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Fast Spatiotemporal Correlation Spectroscopy to Determine Protein Lateral Diffusion Laws in Live Cell Membranes

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each molecule, but we calculate population behavior using all molecules in a
given region of the membrane. First, fast imaging of a given region on the
membrane is achieved. Then, acquisitions at increasing time delays are corre-
lated, for example each 2, 3, n repetitions. If particles diffuse, the width of the
peak of the spatial autocorrelation function increases as the time delay between
frames increases. Fitting of the series of autocorrelation functions enables to
extract the actual protein ‘diffusion law’ from imaging, in the form of a
mean square displacement vs time-delay plot (imSD). The imSD yields a quan-
titative view of the temporal evolution of the average molecular positions with
nanometer accuracy, and no need for interpretative models. We demonstrate
the potentiality of our approach by studying the regulation of protein lateral
diffusion in live cell membranes. By using a GFP-tagged variant of the Trans-
ferrin Receptor (TFR) we are able to observe the regulation of protein diffusion
impacted by the cytoskeleton meshwork on μm-sized membrane regions in the
micro-to-milli-second time range. We show that our approach can successfully
recover TFR diffusion parameters over many microns, and their variation in
response to drug treatments or temperature shifts. Potential extension of this
method to the 3D intracellular environment and differences with respect to
other approaches will be discussed.

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Fast Spatiotemporal Correlation Spectroscopy to Determine Protein
Lateral Diffusion Laws in Live Cell Membranes
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Here we present a straightforward image correlation analysis method to study
the dynamics of fluorescently-labeled plasma-membrane proteins in live cells
with high spatiotemporal resolution1. Notably, we don’t extract and track