C190-E262

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Technical Report

Incorporating Analytical Intelligence into the Integrated i-Series—New Analytical Workflow Automation

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Abstract:

Significant progress has been made in automating analytical operations as more efficient and flexible work styles are required. The integrated i-Series contains all the functions required for LC analysis in a compact unit. These functions have been optimized for ease of operation and maintenance. In addition to the exceptional instrument performance offered in previous models, the new i-Series (LC-2050/LC-2060) models also feature Analytical Intelligence functionality for supporting automation of analytical operations and ensuring acquisition of highly reliable data. Analytical Intelligence is a new concept for analytical instruments offered by Shimadzu. Analytical Intelligence consists of systems and software that simulate expert operators automatically determining whether or not conditions and results are good or bad, providing feedback to users, and solving common problems. It increases data reliability by compensating for any differences between users in their instrument knowledge or experience. This Technical Report bulletin describes the new Analytical Intelligence functionality included in the new i-Series.

Keywords: Analytical Intelligence, i-Series, auto-startup, FlowPilot, mobile phase monitor, i-PeakFinder™, i-PDeA II

1. Background

As users demand higher operating efficiencies and more flexibility in working practices, what is considered the ideal for LC analytical processes is beginning to change significantly. Users want an environment where equivalent analytical operations and data analysis can be performed to obtain identical results, even by users not located in the laboratory or users unfamiliar with operating the system.

Analytical and testing operations often require fundamental knowledge about analytical chemistry and experience-based expertise. Experienced analysts have a good understanding of the principles underlying analytical techniques and systems and are able to apply their expertise gained from past experience to avoid problems and obtain highly reliable data. In contrast, it is difficult for analysts with minimal experience to predict potential risks in advance and analyze samples with corresponding countermeasures implemented. In addition, during data analysis, it is much more likely that an expert analyst will discover hidden problems in the data.

Overall operating efficiency taking into consideration data reliability and instrument uptime rate, etc., is dependent not only on analysis cycles, throughput, and other factors that can be resolved with instruments and software, but is also greatly dependent on the knowledge and skill level of users. Furthermore, whereas improving the knowledge and skill level of users requires a time-consuming process of training personnel, the number of expert analysts available in the analytical workplace is dwindling and the proportion of analysts with minimal experience is increasing. This trend is a major issue currently being faced by the analysis and testing industries.

ANALYTICAL INTELLIGENCE

- Automated support functions utilizing digital technologies, such as M2M, IoT, and Artificial Intelligence (AI), that enable higher productivity and maximum reliability.
- Allows a system to monitor and diagnose itself, handle any issues during data acquisition without user input, and automatically behave as if it were operated by an expert.
- Supports the acquisition of high quality, reproducible data regardless of an operator's skill level for both routine and demanding applications.

2. Analytical Intelligence in Integrated LC System i-Series

ANALYTICAL INTELLIGENCE

That issue cannot be resolved by only improving work efficiency achieved through improvements in the basic performance of instruments or operability of software. It can only be truly solved if highly reliable results can be acquired at any time by any users, regardless of their knowledge or skill.

Analytical Intelligence is a new concept for analytical instruments offered by Shimadzu. It automates the expertise of expert analysts who avoid common pitfalls to ensure that equally high quality data can be acquired by anyone. As shown in Fig. 1, Analytical Intelligence reduces the risk of system problems by automating mobile phase volume checks and column equilibration.

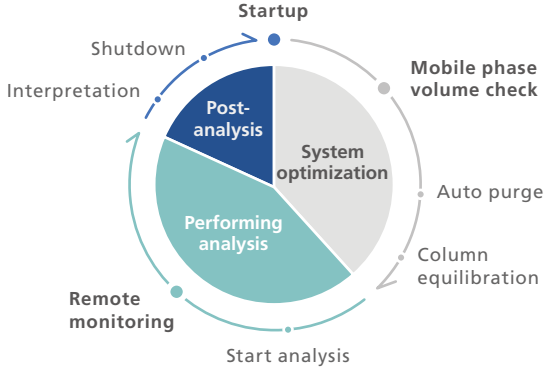

Fig. 1 Workflow of LC Analysis

1 Analytical & Measuring Instruments Division

2. Integrated LC System i-Series

The integrated LC System i-Series contains all the functions required for LC analysis in a compact unit. These functions have been optimized for ease of operation and maintenance with an intuitive touch panel (See Fig. 2). LC-2050/LC-2060 models feature robust hardware performance with a solid reputation plus new Analytical Intelligence functionality for supporting analysis.

Fig. 2 Integrated LC System i-Series (LC-2050/LC-2060)

3. FlowPilot Enabling Fully Automated Workflow for Analysis

FlowPilot enables fully automated workflow for analytical operations from startup and system suitability test (SST) to analysis and shutdown.

3-1. Intelligent Start-up with FlowPilot

When starting up the system and equilibrating the column, it is well known that pressure shock can affect column performance by reducing column lifetime and leading to channeling, which results in peak-splitting in the corresponding chromatogram. Expert analysts will gradually increase the flowrate as the column temperature is controlled to prevent exposing the column to any excessive pressure loads.

When the i-Series auto-startup function starts up the system at the specified date and time, the FlowPilot function starts equilibrating the column by gradually increasing the mobile phase flow rate as the column temperature increases. That means the system automatically replaces the manual operations of expert analysts to avoid column damage and finishes preparing the system (Fig. 3). The FlowPilot status during execution can even be confirmed on the touch panel (Fig. 4).

3-2. Automation of Entire Analytical Procedures

The FlowPilot function can be coupled with the warm-up function and scheduled depending on the user requirements. The system can also be evaluated automatically using the automatic SST function. Scheduled shutdown automatically turns off the system and switches it to power-saving mode when all analytical operations are complete.

The combination of these functions allows the user to fully automate an entire analytical cycle: Shutdown → Start-up → SST → Analysis → Results report → Shutdown (Fig. 5).

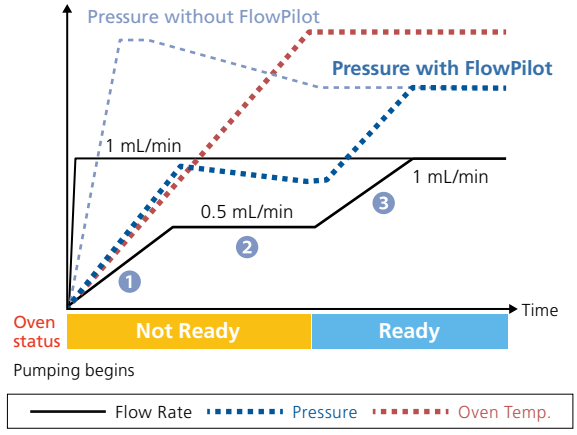

Fig. 3 Diagram of System Pressure Profile during Start-up with the FlowPilot Function

Fig. 4 Touch Panel when FlowPilot Function is used

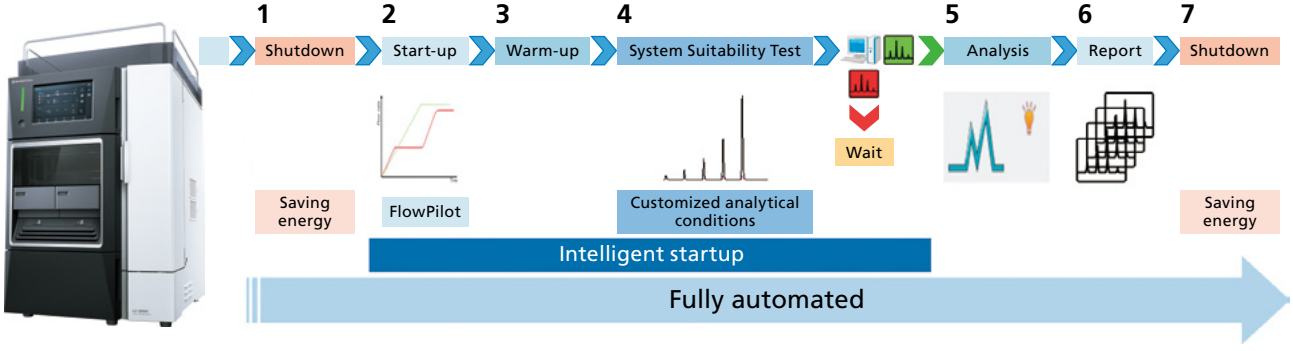

Fig. 5 Workflow Diagram showing the Fully-automated Operation of LC Analysis

3-3. Fully-automated SST

SST are used to verify that the chromatography system is adequate for the intended analysis. The tests are based on the concept that the equipment, electronics, analytical operations, and samples analyzed constitute an integrated system that can be evaluated as such. SST is mandatory in USP, FDA, and EP standards to check and ensure the ongoing performance of analytical systems. Nevertheless, several different parameters can be evaluated depending on the system and the analytical conditions. For this reason, there is a growing demand for a degree of flexibility in the set-up of SST parameters and possibilities for their customization in modern LC systems.

SST parameters are embedded in the analytical method file. This means that users can easily create an SST with specific analytical conditions, in which selected parameters are evaluated (e.g. number of theoretical plates, tailing factor, resolution, capacity factor *k*). After creating the SST, it is possible to choose when to run the SST during a batch analysis (at the beginning, after analysis of some samples or at the end of the batch).

Once the SST is complete, a "pass" or "fail" result is issued depending on the previously-selected criteria, and this result will then trigger specific actions based on user preferences (Refer to Technical Report C190-E227).

4. Mobile Phase Monitor Prevents Mobile Phase Depletion

Mobile phase levels must be appropriately managed because running out of mobile phase during an analysis not only causes the analysis to fail, but can also damage expensive analytical columns. A mobile phase monitor can be used to measure the amount of mobile phase remaining in real time, and is operated in combination with LabSolutions™ or dedicated software to check the mobile phase level.

Previously, LabSolutions could be used to calculate an estimated value of the remaining mobile phase level based on the volume consumed, but the MPM-40 unit (Fig. 6) is configured with a weight sensor and controller that can be used to calculate the level based on the actual mobile phase weight. The MPM-40 sends the current quantity inside the mobile phase bottle to a computer or smartphone in real time via a LAN connection. Dedicated MPMChecker™ software then graphically displays the remaining level (Fig. 7). When the remaining quantity of mobile phase decreases to the specified level, a warning (orange) or error (red) signal is emitted to notify the user. It also stops the LC system if specified criteria are satisfied. (Refer to Technical Report C190-E226)

Two types of bottle holders are available for holding either 1-liter bottle or large 2 to 5-liter bottles.

Fig. 6 MPM-40

Fig. 7 MPMChecker™

5. Accurate Peak Detection without Manual Peak Integration Automatic Peak Integration Using i-PeakFinder

Given increasingly fast analysis capabilities and shorter data acquisition times, if manual operations are required for integrating chromatogram peaks, then the data processing step becomes a bottleneck that prevents truly improving operational efficiency. Therefore, automating the peak integration process is essential. However, for chromatograms with a large number of peaks from contaminant components and target components, automating the peak integration process while eliminating the effects of baseline fluctuations and unseparated peaks can require complicated steps, such as configuring detailed settings for a peak integration program. Also, manual peak integration processes are prone to causing differences between individual operators, which reduces the consistency of quantitation values.

i-PeakFinder, which is one of the peak integration algorithms available in LabSolutions, uses a completely automated integration function to accurately detect peaks, as shown below, without the need to specify special parameter settings (Fig. 8).

- Shoulder peaks can be detected very accurately.
- Baseline processing can be changed easily.
- Reliable peak tracking enables improved reproducibility.
- Peaks can be integrated correctly even with variability from baseline drift.

With applicable parameter settings available for a wide range of complex chromatogram patterns, i-PeakFinder can output highly accurate peak integration results even when processing large quantities of data at the same time. i-PeakFinder is part of the standard functionality included with LabSolutions software, so it can be used for chromatograms obtained with non–i-Series LC systems as well. (Refer to Technical Reports C191-E044, C190-E243)

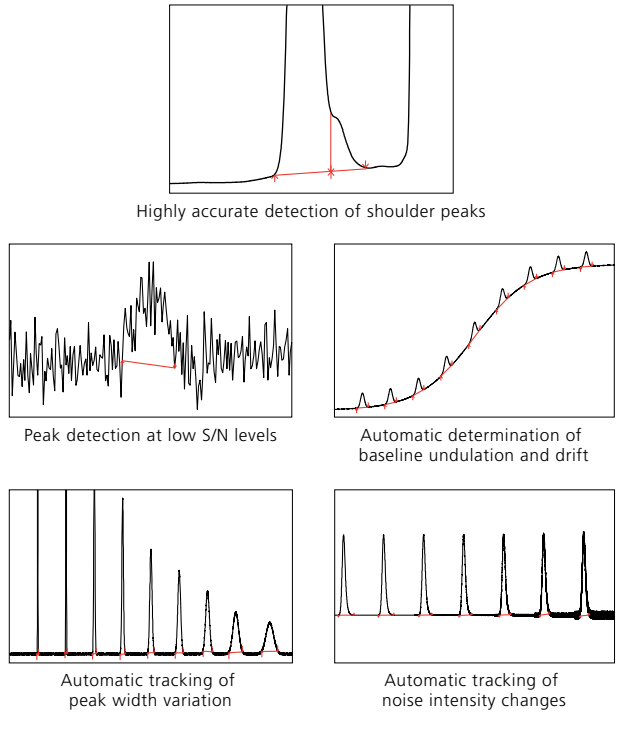

Fig. 8 Example of Automatic Peak Integration Using i-PeakFinder

6. Separating Unseparated Peaks Using a PDA Detector Detecting Overlapping Peaks with i-PDeA II

If there are other peaks present near target component peaks, such as when analyzing multiple components simultaneously, checking for synthesis, or analyzing samples with many contaminant components, to ensure quantitative accuracy, it is important to check for any peaks eluted together with target peaks and overlapping in the chromatogram. However, in reality, checking for such peaks is quite difficult unless a mass spectrometer or any other instrument with high selectivity is used for detection. Also, if unseparated peaks are discovered, it usually requires reassessing peak separation in the column.

i-Series models equipped with a PDA unit (LC-2050C 3D or LC-2060C 3D) can use a unique data analysis technique in Intelligent Peak Deconvolution Analysis II (i-PDeA II) functionality to isolate target peaks from unseparated peaks. The i-PDeA II data analysis technique extracts target peaks from unseparated peaks by analyzing photodiode array (PDA) detector data using the chemometric multivariate curve resolution alternating least squares (MCR-ALS) method. The technology uses a PDA detector to identify overlapping peaks that were not adequately separated by the column and either separates those peaks in the chromatogram or determines the UV spectrum of each peak. Consequently, it can be used to check for impurity peaks hidden by key component peaks, extract chromatograms for individual components (Fig. 9 (b)), or confirm peak purity (Fig. 9 (c)). (Refer to Technical Report C191-E042)

7. Conclusions

Based on a completely new concept, Analytical Intelligence consists of various supporting functionality that was developed for the purpose of promoting higher efficiency through workflow improvements, while also ensuring the reliability of data from instrumental analysis. Automatic operation of the system which simulates operation by an expert analyst reduces the risk of system problems. Consistent data analysis results are provided by automating the operations that tend to result in variability between individual operators and by automatically identifying overlapping peaks that are easily overlooked.

LC-2050/LC-2060 have various functions of Analytical Intelligence in addition to their excellent basic performances, and contribute to maximizing system utilization rates and improving operating efficiency by always acquiring data that is consistently highly reliable and by avoiding system problems, regardless of knowledge and skill level of users.

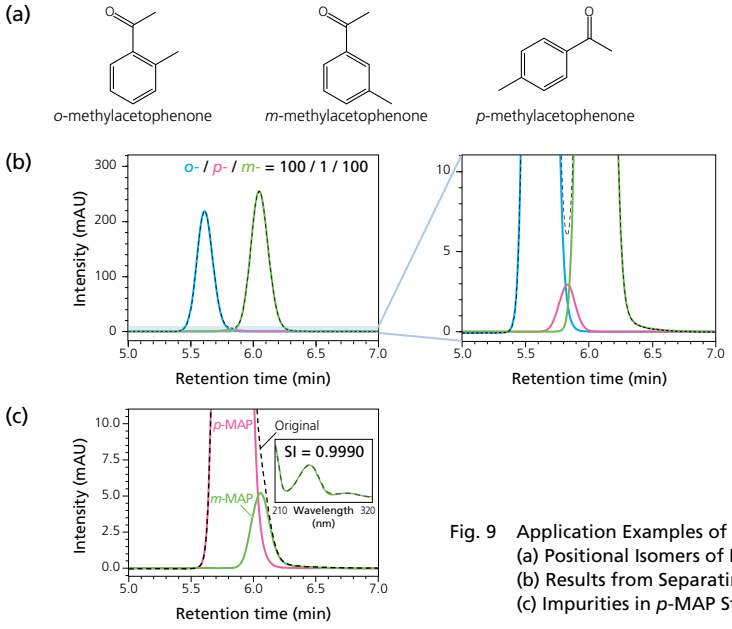

Fig. 9 Application Examples of Peak Separation Algorithm using i-PDeA II
(a) Positional Isomers of Methylacetophenone
(b) Results from Separating a Mixture Sample of *o*-MAP, *m*-MAP, and *p*-MAP
(c) Impurities in *p*-MAP Standard Sample

First Edition: January, 2021

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3655-01101-PDFNS