

Atomic force microscopy in biomedical research

Methods and protocols

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Pier Carlo Braga and Davide Ricci are old friends not only for those researchers familiar with Atomic force microscopy (AFM) but also for those beginners (like the undersigned) that already enthusiastically welcomed their 2004 edition (for the same Humana press printing types) of *Atomic force microscopy: Biomedical methods and applications*, even though I never had used the AFM. That book was much intended to overview the possible AFM applications for a wide range of readers so that they can be in some way stimulated toward the AFM use. In fact, the great majority of scientists is afraid both of the technology behind AFM (that is naturally thought highly demanding in term of concepts not so familiar to biologists and physicians) and of the financial costs: both these two factors are conceived unapproachable by the medium range granted scientist usually not educated in terms of biophysics and electronic background.

Now, one of the great merits of both the two books that Pier Carlo Braga and Davide Ricci edited (with substantial writing contributions by them both, since several chapters are directly write down by the two editors themselves or by some of their associate colleagues) is just the ability to drive the majority of us out of the foggy view *In the forests of the night to show to the readers the burning bright that AFM can burn the fire of thine eye*. The reader will recognize that I am quoting (in a personal manner!) William Blake's *The Tyger!* from *Songs of Experience*, 1794 – but I thought that there were no other better way to recall the powerful pico level (molecular level) that AFM can provide to scientists well behind of the *nano* (sub-cellular) level of electron microscopy (EM) or the *micron* (cellular) level of optical microscopy (OM).

Not to say of the sample's preparation! So simple when compared not only to the tremendously time consuming and laborious EM preparations but also when compared to the standard procedure for any types of OM preparations. In addition, one have always to remember that we are so used to reason in terms of fixed (dead) biological samples standing on glass or plastics or metal supports (which is definitely not *natural* at all), while one of the many advantages of AFM is precise-

ly that of being a powerful tool for studying the effects of biophysical cues on cell behaviour with the extraordinary capacity to work in different environments (air, liquid or vacuum) in real time: a dream for any microscopists. AFM belongs to the scanning probe microscopes family that, depending on the type of interaction measured, take different names like STM (Scanning Tunneling Microscopy, developed by Gerd Binnig and Heinrich Rohrer at the IBM lab in Zurich in 1981, few years they developed the first AFM) and SNOM (Scanning Near field Optical Microscopy) and do not use lenses or electrons: it directly explores the surface of the samples providing a 3-D topographical dataset that dedicated softwares are able to transform in understandable (!) visual presentation on monitors. The result is a very high magnification with a very high resolution of the samples that, in addition, can be moved and touched thus providing *not only morphological, but also chemical and physical structural information* as pointed out by the editors in their preface.

The book is divided in six parts. Part I is entirely devoted to the basics of AFM, consisting of three chapters written by Pier Carlo Braga, Davide Ricci and some of their associates. Part II illustrate the molecule imaging, detailing these studies in eight chapters; among others I found quite interesting the AFM of *ex vivo* amyloid fibrils considering that more than 25 diseases are related to amyloid/amyloid-like deposition, the AFM of proteasome assemblies, the AFM of isolated mitochondria, the AFM of human metaphase chromosomes. Part III deals with the nanoscale surface analysis and cell imaging presenting in seven chapters virus-cell interactions (the reader must recall that AFM is a surface techniques, thus by using enzymatic or chemical digestion even internal virions structures can be revealed, as well as DNA and RNA), the ultrastructure of *Trypanosoma cruzi* epimastigote forms (the causative agent of the Chagas disease), the growth cones of (chick) living spinal cord neurons, the ultrastructural features of pathological human erythrocytes and sperm. Part IV and part VI are those present a major task for a reader like me: they are concerned with non-topographical applications (force spectroscopy) and AFM as a nanotool. Quite fascinating, we are told about the mechanobiology of living cells (e.g., microelastic heterogeneity) and AFM studies of receptor-ligand interactions (Part IV) and the combined use of AFM and fluorescence microscopy or the AFM as a nanorobot (part VI). Part V is much more palatable for my brain, dealing with more familiar investigations of the drug action such as the AFM study of circular DNA changes brought about by the administration of vincristine and aspirine, the thymol induced

alterations in *Candida albicans* infections and the imaging of bacterial shape and surface before and after antibiotics treatment.

At this point of my reading I am quite sure I will be in touch with an atomic force microscopist: I need it!!

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