# Nucleic Acids
# Why do I care?

# Nucleic Acids
# Why do I care?

Proteins do everything, right?

# 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…

DNA

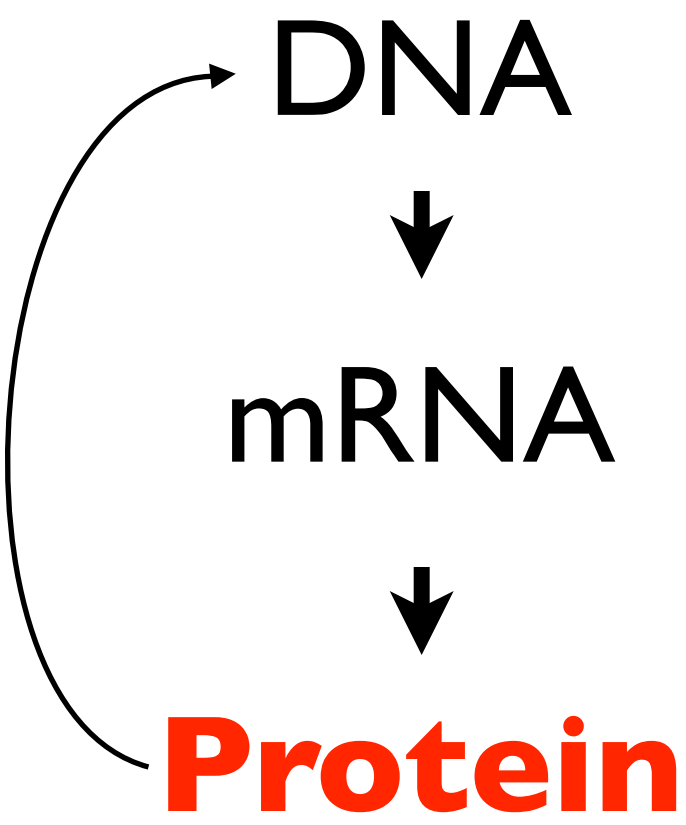
↓

mRNA

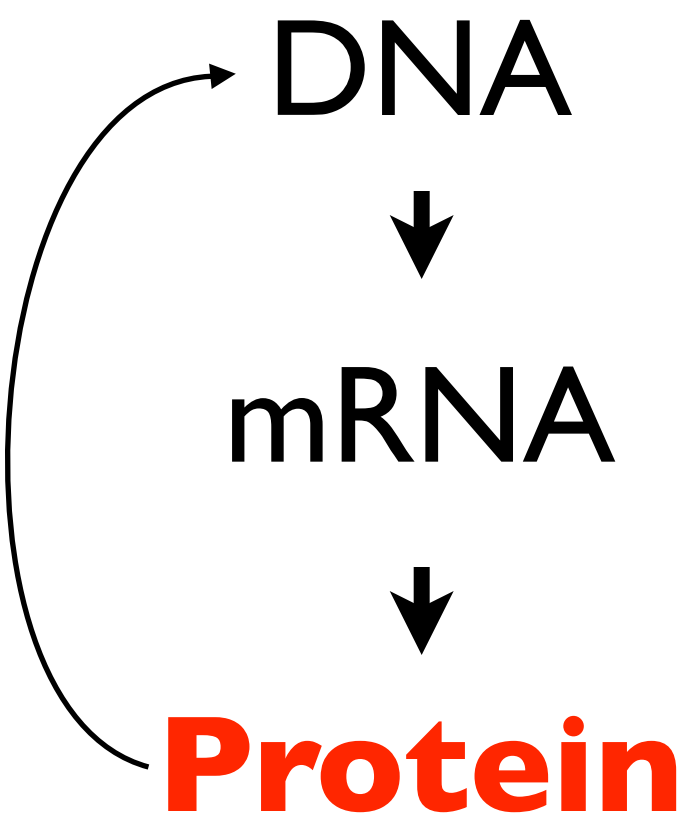
↓

**Protein**

# In the beginning…

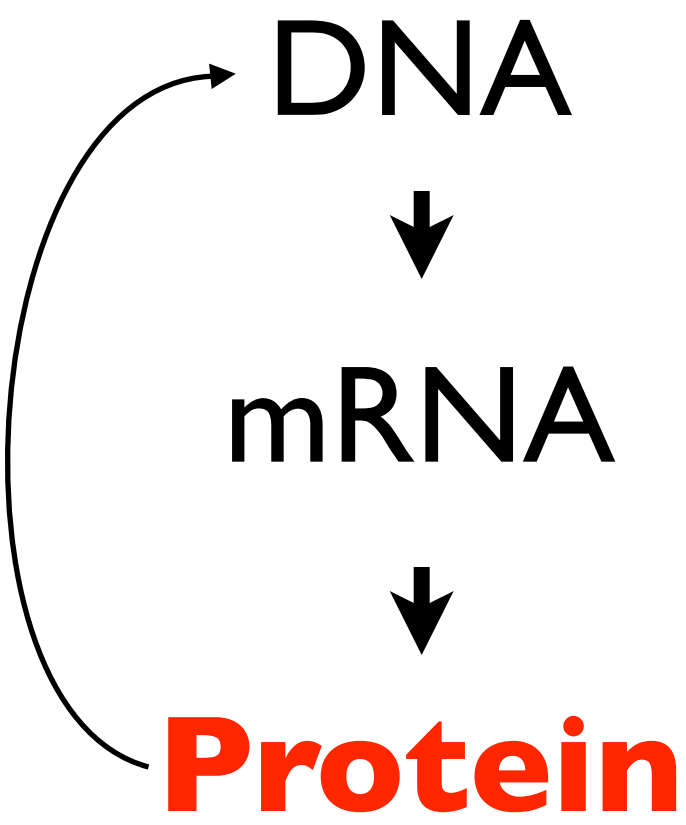


# In the beginning…




Archival information storage

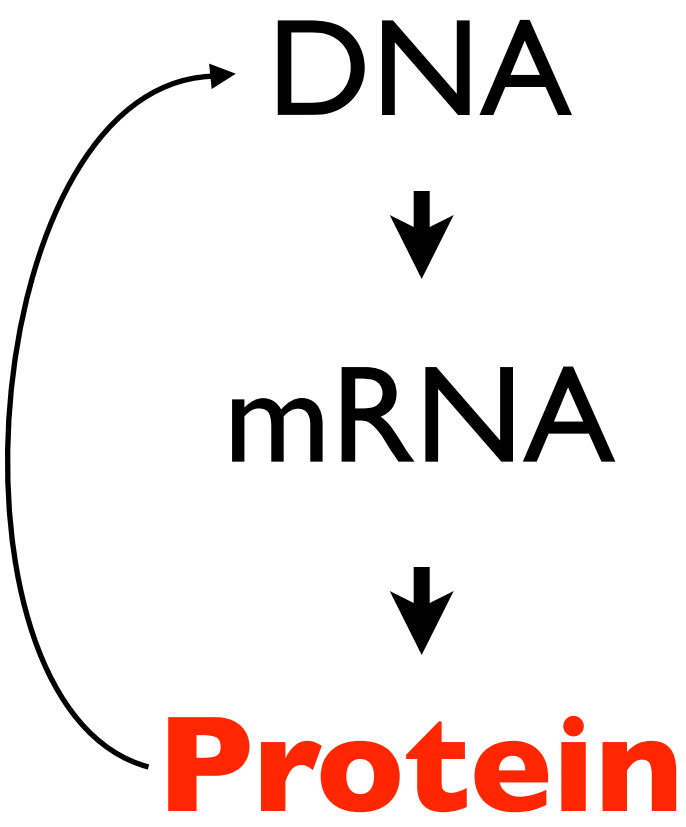
# In the beginning…




Archival information storage

Transient information storage

# In the beginning…

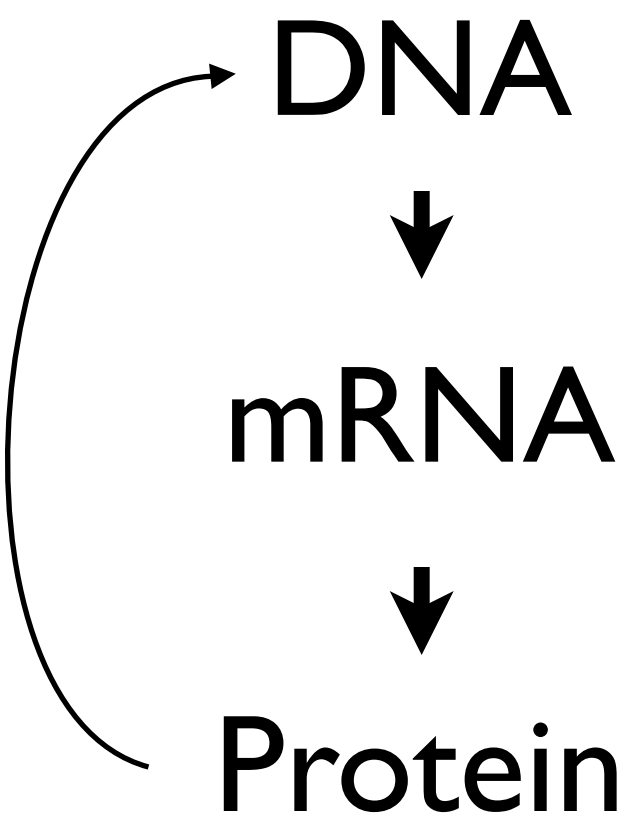



Archival information storage

Transient information storage

Catalysis, structure, regulation, et al.

# Chicken & Egg?

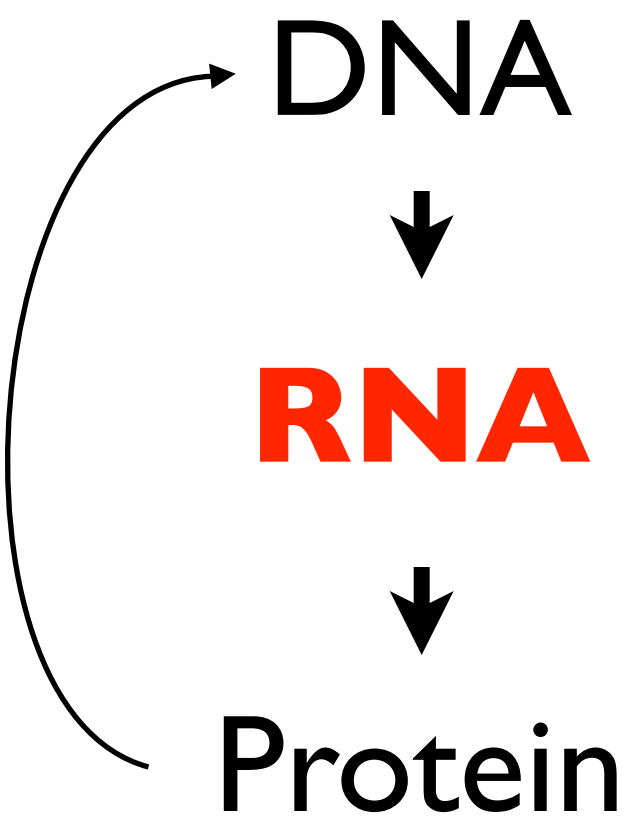



Archival information storage

Transient information storage

Catalysis, structure, regulation, et al.

# RNA can do everything



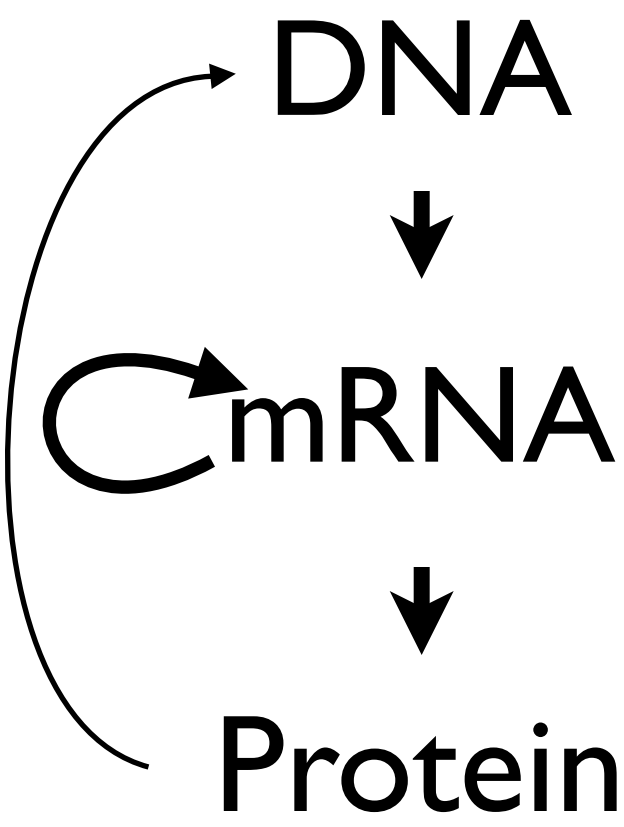

Archival information storage

Transient information storage
**Catalysis!**

1980-2000

Catalysis, structure, regulation, et al.

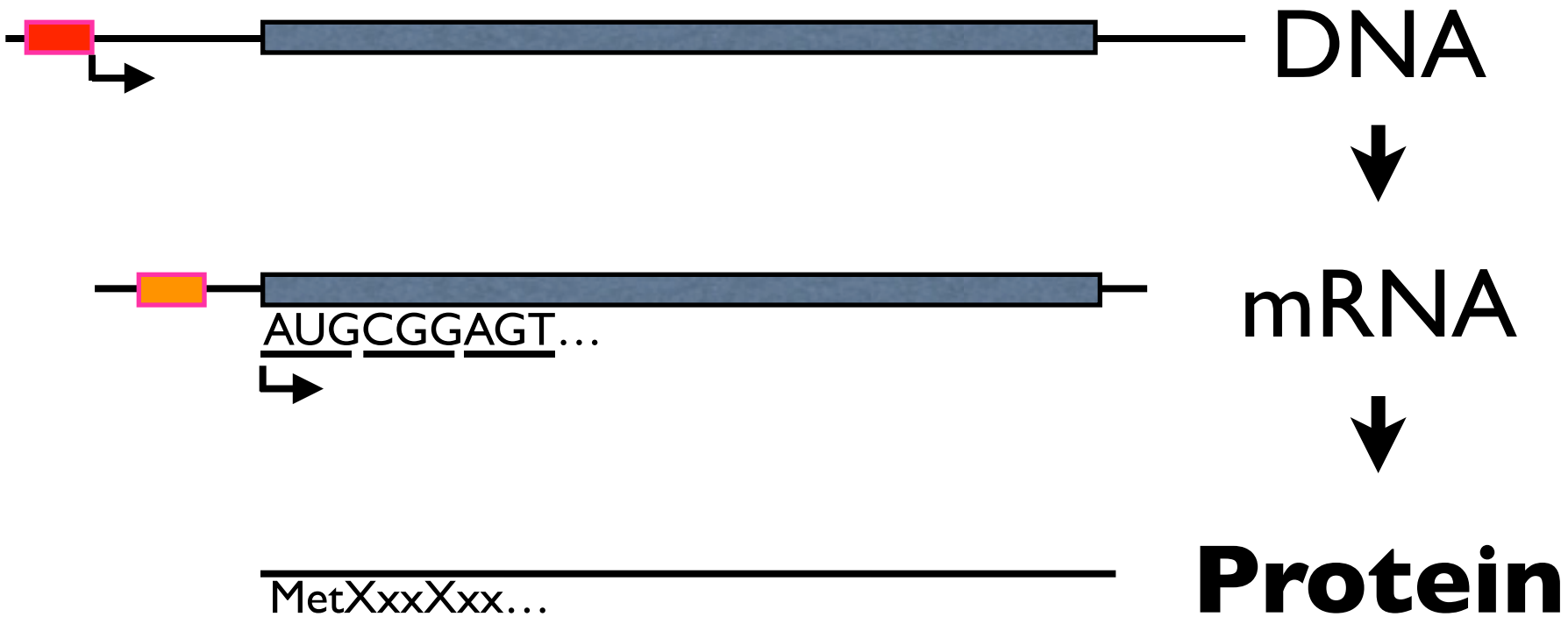
# RNA - primordial molecule




So we accepted that RNA was probably the first, primitive do-everything biomolecule.

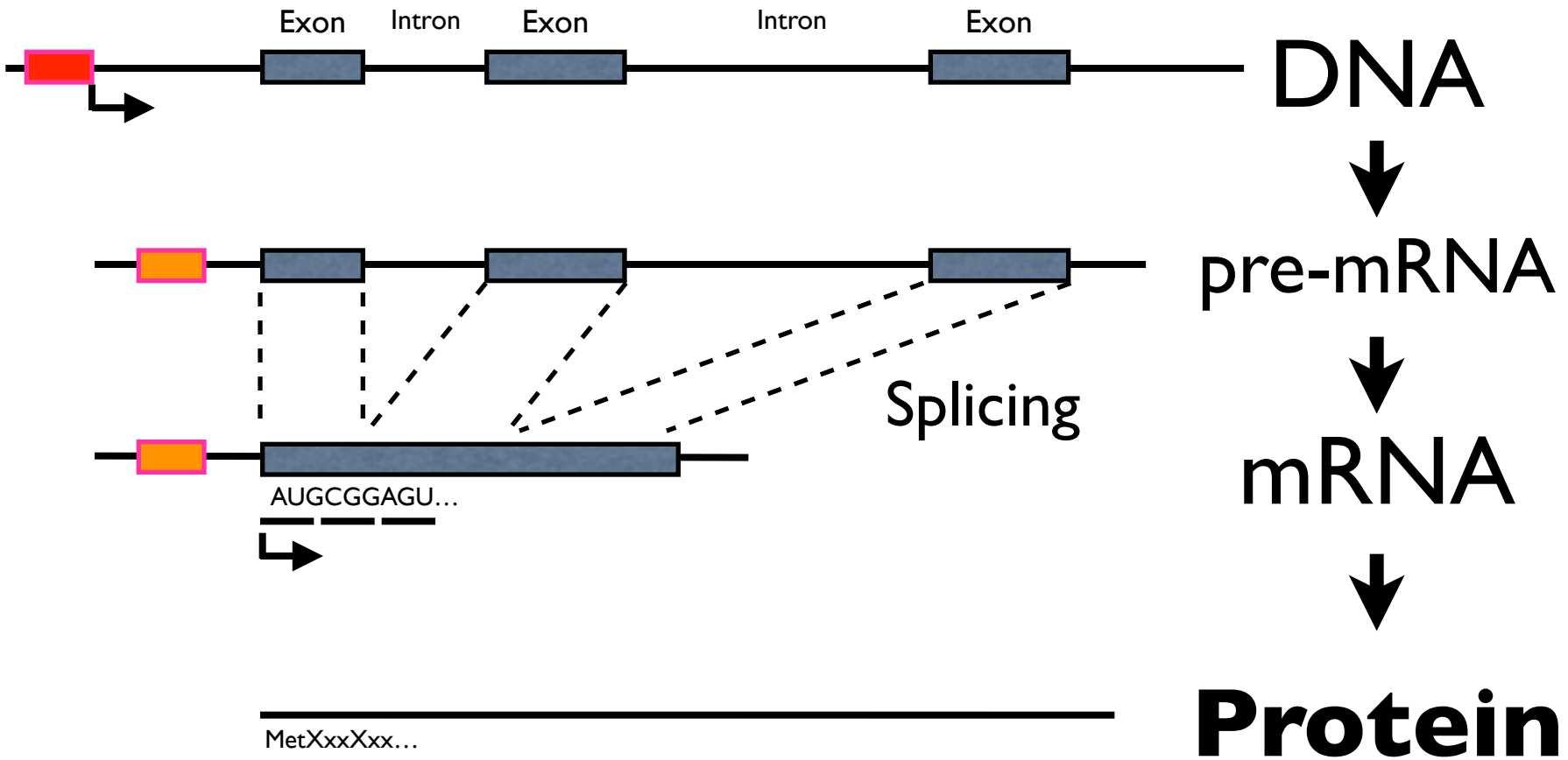
But **proteins** came along to supplant everything and make the world, evolutionarily, what it is today. All hail the protein!

# Seems simple…

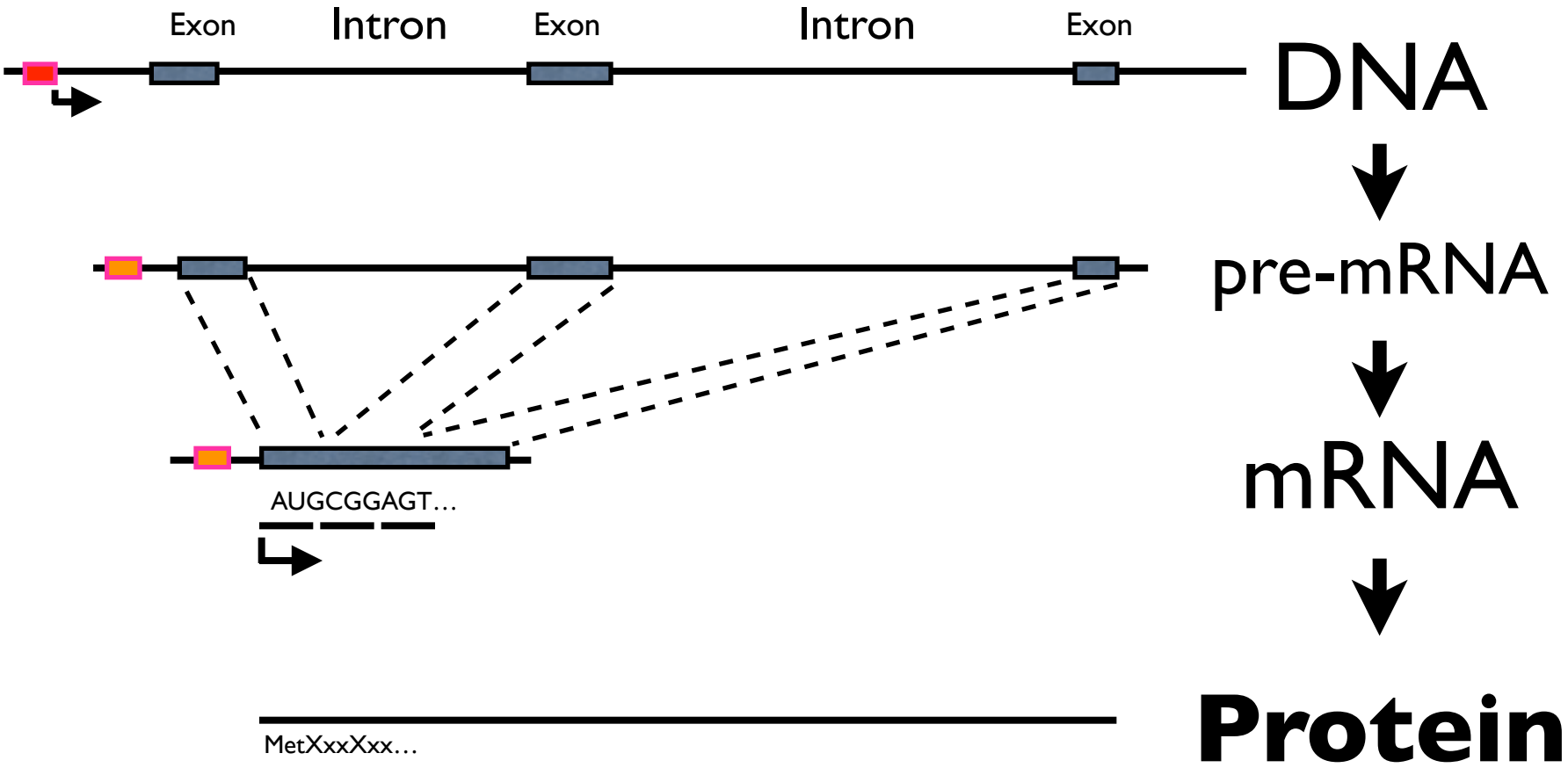


# Seems simple?

# Even more complicated…

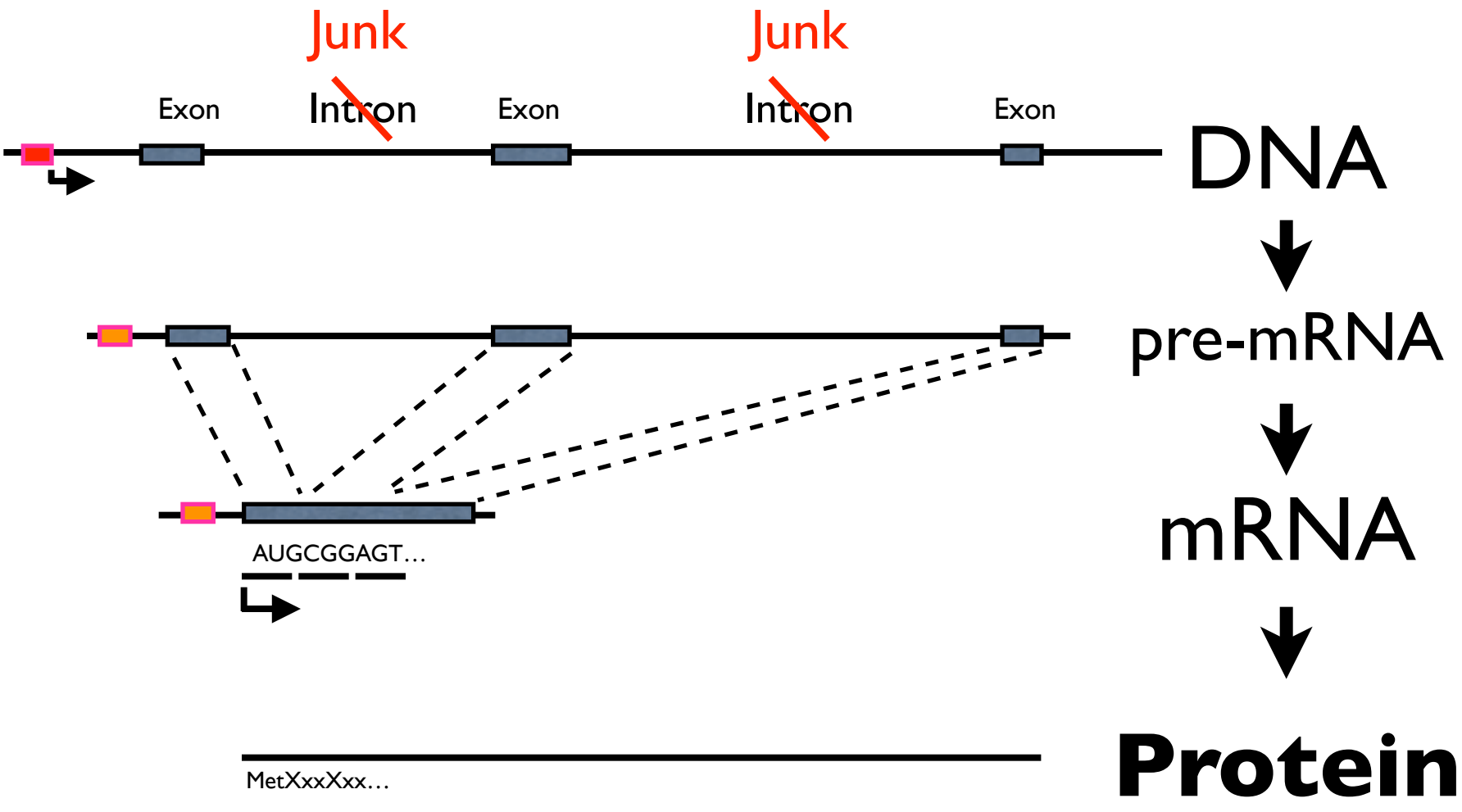


# Reality…


Exon
Intron
Exon
Intron
Exon
DNA
pre-mRNA
mRNA
AUGCGGAGT…
MetXxxXxx…
Protein

# Reality…

## and our perception of it



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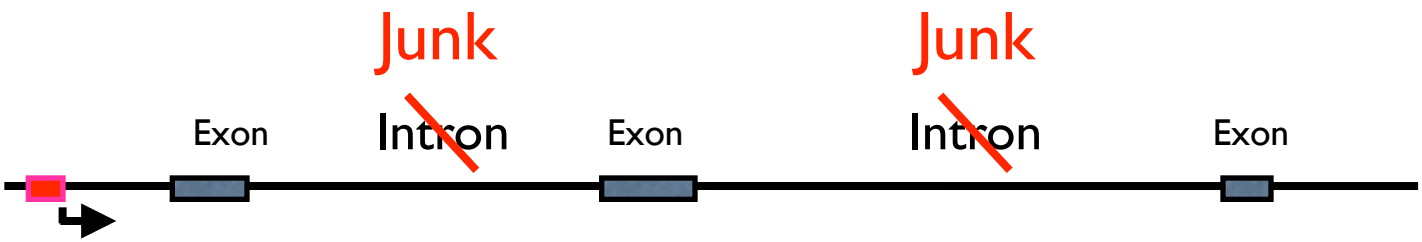

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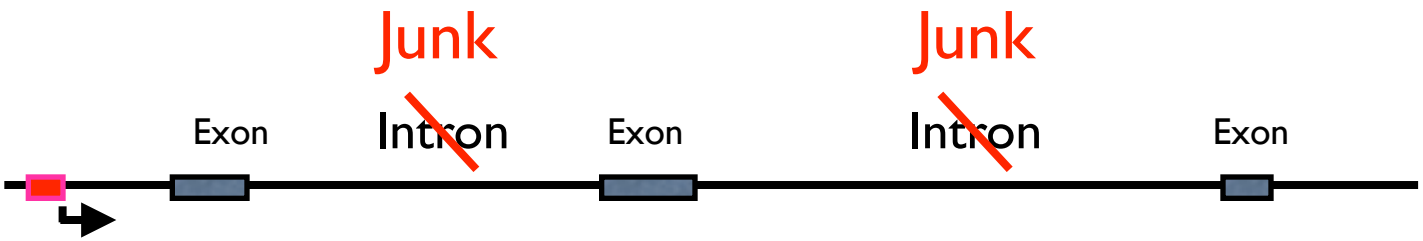


# Genome project goals

Identify and characterize the proteins.
What are their structures?
What do they do?
How do they interact?

# 20th Century View

Polymerases

Kinases

Hydrogenases

Receptors

Oxygenases

Proteases

# 20th Century View

Polymerases

Kinases

Hydrogenases

Receptors

Oxygenases

Proteases

Nucleic acids → Trash

# 21st Century News

## Genome project

Number of protein-encoding genes in the human genome: 25,000

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Number of protein-encoding genes in the 1,000 cell *C elegans* genome: 19,500

Number of protein-encoding genes in the corn genome: 40,000

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How? RNA editing and alternative splicing

Up to 3/4 of all human genes are subject to alternative editing

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Number of different proteins: ≫25,000

How? RNA editing and alternative splicing

Up to 3/4 of all human genes are subject to alternative editing

The prevalence of alternative editing appears to increase with an organism's complexity

# 21st Century News

## Genome project

### How? RNA editing and alternative splicing

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### How? RNA editing and alternative splicing

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Humans have the highest number of introns per gene of any organism

# 21st Century News

## Genome project

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Humans have the highest number of introns per gene of any organism

At least 15% of of the gene mutations that produce genetic diseases and cancers do so by effecting pre-mRNA editing

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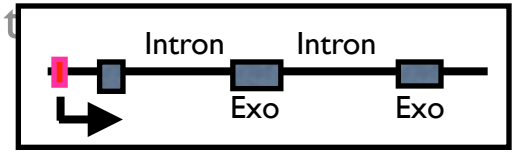


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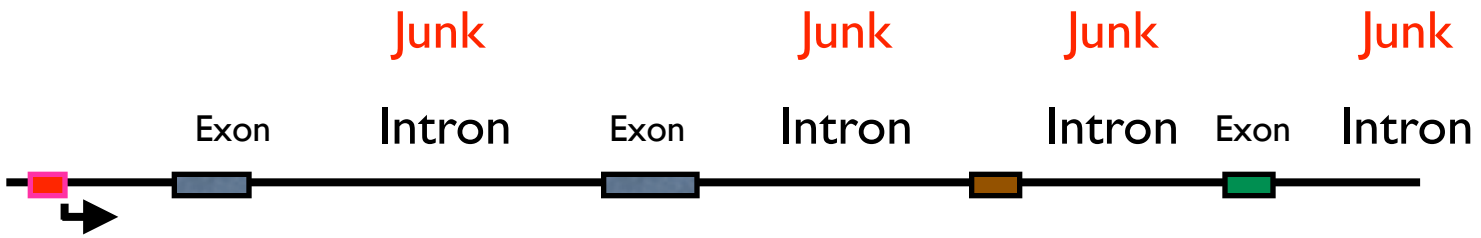
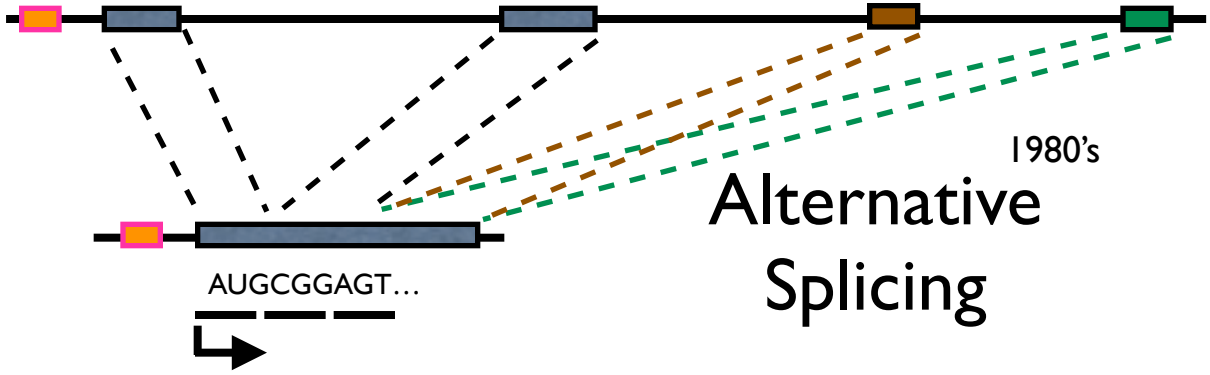
# 21st Century News




DNA

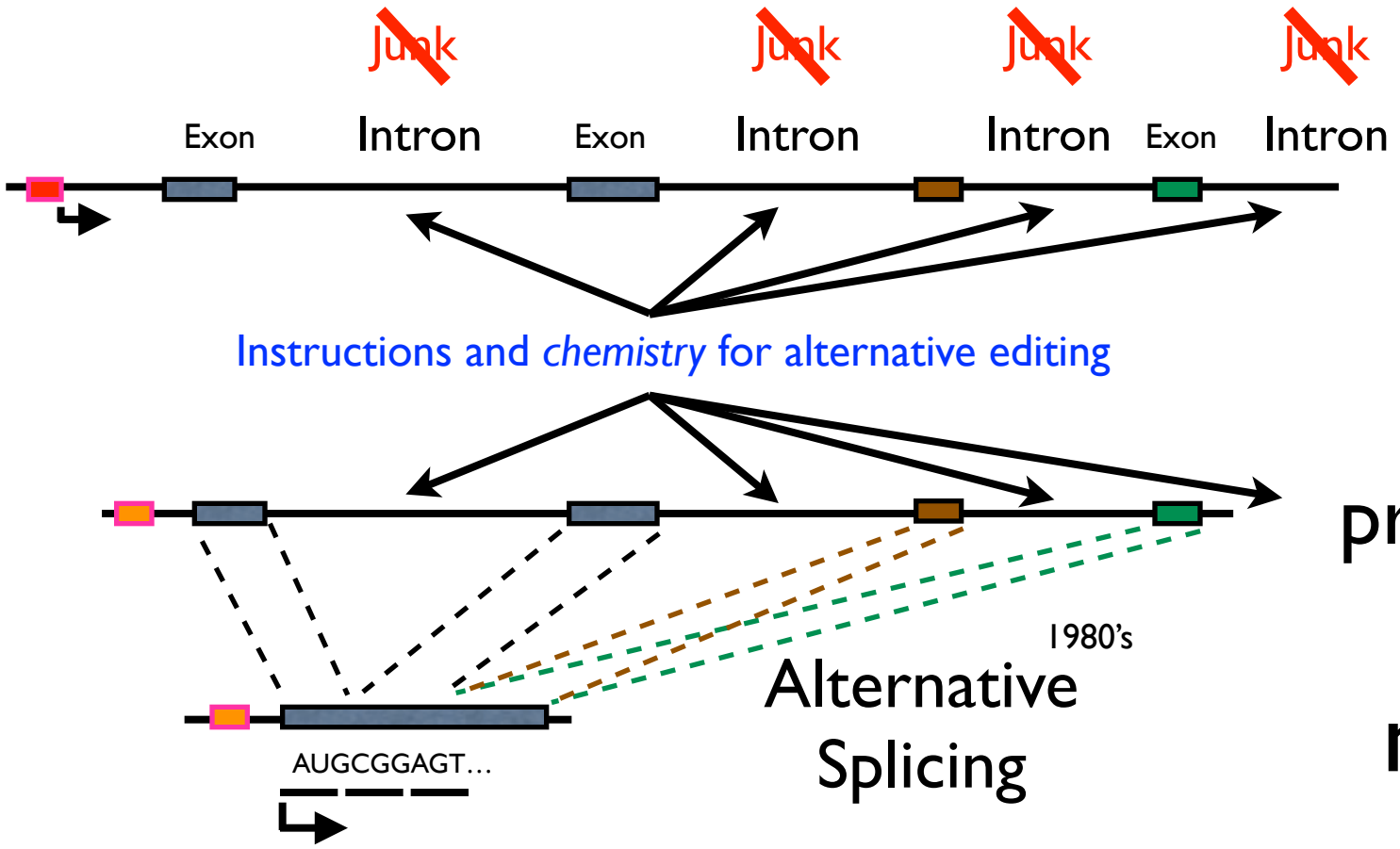



pre-mRNA

mRNA

**Protein**

# 21st Century News




DNA

pre-mRNA

mRNA

**Protein**

# Back in the lab…

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With the advent of PCR, nucleic acids have been recognized as extremely powerful combinatorial tools in the test tube

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Can create riboswitches

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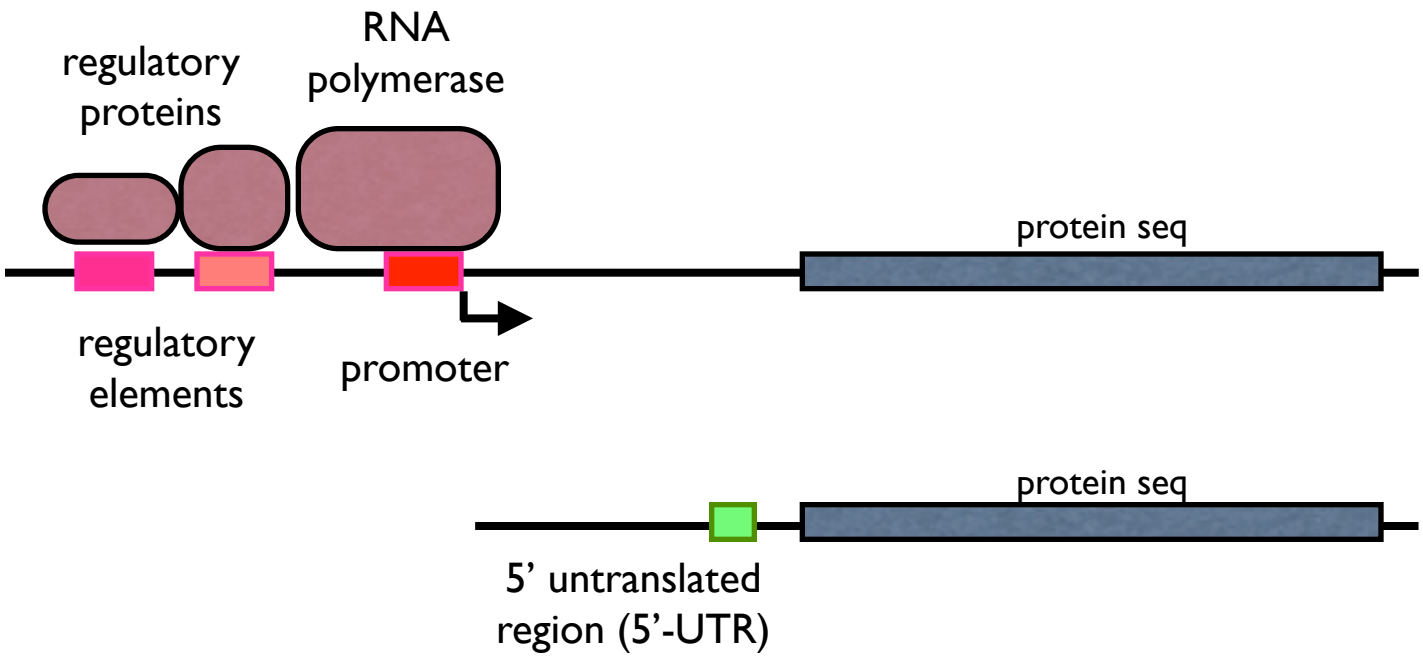
Aptamers can be selected that bind to "your favorite molecule"

Can create riboswitches

Ron Breaker:
"if it's so easy for us, I'll bet nature exploits this"

# More gene regulation




DNA

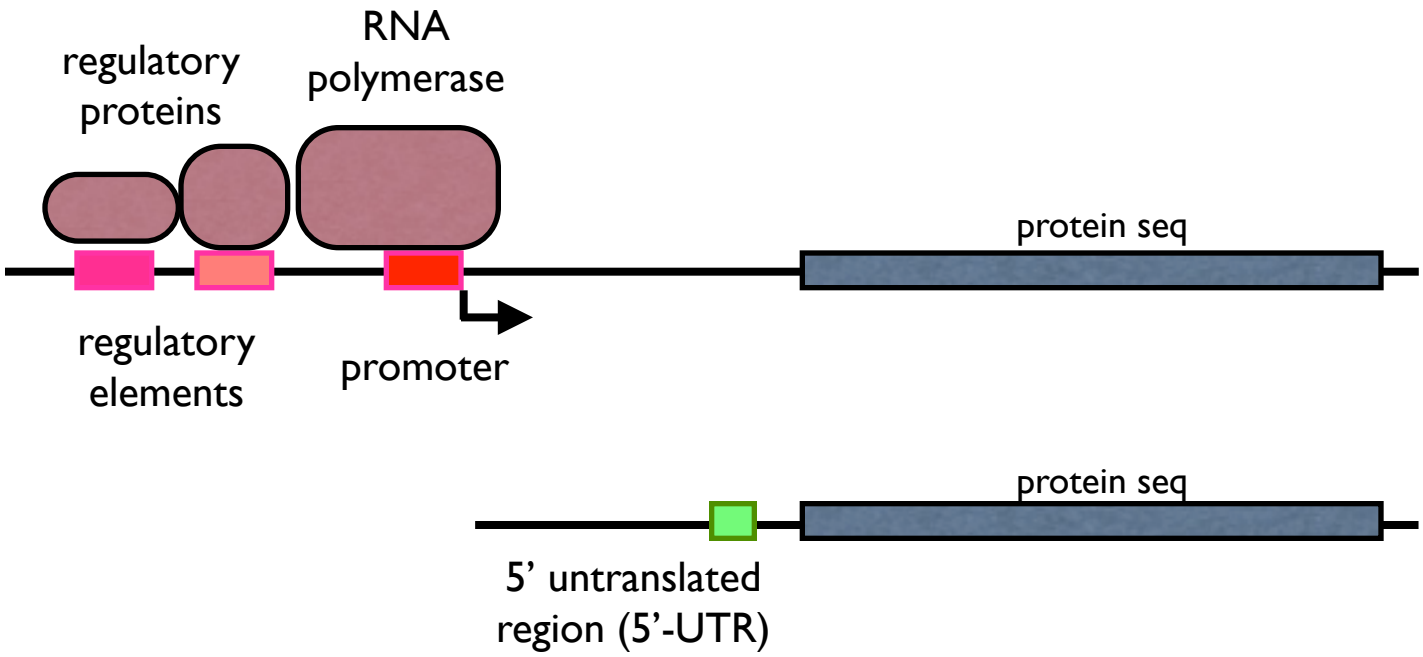
↓

mRNA

↓

Protein

# More gene regulation




DNA

↓

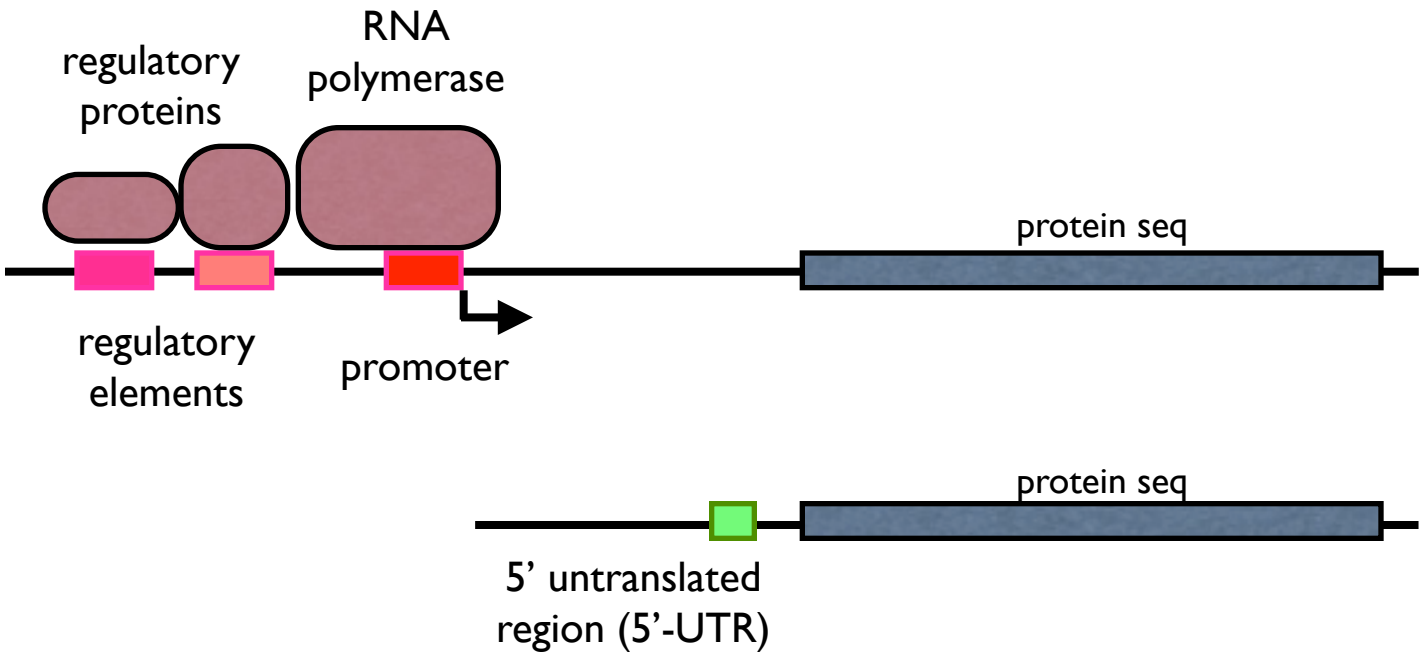
mRNA

↓

Protein

Ron: search for genes with no known protein regulator and which have a highly conserved 5' UTR

# More gene regulation

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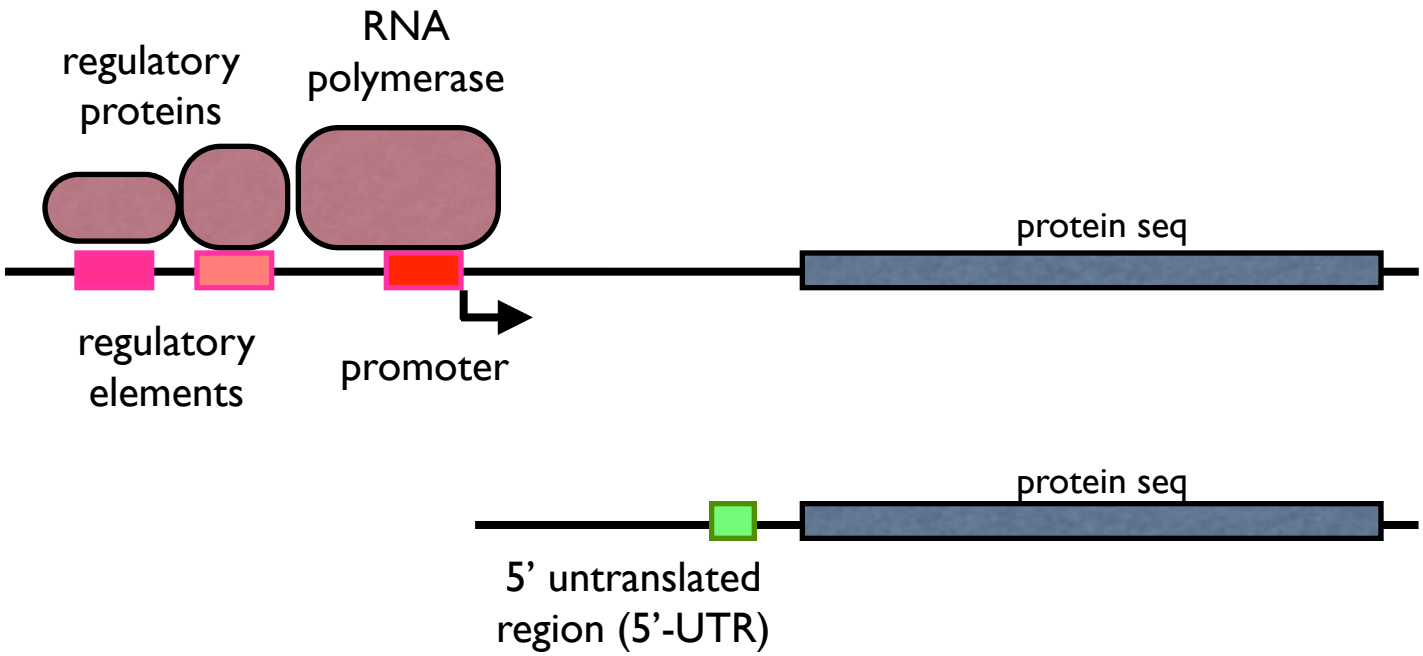
Ron: search for genes with no known protein regulator and which have a highly conserved 5' UTR

Does RNA from that conserved 5' UTR bind the product or substrate of the encoded enzyme?

# More gene regulation




DNA

↓

mRNA

↓

Protein

Ron: search for genes with no known protein regulator and which have a highly conserved 5' UTR

Does RNA from that conserved 5' UTR bind the product or substrate of the encoded enzyme?

**2004**

↘ One week: a Nature paper!

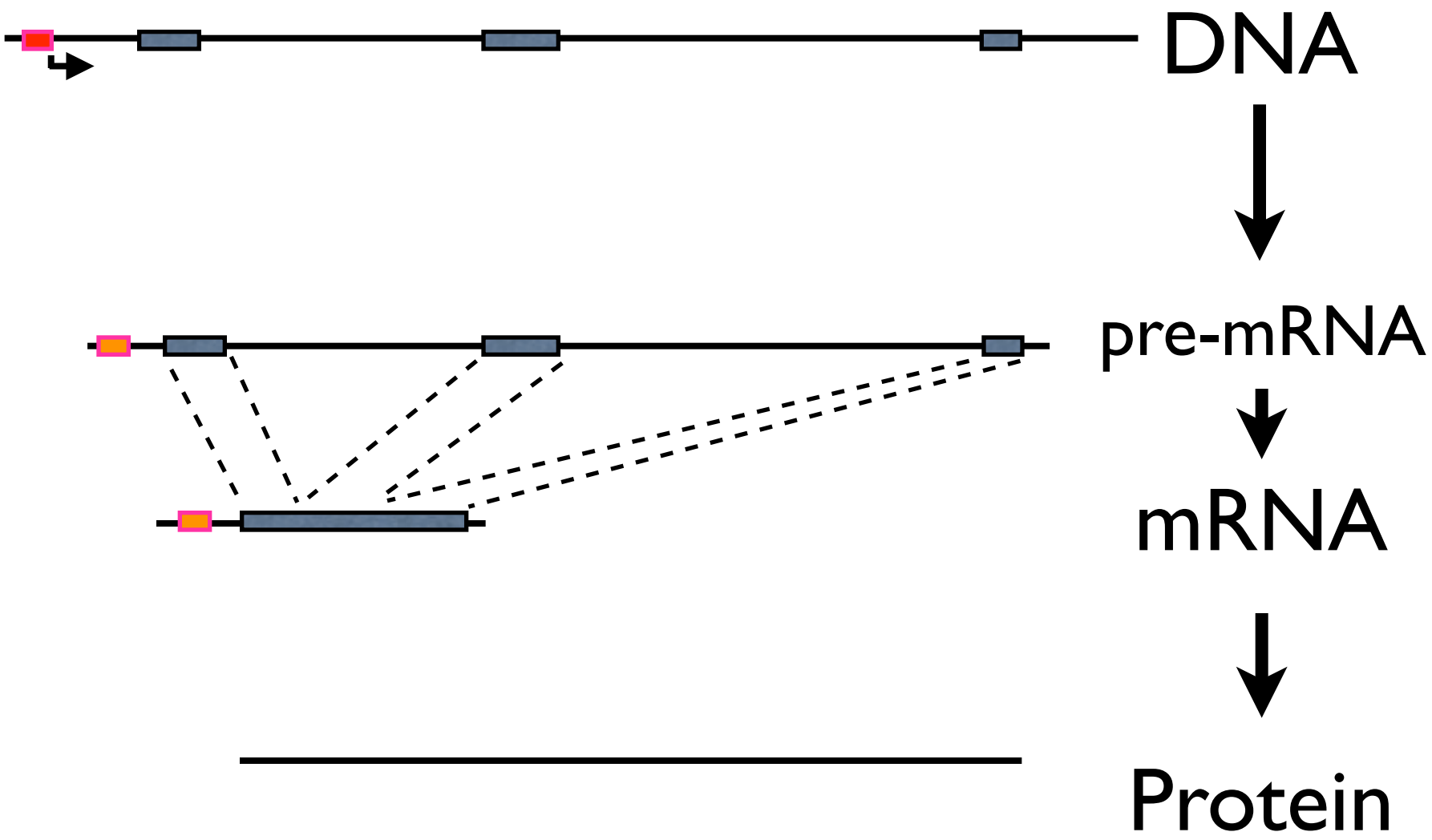
# Project Encode (2007)

(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

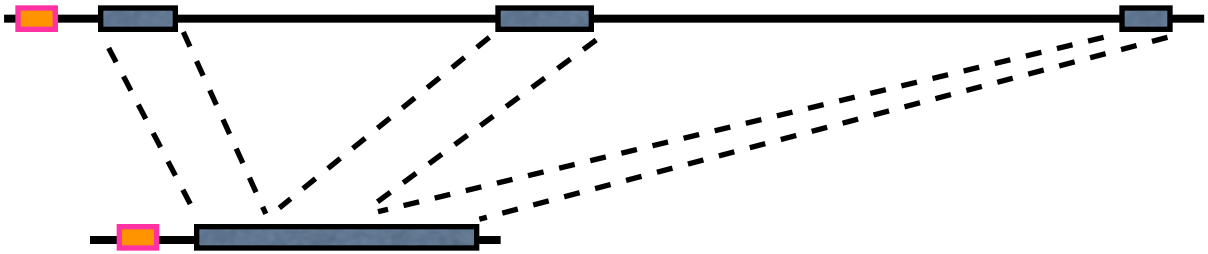


# 21st Century Opportunities

DNA

early '80s, but…

Alternative splicing

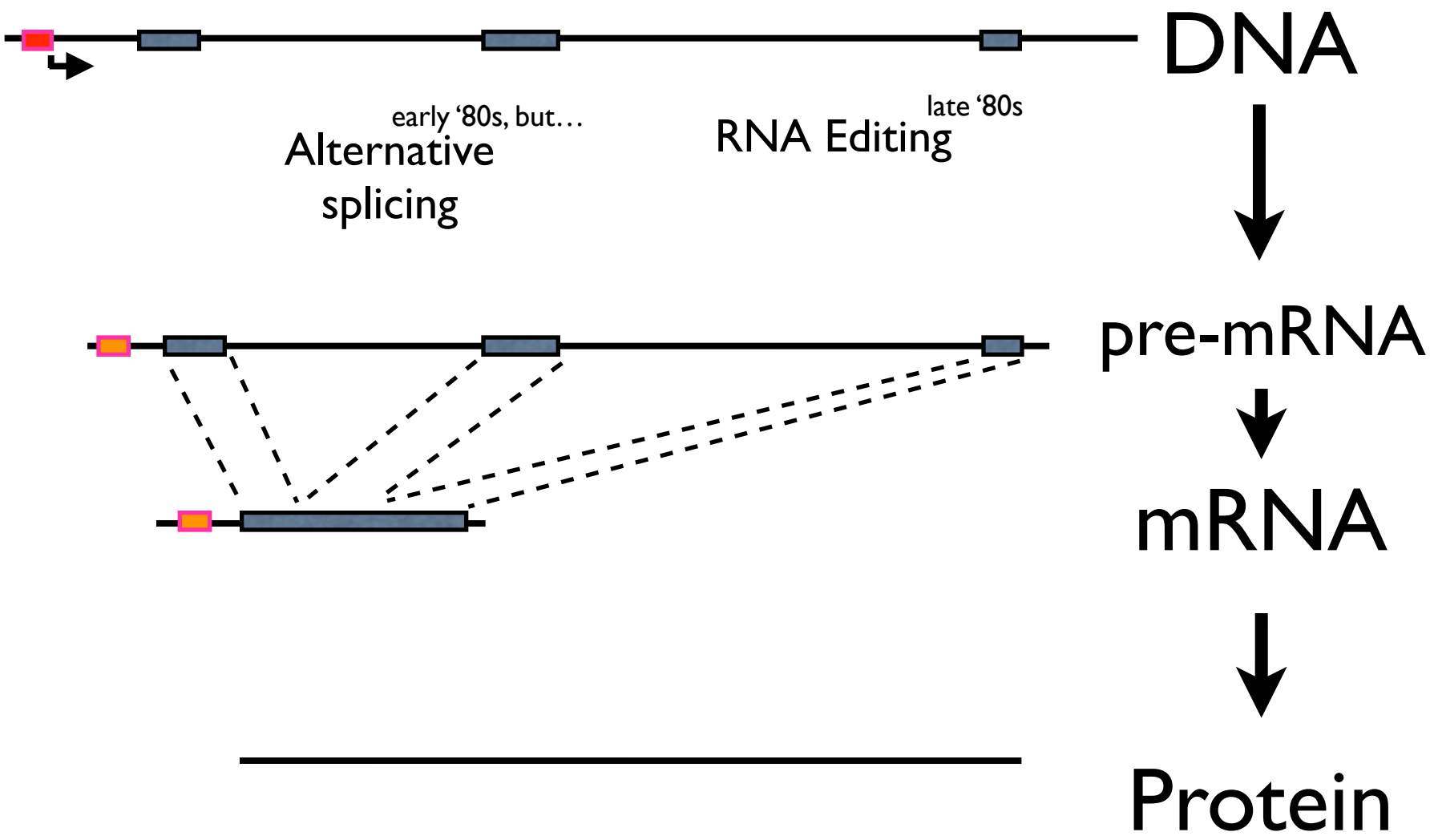


pre-mRNA

mRNA

Protein

# 21st Century Opportunities



# 21st Century Opportunities

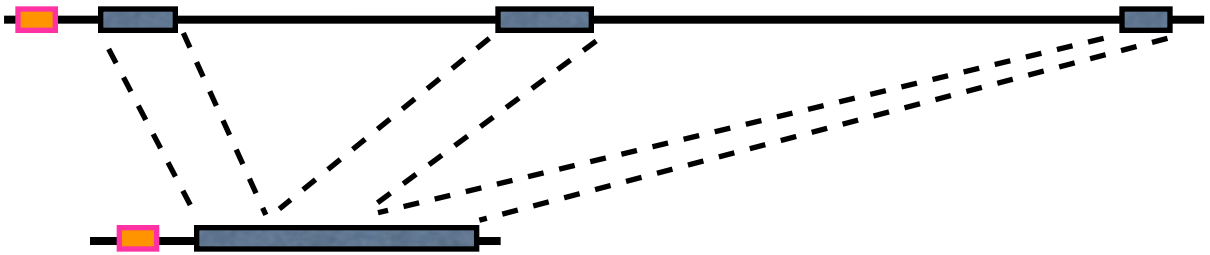
DNA

early '80s, but…

Alternative splicing

late '80s

RNA Editing



pre-mRNA

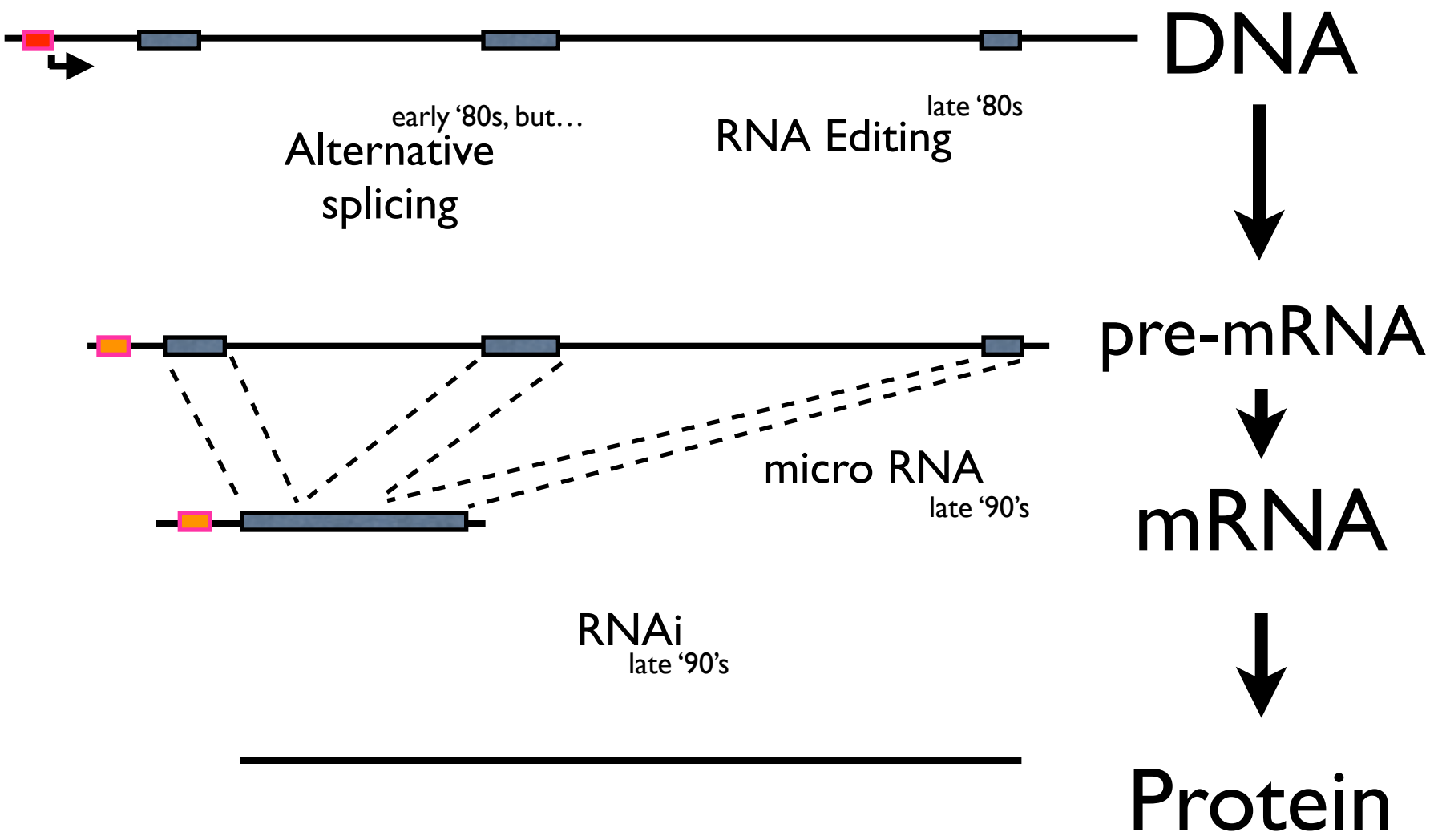
mRNA

RNAi

late '90's

Protein

# 21st Century Opportunities



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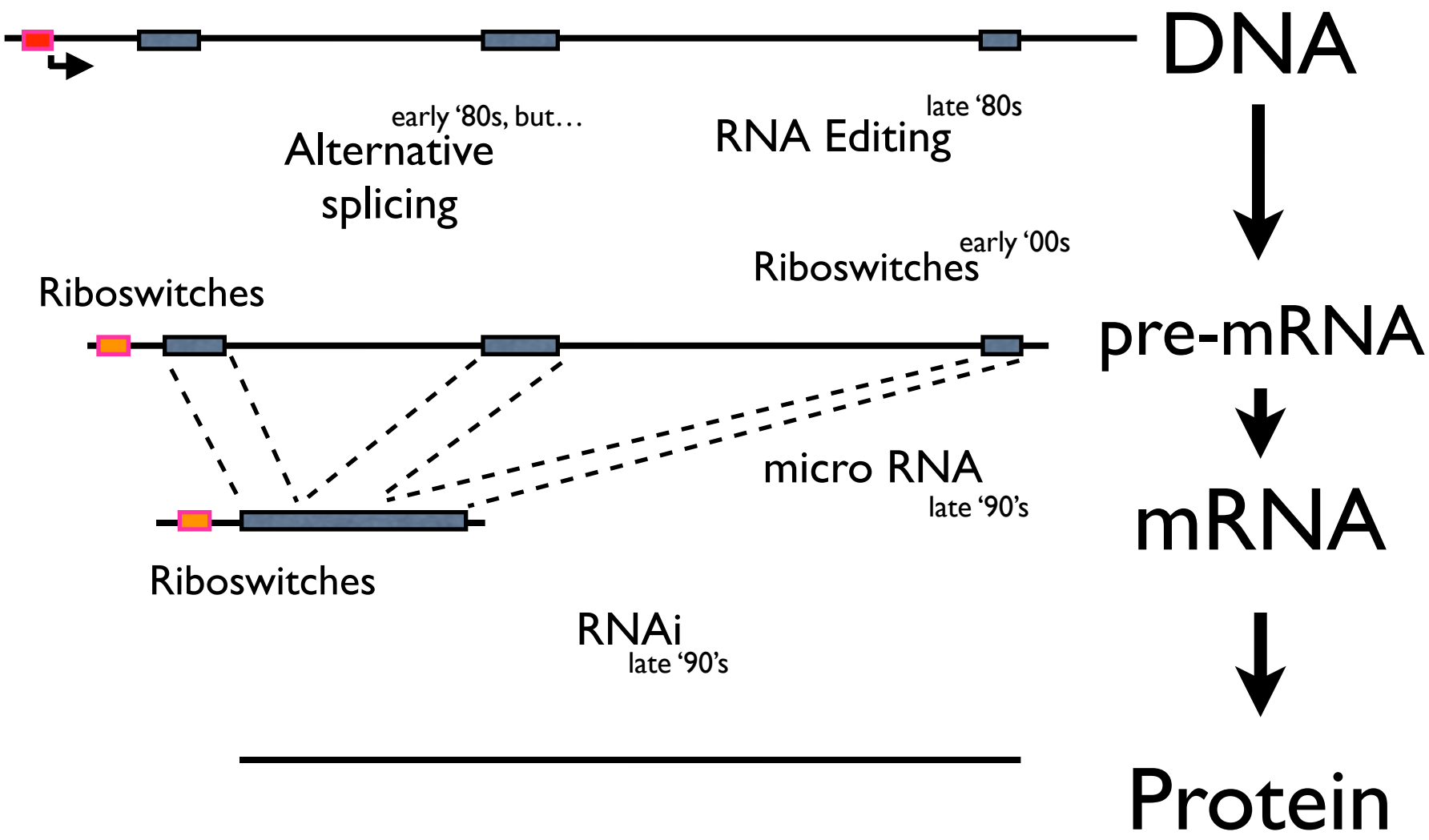


# 21st Century Opportunities

DNA

early '80s, but…

Alternative splicing

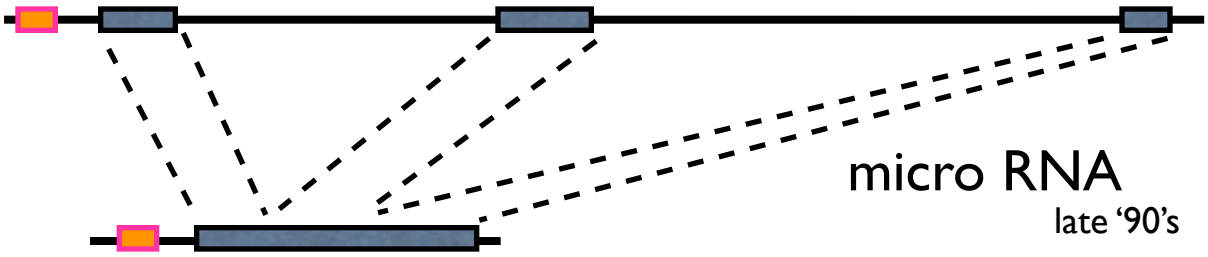
late '80s

RNA Editing

early '00s

Riboswitches

Riboswitches



pre-mRNA

micro RNA

late '90's

mRNA

Riboswitches

RNAi

late '90's

2010

To be discovered…

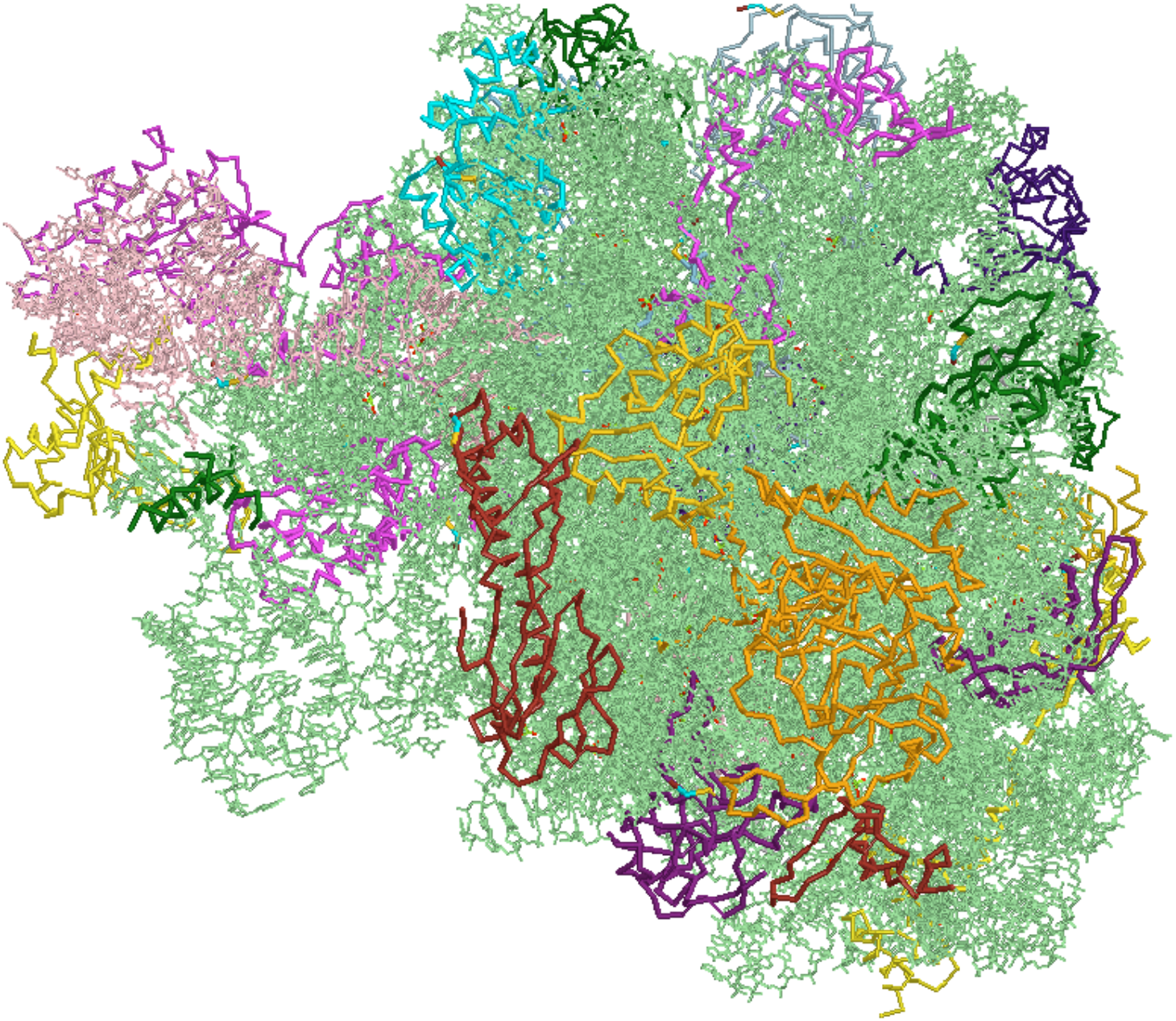
"so 20th century"

Protein

# Large Macromolecular Complexes

# Ribosome

An RNA machine with protein cofactors



# What stabilizes protein structures?

What stabilizes protein structures?

What *directs* protein structures?

# The DNA Duplex

# The DNA Duplex

What stabilizes the duplex?

# The DNA Duplex

What stabilizes the duplex?

What *directs* duplex structure?

# Which is more stable?

(which has a higher melting temperature?)

**ACCGCCACCGAAG**

**TGGCGGTGGCTTC**

or

**ACCGCCACCGAAG**

**TGGCGGTGGCTTA**

# Which is more stable?

(which has a higher melting temperature?)

**ACCGCCACCGAAG**
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51.6° C

or

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51.6° C

or

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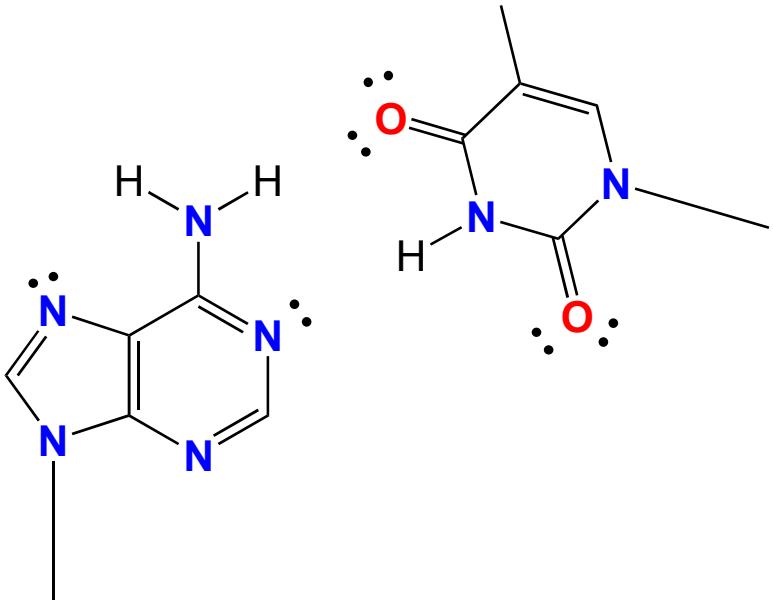
52.5° C

Calculations from http://www.idtdna.com/analyzer/Applications/OligoAnalyzer/


H
H
N
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N
O
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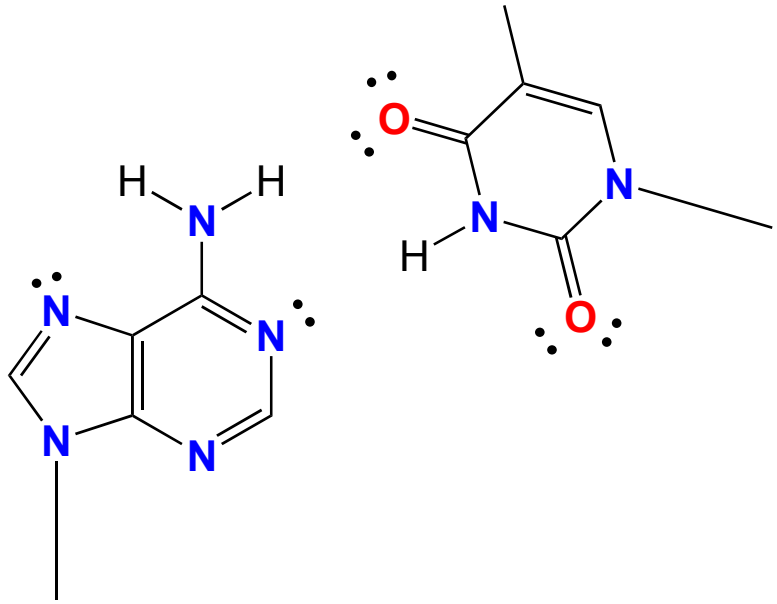
H
O

H
H
N
N
N
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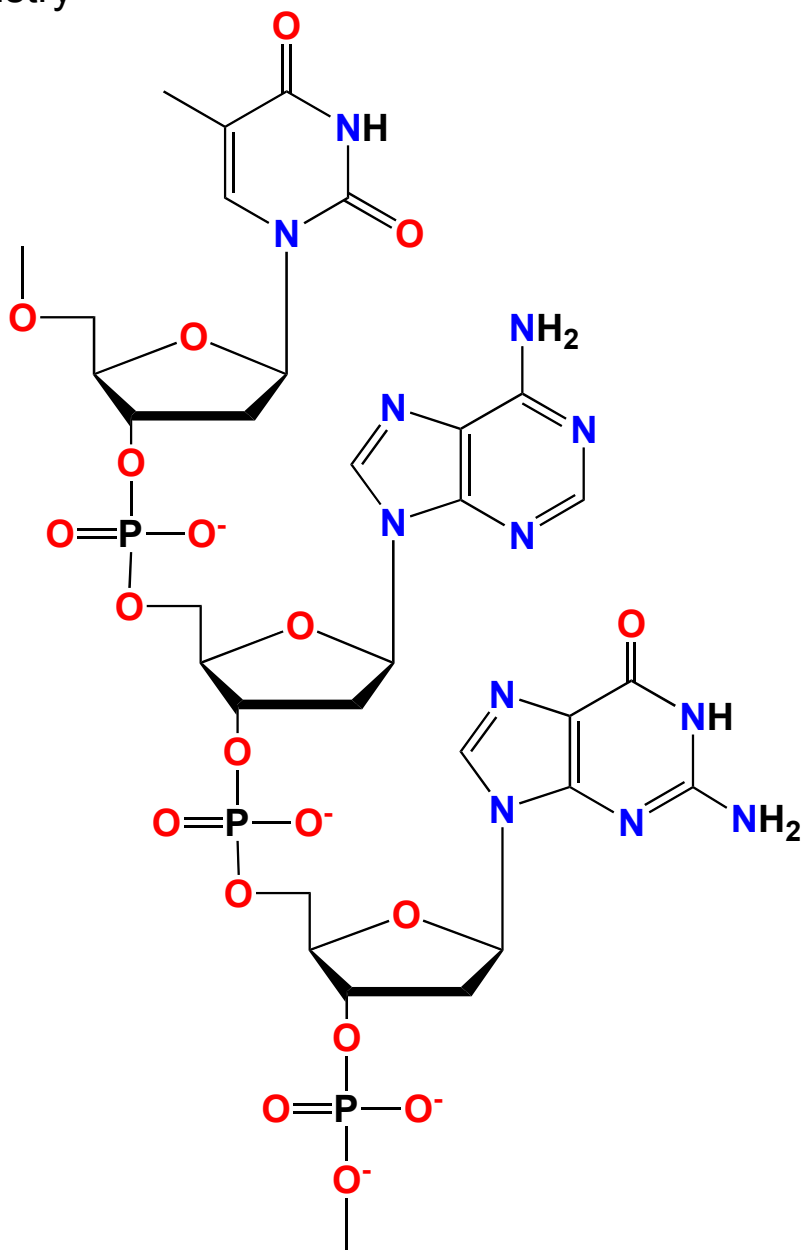
N
H
O

# DNA

A look at the Chemistry



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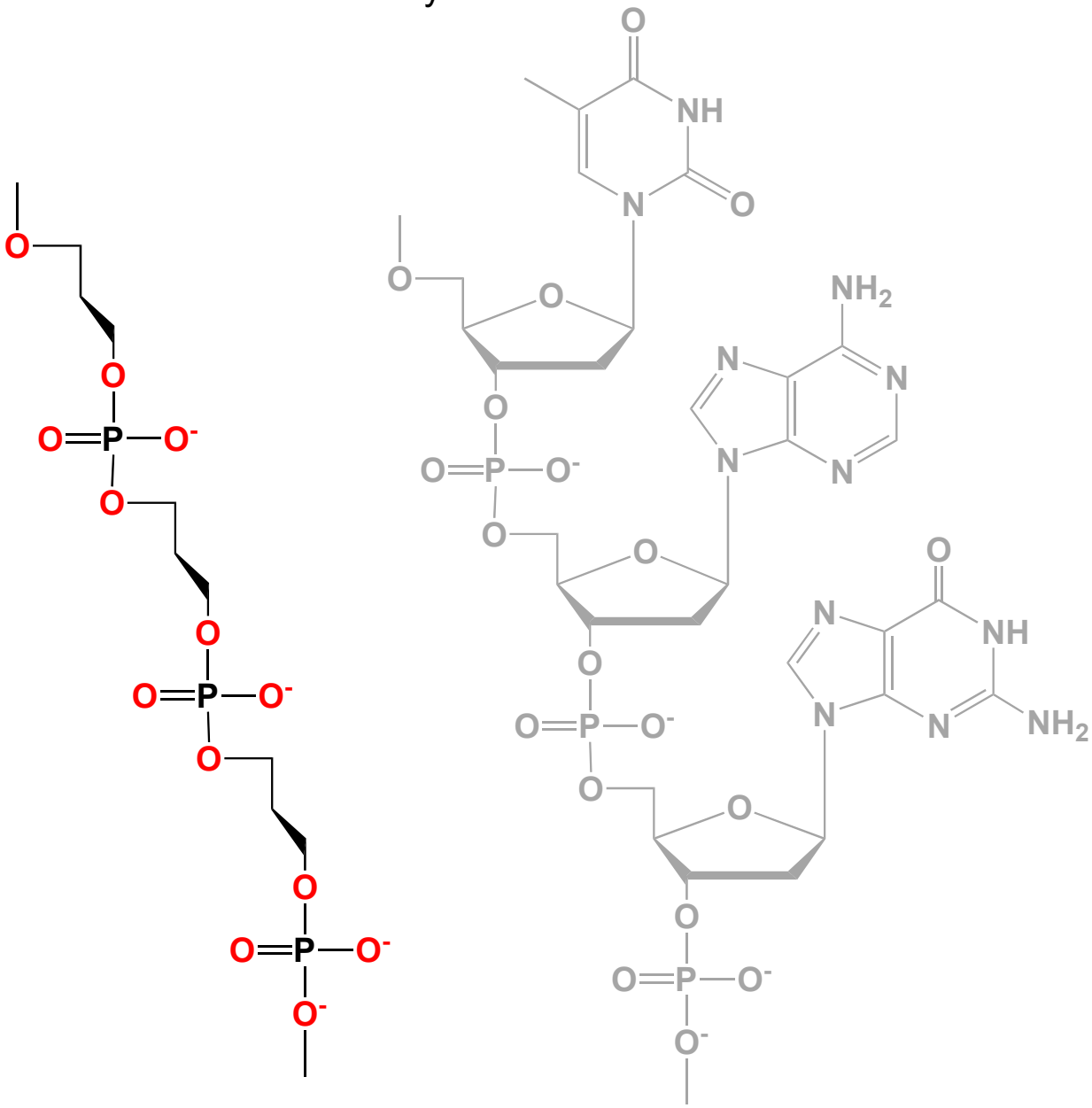

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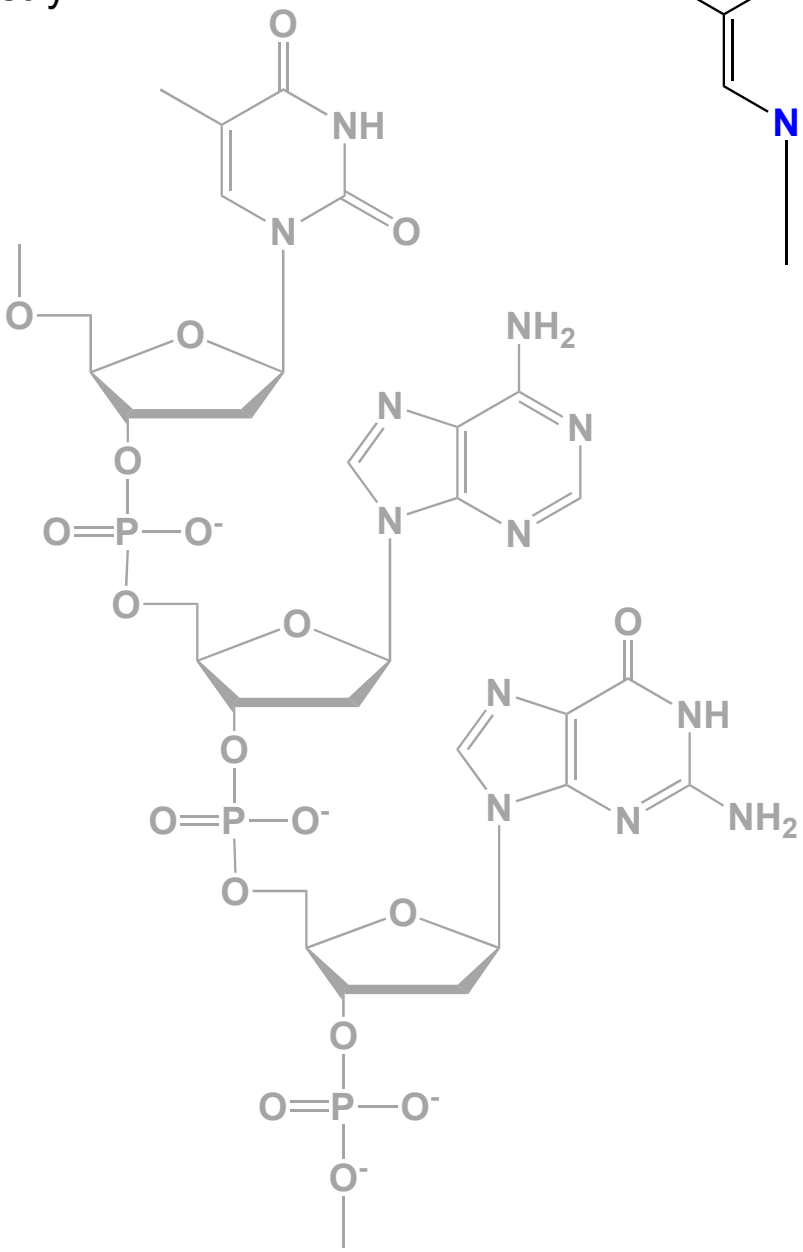

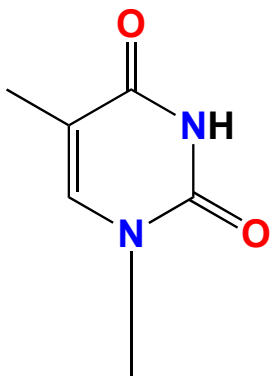

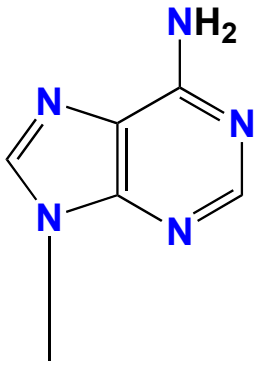

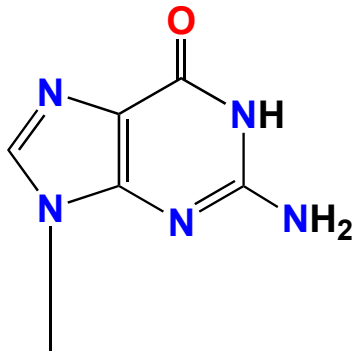

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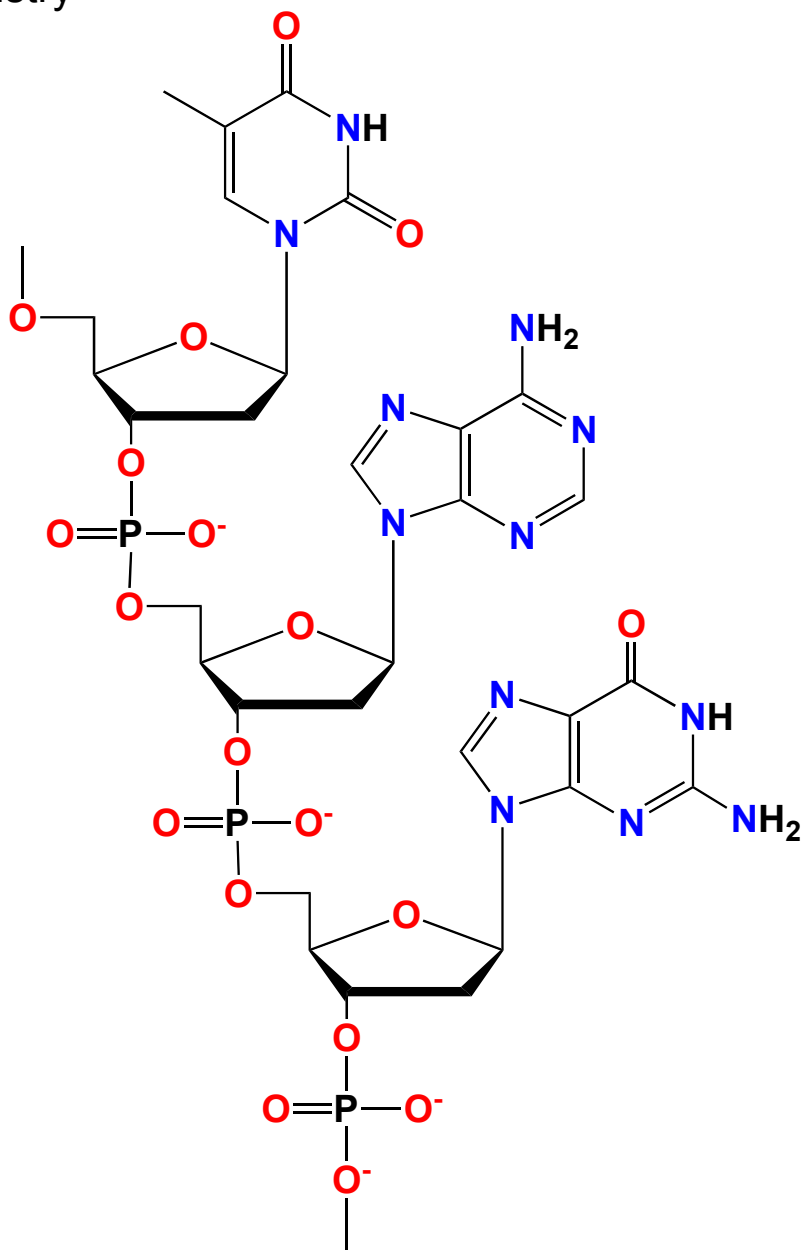

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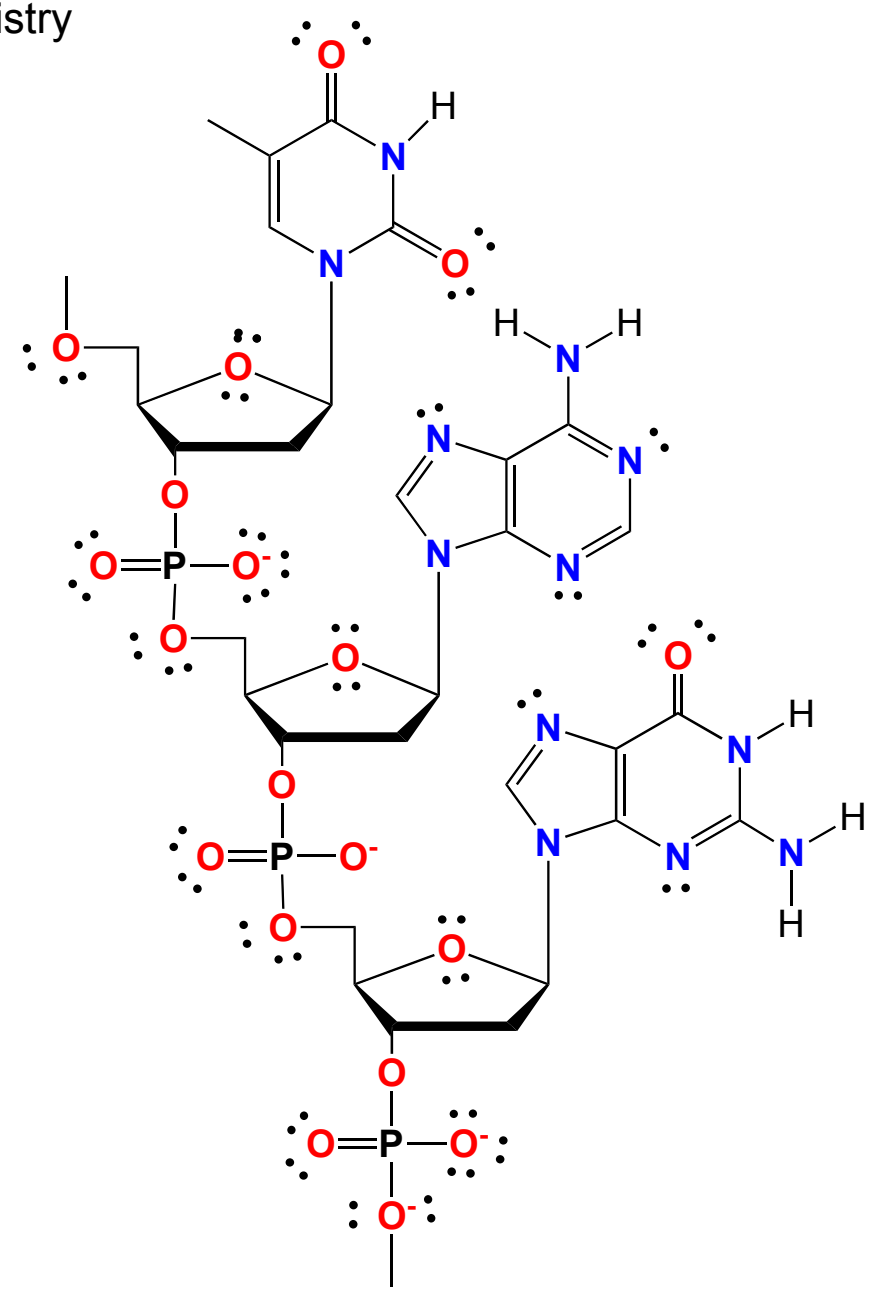

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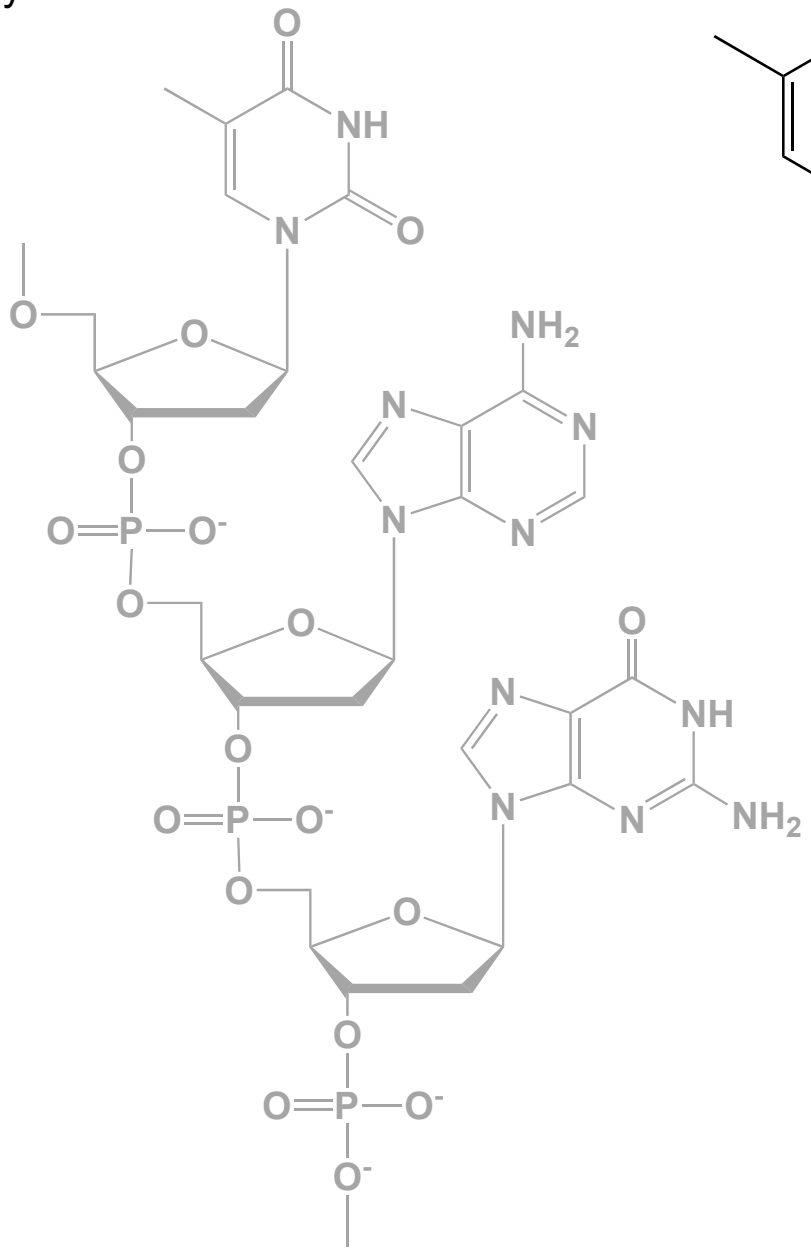


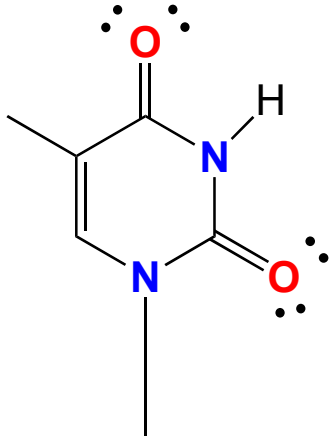

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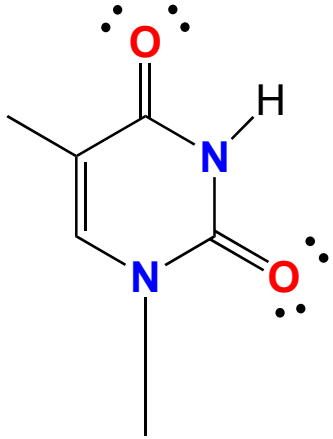
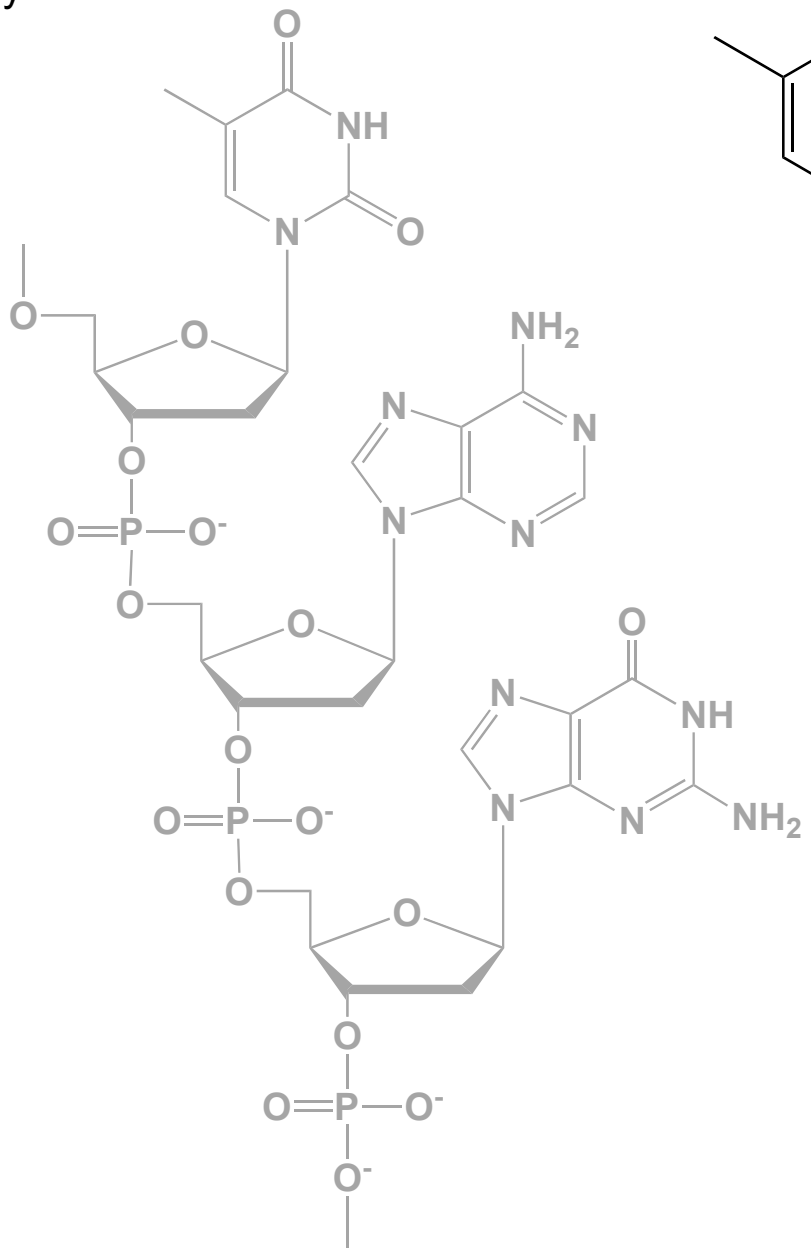
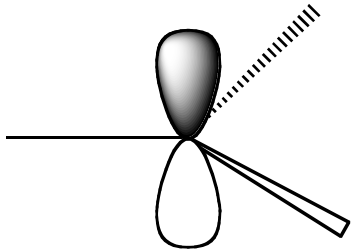
A look at the Chemistry

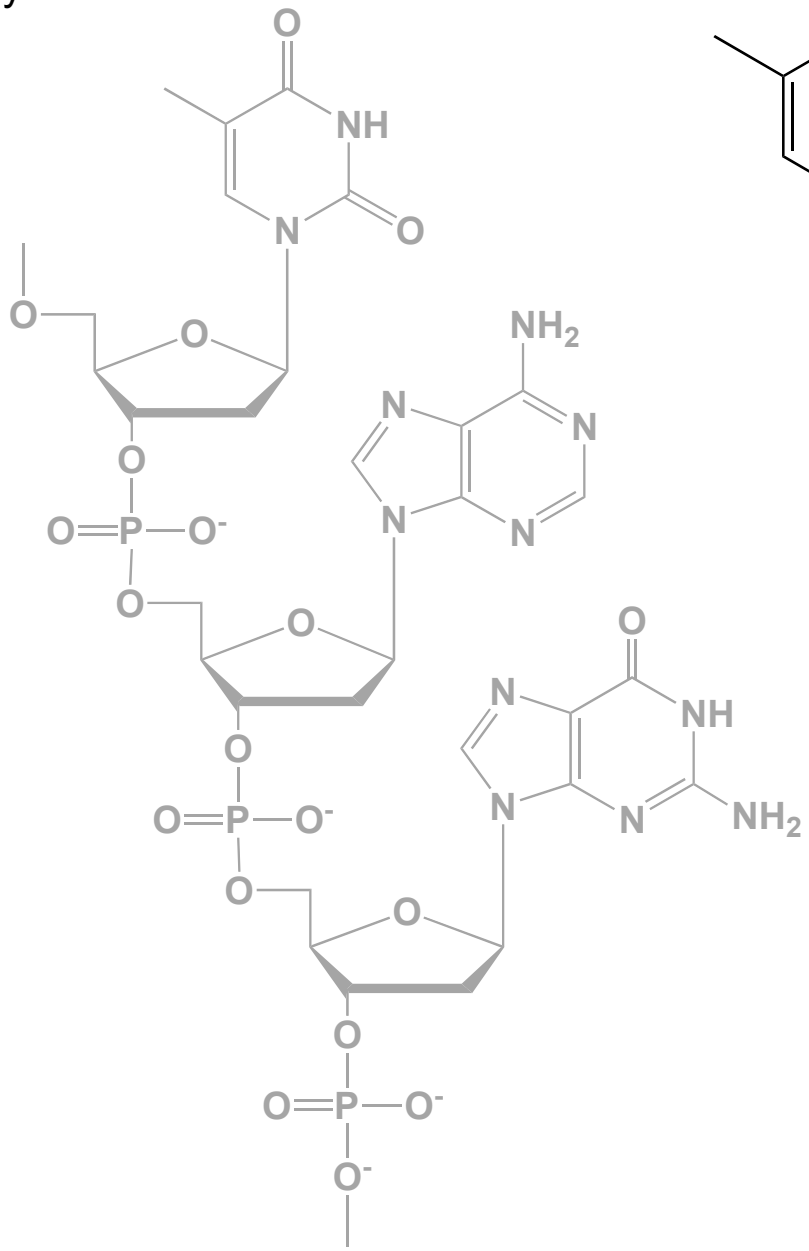


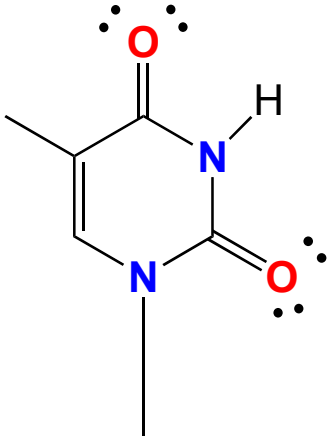


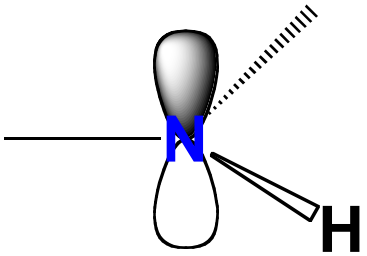


# DNA

A look at the Chemistry

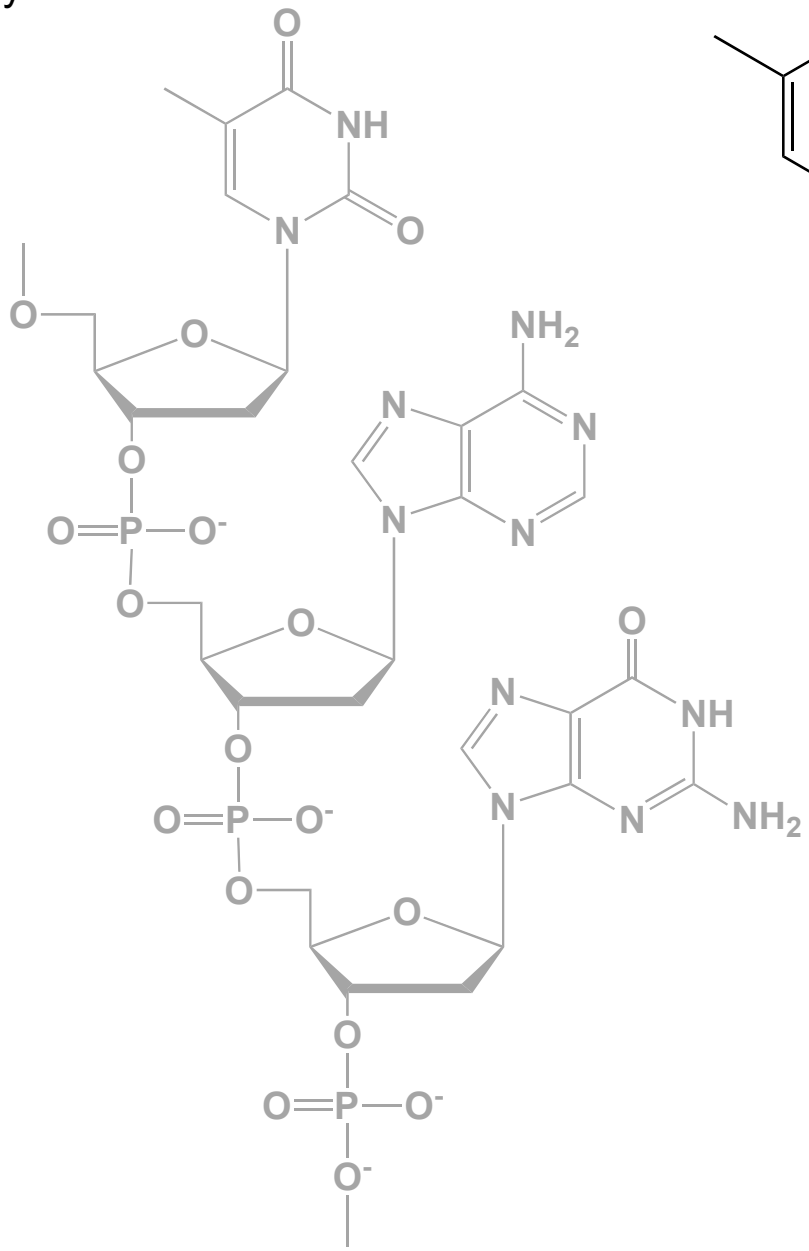


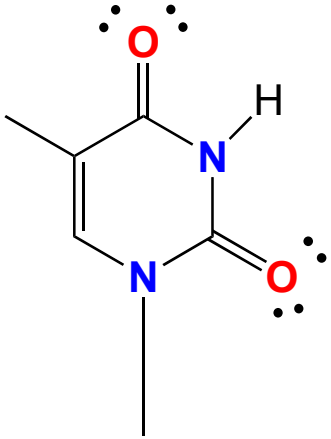



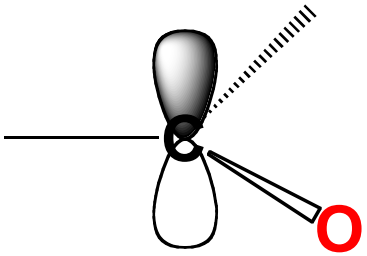



# DNA

A look at the Chemistry

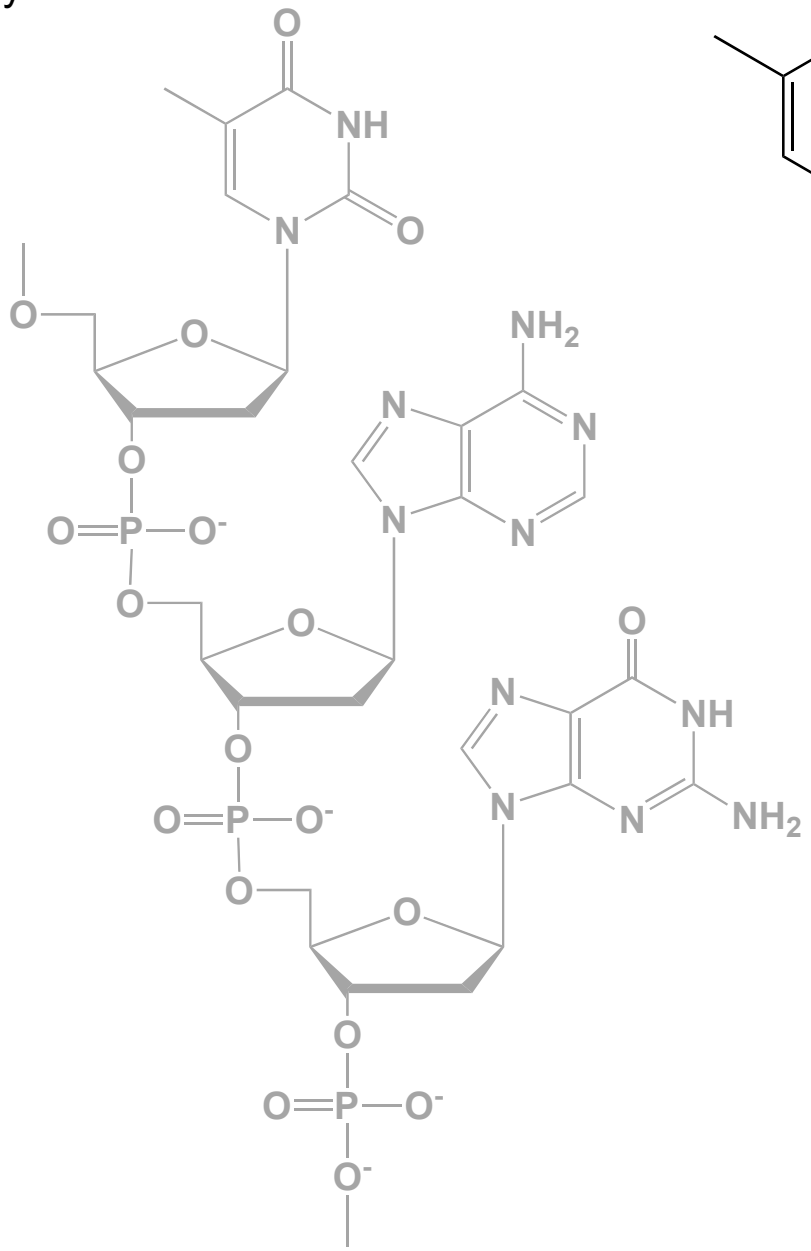


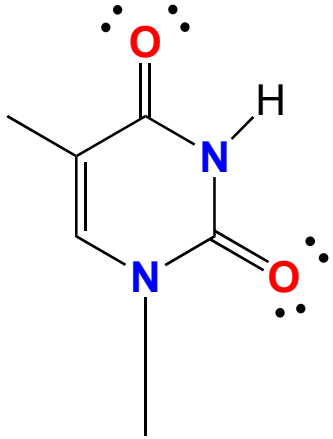



# DNA

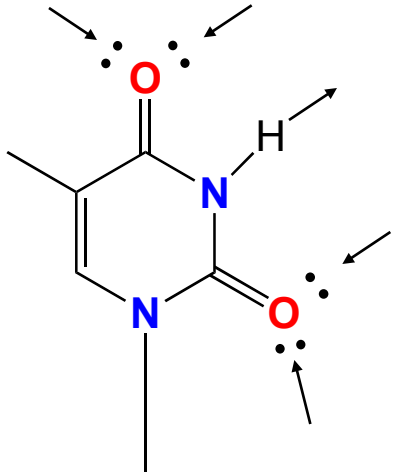
A look at the Chemistry

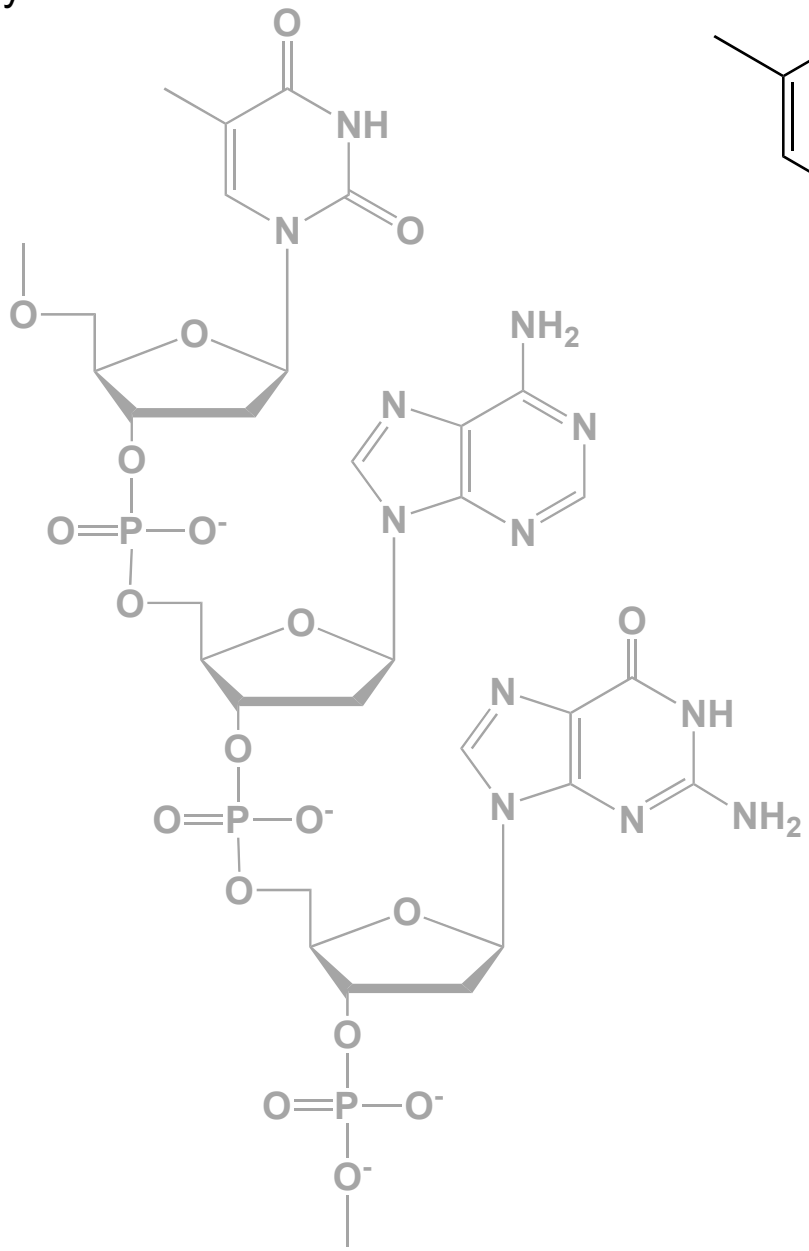


# DNA

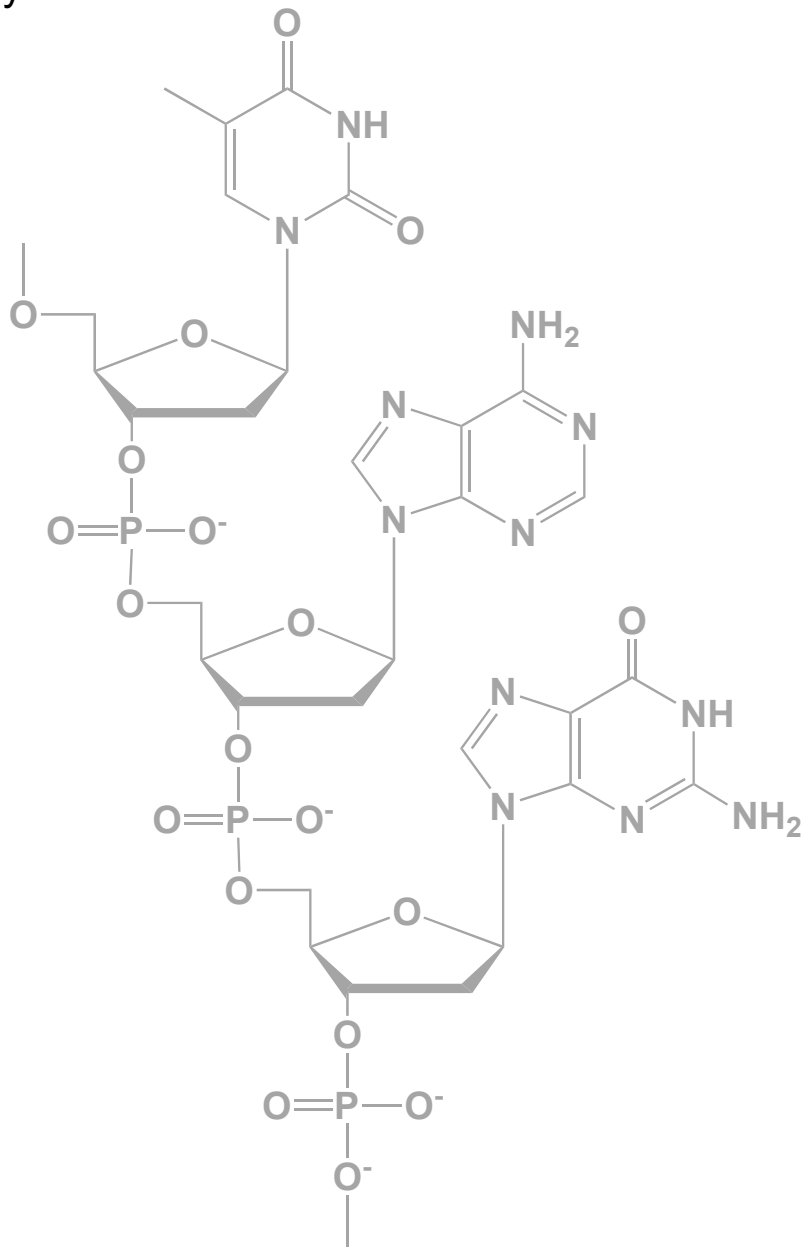
A look at the Chemistry

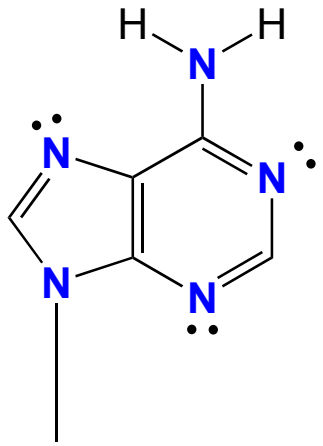


# DNA

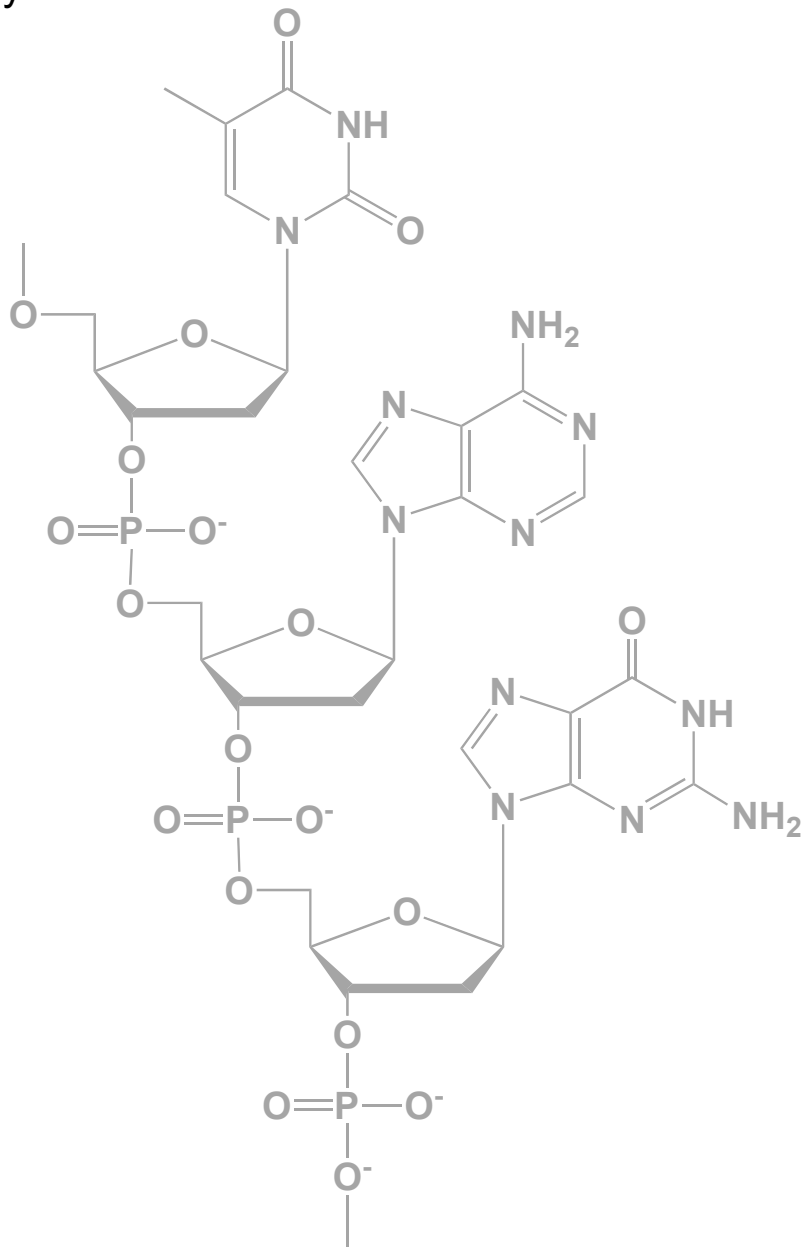
A look at the Chemistry

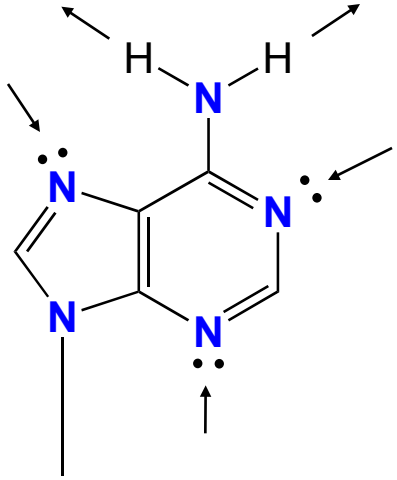




# DNA

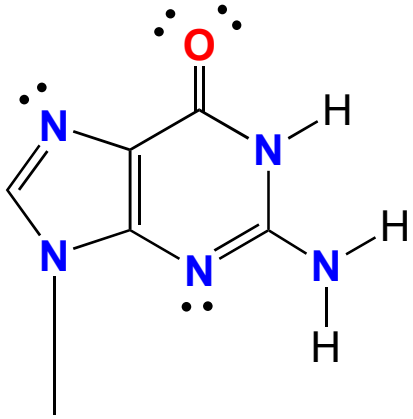
A look at the Chemistry

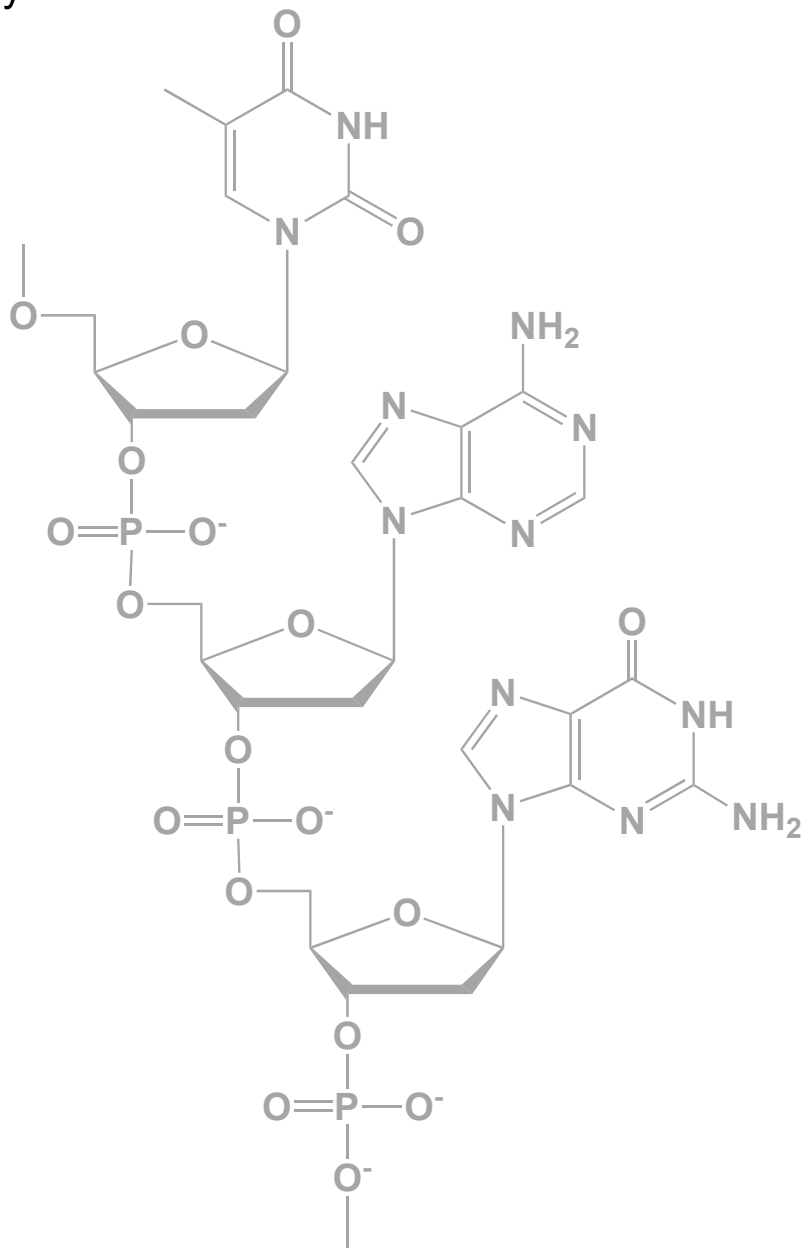




# DNA

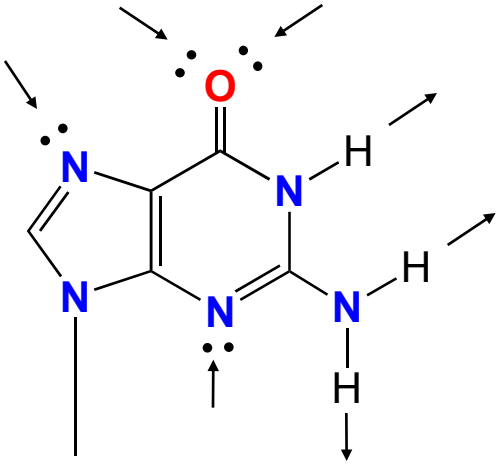
A look at the Chemistry

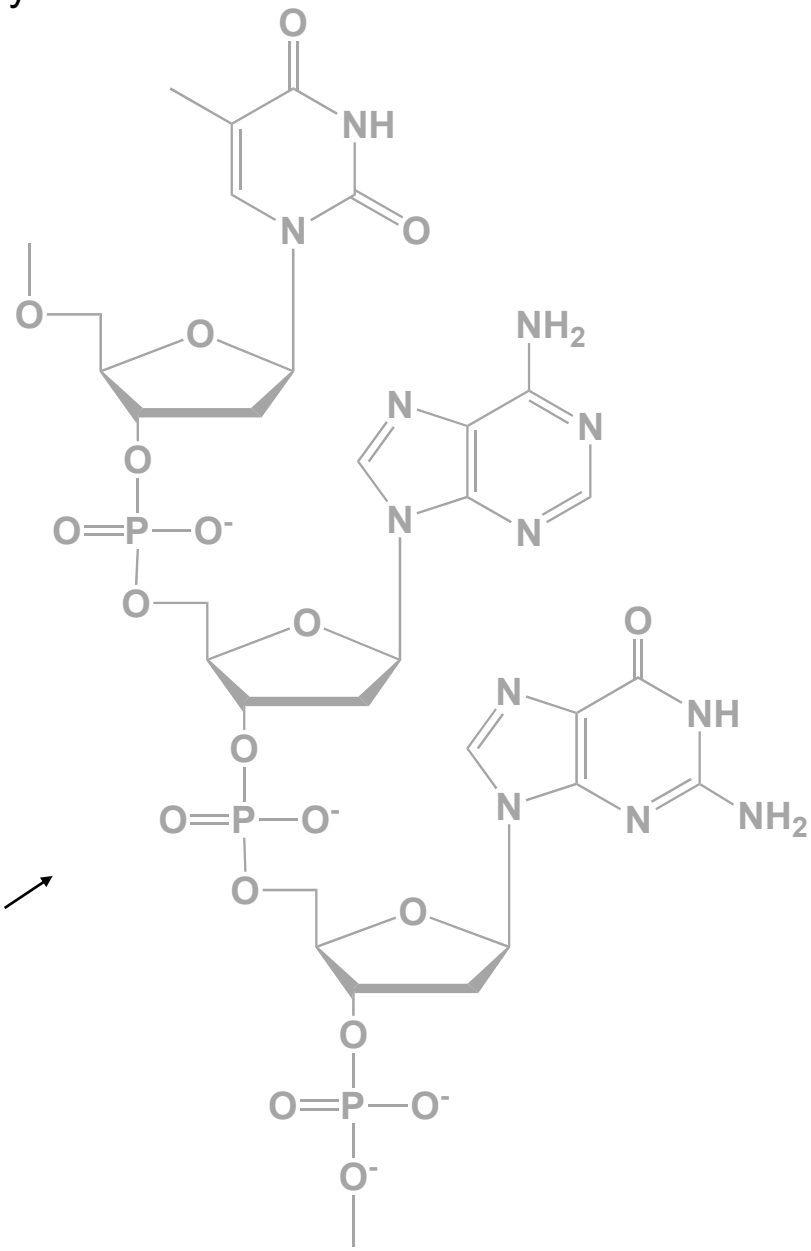




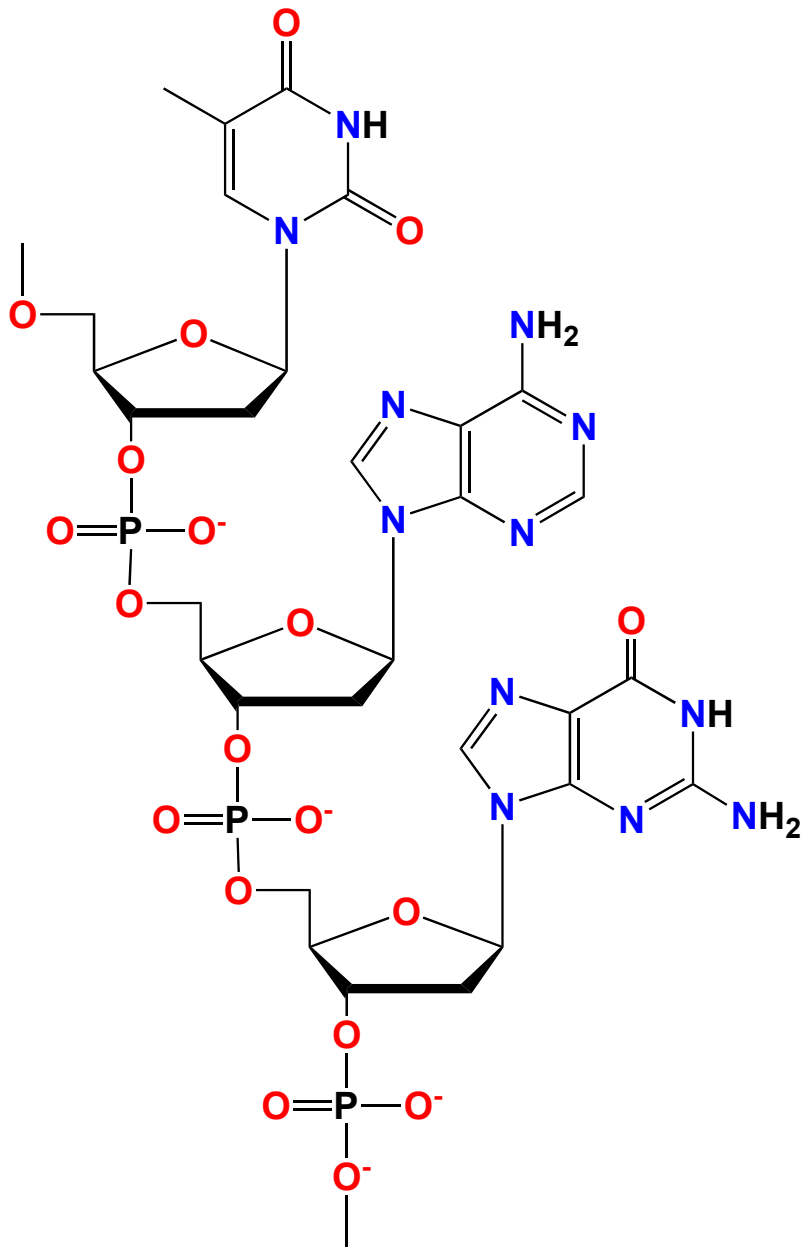
# DNA

A look at the Chemistry

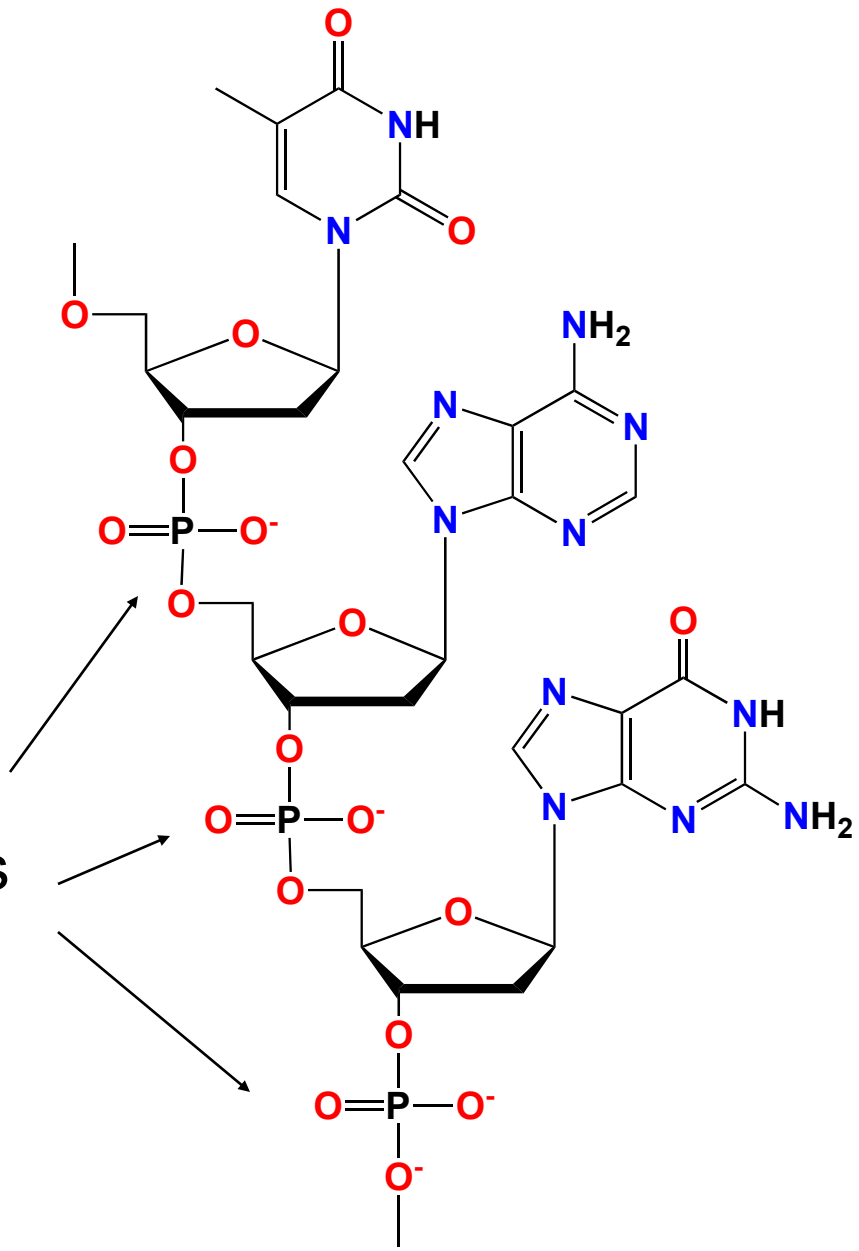




# What forces are important?

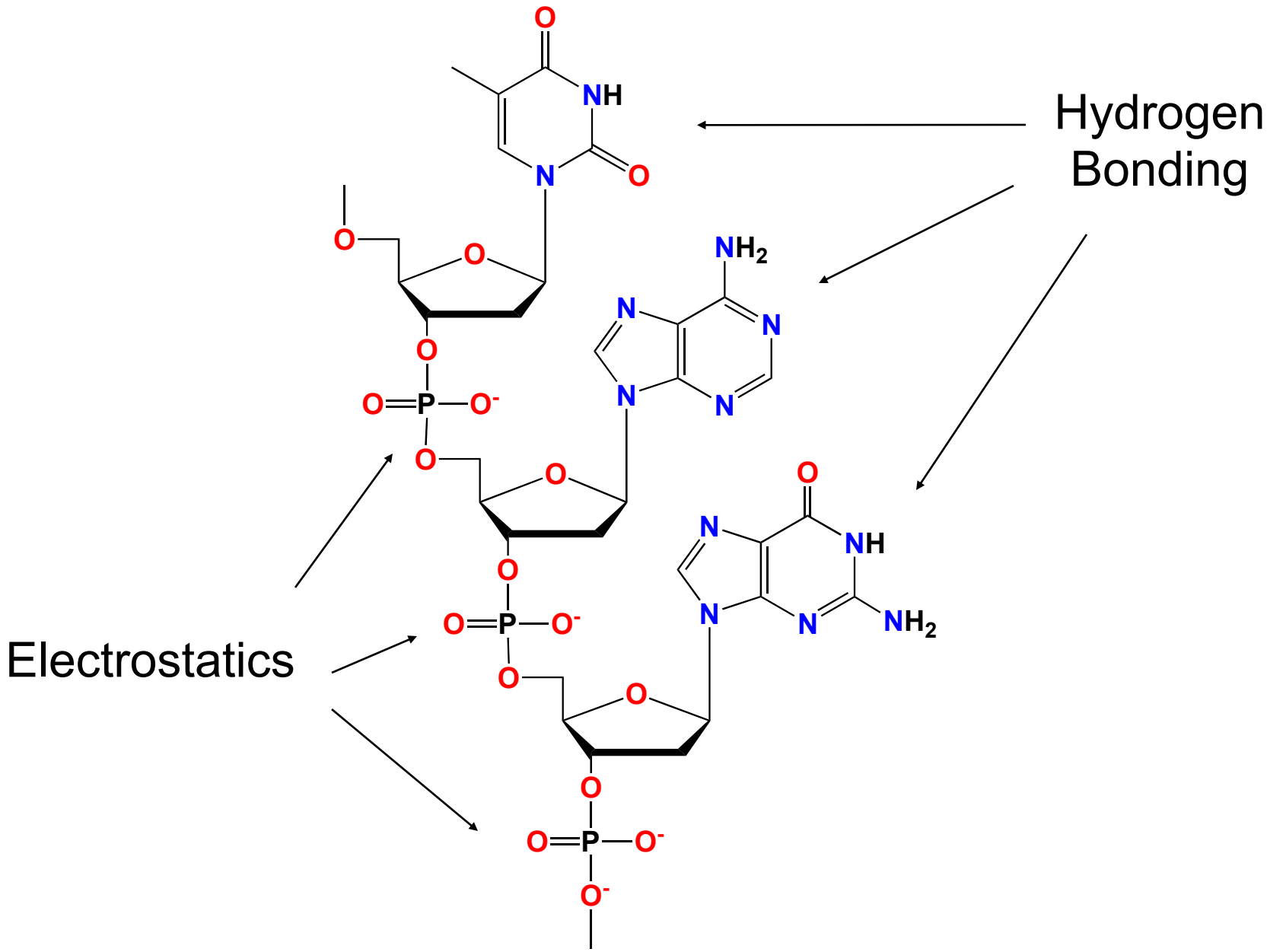


# What forces are important?

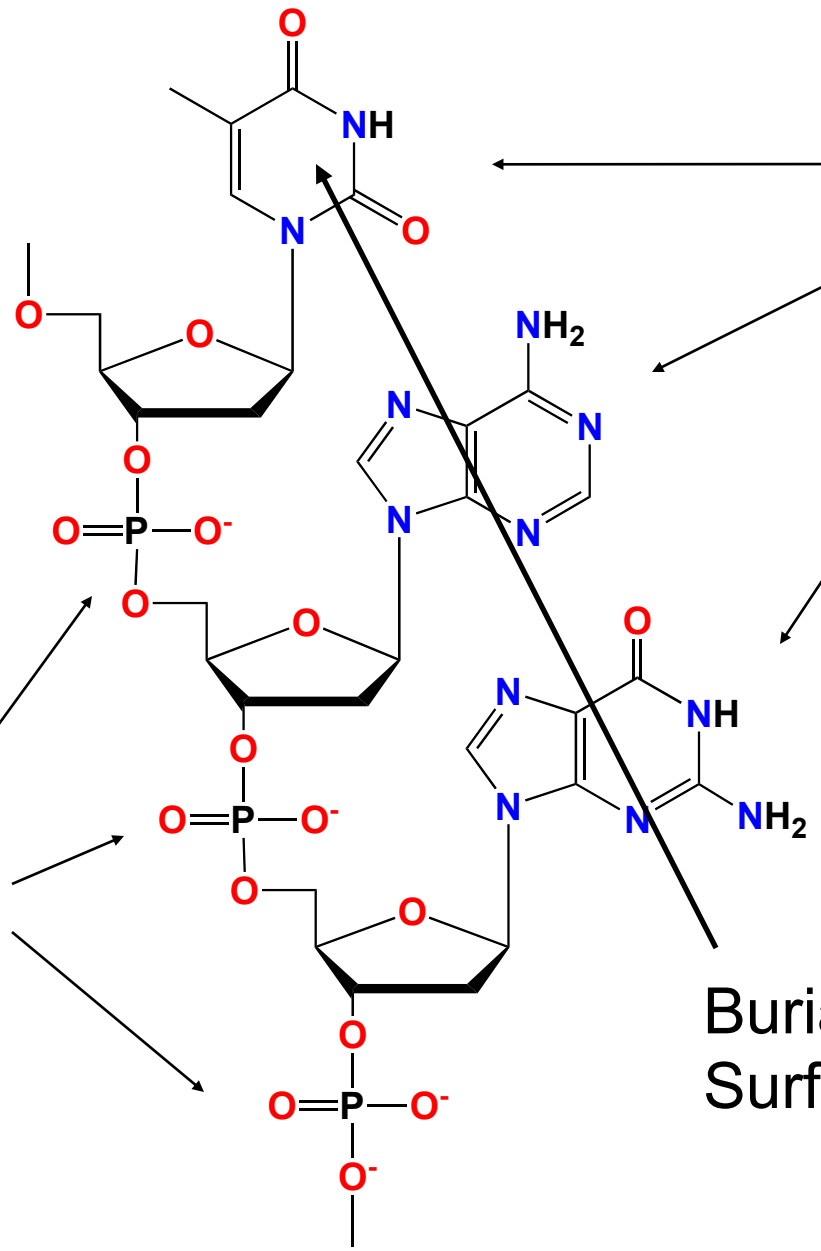



Electrostatics

# What forces are important?



# What forces are important?




Hydrogen Bonding

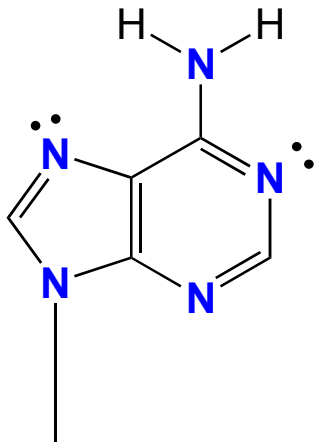
Electrostatics

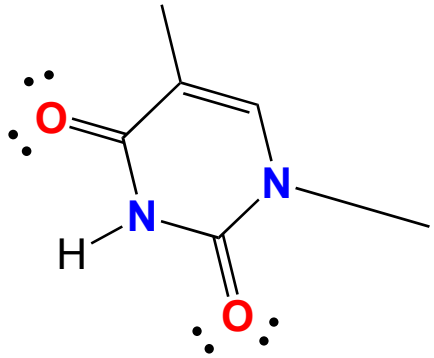
Burial of Hydrophobic Surface & Stacking

# Base Pairing

(Donors matched to Acceptors)

A



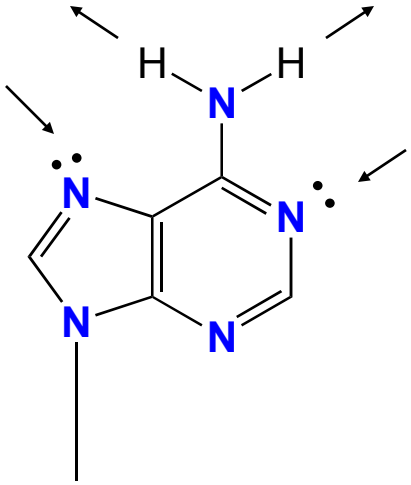



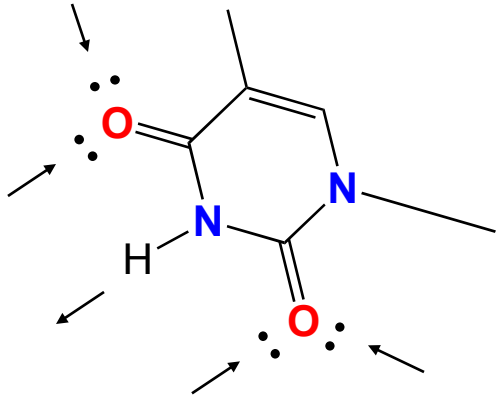

T

# Base Pairing

(Donors matched to Acceptors)

A

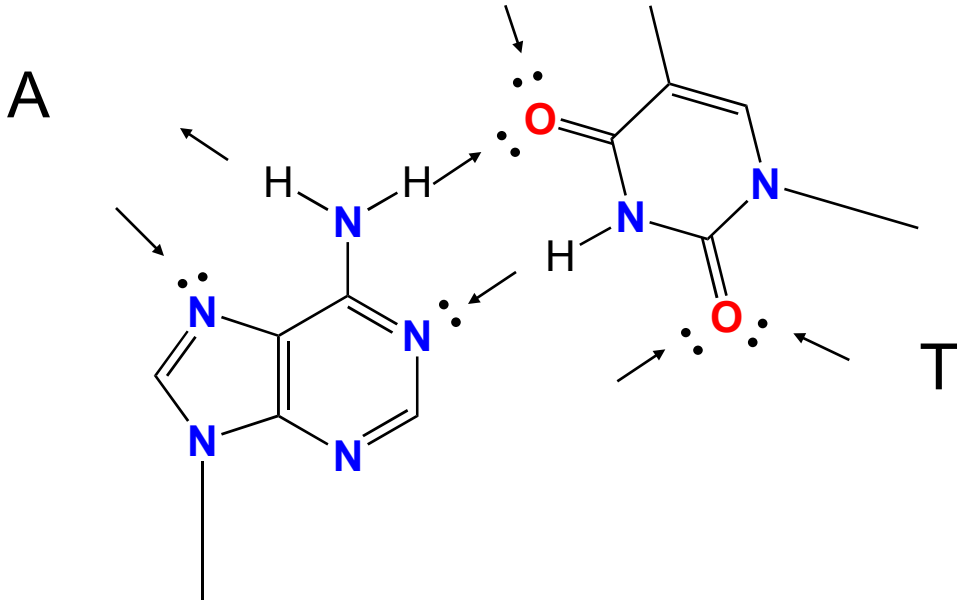



T

# Base Pairing

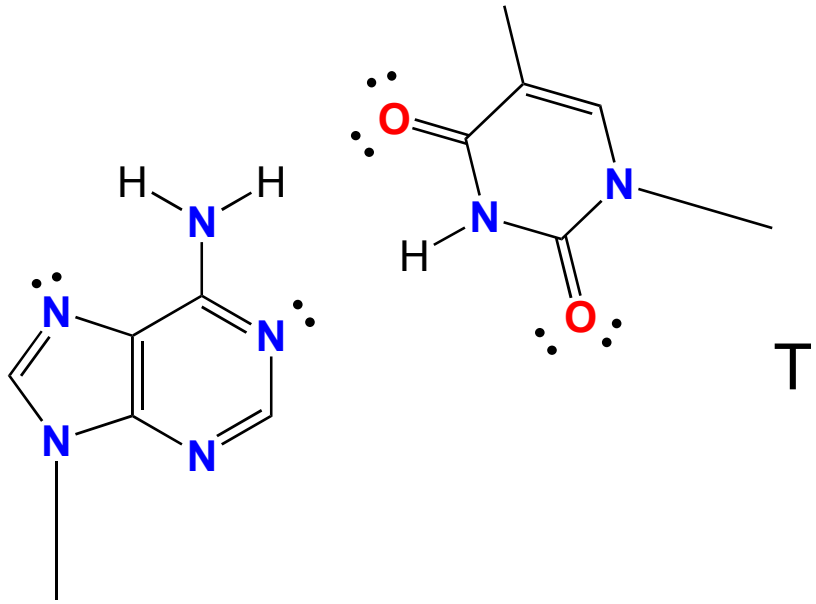
(Donors matched to Acceptors)



# Base Pairing

(Donors matched to Acceptors)

A



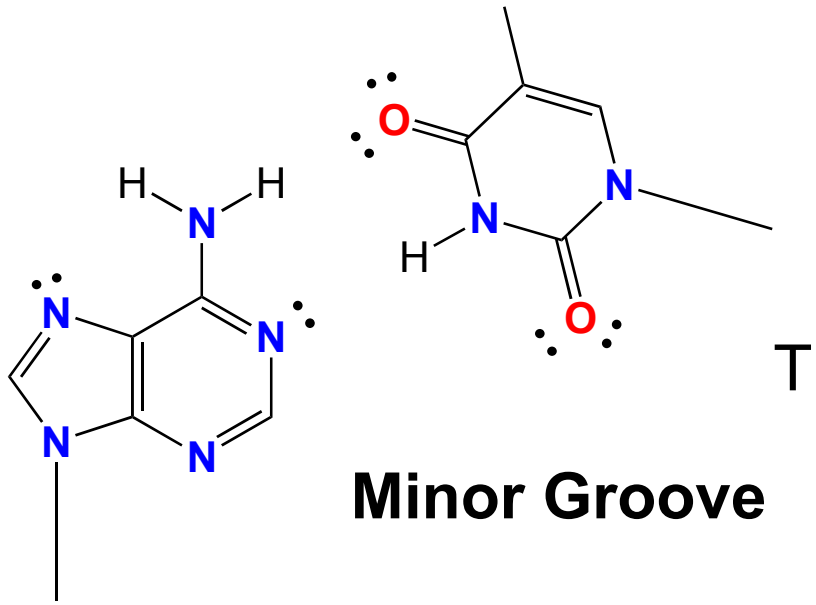

T

# Base Pairing

(Donors matched to Acceptors)

**Major Groove**

A

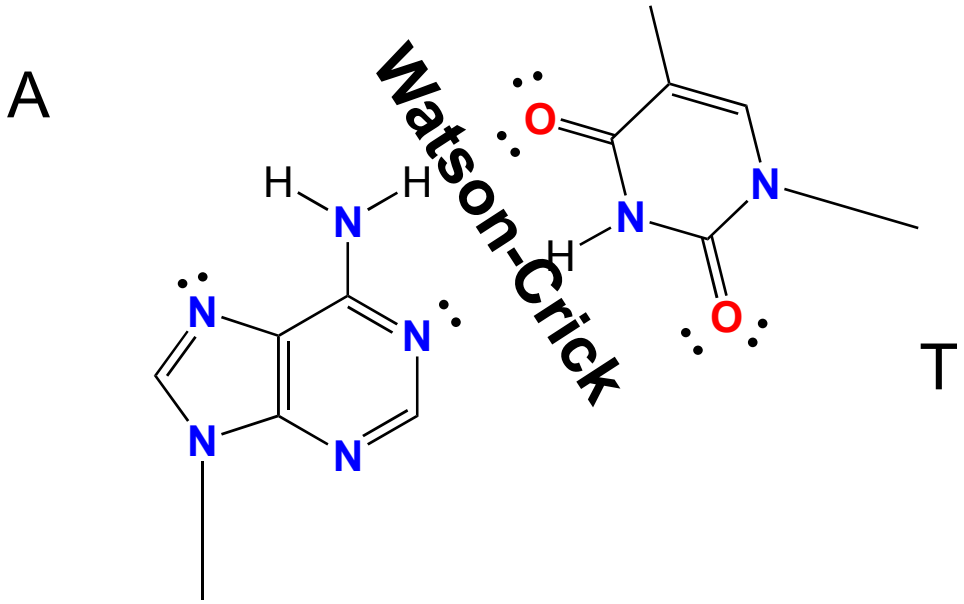



T

**Minor Groove**

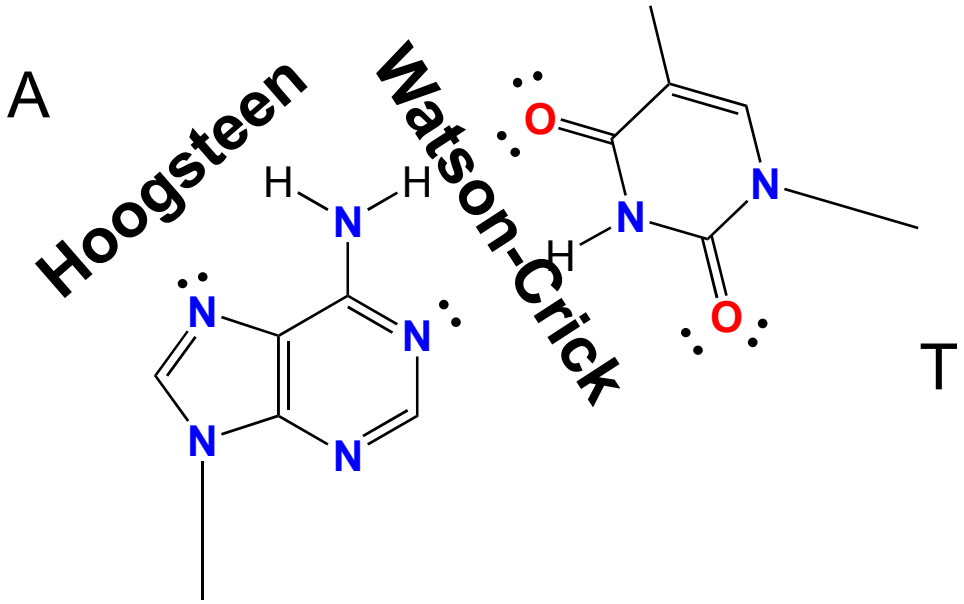
# Base Pairing

(Donors matched to Acceptors)



# Base Pairing

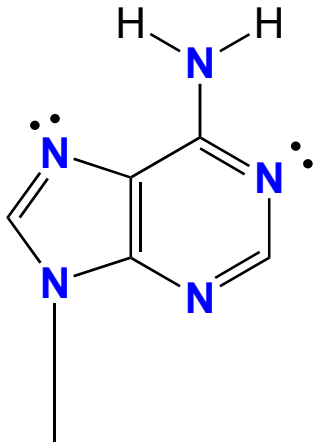
(Donors matched to Acceptors)

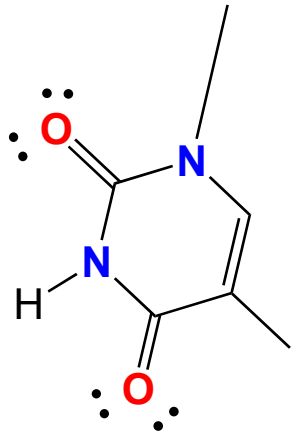


# Base Pairing

(Donors matched to Acceptors)

A



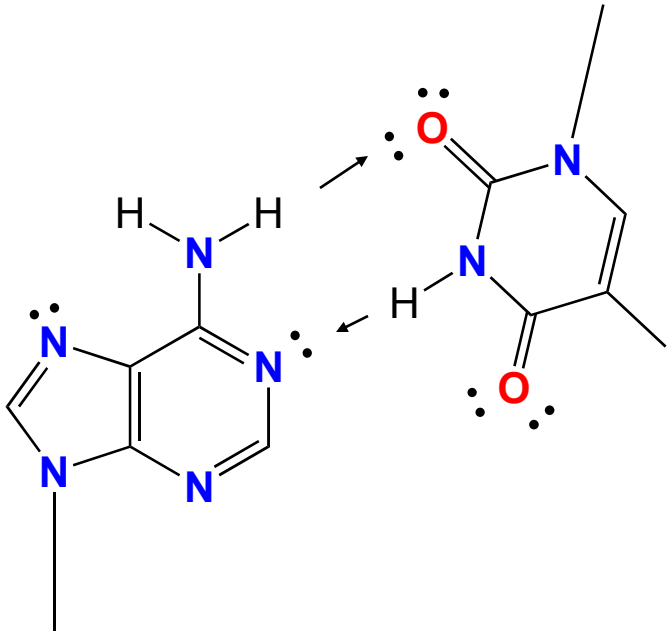




T

# Base Pairing

(Donors matched to Acceptors)

A

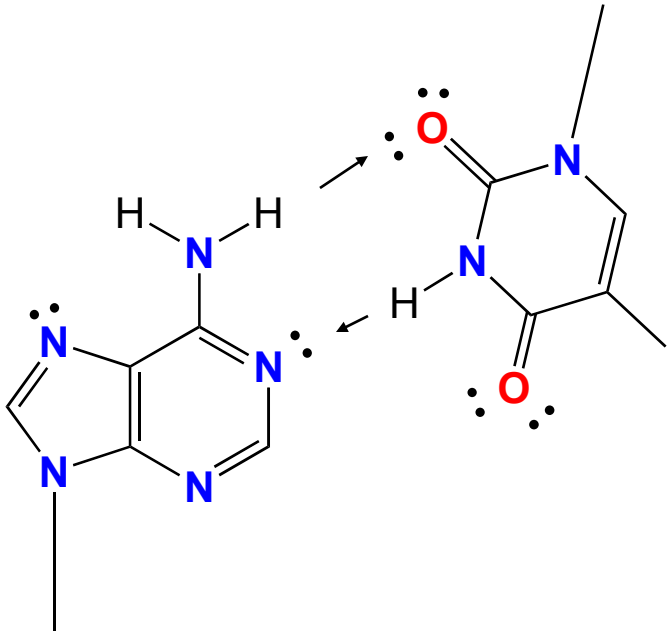



T

# Base Pairing

(Donors matched to Acceptors)

A



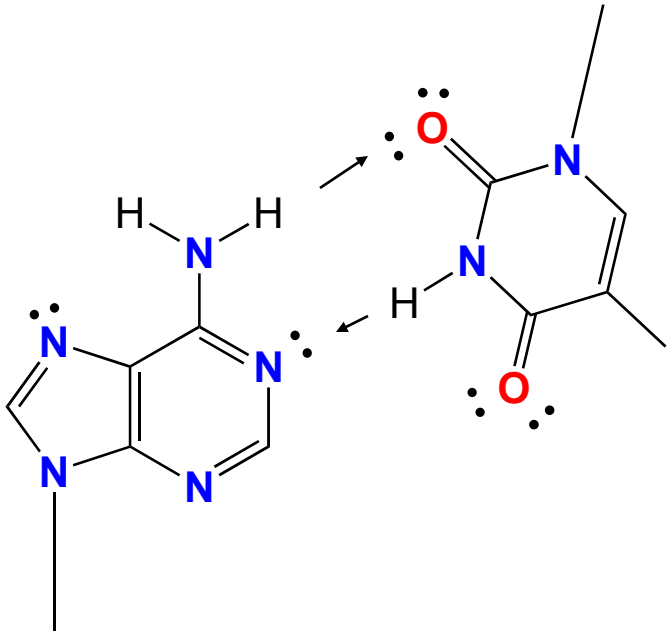

T

Good base pairing

# Base Pairing

(Donors matched to Acceptors)

A

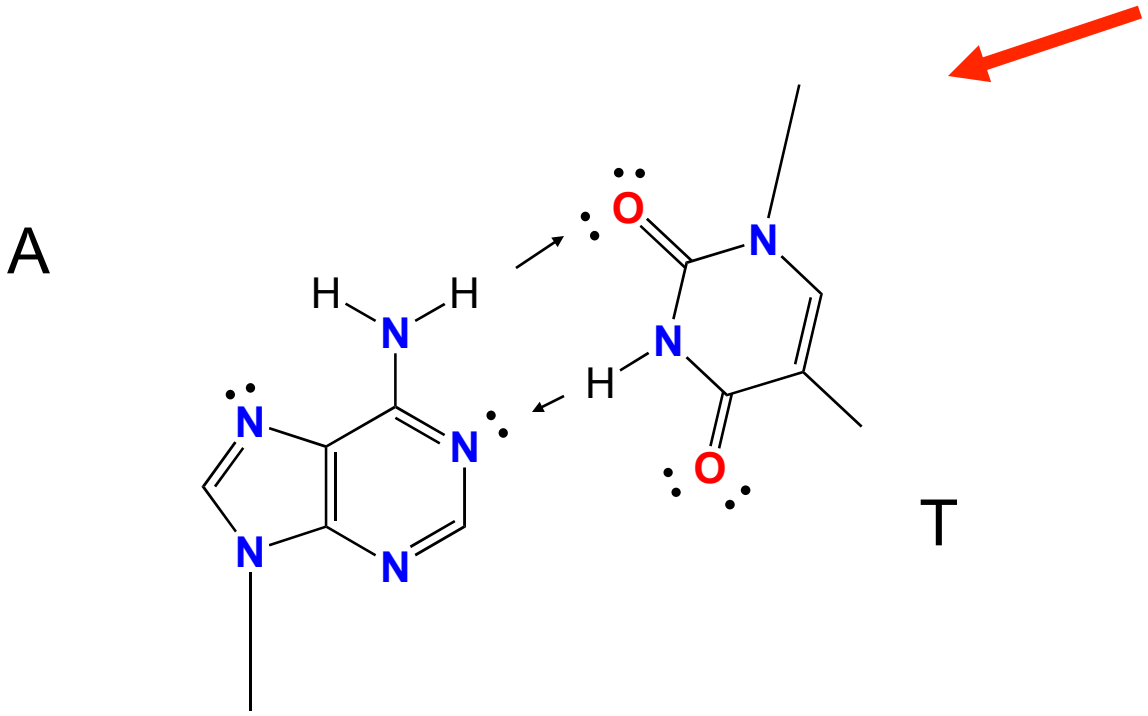



T

Good base pairing
Watson-Crick facing

# Base Pairing

(Donors matched to Acceptors)

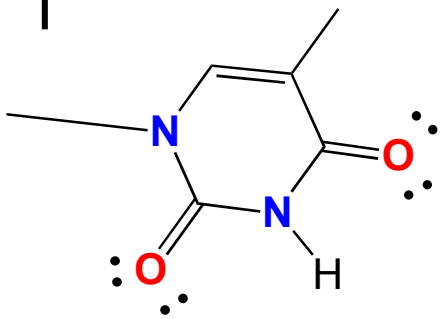


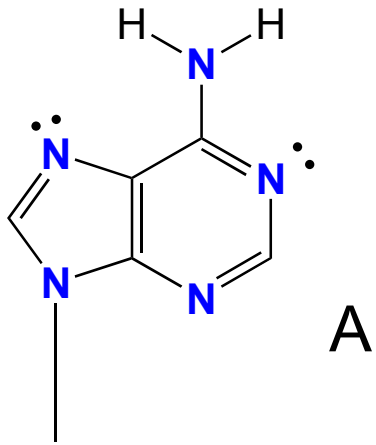

Good base pairing
Watson-Crick facing
but *Anti-Watson-Crick* orientation

# Base Pairing

(Donors matched to Acceptors)

T



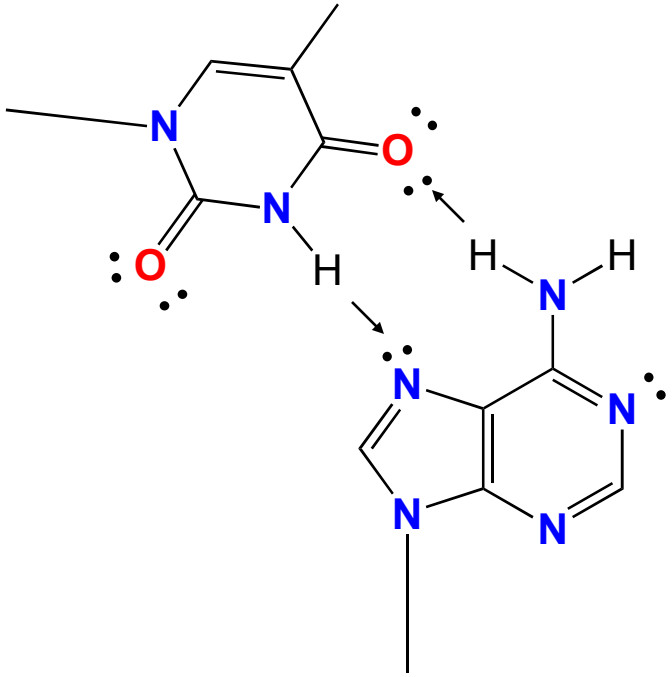




A

# Base Pairing

(Donors matched to Acceptors)

T

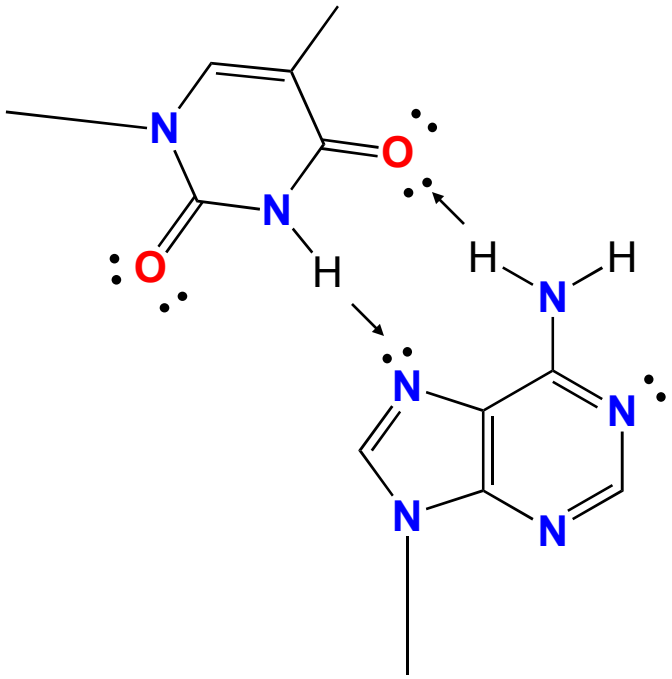



A

# Base Pairing

(Donors matched to Acceptors)

T



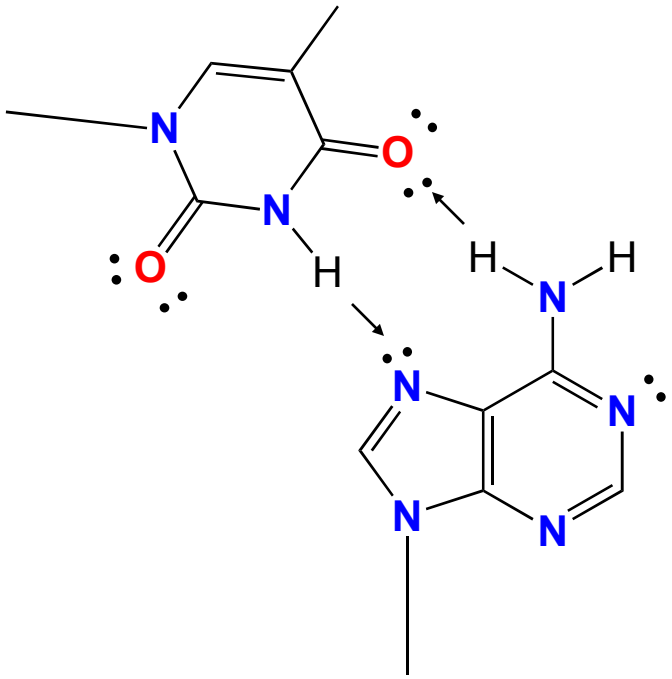

A

Good base pairing

# Base Pairing

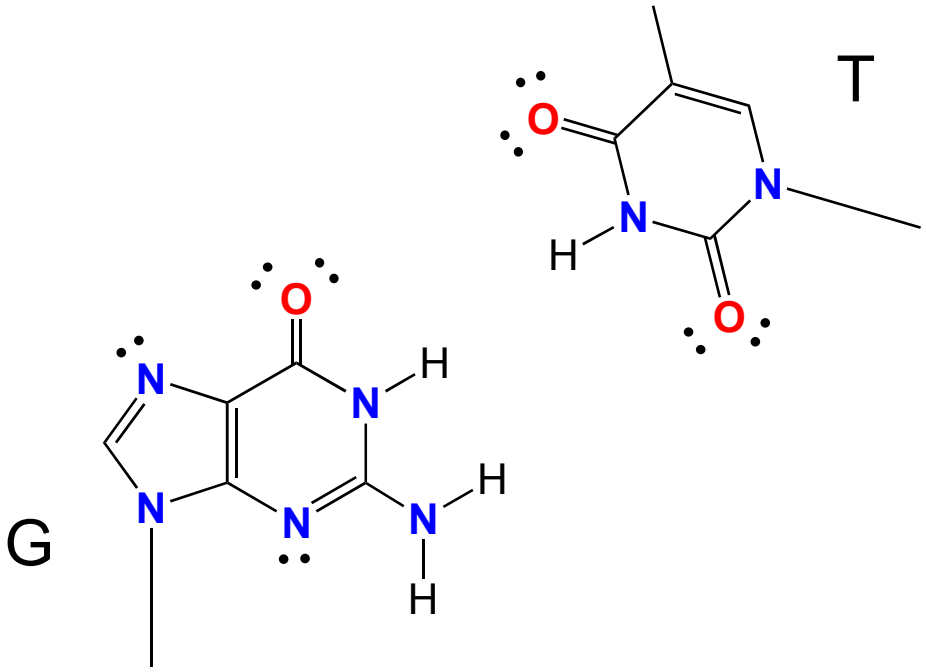
(Donors matched to Acceptors)

T




A

Good base pairing
WC-Hoogsteen facing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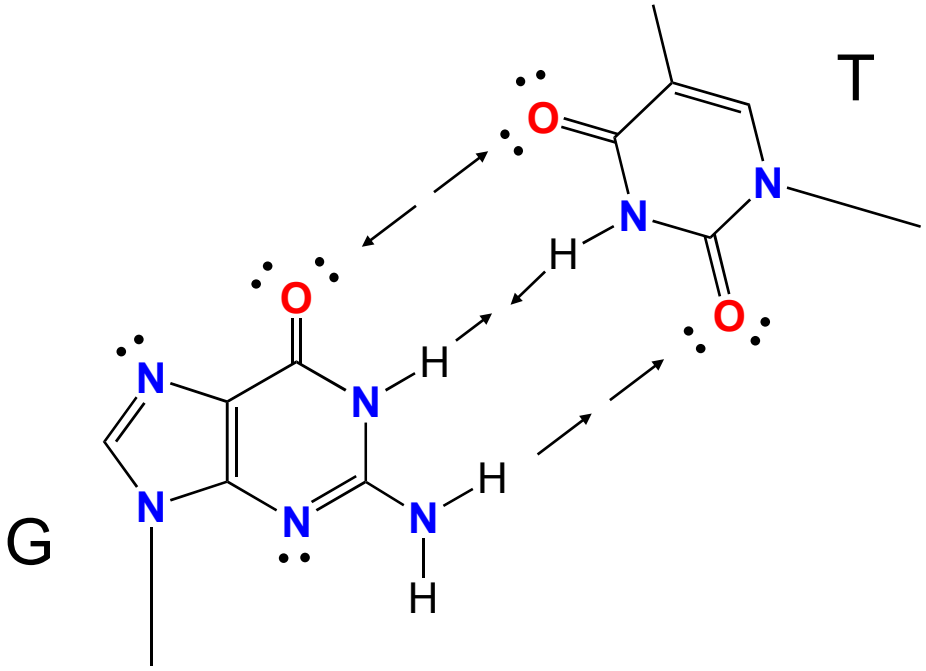
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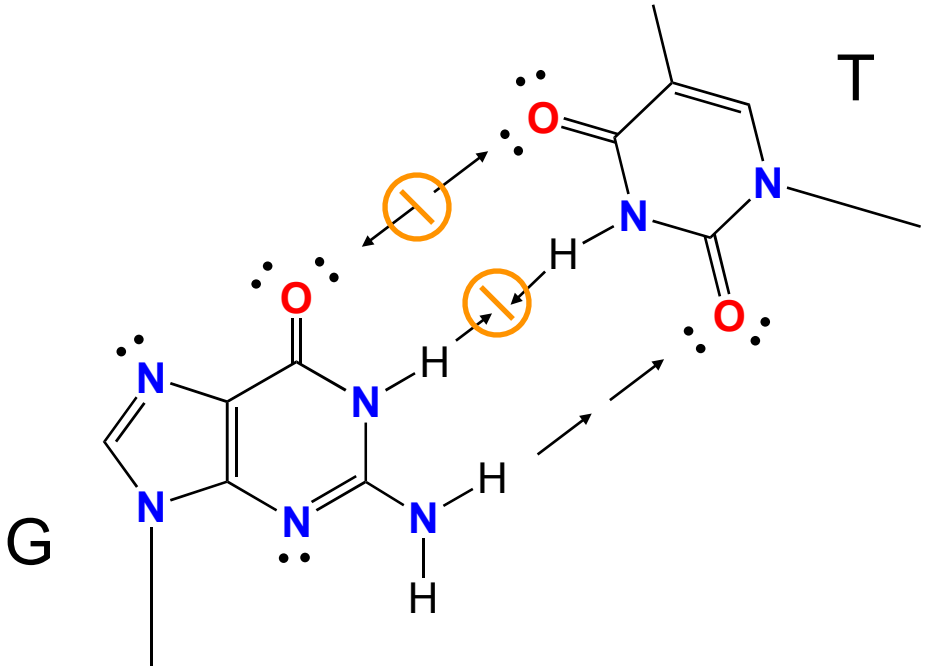
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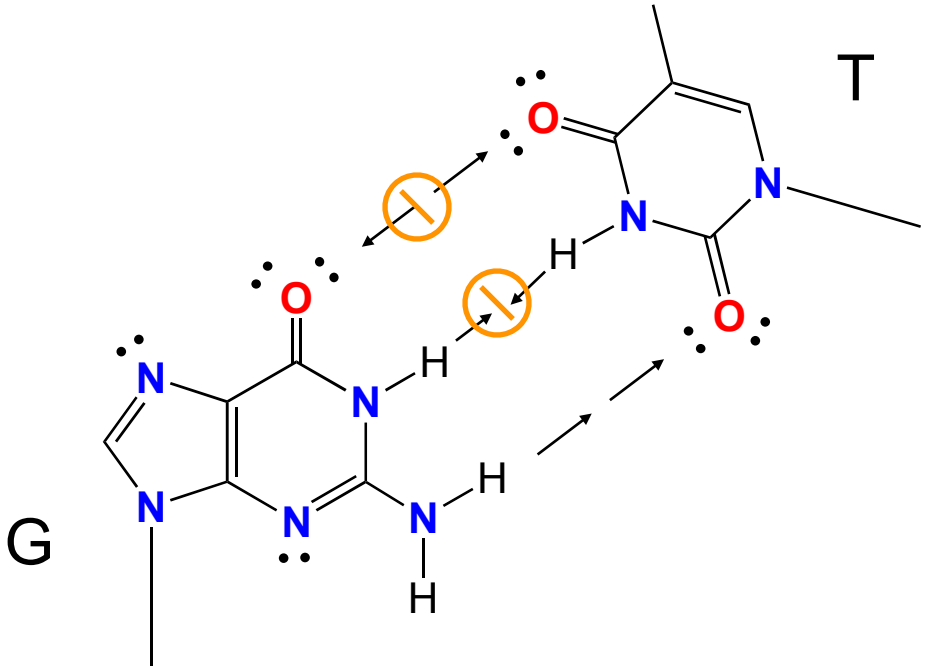
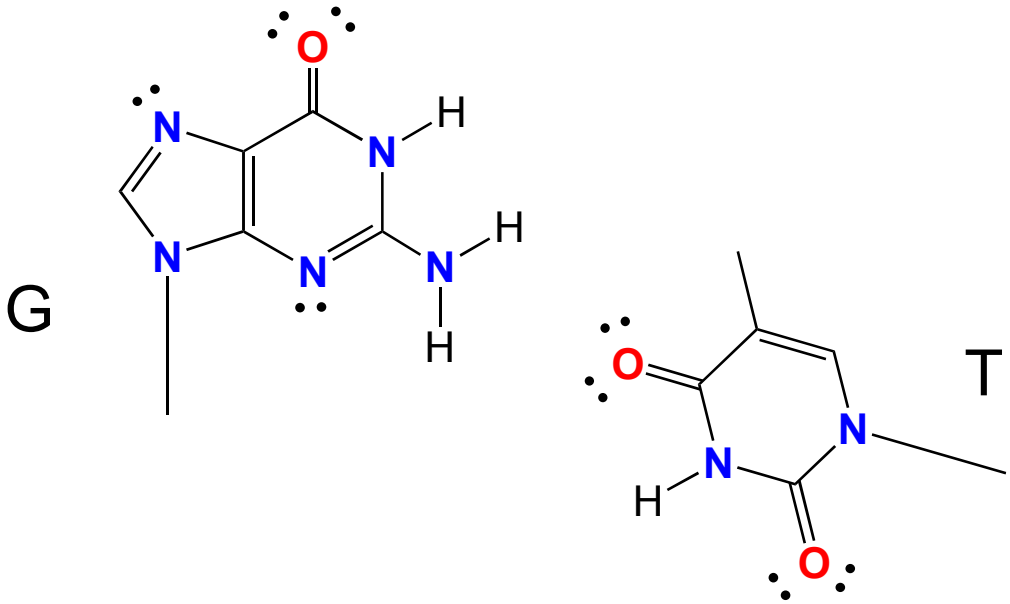
# Bad Base Pairing

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




G
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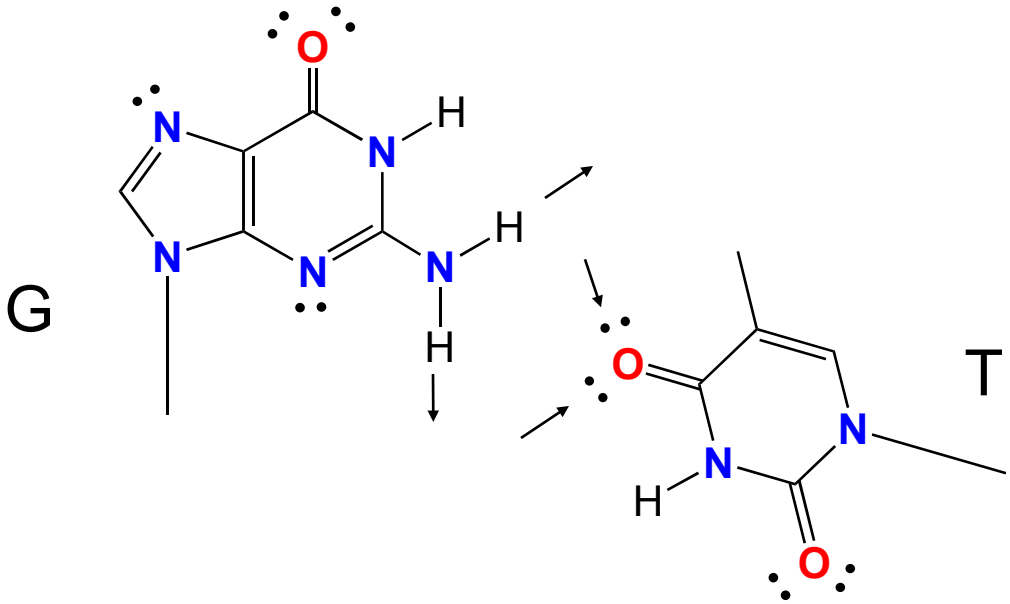
G
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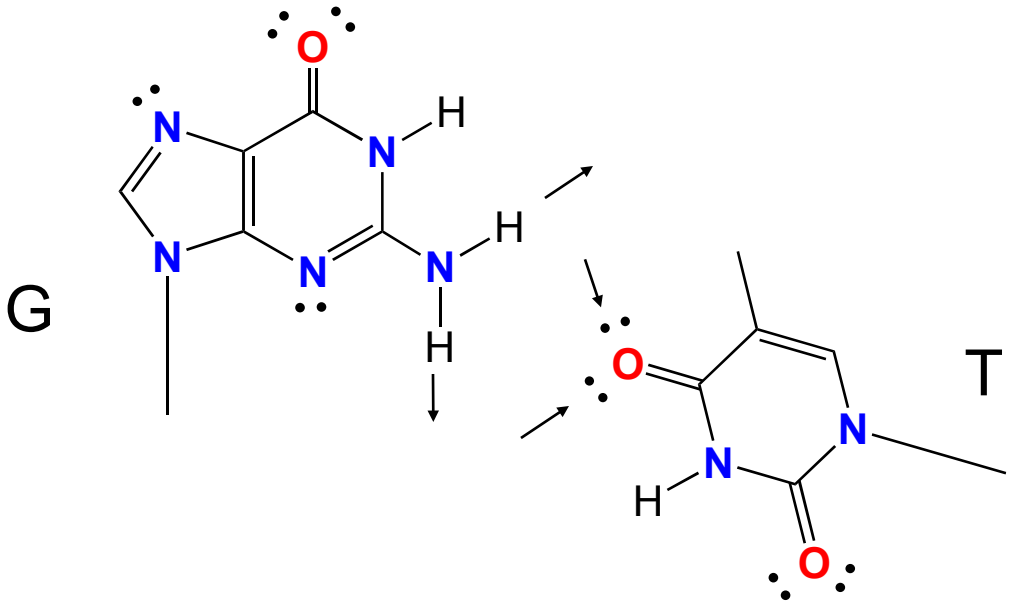
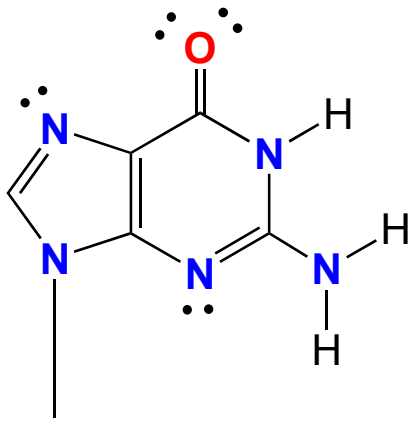
# Bad Base Pairing

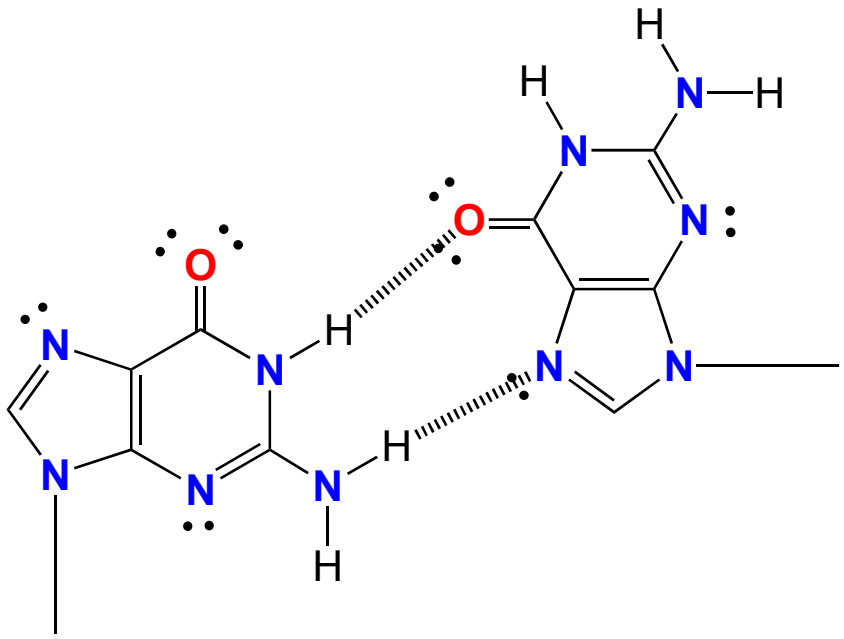
(Donors to Acceptors with ***terrible angles***)



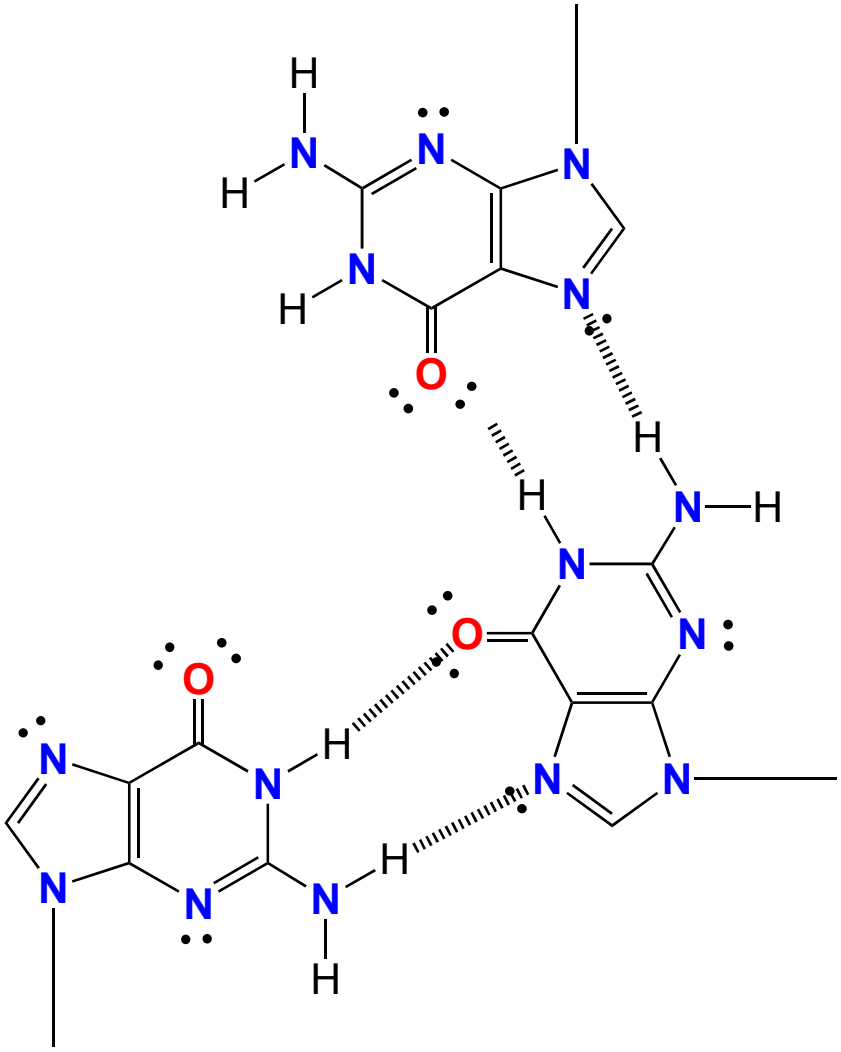
# Wild (but good) Base Pairing



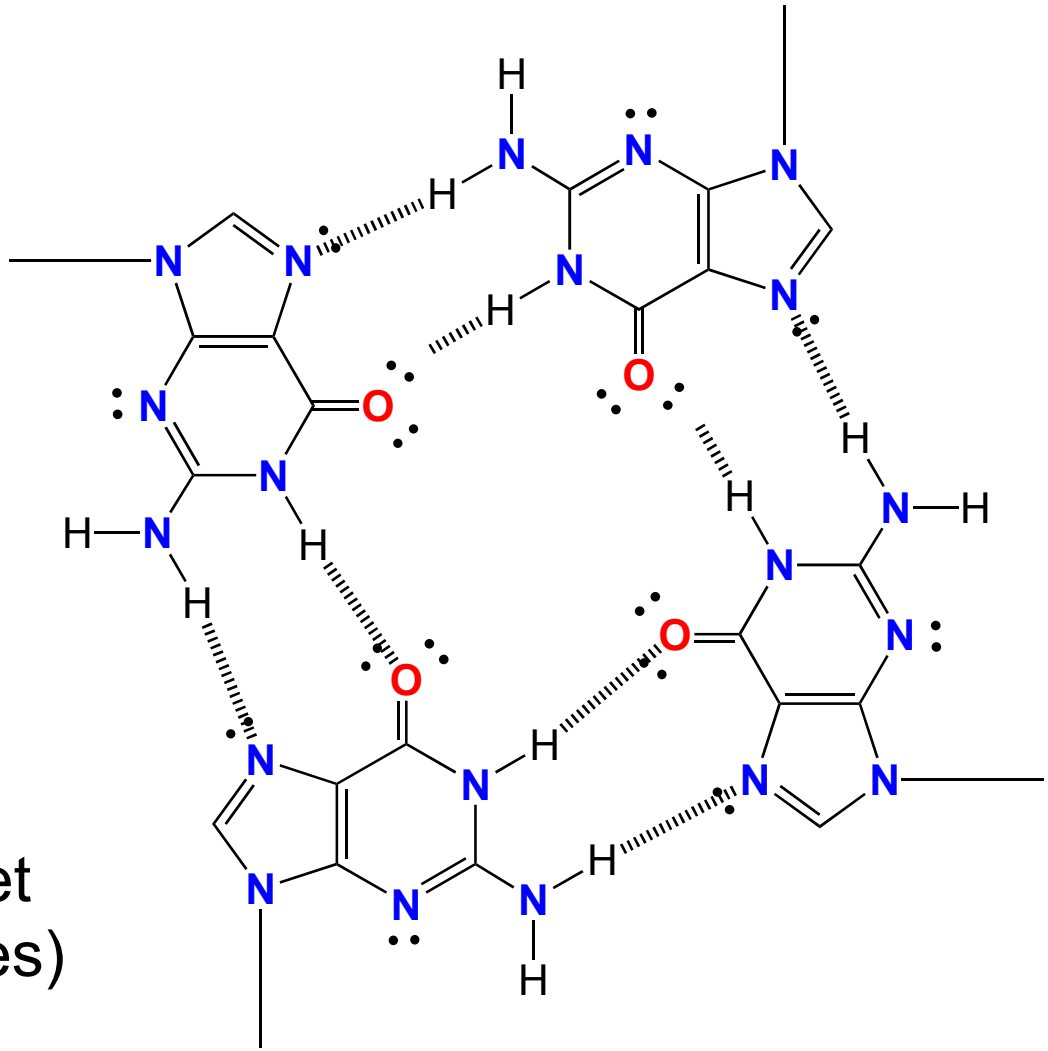
# Wild (but good) Base Pairing



# Wild (but good) Base Pairing

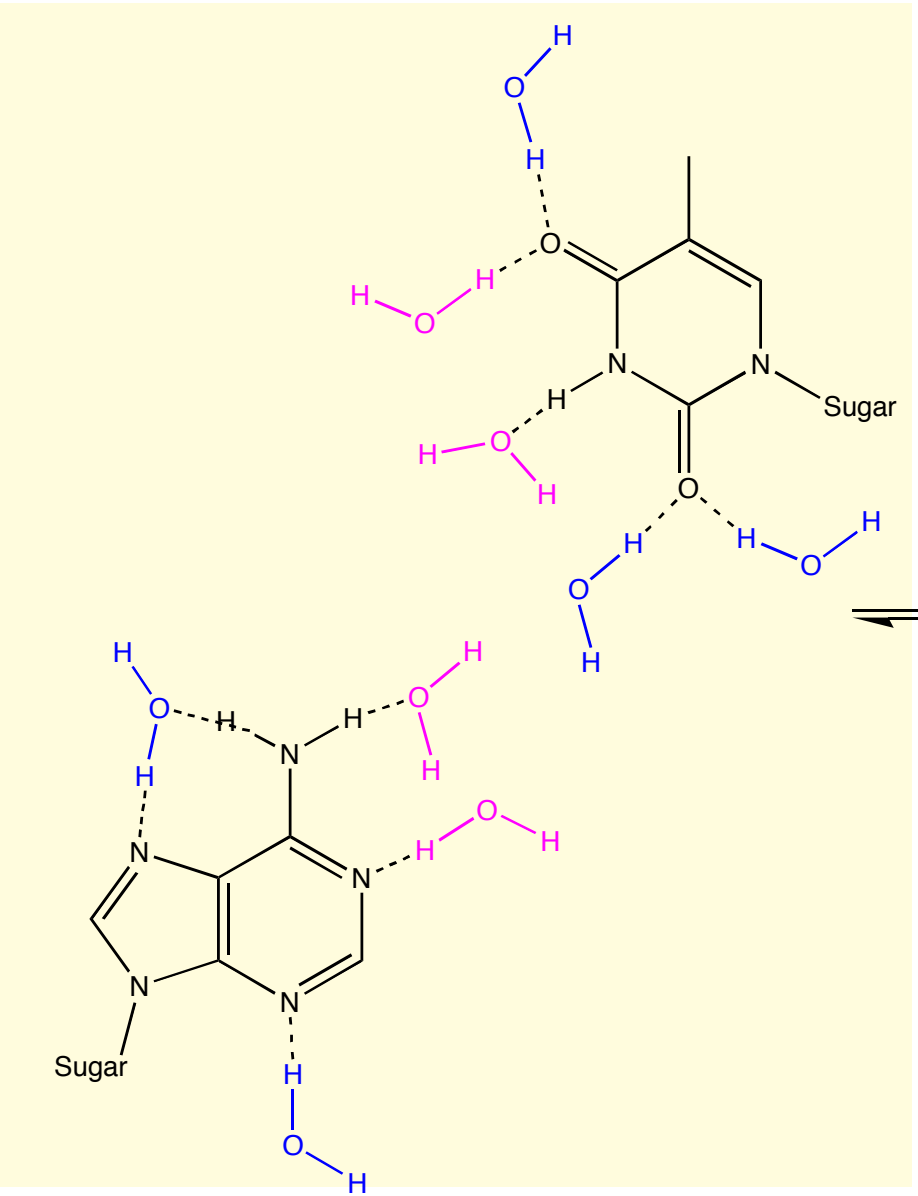


# Wild (but good) Base Pairing



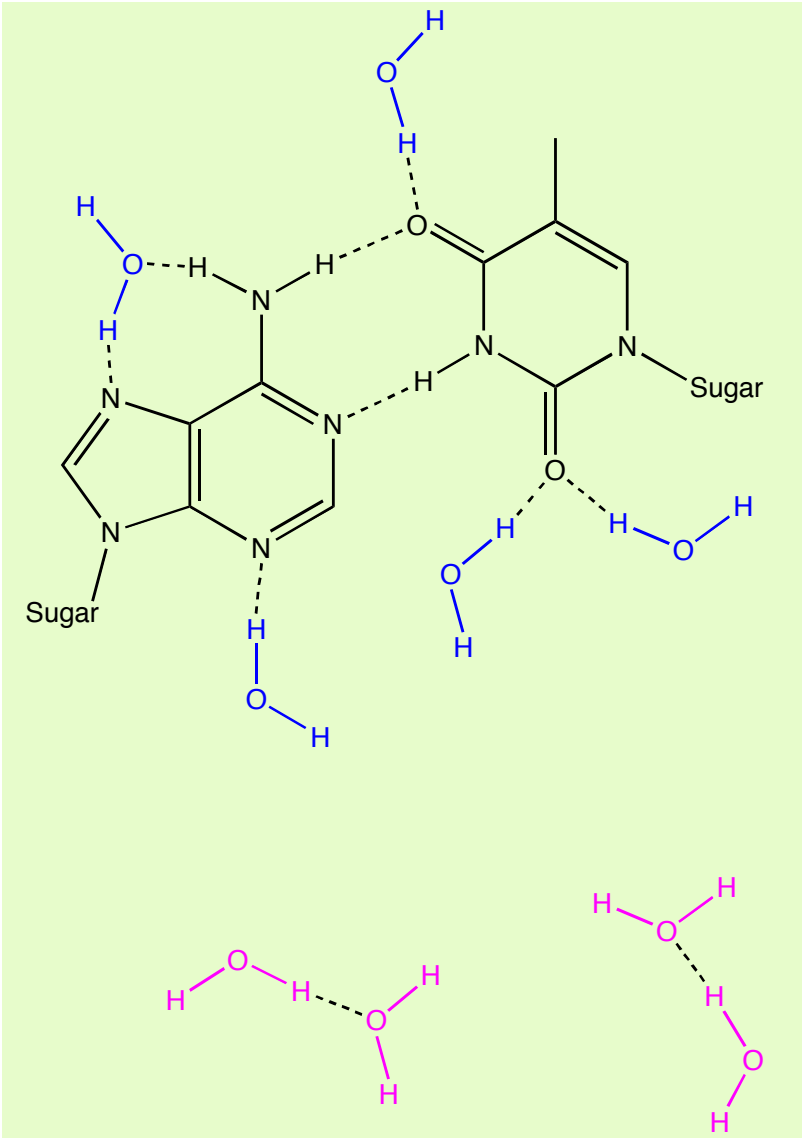
G-quartet
(Telomeres)

# AT Base Pair

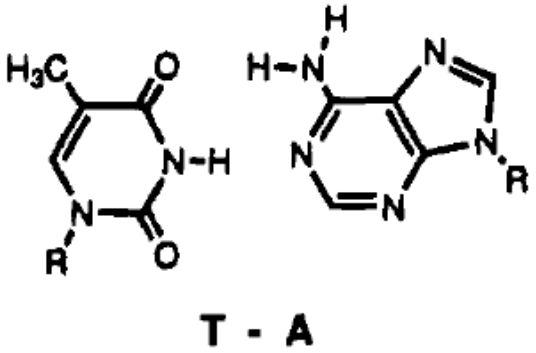



Ten H-Bonds

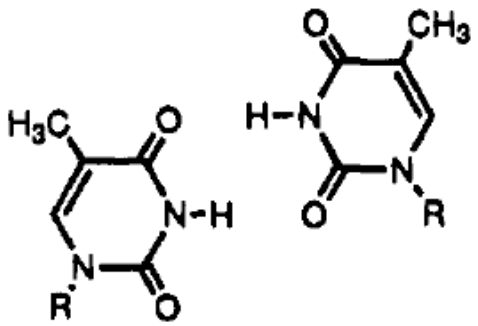
Ten H-Bonds



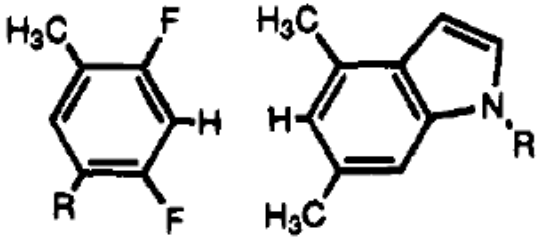
# How important are H-bonds in DNA?



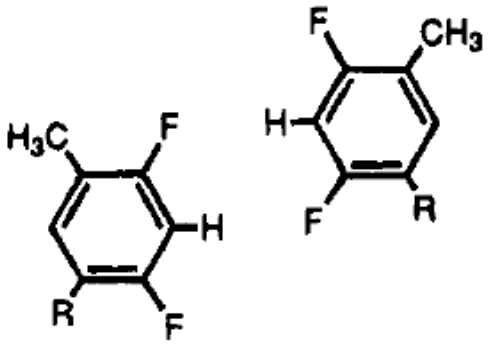
T - A



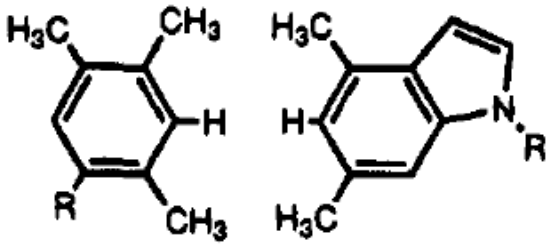
T - T



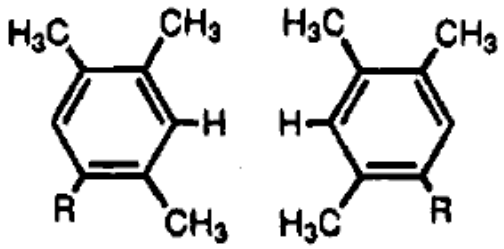
F - D



F - F



B - D



B - B



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| 5′-CTTTTCFTTCTT<br>3′-GAAAAGGAAGAA | 23.0 | 8.0 |
| 5′-CTTTTCFTTCTT<br>3′-GAAAAGTAAGAA | 20.2 | 7.3 |
| 5′-CTTTTCBTTCTT<br>3′-GAAAAGAAAGAA | 21.0 | 7.5 |
| 5′-CTTTTCBTTCTT<br>3′-GAAAAGCAAGAA | 22.9 | 7.8 |
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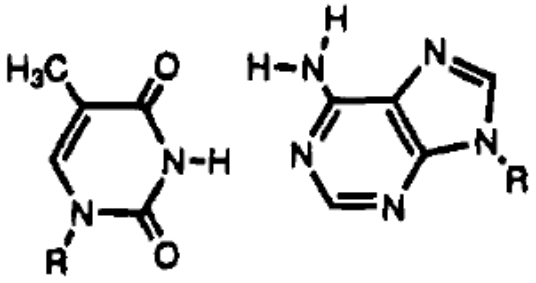
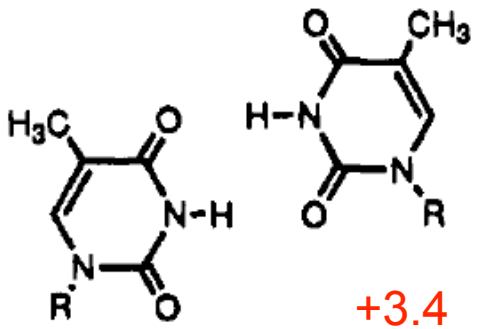
# How important are H-bonds in DNA?

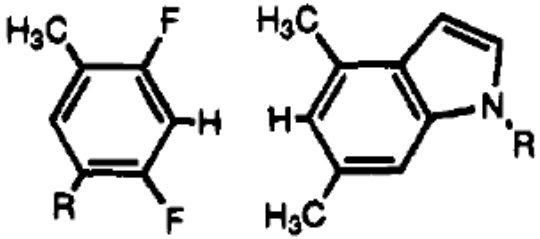


T - A

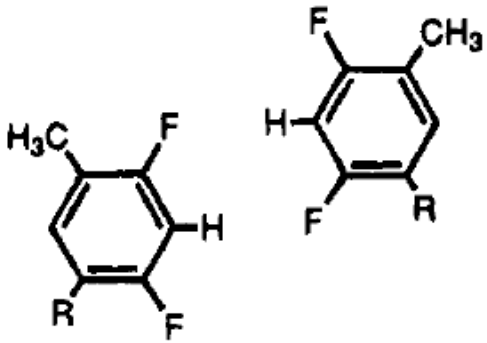


T - T

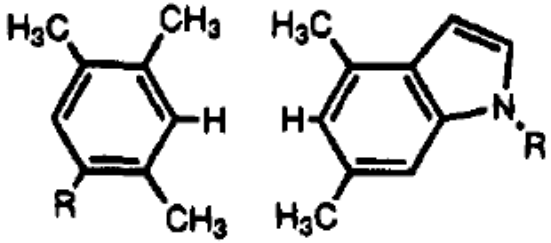
+3.4



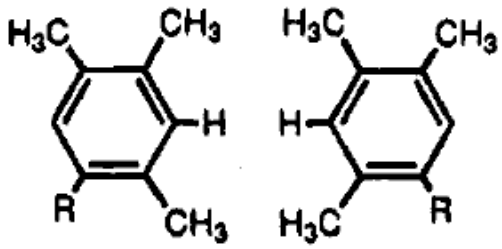
F - D



F - F



B - D



B - B

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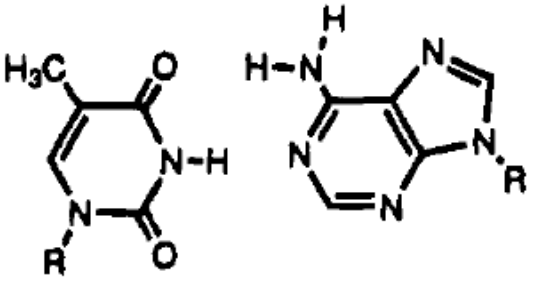
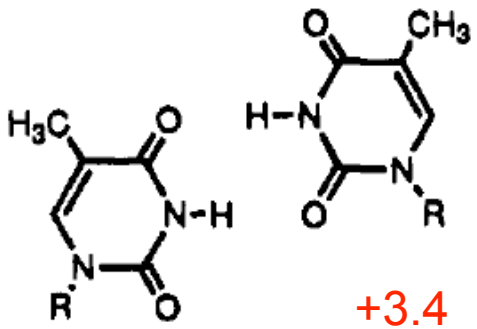
# How important are H-bonds in DNA?

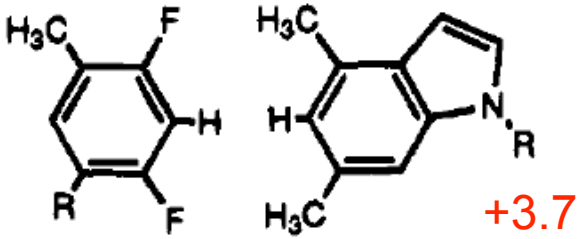


T - A



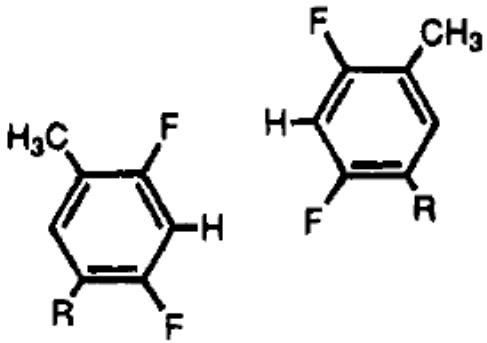
T - T

+3.4

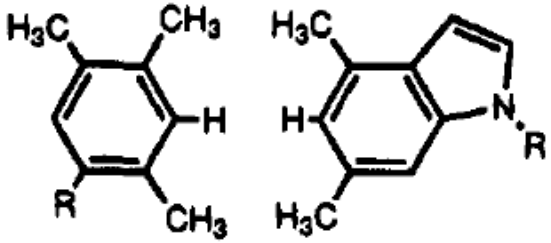


F - D

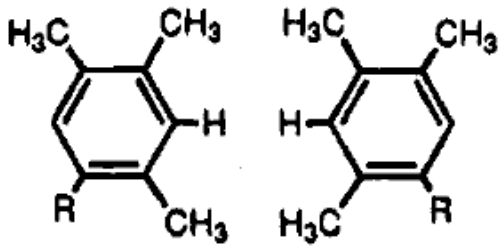
+3.7



F - F



B - D



B - B

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

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| 5′-CTTTTCBTTCTT<br>3′-GAAAAGAAAGAA | 21.0 | 7.5 |
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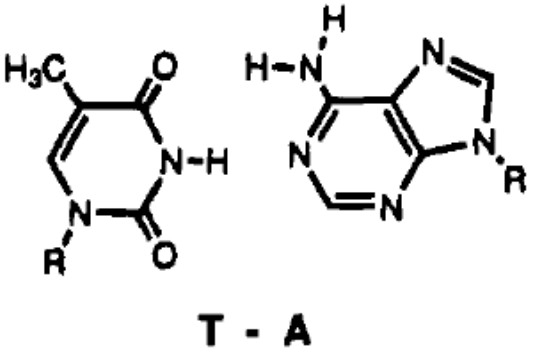
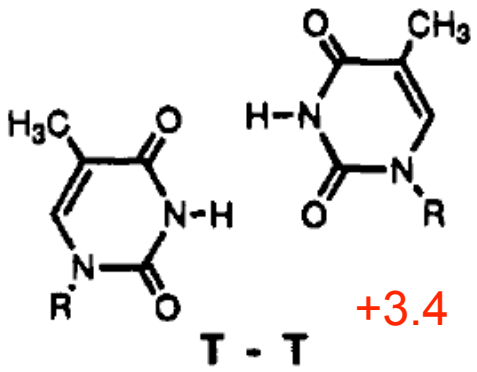
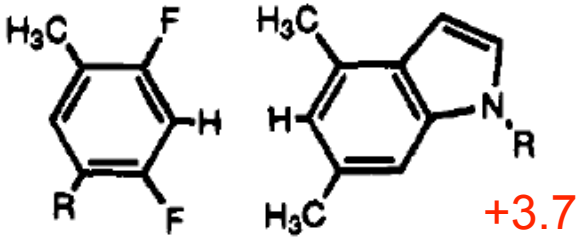


T - A



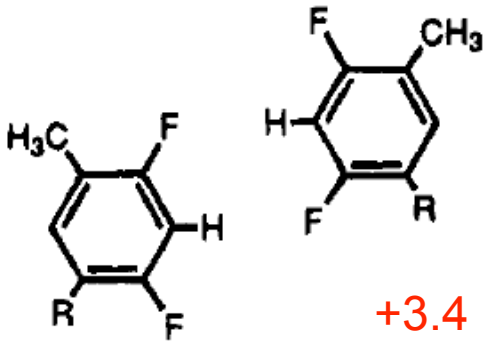
+3.4

T - T



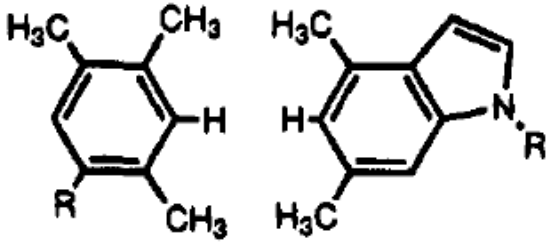
+3.7

F - D

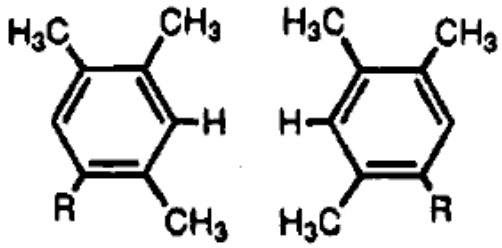


+3.4

F - F



B - D



B - B

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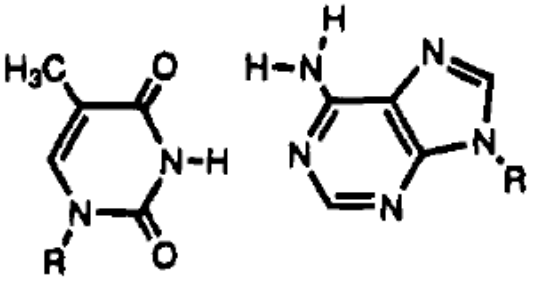
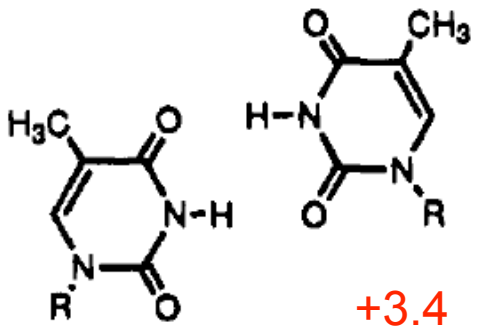
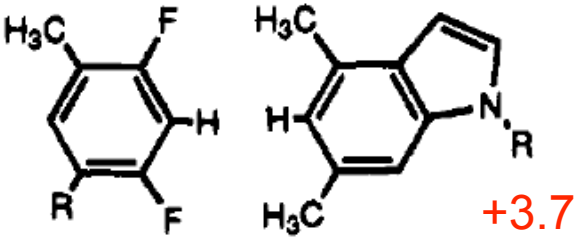


T - A



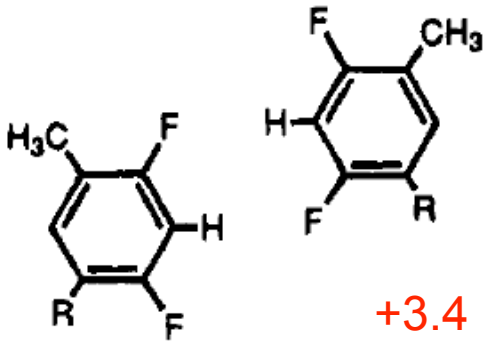
+3.4

T - T



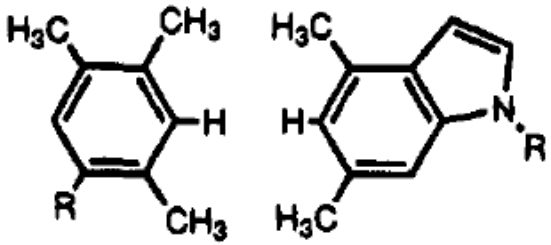
+3.7

F - D



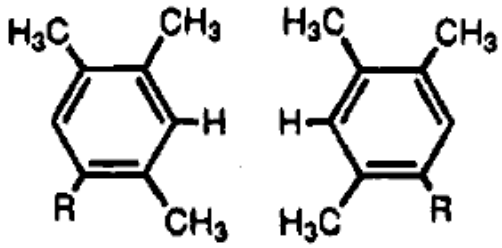
+3.4

F - F



+3.5

B - D



B - B

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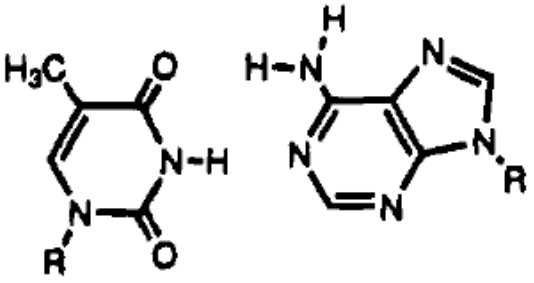
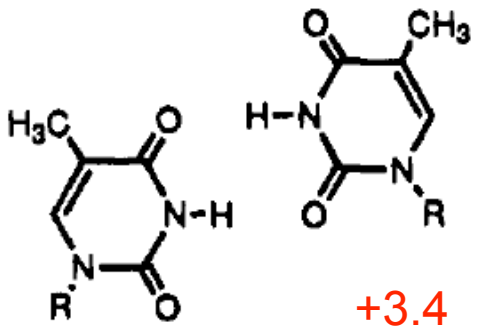
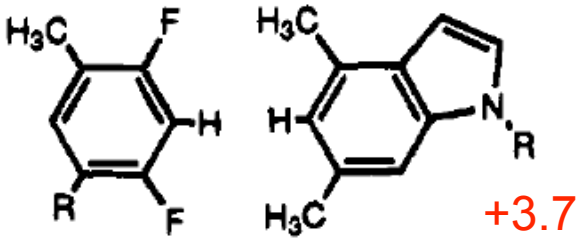


T - A



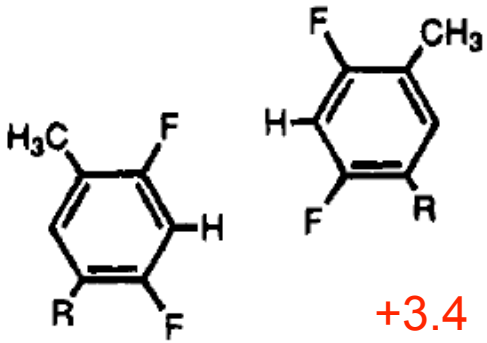
+3.4

T - T



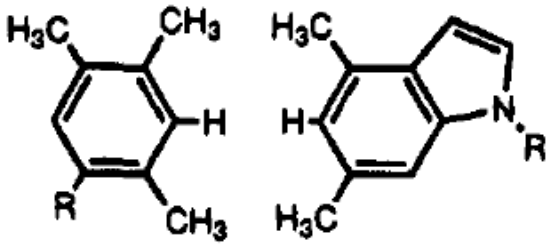
+3.7

F - D



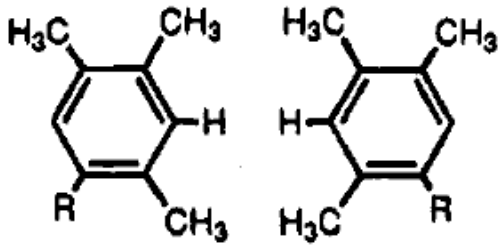
+3.4

F - F



+3.5

B - D



+3.0

B - B

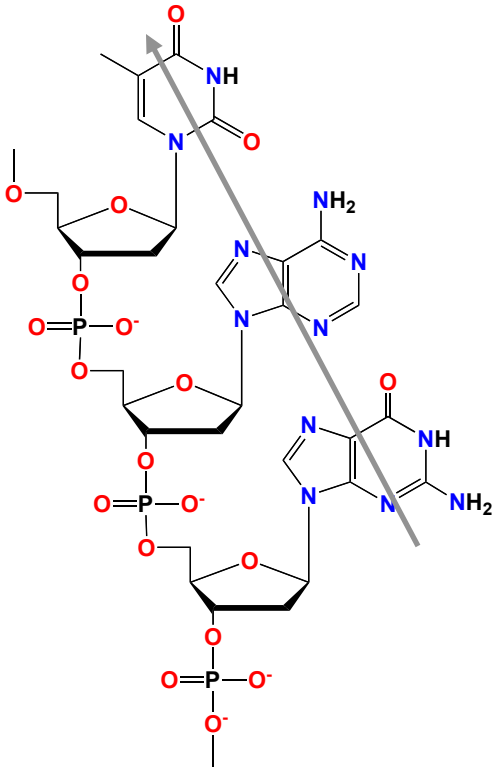
*J. Am. Chem. Soc., Vol. 117, No. 7, 1995* 1867

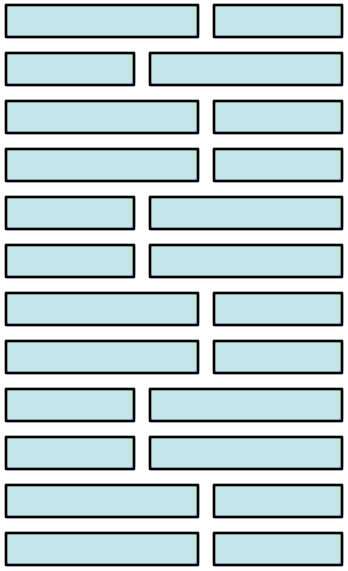
**Table 1.** Free Energies and Melting Temperatures for Dodecamer Duplexes Containing a Variable T−X, F−X, B−X, or D−X Base Pair (X = A, T, C, G)

| duplex | $T_m$ (°C) [a] | $-\Delta G°_{25}$ (kcal) |
|---|---|---|
| 5′-CTTTTCTTTCTT<br>3′-GAAAAGAAAGAA | 39.4 | 12.3 |
| 5′-CTTTTCTTTCTT<br>3′-GAAAAGCAAGAA | 26.4 | 8.7 |
| 5′-CTTTTCTTTCTT<br>3′-GAAAAGGAAGAA | 30.7 | 9.3 |
| 5′-CTTTTCTTTCTT<br>3′-GAAAAGTAAGAA | 27.1 | 8.9 |
| 5′-CTTTTCFTTCTT<br>3′-GAAAAGAAAGAA | 21.4 | 7.4 |
| 5′-CTTTTCFTTCTT<br>3′-GAAAAGCAAGAA | 25.0 | 8.2 |
| 5′-CTTTTCFTTCTT<br>3′-GAAAAGGAAGAA | 23.0 | 8.0 |
| 5′-CTTTTCFTTCTT<br>3′-GAAAAGTAAGAA | 20.2 | 7.3 |
| 5′-CTTTTCBTTCTT<br>3′-GAAAAGAAAGAA | 21.0 | 7.5 |
| 5′-CTTTTCBTTCTT<br>3′-GAAAAGCAAGAA | 22.9 | 7.8 |
| 5′-CTTTTCBTTCTT<br>3′-GAAAAGGAAGAA | 20.1 | 7.6 |
| 5′-CTTTTCBTTCTT<br>3′-GAAAAGTAAGAA | 20.3 | 6.7 |
| 5′-CTTTTCDTTCTT<br>3′-GAAAAGAAAGAA | 20.8 | 7.4 |
| 5′-CTTTTCDTTCTT<br>3′-GAAAAGCAAGAA | 22.2 | 7.6 |
| 5′-CTTTTCDTTCTT<br>3′-GAAAAGGAAGAA | 19.7 | 7.4 |
| 5′-CTTTTCDTTCTT<br>3′-GAAAAGTAAGAA | 17.6 | 6.9 |

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

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



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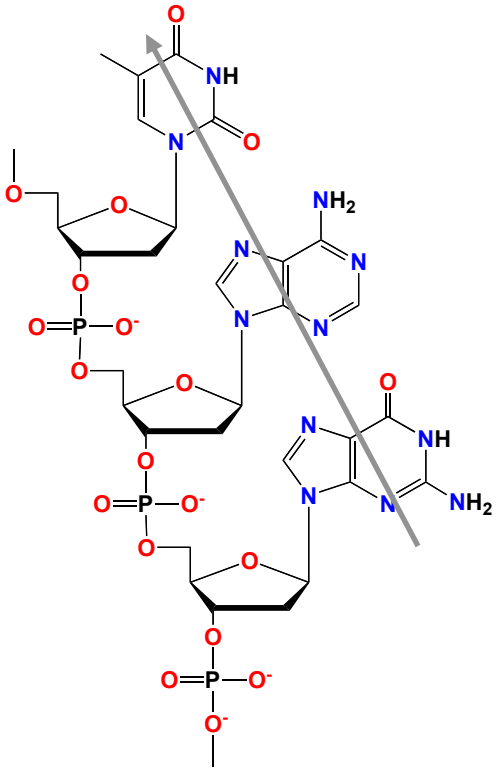
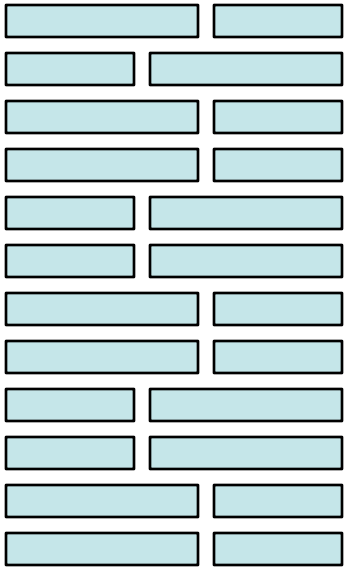
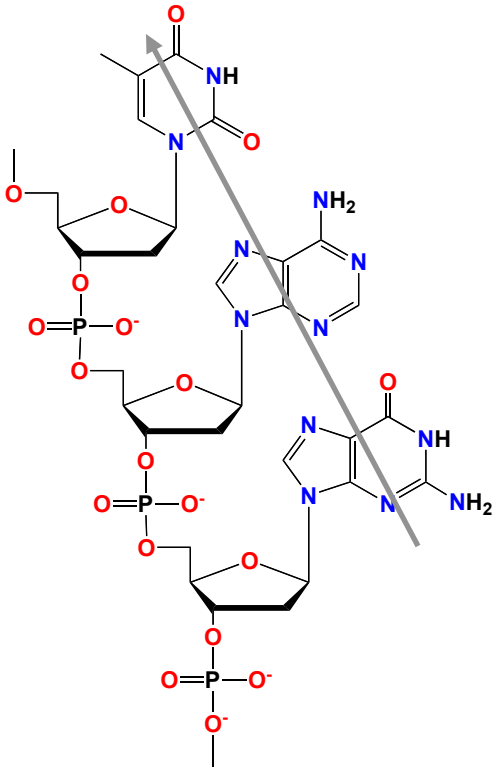
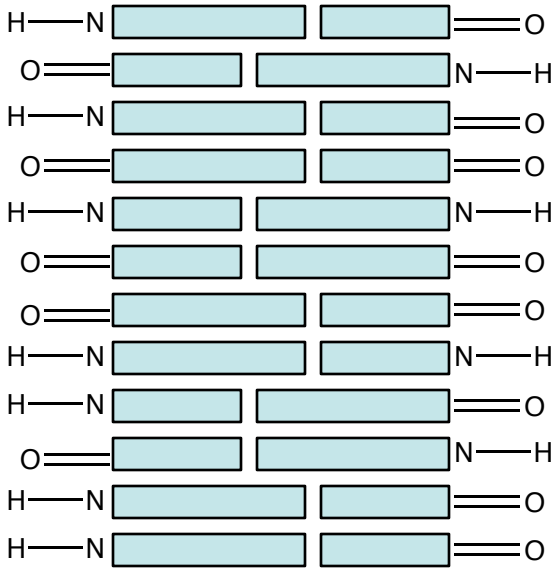




Flat faces are nonpolar

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

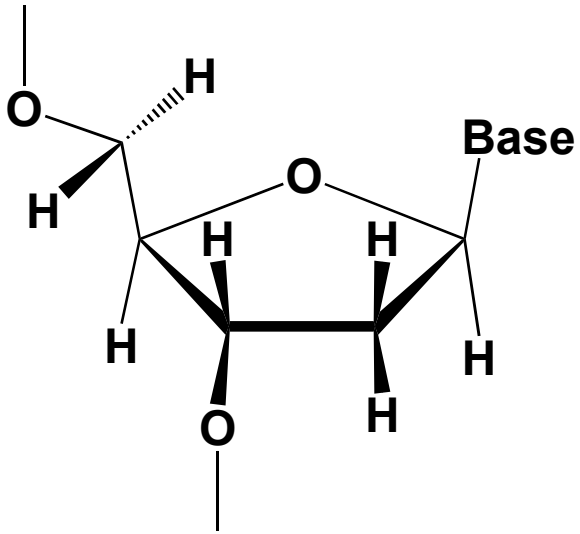


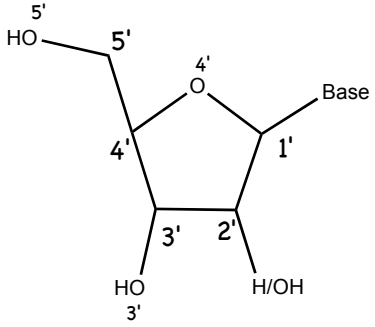


Flat faces are nonpolar
Edges are very polar (can H-bond)

# Other chemical constraints

# Furanose Sugar Ring



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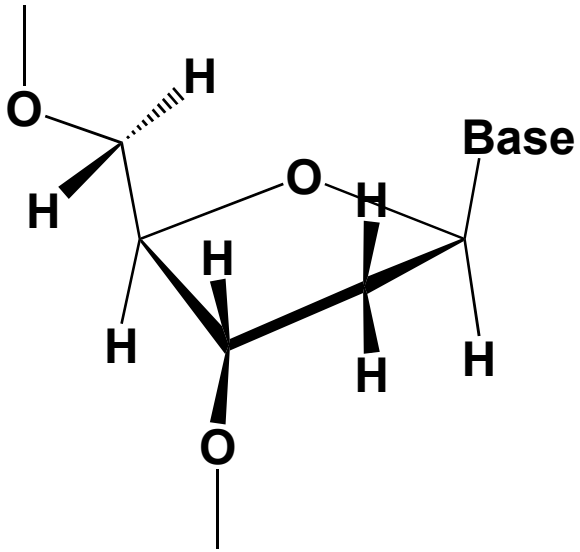


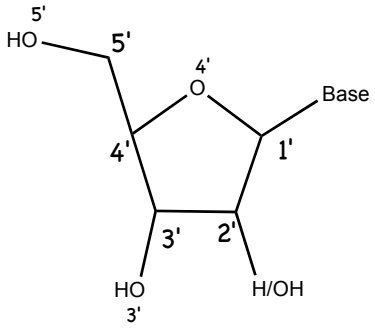

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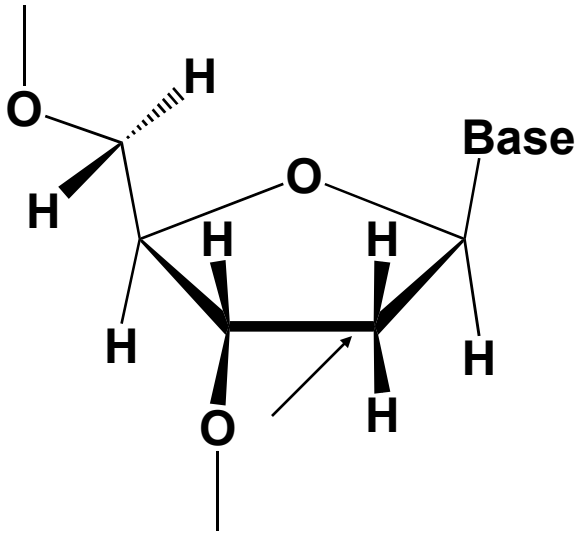
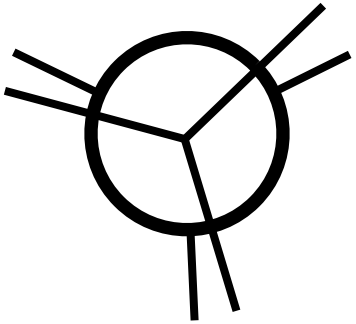
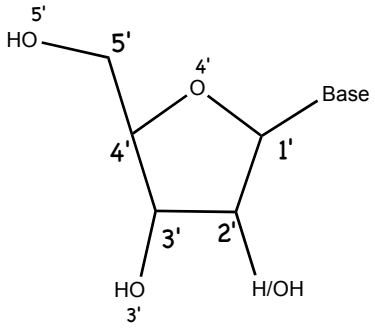
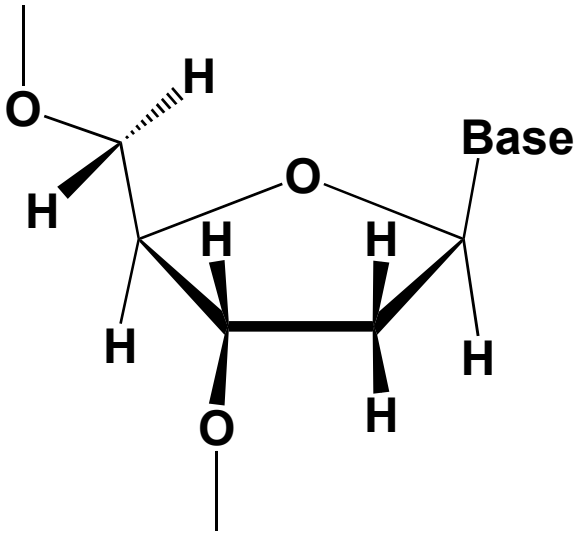
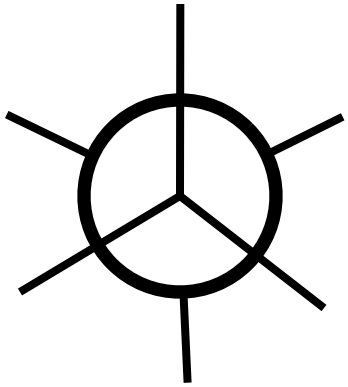


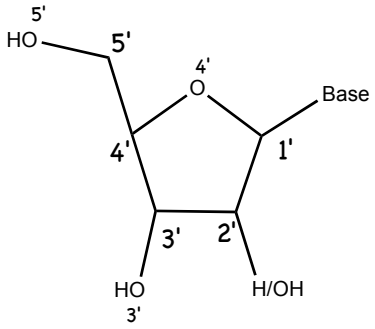





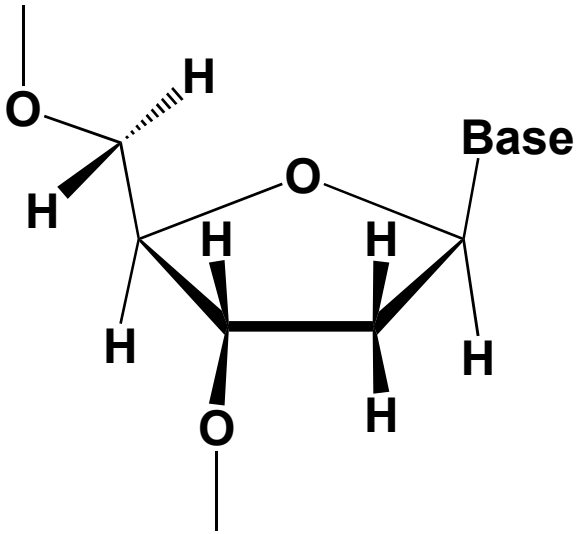
# Furanose Sugar Ring

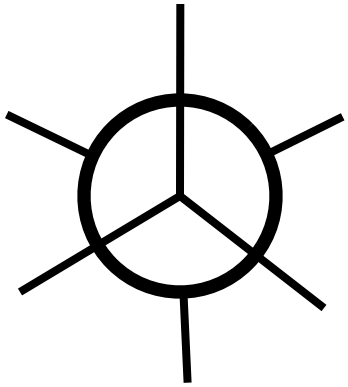


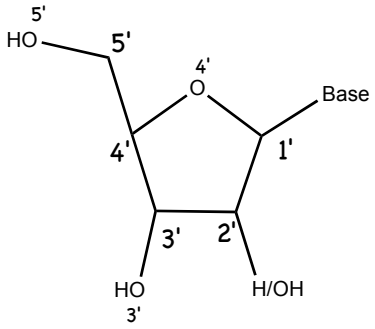



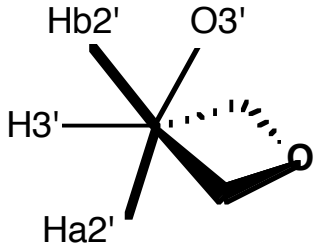


# Furanose Sugar Ring

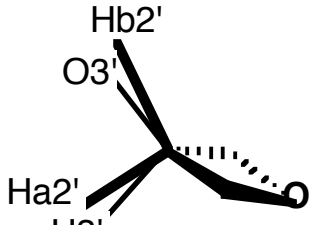




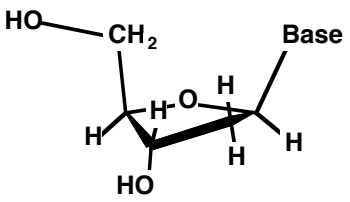




Staggered
Puckered

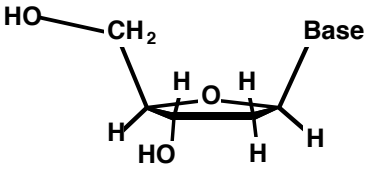



Eclipsed
Planar

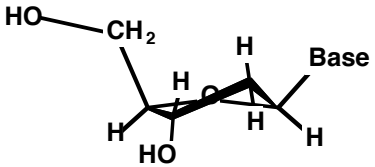
# Furanose Sugar Ring




C3' exo



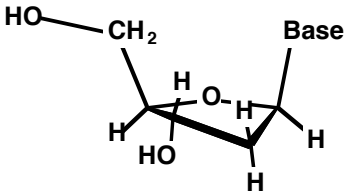

Unpuckered



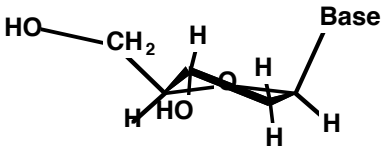

C2' endo

endo

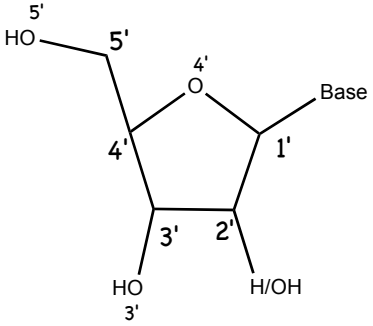
exo

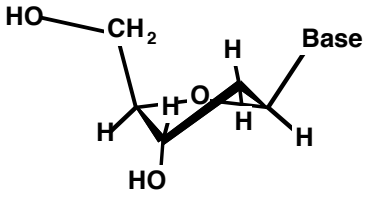



C2' exo

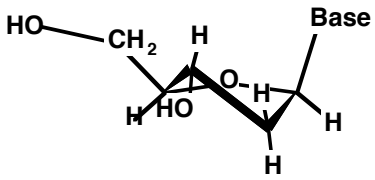



C3' endo

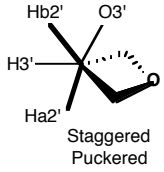


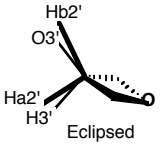

C2' endo - C3' exo




C2' exo - C3' endo




Staggered
Puckered




Eclipsed
Planar

# Hoogsteen vindicated

**Letters to Nature**

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

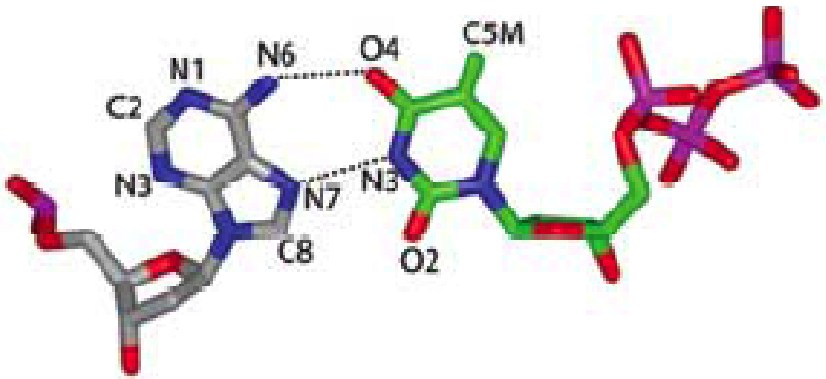
## Replication by human DNA polymerase-ι occurs by Hoogsteen base-pairing

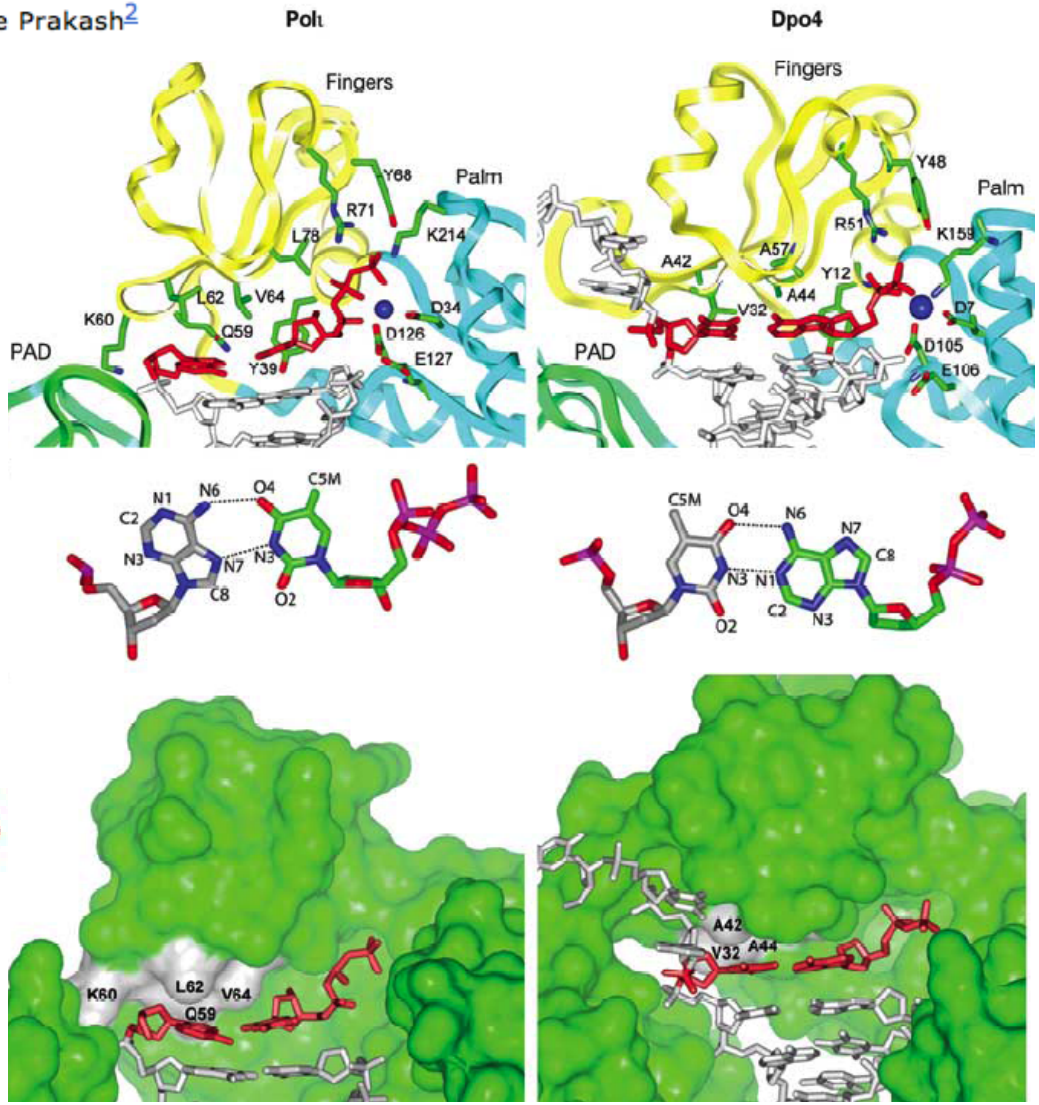
Deepak T. Nair[1], Robert E. Johnson[2], Satya Prakash[2], Louise Prakash[2] and Aneel K. Aggarwal[1]

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 (eg, damaged Watson-Crick face of G).



# Hoogsteen vindicated

**But… perhaps not…**

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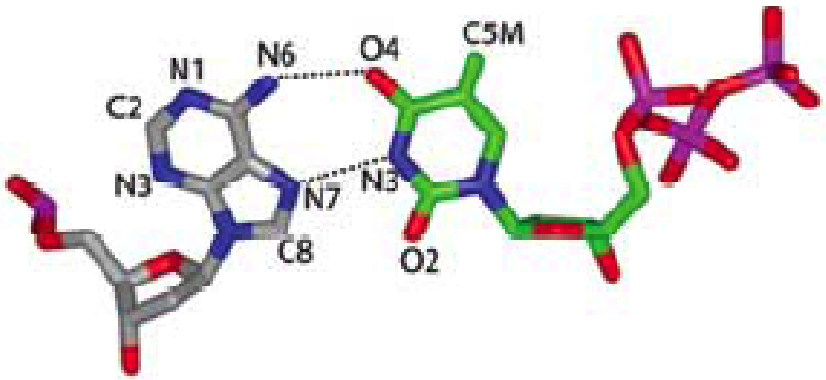
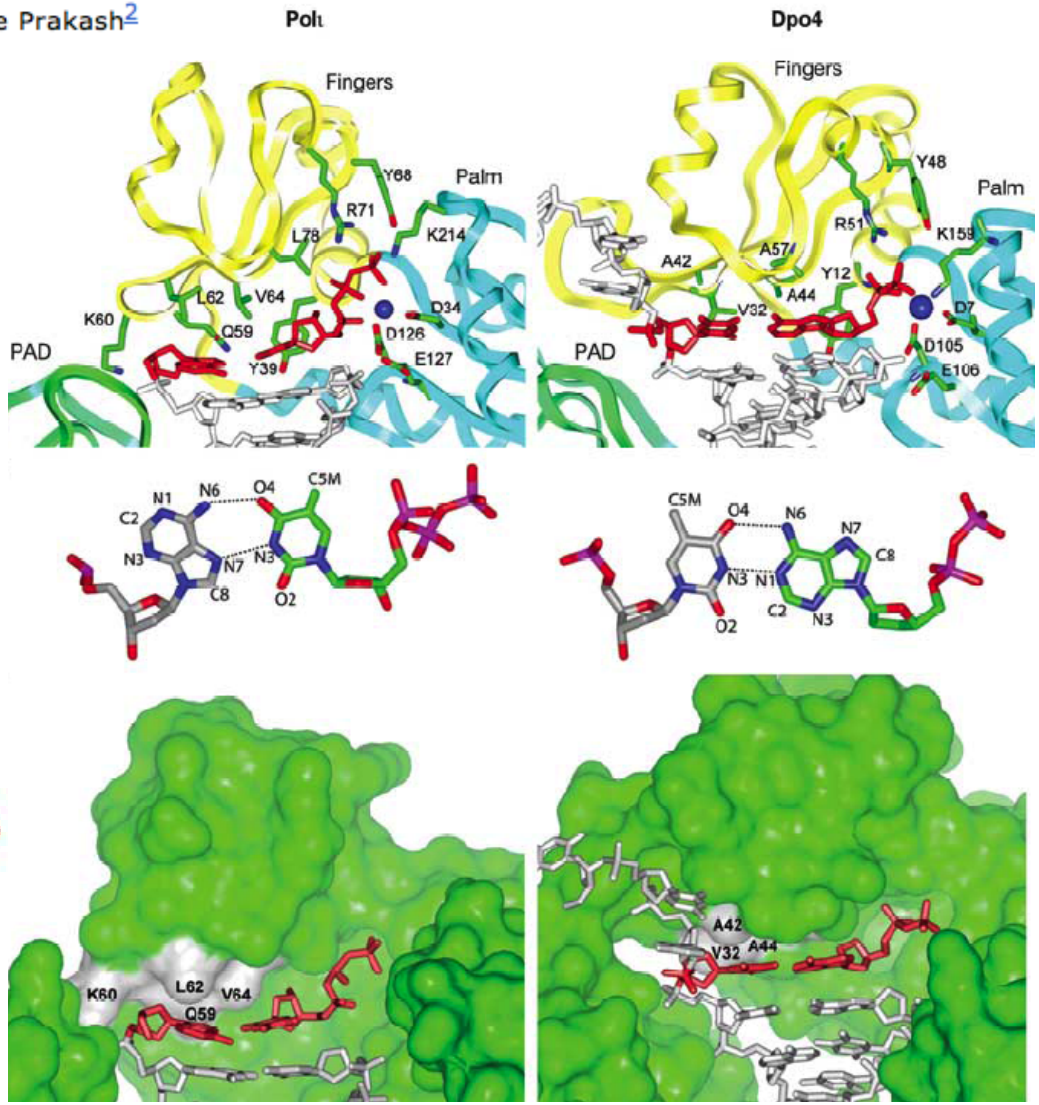
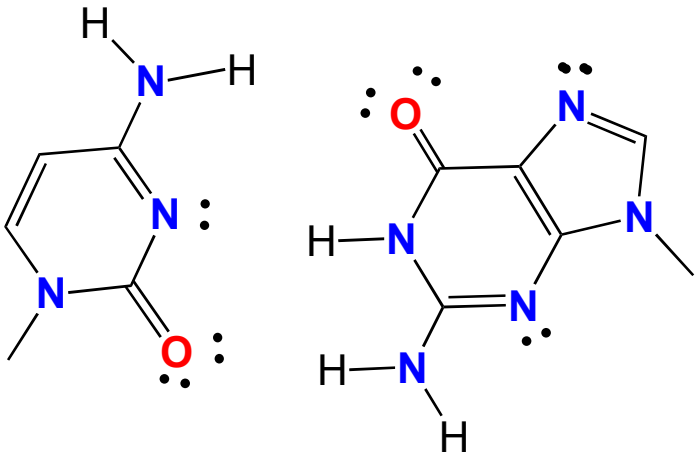


# Why is Watson-Crick so good?

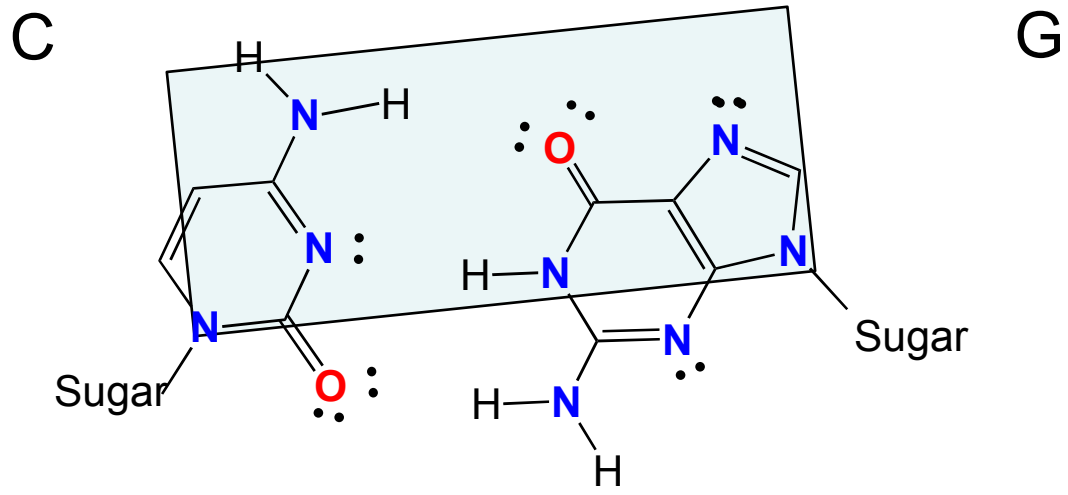
C




G

All four WC base pairs
are
***isosteric***

# Why is Watson-Crick so good?




All four WC base pairs
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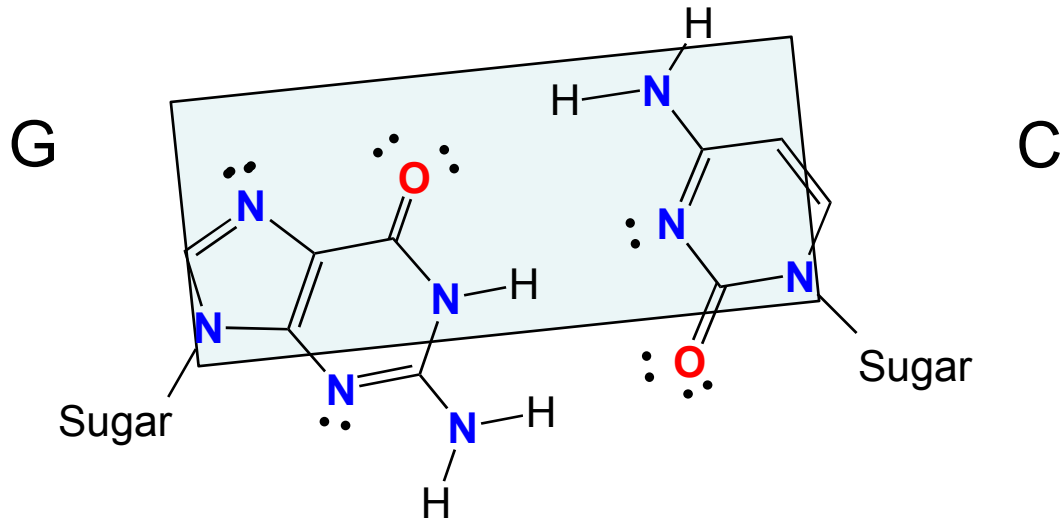


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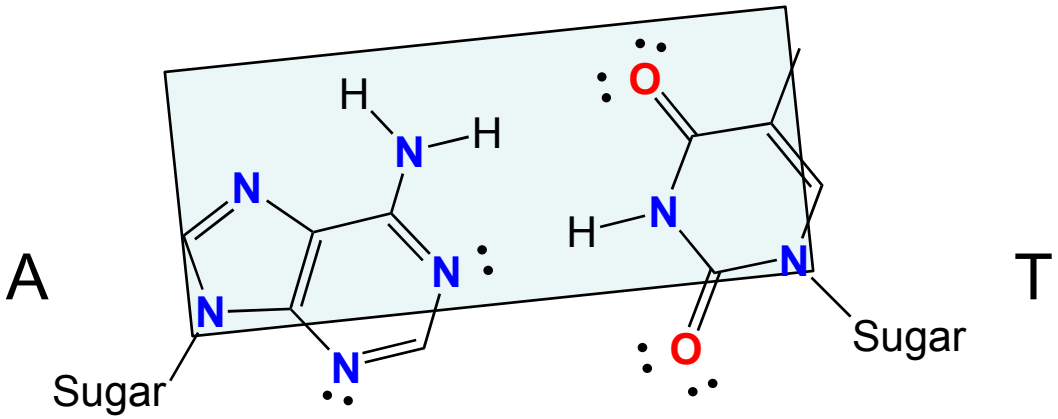


All four WC base pairs
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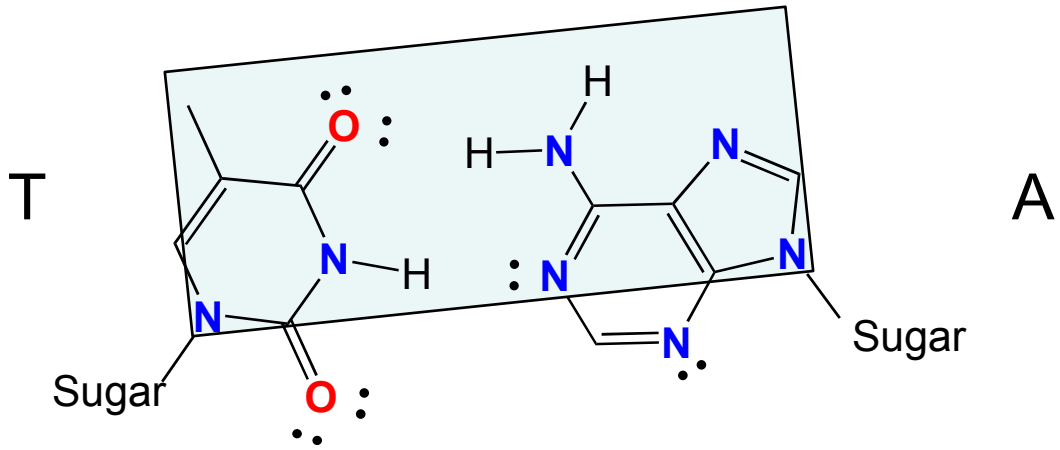
***isosteric***

# Why is Watson-Crick so good?




All four WC base pairs
are
***isosteric***

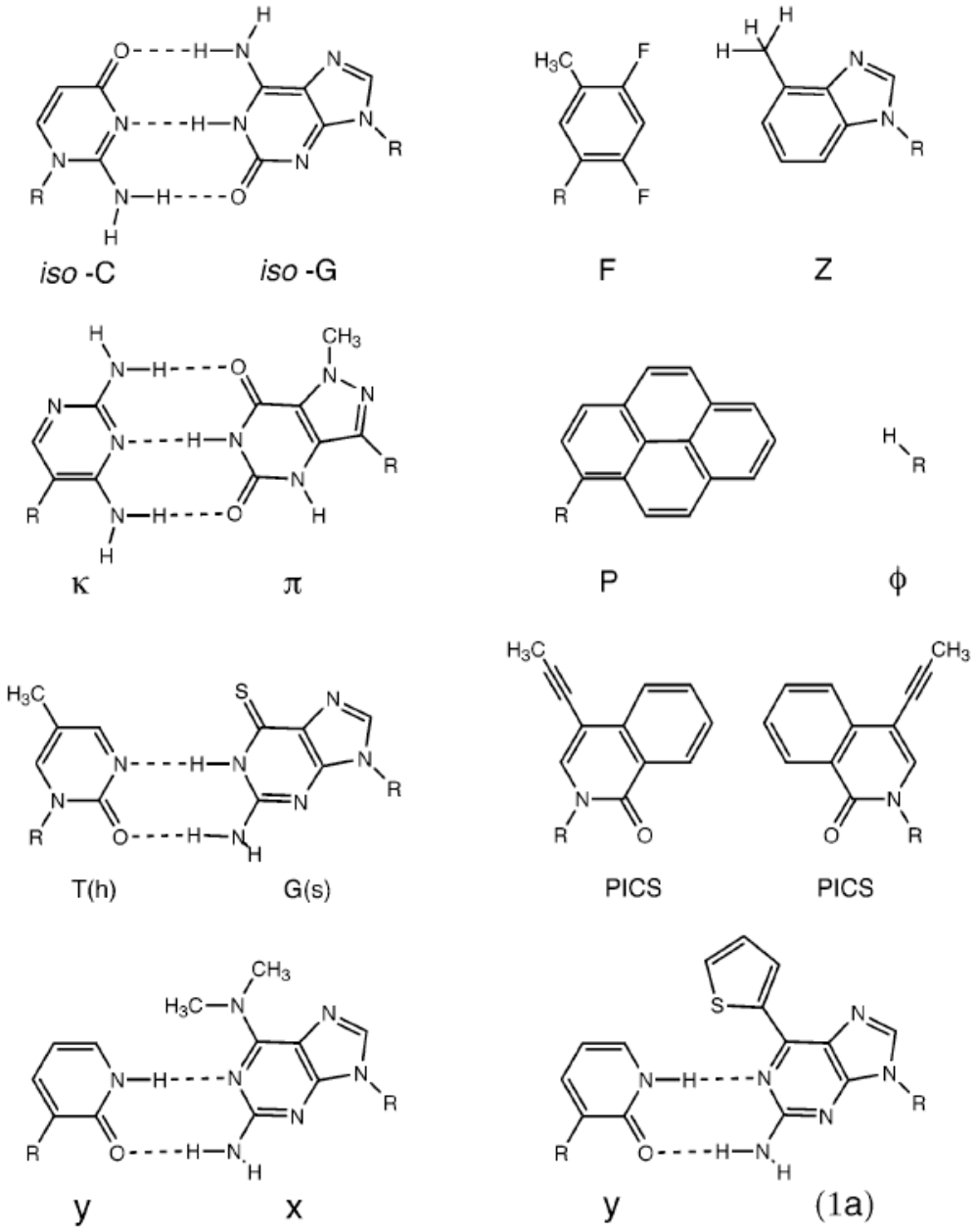
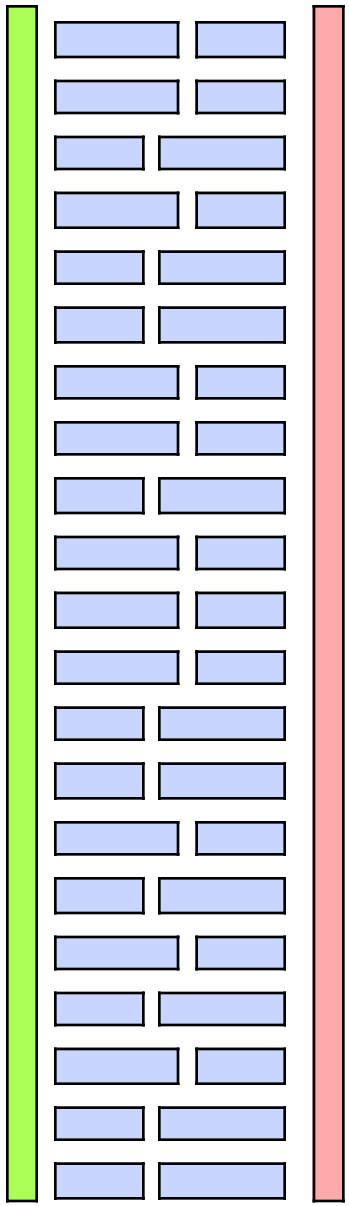
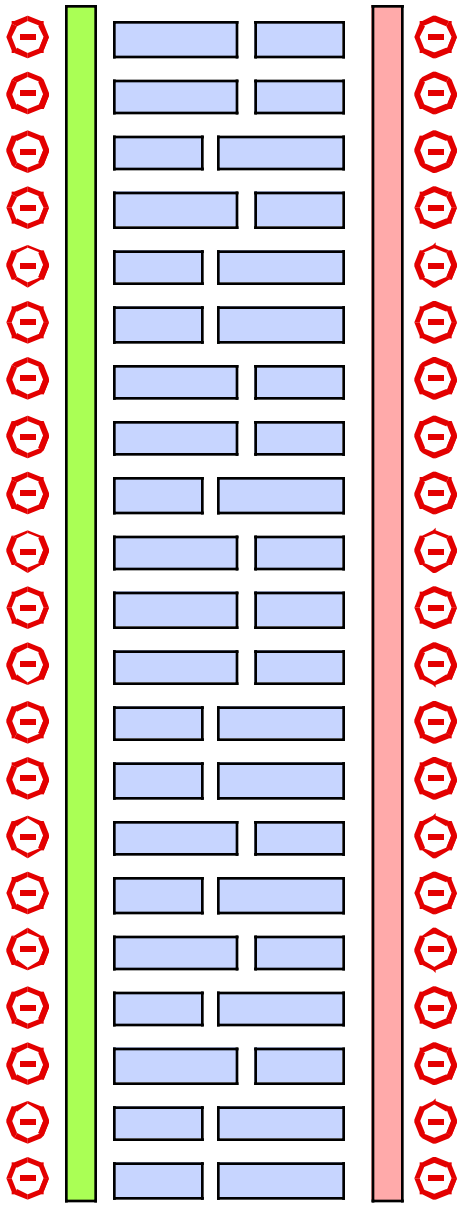



**FIGURE 7.** Examples of DNA base replacements designed to form stable pairs and/or to be replicated selectively by DNA polymerase enzymes.[17,23,24,49,54,55]

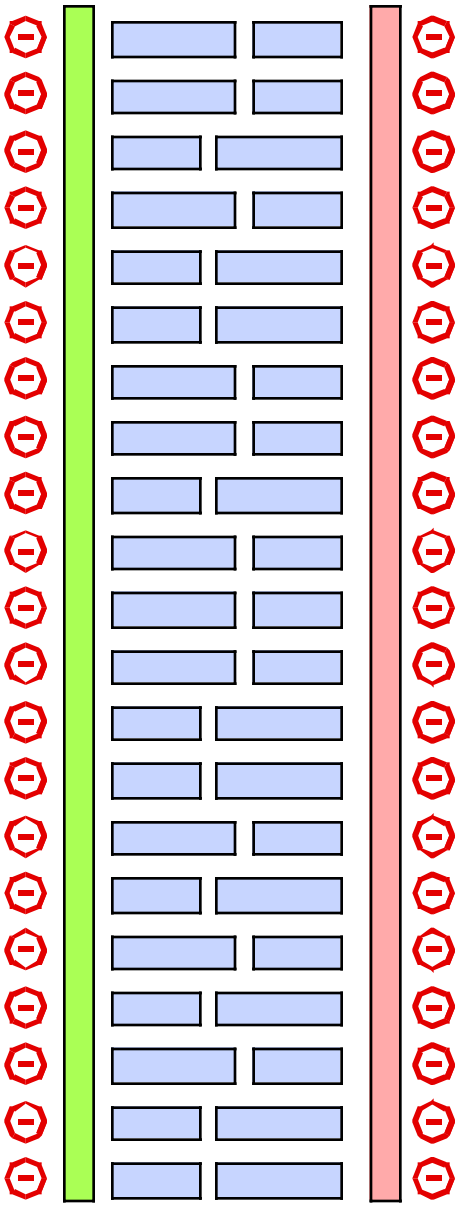
# Bases that polymerases like

# Why ***a helix***?

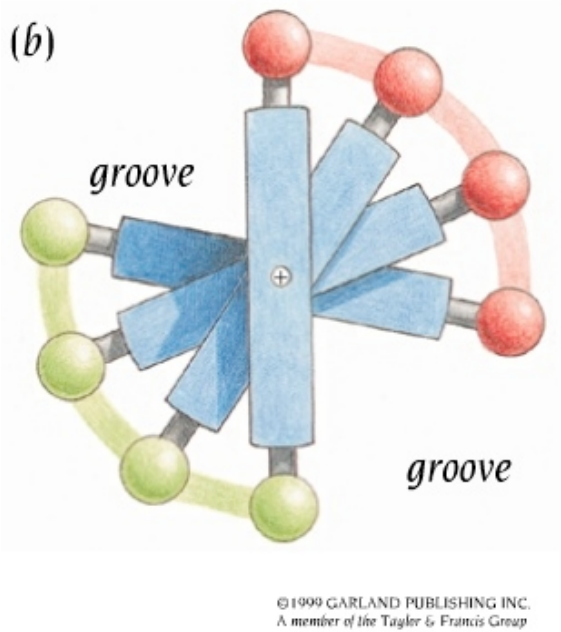




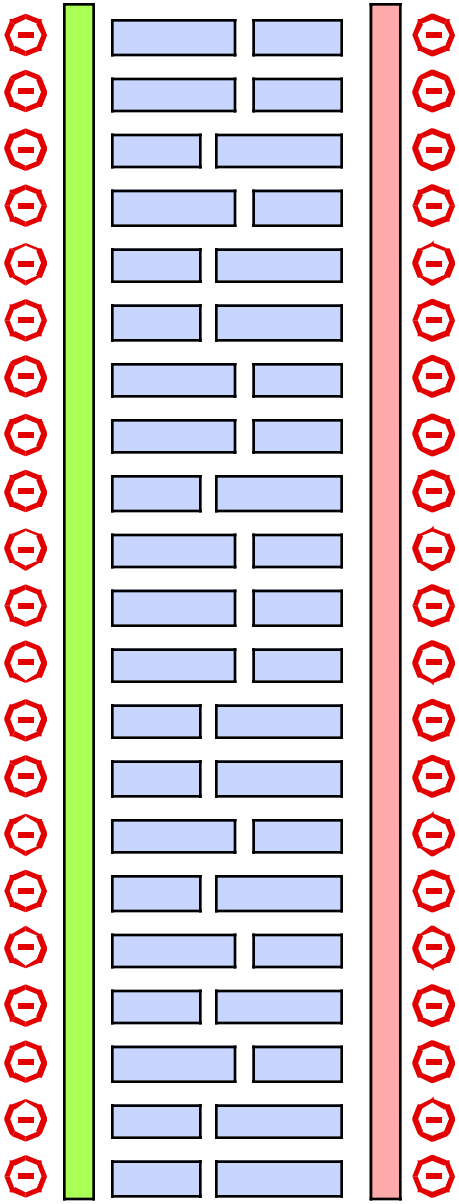
# Why ***a helix***?

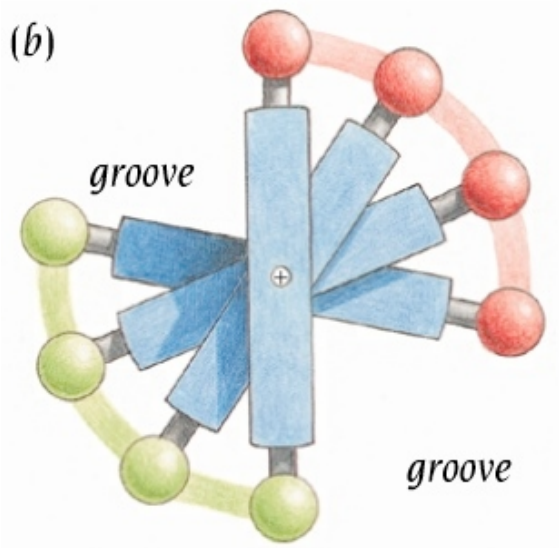


# Why ***a helix***?

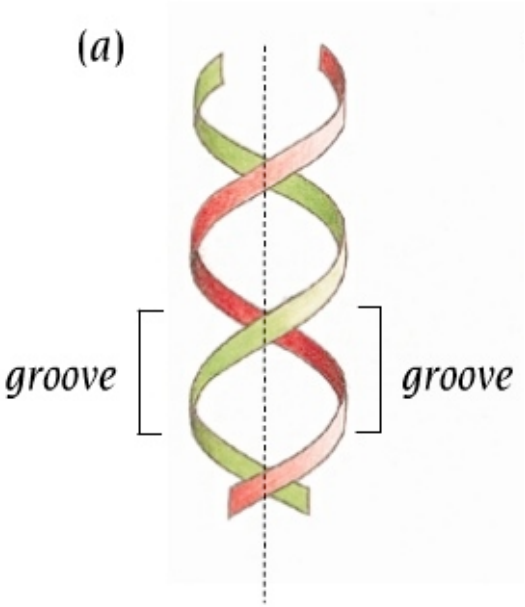


# Why ***a helix***?

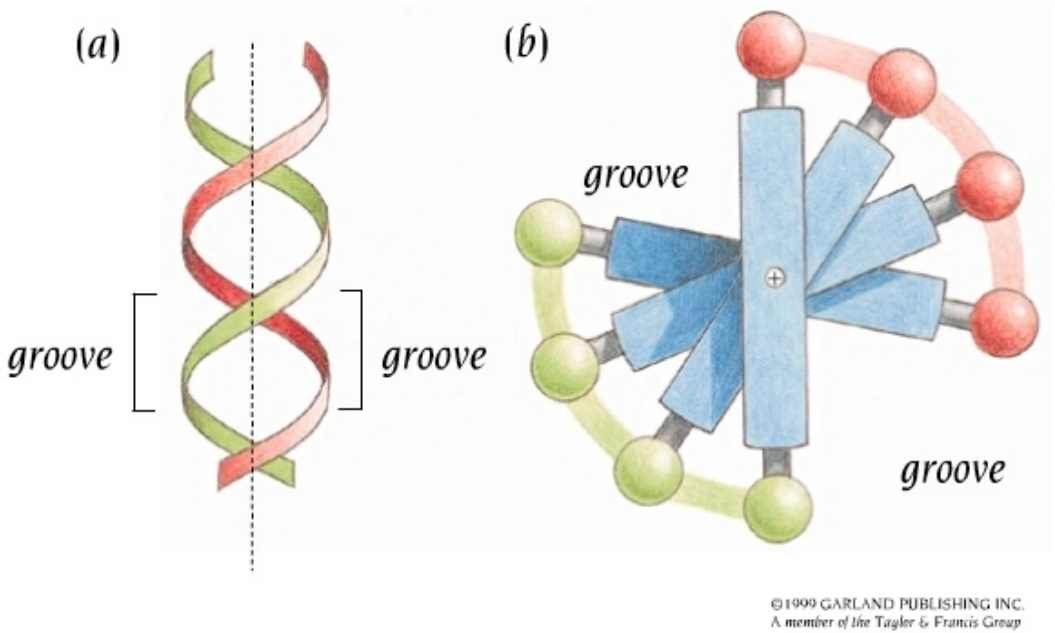




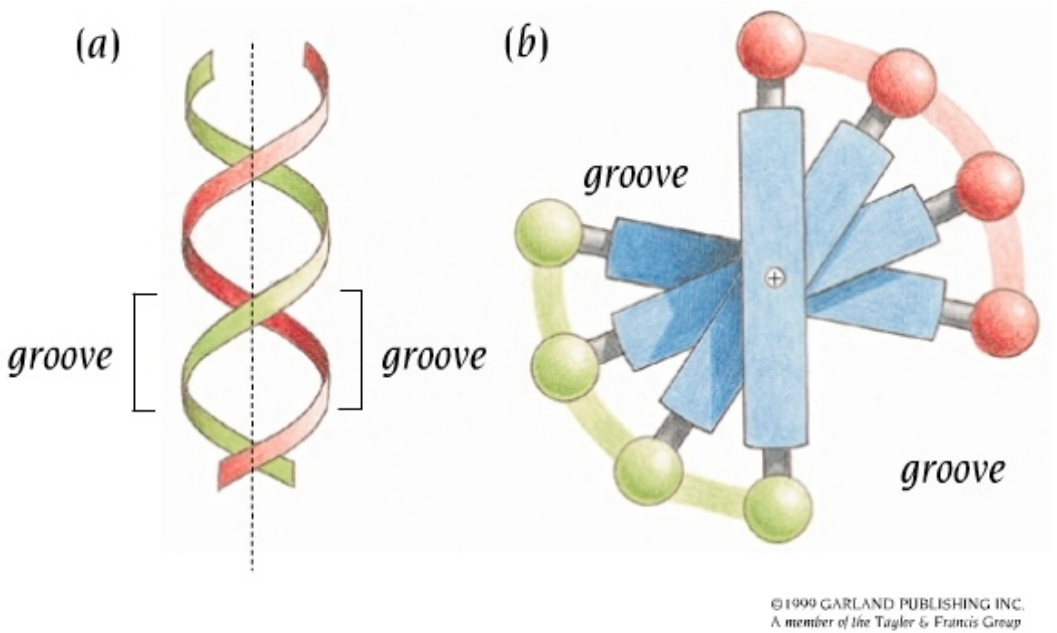


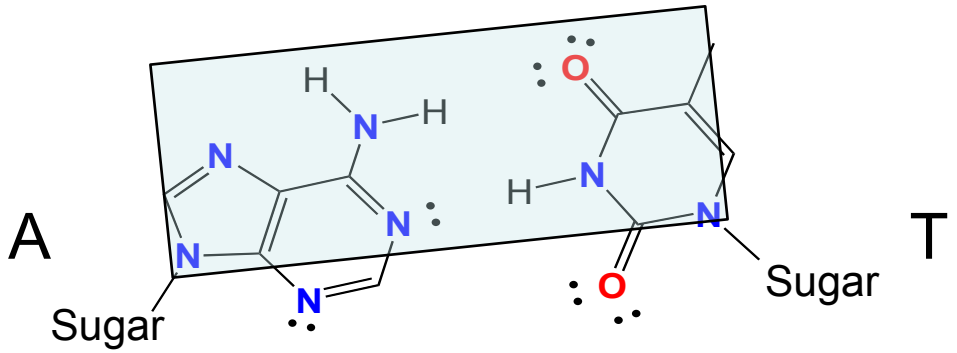
# Why ***major*** and ***minor*** grooves?



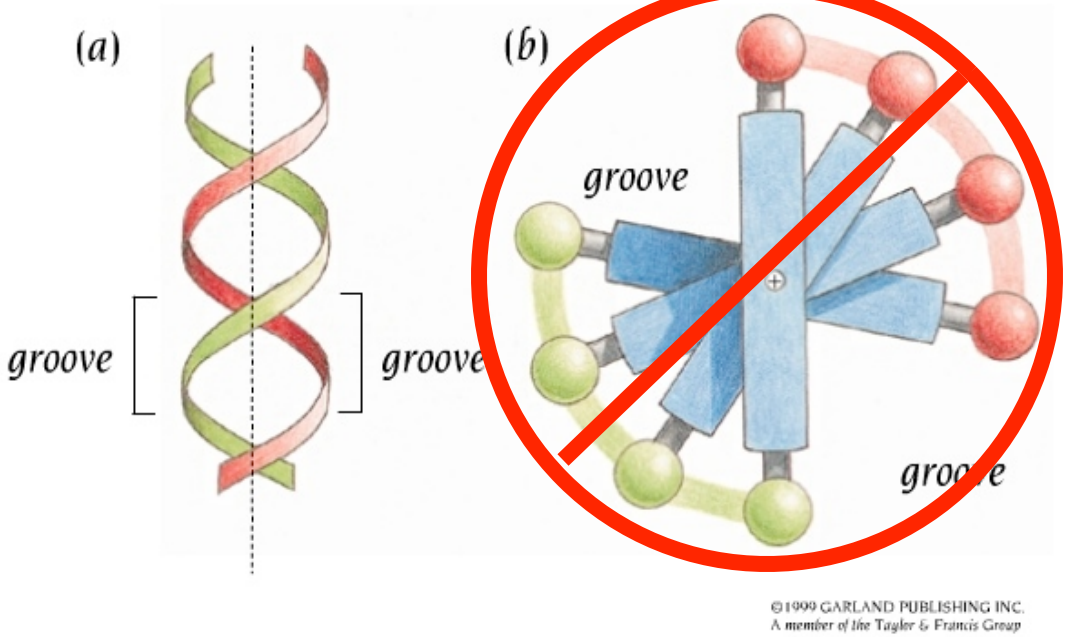
# Why ***major*** and ***minor*** grooves?

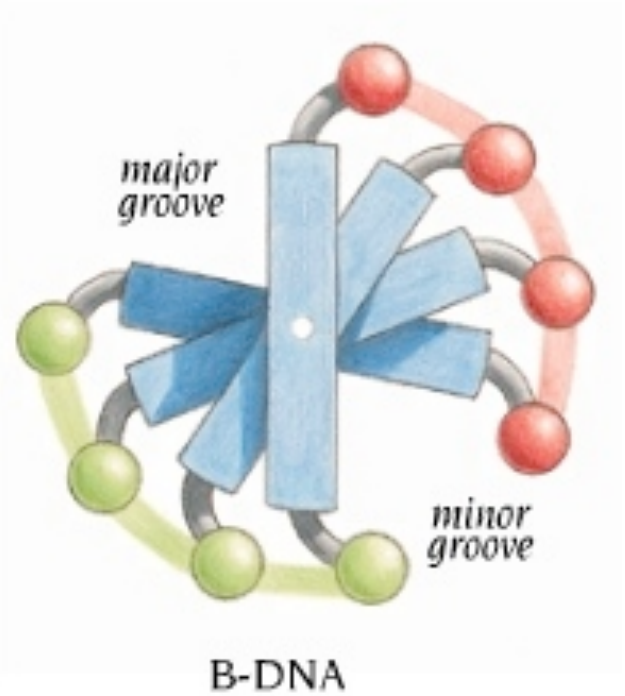


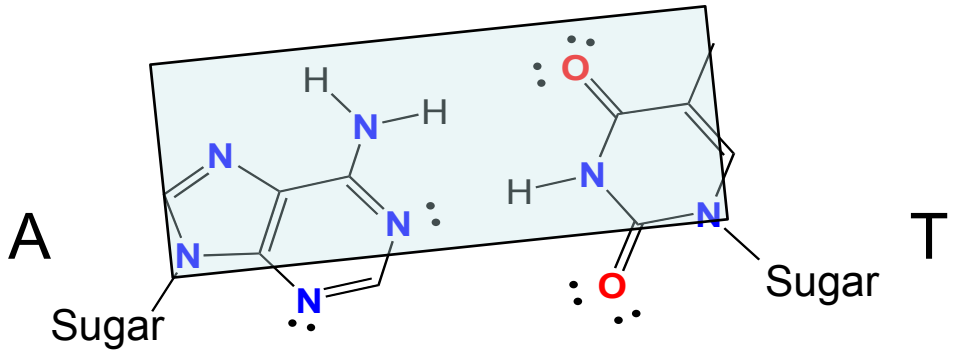


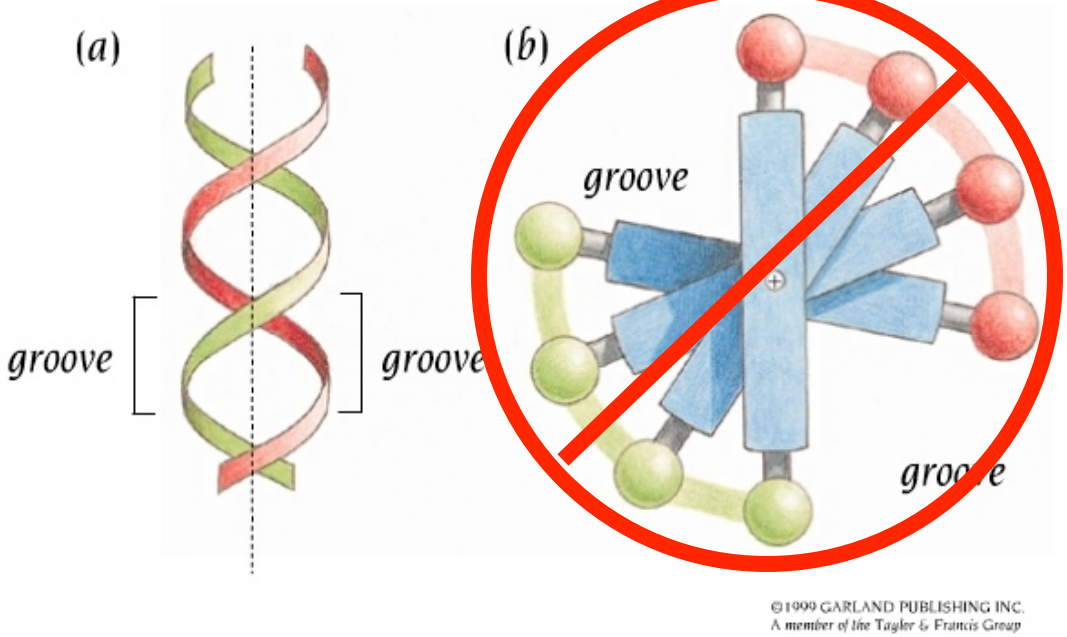
# Why ***major*** and ***minor*** grooves?

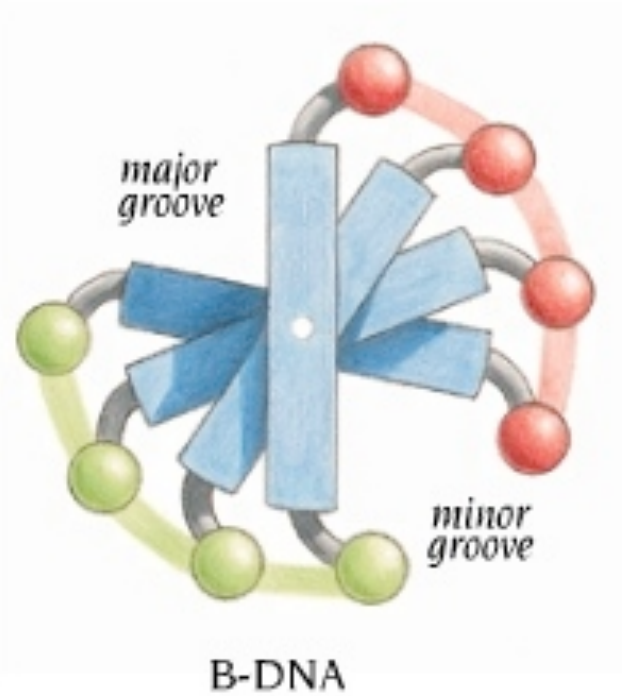


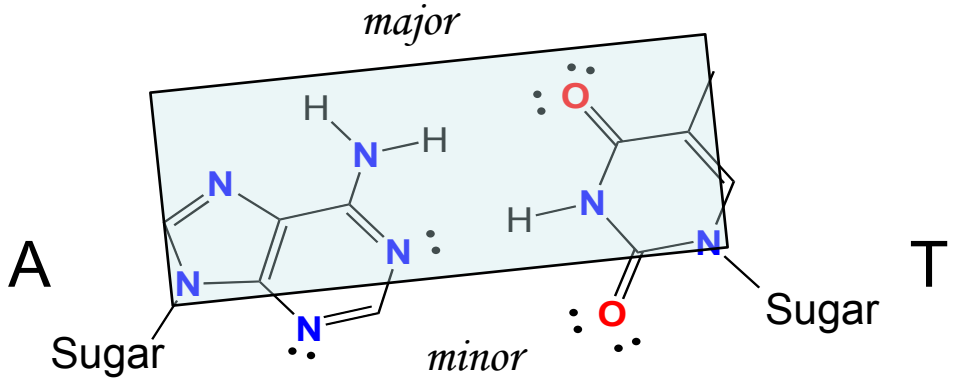



# Why ***major*** and ***minor*** grooves?



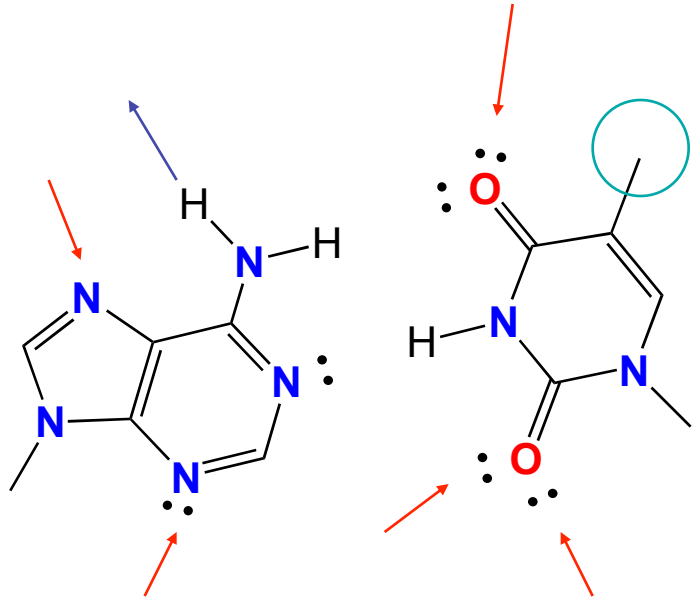



# Why is the major groove so good?

*Major Groove*

A



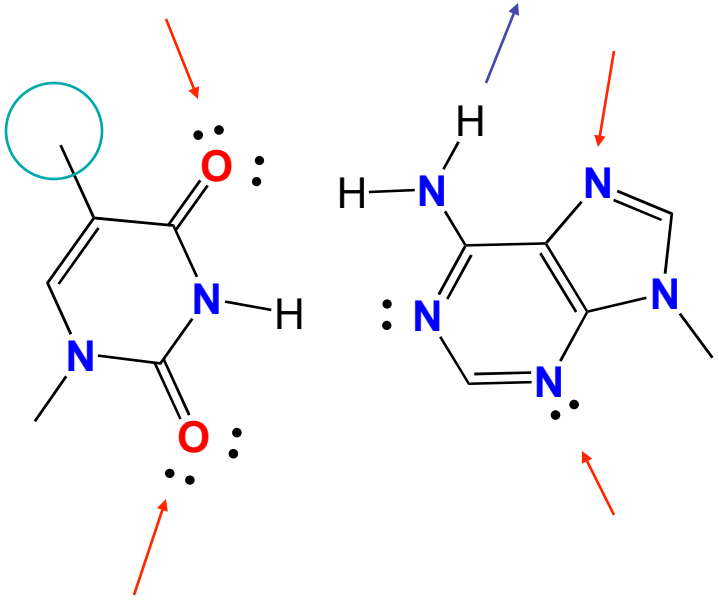

T

*Minor Groove*

# Why is the major groove so good?

*Major Groove*

T



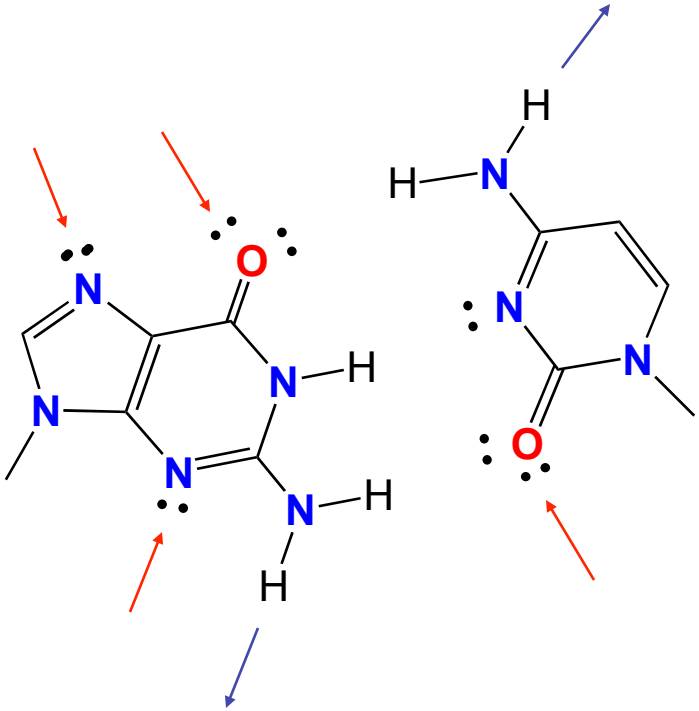

A

*Minor Groove*

# Why is the major groove so good?

*Major Groove*

G

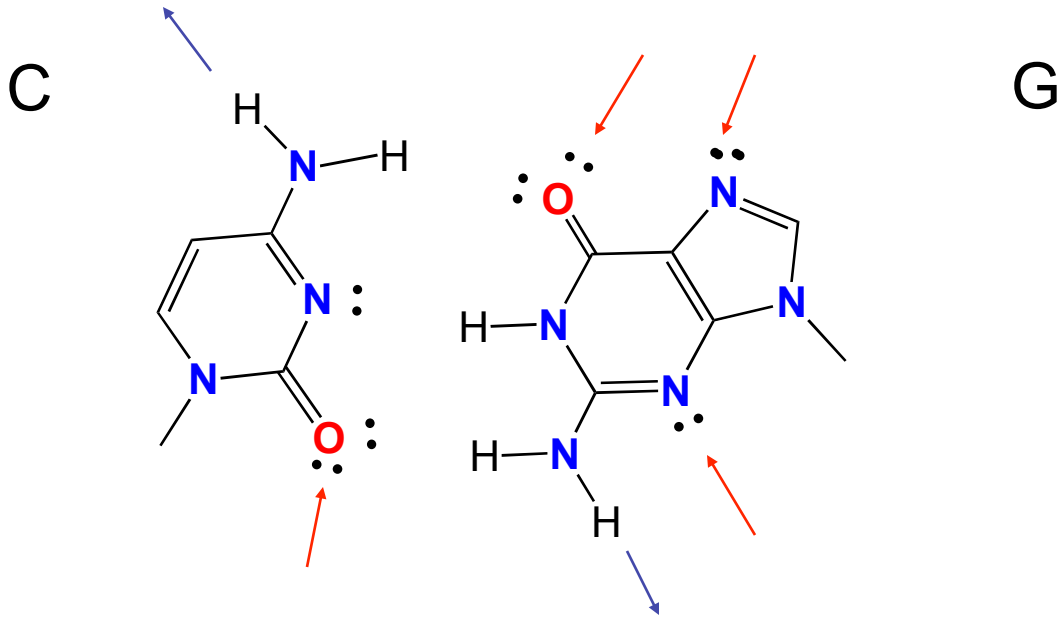



C

*Minor Groove*

# Why is the major groove so good?

*Major Groove*




*Minor Groove*

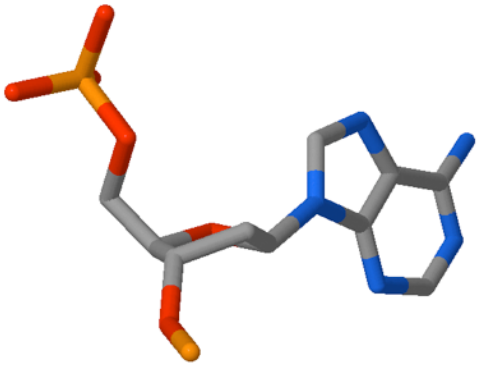
# B-form DNA

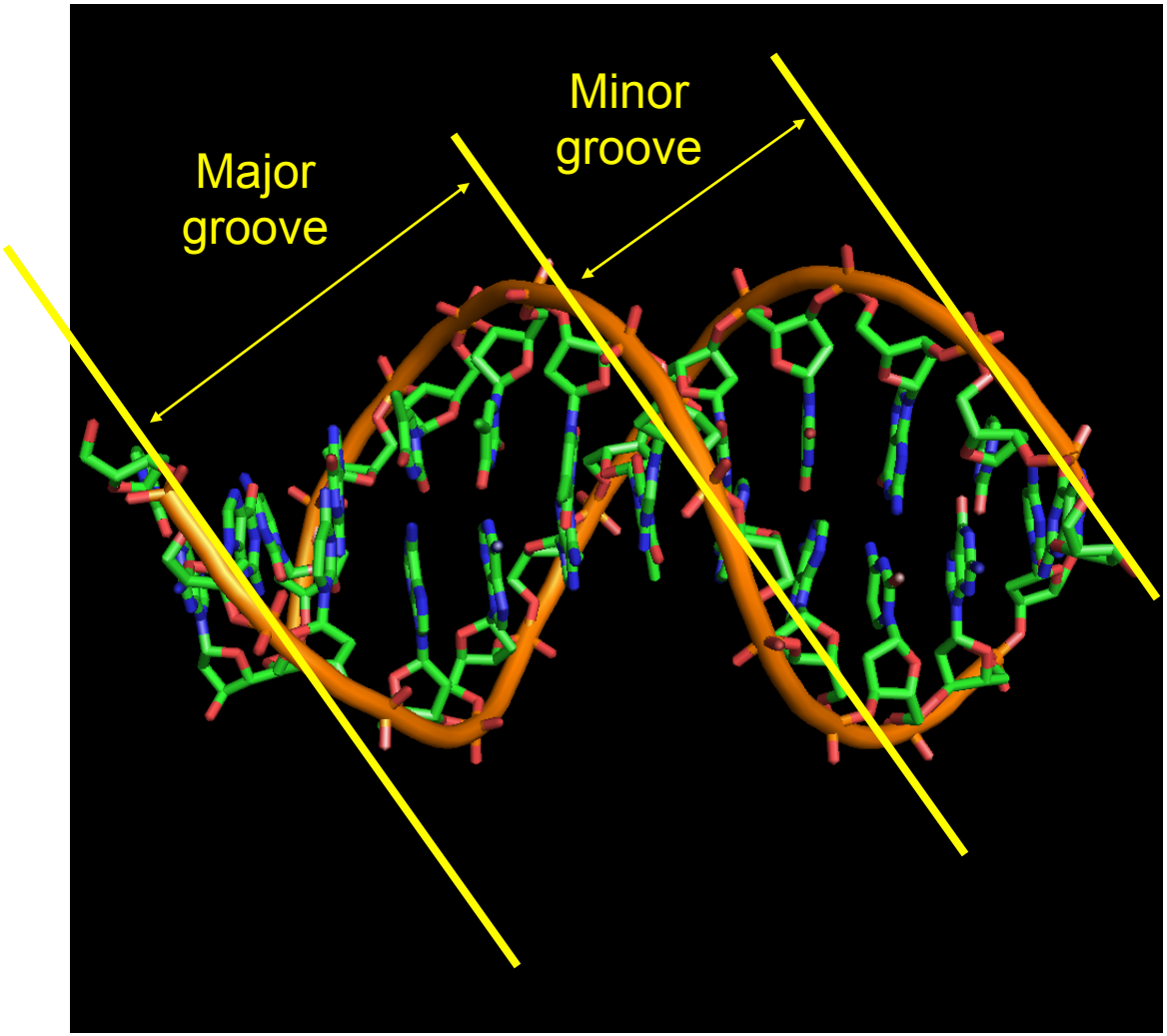
B-form

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

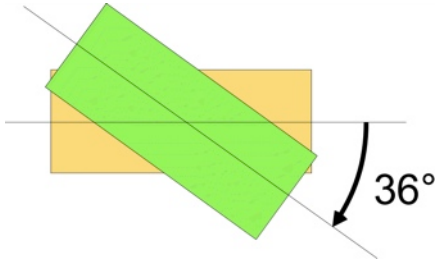
Minor groove depth = 7.5Å
Major groove depth = 8.8Å





# B-form DNA

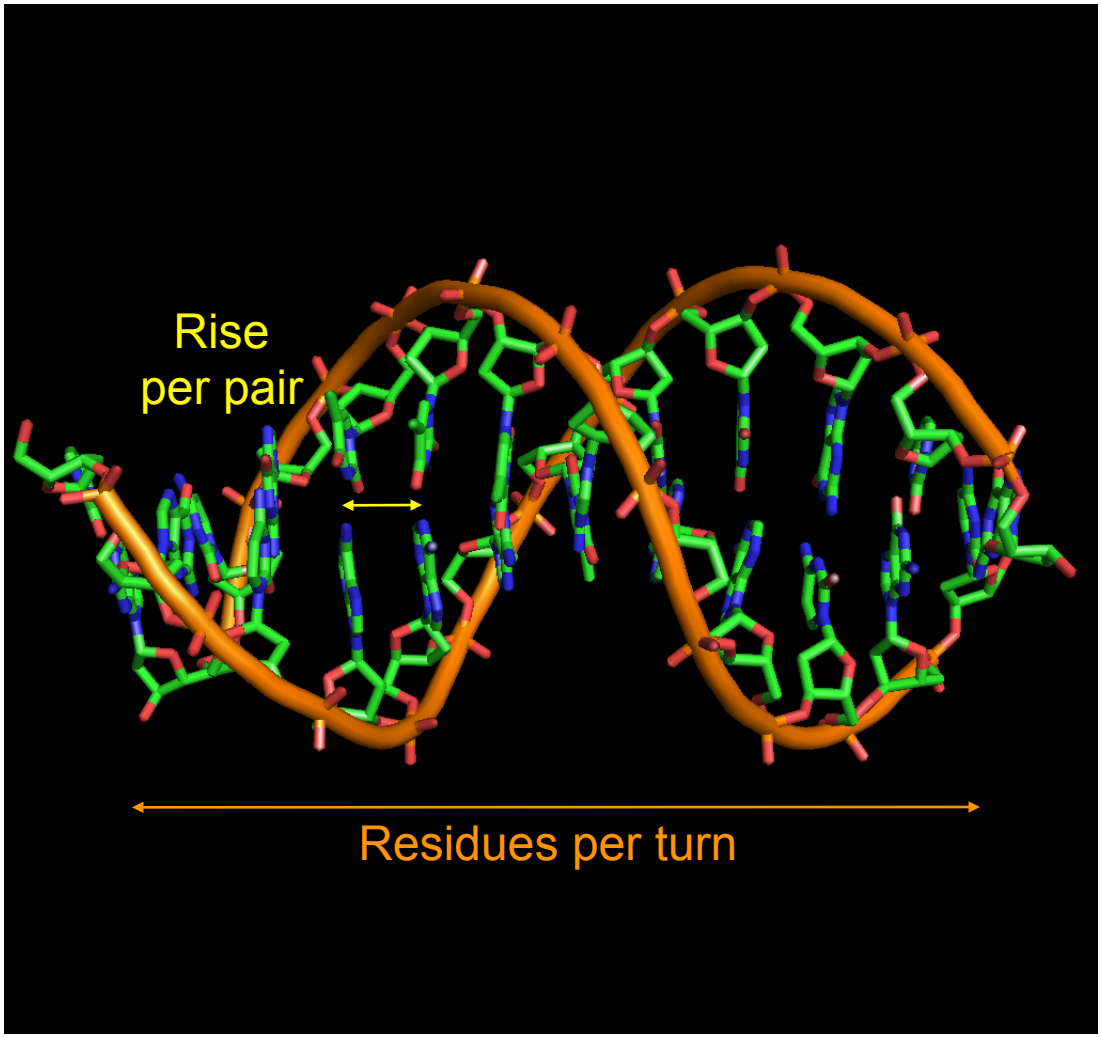
Residues per turn =10
Twist per base pair = 36°




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

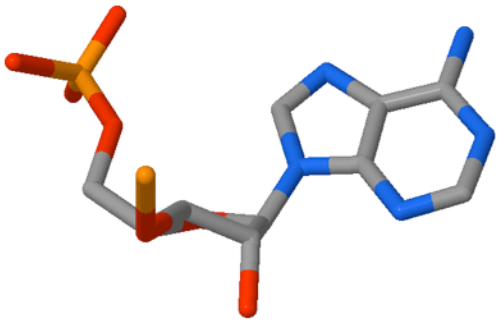


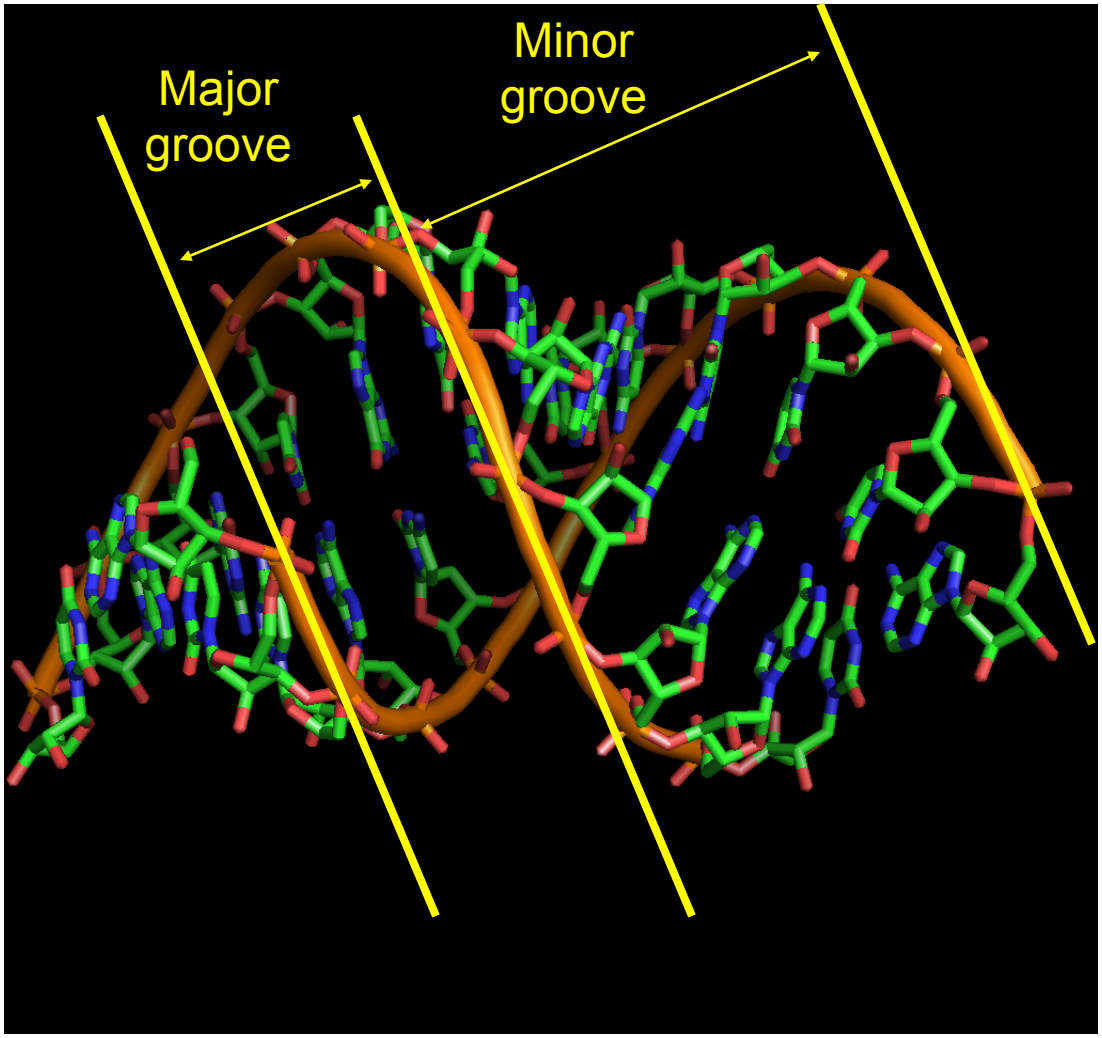
# A-form RNA

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

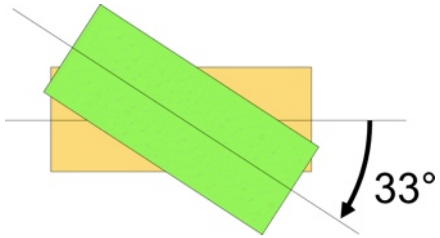
Minor groove depth = 2.8Å
Major groove depth = 13.5Å





# A-form RNA

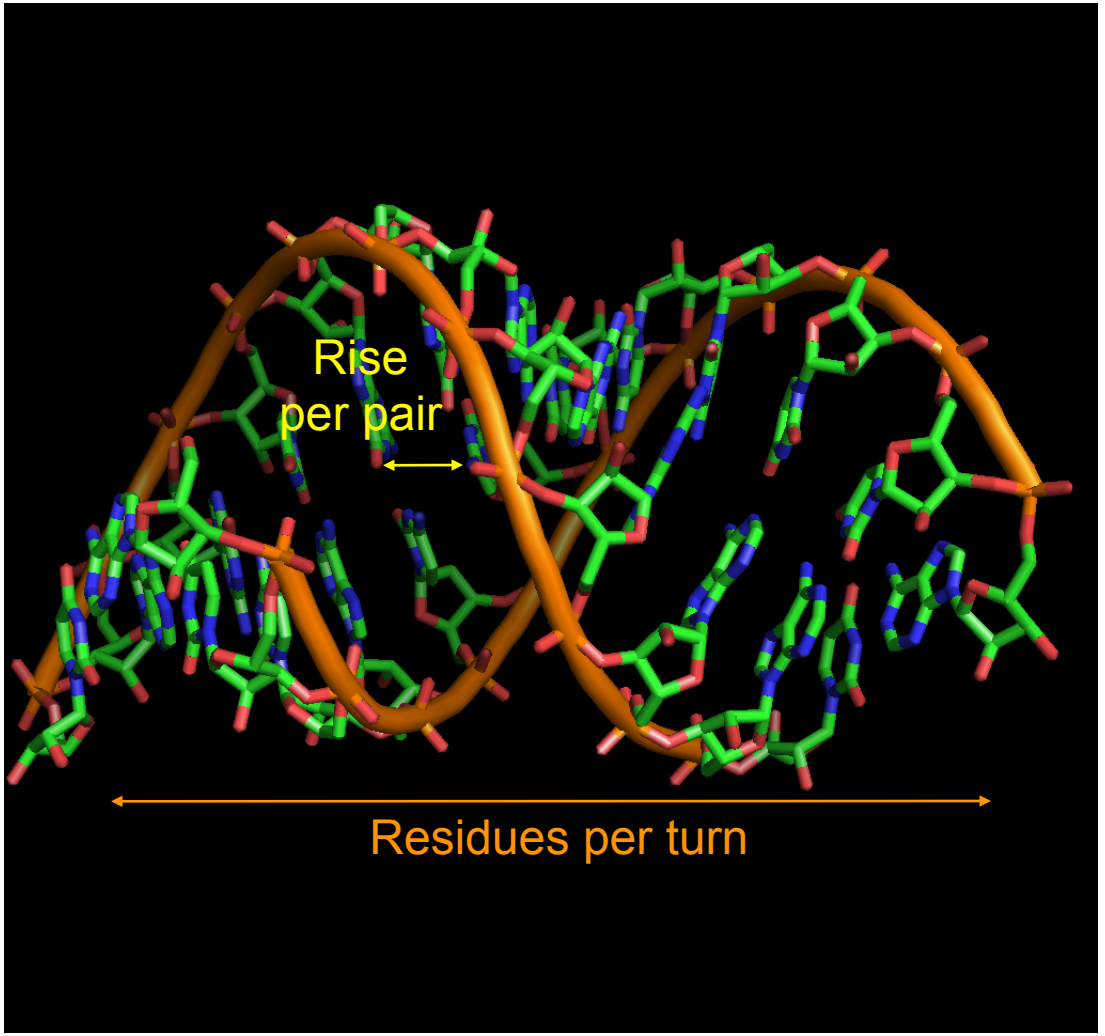
Residues per turn =11
Twist per base pair = 33°



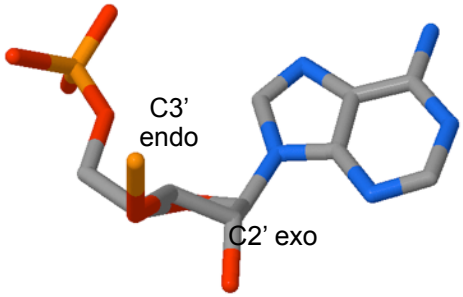

Rise per pair = 2.9Å
c3'-endo

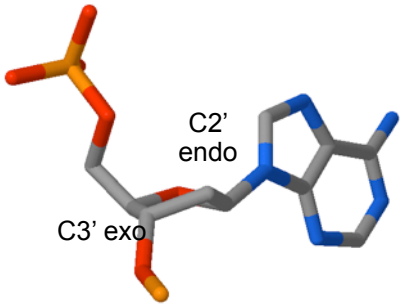
Minor groove width = 11Å
Major groove width = 2.7Å

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



# Compare




## A-form (RNA)

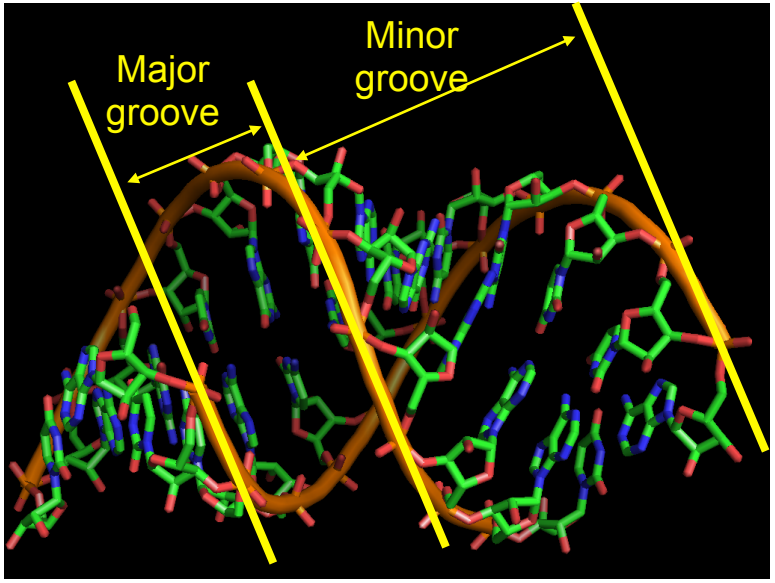
Minor groove width = 11Å
Major groove width = 2.7Å

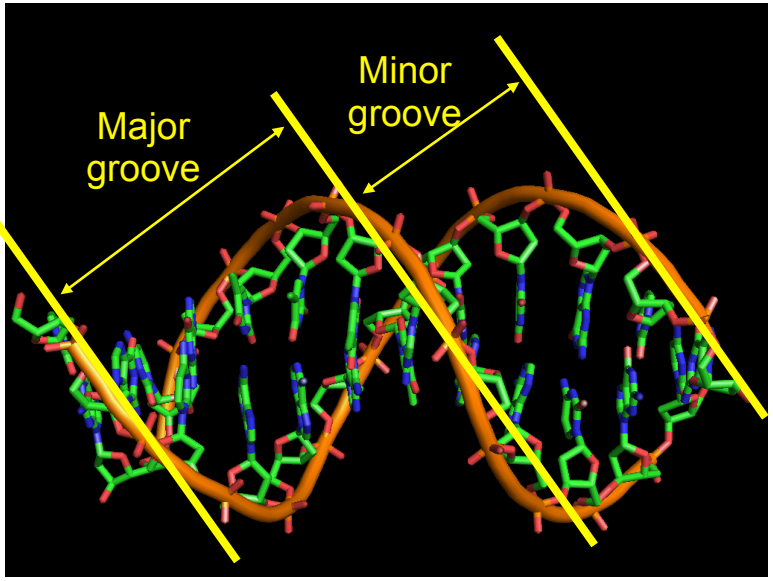
Minor groove depth = 2.8Å
Major groove depth = 13.5Å

## B-form (DNA)

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

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



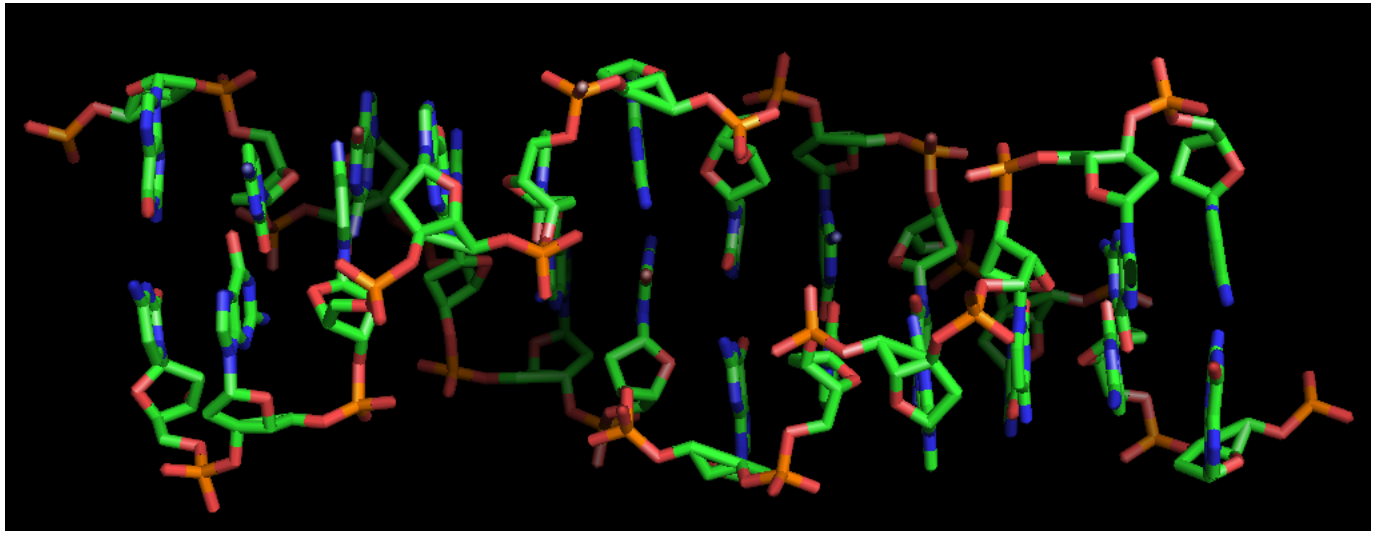
# Z-DNA

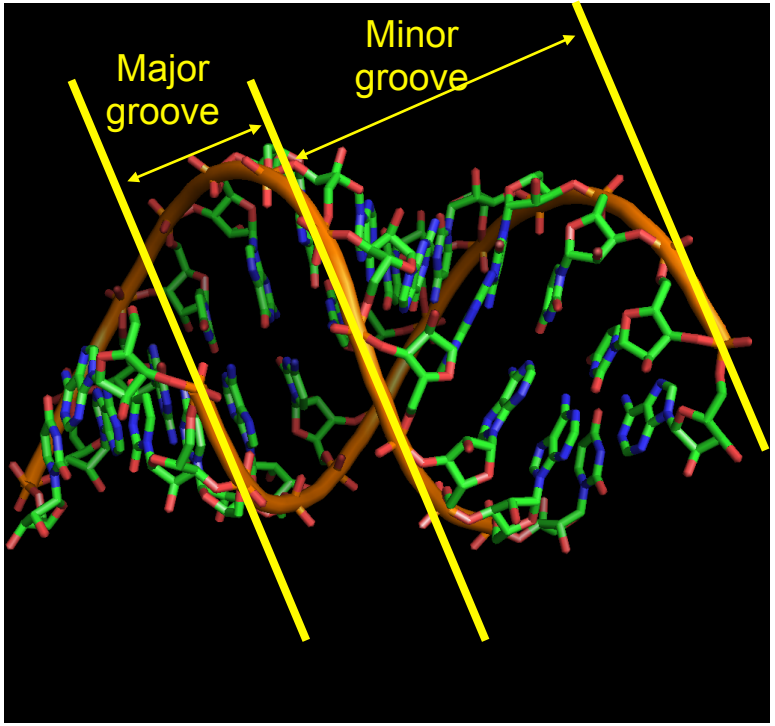
Residues per turn =12
Twist per base pair = -9 / -51°

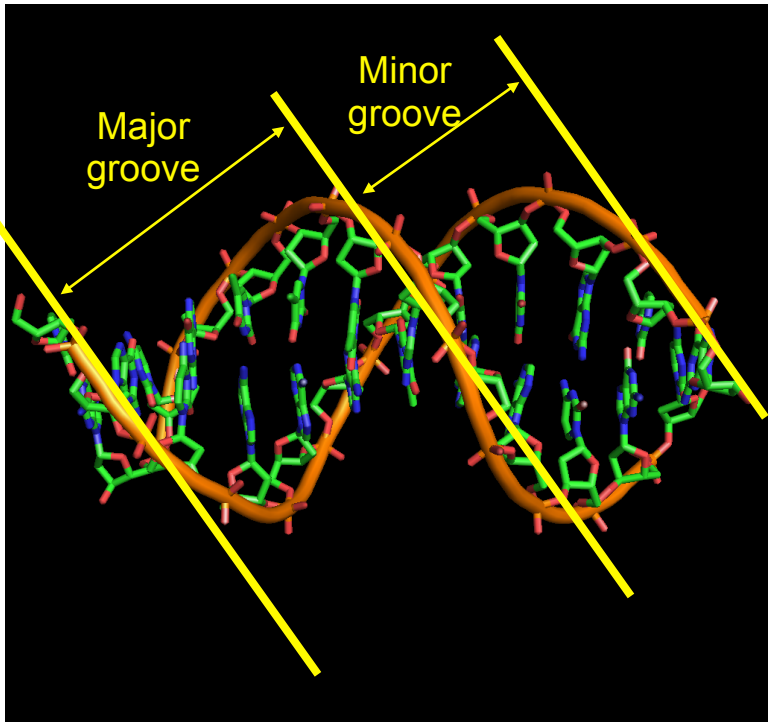
Rise per pair = 3.7Å
c3'-endo(syn) / c2'-endo

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

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

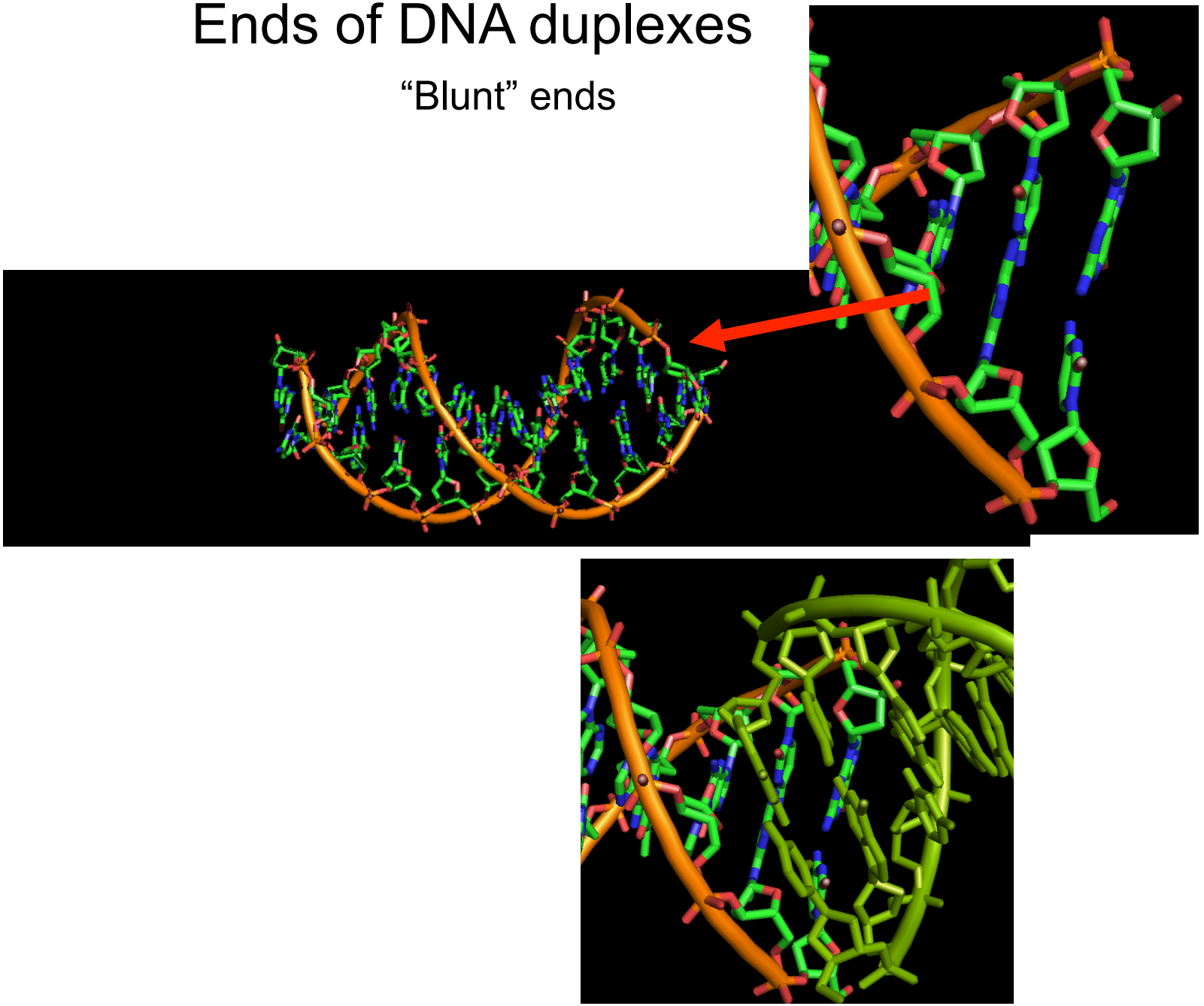




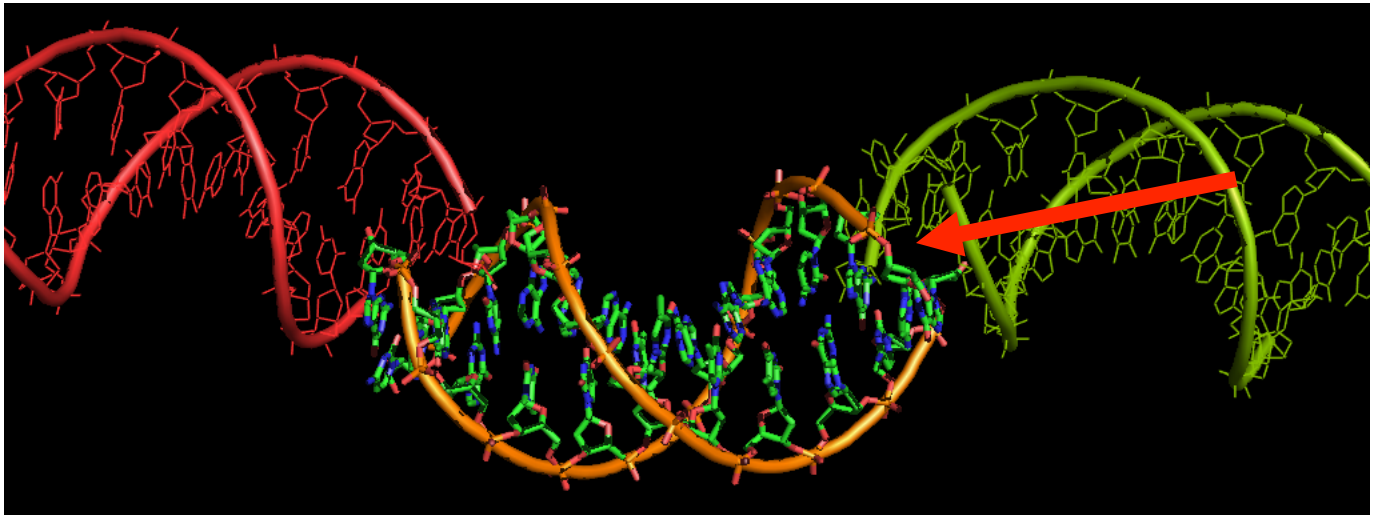
# Ends of DNA duplexes

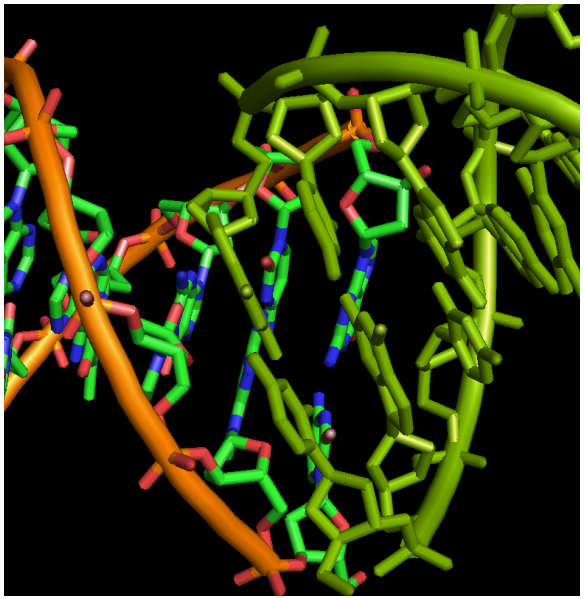
"Blunt" ends



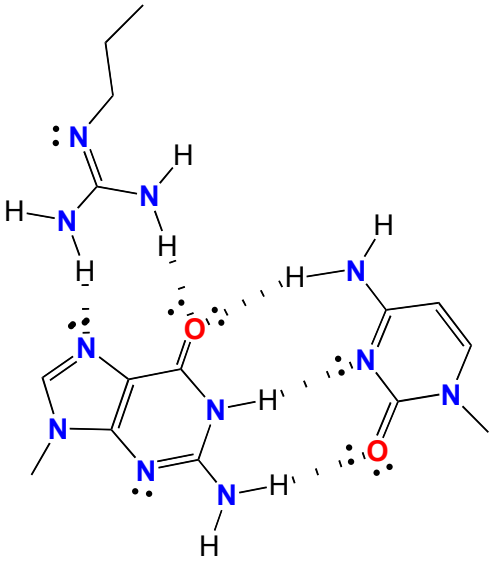
# Ends of DNA duplexes

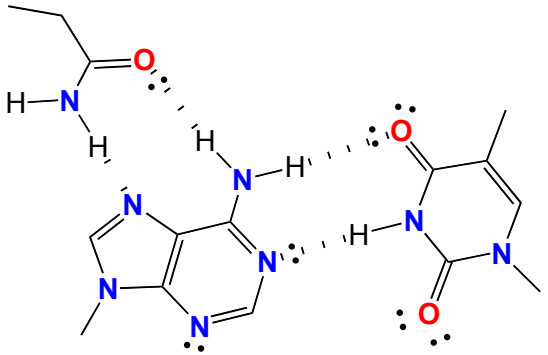
"Blunt" ends



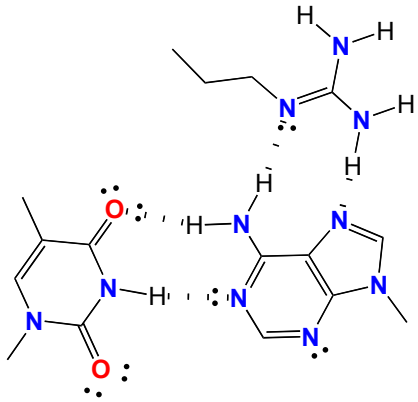


# Protein - Nucleic Acid Interactions





Major Groove Interactions

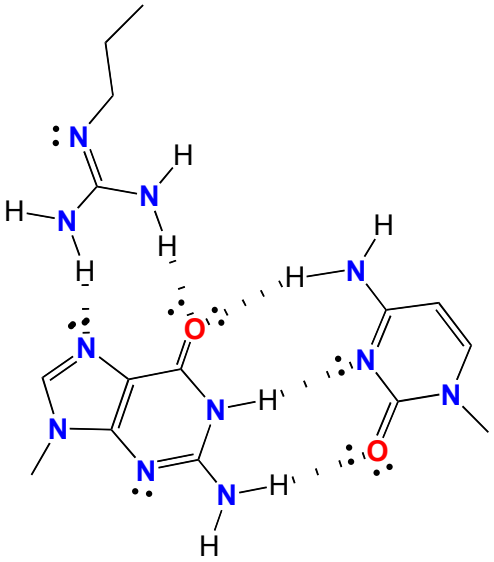


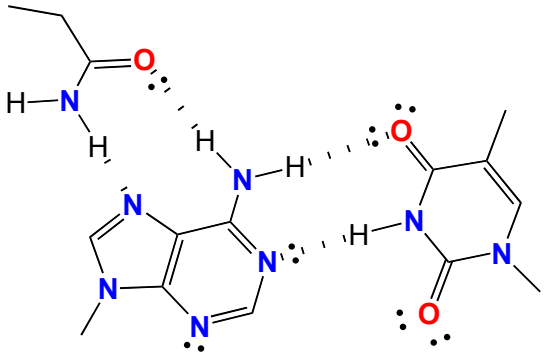
# Protein - Nucleic Acid Interactions

Gln

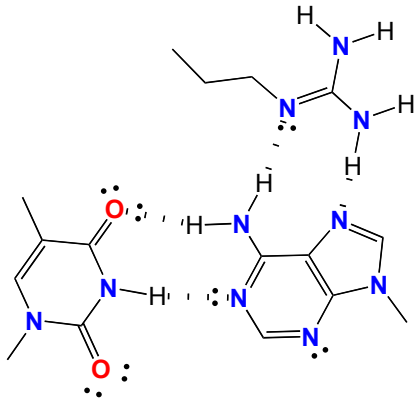
Asn

Arg

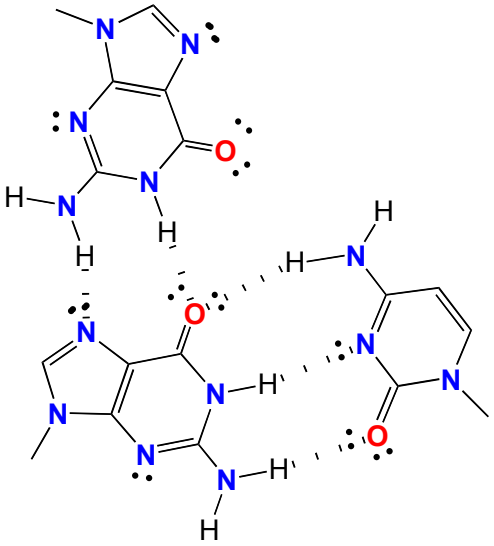


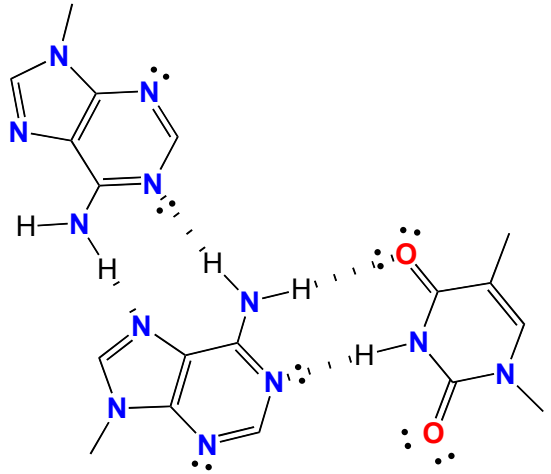


Major Groove Interactions

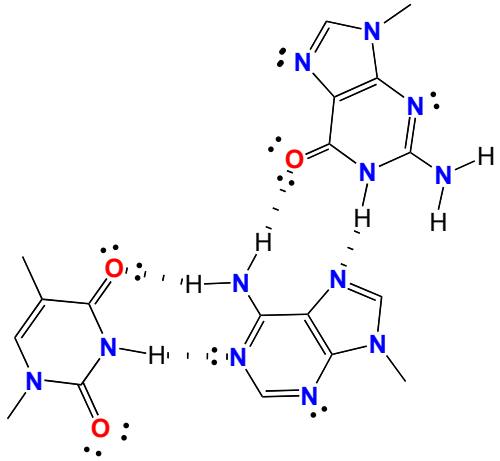


# Nucleic Acid “Triples / Platforms”



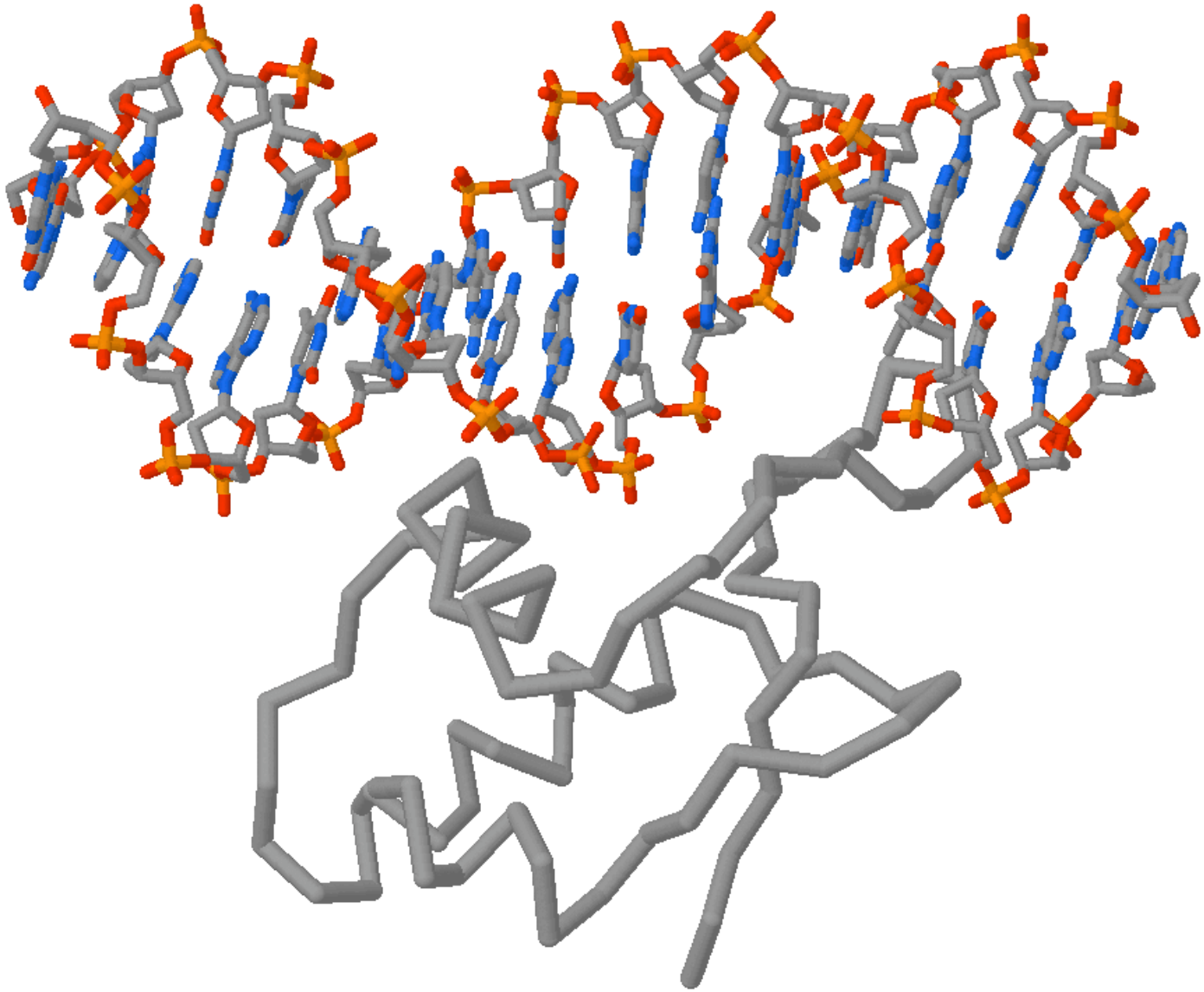


Major Groove Interactions



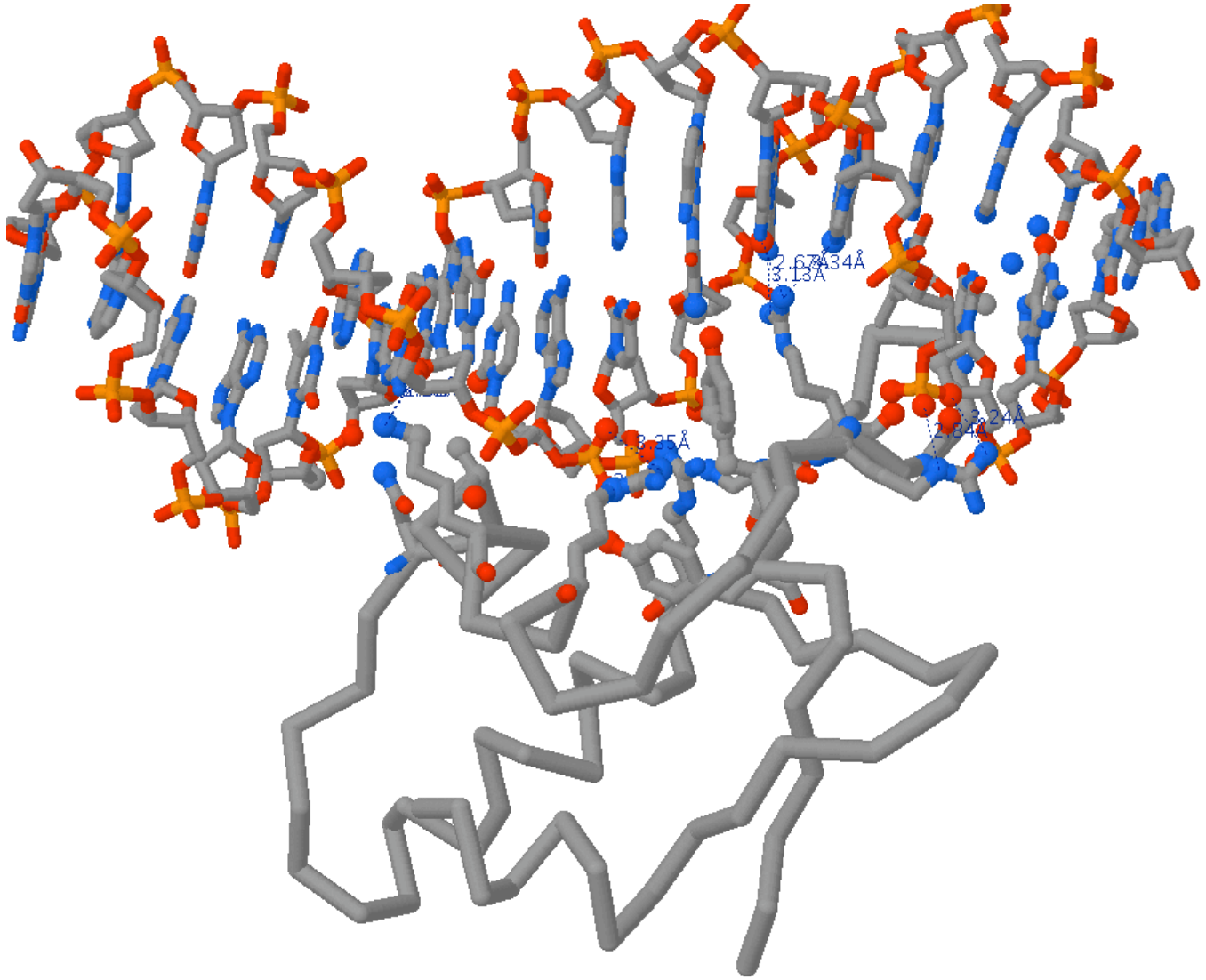
# Winged Helix DNA Binding Domain

Classic helix-turn-helix



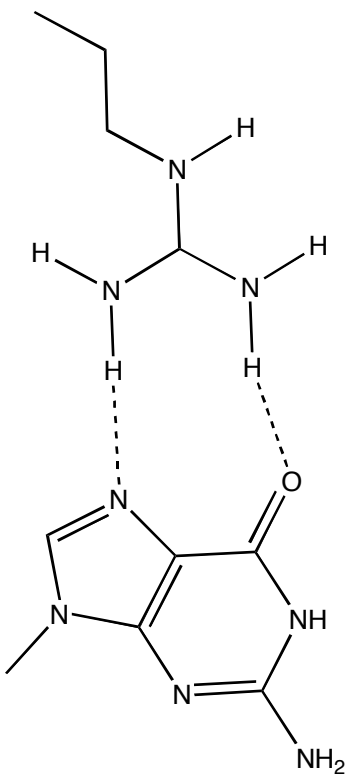
# Winged Helix DNA Binding Domain

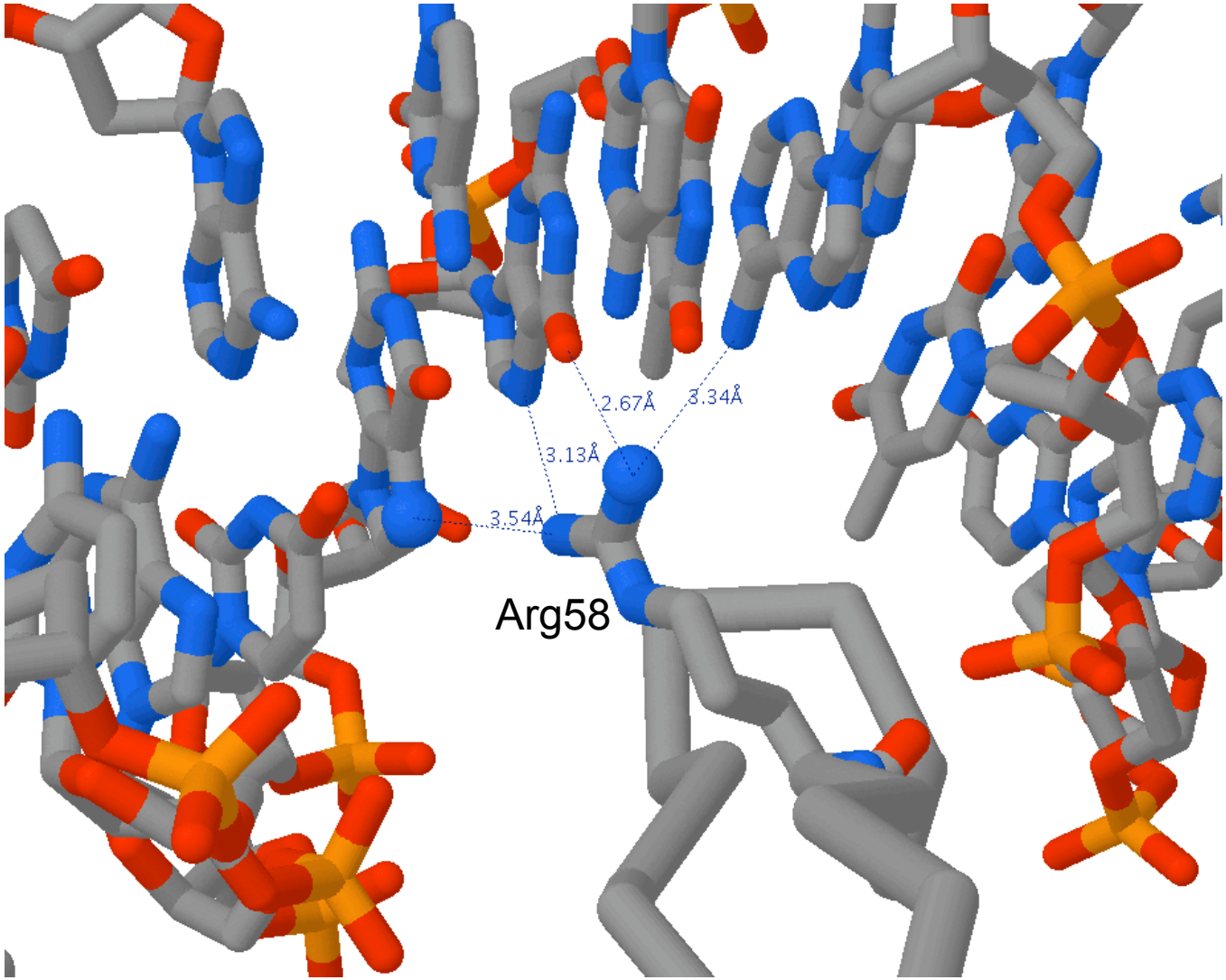
Classic helix-turn-helix



# Winged Helix DNA Binding Domain

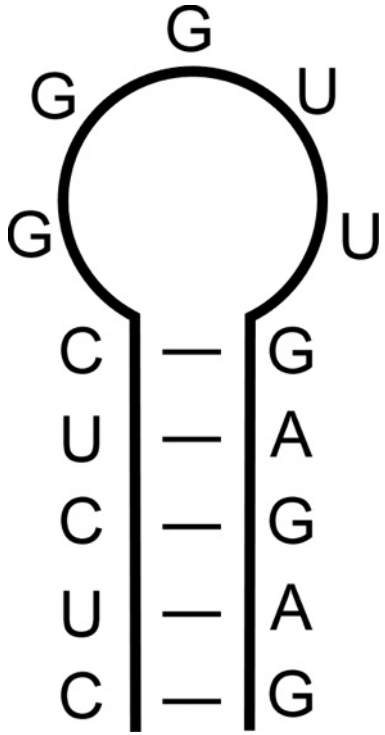
## Classic helix-turn-helix

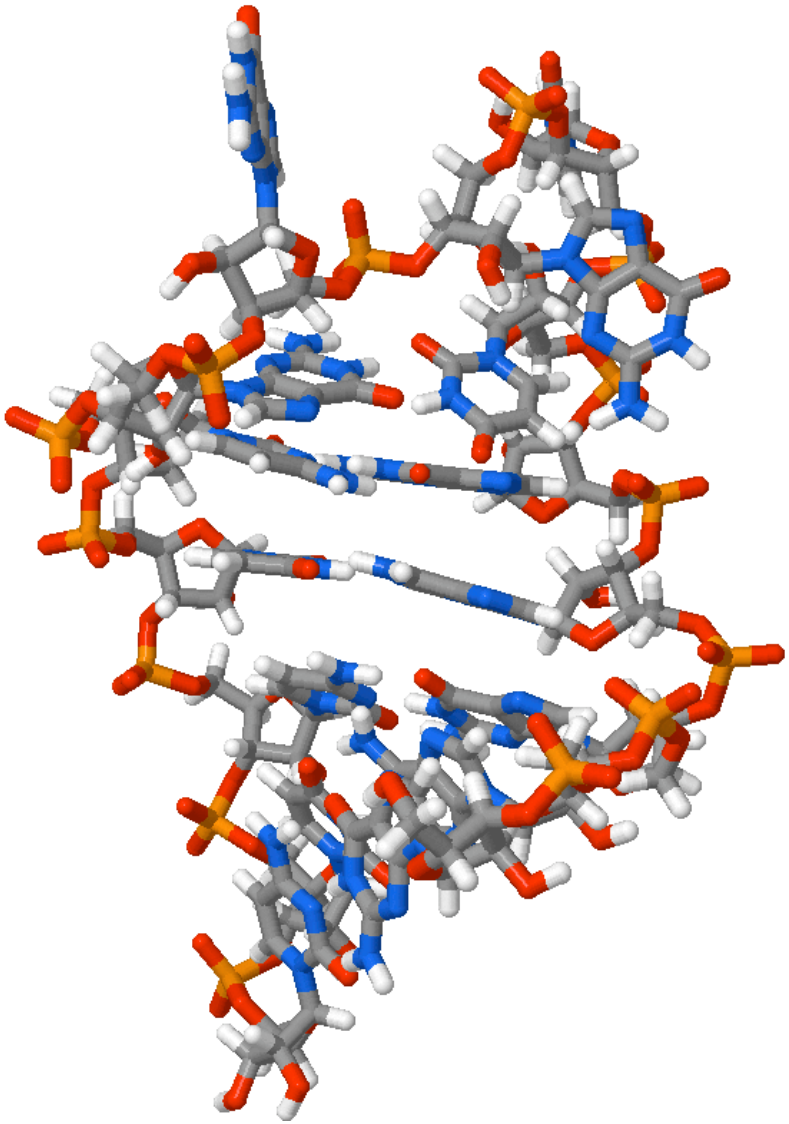


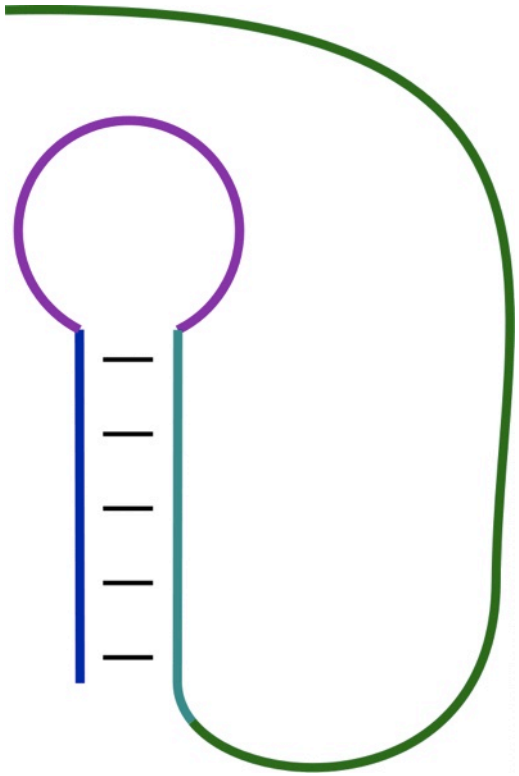

Hrfx1 bound to its X-box binding site

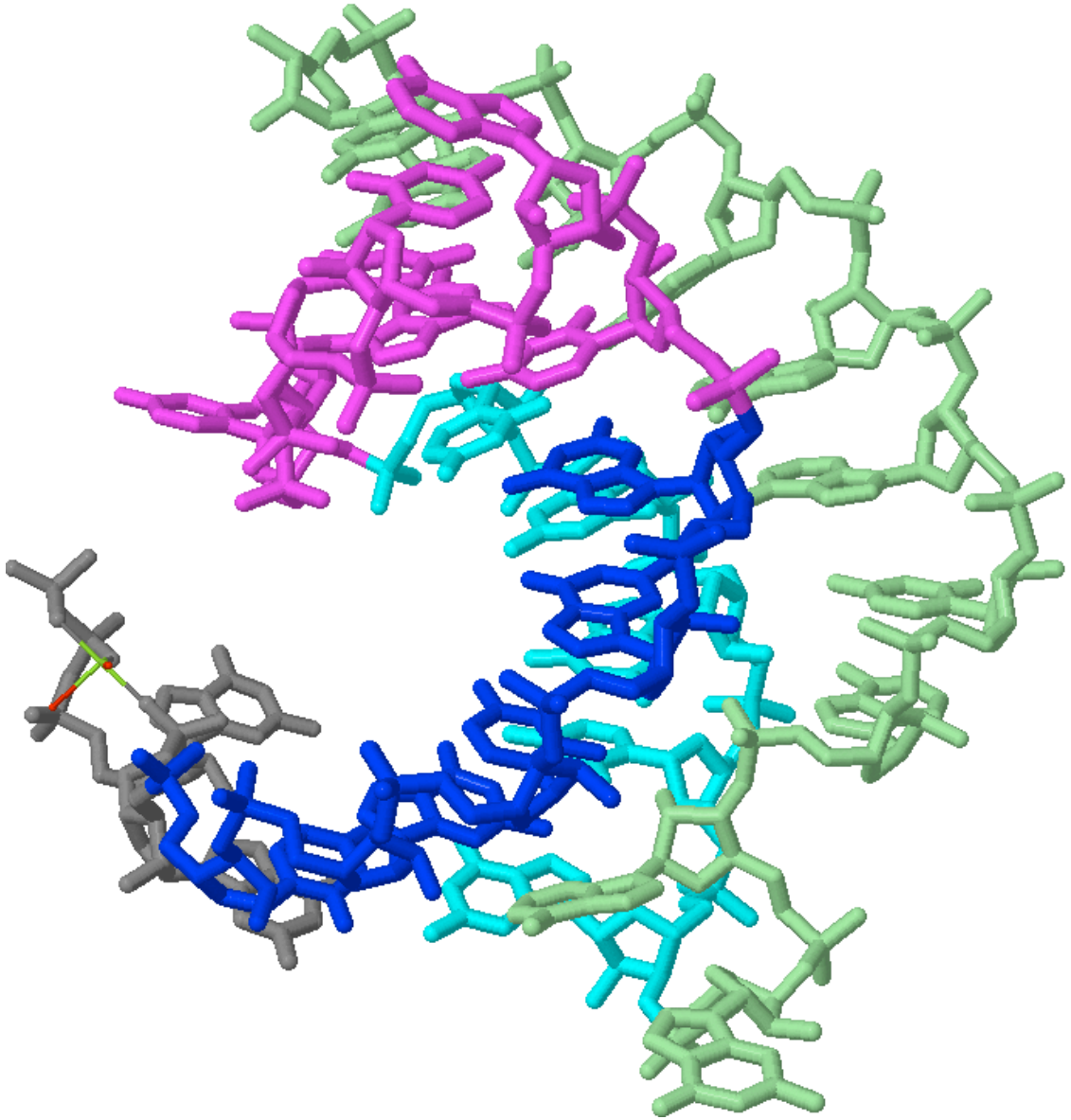
# Simple Structure - Hairpin



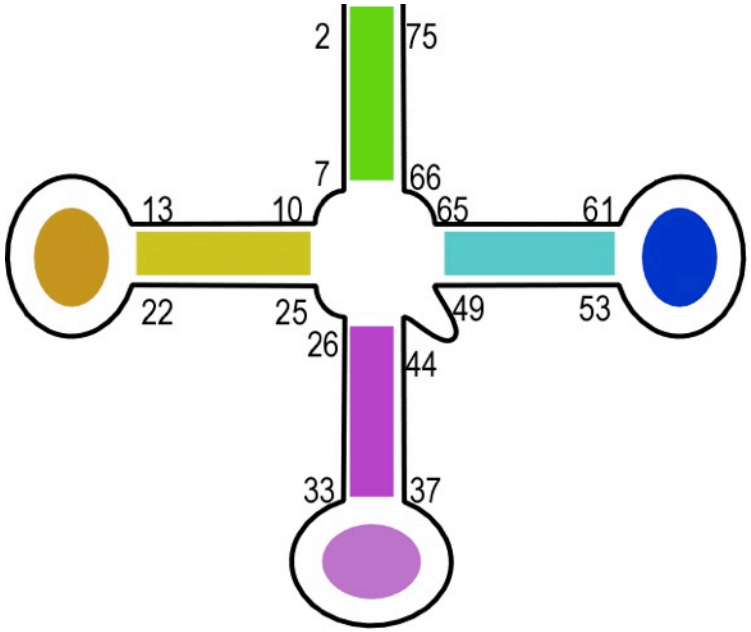



# Classic Structure - Pseudoknot

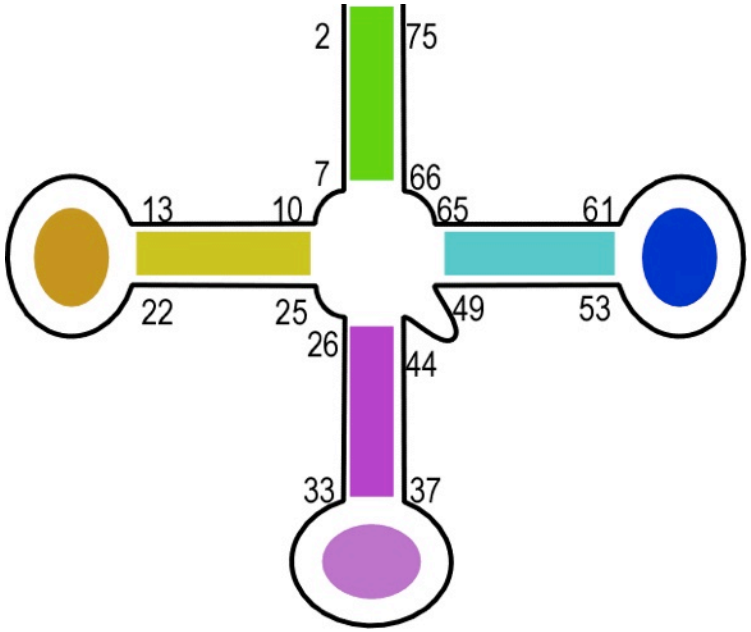


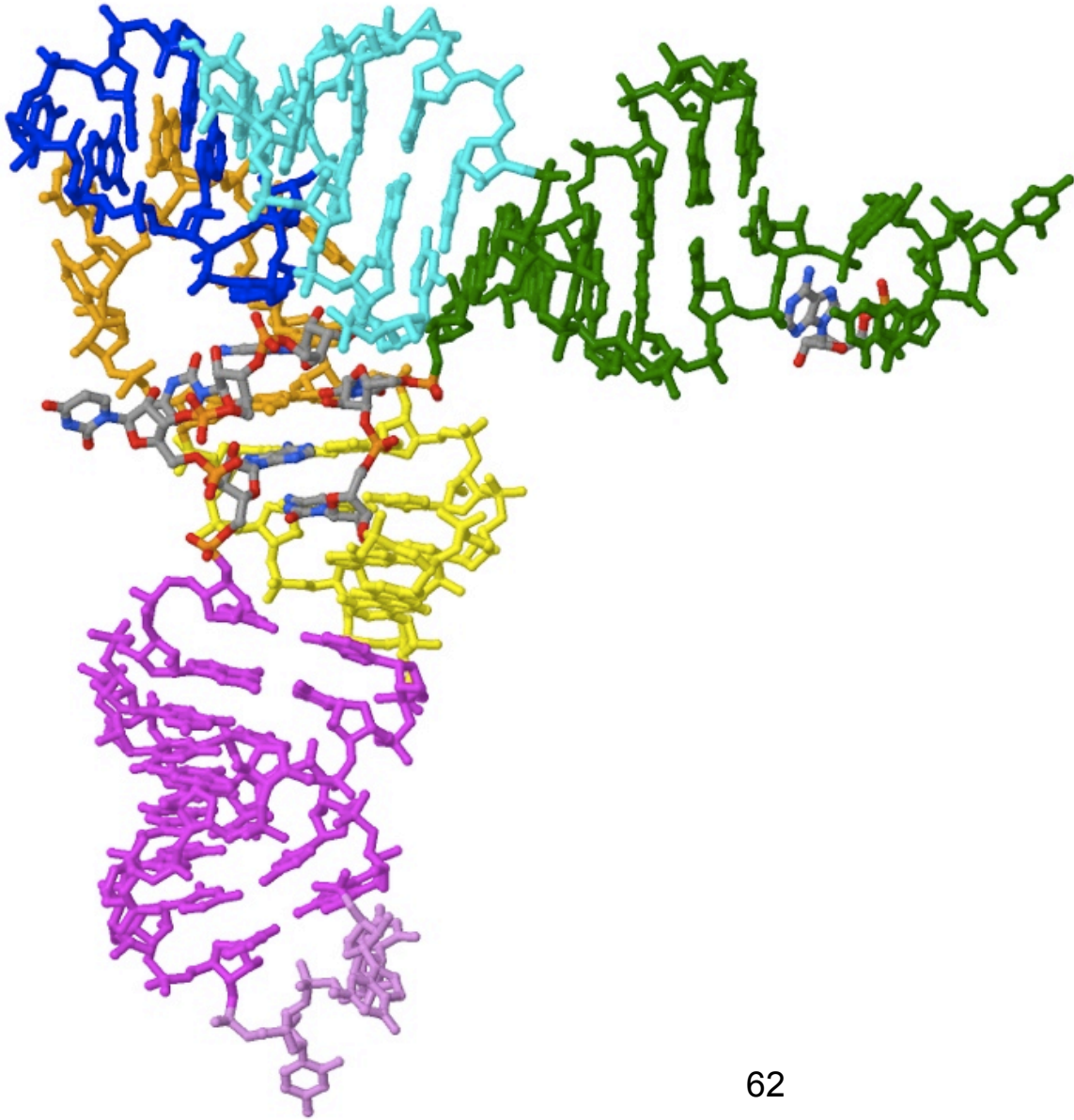


# tRNA

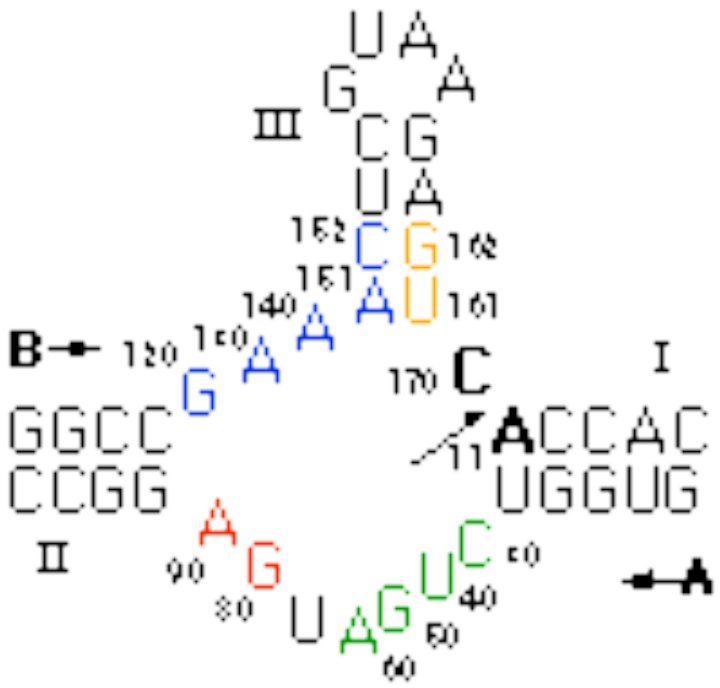


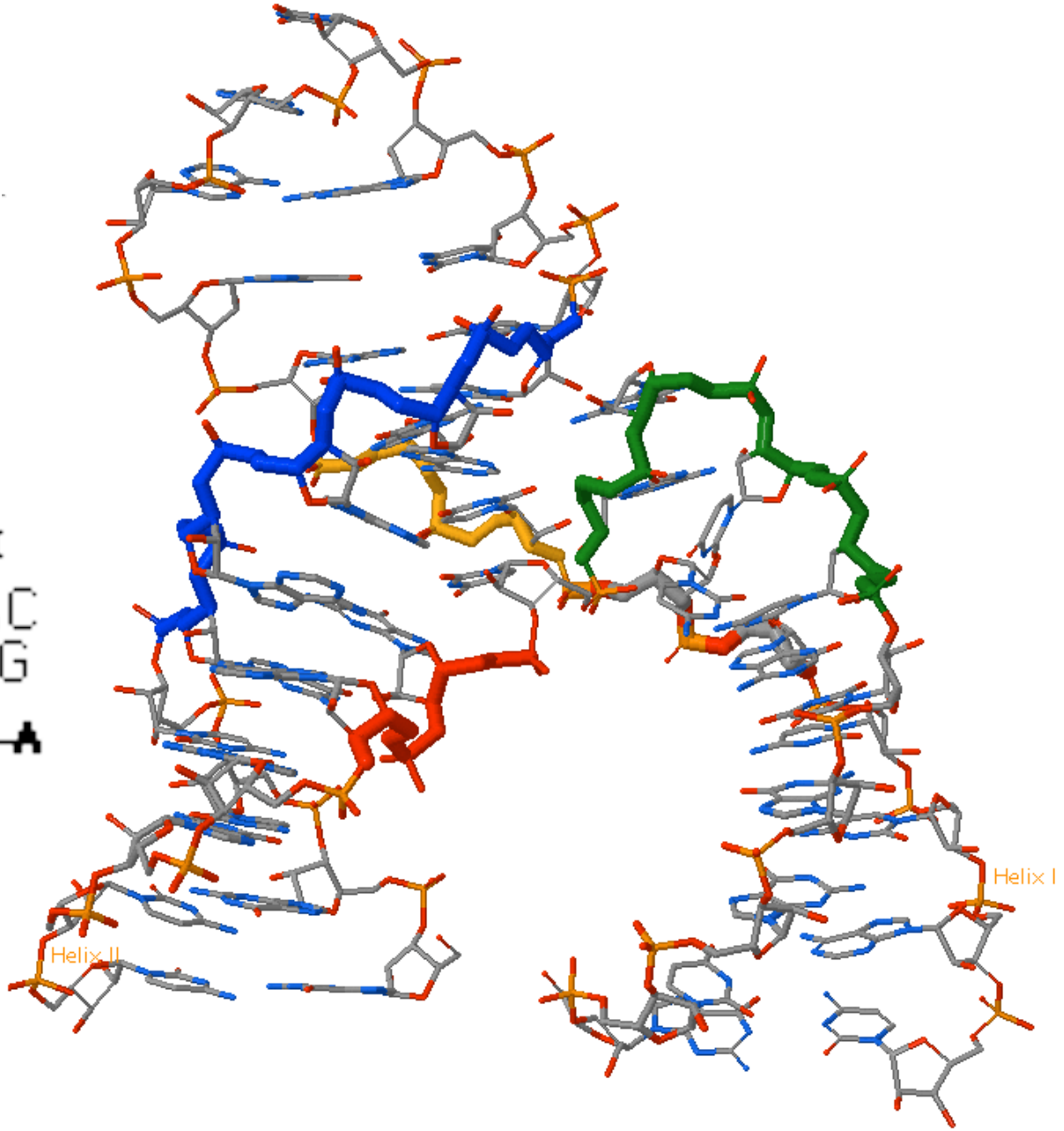
# tRNA



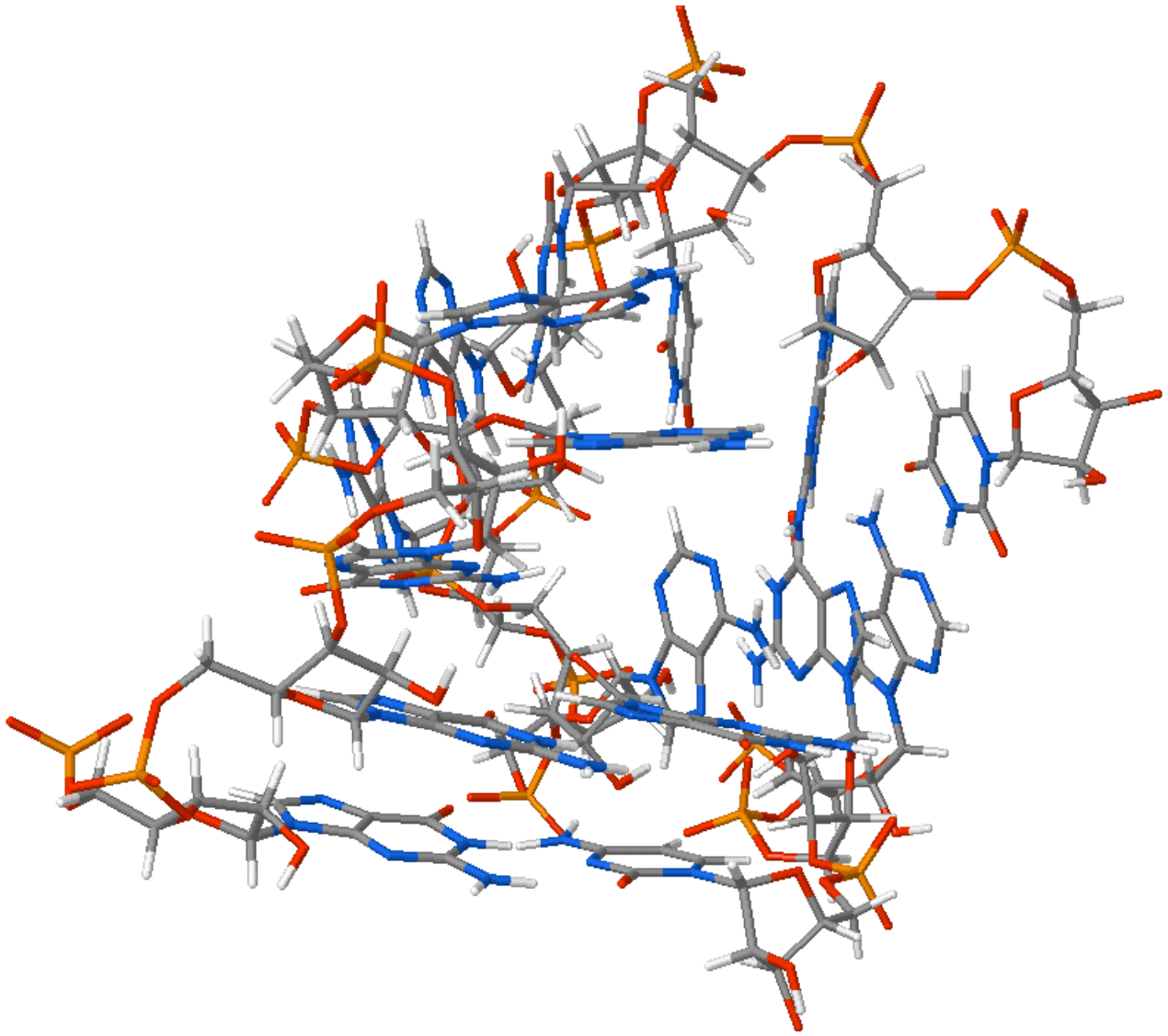



# Hammerhead Ribozyme

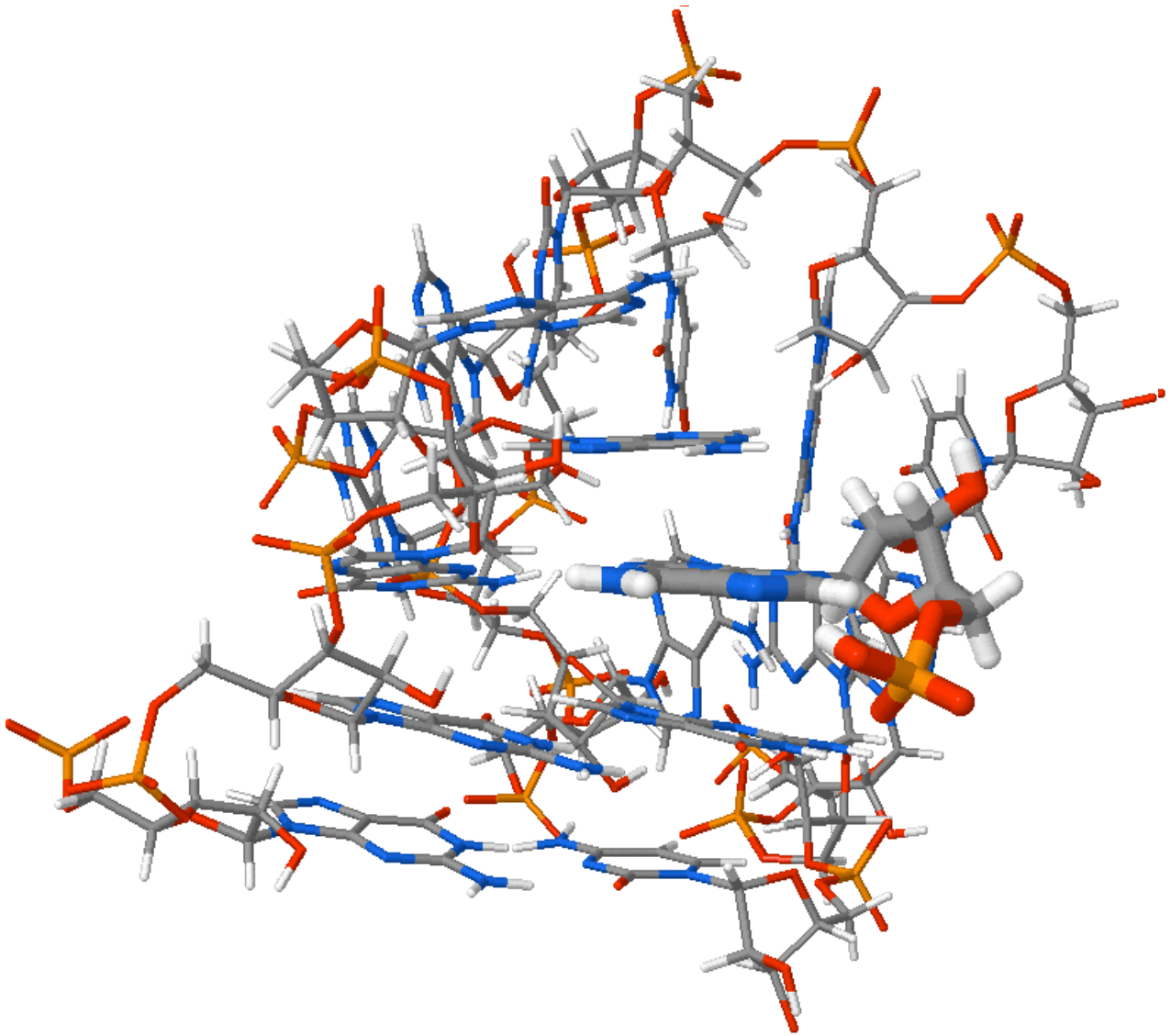


# AMP Aptamer



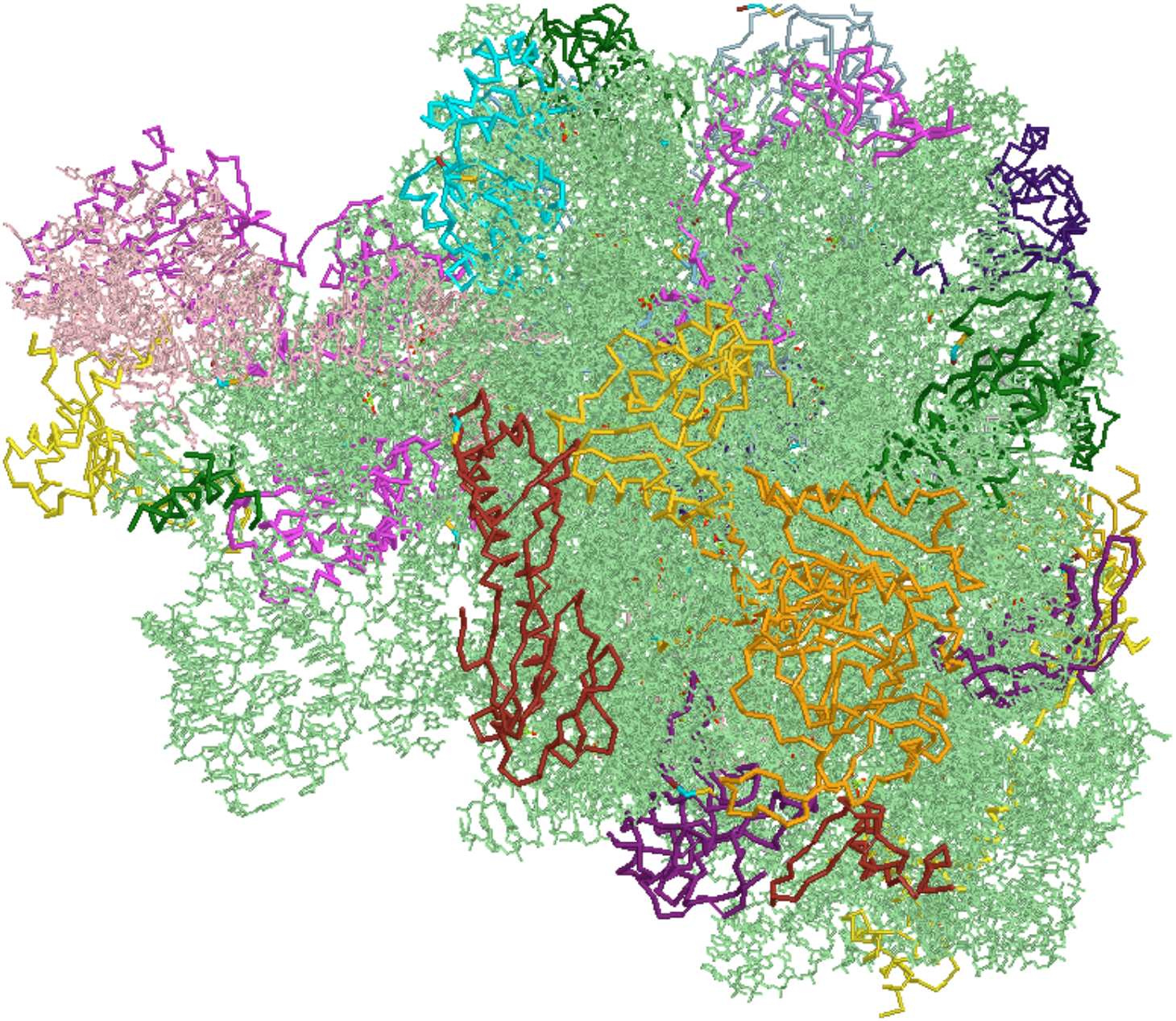
# AMP Aptamer



# RNA

# Ribosome

An RNA machine with protein cofactors

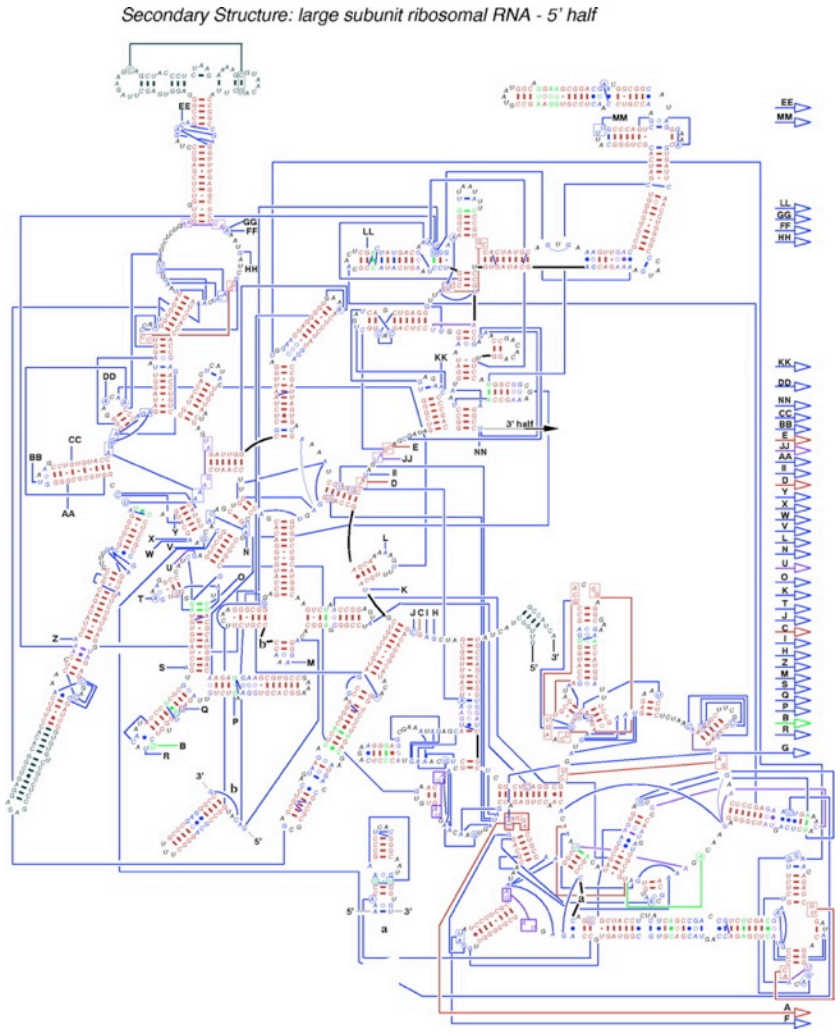


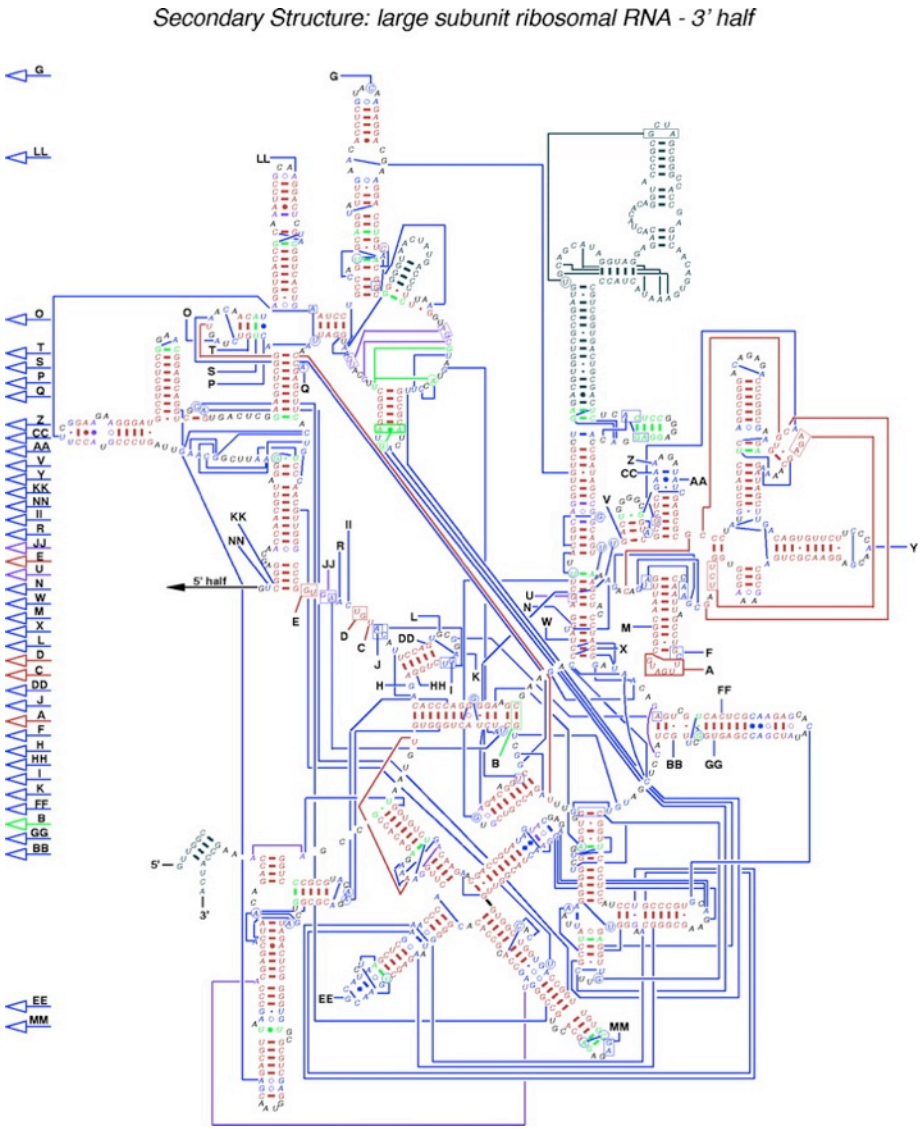
# Ribosome - Secondary Structure

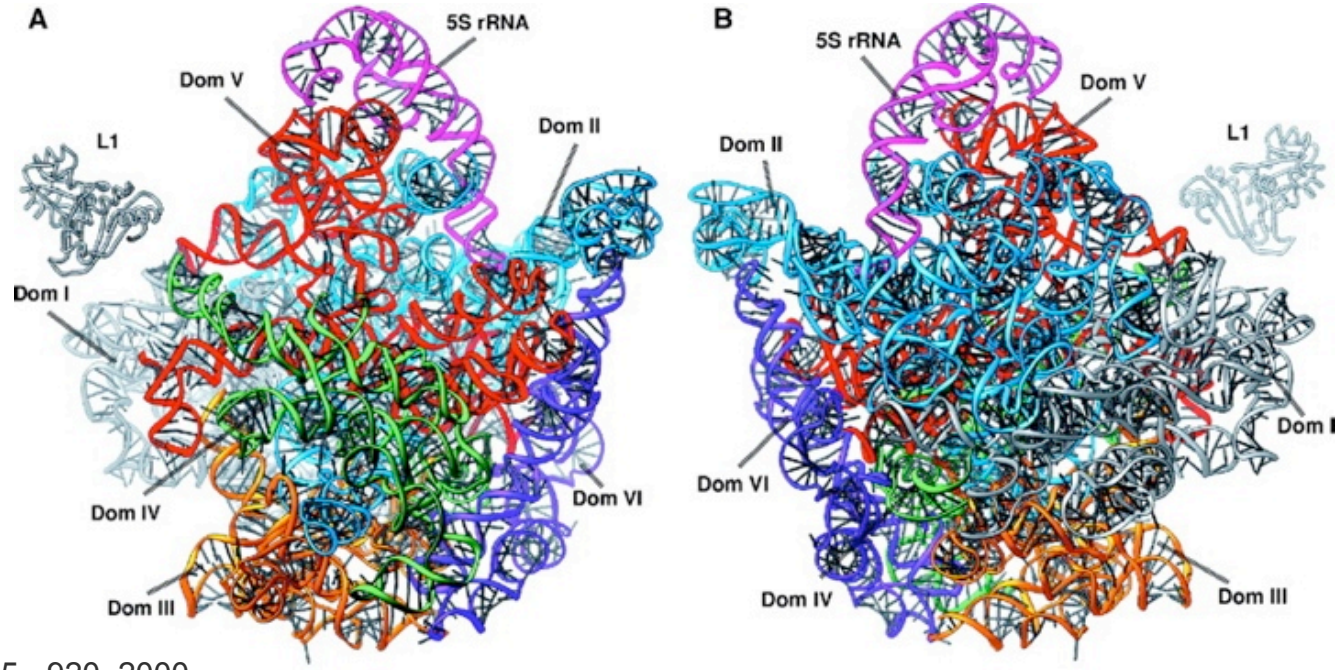
Science 289(5481), 905 - 920, 2000

**The Complete Atomic Structure of the Large Ribosomal Subunit at 2.4 Å Resolution**

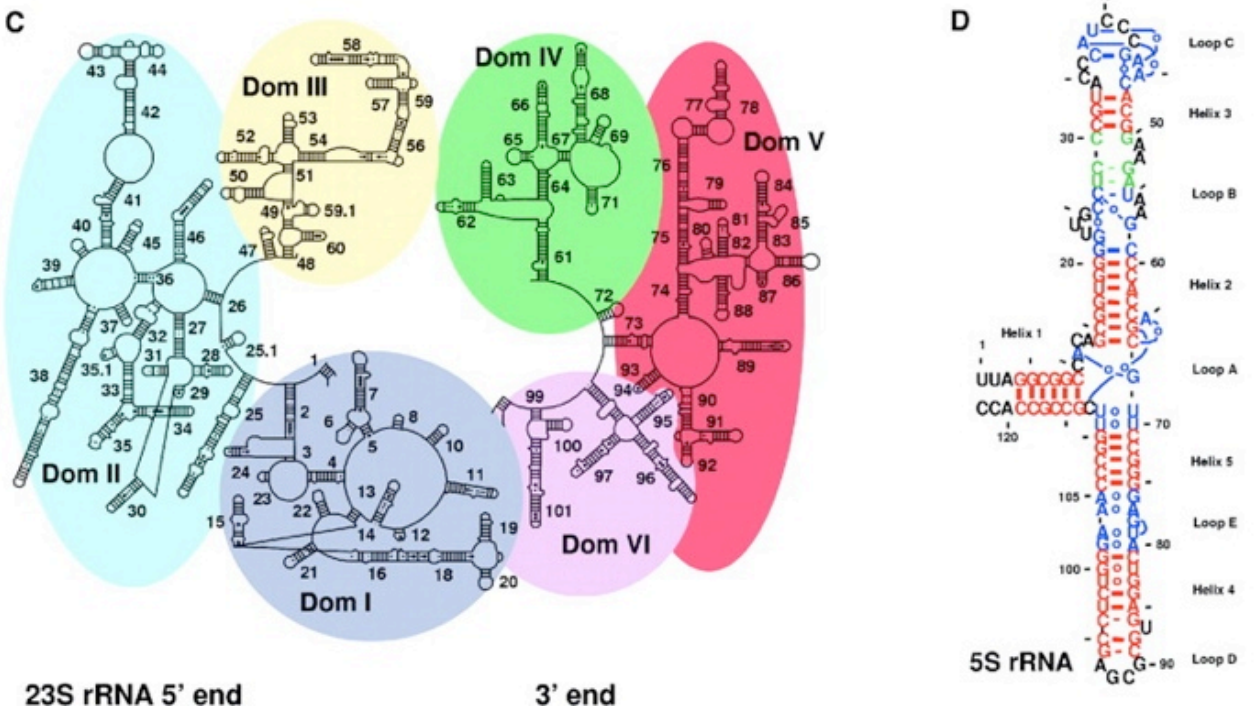
Ban, Nissen, Hansen, Moore, & Steitz






Science 289(5481), 905 - 920, 2000

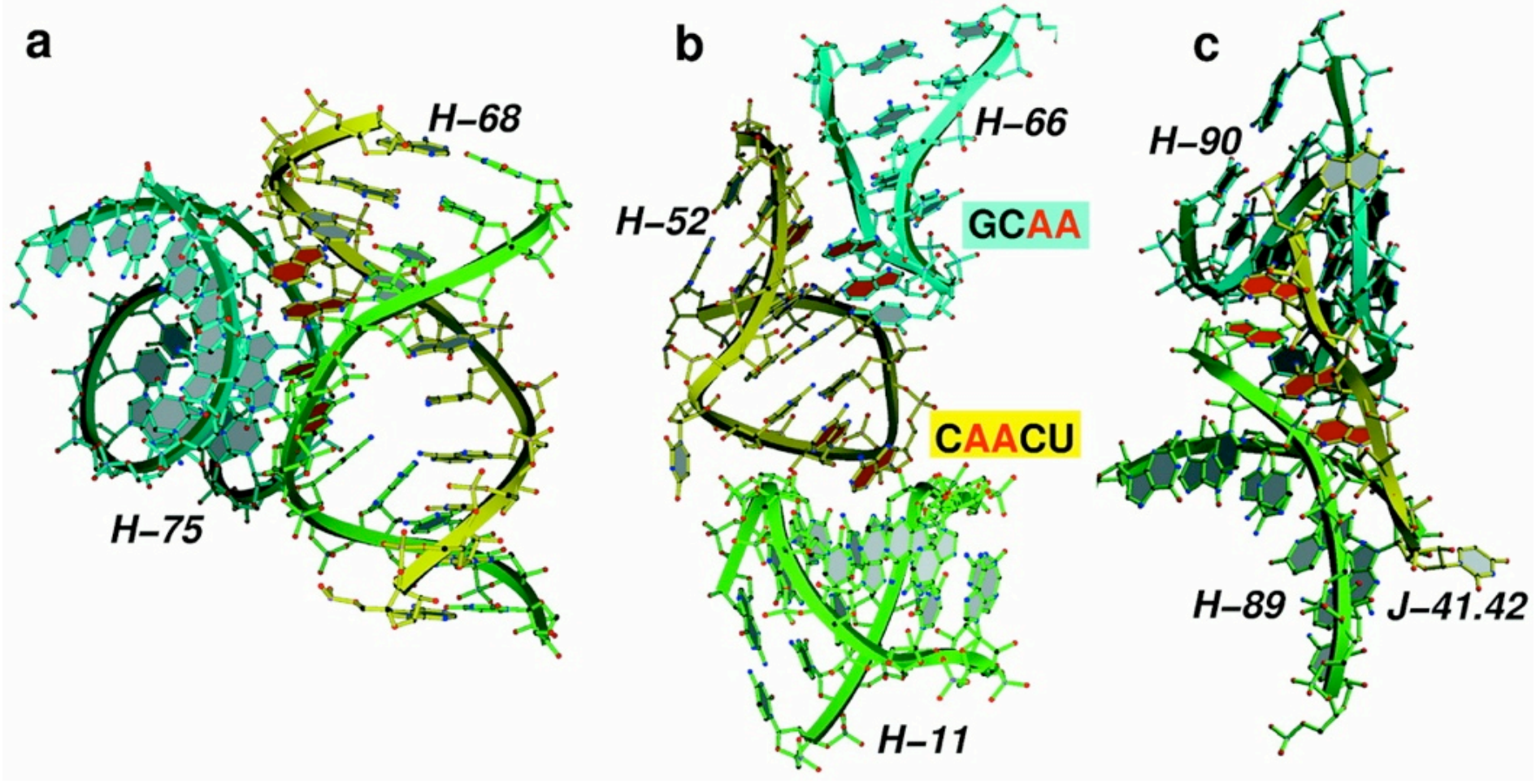


PNAS 98(9), **4899-4903**, 2001

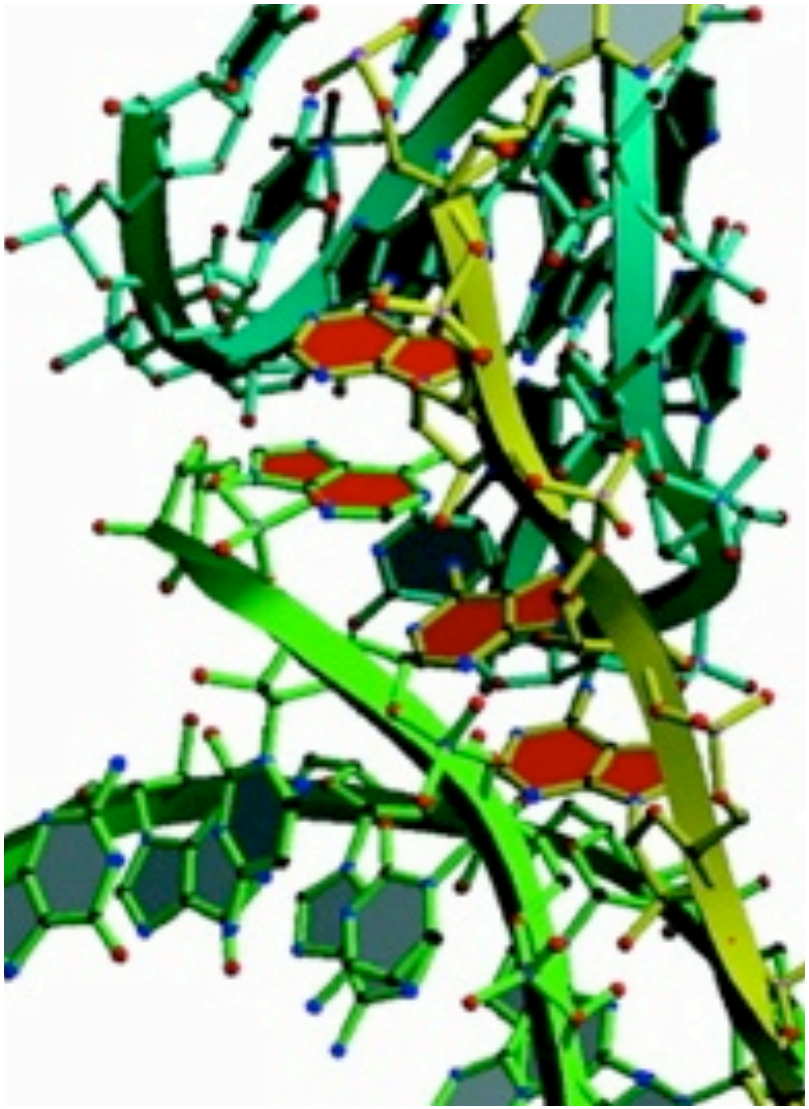
**RNA tertiary interactions in the large ribosomal subunit: The A-minor motif**

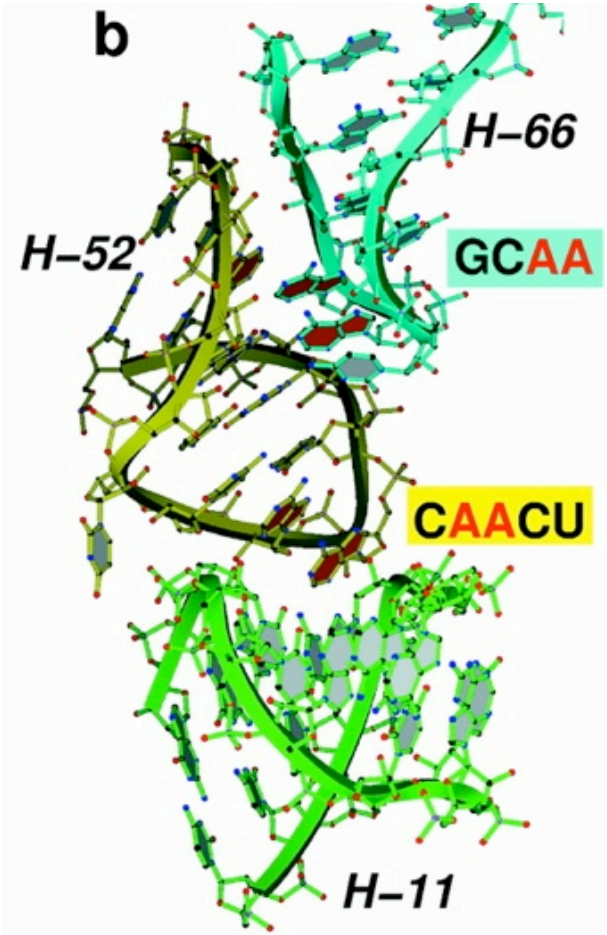
Nissen, Ippolito, Ban, Moore, & Steitz

# The Ribosome: a wealth of RNA structure



PNAS 98(9), **4899-4903**, 2001





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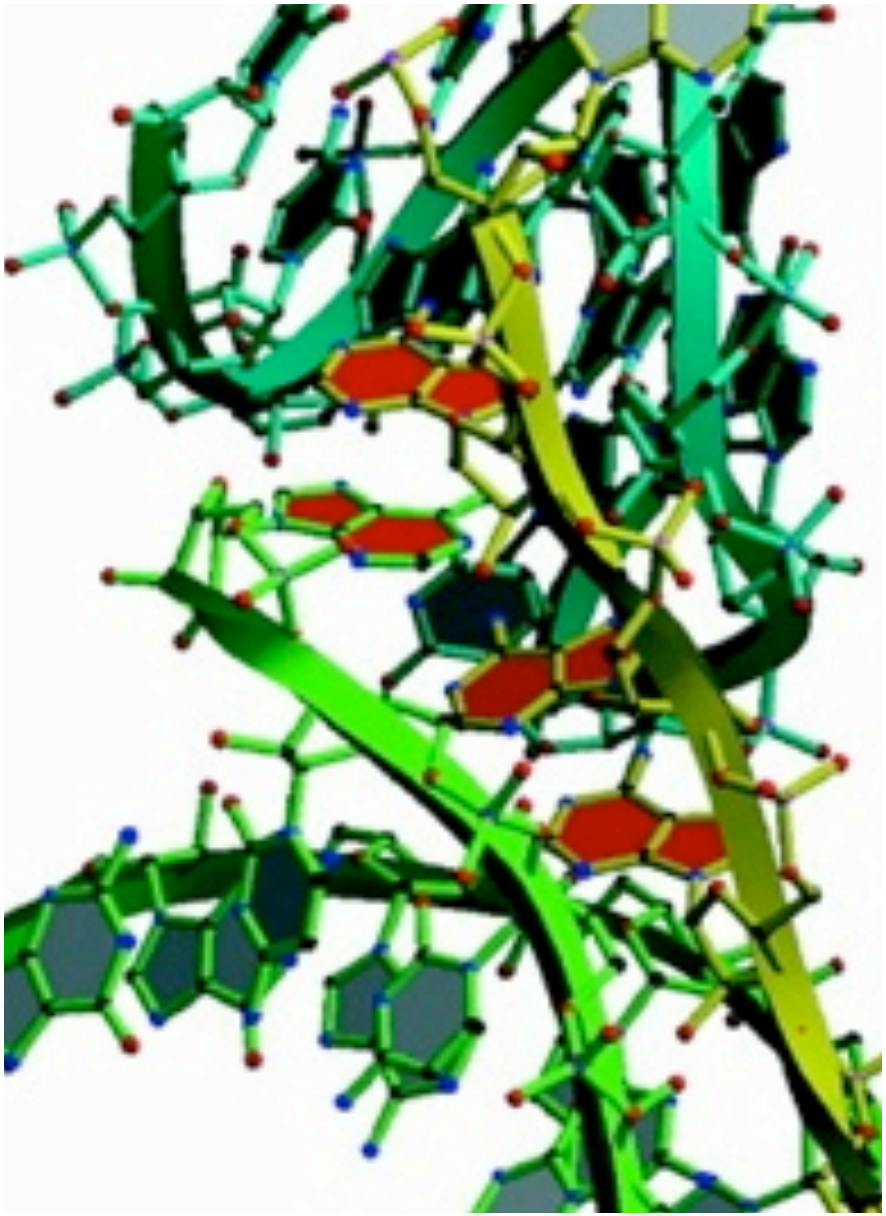

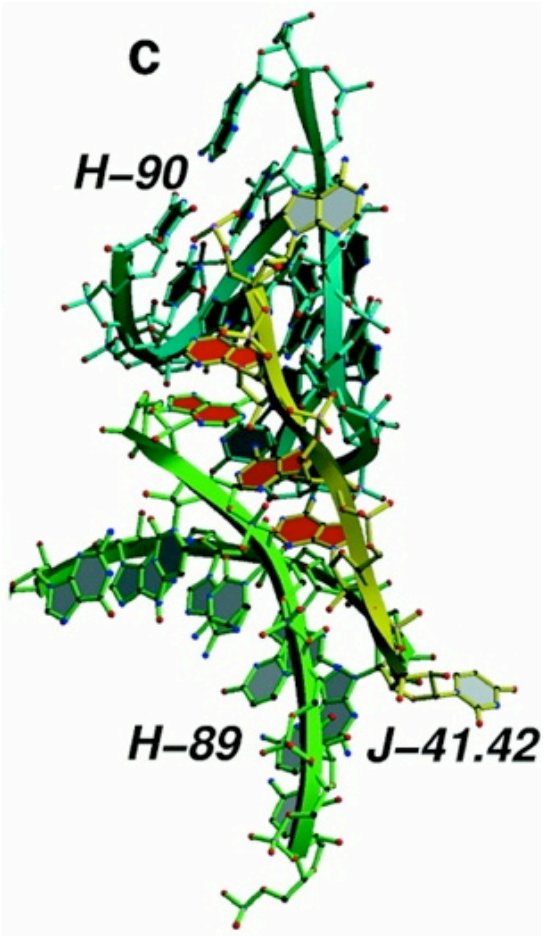

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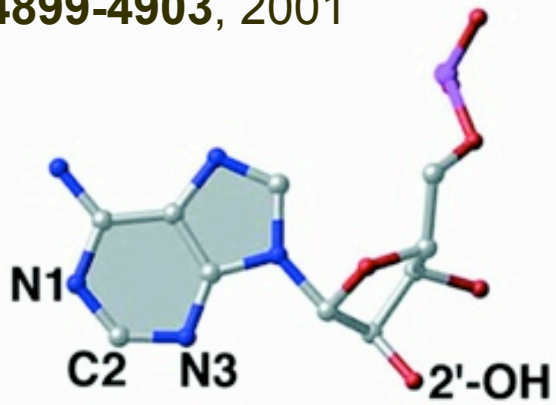
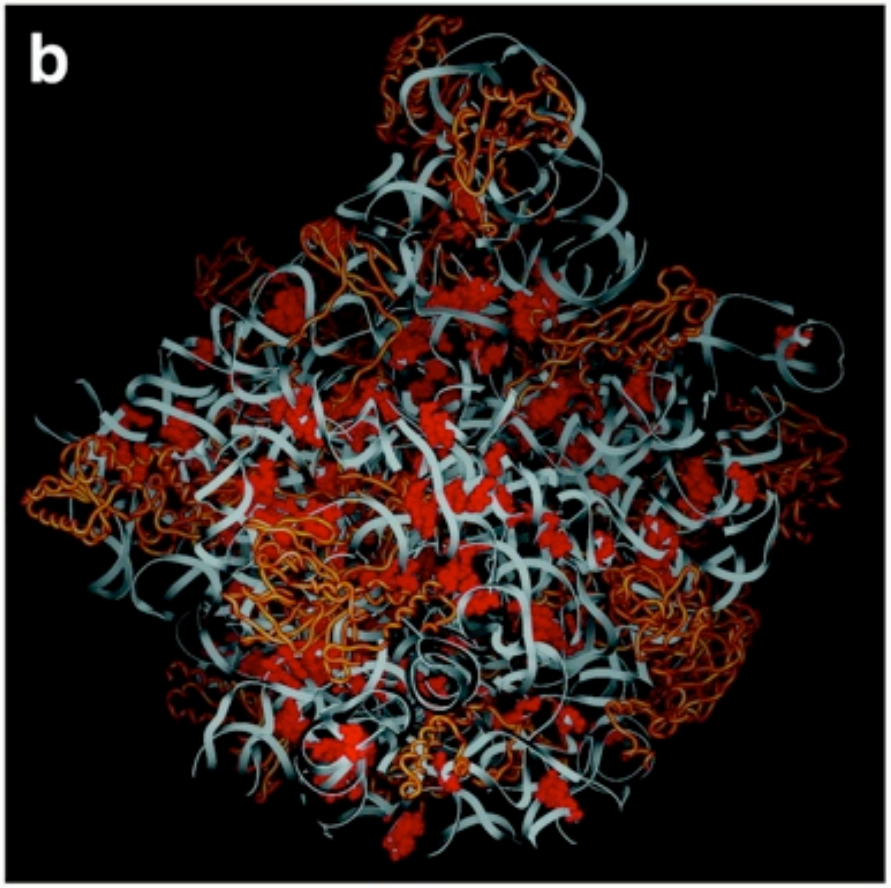
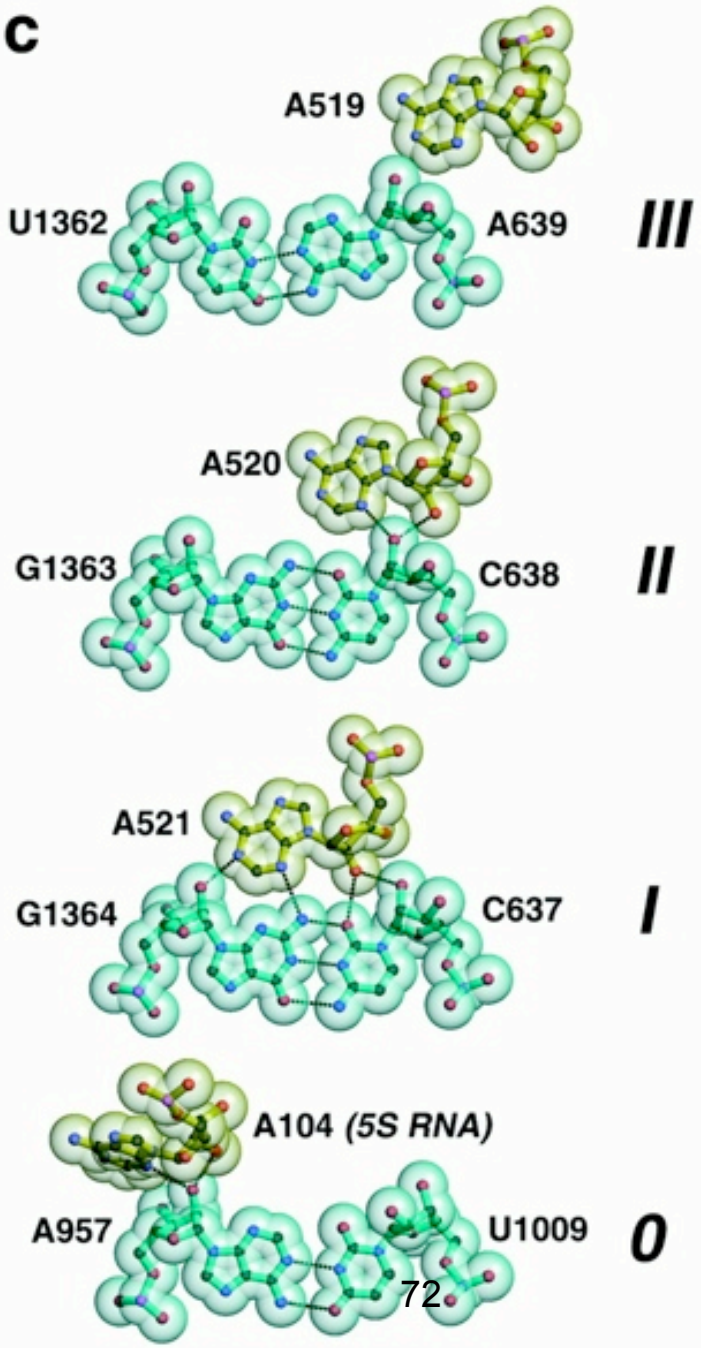
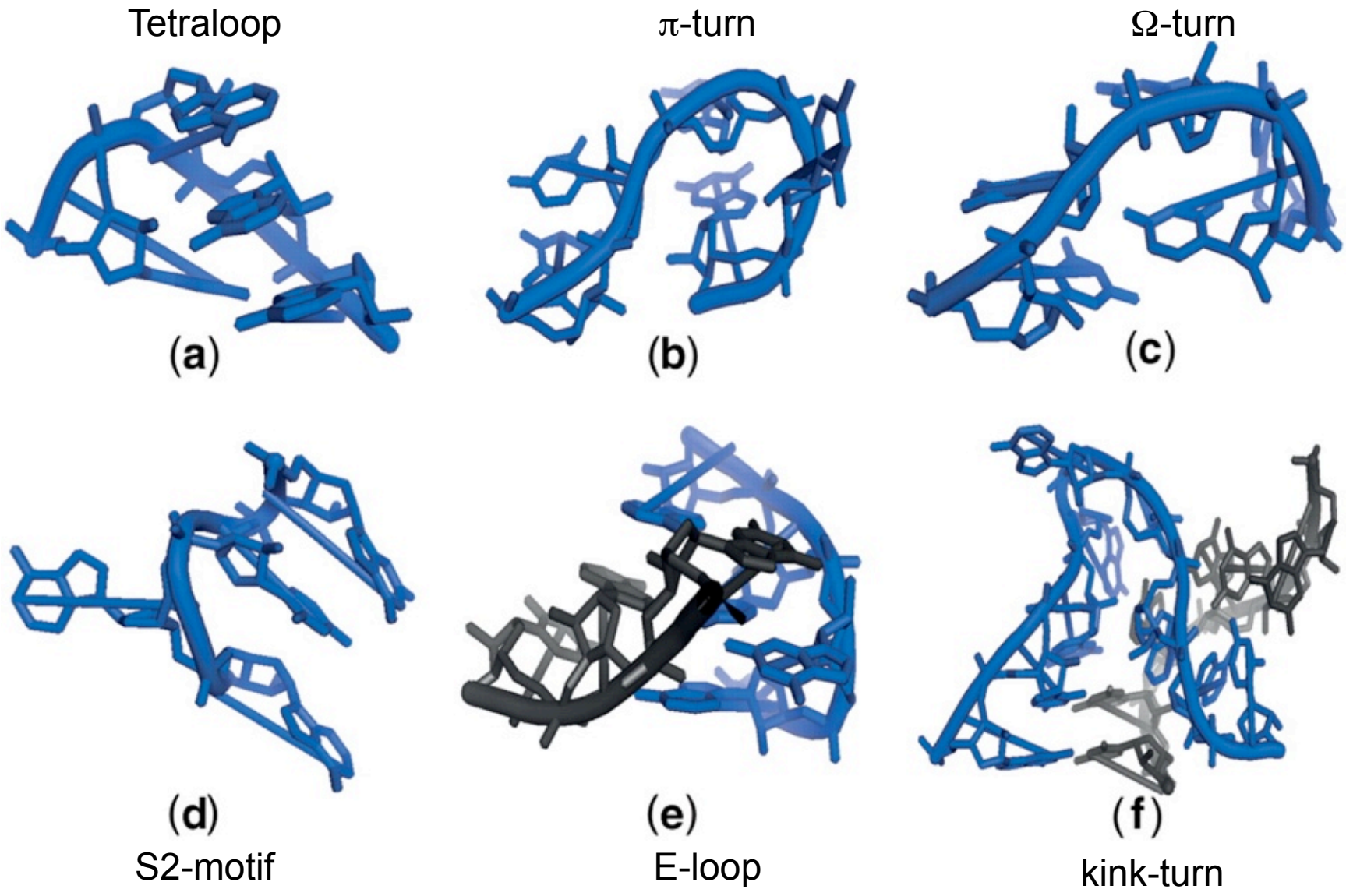


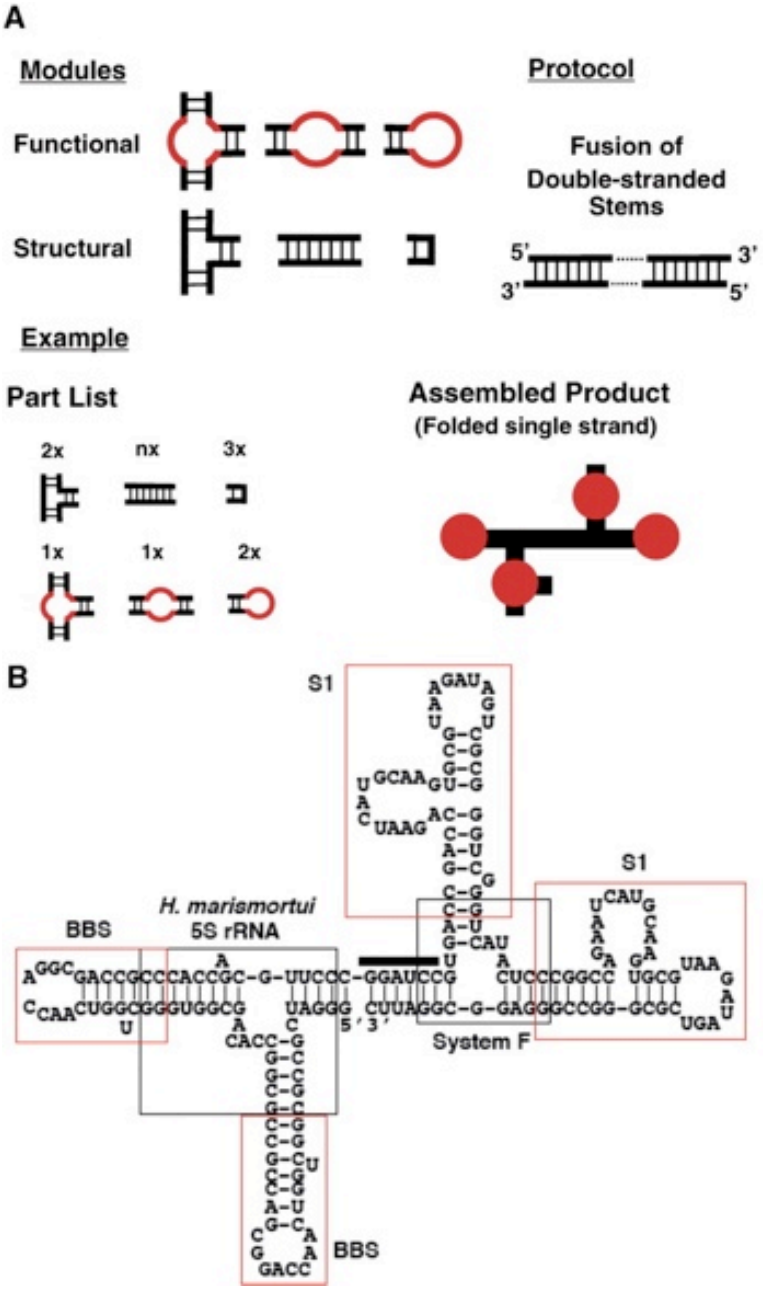



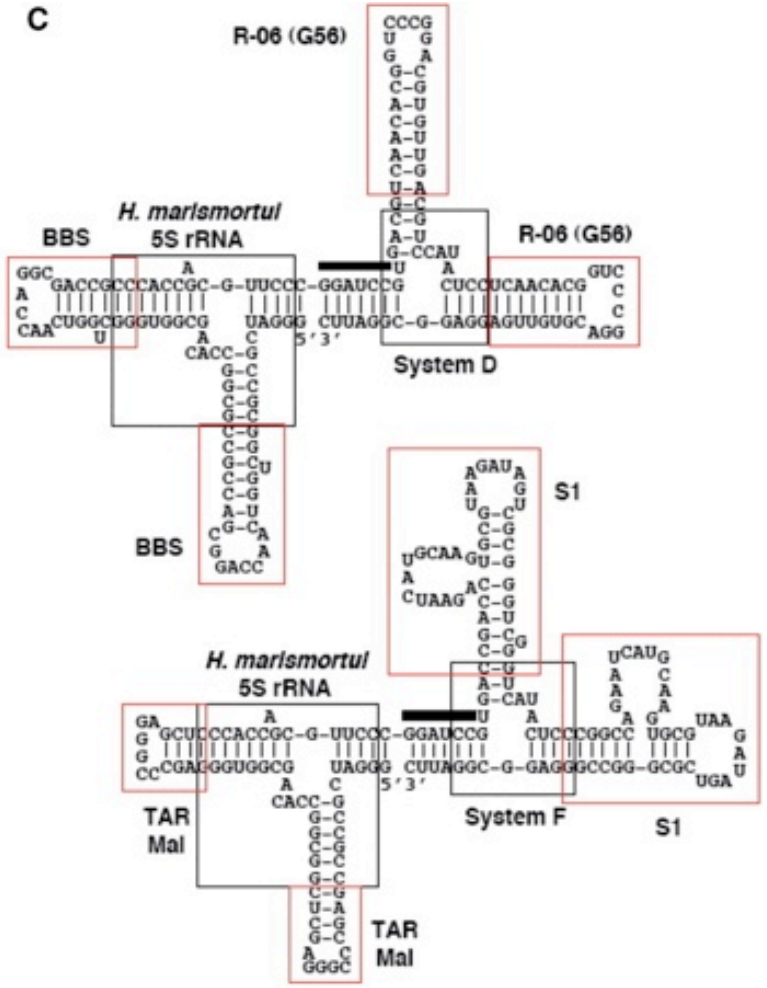
# Structural Motifs

Nucleic Acids Research, 2009, Vol. 37, No. 4 **e29**



# Where to from here? Modular Construction




Xu and Shi, "Composite RNA aptamers as functional mimics of proteins"

Nucleic Acids Research 2009 37(9):e71

# Which is more stable?

(which has a higher melting temperature?)

**ACCGCCACCGAAG**

**TGGCGGTGGCTTC**

or

**ACCGCCACCGAAG**

**TGGCGGTGGCTTA**

# Which is more stable?

(which has a higher melting temperature?)

**ACCGCCACCGAAG**
**TGGCGGTGGCTTC**

51.6° C

or

**ACCGCCACCGAAG**
**TGGCGGTGGCTTA**

# Which is more stable?

(which has a higher melting temperature?)

**ACCGCCACCGAAG**
**TGGCGGTGGCTTC**

51.6° C

or

**ACCGCCACCGAAG**
**TGGCGGTGGCTTA**

52.5° C

Calculations from http://www.idtdna.com/analyzer/Applications/OligoAnalyzer/