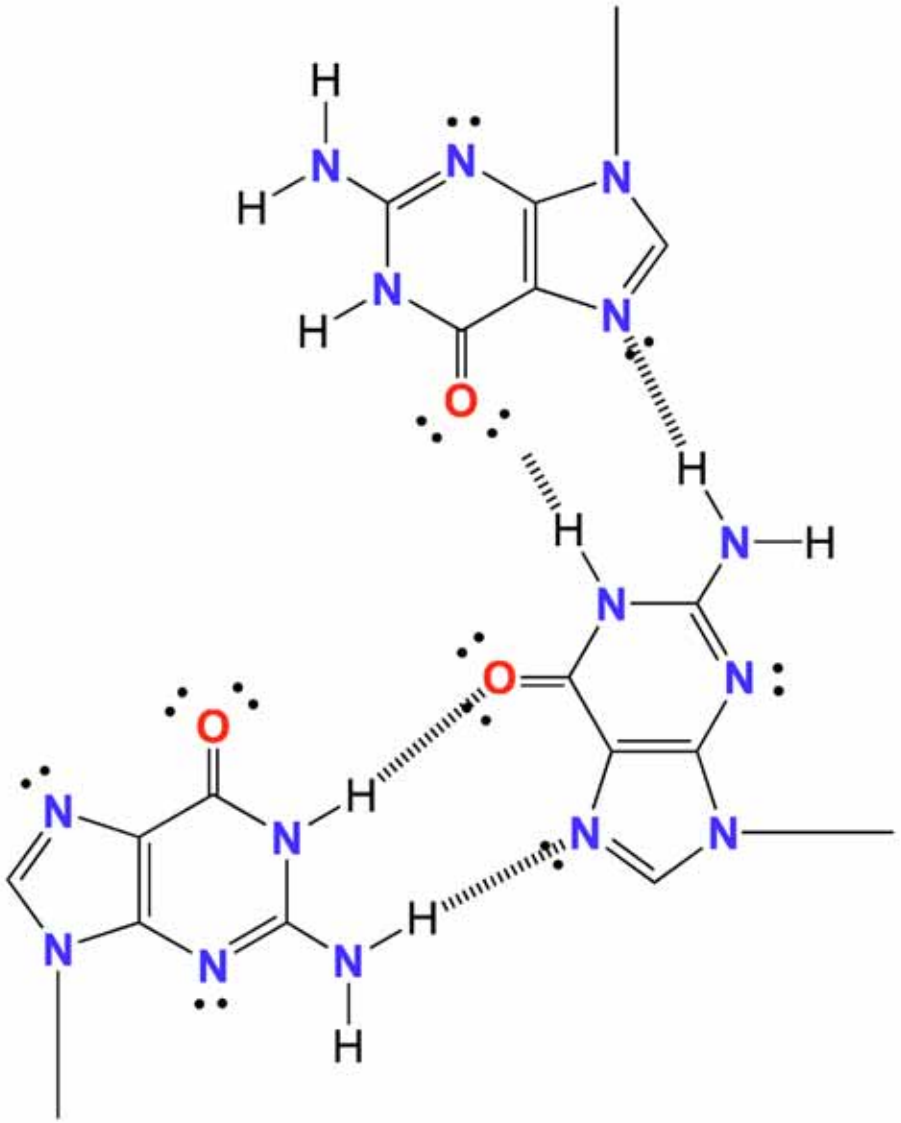
Wild (but good) Base Pairing



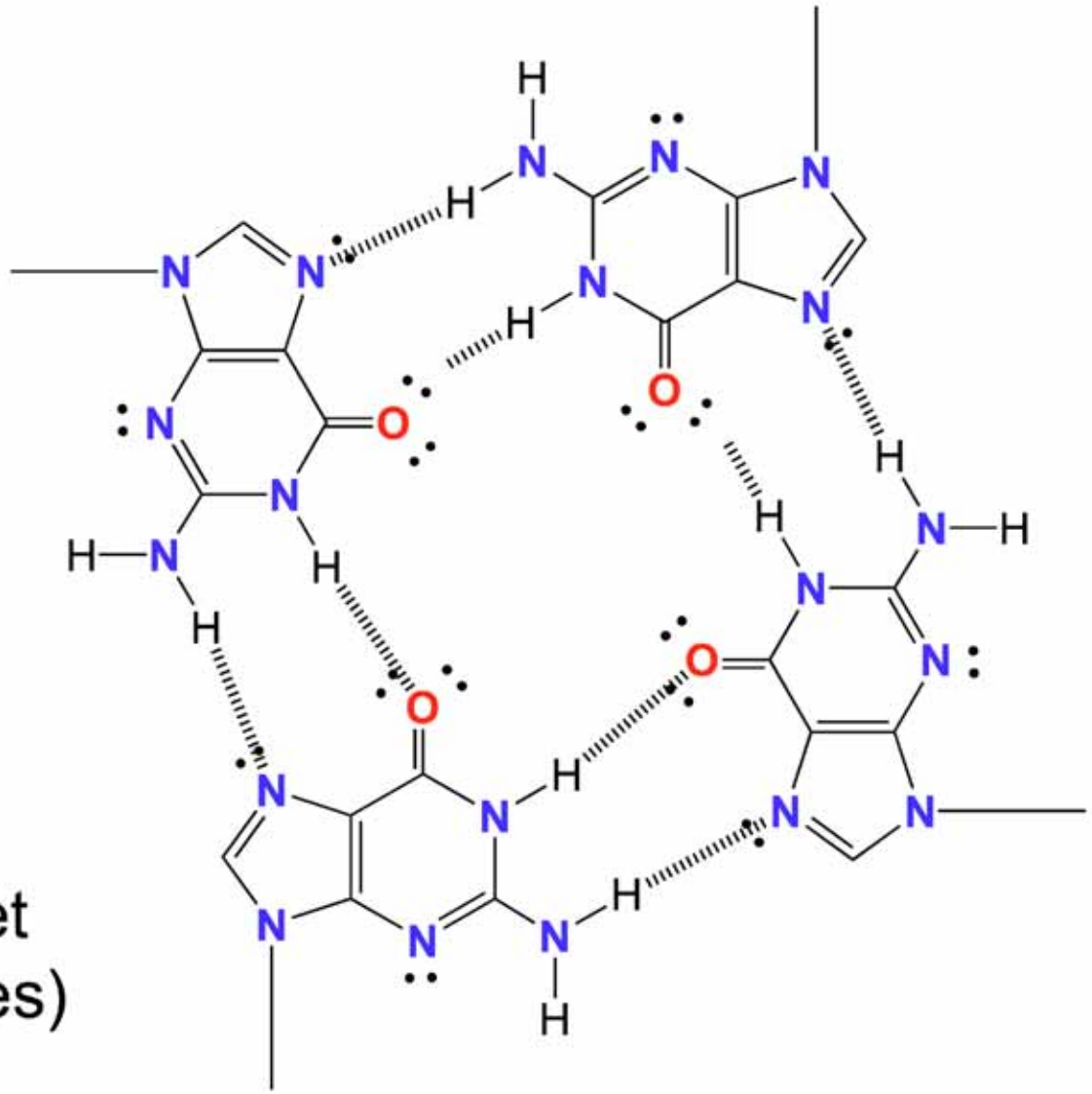
Wild (but good) Base Pairing



Wild (but good) Base Pairing

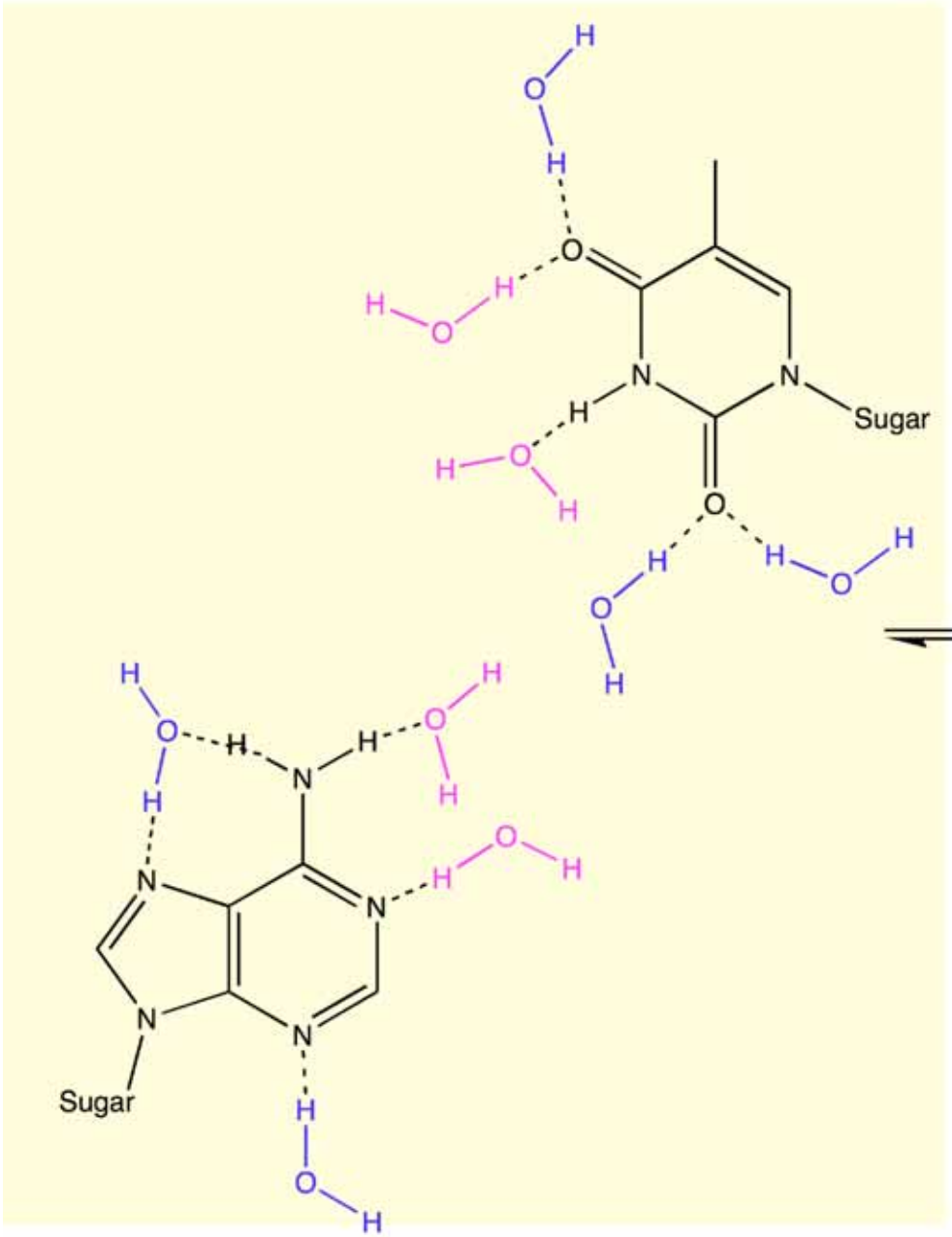


Wild (but good) Base Pairing

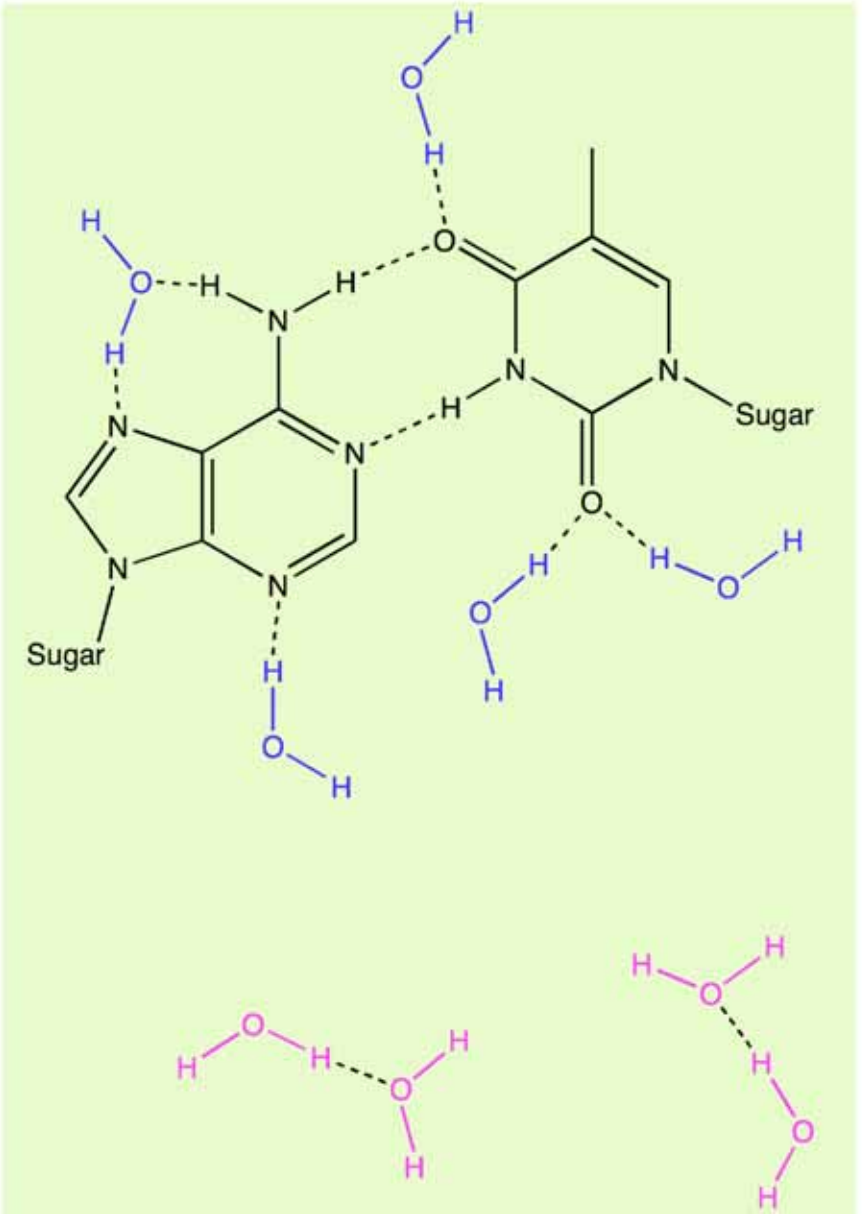


G-quartet
(Telomeres)

AT Base Pair

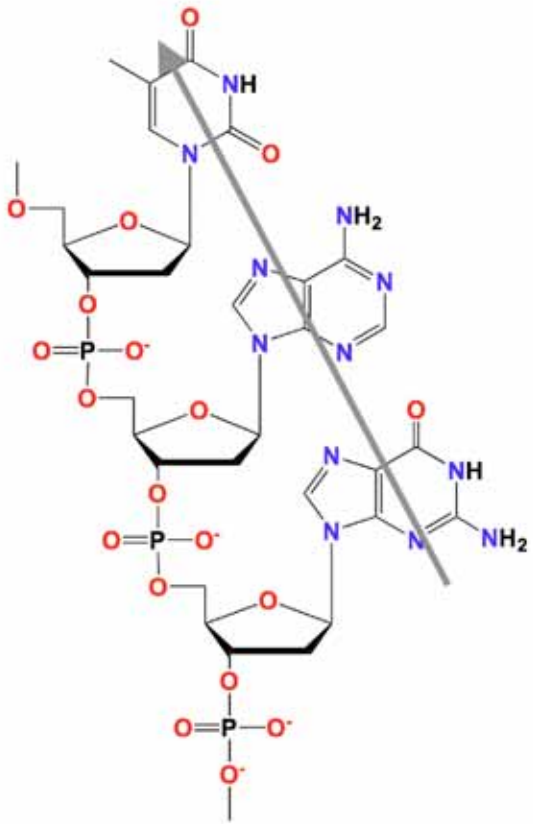


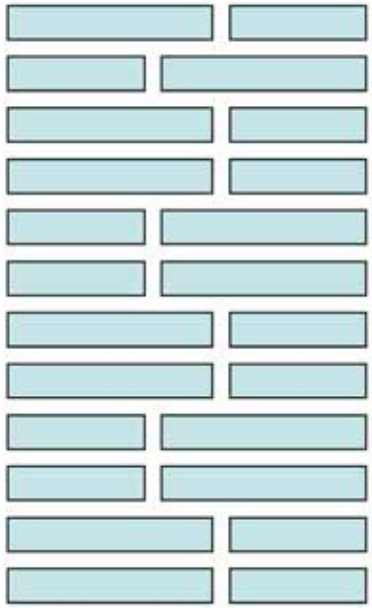
Ten H-Bonds



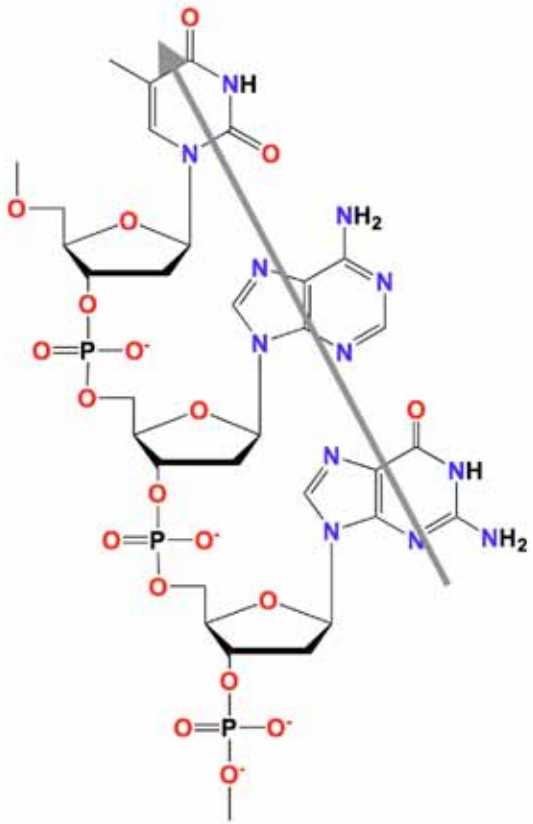
Ten H-Bonds

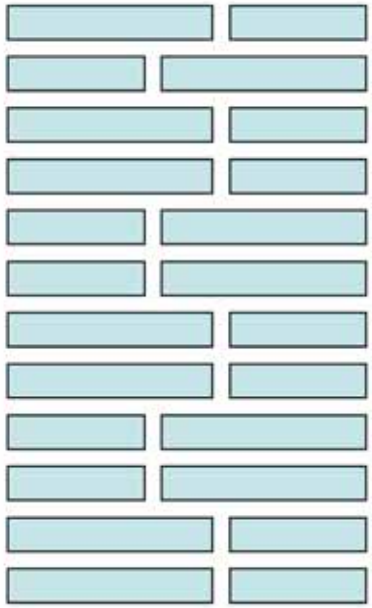
Burial of hydrophobic surface drives helix formation (hydrophobic core / stacking interactions)





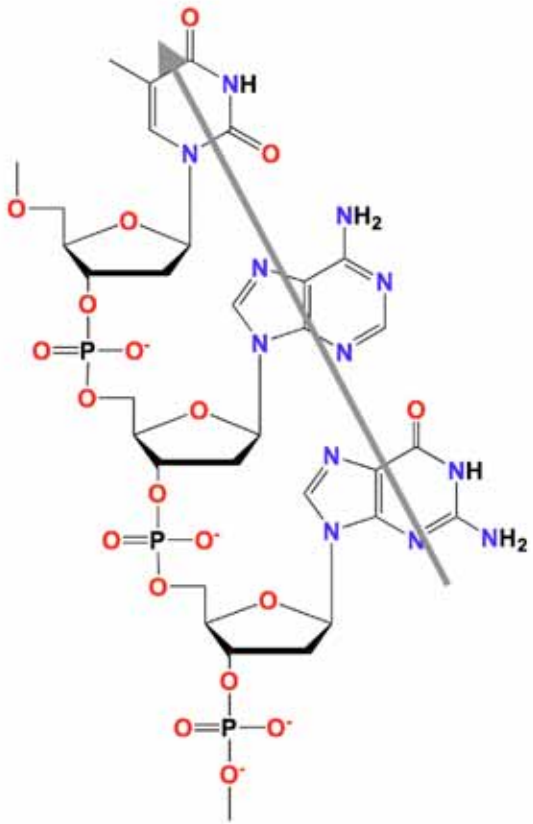
Burial of hydrophobic surface drives helix formation (hydrophobic core / stacking interactions)

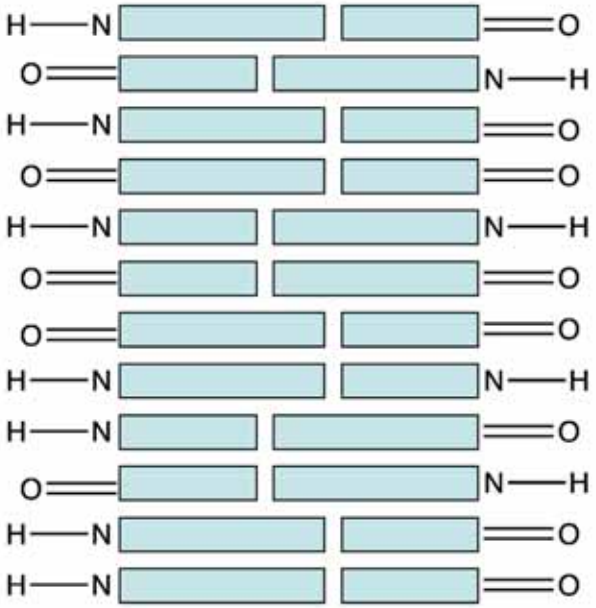




Flat faces are nonpolar

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

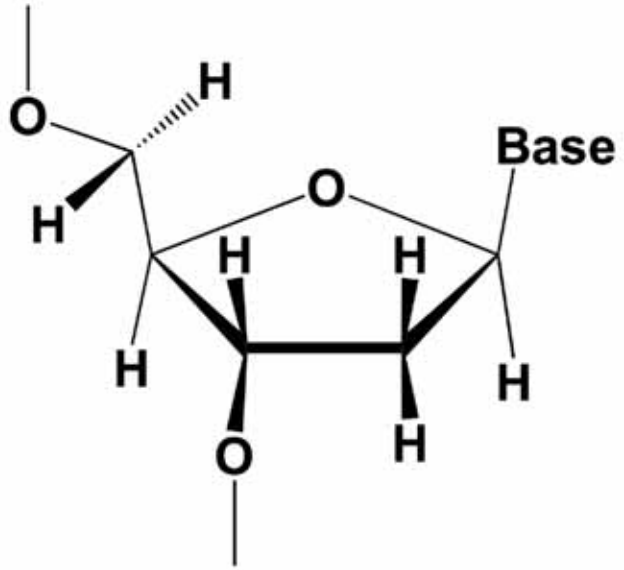




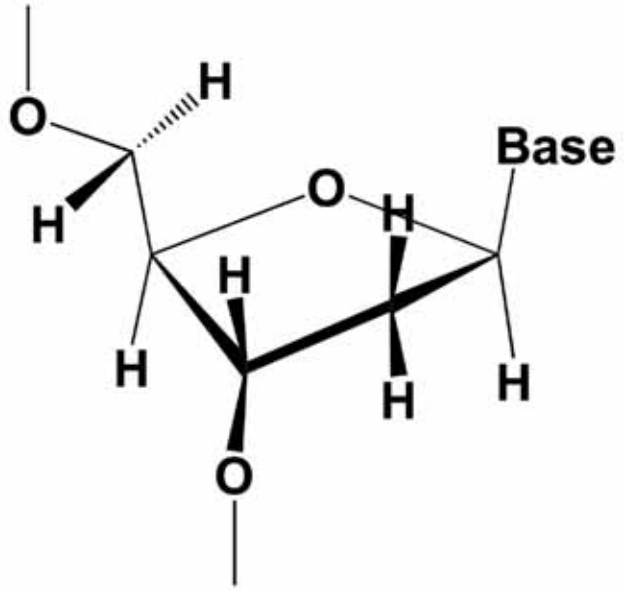
Flat faces are nonpolar
Edges are very polar (can H-bond)

Other chemical constraints

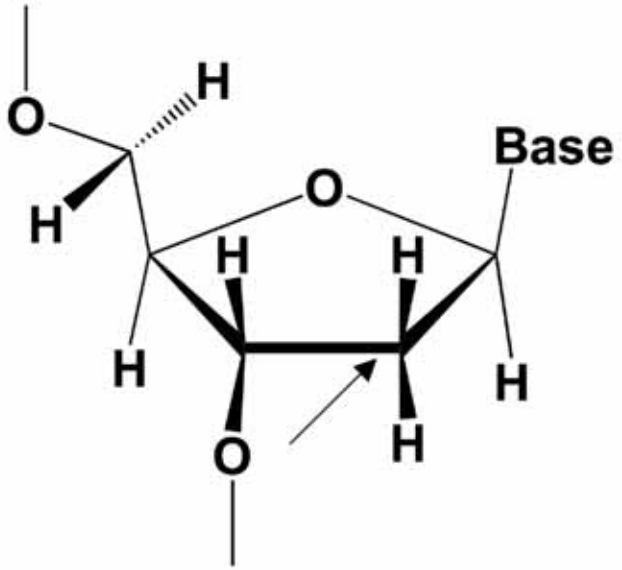
Furanose Sugar Ring

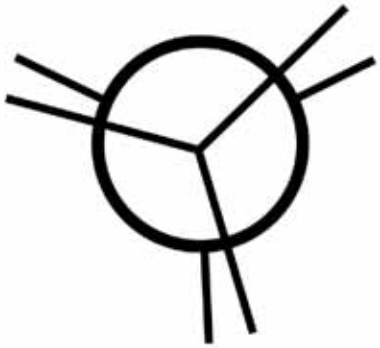


Furanose Sugar Ring

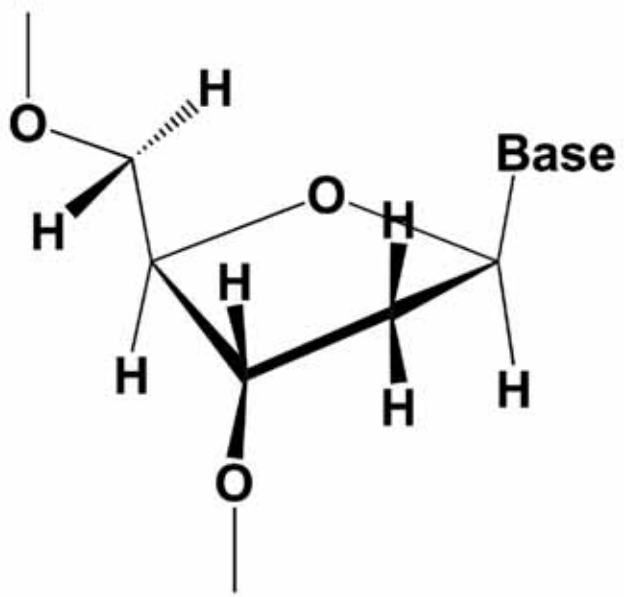


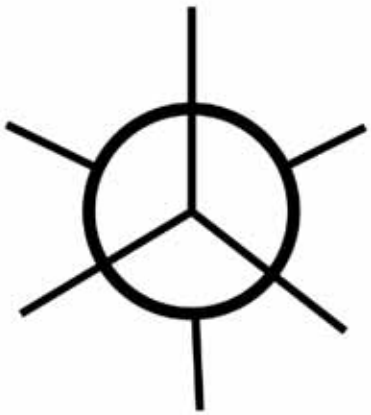
Furanose Sugar Ring



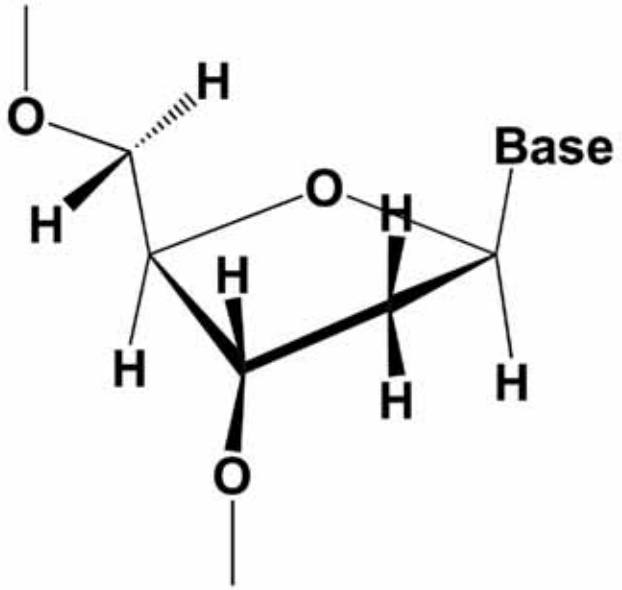


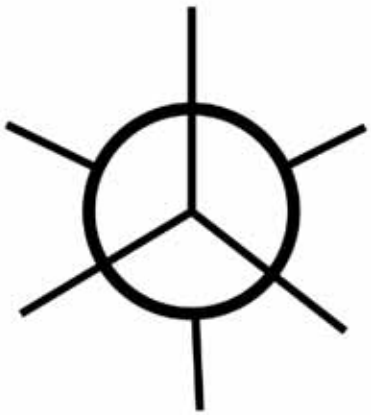
Furanose Sugar Ring

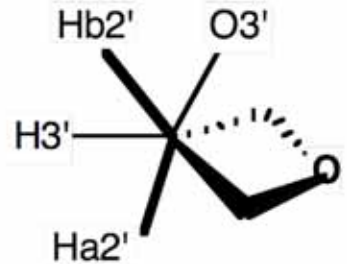




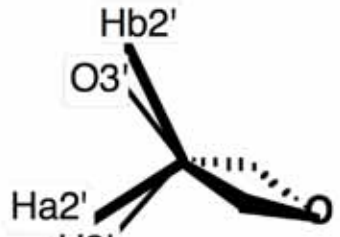
Furanose Sugar Ring





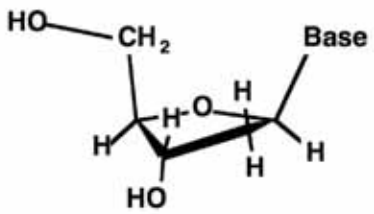


Staggered
Puckered

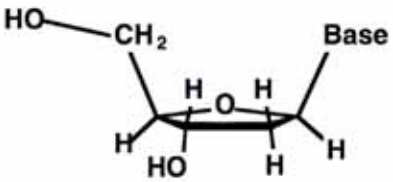


Eclipsed
Planar

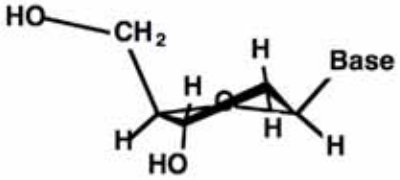
Furanose Sugar Ring



C3' exo



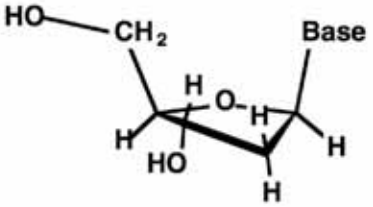
Unpuckered



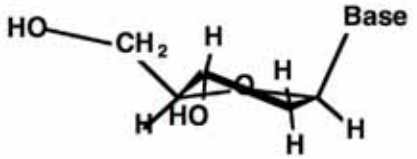
C2' endo

endo

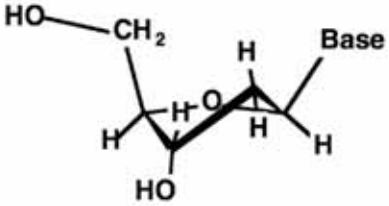
exo



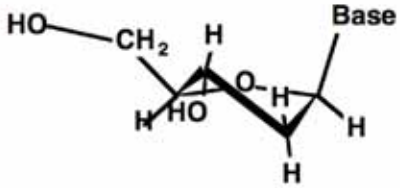
C2' exo



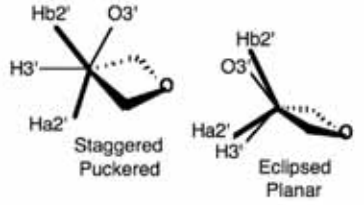
C3' endo

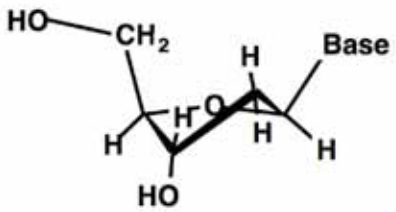


C2' endo - C3' exo

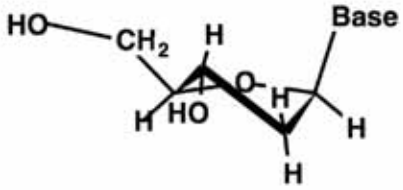


C2' exo - C3' endo





C2' endo - C3' exo



C2' exo - C3' endo

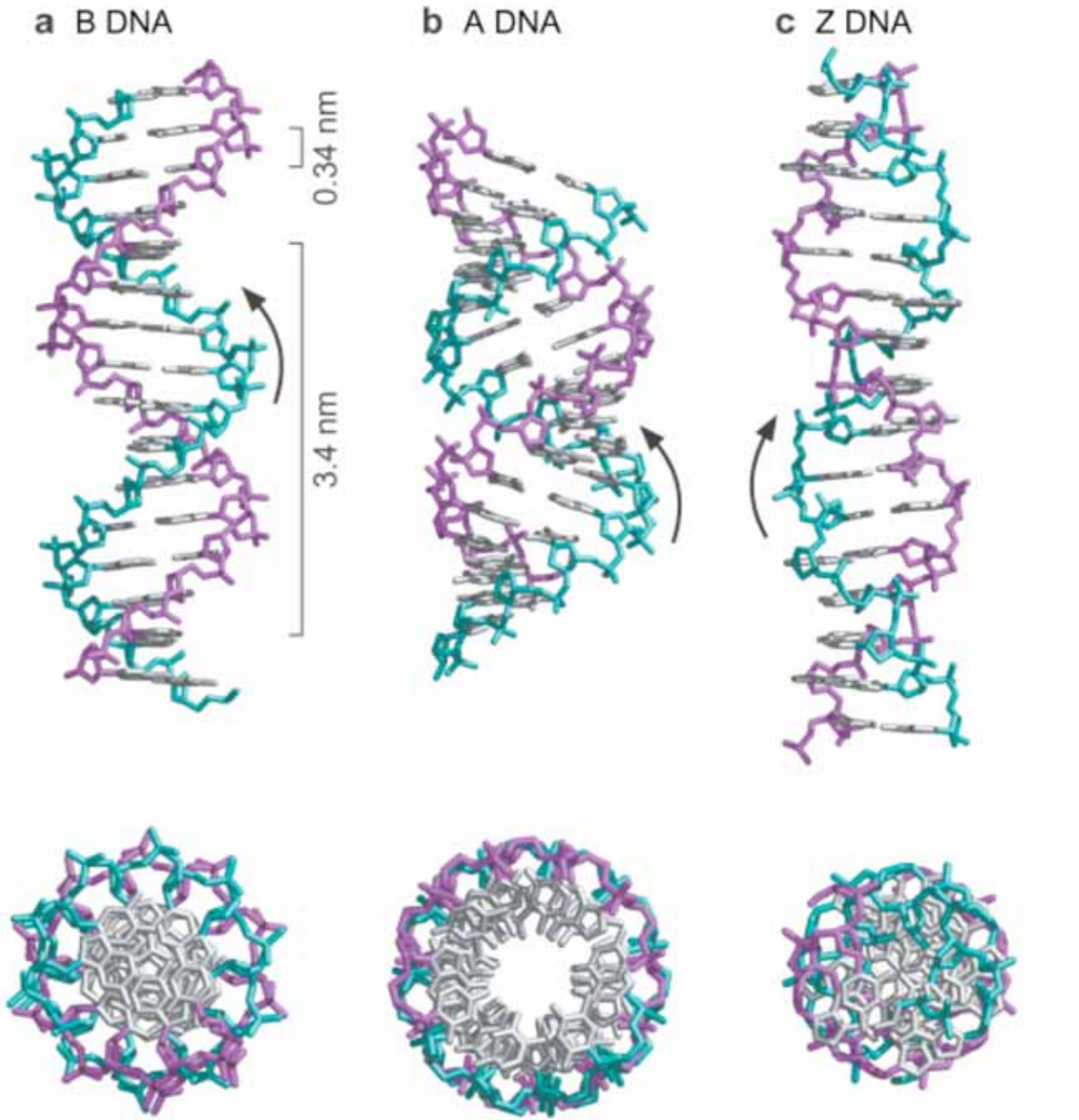


TABLE 6-2 A Comparison of the Structural Properties of A, B, and Z DNAs as Derived from Single-Crystal X-Ray Analysis

	Helix Type		
	A	**B**	**Z**
Overall proportions	Short and broad	Longer and thinner	Elongated and slim
Rise per base pair	2.3 Å	3.32 Å	3.8 Å
Helix-packing diameter	25.5 Å	23.7 Å	18.4 Å
Helix rotation sense	Right-handed	Right-handed	Left-handed
Base pairs per helix repeat	1	1	2
Base pairs per turn of helix	~11	~10	12
Rotation per base pair	33.6°	35.9°	−60° per 2 bp
Pitch per turn of helix	24.6 Å	33.2 Å	45.6 Å
Tilt of base normals to helix axis	+19°	−1.2°	−9°
Base-pair mean propeller twist	+18°	+16°	~0°
Helix axis location	Major groove	Through base pairs	Minor groove
Major-groove proportions	Extremely narrow but very deep	Wide and of intermediate depth	Flattened out on helix surface
Minor-groove proportions	Very broad but shallow	Narrow and of intermediate depth	Extremely narrow but very deep
Glycosyl-bond conformation	*anti*	*anti*	*anti* at C, *syn* at G

Source: Adapted from Dickerson R. E. et al. 1982. *CSHSQB* 47: 14. Copyright © 1982 Cold Spring Harbor Laboratory Press. Used with permission.

Hoogsteen vindicated

Letters to Nature

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

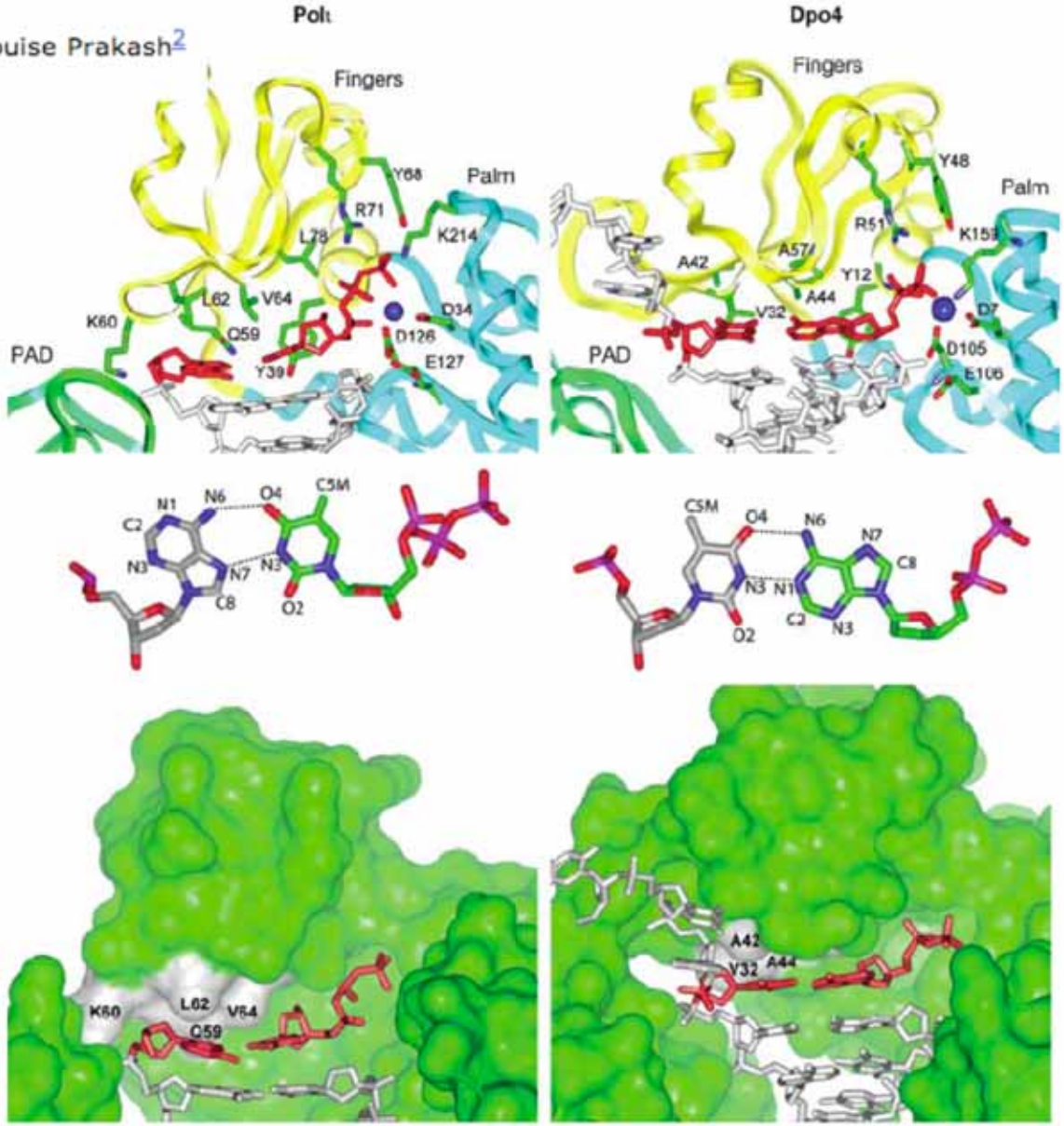
Replication by human DNA polymerase-ι occurs by Hoogsteen base-pairing

Deepak T. Nair[1], Robert E. Johnson[2], Satya Prakash[2], Louise Prakash[2] and Aneel K. Aggarwal[1]

A crystal structure from 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.



Hoogsteen vindicated

But… perhaps not…

Letters to Nature

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

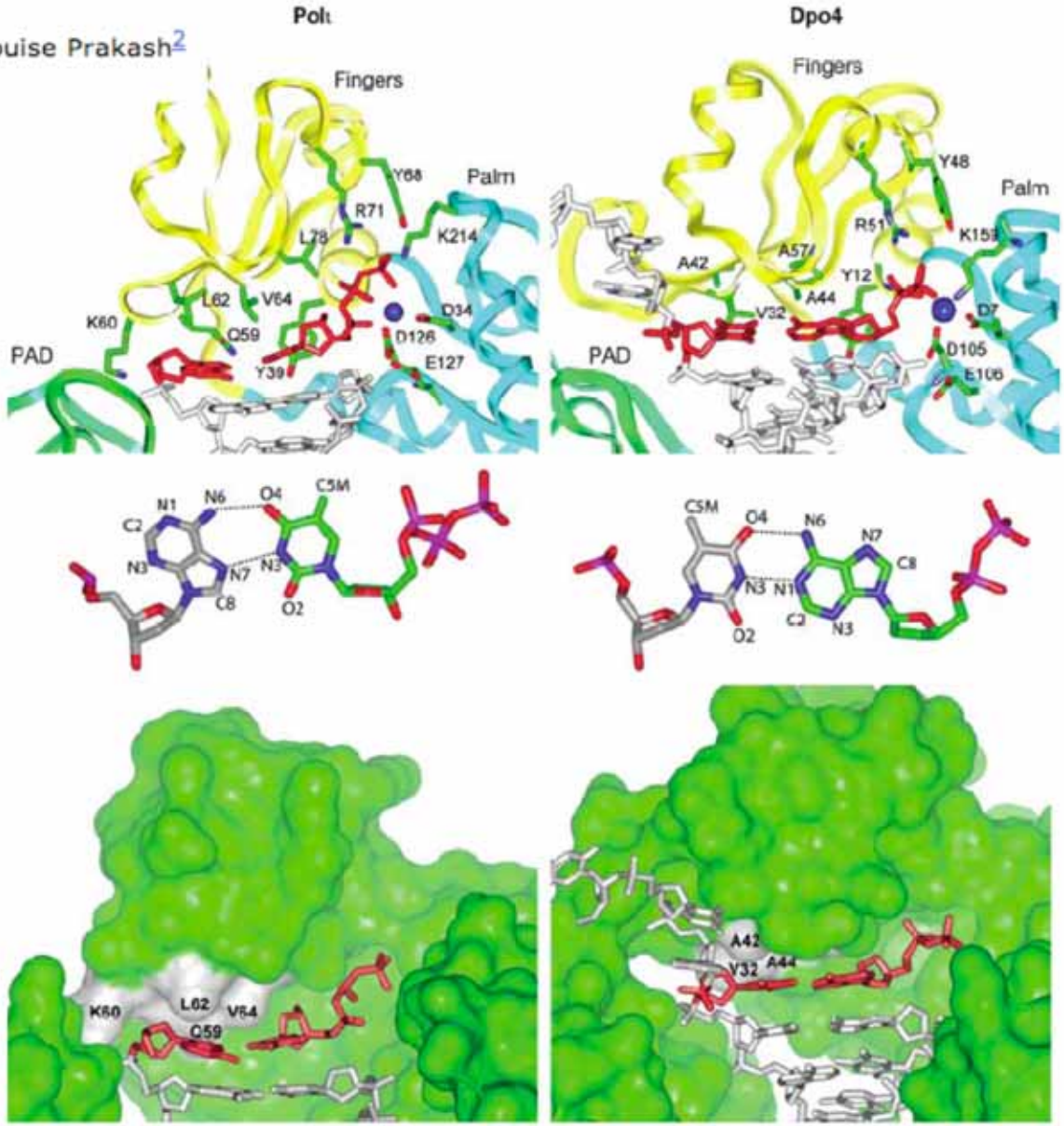
Replication by human DNA polymerase-ι occurs by Hoogsteen base-pairing

Deepak T. Nair[1], Robert E. Johnson[2], Satya Prakash[2], Louise Prakash[2] and Aneel K. Aggarwal[1]

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

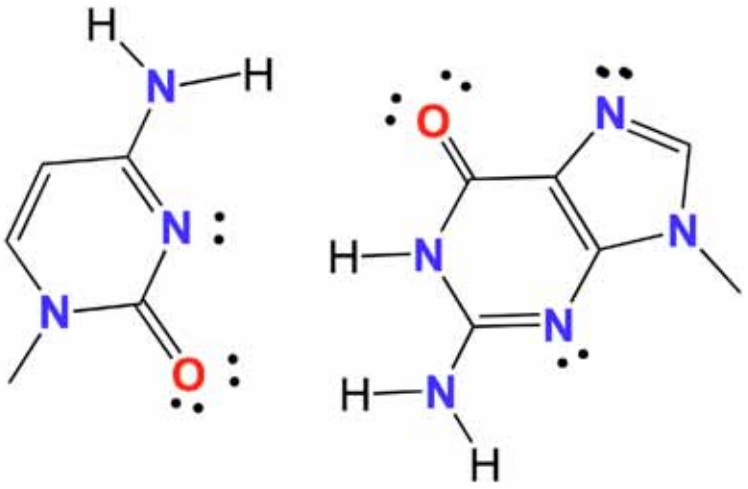
This supports biochemical studies that had been suggesting such a pairing.

This polymerase is good at bypassing lesions in the DNA.



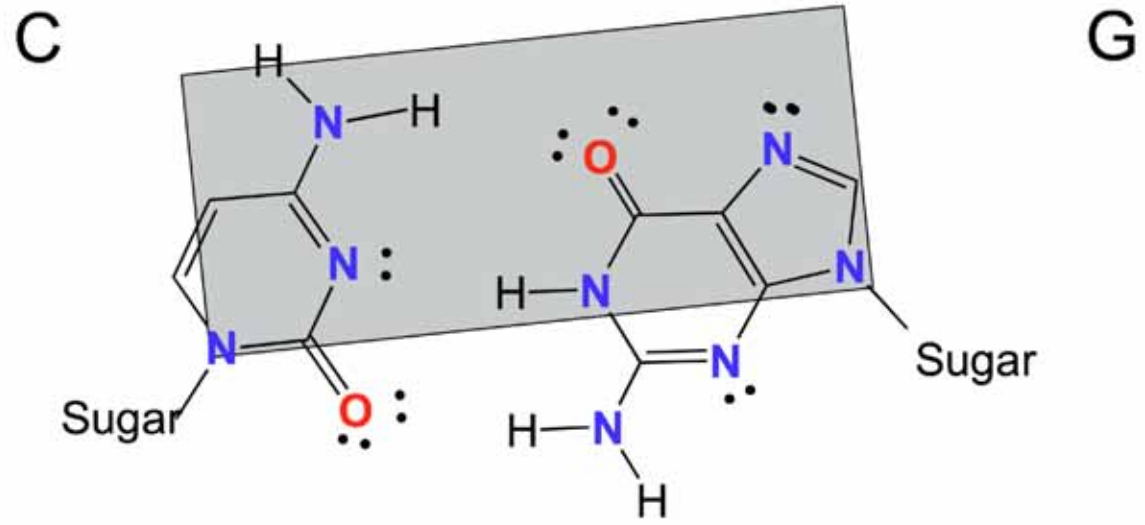
Why is Watson-Crick so good?

C

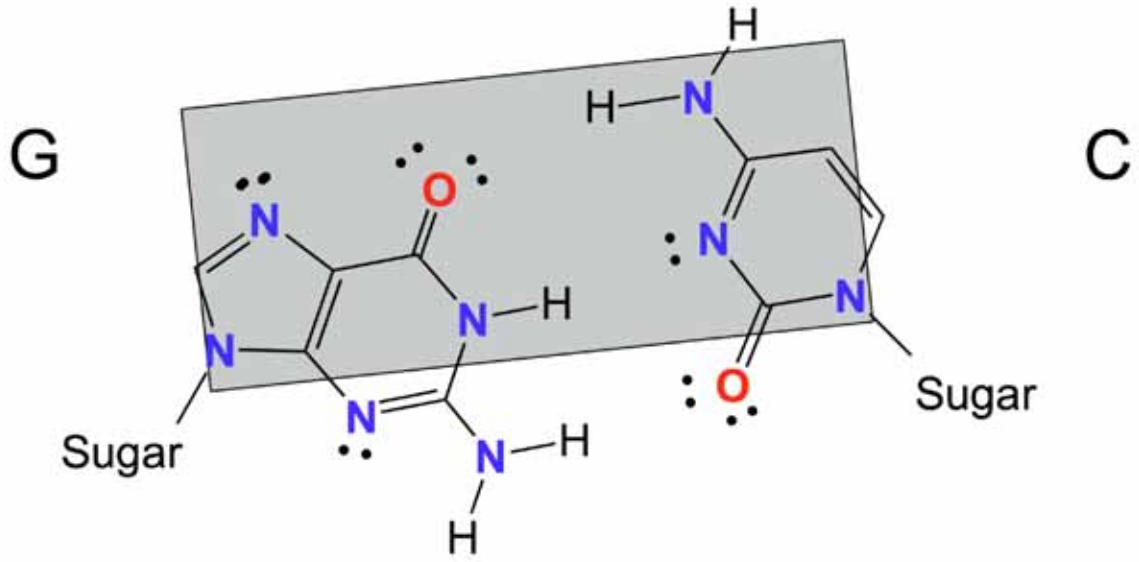


G

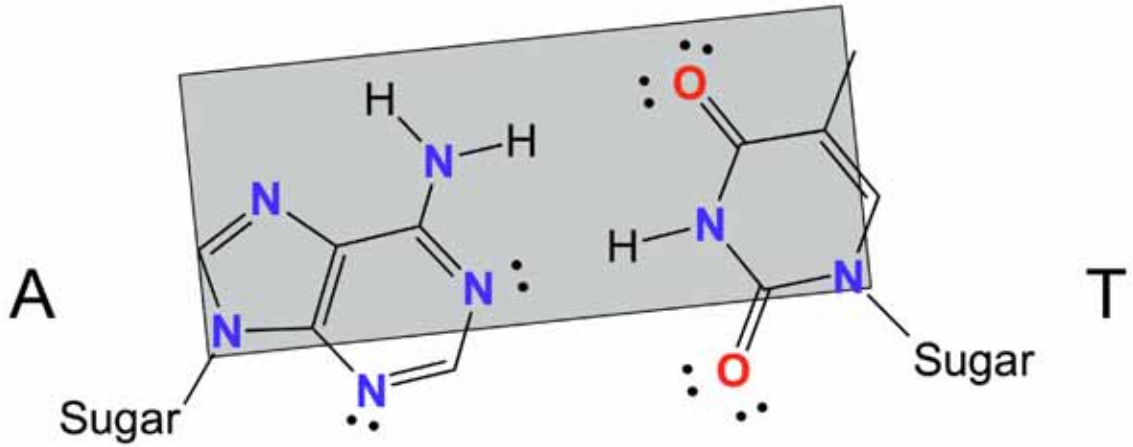
Why is Watson-Crick so good?



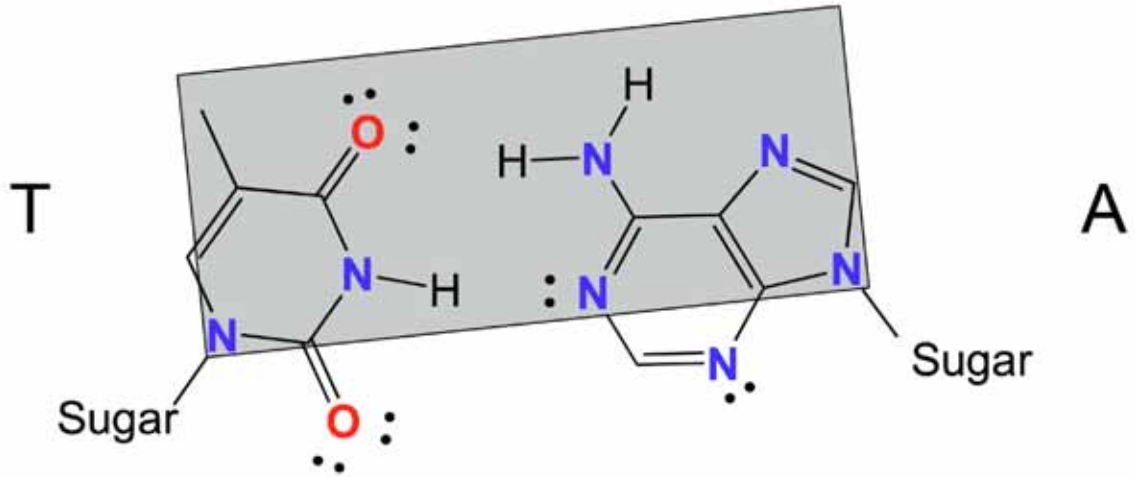
Why is Watson-Crick so good?



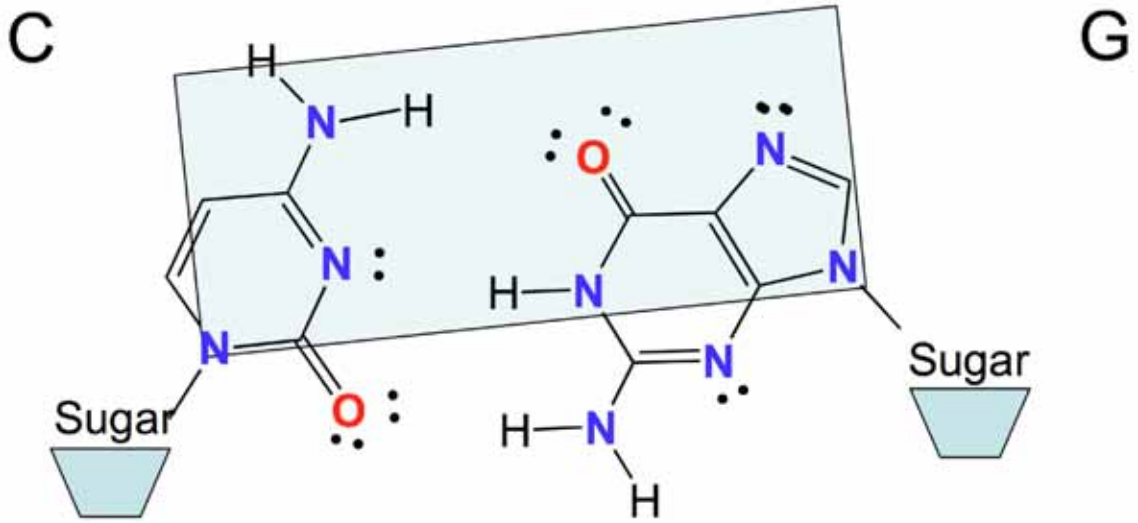
Why is Watson-Crick so good?



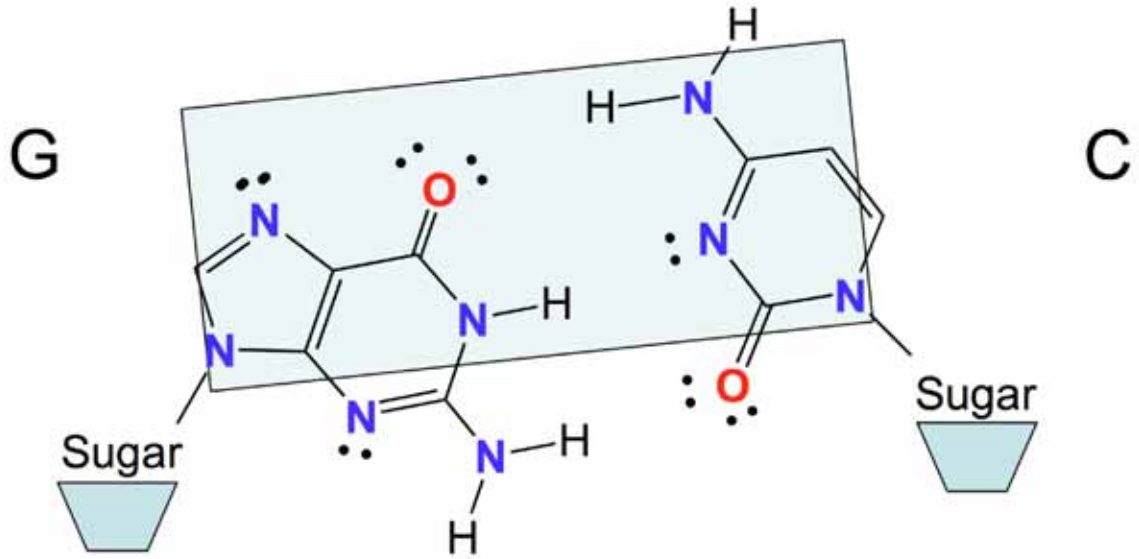
Why is Watson-Crick so good?



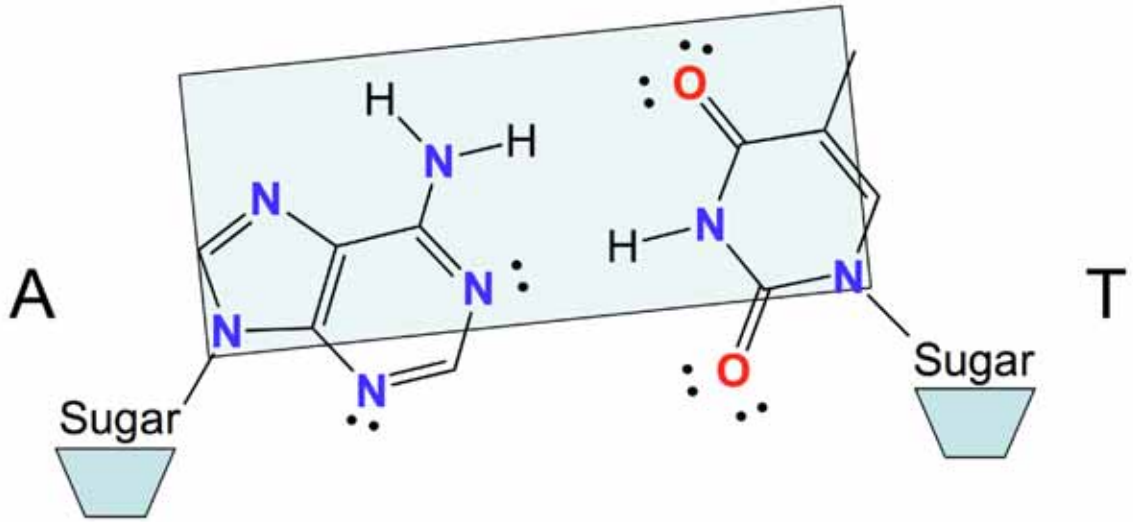
Why is Watson-Crick so good?



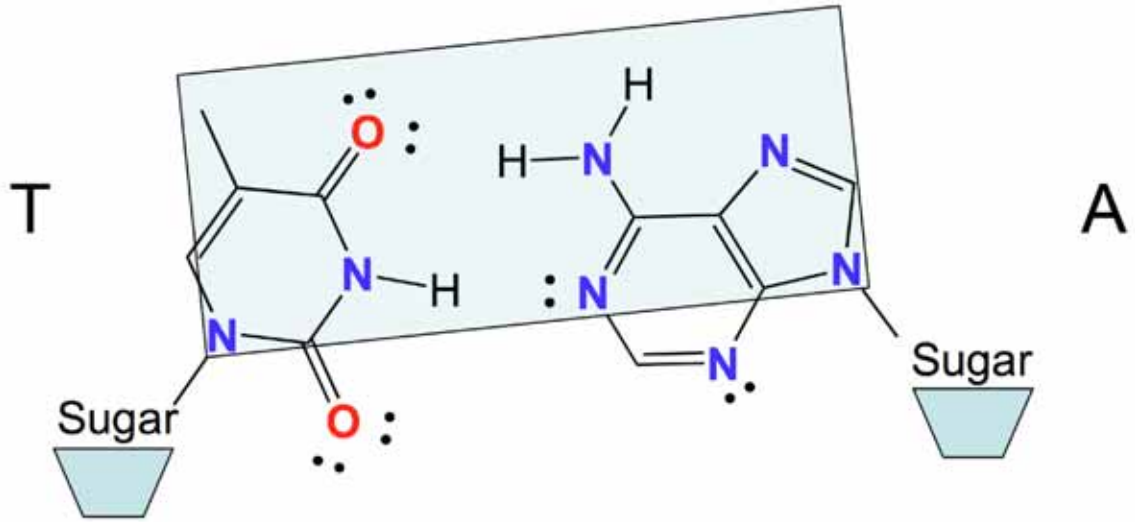
Why is Watson-Crick so good?

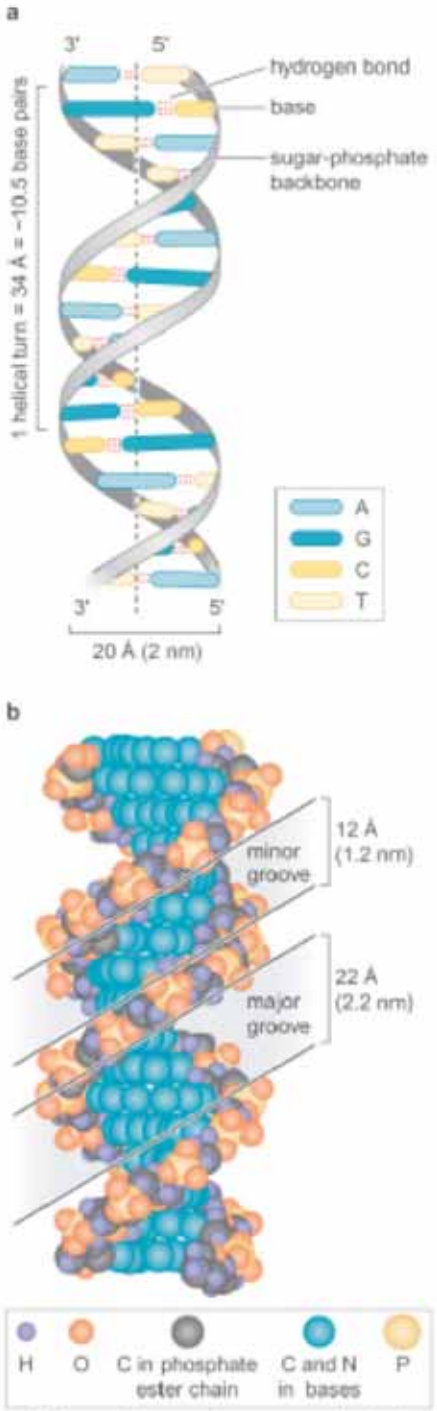


Why is Watson-Crick so good?



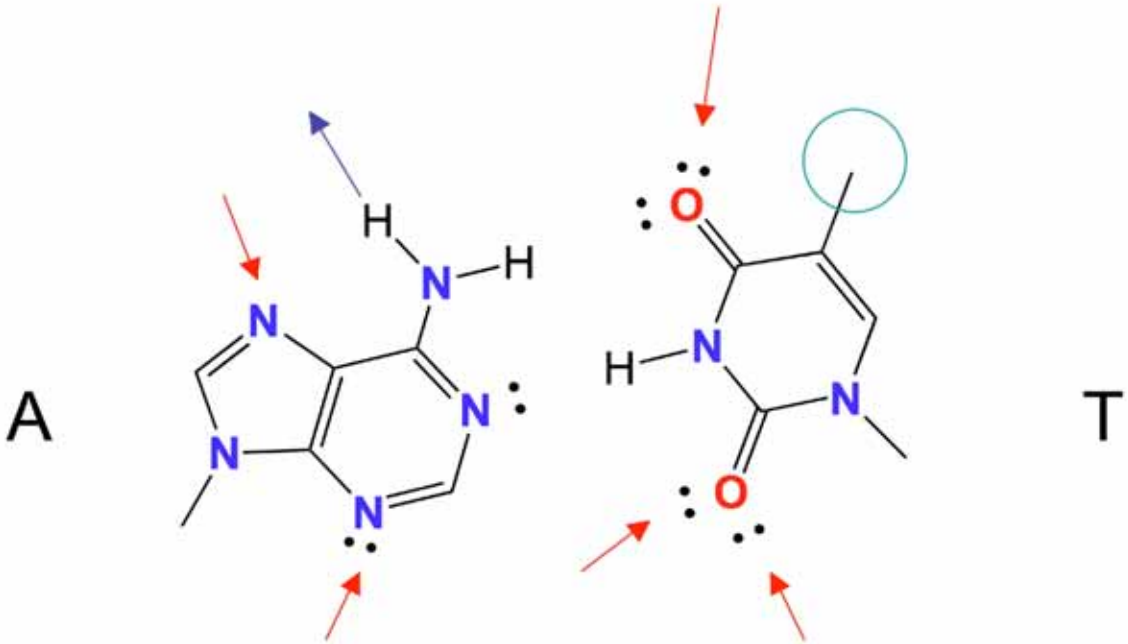
Why is Watson-Crick so good?





Why is the major groove so good?

Major Groove

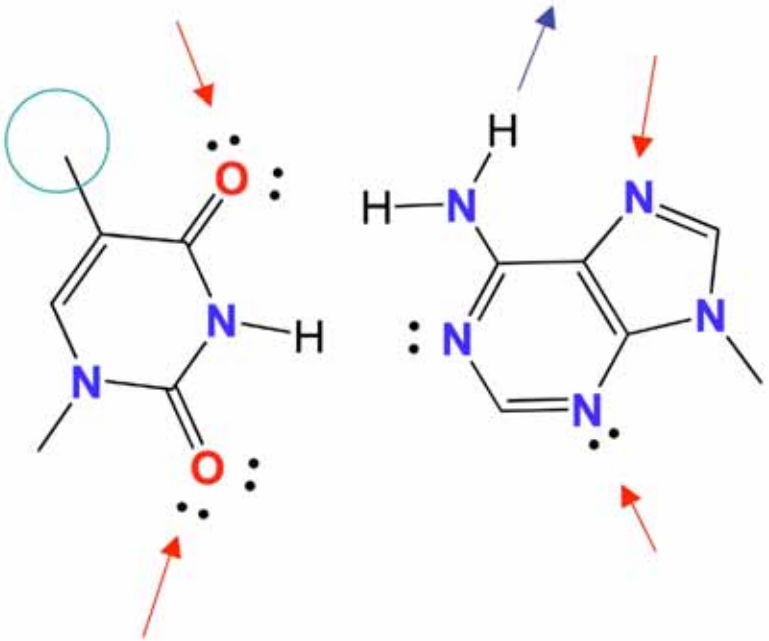


Minor Groove

Why is the major groove so good?

Major Groove

T

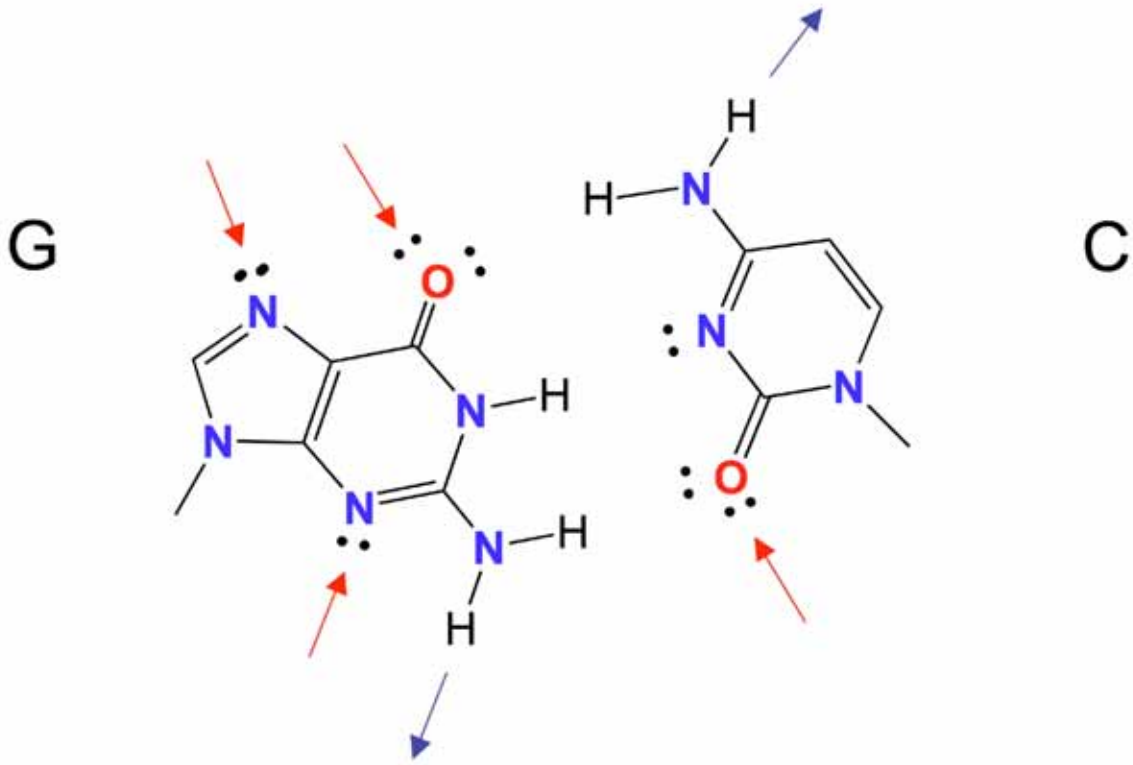


A

Minor Groove

Why is the major groove so good?

Major Groove

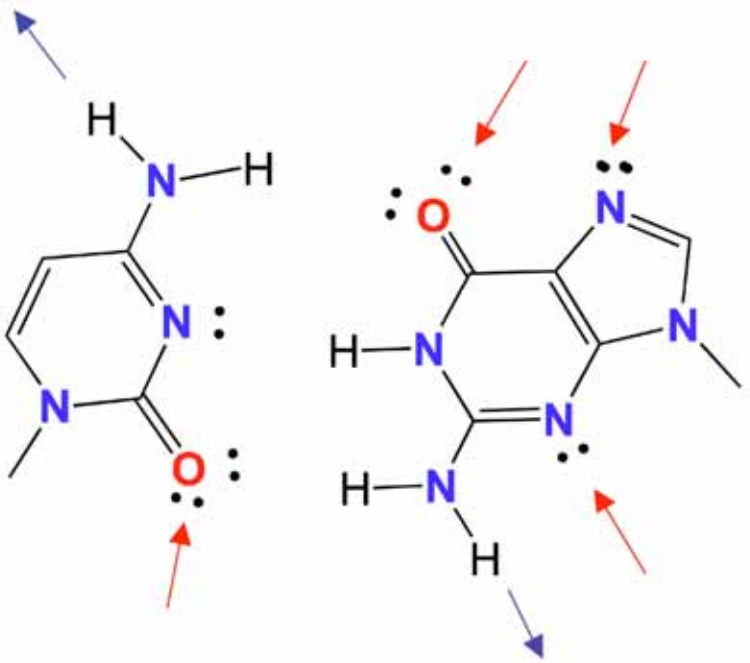


Minor Groove

Why is the major groove so good?

Major Groove

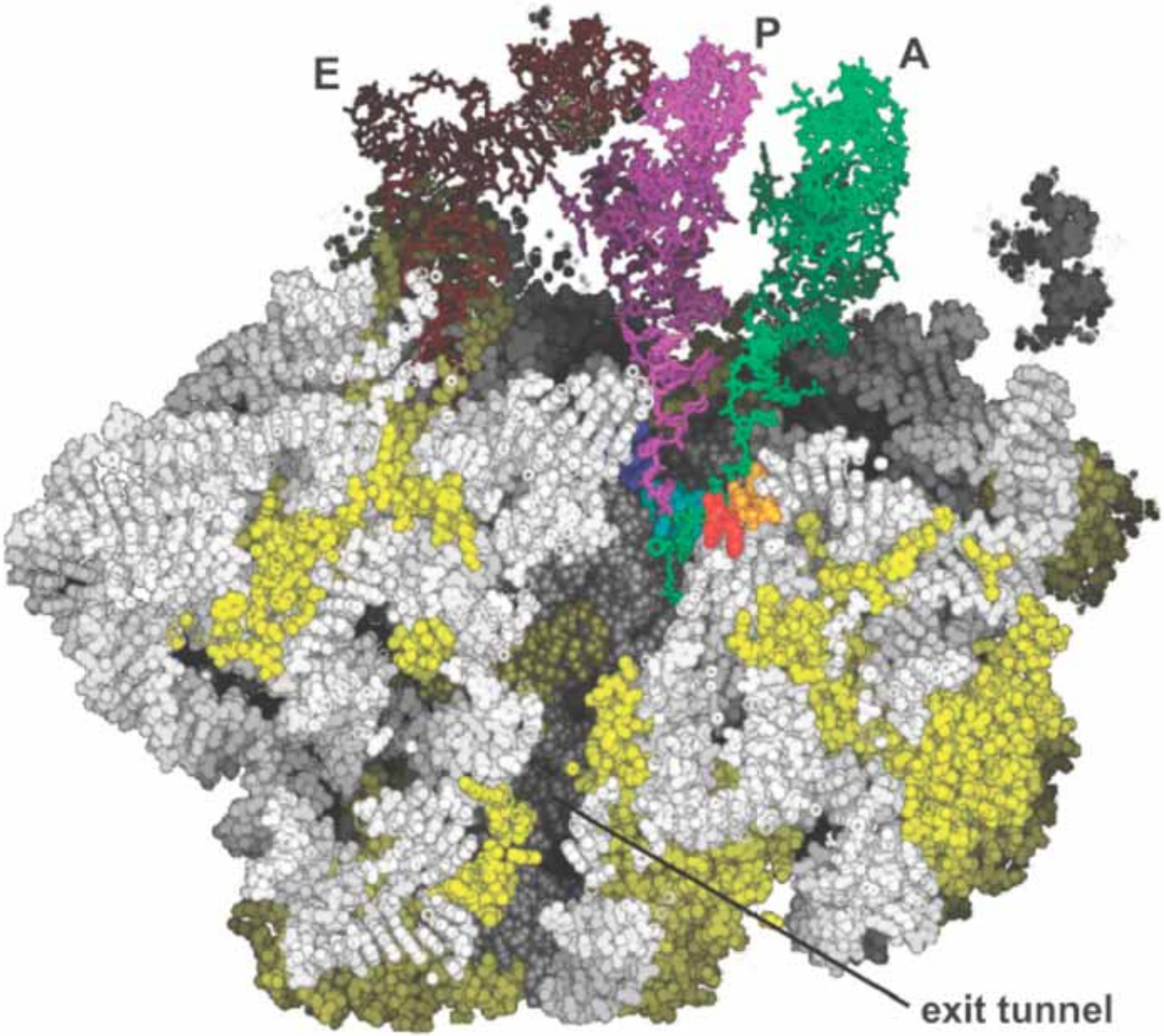
C



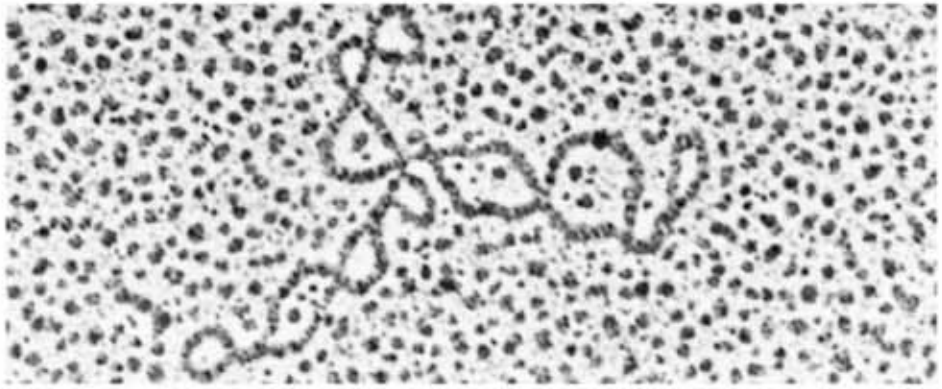
G

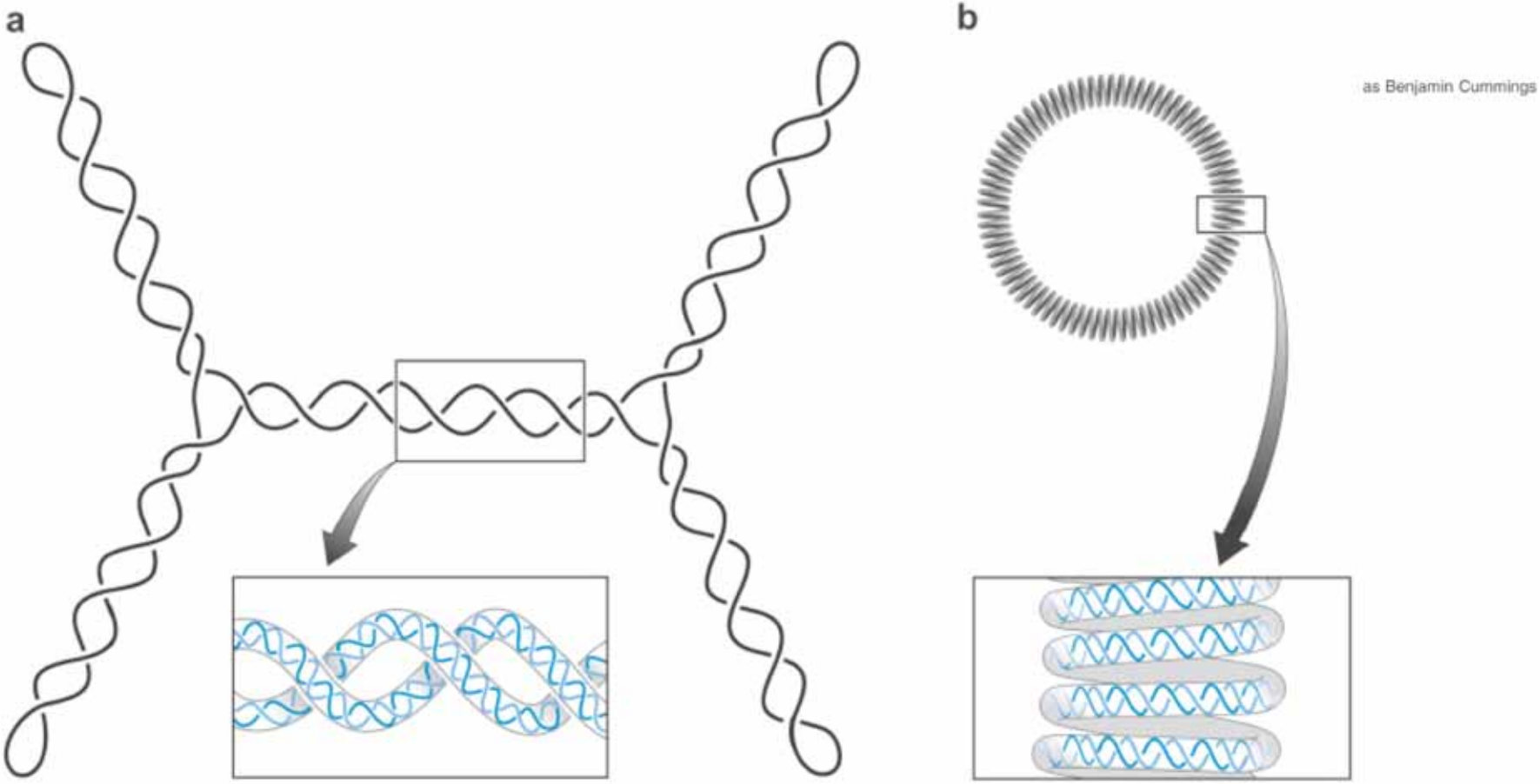
Minor Groove

Ribosome

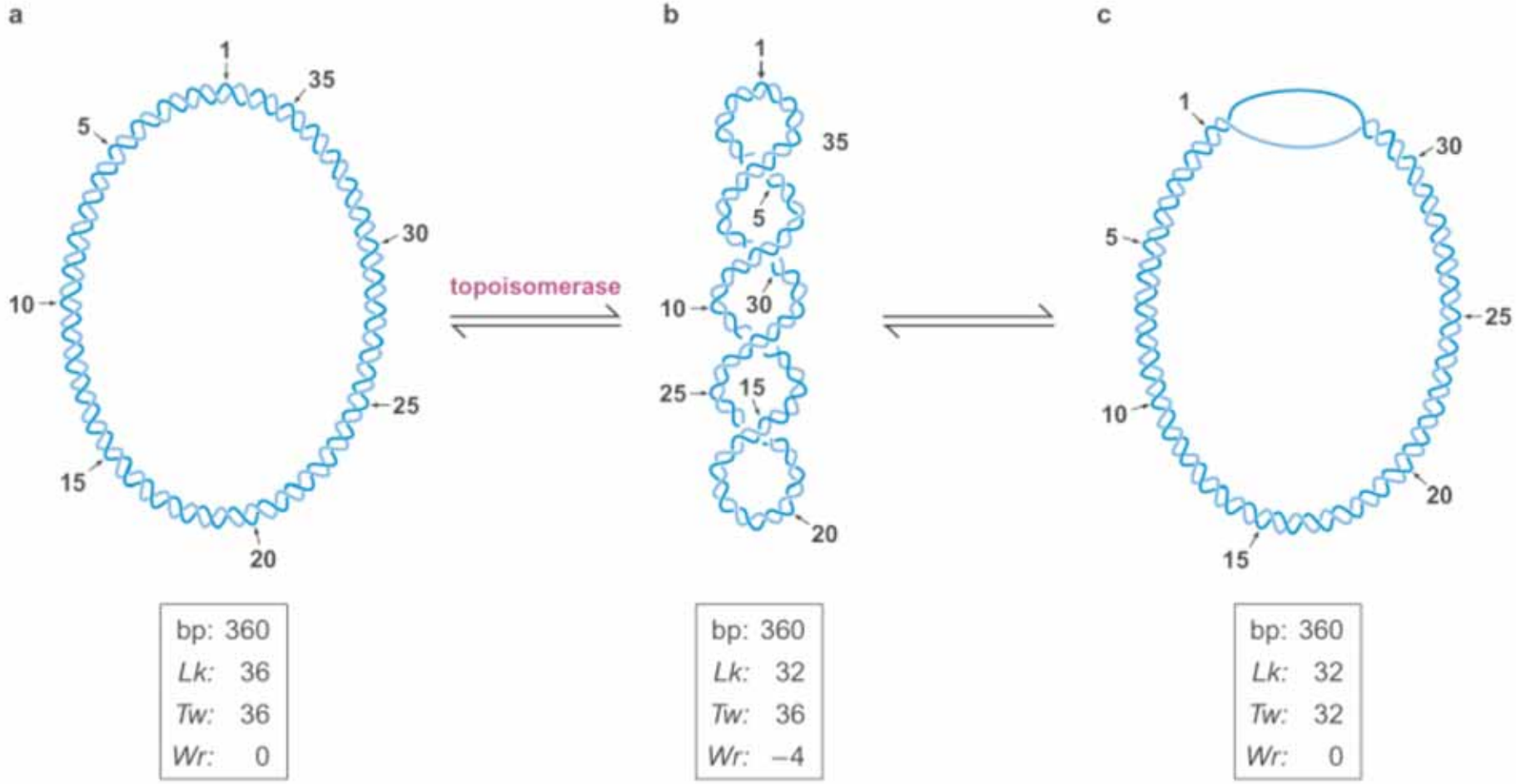


Supercoiling

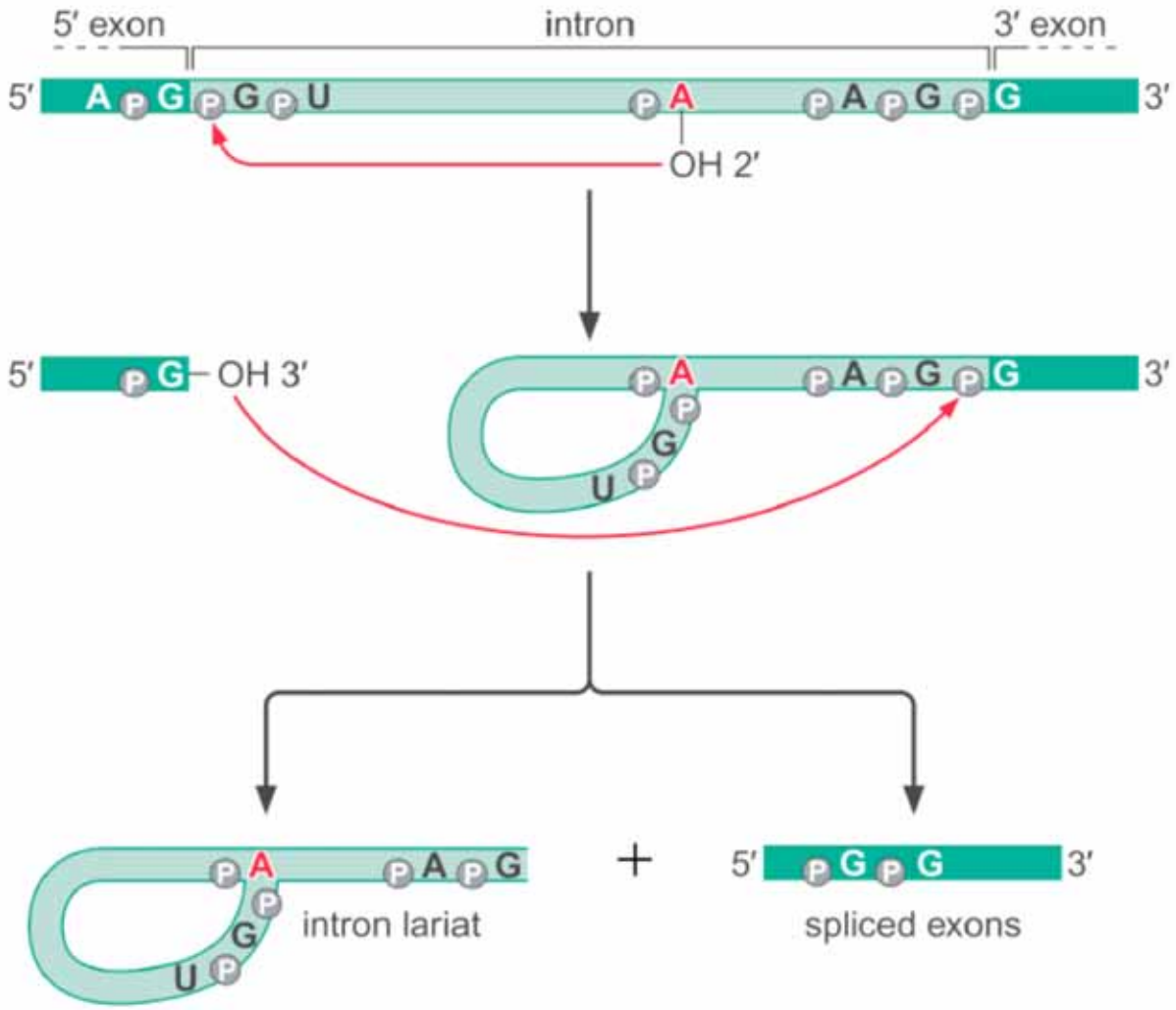




Supercoiling



RNA Splicing



Translation