

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

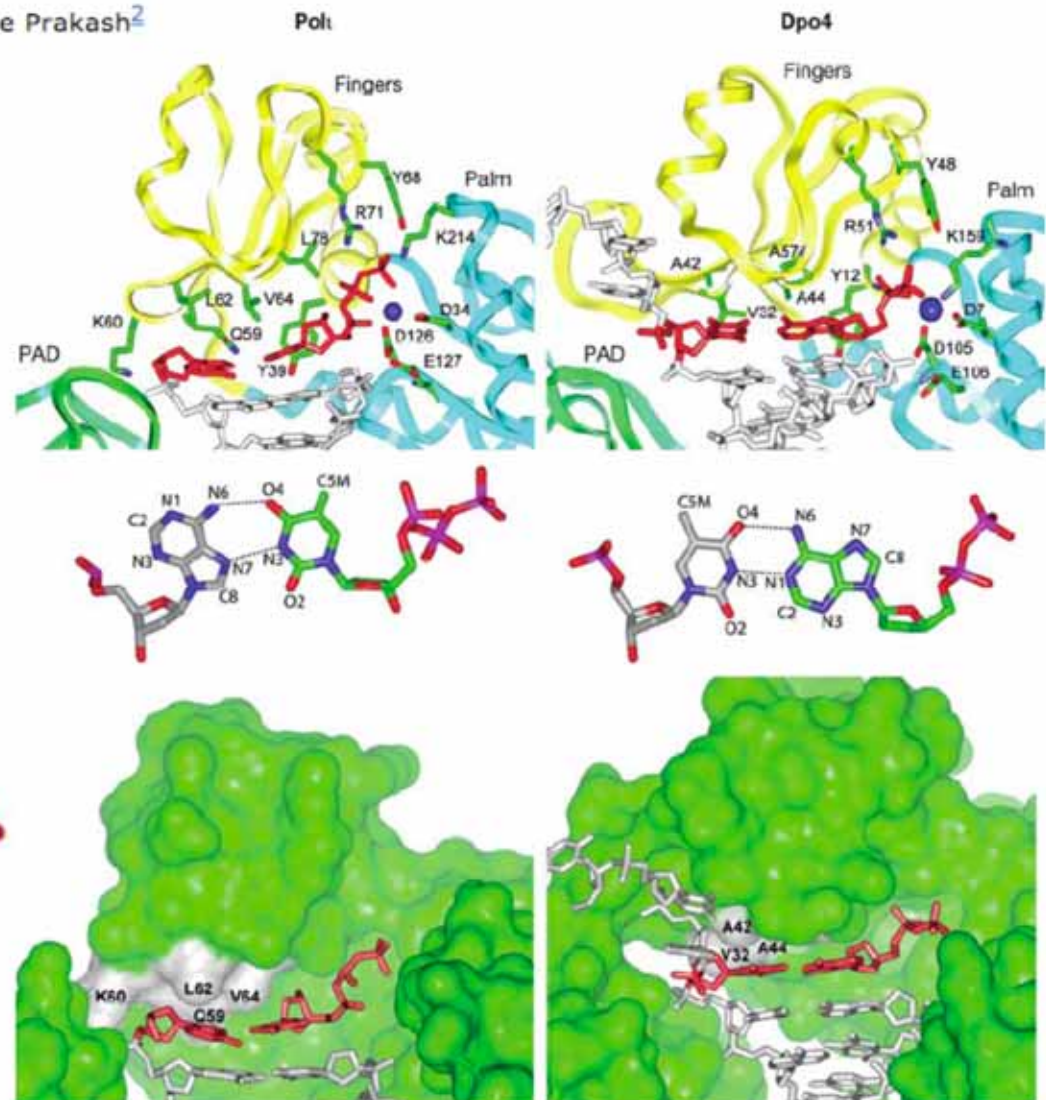
Deepak T. Nair¹, Robert E. Johnson², Satya Prakash², Louise Prakash² and Aneel K. Aggarwal¹

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

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

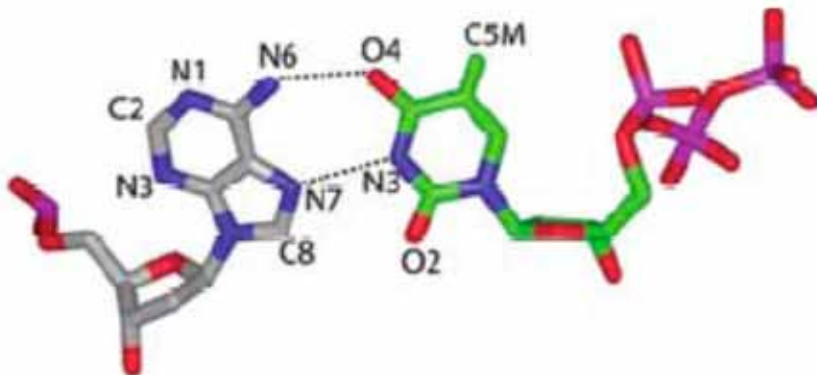
This polymerase is good at bypassing lesions in the DNA (eg, damaged Watson-Crick face of G).

Hoogsteen vindicated

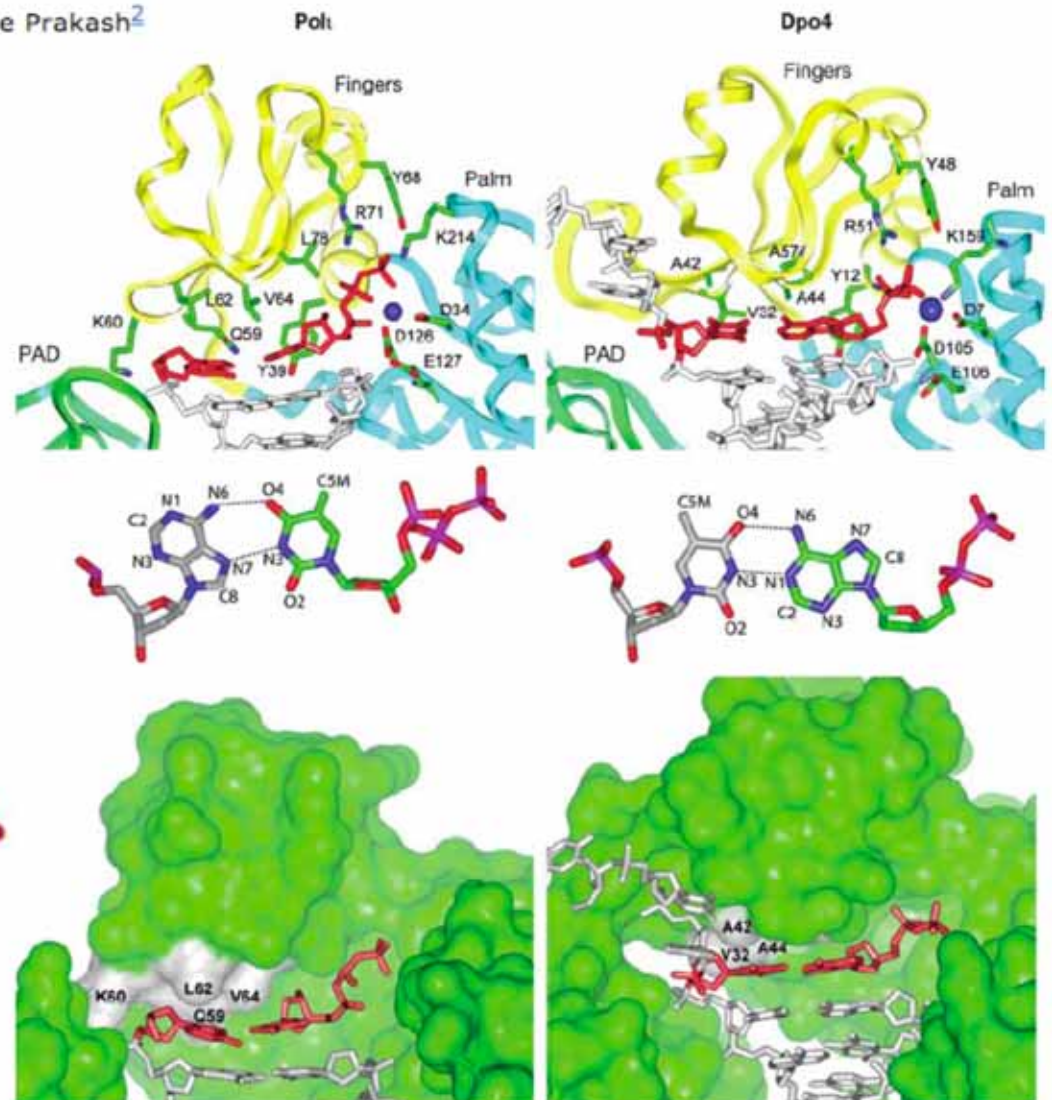


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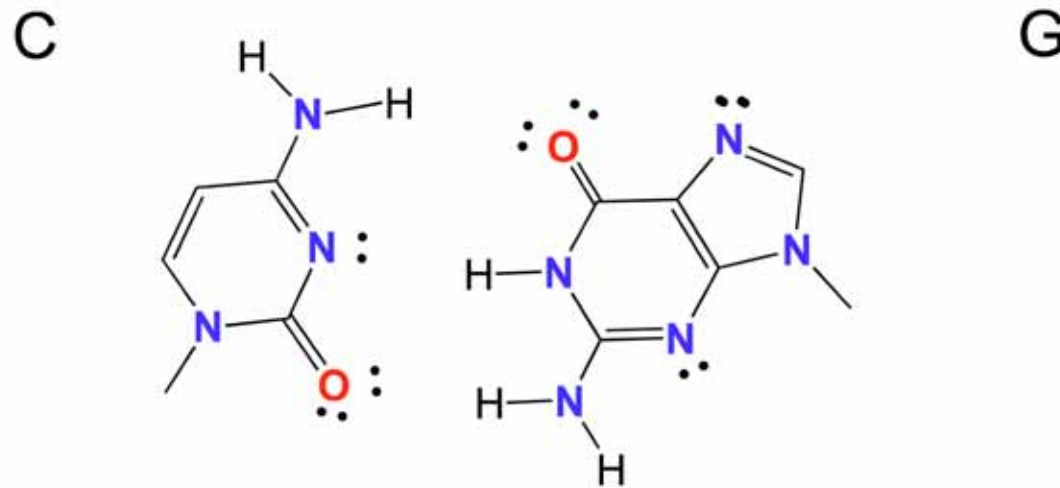
This polymerase is good at bypassing lesions in the DNA (eg, damaged Watson-Crick face of G).



But... perhaps not...

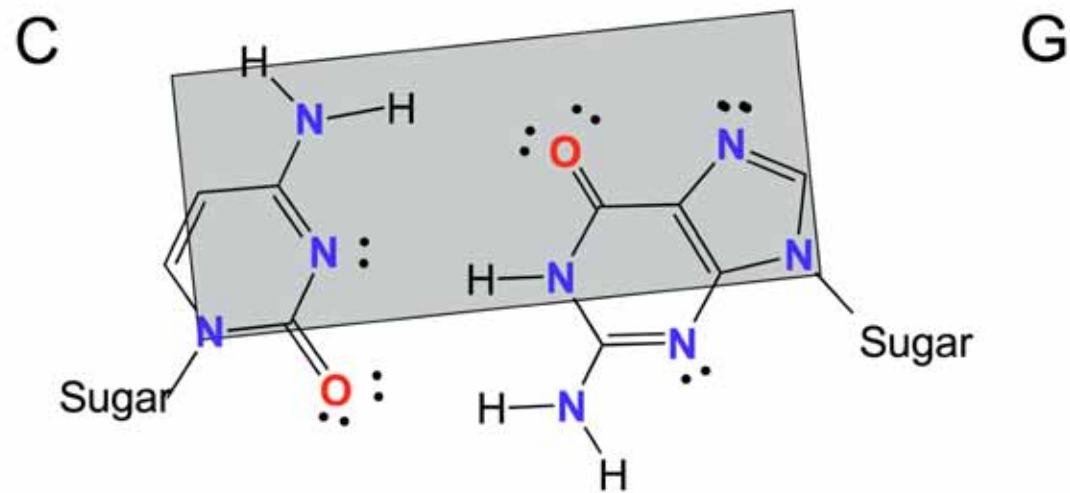


Why is Watson-Crick so good?



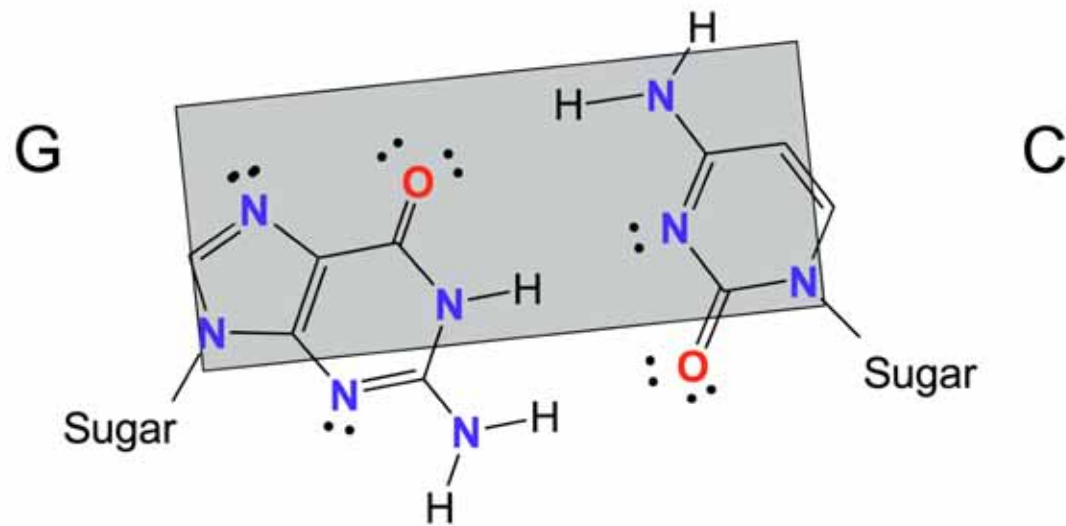
All four WC base pairs
are
isosteric

Why is Watson-Crick so good?



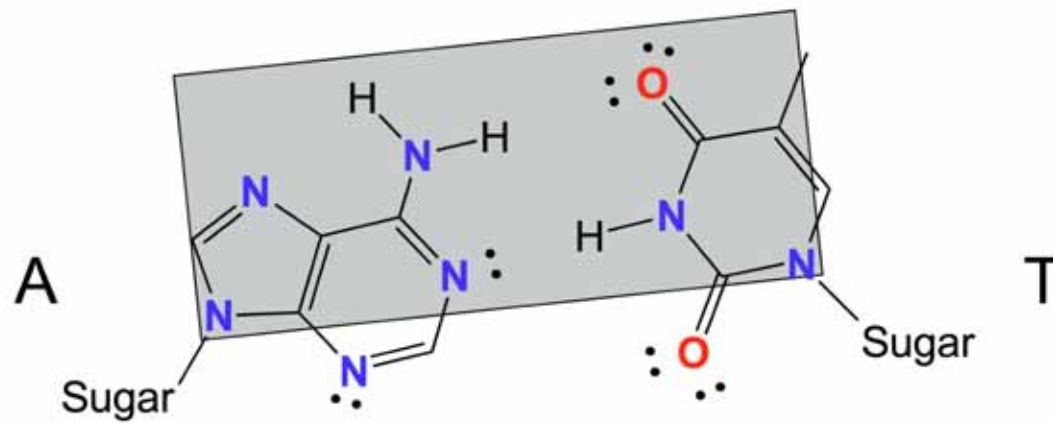
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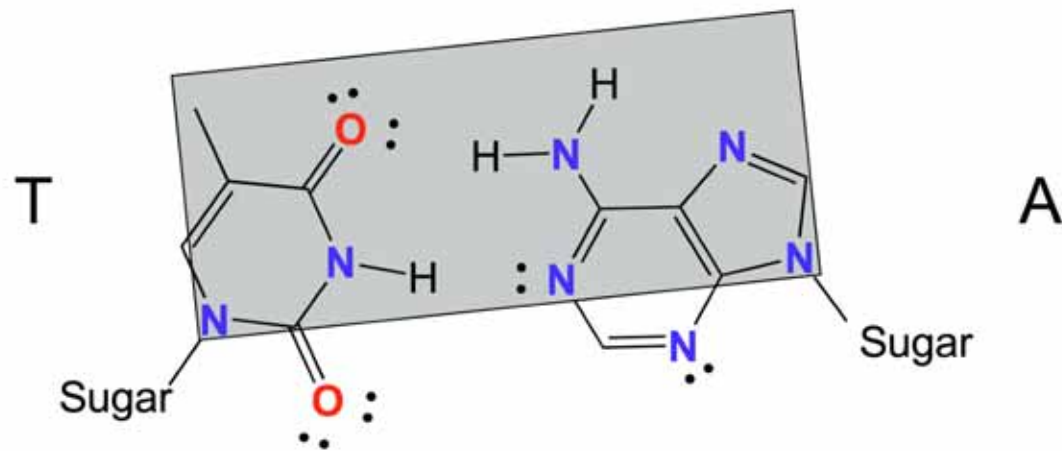
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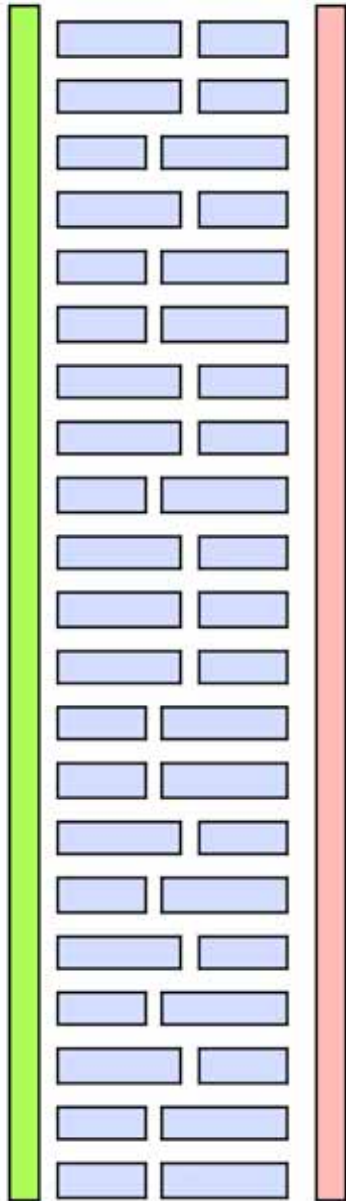
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Why is Watson-Crick so good?

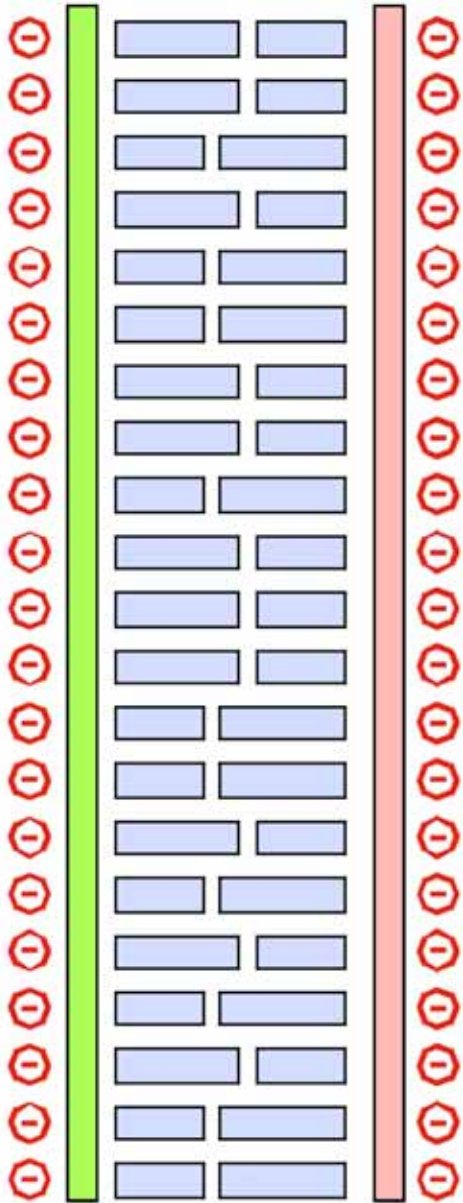


All four WC base pairs
are
isosteric

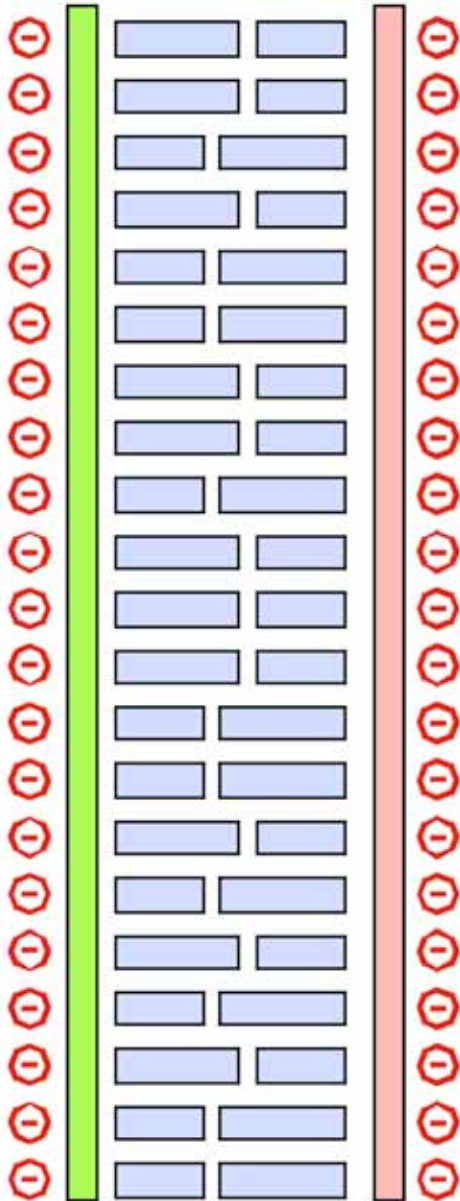
Why *a helix*?



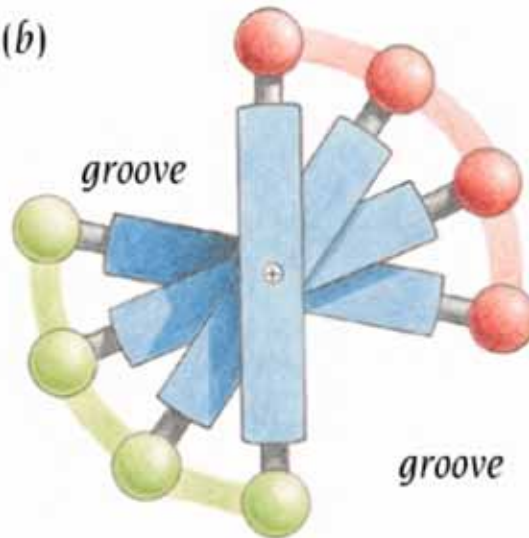
Why *a helix*?



Why *a helix*?

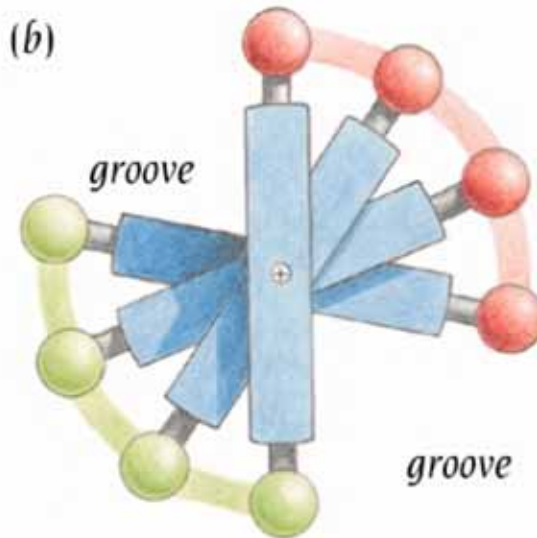
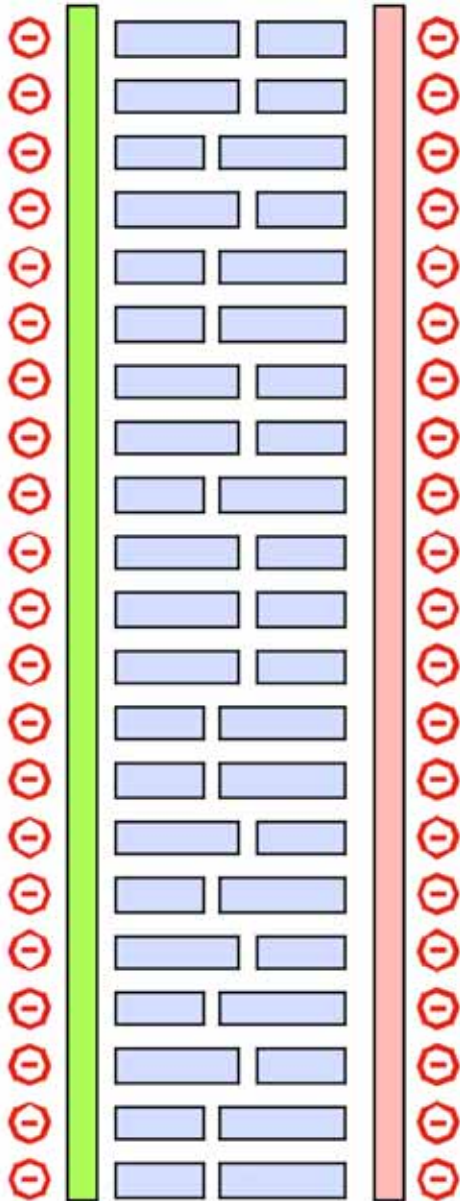


(b)

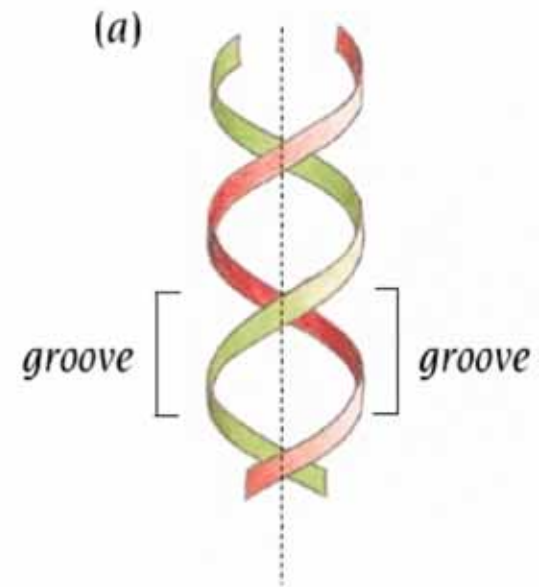


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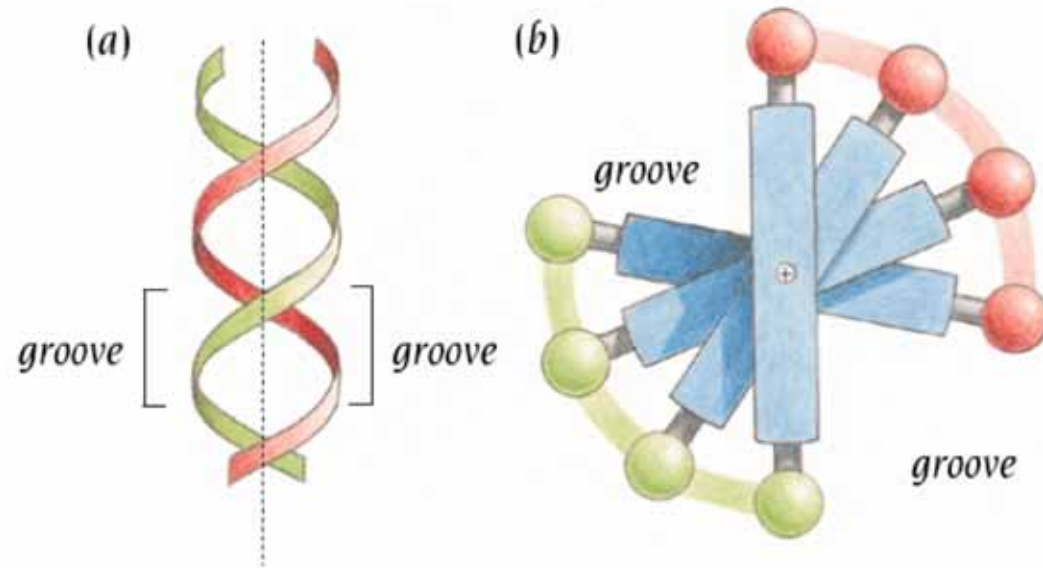
Why *a helix*?



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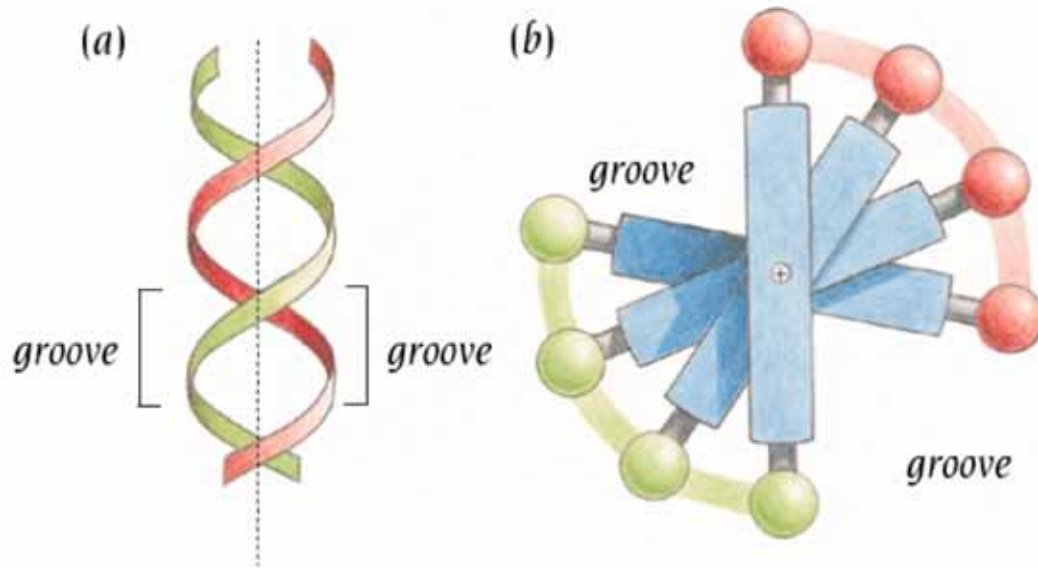


Why *major* and *minor* grooves?

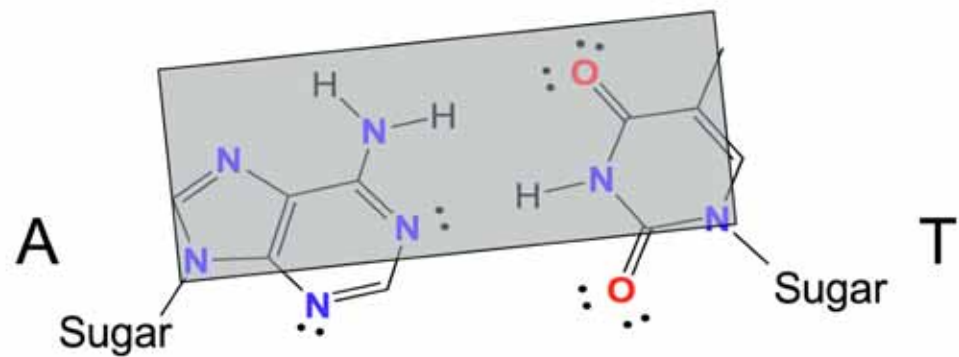


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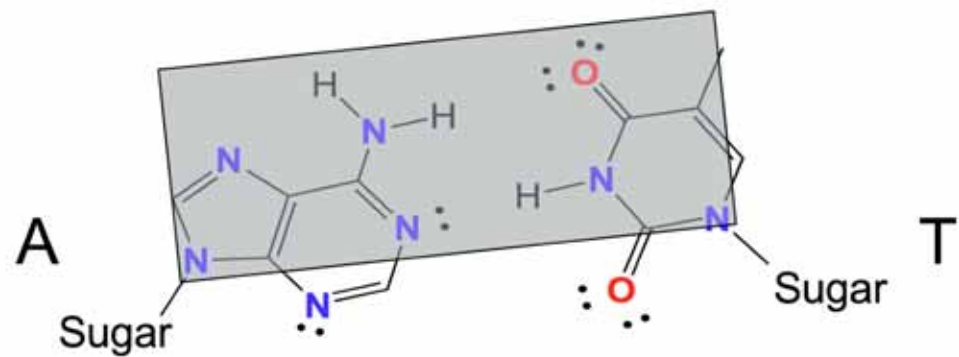
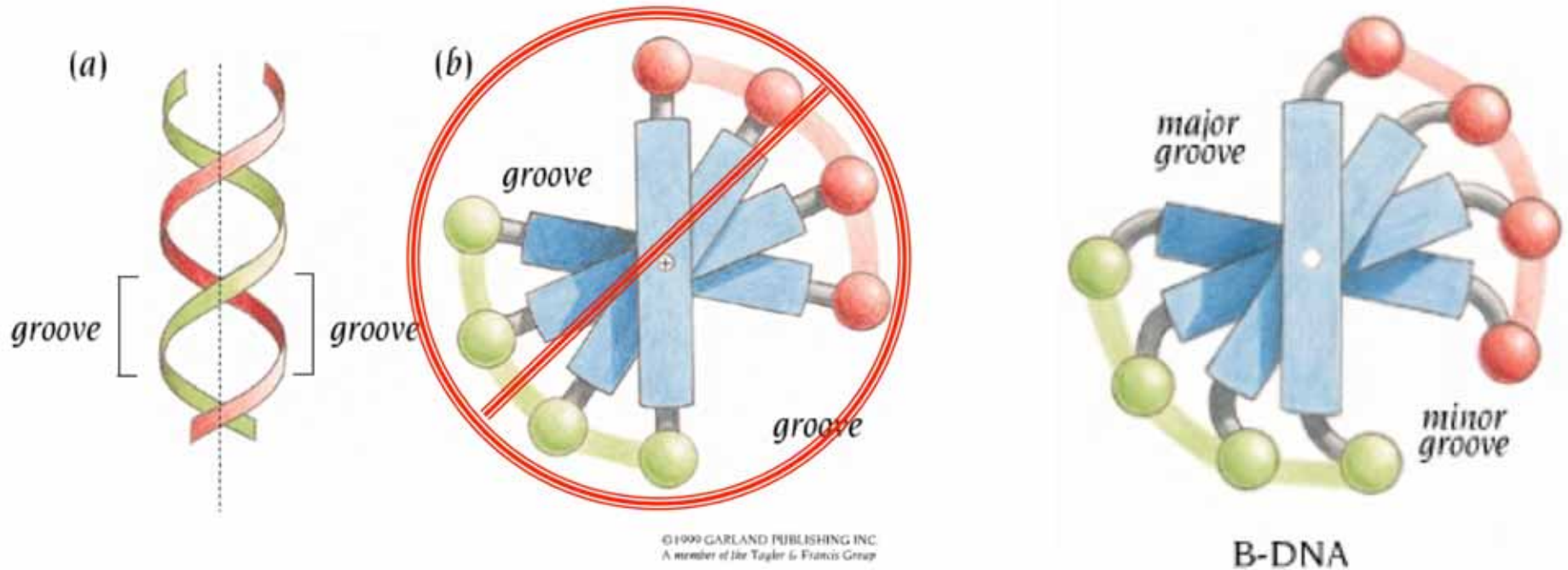
Why *major* and *minor* grooves?



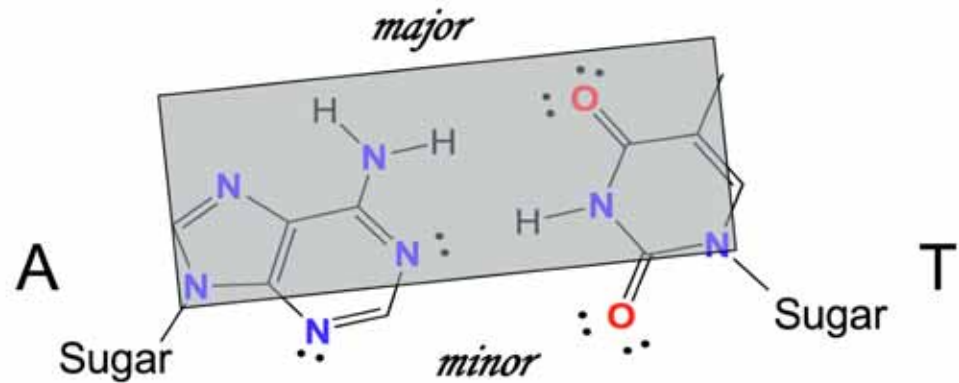
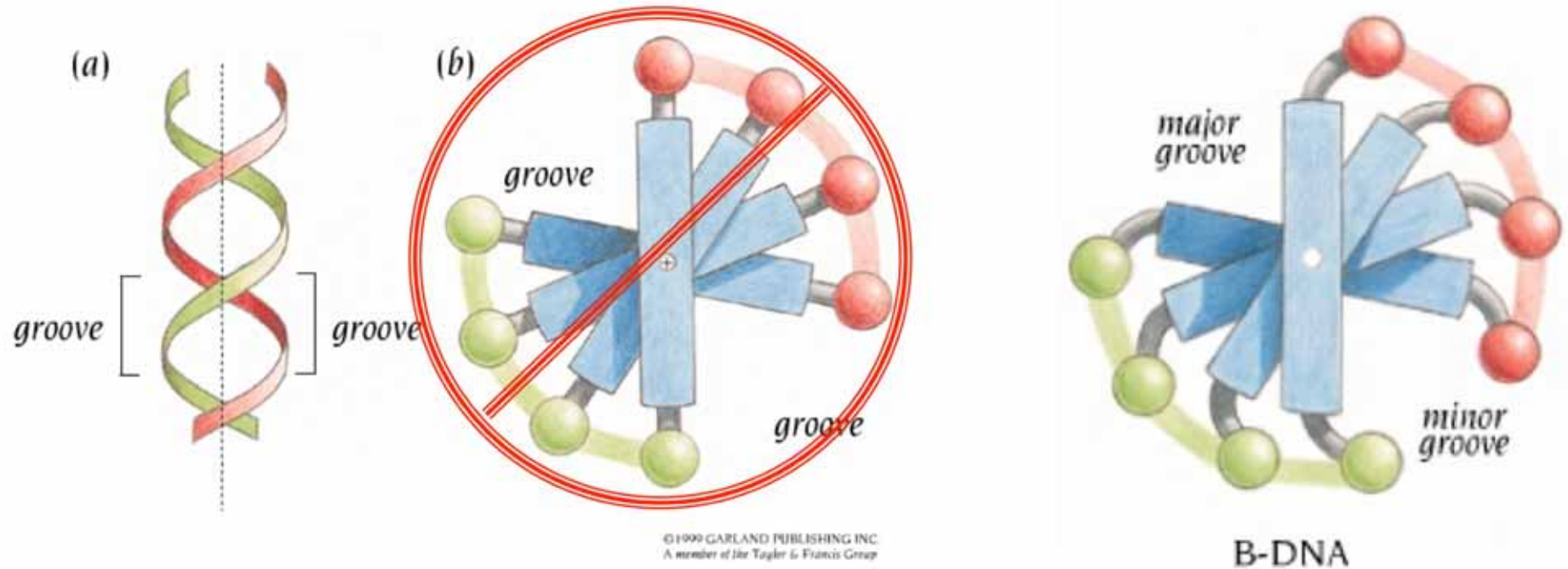
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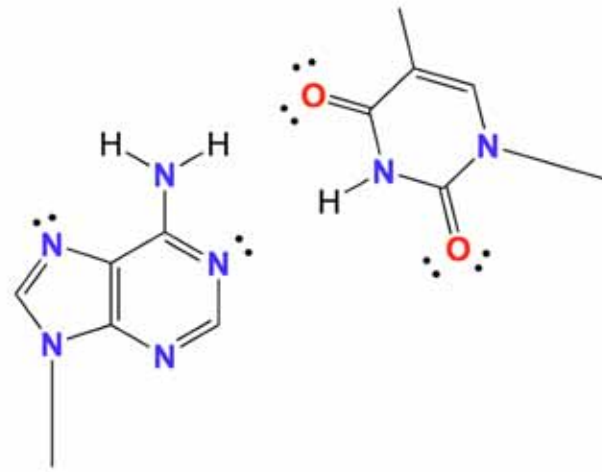
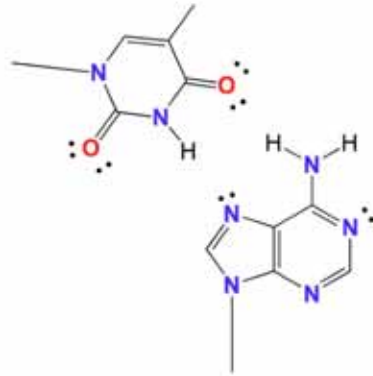
Why *major* and *minor* grooves?



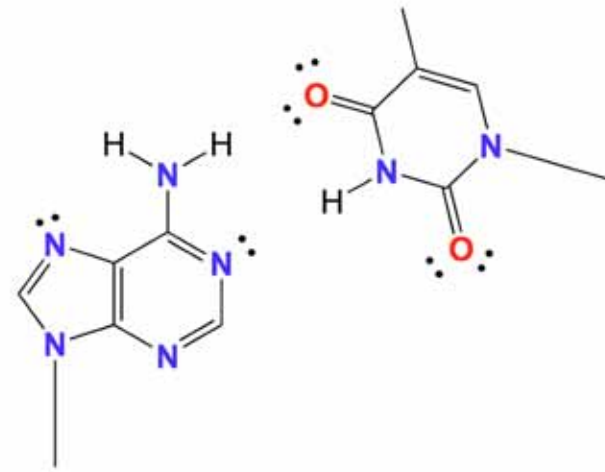
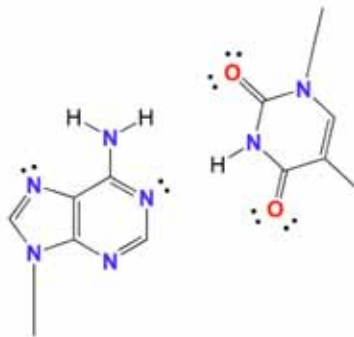
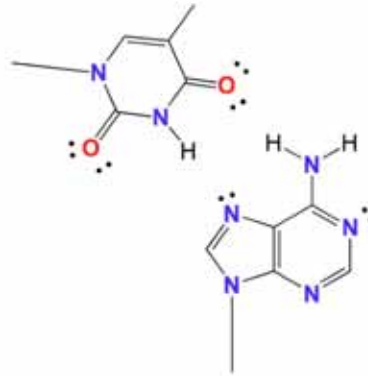
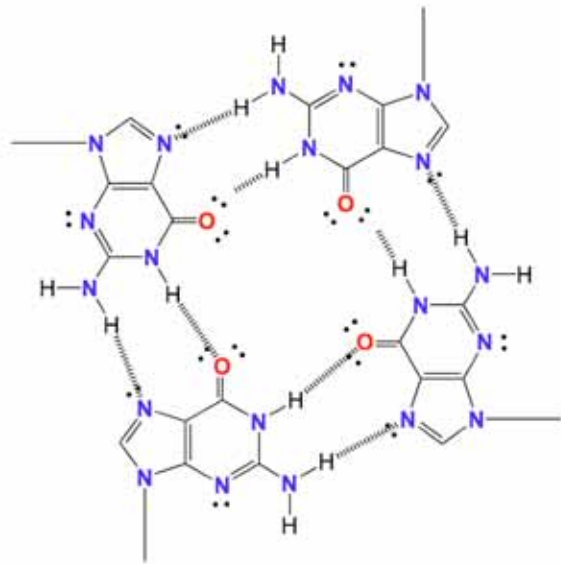
Why *major* and *minor* grooves?



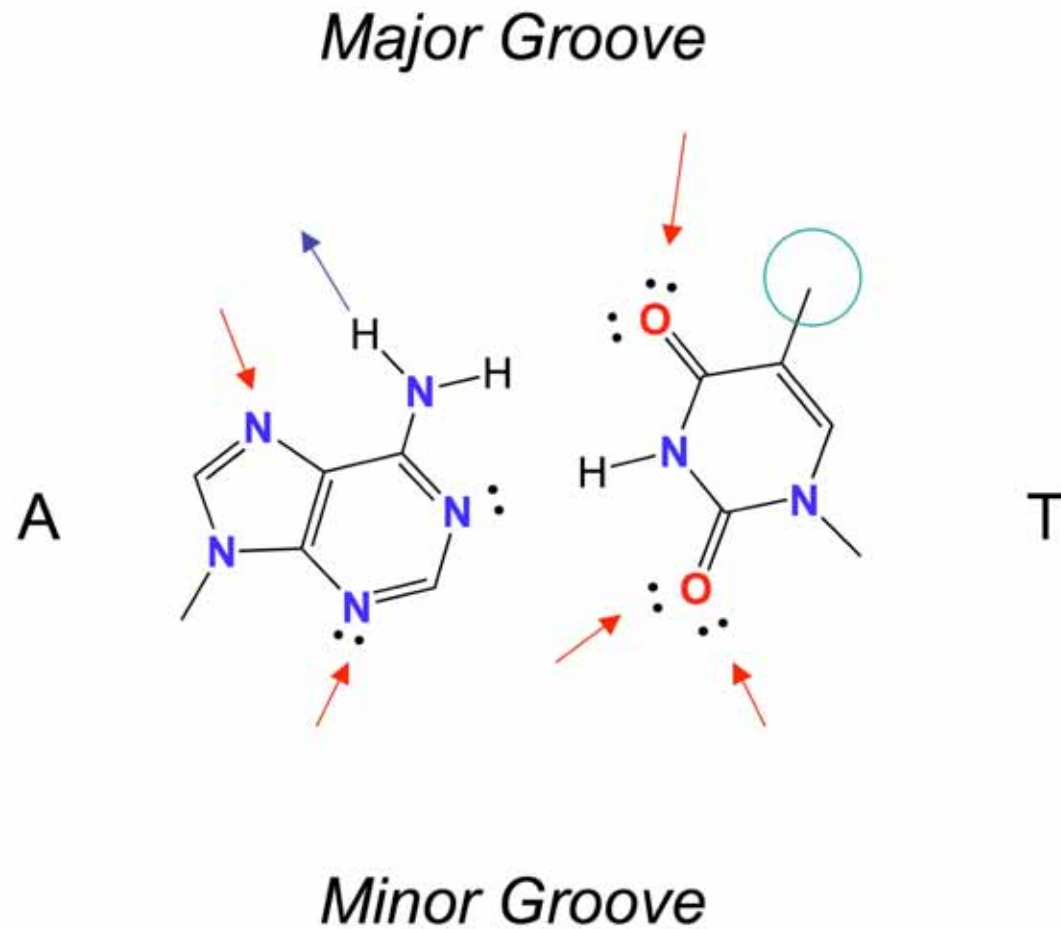
Nucleic Acid - Nucleic Acid Recognition



Nucleic Acid - Nucleic Acid Recognition

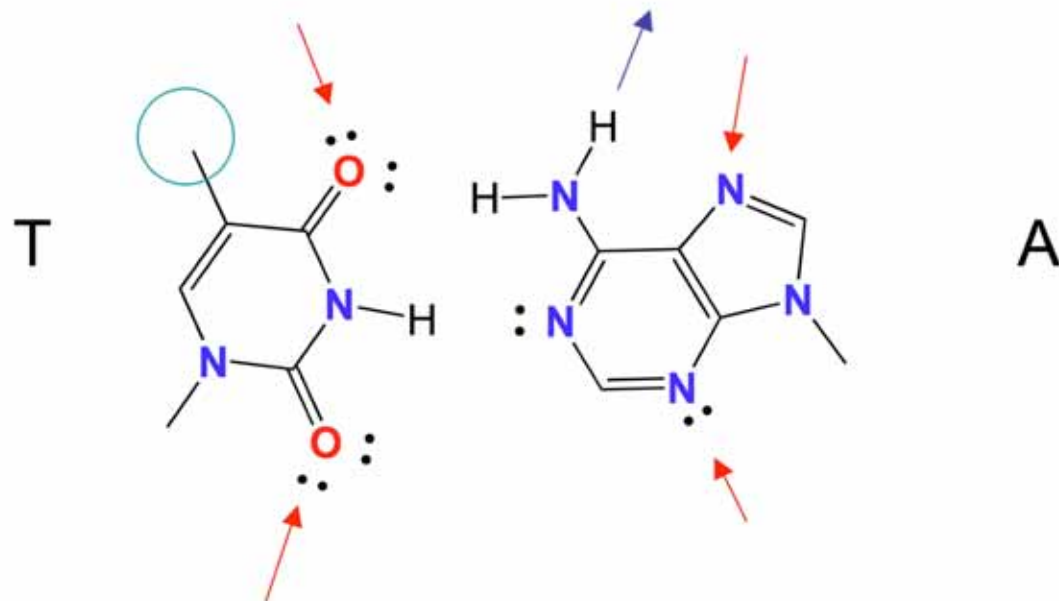


Why is the major groove so good?



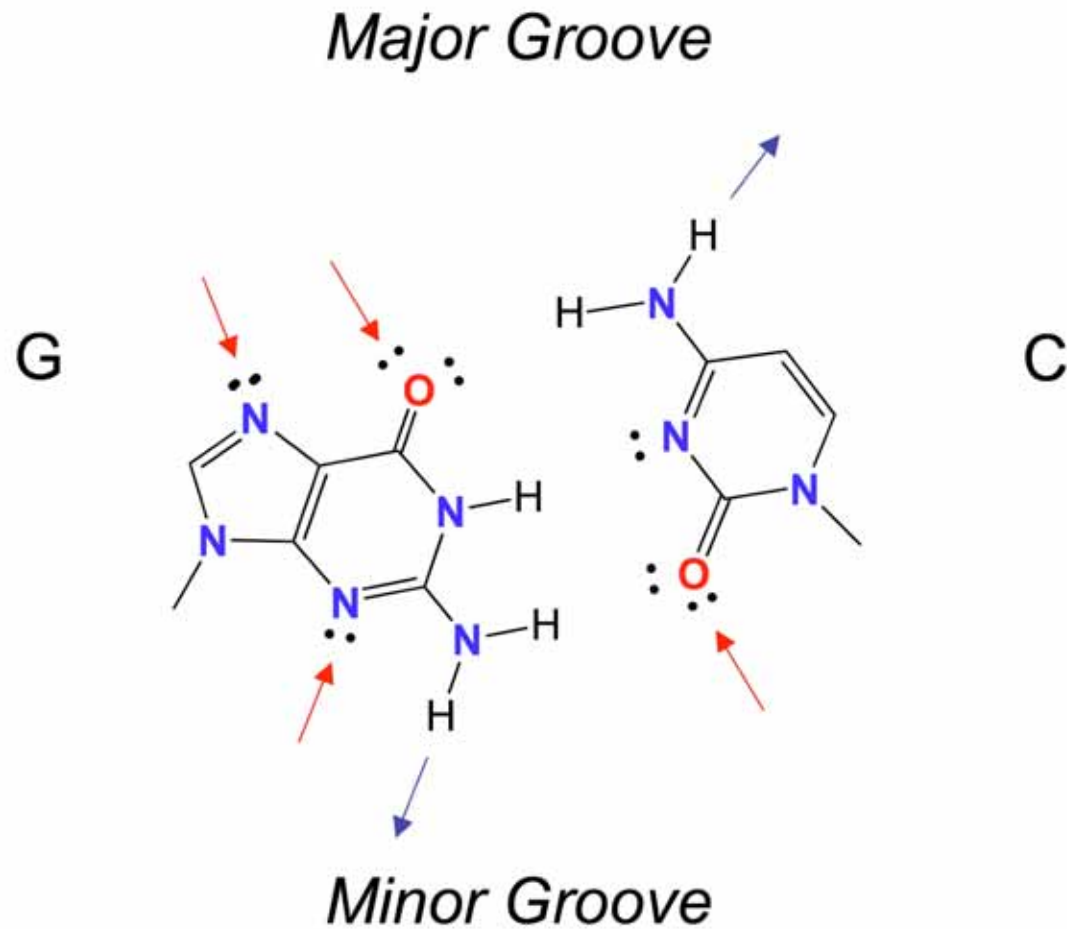
Why is the major groove so good?

Major Groove



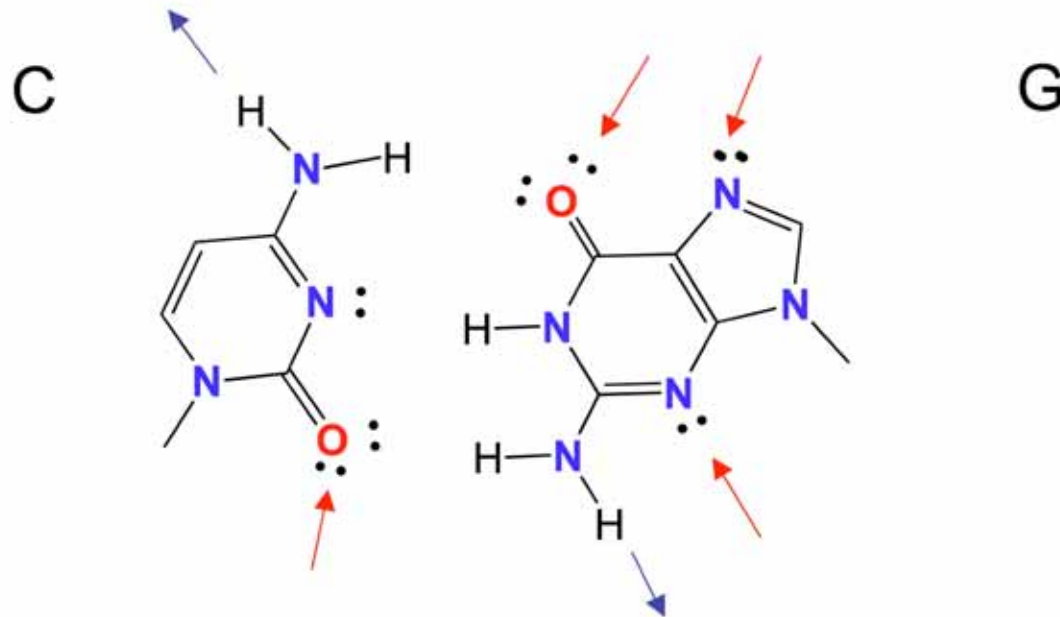
Minor Groove

Why is the major groove so good?



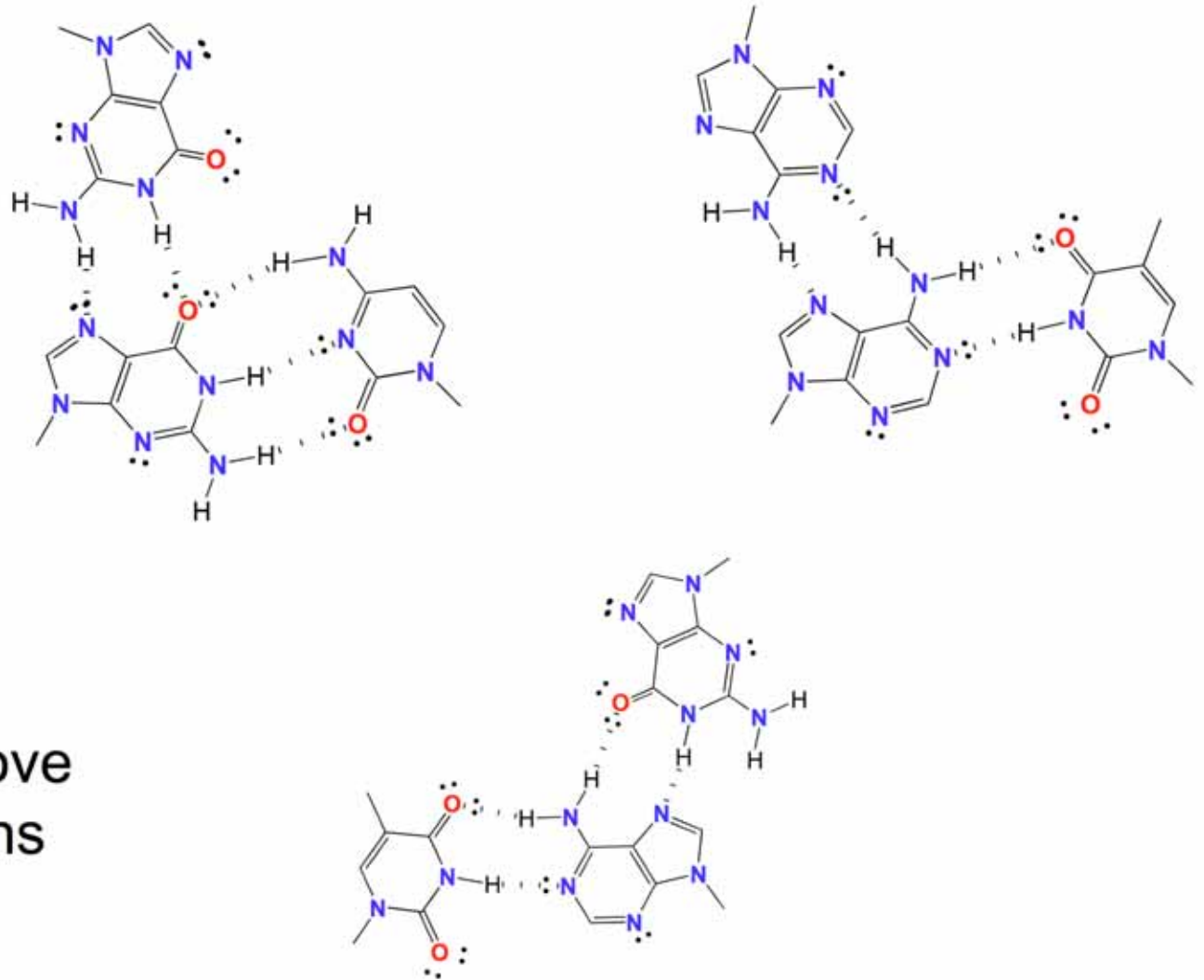
Why is the major groove so good?

Major Groove



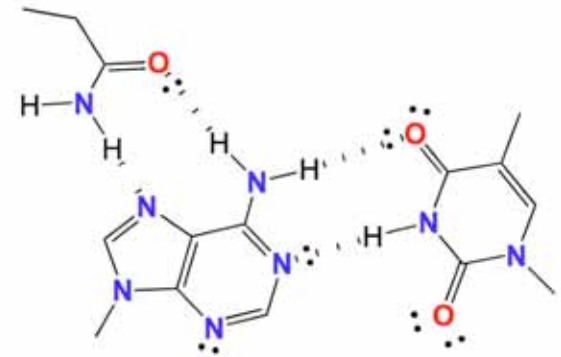
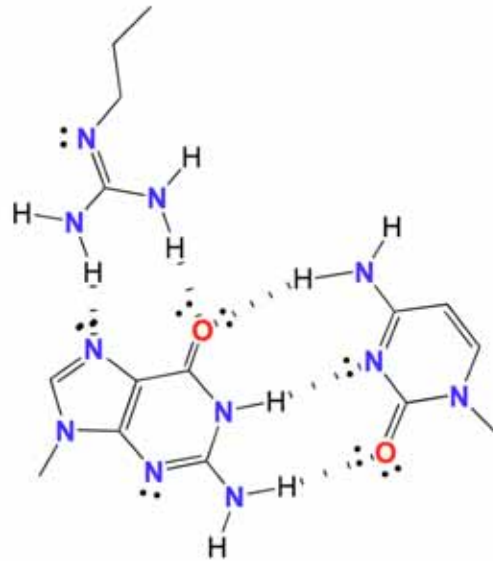
Minor Groove

Nucleic Acid “Triples / Platforms”

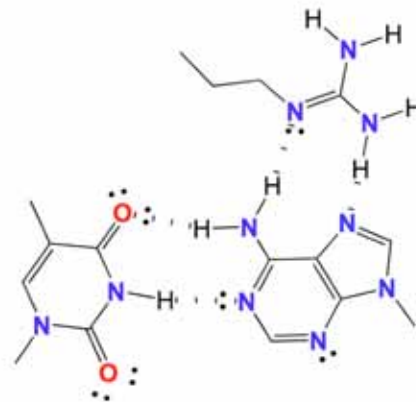


Major Groove
Interactions

Protein - Nucleic Acid Interactions



Major Groove
Interactions



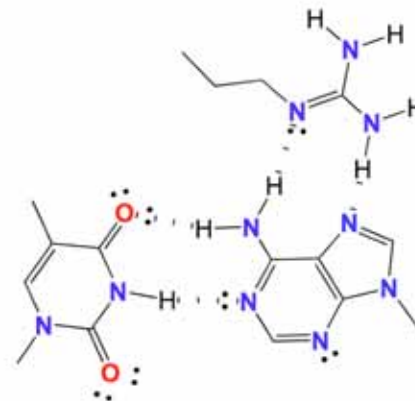
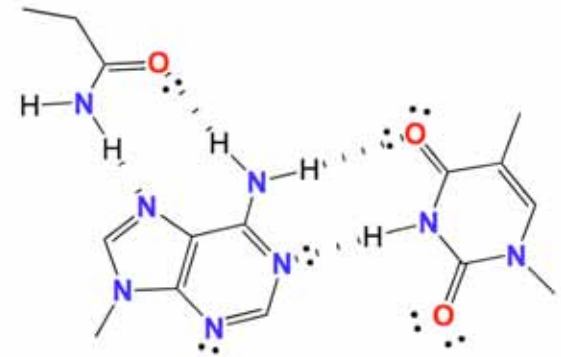
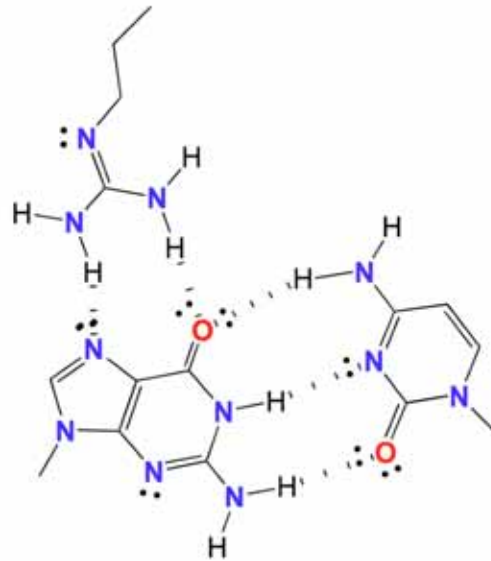
Protein - Nucleic Acid Interactions

Gln

Asn

Arg

Major Groove
Interactions



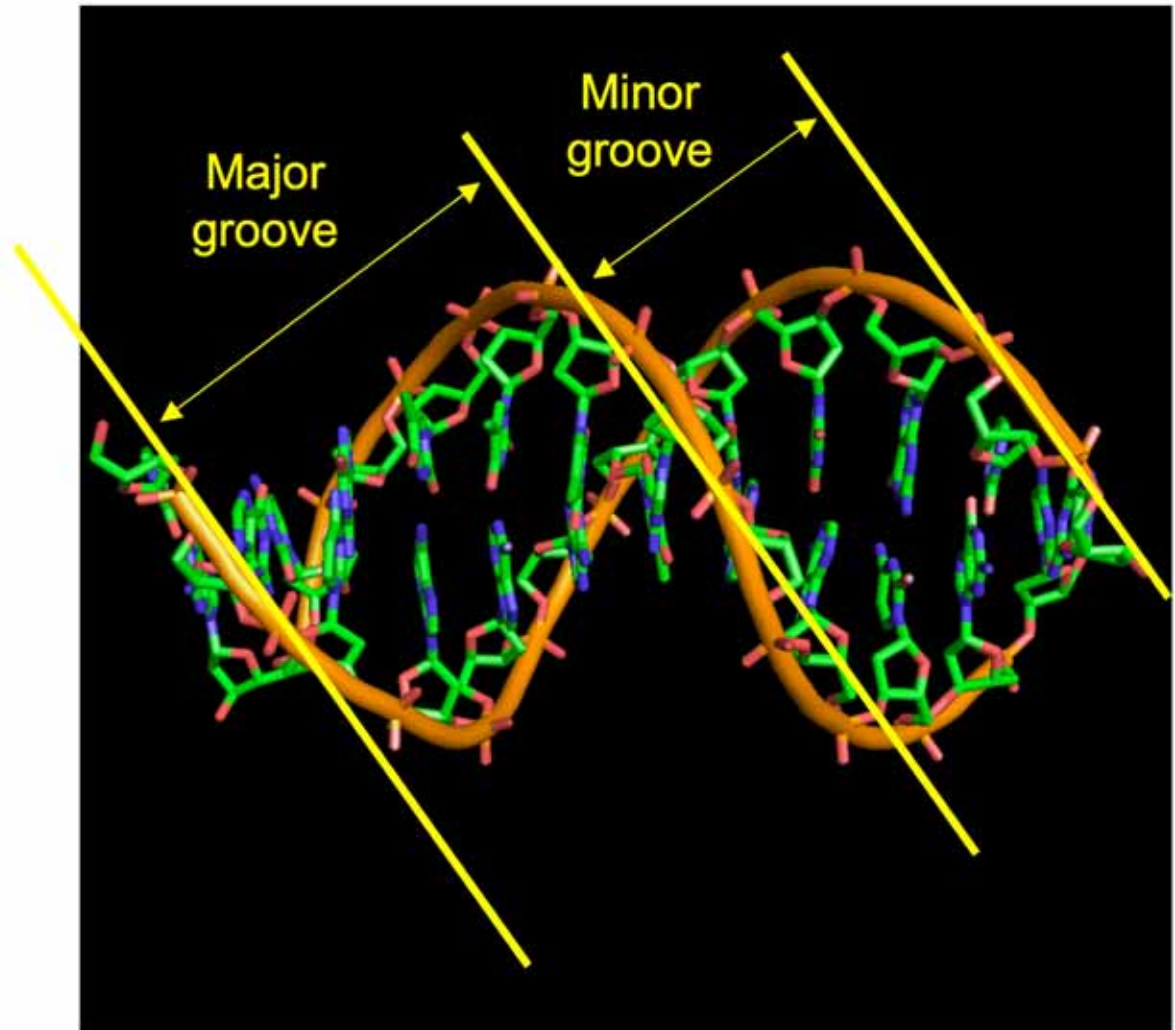
B-form DNA

B-form

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

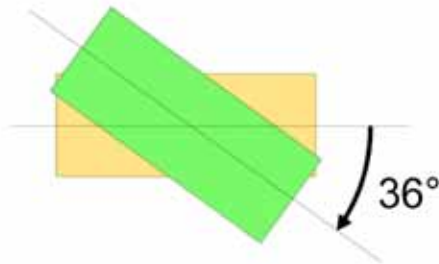
Minor groove width = $5.7\text{\AA}$
Major groove width = $11.7\text{\AA}$

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



B-form DNA

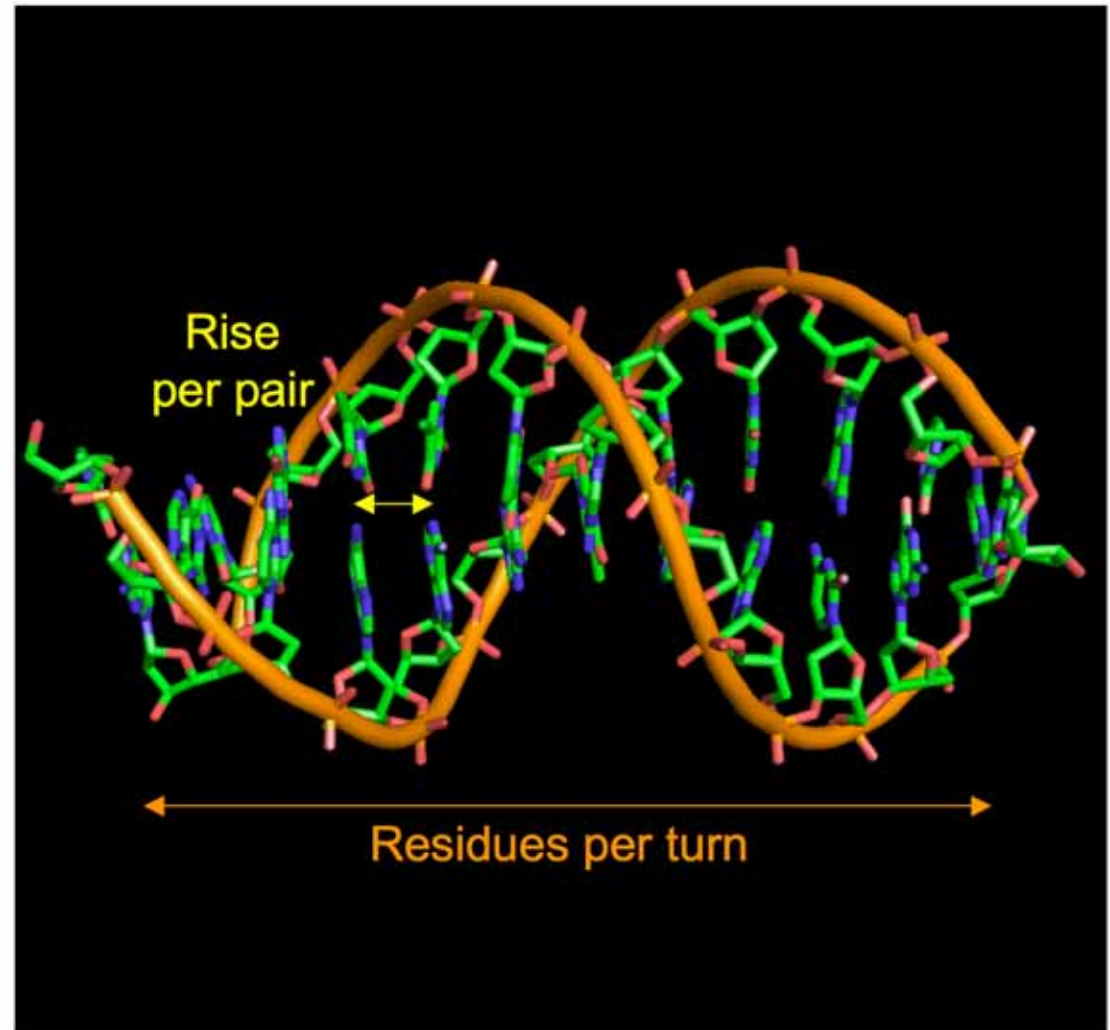
Residues per turn = 10
Twist per base pair = 36°



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

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

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

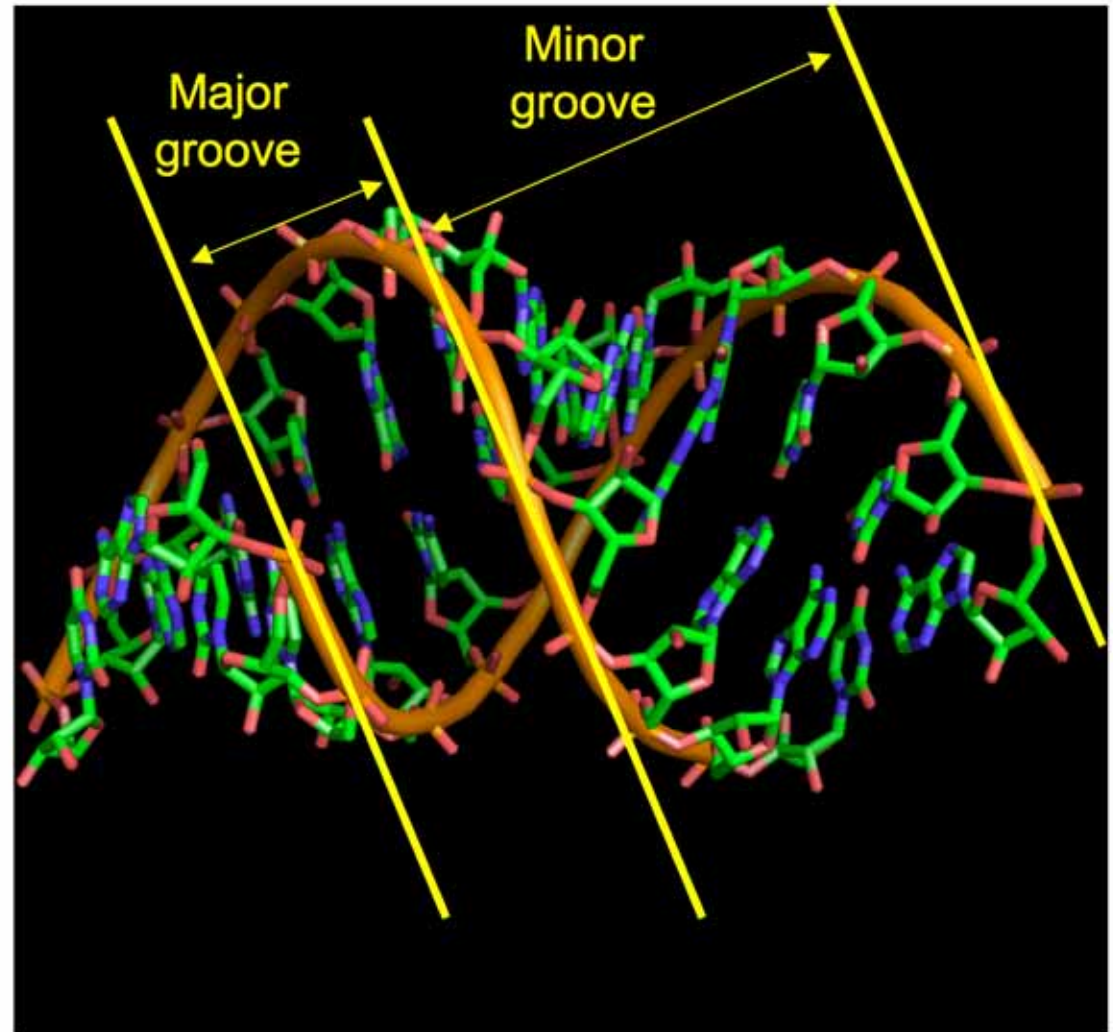


A-form RNA

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

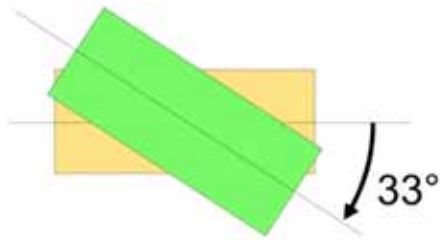
Minor groove width = $11\text{\AA}$
Major groove width = $2.7\text{\AA}$

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



A-form RNA

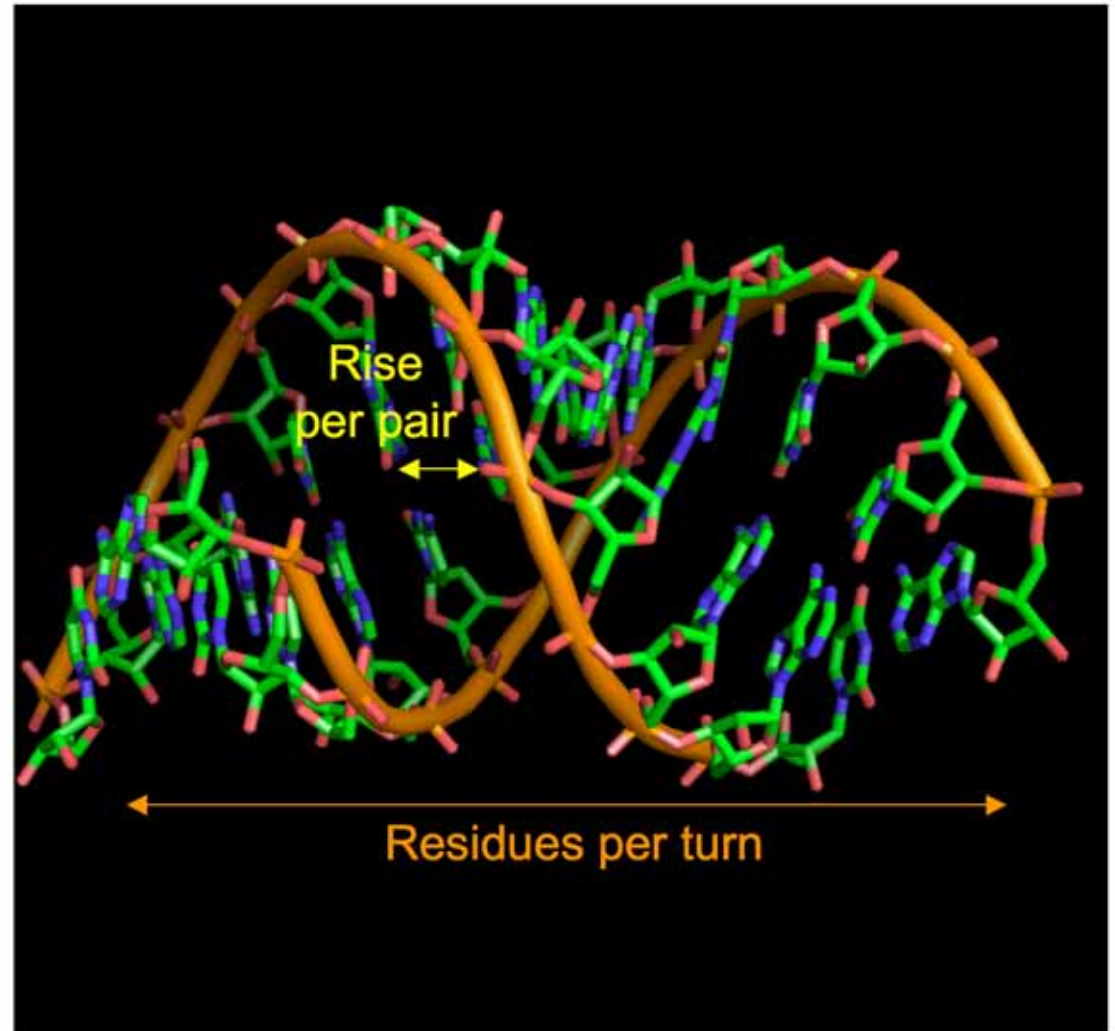
Residues per turn = 11
Twist per base pair = 33°



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

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

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

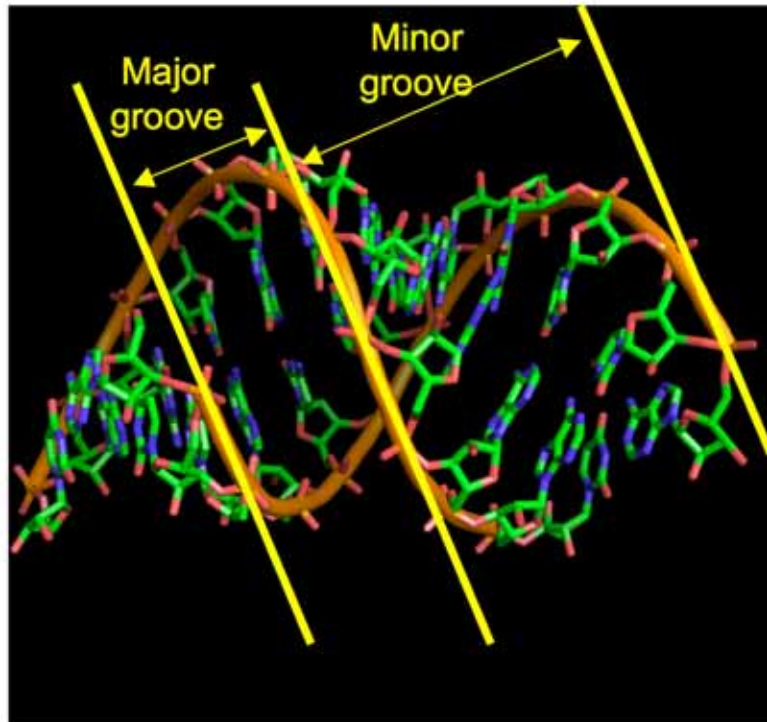


Compare

A-form (RNA)

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

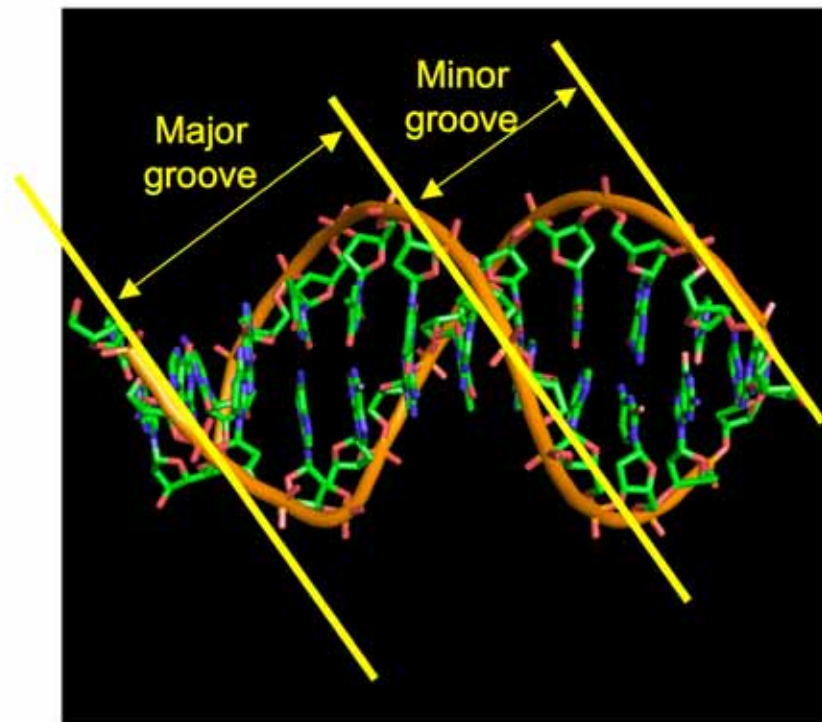
Minor groove depth = $2.8\text{\AA}$
Major groove depth = $13.5\text{\AA}$



B-form (DNA)

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

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



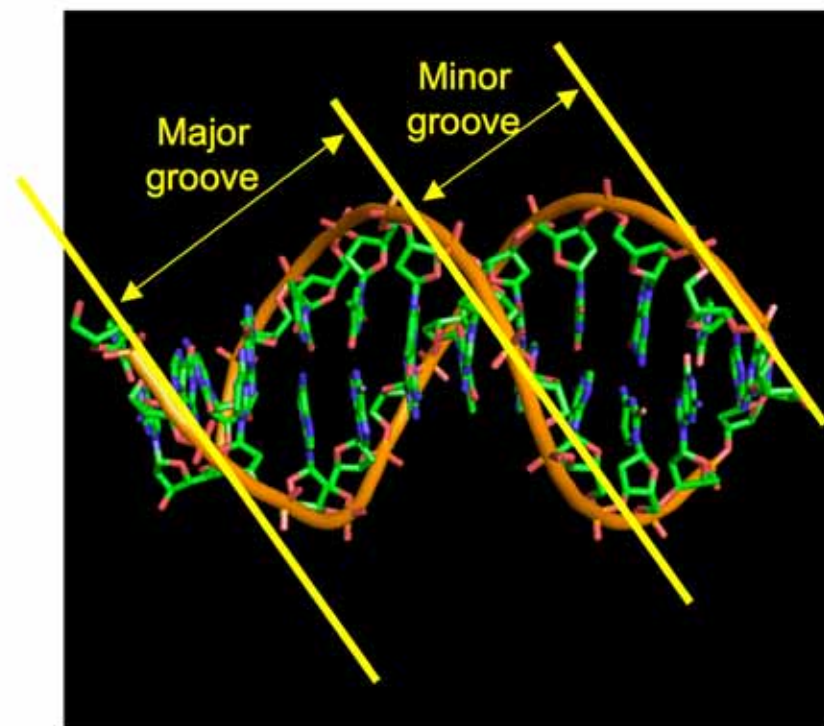
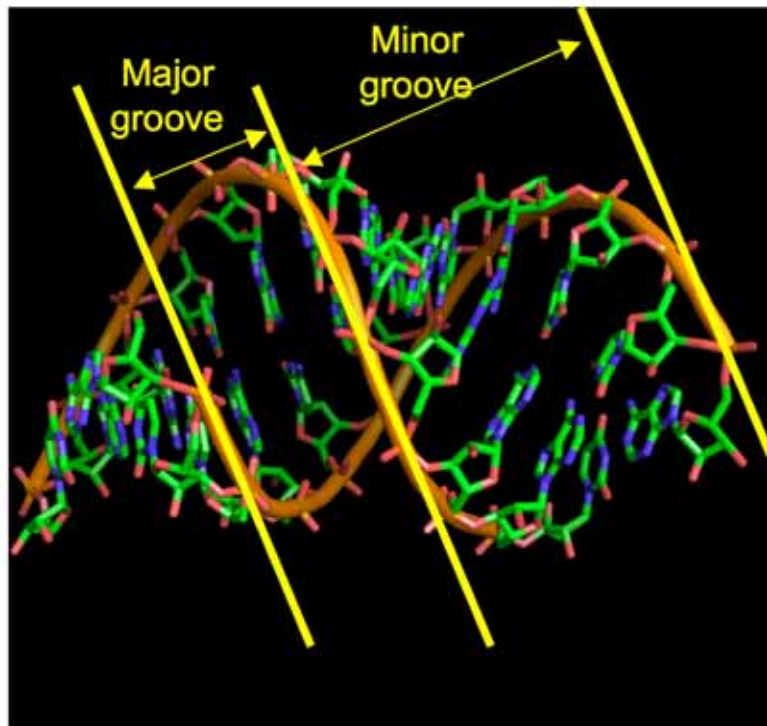
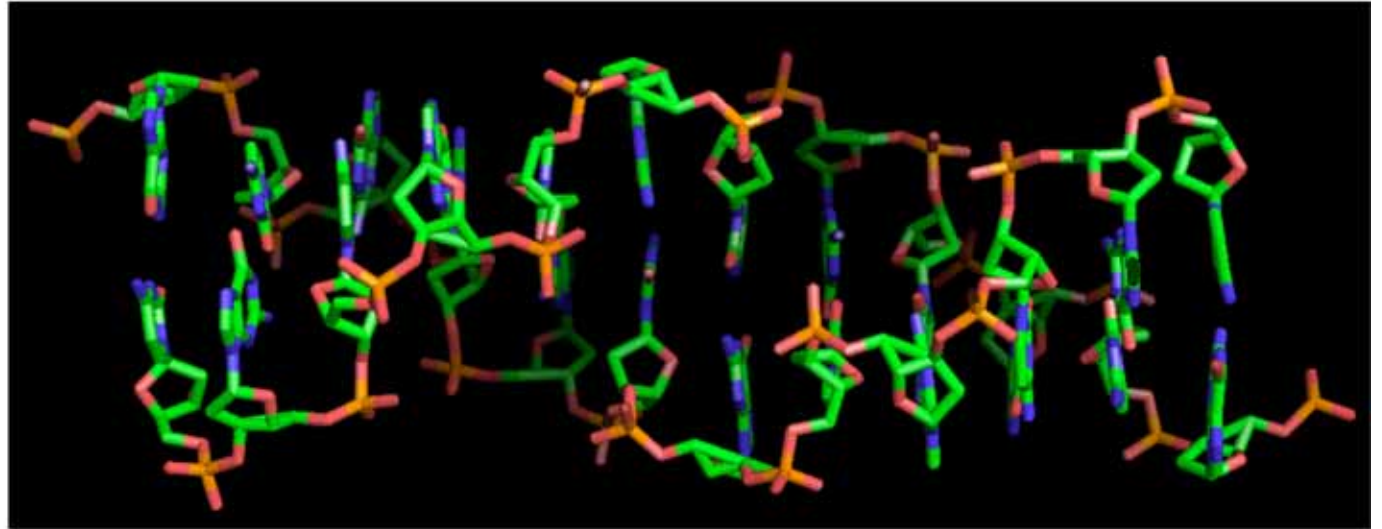
Z-DNA

Residues per turn = 12
Twist per base pair = $-9 / -51^\circ$

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

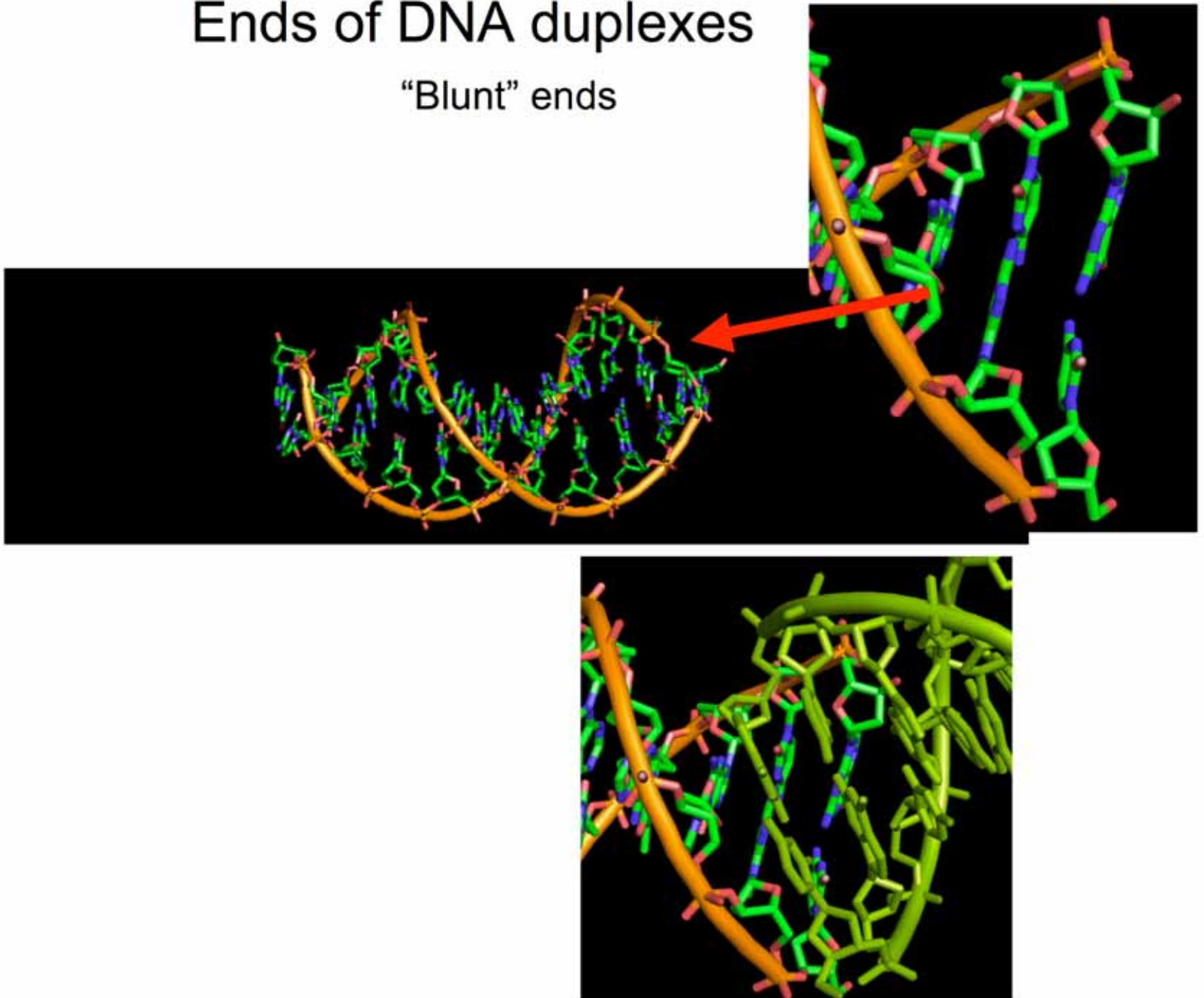
Minor groove width = $2.0\text{\AA}$
Major groove width = $8.8\text{\AA}$

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



Ends of DNA duplexes

"Blunt" ends



Ends of DNA duplexes

“Blunt” ends

