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3D numerical simulations on GPUs of hyperthermia with nanoparticles by a nonlinear bioheat model

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ABSTRACT

This paper deals with the numerical modeling of hyperthermia treatments by magnetic nanoparticles considering a 3D nonlinear Pennes' bioheat transfer model with a temperature-dependent blood perfusion in order to yield more accurate results. The tissue is modeled by considering skin, fat and muscle layers in addition to the tumor. The FDM in a heterogeneous medium is employed and the resulting system of nonlinear equations in the time domain is solved by a predictor–multicorrector algorithm. Since the execution of the three-dimensional model requires a large amount of time, CUDA is used to speedup it. Experimental results showed that the parallelization with CUDA was very effective in improving performance, yielding gains up to 242 times when compared to the sequential execution time.

1. Introduction

Thermal therapies based on electromagnetic radiation have demonstrated great results because of the capability of heating and/or thermoablation of biological tissues at localized areas. However, classical hyperthermia treatment techniques that adopt microwaves, radiofrequency waves and laser devices generally have some drawbacks, especially in deep-seated tumors, such as focusing energy, heat unintentionally targets like healthy tissue, etc. [1].

On the other hand, low frequency alternating magnetic field based therapies have been shown to be quite effective without the shortcomings of the standard electromagnetic therapies. Early studies on the use of magnetic fields in the treatment of tumors [2,3] have employed thermal ferromagnetic seeds surgically implanted, which causes a limitation of its application at deep-seated tumors. Furthermore, the effectiveness of this technique greatly depends on the correct orientations of the seeds; nonetheless, these studies were important to develop the next generation of treatment that utilizes magnetic fluids. This technique is known as magnetic fluid hyperthermia (MFH) in which the fluid is composed by nano- or microscale particles that produce heat when they are stimulated by alternating magnetic fields. It is worth noting that this kind of treatment does not present the problems in applications of the aforementioned one [4].

Hyperthermia has been used to treat various types of cancers [5], among them we can mention carcinomas. The most studied nanoparticles in hyperthermia cancer treatments are probably iron oxides magnetite Fe_3O_4 and maghemite $\gamma - Fe_2O_3$ due to their biocompatibility [6]. Among different devices to deliver the nanoparticles to the tumor target, this paper will be focused on the direct injection into the extracellular space of the tumor. The advantage of direct injection is the possibility of multiple injection sites able to handle any tumor shape in an easy manner.

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There are previous studies (or experiments) about this treatment in liver [7], breast [8] and prostate [9] tumors. These experiments are similar to, for instance, those carried out by [10] showed the feasibility of this treatment using magnetic nanoparticles. It also revealed that the success of the treatment is the ability of heating a specific tumor area above 43 °C with a minimal damage at the healthy tissue [5]. Furthermore, [11] showed that hyperthermia treatment kills (destroy) tumor cells not just with heating by also with induction of the immune response.

The well-known Pennes' equation is employed to describe the heat diffusion due to the hyperthermia treatment [5,12–14]. The main objective of this study is to simulate a hyperthermia treatment of tumors with irregular shapes seated at the muscle layer, where the tissue domain regarding the simulation contains skin, fat and muscle layers. The finite difference method with centered difference for the spatial discretization and with a predictor–multicorrector scheme for the time discretization is adopted to solve the three-dimensional model.

An encouraging previous study about hyperthermia simulation with magnetic nanoparticles in a two-dimensional domain and using OpenMP [15] achieved speedups around 35 on a 64-core machine. In this way, aiming at improving the performance of the code even more, an alternative parallel version has been developed. In fact, the parallel version was implemented using compute unified device architecture (CUDA), a parallel computing platform and programming model that uses graphics processing units (GPUs) as target hardware. A GPU is a single instruction multiple thread (SIMT) parallel architecture, in which one instruction can be executed simultaneously using multiple data in a pipeline [16]. This paper presents the implementation details as well as the results obtained when executing the parallel code on the GPU-based low-cost hardware platform. The GPU-based version of the code achieved a speedup of 242.

To the best of our knowledge no previous studies of applying GPU-based parallel implementation of hyperthermia cancer treatment using magnetic nanoparticles have been developed. Furthermore, this study joins the steady-state solution of a tumor tissue with 3 different types of tissue layer (*i.e.*, tissue properties) with the transient solution by using the steady-state solution as an initial condition, and compares a linear model with a nonlinear one taking into account a constant blood perfusion rate as well as a temperature dependent one. Although there is no previous work that we are aware of that applies GPU in hyperthermia cancer treatment simulation, other works present a GPU-based implementation of distinct equations using a numerical method similar to the one used in this work [17–19].

This paper is organized as follows. The first two sections present a brief theoretical background of the hyperthermia treatment with magnetic nanoparticles and explain how Pennes' hyperthermia model is applied. Then the numerical method used in this work as well as its parallel implementation in CUDA and the computed numerical results are presented. Finally, the last section presents our conclusions and plans for future works.

2. Problem statement

Generally speaking, hyperthermia with nanoparticles can be used as a minimally invasive treatment for destroying tumors in living tissue. The goal is to heat the tumor up to a temperature threshold above the normal physiological one in order to destroy its cells by necrosis while maintaining the damage of the healthy tissue as minimal as possible. This process can be mathematically modeled by the well-known Pennes' equation. Hence, consider that the living tissue containing the tumor is represented by an open bounded domain $\Omega \subset \mathbb{R}^3$ and $I = (0, t_f] \subset \mathbb{R}^+$ is the time interval of the treatment, Pennes' equation can be defined as [12,20]:

$$\nabla \cdot \kappa \nabla T + \omega_b(T) c_b (T_a - T) + Q_m + Q_r = \rho c \frac{\partial T}{\partial t}, \quad \text{in } \Omega \times I \tag{1}$$

where $T : \Omega \times I \to \mathbb{R}^+$ denotes the tissue temperature field, $\rho, c : \Omega \to \mathbb{R}^+$ stand for the density and the specific heat of the tissue, respectively and $c_b : \Omega \to \mathbb{R}^+$ the specific heat of the blood. The thermal conductivity is assumed to be isotropic but inhomogeneous, *i.e.*, $\kappa : \Omega \to \mathbb{R}^+$. Since the heat transfer between the tissue and the blood through the micro-vascular network, which is represented by the term containing the blood perfusion rate ω_b with T_a being the arterial temperature, is very sensitive to the temperature increase, a temperature-dependent (nonlinear) blood perfusion rate is here considered, *i.e.*, $\omega_b : \Omega \times \mathbb{R}^+ \times I \to \mathbb{R}^+$. The metabolic heat generation is represented by $Q_m : \Omega \to \mathbb{R}^+$ while $Q_r : \Omega \times I \to \mathbb{R}^+$ is the external heat generated by the nanoparticles.

Finally, in a well-posed problem, proper boundary conditions on a Lipschitz continuous and piecewise smooth boundary $\Gamma = \partial\Omega$ and an initial condition at $t = 0$ must be specified, *i.e.*

$$\alpha T + \beta \nabla T \cdot \mathbf{n} = f, \quad \text{on } \Gamma \times I \tag{2}$$

$$T(\cdot, 0) = T_0, \quad \text{in } \Omega \tag{3}$$

in which $f : \Omega \times I \to \mathbb{R}^+$ is the prescribed temperature (Dirichlet) or flux (Neumann or Robin), depending on the choice of the functions $\alpha, \beta : \Omega \to \mathbb{R}^+$ with $\mathbf{n}$ being the outward unit normal vector.

In order to initialize the hyperthermia process it is necessary to specify an initial temperature T_0. This is accomplished by solving the following steady-state version of Eq. (1) without external heat generation:

$$\nabla \cdot \kappa \nabla T + \omega_b c_b (T_a - T) + Q_m = 0, \quad \text{in } \Omega. \tag{4}$$

Indeed prior to hyperthermia treatment we have $Q_r = 0$ and now the metabolic heat generation plays a very important role into the solution. Because tumors are generally more vascularized than the normal tissue, the first has a greater value