

在生命科学领域中,生物体的摄入行为、耐受性和积聚效应是药学和 毒理学研究必须关注的。而这些领域中,快速对个别细胞中元素含量 以及细胞群落中元素含量分布进行测定是非常关键的。

传统的细胞摄入行为分析方法需要复杂的样品制备和仪器分析过程, 耗时费力,还只能得到定性的或者细胞群落的平均定量信息。借助 PerkinElmer 的 NexION<sup>®</sup> ICP-MS 平台,配合专利的 Asperon ™单细胞 雾室及 Syngistix ™操作软件单细胞模块,可以实现定量分析单个细胞 内金属成分的独特功能。这一功能可以区分细胞内原有金属成分和后 摄入的离子或纳米颗粒,为药物传输、毒理学评估、生物耐受性评估、 生物累积性机理等研究提供更为适宜的手段。

### PerkinElmer 单细胞 ICP-MS 解决方案包括:

- 专门设计的进样系统,确保细胞在被传输至离子化区域之前保持 完整;
- •专用软件模块, 直观易用, 有效提升分析工作的自动化程度;
- 超群的数据采集速率(高达 100,000 数据点 / 秒),为精确剖析提供可能。



NexION 2000 ICP-MS

### 借助这些独特功能可以实现:

- 单个细胞内待测元素的含量,精确至 ag/cell;
- •细胞群落中待测元素在各个细胞中的分布;
- 含有某待测元素的细胞的数量;
- •细胞水平的曝露或给药/响应信息;
- 单个细胞内纳米颗粒的数量。

For more information, visit perkinelmer.com/NexION2000

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# Single Cell ICP-MS Sample Introduction and Automation Kits

Traditional methods for measuring single cell uptake rates can be a time-consuming process with long instrument analysis and sample preparation time, often leading to qualitative or population-averaged results. PerkinElmer's award-winning NexION® ICP-MS Single Cell Analysis System, with its proprietary Asperon<sup>™</sup> Single Cell Spray Chamber, Single Cell Micro DX Autosampler, and the Syngistix<sup>™</sup> Single Cell Software Module, offers a first-to-market complete solution to quantitatively measure the metal content in individual cells, unveiling new capabilities to study intrinsic metals content and the uptake of dissolved (ionic) and nanoparticulate metals into cells, providing new insights into drug delivery, mobilization/immobilization of metal content, bioavailability, and bioaccumulation mechanisms.

- The Asperon Single Cell Spray Chamber is a proprietary sample introduction system that ensures cells are delivered intact to the ionization source.
- The Single Cell Micro DX Autosampler is a microfluidic automation platform that enables single-digit microliter sample handling, cell resuspension through user-defined agitation protocol and accommodates most microwell plates.
- The Syngistix Single Cell Application Module is a dedicated software module that delivers ease-of-use, data processing and automation.

And to further simplify the process, we offer Single Cell ICP-MS Sample Introduction and Automation Kits that deliver everything you need for single cell analysis with your NexION ICP-MS. See page 2 for more details on these kits.





|   | QTY. | PART NO. |
|---|------|----------|
| Single Cell Kit for NexION 1000/2000            |      | N8150032 |
| Includes:                                       |      |          |
| Asperon Spray Chamber                           | 1    | N8152493 |
| Spray Chamber Drain Line                        | 1    | N8152494 |
| Spray Chamber Addition Gas Tee 1/8 Fitting      | 1    | N8152495 |
| MEINHARD <sup>®</sup> HEN Single Cell Nebulizer | 1    | N8152496 |
| Sample Line for MEINHARD® HEN Nebulizer         | 1    | N8152489 |
| UV Light Shield                                 | 1    | N8152497 |
| Plasma Light Shield                             | 1    | N8152377 |
| Fixed 2.0 mm Injector UHP Quartz Torch          | 1    | N8152428 |
| Torch Cassette White                            | 1    | N8152432 |
| Torch Injector Nut                              | 1    | N8152451 |
| Syngistix Single Cell Software Module           | 1    | N8150321 |
| CTFE Male Barb Fitting                          | 2    | N8145017 |
| CTFE Female Barb Fitting                        | 2    | N8145018 |
| Orange/Red 0.19 mm i.d. PVC pkg. 12             | 1    | N8152401 |
| Orange/Red MP2 PVC Flared 0.19 mm pkg. 12       | 1    | N8145195 |
| Autosampler Probe 0.15 mm                       | 1    | N0777221 |
|   |      |          |

Single Cell Automation Kit for NexION 1000/2000\*

Cell Kit (N8150032).

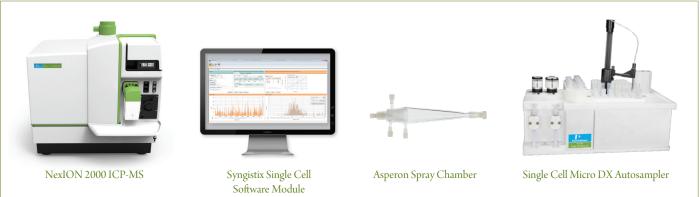
|   | QTY. | PART NO. |
|---|------|----------|
| Single Cell Kit for NexION 300/350              |      | N8140032 |
| Includes:                                       |      |          |
| Asperon Spray Chamber                           | 1    | N8152493 |
| Spray Chamber Drain Line                        | 1    | N8152494 |
| Spray Chamber Addition Gas Tee 1/4 Fitting      | 1    | N8142045 |
| MEINHARD <sup>®</sup> HEN Single Cell Nebulizer | 1    | N8142046 |
| Sample Line for MEINHARD® HEN Nebulizer         | 1    | N8152489 |
| UV Light Shield                                 | 1    | N8142047 |
| Quartz Injector 2 mm                            | 1    | N8145508 |
| Syngistix Single Cell Software Module           | 1    | N8150321 |
| CTFE Male Barb Fitting                          | 2    | N8145017 |
| CTFE Female Barb Fitting                        | 2    | N8145018 |
| Orange/Red 0.19 mm ID Flared PVC pkg. 12        | 1    | N0773111 |
| Autosampler Probe, 0.15 mm                      | 1    | N0777221 |
|   |      |          |

Make-up Gas Mass Flow Controller **Upgrade for NexION** 

W1028686

#### Single Cell Automation Kit for NexION 300/350\* N8140039

\*Includes Single Cell Micro DX Autosampler. Does not include Single



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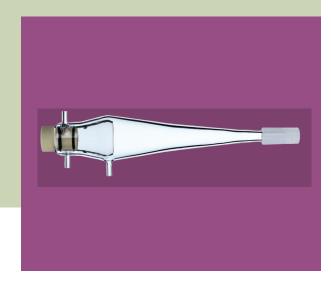
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Cell Kit (N8140032). \*Includes Single Cell Micro DX Autosampler. Does not include Single

N8150039

PerkinElmer Asperon<sup>™</sup> Spray Chamber: Delivering "Intact Individual Cells" to the ICP-MS Plasma

## **ICP-Mass Spectrometry**



#### Introduction

Single Cell ICP-MS (SC-ICP-MS) is a technique that allows for the analyses and quantification of metal content in an individual cell. This technique can be used to quantify the uptake and bioaccumulation of metals and metal nanoparticles in to cells, as well as the intrinsic metals within the cells themselves which can be a measure of metabolomic changes related to cell stress or lifecycle. SC-ICP-MS is able to give information on:

- Metal content per cell
- Metal distribution in the cell population
- Number of cells containing metal or metal nanoparticles
- Number of nanoparticles per cell

The experience and expertise of the scientists at PerkinElmer was used to develop and optimize all of the parameters required to properly handle cells and deliver them individually and intact to the ICP-MS. The SC-ICP-MS package includes:

- Single Cell micro flow autosampler
- Single Cell kit (Asperon<sup>™</sup> spray chamber, high efficiency nebulizer and connections)
- Syngistix<sup>™</sup> Single Cell Application Module Software

This technical note explains methods for Single Cell - ICP-MS system validation. Optimization of sample flow rate for optimal cell transport efficiency into the plasma, quantification of the mass of metal per cell using a standard reference material, and comparison of total digested metal in a sample compared to manufactures data.

For information related to sample preparation or workflow, please consult white paper: Single Cell ICP-MS Analysis: Quantification of Metal content at the cellular level<sup>1</sup>.

#### **Methods**

#### **ICP-MS Instrumental Conditions**

All analyses were carried out on a PerkinElmer NexION® ICP-MS series using two types of spray chambers: baffled cyclonic and Asperon<sup>™</sup>. The conditions used for both spray chambers are shown in Table 1.

#### Table 1. ICP-MS Conditions for Acid-Digested Beads and SC-ICP-MS.

| Parameter                                   | ICP-MS   | SC-ICP-MS                           |  |  |
|---|--|-------------------------------------|--|--|
| Spray Chamber                               | Baffled Cyclonic   | Asperon™                            |  |  |
| Nebulizer                                   | Glass Concentric   | High Efficiency<br>Glass Concentric |  |  |
| Injector                                    | 2 mm Quartz  | 2                                   |  |  |
| RF Power (W)                                | 1600 W   | 1600 W                              |  |  |
| Spray Chamber Path                          | Cyclonic   | Linear Pass                         |  |  |
| Neb Gas Flow<br>(mL min <sup>-1</sup> )     | 0.92   | 0.32                                |  |  |
| Make Up Gas<br>(mL min <sup>-1</sup> )      | 0  | 0.7                                 |  |  |
| Sample Flow Rate<br>(mL min <sup>-1</sup> ) | 0.283  | 0.015                               |  |  |
| Sample Required For<br>Analysis (µL)        | 800-1000   | 100-200                             |  |  |
| Elements                                    | <sup>140</sup> Ce, <sup>151</sup> Eu, <sup>153</sup> Eu, <sup>165</sup> Ho, <sup>175</sup> Lu, <sup>197</sup> Au |                                     |  |  |



Polymer beads (Fluidgem, USA): Polymer beads laced with lanthanide metals (<sup>140</sup>Ce, <sup>151</sup>Eu, <sup>153</sup>Eu, <sup>165</sup>Ho and <sup>175</sup>Lu) were used as a suitable reference material due to the similarity in size (2.5  $\mu$ m) and density (1.05 g/cm<sup>3</sup>) to cells. The presence of lanthanides in the beads enables them to be measured using SC-ICP-MS. Although the size cut-off for the baffled cyclonic spray chamber is in the 1-5 um range,<sup>2,3</sup> the transport of these larger beads (2.5  $\mu$ m) is low, as illustrated later in Figure 2. The beads were supplied at a concentration of 330,000 beads per mL and diluted 10 fold for analysis. The mass of metal per bead can be found in Table 2.

#### Table 2. Supplier information on lanthanide laced polystyrene beads.

| From Supplier |                        |                   |  |  |  |
|---------------|------------------------|-------------------|--|--|--|
| Element       | Atoms Per Bead (± 15%) | Mass (ag) (± 15%) |  |  |  |
| Ce 140        | 19.9E6                 | 4626.26           |  |  |  |
| Eu 151        | 11.3E6                 | 2833.38           |  |  |  |
| Eu 153        | 12.0E6                 | 3048.75           |  |  |  |
| Ho 165        | 7.6E6                  | 2082.32           |  |  |  |
| Lu 175        | 9.8E6                  | 2847.82           |  |  |  |

Standards for SP-ICP-MS and SC-ICP-MS: Standards of 1, 2 and 3 ppb <sup>140</sup>Ce, <sup>151</sup>Eu, <sup>153</sup>Eu, <sup>165</sup>Ho and <sup>175</sup>Lu were prepared for measuring the mass of metals in the polystyrene beads. All standards for SC-ICP-MS were prepared in ultra-pure water. The transport efficiency was determined with the 60 nm Au NPs (NIST 8013) at a concentration of 50,000 part. mL<sup>-1</sup>.

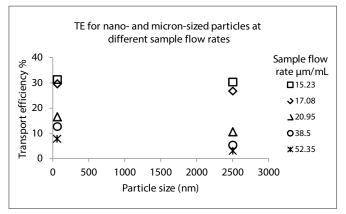
Digestion of polystyrene beads: Digestion was accomplished by placing 5 mL of the bead suspension into a Teflon digestion vessel with 5 mL of hydrogen peroxide (Optima grade) and 10 mL of nitric acid (Optima grade). The mixture was allowed to sit for 10 minutes to allow gasses to be released from any initial reactions before the vessels were sealed. The beads were then digested in a Titan MPS<sup>™</sup> Microwave (PerkinElmer), following the program in Table 3. After they had cooled, the samples were diluted to 2% acid for analysis. Standards of 10, 50, 100 and 200 ppb Lu, Eu, Ho and Ce were matrix-matched to the samples for ICP-MS analysis. Ge and In were spiked into the samples as internal standards.

#### Table 3. Conditions for microwave acid digestion of polystyrene beads.

| Stage | Temperature<br>(°C) | Pressure<br>(bar) | Ramp<br>(min) | Ramp<br>(min) | P<br>(%) |
|-------|---------------------|-------------------|---------------|---------------|----------|
| 1     | 150                 | 70                | 2             | 5             | 60       |
| 2     | 190                 | 75                | 2             | 10            | 80       |
| 3     | 210                 | 80                | 2             | 15            | 90       |
| 4     | 50                  | 80                | 1             | 10            | 0        |
| 5     | 50                  | 0                 | 0             | 0             | 0        |

#### **Gas and Sample Flows Optimization**

The make-up and nebulizer gas flows and sample flow rate had to be optimized to allow for equal transport of nano- and micron sized objects through the introduction system. Figure 1 shows the transport efficiency for nano- and micron-sized objects through the introduction system for different sample flow rates. It can be seen that as the sample flow rate decrease the transport efficiency for both nano- and micron sized objects increases and the difference between their transport gets less pronounced with a transport efficiency of about 31 % for both the 60 nm Au NIST standards and the lanthanide doped micron beads (Fluidigm). The optimized conditions for this system can be seen in Table 1.



*Figure 1.* Optimization of sample flow rates through the introduction system to maximize the transport of nano- and micron-sized objects into the plasma.

#### Transport Efficiency Validation: Baffled Cyclonic vs Asperon<sup>™</sup> Spray Chamber

A comparison study of the transport efficiency of nano- and micron-sized particles between the baffled cyclonic and Asperon<sup>™</sup> spray chambers is shown in Figure 2. The systems were both optimized for maximum intensities while keeping oxide and double charge formation below 2.5% (Table 1). It can be seen in Figure 2 that both introduction systems transport a sufficient amount of NPs (NIST 8013 60 nm Au NPs) into the ICP-MS to provide a statistically significant measure of the mean and standard deviation of the NPs (either in diameter or mass per NP) and particle number concentration showing that both systems work equally well for nanoparticles. However the number of micron sized particles transported by the baffled cyclonic spray chamber is low, with only a few beads being analysed compared to the Asperon<sup>™</sup> chamber, where a significant number of beads were counted.

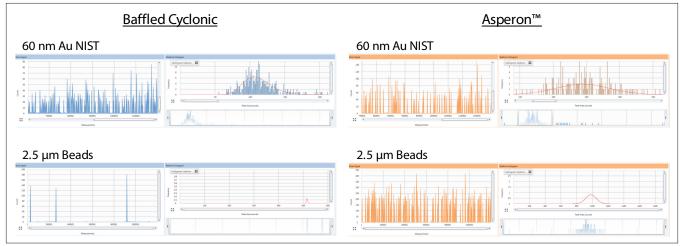


Figure 2. Real time screen shots comparing the number of Au NIST 60 nm NPs and 2.5 µm polystyrene beads making it to the plasma for the baffled cyclonic and Asperon spray chambers.

As shown in Table 4, the TEs for the 2.5 µm polystyrene beads and 60 nm Au NPs in the baffled cyclonic spray chamber are  $0.04 \pm 0.02$  % and  $2.42 \pm 0.06$  %, respectively, which is significantly different (p < 0.05, Student's t-distribution). This translates to approximately  $3.5 \pm 1.9$  beads per minute reaching the plasma in a suspension containing 33,000 beads mL<sup>-1</sup> and  $342.3 \pm 8.7$  NPs per minute for a suspension containing 50,000 NPs mL<sup>-1</sup>. Clearly the cyclonic spray chamber is not suitable for single cell analysis. In contrast the Asperon<sup>TM</sup> spray chamber has a TE which is not significantly different for the beads or the NPs:  $31.33 \pm 2.54$  % and  $30.31 \pm 1.85$  %, respectively. This corresponds to  $229.5 \pm 19.5$  NPs and  $208.3 (\pm 12)$  micron sized beads for suspensions containing 50,000 particles mL<sup>-1</sup> and 33,000 beads mL<sup>-1</sup> respectively.

# Quantitative Validation: Measurement of Metal Mass per Bead

The polymer beads are doped with lanthanide metals ( $^{140}Ce$ ,  $^{151}Eu$ ,  $^{153}Eu$ ,  $^{165}Ho$  and  $^{175}Lu$ ) at the concentrations shown in Table 5, as

supplied by the manufacturer. The mean mass of metal per bead as measured by SC-ICP-MS can also be seen in Table 5. Comparing the experimental data with the supplied concentrations, there is no statistical difference (all p values >> 0.05) between the mean mass provided by the supplier and those quantified using SC-ICP-MS. The number of beads per mL was measured to be 34,821 (± 661.7) having no statistical difference to the manufactures value of 33,000 (± 1650).

## $\it Table$ 4. A comparison of the number of nano and micron sized particles entering the ICP-MS and subsequent TEs.

| Spray Chamber   | Baffled<br>Cyclonic | Asperon™       |
|---|---------------------|----------------|
| TE 60 nm NIST (%)   | 2.42 (±1.85)        | 31.33 (± 2.54) |
| Number of 60 nm NIST NPs<br>Measured in a One Minute Scan | 342.3 (± 8.7)       | 229.5 (±19.1)  |
| TE 2.5 um beads (%)                                       | 0.04 (± 0.02)       | 30.31 (±1.85)  |
| Number of 2.5 um Beads<br>Measured in a One Minute Scan   | 3.5 (± 1.9)         | 208.3 (±12)    |

Table 5. Metal Content per Bead and Bead Concentration: A Comparison of SC-ICP-MS vs. Certificate Values.

| Element                | Data Provided by Supplier |              |              |       | Measure | ed by SC-IC | P-MS (Ag P | er Bead) |       |
|------------------------|---------------------------|--------------|--------------|-------|---------|-------------|------------|----------|-------|
|                        | Atoms Per<br>Bead (±15%)  | Mass<br>(ag) | Size<br>(nm) | 1     | 2       | 3           | 4          | Average  | STDEV |
| Ce 140                 | 19.9E6                    | 4626         | 109.7        | 4250  | 4561    | 4750        | 4699       | 4632     | 95    |
| Eu 151                 | 11.3E6                    | 2833         | 101.1        | 2961  | 3012    | 3123        | 3075       | 3043     | 61.6  |
| Eu 153                 | 12.0E6                    | 3049         | 103.6        | 2904  | 33240   | 3114        | 3061       | 3080     | 120.4 |
| Ho 165                 | 7.6E6                     | 2082         | 76.8         | 2157  | 2228    | 2576        | 2354       | 2329     | 159.3 |
| Lu 175                 | 9.8E6                     | 2848         | 82.1         | 2921  | 2228    | 2965        | 2982       | 2889     | 68.8  |
| Number of<br>Particles |                           |              |              | 34323 | 33145   | 34696       | 34821      | 34246    | 661.7 |

The total metal content of the bead suspension was established after acid digestion and was found not to be statistically different from those calculated from the mass per bead and bead number measured by SC-ICP-MS (Table 6).

#### Table 6. Total amount of metal in bead suspension after acid digestion.

| Element | Values From<br>Supplier (ppb) | Measured<br>Values (ppb) |
|---------|-------------------------------|--------------------------|
| Ce 140  | 152.67                        | 160.3 (7.4)              |
| Eu 151  | 93.50                         | 71.6 (7.6)               |
| Eu 153  | 100.61                        | 80.6 (8.0)               |
| Ho 165  | 68.72                         | 67.8 (8.4)               |
| Lu 175  | 93.98                         | 83.9 (8.1)               |

### Conclusion

This work has shown that the new, dedicated SC-ICP-MS introduction system (Asperon<sup>™</sup>) provides increased transport of micron-sized objects into the ICP-MS compared to traditional introduction systems. Coupled with the fast data acquisition capabilities of the NexION, the Asperon<sup>™</sup> has allowed for the quantification of masses from micron sized objects down to the attogram per bead level as well as providing accurate measurements of the number concentration of the beads per millilitre.

#### References

- 1. PerkinElmer Inc., Single Cell ICP-MS Analysis: Quantification of Metal Content at the Cellular Level, 2017
- Schaldach, G.; Berger, L.; Razilov, I.; Berndt, H., Characterization of a cyclone spray chamber for ICP spectrometry by computer simulation. *Journal of Analytical Atomic Spectrometry* 2002, 17, (4), 334-344.
- 3. Matusiewicz, H.; Slachcinski, M.; Almagro, B.; Canals, A., Evaluation of Various Types of Micronebulizers and Spray Chamber Configurations for Microsamples Analysis by Microwave Induced Plasma Optical Emission Spectrometry. *Chemia Analityczna* 2009, 54, (6), 1219-1244.

#### **SC-ICP-MS** Components

| Component                                   | Part Number<br>NexION 2000 | Part Number<br>NexION 3x0 |
|---|----------------------------|---------------------------|
| Single Cell Micro<br>Flow Autosampler       | N8150039                   | N8140039                  |
| Single Cell Kit                             | N8150032                   | N8140032                  |
| Syngistix Single Cell<br>Application Module | N8150321                   | N8150321                  |

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## **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<sup>™</sup> 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<sup>®</sup> 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

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



## 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<sup>™</sup> 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.

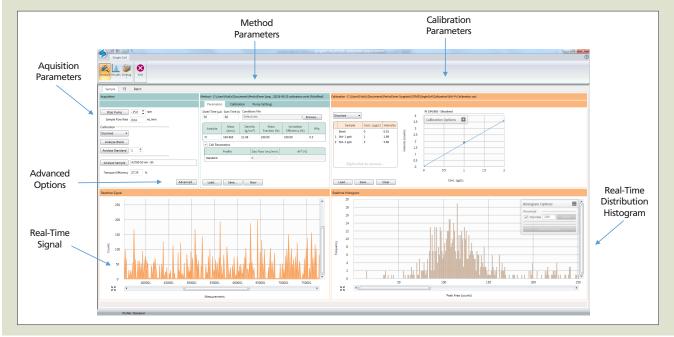


Figure 1. Analysis panel in Syngistix Single Cell Application Module.

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.

| 2<br>aly | sis Resu    | its Debug             |                             |                    |                              |                             |
|----------|-------------|-----------------------|-----------------------------|--------------------|------------------------------|-----------------------------|
| s        | ample       | TE Batch              |                             |                    |                              |                             |
| qui      | isition -   | [Untitled] [Modified] |                             |                    |                              |                             |
|          |             |                       |                             |                    |                              |                             |
|          | aset Fold   |                       |                             |                    |                              |                             |
| _        | rowse       |                       | ungistiv\ICPMS\SingleCell\D | atacet             |                              |                             |
| D        |             |                       |                             | Jusee              |                              |                             |
|          | A/S<br>Loc. | Sample ID             | Measurement<br>Action       | Method             | Sample Flow<br>Rate (mL/min) | Transport<br>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             |                              |                             |
|          |             |                       | Select Action               | Browse             |                              |                             |
| 9        |             |                       |                             |                    |                              |                             |
| 9<br>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.

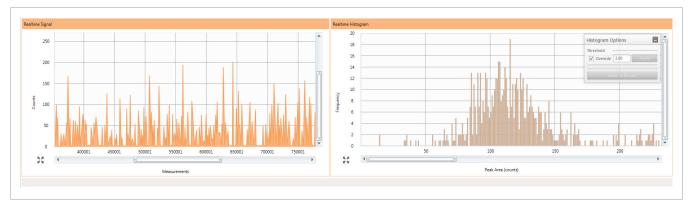


Figure 4. Snapshot of Analysis panel during data acquisition, showing the real-time signal (left) and frequency vs. peak area histogram (right).

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 guantification 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.

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## **ICP - Mass Spectrometry**

#### **Key Features:**

- Reliably delivers intact cells to the ICP plasma
- Consistently runs small-volume samples at micro flow rates
- Efficiently agitates samples prior to analysis, ensuring cells are suspended prior to analysis
- Decreases sample uptake and wash time
- Accommodates a wide range of sample racks and well plates

# Single Cell Micro DX Autosampler

The Single Cell Micro DX Autosampler is a microfluidic automation platform for biological samples. It is part of PerkinElmer's award-winning NexION® ICP-MS Single Cell Analysis System, which offers a first-to-market complete solution to quantitatively measure the metal content in individual cells, unveiling new capabilities to study intrinsic metals content and the uptake of dissolved (ionic) and nanoparticulate metals into cells. The NexION ICP-MS Single Cell Analysis System provides new insights into drug delivery, mobilization/immobilization of metal content, bioavailability, and bioaccumulation mechanisms.

The Single Cell Micro DX Autosampler enables single-digit microliter sample handling, cell resuspension through user-defined agitation protocol and accommodates most microwell plates. It gently agitates the sample, precisely and accurately loads the sample loop, and smoothly delivers the content of the loop to a microflow high efficiency nebulizer (HEN) at defined rates from 10-100 µL/min. It ensures reliable delivery of intact cells to the ICP plasma while minimizing sample uptake and wash time (Figure 1).

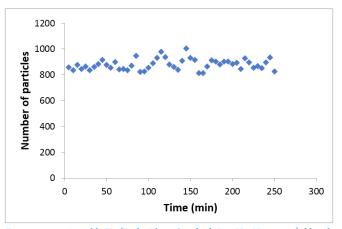


Figure 1. 50 nm Au gold NPs (PerkinElmer Standards Part No. N8151035) diluted at 100,000 particles per mL in UHP water simulating cells. A sample was measured every five minutes for 250 minutes (50 injections). Great stability with 877 ( $\pm$  4%) particles per injection.



## **Specifications**

#### Dimensions

- Height: 438 mm (17.25 in)
- Width: 452 mm (17.8 in)
- Depth: 222 mm (8.75 in)
- Weight: 13.6 kg (30 lbs)

#### **Power Requirements**

- 24V DC switching power supply, 8.3A (included)
- Input power: 100-240 VAC ± 10%, 50-60 Hz

### **Environmental Conditions**

- Ambient operating temperature: 15 °C to 35 °C
- Ambient operating humidity: 20 to 80% RH non-condensing

#### **Minimum PC Specification**

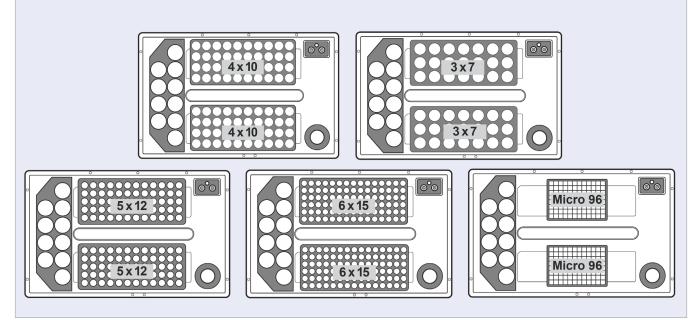
• All versions of Microsoft® Windows® including Vista, Windows® 7 and Windows® 10

#### **Electrical Connections**

- RS-232 with USB and IEEE-488 options
- 3 External Switches In/Out

### Sample Racks

The Single Cell Micro DX Autosampler can hold a wide range of sample racks for both large- and small-volume vials.



*Figure 2.* Examples of available rack configurations.

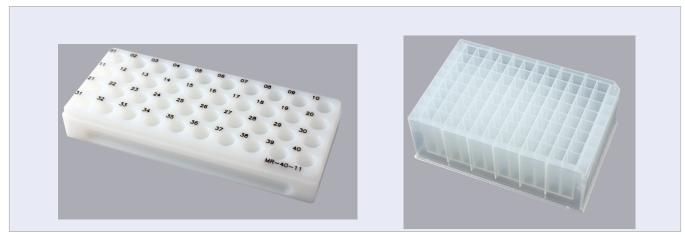


Figure 3. Available rack options - Left: 40-Position Micro Standards Rack; Right: 96-Well 2 mL Microtiter Plate Square Well.

## **Ordering Information**

| Description  | Part No. |
|--|----------|
| Single Cell Automation Kit for NexION 1000/2000 ICP-MS           | N8150039 |
| Single Cell Automation Kit for NexION 300/350 ICP-MS             | N8140039 |
| 1.0 mL PFA Vials Pkg. 10   | N0777403 |
| 2.0 mL PFA Vials Pkg. 10   | N0777404 |
| 21-Position Micro Rack 14 mm ID Qty. 1                           | N0777229 |
| 40-Position Micro Standards Rack for 28 mm Vials Qty. 1          | N8152541 |
| 96-Well, 2 mL Microtiter Plate Square Well, Polypropylene Pkg. 5 | N0777239 |
| 96-Well, 500 µL Microtiter Plate, Polystyrene Pkg. 5             | N8145354 |

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