Contrast agents for photoacoustic imaging

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In photoacoustic imaging, a pulsed laser is used to irradiate tissue but instead of measuring photons to obtain an image of anatomical structures hidden inside, ultrasound is measured. This is because different structures situated in the tissue can absorb light to different extents; this absorbed energy is converted into ultrasonic waves through the thermoelastic effect. The resulting pressure build up relaxes with the propagation of a stress wave which lies in the ultrasound frequency range. By analyzing the ultrasonic waves produced by the absorbing structures, it is possible to reconstruct the position, size, shape and optical properties of these structures. The technique has great potential in the detection and imaging of cancerous tissue; cancers are usually characterized by angiogenesis-driven higher absorption compared with healthy tissue. Laser light in the near-infrared (NIR) region is used to image deeper structures due to higher penetration depths at these wavelengths.

However, in the near-infrared wavelengths, the absorption coefficient of blood, the natural photoacoustic source is low. In order to enhance the photoacoustic effect in deeper structures, we require contrast agents. Contrast agents in general must be biocompatible and highly specific to the disease, and specifically for photoacoustic imaging, they must have high absorption coefficients.

Special physical and optical properties of gold nanorods recommend them as contrast agents for photoacoustic imaging. In the absorbance spectrum, these particles presents two peaks, the one around 520 nm in the green is called tranverse plasmon peak and the other one is red shifted and called longitudinal plasmon (LP) peak. By changing the size and aspect ratio of these gold nanorods is it possible to tune the position of the longitudinal plasmon peak to any desired wavelength in the NIR region. Using an appropriate conjugation of gold nanorods with specific proteins, it is desired to accumulate a large number of a particles a cancer site. The photoacoustic effect generated by the accumulated gold nanorods when excited at the wavelength corresponding to the LP peak should then be higher than blood, allowing higher sensitivity, better
resolution and finally better images for the photoacoustic technique. These proposed applications of light interactions with gold nanorods require the accurate estimation of their optical properties.

We are using computer simulations and photoacoustic measurements to find what are the optimum physical and optical properties of gold nanorods to be used successfully as contrast agents in photoacoustic imaging. The gold nanorods were synthesized in our laboratory with various sizes and aspect ratios using a slightly modified protocol from [1]. Using information about sizes and aspect ratio determined from HRSEM (High Resolution Scanning Electron Microscopy) images, we simulate their optical properties using the Discrete Dipole Approximation method [2] using the code (DDSCAT 6.1) developed by Draine and Flatau [3]. Figures 1a), b) and c) show the results of synthesis of a typical sample of gold nanorods and their simulated and experimentally derived optical properties. The absorbance spectra were measured using a VIS-NIR spectrophotometer.

The position of the simulated longitudinal plasmon peak is shifted compared with the one measured experimentally. This difference can be due to the uncertainties in dielectric function of gold and the local refractive index.

From simulations, we conclude that in the case of our synthesized particles, the absorption dominates the extinction of light. We used photoacoustic imaging to determine the optical absorption properties of gold.

Photoacoustic theory predicts that the amplitude of the generated photoacoustic signal is directly proportional to the absorption coefficient of the irradiated substance.

![Figure 1a) HRSEM picture of gold nanorods with aspect ratio of 2.26; b) Simulated and measured extinction spectrum for particles with aspect ratio of 3.1 (length 52 nm and width 16.8 nm); c) Simulated extinction, absorption and scattering efficiencies for gold nanorods with the 3.1 aspect ratio. Only the interval between 700 nm-900 nm is shown for a better visualization.](image-url)
In these experiments, we irradiate solutions of gold nanorods with a Q-switched Nd:YAG OPO laser with emission wavelength from 700 nm to 900 nm and 10 ns pulse widths. The photoacoustic signal generated by the nanoparticles is measured with an ultrasound detector [4]. The shape of the photoacoustic spectra was compared with the extinction spectra measured using a spectrophotometer. Our experimental photoacoustic spectra agree well with the spectrophotometrically determined spectra as shown in Fig. 2. These results confirm qualitatively the validity of the theoretical model used to simulate optical properties.

Conclusions.

We have succeeded in synthesizing gold nanorods with various sizes and aspect ratios. We are in the process of studying their optical properties experimentally and theoretically. The results recommend the synthesized particles for applications where high optical absorption is required. Such applications are photoacoustic imaging, photoinduced local hyperthermia, photoinduced cell lysis due to generation of shock waves and bubble cavitation. Photoacoustic spectroscopy can be used to determine easily the shape of the absorption spectra showing at what wavelength the conversion light energy to heat is maximum. Work is in progress to validate quantitative the simulated optical properties. The possible nonlinear effects as bubble formation around gold nanoparticles are currently being investigated.

References


