Laboratory Automation: Unsolved Problem of Small and Medium-sized Enterprises

Many of us will relate to this: laboratory automation comes with benefits like quality and efficiency improvements; however, manufacturers make laboratories pay dearly for that. Thus, for small and medium-sized enterprises (SMEs), high investments in laboratory automation often do not pay off, since laboratory automation must be cost-effective and flexible to use. Does this even exist on the market – a flexible and user-friendly laboratory automation system that also fits into the budget?

For years, total laboratory automation (TLA) has been an important factor to increase the efficiency and quality of bioanalytical laboratory processes [1]. Despite TLA attempts, 182 German laboratories were able to rapidly increase their sample throughput from 90,000 to nearly 2.8 million PCR analyses per week during the pandemic [2]. Considering such a throughput, it is not surprising that the purchase of these systems – despite investment costs of millions – amortizes after only a few years. In addition to economic aspects, laboratory automation is also interesting because processes usually become more efficient, and the safety of laboratory personnel improves. In clinical environments, patients especially benefit from higher quality and faster analysis results [3].

At the same time, it becomes obvious that these systems are unsuitable for laboratories of small and medium-sized enterprises (SMEs) and for research laboratories with no commercial interest.

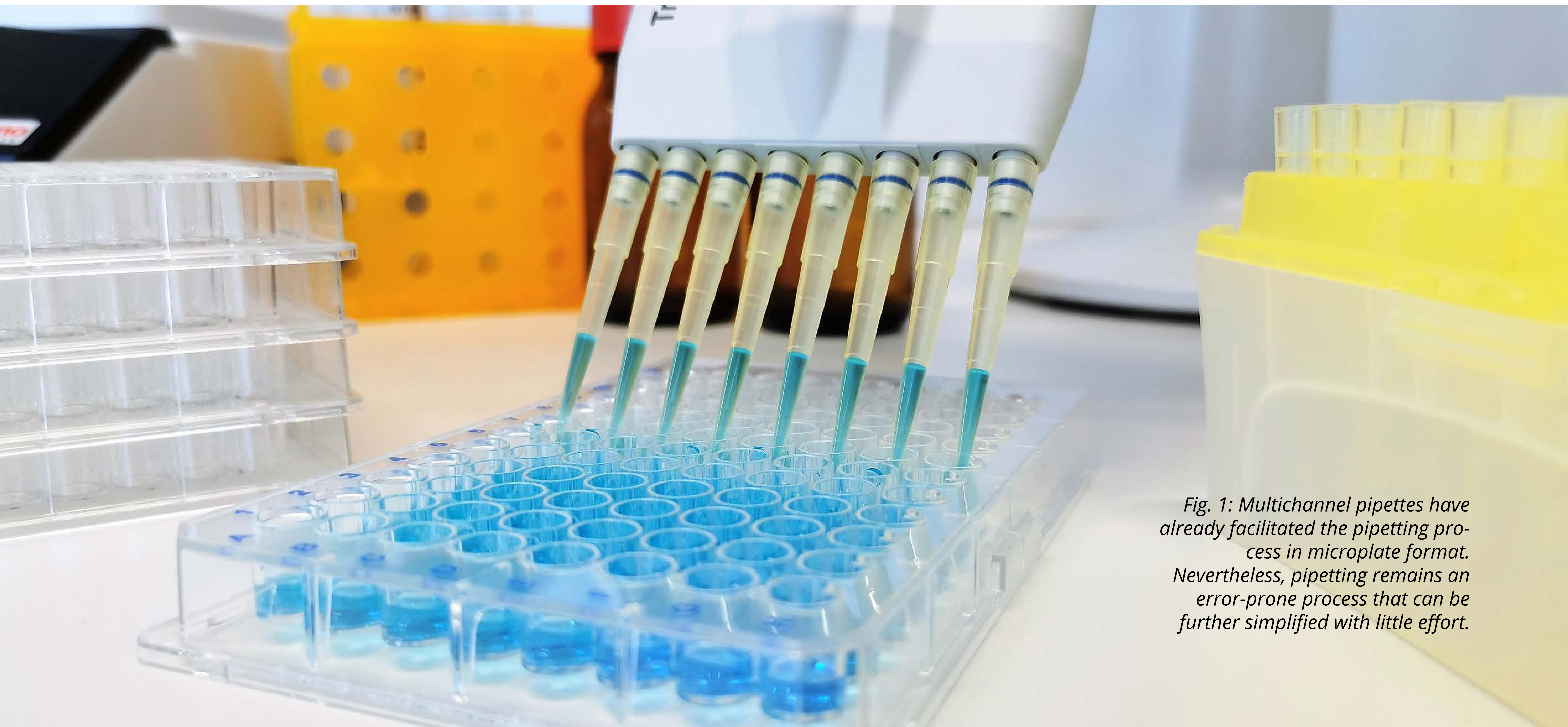

Fig. 1: Multichannel pipettes have already facilitated the pipetting process in microplate format. Nevertheless, pipetting remains an error-prone process that can be further simplified with little effort.

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Studied biochemistry and received his Ph.D. in protein and neurochemistry in Germany and the USA in 2005. After a 2-year research stay at Lund University, Sweden, he obtained his habilitation in 2013 in Germany in the field of bioanalytics as part of a start-up project. After 4 years in different leading positions in the pharmaceutical industry, he accepted an offer for a professorship position in bioanalytics and laboratory automation at Albstadt-Sigmaringen University, in 2018.

Not only the enormously lower sample throughput argues against the establishment of TLA but often these types of laboratories perform different analyses on a daily basis, depending on the order or project. This means that large laboratory automation equipment is usually not economically viable for SMEs to operate. Based on these realities, three basic requirements of SMEs for laboratory automation systems appear:

- the systems should be inexpensive to purchase;
- optimal for small throughputs;
- flexible and user-friendly in their application.

Monotonous and Repetitive Activities in Smaller Laboratories

Although the diversity of laboratory processes is greater in SMEs, repetitive and monotonous activities are also found in them, which are ideally suited for automation. Since monotonous activities can lead to errors, automation has a high potential for quality improvements in this kind of application [2]. One of such monotonous activities is the pipetting process. Not only interindividual inaccuracies can be as high as 8% (at 10 µL), depending on the volume to be pipetted, but mix-ups, for example when pipetting in microplates, are also common errors [4,5]. The quality and reproducibility of analytical results, especially in bioanalysis, often depend directly on the quality of the pipetting process. Some manufacturers have recognized this problem, and a number of low-cost products have appeared on the market that can (semi-)automate the pipetting process relatively easily.

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Type	Model/Series	Vendor	Channel size	Volume range	Number of pipetting modes	Control
Electronic pipettes	Transferpette electronic	BRAND	1, 8, 12	0,5 – 5.000 µL	4	Pipette
	Xplorer/ Xplorer Plus	Eppendorf	1, 8, 12, 16, 24	0,5 - 10.000 µL	5/10	Pipette
	Pipette +	Andrew Alliance	1, 8, 12	10 – 10.000 µL	8	Pipette or software (PC/Tablet)
Pipetting stations	epMotion 96	Eppendorf	96	0,5 - 1.000 µL	7	Software (iPod)
	Mini 96	Integra	96	0,5 - 1.250 µL	10	Pipette
	VIAFLO 96/ 384		24, 96 /384	0,5 - 1.250 µL		
Pipetting robots	OT-2 Liquid Handler	Opentrons	1, 8	1 – 1.000 µL		Software (PC)
	Andrew +	Andrew Alliance	see Pipette +			Software (PC)

Table 1: Comparison of inexpensive pipetting automation systems [6-10].

Simplify Manual Operations

The easiest and most inexpensive method to automate the pipetting process is the use of electronic pipettes, which can be found in the product range of many pipette manufacturers. In addition to pipetting, electronic pipettes often handle further functions, such as mixing, dispensing, or aspiration.

Table 1 compares the characteristics of electronic pipettes from several manufacturers, including BRAND and Eppendorf. Depending on the channel size, these pipettes can be purchased from BRAND for between €350–800, while Eppendorf offers pipettes of the Xplorer series for approximately €620–1,600 [6,7]. The Swiss company, Andrew Alliance, goes one step further with its Pipette + product series (Table 1): pipetting protocols can be visually planned on a PC or tablet and can then be transferred to the electronic pipettes via Bluetooth. For example, dilution series can be calculated automatically or the software can be used as a step-by-step guide when performing in the lab, minimizing the risk of mix-ups [8].

Despite the use of multichannel pipettes, pipetting steps can add up to a large number of repetitions. For steps like substrate addition, 96-channel pipetting stations – such as the epMotion 96 system from Eppendorf or pipetting solutions from Integra (Table 1) – are suitable. The wells of a microplate can be processed simultaneously at the push of a button. Depending on the model, Integra enables the use of a 384 pipetting head [9]. These types of systems also offer a variety of different modes, such as dilution, reverse pipetting, or multiple acquisitions.

Probably the most significant advantage of electronic pipettes is that the pipetting process can be more standardized, for example, through specified aspiration and dispensing speeds. This improves analytical results regarding reproducibility and precision. Using 96-channel pipetting stations, reactions can be stopped simultaneously, which benefits the optimization of time-dependent experiments. In addition, the operation of electronic pipettes makes life easier for laboratory personnel. While pipetting and other techniques (especially mixing) previously required the force of operators, the various functions of electronic pipettes are triggered by pushing a button or even automatically. Another advantage of such pipettes is their compatibility with conventional pipette tips. Manual pipettes can therefore still be used without having to commit to one variant when purchasing tips. With a price range from €350 to a maximum of €20,000 (the most expensive variant of epMotion 96 from Eppendorf), the presented pipettes offer not only affordable automation systems but also enable the flexible use of an essential laboratory process in partial automation.

Inexpensive Pipetting Robots

With increasingly affordable robotics technology, the possibilities to automate entire experiments become more reasonably priced.

Probably the most affordable commercial system for fully automated pipetting is the OT-2 Liquid Handler from Opentrons starting at approximately €5,000. The housed system has a 3-axis robot that can be equipped with different pipetting heads (Table 1). The deck of the liquid handler owns space for 11 units (e.g., microtiter plates and tip or tube reservoirs). Small devices such as a thermoblock can also be purchased. Opentrons also offers preconfigured decks for specific applications, such as nucleic acid purification. Depending on its features, the OT-2 liquid handler can cost up to €20,000 [10].

A similar system is the Andrew + pipetting robot, offered by Andrew Alliance. The special feature of this system is that it uses the electronic pipettes of the Pipette + series for the automation system. This means the robotic arm grips the required pipette and uses it to access the 11 available unit positions that are located in front of the robot system. Starting at approximately €20,000, the pipetting robot and associated pipettes can be purchased in various volumes and channel sizes – as with Opentrons, optionally with additional vessel stands and small devices [8].

By now, both automated pipetting robots come along with a user-friendly operator interface. In addition to the advantages concerning reproducibility and productivity, laboratory personnel can leave the working space to perform other tasks. Although various methods can be flexibly used, the range of applications is limited due to the relatively small usable area. The acquisition of additional modules is also cost-intensive and frustrating, because equipment such as the thermoblocks already exist in the laboratory but are not compatible with the system.

Automating Existing Devices

There is no doubt that an inexpensive, flexible laboratory system is desired by SMEs. Since laboratory personnel usually are not involved in automation and robotic systems, a user-friendly system is required. Although systems like OT-2 or Andrew + meet these requirements, existing laboratory equipment such as shakers cannot be integrated into these systems. Enormous diversity and a lack of software interfaces for communication between instruments make this largely impossible. The idea of the SiLA consortium to harmonize standards in order to simplify cost-effective laboratory automation is a step in the right direction but requires new instrument acquisitions.

A system that can be flexibly used, that is mobile and can be used at different workplaces, and that uses existing laboratory equipment does not yet exist on the market.

Together with industrial partners from the Lake Constance region, a novel approach is currently being created to make a further contribution to cost-effective and flexible laboratory automation.

One of the aspects of the concept is that existing laboratory equipment can be integrated into the automation process without great effort. In addition, the system should also be able to perform software-based activities, such as operating the analysis software of a measuring device.

The QR code below links to a video introducing the new approach called "LARS" and to a 4-minute survey asking you as a potential user to submit your requirements to be considered in the current development phase.

Outlook

There are definitely already inexpensive laboratory automation systems on the market that could be suitable for SMEs. Nevertheless, there is still a lot to be done, especially regarding flexibility and the inclusion of existing laboratory equipment into new laboratory automation solutions. As the market challenges have been recognized in the meantime, it is to be expected that further affordable and flexible laboratory automation solutions for SMEs will be offered commercially in the nearby future.

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