

**DEVELOPMENT OF PHOTOCROMIC CALCIUM INDICATORS BASED ON
REVERSIBLY SWITCHABLE FLUORESCENT PROTEINS**

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In the last two decades, fluorescence microscopy has become an indispensable tool for the real-time study of biomolecules and biochemical pathways in living cells, tissues, and whole animals. The discovery and development of fluorescent proteins (FPs), and recent advances in diffraction-unlimited far-field optical microscopy have revolutionized modern-day biological research even further.[1] However, the labels remain a limiting factor, especially for super-resolution microscopy where the demands are considerably high.[2] Many of these techniques require the use of ‘smart labels’ such as reversibly photoswitchable fluorophores.[3] Engineered fluorescent proteins have provided some of the best-performing smart labels, and as a result are frequently used for advanced fluorescence imaging. However, in the majority of cases these uses have remained limited to visualizing the locations of the fluorophores, rather than being useful as biosensors.

In this project we combine these interesting implementations of FP technology in order to create highlightable biosensors, based on fluorescent proteins (e.g. rsEGFP[4], Dronpa[5]). These hybrid tools would enable interaction measurements and sensing in living biological systems, on a nanoscale.

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