New Look At DNA Hints At Origin Of Ultraviolet Damage

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Chemists at Ohio State University have gained new insight into how sunlight affects DNA. And what they found overturns ideas about genetic mutation that originated decades ago.

In the current issue of the journal Nature, Bern Kohler and his colleagues report that DNA dissipates the energy from ultraviolet (UV) radiation in a kind of energy wave that travels up the edge of the DNA molecule, as if the energy were climbing one side of the helical DNA "ladder."

The finding lends insight into how DNA damage occurs along the ladder's edge.

It also counters what scientists proposed in the 1960s: that UV causes mutations by damaging the bonds between base pairs – the horizontal "rungs" on the ladder. The new study shows that UV energy moves vertically, between successive bases.

In undamaged DNA, there are no chemical bonds between vertically stacked bases. But the bases do interact electronically, which is why Kohler thinks they form an efficient conduit for UV energy to flow through.

"Even though paired bases are connected by weak chemical bonds, it's the interactions that take place without chemical bonds – the interactions between stacked bases – that are much more important for dissipating

UV energy," Kohler said.

The Nature paper builds on work from five years ago, when the associate professor of chemistry and his team first discovered that single DNA bases convert harmful UV energy to heat to prevent sun damage in the same way that sunscreen molecules protect sunbathers.

Back then, they studied only single bases floating in water. They hit the bases with a kind of UV strobe light, and saw that the energy was released as heat in less than one trillionth of a second.

Their new experiments show that the behavior of full DNA differs profoundly from that of isolated bases. When the chemists turned their strobe light on whole strands of novel DNA, the UV energy still changed to heat eventually, but the energy dissipated a thousand times more slowly.

That's an eternity in the DNA universe, where scientists need to use special equipment just to see these ultra-fast chemical reactions happen. Yet, Kohler's team saw no evidence that the UV affected the chemical bonds between the base pairs. They surmised that the UV energy was leaving the molecule by traveling along the edges instead.

"This slow relaxation of energy is utterly different from the mechanism in single bases that transforms the energy into heat in less than a trillionth of a second," Kohler said.

"Eventually, the energy does turn into heat, but the important point is that the energy is retained within the molecule for much longer times," he added. "This can cause all kinds of photochemical havoc."

It could be that when base pairs are aligned in their natural state in a DNA strand, the electronic interactions along the stack provide an easier

way for DNA to rid itself of UV energy, compared to passing the energy back and forth between the two bases in a base pair as scientists have previously thought.

In fact, it was the brilliance of James Watson and Francis Crick's discovery of the structure of DNA that kept this secret hidden for so many years, Kohler said. Their work revealed that the DNA helix was composed of paired bases, and that discovery led researchers to focus on how UV energy might interact with base pairs.

"In fact, so much attention has been paid to base pairing that this other interaction, base stacking, has been neglected," Kohler said.

Base stacking is frequently overlooked, he admitted, because the ladder terminology that we use to describe DNA structure makes us think that there are open spaces between successive rungs of base pairs.

A better analogy would be a stack of coins, he said. Bases are stacked right on top of each other.

Here's what he and his team suspect is happening during the UV energy wave: as sunlight warms our skin, UV photons are absorbed by the bases, causing their electrons to vibrate. These high-energy vibrations nudge the atoms in the bases around, but only along one edge of the DNA ladder at a time.

If all goes well, the DNA returns to normal after the energy wave passes. But some of the time, the atoms don't return to their original positions, and new chemical bonds are formed.

Scientists know that such accidental bonds create "photolesions" – injuries that prevent DNA from replicating properly. The details of the process aren't fully understood, but studies suggest that photolesions

cause genetic mutations that lead to diseases such as cancer.

This new research helps explain why most photolesions are formed between bases on the same side of the DNA strand.

Scientists believe that proteins in the body repair DNA by removing photolesions and filling in new material, using the remaining DNA strand as a template.

If UV damage is confined to one side of the DNA double helix or the other, then the undamaged side makes an easy template for the proteins to follow. But if both sides of a strand were damaged, then the template would effectively be missing.

The Nature paper highlights the shortcomings of previous studies, which applied results from isolated base pairs to the full DNA molecule. "It turns out that you can't extrapolate the results of base pairs to whole strands of DNA," Kohler said.

The discovery has clear implications for biology, since it can help explain the DNA repair process.

"The ability to observe what happens to electronic energy in DNA on such short time scales also extends the hope that methods such as ours can finally determine how DNA is damaged by UV light in the first place," Kohler said.

The Ohio State chemists are now testing other DNA strands. For simplicity, they first wanted to compare the behavior of single Adenine and Thymine bases with strands entirely composed of those two bases. That is the work described in Nature.

Kohler's team includes Carlos E. Crespo-Hernández and Boiko Cohen,

both postdoctoral researchers in the Department of Chemistry at Ohio State. Their work was sponsored by the National Institutes of Health and the Alexander von Humboldt Foundation, and was performed at Ohio State's Center for Chemical and Biophysical Dynamics, which is funded by the National Science Foundation.