University of Basel

Swiss Nanoscience Institute

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In vivo Monitoring of a New-to-Nature Catalytic Event by Super-Resolution Nanoscopy

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Short project description Chemical reactions are the foundation of Life, yet observing these in la iving cell with molecular precision remains a nearly unmet challenge. In this project, we propose to visualize, in real time and with unprecedented spatial resolution, a new-to-nature catalytic reaction occurring on the surface of living *E. coli* cells. With this goal in mind, we will combine an artificial metalloenzyme (ArM) that catalyzes a ring-closing olefin metathesis reaction (RCM) with MINFLUX, the most precise super-resolution microscopy technique currently available—the D-BSSE in Basel has recently purchased such an instrument. By engineering a profluorogenic substrate that becomes fluorescent upon RCM catalyzed by the ArM anchored on the outer membrane of the bacterium, we will track both the ArM's motion and its catalytic RCM activity at the single-molecule level. This proof-of-principle study represents the first attempt to use MINFLUX to monitor a chemical reaction in vivo. Beyond its immediate novelty, this approach has the potential to transform how we study bioorthogonal chemistry in live cells, opening the door to applications ranging from metabolic pathway visualization to targeted drug activation in disease models. This interdisciplinary effort combines expertise in chemical biology, catalysis, and nanoscopy to push the boundaries of what can be observed in living systems.