Are Gold Clusters in RF Fields Hot or Not?

Hong Koo Kim *et al.*

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circular RNA in cells caused mRNAs containing miR-7 binding sites to also decrease in number, indicative of increased binding of miR-7 to these mRNAs leading to their degradation (*6*, *9*).

Additional circular RNAs may function similarly to regulate the activity of other microRNAs because, in general, microRNA binding sites are abundant in circular RNAs (*6*). For example, in the mouse, sex-determining region Y (*Sry*) plays a key role in testes development and generates a circular RNA that contains 16 miR-138 binding sites (*9*). Circular RNAs thus join a growing class of naturally occurring microRNA "sponges," which includes competing endogenous RNAs and pseudogene (nonfunctional gene) RNAs (*12*). Compared to competing endogenous RNAs and pseudogene RNAs, however, circular RNAs are likely much more potent microRNA sponges as they are expressed in greater amounts and contain many more microRNA binding sites. Furthermore, unlike competing endogenous RNAs, circular RNAs appear to be resistant to RNA degradation triggered by microRNAs and thus could have long half-lives (*9*).

Beyond regulating microRNAs, circular RNAs may bind and sequester RNA-binding proteins or even base pair with RNAs besides microRNAs, resulting in the formation of large RNA-protein complexes. Other circular RNAs may produce proteins, given that synthetic circular RNAs can be efficiently translated (*13*). As even linear mRNAs are thought to circularize during translation through protein-protein interactions between factors binding the 5′ and 3′ ends of the mRNA, RNA circularization, whether by direct covalent bonds or noncovalent means such as protein bridging or Watson-Crick base pairing, may be much more common than is currently appreciated. The discovery of such a large class of previously unknown RNAs also raises the question of what other RNAs might have been missed. Considering that RNA structural elements, such as triple helices, efficiently prevent degradation from RNA termini (*14*), it is becoming increasingly clear that the cell uses a myriad of distinct ways to process and stabilize RNA molecules.

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CHEMISTRY

Are Gold Clusters in RF Fields Hot or Not?

Heating of gold nanoparticles by radio-frequency waves, which is of interest for clinical applications, can occur if the nanoparticles are made magnetic.

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Nanoparticles are finding increasing applications in diagnostics, imaging, and therapeutics in biology and medicine. Gold nanoparticles (Au NPs) have received a great deal of interest because of their distinctive optical, electronic, and molecular-recognition properties, as well as biocompatibility. One promising yet ambitious application for Au NPs is noncontact hyperthermia of cancer. By attaching tailor-made ligands, Au NPs can recognize and lock onto receptors on the surface of tumor cells. Under illumination by light, Au NPs can absorb radiation energy and selectively heat and destroy tumor volumes without collateral damage to neighboring healthy tissue. This type of noninvasive, specific, active targeting with Au NPs is highly desirable from a clinical perspective, but its use in cancer intervention has yet to be demonstrated.

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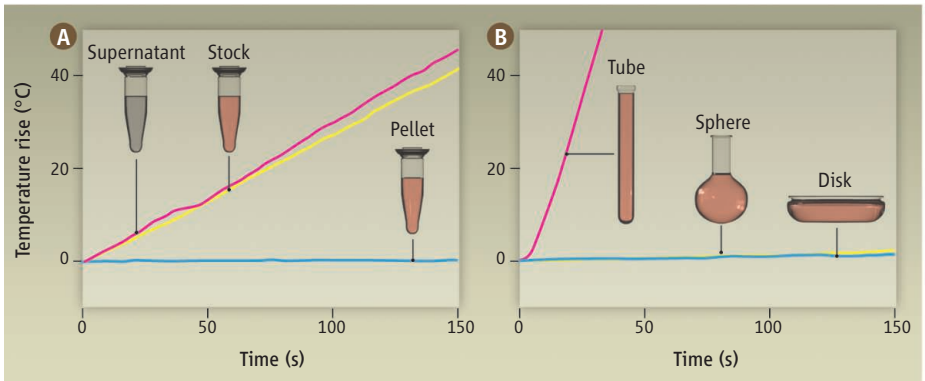
The use of radio-frequency (RF) waves instead of light for heating Au NPs is appealing because of the larger penetration depth of RF waves in tissue, which would increase the tissue volumes that can be interrogated. A number of experimental studies have reported increased tumor cell destruction in the presence of Au NPs. One capacitive RF apparatus, in which a 13.56-MHz RF field is applied across two parallel plate electrodes (*1*), can produce marked heating (*1*–*3*). Moran *et al*. hypothesized that the increased heat dissipation in Au NP solutions was caused by increased Joule (resistive) heating in Au NPs (*3*). By implicitly assuming that the applied electric field penetrates through the Au NP without attenuation (i.e., no shielding effect of free electrons in the metal), a phenomenal amount of power dissipation was calculated for Au NPs and was used to explain the observed solution heating.

This type of Joule heating of Au NPs by RF fields has been disputed on both experimental and theoretical grounds (*4*, *5*). Li *et al*. showed that the heating of Au NP solutions arose from the background ionic solution, not the Au NPs themselves. After separating out Au NPs from the solution via centrifugation and resuspending them in deionized water, negligible RF absorption was observed for a variety of Au NPs ranging in size from 5 to 200 nm. These findings contradict previous conclusions about the heating rate dependence on particle size and concentration and disprove the hypothesis that Au NPs directly absorb RF energy.

Unlike the case at optical frequencies, where a photothermal effect can arise from electromagnetic field penetration into the particle, Au NPs respond differently to RF fields. Given the low oscillation frequency of RF energy, free electrons in metals respond essentially instantaneously and their drift cancels the incident electric field. This shielding effect renders Au NPs unheatable by RF electric fields; any observed heating is Joule heating of the ionic solvent (*6*).

McCoy *et al*. now report RF heating of gold cluster solutions tested in an inductively coupled RF apparatus—that is, inside a coil where the magnetic field dominates over the electric field (*7*). First, *p*-mercaptobenzoic acid (pMBA) was used to create a fixed-size crystalline nanocluster, $Au_{102}(pMBA)_{44}$.



Rethinking RF heating of gold nanoparticle solutions. (**A**) Absorption of RF energy by solutions containing gold nanoparticles is caused by Joule heating of the background ionic solution (supernatant), not by gold nanoparticles (pellet). Sample volume, 0.5 ml. (**B**) Joule heating further depends on the shape of media confinement. A thin tube (0.65 ml) oriented parallel to the electric field heats faster than a sphere (1 ml) or a disk (1 ml). RF power, 25 W; Au NP concentration, 6×10^{-3} weight %.

These Au nanoclusters (Au NCs) can be considered as closed-shell, nonmagnetic superatoms that are not susceptible to RF fields. McCoy *et al*. report that the Au NCs become paramagnetic when oxidized with $KMnO_4$, so that they can be heated by magnetic fields, similar to the heating of magnetic NPs (such as iron oxide NPs) in oscillating magnetic fields. In this type of heating, particles can rotate within the stationary solvent (Brownian relaxation) or magnetic dipoles can rotate within the particle (Néel relaxation).

McCoy *et al*. claim that other previously reported experiments might have contained unintentionally magnetic Au NPs in oscillating magnetic fields, partially accounting for the observed NP-dependent heating. Most previous reports of Au NP heating, however, used NPs with diameters of 5 nm or larger, and superatom stabilization and potential superatomic paramagnetism are unlikely in that size range.

The work by McCoy *et al*. represents an important technical advance, but more work is needed to understand the underlying mechanisms and to develop the technology for use in RF hyperthermia. Much of the heating observed with their Au NCs is modest and substantially less than that reported in previous work on RF heating of solutions and for magnetic heating of iron oxide NPs. Furthermore, considering that most tissues have an ionic background, Joule heating of the background media is expected to be an important factor that will affect the selectivity of RF heating.

Joule heating further depends on operating frequency (*8*) and the shape and geometry of media confinement. Recently, we reported excellent RF heating of ionic solutions at 13.56 MHz, but the shape of the container holding the NP solution (or any conductive solution) played an important role (see the figure) (*9*). Hence, heating applications must be considered in light of container shape. For example, a long, thin object immersed in an RF field and oriented parallel to the electric field will allow greater field penetration into the interior relative to a low, flat object. The slight heating of solutions in a dish with electric field perpendicular to the dish surface may be mainly a geometric effect, rather than a material property of the solution, because depolarization fields develop at dielectric interfaces in response to RF electric fields.

Similar effects are expected with the size and shape of the whole body or individual organs. At a smaller scale, capillaries and microvasculature would also have an important effect on the efficacy of local heating by RF fields. Considering the complex nature of radio-wave interactions in tissues in vivo, further studies are needed to develop optimal RF hyperthermia targeting strategies.

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GEOPHYSICS

Melting Earth's Core

Yingwei Fei

Studies of melting iron at extreme temperature and pressure provide a better understanding of the temperature of Earth's core.

Earth's predominantly iron core is under extreme pressures that range from 136 to 364 GPa (100 GPa ~ 1 million atm). The core consists of an outer layer that is molten and a solid inner core. The temperature of the core region can be estimated if the melting temperature of iron under such extreme pressures can be determined. Pressures and temperatures corresponding to the conditions at the core can be generated in the laboratory by using two gem-quality single-crystal diamonds coupled with laser heating (see the figure). The challenge, however, is how to accurately determine the melting point under such extremes. On page 464 of this issue, Anzellini *et al*. (*1*) use fast in situ synchrotron x-ray diffraction to study melting in the laser-heated diamond-anvil cell. The accurate determination of the melting temperature of iron provides an important constraint on the core temperature, which is essential to understanding how the dynamic Earth works, including its heat budget, generation of its magnetic field, and the thermal evolution of the planet.

The primary experimental methods used to induce the melting of iron at extreme pressures are dynamic shock compression with a light-gas gun (*2*) and static compression in the diamond-anvil cell with laser heating (*3*, *4*). Along the pressure-temperature path of shock-compression experiments, melting is detected as an abrupt decrease in the sound velocity with increasing shock pressure, but the shock-temperature determination is dependent on having an accurate thermodynamic model. By contrast, the temperature of melting in the laser-heated

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