High Resolution, Sensitivity, and Speed.

Identity, Purity and Charge Heterogeneity with the PA 800 Plus Capillary Electrophoresis System

SCIEX

Answers for Science.
Knowledge for Life.™

Consistent, Confident and Compliant Data

Good analytical technologies provide comprehensive characterization and facilitate regulatory compliance.

Established techniques capable of generating results with a high level of accuracy, sensitivity, reproducibility, and flexibility are paramount.

Research Analysts handling protein therapeutics need:

- Automated qualitative and quantitative analyses
- Proven functionality enabling maximum operational efficiency
- Flexible method development as well as simple routine operation across a range of molecules
- Robust, industry validated applications that are globally transferrable

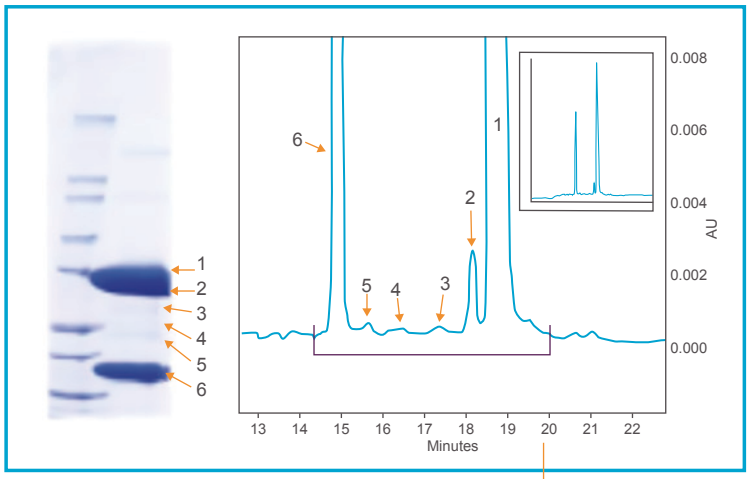
The PA 800 Plus Pharmaceutical Analysis System is a robust analytical platform that provides consistent, confident & compliant data, with easy-to-use software for the development and QC of biologics.

Both Sensitivity and High Resolution are Critical

Protein Purity Characterization Below 0.1%

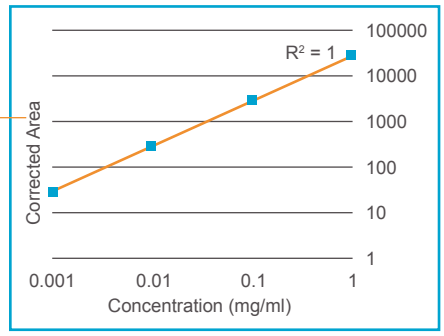
Association of low-level impurities with therapeutic proteins can mean the difference between the success and failure of a biotherapeutic.

The PA 800 Plus modular UV and Laser Induced Fluorescence (LIF) detection provides at least 3 orders of magnitude of impurity detection – 0.1% and 0.01% respectively.



Comparison of SDS-PAGE and capillary-based SDS method for separation of reduced IgG. Peak 1 and 6 correspond to IgG heavy and light chain respectively. Peak 2 is non-glycosylated heavy chain. Peak 3 - 5 are heavy chain degradation products.

Contrary to slab gel, CE-SDS can resolve non-glycosylated heavy chain (peak 2) from glycosylated heavy chain (peak 1), and can quantitate it too as per regulatory requirements.



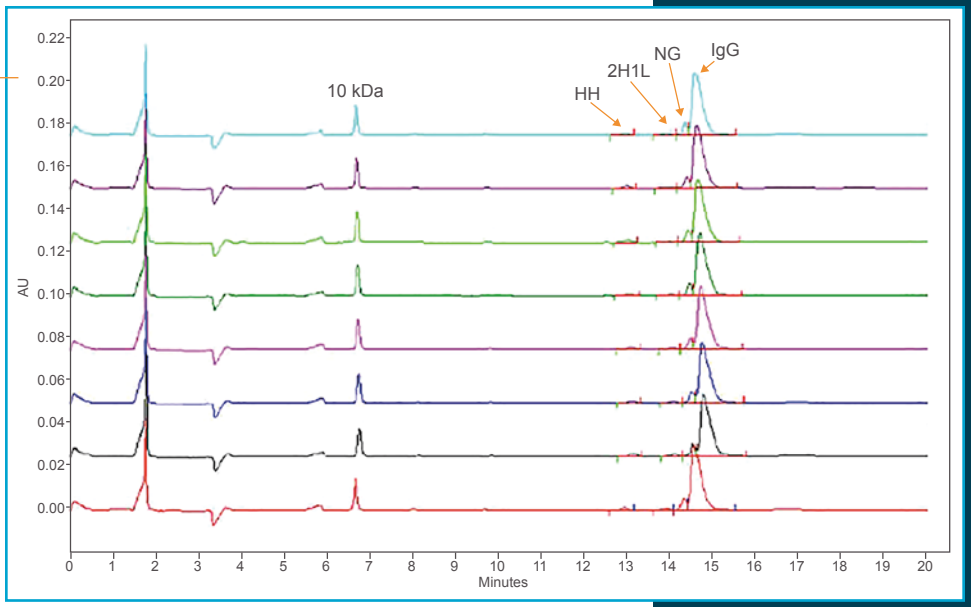
Characterization of impurities down to 0.01% with confidence requires 3 orders of linear dynamic range of detection and quantitation, which is provided by the PA 800 Plus Pharmaceutical Analysis System.

High-Speed Separations When Time is of the Essence

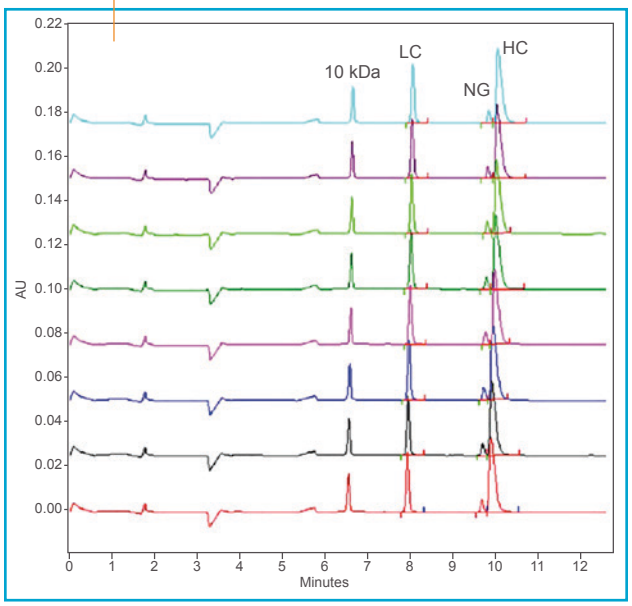
Protein Purity Characterization in <12-18 min.

A simple modification of the high resolution IgG assay (from previous page) is all it takes to increase the speed of separation without compromising assay sensitivity, or reproducibility, and all with minimal impact on resolution. This reduction in separation time is ideal for those occasions when you have large sample sets or are in a production environment and need to produce high-quality answers fast.

Fast CE-SDS separations results with minimal impact on resolution while retaining excellent assay reproducibility for both reduced and non-reduced IgG analyses on the PA 800 Plus.



Raw reproducibility data of Non-Reduced IgG purity in less than 18 minutes

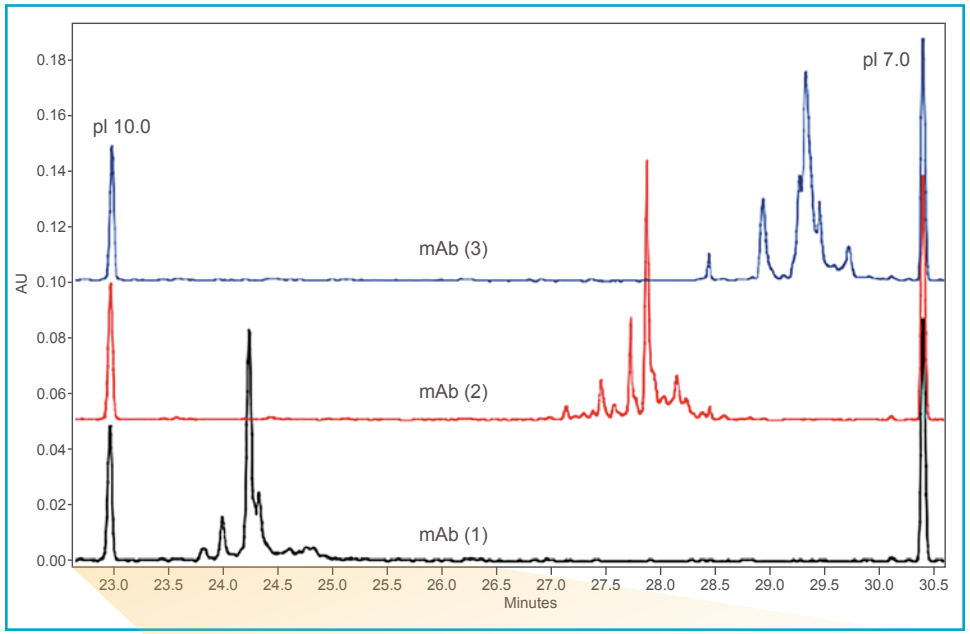


Raw reproducibility data of Reduced IgG purity in less than 12 minutes.

Confidently Assess Protein Stability

Highest Resolution Charge Heterogeneity Capillary Isoelectric Focusing (cIEF) Workflow Solution

Protein stability can be tightly linked to the effect of environmental conditions on charge heterogeneity. The SCIEX cIEF workflow on the PA 800 Plus System has been proven robust and portable. Universal or platform methods can also be created – significantly decreasing method development efforts, simplifying workflows with a single method for molecules across a wide pI range.



cIEF workflow can be established as a standard platform assay across a wide pI range, resulting in simplication of analytical workflows

To provide you with greater sensitivity of analysis, ultra high resolution cIEF is capable of achieving separation between isoforms as closely related as 0.03 pI units.

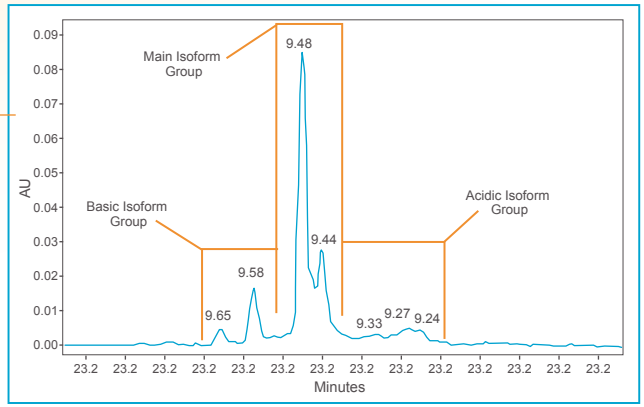


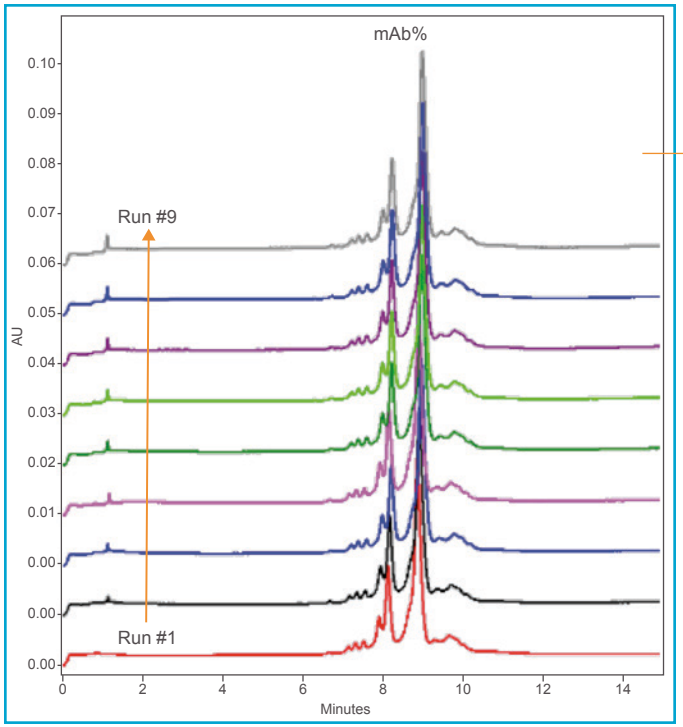
Figure 7: mAb (1) Peak Profile. A close up view of the mAb #1 cIEF separation.

Simplify Your Sample Prep

High Throughput Charge Heterogeneity Made Easy

When determining charge heterogeneity on the PA 800 Plus, capillary zone electrophoresis (CZE) - a simple buffer CE technique - results in faster separation compared to LC and other CE methods. CZE offers you many other advantages, including reduced sample preparation complexity and minimal required optimization. As a result, CZE is being adopted by a growing number of organizations.

Parameter	SCIEX cIEF	CZE	non-SCIEX cIEF	CEX (pH gradient)
Resolution	Very good	Good to very good	Moderate to good	Good to very good
Analysis time	20-25 min	18-21 min (incl. rinsing)	20-25 min (incl. rinsing)	90 min
Applicability to mAbs without modification of the method	75%	100%	65%	~80%
Buffer consumption	Very low	Very low	Very low	720 ml / 8 runs
Injection concentration	0.3 - 04 mg/ml	0.009 - 3.6 mg/ml	0.3 - 0.4 mg/ml	0.006 - 3.6 mg/ml
	SCIEX data	Novartis data, see webinar		



CZE separations are performed with high reproducibility, ideal for multi-user, multi-instrument organizations

Learn More. Watch the SCIEX Webinar Series.

MAb Charge Heterogeneity Analysis by CZE, Part 1: Results of an Intercompany Robustness Study

Dr. Bernd Moritz, Hoffman-La Roche, Pharmaceutical Division, Basel, Switzerland

MAb Charge Heterogeneity Analysis by CZE, Part 2: A Case Study from Merck Sharp & Dohme

Dr. Joop Waterval and Tijmen Verwij, Merck Sharp & Dohme, Netherlands

MAb Charge Heterogeneity Analysis by CZE, Part 3: A Test Method Fit for QC Testing

Dr. Marc Hassel, Novartis Pharma AG, Basel, Switzerland

“PA 800 Plus has been validated for ...”

Read extensive intercompany studies assessing the practical application of CE-SDS, cIEF, and CZE, were performed across the biopharmaceutical industry effectively validating these assays.

Multi-Site N-glycan mapping study 1: Capillary electrophoresis – laser induced fluorescence

mAbs. Volume 6, Issue 6, 2014

N-Glycan

Evaluation of capillary zone electrophoresis for charge heterogeneity testing of monoclonal antibodies

Journal of Chromatography B, 983–984 (2015) 101–110

CZE

U.S. Pharmacopeial Convention

In 2016 the US Pharmacopeial convention (USP) published Chapter <129> describing application of CE-SDS and glycan analysis for the characterization of monoclonal antibodies.

A Series of Collaborations Between Various Pharmaceutical Companies and Regulatory Authorities Concerning the Analysis of Biomolecules Using Capillary Electrophoresis

Chromatographia (2011) 73:1137–1144

CE-SDS

Intercompany Study to Evaluate the Robustness of Capillary Isoelectric Focusing Technology for the Analysis of Monoclonal Antibodies

Chromatographia (2011) 73:1137–1144

cIEF

Notable Publications and Tech Notes

Proven CE Robustness for Biopharmaceutical Quality Control and Method Transfer

A Series of Collaborations between Various Pharmaceutical Companies and Regulatory Authorities Concerning the Analysis of Biomolecules Using Capillary Electrophoresis. *Chromatographia* 2006, 64, September (No. 5/6).

Salas-Solano O et al. (2011) Intercompany Study to Evaluate the Robustness of Capillary Isoelectric Focusing Technology for the Analysis of Monoclonal Antibodies. *Chromatographia*. 73:1137-1144

Evaluation of capillary zone electrophoresis for charge heterogeneity testing of monoclonal antibodies. *J Chromatogr B Analyt Technol Biomed Life Sci.* 2015 Mar 1;983-984:101-10.

Capillary Electrophoresis in Quality Control: PART I: Application for Therapeutic Proteins.

Capillary Electrophoresis in Quality Control: PART II: CE-SDS: Method Development and Robustness.

Quantitative and automated protein purity & heterogeneity analysis by CE-SDS

IgG Purity/Heterogeneity and SDS-MW Assays with High-Speed Separation Method and High Throughput Tray Setup.

Assay of IGG Purity and Heterogeneity Using High-Resolution Sodium Dodecyl Sulfate Capillary Gel Electrophoresis.

Automation of CE-SDS Sample Preparation for PA 800 plus IgG Purity/Heterogeneity Assays Using a Biomek 4000 Automation Workstation.

Quantitative & robust protein charge heterogeneity analysis

Analysis of Monoclonal Antibody Charge Variants by Capillary Zone Electrophoresis. High-Resolution cIEF of Therapeutic Monoclonal Antibodies: A Platform Method Covering pH 4-10.

SCIEX Biologics Characterizations Solutions

For more information on SCIEX Biologics Characterization Solutions download the SCIEX Biologics Analytical Characterization Compendium

For an extensive collection of recorded webinars and events on CE, click here

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Answers for Science.
Knowledge for Life.™

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