

Journal club



IS CHROMATIN HELICAL?

A long-standing question in eukaryotic cell biology and genomics is whether the interphase chromatin fibre has a foundational geometric structure — or at least one that persists over some longitudinal segment of a chromosome. Two recent studies asked if there is any regular, higher-order folding of the fibre beyond simple apposition, that is, the ‘globule’ which results when a polymer falls back on itself in the absence of any particular infrastructure.

Court *et al.* used chromosome conformation capture to interrogate gene-rich regions of mouse and human chromatin and reported that, in both organisms, there is an unanticipated intrinsic constraint. This presents as a 90–100 kb modulation of contact frequencies, which they interpret as a non-linear shape of these chromatin regions and which is most statistically satisfied when modelled as a helix. However, two issues arise. First, the amplitude

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of the helical periodicity is quite small, but we have no way of anticipating the degree to which an underlying helical geometry would be dampened under the interrogation conditions used. Second, both the active and silenced regions of the gene-rich regions of euchromatin studied are constantly influenced by all sorts of effectors. So, would the evidence for helicity have been more or less persuasive if the chromatin regions examined had been uniformly active or repressed?

A few months later, Sheffer *et al.* provided a compelling case that, at least over short distances, the 30-nm-long fibre organization of chromatin in the transcriptionally silent avian erythrocyte nucleus has a helical repeat. This was based on some of the most impressive cryo-electron microscopy of chromatin published to date. The helix is a two-start, left-handed spiral that has ~6.5 nucleosomes per 11 nm. The helical geometry causes the nucleosomes to be facing inward and to present as discrete ‘islands’ along the helix, rather than being spatially interdigitated (as would be the case in the aforementioned passively collapsed polymer).

Finally, a study by Umbarger *et al.* now finds that a bacterial chromosome (without nucleosomes, of course), also has a helical geometry, suggesting that this contour was at hand even before cells had nuclei. There had never been any reason a priori to think that the double helical structure of DNA would ‘reach through’ and impose a helix onto chromosomes themselves, yet this beguiling possibility now stands before us.

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ORIGINAL RESEARCH PAPERS Court, F. *et al.* Modulated contact frequencies at gene-rich loci support a statistical helix model for mammalian chromatin organization. *Genome Biol.* **12**, R42 (2011) | Scheffer, M. P., Eltsov, M. & Frangakis, A. S. Evidence for short-range helical order in the 30-nm chromatin fibers of erythrocyte nuclei. *Proc. Natl Acad. Sci. USA* **108**, 16992–16997 (2011) | Umbarger, M. A. *et al.* The three-dimensional architecture of a bacterial genome and its alteration by genetic perturbation. *Mol. Cell* **44**, 252–264 (2011)