Laboratory Automation in the Life Sciences: Recent Achievements and Future Challenges

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The automation of lab instrumentation has helped to standardise manual tasks and minimise the effects of human error – but scientists continue to push the boundaries, challenging contemporary technologies to not only improve efficiency, but also to pave the way for imaginative new applications.

Images: Tecan Schweiz AG

Figure 1: Integrated Labcyte® Echo™ 555 for acoustic dispensing of nanolitre volumes and downstream processing and liquid handler for subsequent downstream processing

Automation is becoming increasingly commonplace in the life science laboratory due to the growing demands for productivity in speed, accuracy, throughput and efficiency. Helped by advancing technology, modern automated systems are already capable of a wide range of functions that were previously performed by slow, tedious, manual labour. Instrumentation continues to evolve, and is poised to tackle tasks that were not even conceivable just a few years ago. Originally used mainly by the big pharmaceutical and biotechnology companies, laboratory automation technology has rapidly developed to satisfy a wider audience of scientists in the life science industry. Automation companies not only produce automation for specific customer needs but also smaller, easy-to-use systems that are much more accessible to scientists to satisfy their general needs.

THE IMPORTANCE OF CLOSE COOPERATION

Many of the most significant improvements to automated solutions have been instigated by a strong line of communication between instrument manufacturers and laboratory scientists. The larger automation companies, in particular, recognise the importance of fully understanding a user's specific needs and challenges, not just in terms of the function of the instruments, but also from an application standpoint. An example where this has been extremely successful is in cell biology research, where automation of cell maintenance and cell-line generation has presented its own unique set of challenges. Having started as basic cell-feeding stations, the latest comprehensive automated cell biology solutions are proving invaluable in biomedical research fields, including stem cell research, transplantation medicine and high-throughput monoclonal antibody production.

Modern automated cell culture workstations can operate unattended over whole weekends and process many cell lines in parallel. It is essential that the complex processes involved – such as cloning, transfection, cell maintenance, routine subculturing, harvesting adherent cells and accounting for the varying responses of different cell lines – are all automated while still maintaining sterile conditions. The development and

Figure 2 (top): Integration of the ForteBio Octet® 384 on the Tecan Freedom EVO® for automated, high-throughput Dip and Read™ biosensor assays

Figure 3 (bottom): The Tecan TouchTools Suite™ offers researchers a unique user experience with its special user interface

integration of specialised readers within the systems to measure cell counts, confluency, viability and mycoplasma contamination ensures that reproducible batches of cells suitable for repeatable experimentation are efficiently provided. Automated processing and monitoring of cell cultures can effectively simulate miniaturised bioreactors, allowing the testing of variables in parallel-processed cultures and yielding valuable data that can be scaled up for larger volume culture set-ups.

SOLVING PROBLEMS – AUTOMATION FOR PROCESS DEVELOPMENT IN BIOPHARMA

Instrument manufacturers continue to concentrate on the development of products, which can handle miniaturised, automated processing in parallel, and substantially shorten the time spent on process development. The throughput, precision and robustness of modern automation platforms ensure reproducible and scalable results, and bring increased efficiency to process development and high-throughput screening applications. The developer can investigate a much larger set of parameters with minimal hands-on time, and so can devote more time to gaining quickly a greater overall understanding of the workflow and making better informed decisions for process optimisation. The data recorded are also valuable from a regulatory perspective, and help define dependable manufacturing methods.

Miniaturisation has also led to the advent of nano-pipetting; new and innovative technologies have been developed that accurately dispense sub-microlitre volumes. This facility allows smaller assay volumes for economical use of samples and reagents in applications such as sample and matrix application to plates for MALDI mass spectrometry as well as protein crystallography. Acoustic methods of sample delivery are particularly useful for eliminating serial dilution steps in the rapid and accurate determination of IC50 of compounds in biopharmaceutical laboratories. Combined with liquid handling automation, all aspects of the pre- and post-processing of the transferred samples are completed by the instrument.

The ability to handle higher workloads brings an additional need for more efficient and flexible compound and sample management systems. The latest systems have been developed with this in mind in order to suit the needs of laboratories of different sizes and dealing with varied sample types. These systems automatically perform sample storage and retrieval, for repositories of up to millions of biological or chemical samples and at a range of temperatures, boosting the quality and efficiency of management of sample libraries.

QUALITY AND REGULATORY COMPLIANCE

The demand for regulatory compliance, particularly applicable for clinical diagnostic processes, has meant that major instrument manufacturers have made great efforts to develop and validate their products to comply with clearly defined quality standards. The EU's *in vitro* diagnostics directive (IVD-D) and the US Food and Drug Administration's quality systems regulation (QSR), as well as the ISO13485 international standard for the design and manufacture of medical devices, all exist to maintain strict quality standards. Quality control steps are often standard in software that accompany automation systems, and several vendors also offer quality assurance consultation of data generated by automated systems, covering verification and calibration of liquid handling, and regulatory compliance protocols.

COMPLETE SOLUTIONS – WORKFLOW AUTOMATION CONCEPT, CLOSED-LOOP AUTOMATION

As the benefits of laboratory automation become increasingly clear to scientists, demand has grown and laboratory managers are looking for single-source providers to automate every aspect of their laboratory workflows, encompassing all tasks from sample management, robotic processing, detection and data collection. The complicated and potentially time-consuming task of developing and validating the elements of their workflow is increasingly being addressed by those manufacturers, which can offer solutions. The researcher benefits from the reduction in development time, as well as the costs of development, with the adoption of standardised solutions within their workflow.

The latest solutions feature closed-loop automation of the workflow – from compound management through to data acquisition – to allow informed decision-making.

Figure 4: Compact modular platforms like the Tecan Cavro® Omni Robot offer a cost-effective solution for application automation

Sample tracking becomes ever more important when transferring samples from multiple instruments. Laboratory information management systems (LIMS) are increasingly being used to control the important link between sample identification and results. User interaction is almost entirely through a software interface that is fully integrated into this control mechanism. Another trend is remote monitoring of systems, which allows users to monitor an instrument's status through any networked computer or mobile device with a web browser, thereby increasing walk-away time and process security. The status of the system is immediately visible and the user can easily see if any interaction is needed. Remote monitoring can be particularly useful if the instrument is in a clean room, biosafety cabinet or cold room where laboratory access is difficult or could risk assay contamination.

The latest systems are also being developed for ease of use, with user-friendly application software and a simple user interface, offering a unique, appealing user experience. This trend has reduced the dependency of laboratories on technical support personnel specialised in automation systems that previously were essential for maintaining correct operation of complex instruments. A pipetting robot is a capital investment, which should be maximised, and programmes – such as Tecan's patent pending Instant Pipetting™ – achieve this by making automation more accessible than ever before. The easy-to-use touch-screen user interface enables users of any skill level to use the robot for daily pipetting tasks, without any need for programming. The requested actions will be completed in real time and, by increasing the use of the robot and thus reducing idle times, return on investment is maximised.

FUTURE CHALLENGES

In recent years, as automation instrumentation has improved, scientists have simply pushed the boundaries of expectation even further, challenging contemporary technologies not only to improve efficiency and speed, but also to pave the way for imaginative new applications.

Recent trends lean towards smaller robotic instruments, using technology to offer high-end performance in compact platforms – although there is still a place in the market for large, integrated multi-unit systems, and these continue to be developed and customised for laboratories processing larger throughputs. The challenge for manufacturers is to provide ease in integration while working within the confines of laboratory spaces. Manufacturers have maximised the space efficiency of laboratory platforms by positioning additional modules on or around the worktable and even using the space below the deck for positioning additional modules for storage by robotic arms.

While one trend is moving towards larger, highly-customised automation, there exists another trend to work towards smaller platforms dedicated to standardised applications. The smaller, economical propositions allow even small organisations to benefit from automated systems, and are also useful as flexible alternatives for larger companies hoping to equip multiple laboratories with multiple systems. These simplified, modular platforms offer flexibility, allowing the instruments to be constructed to suit the end-users' needs, as well as offering a compact system that is capable of several functions. Smaller systems are also attractive in the economical usage of bench space. Furthermore, the demand for laboratory automation to offer whole solutions means that these smaller robotic platforms are increasingly designed so that user involvement is reduced and the learning curve is minimised. This development is particularly apparent in clinical diagnostics applications, where reducing user involvement is desired for reasons of safety and regulation.

Specific challenges – such as the freeze-thaw problem in compound management – are still a top priority for many instrument manufacturers; these are being tackled, for example, with innovative solutions for cherry-picking and single-use tube technology in an environmentally controlled storage system. With innovation in instruments comes further development in laboratory logistics and consumables like disposable tips and other plastic labware. For example, forward-thinking manufacturers are designing superior logistics into the delivery of consumables, such as stacked or nested pipette tips and multi-well plates to make savings on storage space.

Automated liquid handling and robotic manipulation in the laboratory has come along in leaps and bounds, addressing many of the problems commonly faced by scientists. With the constant pressure to improve productivity and efficiency, automation has helped to standardise manual tasks and minimise the effects of human error, as well as achieving new standards in accuracy, speed and throughput.

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