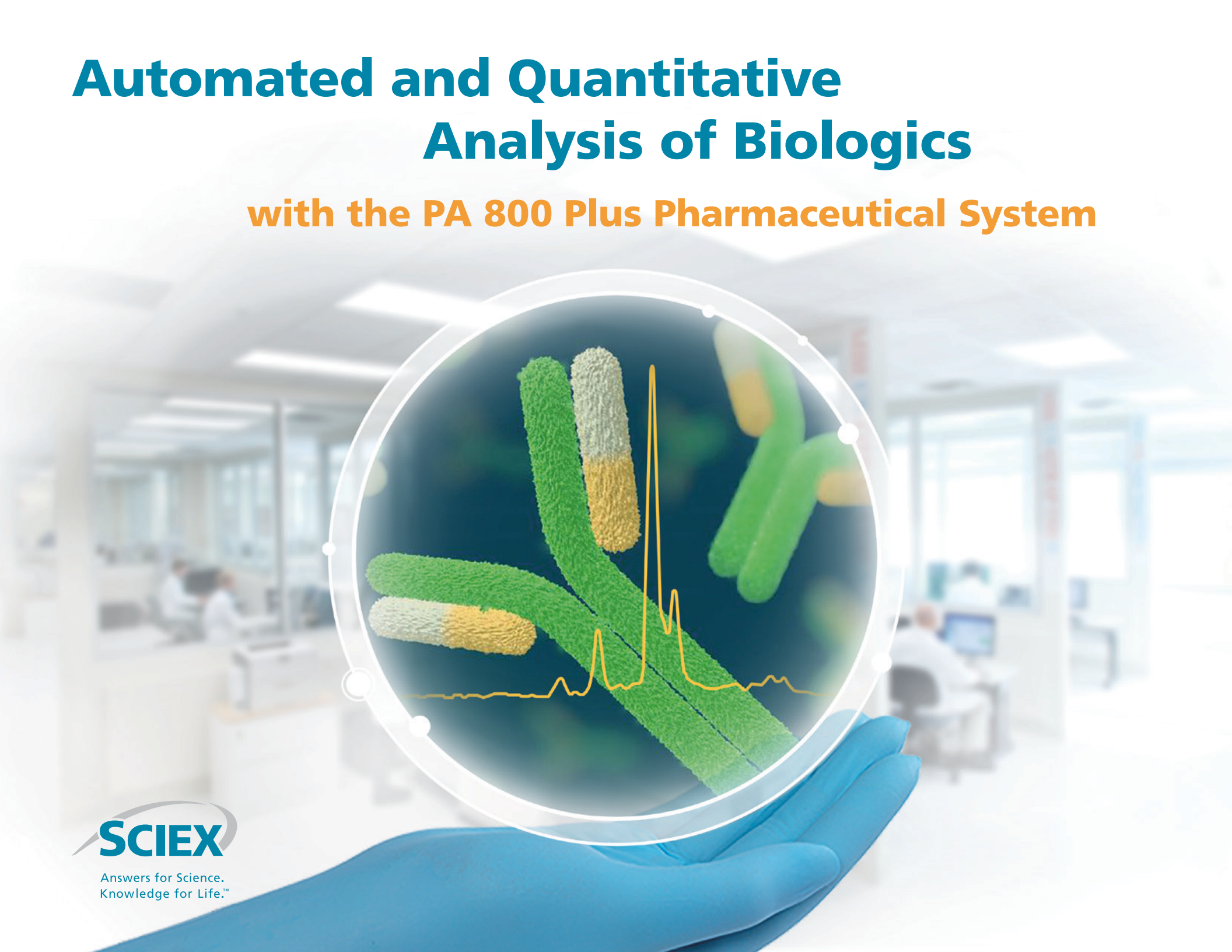
# Automated and Quantitative Analysis of Biologics

## with the PA 800 Plus Pharmaceutical 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 therefore, paramount to biopharmaceutical analyses within your lab.

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

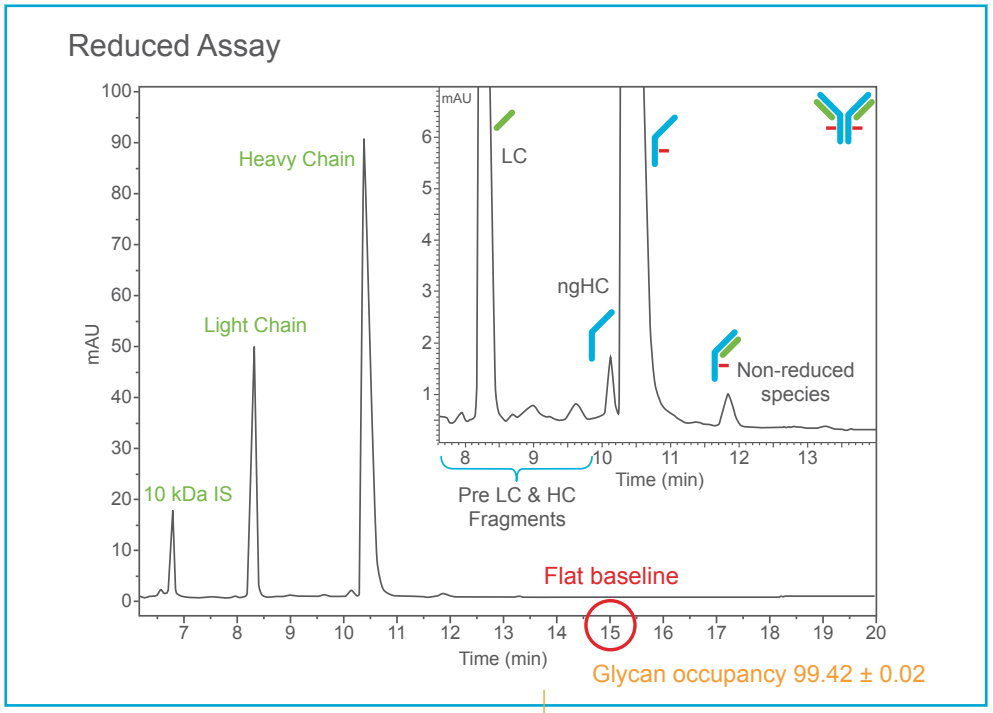
The PA 800 Plus Pharmaceutical Analysis System is a robust analytical platform that provides consistent, confident & compliant data, with easy-to-use software for the development and QC of biologics.

## Exceed Sensitivity and Resolution Requirements

### 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.

Have confidence in your results with SCIEX CE-SDS, the gold standard adopted by biopharma for this application.




Capillary-based SDS method for separation of reduced NIST mAb, in less than 15 minutes.

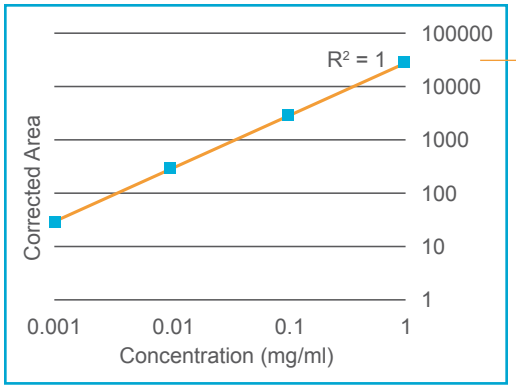
Contrary to slab gel, CE-SDS can resolve non-glycosylated heavy chain from glycosylated heavy chain, and can quantitate it too, as per regulatory requirements.

# Complete Your Protein Purity Characterization in <18 Minutes

Time is of the essence. Workloads are high. Achieve more and make every minute count without impacting the quality of your data, with fast, accurate and reproducible separations.

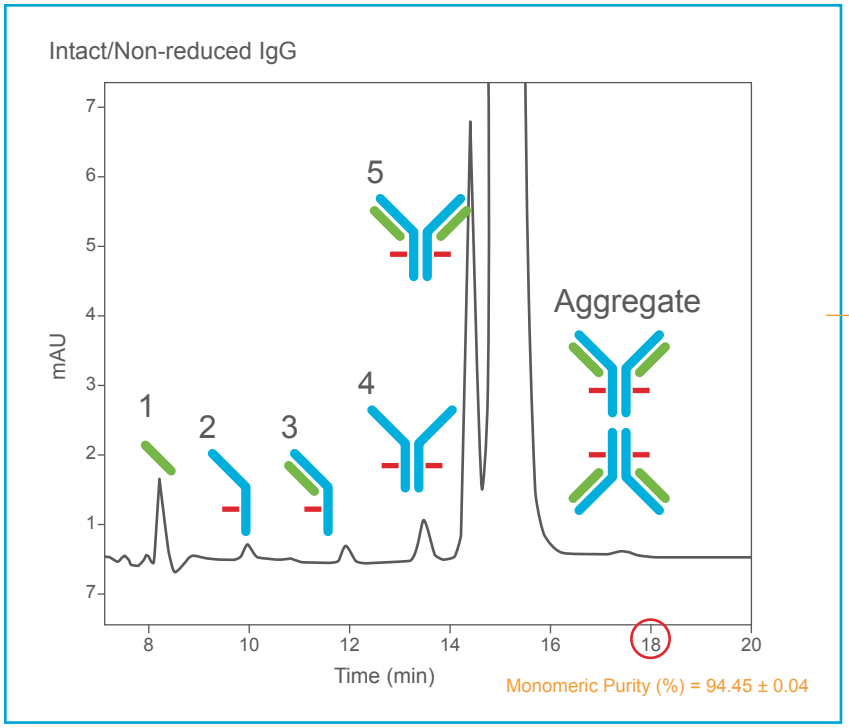
## Protein Purity Characterization in <12-18 min.

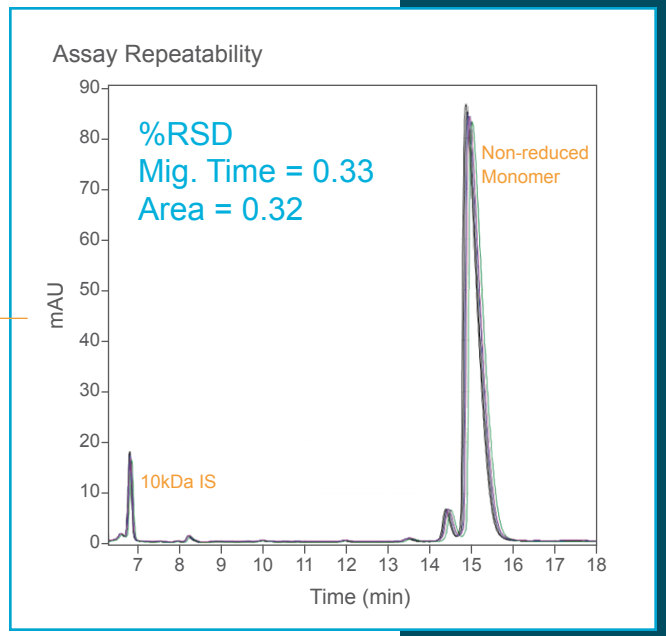
Gain excellent assay reproducibility for both reduced and non-reduced IgG analyses on the PA 800 Plus.




Achieve maximum sensitivity with the PA 800 Plus modular UV and Laser Induced Fluorescence (LIF) detection – providing at least three orders of magnitude of impurity detection – 0.1% and 0.01% respectively.

## Rapidly Assess Monomeric Purity



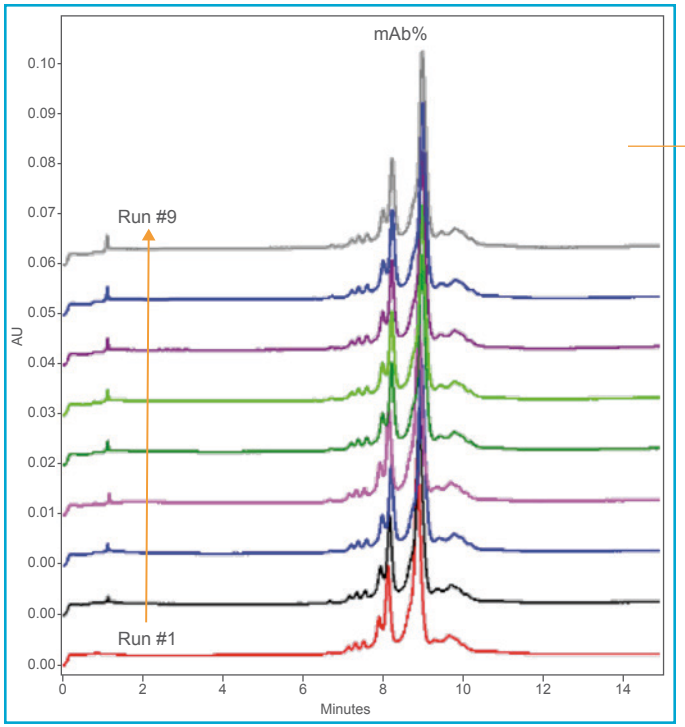




6 overlaid traces demonstrate the assay repeatability as the migration time and peak area RSDs are less than 0.5%

# High Throughput Charge Heterogeneity Made Easy

## Rapid Charge Variant Analysis Made Easy

When used on the PA 800 Plus, Capillary Zone Electrophoresis (CZE) offers faster separation results than other LC and CE methods. Additionally, you'll find CZE offers many other advantages for your lab.




CZE separations are performed with high reproducibility and are ideal for multi-user/ multi-instrument environments.

## 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

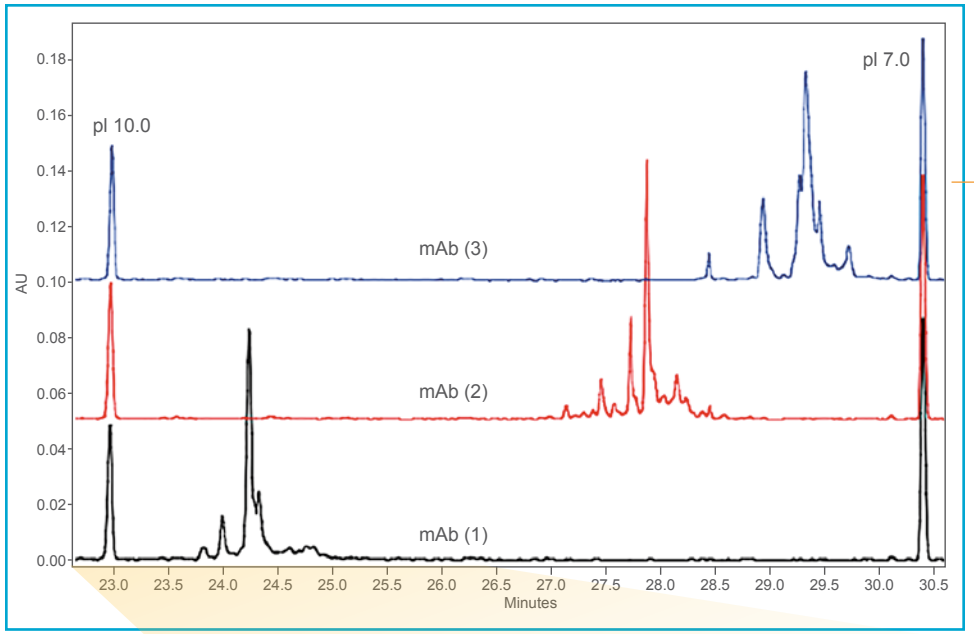
| Parameter | SCIEX cIEF | CZE | non-SCIEX cIEF | CEX (pH gradient) |
|---|---|---|---|---|
| Resolution | Very good | Good to very good | Moderate to good | Good to very good |
| Analysis time | 20-25 min | 18-21 min (incl. rinsing) | 20-25 min (incl. rinsing) | 90 min |
| Applicability to mAbs without 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 | | |

- **Screen charge variants in 10 minutes**
- **Save time with fast, simple sample preparation**
- **Same method applies to a wide range of pI**

# Highest Resolution Charge Heterogeneity Capillary Isoelectric Focusing (cIEF)

## Confidently Assess Protein Stability

The SCIEX cIEF workflow on the PA 800 Plus System has proven robust and portable. Universal or platform methods can also be created – significantly decreasing method development efforts and 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, simplifying workflows.

Ultra high resolution cIEF is capable of achieving separation between isoforms as closely related as 0.03 pI units.

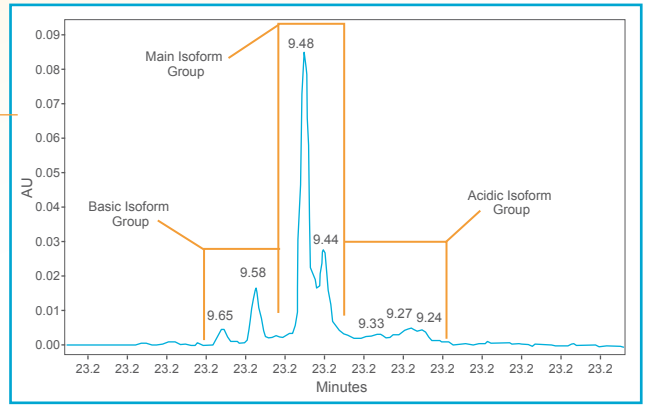



Figure 7: mAb (1) Peak Profile. A close up view of the mAb #1 cIEF separation.

# Rapid, Precise Glycan Analysis

SCIEX offers high throughput semi-quantitative glycan screening for clone selection and process control as well as fast glycan analysis for biologics characterization from standard mAbs to complex proteins – all using the same award-winning chemistry.

In addition, SCIEX LC-MS and CESI-MS solutions can accurately determine intact and subunit level glycoprotein profiles for comparability reasons, as well as obtain site specific glycan information at the peptide level.

## Simplify your Workflow
## One Chemistry from Clone Selection Through QC

### Resolve Critical Microheterogeneity Information with Fast Glycan Technology

Glycosylation is critical for the efficacy, clearance, and immunogenicity of biologics. Incorrect glycan species associated with a biologic, like a monoclonal antibody (mAb), can lead to an increase and/or decrease in antibody or complement dependent cellular cytotoxicity. SCIEX Fast Glycan Technology gives you the power to rapidly resolve microheterogeneity and helps you profile glycans that could lead to changes in function, efficacy and clearance of a biologic.


### Sciex Award-Winning Fast Glycan Technology Takes You from Intact Proteins to Glycans with Sample Prep

- as quick as about an hour for a few samples
- or in <2 hours for 96 samples, using automation

With software that provides Immediate Glycan Identification.

## Make Confident Decisions on Clone Selection and Cell Culture Optimization in Real-time

### Easily Screen Large Sample Cohorts, with the C100HT Biologics Analyzer

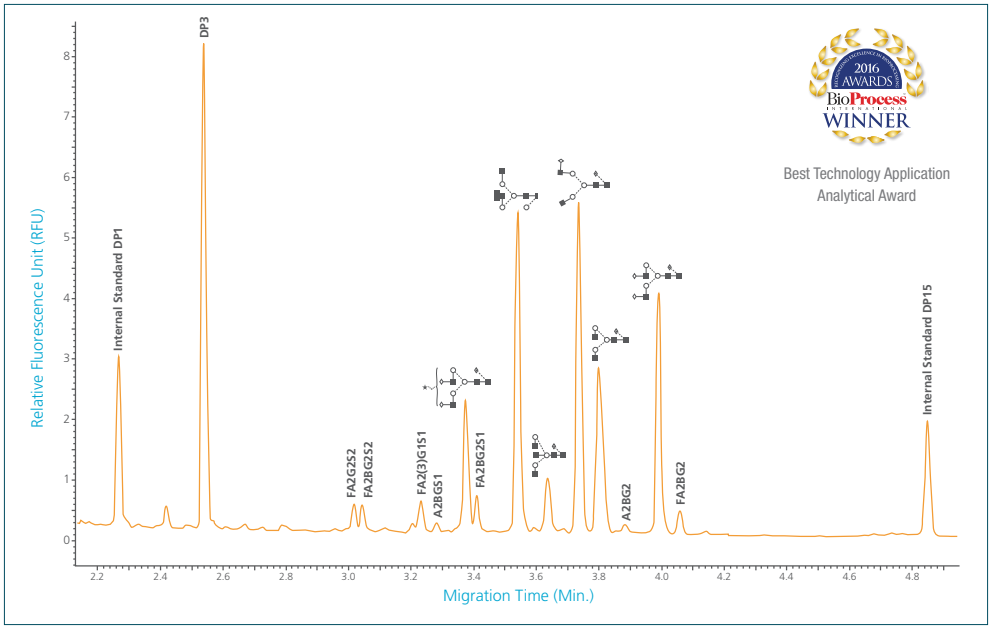
Just mouse over any well and see why the sample passed (green) compared to your acceptance criteria, or failed (red). Parameters can be easily changed if desired.

# Characterize Glycans in Record Time

## Glycoprotein to Identified Glycans within 90 minutes

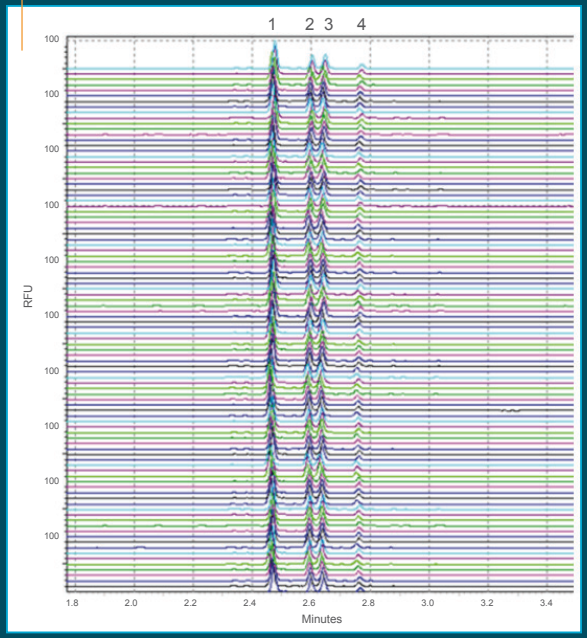
When paired with the PA 800 Plus, SCIEX Fast Glycan Labeling and Analysis technology delivers rapid glycan heterogeneity identification, capable of profiling your glycans in record time.

Combining simplified sample preparation, rapid separations and automated glycan identification, you can make confident decisions quickly by running glycans up to five-times faster than HILIC – including sialylated N-glycans.


| Obtaining High Resolution Glycan Analysis Has Traditionally Required Patience | | | |
|---|---|---|---|
| | **HILIC UHPLC** | **Conventional CE** | **SCIEX Fast Glycan CE** |
| Sample Prep | 30-min to 24-hours | 4-hours | **1-hour** |
| Separation Time | 17- to 45-min | 15- to 20-min | **5-min** |
| Immediate ID | — | — | ✔ |

Get repeatable results with exclusive recirculating liquid coolant to control separation temperature.




Raw data illustrating rapid and highly reproducible CE-LIF analysis of APTS labeled IgG glycans prepared in a 96-well plate format using automated liquid handling.

Optimize your workflows through the use of automated sample preparation, resulting in high resolution separation data with excellent reproducibility across large sample sets.

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

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

usp™

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

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

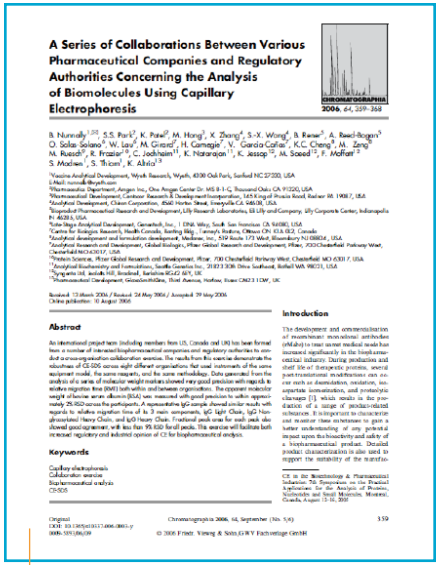
mAbs. Volume 6, Issue 6, 2014

N-Glycan

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

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

CZE



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.

# Notable Publications and Tech Notes

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

High Resolution and high speed glycan analysis for microheterogeneity determination

Rapid sample preparation and analysis of monoclonal antibody Nglycans by magnetic bead technology and CE-LIF.

CE Separation of N-Linked Oligosaccharides Released From Recombinant Monoclonal Antibody.

Fully automated sample preparation with ultrafast N-glycosylation analysis of therapeutic antibodies.

High fidelity glycan sequencing using a combination of capillary electrophoresis and exoglycosidase digestion.

SCIEX Biologics Characterizations Solutions

SCIEX Biologics Analytical Characterization Compendium

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

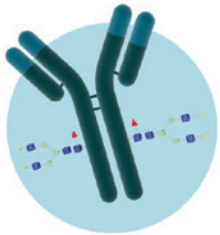
# It’s Time to Reduce Complexity in Biologics Characterization

Glycan Analysis is part of the SCIEX 360° solution for Biologics Characterization. You can advance your characterization workflows with our full-circle product portfolio, including application-focused systems, software and services designed specifically for biologics analyses. SCIEX innovation can help you speed routine tasks as well as simplify your most complex characterization challenges. Now you can achieve insights faster and with greater confidence than you ever thought possible. Find out more at sciex.com/biologics-characterization.

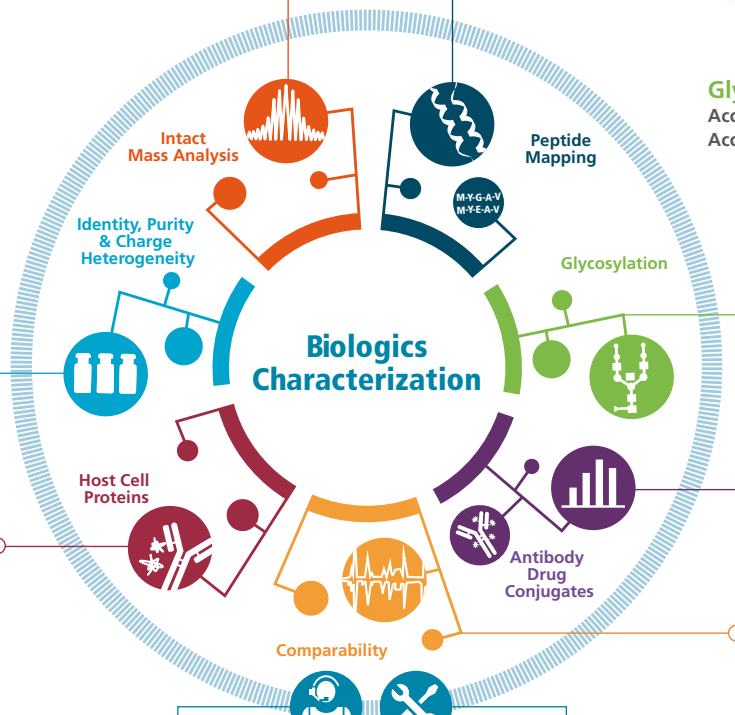
**Intact Mass Analysis**
Accuracy + Sensitivity = Confidence

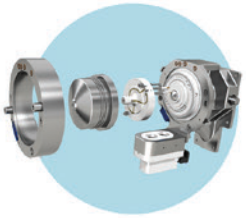
**Peptide Mapping**
Deeper Information, Faster

**Identity, Purity & Charge Heterogeneity**
High Resolution, Sensitivity, & Speed



**Glycosylation**
Accurate Analysis. Accelerated Results.



**Antibody Drug Conjugates**
DAR, Demystified


**Host Cell Proteins**
Nothing Hides from SWATH® Acquisition


**Comparability**
Click. Compare. Report.

**SCIEX Support**
Team with our Biologics Experts

**SCIEX Service**
Maximize Uptime

# Network Your Way to Success

## Discover How the SCIEX Success Network Speeds and Simplifies Your Path to Answers

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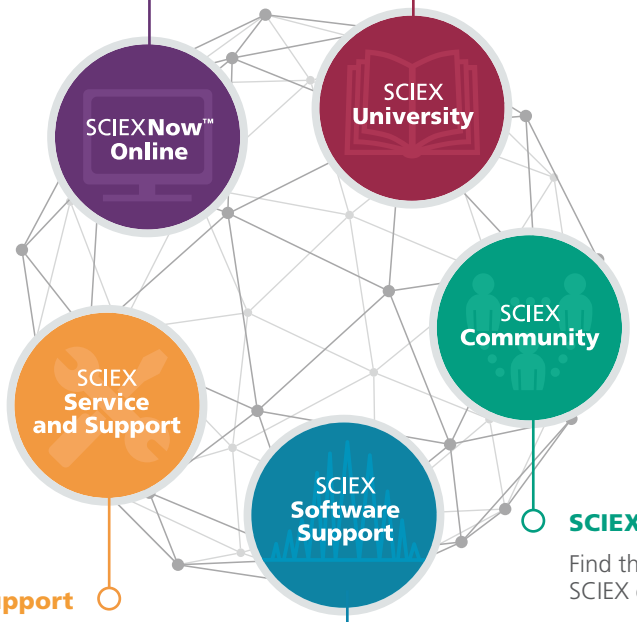
The everything, anytime destination for all your SCIEX support needs

**SCIEXUniversity**

The most diverse and flexible learning options available




**SCIEX Community**

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Answers for Science.
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RUO-MKT-03-4556-C 05/2018

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