ACD/Labs' solutions for more robust, less time-consuming separations

4 Software Strategies to Master Method Development

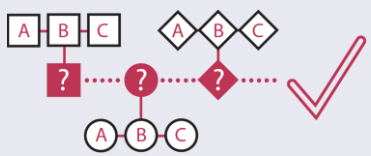
ACD/Labs®

Contents

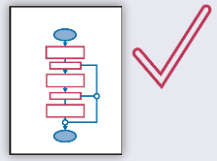
Why Method Development Software?

Traditional chromatographic approaches do not address the growing experiment complexity, greater regulatory requirements, and shrinking analytical staff complements of modern laboratories. Particularly, native instrument software is insufficient to accomplish project goals.

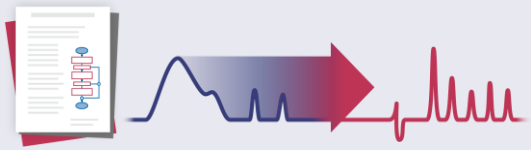
Chromatographers need advanced informatics solutions to ensure:



Method development is no longer a trial-and-error adventure



Identifying an optimal method is simple and straightforward



Experiments follow a comprehensive Quality by Design (QbD) strategy

Past work is easily accessible and shareable

Method Development Software Ensures:

Compliance with QbD Regulations

For separation scientists, QbD principles require a rational approach to method development and reporting, that ensures quality and safety through sound science and diligent risk management.

Elimination of Trial-and-Error Method Development

An empirical approach that haphazardly varies method parameters without clear rationale is not supported by regulatory agencies. This strategy demands a high resource and time cost that may require dozens of test runs and take weeks to accomplish.

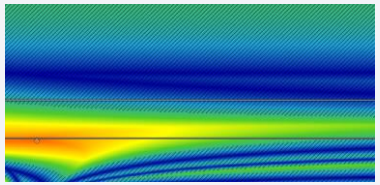
Simple & Straight-Forward Data Management

Separation scientists produce a lot of chromatographic data, which must be united with downstream results (UV, MS, etc.) to complete projects.

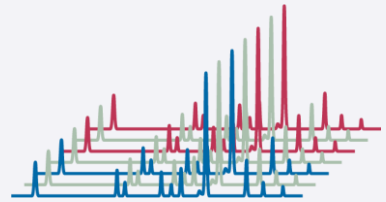
Native instrument software may archive and organize separations but does not offer comprehensive analytical data management options.

QbD Chromatography Best Practices

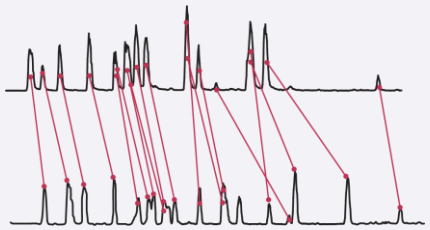
One software system:
Plan, execute, and evaluate experiments in one software system



Perform Systematic Optimization:
Thoroughly investigate the full Design of Experiment (DoE) space



Simulate Separations:
Model chromatograms to achieve method robustness



Track Peaks Algorithmically:
Use matching tools to ensure accuracy

Ensure Effective Data Management:
Comprehensively record all design and analysis decisions

Master Method Development

	Your Need:	Our Solution:
1. Set-up	Efficient Method Design *Create robust methods, in less time*	Column, pH, and Buffer Selection Tools Project Management Interface
2. Screen	Full Experimental Control *Execute optimized methods easily*	Method Strategy Builder Automated Method Execution Peak Tracking Tool
3. Simulate	Calculation of Optimal Conditions *Generate methods that align to success criteria*	Simulation Engine with Chemically Intelligent Separation Models
4. Study & Store	Complete Reporting & Databasing Capabilities *Store live results to simplify collaboration & reporting*	QbD Reporting Tool Comprehensive Databasing

Set-Up

Successful separations begin with sound parameter selection. Choosing an informed starting point and outlining an efficient optimization approach is critical.

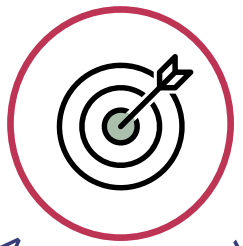
ACD/Labs simplifies the initial stages of method development by enabling rational condition identification based on accurate physicochemical and column parameters, for key compounds of interest. These parameters can then be used to calculate the most suitable initial method conditions—column, buffer, pH—using a variety of onboard selection tools.

Identify an orthogonal set of columns

Select initial pH values using accurate pK_a and log*D* estimates

Automatically calculate buffer concentrations that achieve target pHs

Select Initial Conditions:



Set-Up

1. Identify an Orthogonal Set of Columns

Use ACD/Labs' column selection tool to reliably collate a group of orthogonal columns for screening experiments. Further filter lists based on the compound class of interest and readily add new columns to the onboard database to diversify screening options. Compiling a diverse list of appropriate columns is the first step to designing an effective and efficient separation strategy.

- ☑ Diversify method screening options
- ☑ Increase method selectivity for target compound classes

Set-Up: Select Suitable pH & Buffer Combinations

Choose initial pH values using accurate pK_a and log*D* estimates, then automatically calculate buffer concentrations that achieve target pHs.

2. pH Selection Tool

- Calculate the most suitable pH values for separations based on target structures
- Array target compound log*D* curves to visualize ideal pH values based on phase distribution

☑ Reduce the number of experiments, save time

☑ Enable rational selection of method conditions (a QbD recommendation)

3. Buffer Suggestion Tool

- Calculate experimental buffer concentrations required to achieve target pH values
- Design precise buffer/solvent systems for optimal separations

☑ Eliminate errors from calculating buffer concentrations manually

Results

80%
Reduction in method development time

25-Fold
Improvement in method quality

Read the full case study

Achieving Better, Faster Method Development at Janssen Pharmaceuticals

The Challenge

At Janssen, small molecule method development for impurity identification was trial-and-error. Chromatographic parameters were typically selected at random and adapted in several experiments. This required manual evaluation of several raw chromatographs that was very complex and time-consuming, resulting in a non-optimal method.

The Solution

Adoption of an updated separation strategy that included ACD/AutoChrom enabled an 80% reduction in method development time and a 25-fold improvement in method quality, relative to the trial-and-error approach. Further, automation of raw data evaluation provided significant personnel cost savings.

Screen

Easily Enumerate a Strategy

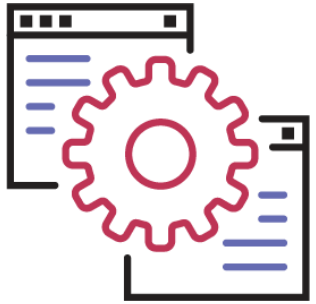
Seamlessly convert your list of experiments into a stepwise method strategy that intelligently screens and optimizes key conditions.

- Readily compile a list of screening experiments to test the sets of initial conditions selected during separation set-up.
- Automatically enumerate the experiment list into an iterative method strategy to organize screening experiments.

Automate Method Execution

Connect directly to Waters Empower and Agilent Chemstation systems to streamline workflows and transcribe error-free method conditions.

- Track peaks automatically to match all components between runs with ease.
- Define all separation parameters, instruct the instrument to execute experiments via CDS, and suggest the next experiment to perform.



Case Study Dow AgroSciences

The Challenge

The analytical R&D team at Dow AgroSciences sought to increase efficiency in chromatographic method parameter screening, as complex methods for new formulations could take up to several months to develop and validate. They partnered with ACD/Labs to enable a more consistent and effective method development approach.

The Solution

Implementation of AutoChrom® produced high-quality methods that consistently performed as expected over several months. Plus, automatic component tracking led to greater confidence in separation results, as the software identified peaks that may have been missed by manual analyses.

- ☑ Greater confidence in separation results
- ☑ More consistent and effective method development approach

> We have spent several months developing a method without successfully resolving a critical pair of peaks. Using the software, we managed to generate a method that resolved those peaks in less than 48 hours.

Read the full case study

Simulate

Choose initial pH values using accurate pK_a and log*D* estimates, then automatically calculate buffer concentrations that achieve target pHs.

Generate a Method with Ideal Suitability

Simulate separations to predict the impact of adjusting method conditions, without the need to perform countless experiments.

- Visualize resolution maps that are color-coded according to the success criteria that determine unsuitability in each region
- Perform simulations to produce methods that better align with predefined success criteria

☑ Directly observe the relationship between specific success criteria and suitability

Further Optimize via Robustness Testing

Refine suitable methods further by testing robustness in order to achieve optimal conditions. Readily assess several variables including flow rate, temperature, gradient, pH, buffer, and solvent ratio.

- Evaluate robustness automatically by generating a list of iterative experiments derived from the method of interest

☑ Quantify the predicted impact of changing method conditions on separations

Protein & Peptide Simulation

Results

<1%
Deviation between calculated and experimental RTs

Same Accuracy
Modelling RPC & IEC gradient chromatography for proteins & small molecules

Read the application note

Adapting Retention Models to Support Optimized Separation of Proteins & Peptides

The Challenge

The growing interest in biological drugs has led to proteins and peptides becoming analytes of increasing importance in pharmaceutical laboratories. However, commercial retention modeling of common chromatographic techniques used to separate these molecules, reversed phase chromatography (RPC), and ion exchange chromatography (IEC) has lagged behind biopharmaceutical demand.

The Solution

Adaptation of ACD/Method Selection Suite to model protein and peptide separations via RPC & IEC gradient chromatography demonstrated equivalent accuracy to small molecule simulations. Notably, a 2nd order temperature model was required to correctly model retention behavior of proteins due to its influence on protein structure (folded/unfolded).

Study & Store

A wealth of optimal separation methods and quality chromatographic data is useless if it can't be effectively shared, re-used, or re-purposed.

In addition to industry-leading method development and data analysis solutions, ACD/Labs also provides valuable tools to effortlessly communicate and collaborate on chromatography projects.

Readily generate comprehensive reports, including all method development details and analytical interpretations, and easily save pertinent methods and results to shared databases.

Process & Interpret All Data

- ☑ Automate repetitive tasks

Produce Comprehensive Reports

- ☑ Rational method generation
- ☑ Ensure data traceability

Collaborate Easily via Databasing

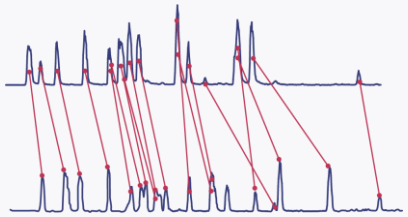
- ☑ Preserve critical knowledge
- ☑ Support collaboration

Study & Store

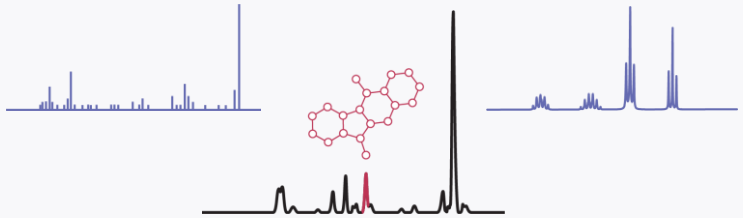
Process & Interpret All Data

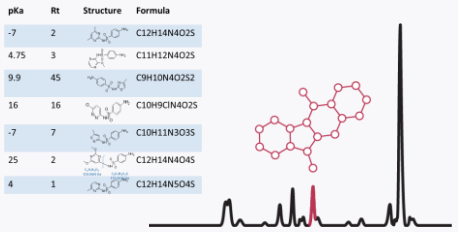
Unite chromatographic results with associated project data, importable from virtually all instrument vendors, to readily perform collective processing and interpretation functions.

Perform routine processing including peak smoothing, peak picking, and baseline correction



Assign a structure to a peak to view its consistency with MS data and/or verify alignment with NMR spectra





pKa	Rt	Structure	Formula
-7	2		C12H14N4O2S
4.75	3		C11H12N4O2S
9.9	45		C9H10N4O2S2
16	16		C10H9ClN4O2S
-7	7		C10H11N3O3S
25	2		C12H14N4O4S
4	1		C12H14N5O4S

Query analytical databases for experimental spectra and overlay results with project data

Create macros to automate repetitive tasks

Study & Store

Produce Comprehensive Reports

Perform straightforward reporting that clearly communicates method and experimental parameters and follows QbD principles.

- Capture complete project information in one document, that also includes instrument configuration to ensure data traceability
- Arrange information in a logical format that provides comprehensive evidence of rational method generation and justifiable data analysis
- Choose from a series of available report elements:
  - Instrument configuration
  - Method strategy
  - Method condition selection
  - Optimization decisions
  - Method operable design region (MODR)
  - Chromatograms
  - Chemical structures
  - Peak tables

Collaborate Easily via Databasing

Enable intuitive storage of multi-technique results, along with their interpretation(s), to preserve critical knowledge and support collaboration.

- Search databases by numerous spectral, structural, and text parameters
- Generate comprehensive experimental databases that can be viewed in a variety of configurations (default, table, tile, etc.)

Case Study Friedrich-Schiller-Universität Jena (FSUJ)

The Challenge

Drs. Peter Bellstedt and Nico Ueberschaar oversee analytical techniques at the FSUJ Faculty of Chemistry and Earth Sciences. They were eager to consolidate analytical data management across the department and reduce the experimental costs, time, and effort of analyses that were inefficiently distributed across multiple instruments in different laboratories.

The Solution

Implementation of various ACD/Labs tools provided access to a centralized database for housing all experimental methods, data, and analyses, eliminating a major data distribution bottleneck. New findings can now be seamlessly incorporated into ongoing projects, and previously stored data is readily available for reexamination and reinterpretation.

☑ Reduce experimental costs, time, and effort of analyses

> Whereas prior to software implementation key analytical technique knowledge was isolated in different working groups…now all methodologies and data are housed in a centralized server environment for easy sharing between individuals and laboratories.

Read the full case study

Next Steps

ACD/Labs has a variety of tools designed to fit the needs of any separation scientist and is ready to help you with all stages of your method development projects:

1. **Set-Up:** Create robust methods, in less time
2. **Screen:** Easily execute optimized methods
3. **Simulate:** Calculate optimal conditions
4. **Study & Store:** Simplify collaboration and reporting

Is your organization ready to save time and effort on method development strategies? Do you want to:

- Eliminate trial-and-error method development?
- Incorporate QbD principles into separation strategies?
- Support simple and straightforward generation of optimal methods?
- Ensure that previous projects are easily accessible and shareable?

To learn more about how ACD/Labs can help you achieve this, contact us to get more information.

Contact Us