Single-Molecule
Optical Detection,
Imaging and Spectroscopy

edited by
T. Basché,
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Techniques for detection and controlled manipulation of single particles such as atoms, molecules, proteins or nanocrystals have been continuously emerging during the past ten years. Scanning tunneling microscopy and atomic force microscopy allowed for the first time the imaging of single atoms and molecules on surfaces in real space. The optical detection of single particles was first realized by imaging the fluorescence of single atomic ions stored in radiofrequency traps. The present book is dedicated to a survey of optical methodologies to detect and image single organic dye molecules (single fluorophores) in solids, on surfaces and in liquids.

Optical experiments at the single-molecule level hold promise for novel and unexpected achievements in different fields of science. In a single-molecule experiment the usual averaging over large populations is absent and inhomogeneous distributions of different origins that complicate measurements on large ensembles are eliminated. Various kinds of spectroscopy and microscopy and some clever combinations of both can be employed to detect single molecules in the condensed phase between liquid helium temperatures and room temperature. The range of techniques and experimental conditions available spans a very broad research arena, which includes quantum optics, the probing of dynamical interactions in solids and on surfaces on a nanoscopic scale, trace analysis and rare event screening in liquids, as well as studies of molecular processes in systems of biological interest.

The wide range of potential applications demonstrates that the topic of single-molecule detection and spectroscopy is quite interdisciplinary. As such, the book is intended for researchers, graduate students and advanced undergraduates in the field of chemical physics, solid-state physics, analytical chemistry, laser spectroscopy, photochemistry and photophysics of molecules, fluorescence spectroscopy, fluorescence microscopy and molecular biology. The book provides thorough introductions to the various methodologies, which makes it also useful for newcomers who wish to enter the field. Since optical experiments at the single-molecule level are a very rapidly expanding area of research a comprehensive list of references is available at the end of each section of the book.

The book is organized according to the different techniques that are used for single-molecule detection. Chapter 1 which is divided into six sections is devoted to single molecule studies in solids at low temperature. Section 1.1 introduces the field by reviewing the physical principles, methods and experimental techniques of high-resolution spectroscopy of single impurity molecules in solids. Section 1.2 treats the single-molecule excitation lineshape, dispersed fluorescence spectra and quantum
optical experiments. Fluorescence microscopy, lifetime measurements, polarization effects and external perturbations by electric fields or hydrostatic pressure are discussed in section 1.3. The absorption lines of single molecules in solids at low temperatures often undergo frequency jumps (spectral shifts). This behaviour is described in section 1.4, and analyzed theoretically in section 1.5. The last section (1.6) of chapter 1 is devoted to magnetic resonance experiments on single molecular spins with or without an applied magnetic field and to the study of spin coherence.

In chapters 2 and 3 microscopic techniques suitable for single-molecule detection are described. Chapter 2 portrays near-field optical microscopy, a technique with sub-diffraction limited spatial resolution. A qualitative introduction into the basics of near-field optical microscopy is given as well as a synopsis of the various results that were achieved in single-molecule imaging and spectroscopy using this technique. The book concludes with a survey of the potential of single-molecule detection in analytical chemistry (chapter 3). Several microscopic techniques for single-molecule fluorescence detection in solution are outlined followed by applications of single-molecule detection in DNA sequencing and capillary electrophoresis.

The editors hope that the present volume will furnish the reader with a thorough understanding of the basic principles of the very rapidly expanding field of single-molecule detection and spectroscopy in the condensed phase. We would be particularly delighted if the book would also serve yet another purpose, namely to stimulate new research directions in this exciting area. We are grateful to S. Mais for technical assistance and to Dr. T. Mager and Dr. M. Baer from VCH publishers for their assistance and constructive help in preparing this book.

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T. Basché
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U. P. Wild
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