



# Theoretical analysis of coupled thermal and denaturation processes in living tissues subject to a uniform surface heating condition



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## ABSTRACT

In this work, we develop a theoretical study of the thermal and denaturation processes in a biological tissue subject to a surface heating, when coupled effects of dynamic changes of blood perfusion and temperature-dependent physical properties are taken into account. To analyze this phenomenon, the governing equations were appropriately nondimensionalized, where a suitable Damköhler number appears, which measures the competition between the denaturation time and the characteristic thermal diffusive time of tissue. In order to determine the denaturation front, situation that occurs when tissue has been completely denatured, we show the existence of a critical value of this dimensionless number for each time, which represents an eigenvalue in the mathematical model. Important results of the proposed model indicate that the denatured region, and the time required for carrying out this thermal process are substantially modified in comparison with the case of constant physical properties. In addition, the magnitude of the applied thermal energy source, the biological resistance of tissue to thermal attack and the blood perfusion are very important aspects that must be considered in those medical treatments that make use of rehabilitation therapies by thermal processes.

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## 1. Introduction

In recent decades, the study of heat transfer in biological tissues has taken a relevant importance due to the medical interest for applying this fundamental knowledge to the thermal detection of cancerous tumors [1–4], and for the destruction of dangerous tissues [5,6]. In the last years, the number of patients associated with different illness caused for cancerous tumors has increased exponentially, implying serious problems in the health care and in the economy of the world [1]. Therefore, many researchers have proposed different alternatives to develop new techniques or methodologies, cheaper and less invasive to detect or destroy dangerous tissues. In the first case, for the detection of tumors, cancerous cells have an extensive heat emission, which causes a perturbation in the corporal temperature field. The above property of tissue allows us to confirm the existence of cancerous cells using corporal thermography [7]. On the other hand, in order to destroy dangerous tissues with thermal therapies, innumerable medical methodologies of hyperthermia or hypothermia have been proposed, such as: laser, photocoagulation, magnetic fluids, magnetic particles,

electromagnetic radiation, ultrasound, heating or cooling by energy fluxes or direct contact [8–14].

Theoretical studies in the specialized literature about thermal processes in biological tissues are based on the well-known bio-heat transfer equation or Pennes equation [15,16], the thermal wave equation (TW) [17,18], and the dual phase lag model (DPL) [19–22]. In addition, the heat transfer in biological tissues has also been modeled mathematically by considering it as a porous medium [23–27]. Recently, some variations of the mentioned mathematical models have been developed by introducing interactions between two or more tissues with different properties (conjugated phenomenon of the layers of the skin, tumor-tissue or veins-tumor-tissue). On the other hand, although there are several works concerning the thermal propagation through biological tissues, the study of thermal damage or denaturation of tissues is limited. In order to quantify the thermal denaturation process, the Arrhenius burn integration approach proposed by Moritz and Hernández [28] has been widely used. The degree of thermal denaturation or thermal damage,  $\Omega$ , satisfies the following equation:

$$\frac{d\Omega}{dt} = A \exp\left(\frac{-E_a}{RT}\right), \quad (1)$$

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## Nomenclature

### Symbol definition

$A$	kinetic frequency factor, $s^{-1}$
$B_b$	constant defined in Eq. (3)
$b_k$	coefficient of the variable thermal conductivity, $K^{-1}$
$b_m$	coefficient of the variable metabolic heat, $K^{-1}$
$b_w$	coefficient of the variable blood perfusion, $K^{-1}$
$c_b$	specific heat of the blood, $J/kg\ K$
$c_p$	specific heat of tissue, $J/kg\ K$
$Da$	Damköhler number defined in Eq. (17)
$Da_{Deg}$	critical value of the dimensionless Damköhler number
$Deg$	denaturation rate of living tissue
$E_a$	activation energy, $J/mol$
$\bar{E}_a$	dimensionless parameter that measures the biological resistance of tissue to thermal attack
$k$	thermal conductivity, $W/m\ K$
$Pe_b$	Péclet number associated to the blood perfusion
$\dot{q}_m$	rate of metabolic heat production per unit volume, $W/m^3$
$\dot{q}_w$	net rate of energy added by the blood per unit volume, $W/m^3$
$R$	universal gas constant, $J/mol\ K$
$t$	time, $s$
$t_{Deg}$	denaturation time, $s$
$t_{th}$	characteristic diffusive time, $s$
$T$	local tissue temperature, $K$
$T_a$	arterial temperature, $K$

$T_s$	temperature of the heating source, $K$
$W_b$	volumetric blood perfusion rate per unit tissue volume, $m^3/m^3\ s$
$x, y, z$	dimensional coordinates, $m$

### Greek letters

$\alpha$	thermal diffusivity, $m^2/s$
$\beta_1, \beta_2$	dimensionless geometric parameters
$\theta$	dimensionless temperature
$\theta_s$	dimensionless temperature of the heating source
$\theta_w$	dimensionless parameter relates with the arterial and referent temperatures
$\rho$	density of tissue, $kg/m^3$
$\rho_b$	density of blood, $kg/m^3$
$\tau$	dimensionless time
$\Gamma_w$	dimensionless parameter, defined as $\Gamma_w = b_w/b_k$
$\Gamma_m$	dimensionless parameter, defined as $\Gamma_m = b_m/b_k$
$\Gamma_\Omega$	dimensionless parameter, defined as $\Gamma_\Omega = 1/b_k T_0$
$\Omega$	thermal damage
$\Delta T$	characteristic temperature difference, $K$
$\chi, \eta, \xi$	dimensionless coordinates

### Subscripts

0	reference temperature
r1	denatured region
r2	living tissue region

where  $A$  is a material parameter (frequency factor),  $E_a$  is the activation energy,  $R$  is the universal gas constant, and  $T$  is the absolute temperature.

Studies carried out in past years about thermal denaturation of tissues have been conducted by using uncoupled mathematical models (Pennes, TW and DPL). This means that the temperature field in tissue is first obtained by solving the governing equations of bioheat transfer and the solution is then used as the input of the thermal damage model, obtaining the corresponding denaturation, i.e., there are not dynamic changes in physical and biological properties in a simultaneous manner. Dai et al. [29] developed a mathematical model based on the Maxwell–Cattaneo thermal flux law, for predicting the temperature distribution and thermal damage suffered by the skin due to radiation heating. The above model takes into account large thermal relaxation times of tissue and the effects of high thermal radiation. The results show that the Pennes equation overpredicts the temperature in tissues. In the same direction, Zhou et al. [30] investigated the thermal damage in laser-irradiated biological tissues; they employed a DPL model and a numerical technique based on the finite volume method (FVM). Their results show that for early time stages of the phenomenon, the temperature profile and the thermal damage are affected substantially in comparison against Pennes equation. On the other hand, experimental and numerical works, based on the Pennes equation, were conducted by Abraham and co-workers [31–33]. Here, the thermal injury of the skin tissue was studied, when it is placed in contact with an object or fluid (water) that is found at temperatures between 50 and 90 °C during different periods of time. Their principal results show that in order to obtain a great depth of damage, the temperature of the heating source and the time of the thermal process have to be increased. In all works mentioned, temperature-dependent properties and dynamic changes of the physical and biological properties were omitted.

In the recent literature, there are only a few works, based on the Pennes equation, where variations in physical properties are taken into account. In this direction, Gupta et al. [5] incorporated in their numerical analysis a linear variation of the metabolic heat with the temperature. In the same context, Keangin and co-workers [34,35] studied numerically the interstitial microwave ablation (MWA), using an electromagnetic microwave coaxial antenna for treating cancerous tumors with localized heating. They included the influence of temperature on physical and biological properties (thermal conductivity, blood perfusion, electrical conductivity). On the other hand, in the case of dynamic changes of biological properties, He and Bischof [36] proposed a coupled mathematical model between the thermal propagation and the denaturation process of tissues, by means of a correction function, and the degradation of the blood perfusion was incorporated in the thermal analysis. In the same context, the works of Abraham and Sparrow [37] and Museux et al. [38], reported the use of similar models considering the manner in which the degradation of blood perfusion is introduced in the thermal analysis, evaluating the blood perfusion for different levels of denaturation. Their results show that the dynamic relationship between temperature and denaturation affects substantially the accumulated thermal denaturation of tissues. In order to cover all degradation levels of blood perfusion and to extend the analysis of dynamic interactions between temperature fields and denaturation processes, Zhang and his collaborators [14,39,6] introduced an exponential model of blood perfusion degradation associated to thermal denaturation when tissue is being heated by laser emissions. These authors analyzed the interaction between two different tissues when one is subjected to thermal therapy, the effect of the heat transfer in the accumulated denaturation during laser-induced interstitial thermo-therapy (LITT) for different laser sources, and the dynamic change of physical and biological properties. Although these authors take into account the temperature dependence of physical properties and the

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