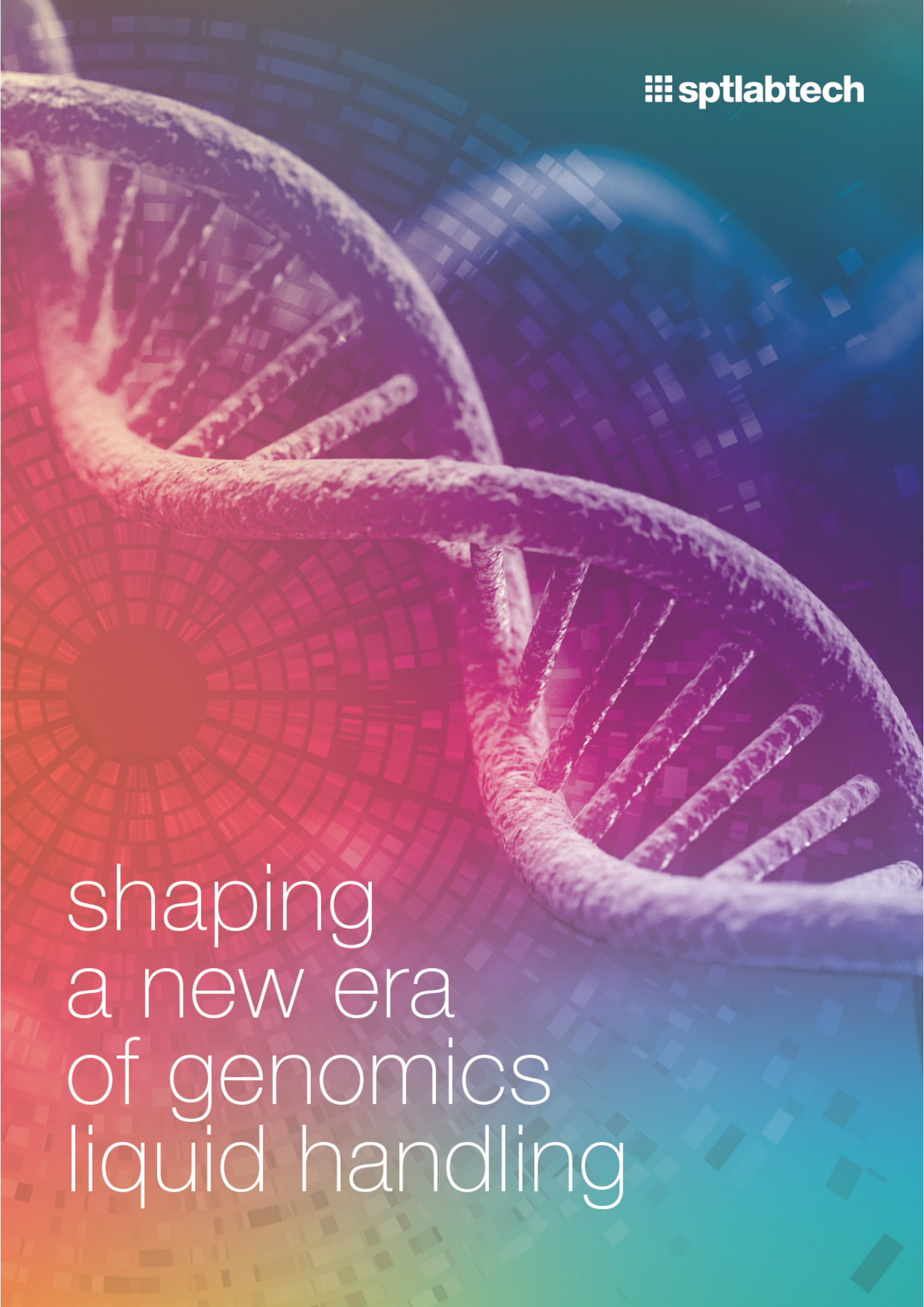
sptlabtech



shaping a new era of genomics liquid handling

introduction

Next-generation sequencing (NGS) has revolutionized genomic research by empowering researchers to sequence genomes at speed. The adoption of powerful genomic techniques has expanded beyond research into clinical settings – opening up new scientific avenues and commercial markets. To harness the full potential of transformative methods, scientific leaders need robust and innovative solutions that can overcome workflow bottlenecks and increase throughput and efficiency. Automated instrumentation is already playing a vital role in underpinning genomic advances as laboratories respond to increased research demand and accelerating sample volumes.

Yet, sample management workflows still present multiple opportunities for optimization to assure sample integrity, automate repetitive tasks, and increase efficiency.

The tasks of pipetting, mixing, dispensing, incubating, and shaking are integral to genomics research. Therefore, automated liquid-handling technology represents a particularly significant opportunity to reduce costs and improve the efficiency of sequencing. With capabilities and functionality developing at a pace, the implementation of solutions poses several considerations for laboratory leaders.

This report summarizes these opportunities and considerations, shares snapshots from our qualitative research with NGS customers about their library preparation experiences, and proposes a vision for the future.

> *Automatic liquid-handling systems have the potential to significantly optimize genome sequencing outputs, both in time and costs.*
>
> *– Tegally, H. San, J.E., Giandhari, J. et al.*

contents

key opportunities and considerations

Automation will deliver better value

Automated liquid handling solutions stand to deliver exceptional ongoing value to NGS laboratories. Research scientists are highly skilled and expensive resources, and it is essential that we direct scientists' energy and expertise away from repetitive, manual tasks and towards areas that deliver the most advantage, such as designing experiments and analyzing results.

Automated liquid handling in NGS applications enables higher throughput by using multi-well 96 and 384 well plates, dramatically increasing reliability, accuracy, and speed. This higher throughput allows labs to generate more data from their available budget and ensure worthwhile research investment.

While there is naturally an upfront capital cost when investing in any automated liquid handling system, laboratories can recoup this initial outlay swiftly with the demonstrable efficiency and productivity gains, as well as the reduction in required consumables. New, affordable automated liquid handling technologies accessible for all will help democratize access to this transformational approach.

> *Beyond cost, robots can also carry out tedious and repetitive tasks tirelessly and accurately, presenting a huge advantage over manual liquid-handling. Not only would this help cut down costs associated with manual labor, it would also mean that highly skilled life scientists would not have to spend long hours pipetting liquids anymore.*
>
> *– Tegally, H. San, J.E., Giandhari, J. et al.*

Space is often a limiting factor

Automation technologies demand substantial square footage, and when deciding which instruments to choose, there are complex trade-offs that often include bench space considerations. Laboratory space is an issue across organization types, from academic research to larger pharmaceutical companies. Eliminating redundancies in equipment by considering multi-functional technologies with a more compact footprint would offer numerous benefits. These include lower direct costs, lower environmental impact, and a greater per square footage investment return.

accessible technologies with intuitive software can remove the 'fear factor' from controlling the automated instrument

Ease of use

In the past, implementing automation solutions has relied on an in-house ‘expert’ to control and manage the robot. Identifying more accessible technologies with intuitive software can remove the 'fear factor' from controlling the automated instrument and empower every researcher within the lab with the tools to boost productivity and quality. Software has historically been an afterthought, and many software packages have evolved incrementally over 20 years or more, building complexity on complexity. A few recent products in the market are bucking that trend to put software at the forefront of the user experience and make approachable graphical user interfaces that are intuitive and quick to learn.

Another emerging trend is the shift from the reliance on the instrument vendor for new protocols. This derives from easier to use software requiring less input from vendor experts and the emergence of cloud-based protocol sharing. Whilst many vendors provide access to new protocols, they can become a bottleneck in curating and distributing them.

What our industry colleagues reveal about their experiences in automated liquid handling for genomic research

We have asked our industry colleagues to share their insights and experiences in implementing liquid handling automation for next-generation sequencing. Below we share some snapshots of their experiences.

Over 80% of respondents surveyed were using three or more automated liquid handling systems for library preparation. This fact reflects the challenge of multiple systems contributing to laboratory crowding, addressable with the use of more multi-functional technologies.

Over 50% of our respondents were most commonly using 384 well plates with a further 31% using mainly 96 well plates and some 384 well plates for library preparation reactions.

If miniaturized protocols were available, **62%** of our respondents would miniaturize all or most of their weekly library preparation. This reflects an overall drive towards enabling greater efficiency within these workflows.

"As an academic relying on shared facilities, laboratory space is a problem for me."

"We rely heavily on the robot experts in our lab and when they are not around other users are nervous about using the robots"

"Our priority now is to start automating liquid handling processes that are currently manual."

“Manual library preps are extremely time consuming and prone to error - we want our scientists focused on analyzing data not generating it”

A future vision for liquid handling automation for next-generation sequencing

More cost-effective, flexible, and easy-to-use liquid handling automation for next-generation sequencing would democratize greater library preparation efficiency for laboratories of all sizes.

The rewards of fully harnessing the power of automation in next-generation sequencing will be substantial with as yet unrealized potential for increased productivity across thousands of laboratories. With every new insight having the potential to contribute to another important discovery, who knows where that future may lead?

next-generation sequencing is transforming healthcare – where are we now, and what does the future hold?

Advances in next-generation sequencing have powered a genomic revolution. From early beginnings and painstaking processes, methods have advanced significantly, opening endless research avenues. As of 2021, it is possible to sequence a human genome within a single day, and we are fast approaching the much-anticipated $100 genome. As speed and throughput have increased, the applications for these powerful genomic techniques have expanded beyond research into a more diverse range of clinical settings.

The first high-level trend shaping the sector is the increased demand for next-generation sequencing across personalized medicine, genetic testing and other applications. The second fundamental factor is the scale of advances in sequencing techniques and associated technologies that have enabled greater adoption and increased the breadth of possibilities for genomic research.

Research demand

Several key areas are shaping the ongoing boom in global research demand, all underpinned by far greater accessibility in terms of costs and technology. Approaches that were once the preserve of a limited pool of researchers in specific academic centers and regions are now geographically widespread and adopted into a range of clinical and research settings.

Genetic sequencing for infectious disease surveillance

Even as the worst of the SARS-COV-2 pandemic passes, at least in the developed world, genetic sequencing will continue to play an essential role in managing the global SARS-COV-2 disease burden and monitoring transmission and variants. Sequencing is now firmly embedded in worldwide healthcare systems as a critical tool for identifying and surveying infectious diseases.

Genomic profiling for personalized therapeutics

Once an aspirational goal, personalized therapeutics have now become a reality, especially within oncology indications. With these new medicines comes a need for genomic profiling supported by next-generation sequencing. In a recent its presentation, Illumina highlighted 55 approved drugs that require genomic testing to identify whether they are suitable for the specific patient. More similar medicines are on the horizon as biomarker-driven clinical development becomes increasingly mainstream.

Sequencing for other clinical applications

Next-generation sequencing is used across many clinical applications, and essential tests are now available in most regions for risk assessment, disease screening, and reproductive health. Sequencing also plays a vital role in the diagnosis of rare and suspected genetic conditions, and 'long-read' sequencing technologies now provide a more comprehensive view of variation in a genome to improve detection. A team of scientists from Stanford used a novel sequencing method from PacBio to successfully identify a novel structural variant in a gene associated with Carney syndrome, for a patient who had suffered repeated tumors. This breakthrough came after eight years of genetic analyses that had produced no concrete results.

As technologies become less costly and easier to access, the increased uptake of genetic testing is set to continue. Innovative developments such as Oxford Nanopore's real-time portable sequencing have the potential to transform point-of-care treatment. For example, Oslo University Hospital used the technology to classify brain tumors in just over 90 minutes- fast enough to inform in-process surgical strategy and drastically improve patient outcomes.

Technology advances

Technology advances encompass faster, more cost-effective and more informative sequencing techniques, alongside a step-change in analytical power through artificial intelligence and deep learning approaches.

Multi-omics growth

One of the most promising developments is the ability to capture multi-omics data, allowing researchers to gain a deeper level of biological knowledge beyond the genome and explore the transcriptome, proteome, and metabolome. These dynamic datasets yield transformative insights about the drivers of disease to enable breakthroughs in drug discovery. Growth in this field is driving further demand for sequencing technologies and supportive solutions.

AI advances to unlock the power of large datasets

Reduced sequencing costs and new techniques have facilitated more ambitious projects and generated an explosion in available data. For instance, low-pass Whole Genome Sequencing (WGS) involves high-throughput sequencing of the entire human genome at low coverage. It delivers a much more cost-effective approach to measuring genetic variation at high throughput for large genomics projects.

by making automation a reality for laboratories of all sizes, we can empower the next phase of genomic innovation

Artificial intelligence and data science are helping to transform this increasingly vast volume of data into an asset that can inform a better understanding of diseases, support more efficient drug discovery, and improve clinical decision-making. For example, Illumina's SpliceAI, a state-of-the-art deep neural network, helps research scientists to identify mutations in patients with autism. At the same time, its TruSight Software Suite uses advanced analytical techniques to translate sequencing data into meaningful results for rare diseases. The availability of these superior computational methods to extract insight efficiently will further drive appetite for sequencing in research, drug discovery and clinical applications.

Where next?

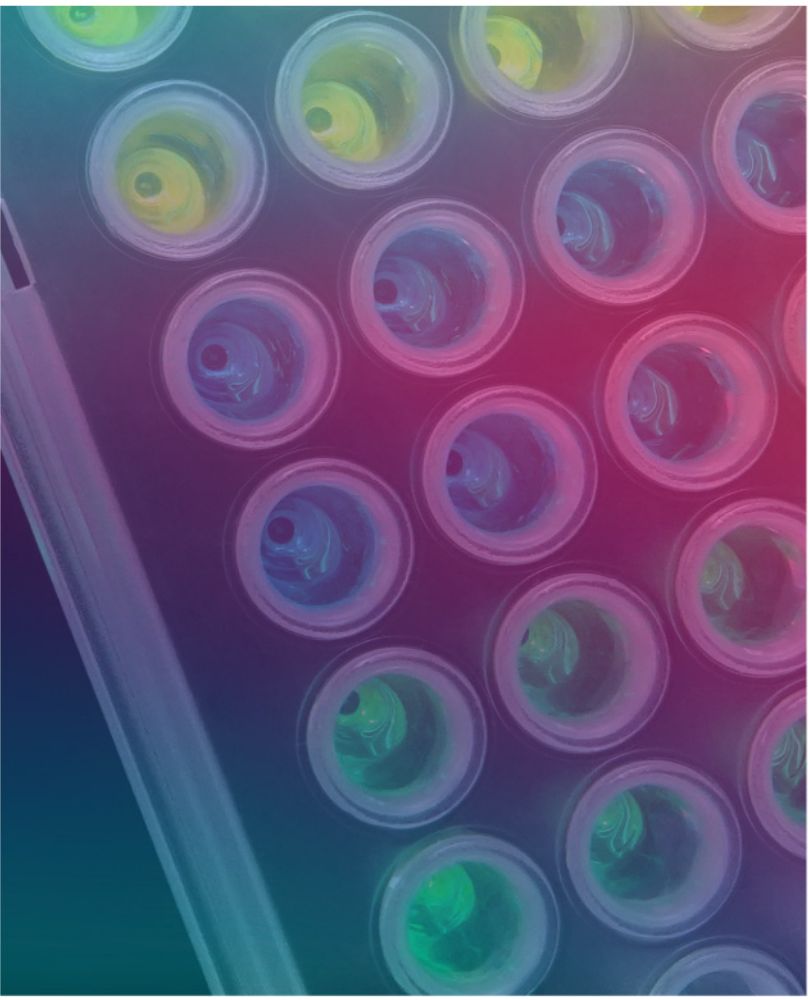
Against the backdrop of this transformational progress in sequencing techniques, there are still challenges to overcome. All too often, sample and library preparation methods cause workflow bottlenecks and inhibit researchers from maximizing the value of their research. As lower costs have enabled access to next-generation sequencing techniques for a broader range of research settings, we must also democratize access to transformative automated liquid handling solutions for genomics that can support throughput without compromising accuracy. Genuinely accessible solutions need to consider efficient use of available space, multi-functionality, simplicity for all researchers, and cost-effectiveness. By making automation a reality for laboratories of all sizes, we can empower the next phase of genomic innovation.

in the modern genomics lab, automation is accessible for all

In his book, "Seven Habits of Highly Effective People", Stephen Covey tells the story of a woodcutter attempting to chop down a tree with a blunt saw. Despite the frustration of working with this ineffective tool, the woodcutter carried on, saying he was too busy to stop and sharpen it. Of course, had he taken that time, he would have been able to complete the task efficiently with a sharp saw instead of laboring in vain. This principle of stopping to 'sharpen the saw' applies closely to our efforts to make our laboratory workflows more productive and efficient through automated liquid handling technologies. Indeed, the rapid expansion of genomics applications and research programs means that automated sample and library preparation is becoming a necessity for next-generation sequencing laboratories to enable them to keep up with demand. Sharpening the saw and ensuring we have the right technologies and systems in place is more important than ever.

Liquid handling solutions don't require an in-house automation expert

While the advantages of liquid handling automation are well-documented – greater speed, improved accuracy and precision and reduced costs – bringing in new tools and technologies can still be a daunting process. One of the inhibiting factors is the fear that automating might make the day-to-day activity more challenging initially because of the perceived need for extensive upfront training and reliance on dedicated experts to handle the system on an ongoing basis. This concern may be grounded in a kernel of truth because, unfortunately, there are stories of labs having invested in a complex system that only one team member was able to operate. When that 'automation expert' moved on, the instrument remained untouched in the corner – a waste of space and investment. More fundamentally, such implementation hiccups, however rare, increase hesitancy about bringing on transformational technologies.



However, we are now in a world where powerful automated liquid handling solutions can be implemented by any genomics laboratory using existing expertise, without the need for an in-house automation 'expert'. So, the future of liquid handling automation – like NGS sequencing itself – will be democratic and available more widely than in the past.

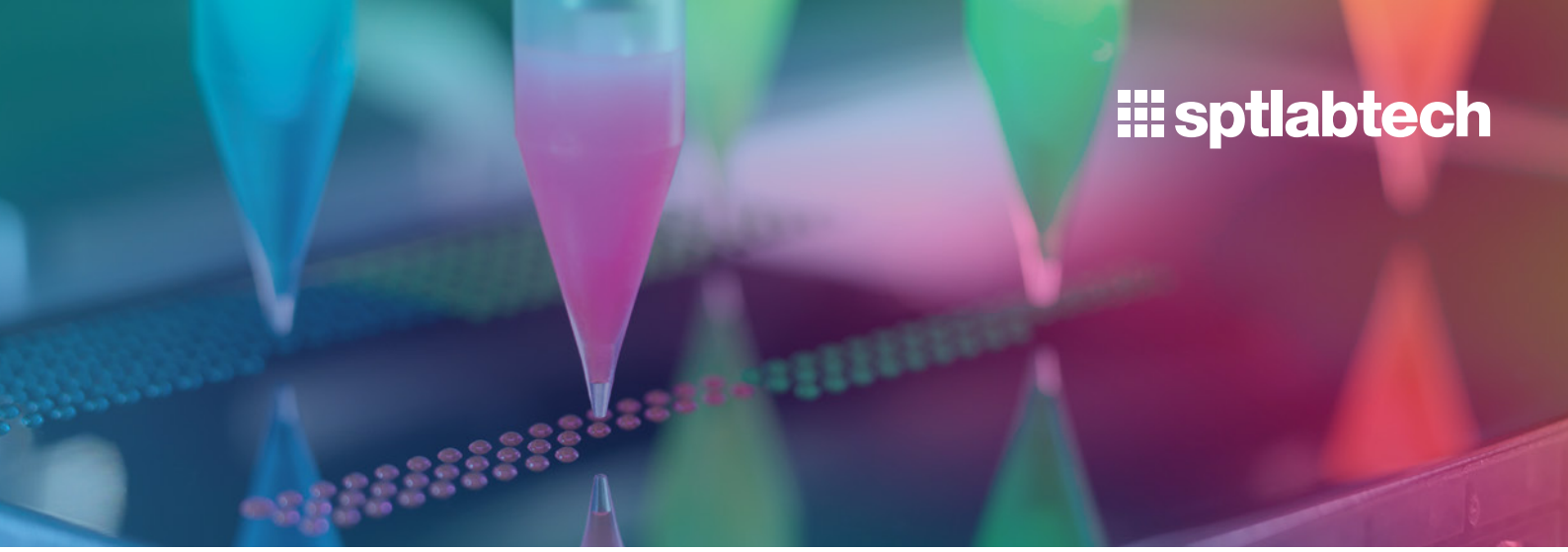
A significant development in this democratization journey is more intuitive software that removes the 'fear factor' from controlling the automated instrument. In liquid handling automation, software has often been an afterthought and many software packages have evolved incrementally over 20 years or more building complexity on complexity. A few recent products in the market are bucking that trend to put software at the forefront of the user experience and making approachable graphical user interfaces that are intuitive and quick to learn. This is a welcome development. Nowadays we are all used to adopting new software on a daily basis on our smartphones, so why should automated liquid handling be any different?

Revolutionizing NGS library preparation

Another emerging trend is the shift from the reliance on the instrument vendor for new protocols. This in part flows naturally from easier to use software requiring less input from vendor experts, but also the emergence of cloud-based protocol sharing. While many vendors do provide access to new protocols, they can become a bottleneck in curating and distributing them. Cloud based peer-to-peer sharing removes this bottleneck. Unfortunately, many current software packages make it very difficult to transfer protocols between systems with different configurations. Going forward, vendors that can enable peer-to-peer sharing of expertise in an easily transferable way between systems are likely to gain adoption.

Similarly, liquid handling instruments designed with ease of use in mind and training that quickly equips users of all levels to get up and running with their applications contribute to greater adoption of automated approaches.

Implementing a new automation solution is as much a human as a technology issue. Freeing highly qualified staff from laborious, repetitive tasks and enabling them to spend more time on rewarding scientific investigation, while providing access to new automation skills can ultimately improve their job satisfaction and enable greater innovation and productivity. In the modern-day genomics laboratory, everyone has the tools to be an automation expert and unlock the potential of efficiency gains for better scientific breakthroughs.



dedicated automated liquid handling technologies deliver better value

Four ways automation helps deliver better value in genomics research

In the dynamic, fast-paced landscape of genomics research, laboratory heads are constantly challenged to do more with less and deliver greater value from their investment. With the cost of next-generation sequencing reducing year on year, there remain significant opportunities to maximize research value by adopting liquid handling automation to streamline library preparation. Traditional multi-step library preparation protocols to prepare a sample for sequencing are time-consuming, error-prone, and costly. Dedicated automated liquid handling technologies can overcome these challenges to help laboratory leads research productivity and deliver better value. Below are four areas to consider:

1. Making better use of valuable people

Research scientists are exceptionally valuable resources, particularly in today's buoyant, candidate-led market with skills shortages in many key areas. It's essential that we direct scientists' energy and expertise towards areas that add the most value, such as designing experiments and analyzing results. Where there is over-reliance on manual processes, expensive and highly qualified researchers are forced to spend their time on repetitive tasks instead of investing effort where their skills matter most. By implementing an automated approach to library and sample preparation, resources can be redirected where they are most impactful. In addition, relieving researchers of the burden of repetitive tasks and alleviating pipetting strain improves job satisfaction, leading to improved staff retention and reduced hiring costs.

2. Reducing the cost of consumables

Enzymatic reagents used in genomics research are both challenging to work with and costly. Traditional manual processes and protocols use more sample volume and reagent than is often required for the experiment, resulting in inefficiency and cost wastage. Miniaturization techniques are now commonly used within high-throughput screening (HTS) assays. Genomics workflows are also extremely well suited to a range of lower volumes – depending on the application – which saves the laboratory cost and reagent.

3. Increasing throughput and generating more data from budget

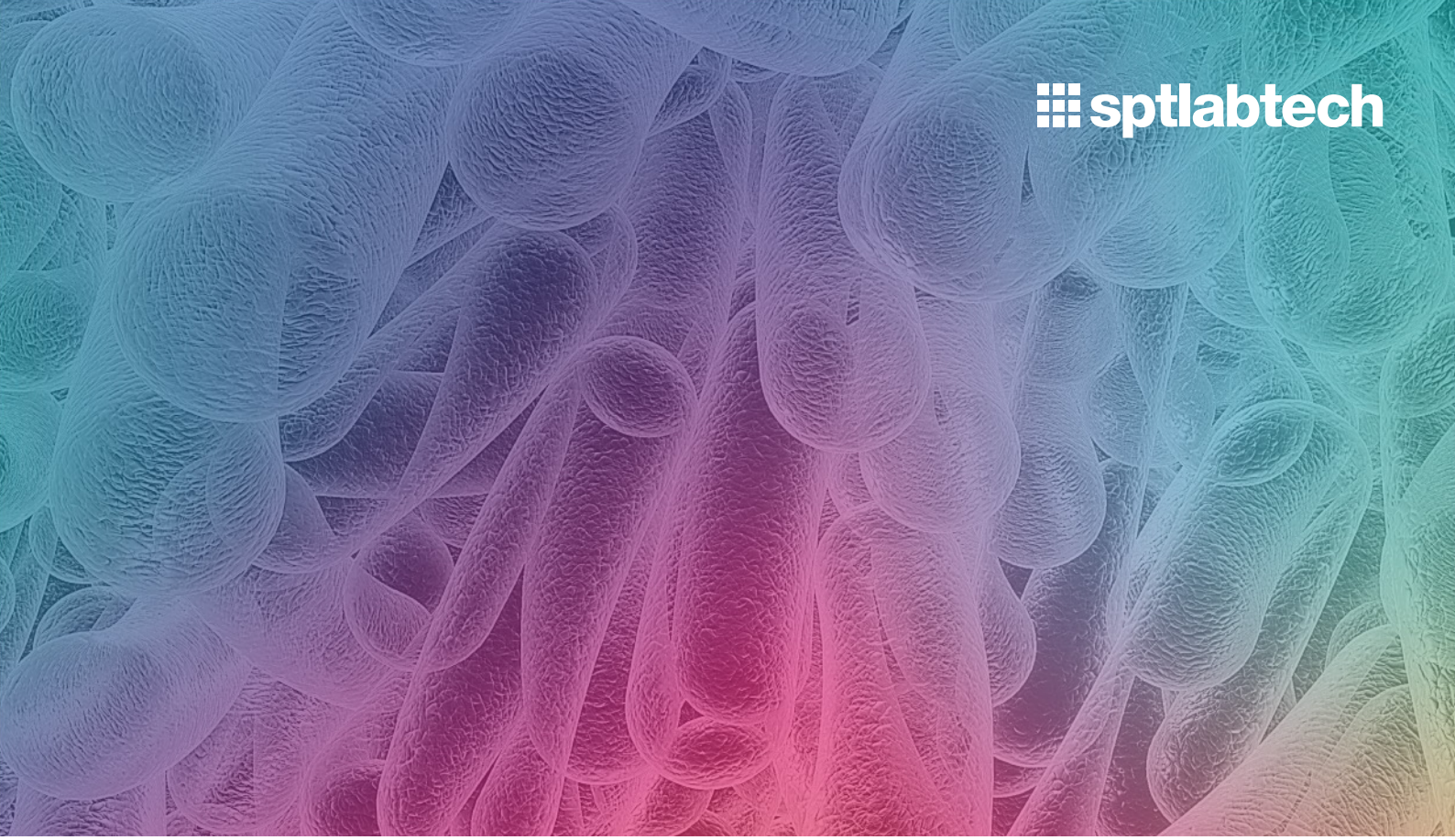
Automated liquid handling in NGS applications dramatically increases reliability, accuracy, and speed, facilitating the use of multi-well 96 and 384 well plates, even for complex experiments where multiple reagents are required. This higher throughput, combined with reduced costs, enables labs to generate more data from their available budget and ensure worthwhile research investment.

4. Mitigating the upfront capital investment with affordable systems

While there is naturally upfront capital expenditure when investing in any automated liquid handling system, laboratories can recoup this initial outlay swiftly with the demonstrable efficiency and productivity gains, as well as the reduction in required consumables.

Historically automated systems have had a high price point, but increasingly there is a notable trend towards democratization with more affordable technologies that are accessible for all. In the past, complete liquid handling automation was often only achieved by bringing together several instruments to accomplish the individual tasks of pipetting, dispensing, incubating, and shaking. As instrumentation capabilities advance, multi-functional technologies are increasingly realistic propositions. If one system can deliver all tasks, this also mitigates that upfront outlay and makes the investment more feasible for laboratories of all sizes. Developing a compelling return on investment case becomes even more straightforward with more cost-effective options to take those first steps into NGS liquid handling automation.

Increasingly, life sciences leaders consider value rather than simply cost when making investments in automation technology. This approach makes perfect sense given the step-change in productivity that automation can deliver and the high potential gains for more successful drug development, disease understanding, and human health.



could multi-purpose technologies help tackle the laboratory space conundrum?

The scale of next-generation sequencing is expanding, and the efficiency of the sequence generation process has improved significantly over time. However, library and sample preparation bottlenecks remain troublesome inhibitors of productivity and speed in genomic research. Eager to overcome these obstacles, laboratory leaders have increasingly adopted automated solutions to tackle various aspects of the liquid handling workflows required for genomics studies. With a life sciences boom fueling a rapid uplift in genomic research demand, embracing liquid handling automation solutions is now imperative for laboratories of all sizes.

eliminating redundancies in equipment by considering multi-functional technologies with a more compact footprint would offer numerous benefits.

Inefficient use of valuable laboratory space

There are many challenges to automation adoption in genomic research – one of which is the simple matter of precious available laboratory space. Automation technologies often demand substantial square footage, and when deciding which instruments to choose, there are complex trade-offs that include bench space considerations. Beyond these inherent space requirements, automated liquid handling for NGS is naturally challenging, incorporating multiple essential tasks, including pipetting, dispensing, incubating, and mixing.

All too often, full automation can only be accomplished by bringing together multiple single-task instruments and additional accessories into an integrated workflow. With each separate task integral to the research effort, it is, of course, critical to have the right tool for the right job. Genomics workflows require reliable, precise and accurate pipetting and dispensing of challenging liquids such as enzymatic reagents and beads, often at very low volumes. Shaking and incubation tasks also benefit from the efficiency improvements of automation. Nevertheless, the current need for multiple single-purpose technologies and several instruments may result in inefficient use of valuable laboratory space.

In the UK alone, recent press has highlighted a severe lack of laboratory space supply in London, Cambridge, and Oxford research centers, with rents tipping upwards of £100 per square foot.

With a thriving life Sciences Industry and research investment at an all-time high, laboratory space is at a premium, bench space for equipment is becoming scarce and expensive. This reality puts heightened pressure on facilities to maximize the return on any instrument investment and their overall infrastructure. In the UK alone, recent press has highlighted a severe lack of laboratory space supply in London, Cambridge, and Oxford research centers, with rents tipping upwards of £100 per square foot. This demand is apparent around the world, including in US biotech hotspots such as Boston where 50% of the five million square feet lab construction slated for completion by the end of 2022 is already leased. While larger pharmaceutical companies may have greater flexibility of resources and space, any facility needs to consider how they use their layout to ensure the maximum research productivity from every inch of their laboratory.

Multi-purpose technologies for liquid handling and other applications

Eliminating redundancies in equipment by considering multi-functional technologies with a more compact footprint would offer numerous benefits. These include lower direct costs, lower environmental impact, and a greater return on per square footage investment.

The solutions may be more accessible than we think. With technologies continuing to advance at a pace, robust multi-purpose technologies incorporating liquid handling and other key application processes could deliver exceptional performance within a single unit and are now becoming a real possibility. Such innovations stand to offer the space-saving research productivity and uptime boost that laboratory leaders so desperately need.

towards a more sustainable lab: what opportunities do we have to reduce waste?

Environmental sustainability is high on the agenda for governments worldwide, with private companies, public bodies and academic centers all playing a part in reducing the burden on the world around us. Unfortunately, laboratory research is particularly resource-intensive, consuming energy and water at greater levels than other sectors and producing vast quantities of plastic waste – a staggering 5 million tons every year. MyGreenLab, a non-profit organization devoted to creating a culture of sustainability in science, notes that this volume of plastic waste could cover an area 23x the size of Manhattan. These are striking figures, and with limited options for recycling the plastic products generated by laboratories, the situation is of deep concern. Against the backdrop of rising research demand in high-growth areas such as genomics, it's an opportune moment for laboratories to explore how to use resources better and reduce this environmental burden.

> *Never doubt that a small group of thoughtful, committed citizens can change the world. Indeed, it is the only thing that ever has.*
>
> *– Margaret Mead*

Sustainable laboratory practices

The advice from sustainable laboratory initiatives like MyGreenLab concerning waste is to follow the three ‘Rs’, reduce, reuse, and recycle and explore how each method could be adopted within the specific setting. Getting the basics right also matters – for example, the good practice of inventory management is essential for controlling costs and also supports oversight over sustainability practices. Making sustainability a factor in procurement strategy is another tactic many laboratories are now employing – since consolidating orders can significantly reduce waste.

It’s well known that consumables including tips, reagents and reaction tubes are the primary source of plastic waste from the laboratory, often resulting in numerous sacks per day from a single facility. 'Green' options for disposal of these items are limited due to contamination, but not all waste is hazardous so laboratories may work proactively with waste management providers to identify any opportunities for recycling. Yet, with consumables, perhaps the most powerful tactic laboratories can employ is to eliminate waste before it occurs by reducing use. There are already options available that

already contribute to this effort, including liquid handling solutions that mitigate waste of tip and reagent resources. For example, SPT Labtech’s dragonfly uses non-contact reagent dispensing, allowing a single tip to be used for multiple plate runs, dramatically reducing the number of tips required. Miniaturization, where we scale down the volume of a reaction mixture or assay, is another opportunity for environmental improvement by reducing waste of both reagent and sample. SPT Labtech’s mosquito and dragonfly instruments support these increasingly adopted miniaturized workflows. Indirectly, by reducing time at the bench for individual researchers, automated solutions can also lessen the use of other single-use plastics like gloves.

Innovative solutions for greener labs

Beyond this, innovative solutions such as automated washers that sanitize tips for reuse, and microplate washing technologies are now entering the field, and we will watch with interest to see how these approaches develop.

At a higher level, it's also crucial to think carefully about what technologies we choose in the laboratory to ensure that the scientific output justifies the environmental footprint. For example, investing in an instrument that is too complex for use by many of the research team is a questionable use of resources and does not reflect sustainable practice.

There is a great deal to explore and address in the journey towards greener research practices, yet the positive outcomes of embracing sustainability are multi-fold. Laboratories investing in sustainable approaches stand to benefit from stronger community spirit and motivation as well as derive cost efficiencies. A sustainability focus can also help inspire better science by encouraging us to think creatively, streamline processes and "do more with less", generating a more significant scientific return on our investment- while protecting our world for the next generation of scientists.

firefly®
an all-in-one solution

firefly® is a revolutionary, all-in-one liquid handling platform for genomics. It simplifies NGS library prep workflows by combining novel pipetting, dispensing, incubating, and shaking technologies within a single, compact instrument.

This groundbreaking platform helps genomic laboratories drive even bigger breakthroughs with accessible access to multi-functional automation. Underpinned by powerful, intuitive software, firefly empowers labs to:

- Simplify and integrate their genomic liquid handling workflows
- Achieve accurate and repeatable nanoliter to microliter pipetting regardless of liquid viscosity or environmental conditions
- Boost efficiency and flexibility with novel dispensing technology
- Fast-track collaboration via a peer-to-peer cloud-based network

Learn more about firefly®