Study sheds light how amino acid side chains and peptide secondary structure change electron transport

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(Phys.org)—In an effort to understand how to meld electronics with biochemistry, known as bioelectronics, several research groups have studied how electronic charges travel through peptides. Proteins are made of peptides and peptides are made of amino acids. A group of experimentalists and theorists from the Weizmann Institute of Science investigated how amino acid side chains, peptide length, and peptide secondary structure affect electron transport by anchoring varieties of peptide chains between two gold electrodes. They found that the side chain as well as secondary structure directly affects electron transport. Their work appears in the *Journal of the American Chemical Society*.

Typically, electron transfer is studied in proteins using electrochemical or spectroscopic methods. Instead, Sepunaru et al. used a solid-state molecular junction between two gold electrodes in which they made monolayers of homo-peptides, or peptides consisting of varying numbers of repeating amino acids. They investigated conductance as a function of bias voltage and temperature for three different systems: 1) homo-peptides of similar length, but different side chains, 2) homo-peptides of different lengths (i.e., different numbers of amino acids), and 3) homo-peptides of similar length, but different secondary structures. Additionally, in each of these experiments, they looked at the gas phase frontier molecular orbitals using optimally-tuned range-separated hybrid DFT calculations on conformations of the peptides that were optimized by molecular dynamics, to understand differing electron transport

properties. All peptides were functionalized with mercaptopropionic acid to provide a chemical linker to the gold electrode.

In their first experiment, Sepunaru et al. tested four different homopeptides composed of seven amino acids. Specifically, they looked at alanine, glutamic acid, tryptophan, and lysine. All of the peptides had a similar length (approximately 25 Å).

Their results showed that electron transport changes with different amino acid side chains. Tryptophan was found to be the best conductor, followed by lysine, then glutamic acid, and alanine. There is a significant difference among the four peptides with tryptophan's electron transport rate measuring almost twenty-fold larger than alanine's. The authors attribute this to the differences between the HOMO energy levels for each of the peptide chains.

All of the peptides were neutral when tested. The authors wondered whether protonating lysine and deprotonating glutamic acid, thus making a charged peptide, would affect electron transport rates. They found that the protonated hepta-lysine peptide had a much higher conductance, while the deprotonated hepta-glutamic acid peptide had a lower conductance that was comparable to alanine. They also found that the energies of the gas phase occupied and unoccupied molecular orbitals decreased upon protonation and increased upon deprotonation, confirming the importance of the frontier energy levels for electron transport.

In their second experiment, Sepunaru et al. investigated how length of peptide chain affects electron transport. They used homo-tryptophan peptide chains comprised of four, five, six and seven amino acids. They found that the electron transport rate decreased gradually with an increase in peptide length, which is typical for electrode-monolayer systems. However upon closer inspection, the electron transport rate

decreases exponentially with increasing length and it was not temperature dependent. Both of these factors mean that electron transport may be due to tunneling effects.

Finally, the last experiment was to see whether peptide secondary structure affects electron transport. Comparisons were made between extended and helical alanine and lysine peptides. Both will tend to form a helix when the peptide is twenty amino acids long, so the 20-mer extended and helical versions of alanine and lysine were compared with each other and these were compared to the corresponding heptamer peptides.

The authors saw a marked increase in conductance with the helical structure compared to the extended peptide structure. They report that the HOMO-LUMO gap decreases in the helical structure, and the charge is distributed over more of the molecule compared to the extended peptide, indicating that there is a difference in electron delocalization between the extended peptide and the helix.

This study shows that peptide composition and peptide secondary structure directly affect electron transport through a peptide. Sepunaru et al.'s work builds on prior models of electron transport through proteins, providing further insights that can be applied to constructing bioelectronics systems.

More information: "Electronic transport via homo-peptides: The role of side chains and secondary structure" *J. Am. Chem. Soc.*, Just Accepted Manuscript, DOI: 10.1021/jacs.5b03933

Abstract
Many novel applications in bioelectronics rely on the interaction between biomolecules and electronically conducting substrates. However, crucial knowledge about the relation between electronic transport via peptides

and their amino-acid composition is still absent. Here, we report results of electronic transport measurements via several homo-peptides as a function of their structural properties and temperature. We demonstrate that the conduction through the peptide depends on its length and secondary structure, as well as on the nature of the constituent amino acid and charge of its residue. We support our experimental observations with high-level electronic structure calculations and suggest off-resonance tunneling as the dominant conduction mechanism via extended peptides. Our findings indicate that both peptide composition and structure can affect the efficiency of electronic transport across peptides.