The protein that assesses distances

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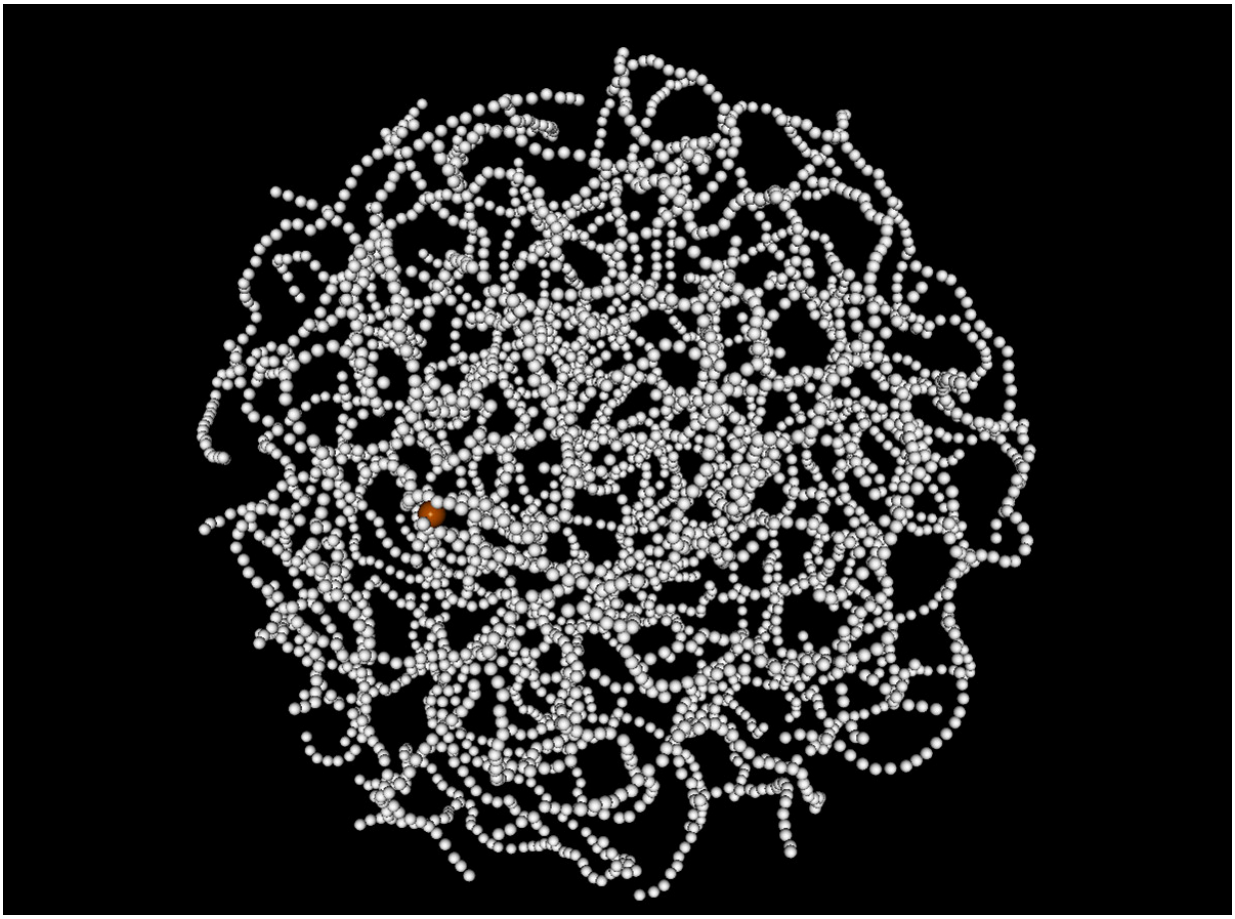

DNA. Credit: Ana Maria Florescu

A protein of the ISWI family (Imitation Switch, or nucleosome remodelling motors) is endowed with a special property: despite having no organ of sense it is nonetheless able to assess the length of DNA

strands. A study just published in the Journal of Statistical Mechanics: Theory and Experiment and carried out by SISSA, the MAX Planck Institute and the NIH has discovered how it works.

Picture a chromosome as a string of beads. The beads are in fact called nucleosomes and are formed by the DNA strand that makes up the chromosome itself, tightly wrapped around proteins, called histones, which act a bit like spools. Nucleosomes are joined to one other by a segment, of varying length, of the same strand of DNA. The "beads" can be moved along the strand, grouped close together or moved apart, by the action of special proteins called "remodelling motors". One type of these motors arranges the nucleosomes equidistantly on the "string of beads". To know where to move the nucleosomes, the motors need to assess the length of the segments joining them. And this is where the question arises: how can a single molecule "sense" how long a piece of DNA is?

Ana Maria Florescu, research scientist at the International School for Advanced Studies (SISSA) in Trieste, and Kuni Iwasa, from the US National Institutes of Health (NIH), have answered this question by means of a theoretical study. Both Florescu and Iwasa were at the Max Planck Institute for Physics of Complex Systems in Dresden when they started their work for this research. "It is indeed a 'sensory' issue, but let's not forget we are dealing with protein complexes, which don't have organs of sense", explains Florescu.

Florescu and Iwasa were inspired by previous experimental results, and they constructed a model of the system (nucleosomes, strands and remodelling motors, immersed in a fluid environment).

"What we observed in our calculations is that the longer the DNA segment between one nucleosome and the next the shorter the time it takes the motor to bind to it". In fact the strands immersed in fluid tend

to fluctuate randomly and the magnitude and speed of their movement depend on the length of the segment. In practice, the shorter the segment, the faster it oscillates: "in this case, the molecule has more trouble capturing the segment, and it cannot carry out its action until it binds to it". The time it takes the motor to bind to the segment is therefore an indicator of the length of the segment itself.

Unpacking the strand to allow DNA to work

The ultimate function of DNA is protein synthesis, a process that starts with the first crucial step of gene transcription: pieces of code contained in the genes are copied to be used as a matrix to build new proteins. For this to happen, the nitrogen bases that make up the DNA strand need to be accessible. When they are tightly packed around the histones, they are unusable. Their rearrangement by the remodelling motors is crucial for freeing them.

"DNA is tightly packaged because otherwise it wouldn't fit inside the cell nucleus, as we're talking about over two metres of strand in total if we consider the complete human genome. This, though, has the disadvantage of having to unpack it each time it's needed, a task carried out by the remodelling motors that make the chromatin strand accessible so that the transcription process can take place" explains Florescu.

So it is easy to understand how important these remodelling molecules are for the body's health: a breakdown of the mechanism blocks transcription and thus protein synthesis. And, indeed, "some studies have linked certain types of cancer with the absence or limited presence of remodelling motors", concludes Florescu.

More information: Kuni H Iwasa et al. A molecule that detects the length of DNA by using chain fluctuations, *Journal of Statistical Mechanics: Theory and Experiment* (2016). DOI:

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