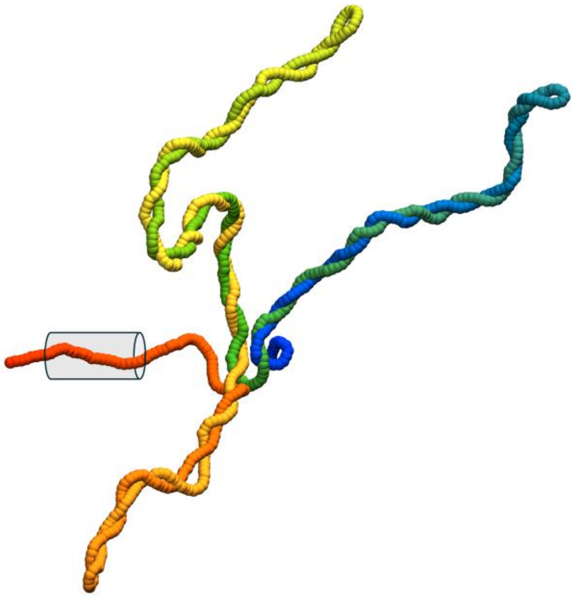
PRESS RELEASE

Twisted Strand of Life: Nanopores Reveal DNA Entanglements

Plectonemes are DNA supercoils that can form when the molecule passes through extremely narrow channels. This is the conclusion of a study published in Physical Review X, which offers new perspectives for studying genome organization.



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They are called plectonemes. They are the analog of the twisted tangles of telephone cords, and can form in DNA that is pulled through a nanoscale channel. This is the finding of a study led by Ulrich Keyser from the University of Cambridge and Cristian Micheletti from SISSA-Scuola Internazionale Superiore di Studi Avanzati in Trieste, conducted in collaboration with Antonio Suma from the Interuniversity Department of Physics of the University of Bari and Politecnico of Bari and the team of Aleksei Aksimentiev from the University of Illinois.
By combining experiments and simulations, the international team revealed what happens when a DNA strand is pulled through a nanopore. The fluid flow accompanying DNA translocation generates a torsion that propagates upstream along the double helix, causing the formation of plectonemes, or supercoils. These tangled structures produce a characteristic signature in the current measured during translocation, a property that had previously gone unnoticed, and possibly confused with the much shorter signal produced by DNA knots.

Studying DNA supercoils is relevant to understanding how genomic DNA is organised in the cell nucleus, where plectonemes may help to maintain order and compactness in chromosomes. The use of nanopores may therefore open new perspectives for studying the action of specific enzymes responsible for generating and eliminating supercoils. The research is published in Phys Rev. X.

Knot or not? What simulations tell us

“The current signatures detected during DNA translocation by Keyser's lab at the University of Cambridge exhibited some highly unusual and unexpected features.", says Cristian Micheletti of SISSA. "They clearly indicated the passage of entanglements, yet they occurred too frequently to be due to random knots, virtually the only type of entanglement known and studied previously. Moreover, their frequency increased with the pulling force. We searched for alternative explanations, including the formation of plectonemes due to DNA twisting inside the nanopore, an already known phenomenon.”.
To test this hypothesis, the researchers turned to models and simulations. Antonio Suma of the University of Bari explains: “We demonstrated that the twisting of a short section of DNA in the nanopore propagates upstream along long stretches of the strand, leading to the formation of intricate and stable supercoils. We then used the models and simulations as a 'virtual microscope' to distinguish the signals produced by the passage of plectonemes from those of knots . This is important for several reasons".

The impact of the research: from fundamental research to biosensors

Micheletti clarifies: "This study provides valuable insights for interpreting the electrical signals recorded during DNA passage through nanopores. Discriminating between knots and plectonemes based on signal duration will enable a more detailed understanding of DNA organization, integrity, and possible damage”. He continues: "The implications can go further. Knots and plectonemes are also present in genomic DNA. Understanding how chromosomes are maintained in a compact and functional form by specific enzymes remains one of the key challenges of molecular biology. Our study paves the way for using nanopores as tools to investigate the activity of these molecular machines, mapping the conditions under which they generate or eliminate supercoils".
Antonio Suma concludes: "The study demonstrates a twofold advantage of employing DNA translocation: not only can it be used to create complex structures such as supercoils, but it enables their detection. This provides an ideal platform for investigating DNA organisation at scales that have so far remained largely unexplored".

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