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Technical Report

A New Peak Integration Algorithm for LabSolutions

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Abstract:

The time required to analyze large quantities of data obtained from the increasingly quick analyses and increasingly prevalent simultaneous multicomponent analyses in recent years has become a challenging issue. In addition, the strengthening of regulations associated with data integrity has given rise to demands for automated and simplified manual methods for integrating the areas of problematic chromatogram peaks. Herein, we introduce a new peak integration algorithm for LabSolutions, i-PeakFinder, which is designed to resolve these issues.

Keywords: Data processing, peak integration, algorithm

1. Introduction

i-PeakFinder, a new peak integration algorithm for LabSolutions, is a completely automated integration function that can detect peaks with high levels of accuracy without requiring special parameter adjustments. In addition, this algorithm has adjustable parameters that allow the integration function to be applied to a wide range of complex chromatogram patterns. Furthermore, the adjustable parameters allow to output highly accurate peak integration results from large quantities of data, even for batch analysis.

2. Features of i-PeakFinder

With Shimadzu's traditional peak integration methods or competitor methods, some complex chromatograms require time programming in addition to the typical parameter adjustments for peak integration. However, i-PeakFinder can perform peak integration of these chromatograms just with simple parameter adjustments. This peak integration function has the following features:
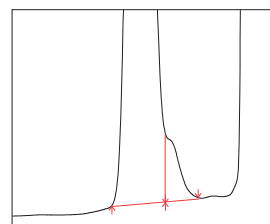
- Highly accurate detection of shoulder peaks
- Simple adjustment of peak-baseline processing
- Improved peak-baseline positioning that results in improved reproducibility
- Performing accurate peak integration even with variabilities caused by baseline drift

Shimadzu also emphasizes on compatibility, so LabSolutions can also be used with the traditional peak integration methods (Chromatopac mode). Switching between the traditional peak integration and i-PeakFinder methods during analysis is easy, allowing the user to select an appropriate peak integration method for the circumstances. This includes selecting a traditional method for compatibility with past data. Fig. 1 shows examples of using the completely automated integration function to analyze typical peaks.

2-1. Highly Accurate Detection of Shoulder Peaks

i-PeakFinder can accurately detect shoulder peaks. In cases wherein manual peak integration is required to distinguish and detect the shoul-

der and main peaks using traditional peak integration methods, i-Peak-Finder can automatically detect shoulder peaks while maintaining consistent peak detection sensitivity throughout the entire chromatogram. In general, it is difficult to automatically detect considerably small shoulder peaks, as shown in Fig. 2; however, i-PeakFinder can even detect such peaks automatically based on the threshold judgment.
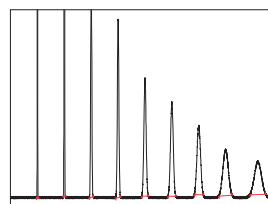

Highly accurate detection of shoulder peaks
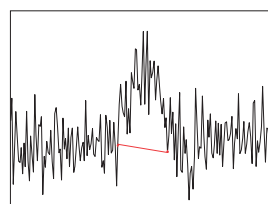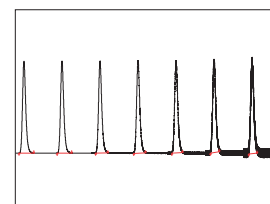

Peak detection at low S/N levels
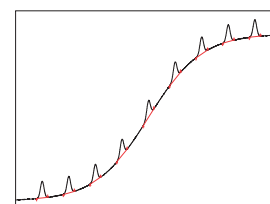
Automatic determination of baseline undulation and drift

Automatic tracking of peak width variation

Automatic tracking of noise intensity changes

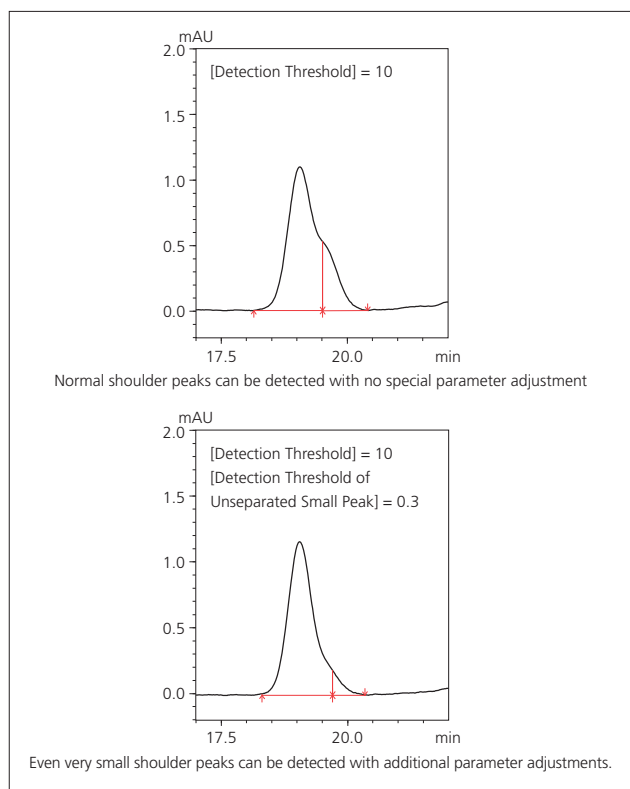Fig. 1   i-PeakFinder's Completely Automated Integration Function

Normal shoulder peaks can be detected with no special parameter adjustment

[Detection Threshold] = 10

[Detection Threshold] = 10
[Detection Threshold of Unseparated Small Peak] = 0.3

Even very small shoulder peaks can be detected with additional parameter adjustments.

Fig. 2   Examples of Shoulder Peak Detection

2-2. Simple Adjustment of Peak-baseline Processing

Accurate detection of impurity peaks is essential for pharmaceutical quality control and other applications. Impurity peaks are often fused at the base of a major peak, and quantitative results obtained via area normalization can vary depending on the method used for peak-baseline processing. The method used for peak-baseline processing also differs based on the samples and testing objectives. With traditional methods, performing a specific type of peak-baseline processing requires the user to include time programming or perform peak integration manually.

However, i-PeakFinder has adjustable parameters in its basic settings for performing a specific type of peak-baseline processing, allowing the user to easily implement the optimum peak-baseline type in each situation. Fig. 3 shows a list of peak-baseline type in the settings window, Fig. 4 shows the result of peak-baseline type setting of an impurity peak that is fused at the base of a major peak, and Table 1 summarizes the quantitative results obtained via area normalization with different peak-baseline type settings. Peak-baseline processing appropriate for a particular situation can be simply performed by changing a few basic parameters.
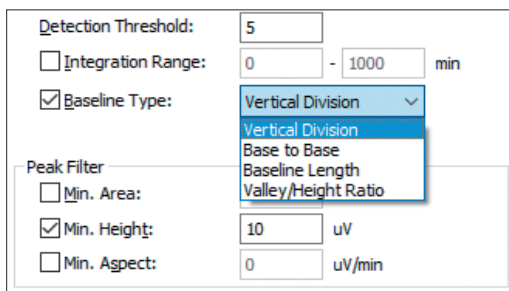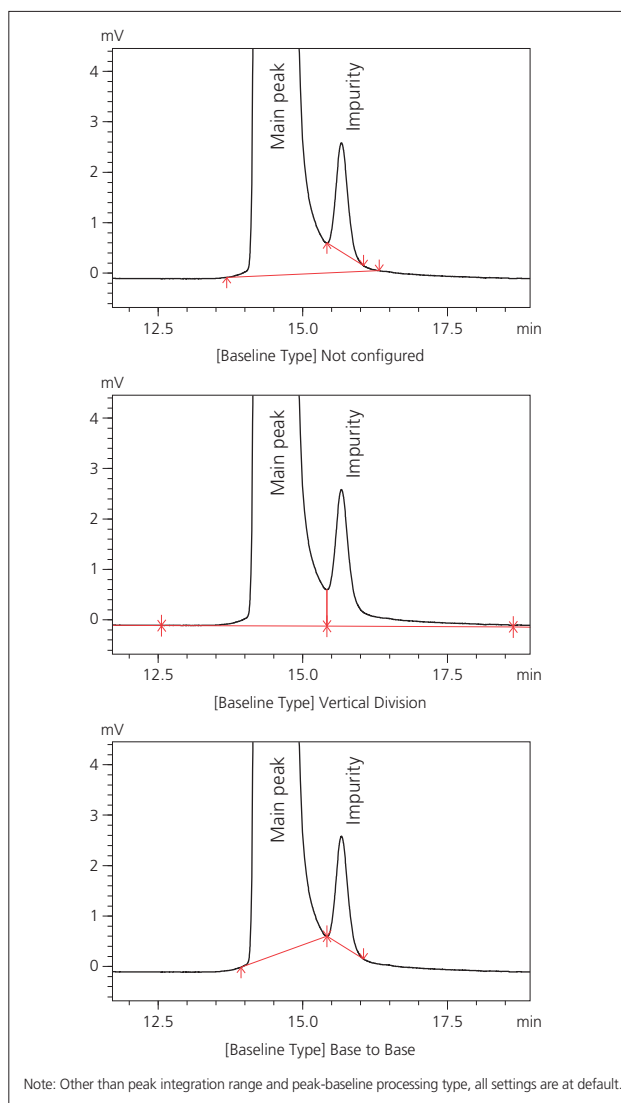

Fig. 3   Peak-baseline Type Settings

[Baseline Type] Not configured

[Baseline Type] Vertical Division

[Baseline Type] Base to Base

Note: Other than peak integration range and peak-baseline processing type, all settings are at default.

Fig. 4   Peak-baseline Processing Example

Table 1   Quantitative Results Obtained via Area Normalization with Different Methods of Peak-baseline Type

	Not configured	Vertical Division	Base to Base
Main peak	99.681	99.448	99.680
Impurity	0.160	0.338	0.160

2-3. Improved Peak-Baseline Positioning for Enhanced Reproducibility

When a target component is separated with peak tailing or leading in some cases, using a traditional peak integration method would result in variability in the calculated peak areas depending on which point along the trailing and leading edge was defined as the peak base. This affected the reproducibility of area results.

With i-PeakFinder, the user can adjust the height at which the start and end of a peak-baseline needs to be defined so that peak-baseline processing is consistent even with tailing and leading peaks.

The reproducibility of results obtained using the traditional method and i- PeakFinder is summarized in Table 2 for the chromatogram shown in Fig. 5. In the example below, the peak area results obtained using i-PeakFinder exhibit superior reproducibility compared to the traditional method.
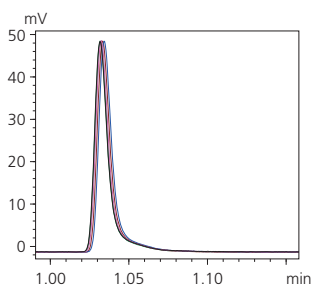
mV
50
40
30
20
10
0

1.00   1.05   1.10   min

Fig. 5   Chromatogram with Peak Tailing (N=5)

Table 2   Comparison of Area Reproducibility Between the Traditional Method and i-PeakFinder

	i-PeakFinder	Traditional method
%RSD	0.106	0.275
Processing	Peak-baseline Type: Base to Base Peak-Baseline Height* 2	Width: 1 s Slope: 2000 uV/min

* Described in more detail later in the article

3. Setting Parameters

i-PeakFinder not only performs highly accurate peak integration with default settings but also includes more detailed settings for adjusting the peak detection conditions (peak width and peak-baseline start and end heights) and peak-unifying conditions that determine how to combine multiple peaks. The most important of these settings will be explained here.

3-1. Basic Peak Detection Parameters

The basic parameters that allow the user to adjust peak detection conditions are the peak-baseline type mentioned above, peak detection threshold, and peak integration range. Using the detection threshold setting, the peaks below a certain threshold are not detected based on the estimated noise level calculated using a proprietary algorithm. Decreasing the peak detection threshold value allows the detection of smaller peaks. The peak integration range specifies the time range during which peaks will be detected. Fig. 6 shows the change in results produced by changing the peak detection threshold from the default setting of 5 to 2,000. These intuitive controls allow the user to detect or not to detect small peaks with a simple adjustment. Fig. 7 shows an example of adjusting the peak integration range. Without adjusting the peak integration range, all peaks fall within the range and the peak-baseline is affected by negative peaks. Setting the peak integration range to exclude negative peaks allows the user to configure an appropriate baseline.
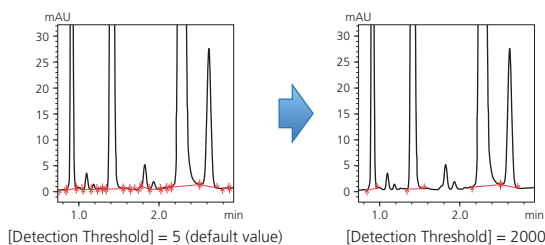

[Detection Threshold] = 5 (default value)   [Detection Threshold] = 2000

Fig. 6   Peak Detection Threshold

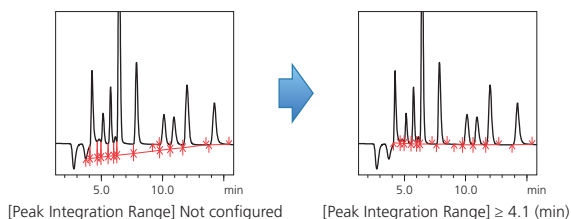[Peak Integration Range] Not configured   [Peak Integration Range] ≥ 4.1 (min)

Fig. 7   Peak Integration Range

3-2. Detailed Peak Detection Settings

For complex chromatograms, adjustments of the detection threshold, peak integration range, and peak-baseline type may not be enough to obtain the desired peak integration results. i-PeakFinder is compatible with a wide variety of chromatograms and allows the user to configure more detailed peak detection conditions. Some of these detailed settings are described below:

(1) To Detect Peaks Not Affected by Noise [Minimum Half Width]

Smoothing is sometimes performed on chromatograms obtained via LCMS. If the noise frequency is close to the peak frequency, then it becomes difficult to determine peaks automatically and single peaks may be recognized as multiple peaks. In this situation, configuring the minimum half width setting ignores noise smaller than that value and ensures that peaks with a FWHM value above the set minimum value are detected among the peaks with a wide wave profile due to smoothing. Fig. 8 shows the difference made by increasing the minimum FWHM value. This feature is useful when noise can be observed in a peak.

[Minimum Half Width] Not configured   [Minimum Half Width] = 2
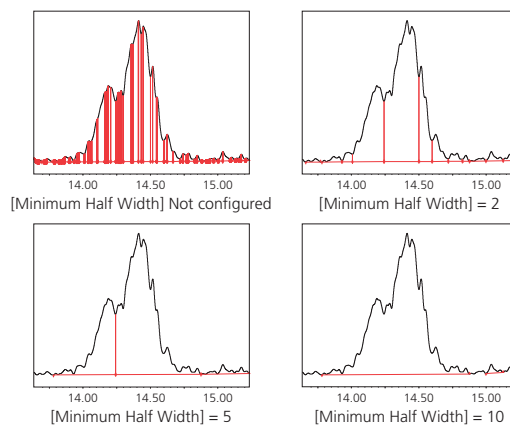[Minimum Half Width] = 5   [Minimum Half Width] = 10

Fig. 8   Example Configuration of Minimum FWHM

(2) To Ensure Peak Area Accuracy and Linearity [Peak Baseline Height]

With tailing peaks and chromatograms with a large amount of baseline noise, the peak start and end points can vary depending on the data, which can reduce area accuracy. By using the peak-baseline height setting, the peak start and end points are recognized as the product of a value entered for peak-baseline height and noise intensity calculated using a proprietary algorithm. Consequently, the larger the peak-baseline height value is, the higher the peak-baseline is positioned.

Using this setting provides good reproducibility in the determination of peak- baseline start and end points. This improves peak area reproducibility, as mentioned earlier in Table 2, and provides linearity across results obtained for a target component at different concentrations. Fig. 9 shows an example configuration of peak-baseline height where the baseline length of the tailing peaks is adjusted by specifying the peak-baseline height.
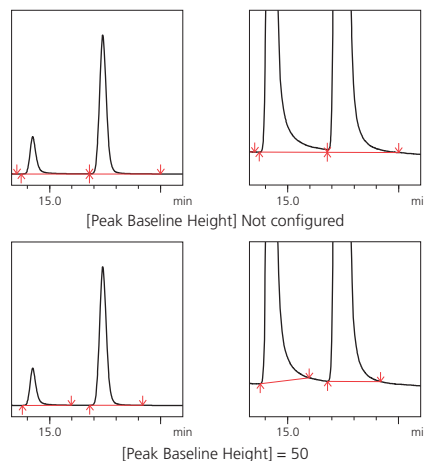

[Peak Baseline Height] Not configured
[Peak Baseline Height] = 50

Fig. 9   Example Configuration of Peak-Baseline Height for Tailing Peaks

3

(3) To Avoid Recognizing Long-Period Undulations as Peaks
[Maximum Half Width]

The maximum half width, which is the opposite of the minimum half width, is a parameter that can be specified to ignore larger peaks as baseline undulations. For example, Fig. 10 shows baseline drift appearing as a large baseline bulge that could be recognized as a peak. This undulation can be removed by specifying a maximum FWHM.

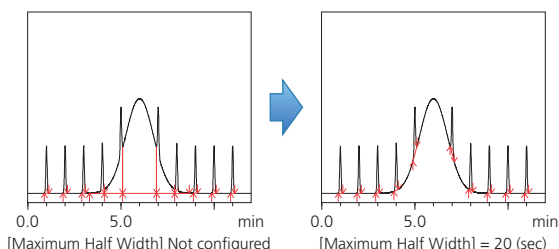[Maximum Half Width] Not configured   [Maximum Half Width] = 20 (sec)

Fig. 10   Example Configuration of Maximum FWHM

(4) To Unify Fused Peaks into a Single Peak
[Unify Peaks by Separation Width]

The minimum half width setting is used to avoid mistakenly recognizing noise as peaks, while unifying peaks by separation factor is used to combine fused peaks into a single peak. Fig. 11 shows three fused peaks. Configuring this setting will unify the two side peaks into the larger peak. Note that this setting is only effective for baseline intervals containing fused peak.

[Unify Peaks by Separation Width] Not configured   [Unify Peaks by Separation Width] = 2
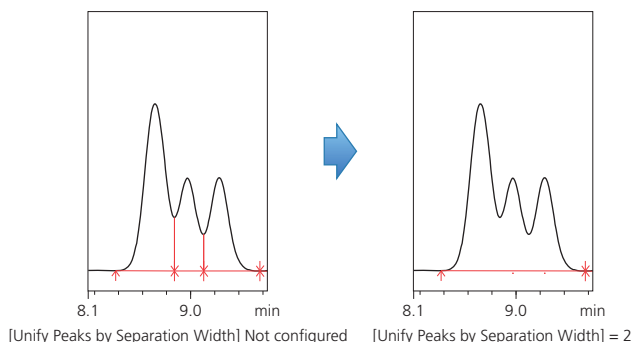
Fig. 11   Example of Unifying Unresolved Peaks

(5) To Decide Whether to Recognize Shoulder Peaks
[Unify Peaks by Shoulder Ratio]

When impurities were fused as shoulder peaks at the base of a main component peak, the traditional peak integration method required time programming or manual peak integration to detect the shoulder peak. i-PeakFinder allows easy detection of shoulder peaks and also allows the user to decide whether to recognize (or not) impurity peaks based on a threshold ratio of the main component peak height to the shoulder peak tangential height. Fig. 12 shows an example of shoulder peak detection implemented without time programming or manual peak integration and an example of using the threshold value to unify the shoulder peak with the main component peak. Configuring a threshold value can also be used as a condition for deciding whether to recognize impurity peaks.
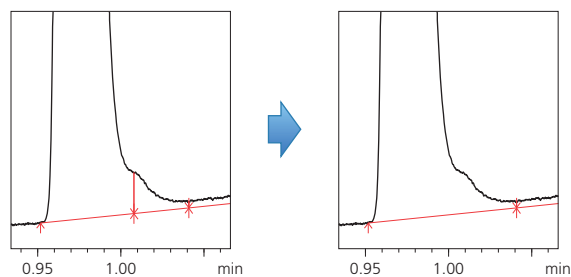

[Unify Peaks by Shoulder Ratio] Not configured   [Unify Peaks by Shoulder Ratio] = 0.01 (%)

Fig. 12   Example of Setting a Threshold for Recognizing Shoulder Peaks

4. Customizable Default Values

The i-PeakFinder parameters can be configured as the default values of methods. For example, if a user decides to use vertical division as the peak-baseline type, specifying vertical division as the default setting can omit the effort involved in adjusting the parameter for each new analysis. LabSolutions is an integrated workstation capable of controlling a range of different instrument models. However, the HPLC and GC systems occasionally require different default peak integration settings. Accordingly, default settings can be specified for each type of instrument (Fig. 13).
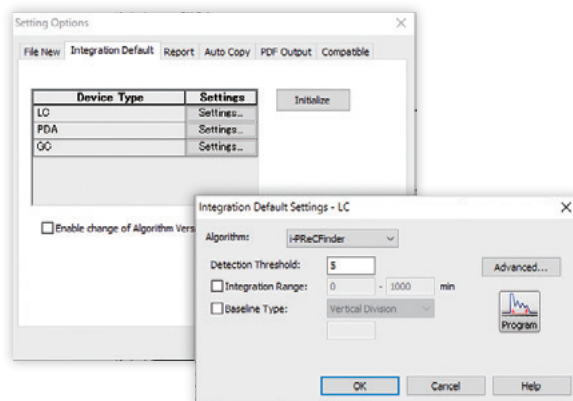

Fig. 13   The Default Settings Window

5. Summary

i-PeakFinder, a new peak integration algorithm developed by Shimadzu, can perform either automated peak integration or peak integration with simple settings adjustments, even for cases in which the traditional peak integration method requires time programming or manual peak integration for individual data sets. i-PeakFinder also allows the user to easily configure the peak-baseline type and perform accurate peak integration of small peaks.

Furthermore, i-PeakFinder can quickly and easily process large quantities of data without errors and improve the efficacy and reliability of analytical operations.

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