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A2_2 Nanoparticle Hyperthermia Heat Transfer

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Abstract
This paper attempts to model the heating of a tumour by superparamagnetic iron oxide nanoparticles of diameter 15nm in an alternating 1T magnetic field. It was calculated that in such a field alternating at the maximum angular frequency of the particles that the required 2.5K rise in temperature required for cell death could be achieved in 10 minutes using a minimum number of nanoparticles in the order of 10^8, assuming that all nanoparticles injected reached the target cells and that all of the heat was transfered to the tumour.

Introduction
One of the more significant areas of research in current nanoscience is the concept of magnetic nanoparticle hyperthermia. This is the process by which nanoparticles formed of clusters of atoms can be spun at high frequency by applying an alternating magnetic field. This is made possible by the superparamagnetism of sufficiently small particles, which means that, as the magnetic field alternates, the alignment of the nanoparticles magnetic moment will flip back and forth. This is used to apply a heating effect to individual cells within a body; this can be used for many purposes from helping image cells affected by disease to actually destroying cancerous cells. This paper will attempt to calculate a theoretical value of the power output of a single nanoparticle, and its heating effect on a tumour cell, with a view to destroying the cell.

Calculating Nanoparticle Angular Frequency
Assuming the nanoparticle being used is a spherical iron oxide nanocluster composed of $\sim 20000 Fe_3O_4$ (also referred to as magnetite) molecules, this would imply a radius of approximately 7.5nm, and a volume of $1.767 \times 10^{-24} m^3$ (these are fairly standard sizes for use in hyperthermia research [1]). This particle would be bound covalently, to an enzyme or a monomer that will bond to the cell wall of a target cell; in this case, an average cancer cell. An alternating magnetic field is applied; with particles of this low volume, the entire particle will form a single magnetic moment, thus becoming superparamagnetic, though only while above the blocking temperature (the temperature below which the magnetisation curve will undergo hysteresis), which for a particle of radius 7.5nm, is about 200K [5]. This is acceptable, as for any medical procedure, the nanoparticle will be at body temperature $\sim$ 310K. The applied magnetic field strength B is 1 Tesla, being generated by a similar system to an MRI, and the magnetisation is close to the saturation point for iron oxide particles. Being dependent on size, the magnetisation saturation has to be measured; for particles of diameter 13nm this is measured to be 54.7emu/g $\pm$ 1emu/g, so this is the value that will be used for magnetisation. The first step in calculating the power output of the particles is to calculate the maximum angular frequency that can be reached by the particles magnetic moment flipping its alignment within the applied field. This is given by the following formula [2]:

$$\omega_{max} = \frac{BM}{6\eta} \tag{1}$$

where B is the magnetic field strength, M is the magnetisation and η is the viscosity of the medium in which the particle is rotating, which for this model will be water (=0.7mPa.s) [3]. This results in a maximum angular frequency of 13000 rad s^{-1}.

Calculating Rate of Heat Output
Knowing this angular frequency, the maximum rate of energy transfer to the medium can be calculated using [2]:

$$\frac{dU}{dt} \approx \frac{4}{3}\pi r^3 BM\omega_{max} \tag{2}$$

where r is the radius. Using all the known values for the model, this formula produces a heat transfer rate of $1.259 \times 10^{-}18 Js^{-1}$ per nanoparticle. Assuming that a cancer cell has a density of $\rho = 920 kg.m^{-3}$,

a specific heat capacity of C=3000 $JKg^{-1}K^{-1}$ and a radius of $a = 5\mu m$ [4], the resulting temperature change after a given change in time Δt is found by:

$$dT = \frac{dU}{dt}\frac{\Delta t}{\frac{4}{3}\pi a^3 c\rho} \tag{3}$$

This means that the temperature change after one second due to one nanoparticle in a single cell is 7.19×10^{-8}K, after one minute it is 4.314×10^{-6}K; bearing in mind that a standard exposure for medical purposes would be closer to ten minutes, after which the temperature will have changed by 4.314×10^{-5}K per nanoparticle attached to the cell. Taking into consideration the fact that cell death occurs at a minimum of 313K, and taking the cells initial temperature to be the core temperature of 310.5K, the required temperature rise for the destruction of a cancer cell is at least 2.5K. This means that, to kill a single cell within 10 minutes of solid exposure, there would have to be approximately 57950 nanoparticles attached to it. Given a tumour of $1cm^3$ in volume, and assuming all the cells are uniform with the one above and tightly packed, the minimum number of nanoparticles required to enact cell-death within 10 minutes is 2.387×10^8.

Discussion

The above result may seem high at first glance, especially for a minimum, however it should be pointed out that the required particles, given the starting dimensions of the model, would only fill $4.218 \times 10^{-16}m^3$. To put this in perspective, in an experiment at the University of Georgia [1], a dose of 0.5mL of specially prepared nanoparticles were produced and injected into a rat with a cancerous tumour. The solution was largely a suspension of the monomers required to attach to the target cells, with a concentration of $0.3gmL^{-1}$ comprised purely of nanoparticles. This approximates to 1.008×10^{17} of the nanoparticles described in this model, which is vastly more than the minimum requirement. It should be pointed out that this model is heavily limited and that additional nanoparticles need to be injected due to a number of losses that are unaccounted for. Firstly, not all of these particles are guaranteed to attach to the target cells; despite targeting, they may still bond to the wrong type of cell, or just float in the blood stream until they are filtered out. The heat can also not be assumed to be perfectly transferred between the particle and the cell, as much of the heat will be absorbed by the surrounding medium, namely other cells and bodily fluids. The amount of heat these absorb would be dependent on how the nanoparticles are bonded to the cells. The predicted power output is also an absolute maximum, derived from a maximum angular frequency, which would be reduced by several different factors, such as a lower body temperature at the skin surface or by relaxation times (Neél and Brownian).

Conclusion

While the result found by this paper is a feasible estimate for a maximum power and for minimum required number of nanoparticles, the model is quite limited by the various unaccounted factors. The main problem arises from the fact that most of these factors can only be found by way of direct measurement, meaning that practical testing has to be done in order to refine the model. Fortunately, this particular area is currently undergoing a lot of testing. However, another issue that may require investigation is how this model would vary with shape with regards to the anisotropy factor of the particles, a variable that effects how it interacts with the applied field.

References

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