PRODUCT NOTE

ICP - Mass Spectrometry

Key Features:

- Proprietary sample introduction system ensures efficient transport of cells to the plasma
- Dedicated software module provides ease of use and automation
- Unmatched data acquisition speed for accurate profiling

Syngistix Single Cell Application Software Module for NexION ICP-MS Systems

Introduction

The detection of metals in a single cell offers an exciting and novel approach to understanding cellular mechanisms when examining the uptake of drugs, environmental contaminants, nutrients, and/or nanoparticles. Traditionally, metal content in cells was measured quantitatively by digesting large numbers of cells and assuming every cell in the population contains an equal amount of metal or qualitatively using either light or electron microscopy, a technique that is both time consuming and only measures a small selection of the population.

By coupling mathematical simulations with experimental work, PerkinElmer scientists have developed a proprietary Single Cell Sample Introduction System and dedicated software – Syngistix™ Single Cell Application Software Module. The Single Cell Sample Introduction System ensures successful delivery of individual cells to the ICP-MS plasma without disrupting or rupturing their membranes. The Syngistix Single Cell Application Software Module, the focus of this product note, benefits from the unmatched speed of acquisition of PerkinElmer's NexION® ICP-MS family of instruments (100,000 pts/sec) delivering a unique solution to detect and quantify metal content at the cellular level.

Capabilities Overview For Single Cell Acquisition

- Reporting in mass-per-cell
- Reporting number of cells containing metal
- Handling small sample volumes
- Quantifying low cell numbers

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For the Better

Proprietary Single Cell Sample Introduction System

Critical to the success of this software module is the new **Single Cell Sample Introduction System** which combines the Asperon™ spray chamber and an all-new autosampler that complement each other to deliver cells to the ICP-MS plasma in a very efficient manner. Conventional spray chambers are designed to limit the size of the aerosol droplets entering the ICP-MS plasma. However, PerkinElmer's unique Asperon spray chamber is designed to allow cells as large as 50 µm to enter the plasma utilizing a tangential flow pattern that ensures proper cell transportation. This technology, combined with a dedicated autosampler capable of handling micro-volume samples, offers researchers the capability to do more with less sample volume.

Dedicated Software Module

PerkinElmer's **Syngistix Single Cell Application Software Module** is the first commercially available software designed specifically for single cell analysis by ICP-MS, combining real-time single-cell acquisition with fast data processing capable of handling the large amounts of data generated, for routine analytical use. This module is an extension of PerkinElmer's Syngistix for ICP-MS software for the NexION series of ICP-MS instruments. Through a combination of unique hardware, patented software algorithms, and scientific knowhow, this package provides users with several important cellular characteristics, including:

- Mass of metal per cell
- Mass distribution
- Concentration of cells containing metal or nanoparticles
- Number of nanoparticles per cell
- Ability to differentiate between ionic and particulate fractions
- Ability to clearly separate between exogenous ions and those endogenous to the cell

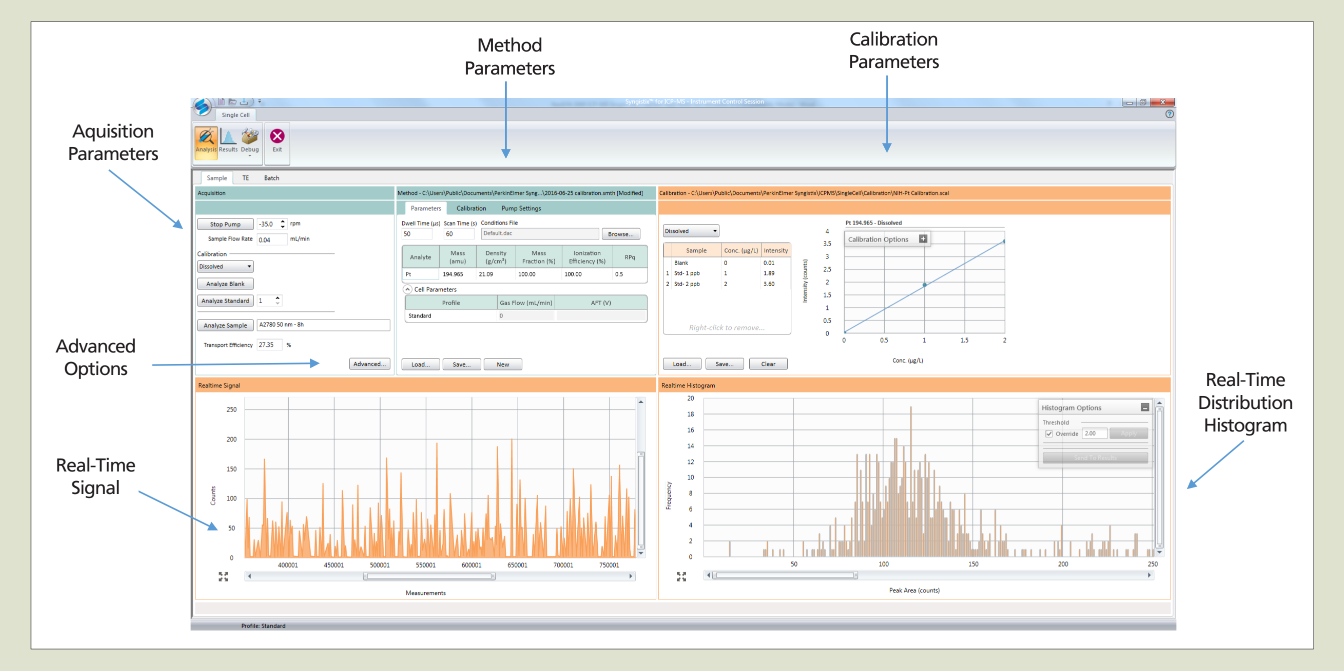
All this is accomplished through a single interface that eliminates the need for labor-intensive data processing.

Ease of Use

The Syngistix Single Cell Software Module incorporates all single-cell analysis needs into an intelligent workflow. The Analysis panel (Figure 1) contains all the parameters necessary to set up methods and batches:

- An analyte drop-down menu
- Analytical mode selection (Standard or Reaction)
- Multi-point calibrations (both particle and dissolved)
- Advanced features for ultimate flexibility

All results are displayed in real time, both as intensity vs. time and as a background-corrected histogram showing the mass distribution – all made possible with the software capability to automatically detect and assign pulse detection thresholds, one of the many unique features of the Syngistix Single Cell Application Software Module. With this powerful combination of method and data acquisition parameters, a great deal of flexibility is offered for a wide variety of laboratory operations.



Acquisition

Stop Pump -35.0 rpm

Sample Flow Rate 0.04 mL/min

Calibration: Dissolved

Analyze Standard 1

Analyze Sample A2780 50 nm - 8h

Transport Efficiency 27.35 %

Method - C:\Users\Public\Documents\PerkinElmer Syng...\2016-06-25 calibration.smth [Modified]

Dwell Time (µs) 50

Scan Time (s) 60

Conditions File Default.dac

Analyte	Mass (amu)	Density (g/cm³)	Mass Fraction (%)	Ionization Efficiency (%)	RPq
Pt	194.965	21.09	100.00	100.00	0.5

Cell Parameters

Profile	Gas Flow (mL/min)	AFT (V)
Standard	0	

Calibration - C:\Users\Public\Documents\PerkinElmer Syngistix\ICPMS\SingleCell\Calibration\NIH-Pt Calibration.scal

Dissolved

	Sample	Conc. (µg/L)	Intensity
	Blank	0	0.01
1	Std- 1 ppb	1	1.89
2	Std- 2 ppb	2	3.60

Threshold ☑ Override 2.00

Figure 1. Analysis panel in Syngistix Single Cell Application Module.

The Results panel (Figure 2) allows users to review and interact with the data once it has been processed. Options include:

- Changing the threshold and bin sizes
- Setting integration parameters
- Applying both ionic and particle calibrations.

With this intelligent workflow, users will be able to focus on what matters most – the results.

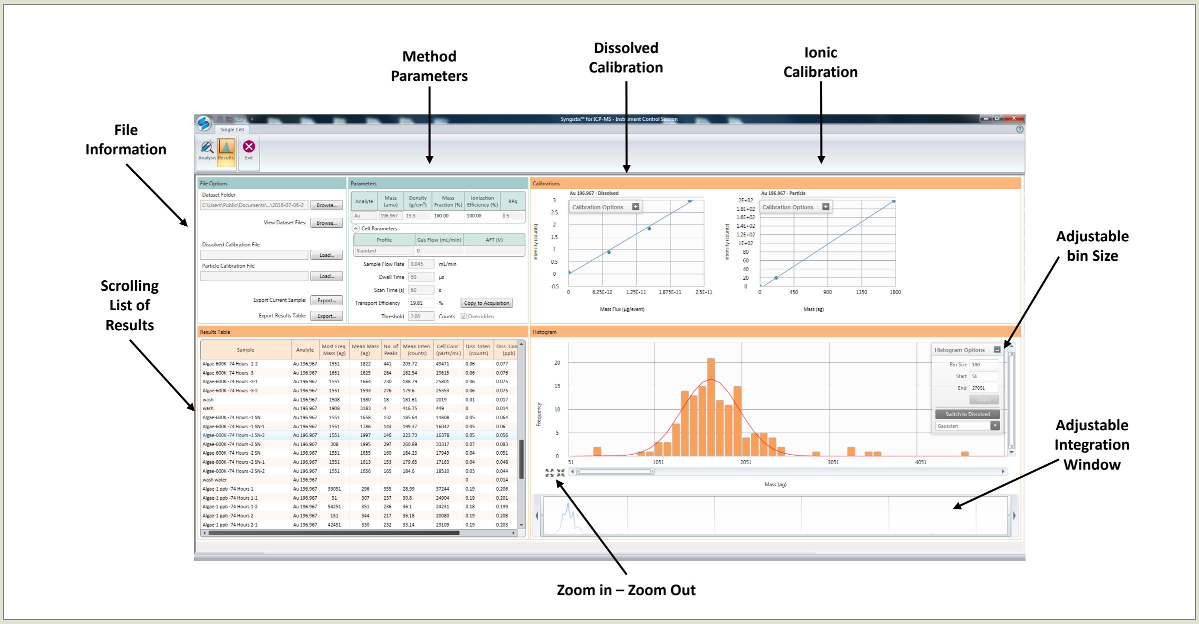


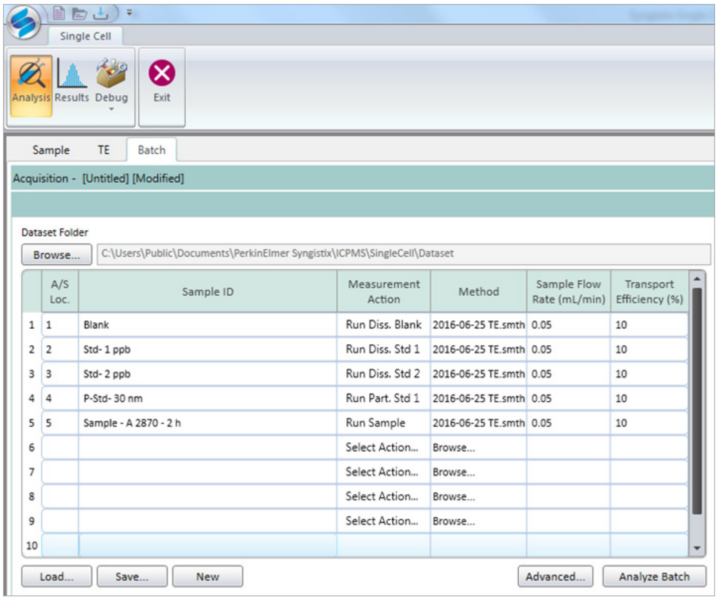
Figure 2. Results panel in Syngistix Single Cell Application Module.

Automation

Using the Batch functionality available in the Syngistix Single Cell Application Module (Figure 3), the user can create sample lists with multiple methods and calibrations (ionic and/or particulate) and run them automatically. This functionality allows for high throughput, maximum flexibility, and eliminates the need for manual intervention.

Unmatched Data Acquisition Speed

The duration of the signal emitted from the bursting event of the cell in an ICP is only a few hundred microseconds. As a result, in order to get enough data points to fully capture this signal, the instrument should be capable of taking a reading every 50 microseconds (minimum eight points per peak at 400 microsecond wide peaks), thereby acquiring upwards of 20,000 points/second. Not only is the NexION ICP-MS capable of acquiring at 100,000 points/sec, but also the Syngistix Single Cell Application Module is powerful enough to handle the large quantity of data generated while being able to clearly distinguish between exogenous and endogenous ions, providing an essential tool to analysts.



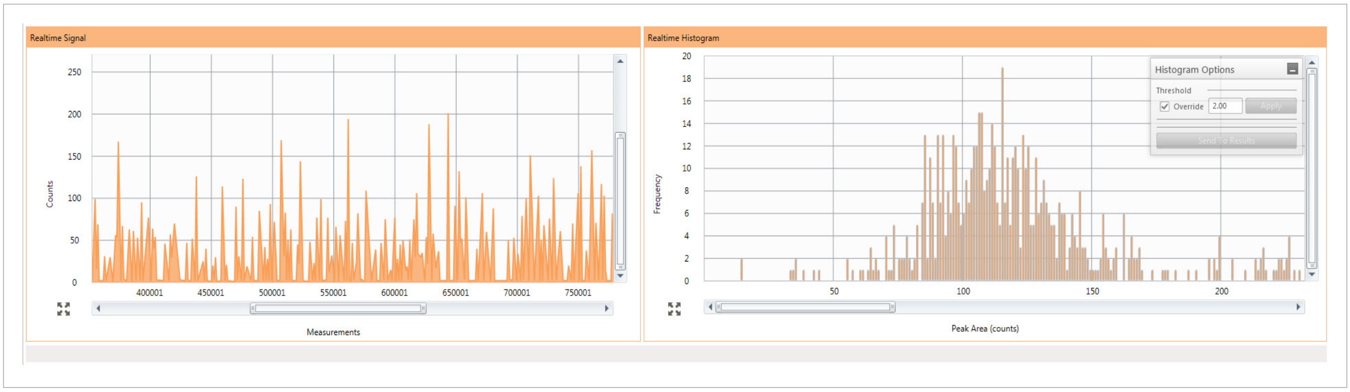
Acquisition - [Untitled] [Modified]

Dataset Folder: C:\Users\Public\Documents\PerkinElmer Syngistix\ICPMS\SingleCell\Dataset

	A/S Loc.	Sample ID	Measurement Action	Method	Sample Flow Rate (mL/min)	Transport Efficiency (%)
1	1	Blank	Run Diss. Blank	2016-06-25 TE.smth	0.05	10
2	2	Std- 1 ppb	Run Diss. Std 1	2016-06-25 TE.smth	0.05	10
3	3	Std- 2 ppb	Run Diss. Std 2	2016-06-25 TE.smth	0.05	10
4	4	P-Std- 30 nm	Run Part. Std 1	2016-06-25 TE.smth	0.05	10
5	5	Sample - A 2870 - 2 h	Run Sample	2016-06-25 TE.smth	0.05	10
6			Select Action...	Browse...		
7			Select Action...	Browse...		
8			Select Action...	Browse...		
9			Select Action...	Browse...		
10						

Figure 3. Batch view in Syngistix Single Cell Application Module.

With the Syngistix Single Cell Application Module, data can be viewed as it is being acquired in real time: individual single cell events are displayed, and the metal content is converted to a background-corrected intensity histogram, which continuously updates during data acquisition, thanks to the module's automated threshold detection. Figure 4 is a snapshot of the Analysis panel taken during data acquisition, showing both the real-time signal and histogram. The real-time display of results is unique to PerkinElmer's Syngistix Single Cell Application Module and provides users with instant information on the sample being analyzed, including whether further dilutions are necessary to avoid cell coincidence.



Threshold

☑ Override 2.00

Figure 4. Snapshot of Analysis panel during data acquisition, showing the real-time signal (left) and frequency vs. peak area histogram (right).

Once data acquisition has been completed, the Results environment allows the user to review the data, both through a Results table and accompanying histograms. These formats allow for ease of verification, offering a multitude of additional information. The user can interact with the data in the histogram for each sample and adjust a variety of parameters, including:

- Dynamic fitting window
- Bin range
- Peak fit (Gaussian, log normal, maximum intensity)

Last but not least, the Syngistix Single Cell Application Module provides two different types of export functions, allowing data to be shared with collaborators or colleagues:

- The Results table can be exported for quick review
- All the information on a single sample (including sample data, mass and intensity histograms, as well as calibration information) can be exported for post-processing for other data manipulations.

The Syngistix Single Cell Application Software Module is the ideal tool for laboratories analyzing the metal content in cells, either from cellular uptake of metals (dissolved or metallic nanoparticles) or measuring the intrinsic metal content of the cell. This unique application module allows the differentiation and quantification between the dissolved and cellular fractions of the same analyte. The following variety of information can be determined in a single analysis without the need for subsequent data processing: mass per cell, mass distribution in a cell population, concentration of cells containing metal or nanoparticles, and number of nanoparticles per cell. Coupled with the NexION series ICP-MS instruments, the Syngistix Single Cell Application Module is the world's first single cell ICP-MS dedicated analysis software, delivering speed, flexibility, automation, and ease-of-use.

PerkinElmer, Inc.
940 Winter Street
Waltham, MA 02451 USA
P: (800) 762-4000 or
(+1) 203-925-4602
www.perkinelmer.com

For a complete listing of our global offices, visit www.perkinelmer.com/ContactUs

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