

Automated Analysis of Open-Access HPLC Instrumentation Metrics

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All modern chromatographic software products gather information on each experiment and compile this data into text files. These files contain a wealth of information that can be used to track valuable metrics of instrument performance. By importing these metrics into data analysis software, researchers can easily visualise performance parameters such as retention times, peak heights, and intensities of samples across multiple systems simultaneously, while receiving updates in real time. This article discusses the utilisation of data analysis software for chromatographic system tracking in order to increase overall productivity and efficiency.

Introduction

Analysis of QC standards for analytical instruments within a laboratory setting is a time consuming, albeit necessary process, often requiring dedicated technician support. As the number of dedicated open access instruments grows in an organisation, the routine task of maintaining and tracking instrument performance becomes resource intensive for analytical teams. Working in an open-access setting within Novartis Global Discovery Chemistry at NIBR Cambridge, there are over 20 analytical and preparative HPLC and LCMS systems that are set up to run automated QC standards multiple times a day to ensure optimal instrument performance. This workflow utilises

analytical HPLC instruments to obtain an initial separation profile that aids chemists in method selection on a preparative scale. The retention times observed on analytical instruments are used to choose focused gradients for large scale preparative separations; therefore the accuracy and consistency of the analytical retention times is vital for the efficient purification of reaction products.

In order to streamline the QC process, innovative ways to compile and monitor data generated within QC reports were examined. Longer term trends such as system utilisation or uptime are difficult to track and visualise, but these can play a large role in the efficiency of a chromatographic operation. Data analysis

software has been utilised to visualise large data sets with many parameters in order to gain insight to discover and even predict future outcomes by analysing trends [1]. Data visualisation software from TIBCO (Spotfire) has been utilised within corporations ranging from scientific research institutes to financial institution data analytics departments, and was selected over various other programs for its proven versatility and visual data rendering capabilities [2].

Software utilised

Waters Masslynx data processing software v4.1 and TIBCO Spotfire v4.0.3.

QC Tracking

The main goal of monitoring our data was to track the chromatographic characteristics of standards run across multiple instruments. Instruments of the same type were standardised and QC datasets were collected over a period of several months. Averages of chromatographic data (retention time, peak height, peak width, absorbance, etc.) were recorded and used to determine a starting value within scatter plots. Limits were then determined to allow for unavoidable fluctuations in these values. These plots then give an easy way to visualise instrument performance and assign a QC pass or fail.

By regularly checking these plots, it becomes much easier to monitor, and to determine when instruments require

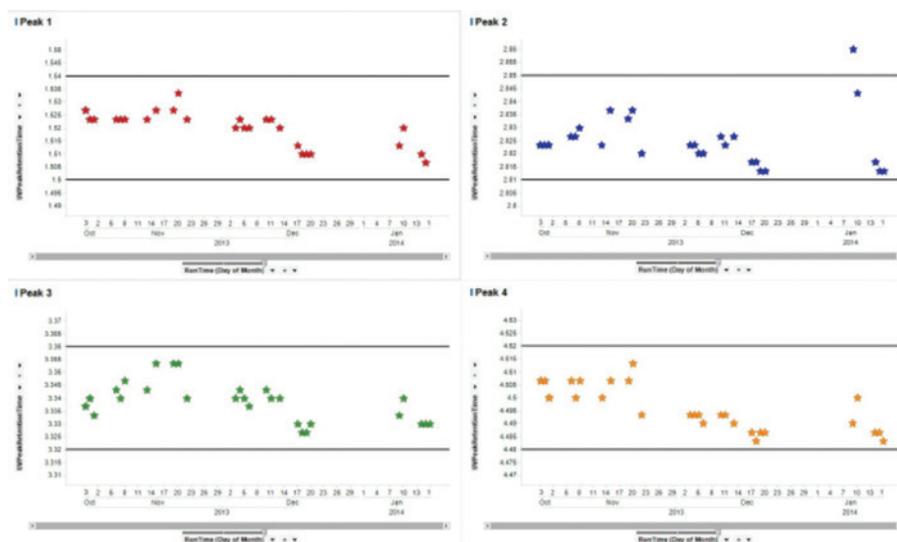


Figure 1: Tracking of retention times for standards is easily visualised

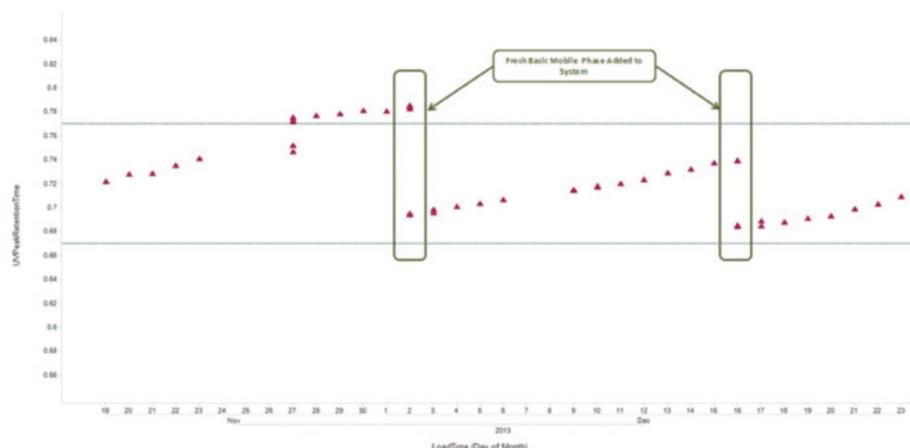


Figure 2: Time points at which the basic modifier was replenished resulting in an adjustment of the standard retention time.

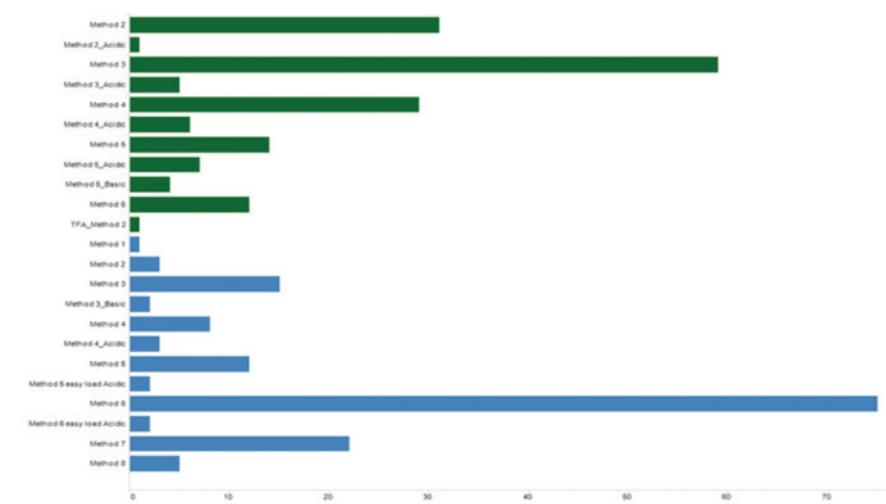


Figure 3: Purification method selection metrics for different projects

maintenance due to results that are not within specification. Previously undetected system changes were also evident through these visualisations. It was apparent on basic pH systems which utilise ammonium hydroxide as a modifier, that there is a clear trend in retention time shifts as the basic buffer additive appears to be evaporating over time.

Visualisations such as this have been beneficial in aiding the standardisation of open access analytical instruments, where the retention times have a critical impact on the determination of focused gradients for preparative purifications. When a retention time shifts on an analytical system due to system performance an incorrect purification methodology may be selected based upon this inaccurate analytical representation.

Although this is not a substitute to a researcher personally inspecting an instrument, the ability to collate performance parameters of instruments located within different laboratories or even different buildings can dramatically impact response times to malfunctioning HPLCs.

Injection Tracking

The Waters Openlynx software allows chemists to input specified information fields upon logging in a purification sample. Part of the login process has been configured to require the chemist to input project information prior to the injection of the sample. This aspect enables the ability to link project to metrics

such as method and instrument selection, number of injections, and use per chemist, thus combining information that was not readily tracked previously.

The “analytical scout-to-purification” workflow utilises focused gradients for preparative purifications based on retention times from analytical injections. Shown in Figure 3 is a plot of the varying focused gradient selections among two projects. Analysing metrics such as this can lead to the creation of customised methods within the open access framework for high demand specialty purifications. The spread of purification methods is very different based upon lipophilicity of samples. This can be seen in Figure 3 where for one project (green) the most utilised method was method 3 where compounds require low% acetonitrile gradients because they are more hydrophilic in nature. The other project (blue) utilised method 6 where compounds require more shallow high% acetonitrile gradients because they are more hydrophilic in nature.

Detector/ LC Performance

In monitoring the peak shape of standard runs, the performance of a specific instrument can be qualified. Peak height, width, and signal intensity are just a few parameters that can be tracked to ensure that detectors are functioning properly. These simple automated checks enable technicians to quickly focus on instruments where “hands on” maintenance is required on a daily basis. Instrument failures such as sample precipitation, column performance (peak width and retention time variation) and QC standard mass accuracy can be more simply tracked and instrument up-time can be more easily tracked. This gives a visual performance metric to all chemists and is shown in Figure 4 and demonstrates the usefulness of tracking performance metrics in this manner.

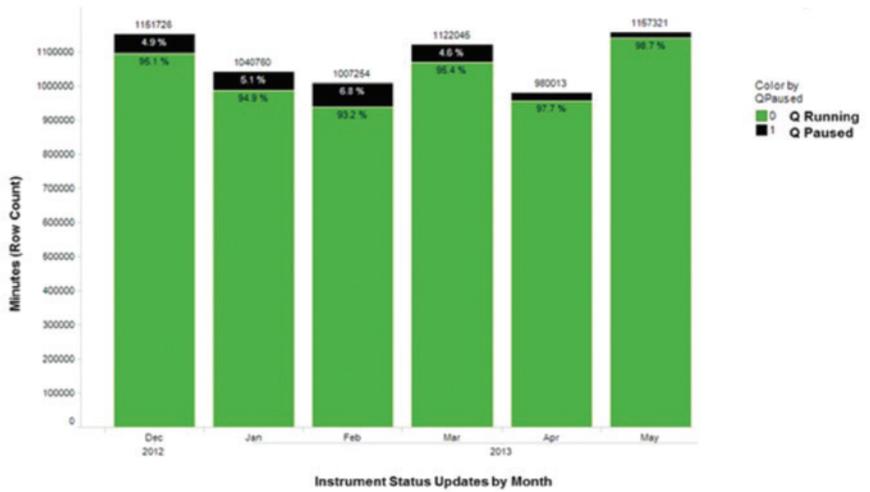


Figure 3: Purification method selection metrics for different projects

Conclusion

The initial goal of implementing data analysis software was for tracking QC runs, although a lasting impact was obtained from the unexpected additional metric information that this workflow gathered. The collation of specific project information and utilisation rates, allows for tailored chromatographic methods for high demand purifications. Daily

operations become more streamlined as technicians are able to quickly identify and resolve issues remotely, while also performing simple preventative maintenance steps that minimises down time and increases column life. Predicting and planning for potential issues can be significantly improved by analysing column performance metrics through routine automated information

tracking tests for chromatographic instruments.

References

(1) B. Evelson, *The Forrester Wave™: Self Service Business Intelligence Platforms, Q2 2012*. (Forrester Research Inc. 2012)

(2) T. Kucera, D. White, *Predictive Analytics for Sales and Marketing*. (Aberdeen Group, A Harte-Hanks Company 2012)

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Kinesis is pleased to announce that it has been appointed the exclusive distributor for the Rapid Extraction System (RES) developed and manufactured by CambTEK Limited. Under this agreement Kinesis will be responsible for sales and service of the RES throughout the UK and Ireland. The RES was developed by CambTEK to address the long-standing issues of poor productivity and quality of data of solid dose testing, within the pharmaceutical and food industries. The RES is built on a scientific understanding of dissolution and liquid flow as opposed to the traditional invasive homogenization and automation of human processes. It is a very intuitive and user-friendly scientific instrument that will substantially ease bottlenecks in sample preparation for food and drugs companies.

As part of this agreement Kinesis will support a recently announced co-marketing agreement between CambTEK and Agilent Technologies to provide a combined solution for Liquid Chromatography and Sample Preparation.

At the end of 2013 CambTEK Limited signed an exclusive multi-territory distribution agreement with the Kinesis Group:

Kinesis is the exclusive distributor of the CambTEK RES system in the United Kingdom and Ireland; USA and Canada; Germany; Austria; Switzerland; Italy; Croatia; Slovenia; Ukraine; Baltics (Latvia, Lithuania, Estonia) Serbia; Romania; Turkey; Bulgaria; Kosovo; Azerbaijan; Albania; Greater China (mainland China, Hong Kong, Macao); Middle East (Saudi Arabia, Jordan, Lebanon, UAE, Kuwait, Qatar, Egypt). Kinesis is a non exclusive distributor of the CambTEK RES system in Russia.

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Simultaneous Determination of Amlodipine and Its Counterion Besylate

Thermo Fisher Scientific has developed a simple, rapid, reliable, and accurate high-performance liquid chromatography (HPLC) method for the simultaneous determination of amlodipine and besylate in an amlodipine besylate drug substance. Application Note 1087: Simultaneous Determination of Amlodipine and Its Counterion Besylate by HPLC demonstrates that this method requires only 8 minutes per analysis using a column designed for pharmaceutical analysis and ultraviolet detection. In addition, combining the analysis of the active pharmaceutical ingredient (API) and counterion into a single method saves times, reduces mobile phase consumption, and minimizes waste.

Amlodipine besylate is a commonly prescribed drug product. During the drug manufacturing process, HPLC techniques are frequently used to analyze the API, but often lack the sensitivity to reliably identify the counterion. Although the current U.S. Pharmacopeia monograph for determining amlodipine besylate describes an HPLC method for separating the API, it has no method to determine the besylate counterion. Thus, this new approach gives drug manufacturers the ability to simultaneously determine both amlodipine and its counterion besylate in a single method.

This application brief and many others can be found at www.thermoscientific.com/dionex under the Documents tab.