



BioPhase 8800 system

TAKE

CHARGE

Getting to know the BioPhase 8800 system

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The Power of Precision

Introduction

Since the 1980s, therapeutic proteins such as monoclonal antibodies (mAbs) have been successfully applied in the treatment of cancer, autoimmune diseases and other ailments, delivering relief, remission and extending the lifespan of many patients.¹ Typical of complex proteins, mAbs are susceptible to post-translational modifications (PTMs). In some instances, these PTMs are capable of inducing instability, often the result of charge heterogeneity in the protein. Also common to the manufacture of mAbs are product and process-related impurities, such as clipped products, aggregation and fragmentation. All these factors could potentially affect the protein structure and biological activity.² Assessments of purity and charge heterogeneity are essential to the protein characterization process at different stages of therapeutic protein manufacturing. However, as biopharmaceutical manufacturers increase the number of drug candidates in their development pipelines, analytical characterization of growing sample numbers often becomes a major bottleneck.

The BioPhase 8800 system [Figure 1] represents the next generation of capillary electrophoresis instrumentation from SCIEX.

With the BioPhase 8800 system, scientists engaged in analytical method development involving characterization strategies—such as molecular stability and degradation studies, optimization of storage conditions or investigation of other critical quality attributes—are able to apply routine workflows to an increased number of samples.

The multi-capillary separation environment of the BioPhase 8800 system fosters flexibility and efficiency due to its parallel processing capability, reducing analysis time to days rather than weeks or months.³

This technical note highlights the main hardware features of the BioPhase 8800 system, which empowers the user to perform lengthy characterization workflow studies of hundreds of samples in record time—an activity only possible in a multi-capillary environment.



Figure 1. The BioPhase 8800 system.

Key features

- Multi-capillary system capable of performing up to 8 separations simultaneously, enabling parallel sample analysis
- Integrated optics module enables the use of both UV and LIF detection in a single sequence through automated switching via software controls
- Utilizes ANSI-compliant 96-well plates for samples and reagents, allowing for automated sample and reagent preparation
- Circulating liquid-based cartridge temperature control tightly controls separation temperature



The multi-capillary cartridge

The BioPhase 8800 system cartridge was designed to accommodate 8 capillaries and the heat load generated during a separation. The cartridge (Figure 2) is available fully assembled, eliminating the need for end-user assembly. The cartridge design enables it to efficiently accommodate liquid cooling with an operational temperature range of 20–40° C.

Currently, there are 2 capillary cartridge types available for the BioPhase 8800 system: bare-fused silica for CE sodium dodecyl sulfate (CE-SDS), and neutral coated for capillary isoelectric focusing (cIEF) applications. The total length of the capillaries used in both cartridge types is 30 cm. The effective length is 20 cm, and the inner diameter is 50 µm for both types of cartridges. The capillary windows are supported by an 8-slit aperture, measuring 100 µm width x 3 mm height.

The innovative design of the pre-assembled cartridge is easy to handle and incorporates 8 gold-plated cannula electrodes. Each cannula engages with the high-voltage power supply to deliver voltage for separation. The cannula design allows for concentric positioning of capillaries on the inlet side, enabling efficient interaction with the BioPhase 8800 system 96-well plates. On the outlet side of the cartridge, capillaries are bundled and exit in parallel to the electrode. When inside the cartridge body, the capillaries are immersed in a liquid environment capable of efficient Joule heating dissipation. The cartridges are equipped with a unique chip that tracks serial number, lot number, the total number of runs, date in service, expiration date, manufacturing date and capillary dimensions.

This feature facilitates the electronic record-keeping of the cartridge's usage history.



Figure 2. The BioPhase 8800 system 8-capillary cartridge.

The sample and reagent plates

The 96-well sample and reagent plates used in the BioPhase 8800 system conform with ANSI guidelines, allowing sample and reagent preparation using automated liquid-handling processes. The inlet reagent plate (Figure 3A) has a square well design, facilitating a robust seal around each well, enabling high-pressure rinses and the high-volume capacity necessary for robust electrophoretic separations. The inlet sample plate (Figure 3B) has the traditional round wells with a conical bottom to reduce the minimum volume required for injections. The recommended sample volume required is 100 µL.

The outlet plate (Figure 3C) is the same for both sample and reagent positions. The outlet plate design offers 12 high-capacity wells designed to capture the effluent of 8 capillaries. The overall capacity of each trough is 6 mL. A typical method requires 2.8 mL of buffer (for separation) and water (for capillary dip and protection), as well as 1.5 mL of water for waste.

Plate transport occurs in only 2 axes, minimizing the need for post-installation alignment correction.

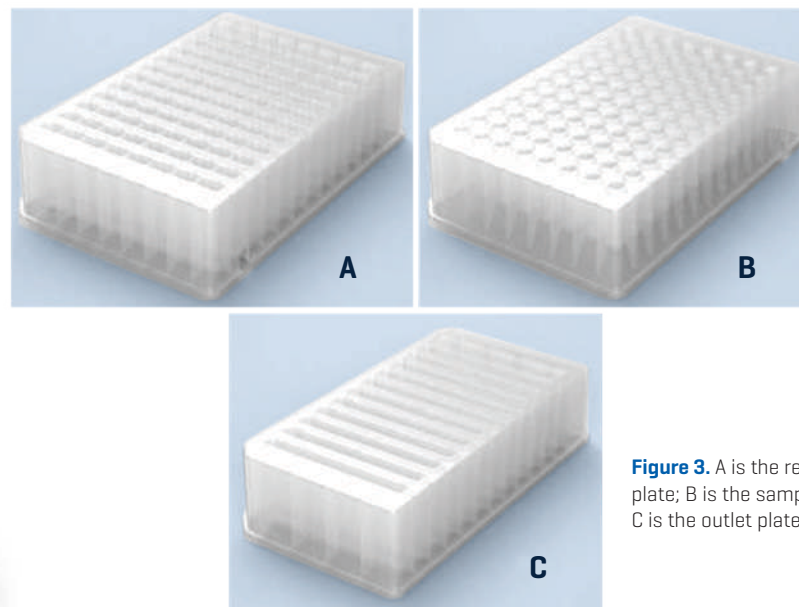


Figure 3. A is the reagent plate; B is the sample plate; C is the outlet plate.

The integrated optical system

The BioPhase 8800 system is equipped with both UV and LIF detection options. UV and LIF detection systems are integrated and method-driven, allowing users to take advantage of both detection modes in the same sequence. For example, it is possible to run labeled and unlabeled adeno-associated viruses (AAVs) in the same sequence², thus, saving time during method development.

Table 1 shows the typical LOQ/LOD for UV and LIF detectors using the CE-SDS application.

Detector type	LOD	LOQ
UV	2.5 µg/mL	5.0 µg/mL
LIF	4.0 ng/mL	10.0 ng/mL

Table 1. LOQ/LOD for UV and LIF detectors using the CE-SDS application.

The BioPhase 8800 system is equipped with 220 and 280 nm transmittance filters coated with reflective optics, allowing for excellent durability and integrity over time. The UV and LIF filter assemblies can be replaced or exchanged through a side access panel in less than 1 minute.

The BioPhase 8800 system uses a step scanning approach to direct the excitation light source to each capillary individually. The selected data rate determines the scanning rate. The data rates available on the UV detector are limited to 1 Hz, 2 Hz, 4 Hz and 8 Hz. The LIF detector is limited to 2 Hz, 4 Hz, 8 Hz and 10 Hz. For best analysis results, it is recommended that the data rate is set so that 16 to 25 data points are collected within the span of the peak. At a minimum, when setting up a new method, the value of the data rate should follow this simple equation:

data collection rate x peak width at half height = 8

For example, if the peak width at half height is 2 seconds, the data collection rate is 4 Hz.

The pressure delivery system

The pressure system on the BioPhase 8800 system is based on a high-capacity syringe pump capable of delivering a maximum pressure of 80 psi for capillary rinses that must push highly viscous solution through the capillary tube. The system can also apply pressure on both inlet and outlet sides of the capillary. The maximum pressure that can be applied on both sides is 20 psi. For robust injection conditions and reproducible area count, it is essential to have the proper combination of pressure [psi] and duration of sample injection [seconds] in the method time program. Table 2 shows the recommended minimum injection time in seconds and the pressure value in psi for the injection step.

The high-voltage delivery system

The high-voltage power supply can handle a maximum total current output of 600 microamps during a separation. This translates into approximately 2.3 W of power applied across the capillary array, which is an important feature allowing for safe operation of the BioPhase 8800 system.

The system applies high voltage across all 8 capillaries present in the cartridge in a parallel arrangement, exposing each to the same voltage. Additionally, since each capillary has a dedicated buffer well, it is possible to monitor the total current generated or the individual current for each of the 8 capillaries using the touchscreen front panel. Another useful feature is the ability to limit the current during a separation to maintain the capillary cartridge longevity.

Pressure [psi]	Minimum injection time [s]
0.1	0.1
0.2	0.2
0.3	0.3
0.4	0.3
0.5	0.4
0.7	0.6
2.0	1.6
5.0	3.3
9.5	5.1
25	8.2

Table 2. Pressure vs. minimum time relationship for robust sample injection.





The sample storage system

The sample plates are stored protected from light and in a temperature-controlled chamber where thermoelectric device is used to cool or heat the air circulating along the bottom of the sample plate. The air flow was designed to uniformly control temperature across the whole sample plate. Additionally, the sample chamber design allows for the desired temperature to be reached within minutes. These features are critical for onboard sample stability. The operational range of the sample changer is from 4 to 37° C.

Conclusions

- ▶ Aiming to reduce the complexity of operation, the BioPhase 8800 system has an innovative approach to detection, where switching between UV and LIF detection is seamless and straightforward. The integrated modular detection makes it easy to switch from 1 assay to the next without user intervention.
- ▶ The cartridge is equipped with a highly efficient cooling exchange device to control Joule heating. Cartridges also contain a chip where the history of the cartridge is stored, potentially helping with electronic record-keeping compliance requirements.
- ▶ The sample and reagent plates are designed to ANSI standards, allowing sample prep workflows to be fully compatible with automated liquid handling.
- ▶ The high-voltage delivery system was built to meet the demand required in a multi-capillary, simultaneous-separation environment while retaining safety in operation. Similarly, the pressure delivery system was engineered to deliver accurate and consistent pressure for both injections and rinses across the plate.
- ▶ The compact design of the sample plate chamber allows for tight temperature control of the sample compartment, which is critical for onboard sample stability.
- ▶ The multi-capillary separation format provides flexibility and efficiency due to its sample parallel-processing capabilities, considerably reducing method development and characterization timelines.

References

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