

## Multifunctional Super-resolution Microscopy through Multidimensional Single-molecule Spectroscopy



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### LECTURE ABSTRACT

Recent advances in super-resolution microscopy methods based on single-molecule imaging (single-molecule localization microscopy; SMLM) have led to ~10 nm spatial resolution and exciting new biology. We are advancing beyond the structural (shape) information offered by existing methods, to reveal (intracellular) *functional* parameters, including chemical polarity, diffusivity, and reactivity, with nanoscale resolution and single-molecule sensitivity. To this end, we have been developing new strategies to perform high-throughput, multidimensional single-molecule spectroscopy in the wide-field. In particular, with spectrally resolved SMLM, we encoded functional parameters into the emission spectra of single probe molecules, and so unveiled rich, nanoscale functional and compositional heterogeneities in the membranes of live mammalian cells and in phase-separated surface processes. With single-molecule displacement/diffusivity mapping (SMdM), we mapped out intracellular diffusivity with unprecedented spatial resolution and fidelity, and hence discovered that diffusion in the mammalian cytoplasm and nucleus are both spatially heterogeneous at the nanoscale, and identified the net charge of the diffuser as a previously overlooked, key determinant of diffusion rate. By adding remarkably rich *functional* dimensions to the already powerful super-resolution microscopy, we thus open up new ways to reveal fascinating local heterogeneities in both live cells and chemical systems.

### SPEAKER BIOSKETCH

Ke Xu is an assistant professor in Chemistry and a Chan-Zuckerberg Biohub Investigator at UC-Berkeley. Dr. Xu received his B.S. from Tsinghua University, did his Ph.D. work with Prof. Jim Heath at Caltech, and his postdoc work with Prof. Xiaowei Zhuang at Harvard University. Dr. Xu joined the Department of Chemistry at UC-Berkeley in the summer of 2013. His current research develops new physicochemical tools to interrogate biological, chemical, and materials systems at the nanoscale with extraordinary resolution, sensitivity, and functionality. To this end, his lab takes a multidimensional approach that integrates advanced microscopy, spectroscopy, cell biology, and nanotechnology. Dr. Xu is a Sloan Research Fellow, a Packard Fellow for Science and Engineering, a Beckman Young Investigator, and a Pew Biomedical Scholar, and has received an NSF CAREER Award, an NIH Director's New Innovator Award, and the Talented 12 by *C&EN*.

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