MAX-PLANCK-INSTITUT
für die Physik des Lichts

PRESS RELEASE

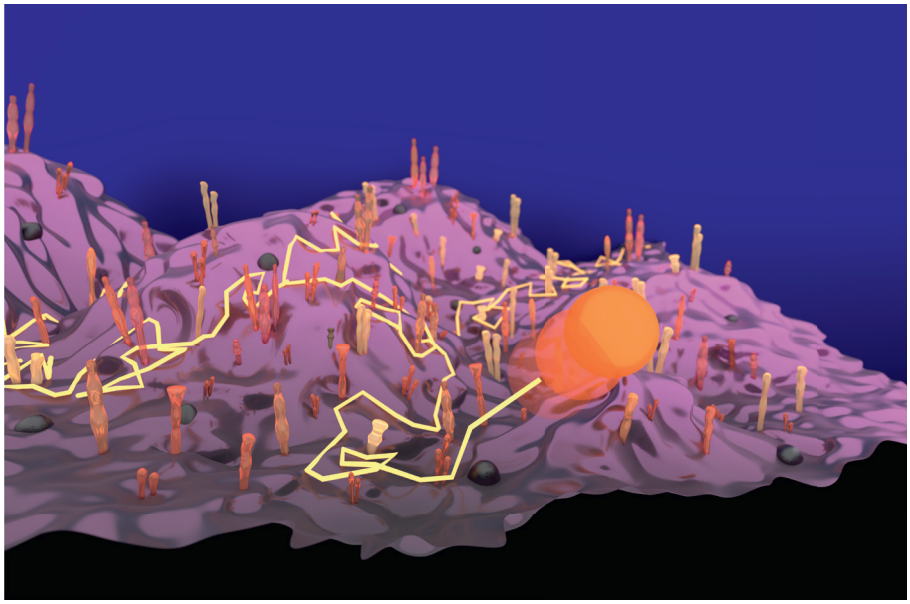
FOLLOWING A PROTEIN NANO-ROVER ON THE CELL MEMBRANE

ERLANGEN, 15 APRIL 2019

The human body is composed of billions of cells, each one representing the smallest self-sustaining unit of life. We know that surfaces of our cells are carpeted with a layer of densely crowded molecules which rush about in a perpetual frenzy. In the blink of an eye, these molecules undergo thousands of collisions with one another as well as with the perilously rough nanoscale terrain upon which they reside. The function of the cell as a whole emerges out of the sum of these interactions. How does being constantly bumped and corralled, knocked and propelled permit a protein to operate? The details of these events have long evaded even the best of conventional imaging microscopies.

Now, scientists at the Max Planck Institute for the Science of Light (MPL) and the newly established Max-Planck-Zentrum für Physik und Medizin can watch this molecular mobility in 3D in both real time and slow motion. With a technique called Interferometric Scattering (iSCAT) microscopy, invented in their laboratories, they can now watch the nanoscale motion of proteins on the cell surface at a very fast speed.

To monitor the motion of single proteins, the scientists attached a tiny gold nanoparticle, the size of 20 nm, to the protein of interest. The gold particle acts as a reflective "backpack", rendering the protein distinct from its neighbours. By illuminating the sample with laser light, the team exploits interference to amplify the weak light that is scattered from the gold backpack. The resulting iSCAT image provides exquisite sensitivity, allowing the researchers to locate the position of the protein with nanometre precision, a length scale comparable to the size of the protein. *"Detecting tiny things with iSCAT is nothing new for us"* boasts Prof Sandoghdar, who led the research. *"We've been able to detect single isolated proteins with high sensitivity for some time now, the challenge here lies in distinguishing the desired signal of a small particle against a large complex background that is unfortunately provided by the cell"*.



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"We used several advanced analysis techniques to decipher the characteristic signature of a gold nanoparticle from a hugely inhomogeneous image to establish three-dimensional trajectories", explained Reza Gholami, a doctoral student in the team. *"Scattering microscopy allows us to follow the same protein for tens of minutes and even hours if we wanted"* explains Richard Taylor, the lead author and a postdoctoral fellow. *"This is completely out of the scope of existing fluorescence microscopes."* Another important advantage of iSCAT microscopy is its remarkable speed, allowing the researchers to also monitor every tiny step of the protein within a few microseconds.

"This technology allows us to watch the proteins as they take part in vital processes such as endocytosis and directed trafficking – all in a detail never before thought possible" remarks Alex Schambony, who is a co-author and professor of biology at Friedrich Alexander University of Erlangen-Nuremberg (FAU). Such information is important for understanding cellular operation at the molecular level, where chemical structure works hand in hand with physical mobility. Their microscopy could also prove useful in unravelling the effect genetic mutations play on protein mobility. Understanding the molecular basis of pathologies is a key step in the development of novel therapeutic approaches.

The team is hoping to apply iSCAT to gain unprecedented insight into fundamental cellular mechanisms. *"Our technique can be easily combined with other conventional methods, and we believe soon one ought to be able to watch the entire life cycle of a protein or a virus"* stated Sandoghdar. For those brave enough to bridge gaps between physics and lifesciences, there remains much to be explored in the nano-world of the cell.

Further reading: **Taylor *et al.* "Interferometric scattering microscopy reveals microsecond nanoscopic protein motion on a live cell membrane" Nature Photonics, X (2019), DOI: 10.1038/s41566-019-0414-6.**

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