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Comment on: Chromatin fiber functional organization: some plausible models by A. Lesne and J.-M. Victor

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The physical properties of complexes between, say, polymers, colloids etc. can be usually derived from the physical properties of its constituents and this is also true for chromatin. For instance, the elastic properties of a chromatin fiber (its bending, twisting and stretching moduli) can be in principle derived from the elasticity of the DNA linker backbone and the interaction between the nucleosomes. In their contribution Lesne and Victor [1] advocate an additional point that strongly enriches the picture in the case of chromatin: there is also a flow in the other direction, i.e., through the course of evolution higher-order structures have stamped their features in some way onto its smaller subunits.

The clearest example given in Ref. [1] is the nucleosome gaping mechanism: a gaping within the histone core might be beneficial for nucleosomes organized inside a chromatin fiber. Whether this mechanism is actually at work inside such fibers is still an open question [2] but it serves in any case as an example for how the chromatin fiber might leave an imprint on its subunits, the nucleosomes.

That there are feedback loops such that e.g. the chromatin fiber affects the nucleosome structure is certainly true but that this goes down to the DNA level (as mentioned in the concluding part of their contribution [1]) has to be taken with a grain of salt: DNA also exists in prokaryotes where chromatin is absent. DNA should thus better be considered as a given boundary condition under which the chromatin complex has evolved. But clearly in eukaryotes where DNA contains so much "junk" sequences there is still some degree of freedom: the basepair sequence of non-coding sequences themselves. Indeed some basepair stretches clearly reflect the presence of higher-order structures in so-called nucleosome positioning sequences (there exist probably also less direct repercussions of the higher-order structures in the basepair sequence as discussed in Ref. [4] of this volume). Some basepairs steps are, for instance, more flexible than others (via the rolling degree of freedom) and others might lead to an intrinsic curvature of the DNA chain [5]. A DNA stretch featuring the appropriate basepair sequence can be more easily wrapped onto a histone octamer. Such a nucleosome positioning sequence might serve as a switch where e.g. under "normal" circumstances the nucleosome is present, but at other times it might be actively pushed away from that location. Important is here that nucleosomes are usually not only translationally positioned but even much more so rotationally positioned due to the anisotropic bendability of the DNA wrapped around [6]. That means that such a positioned nucleosome will induce a "kink" at a well-defined position with a well-defined rotational orientation between the DNA entering and exiting the positioned nucleosome.

I would also like to mention another example where the interplay of the different levels becomes especially clear. The chromatin fiber is hold together by the linker DNA. Suppose that we have a piece of chromatin fiber where the geometrical parameters of its *unbent* linkers are such that the resulting fiber would feature a relatively open structure with some free space between all its nucleosomes (similar to the one in Fig. 3(a) in [1]). Now the interaction between nucleosomes results to a large extent from the histone tails, flexible cationic extensions of the core histone proteins. The cell can biochemically control the charges of these tails via acetylation ("uncharging") and deacetylation ("charging") which in turn presumably has a strong impact on the nucleosome-nucleosome interaction via the tail-bridging effect [6]. Suppose all the nucleosomes of the fiber are deacetylated. In this case the nucleosomes are very sticky due to the tail-bridging effect and presumably the fiber is a collapsed, dense structure with the linker DNA being bent and twisted out of the unrelaxed conformation. On the other hand, when the nucleosomes are acetylated the nucleosome-nucleosome attraction is strongly reduced, the linker DNA relaxes and as a result the fiber is very open and overall very flexible. Whereas in the former case the DNA inside the fiber is inaccessible and genes associated with this piece are silenced, in the latter case one has an active open fiber with each gene being ready for transcription. This picture illustrates how the interplay of three levels, that of the highly elastic DNA linker and its geometry (representing a spring under tension for the dense structure), that of

the biochemically tunable nucleosomes (with the charged lysine groups on its tails being a locally tunable "salt concentration") and that of the chromatin fiber are strongly interlinked. Through the course of evolution the lengths, charges and positions of the histone tails might have been adjusted to allow such a switching mechanisms between open and closed fibers to take place.

Chromatin is a highly complex structure where specific and more general principles work in parallel and that on several length scales. Many of those principles will only reveal themselves when one comprehends the chromatin complex as a whole structure and not as a sequence of fairly independent hierarchical compaction levels – and this is beautifully formulated in the contribution by Lesne and Victor [1]

References

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