Workflow and Project Management in Chromatographic Method Development

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NJUM September 25, 2007

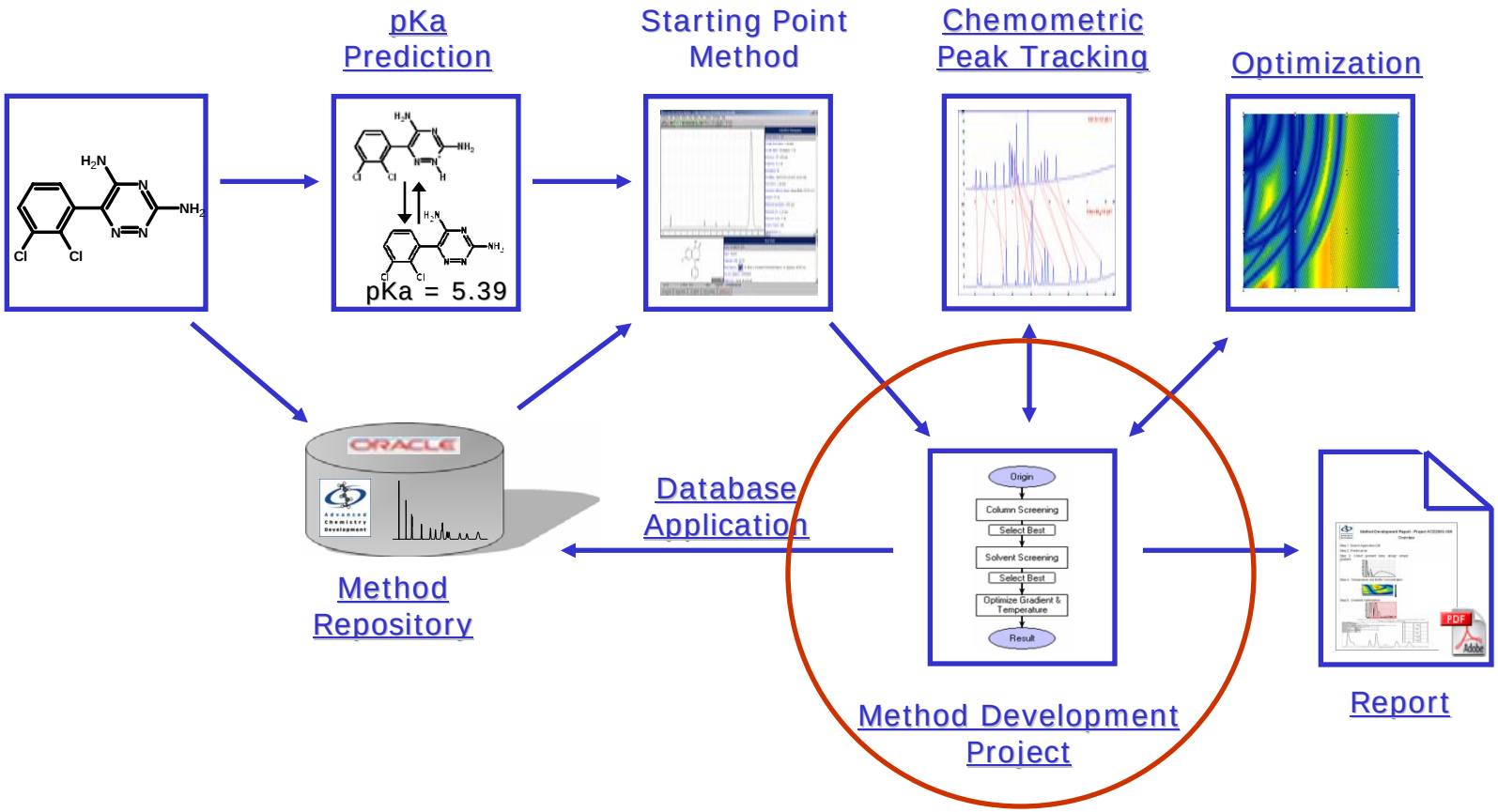
Advanced Chemistry Development, Inc. (ACD/Labs)

Visionary Software Advancing Research

Outline

- Overview of MDS
- Project Management
- Tour of the Method Development Console
- Strategies
- Data Management from a Method Point of View
- Composite samples – a new concept in method development

A Better Method Development Workflow



The Need for Project Management

- There are *lots* of data associated with a sample
  - We need a way to link/group/manipulate these datafiles in a way that's logical to method development
  - We must have a way to overview huge amounts of hyphenated data quickly.
- Method development projects are typically multi-session:
  - State of project needs to be retained
  - Information needs to be sorted
- Information transfer was one-way:
  - Resolution maps received information and built models, but no part of the decision-making was linked to the data
- When a method is delivered, it's not always clear why it was designed that way
  - We need to communicate what was done, and why

Project Management for Chromatographic MethDev

- Method Development Strategies:
  - Creation
  - Management
  - Communication
- Hyphenated data management
- Online workflow support

A Tour of the Method Development Console

ACD/AutoChrom: Task - [Task @ Virtual Mode >> C:\Documents a...ed\Project 2\project_LCMS_UV_stage 4.awx]

Workspace Screen Forms Instrument Tools Manage Task Planning ACD/Labs Help

Rej Irrel Start Stop Complete Execute Discard Suggest Accept

Components

#	Name	Mass	tR	Width	As	Area	Conc.
18	340.19	339.19	9.45	0.22	0.8	0.034	
12	368.2	367.19	8.59	0.19	1.1	0.001	0.003
15	396.2	395.2	11.61	0.17	0.9	0.001	0.004

Wave browser

Assistant

Column & Buffer Selection

Now you are allowed to stop the task.

Alternatively you are able to compare the following experiments from the wave:

XBridge C18 & pH 2.5
XBridge Shield & pH 2.5
XBridge Phenyl & pH 2.5
Platinum EPS C18 & pH 2.5
Curosil PFP & pH 2.5
XBridge C18 & pH 4.8
XBridge Shield & pH 4.8
XBridge Phenyl & pH 4.8
Platinum EPS C18 & pH 4.8

Assistant / Method / Strategy / Spectrum / Chromatogram / Notes / Picture

Waves

#	Wave	Status	Attribute
1	Column & Buffer	Planned	

Query for Signals

Query	Qty
All Signals	120
Selected Si...	6
Chromatogr...	0
Spectral Data	120
Processed ...	120
Table of Pe...	120
MS Detector	60
UV Detector	60
S5	40
S6	40
S7	40
XBridge C18	24
XBridge Shi...	24

Signals

W1_COL1_25_S5.raw[1,MS]
W1_COL1_25_S5.raw[34,DAD]
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W1_COL4_25_S5.raw[28,DAD]
W1_COL5_25_S5.raw[1,MS]
W1_COL5_25_S5.raw[29,DAD]
W1_COL1_48_S5.raw[1,MS]
W1_COL1_48_S5.raw[14,DAD]
W1_COL2_48_S5.raw[1,MS]
W1_COL2_48_S5.raw[17,DAD]

Experiments

Experiment	Rs Score	Total	205.14	309.18	426.1
XBridge C18 & pH 2.5	0.376	22/31	5.1	5.69	8
XBridge Shield & pH 2.5	0.539	24/31	5.26	5.78	8
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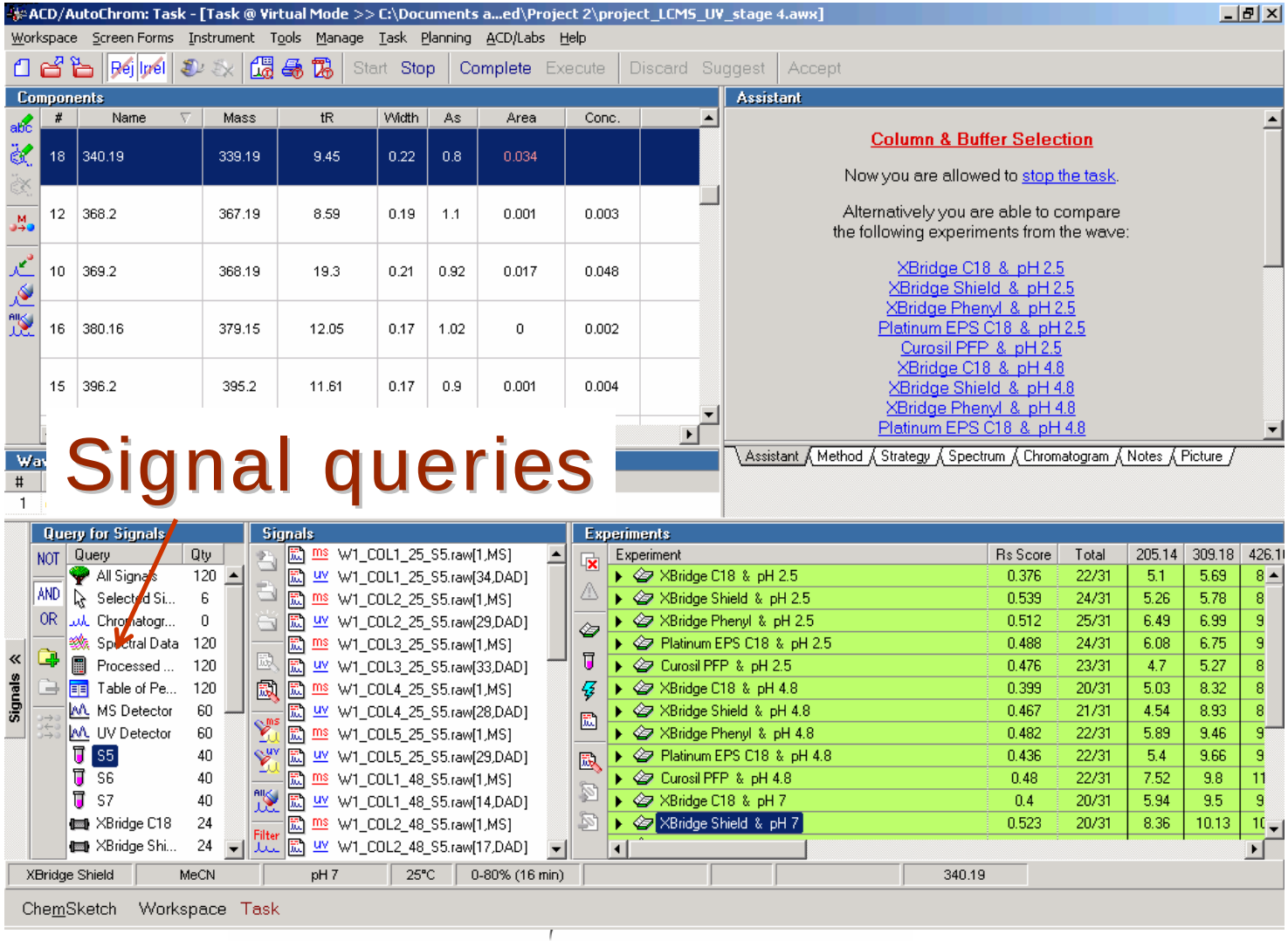
Curosil PFP & pH 4.8	0.48	22/31	7.52	9.8	11
XBridge C18 & pH 7	0.4	20/31	5.94	9.5	9
XBridge Shield & pH 7	0.523	20/31	8.36	10.13	10

XBridge Shield | MeCN | pH 7 | 25°C | 0-80% (16 min) | 340.19

ChemSketch Workspace Task

A Tour of the Method Development Console



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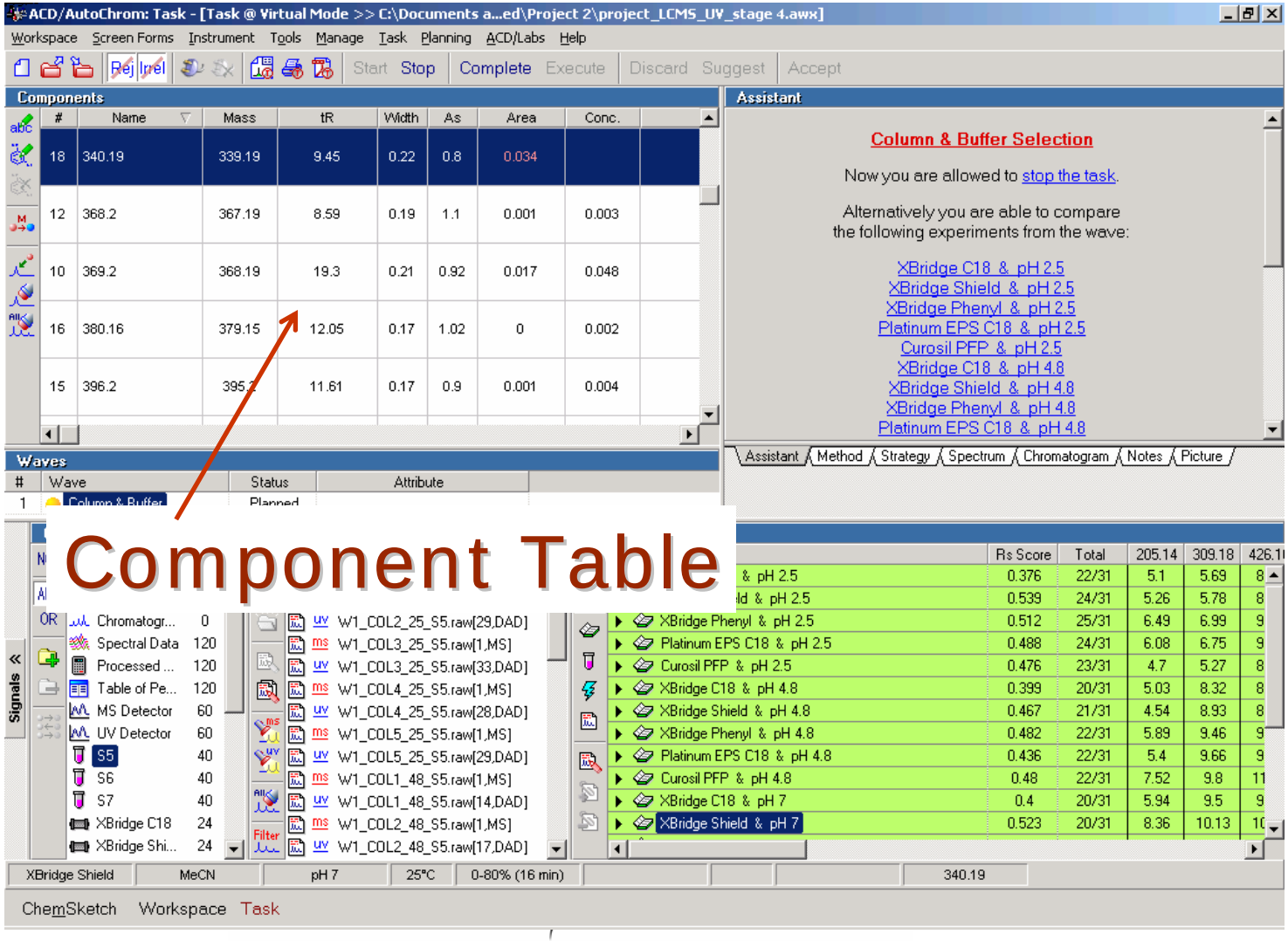

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ChemSketch Workspace Task

Experiments

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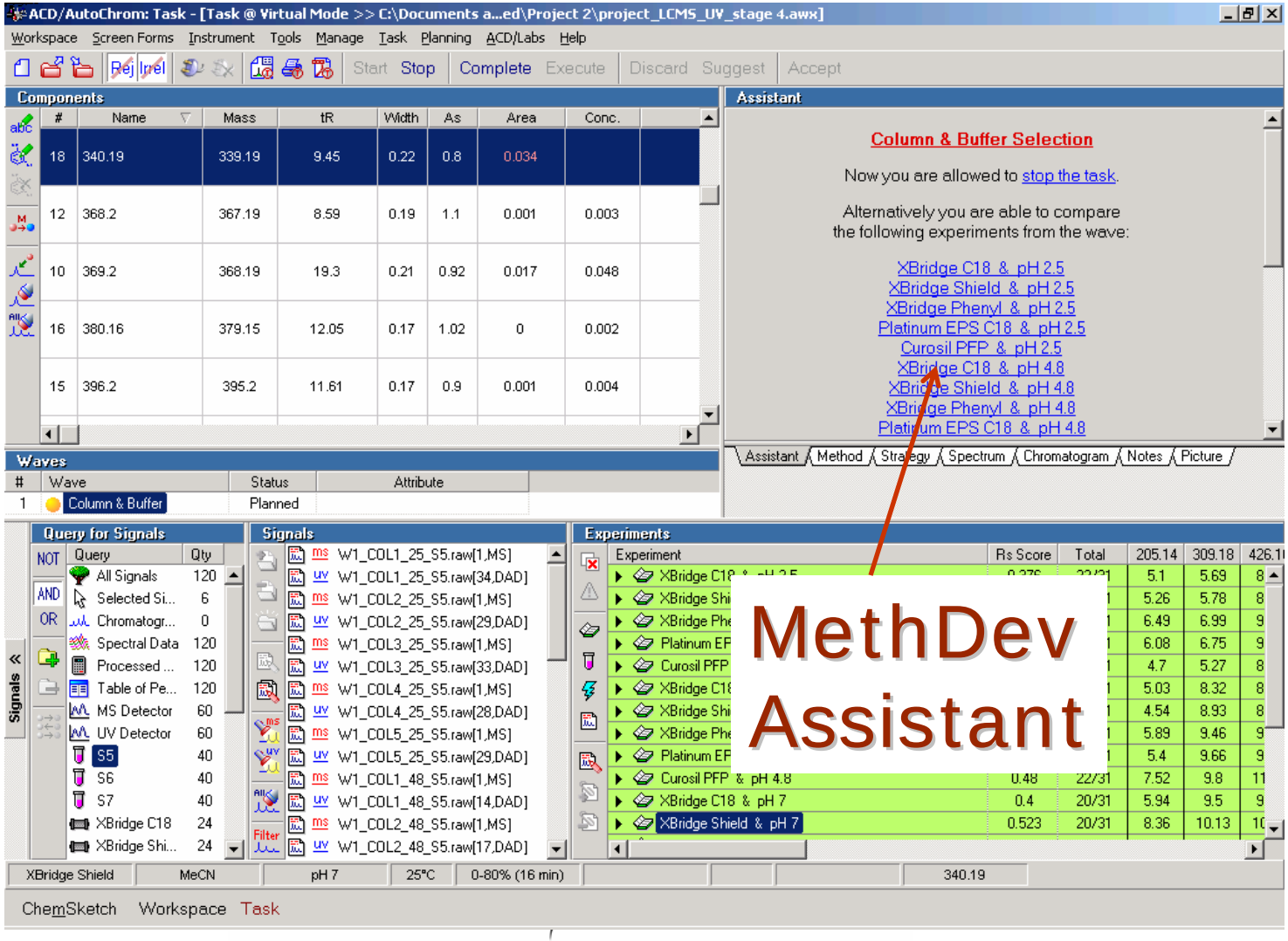

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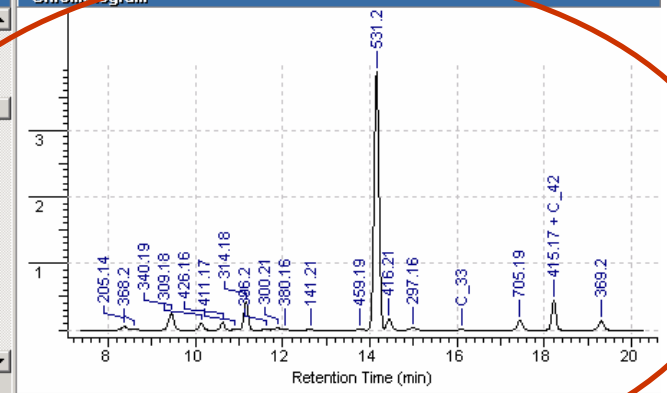
Chromatogram



Assistant | Method | Strategy | Spectrum | Chromatogram | Notes | Picture

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NOT AND OR

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ChemSketch Workspace Task

Workflow Support

- Method development is typically multi-session:
  - Design wave
  - Collect data
  - Process (UV-MAP, MS-MAP, reconcile)
  - Review
  - ...Repeat...
- It can be challenging:
  - Where was I?
  - Where is the data from a given injection?
  - What do I do next?

Visionary Software Advancing Research

The MethDev Assistant

- Remembers where you are in your work
- Hyperlinks to the next step in the project/strategy
- Evaluates extracted information
- Designs experiments for each method development wave in light of the strategy, and the elution data

The Assistant

Assistant

Column & Buffer Selection

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the following experiments from the wave:

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Platinum EPS C18 & pH 4.8
Curosil PFP & pH 4.8
XBridge C18 & pH 7
XBridge Shield & pH 7
XBridge Phenyl & pH 7
Platinum EPS C18 & pH 7
Curosil PFP & pH 7
XBridge C18 & pH 9
XBridge Shield & pH 9
XBridge Phenyl & pH 9
Platinum EPS C18 & pH 9
Curosil PFP & pH 9

and choose the best one using your own criteria
or with assistance of ACD/LC Simulator.

When the best experiment (in your opinion) is selected,
you should complete the current wave.

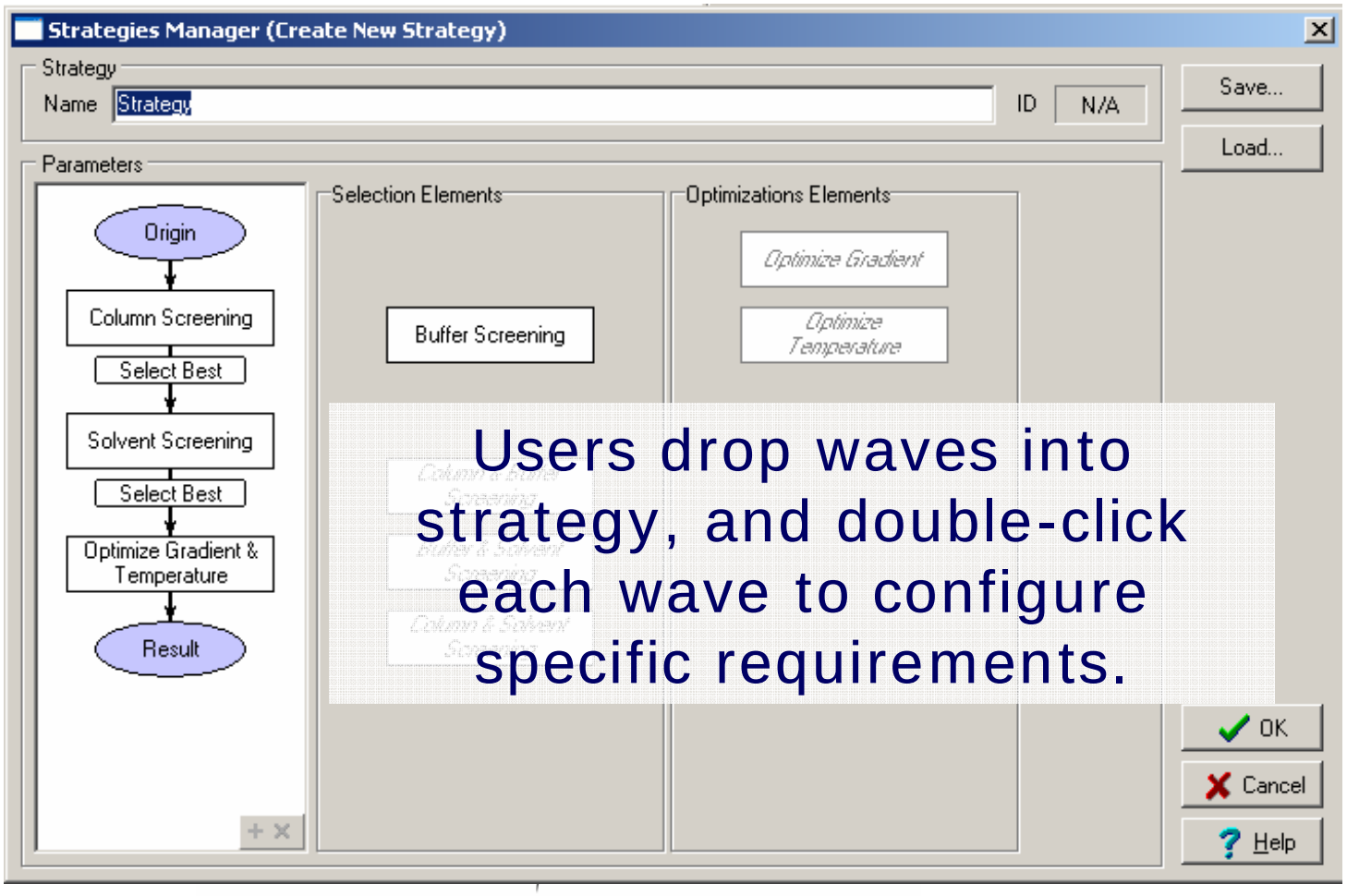
Assistant | Method | Strategy | Spectrum | Chromatogram | Notes | Picture

Compliance to Procedures

- Most groups have accepted, validated MethDev procedures.
- Are SOPs followed?
- How much time is spent on training new staff?
- When SOPs are ignored, quality suffers and unnecessary experiments are performed.

MDS Strategy Manager

Strategy Builder



Users drop waves into strategy, and double-click each wave to configure specific requirements.

MDS Strategy Manager

- Design and management of strategies
- Links between strategy and project
- Automatic “next injection” design through MethDev Assistant
- The MethDev Project Viewer allows reviewers to see the exact strategy followed.

Effective Reporting

- What was done? Why?
- Process auditing
- Facilitates:
  - Validation
  - Troubleshooting

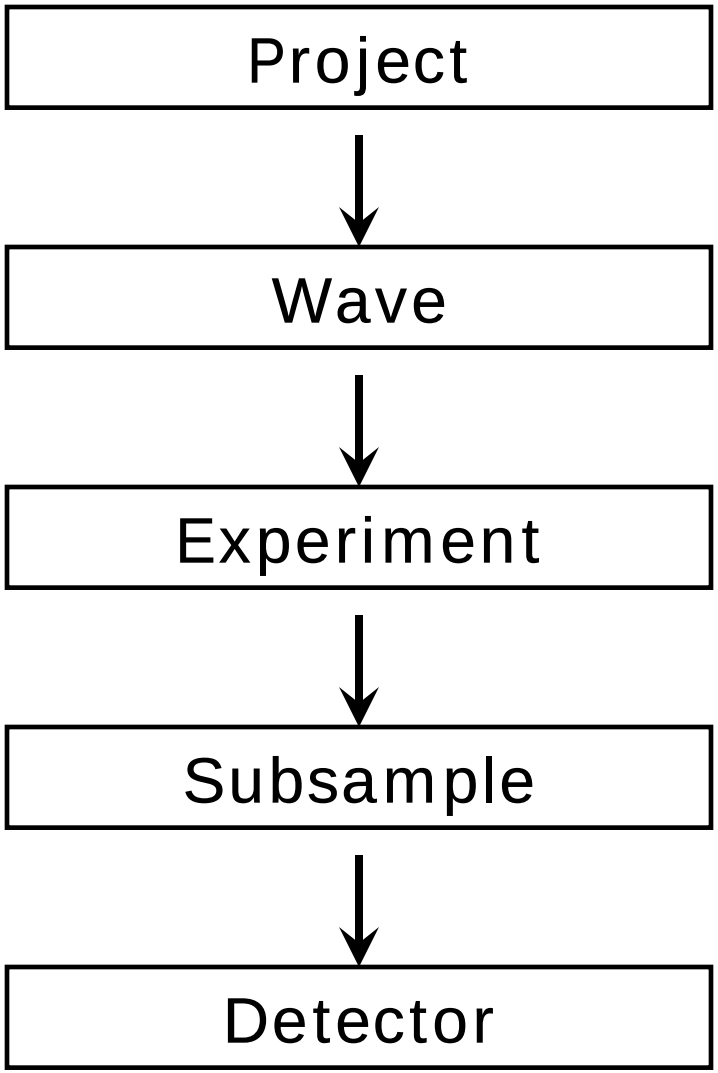
Project Reports

- The method development console contains a complete report of all injections/methods/elution data:
  - Grouped by wave
  - Component spectral views
  - Quick-view chromatograms
  - Links to full hyphenated data and retention models

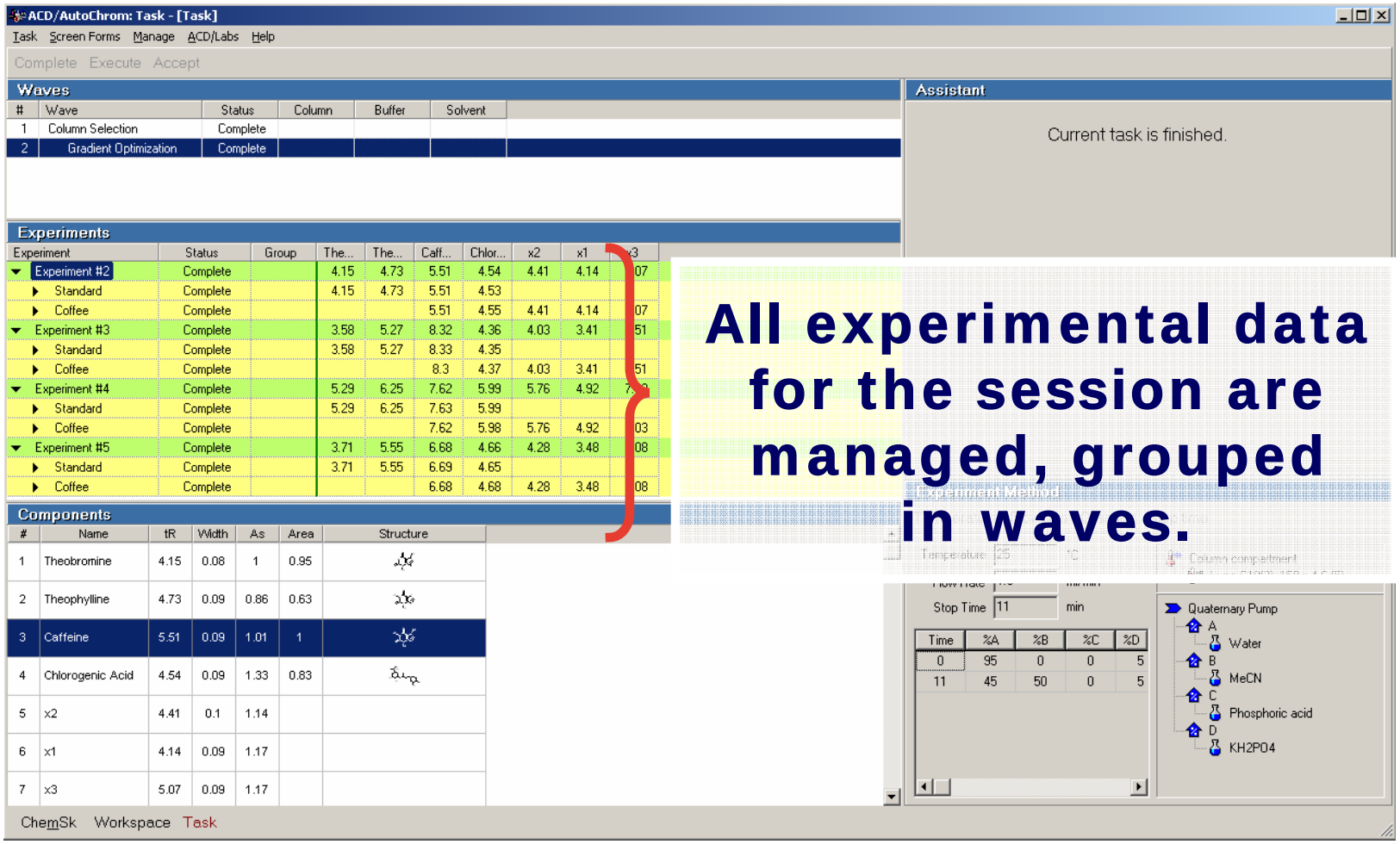
Data Organization

- The MDS interface is designed specifically for transparent communication of method development work
- Wave data are arranged hierarchically

Data Hierarchy

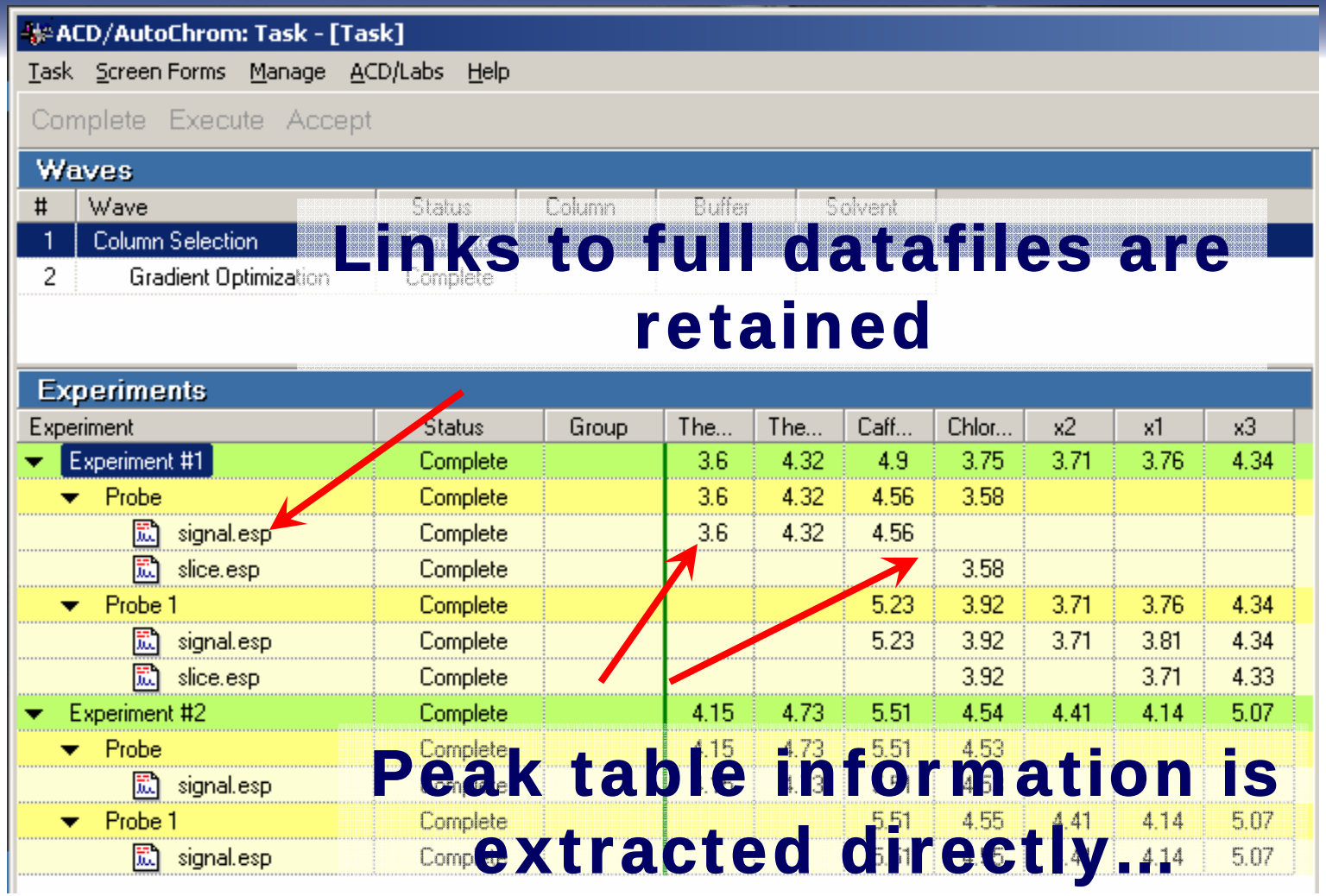


Managing Experimental Information



All experimental data for the session are managed, grouped in waves.

Hyphenated Data Management



Links to full datafiles are retained

Peak table information is extracted directly…

Hyphenated Data Management

ACD/AutoChrom: Task - [Task]

Task Screen Forms Manage ACD/Labs Help

Complete Execute Accept

Waves

#	Wave	
1	Column Selection	Complete
2	Gradient Optimization	Complete

...and summarized in an overall peak table.

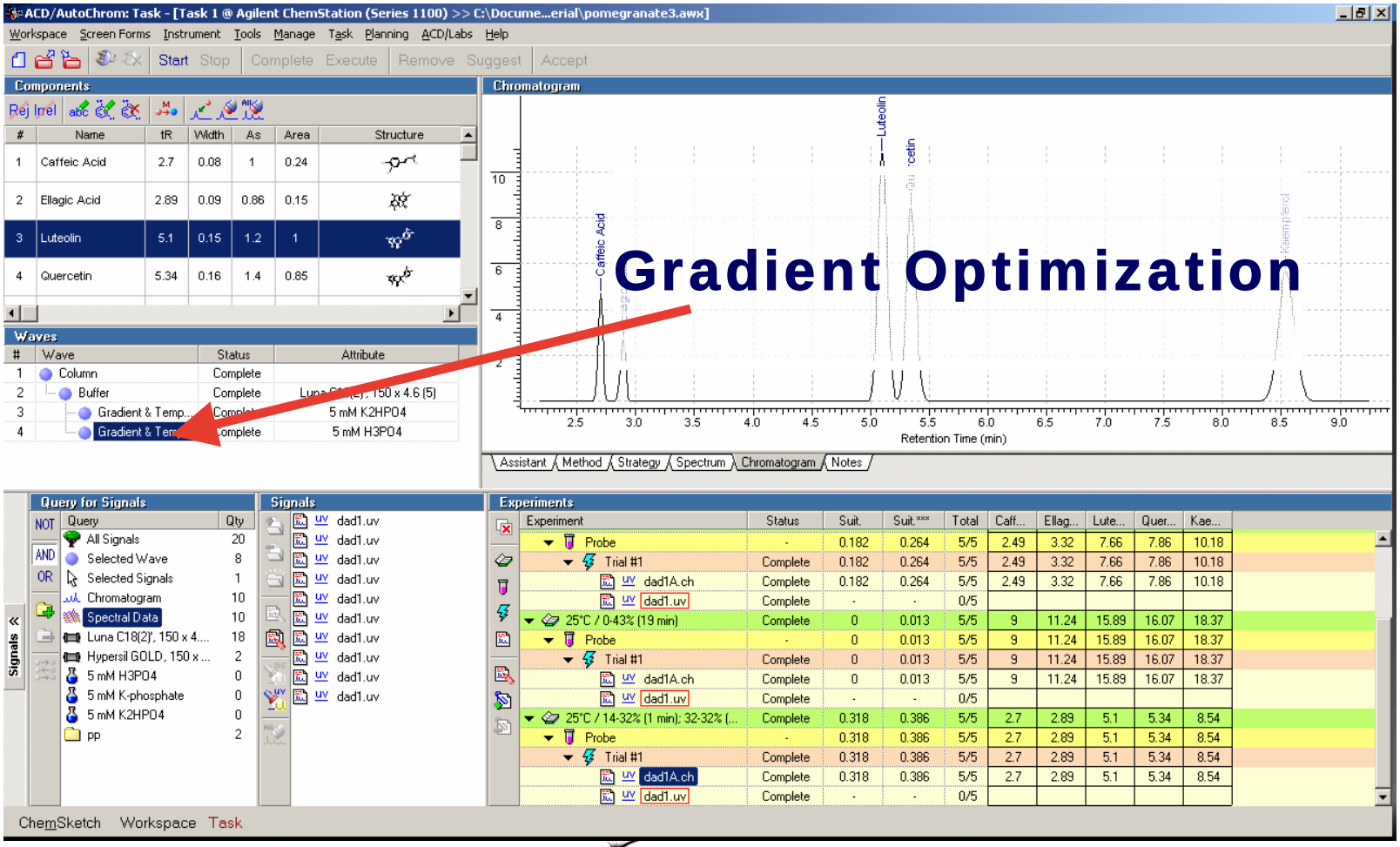
Experiments

Experiment	Status	Group	The...	The...	Caff...	Chlor...	x2	x1	x3
Experiment #1	Complete		3.6	4.32	4.9	3.75	3.71	3.76	4.34
Probe	Complete		3.6	4.32	4.56	3.58			
signal.esp	Complete		3.6	4.32	4.56				
slice.esp	Complete					3.58			
Probe 1	Complete				5.23	3.92	3.71	3.76	4.34
signal.esp	Complete				5.23	3.92	3.71	3.81	4.34
slice.esp	Complete					3.92		3.71	4.33
Experiment #2	Complete		4.15	4.73	5.51	4.54	4.41	4.14	5.07
Probe	Complete		4.15	4.73	5.51	4.53			
signal.esp	Complete								
Probe 1	Complete				5.51	4.55	4.41	4.14	5.07
signal.esp	Complete							4.14	5.07

Peak table information is extracted directly...

Managing Method Development Sessions

Linking multiple method development waves



Extracted Component Spectra

ACD/AutoChrom: Task - [Task @ Virtual Console >> D:\My Documents\Margare...hrom\AutoChrom\DEMO\demo.awx]

Workspace Screen Forms Instrument Tools Manage Task Planning ACD/Labs Help

Start Stop Complete Execute Remove Suggest Accept

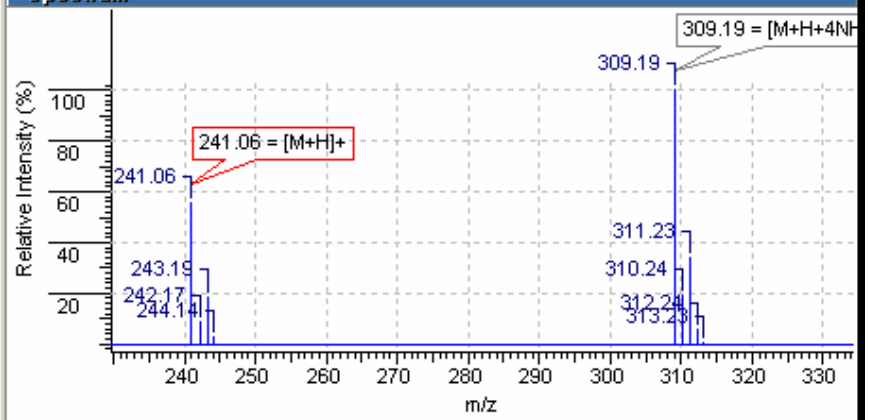
Components

#	Name	tR	Width	As	Area
1	241.06	9.02	0.26	1	1
2	426.28	8.37	0.24	1	1
3	314.21	11.65	0.33	1	1
4	300.2	12.32	0.35	1	1
5	416.28	10.78	0.31	1	1

Waves

#	Wave	Status	Attribut
1	Column & Buffer	Complete	

Spectrum



Assistant Method Strategy Spectrum Chromatogram Notes

Experiments

Experiment	Status	Min Rs	Rs Score	Total	241.06	426.28	314.21	300.2	416.28	297.22	531.27
XBridge C18, 150 x 4.6 (3.5) & ...	Complete	1.088	0.918	11/11	8.56	8.89	10.37	10.77	11.19	11.95	12.24
S1	-	1.088	0.918	11/11	8.56	8.89	10.37	10.77	11.19	11.95	12.24
XBridge Shield RP18, 150 x 4.6 ...	Complete	0.877	0.9	11/11	8.97	8.27	11.45	12.13	10.86	13.69	13.36
S1	-	1.726	1	11/11	9.02	8.37	11.64	12.32	10.78	13.57	13.35
Trial #1	Complete	1.726	1	11/11	9.02	8.37	11.64	12.32	10.78	13.57	13.35
uv W1_COL2_10_4...	Complete	1.725	1	11/11	9.02	8.37	11.63	12.31	10.78	13.56	13.35
ms W1_COL2_10_4...	Complete	0.562	0.8	11/11	9.02	8.37	11.65	12.32	10.78	13.57	13.35
S5	-	0.233	0.725	11/11	8.92	8.18	11.25	11.94	10.94	13.81	13.37
XBridge Phenyl, 150 x 4.6 (3.5) ...	Complete	1.371	0.974	11/11	8.64	7.68	11.39	11.12	9.48	11.59	11.95

Signals

ChemSketch Workspace Task

Composite Samples

Composite Chromatogram Examples

- (Trivial) individual standards injected separately
- Blank, and sample
- Standard(s) and “real sample”
- *Forced-degradation samples*

A Data Explosion

- Forced degradation samples:
  - Complex
  - Low level, unknown impurities
  - Multiple samples – one method
    - Standards
    - Blanks
    - Forced degradation – HOOH, H^+, OH^-, etc.
  - LOTS of hyphenated data

Visionary Software Advancing Research

Forced Degradation: Too Much Data?

- Each set of chromatographic conditions can give 18 (!) traces:
  - 6 subsamples
  - 3 detectors
- All elution data must be cross-correlated and transferred to method design software

Support for Composite Samples

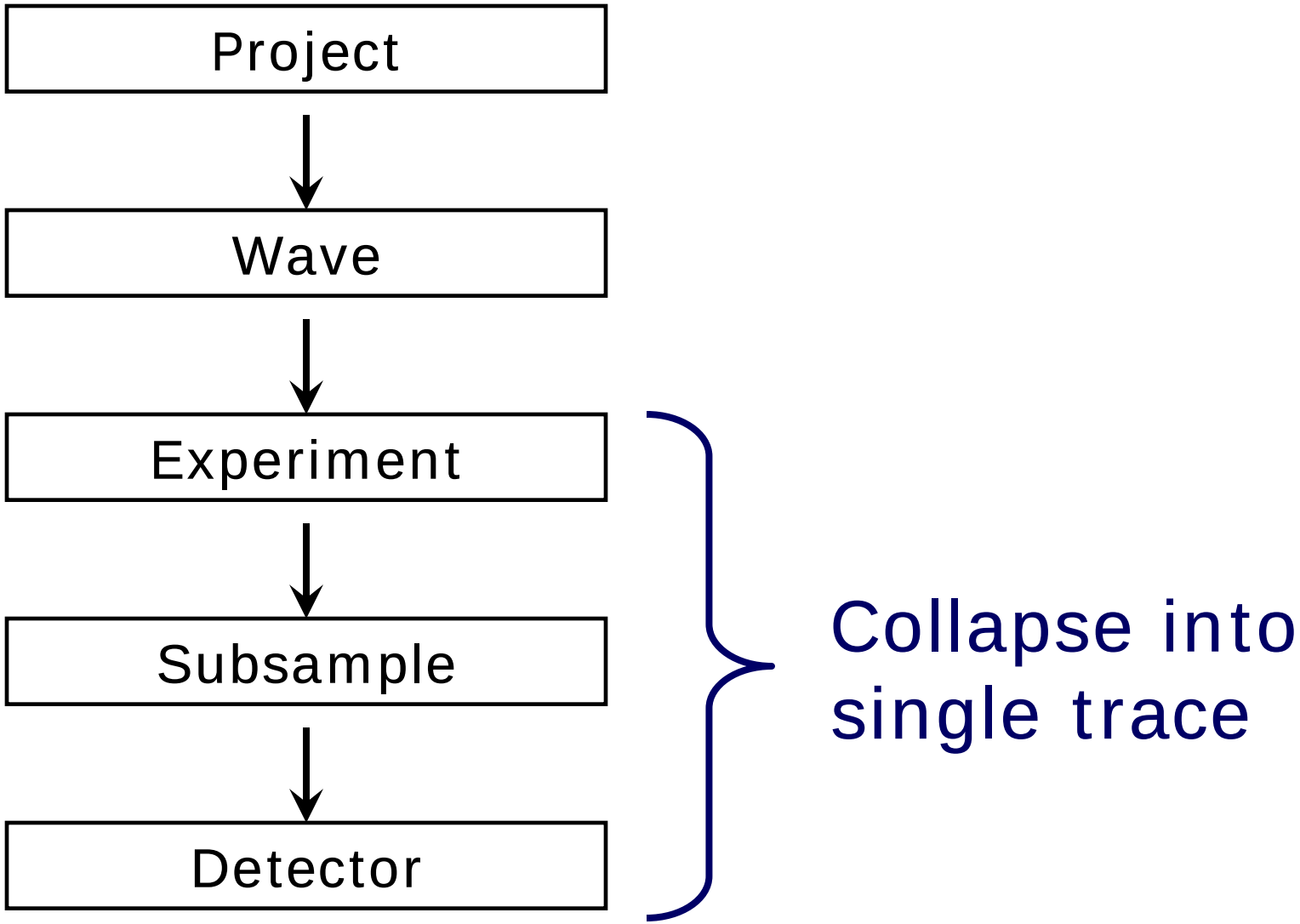
- The Method Development Console can manage multiple injections for each method
- Components can be unique to one subsample, or shared
- Components must be reconciled

Software can simplify this process

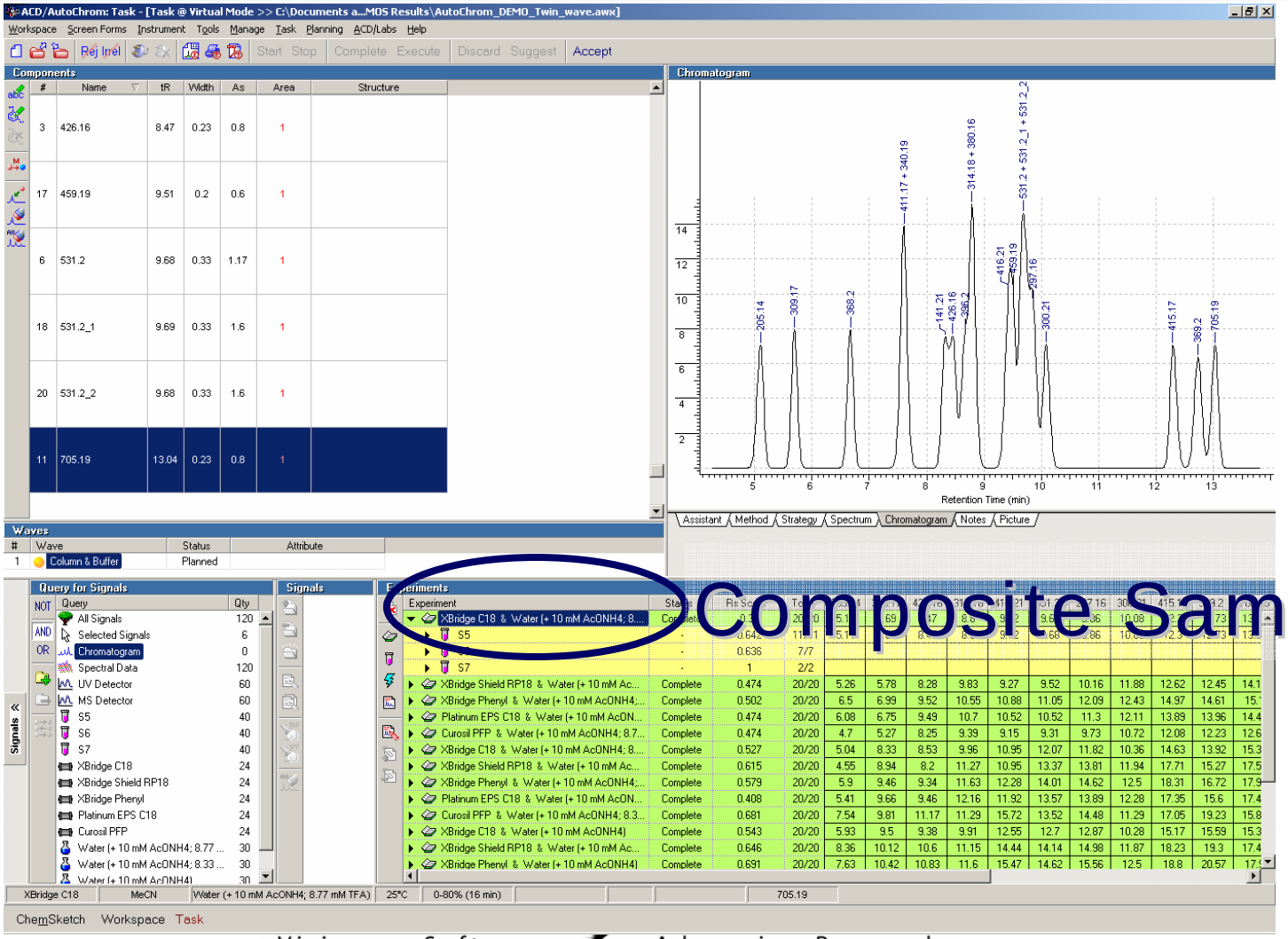
The Composite Sample

- Components in multiple vials must be treated as one overall sample
- Inject separately, and then correlate post-injection
- Determine which peaks are shared, and which are unique
- “collapse” all peaks into one overall composite chromatogram

The Composite Chromatogram



Composite Chromatogram View

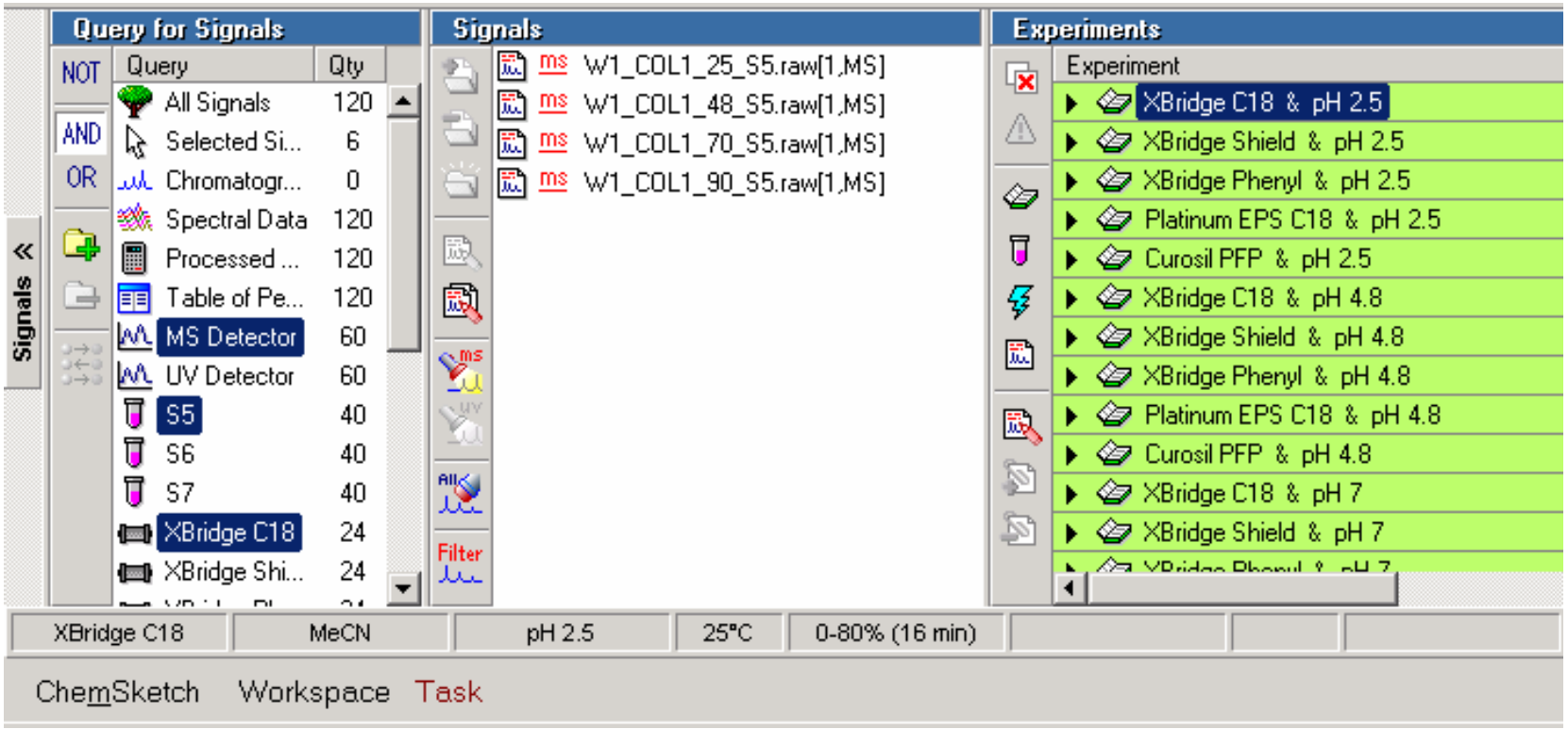


Composite Sample

Signal Queries

- Data must be sorted and manipulated in groups:
  - Processing
  - Peak matching
  - Reconciliation
- Signal query system allows for logical grouping of signals according to MethDev objectives

Grouping Signals



In a few seconds, chromatographers can select from hundreds of traces to process/match/reconcile.

Benefits of Project Management

- Easier organization of data files
  - Workflow-centric data organization
- Every data file is linked to the decision-making tool
  - Change a peak assignment, and immediately view the effect on the decisions
- Track common components across *different detectors*
- Track common components across *different subsamples*
- Workflow support with the MethDev assistant
- Fast overviews of gigabytes of data:
  - Spectra
  - chromatograms