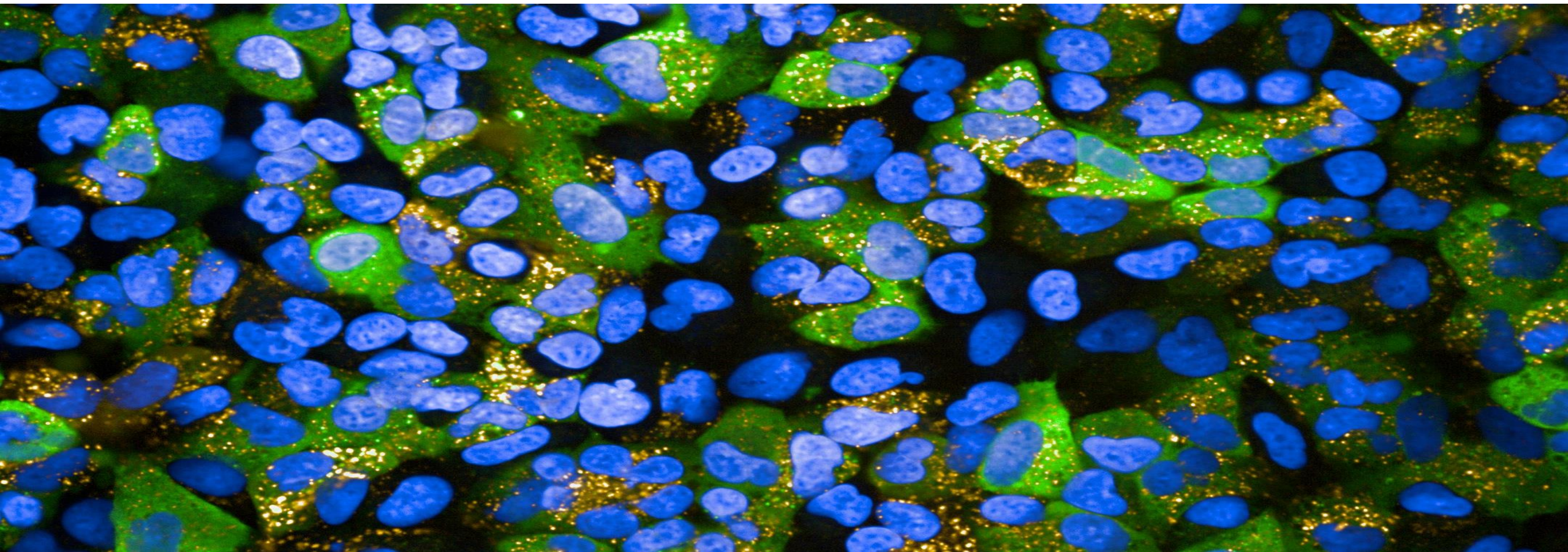


# PerkinElmer 高分辨单细胞-ICP-MS技术与应用



- 朱敏, [min.zhu@perkinelmer.com](mailto:min.zhu@perkinelmer.com), 15301601129
- 21<sup>th</sup>, Sep, 2018

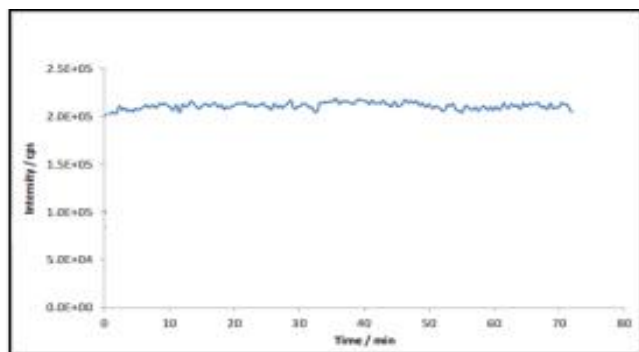


## 单颗粒、单细胞 SP-ICP-MS分析技术

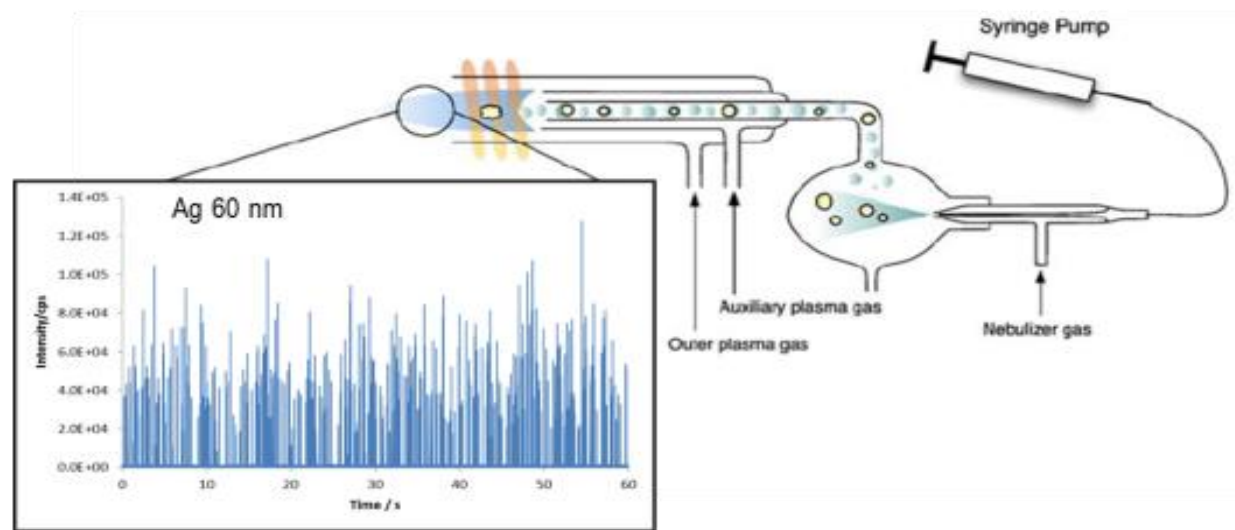
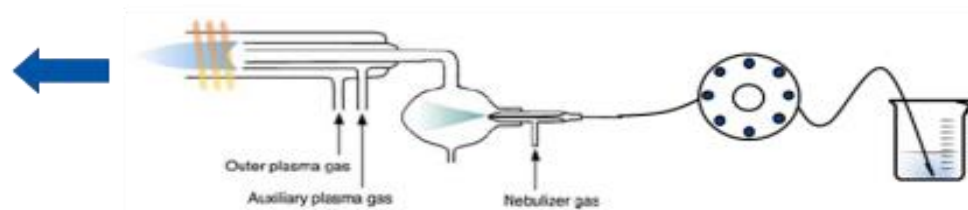
- PerkinElmer 公司极力倡导的单颗粒、单细胞ICP-MS(single particle-ICPMS)技术被公认为一种定性和定量测定含有特定元素的低浓度的单颗粒最有前途的方法。
- 单颗粒目标可以是纳米粒子，也可以是PM2.5/PM10等大气粉尘颗粒物，或者合成的超细颗粒物及包合物等，更可以是生命科学研究前沿的细胞，藻类，病毒等活体小颗粒型目标物。
- 相对传统的元素监测方法，SP-ICP-MS技术可快速有效并提供更多的信息：它能够测定颗粒尺寸分布、颗粒个数，颗粒内部元素的浓度、颗粒外部溶解出来的元素浓度等。而且，它能够区分含有不同元素的特定粒子。



# 常规ICP-MS测定与SP-ICP-MS单颗粒测定的区别

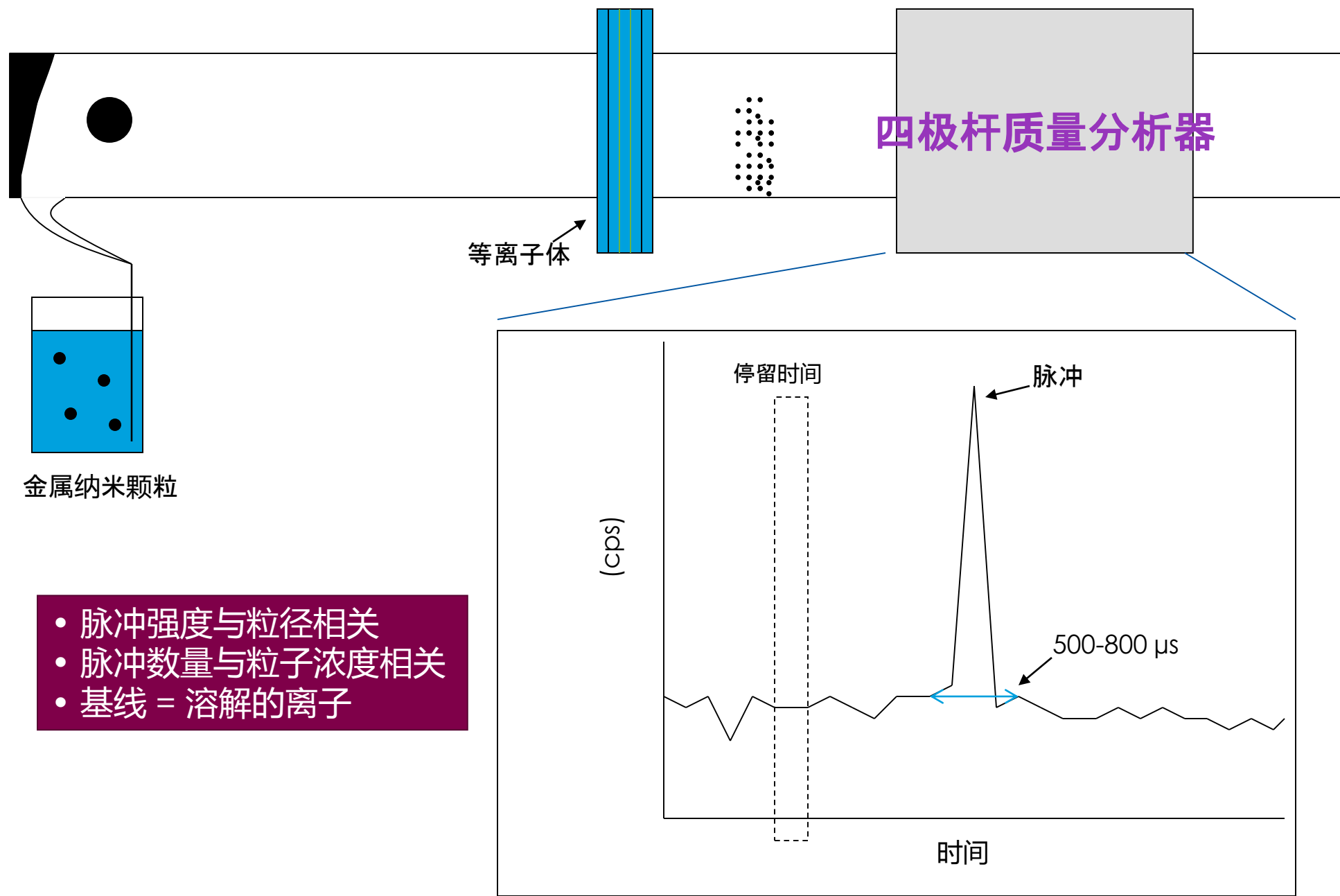


连续稳定的信号（溶液）



单独的信号（纳米粒子）

# SP-ICP-MS 单颗粒测定原理



## Single Particle Inductively Coupled Plasma Mass Spectrometry: A Powerful Tool for Nanoanalysis

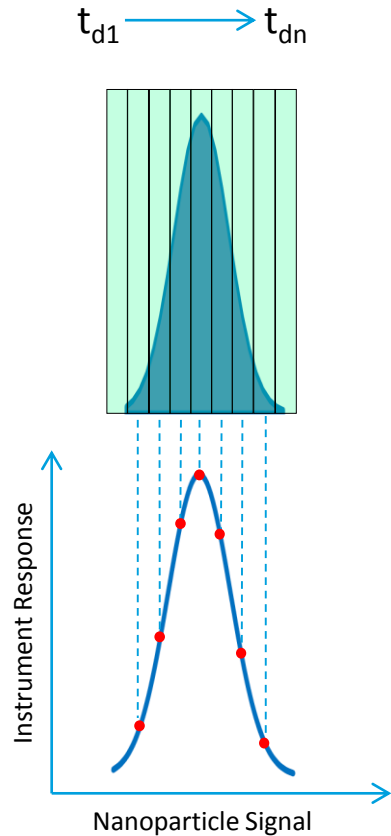
Table 1. Size and Element Mass Detection Limits Reported for Selected Nanoparticles Determined by SP-ICPMS

nanoparticle	LOD <sub>size</sub>	LOD <sub>mass</sub>	ref
Ag	18 nm	32 ag	15
	<20 nm	<44 ag	20
	20 nm	44 ag	34,28
	33 nm	200 ag	21
	30 nm	535 ag	22
Au	21 nm	94 ag	21
	25 nm	158 ag	13
	17 nm	331 ag	22
U	10 nm	106 ag	22
Al <sub>2</sub> O <sub>3</sub>	30 nm	30 ag	9
ZrO <sub>2</sub>	70 nm	755 ag	10
ThO <sub>2</sub>	80 nm	2.4 fg	11
TiO <sub>2</sub>	100 nm	1.3 fg	9
FeOOH (goethite)	200 nm	10 fg	9

At present, SP-ICPMS is particularly suitable for NPs consisting of one element only and sizes higher than ~20 nm. In order to enhance size detection limits and implement multielement capabilities for heterogeneous NPs, improved commercially available ICPMS instruments are needed.

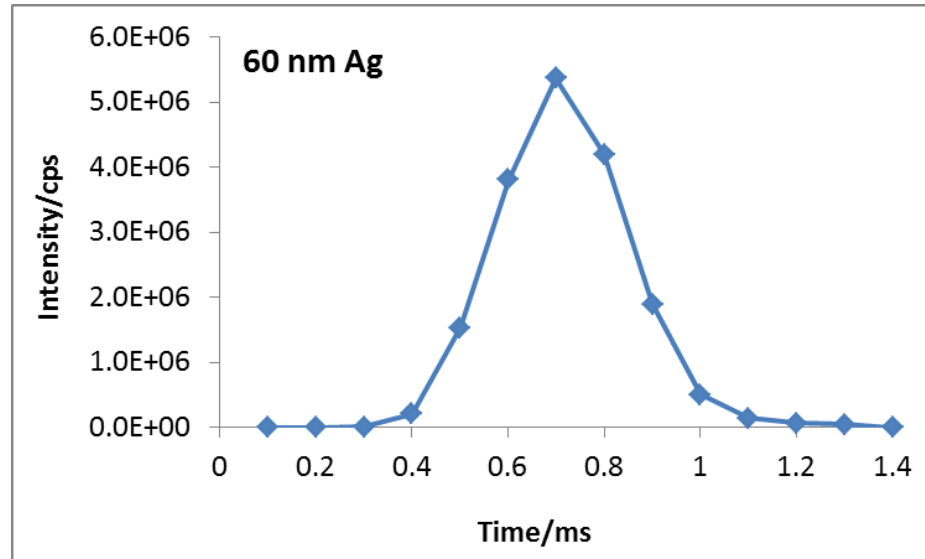
Because the duration of the transient signal generated by an individual NP is in the range of hundreds of microseconds, the multielement detection of transient signal generated by individual NPs involves the use of simultaneous or fast scanning instruments, able of recording full spectra of a mass range of interest at frequencies around  $10^5$  Hz.<sup>45</sup> Apart from

# NexION高分辨单颗粒ICP-MS的快速数据采集能力



## NexION 系列ICP-MS:

- 最短驻留时间可达10  $\mu\text{s}$ ，单质量数据采集能力可达100000点每秒
- 专利的数据处理算法获得实时信号分析与背景信号校正



**United States Patent Application Publication**  
 (19) **United States**  
 (12) **Patent Application Publication**  
 Bazarzan et al.  
 (10) **Pub. No.:** US 2015/0235833 A1  
 (43) **Pub. Date:** Aug. 20, 2015

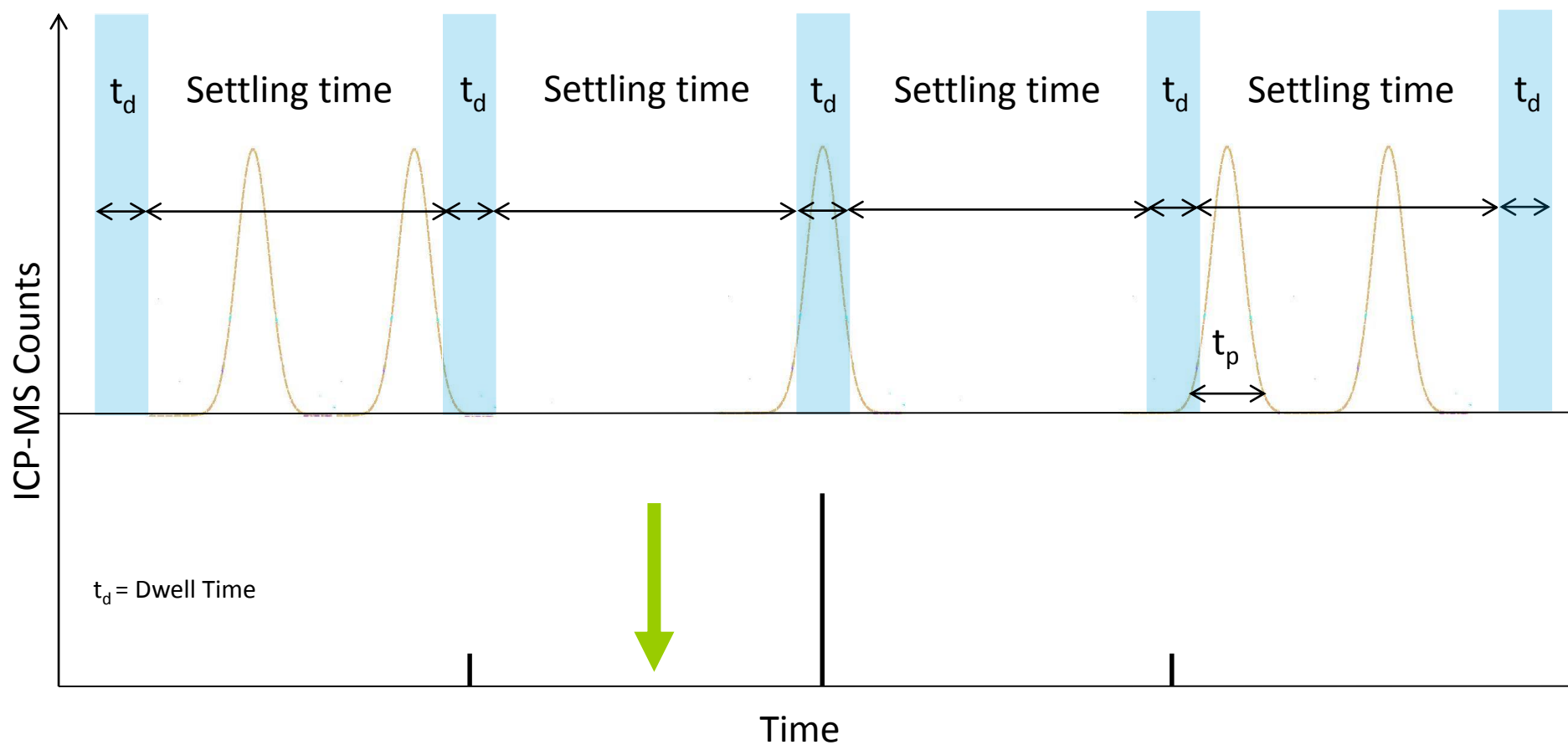
**Publication Classification**  
 (51) **Int. Cl.** H01J 49/20 (2006.01)  
 (52) **U.S. Cl.** CPC: 1011 49/105 (2013.01)  
 (57) **ABSTRACT**  
 The present disclosure provides methods and systems for automated analysis of spectrometry data corresponding to particles of a sample, such as large data sets obtained during single particle mode analysis of an inductively coupled plasma mass spectrometer (SP-ICP-MS). Techniques are presented herein that provide appropriate smoothing for rapid data processing without an accompanying reduction (or with an acceptably negligible reduction) in accuracy and/or precision.

**Flowchart of the data processing method:**

```

    graph TD
        RawData[Raw Data 102] --> Background[Background Determination 104]
        RawData --> PeakDetection[Peak Detection 106]
        RawData --> PeakArea[Peak area Determination 108]
        RawData --> Histogram[Constructing Intensity Histogram 110]
        RawData --> SizeHistogram[Constructing Size Histogram 112]
        RawData --> Statistical[Calculating Statistical Data for the Particle Sample 114]
    
```

## 单颗粒-ICP-MS技术对仪器的要求

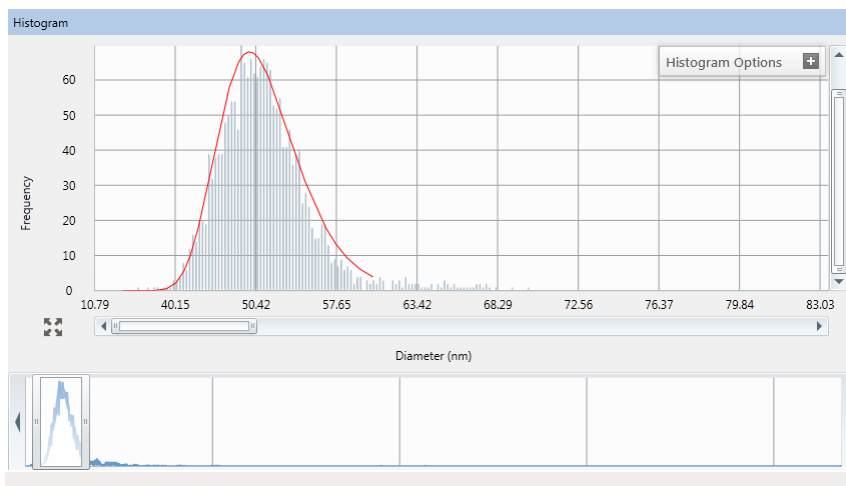


1、不准确的信号

2、不准确的尺寸、颗粒浓度、线性、样品适应性等

# 驻留时间对单颗粒 -ICP-MS分析技术的影响

200 000 part/mL dwell time (50  $\mu$ s)



200 000 part/mL dwell time (3000  $\mu$ s)

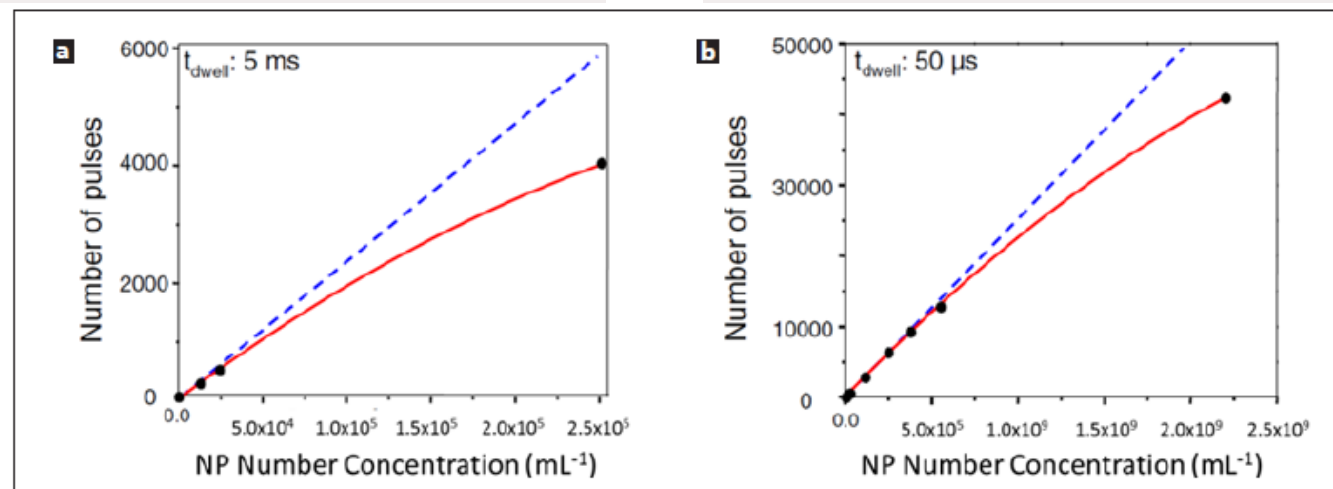
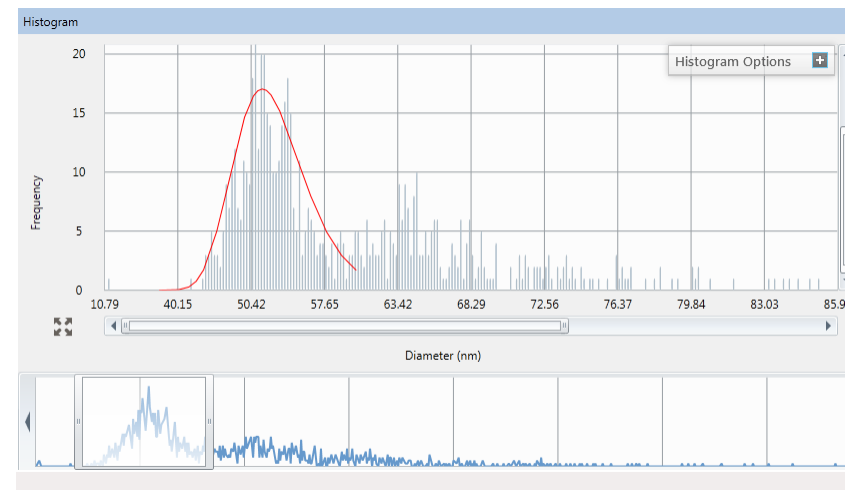


Figure 2. Number concentrations at dwell times of 5 ms (a) and 50  $\mu$ s (b). Blue line = theoretical calculations; red line = experimental results (60 nm Au NPs, acquisition time = 60 sec).



# 驻留时间对单颗粒-ICP-MS分析技术的影响

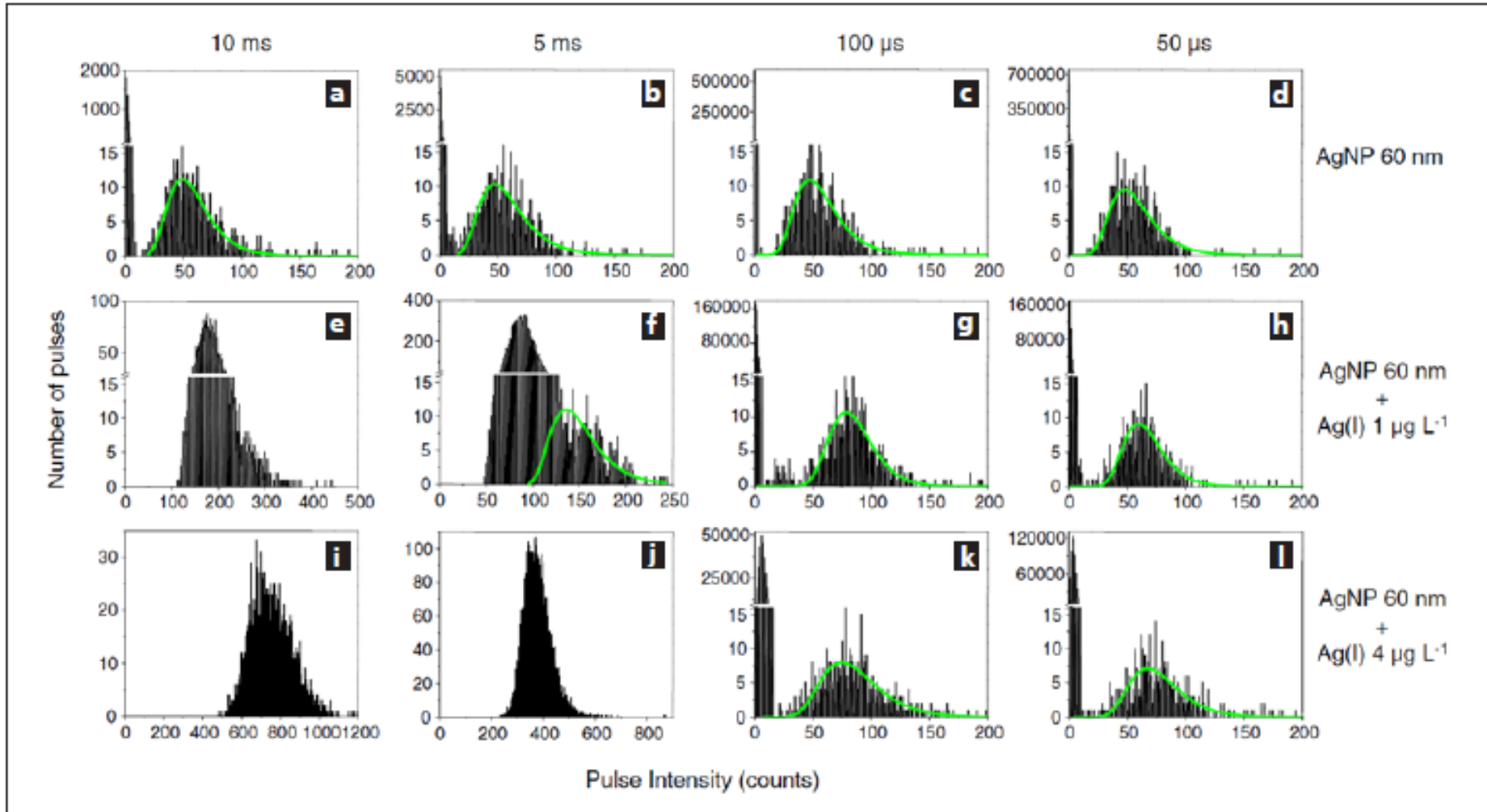
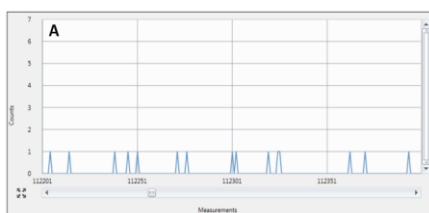
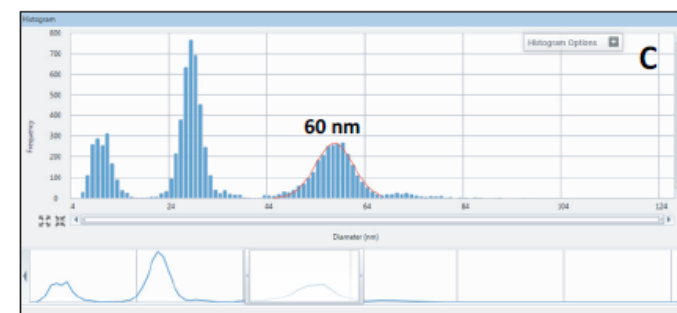
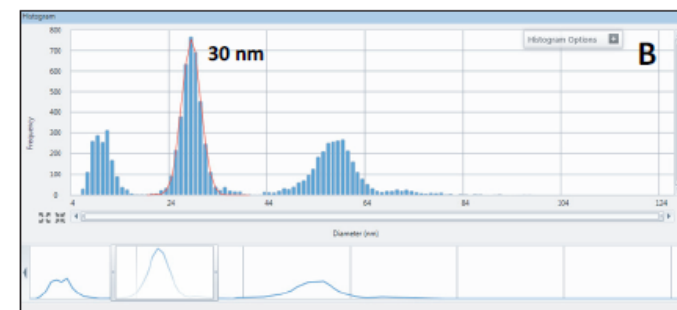
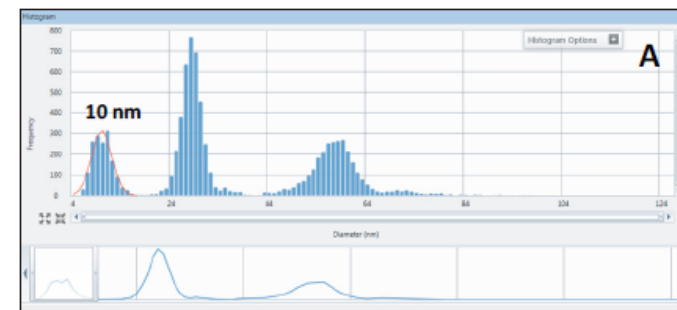


Figure 3. Size distribution histograms for: 60 nm Ag NPs (a-d); 60 nm Ag NPs + 1  $\mu$ g/L dissolved Ag (e-h); and 60 nm Ag NPs + 4  $\mu$ g/L dissolved Ag (i-l). All solutions contained Ag NPs at a concentration of 25,000 part/mL and were analyzed with dwell times of 10 ms (a, e, i), 5 ms (b, f, j), 100  $\mu$ s (c, g, k), and 50  $\mu$ s (d, h, l).

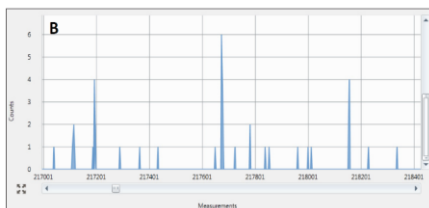
# 精确测定10 nm Au 纳米颗粒的粒径和数量

表 6. 不同粒径纳米颗粒混合物的分析。

同样的样品	NIST 8011 - 10 nm			NIST 8012 - 30 nm			NIST 8013 - 60 nm		
	标称粒径 (nm)	平均粒径 (nm)	颗粒浓度 (PART/mL)	标称粒径 (nm)	平均粒径 (nm)	颗粒浓度 (PART/mL)	标称粒径 (nm)	平均粒径 (nm)	颗粒浓度 (PART/mL)
1	9	8.9	20,058	28	28.3	49,411	57	56.6	31,295
2	9	8.9	20,622	28	28.3	49,391	57	56.7	31,007
3	9	8.7	21,327	28	28.2	49,763	57	57.0	31,585
均值	9	8.8	20,669	28	28.3	49,522	57	56.8	31,296
% RSD	0.0	1.3	3.1	0.0	0.2	0.4	0.0	0.4	0.9



Blank



10 nm Au

Table 4. Particle Size Results Determined with Particle and Dissolved Calibrations.

Sample	Certificate Value (by TEM; nm)	Particle Calibrations (nm)	Dissolved Calibrations (nm)
NIST 8011	8.9 ± 0.1	8.8 ± 0.03	8.8 ± 0.03
NIST 8012	27.6 ± 0.1	27.8 ± 0.06	27.9 ± 0.03
NIST 8013	56 ± 0.51	56.1 ± 0.37	56.2 ± 0.30

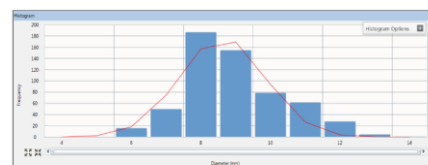


Figure 4. Particle size distribution for NIST 8011 10 nm Au NPs, fitted with a Gaussian distribution.

# 高分辨单颗粒ICP-MS实现金纳米棒表征

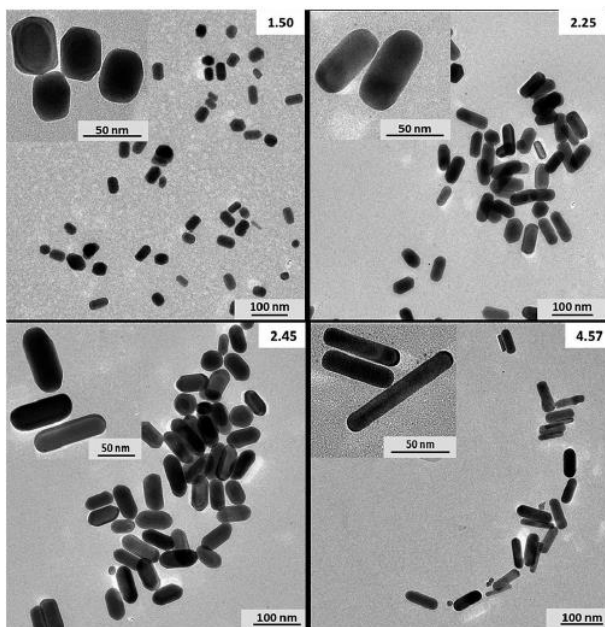


Table 1 ICP-MS instrumental settings and

Parameter/device	NexION 350
RF power	1400 W
Plasma gas flow rate	20.0 L min <sup>-1</sup>
Carrier gas flow rate	1.05 L min <sup>-1</sup>
Plasma sampling depth	4 mm
Measurement mode	TRA
Dwell time	20 μs
Acquisition time	60 s
Nebulizer	MicroMist
Spray chamber	Cyclonic

Table 3 Calculated width and length data for nanorods as determined by high resolution spICP-MS measurements. The relative error is calculated with respect to the data shown in Table 2

Width (nm)	Length (nm)	Rel. error for the width (%)	Rel. error for the length (%)
30.9	47.5	1.4	1.0
32.9	66.7	2.3	1.6
30.3	63.7	4.3	2.7
29.9	67.8	4.9	3.0
17.2	46.3	1.7	1.1
28.9	85.2	5.4	3.1
15.9	55.7	4.8	2.7
15.9	74.7	1.6	1.9

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Cite this: DOI: 10.1039/c7ja00306d

## Dimensional characterization of gold nanorods by combining millisecond and microsecond temporal resolution single particle ICP-MS measurements†

Ildikó Kálomista,<sup>a</sup> Albert Kéri,<sup>a</sup> Ditta Ungor,<sup>b</sup> Edit Csapó,<sup>bc</sup> Imre Dékány,<sup>b</sup> Thomas Prohaska<sup>cd</sup> and Gábor Galbács<sup>de\*</sup>

A systematic investigation of single particle inductively coupled plasma mass spectrometry (spICP-MS) signal profiles recorded with normal (ms-range) and high (μs-range) temporal resolution for spherical and rod-shaped gold nanoparticles was performed. The experiments with nanorods were carried out on hemispherically capped cylindrical particles synthesized in the aspect ratio range from 1.5 to 4.5. A comparison of NP signals and time profiles for spherical and rod-shaped NPs revealed that (i) the volume of the particles can be assessed by conventional spICP-MS measurements using a joint, linear calibration

# 高分辨单颗粒ICP-MS实现单颗粒的双元素检测能力

## 颗粒的多元素扫描

Syngistix™ for ICP-MS - Instrument Control Session

Quantitative Analysis Method - [Untitled][Modified]

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

Sweeps / Reading Est. Reading Time MassCal File  
1 0:00:00.004 default.tun

Readings / Replicate Est. Replicate Time Conditions File  
25000 0:02:00.000 default.dac

Replicates Est. Sample Time  
1 0:02:00.000

Enable QC Checking

Int Std	Analyte	Mass (amu)	Scan Mode (*)	MCA Channels	Dwell Time per AMU (ms)	Integration Time (ms)	Corrections	Profile (*)	Ammonia Flow	Helium Flow	Oxygen Flow	RP a	RP q
1	Li	7.016	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
2	Be	9.0122	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
3	Na	22.9898	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
4	Mg	23.985	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
5	K	38.9637	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
6	Ca	42.9588	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
7	Sc	44.9559	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
8	Ti	47.948	Peak Hopping	1	0.1	2500	Ca	Standard	0	0	0	0	0.25
9	V	50.944	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
10	Cr	51.9405	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
11	Mn	54.9381	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
12	Fe	56.9354	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
13	Co	58.9332	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
14	Ni	59.9332	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
15	Cu	62.9298	Peak Hopping	1	0.1	2500		Standard	0	0	0	0	0.25
16													
17													
18													
19													
20													
21													
22													
23													
24													
25													
26													
27													
28													
29													

Profile: Standard

## 单颗粒的双元素同时分析

Nano

Analysis Results Exit

Sample TE Batch

Acquisition Method: C:\Users\Public\Documents\PerkinElmer Syngistix\ICPMS\Nano\...\Au-Lu method.nmth

Parameters Calibration Pump Settings Sampling Device

Stop Pump -5.0 rpm

Sample Flow Rate 0.01 mL/min

Calibration Particle Au 196.967

Analyze Blank Analyze Peak Shape

Analyze Standard 1

Analyze Sample Au NP+Beads -6

Transport Efficiency 66 %

Dilution Factor 1

Advanced...

Analyte	Mass (amu)	Structure	Density (g/cm <sup>3</sup> )	Mass Fraction (%)	Ionization Efficiency (%)	RPq
Au	196.967	None	19.3	100.00	100.00	0.25
Lu	174.941	None	9.841	100.00	100.00	0.28

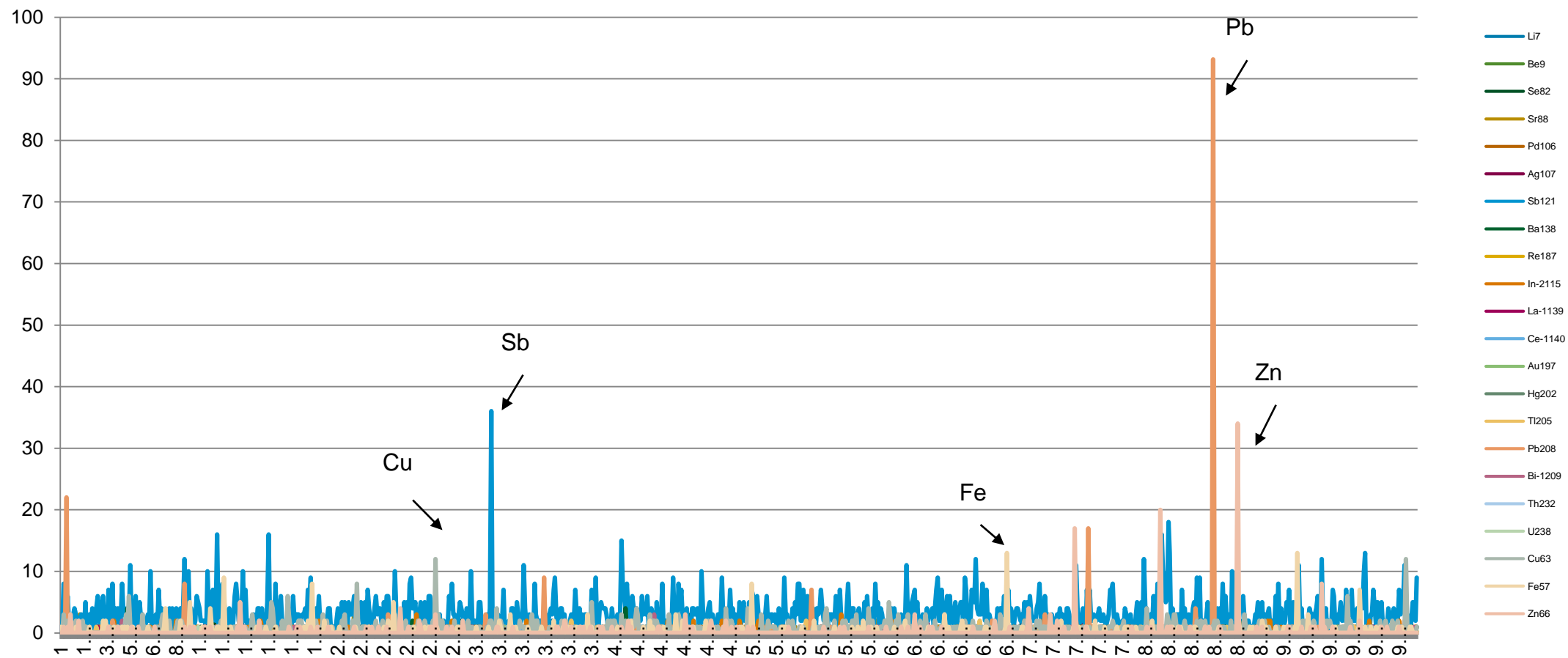
Cell Parameters

Profile	Gas Flow (mL/min)	AFT (V)
Ammonia DRC	0.35	50

Conditions File Default.dac

Load... Save... New

# 颗粒的多元素扫描





# 颗粒的多元素扫描-污水处理厂淤泥中发现大量纳米颗粒

DOI: 10.1021/acs.est.6b05931

## 7. Occurrence of Ti-, Fe- and Zn- NPs and dissolved elements in sludge samples

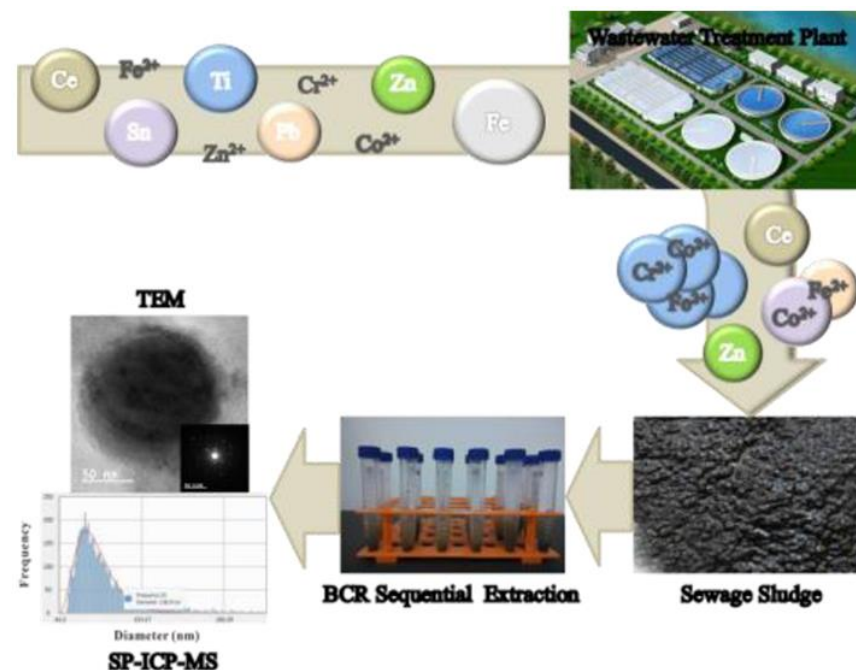
Table S6. Occurrence of Ti-, Fe- and Zn- NPs and dissolved elements in sludge samples

Sample Sites	Chemical Fractions	Ti			Fe						Zn				
		Most Freq. Size (nm)	Part. Conc. (Parts/g)	Diss. Conc. (µg/g)	Most Freq. Size (nm)						Most Freq. Size (nm)	Part. Conc. (Parts/g)	Diss. Conc. (µg/g)		
		TiO <sub>2</sub>	Fe <sub>2</sub> O <sub>3</sub>	Fe <sub>3</sub> O <sub>4</sub>	FeS/FeOOH	FeS <sub>2</sub>	Fe <sub>7</sub> S <sub>8</sub>	ZnO	ZnS						
S4	Acid-exchangeable fraction	64	1.96E+09	10.00	57	56	60	66	62	3.83E+09	1311.25	45	53	9.86E+10	718.75
	Acid-exchangeable fraction duplicate	64	1.91E+09	9.89	58	58	62	68	64	4.17E+09	1406.25	45	53	9.64E+10	717.50
S5	Acid-exchangeable fraction	64	6.20E+09	51.50	47	46	50	54	51	2.65E+10	2095.00	45	53	2.41E+10	1280.00
	Acid-exchangeable fraction duplicate	64	6.70E+09	52.25	47	46	50	54	51	2.50E+10	2080.00	45	53	2.15E+10	1253.75
S10	Acid-exchangeable fraction	71	6.46E+08	21.93	47	46	50	54	51	4.09E+10	4497.46	45	53	1.92E+10	1230.00
	Acid-exchangeable fraction duplicate	71	7.67E+08	22.60	47	46	50	54	51	3.34E+10	4379.60	45	53	2.22E+10	1247.50
S11	Acid-exchangeable fraction	29	1.92E+08	2.61	56	56	57	57	58	7.20E+10	176.50	--	--	--	267.50
	Acid-exchangeable fraction duplicate	29	2.07E+08	2.74	59	59	60	60	61	7.47E+10	184.50	--	--	--	270.00
S12	Acid-exchangeable fraction	35	2.85E+07	4.89	49	49	50	50	51	2.40E+10	129.50	--	--	--	527.50
	Acid-exchangeable fraction duplicate	36	2.84E+07	5.55	51	51	52	52	53	2.20E+10	125.50	--	--	--	526.00
S14	Acid-exchangeable fraction	81	1.06E+09	25.00	57	56	60	66	62	9.78E+08	2096.62	45	53	2.07E+10	303.13
	Acid-exchangeable fraction duplicate	81	1.11E+09	25.10	54	53	57	62	59	7.53E+08	2126.10	45	53	2.16E+10	303.75
S15	Acid-exchangeable fraction	76	1.00E+09	68.40	52	52	56	61	58	1.46E+10	1051.10	45	53	8.70E+10	705.00
	Acid-exchangeable fraction duplicate	76	8.77E+08	65.70	54	53	57	62	59	1.33E+10	1049.99	45	53	9.06E+10	702.50
S17	Acid-exchangeable fraction	71	3.67E+09	30.75	55	54	58	63	60	9.02E+09	2475.44	45	53	7.03E+10	668.75
	Acid-exchangeable fraction duplicate	71	3.99E+09	31.35	56	55	59	64	61	7.51E+09	2467.86	45	53	6.87E+10	662.50
S18	Acid-exchangeable fraction	76	1.20E+09	11.04	51	51	55	60	57	2.93E+09	2705.41	48	57	2.77E+10	1303.75
	Acid-exchangeable fraction duplicate	76	1.17E+09	10.95	57	57	60	66	63	2.18E+09	2719.47	48	57	3.17E+10	1306.25
S19	Acid-exchangeable fraction	71	1.96E+09	15.88	55	54	58	63	60	3.13E+10	5598.12	45	53	5.51E+09	993.75
	Acid-exchangeable fraction duplicate	71	1.88E+09	15.70	54	53	57	62	59	3.58E+10	5630.98	45	53	5.23E+09	991.25
S20	Acid-exchangeable fraction	71	5.20E+08	12.08	51	51	55	60	57	2.88E+10	17302.01	41	48	1.20E+11	2140.00
	Acid-exchangeable fraction duplicate	71	5.25E+08	13.05	51	51	55	60	57	3.43E+10	17606.29	41	48	9.40E+10	2007.50
S21	Acid-exchangeable fraction	71	1.01E+09	12.70	56	55	59	64	61	3.25E+10	17885.81	45	53	6.27E+11	5340.00
	Acid-exchangeable fraction duplicate	71	1.02E+09	12.75	57	57	60	66	63	3.79E+10	18137.15	45	53	5.94E+11	5400.00
S23	Acid-exchangeable fraction	76	1.21E+09	34.85	50	50	53	59	55	1.35E+09	2271.79	45	53	4.15E+10	585.00
	Acid-exchangeable fraction duplicate	76	1.22E+09	35.13	50	50	53	59	55	1.13E+09	2274.63	45	53	3.45E+10	573.75
S26	Acid-exchangeable fraction	71	1.77E+08	34.00	58	58	62	68	64	1.77E+10	6712.06	41	48	4.88E+10	140.00
	Acid-exchangeable fraction duplicate	71	1.83E+08	33.80	58	58	62	68	64	1.62E+10	6742.84	41	48	5.00E+10	143.13
	Reducible fraction	97	5.02E+07	21.74	--	--	--	--	--	--	--	--	--	--	--
	Reducible fraction duplicate	96	5.08E+07	21.92	--	--	--	--	--	--	--	--	--	--	--
	Oxidizable fraction	98	1.95E+08	39.61	--	--	--	--	--	--	--	--	--	--	--
	Oxidizable fraction duplicate	97	1.92E+08	37.73	--	--	--	--	--	--	--	--	--	--	--

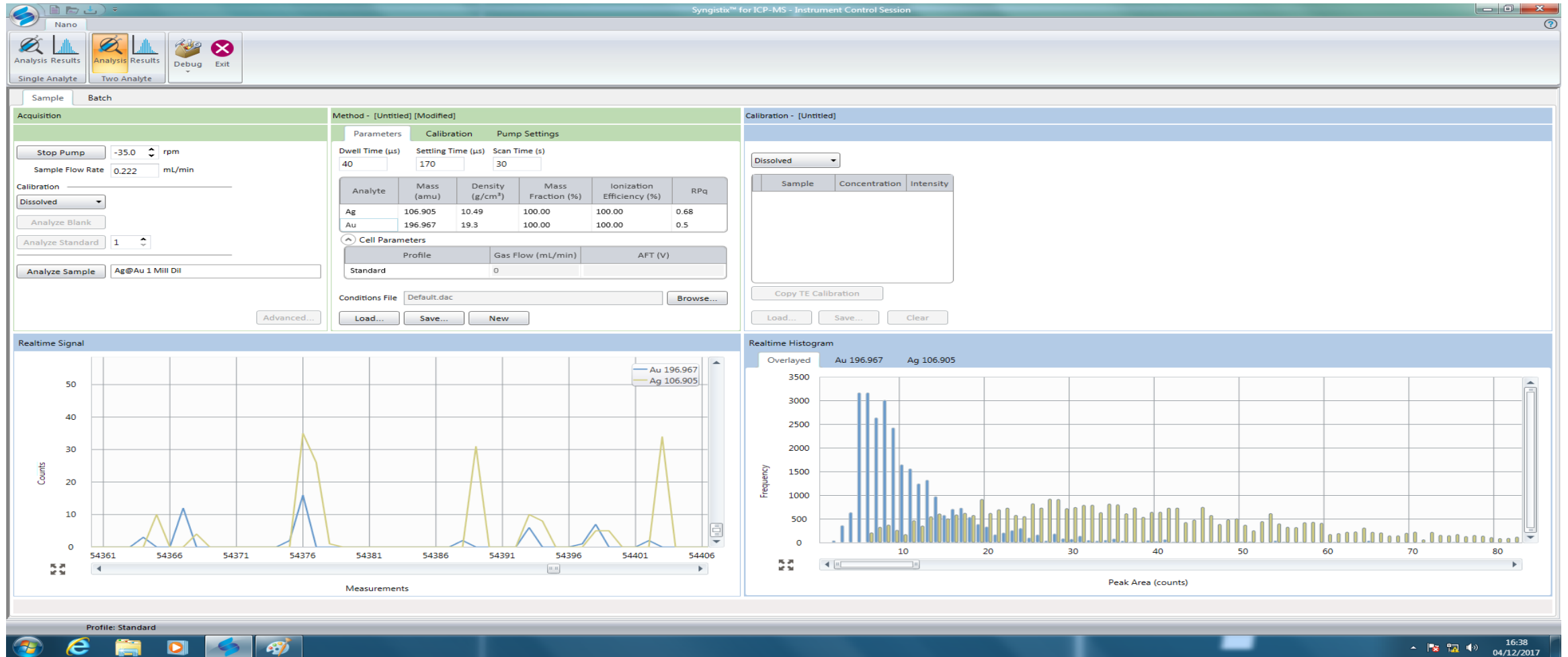
--: Not Tested

## Environmental Risk Implications of Metals in Sludges from Waste Water Treatment Plants: The Discovery of Vast Stores of Metal-Containing Nanoparticles

Feiyun Tou,<sup>†</sup> Yi Yang,<sup>\*,†,‡,§</sup> Jingnan Feng,<sup>†</sup> Zuoshun Niu,<sup>†</sup> Hui Pan,<sup>†</sup> Yukun Qin,<sup>†</sup> Xingpan Guo,<sup>†</sup> Xiangzhou Meng,<sup>§</sup> Min Liu,<sup>†</sup> and Michael F. Hochella<sup>||,⊥</sup>

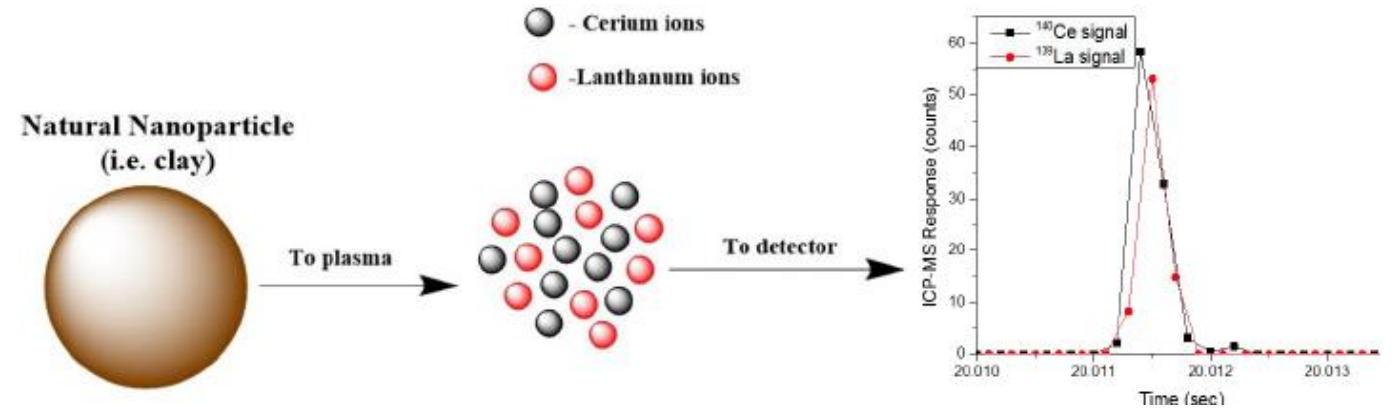


# 单颗粒双元素同时分析 ( Au@Ag )

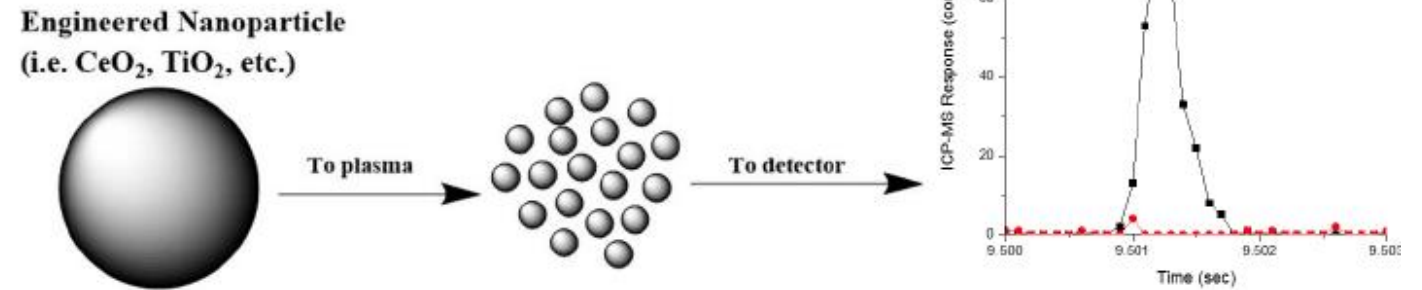


# 单颗粒双元素同时分析

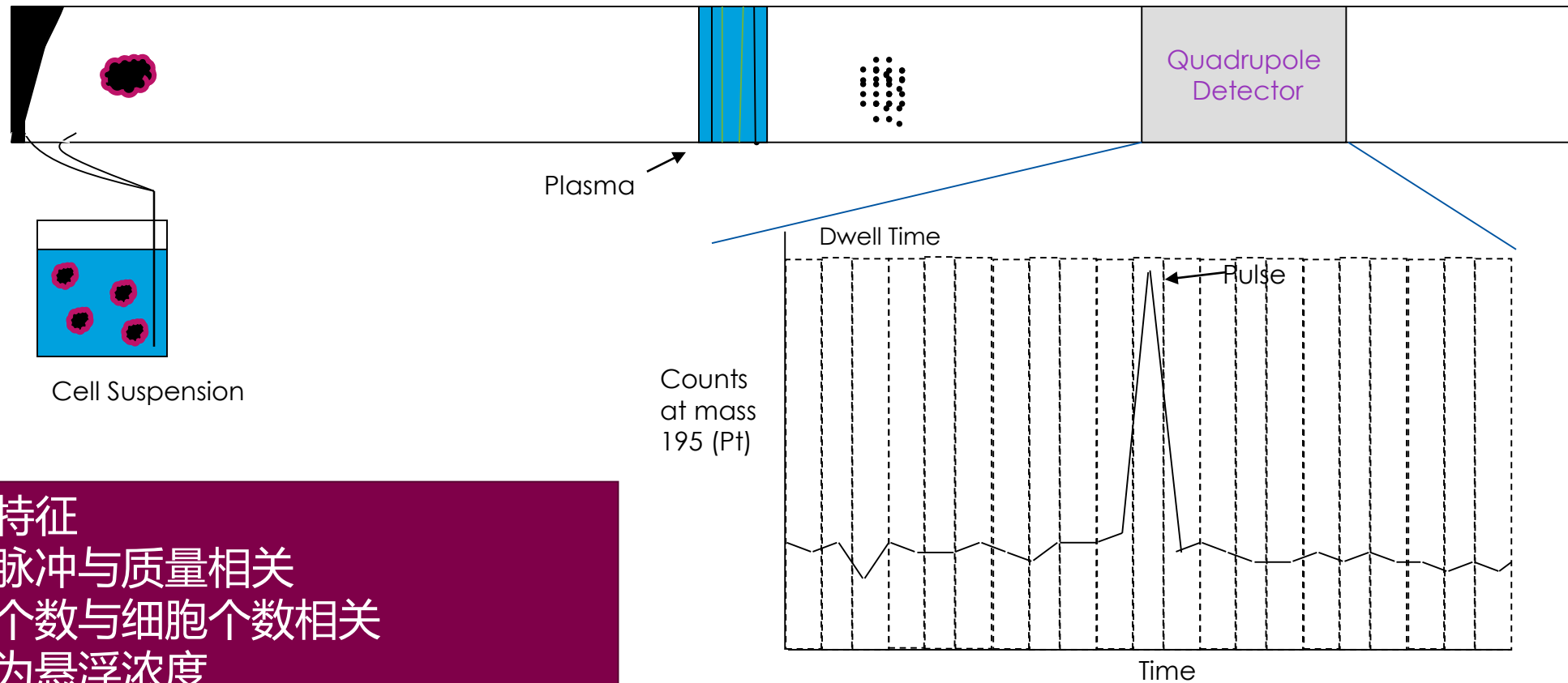
- Natural clay is composed of a 2:1 ratio of Ce:La



- Engineered CeO NP is composed of Ce

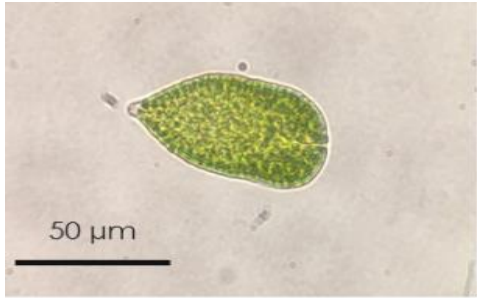


# Single Cell ICP-MS 工作原理

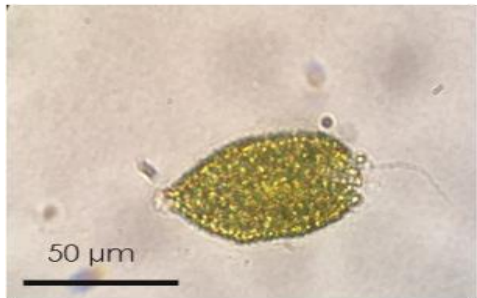


- 元素特征
- 信号脉冲与质量相关
- 脉冲个数与细胞个数相关
- 基线为悬浮浓度

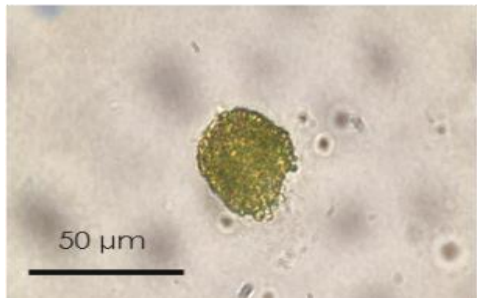
# SP-ICP-MS单颗粒用于细胞、藻类、细菌等生物分析



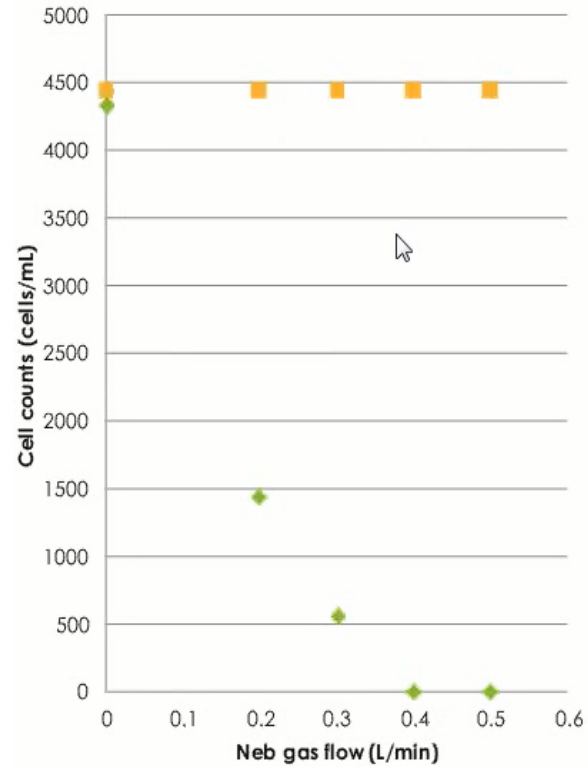
Stock  
Before Nebulization



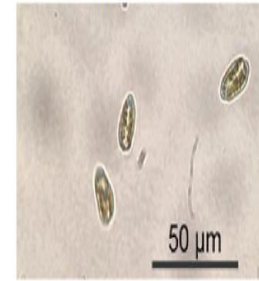
After Nebulization  
Neb gas 0.3



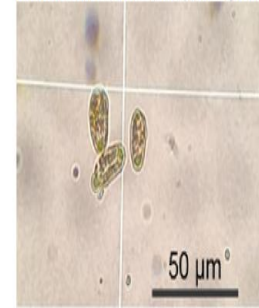
After Nebulization  
Neb gas 0.4



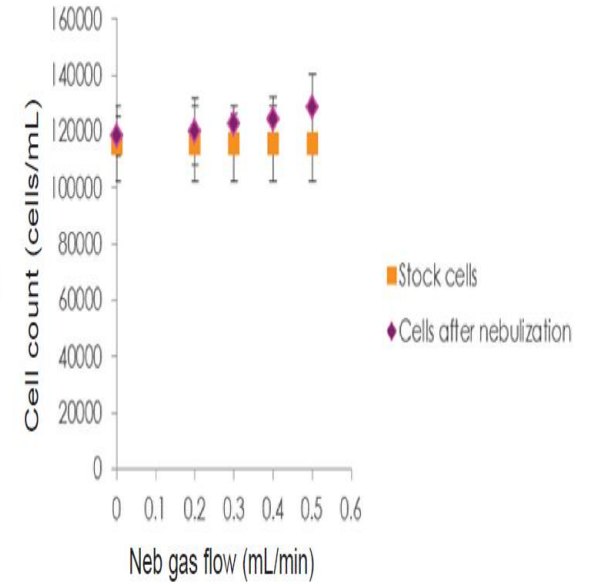
A: Before nebulization



B: After nebulization (Neb gas 0.4)



C: Number of viable cells vs. nebulizer gas flow





## SP-ICP-MS单颗粒用于细胞、藻类、细菌等生物分析

- Nanoparticles < 0,1  $\mu\text{m}$
- **Aerosol-droplets**  $\sim 4 \mu\text{m}$
- Yeast cells 2 - 10  $\mu\text{m}$
- Algae cells 1 - 100  $\mu\text{m}$

- 传统ICP-MS雾化器不适合细胞、藻类、细菌等生物分析



Asperon™ Linear Path



旋流雾室



Scott 双通道雾室

# Asperon™ 单细胞雾室与传统旋流对比

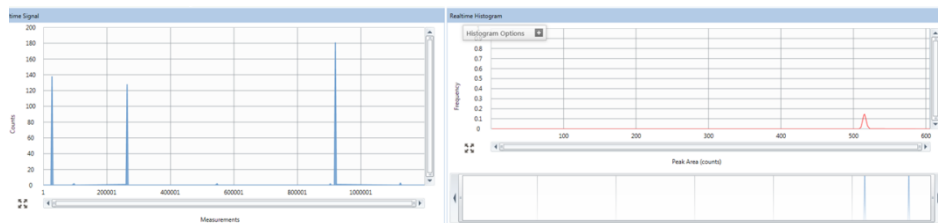
Spray chamber	Baffled Cyclonic	Asperon™
Neb gas flow (mL/min)	0.92	0.32
Make up gas (mL/min)	0	0.7
Sample flow rate (mL/min)	0.283	0.015
TE 2.5 $\mu$ m beads (%)	0.04	30.84
TE 60 nm NIST (%)	5.42	31.33



Asperon™ Linear Path

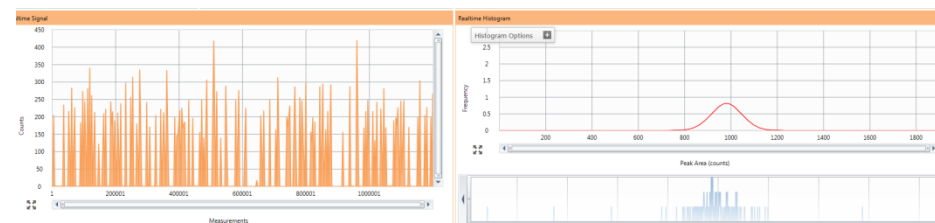
Baffled Cyclonic

2.5  $\mu$ m Beads

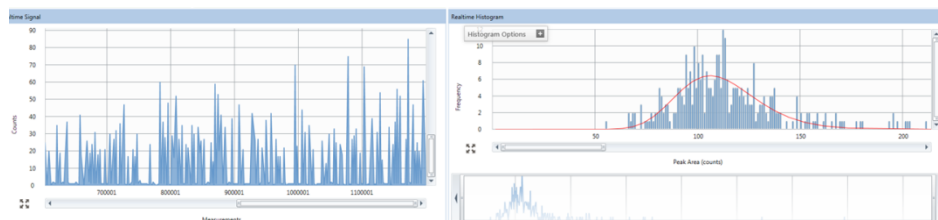


Asperon™

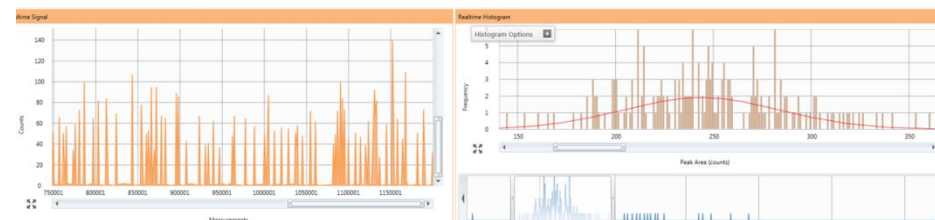
2.5  $\mu$ m Beads



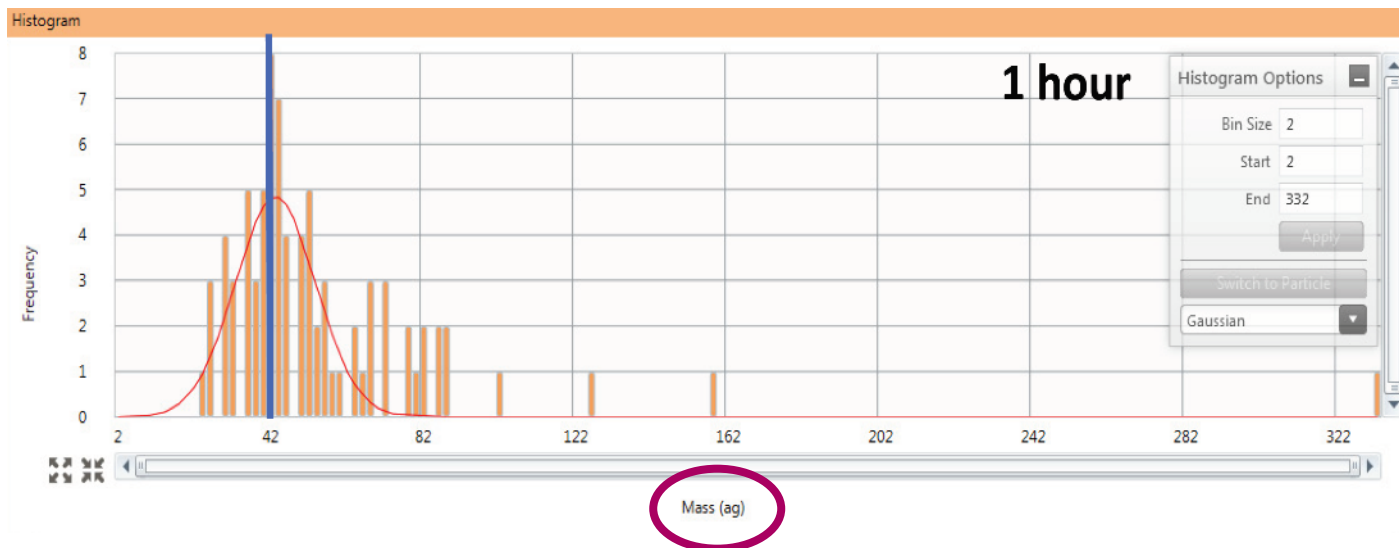
60 nm Au NIST



60 nm Au NIST



# Single cell 软件– 在 attogram (ag) 水平上的分析



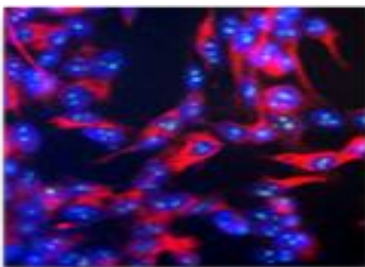
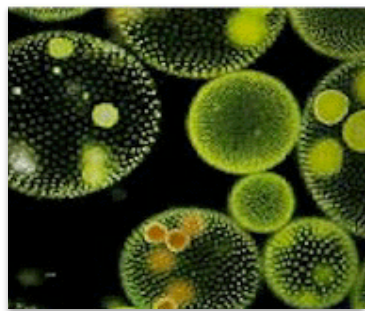
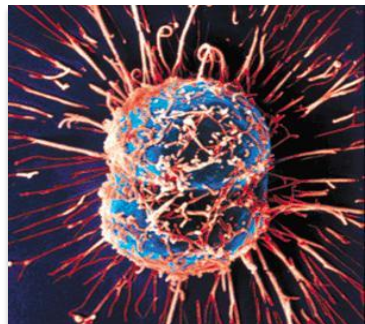
Prefix		$10^n$	Decimal	English Word		Platinum Atoms
		$10^0$	1	one		
deci	d	$10^{-1}$	0.1	tenth		
centi	c	$10^{-2}$	0.01	hundredth		
milli	m	$10^{-3}$	0.001	thousandth	mg Pt	
micro	$\mu$	$10^{-6}$	0.000001	millionth	$\mu$ g Pt	
nano	n	$10^{-9}$	0.000000001	billionth	ng Pt	
pico	p	$10^{-12}$	0.000000000001	trillionth	pg Pt	3,000,000,000
<b>femto</b>	<b>f</b>	<b><math>10^{-15}</math></b>	<b>0.000000000000001</b>	<b>quadrillionth</b>	<b>fg Pt</b>	<b>3,000,000</b>
<b>atto</b>	<b>a</b>	<b><math>10^{-18}</math></b>	<b>0.000000000000000001</b>	<b>quintillionth</b>	<b>ag Pt</b>	<b>3,000</b>
zepto	z	$10^{-21}$	0.000000000000000000001	sextillionth	zg Pt	3

## 单细胞ICP-MS准确分析镧系金属标记的聚苯乙烯珠

- 含有镧系金属的聚苯乙烯珠
- 尺寸：2.5  $\mu\text{m}$
- 进样 33,000 part./mL

From supplier				Measured using ionic calibrations in SC-ICP-MS (ag)					
Element	Atoms per bead ( $\pm 15\%$ )	Mass (ag)	Size (nm)	1	2	3	4	Average	STDEV
Ce 140	19.9E6	4626.26	109.7	4519.76	4560.64	4749.98	4698.90	4632.32	94.98
Eu 151	11.3E6	2833.38	101.1	2960.52	3011.75	3122.76	3075.32	3042.59	61.61
Eu 153	12.0E6	3048.75	103.6	2903.66	3239.50	3113.54	3061.42	3079.53	120.42
Ho 165	7.6E6	2082.32	76.8	2157.37	2227.98	2576.47	2354.24	2329.02	159.33
Lu 175	9.8E6	2847.82	82.1	2920.82	2779.02	2965.16	2892.10	2889.28	68.77
Number particles				34323	33145	34696	34821	34246	661.67

# 单细胞-ICP-MS应用



- 癌症研究
- 药物设计
- 环境毒理学
- 生物技术和细胞科学
- ○ ○ ○



# 基于单细胞-ICP-MS 的卵巢癌细胞对顺铂吸收研究新方法



APPLICATION NOTE

ICP - Mass Spectrometry

Authors:  
 Lauren Amable  
 National Institute on Minority Health and Health Disparities, National Institutes of Health Bethesda, MD

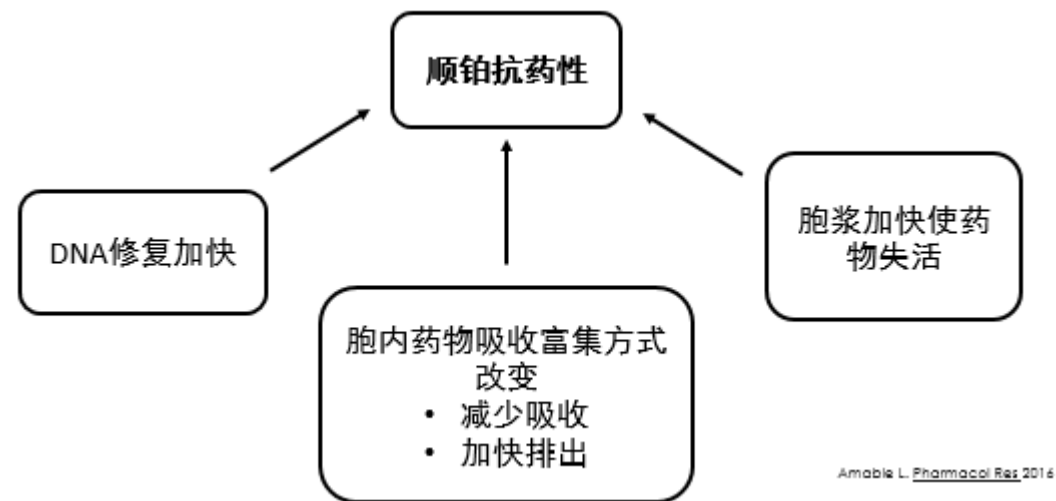
Stan Smith  
 Chady Stephan  
 PerkinElmer, Inc.  
 Shelton, CT

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

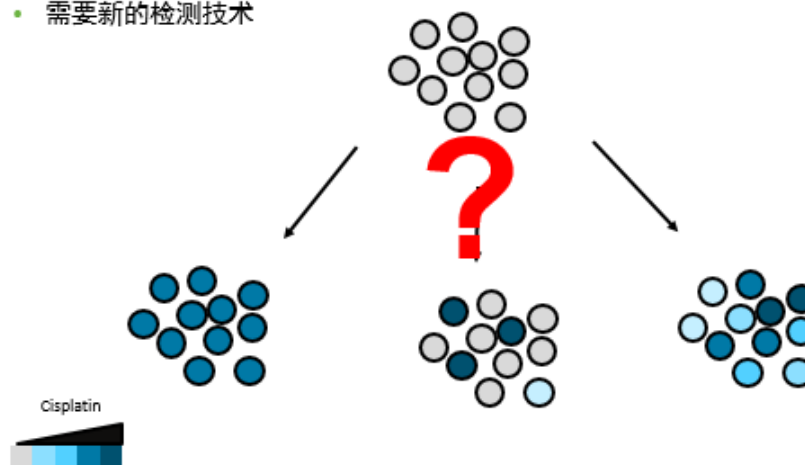
**Introduction**  
 Cisplatin, carboplatin, and oxaliplatin are the most widely used of platinum-based cancer chemotherapy drugs in the Western world. Cisplatin's effectiveness is due to its ability to bind to the DNA, resulting in DNA-platinum (Pt) adducts, which bend the DNA. The cells must then repair the DNA damage, otherwise DNA replication is blocked resulting in cell death!

Many cancers are initially sensitive to platinum-based treatment, but patients frequently relapse with tumors displaying resistance to further cisplatin therapy<sup>1</sup>. Cisplatin drug resistance is due to three major molecular mechanisms: increased DNA repair, increased cytosolic inactivation, and altered cellular accumulation. Decreased cellular uptake or increased cellular export of cisplatin constitutes the mechanisms involved in altered cellular accumulation<sup>1</sup>.





- 传统AA, ICP, MAS技术只能测定吸收平均值, 无法区分细胞间差异
- 顺铂以及其他药物的吸收存在特异性, 即吸收/不吸收; 吸收多与少的差异
- 需要新的检测技术



# 基于单细胞-ICP-MS 的卵巢癌细胞对顺铂吸收研究新方法



APPLICATION NOTE

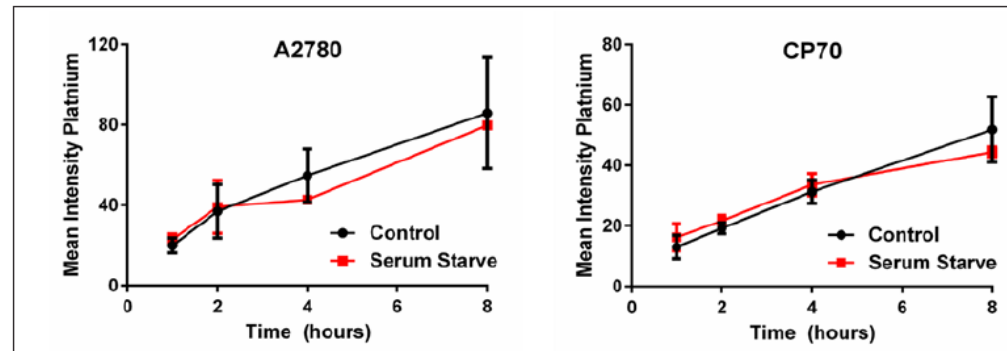
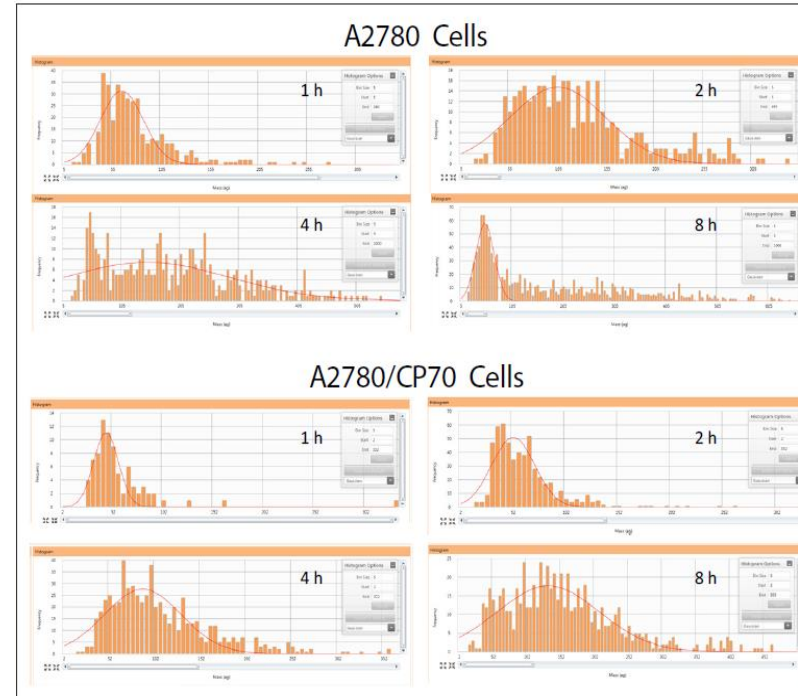
ICP - Mass Spectrometry

**Authors:**  
 Lauren Amable  
 National Institute on Minority Health and Health Disparities, National Institutes of Health Bethesda, MD  
  
 Stan Smith  
 Chady Stephan  
 PerkinElmer, Inc.  
 Shelton, CT

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# 基于单细胞-ICP-MS 对金纳米颗粒吸收



**APPLICATION NOTE**

**ICP - Mass Spectrometry**

**Authors:**  
 Stefan Wilhelm  
 Stephenson School of Biomedical Engineering  
 University of Oklahoma  
 Norman, Oklahoma

Ryan C. Benzen, Naga Rama Kathapala,  
 Anthony W. G. Burgitt  
 Chemistry and Biochemistry  
 University of Oklahoma  
 Norman, Oklahoma

Ruth Merrifield, Chady Stephaan  
 PerkinElmer, Inc.  
 Woodbridge, Canada

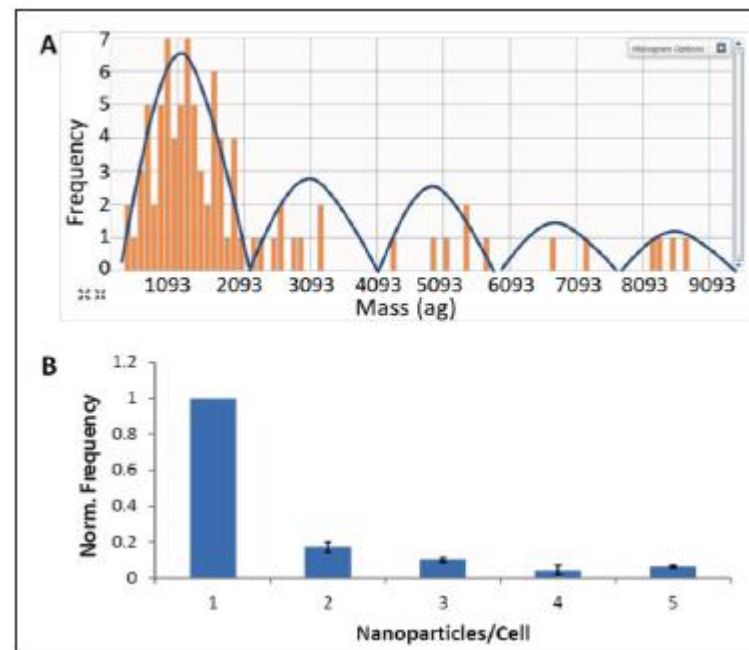
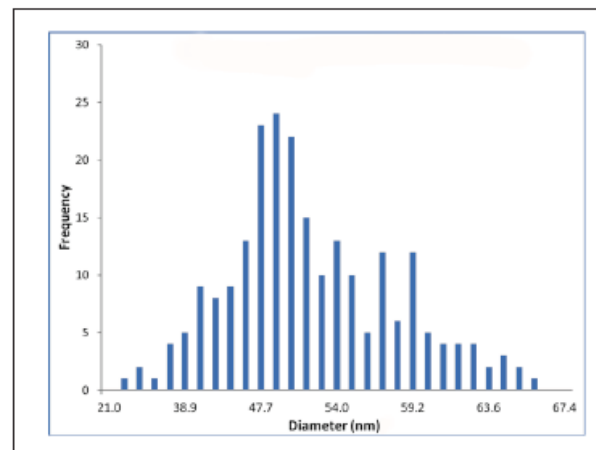
## Quantification of Gold Nanoparticle Uptake into Cancer Cells using Single Cell ICP-MS

### Introduction

Cancer is a disease that is characterized by the uncontrolled growth and spread of abnormal cells. According to the American Cancer Society, cancer is the second most

common cause of death in the US.<sup>1</sup> Current treatments for various cancers include surgery, radiation, immunotherapy, and chemotherapy. Although these conventional therapies may improve patients' overall survival and quality of life, they also have several limitations. For example, in conventional cancer chemotherapy, small-molecule-based cancer therapeutics distribute non-specifically throughout the entire human body. The consequence is that these drugs do not only kill cancer cells but also destroy healthy cells in the body causing severe side effects for cancer patients,<sup>2</sup> leading to a need for new therapies that can target diseased cells.

Nanoparticles (NPs) have been of significant interest over the last two decades as they offer attractive benefits for drug delivery to overcome limitations in conventional chemotherapy.<sup>3</sup> Nanoparticles can be engineered to carry both drugs and imaging probes to simultaneously detect and treat cancer. They may also be designed to specifically target diseased tissues and cells in the body. A number of nanoparticle-based cancer therapeutics have been approved for clinical use and/or are currently under development.<sup>4,5</sup> Advantages that rationally engineered nanoparticles may offer over conventional small-molecule drugs include: (i) prolonged circulation time in the body; (ii) reduction of non-specific cellular uptake and undesirable off-target and side effects; and (iii) improvement in cellular interactions through specific cancer cell targeting moieties.



# 基于单细胞-ICP-MS的淡水藻类对金纳米颗粒和金离子的摄入行为研究



## APPLICATION NOTE

### ICP -Mass Spectrometry

#### Authors

Ruth Merciful<sup>1</sup>  
Janis Lead<sup>1</sup>  
Chady Stephan<sup>2</sup>

<sup>1</sup>Center for Environmental NanoScience and Risk (CENR), Arnold School of Public Health, University of South Carolina, SC

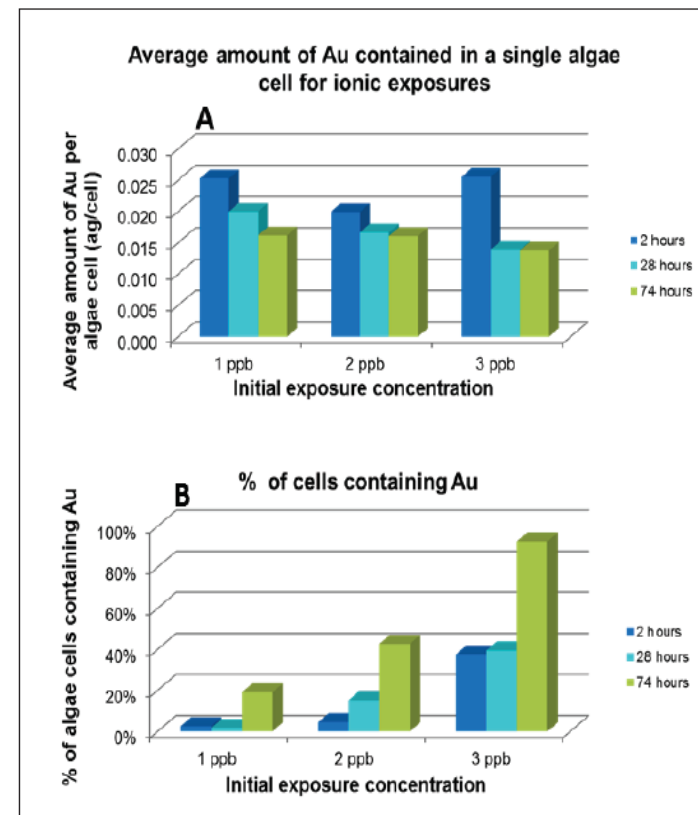
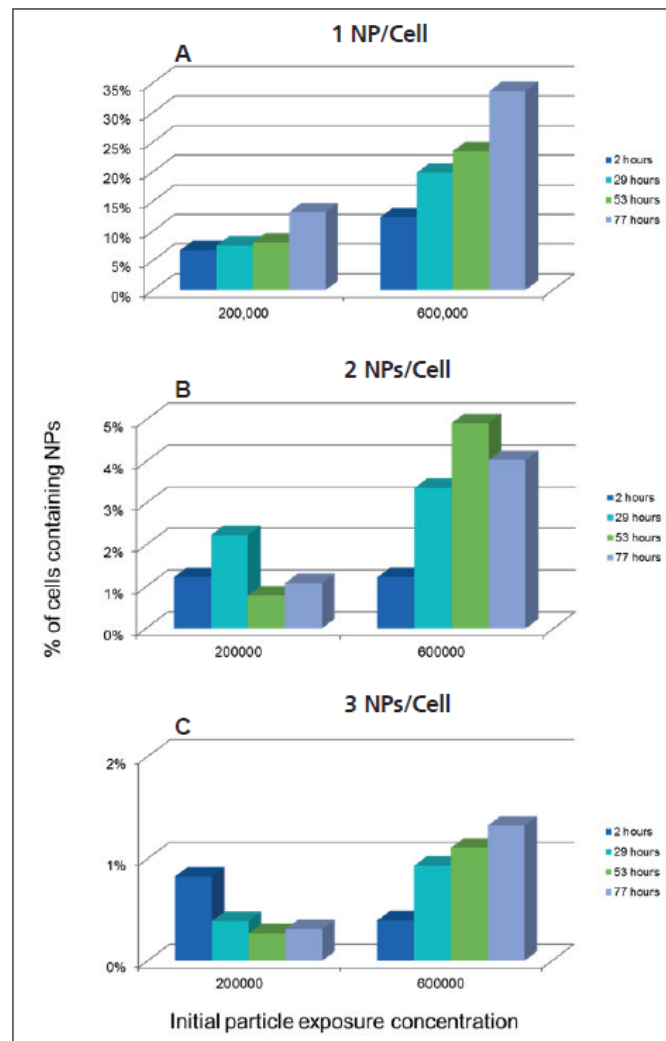
<sup>2</sup>PerkinElmer Inc., Shelton, CT

## Monitoring the Uptake of Nanoparticles and Ionic/Dissolved Gold by Fresh Water Algae using Single Cell ICP-MS

### Introduction

The uptake of metals into individual cells is of interest to both environmental<sup>1</sup> and human health<sup>2,3</sup> studies, whether the metal is dissolved or exists as nanoparticles (NPs).

Currently, cellular metal content is studied by removing the cells from their culture media (either by centrifugation or filtration), washing with fresh media solution, and then acid-digesting them for analysis by ICP-MS<sup>4</sup>. This methodology gives the total metal or particle content in a given number of cells rather than on a per-cell basis. As such, the metal concentration of an individual cell relies on the assumption that all cells accumulate the same amount of ionic or nanoparticulate metal. This assumption is not always true, as demonstrated by techniques such as transmission electron microscope (TEM)<sup>5</sup>, scanning electron microscope (SEM)<sup>6</sup>, and fluorescent tracking<sup>7</sup>. These microscopy techniques allow visualization of NP uptake into cells but are time consuming and prone to artifacts. TEM and SEM are qualitative, and labelling may give false positives where the label-NP complexes are not persistent.





# 基于单细胞-ICP-MS的淡水藻类对金纳米颗粒和金离子的摄入行为研究



**APPLICATION NOTE**

**ICP -Mass Spectrometry**

**Authors**  
 Ruth Mercifield<sup>1</sup>  
 Janis Lead<sup>1</sup>  
 Chady Stephan<sup>2</sup>

<sup>1</sup>Center for Environmental NanoScience and Risk (CENR), Arnold School of Public Health, University of South Carolina, SC

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# 单个细菌中铁含量的测定



**APPLICATION NOTE**

## ICP - Mass Spectrometry

**Author:**  
Mariko Ishihata  
Jennifer Woolcock  
Michael E. P. Murphy

Department of Microbiology and Immunology, Life Sciences Centre, University of British Columbia, Vancouver, BC Canada

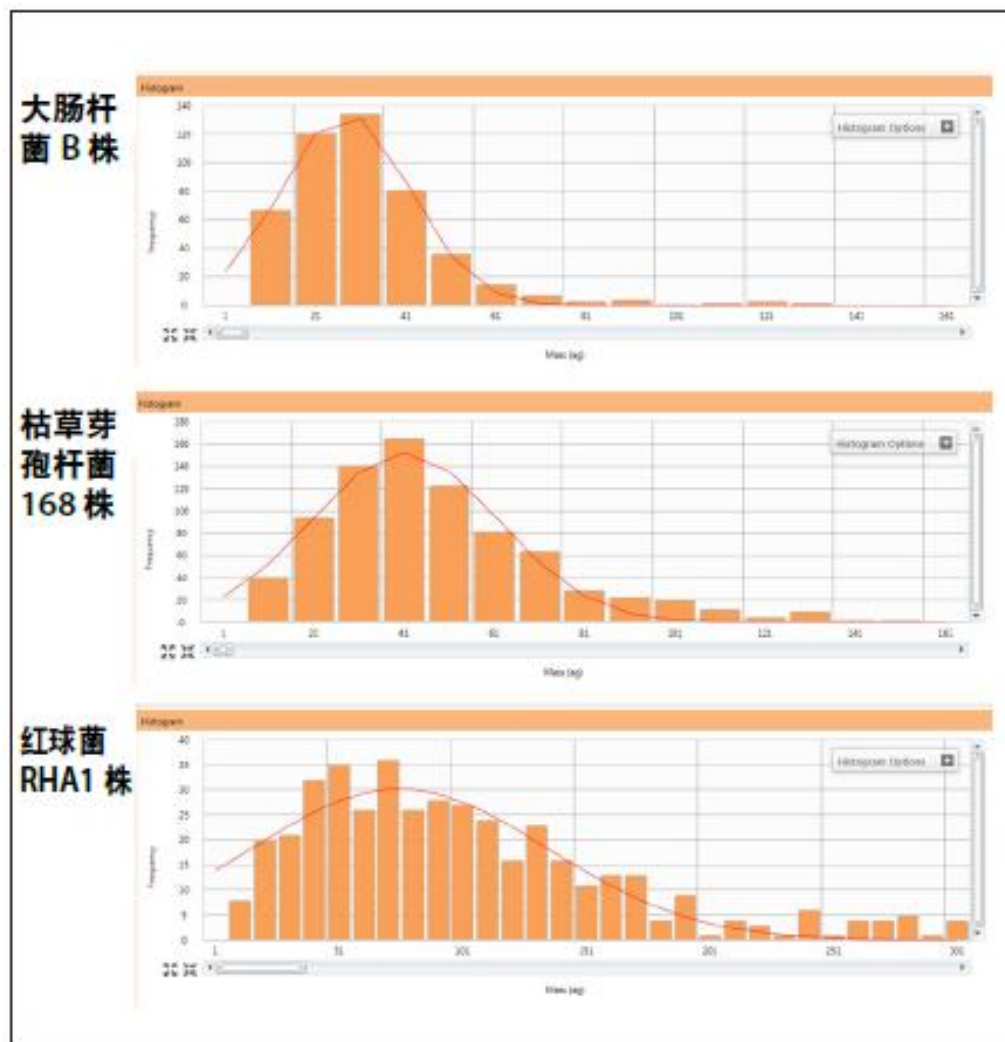
Ruth Merrifield  
Chady Stephan  
PerkinElmer, Inc.  
Woodbridge, ON Canada

## Iron Content Measurement in Individual Bacterial Cells Using SC-ICP-MS

### Introduction

Iron is an essential metal cofactor for diverse biological processes within the bacterial cell. It is often a growth-limiting nutrient in bacteria,

and the total iron quota for a cell will depend on the cells' growth states and metabolic requirements. Bacteria have evolved complex systems to regulate iron levels within the cell.<sup>1</sup> Excess soluble iron within the cell is toxic due to formation of reactive oxygen species that damage cellular components, meaning that iron levels must be tightly regulated. However, the variability of iron regulation within individual cells and throughout cell populations has not been determined. Quantifying iron in bacterial cells in near real time could provide insight into the limits of bacterial iron tolerance when defining the effects of growth conditions and stress responses, including those due to antibiotics. Interestingly, some mineral clays and clay extracts that are bactericidal are high in dissolved iron, which may disrupt bacterial iron homeostasis, leading to death.<sup>2</sup> Moreover, monitoring iron levels within single cells will provide the distribution of cellular iron to determine the homogeneity of a population.





# 单个细菌中铁含量的测定



**APPLICATION NOTE**

**ICP - Mass Spectrometry**

**Author:**  
 Mariko Iwabata  
 Jennifer Woolcock  
 Michael E. P. Murphy

Department of Microbiology and Immunology, Life Sciences Centre, University of British Columbia, Vancouver, BC Canada

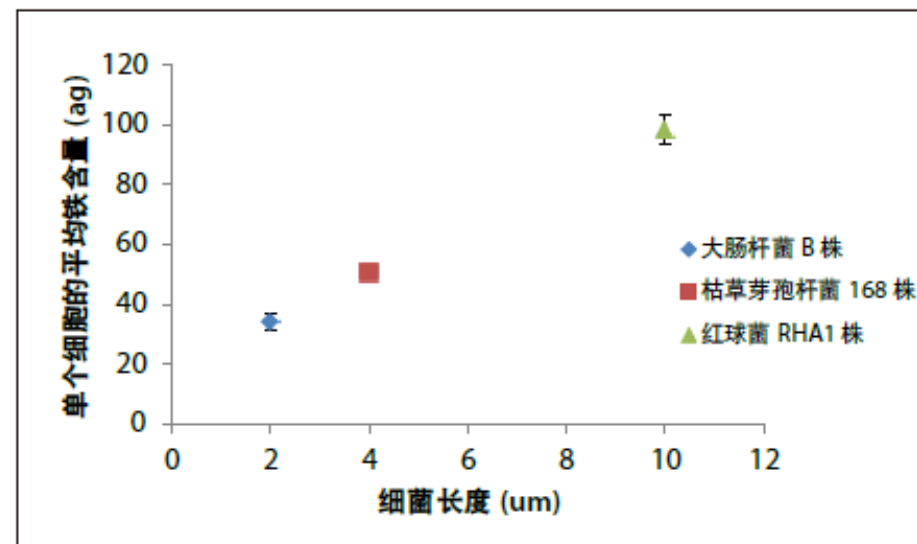
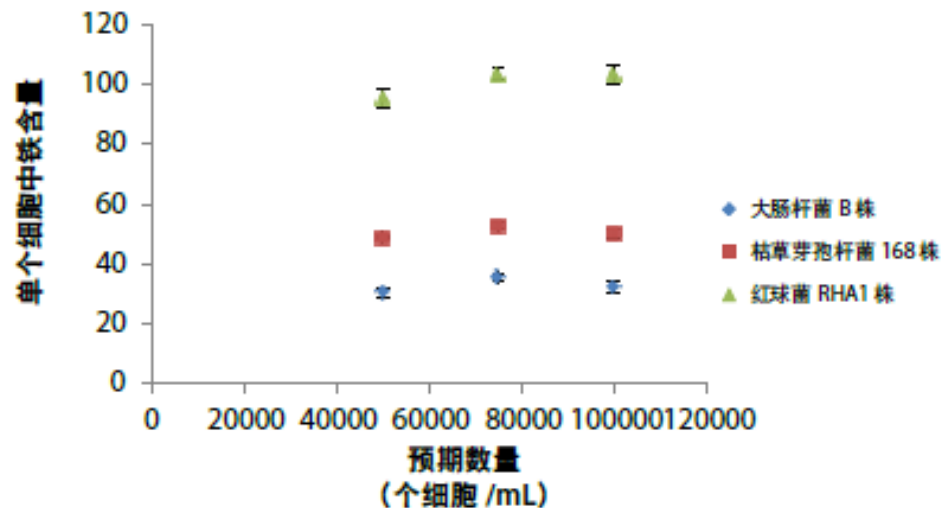
Ruth Merrifield  
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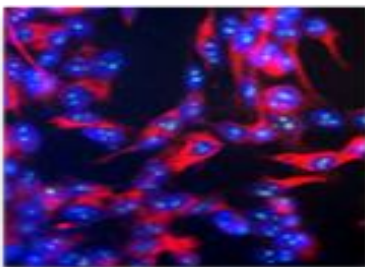
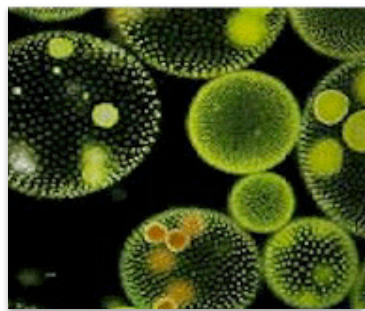
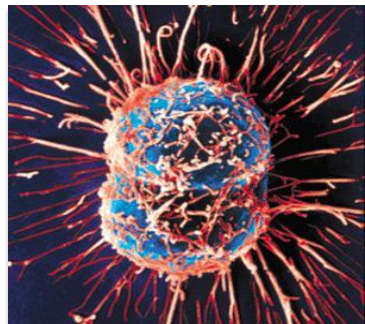
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# 单细胞-ICP-MS应用



- 癌症研究
- 药物设计
- 环境毒理学
- 生物技术和细胞科学
- ○ ○ ○





谢 谢!