But this level of automation brought technical challenges. Specialist consultancy The Automation Partnership (TAP) in Royston, UK, worked with Cyprotex to adapt TAP's proprietary BasePlate liquid-handling robots to Cyprotex's particular requirements. Cyprotex also automated many of its analytical instruments to run standardized tests on compounds coming through the high-throughput process.

Cyprotex is now in a position to extend its automated systems to carry out a wider range of important assays. "We think automation gives us a screening capacity that is at least an order of magnitude higher than a typical pharmaceutical company, at a unit cost that is possibly 20-fold less," says Leahy.

Small is beautiful

Benchtop automated liquid handling and sample-dispensing systems are now routine in most life-science laboratories. Such systems will become even more ubiquitous with the introduction of a new wave of lower-cost modular devices with much the same functionality as the systems used by big-pharma labs. "The pharma labs have the deepest pockets, but a new generation of automated systems is becoming available that's more the 'Volkswagen' of the market," says Felder.

Xiril, a young Swiss company founded in Hombrechtikon by a team of specialists in robotic liquid-handling, has a range of pipetting robots that costs about 20–30% less than comparable systems. The Xiril robots are primarily aimed at low-to-medium-throughput operations, particularly for processes that have not yet been automated.

"We believe we can fill a market for liquid-handling processes that are often done manually, even in labs that are highly automated," says the firm's chief executive Heinz Abplanalp. Xiril has also developed automated systems for magnetic-bead separation.

At the more expensive end of the liquid-handling market, the trend is towards increasing miniaturization. Given the high cost of many reagents used in biomedical experimentation, considerable savings can be made simply by using less. Allegro Technologies, a Dublin-based company spun out of Trinity College, has the proprietary technology to dispense droplets up to 1,000 times smaller than those from standard equipment. The company claims that this could reduce the cost of some experiments sixfold.

Allegro's latest range of pipetting systems uses electromagnetically controlled valves to deliver droplets of 20 microlitres down to 20 nanolitres in volume. The firm has licensed its technology to US instrument manufacturers Gilson of Middleton, Wisconsin, and Beckman Coulter in Fullerton, California, and has also put the pipettes into its own robotic system.

Being able to manipulate tiny volumes of liquid means that entire lab processes can be miniaturized. Using technology developed for the semiconductor industry, chips a few centimetres square can be etched with microscopic channels in which routine preparation procedures and assays can be carried out.

Caliper Technologies in Mountain View, California, was the first to market these 'lab-on-a-chip' devices. Its 250 HTS system can use a range of chips for enzymatic or cell-based drug screens; some assays require fewer than 500 cells.

Caliper's chips use small electrical currents or vacuum-based pressure techniques to move fluids through the channels. Gyros in Uppsala, Sweden, is developing a range of microlabs for processes such as protein purification in the form of compact discs. A robotic workstation loads the CD with reagents and spins it at precisely controlled speeds, driving the fluids through the channels by centrifugal acceleration. Gyros's first product, the Gyrolab MALDI, can prepare up to 96 protein samples simultaneously for mass spectrometry. Tecan has also launched a similar product — its LabCD devices for pharmacological assays.

Action stations

Workstations, stand-alone automated solutions for specific lab tasks such as DNA sequencing or immunoassay tests, continue to be dominated by established

CULTURAL REVOLUTION

Cell culture, either for the cells themselves or their products, is traditionally a manual process that demands hours of repetitive, painstaking work to ensure absolute sterility under exacting conditions. Growing a mammalian cell culture for use in a screen for drug activity or toxicity typically takes 48 hours, so almost half the working week is gone before screening can begin.

But with automated cell-culture systems, screening could start on Monday morning on cultures left to grow over the weekend. Robotic systems can also provide a consistency of procedure and sterility that the best technicians cannot match, ensuring less variability between batches.

The Automation Partnership (TAP) in Royston, UK, introduced its pioneering Cellmate workstation in the late 1980s for the relatively large-scale production of therapeutic reagents and vaccines. This has now been joined by a new system, SelecT, developed in association with a consortium of six major drug companies, including GlaxoSmithKline and Pfizer.

SelecT is aimed at labs that need an automated system for processing up to 168 different mammalian cell lines simultaneously, making it ideal for multiple batches. The system can automatically maintain, expand, process and harvest multiple cell lines, assess their viability, and distribute them onto a maximum of 300 microtitre plates. "Cellmate is not so good at dealing with just-in-time production of ready-to-go microplates," says Mark Beggs, head of consulting at TPA. "SelecT can handle all the capabilities you need to take cells through to incubation to microplates."

Other commercial systems provide an even greater level of integration. Cytogration, a subsidiary of Brandel in Rockville, Maryland, has developed a robotic system that performs both cell culture and screening assays for drug candidates. The standard system handles up to 504 plates, and automates cell production, preparation of membrane-bound cells and *in vitro* screening.

An automated system has primarily to maintain a stable environment and reduce the risk of contamination, says Sean Sales, applications consultant at RTS Life Sciences in Manchester, UK. The system also needs to be dynamic in terms of knowing everything, so that the robot itself isn't slowing things down, he says. RTS has developed a flexible cell-culture system called acCellerator which has a very simple liquid-handling method and three parallel robot arms to process the flasks and plates in parallel. "It has a number of peristaltic pump units that allow a very short liquid line for reagents, so you don't have a lot of tubing to change over between cell lines," says Sales. T.C.

The acCellerator: flexible cell culture from RTS.