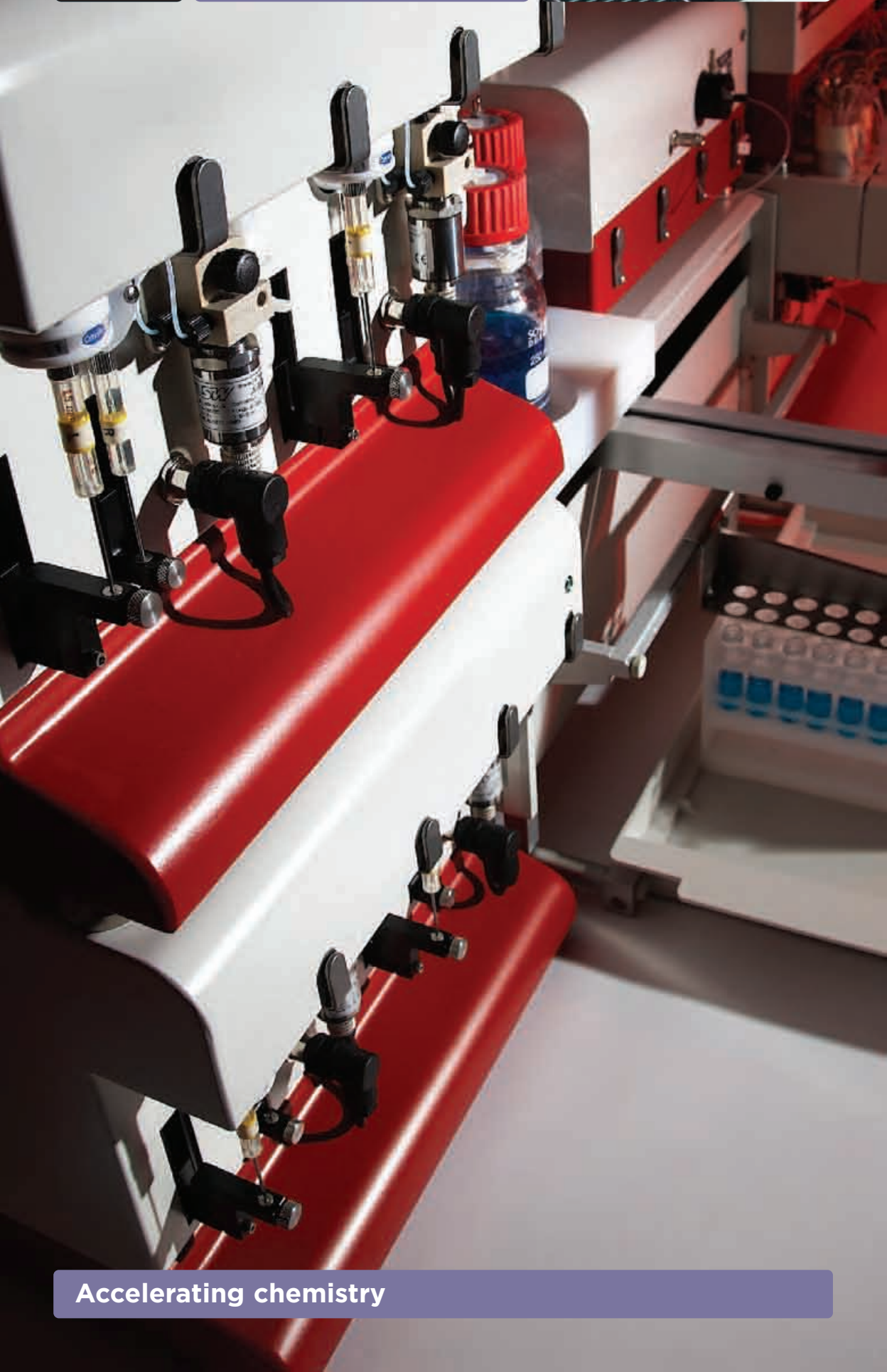




syrris

africa

automated
flow chemistry



Accelerating chemistry

What is Africa?

Africa is a fully automated, flexible and easy-to-use microreactor system. The Africa system allows R&D chemists working in discovery and process development to accelerate compound synthesis and reaction optimization.

Africa benefits

- **Walk away synthesis:** Fully automated hardware is controlled by the Africa software to enable unattended runs. Reagents are injected and products are collected automatically.
- **Faster reactions:** Increase reaction rates over 100 fold by superheating reactions significantly above reflux e.g. dichloromethane to 100°C, acetonitrile to 150°C and water to 170°C.
- **Cleaner reactions:** Reduced impurities via excellent, reproducible reaction control and optional use of solid phase reagents/catalysts/scavengers.
- **Inline aqueous work-up:** The Flow Liquid Liquid Extraction Module (FLLEX) enables two immiscible phases to be mixed and separated in flow, immediately following the reaction.
- **Online analysis:** A sample of reaction mixture can be taken, diluted and analyzed by HPLC in an entirely automated fashion.
- **Scale-up:** Production rates up to kg overnight.
- **Rapid development:** Reaction time, temperature and equivalents can be rapidly varied using mg of substrate.
- **Reactions not possible with batch synthesis:** Extremely quick reaction times, reagent additions, temperature changes and quenches are possible.
- **Automated blockage protection:** Pressure sensors continually monitor every flow channel.
- **Wide temperature range:** Heat reactions up to 300°C or cool down to 0°C.
- **Chemically resistant:** Glass and PTFE/fluoropolymer wetted parts allow the widest range of chemistry possible.
- **Customisable:** Systems are made up of functional modules, allowing each system to accurately match the need of the application.
- **Safer reactions:** Only small amounts of material react at any time, minimising exotherms and the quantity of any hazardous intermediates.



Top: The FLLEX (Flow Liquid Liquid EXtraction) module allows inline aqueous work-up.

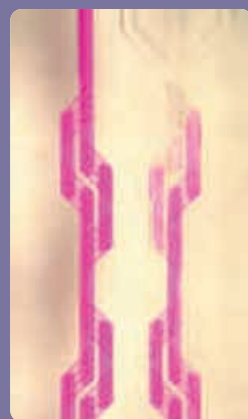
Far left: The Reagent Injection Module can access 100s of compounds and inject them into the microreactor.

Left: The Heater Cooler Module can heat microreactors up to 300°C or cool down to 0°C.

Applications

Africa has the following applications in discovery and process chemistry:

- Reaction optimization
- Library synthesis
- Preparative synthesis up to kg overnight
- Automated work-up
- Transfer of batch experiments to flow
- Process screening
- Reaction development
- Solid phase flow chemistry
- Flow process design
- Hazards chemistry



Other applications include:

- Forced degradation
- Nanoparticle synthesis
- Virus inactivation
- ADME - LogD analysis
- Kinetic studies

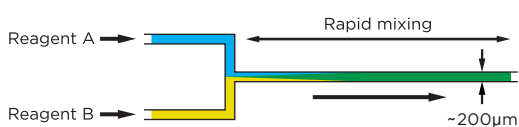
Left: Africa's automation allows unattended operation of hundreds of experiments.

Above: The Africa micromixer offers total mixing in less than four milliseconds.

Flow chemistry (sometimes referred to as plugflow, microchemistry, or continuous flow chemistry) offers exciting opportunities to integrate traditionally separate processes and increase the pace of discovery and development.

Mixing by diffusion

In a batch reactor (e.g. a round bottom flask), reagents mix by turbulent flow - a chaotic, non-reproducible flow regime. In Africa microreactors, flow is laminar, and reagents mix by diffusion across the 200 μ m wide channel. The time taken to mix in this way is in the order of seconds. Laminar flow offers high quality, reproducible mixing.



Easy Pressurization

Using the Africa Pressurization Module it is safe and easy to apply elevated pressure to the whole flow channel. Reactions may be heated to well above the boiling point of the solvent, increasing reaction rates and reducing reaction time.

Africa flow chemistry examples

Homogeneous and heterogeneous catalysis:

Suzuki, Heck, Grubbs metathesis

Multicomponent reactions:

Passerini 3CR, Biginelli 3CR, Ugi 4CR

Deprotection chemistry:

BOC, MOM, methyl ester

Ring formations:

Benzimidazole, Diels Alder, 1,3,4 Oxadiazole, Fischer indole, 1,3 Thioamidazole, 1,2,3 Triazole

Oxidations and reductions:

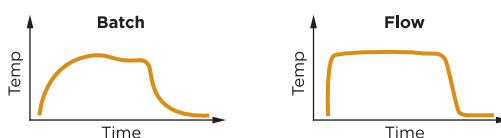
Borohydride, Borane, Reductive amination, Dess Martin

General syntheses:

Aldol, Biphasic Schotten-Baumann, Amide couplings, Elimination, Esterification, Wittig, SNAr, SN1, Mitsunobu

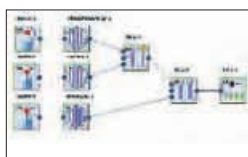
High surface area to volume ratio

The surface area to volume ratio of the reaction mixture in a flow reactor is 1000s of times greater than a flask. Thus heat can be transferred to or from the reaction mixture much more rapidly than in a batch reactor. A constant temperature can be maintained for exo or endothermic reactions improving consistency and yield.

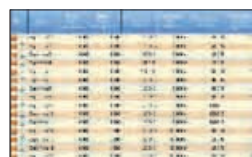


Integration of chemical processes

Traditionally separate functions such as synthesis, work-up and analysis are integrated into a compact, continuous process - saving space, reducing handover delays, and increasing the speed of drug discovery and development.



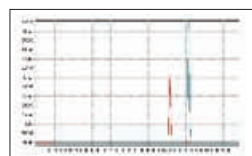
1. Define the fluidics



2. Enter reaction conditions



3. Run experiment



4. View HPLC data



Africa software

The Africa software automatically controls each module and all the timings related to injection, sampling and collection. Only 'chemist familiar' terms, e.g. concentrations, equivalents, volumes and times need to be entered rather than flow rates. Graphs can be plotted real time and exported to .csv files with experimental reports. When using the AFRICA HPLC modules, chromatograms can be displayed, integrated and tabulated.

Key applications

Africa is the most sophisticated and flexible microreactor system available. Reaction optimization, library synthesis or preparative synthesis can be performed with work-up and analysis in an entirely automated fashion.

Rapid reaction optimization

Africa can automatically vary reaction time, temperature, reagents and equivalents. Quantitative analysis of every reaction by HPLC gives integrated data with minimal effort.



Samples experiencing different reaction conditions move through the flow reactor.

Advanced library synthesis

The Reagent Injection and Product Collection Modules enable the use of hazardous reactions or reagents, superheated reactions, multi-step reactions, online aqueous work-up, online analysis and custom reaction conditions for certain reagents/substrates in library format.



Different compounds in a library flow through the reactor, separated by solvent.

Synthesis

Africa tube reactors synthesize g-kg quantities of product overnight whilst maintaining the benefits of flow e.g. reproducible, low quantities of hazardous intermediates, rapid removal of heat from exothermic reactions and fast reaction rates due to superheating.



Utilize the benefits of flow chemistry to continuously synthesize g-kg overnight.

LogP/LogD analysis

FLLEX (Flow Liquid Liquid Extraction) technology, coupled with on line analysis can be used to generate automated LogP/LogD data. Studies performed in collaboration with a major pharmaceutical have demonstrated more accurate results than their contract shake flask method.

Temperature verses time studies

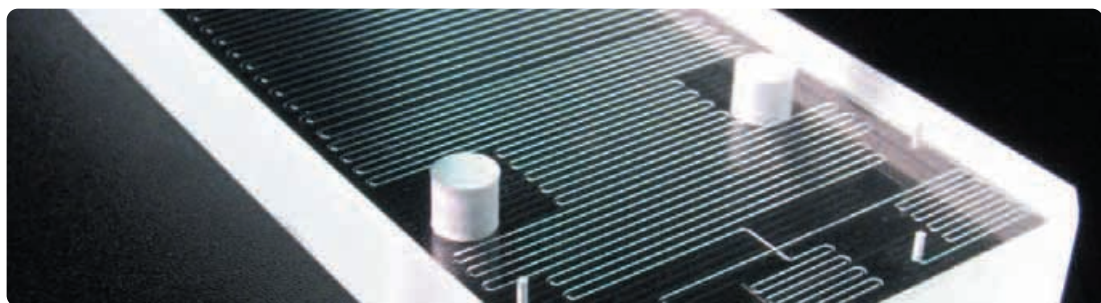
Africa offers rapid, accurate sample heating (to within 0.1°C) and can access temperatures only available in pressurized systems. Conditions not possible in batch such as accurately heating a sample for only a few seconds are easily created.

Example 1. Forced degradation

Africa can accelerate decomposition processes beyond their natural rate to investigate the kinetics of the process. This can predict shelf-life in a fraction of the time and in an automated fashion.

Example 2. Virus inactivation

The Africa system has successfully demonstrated heat inactivation of a virus in a mammalian cell culture process stream used in the manufacture of therapeutic proteins and antibodies.



Above: Glass micro reactors offer control of mixing and reaction temperature with high chemical resistance.

Far left: The Sampler and Dilutor allows a sample of the reaction to be automatically diluted and analyzed by HPLC.

Left: Africa's high precision syringe pumps are chemically resistant.

The Africa system



The full Africa system
Africa is the most sophisticated and flexible microreactor system available. Reaction optimization, library synthesis or preparative synthesis can be performed with work-up and analysis in an automated fashion.

Africa modules

Africa systems	Part number	B	S	SC	SH	SA	SF	SFC	SAH	SAHF
Reagent pump	2100140	●	2	2	2	2	2	2	2	2
Reagent store	2100150	●	●	●	○	●	●	●	○	○
Reagent injection	2101431	○	○	○	●	○	○	○	●	●
62.5µl chip 2 input	2100141	2	2	2	2	2	2	2	2	2
62.5µl chip 3 input	2100142	2	2	2	2	2	2	2	2	2
250µl chip 2 input	2100143	2	2	2	2	2	2	2	2	2
250µl chip 3 input	2100144	2	2	2	2	2	2	2	2	2
1000µl chip 2 input	2100145	2	2	2	2	2	2	2	2	2
1000µl chip 3 input	2100146	2	2	2	2	2	2	2	2	2
Micromixer chip	2101411	○	○	○	○	○	○	○	○	○
4ml tube reactor	2100632	○	○	○	○	○	○	○	○	○
16ml tube reactor	2100633	○	○	○	○	○	○	○	○	○
Chip holder	2100147	2	2	2	2	2	2	2	2	2
Heater/cooler	2100090	●	●	●	●	●	●	●	●	●
Tube reactor heater	2100640	○	○	○	○	○	○	○	○	○
Pressurisation module	2100701	●	●	●	●	●	●	●	●	●
FLLEX	2100700	○	○	○	○	○	●	●	○	●
Sample and dilutor	2100389	○	○	○	○	●	○	○	●	●
HPLC pump	2100140	○	○	○	○	●	○	○	●	●
UV detector	2100391	○	○	○	○	●	○	○	●	●
Product collection	2100806	○	○	●	●	○	○	●	●	●
PC and software	2100724	●	●	●	●	●	●	●	●	●

Standard ● Option ○



Reagent pump

Each pump module has two continuous high precision flow channels with a flow rate range of 2.5–2500µl/min.



Reagent injection

This module aspirates reagent solutions from a robot deck and pre-pressurizes them before automatically injecting them into the reactor.



Micro and tube reactors

Glass microreactors (62.5µl, 250µl and 1ml) and PTFE tube reactors (4ml and 16ml) are available for reaction optimization of mg and scale up synthesis of g–kg.



Heater cooler

Up to two glass micro-reactors are held in the heater cooler, each with a customizable temperature range of 0–150°C or 40–300°C.



Pressurisation

This module allows pressurization of the reactor to at least 7 bar (105bar) enabling superheating to 60–120°C above atmospheric reflux temperature.



FLLEX

Flow Liquid-Liquid Extraction uses advanced membrane separation technology to enable aqueous work-up of any reaction with separation.



Sampler and Dilutor with HPLC

The Sampler and Dilutor takes a 5µl sample from the flowing reaction stream, dilutes it and loads it into the HPLC.



Product collection

This module allows reactions to be automatically collected in separate tubes, vials etc. and unwanted solvent flow to be diverted to waste.

Distributor



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