NUS researchers identify a novel double-stranded DNA structure

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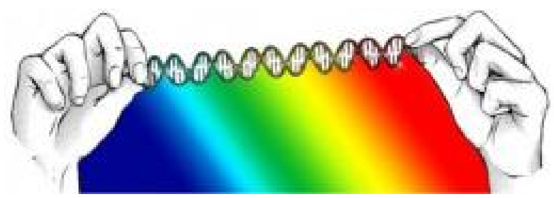

This novel double-stranded DNA structure produced through mechanical stretching has been successfully demonstrated by researchers from the National University of Singapore. Credit: National University of Singapore

By way of mechanical stretching, National University of Singapore researchers identify a novel double-stranded DNA structure, thus successfully resolving a 16-year-old scientific debate over the existence of a double-stranded DNA structure.

Double-stranded DNA has often been described as a right-handed helical structure, known as B-DNA. To perform its multiple functions, double-stranded DNA has multiple structures depending on conditions. For example, the melted DNA bubble forms during transcription elongation and the left-handed helical Z-DNA forms hypothetically during transcriptional regulations.

Scientists have been proposing a novel form of double-stranded DNA structure since 1996. Referred to as 'S-DNA', it is produced from stretching the B-form DNA beyond a certain 'transition force' of around 65 pN to approximately 1.7-fold in length (termed as DNA overstretching transition). Its existence has sparked a 16-year scientific debate since it was proposed, as many other evidences suggested that DNA overstretching transition was merely a force-induced DNA melting transition, leading to peeled-apart single-stranded DNA.

At National University of Singapore (NUS), the research was led by Associate Professor Jie Yan, from the Department of Physics, Faculty of Science and Mechanobiology Institute, Singapore. It succeeded in demonstrating the intricacies of the DNA mechanics in highly sensitive single-DNA stretching experiments.

Assoc Prof Yan and his team found that DNA overstretching may involve two transitions that are distinct in their transition kinetics, namely, a slower hysteretic peeling transition to peeled-apart single-stranded DNA and a faster non-hysteretic transition to an unknown DNA structure. However, whether the unknown DNA structure produced from the non-hysteretic transition is the S-DNA or two single-stranded DNA strands through inside-DNA-melting, remains a question.

Their findings were published in Nucleic Acids Research.

In another recent work published in *Proceedings of the National Academy of Sciences*, Assoc Prof Yan and co-researchers examined the thermodynamics associated with the two transitions. They found that the non-hysteretic transition was associated with a small negative entropy change, in contrast to the large positive entropy change found during the hysteretic peeling transition. This result strongly favors DNA re-arrangement into a highly ordered, non-melted state during the non-hyteretic transition. They also demonstrated that the selection between the two transitions was dependent on DNA base-pair stability and could be represented in a multi-dimensional phase diagram.

Their results not only brought clarity to the scientific debate of whether S-DNA exists, but also provided important insights to the possible structures and functions of the mysterious S-DNA.

Given its elongated structure, the S-DNA may be a potential binding substrate for DNA intercalators, including those used in chemotherapeutic treatment to inhibit DNA replication in rapidly growing cancer cells. In cells, many DNA-binding proteins utilize side chain intercalation to distort the DNA backbone. Therefore, the S-DNA may also be a potential binding substrate for these proteins that occur in living organisms.

Provided by National University of Singapore