

# Researchers unravel mystery of DNA conformation

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An iconic photograph (<http://img.timeinc.net/time/80days/images/530228.jpg>) of Nobel laureates Drs. Francis Crick and James Watson show the pair discussing with a rigid model of the famous double helix.

The interaction represented produced the famous explanation of the structure of [DNA](#), but the model pictured is a stiff snapshot of idealized DNA. As researchers from Baylor College of Medicine and the University of Houston note in a report that appears online in the journal *Nucleic Acids Research*, DNA is not a stiff or static. It is dynamic with high energy. It exists naturally in a slightly underwound state and its status changes in waves generated by normal cell functions such as [DNA replication](#), transcription, repair and recombination. DNA is also accompanied by a cloud of counterions (charged particles that neutralize the genetic material's very negative charge) and, of course, the protein macromolecules that affect DNA activity.

"Many models and experiments have been interpreted with the static model," said Dr. Lynn Zechiedrich, associate professor of [molecular virology](#) and microbiology at BCM and a senior author of the report. "But this model does not allow for the fact that DNA in real life is transiently underwound and overwound in its natural state."

DNA appears a perfect spring that can be stretched and then spring back to its original conformation. How far can you stretch it before something happens to the structure and it cannot bounce back? What happens when

it is exposed to normal cellular stresses involved in doing its job? That was the problem that Zechiedrich and her colleagues tackled.

Their results also addresses a question posed by another Nobel laureate, the late Dr. Linus Pauling, who asked how the information encoded by the bases could be read if it is sequestered inside the DNA molecular with phosphate molecules on the outside.

It's easy to explain when the cell divides because the double-stranded DNA also divides at the behest of a special enzyme, making its genetic code readily readable.

"Many cellular activities, however, do not involve the separation of the two strands of DNA," said Zechiedrich.

To unravel the problem, former graduate student, Dr. Graham L. Randall, mentored jointly by Zechiedrich and Dr. B. Montgomery Pettitt of UH, simulated 19 independent DNA systems with fixed degrees of underwinding or overwinding, using a special computer analysis started by Pettitt.

They found that when DNA is underwound in the same manner that you might underwind a spring, the forces induce one of two bases - adenine or thymine - to "flip out" of the sequence, thus relieving the stress that the molecule experiences.

"It always happens in the underwound state," said Zechiedrich. "We wanted to know if torsional stress was the force that accounted for the base flipping that others have seen occur, but for which we had no idea where the energy was supplied to do this very big job."

When the base flips out, it relieves the stress on the DNA, which then relaxes the rest of the DNA not involved in the base flipping back to its

"perfect spring" state.

When the molecule is overwound, it assumes a "Pauling-like DNA" state in which the DNA turns itself inside out to expose the bases -- much in the way Pauling had predicted.

Zechiedrich and her colleagues theorize that the base flipping, denaturation, and Pauling-like DNA caused by under- and overwinding allows DNA to interact with proteins during processes such as replication, transcription and recombination and allows the code to be read. And back to the idea of the "perfect spring" behavior of the DNA helix - "This notion is entirely wrong," said Zechiedrich. "Underwinding is not equal and opposite to overwinding, as predicted, not by a long shot, that's really a cool result that Graham got."

More information: The report is available free at [nar.oxfordjournals.org/cgi/con ... 0&resourcetype=HWCIT](http://nar.oxfordjournals.org/cgi/con...0&resourcetype=HWCIT)

Source: Baylor College of Medicine ([news](#) : [web](#))

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