Exposure assessment method for products containing nanomaterials using a gas sample introduction system for ICP-MS

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Abstract
General aerosol-measuring instruments allow real-time measurements of air particle concentrations. However, these measurements cannot distinguish free particles from target nanomaterials because they do not differentiate nanomaterials. The purpose of this study is investigation of the quantitative nature of atmospheric nanoparticles using GED (Gas Exchange Device)-ICP-MS to detect and measure nanoparticles as an element. The per particle signal intensity increased proportionally to the volume until the particle size reaches 120 nm. For all particle sizes from 20 nm to 160 nm, the measured values of FMPS (Fast Mobility Particle Sizer) were consistently higher than those for ICP-MS. The system will be able to adapt to an exposure assessment of CNT (Carbon Nanotube) because carbon-base materials can be identified and quantified as long as an index element can be found.

1. Introduction
Nanomaterials in the air are usually measured using aerosol-measuring instruments or by collecting particulates in filters and impactors. ISO and NIOSH in 2008 and 2009, respectively, published reports on measurement methods of nanomaterials in work environments [1, 2]. They suggest using Condensation Particle Counters (CPC) and Optical Particle Counters (OPC) for the preliminary evaluation of nanomaterials in a work environment. These aerosol-measuring instruments allow real-time measurements of air particle concentrations in a matter of seconds to minutes. However, these measurements cannot distinguish free particles from target nanomaterials because they do not differentiate nanomaterials.

The New Energy and Industrial Technology Development Organization (NEDO) has provided guidance on measurement methods for nanomaterials such as carbon nanotubes (CNT). These methods...
include instrumental measurements, quantification using filter-collected materials, and observations using an electron microscope. NIOSH recommends the aerosol carbon analysis method (NIOSH 5040) to quantify filter-collected materials [3], and has reported practical measurement examples [4, 5]. Another study quantified nanomaterials using contaminating metal catalysts in CNTs [6]. All of these examples evaluated CNT by weight concentration. On the other hand, other studies have estimated the atmospheric concentrations of CNT by measuring the number of fibers and aggregates obtained via aerosol-measuring instruments or collected on filters [7].

Although exposure assessments of nanomaterials in actual products have been reported, simulated discharge tests using aerosol-measuring instruments show that small amounts of particles are difficult to detect because they are masked by background particles measuring in the range of $10^3$–$10^4$ parts/cm$^3$. Additionally, nanosized particles other than the target nanomaterial may be present. For example, an increase in particulate concentration has been observed due to the simulated test environment from sources such as active motors in machinery and particles derived from friction of volatile components [8].

For these reasons, a highly sensitive method to differentiate small amounts of target nanomaterials from other nanosized particles is required. Although many previous exposure assessments of nanomaterials have been conducted in work environments, they have focused on measuring one single particle at relatively high concentrations. However, few studies have been published regarding the evaluation of nanomaterials contained in products in the marketplace.

### 2. Objective

A Gas Exchange Device (GED; GED-01, J-SCIENCE LAB) [9, 10] is developed to quantify atmospheric particles by direct ICP-MS. This device negates the need for pre-processing steps such as sample collection, breakdown, and dilution, enabling continuous and highly sensitive measurements. Moreover, shortening the integration time of ICP-MS allows single particles to be detected because the signal intensity can be used to estimate the particle count and particle size.

Conventional ICP-MS analysis of gas samples involves dissolving atmospheric particulates collected on a filter in acid and using the dissolved solution for measurements. These methods reduce the weight concentrations of samples such as nanomaterials, and consequently require long-term collection to increase the weight. Other challenges include the need for pre-processing steps and contamination risks during pre-processing.

This study investigates the quantitative nature of atmospheric nanoparticles using GED-ICP-MS. To measure nanoparticles introduced to the plasma of ICP-MS, liquidification, vaporization, and ionization must occur at 1-ms intervals. However, ionization cannot be completed if the particle size exceeds the critical particle size, which reduces the analytical precision. Additionally, the rate of ionization depends
on particle composition. In particular, metal oxides with high boiling and melting points undergo incomplete ionization. Specifically, we aim to identify the critical particle size by investigating the correlation between particle size and particle counts obtained through ICP-MS of titanium oxide nanoparticles. Additionally, we can increase the signal intensity of GED-ICP-MS by nebulizing a Ti solution with a known concentration. In this way, we determine the amount of elemental metal per element count and the quantitative factor for Ti.

3. Methods

3.1. Generation of titanium oxide nanoparticles
We generated titanium oxide nanoparticles and measured the particle size distribution using a Fast Mobility Particle Sizer (FMPS; FMPS3091, TSI). The sample was a titanium oxide MPT-429 (Ishihara Sangyo Kaisha, Ltd.) diluted 100-fold in a buffer solution. The buffer solution was an ammonium acetate solution (20 mM, pH 8) prepared by dissolving ammonium acetate (0.77 g) in ultrapure water (500 mL) and adding ammonium hydroxide (0.75 mL). Titanium oxide nanoparticles were generated using the Electrospray 3480 (TSI) and applying a voltage of 2.30 kV to the particulate suspension to create small charged droplets.

The electrospray was connected to the FMPS via a conductive tube in order to measure the size distribution of titanium oxide particles. The flow rate of the electrospray was 1.1 L/min, while the sample intake rate of the FMPS was 10.0 L/min; we adjusted the inter-device flow rate by creating branching pathways between the devices and attaching HEPA filters (ADVANTEC) in the tubes. Additionally, we removed the water content released with the particles by passing the released particles through a diffusion drier (TSI).

3.2. Ionization of particles
The signal intensity (counts per second, cps) using an ICP-MS (iCAP-Q, Thermo Fisher Scientific) when particle ionization is complete within the plasma is proportional to the particle volume. We used ICP-MS to confirm the ionization by measuring the signal intensity and particle counts of standard particles.

A 100-fold diluted titanium oxide solution in a buffer was supplied to the electrospray to generate particles. By introducing this output to a Differential Mobility Analyzer (DMA, Model EMC, Tsukasa Sokken Co., Ltd), we changed the applied voltage and classified the particle size in 10-nm intervals from 20 nm to 160 nm. The sheath flow rate was 5.0 L/min controlled by solenoid valve flow controller. After classification by DMA, we simultaneously measured the particle counts by FMPS and the signal intensity of $^{48}$Ti by ICP-MS. The flow rates of the electrospray and ICP-MS were 1.1 L/min and 0.23
L/min, respectively, while the aerosol flow rate to the DMA and sample flow rate to the FMPS were 0.25 L/min and 8.0 L/min, respectively. A branch and HEPA filter (ADVANTEC) was introduced before the sample entrance to the FMPS to adjust flow rate (Figure 1).

3.3. Quantification of titanium
To determine the amount of elemental metal per 1 cps signal intensity, we first created a standard particle solution. A Ti standard solution (Kanto Kagaku), which was used as a standard solution for metals during quantitative analysis with ICP-MS, was diluted in 3% nitric acid and an In standard solution (Kanto Kagaku) was added to this dilution to provide an index element. We adjusted the concentration of In and Ti to 250 ppb and 10 ppb, respectively. We also created an In standard solution with a concentration of 1 ppb by diluting the original standard solution in 6% nitric acid.

These solutions were nebulized using a desolvating sample introduction device (APEX, Elemental Scientific Inc.) for ICP-MS. The solvent in the sample was removed by passing the aerosol through a film. In this way, only the particulate component of the solution was measured. A four-way stopcock was attached to the exit mouth of the APEX with one of the outlets attached between the gas exchange device and the ICP-MS, and the other outlet attached to a syringe filter. Argon gas was introduced to the particle nebulizing device at a flow rate of 300 mL/min (Figure 2).
Figure 2. Device setup to quantify elemental titanium.

We initially measured the signal intensity of elemental Ti using the APEX to nebulize the desolventized standard solution and introduced this processed solution to the ICP-MS. Next, we redirected the APEX output through the stopcock to the syringe filter (DISMIC®-25CS080AS, ADVANTEC) for five minutes to collect particulate matter. Afterwards the filter was attached to a syringe dripping 10 mL of 6% nitric acid at a rate of 1 drop per second. The extracted liquid was nebulized again. Then we determined the per second metal emission rate by measuring the signal intensity of In by ICP-MS. Next we nebulized the In standard solution diluted to 1 ppb and measured the signal intensity of In by ICP-MS.

4. Results

Figure 3 shows the particle size distributions before and after drying when the particles are introduced directly to FMPS. A reduction in the particle count concentration occurs for particles between 30 and 60 nm after passing through a diffusion drier. Furthermore, the 60-second average for the total particle count concentration decreases 18.5% from 65,500 cm$^{-3}$ prior to drying to 53,400 cm$^{-3}$ after drying.

Figure 3. Particle size distribution before and after drying.
Particle concentrations for each size classification determined by DMA were measured using FMPS as well as the signal intensity by ICP-MS (Table 1). The blank reading taken before particle generation was subtracted from each measurement to determine the particle concentration and the signal intensity.
Table 1. Particle count and Ti signal intensity.

| Particle size (nm) | Number of particles (particles) | Signal intensity (cps) |
|-------------------|---------------------------------|------------------------|
| 20                | 73                              | 0                      |
| 30                | 58                              | 0                      |
| 40                | 94                              | 0                      |
| 50                | 189                             | 243                    |
| 60                | 317                             | 2122                   |
| 70                | 461                             | 5871                   |
| 80                | 437                             | 9336                   |
| 90                | 392                             | 12148                  |
| 100               | 256                             | 12506                  |
| 110               | 172                             | 9828                   |
| 120               | 92                              | 6359                   |
| 130               | 75                              | 3916                   |
| 140               | 50                              | 2591                   |
| 150               | 40                              | 1656                   |
| 160               | 26                              | 1419                   |

We assumed that the particles are spherical, and then determined the volume per particle as well as the total volume for all particles of a given size (Table 2).

Table 2. Number of particles per size classification and the total volume.

| Particle size (nm) | Volume \( \times 10^4 \text{ nm}^3 \) | Number of particles (particles) | Total volume \( \times 10^6 \text{ nm}^3 \) |
|--------------------|----------------------------------------|---------------------------------|----------------------------------|
| 20                 | 0.419                                  | 73                              | 0.306                            |
| 30                 | 1.41                                   | 58                              | 0.814                            |
| 40                 | 3.35                                   | 94                              | 3.15                             |
| 50                 | 6.54                                   | 189                             | 12.4                             |
| 60                 | 11.3                                   | 317                             | 35.9                             |
| 70                 | 18.0                                   | 461                             | 82.7                             |
| 80                 | 26.8                                   | 437                             | 117                              |
| 90                 | 38.2                                   | 392                             | 150                              |
| 100                | 52.4                                   | 256                             | 134                              |
| 110                | 69.7                                   | 172                             | 120                              |
| 120                | 90.5                                   | 92                              | 83.3                             |
| 130                | 115                                     | 75                              | 86.0                             |
| 140                | 144                                     | 50                              | 71.7                             |
| 150                | 177                                     | 40                              | 70.0                             |
| 160                | 214                                     | 26                              | 56.1                             |

Figure 4 shows the total volume and the signal intensities per particle size classification. A clear peak
is observed for both the total volume and the signal intensity at particle sizes of 90–100 nm. Moreover, the patterns for the total volume and the signal intensity begin to separate at particle sizes greater than 120 nm.

![Figure 4. Relationship between the ICP-MS signal intensity and the total volume of particles.](image)

The ICP-MS-measured signal intensity of a Ti standard solution adjusted to 10 ppb is 17,963 cps. Using this intensity, we calculated the amount of Ti per count by determining the amount of Ti nebulized per second. The signal intensities of In in the standard and extracted solutions are 44,718 cps and 55,309 cps, respectively. Furthermore, the extracted volume is 10 mL and the concentration of the standard solution is 1.0 ng/mL. Using these values, we calculated the amount of In (ng) in the extracted solution using Equation 1-1.

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Extracted Solution In Amount (ng) = Concentration Standard Solution (ng/mL) × Extracted Solution In signal intensity (cps) × Standard Solution In signal intensity (cps) × Extracted Solution volume (mL)
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\[ = 12.4 \text{ ng} \] (Equation 1-1)

This is equivalent to the amount of In nebulized in five minutes. We then determined the amount of
Ti in the extracted solution as well as the rate per second of nebulization. The concentration of In in the standard particle solution is 250 ng/mL, whereas the concentration of Ti is 10 ng/mL. Using these values, the rate per second of Ti nebulization is calculated using Equation 1-2.

\[
\text{Per second Ti nebulization (ng)} = \frac{\text{Extracted Solution In Amount (ng)} \times \text{Extracted Solution Ti concentration (ng/mL)}}{\text{Extracted Solution In concentration (ng/mL)}} \div 300 \text{ sec} = 0.00165 \text{ (ng/sec)}
\]

(Equation 1-2)

Since this value corresponds to the signal intensities shown in Table 1, the amount of Ti per count can be determined using Equation 1-3.

\[
\text{Ti amount per count (ag/count)} = \frac{\text{Rate of Ti nebulization per second (ng/sec)}}{\text{Standard Solution signal intensity (cps)}} \times 10^9
\]

(Equation 1-3)

Given the equation above, we calculated the conversion factor for Ti amounts per count as 91.8.

5. Discussion
First, we considered the ionization of titanium oxide particles. Figure 5 plots the per particle relationship between the volume and the signal intensity to confirm a proportional relationship between the particle volume and the signal intensity.
Figure 5. Signal intensity per particle volume.

The per particle signal intensity increases proportionally to the volume until the particle size reaches 120 nm (volume: 90.5×10⁴ nm³). To confirm the correlation, we extracted the particle sizes between 20 nm and 120 nm from Fig. 5 and determined the relationship between the particle volume and the signal intensity (Figure 6).
**Figure 6.** Relationship between the volume and the signal intensity for particle sizes 20–120 nm.

A plot of the linear approximation for the points indicates that the correlation coefficient is R = 0.994. The critical particle size is 120 nm, and we believe that particles below this size are completely ionized in the plasma. Consequently, GED-ICP-MS effectively measures nanoparticles as defined by ISO (Dp < 100 nm).

Next, we considered the validity of the conversion factor for the Ti amounts per count as determined by ICP-MS (91.8). Because gases discharged at 1.1 L/min from the DMA are branched to the ICP-MS at 0.23 L/min and FMPS at 0.87 L/min (Figure 1), we converted the values measured by ICP-MS and FMPS to the particle amounts, and determined the particle amounts by classification by DMA after adjusting for the flow rate. Similar values confirm the validity of the conversion factor. First, we determined the particle amount from the measured values of ICP-MS. Using the signal intensities in Table 1 and Equation 1-4, we calculated the per second amount of Ti introduced to ICP-MS. As a measure of the detection sensitivity for ICP-MS, we used a value of 0.1% for the ion transmittance (detected ions/introduced ions).

\[
\text{Amount of introduced Ti (g/sec)} = \text{Ti signal intensity (cps)} \times 91.8 \text{ (ag/count)} \times 10^{-18} \div \text{Ion transmittance}
\]

(Equation 1-4)

Next, we determined the per second particle mass introduced to FMPS from the particle counts shown in Table 2. For this calculation, we used 10,000 cm³/min as the flow rate for FMPS and 4.23 g/cm³ as the density of titanium oxide.

\[
\text{Particle amount (g/sec) = Total volume (mm}^3/\text{cm}^3) \times \text{Flow rate (cm}^3/\text{sec}) \times 10^{-21} \times \text{Density of titanium oxide (g/cm}^3)
\]

(Equation 1-5)

Finally, we adjusted the Ti amounts for ICP-MS calculated using Equation 1-4 and the particle amounts for FMPS calculated using Equation 1-5 by the flow rate. We assumed that the distribution of particles classified by DMA for each device is proportional to its flow rate. Figure 7 and Table 3 show the adjusted values after classification.

**Table 3.** Particle amounts introduced into each device per particle size classification.
Figure 7. Calculated particle amounts from the measured values per size classification.

For all particle sizes, the measured values of FMPS are consistently higher than those for ICP-MS, with a tolerance of approximately 20.1% for the peak particle size; however, both sets of values roughly align. One reason for the higher FMPS values may be that measurements are made without distinguishing the particles, meaning that the values may contain counts for contaminants such as silica in the dispersant for titanium oxide or other unrelated particles. Regardless, our results show that GED-ICP-MS can be used to quantify nanomaterials continuously with a high sensitivity. Carbon-based
materials such as CNT can be identified and quantified as long as an index element can be found in the CNT.

The selection of 1) intentionally included nanomaterials in a given product, 2) composite nanomaterials containing intentionally included nanomaterials and other materials, and 3) spontaneously generated nanomaterials remain challenging in per aerosol assessments of products containing nanomaterials. Previously proposed assessment methods, including particle concentrations and weight concentrations, are inadequate to distinguish the different types of nanomaterials. Although electron microscopy can differentiate among these types of nanomaterials, quantification requires an enormous amount of effort. In our proposed method, the status of nanomaterials described in 1) or 2) can be monitored, enabling safe aerosol assessments, even though it cannot yet distinguish among these types. By applying our setup to a simulated emission test, we expect that our method will be used for aerosol assessments of actual products containing nanomaterials.

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