PREFACE

This volume contains the lectures and seminars given at the NATO Advanced Study Institute on "From cell to proteins: Imaging nature across dimensions", held in Pisa, Italy in September, 2004. The Institute was sponsored and mainly funded by the Scientific Affairs Division of NATO. The European Biophysical Societies' Association also supported the School and contributed to its success. It is my pleasant duty to thank these institutions. This ASI offered updated information on how many information we are able to achieve in the exploration of the inner details of biological specimens in their native structure and composition.

How deep we can see inside Nature smallest secrets? Will it be possible someday in a near future to investigate living structures at atomic level? This area of study is very interdisciplinary, since it uses and it is based on the principles and techniques of biology, physics, chemistry, mathematics, and engineering to elucidate the structures of biological macromolecules, of supramolecular structures, organelles, and cells. Scientists from very different backgrounds contributed to the understanding of this fast developing field of research, which has seen considerable progress during the last years. These revelations came not (only) through biochemistry and molecular biology, but through staggering improvements of microscopy.

The widest range of dimensions is covered by the electron microscope (EM): it can image whole cells, their organelles, cytoskeleton and supramolecular assemblies, as well as individual biomolecules, their submolecular structure and, ultimately, individual atoms. Recently, the scanning force microscope (SFM) has opened completely new perspectives for analyzing the surface topography of biological matter in its aqueous environment at a resolution comparable to that achieved by EM. Most exciting, the SFM is the first imaging device allowing direct correlation between structural and functional states of biomolecules at submolecular resolution. The developments of implementation of laser beam and stage scanning systems incorporating confocal optics, the advent of new electro-optical detectors with great sensitivity, linearity, and dynamic range, the possibility of 2D fast image enhancement, reconstruction, analysis and 3D display, and application of luminescence techniques gives the possibility to investigate the chemical and molecular details of life processes, and we can say that this digital approach, comprehending FLIMT and FRET techniques combined with the use of quantum dots, can probe the spatio-temporal organization of cell metabolism. Moreover, through the use of antibody labelling and confocal or multiphoton microscopy joined to algorithms for image restoration, it is now commonplace to distinguish and study structures an order of magnitude below the theoretical limit of resolution of the light microscope (about 250 nm). Also, individual 20 nm particles carrying

specific protein probes can be seen, for example tracking across the surface of a living cell.

We can conclude that with the microscope we can explore the microcosm, from tissues to cells and all the way down to molecules and atoms, and that this ASI represented a successful opportunity for carrying on and implementing an interdisciplinary approach to the study of theoretical and practical aspects of this research field.

The first part of the book deals with a general overview of the state of the art of microscopy including theoretical aspects, whereas the second part deals with uses and applications of the different kind of microscopes.

I do hope this book has caught the spirit in which the ASI was conceived.

Paolo Gualtieri

Director of the ASI "From cell to proteins: Imaging nature across dimensions"