Effect of Nucleosome Positioning on Chromatin

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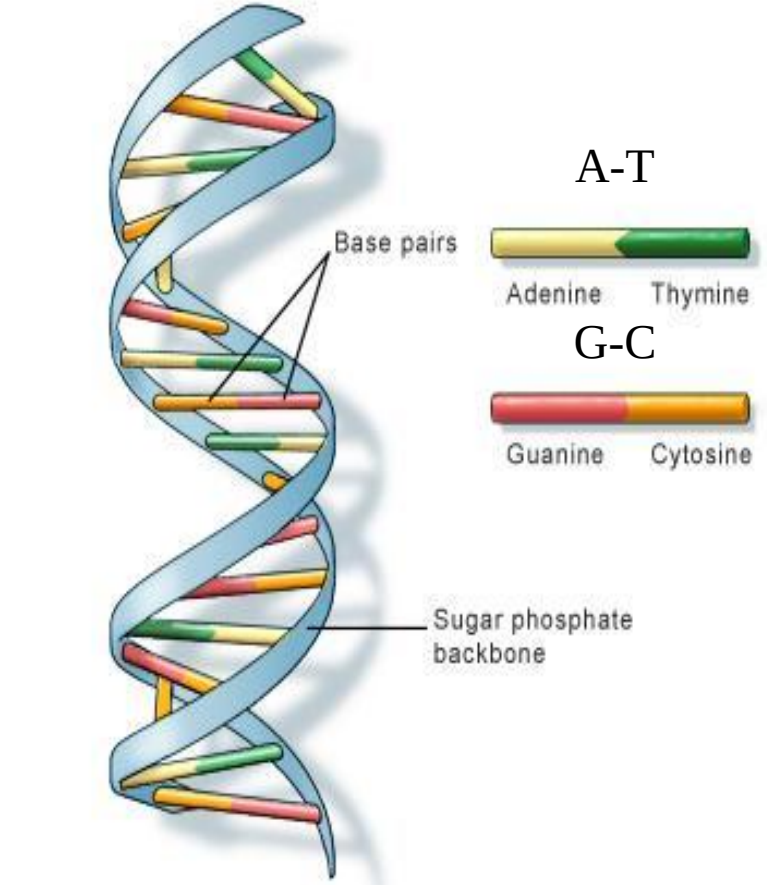
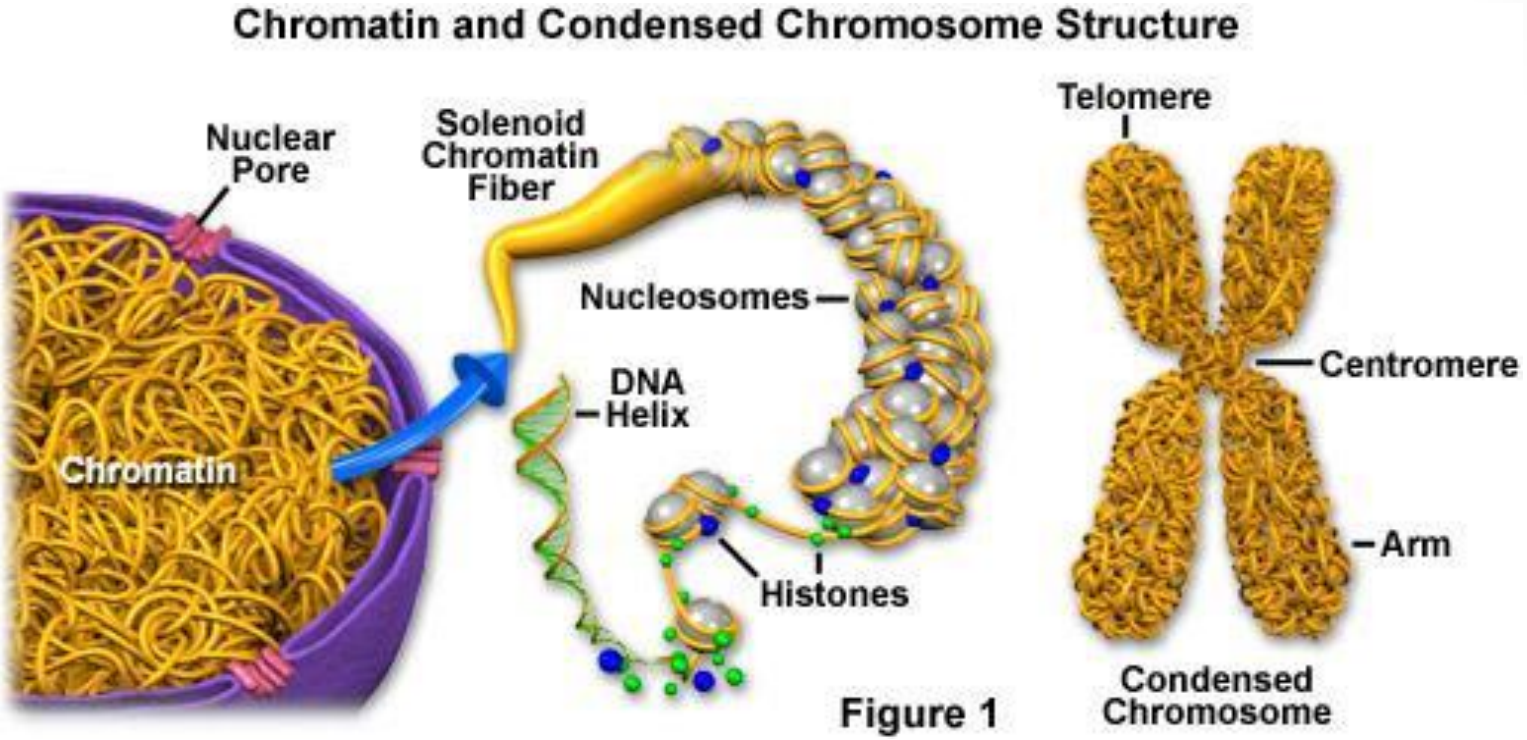
DNA

- DNA, which is located in our cell nucleus, is the carrier of genetic information in our body.
- Same DNA in almost every cell of our body.
- Forms a double-helical structure and contains a backbone and base pairs (A-T, G-C).



Chromatin

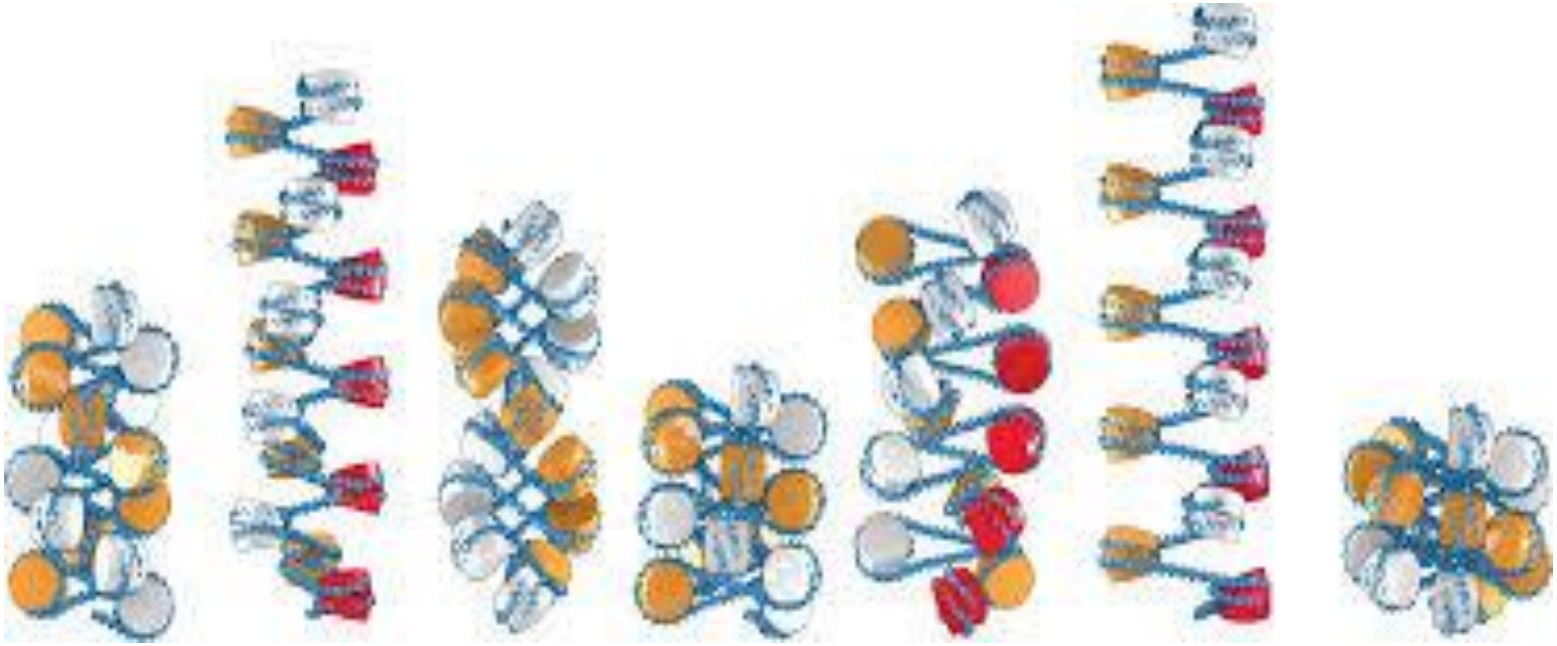


Davidson, Michael and The Florida State University. Chromatin and Chromosomes. 10 May 2005. <http://micro.magnet.fsu.edu/cells/nucleus/chromatin.html >

- Chromatin consists of DNA and histones (other proteins).
- Eight histones form an octamer core.
- DNA wraps around the octamer core (roughly 150 base pairs) to form a nucleosome core particle.

Nucleosome Positioning on Chromatin

- Position of nucleosomes on chromatin determined by DNA linker length (number of free intervening DNA base pairs)

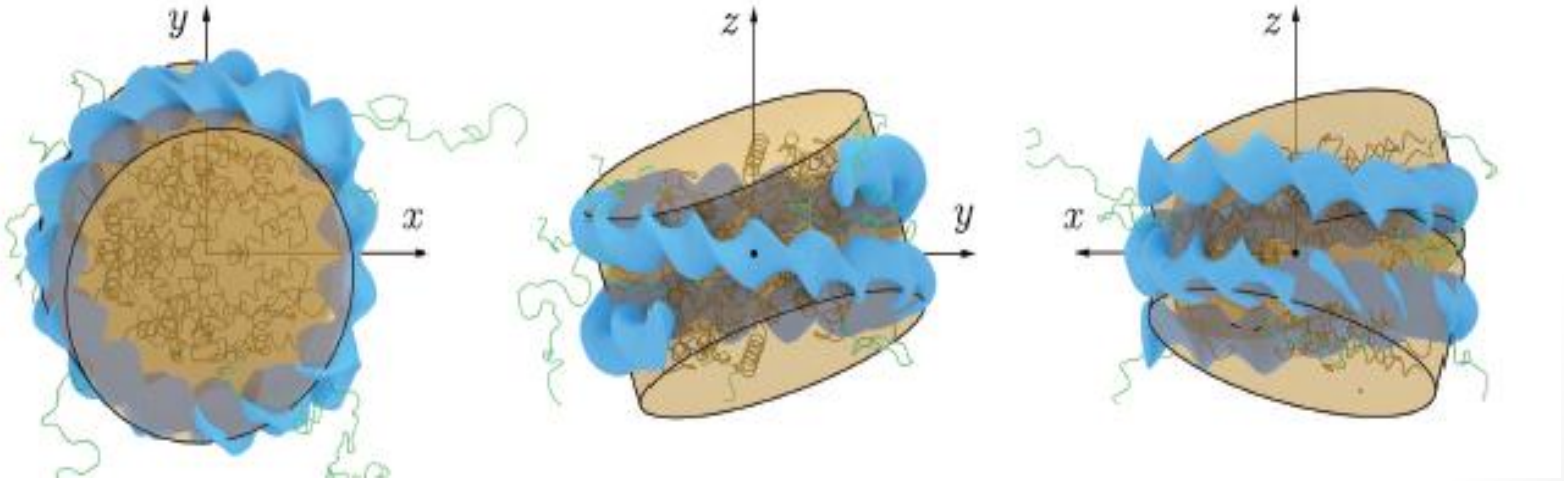


25bp 30bp 32bp 35bp 37bp 40bp 45bp

bp = base pairs

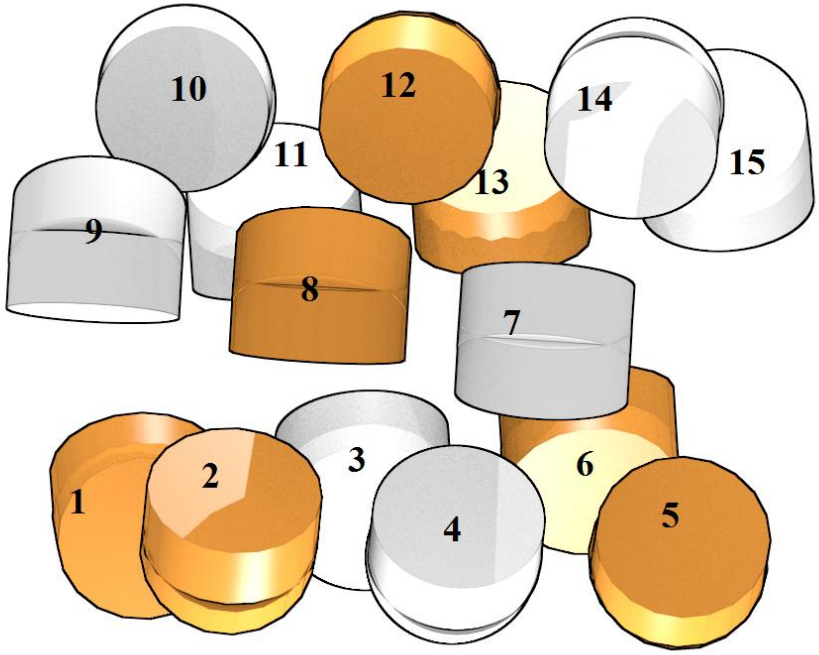
Geometry of Nucleosomes

- Analyze the chromatin fiber at nucleosome level as rigid bodies
- Each nucleosome can be described with an origin (global position vector) and three additional vectors describing the xyz axes in the global reference frame



Data

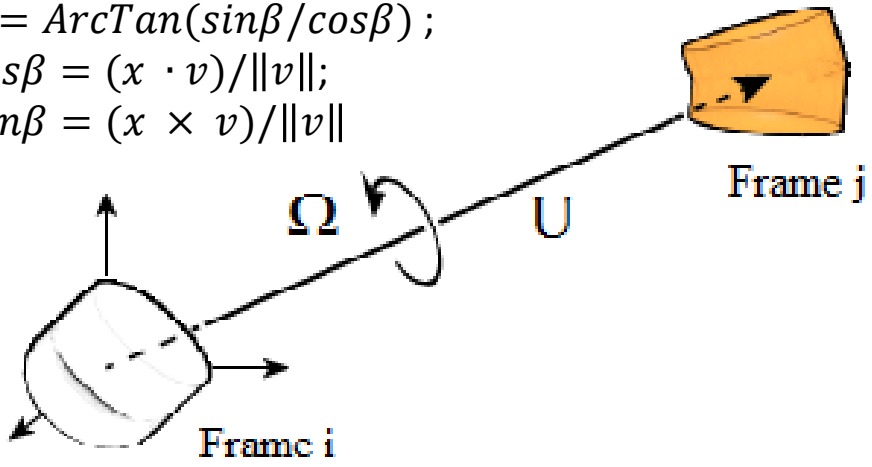
- Monte Carlo Markov Chain simulations of chromatin fiber consisting of 20 nucleosomes for a wide range of linker lengths (15bp to 80bp)
- For each linker length, around 20,000 configurations are obtained.

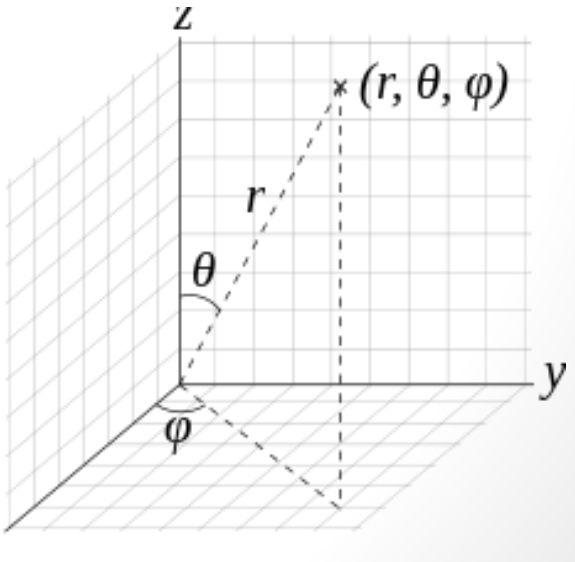


Parameters

- Obtain geometric parameters by looking at each nucleosome pair (i, j) where j > i and i ranges from 1 to 20
- $\underline{p}(i, j) = < \Omega , \alpha , \beta, \theta, \psi, r >$
- Ω , α , and β describe the rotation between two nucleosome frames. (α and β are spherical coordinates describing axis of rotation U with respect to frame i)
- θ, ψ, and r describe the translation between two frames

- $(z \cdot U) = \|z\|\|U\|cos\alpha$
- $\beta = ArcTan(sin\beta/cos\beta)$;
  $cos\beta = (x \cdot v)/\|v\|$;
  $sin\beta = (x \times v)/\|v\|$





http://en.wikipedia.org/wiki/Spherical_coordinates

Covariance Matrices

- Use of circular means for angular parameters
  - $\{\alpha_i\}$ = series of angles, N = number of configurations

$$\tan\langle\alpha\rangle = \frac{\langle\sin\alpha\rangle}{\langle\cos\alpha\rangle} = \frac{\sum_{i=1}^{N}\sin\alpha_i}{\sum_{i=1}^{N}\cos\alpha_i}$$

- Determine the covariance matrices for the parameters for each pair of nucleosome.

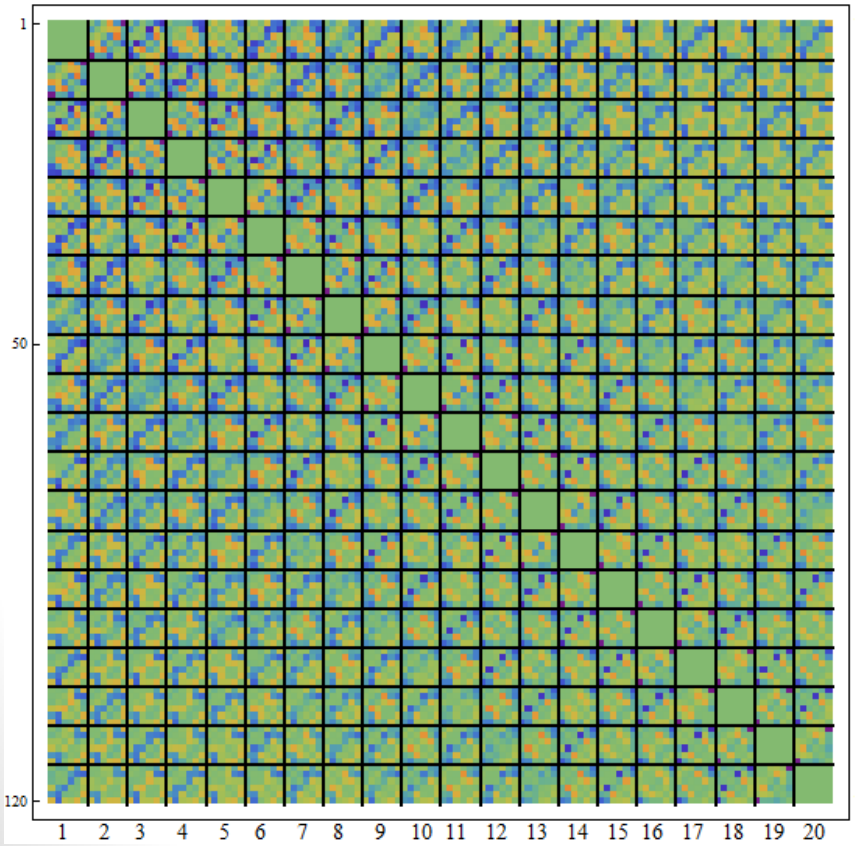
$$\boldsymbol{\sigma}(i,j) = \left\langle \left(\underline{p}(i,j) - \underline{\overline{p}}(i,j)\right)\left(\underline{p}(i,j) - \underline{\overline{p}}(i,j)\right)^{\mathsf{T}} \right\rangle$$

- Full fiber covariance matrices for different linker lengths to determine patterns as to which pairs of nucleosomes have a greater correlation value with each other.

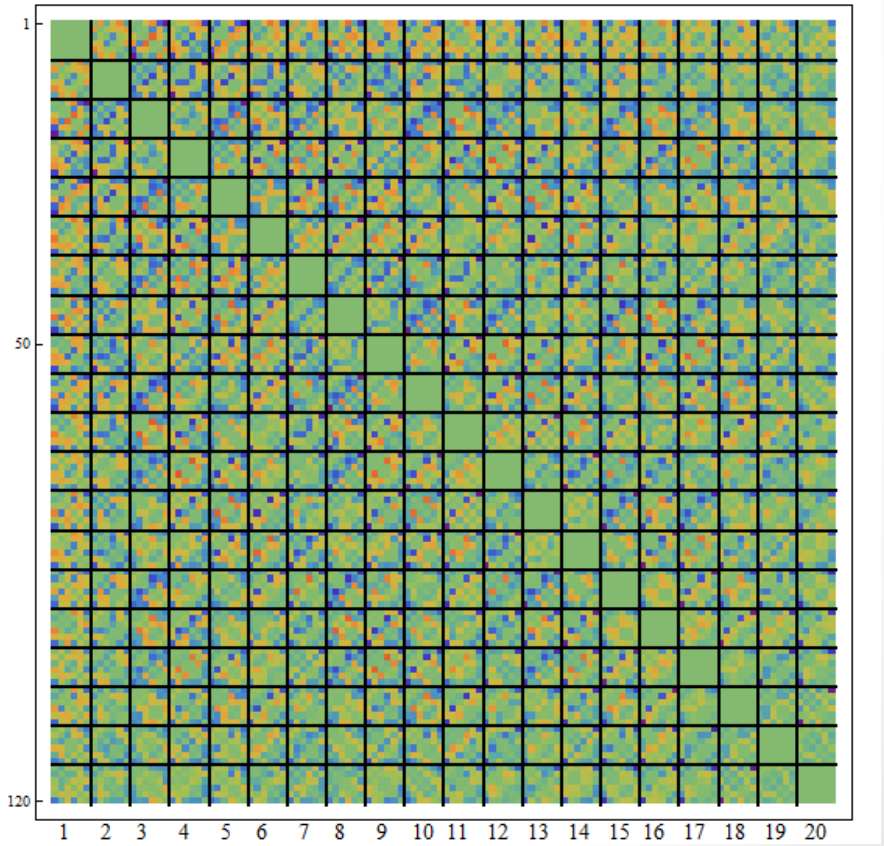
Covariance Matrix: 30bp vs. 35bp

- Each block is the covariance matrix for the parameters of pair (i, j)

30bp



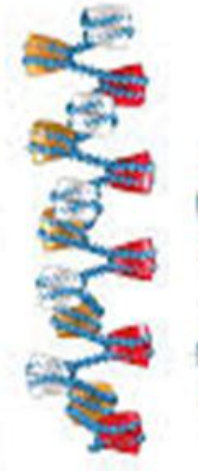
35bp



Nucleosome Number

Conclusion

- Differences in covariance matrices and correlation between nucleosome pairs due to different configurations of chromatin fiber.
- Some chains more compact than others depending on linker length.
- Difference in chromatin models for linker lengths with integral base pairs and half-integral base pairs



30bp

35bp

Current Work

- Through Principal Component Analysis (PCA), the eigenvector corresponding to largest eigenvalue for each of the 6x6 covariance matrices describes the predominant variation for the different parameters.
- By using the mean parameters and the eigenvectors obtained, build a series of models between a nucleosome pair (i ,i +1) to see how the nucleosomes move with respect to each other.
- This can be used to generate a polymer model.