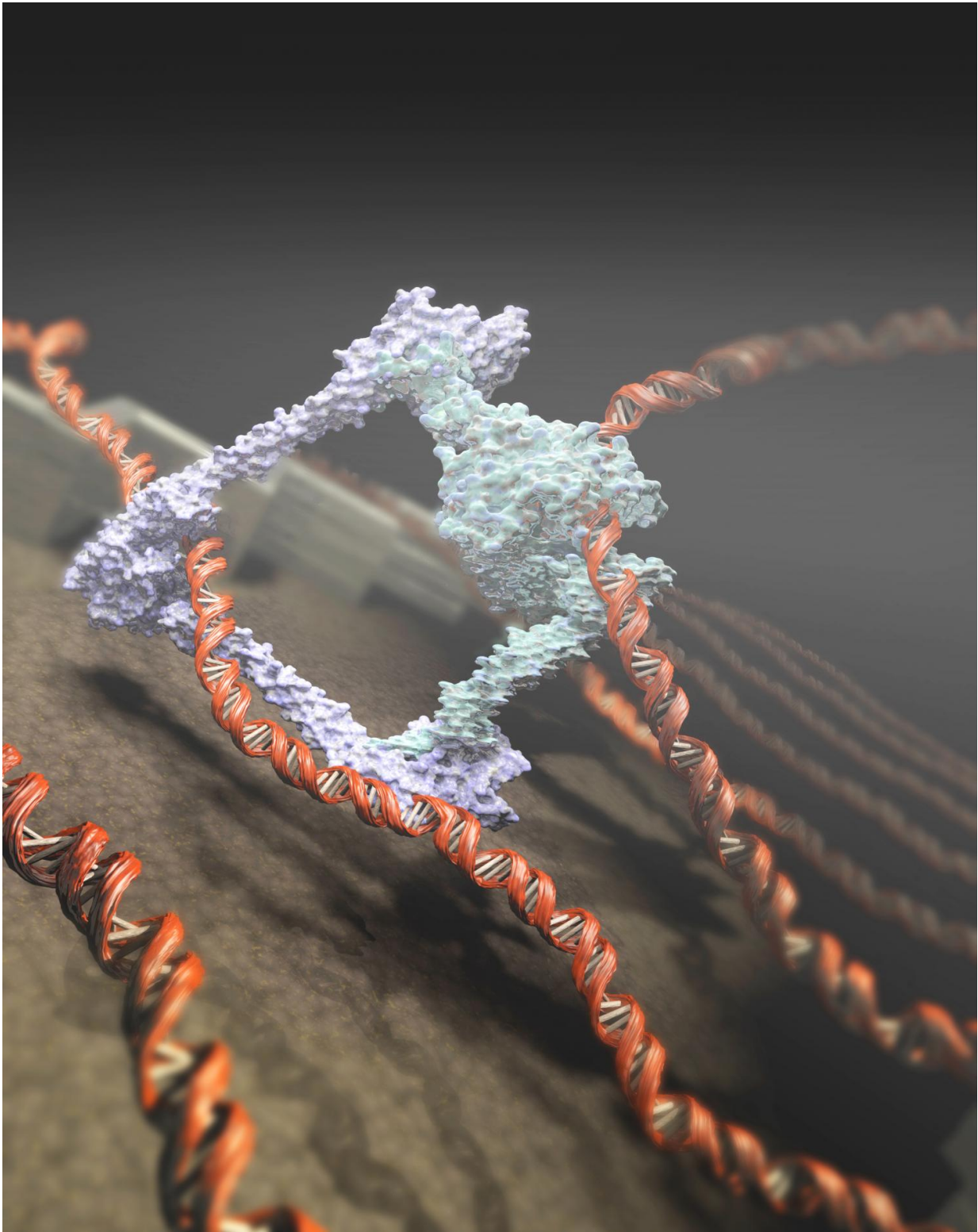


Chromosome motor discovery supports DNA loop extrusion

September 7 2017



Artist impression of Condensin, moving over DNA. Credit: Tremani/Cees Dekker Lab TU Delft

It is one of the great mysteries in biology: How does a cell neatly distribute its replicated DNA between two daughter cells? For more than a century, we have known that DNA in the cell is comparable to a plate of spaghetti—a jumble of intermingled strands. When cells divide, they have to pack two metres of DNA into tidy little packages—chromosomes. This packing is induced by proteins called condensin, but scientists are split regarding the actual mechanism. One argument holds that the protein works like a hook, randomly grasping somewhere in the jumble of DNA and tying it all together. Another holds that the ring-shaped protein pulls the DNA inward to create a loop. In a new study reported in *Science*, researchers from TU Delft, Heidelberg and Columbia University give the oop-extrusion argument a significant boost, demonstrating that condensin does, indeed, have the putative motor function required for this dynamic.

As early as 1882, the renowned biologist Walter Flemming recorded the process of condensation of DNA. Looking through a microscope, he saw how a cell neatly organised the bundles of DNA and subsequently divided them into two new [cells](#). However, the exact details of this process have remained a mystery for more than 100 years.

"There are different schools on this question within the field of cell biology," explains nanobiologist and head of research Cees Dekker from TU Delft's Kavli Institute. "In recent years, the hypothesis that condensin extrudes loops has been winning ground, supported by computer simulations. The idea is that that the ring-shaped condensin grabs the DNA and pulls it through its ring in a loop-like fashion. This is only possible if the [protein](#) has motor activity. One problem with this loop extrusion model was that up until now, a motor function of this kind had not been detected. In addition, too much energy would be required to pull the loops through the ring, far more than the fuel usage that was

observed for condensin."

Motor function

In their article in *Science*, the researchers show for the first time that condensin does have a [motor function](#). They positioned DNA molecules that were stretched on a surface and added condensin proteins, each fitted with a light-emitting quantum dot to enable observation. "We observed how condensin does, indeed, translocate along the DNA. This only happened if fuel was present, in this case the molecule ATP – the petrol that powers all processes in a cell," explains Jorine Eeftens, graduate student at Delft and one of the first authors. "The results also show that condensin takes extremely large steps on the DNA, and therefore needs significantly less ATP than previously thought." In the second stage of their research, the researchers replaced the light-emitting quantum dot on the condensin with a light-emitting string of DNA. They once again witnessed condensin moving in the same way. Condensin is therefore able to move a piece of DNA in relation to another, which corresponds with the idea of loop formation.

"The exact underlying mechanism is still open to discussion. But this discovery is certainly an enormous boost to the loop extrusion camp. We have also shown that the amount of energy used is a lot less than previously thought," says Cees Dekker.

The research represents a significant step in the fundamental understanding of cells, but it is also relevant for medical research. Problems with the protein family to which condensin belongs, the SMC proteins, are related to hereditary conditions such as Cornelia de Lange Syndrome. Condensin is also crucial in the organisation of the chromosomes during cell division, and errors in the process can result in cancer. A better understanding of these processes is vital for tracking down the molecular origins of serious illnesses.

More information: The condensin complex is a mechanochemical motor that translocates along DNA, *Science*, 7 September 2017.
[science.sciencemag.org/lookup/ ... 1126/science.aan6516](https://science.sciencemag.org/lookup/.../1126/science.aan6516)

Provided by Delft University of Technology

Citation: Chromosome motor discovery supports DNA loop extrusion (2017, September 7)
retrieved 26 June 2024 from <https://phys.org/news/2017-09-chromosome-motor-discovery-dna-loop.html>

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