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Case Study - C1

Reaction Monitoring, Scheduling and Control

User Requirements

When Anachem realised that their customers working in Process Development needed a solution to run parallel reactions with different conditions, Anachem approached Aitken Scientific. Anachem supply reaction racks offering temperature and stirring control, an XY sampler for liquid handling, interchangeable racks for reagents, and HPLC systems for analysing the samples. What Anachem required was the software to allow users to define different tasks for each vessel, and then run the tasks in an optimal way. This new product was called ReactArray.

A typical workstation can be seen in Figure 1, consisting of a standard Gilson 215 sampler, fitted with reagent racks, and a temperature controlled rack for the reactions.

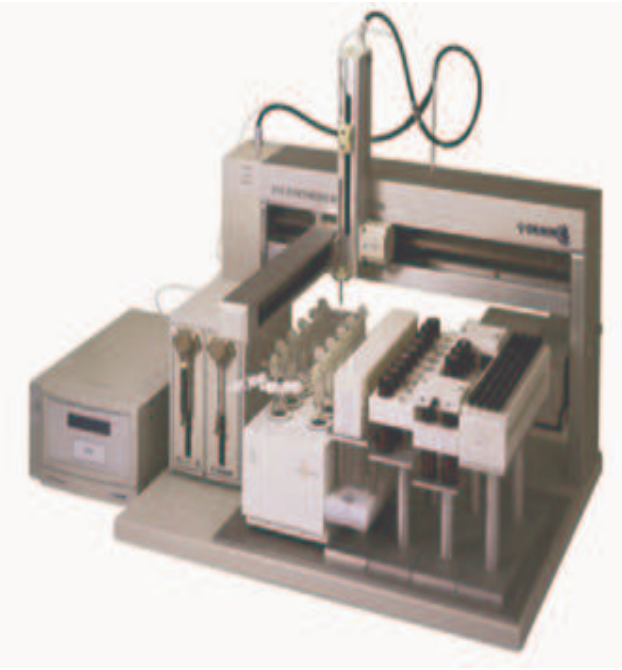

Figure 1. The ReactArray Hardware

Designing the solution

Anachem invited scientists from the leading pharmaceutical companies to act as a study group while Aitken Scientific helped to define what the software should look like. The initial requirements included direct instrument control, the ability for the user to define the bed layout from standard components, and to define a sequence of tasks, for example aspirate, dispense, wash, mix and sample. (Figure 2)

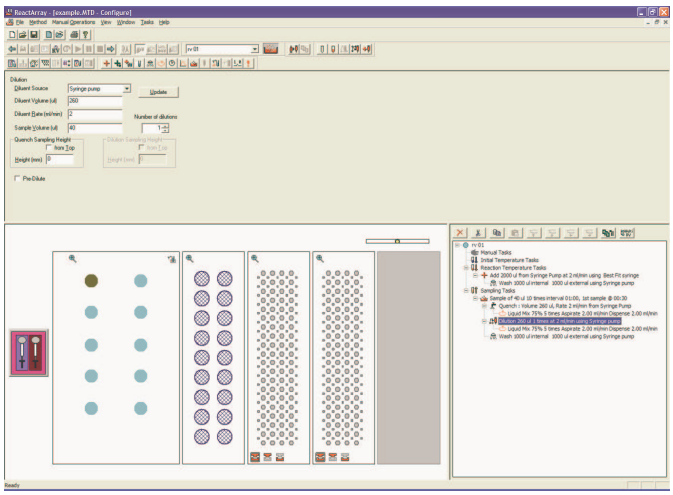

Figure 2. The ReactArray Workstation task editing screen

Scheduling

The key requirement for the system was to allow users to mix the various reaction components together using the sampler, and then take and analyse aliquots of the reacting mixture at intervals. If processing only one reaction, the hardware is idle for long periods. However, if a scheduler is provided, the idle periods could be used to process another reaction vessel in parallel.

The scheduler calculates the time periods when the sampler is busy transferring liquids, and also calculates the time periods when the HPLC is busy running and analysing samples. Optimal operation can be achieved by interleaving the reaction vessels to take advantage of the gaps in each individual vessel's reaction conditions.

To calculate the times accurately requires a knowledge of the timing of each minor operation. An example of the schedule can be seen in Figure 3.

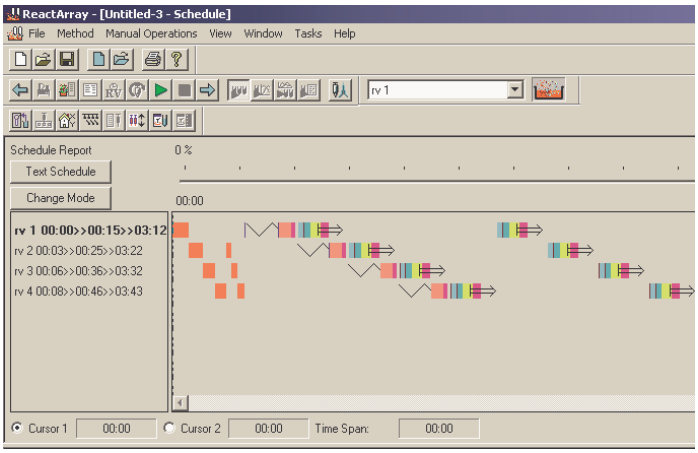

Figure 3 - The graphical display of the schedule

Data Handling

After the initial release of the system, it was realised that Process Development chemists needed extra calculations and features compared to traditional HPLC data analysis. For this reason, Aitken Scientific were asked to look into whether a custom data handling package could be added to ReactArray.

ReactArray Data Manager (RDM)

The result of the investigation was a design for a new HPLC data handling package which included the extra features required. This was developed as a separate application which integrates with the ReactArray control software. One package can be used without the other, so data can be analysed and reported on separately from method development. The two packages work together when controlling the hardware, and collecting data in real time.

Features of RDM

RDM was designed as a complete replacement chromatography package. It handles the collection of raw data directly from the hardware, display of chromatograms, peak locating, peak area and height, timed events and baseline correction with database storage of methods and data. Additional features were incorporated such as the ability to perform a scout run, which allows the user to define the peaks of interest for the main run.

Further benefits

The ability to calculate and display peak profiles is a key feature for Process Development, where the aim is to reduce the reaction time needed to produce the optimal drug quantity. This can be seen in figure 4 below, where many profile plots are overlaid on each other. Each profile graph shows how a selected peak changes with time.

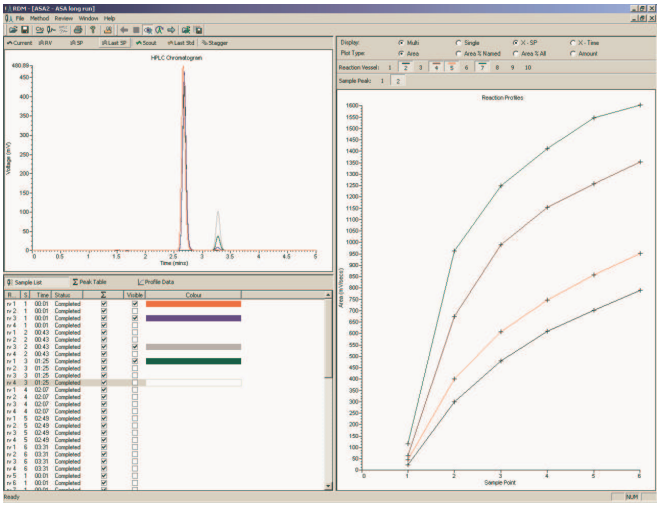

Figure 4 - RDM with chromatograms on the top left, the peak table on the bottom left, and the right hand pane showing the peak profiles.

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