DNA enzyme's speed confirms physics law

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UC DAVIS (US) — Scientists have used a protein that unwinds DNA to show that the ergodic theorem can be demonstrated by a collection of individual protein molecules.

The ergodic theorem, proposed by mathematician George Birkhoff in 1931, holds that if you follow an individual particle over an infinite amount of time, it will go through all the states that are seen in an infinite population at an instant in time. It's a fundamental assumption in statistical mechanics—but difficult to prove in an experiment.

Using technology for watching single enzymes at work, the researchers found that when they paused and restarted a single molecule of the DNA-unwinding enzyme RecBCD, it could restart at any speed achieved by the whole population of enzymes.

Straight from the Source

Read the original study [1]

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"It's pretty impressive," says Daniel Cox, a physics professor at the University of California, Davis, who was not involved in the work. "The laws of physics should apply to biological systems, and it turns out they do."

The results, published in *Nature* [1], also have implications for understanding how proteins fold into their correct shape, for exploring interactions between drugs and their targets, and for engineering enzymes for new functions.

UC Davis graduate student Bian Liu and Professor Steve Kowalczykowski weren't attempting to test laws of physics when they began the work. They wanted to know why RecBCD, an enzyme that unwinds DNA in *E. coli* bacteria, showed so much variability in its rate of action.

RecBCD attaches to and moves along DNA, unwinding the double helix into two separate strands. It has two jobs in the cell: to allow damaged DNA to be repaired, and to break down invading "foreign" DNA from viruses.

In 2001, Kowalczykowski's laboratory, with the late professor Ronald Baskin, developed a technique to trap single molecules of RecBCD and watch them at work on a strand of DNA in real time. They have since exploited the method to study how DNA is repaired—in humans, a vital process in protecting against cancer and developmental defects.

"Ever since the original experiments, we've noticed RecBCD molecules have quite a broad range of speeds," says Kowalczykowski, a member of the department of microbiology and molecular genetics and the UC Davis Cancer Center.

Liu used the single-molecule visualization technique to measure the rates of hundreds of RecBCD molecules, finding bell-shaped curves for the whole population.

One explanation could be that a large proportion of the proteins were not folded properly and were "trapped" in an inefficient state. However, mild heat or unfolding treatments, which should have allowed the proteins to relax into their correct folded state, had no effect.

Fuel and speed

RecBCD usually runs for about a minute before stopping spontaneously. Liu found that he could stop the enzyme early by taking away ATP, the chemical fuel that makes the enzyme work.

When he brought back the fuel, he found that the enzymes started up again—but at a random speed, not related to their previous rate. Overall, the individual RecBCD proteins could restart at any speed within the bell-shaped spread shown by all the proteins.

The experiment shows that RecBCD can move through a wide range of slightly different conformations in which it works at slightly different speeds. However, when it is attached to a step on the DNA ladder, it is locked in shape. Because the time for the enzyme to move from step to step along DNA is shorter than the time it needs to change conformation (about one second), it remains in the same conformation as long as it is moving along DNA, Kowalczykowski says.

What is the point? Why not just have all the enzymes work at one, optimal rate? Having this important enzyme able to operate at a range of speeds might give the cell flexibility to respond to rapidly changing conditions, Kowalczykowski says.

For example, degradation of foreign DNA is a process that needs to go quite fast: copying and repairing DNA might require the enzyme to work more slowly, in combination with other proteins.

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Source: UC Davis [2]
