Mechanical forces could affect gene expression

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(PhysOrg.com) -- University of Michigan researchers have shown that tension on DNA molecules can affect gene expression---the process at the heart of biological function that tells a cell what to do.

Scientists understand the chemistry involved in gene expression, but they know little about the physics. The U-M group is believed to be the first to actually demonstrate a mechanical effect at work in this process. Their paper is published in the current edition of *Physical Review Letters*.

"We have shown that small forces can control the machinery that turns genes on and off. There's more to gene regulation than biochemistry. We have to look at mechanics too," said Jens-Christian Meiners, associate professor in the Department of Physics and director of the biophysics program.

A better understanding of how cells regulate themselves could lead to new insights into how the process could fail and lead to disease.

"When cells start to misinterpret regulatory signals, cardiac disease, birth defects, and cancer can result. In fact, mechanical signals have been implicated as a culprit in a variety of pathologies," said Joshua Milstein, a research fellow in the Department of Physics.

To perform their experiment, the scientists used custom "optical tweezers," or lasers, to pull on the ends of bacterial DNA strands with 200 femtonewtons of force, said Yih-Fan Chen, a doctoral student in the

Department of Biomedical Engineering. Chen designed and built the tweezers.

The force they used corresponds roughly to the weight of one-billionth of a grain of rice.

In segments of DNA that were tethered to a microscope slide, the scientists observed a 10-fold decrease in the rate at which the strands looped in on themselves.

DNA looping prevents genes within the loops from being expressed. A common mechanism for gene regulation, it also occurs in complex organisms including humans. Specialized proteins act as buckles to connect distant points on the DNA to form the loops. That's the chemistry part. The challenge for physics is to understand how the DNA bends so those distant points can come together.

While this experiment was performed on free DNA, the scientists say forces as much as 100 times stronger are regularly created inside cells as contents shift and buffet each other.

"If we can basically shut this process down with the tiniest force, how could all these larger forces not have an impact on gene expression?" Milstein said.

Meiners and his team are striving for a quantitative understanding of this biological process. He likens the current state of our understanding of gene expression to a diagram. He is searching for equations, and these results begin to provide that.

"We can tell you how long you'll have to wait for a DNA loop to form based on how much force you apply to the DNA," Meiners said. "We're one step closer to understanding cells quantitatively."

More information: The paper is called "Femtonewton Entropic Forces Can Control the Formation of Protein-Mediated DNA Loops." prl.aps.org/abstract/PRL/v104/i4/e048301

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