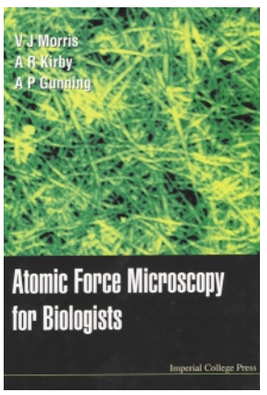
Another step towards biomolecular microscopy



Atomic Force Microscopy for Biologists
by V. J. Morris, A. R. Kirby and A. P. Gunning
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Scott Fraser

Microscopy has entered a second golden age in which it is offering critical insights into the structure and function of molecular machines. The light microscope arose from the humble beginnings of a simple lens used to enlarge the retinal image of a specimen by allowing it to be moved closer to the viewer's eye. It was refined in the early years of the last century as the compound microscope, capable of delivering images either to the eye or to film, approached the theoretical limits of performance. Given this, it became the principal tool for investigation into the structure and potential function of cells and tissues. The significant limitations of light microscopy for most of the 20th century were resolution and contrast — the highest-resolution images required fixation and staining of the preparation. Electron microscopy offered increased resolution, but not freedom from the need to process specimens. Thus, insights into biological processes could only be deduced from structures that were no longer capable of functioning.

The past two decades have seen these barriers largely eliminated by the development of techniques that can follow biological processes as they take place; these tools range from video-enhanced light microscopy and laser-scanning confocal microscopy to scanned-probe microscopy. Scanned-probe microscopes (SPMs) are a family of instruments (now numbering at least twenty) that raster-scan a probe over the surface of a specimen. The piezo-electric stage used is capable of movement at the atomic scale, offering the promise of remarkable resolution. The founding member of the SPM family, the scanning tunnelling microscope (STM), uses the very steep distance dependence of the tunneling current between a tip and a specimen to monitor the distance between the two. Sample topography is then recorded as the excursions of the z-axis voltage required to maintain a constant tunneling current as the tip is scanned in the x and y dimensions by the piezoelectric transducer. Mapping the surface topography of specimens in this manner generated such startling atomic images that the invention of the STM was recognized with the 1986 Nobel Prize for physics. The atomic-force microscope (AFM) uses a similar scanning mechanism, but generates image contrast differently — by measuring the deflection of a micro-machined silicon-oxynitride cantilever with an integral tip. Interactions with the specimen deflect the cantilever from its equilibrium position, which can be monitored by a laser beam reflected from the back of the cantilever into a position-sensitive detector. In its simplest form, AFM measures the surface topography by monitoring the cantilever deflection as the specimen is raster-scanned. Thus, any variant of AFM that alters the tip–specimen interaction (charge, chemical bonds, etc.) can be used to generate useful contrast from an SPM. In principle, SPMs should provide resolution of biological specimens that is comparable to or better than that obtainable with electron microscopes, but in more biologically relevant imaging environments such as physiological buffers.

Atomic Force Microscopy for Biologists fills an important niche by providing an introduction to AFM that will be understandable to a wide range of scientists. The book offers an overview of the key components common to all SPMs, explaining the theory of their operation as well as the limitations in their performance. In a little more than three hundred pages, the authors are thus able to offer the reader an overview of what can and, more importantly, what cannot be deduced from AFM data. The book presents the techniques and the special concerns relating to obtaining AFM data from specimens ranging from proteins and membranes to a variety of entire cells. The book is far too brief to be considered a laboratory guide, but this is a strength, not a weakness. The recipes and details expected in a lab manual would make a book that is very unlikely to reach a broad audience. Much as computer manuals seem to make the best sense to those who already know the answer to a question, lab manuals usually serve best to inform those already familiar with at least the basics of an approach. *Atomic Force Microscopy for Biologists* takes care to offer enough detail to be substantial, but avoids the temptation to heap too many details on the reader. In the last few pages it offers a brief mention of other SPMs that are related to AFM. These few words inform the reader of emerging technologies and give a brief introduction to their mechanisms of operation. I recommend *Atomic Force Microscopy for Biologists* because the reader is offered an introduction of sufficient brevity to actually be read and of sufficient depth to help in defining the potential uses of SPMs in his or her own research.

Scott Fraser is at Caltech, Pasadena, California 91125, USA
e-mail: sefraser@caltech.edu

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