Uniqsis FlowSyn Frequently Asked Questions (FAQs)

Q: What is the maximum usable pressure of the standard FlowSyn

A: All new standard FlowSyn units are rated to 1000psi (or 70bar). However this maximum is only possible when using Stainless Steel or Hastelloy™ coil reactors. When using Teflon or PFA coil reactors the pressure is automatically limited to 200psi (or 14bar) for safety.

Q: What is the maximum temperature the standard Uniqsis FlowSyn can reach?

A: The standard FlowSyn includes 2 separate heating modules. The coil reactor unit (homogeneous) can be heated to 260°C and the column reactor unit (heterogeneous) can be heated to 150°C. The temperature of each reactor has been calibrated so that the temperature of the solution is accurate to ±1°C.
The maximum temperatures are achievable using the Stainless Steel coil reactor (260 °C).
For Teflon and PFA coil reactors the system limits the maximum temperature to 150°C this ensures that the tubing is not damaged by over-heating.

Q: How chemically resistant is FlowSyn?

Uniqsis fit modified high pressure pumps that *do not* contain PEEK to all FlowSyns (PEEK is an excellent engineering polymer but has poor compatibility with concentrated mineral and organic acids and very strong organic bases). Wetted parts are fabricated from sapphire, ruby, Kel F, Hastelloy™ and carbon filled PTFE.
FlowSyn can be specified whereby the flow path is fabricated from different materials that the user may select to best meet the requirements of their chemistries as cost-effectively as possible

	Flow Path	P_{max}	T_{max}	Chemical Compatibility
FlowSyn Standard:	PEEK and PTFE	1000psi	260/150°C	Good
FlowSyn PTFE:	All PTFE	300psi	150°C	Excellent
FlowSyn Steel	PTFE and 316 Stainless Steel	1400psi	260/150°C	Very good
FlowSyn Hastelloy™:	PTFE and Hastelloy™	1400psi	260/150°C	Excellent

In coming to a decision as to what is the best system for you, you should consider the following factors:
(i). A full PTFE flow path offers the broadest chemical resistance, particularly to concentrated mineral acids – but lacks the physical strength to operate safely at very high pressures.

(ii). Stainless Steel offers a good compromise with the strength to safely operate at high pressures with permanently swaged 316SS tubing and has broad chemical resistance; so long as it is not exposed to high concentrations of HCl.
(iii). Hastelloy offers the best combination of chemical resistance combined with high pressure capability – but is the most expensive.

For many scientists, the standard PEEK and PTFE flow path will be more than adequate.

If you would like more information or assistance in making your choice, please don't hesitate to contact Uniqsis directly.

Q: What safety features are incorporated within FlowSyn?

A: The FlowSyn™ system has been designed with a number of safety features to protect you and your working environment in the event of a failure: There are 4 main safety features. Constant alarm-linked pressure monitoring for under- and over-pressure. If a leak or pressurisation above the safe limit is detected, the pumps stop.

- All pressure-critical parts pressure tested and rated; pressure limits automatically set by FlowSyn™ according to the reactor material.
- Unique to FlowSyn is that all pressurised parts are contained within the Plexiglass safety cover which has an alarmed safety interlock to warn the user not to open during operation.
- An over-temperature alarm/cut-out protects the system from over-heating.

Q: Can I rewind my coil reactor?

A: Cetainly! The Coil reactors have been made so that the tubing can be quickly and easily replaced by the user.

This is both pragmatic and cost-effective, because blockages do occur from time to time, and PTFE tubing should be replaced periodically to reduce the risk of potential rupture (after every 10 - 20 uses is recommended). [Repeated pressure and heat cycling of thermoplastic materials causes fatigue.]
Our competitors insist that you repeatedly purchase expensive new coil reactors each time. Uniqsis make it as easy as possible for you to re-wind your own.
It takes a matter of minutes! We can even provide tubing in bulk quantities to reduce the cost as much as possible.

Of course, we are more than happy to re-wind your coil reactors for you, but this is only really worth considering where the coils are made of metal (Stainless Steel or Hastelloy).

Q: How many reagents can be used for a reaction?

A: As standard FlowSyn has 2 channels to introduce reagents, however you can premix reagents and there is an option of a third channel including a high pressure pump that is controlled by the FlowSyn.

Q: What happens if there is a problem with pressure?

A: The FlowSyn has active pressure monitoring and will detect a pressure increase or decrease. An alarm will sound to alert the user to the problem, after a defined time the pumps and heaters will shutdown. If the pressure change is such that it indicates a leak or blockage then the pumps etc. will immediately stop.

Q: When should we consider using a static mixer chip/reactor?

A: A key benefit of flow chemistry derives from the ability to control both mixing and temperature of reactions with a precision that is very difficult, or impossible, to achieve in batch reactors. This leads to reproducible scaleability and the ability to safely contain exotherms.
However, as the channel dimensions of the flow reactor increase (above approx 0.5mm id), the rate of mixing by simple diffusion decreases markedly (Fick's Law). Therefore very rapid reactions (that are typically exothermic) can become rate limited and unpredictable because mixing is too slow. Under these circumstances it is advantageous to utilise a static mixer that dynamically mixes reagent streams and does not rely upon slow diffusional mixing in wide channels.
Uniqsis offer all glass static mixers that have relatively wide channels to minimise the risk of blockages and make cleaning easier if they do occur. The channels incorporate a special geometry that promotes dynamic mixing.

Q: What happens if a pump malfunctions during an experiment and doesn't pump properly.

A: FlowSyn *automatically* monitors the performance of both pumps individually.

If an air bubble is detected, or a check valve malfunctions, an audible alarm sounds. If the user does not correct the problem within 60 seconds, FlowSyn will abort the experiment and stop to avoid contaminating the product already collected and wasting starting materials.
Usually repriming the FlowSyn 'on the fly' (there is no need to de-pressurise the system or allow the reactors to cool down before doing this) will resolve the problem, and the experiment can continue.

It is possible for the user to adjust the sensitivity of this detector, or switch it off completely if they prefer.

Q: Can I pump organometallic bases such as LiHMDS and BuLi using FlowSyn.

A: Yes, this is certainly possible, however, we recommend that you adhere to the following guidelines:

- The organometallic should not contain precipitate. If so, it is advisable to use an in-line filter.
- All solvents should be anhydrous, and the stock bottles inerted under a N_2 or Ar blanket (tubing from a low pressure gas manifold can be terminated with the ends of disposable syringes and these can be inserted directly into our recommended bottle tops). A short length of wide-bore SS tubing can be inserted directly through Sure-Seals and connected directly to the FlowSyn using standard fittings.
- The flow path should be thoroughly flushed through with an anhydrous solvent (eg THF) before any moisture sensitive or air sensitive reagents are pumped.
- We recommend that you fit a **Backflush Kit (UQ-7210)** to the pump heads. Salts (amongst other things!) derived from hydrolysis of organometallic reagents tend to accumulate between the high and low pressure pump seals. These should be removed periodically by either dissembling the 2 halves of the pump heads, or more conveniently, by flushing with a suitable cleaning solvent using the Backflush Kit (eg 1:1:1 [AcOH:THF:H_2O] or [AcOH:THF:DMF]).
- The FlowSyn should be flushed with a cleaning solvent (1:1:1 [AcOH:THF:H_2O] works well) after use, and then stored in ^{i}PrOH.

This protocol should ensure that your FlowSyn performs reliably.

Q: Is it always necessary to store the FlowSyn in ^{i}PrOH after use?

A: It is very important, particularly if you pump reagent solutions through the pump heads, to clean them out thoroughly after use and then store them in a benign solvent. ^{i}PrOH is particularly good because it helps to ensure that the check valves in the pump heads are conditioned properly.
Other clean solvents are also suitable overnight, however, we recommend ^{i}PrOH for prolonged storage of the FlowSyn.
If you are using a fluorous system solvent (for plug flow work), we recommend that you do not routinely switch back to ^{i}PrOH to store the system in overnight. Leave it primed with the fluorous solvent. Conditioning the check valves to give stable flow can be particularly problematic and require prolonged flushing in these cases.

Q: What about changing between immiscible solvents?

A: If you wish to pump a solvent that is not miscible with the solvent that is currently in the pump head(s), then it is very important to first thoroughly flush the pump heads with a solvent which is fully miscible with both solvents.
This will ensure that the check valves are properly conditioned and that the pumps will give a stable flow.
A good example is when switching between water and toluene. DMF is a good choice of intermediate flush solvent in this case.
Fluorous solvents pose a particular problem. However, MeOH can be effective in these cases.
However, if you subsequently intend to pump a solvent that is not miscible with ^{i}PrOH then you should ensure that any residual ^{i}PrOH is thoroughly washed out of the pump heads and check valves using a solvent that is miscible with both solvents.

This applies whenever you wish to change between immiscible solvents. Always flush thoroughly with a solvent that has miscibility with both solvents.

Q: Can FlowSyn be used to produce compound libraries or handle multiple reagent sets for, say, reaction profiling?

A: Yes, certainly!

Generally for compound library preparation, the individual monomers are introduced into the flow stream using sample loops. This has the added advantage that because because only solvent and not reagent solutions are pumped *through* the pump heads, the pump heads need less maintenance and cleaning.
However, since the sample loops have to be filled by hand with a syringe, this means that you need to keep going back to the machine …. Until now, that is!

☆ As as upgrade, we now offer a bolt-on package (**FlowSyn Auto-LF Package**) that will automatically wash and refill the sample loops from a pre-determined set of reagents.
So you can design your combinatorial array upfront and the flow reactor will automatically run the chemistry and prepare the compound library completely unattended.

In a similar way, this set up can be used for reaction profiling using a set of different reagents (say bases or coupling reagents, for example).

☆ Also, because the sample loop refilling and product collection and/or fractionation are handled separately, then the system will typically start to fill the sample loops for the next experiment before the current experiment has actually finished. Loop loading is a relatively slow process, and therefore this saves a considerable amount of time when experiments are processed serially using a single flow reactor.

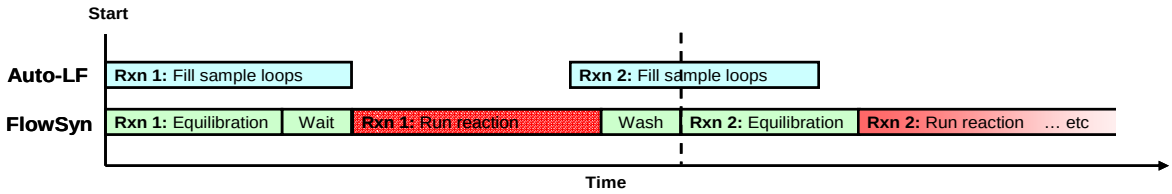
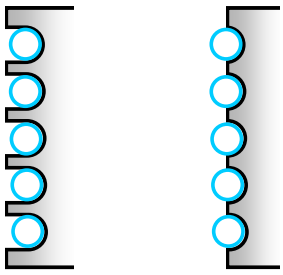


Fig. Running Flow Reactions in Sequence: Representative Time Course

Q: What is the difference between HT and LT PTFE coil reactors?

A: Perfluoroelastomers such as PTFE and PFA soften considerably at elevated temperatures and this leads to stretching of the tubing when pressurised. Consequently, the tubing can expand and lose intimate contact with the metal mandrel of the coil reactor which compromises heat transfer and therefore temperature stability.



This in effect limits the maximum temperature that LT (low temperature) Coil Reactors can be heated to approximately 100^{o}C.

The HT (high temperature) Coil Reactor design, however, incorporates deeper channels (grooves) such that the tubing locates in a 'micro oven' environment. This allows more movement of the tubing before a stable temperature environment is compromised. HT coil reactors can therefore be heated up to a maximum of 150^{o}C.

☆ An additional, and important, benefit of the FlowSyn coil reactor design is that if a coil reactor ruptures when under pressure and the contents expelled, then these are safely contained within the glass cover.

The pumps will stop immediately to minimise any spillage, however, any liquid escaping from the reactor (the largest coils we offer contain 50 mL) will simply drain into the PTFE coated reactor containment tray.

Replacement or repair of the coil is straightforward and clean up of the instrument is quick and easy. This is NOT the case with hot air (convector) heating systems where not only can the coil reactor not be repaired, but the inside of the instrument becomes contaminated and the unit has to be dissembled and decontaminated. A major undertaking!