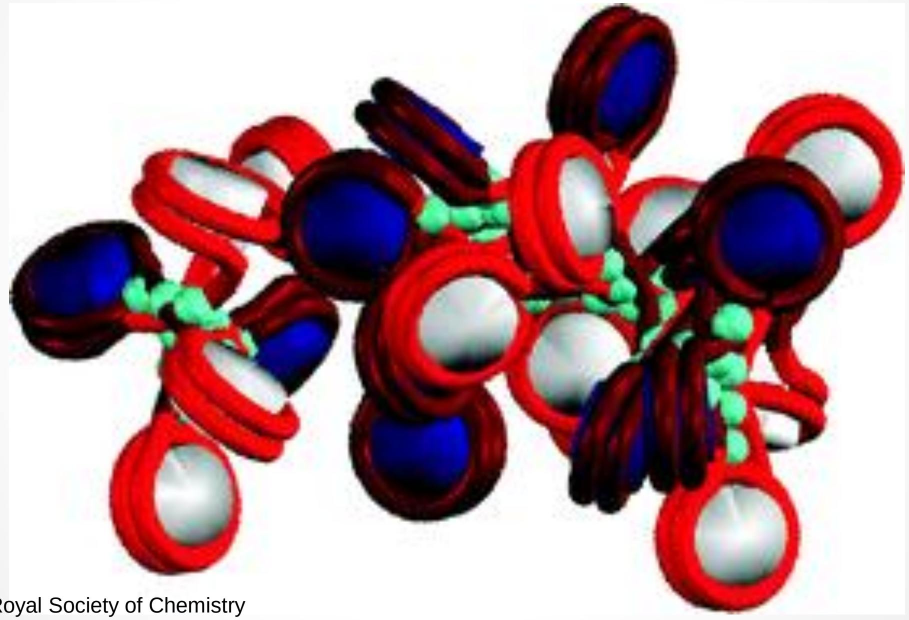
Chromatin Folding



Royal Society of Chemistry

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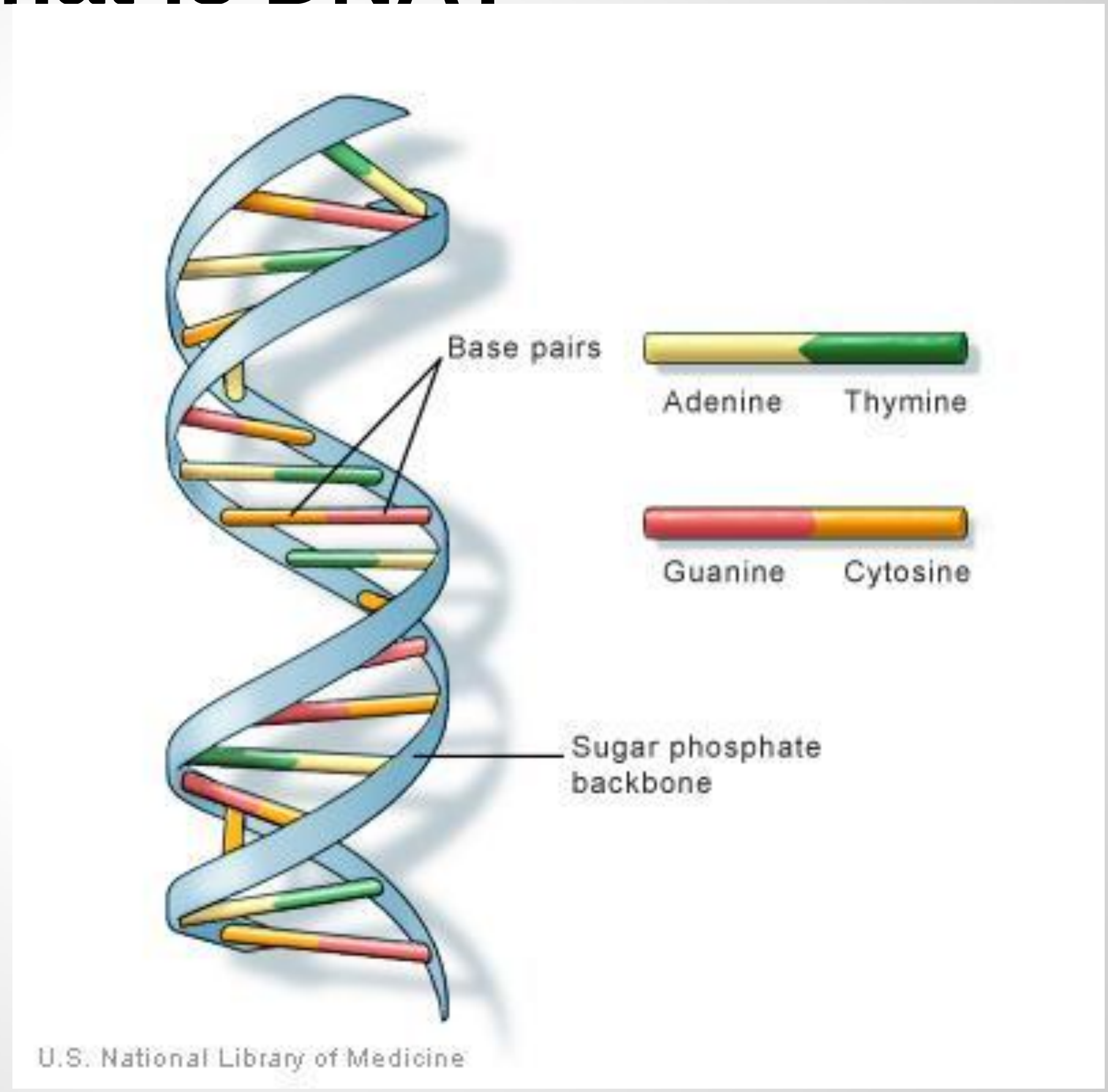
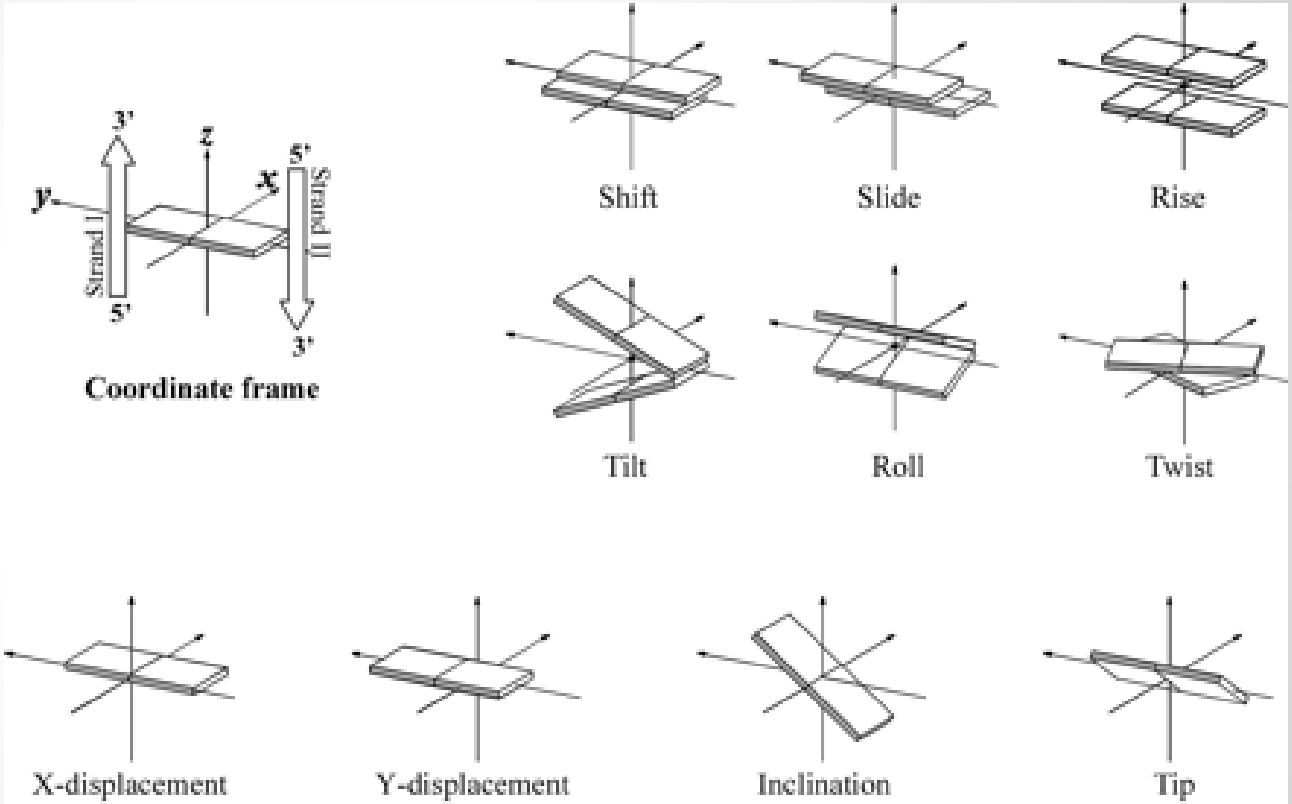
What is DNA?

- Carrier of genetic information
- About 2m long, DNA is fit into a cell nucleus with diameter 10 microns.
- Same DNA in every cell of our body
- Double-Helical structure that repeats for every 10bp
- Consists of a backbone (sugar-phosphate) and base pairs (adenine (A), thymine (T), guanine (G), and cytosine (C))



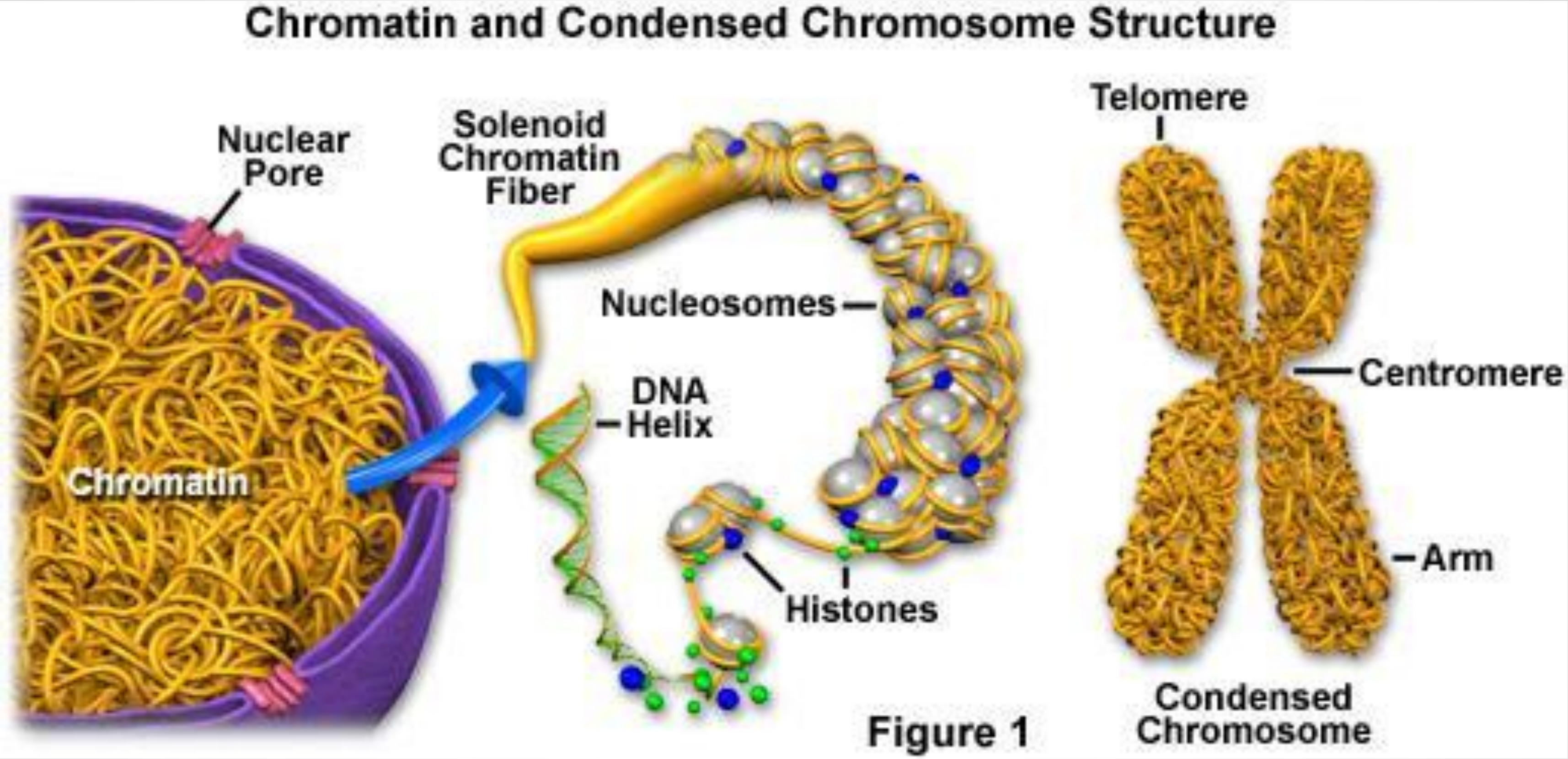
Base Pair Geometry

- Base pairs modeled as rigid bodies
- Double helix is described by the relative orientations of successive base pairs
- There are 6 types of coordinates to describe base pair conformation
- 3 angles and the 3 components of translation



Nucleic Acids Research. Oxford University Press. 2013.
http://nar.oxfordjournals.org/content/31/12/2975/F1.expansion

Chromatin

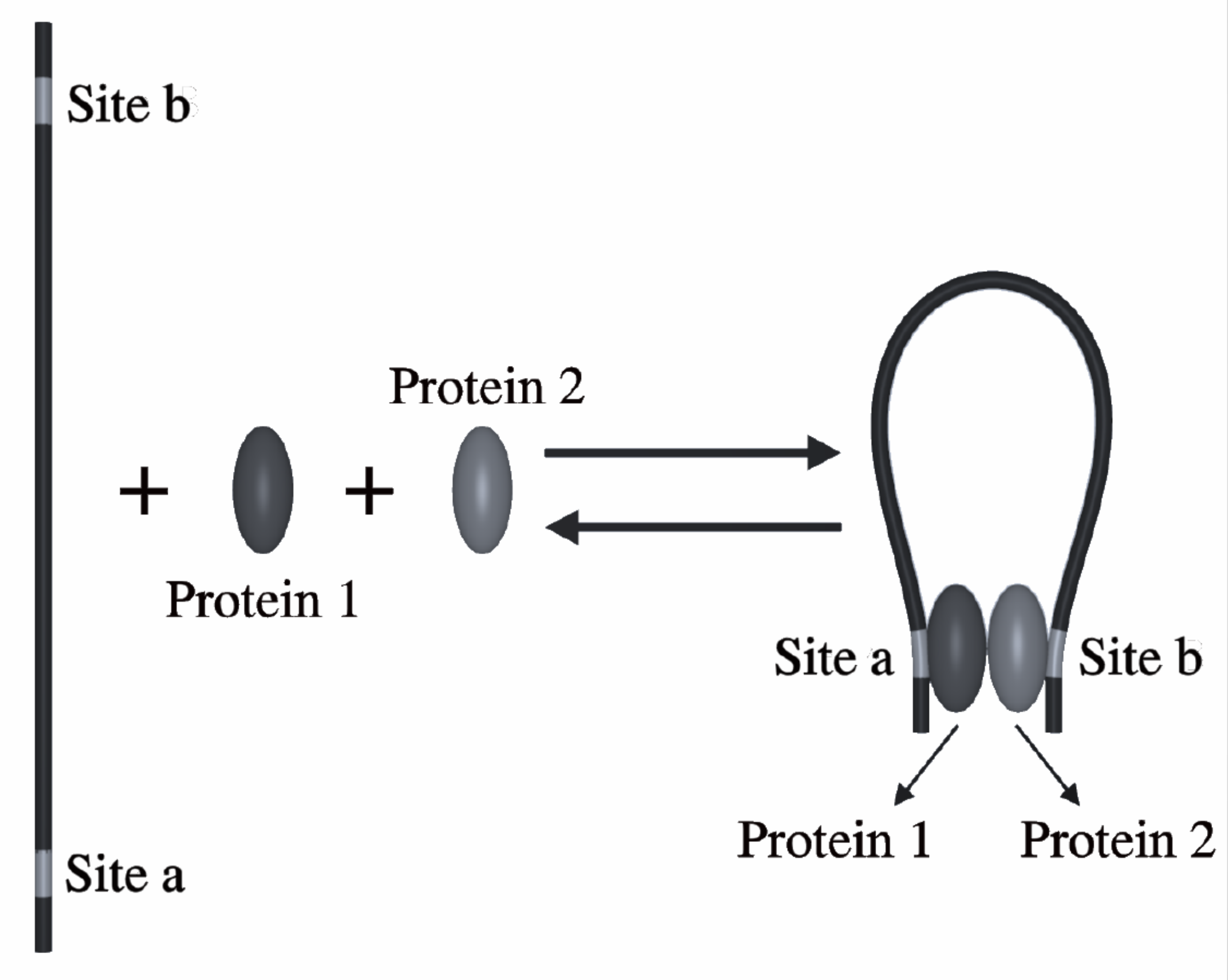


Davidson, Michael and The Florida State University. Chromatin and Chromosomes. 10 May 2005. <http://micro.magnet.fsu.edu/cells/nucleus/chromatin.html >

- Chromatin consists of DNA and histones (and other proteins).
- An octamer core is formed by 8 histones
- DNA wraps around the octamer core (roughly 150-bp) to form a nucleosome core particle

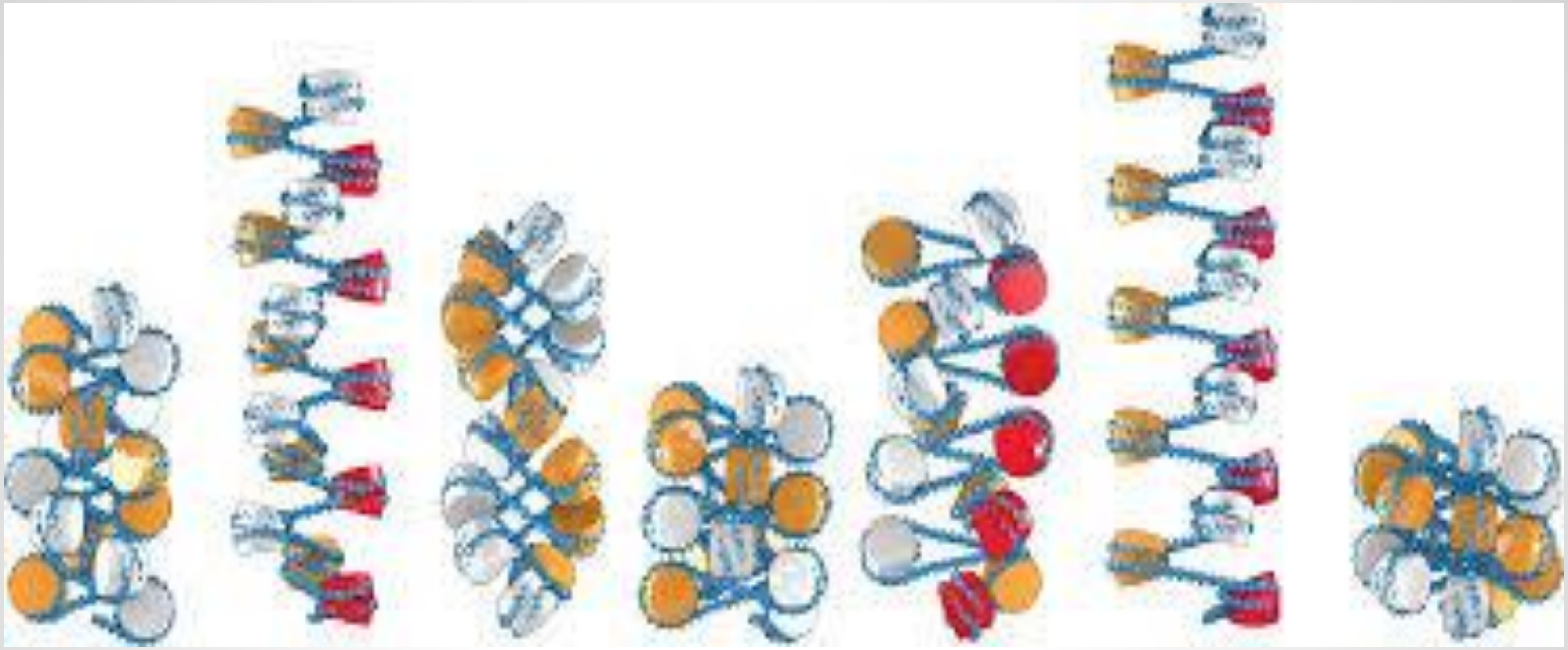
Long-Distance Communication

- Gene expression entails looping frequently
- Proteins 1 and 2 which bind at sites a and b must come in contact for biological processing
- Proteins mediate the looping of DNA



How chromatin architecture affect and/or control looping?

Chromatin Architecture and Nucleosome Positioning

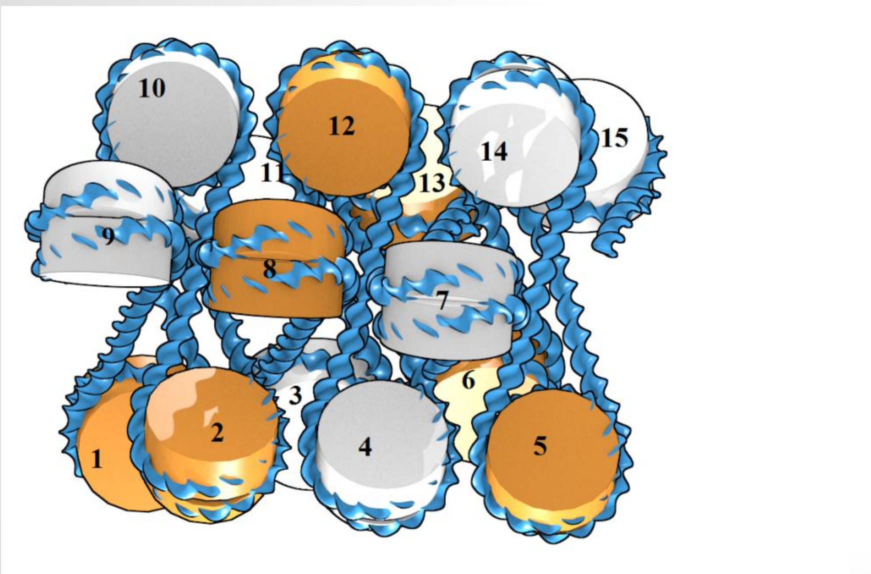


25bp 30bp 32bp 35bp 37bp 40bp 45bp

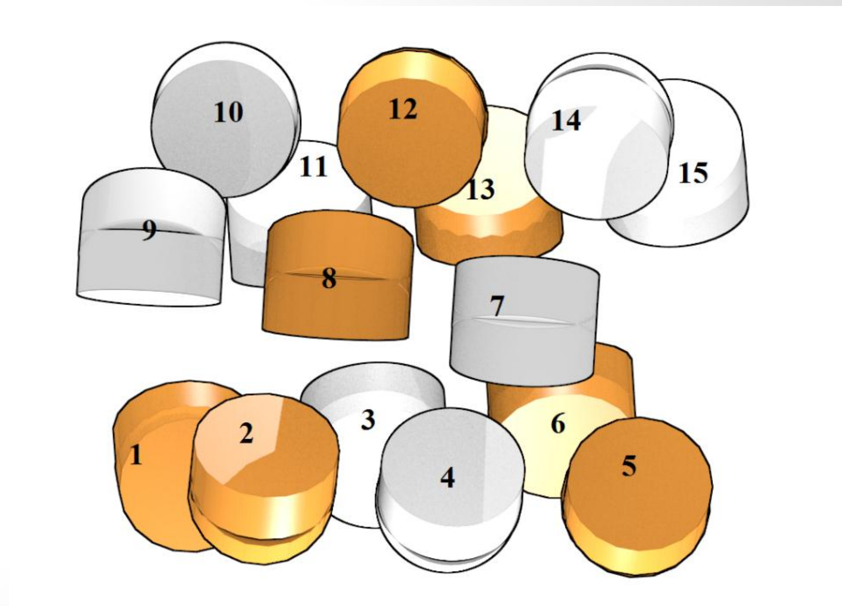
- The spacing of nucleosomes (the number of free base pairs) controls the chromatin architecture
- Ex) 35 bp more compact and 40bp more spread out in the chromatin

Geometry of Chromatin

Nucleosomes + Linker DNA



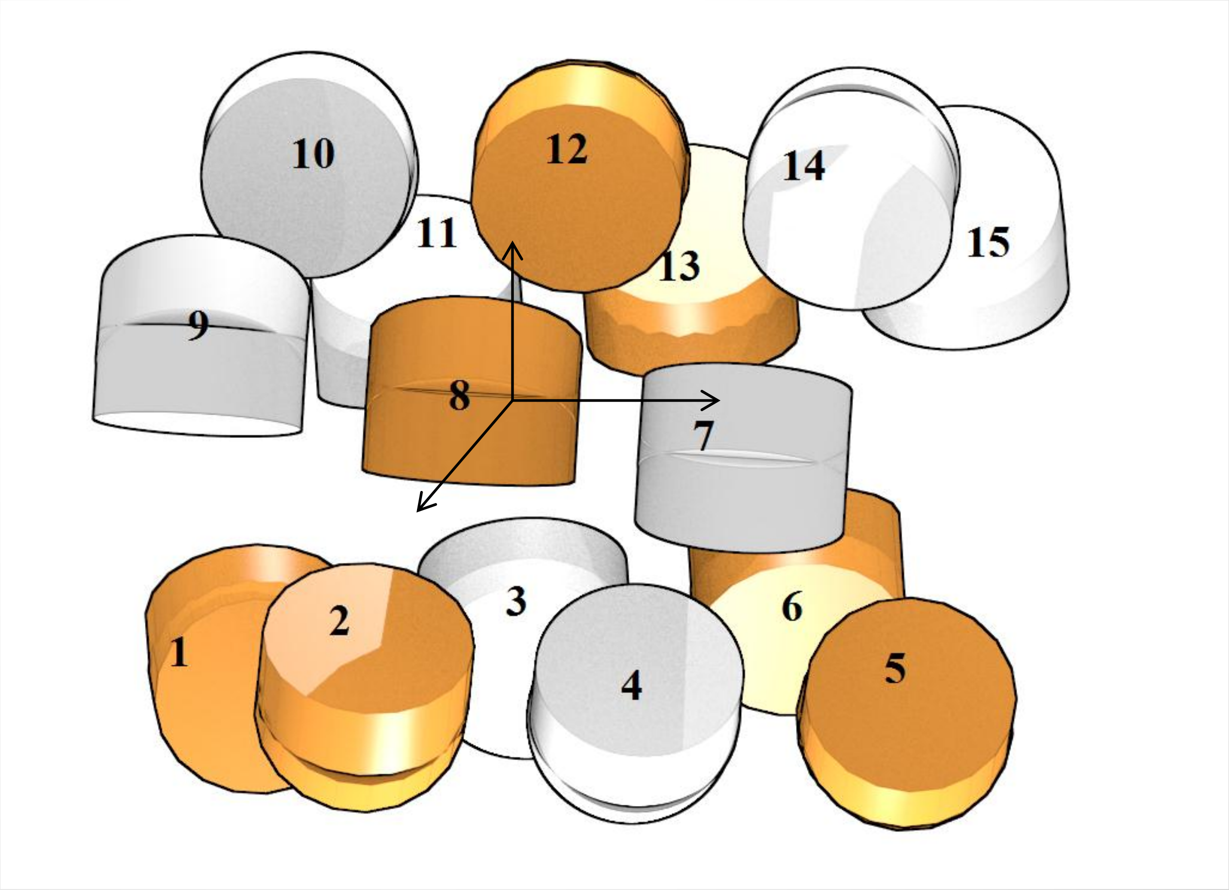
Nucleosomes Only



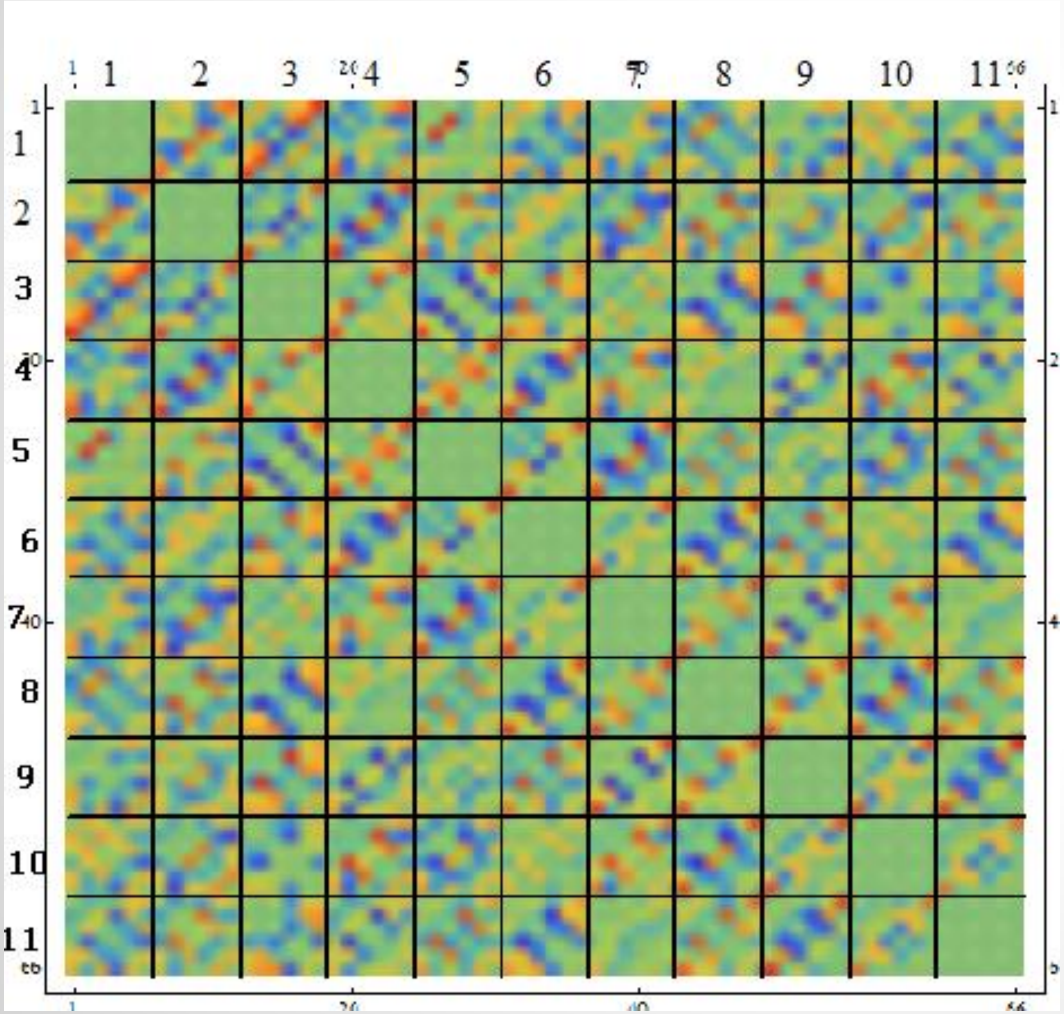
Project : Look at the interaction between nucleosomes.

Geometry of Chromatin

- Chromatin can be viewed at a nucleosome level as rigid bodies.
- Ex.



Chromatin Fiber Covariance Matrix



- A covariance matrix consisting of all pairs of nucleosomes for the chromatin fiber was obtained.
- Each square is 6x6 covariance matrix for the pair (i,j).

PROBLEM

- From the effect of nucleosome positioning on chromatin architecture, determine a spring constant describing the bending and flexibility of the chromatin for different linker lengths.
- Design coarse-grained models of chromatin based on effective potentials for nucleosome interactions (covariance analysis).