Information Relating to “From Holliday Junctions to Halogen Bonds”: A Seminar by Dr. Pui Shing Ho
9-6-06

Nathan Alexander

Holliday Junctions

- The point of crossing over for two homologous recombinating DNA strands

Mathews, C., van Hold, K.E., Ahern, K. *Biochemistry,* 3. Benjamin/Cummings: San Francisco, 2000.

DNA

- Contains nucleic acid molecules cytosine (C), thymine (T), adenine (A), guanine (G)
  - A pairs with T
  - C pairs with G
- Can adopt different conformations
  - B-DNA: stereotypical helix
  - A-DNA: slightly distorted helix

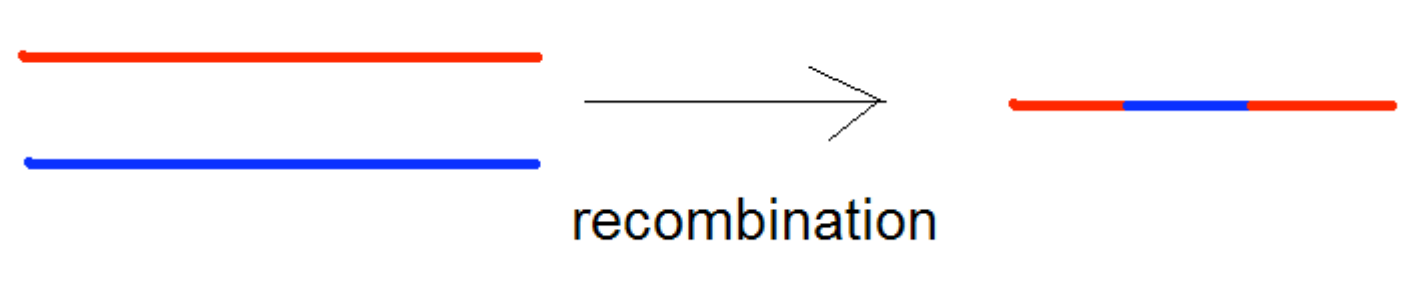
- DNA Sequence: a series of nucleic acids

  ex. CTACGGCA

- Brandt F. Eichman, Jeffery M. Varagason, Blaine H.M. Mooers, and P. Shing Ho (2000) "The Holliday junction in an inverted repeat DNA sequence: Sequence effects on the structure of four-way junctions", *Proc. Natl. Acad. Sci., USA*, **97**, 3971-3976.

Recombination

- The mixing of separate DNA to form new DNA

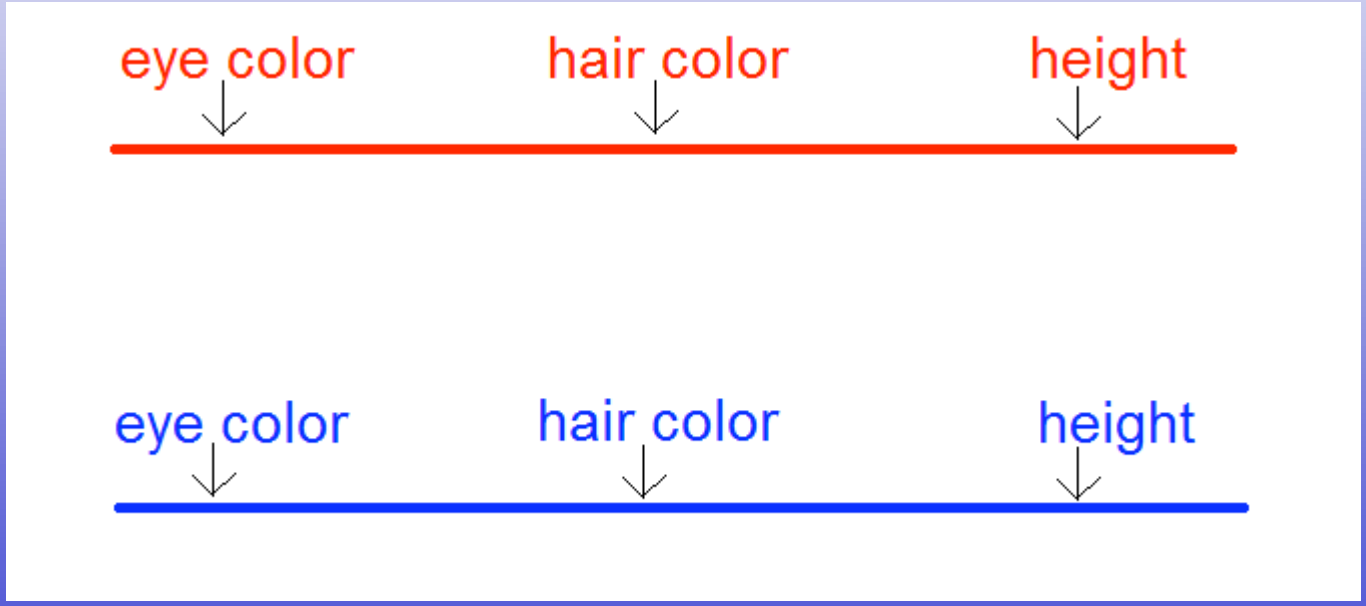


Allows genetic variation and mixing

Mathews, C., van Hold, K.E., Ahern, K. *Biochemistry,* 3. Benjamin/Cummings: San Francisco, 2000.

Homologous DNA

- DNA strands that carry genetic information at the same locus.



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Holliday Junctions

- The point of crossing over for two homologous recombinating DNA strands

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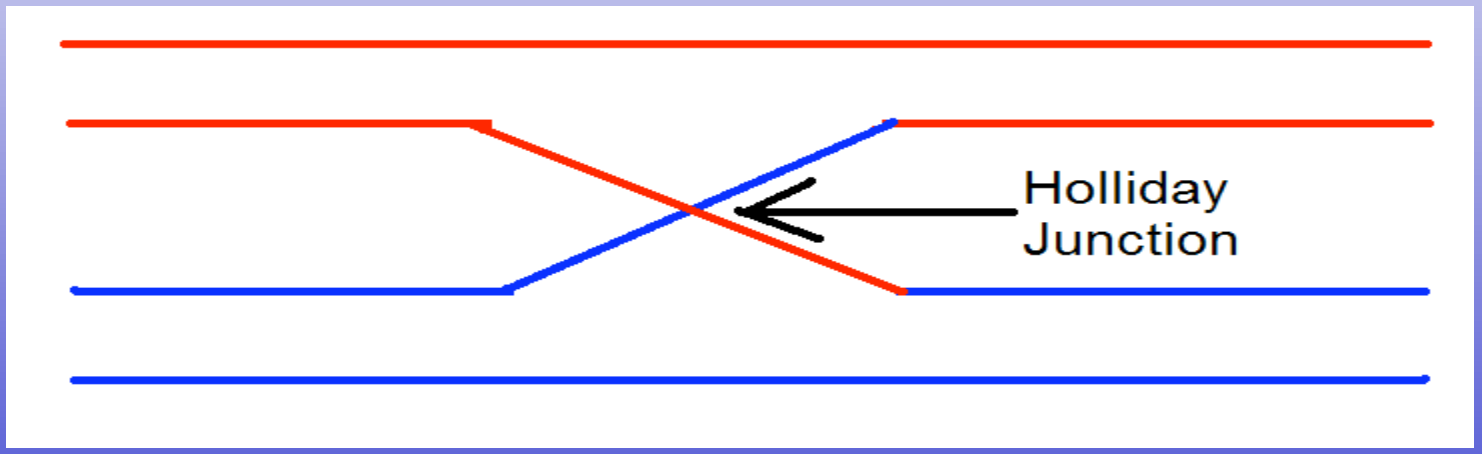
If these are two double-helix lengths of homologous DNA

Then these are two double-helix lengths of homologous DNA during recombination



Mathews, C., van Hold, K.E., Ahern, K. *Biochemistry,* 3. Benjamin/Cummings: San Francisco, 2000.

Holliday Junctions

- First proposed by Robin Holliday in 1964 to explain how homologous recombination takes place
- Holliday junctions are brief intermediates in the process of recombination and are also involved in DNA maintenance/repair

Mathews, C., van Hold, K.E., Ahern, K. *Biochemistry,* 3. Benjamin/Cummings: San Francisco, 2000.

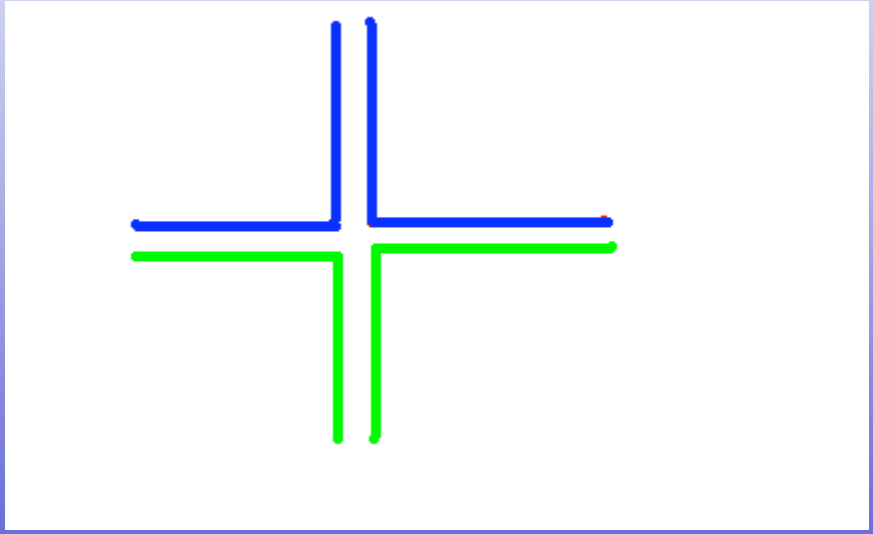
Holliday Junctions

- There are two main types of Holliday junctions
  - Open-X
  - Stacked-X

- Watson, J., Hays, F. A., and Ho, P. S. (2004) "Definitions and analysis of DNA Holliday junction geometry", *Nucleic Acids Res.*, **32:** 3017-3027 (cover article).

Open-X Holliday Junction

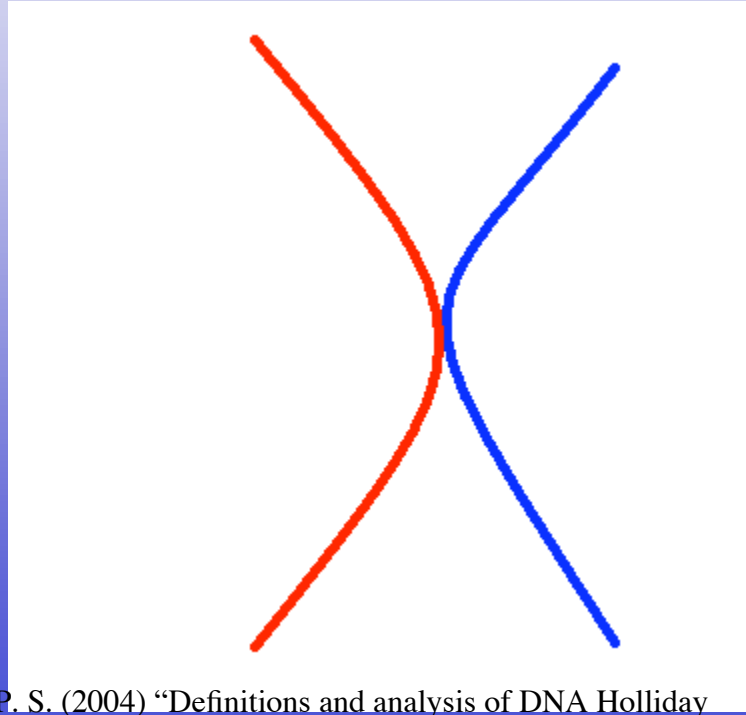
- Imagine as a road intersection
  - Ex. 2 DNA strands during recombination



- Watson, J., Hays, F. A., and Ho, P. S. (2004) "Definitions and analysis of DNA Holliday junction geometry", *Nucleic Acids Res.*, **32:** 3017-3027 (cover article).

Stacked-X Holliday Junction

- Imagine as an X
  - Ex. DNA strands in recombination



- Watson, J., Hays, F. A., and Ho, P. S. (2004) "Definitions and analysis of DNA Holliday junction geometry", *Nucleic Acids Res.*, **32:** 3017-3027 (cover article).

Dr. Pui Shing Ho Recent Papers

"The Holliday junction in an inverted repeat DNA sequence: Sequence effects on the structure of four-way junctions"

- Brandt F. Eichman, Jeffery M. Varagason, Blaine H.M. Mooers, and P. Shing Ho (2000) "The Holliday junction in an inverted repeat DNA sequence: Sequence effects on the structure of four-way junctions", *Proc. Natl. Acad. Sci., USA*, **97**, 3971-3976.

Inverted Repeat DNA Sequence

Inverted Repeat DNA Sequence

- The series of nucleic acids mirrors itself after a certain period but the A's switch to T's and C's switch to G's
  - Ex. CGAATATTCG

- Brandt F. Eichman, Jeffery M. Varagason, Blaine H.M. Mooers, and P. Shing Ho (2000) "The Holliday junction in an inverted repeat DNA sequence: Sequence effects on the structure of four-way junctions", *Proc. Natl. Acad. Sci., USA*, **97**, 3971-3976.

"The Holliday junction in an inverted repeat DNA sequence: sequence effects on the structure of four way junctions"

- Examined the crystal structure of the Holliday junction formed by the inverted repeat DNA sequence CCGGTACCGG
- Had actually wanted to use the sequence for a different experiment but it just happened to form a Holliday junction so they examined it

- Brandt F. Eichman, Jeffery M. Varagason, Blaine H.M. Mooers, and P. Shing Ho (2000) "The Holliday junction in an inverted repeat DNA sequence: Sequence effects on the structure of four-way junctions", *Proc. Natl. Acad. Sci., USA*, **97**, 3971-3976.

Holliday junction of CCGGTACCGG DNA Sequence

- Four of the sequences come together to form a stacked-X type junction
- Examined interactions of the sequences at the junction
- Conclude ACC sequence is key to junction formation

- Brandt F. Eichman, Jeffery M. Varagason, Blaine H.M. Mooers, and P. Shing Ho (2000) "The Holliday junction in an inverted repeat DNA sequence: Sequence effects on the structure of four-way junctions", *Proc. Natl. Acad. Sci., USA*, **97**, 3971-3976.

Dr. Pui Shing Ho Recent Papers

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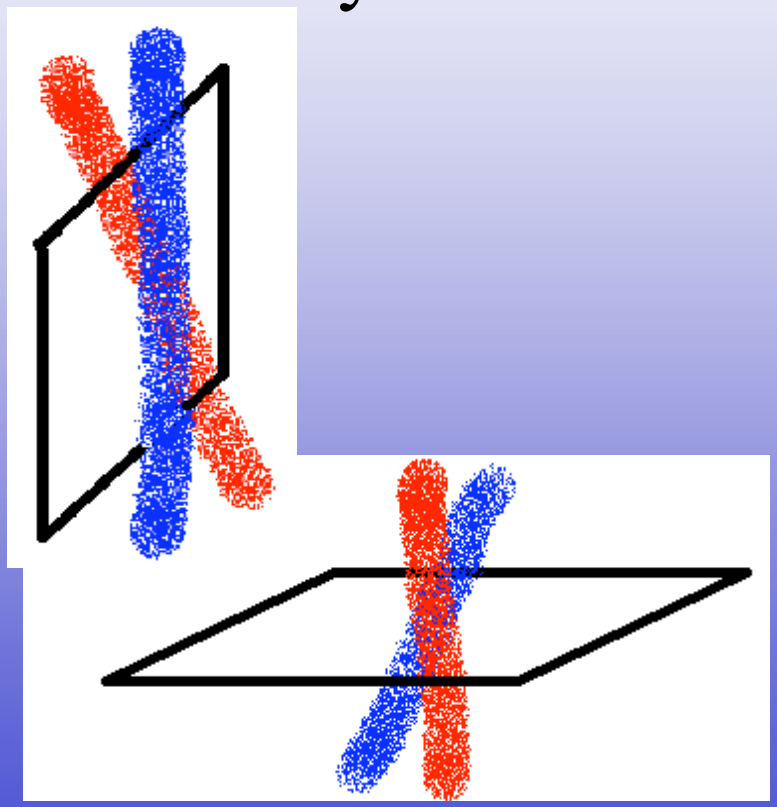
Watson, J., Hays, F. A., and Ho, P. S. (2004) "Definitions and analysis of DNA Holliday junction geometry", *Nucleic Acids Res.*, **32:** 3017-3027 (cover article).

- Holliday junction geometry varies
- Defined parameters that can be used to describe Holliday junctions so that solved structures and any future solved structures can be compared.
- Also described the methodology for obtaining the parameters.

- Watson, J., Hays, F. A., and Ho, P. S. (2004) "Definitions and analysis of DNA Holliday junction geometry", *Nucleic Acids Res.*, **32:** 3017-3027 (cover article).

Holliday junction geometry

- Junction geometrically is defined by two planes
  - "resolving plane"
    i.e. vertical plane
  - "bisecting plane
    i.e. horizontal plane



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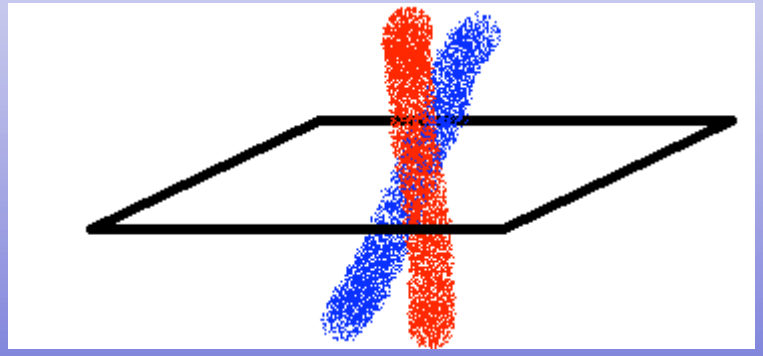
Describing a Holliday junction

- J_{slide}
- Interduplex Angle
- J_{twist}
- J_{roll}

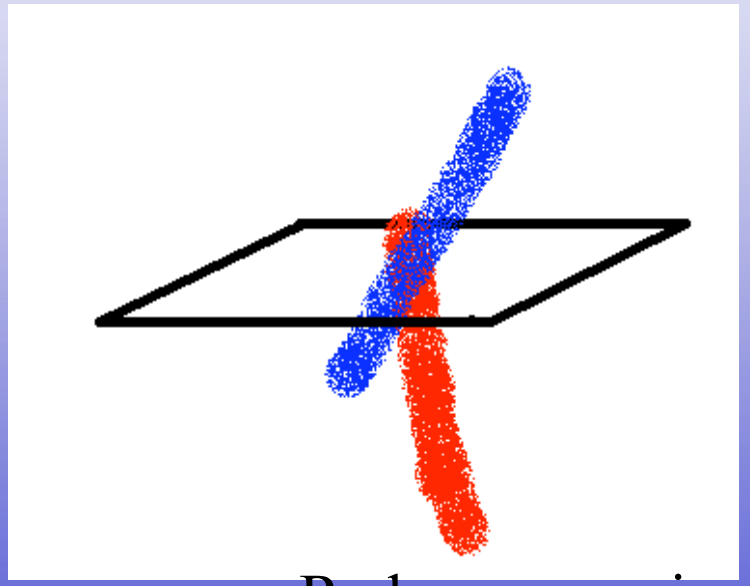
- Watson, J., Hays, F. A., and Ho, P. S. (2004) "Definitions and analysis of DNA Holliday junction geometry", *Nucleic Acids Res.*, **32:** 3017-3027 (cover article).

J_{slide}

- How far up or down one DNA sequence is relative to the other



Sequences are vertically aligned

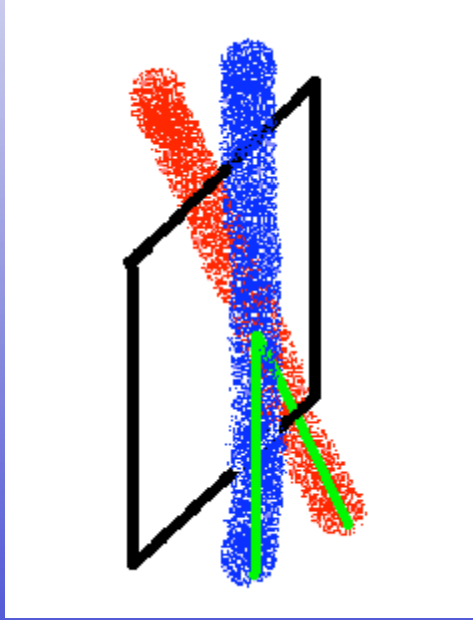


Red sequence is slid downward

- Watson, J., Hays, F. A., and Ho, P. S. (2004) "Definitions and analysis of DNA Holliday junction geometry", *Nucleic Acids Res.*, **32:** 3017-3027 (cover article).

Interduplex Angle (IDA)

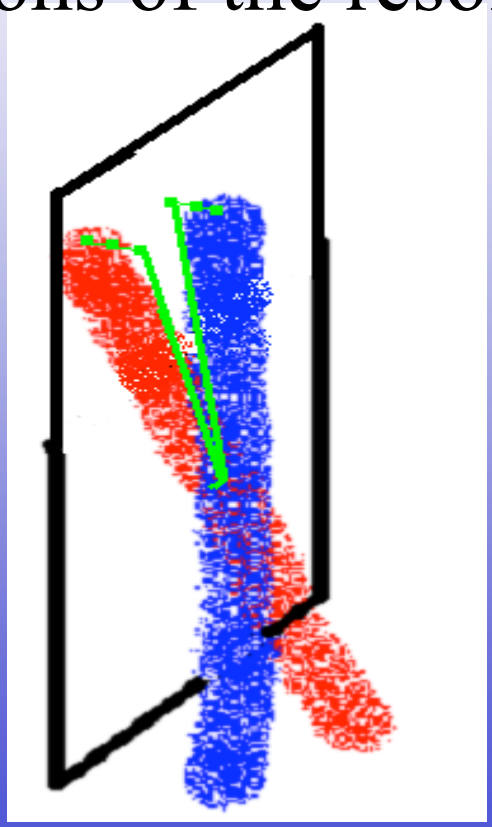
- Angle formed by the DNA sequences' helices with the center Holliday junction as the vertex



- Watson, J., Hays, F. A., and Ho, P. S. (2004) "Definitions and analysis of DNA Holliday junction geometry", *Nucleic Acids Res.*, **32:** 3017-3027 (cover article).

J_{twist}

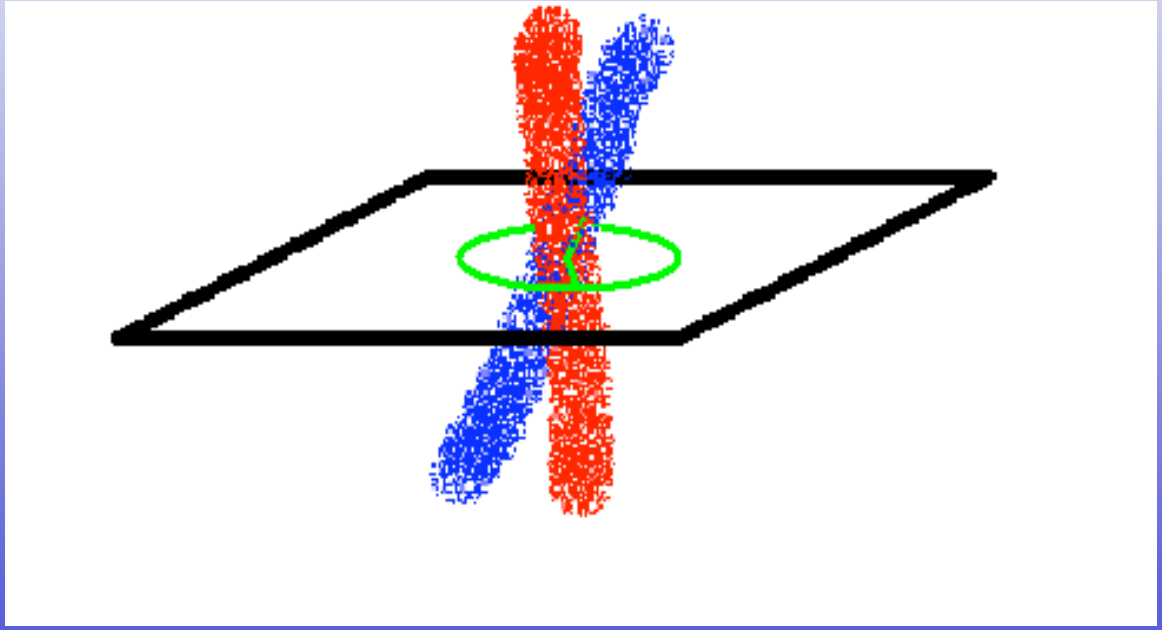
- The angle between the DNA sequences as measured by squishing the helical axes onto the two dimensions of the resolving plane



- Watson, J., Hays, F. A., and Ho, P. S. (2004) "Definitions and analysis of DNA Holliday junction geometry", *Nucleic Acids Res.*, **32:** 3017-3027 (cover article).

J_{roll}

- The angle between the DNA sequences as measured along the bisecting plane



- Watson, J., Hays, F. A., and Ho, P. S. (2004) "Definitions and analysis of DNA Holliday junction geometry", *Nucleic Acids Res.*, **32:** 3017-3027 (cover article).

Dr. Pui Shing Ho Relevant Papers

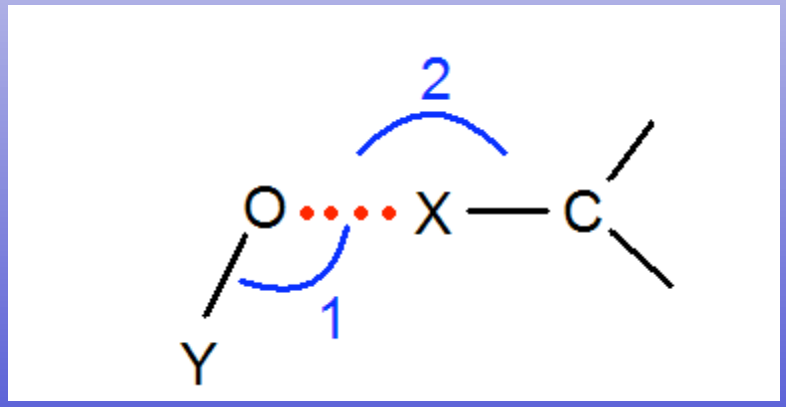
- Auffinger, P., Hays, F. A., Westhof, E., and Ho, P. S. (2004) “Halogen bonds in biological molecules”, *Proc. Natl. Acad. Sci., USA*, **101**: 16789-16794.

Auffinger, P., Hays, F. A., Westhof, E., and Ho, P. S. (2004) "Halogen bonds in biological molecules", *Proc. Natl. Acad. Sci., USA*, **101**: 16789-16794.

- Halogens are important throughout biology
  - Ex. Thyroid hormones are halogenated molecules
- Could not explain the conformations of halogenated DNA sequences due to lack of knowledge about halogen bonds
- Current study closes knowledge gap by
  - investigating geometry of halogen bonds in biological molecules
  - Investigating potential for electron movement (polarizability) within halogen atoms in a biological environment

Halogen Bonding

- Halogens include F, Cl, Br, I
  - Halogenated molecule contains F, Cl, Br, or I
- Similar to hydrogen bonding
- Geometry defined by Θ_1 Θ_2

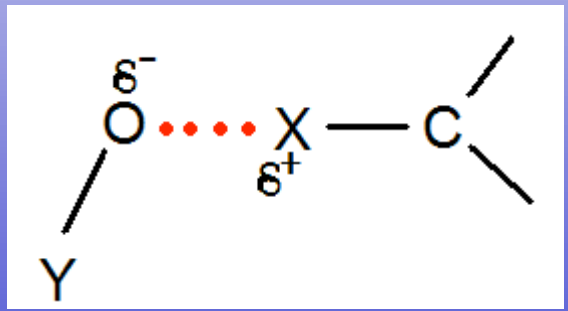


Y=C, P, or S
X=F, Cl, Br, or I
•••• = Halogen bond

- Auffinger, P., Hays, F. A., Westhof, E., and Ho, P. S. (2004) "Halogen bonds in biological molecules", *Proc. Natl. Acad. Sci., USA*, **101**: 16789-16794.

Halogen Bonding

- In order to halogen bond, the halogen must be able to be polarized so that it has a partial positive charge available to be attracted to the partial negative charge of the opposing oxygen



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Halogen Polarizability

- Electrostatic potential
  - Quantum mechanical calculation that can provide information about polarization of an atom
- F < Cl < Br < I
- The study shows that iodine is involved in the most halogen bonding between biological molecules, which makes sense since it is most polarizable

- Auffinger, P., Hays, F. A., Westhof, E., and Ho, P. S. (2004) "Halogen bonds in biological molecules", *Proc. Natl. Acad. Sci., USA*, **101**: 16789-16794.

Further Pui Shing Ho Papers

- **If you are interested, listed below are a few more papers you could look at:**

- Hays, F.A., Teegarden, A., Jones, Z., Harms, M., Raup, D., Watson, J., Cavaliere, E., and Ho, P.S. (2005) "How sequence defines structure: A crystallographic map of DNA structure and conformation", *Proc. Natl. Acad. Sci., USA*, **102**: 7157-7162.

- Hays, F. A., Schirf, V., Ho, P.S., and Demeler, B. (2006) "Solution formation of Holliday junctions in inverted-repeat sequences", *Biochemistry*, **45**, 2467-2471.

- Khuu, P., Voth, A. R., Hays, F. A., and Ho, P. S. (2006) "The stacked-X DNA Holliday junction and protein recognition", *J. Mol. Recog.*, **19**: 234-242.

Thank You!