



Operation Manual



600192
Rev. 1

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Section 1: Introduction

Introduction

About This Manual

This manual (PN 600192) describes the operation and maintenance of the Liberty1™ Automated Microwave Peptide Synthesizer. The manual is intended for use by both novice and experienced users.

This introductory section contains a list of common abbreviations and units used throughout the manual, as well as important information for the safe operation of the unit. The manual assumes that the Liberty1 was installed by a CEM certified service technician.

This manual refers to PepDriver1™ version 3.6.2.0 for all software information, including screenshots and technical information. The latest version of PepDriver1 can be downloaded from CEM's website at <http://www.cem-technet.com>. A registered account is required for download.

Additional information is available in the Appendices (PN 600193), which can be found on the included CD-ROM (PN 900105).

Common Abbreviations and Units

Abbreviation	Definition
°C	degrees Celsius
°F	degrees Fahrenheit
AA	amino acid
ACP	acyl carrier protein 65-74
Amp	ampere
Boc	<i>tert</i> -butoxycarbonyl
<i>t</i> Bu	<i>tert</i> -butyl
DIEA	diisopropylethylamine
DMF	<i>N,N'</i> -dimethylformamide
E _a	energy of activation
Fmoc	9-fluorenylmethoxycarbonyl
g	gram
h	height
HATU	<i>N</i> -((dimethylamino)-1H-1,2,3-triazolo-4,5-bi-pyridin-1-yl-methylene) <i>N</i> -methylmethan-aminium hexafluorophosphate <i>N</i> -oxide
HBTU	2-(1 H-benzotriazol-1-yl)-1,1,3,3-tetramethyl-uronium hexafluorophosphate
HCTU	<i>O</i> -(6-chlorobenzotriazol-1-yl)- <i>N,N,N',N'</i> -tetramethyluronium hexafluorophosphate
HOAt	1-hydroxy-7-azabenzotriazole
HOBt	1-hydroxybenzotriazole
Hz	Hertz
ID	inner diameter
L	liter
l	length
m	meter
meq	milliequivalent
mg	milligram
MHz	megahertz
mL	milliliter

Abbreviation	Definition
mm	millimeter
mM	millimolar
mmol	millimole
MW	molecular weight
NMP	1-methyl-2-pyrrolidone
OAt	7-azabenzotriazole
OBt	benzotriazole
OD	outer diameter
PN	part number
psi	pounds per square inch
PyAOP	(7-Azabenzotriazol-1-yloxy) tripyrrolidinophosphonium hexafluorophosphate
PyBOP	(Benzotriazol-1-yloxy) tripyrrolidinophosphonium hexafluorophosphate
RV	reaction vessel
s	seconds
TBTU	O-(Benzotriazol-1-yl)- <i>N,N,N',N'</i> - tetramethyluronium tetrafluoroborate
Trt	trityl
VAC	volts of alternating current
W	Watts
w	width



How to Obtain Support

Applications Support

For the latest Liberty1 applications information, go to <http://www.cem.com/bioscience>. The CEM Bioscience website contains downloadable applications notes, a listing of recent microwave peptide synthesis publications, and more.

CEM is proud to provide applications support for any peptide synthesis related questions from a team of trained chemists with a complete peptide synthesis lab. For applications support, call (800) 726-3331 (inside the US) or (704) 821-7015 and ask for “Peptide Applications”, or email CEM Liberty1 applications support at peptides@cem.com.

Technical Support

For the latest technical support information, go to <http://www.cemservice.us>. The CEM Service website provides access to the CEM Knowledge Base, which contains helpful troubleshooting information. From the website requests for phone or email support can also be submitted.

CEM is proud to provide technical support for the Liberty1 from a team of specially trained Service Technicians. For technical support in the US and Canada, call (800) 726-5551 or (704) 821-7015 and ask for “Liberty1 Service”. For technical support outside the US and Canada, contact your local CEM Subsidiary or Distributor.

Requested Information

When contacting CEM for support, please provide the following information about the instrument:

- Liberty1 Serial Number
- Liberty1 Firmware Version
- Discover Serial Number
- Discover Firmware Version
- PepDriver1 Version Number and Build Number
- The Run History report for the synthesis that was running when the error occurred (see p. 51)

Serial numbers, firmware versions, and software version can be found within PepDriver1 by clicking the Help Menu (not the Help Button) and selecting About PepDriver1.

Contact CEM

CEM Corporation Headquarters

Toll-Free Phone (US/Canada): (800) 726-3331
 Phone: (704) 821-7015
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Buckingham
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Email: info.uk@cem.com

CEM Distributors

For a complete list of distributors of CEM products, including contact information, go to the CEM website (<http://www.cem.com>), select Contact Us, and then select Distributors.

Safety Information

Safety Notations

This manual uses three safety alert words at points in the documentation where the user should be aware of potential hazards. The safety alerts are shown in color-coded boxes. The three words—NOTE, CAUTION, and WARNING—indicate differing levels of observation or action as described below:

NOTE

A NOTE is intended to provide emphasis of procedures that may be misinterpreted or overlooked, or to otherwise clarify confusing situations.

CAUTION

A CAUTION is intended to provide essential information and to emphasize procedures which, if not strictly followed, may result in improper instrument operation.

WARNING

A WARNING is intended to provide emphasize dangerous or hazardous conditions which may result in personal injury to the user and damage or destruction of the instrument.



Safety Information

Fume Ventilation

The Liberty1 operates as a semi-closed system, with minimal venting of any hazardous solvent fumes through the vent line coming from the Waste Reservoir. The vent line from the Waste Reservoir must be vented into a proper chemical fume hood or exhaust line no longer than six feet (6')/two meters (2 m) from the instrument.

In addition, adequate ventilation should be provided for preparation of reagents and solvents for use on the system. All solvent bottles and the Waste Reservoir should be placed into proper secondary containers to minimize the risk of exposure.

Waste Disposal

Waste produced by the Liberty1 can be hazardous. For detailed information on the safety requirements for the chemicals used on the Liberty1, refer to the appropriate MSDS documents.

WARNING

Handle all waste under a fume hood, and wear suitable protective clothing.
Dispose of all waste in accordance with all applicable local, state, and federal health and safety recommendations.

System Requirements

Bench and/or Fume Hood Space

The Liberty1 should be positioned on the bench such that access to the electrical outlets for the system is not restricted. The Liberty1 requires the following space for system components:

Liberty1 Instrument (Discover Module and Liberty1 Module):

30" (w) x 24" (d) x 26" (h) [76 cm (w) x 61 cm (d) x 66 cm (h)]

(Depth includes 3" (7.62 cm) clearance behind instrument for unimpeded airflow at rear fan ducts)

CEM Supplied Controller:

Laptop:

12.5" (w) x 9.9" (d) x 15.5" (h) [32 cm (w) x 25 cm (d) x 39 cm (h)]

(Height includes 14.1" (35.8 cm) display)

Desktop:

Minitower: 7.4" (w) x 17.5" (d) x 16.1" (h) [19 cm (w) x 44.5 cm (d) x 41 cm (h)]

Monitor: 16" (h) x 8" (d) x 20" (h) [41 cm (h) x 20 cm (w) 51 cm (h)]

External Reagent Bottles:

13" (w) x 18" (d) x 15" (h) [33 cm (w) x 46 cm (d) x 38 cm (h)]

(Left side of instrument, facing front of instrument)

Waste Reservoir:

10" (w) x 16" (d) x 18" (h) [25 cm (w) x 41 cm (d) x 45.72 cm (h)]

(Must be vented into fume hood)

Approximate overall dimensions for Liberty1 and external reagents:

43" (w) x 24" (d) x 26" (h) [109 cm (w) x 61 cm (d) x 66 cm (h)]

Environmental Conditions

The Liberty1 is designed for indoor use only.

Temperature Range: 50 °F – 85 °F (10 °C – 29 °C)

Relative Humidity Range: 0 – 85%

Inert Gas Source

The Liberty1 requires an inert gas source (either high purity grade nitrogen or argon) capable of supplying 25 psi (20 L/min flow) within ten feet (10')/three meters (3 m) of the right side of the instrument.

Electrical Requirements

The Liberty requires electrical power of 120 VAC (60 Hz, 1.7 A) (or 240 VAC [50 Hz, 1.7 A] where applicable). Specific power requirements (120 VAC vs. 240 VAC) can be found on the nameplate affixed to the rear of the Liberty module and on the side of the Discover module.

Four (4) grounded electrical connections providing a total of 10 A are required for all components:

Liberty Module power cord

Discover Module power cord

Router power cord

Controller (laptop computer) power cord

NOTE

Five (5) grounded electrical connections providing a total of 10 A are required when using the desktop computer controller option: Liberty module, Discover module, router, controller minitower, controller monitor.

NOTE

Optionally, the router can be powered directly from the Liberty1 Module without the need for an external electrical connection (using Router-Serial Power Cable, PN 243290).

Fuse Replacement

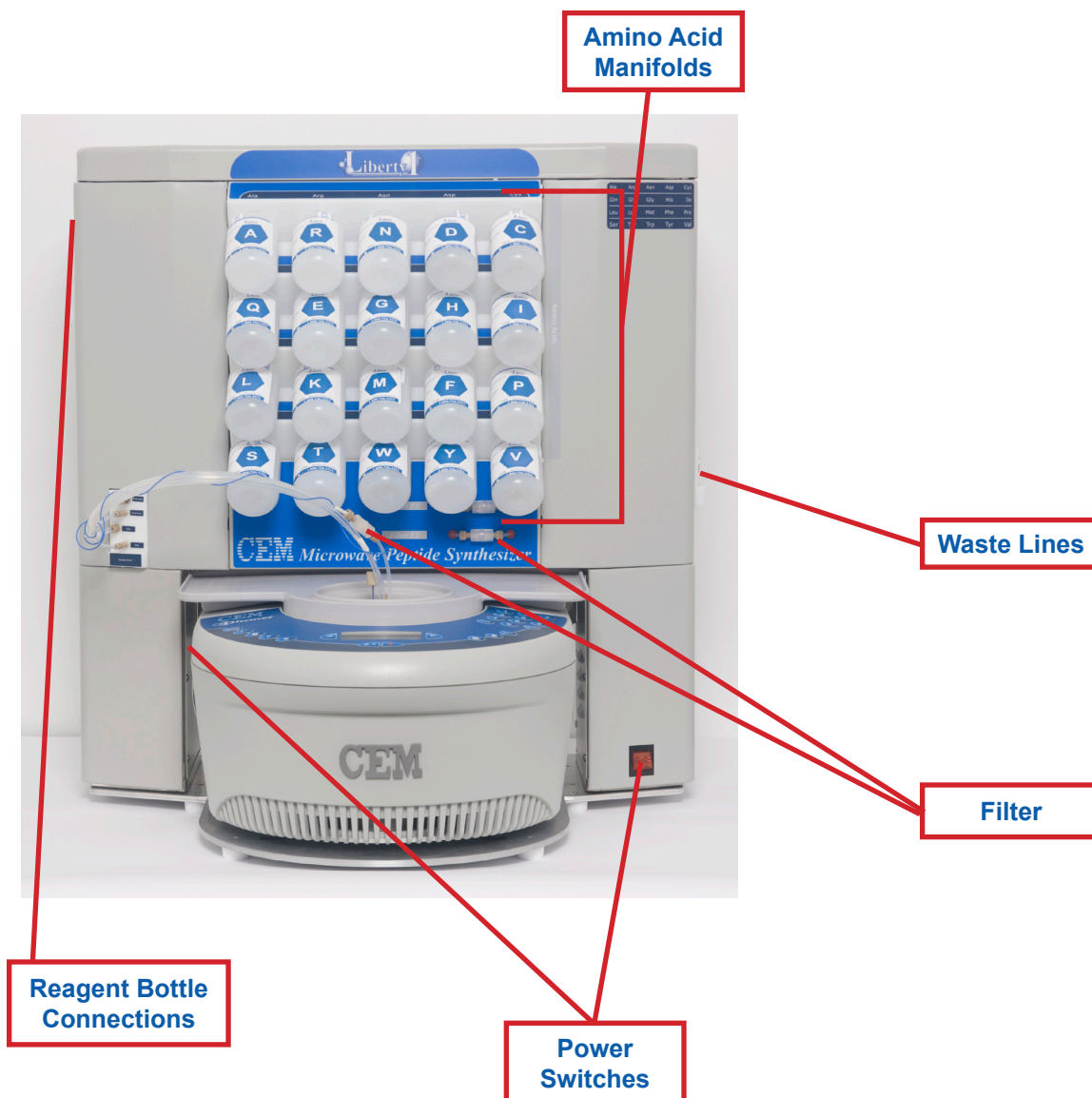
The Liberty has two operator replaceable fuses located in the power inlet module (at the rear of the instrument, where the power cord connects to the Liberty). The fuses are rated F 250 V 2 A. The fuses (PN BR188250) are North American style, 1.25" x 0.25" (3.2 cm x 0.7 cm) size.

Section 2: Operation of the Liberty1

Introduction to the Liberty1

The Liberty1 Automated Microwave Peptide Synthesizer is the latest automated microwave peptide synthesizer. Built on CEM's flexible Discover microwave platform, the Liberty1 is capable of synthesizing peptides on scales ranging from 0.05 to 5 mmol faster and more efficiently than conventional synthesizers thanks to the system's patented circular microwave cavity.



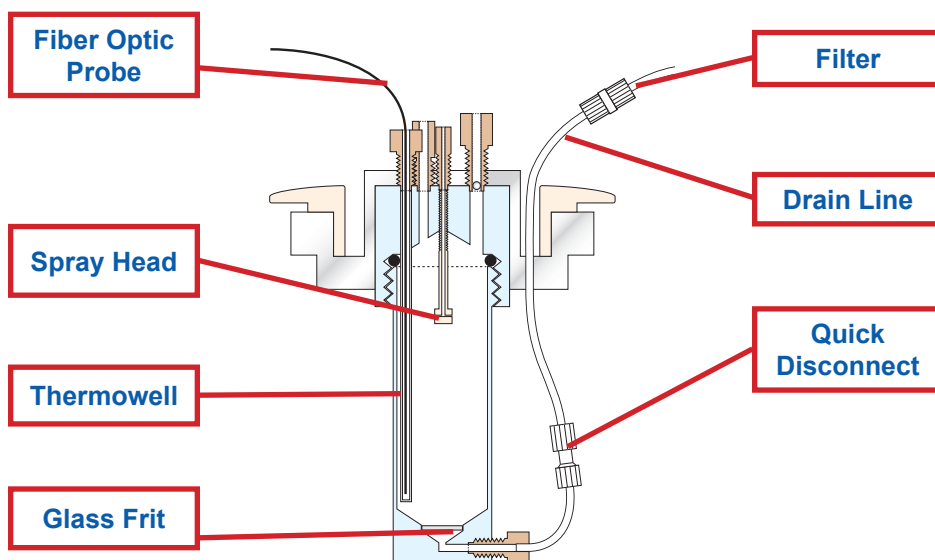


Components and Parts

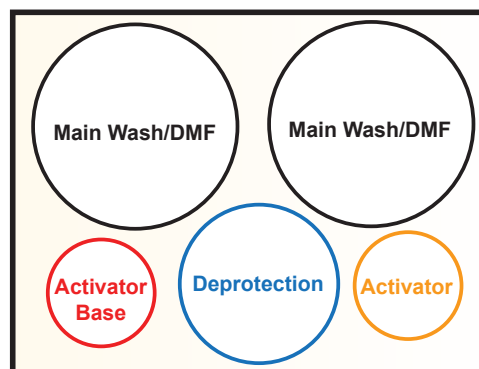
- **Liberty1 Module:** The Liberty1 handles all of the fluid transfer into and out of the reaction vessel. In addition, the Liberty1 manages communications with the computer controller and the Discover during peptide synthesis.
- **Discover Microwave Reactor:** The Discover microwave reactor holds the reaction vessel and generates the microwave energy used to irradiate the sample. The Discover is capable of operating independently of the Liberty1.
- **Power Switches:** There are two power switches, one for the Discover and one for the Liberty1. Both switches must be on to operate the Liberty1.
- **Reagent Bottles:** Bottles for activator, activator base, deprotect, and main wash (DMF) connect to the manifold on the side of the Liberty1 using caps (GL45 for activator, activator base, and deprotect, 4L for main wash) and tubing assemblies. The reagent bottles sit in a secondary containment tray. Replacement caps for using GL45 bottles for DMF are available (p. 95).

- **Amino Acid Manifolds:** There are 20 positions on the manifold for amino acids, each corresponding to a specific amino acid. Each position is labeled using the 3 letter abbreviations of the amino acids. These positions are designed for use with 125 mL plastic bottles.
- **Reaction Vessel:** The reaction vessel (not shown, see p. 20) is where the synthesis takes place. Reagents are added to the vessel and washed out throughout the synthesis of the peptide. There are different size vessels that can be used depending on the scale of the synthesis.
- **Fiber Optic Temperature Probe:** The fiber optic probe is inserted in the top of the reaction vessel. It allows the system to monitor the temperature of the reaction vessel.
- **Waste Lines:** The waste lines carry all of the system's waste out into an external waste container. The waste container is equipped with a level sensor and will trigger the system to pause if the container is full.
- **Filters:** There are three in-line filters on the system. These filters should be changed regularly as part of routine maintenance.
- **Optional Features**
 - **DMF Keg:** An optional 20 L steel keg (not shown) is available for the DMF position. This keg allows for synthesis of longer peptides where total solvent usage would otherwise be a limitation.
 - **Capping Option:** An optional position for acetic anhydride (including necessary additional valves, tubing, bottle, and bottle cap, not shown) is available to allow for capping reactions on the Liberty1.
 - **10 mL Reaction Vessel:** A smaller reaction vessel assembly (not shown) is available to allow synthesis on scales as low as 0.025 mmol.

Reaction Vessel Components



Reagent Bottles



Introduction to PepDriver1

The operation of the Liberty1 is controlled through the PepDriver1 software package. The Liberty1 includes an external computer controller (either a laptop or desktop Windows PC) for running PepDriver1. This computer is connected to the Liberty1 and the Discover through an ethernet connection.

CAUTION

PepDriver1 is designed to operate in Windows XP and/or Windows 7 using default display conditions.

In Windows XP, increasing the window font size (from the Display Properties window) to Large Fonts or Extra Large Fonts will cause PepDriver1 to display improperly and may impact the operation of PepDriver1.

In Windows 7, increasing the display size from smallest (100% to medium (125%) (from the Display link in the Personalize window) will cause PepDriver1 to display improperly and may impact the operation of PepDriver1.

PepDriver1 Terminology

Throughout this manual, specific terms will be used to describe the various functions within PepDriver1.

- **Microwave Method:** The specific parameters used in a Microwave step within a cycle. Microwave Methods can be created or modified using the Microwave Editor (p. 24).
- **Cycle:** The specific steps used for each residue within a given sequence. Cycles can be created or modified using the Cycle Editor (p. 27).

- **Sequence:** The specific peptide to be synthesized in a given method. Sequences can be created or modified using the Sequence Editor (p. 30).
- **Method:** The specific parameters used to synthesize a peptide. For each method, a sequence is selected, and then parameters (individual coupling cycles for each residue, C-terminus type, final deprotection, etc.) are also selected as part of the method. Methods can be created or modified using the Method Editor (p. 33).
- **Run:** A specific instance of a method being loaded and started in PepDriver1. A Run History file is recorded for each run.

PepDriver1 Main Screen

The screenshot shows the PepDriver1 software interface. Callout boxes point to the following elements:

- Control Buttons:** Start, Pause, Stop
- Menu Buttons:** Methods, Sequences, Cycles, Setup, Maintenance, Calculator
- Estimated Time Remaining:** 04:59:17
- Peptide Synthesis Status:** VQAAIDYING
- Resin Indicator:** 1
- Tabs:** Methods, Queue, Current Run, Run History
- Method Detail:** ACP
- System Status Line:** 15.5 PSI, 41 C, Liberty Connected, Discover Connected, Waste, Microwave

Step	Amino Acid	Specific Derivative	MW	Cycle Name
1	Gly	Resin	57.052	Standard - Resin
2	Asn	Fmoc-Asn(Trt)-OH	114.105	0.10-Single
3	Ile	Fmoc-Ile-OH	113.161	0.10-Single
4	Tyr	Fmoc-Tyr(Obt)-OH	163.178	0.10-Single
5	Asp	Fmoc-Asp(Obt)-OH	115.089	0.10-Single
6	Ile	Fmoc-Ile-OH	113.161	0.10-Single
7	Ala	Fmoc-Ala-OH • H ₂ O	71.079	0.10-Single
8	Ala	Fmoc-Ala-OH • H ₂ O	71.079	0.10-Single
9	Gln	Fmoc-Gln(Trt)-OH	128.132	0.10-Single
10	Val	Fmoc-Val-OH	99.134	0.10-Single
11	None	Final Deprotection		0.10

Control Buttons

- **Start:** This button starts the first method in the queue, or resumes a stopped method.
- **Pause:** This button pauses or unpauses the current method.
- **Stop:** This button stops the current method. PepDriver1 will finish the operation it is currently performing before stopping the method.

Menu Buttons

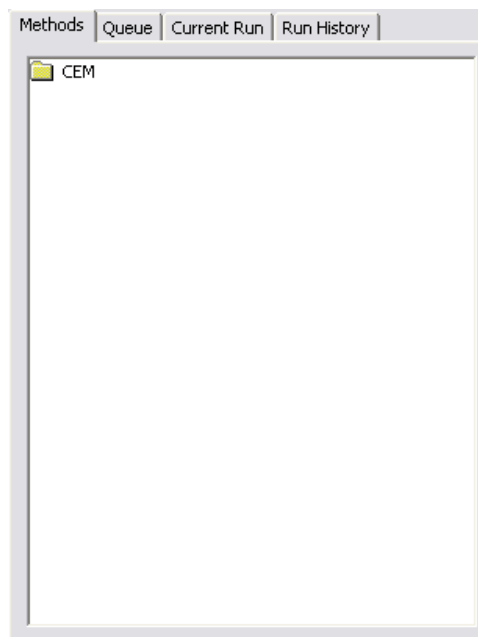
- **Methods:** This button opens the Method Editor. From the Method Editor, specific parameters for each synthesis can be programmed.
- **Sequence:** This button opens the Sequence Editor, where peptide sequences are entered to be used in methods.
- **Cycles:** This button opens the Cycle Editor. From the Cycle Editor, cycles can be created or edited for use in any part of a method.
- **Setup:** This menu contains the Microwave Editor, Default Cycle Editor, PepDriver1 Options Menu, and Communication options. From this menu, User Accounts can also be accessed.
- **Maintenance:** From this menu, the Maintenance and Diagnostics screens can be accessed. The Maintenance Screen allows for cleaning, volume calibration, sensor calibration, and pressure calibration. The Diagnostics Screen contains information about the sensors, valves, and delay times for the system.
- **Calculators:** This menu contains the Reagent and Usage calculators. The Usage Calculator will calculate the amount of each reagent solution needed for the currently loaded methods. The Reagent Calculator can then be used to calculate how to make each of the stock solutions for the loaded methods (including activator, activator base, deprotection, cleavage, and amino acids).

Indicators

- **Resin Indicator:** The Resin Indicator shows the status for the currently loaded method: green when ready to run, red when stopped, blue when complete.
- **Peptide Synthesis Status:** This displays the peptide sequence being synthesized and indicates the status of the synthesis.
- **Current Method Detail:** This window displays the currently selected method. When a method is running, the current step is indicated in yellow.
- **System Status Line:** The left box indicates the specific command the Liberty1 is currently executing. The current temperature and pressure readings are displayed next to the command indicator. Two indicators show the computer's communication status with the Liberty1 and the Discover. The waste full and spill tray warnings are also seen here. On the right, there is an indicator that shows whether the microwave is running.

Tabs

- **Methods:** From this tab, methods are loaded into the resin position.



- **Queue:** From this tab, the Method can be started from any step.

The screenshot shows the 'Queue' tab selected. The interface has a tab bar at the top with 'Methods', 'Queue', 'Current Run', and 'Run History'. Below the tabs, there is a table with the following data:

Priority	Load Resin	Method	Location	Status
1	No	ACP	1	Ready

Below the table, there is a large grey rectangular area.

- **Current Run:** This tab displays the Method that is currently running.

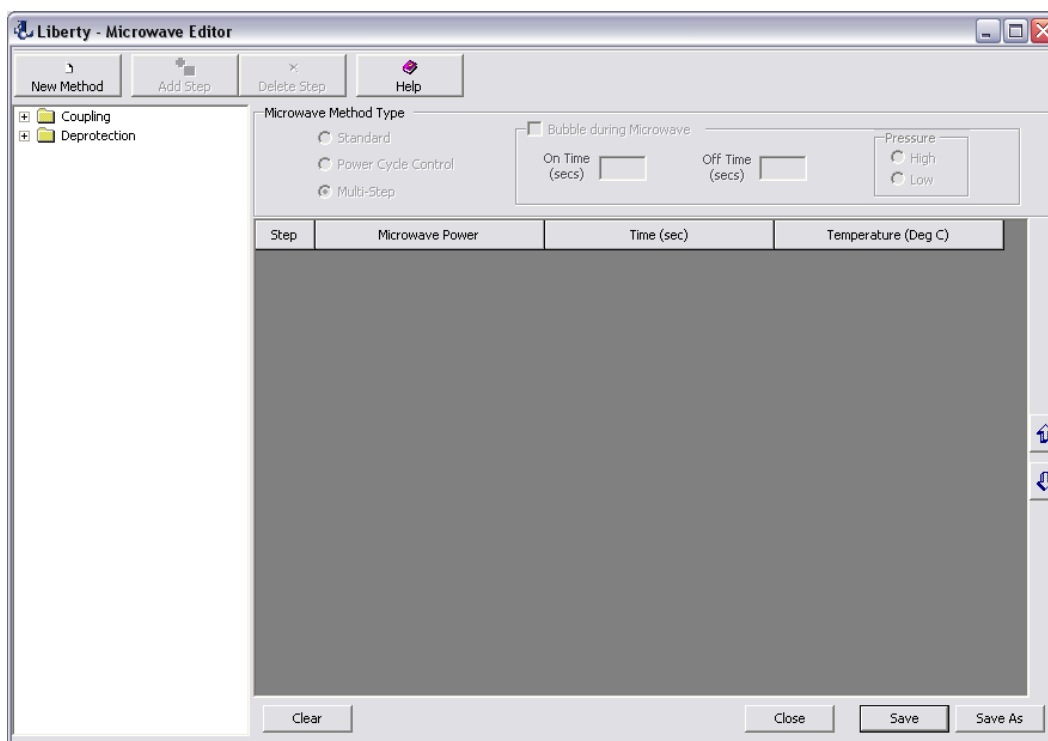
Methods	Queue	Current Run	Run History	
Priority	Load Resin	Method	Location	Status
1	Yes	ACP	1	Running

- **Run History:** From this tab, detailed logs of each Method that has been run can be accessed. In addition, Method Reports can be generated for each Method that has been run.

Methods	Queue	Current Run	Run History
Run History Data			
01-2008			
01-2009			
02-2007			
02-2009			
03-2008			
03-2009			
04-2008			
04-2009			
05-2008			
05-2009			
06-2008			
06-2009			
07-2008			
07-2009			
08-2008			
08-2009			
09-2006			
09-2008			
10-2008			
11-2008			
12-2008			

Editors

Microwave Editor



The Microwave Editor allows for the control and customization of the microwave steps of any cycle. By editing the power and duration of a microwave step difficult peptides can be synthesized with higher purity and yield.

The Microwave Editor can be accessed by clicking the Setup Button on the PepDriver1 main screen and selecting Microwave Editor from the menu.

Microwave Method Folders

The Microwave Editor contains separate folders for each type of microwave method. Within each method folder, there are subfolders for each scale, allowing for the development of optimized microwave methods for each scale. A microwave method will only appear in the Cycle Editor when creating a cycle of the same scale.

PepDriver1 comes with optimized default microwave methods for deprotection and coupling.

Microwave Method Types

- **Standard:** A Standard method applies a set microwave power until the set temperature is reached, and then turns off the microwave until the temperature drops to 5 °C below the set temperature. The total agitation time can also be selected.
- **Multi-Step:** Multi-Step methods allow for a single microwave method to use multiple power, temperature, or time settings.

Creating a New Microwave Method

Microwave methods allow for detailed control of the microwave heating and reaction time for each step in the synthesis. The Microwave Editor allows the user to select the microwave time, microwave power, maximum temperature, and sample agitation.

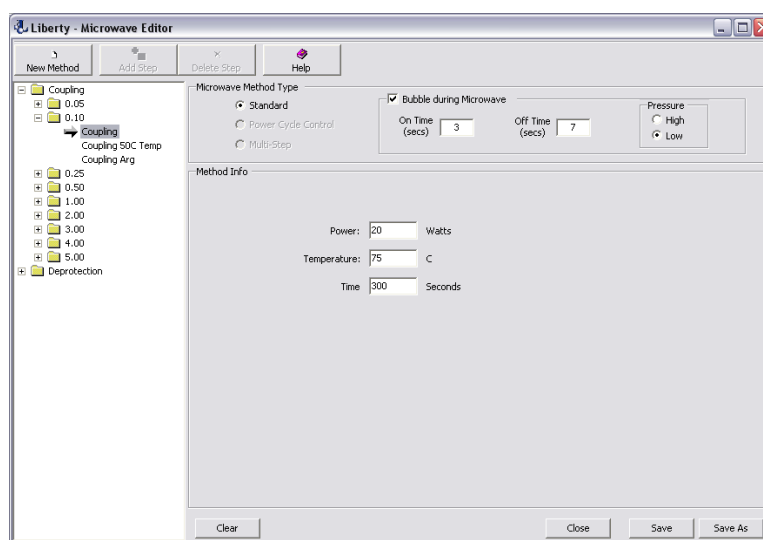
1. Open the folder of the appropriate method type, then open the subfolder for the appropriate scale.

NOTE

A microwave method saved in a specific scale folder will only be available for use in Cycle Editor for cycles created in the same scale folder.

2. Click the New Method button.
3. The new method will appear in the selected folder. Enter a name for the method and press Enter.
4. Select the type of microwave method to make.

4.1. Standard

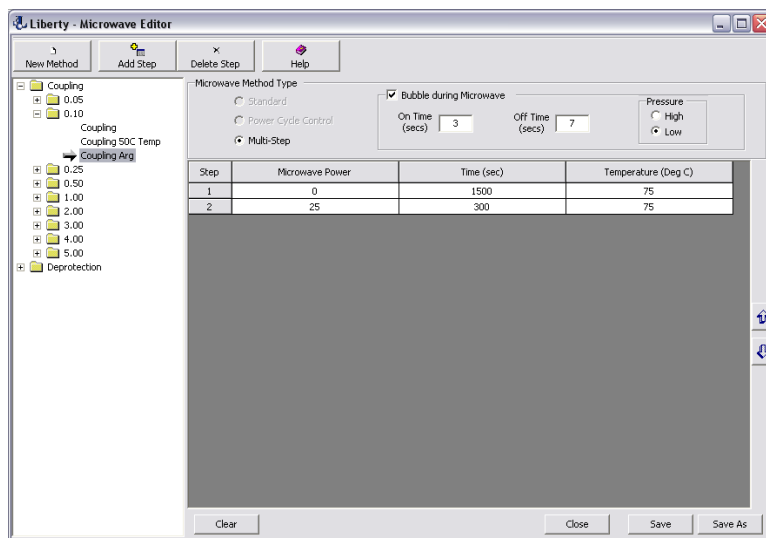


- 4.1.1. Enter the desired microwave power setting (in Watts), maximum temperature (in °C), and time for the microwave step (in seconds).
- 4.1.2. If agitation is desired during the microwave step, check the box for Bubbling During Microwave. Enter the amount of time to bubble and the time between each bubbling. (Bubbling is enabled by default. The default setting is 3 seconds On Time, 7 seconds Off Time, low pressure)

CAUTION

High Pressure bubbling is not recommended as this can deposit resin on the top of the reaction vessel. This can lead to poor synthesis quality, product loss, and contamination between syntheses.

4.2. Multi-Step



- 4.2.1. Enter the microwave power (in Watts), time (in seconds), and maximum temperature (in °C) for the first step in the method.
- 4.2.2. Add the next step to the microwave method by clicking the Add Step button, and then enter the power, temperature, and time settings for the second step.
- 4.2.3. Repeat step 4.2.2. for each step in the method.
- 4.2.4. If agitation is desired during the microwave step, check the box for Bubbling During Microwave. Enter the amount of time to bubble and the time between each bubbling. (Bubbling is enabled by default. The default setting is 3 seconds On Time, 7 seconds Off Time, low pressure.)

CAUTION

High Pressure bubbling is not recommended. Bubbling at high pressure can deposit resin on the top of the reaction vessel. This can lead to poor synthesis quality, product loss, and contamination between syntheses.

5. Save the method by clicking the Save button.

Editing an Existing Microwave Method

The Microwave Editor allows for settings on existing methods to be modified and saved as needed. The most common reason to modify an existing method is to increase or decrease the microwave power to optimize peptide synthesis. To modify an existing method:

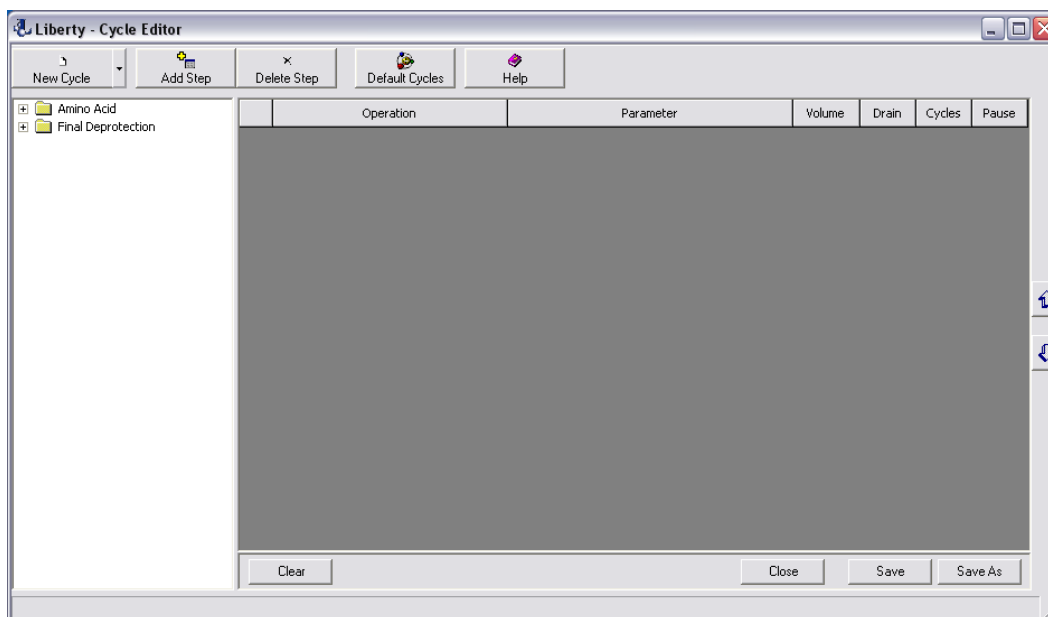
1. Open the folder of the appropriate method type, then open the subfolder for the appropriate scale.
2. Click on the microwave method to be modified.
3. Make any changes as needed.
4. Click Save to save the changes to the method.

Copying and Modifying an Existing Microwave Method

Often, it is easier to copy and modify an existing microwave method rather than creating an entirely new method. Methods can easily be duplicated and modified within the Microwave Editor, and then be moved to different scale folders as needed. To copy an existing method:

1. Open the folder of the appropriate method type, then open the subfolder for the appropriate scale.
2. Right click on a microwave method and select Copy Method.
3. The new method will appear named "Copy of (method name)". Type a new name and press Enter.
4. Any settings in the method can be changed. If the copied method was a Multi-Step method, steps can also be added or deleted by using the Add Step and Delete Step buttons.
5. When all changes have been made, click Save to save the modified method.
6. If the new method is to be used at a different synthetic scale, drag the method from the folder it was created in to the appropriate folder.

Cycle Editor



The Cycle Editor allows for the full control and customization of any step of a synthesis. This allows for optimization of each step of a given peptide synthesis.

The Cycle Editor can be accessed by clicking on the Cycles Button on the main screen of PepDriver1, or by clicking the Cycle Editor button from the Method Editor.

Cycle Folders

The Cycle Editor contains separate folders for each type of cycle. Within each cycle folder, there are subfolders for each scale, allowing for the development of optimized cycles for each scale. A cycle will only appear in the Method Editor when creating a method of the same scale.

PepDriver1 comes with optimized default cycles for resin transfer, amino acid addition, final deprotection, and cleavage for each of the available synthetic scales.

Cycle Types

- **Amino Acid:** Amino acid cycles control how the deprotection and coupling steps of one amino acid in the sequence occur.
- **Final Deprotection:** Final deprotection cycles control the removal of the N-terminal protecting group, and also allow for N-terminal acetylation of the peptide before cleavage.

Creating a Cycle

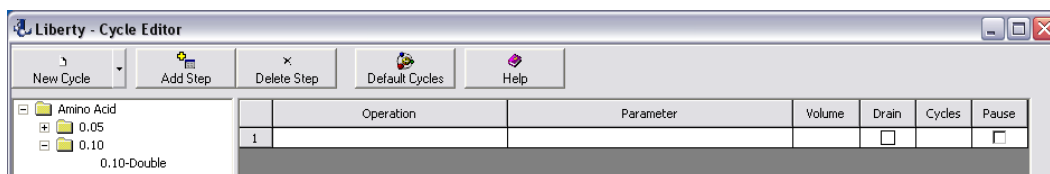
Cycles allow for detailed control of each action taken in a given step of a peptide synthesis run. PepDriver1 comes with default cycles of each type for each synthetic scale; however, cycles can be customized to accomplish a number of non-standard chemistries. To create a new cycle:

1. Click the New Cycle button at the top of the Cycle Editor window and select the type of cycle to be created.

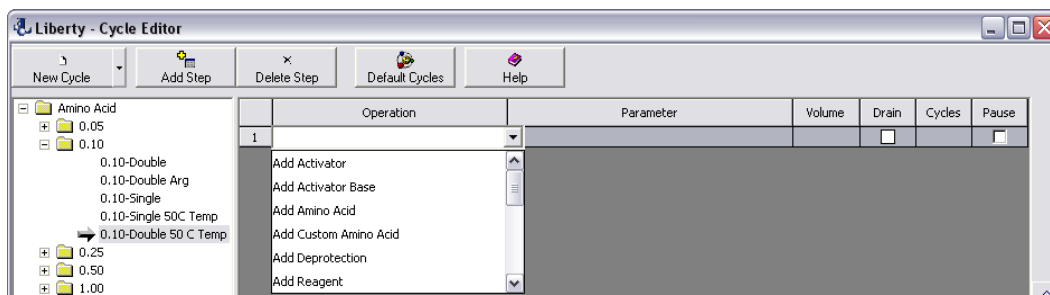
NOTE

A cycle saved in a specific scale folder will only be available for use in Method Editor for methods created at that scale.

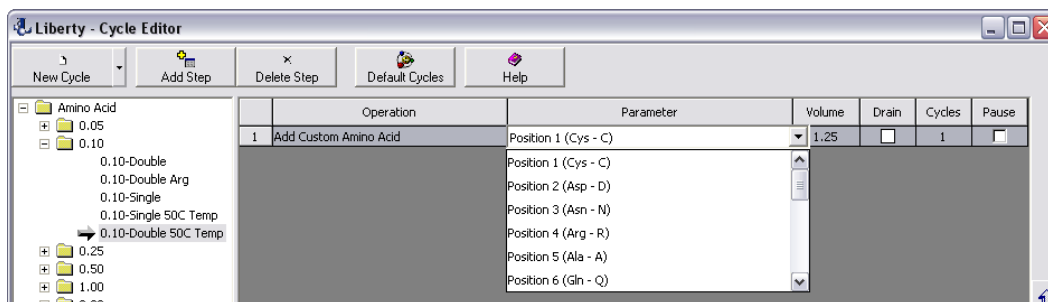
2. The cycle will appear in the appropriate folder. Enter a name for the cycle and press Enter.
3. Step 1 will appear in the cycle window.



4. Click the Operation box and select the operation to be performed. (For a full list of available operations, see Appendix 3: Operations in the Cycle Editor.)



- The default parameter and volume for the chosen operation will appear in the appropriate boxes. Click on the Parameter box to select a different parameter. Click on the volume to enter the desired volume.

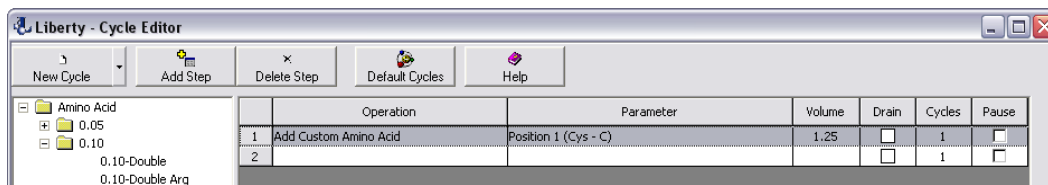


- If the Drain box is checked, the reaction vessel will be drained using a filtered drain after the operation is carried out. Uncheck the box to leave any liquid reagents in the vessel.
- Enter the number of times the operation is to be carried out in the Cycles box.
- If the Pause box is checked, the method will be paused after the operation is carried out. To insert a pause, check the box.

NOTE

The method will not resume until the user presses the Start button on the main screen of PepDriver1.

- Click the Add Step button to add a new step to the cycle.



- Repeat steps 3 through 9 until the cycle is fully programmed.
- Click Save to save the cycle.

Editing an Existing Cycle

The Cycle Editor allows for settings on existing cycles to be modified and saved as needed. To modify an existing cycle:

- Open the folder for the appropriate cycle type, then open the subfolder for the appropriate scale if necessary.
- Click on the cycle to be modified.
- Make any changes as needed.
- Click Save to save the changes to the cycle.

Copying and Modifying an Existing Cycle

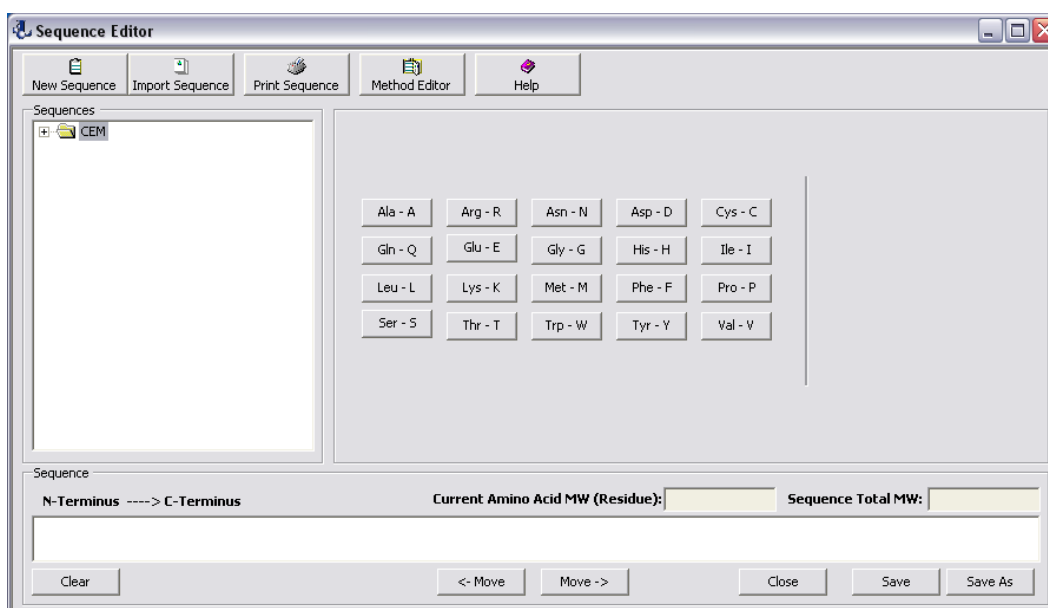
Often, it is easier to copy and modify an existing cycle rather than creating an entirely new cycle. Cycles can easily be duplicated and modified within the Cycle Editor, and then they can be moved to different scale folders as needed. To copy an existing cycle:

1. Open the folder of the appropriate method type, then open the subfolder for the appropriate scale if necessary.
2. Right click on a cycle and select Copy Cycle.
3. The new cycle will appear named "Copy of [cycle name]". Type a new name and press Enter.
4. Any setting can be changed. Steps may be added or deleted as necessary using the Add Step and Delete Step buttons.
5. When all changes have been made, click Save to save the modified cycle.
6. If the new cycle is to be used at a different synthetic scale, drag the cycle from the folder it was created in to the appropriate folder.

NOTE

When copying a cycle to use with a different scale, verify that the volumes used are appropriate for the new scale before using the cycle.

Sequence Editor



Peptide sequences to be synthesized are entered in the Sequence Editor. The Sequence Editor allows for the use of all twenty standard amino acids. In addition, the Sequence Editor will automatically calculate the total molecular weight of the peptide sequence.

The Sequence Editor can be accessed by clicking on the Sequences button on the PepDriver1 main screen, or by clicking the Sequence Editor button from the Method Editor.

Creating a New Sequence

1. Open the appropriate folder for the new sequence.
2. Click the New Sequence button.
3. The new sequence will be created in the selected folder. Enter a name for the sequence (the default is "New Sequence") and press Enter.
4. The amino acids for the sequence can be entered in two ways:
 - 4.1. Click the amino acid buttons:
 - 4.1.1. Click the white Sequence box at the bottom of the Sequence Editor.
 - 4.1.2. Click the button corresponding to first (N-terminal) amino acid. The one letter abbreviation will appear in the Sequence box.
 - 4.1.3. Repeat step 4.1.2. for the remaining amino acids.
 - 4.2. Type in the one letter abbreviations:
 - 4.2.1. Click the white Sequence box at the bottom of the Sequence Editor.
 - 4.2.2. Type the sequence (N-terminus to C-terminus) using the one letter abbreviations.
5. Click Save to save the sequence.

Modifying a Sequence

If a sequence is entered incorrectly, there are a few ways to correct the error.

To insert an amino acid:

1. Right-click on the amino acid that will come after the inserted amino acid.
2. Select Insert Amino Acid.
3. A box will pop up stating that the next amino acid entered will be inserted before the current amino acid. Click OK to close the box.
4. Click on the desired amino acid button or type the one letter abbreviation of the desired amino acid.

To delete an amino acid:

1. Right-click on the amino acid.
2. Select Remove Amino Acid.

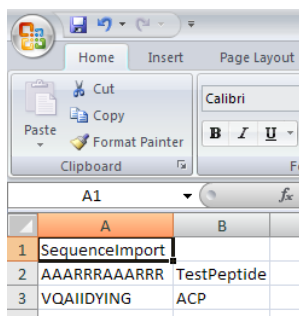
To move an amino acid within a sequence:

1. Click on the amino acid to be moved.
2. Click the Move Left (<-Move) or Move Right (Move->) buttons at the bottom of the Editor window to move the amino acid one position in the indicated direction. Repeat as needed until the amino acid is in the correct position.

Importing a Sequence

PepDriver1 includes an option for importing sequences from external documents such as Microsoft Word documents, PDF documents, or webpages. This is especially useful for longer sequences because it minimizes the possibility of incorrectly entering the sequence.

1. Create a Microsoft Excel spreadsheet containing the sequence or sequences to be imported.
 - 1.1. In Excel, create a new document.
 - 1.2. In cell A1, enter the words SequenceImport (without a space between the words).
 - 1.3. Highlight the sequence in the source document (PDF, webpage, etc.) and press Ctrl+C (or right-click and select Copy).
 - 1.4. Paste the sequence into the first open cell in column A of the Excel spreadsheet.
 - 1.5. Enter a name for the sequence in column B.

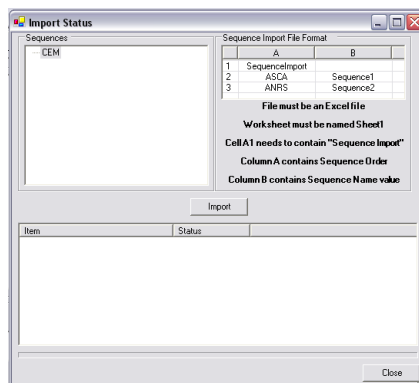


- 1.6. Repeat steps 1.3 through 1.5 for any other sequences to be imported.
- 1.7. Save the file and close Excel.

NOTE

If using Excel 2007 or later, the file must be saved as an Excel 97-2003 compatible file (.xls, not .xlsx). The file name must be in English.

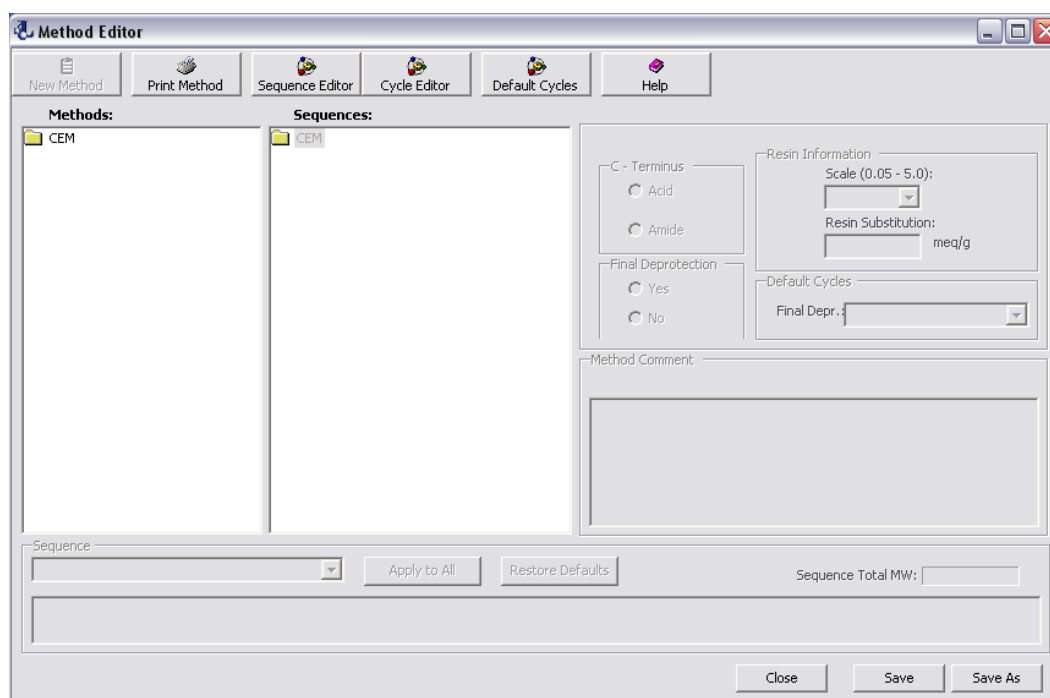
2. From PepDriver1, open the Sequence Editor.
3. Click Import Sequence to open the Import window.



4. In the Import window, open the destination folder for the sequences.
5. Click Import. In the window that appears, select the Excel document created earlier and click Open.
6. The Import window will be updated to reflect the successful import of the sequences. The imported sequences are now available for use in the Sequence Editor and Method Editor.

Item	Status
Sequence #1	Imported
Sequence #2	Imported

Method Editor



The Method Editor is used to program the specific conditions to be used for a given synthesis. Once a sequence is selected, several options for the run can be configured that will determine the specific steps to be used in the synthesis.

The Method Editor can be accessed by clicking the Methods button on the PepDriver1 main screen, or by clicking the Method Editor button from the Sequence Editor.

Creating a New Method

1. Open the appropriate folder in the Methods box for the new method.
2. Click the New Method button.
3. Enter a name for the method and press Enter.
4. Open the appropriate folder in the Sequences box, and click on the desired sequence. The sequence will then be loaded into the sequence box at the bottom

of the Method Editor window.

5. Select the synthetic scale (0.05 mmol to 5.0 mmol) from the Resin Information box.

NOTE

The scale must be selected before changing any other parameters, as each scale has specific default options that will be loaded upon selection.

NOTE

The 125 mL vessel must be used for syntheses above 0.25 mmol.
The 10 mL vessel assembly must be used for syntheses below 0.1 mmol.

6. The remaining options can now be selected.
 - 6.1. C-Terminus: This corresponds to the type of resin used. Selecting Acid assumes the resin is preloaded (the first amino acid is already attached) and therefore skips that coupling. If the resin is not preloaded, Amide should be selected.
 - 6.2. Final Deprotection: If No Final Deprotection is selected, the N-terminal Fmoc group will not be removed from the peptide prior to cleavage.
 - 6.3. Default Cycles:
 - 6.3.1. Final Deprotection: By default, the N-terminal Fmoc group is removed and left as the free amine.
7. Enter the substitution value in the Resin Substitution box. This value is provided by the supplier of the resin, and is usually expressed in mmol/g or meq/g

NOTE

The substitution value entered here will not affect the operation of the Liberty1. It is only needed for the Usage Calculator to calculate how much resin is required for the synthesis.

8. Assign cycles for each residue in the sequence that will not use the default cycle.

NOTE

Each amino acid is assigned an optimized default coupling cycle. By default, the Double Arg cycle is used for arginine, and the Single 50 C cycle is used for cysteine and histidine. The Single coupling cycle is used for all other amino acids. To restore all amino acids in a sequence to the default cycles, click the Restore Defaults button.

- 8.1. Click on the amino acid to highlight it.
- 8.2. Click on the drop-down box above the sequence and select the desired cycle. This will change the cycle for that highlighted amino acid only.

NOTE

Amino acids assigned cycles other than the default will be highlighted in yellow in the Method Editor.

- 8.3. To change the cycle for all amino acids to the selected cycle, click Apply to All button on the left.
9. When the method is complete, click Save to save the method.

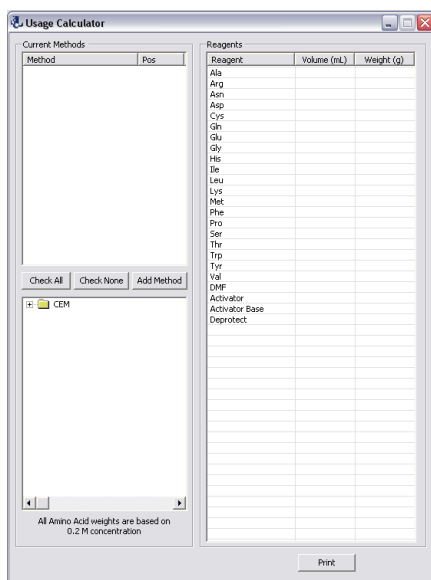
Modifying an Existing Method

1. Open the Method Editor.
2. Open the folder containing the method in the Methods window.
3. Click on the method to be modified. The sequence will automatically be selected and loaded.
4. Make any changes to the method as needed.
5. Click Save to save the changes to the method.

Calculators

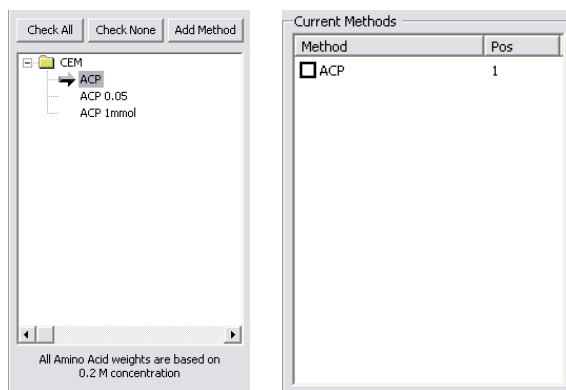
PepDriver1 contains two calculators that allow for easy determination of reagent needs and reagent preparation: the Usage Calculator and the Reagent Calculator. These calculators are accessed from the Calculator Button on the PepDriver1 main screen.

Usage Calculator



The Usage Calculator can be used to determine the amount of each reagent needed for a given method. Multiple methods can be loaded into the calculator, so that sufficient reagents can be loaded onto the Liberty1 for multiple peptides. To use the Usage Calculator:

1. Click on the Calculator button, and select Usage from the menu.
2. From the Methods box at the bottom left of the Usage Calculator, select the method to be included in the calculation and click the Add Method button. The method will appear in the Current Methods box on the top left of the Usage Calculator.



3. Repeat step 2 for each method to be included in the calculation.

- Click the Check All button to calculate the combined reagent usage for all loaded methods.

The Usage Calculator window displays the following data:

Current Methods		Reagents	
Method	Pos	Reagent	Weight (g)
<input checked="" type="checkbox"/> ACP	1	Ala	2.30
<input checked="" type="checkbox"/> ACP 1mmol	1	Arg	2.27
		Asn	1.56
		Cys	2.32
		Glu	2.62
		Gly	
		His	
		Ile	
		Leu	
		Lys	
		Met	
		Phe	
		Pro	
		Ser	
		Thr	
		Tyr	1.75
		Val	1.29
		DMF	4262
		Activator	70
		Activator Base	35
		Deprotect	638

Buttons: Check All, Check None, Add Method

Tree view: CEM > ACP > ACP 0.05 > ACP 1mmol

Footer: All Amino Acid weights are based on 0.2 M concentration

- To exclude a selected method from the calculator, click the box next to the method name in the Current Methods box to unselect it. The calculator will automatically update the total usage for each reagent.

The Usage Calculator window displays the following data after excluding ACP 1mmol:

Current Methods		Reagents	
Method	Pos	Reagent	Weight (g)
<input checked="" type="checkbox"/> ACP	1	Ala	0.37
<input type="checkbox"/> ACP 1mmol	1	Arg	0.60
		Asn	0.41
		Cys	0.61
		Glu	0.42
		Gly	
		His	
		Ile	
		Leu	
		Lys	
		Met	
		Phe	
		Pro	
		Ser	
		Thr	
		Tyr	0.46
		Val	0.34
		DMF	1567
		Activator	10
		Activator Base	5
		Deprotect	176

Buttons: Check All, Check None, Add Method

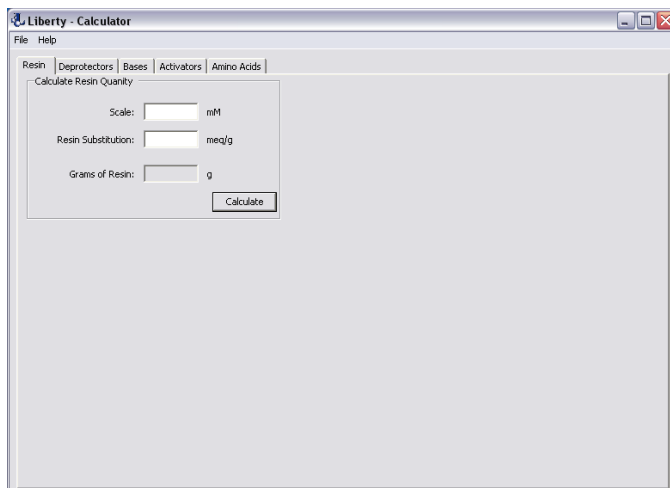
Tree view: CEM > ACP > ACP 0.05 > ACP 1mmol

Footer: All Amino Acid weights are based on 0.2 M concentration

- To print a Usage Report, click the Print button at the bottom of the Usage Calculator. This will open the report as a PDF which can be printed or saved for future reference.

Reagent Calculator

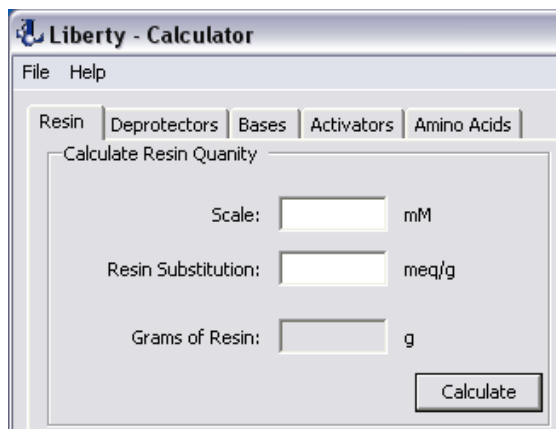
The Reagent Calculator can be used to determine how to prepare all reagents to be loaded on the system at the correct concentrations. There are five tabs: Resin, Deprotectors, Bases, Activators, and Amino Acids.



NOTE

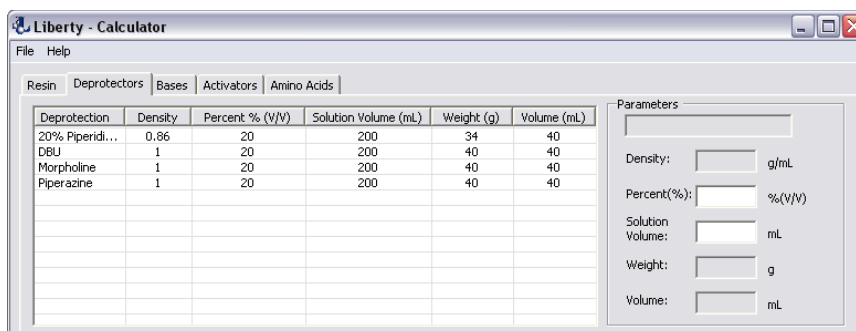
The Reagent Calculator contains a library of common reagents. The Liberty1 is not limited to only these reagents; however, the Reagent Calculator can only perform calculations using reagents in the library.

Resin Calculator



1. Enter the scale for the synthesis.
2. Enter the resin substitution value in the Resin Substitution box. This value is provided by the supplier of the resin, and is usually expressed in mmol/g or meq/g.
3. Click Calculate. The required mass of resin will be reported in the Grams of Resin box (in grams).

Deprotection Calculator



Deprotection	Density	Percent % (V/V)	Solution Volume (mL)	Weight (g)	Volume (mL)
20% Piperidi...	0.86	20	200	34	40
DBU	1	20	200	40	40
Morpholine	1	20	200	40	40
Piperazine	1	20	200	40	40

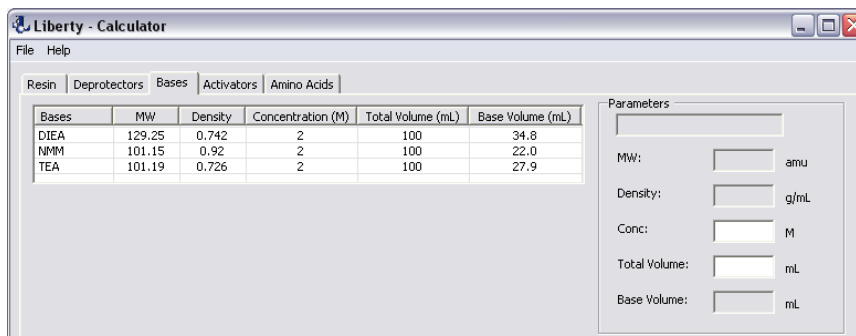
1. Click on the desired deprotection reagent from the list.
2. Enter the desired concentration (in percent volume).

CAUTION

The default concentration is 20%. Piperazine should be prepared at a 5% solution due to its solubility in DMF.

3. Enter the total volume of deprotection solution required.
4. Click Calculate. The calculator will report the required amount of deprotection reagent in milliliters (for liquids) and grams (for solids).

Activator Base Calculator



Bases	MW	Density	Concentration (M)	Total Volume (mL)	Base Volume (mL)
DIEA	129.25	0.742	2	100	34.8
NMM	101.15	0.92	2	100	22.0
TEA	101.19	0.726	2	100	27.9

1. Click on the desired base from the list.
2. Enter the desired concentration (in M)

CAUTION

The default concentration is 2 M. DIEA should be prepared using NMP as the solvent because of its miscibility in DMF.

3. Enter the total volume of activator base solution needed.
4. Click Calculate. The calculator will report the required amount of base in milliliters.

Activator Calculator

Activators	MW	Concentration (M)	Volume (mL)	Weight (g)
HATU	381	0.5	100	19
HBTU	379.3	0.5	100	19
HCTU	413.7	0.5	100	21
HOBT	135.1	0.5	100	7
HOBT H2O	153.15	0.5	100	8
PyAOP	521.4	0.5	100	26
PyBOP	520.3	0.5	100	26
TBTU	321.1	0.5	100	16

1. Click on the desired activator from the list.
2. Enter the desired concentration (in M). The default is 0.5 M.
3. Enter the total volume of activator solution needed.
4. Click Calculate. The calculator will report the required amount of activator in grams.

Amino Acid Calculator

Amino Acid	Specific Derivative	Volume (mL)	Conc (M)	Weight (g)
ALA	Fmoc-Ala-OH • H ₂ O	100	0.2	6.227
ARG	Fmoc-Arg(Pbf)-OH	100	0.2	12.975
ASN	Fmoc-Asn(Trt)-OH	100	0.2	11.934
ASP	Fmoc-Asp(OtBu)-OH	100	0.2	8.229
CYS	Fmoc-Cys(Trt)-OH	100	0.2	11.714
GLN	Fmoc-Gln(Trt)-OH	100	0.2	12.214
GLU	Fmoc-Glu(OtBu)-OH	100	0.2	8.510
GLY	Fmoc-Gly-OH	100	0.2	5.946
HIS	Fmoc-His(Trt)-OH	100	0.2	12.394
ILE	Fmoc-Ile-OH	100	0.2	7.068
LEU	Fmoc-Leu-OH	100	0.2	7.068
LYS	Fmoc-Lys(Boc)-OH	100	0.2	9.371
MET	Fmoc-Met-OH	100	0.2	7.429
PHE	Fmoc-Phe-OH	100	0.2	7.749
PRO	Fmoc-Pro-OH	100	0.2	6.748
SER	Fmoc-Ser(tBu)-OH	100	0.2	7.669
THR	Fmoc-Thr(tBu)-OH	100	0.2	7.949
TRP	Fmoc-Trp(Boc)-OH	100	0.2	10.532
TYR	Fmoc-Tyr(tBu)-OH	100	0.2	9.191
VAL	Fmoc-Val-OH	100	0.2	6.788

1. To calculate a specific amino acid, click on that amino acid in the list so that it is highlighted and then click the Selected box. To calculate all amino acids at the same volume, click the All box.
2. Enter the total volume of amino acid solution.
3. Click Calculate. The calculator will report the required amount of amino acid(s) in grams.

Setting up a Synthesis

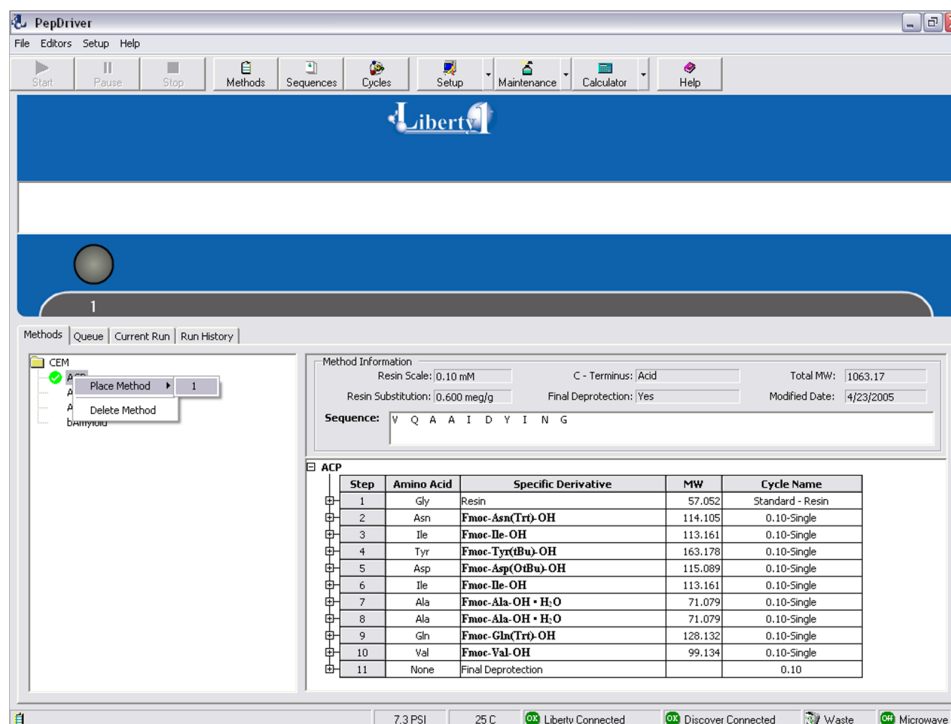
Configuring Methods to Run

Loading a Method

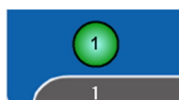
Once a method has been created and saved in the Method Editor, it is available from the Methods tab on the main PepDriver1 screen. Methods can be loaded to run in two ways.

To load by clicking:

1. Open the appropriate folder in the Methods tab.
2. Right-click on the desired method, select Place Method.



3. The resin position in PepDriver1 will turn green, indicating the method is loaded and ready to run.



To load by dragging:

1. Open the appropriate folder in the Methods tab.
2. Click on the desired method, and drag the method to the resin position.
3. The resin position in PepDriver1 will turn green, indicating the method is loaded and ready to run.

Preparing Reagents

Standard Concentrations

The Liberty1 uses stock solutions of all reagents. The default cycles are designed to deliver enough of each stock solution to give 5 eq of amino acid and activator and 10 eq of activator base for each coupling. The table below details the standard concentrations used on the Liberty1.

Reagent	Standard Concentration	0.05 mmol Scale Concentration
Activator	0.5 M	0.25 M
Activator Base	2 M	1 M
Amino Acid	0.2 M	0.2 M

NOTE

When working on 0.05 mmol scale, due to the size of the sample loops used for reagent delivery, activator and activator base should be made at half the standard concentration. Amino acids do not need to be diluted.

NOTE

Amino acid, activator, activator base, and deprotection solutions can be used for up to two weeks. Some amino acids, notably His, will begin to crash out of solution after two weeks.

Preparing Activator Solution

1. Weigh out the appropriate amount of the desired activator (as calculated using the Usage and Reagent Calculators) and transfer to a 250 mL amber glass bottle.

NOTE

Some activators, especially the aminium activators such as HBTU, are light sensitive and should be prepared in an amber glass bottle.

2. Add the appropriate volume of DMF.
3. Put a cap on the bottle. Gently swirl the bottle to ensure that all of the activator has gone into solution.

NOTE

Some activators, notably HBTU, may take up to 10 minutes to fully go into solution.

Preparing Activator Base Solution

1. Measure out the appropriate amount of activator base and transfer to a clear 250 mL glass bottle.

2. Add the appropriate volume of NMP to give the correct final volume.

NOTE

CEM recommends using DIEA as the activator base. When using DIEA, NMP must be used as the solvent because DIEA is not miscible in DMF at the standard concentration of 2 M. The final concentration of DIEA in the reaction vessel is low enough that miscibility is not an issue.

3. Put a cap on the bottle. Gently swirl the bottle to ensure all of the activator base has gone into solution.

Preparing Amino Acids

CEM offers a full line of pre-weighed amino acids in 5 mmol, 10 mmol, and 20 mmol sizes. It is not required to use the pre-weighed amino acids.

To use CEM pre-weighed amino acids:

1. Open the bottles, breaking the safety seals.
2. Add the appropriate amount of DMF to each bottle (25 mL for 5 mmol bottles, 50 mL for 10 mmol bottles, and 100 mL for 20 mmol bottles).
3. Replace the caps and shake vigorously to ensure all amino acid has gone into solution.

To use bulk amino acids:

1. Weigh out the appropriate amount of the amino acid as calculated using the Usage and Reagent Calculators.
2. Transfer the amino acid to a clean 125 mL plastic bottle.
3. Add the appropriate volume of DMF to the bottle.
4. Place a cap on the bottle and shake vigorously to ensure the amino acid has fully gone into solution.

Preparing Deprotection Solution

1. Measure out the appropriate amount of deprotection reagent as calculated using the Usage and Reagent Calculators.
2. Transfer the deprotection reagent to a 1 L clear glass bottle.
3. Add the appropriate volume of DMF to give the correct final volume as calculated in the Reagent Calculator.
4. Add HOBt if necessary.

NOTE

For sequences susceptible to aspartimide formation, CEM recommends the addition of 0.1 M HOBt to the deprotection solution as this significantly reduces levels of aspartimide. The appropriate mass of HOBt can be calculated in the Reagent Calculator under the Activators tab. Enter the total volume of deprotection and change the concentration to 0.1, then click Calculate.

- Place a cap on the bottle. Swirl the bottle gently to ensure the deprotection reagent (and HOBt, if used) has fully gone into solution.

Setting up the Liberty1

Loading Reagents onto the Liberty1

NOTE

All reagent positions must have a bottle in place. If a given reagent is not required for a synthesis, connect an empty bottle to that position.

- Connect amino acid bottles to the appropriate positions on the system. Connect empty amino acid bottles to all unused amino acid positions.
- Load activator, activator base, and deprotection using the Change Bottle command. (For more information about the Change Bottle command, see p. 59.)
 - Click on the Maintenance button in PepDriver1 and select Maintenance.
 - Select the appropriate reagent from the pull-down box next to the Change Bottle button, then click Change Bottle.
 - The Change Bottle window will appear. Follow the onscreen instructions to depressurize and remove the existing bottle.
 - Ensure the dip tube has a dip tube filter in place, then screw the cap onto the deprotection bottle.
 - Click Next to continue with the Change Bottle procedure. The Liberty1 will automatically pressurize the bottle and ensure the lines are filled and ready to add.
- Check the level of DMF remaining in the DMF bottles. If more DMF is required, use the Change Bottle command (p. 59) to replace the bottles.

NOTE

The two bottles of DMF should have approximately equal amounts of solvent.

- Click on the Maintenance button in PepDriver1 and select Maintenance.
- Select Main Wash from the pull-down box next to the Change Bottle button, then click Change Bottle.
- The Change Bottle window will appear. Follow the onscreen instructions to depressurize the existing bottles.
- Slowly loosen one of the DMF bottle caps to release any residual pressure, then remove both caps.
- Ensure each dip tube has a dip tube filter in place, then screw the caps onto the new solvent bottles.
- Click Next to continue with the Change Bottle procedure. The Liberty1 will automatically pressurize the bottles and ensure the lines are filled and

ready to add.

4. Add the resin to the reaction vessel.
 - 4.1. Use the Reagent Calculator to determine the amount of resin required for the synthesis.
 - 4.2. Remove the reaction vessel from the microwave cavity.



- 4.3. Disconnect the filtered drain line from the vessel body.



- 4.4. Disconnect the vessel body from the attenuator.



- 4.5. Weigh the appropriate amount of dry resin into the vessel body.



NOTE

The large (125 mL) vessel is necessary for reactions of 0.5 mmol scale or higher. Weigh the resin into the appropriate vessel body for the method scale.

- 4.6. Connect the vessel body to the attenuator.
- 4.7. Connect the filtered drain to the vessel body.
- 4.8. Place the vessel back into the microwave cavity, securing the attenuator.

Changing the Reaction Vessel

When working on large or small scales, the reaction vessel will need to be swapped out for one of an appropriate volume. The large (125 mL) vessel is necessary for reactions of 0.5 mmol scale or higher. The small (10 mL) vessel is necessary for reactions of 0.05 mmol scale or lower.

125 mL Reaction Vessel

1. Remove the 35 mL (Standard) reaction vessel from the microwave cavity.
2. Disconnect the filtered drain line from the vessel body.
3. Disconnect the vessel body from the attenuator.
4. Connect the 125 mL vessel body to the attenuator.
5. Connect the filtered drain line to the 125 mL vessel body, being careful not to crossthread or overtighten the fitting.
6. Place the vessel back into the microwave cavity, securing the attenuator.
7. Perform a Reaction Vessel Leak Check (see p. 84).

10 mL Reaction Vessel

1. Remove the 35 mL (Standard) reaction vessel from the microwave cavity.
2. Slide the fiber optic clip off of the thermowell, then carefully remove the temperature probe from the thermowell.
3. Disconnect the four lines from the manifold on the front of the Liberty.
4. Place the 10 mL vessel into the microwave cavity, securing the attenuator.
5. Connect the four line from the 10 mL vessel to the manifold on the front of the Liberty, ensuring each line is connected to the correct position.
6. Insert the temperature probe into the thermowell, ensuring the probe is inserted to the bottom of the thermowell. Slide the fiber optic clip onto the thermowell.
7. Perform a Reaction Vessel Leak Check (see p. 84).

Running the Liberty1

Preparing the Liberty1 to Run

1. Verify the level of the waste container to ensure there is sufficient room before starting another synthesis.
2. Verify the nitrogen supply to ensure there is sufficient nitrogen to complete the synthesis.
3. Verify that all amino acids required for the synthesis are loaded in the appropriate

positions, and that empty bottles are connected to all other positions.

4. Verify the levels of the wash solvent (DMF) to ensure there is sufficient solvent.
5. Verify that the fiber optic probe is fully inserted into the thermowell.

WARNING

If the probe is not inserted all the way to the bottom of the vessel the Liberty1 will not accurately measure the temperature, and significant overheating of the vessel can occur. This will result in poor synthesis quality and/or serious damage to the vessel.

6. Verify that the method is correct by looking at the steps outlined in the Method box. If there are any errors, make corrections and reload the method.
 - 6.1. Right-click on the green resin indicator and select Clear Method.
 - 6.2. To correct the method:
 - 6.2.1. Open the Method Editor. In the Methods box on the left, open the folder where the method was saved. Click on the method to load it.
 - 6.2.2. Make any corrections as needed (see p. 35).
 - 6.2.3. Click Save to save the method, then close the Method Editor.
 - 6.2.4. Load the corrected method as described above.
 - 6.3. To correct the sequence:
 - 6.3.1. Open the Sequence Editor. In the Sequences box on the left, open the folder where the sequence was saved. Click on the sequence to load it.
 - 6.3.2. Make any corrections as needed (see p. 31).
 - 6.3.3. Click Save to save the sequence, then close the Sequence Editor.
 - 6.3.4. Open the Method Editor and correct the method as described above.

Running the Liberty1

1. Click the Start button at the top of the PepDriver1 main screen.

NOTE

If the Method is for 0.5 mmol scale or larger, a warning to verify that the 125 mL reaction vessel is connected will pop up. Click OK to continue.

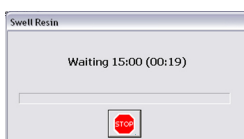
2. The Liberty1 will go through a series of initialization steps.
3. The outline of the resin position will turn yellow to indicate the method is running.



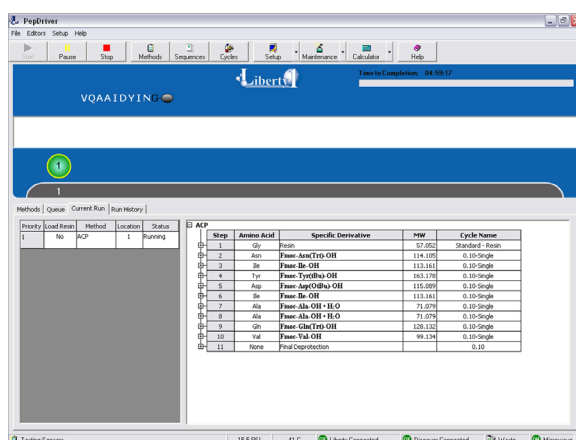
4. The Liberty1 will run a leak check on the reaction vessel to ensure the vessel is

properly connected. This option may be disabled from the Setup menu under Options.

5. The Liberty1 will perform a sensor test to ensure all sensors are operational. This option may be disabled from the Setup menu under Options.
6. Once all initialization and testing is complete, the Liberty1 will enter a wait state for 15 minutes to allow the resin to swell. The time remaining (in seconds) will be displayed in the Swelling box. This option may be disabled from the Setup Menu under options.



During the run, the status of the peptide is displayed above the resin indicator. The estimated time remaining is indicated in the top right. The current step of the method is highlighted in yellow in the Current Method Display.



7. Following final deprotection (if selected), the resin indicator on the PepDriver1 main screen will turn blue, indicating the method was successfully completed.



Generating Reports

Method Reports

Method reports record all settings selected in the Method Editor when creating the method. Method reports are created as PDF files, which can be saved and printed to allow for easy recording of experimental parameters.

A method report consists of two sections. The first section contains information about the synthesis parameters: the sequence with calculated molecular weight, the selected C-terminus (acid or amide), the resin parameters (loading, scale), and a list of the cycles selected for each residue in the sequence. The second section shows every cycle used in the method, including the final deprotection and cleavage cycles. This section includes a full outline of each cycle, providing a record of exactly what was performed at each step.

Creating a Method Report

From the Method Editor:

1. Open the Method Editor.
2. Open the folder containing the method in the Methods window.
3. Click on the method to be reported.
4. Click the Print Method button. The Report Viewer window will open, and the method report will be rendered as a PDF.

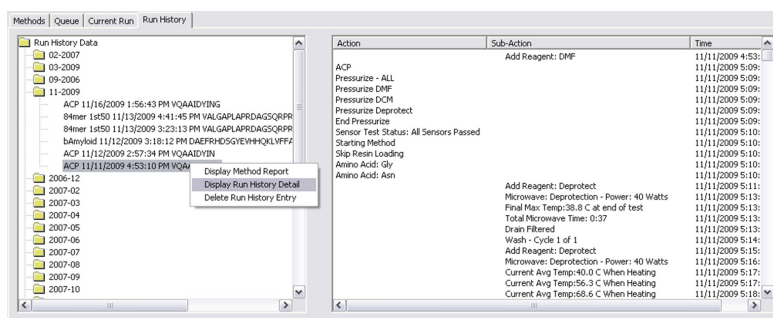
NOTE

The Report Viewer window does not allow scrolling between pages. To view the next page in the report before saving, click the Next Page button, located next to the page number box.

5. Click Save As PDF to save the report.

From the Run History Tab:

1. Open the folder for the month in which the method was run.
2. Right-click on the specific run to be reported and select Display Method Report.



3. The Report Viewer window will open, and the method report will be rendered as a PDF.
4. Click Save As PDF to save the report.



Sample Method Report

ACP

Total MW: 1093.17

Method

Sequence: **VQAADNYING**

C-Terminates: Acid

Resin	Cycles
Scale: 0.10	Resin: Standard - Resin
Substitution: 0.8	
Resin Load: No	Final Deprotection: 0.10

Method Comments:

Modified Date: 4/23/2005 4:41:20 PM

None

Amino Acids

Amino Acid	Specific Derivative	Cycle
Gly - G	Fmoc-Gly-OH	Standard - Resin
Asn - N	Fmoc-Asn(Trt)-OH	D.10-Single
Ile - I	Fmoc-Ile-OH	D.10-Single
Tyr - Y	Fmoc-Tyr(Bzl)-OH	D.10-Single
Asp - D	Fmoc-Asp(Delta)-OH	D.10-Single
Ile - I	Fmoc-Ile-OH	D.10-Single
Ala - A	Fmoc-Ala-OH · H ₂ O	D.10-Single
Ala - A	Fmoc-Ala-OH · H ₂ O	D.10-Single
Gln - Q	Fmoc-Gln(Trt)-OH	D.10-Single
Val - V	Fmoc-Val-OH	D.10-Single

Amino Acid Cycle - 0.10-Single

No	Operation	Parameter	Volumetric (L)	Drain	Cycles	Pause
1	Clean Resin Dip Tube			Yes	1	No
2	Wash - Top	DMF	7.0	Yes	1	No
3	Add Deprotection		7.0	No	1	No
4	Microwave Method	Initial Deprotection		Yes	1	No
5	Wash - Top	DMF	5.0	Yes	1	No
6	Add Deprotection		7.0	No	1	No
7	Microwave Method	Deprotection		Yes	1	No
8	Wash - Top	DMF	7.0	Yes	1	No
9	Wash - Bottom	DMF	7.0	Yes	1	No
10	Wash - Top	DMF	7.0	Yes	1	No
11	Clean Resin Dip Tube			Yes	1	No
12	Wash - Top	DMF	7.0	Yes	1	No
13	Add Amino Acid		2.5	No	1	No
14	Add Activator		1.0	No	1	No
15	Add Activator Base		0.5	No	1	No
16	Microwave Method	Coupling		Yes	1	No
17	Wash - Top	DMF	7.0	Yes	1	No
18	Wash - Bottom	DMF	7.0	Yes	1	No
19	Wash - Top	DMF	7.0	Yes	1	No

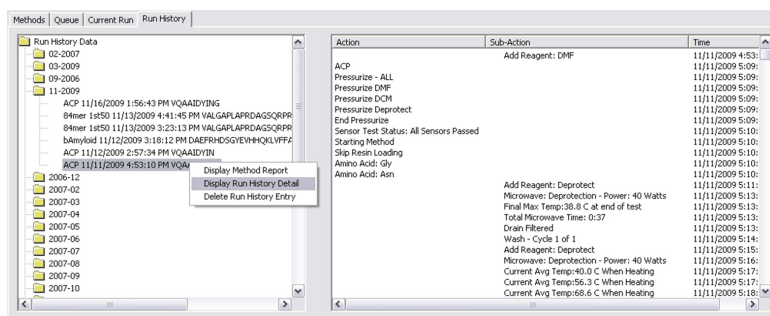
Run History Reports

Run History Reports record each command executed by PepDriver1 during a run with a date/time stamp. In addition, a Run History Report records any system errors that occur, allowing for easy diagnosis and troubleshooting of failed syntheses.

Creating a Run History Report

From the Run History tab:

1. Open the folder for the month in which the method was run.
2. Right-click on the specific run to be reported and select Display Run History Detail.



3. The Report Viewer window will open, and the method report will be rendered as a PDF.
4. Click Save As PDF to save the report.

Sample Run History Report

ACP		Started: 11/11/2009 4:53:10 PM
Run History		
Action	Sub-Action	Time
Add Reagent: DMF		11/11/2009 4:53:17 PM
DMF (2.424)		11/11/2009 4:53:36 PM
ACP		11/11/2009 5:09:23 PM
Pressurize - ALL		11/11/2009 5:09:23 PM
Pressurize DMF		11/11/2009 5:09:23 PM
Pressurize DCM		11/11/2009 5:09:27 PM
Pressurize Deprotect		11/11/2009 5:09:36 PM
End Pressurize		11/11/2009 5:09:36 PM
Sensor Test Status: All Sensors Passed		11/11/2009 5:10:03 PM
Starting Method		11/11/2009 5:10:37 PM
Ship Resin Loading		11/11/2009 5:10:37 PM
Amino Acid: Gly		11/11/2009 5:10:37 PM
Amino Acid: Asn		11/11/2009 5:11:45 PM
Add Reagent: Deprotect		11/11/2009 5:11:45 PM
Deprotect (2.303, 7)		11/11/2009 5:12:12 PM
Microwave: Deprotection - Power: 40 Watts		11/11/2009 5:13:00 PM
Final Max Temp:38.0 C at end of test		11/11/2009 5:13:30 PM
Total Microwave Time: 0:37		11/11/2009 5:13:30 PM
Drain Filtered		11/11/2009 5:13:30 PM
Wash - Cycle 1 of 1		11/11/2009 5:14:23 PM
DMF (2.102, 4)		11/11/2009 5:14:41 PM
Add Reagent: Deprotect		11/11/2009 5:15:32 PM
Deprotect (2.303, 8)		11/11/2009 5:16:01 PM
Microwave: Deprotection - Power: 40 Watts		11/11/2009 5:16:48 PM
Current Avg Temp:60.0 C When Heating		11/11/2009 5:17:23 PM
Current Avg Temp:56.3 C When Heating		11/11/2009 5:17:52 PM
Current Avg Temp:58.6 C When Heating		11/11/2009 5:18:23 PM
Current Avg Temp:77.2 C When Heating		11/11/2009 5:18:53 PM
Current Avg Temp:77.0 C When Heating		11/11/2009 5:19:22 PM
Final Max Temp:77.2 C at end of test		11/11/2009 5:19:54 PM
Total Microwave Time: 3:05		11/11/2009 5:19:55 PM
Drain Filtered		11/11/2009 5:19:55 PM
Wash - Cycle 1 of 1		11/11/2009 5:20:37 PM
DMF (2.302, 3)		11/11/2009 5:20:57 PM
Wash Bottom - Cycle 1 of 1 - Bottom		11/11/2009 5:21:40 PM
DMF Bottom (2.622, 3)		11/11/2009 5:22:00 PM
Wash - Cycle 1 of 1		11/11/2009 5:22:37 PM
DMF (2.262, 3)		11/11/2009 5:22:48 PM
Wash - Cycle 1 of 1		11/11/2009 5:23:58 PM
DMF (2.002, 2)		11/11/2009 5:24:42 PM
Add Amino Acid: Asn (3)		11/11/2009 5:25:10 PM
Add Reagent: Activation/React		11/11/2009 5:25:21 PM
Microwave: Coupling - Power: 20 Watts		11/11/2009 5:31:42 PM
Chem: Coupling		11/11/2009 5:31:48 PM
Current Avg Temp:43.4 C When Heating		11/11/2009 5:32:10 PM
Current Avg Temp:58.7 C When Heating		11/11/2009 5:32:47 PM
Current Avg Temp:58.0 C When Heating		11/11/2009 5:33:17 PM
Current Avg Temp:58.7 C When Heating		11/11/2009 5:33:49 PM
Current Avg Temp:75.2 C When Heating		11/11/2009 5:34:17 PM
End Chem		11/11/2009 5:34:48 PM
Current Avg Temp:77.0 C When Heating		11/11/2009 5:35:47 PM
Current Avg Temp:80.7 C When Heating		11/11/2009 5:35:10 PM
Current Avg Temp:77.8 C When Heating		11/11/2009 5:35:47 PM
Current Avg Temp:76.6 C When Heating		11/11/2009 5:36:17 PM

Section 3: Quick Setup Guide

Liberty1 Setup

Create and Load the Method

1. Create a new sequence.
 - 1.1. Open Sequence Editor by clicking on the Sequence button at the top.
 - 1.2. Click on the folder where the sequence should be saved, then click the New Sequence button.
 - 1.3. Enter a name for the sequence and press Enter.
 - 1.4. Enter the sequence either by clicking on the amino acid buttons or by typing the one letter abbreviations for the amino acids into the Sequence box.

NOTE

The amino acids in the sequence should be entered from N-terminus to C-terminus.

- 1.5. Click Save, then close the Sequence Editor.
2. Create a new method.
 - 2.1. Open the Method Editor by clicking on the Methods button.
 - 2.2. Click on the folder where the method should be saved, then click New Method.
 - 2.3. Enter a name for the method and press Enter.
 - 2.4. Choose the desired sequence from the appropriate folder in the Sequences window. The selected sequence will be loaded into the Sequence box.
 - 2.5. Select all method parameters:
 - 2.5.1. Resin Information:
 - 2.5.1.1. Scale: Select the scale for the synthesis of the peptide (0.05 mmol to 5.0 mmol).

CAUTION

The 125 mL reaction vessel must be used for syntheses above 0.25 mmol.
The 10 mL reaction vessel should be used for syntheses below 0.1 mmol.

- 2.5.1.2. Resin Substitution: The resin substitution can be found on the bottle of resin and it will be labeled either meq/g or mmol/g.

NOTE

The substitution value entered will not affect the operation of the Liberty1. It is only needed for the Usage Calculator to calculate how much resin is required for the synthesis.

- 2.5.2. C-terminus: If using preloaded resin (the resin already has the first amino acid attached), select Acid. Otherwise, select Amide.
- 2.5.3. Final Deprotection: Select Yes to remove the final Fmoc from the N-terminus of the peptide.
- 2.5.4. Default cycles:
- 2.5.4.1. Resin: After the scale is selected, the default Resin Transfer cycle will be loaded for the appropriate reaction vessel. Ensure the correct vessel is connected to the Liberty1.
- 2.5.4.2. Final Deprotection: Select the desired final deprotection cycle.
- 2.6. Click Save to save the method. Close the Method Editor
3. From the main screen of PepDriver1, load the method by clicking on the appropriate method in the Method Tab and dragging it to the resin indicator at the top of the screen. The resin indicator should turn green.

Prepare Reagents

4. To determine the amount of each reagent needed and how to prepare them, use the Usage and Reagent Calculators
- 4.1. Click on the Calculator button and select Usage from the menu. From the Methods window in the calculator, select the method to be run. Check the box next to the method name to calculate the amount of each reagent required. Click Print at the bottom of the calculator to generate a PDF that can be printed or saved.
- 4.2. Click on the Calculator button and select Reagent from the menu.
- 4.2.1. Resin: Enter the scale of the synthesis and the resin substitution to determine the mass of resin needed.
- 4.2.2. Other Reagents: For the other reagents, click on the appropriate tab (Activator, Base, Deprotection) and then select the appropriate reagent from the list. Enter the concentration and volume needed on the right and click Calculate.
5. Load all reagents onto the Liberty1.
- 5.1. Dissolve each amino acid in the correct volume of solvent in a 125 mL bottle. Connect each bottle onto the corresponding position for that amino acid on the manifold.
- 5.2. Connect an empty 125 mL bottle to any unused amino acid positions.

- 5.3. Dissolve activator in the correct volume of solvent in a 250 mL amber glass bottle. Use the Change Bottle command (see p. 57) to replace the activator bottle connected to the Liberty1.
 - 5.3.1. Click on the Maintenance button at the top of the screen and select Maintenance in the drop down box.
 - 5.3.2. On the right hand side of the Maintenance window, under Cleaning, choose the reagent in the first box to be removed and then click Change Bottle. Follow the onscreen instructions to replace the bottles.
- 5.4. Dissolve activator base in the correct volume of solvent in a 250 mL clear glass bottle. Use the Change Bottle command (see p.57) to replace the activator base bottle connected to the Liberty1.
 - 5.4.1. Click on the Maintenance button at the top of the screen and select Maintenance in the drop down box.
 - 5.4.2. On the right hand side of the Maintenance window, under Cleaning, choose the reagent in the first box to be removed and then click Change Bottle. Follow the onscreen instructions to replace the bottles.
- 5.5. Add the correct volume of deprotection reagent to a 1 L bottle, then add the correct amount of DMF. Use the Change Bottle command (see p. 57) to replace the deprotection bottle connected to the Liberty1.
 - 5.5.1. Click on the Maintenance button at the top of the screen and select Maintenance in the drop down box.
 - 5.5.2. On the right hand side of the Maintenance window, under Cleaning, choose the reagent in the first box to be removed and then click Change Bottle. Follow the onscreen instructions to replace the bottles.
- 5.6. Check the DMF bottles to ensure there is enough solvent to complete the synthesis. If the solvent need to be replaced, use the Change Bottle command (see p. 57) to replace the solvent bottles connected to the Liberty1.
 - 5.6.1. Click on the Maintenance button at the top of the screen and select Maintenance in the drop down box.
 - 5.6.2. On the right hand side of the Maintenance window, under Cleaning, choose the reagent in the first box to be removed and then click Change Bottle. Follow the onscreen instructions to replace the bottles.

Ensure the Liberty1 is Ready to Run

6. Verify that the waste container has sufficient capacity.
7. Verify that the fiber optic probe is fully inserted into the thermowell.

WARNING

If the probe is not inserted all the way to the bottom of the vessel the Liberty1 will not accurately measure the temperature, and significant overheating of the vessel will occur. This will result in poor synthesis quality and/or serious damage to the vessel.

8. Verify that the method is correct by looking at the steps outlined in the Method box. If there are any errors, make corrections and reload the method.
 - 8.1. Right-click on the green resin indicator and select Clear Method.
 - 8.2. Open the Method Editor. In the Methods box on the left, open the folder where the method was saved. Click on the method to load it.
 - 8.3. Make any corrections as needed. Click Save the save the method, then close the Method Editor.
 - 8.4. Load the corrected method as described in step 3.
9. If the method is correct and all reagents are attached to the Liberty1, press the Start button at the top of the screen to begin the synthesis.

NOTE

If the Method is for 0.5 mmol scale or larger, a warning to verify that the 125 mL reaction vessel is connected. Click OK to continue.

Section 4: Maintenance of the Liberty1

Routine Maintenance

A routine maintenance protocol is vital for the long-term operation of the Liberty1. Further details about the maintenance procedures can be found in the Liberty1 Maintenance Procedures Manual (PN 600765). The Liberty1 Maintenance Procedures Manual also contains twelve months of maintenance logs for recording and maintaining maintenance records.

Daily Maintenance

- Inspect the instrument for any visible signs of leakage in all spill trays, any flat areas inside the Liberty1, and inside the cavity of the Discover.
- Check the level in the waste container and empty if necessary.
- Ensure the fiber optic probe is fully inserted into the thermowell on the reaction vessel.

Weekly Maintenance

- Replace the two inline filters (PN 172105-M):
 - F2 filter (front of Liberty1)
 - F3 (reaction vessel drain line)

Biweekly Maintenance

- Replace dip tube filters (PN 167485-M)
- Backflush all positions except Main Wash/DMF. (See Performing a Backflush, p. 60, for details.)

Monthly Maintenance

- Perform a sensor calibration on all sensors. (See Performing a Sensor Calibration, p. 67, for details.)
- Perform a volume calibration for all additions. (See Performing a Volume Calibration, p. 62, for details.)
- Verify the performance of the filtered drain by adding 10 mL of DMF to the reaction vessel and then performing a filtered drain. The reaction vessel should drain 10 mL of DMF within 10 seconds. If the drain takes longer than 10 seconds, replace the F3 filter and try again. If the drain still takes longer than 10 seconds, replace the reaction vessel.
- Inspect the reaction vessel for particulate accumulation, particularly on the top of the vessel.

- Review recent run history reports (see Run History Reports, p. 51, for details) to ensure that the Liberty1 is heating properly. The temperature for a coupling should reach 75 °C within 70 seconds. If the Liberty1 is not reaching temperature in time, increase the power setting in the Microwave Editor (see Editing an Existing Microwave Method, p. 26 for details). If the Liberty1 is routinely heating to above 83 °C, decrease the power setting in the Microwave Editor.

Semiannual Maintenance

- Replace the reaction vessel body.
- Verify the proper operation of the waste sensor.

Standby Procedure

If the Liberty1 will be idle for a period of two weeks or more:

- Remove all reagents (amino acids, activator, activator base, deprotection) from the system.
- Backflush all positions except Main Wash/DMF.
- Remove the wash solvent and perform a backpurge on that position to empty the lines.

Prior to using the Liberty1 after it has been in Standby:

- Connect the main wash solvent using the Change Bottle command to properly prime the lines and pressurize the bottles.
- Perform a backflush on all positions except Main Wash/DMF.
- Perform a Sensor Calibration on all sensors. (See Performing a Sensor Calibration, p. 67, for details.)
- Perform a Volume Calibration for all additions. (See Performing a Volume Calibration, p. 62, for details.)

Maintenance Screen

The Maintenance screen is accessed by clicking on the Maintenance button on the PepDriver1 main screen and selecting Maintenance. From the Maintenance Menu, a number of important maintenance procedures and manual system commands can be accessed.

Cleaning Tab

Maintenance

Cleaning | Volume Calibration | Sensor Calibration | Pressure Calibration

Backflush

Reagent	Date Backflushed
<input type="checkbox"/> Cys - C	1/7/2010
<input type="checkbox"/> Asp - D	1/7/2010
<input type="checkbox"/> Asn - N	1/7/2010
<input type="checkbox"/> Arg - R	1/7/2010
<input type="checkbox"/> Ala - A	1/7/2010
<input type="checkbox"/> Gln - Q	1/7/2010
<input type="checkbox"/> Glu - E	1/7/2010
<input type="checkbox"/> Gly - G	1/7/2010
<input type="checkbox"/> His - H	1/7/2010
<input type="checkbox"/> Ile - I	1/7/2010
<input type="checkbox"/> Pro - P	1/7/2010
<input type="checkbox"/> Phe - F	1/7/2010
<input type="checkbox"/> Met - M	1/7/2010
<input type="checkbox"/> Lys - K	1/7/2010
<input type="checkbox"/> Leu - L	1/7/2010
<input type="checkbox"/> Ser - S	1/7/2010
<input type="checkbox"/> Thr - T	1/7/2010
<input type="checkbox"/> Trp - W	1/7/2010
<input type="checkbox"/> Tyr - Y	1/7/2010
<input type="checkbox"/> Val - V	1/7/2010
<input type="checkbox"/> Main Wash	
<input type="checkbox"/> Deprotect	1/7/2010
<input type="checkbox"/> Activator	1/7/2010
<input type="checkbox"/> Activator Base	1/7/2010

☐ Select All

Backflush Backpurge

Clean

Change Bottle Reagent: Activator Base mL: 2

Add Deprotect

Depressurize Deprotect

Clean All Manifolds

Prime Cys - C

Liberty1 Purge

Wash

Wash

Reagent: Main Wash Cycles: 1 Volume: 10

Location: ☒ Top ☐ Bottom

Drain

Filtered

System Tests

Test System

Leak Test Test Sensors

AllValvesOff

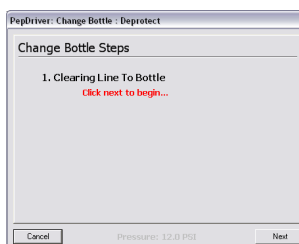
- **Clean**
 - **Change Bottle:** Clicking this button begins the Change Bottle procedure for the reagent selected from the pull-down menu. (For more information about using Change Bottle, see Using the Change Bottle Command, p. 59).
 - **Add:** Clicking this button will add the reagent selected from the pull-down menu to the reaction vessel at the volume selected from the second pull-down menu.
 - **Depressurize:** Clicking this button will vent any pressure from the reagent selected from the pull-down menu.
 - **Clean All Manifolds:** Clicking this button will begin a cleaning procedure for all manifolds on the system. This cleaning only cleans the manifolds and any internal tubing; it does not affect the dip tubes or any bottles connected to the

system.

- **Prime:** Clicking this button will prime the lines for the reagent selected from the pull-down menu.
- **Liberty1 Purge:** Clicking this button will purge all liquid from all lines and manifolds on the system.
- **Wash:** Clicking this button adds the selected volume of Main Wash (DMF) to the reaction vessel from either the top or the bottom, then performs a filtered drain.
- **Drain Filtered:** Clicking this button drains the contents of the reaction vessel through the glass frit on the bottom of the reaction vessel and through the inline filter out to waste. Any solid reagents will remain in the reaction vessel.
- **Backflush**
 - **Backflush:** Clicking this button will perform a backflush on the reagent(s) selected from the list. (For more information about using the Backflush command, see Performing a Backflush, p. 60.)
 - **Backpurge:** Clicking this button will perform a backpurge on the reagent(s) selected from the list.
- **System Tests**
 - **Leak Test:** Clicking this button brings a full leak check of the system. (For more information about the leak testing procedure, see Test System, p. 79.)
 - **Test Sensors:** Clicking this button begins a full sensor test of the system. (For more information about the sensor test procedure, see Test System, p. 81.)
 - **Test System:** Clicking this button opens the Test System menu, which contains a number of diagnostic tests and troubleshooting procedures.

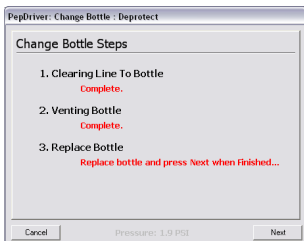
Using the Change Bottle Command

1. Click on the pull-down menu to select the reagent to be changed, then click the Change Bottle button.
2. The Change Bottle window will appear. Click Next to begin the Change Bottle procedure.



3. The Liberty1 will clear the line to the bottle, and then vent the pressure to the bottle.

- The Change Bottle window will indicate it is safe to remove the bottle. Remove the old bottle from the system and connect a fresh bottle.



- Click Next to continue. The Liberty1 will pressurize the bottle and prime the lines. Once the lines are primed, click Close to close the Change Bottle window and return to the Maintenance screen.

Performing a Backflush

NOTE

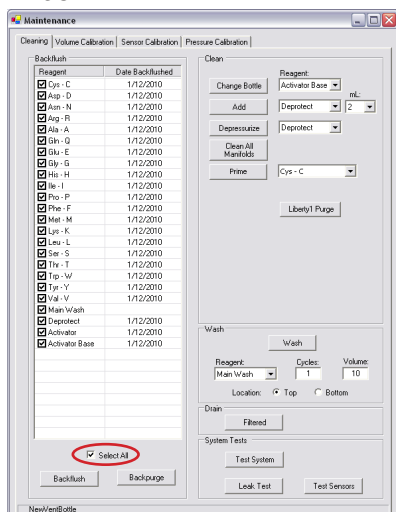
For detailed instructions on performing a backflush, see the Liberty1 Maintenance Procedures manual, PN 600765.

- Remove the bottles for all positions to be backflushed. Remove the diptube filters, then connect empty bottles to all positions to be backflushed.
- Ensure that all reagent positions have a bottle connected.

NOTE

All reagent positions on the Liberty1 must have a bottle connected to perform a backflush. The Change Bottle command should be used to connect empty bottles for Deprotection, Activator, and Activator Base.

- From the Cleaning Tab, check the box next to each position to be backflushed. To backflush all reagents, click Select All and then uncheck the box for Main Wash.

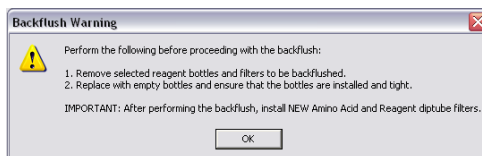


<input checked="" type="checkbox"/>	Tyr - Y	1/7/2010
<input checked="" type="checkbox"/>	Val - V	1/7/2010
<input type="checkbox"/>	Main Wash	
<input checked="" type="checkbox"/>	Deprotect	1/7/2010
<input checked="" type="checkbox"/>	Activator	1/7/2010
<input checked="" type="checkbox"/>	Activator Base	1/7/2010

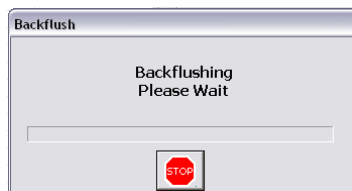
NOTE

Main Wash (DMF) should not be backflushed.

- Click the Backflush button. A warning box will pop up. Verify that dip tube filters have been removed from all positions to be backflushed and that empty bottles have been connected and tightened. Click OK to continue.



- A progress window will pop up showing the progress of the backflush procedure for all amino acids. The status for each step of the backflush procedure will be displayed on the System Status line of the PepDriver1 main screen.



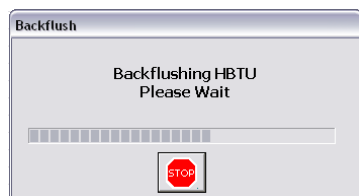
NOTE

Before backflushing any amino acid positions, the system will go through a pressurization/depressurization step, which can take up to five minutes to complete. Progress of this step will be displayed on the System Status Line of the PepDriver1 main screen.

- Once all amino acid positions have been backflushed, the checkboxes will be cleared and the date will be updated to the current date.

Reagent	Date Backflushed
<input type="checkbox"/> Cys - C	1/12/2010
<input type="checkbox"/> Asp - D	1/12/2010
<input type="checkbox"/> Asn - N	1/12/2010
<input type="checkbox"/> Arg - R	1/12/2010
<input type="checkbox"/> Ala - A	1/12/2010
<input type="checkbox"/> Gln - Q	1/12/2010
<input type="checkbox"/> Glu - E	1/12/2010
<input type="checkbox"/> Gly - G	1/12/2010
<input type="checkbox"/> His - H	1/12/2010
<input type="checkbox"/> Ile - I	1/12/2010
<input type="checkbox"/> Pro - P	1/12/2010
<input type="checkbox"/> Phe - F	1/12/2010
<input type="checkbox"/> Met - M	1/12/2010
<input type="checkbox"/> Lys - K	1/12/2010
<input type="checkbox"/> Leu - L	1/12/2010
<input type="checkbox"/> Ser - S	1/12/2010
<input type="checkbox"/> Thr - T	1/12/2010
<input type="checkbox"/> Trp - W	1/12/2010
<input type="checkbox"/> Tyr - Y	1/12/2010
<input type="checkbox"/> Val - V	1/12/2010
<input type="checkbox"/> Main Wash	

- When backflushing other reagent positions (Deprotection, Activator, Activator Base), a progress window will pop up showing the progress for each position. As each position is backflushed, the checkbox will be cleared and the date updated to the current date.



<input type="checkbox"/> Deprotect	1/12/2010
<input type="checkbox"/> Activator	1/12/2010
<input checked="" type="checkbox"/> Activator Base	1/7/2010

- Once all positions have been backflushed, remove the bottles from those positions and dispose of the liquid.

Volume Calibration Tab

Position	Delivery	Volume	Rate (mL/s)	Flow(Cal/Current)(s)	Date
1	Add DMF - Top	10.00	1.336	2.4 / 2.2	11/11/2009
7	Add Deprotect - Top	10.00	1.305	3.7 / 4.0	11/11/2009
8	Add DMF - Bottom	10.00	1.334	2.8 / 2.1	11/11/2009

Reagent Calibration | Large Scale Calibration

Delivery

Drain

Backup

The Volume Calibration tab allows for the calibration of the timed delivery of reagents to the reaction vessel. Reagent calibration should be performed monthly as part of routine maintenance.

In addition, the Volume Calibration tab allows for the calibration of amino acids at large scale. For additions of more than 11 mL, the Liberty1 switches from a sample loop to a timed addition to reduce the time required for each addition.

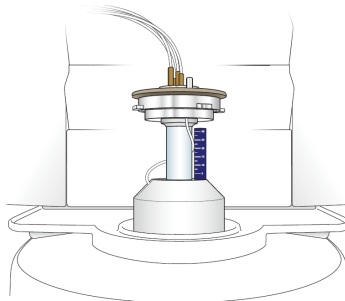
Performing a Volume Calibration

NOTE

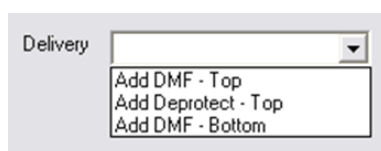
For detailed instructions on performing a volume calibration, see the Liberty1 Maintenance Procedures manual, PN 600765.

1. Place the reaction vessel into the volume calibration stand (PN 576250).
 - 1.1. Remove the reaction vessel assembly from the cavity of the Discover.
 - 1.2. Set the volume calibration stand on top of the cavity opening, with the graduations on the right.

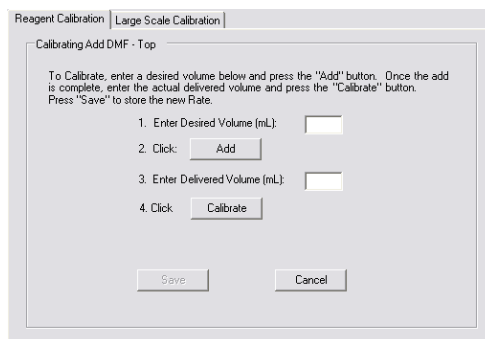
- 1.3. Insert the reaction vessel into the calibration stand so that the drain line from the bottom of the vessel fits into the slot on the left of the stand.



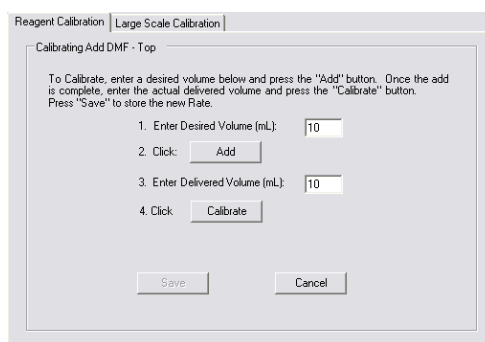
2. From the Volume Calibration tab, click on the Delivery pull-down to select the reagent to calibrate.



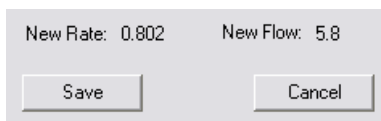
3. Once a reagent has been selected, click Calibrate to begin the calibration procedure.



4. Enter the volume to be used for calibration, then click Add. Typically, 10 mL of reagent are used for calibration.
5. The selected reagent will be added to the reaction vessel through the sprayhead. Once the addition is finished, measure the volume delivered to the reaction vessel using the graduations on the calibration stand.
6. Enter the amount of reagent delivered to the reaction vessel.



7. Click Calibrate. Two values will be displayed below the Calibrate button, New Rate and New Flow. Click Save to save the new calibration values.

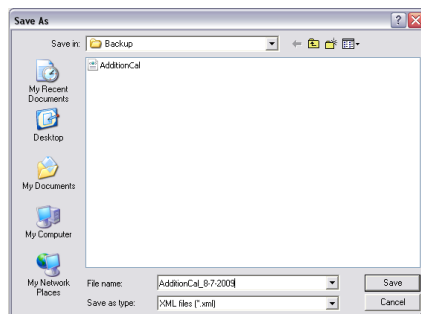


8. Click the Filtered Drain button to empty the reaction vessel.

Importing and Exporting Volume Calibration Values

To create a backup copy of the current volume calibration values:

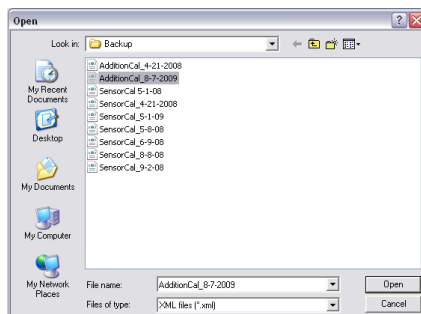
1. From the Volume Calibration tab, click Export.



2. Enter a name for the backup file, and then click Save.

To restore previous volume calibration values from a backup file:

1. From the Volume Calibration tab, click Import.
2. Select the backup file to be restored, and then click Open.



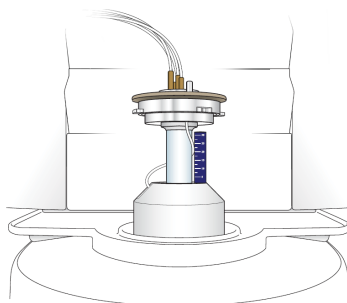
NOTE

When importing values from a backup file, the current calibration values for all reagents will be discarded.

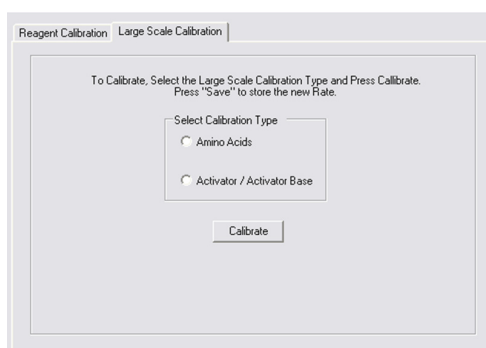
Performing a Large Scale Calibration

1. Place the reaction vessel into the volume calibration stand (PN 576250).
 - 1.1. Remove the reaction vessel assembly from the cavity of the Discover.
 - 1.2. Set the volume calibration stand on top of the cavity opening, with the graduations on the right.

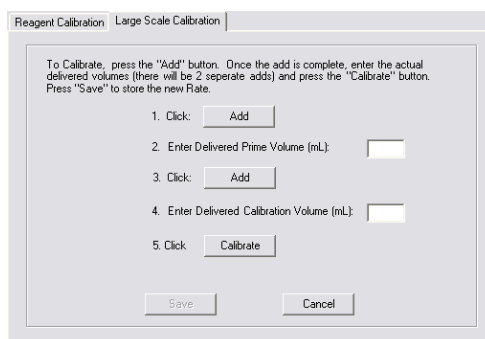
- 1.3. Insert the reaction vessel into the calibration stand so that the drain line from the bottom of the vessel fits into the slot on the left of the stand.



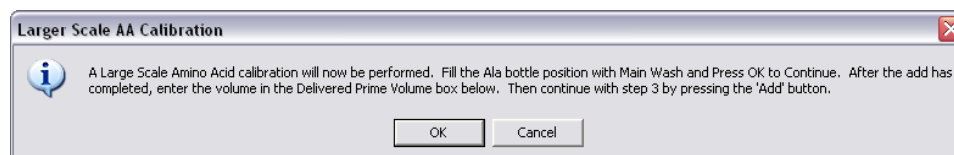
2. From the Volume Calibration Tab, click on the Large Scale Addition Tab.



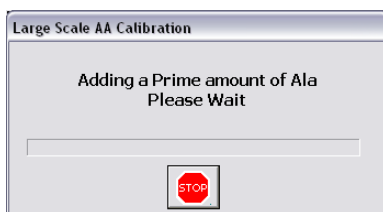
3. Select the desired reagent and click Calibrate.
4. Click the first Add button to begin the calibration procedure.



5. A warning box will pop up to confirm that Main Wash (DMF) has been added to the appropriate position for the calibration procedure. Ensure sufficient DMF (approximately 30 mL) is connected and click OK.



- A prime volume of DMF will be added to the reaction vessel.

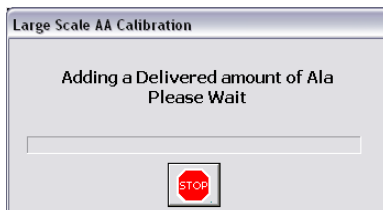


Once the addition is finished, measure the volume delivered to the reaction vessel using the graduations on the calibration stand.

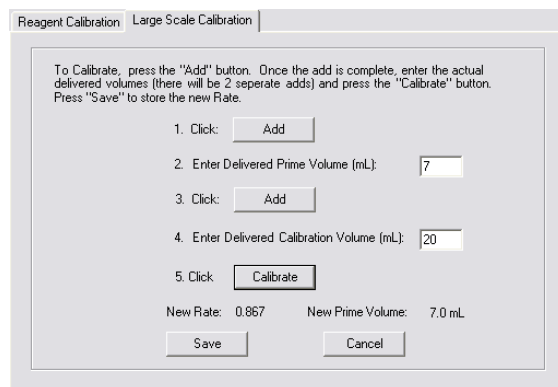
- Enter the delivered volume in the Prime Volume box, and then click the second Add button.
- The solvent will be automatically drained from the reaction vessel. Following the filtered drain, the Liberty1 will add a delivery volume of DMF to the reaction vessel (approximately 20 mL).



Once the addition is finished, measure the volume delivered to the reaction vessel using the graduations on the calibration stand.



- Enter the delivered volume in the Delivered Calibration Volume box, and then click Calibrate. Two values will appear below the Calibrate button: New Rate and New Prime Volume. Click Save to save the new calibration values.



Sensor Calibration Tab

Sensor	Current Threshold	New Threshold	Calibration Date
<input type="checkbox"/> X1	311		10/16/2009
<input type="checkbox"/> X2	259		10/16/2009
<input type="checkbox"/> A1	311		10/16/2009
<input type="checkbox"/> A2	307		10/16/2009
<input type="checkbox"/> A3	238		10/16/2009
<input type="checkbox"/> A4	235		10/16/2009
<input type="checkbox"/> A5	268		10/16/2009
<input type="checkbox"/> A6	270		10/16/2009
<input type="checkbox"/> A7	231		10/16/2009
<input type="checkbox"/> A8	242		10/16/2009
<input type="checkbox"/> A9	261		10/16/2009
<input type="checkbox"/> A10	267		10/16/2009
<input type="checkbox"/> A11	295		10/16/2009
<input type="checkbox"/> A12	311		10/16/2009
<input type="checkbox"/> A13	237		10/16/2009
<input type="checkbox"/> A14	313		10/16/2009
<input type="checkbox"/> A15	262		10/16/2009
<input type="checkbox"/> A16	240		10/16/2009
<input type="checkbox"/> A17	253		10/16/2009
<input type="checkbox"/> A18	245		10/16/2009
<input type="checkbox"/> A19	267		10/16/2009
<input type="checkbox"/> A20	255		10/16/2009
<input type="checkbox"/> X9	246		10/16/2009
<input type="checkbox"/> X10	247		10/16/2009
<input type="checkbox"/> X11	277		10/16/2009
<input type="checkbox"/> X12	293		10/16/2009
<input type="checkbox"/> X13	283		10/16/2009
<input type="checkbox"/> LS1	266		10/16/2009
<input type="checkbox"/> LS2	NA	NA	

Backup
Import
Export

Calibration
☒ Select All
Calibrate
Save

Test
Test Sensors

The Sensor Calibration tab allows for the calibration of the sensors used to monitor the addition and transfer of reagents in the Liberty1. Sensor calibration should be performed monthly as part of routine maintenance.

Performing a Sensor Calibration

NOTE

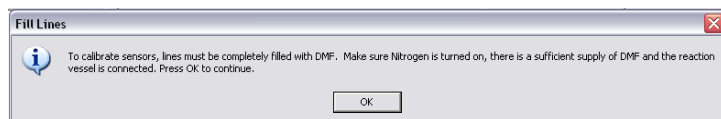
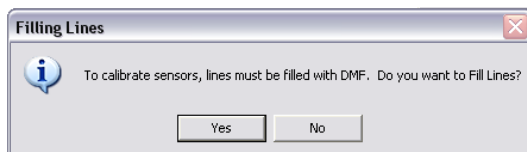
For detailed instructions on performing a sensor calibration, see the Liberty1 Maintenance Procedures manual, PN 600765.

1. Open the Sensor Calibration tab. PepDriver1 will load the current calibration values for each sensor.
2. Check the Select All box. This will select all sensors except LS2.

NOTE

LS2 does not need to be routinely calibrated. A separate calibration procedure is required for this sensor. Contact CEM Service for help if these sensors require calibration.

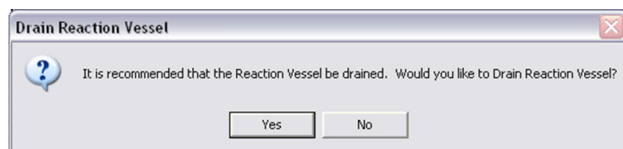
- Click Calibrate to begin the sensor calibration procedure.
- A series of warning boxes will pop up to ensure sufficient DMF is loaded on the Liberty1 for the test. Verify there is sufficient DMF in the Main Wash bottles (approximately 75 mL) and click OK.



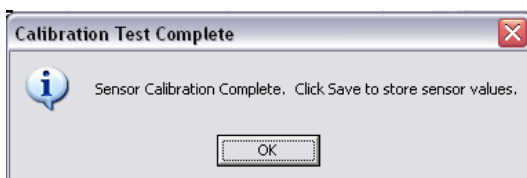
- The instrument will pressurize the DMF bottles and then fill all manifolds and tubing with DMF. Once this is complete, the calibration procedure will begin. As each sensor is calibrated, the updated calibration value is displayed in the New Threshold column. The entire process should take approximately 5 minutes.

Cleaning Volume Calibration Sensor Calibration Pressure Calibration			
Sensor	Current Threshold	New Threshold	Calibration Date
<input checked="" type="checkbox"/> X1	311	312	10/16/2009
<input checked="" type="checkbox"/> X2	259	259	10/16/2009
<input checked="" type="checkbox"/> A1	311	315	10/16/2009
<input checked="" type="checkbox"/> A2	307	304	10/16/2009
<input checked="" type="checkbox"/> A3	238		10/16/2009
<input checked="" type="checkbox"/> A4	235		10/16/2009
<input checked="" type="checkbox"/> A5	268		10/16/2009
<input checked="" type="checkbox"/> A6	270		10/16/2009
<input checked="" type="checkbox"/> A7	231		10/16/2009
<input checked="" type="checkbox"/> A8	242		10/16/2009
<input checked="" type="checkbox"/> A9	261		10/16/2009
<input checked="" type="checkbox"/> A10	267		10/16/2009
<input checked="" type="checkbox"/> A11	295		10/16/2009
<input checked="" type="checkbox"/> A12	311		10/16/2009
<input checked="" type="checkbox"/> A13	237		10/16/2009
<input checked="" type="checkbox"/> A14	313		10/16/2009
<input checked="" type="checkbox"/> A15	262		10/16/2009
<input checked="" type="checkbox"/> A16	240		10/16/2009
<input checked="" type="checkbox"/> A17	253		10/16/2009
<input checked="" type="checkbox"/> A18	245		10/16/2009
<input checked="" type="checkbox"/> A19	267		10/16/2009
<input checked="" type="checkbox"/> A20	255		10/16/2009
<input checked="" type="checkbox"/> X9	246		10/16/2009
<input checked="" type="checkbox"/> X10	247		10/16/2009
<input checked="" type="checkbox"/> X11	277		10/16/2009
<input checked="" type="checkbox"/> X12	293		10/16/2009
<input checked="" type="checkbox"/> X13	283		10/16/2009
<input checked="" type="checkbox"/> LS1	266		10/16/2009
<input type="checkbox"/> LS2	NA	NA	

- When calibration is complete, a window will pop up suggesting performing a filtered drain. Click OK to drain the reaction vessel.



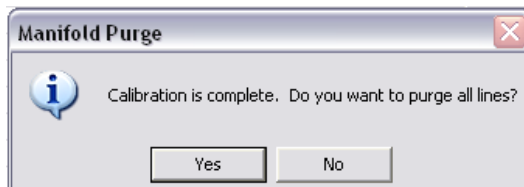
- After the filtered drain, a window will pop up stating that the procedure is complete. Click OK to close the window.



8. Click Save to save the new calibration values. As each value is saved, the New Threshold column will be cleared and the Current Threshold values will be updated with the new calibration value.

Cleaning Volume Calibration Sensor Calibration Pressure Calibration			
Sensor	Current Threshold	New Threshold	Calibration Date
<input type="checkbox"/> X1	312		11/13/2009
<input type="checkbox"/> X2	259		11/13/2009
<input type="checkbox"/> A1	315		11/13/2009
<input type="checkbox"/> A2	304		11/13/2009
<input checked="" type="checkbox"/> A3	238	235	10/16/2009
<input checked="" type="checkbox"/> A4	235	233	10/16/2009
<input checked="" type="checkbox"/> A5	268	271	10/16/2009
<input checked="" type="checkbox"/> A6	270	271	10/16/2009
<input checked="" type="checkbox"/> A7	231	229	10/16/2009
<input checked="" type="checkbox"/> A8	242	241	10/16/2009
<input checked="" type="checkbox"/> A9	261	259	10/16/2009
<input checked="" type="checkbox"/> A10	267	269	10/16/2009
<input checked="" type="checkbox"/> A11	295	296	10/16/2009
<input checked="" type="checkbox"/> A12	311	310	10/16/2009
<input checked="" type="checkbox"/> A13	237	237	10/16/2009
<input checked="" type="checkbox"/> A14	313	311	10/16/2009
<input checked="" type="checkbox"/> A15	262	261	10/16/2009
<input checked="" type="checkbox"/> A16	240	241	10/16/2009
<input checked="" type="checkbox"/> A17	253	251	10/16/2009
<input checked="" type="checkbox"/> A18	245	246	10/16/2009
<input checked="" type="checkbox"/> A19	267	265	10/16/2009
<input checked="" type="checkbox"/> A20	295	294	10/16/2009
<input checked="" type="checkbox"/> X9	246	244	10/16/2009
<input checked="" type="checkbox"/> X10	247	246	10/16/2009
<input checked="" type="checkbox"/> X11	277	275	10/16/2009
<input checked="" type="checkbox"/> X12	293	292	10/16/2009
<input checked="" type="checkbox"/> X13	283	283	10/16/2009
<input type="checkbox"/> LS1	266	267	10/16/2009
<input type="checkbox"/> LS2	NA	NA	

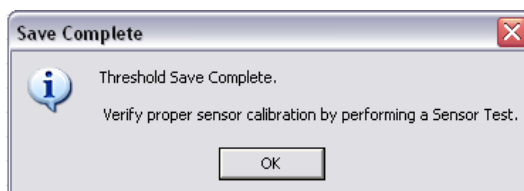
9. Once all the new calibration values are saved, a window will pop up to purge the lines of DMF. Click Yes to empty the lines, or click No to leave the lines filled.



NOTE

The first step of a Sensor Test is to fill the lines. To conserve DMF, click No to leave the lines filled if a Sensor Test will be performed.

10. A window will pop up suggesting running a Sensor Test. Click OK to close the window.



11. Click the Test Sensors button to begin a Sensor Test.

NOTE

For information on performing a Sensor Test, see Test Sensors, p. 81.

Importing and Exporting Sensor Calibration Values

To create a backup copy of the current sensor calibration values:

1. From the Sensor Calibration tab, click Export.
2. Enter a name for the backup file, and then click Save.

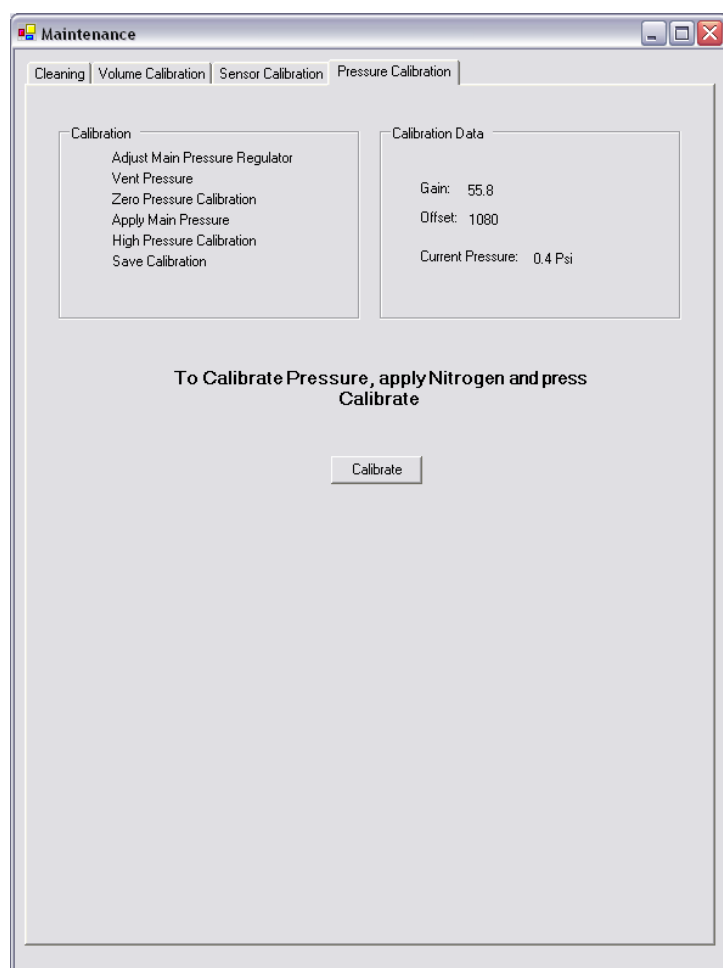
To restore previous sensor calibration values from a backup file:

1. From the Sensor Calibration tab, click Import.
2. Select the backup file to be restored, and then click Open.

NOTE

When importing values from a backup file, the current calibration values for all sensors will be discarded.

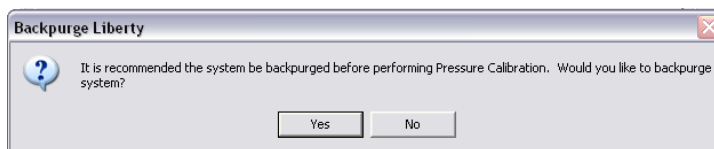
Pressure Calibration Tab



The Pressure Calibration tab allows for the calibration of the pressure sensor on the Liberty1. Pressure calibration is not necessary for routine maintenance; a calibration should only be done as part of a troubleshooting protocol as advised by CEM Service.

Performing a Pressure Calibration

1. Click Calibrate to begin the calibration procedure. A warning will pop up about performing a backpurge. Click Yes to backpurge the system before calibrating.



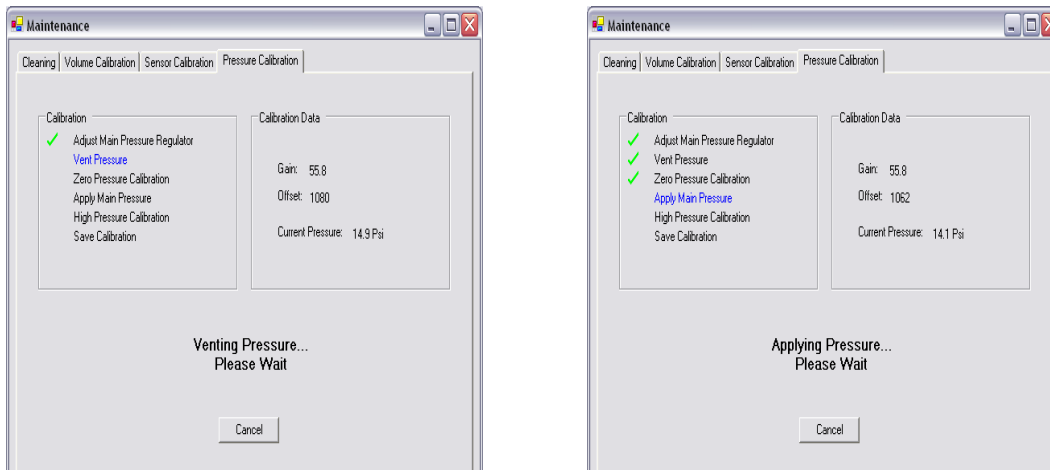
NOTE

Put empty bottles on all positions before performing a backpurge.

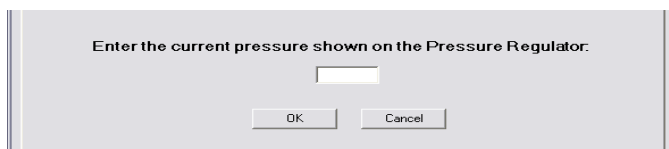
2. Adjust the pressure on the main pressure regulator in the Liberty1 to 16 psi, and then click OK to continue the calibration.



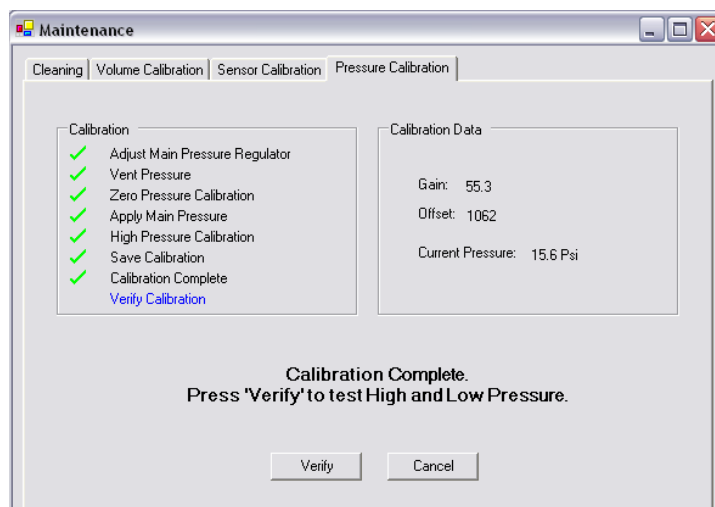
- The Liberty1 will vent the pressure on the entire system to get a zero pressure reading, and then apply pressure to get a main pressure reading.



- Look at the pressure regulator on the Liberty1 and enter the current reading. Click OK to continue the calibration.



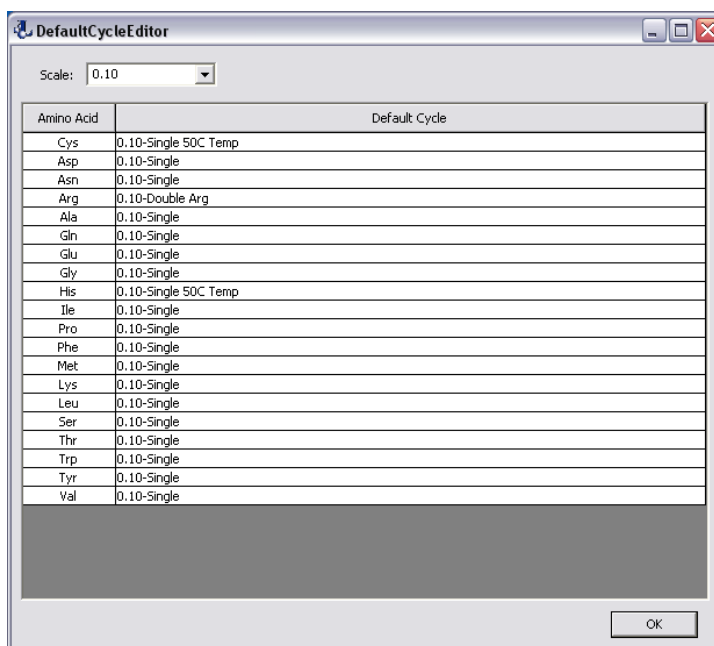
- The software will save the calibration values automatically. Click Verify to test the pressure readings.



- The Test System screen will automatically open and begin performing a Pressure Adjustment to confirm the pressure is within the correct range.

Section 5: Advanced Features

Default Cycle Editor



The Default Cycle Editor is accessed by clicking the Setup button and selecting Default Cycle Editor. The Default Cycle Editor allows the user to assign a default Amino Acid Cycle to each amino acid. Different cycles can be assigned for different scales, allowing for the use of higher power or more agitation at higher synthesis scales.

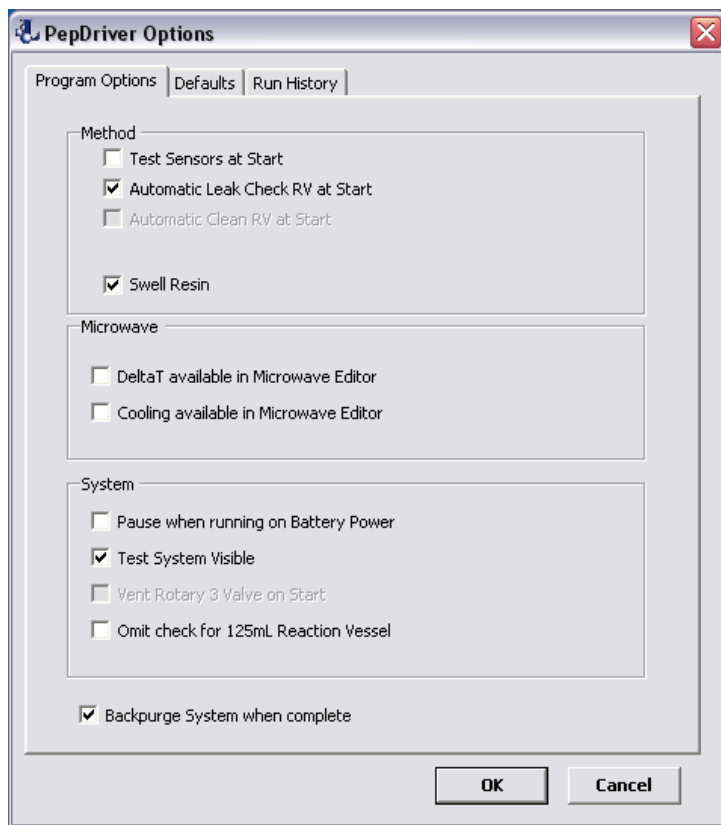
Changing Default Cycles

1. Open the Default Cycle Editor by clicking the Setup button and selecting Default Cycles.
2. Select a scale from the Scale pull-down menu.
3. Click on the cycle next to the an amino acid and select the desired cycle from the pull-down.
4. Click OK to save the new default cycles.

Options Menu

The Options Menu can be accessed by clicking the Setup button from the PepDriver1 main screen and selecting Options. The Options menu allows configuration of a number of important system functions.

Program Options Tab



- **Method Options**
 - **Test Sensors at Start:** When this option is enabled, the Liberty1 will perform a full Sensor Test before starting the first method in the queue. This option is disabled by default.
 - **Automatic Leak Check RV at Start:** When this option is enabled, the Liberty1 will perform a leak check of the reaction vessel before starting the first method in the queue. This option is enabled by default.
 - **Swell Resin:** When this option is enabled, the Liberty1 will add 10 mL of Main Wash/DMF to the reaction vessel and then enter a wait state for 15 minutes to swell the resin. This option is enabled by default.

- **Microwave Options**

- **DeltaT Available in Microwave Editor:** When this option is enabled, the delta T value can be changed when programming a microwave method in the Microwave Editor.

NOTE

During a microwave method, microwave power will only be applied until the temperature reaches the programmed temperature. At that point, the power will be turned off until the temperature drops to below the delta temperature value. This reduces the risk of overshooting the temperature and improves the quality of the synthesis. The default value for delta T is 5 degrees.

- **Cooling Available in Microwave Editor:** When this option is enabled, air cooling can be enabled when programming a microwave method in the Microwave Editor.

NOTE

During a microwave method, if air cooling is enabled, and the air cooling line is connected to the Discover and to a nitrogen source, a stream of air will be blown over the reaction vessel. This will decrease the time needed for the temperature to drop below the delta T and for the microwave power to resume. Air cooling is not recommended for peptide synthesis.

- **System Options**

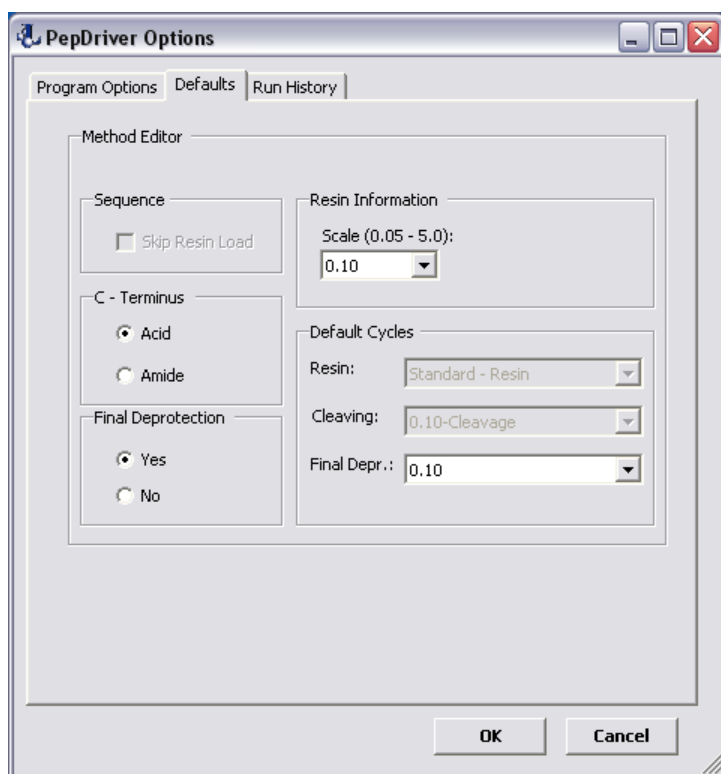
- **Pause When Running on Battery Power:** When this option is enabled, PepDriver1 will pause the current method in the event the laptop computer switches to battery power. This is critical in the event of power failure. This option is enabled by default.
- **Test System Visible:** When this option is enabled, the Test System button is visible on the Cleaning Tab of the Maintenance Screen. This option is enabled by default.
- **Omit Check for 125 mL Reaction Vessel:** By default, if a method of 0.5 mmol scale or higher is loaded into the queue, PepDriver1 will prompt the user to check that the correct reaction vessel is installed.

CAUTION

The 125 mL reaction vessel must be used for syntheses above 0.25 mmol. Using the 35 mL reaction vessel for large syntheses will result in overfilling of the vessel, loss of product, and possible damage to the instrument.

- **Backpurge System when complete:** When this option is enabled, the Liberty1 will perform a full backpurge of the system following the completion of the loaded method, removing all solvent from all lines. This option is enabled by default.

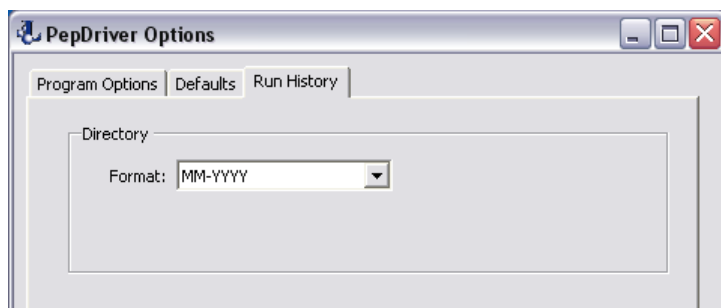
Defaults Tab



The Defaults Tab is used to select the default settings for all options in the Method Editor. To change the default settings:

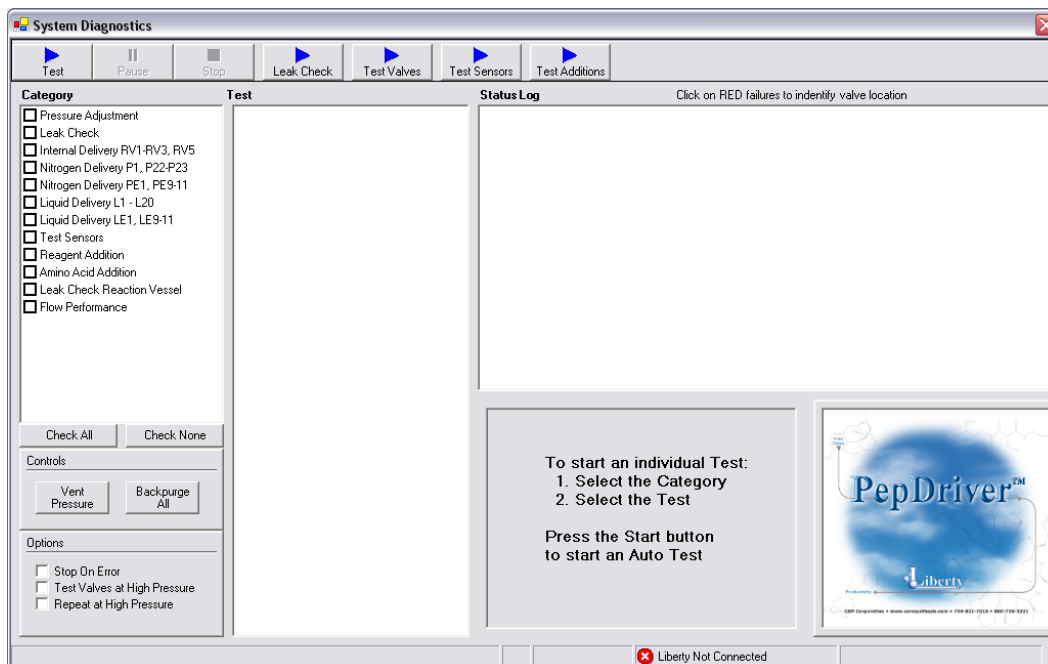
1. Select a scale from the Resin Information box.
2. Make any changes to the other settings.
3. Click OK to save the changes.

Run History Tab



The Run History tab is used to select the format for naming the folders into which run history files are saved. Folders can be named in either American (Month-Year) or European (Year-Month) format.

Test System Screen



The Test System screen contains a number of diagnostic tests that can be used to troubleshoot the performance of the Liberty1. The Test System screen is accessed by clicking the Maintenance button, selecting Maintenance, and then clicking the Test System button from the Cleaning tab of the Maintenance menu.

There are four Quick Test buttons at the top of the Test System screen: Leak Check, Test Valves, Test Sensors, and Test Additions. Clicking any of these buttons will automatically select the appropriate categories and begin the necessary tests.

To perform a specific test:

1. Check the box next to the desired test category in the Category window.
2. Click the name of the category. The tests within that category will appear in the Tests window.
3. Click Test to run all the tests in the selected category, or double-click on a specific test to run only that test.

Once a test is complete, a green check mark will appear if the test was passed, or a red X will appear if the test was failed. Details about the results will be recorded in the Status Log window.

Pressure Adjustment

Category	Test
<input type="checkbox"/> Pressure Adjustment	Adjust Main Pressure
<input type="checkbox"/> Leak Check	Adjust Low Pressure
<input type="checkbox"/> Internal Delivery RV1-RV3, RV5	
<input type="checkbox"/> Nitrogen Delivery P1, P22-P23	
<input type="checkbox"/> Nitrogen Delivery PE1, PE9-11	
<input type="checkbox"/> Liquid Delivery L1 - L20	
<input type="checkbox"/> Liquid Delivery LE1, LE9-11	
<input type="checkbox"/> Test Sensors	
<input type="checkbox"/> Reagent Addition	
<input type="checkbox"/> Amino Acid Addition	
<input type="checkbox"/> Leak Check Reaction Vessel	
<input type="checkbox"/> Flow Performance	

Controls

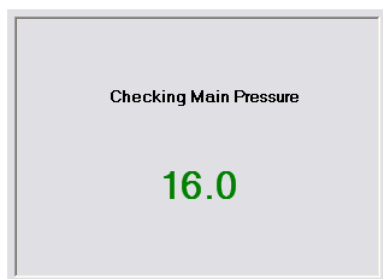
Options

☐ Stop On Error
 ☐ Test Valves at High Pressure
 ☐ Repeat at High Pressure

The Pressure Adjustment category contains two tests: Adjust Main Pressure and Adjust Low Pressure. These two tests are used to ensure the high and low pressure regulators are adjusted to within the standard operating parameters.

Main Pressure Adjustment

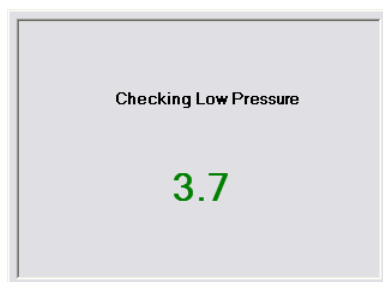
1. Select the Pressure Adjustment category, and then double-click on the Adjust Main Pressure test.
2. The current pressure reading (in psi) will be displayed in the status box. The reading will be displayed in green if the value is within the standard operating parameters (15-17 psi), and in red if it is outside the standard parameters.



3. If the pressure reading is outside the range, the status box will display instructions for adjusting the pressure regulator. The pressure reading will be displayed in real time. Adjust the regulator until the reading is between 15 and 17 psi.

Low Pressure Adjustment

1. Select the Pressure Adjustment category, and then double-click on the Adjust Low Pressure test.
2. The current pressure reading (in psi) will be displayed in the status box. The reading will be displayed in green if the value is within the standard operating parameters (2.5-4.5 psi), and in red if it is outside the standard parameters.



3. If the pressure reading is outside the range, the status box will display instructions for adjusting the pressure regulator. The pressure reading will be displayed in real time. Adjust the regulator until the reading is between 2.5 and 4.5 psi. Contact CEM Service for help adjusting the low pressure regulator.

Leak Check

Category	Test
<input type="checkbox"/> Pressure Adjustment <input checked="" type="checkbox"/> Leak Check <input type="checkbox"/> Internal Delivery RV1-RV3, RV5 <input type="checkbox"/> Nitrogen Delivery P1, P22-P23 <input type="checkbox"/> Nitrogen Delivery PE1, PE9-11 <input type="checkbox"/> Liquid Delivery L1 - L20 <input type="checkbox"/> Liquid Delivery LE1, LE9-11 <input type="checkbox"/> Test Sensors <input type="checkbox"/> Reagent Addition <input type="checkbox"/> Amino Acid Addition <input type="checkbox"/> Leak Check Reaction Vessel <input type="checkbox"/> Flow Performance	Leak Check Nitrogen Circuit
<div> <div>Check All</div> <div>Check None</div> </div> <div> <div>Controls</div> <div> <div>Vent Pressure</div> <div>Backpurge All</div> </div> </div> <div> <div>Options</div> <div> <input type="checkbox"/> Stop On Error <input type="checkbox"/> Test Valves at High Pressure <input type="checkbox"/> Repeat at High Pressure </div> </div>	

The Leak Check category contains a test to ensure none of the manifolds on the system are leaking. To perform a Leak Check:

1. Select the Leak Check category, and then click Test.

2. The Liberty1 will purge all manifolds, and then pressurize the system.
3. The pressure will be monitored for a set amount of time, during which the current drop in pressure at the manifold being tested will be displayed in the status box.



4. If the pressure drops more than 0.4 psi, the system will fail the Leak Check. For help with troubleshooting a leaking manifold, see the Troubleshooting section of this manual or contact CEM Service.



Internal, Nitrogen, and Liquid Delivery Tests

There are three types of delivery tests available in Test System: Internal Delivery, Nitrogen Delivery, and Liquid Delivery. Each category corresponds to a specific flow path within the Liberty1, and each contains individual tests of each valve in that path. The delivery tests are intended to test the function of each valve on the system.

The Internal Delivery category tests the RV valves. There are two categories of Nitrogen Delivery tests: the P valves and the PE valves. There are two categories of Liquid Delivery test: the L valves and the LE valves.

Setting Up the Liberty1 for a Delivery Test

Before beginning a delivery test, certain precautions need to be taken to ensure accurate test results:

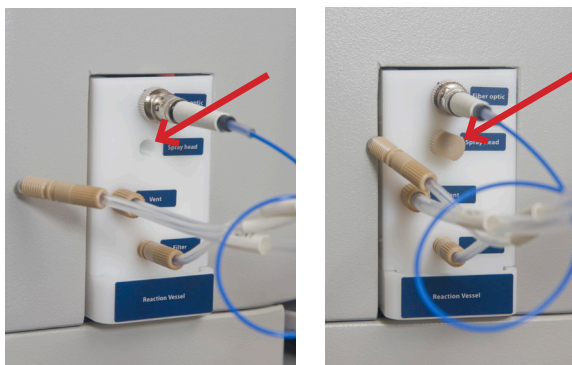
1. Remove all reagents (amino acids, activator, activator base, deprotection, and Main Wash) from the system.
2. Remove the dip tube filters from all dip tubes.

CAUTION

If leaving bottles in place, ensure the bottles are loose enough to allow pressure to escape. Tightening the bottles will result in false failures.

3. Perform a backpurge on all positions to ensure the lines are free of liquid.
4. Loosen or remove any bottles connected to the reagent positions (amino acids, activator, activator base, deprotection, and Main Wash).

5. Disconnect the spray head line from the reaction vessel manifold on the front of the Liberty1 and connect a plug (PN 167800) to that position.



Performing a Delivery Test

1. Select the category of delivery test, and then double-click on the individual valve to be tested in the Test window (or click Test to test all valves within the category).
2. The Liberty1 will vent all pressure from the lines. The valve will be closed and the line pressurized, then the nitrogen turned off. The Liberty1 will wait to see if there is a decrease in pressure. A decrease in pressure indicates the valve is leaking, and will cause the test to fail. If the test fails, contact CEM Service for help with troubleshooting.
3. The valve will then be opened and the pressure should vent. Failure to vent pressure indicates the valve is not opening or the line is restricted, and will cause the test to fail. If the test fails, contact CEM Service for help with troubleshooting.

Test Sensors

Category	Test
<input type="checkbox"/> Pressure Adjustment <input type="checkbox"/> Leak Check <input type="checkbox"/> Internal Delivery RV1-RV3, RV5 <input type="checkbox"/> Nitrogen Delivery P1, P22-P23 <input type="checkbox"/> Nitrogen Delivery PE1, PE9-11 <input type="checkbox"/> Liquid Delivery L1 - L20 <input type="checkbox"/> Liquid Delivery LE1, LE9-11 <input type="checkbox"/> Test Sensors <input type="checkbox"/> Reagent Addition <input type="checkbox"/> Amino Acid Addition <input type="checkbox"/> Leak Check Reaction Vessel <input type="checkbox"/> Flow Performance	Test X(1,2,9-13) & A(1-20) Sensors Test Sensors LS1 - LS2

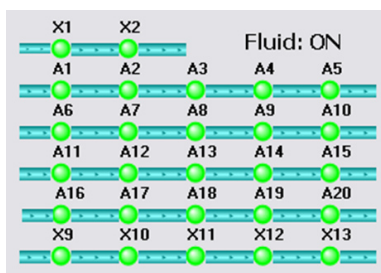
The Sensor Test is the most commonly used category in the Test System screen. A Sensor Test should be performed after every sensor calibration. To perform a Sensor Test:

1. Select the Test Sensors category, and then click Test.

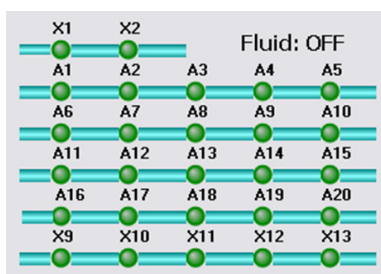
2. A warning will pop up to confirm that there is sufficient DMF for the test and that the waste container is connected. Verify the DMF supply and that the waste container is not full, then click OK.



3. The Liberty1 will purge the lines. The sensors for the test will be displayed in the status window.
4. The Liberty1 will fill the line with DMF. As each sensor detects liquid, the corresponding indicator in the status window will turn bright green.



5. The Liberty1 will turn off the DMF flow and empty the line. As each sensor stops detecting liquid, the corresponding indicator in the status window will dim.



6. If a sensor fails the test, a red X will appear next to the test in the Test window, and the specific sensor that failed will be recorded in the status log. If any sensors fail, contact CEM Service for troubleshooting help.
7. During the test, solvent will be added to the reaction vessel. At the end of the test, the Liberty1 will automatically drain the reaction vessel.

NOTE

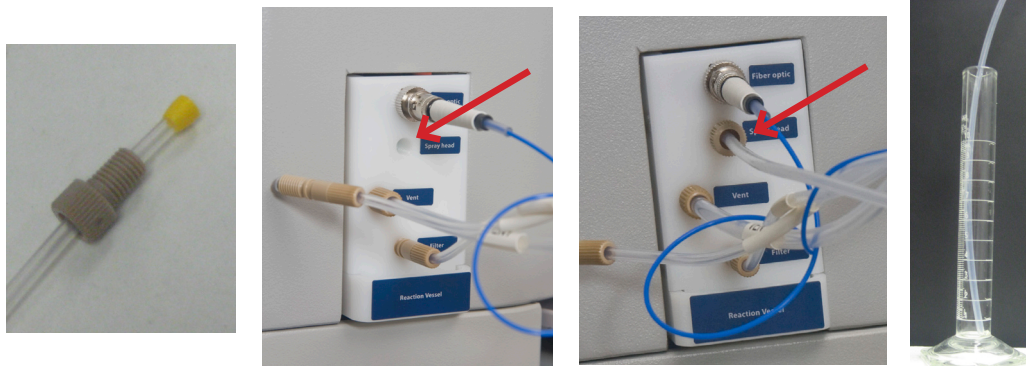
A Sensor Test can also be started from either the Cleaning tab or the Sensor Calibration tab by clicking the Test Sensors button. Clicking Test Sensors from either tab will open the Test System screen and automatically select and begin a Sensor Test.

Reagent and Amino Acid Addition

There are two types of addition tests available in Test System: Reagent and Amino Acid. The addition tests are intended to verify that the sample loops for each of these positions are delivering the correct volume.

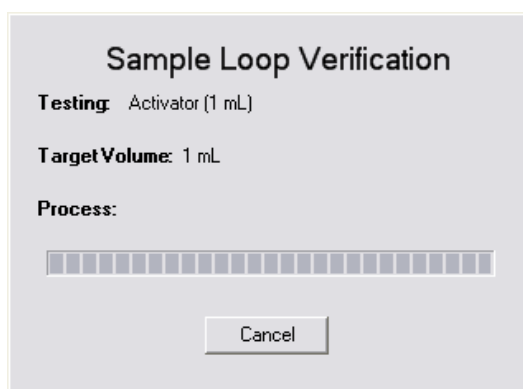
To perform an Addition Test:

1. Disconnect the sprayhead line from the manifold on the front of the Liberty1. Connect a piece of 1/8" OD tubing (PN BR199116) to the manifold using a nut (PN 167810) and yellow ferrule (PN 164315).



Place the open end of the tubing into a 10 mL graduated cylinder.

2. Select the category of addition test, and then double-click on the individual position to be tested in the Test window (or click Test to test all additions within the category).
3. The Liberty1 will begin adding one sample loop of the selected reagent. The progress of the addition and the target volume will be displayed in the status window.



4. When the addition is complete, verify the volume delivered to the graduated cylinder. If the delivered volume is more than 0.3 mL different from the target, contact CEM Service for troubleshooting assistance.

Leak Check Reaction Vessel

The Reaction Vessel Leak Check should be performed any time the reaction vessel has been disconnected from the system. In particular, a leak check should be performed when switching between the 125 mL, 35 mL, and 10 mL vessels, or after any test that requires disconnecting the spray head line.

To perform a Reaction Vessel Leak Check:

1. Select the Leak Check Reaction Vessel category, and then click Test.
2. A warning will pop up to confirm that the reaction vessel is connected and secure. Verify the reaction vessel is properly connected, then click OK.
3. The Liberty1 will pressurize the reaction vessel.



4. The pressure will be monitored for a set amount of time, during which the current drop in pressure at the manifold being tested will be displayed in the status box.

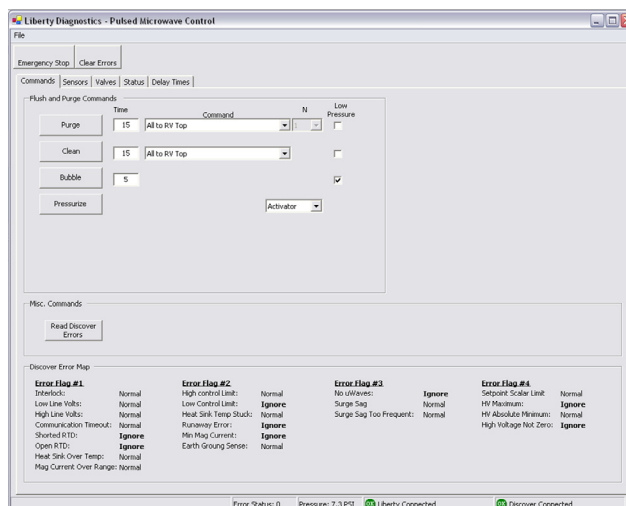


5. If the pressure drops more than 0.4 psi, the reaction vessel will fail the Leak Check. (For help with troubleshooting a leaking reaction vessel, see p. 115 or contact CEM Service.)

Diagnostics Screen

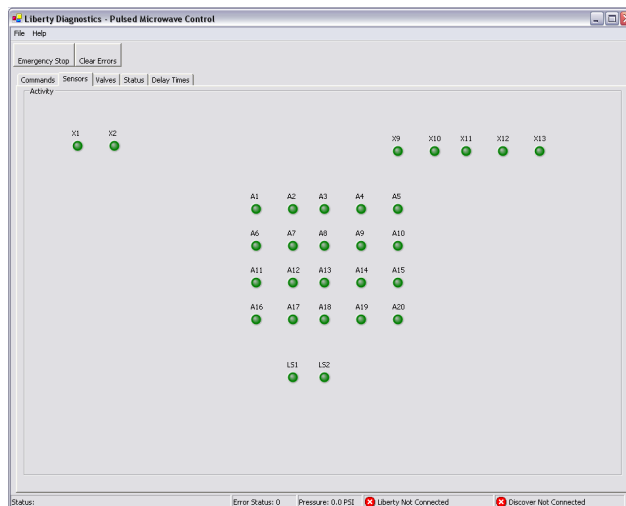
The Diagnostics Screen contains a number of reports and manual controls that are not intended for normal use. In general, the Diagnostics screen should only be used under the advice of a trained CEM Service Technician.

Commands Tab



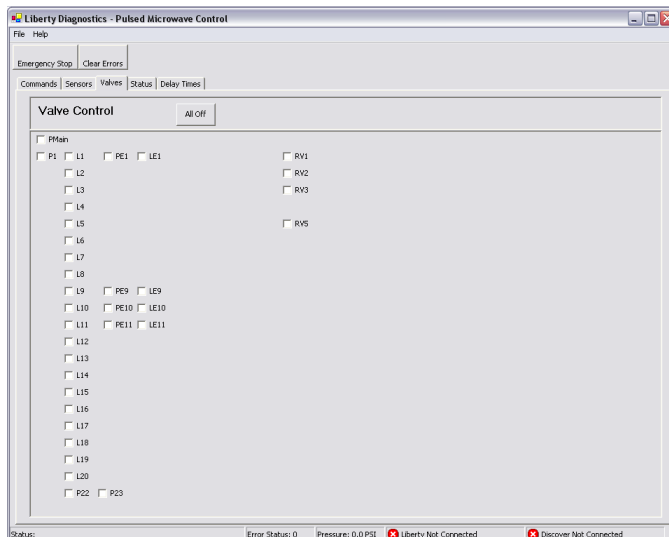
The Commands tab allows for the manual execution of all system commands. In addition, the Read Discover Errors button will detect any firmware errors in the Discover.

Sensors Tab



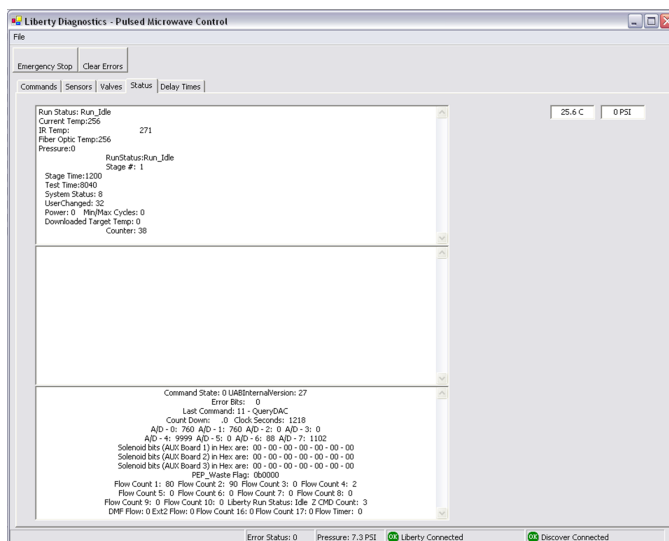
The Sensors tab displays the current status (on or off) of each sensor on the system. Sensors are on when they are seeing liquid, as shown by the bright green indicator.

Valves Tab



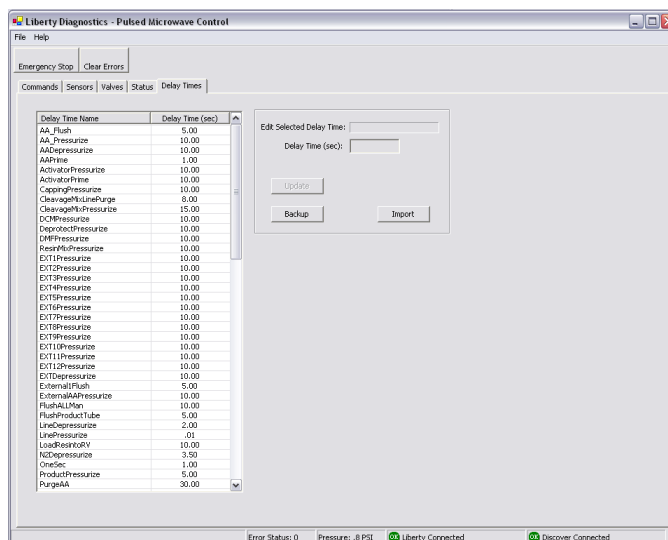
The Valves panel allows for the manual control of each valve on the system. Checking the box next to a valve opens that valve. Unchecking the box closes the valve. Clicking the All Off button unchecks all valves.

Status Tab



The Status tab contains diagnostic information about the current status of the Liberty1.

Delay Times Tab



The Delay Times tab is used to change the delay times for various system commands and parameters.

To change a delay time:

CAUTION

Do not change a delay time without consulting with a trained CEM Service Technician. Incorrect delay times can result in poor synthesis quality and instrument malfunction.

CAUTION

Before changing any delay times, click the Backup button to save a backup file of all current delay times.

1. Click on the delay time to be changed in the list.
2. Enter the new delay time in the Delay Time (sec) box on the right.
3. Click Update to save the new delay time.

Section 6: Troubleshooting

Problem	Possible Solution
Empty Amino Acid Bottle Error	<ul style="list-style-type: none"> • Replace the empty bottle with fresh reagent. • If the bottle is not empty, ensure bottle is securely connected to the manifold. • If the bottle is not empty, replace the dip tube filter. • If the error still occurs, perform a sensor calibration. • If the error still occurs, contact CEM Service.
Empty Activator, Activator Base, or Deprotection	<ul style="list-style-type: none"> • Replace the empty bottle with fresh reagent. • Ensure the bottle is not cracked. • If the bottle is not empty, ensure bottle tubing is securely connected to the manifold and that the cap is tightly closed. • If the bottle is not empty, replace the dip tube filter. • If the error still occurs, perform a sensor calibration. • If the error still occurs, contact CEM Service.
F2 Restriction Error	<ul style="list-style-type: none"> • Replace the F2 filter. • Replace the dip tube filter for the reagent being added. • If the error still occurs, contact CEM Service.
F3 Restriction Error	<ul style="list-style-type: none"> • Replace the F3 filter. • If the error still occurs, replace the reaction vessel. • If the error still occurs, contact CEM Service
Waste Full Error	<ul style="list-style-type: none"> • Empty the waste container. • If the waste container is not full, ensure the sensor is not engaged (in the up position). • If the error still occurs, contact CEM Service.
Nitrogen Pressure Errors	<ul style="list-style-type: none"> • Verify the nitrogen source is functional. • Verify the pressure setting on the Main Pressure Regulator is between 15 and 17 psi. • Perform a Leak Check (p. 77), then contact CEM Service.
Reaction Vessel Fails Leak Check	<ul style="list-style-type: none"> • Verify the tubing connections to the manifold on the front of the Liberty1 are tight and not cross-threaded • Verify the vessel body is tightly connected to the attenuator • Verify the PEEK fitting on the drain line is tightly connected to the bottom of the reaction vessel • Verify the quick disconnect on the drain line is tightly secured • If the vessel still fails the Leak Check, contact CEM Service

Tips for Recovering from Errors

- If an error occurs on a wash step, an Add Amino Acid step or an Add Deprotection step, and the method has been stopped for more than 30 minutes, manually reswell the resin before restarting the method.
- Click Stop to stop the method. Perform any maintenance (replacing filters or bottles) as needed to correct the error.
- Open the Maintenance Screen by clicking the Maintenance button and selecting Maintenance.
- Click Filtered Drain to perform a filtered drain.
- Add 14 mL of DMF: Select Main Wash/DMF and 14 from the pulldowns next to the Add button, then click Add.





CAUTION



If using the 10 mL vessel, only add 6 mL of solvent to avoid overfilling the vessel.

- Allow the resin to swell for approximately 15 minutes, then click Filtered Drain.
- Close the Maintenance Screen.
- To restart the method, from the Current Run tab, right-click on the appropriate step (the wash step or Add Amino Acid step the method stopped on), and select Restart Method.
- If an error occurs on an Add Activator or Add Activator Base step, perform a filtered drain and reswell the resin as above, except restart with the Add Amino Acid step.



Section 7: Spare Parts and Consumables

Reaction Vessel Parts

Part Number	Name	Description	Picture
516015	30 mL Reaction Vessel Assembly	Standard reaction vessel attenuator used for the Liberty1 with the 30 mL and 125 mL reaction vessels	
516095	10 mL Reaction Vessel Assembly	Modified reaction vessel attenuator specifically designed for use with the 10 mL reaction vessel	
167260	30 mL Reaction Vessel Body	Standard 30 mL Teflon reaction vessel body that connects to the standard reaction vessel attenuator	
542415	125 mL Reaction Vessel Body	Large 125 mL Teflon reaction vessel body that connects to the standard reaction vessel attenuator	

Part Number	Name	Description	Picture
167765	10 mL Reaction Vessel Body	Small 10 mL Teflon reaction vessel that connects to the 10 mL vessel attenuator	
314325	Fiber Optic Temperature Probe	Replacement temperature probe for monitoring reaction temperature	
167750	Reaction Vessel Spray Head	Replacement spray head used in both the Standard and 10 mL reaction vessel attenuators	(not pictured)





Filters

Part Number	Name	Description	Picture
167485-M	Dip Tube Filters	Replacement filters for all reagent dip tubes (bag of 50 filters)	
172150-M	Inline Filters	Replacement filters for F1, F2, and F3 positions (box of 25)	





Solvent Keg

Part Number	Name	Description	Picture
908515	20 L Solvent Keg Kit	Optional steel keg with bladder for use as 20 L DMF reservoir (includes keg and all necessary tubing)	(not pictured)



Bottles

Part Number	Name	Description	Picture
167550	1 L Glass Bottle (Clear)	Standard 1 L glass bottle for use on deprotection and capping positions	
167505	250 mL Glass Bottle (Clear)	Standard 250 mL glass bottle used on activator base and cleavage positions	
167506	250 mL Glass Bottle (Amber)	Standard 250 mL amber glass bottle used on activator position	
167155-M	125 mL Polypropylene Bottle	Standard 125 mL plastic bottles used on amino acid manifolds (bag of 24)	

Bulk Tubing and Fittings

Part Number	Name	Description	Picture
BR199116	0.125" (1/8") Teflon Tubing	1/8" OD tubing	(not pictured)
164305	0.125" (1/8") High Purity PFA Tubing	1/8" OD PFA tubing	(not pictured)
167810	1/8" Tubing Fitting	PEEK nut used for 1/8" OD tubing connections	
164315	1/8" Tubing Ferrule	Yellow ferrule for use with PEEK nut for 1/8" tubing (PN 167810)	
BR199117	0.188" (3/16") Teflon Tubing	3/16" OD tubing	(not pictured)
167315	3/16" Tubing Fitting	PEEK nut used for 3/16" OD tubing connections	
167320	3/16" Tubing Ferrule	Blue ferrule for use with PEEK nut for 3/16" tubing (PN 167315)	



Bottle Tubing Assemblies

Part Number	Name	Description	Picture
167693	Bottle Tubing Assembly, Black	Tubing assembly used to connect a single DMF bottle or the DMF TEE assembly (PN 167971) to the manifold	
167673	Bottle Tubing Assembly, Blue	Tubing assembly used to connect the deprotection bottle to the manifold	(see 167693)
167668	Bottle Tubing Assembly, Red	Tubing used to connect an external activator base bottle to the manifold	(see 167693)
167663	Bottle Tubing Assembly, Orange	Tubing assembly used to connect an external activator bottle to the manifold	(see 167693)
167971	DMF TEE Assembly	Tubing used to connect two DMF bottles to the manifold	


O-Rings

Part Number	Name	Description	Picture
BR198116	4 L Bottle Cap O-Ring	Large O-ring used with 4 L bottle caps (PN 167569)	(not pictured)
172089	2-way Valve O-Ring	O-ring used with standard 2-way valves (PN 167850)	(not pictured)
174000	CALRES Valve O-Ring	O-ring used with PTFE 2-way valves (PN 167855)	(not pictured)
167731	Reaction Vessel O-Ring	O-ring uses to seal the top of the reaction vessel to the attenuator assembly	(not pictured)


Bottle Caps


Part Number	Name	Description	Picture
167569	4 L Bottle Cap Assembly	Teflon bottle cap with diptube for use with a 4 L bottle with a Wheaton-style neck (uses O-ring, PN BR198116, to seal)	
167559	GL-45 Bottle Cap Assembly	Teflon bottle cap with dip tube for use with an external bottle	

Dip Tubes


Part Number	Name	Description	Picture
167500-M	Amino Acid Dip Tube Assemblies	Dip tubes used for each amino acid position (package of 20)	

Valves and Valve Wiring

Part Number	Name	Description	Picture
167850	2-Way Valve	Main 2-way valve used on the Liberty1	

Part Number	Name	Description	Picture
167980	3-Way Valve (X-style)	Main 3-way valve used on the Liberty1	
243405	X-Style Valve Wire Assmebly	Wiring assembly used to connect valves to valve controller boards (used with PN 167980)	(not pictured)


Liquid Sensors

Part Number	Name	Description	Picture
243097	Liquid Sensor	Liquid sensor used to monitor fluid transfer in the Liberty1	
243395	Sensor Wire Assembly	Wiring assembly used to connect liquid sensors (PN 243097) to sensor board	(not pictured)

Waste Container

Part Number	Name	Description	Picture
167536	20 L Waste Carboy	20 L solvent waste container used with the Liberty1	(not pictured)
576155	Waste Cap with Level Sensor Assembly	Cap for waste container with waste level sensor and all required tubing to connect to the Liberty1	(not pictured)
167790	Waste Cap	Cap for 20 L solvent waste container	(not pictured)
243115	Waste Sensor Wire Harness	Cable that connects the level sensor to the Liberty1	(not pictured)
167970	Waste Tubing Assembly	Tubing assembly that connects the waste cap to the Liberty1	(not pictured)

Accessories and Tools

Part Number	Name	Description	Picture
567250	Reaction Vessel Calibration Stand	Stand used to hold the reaction vessel for volume calibrations	
167945	250 mL Polypropylene Flask	Plastic flask for preparing reagents and transferring waste	(not pictured)
167950	10 mL Polypropylene Graduated Cylinder	Plastic graduated cylinder used for routine maintenance	(not pictured)
163456	Screwdriver	Multibit screwdriver	(not pictured)
167990	Preset Torque Wrench	Calibrated torque wrench for tightening all 2-way valves	(not pictured)
167975	Ball Point Hex Bit	Hex bit for use with torque wrench (PN 167975)	(not pictured)
BR301510	Allen Wrench Set	Complete set of allen (hex) wrenches. 5/64" size is required for replacement of X-style 3-way valves.	(not pictured)
167961	Fitting Tightener Tool	Metal tool for tightening 1/8" outer diameter PEEK fittings (PN 167810)	(not pictured)
167955	Chemical Bottle Labels	Safety labels for all reagent bottles	(not pictured)
167922	Discover Spill Tray	Large spill tray to protect the microwave from solvent spills	(not pictured)
BR196113	Screws for Discover Spill Tray	Screws for use with spill tray (PN 167992)	(not pictured)
BR198728	Washers for Discover Spill Tray	Washers for use with spill tray (PN 167992)	(not pictured)
167973	Fiber Optic Clip	Clip to secure the fiber optic probe in the thermowell	(not pictured)

Part Number	Name	Description	Picture
576200	Thermowell Assembly	Replacement thermowell for use with either the standard or 10 mL reaction vessels	(not pictured)
194215	External Reagent Tray	Secondary containment tray for external reagent bottles	(not pictured)
167988	Reagent Wash Bottle	Wash bottle for transferring resin to the reaction vessel	(not pictured)

Circuit Boards

Part Number	Name	Description	Picture
576020	CPU Board	Main CPU board for the Liberty1	(not pictured)
576006	Valve Controller Board	Valve controller board for the Liberty1	(not pictured)
576040	Sensor Board	Sensor controller board for the Liberty1	(not pictured)
314345	Temperature Board	Board for control of fiber optic temperature probe	(not pictured)
576105	Pressure Board Assembly	Board for detecting pressure on the Liberty1	(not pictured)

Computer Accessories

Part Number	Name	Description	Picture
274205	Network Cable (Green)	10' ethernet cable	(not pictured)
274200	Network Cable (Black)	4' ethernet cable	(not pictured)
243290	Router-Serial Power Cable	Adaptor cable used to power the router directly through the Liberty1	(not pictured)

Regulators

Part Number	Name	Description	Picture
576195	Main Pressure Regulator	Regulator for main (high) nitrogen pressure	(not pictured)
576015	Low Pressure Regulator	Regulator for low nitrogen pressure	(not pictured)

Documentation

Part Number	Name	Description	Picture
600192	Liberty1 Operations Manual	Operations manual for the Liberty1	(not pictured)
600193	Liberty1 Manual Appendices	Appendices to the operations manual for the Liberty1	(not pictured)
600765	Liberty1 Maintenance Manual	Guide to routine maintenance procedures for the Liberty1	(not pictured)
600770	Liberty1 Diagram	Diagrams of valve and manifold locations	(not pictured)
600760	Liberty1 Fluid Circuit Diagram	Diagram of fluidics pathways for the Liberty1	(not pictured)

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