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Technical Report

New Analytical Intelligence Concept —Support for Automating Analytical Operations

The idea to support the novel workflow automation for analytical and testing operation

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ANALYTICAL INTELLIGENCE

Abstract:

Significant progress has been made in automating analytical operations in an effort to improve productivity and prevent human errors. Nevertheless, differences in the functionality, performance, and operability of instruments and software and also in the level of analytical chemistry knowledge and expertise can affect the reliability of results and the condition of instruments. 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 Nexera™ series.

Keywords: Analytical Intelligence, Nexera series, auto-startup, FlowPilot, mobile phase monitor, auto-diagnostics, auto-recovery, i-PeakFinder, and i-PDeA II

1. Issues Involved in Improving Workflow for Analytical Operations

When systems equipped with autosampler-based automatic injection functionality and workstations with the capability of using such autosampler functionality to acquire data based on specified parameter settings became available, it resulted in automated instrumental analysis and it significantly changed how analytical operations are performed. Automated data acquisition enabled continuous analysis at night or at other times when facilities are closed, which not only dramatically improved operating efficiencies, but also reduced the risks of variability or errors associated with manual operations and improved data reliability.

However, 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.

2. Analytical Intelligence

ANALYTICAL INTELLIGENCE

That issue cannot be resolved by only shorter analysis times or higher throughput 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 user, regardless of their knowledge or skill. Making that a reality requires an unprecedented new policy.

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 in instrument knowledge or experience of users. This document describes the new Analytical Intelligence functionality included in the new Nexera series ultra high performance liquid chromatographs.

3. Analytical Intelligence Functionality in Nexera Series Systems

Typical liquid chromatography workflow involves several risks that could interrupt continuous analysis or compromise data reliability (Fig. 1).

- Column damage from sudden starting of solvent delivery
- Analysis interruption and column damage due to depletion of mobile phase
- Negative impact on chromatograms from using a defective column
- Retention time delay due to solvent delivery becoming unstable
- Poor quantitative reproducibility due to variability in peak integration.
- Poor quantitative accuracy due to overlapping peaks from coeluting components.

The next section explains how Analytical Intelligence helps minimize each of the above risks when using Nexera series systems. For more details, refer to individual Technical Report bulletins that describe the respective functionality.

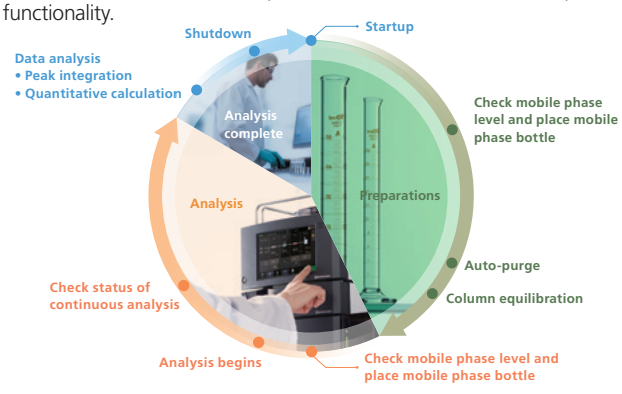

Fig. 1 Work flow of LC analysis

1 Analytical & Measuring Instruments Division

3-1. Automatic Startup and FlowPilot

When starting up the system and equilibrating the column, expert analysts will gradually increase the flowrate as the column temperature is controlled to prevent exposing the column to any excessive pressure loads. Repeatedly starting solvent delivery too abruptly, without the above steps, can cause column damage. When the Nexera 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 flowrate 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. (Refer to Technical Report C190-E227.)

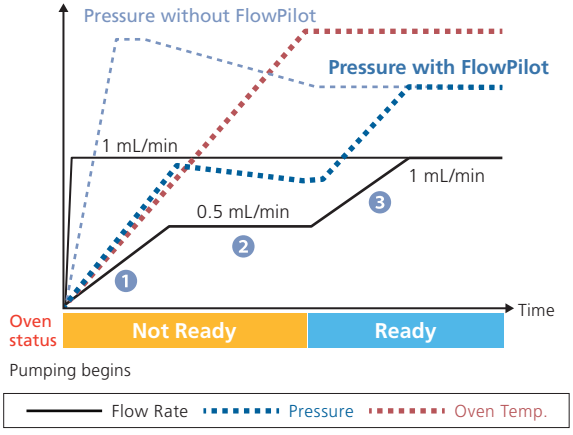

Fig. 2 Diagram of system pressure profile during start-up with the FlowPilot function

3-2. Mobile Phase Monitor Prevents Mobile Phase Depletion

Using the mobile phase monitor prevents depletion of mobile phase and eliminates the need to visually check the level. It also eliminates the need to perform bothersome consumption rate calculations.

The MPM-40 unit (Fig. 3), which comprises a weight sensor and controller, 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. 4). When the remaining quantity of solution 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. LabSolutions prevents interruption of analysis due to insufficient mobile phase by comparing the predicted usage volume to the volume available before starting each analysis and notifies the user if there is not enough available (Fig. 5). The function also reduces the risk of bubbles getting inside the column and prevents loss of scarce samples caused by injecting samples when the mobile phase supply is depleted. (Refer to Technical Report C190-E226.)

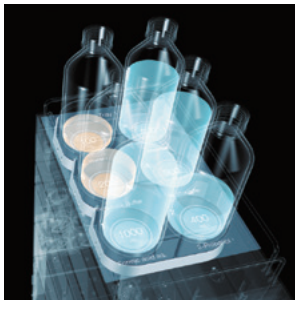

Fig. 3 MPM-40

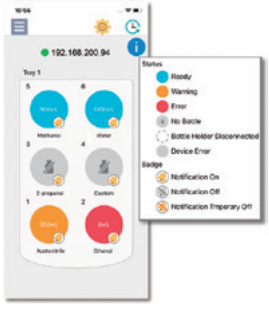

Fig. 4 MPMChecker

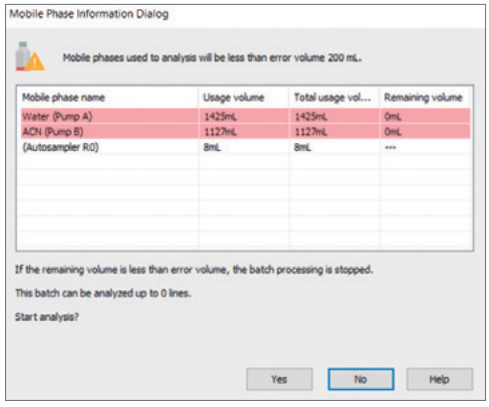

Fig. 5 Warning Window when Using LabSolutions™

3-3. Collective Management of Columns and Visualization of Column Condition CMD and Column Data Browser

Reliable quantitation is premised on separation by maximizing the inherent performance capabilities of columns. On the other hand, given that columns are consumables, their performance will gradually decrease as sample contaminant components accumulate and the column deteriorates over time. They can also become damaged suddenly, such as if insoluble substances from a sample are accidentally injected. To ensure columns with adequate performance are always used, column performance must be managed or usage history routinely recorded, which is not a simple matter if columns are shared by multiple users or the number of columns is large.

Therefore, the Nexera series column management function collects various information during column use, such as injection pressure, links the information to a LabSolutions data file, and stores it in a database. It can be used with all sorts of columns, regardless of the column type or brand, so that information about all columns can be checked at a glance using the column data browser (Fig. 6). A list of all registered columns can be displayed or the usage history or most recent chromatogram visually checked for the selected column, which means column condition can be confirmed without spending extra time.

Note: An optional column management device (CMD) and Nexera series-compatible LabSolutions DB/CS version software are required in order to use the new functionality for column management.

Fig. 6 Example of Column Data Browser Display

3-4. Automatic Detection and Resolution of Solvent Delivery Problems during Analysis by Auto-Diagnostics and Auto-Recovery Functions

Due to degassing unit and solvent delivery unit performance improvements in recent years, problems occur much less often now than they used to, but in rare cases bubbles that form within HPLC/UHPLC flow channels can cause solvent delivery problems if they enter the solvent delivery pump. That can cause retention time and area value fluctuations, baseline instability, peak shape distortion, or other problems that can significantly reduce the reliability of quantitative results. If such a problem occurs, the user must manually stop the current analysis and implement corrective measures, such as purging the flow channels. That means that if air bubbles appear in flow channels during unattended operation, the same analysis must be repeated the next day.

The auto-diagnostics and auto-recovery functions included in Nexera series solvent delivery pumps detect abnormal pressure fluctuations (pulsation) caused by bubbles in flow channels and automatically purge the pump to restore the system to normal. Consequently, instead of the user, the instrument monitors and manages the relationship between easily overlooked chromatogram abnormalities and flowrate changes that can cause pulsation, thereby preventing analysis failures. (Refer to Technical Report C190-E225.)

Note: This function can also be switched OFF in settings.

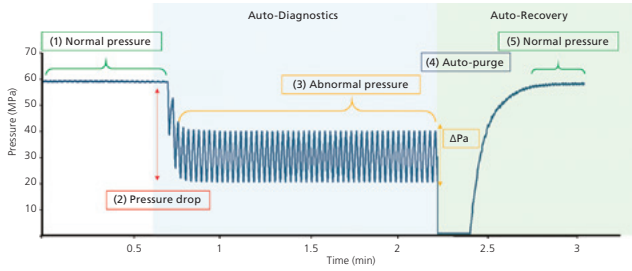

Fig. 7 Diagram of Auto-Diagnostics and Auto-Recovery Functions

3-5. 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-Nexera series LC systems as well. (Refer to Technical Reports C191-E044 and C190-E243.)

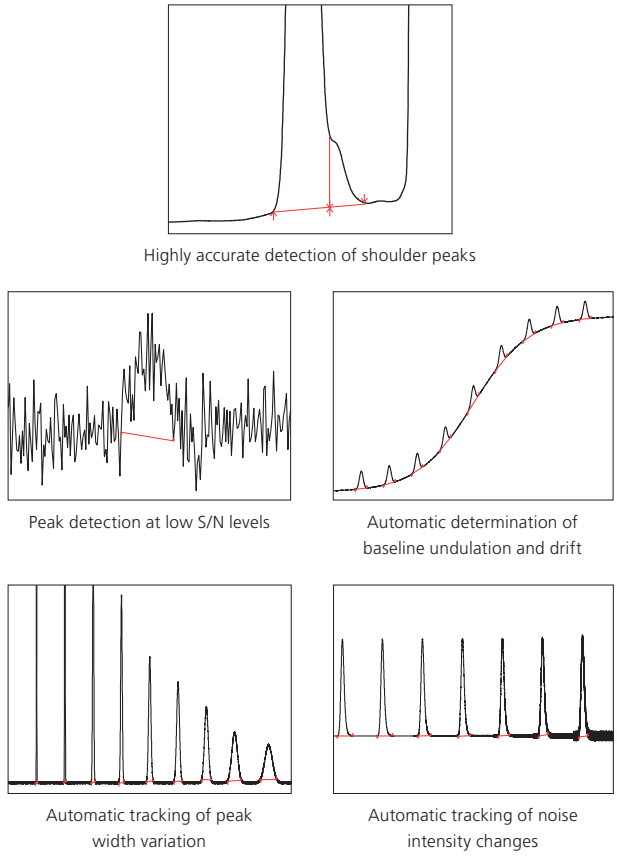

Fig. 8 Example of Automatic Peak Integration Using i-PeakFinder

3-6. 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 impurities simultaneously, 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.

The i-PDeA II (Intelligent Peak Deconvolution Analysis 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 C191-0078.)

Note: This function can be used with LabSolutions and SPD-M20A/M30A/M40 detectors.

4. 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 and enables any problem to be solved if an unlikely event occurs. 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. Analytical Intelligence contributes 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.

We also plan to add additional new Analytical Intelligence functionality in the future. In that way, the Nexera series systems currently in use can continue to be improved by adding new functionality as needed. Analytical Intelligence will undoubtedly significantly change how analysis and testing operations are performed.

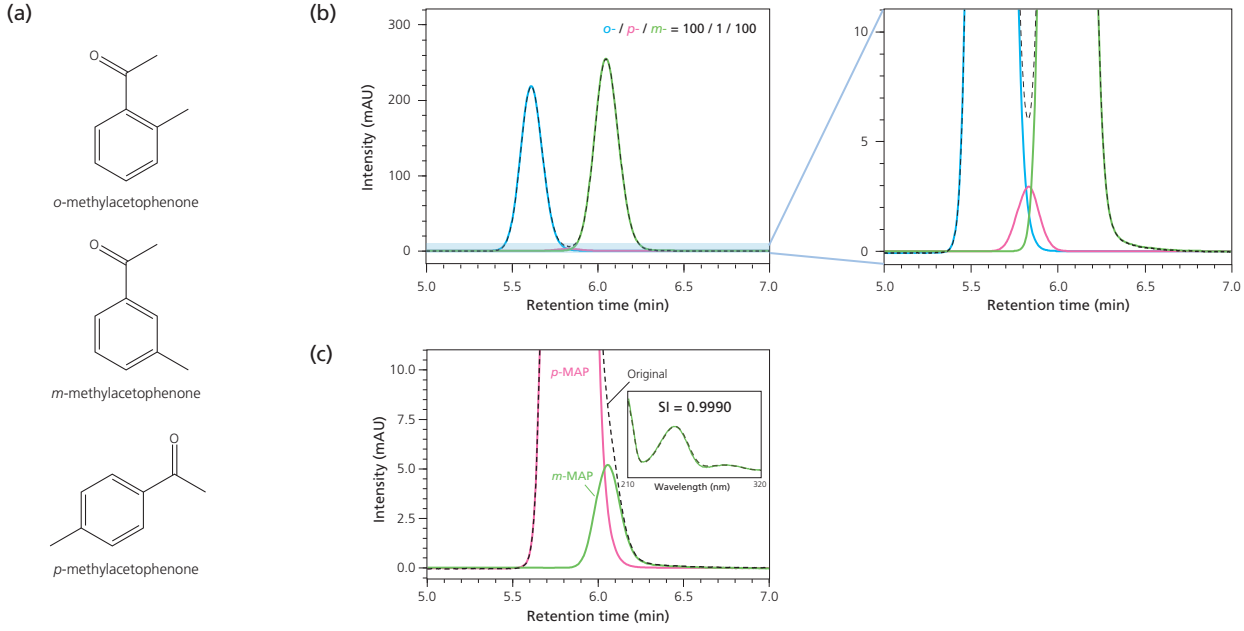

Fig. 9 (a) Positional Isomers of Methylacetophenone
(b) Results from Separating a Mixture Sample of o-MAP, m-MAP, and p-MAP
(c) Impurities in p-MAP Standard Sample

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