Atom Distance and the Interaction between DNA and Acetylated Histone Tails

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What can we do with molecular modeling systems? Can we use MM-MD systems to simulate histone modification?

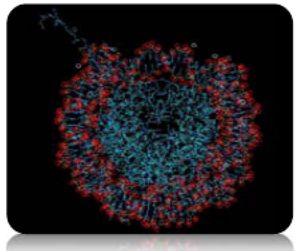
Introduction

Transcription is the way in which our cells create proteins from our DNA. Cells are not continuously transcribing DNA to RNA. While idle, DNA is wrapped snug around a histone core, collectively called a nucleosome (Figure 1). Nucleosomes are made of four pairs histones: H2A, H2B, H3, and H4. When DNA needs to be transcribed, the histone or DNA can be modified to release the histones hold on the DNA.

The H3 and H4 histones tails are rich in basic amino acids, giving them a positive charge at a physiological pH. DNA phosphate backbone is negatively charged. Histone acetyl transferases (HATs) can add acetyl groups to lysines on the H3 and H4 tails to remove the electrostatic attraction (hydrogen bond) between the hydrogen on ε amine group of the lysine residue and the phosphate of the DNA backbone. This causes in increase in distance between the phosphate and amine group allowing for transcription to take place.

Method

With the amino acid sequence known for the H3 histone, a peptide chain of the second ten amino acids and an arbitrary DNA chain was constructed with HyperChem Realease7.52. These structures underwent a geometry optimization and then a molecular dynamics calculation at 310K (body temperature on the Kelvin scale). The distance between the nitrogen on the ε amine group of the lysine residue and the closest oxygen of a DNA phosphate group will be measured before and after acetylation and the two distances will be compared.



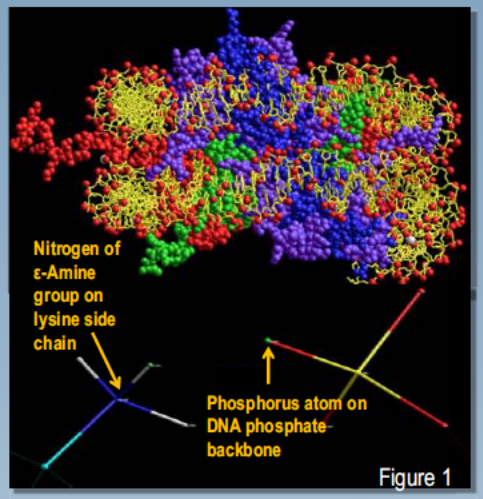


Figure 1

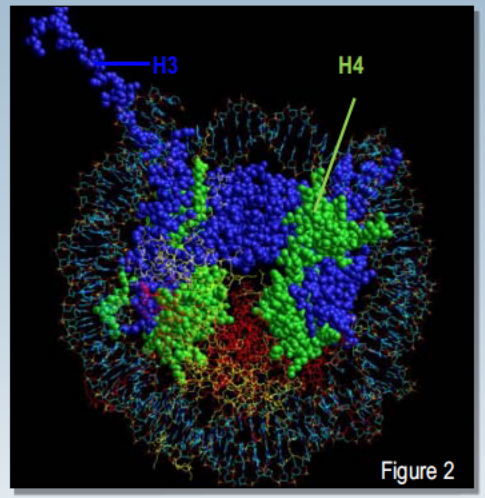


Figure 2

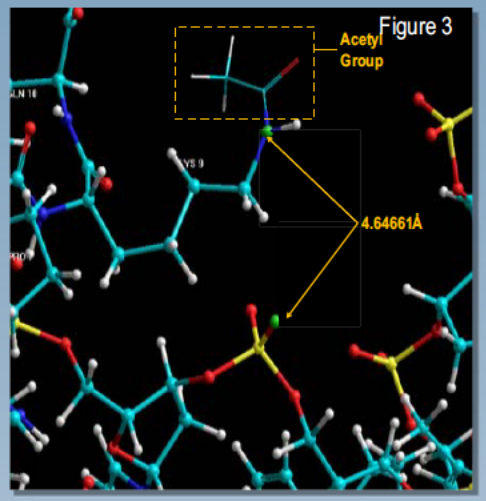


Figure 3

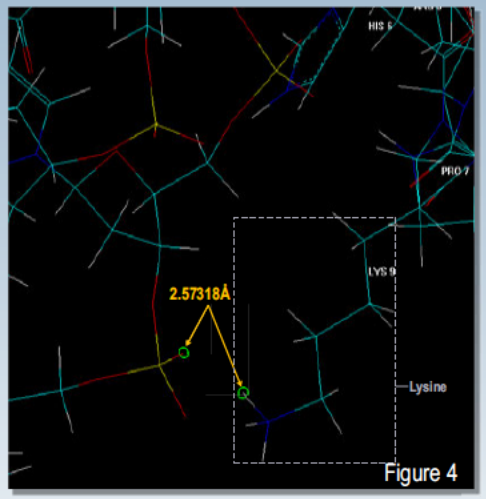


Figure 4

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Results

The distance between the nitrogen of the ε amine group of the lysine residue and the closest oxygen atom on the DNA phosphate group was measured, yielding a distance of 2.57318Å (Figure 4).The same lysine was then acetylated and a molecular dynamics calculation was done, now yielding a distance of 4.64661 Å (Figure 3).

Discussion

A hydrogen bond usually has a bond distance of about 2.6Å 3.5Å between the donor and acceptor atoms. In this study, we see that when simulating histone acetylation in HyperChem Release 7.52, before acetylation, these circumstances were met with a distance of 2.57318Å. The distance post acetylation was beyond that of a hydrogen bond. These results were consistent with the concept of n acetylation in histone tails being indicative of transcriptionally active DNA.

References

1. PBD ID: 1AOI
K. Luger, A.W. Mader, R.K. Richmond, D.F. Sargent, T.J. Richmond (1997) Crystal structure of the nucleosome core particle at 2.8 A resolution.

2. IBI Biosolution. Hydrogen Bond Interactions. IBI Biosolution. Hydrogen Bond Interactions. http://pipe.ibibiosolutions.com/Hydrogen%20Bond.html (accessed March 10, 2013).