

Biomolecules: Trying Nanometer Measurement for Size

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As part of a comparative international study, researchers have successfully tested and validated a method of investigating dynamic protein structures.

The precise measurement of biomolecules can play a critical role in improving our understanding of fundamental life processes. In a large-scale comparative study involving 19 laboratories around the globe, a team working with [LMU](#) scientists Professor Thorben Cordes and Professor Don C. Lamb, alongside Professor Claus Seidel of [HHU](#) in Düsseldorf and Dr. Anders Barth of [Delft University of Technology](#), has now tested a method of measuring the precise dimensions and comparability of biomolecules. Their findings are published in [Nature Methods](#).

Proteins are the fundamental building blocks of life. Every animal, every plant and every microorganism is made up of proteins and only 'works' on the basis of countless complex processes that are controlled by the interplay of different proteins. It is therefore no wonder that science has a keen interest in a better understanding of these biochemical all-rounders.

The problem is that we cannot simply measure them with a ruler. Researchers thus have to resort to a whole toolbox full of different investigative methods in order to arrive at an accurate picture of what proteins look like, how they behave and how they work.

How do you measure moving protein structures?

The single-molecule FRET analysis is especially well suited to this purpose. It makes use of what is known as Förster resonance energy transfer (FRET), where energy from an excited chromophore is transferred without radiation to a second light-sensitive molecule. By artificially inserting color molecules (chromophores) in the biomolecules under investigation,

it becomes possible to measure extremely small distances in the sub-nanometer range.

This approach already works quite well to measure distances between different molecules. The structure of DNA strands can likewise be examined fairly reliably. Compared to DNA, however, performing similar operations with proteins is considerably trickier. Proteins are more varied and, above all, more mobile, which makes them much more difficult to analyze.

Notwithstanding, the researchers conducting the study have now been able to establish the process for movable proteins too – successfully enough to achieve precise and reproducible results. For example, they were able to measure not only tiny distances within the protein complexes but also to observe structural differences as proteins changed their shape.

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Visualization of the measurement of proteins with the FRET method.

The laboratories taking part in the study were able to measure such structural changes to within one nanometer, and that on time scales of less than a millisecond. This astonishing precision shows that even dynamic protein systems can be reproducibly measured with FRET.

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The researchers are convinced: Another versatile and reliable instrument has now been added to structural biologists' toolbox. Their hope is that the resultant data will also improve the accuracy of AI-based predictions and thereby further advance our understanding of dynamic processes in proteins.

Read the [original article](#) on LMU Munich.