First videos to show the helix of 'dancing DNA' developed by scientists

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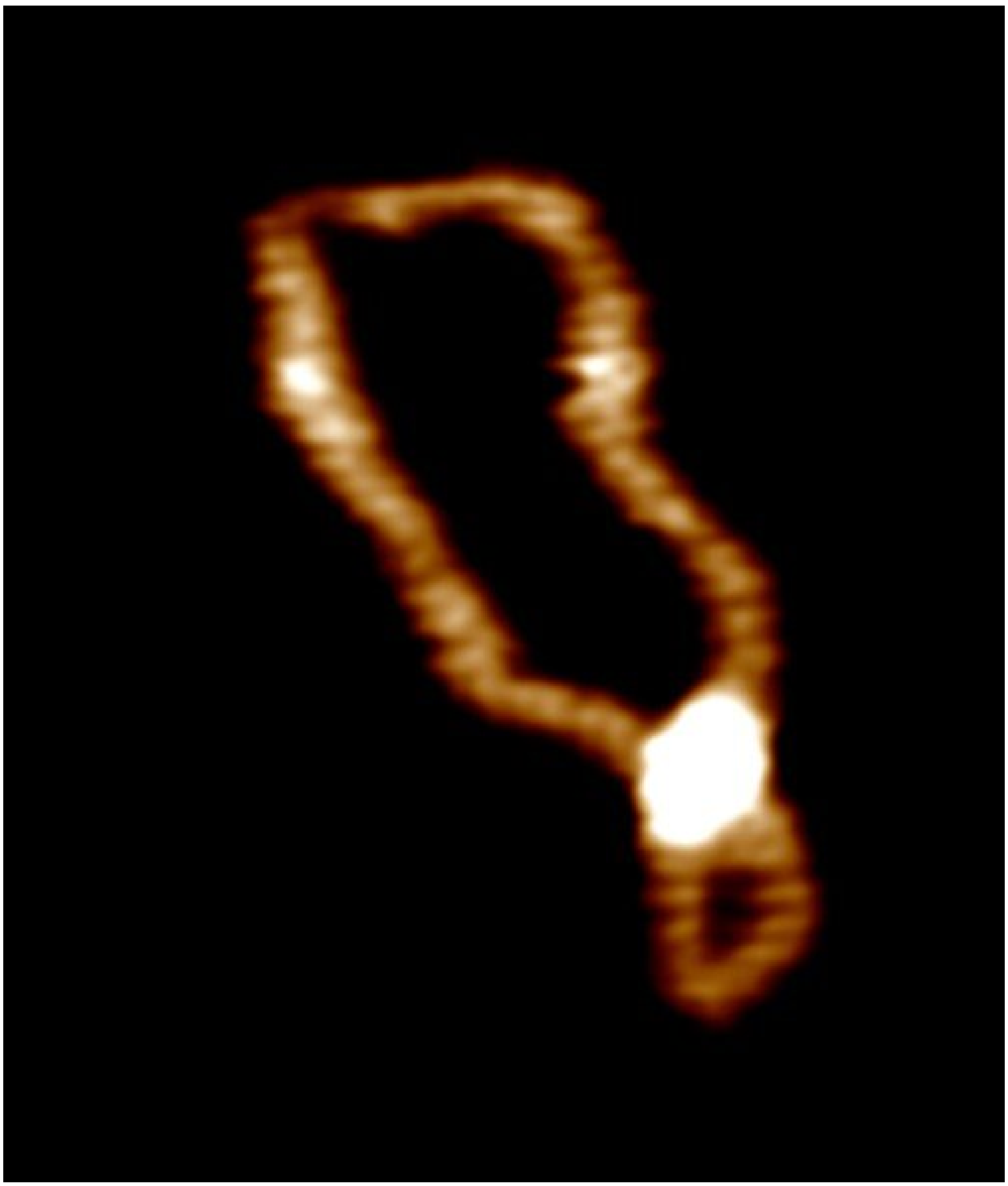


The team looked at DNA minicircles, which are special because the molecule is joined at both ends to form a loop. Credit: University of York

Videos allowing us to see for the first time how small circles of DNA adopt dance-like movements inside a cell have been developed by researchers at universities in Yorkshire.

The footage, developed by a team of scientists from the Universities of York, Sheffield and Leeds, are based on the highest resolution images of a single molecule of DNA ever captured. They show in unprecedented detail how the stresses and strains that are placed on DNA when it is crammed inside cells can change its shape.

Microscopy

Previously scientists were only able to see DNA by using microscopes that are limited to taking static images. But now the Yorkshire team has combined advanced atomic force microscopy with supercomputer simulations to create videos of twisted molecules of DNA.

The images are so detailed it is possible to see the iconic double helical structure of DNA, but when combined with the simulations, the researchers were able to see the position of every single atom in the DNA and how it twists and writhes.

Every human cell contains two meters of DNA. In order for this DNA to fit inside our cells, it has evolved to twist, turn and coil. That means that loopy DNA is everywhere in the genome, forming twisted structures which show more dynamic behavior than their relaxed counterparts.

The team looked at DNA minicircles, which are special because the molecule is joined at both ends to form a loop. This loop enabled the researchers to give the DNA minicircles an extra added twist, making the DNA dance more vigorously.

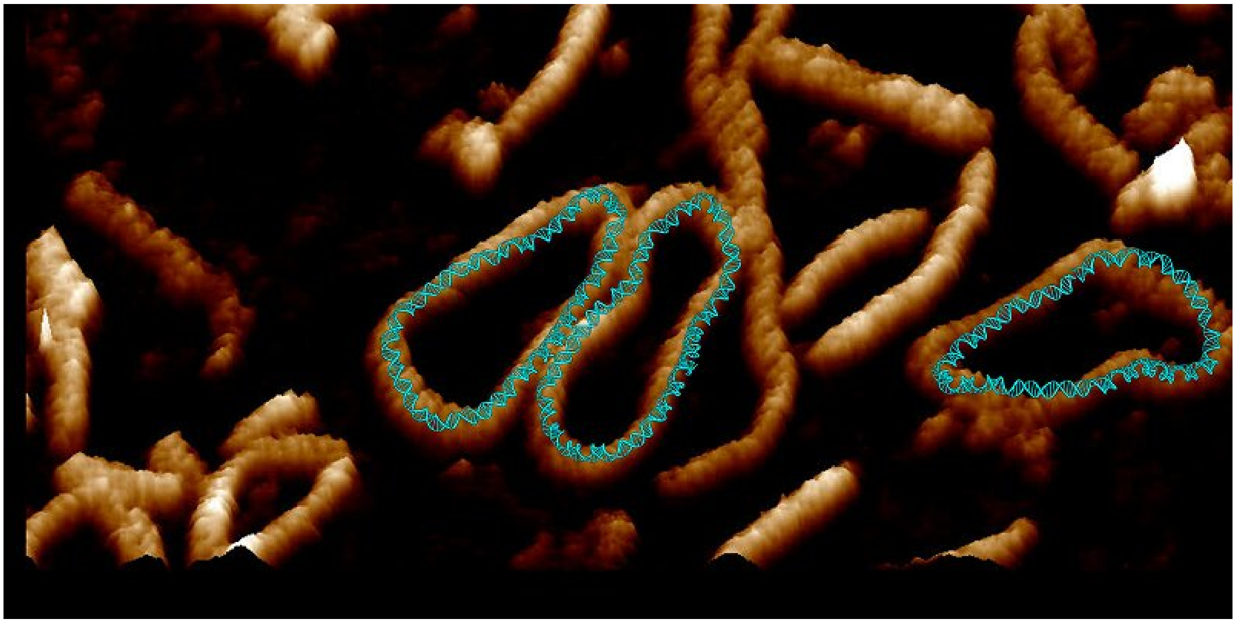
Dynamic

When the researchers imaged relaxed DNA, without any twists, they saw that it did very little. However, when they gave the DNA an added twist, it suddenly became far more dynamic and could be seen to adopt some very exotic shapes. These exotic dance-moves were found to be the key to finding binding partners for the DNA, as when they adopt a wider range of shapes, then a greater variety of other molecules find it attractive.

Previous research from Stanford, which detected DNA minicircles in cells, suggests they are potential indicators of health and aging and may act as early markers for disease.

As the DNA minicircles can twist and bend, they can also become very compact. Being able to study DNA in such detail could accelerate the development of new gene therapies by utilizing how twisted and compacted DNA circles can squeeze their way into cells.

Dr. Agnes Noy, EPSRC Early Career Fellow and lecturer in the Department of Physics at the University of York, who did the theoretical modeling in the study, said: ""The computer simulations and microscopy images agree so well that they boost the resolution of experiments and enable us to track how each atom of the double helix of DNA dances."



A visualisation of a DNA minicircle. Credit: University of Leeds

Challenging

Dr. Alice Pyne, lecturer in Polymers & Soft Matter at the University of Sheffield, who captured the footage, said: "Seeing is believing, but with something as small as DNA, seeing the helical structure of the entire DNA molecule was extremely challenging.

The videos we have developed enable us to observe DNA twisting in a level of detail that has never been seen before."

Professor Lynn Zechiedrich from Baylor College of Medicine in Houston Texas, U.S., who made the DNA minicircles used in the study said, "Dr. Pyne and her co-worker's new AFM structures of our supercoiled minicircles are extremely exciting because they show, with remarkable detail, how wrinkled, bubbled, kinked, denatured, and strangely shaped they are which we hope to be able to control someday."

Dr. Sarah Harris, associate professor in the School of Physics and Astronomy at the University of Leeds, who supervised the research, said: "The laws of physics apply just as well to the tiny looped DNA as to sub-atomic particles and galaxies. We can use supercomputers to understand the physics of twisted DNA. This should help researchers such as Professor Zechiedrich design bespoke minicircles for future therapies."

More information: Base-pair resolution analysis of the effect of supercoiling on DNA flexibility and major groove recognition by triplex-forming oligonucleotides. *Nat Commun* 12, 1053 (2021). doi.org/10.1038/s41467-021-21243-y

Provided by University of York

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