

FlowSyn™ – The Continuous Flow Reactor from Uniqsis
Designed by chemists for chemists

UNIQSIS
Accessible flow chemistry

 **interchim®**

FlowSyn™ from Uniqsis

The FlowSyn continuous flow reactor has been designed by chemists, for chemists. Whether you are new to flow chemistry or an advanced user, Uniqsis offers a range of accessible modules with outstanding chemical compatibility and proven reliability.

High Performance

- Accurate, uniform temperature control from -70°C to +260°C
- Pressure up to 1400 psi: Perform superheated reactions routinely
- Automated reactions: Allows unattended operation
- Maximum reproducibility thanks to specially designed mixers and reactors
- Chemical compatibility: Choose stainless steel or PTFE flow path
- Excellent reaction visibility

Flexible

- Perform an extensive range of chemistries from mg to kg
- Choose from modules for reaction profiling and optimisation, and library synthesis
- Choose from reactors for homogeneous and heterogeneous reactions
- Switch between configurations in minutes
- Add extra pump modules for downstream additions
- Choose between manual and automated control
- Suited for a single user or for open access

Safe

- All pressurised parts contained within a Plexiglass alarmed safety cover
- Automatic shutdown in the event of a leak or blockage
- Pressure and temperature limits automatically determined depending on system configuration
- High performance connections and tubing prevent tubing blow-outs

Uniqsis

Located in Cambridge, England, Uniqsis has a team of flow chemists and engineers developing innovative technology for the flow chemistry market.

At the forefront of flow reactor design, FlowSyn is the platform of choice within major pharmaceutical companies and academic research laboratories around the world.

Contact us for:

- Assistance in choosing your FlowSyn configuration
- Application support and training
- After sales service and preventative maintenance options

www.uniqsis.com

FlowSyn – Range overview

FlowSyn

For single reactions

- Superheated reactions up to +260°C (1400 psi)
- Small scale cooled reactions down to -70°C
- Run seamless scale up reactions
- Continuous or plug flow
- Segmented flow



FlowSyn Multi-X

For multiple reactions

- Automatically run sequential experiments
- Reagent scanning, reaction profiling and optimisation
- Explore a range of reaction conditions: temperature, residence time and stoichiometry



FlowSyn Auto-LF

For multiple experiments with multiple reagents

- The ultimate tool for combinatorial experiments
- Compound library synthesis
- Reagent scanning and reaction optimisation
- Concentration studies



FlowSyn Cold

For low temperature reactions

- Large scale cooled reactions down to -70°C
- Exothermic reactions
- Compatible with all existing coil reactors



Accessories

Coil Reactors

For homogeneous reactions

- Small reactors for minimal reagent usage
- Larger reactors for increased throughput and residence time

Column Reactors

For heterogeneous reactions

- Pack your own catalyst, solid supported reagents and scavenger resins

Mixer Blocks

For efficient mixing

- Fast, exothermic reactions
- Bi-phasic reactions
- Small scale reaction optimisation
- Pre-mix for large scale reactions

External Pump

For additional reagent channel

- A + B + C reaction
- 2 stage reaction
- Quench

FlowSyn Your flexible research tool

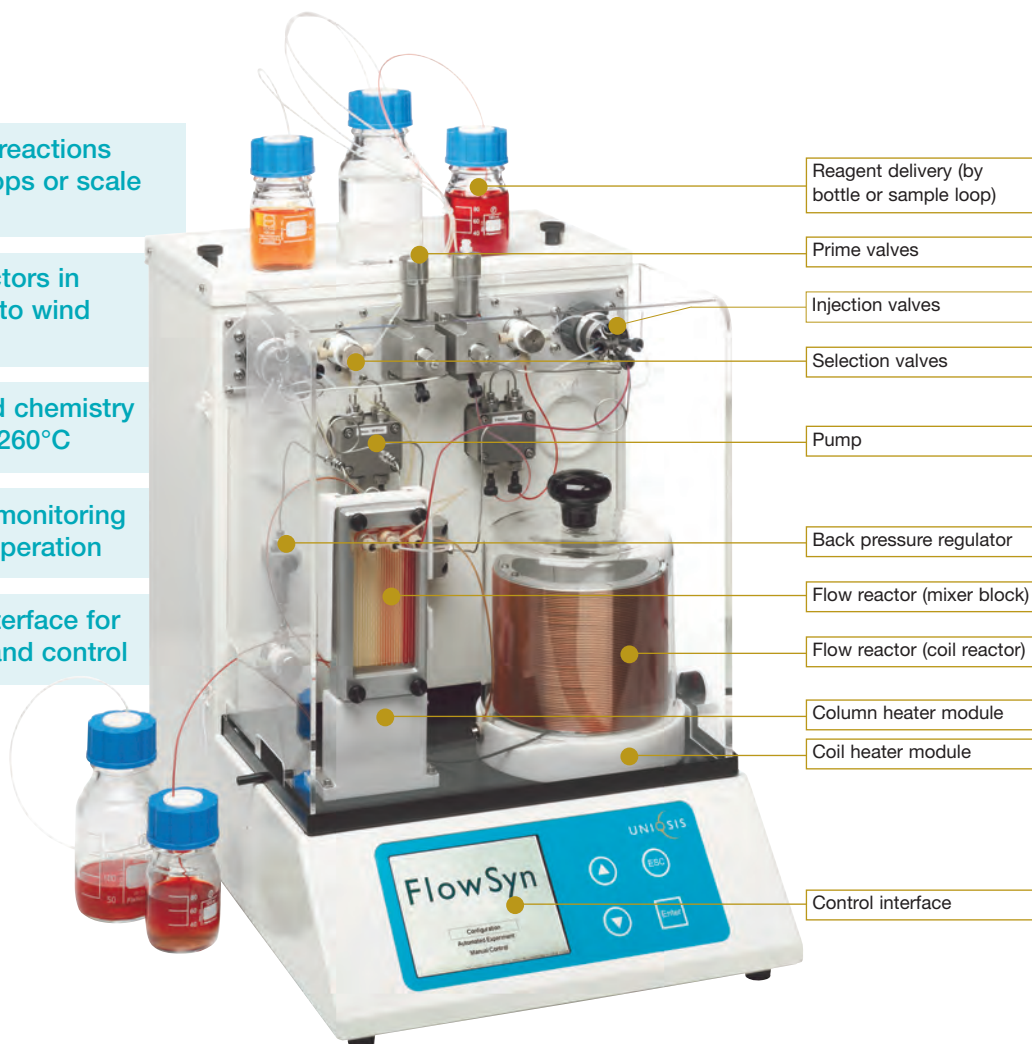
Run small scale reactions using sample loops or scale up using bottles

Interchange reactors in minutes. Option to wind your own coils

Run superheated chemistry routinely up to +260°C

Active pressure monitoring for unattended operation

Easy, intuitive interface for reaction set up and control



Reagent delivery (by bottle or sample loop)

Prime valves

Injection valves

Selection valves

Pump

Back pressure regulator

Flow reactor (mixer block)

Flow reactor (coil reactor)

Column heater module

Coil heater module

Control interface

Configuration options

	FlowSyn	FlowSyn PTFE	FlowSyn Steel	FlowSyn Hastelloy®
Flow Path	PEEK and PTFE	All PTFE	PTFE* and 316 Stainless Steel	PTFE* and Hastelloy®
Pmax /psi	1000	300	1400	1400
Tmax /°C Coil/Column	+260/+150	+150	+260/+150	+260/+150
Chemical Resistance	Good	Excellent	Very Good	Excellent

*Note PTFE is only used for low pressure components in the flow path in these configurations.

FlowSyn in Detail

A fully integrated, easy to use continuous flow reactor

Reagent Delivery

Choose your method of reagent/solvent delivery – bottles or loops

Reagent solutions can be delivered from bottles (for continuous processing) or sample loops (for small scale, plug flow reactions).

Selection valves

For switching between reagent solutions and cleaning solvent.

Chemically resistant sample injection valves

The bespoke sample injection valves offer high chemical resistance to concentrated mineral acids such as nitric and sulfuric acids. The valve has been specifically designed with 1.0 mm internal channel diameter to minimise the risk of blockages.

Pumps, Priming and Pressure

Two independent flow channels driven by chemically resistant high-pressure pumps

FlowSyn pumps have been specially modified to improve chemical resistance (no PEEK!). These chemically inert high-pressure pumps deliver total flow rates adjustable from 0.01 to 20.0 ml/min. FlowSyn automatically monitors each high-pressure reagent channel and will alert the user if there is an air bubble or inconsistent pumping during an experiment. If the situation is not resolved within 60 seconds, FlowSyn will abort the experiment.

Convenient dedicated priming ports

FlowSyn pumps can be easily primed without disconnecting any fittings, and the system itself purged of air using the dedicated 'Prime' function.

Back pressure regulator

FlowSyn uses interchangeable, fixed back pressure regulator cartridges to maintain constant pressure during an experiment.

Reactor Modules

Coil Heater

The electronically controlled coil heater module has been designed for fast heat up. Reactor temperature is calibrated for accurate temperature control that is consistently maintained throughout the whole reaction.

- Glass insulated cover
- Allows use of different sized reactors
- Maximum temperature +260°C

Column Heater

Adapts for columns of different sizes.

- Maximum temperature +150°C
- Also houses glass mixing blocks
- Can be liquid or gas cooled

Gas-cooled heat exchanger

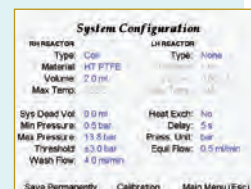
Allows you to pre-heat reagents prior to entering column.

Allows you to cool product solutions below the solvent boiling point before exiting the pressurised reaction – essential when performing reactions above the boiling point of the solvent (superheating).

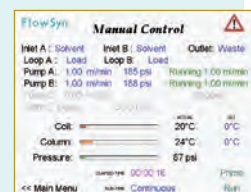
FlowSyn Control Interface

FlowSyn has an in-built graphical control interface making it very easy and quick to set up reactions.

Configuration – When setting up the reactors, FlowSyn will automatically set maximum pressure and temperature limits based upon the materials the reactors are made from.



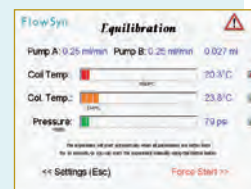
All components (pumps, reactors and valves) can be independently controlled from within the Manual Control screen. In this way, pumps and reactors can be quickly primed before starting any reactions.



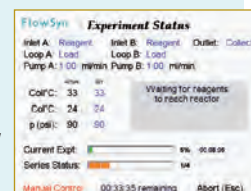
Automated Control – Set up a reaction in minutes. FlowSyn will do the calculations for you, e.g. set the reaction time and FlowSyn will work out the flow rate.



To ensure consistent and reproducible results, FlowSyn equilibrates to reaction temperature using system solvent before allowing any reagent solutions into the reactor(s).



When up to the desired temperature, FlowSyn introduces the reagents, and the reaction begins. Throughout the reaction you can see the progress. At the end of the reaction FlowSyn will automatically wash the whole flow path with clean solvent.



FlowSyn Multi-X

Multiple experiment package for multiple reactions



Run up to 10 experiments with varying reaction temperature, time and stoichiometry

Perform sequential reaction profiling and optimisation

FlowSyn controls the fraction collector – no PC required!

Unattended operation – allows overnight optimisation

Why should I collect the steady state?

Generally, only the material at the steady state has a product distribution that is truly representative of a scale up result

Flow chemistry is an excellent method for reaction profiling and optimisation, particularly prior to scale up. High reproducibility of results, coupled with short processing times, allows rapid exploration of a range of reaction conditions.

The FlowSyn Multi-experiment package (FlowSyn Multi-X) consists of either a Gilson FC203B or FC204 fraction collector and an enhanced FlowSyn control interface.

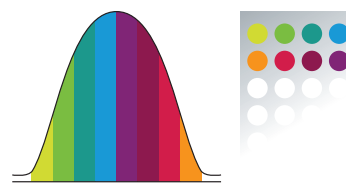
The FlowSyn can be programmed to perform up to 10 sequential experiments and then will run unattended and collect the output of each experiment according to the collection protocol selected ('fractionate' or 'optimise').

Reaction outputs can be either simply 'fractionated' or collected using a dedicated optimisation rack whereby each reaction plug is collected into a single vial and an aliquot is directly sampled into a 2 ml LCMS vial for subsequent analysis.

Sample collection options

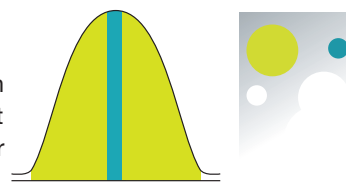
Fractionate

Select the arrangement and number of vials to be collected for each experiment. This is a useful method to model the dispersion curve.



Optimise

Each reaction is collected into a 20 ml vial and an aliquot taken at the steady state point into a 2 ml LCMS vial for subsequent analysis.





FlowSyn Multi-X: FC203B option

- Small footprint
- 1 rack position



FlowSyn Multi-X: FC204 option

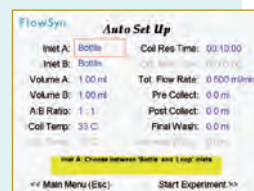
- High throughput
- 4 rack positions

Set up

Setting up the FlowSyn Multi-X is a very straightforward process:

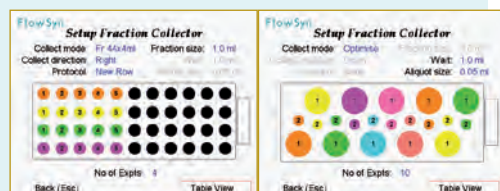
Step 1

– Set up a single 'template' reaction



Step 2

Choose collection mode: fractionate or optimise



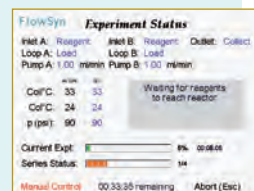
Step 3

Edit individual experiments in 'Table View'

Expt	Vol A	Vol B	Rate	Coil Temp	Flow Rate
1	1.0	1.0	1:1	33	00:05:59 2.01
2	1.5	0.5	3:0:1	33	00:05:59 2.00
3	1.0	1.0	1:1	33	00:02:59 5.15
4	1.0	1.0	1:1	33	00:00:20 24.83

Total 4.5 3.5
Back Sort Start >>>

Check reaction progress in 'Experiment Running'



Review reaction summary



FlowSyn Auto-LF

For automated combinatorial experiments



Run up to 10 experiments with multiple reagent inputs

Powerful, intuitive PC interface

Efficiently loads and collects reactions simultaneously

FlowSyn Automated Loop Filling (FlowSyn Auto-LF) is an optional module which enables you to perform automated combinatorial experiments, i.e. to run multiple experiments with multiple reagent inputs

- Automatically prepare focussed combinatorial compound libraries in flow
- Optimise reactions and perform reagent screening using multiple starting materials (e.g. base or coupling reagent screen)
- Integrated wash steps to prevent cross-contamination
- Simultaneous loop filling and fraction collection to save processing time
- Electrically operated selection valve – no injection ports to block!
- Continuously monitor flow reactor progress and performance in real time – interactive displays of pressure and temperature
- Save experiment log files

With its many capabilities FlowSyn Auto-LF is a powerful and highly versatile research tool enabling you to harness the power of flow chemistry to deliver more compounds faster.

- **Flexible:** Each reaction can have a different set of conditions.
- **Efficient:** Separate Sampler and Fraction Collector enables loop filling for the next experiment to begin before the current experiment has finished, significantly reducing series run times
- **Reliable:** No injection port to leak or block; fully integrated robust wash protocols minimise the risk of cross-contamination.
- **Versatile:** Partial, full or over-filling of sample loops possible
- **Accurate:** Sampler can be calibrated to position samples precisely within sample loops.
- **Powerful:** Independent, manual control of Sampler, real-time reaction monitoring and data logging
- **Easy to set up:** Multiple experiments quickly programmed via familiar user interface
- **Compact:** Stacked small format XYZ Sampler and Fraction Collector minimises valuable fume cupboard space.

Programming FlowSyn Auto-LF

FlowSyn Auto-LF is programmed with dedicated software supplied on a notebook as part of the system. The user interface is organised in a similar way to the standard FlowSyn graphical interface and is very straightforward to use. All the control screens (Configuration, Manual Control, Experiment Setup and Logging) are conveniently accessed by selecting the relevant 'tab'.

Setting up experiments

FlowSyn Auto-LF has been designed by chemists for chemists, so setting up experiments is straightforward and intuitive:

- Enter a series of combinatorial experiments into the spreadsheet style user interface running on the FlowSyn notebook.
- Place the reagent solutions into the sample rack (these may be septum capped to minimise evaporation). The compact XYZ sampler then automatically selects and loads the solutions into the FlowSyn sample loops.
- Solutions are initially loaded into an intermediate holding coil. Air bubbles can be incorporated to prevent sample dispersion and dilution during the sample loop loading process.
- Each reagent solution is then transferred directly to the appropriate sample loop. An electrically operated selection valve is utilised to avoid the need for unreliable injection ports.
- All transfer lines are rigorously washed between operations to eliminate any possibility of cross contamination.

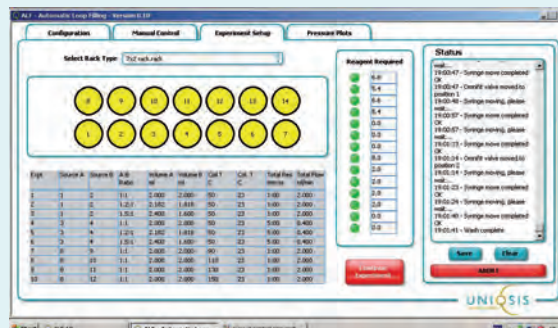


Experiment Setup

Use the 'Experiment Setup' screen to build the set of combinatorial reactions you plan to run. Simply select your desired reagent rack layout and associate the different solutions.

Your plan is displayed as a spreadsheet that summarises all the reaction conditions, each of which can be completely different.

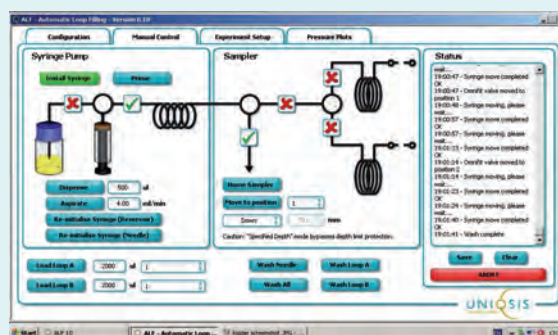
The volumes of reagent solutions are automatically accumulated, and an error message is displayed if any of these inadvertently exceeds the maximum permissible vial volume.



Manual Control

You can control the Sampler and associated syringe pump independently via the Manual Control screen. Simply select the desired flow path by clicking on the check boxes on the schematic. This feature is particularly useful when assembling or calibrating a new hardware configuration.

A number of macros are included to simplify some common operations.

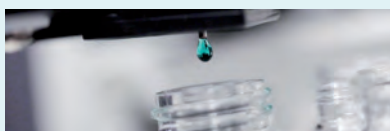


Data Logging

You can view pressure and temperature plots in real time during an experiment by switching to the 'Pressure Plots' screen. This data allows you to quickly survey the performance of the flow reactor and confirm that all is well.

You can subsequently save and download the pressure and temperature profiles for archiving.

In addition, all the control screens have a 'Status' window summarising the individual automated operations performed in a run. These can also be saved as a record of the experiment.



FlowSyn Cold

For low temperature experiments



Perform large scale continuous experiments between -70°C and +150°C

Run multiple low temperature experiments automatically*

Integrated gas purge avoids ice formation

Precise temperature control via internal coil module probe

Temperature controlled mixing blocks

Flow chemistry is an ideal tool for performing fast exothermic chemistries such as metallations. The high surface area/volume ratio of the tubing reactors allows heat generated by a chemical reaction to be rapidly dissipated. However, active cooling may be needed, particularly if there is a requirement to perform a reaction below ambient temperature.

FlowSyn Cold is a stand-alone reactor module which, when coupled with FlowSyn and a recirculating chiller, allows you to perform reactions between -70°C and +150°C (the temperature range will be determined by the chiller).

FlowSyn Cold works with the standard FlowSyn coil reactors from 2 ml to 20 ml volume, allowing for seamless scale up.

For temperature controlled mixing we recommend pairing with the mixer block holder which is also temperature controlled.



Reactions are clearly visible with PFA or PTFE reactors when a nitrogen line is connected to the purging inlet to prevent condensation and ice formation.

Chiller control

The FlowSyn in-built interface can be used to communicate with an external recirculating chiller such as the Huber Tango, Unistat® or Petite Fleur. A temperature probe located inside the FlowSyn Cold module ensures that accurate and uniform temperatures are maintained over the course of the reaction. When using FlowSyn Multi-X, multiple reactions at varying temperatures can be performed automatically.



FlowSyn Cold heats too!

Using a heating recirculator and suitable thermal fluid, FlowSyn Cold can be heated to +150°C, making it ideal for performing multi-step reactions where two temperature zones are required.

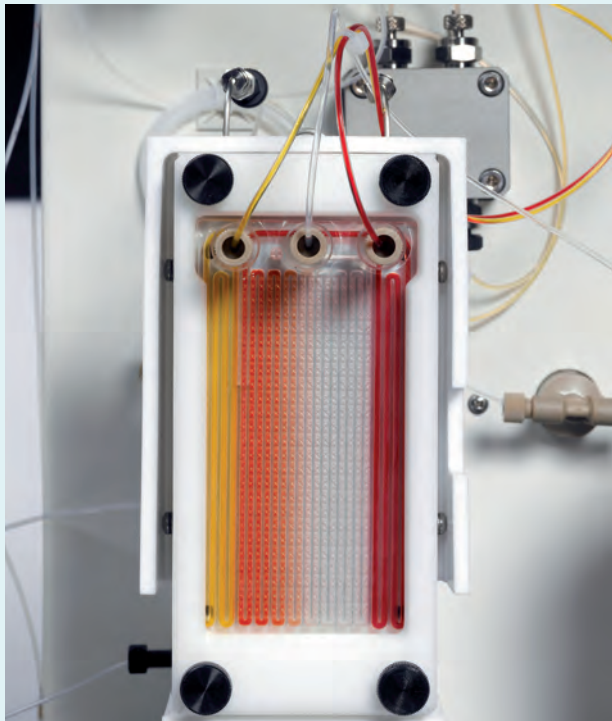
Can I do multiple step chemistries?

Yes – up to 3 temperature zones and 3 reagent inputs are available.

* Requires FlowSyn Multi-X and external chiller such as Huber Tango, Unistat® or Petite Fleur

Accessories: Mixer blocks

For efficient mixing



Fast, turbulent mixing in 1 mm id channels

Vital for temperature control of rapid exothermic reactions

Manufactured from chemically inert borosilicate glass

Simple connections – easy to use



To achieve high reproducibility and facilitate scale up, it is important to control both mixing and temperature, particularly for highly exothermic or fast mixing-dependent reactions.

On a small scale, the narrow channels of the FlowSyn system provide good control of mixing by diffusion, and in these cases the standard mixer is adequate.

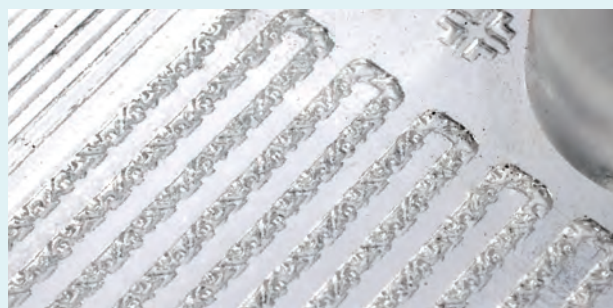
For higher throughput applications or where diffusion is slow, Uniqsis has designed a range of ingenious glass static mixer blocks (also known as 'chips') to provide efficient turbulent mixing throughout the block.

Precision machined from glass and chemically inert, these blocks incorporate narrow channels with active mixing geometries that promote both diffusional and turbulent mixing, as well as functioning as very efficient heat exchangers. A typical mixer block has a 2 ml total volume, with two inlets and one outlet. The 1 mm id channels are wider than most glass 'chips' to minimise blockages.

Mixer blocks can be attached to the FlowSyn column module or to FlowSyn Cold. Both positions can be heated and cooled. Reagents are tempered prior to mixing.

Applications

- Fast, exothermic reactions
- Precise temperature controlled mixing
- Pre-mix for high flow rate (scale up) experiments
- Small scale reaction optimisation
- Bi-phasic reaction / quench



Channels are designed and precision machined to promote turbulent mixing and minimise blockages

What pressure and temperature can the mixer block withstand?

Each individual block is pressure tested to 40 bar and can be used at -70°C to +150°C.

Accessories: Coil reactors

For homogeneous reactions



Widest range of coil reactors for mg to kg reactions

Excellent reaction visibility in perfluoropolymer coil reactors

Specifically designed for fast heat up and accurate temperature control

Change coils in seconds with our patented reactor design

Easily re-wind the tubing in the event of a blockage

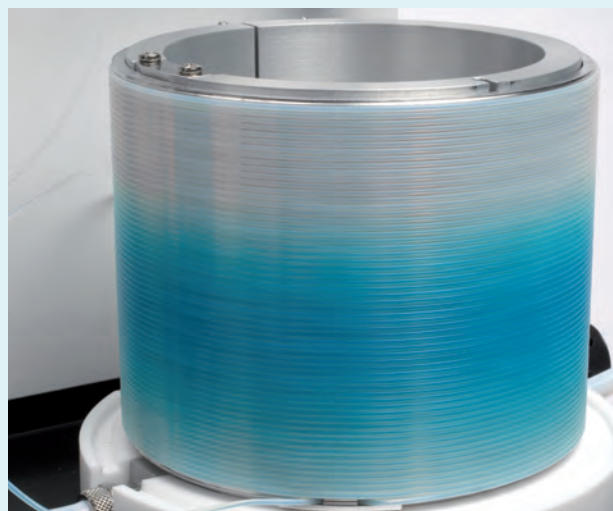
FlowSyn coil reactors consist of 1mm id tubing wound around an aluminium 'mandrel'. They have been designed to allow you to rapidly switch between different sizes and materials for different reactions, making FlowSyn an ideal research tool.

Coil reactors heat up rapidly and retain a uniform temperature throughout the whole reaction, guaranteeing reproducibility of reactions.

Smaller volume coils can be used for small scale reactions, allowing the minimal amount of material to be used.

Larger scale reactors are suitable for scale up experiments or when a longer residence time is required.

Reaction size is not limited to coil volume!



Scale up

Maximising throughput (g/hr) is of key importance for scale up. Large scale coils (identified with * in table) have 1.6mm id channels to increase overall volume. To ensure optimum mixing and heating performance, we recommend using a mixer block to pre-heat and pre-mix reagents.

Can the coils be used for sub-ambient reactions?

Yes – All coils can be used with FlowSyn Cold to -70°C.

	PTFE	PFA	Stainless Steel	Hastelloy®
Size/ ml	25*	2, 5, 14	2.5, 5, 10, 20, 40*	1.4, 2.9, 5.8, 11.6
Pmax /psi	200	200	1400	1400
Tmax /°C	+150	+150	+260	+260
Chemical Resistance	Excellent	Excellent	Very Good	Excellent

Accessories: Column reactors

For heterogeneous reactions



Adjustable column for varying reaction scale

Pack your own reagents, catalysts and scavengers

For reactions or purification up to +150°C and 600 psi

Using solid supported reagents, catalysts and scavengers in a flow reactor offers significant benefits.

- Convenient for 'Catch and release' reaction protocols
- Scavengers used for in-line purification
- Using immobilised reagents and catalysts can often avoid the need for subsequent product purification.

Uniqsis column heater will accept 10 mm id x 100 mm OMNIFIT® glass columns with enhanced PEEK adjustable end fittings. The column length can be easily adjusted to allow for varying amounts of material.

6.6 mm id columns can also be used with column adapter inserts.

Accessories: External pump

For additional reagent channel



3rd channel controlled by FlowSyn interface

Use for multi-component or multi-2 step reactions (A + B + C reactions)

FlowSyn has two pumping channels as standard. When more than two reagents are used, non-reactive starting materials can be pre-mixed. However, if three separate inlets are required, an external pump offers this flexibility. The pump is simply plumbed in-line: either at the mixer, or further down-stream for a quench/2 step reaction. The pump is automatically recognised and can be controlled by the FlowSyn.

FlowSyn™ Specification

Component	Operating specification
2 x High pressure pumps	<ul style="list-style-type: none"> • Combined flow 0.01 to 20.0 ml/min • Wetted materials Hastelloy®, ceramic, sapphire and ruby (limited to 1400 psi) • All Hastelloy® pump heads available as custom option • Third pump available as an option – controlled from the FlowSyn
2 x Pump priming valves	<ul style="list-style-type: none"> • Enables easy priming of pumps, available in PEEK, glass filled PTFE, stainless steel or Hastelloy®. Each port holds a back pressure valve and transducer
2 x Loop injection valves	<ul style="list-style-type: none"> • Electrically operated high pressure, chemically inert injection valve with stainless steel stator and perfluoropolymer rotor seal • Top loading syringe port • Sample loops are available in PTFE, PFA, stainless steel and Hastelloy® between 1 ml and 20 ml
Pressure monitoring system	<ul style="list-style-type: none"> • 3 pressure transducers to monitor individual pump performance and system reaction pressure; an internal algorithm detects bubbles, leaks or system blockages
Mixers	<ul style="list-style-type: none"> • An 'arrowhead' mixer is included as standard, available in PTFE, stainless steel or Hastelloy®. Other borosilicate glass static mixer/ reactor chips are available in 2ml
Coil heating module	<ul style="list-style-type: none"> • Ambient to +260°C. Over temperature protection cut-out
Column and static chip heating module	<ul style="list-style-type: none"> • Maximum temperature +150°C. Sub-ambient temperatures with external chiller. Holds 10 mm id columns • The column module is easily removed to hold the static mixer/reactor chip • Integral heat exchanger for pre or post reaction heating and cooling
Back pressure regulators	<ul style="list-style-type: none"> • Cartridges available up to 1000 psi • PEEK wetted parts as standard. Also available in stainless steel, PTFE and Hastelloy®
Graphical User Interface	<ul style="list-style-type: none"> • High resolution TFT display and touch panel keypad
Dimensions	<ul style="list-style-type: none"> • 360 mm (width) x 540 mm (depth) x 480 mm (height)
Weight	<ul style="list-style-type: none"> • 32 kg unpacked
Power supply	<ul style="list-style-type: none"> • 100 V to 240 V 50/60Hz max current
Compatibility	<ul style="list-style-type: none"> • FlowSyn is compatible with FlowSyn Multi-X, FlowSyn Auto-LF and FlowSyn Cold. For additional information, please contact Uniqsis

Safety

The FlowSyn™ meets the requirement of the International Standard IEC 61010-1, safety for electrical equipment for measurement, control and laboratory use and IEC 61010-2-010 requirement for laboratory equipment for the heating of chemicals and materials.

CE mark

The FlowSyn equipment bears a CE mark to indicate that it meets the requirements of all applicable European directives.

Compliance with the low voltage directive is demonstrated by meeting EN 61010 and compliance with EMC directives by meeting EN 61326-1:EMC requirements for electrical equipment. The FlowSyn meets the EN61236-1 Class A and as such the equipment is suitable for use in establishments other than domestic and those sharing their mains supply with domestic premises.

The EMC tests results were carried out by a registered external test house. We hold a full technical file of the results.

Quality

The equipment is built under and complies with the requirements of BS EN ISO 9001:2000.

It is Uniqsis policy to ensure that products are fit for their intended purpose, perform reliably and are backed by fast and efficient customer service.

Warranty

Uniqsis offers 12 months warranty from date of installation covering materials and workmanship.