lab2lab

application note

TTP Labtech's lab2lab: a virtual analytical instrument in every laboratory

introduction

It is essential for medicinal chemists to have easy access to analytical instrumentation for reaction monitoring and product analysis. Ideally instruments need to be in close proximity to scientists' work areas; however, the high capital cost and maintenance overheads associated with such instrumentation makes it unfeasible to support instruments such as LC-MS in every medicinal chemistry lab.

TTP Labtech has developed an automated laboratory transport and management system for connecting remote research laboratories to a central analytical instrument facility. Run by software compatible with the scientists' electronic notebook (ELN), lab2lab connects to existing analytical instrumentation such as HPLC, LCMS, GC/MS, UPLC and NMR.

the lab2lab system

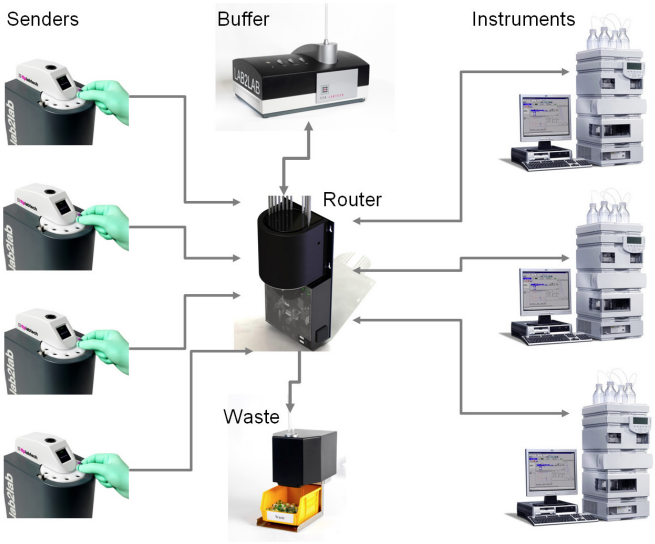

fig. 1 lab2lab schematic: the Router controls the flow of sample microtubes from Sender units, to analytical instrumentation, on to waste and/or retrieval bins.

lab2lab comprises a small bench top multi tube Sender, connected by pneumatic transport pipes via a Router to a Buffer. The Router controls the flow of sample microtubes to a temporary storage area (Buffer) and then onto the Receiver unit of analytical instruments and then onto either a waste or retrieval Bin. The flexible delivery tubing connecting the system together uses low pressure compressed air to transport sample microtubes up to 800–1000 metres in distance.

lab2lab's software enables samples to be continuously presented for analysis whilst the preceding sample's data is still being analysed, ensuring that instruments are working to the highest capacity.

At the bench, the scientist prepares a sample for analysis by placing it in a 2D barcoded 500 µL microtube and seals it with a septum cap.
The barcode is scanned and the scientist logs the details of the sample and the required method of analysis into the software.

The sample is then transported pneumatically to the Router where it is distributed to the Buffer or the appropriate analytical instrument.

Once the sample has been analysed, the results are collected and returned via the network to be captured in the scientist's electronic lab notebook. The sample may then be sent to waste or retained in the system for further analysis.

case study

In 2009, the Horsham sector of Novartis Global Discovery Chemistry initiated a project with TTP Labtech to develop a system to automate sample analysis, connecting remote medicinal chemistry labs to instruments in a central analytical laboratory. The early phase of the lab2lab system integration involved the linking of six medicinal chemistry laboratories to a Waters Acquity UPLC-MS and an Agilent HPLC instruments for reaction monitoring.

Further expansion of the lab2lab network involved the linking of two additional Waters Acquity UPLC-MS instruments, one normal phase HPLC and two SFC HPLCs with aurora units, with five single tube Senders and two multi-tube Senders based in six separate medicinal chemistry laboratories. These analyzers were existing instrumentation owned by Novartis and did not require modification to integrate them with the lab2lab system. In this study, samples were submitted to these instruments by more than 50 scientists working in these laboratories.

enhancing the medicinal chemist's workflow

In the drug discovery workflow, the frequency of sample submission to analytical instrumentation is dependent on several factors including the difficulty of the chemistry, the type of synthetic reaction and the number of scientists working on a particular project. The number of samples sent for analysis may therefore vary widely throughout the day.

When sample analysis is required, the scientist tends to collect together a number of samples and manually transport them to the analytical lab, submitting samples in a batch to a chosen instrument. This can only prove time-consuming and tedious but can also deter scientists from analyzing intermediate stages of a reaction series which may result in valuable information being overlooked.

Using lab2lab, chemical analysis can be performed without the scientist having to leave the bench. This significantly reduces the time involved in

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manual sample transport and queues for preferred instruments as samples are automatically distributed equally between instruments.

In periods where large numbers of samples are submitted, lab2lab's Buffer gives the scientist the opportunity to store and prioritise samples. Samples can be sent during the course of a chemical reaction, allowing rapid analysis of intermediate reactions, allowing them to be modified or stopped. In addition, lab2lab's software allows the scientist to edit the methods of analysis after microtube submission and to send it to further analytical equipment.

increased analytical throughput and speed

In this case study, a comparison of the time taken for a scientists to physically submit a sample microtube to UPLC-MS instrumentation and to receive data into their ELN with lab2lab's system was carried out. Data included samples which had been submitted for multiple methods, including samples which were submitted using methods which would take longer than the standard 2 minute reaction monitoring analysis. In this study, on a single day 180 samples were manually submitted to two Acquity LS-MS instruments and the average time taken for the results to be returned was 11 minutes, 34 seconds (Figure 2).

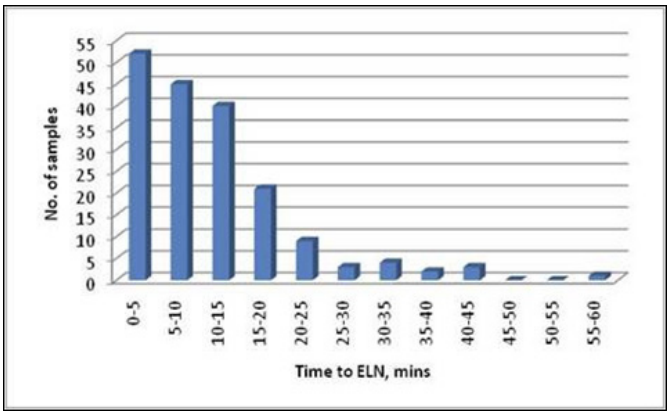

fig. 2 Average time taken for manual submission of 180 samples to two Acquity LS-MS instruments on a single day.

discussion

The lab2lab advantage may be summarised as:

- Efficient use of scientists' and instrument time as samples are sent to the shortest queue.
- Safe, secure transport and tracking of samples
- May be installed in existing labs onto existing instrumentation
- Simple to expand system
- Does not prevent instruments being used offline from lab2lab
- Long transportation distances are possible
- Cost effective

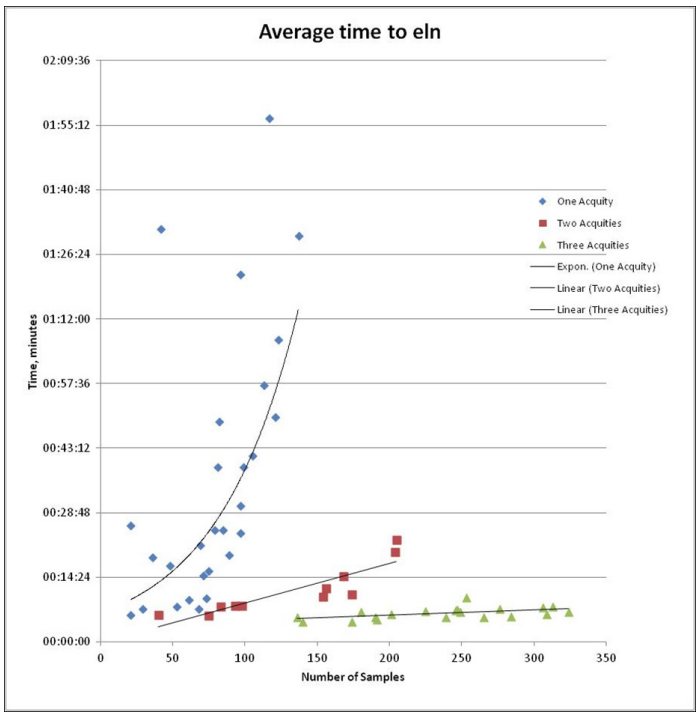

fig. 3 Average time taken from sample submission to data arriving in an Electronic Note Book (ELN) using lab2lab. Each point on this graph represents a single day, and shows the samples submitted by more than 50 scientists working in the six medicinal chemistry labs.

A number of advantages can be seen as a result of sending samples for analysis via lab2lab. Most significantly, the ability to achieve increased sample throughput and rapidly obtain results with minimal manual effort enables the scientist to concentrate on other more relevant scientific tasks.

Figure 3 shows the average time taken to obtain results from UPLC-MS instrumentation, plotted against the number of samples run on each day (here each point on the graph represents a single day). This figure also shows the response of either one, two and three UPLC-MS instruments. Here it was observed that, as the number of samples per day increased to more than 100, a single UPLC-MS instrument struggles to cope. However, increasing the number of instruments on the system significantly reduced the time to ELN for data, even for increasing sample numbers.

conclusion

This case study presents a comparison of traditional methods of analysis against analysis using lab2lab that clearly demonstrates significant savings in time and manual effort by the medicinal chemist, increasing workflow and efficiency.

lab2lab has the potential to link scientists working in different disciplines connecting synthesis to purification, then to compound management and biological assay. This vision of a fully automated system from synthesis to purity to biological testing is a "revolution in compound management" and can contribute to a reduction in the time taken to develop a new chemical entity into a drug molecule.

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