SUB-MOLECULAR RESOLUTION USING CRYOGENIC COLOCALIZATION MICROSCOPY

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The significance of super-resolution microscopy beyond the diffraction barrier of resolution was recognized by the Nobel Prize in Chemistry last year. One popular method employs pinpointing the position of single fluorophores, whereby the center of the point-spread function can be determined with arbitrary localization precision depending on the available signal-to-noise ratio. At room temperature, the signal of a fluorophore is limited by photobleaching resulting in typical localization precisions on the order of about ten nanometers. We have already demonstrated Angstrom localization precision made possible by the substantial enhancement of the molecular photostability at cryogenic temperatures [1]. Recently, we verified the feasibility of our colocalization microscopy method for cryogenic distance measurements by resolving two fluorophores on the backbone of a double-stranded DNA at nanometer separation [2].

Here, we present our progress towards measuring intramolecular distances in proteins [3]. We perform colocalization of multiple fluorophores attached to model proteins in order to resolve sub-molecular structure. These proof-of-principle experiments hold the promise to ascertain structural information about biomolecules that are incompatible to conventional methods like x-ray scattering. We discuss the important challenges of the technique as well as its potential for further improvement.