Advanced Informatics for Peak Detection and Quality Assurance with Comprehensive Two-Dimensional Liquid Chromatography (LCxLC)

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Comprehensive two-dimensional liquid chromatography (LCxLC) is a powerful new technology for advanced separations. LCxLC has promising applications in foods, essential oils, polymers, life sciences, and other fields. The information-rich data generated by LCxLC is large and complex, so automated processing is essential. Therefore, LCxLC data processing operations must be flexible, but configuring automated processing and assuring the quality of results are challenging tasks.

New methods and tools for optimizing automated processing and rapid quality assessment (QA) provide multiple visualizations and convenient graphical user interfaces (GUIs) to ensure more reliable data processing. *Interactive Blob Detection* allows users to precisely configure blob detection parameters for more reliable peak detection. *QA Rapid Screen* allows users to define sophisticated quality metrics, then quickly visualize results, correct any problems, and approve QA reports.

Interactive Blob Detection

Goals & Objectives

Interactive Blob Detection supports the creation of blob/peak detection filters and setting filter parameters to reduce false peak detections (e.g., caused by noise) without missing important chemical peaks. Blob filters are expressed in the Computer Language for Identifying Compounds (CLIC)™ and parameters can be set interactively with sliders to adjust minimum, maximum, and/or range values. Multiple filters can be used in concert to provide highly effective peak detection with greatly reduced false peak detections.

Interactive Blob Detection

The initial blob detection is implemented with very low built-in thresholds on peak size and intensity. Such settings result in many false (and/or undesired) peak detections. For example, the screenshots here show peak detections for a taxane standards mix. The fourteen standards are detected, but two small impurities also are detected.
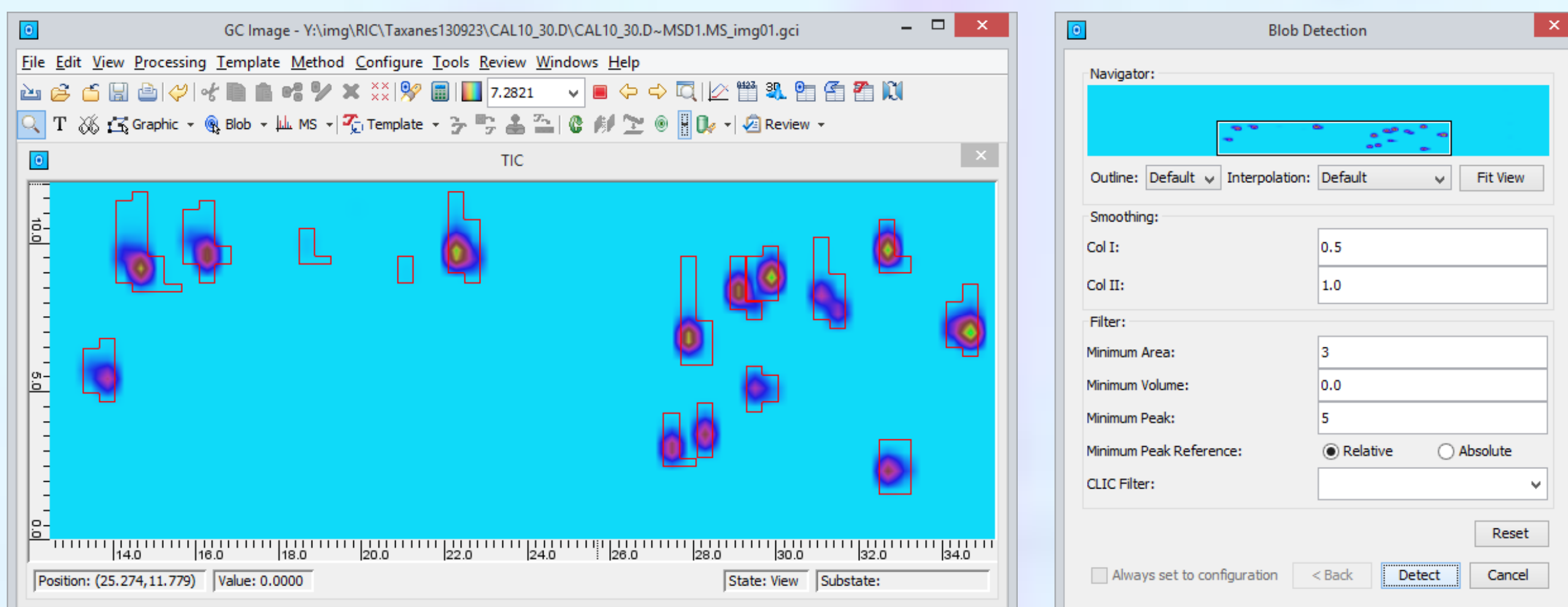
The undesired peaks can be filtered based on a threshold on the volume (i.e., the total intensity of the 2D peak). The slider sets the threshold value and the visualization allows the filter parameter to be set quickly so that only the peaks for the standards are detected.
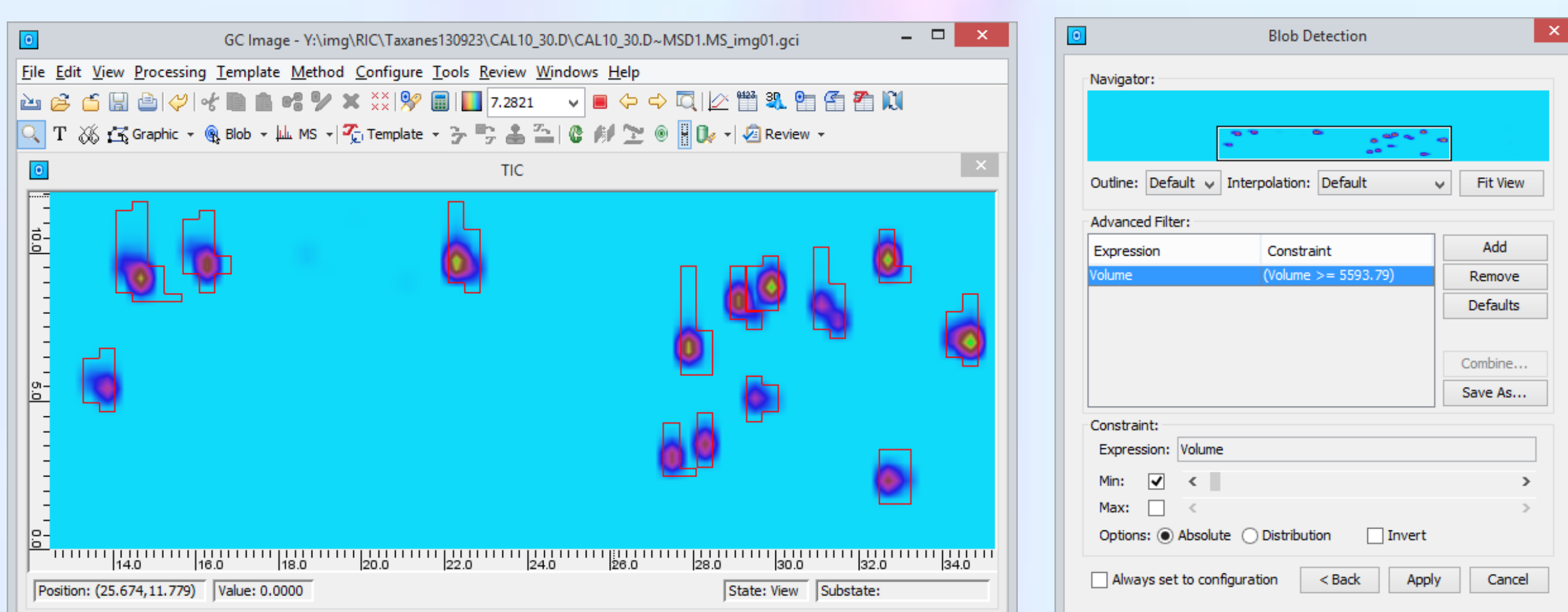
Filters can be implemented to constrain peak size, peak shape, retention times, signal intensity, signal-to-noise ratio, etc., then combined to achieve higher-quality peak detection.

Current Research

Current research is evaluating the effectiveness of various attributes for blob detection filters. This research deems peaks that can be matched reliably between replicate samples to be true peak and then constructs confusion matrices that can be used to optimize the tradeoff between false detections (false positives) and missed peaks (false negatives).

QA Rapid Screen

Goals & Objectives

QA Rapid Screen provides methods and tools to rapidly assure that LCxLC analytical results meet quality requirements. It supports:

- Automated QA for formal quality requirements, with reporting tools.
- Powerful quantitative measures for quality indicators, with tools for sorting and visualization.
- Multi-view visualization for inspection and quality assessment.
- Facilities for re-processing data to improve analytical quality.

Formal, Quantitative QA Metrics

Quantitative metrics with Computer Language for Identifying Compounds (CLIC). Examples of quality indicators:

- Chromatographic, e.g., peak shape, resolution, etc.
- Spectral, e.g., spectral purity, qualifier ion ratio.
- Identity, e.g., MS match factor, retention index, mass defect, etc.

Individual metrics or expressions combining metrics (e.g., with AND). Metrics can be global (for all peaks/features) or local (for specific peaks/features).

QA Operations

1. Configure QA metrics, views, and layout.
2. Rapidly navigate peak/feature tables ordered by quality indicators.
3. Review visualizations and reprocess data as necessary.
4. Approve or reject peaks/features, then generate QA report.