Scientific article

Overcoming Implementation Challenges for High-Throughput Workflows with the STAR Q SP/AS Instrument

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Abstract: Increased dependence on DNA profiling in criminal investigations is resulting in ever higher submissions of casework samples to forensic laboratories. To address this rising demand, labs are looking to high-throughput automation to purify their samples and prepare them for DNA analysis. The majority of relevant options for automation involve "open" liquid handlers, and these systems normally are burdened with a number of challenges, making adoption difficult or potentially preventing it entirely. Here we review these challenges and describe how the STAR Q SP/AS instrument circumvents many of them, offering a new alternative for high-throughput "turnkey" automation.

Introduction

DNA profiling for human identification has been a mainstay of forensic science since its inception in the 1980s. Today's methods offer unprecedented sensitivity and tolerance to inhibitors typically encountered in casework exhibits while delivering results at a much lower cost. This in turn has stimulated a growing demand from police for DNA testing from ever more challenging samples and from increasingly minor crimes. The latest ENFSI report on DNA databases described a total of 1.6 million crime stains loaded to Europe's DNA databases, and the FBI's CODIS NDIS holds 730,000 crime stain profiles, both demonstrating the scale of this DNA proliferation (1, 2). Laboratories have responded to this propagation in several ways, such as workflow streamlining, but the greatest change has been the adoption of automation systems to enable high numbers of samples to be processed in a standardized manner with reduced human intervention.

High-throughput instruments have been used in particular for automation of sample purification and assay setup prior to PCR. Such automation requires liquid handling systems capable of ▷

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customization to perform a wide range of protocol-specific pipetting and sample manipulation steps. However, optimizing these "open" liquid handling platforms for such a wide range of sample processing presents some significant challenges, preventing adoption by many forensic labs. "Open" platforms are those with a fully configurable deck layout and pipetting arm, enabling definition of specific sample and reagent handling steps for any given DNA processing workflow. The challenges associated with the adoption of such "open" platforms include a lengthy optimization procedure to evaluate all variables in a process; the time, manpower, skills and expertise required for such exhaustive testing; and the impact this work has on the day-to-day operations of the lab, when the scientists required for the development effort are not available for routine casework. The net outcome of this is an implementation process that may not be completed to the standard required and that will almost certainly take many months.

QIAGEN's STAR Q SP/AS instrument has been designed to address these specific challenges, offering a turnkey high-throughput automation workflow, with all hardware, chemistry and protocols optimized and ready for implementation. The system offers all the benefits of "open" liquid handlers, such as customization to perform any DNA sample processing step involving liquid handling.* However, with pre-validated protocols for QIAGEN's sample prep chemistry and the ability to prepare assays for any commonly used commercial quantification or STR kit, the instrument can be implemented and validated at a fraction of the time, cost and effort required for "open" platforms from instrument-only providers. Here we examine the benefits of adopting the STAR Q SP/AS to achieve a high-throughput crime stain sample workflow, relative to other "open" liquid handling platforms.

Current automation implementation challenges

1. Identification of extraction chemistry

Any workflow needs to start with the identification of an extraction chemistry that works, manually, with all major sample types processed by a laboratory. This is a time-consuming process since automated, single batch processing will prevent variations in factors such as incubation times and elution volumes to get the best results from different samples. It can take several months to optimize a single, manual protocol to meet your current lab's success rates, with no guarantee of success.

2. Identification of a liquid handler

The liquid handler needs to accommodate factors such as the deck space requirements, heating and shaking steps, file handling, support needs moving forward, and security of supply. Again, months may be required to identify the appropriate instrument.

3. Making the manual protocol work on the automated handler

Moving away from individual sample tubes requires the sourcing of hardware and labware that successfully replicates your manual process, before determining how DNA yields and quality compare against the manual protocol. This typically requires a minimum 3–6-month testing phase, during which factors such as shaking times, binding times, wash volumes, drying times, and mixing of magnetic beads may need adjusting. This work is likely to require expensive application support from the manufacturer.

4. Assay and normalization protocol setup

Depending on the size of the development team, it may not be possible to work on quantitation and STR setup at the same time. If this is the case, a further 3–6-month development time may be required to fine-tune the handling of reagents. Aspects such as standard curve creation and ensuring efficient mixing and pipetting for samples and master mix will take time. In particular protocols for normalization of your samples prior to PCR will take considerable effort. Once again, support from your instrument provider will be required here.

5. Integration with LIMS

Once protocols have been optimized, incorporation of the LIMS and file transfers is required. This will likely take a minimum of a month to ensure that data transfer is working appropriately.

6. R&D and automation expertise

Underpinning this whole process is experience in both automation and research and development. Without this know-how, the task of developing and implementing a new automation workflow is almost certain to be unsuccessful.

* With support from QIAGEN or its partners.

Case study

The United Kingdom Forensic Science Service (FSS) implemented a new high-throughput workflow involving Hamilton STARline automation and QIAGEN® magnetic bead chemistry in 2009. A team of four scientists, experienced in automation and DNA workflow optimization, worked full-time on the project with an IT LIMS specialist ensuring full LIMS integration. This project was 6 months in development and a further 3 months for validation.

The FSS example can be considered a success, in that DNA results were not compromised and the final workflow was implemented and accredited to ISO 17025 within 12 months. Many automation projects never overcome the hurdles described above and are terminated early.

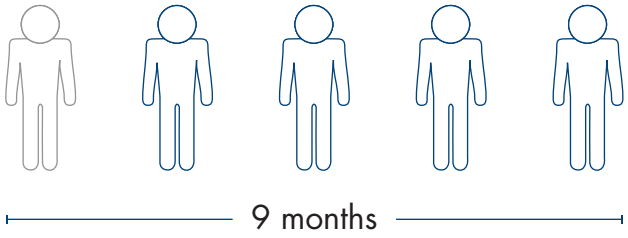

Figure 1. Effort required to implement a new high-throughput automation workflow at the UK Forensic Science Service. 4 scientists and 1 IT specialist for 9 months. Support from the instrument supplier is in addition.

STAR Q SP/AS Instrument

QIAGEN's STAR Q SP/AS has been developed in partnership with Hamilton Robotics. The platform combines Hamilton's experience in high-throughput, precision liquid handling with QIAGEN's expertise in the development of sample preparation and assay setup workflows for human identity. The final workflow is based on QIAGEN's trusted Investigator® chemistry for sample preparation, ensuring the highest possible yields of inhibitor-free DNA, produced using QIAGEN's ISO-18385 forensic DNA grade consumables. The system has several benefits over traditional "open" liquid handlers, as follows.

1. Pre-validated protocols

Questions over compatibility of manual methods with instrumentation are completely removed with optimized and validated protocols for QIAGEN chemistry. All hardware, protocols and workflow steps have been developed with QIAGEN's magnetic bead chemistry in mind to ensure a seamless workflow, capable of best-in-class DNA recovery, without the need for optimization in your lab. Developmental validation data is available to demonstrate that success rates are comparable to other, lower throughput solutions, ensuring no compromise in performance.

2. Fast and painless implementation

Because protocols are established, the months of development and optimization required for more traditional automation platforms is completely removed and implementation is extremely efficient. Once the instrument has been installed by a qualified engineer and its basic performance verified, your own in-house validation according to ENFSI and/or SWGDAM guidelines can then be performed, either on your own or with QIAGEN's full support.

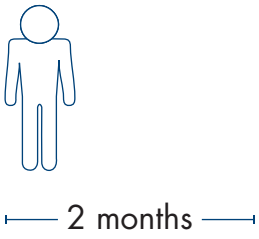

Figure 2. Fast implementation. The STAR Q SP/AS can be up and running within two months of delivery: 1 person, working with QIAGEN, for 2 months.

3. Training

As part of the implementation process for the STAR Q SP/AS Instrument, QIAGEN delivers a detailed training program to ensure your team understands the science behind their new workflow. This is essential to enable them to run the workflow competently and to address any questions raised by accreditation bodies.

4. Substantial cost savings

As described above, typical protocol development on open platforms requires days or weeks of programming from the instrument provider, and this cost is passed on to the customer in the final instrument price. Because QIAGEN's protocols are ready to go these costs are not incurred and the STAR Q SP/AS is typically more cost-effective than other options.

5. Maximum flexibility

Although the STAR Q SP/AS comes with all protocols for QIAGEN chemistry pre-installed, it is still based on the Hamilton STAR instrument and so has the flexibility to be configured to meet any laboratory needs both now and in the future. QIAGEN understands that labs want this flexibility and future-proofing in their automation, and so our trained application specialists will work with any customer to explore other changes if required down the road.

6. Peace of mind with guaranteed support

Most liquid handlers do not provide the chemistry, which needs to be sourced from another supplier. The end user therefore has responsibility not only for developing their protocols but also for maintaining and troubleshooting them in case of problems down the road. Because QIAGEN provides the full workflow the responsibility rests with us. Although highly unlikely to occur, any problems with your workflow will trigger the full support of QIAGEN, with our technical service and forensic application specialists taking the lead in getting your lab back up and running in the shortest possible time.

Summary

Modern forensic science laboratories are under increasing pressure to expand their capacity to handle higher volumes of DNA analysis. This inevitably needs to be achieved with no compromise of results or quality and with minimal downtime to their core operations during the adoption process. However, developing, evaluating and optimizing automation workflows to address these needs will always take considerable expertise, cost, time and effort for challenging forensic samples. The paradox inherent in this requirement prevents many labs from adopting new automation and in turn means DNA profiling is yet to meet its full potential. The STAR Q SP/AS Instrument has been developed specifically to address this problem and presents a unique solution to labs wishing to increase throughput cost-effectively and in the shortest possible time.

References

1. ENFSI Survey on DNA databases in Europe (December 2015)
   http://www.enfsi.eu/sites/default/files/documents/enfsi_survey_on_dna_databases_in_europe_december_2015_final_0.pdf
2. CODIS – NDIS Statistics (October 2016)
   https://www.fbi.gov/services/laboratory/biometric-analysis/codis/ndis-statistics

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