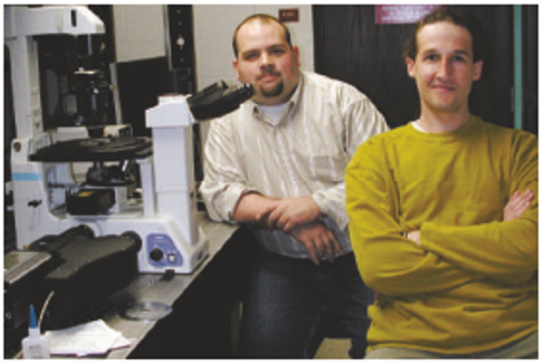
and 100× magnification objectives. "We achieved a numerical aperture of 1.49," says Schwartz, "and that's just under the theoretical limit for imaging with glass."

### Putting it all together

Modern imaging experiments have become very complex, generating huge amounts of multidimensional data. Although microscope manufacturers will typically provide reasonably effective tools for image processing and analysis, many users also opt for third-party software with more extensive analytical capabilities.

MetaMorph from Molecular Devices of Sunnyvale, California, integrates hardware control with a large toolbox of resources for multidimensional imaging, including a range of 'application modules' for image processing. "These are specific segmentation and analysis modules where, rather than having the user write macros, we've automated the entire process by having one dialogue box that helps segment your image and gives you relevant measurements," says product manager Magali Tranié.

Imaris from Bitplane in Zurich, Switzerland, also uses a module-based approach for segmentation and analysis of multidimensional images. "You can click on any object that you see and immediately, in the same screen, get the statistics for that particular object," says vice-president and director of sales Michael Wussow. "The same is true in reverse — we have an interactive sorting tab, where you move a bar on a histogram and things will appear or disappear depending on whether or not they meet your criteria." Bitplane also allows users to code their own routines, and hosts a number of user-generated plug-ins on its webpage.



K. ELICEIRI

**Kevin Eliceiri and Curtis Rueden have worked together to develop open-source solutions for the imaging community.**

Improvision of Coventry, UK, recently released the latest version of its Volocity package, which consists of four products — Acquisition, Visualization, Quantitation and Restoration — that can also be integrated. Among Volocity's strengths are its object detection and tracking capabilities, and powerful rendering techniques. "Every voxel within the image set is computed by the Volocity rendering engine," says senior marketing specialist Nicky Francis. "So it isn't a surface rendering technique, but a fully interactive volume-rendering technique. This makes it much more true-to-life."

Numerous other powerful commercial options are available, but the academic community has also stepped up to provide a variety of open-source solutions. Among the most popular is ImageJ, developed at the US National Institutes of Health by Wayne Rasband. ImageJ is a multipurpose imaging tool, maintained by Rasband but powered by a highly active user community. "There are about 400 plug-ins on our webpage, contributed by more than 100 people," says Rasband. Another popular program is VisBio, developed by the LOCI's Curtis Rueden for working with multidimensional data. According to Kevin Eliceiri, co-director of the LOCI, such tools complement commercial products. "The goal is to fill in the gaps," he says. "There are needs that often cannot yet be met by the commercial community because they either represent too small a market or are emerging techniques." Such projects have also meshed with the efforts of the Open Microscopy Environment (OME) to develop tools that aid collection and sharing of complex image data (see 'Tower of Babel').

Software — and hardware — requirements will only grow more severe as scientists attempt to coax increasingly complex data from smaller numbers of photons. Technology aside, the underlying challenges for this field remain clear and simple. "There are three issues in microscopy that never change — I want the best resolution, I want the best sensitivity and I want the best speed," says Nikon's Schwartz. "And it's really difficult to get all three." ■

**Michael Eisenstein is technology editor for *Nature* and *Nature Methods*.**

## TOWER OF BABEL

**The Open Microscopy Environment (OME) first emerged from the recognition that an explosion in imaging data was imminent. Image files were becoming bigger and more complex, representing copious data on numerous parameters as well as experiment-specific 'metadata'. "The ability to provide links between an image, any processed versions of an image, the data describing the acquisition of that image, and any analytical results generated about that image is a critical capability," says Jason Swedlow of the University of Dundee, UK.**

**When Swedlow, along with Ilya Goldberg at the US National Institute on Aging, Peter Sorger at the Massachusetts Institute of Technology, and researchers at the Laboratory for Optical and Computational Instrumentation (LOCI) at the University of Wisconsin at Madison, officially launched the OME in 2001, the development of a universal file format was a top priority. "Proprietary file formats are one of the biggest problems in modern microscopy," says the LOCI's Kevin Eliceiri. "There are about 30 or 40 major microscopy file formats, so we're speaking all of these different languages — it's the Tower of Babel."**

**To combat this, the OME has developed a file format called OME-XML, which retains both image pixel data and experimental metadata in a readable XML-based file. The LOCI has since refined this format as the OME-TIFF, which still encapsulates metadata in XML but stores pixel data in a TIFF format. "We have the best of both worlds now, in that TIFF is probably the closest there is to a universal image format," says Eliceiri.**

**The OME also offers open-source software for image management and analysis, which uses these new formats. Swedlow acknowledges that OME software may prove challenging for less computer-savvy users, but says the developers are working hard to make it easier to use. Meanwhile, a growing number of commercial packages now not only recognize the OME formats, but also record data into them. Indeed, the efforts of Swedlow and his colleagues have won accolades from several manufacturers. "Maybe up to 15 or 20% of our development resources go towards reader updates," says Michael Wussow of Bitplane in Zurich, "so we really like this idea of an Open Microscopy Environment."**

J. SWEDLOW

**Jason Swedlow helped launch the Open Microscopy Environment.**

**The OME also intends to tackle another weighty issue: handling and browsing increasingly bulky data sets. "We currently store about 50 terabytes of data from our imaging facility," says Swedlow, "and the OME's goal is to provide software to handle data on this scale." Of course, software isn't the whole answer, and significant investment in hardware and network infrastructure will be necessary for labs serious about imaging. "An enterprise-scale data-storage facility doesn't sound like hypothesis-driven research," says Swedlow, "but it is a required tool for hypothesis-driven research using imaging."** M.E.



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