Microscopy provides key tools for fields from semiconductor manufacturing to materials science to proteomics. As the application areas have expanded, so have the technologies. In light-based microscopy alone, contenders include optical, confocal, near-field scanning optical microscopy (NSOM), Raman, and polarized light.

With microscopy playing such a key role in enormous industries such as biomedicine and semiconductor manufacturing, it is logical to wonder about market size. A recent study released by Trimark Publications (New York, NY) estimated the total microscopy market in 2000 at $811 million. According to Barbara Foster, president and CEO of Microscopy/Marketing & Education Inc. (Springfield, MA), the question is flawed. "If there is any one concept that characterizes the microscopy market, it is heterogeneity. Each of the areas you mentioned is a market unique unto itself, with its own engineering requirements, its own applications requirements, and its own business issues. To ask the blanket question how big is the market just doesn’t make any sense. It’s just too varied."

If one trend has been toward the proliferation of microscopy technologies, another trend has been toward convergence. Biologists and materials scientists are increasingly working with hybrid systems. "[We’re] coming in with the fluorescence microscopy on the bottom and an NSOM on the top," says David Piston, a professor at Vanderbilt University (Nashville, TN). "We’ve been using more wavelengths, maybe infrared with the near-field scanning and then visible light with total internal reflectance. The reason you want to have all these things done simultaneously is that the whole push is to go to live cells, to dynamics."

Spectroscopic techniques, in particular, provide powerful new capabilities. Although microscopy has been taking advantage of spectroscopic techniques since the 1930s, it is only recently that the technologies have become powerful enough to spawn significant advances. "With the advent of both Raman confocal and micro FTIR [Fourier transform IR], we are finally seeing the real convergence of microscopy and spectroscopy," says Foster. "We can not only image the specimen, we can get the chemical fingerprint."

Of course, the drive for more information manifests here, as well, as biologists seek multispectral capabilities to monitor more mechanisms. "I think we’ve gone just about as far as we can go measuring one thing at a time," says Piston. "People can tag a protein with a fluorescent marker, watch it move around the cell. But then you say..."
look, at one point it sticks to the membrane. Now you want to know what it's sticking to and then you want to know if that thing is being recruited at the same time, so you need to do two [colors], then you need to do three.” And the beat goes on. Fortunately, widefield fluorescence microscopes and confocal microscopes allow users to take an entire spectra all at once, then deconvolve it into separate components.

But along with benefits, hybridization brings challenges. “The good news is that we're going to be able to do a different level of analysis than we've ever been able to do before. The bad news is that it's going to require a learning curve,” says Foster. Multifunction instruments mean teaching users multiple levels of operation, sample preparation, software, and image management.

Piston teaches an annual course for microscopy users. Class size is 25; he receives hundreds of applications, he says. “People know how to turn the knobs and take the data but now they want to take three colors at once, four colors at once,” says Piston. The challenges lie not just in operating the instrument but in managing the data. “The data that comes out of these things now is so complicated, it's so rich and there's just a lot of it. You need to ask the right questions, and then you need to take the right data, and then you need to be able to reduce it in a way that tests your hypothesis and is also presentable to the public.”

Image databases are beginning to become important. “There are efforts in the United States and Europe to get some sort of common image format or at least compatible formats and common databases,” says Jose Carrascosa, professor at the Centro Nacional de Biotecnología and the Campus de la Universidad Autónoma de Madrid in Spain. The Open Microscopy Environment (www.openmicroscopy.org) is a start. This consortium-based effort is focused on building an open-source software system for quantitative biological microscopy.

Networking has other implications for microscopy, says Carrascosa. “Automation of electron microscopy is becoming a hot issue in the field and it will be based on more computerized microscopes, more automatic sample handling, data collection and storage, and even the data processing,” he says. Automation could give the speed required for certain applications such as high-throughput drug screening, as well as provide other possibilities. “You can even use microscopes in remote settings,” he adds. Given the cost of these instruments, this is a decided benefit.

Technology just continues to roll forward at a fast pace. “We are always astounded when someone goes to outer space and yet thousands of microscopists are going to inner space every day,” says Foster. “I just think that microscopy is an extremely exciting place to be at the moment.”

Illustration by Bill Bruning