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Heating Mechanisms in Gold Nanoparticles at Radio Frequencies

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***Abstract*—Gold nanoparticles are under study as a potentially viable mechanism for hyperthermia tumor treatment in two regimes of the electromagnetic spectrum: laser and radio frequency excitation. Gold nanoparticles, nanorods and nanoshells have been applied with visible laser sources that excite the particles at or near their plasmon resonance frequency, and this mechanism has been well studied. The physical processes that describe the experimentally observed heating at radio frequencies (13.56 MHz) are not as well understood. Differing results have been reported in semi-solid phantom materials and liquid phase suspensions. This numerical modeling study was undertaken to inspect the relative importance of several candidate physical processes.**

I. Introduction

THE extremely small size of nanoparticles changes the relative significance of many effects that are normally of negligible or little consequence in larger systems. This is particularly true for viscous forces in fluid media, which partially accounts for the extremely slow settling velocity of nano particles (NP) in suspension. Other forces of augmented influence include Brownian motion and buoyancy forces. Nano particle heating has been well studied at optical frequencies, where plasmon resonance effects dominate the heating mechanism. The problem of heating at much lower radio frequencies has not been well elucidated to this point, and remains somewhat controversial. Colloidal gold already has FDA approval for treatment of arthritis by internal administration. Given that some considerable effort is being expended toward establishing a clinical application for gold nano particles in cancer therapy, it is important to resolve this particular aspect of the problem to put the discussion on a firm physical basis.

A. Experimental Observations

There have been several recent experimental studies that observe significant heating with gold nano particles of 5 nm diameter in tissues at industrial, scientific and medical (ISM) radio frequencies (RF).[1-4] Moran et al. [5] have attributed the remarkable heating measured in experiments with small gold nanoparticles, 5 nm diameter at 13.56 MHz, to an increased effective electrical resistivity due to their extremely small size. The rationale given was based on experimental work by Wiley et al. [6] on silver nano-beams. However, the 2006 Wiley paper noted only an increase in effective resistivity of the silver by a factor of approximately 2 over the bulk value, and the bulk electrical conductivity of gold is in the neighborhood of 4.5×10^7 (S m^{-1}) — consequently, it seems unlikely that internal joule losses in the particle form a complete description of the experimentally observed RF heating. In an as yet unpublished series of experiments Chen and Borelli [7] measured no RF heating attributable to gold nanoparticles suspended in combination Agarose and Carrageenan phantoms (as typically used in hyperthermia work), except that due to the ionic content of the bulk phantom material in the absence of nano particles. Also, recent experiments by Li *et al*. [8] in colloidal suspensions of gold NPs have failed to show any net increase in RF heating over that of the supernatant NP suspension medium alone, and no significant heating in re-suspended Au NPs in a non-conducting medium.

B. Physical Principles in Radio Frequency Heating

If there is a pertinent fundamental mechanism for preferential heating induced by gold nano particles in solution it is completely unclear at this point. The major difference between a liquid suspension and a phantom distribution is that the particles can move in a liquid suspension.

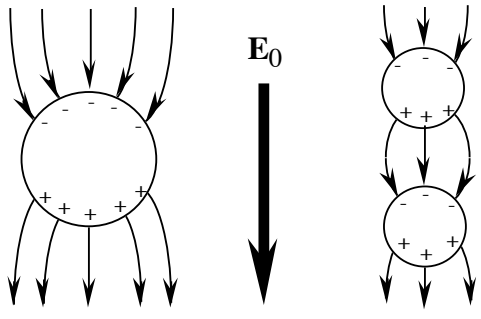

Fig. 1. Induced dipole surface charge in a uniform electric field, $\mathbf{E}_0$. a) Single sphere with symmetric charge distribution. b) Two spheres in close proximity: surface charge distribution results in a mutually attractive force between the spheres.

In both phantoms and liquid suspensions the presence of the conducting particles distorts an electric field and results in increased volume power density at the particle surface.

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Here we inspect several possible mechanisms and their relative magnitudes of importance.

A metallic sphere in a dielectric medium refracts the electric field to satisfy the boundary conditions: the tangential E-field component must be zero. The classical analytical solution for a conducting sphere in a uniform electric field, $\mathbf{E}_0 = -E_0\,\mathbf{a}_z$ (V m^{-1}) — as in Fig. 1 — has a surface electric field of:[9]

$$\mathbf{E} = -3E_0\,cos(\theta)\mathbf{a}_r \qquad (1)$$

where: θ = the azimuthal angle, r is the radial coordinate, and **a** is the direction unit vector.

The E-field refraction results in a spatially distributed surface charge, ρ_S (C m^{-2}):

$$\rho_S = -3\varepsilon E_0\,cos(\theta) \qquad (2)$$

where ε is the surrounding medium permittivity (F m^{-1}). The concentrated electric field at the surface results in an increased volume power density, Q_{gen} (W m^{-3}) = $\sigma\,|\mathbf{E}|^2$.

In Fig. 1b, two particles in proximity co-linear with the applied E-field have induced surface charge distributions that result in a force of attraction between them. Co-linear particles suspended in water can move relatively freely since the "noble metal" property of gold means that the interactive surface forces contributing to viscous losses will be extremely weak. It is not unlikely that particles in liquid suspension may accelerate and collide, thus dissipating energy. Certainly, the experimentally-observed tendency for gold nano particles to cluster together [2] may be due, in part at least, to these induced attractive forces.

II. Numerical Model Studies

Numerical models of individual and grouped gold nano particles were implemented in Comsol (Comsol Inc. Burlington, MA). It is not productive to model the transient temperature rise in these small model spaces (on the order of 10^{-20} m^3) because the heat transfer effects are amplified uncontrollably — a transient thermal model must have at least one Dirichlet-like boundary to ensure stability. That problem is inherently a multi-scale modeling problem, and outside of the scope of this investigation. The electric field models alone are adequately instructive for these purposes.

A. Single Particle Electric Field Calculations

A numerical model of one of the representative experiments described by Gannon *et al.* [2] was executed to study the relative contributions of the electric field refraction and internal joule heating in the particle. The specific experiment under study had a 5 nm diameter gold nano particle concentration of 67 (μM L^{-1}) exposed to 13.56 MHz at 200 W in their system, *i.e.* an estimated electric field strength of 10^4 (V_{rms} m^{-1}). After 300 s of exposure the measured temperature was 90 °C.

The Comsol numerical model (Fig. 2) is a 2D axisymmetric (in cylindrical coordinates, the r, z plane) quasi-static E-field model of a 5 nm diameter gold particle in a 0.3 µm high by 0.1 µm radius cylinder of medium at that field strength. An approximately uniform applied E-field was created by a constant potential boundary at z_{max} = +0.3 µm, V = 4.24 (mV_{peak}). The z = 0 plane is a symmetry boundary set to V = 0, which simulates a virtual boundary of – 4.24 mV at z = -0.3 µm. The electrical conductivity of the surrounding medium was 0.1 (S m^{-1}) (relative permittivity = 80) and the electrical conductivity of the gold particle was 4.5 x 10^7 (S m^{-1}). The problem is quasi-static because the maximum size of the model space (< 1µm) is many orders of magnitude smaller than a wavelength at these frequencies (approximately 2 m).

At 10^4 (V_{rms} m^{-1}) electric field strength the volume power density in the surrounding medium is 1 x 10^7 (W m^{-3}), while inside the particle it is 0.27 (W m^{-3}) — hardly adequate to provide measurable internal heating in any sense. The surface charge, (2), has effectively canceled the electric field: 10^4 outside the particle and 7.7 x 10^{-5} (V_{rms} m^{-1}) inside the particle — with 3.0 x 10^4 (V_{rms} m^{-1}) maximum at the top surface, a 3-fold increase over the baseline applied field.

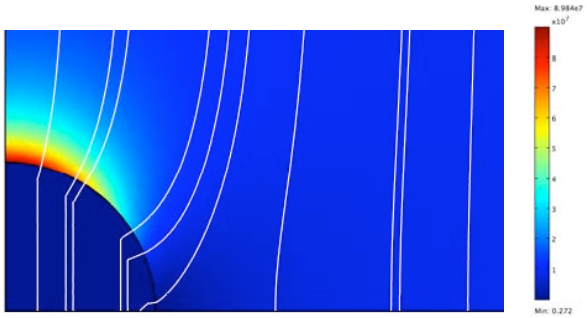

Fig. 2. Volume power density, Q_{gen} in color scale between 0.27 (dark blue) and 9 x 10^7 (W m^{-3}) (red). Refraction in the electric field (streamlines) is also shown.

In this case the presence of the particle has not contributed to the overall coupled power. In the absence of the particle the model space would have 9.425 x 10^{-14} (W) total power. Subdomain integration gives a total coupled power with the particle hemisphere in place of 9.413 x 10^{-14} (W) — a net decrease of 1.2 x 10^{-16} (W), which would not be expected from integration of the analytical solution and is most likely due to accumulated error in the extremely small geometry.

The nano particle does focus the heating in a narrow location, so placement is an important consideration. Other models with larger 50 nm particles suggest that a very slight positive contribution to the overall resistive heating is realized — but in any case not enough to contribute significant heating to the model space.

B. Comparison to Analytical Approximations

The numerical model case can be compared to analytical approximations based on (2). The second hypothesis under

investigation is that particles in proximity experience an attractive force that causes them to move together in the liquid suspension medium. For this preliminary analysis we neglect the Brownian motion and buoyancy effects.

From Fig. 1b the attractive force is due to the two hemispherical cap surface charges. The total charge on a hemispherical cap, q_h (C) is:

$$q_h = -3\,\varepsilon\,E_0 \int_0^{\pi/2}\int_0^{2\pi} R^2\, cos(\theta)\, sin(\theta)\, d\phi\, d\theta = -3\,\varepsilon\,E_0 R^2 \qquad (3)$$

where R = the particle radius (m). The charge results in an attractive (i.e. negative) force between the particles on both half-cycles of the waveform:

$$F_q = -\frac{9}{4}\,\pi\,\varepsilon\,E_0\left(\frac{R^2}{h}\right)^2 \qquad (4)$$

where h = the distance between particle centers (m).

The drag force, F_D, on spherical particles may be estimated from Stokes' result:

$$F_D = 6\,\pi\,\mu\,R\,U_d \qquad (5)$$

where: μ = fluid viscosity (N s m^{-2}) and U_d = the particle drift velocity (m s^{-1}). The drift velocity is created by the Coulomb force from (4), so:

$$U_d = \frac{9}{24}\frac{\varepsilon E_0}{\mu}\left(\frac{R^3}{h^2}\right) \qquad (6)$$

which increases as h decreases. For the conditions of the numerical model, and using μ = 1.0 x10^{-3} (N s m^{-2}), U_d = 26.6 (R^3/h^2) — at h = 4R = 10 nm U_d = 4.16 x 10^{-9} (m s^{-1}).

The particles would require on the order of seconds to collide, hardly a sufficient velocity for the collision to result in much energy dissipation since the kinetic energy of a 1.82 x 10^{-16} (kg) gold particle at that velocity is only about 1.57 x 10^{-33} (J).

In terms of a 67 (μM L^{-1}) uniform dispersion, we expect approximately 1.32 x 10^{-5} (kg L^{-1}) of gold, or a volume fraction of 6.84 x 10^{-5} %. The particle separation distance in a uniform dispersion would average about 24 μm, consequently the average attractive force and approach velocity are negligibly small in a uniform dispersion. This mechanism makes no significant contribution to heating.

C. Clustered Nano Particles

The single particle model results do not support heating; however, the weak attractive forces do support the tendency of the particles to cluster. An additional 3D model of a 9-particle cluster with inter-particle separation distance of 7.5 nm (2.5 nm space between particles) was constructed to study the effect of clustering.

In the model result of Fig. 3 the electric field is in the -Z direction (i.e. down) and the particle cluster is in the X-Z plane. The maximum volume power density near the cluster is the same as in the single particle model, nominally 1.4 x 10^8 (W m^{-3}), or approximately 10 times the power density in the surrounding medium. The total power in this much larger 3D volume is reduced by 0.96 x 10^{-17} (W) due to clustering. However, we might achieve a net power gain when 100s of particles cluster together, as shown in the electron micrographs of the previous studies.[3, 5, 10]

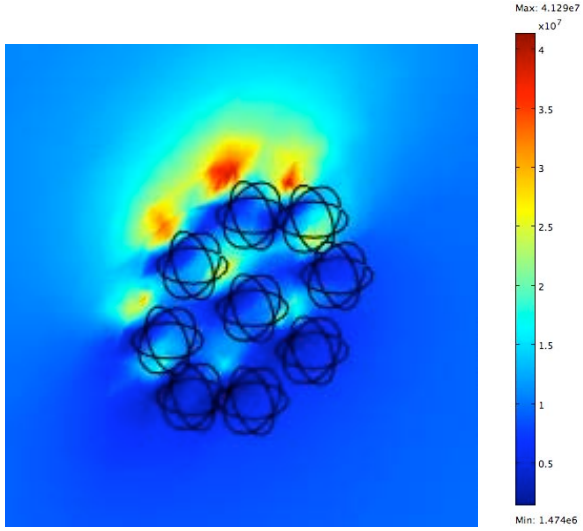

Fig. 3. A cluster of 9 Au NPs of 5 nm diameter at the same applied electric field strength, $-E_z$, has a similar maximum volume power density, Q_{gen} = 5 x 10^7 (W m^{-3}); however the effect of clustering is to focus power in the model space. The display plane is immediately behind the plane of the nanoparticles.

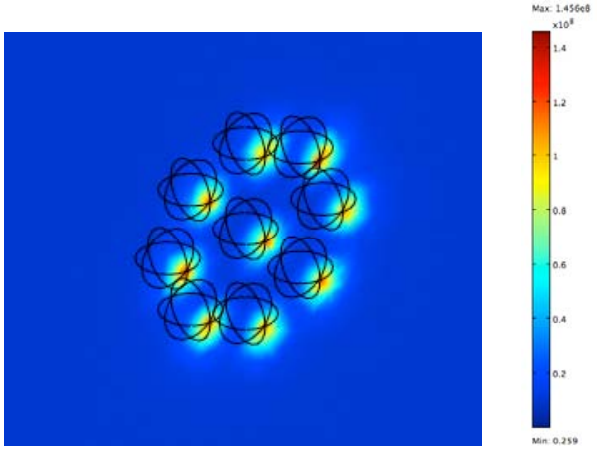

Fig. 4. The same 9-particle sheet exposed to a Y-polarized E-field shows no particle shadowing effect, and maximum power density Q_{gen} = 1.5 x 10^8 (W m^{-3}). The plot plane shown is at Y = 92.5 nm, or just at the proximal surface of the particles.

Also visible in Fig. 3 is the effect of "shadowing" by particles proximal to the E-field source. If the E-field polarization were changed from -Z to +Y polarization all of

the particles in the sheet would be "proximal", as it were. That model result, for all other conditions unchanged, is shown in Fig. 4.

III. Conclusion

The numerical model work and analytical estimates support the experimental measurements of Li *et al*. [8] in which they were not able to measure any significant heating attributable to the gold nano particles alone when suspended in a non conductive medium. In their experiments all of the measured heating could be explained by RF field interaction with the semiconducting suspending medium, the "supernatant". This is the reasonable result, of course: the analytical calculations and numerical models both confirm that the dominant heating mechanism is concentration of the electric field in the surrounding medium at the surface of the conductive nano particle. Consequently, suspending the particles in a non-conducting medium completely removes all of the heating mechanism. In that sense, it is completely unfair to condemn the gold nano particles on the basis of their experiment alone. It is equally incorrect to attribute the experimental heating results in tissues to the presence of the gold nano particles alone,[2] when, in fact, the applied electric fields are strong enough to cause substantial heating in the semi conducting fluids even in the absence of the nano particles. None of the other possible mechanisms studied are capable of adding any significant heating to the suspensions.

Clusters of the nano particles in a semiconducting solution do focus some enhanced heating in a very narrow volume immediately adjacent to the particles due to the E-field boundary conditions at the particle/semiconductor interface. Consequently, if located on a sensitive structure, such as a membrane surface, they may provide some therapeutic advantage; however, there is no compelling argument for enhanced heating in dispersed particle spaces among the several candidate mechanisms that were studied.

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