



Automation and the Next Generation Sequencing Workflow

Factors to Consider

Next generation sequencing (NGS) has revolutionized genomics, enabling entire genomes to be sequenced more efficiently than ever before. However, the typical NGS workflow is less revolutionary, with numerous manual steps and challenges that include cost, throughput, and variability. Traditional methods for sample preparation and data analysis can be extremely time consuming with numerous opportunities for error.

Automation provides a solution for many of these challenges, and increases precision by reducing sample-to-sample variability. Nonetheless, choosing the right automation instrument or instruments for your NGS workflow is a complex process. For the best integration of automation into your lab, evaluate these four factors before making any decision:

- How will automation impact your processes?
- What are your automation options?
- How much of a learning curve will there be?
- Will your automation solution expand to meet future needs?



Agilent Technologies

Automation and your NGS processes



Figure 1. General NGS workflow.

Automation's key benefit is accelerating the speed and accuracy of routine steps, and there are multiple opportunities for automated liquid handling in a typical NGS workflow. To see how automation can be applied to library preparation, Figure 2 shows the manual and automated workflows for library construction on the Illumina sequencing platform.

In this example, SPRI purification reduces the number of steps. And, while automation decreases the number of steps required, the more significant finding is that it also decreases the time needed for preparation, selection, and capture – by 50%.

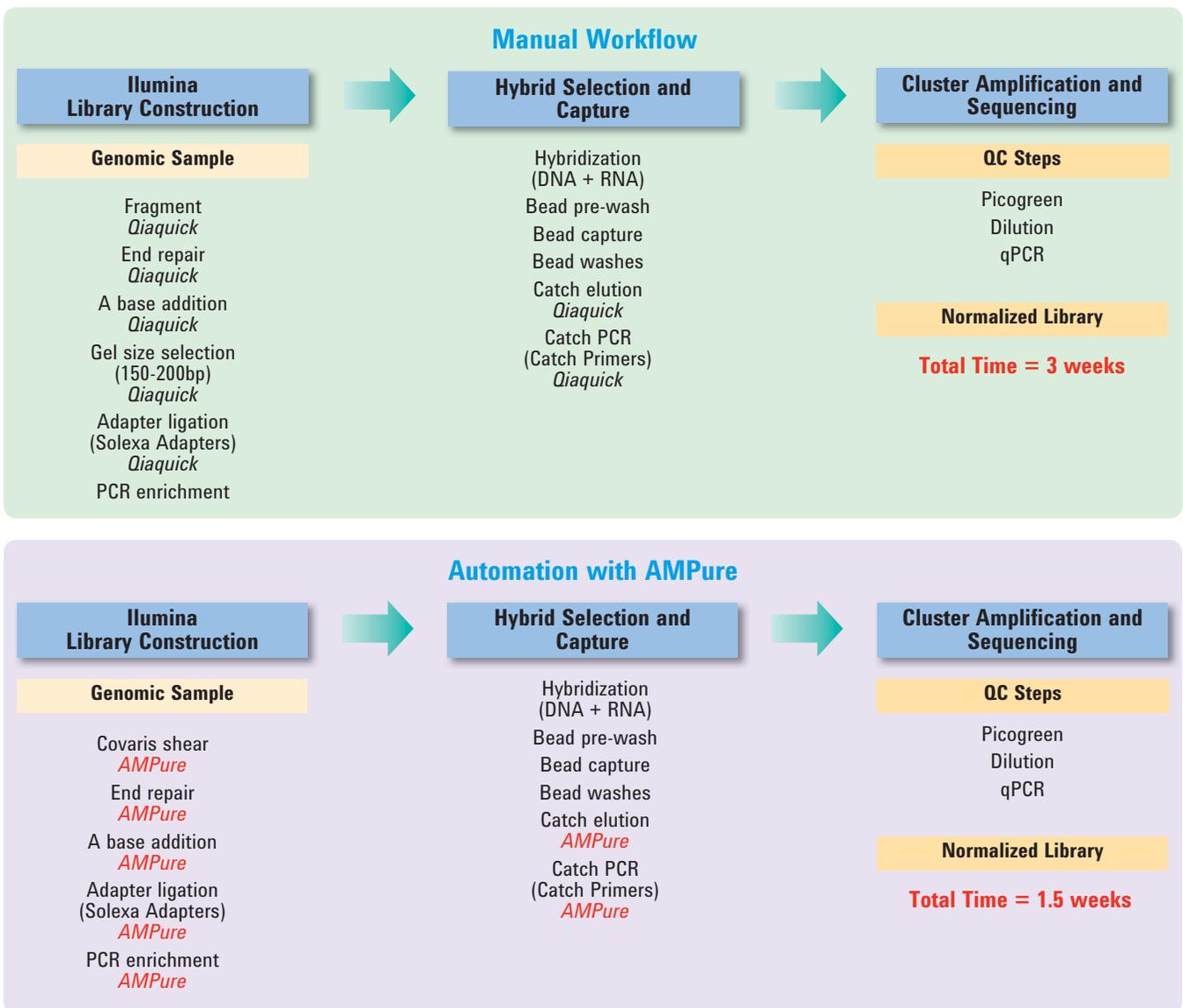
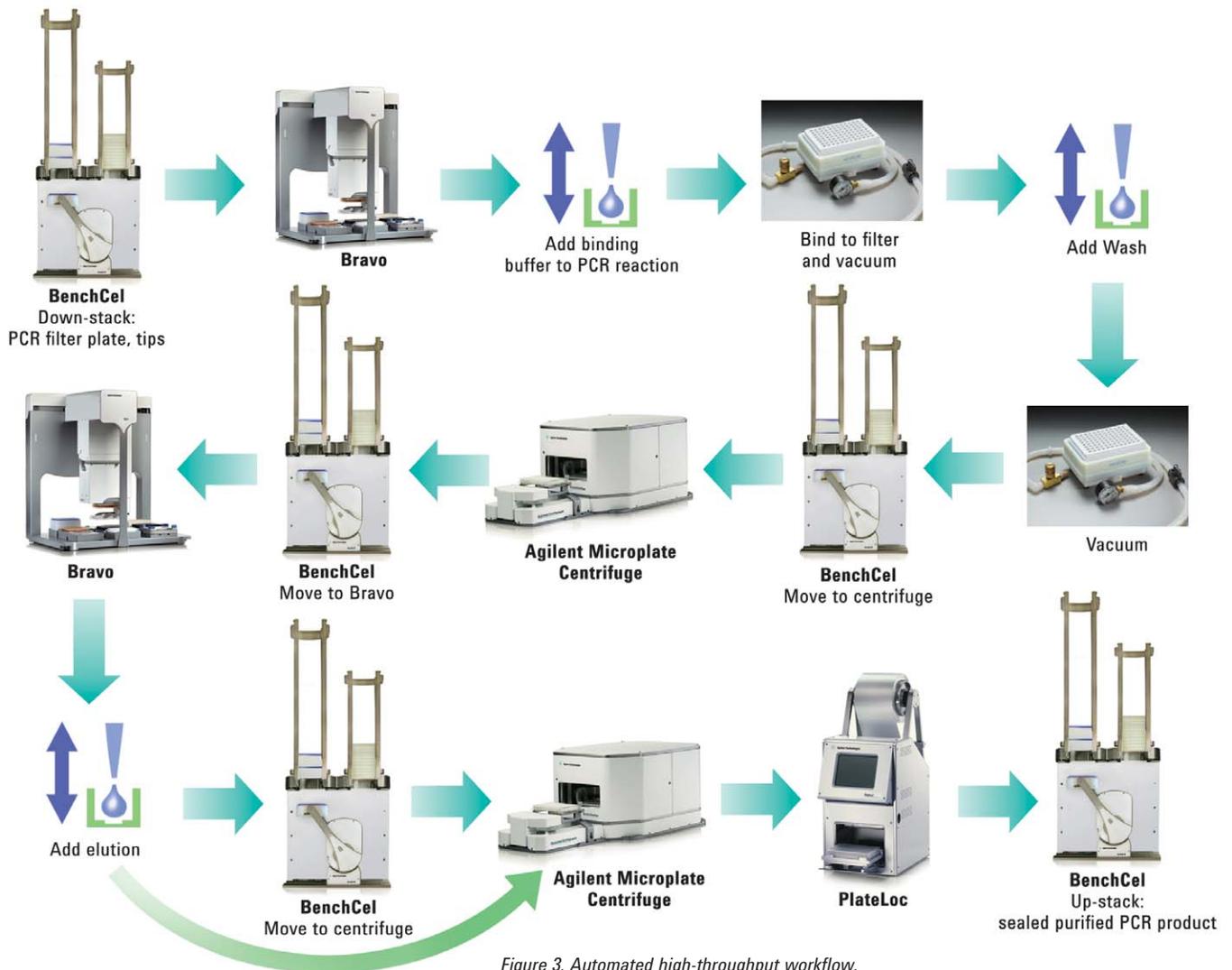


Figure 2. Library construction on Illumina platform.



Do you use vacuum and spin filtration for your purification? Figure 3 illustrates what this might look like for a fairly high-throughput workflow with automation.

Additional Acceleration: Target Enrichment

Bead-based target enrichment protocols like those used in the SureSelect Target Enrichment Kits and SureSelect Human All Exon Kits enable you to sequence only the genomic regions of interest, improving experimental efficiency by orders of magnitude. These protocols are easily implemented and highly scalable, enhancing the speed and accuracy advantages of the Bravo Automated Liquid Handling Platform.

Automation options

Consider your lab's entire workflow. There are various automation solutions – from the Vertical Pipetting Station to the BenchCel Workstation to the BioCel System, to meet a range of throughput needs. Automation will improve accuracy and consistency – do you also need a complete walk-away solution? A range of automation devices are available to accommodate different lab needs.

Agilent's Bravo Automated Liquid Handling Platform delivers high-accuracy pipetting over a wide volume range, with the flexibility to accommodate different plate formats and a unique, open design that facilitates integration into additional workflow automation. Incorporating the Bravo Automated Liquid Handling Platform into your research can greatly reduce the amount of time you spend preparing and checking the quality of your next generation sequencing libraries, and increase precision by reducing sample-to-sample variability.

If your lab requires higher throughput, you may wish to add a more comprehensive automated system. Agilent's BenchCel Microplate Workstation provides the flexibility, scalability, and throughput of a full-size system in a compact, benchtop platform. Controlled by the Agilent VWorks software, the most flexible and efficient scheduling software available, BenchCel Workstations can be adapted for both complex and simplistic application workflows, delivering more walk away time and greater throughput when compared to traditional manual methods.

For ultra high-throughput, high-productivity labs, you may need to move off the benchtop. Agilent's free-standing BioCel automation system is enabled by the teachable Direct Drive Robot (DDR). This highly flexible system can be customized with other Agilent automation modules, or third-party instruments to meet your lab's needs.



Figure 4.

Benchtop options:

A. Bravo Automated Liquid Handling Platform

B. BenchCel Microplate Workstation

Free-standing productivity:

C. BioCel System

How much of a learning curve will there be?

A single device like the Bravo Automated Liquid Handling Platform is simple and straightforward to use. However, if you have multiple automation devices (such as robots, liquid handlers, readers, washers, and others), you need to consider the time needed to master all of them. Are the software and device menus easy to understand? Will all your automation devices work together?

Agilent VWorks Automation Control software integrates your automation devices. An intuitive graphical user interface makes it simple to create new protocols, connect and configure devices, run protocols, and monitor progress. A single scalable and dynamic software in your lab means that you can reduce training costs and maximize productivity while expanding into a complex network of devices.

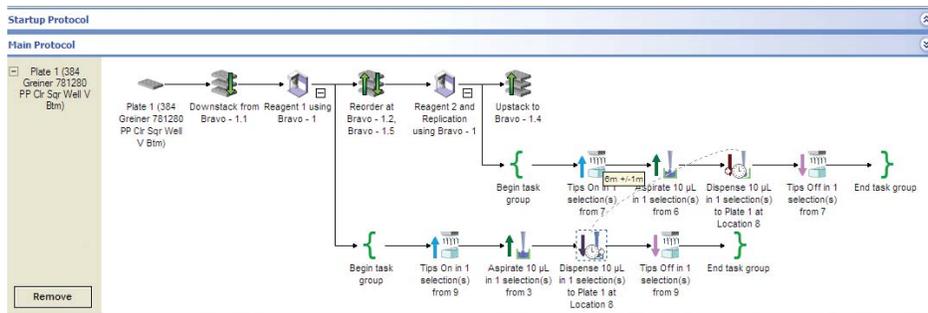
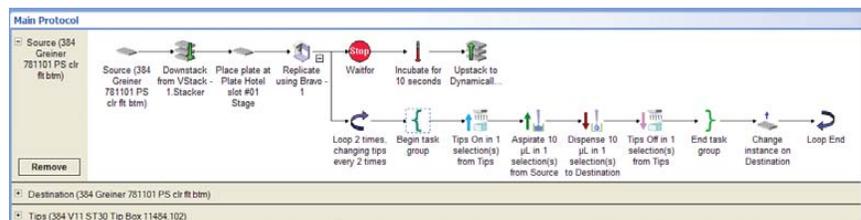


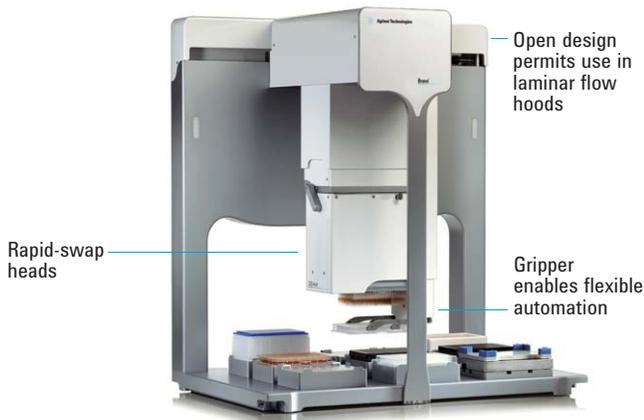
Figure 5. Agilent VWorks: the most powerful and flexible automation control software in industry, and an integral part of workflow implementation.



Will your automation solution expand to meet future needs?

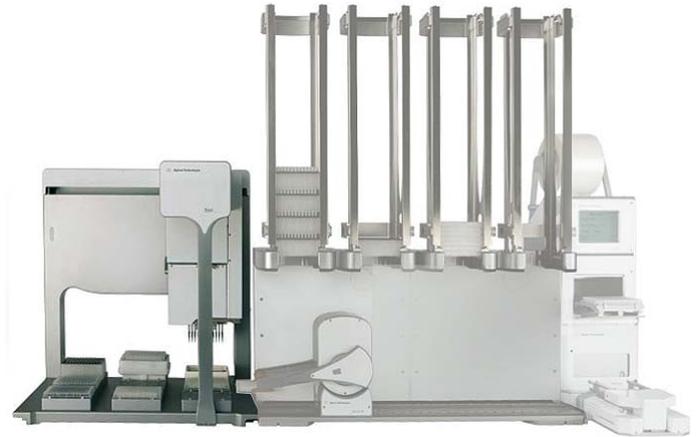
What are your needs now, and what will they be a year from now? Agilent's automation solutions are designed to work together, with VWorks Automation Control software making it as easy to run 10 instruments as it is to run one. The Bravo Automated Liquid Handling Platform and BenchCel Workstations are specifically designed to scale up.

A. Bravo Automated Liquid Handling Platform: versatile design



With fast, compact, quiet operation, the Bravo Automated Liquid Handling Platform features best-in-class precision and accuracy, and no electronics below the deck.

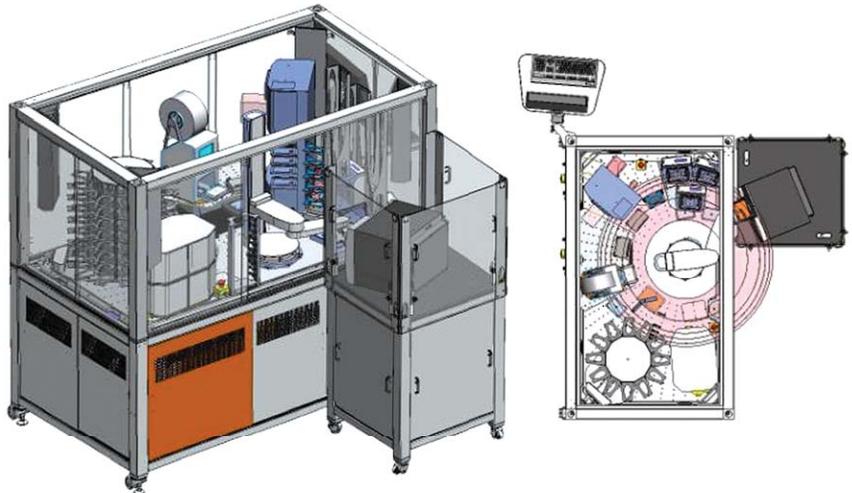
B. BenchCel Workstation: additional capacity



Scale as your workflow requires. BenchCel Workstations can be used in both complex and simple applications, delivering more walk-away time and greater throughput compared to traditional manual methods.

C. BioCel System: ultimate throughput and walk-away freedom

Figure 6.
Meeting varying throughput needs:
A. Bravo Automated Liquid Handling Platform
B. BenchCel Microplate Workstation
C. BioCel System



Scale up to a BioCel for many plates (side and top view). The new Direct Drive Robot brings speed and precision to the BioCel System that is both affordable and easily expandable. With modular cells, options for various enclosures, and environmental control, BioCel Systems are tailored to your individual needs, and deliver the longest walk-away time and throughput of any integrated system.

Real-life workflow: Broad Institute

The Broad Institute is one of the world's leading genomic research organizations. An evaluation of three manufacturer's liquid-handling systems led the Institute to choose the Bravo Automated Liquid Handling Platform, with size and tip-loading convenience as deciding factors. Using an automated workflow with target enrichment (Figure 7) has enabled the number of experiments per sequencer to

increase from ~1,000 to more than 10,000 per year, and achieve other benefits, including:

- Decreased sample process time
- Decreased sample-to-sample variability
- Increased yield when compared to manual method
- Increased capacity from 12 to 96 samples/per technician

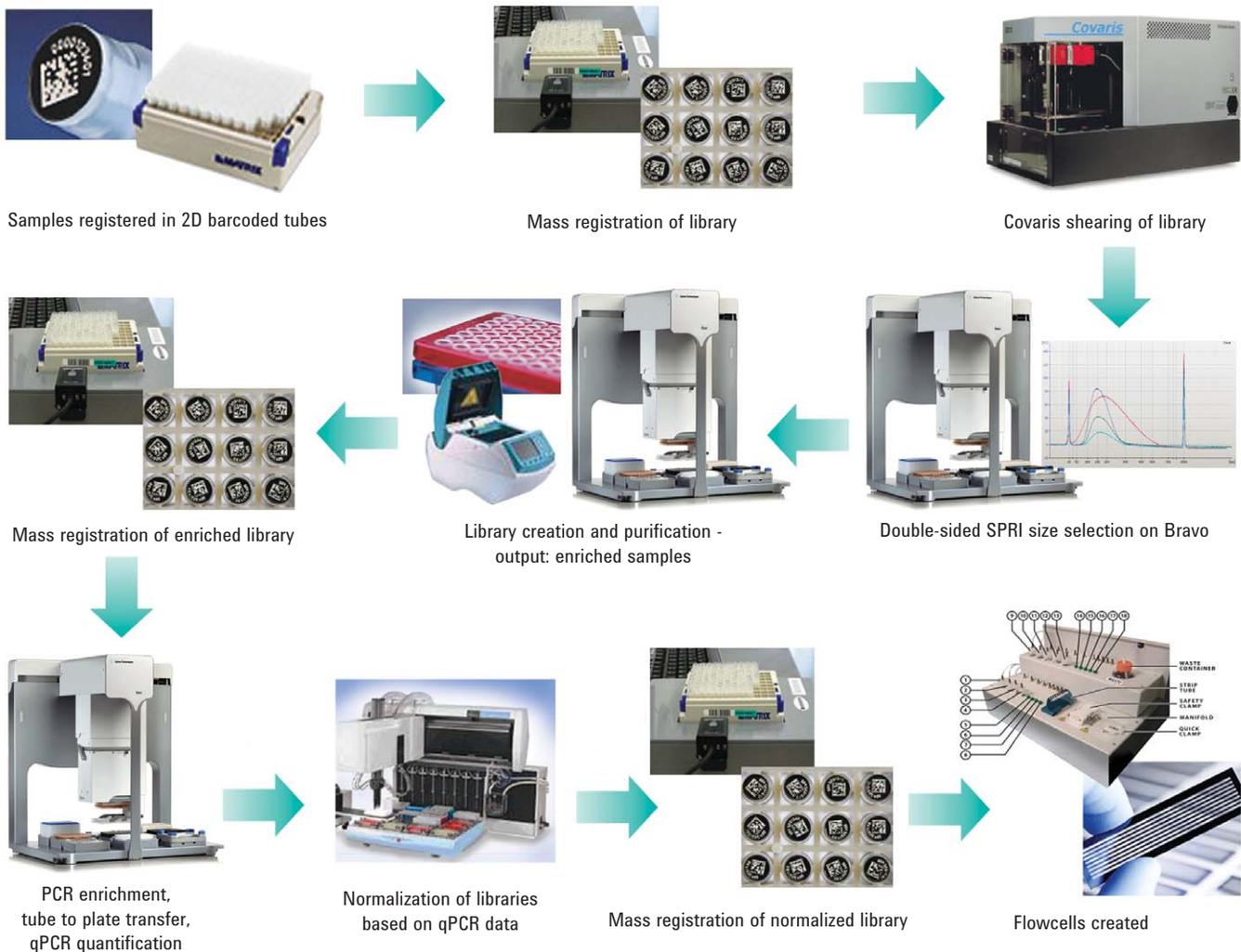


Figure 7. Creation of enriched library at the Broad Institute.

Consider Agilent

At Agilent, we understand the importance of the four key factors we've been discussing, and we have included each as a core objective in our automation solutions platform. We build in quality from the start by using ISO-certified processes to develop and test procedures for all of our automation solutions.

In addition to proven machines and compatible consumables and accessories, we provide the expertise you need to ensure optimal results in your work. Agilent Automation Solutions are backed by knowledgeable scientists who can provide customized support and services for your specific applications.

When you're ready to consider automation for your next generation sequencing needs, consider Agilent's automation products. If you have any questions about the best options for your lab, talk to your Agilent Representative about how to best simplify and accelerate your NGS workflow.

Application notes

Find out how automation has been implemented in a variety of NGS laboratories.

1. Automation of Agencourt AMPure Purification Kit for the Purification of Next-Generation Sequencing Sample Preparation Reactions on the Agilent Bravo Automated Liquid Handling Platform (5990-3532EN).
2. Automation of Stratagene Absolutely RNA 96 Microprep Kit with the Bravo Automated Liquid Handling Platform (5990-3558EN).
3. Complete Automation of Quantitative Polymerase Chain Reaction Assays on the Agilent Bravo Automated Liquid Handling Platform (5990-4522EN).
4. Automating the CGH/CNV Workflow with the Bravo Automated Liquid Handling Platform (5990-4660EN).

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