Chromatography Data Systems Market in India

- Nitin M. Kabbin

Chromatography is probably the most widely used analytical technique today. This science of separation serves a wide range of industries from pharmaceutical to petrochemicals, from food to agro chemicals and many more. Computing Integrators, the precursors of chromatography software and modern Chromatography Data Systems (CDS) have been relied upon to provide the intermediate or the final result of analysis. Though an integral part of a chromatograph, Computing Integrators and CDS have employed distinct technology than those used in the chromatograph itself. There have therefore been a number of companies excelling in software and data processing but not necessarily in chromatographs.

History

Few decades ago when strip chart recorders were the only means of recording chromatography data , computing areas of peaks over a wide range was equally daunting as performing the experiment itself. The early microprocessors lent themselves very well to ease this seemingly trying task. A range of Computing Integrators were launched by companies like Spectra Physics, Hewlett Packard, Shimadzu, LDC Milton Roy and many others. They varied from just printing peak heights and areas to printing full chromatograms and results usually on thermal paper. Forgetting to photocopy these printouts left the slate clean in a few months.

The exponential rise in semiconductors, computing speed and software has revolutionized many technologies and chromatography data processing was an ideal candidate. The industry has seen evolution from the basic DOS based software to a modern CDS which provides a wide range of features going far beyond their immediate tasks.

Basic challenges

Even though the luxury of hindsight allows us to mock at some of the earliest integrators and software, the primary challenges have remained unchanged. For a purist computing proper areas and heights of peaks under trying conditions is still the primary job of a CDS. The tasks can be divided as integration of peaks and data processing & management.

Market Dynamics in India

- **With compliance, training and networking gaining importance many companies are looking for Chromatography Data Systems which offer multi vendor control and other features which can increase laboratory efficiency and productivity.**
- **Though industries rely heavily on chromatography analysis a need is felt to integrate other instruments into a single software and provide one solution for all laboratory data processing and management needs.**

Digitizing the detector signals is the first step for a CDS. The analog to digital converter (ADC) has to retain the dynamic range the detector offers and make no significant contributions to the noise of the system. ADCs usually measure the heights of signals at a given frequency. ADCs of the continuous integration type are more suitable for a CDS as they give a measure of area rather than height. They also have certain filtering built in however there is a trade off between sampling frequency and resolution. In most modern GCs and HPLCs digitizing is carried in the instrument itself.

Once in the digital domain the signal is filtered. Filtering is the general process of separating noise from true signal. This is possible only if the two have some distinguishing features which in this case is the signal frequency. Though this goes unnoticed by many users the quality of filtering has a great impact on integration. The most popular algorithm is the Least Squares method propounded by Savitzky and Golay and its variants. Many CDS offer a range of filter algorithms for the users to choose. These options though welcomed by the discerning user tend to confound the lay users and hence are tucked away in some corner making them available yet invisible. The filtering parameters the user selects are in the form of peak widths, peak slices etc. Given the different

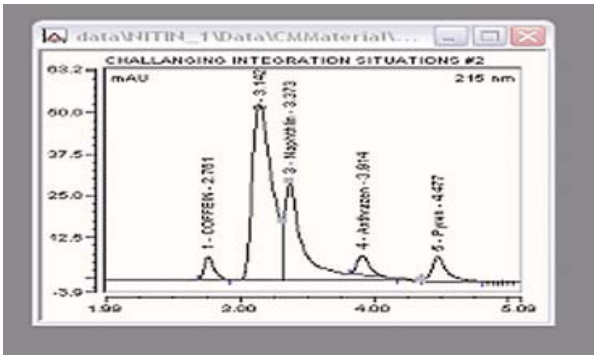
NITIN M. KABBIN

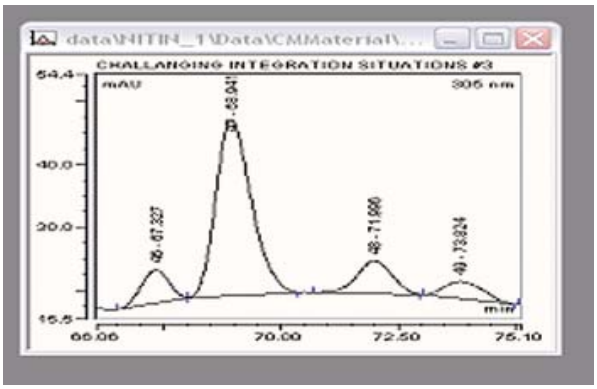
Nitin Kabbin completed his post graduation in Computer Sciences from IIT Mumbai in 1983. He then joined Netel Chromatographs as R&D Engineer and was involved in designing Gas Chromatographs and other analytical instruments. After a brief stint at Netel Chromatographs he launched his own venture in early 1986 under the style of Indtech Instruments Pvt. Ltd. The company focused on design and manufacture of Computing Integrators and software for Chromatography. In 1989 this was the first indigenously designed product of its kind. In 2005 he established Dionex India Pvt. Ltd, a joint venture subsidiary of Dionex Corporation USA and Indtech and is currently the Managing Director looking after Dionex operations in South Asia.

chromatography techniques peak shapes can range from razor sharp for a capillary GC to the mounds of a GPC. It is however essential that filtering should not lead to peak distortion. Filtering readily eliminates high frequency noise. Discrimination from baseline perturbations requires more subtle techniques as their characteristic frequencies are similar to peaks. Lower frequencies emanating from drifting baselines due to temperature programming in a GC or gradient runs in a HPLC need appropriate baseline corrections.

It is taken for granted that peak area is the fundamental measure of sample composition than peak height. Yet height is more appropriate for flow sensitive detectors like UV-Vis detectors and area is the better choice for mass sensitive detectors like FID. The advances in instrumentation in terms of flow precision ensure that both area and height are equally representative of the sample composition. Peak start, end and apex detection are the basic function of a CDS. Different software have varying approaches but all of them require some inputs from the user to discriminate signal from noise. The sophistication of algorithms determines the number of parameters required for consistent detection of peaks from run after run. Frequent requirement of manual integration should be seen as the ultimate surrender of the detection algorithm. Peak apex is generally found by fitting a quadratic curve at the top.

Apportioning proper peak areas and heights is the next challenge. The ideal chromatogram should have Gaussian bells separated by a flat baseline. The real conditions are seldom ideal, merged peaks need to be resolved and drifting baselines corrected for. The goal is to try and overcome the imperfection in separations and give areas and heights which can still be fairly accurate about the sample composition. A number of features like vertical drops, tangent skim, valley to valley corrections take care of the situation, but it is important for the user to apply these properly based on the knowledge of sample and instrument conditions. Once the proper areas, heights and retention times are computed a wide range of calculations like correcting for detector responses, linearity curves, identification of peaks etc. are performed.





Examples of Perpendicular drops, skimming and valley to valley corrections

Data Management

Increasingly success and failures of CDS are determined by their data management capabilities than anything else. The demands of GLP and requirements of regulatory bodies especially those in the pharmaceutical industry have added a new dimension to CDS. This area in the realm of Information Technology has transformed a CDS from a integration software to a comprehensive solution provider. Of the all the guidelines the 21 CFR part 11 of US FDA has had a significant impact on design of CDS. The key features of a modern CDS are:

Data Security

Chromatography data generated and created by users should be secured in a way to prevent unauthorized access from within and outside if the application. Elaborate user management can create different user levels which authorizes or restricts various functions e.g. create / modify / delete method flies or program / sequence / report formats. At the same time user management also defines access rights to instruments. Care is also taken to protect the data tampering from outside the application. Data bases are employed to store entire or part of data for both security and ease of management.

Audit Trails

Traceability is the buzz word today. With comprehensive audit trails one always has the documentation needed to defend the results and at the same time the auditor can view the history of the data under scrutiny. An audit trail needs to log every event related to instrument control and data acquisition. Every change to base line, method files and report formats needs to be tracked. All security related events like logins, password changes, privilege changes and electronic signatures events have to be recorded.

Validation

Establishing correct performance of instruments and software is of paramount importance and this has become a specialized area in itself. A CDS should ensure it has all the features to validate performance of instruments and software once it has

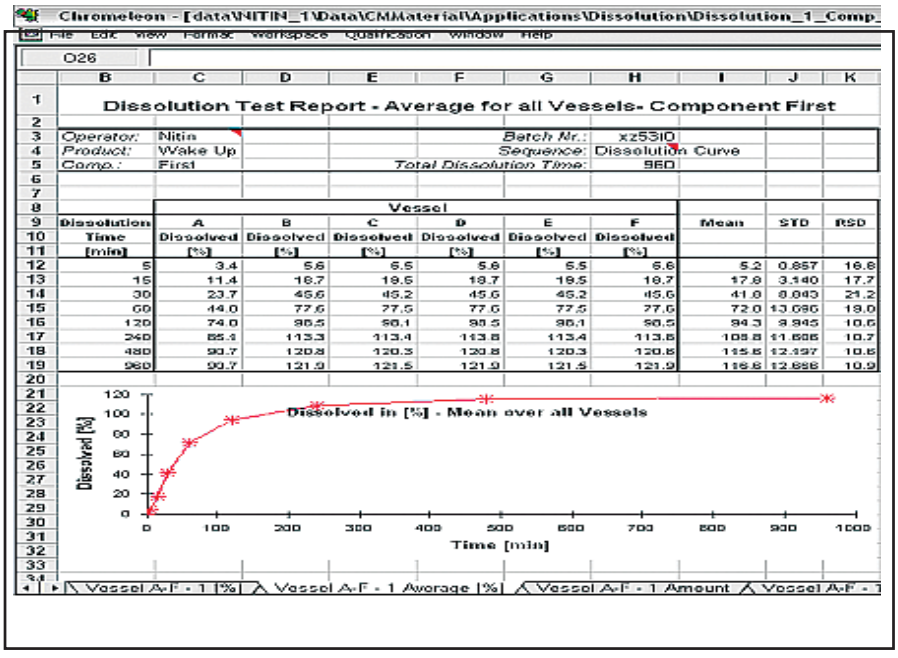
been installed. Most CDS come with a certificate of compliance from the designer guaranteeing performance of the software. The validation procedures are also open to scrutiny at vendor sites.

Electronic Signatures

21 CFR part 11 laid down guidelines for Electronic signatures when data is submitted in an electronic form. Large installations find electronic signatures useful not only from compliance point if view but as a step towards a paperless laboratory.

Multi Vendor Control

CDS naturally control the instru-ments from the same company, but increasingly multi vendor control is sought after for various reasons. Pockets of excellence lead to some instruments being better for an application and the inability of a good CDS to control it is seen as a major handicap. In a networked environment a multi vendor control allows methods to be seamlessly transferred from one instrument to another. Reporting is uniform irrespective of the brand of GC / HPLC. For large pharmaceutical companies training burdens are reduced as only one software needs to be learnt. Choice of future hardware purchases are also kept open.



Example of automated custom calculation for dissolution profile.

Customized Calculations

One of the most important functions of any CDS is reporting of processed data. If it is not possible to use the application to report data in accordance with the laboratory requirements, it becomes necessary to transcribe or export data to other software applications. This process is time consuming and error prone and is one of the major bottlenecks that laboratories have in transforming chromatography data into useful information.

Operation in a networked environment

In recent years, the trend for many laboratories has been to move from storing data on single workstations to storing data on a central server. The main reasons being easier data access, data management and comparison. Although the benefits are clear, there are several challenges that a CDS has to meet. One of the important aspects is how network failures or server crashes are handled. Ensuring uninterrupted operations of instruments in these events and data integrity is highly desirable.

With all the above it may appear that a modern CDS is a complex package which under the garb of compliance is extremely difficult to use. Therein lies the challenge to provide all the features with ease of use. The success of a technology is also measured by the ease with which it can be operated by users at different levels.

Indian scenario

In India the first and the only Computing Integrator was developed by Indtech Instruments in 1989 which was followed by PC based software by few companies. These indigenous developments chiefly met the local GC manufacturers and few HPLC requirements. They came at a time when importing Computing Integrators and software was not easy. As the imports were liberalized and GCs and HPLCs came with full PC control the trend was to stick to the software of the instrument manufacturer. Now with compliance, training and networking gaining importance many companies are looking for CDS which offer multi vendor control and other features which can increase laboratory efficiency and productivity.

Future trends

Though industries like pharmaceutical and petrochemicals rely heavily on chromatography analysis a need is felt to integrate other instruments into a single software and provide one solution for all laboratory data processing and management needs. Some solutions are available but they still lack a wider appeal as they cater to instruments from one manufacturer or have gaps in terms of full control. It will be ideal if the manufacturers can arrive at a protocol sharing agreements so that future solutions are easy to implement. ■