

Digital Advanced Laser Polarimeter, Gradient Mixer, Column Selector, Injector/Collector AutoMDS, AutoPrep, AutoCCC/CPC, Spectral Deconvolution, Chiral Deconvolution Improve Productivity in HPLC, CCC/CPC, SMB/MCC, Reaction, Process Applications Integration/Installation, Support, Training, Purification, Custom HW/SW Systems

AutoPrep Systems (Automated Preparative Purification)

PDR started developing AutoMDS and AutoPrep Software in 1998. PDR had previously developed the ALP (Advanced Laser Polarimeter), was operating a fast-pace contract purification service, and were unhappy with available software. PDR needed walk-away automation for method development and preparative purification to rapidly purify previously unknown compounds for big-pharma in the range of 1-1000 grams. PDR still continues aggressive development and improvement of AutoMDS and AutoPrep software. AutoPrep can run continuously without attention; assuming adequate solvent, waste, and sample solution. AutoPrep features include the following.

- 1. <u>Methods and sequences only contain chromatographic parameters</u> so all systems have same user interface whether analytical method development or larger-scale preparative purification. Our device drivers translate chromatographic parameters into device-specific commands. Methods, sequences, and user interface are independent of hardware idiosyncrasies. For example, HPLC and CCC/CPC applications have the same user interface, but much different methods.
- Each method can have multiple unique cycles and each method and/or cycle can be repeated many times. For example, a CCC/CPC method usually contains 3 or 4 different cycles pumping different solutions at different flow rates and the method is repeated many times. Whereas an HPLC preparative purification method usually contains a single cycle repeated many times. Repeating a cycle is continuous, does not restart the method, and allows overlapping (stacking) of injections.
- 3. <u>Method Development and Preparative Purification software are identical</u>, except for configuration settings. User interface is consistent and software upgrades apply to all products. Software is modular so new features and improvements can be released often and upgrades are very easy to apply.
- 4. <u>Parameters can be changed during a run</u>. You can start a preparative purification run with conservative injection volume and injection spacing (stacking), then increase injection volume and reduce injection spacing to improve productivity as the system equilibrates and results are clear. This helps improve productivity in purification jobs requiring many injections and high purity. Stopping a run only to change parameters is never required.
- Peak collection decisions can be made in real-time using derivative (slope) and +/- sign of DALP derivative, rather than time. Time works OK if elutions are stable, but peak derivative collections follow shifting or changing peaks accurately. This can be very important to purity and recovery during long-running purifications by compensating for minor changes in eluent and sample solution.
- 6. <u>Method and Sequence Editors</u> use a spreadsheet format that is very good for building, editing and monitoring methods and sequences.
- 7. <u>Repeats/Runtime</u> display clearly shows job progress and end times helping you schedule liquid management, other activities, and following jobs.

Repeats/Runtime			
Methods: waiting/done	9 /	(2
Cycles: waiting/active/done	1/	1/	1
Minutes: done/remaining	12.02 /	1	9.48
Expected method end time:	Oct 11, 2022 3:16:24 PM		
Expected run end time:	Oct 11, 2022 6:30:41 PM		

8. <u>Realtime 2D and 3D Plots</u> show detector data in real time continuously.





AutoPrep Example from 2019 job at PDR

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Prep Predictor LC

- \geq Parameters can be changed while method is running making it easy to optimize productivity as conditions equilibrate or change.
- \geq Typical installation: AutoPrep software, Injector/Collector module, Custom Installation with your pumps and UV, Optimization for your applications, and Training.

Spreadsheets:

Prep Predictor spreadsheets predict number of injections, run time, and volumes, so jobs are predictable: you always know what to expect. Useful for pragmatically comparing methods, solvent management, project costing, scheduling, etc. Often the largest separation is not really the best method for purification.

Injector/Collector:

Injector/Collector, see photo at right, can be built for 1/16- or 1/8-inch OD tubing and any size loop. Sample solution is drawn in at top of loop and pump flows into bottom of loop. Thus, sample solution does not get diffused traveling length of loop and sample solution does not go into syringe because syringe sucks eluent from bottom of loop drawing sample solution into top of loop.

For larger tubing sizes and/or customers preferring open/close (rather than rotating) collection valves we have a universal valve driver module that can actuate any size or type of valve (electrical, pneumatic, etc.).

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AutoPrep:

AutoPrep is very easy to use and can reliably make 1000s of unattended injections for big jobs. The Recalculate feature instantly shows result of peak detection and collection changes on a test run chromatogram, eliminating the need for more test runs and making setup quick and easy to optimize. If method settings are changed while method is running, AutoPrep adapts appropriately and records changes.

AutoPrep Advantages:

DALP, AutoMDS, AutoPrep

HPLC/UHPLC/SFC/CCC/SMB/PAT

- Direct control of existing or new pumps and detectors.
- ≻ Injections made with syringe/loop/valve or another pump for large-scale installations.
- ≻ Collections made with rotary valve or open/close valves of any type or size.

Spectral

Deconvolution

- \triangleright Setup, operation, and monitoring are very easy and robust.
- \triangleright Recalculate feature instantly shows result of changing collection parameters on test run.
- \triangleright Detection and Collection can adapt to variations in real-time.
- \geq Collect based on time, voltage (amplitude), slope (derivative), +/- polarity, ee, and logical combinations.

Material to be Separated	6	200.000
to to all the design of the second	and the l	00.0
Injection Concentration	mg/mL	90.0
Injection volume	mL	1.000
Material per injection	mg	90.000
Number of Injections		2222.2
Cycle Time	min	10.0
Time Req'd	Hours	370.4
Time Req'd	Days	15.4
Flow Rate	mL/min	20.0
Total Eluent Reg'd	L	444.4
Solvent B	%	35.0
Total Solvent A Reo'd	1	288.9
Total Solvent B Reg'd	L.	155.6
Total Eluent Collected	L.	311.1
Fraction 1 Open	min	5.00
Fraction 1 Close	min	7.00
Eluent Collected, Fraction 1	L	88.9
Fraction 2 Open	min	8.00
Fraction 2 Close	min	13.00
Eluent Collected, Fraction 2	L	222.2
Column, ID	cm	2.1
Column, Packed Length	cm	25.0
CSP Density	g/cc	0.6
(betclusted)		52.0

Material to be Separated	£	20.000
Injection Concentration	mg/mL	20.0
Injection Volume	mL	3.000
Material per Injection	mg	60.000
Number of Injections		333.5
Cycle Time	min	5.0
Time Reg'd	Hours	27.3
Time Req'd	Days	13
Flow Rate	mL/min	50.0
Total Eluent Reg'd	L	83.3
Modifier	%	25.0
Total CO2 Regid	B	439.
Total CO2 Reg'd	50 lb Tanks	8.78
Total Modifier Reg'd	L	20.1
Total Modifier Collected	L.	17.9
Fraction 1 Open	min	5.20
Fraction 1 Close	min	6.70
Eluent Collected, Fraction 1	L	25.
Modifier Collected, Fraction 1	L	6.3
Fraction 2 Open	min	7.0
Fraction 2 Close	min	9.8
Eluent Collected, Fraction 2	L	46.
Modifier Collected, Fraction 2	L	11.
Column, ID	cm	2
Column, Packed Length	cm	25.
CCD Density	g/cc	0.0
Cor Density		









DALP, AutoMDS, AutoPrep Spectral HPLC/UHPLC/SFC/CCC/SMB/PAT Deconvolution Digital Advanced Laser Polarimeter, Gradient Mixer, Column Selector, Injector/Collector AutoMDS, AutoPrep, AutoCCC/CPC, Spectral Deconvolution, Chiral Deconvolution Improve Productivity in HPLC, CCC/CPC, SMB/MCC, Reaction, Process Applications Integration/Installation, Support, Training, Purification, Custom HW/SW Systems

AutoPrep Examples:



AutoPrep Example from 2019 job at PDR Notice blue injector markings at top and blue collection markings at bottom: all actions are recorded.





AutoPrep with Agilent



AutoPrep with JCT 1L CCC

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