Research lines in Hyperthermia at the Bioinstrumentation Laboratory of the Centre for Biomedical Technology

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Introduction

The Bioinstrumentation Laboratory belongs to the Centre for Biomedical Technology (CTB) of the Technical University of Madrid and its main objective is to provide the scientific community with devices and techniques for the characterization of micro and nanostructures and consequently finding their best biomedical applications.

Specifically, the aim of the hyperthermia methods used in The Bioinstrumentation Laboratory is the development of thermal therapies, some of these using different kinds of nanoparticles, to kill cancer cells and reduce the damage on healthy tissues.

Magnetic Hyperthermia

The Magnetic hyperthermia use the effect produced by irradiation of alternating magnetic field in magnetic fluids, in order to study the thermal behavior of the magnetic nanoparticles (MNPs). The working frequency range of our device is 9KHz-2MHz.

Research Line

- Behavior of the MNPs embedded in different viscous medium, example: Water, Agar.
- Study of samples with different concentrations of MPNs.
- Equipment Optimization, in order to provide the best performance possible.
- Characterization of temperature change using different excitation signals.

Properties

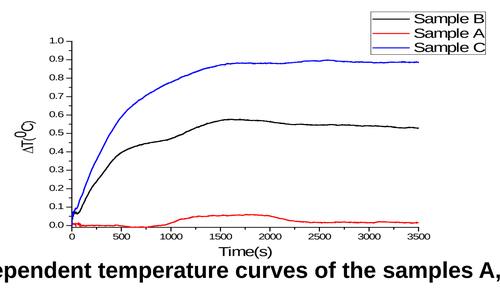
The device was completely designed and built by our research group, and has the following capabilities:

- It can achieve a wide range of working frequencies from 9 KHz to 2MHz.
- Study of samples with different concentrations of MPNs.
- It is possible to use different excitation signal

An Example of our studies is shown in figures 1, and parameters used are in table I.

H - 0.35 KA/m, *f* - 400KHz, 0.5ml		
N-Sample	**Sample**	**Concentrations**
A	Agar	-
B	Magnetite(D-12nm)-Agar	200mg/ml
C	Magnetite(D-12nm)-Agar	300mg/ml

Description of the samples used for the study.

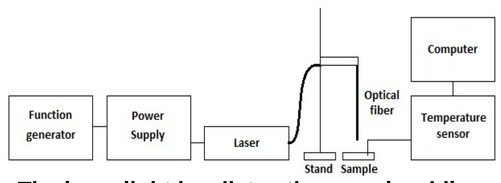


Time-dependent temperature curves of the samples A,B, C.

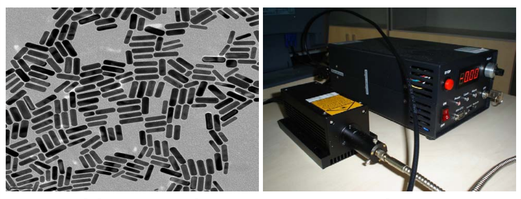
Optical Hyperthermia

The Surface Plasmon Resonance (SPR) in gold nanoparticles exposed to a laser light, results in a strong enhancement of light absorption. Furthermore, gold nanoparticles convert the absorbed light into localized heat quickly. These properties allows the development of hyperthermia therapies for cancer treatment.

Hyperthermia device



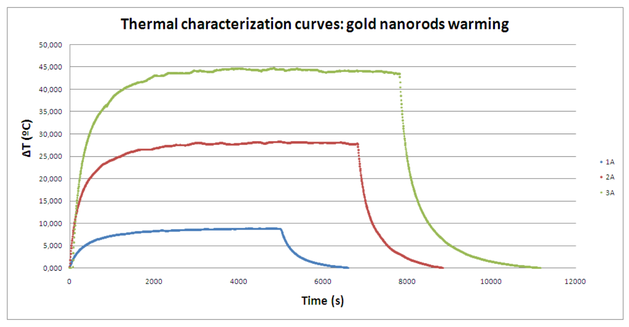
The laser light irradiates the sample while a temperature sensor controls the warming



Gold nanorods (808 nm, Nanopartz™)

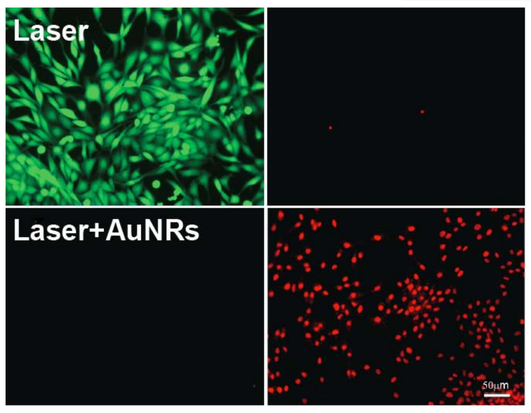
CW laser (MDL H808, CNILaser)

Thermal characterization

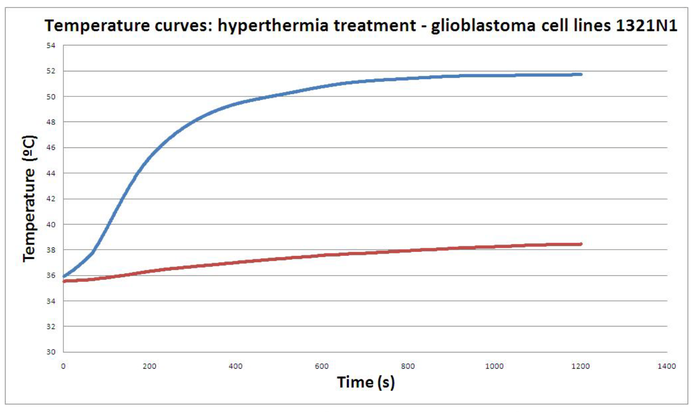


These curves show that a higher power of the laser source produces more plasmonic excitation and consequently, a higher temperature is reached. Temperature curves using different configurations of the hyperthermia device are essential to develop a thermal model.

Results



IP/Calcein essay in samples of glioblastoma cell lines and gold nanorods 24 h after the irradiation (alive cells: green-left, dead cells: red-right)



Temperature curves in the culture medium of glioblastoma cell lines irradiated with the laser source. (Blue curve: cells + nanorods + laser, red curve: cells + laser).

MRI Hyperthermia

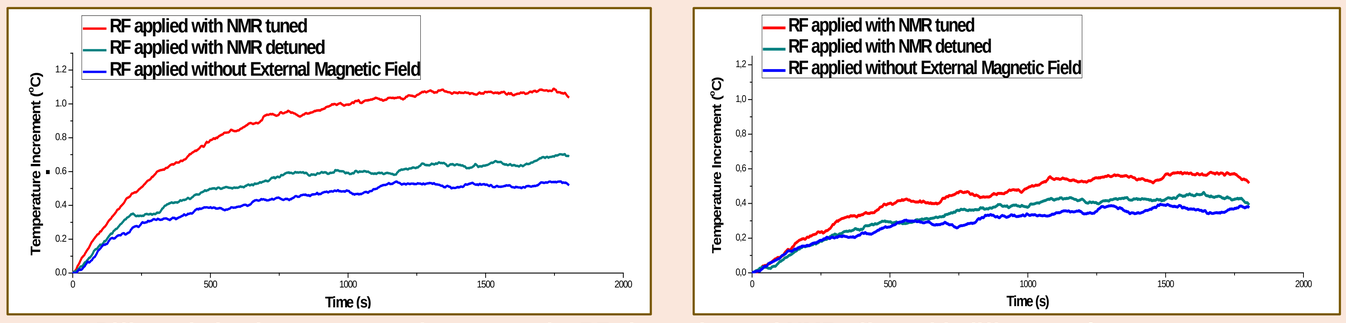
The Bioinstrumentation Laboratory in collaboration with the Mexican company MRI-DT have recently implemented a new research line on Nuclear Magnetic Resonance Hyperthermia, which is sustained on patent US 7,423,429B2 owned by this company and developed by Eng. Lázaro Eusebio Hernández Pérez. This investigation is based on the use of clinical MRI equipment not only for diagnosis but for therapy. We thanks to Mr. Javier Núñez Peláez for sponsoring the project.

Research Line

- Differentiation in temperature increments in diverse samples by RF absorption and NMR effect.
- Differentiation in Nuclear Magnetic Resonant frequency between healthy and cancer cells; and other biomolecular targets.
- Pulse sequence design to produce heating and cooling in biological samples.

Final Goal

The final goal of this research line is to produce fast excitation and relaxation mechanism that generates temperature increase of the tumor, causing cellular death or metabolism malfunction that stops cellular division. To only produce this effect in cancer cells when the whole body is irradiated, it is necessary to determine the specific resonant frequency of the target, using the information contained in the spectra of the area of interest. Then, special RF pulse sequence is applied to produce hyperthermia.



Differentiation in temperature increments by RF absorption and NMR effect with different pulse sequences.

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