Lab-management software and electronic notebooks are here — and this time, it's more than just talk.

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BY JIM GILES

The basement room in the James H. Clark Center contains all the trappings of a modern imaging laboratory. An X-ray scanner hums away in a corner. A miniature magnetic resonance imaging (MRI) machine, designed to scan the brains of mice, sits nearby. It's the kind of set-up that researchers at well-funded institutions such as Stanford University in California, the centre's home, have come to expect.

One piece of equipment, however, is conspicuous by its absence: the humble paper notebook. Michelle James uses her iPad to jot down notes, check protocols and monitor the progress of her experiments on techniques for the early detection of Alzheimer's disease. Since she first brought the device into the lab around four months ago, it has essentially replaced her former hardback notebook. "Paper has nothing to offer me," declares James.

It's a refrain heard in more and more labs. Some groups have ditched notebooks in favour of software from Google, such as free-to-use tools for sharing documents, spreadsheets and calendars. Others are finding that software designed specifically for lab workers has evolved to the point where it can reliably do a range of tasks, from tracking reagent supplies to sharing protocols. The era of the paperless lab, decades in the making, seems finally to have arrived.

Now that it's here, adopters say that a paperless laboratory seems to offer real advantages. Bench researchers say that digital notebooks help them track their experiments in more detail. Lab heads report being able to follow and focus projects more efficiently when documentation is tailored to their needs, accessible online and shared among colleagues. In some cases, digital notebooks could even help researchers to find connections or extract results from systematically stored data. "The efficiency thing is nice," says Jonathan Hirsch, founder of Syapse, a company based in Palo Alto, California, that develops the software James uses to manage and share her results. "But understanding your data better is what gets people really excited."

GOING PAPERLESS, AGAIN

If these claims sound familiar, that may be because the paper notebook's obituary has been written many times before. The paperless laboratory was "nascent" ten years ago, according to one American Chemical Society journal. Electronic notebooks are "ready for prime time", said Douglas Perry, a bioinformatics expert, in a *Nature* News Feature from 2005 (see *Nature* **436,** 20–21; 2005).

Yet most early notebook-software programs had limited impact, often because they weren't easy enough to use. Some worked only with specific file types, for example, or had cumbersome data-entry mechanisms. Such drawbacks have not stopped digital notebooks from taking off within the pharmaceutical industry, where companies have the funds to customize the

systems and can mandate that employees use them. But for academics, these shortcomings were deal-breakers. "Everything we tried was really crappy," says Sriram Kosuri, a bioengineer at Harvard Medical School (HMS) in Boston, Massachusetts, who experimented with many of the older packages.

Things have changed, thanks in part to the arrival of free or cheap sharing tools that are easy to use and configure. These tools, from storage systems such as Dropbox to the products offered by Google and others, rely on fast and reliable Internet connections and cloud-based storage. They provide a quick and cheap way to set up a basic lab infrastructure for sharing methods, data and other records.

At William Shih's synthetic-biology lab at HMS, researchers store records on a password-protected network of interlinked pages that any group member can edit. His team built it using MediaWiki, the free-to-use software that powers Wikipedia. A page for an ongoing experiment, for example, can easily be updated to note changes in a protocol or to include a graph of the latest results.

Team members log on to the site through laptops or their iPads, which they wrap in ziplock bags before venturing to the bench. "Even with a finger in a glove we can still get touch-screen sensitivity," says Shih. When researchers want to sketch out an idea — an essential process in a lab working on self-assembling nanostructures — they use Adobe Ideas, software that, for US$10 or less, makes it possible to construct detailed images on touch-screen devices.

But these general-purpose tools don't always satisfy researchers' needs. Some note-taking software, for example, does not handle tables well. And although MediaWiki is very flexible, some users say that it has a clunky interface for putting in text. This means that the race to create a good digital notebook — one that is both flexible and tailored to researchers' requirements — is still on.

GETTING PLUGGED IN

Jonathan Gross is one of the front runners in that competition. Gross began creating lab software when he was a plant-biology researcher at the Hebrew University of Jerusalem. The tools he built gained a following among his colleagues and, in 2007, he quit the lab to found BioData, a company based in Rosh Ha'ayin, Israel, that develops lab-management software. (BioData was purchased in 2010 by Digital Science, a sister company to Nature Publishing Group.)

Alex Kentsis, a paediatric oncologist and haematologist at HMS, is an early adopter of Gross's software. "Prior to BioData we had a makeshift operation," he says. His group used to swap files over shared drives, and Kentsis kept track of the lab's progress using an Excel spreadsheet in which each column represented a project and each row an activity. It worked, but only kind of. External collaborators could not access the shared drives, and the spreadsheet required constant maintenance and was hard to interpret.

BioData's software, which was relaunched last December as Labguru, tackles those problems. It's an online home for any information associated with scientific research, from protocols and results to images and related papers. The material is grouped by project, which Gross says makes it easy to track progress and to assemble the components of a paper. A tagging system makes it possible to group experiments that share a common component, such as a specific gene or cell line. External collaborators can use a password to access a specific project, which can be done from anywhere because the data are stored in the cloud.

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Gross plans to add new functions: he says he is in discussions about integrating his system with *Nature Protocols*, a journal dedicated to recipes for lab procedures, and Addgene, a repository of information on genetic-research tools called plasmids. The hope is that Labguru users can seamlessly pull information from the external databases. "It's about making researchers' lives as easy as possible," says Gross.

Labguru is aimed at life-science labs, but there are alternatives for other fields. Andrew Phillips, a chemist at Yale University in New Haven, Connecticut, uses iLabber, a product from Stockholm-based Contur Software. The selling point for Phillips was iLabber's ability to handle a chemist's daily tasks, such as drawing molecular structures and calculating expected yields. "It's chemically savvy," says Phillips, who says he pays $150 per user per year. Labguru charges academic labs a similar fee.

At Syapse, Hirsch also has ambitious plans. The company's software, Syapse Discovery, is undergoing testing in around 45 US labs. It combines the project-based structure of iLabber and Labguru with a layer of semantic technology that 'knows' the data that researchers upload. For example, the Syapse software can automatically recognize that data are from a particular lab machine, such as a microarray or MRI, and apply 'time' and other appropriate headings to it. For other data, Syapse Discovery has a system that allows researchers to quickly select labels from a drop-down list.

With the tagging in place, researchers can use the software to run complex tasks that would generally require coding skills. Users might ask it to scan multiple experiments and to build a table that combines all results on a specific gene. Or, in a clinical setting, they might ask it how an experimental drug is affecting patients with a particular constellation of symptoms. "We want to give people the ability to access this information without them having to learn programming," says Hirsch.

END OF AN ERA?

All of this hints at a future in which iPads and other devices do more than just replace notebooks. Kentsis points to a study of his into a therapy for acute myeloid leukaemia. Only when he looked at the milestones he had highlighted in BioData did he realize that a key piece of evidence — additional results on the extent to which drug resistance developed — was missing. The task could have been done using pen and paper, but BioData made it quicker. "It's been easier to see project arcs and to direct research towards more important questions," says Kentsis.

Digital notebooks may also help researchers to probe correlations that are too time-consuming to pursue using paper-based records. Archana Shenoy, a stem-cell biologist at the University of California, San Francisco, has been using Syapse Discovery for six months. She thinks that it can help to shed light on one of the frustrations of her field: cell lines that die without apparent cause.

With a paper notebook it is almost impossible to correlate the myriad factors that might affect cell survival. But with Syapse Discovery, Shenoy can quickly record data ranging from the carbon dioxide levels in a cell incubator to the date when a new batch of reagents arrives. When the search capability is up and running, she will be able to look for correlations between these factors and the fate of her cells. "It's something everybody wonders about," she says. "What is causing these little changes?"

Yet it's unclear how much impact the new programs will have. Expense is one issue: not every lab can afford to equip its members with laptops or iPads. Practicality is another: some labs don't allow laptops near the bench because of the risk of spills. But ultimately, these tools, like the earlier iterations of digital notebooks, will live or die on the basis of their usability.

The greatest challenge for Syapse, BioData and their rivals is not to create a tool that can do everything, but one that, like the intuitive software produced by Apple, is fundamentally easy to use. The initial feedback from James and others suggests that the latest generation of lab software might be able to do both. If so, it might finally be time to turn the page on the notebook. ■

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