Miniaturisation in GC Laboratories - the Holistic Picture

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Supply and demand issues, particularly in the last few years during the recession, have caused contract laboratories [1] to review the cost of their operations more stringently than ever; areas that provide potential financial savings include consumable rationalisation, process efficiencies, method miniaturisation, all the way to the biblical improvements e.g. lab re-arrangements and Laboratory Information Management Systems (LIMS).

Method miniaturisation is the scaling down of as many instrumental and analytical parameters as possible to optimise efficiency and it has multiple practical benefits in itself. In addition, it has the added attraction of ensuring multiple on-going financial savings or rapid paybacks for a one-off capital expenditure.

In its purest form, miniaturising a method involves looking at the sample extraction solvent, the extraction technique, the injection onto the instrument, the separation on column, the quantification via the detector and finally the general cycle time of one analytical run to the next. We are also aiming to make the method more robust which should improve quality, to give us at least the same if not better Limit of Detection (LOD), but deliver the result far more quickly and hence more cost effectively. Remember, time is money in a contract lab.

Why change the extraction solvent?

We may then be able to inject more solvent, giving better sensitivity or enabling less initial sample to be extracted, and also start the analytical run at a higher temperature meaning shorter cycle times. Old environmental soil methods, for example, traditionally used dichloromethane (boiling point 39.6˚C) whereas that of a mixture of hexane/acetone (90:10 v:v) will be nearer 68˚C. The latter still has some polarity, the extraction efficiency will be sufficient (and can be performance-checked by a Proficiency Testing scheme if need be), yet the starting oven temperature for solvent focussing can be increased from 35˚C to 60˚C, saving a lot of cycle time. Added benefits of the proposed solvent mixture are that it is more environmentally friendly and has less health and safety issues.

Table 1: Polarity indices

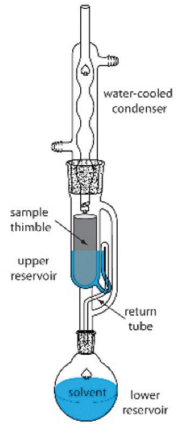
Solvent	Polarity index
Dichloromethane	~3.1
Hexane	~0.1
Hexane/Acetone (90:10)	~0.56

Extraction techniques for solids have typically evolved through speed and capacity [2], as efficiency has historically been universally satisfactory. Any piece of equipment that can run more samples in parallel, per unit space, should be investigated in this process. Whilst presenting a beginner's training course in GC in late January this year, I was honestly asked about soxhlet extraction, yes it was in a research laboratory but I can almost certainly guarantee it will be in use in a contract lab somewhere, one sample at a time is NOT high throughput and there are other, quicker methods that give the same recoveries, such as soxtherm, sonication or orbital shaking.

Why change the injection technique?

For sample matrices where large volumes have traditionally been necessary, i.e. waters, something fundamentally more intelligent has been required, as laboratory space quickly becomes prohibitive in such instances. To miniaturise environmental water analysis to the same scale as soil analysis, the technique of Large Volume Injection [3] (LVI) is often used. This enables the user to get more analyte onto the column by expertly injecting a hundred times more sample dissolved in solvent but then venting almost all of the latter leaving the concentrated analytes of interest to

Soxhlet
1 sample/hr



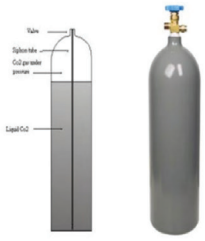
Soxtherm
6 samples/hr

Sonicator
60 samples/hr

Orbital shaker
600 samples/hr

Diagram 2: Evolution of semi-volatile soil extraction

Liquid CO_2 for PTV inlet



Gerstel CIS4 Peltier system

JAS Unis Peltier system

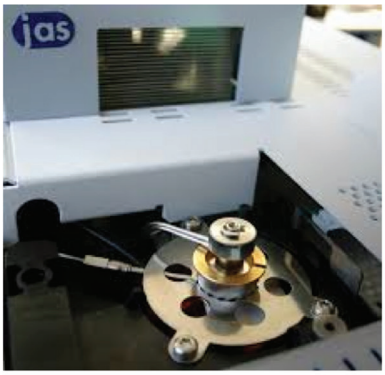


Diagram 3: Evolution of Large volume injection

pass through the column and be resolved. Benefits can be a smaller initial sample volume, smaller extraction solvent volume and then additionally no solvent evaporation, the latter can lead to analyte loss through sample transfers. Traditionally Polycyclic Aromatic Hydrocarbon (PAH) analysis from water has been performed by liquid/liquid extraction of a 500ml water sample, with 100ml DCM, evaporated to 1ml and 1ul injected; with LVI 50ml of water is extracted with 2ml pentane and 100µl of solvent injected in solvent vent mode with no subsequent requirement for evaporation, saving time and money on sample bottles, solvent and time from extraction to vialling/running.

Historically it would have been normal practice to use a cryogenic gas to get sufficient temperature differential between the solvent of use and the first eluting target compound but recent advances have moved to Peltier cooling using an ethanol/water mix (still not ideal as the control equipment is cumbersome and the solution needs periodic replacement) and since on to modern solvent-free Peltier cooling elements.

The payback in method miniaturisation is rapid even for small environmental labs (~£1 million turnover), a period of seven months would not be untypical to see the payback for a modern LVI capability.

Table 4: Cost benefit analysis / cost per sample table

	35 PAH waters / day LLE	35 PAH waters / hr LVI	6 PAH soils / hr soxtherm	60 PAH soils / hr sonicate
analyst cost £	1.5	0.18	1.1	0.1
standards solvents etc. £	0.25	0.01	0.5	0.1
vessels £	0	0.14	0	0.14
extraction cost per sample £	1.75	0.33	1.6	0.34

Why change the column dimensions or carrier gas?

By using a shorter, narrower column, with a thinner film and increasing gas flows and oven temperature ramp rates, it is possible to shorten run times considerably with little or no loss in resolution or signal-to-noise ratio. Method translation software has been developed [4] and is freely available to assist analysts.

Further possible improvements include using more efficient carrier gases like hydrogen, which compared to helium has a larger linear velocity. Whilst hydrogen is known to be reactive to certain compounds, using a PTV inlet with cool injection reduces the likelihood of artefact production, leaving the major gains of improved efficiency, better signal to noise ratios and further reduced run times.

Why change the detection technique?

Specific detectors such as Electron Capture Detectors (ECD) can bring 1-2 orders of magnitude greater sensitivity but may not be viable with large analytical suites where functional groups can be present or absent and identification of unknowns may be

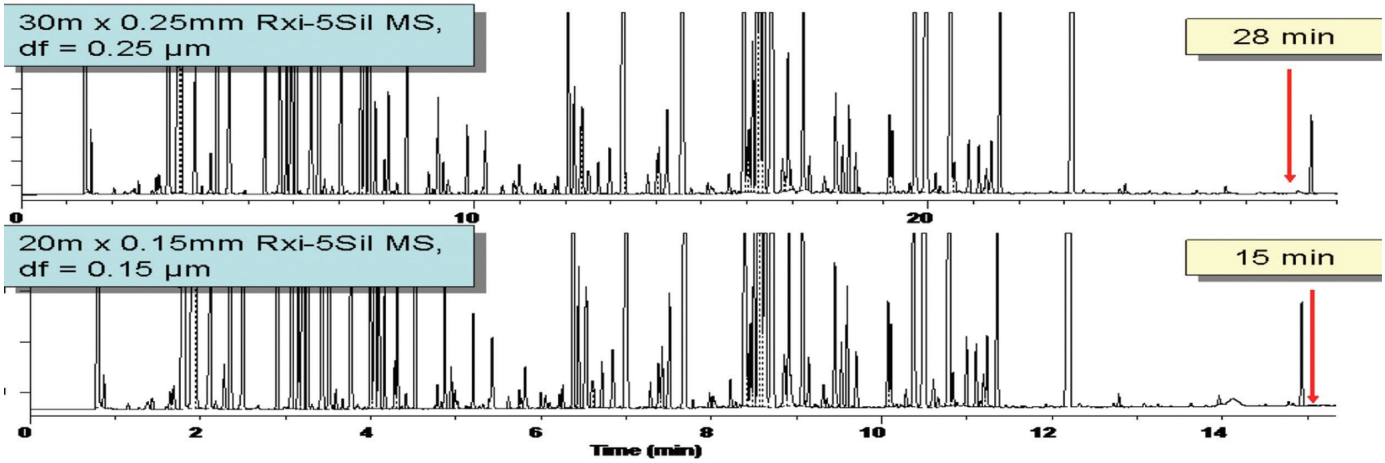


Diagram 5: Moving to a shorter column but keeping phase ratio the same reduces run time but preserves selectivity

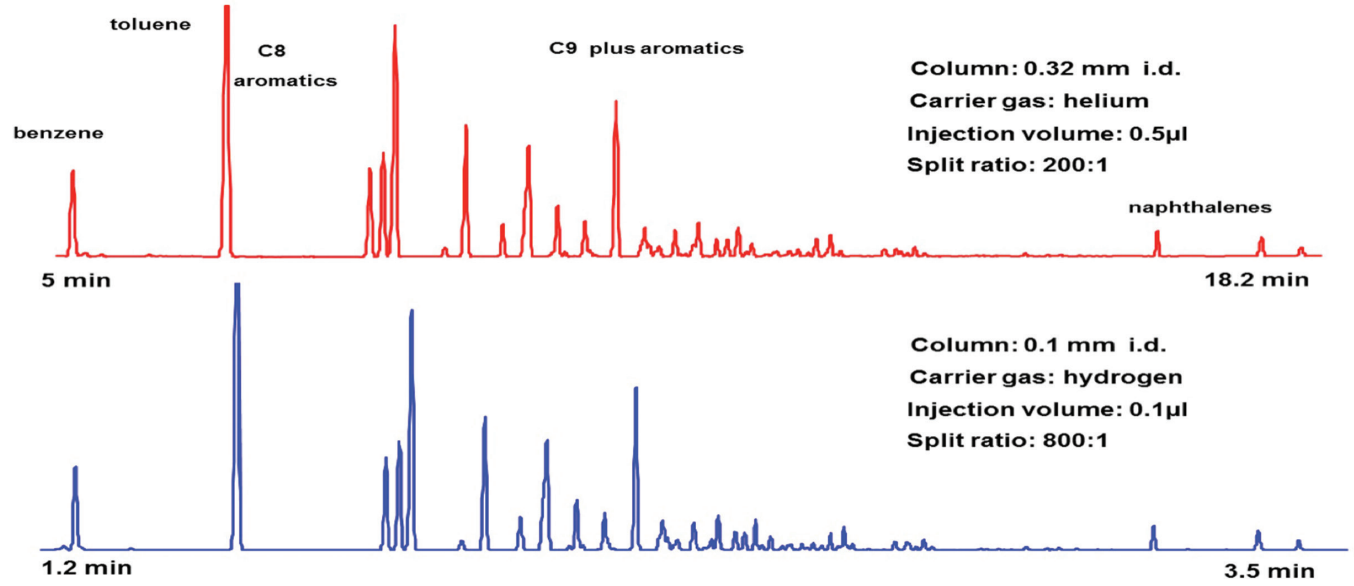


Diagram 6: Utilising further variables gives even more productivity gains

very important. Gas Chromatography Mass Spectrometry (GCMS) may consequently be required and in moving from SCAN* analysis to SIM**, the higher sensitivity may enable the scaling down of front end extraction volumes.

*SCAN analysis within GCMS spends the finite time available scanning every signal mass across a wide range consequently enabling the identification of unknowns from probability based library matching.

**In comparison SIM analysis searches for 1-12 different ions only, within any given time window, giving more data points per peak, as more cycles per second and longer dwell times on each ion are enabled.

For those with healthy capex budgets, modern instrumentation allows synchronous SIM/SCAN enabling simultaneous qualitative analysis of unknowns with accurate quantitation of targets.

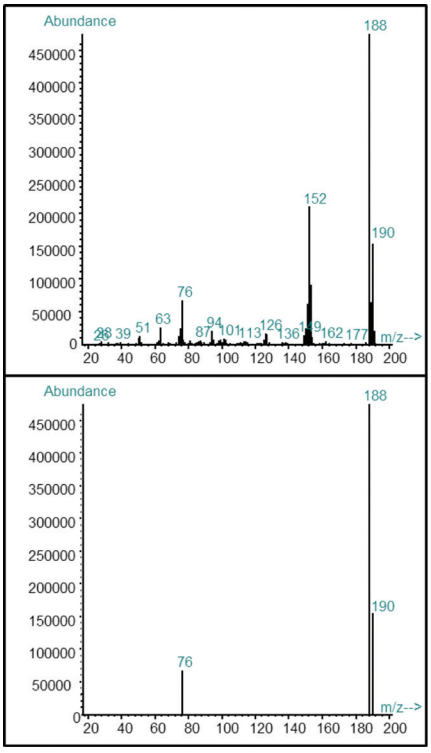


Diagram 7: SIM has less noise and allows more ions of the m/z range through to the MS detector therefore giving higher sensitivity than SCAN

How can we further shorten the cycle time?

The longest time delay in any GC cycle is the oven cooling down. As the typical GC oven heating process is very inefficient (fundamentally it is heating up air in an oven), improvements have been steadily introduced over history varying from the futuristic (encapsulating the capillary column in a heated metal shield thereby reducing the air volume that is required to be heated and cooled) to the less mechanically challenged (high efficiency secondary cooling fans blowing cold air through the GC oven flap at the end of the cycle). Other developments have included thermally stable oven pillows to reduce the volume of air in the oven to secondary heating elements within ovens that accelerate the GC ramp rate. Some broad-minded laboratories have vented the heat from the GCs through chimneys that feed into ductwork and exhausted it from the building courtesy of a robust fan. All GC analysts are extremely thankful in the summer for the latter technology but strangely less so in the winter. All of the above solutions have one thing in common, they shorten cycle times and therefore save money by improving delivery.

How do consumable savings then arise?

Looking at miniaturising water analysis methods for PAHs or Total Petroleum Hydrocarbons (TPH) from liquid/liquid extraction to large volume injection, small disposable glass vials (60ml) will replace large cumbersome separating funnels (one litre), saving time, reducing courier costs and negating the need for washing glassware. Similarly, certified EPA vials used in soil analysis - whilst being excellent quality and the industry vessel of choice - are most certainly not the cheapest, other cheaper fit-for-purpose alternatives exist.

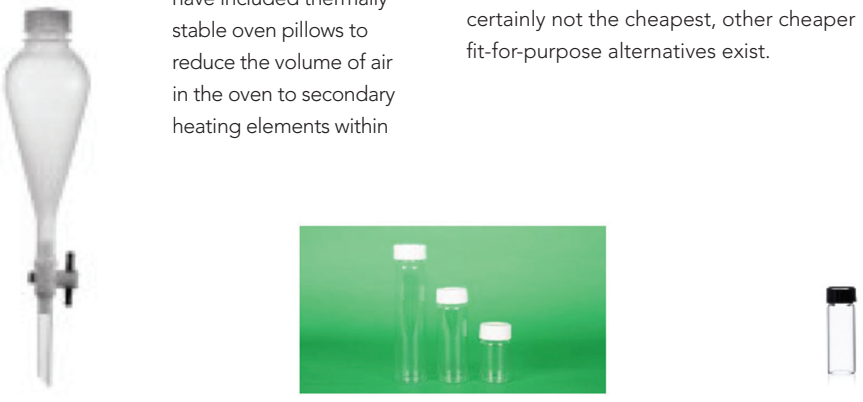


Diagram 8: Cumbersome extraction to miniaturised high cost to miniaturised low cost

How do process improvements then arise?

Space is often at a premium in older laboratories. After water analysis methods are miniaturised, such small volumes of solvent and such small vessels are used that the space required in a fume cupboard becomes negligible. The extra space can be taken by an efficient soil extraction system that once again took a whole fume cupboard to itself. No queuing means no time loss. The more efficient use of work space can also promote health and safety and might negate the need for a shift system, a shift premium, unsociable working hours and any extra energy costs involved.

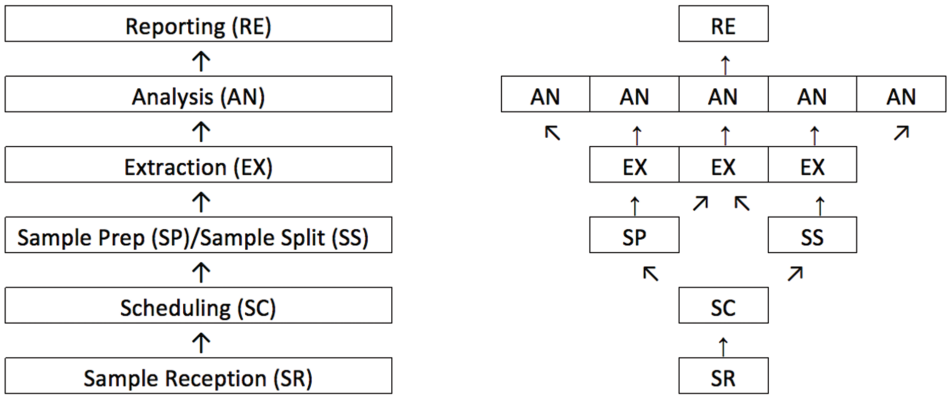


Diagram 9: Floor schematic of push lab v compartmentalised

Biblical improvements:

How do lab re-arrangements then arise?

Allying the space savings and method miniaturisations described in previous paragraphs has led laboratories to regard their operations as manufacturing enterprises. The ideal in any modern lab is to have a 'push' ethos. If as many methods as possible have been miniaturised it is perfectly feasible to gear the "front end" of a laboratory into a sample-splitting area. Here, each sample aliquot (whether it be a soil or water sample within an Environmental Lab) will be weighed into a vial that is then used for the extraction, this will save several people constantly going back to the original container, on a shelf or in a fridge, to sub-sample. These aliquots are then pushed down to the extraction department who in turn send the extracts, when completed, on to the instrumental analysts who then provide the results to the reporting teams for final delivery to the customer. If everyone can see the work coming, they are more likely to be focussed on delivery. Old style compartmentalised labs do not promote flow through the system, in fact they are more likely to ensure samples (and analysts!) go missing.

Finally, when it comes to multiple beneficiaries and when done well, the largest scale improvement a lab can effect is a LIMS system. These enable the tracking of each and every sample, via its own unique identification number and/or barcode, through the entire analytical workflow from site sampling all the way to the customer's e-mail address. Data is not the only thing housed within a LIMS, anything to do with the whole laboratory, including management and quality details, can be stored, giving all users multiple benefits. The biggest wins are improved quality, the chance to track key variables and real time analysis of samples within a workflow. Other major benefits are that:

- Instrumental link-to-lims allows error-free transcription of often hundreds of results in minutes rather than the laborious cut-and paste of old and other more minor kit can be connected i.e. balances for sample weighing and label printers for automated labelling.
- Report viewing is a useful option, automated reporting once again eliminates cutting and pasting and the inherent errors that can arise and advanced reporting formats (which are becoming increasingly requested) are easily incorporated into the software.
- The LIMS system becomes a database that can be interrogated for management reports or trend analysis via KPIs.
- The systems themselves are easily administered in-house in a part-time capacity by anyone with basic IT skills.
- Everything moves towards becoming electronic, reducing the paper trail.
- Real time analysis of samples in the work process is enabled so labour can be re allocated to remove bottlenecks.
- Archiving of old suites is easily enabled reducing errors in scheduling.
- A rapid search facility becomes available.
- Audit trails are accumulated in the background and swiftly retrievable, user administration status can be set at several levels to protect security and ensure training has been received before extra responsibility is taken.
- Most new systems come with associated web portals enabling the customer to remotely view or trend results.

In conclusion there is a lot to consider in implementing these processes, but a little time spent miniaturising methods and processes could provide better analysis quality and limits of detection, considerable on-going financial savings and a large amount of re-investable time. As Professor Walt Jennings once said "the only place you can afford to lose time is academia".

Acknowledgements:

Agilent
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References:

[1] Alcontrol Hawarden, Exova Hillington, Derwentside Envronmental Testing Services, BLC Leather Technology Centre, Exova Saudi Arabia, Chemtest, ESG, Nicholls Colton Group.

[2] USEPA SW-846 Revisions 1 to 5 —Test Methods for Evaluating Solid Waste, Physical/Chemical Methods, contains USEPA 8270 method - semivolatile organic pollutants in solid waste, soil, water, and air matrices using GCMS.

[3] Available from the Agilent website - GC method translation software, Windows 7 compatible - last update 20/03/2015

[4] Large Volume Injection with Solvent Venting - Application to Trace Detection of Analytes in Water - A. Hoffmann, K. MacNamara, Gerstel GmbH & Co. KG, Eberhard-Gerstel-Platz 1, D-45473 Mülheim an der Ruhr, Germany