SPOTLIGHT feature

LIMS & Lab Automation

Driving Productivity in Protein Purification

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Crucial to the successful operation of any research laboratory is the ability to efficiently generate purified proteins for further investigation and analysis. In addition to timely delivery, researchers also demand a protein product which is pure, stable and active – it is crucial for antibodies to have the necessary binding activity and enzymes must be fully functional.

How a laboratory, or indeed a company or institution as a whole, goes about addressing these needs, can vary significantly and there are a range of technologies, workflows and organisational structures that can be implemented.

Challenges to Productivity

Identifying and understanding current bottlenecks and challenges to protein purification is the first step towards improving productivity to deliver positive business benefits.

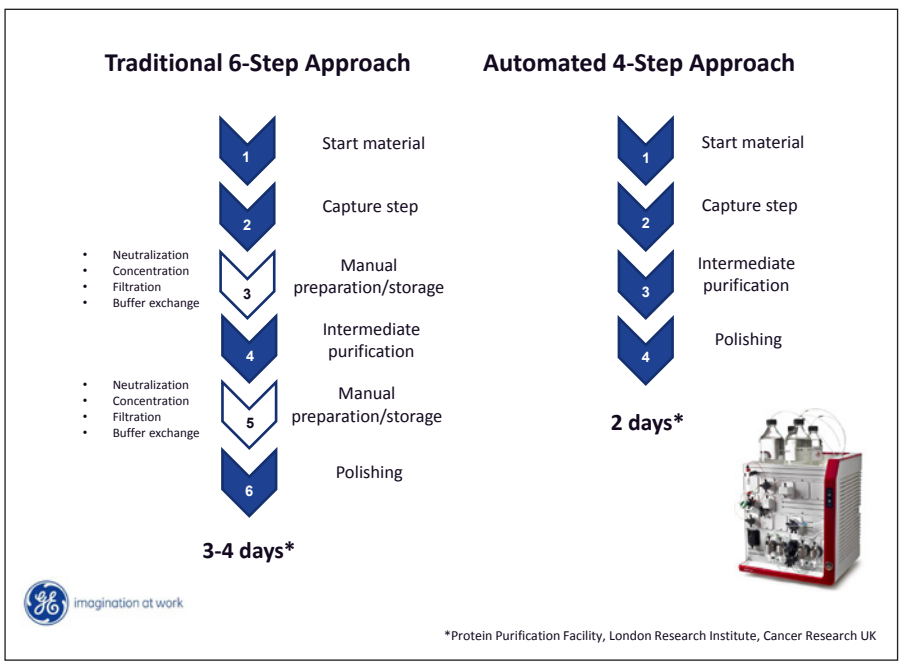
As a global supplier of specialist protein research tools, Abcam intimately understands these challenges as it works to provide large numbers of high-quality complex protein-based products to researchers with varying requirements. The company utilises a number of chromatography systems for protein purification across multiple sites globally. Increasing demand globally, created a need to increase production of small volumes of high-quality proteins at high throughput consistently, irrespective of geographic location, from its existing workforce. This challenge was coupled with the requirement to maintain levels of expertise and technical support, thereby potentially increasing pressure on in-house experts.

Similarly, the Protein Purification Facility (PPF) at the London Research Institute (LRI), Cancer Research UK (CRUK) expresses and purifies recombinant proteins for applications with high quality demands such as x-ray crystallography and downstream analysis of functional activity e.g. binding and/or enzymatic activity. Critical to success is minimising hands-on interaction with the proteins, many of which are highly sensitive, to preserve enzymatic activity. As a consequence, speed and access to instruments are key considerations. An internal review of all operations across the PPF identified that the existing batch-based purification approach, involving significant amounts of hands-on work, could be targeted for streamlining, to increase output and improve throughput.

Practical Approaches to Improving Productivity

Once the bottlenecks in a protein purification workflow have been identified and understood, it is necessary to evaluate options for addressing them.

Productivity in protein purification can be improved through use of automation that reduces hands-on technical requirements, reducing the chances of error and streamlining production efficiency and work effort. Simplification in the use of equipment can support fast set-up of protocols and improve utilisation while maintaining flexibility and the ability to carry out complex procedures. Standardised approaches, in addition to improved system design, reduces training requirements, boosting productivity for experienced scientists while opening up protein purification technologies to researchers who are not necessarily protein purification experts. As resource utilisation is improved the overall output from available instruments can increase significantly, ultimately leading to fewer instruments required, which in turn means savings on maintenance work, service support contracts and lab space.



Globally Distributed Manufacturing Delivered through Standardisation

The purchase of multiple automated protein purification systems by Abcam has further enhanced both productivity and quality, and has been used to support its latest innovations, specifically, the manufacture of its Alexa Fluor®-conjugated secondary antibody product range. Innovation, in-house manufacturing, and quality are significant factors in the success of Abcam today, and the decision to automate over traditional hands-on approaches was to ensure quality of the final product (monitoring & control of process parameters), in addition to increased productivity/throughput. After the Alexa Fluor®-conjugated secondary antibody range was launched in December 2012 production batch sizes needed to scale up 5-fold to meet sales demand and generate sufficient stock. ÄKTA™ pure (from GE Healthcare) was flexible enough to allow scale-up of production, whilst maintaining necessary throughput.

Having a global customer base meant that global standardisation was important, as was security of supply. A combination of increased in-house production, as well as developing relationships with multiple suppliers, enabled Abcam to maintain provision of its large catalogue of protein research tools without any reduction in levels of expertise and technical support. Platforms such as the ÄKTA protein purification systems permit the production of the same protein to a consistent standard at any of Abcam's international sites. This arrangement allows faster restock of products to maintain customer supply despite the increased demand. The interoperability that exists across the ÄKTA systems range allows Abcam's protein purification scientists to move easily between different system sizes in order to maximise cost-effectiveness.

Purification Time Halved through Automated Workflow

By moving to automated protein purification systems (ÄKTA pure from GE Healthcare) at the PPF at CRUK, the continuous running of the instruments is now possible. For example, a batch of labile GST-tagged kinases would previously take 3-4 working days but can now be left overnight to run so it is purified within 2 working days. The increased flexibility of the automated workflow means that, at the initial stages of developing a protocol, challenges in purification can be overcome creatively. Then, once a good protocol has been achieved, it can be formalised for simple re-use. For example, proteins that precipitate quickly after being eluted from a column, especially when left to run overnight, can now be directly loaded into a buffer exchange column. In addition, the increase in automation eliminated a manual step, meaning less manual protein handling and resulting in higher protein quality and yields.

Save Scientists' Time Through Intuitive Software

Methods for ÄKTA protein purification systems are set up through the 'drag and drop' interface of the UNICORN™ control software, which has enabled scientists at Abcam and CRUK to put together easy-to-use, intuitive protocols quickly, and also reduced the training need. For Abcam, movement from development into production, whilst maintaining flexibility, is supported by the fact that this easy-to-program software is installed platform-wide. For CRUK, the fact that many of the columns it uses are pre-programed into the software saves further time.

Conclusions

At Abcam, use of automated protein purification platforms such as ÄKTA pure has helped to achieve improved process economy, while reducing the length of training and allowing innovative processes to be set up quickly. Use of an easy-to-use, automated system for protein purification has resulted in significant improvements to team productivity while facilitating the global uptake of innovative methods developed in-house.

At CRUK, the introduction of an automated protein purification platform was able to more than halve the time for a typical protein purification run, whilst maintaining the flexibility required for the set-up of more challenging proteins.

Addressing bottlenecks in protein production and purification with the application of controlled, automated and standardised purification platforms is a key step to driving innovation. Straightforward and easy-to-learn workflows allow for quick programming of protocols and sharing across multiple sites, enabling users to achieve a standardised level of protein purification, and resulting in efficient production of pure and functional proteins.

Next Generation Sequencing Applications Automated

Beckman Coulter Life Sciences, through a partnership with New England Biolabs®, Inc (NEB®), offers automated methods to improve processes and throughput in next generation sequencing (NGS) sample preparation. Under the agreement, Beckman Coulter will use its extensive experience in automated NGS sample prep to develop, distribute and support automation for NEB's NEBNext® sample preparation reagent kits. NEB will provide technical expertise on the reagents, chemistry and protocols.

Fiona Stewart, Product Marketing Manager for Next Generation Sequencing at NEB said: "We are delighted to have formed this productive partnership with Beckman Coulter Life Sciences. With fast, streamlined workflows requiring fewer components and fewer steps, the NEBNext kits are ideally suited for automation. In combination with Beckman's trusted automation solutions, NEBNext reagents enable robust performance, even with low input amounts and challenging samples."

Optimised methods for the NEBNext kits are built on Beckman Coulter's proven Biomek liquid handling platforms, and each solution includes a unique group of Biomek methods to address a specific NEBNext kit protocol. To improve overall workflows, methods are also included that automate Beckman Coulter's AMPure XP kit for DNA purification, the SPRIselect kit for high throughput DNA size selection, and the qPCR setup and normalisation processes.

"Beckman Coulter's focus on providing our NGS customers a top-notch portfolio of automated sample prep solutions makes a partnership with NEB, a world leading provider of quality reagent systems for molecular biology research, a natural fit," said Alisa Jackson, Senior Marketing Manager, Automated Genomics Solutions at Beckman.

The first collection of automated NEBNext methods were developed on the NGS configurations of the Biomek 4000 and the Biomek FXP Dual Arm Multi 96 and Span 8 platforms in collaboration with scientists from several institutions, including the European Molecular Biology Laboratory (EMBL), and the Genomics and Molecular Biology Shared Resource (GMBSR) at the Geisel School of Medicine at Dartmouth and the Norris Cotton Cancer Center. The methods create up to 96 sequence-ready libraries that generate quality results on Illumina® and Ion Torrent™ sequencing platform.

Methods available today are NEBNext Ultra™ Directional RNA, NEBNext Ultra DNA (including for ChIP-Seq) for Illumina NGS and NEBNext Fast DNA Fragmentation & Library Prep for Ion Torrent. Other methods, including for NEBNext ribosomal RNA depletion and the NEBNext Small RNA reagent kits, are expected to follow later in the year.

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Patent for Automated Ultrasonic Blockage Detection and Cleaning in Microplate Washers Awarded

BioTek has been awarded US Patent 8,858,718, covering the use of ultrasonic devices to check for clogged manifold tubes and to clean the manifold tubes of a microplate washer automatically. The two features are known as Verify™ and Ultrasonic Advantage™ and are available in BioTek's 405 family of microplate washers.

Using Verify technology on the 405 washer, the user can run an automated routine to check for blockages, typically caused by protein or salt build-up in the aspirate and dispense tubes of the 405's manifold. Verify uses ultrasonic pulses to determine that the volume dispensed or aspirated per tube meets specified variation limits. Potential blockages are reported visually via the onboard touchscreen display or software or via the LHC™ PC software. If blockages are noted, the user can proceed to run an automated cleaning routine using the Ultrasonic Advantage trough to immerse and efficiently clean all manifold tubes. The two functions help prevent potential assay failure and equipment downtime commonly caused by blockages in the small diameter tubes of the microplate washer.

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New Options for Cavro® Omni Robot Launched at AACC's Clinical Lab Expo

Tecan has extended the flexibility of its popular Cavro® Omni Robot with the introduction of embedded control functions and the option to select single axis configurations. Unveiled with the launch of the Cavro Omni Robot Version 4.0 at the AACC's 2014 Clinical Lab Expo, these latest updates will make it even easier to configure the Cavro Omni Robot to suit specific applications or instrument designs. The robot's new Embedded Command Processor Mode allows direct communication for precise control and coordination of axis movements and liquid handling operations. This OS-independent command schema allows line commands to be sent directly to the robot using virtually any computer or custom control board, complementing the existing Windows®-based Command Processor Mode for greater integration flexibility.

The modular design of the Cavro Omni Robot allows users to choose from various lengths and orientations of all three axes, including a choice of single or dual arm X-axis configurations. To ensure there is a Cavro Omni for virtually every application, it is now also possible to choose any combination of X-Y or Y-Z axes, offering instrument designers the option to create their own axes without the time and expense of developing a complete liquid handling solution. These latest updates further extend the versatility of the Cavro Omni Robot and, together with the system's extensive choice of liquid handling options and finishes, provide exceptional flexibility for OEM liquid handling applications

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