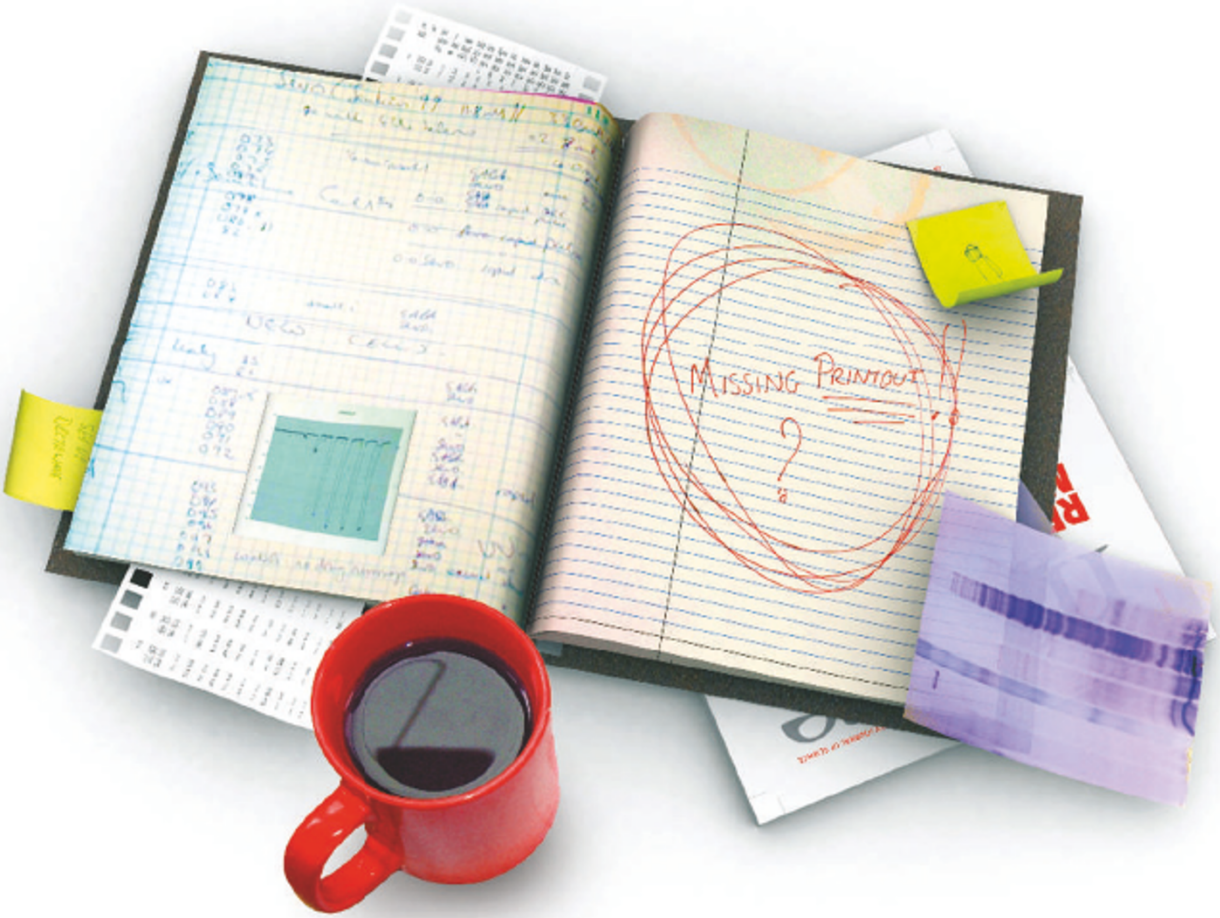


C. DARKIN

A new leaf

Record-keeping in the lab has stayed unchanged for hundreds of years, but today's experiments are putting huge pressure on the old ways. Declan Butler weighs up the pros and cons of electronic alternatives to that dog-eared notebook.

Pity the poor lab notebook. Almost everyone is publishing, sharing and searching information in electronic form, from biological and literature databases to blogs of their latest ideas. But lab notebooks are stuck in a time warp, still handwritten, on paper. Many scientists can barely understand their own scribblings from last week, let alone five years from now — as anyone who has had to decipher the hieroglyphics of a co-worker can testify.

We've been promised the 'paperless lab' since the early 1990s, but it hasn't taken off. Now, almost every laboratory is struggling with an explosion of data, much of it generated by automated instruments. An electronic version of the lab notebook can fully integrate with all these digital data and images. But most researchers continue to make fuzzy printouts of gels and data tables, and glue them on to the leaves of their notebooks.

Things may finally be changing, however. E-notebooks are ready for prime time, says Douglas Perry, a laboratory informatics expert at the Indiana University School of Informatics in Indianapolis. New products are being rolled out across the pharmaceutical industry by a growing army of vendors, he says, noting that the industry's massive investment in e-notebooks has helped the technologies to mature.

So far, academia has been slower to respond. But labs that have switched from paper say e-notebooks have made life easier, improved quality, and revolutionized the way they share data and results.

At Sweden's Karolinska Institute, bench scientists at the Centre of Excellence in Structural Genomics quickly adapted to their new paperless lab. They are using an e-notebook made by Stockholm-based Contur Technology. "It's intuitive, and easy to get started," says Johan Weigelt, the centre's chief scientist. "People got rid of their paper notebooks immediately."

Weigelt says the e-notebook lets scientists share everything: "the bioinformatics, expression data, sequence analysis and all the molecular biology, protein purification, crystallization and structural determinations".

Pål Stenmark, a Karolinska postdoc, says his co-workers find the e-notebook gives them easy access to each other's results. "You don't have to ask each other for protocols. You can read exactly what the other person did," he says.

Knowing that others regularly dip into his e-notebook has also prompted Stenmark to spruce up his own note-taking. "You have to be a bit more particular when writing; that's good because it's easy to be sloppy when writing a personal lab book." And when you can't find that crucial protocol? "It's also very nice to be able to search your own lab book."

Although the data entry 'pages' of an e-notebook look like a typical web form, they are dynamic not static. Once an experiment is set up, data is automatically captured and stored in a structured database, often alongside instrument settings. And where a compound, protein or gene is mentioned, it can be hyperlinked to structure and sequence data on the web.

You can add notes as you go along, compute or analyse results directly in your notebook, and store those in turn. Once the experiment is over, click on the 'submit experiment' button, and the computer gives it an indelible date and timestamp, and you sign it off with an encrypted digital signature. The pages can now never be modified by anyone, although comments can be added later, each with their own timestamp and signature.

It is this electronic security, and the need for detailed documentation to protect legal challenges to their inventions, that has driven drug companies to embrace e-notebooks. They also meet the US Food and Drug Administration's strict standards for record keeping for clinical trials and regulatory approvals, and may help discourage misconduct.

But the biggest advantage of going electronic should appeal to both industry and academia alike. With paper records, vast amounts of data lie unused and effectively hidden, whereas e-notebooks allow results to be instantly shared with collaborators. The pitfalls of paper are estimated to cost the drug industry alone over $1 billion annually in lost opportunities and duplicated research.

However, installing new software on scientists' computers, and simply telling them to use it, is not enough. Most software needs to be customized to the working habits and research needs of individual groups, which means an investment of time and energy.

Experience shows that scientists won't adopt e-notebooks, if it means taking on additional computing tasks, unless it also makes their job markedly easier. Software has to adapt to the user, not the other way round. The Paris-based pharmaceutical giant Sanofi-Aventis spent years working with a French software provider, Klee Group, to develop a product (now available commercially as Kalabie) that met the specifications its scientists needed.

Cut to size

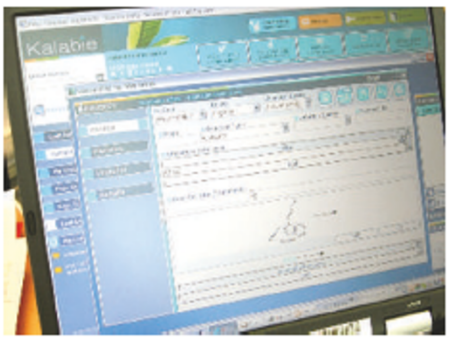
Customizing e-notebooks is proving more difficult in academia than in industry. Industry research groups are typically large and well-funded, with clearly defined project management and workflows, and generous IT support.

"Academics simply don't have funds for software that needs customizing to their situation, and there are almost as many different situations as there are labs," says Robert Cannon, a computational neuroscientist at Edinburgh University and founder of the Edinburgh-based notebook company Axiope.

And experimental protocols are continually changing. But redesigning the pages of e-notebooks, and adding fields and tables, usually entails modifying the structure of the underlying database. That requires the skills of database engineers, a luxury few labs enjoy.

Apart from a handful of big international collaborations that have database managers, such as CERN's Large Hadron Collider, most academic research is investigator-driven and small-scale. Academic groups are often scattered across disciplines, and are perhaps overly creative in inventing different ways of working.

Academic e-notebooks need to include user-friendly tools allowing researchers to customize them without demanding computing skills, says Gwen Jacobs, who heads the open-source NeuroSys neuroscience e-notebook system at Montana State University, Bozeman. "Any system must be flexible enough to handle any type of data, and any experimental protocol," she says.



Note well: e-notebooks like SmartTea (top) and Kalabie are nudging paper records out of the picture.

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KLEE GROUP

"The nice thing about NeuroSys is that researchers can customize their templates and build user interfaces without a database administrator," says Maryann Martone, scientific coordinator of the Mouse Biomedical Informatics Research Network, based in La Jolla, California. Martone is carrying out an "exhaustive evaluation" of commercial and open-source e-notebooks.

Although most e-notebook vendors focus on the lucrative market in industry, Contur, Axiope and Rescentris in Columbus, Ohio, among others, are bringing out products targeting the needs of computer-illiterate academics.

And if you are keen to try one for free, you can download a basic open source Electronic Laboratory Notebook (http://collaboratory.emsl.pnl.gov). It lacks the cutting-edge database features of commercial products, but allows any group to share notebooks online and create templates for data entry. It also has a suite of data-analysis tools. The system was built by a group led by Jim Myers, a pioneer in e-notebooks at the Pacific Northwest National Laboratory in Richland, Washington.

Besides freeing academics from paper, electronic notebooks herald much deeper changes to the way science is practiced. Blogging has transformed communication on the web, and once scientists start making their e-notebooks available online — if only to remote collaborators — there will be a revolution in data sharing, predict observers.

Rather than spending time collecting their own data, scientists will organize themselves around shared data sets, much as astronomers do, says Monica Schraefel, a computer scientist at the University of Southampton, UK. Her SmartTea e-notebook project aims not just to get paper out of chemist's labs, but to get their experiments out to external collaborators as soon as they're finished.

Track records

Schraefel's group is also helping the scientists who barely use paper at all: bioinformaticians. "Whereas chemists have 400 years' practice using a lab book for their experiments, bioinformaticians, who do all their work on a computer, have none," she says.

In bioinformatics research, software is used to analyse data from big biology databases such as GenBank and Swiss-Prot. The 'results' are often strewn across thousands of computer files that the researchers struggle to organize.

"The strategies we've seen them invent to keep track of their work are amazing — and they fail," says Schraefel. "It gets to the point, they tell us, where it's easier to run an experiment again than to try to find the data. Great."

And if bioinformaticians can't keep track of the mess on their own hard drives, what hope do they have of sharing results with colleagues? Schraefel is tackling this problem by building unobtrusive software dubbed MyTea, which runs in the background and tracks related files and notes. The idea, she says, is to create "representations of work in progress that can be shared" — in short, lab notebooks.

Whatever form e-notebooks take, some are concerned about how robust archived copies will be. "I'm very nervous about the fragility of digital information," says Martone. "We can still read papyri and stone monuments from over 2,000 years ago. We sometimes can't read digital files from 10 years ago."

But Stenmark points to the "disastrous" risk of losing a paper notebook, perhaps in the train on the way home from a lab party. He sleeps easier knowing his e-notebook is automatically backed up nightly to multiple locations.

And those attached to their dog-eared lab books shouldn't worry: even the drug industry is reluctant to abandon paper completely. Although electronic digital signatures and time stamps are now legally accepted, they haven't yet been tested in a court case. So companies that have gone electronic are playing it safe. After each experiment is submitted to the e-notebook, managers print it out, have the researcher and a witness sign each page using a pen, and lock the lot in a safe. ■

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