



AUTOMATION 101

THE CASE FOR AUTOMATED SAMPLE PREPARATION IN ANALYTICAL LABORATORIES



The Importance of Sample Preparation

Where GC-MS or LC-MS is used to make chemical measurement of environmental samples, there is always a need to prepare the samples before performing the analysis. This can be as simple as adding internal standards and surrogates or it can be complex and include extraction from the matrix, pre-concentration or derivatisation. When these tasks are carried out by hand, they are the most time consuming, expensive and error-prone part of the whole analytical process.



*The Newest Mass Spectrometers Offer High Sensitivity that is Very Valuable in this Context
Credit: Anatune*

The Truth About Automation

Automating sample preparation addresses all three of these issues. Sample preparation is repetitive and can be tedious when done by hand. Machines free-up skilled analysts for more valuable employment, they can do routine work at a lower cost, and, importantly, treat every sample exactly the same.

There are understandable fears, that the increased use of robotics in the laboratory, puts people's jobs at risk. These fears are unfounded, but have to be addressed, otherwise they remain an obstacle to achieving the considerable benefits available.

In more than two decades of direct involvement in laboratory automation, I have never come across any example where the installation of a laboratory robot has cost anyone their job and there are good reasons to believe this will never be the case.

When automation is successfully introduced, costs fall and data quality improves. These factors act to increase the demand for a laboratory's services and so sample numbers increase in response to the change. Since there are always parts of the analytical process that haven't been automated, the machines create more, but different, work for humans to do. The fear is rooted in the mistaken belief that there is only a fixed amount of work to be done. This is what economists call the "Lump of Labour Fallacy".

Automation is the key to improving the productivity of any laboratory.

What is more, robots change the way people spend their time at work in a positive way, since the machines always get to do the most tedious, unpleasant and hazardous tasks.

At the risk of sounding like a cut-price Carl Sagan, consider the second

law of thermodynamics. As humans, we exist to create tiny islands of structure within a vast cosmic tide of disorder. Automation and artificial intelligence enables us to make those islands slightly larger, but will never reverse the direction of entropy!

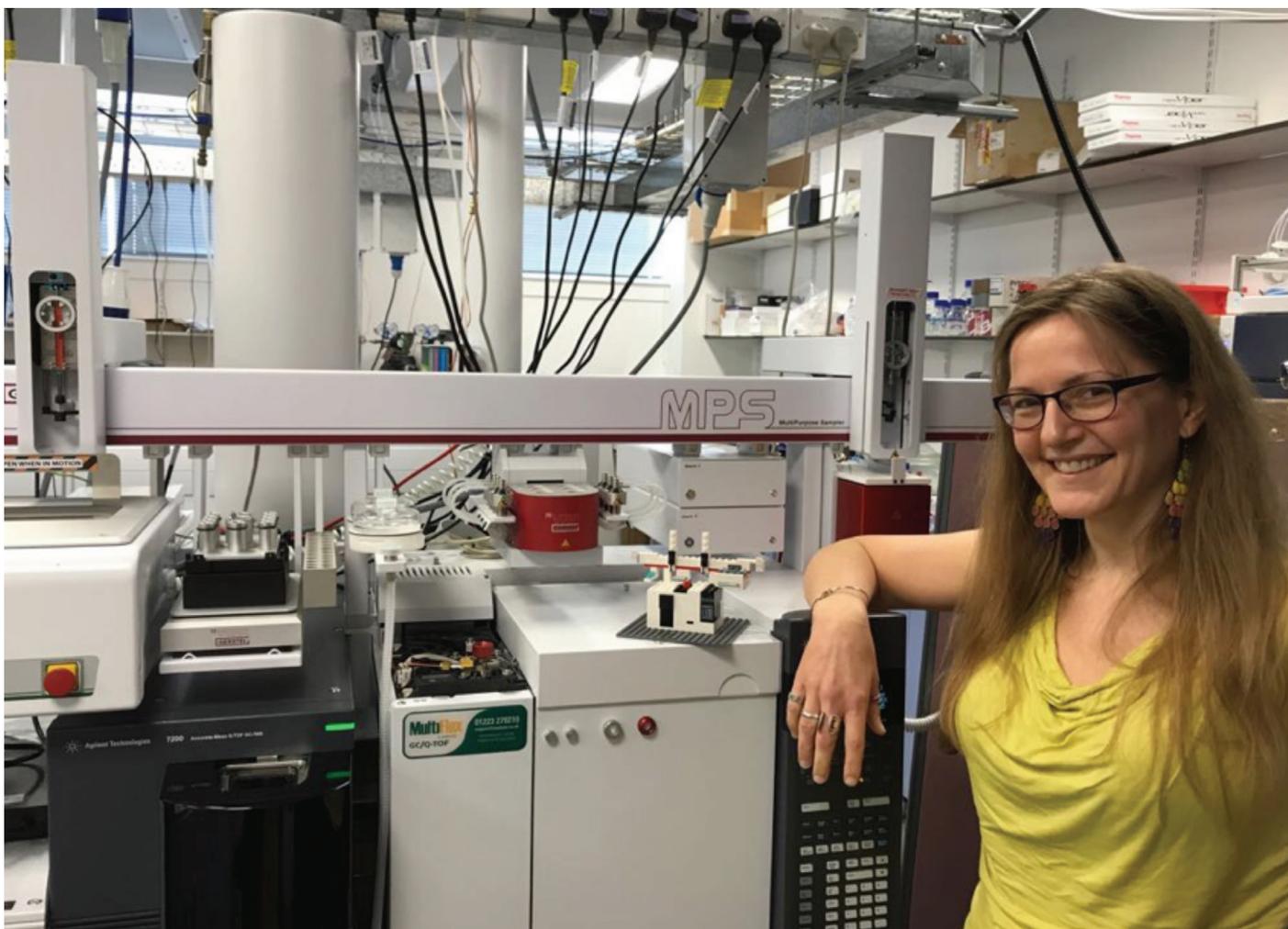
The Tipping-Point

As far as sample prep automation is concerned, small is beautiful. Small samples are cheaper and easier to automate, the sample preparation is always quicker and the health, safety and environmental footprint of the whole analysis is reduced.

Ultimately, the minimum sample size you can work with is limited by the sensitivity of the mass spectrometers available. Every new generation of mass spectrometer offers improved performance and in the last few years, we have passed a tipping point where virtually any analysis can be performed with samples of 40µl or less. In parallel, the range of modules available to perform all of the different sample preparation functions is now close to complete and the great majority of sample preparation procedures, can be adapted to run automatically and without human involvement.

Automated Sample Preparation – The Benefits

The largest gains come when you are clear about, and target, the benefit that is most important to you. Automated solutions can be very different, depending upon the issues that you prioritise. As a consequence, it is worth looking at the various benefits on offer in some detail.



Automated Sample Preparation in a Non-Routine Setting at the University of Edinburgh
Credit: Dr Hannah Florance, University of Edinburgh

Sample prep automation offers the most obvious advantages to analysts involved in routine measurements, however it offers different, equally significant advantages for analysts involved in non-routine; method development, trouble-shooting and research. We'll look at both cases. Firstly, the benefits for analysts working in a routine lab environment:

Sample Prep Automation in the Production Setting

The ability to run more samples. One way of solving a capacity problem, is by increasing staffing, instrumentation and bench space, this a conventional, but costly solution. Automation of sample preparation can free-up staff, enable 24-hour operation of existing instrumentation and often enables better use to be made of the space available. It should always be your first option.

In some circumstances, getting more samples run per day, means more samples can be charged as premium, fast turnaround samples.

Lower costs per sample Reducing or eliminating the amount of labour spent on each sample is often where the biggest savings can be made, however, costs also come down when expensive analytical instruments are worked harder. Miniaturisation of the method is part of the automation bundle and the costs associated with the purchase and disposal of reagents is also lower.

Better use of analyst's skills. Time saved on routine sample preparation is time that analysts can spend on more rewarding tasks such as method development, data interpretation or interaction with clients. These are tasks that enable analysts to add the most value and by relieving the tedium of repetitive sample preparation can only help in

retaining experienced staff members.

Elimination of operator technique. When a method has to be used in a number of different laboratories, automated sample preparation will eliminate much of the variability in results attributable to different operators. As a consequence, data quality becomes more consistent from one site to another.

Improvements in accuracy and precision. In general, a robot will match the accuracy and precision of a skilled analyst who is fully focused on the job in hand. However, a robot won't get tired, have off-days or go on holiday.

Reduce the use of solvents and reagents. Reagents are expensive to buy, store and to dispose of. On many occasions, automation results in the whole sample prep being scaled down. There are obvious cost savings to be had coupled with a reduction in environmental footprint.

Reduce staff exposure to hazardous materials. From a health and safety perspective, automated sample preparation, physically separates the analysts from solvents and reagents and so reduces their exposure to hazards.

Get faster sample turn-arounds. On occasion, there can be huge value to analysing samples more quickly – this is especially true if the analytical data can be used for the control of an industrial process. Fully automated, just-in-time sample preparation is the missing link that enables high-performance laboratory grade GC-MS and LC-MS to generate compositional information in real-time without the constant attention of an operator.

Table 1. Automation modules are available to support the most complex sample preparation requirements.

Type of Analyte	Automation Possibilities
Volatile, medium to low polarity	Static headspace, dynamic headspace, solid phase micro extraction, stir bar sorptive extraction, purge & trap, thermal desorption
Volatile, high polarity	Derivatisation
Semi-volatile to involatile	Liquid-liquid extraction, dispersive liquid-liquid micro extraction, solid phase extraction, solid-liquid extraction, matrix removal, pre-concentration
All	Addition of standards and reagents, mixing, filtering, centrifugation

The Role of Automated Sample Preparation in Non-Routine Analysis

Method development is a time consuming and costly activity. In most labs, it is a task reserved for the most experienced analytical chemists and the process can take anything from a few weeks to several months to complete.

Method development involves the exploration of a set of variables, in a systematic fashion, with the aim of finding the optimum set of conditions for a robust method that yields data of an appropriate quality and cost.

In method development, it is vital to:

1. Vary the parameters under investigation in a stepwise fashion automatically.
2. Tightly fix all other parameters, so that the effect of varying a target parameter isn't obscured by random variations elsewhere.

Manual sample preparation is a significant source of unwanted variation. Automating sample preparation, makes method development a more straightforward and predictable process and saves a great deal of time.

With more analysts taking a Design of Experiment (DoE) approach to method development, (where several parameters are adjusted simultaneously in a systematic way), automated sample preparation is a logical partner. The experience of our laboratory is that, together, the combination of full automation and DoE enables us to reduce the number of experiments needed to complete the development of a method by at least 50%. This has a huge impact upon the amount of work that our laboratory is able to complete.

For research into biological samples and other complex materials, it is often the case that significant variations in composition between samples are subtle, and chemometrics is used to tease out differences that are hard to spot by eye. Automated sample preparation ensures that every sample is processed in an identical fashion, random variation is minimised and real sample-to-sample differences become more apparent.

Implementation

The path to the successful implementation of automated sample preparation is well trodden, especially so in the field of environmental analysis, where the bulk of the work carried out is with similar matrices and similar suites of analytes. Whatever you may want to do, the chances are, that someone has already done something similar. Knowing that what you want to do is possible, is a great jumping off point.

As always, a systematic approach is most likely to yield a satisfactory outcome and the following process is one that has proved itself to offer the greatest chance of success, with the minimum of risk.

1. Start with a robust manual method. If necessary, de-bug your manual method to ensure you are automating a process that is intrinsically sound.
2. Be clear on your objectives and priorities.
3. Using your current standard operation procedure (SOP), carry out a desk study to see what adjustments your SOP will require to be compatible with the automation platform you intend to use.
4. Test the adjusted method manually to ensure you can obtain results that are comparable to your current method.
5. Conduct a cost/benefit analysis. Check that there is a case to be made and that you have all the support needed to take the project further.
6. In collaboration with the platform vendor, configure a robot to perform the new automated process. Run the same batch of test samples both automatically, and by hand and compare the quality of results delivered via the two routes.

Assuming that the automated data is at least as good as that generated by your current method, you should have everything you need to write a strong justification for the investment required.

Conclusions

The points made here are derived from more than twenty years work with successful laboratory automation projects, backed by numerous case studies.

Some analysts have embraced automation and seen the fortunes of their laboratories blossom. Client samples are the lifeblood of every analytical laboratory and are remarkably mobile. They are easily shipped anywhere in the World and will flow to those laboratories that offer the best combination of quality and cost. In my experience, to be the best, you have to make good use of sample prep automation.

A significant tipping point has been passed. Analytical laboratories, are still heavily reliant upon manual sample preparation, while suddenly everything is in place for the change to automation to happen. A commitment to sample prep automation, together with an entrepreneurial mind-set and some old-fashioned hard work, will give your laboratory a clear path to becoming a leader in your area of specialisation.

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