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Thermal Diffusivity Determination of Protoporphyrin IX Solution Mixed with Gold Metallic Nanoparticles

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Abstract Nanoparticles appear to be ideally suited for applications in targeted thermal effects in medical therapies and photothermally activated drug delivery; all depend critically on the thermal transport between the nanoparticles and the surrounding liquid. In this work thermal lens spectroscopy (TLS) was used to determine the thermal diffusivity of protoporphyrin IX (PpIX) solutions mixed with gold metallic nanoparticles. PpIX disodium salt (DS) was used in a HCl solution at 25%. Fluids containing gold (Au) nanoparticles at different concentrations were prepared and added to the PpIX solutions. For each solution, UV–Vis spectroscopy was used to obtain the optical absorption spectrum, and transmission electron microscopy (TEM) was used to obtain the gold nanoparticle size. From the TLS signal intensity, it was possible to determine the characteristic time constant of the transient thermal by fitting the theoretical expression to the experimental data. From this characteristic time, the thermal diffusivity was obtained for each solution. The results show that the thermal diffusivity of PpIX mixed with gold nanoparticles increases with an increase of the nanoparticle metallic concentration.

Keywords Nanoparticles · TEM · Thermal lens · Thermal properties of small particles

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1 Introduction

Metal nanoparticles have been proposed as targeted thermal agents for use in medical therapies and drug delivery [1–4] and could extend the precision of thermal effects below cellular dimensions [4]. Gold nanoparticles are leading candidate materials for these applications due to their biocompatibility and also because well-developed surface chemistries are available to functionalize Au nanoparticles for attachment to selected biological molecules or materials. Many research groups have studied how the environment of a nanoparticle affects the decay of the particle temperature [5–8] but these data, in most cases, have not been analyzed quantitatively to extract information about the thermophysical properties or microstructure of the material surrounding the nanoparticles. On the other hand in the photodynamic therapy (PDT), porphyrins are currently used as photo-sensitizers of cancerous tumors; thus, it is important to measure their distribution in tissues, mainly in relation to the possible side effects after their injection into patients [9].

Among these porphyrins the protoporphyrin IX (PpIX), which is induced by δ-aminolevulinic acid (ALA) being accumulated in high concentrations in cancerous cells and low concentrations in normal cells [9], stands out. Thus, it is important to determine the thermal diffusivity of the nanoparticles and the surrounding liquid (PpIX and water) in order to know the heat transfer between the photosensitizers and nanoparticles with possible applications of treatment for cancerous tumors. Thermal lens spectroscopy (TLS) offers some advantages in the field of photosensitization because one of the most distinctive features of this technique is its capability for the analysis of semitransparent samples, as well as its high sensitivity. This time-resolved method can be used to follow the thermal lens development over a short time, and also the optical absorption coefficient and thermal diffusivity of a sample can be measured in an absolute sense [10]. Furthermore, it has been demonstrated that the dual-beam thermal-lens measurement is independent of scattered light [11,12]. TLS, therefore, is suitable for thermal-diffusivity measurements of the nanoparticles and surrounding liquid. The purpose of this work is to determine the thermal diffusivity of PpIX solutions at different concentrations of gold metallic nanoparticles.

2 Materials and Methods

Gold nanoparticles in aqueous solution were synthesized using ascorbic acid (AA) as a reducing agent [13]. The reduction of $HAuCl_4$ was carried out as follows: solutions of $HAuCl_4$ (0.033 mmol in 25 ml of water) and poly (N-vinyl-2-pyrrolidone) (PVP, 25 mg in 20 ml of water) were prepared by dissolving the $HAuCl_4$ crystals and PVP in water. Both solutions were mixed to produce an Au (III) ion solution containing PVP. Then an aqueous solution of AA (0.033 mmol in 5 ml of water) was added to the resulting solution at room temperature. A colloidal solution containing metallic particles was formed after the addition of AA solution to the mixture solution. Three solutions of PpIX disodium salt (5 ml, 400 $\mu g \cdot ml^{-1}$, to 25% of HCl) were mixed at room temperature with 1, 2.5, and 5 ml of the colloidal Au solution to produce PpIX–Au nanocluster systems. The volume was adjusted to 10 ml with water and was placed in a quartz cuvette with 1 cm thick wall for the optical and thermal measurements. The experiments were performed at room temperature.

A Shimadzu UV–Vis 3101PC double-beam spectrophotometer was used to record the absorption spectra of the fluids. Particle sizes and size distribution were evaluated by TEM, using a JEOL-JEM200 microscope. For TEM observations, a drop of colloidal solution was spread on a carbon-coated copper micro-grid and dried subsequently in vacuum. Gold particles with an average size of 14.3 nm were measured. The TL effect of such PpIX–Au nanocluster assemblies was based on laser-induced heating and time-resolved monitoring of the thermal effects in the nanoliquids.

3 Thermal Lens Measurements

In the dual-beam thermal lens measurements, a sample is placed in a TEM_{00} Gaussian laser beam (excitation beam), and a temperature rise is produced by non-radiative decay processes following the optical energy absorption. Since the refractive index of the sample changes with temperature, a refractive index gradient is produced, creating a lens-like optical element, the so-called thermal lens. A weak TEM_{00} Gaussian laser beam (probe beam), which is co-linear with the excitation beam passing through the thermal lens, will be affected, resulting in a variation in its spot size and hence the intensity at the sample that can be obtained. A theoretical model for a continuous-wave (CW) laser-induced mode-mismatched dual-beam TLS has been developed, and the variation of the intensity in the center of the probe beam, caused by the thermal lens, can be expressed as [10,14]

$$I\,(t) = I(0)\left[1 - \frac{\theta}{2}\tan^{-1}\left(\frac{2mV}{\left[(1+2m)^2 + V^2\right]\frac{t_\mathrm{c}}{2t} + 1 + 2m + V^2}\right)\right]^2 \tag{1}$$

where

$$m = \left(\frac{\omega_{1\mathrm{p}}}{\omega_\mathrm{e}}\right)^2; \quad V = \frac{Z_1}{Z_\mathrm{c}}; \quad \theta = -\frac{P_\mathrm{e}A_\mathrm{e}l_0}{k\lambda_\mathrm{p}}\left(\frac{\mathrm{d}n}{\mathrm{d}T}\right)_p$$

and

$$t_\mathrm{c} = \frac{\omega_\mathrm{e}^2}{4D} \tag{2}$$

Here $I(0)$ is the initial intensity when t or θ is zero, P_e is the excitation beam power (W), A_e is the absorption coefficient (cm^{-1}), l_0 is the sample thickness, λ_p is the probe beam wavelength (cm), dn/dT is the refractive index change of the sample with temperature (K^{-1}), $Z_c = \pi\omega_{0p}^2/\lambda$ is the confocal distance (cm), Z_1 is the distance from the probe beam waist to the sample, $D = \kappa/(\rho c)$ is the thermal diffusivity of the sample ($\mathrm{cm}^2 \cdot \mathrm{s}^{-1}$), κ is the thermal conductivity ($\mathrm{J} \cdot \mathrm{s}^{-1} \cdot \mathrm{cm}^{-1} \cdot \mathrm{K}^{-1}$), ρ is the density of the sample ($\mathrm{g} \cdot \mathrm{cm}^{-3}$), c is the specific heat of the sample ($\mathrm{J} \cdot \mathrm{g}^{-1} \cdot \mathrm{K}^{-1}$), and

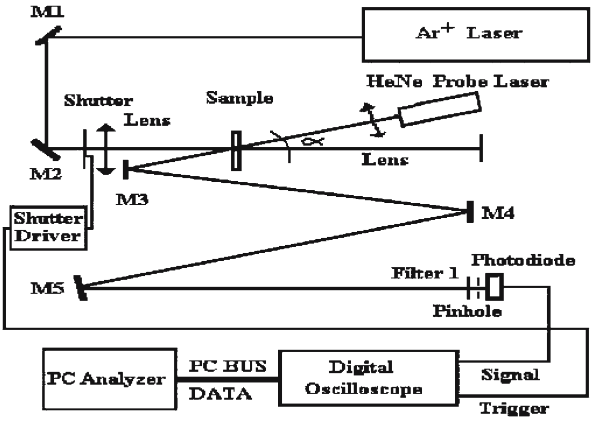

Fig. 1 Schematic representation of the thermal lens (TL) experimental setup

t_c is the characteristic thermal time constant (s). ω_e, Z_c, ω_{1p}, and ω_{0p} can be obtained from the spot-size measurements [10], and θ and t_c can be determined by fitting Eq. (1) to the measured time-resolved intensity signal data, $I(t)$. The thermal diffusivity, D, can be determined from t_c in Eq. (2). The mathematical expression in Eq. (1) is simple and convenient to use.

4 Experimental

The experimental apparatus for time-resolved measurements of gold nanoparticles in water solution samples is show in Fig. 1. The excitation laser is an Ar+ laser, at $\lambda = 514\,\text{nm}$, which was focused by a converging lens ($\omega_e = 40\mu\text{m}$), and the sample was placed at the focal plane lens. Exposure of the sample to the excitation beam was controlled by means of a shutter, which was connected directly to the trigger of a digital oscilloscope. A He–Ne laser probe beam of 4 mW was focused with a lens. The probe beam was incident on the sample and carefully centered to pass through the thermal lens to maximize the thermal-lens signal. After passing through the sample, the probe beam was reflected by mirrors M_3, M_4, and M_5 to a pinhole mounted before a photodiode or photodetector. A band-pass filter 1, at the He–Ne laser wavelength, was placed over the photodiode to prevent stray light from entering the photodetector. The spot size of the probe beam at the pinhole was 10 cm because of scattering by the sample, and the radius of the pinhole used here was 0.5 cm. The output of the photodiode was coupled to the digital oscilloscope. The parameters of the experimental setup such as ω_e, Z_c, ω_{0p}, and ω_{1p} were measured as described in [10].

5 Results and Discussion

Figure 2 shows a typical optical absorption spectrum of a PpIX solution and samples PpIX(1), PpIX(2), and PpIX(3) with Au particle concentrations of 0.001008, 0.00504, and 0.01008 mmol in 25 ml of water, respectively. In the spectrum it is possible to

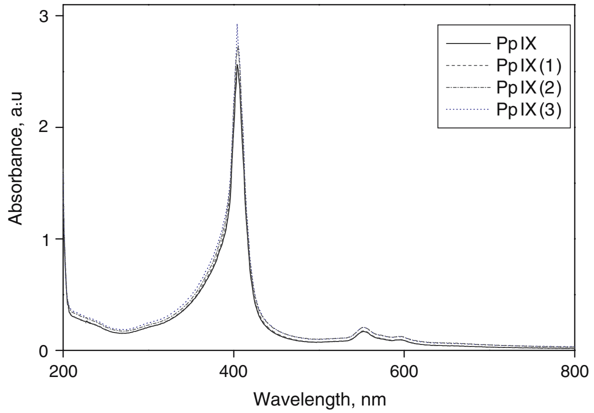

Fig. 2 Optical absorption spectra of PpIX and PpIX containing Au nanoparticles prepared with different concentrations of metal ions

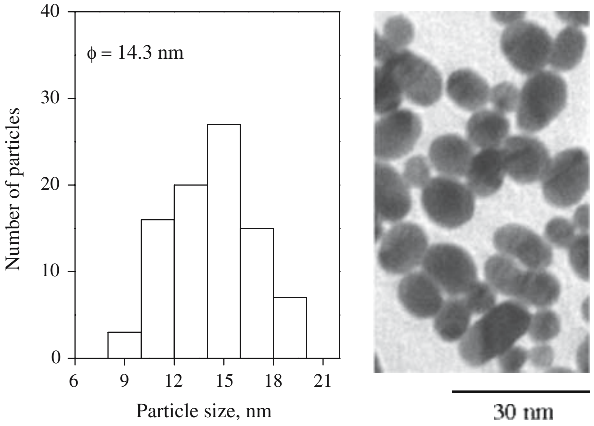

Fig. 3 Electron micrograph and particle size histogram of Au nanoparticles prepared with concentration of metal ion of 0.096 mmol in 50 ml of water. Average size ϕ is reported

observe that PpIX has a strong optical absorption band with a maximum at 404 nm, which is known as the Soret band, characteristic of porphyrins [15], and also another characteristic peak appears at 552 nm. For the samples that have a PpIX solution with nanoparticles (PpIX (1), (2), and (3)), it is observed that there is a little shift in the positions of the bands, approximately 1 nm. Also, it is possible to see that the intensity of PpIX (2.55 a.u.) increases proportionally with the nanoparticle concentration; for example, the peak of PpIX (3) is increased to 2.99 a.u. Figure 3 shows the TEM image and the corresponding size distribution of the Au nanoparticles. Formation of nanoparticles is clear from the TEM micrograph with an average size of 14.3 nm.

Figure 4 shows the normalized time resolved thermal-lens signal of the PpIX solution without gold metallic nanoparticles; symbols (o) represent the experimental points and the solid line corresponds to the best fit of Eq. (1) to the experimental data with θ and t_c as adjustable parameters. From this fit the values of $\theta = 0.37 \pm 0.06 \times 10^{-2}$ and

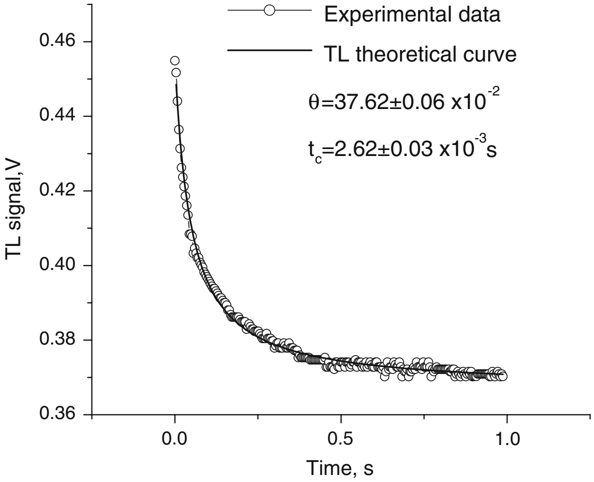

Fig. 4 Time evolution of the TL signal for PpIX solution. Symbols represent the experimental data, and solid line represents the best fit of Eq. (1) to the experimental data

Table 1 Adjustable Parameters t_c and θ, Obtained from the Best Fit of Eq. (1) to TL Experimental Data and Corresponding D Values Calculated from Eq. (2)

Sample	$t_c(10^{-3}\text{s})$	$\theta \times 10^{-2}$	$D(10^{-4}\,\text{cm}^2 \cdot \text{s}^{-1})$
PpIX	2.62 ± 0.03	37.62 ± 0.06	15.26 ± 0.17
PpIX(1)	2.02 ± 0.03	44.59 ± 0.12	19.80 ± 0.29
PpIX(2)	1.91 ± 0.02	40.83 ± 0.07	20.94 ± 0.23
PpIX(3)	1.56 ± 0.02	33.08 ± 0.08	25.64 ± 0.32

$t_c = 2.62 \pm 0.03 \times 10^{-3}$ s were obtained, which corresponds to the thermal diffusivity $D = 15.26 \pm 0.1710^{-4}$ cm $^2 \cdot \text{s}^{-1}$. This value is close to the thermal diffusivity of water ($D_{water} = 14 \times 10^{-4}\,\text{cm}^2 \cdot \text{s}^{-1}$) [16]. Figure 5 shows the transient thermal lens signal for PpIX(1) sample. From the best fit of Eq. (1) to the experimental data, the thermal diffusivity of this sample was obtained. Similar TL signal evolution was obtained for PpIX(2), and PpIX(3) samples and their corresponding thermal diffusivities were obtained. Table 1 summarizes the thermal diffusivity values obtained from the fit of Eq. (1) to experimental data. It can be seen that there is an increase in the fluid thermal diffusivity when the Au particle concentration increases.

A possible explanation for this incremental increase in the thermal diffusivity when the Au particle concentration increases, is due to the strong electrostatic interaction between the cationic PpIX and the negatively charged Au nanoparticles. This interaction implies a higher nanoparticle concentration per volume unit in the PpIX, which implies an increase in the optical absorption peak intensity (see Fig. 2) [17]. A laser excitation would lead to the generation of hot electrons that are rapidly thermalized by electron–phonon scattering [18]. The energy deposited into the phonon modes is subsequently transferred to the surrounding medium. Then when the particle concentration

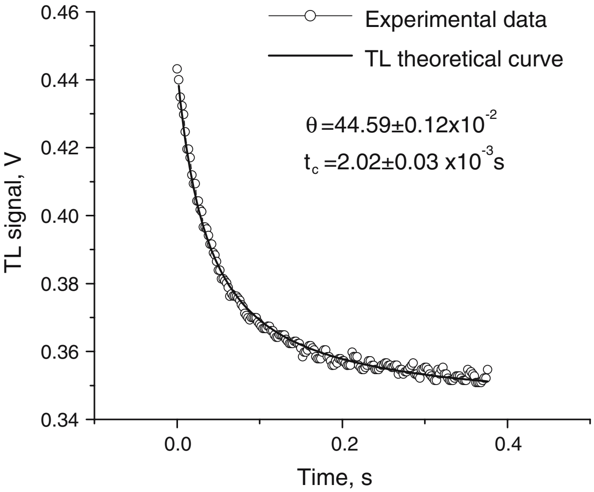

Fig. 5 Time evolution of the TL signal for PpIX (1) with gold nanoparticles. Symbols represent the experimental data, and solid line represents the best fit of Eq. (1) to the experimental data

is increased in PpIX, the optical absorption intensity is increased, as well as the thermal diffusivity of the surrounding medium (see Table 1).

6 Conclusions

From TL the thermal diffusivity of PpIX and PpIX mixed with gold nanoparticles at different concentrations was obtained in aqueous solutions. The results show that the thermal diffusivity of PpIX mixed with gold nanoparticles increases with the Au particle concentration. The determination of this thermal parameter is very important in PDT in order to know the heat transfer between photosensitizers (such as porphyrins) and nanoparticles that are being studied in cancerous tumor treatment.

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References

1. K. Hamad Schifferli, J.J. Scwartz, A.T. Santos, S.G. Zhang, J.M. Jacobson, Nature **415**, 152 (2002)
2. C. Loo, A. Lin, L. Hirsch, M.H. Lee, J. Barton, N. Halas, J. West, R. Drezck, Technol. Cancer Res. Treat. **3**, 33 (2004)
3. D.P. O'Neal, L.R. Hirsch, N.J. Halas, J.D. Payne, J.L.West, Cancer Lett. **209**, 171 (2004)
4. G. Huttmann, R. Birngruber, IEEE J. Sel. Top. Quant **5**, 954 (1999)
5. S. Link, A. Furube, M.B. Mohamed, T. Asahi, H. Masuhara, M.A. El-Sayed, J. Phys. Chem. B **106**, 945 (2002)
6. J.Y. Bigot, V. Halte, J.C. Merle, A. Daunois, Chem. Phys. **251**, 181 (2000)

7. J.Z. Zhang, Acc. Chem. Res. **30**, 432 (1977)
8. M.B. Mohamed, T.S. Ahmadi, S. Link, M. Braun, M.A. El-Sayed, Chem. Phys. Lett. **343**, 55 (2001)
9. J.C. Kennedy, R.H. Pottier, D.C. Pross, J. Photochem. Photobiol. Biol. B. **6**, 143 (1990)
10. J. Shen, R.D. Lowe, R.D. Snook, Chem. Phys. **165**, 385 (1992)
11. J. Shen, R.D. Snook, J. Appl. Phys. **73**, 5286 (1993)
12. S.M. Brown, M.L. Baesso, J. Shen, R.D. Snook, Anal. Chim. Acta. **282**, 711 (1993)
13. J. Park, V. Privman, E. Matijevic, J. Phys. Chem. B. **105**, 11630 (2001)
14. J.F. Sánchez-Ramírez, J.L. Jiménez-Pérez, R. Carbajal-Valdez, A. Cruz-Orea, R. Gutierrez-Fuentes, J.L. Herrera-Pérez, Int. J. Thermophys. **27**, 1181 (2006)
15. M. Gouterman, in *In the Porphyrins*, vol. III, *Physical Chemistry*, Part A, Chap. 1, ed. by D. Dolphin (Academic, London, 1978)
16. R.C. Weast (ed.), *Handbook of Chemistry and Physics*, 67th edn. (Chemical Rubber Co., Boca Raton, Florida, 1986–1987)
17. P. Mulvaney, Langmuir **12**, 788 (1996)
18. N. Chandrasekharan, P.V. Kamat, J. Hu, G. Jones, II J. Phys. Chem. B **104**, 11103 (2000)