

## Functional THG microscopy with plasmon-resonance enhancement in silver nanoparticles

Shi-Wei Chu, Szu-Yu Chen, Tsung-Han Tsai, Cheng-Chi Cheng, Tzu-Ming Liu, and Chi-Kuang Sun

Graduate Institute of Electro-Optical Engineering, National Taiwan University, Taipei, 10617 Taiwan, R.O.C.

Tel: +886-2-23635251 ext. 406. FAX: +886-2-23677467. Email: sun@cc.ee.ntu.edu.tw

Shr-Bin Wu, Sajal Biring, Juen-Kai Wang, and Yu-Lin Wang

Institute of Atomic and Molecular Sciences, Academia Sinica, Taipei 10617, Taiwan, R.O.C.

**Abstract:** Functional third-harmonic-generation (THG) microscopy is proposed/demonstrated by labeling the samples with silver nanoparticles. Over 100-fold THG enhancement can be observed by coinciding the signal frequency with the surface-plasmon-resonance frequency of <50-nm silver nanoparticles.

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THG has been proved to be a powerful noninvasive microscopic probe for subcellular structural imaging in bio-specimens [1] with the advantages including no energy deposition due to virtual-level-transitions and high resolution due to high-order nonlinearity. Current functional imaging, however, has to rely on fluorescence probes to label the specific target molecules or organelles while the light-stimulated fluorescence processes will cause optical bleaching/damage due to required absorption. Here we propose/demonstrate functional THG imaging utilizing plasmon-resonance in silver nanoparticles. For biological imaging, to avoid strong ultraviolet absorption, THG wavelength has to be in the visible range, requiring a fundamental wavelength longer than 1200-nm. However, the plasmon-resonance frequencies of noble metal nanoparticles fall in the visible range (blue for silver and yellow for gold). By adjusting aspect ratio, the plasmon-resonance frequency of gold nanoparticles can be red-tuned to near 800-nm with ~200-nm particle width [2], which is too large for the interested targets. Therefore, it is impractical to match the resonance frequency of gold nanoparticles with the >1200-nm light. On the other hand, it is straightforward to match the generated-THG with gold nanoparticle resonance frequency (~550-nm wavelength) yet the 1650-nm fundamental light will suffer from strong water absorption and is not suitable for biological research. In this presentation we will demonstrate that, for the first time, by coinciding the THG frequency with the plasmon-resonance frequency (~410-nm wavelength) of <50-nm silver nanoparticles, over 100-fold THG enhancement can be observed due to local field effects, while the fundamental wavelength (1230-nm) is located in the penetration window in common biological tissues [3]. Deep-tissue functional THG imaging can thus be realized by attaching the silver nanoparticles onto target proteins or molecules. Such metal nanoparticle labeling technique is routinely used in electron microscopy, which does not allow *in vivo* observation inside specimens. THG microscopy, on the other hand, can provide depth-resolved functional images in live cells without damage.

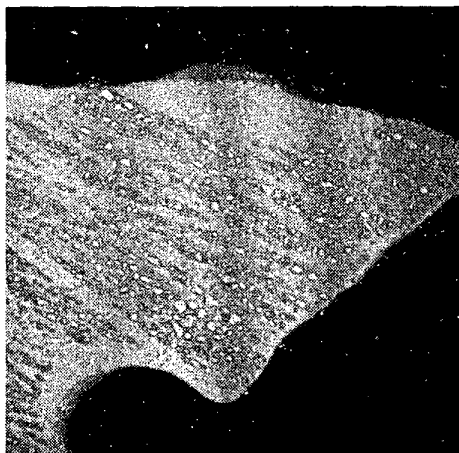


Fig. 1. A scanning THG microscopic image on a water-glass interface demonstrating the strong THG enhancement through silver nanoparticles. Note the contrast (>100:1) between regions with and without silver nanoparticles. Image size: 700×700- $\mu\text{m}^2$ .

**References**

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