# An Electrifying DNA Debate

## New evidence explains how DNA conducts charge

By CORINNA WU

Look at a long, thin piece of DNA and it's not hard to think of it as a wire. Look more closely at its atomic structure and it's even easier to think of DNA that way.

Two single strands twirl together into a double helix—a twisted ladder with rungs formed by pairs of complementary molecular bases. Electron orbits within the base pairs extend above and below each rung of the ladder, overlapping with their counterparts from neighboring rungs and creating a continuous pathway through the molecule.

Other polymers with similar systems, known as pi-stacks from the name of the orbitals that overlap, conduct electricity easily. For many years, researchers wondered, Could DNA do the same?

Some provocative experiments done several years ago by Jacqueline K. Barton of the California Institute of Technology in Pasadena and her colleagues indicated that the answer is yes. Their results suggested that electrons move through DNA with amazing ease over long distances. In effect, DNA acts like a "molecular wire," Barton said.

Many other researchers, however, were not so sure. Their own experiments suggested that electrons didn't travel through DNA with such impunity. The electrons took a slower pathway instead of a fast "pi-way" through the center of the DNA molecule, they believed. Barton's experiments ignited a controversy that has endured to this day.

New evidence, however, may bring researchers closer to resolving this contentious debate. As scientists delve into the details of DNA's electrical properties, they've found the picture to be much more complicated than they originally thought. Researchers once on opposite ends of the spectrum of opinions are fitting the disparate results into a common framework. The question no longer is whether DNA can conduct, but how well and under what circumstances.

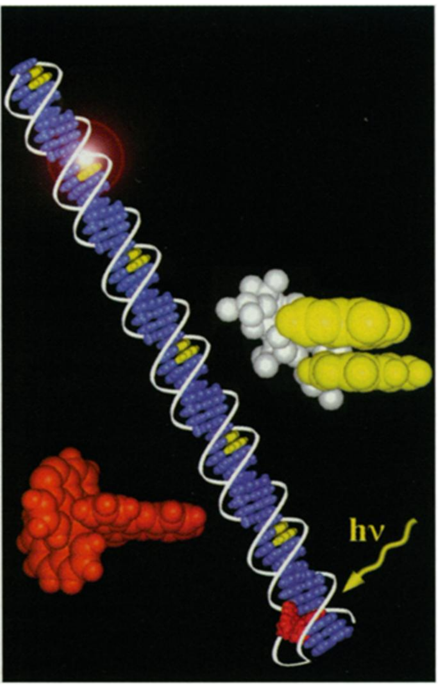
By understanding how charge moves within DNA, researchers hope to learn how radiation causes genetic damage and maybe even how DNA repairs itself.

About a decade ago, while at Columbia University, Barton and her colleague Nicholas J. Turro designed an ingenious experiment to probe the ability of electrons to zip through DNA's pi-stack. They chose two molecules that slipped in, or intercalated, between the rungs of the ladder.

First, they slipped an electron-donating ruthenium complex into the DNA helix. When the researchers shone light on it, the ruthenium complex glowed. Next, they added an electron-accepting rhodium complex, and the glow disappeared.

To come up with an explanation for these findings, Barton and her colleagues assumed electrons could travel within the pi-stack. Shining light on the DNA excites an electron in the ruthenium complex to a higher energy state; when that electron falls back to its original state, the excess energy comes out in the form of a photon of light.

Barton




*A photon of light hits a charge-donating molecule (red) that has slipped into a strand of DNA. The charge travels along the DNA, which contains several pairs of guanine bases (yellow), and oxidizes one of the bases (white flash).*

When the DNA also contains a rhodium complex, however, the excited electron moves to that complex, and no light emerges.

Other scientists expressed skepticism at the findings. Although some synthetic organic polymers do conduct electricity, biological molecules, such as proteins, had not shown such evidence of conductance. "To the protein community, it was outrageous," Barton says. "The outside world didn't have any theory for this," Turro adds.

Barton admits that the critics had a point. Her studies depended on a negative observation—the quenching of luminescence. That left open the possibility that the electron-accepting molecules might be clustering around the electron-donating complexes, thus short-circuiting the glow.

To address these concerns, the researchers tethered an electron-donor molecule to one end of a short strand of DNA. They found that the tethered molecule luminesced. When they also attached an acceptor molecule to the other end, the luminescence vanished. In these experiments, they felt certain that the intercalators would stay a fixed distance—0.4 nanometers (nm)—apart and that the electrons would have nowhere to go except between the rungs of the DNA ladder.

It had taken nearly 5 years of work to synthesize the molecules for the experiment, says Turro, but the results in 1993 convinced Barton and her colleagues of the reality of fast electron transfer through the pi-stack.

Contradictory results from other groups soon intensified the debate. Chemists characterize the speed of this type of transfer with an experimentally determined quantity they call beta. In proteins, beta is equal to about 1, which means that electrons move along them only with great difficulty. Barton's measurements on DNA revealed a beta of 0.2, indicating that electrons zip along the strand with very little resistance.

Using a slightly different system of donors and acceptors attached to DNA, a second group at Caltech arrived at a lethargic beta value of about 1.

Anthony Harriman of the Louis Pasteur University in Strasbourg, France, devised a system in which donors and acceptors intercalate into DNA, with random separations. He excited luminescence and traced how quickly the light died away. If electron transfer is fast, he argues, luminescence should fade quickly regardless of the distance between donors and acceptors. If electrons have trouble moving along DNA, however, the speed of decay should depend strongly on separation.

Using nearly 40,000 such measurements, Harriman assembled a statistical profile of the luminescence. "No other technique can give you data you can fit so accurately," he claims. His results suggested an electron-transfer rate similar to that for a protein.

He casts doubt on the results obtained with tethered intercalators. "The molecules are so hard to make, no one has been able to duplicate the work yet," Harriman complains. "If it's so exotic that others can't repeat it, that's a ridiculous state of affairs."

Several other groups staked out a middle ground between the two extremes. They measured intermediate beta values. To them, DNA appeared to conduct better than a protein but still not as well as a true molecular wire.

For example, Frederick D. Lewis and his colleagues at Northwestern University in Evanston, Ill., designed a molecular system to study how electron transfer depends on distance. Using only the paired bases adenine and thymine, they synthesized short strands of DNA having a molecule called stilbene at one end. Stilbene serves as an electron acceptor. At various locations along the strand they inserted the other pair of DNA bases, guanine and cytosine. The easily oxidized guanine served as the electron donor.

The researchers found that electron transfer indeed depended on strand length. They calculated a DNA beta value of about 0.6—which translates into a rate midway between the values obtained by Barton and Harriman.

Despite the reports of slower conductance, Barton feels that she and her coworkers have clearly demonstrated fast conduction through the pi-stack. She doesn't rule out the slower conductances, however. "Everyone was getting different results," she says. "If you think about the controversy, [the mechanism] had to be complicated."

Theoretical work on the mechanism of the electron transfer has shed some light on this quandary. Assuming that electrons tunnel through the pi-stack, David Beratan of the University of Pittsburgh and his colleagues have modeled three experimental systems: Harriman's, Barton's, and one devised by Barton's colleague Thomas J. Meade. So far, the theoretical models predict slow electron-transfer rates that drop with increasing distance between donor and acceptor molecules. Such models are consistent with Meade's and Harriman's results but not with Barton's, Beratan says.

He suggests, however, that more-sophisticated theoretical models may explain some of the discrepancies in these experimental results. Tunneling through the pi-stack turns out to be slow, but if the electrons travel by way of some other mechanism, they could potentially move much faster, says Beratan.

For example, Gary B. Schuster and his colleagues at the Georgia Institute of Technology in Atlanta have suggested a hopping mechanism, in which the charge leaps from the donor to a base to another base and so on down the line to the acceptor. In this case, Beratan explains, the electron could move very fast, perhaps rapidly enough to get the low beta value seen by Barton and her group.

In fact, the observations in any given experiment might result from a mixture of two mechanisms. Schuster and his coworkers have recently proposed that electrons travel via a series of short pi-ways in the DNA strand, hopping from the end of one pi-way to the beginning of the next. They describe their model in the July 20 PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES (PNAS).

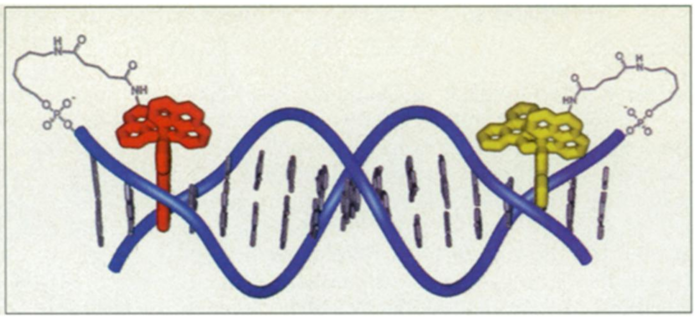
"The introduction of charge in DNA causes a distortion [of the DNA strand] to stabilize the charge," says Schuster. This distortion brings the energy levels of the orbitals constituting the pi-stack closer together, thus facilitating the charge's movement through the DNA strand. Furthermore, thermal motions of the DNA—known as phonons—push the charge down the strand. Schuster's group calls this hybrid process "phonon-assisted polaron hopping."

"We've come to realize that DNA is not a static structure," says Schuster. "Mechanisms that don't consider this distortion are incomplete."

Barton's latest experiments, done in collaboration with her Caltech colleague Ahmed H. Zewail, support the importance of physical distortions and thus add to the evidence for a hybrid mechanism.

Zewail's specialty is probing extremely fast chemical reactions with lasers. Using his technique, the researchers were able for the first time to directly measure the speed of an electric charge along a DNA molecule. They found that it takes 5 picoseconds (ps) for a charge to travel 0.10 to 0.17 nm. However, the rate depends on the access that electrons have to the pi-stack. If the donor shifts away from the pi-stack, the charge takes 75 ps to travel the same distance.

"The sensitivity to the pi-stacking is extraordinary," Barton says. She and Zewail describe their findings in the May 25 PNAS.


Barton

*An electron-donating ruthenium complex (red) and an electron-accepting rhodium complex (yellow) slip in between the bases of a DNA molecule. The complexes are chemically tethered to the ends of the strand so that they will remain a fixed distance apart.*

If DNA does conduct electricity, wouldn't Mother Nature have noticed? "DNA isn't just some polymer," says Barton. Its role as the carrier of genetic information suggests that organisms might take advantage of its electrical properties somehow. "The fact that DNA can transfer electrons probably has some biological implications, but no one knows what they are," says Schuster.

Researchers can speculate, though. Since the 1960s, radiation biologists have wondered whether the effects of gamma rays can travel down DNA and cause damage.

In 1996, Barton found that light shone on a tethered intercalator can oxidize pairs of adjacent guanines located farther down the DNA strand. Some biological molecules, such as tryptophans, can be intercalated into DNA, she adds. Perhaps some carcinogens wreak havoc with DNA by inserting themselves into the pi-stack.

Ironically, DNA might also repair itself with this process. Barton has found that electron transfer can fix a mutation known as a thymine dimer, in which two thymines on the same DNA strand bond together.

One encouraging finding suggests that cells might actually have the equipment to modulate the electrical properties of DNA. Barton's group reports that an enzyme known as methyltransferase, which is ordinarily involved in DNA repair, can interrupt electron transfer by inserting an insulating chemical group into the pi-stack. The researchers report their finding in the June 16 JOURNAL OF THE AMERICAN CHEMICAL SOCIETY.

The debate over electron transfer, at times, has gotten quite huffy. Is the latest evidence of a hybrid mechanism in DNA strong enough to settle the issue?

"No!" Barton declares. "I think the tide is moving in that direction, though. This is the first time we've measured what the rate is. Now, we can begin to talk about the mechanism."

Though the exchanges between scientists researching this area are sometimes harsh, Barton feels they have lifted the quality of the research. "It pushes you to do better and better experiments. The more you learn, the more questions you have," she says.

Schuster says that the saga of electron transfer in DNA exemplifies the scientific process: provocative initial observations, preliminary explanations, and finally, refinements of those theories.

"Science is a search for the truth," he says. "Now, we're beginning to circumscribe the truth." □

# Astronomy

## New moons make Uranus the champ

Astronomers have discovered two small bodies that are almost certainly moons of Uranus. If the discovery is confirmed, this distant planet would have 20 known moons—more than any other planet in the solar system. The former champion, Saturn, would become the runner-up, with 18 satellites.

J.J. Kavelaars of McMaster University in Hamilton, Ontario, and his colleagues announced their finding in a July 27 circular of the International Astronomical Union. The team used the 3.5-meter Canada-France-Hawaii Telescope atop Hawaii's Mauna Kea to spy objects in the outer solar system's reservoir of comets, the Kuiper belt, as well as to search the vicinity of Uranus. A search within 100 million kilometers of the planet revealed only the two bodies.

There's a small possibility, says Kavelaars, that these small bodies are not satellites of Uranus but escapees from the Kuiper belt that are orbiting the sun. However, both the location and the speed of the faint objects—they lie near Uranus and appear to move with the planet—make that possibility remote, he says. The researchers estimate that each body has a diameter less than 20 km and resides several million kilometers from the planet.

Two years ago, using the 5-meter Hale Telescope on Palomar Mountain near Escondido, Calif., Kavelaars and his colleagues discovered the 16th and 17th moons of Uranus (SN: 12/6/97, p. 360). This past spring, Erich Karkoschka of the University of Arizona in Tucson, found an 18th moon in images taken by the Voyager 2 spacecraft as it flew past the planet.

The moons found by Kavelaars' team in 1997, as well as the objects announced in July, share an unusual trait. They are the only bodies with orbits inclined relative to the planet's equator.

Kavelaars suggests that soon after Uranus formed, two chunks of debris that resided near the planet collided and broke into fragments. The fragments then passed through gas in Uranus' young, bloated atmosphere that slowed them down until they were captured by the planet's gravitational field.

If the collision theory is correct, Uranus may have several more moons, but most would be too small and dim to detect, Kavelaars says. *—R.C.*

## Extrasolar planet with an Earthlike orbit

Tracking the wobbling motion of several hundred nearby stars, astronomers over the past 4 years have found evidence of some 20 planets outside the solar system. The latest find, announced July 29, stands out from the crowd. Its orbit more closely resembles that of Earth than any extrasolar planet previously found.

The planet lies an average of 137 million kilometers from its parent, the sunlike star iota Horologii. That's 92 percent of the distance between Earth and the sun. The planet's mass, however, is at least 2.26 times that of Jupiter, or 718 times that of Earth, report Martin Kürster of the European Southern Observatory in Santiago, Chile, William D. Cochran of the University of Texas at Austin, and an international team of colleagues.

Rather than having a solid surface, the planet is most likely a giant blob of noxious gases like Jupiter and is unlikely to support life, Cochran says. However, "if such a planet has a system of satellites around it, they would be an excellent place for life to develop," he adds.

Geoffrey W. Marcy of San Francisco State University and the University of California, Berkeley says there's another reason he finds the new object intriguing. Like the other 11 extrasolar planets that reside farther than 29 million km (20 percent of the Earth-sun distance) from their parent star, this one has an elliptical orbit. "This new planet adds to the suspicion that our solar system with its neat, circular, coplanar orbits, may be the exception rather than the rule." *—R.C.*