

PREFACE

Ever since Feynman's suggestion in the early 1960s that "there's plenty of room at the bottom," single-molecule tools have seen an exponential rise in popularity (note that exponentially increasing rates are characteristic of explosions!). One can hardly go to a Biophysical Society meeting these days without being impressed by the literally thousands of posters and seminars that show data exploiting the unique capabilities of single-molecule probing techniques. Among their benefits are that they: (i) can directly observe events at the molecular level; (ii) reveal rare and/or transient species and heterogeneities along a reaction pathway, which are often lost in ensemble averages; (iii) can directly access the low copy numbers (typically 1–1000) of any specific biopolymer in a single cell; (iv) afford counting and nanometer-accuracy localization of molecules in spatially distributed samples such as a cell; (v) enable the ultimate miniaturization and multiplexing of biological assays such as DNA sequencing; (vi) allow of the direct measurement of the mechanical forces affecting and enacted by biopolymers; and (vii) yield standard population-averaged information from the statistics of many single-molecule observations. A half-century of single-molecule tool development has yielded technical advances that have demonstrated each of these advantages, and more are sure to emerge.

Yet in any field enjoying increasing popularity, there inevitably comes a crossroads, which inspired MIE volumes 472 and 475. To advance beyond being used or studied only by a limited (and eventually vanishing) group of specialists, a set of tools or area of research needs to find more widespread appreciation. Many methods that are commonplace in labs today – such as gel electrophoresis, PCR, and sequencing – made that transition from specialist's art to general practitioner's basic tool by a combination of being very appealing and becoming easy to master. The two MIE volumes are aimed to facilitate this transition by, often for the first time, revealing for a broad selection of single-molecule tools those details that pioneering specialists rarely have the space to cover in their research publications.

Compiling methods from an emerging field is a daunting task, since new tools are developed nearly daily. The resulting selection is by necessity incomplete, limited by both the availability of contributors and my gaps in knowledge. Yet through the vigorous response to my solicitation of articles, what was planned as one volume became two, somewhat loosely organized by theme. While editing each of these works, I became increasingly impressed by the consistently superb quality of the contributions, in

terms of both style and substance. I am therefore very grateful to John Abelson for convincing me to take on the job as editor, and trusting me with it, to the phenomenal group of authors (some of which even made the deadline), and to the staff at Elsevier for allowing me to divide the contributions into two volumes and supporting me in numerous other ways. My hope is that the hard work by everyone involved bears fruit and helps spread the word and enthusiasm about the power of single-molecule tools.

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