Nano-thermometers by Quantum Mechanics

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***Abstract*—**Scientists have recently announced the measurement of temperatures inside living cells using nano-thermometers. The nano-thermometers are submicron NPs of semiconductor materials called QDs that are small enough to enter the cell. . NP stands for nanoparticles. To perform the temperture measurements, the QDs are excited with laser light to obtain their emission spectra from which temperatures are inferred by comparison with experimental spectra taken at known temperatures. However, the QD spectra assume the laser light does not affect their temperature which is valid providing the QDs are in contact with the relatively massive macroscopic cell. However, if the QDs move, contact with the cell is lost and the isolated QDs will respond differently to the laser excitation. Classically, the QDs increase in temperature by absorbing laser light, but this does not happen. Quantum mechanics (QM) requires the heat capacity of the QD to vanish, thereby precluding any increase in QD temperature. Instead, the conservation proceeds by the QED induced creation of photons within the QD, the QED photons confined by TIR. QED stands for quantum electrodynamics and TIR for total internal reflection. The TIR confinement of QED photons is enhanced by the fact the absorbed laser light is concentrated solely in the TIR mode because QDs have a high surface to volume ratio. In moving QDs, the QD spectrum is the consequence of absorbed laser light that is not related to the cell temperature. A clarification of what the nano-thermometers are actually measuring is presented and extensions made to measurements of cell temperatures by Raman shifts.

Keywords **—** Nano-thermometers, cell temperatures, quantum mechanics, spectra, Raman shifts.

I. Introduction

NANO-THERMOMETERS offer the promise of understanding how chemical reactions in the cells of the human body maintain an almost constant temperature. Chemical reactions inside a cell normally occur only at a much higher temperature than body temperature. Metabolic reactions therefore utilize enzymes to increase chemical reactivity at body temperature. Cell temperature itself is therefore inconsequential compared to enzymes in driving metabolic reactions. Hence, the notion that temperature is one of the most important physical factors in a chemical reaction inside a cell can safely be dismissed. Nevertheless, temperatures within living cells are important in understanding how enzymes control body temperature.

Scientists have recently reported [1] the measurement of temperatures inside mouse cells using nano-thermometers of QDs. Temperature measurements [1-3] are made by exciting the QDs with a laser to obtain the QD fluorescent spectra, the QD temperatures inferred from experimental QD spectra taken at known temperatures.

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The measurement of cell temperatures based on laser excited QD fluorescent spectra has been proposed before. A summary [4] of nano-thermometers describes various designs directed to temperature measurements. Indeed, the fabrication of thermocouples by nano-lithography has even led [5] to US patents. But what the nano-thermometer designs actually measure including QM constraints on the measurement is not discussed. In this paper, the validity of cell temperature measurements from QD fluorescent spectra is discussed.

II. Problem

QM requires the heat capacity of QDs to vanish, and therefore the QD temperature does not increase during laser excitation. What this means is the QD remains at the local temperature of the cell where it is attached. Upon laser excitation, a portion of the QD fluorescence is absorbed by the cell, but because of its massive size the cell relative to the QD does not change it temperature significantly, and therefore the QD spectra is indeed a valid measure of the cell temperature. However, if the QDs move and lose contact with the cell, the QD temperature still does not increase, but QD fluorescence increases because it is no longer dissipated in part by the cell. Therefore, QD spectra from moving QDs give false cell temperatures. Valid cell temperature measurements require the QDs to be in contact with the cell, a condition that cannot always be satisfied.

III. Proposed Mechanism

By the theory of QED induced radiation, the observed VIS fluorescence is a consequence of absorbed EM energy that includes not only metabolic heat, but also the light from the laser excitation. Since absorbed EM energy in a QD is not conserved by an increase in temperature, conservation proceeds by the frequency up-conversion of the absorbed EM energy to their TIR confinement frequencies. TIR is enhanced by the fact QDs having a high surface to volume ratios concentrate the absorbed EM energy in their surface thereby providing the confinement necessary to create the high-energy QED photons. Subsequently, the QED photons as the EM source excite the lower energy VIS fluorescent state. All this occurs without an increase in QD temperature.

IV. Theory

QM precludes temperature increases in QDs. Supramicron cells are macroscopic and do indeed increase in temperature during laser and metabolic heating. Fig. 1 show QDs in contact with and removed from the cell. Under laser excitation, their QD spectra are likely to differ.

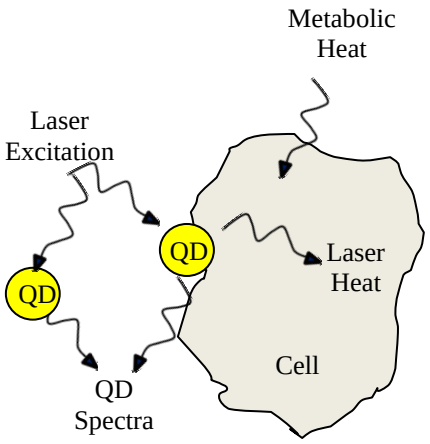

Fig. 1 QD fixed to and removed from the Cell

A. QM Restrictions

To understand how QED photons are created in QDs, consider the QM restriction on heat capacity in conserving heat by an increase in temperature. Unlike classical physics, the heat capacity of the atom by QM depends on its TIR confinement and thermal wavelength $\lambda_T = hc/kT$. Here, h is Planck's constant, c the speed of light, k Boltzmann's constant, and T absolute temperature. At 300 K, the Einstein-Hopf relation for the average Planck energy of the harmonic oscillator in terms of kT is shown in Fig. 2.

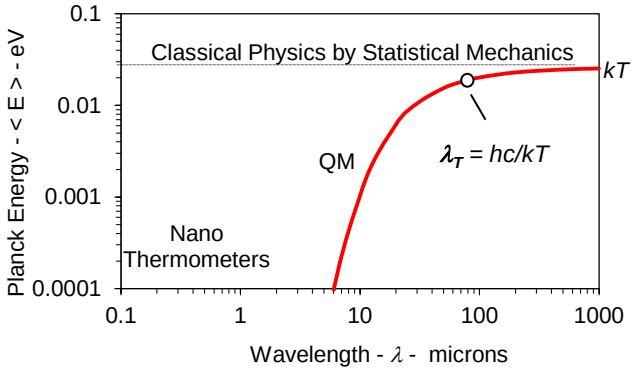

Fig. 2 Classical and QM Oscillators - Heat Capacity at 300 K

Unlike classical oscillators allowing the atom to have heat capacity at all wavelengths, QM oscillators only have heat capacity for $\lambda > \lambda_T$ and restrict heat capacity for $\lambda < \lambda_T$. At 300 K, λ_T = 50 microns. Fig. 2 shows the heat capacity is less than kT for $\lambda < \lambda_T$ and is only available for $\lambda > \lambda_T$. For QDs having λ < 1 micron, QM by requiring heat capacity to vanish precludes any increase in temperature upon absorption of EM radiation.

A. TIR Confinement

QDs lack heat capacity and cannot conserve absorbed heat by an increase in temperature. Instead, conservation proceeds by the QED induced frequency up-conversion of the absorbed laser light to the TIR confinement frequency of the QD. Since QDs have high surface to volume ratios, the absorbed EM energy is confined by TIR almost entirely in the QD surface. The TIR confinement is momentary and occurs only upon absorption of EM energy, and therefore the TIR confinement effectively sustains itself.

Similar to creating QED photons of wavelength λ by supplying EM energy to a QM box with sides separated by $\lambda/2$, the absorbed EM energy is frequency up-converted to the QD diameter D. The QED photon energy E and frequency f are:

$$E = hf, \quad f = \frac{c}{\lambda}, \quad \lambda = 2nD \tag{1}$$

where, n is the refractive index of the QD. For rutile and anatase TiO_2, n = 2.7 and 2.55, respectively.

B. QED Photon Rate

Classical heat transfer conserves EM energy by an increase in temperature, but is not applicable to QDs because of QM restrictions on heat capacity. Instead, the power P of the laser light is conserved by creating numbers N_P of QED photons inside the QD. The QED photon rate is,

$$\frac{dN_P}{dt} = \frac{\eta P}{E} \tag{2}$$

where, t is time. Only a fraction η of the power P creates QED photons, the remainder (1-η) is lost For ηP = 1 nW and rutile TiO_2, the QED photon energy E and rate dN_p/dt in terms of QD diameter D, are shown in Fig. 3.

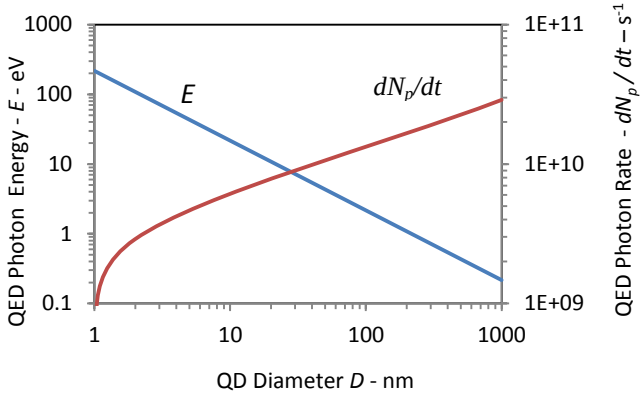

Fig. 3 QED Photon Energy and Rate at ηP = 1 nW

V. DISCUSSION

A. Intra-cellular Temperature Gradients

The claim [1] that QDs show temperature gradients develop in cells under metabolic heat requires qualification. QDs in contact with or fixed to the cell become part of a macroscopic surface and spontaneously acquire the cell temperature as shown in Fig. 3. Upon laser irradiation, QM precludes any QD temperature increase. Instead, QED photons are created inside the QD that excite the QD spectrum from which the cell temperature may be inferred.

However, the QDs may also move and become free from the cell as shown in Fig. 3. For a short time at least, the temperature of the free QDs is the same as that of the cell. Laser light creates QED photons and QD spectra just as for the fixed QDs. But the QD spectrum for free QDs will be more intense because the cell dissipates the intensity of fixed QDs. Indeed, the difference in measured temperatures by QDs that are fixed and free is observed in (Fig. 2d and inset of [1]). The free QDs are most likely producing the bright red images shown in (Fig. 1b of [1]).

Both fixed and free QD spectra are valid indications of cell temperature, but fixed QD spectrum having a lower intensity occurring over a longer period-of-time are more representative of cell temperature. To distinguish between the QD spectra would appear to require waiting until the QD spectrum stabilizes.

B. Intra-cellular Temperature Gradients

The 18 nm QDs are assumed [2] capable of up-converting laser light at 980 nm to higher energy green light at 515 and 535 nm. A 2-photon process of energy transfer from Yb3+ to Er4+ is proposed to explain the up-conversion. However, the 2-photon process cannot explain the UV absorption typical of QDs that far exceeds that at the plasmon resonances in the VIS.

The QD absorption in the UV depends on the material, but a general description [6] typically shows lower plasmon absorption. Consistent with the UV-VIS spectrum of QDs, the creation of QED photons at energies beyond the UV are the EM source that excites the fluorescent VIS and IR Raman states. Provided the QDs are in contact with the cell, the temperature of the QD inferred from QD spectra is a valid determination of cell temperatures. However, it is not known if the QDs in (Fig. 1B of [2]) were or were not in contact with the cuvette during calibration of the QD spectra.

Earlier work [3] in nano thermometry using the fluorescence from supramicron YAG:Ce phosphor particles was extended to 30 nm NPs of Y_2O_3:Eu^{3+} to probe the structure of brain phantom gelatins. The NPs were applied over a cm spot and adhered well to in a 5.5×3.5×0.5 cm aluminum plate. The aluminum substrate temperature was controlled from 10 to 77 K. The NPs were irradiated with a 4 ns pulse of 300 μJ with a nitrogen (337 nm) laser and left emit light to a photomultiplier. By recording the dependence of the fluorescence decay lifetime at the substrate temperature, decay lifetimes were correlated with substrate temperature, thereby allowing unknown temperatures to be determined from lifetimes calibrations. Provided the NPs are in contact with the substrate, the lifetimes are valid estimates of temperature, but as described above, the problem is one does not know if this is so. If not, the absorbed laser radiation excites the NPs to emit the Y_2O_3:Eu^{3+} spectra independent of temperature.

C. Cancer and QD Temperatures

Cancer cells are typically 10-20 microns and by QM are macroscopic allowing temperatures to increase under metabolic heating. In contrast, QDs are submicron and under heating cannot increase in temperature. Provided the QDs remain in contact with the cancer cell, the cell temperature measurement [3] based on QD spectra is valid, but if the QDs come-off the cell, the absorbed laser excitation is emitted as fluorescent QED radiation having nothing to do with the temperature of the cell.

Similarly, NPs attached to cancer cells are thought [7] to absorb penetrating NIR radiation and undergo necrosis by heating to temperatures of 45 C. However, increasing the temperature of NPs is precluded by QM. What this means is the cancer cell is actually killed by the UV and higher content in the QED emission from the NPs. Heating occurs when the UV is absorbed in tissue more than a few microns from the NP. But even biologic NPs can lead [8] to DNA damage and cancer.

D. Upconversion fluorescence imaging

Conventional fluorescence imaging is based on single-photon excitation where high-energy laser light is used to excite lower energy fluorescence. However, the high-energy laser light causes DNA damage and is limited by the short penetration depth in biological tissues. Upconversion fluorescence imaging offers the advantage of using low energy NIR light thereby avoiding DNA damage while allowing deeper penetration of tissue.

Upconversion is thought [9] to occur by two or more low energy photons — usually in the NIR — to excite the higher .energy fluorescence. However, QED radiation differs in that the NIR photons are considered as just another form of EM energy that upon absorption is frequency up-converted to the TIR resonance of the QD. Indeed, the Planck energies at the frequencies of TIR resonance act as a source of EM energy to excite not only QD fluorescence, but even higher QD states. Indeed, QED induced radiation may be the source of multi-photon excitation itself.

VI. EXTENSIONS

The QD emission spectrum depends on photons, but phonon confinement mechanisms [10-12] are also proposed using NPs to measure cell temperatures. Raman shifts of laser excited NPs based on phonon confinement are used to measure cell temperature from experimental correlations of NP size with temperature dependent grain growth.

A.. Record of Thermal Events

Nano-thermometers of NPs based on phonon confinement are thought [10] to not only measure the thermal environment, but also record their temperature-time history. Moreover, NPs allow measurement of temperatures in an explosion that cannot be measured using conventional thermometers.

However, the NPs are subject to the same QM restrictions on temperature measurements described for fluorescent QDs, i.e., the NPs must be attached or fixed to the cell surface during the measurement. NPs free and floating in space can absorb EM radiation from an explosion, but by QM cannot increase in temperature. The QED photons created inside the NP have high Planck energy and may ionize the NP. Subsequently, electron emission leaves the NP in a highly charged positive state subject to disintegration by Coulomb explosion. Even if not ionized, the NPs emit their QED radiation to the surroundings

without changing NP temperature. Regardless, the temperature-time history cannot be retrieved. The phonon confinement model therefore cannot provide the basis for correlation with NP temperature by Raman scattering.

B. Validity of Phonon Confinement

Unlike the physical basis for the TIR confinement of photons, phonon confinement is phenomenological. But TIR confinement in NPs also occurs upon laser excitation in Raman shift measurements. Although phonon confinement as a theory is sometimes [12] questioned, the correlation of Raman shifts with the growth of NPs at temperature over a time should be valid for a specific type of NP.

VII. Summary and Conclusions

1. Provided the QDs are in contact or fixed to the cell, QM allows them to acquire the cell temperature. Analysis of the QD spectrum obtained by exciting fixed QDs with a laser provides a valid estimate of cell temperature, i.e., the cell temperature varies [1] less than about 1 C.

2. However, if the QDs move and lose contact with the cell, QM precludes any temperature response of QDs under laser excitation, and instead QED photons are created inside the QDs that excite VIS fluorescent modes giving false cell temperature measurements, i.e., temperature differences [1] vary up to 10 C.

3. The hypothesis that cells use differences in temperature as a way to communicate is unlikely because fixed cell temperatures are less than 1 C. Instead, cells may use natural QDs of attached sub-micron proteins to communicate their temperature by EM signaling using QED induced EM radiation.

4. The validity of NPs in phonon confinement to measure cell temperature is limited by QM for the same reasons described above for temperatures measured using QD spectra.

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