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Inductively Coupled Plasma Mass Spectrometry (ICP-MS)

*Hui Chen, PhD
MSC, RRC, UIC*

HUMAN HEALTH • ENVIRONMENTAL HEALTH

Jan 24th, 2019

UIC ICP MS introduction

- ICP MS Principle
- Unique Features of Nexlon 2000s
- Assays Currently Available on 2000s
- Assays in Development on 2000s

What is ICP-MS?

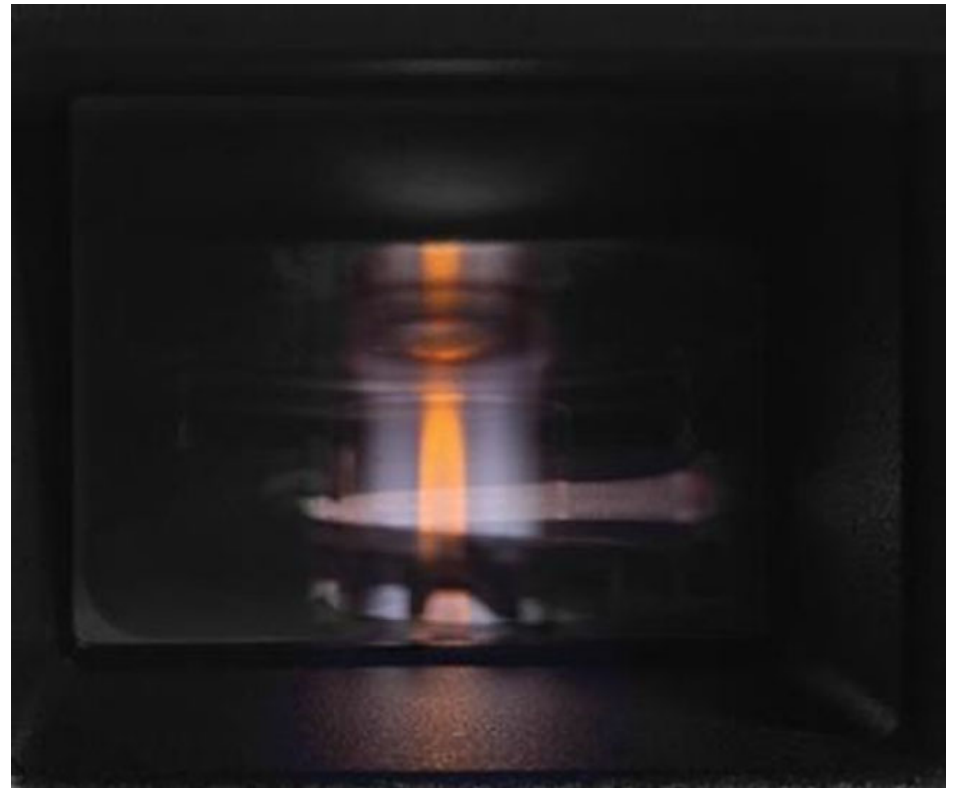
- Technique for trace elemental analysis
 - Commercially available since 1983
- Detection limits in the ppq-ppb range for most elements
- Ability to determine isotope ratios
- Ability to determine elements in single particles
- Ability to determine elements in single cells



NexION 2000s ICP-MS

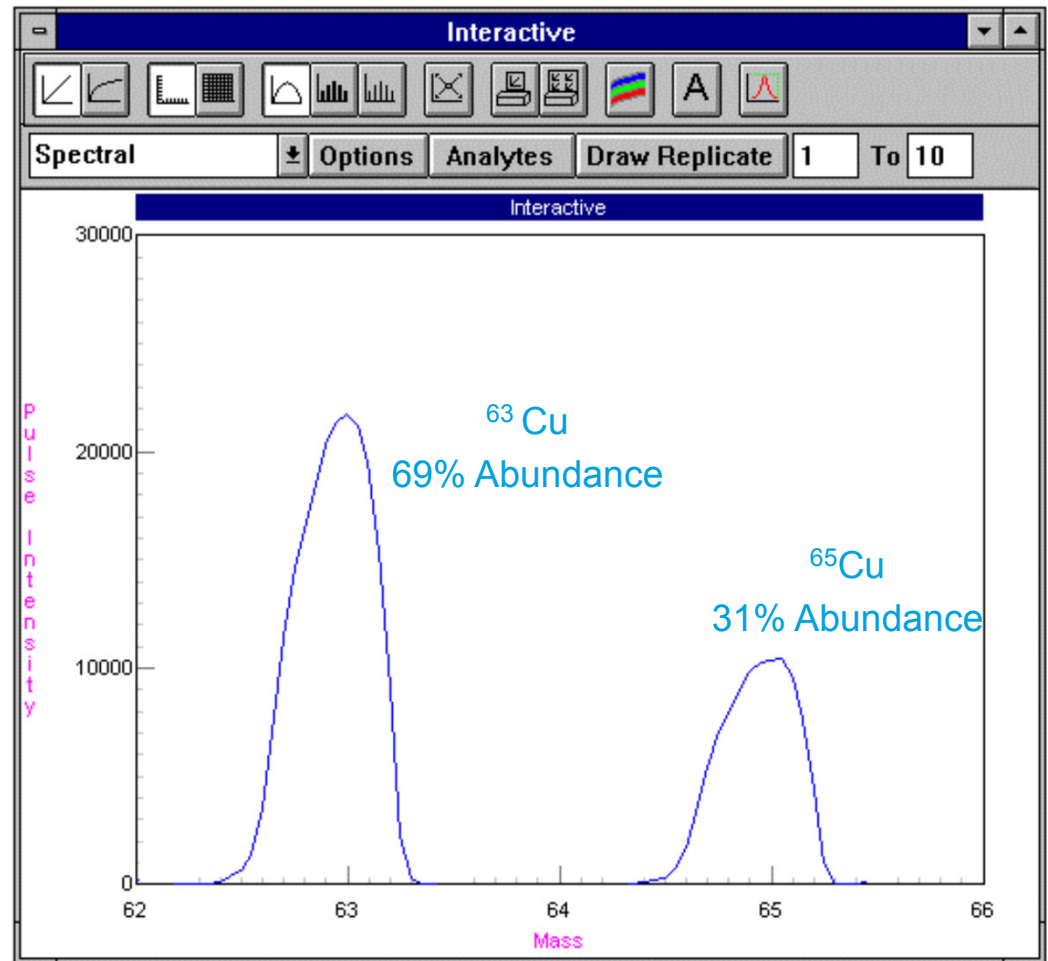
How Does ICP-MS Work?

- Elements in sample are volatilized and ionized by argon ICP (Inductively Coupled Plasma)
- Ions are focused into a quadrupole mass spectrometer
- Ions for each element are “counted” by the detector
- Instrument is calibrated daily by analysis of solutions of known elemental concentration



Isotopes and Mass Spectra

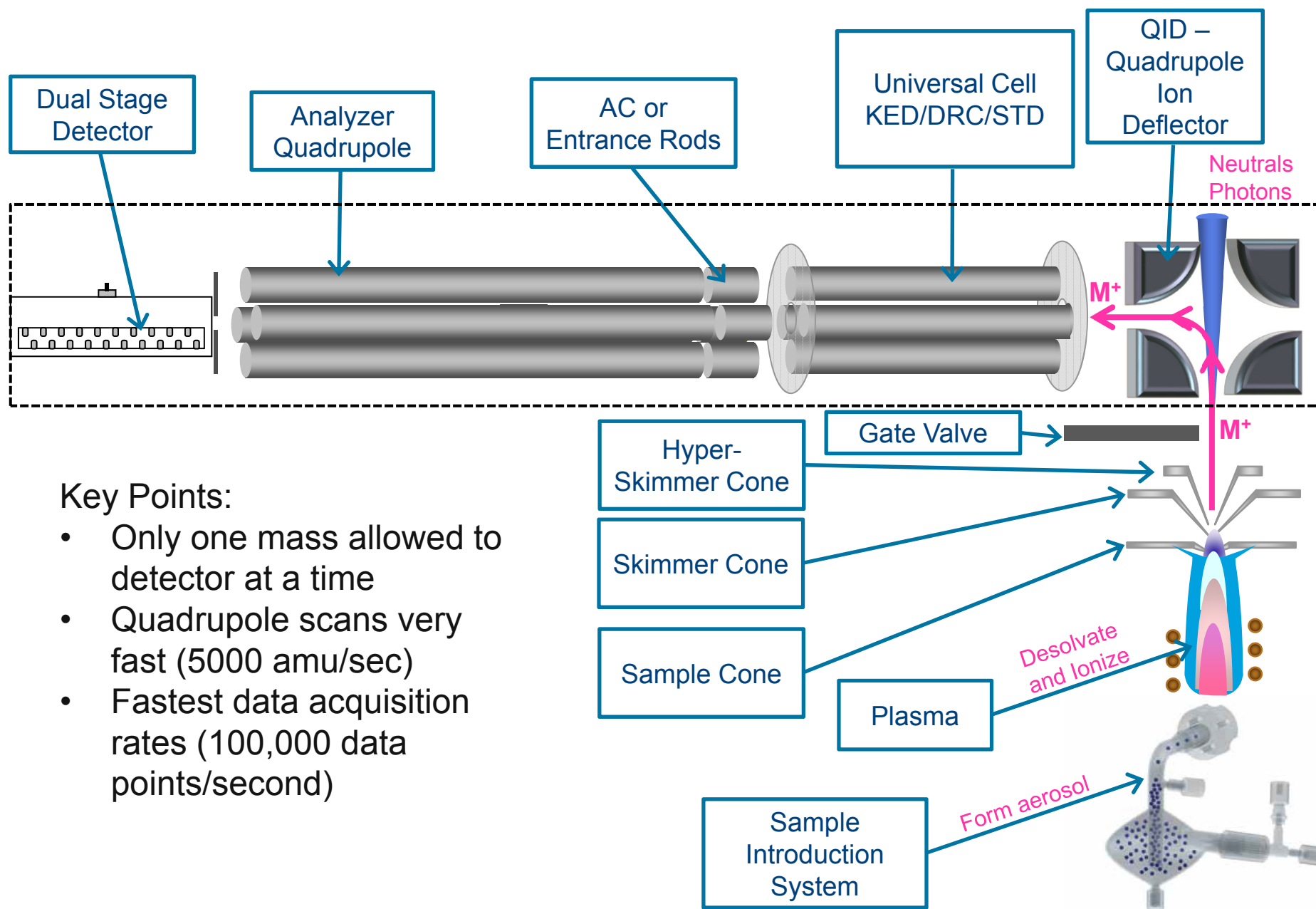
- Isotopes of an element differ in the number of neutrons in the nucleus
- Cu Atomic Number 29
 - ^{63}Cu has 34 neutrons
 - ^{65}Cu has 36 neutrons
- The mass spectrum of Cu consists of two peaks of the above isotopes and their relative intensities will be a function of the isotopic abundance



Feature of Nexlon 2000s

- *A dedicated SMARTintro™ High Purity sample-introduction module minimizes contamination and delivers low background equivalent concentrations (BECs))*
- *Built-in cold plasma capabilities which, combined with Reaction mode, deliver PPQ detection limits*
- ***Three quadrupoles, three gas channels, and three modes of operation combine to offer better interference removal, delivering better detection limits/improved data accuracy***
- ***The industry's fastest data acquisition speed on the market (100,000 points/sec) to handle any particle size***
- *A new solid-state RF generator with revolutionary LumiCoil™ technology – first ICP-MS RF coil that requires no maintenance or cooling*
- ***Triple Cone Interface with Quadrupole Ion Deflector, delivering no maintenance beyond the cones***
- *Small footprint to minimize bench space*
- *Syngistix™ software provides an intuitive interface that mirrors your workflow, with left-to-right, icon-based navigation that guides you through your analysis. Plus, it's a cross-platform solution, easing the transition from technique to technique*
- *Built-in Radian™ Remote Monitoring Service provides real-time monitoring of your NexION system's diagnostic parameters, enhancing laboratory productivity*

How Does It Work - Ion Path of the NexION 2000



Universal Cell

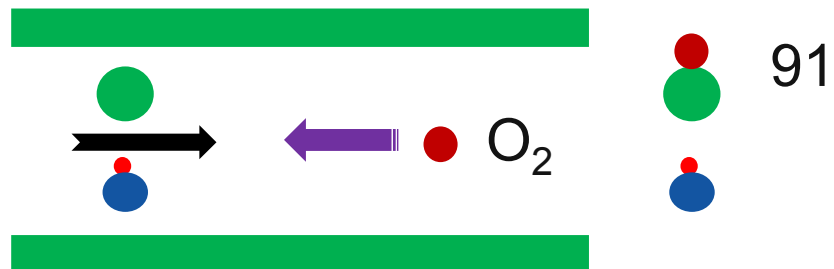
STD



KED



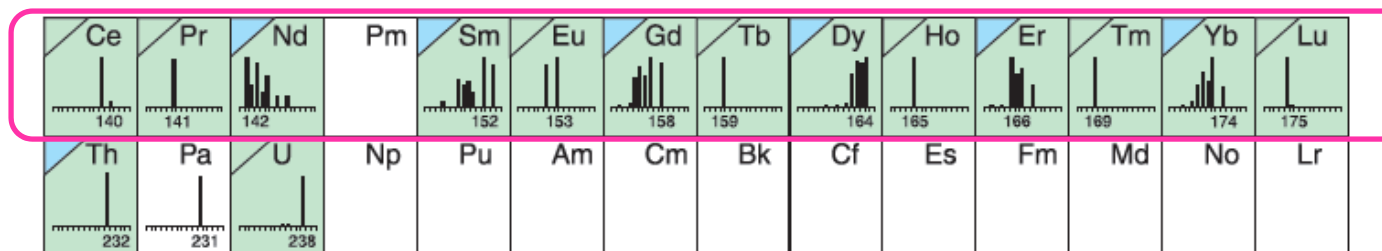
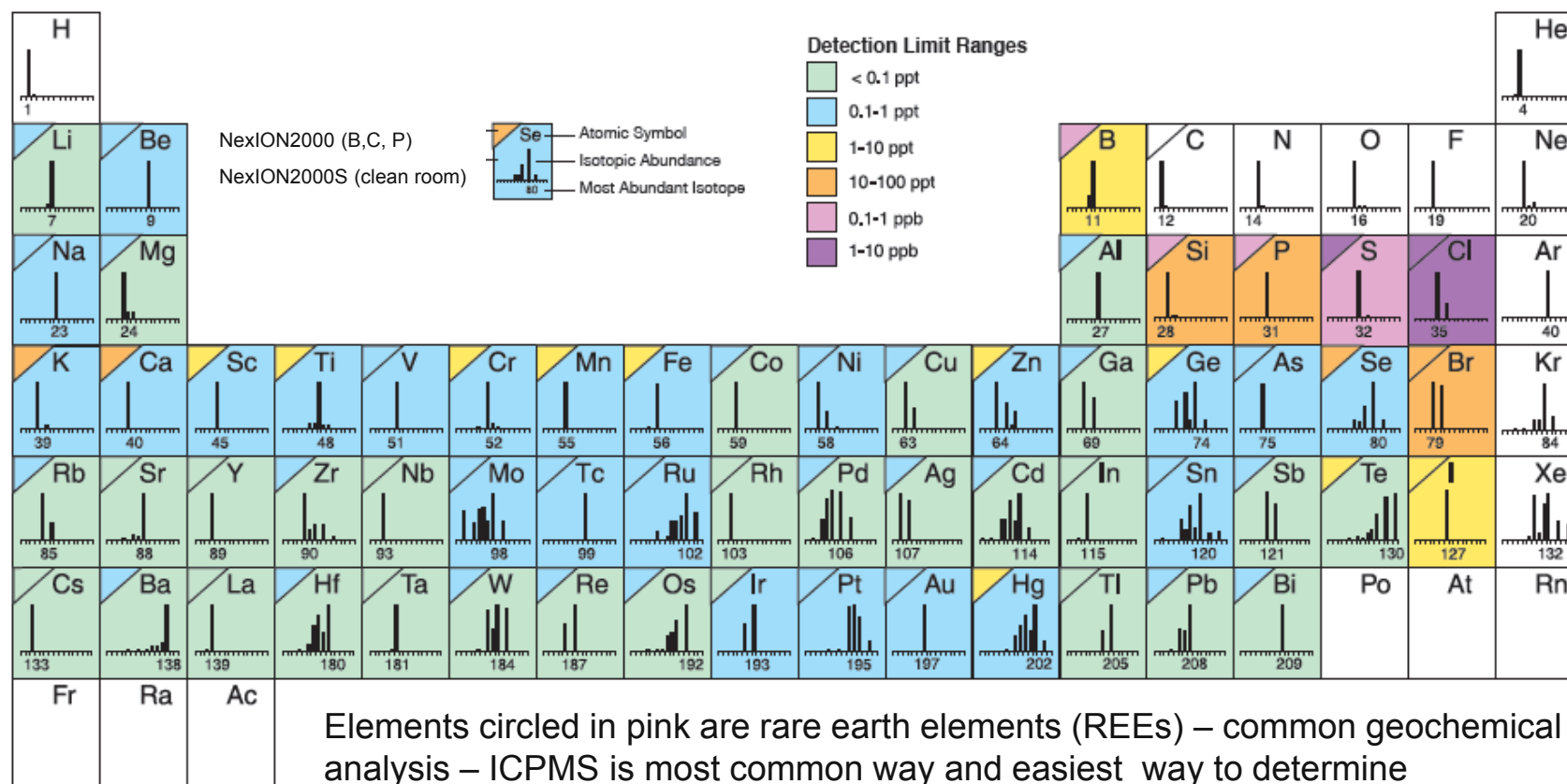
DRC



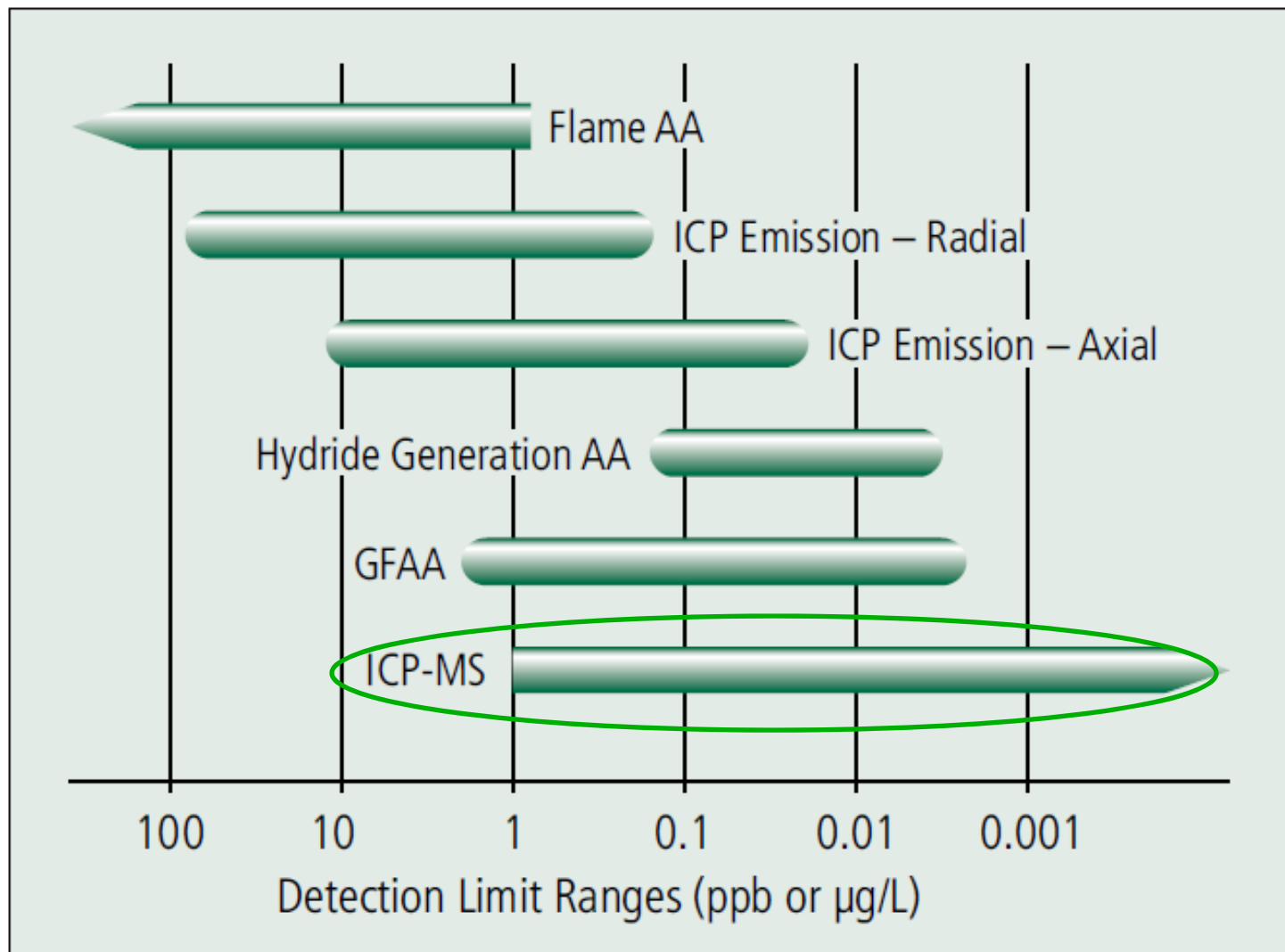
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What Elements Can Be Determined by ICP-MS?

If the box is shaded it can be determined!



Comparison of Detection Limit Ranges



Analytical Working Range Rivals ICP-OES...

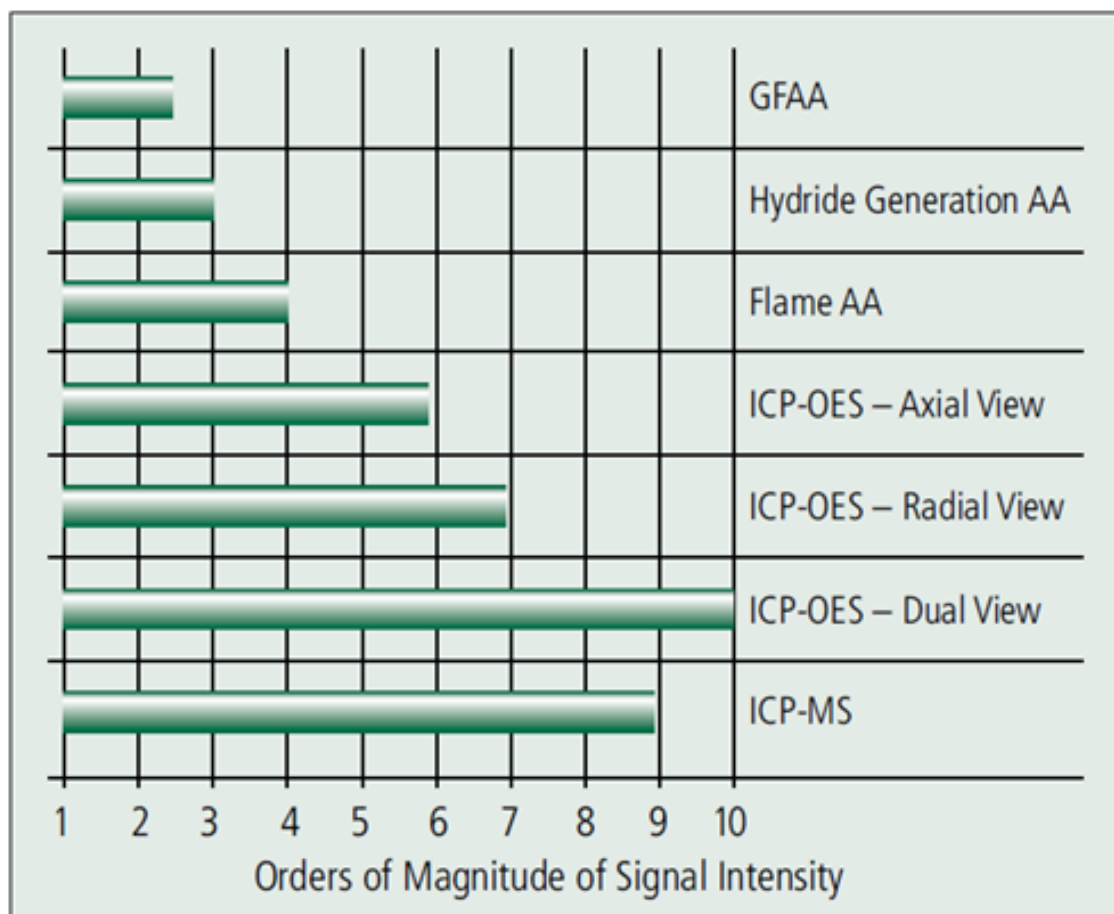
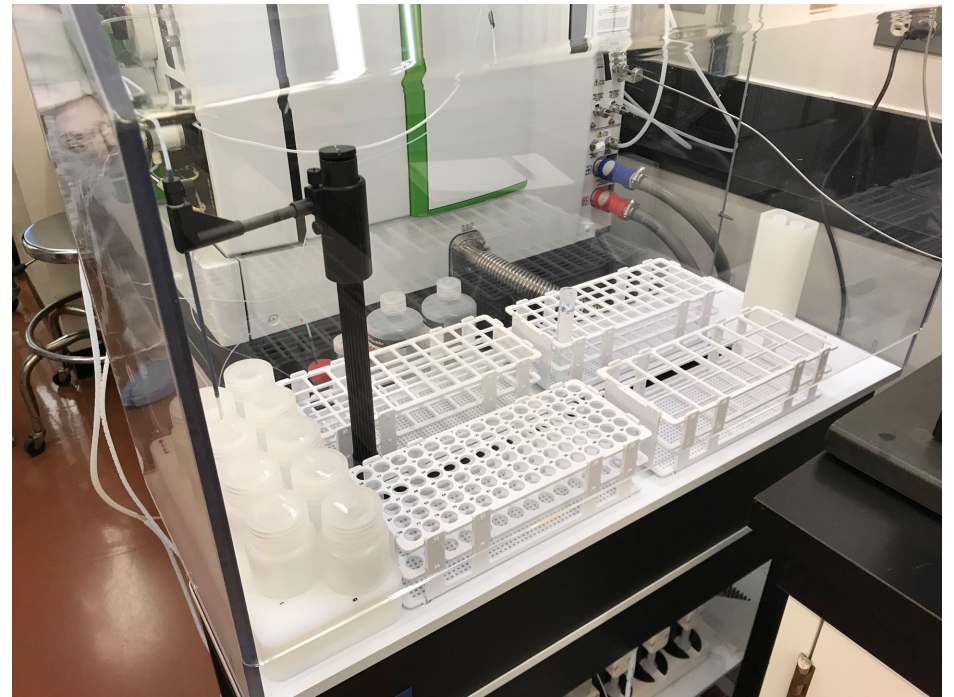
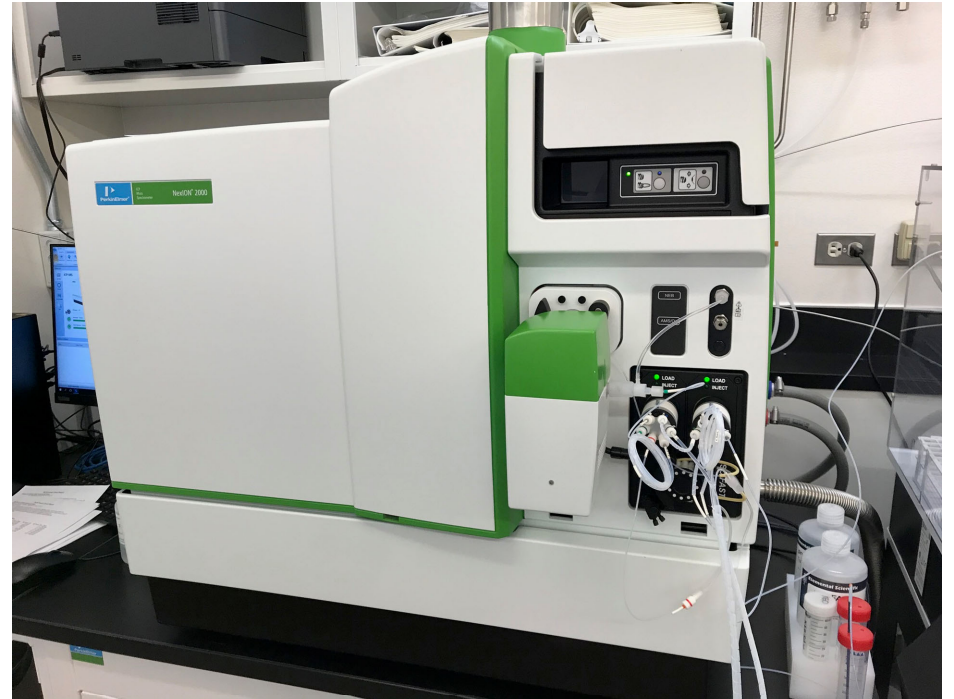


Figure 7. Typical analytical working ranges for the major atomic spectroscopy techniques.

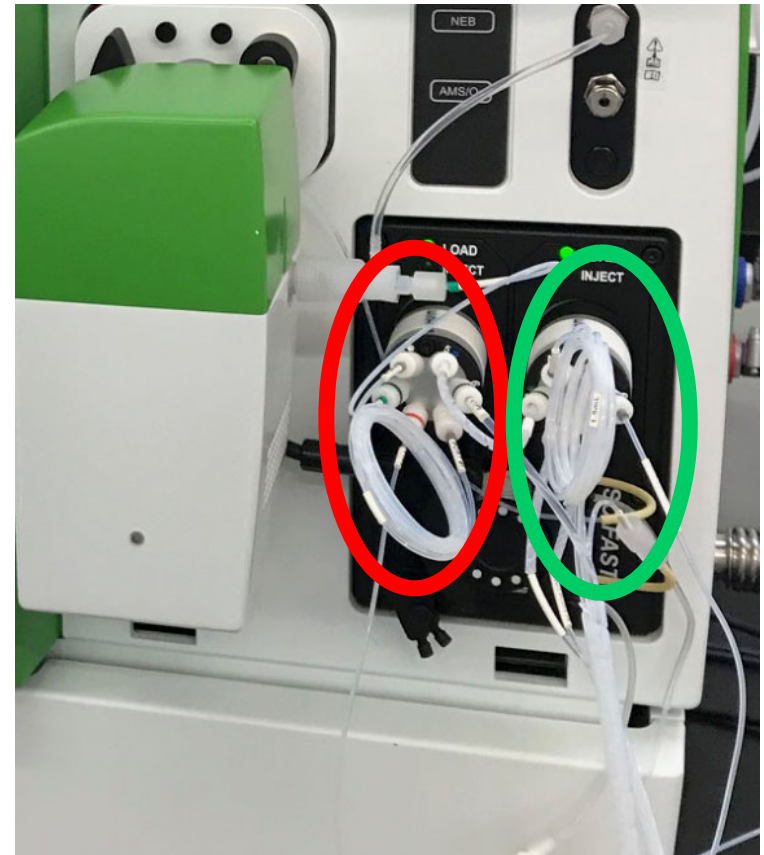
NexION 2000 can use Extended Dynamic Range (EDR) Mode to extend linear working ranges for high concentration elements

Nexlon 2000s in clean room of NCF



NexION 2000 Productivity Enhancements - PrepFAST

- Automated Standards Preparation
 - Automatic dilution from 1-2 Stock Solutions
- Automated Dilutions
 - Up to 400-fold dilutions
 - Pre-determined or based on QC results
- Contamination Control
 - System made of inert PFA
 - Reduced contamination
 - Reduced carryover
- High Throughput
 - 2 load/injector valves



Save Time on Analysis

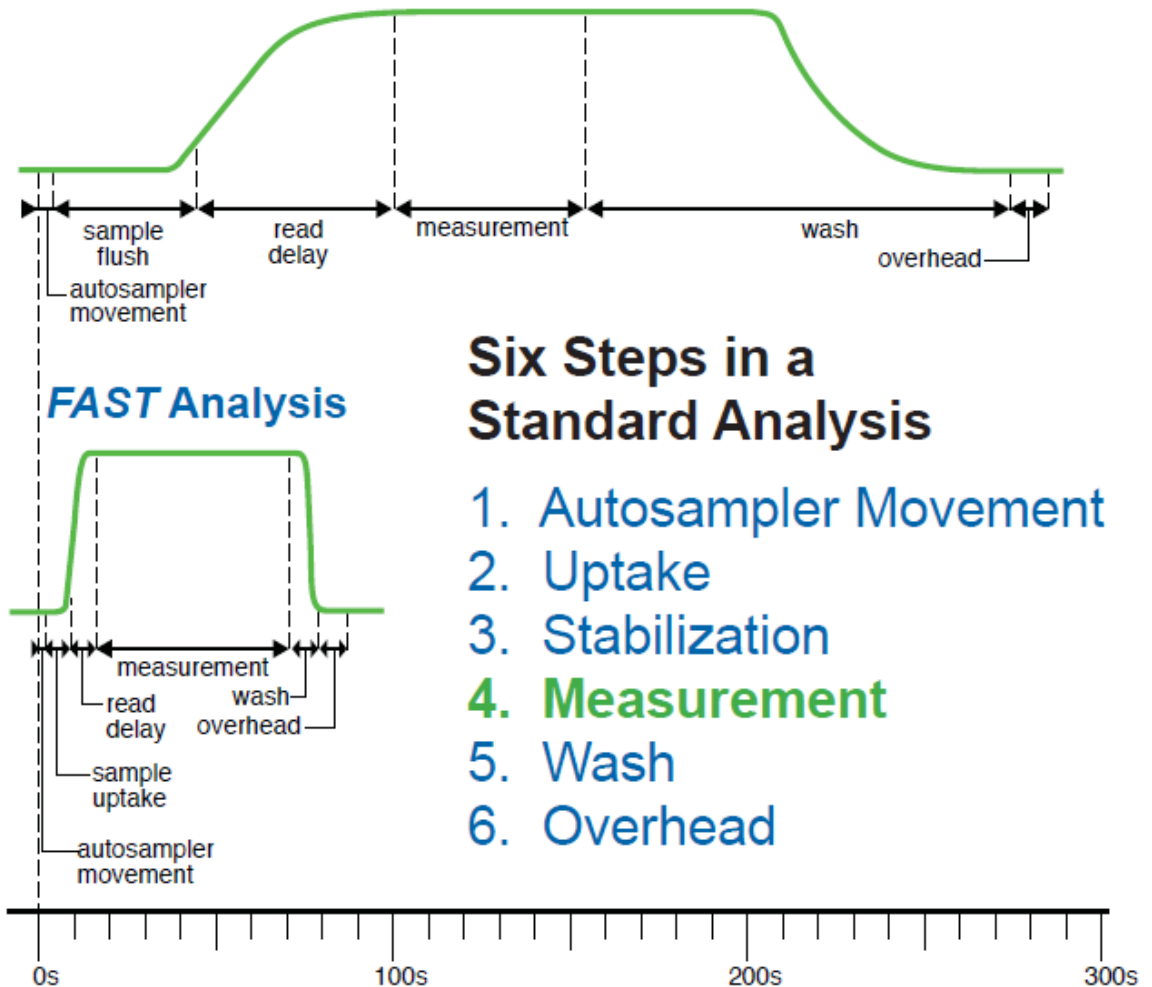
FAST is:

- Reliable, high-throughput, automated sample introduction system

Benefits of FAST:

- ~ 3 times faster than conventional autosampler systems.
- Handles even the most demanding high-matrix samples.

Normal Analysis



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Save Time on Preparation

prepFAST for NexION 2000 Features

Quantitative Analysis Method - C:\Users\Public\Documents\PerkinElmer Syngistix\ICPMS\Method\5x myMethod_NexION 2000.r

Timing | Processing | Equation | Calibration | **Sampling** | Devices... | QC... | Report | Notes

Peristaltic Pump

	Time (sec)	Speed (+/- rpm)
Sample Flush	0	18.0
Read Delay	40	18.0
Analysis		18.0
Wash	40	18

☒ Peristaltic Pump Under Computer Control

Auto Diluter

Dil. Factor: 5 Dil. To Vol. (mL): 10

1st. Dil. Pos: 1 Probe Purge Pos.: 10

Sampling Device

(None)

ESI prepFAST

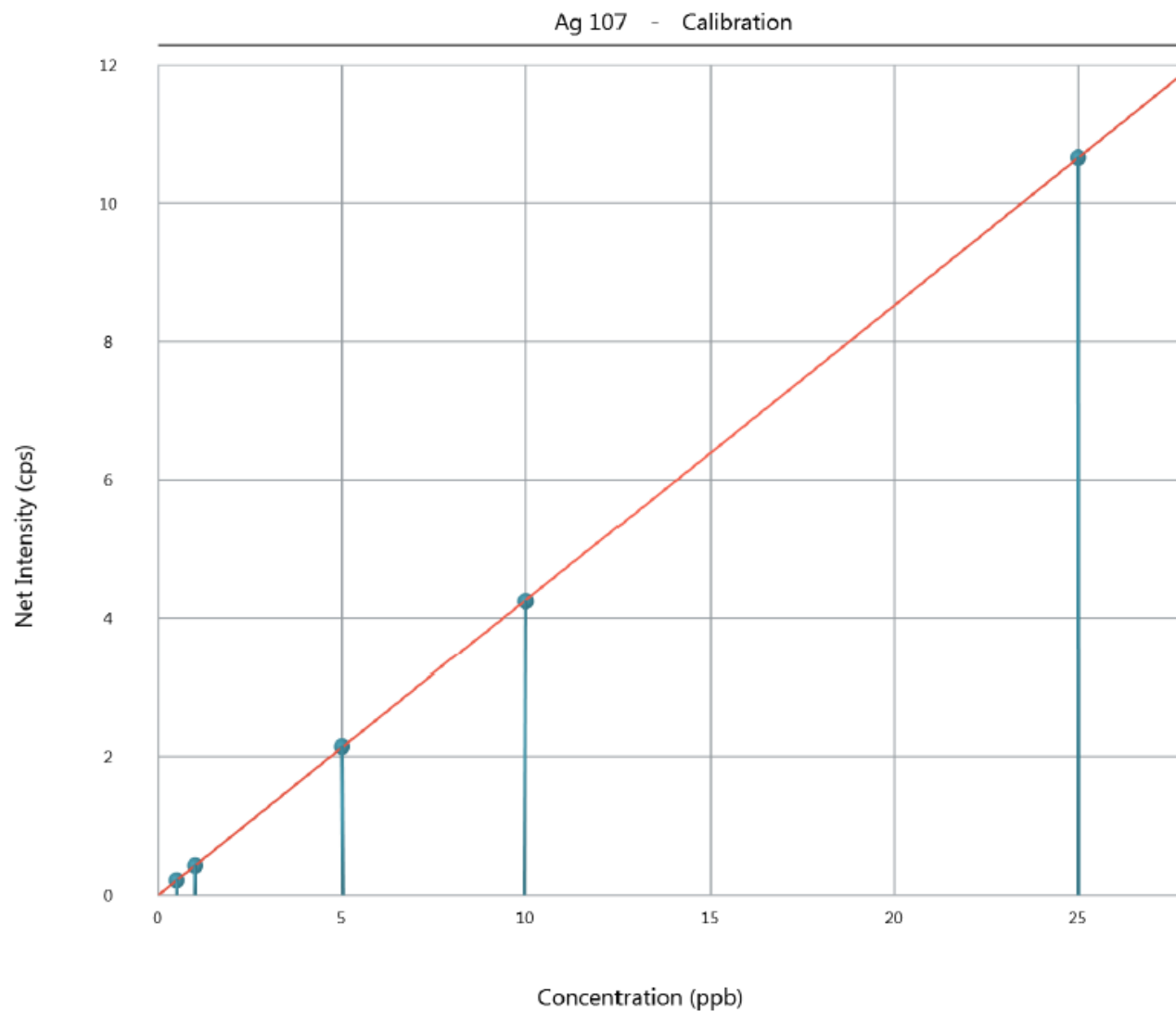
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	Standard	Solution ID	A/S Loc.	Wash Override (sec)
1	Blank	Blank	1	
2	Standard 1	5ppb	2100	
3	Standard 2	25ppb	2020	
4	Standard 3	100ppb	2005	
5	Standard 4	250ppb	2002	

Autocalibration

Autocalibrate from one or more standards with ease by entering the location of the standard, dilution factor, and concentration of elements in the standard. Syngistix will automatically calculate the concentrations of elements for each calibration point.

Ag107 Autocalibration Curve From Stock Standard



Save Time on Analysis

The screenshot displays the Syngistix software interface. The top menu bar includes 'Syngistix' and 'Applications'. Below this, there are several icons for different functions: Control Diagnostics, SmartTune, Conditions, LogBook, Method (highlighted with a red box), Sample, Dataset, Reporter, Realtime, Interactive, CalibView, Scheduler, and Review. The main window shows a 'Quantitative Analysis Method' configuration for 'C:\Users\Public\Documents\PerkinElmer Syngistix\ICPMS\Method\5x myMethod_NexION 2000.mth'. The 'Auto Diluter' section is highlighted with a red box, showing a 'Dil. Factor' of 5. The 'Sampling Device' is set to 'ESI prepFAST'. A table for the 'Peristaltic Pump' is also visible.

	Time (sec)	Speed (+/- rpm)
Sample Flush	0	18.0
Read Delay	40	18.0
Analysis		18.0
Wash	40	18

Below the main window, a 'Manual Batch' dialog box is open, showing a table of batch analysis data. The table has columns for Batch Index, A/S Loc., Batch ID, Sample ID, Measurement Action (*), Method (*), and Description. Rows 4, 7, and 8 are highlighted with red boxes.

Batch Index	A/S Loc.	Batch ID	Sample ID	Measurement Action (*)	Method (*)	Description
1	1	1	Sample1	Run Sample	5x mymethod.mth	
2	101	2	Sample2	Run Blank, Stds. and Sample	5x mymethod.mth	
3	102	3	Sample3	Run Sample	5x mymethod.mth	
4	103	4	Sample4	Run Diluted Sample	5x mymethod.mth	
5	201	5	Sample5	Run Sample	20x mymethod.mth	
6	202	6	Sample6	Run Sample	20x mymethod.mth	
7	203	7	Sample7	Run Diluted Sample	20x mymethod.mth	
8						
9						

Sample Autodilution

A dilution factor can be independently defined for each sample in the Sample List. Syngistix automatically corrects the sample results and reports the undiluted concentration in each vial.

Save Time on Analysis

Automated Over-range Dilutions

Syngistix Applications

Control Devices SmartTune Conditions LogBook Method Sample Dataset Reporter

Instrument Optimize Analyze

Samples - C:\Users\vm\Documents\PerkinElmer Syngistix\ICPMS_vm\Sample\pre

Manual Batch

Analyze Batch Sample Template... Summary... Build Run List...

☐ Use Manual Sampling (No autosampler)

Batch Index	A/S Loc.	Batch ID	Sample ID	Measurement Action (*)	Method (*)	Description	Sample Type (*)
1	1	1	Sample1	Run Sample	5x mymethod.mth		Sample
2	101	2	Sample2	Run Blank, Stds. and Sample	5x mymethod.mth		Sample
3	102	3	Sample3	Run Sample	5x mymethod.mth		Sample
4	103	4	Sample4	Run Diluted Sample	5x mymethod.mth		Sample
5	201	5	Sample5	Run Sample	20x mymethod.mth		Sample
6	202	6	Sample6	Run Sample	20x mymethod.mth		Sample
7	203	7	Sample7	Run Diluted Sample	20x mymethod.mth		Sample
8	204	8	Sample8	Run Sample	20x 250ppb max.mth		Sample

Syngistix Applications

Control Devices SmartTune Conditions LogBook Method Sample Dataset Reporter Realtime Interactive CalibView Scheduler Review

Instrument Optimize Analyze Results Work Flow

Quantitative Analysis Method - C:\Users\vm\Documents\PerkinElmer Syngistix\ICPMS_vm\Method\20x 250ppb max.mth

Timing Processing Equation Calibration Sampling Devices... QC... Report Notes

	Analyte	Mass (amu)	QC Action Priority	Sample Lower (Conc.)	Sample Upper (Conc.)	Sample Conc SD	Sample Conc RSD
2	Co	58.9332	3				
3	Ce	139.905	4				
4	Pb	207.977	5				
5	U	238.05	6				
6	Be	9.0122	1		250		

	Measurement	Action 1 (*)	Action 1 Data	Action 2 (*)	Action 2 Data
21	Be 9 Lower	Continue		Continue	
22	Be 9 Upper, S, EEE	Wash for X, Dilute and Rerun Current	25 seconds	Continue	
23	Be 9 Std Dev	Continue		Continue	
24	Be 9 RSD	Continue		Continue	

Calibration QC Stds. QC Measurement Frequency QC Std. Int. Stds. Calibration Stds. Sample Int Stds. Sample

Sample Overrange Dilution

Sample limits can be defined for each analyte in the NexION 2000 method. Any analyte detected in excess of the upper limit will be automatically diluted and reanalyzed.



Assays on Nexlon 2000s

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The Analysis of Drinking and Natural Waters using the NexION 2000 ICP-MS

- NexION® 2000 ICP-MS can analyze drinking and natural waters in Standard mode in accordance with U.S. EPA Method 200.8
 - Accuracy
 - Stability
 - Detection Limits
- Unique ability to selectively suppress high-level elements without affecting other masses

Analyte

Aluminum	(Al)
Antimony	(Sb)
Arsenic	(As)
Barium	(Ba)
Beryllium	(Be)
Cadmium	(Cd)
Chromium	(Cr)
Cobalt	(Co)
Copper	(Cu)
Lead	(Pb)
Manganese	(Mn)
Mercury	(Hg)
Molybdenum	(Mo)
Nickel	(Ni)
Selenium	(Se)
Silver	(Ag)
Thallium	(Tl)
Thorium	(Th)
Uranium	(U)
Vanadium	(V)
Zinc	(Zn)

The Analysis of Soils and Waters in Accordance with U.S. EPA Method 6020B using the NexION 2000 ICP-MS

- NexION® 2000 ICP-MS can easily analyze waters and soils in accordance with U.S. EPA Method 6020B
 - Accuracy
 - Stability
 - Detection Limits
- SMARTintro™ High Throughput/High Matrix sample introduction module
 - Increases productivity without sacrificing performance

Element	Symbol	Element	Symbol
Aluminum	Al	Selenium	Se
Antimony	Sb	Silver	Ag
Arsenic	As	Sodium	Na
Barium	Ba	Thallium	Tl
Beryllium	Be	Vanadium	V
Magnesium	Mg	Zinc	Zn
Manganese	Mn		
Mercury	Hg		
Nickel	Ni		
Potassium	K		
Cadmium	Cd		
Calcium	Ca		
Chromium	Cr		
Cobalt	Co		

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The NexION 2000: A Perfect Tool for the Determination of Trace Elements in Blood and Serum

- Accurate, stable analysis of blood and serum
- Unique RF generator allows matrix-matched or aqueous calibrations
- Four modes for optimal performance

Element	Certified (µg/L)	Measured (µg/L)	Recovery	Measured (µg/L)	Recovery
Cr	58.7	56.8	97%	53.5	91%
Mn	92.0	84.9	93%	86.0	93%
Se	579	556	96%	550	95%
As	90.3	80.1	92%	13.7	94%
Cd	14.5	13.4	92%	13.7	94%
Hg	51.1	51.8	101%	52.5	103%
Tl	47.8	44.7	94%	48.0	101%
Pb	604	605	100%	605	100%

Sample Type	Element	Mass	Analysis Mode	Cell Gas
Blood	Cr	52	Reaction	NH ₃
	Mn	55	Reaction	NH ₃
	Se	78	Reaction	O ₂
	AsO	91	Reaction	O ₂
	Cd	114	Reaction	O ₂
	Hg	202	Reaction	O ₂
	Tl	205	Standard	---
	Pb	208	Standard	---
Serum	Cr	52	Reaction	NH ₃
	Cu	63	Collision	He
	Zn	66	Collision	He
	Se	78	Reaction	O ₂
	Cd	114	Reaction	O ₂
	Hg	202	Reaction	O ₂

The Analysis of Urine for Trace Elements using the NexION 2000 ICP-MS

- Accurate, stable analysis of urine
- Unique RF generator allows matrix-matched or aqueous calibrations
- Four modes for optimal performance

Element	Certified (µg/L)	Experimental (µg/L)	% Recovery
Cr	4.07	3.97	98
Mn	3.91	3.88	99
Co	2.03	1.94	96
Ni	5.92	5.94	100
Cu	36.7	36.7	100
As	43.0	42.3	98
Se	29.9	28.6	96
Mo	23.9	23.0	96
Cd	2.46	2.37	96
Hg	2.30	2.62	114
Sb	11.1	11.2	101
Tl	7.24	7.12	98
Pb	24.0	22.5	94

Element	Mass	Analysis Mode	Cell Gas
Cr	52	Reaction	Ammonia
Mn	55	Reaction	Ammonia
Co	59	Collision	Helium
Ni	60	Collision	Helium
Cu	63	Collision	Helium
AsO	91	Reaction	Oxygen
Se	78	Reaction	Oxygen
Mo	95	Collision	Helium
Cd	111	Reaction	Oxygen
Sb	121	Standard	---
Hg	202	Reaction	Oxygen
Tl	205	Standard	---
Pb	208	Standard	---

Testing & Validation of Various Antacids for Class 1 & 2A Elemental Impurities in Pharmaceutical Products Following ICH Q3D & USP <232>/<233>

- NexION® 2000 ICP-MS can easily analyze some of the highest-matrix drug products in accordance with USP <232>
 - Accuracy
 - Repeatability
 - Ruggedness
 - System Suitability
- Instrument design considerations simplify analysis and maintenance
 - Universal Cell
 - Triple Cone Interface
 - Quadrupole Ion Deflector (QID)
 - All Matrix Solution (AMS)
 - SMARTintro™ High Throughput/High Matrix sample introduction system

Element	Mass	Universal Cell Mode	Internal Standard
Na	23	Collision - Helium	⁷¹ Ga
Mg	24	Collision - Helium	⁷¹ Ga
Al	27	Collision - Helium	⁷¹ Ga
Ca	43	Collision - Helium	⁷¹ Ga
V	51	Collision - Helium	⁷¹ Ga
Co	59	Collision - Helium	⁷¹ Ga
Ni	60	Collision - Helium	⁷¹ Ga
As	75	Collision - Helium	⁷² Ge
Cd	111	Collision - Helium	¹¹⁵ In
Hg	202	Collision - Helium	¹⁵⁰ Tb
Pb	206 + 207 + 208	Collision - Helium	¹⁵⁰ Tb

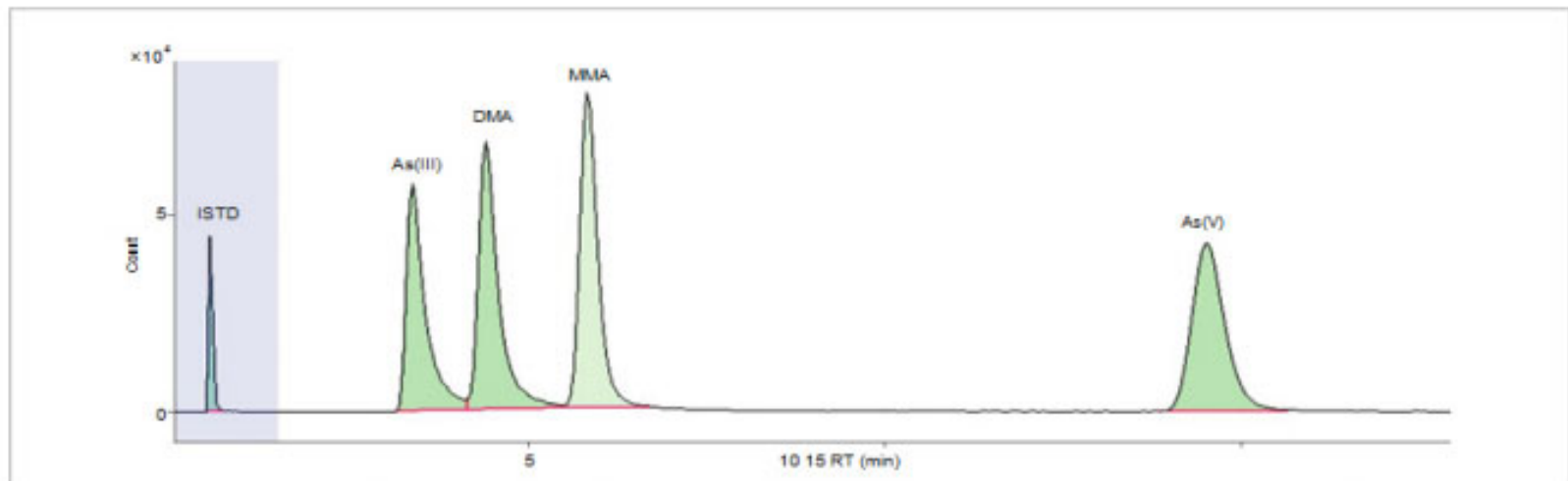


Assays in Development

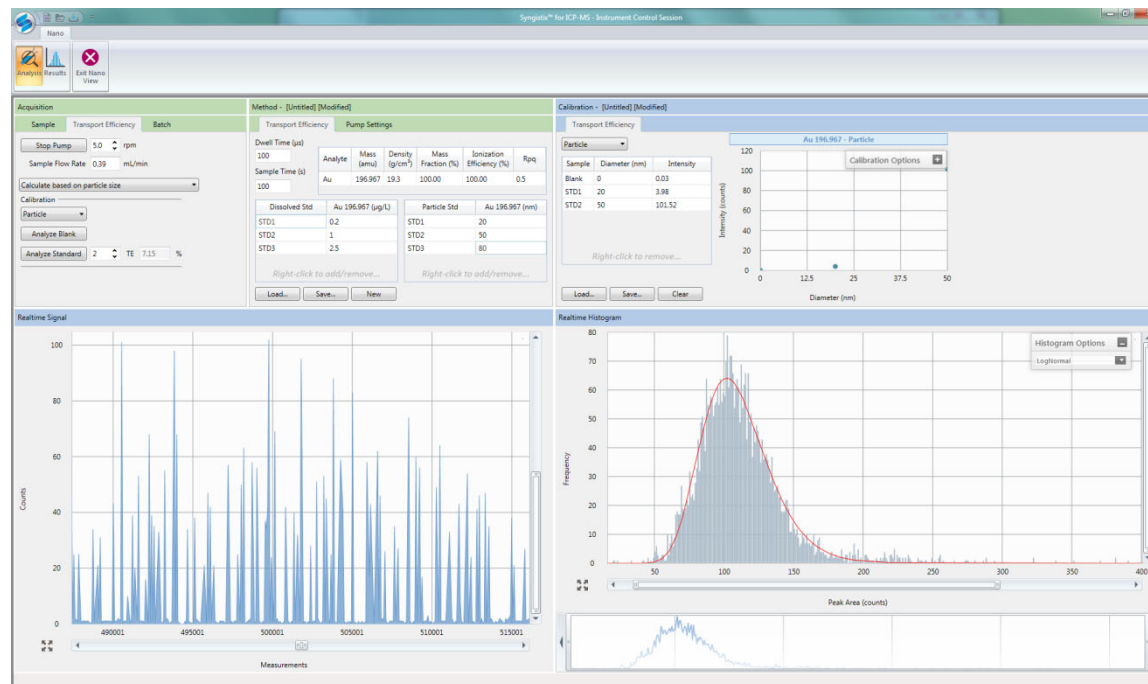
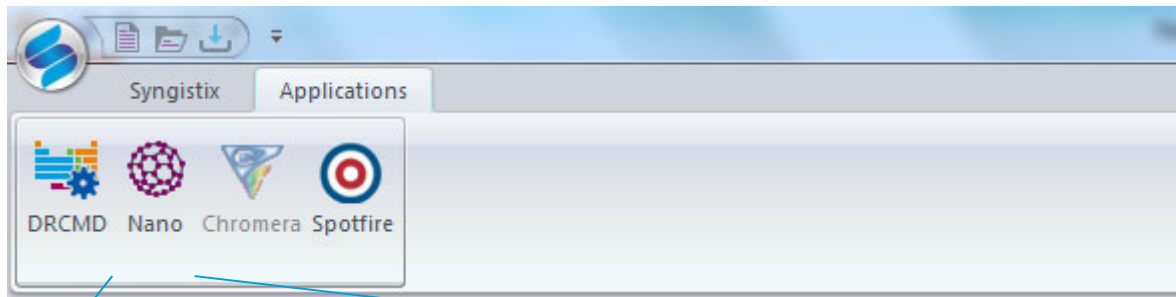
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Arsenic Speciation Analysis (*New Chromera is coming*)

- Toxicity of elements depends on chemical form of the element
 - As – inorganic (As⁺³/As⁺⁵)
 - As – organic (MMA, DMA, AsB)
- Separate species using chromatography
 - HPLC or GC
- Detect element – retention time identifies species



Nano Particle Analysis

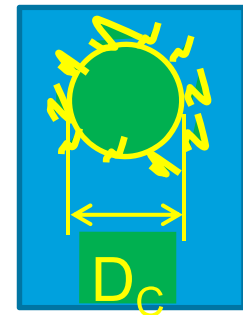


NexION™ Syngistix
Nano Application Module

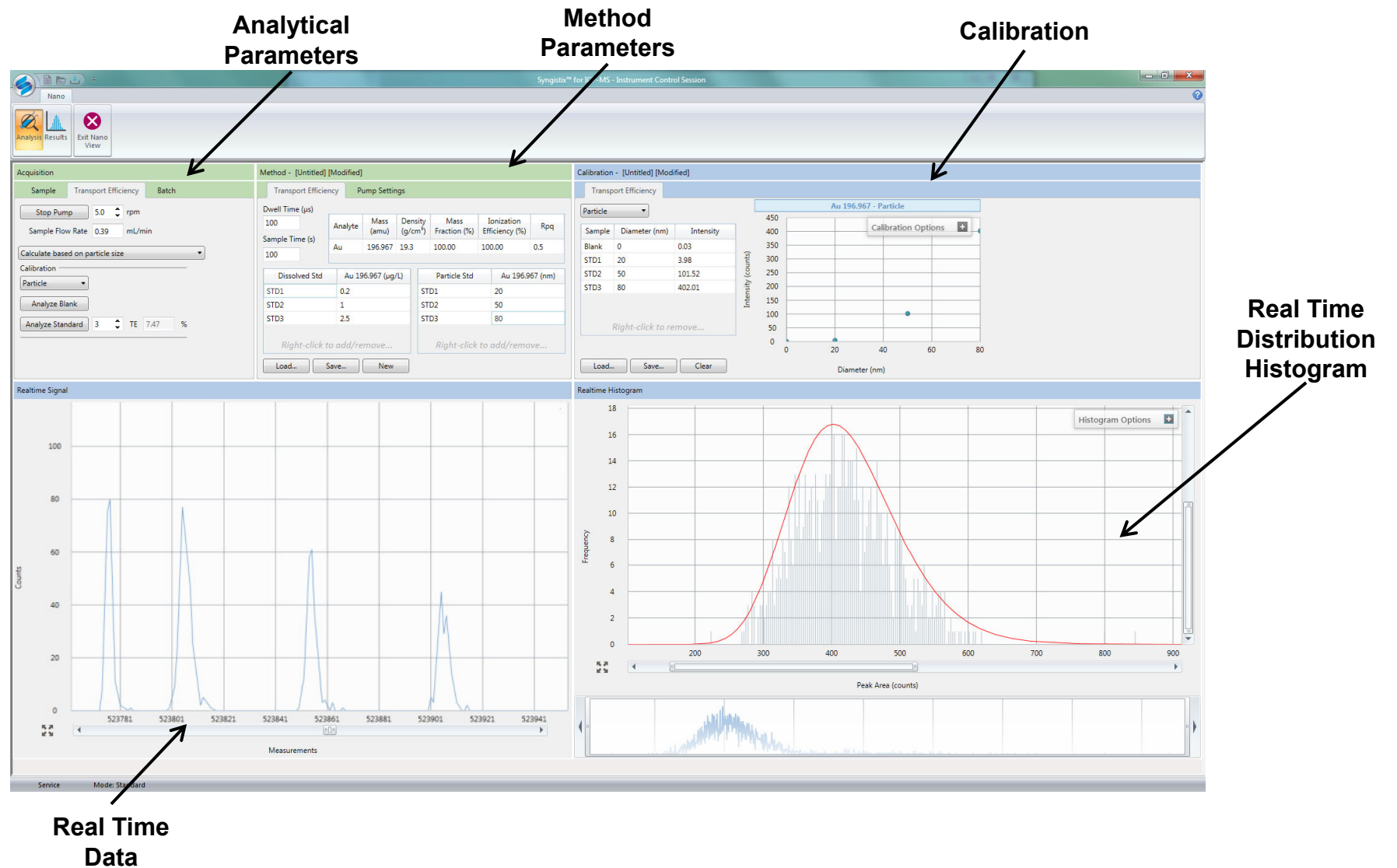
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Single Particle ICP-MS – What is it?

- A new advancement in ICP-MS applications allowing the measurement of individual inorganic nanoparticles
- A technique that allows the differentiation between ionic (M^+) and particulate signal (nanoparticles) in a wide variety of matrices without any prior separation
- It is element specific, and provides composition, ionic and particle concentration, size and size distribution
- Allows the analysis of nanoparticles at low concentrations (as low as 50 part/mL)
- Measures the core size of nanoparticles
- Tracks nanoparticles dissolution and agglomeration



Syngistix Nano Application Module – Analysis Tab



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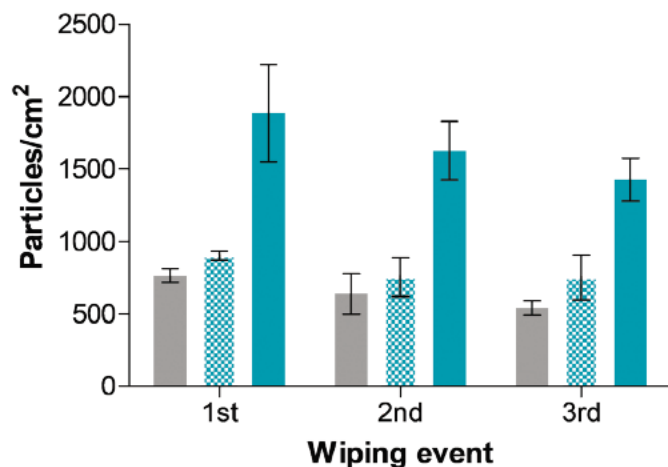
Transport of Nanoparticles Via Physical Contact

- Antimicrobial coatings

Product	Description	Nanoparticle	Notes
Silicone Keyboard Covers	Antimicrobial Properties	Ag	Advertised That Contains Ag NPs
	No Antimicrobial Properties	---	Control; No Claim of Antimicrobial Properties
Wooden Blocks	CuO-containing Paint	CuO	Contains CuO NPs
	Paint Without CuO	---	Control; Certified Not to Contain CuO NPs



- Ag NP transfer from keyboard covers



Transport of Nanoparticles From Coated Surfaces Through Physical Contact

Introduction

With the growing use and incorporation of nanoparticles (NPs) into consumer products, concern about human exposure

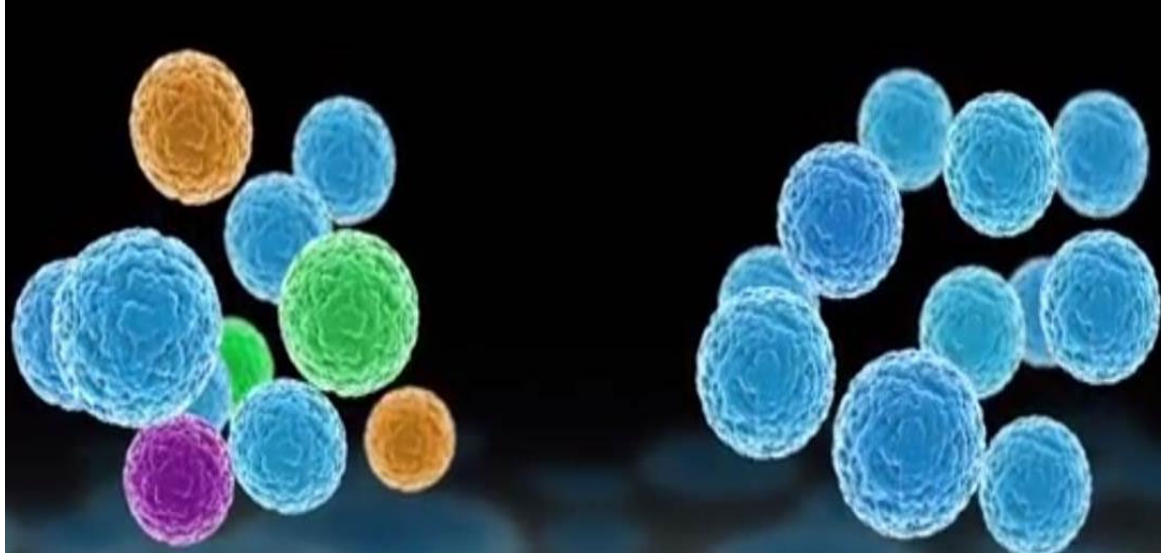
to NPs has also increased, leading to the question: Are nanoparticles in consumer products transferred to humans? Since user interaction with these products occurs mostly via physical interaction, it is important to understand how NPs are transferred through physical contact.

This work explores the transfer of nanoparticles from nano-enabled surfaces to wipes, focusing on several characteristics of nanoparticle release: total mass concentration, particle number concentration, and particle size distribution. Because of their wide use due to antimicrobial properties, silver (Ag) NPs were examined, along with CuO NP transfer from painted surfaces. A more detailed description of this work is available¹, so only an overview will be given here.



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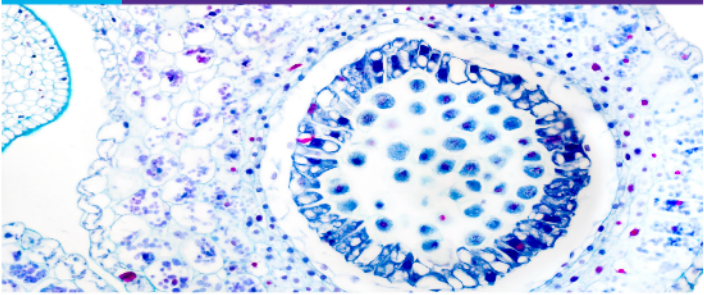
Single Cell ICP-MS: Metal content at the cellular level



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What is Single Cell ICP-MS?

WHITE PAPER
An Introduction to Single Cell ICP-MS Analysis



Introduction

The introduction and development of Single Particle ICP-MS (SP-ICP-MS) has opened a new area of research which allows the rapid detection and analysis of metal based particles in a variety of matrices and applications.^{1,2} The key feature of SP-ICP-MS is that it allows discrete pulses of positively charged ions to be detected and measured in a time resolved manner using microsecond (µs) data acquisition rates. This advance in data acquisition capabilities is opening up a number of new application areas. In this white paper, we will introduce the concept of Single Cell ICP-MS (SC-ICP-MS), where individual cells are rapidly analyzed for metal content. Before delving into SC-ICP-MS, let's briefly review the theory of SP-ICP-MS.

SP-ICP-MS: A Brief Review

Comprehensive descriptions of SP-ICP-MS are available,^{1,2} so only a brief review will be given here. When a nanoparticle enters the plasma, it is completely ionized, producing a burst of ions which can be detected with ICP-MS. While conventional ICP-MS looks at a continuous signal, the output from SP-ICP-MS looks at discrete signals: one nanoparticle yields one ion burst, with the intensity of the resulting signal being related to the size of a particle (nm) and the number of pulses being related to the particle concentration (part/mL).

The key to SP-ICP-MS is rapid, continuous measurement, which minimizes the chance of more than one particle being detected at the same time and ensures that particles are all counted. These tasks can be accomplished with ICP-MS instrumentation which contains fast electronics and eliminates the quadrupole

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PerkinElmer
For the Better

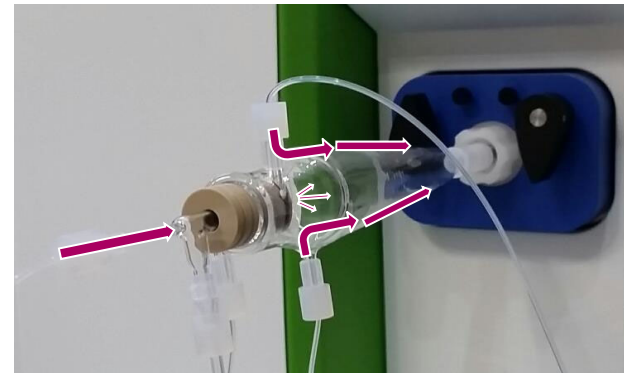
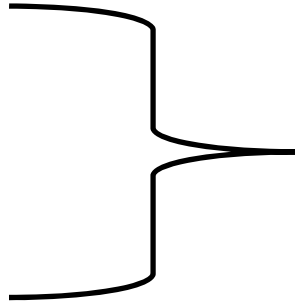
Single Cell - ICP-MS is an emerging technology allowing users to:

- Differentiate between ionic metal concentration in culture media and in individual cells without any sample preparation
- Monitor metal and nanoparticles content within single cells
 - Intrinsic metal content
 - Uptake of metals within a cell
 - Uptake of nanoparticles
 - Number of nanoparticles within a cell
- Handle low cell numbers compared to conventional methods

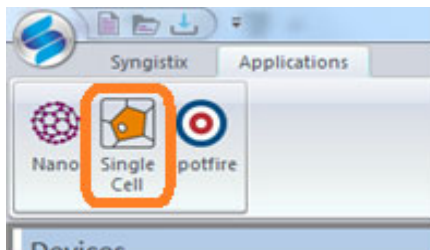
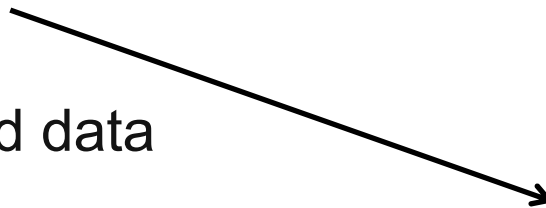
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Single Cell ICP-MS

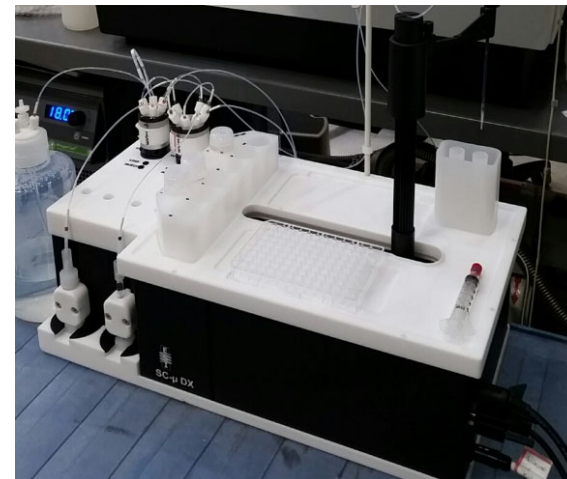
- Nebulization of cells
- Transport of cells into the plasma
- Automation
- Software and data treatment



Asperon™ Spray Chamber

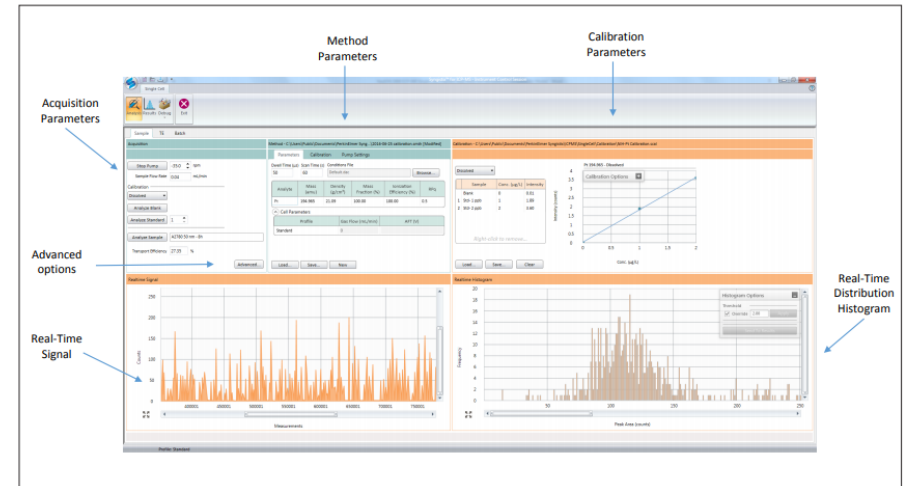
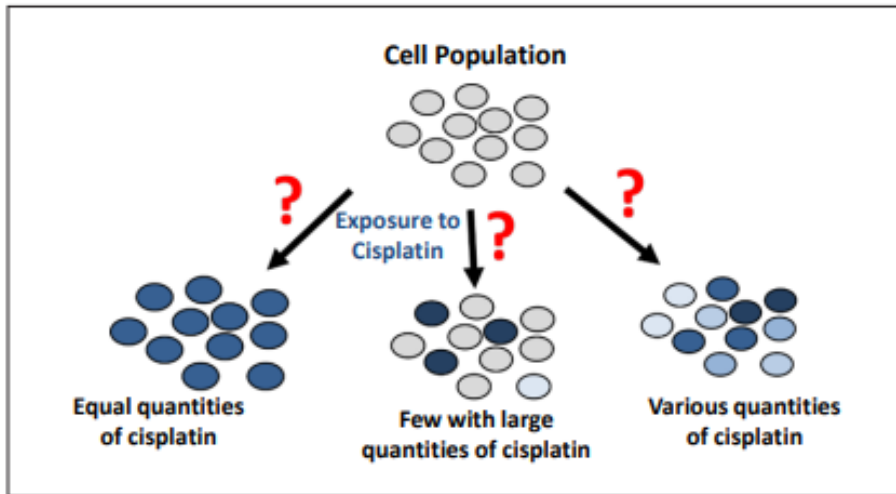


Application Software

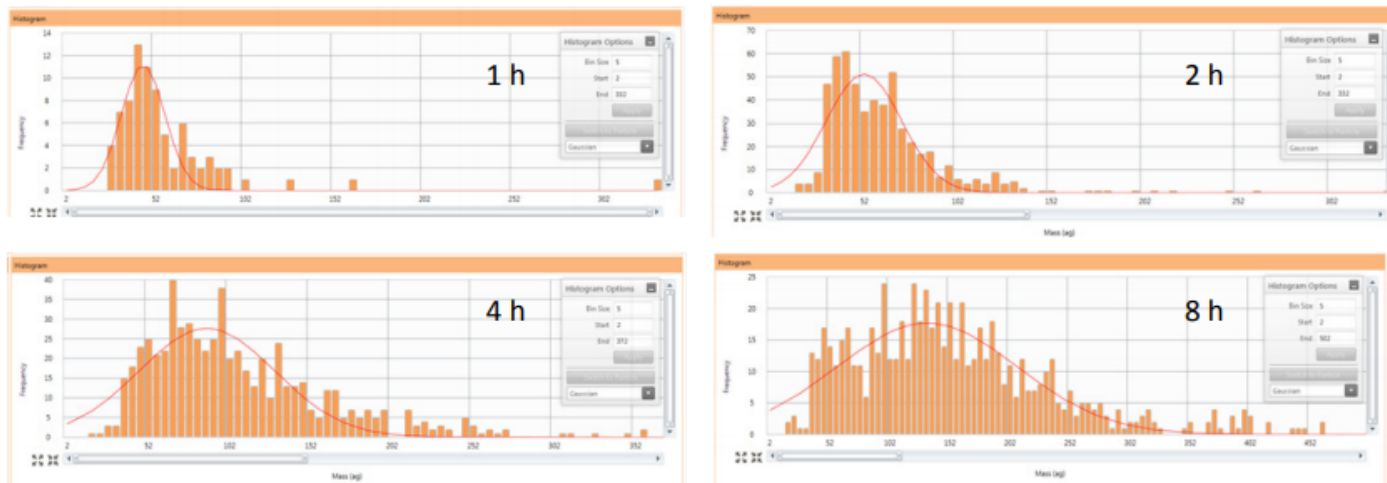


microFAST for Single Cell

New Research Evaluating Cisplatin Uptake in Ovarian Cancer Cells by Single Cell ICP-MS



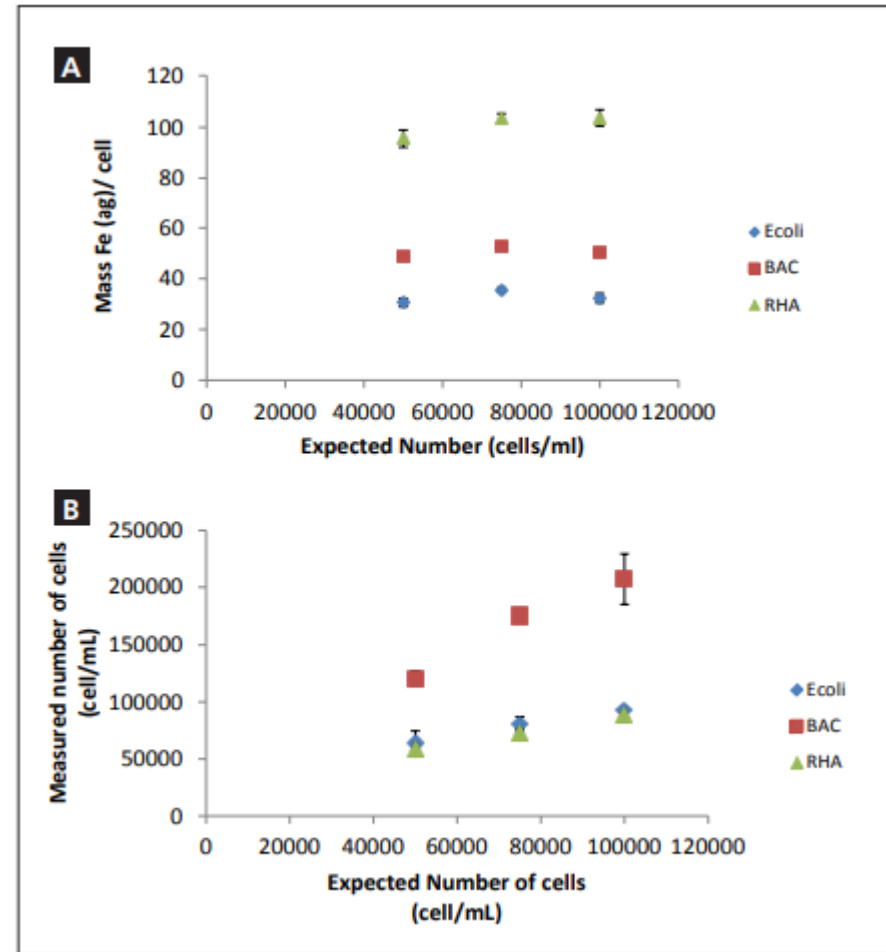
A2780/CP70 Cells



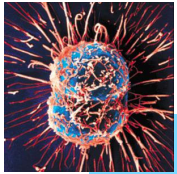
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Iron Content Measurement in Individual Bacterial Cells Using Single Cell ICP-MS

- **Intrinsic/nutrient metals:** Single Cell ICP-MS is an essential tool for quantifying nutrient metals
- **Iron mass per cell:** SC-ICP-MS allows for the quantification of the relationship between the size of the cell and the Fe concentration
- **Stress conditions:** SC-ICP-MS enables monitoring the change in intrinsic/nutrient metal per cell, which can change due to cell stress conditions



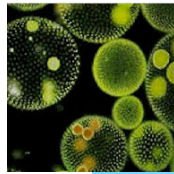
Benefits of Single Cell



1

Cancer & Drug Research

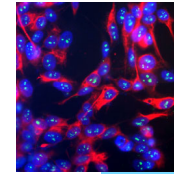
- Metal-based drugs
- Drug discovery and development
- Drug delivery
- Center For Disease Control And Prevention



2

Environmental Toxicology

- Environmental and Marine Science centers
- Institute of Plant Physiology and Ecology
- Center for Eco-Environmental Sciences



3

Biotech and cellular science

- Department of Molecular & Cellular Biology
- Department of Biological Sciences

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