Electrons travel through proteins like urban commuters

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For Duke University theoretical chemist David Beratan, the results of his 15 years of studying how electrons make their way through some important protein molecules can be summed up with an analogy: how do big city dwellers get from here to there?

It's often swiftest to take the subway, Beratan notes, but riders may sometimes elect to alter their route by exiting the train for a short cab ride or a walk down the street. And they also may have to work around a route that is temporarily out of service.

In the Friday, Feb. 2, issue of the journal *Science*, Beratan and two co-authors use similar logic to describe their unified description of electron movements through certain "electron-transfer" proteins that lie at the heart of many processes essential for life. Such processes include harvesting light in photosynthesis in plant cells and generating energy in animal cells.

"I think we have discovered the physical framework for thinking about all such protein electron-transfer chemistry," Beratan said. "Having this rule book in place will let scientists pose some hard but interesting questions about evolutionary pressures on protein structures.

"Another payoff may be new insight for designing biologically based artificial systems that, for instance, can capture solar energy or make fertilizer from air," he added.

For more than 50 years, theoreticians have been pondering the most likely itineraries that electrons follow through electron-transfer proteins, Beratan said. These proteins "are believed to shuttle electrons around, one at a time, but not to do any chemistry that involves the forming or breaking of chemical bonds," he said.

Earlier theoretical work from Beratan's group indicated that electrons can take short cuts through the proteins by following the spooky guidelines of quantum mechanics.

That means the electrons may sometimes leak from one chemical bond to a neighboring bond, he said. They also can take forbidden walks on the wild side by tunneling through open space.

Those findings prompted scientists to conjecture that electron-transfer proteins actually evolved their shapes to allow electrons the option of using quantum rules in negotiating molecular folds and crevices. The possibilities of such quirky routing options have vastly increased the challenge for theoreticians such as Beratan.

Using ever larger networks of computers to calculate the most favorable routes of electron travel, Beratan and his colleagues analyze these proteins in much the same way that commuters pore over transportation maps to plot the fastest destination routes.

The key insight to their current study arose from understanding that as the proteins' atoms jiggle around, the "subway maps" change dynamically.

Beratan said their extended computer analyses have been aided by an experimental team from the California Institute of Technology that has been documenting where electrons are moving by attaching extra chemical groups at various positions on protein surfaces. Shining laser

light on these chemical groups enables researchers to monitor the movement of electrons.

The Caltech experiments, prompted in part by the predictions of Beratan's group, showed several years ago that the swiftest electron routes can sometimes be longer than expected, because electrons move fastest along chemically bonded pathways.

In contrast, electrons move much slower if they must tunnel through empty space. But the through-space routes can actually prove optimal if they enable electrons to make major shortcuts.

"You can think about a through-bond network being analogous to taking a subway route, and a through-space connection being analogous to walking or taking a bus between subway stops," Beratan said.

New analyses reported by Beratan's group have uncovered that more complicated routings are important in some electron-transfer proteins. There can be multiple pathways that fluctuate in importance as the protein atoms move around. "We can capture those pathway fluctuations only by doing combined quantum mechanical and classical, standard calculations, which we're now able to do," he said.

The new report describes the mixed quantum-classical analysis of likely electron pathways in the electron-transfer protein cytochrome b562.

The analysis uncovered that at seven locations on the protein, electrons took multiple fluctuating pathways. "So there is always a rapid commuter route available, even if the favorite train is out of order," he said.

In two other locations, the protein offers only one dominant but slow route. There the electron has no choice but to tunnel through an

especially slow bottleneck presented by the protein's structure.

"After we saw this compelling bimodal behavior in cytochrome b562, we wondered whether this behavior was general among electron-transfer proteins," Beratan said. "And we've found that all of the proteins we have looked at have this same behavior.

"I think we're able to explain why there is this dichotomy, and why some electron-transfer rates have a quite remarkable dependence on protein structure while others don't," he said. "I believe we now have a unified view of many years' worth of experimental data."

Source: Duke University