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Determination of functionalized gold nanoparticles incorporated in hydrophilic and hydrophobic microenvironments by surface modification of quartz crystal microbalance

Tsui-Hsun Wu[a,f], Shu-Chuan Liao[b], Ying-Fang Chen[c], Yi-You Huang[a], Yi-Syuan Wei[d], Shu-Ju Tu[e,**], Ko-Shao Chen[d,*]

[a] Institute of Biomedical Engineering, College of Engineering, College of Medicine, National Taiwan University, Taipei, Taiwan, ROC
[b] Center of Thin Film Technologies and Applications, Mingchi University of Technology, Taipei, Taiwan, ROC
[c] Department of Dentistry, Yun-Lin Branch, National Taiwan University Hospital, Dou-Liu, Yun-Lin, Taiwan, ROC
[d] Department of Materials Engineering, Tatung University, 40 Zhongshan North Road, 3rd Section, Taipei 104, Taiwan, ROC
[e] Department of Medical Imaging and Radiological Sciences, Chang Gung University, 259 Wen-Hwa, 1st Road, Kwei-Shan, Tao-Yuan 133, Taiwan, ROC
[f] Institute of Medical Mechatronics, Chang Gung University, Tao-Yuan, Taiwan, ROC

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ABSTRACT

In this study, plasma deposition methods were used to immobilize Au electrode of a quartz crystal microbalance (QCM) to create different microenvironments for mass measurement of various modified Au nanoparticles (AuNPs). AuNPs were modified by 11-mercaptoundecanoic acid (MUA) and 1-decanethiol (DCT) for potential applications to drug release, protective coatings, and immunosensors. We aimed to develop a highly sensitive and reliable method to quantify the mass of various modified AuNPs. The surface of AuNPs and Au electrode was coated with polymer films, as determined by Fourier transform infrared spectroscopy and atomic force microscopy. Measurements obtained for various AuNPs and the plasma-treated surface of the Au electrode were compared with those obtained for an untreated Au electrode. According to the resonant frequency shift of QCM, a linear relationship was observed that significantly differed for AuNPs, MUA-AuNPs, and DCT-AuNPs (R^2 range, 0.94–0.965, 0.934–0.972, and 0.874–0.9514, respectively). Compared to inductively coupled plasma and micro-computerized tomography, the QCM method with plasma treatment has advantages of real-time monitoring, greater sensitivity, and lower cost. Our results demonstrate that surface modifications measured by a QCM system for various modified AuNPs were reliable.

1. Introduction

Gold nanotechnology has promising biomedical applications in the fields of drug delivery, biomedical imaging, implants, and biosensors [1–4]. Gold exhibits interesting optical phenomena in the visible wavelength range [5]. When assembled into a close-packed structure, its optical properties change dramatically owing to the interaction of the particles and local electromagnetic fields [6]. Some gold nanoparticles (AuNPs) have been modified with various substrates to change their external physical and chemical properties—such as by coating with polymers, liposomes, and superparamagnetic iron oxide (SPIO)—for drug release and image diagnosis in various biomedical applications [7–13]. In fact, AuNPs have better resolution than SPIO used for micro-computerized tomography (micro-CT) imaging. The virtue of modification of surface properties of AuNPs has led to their applications in the field of medical therapy, such as drug protection and thermal radiation [14,15].

In biomedical applications, 11-mercaptoundecanoic acid (MUA) is used as a hydrophilic material to modify the surface of AuNPs by self-assembly to enhance its hydrophilicity [16], while 1-decanethiol (DCT) is used to enhance its hydrophobicity [17]. MUA-AuNPs, through interactions between the carboxylate group of MUA and the amine groups of melamine, form a stable complex for selective enrichment of target cells, detection of binding with AchE, or DNA delivery applications [18]. Sitaula et al. used DCT as a protective coating on drugs to prevent biochemical reactions that can damage the drug before it binds to the target cell [19]. In general, it is difficult to measure the mass of AuNPs by an instrument. Moreover, it is particularly desirable to obtain information on the status of nanoparticles in real time in order to use AuNPs as a modal drug delivery system, indicator, or biosensor. Surface quantification techniques such as Raman spectroscopy, Fourier transform

* Corresponding author. Tel.: +886 2 2592 5252 3411x16; fax: +886 2 2593 6897.
** Corresponding author.
E-mail addresses: sjt@cgu.edu.tw (S.-J. Tu), kschen@ttu.edu.tw (K.-S. Chen).

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infrared (FTIR) spectroscopy, quartz crystal microbalance (QCM), atomic force microscopy (AFM), and Inductively coupled plasma-optical emission spectrometry (ICP) [20–23] have been used to analyze surface modification or quantify the mass of AuNPs. Some of these methods are qualitative for nanoparticles, and few tools are available for quantitative analysis. ICP has been used as a standard method to measure the mass of AuNPs. However, the ICP process requires samples to be prepared as a homogenous suspension. In particular, the aggregation and deposition of some of the particles after modification reduces the measurement accuracy. Micro CT has been used to quantitatively determine the uptake of AuNPs in cells or model laboratory animals and has been considered to be a useful tool. QCM is a piezoelectric resonator that has been widely used as a biosensor and has been shown to detect coagulation time and large and small particles such as bacteria, viruses, DNA, and proteins [24–26]. In essence, it is a highly sensitive balance in which changes in frequency indicate a proportional change in mass or viscoelasticity depending on the piezoelectric, and simultaneous monitoring of dissipation provides useful information on the Au electrode [27]. These techniques are well established for studying the absorption of substrates—for example, the absorption of polyelectrolytes or proteins on a variety of model substrates. A change in the surface-bound mass will result in a shift in resonance frequency. In liquid conditions or in air, the change in frequency is directly proportional to mass and can be accurately estimated using the Sauerbrey equation [28], which is used to characterize the various surface modifications of AuNPs. This is a new strategic measurement technique to characterize the properties of AuNPs.

Recently, surface modification by the plasma deposition (P-D) method is often used to solve the adhesion problem between the coating and the substrate. This method can induce free radicals and peroxide groups on the surface of the treated substrates. The films deposited on the substrate offer many advantages, such as good adhesion to substrates, excellent uniformity, easy preparation, thickness control, and pin-hole-free formation. By using plasma treatment, the P-D method can easily modify the physicochemical properties of various surfaces in a short period. The main reactions occurring during plasma treatment on the substrate surface are etching, cleaning, crosslinking, grafting, and other chemical reactions depending on the presence of active species in the plasma. The dimension of the deposited particles is limited by the size of the chamber, and hydrogen atoms can easily form a bond with the deposited Si layer at low temperature [29]. In the biomedical applications, AuNPs is used in image analysis and thermotherapies where more accurate dosages are required for in vitro and in vivo examinations. Here, we use changes in the surface electrode properties induced by the P-D method, which creates suitable conditions for easy, accurate, and reliable measurements of various properties of AuNPs.

2. Methods and materials

2.1. Synthesis and modification of AuNPs

AuNPs were synthesized by the chemical reduction method. Hydrogen tetrachloroaurate(III) tetrahydrate (chloroauric acid) ($HAuCl_4{\cdot}4H_2O$, 0.1 mM) was dissolved in deionized water, and the solution was heated up to 60 °C for 10 min. A solution of 38.8 mM trisodium citrate was added, and the solution was boiled for 10 min. Boiling was continued until the AuNPs changed into a wine red color and showed an absorption spectrum with a peak at approximately 530 nm. MUA-AuNPs were synthesized by adding MUA (10 mM, 200 mL, Lot. 674427, Sigma) to a solution of citrate-capped AuNPs (200 mL, 0.15 mM). The reaction was allowed to occur under stirring at 30 °C for 2 h. The resulting solution was equilibrated at ambient temperature overnight. DCT-AuNPs were synthesized by adding DCT (0.15 mM, 200 mL, Lot. D1602, Sigma) to AuNPs after rapidly stirring the microemulsion for 10 min. To remove the reaction reagents, all the AuNP solutions were centrifuged at 3000 rpm for 10 min and then washed with deionized water. After 3 centrifugation/washing cycles, the supernatant was removed until the residual volume was 3–6 μL and stored at 4 °C [29].

2.2. Plasma deposition treatment on polished Au electrodes of the QCM

A QCM-D instrument (MELL SB01B) from Smell Biotechnology Co. Ltd., Taiwan, was used. The QCM device, made from an AT-cut quartz crystal with gold electrodes on both sides and a basic resonant frequency of 10 MHz, was purchased from Taitien Electronics Co., Taiwan. The P-D method reactor system includes a bell-jar reaction chamber and 13.56-MHz radiofrequency generator (CVD model: PD-2S, SAMCO, Japan). The gold QCM electrode was a modification of hexamethyldisslazane (HMDSZ) by the P-D method (input power: 30 W, 100 mTorr, 180 s). After HMDSZ was deposited on the Au electrode, it was treated with O_2 gas at 70 mTorr for 1 min, with an input power of 100 W. The processes performed to modify hydrophobicity and hydrophilicity of the QCM gold electrodes were HMDSZ treatment and HMDSZ with O_2 plasma deposition, respectively.

The QCM-D technique enables in situ studies of mass change at the solid/liquid interface due to adsorption, desorption, and swelling. The piezoelectric quartz crystal oscillates at a resonant frequency f_0, which decreases or increases when mass changes are sensed on the surface of the crystal. If the layer on the electrode surface is evenly distributed, rigidly attached, fully elastic, and small compared to the mass of the crystal, the shift in the resonant frequency is related to the mass change by the Sauerbrey equation.

The resonant frequency of the piezoelectric depends on the total oscillating mass, including the water coupled to the oscillation. Determination of whether the film on the sensor surface is rigid or water-rich and mobile (soft) is possible only by measuring several frequencies and the dissipation.

We treated the electrode surface of a QCM with HMDSZ and O_2 plasma for creating hydrophobic and hydrophilic environments for substrate interactions by the P-D method (Fig. 1B) [29]. Our results demonstrate a simple technique to increase the sensitivity of the QCM to measure various modified AuNPs surfaces (Fig. 1A), and to potentially expand biomedical-related applications.

2.3. Chemical concentrations and morphological observations

Various AuNPs were prepared and validated in a multistep process. First, the average nanoparticle diameter was obtained from transmission electron microscopy (TEM) measurements (Hitachi 800 TEM/STEM, Japan), and evaluated by measuring the ζ potential (Nano-Zs, Zeta Sizer, USA). Infrared absorption spectroscopy (FTIR, JASCO FT/IR-6200, Japan) was used to illustrate the chemical structure of the thin films in the reflection mode.

Suspensions of AuNPs, MUA-AuNPs, and DCT-AuNPs were immersed on the surface of Au electrode of the QCM by series dilution and dried in the incubator for 24 h at 30 °C. The films were then scratched using a sharp needle, and the scratched area was scanned by AFM (1 μm × 1 μm, Digital Instrument, NS3a controller with D3100). The height difference between the revealed substrate and the intact areas of the film determined the film thickness. The images were scanned in the tapping mode with cantilevers (Non-Contact/Tapping™ sensors NCH-50). The radius of curvature for the tip was less than 10 nm, and the typical resonance frequency