Anionic gold ions desorbed from gold nanorods and nanospheres

Tomoki Nishi1 · Yasuro Niidome1

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Abstract
The desorption and ionization of gold anions and cations from gold nanorods and nanospheres were investigated using a matrix-assisted laser desorption/ionization mass spectrometry instrument. The signal intensities of the gold anions from nanorods with a volume of $4.8 \times 10^3$ nm$^3$ were about 28 times larger than the signal intensities of gold anions from nanospheres of similar volume. Gold cations did not show a remarkable difference depending on the nanoparticles’ shapes. The unique desorption behavior of gold anions suggests their potential as reporter ions in mass spectrometry.

Keywords Mass probe · Gold nanorod · Laser-induced desorption · Ionization · Metal anions · Gelatin section

Introduction
Gold nanoparticles have been developed as a mass probe for imaging mass spectrometry of tissue sections using a conventional mass spectrometer designed for matrix-assisted laser desorption/ionization mass spectrometry (MALDI-MS) [1, 3–10]. The irradiation of 355-nm pulsed-laser light in an MALDI-MS instrument causes preferential desorption of gold cations (Au$^+$, Au$_2^+$, Au$_3^+$) in the absence of matrix molecules. The gold cations act as reporter ions to represent the distribution of target molecules. We have found that gold ion signals showed good linearity and remarkable limits of detection, even when an insulating porous membrane was used as a substrate for gold nanoparticles [1, 5, 6]. The ionization efficiency was dependent on the sizes and shapes of the gold nanoparticles [6, 11]. Previous works have shown that gold nanoparticles could be a highly sensitive mass probe for investigating the distribution using a conventional MALDI-MS instrument.

In previous mass probe developments, cations were used as reporter ions. The triphenyl methane moiety [12] and the hexadecyltrimethylammonium [13] are organic species that could be used as a mass probe. In conventional MALDI processes, proton (H$^+$) or sodium ion (Na$^+$) adducted species are major targets. The positive mode is the default mode of an MALDI-MS machine; however, the polarity of the ions is irrelevant to mass probe spectrometry. Cationic gold ions (Au$^+$, Au$_2^+$, Au$_3^+$) have been used as reporter ions, but the use of gold anions as reporter ions cannot be excluded. The desorption of gold cations by laser irradiation occurs with compensating amounts of anions. Here, we investigated the ionization efficiencies of gold anions (Au$^-$, Au$_2^-$, Au$_3^-$) depending on the shapes and sizes of gold nanoparticles. The discrimination of interfering organic ions whose $m/z$ values overlap with those of the gold ions is an issue to conduct reliable and reproducible mass probe analysis. The interfering organic ions should be different concerning both the anion and cation sides. The analysis of gold anions in addition to gold cations will contribute to the discrimination of gold ion signals, whose intensities are comparable with those of the interfering organic ions. To the best of our knowledge, this is the first report to discuss the possibility of anionic gold ions functioning as reporter ions in mass spectrometry.

Experimental
Reagents and chemicals
All chemicals were commercially available and used without further purification. A thiol-terminated derivative of polyethylene glycol (noted as mPEG-SH, Mw: 2000) and
poly(vinylpyrrolidone) (PVP, Mw: 15,000) were obtained from NOF and TCI, Japan, respectively. Gelatin was obtained from Wako, Japan.

Seven kinds of nanorods having different aspect ratios were prepared by a seeding method in cationic amphiphile solutions described in a previous paper [14]. Details are shown in the supporting information. The nanorods were wrapped with mPEG-SH and PVP, [2] and irradiated by pulsed-laser irradiation at 532 nm (Nd-YAG laser, ~ 10 ns, 20 Hz) to obtain spherical gold nanoparticles [15]. The energy of the pulsed-laser light was 4–6 mJ/pulse. The spectroscopic properties (Fig. S3) and scanning electron microscope (SEM) images of nanoparticles (Figs. S4 and S5) are shown in the supporting information.

To evaluate the laser desorption/ionization efficiencies of the gold nanoparticles, the nanoparticles were dispersed in 10 wt% gelatin solutions [11]. The absorbance of the nanoparticle-gelatin solutions was kept constant (0.043 cm⁻¹ at 355 nm), independent of the shapes and sizes of the gold nanoparticles. The concentration of gold atoms in the gelatin solutions was about 10 µM. The hot gelatin solutions were cooled in a plastic tray (about 10 × 10 mm), and frozen in a dry-ice bath. The samples were sliced into sections (10 µm) at − 20 °C using a cryomicrotome (HYRAX C 50, Carl Zeiss). The sections were placed on an ITO plate and analyzed by an MALDI-MS instrument.

Apparatus

A scanning electron microscope (SEM, S-4100H Hitachi Hitech, Japan) was used to observe the shapes of the nanoparticles. A Q-switched Nd-YAG laser (Polaris III, New Wave Research, USA) was used to transform the nanorods into nanospheres. Mass spectrometry was performed by an MALDI-MS instrument (Autoflex Speed, Bruker, USA). A typical set of experimental conditions for the mass spectrometer involved the use of the negative ion mode; reflector: on; laser power 90%; shot counts 200; and random walk 5 shots/spot. The laser irradiated 5 shots at one spot, and then the sample plate moved to another spot for the next 5 shots. Forty spots were randomly selected; thus, the mass signal intensities of 200 shots were averaged.

Results and discussion

Spectroscopic and morphological properties of nanorods and nanospheres are listed in Table 1. Extinction spectra (Fig. S3) and SEM images (Figs. S4 and S5) are shown in the supporting information. Their longitudinal surface plasmon (SP) bands were found in the near-infrared (near-IR) region from 917 to 1269 nm [16–18]. The sample numbers (i–vii) correspond to the order of the peak wavelengths of the longitudinal SP bands. The clear SP bands in the near-IR region indicate that the nanorods were uniform and dispersed in the solution without forming aggregates. Pulsed-laser irradiation (at 532 nm, 10 ns) of the nanorods transformed them into spherical nanoparticles (see Figs. S4 and S5). Spectral changes and SEM images before and after laser irradiation consistently indicated that the laser-induced transformation occurred without a change in the volume of the nanoparticles. Samples (i) and (vi), however, showed insufficient shape uniformities (see Fig. S5). Samples (i) and (vi) were omitted from evaluations of the laser-desorption efficiencies of spherical nanoparticles.

The peak positions of the longitudinal SP bands were dependent on the aspect ratios of the nanorods (longitudinal length/transverse length) and independent of the volumes; sample (iii) was the smallest one, and sample (vi) was the bulkiest one. Sample (i) contained some nanorods even after the laser irradiation. The bulkiest sample (vi) formed precipitates after laser irradiation, which resulted in a large size distribution. Therefore, we used five kinds of spherical nanoparticles (ii–v and vii).

The process for dispersing the nanorods was the same as that used in our previous paper [11]. The nanorods in gelatin solutions gave gold cations (Au⁺, Au₂⁺, and Au₃⁺) quantitatively (see Fig. S6 in the supporting information). The dependence of the mass signal intensities on their volumes

| Table 1 Optical and morphological properties of nanoparticles |
|-------------------------------|--------|------------------|------------------|
| Nanorod | SP peak Position/nm | Aspect ratio | Volume/10³ nm³ | Nanosphere | Diameter/nm | Volume/10³ nm³ |
| (i) 506 | 1269 | 10 ± 2 | 5.8 ± 1.8 | – | – |
| (ii) 507 | 1168 | 8.5 ± 2 | 11 ± 3 | 26 ± 3 | 9.8 ± 2 |
| (iii) 507 | 1095 | 8.3 ± 2 | 4.0 ± 0.8 | 19 ± 2 | 3.6 ± 2 |
| (iv) 509 | 1004 | 6.3 ± 1 | 14 ± 3 | 30 ± 1 | 15 ± 2 |
| (v) 511 | 964 | 5.4 ± 0.7 | 22 ± 7 | 33 ± 3 | 20 ± 6 |
| (vi) 515 | 950 | 4.9 ± 0.4 | 60 ± 12 | – | – |
| (vii) 515 | 917 | 4.5 ± 0.7 | 53 ± 12 | 46 ± 3 | 53 ± 10 |
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was consistent with the results presented in our previous paper discussing the ionization properties of gold nanostars [11]. In our present work, gold nanorods with volumes smaller than $10^4$ nm$^3$ showed mass signal intensities that were roughly 3 times larger than those of spherical particles having the same volumes; in contrast, larger nanorods and nanospheres showed comparable signal intensities.

Figure 1 shows a typical mass spectrum obtained from the gelatin section in a negative mode. Au$^-$, Au$_2^-$, and Au$_3^-$ ions were found in the spectrum, indicating their desorption from the gelatin section by laser irradiation from an MALDI-MS instrument. The gold anions, as well as gold cations, could function as reporter ions to investigate the distribution of gold nanoparticles in a section.

The sums of the mass signal intensities of the three gold anions (Au$^-$, Au$_2^-$, and Au$_3^-$) were plotted against the volumes of the nanoparticles (Fig. 2). The filled circles in Fig. 2 show the mass signal intensities obtained from nanorods. Larger nanorods gave larger signals, consistent with the results of the gold cations (Fig. S6); however, the differences between the signal intensities of the nanorods and the nanospheres were remarkable. The smallest nanorods (iii) ($4.8 \times 10^3$ nm$^3$) showed signal intensities that were about 28 times larger than those of the nanospheres (nanorod 6820; nanosphere 242). The second-largest nanorods (vii) ($53 \times 10^3$ nm$^3$) showed signal intensities of 1.9 times larger than those of the nanospheres (nanorod 13,276; nanosphere 7055).

In our experimental condition, the gold anions were dominant anionic species desorbed from a gelatin section. The desorption of organic anions seemed to be much less efficient than that of gold anions. The preferential desorption would be a factor that enhances the desorption of gold anions from nanorods.

In this work, we have found that gold anions desorbed from gold nanoparticles with desorption efficiencies that were dependent on the sizes and the shapes of the nanoparticles. The differences in the desorption behaviors between gold cations and anions were remarkable, suggesting a new strategy to design a mass probe employing the desorption of anions as reporter ions. At the present stage of this work, the mechanisms by which the shapes of the nanoparticles affect the desorption processes have not been proven. The study of anions as reporter ions has just started. Further investigation will reveal the potential of the anionic species as reporter ions.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.2116/analsci.21N027.

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