Genome Folding and Function
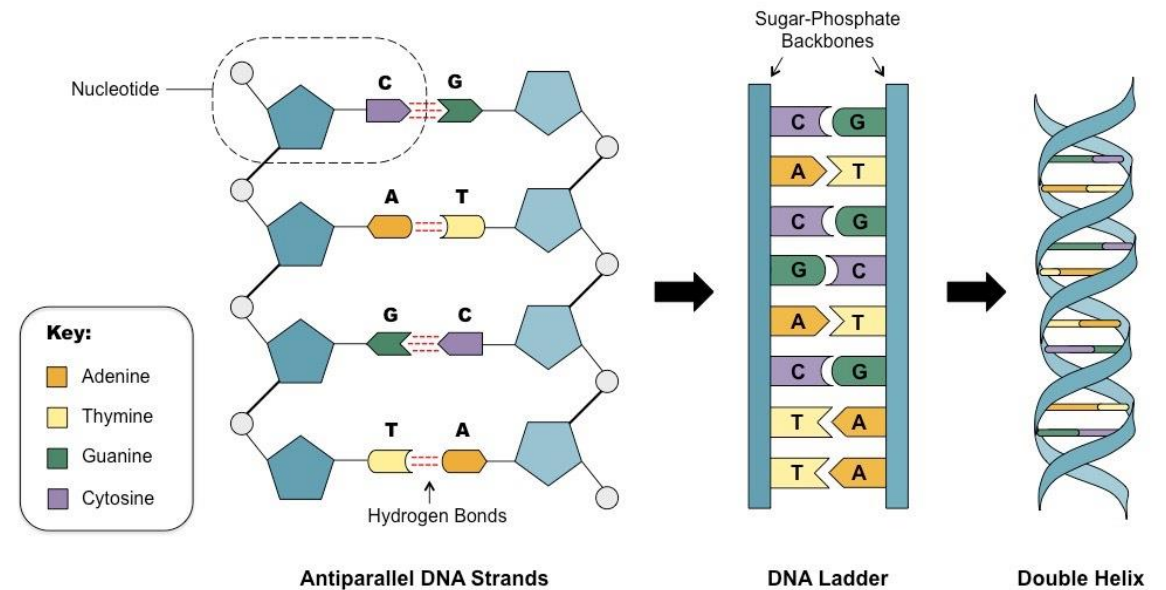
ZOE WEFERS

MENTOR: WILMA OLSON

# DNA: A Biological View

- DNA is a biological molecule that encodes genetic information

- 4 types of nucleic acid bases, adenosine (A), cytosine (C), guanosine (G), thymidine (T)
  - Base Pairs: A pairs with T, and C pairs with G

- Double helix structure - stiff
  - CACGACTT

- Bending and twisting DNA minicircles changes its elastic energy – how can we model this?

- DNA circles – found in cancers, used to deliver genetic messages, packaging in nucleus

Nucleotide

C G

A T

G C

T A

Key:
- Adenine
- Thymine
- Guanine
- Cytosine

Hydrogen Bonds

Antiparallel DNA Strands

Sugar-Phosphate Backbones

C G
A T
C G
G C
A T
C G
T A
T A

DNA Ladder

Double Helix

# DNA: A Mathematical View

- Model each base pair as rigid rectangle
  - Relation between adjacent base pairs can be represented by 6 parameters: Shift, Slide, Rise, Tilt, Roll, Twist

- Total elastic energy = sum of the elastic energy of base pair steps

- Elastic energy is sequence dependent- by dimers
  - AA, CC, AC, CA,

Shift (Dx)

Tilt (τ)

Slide (Dy)

Roll (ρ)

Rise (Dz)

Twist (ω)
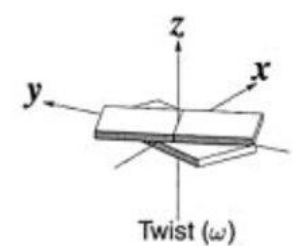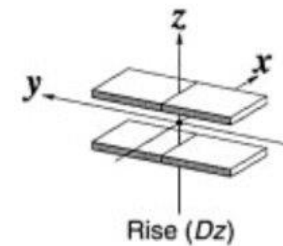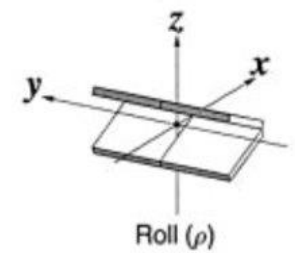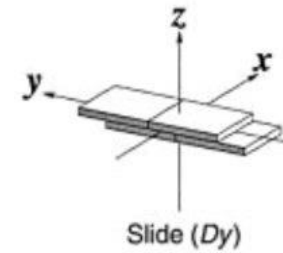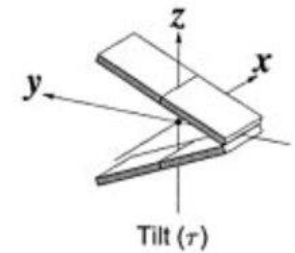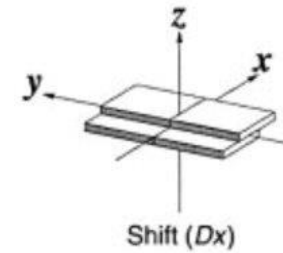
emDNA Software

- Core Idea: DNA will move to achieve least elastic energy
  - Can be modeled by gradient descent-like algorithm

- Can slowly freeze certain parameters to model protein binding to DNA
  - Effects the minimum energy conformation

- Can impose end conditions --> allow us to model DNA minicircles and loops

- Currently minimizes elastic energy with respect to dimer optimal conditions
  - New evidence that optimal conditions vary by tetramers
  - C-AT-G different than C-AT-C
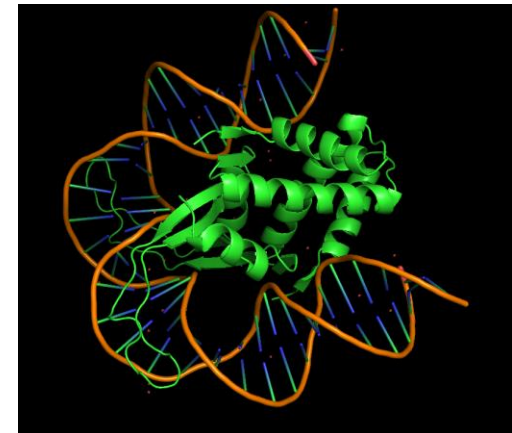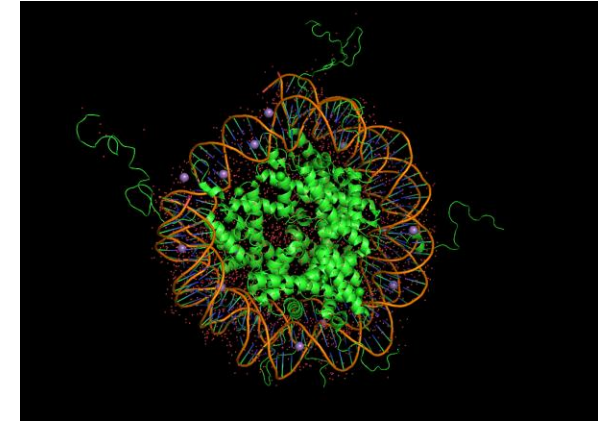
My Goals:

- Adapt the program to minimize the elastic energy with respect to energetically optimal tetrameric base-pair steps

- Use the modified program to see how the minimum energy conformations achieved by specfic DNA sequences changes
  - Small changes in twist (1-2º) , but times 150 base pairs --> significant effects on final conformation

References and Acknowledgments

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