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## Molecular scales on biological membranes: Mass-Sensitive Particle Tracking

Biophysicists at the Max Planck Institute of Biochemistry have developed a new method to determine location and size changes of unlabeled proteins on membranes via their mass.

**A large proportion of biologically relevant processes take place at membranes. Studying the dynamics of these processes in real time and without disturbing the biological system is still a major methodological challenge. A team led by Petra Schwille, director at the MPI of Biochemistry (MPIB), and Nikolas Hundt from the Ludwig-Maximilians-Universität München (LMU) has now developed a new method for this purpose: Mass-Sensitive Particle Tracking (MSPT). Using MSPT, the movements and reactions of individual unlabeled proteins on biological membranes can be determined solely by their mass. The method has been published in *Nature Methods*.**

Cellular processes on membranes are often fast and short-lived. Molecules assemble briefly, separate again, interact with different partners and move along or through the membrane. It is therefore important to not only study static snapshots of these processes, but also to understand their dynamics. But how can this be achieved methodically? Petra Schwille from the MPIB and Nikolas Hundt from the LMU together with their team have developed the method Mass-Sensitive Particle Tracking – MSPT, which allows to analyze proteins during dynamic processes on membranes.

### Analysis of dynamic processes on biological membranes

The starting point for the biophysicists were recent advancements in mass photometry, which could already be used to determine the molecular mass of unlabeled molecules in solution. What is new about MSPT is that the dynamics of membrane-associated proteins can now be tracked in their biologically plausible environment. In this process, individual proteins are identified by their molecular mass without the need for labeling. Frederik Steiert, one of the first authors of the publication, says: "We can now track directly on biological membranes what mass individual proteins have, how they move and how they interact. This allows us to study the dynamics of biological systems in greater detail." Analyzing dynamic processes is particularly important in biology as many processes at the membrane are transient.



### Mass determination by light scattering

What principles is the new method based on? When light hits a particle, the light is scattered. The intensity of the scattered light depends on the mass of the particle. Videos in which individual proteins on membranes are made directly visible are recorded with a microscope. With the aid of analysis software, these proteins can be tracked and their scattering signal, and thus their mass, can be determined. This is currently possible for proteins with a molecular weight of at least 50 kDa, i.e. for a large part of all known proteins. Another advantage of the new MSPT method is that proteins do not have to be labeled. Labelling can be achieved, for example, by attaching fluorescent tags to molecules. However, labeling poses the risk that proteins could be impaired in their function or that the fluorescent labels could bleach during the experiment. By using MSPT, in contrast, methodological problems that can arise from labeling are prevented.

### MinDE protein system

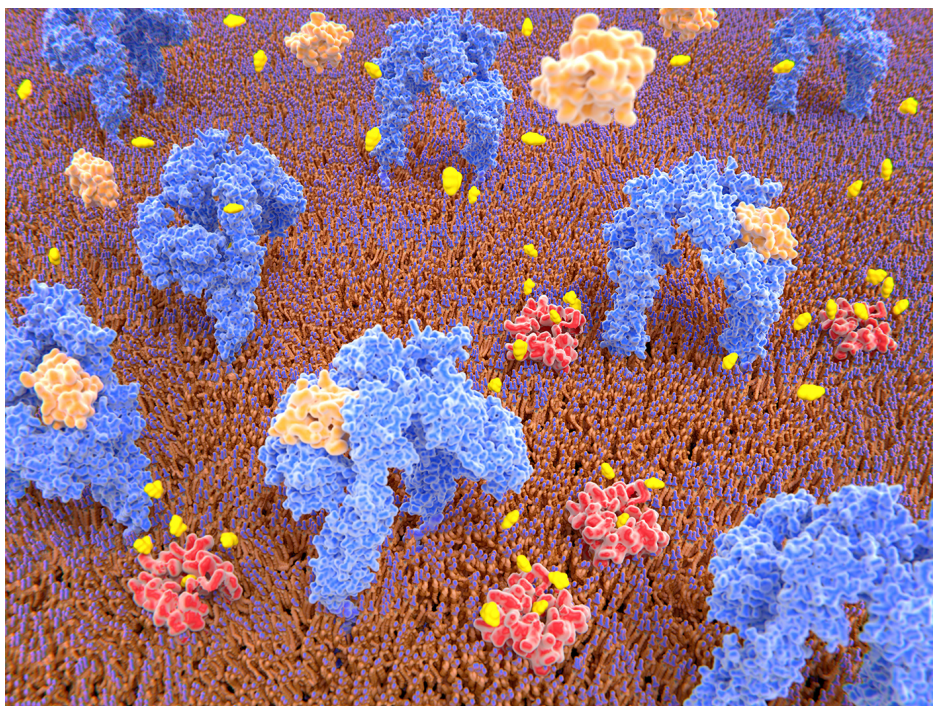
To demonstrate the potential of the method for biological questions, the biophysicists used an established system from the Schwille laboratory: the MinDE protein system from the bacterium *Escherichia coli* (*E. coli*). MinD and MinE proteins are involved in *E. coli* cell division. Tamara Heermann, another first author, says: "The method permits us to characterize properties of dynamical systems that were previously not measurable. This allowed us not only to verify established findings about the Min system, but also to gain new insights." By using MSPT, the team was able to show that the complexes of MinD proteins are larger than initially thought. In addition, the experiments provide first insights that MinE can act as a connecting piece for MinD proteins and that it can thus initiate the membrane release of larger complexes.

As reported in the new *Nature Methods* paper, MSPT provides valuable insights for elucidating dynamic processes at biological membranes. However, the researchers are continuously working on improving the method even further. In the future, the method should also be applicable for integral membrane proteins and it should allow the detection of even smaller proteins.

### Original Publication:

T. Heermann, F. Steiert, B. Ramm, N. Hundt and P. Schwille: Mass-sensitive particle tracking to elucidate the membrane-associated MinDE reaction cycle, *Nature Methods*, October 2021

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**Caption:**

The new method Mass-Sensitive Particle Tracking (MSPT) allows the analysis of molecular mass, movement and interaction of proteins on biological membranes.

Photo: Juan Gärtner – AdobeStock

**About Petra Schwille**

Petra Schwille studied physics and philosophy at the Universities of Stuttgart and Göttingen. She received her doctorate in the laboratory of the Nobel laureate Manfred Eigen at the MPI for Biophysical Chemistry. After a postdoctoral stay at Cornell University, Ithaca, New York, USA, she returned to Germany in 1999 to the MPI for Biophysical Chemistry, where she led her own junior research group. In 2002, she was appointed as the Chair of Biophysics to the Biotechnology Center of the TU Dresden (BIOTEC), which she held until April 2012. Since 2011 she is director at the MPI of Biochemistry and heads the department "Cellular and Molecular Biophysics". Since 2012 she has been honorary professor at the Faculty of Physics of the LMU. Petra Schwille has been awarded several prizes, including the Philip Morris Research Award 2004, the Gottfried Wilhelm Leibniz Prize 2010 and the Bavarian Maximilian Order 2018.

**About the Max Planck Institute of Biochemistry**

The Max Planck Institute of Biochemistry (MPIB) belongs to the Max Planck Society, an independent, non-profit research organization dedicated to top-level basic research. As one of the largest Institutes of the Max Planck Society, about 800 employees from 45 nations work here in the field of life sciences. In currently about 35 departments and research groups, the scientists contribute to the newest findings in the areas of biochemistry, cell biology, structural biology, biophysics and molecular science. The MPIB in Munich-Martinsried is part of the local life-science-campus in close proximity to the Max Planck Institute of Neurobiology, a Helmholtz Center, the Gene-Center, several bio-medical faculties of the Ludwig-Maximilians-Universität München and the Innovation and Founding Center Biotechnology (IZB).



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