Preface

The invention and development of the optical microscope in the seventeenth century revealed the presence of a previously unseen and unimaginable world within and around us. Our lives would not be what they are today if optical microscopy had never existed or if it had not helped us to understand better what we are, how we function, and how we can improve our condition – first in the fields of biology and medicine, and then in many other fields.

Another great step was made with the introduction of transmission and scanning electron microscopy in the 1930s, which was initially integrated with optical microscopy but subsequently developed its own identity and technology and opened up new horizons in human knowledge.

Starting in 1986, further technological advances led to the development of atomic force microscopy (AFM), which is completely different from its predecessors: instead of being based on lenses, photons, and electrons, it directly explores the surface of the sample by means of a local scanning probe while the use of dedicated software allows the results to be visualized on a monitor.

AFM has a number of special characteristics: very high magnification with very high resolution; minimal sample preparation (none of the dyes of optical microscopy, or the vacuum, critical point, or gold sputtering required by scanning electron microscopy); real three-dimensional topographical data that allow us to obtain different views of the samples from a single collected dataset; and the ability to work in a liquid in real time, thus making it possible to study the dynamic phenomena of living specimens in their biological environment and under near-physiological conditions.

Over the years, an increasing number of researchers have started to use AFM and, in addition to a wide range of scientific articles, there are now also various books on the subject. In 2004, we edited a book published by Humana Press (*Atomic Force Microscopy: Biomedical Methods and Applications*) that described a series of practical AFM procedures in various applications with the aim of stimulating researchers to use the technique. We were therefore surprised when Humana Press proposed the publication of a second book on the subject so quickly after the first, and hesitated to accept the challenge. However, upon further reflection, we had to agree that the sheer breadth and originality of the new applications that have emerged since the first book was published more than justified this further review. The reason is quite simple: AFM is no longer simply just another form of microscopy, but has given rise to a completely new way of using microscopy that fulfils the dreams of all microscopists: being able to touch, move, and interact with the sample while it is being examined, thus making it possible to discover not only morphological, but also chemical and physical structural information.

Optical microscopy made it possible to talk at the "micron" level (cells), and transmission and scanning electron microscopy introduced the idea of the "nano" level (sub-cellular), but still only in two dimensions; however, when speaking of AFM, it is not only usual to talk in three-dimensional "nano" terms, but it is also already possible to talk

at the "pico" level (molecular). Together with continuous technical improvements, the reaching of this new dimensional range means that AFM can provide an opportunity to interact with individual molecules, observing them while we touch them and move them around in order to be able to discover their physical characteristics. All of this has also led to the development of a parallel "nano-technology" insofar as an AFM workstation has become a "nano-robot" that can dynamically interact with and manipulate samples on a "nano-scale", and acquire information of sub-pico Newton "force spectroscopy" data on which to base the study of "nano-biology". Functionalizing the AFM tip has made it possible to obtain "nano-biosensors" that can be used in the field of dynamic biomolecular processes in ways that could not even be imagined just a few years ago. Finally, combining AFM with other microscopic techniques, such as confocal or fluorescence microscopy is now being actively explored, and a number of interesting synergies have been discovered.

This book brings together different types of applications in order to provide examples from different fields in the hope that this will stimulate researchers to apply their ingenuity in their own specialization and allow them to add significant originality to their studies.

We gratefully acknowledge all of the contributions of our colleagues, each of whom donated their experience in order to cross-fertilize this new and fascinating technology.

"GOD BLESS MICROSCOPY (ALL TYPES)
…AND MICROSCOPISTS TOO"

because they show us what and how wonderful life is.

Milan, Italy ***Pier Carlo Braga***
Genoa, Italy ***Davide Ricci***