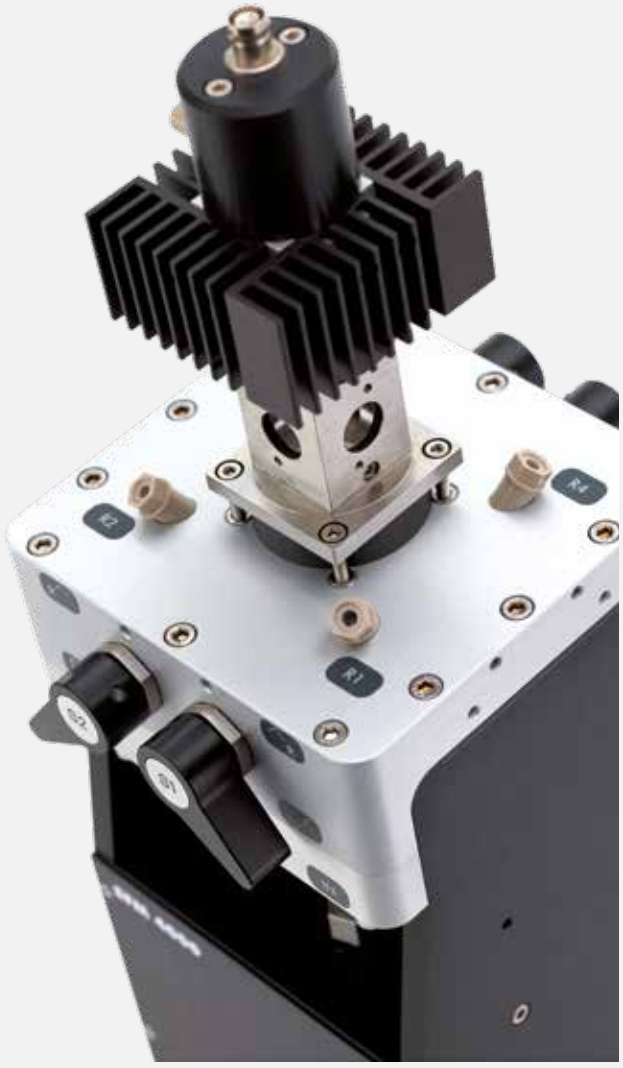
STOPPED FLOW

BioLogic

SFM Series.

Rapid kinetics and spectroscopy



SFM-2000/3000/4000
Unparalleled performance and modularity.

The SFM-2000/3000/4000 stopped-flow systems are the result of over 30 years of R&D and constant innovation

Timeline: From strength to strength.
The evolution of the SFM Series

Introduced to the market in 1987, the SFM-3 was the world's first three syringe stopped-flow system incorporating independent stepping motor technology, Berger Ball mixers and an electro-valve hard-stop.

In 1992 the four syringe **SFM-4** brought triple mixing capability to the rapid kinetics field, increasing the range of applications available.

1999 was a milestone year with the introduction of the two syringe **SFM-20**, the **SFM-300** and **SFM-400**. The **SFM-300**/**400** reduced the size of instrument, dead volume, sample consumption, and dead time by nearly a factor of two. The **SFM-300** also brought dead time down to 200 µs based on published results, making it the benchmark system for ultra rapid reactions.

2011 marked the launch of the third generation **SFM-2000**/**3000**/**4000** systems. With a common drive chassis, this generation offers simpler upgrades to three or four syringes, smaller dead volume, and improved overall performance.

SFM 2000/3000/4000

UNIQUE FEATURES

- Independent stepping motor control for each syringe
- Automatic concentration dependent studies
- Fully programmable mixing ratios with Bio-Kine interface
- Ratios can be changed without syringe or hardware changes
- µl precision - No pressure artifacts
- Modularity from SFM-2000 to SFM-3000 and SFM-4000
- Quench-flow capabilities using optional quench valve

Outstanding performance and unsurpassed flexibility make the **SFM-2000/3000/4000** family the benchmark rapid kinetics mixers for today's laboratory.

All BioLogic **SFM mixers use independent stepping motor technology**, for full independent control of volume, flow rate and drive power in each syringe.
Precise control allows mixing ratios from 1:1 to 1:100 to be achieved quickly and repeatedly.
A series of shots at various concentrations can be programmed and run quickly without refilling or changing syringes. BioLogic's stepping motor drive technology has proven itself to be the best in it's field, in terms of perfomance and reliability, for over thirty years. Flexible ratio control, precision, accuracy, speed and the ability to handle extreme viscosity ranges are well known features of BioLogic systems.

Advanced Berger-Ball technology mixers are used to provide the best turbulent mixing over the widest range of flow, viscosity and temperature conditions. Berger-Ball technology offers outstanding consistency and repeatability over T-style mixers.

The SFM stopped-flow family is is the most versatile system available. **The instruments are easily adaptable and expandable to a wide variety of rapid mixing techniques and applications**. A single SFM can be switched from optical stopped-flow, to chemical quench flow, to freeze quench, to automatic titration, to cryo operation, to a beam-line, all in minutes, with off-the-shelf options.

All of these accessories, and more, are user changeable enabling you to adapt the **SFM-2000/3000/4000** to your research needs in the lab, without buying a new system.

GENERAL SPECIFICATIONS

- SFM-2000: single mixing
- SFM-3000: single and double mixing
- SFM-4000: single, double and triple mixing
- Independent syringe control of volume
- Independent control of flow rate
- 200 µs dead time
- Mixing ratio 1:1 to 1:100
- Low dead volume 88 µl
- Sample economy
- Automated concentration dependent studies
- Compatible with: MOS-LED, MOS-200/200M, MOS-500, MOS-450/AF-CD, MOS-DA, MCS-200
  High level of modularity with external (non-BioLogic) instruments

Key Benefits

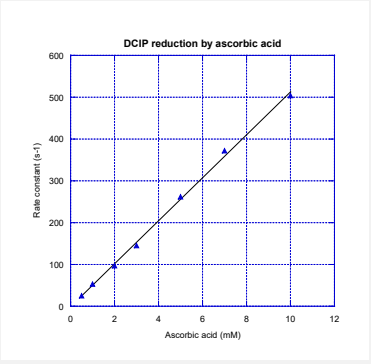
Mixing performance

The precision of sample delivery with stepping motors is outstanding.

The BioLogic design delivers µl precision and accuracy at all flow rates. Turbulent mixing is achieved over a wide viscosity and mixing ratio range, which makes the SFM the perfect instrument for all rapid kinetics conditions.

The reduction of DCIP by ascorbic acid illustrates SFM mixing consistency and speed. A standard configuration with three 10 ml syringes is used, with buffer in syringe 1, ascorbic acid in syringe 2, and DCIP in syringe 3. Ascorbic acid concentration is varied by changing the mixing ratio from 19:1:20 to 0:20:20 in Bio-kine software.

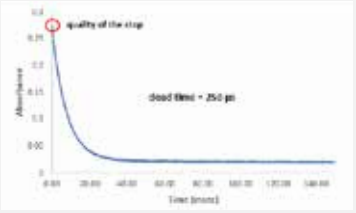
As the syringes do not need to be reloaded between shots, a full series of experiments can be performed in less than a minute.



Dead time performance and stop quality

With independent stepping motors driving the syringes, the user has full control of flow velocity. The accuracy of flow rate delivery can easily be checked by measuring faster dead time with increasing flow rates.

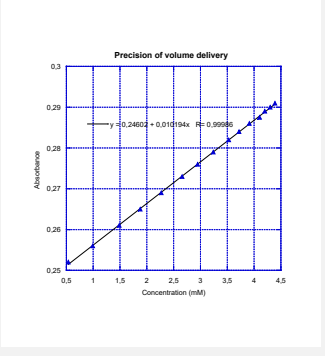
Dead times to 200 µs can be obtained with the micro-cuvette option. Measurement of low dead time is enhanced with the responsive hard-stop electro-valve and a pre-trigger. Flow in the cuvette is stopped instantly without the pressure artifacts common observed with systems using stop syringes. A pre-trigger is user selectable to check that the mixing reaches a stationary state before the flow stops.



Volume performance

Dead volumes have been reduced by a factor of two with BioLogic's latest SFM mixers. All internal volumes have been reduced to minimize priming requirements. Sub-micro-liter precision stepping motors maximize the precision of volume delivery.

The plot illustrates the linear performance of an absorbance check in titration mode by performing consecutive injections of 10 µl, 5 µl, and 2 µl steps (see figure on the right).



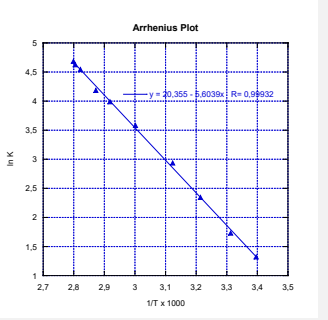
Change your cuvette in 30 seconds!

A wide choice of cuvettes and the ability to change them quickly is essential in rapid kinetics experiments. The SFM-2000/3000/4000 models deliver both these important capabilities. A choice of 10 cuvettes is available with light path from 0.75 mm to 10 mm, and volumes from 3 µl to 50 µl (cuvettes with dual light path are available: for example 1 cm and 1 mm). Fluorescence optimized cuvettes with a short light path (0.8 mm) are available to minimize inner filter effects.

The SFM has been designed so that the user can change the cuvette in seconds, without dismantling the system or draining the temperature circuit. SFM series stopped-flows have been designed to work seamlessly with your experiment.

You don't need to change the configuration of your experiment to suit your instrument. The SFM series works **with** your existing setup.

Precise temperature control



All driving syringes, delay lines, mixers and mixing chambers can be temperature controlled by connecting a water bath circulator.
The same circuit is used for the entire cooling path to prevent a temperature gradient observed when different circuits are used for syringes and cuvettes.
Options for individual syringe temperature control or individual mixing chamber temperature control are available if multiple control temperatures are needed.

An optional temperature probe is available for installation on the observation cuvette; it provides a temperature readout in Bio-kine software with a 0.1°C precision.

High-level performance, reliability and modularity

SFM Series instruments have a proven track record of reliability and performance, even after many years of use. We often hear from clients who state that instruments bought years ago still work like new. Routine maintenance can be easily carried out by users themselves, with inexpensive parts.

SFM stopped flows were designed with modularity in mind and can easily be used for both traditional and specialist applications. Easy access to the mixing head makes external coupling possible, for example: laser excitation, flash photolysis or coupling to a streak camera.

For highly specific needs Our R&D team also provides special development services and can customize your instrument. Our expertise includes electronic, optical, software and mechanical engineering.

So, when you invest in an SFM stopped-flow, you invest in an instrument that will withstand the tests of time and the rigors of the laboratory – an instrument that will grow with your needs and help you take your research to the next level.

Please contact your local representative or BioLogic's head office for details.

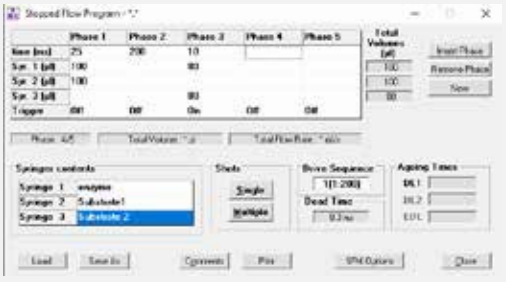
Bio-Kine: Powerful, intuitive software

Single mixing applications

Two levels of operation are provided for mixer control. The first level is designed for rapid and easy experiment design.

The user sets the mixing ratio, the size of the cuvette and the volume of samples. Color coded windows display calculated values and alert the user to out of range conditions. The estimated dead time is automatically displayed, and a pretrigger is also available to be sure the stationary state is reached accurately.
This interface is ideal for routine mixing designs, occasional users, or students.

Multi mixing applications

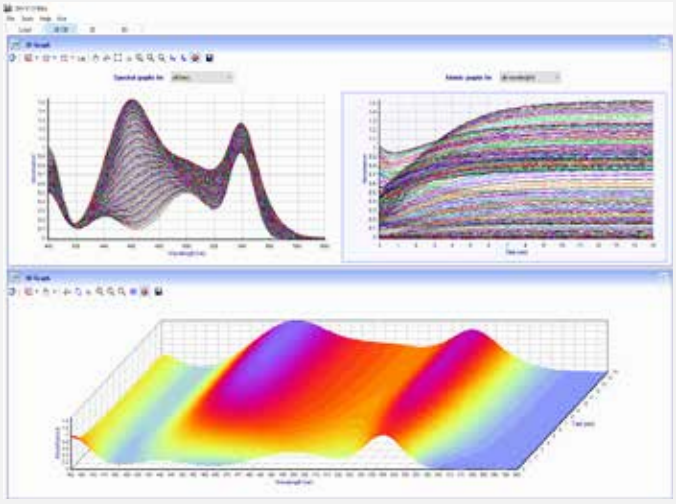


The easy to use interface allows sophisticated and unrestricted instrument programming. This is ideal for multi-step sequences such as double jump experiments. It can also be used to include a pre-washing phase and for coupling with external devices, (synchrotron lines for example).

In a double mixing application, samples 1 and 2 are mixed in phase 1 before incubation in phase 2. Then, it is mixed with a third reactant in phase 3, and the second kinetics is followed optically.

Estimated dead time and ageing time are automatically calculated by the software. This mode is also suitable for chemical quench, freeze quench and optical quench modes. In these applications ageing time is also automatically calculated according to user's parameters.

Global Fitting / SVD analysis



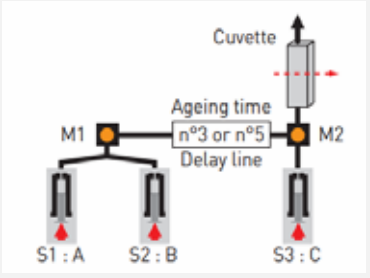
BioLogic provides SVD (Single Value Decomposition) analysis tools with all new mixers. This feature is ideal to analyze data generated by diode array detectors, and multi-wavelength data generated by MOS-200/M and MOS-500.

It includes:

- Automatic estimation of number of vectors,
- Fast SVD analysis,
- Global fitting with residual analysis (2D and 3D),
- Levenberg-Marquardt and Simplex fit algorithms,
- Large selection of kinetics models,
- Data import from clipboard or text files.

SAVE SAMPLES, TIME and MONEY.
Independent stepping motors offer endless possibilities for automation.

Automatic variation of ageing time

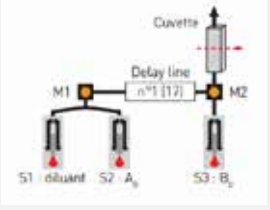


This protocol was designed to automate double jump experiments, such as folding/unfolding experiments. Samples A and B are mixed and then aged according to pre-defined times. After incubation the aged solution is mixed with sample C so the second kinetics can be observed optically.

The user defines the mixing ratios for the 3 reactants, then enters the ageing times he wants to reach.

Bio-Kine automatically calculates the optimum sequence based on user parameters, (cuvette, mixer, flow rate), and displays the corresponding dead time. Each ageing step can be repeated for averaging. This mode is also available for external detectors.

Automatic concentration dependence studies



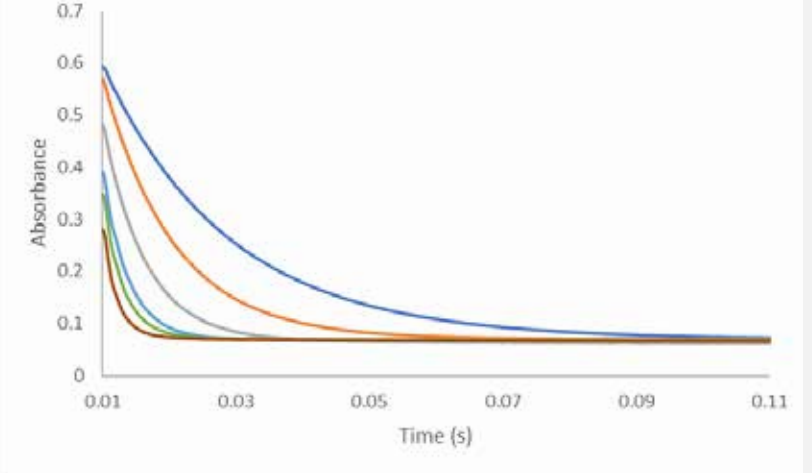
This protocol studies the reaction A+B by varying the concentration of A at each shot while keeping B constant. The first mixer is used to set the concentration of A by mixing A with buffer.
Then A is mixed with B in the second mixer and the reaction is followed optically. The dead time is identical for all concentration steps.

The user enters the mixing ratio between A and B at each mixing step, and the final concentration of A required. Bio-Kine automatically calculates the optimum volume to push from each syringe.

Mixing ratios can be varied
from 1:1 to 1:20 using the same configuration.

Each concentration step can be repeated for averaging, and concentrations at each step are automatically saved with data to facilitate data analysis.

This mode is also available when using an external detector. The method is ideal for rapidly collecting data for Chevron plots.

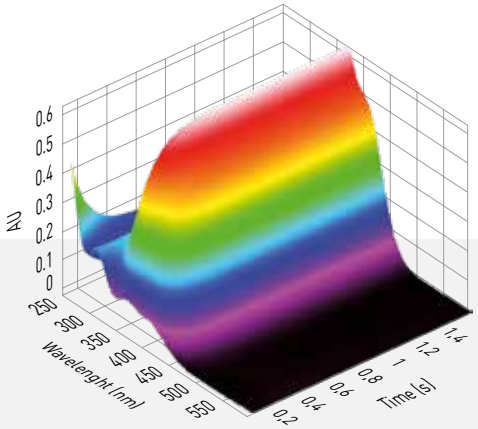


Optical coupling

MOS-200/200M

Absorbance, fluorescence, chemiluminescence, and 90° light scattering

The MOS-200/200M are perfect for all basic rapid kinetics studies, with data acquisition down to 10 μs resolution. The systems include a manual or motorized monochromator, dual light source, and high sensitivity photomultiplier (PMT).
Multiple detector and T-format anisotropy options are available. The motorized model offers full automation for multiwavelength studies.



MOS-DA

Diode array spectrometer

The fastest Diode Array spectrometers on the market for UV, visible and near IR, with speed down to 0.4 ms/spectra. The instrument includes a high-quality 3D software interface. SVD analysis is also available through BioLogic's proprietary software package.

MCS-200

Conductivity detector

MCS-200 is a detector used to measure conductivity change. Conductivity detection is ideally suited to inorganic reduction/oxidation reaction, proton exchange, metal ligand binding and micelle formation from surfactants. Conductivity can bring complementary information to optical measurements. The MCS-200 includes a special cuvette with embedded gold electrodes in the cuvette walls. Conductivity measurements are based on impedance spectroscopy and the MCS can also be operated as a standard potentiostat.

MOS-500

Absorbance, fluorescence, circular dichroism, ORD, LD, fluorescence anisotropy and 90° light scattering

MOS-500 uses an innovative and patented three stage wavelength selection system making it the most advanced kinetics and steady state spectrometer on the market. MOS-500 includes a double light source Xe/Xe(Hg). No purging of optics is needed in kinetics mode, and there is no need to handle lamps for operation.
Time resolution to 10 μs. Bio-Kine control software allows full automation and multi-wavelength experiments with automatic spectral reconstruction.

Applications

Biochemistry

Protein folding/unfolding

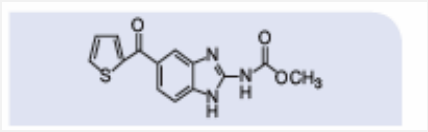
Independent syringes and completely variable mixing ratios make the SFM-2000/3000/4000 the ideal system for studying protein folding. These studies often involve mixing solutions of up to 2000 cp viscosity, which is easily carried out with our specially designed microvolume Berger Ball mixers.

For reactions longer than 10-15 seconds, a unique high density mixer is available to minimize convection artifacts. The flexibility of mixing ratios and differing sample viscosities offered by the SFM give the user unmatched control of experiment design and sample economy.

Water & ion transport in vesicles

A common stopped-flow application is the fast tracking of transient kinetics of water or solute transport, across the membranes of small, (10-500 nm scale), pressure sensitive vesicles. With the SFM's precise control of total flow rate, and a synchronized electro-valve to stop sample flow, sheer forces and over pressure artifacts are minimized. This combination minimizes changes in vesicle integrity.

The SFM coupled to one of our spectrometers is an ideal system for 90° light scattering and fluorescence which is often used to follow such reactions in blood cells, aquaporins, liposomes, and for water purification applications.

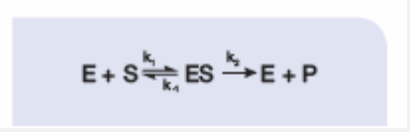


Organic & inorganic chemistry

Structural changes

Understanding reaction mechanisms and characterizing the structure of reaction intermediates are common goals in organic and inorganic chemistry. These reactions often occur in organic solvents, requiring instruments that can maintain design function and performance in an aggressive environment. The SFM-2000/3000/4000 mixer components and optional Kalrez O-ring set easily withstand exposure to solvents such as THF and toluene.

For studies where a reactant is oxygen sensitive, the SFM anaerobic option provides a simple and reliable way to perform an experiment in an oxygen limited environment. A -90°C cryogenic option is available to capture intermediates with very short life times.



Enzyme kinetics

Ligand binding conformational changes

Single and multi-substrate reactions can be followed with stopped flow techniques to study the catalytic mechanism of an enzyme, and to learn about its role in the cell. Mechanisms can be investigated by changing reactant concentrations, and by adding fluorescent dyes to the protein to enable observation of movements during reactions. With independent stepping motors, users can change mixing ratios after each shot without refilling the system, so a series of concentration studies can be performed rapidly. Bio-Kine's analytical tools provide immediate information about the reaction mechanism.

Endless opportunities for applications : micelles, second messenger, drug design, polymerization, and more.

Options

mT-jump

The mT-jump head replaces the standard SFM observation head. mT-jump achieves temperature changes by mixing two solutions of initial temperatures T1 and T2. The final temperature (T3) of the mixture is calculated from the initial temperatures T1 and T2 and the mixing ratio of the two solutions. A T-jump with a dead time of 0.7 ms can be measured.

Reactions can be followed with a ms resolution. A cooling or heating jump of up to 40°C is possible.

It is compatible with all stopped-flow models in all modes of observation such as circular dichroism, fluorescence, absorbance, and fluorescence anisotropy. With this accessory, protein folding and refolding can easily be studied without adding denaturant to the protein!

Titration

The titration head replaces the standard SFM observation cell in seconds. It is designed to accept standard 1 x 1 cm cells, and includes a magnetic stirrer for continuous sample mixing. Temperature is controlled through the stopped-flow circulation loop. Three detection windows are provided for measurements, and a 5.5 mm diameter port is available for external devices such as pH electrodes, nitric oxide electrodes, and temperature probes.

The programmable titrator takes advantage of high precision stepping motors for accurate micro-volume delivery of solutions. Volumes as low as 2 µl can be injected using a 1.9 ml syringe. Concentration steps are user-defined.

Automatic increment functions are available, including a function to change the increment during titration. Bio-Kine automatically tracks solution volumes, and alerts the user to out of range conditions. This prevents an experiment from running out of solution during the sequence.

Customisation

The SFM-2000/3000/4000 observation head was designed to allow easy coupling to external devices. Optional heads and adaptors have been designed for neutron scattering, EPR, large and small angle X-ray, multi-angle light scattering, FT-IR, and conductimetry. Connection options are available for some third party spectrophotometers, fluorimeters, EPR, and other systems. If you have a system and want to connect it to stopped-flow mixer, contact us with the details and we can advise you on what options are available.

Easy interfacing

- Fiber optic accessory
- Single and double light links
- Umbilical connection

Quench-flow

SFM-3000 and SFM-4000 systems can be converted quickly to top performance quench-flow operation by exchanging the stopped-flow observation head for a quench-flow collecting valve.

Ageing times are varied by selecting delay lines. Mixing is made in continuous flow mode, interrupted flow mode, or in BioLogic's unique pulse mode (single mixing applications only).

BioLogic's stepping motor technology controls flow rate precisely from Bio-Kine software. Long calibration procedures to estimate the flow rate are not required. The SFM drive delivers the exact requirements, every time.

Freeze quench

The freeze quench accessory consists of an umbilical connector, a set of ageing loops, a diverting electrovalve, and a dewar with a sample holder.

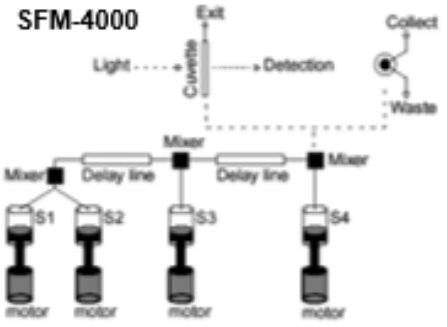
Reactants are loaded in the mixer syringes, then the reaction is initiated by mixing 2 or more solutions. The reaction is aged for a user-defined time inside the calibrated ageing loops. A built-in ejection nozzle at the exit of the ageing loop sprays the aged solution towards the dewar.

Freeze quench techniques are extensively used to study metallic reaction centers in metalloproteins and metalloenzymes. Different sample holder are available for XAFS, EPR, NMR or Mossbauer spectroscopy.

Independent stepping motors remove all limitations of single drive mechanisms, and mixing ratios can be changed freely just as in stopped-flow observation mode. The SFM-4000/Q is the only system in the world with four independent syringes and 3 mixers.

It is a **unique** system for triple mixing applications, such as De/H exchange experiments or radioactive labeling. The user controls two ageing times from the software, a series of experiments can be carried out rapidly.

A large number of academic papers citing our instruments is available online.



SPECIFICATIONS :

Drive mechanism: independent stepping motors

Number of syringes	2 (SFM-2000), 3 (SFM-3000), or 4 (SFM-4000)
Number of stepping motors	1 per syringe
Precision of stepping motors	10.4 nl per microstep
Number of mixers	1 (SFM-2000) 2 (SFM-3000) or 3 (SFM-4000)
Mixer type Berger-Ball	Mixer or optional HDS
Stop mechanism	Electrovalve

Syringes

Syringe material	PEEK
Syringe size	10 ml (6.8 ml, 3.6 ml and 1.9 ml are optional)
Anaerobicity	Anaerobic operation standard

Sample consumption

Priming volume	from 88 µl per syringe
Flow rate range	0.003 to 10 ml/s (per syringe)
Mixing ratio fully variable	From 1:1 to 1:100
Minimum injection volume	10-25 µl depending on syringe size in stopped-flow mode
Minimum injection volume in titration mode	2 µl

Observation head

Number of detection windows	3
Cuvette	Quartz: from 0.75 mm to 1 cm
Optional	Capillary for X-ray measurements
Minimum dead time	0.2 ms using microcuvette (0.8 mm light path), < 0.7 ms using smallest standard cuvette
Material	PEEK, Viton Full solvent compatibility using Kalrez o rings (option)

Note

Bio-Kine software and a USB connected hardware interface are included with the SFM-2000/3000/4000. A PC is required for controlling the SFM system(Windows XP, Vista, 7 or 10 operating systems).

Temperature control

Temperature range	-20°C to +85°C (standard) Down to -90°C using cryo-option Up to 160°C using high temperature umbilical and mixing head
Temperature control	Water bath circulation (optional)
Temperature probe	Optional PT100 allows direct reading of temperature in Bio-Kine

Synchronization with detection

Trigger	Fully programmable; 5V TTL trigger in/out available
Optical coupling	Fiber optics or direct attachment

Compatible detection devices

MOS-LED	Absorbance, fluorescence, dual absorbance
MOS-200/200M	Absorbance, fluorescence, 90° light scattering, T-format anisotropy (optional)
MOS-DA	Diode array, absorbance
MOS-500	Absorbance, fluorescence, 90° light scattering,
MCS-20	Circular dichroism, anisotropy (EMFA) conductivity

General

Dimensions	200 x 197 x 522 mm
Weight	12 kg (SFM-2000), 13 kg (SFM-3000),14 kg (SFM-4000)
Communication	USB
Power	110 V-220 V

Upgrades

Chemical quench-flow
Freeze quench (EPR, Mossbauer, NMR, XAFS)
EPR stopped-flow
Upgrade to SFM-3000 and SFM-4000
XAFS head
Neutron scattering head
Titration
Optical quench

Specifications are subject to change