W. E. Moerner, Stanford University

Title: Single Molecules as Light Sources for Super-resolution Imaging and Probes for Single Biomolecules in Solution

Abstract: Since the first optical detection and spectroscopy of a single molecule in condensed matter (PRL (1989)), much has been learned about the ability of single molecules to probe local nanoenvironments and individual behavior in biological and nonbiological materials in the absence of ensemble averaging that can obscure heterogeneity. Using the fact that light acts at a distance with little perturbation, single-molecule fluorescence imaging has enabled both materials science studies as well as biophysical measurements in cells. However, the single-molecule emitter can also act as a nanoscale light source which yields enhanced spatial resolution beyond the diffraction limit when combined with optical control of the single emitters (WEM, J. Microsc. (2012)). Using the native photoinduced blinking and switching of enhanced yellow fluorescent protein (Dickson et al., Nature (1997)) we can achieve sub-40 nm super-resolution imaging of a variety of protein structures in the bacterium *Caulobacter crescentus*. With a fluorescently-labeled toxin, the locations of voltage-gated sodium channels on the surface of neuronal cells can be observed in near-real time.

In terms of methods, a new scheme for 3D imaging based on a double-helix point spread function enables quantitative tracking of single mRNA particles in living yeast cells with 15 ms time resolution and 25-50 nm spatial precision (Thompson et al., PNAS (2010)), and this approach has been used to define the 3D spatial structure in bacterial (Lew et al., PNAS (2011)) and mammalian cells (Lee et al. Appl. Phys. Lett. (2012)). Moving away from nanoscopy, it is often important to study a single biomolecule in solution without surface attachment or confinement. To do this, we use a machine called the Anti-Brownian ELectrokinetic (ABEL) trap which provides real-time suppression of Brownian motion, and this device has been used to explore the photodynamics of single copies of antenna proteins, chaperonins, and redox enzymes (Wang et al. Acc. Chem. Res. (2012)). The examples provided here illustrate some of the frontiers where the power of optics and lasers applied to single-molecule spectroscopy and imaging is yielding new insights into the behavior of complex systems.

Biography: W. E. (William Esco) Moerner, the Harry S. Mosher Professor of Chemistry and professor, by courtesy, of Applied Physics, conducts research in physical chemistry of single molecules, biophysics, nanoparticle trapping, and nanophotonics. He earned three bachelor's degrees from Washington University in 1975 and master's and doctoral degrees from Cornell University in 1978 and 1982. From 1981 to 1995, he was a research staff member at IBM, receiving two IBM Outstanding Technical Achievement Awards. Moerner was Guest Professor of Physical Chemistry at the Swiss Federal Institute of Technology from 1993 to 1994 and Professor and Distinguished Chair in Physical Chemistry at the University of California-San Diego from 1995 to 1998, the year he joined the Stanford faculty. He spent time as the Robert B. Woodward Visiting Professor at Harvard University in 1997-1998. He was elected Fellow of the American Physical Society in 1992 and received the society's Earle K. Plyler Prize for Molecular Spectroscopy in 2001 and the Irving Langmuir Prize in Chemical Physics in 2009. His other elected fellowships include the Optical Society of America, the American Academy of Arts and Sciences, the Australian Academy of Sciences and the American Association for the

Advancement of Science. He was elected Member of the National Academy of Sciences in 2007, received the Pittsburgh Spectroscopy Award in 2012, and received the Wolf Prize in Chemistry (with Allen Bard) in 2008.