Syro

User Manual

Biotage®

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1 System Description

Syro is a programmable peptide synthesizer that is capable of parallel synthesis at room temperature. When using Biotage® Syro *Wave*™, which is a Syro system supplied with a microwave instrument (Biotage® Initiator), it is also possible to perform microwave assisted synthesis at 40°C to 80°C. All Syro systems are controlled by a computer running the Syro XP software.

1.1 Syro I

The Syro I system consists of the following parts:

- An amino acid rack with 40 positions for 50 ml amino acid vessels or an amino acid combi rack with 25 positions for 50 ml amino acid vessels and 25 positions for 15 ml pre-activation vessels.
- A system solvent bottle.
- Five reagent bottles, 2 x 500 ml and 3 x 200 ml.
- A reactor block with 24 positions for 2, 5 and 10 ml reactor vials or a reactor block with 48 positions for 2 ml reactor vials.
- A robot arm with a needle for measuring and dispensing liquids using two 5 ml syringe pumps.
- A vacuum pump for emptying reactor vials.
- A wash station with a waste port and a wash well.
- Two waste containers.

Figure 1. The Syro I system.

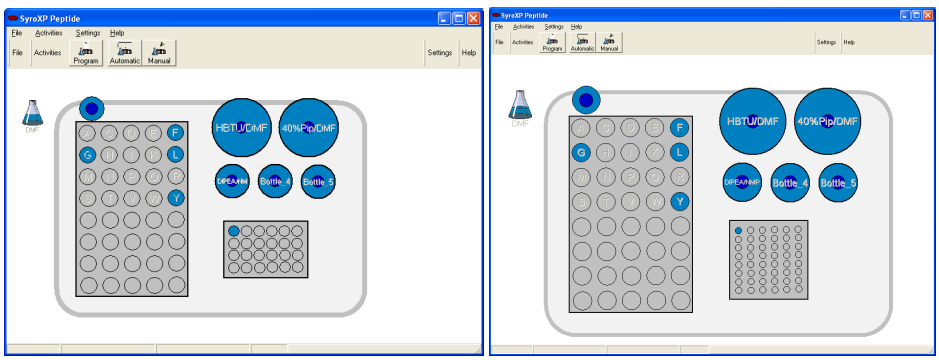


Figure 2. Examples of Syro I software layout with 24-position reactor block (left) and 48-position reactor block (right).

1.2 *Syro II*

The Syro I system consists of the following parts:

- An amino acid rack with 40 positions for 50 ml amino acid vessels or an amino acid combi rack with 25 positions for 50 ml amino acid vessels and 25 positions for 15 ml pre-activation vessels.
- Three system solvent bottles.
- Seven reagent bottles, 3 x 500 ml and 4 x 200 ml.
- Two reactor blocks with 24 positions for 2, 5 and 10 ml reactor vials or two reactor blocks with 48 positions for 2 ml reactor vials.
- Two robot arms with needles for measuring and dispensing liquids using four syringe pumps, one 5 ml syringe pump for amino acid addition and three 10 ml syringe pumps for solvent wash and reagent addition.
- A vacuum pump for emptying reactor vials.
- Two wash stations with a waste port and a wash well.
- Two waste containers.

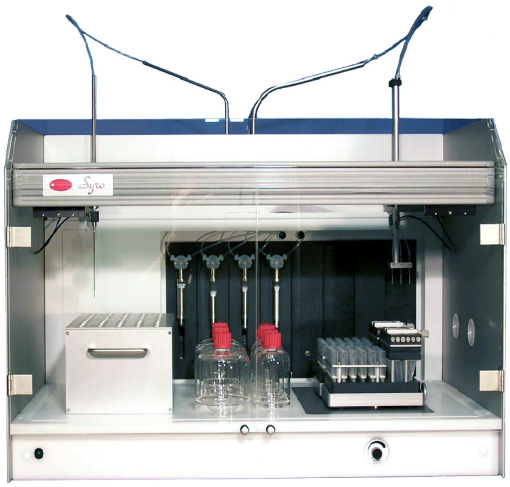


Figure 3. The Syro II system.

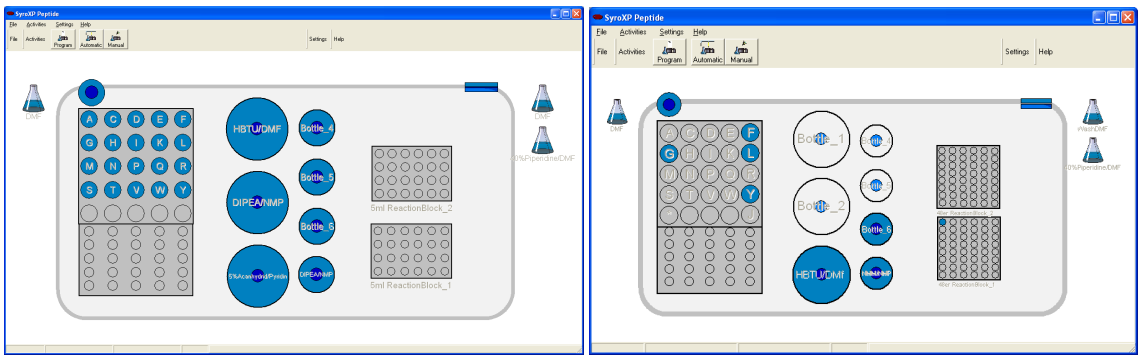


Figure 4. Examples of Syro II software layout with 24-position reactor blocks (left) and 48-position reactor blocks (right).

1.3 *Biotage® Syro Wave™*

The Syro *Wave* system consists of a peptide synthesizer (Syro) and a microwave instrument (Initiator). The peptide synthesizer consists of the following parts:

- An amino acid rack with 32 positions for 50 ml amino acid vessels or an amino acid combi rack with 25 positions for 15 ml amino acid vessels and 25 position 15 ml pre-activation vessels.
- A system solvent bottle.
- Five reagent bottles, 2 x 500 ml and 3 x 200 ml.
- A reactor block with 24 positions for 10 ml reactor vials. Can only be used when not using Initiator.
- A robot arm with a needle for measuring and dispensing liquids using one 5 ml syringe pump.
- A vacuum pump for emptying reactor vials.
- A wash station with a waste port and a wash well.
- Two waste containers.

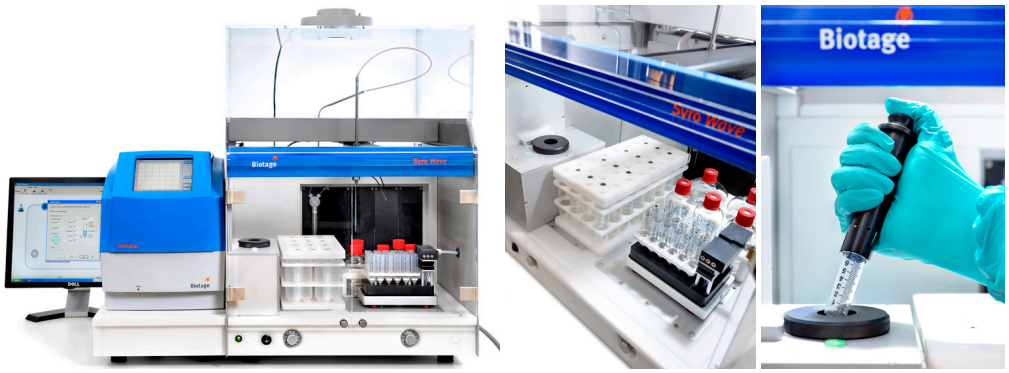


Figure 5. The Syro *Wave* system.

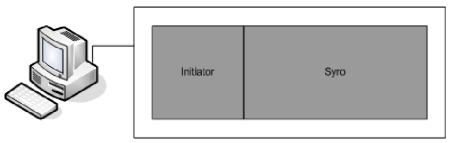


Figure 6. Syro *Wave* main components.

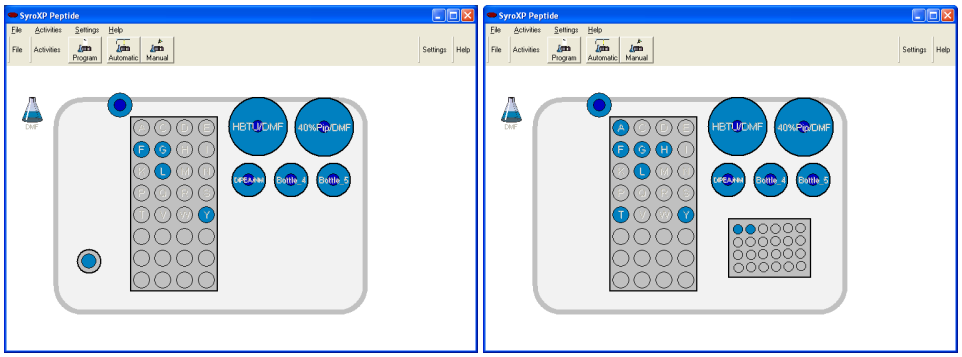


Figure 7. Examples of Syro *Wave* software layout with microwave assisted synthesis (left) or parallel synthesis (right).

1.3.1 Microwave Instrument (Biotage® Initiator)

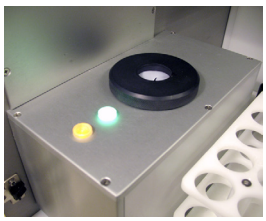
Reactions performed inside the microwave cavity are regulated by means of time and temperature. The time parameter specifies the length of reaction time at the target temperature.

When the reactor vial has been inserted into the microwave cavity and the synthesis has been started, high-frequency microwaves (2.45 GHz), generated by the magnetron, heat the reaction mixture. During the heating process, the reaction mixture is continuously agitated by means of the vortexer located underneath the microwave cavity.

The microwave instrument is equipped with a touch screen used for synthesis monitoring and shut down of the instrument. The instrument status is displayed in the touch screen's right-hand panel:

- Idle or Paused = Initiator is not processing.
- Processing = Initiator is processing, but the magnetron is switched off.
- Magnetron On = Initiator is processing and the magnetron, which generates microwaves, is switched on.

LEDs on the Microwave Cavity



Both LEDs lit.	Both LEDs are lit during startup and shutdown of the Initiator.
No LED lit.	The Initiator is switched off or disconnected. **Warning!** If the Initiator is switched on and no LED is lit, shut down the system and contact Biotage® 1-Point Support™.
Only green LED lit.	The Initiator is switched on but the magnetron is switched off, i.e. **no** microwaves are being generated.
Only orange LED lit.	The magnetron is switched on, i.e. microwaves are being generated. **Warning!** Keep your hands away from the microwave cavity when the system generates microwaves. It is only safe to insert reactor vials etc into the microwave cavity when the green cavity LED is lit and the orange LED is not.

1.4 Liquid Handling

The needle is used for detecting liquid and to aspirate and dispense liquid into bottles, vessels and vials on the system's work surface using the integrated syringe pump(s). Tasks supported by the system include single pipetting, multi-pipetting, and dilutions.

After completion of a liquid handling function, the robot arm moves the needle to the wash station. At the wash station, excess liquid is discarded through the waste port and the needle is rinsed both externally and internally using system solvent. The system solvent is pumped through the needle, flows into the wash well and rinses the outside of the needle, and then overflows into the waste port, which is connected to a waste reservoir below the system.

There are two wash methods depending on whether the liquid-level detection is used or not:

- If the detection mode is turned on (default), only the tip of the needle is washed.
- If the detection mode is turned off, the full length of the needle is washed.

For syringe pump volume range, resolution, and accuracy; see the technical specifications on page 41.

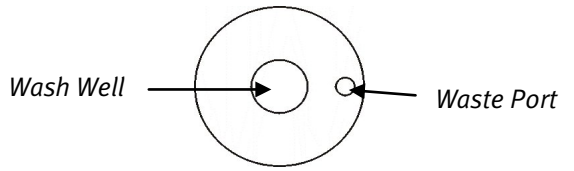


Figure 8. Wash station.

1.5 Electrical Connections

1.5.1 Syro

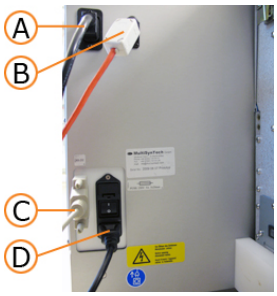


Figure 9. Electrical connections on Syro.

A. Power to the Initiator (when using Syro *Wave*) or the external fan supplied and installed by Biotage (when using Syro I or Syro II). No other equipment must be connected to this outlet.

B. Control signal to the vacuum pump.

C. RS-232 port. Used to connect the Syro to the system computer using the RS-232 cable supplied with the system.

D. Mains power inlet and power switch.

1.5.2 Biotage® Initiator

Note that the Initiator is only used with the Syro *Wave* system.

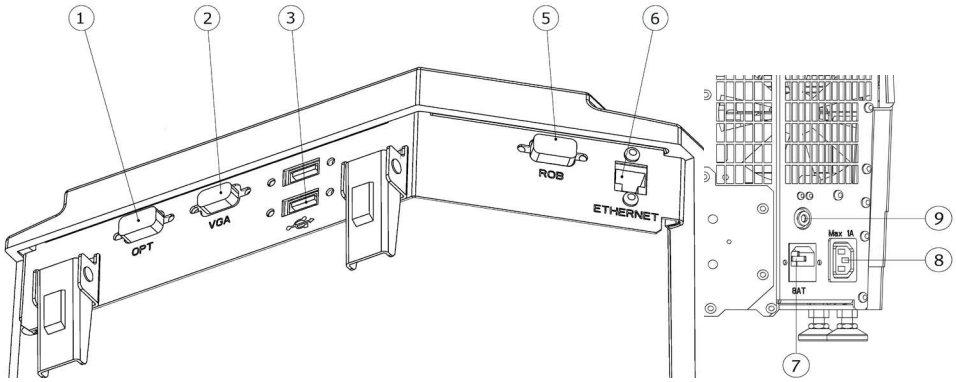


Figure 10. Connections on Initiator.

1. Only used by Biotage service engineer.
2. VGA port. Used to connect an external screen to the Initiator.
3. USB ports. Only used by Biotage service engineers.
5. Not used.
6. Ethernet port. Used to connect the Initiator to the system computer (running the Syro XP software) using the RJ-45 Ethernet cable supplied with the system.
7. Power inlet. Connected to Syro.
8. Not used.
9. Not used.

1.5.3 Vacuum Pump

Figure 11. Electrical connections on the vacuum pump.

A. Mains power inlet.

B. Control signal from the Syro.

1.6 Syro XP Software

The Syro XP software is used to set up and control peptide synthesis on all Syro systems. The systems are delivered with a library of common reaction steps and synthesis cycles. You can also set up your own steps and cycles.

The software also includes a calculation function that calculates the amounts of amino acids, reagents, and solvents needed for a synthesis.

1.6.1 Definitions of Chemfile, Workfile, Sequence List, and Synthesis File

The following files are used in the Syro XP software:

- **Chemfile (*.cmf):** A file that normally covers all the commands for a reaction step (fill, reaction, empty, and wash). The system is delivered with a library of chemfiles, which includes common reaction steps such as Fmoc deprotection, deprotection wash, coupling, and coupling wash.
- **Workfile (*.wkf):** A file that normally covers all the commands for an entire synthesis cycle, for example:

  Single coupling.wkf

  Fmoc-Deprotection.cmf

  Wash DMF, DCM.cmf

  Coupling.cmf

  Wash DMF.cmf

  Acetylation.cmf

  Wash DMF, NMP.cmf

  The system is delivered with a library of workfiles with common synthesis cycles.
- **Sequence list (*.txt):** A text file including the peptide sequence or sequences used for the synthesis.
- **Synthesis file (*.syn):** A file containing all the cycles for a complete synthesis as well as the positions on the system's work surface and the contents of the bottles and vessels to be used. A synthesis file is generated by opening a sequence list and then assigning workfiles to the individual synthesis cycles.

2 Operation

Warning

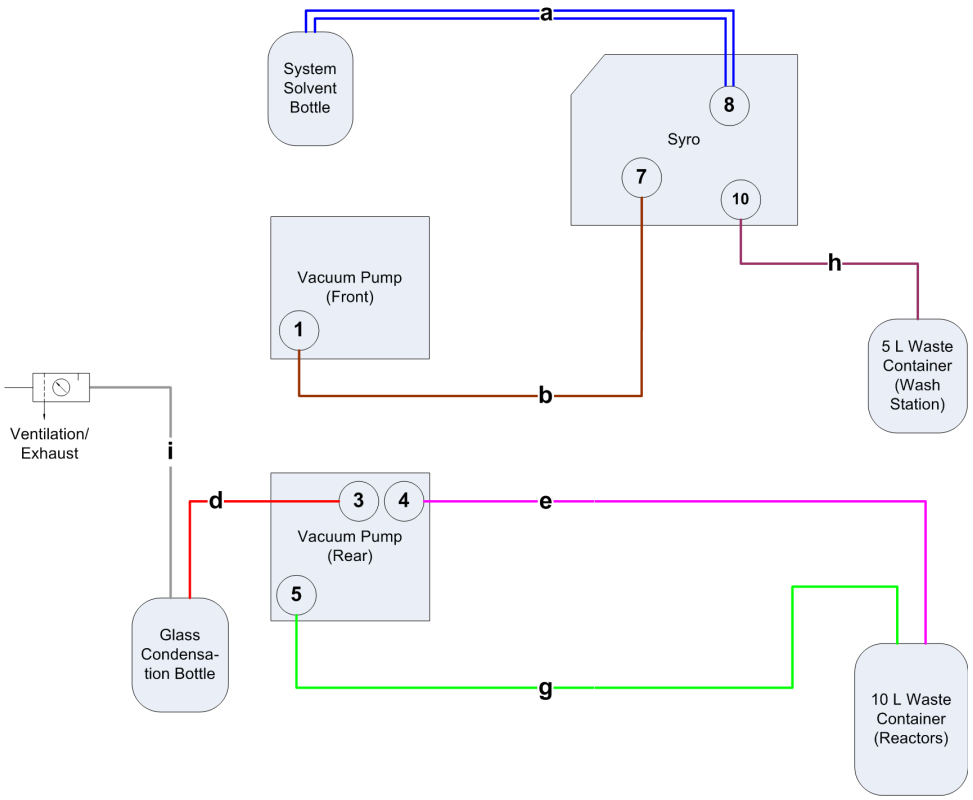
- Before performing any procedures in this chapter, please read and observe the safety requirements in the “Syro Installation and Safety” document. Failure to follow those requirements may result in personal injury and/or equipment damage.

Notice

- Before operating the system, ensure that all connections are properly connected and that the waste containers are not full.

2.1 Check Tube Connections

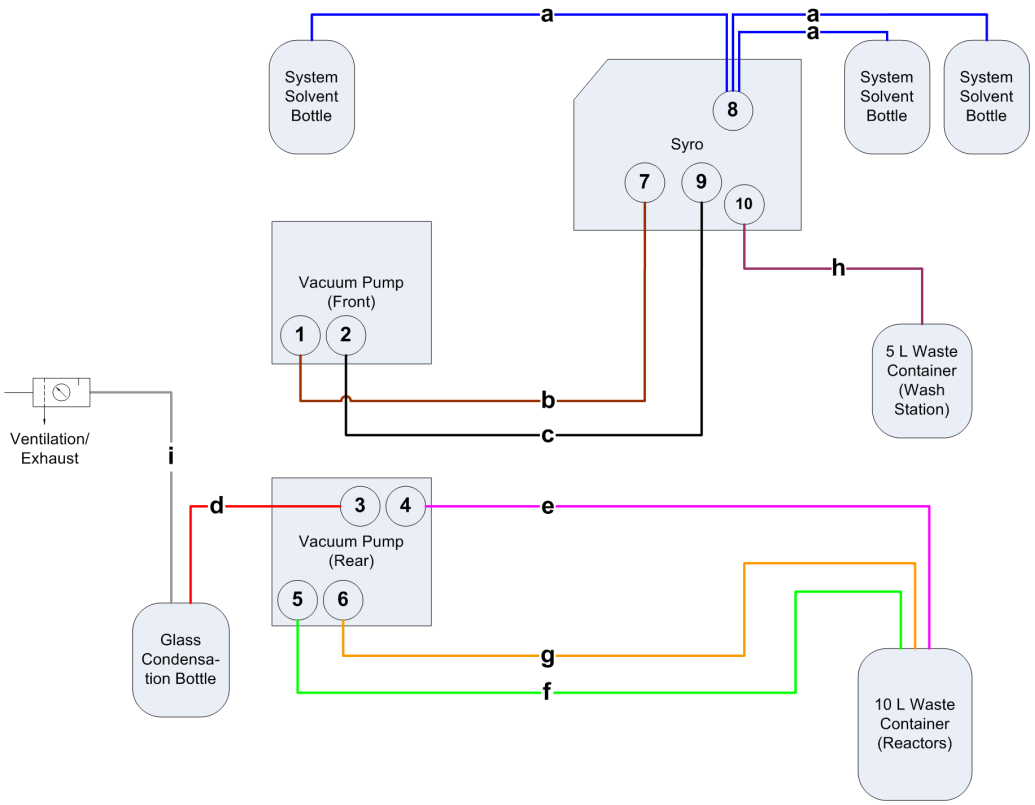
2.1.1 Syro I Tubing Diagram



Tube	From/to	Purpose	Type
a	8	Two system solvent (DMF) inlets	∅3 mm PTFE
b	1/7	Reactor block vacuum drain	∅6 mm polypropylene
d	3	Vacuum pump exhaust	∅6 mm polypropylene
e	4	Vacuum pump inlet	∅6 mm polypropylene

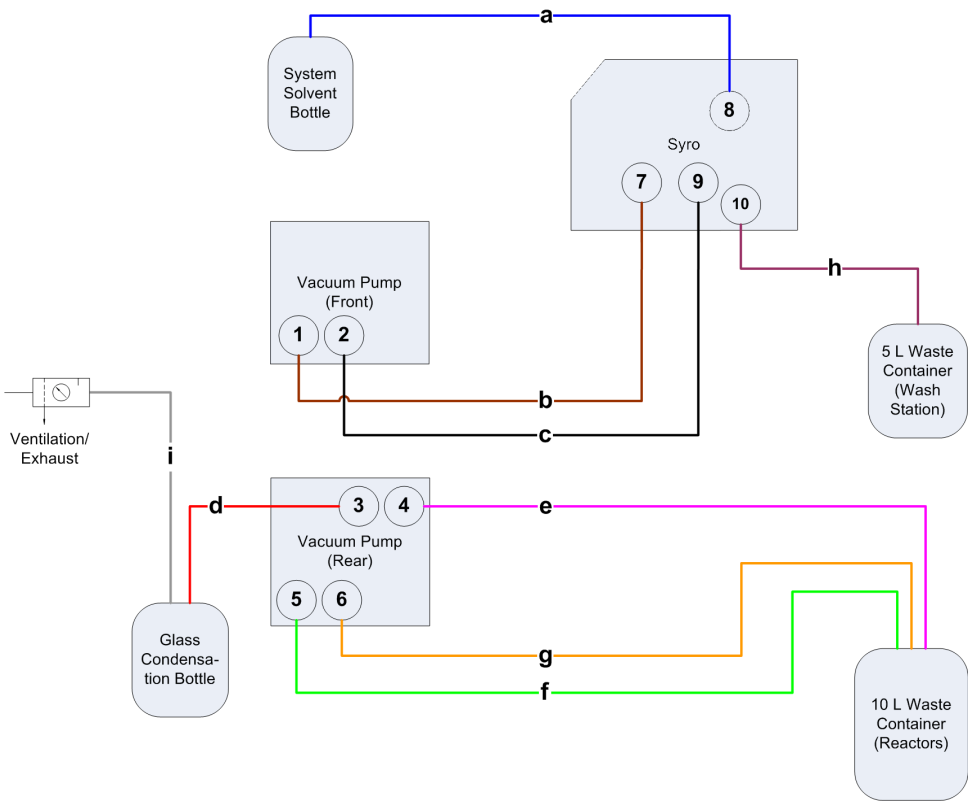
g	5	Vacuum pump drain	∅6 mm polypropylene
h	10	Wash station drain	∅10 mm polypropylene
i		Exhaust from vacuum pump/condensation bottle	∅6 mm polypropylene

2.1.2 Syro II Tubing Diagram



Tube	From/to	Purpose	Type
a	8	Three system solvent inlets	∅3 mm PTFE
b	1/7	Reactor block vacuum drain	∅6 mm polypropylene
c	2/9	Reactor block vacuum drain	∅6 mm polypropylene
d	3	Vacuum pump exhaust	∅10 mm polypropylene
e	4	Vacuum pump inlet	∅6 mm polypropylene
f	5	Vacuum pump drain 1	∅6 mm polypropylene
g	6	Vacuum pump drain 2	∅6 mm polypropylene
h	10	Wash station drain	∅10 mm polypropylene
i		Exhaust from vacuum pump/condensation bottle	∅6 mm polypropylene

2.1.3 Biotage® Syro *Wave*™ Tubing Diagram



Tube	From/to	Purpose	Type
a	8	System solvent (DMF) inlet	∅3 mm PTFE
b	1/7	Reactor block vacuum drain	∅6 mm polypropylene
c	2/9	Microwave reactor block vacuum drain	∅6 mm polypropylene
d	3	Vacuum pump exhaust	∅6 mm polypropylene
e	4	Vacuum pump inlet	∅6 mm polypropylene
f	5	Vacuum pump drain 1	∅6 mm polypropylene
g	6	Vacuum pump drain 2	∅6 mm polypropylene
h	10	Wash station drain	∅10 mm polypropylene
i		Exhaust from vacuum pump/condensation bottle	∅6 mm polypropylene

2.2 Start Up and Shut Down the System

Warning

- The system must be electrically grounded (earthed). Connect only to a properly grounded outlet. Keep mains plugs easily accessible in case the system needs to be disconnected quickly from mains power.
- The Initiator must be connected to the power outlet at the rear left side of the Syro (see A in Figure 9 on page 5). No equipment other than the Initiator (when using Syro *Wave*) or the external fan supplied and installed by Biotage (when using Syro I or Syro II) must be connected to this outlet.
- Sharp corners may exist at the rear of the system. Exercise caution when working with the system.
- Do not operate a damaged system. If the system has been damaged and does not function properly, shut it down and contact Biotage 1-Point Support immediately.

Note

- We recommend that you do not run any other programs (including anti-virus programs) than Syro XP on the system when the system is processing.
- If using a Syro *Wave* system and the Initiator is not to be used for a period of time, shut it down as described in steps 1a and 1b in the "Shut Down the System" section on page 12.
- If using a Syro *Wave* system, both LEDs on the cavity cover should be lit during startup and shutdown of the Initiator; see the LED description on page 4.

2.2.1 Start Up the System

1. Switch on the Syro. The power switch is located at the rear left side of the system.
2. If using a Syro *Wave* system, switch on the Initiator. The power switch is located at the front of the system.
3. Switch on the system computer and log on to Windows.
4. To start the Syro XP software, double-click the SyroXP shortcut ( ) on the system computer's desktop. The **Password** dialog opens.
5. Enter the password and click **OK**.

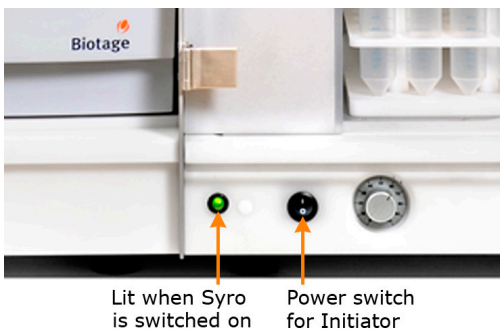


Figure 12. The LED at the front is lit when the Syro is switched on (Syro *Wave* shown).

2.2.2 Shut Down the System

1. If using a Syro *Wave* system, shut down the Initiator:
    a. When the Initiator is not processing, press **Main Menu**/**Log Out** and then **Shut Down** on the touch screen.
    b. When the message “It is now safe to turn off the system” appears, switch off the Initiator. The power switch is located at the front of the system.
2. When the system is not processing, shut down the system computer running the Syro XP software:
    a. Shut down all software.
    b. Select **Shut Down**/**Turn Off** from the Windows **Start** menu.
    c. Select **Shut Down** from the drop-down list in the **Shut Down Windows** dialog or click **Turn Off** in the **Turn off computer** dialog.
3. When Windows has shut down, switch off the Syro. The power switch is located at the rear left side of the system.
4. If required, unplug the power cord from the power outlet at the rear left side of the system.

2.3 Start the Syro XP Software

Double-click the SyroXP shortcut ( ) on the system computer's desktop.

2.4 Set Up the Work Surface

The system is delivered with one robot setup for each possible bottle, rack, and block configuration. If you are missing a robot setup, please contact your local Biotage representative. If you are using various chemical configurations, it is advisable to prepare a separate setup for each configuration. You can prepare a new setup by copying an existing one and modifying it; see page 29.

To select the robot setup to be used for your peptide synthesis:

1. Select **Robot setup** from the **Settings** menu. The **Setup settings** dialog opens.
2. Select the desired robot setup from the **Actual** drop-down list.
3. Click the **Use settings** button.
4. The software has to be restarted for the new settings to take affect; click **OK** in the **Information** dialog that opens and then double-click the SyroXP shortcut ( ) on the system computer's desktop.
5. Ensure that all the necessary chemicals are defined correctly in the current robot setup. To print lists with the chemical data for the current robot setup, see page 22. To create a new robot setup or modify the current setup, see page 29. If not all the required amino acids are defined, just ensure to turn off the **Fixed AminoAcid positions** option when generating the synthesis file (see page 18) and the system will populate the amino acid rack with the required amino acids according to the sequence(s).

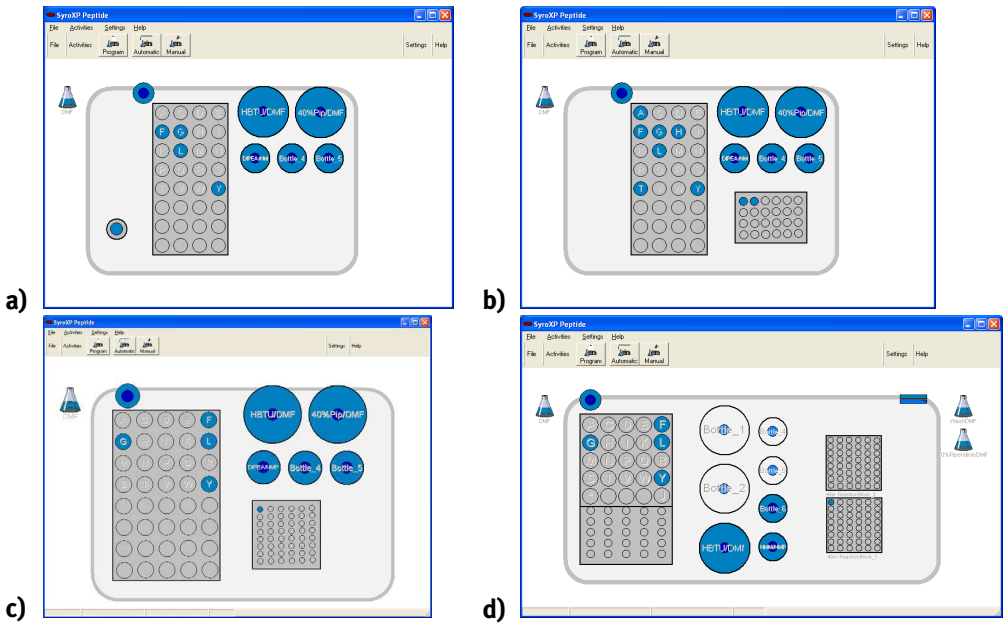


Figure 13. Different Syro XP software layouts; a) Syro *Wave* with microwave assisted synthesis, b) Syro *Wave* with parallel synthesis (using a reactor block with 24 positions), c) Syro I with a reactor block with 48 positions, and d) Syro II with two reactor blocks with 48 positions each.

2.5 Set Up a Synthesis

Note: For Syro *Wave*, we do not recommend the use of microwave heating during the Fmoc deprotection step due to the potential risk of promoting side reactions such as aspartimide formation and epimerization.

2.5.1 Create a Sequence List

1. Open Notepad or a similar text editor.
2. Enter the peptide sequence or sequences used for the synthesis using one-letter codes.

   All letters and numbers between 0 and 9 are permitted. Use uppercase letters for L-amino acids and lowercase letters for D-amino acids. The number of characters for a sequence is restricted to a maximum of 80. Note that a sequence may not contain any spaces.

   You can also use an inline scale factor by writing <*scale factor*> at the end of a line. The scale factor range is between 0.1 and 2.0. The volumes in the used workfiles are then multiplied by this factor for this sequence. If using the same scale factor for all the sequences in the sequence list, set the scale factor when generating the synthesis file; see page 18.

   A sequence must be completed by pressing the **Enter** key. When performing parallel synthesis, the lines in the sequence list correspond to the reactor block positions. The first sequence (line 1) goes to position A1, the second (line 2) to A2, and so on.
3. Save the text file (*.txt) in your Syro library. The library is by default available at My Documents\SyroXP\Library. To change the location of the library, see page 32.

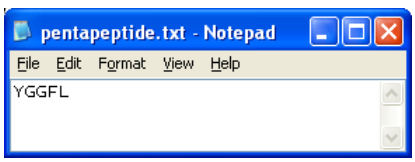


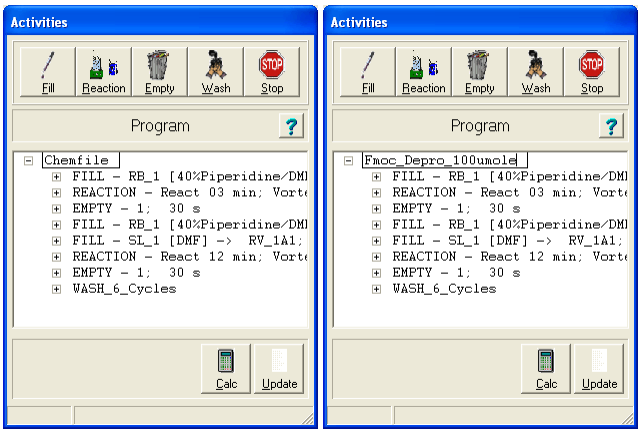
Figure 14. An example of a sequence list created in Notepad.

2.5.2 Create a Chemfile

A chemfile normally covers all the commands for a reaction step (fill, reaction, empty, and wash). The system is delivered with a library of chemfiles that includes common reaction steps such as Fmoc deprotection, deprotection wash, coupling, and coupling wash.

To create a chemfile:

1. Select **Program** from the **Activities** menu. The **Activities** window opens with a **Program** field and a command bar.
2. Add the desired commands, see “Add a Fill Command” below, “Add a Reaction Command” on page 15, “Add a Wash Command” on page 16, “Add an Empty Command” on page 17, “Add a Stop Command” on page 17, and “Move, Copy, Edit, and Delete a Command” on page 17.
3. When you have completed the list of commands, click the word Chemfile twice in slow succession and enter the name of the chemfile.



4. Validate the chemfile by clicking the **Update** button in the **Activities** window.
5. Save the chemfile; select **Save** from the **File** menu. Ensure to save the file as a chemfile, i.e. select **Chemfile** in the **Save as type** drop-down list in the **Save As** dialog that opens.

Add a Fill Command

The fill command is used to aspirate and dispense liquid into bottles, vessels, and vials on the system's work surface using the integrated syringe pump(s).

Note: The fill command is completed by clicking the **Ready** button in the **Fill Option** toolbar. To undo a command, click the **Undo** button.

1. In the **Activities** window, click the **Fill** button. The **Activities** window disappears.
2. On the work surface, select the position containing the liquid that you want to distribute.

   To distribute several successive amino acids, first select the **Source multiple linear** option in the **Fill Option** toolbar and then select the start and end positions in the amino acid rack or the combi rack (used for pre-activation).

   To distribute amino acids from a random peptide sequence list, click the **AminoAcidList** button in the **Fill Option** toolbar and then select position A1 on the reactor block. Enter the distribution volume, a value between 0.1 and 30000 µl, in the **Fill** dialog that opens and click **OK**. Proceed to step 4 below. **Note:** This command may only be used in Chemfiles that are going to be used to prepare Workfiles and Synthesis files. They cannot be executed individually.

   Source positions are highlighted in yellow on the work surface.

3. Select the target position and enter the distribution volume, a value between 0.1 and 30000 µl, in the **Fill** dialog that opens and click **OK**.

   To distribute to several positions, select the positions one after the other.

   To distribute to several direct successive positions within the amino acid rack, combi rack (used for pre-activation), or the reactor block, first select the **Destination multiple linear** option in the **Fill Option** toolbar and then select the start and end positions.

   A different distribution volume can be entered for each target position. To use the same fill volume for all positions, select the **Use Volume for each position** option in the **Fill** dialog.

   Target positions are highlighted in green on the work surface.

4. When you are done, click the **Ready** button in the **Fill Option** toolbar. The fill command appears in the **Activities** window.

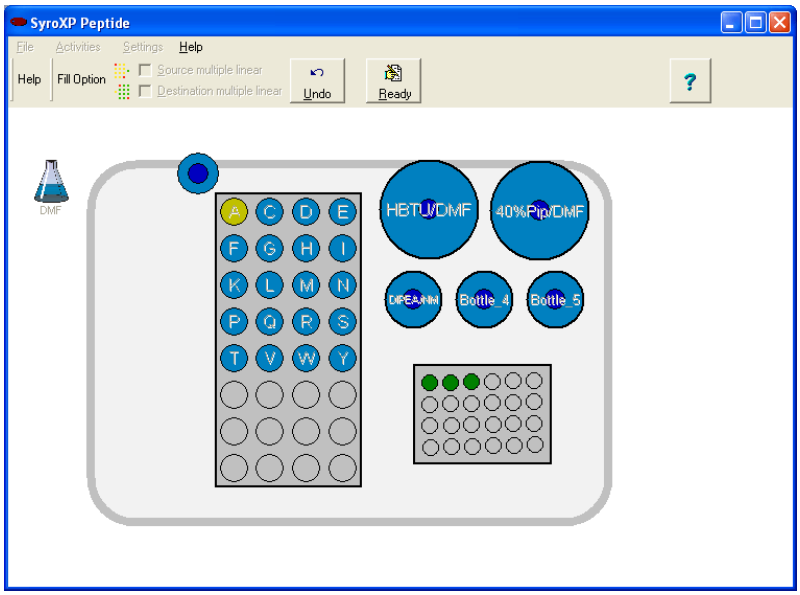


Figure 15. Source positions are highlighted in yellow and target positions in green.

Add a Reaction Command

1. In the **Activities** window, click the **Reaction** button. The **Reaction** dialog opens.
2. Enter the reaction time.
3. If using a robot setup for microwave assisted synthesis (Syro *Wave*), enter the target temperature. Note that the time parameter specifies the length of reaction time at the target temperature and that the reaction mixture will be continuously agitated by means of the vortexer located underneath the microwave cavity.

   To change back to room temperature, enter “RT” in the **Reactor** text box.

4. If using a robot setup for parallel synthesis, set the intervals for the vortexer:

   - **Vortex time:** Shows how long the agitation is to be active. The recommended value during solid phase synthesis is 10 to 20 seconds. The valid range is from 0 (zero) to 59 minutes and 59 seconds.
   - **Break time:** Shows how long the agitation is to be paused.

   The Vortex time commences and is followed by the Break time.

5. When you are done, click **OK**. The reaction command appears in the **Activities** window.

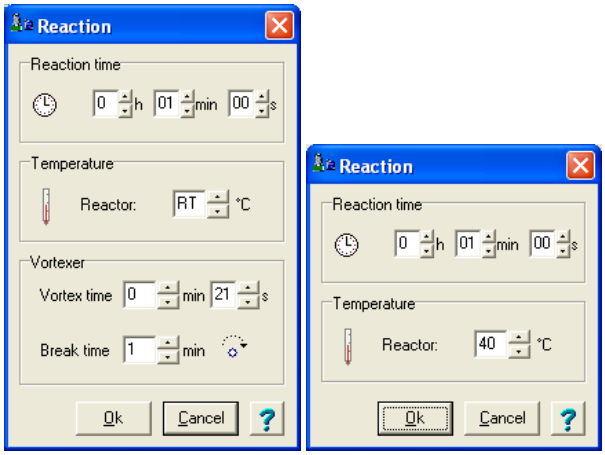


Figure 16. When using a Syro *Wave* system and the temperature is set to ≥ 40°C, the vortexer parameters are hidden in the Reaction dialog.

Add a Wash Command

The wash command is used for washing the reactor. The command is made up of a fill command, a reaction command, and an empty command.

Note: The wash command is completed by clicking the **Ready** button in the **Fill Option** toolbar. To undo a command, click the **Undo** button.

1. In the **Activities** window, click the **Wash** button. The **Activities** window disappears.
2. On the work surface, select the wash solvent. The position is highlighted in yellow.
3. Select the target position and enter the amount of the wash solvent to be distributed in the **Wash** dialog that opens.

   To wash several positions, select the destination positions one after the other on the reactor block(s) or select the **Destination multiple linear** option in the **Fill Option** toolbar and select the start and end positions.

   A different distribution volume can be entered for each target position. To use the same wash volume for all positions, select the **Use Volume for each position** option in the first **Wash** dialog.

   Target positions are highlighted in green on the work surface.
4. Click the **Ready** button in the **Fill Option** toolbar. The **Reaction** dialog opens.
5. In the **Reaction time** text boxes, enter the hold time after the wash solvent has been added and before the empty command is executed.
6. If using a robot setup for microwave assisted synthesis (Syro *Wave*), it is possible to heat the reactor vial during the hold time. If desired, enter a heating temperature.
7. If using a robot setup for parallel synthesis, enter the vortex time (approx. 5–20 seconds) and the break time and click **OK**. The **Empty** dialog opens.
8. If using a Syro II system, select the reactor block to be emptied:
   - **Empty 1**: The reactor block at the front.
   - **Empty 2:** The reactor block at the back.
9. Enter the time for vacuum draining, approximately 20–40 seconds depending on the volume and click **OK**. The **Wash** dialog opens.

   Note: For optimal reaction conditions, keep the empty time as short as possible.
10. Enter the number of wash cycles and click **OK**. The wash command appears in the **Activities** window.

Add an Empty Command

The empty command is used for draining the reactor vials.

1. In the **Activities** window, click the **Empty** button. The **Empty** dialog opens.
2. If using a Syro II system, select the reactor block to be emptied:
    - **Empty 1**: The reactor block at the front.
    - **Empty 2:** The reactor block at the back.
3. Enter the time for vacuum draining, approximately 20–40 seconds depending on the volume. For optimal reaction conditions, keep the empty time as short as possible.
4. When you are done, click **OK**. The empty command appears in the **Activities** window.

Add a Stop Command

The stop command can be used for example if a complicated coupling needs to be checked or if an amino acid or reagent has to be added manually. The following commands will not be executed until you have resumed the synthesis.

1. In the **Activities** window, click the **Stop** button. The **Stop** dialog opens.
2. Enter a text to display when the stop command is executed, consisting of a maximum of 20 characters.

Move, Copy, Edit, and Delete a Command

To move a command, click it and hold down the left mouse button while dragging the command to the desired position.

To copy and paste a command:

1. Right-click the command and select **Copy** from the context menu.
2. Right-click the command you want to insert the copied command above and select **Insert** from the context menu.

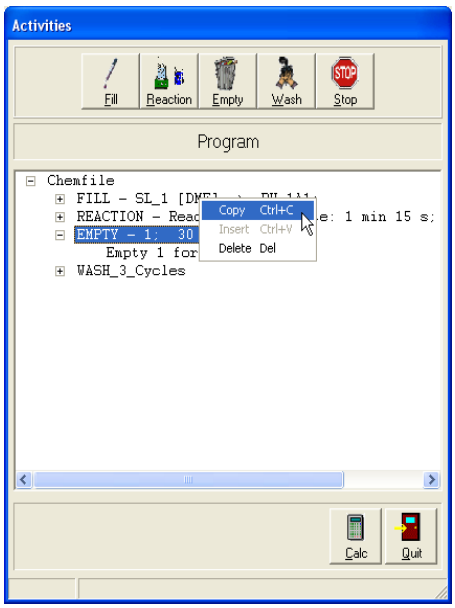


Figure 17. Right-click a command to open a context menu with Copy, Insert, and Delete.

To edit a command:

1. Expand the command.
2. Click the line that you want to edit twice in slow succession. A frame appears around the line and the cursor appears at the end of the line.
3. Make the desired modifications.
4. The changes are adopted by selecting another line.

To delete a command, either select it and press the **Delete** key or right-click it and select **Delete** from the context menu. Confirm the deletion by clicking **Yes** in the **Confirm** dialog that opens.

2.5.3 Create a Workfile

A workfile normally covers all the commands for an entire synthesis cycle. A workfile is created by combining chemfiles into one file. The system is delivered with a library of workfiles with common synthesis cycles.

To create a workfile:

1. Select **Program** from the **Activities** menu. The **Activities** window opens with a **Program** field and a command bar.
2. Add the desired chemfiles. To add a chemfile:
    a. Select **Library** from the **File** menu. The **Open** dialog opens.
    b. Select **Chemfile** in the **Files of type** drop-down list.
    c. Select the chemfile that you want to add and click **Open**.
3. If you want to add a fill, reaction, wash, empty, and/or stop command to the workfile, see the instructions on page 14–17. The command is added at the end of the selected reaction step. To move, copy, edit, or delete a command, see page 17.
4. When you have completed the synthesis cycle, validate the workfile by clicking the **Update** button in the **Activities** window.
5. Save the workfile; select **Save** from the **File** menu. Ensure to save the file as a workfile, i.e. select **Workfile** in the **Save as type** drop-down list in the **Save As** dialog that opens.

2.5.4 Generate a Synthesis File

A synthesis file contains all the cycles for a complete synthesis as well as the positions on the system's work surface and the contents of the bottles and vessels to be used. A synthesis file is generated by opening a sequence list and then assigning workfiles to the individual synthesis cycles.

To create a synthesis file:

1. Open the sequence list to be used:
    a. Select **Library** from the **File** menu. The **Open** dialog opens.
    b. Select **SequenceList** in the **Files of type** drop-down list.
    c. Select the list that you want to use and click **Open**. The **ImportData** dialog opens.
2. If the list contains several sequences, the list can be sorted by length (with the longest at the top) by clicking the **Sort** button. This feature is relevant when using Syro II.
3. Click **OK**. The **Generate** dialog opens.
4. Assign workfiles to all cycles; select one cycle at a time using the ◂ and ▸ buttons and then select its workfile in the **Workfile** drop-down list. Note that only the Workfiles that have been saved in the

Syro XP library will be displayed. The library is by default available at My Documents\SyroXP\Library. To change the location of the library, see page 32.

To assign the same workfile to several cycles, select the start cycle using the ◂ and ▸ buttons and then enter the end cycle in the **until cycle** text box.

To decrease the number of cycles, use the ▾ button.

5. Enter the scale factor in the **Scale factor** text box. All volumes in the used workfiles are multiplied by this factor.
6. Turn on or off the following generate options:
   - **AminoAcid Priority:** When turned on, the system populates the amino acid rack in priority order. When turned off, the system populates the amino acid rack in alphabetical order.
   - **AminoAcid volume check:** When turned on, the system creates additional vessels for amino acids whose total volumes exceed the volume of one vessel.
   - **Fixed AminoAcid positions:** When turned on, the current amino acid rack setup will be used. When turned off, the system populates the amino acid rack with the required amino acids according to the sequence(s).

     Note: If this option is turned off, ensure that all the symbols contained in the sequence(s) are defined in the current rack setup. Data import will be cancelled if a definition is missing or if an incorrect symbol has been used.
7. To generate a synthesis file, click the **Generate** button. The synthesis file is opened in the **Activities** window.
8. Save the synthesis file; select **Save** from the **File** menu. Ensure to save the file as a synthesis file, i.e. select **Synthesis** in the **Save as type** drop-down list in the **Save As** dialog that opens.

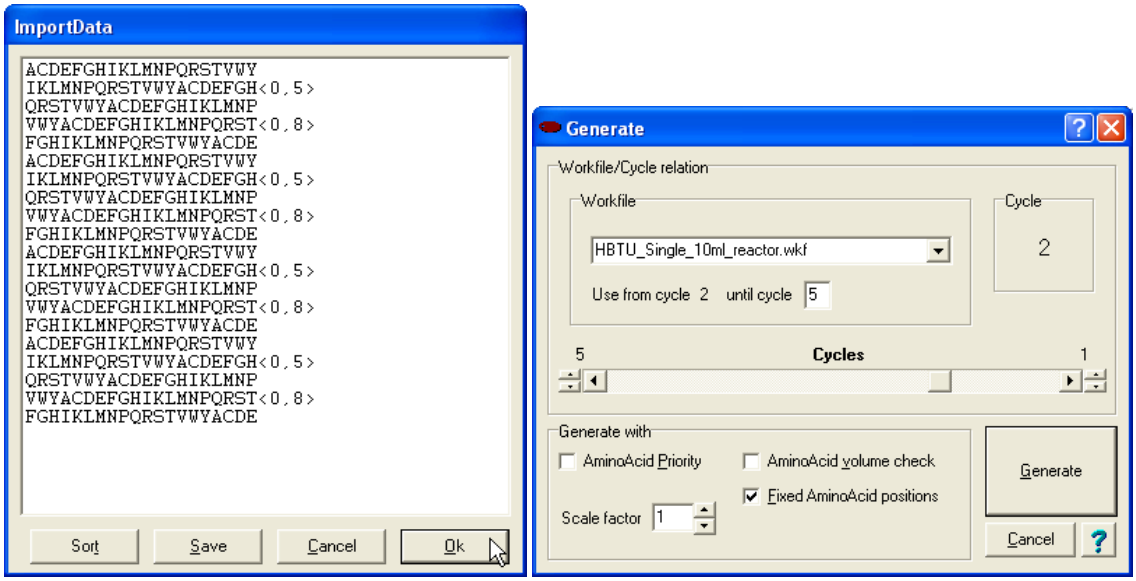


Figure 18. ImportData and Generate dialogs.

2.5.5 Pre-Activate Amino Acids

Pre-activation of the amino acids can be performed for all the synthesis cycles or just for individual ones and the amino acids in a cycle can be activated in parallel or individually directly prior to their distribution.

1. Open the synthesis file:
    a. Select **Library** from the **File** menu. The **Open** dialog opens.
    b. Select **Synthesis** in the **Files of type** drop-down list.
    c. Select the file that you want to use and click **Open**. The synthesis file is opened in the **Activities** window.
2. Right-click the synthesis cycle that you want to pre-activate and select **Pre-Activate** from the context menu. The **Information** dialog opens, requesting you to select the base.
3. Click **OK** and select the base bottle on the work surface. The **Information** dialog opens, requesting you to select the activator.
4. Click **OK** and select the activator bottle. The **Pre-activation** dialog opens.
5. Enter the base and activator volume. The amino acid volume will be adjusted automatically.
6. Select the desired pre-activation options:
    - **Pre-activate all remaining cycles:** If turned on, all successive cycles will also be pre-activated. If turned off, only the selected cycle will be pre-activated.
    - **Single preactivation:** If turned on, the amino acids are distributed to their pre-activation container, activated, and distributed to the reactor vial or vials one after the other according to their priority. The priority is defined in the robot setup; see page 29. The highest priority is 1. If turned off, all the amino acids in a cycle are distributed to the pre-activation containers and activated at the same time.
7. Right-click the **Base volume** label and select the sequence for distributing the reagents to the pre-activation containers from the context menu. As a rule, the sequence is amino acid first, the activator second, and the base last.
8. When you are done, click **OK** in the **Pre-activation** dialog. The pre-activation command appears in the **Activities** window.
9. Save the synthesis file; select **Save** from the **File** menu. Ensure to save the file as a synthesis file, i.e. select **Synthesis** in the **Save as type** drop-down list in the **Save As** dialog that opens.

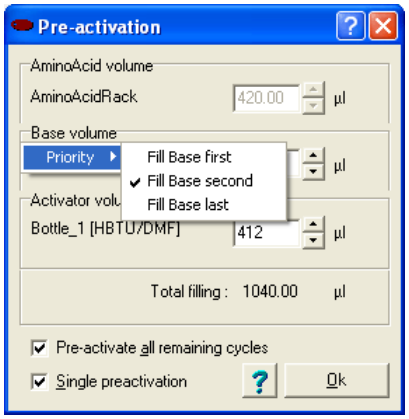


Figure 19. Pre-activation dialog.

2.6 Prepare and Load Chemicals

Warning

- Reagent and solvent bottles should be positioned on or below the work surface.
- Do not fill a reactor vial above or under the stated volume range when using the microwave unit available with the Syro *Wave* system. The volume range is 0.8–1.1 ml for the 2 ml reactor vial, 1.6–3.2 ml for the 5 ml reactor vial, and 3.2–6.4 ml for the 10 ml reactor vial.
- Keep your hands out of range of the robot arm(s) and the needle(s) when the system is in use, and when pausing or stopping the processing, until the robot arm or arms have stopped moving. The robot arm operates without a warning signal. There is a risk of personal injury.

Notice

- In order to maintain compliance, only consumables and accessories supplied by Biotage must be used in the system (see page 38).
- It is each user's responsibility to study the Material Safety Data Sheet (MSDS) for each chemical used. Handle chemical and liquid waste according to the MSDS and to local/national guidelines on laboratory safety procedures. In case of spillage, the MSDS contains instructions for decontamination, including what decontamination agent to use for safe operation as well as information about any protective equipment required.

2.6.1 Calculate and Print a Load List

1. Open the synthesis file to be used:
    a. Select **Library** from the **File** menu. The **Open** dialog opens.
    b. Select **Synthesis** in the **Files of type** drop-down list.
    c. Select the file that you want to use and click **Open**. The synthesis file is opened in the **Activities** window.
2. Click the **Calc** button. The **CalcStart** dialog opens.
3. Enter the start and end cycle for the calculation. For example, for preloaded resins enter 2 as the start cycle and turn on the **Calculate all** option. All the required reagents for all the cycles starting with cycle 2 are then calculated.
4. Click **OK**. A calculation is performed and a list displays the amounts of amino acids, reagents, and solvents needed for the synthesis. The calculation program considers the volume of solid matter and the defined density and factor for reagents.
5. To modify the calculation, enter the changes and click the **Recalculation** button. The following parameters can be modified:
    - The resin load.
    - The resin amount. If you want to use preloaded resin, click the **preloaded resin** button and enter the resin amount. The resin you have to weigh is then given by the calculation.
    - The number of equivalents of amino acids, with reference to the loading of the resin.
6. To print the load list, click the **Print** button and then the button in the **Calculation protocol** window that opens.

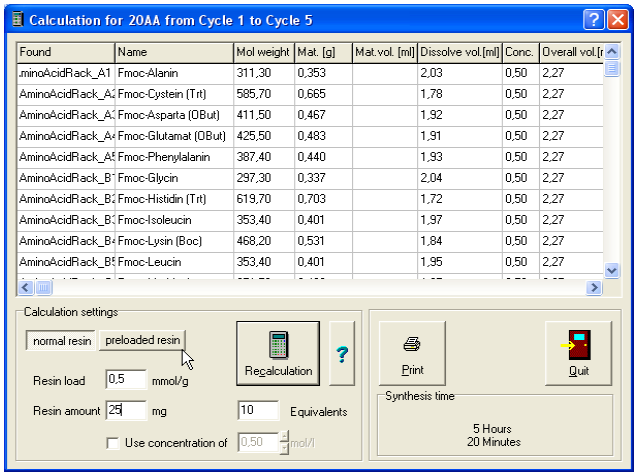


Figure 20. Syro XP calculation window.

2.6.2 Print Lists of Chemicals and Sequences Assigned to the Work Surface

1. Select **Print** from the **File** menu.
2. Select the desired print option:
   - **Solvents:** A list of all the solvents and reagents defined in the current robot setup.
   - **Amino acids:** A list of all the amino acids assigned to the amino acid rack. The following information is included for each amino acid: position on the rack, name, code, short code, priority, molecular weight, mass, and density. For a description on the parameters, see step 7 in “Create or Modify a Robot Setup” on page 29.
   - **Sequences:** A list of all the peptide sequences assigned to the reactor block positions or the sequence assigned to the microwave cavity. The following information is included for each sequence: position on the work surface, yield, average mass, and preloaded resin.
3. Click the **Preview** button. The **Print Preview** dialog opens.
4. To print the list, click the button.

2.6.3 Prepare Chemicals

Solvents

Use at least the volume shown in the load list. Please ensure that no foreign matter (e.g. molecular sieve) is present in the bottle(s). If necessary, filter the solvent(s).

Reagent Solutions

Prepare the reagent solutions according to the load list. **Note:** The reagent bottles are handmade (not uniform) and have to go into their designated places, see labels on the bottles and the illustration below.

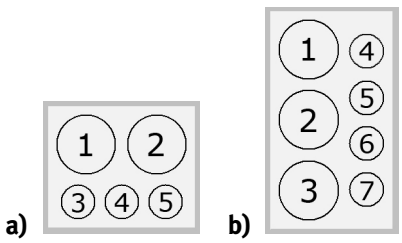


Figure 21. Reagent bottle positions for a) Syro I and Syro *Wave* and b) Syro II.

Resins

For each synthesis, weigh the resin and pour it into an empty reactor vial. The required weight is shown in the load list. We recommend that only resins with a bead size in the range of 100 to 200 mesh are used.

Amino Acids

Weigh the amino acids and pour them into empty amino acid vessels. The required weights are shown in the load list. Larger chunks should be broken up.

Pipette the required amount of solvent (see the load list or the solubility table on page 44) into the vessels and leave the amino acids standing at room temperature for about 30 minutes. Speed up the dissolving procedure by using an ultrasonic bath until the amino acids have become fully dissolved. Remove any solid components as they may block the needle.

2.6.4 Load Chemicals

Ensure to load the amino acid vessels and reagent and solvent bottles according to the software layout. To print lists with the amino acids, solvents, reagents, and sequences and their positions on the work surface, see page 22.

Note: The reagent bottles are handmade (not uniform) and have to go into their designated places, see labels on the bottles and the illustrations in section 2.6.3.

To prevent the risk of spillage in the microwave cavity, insert reactor caps (from Biotage) into the reactor vials that are to be heated in the cavity. See “Consumables and Accessories” on page 38.

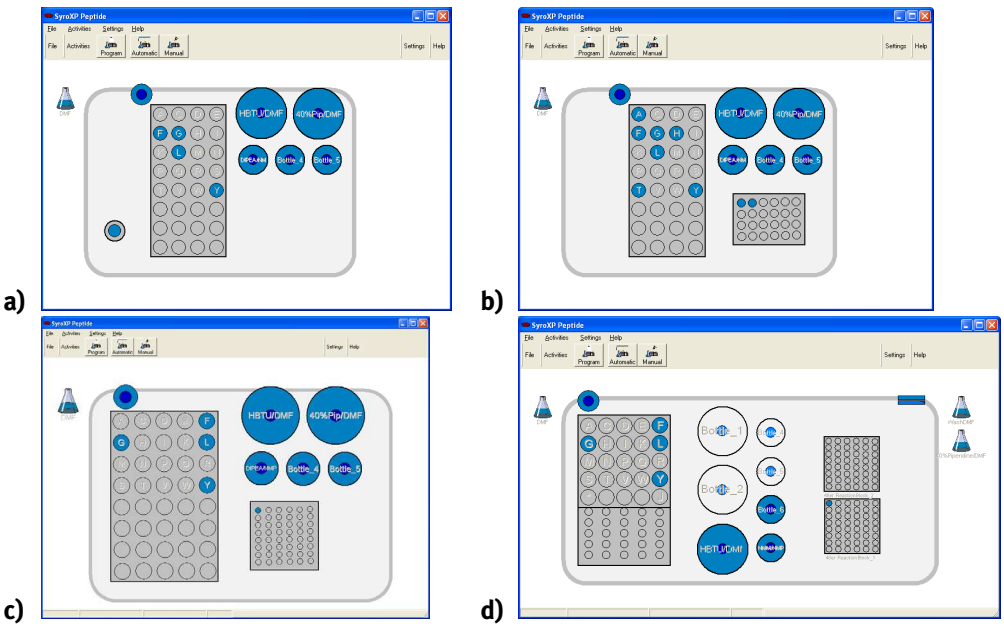


Figure 22. Examples of software layout; a) Syro *Wave* with microwave assisted synthesis, b) Syro *Wave* with parallel synthesis (using a reactor block with 24 positions), c) Syro I with a reactor block with 48 positions, and d) Syro II with two reactor blocks with 48 positions each. The blue positions are used in the synthesis.

2.7 Prime the System

Warning

- Reagent and solvent bottles should be positioned on or below the work surface. If leakage is observed, shut down the system as described on page 12, disconnect the power cord, and follow the instructions for cleaning the exterior of the system in the “Maintenance” chapter.
- Keep your hands out of range of the robot arm(s) and the needle(s) when the system is in use, and when pausing or stopping the processing, until the robot arm or arms have stopped moving. The robot arm operates without a warning signal. There is a risk of personal injury.
- Keep the system doors closed while the system is dispensing liquids. There is a risk of personal injury.

Before you start a synthesis, you might need to prime the system to:

- Remove any air bubbles from the pump and the tubing by flushing them with system solvent.
- Empty the tubing of solvent used in the previous run and fill them with the new system solvent.

To prime the system:

1. Ensure that all connections are properly connected; see page 8.
2. If necessary, empty the waste containers according to the instructions on page 35.
3. Select **Manual** from the **Activities** menu. The **Activities** window opens with a **Manual** field and a command bar.
4. Click the **Fill** button. The **Activities** window disappears.
5. On the work surface, select the system solvent. The position is highlighted in yellow; see Figure 27 on page 36.
6. Select a/the wash station and enter 5000 µl in the **Fill** dialog that opens and click **OK**. The position is highlighted in green on the work surface; see Figure 27 on page 36.
7. When you are done, click the **Ready** button in the **Fill Option** toolbar. The fill command appears in the **Activities** window.
8. Right-click the fill command and select **Copy** from the context menu.
9. Right-click the fill command and select **Insert** from the context menu. The system will now be primed twice with 5000 µl of system solvent.
10. If using a Syro II system, repeat steps 2 to 7 above for the other robot arm, i. e. select the other wash station as the target destination.
11. Validate the chemfile by clicking the **Update** button in the **Activities** window.
12. Close the system doors.
13. To start priming, click the **Execute** button. A **Stop** button appears instead of the **Execute** button. If you are priming to remove air bubbles, click the **Stop** button when no air bubbles can be observed.

Tip! Save the chemfile and use it the next time you need to prime the system. To enter the name of the chemfile, click the word Chemfile twice in slow succession and enter the name of the file.

2.8 Run a Synthesis

Warning

- Reagent and solvent bottles should be positioned on or below the work surface. If leakage is observed, shut down the system as described on page 12, disconnect the power cord, and follow the instructions for cleaning the exterior of the system in the “Maintenance” chapter.
- Keep your hands out of range of the robot arm(s) and the needle(s) when the system is in use, and when pausing or stopping the processing, until the robot arm or arms have stopped moving. The robot arm operates without a warning signal. There is a risk of personal injury.
- Keep the system doors closed while the system is dispensing liquids. There is a risk of personal injury.
- Do not fill a reactor vial above or under the stated volume range when using the microwave unit available with the Syro *Wave* system. The volume range is 0.8–1.1 ml for the 2 ml reactor vial, 1.6–3.2 ml for the 5 ml reactor vial, and 3.2–6.4 ml for the 10 ml reactor vial.

1. Prepare the amino acids, reagents, and solvents according to the load list; see page 21.
2. When the system is not processing, load the amino acid vessels, reactor vials, and the solvent and reagent bottles onto the work surface according to the software layout. If using a robot setup for microwave assisted synthesis (Syro *Wave*), load the reactor vial into the microwave cavity using the vial loading tool supplied with the system. If the septum at the cavity opening is broken or distorted, replace it.

   Note: The reagent bottles are handmade (not uniform) and have to go into their designated places, see labels on the bottles and the illustrations in section 2.6.3.

Figure 23. Vial loading tool

3. Ensure that all connections are properly connected; see page 8.
4. If necessary, empty the waste containers according to the instructions on page 35.
5. If necessary, prime the system according to the instructions on page 24.
6. Select **Automatic** from the **Activities** menu.
7. Open the synthesis file to be used:
   a. Select **Library** from the **File** menu. The **Open** dialog opens.
   b. Select **Synthesis** in the **Files of type** drop-down list.
   c. Select the file that you want to use and click **Open**. The synthesis file is opened in the **Activities** window.
8. Validate the synthesis file by clicking the **Update** button in the **Activities** window.

9. Select the cycle or command in the synthesis file with which you want to start the synthesis. The selected cycle or command is highlighted in blue.
10. Close the system doors.
11. To start the synthesis, click the **Execute** button. When the synthesis starts, a **Stop** button appears instead of the **Execute** button.

2.9 Monitor the Synthesis

The reaction step in progress is highlighted in blue in the **Activities** window in the SyroXP software.

2.9.1 Monitor the Heating Process (Biotage® Syro *Wave*™)

Warning

- Keep your hands away from the microwave cavity when the system generates microwaves, i.e. when **Magnetron On** is displayed on the touch screen. It is only safe to insert reactor vials etc into the microwave cavity when the green cavity LED is lit and the orange LED is not (see page 4).

During a reaction step performed in the microwave cavity, a heating graph with real time measurements of temperature and applied power is displayed both on the touch screen and the system computer.

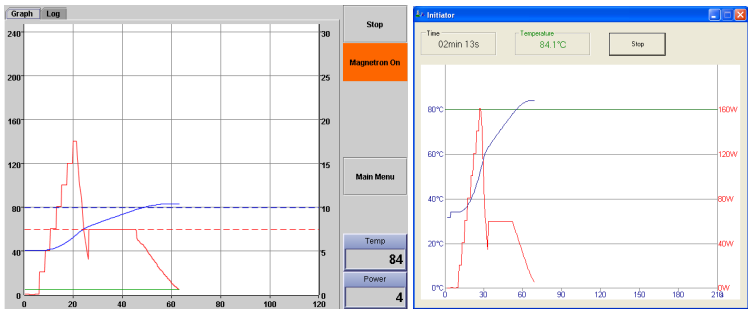


Figure 24. The heating graph displayed on the touch screen (left) and on the system computer (right).

2.10 Pause or Abort a Synthesis

Warning

- Keep your hands out of range of the robot arm(s) and the needle(s) when the system is in use, and when pausing or stopping the processing, until the robot arm or arms have stopped moving. The robot arm operates without a warning signal. There is a risk of personal injury.

You can stop the synthesis at any time using the **Stop** button, except for when a reaction is in progress (see "Abort a Reaction in Progress" below), and restart it at any step of the cycle (click the **Execute** button).

If you want to perform additional tasks and then resume the synthesis, use the manual programming feature (see page 28). When you are done and want to resume the synthesis, click the white area inside the **Activities** window (the step at which the synthesis was stopped is selected) and click the **Execute** button.

Note: If a fill command is aborted while a pump task is in progress, the (aspiration or dispense) task will be completed before the fill command is aborted and no further commands are sent to the pump or arm.

2.10.1 Abort a Reaction in Progress

Warning

- Keep your hands away from the microwave cavity when the system generates microwaves, i.e. when **Magnetron On** is displayed on the touch screen. It is only safe to insert reactor vials etc into the microwave cavity when the green cavity LED is lit and the orange LED is not (see page 4).

Parallel Synthesis

Abort a reaction in progress by clicking the **Close** button in the **Reaction** dialog. Three buttons appear in the lower part of the **Activities** window:

- **Continue:** Resumes the reaction command.
- **Skip:** Aborts the reaction command and starts the following command in the synthesis file.
- **Stop:** Aborts the synthesis. The message "Process stopped, Protocol (Log) saved" appears and the robot arm and pump initialize. The **Activities** window remains open with the step at which the synthesis was stopped selected (highlighted in blue). If you do not want to resume the synthesis, close the window. To open the synthesis log, with information on where and when synthesis was aborted, see page 28.

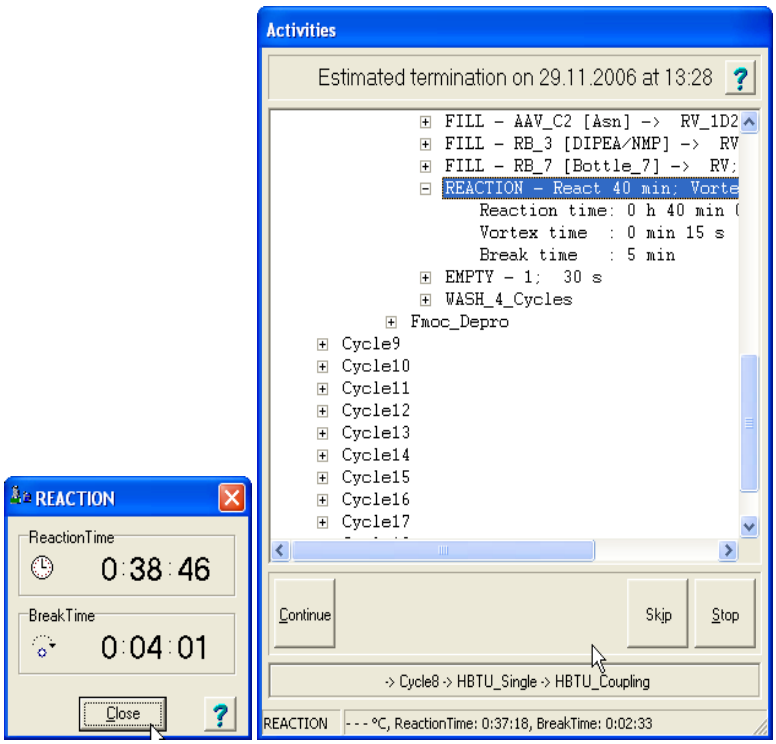


Figure 25. Abort a reaction in progress by clicking the Close button in the Reaction dialog. Three buttons appear in the lower part of the Activities window, Continue, Skip, and Stop.

Microwave Synthesis (Biotage® Syro *Wave*™)

Abort a reaction in progress by pressing the **Stop** button on the touch screen or clicking the **Stop** button in the **Initiator** dialog on the system computer. It is also possible to use the same abort procedure as for parallel synthesis; see above.

2.11 Cleavage of Peptides from Resin

For parallel peptide synthesis, we recommend that you use the Transfer Unit, which is available as an accessory. Please refer to the instruction video on our website www.biotage.com.

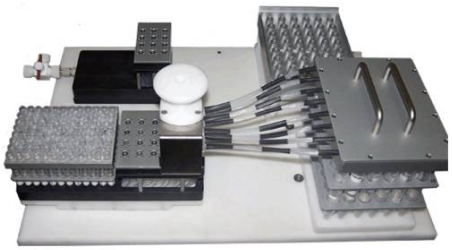


Figure 26. Optional Transfer Unit.

2.12 Print a Chemfile, Workfile, or Synthesis File

1. Select **Print** from the **File** menu.
2. Select the desired print option:
    - **Chem-/Workfile:** All the commands in a saved chemfile or workfile.
    - **Syntheses:** All the commands in a saved synthesis file.
3. Click the **Preview** button. The **Open** dialog opens.
4. Select the file (*.cmf, *.wkf, or *.syn) to print and click the **Open** button. The file is opened in the **Operations** dialog.
5. To print the file, click the **Print** button.

2.13 View and Print a Synthesis Log

Logs are saved using the date and time they were created in the library (yearmonthday_hourminute.rtf). To display the log for the current or a performed synthesis:

1. Select **Library** from the **File** menu. The **Open** dialog opens.
2. Select **Protocol** in the **Files of type** drop-down list.
3. Select the log that you want to open and click **Open**. The log is opened in the **Operations** dialog.
4. To print the log, click the **Print** button.

Note: To open the latest synthesis, select **Protocol** from the **File** menu. The log is opened in the **Operations** dialog.

2.14 Use the Manual Programming Feature

If you want to perform a system task during a synthesis:

1. Stop the synthesis in progress; see page 26.
2. Select **Manual** from the **Activities** menu. The **Activities** window opens with a **Manual** field and a command bar.
3. Add the desired command or command (see the instructions on page 14–17) and click the **Execute** button.

4. When you are done and want to resume the synthesis, click the white area inside the **Activities** window with the **Program** field, the step at which the synthesis was stopped is selected, and click the **Execute** button.

2.15 Change System Settings

2.15.1 Create or Modify a Robot Setup

A robot setup contains the chemical data, position coordinates, and the diameter of all bottles, reactor vials, and vessels on the work surface. It also contains the speed for aspiration and dispensing and settings for fluid detection. The system is delivered with one robot setup for each possible bottle, rack, and block configuration for the system. If you are missing a robot setup, please contact your local Biotage representative.

If you are using various chemical configurations, it is advisable to prepare a separate setup for each configuration. You can prepare a new setup by copying an existing one and modify it. To print lists with the defined chemical data for the amino acids, solvents, and reagents in the current robot setup, see page 22.

To create a new robot setup or change the chemical data in an existing one and, if desired, enable or disable the liquid detection:

1. Select **Robot setup** from the **Settings** menu. The **Setup settings** dialog opens.
2. Select the robot setup to modify or to base the new setup on from the **Actual** drop-down list.
3. To create a new robot setup:
    a. Click the **Copy** button. The **Copy settings** dialog opens.
    b. Select the settings you want to copy and click the **Copy now** button.
    c. In the **Setup settings** dialog, enter the name of the new setup in the **New** text box and click **OK**.
4. Click the **Use settings** button.
5. The software has to be restarted for a new setup to be used; click **OK** in the **Information** dialog that opens and then double-click the SyroXP shortcut ( ) on the system computer's desktop.
6. If you have copied a robot setup for microwave assisted synthesis:
    a. Select **Robot setup** from the **Settings** menu. The **Setup settings** dialog opens.
    b. Click the **Use settings** button. This activates the **General** button in the **Settings** toolbar.
    c. Click the **General** button. The **General settings** dialog opens.
    d. Press **F2**.
    e. Select the **Control unit** tab and enter the complete address to the InitiatorAPI.exe file, which is normally C:\Program Files\MultiSynTech\Initiator\bin\InitiatorAPI.exe.
    f. Click **Save** and then **Quit**.
7. To edit the chemical settings for a position on the work surface, right-click the position and select **Name** from the context menu. The **Settings** dialog opens. Enter the desired settings.

    The following parameter can be set for all positions on the work surface:

    - **Name:** The complete name of the chemical. Either enter the name or select it from the drop-down list.

    The following parameters can be set for amino acids:

    - **Code:** Multi-character code, e.g. three-letter code. Entries of up to 8 characters are possible.

- **Short code:** One-letter code. All letters and numbers between 0 and 9 are permitted. Use uppercase letters for L-amino acids and lowercase letters for D-amino acids.
- **Priority:** If single pre-activation is performed (see "Pre-Activate Amino Acids" on page 20), the amino acids will be pre-activated according to their priority and are directly distributed following pre-activation. 1 is the highest priority level. The rack position (alphabetic order) is taken into consideration for identical priorities.
  If the amino acid rack is populated in priority order (the **AminoAcid Priority** option is turned on when generating a synthesis file), the amino acid with the highest priority level is in position A1 on the amino acid rack, the second highest in position A2, and so on.
- **Resin load:** The loading of the preloaded resin for the amino acid.
- **Protected mol weight:** The molecular weight of the protected amino acid. The entry is used to calculate the original weighed in quantities.
- **Monoisotopic mass** and **Average mass:** The respective mass of the unprotected amino acid. The entry is used to calculate the molecular mass of the peptide.
- **Density:** The density of the original weighed in quantities for a liquid amino acid.

The following parameters can be set for reagents and solvents:

- **Factor:** The Factor parameter is applied to the calculation used to change the ratio of amino acid compared to reagents.
- **Mol weight:** The molecular weight of the reagent or solvent.
- **Density:** The density of the reagent or solvent.
- **Use reagent as:** Three options are available; Otherwise, Base, and Activator. (Only reagents.)

The following parameters can be set for the positions on the reactor block or the microwave cavity position:

- **N-terminal:** Four options are available; Hydrogen, N-Formyl, N-Acetyl, and New (create another one).
- **C-terminal:** Three options are available; Free Acid, Amide, and Test (create another one).
- **Monoisotopic mass** and **Average mass:** The respective mass of the unprotected amino acid. This entry is used to calculate the molecular mass of the peptide.

Note: If required data is missing for a position, the position is highlighted in red.

8. To enable or disable the detection mode:
   a. Right-click a position on the work surface and select **Adjustment** from the context menu. The **Robot Setup** dialog opens.
   b. Select the **Liquid handling** tab.
   c. Select the desired detection sensitivity setting.
   d. Click the **Save** button.

   Note: If you need to change any other settings in this adjustment view, please contact your local Biotage representative for instructions.

Export and Import Robot Setups

To export a robot setup to a diskette or to the hard disk and e.g. use it on another Syro system with the same configuration:

1. Select **Robot setup** from the **Settings** menu. The **Setup settings** dialog opens.
2. Click the **Save registry to disc** button.

To import a robot setup:

1. Select **Robot setup** from the **Settings** menu. The **Setup settings** dialog opens.
2. Click the **Restore registry** button.

2.15.2 Change General Liquid Handling Settings

To change the general liquid handling settings for the current robot setup:

1. Select **Robot setup** from the **Settings** menu. The **Setup settings** dialog opens.
2. Click the **Use settings** button. This activates the **General** button in the **Settings** toolbar.
3. Click the **General** button. The **General settings** dialog opens.
4. Make the desired changes. The following parameters are available:
    - **Gas gap Systemliquid:** The amount of air (inert gas bubble) that is drawn into the needle before an amino acid or reagent is aspirated. It reduces diffusion between the chemical and the system solvent.
    - **Buffer volume:** Additional volume that is used to compensate for diffusion. When the amino acid or reagent has been distributed, the buffer volume is discarded.
    - **Gas gap transport:** The amount of air (inert gas bubble) that is drawn into the needle after an amino acid or reagent has been aspirated. This prevents drips when the arm is in motion.
    - **Flush Min.:** This is the minimum volume in which the needle is washed after distributing an amino acid or reagent. The wash volume normally equals 2.5 times the distribution volume.
    - **Automatic Flush:** If turned on, the system washes the needle after a fill command.
    - **Substeps after detection:** Number of steps that the needle travels downwards after it has detected the surface of the liquid. This ensures that the needle is in the solution, when the suction procedure starts.
    - **Vortexer while Fill onto Reaction Block:** If turned on, the reactor block is continuously agitated during a fill command. (This parameters is only enabled when using a robot setup for parallel synthesis.)
    - **Number of Bottles, Racks & Blocks:** These settings shall not be changed. The system is delivered with one robot setup for each possible bottle, rack, and block configuration. If you are missing a robot setup, please contact your local Biotage representative.
    - **Mix preact.:** The number of mixing steps for the pre-activation liquid. Mix process: The needle traverses into the pre-activation vessel to the Z max position and draws out 70% of the pre-activation solution (5 ml max) plus the buffer volume. The needle subsequently traverses to the Z dispense position and pumps the liquid back into the pre-activation vessel. (This parameter is only enabled when using a robot setup with a combi rack for pre-activation.)
    - **Clean preact. vessels:** If turned on, the pre-activation vessels will be washed with the same volume of solvent as the liquid volume used in the pre-activation. If turned off, the pre-activation vessels will just be emptied with suction.
5. When you are done, click the **Save** button.

6. To close the **General settings** dialog, click the **Quit** button.
7. To exit the general settings mode, click the **Robot setup** button in the **Settings** toolbar.

2.15.3 Change Password and Location of Library

The library is by default available at My Documents\SyroXP\Library. To change the location of the library and/or the password for the Syro XP software:

1. Double-click the **Administrator** shortcut ( ) on the system computer's desktop. The **Administrator** dialog opens.
2. Change the location of the library and/or the password. Note that the location of the library is only changed for the robot setup in use.
3. When you are done, click the **Set** button.

3 Maintenance

Warning

- When it is required that the system is switched off, check that the power switch or switches (Syro *Wave* has two) are switched off, or that the power cord is disconnected.
- Covers and safety shields may only be removed by an authorized Biotage service engineer. Potential electrical hazard exists due to high voltage circuits inside the system.
- The system uses double pole fusing. Use only exact replacement fuses. Incorrect fuses create a potential fire hazard.
- Sharp corners may exist at the rear of the system. Exercise caution when working with the system.
- Pinch risk exists at the rear of the system where the robot arm(s) move. Exercise caution when working with the system and always shut it down before accessing the rear.
- Service or adjustments, other than those described in the "Maintenance" chapter, shall be made only by an authorized Biotage service engineer.
- Do not operate a damaged system. If the system has been damaged and does not function properly, shut it down and contact Biotage 1-Point Support immediately.

Notice

- The system shall be unpacked, installed, or re-located only by an authorized Biotage service engineer.
- In order to maintain compliance, only consumables and accessories supplied by Biotage must be used in the system; see page 38.
- It is each user's responsibility to study the Material Safety Data Sheet (MSDS) for each chemical used. Handle chemical and liquid waste according to the MSDS and to local/national guidelines on laboratory safety procedures. In case of spillage, the MSDS contains instructions for decontamination, including what decontamination agent to use for safe operation as well as information about any protective equipment required.

3.1 Clean the Exterior of the System

Note: If using a Syro *Wave* system and the touch screen on the Initiator has been contaminated by chemicals, it must be cleaned immediately.

To clean the exterior of the system:

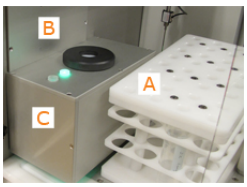
1. Shut down the system; see page 12.
2. When the system has shut down, disconnect the power cord.
3. Clean the touch screen (only available on Syro *Wave* systems) and the exterior of the system, using a soft and clean cloth. The cloth can be dry or lightly dampened with a neutral detergent or alcohol.
4. When you are done cleaning the system, connect the power cord and switch on the system; see page 11.

3.2 Clean the Microwave Cavity and IR-sensor (Biotage® Syro Wave™)

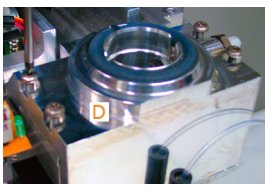
The microwave cavity and IR-sensor must be cleaned after the occurrence of a vial breakage or leakage. Note that only the Syro *Wave* system is equipped with a microwave unit.

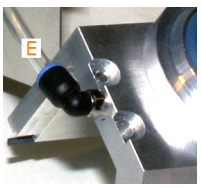
You need the T20 Torx screwdriver and the Philips screwdriver supplied with the system, a vacuum cleaner, a soft lens cleaning tissue (or similar), cotton swabs, soft and clean cloths, an emery cloth, pressurized air, water, and/or alcohol. The cleaning solution is dependent on the residues inside the cavity.

1. If the system is processing and you need to clean the microwave cavity at once, abort the synthesis as described on page 26.
2. Shut down the system and disconnect the power cord; see page 12.
3. Remove the amino acid rack (A).

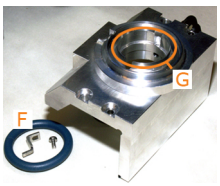


4. Remove the cavity wall panel (B) by removing the screws.
5. Remove the cavity cover (C).
6. If a reactor vial is located in the microwave cavity, remove it using the vial loading tool supplied with the system.
7. Remove the service lid (D) by removing the four screws and disconnecting the air tubing (E). Push in the collar against the fitting and pull the tubing out.



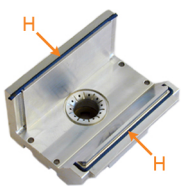


8. Remove the cavity lid seal (F) by removing the screw and carefully pulling out the lid seal.



9. Clean the cavity lid seal with water or alcohol containing mild soap. Do not use aromatic or chlorinated solvents.

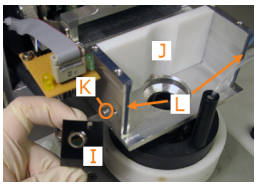
   Note: If the cavity lid seal is broken or distorted, it has to be replaced.
10. Clean the service lid using a cloth.
11. Clean the seal slot (G) using an emery cloth.
12. Ensure that the service lid and all its parts are dry and that the two service lid seals (H), on the back of the service lid, are in place. If a seal is broken or distorted, contact Biotage 1-Point Support.



13. Put the cavity lid seal (F) back in place.

    Note: Do not tighten the screw too hard.

14. Remove the IR-sensor (I) from the microwave cavity by removing the screw.



15. Clean the IR-sensor using a soft lens cleaning tissue (or similar) lightly dampened with distilled water, alcohol, or Kodak lens cleaner. Do not scratch the surface. If the IR-sensor is broken, contact Biotage 1-Point Support.
16. Remove the burst wall (J) and clean it using a cloth. If the burst wall is broken or distorted, contact Biotage 1-Point Support.
17. Remove as much as possible of the spill with a soft and clean cloth and then vacuum the microwave cavity, if possible.
18. Clean the microwave cavity, including the IR-housing (K), using pressurized air, a cloth, and cotton swabs.
19. Ensure that all parts are dry and that the two service lid seals (L), on the side of the cavity wall, are in place. If a seal is broken or distorted, contact Biotage 1-Point Support.
20. Reassemble the IR-sensor, burst wall, service lid, and air tubing.
21. If the vortexer needs to be cleaned:
    a. Carefully remove the Initiator. **Note:** Two persons are required when lifting the Initiator.
    b. If required, vacuum the vortexer.
    c. Clean the vortexer using a soft and clean cloth lightly dampened with alcohol.
    d. Carefully put the Initiator back in place.
22. Clean the work surface below the microwave cavity using a soft and clean cloth lightly dampened with a neutral detergent or alcohol.
23. Put the cavity cover and the amino acid rack back in place.
24. Remount the cavity wall panel on the cavity wall.
25. Connect the power cord and switch on the system; see page 11.

3.3 Clean the Tubing

If the system is not to be used for two weeks or more, clean the tubing as described below.

1. When the system is not processing, move the system solvent tube to a container containing ethanol.
2. Flush the system twice with 5000 µl of ethanol. If using a Syro II system, repeat for both arms. Use the same procedures as when priming the system; see page 24.

3.4 Empty a Waste Container

1. Remove the cap. Note that the cap can be removed without disconnecting the waste tube.
2. Empty the waste container.
3. Remount the cap and put the container in a safe and steady position below the system.

3.5 *Empty the System of System Solvent*

Before handing over the system for service or re-location, it should be emptied of system solvent (see below) and cleaned from harmful residues (see page 33).

1. Select **Manual** from the **Activities** menu. The **Activities** window opens with a **Manual** field and a command bar.
2. Click the **Fill** button. The **Activities** window disappears.
3. On the work surface, select the system solvent. The position is highlighted in yellow.
4. Select a/the wash station and enter 5000 µl in the **Fill** dialog that opens and click **OK**. The position is highlighted in green on the work surface.
5. When you are done, click the **Ready** button in the **Fill Option** toolbar. The fill command appears in the **Activities** window.
6. Click the **Stop** button. The **Stop** dialog opens.
7. Enter e.g. "Remove solvent tube" as the text to display when the stop command is executed.
8. Repeat steps 2 to 5 above. Enter 10000 µl in the **Fill** dialog that opens and click **OK**. If using a Syro II system, select the same wash station in step 4 as in the previous fill command.
9. If using a Syro II system, repeat steps 2 to 8 above for the other robot arm, i.e. select the other wash station as the target destination.
10. Validate the chemfile by clicking the **Update** button in the **Activities** window.
11. Close the system doors.
12. To start flushing, click the **Execute** button. A **Stop** button appears instead of the **Execute** button. When the stop command created in steps 6 and 7 is activated, remove the system solvent tube from the ethanol container (to draw air into the system) and resume the synthesis.

Tip! Save the chemfile and use it the next time you need to empty the system of system solvent. To enter the name of the chemfile, click the word Chemfile twice in slow succession and enter the name of the file.

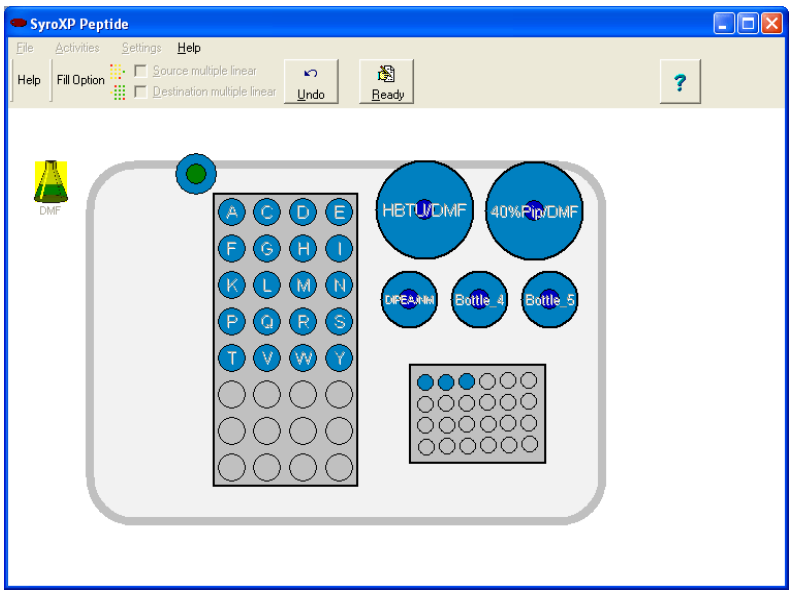


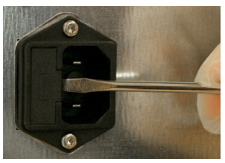
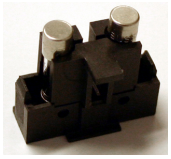
Figure 27. Source position is highlighted in yellow and target position in green.

3.6 Replace the Fuses

3.6.1 Replace the Vacuum Pump Fuses

The two fuses by the power inlet only have to be replaced if they are blown.

1. Disconnect the vacuum pump power cord from the power outlet.
2. Unplug the power cord from the rear of the pump. (You will not be able to remove the fuse holder if the power cord is plugged in.)
3. Loosen the fuse holder by carefully prying under the notch on the holder with a small standard (flat blade) screwdriver; see image below.

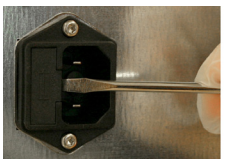
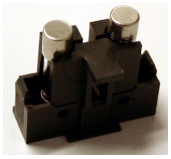



4. Grasp the fuse holder with your fingers and pull it out of the system.
5. Replace the two fuses with new fuses of the same type and rate, T8.0AL250V.
6. Put the fuse holder back in place.
7. If the fuses would blow shortly after being replaced, disconnect the power cable and contact Biotage 1-Point Support.

3.6.2 Replace the Fuses at the Syro Power Inlet

The two fuses by the power inlet only have to be replaced if they are blown.

1. Shut down the system as described on page 12.
2. Disconnect the power cord from the power outlet.
3. Unplug the power cord from the rear left side of the Syro. (You will not be able to remove the fuse holder if the power cord is plugged in.)
4. Loosen the fuse holder by carefully prying under the notch on the holder with a small standard (flat blade) screwdriver; see image below.

5. Grasp the fuse holder with your fingers and pull it out of the system.
6. Replace the two fuses with new fuses of the same type and rate, T8.0AL250V.
7. Put the fuse holder back in place.

3.7 Consumables and Accessories

Part No.	Description	Quantity
V020TF051	PP-Reactor, 2 ml, with PTFE frit	100
öV050TF062	PP-Reactor, 5 ml, with PTFE frit	100
V100TF086	PP-Reactor, 10 ml, with PTFE frit	100
V004PE050	PP-Reactor Tip, 0.4 mL with PE Frit	96
V100TF073	PP-Reactor, 10 mL, with PTFE frit (for Inert Gas)	100
V000LS100	Luer Stoppers	100
Z001RC020	Reactor cap, 2 ml	1
Z001RC050	Reactor cap, 5 ml	1
Z001RC100	Reactor cap, 10 ml	1
354180	Cavity lid seal	1
355741	Syro *Wave* Vial Loading Tool for 24-position reactor block	1
355754	Syro *Wave* Vial Loading Tool for 48-position reactor block	1
S011TU024	Transfer Unit 24-position	1
S011TU048	Transfer Unit 48-position	1
S011TU424	Transfer Unit 24- and 48-position	1
S006VO002	Vortex mixer, stand-alone, holds two reactor blocks	1
Z024UB050	U-block Reactor, 24 x 2-5-10 mL	1
Z048UB020	U-block Reactor, 48 x 2 mL	1
Z096UB020	U-block Reactor, 96 x 2 mL (Syro II only)	1
Z024AK000	Empty Head, 24-position	1
Z048AK000	Empty Head, 48-position	1
Z096AK000	Empty Head, 96-position (Syro II only)	1
411458	Fuse, T8.0AL250V, Syro power inlet and vacuum pump power inlet	1

4 Troubleshooting

Warning

- When it is required that the system is switched off, check that the power switch or switches (Syro *Wave* has two) are switched off, or that the power cord is disconnected.
- Covers and safety shields may only be removed by an authorized Biotage service engineer. Potential electrical hazard exists due to high voltage circuits inside the system.
- Sharp corners may exist at the rear of the system. Exercise caution when working with the system.
- Pinch risk exists at the rear of the system where the robot arm(s) move. Exercise caution when working with the system and always shut it down before accessing the rear.
- Service or adjustments, other than those described in the “Maintenance” chapter, shall be made only by an authorized Biotage service engineer.

Notice

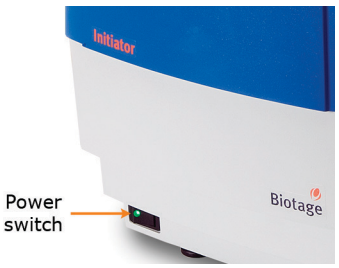
- The system shall be unpacked, installed, or re-located only by an authorized Biotage service engineer.
- In order to maintain compliance, only consumables and accessories supplied by Biotage must be used in the system; see page 38.
- It is each user’s responsibility to study the Material Safety Data Sheet (MSDS) for each chemical used. Handle chemical and liquid waste according to the MSDS and to local/national guidelines on laboratory safety procedures. In case of spillage, the MSDS contains instructions for decontamination, including what decontamination agent to use for safe operation as well as information about any protective equipment required.

4.1 All Syro Systems

- If the system has been damaged and does not function properly, shut it down and contact Biotage 1-Point Support immediately.
- Reagent and solvent bottles should be positioned on or below the work surface. If leakage is observed, shut down the system as described on page 12, disconnect the power cord, and follow the instructions for cleaning the exterior of the system in the “Maintenance” chapter.
- If materials inside the system should ignite, keep the system doors closed, switch off the system, and disconnect the power cord or shut off the power at the fuse or circuit breaker panel.
- If the Syro XP software is not shutdown correctly, it might not start at subsequent attempts. If this occurs, double-click the **Repair.reg** shortcut on the system computer's desktop. Confirm merge of the information into the registry by clicking **Yes** in the **Registry Editor** dialog that opens. Retry starting the Syro XP software.

4.2 Biotage® Syro Wave™ Systems

- In the event of a reactor vial breakage inside the microwave cavity, clean the cavity as described on page 34.
- If the microwave cavity contains trapped objects or moisture, clean the microwave cavity as described on page 34.
- If the system has been switched on according to the instructions on page 11 but the Initiator is not receiving any power, check that the power switch on the Initiator has not been accidentally switched off. Note that two persons are required when lifting the Initiator.



4.3 Technical Support

If you have any other problems with your system than those listed above, please contact Biotage 1-Point Support. See contact information on the back of this document or visit our website www.biotage.com.

When contacting Biotage 1-Point Support, please have the following information ready:

- Your name, address, telephone, fax numbers, and e-mail address.
- Serial number of your Syro system (see the product label at the rear left side of the Syro.
- A brief description of the symptoms or technical problems you are experiencing.

Note that all service or adjustments, other than those described in the “Maintenance” chapter, shall be made only by an authorized Biotage service engineer. Before handing over the system for service, it should be emptied of system solvent and cleaned from harmful residues as described in the “Maintenance” chapter.

5 Technical Specifications

Heating process (Biotage® Syro *Wave*™ only)	
Temperature range	40–80°C
Temperature increase	Typically 2–5°C/sec depending on solvent and power applied
Reaction time	Up to 12 hours. Typically, most reactions require 2 to 15 minutes of irradiation
Pressure range	Run at atmospheric pressure
Power range	0–200 W from magnetron at 2.45 GHz, capped at 60 W during steady state
Reaction volumes	When using the microwave unit: 2 ml reactor vial: 0.8–1.1 ml 5 ml reactor vial: 1.6–3.2 ml 10 ml reactor vial: 3.2–6.4 ml
Agitation	Vortex

Liquid Handling	
Volume range	2 µl to 10 ml
Syringe pump size	Syro I: 2 x 5 ml Syro II: 1 x 5 ml + 3 x 10 ml Syro *Wave*: 1 x 5 ml
Syringe pump resolution	Mechanical resolution is 1/3000 of syringe volume
Syringe pump accuracy	< 1.0% deviation at full stroke
Minimum detectable volume	200 µl

System requirements	
Operating temperature	18–32°C
Storage temperature	0–50°C (32–122°F)
Humidity	Minimum relative humidity 20% RH Maximum relative humidity 85% for temperatures up to 31°C decreasing linearly to 50% relative humidity at 40°C
Altitude	Up to 2000 m
Electrical supply	Syro I/II: Robot EU: 230 V~, 50 Hz (1.5 A) Robot US: 120 V~, 60 Hz (2.5 A) Robot JPN: 100 V~, 50/60 Hz (3.0 A) Vacuum pump EU: 230 V~, 50 Hz (1.4 A) Vacuum pump US: 120 V~, 60 Hz (3 A) Vacuum pump JPN: 100 V~, 50/60 Hz (3.8 A)

	Syro *Wave*: Robot EU: 230 V~, 50 Hz (3.4 A) Robot US: 120 V~, 60 Hz (6.7 A) Robot JPN: 100 V~, 50/60 Hz (8 A) Vacuum pump EU: 230 V~, 50 Hz (1.1 A) Vacuum pump US: 120 V~, 60 Hz (2.6 A) Vacuum pump JPN: 100 V~, 50/60 Hz (2.6 A)
Maximum power consumed	Syro I/II: Robot: 250 W Vacuum pump: 180 W Syro *Wave*: Robot + Initiator: 800 W Vacuum pump: 120 W
Weight	Syro I: 60 kg (132 lbs) Syro II: 85 kg (187 lbs) Syro *Wave*: Syro: 63 kg (138.9 lbs) Initiator: 22 kg (48.5 lbs) Syro + Initiator: 85 kg (187 lbs) Vacuum Pump (Syro I and Syro *Wave*): 12.2 kg (26.8 lbs) Vacuum Pump (Syro II): 16.0 kg (35.2 lbs)
Dimensions (WxDxH)	Syro I: 560 x 700 x 910 mm (22.0” x 27.6” x 35.8”) Syro II: 820 x 700 x 835 mm (32.3” x 27.6” x 35.8”) Syro *Wave*: Syro: 600 x 700 x 910 mm (23.6” x 27.6” x 35.8”) Initiator: 365 x 405 x 415 mm (14.4" x 15.9" x 16.3") Syro + Initiator: 900 x 700 x 910 mm (35.4" x 27.6" x 35.8") Vacuum Pump (Syro I and Syro *Wave*): 260 x 290 x 270 mm (10.2” x 11.4” x 10.6”) Vacuum Pump (Syro II): 380 x 310 x 220 mm (15.0” x 12.2” x 8.7”)Syro I: 560 x 700 x 910 mm (22.0" x 27.6" x 35.8")
Max sound level	70 dB(A)

Interfaces (Biotage® Syro *Wave*™ only)	
Touch screen	6.4"
Ethernet LAN	Complies with IEEE 802.3 (ANSI 8802-3)
USB	USB 1.1

Archiving/back-up and printing
Via the LAN, USB

6 General Information

6.1 Trademark Acknowledgement

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6.3 Consumables and Accessories

In order to maintain compliance, only consumables and accessories supplied by Biotage must be used in the system (see page 38). To order consumables and accessories, see contact information on the back of this document or visit our website www.biotage.com.

6.4 Contact Us

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7 Appendix A: Solubility of Chemicals

7.1 Solubility of Amino Acid Derivatives

The molar concentration in the starting reaction mixture is critical. Therefore, the amino acids should be dissolved in the smallest possible volume of solvent.

Amino Acid Derivates	One-Letter Code	CAS	Solubility (mmol/ml)		
			DMF	NMP	DMA
Fmoc-Ala-OH	A	[35661-39-3]	1.7	2.5	3.3
Fmoc-Arg(Pbf)-OH	R	[154445-77-9]	0.8	0.8	0.8
Fmoc-Asn(Trt)-OH	N	[132388-59-1]	1.1	0.9	--
Fmoc-Asp(tBu)-OH	D	[129460-09-9]	2.5	1.7	2.5
Fmoc-Cys(Trt)-OH	C	[103213-32-7]	2.0	2.0	2.0
Fmoc-Gln(Trt)-OH	Q	[132327-80-1]	1.2	0.8	--
Fmoc-Glu(tBu)-OH	E	[84793-07-7]	2.5	2.5	2.5
Fmoc-Gly-OH	G	[29022-11-5]	3.3	3.3	3.3
Fmoc-His(Trt)-OH	H	[109425-51-6]	0.9	0.9	--
Fmoc-Ile-OH	I	[71989-23-6]	2.5	2.5	2.5
Fmoc-Leu-OH	L	[35661-60-0]	2.5	2.5	2.5
Fmoc-Lys(Boc)-OH	K	[71989-26-9]	2.0	2.0	2.0
Fmoc-Met-OH	M	[71989-28-1]	2.5	2.5	2.5
Fmoc-Phe-OH	F	[35661-40-6]	0.7	1.7	0.5
Fmoc-Pro-OH	P	[71989-31-6]	3.3	3.3	3.3
Fmoc-Ser(tBu)-OH	S	[71989-33-8]	2.5	2.5	2.5
Fmoc-Thr(tBu)-OH	T	[71989-35-0]	2.5	2.5	2.5
Fmoc-Trp(Boc)-OH	W	[143824-78-6]	1.3	1.2	--
Fmoc-Tyr(tBu)-OH	Y	[71989-38-3]	2.0	2.0	2.0
Fmoc-Val-OH	V	[68858-20-8]	3.3	3.3	3.3

7.2 Solubility of Coupling Reagents

Coupling Reagents	CAS	Solubility (mmol/ml)	
		DMF	NMP
DIC (N,N'-Diisopropyl-carbodiimide)	[693-13-0]	3.5	
TBTU (2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium tetrafluoroborate)	[125700-67-6]	0.69	0.38
HBTU (2-(1H-Benzotriazole-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate)	[94790-37-1]	0.64	0.41
HCTU (2-(6-Chloro-1H-benzotriazole-1-yl)-1,1,3,3-tetramethylaminium hexafluorophosphate)	[330645-87-9]	0.5	
PyBOP ((Benzotriazole-1-yloxy)trispyrrolidinophosphonium hexafluorophosphate)	[128625-52-5]	0.98	0.87
HOBt (Hydroxybenzotrialzole)	[2592-95-2]	2.5	3.3
DIPEA (N,N-Diisopropylethylamine)	[7087-68-5]	1.5	2.5
NMM (N-Methylmorpholine) DMF (N,N-Dimethylformamide) NMP (N-Methylpyrrolidinone) Piperidine	[109-02-4] [68-12-2] [872-50-4] [110-89-4]	Compl.	Compl.

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