Introduction to the Special Feature on Single-Molecule Chemistry and Biology

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The advent of experiments in single-molecule chemistry ≈20 years ago (1, 2) generated a new type of molecular spectroscopy and provided new ways of looking at the dynamics and reactions of biomolecules. In ordinary ensemble experiments, one measures the average over a large number of molecules, so that individual differences between molecules are unobservable. Early spectroscopic studies of single molecules in low-temperature solids showed that each molecule in the ensemble had a distinct spectrum, that the individual spectrum was time-dependent, and that the distribution of molecular properties was often counterintuitive.

The next 10 years saw many advances in experimental techniques, which are reviewed in refs. 3–7. In the last few years, further advances in imaging and optics and the use of nanomechanical methods such as laser tweezers and atomic force microscopy have opened the field widely to the study of biomolecular behavior in solution. It is now possible to observe the dynamic behavior of single biomolecules and to study the kinetics of enzyme catalysis, for example, at the single-molecule level. All of these studies have revealed both static and dynamic heterogeneity among the different molecules within an ensemble. In addition, time-dependent single-molecule studies show the inherent and ubiquitous fluctuations in the structure and function of these molecules. This presents a molecular picture of a fluctuating single molecule in a dynamic environment, whereas experiments that study an ensemble of such molecules measure only average quantities. Thus, single-molecule studies provide fundamental data on biomolecules and biological processes and even on processes in single cells that are complementary to those of inherently ensemble or average measurement approaches such as NMR and x-ray crystallography. Single-molecule experiments thus will lead to a better understanding of how the mechanisms and dynamics seen in ensemble experiments are generated from dynamics and fluctuations at the molecular level. Theorists and experimentalists will work closely together to examine dynamics at the molecular level and the foundations of statistical mechanics.

This PNAS special feature focuses on recent advances in single-molecule chemistry and biology, presenting studies on topics ranging from physical properties, such as viscosity, to biological processes. The breadth of these articles clearly shows the power and generality of the method. This newly emergent field will provide significant insights and surprises in the years to come.

For several years, PNAS has published special feature issues on many cutting-edge research topics. Themes of past special features have included tissue engineering, social and behavioral sciences, asymmetric catalysis, science and technology for sustainable development, long-range electron transfer, cluster chemistry and dynamics, interstellar chemistry, nitrogen fixation, eukaryotic transposable elements, genome evolution, and, most recently, coordination chemistry of saturated molecules and high-pressure geoscience. Scheduled for future issues of the journal are special features on multidimensional ultrafast spectroscopy and economics. One objective of these special features is to advance the journal's initiative to expand its coverage of the physical and social sciences and mathematics. PNAS continues to encourage and welcome research articles in all areas of the natural and social sciences and mathematics.

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1. Moerner WE, Kador L (1989) *Phys Rev Lett* 62:2535–2538.
2. Orrit M, Bernard J (1990) *Phys Rev Lett* 65:2716–2719.
3. Nie SM, Zare RN (1997) *Annu Rev Biophys Biomol Struct* 26:567–596.
4. Plakhotnik T, Donley EA, Wild UP (1997) *Annu Rev Phys Chem* 48:181–212.
5. Moerner WE, Orrit M (1999) *Science* 283:1670–1676.
6. Xie XS, Trautman JK (1998) *Annu Rev Phys Chem* 49:441–480.
7. Moerner WE (2002) *J Phys Chem B* 106:910–927.