Positioning of Nucleosomes at DNA Containing Short Periodic Sequences

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Nucleosome distribution, alongside with histone modifications and RNA polymerase II (Pol II) occupancy shows preferential association with exons ("exon-intron marking"), linking chromatin structure and function to co-transcriptional splicing in a variety of eukaryotes [1].

Interestingly the minimal nucleosome repeat length is very close to the distance between adjacent exons in segments of fibrous domains of collagen genes. These loci contain exons coding for periodic (fibrous) segments of coding human (pro)collagens I, II, III, V, VI, IX, XI with a strict $(GGx\text{-}xxx\text{-}xxx)_n$ nucleotide sequence.

Exons of fibrous collagen loci are about 3 times shorter than the average exon length in the genome, inter-exon distance also differs from a genome average distance [2]. In our previous report we suggested that this shortening and exon-intron structure is caused by the interplay of the periodic sequence of DNA necessary for coding for periodic protein molecule and the sequence of nucleosome binding site, which is also quasi-periodic with the different period [2].

Several groups of authors provided the whole-genome nucleoseome positioning data recently. Here we use this data to get an in-depth look on a positioning of nucleosomes at a double-stranded DNA chain containing short periodic sequences, represented by exons of fibrous collagen genes. Centers of nucleosome positions mapped with 1-nt resolution on the human genome (build hg18) were provided as a supplementary online material to [3]. Positions of exons for collagen genes were retrieved from Ensembl; sequences coding chain 1 of corresponding proteins were used.

Relative positions of nucleosome borders and exon borders were determined using the following procedure:

1. For each exon find the nucleosome with the minimal distance between the nucleosome center and the **nearest** exon border.
2. Store a distance between the nucleosome center and the exon border most distant from it.

Histogram of relative positions of nucleosome and exon borders is shown in Fig. 1.

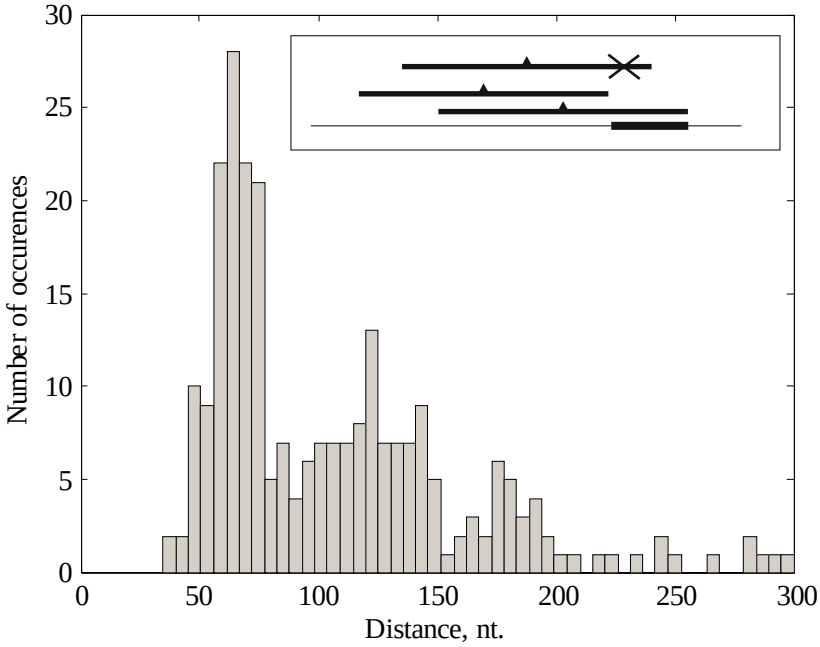

Fig. 1: *Distance between the nucleosome center and the most distant border of the corresponding exon with a periodic sequence (averaged by 5 nt).*

Majority of distances falls into two regions: close to 70 nt and 100-150 nt. This distance distribution can be explained as follows (see caption above the histogram, DNA regions spanned by nucleosomes are shown by upper lines with arrows – nucleosome centers, exon is shown by thicker line). Distance of 65-70 nt (maximum of the histogram), is approximately a half of the 147 nt, the length of double-stranded DNA chain interacting with the nucleosome histone core. Thus the first maximum is formed by exons lying entirely on DNA interacting with nucleosome core; the exon's border most distant from the nucleosome center coincides with the nucleosome border. The second region is formed by exons located outside but not afar of the nucleosome. The exons overlapping with the nucleosome border are depleted.

We can conclude that nucleosomes are predominantly positioned at DNA sequence containing short periodic regions so that one of nucleosome borders coincides with the boundary of a region that is not interacting with the nucleosome core. This behavior agrees with observations of nucleosome positioning preferences on a DNA chain containing exons with "weak" splicing sites [1].

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3. Daniel J. Gaffney, Graham McVicker, Athma A. Pai et al (2012) Controls of Nucleosome Positioning in the Human Genome, *PLOS Genetics*, **8,** 11.