



# What's the Big Deal About Something So Small? Nanoparticles in Food, Consumer Products, and the Environment

---

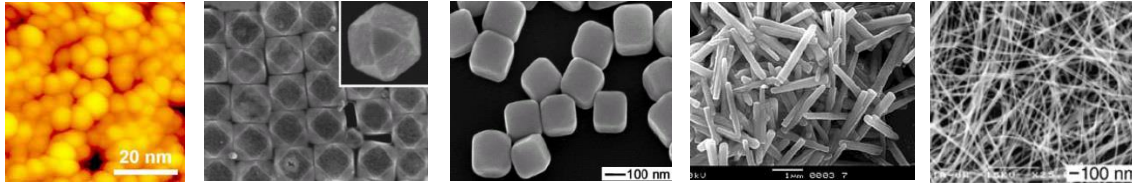
Lindsey Whitecotton  
Applications Chemist

# Agenda

- Nanoparticle Definition and Overview
- Survey of Analytical Techniques
- ICP-MS Based Techniques – benefits and limitations of each
- Single Particle ICP-MS – important considerations
- Single Particle ICP-MS – some results
- ICP-QQQ; unsurpassed analytical capabilities

# What are nanoparticles and where do they come from?

Particles with at least one dimension in the nano-scale (1-100nm)  $10^{-9}$  m



## Natural Sources

Produced by redox reactions, weathering, mining, volcanos, dust storms...



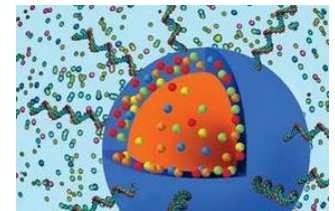
## Unintentionally produced NPs

Emitted to air, water and soil from combustion, wear, metal polishing and metal working, electric motors etc.



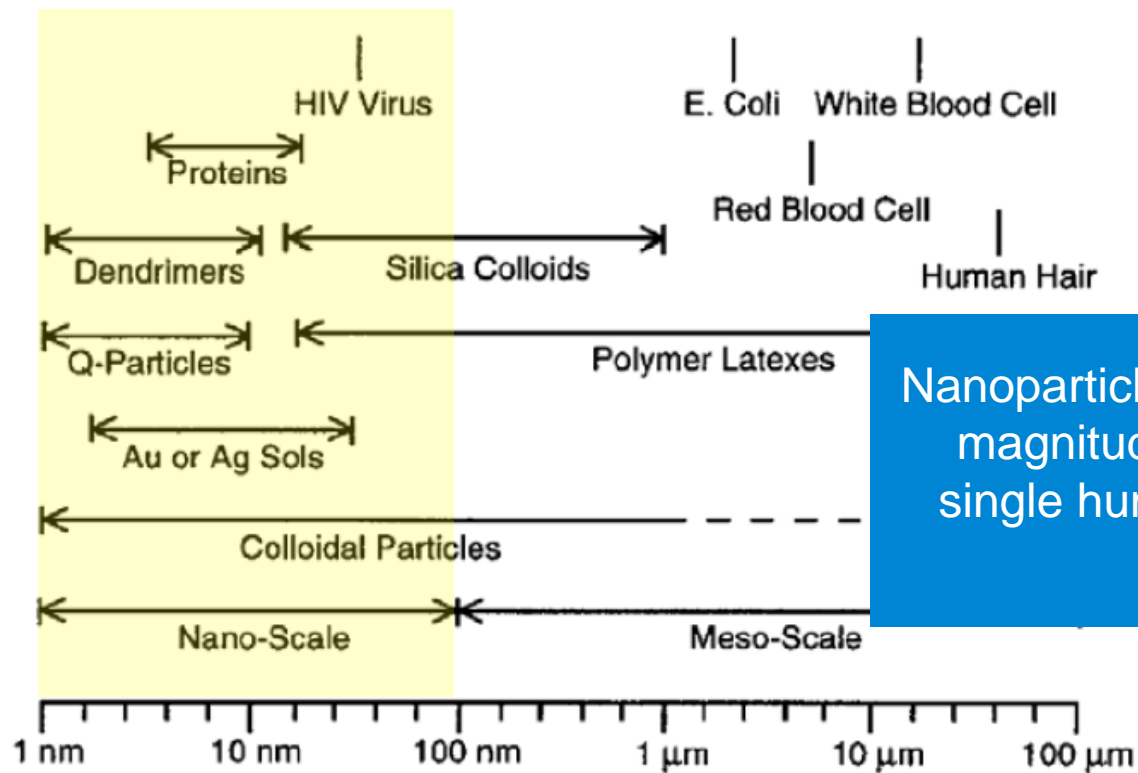
## Engineered NPs

Synthesized for a specific purpose by design



# Relative size of nanoparticles (log scale)

## Colloidal Domain – Characteristic Sizes



Orlin D. Velev

Department of Chemical and Biomolecular Engineering

North Carolina State University

odvelev@unity.ncsu.edu



Agilent Technologies

# Uses of Engineered Nanoparticles

Consumer goods

Pharmaceuticals and Medical Research

Semiconductor manufacturing

Foods and Food packaging

Ceramics

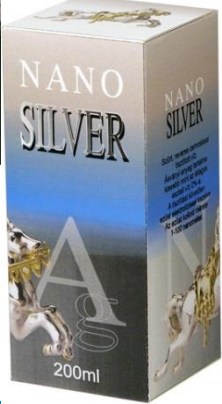
Superconductors

Electronics

Agriculture

Defense

...



# Nanoparticles in the environment - considerations

- Environmental health and safety concerns of nanoparticles
  - ◆ Potential to be released into environment
  - ◆ May be toxic to beneficial microbes
  - ◆ Potential impact on aquatic species
  - ◆ Poorly characterized toxicity to humans
- Analytical needs
  - ◆ Chemical composition
  - ◆ Size and size distribution
  - ◆ Mass/number concentration
  - ◆ Agglomeration state
  - ◆ Shape
  - ◆ Surface area/charge
  - ◆ .....

# Methods for NP characterization

- **Imaging** methods (TEM, SEM, AFM) are often definitive for detection, shape and size determination. Not quantitative nor representative.
- **Spectroscopic/optical** methods (UV-Vis, dynamic light scattering) simple, but subject to interferences. No elemental information.
- **Hyphenated techniques** (Chromatographic (or other online) separation coupled with ICP-MS detection). Allow representative samples, provide good particle size resolution, high elemental sensitivity but no information on individual particles

FFF-ICP-MS

CE -ICP-MS

HPLC-ICP-MS

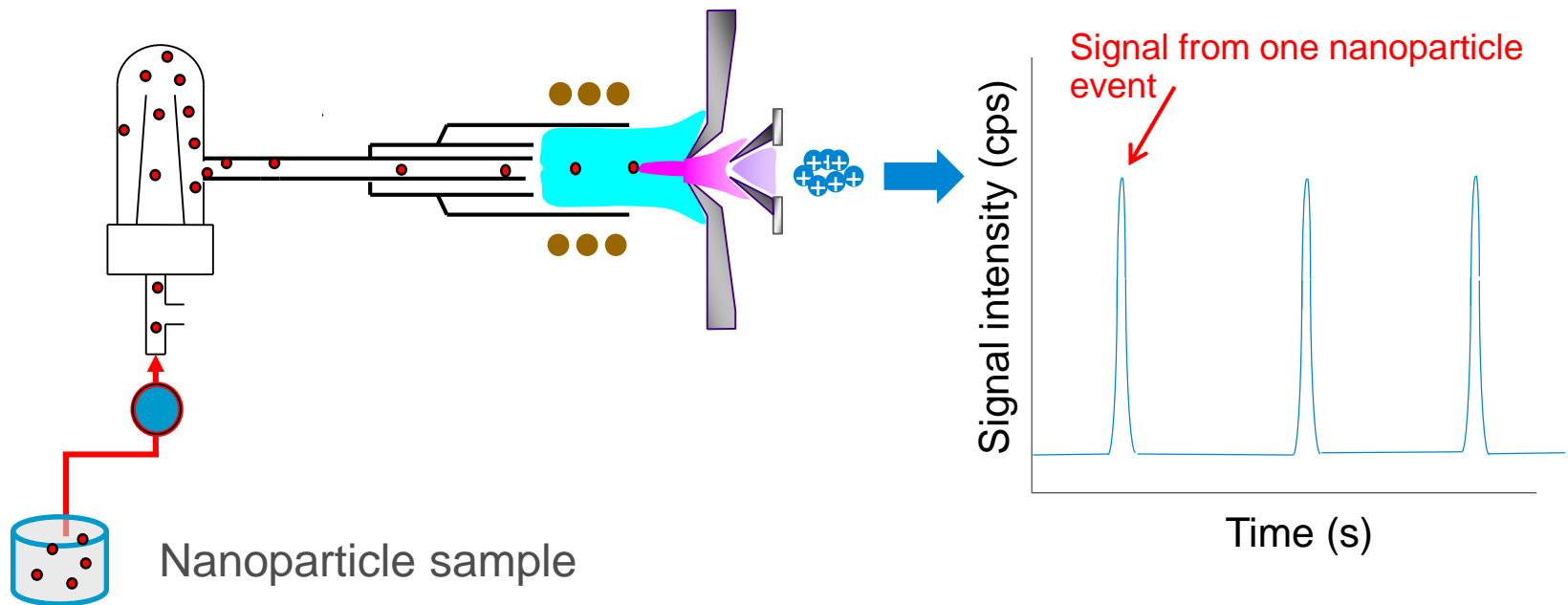


- **Single particle ICP-MS**



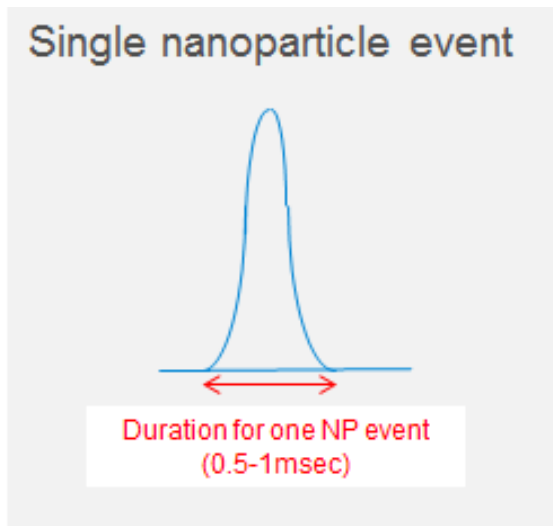
# Methods for NP characterization

- Single Particle - ICP-MS
  - Each nanoparticle gives a transient signal (a plume of ions generated from the particle)
  - Use Time Resolved data acquisition and analysis
  - Particle concentration, particle diameter, composition and size distribution are obtained



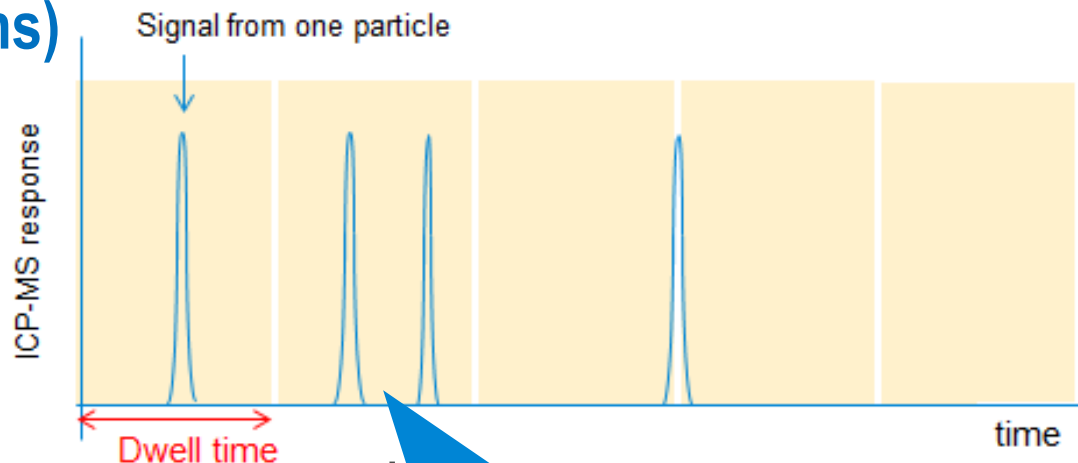
# Some important concepts for single nanoparticle analysis (Dwell Time matters, determining the optimum)

## - Long Dwell Time (> 3-5ms)



Integrated signal for entire dwell time creates a single intensity value for that “scan” including any nanoparticle peaks plus background due to ionic concentration, spectral interferences and instrument background.

Spectrum shown at right



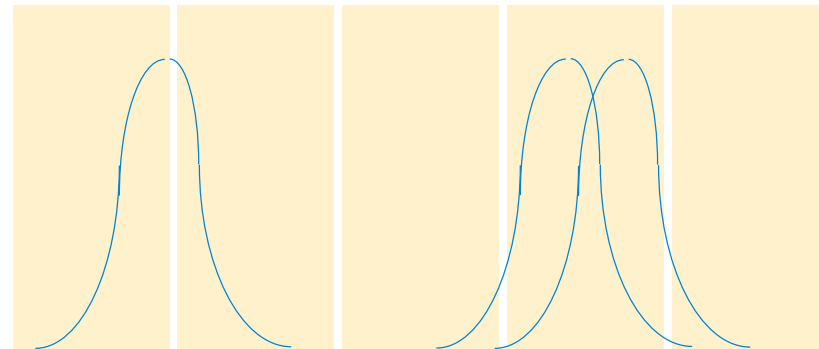
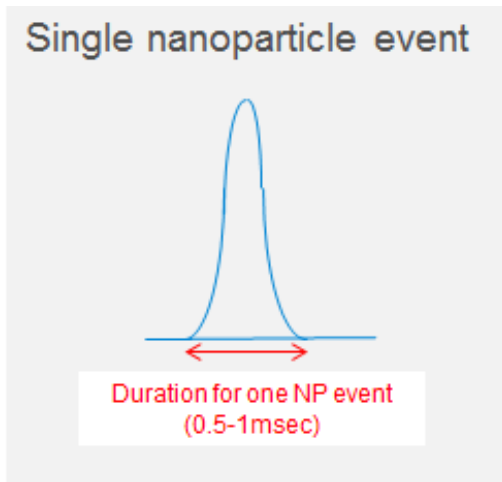
### Important Considerations:

- Correct dilution factor is critical to avoid multiple peaks per scan
- Background contribution to total signal increases with increasing dwell time.

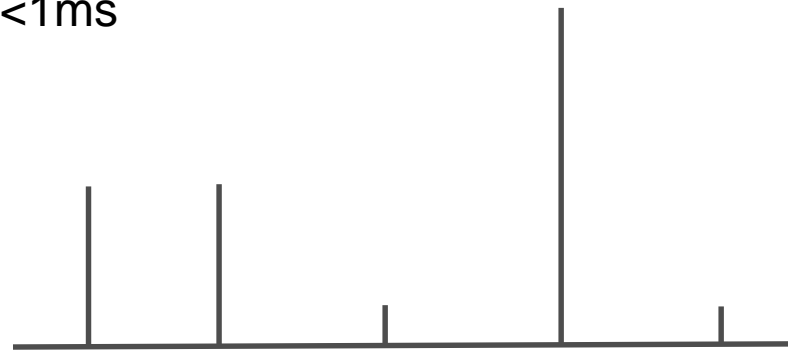


# Some important concepts for single nanoparticle analysis

However...as the dwell time becomes shorter, the nanoparticle signal will begin to decrease with the background, but the potential problem with overlapping peaks is still not solved. Correct dilution is still important.



<1ms



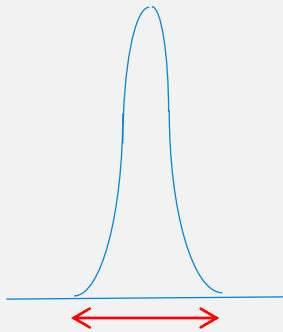
- Just shortening the dwell time alone does not solve the problem
- Need a way to integrate signal over multiple scans to:
  - Accurately quantify signal from single particle
  - Help identify overlapping peaks

# Microsecond Scanning with no Settling Time

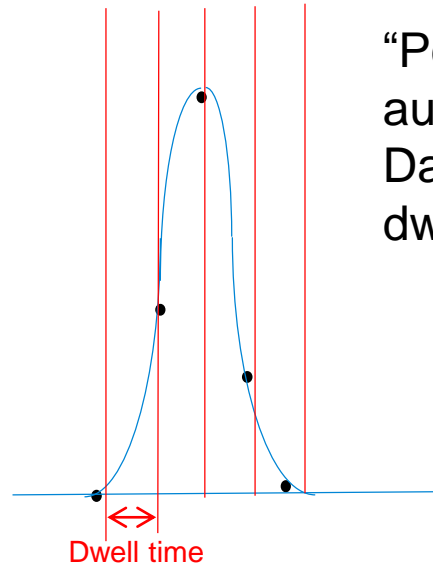
## - Short Dwell Time ( $\ll 1\text{ms}$ )

- Peak Integration Mode

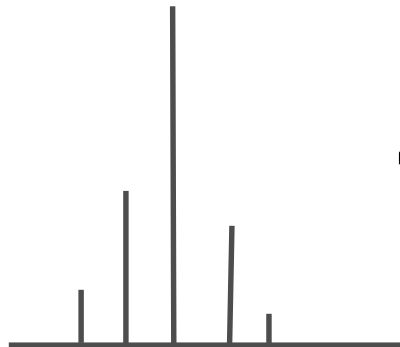
Single nanoparticle event



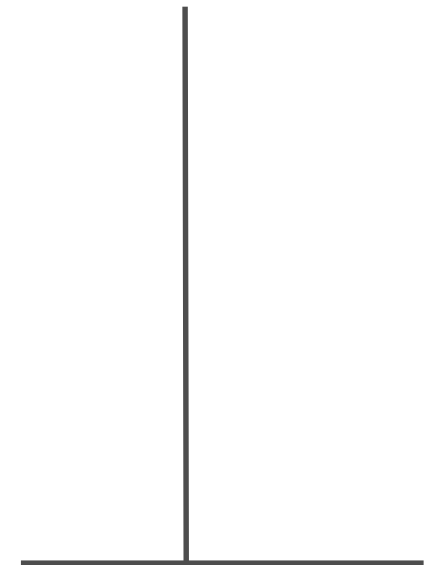
Duration for one NP event  
(0.5-1msec)



“Peak Integration Mode” is automatically enabled by sNP Data Analysis software when dwell time is  $< 1\text{ms}$



$$\Sigma =$$



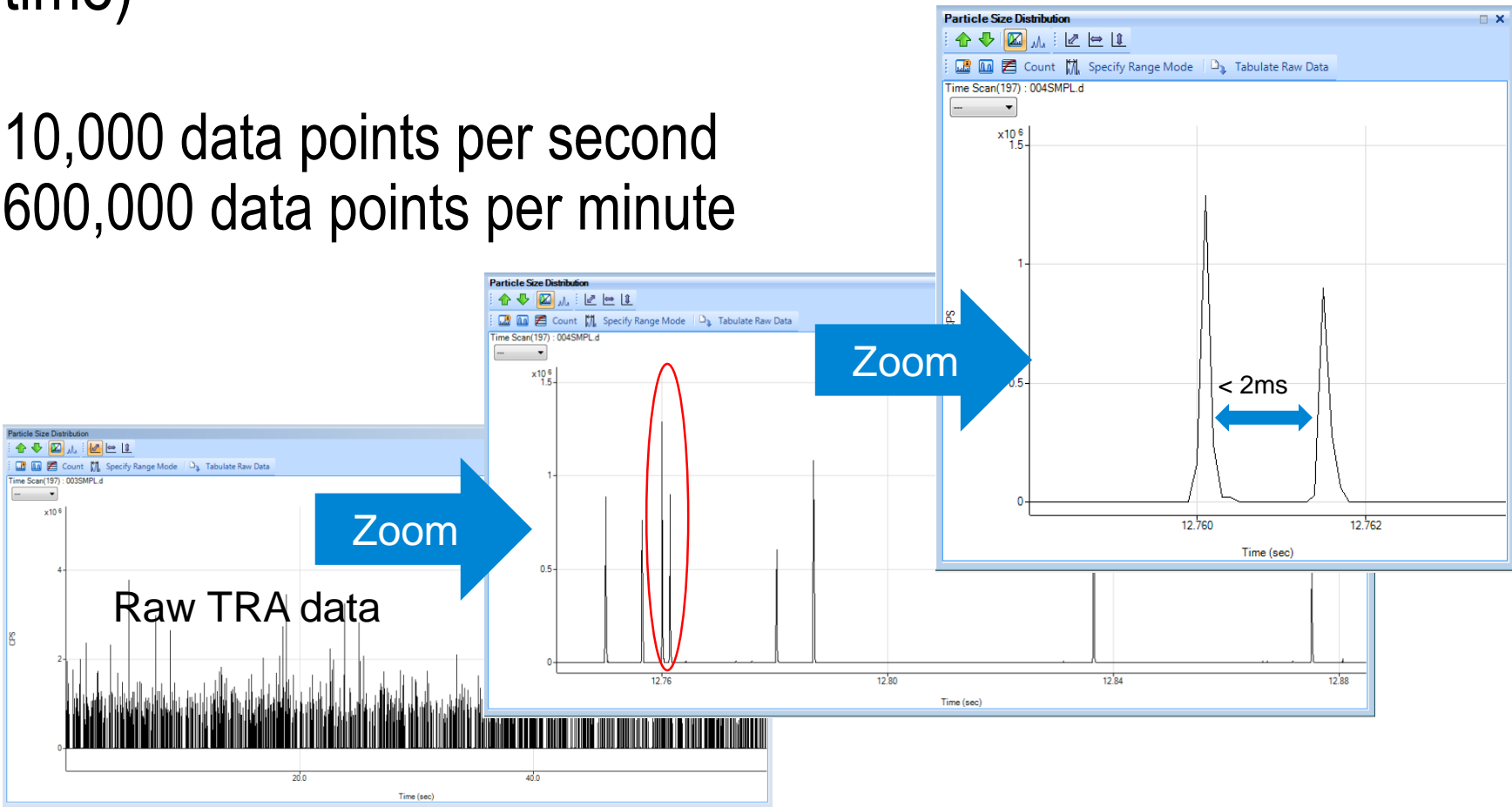
# What about very short dwell times ( $<100\mu\text{s}$ )?

## Minimum Particle Size and ionic concentration

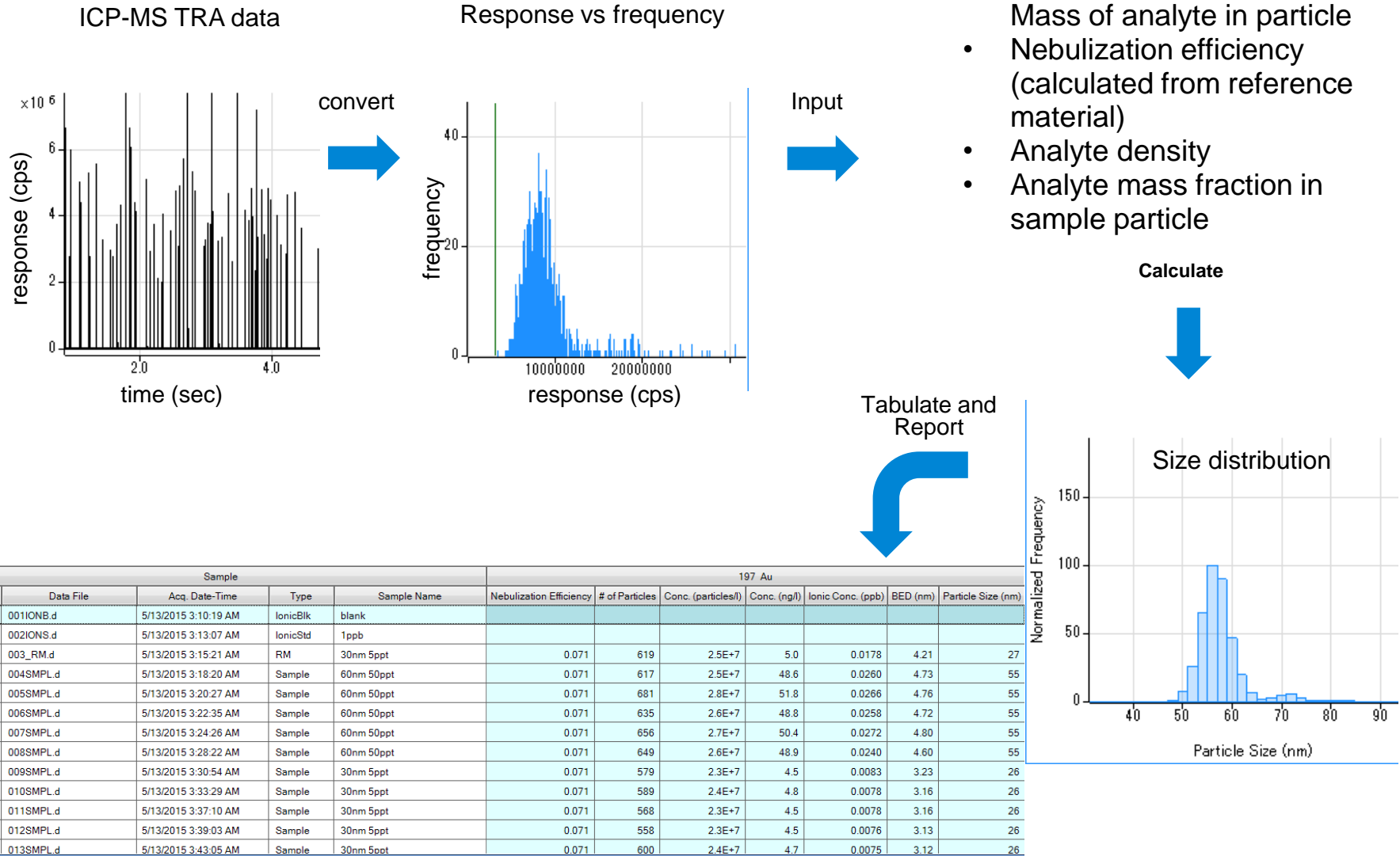
- Minimum Detectable Particle Size is limited by signal/background
- Particle signal decreases as the cube of the diameter so high sensitivity is critical to achieve good particle signal precision
  - 30nm particle generates 1/8 the response of a 60nm particle
  - 15nm particle generates 1/64 the response of a 60 nm particle
  - Background signal doesn't decrease with particle size
  - 1 detected background count at 10 $\mu\text{s}$  dwell time = 100,000cps! Background precision (minimum detectable particle size and ionic concentration) are compromised.
- Particle signal precision decreases with decreasing dwell time
- 100 $\mu\text{s}$  dwell time is a good compromise between background precision and sufficient points to define the nanoparticle peak shape (~5 -10 points/peak)

# Fast TRA on Agilent 7900 (100 $\mu$ s dwell time, no settling time)

10,000 data points per second  
600,000 data points per minute



# Workflow for NP characterization

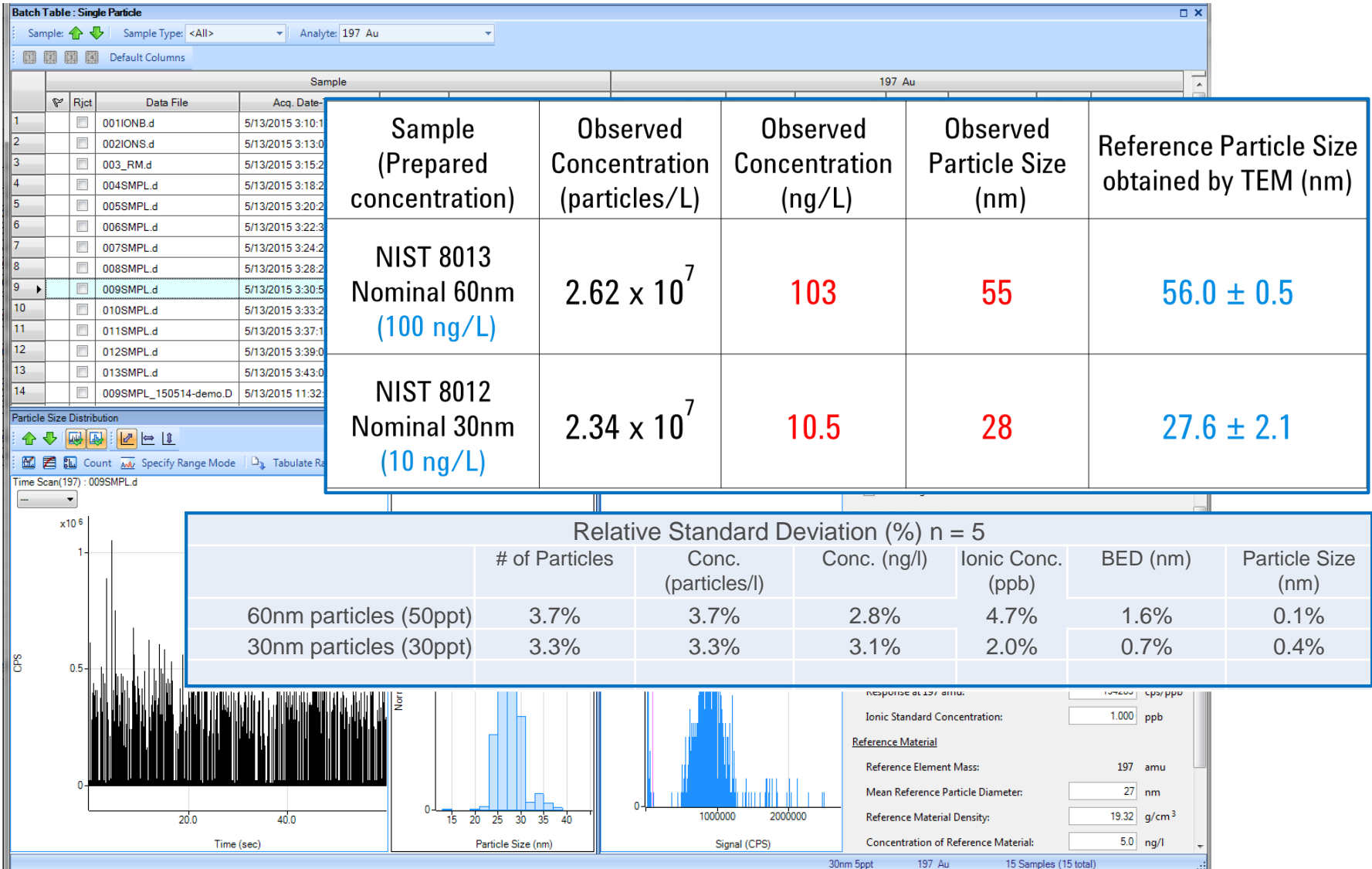


- Analyte response factor > Mass of analyte in particle
- Nebulization efficiency (calculated from reference material)
- Analyte density
- Analyte mass fraction in sample particle

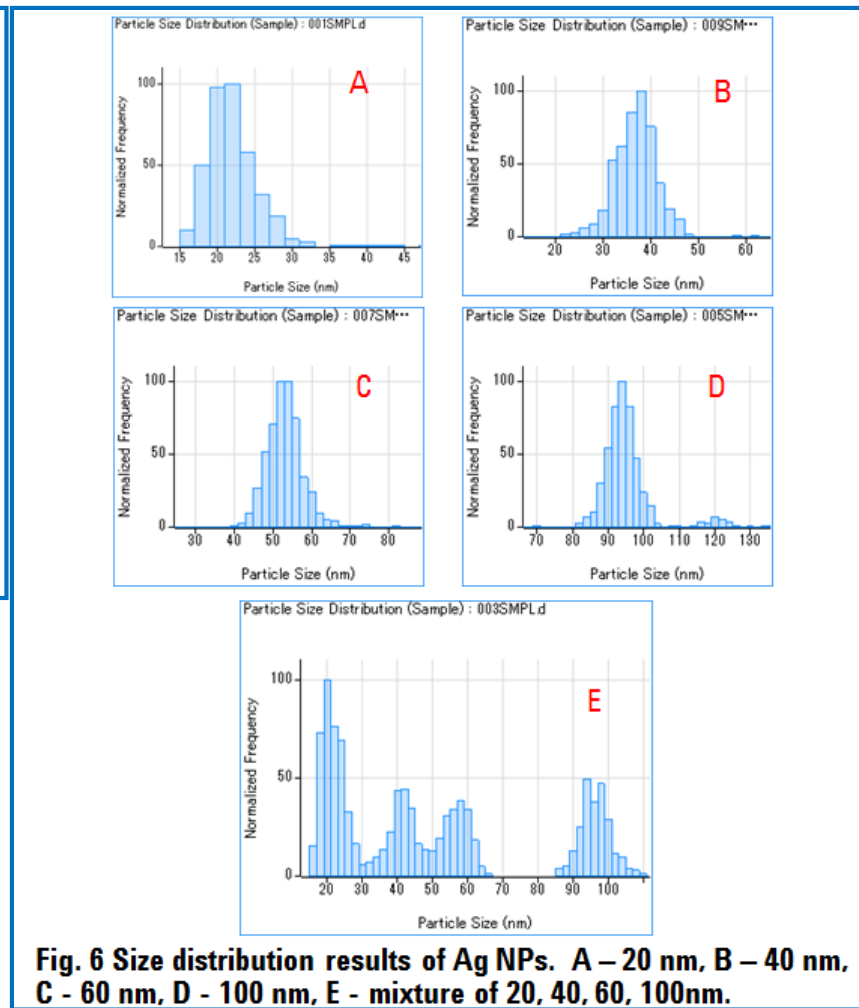
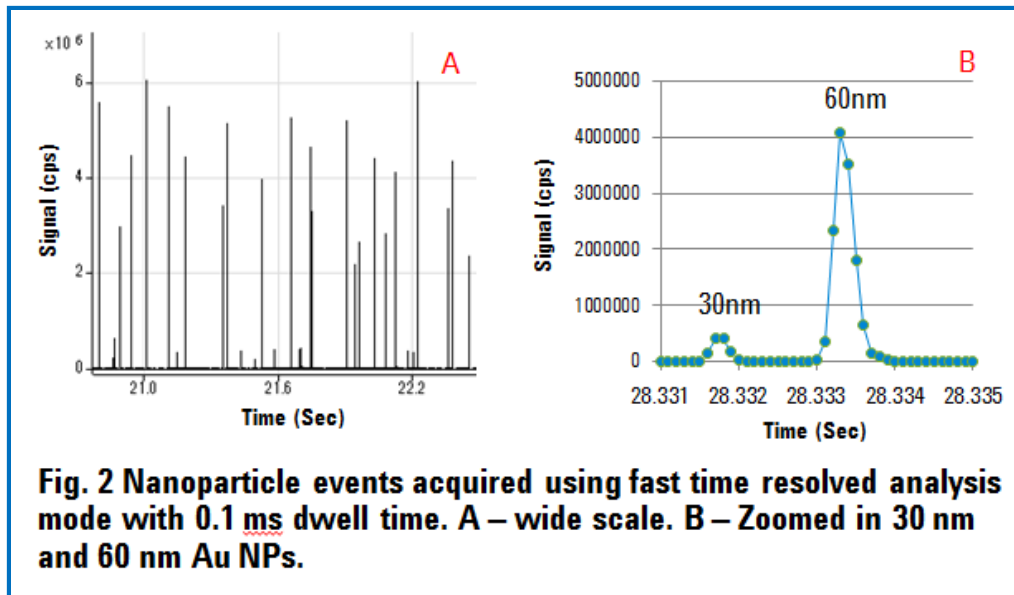
Sample				197 Au						
Data File	Acq. Date-Time	Type	Sample Name	Nebulization Efficiency	# of Particles	Conc. (particles/l)	Conc. (ng/l)	Ionic Conc. (ppb)	BED (nm)	Particle Size (nm)
001IONB.d	5/13/2015 3:10:19 AM	IonicBlk	blank							
002IONS.d	5/13/2015 3:13:07 AM	IonicStd	1ppb							
003_RM.d	5/13/2015 3:15:21 AM	RM	30nm 5ppt	0.071	619	2.5E+7	5.0	0.0178	4.21	27
004SMPL.d	5/13/2015 3:18:20 AM	Sample	60nm 50ppt	0.071	617	2.5E+7	48.6	0.0260	4.73	55
005SMPL.d	5/13/2015 3:20:27 AM	Sample	60nm 50ppt	0.071	681	2.8E+7	51.8	0.0266	4.76	55
006SMPL.d	5/13/2015 3:22:35 AM	Sample	60nm 50ppt	0.071	635	2.6E+7	48.8	0.0258	4.72	55
007SMPL.d	5/13/2015 3:24:26 AM	Sample	60nm 50ppt	0.071	656	2.7E+7	50.4	0.0272	4.80	55
008SMPL.d	5/13/2015 3:28:22 AM	Sample	60nm 50ppt	0.071	649	2.6E+7	48.9	0.0240	4.60	55
009SMPL.d	5/13/2015 3:30:54 AM	Sample	30nm 5ppt	0.071	579	2.3E+7	4.5	0.0083	3.23	26
010SMPL.d	5/13/2015 3:33:29 AM	Sample	30nm 5ppt	0.071	589	2.4E+7	4.8	0.0078	3.16	26
011SMPL.d	5/13/2015 3:37:10 AM	Sample	30nm 5ppt	0.071	568	2.3E+7	4.5	0.0078	3.16	26
012SMPL.d	5/13/2015 3:39:03 AM	Sample	30nm 5ppt	0.071	558	2.3E+7	4.5	0.0076	3.13	26
013SMPL.d	5/13/2015 3:43:05 AM	Sample	30nm 5ppt	0.071	600	2.4E+7	4.7	0.0075	3.12	26



# Precision and Accuracy (NIST 8012 and 8013)



# Analyzing mixtures of different particle sizes



Sample	Observed concentration (particles/L)	Observed concentration (ng/L)	Prepared total concentration (ng/L)	Recovery
60nm (NIST 8013) 50 ng/L + 30nm (NIST 8012) 5 ng/L	4.78 x10 <sup>7</sup>	57.6	55	105%
60nm (NIST 8013) 80 ng/L + 30nm (NIST 8012) 2 ng/L	5.13 x10 <sup>7</sup>	86.1	82	105%

# sNP Analysis

- It has been proven that both Au and Ag sNP can easily be analyzed

## **What about more relevant and complex sNP analyses of analytes that are routinely used around us**

- $\text{TiO}_2$  and  $\text{SiO}_2$  particles are widely used in many industries

$\text{SiO}_2$  : food additives, plastics, adhesives, electronics, paints, etc.

$\text{TiO}_2$  : paints, food colorants, cosmetics, pharmaceuticals, photocatalysts, etc.

- Some include nanoparticles (NPs)

For example, recent research indicated that in E551 ( $\text{SiO}_2$  food additive) at least part of the  $\text{SiO}_2$  is in the nano-size range

- Si and Ti are difficult to measure at trace levels in complex matrices by conventional ICP-MS

**A Rapid, accurate, sensitive technique for characterizing and quantifying smaller  $\text{TiO}_2$  and  $\text{SiO}_2$  NPs is necessary**

# Challenge of Si or Ti Measurement by Conventional Single Quadrupole ICP-MS

- **Interferences**

- Si is interfered by C and N matrices
- Ti is interfered by P, S, Ca, Si and C matrices

These matrices make the  $\text{SiO}_2$  or  $\text{TiO}_2$  NPs analysis in real samples difficult

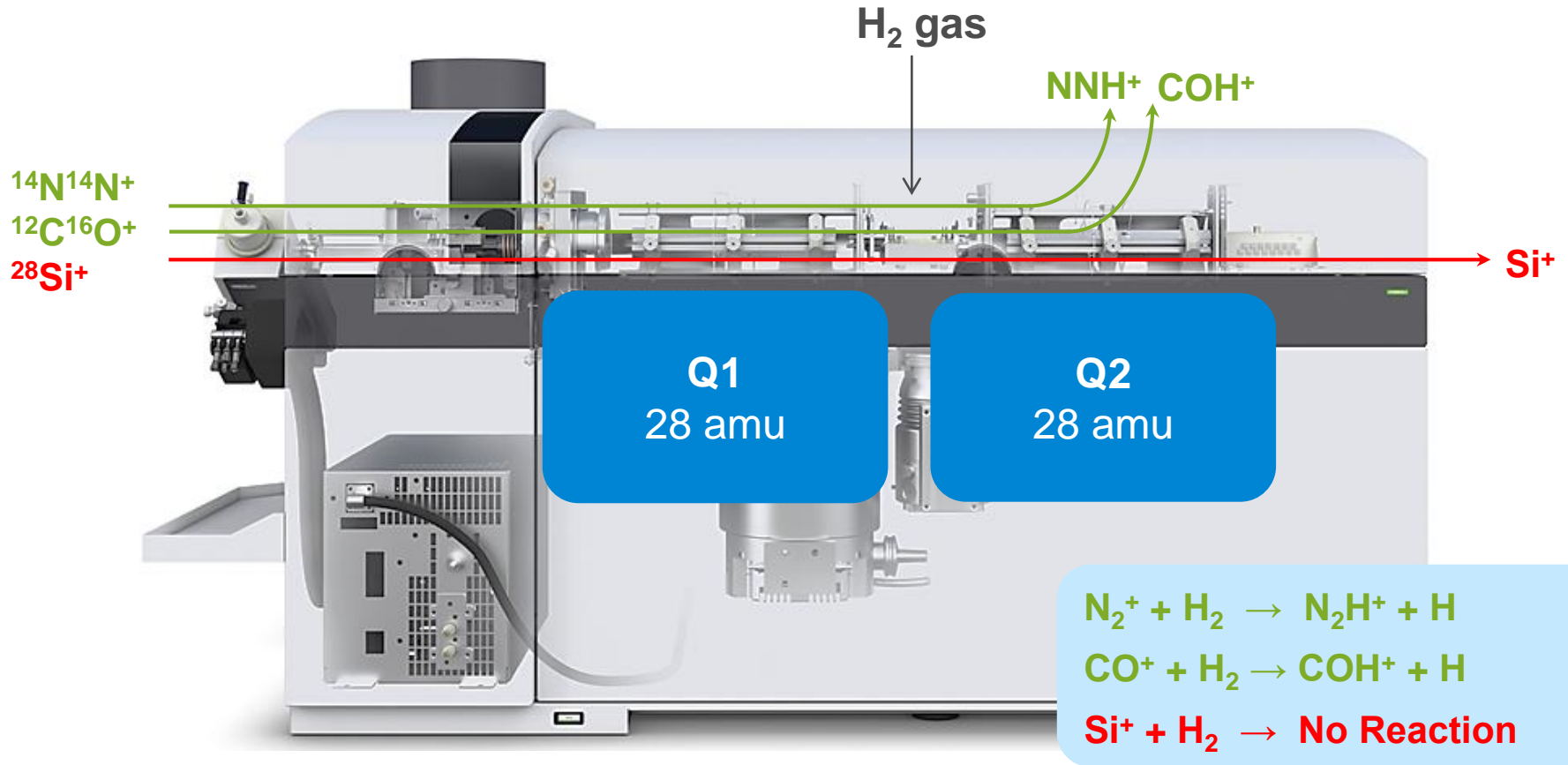
- **$^{48}\text{Ti}$  (74% abundance) cannot be used due to the  $^{48}\text{Ca}$  isobaric interference**

- Less interfered  $^{49}\text{Ti}$  (5.4% abundance) has less sensitivity resulting in limited smaller particle detection

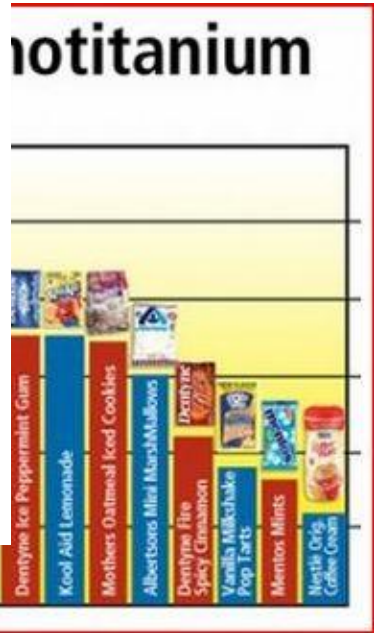
**➔ ICP-QQQ can solve these problems**

# ICP-QQQ technique for Si (on mass method)

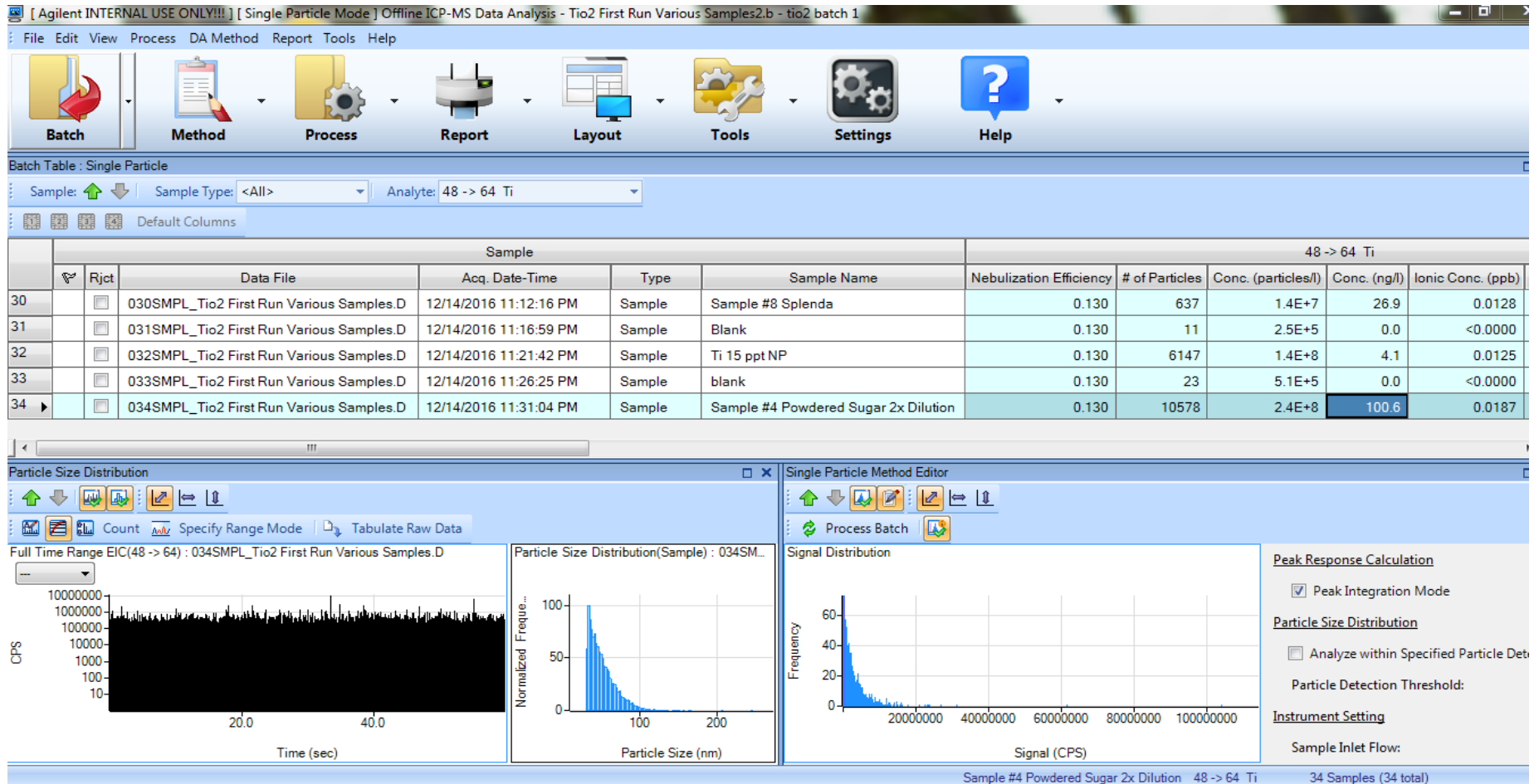
ICP-QQQ uses two quadrupoles separated by a collision/reaction cell



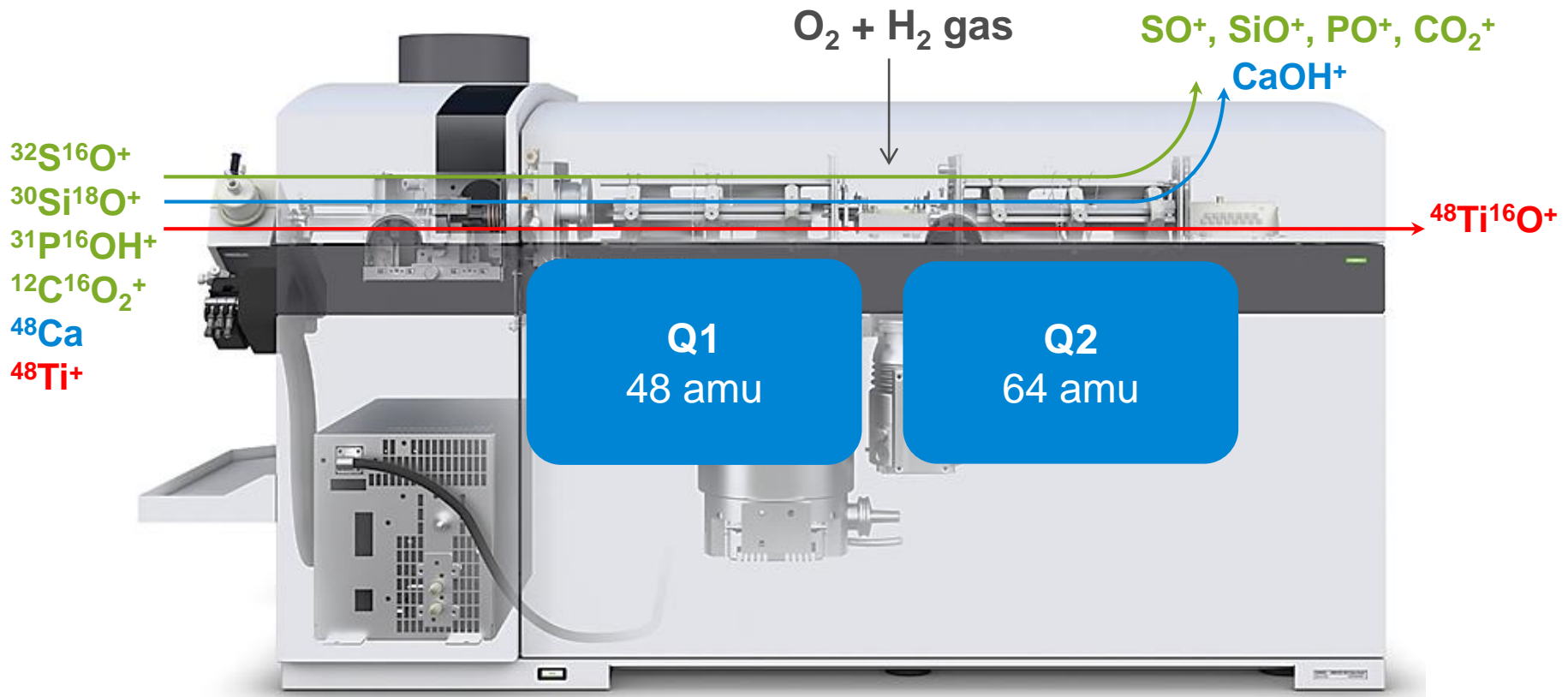
# Food



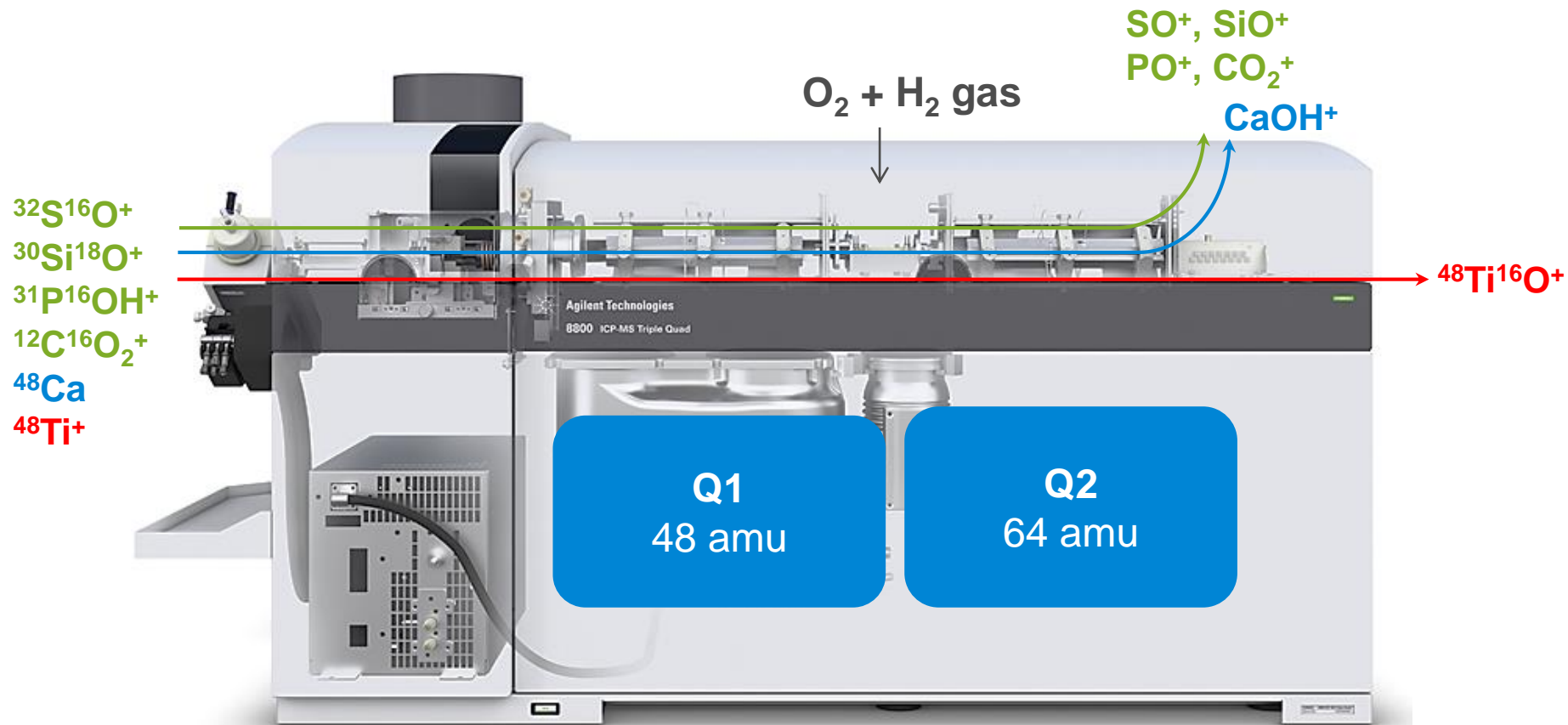
# sNP in Powdered Donuts???



# ICP-QQQ technique for Ti (mass shift method)



# ICP-QQQ technique for Ti (mass shift method)



$SO^+ + O_2 \rightarrow$  No Reaction  
 $SiO^+ + O_2 \rightarrow$  No Reaction  
 $POH^+ \rightarrow PO^+ + H$  (collision)  
 $CO_2^+ + O_2 \rightarrow CO_2 + O_2^+$

$Ca^+ + O_2 \rightarrow CaO^+ + O$  (problem)

$Ti^+ + O_2 \rightarrow TiO^+ + O$

$CaO^+ + H_2 \rightarrow CaOH^+ + H$  (solved)



# Experiments

- Reference Materials and Samples

SiO<sub>2</sub> : nanoComposix, nominal 50, 60, 100, 200 nm

TiO<sub>2</sub> : US research nanomaterials, Rutile and Anatase (common mineral forms of TiO<sub>2</sub>), nominal 30-50 nm

Sunscreen purchased from a local store

- Sample Preparation

SiO<sub>2</sub> : diluted with DI water or 1% ethanol

TiO<sub>2</sub> : [intermediates] diluted with 1% Triton X-100

[working solutions] diluted with DI water, tap water or matrix mixture including 100ppm P, 100ppm S, 50ppm Ca, 50ppm Si and 0.1% ethanol

- ICP-QQQ Conditions

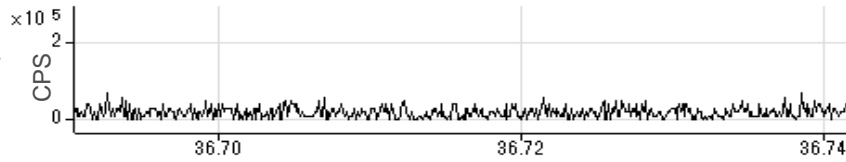
Standard quartz sample introduction system, normal hot plasma condition

Dwell time : 0.1 ms

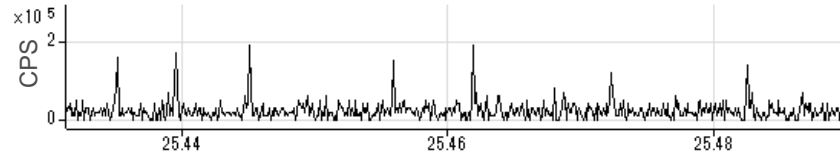
NPs	Measured element	Reaction gas	Mass of Q1	Mass of Q2
SiO <sub>2</sub>	Si	H <sub>2</sub> 2~3 mL/min	28	28
TiO <sub>2</sub>	Ti	O <sub>2</sub> 0.1 mL/min + H <sub>2</sub> 5 mL/min	48	64

# SiO<sub>2</sub> NP signals

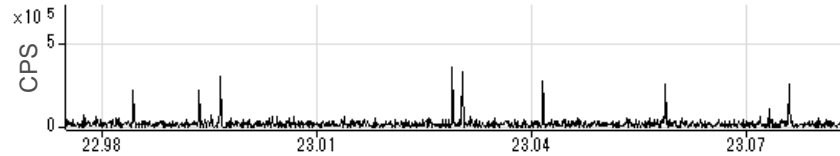
DI water



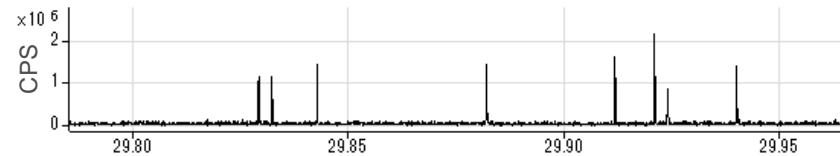
50 nm



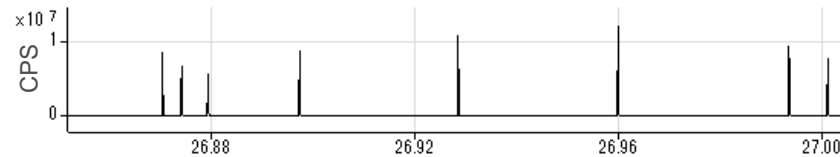
60 nm



100 nm

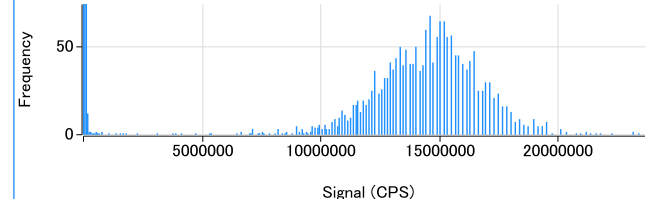
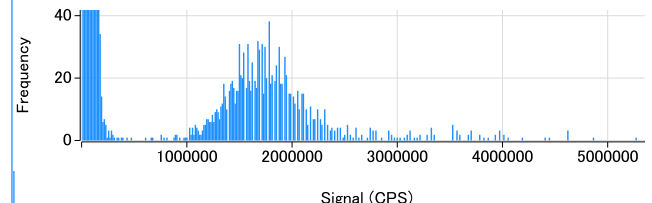
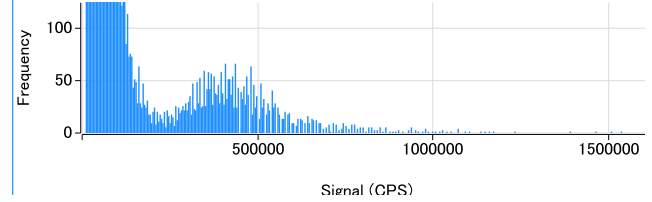
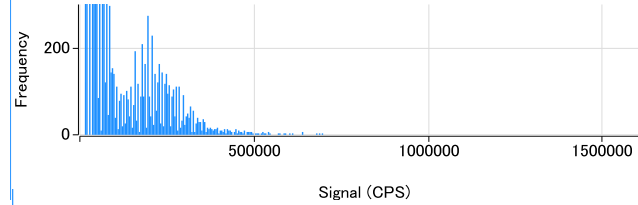
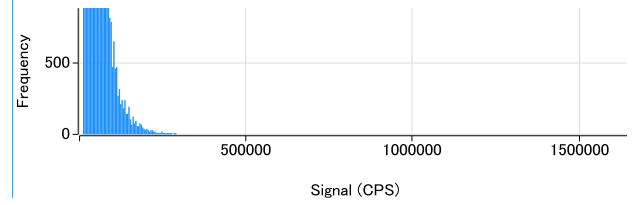


200 nm



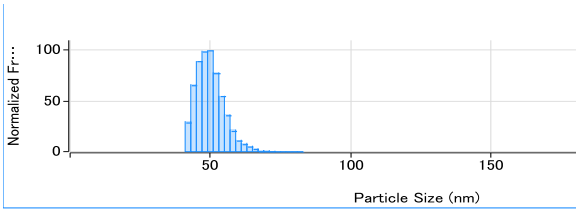
Time (sec)

H<sub>2</sub> MS/MS mode



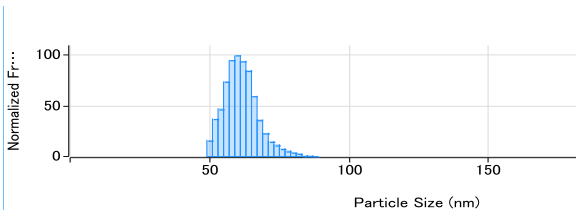
# SiO<sub>2</sub> nanoparticle reference material results

50 nm

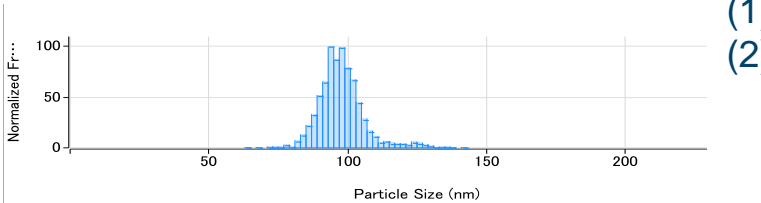


Nominal size (nm)	Median size (nm)	Most Freq. Size (nm)	Mean Size (nm)	TEM Diameter <sup>(1)</sup> (nm)	BED <sup>(2)</sup> (nm)
50	49	50	49	46.3 ± 3.1	23
60	59	58	60	57.8 ± 3.5	22
100	99	100	100	97.0 ± 4.8	25
200	199	204	199	198.5 ± 10.5	25

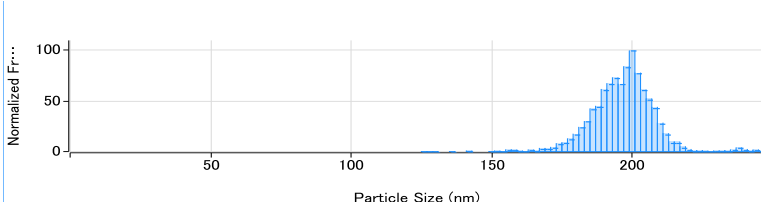
60 nm



100 nm



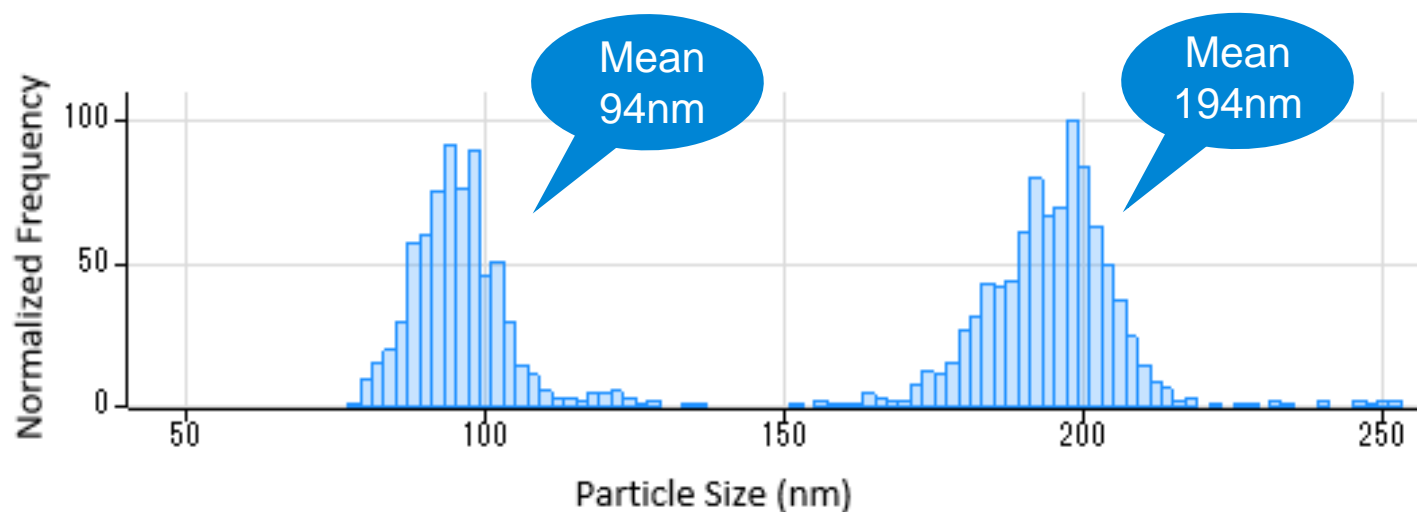
200 nm



- (1) values supplied by nanoComposix
- (2) Background equivalent diameter ~ size detection limit – most likely limited by dissolved Si.

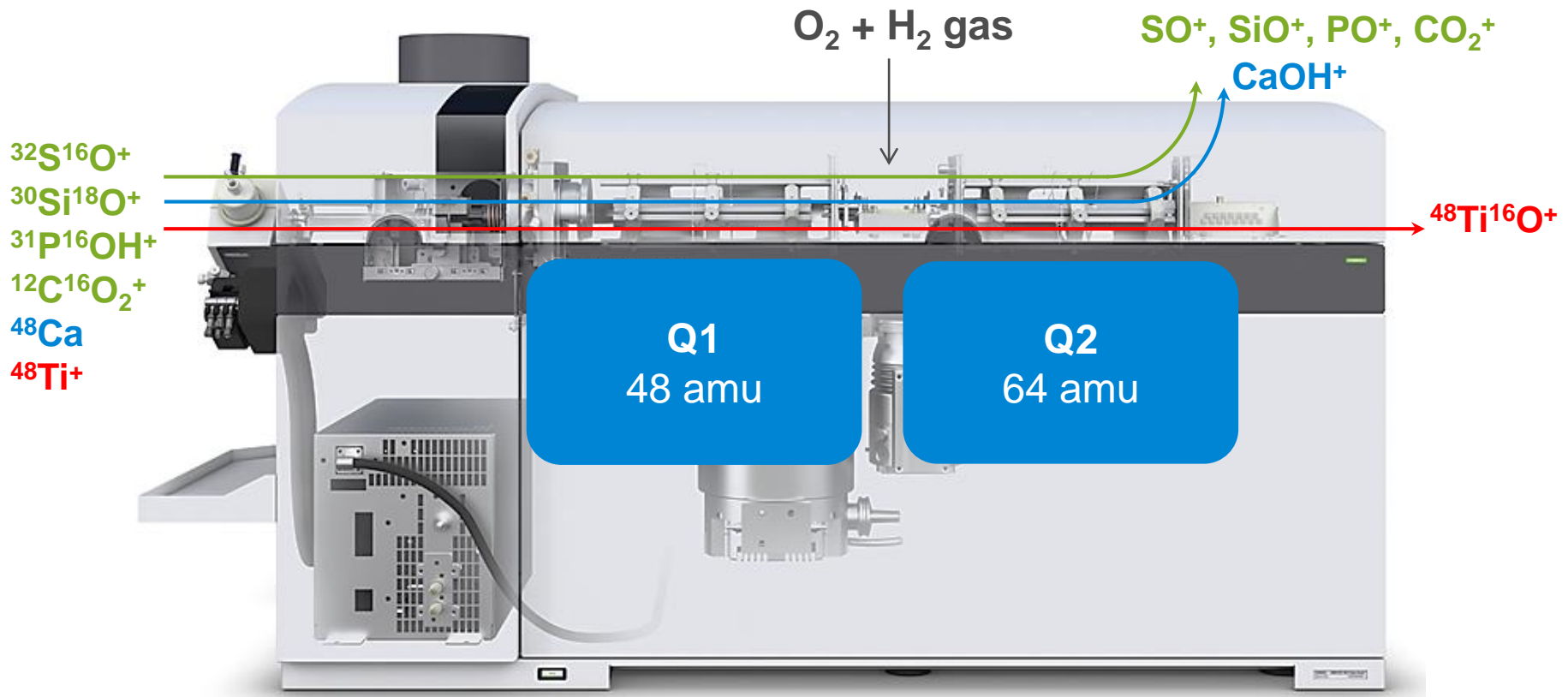
Real samples sometimes contain carbon matrices that cause a CO interference on Si

ICP-QQQ can resolve CO interference problem



Particle Distribution of 100 nm + 200 nm SiO<sub>2</sub> NPs in 1% Ethanol  
BED: 32 nm

# ICP-QQQ technique for Ti (mass shift method)



# TiO<sub>2</sub> analysis - Interference Removal by O<sub>2</sub>-H<sub>2</sub> Mode

## Determining interferences in ionic matrix solutions

Mode	Sensitivity (cps/ppb)	BEC (ppb)	Quantitative result as Ti (ppb)					
			P 100 ppm	S 100 ppm	Ca 50 ppm	Si 50 ppm	Ethanol 0.1%	Matrix mixture
No gas	155000	<b>0.016</b>	1.7	6.0	225	0.39	0.14	261
O <sub>2</sub> + H <sub>2</sub>	79000	<b>0.001</b>	0.010	0.001	0.18	0.054	0.001	0.023

No gas : Single Quad mode, Q2=48

O<sub>2</sub> + H<sub>2</sub> : MS/MS mode, Q1=48, Q2=64

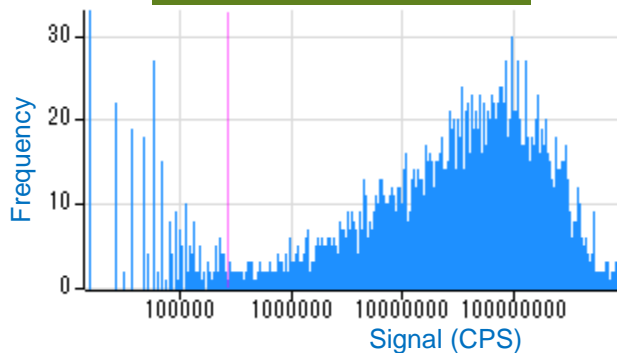
### Advantage of O<sub>2</sub> + H<sub>2</sub> mode

- Can use the most abundant isotope of Ti (mass 48, 73.7% relative abundance) for highest sensitivity
- Can remove almost all interferences including <sup>48</sup>Ca

# TiO<sub>2</sub> NP Samples

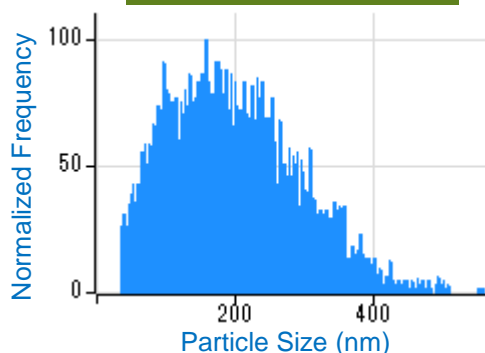
O<sub>2</sub>-H<sub>2</sub> MS/MS mode

Signal Distribution

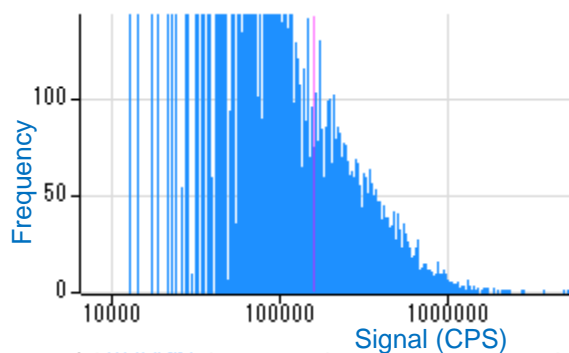


Rutile

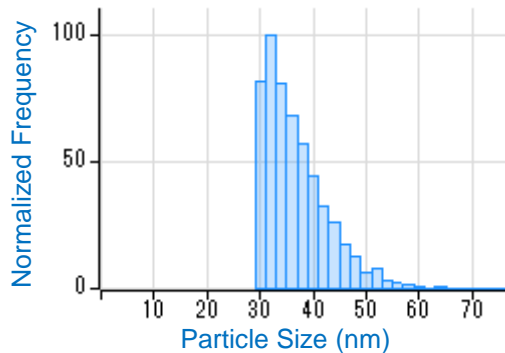
Size Distribution



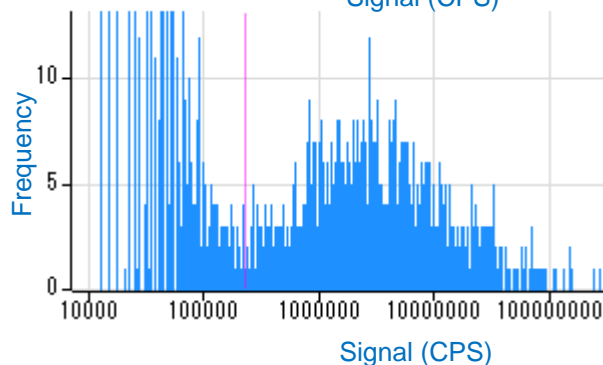
- Strongly aggregated
- Mean size : 200 nm



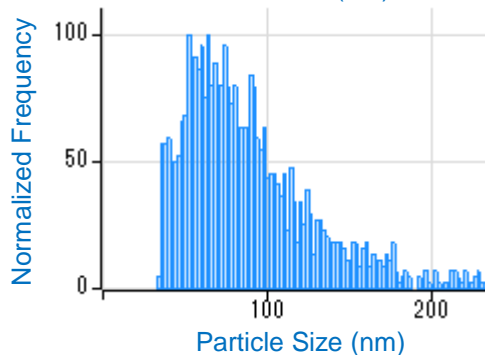
Anatase



- Many small particles
- Mean size : 32 nm
- Nominal reference size: 30-50nm



Sunscreen

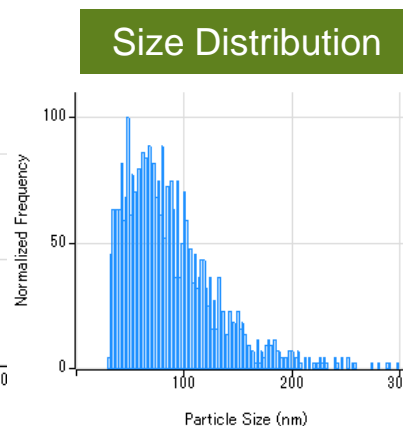
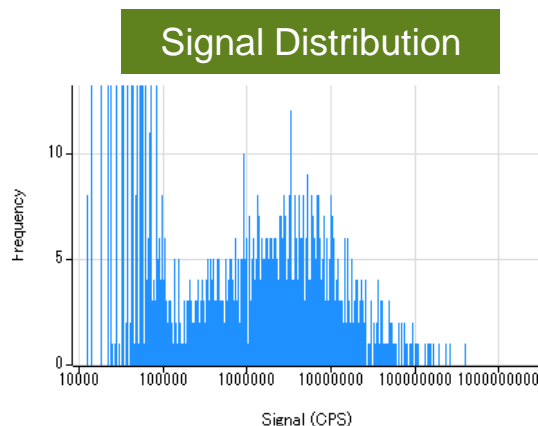


- Mean size : 90 nm
- Good size distribution
- Appropriate to further experiments

# TiO<sub>2</sub> NPs in Matrix Samples

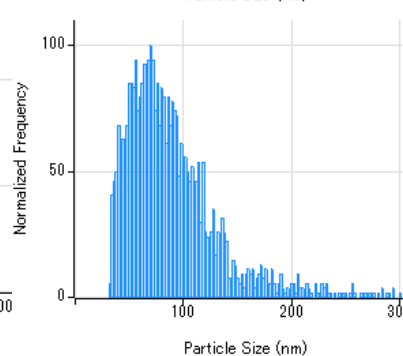
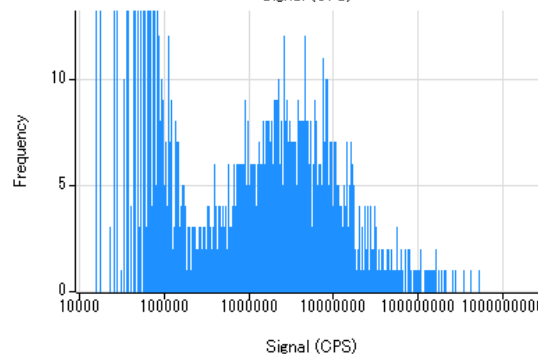
O<sub>2</sub>-H<sub>2</sub> MS/MS mode

Sunscreen  
in DI water



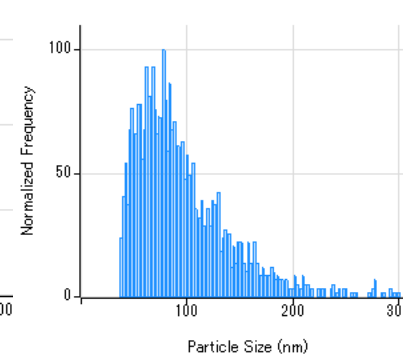
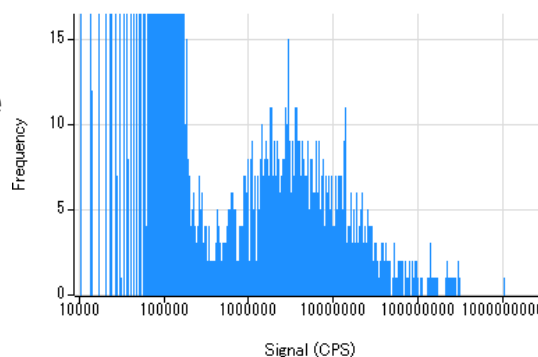
- Mean size : 77 nm
- **BED : 16 nm**

Sunscreen  
in tap water



- Mean size : 79 nm
- **BED : 10 nm**

Sunscreen  
in matrix mixture  
(100ppm S & P,  
50ppm Ca & Si,  
0.1% ethanol)



- Mean size : 84 nm
- **BED : 22 nm**



# Q&A Session

Your questions...

