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Thermal Therapy: Stabilization and Identification

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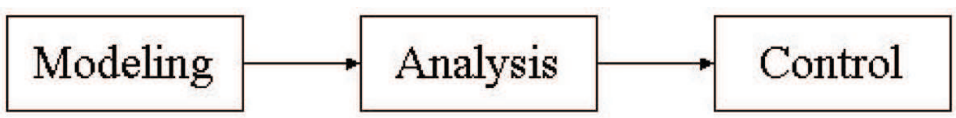
1. Introduction

1.1 Terminology and methods

The physicists, biologists or chemists control, in general, their experimental devices by using a certain number of functions or parameters of control which enable them to optimize and to stabilize the system. The work of the engineers consists in determining theses functions in an optimal and stable way in accordance with the desired performance. We can note that the three main steps in the area of research in control of dynamical systems are inextricably linked, as shown below:



To predict the response of dynamic systems from given parameters, data and source terms requires a mathematical model of the behaviour of the process under investigation and a physical theory linking the state variables of the model to data and parameters. This prediction of the observation (i.e. modeling) constitutes the so-called **direct problem** (primal problem, prediction problem or also forward problem) and it is usually defined by one or more coupled integral, ordinary or partial differential systems and sufficient boundary and initial conditions for each of the main fields (such as temperature, concentration, velocity, pressure, wave, etc.). Initial and boundary conditions are essential for the design and characterization of any physical systems. For example, in a transient conduction heat transfer problem, in order to define a "direct heat conduction problem", in addition to the model which include thermal conductivity, specific heat, density, initial temperature and other data, temperature, flux or radiating boundary conditions are applied to each part of the boundary of the studied domain.

Direct problems are well-posed problem in the sense of Hadamard. Hadamard claims that a mathematical model for a physical problem has to be well-posed or properly problem in the sense that it is characterized by the existence of a unique solution that is stable (i.e. the solution depends continuously on the given data) to perturbations in the given data (material properties, boundary and initial conditions, etc.) under certain regularity conditions on data and additional properties. The requirement of stability is the most important one, because if this property is not valid, then the problem becomes very sensitive to small fluctuations and noises (chaotic situation) and consequently it is impossible to solve the problem.

If any of the conditions necessary to define a direct problem are unknown or rather badly known, an **inverse problem** (control problem or protection problem) results, typically when modeling physical situations where the model parameters (intervening either in the boundary conditions, or initial conditions or equations model itself) or material properties are unknown or partially known. Certain parameters or data can influence considerably the material behavior or modify phenomena in biological or medical matter; then their knowledge (e.g. parameter identification) is an invaluable help for the physicists, biologists or chemists who, in general, use a mathematical model for their problem, but with a great uncertainty on its parameters. The resolution of the inverse problems thus provides them essential informations which are necessary to the comprehension of the various processes which can intervene in these models. This resolution need some regularity and additional conditions, and partial informations of some unknown parameters and fields (observations) given, for example, by experiment measurements.

In all cases the inverse problem is ill-posed or improperly posed (as opposed to the well-posed or properly problem in the sense of Hadamard) in the sense that conditions of existence and uniqueness of the solution are not necessarily satisfied and that the solution may be **unstable** to perturbation in input data (see (Hadamard, 1923)). The inverse problem is used to determine the unknown parameters or control certain functions for problems where uncertainties (disturbances, noises, fluctuations, etc.) are neglected. Moreover the inverse problems are not always tolerant to changes in the control system or the environment. But it is well known that many uncertainties occur in the most realistic studies of physical, biological or chemical problems. The presence of these uncertainties may induce complex behaviors, e.g., oscillations, instability, bad performances, etc. Problems with uncertainties are the most challenging and difficult in control theory but their analysis are necessary and important for applications.

If uncertainties, stability and performance validation occur, a **robust control problem** results. The fundament of robust control theory, which is a generalization of the optimal control theory, is to take into account these uncertain behaviours and to analyze how the control system can deal with this problem. The uncertainty can be of two types: first, the errors (or imperfections) coming from the model (difference between the reality and the mathematical model, in particular if some parameters are badly known) and, second, the unmeasured noises and fluctuations that act on the physical, biological or chemical systems (e.g. in medical laser-induced thermotherapy (ILT), a small fluctuation of laser power can affect considerably the resulting temperature distribution and thus the cancer treatment). These uncertainty terms can have additive and/or multiplicative components and they often lead to great instability.

The goal of robust control theory is to control these instabilities, either by acting on some parameters to maintain the system in a desired state (target), or by calculating the limit of these parameters before the system becomes unstable ("predict to act"). In other words, the robust control allows engineers to analyze instabilities and their consequences and helps them to determine the most acceptable conditions for which a system remains stable. The goal is then to define the maximum of noises and fluctuations that can be accepted if we want to keep the system stable. Therefore, we can predict that if the disturbances exceed this threshold, the system becomes unstable. It also allows us, in a system where we can control the perturbations, to provide the threshold at which the system becomes unstable.

Our robust control approach consists in setting the problem in the worst-case disturbances which leads to the **game theory** in which the controls and the disturbances (which destabilize the dynamical behavior of the system) play antagonistic roles. For more details on this new

approach and its application to different models describing realistic physical and biological process, see the book (Belmiloudi, 2008).
We shall now present the process of our control robust approach.

1.2 General process of the robust control technique

In contrast with the inverse (or optimal control) problems[1], the relation between the problems of identification, regulation and optimization, lies in the fact that it acts, in these cases, to find a **saddle point** of a functional calculus depending on the control, the disturbance and the solution of the direct **perturbation problem**. Indeed, the problems of control can be formulated as the robust regulation of the deviation of the systems from the desired target; the considered control and disturbance variables, in this case, can be in the parameters or in the functions to be identified. This optimization problem (a **minimax problem**), depending on the solution of the direct problem, with respect to control and disturbance variables (intervening either in the initial conditions, or boundary conditions or equation itself), is the base of the robust control theory of partial differential equations (see (Belmiloudi, 2008)).
The essential data used in our robust control problem are the following.

- A known operator $\mathcal{F}$ which represents the dynamical system to be controlled i.e. $\mathcal{F}$ is the model of the studied boundary-value problem such that

$$\mathcal{F}(x,t,f,g,U) = 0, \tag{1}$$

  where (x,t) are the space-time variables, $(f,g) \in \mathcal{X}$ represents the input of the system (initial conditions, boundary conditions, source terms, parameters and others) and $U \in \mathcal{Z}$ represents the state or the output of the system (temperature, concentration, velocity, magnetic field, pressure, etc.), where $\mathcal{X}$ and $\mathcal{Z}$ are two spaces of input data and output solutions, respectively, which are assumed to be, for example, Hilbert and Banach spaces, respectively. We assume that the direct problem (1) is well-posed (or correctly-set) in Hadamard sense.

- A "control" variable φ in a set $U_{ad} \subset \mathcal{U}_1$ (known as set of "admissible controls") and a "disturbance" variable ψ in a set $V_{ad} \subset \mathcal{U}_2$ (known as set of "admissible disturbances"), where $\mathcal{U}_1$ and $\mathcal{U}_2$ are two spaces of controls and disturbances, respectively, which are assumed to be, for example, Hilbert spaces.

- For a chosen control-disturbance (φ,ψ), the **perturbation problem**, which models fluctuations (φ,ψ,u) to the desired target (f,g,U) (we assume that $(f + \mathcal{B}_1\varphi, g + \mathcal{B}_2\psi, U + u)$ is also solution of (1)) and which is given by

$$\tilde{\mathcal{F}}(x,t,\varphi,\psi,u) = \mathcal{F}(x,t,f + \mathcal{B}_1\varphi, g + \mathcal{B}_2\psi, U + u) - \mathcal{F}(x,t,f,g,U) = 0, \tag{2}$$

  where the operator $\tilde{\mathcal{F}}$, which depends on U, is the perturbation of the model $\mathcal{F}$ of the studied system and $\mathcal{B}_i$, for $i = 1,2$, are bounded linear operators from $\mathcal{U}_i$ into $\mathcal{Z}$. In the sequel we denote by $u = \mathcal{M}(x,t,\varphi,\psi)$ the solution of the direct problem (2).

- An "observation" u_{obs} which is supposed to be known exactly (for example the desired tolerance for the perturbation or the offset given by measurements).

[1] Inverse problem corresponds to minimize or maximize a calculus function depending on the control and the solution of the direct problem.

- A "cost" functional (or "objective" functional) $J(\varphi,\psi)$ which is defined from a real-valued and positive function $\mathcal{G}(X,Y)$ by (so-called the **reduced form**)

$$J(\varphi,\psi) = \mathcal{G}((\varphi,\psi),\mathcal{M}(.,\varphi,\psi)).$$

The goal is to find a saddle point of J, *i.e.*, a solution $(\varphi^*,\psi^*) \in U_{ad} \times V_{ad}$ of

$$J(\varphi,\psi^*) \leq J(\varphi^*,\psi^*) \leq J(\varphi^*,\psi) \quad \forall(\varphi,\psi) \in U_{ad} \times V_{ad},$$

i.e. find $(\varphi^*,\psi^*,u^*) \in U_{ad} \times V_{ad} \times \mathcal{Z}$ such that the cost functional J is minimized with respect to φ and maximized with respect to ψ subject to the problem (2) (i.e. $u^*(x,t) = \mathcal{M}(x,t,\varphi^*,\psi^*)$).

We lay stress upon the fact that there is no general method to analyse the problems of robust control (it is necessary to adapt it in each situation). On the other hand, we can define a process to be followed for each situation.

(i) solve the direct problem (existence of solutions, uniqueness, stability according to the data, regularity, *etc.*)

(ii) define the function or the parameter to be identified and the type of disturbance to be controlled

(iii) introduce and solve the perturbed problem which plays the role of the direct problem (existence of solutions, uniqueness, stability according to the data, regularity, differentiability of the operator solution, *etc.*)

(iv) define the cost (or objective) functional, which depends on control and disturbance functions

(v) obtain the existence of an optimal solution (as a saddle point of the cost functional) and analyse the necessary conditions of optimality

(vi) characterize the optimal solutions by introducing an **adjoint (dual or co-state)** model (the characterization include the direct problem coupled with the adjoint problem, linked by inequalities)

(vii) define an algorithm allowing to solve numerically the robust control problem.

Remark 1

1. *In nonlinear systems the analysis of robust control problems is more complicated than in the case of inverse problems, because we are interested in the robust regulation of the deviation of the systems from the desired target state variables (while the desired power level and adjustment costs are taken into consideration) by analyzing the* **full nonlinear** *systems which model large perturbations to the desired target. Consequently the perturbations of the initial models, which show additional operators (and then difficulties), generate new direct problem and then new adjoint problem which, often, seem of a new type.*
2. *If there are no noises (i.e., $\mathcal{B}_2$ vanishes), the problem becomes an inverse problem or model calibration, i.e., find φ in U_{ad} such that the cost functional $J_0(\varphi)$ (in reduced form i.e. in place of the form $\mathcal{G}_0(\varphi, U = M(.,\varphi))$) is minimized subject to the well-posed problem*

$$\mathcal{F}(x,t,f_0 + \mathcal{B}_1\varphi, g, U) = 0, \tag{3}$$

where data (f_0, g) are known (we have supposed that f is decomposed into a known function f_0 and the control φ) and $M(., \varphi) = U$ is the solution of (3), corresponding to φ. Precisely, the problem is : find $(\varphi^*, U^*) \in U_{ad} \times \mathcal{Z}$ solution of

$$J_0(\varphi^*) = \inf_{\varphi \in U_{ad}} J_0(\varphi),$$

and $U^* = M(., \varphi^*)$.

2. Statement of the problem

2.1 Problem definition

Motivated by topics and issues critical to human health and safety of treatment, the problem studied in this chapter derives from the modeling and stabilizing control of the transport of thermal energy in biological systems with porous structures.
The evaluation of thermal conductivities in living tissues is a very complex process which uses different phenomenological mechanisms including conduction, convection, radiation, metabolism, evaporation and others. Moreover blood flow and extracellular water affect considerably the heat transfer in the tissues and then the tissue thermal properties. The bioheat transfer process in tissues is also dependent on the behavior of blood perfusion along the vascular system. An analysis of thermal process and corresponding tissue damage taking into account theses parameters will be very beneficial for thermal destruction of the tumor in medical practices, for example for laser surgery and thermotherapy for treatment planning and optimal control of the treatment outcome, often used in treatment of cancer. The first model, taking account on the blood perfusion, was introduced by Pennes see (Pennes, 1948) (see also (Wissler, 1998) where the paper of Pennes is revisited). The model is based on the classical thermal diffusion system, by incorporating the effects of metabolism and blood perfusion. The Pennes model has been adapted per many biologists for the analysis of various heat transfer phenomena in a living body. Others, after evaluations of the Pennes model in specifical situations, have concluded that many of the hypotheses (foundational to the model) are not valid. Then these latter ones modified and generalized the model to adequate systems, see e.g. (Chen & Holmes, 1980a;b);(Chato, 1980); (Valvano et al., 1984); (Weinbaum & Jiji, 1985); (Arkin et al., 1986); (Hirst, 1989) (see also e.g. (Charney, 1992) for a review on mathematical modeling of the influence of blood perfusion). Recently, some studies have shown the important role of porous media in modeling flow and heat transfer in living body, and the pertinence of models including this parameter have been analyzed, see e.g. (Shih et al., 2002); (Khaled & Vafai, 2003); (Belmiloudi, 2010) and the references therein.
The goal of our contribution is to study time-dependent identification, regulation and stabilization problems related to the effects of thermal and physical properties on the transient temperature of biological tissues with porous structures. To treat the system of motion in living body, we have written the transient bioheat transfer type model in a generalized form by taking into account the nature of the porous medium. In paragraph 3.1, we have constructed a model for a specific problem which has allowed us to propose this generalized model as follows

$$\begin{aligned} c(\phi, x)\frac{\partial U}{\partial t} &= div(\kappa(\phi, U, x)\nabla U) - e(\phi, x)P(x,t)(U - U_a) \\ &\quad - d(\phi, x)K_v(U) + r(\phi, x)g(x,t) + f(x,t) \quad in \;\; \mathcal{Q}, \end{aligned} \tag{4}$$

subjected to the boundary condition

$$(\kappa(\phi,U,x)\nabla U).\mathbf{n} = -q(x,t)(U - U_b)$$
$$-\lambda(x)(L(U) - L(U_b)) + h(x,t) \quad in \;\; \Sigma,$$

and the initial condition

$$U(x,0) = U_0(x) \;\; in \;\; \Omega,$$

under the pointwise constraints

$$\begin{array}{l} a_1 \leq P \leq a_2 \;\; a.e. \; in \; \mathcal{Q}, \\ b_1 \leq \phi \leq b_2 \;\; a.e. \; in \; \Omega, \end{array} \tag{5}$$

where the state function U is the temperature distribution, the function K_v is the transport operator in $\vec{\vartheta}$ direction i.e. $K_v(U) = (\vec{\vartheta}.\nabla)U$, the function L is the radiative operator i.e. $L(U) = \mid U \mid^3 U$. The body Ω is an open bounded domain in $\mathbb{R}^m$, $m \leq 3$ with a smooth boundary $\Gamma = \partial\Omega$ which is sufficiently regular, and Ω is totally on one side of Γ, the cylindre $\mathcal{Q}$ is $\mathcal{Q} = \Omega \times (0,T)$ with $T > 0$ a fixed constant (a given final time), $\Sigma = \partial\Omega \times (0,T)$, $\mathbf{n}$ is the unit outward normal to Γ and a_i, b_i, for $i = 1,2$, are given positive constants. The quantity P is the blood perfusion rate and $\phi \in L^\infty(\Omega)$ describes the porosity that is defined as the ratio of blood volume to the total volume (i.e. the sum of the tissue domain and the blood domain). The volumetric heat capacity type function $c(\phi,.)$ and the thermal conductivity type function of the tissue $\kappa(\phi,U,.)$ are assumed to be variable and satisfy $\nu \geq \kappa(\phi,U,.) = \sigma^2(\phi,U,.) \geq \mu > 0$, $M_1 \geq c(\phi,.) = \mathfrak{r}^2(\phi,.) \geq M_0 > 0$ (where ν, μ, M_0, M_1 are positive constants). The second term on the right of the state equation (4) describes the heat transport between the tissue and microcirculatory blood perfusion, the third term K_v is corresponding to the directional convective mechanism of heat transfer due to blood flow, the last terms are corresponding to the sum of the body heating function which describes the physical properties of material (depending on the thermal absorptivity, on the current density, on the electric field intensity, that can be calculated from the Maxwell equations, and others) and the source terms that describe a distributed energy source which can be generated through a variety of sources, such as focused ultrasound, radio-frequency, microwave, resistive heating, laser beams and others (depending on the difference between the energy generated by the metabolic processes and the heat exchanged between, for example, the electrode and the tissue). The first term in the right of the boundary condition in (4) describes the convective component and the second term is the radiative component. The term h is the heat flux due to evaporation. The function U_a is the arterial blood temperature, the function U_b is the bolus temperature and they are assumed to be in $L^\infty(\mathcal{Q})$ and in $L^\infty(\Sigma)$, respectively.
The function u_0 is the initial value and is assumed to be variable and $\lambda = \sigma_B \epsilon_e$ is assumed to be in $L^\infty(\Gamma)$ where σ_B ($Wm^{-2}K^{-4}$) is Stefan-Boltzmann's constant and ϵ_e is the effective emissivity. The vector function $\vec{\vartheta}$ is the flow velocity which is assumed to be sufficiently regular.

Remark 2

1. *Emissivity of a material is defined as the ratio of energy radiated by a particular material to energy radiated by a black body at the same temperature (the tissue is not a perfect black body). It is a dimensionless quantity (i.e. a quantity without a physical unit). The emissivity of human skin is in the range* $0.98 - 0.99$.

2. *We consider only the boundary effect of the process of radiation, since radiative heat transfer processes within the system are neglected.*
3. *In the physical case there is not absolute values under the boundary conditions (since the temperature is non negative). For real physical and biological data, we can prove by using the maximum principle that the temperature is positive and then we can remove the absolute values.*
4. *For all $\vec{\vartheta}$ sufficiently regular (such e.g. the condition (17)), the linear operator satisfies the following estimate:*
   there exists a constant $\gamma_v \geq 0$ (depending on the norm of $\vec{\vartheta}$) such that

$$\| K(\vec{\vartheta},v) \|_{L^2(\Omega)} \leq \gamma_v \| v \|_{H^1(\Omega)}, \forall v \in H^1(\Omega). \tag{6}$$

5. *The nonlinear scalar function $L : I\!R \longrightarrow I\!R$ is a $C^1(I\!R)$ function and its derivative is given by*

$$L'(v) = 4 \mid v \mid^3 . \tag{7}$$

2.2 Basis for thermal therapy

Cells, vasculature (which supply the tissue with nutrients and oxygen through the flow of blood) and extracellular matrix (which provides structural support to cells) are the main constituents of tissue. Most living cells and tissues can tolerate modest temperature elevations for limited time periods depending on the metabolic status of the individual cell (so-called thermotolerance). Contrariwise, when tissues are exposed to very high temperature conditions, this leads to cellular damage which can be irreversible.

Therapy by elevation of temperature is a thermal treatment in which pathological tissue is exposed to high temperatures to damage and destroy or kill malignant cells (directly or indirectly by the destruction of microvasculature) or to make malignant cells more sensitive to the effects of another therapeutic option, such as radiation therapy, chemotherapy or photodynamic therapy. Many scientists claim that this is due largely to the difference in blood circulation between tumor and normal tissues. Moreover, local tissue properties, in particular perfusion, have a significant impact on the size of treatment zone, for example, highly perfused tissue and large vessels act as a heat sink (this phenomenon makes normal tissue relatively more resilient to treatment than tumor tissue, since perfusion rates in tumors are generally less than those in normal tissues). Consequently, the knowledge of the thermal properties and blood perfusion of biological tissues is fundamental for accurately modeling the heat transfer process during thermal therapy. The most commonly used technique for heating of tumors is the interstitial thermal therapy, in which heating elements are implanted directly into the treated zone, because energy can be localized to the target region while surrounding healthy tissue is preserved. Different energy sources are employed to deliver local thermal energy including laser, microwaves, radiofrequency and ultrasound.

The traditional hyperthermia is defined as a temperature greater than $37.5 - 38.3^o C$, in general in the interval of about $41 - 47^o C$. This thermal therapy is only useful for certain kinds of cancer and is most effective when it is combined with the other conventional therapeutic modalities. Though temperatures are not very high and then cell death is not instantaneous, prolonged exposure leads to the thermal denaturation of non-stabilized proteins such as enzymes and to their destruction, which ultimately leads to cell death. There are various types of hyperthermia as alternative cancer therapy. These include: the regional (heats a larger part of the body, such as an entire affected organ) and local (heats a small area, such as the tumor itself) hyperthermia, where temperatures reach between 42 and 44^oC and the whole body hyperthermia, where the entire body except for the head is overheated to a temperature of about 39 to 41^oC. Heat sensitivity of the tissue is lost at higher temperatures (above 44^oC) resulting in tumor and normal tissues destruction at the same rate. Consequently, in order to minimize damage to surrounding tissues and other adverse effects, we must keep local temperatures under 44^oC, but requires more treatment-time (between 1 and 3 hours). At these low temperatures damage can be reversible. Indeed damaged proteins can be repaired or degraded and replaced with new ones.

For a rapid destruction of tissue, it is necessary to make a temperature rise of at least exceed 50^oC. During thermotherapy, which employs higher temperatures over shorter times (seconds to minutes), than those used in hyperthermia treatment, several processes, as tissue vaporization, carbonization and molecular dissociation, occur which lead to the destruction or death of the tissue. At temperatures above 60^oC, proteins and other biological molecules of the tissue become severely denatured (irreversibly altered) and coagulate leading to cell and tissue death. Temperatures above 100^oC will cause vaporization from evaporation of water in the tissue and in the intracellular compartments and lead to rupture or explosion of cells or tissue components, and above 300^oC tissue carbonization occurs. At these temperatures, an elevated temperature front migrates through the tissue and structural proteins, such as fibrillar collagen and elastin, begin to damage irreversibly causing visible whitening of the tissue and then coagulation necrosis to the targeted tissue. Indeed, structural proteins are more thermally stable than the intracellular proteins and enzymes (involved in reversible heat damage), and consequently tissue coagulation signifies destruction of the lesion.

The actual level of thermal damage in cells and tissue is a function of both temperature and heating time. Using the temperature history, the accumulation of thermal damage, associated with injury of tissue, can be calculated by an approach (based on the well-known Arrhenius model see e.g. (Henriques, 1947)) characterizing tissue damage, including cell kill, microvascular stasis and protein coagulation. For this, we can use the Arrhenius damage integral formulation, which assumes that some thermal damage processes follow first-order irreversible rate reaction kinetics (from thermal chemical rate equations, see e.g. (Atkins, 1982)), for more details see e.g. (Tropea & Lee, 1992) and (Skinner et al., 1998):

$$\mathcal{D}(x,\tau_{exp}) = ln(\frac{C(0)}{C(\tau_{exp})}) = A\int_0^{\tau_{exp}} exp(\frac{-E}{RU(x,t)})dt, \tag{8}$$

where D is the nondimensional degree of tissue injury, U is the temperature of exposure (K), τ_{exp} is the duration of the exposure, $C(0)$ is the concentration of living cells before irradiation exposure and $C(\tau_{exp})$ is the concentration of living cells at the end of the exposure time. The parameter A is the molecular collision frequency (s^{-1}) i.e. damage rate, the parameter E is the denaturation activation energy ($J.mol^{-1}$) and R is the universal gaz constant equal to 8.314 $J.mol^{-1}K^{-1}$. The two kinetic parameters A and E are dependent on the type of tissue and must be determined by experiments a priori. The cumulative damage can be interpreted as the fraction of hypothetical indicator molecules that are denatured and can play an important role in the optimization of the treatment.

Other cell damage models are developed, in recent years, see for example the two-state model of Oden et al. in (Feng et al., 2008) (which is based on statistical thermodynamic principles) as follows:

$$\mathcal{D}(x,\tau_{exp}) = \int_0^{\tau_{exp}} \frac{1}{1+exp(\frac{-E_o(t,U(x,t))}{RU(x,t)})}dt, \tag{9}$$

with the activation energy function $E_0(t,U) = (\frac{\zeta}{U} + at + b)$, where ζ, a and b are known constants determined by in vitro cellular experiments.
In conclusion the cell damage model can be expressed by the following general form

$$\mathcal{D}(x,\tau_{exp}) = ln(\frac{C(0)}{C(\tau_{exp})}) = \int_0^{\tau_{exp}} \mathcal{H}(t,U(x,t))dt, \tag{10}$$

where $\mathcal{H}$ is differentiable on the variable U.

2.3 Outline

We give now the outline of the rest of the chapter. First, the modeling of thermal transport by perfusion within the framework of the theory of porous media is presented and the governing equations are established. The thermal processes within the tissues are predicted by using some generalized uncertain evolutive nonlinear bioheat transfer type models with nonlinear Robin boundary conditions (radiative type), by taking into account porous structures and directional blood flow. Afterwards the existence, the uniqueness and the regularity of the solution of the state equation are presented as well as stability and maximum principle under extra assumptions. Second, we introduce the initial perturbation problem and give the existence and uniqueness of the perturbation solution and obtain a stability result. Third, the real-time identification and robust stabilization problems are formulated, in different situations, in order to reconstitute simultaneously the blood perfusion rate, the porosity parameter, the heat transfer parameter, the distributed energy source terms and the heat flux due to the evaporation, which affect the effects of thermal physical properties on the transient temperature of biological tissues, and to control and stabilize the desired online temperature and thermal damage provided by MRI (Magnetic Resonance Imaging) measurements. Because, it is now well-known that a controlled and stabilized temperature field does not necessarily imply a controlled and stabilized tissue damage. This work includes results concerning the existence of the optimal solutions, the sensitivity problems, adjoint problems, necessary optimality conditions (necessary to develop numerical optimization methods) and optimization problems. Next, we analyse the case when data are measured in only some points in space-time domain, and the case where the body Ω is constituted by different tissue types which occupy finitely many disjointed subdomains. As in previous, we give the existence of an optimal solution and we derive necessary optimality conditions. Some numerical strategies, based on adjoint control optimization (combining the obtained optimal necessary conditions and gradient-iterative algorithms), in order to perform the robust control, are also discussed. Finally, control and stabilization problems for a coupled thermal, radiation transport and coagulation processes modeling the laser-induced thermotherapy in biological tissues, during cancer treatment, are analyzed.
In the sequel, we will always denoted by C some positive constant which can be different at each occurrence.

3. Mathematical modelling and motivation

3.1 Model development

3.1.1 Heat transfer equation

The blood-perfused tumor tissue volume, including blood flow in microvascular bed with the blood flow direction, contains many vessels and can be regarded as a porous medium consisting of a tumor tissue (a solid domain) fully filled with blood (a liquid domain), see

Figure 1. Consequently the temperature distribution in biological tissue can be modelized by analyzing a conjugate heat transfer problem with the porous medium theory. For the tumor tissue domain, we use the Pennes bioheat transfer equation by taking account on the blood perfusion in the energy balance for the blood phase. For the blood flow domain, we use the energy transport equation. The system of equations of the model is then

$$\begin{aligned} & c_s(x)\rho_s(x)\frac{\partial U_s}{\partial t} = div(\kappa_s(U_s,x)\nabla U_s) - c_l(x)w_l(x,t)(U_s - U_a) + Q_s(x,t) + Q_J(x,t), \\ & c_l(x)\rho_l(x)(\frac{\partial U_l}{\partial t} + (\vec{\vartheta}.\nabla)U_l) = div(\kappa_l(U_l,x)\nabla U_l) + Q_J(x,t), \end{aligned} \tag{11}$$

where c_l, c_s, ρ_l, ρ_s, U_l, U_s, κ_l, κ_s, Q_s, Q_J are the specific heat of blood, the specific heat of tissue, the density of blood, the density of tissue, the local blood temperature, local tissue temperature, blood effective thermal conductivity tensor, tissue effective thermal conductivity tensor, metabolic volumetric heat generation and energy source term (which is also called the specific absorption rate, SAR (Wm^{-3})), respectively, and U_a is the temperature in arterial blood. The term $div(\kappa_l(U_l)\nabla U_l)$ is corresponding to the enhancement of thermal conductivity in tissue due to the flow of blood within thermally significant blood vessels and the term $div(\kappa_s(U_s)\nabla U_s)$ is similar to Pennes model. The transport operator is $\vec{\vartheta}.\nabla$ and is corresponding to a directional convective term due to the net flux of the equilibrated blood.

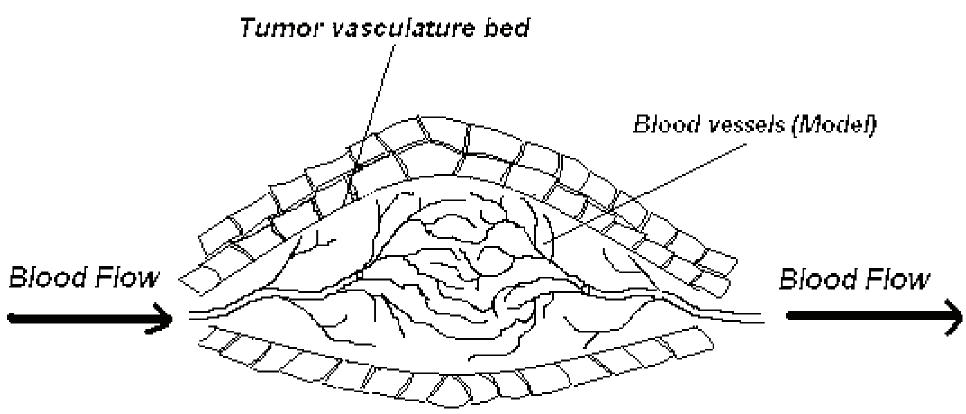


Fig. 1. : Relationship between tumor vascular and blood flow direction

The volumetric averaging of the energy conservation principle is achieved by combining and rearranging the first and the second part of the system (11) with the porous structure (regarded as a homogeneous medium). Under thermal equilibrium and according to the modelization of (Chen & Holmes, 1980a) (the model has been formulated after the analyzing of blood vessel thermal equilibration length) we have then by multiplying the first equation by $(1-\phi)$ and the second equation by ϕ

$$\begin{aligned} & ((1-\phi)c_s(x)\rho_s(x) + \phi c_l(x)\rho_l(x))\frac{\partial U}{\partial t} + div(((1-\phi)\kappa_s(U,x) + \phi\kappa_l(U,x))\nabla U) \\ & + \phi c_l(x)\rho_l(x)(\vec{\vartheta}.\nabla)U + (1-\phi)c_l(x)w_l(x,t)(U-U_a) = (1-\phi)Q_s(x,t) + Q_J(x,t). \end{aligned} \tag{12}$$

Our model incorporates the effect of blood flow in the heat transfer equation in a way that captures the directionality of the blood flow and incorporates the convection features of the heat transfer between blood and solid tissue.

The model (12) is a particular case of the general equation in the system (4), by taking, in the first relation of (4), the heat capacity type function $c(\phi,x)$ as $(1-\phi)c_s\rho_s + \phi c_l\rho_l$, the thermal conductivity capacity type function $\kappa(\phi,U,x)$ as $(1-\phi)\kappa_s + \phi\kappa_l$, the function $e(\phi,x)P(x,t)$ as $(1-\phi)c_l w_l$, the function $d(\phi,x)$ as $\phi c_l\rho_l$, the function $r(\phi,x)$ as $1-\phi$, the function f as Q_J and the function g as Q_s .
To close the model, we must specify boundary conditions.

3.1.2 Boundary conditions

Every body emits electromagnetic radiation proportional to the fourth power of the absolute temperature of its surface. The total energy, emitted from a black body, E_R (Wm^{-2}) can be given by the following Stefan-Boltzmann-Law:

$$E_R = \sigma_B \epsilon_e (U^4 - U_b^4), \tag{13}$$

where $\sigma_B = 5.67.10^{-8} Wm^{-2}K^{-4}$ is the Stefan-Boltzmann constant, U and U_b (K) are the tissue surface temperature and surrouding temperature, respectively and $\epsilon < 1$ (since tissue is not a perfect black body) is the emissivity coefficient.
Convection problems involve the exchange of heat between the surface of the body (the conducting) and the surrounding air (convecting). The thermal energy E_C (Wm^{-2}) can be given by Newton's law of cooling:

$$E_C = q(U - U_b), \tag{14}$$

where, the proportionality function q $(Wm^{-2}K^{-1})$ is the coefficient of local heat convection and U_b is the bulk temperature of the air (assumed to be similar as relation in (13)).
If we assume that the evaporation occurs mainly at the surface, the energy associated with the phase change occurring during evaporation (the heat flux due to evaporation) can be given by the following expression

$$E_V = h_{fg} m_w = -h(x,t), \tag{15}$$

where h_{fg} is the latent heat of vaporization and m_w is the mass flux of evaporating water.
According to the previous relations, the boundary condition can be imposed as follows:

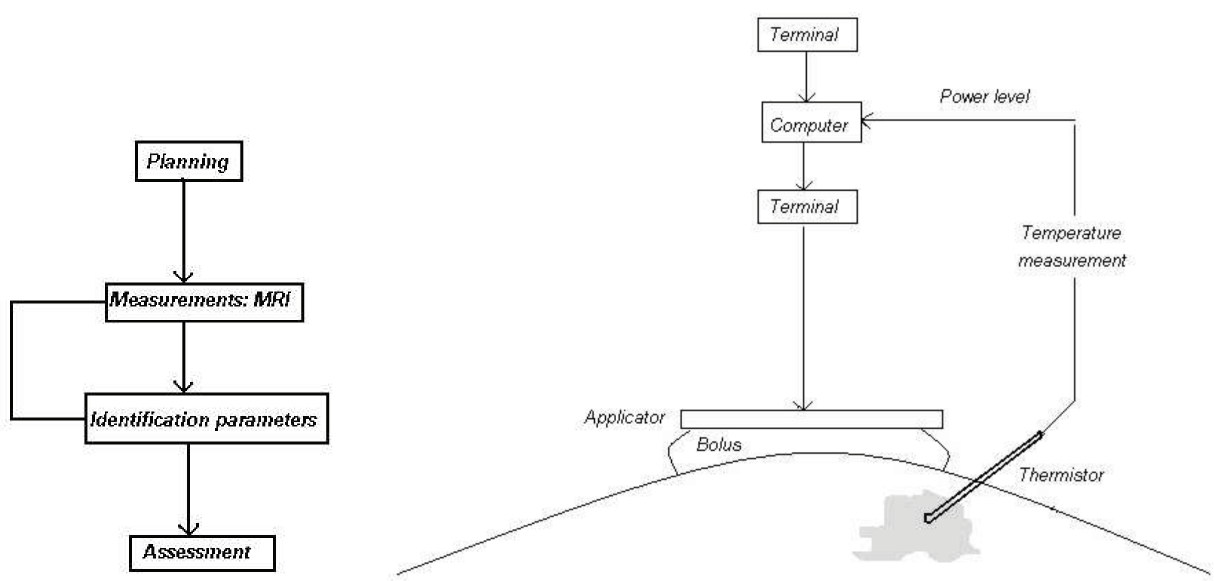
$$-(\kappa(\phi,U,x)\nabla U).\mathbf{n} = E_R + E_C + E_V = q(U - U_b) + \lambda(x)(L(U) - L(U_b)) - h(x,t), \tag{16}$$

where $\lambda = \sigma_B \epsilon_e$ and $L(v) = \mid v \mid^3 v = v^4$ for all positive functions.
We recall now some biological and medical background and motivations to analyse the identification, calibration and stabilization problem.

3.2 Background and motivation

Mathematical modeling of cancer treatments (chemotherapy, thermotherapy, etc) is an highly challenging frontier of applied mathematics. Recently, a large amount of studies and research related to the cancer treatments, in particular by chemotherapy or thermotherapy, have been the object of numerous developments.
As an alternative to the traditional surgical treatment or to enhance the effect of conventional chemotherapy, various problems associated with localized thermal therapy have been intensively studied (see e.g. (Pincombe & Smyth, 1991); (Hill & Pincombe, 1992); (Tropea & Lee, 1992); (Martin et al., 1992); (Seip & Ebbini, 1995); (Sturesson & Andersson-Engels, 1995); (Deuflhard & Seebass, 1998); (Xu et al.,

1998); (Liu et al., 2000); (Marchant & Lui, 2001); (Shih et al., 2002); (He & Bischof, 2003); (Zhou & Liu, 2004); (Zhang et al., 2005) and the references therein). In order to improve the treatments, several approaches have been proposed recently to control the temperature during thermal therapy. We can mention e.g. (Bohm et al., 1993); (Hutchinson et al., 1998); (Köhler et al., 2001); (Vanne & Hynynen, 2003); (Kowalski & Jin, 2004); (Malinen et al., 2006); (Belmiloudi, 2006; 2007) and the references therein. The essential of these contributions has been the numerical analysis, MRI-based optimization techniques and mathematical analysis. For the stabilization of the temperature treatment, see e.g. (Belmiloudi, 2008), in which the author develops nonlinear PDE robust control approach in order to stabilize and control the desired online temperature for a Pennes's type model with linear boundary conditions.
An important application of all bioheat transfer models in interdisciplinary research areas, in joining mathematical, biological and medical fields, is the analysis of the temperature field which develops in living tissue when a heat is applied to the tissue, especially in the clinical cancer therapy hyperthermia and in the accidental heating injury, such as burns (in hyperthermia, tissue is heated to enhance the effect of an accompanying radio or chemotherapy). Indeed the thermal therapy (performed with laser, focused ultrasound or microwaves) gives the possibility to destroy the pathological tissues with minimal damage to the surrounding tissues. Moreover, due to the self-regulating capability of the biological tissue, the blood perfusion and the porosity parameters depend on the evolution of the temperature and vary significantly between different patients, and between different therapy sessions (for the same patient). Consequently, in order to have a very optimal thermal diagnostics and so the result of the therapy being very beneficial to treatment of the patient, it is necessary to identify the value of these two parameters.
The new feature introduced in this work concerns the estimation of the evolution of the blood perfusion and the porosity parameters by using nonlinear optimal control methods, for some generalized evolutive bioheat transfer systems, where the observation is the online temperature control provided by Magnetic Resonance Imaging (MRI) measurements, see Figure2 (MRI is a new efficie



(a) Control process (b) Applicator and measurements

Fig. 2. : Laser-induced thermotherapy and identification

The introduction of the theory of porous media for heat transfer in biological tissues is very important because the physical properties of material have power law dependence on temperature (see e.g. (Marchant & Lui, 2001; Pincombe & Smyth, 1991)) and moreover the porosity is one of the crucial factors determining distribution of temperature during thermal therapies, for example in medical laser-induced thermotherapy (see e.g. the review of (Khaled & Vafai, 2003)). Consequently we cannot neglect the influence of the porosity in the model and then it is necessary to identify, in more of the blood perfusion, the porosity of the material during thermal therapy in order to maximize the efficiency and safety of the treatment. Moreover, the introduction of the nonlinear radiative operator including the cooling mechanism of water evaporation in the model is very important, because the heat exchange mechanisms at the body-air interface play a very important part on the total tissue temperature distribution and consequently we cannot also neglect the influence of the surface evaporation in the model (see e.g. (Sturesson & Andersson-Engels, 1995)). On the other hand we will consider that the source term f and the heat flux due to evaporation h (in the model (4)) are not accurately known.

4. Solvability of the state system

Now we give some assumptions, notations, results and an analysis of the state system (4) which are essential for the following investigations.

4.1 Assumptions and notations

We use the standard notation for Sobolev spaces (see (Adams, 1975)), denoting the norm of $W^{m,p}(\Omega)$ ($m \in \mathbb{N}$, $p \in [1,\infty]$) by $\| \ \|_{W^{m,p}(\Omega)}$. In the special case $p = 2$ we use $H^m(\Omega)$ instead of $W^{m,2}(\Omega)$. The duality pairing of a Banach space X with its dual space X' is given by $< .,. >_{X',X}$. For a Hilbert space Y the inner product is denoted by $(.,.)_Y$. For any pair of real numbers $r,s \geq 0$, we introduce the Sobolev space $H^{r,s}(\mathcal{Q})$ defined by $H^{r,s}(\mathcal{Q}) = L^2(0,T,H^r(\Omega)) \cap H^s(0,T,L^2(\Omega))$, which is a Hilbert space normed by

$$(\| v \|^2_{L^2(0,T,H^r(\Omega))} + \| v \|^2_{H^s(0,T,L^2(\Omega))})^{1/2},$$

where $H^s(0,T,L^2(\Omega))$ denotes the Sobolev space of order s of functions defined on $(0,T)$ and taking values in $L^2(\Omega)$, and defined by, for $\theta \in (0,1), s = (1-\theta)m$, m is an integer, (see e.g. (Lions & Magenes, 1968)) $H^s(0,T,L^2(\Omega)) = [H^m(0,T,L^2(\Omega)), L^2(\mathcal{Q})]_\theta$, $H^m(0,T,L^2(\Omega)) = \{v \in L^2(\mathcal{Q}) | \ \frac{\partial^j v}{\partial t^j} \in L^2(\mathcal{Q}), \forall j = 1,m\}$.
We denote by V the following space: $V = \{v \in H^1(\Omega) | \gamma_0 v \in L^5(\Gamma)\}$ equipped with the norm $\| v \| = \| v \|_{H^1(\Omega)} + \| \gamma_0 v \|_{L^5(\Gamma)}$ for $v \in V$, where γ_0 is the trace operator in Γ. The space V is a reflexive and separable Banach space and satisfies the following continuous embedding: $V \subset L^2(\Omega) \subset V'$ (see e.g. (Delfour et al., 1987)). For $\Omega \subset \mathbb{R}^2$, the space $H^1(\Omega)$ is compactly embedded in $L^5(\Gamma)$ and then $V = H^1(\Omega)$. We can now introduce the following spaces:
$\mathcal{H}(\mathcal{Q}) = L^\infty(0,T,L^2(\Omega)), \mathcal{V}(\mathcal{Q}) = L^2(0,T,V), \mathcal{W}(\mathcal{Q}) = \{w \in L^2(0,T,V) | \frac{\partial w}{\partial t} \in L^{5/4}(0,T,V')\}$ and $\tilde{\mathcal{W}}(\mathcal{Q}) = \{v \in \mathcal{W}(\mathcal{Q}) | v \in L^5(\Sigma)\}$.

Remark 3 *Let $\Omega \subset \mathbb{R}^m$, $m \geq 1$, be an open and bounded set with a smooth boundary and q be a nonnegative integer. We have the following results (see e.g. (Adams, 1975))*
(i) $H^q(\Omega) \subset L^p(\Omega)$, $\forall p \in [1, \frac{2m}{m-2q}]$, with continuous embedding (with the exception that if $2q = m$, then $p \in [1,+\infty[$ and if $2q > m$, then $p \in [1,+\infty]$).

(ii) (Gagliardo-Nirenberg inequalities) There exists $C > 0$ *such that*

$$\| v \|_{L^p} \leq C \| v \|_{H^q}^{\theta} \| v \|_{L^2}^{1-\theta}, \forall v \in H^q(\Omega),$$

where $0 \leq \theta < 1$ *and* $p = \frac{2m}{m-2\theta q}$ *(with the exception that if* $q - m/2$ *is a nonnegative integer, then* θ *is restricted to 0).*
2. If $u \in \mathcal{W}(\mathcal{Q}) \cap \mathcal{H}(\mathcal{Q})$*, then* u *is a weakly continuous function on* $[0, T]$ *with values in* $L^2(\Omega)$ *i.e.* $u \in \mathcal{C}_w([0, T], L^2(\Omega))$ *(see e.g. (Lions, 1961)).*

Definition 1 *A real valued function* Φ *defined on* $\mathbb{R}^q \times D$*,* $q \geq 1$*, is a Carathéodory function iff* $\Phi(\mathbf{v}, .)$ *is measurable for all* $\mathbf{v} \in \mathbb{R}^q$ *and* $\Phi(y, .)$ *is continuous for almost all* $y \in D$*.*

We state the following hypotheses for the functions (or operators) c, d, e, r and κ appearing in the model (4) :

(**H1**) The functions $c = \mathfrak{r}^2 > 0$, $d > 0$, $e > 0$, r are Carathéodory functions from $\mathbb{R} \times \Omega$ into $\mathbb{R}^+$ and $c(., x)$, $d(., x)$, $e(., x)$, $r(., x)$ are Lipschitz and bounded functions for almost all $x \in \Omega$, where $M_1 \geq c(\phi, .) = \mathfrak{r}^2(\phi, .) \geq M_0 > 0$ (where M_0 and M_1 are positive constants).

(**H2**) The function $\kappa = \sigma^2 > 0$ is Carathéodory function from $\mathbb{R}^2 \times \Omega$ into $\mathbb{R}^+$ and $\kappa(., x)$ is Lipschitz and bounded functions for almost all $x \in \Omega$,
where $\nu \geq \kappa(\phi, U, .) = \sigma^2(\phi, U, .) \geq \mu > 0$ (where ν and μ are positive constants).

(**H3**) The function c, d, e, r (resp. κ) are differentiable on φ (resp. on (ϕ, U)) and their partial derivatives are Lipschitz and bounded functions.

We assume that the flow velocities $\vec{\vartheta}$ satisfy the regularity :

$$\vec{\vartheta} \in L^\infty(0, T, W^{1,\infty}(\Omega)) \tag{17}$$

and we denote by K_v^* the adjoint operator of K_v i.e. $K_v^*(u) = -div(\vec{\vartheta} u)$ and we have:

$$\int_\Omega K_v(u) v dx = \int_\Omega K_v^*(v) u dx + \int_\Gamma u v \vec{\vartheta}.\mathbf{n} d\Gamma, \ \ \forall (u, v) \in (H^1(\Omega))^2. \tag{18}$$

Nota bene: For simplicity we denote the values $\mathfrak{h}(\varphi, .)$ by $\mathfrak{h}(\varphi)$, where the function $\mathfrak{h}$ plays the role of c, d, e or r, and the value $\kappa(\phi, U, .)$ by $\kappa(\phi, U)$.

4.2 Some fundamental inequalities and results

Our study involve the following fundamental inequalities, which are repeated here for review:
(i) *Hölder's inequality*

$$\int_D \Pi_{i=1,k} f_i dx \leq \Pi_{i=1,k} \| f_i \|_{L^{q_i}(D)}, \text{ where}$$
$$\| f_i \|_{L^{q_i}(D)} = (\int_D | f_i |^{q_i} dx)^{1/q_i} \ \text{ and } \ \sum_{i=1,k} \frac{1}{q_i} = 1.$$

(ii) *Young's inequality* ($\forall a, b > 0$ and $\epsilon > 0$)

$$ab \leq \frac{\epsilon}{p} a^p + \frac{\epsilon^{-q/p}}{q} b^q, \ for \ p, q \in]1, +\infty[\ and \ \frac{1}{p} + \frac{1}{q} = 1.$$

(iii) *Gronwall's Lemma*

$$\text{If } \frac{d\Phi}{dt} \leq g(t)\Phi(t) + h(t),\ \forall t \geq 0 \ \ then$$
$$\Phi(t) \leq \Phi(0)exp(\int_0^t g(s)ds) + \int_0^t h(s)exp(\int_s^t g(\tau)d\tau)ds,\ \forall t \geq 0.$$

Lemma 1 *For u, v, w sufficiently regular functions and D positive and bounded function we have for all $r \geq 0$*
1. $(D(\mid u \mid^r u - \mid v \mid^r v), u - v)_\Gamma \geq 0,$
2. $\mid (D \mid u \mid^r u, v)_\Gamma \mid \leq C \parallel \mid u \mid^r u \parallel_{L^{\frac{r+2}{r+1}}(\Gamma)} \parallel v \parallel_{L^{r+2}(\Gamma)} = C \parallel u \parallel^{r+1}_{L^{r+2}(\Gamma)} \parallel v \parallel_{L^{r+2}(\Gamma)},$
3. $\mid (D \mid u \mid^r w, v)_\Gamma \mid \leq C \parallel \mid u \mid^r w \parallel_{L^{\frac{r+2}{r+1}}(\Gamma)} \parallel v \parallel_{L^{r+2}(\Gamma)}$ *and*

$$\parallel \mid u \mid^r w \parallel_{L^{\frac{r+2}{r+1}}(\Gamma)} \leq C \parallel u \parallel^{\frac{r}{2}}_{L^{r+2}(\Gamma)} \parallel \mid u \mid^r w^2 \parallel^{\frac{1}{2}}_{L^1(\Gamma)}.$$

Proof. For the proof see (Belmiloudi, 2007).

Definition 2 *A function $U \in \mathcal{W}(\mathcal{Q})$ is a weak solution of system (4) provided*

$$\begin{aligned} &< c(\phi)\frac{\partial U}{\partial t}, v > + \int_\Omega \kappa(\phi, U)\nabla U.\nabla v dx + \int_\Omega d(\phi)K_v(U) v dx \\ &\quad + \int_\Omega e(\phi)P(U - U_a) v dx + \int_\Gamma q(U - U_b) v d\Gamma + \int_\Gamma \lambda(\mid U \mid^3 U - \mid U_b \mid^3 U_b) v d\Gamma \\ &\quad = \int_\Omega r(\phi) g v dx + \int_\Omega f v dx + \int_\Gamma h v d\Gamma \ \ \forall v \in V and \ \ a.e.\ in (0, T), \\ &U(0) = U_0 \ \ in \ \ \Omega, \end{aligned} \tag{19}$$

here $< .,. >$ denotes the duality between V' and V.

4.3 State system

The solvability (existence, uniqueness and stability) of the state system (4) and the boundedness of the solution are the content of the following results, where the existence is proved by compactness arguments and Faedo-Galerkin method, and the boundedness is derived from the maximum principle results. By using similar argument as in (Belmiloudi, 2007) and Lemma 1, combined with these of (Belmiloudi, 2010), we can prove the following results. So, we omit the details.

Theorem 1 *Let assumptions (H1)(H2) be fulfilled.*
(i) Let be given the initial condition U_0 in $L^2(\Omega)$ and source terms (P, ϕ, f, g, h) in $\mathcal{C}_{pt} \times (L^2(\mathcal{Q}))^2 \times L^2(\Sigma)$, where $\mathcal{C}_{pt} = \{(P, \phi) \in L^2(\mathcal{Q}) \times L^2(\Omega) \mid a_1 \leq P \leq a_2$ a.e. in $\mathcal{Q}$ and $b_1 \leq \phi \leq b_2$ a.e. in $\Omega\}$ is the set of functions describing the constraints (5). Then there exists a unique solution U in $\mathcal{W}(\mathcal{Q}) \cap \mathcal{H}(\mathcal{Q})$ of (4) satisfying the following regularity: $\mid U \mid^3 U \in L^{\frac{5}{4}}(\Sigma)$.

(ii) Let $(P_i, \phi_i, f_i, g_i, h_i, U_{0i})$, i=1,2 be two functions of $\mathcal{C}_{pt} \times (L^2(\mathcal{Q}))^2 \times L^2(\Sigma) \times L^2(\Omega)$. If $U_i \in \mathcal{W}(\mathcal{Q}) \cap \mathcal{H}(\mathcal{Q})$ is the solution of (4) corresponding to data $(p_i, \phi_i, f_i, g_i, h_i, U_{0i})$, i=1,2, then

$$\begin{aligned} \parallel U \parallel^2_{\mathcal{H}(\mathcal{Q})\cap\mathcal{V}(\mathcal{Q})} \leq & C_1(\parallel P \parallel^2_{L^2(\mathcal{Q})} + \parallel f \parallel^2_{L^2(\mathcal{Q})} + \parallel g \parallel^2_{L^2(\mathcal{Q})}) \\ & + C_2(\parallel \phi \parallel^2_{L^2(\Omega)} + \parallel h \parallel^2_{L^2(\Sigma)} + \parallel U_0 \parallel^2_{L^2(\Omega)}), \end{aligned}$$

where $U = U_1 - U_2, P = P_1 - P_2, \phi = \phi_1 - \phi_2$, $f = f_1 - f_2$, $g = g_1 - g_2$, $h = h_1 - h_2$ and $U_0 = U_{01} - U_{02}$.

If we suppose now that the functions h, q and U_b satisfy the following hypotheses:

(HS1): h is in $\mathcal{R}_1(\Sigma) = \{h|\ h \in L^2(0,T,H^1(\Gamma)), \frac{\partial h}{\partial t} \in L^2(0,T,L^2(\Gamma))\}$,

(HS2): U_b and q are in $\mathcal{R}_2(\Sigma) = \{v|\ v \in L^\infty(\overline{\Sigma}), \frac{\partial v}{\partial t} \in L^2(0,T,L^2(\Gamma))\}$,

then the following theorem holds.

Theorem 2 *Let assumptions (H1)(H2)(HS1)(HS2) be fulfilled. Let be given the initial condition U_0 in $H^{3/2}(\Omega)$ and data (P,ϕ,f,g) in $\mathcal{C}_{pt} \times (L^2(\mathcal{Q}))^2$. Then the unique solution U of (4) satisfies the following regularity: $U \in \tilde{\mathcal{S}}(\mathcal{Q})$, where*

$$\begin{aligned} &\tilde{\mathcal{S}}(\mathcal{Q}) = \{v \in \mathcal{S}(\mathcal{Q}) \text{ such that } v \in L^\infty(0,T,L^5(\Gamma))\}, \text{with} \\ &\mathcal{S}(\mathcal{Q}) = \{v \in L^\infty(0,T,V) \text{ such that } \frac{\partial v}{\partial t} \in L^2(\mathcal{Q})\}. \end{aligned} \tag{20}$$

Remark 4 (**HS1**) *implies that $h \in C^0([0,T],L^2(\Gamma))$.*

Now, we establish a maximum principle under extra assumptions on the data. In addition to (H1)(H2), we suppose, for a constant u_s such that $0 \le u_s$, the following assumption:

(H4) $0 \le U_a \le u_s$ and $0 \le U_b \le u_s$ for all in $\mathcal{Q}$ and in Σ, respectively.

Then we have the following theorem.

Theorem 3 *Let (H1),(H2) and (H4) be fulfilled. Suppose that the initial data u_0 is such that $0 \le U_0 \le u_s$, a.e. in Ω and $f + r(\phi)g$ is a positive function and satisfies $0 \le f + r(\varphi)g \le M$, a.e. in $\mathcal{Q}$ and for all ϕ such that (5). Then, the weak solution $U \in \mathcal{W}(\mathcal{Q})$ of (4) satisfies, for all $t \in (0,T)$, $0 \le U(.,t) \le m_s = \max(u_s,M)$ a.e. in Ω.*

Proof: Let us consider the following notations: $r^+ = max(r,0)$, $r^- = (-r)^+$ and then $r = r^+ - r^-$.
We prove now that if $U_0 \ge 0$, a.e. in Ω then $U(.,t) \ge 0$, for all $t \in [0,T]$ and a.e. in Ω. According to (Gilbarg & Trudinger, 1983), we have that $U^- \in L^2(0,T,V)$ with $\frac{\partial U^-}{\partial x} = -\frac{\partial U}{\partial x}$ if $U > 0$ and $\frac{\partial U^-}{\partial x} = 0$ otherwise, a.e. in $\mathcal{Q}$. Then, taking $v = -U^-$ in the equation (19) we have (*a.e. in* $(0,T)$)

$$\begin{aligned} \frac{d}{2dt} \parallel \mathfrak{r}(\phi)U^- \parallel^2_{L^2(\Omega)} &+ \int_\Omega \kappa(\phi,U) \mid \nabla U^- \mid^2 dx + \int_\Omega d(\phi)K_v(U^-)U^- dx \\ &+ \int_\Omega e(\phi)pU_aU^- dx + \int_\Omega e(\phi)P(U^-)^2 dx = -\int_\Omega (f + r(\phi)g)U^- dx \\ &+ \int_\Gamma qU_bU^- d\Gamma + \int_\Gamma q(U^-)^2 d\Gamma \\ &+ \int_\Gamma \lambda \mid u \mid^3 (U^-)^2 d\Gamma + \int_\Gamma \lambda \mid U_b \mid^3 U_bU^- d\Gamma. \end{aligned}$$

According to the assumption $U_a, U_b \ge 0$ we find that

$$\frac{d}{2dt} \parallel \mathfrak{r}(\phi)U^- \parallel^2_{L^2(\Omega)} + \int_\Omega \kappa(\phi,U) \mid \nabla u^- \mid^2 dx \le -\int_\Omega d(\varphi)K_v(U^-)U^- dx$$

and then (according to (H1) and (6))

$$\frac{d}{2dt} \parallel \mathfrak{r}(\phi)U^- \parallel^2_{L^2(\Omega)} + \frac{\nu}{2}\int_\Omega \mid \nabla u^- \mid^2 dx \le C \parallel \mathfrak{r}(\phi)U^- \parallel^2_{L^2(\Omega)}.$$

Using the assumption $U_0 \geq 0$ (then $\| U_0^- \|^2_{L^2(\Omega)} = 0$) and Gronwall's lemma, we can deduce that $U(t,.) \geq 0$ for all $t \in (0,T)$ and a.e. in Ω.
To prove that, for all $t \in (0,T)$, $U(.,t) \leq m_s$ *a.e.* in Ω, we choose $v = (U - m_s)^+ \in V$ in the equation (19) and we use the same technique as before by using the following estimate:

$$\int_\Omega (f + r(\varphi)g)(U - m_s)^+ dx = \int_\Omega ((f + r(\varphi)g) - m_s)(U - m_s)^+ dx \\ + \int_{[U \geq m_s]} m_s (U - m_s)^+ dx \leq C \| \mathfrak{r}(\phi)(U - m_s)^+ \|^2_{L^2(\Omega)}. \quad \square$$

5. Uncertainties and perturbation problems

In clinical practice, measurements, material data, behavior of patients and other process are highly disturbed and affected by noises and errors. Consequently, in order to obtain a solution robust to the noises and fluctuations in input data and parameters, it is necessary to incorporate these uncertainties in the modeling and to analyse the robust regulation of the deviation of the model from the desired temperature distribution target, due to fluctuations.
In the following, the solution U of problem (4) will be treated as the target function. We are then interested in the robust regulation of deviation of the problem from the desired target U. So, we now formulate the perturbation problem. Precisely, we develop the **full nonlinear perturbation** problem, which models fluctuations u to the target temperature therapy U, i.e. we assume that U satisfies the problem (4) with data $(U_0, P, \phi, f, g, h, U_a, U_b)$ and $U + u$ satisfies problem (4) with the data $(U_0 + u_0, P + p, \phi + \varphi, f + \xi, g + \eta, h + \pi, U_a + u_a, U_b + u_b)$.
Hence we consider the following system (for a given U sufficiently regular):

$$\begin{aligned} c(\phi+\varphi)\frac{\partial u}{\partial t} &- div(\kappa(\phi+\varphi, U+u)\nabla u) - div((\kappa(\phi+\varphi, U+u) - \kappa(\phi, U))\nabla U) \\ &= -e(\phi+\varphi)(p+P)(u-u_a) - d(\phi+\varphi)K_v(u) + r(\phi+\varphi)\eta + \xi \\ &\quad -(c(\phi+\varphi) - c(\phi))\frac{\partial U}{\partial t} - (e(\varphi+\phi)(p+P) - e(\phi)P)(U-U_a) \\ &\quad -(d(\varphi+\phi) - d(\phi))K_v(U) + (r(\varphi+\phi) - r(\phi))g \quad in \ \mathcal{Q}, \end{aligned}$$

subjected to the boundary condition (21)

$$\begin{aligned} (\kappa(\phi+\varphi, U+u)\nabla u).\mathbf{n} &+ ((\kappa(\phi+\varphi, U+u) - \kappa(\phi, U))\nabla U).\mathbf{n} = -q(u-u_b) \\ &-\lambda(x)((L(U+u) - L(U)) - (L(U_b+u_b) - L(U_b))) + \pi \quad in \ \Sigma, \end{aligned}$$

and the initial condition

$$u(0) = u_0 \ \ in \ \ \Omega.$$

If we set : $\tilde{L}(u) = L(U+u) - L(U)$, $\tilde{L}^b(u_b) = L(U_b + u_b) - L(U_b)$, and $\tilde{\beta}(\varphi) = \beta(\phi + \varphi)$, $\tilde{\kappa}(\varphi, u) = \kappa(\phi + \varphi, U + u)$, where the function β plays the role of c, d, e or r, then System (21) reduces to

$$\begin{aligned} \tilde{c}(\varphi)\frac{\partial u}{\partial t} &- div(\tilde{\kappa}(\varphi, u)\nabla u) - div((\tilde{\kappa}(\varphi, u) - \tilde{\kappa}(0,0))\nabla U) \\ &= -\tilde{e}(\varphi)(p+P)(u-u_a) - \tilde{d}(\varphi)K_v(u) + \tilde{r}(\varphi)\eta + \xi \\ &\quad -(\tilde{c}(\varphi) - \tilde{c}(0))\frac{\partial U}{\partial t} - (\tilde{e}(\varphi)(p+P) - \tilde{e}(0)P)(U-U_a) \\ &\quad -(\tilde{d}(\varphi) - \tilde{d}(0))K_v(U) + (\tilde{r}(\varphi) - \tilde{r}(0))g \quad in \ \mathcal{Q}, \end{aligned} \tag{22}$$

subjected to the boundary condition

$$(\tilde{\kappa}(\varphi,u)\nabla u).\mathbf{n} + ((\tilde{\kappa}(\varphi,u) - \tilde{\kappa}(0,0))\nabla U).\mathbf{n} \\ = -q(u - u_b) - \lambda(x)(\tilde{L}(u) - \tilde{L}^b(u_b)) + \pi \quad in \ \Sigma,$$

and the initial condition

$$u(0) = u_0 \ \ in \ \ \Omega.$$

Remark 5 **(i)** *We can easily verify that $\tilde{c},\tilde{d},\tilde{e},\tilde{r}$ and $\tilde{\kappa}$ satisfy the same hypothesis that c,d,e,r and κ i.e. the assumptions (H1)-(H3).*

(ii) *For simplicity of future reference, we omit the " ~ " on $\tilde{L}$, $\tilde{L}^b$, $\tilde{c},\tilde{d},\tilde{e},\tilde{r}$ and $\tilde{\kappa}$ for the system (22).*

In the sequel we assume that

$$(U_a,\phi) \in L^\infty(\mathcal{Q}) \times L^\infty(\Omega), \ \ (U_b,q) \in \mathcal{R}_2(\Sigma) \ \ \text{and} \ \ U \in \tilde{\mathcal{S}}(\mathcal{Q}). \tag{23}$$

Now we show the existence and uniqueness of the solution to the problem (22), and give some Lipschitz continuity results.

Theorem 4 *Let assumptions (H1)(H2) be fulfilled (with remark 5) and (U_a,ϕ,U_b,q) be given such that (23). We have the following results.*
(i) For the initial condition u_0 in $L^2(\Omega)$ and source terms (p,φ,ξ,η,π) in $L^\infty(\mathcal{Q}) \times L^\infty(\Omega) \times (L^2(\mathcal{Q}))^2 \times L^2(\Sigma)$. There exists a unique solution u in $\mathcal{W}(\mathcal{Q}) \cap \mathcal{H}(\mathcal{Q})$ of (22) satisfying the following regularity: $\mid u \mid^3 u \in L^{\frac{5}{4}}(\Sigma)$.
(ii) Let $(p_i,\varphi_i,\xi_i,\eta_i,\pi_i,u_{0i})$, i=1,2 be two functions of $L^\infty(\mathcal{Q}) \times L^\infty(\Sigma) \times (L^2(\mathcal{Q}))^2 \times L^2(\Sigma) \times L^2(\Omega)$. If $u_i \in \mathcal{W}(\mathcal{Q}) \cap \mathcal{H}(\mathcal{Q})$ is the solution of (22) corresponding to data $(p_i,\varphi_i,\xi_i,\eta_i,\pi_i,u_{0i})$, i=1,2, then

$$\| u \|^2_{\mathcal{H}(\mathcal{Q})\cap\mathcal{V}(\mathcal{Q})} \leq C_1(\| p \|^2_{L^2(\mathcal{Q})} + \| \xi \|^2_{L^2(\mathcal{Q})}) \\ +C_2(\| \varphi \|^2_{L^2(\Omega)} + \| \eta \|^2_{L^2(\mathcal{Q})} + \| \pi \|^2_{L^2(\Sigma)}) + C_3 \| u_0 \|^2_{L^2(\Omega)}, \tag{24}$$

where $u = u_1 - u_2, p = p_1 - p_2, \varphi = \varphi_1 - \varphi_2$, $\xi = \xi_1 - \xi_2$, $\eta = \eta_1 - \eta_2$, $\pi = \pi_1 - \pi_2$ and $u_0 = u_{01} - u_{02}$.

Proof. The proof of this result can be obtained by using a similar technique as in the proof of Theorem 1. So, we omit the details.

6. Robust control and regulation problems

In this section we formulate the robust control problem and study the existence and necessary optimality conditions for an optimal solution.

6.1 Formulation of the control problem

Our problem in this section is to find the best admissible perfusion function p and distributed energy source ξ in the presence of the worst disturbance in the porosity function φ, in the evaporation term π and in the metabolic heat generation type term η. We then suppose that the control is in $X = (p, \xi)$ and the disturbance is in $Y = (\varphi, \eta, \pi)$. Therefore, the function u is assumed to be related to the disturbance Y and control X through the problem

$$\begin{aligned} & c(\varphi)\frac{\partial u}{\partial t} - div(\kappa(\varphi,u)\nabla u) + e(\varphi)(p+P)(u-w_a) + d(\varphi)K_v(u) \\ & \qquad = div((\kappa(\varphi,u)-\kappa(0,0))\nabla U) + r(\varphi)\eta + \xi - (c(\varphi)-c(0))\frac{\partial U}{\partial t} \\ & \qquad\quad + e(0)Pv_a - (d(\varphi)-d(0))K_v(U) + (r(\varphi)-r(0))g \;\; in \;\; \mathcal{Q}, \end{aligned}$$

subjected to the boundary condition

$$\begin{aligned} (\kappa(\varphi,u)\nabla u).\mathbf{n} = & -((\kappa(\varphi,u)-\kappa(0,0))\nabla U).\mathbf{n} \\ & -q(u-u_b) - \lambda(x)(L(u) - L^b(u_b)) + \pi \;\; in \;\; \Sigma, \end{aligned} \tag{25}$$

and the initial condition

$$u(0) = u_0 \;\; in \;\; \Omega,$$

under pointwise constraints

$$\begin{aligned} \tau_1 \le p \le \tau_2 \;\; a.e. \; in \; \mathcal{Q}, \\ \delta_1 \le \varphi \le \delta_2 \;\; a.e. \; in \; \Omega, \end{aligned} \tag{26}$$

where $v_a = U - U_a$ and $w_a = u_a - v_a$, and $u_0 \in L^2(\Omega)$ is assumed to be given.
Let D_i, for $i = 1,2$ be the sets of functions describing the constraints (26) such that

$$D_1 = \{p \in L^2(\mathcal{Q}) : \; \tau_1 \le p \le \tau_2 \;\; a.e. \; in \; \mathcal{Q}\} \;\; \text{and} \;\; D_2 = \{\varphi \in L^2(\Omega) : \; \delta_1 \le \varphi \le \delta_2 \;\; a.e. \; in \; \Omega\},$$

and $\mathcal{K}_i$ for $i = 1,2$ be convex, closed, non-empty and bounded subset of $L^2(\mathcal{Q})$ and $\mathcal{K}_3$ be convex, closed, non-empty and bounded subset of $L^2(\Sigma)$. The studied control problem is to find a saddle point of the cost function $\mathcal{J}$ which measures the distance between the known observations $\mathfrak{m}_{obs}$ and D_{obs} (or known offsets which are given by experiment measurements) , corresponding to the online temperature control and thermal damage via radiometric temperature measurement system, respectively, and the prognostic variables $\gamma u + \delta p$ (in practice the parameters γ and δ satisfy $\gamma \approx \delta$ in muscle and $\gamma \ll \delta$ in fat) and the variation of cell damage function $(\mathcal{D}(x, u + U) - \mathcal{D}(x, U))$ (see paragraph 2.2). Precisely we will study the following robust control problem (**SP**).

find $(X, Y) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$ such that the cost functional (in the reduced form)

$$\begin{aligned} \mathcal{J}(X,Y) = & \frac{a}{2} \parallel (\gamma u + \delta p) - \mathfrak{m}_{obs} \parallel^2_{L^2(\mathcal{Q})} + \frac{b}{2} \parallel \int_0^T \tilde{\mathcal{H}}(t, u(.,t))dt - D_{obs} \parallel^2_{L^2(\Omega)} \\ & + \frac{\alpha}{2} \parallel \mathcal{N}X \parallel^2_{L^2(\mathcal{Q})\times L^2(\mathcal{Q})} - \frac{\beta}{2} \parallel \mathcal{M}Y \parallel^2_{L^2(\Omega)\times L^2(\mathcal{Q})\times L^2(\Sigma)} \end{aligned} \tag{27}$$

is minimized with respect to $X = (p, \xi)$ and maximized with respect to $Y = (\varphi, \eta, \pi)$ subject to the problem (25),

where $a + b > 0$ and $a, b \ge 0$, $\tilde{\mathcal{H}}(t, u) = \mathcal{H}(t, u + U) - \mathcal{H}(t, U)$ with the cell damage function $D(x, u) = \int_0^T \mathcal{H}(t, u(.,t))dt$ (see paragraph 2.2), the matrix $\mathcal{N} = diag(\sqrt{n_1}, \sqrt{n_2})$ and $\mathcal{M} =$

$diag(\sqrt{m_1}, \sqrt{m_2}, \sqrt{m_3})$, are predefined nonnegative weights such that $n_1 + n_2 \neq 0$ and $m_1 + m_2 + m_3 \neq 0, \mathcal{U}_{ad} = D_1 \times \mathcal{K}_1, \mathcal{V}_{ad} = D_2 \times \mathcal{K}_2 \times \mathcal{K}_3$ and $(\mathfrak{m}_{obs}, D_{obs})$ is the target. The coefficient $\alpha > 0$ can be interpreted as the measure of the price of the control (that the engineer can afford) and the coefficient $\beta > 0$ can be interpreted as the measure of the price of the disturbance (that the environnement can afford). The parameters γ, δ are positive with space-time dependent entries and are in $L^\infty(\overline{\mathcal{Q}})$.

Remark 6 *Although D_1 (respectively D_2) is a subset of $L^\infty(\mathcal{Q})$ (respectively of $L^\infty(\Omega)$), we prefer to use the standard norms of the space $L^2(\mathcal{Q})$ (respectively of $L^2(\Omega)$). The reason is that we would like to take advantages of the differentiability of the latter norm away from the origin to perform our variational analysis.*

6.2 Fréchet differentiability and existence result

Let us introduce the following mapping $\mathcal{F} : \mathcal{U}_{ad} \times \mathcal{V}_{ad} \longrightarrow \mathcal{Z} = \tilde{\mathcal{W}}(\mathcal{Q}) \cap \mathcal{H}(\mathcal{Q})$, which maps the source term $(X, Y) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$ of (25) into the corresponding solution u in $\mathcal{Z}$, and assume, in addition, that the assumption (**H**3) holds.
Following the development in (Belmiloudi, 2008), we start by calculating the variation of the operator solution $\mathcal{F}$. For this we suppose that the operator solution $\mathcal{F}$ is continuously differentiable (in weak sense) on $\mathcal{U}_{ad} \times \mathcal{V}_{ad}$ and its derivative (at point $(X, Y) = (p, \xi, \varphi, \eta, \pi)$) $\mathcal{F}'(X, Y) : (H, K) = (\mathfrak{y}, \mathfrak{h}, \psi, \mathfrak{e}, \mathfrak{z}) \in L^\infty(\mathcal{Q}) \times L^2(\mathcal{Q}) \times L^\infty(\Omega) \times L^2(\mathcal{Q}) \times L^2(\Sigma) \longrightarrow w = \mathcal{F}'(X, Y).(H, K) = \lim_{\epsilon \longrightarrow 0} \dfrac{\mathcal{F}(X + \epsilon H, Y + \epsilon K)}{\epsilon}$, where $(X + \epsilon H, Y + \epsilon K) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$, is such that $w = \dfrac{\partial \mathcal{F}}{\partial X}(X, Y)H + \dfrac{\partial \mathcal{F}}{\partial Y}(X, Y)K$ is the unique weak solution of the following system

$$
\begin{aligned}
& c'(\varphi)\frac{\partial(u+U)}{\partial t}\psi + c(\varphi)\frac{\partial w}{\partial t} - div(\kappa(\varphi, u)\nabla w) \\
& \quad -div((\frac{\partial \kappa}{\partial \varphi}(\varphi, u)\psi + \frac{\partial \kappa}{\partial u}(\varphi, u)w)\nabla(u+U)) \\
& \quad +e'(\varphi)\psi(p+P)(u-w_a) + e(\varphi)\mathfrak{y}(u-w_a) + e(\varphi)(p+P)w \\
& \quad +d'(\varphi)\psi K_v(u+U) + d(\varphi)K_v(w) = r'(\varphi)\psi(\eta+g) + r(\varphi)\mathfrak{e} + \mathfrak{h} \quad in \ \mathcal{Q}, \\
& \text{subjected to the boundary condition} \\
& (\kappa(\varphi, u)\nabla w).\mathbf{n} = -((\frac{\partial \kappa}{\partial \varphi}(\varphi, u)\psi + \frac{\partial \kappa}{\partial u}(\varphi, u)w)\nabla(U+u)).\mathbf{n} \\
& \qquad -qw - \lambda(x)L'(u)w + \mathfrak{z} \quad in \ \Sigma, \\
& \text{and the initial condition} \\
& w(0) = 0 \ in \ \Omega,
\end{aligned}
\tag{28}
$$

where $u = \mathcal{F}(X, Y)$. If we put $U_1 = u + U$, $P_1 = p + P$, $V_a = u - w_a$ and $G_1 = \eta - g$, the system (28) can be written as

$$
\begin{aligned}
c(\varphi)\frac{\partial w}{\partial t} & - div(\kappa(\varphi, u)\nabla w) - div((\frac{\partial \kappa}{\partial \varphi}(\varphi, u)\psi + \frac{\partial \kappa}{\partial u}(\varphi, u)w)\nabla U_1) + d(\varphi)K_v(w) \\
& +e(\varphi)P_1 w + e'(\varphi)\psi P_1 V_a + e(\varphi)\mathfrak{y} V_a \\
& +d'(\varphi)\psi K_v(U_1) = -c'(\varphi)\frac{\partial U_1}{\partial t}\psi + r'(\varphi)\psi G_1 + r(\varphi)\mathfrak{e} + \mathfrak{h} \quad in \ \mathcal{Q},
\end{aligned}
\tag{29}
$$

subjected to the boundary condition

$$(\kappa(\varphi,u)\nabla w).\mathbf{n} = -((\frac{\partial \kappa}{\partial \varphi}(\varphi,u)\psi + \frac{\partial \kappa}{\partial u}(\varphi,u)w)\nabla U_1).\mathbf{n} \\ -qw - \lambda(x)L'(u)w + \mathfrak{z} \quad in \;\; \Sigma,$$

and the initial condition

$$w(0) = 0 \;\; in \;\; \Omega.$$

Definition 3 *The system (28) (or (29)) satisfied by w is called the tangent linear model (TLM) or sensitivity problem and w is called sensitivity temperature.*

Using the minimax formulation (of *Ky Fan-von Neumann*) in infinite dimensions presented in chapter 5 of (Belmiloudi, 2008) (see also (Ekeland & Temam, 1976)), we have the following sufficient and necessary conditions for the existence and characterisation of a saddle point.

1. Sufficient conditions for the objective functional $\mathcal{J}$ to admit a saddle point are :
   a) The mapping $\mathcal{P}_Y : \;\; X \longrightarrow \mathcal{J}(X,Y)$ is convex and lower semi-continuous (in a weak topology), for all $Y \in \mathcal{V}_{ad}$.
   b) The mapping $\mathcal{R}_X : \;\; Y \longrightarrow \mathcal{J}(X,Y)$ is concave and upper semi-continuous (in a weak topology), for all $X \in \mathcal{U}_{ad}$.
2. Necessary optimality conditions for a saddle point $(X^*,Y^*) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$ of $\mathcal{J}$, if $\mathcal{P}_Y$ and $\mathcal{R}_X$ are Gâteaux differentiable, are

$$\frac{\partial \mathcal{J}}{\partial X}(X^*,Y^*).(X - X^*) \geq 0 \quad \forall X \in \mathcal{U}_{ad}, \\ \frac{\partial \mathcal{J}}{\partial Y}(X^*,Y^*).(Y - Y^*) \leq 0 \quad \forall Y \in \mathcal{V}_{ad}. \tag{30}$$

From the expression of the cost functional $\mathcal{J}$, which is a composition of Gâteaux differentiable mappings, it follows that $\mathcal{P}_Y$ and $\mathcal{R}_X$ are Gâteaux differentiable. Consequently, in order to prove the convexity of $\mathcal{P}_Y$ (respectively the concavity of $\mathcal{R}_X$), it is sufficient to show that for all $(X_1,X_2) \in \mathcal{U}_{ad} \times \mathcal{U}_{ad}$ (respectively for all $(Y_1,Y_2) \in \mathcal{V}_{ad} \times \mathcal{V}_{ad}$), we have

$$(\mathcal{P}'_Y(X_1) - \mathcal{P}'_Y(X_2)).(X_1 - X_2) \geq 0 \;\; \text{(respectively } (\mathcal{R}'_X(Y_1) - \mathcal{R}'_X(Y_2)).(Y_1 - Y_2) \leq 0)\text{)},$$

where for $i = 1,2$ and for all $(H,K) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$

$$\mathcal{P}'_Y(X_i)H = \lim_{\epsilon \longrightarrow 0} \frac{\mathcal{J}(X_i + \epsilon H, Y) - \mathcal{J}(X_i, Y)}{\epsilon}, \quad \mathcal{R}'_X(Y_i)K = \lim_{\epsilon \longrightarrow 0} \frac{\mathcal{J}(X, Y_i + \epsilon K) - \mathcal{J}(X, Y_i)}{\epsilon}.$$

Using similar arguments as in Chapter 8 of (Belmiloudi, 2008), we can prove that : *there exist constants α_l and β_l such that for all $\alpha \geq \alpha_l$ and $\beta \geq \beta_l$, the operators $\mathcal{P}_Y$ and $\mathcal{R}_X$ are convex and concave, respectively.* We shall prove now that $\mathcal{P}_Y$ (respectively $\mathcal{R}_X$) is lower (respectively upper) semi-continuous for all $Y \in \mathcal{V}_{ad}$ (respectively $X \in \mathcal{U}_{ad}$). Let $X_k \in \mathcal{U}_{ad}$ be a minimizing sequence of $\mathcal{P}_Y$, i.e.,

$$\liminf_{k \longrightarrow \infty} \mathcal{J}(X_k, Y) = \inf_{X \in (L^2(\mathcal{Q}))^2} \mathcal{J}(X, Y).$$

Then, according to the nature of the cost function $\mathcal{J}$, we can deduce that X_k is uniformly bounded in $\mathcal{U}_{ad}$ and we can extract from X_k a subsequence also denoted by X_k such that $X_k \rightharpoonup X_Y$ weakly in $\mathcal{U}_{ad}$. Therefore, by using the same technique as to obtain the estimate (24), the function $u_k = \mathcal{F}(X_k, Y)$ is uniformly bounded in $\mathcal{W}(\mathcal{Q}) \cap \mathcal{H}(\mathcal{Q})$. Consequently, since the injection of $\mathcal{W}(\mathcal{Q})$ into $L^2(\mathcal{Q})$ is compact, these results make it possible to extract from u_k a subsequence also denoted by u_k such that

$$\begin{aligned} & u_k \rightharpoonup u_Y \textit{ weakly in } L^2(0,T;V), \\ & u_k \longrightarrow u_Y \textit{ strongly in } L^2(\mathcal{Q}), \\ & X_k \rightharpoonup X_Y \textit{ weakly in } L^2(\mathcal{Q}) \text{ and } X_Y \in \mathcal{U}_{ad}. \end{aligned} \tag{31}$$

It is easy to prove that u_Y is a solution of (25) with data (X_Y, Y) and according to the uniqueness of the solution of the direct problem (25), we have then $u_Y = \mathcal{F}(X_Y, Y)$. Therefore, since the norm is lower semi-continuous, we have that the map $\mathcal{P}_Y$ is lower semi-continuous for all $Y \in \mathcal{V}_{ad}$. By applying similar argument as in the proof of the previous result we obtain that $\mathcal{R}_X$ is upper semi-continuous for all $X \in \mathcal{U}_{ad}$ (in this case we consider a maximizing sequence $X_k \in \mathcal{U}_{ad}$ of $\mathcal{R}_X$, i.e., $\limsup_{k \longrightarrow \infty} \mathcal{J}(X_k, Y) = \sup_{Y \in \mathcal{Y}_2} \mathcal{J}(\mathcal{X}, \mathcal{Y})$, where $\mathcal{Y}_2 = L^2(\Omega) \times L^2(\mathcal{Q}) \times L^2(\Sigma))$.

In conclusion we have that: *for α and β sufficiently large there exists an optimal solution $(X^*, Y^*) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$ and $u^* \in \mathcal{Z}$ such that (X^*, Y^*) is a saddle point of $\mathcal{J}$ and $u^* = \mathcal{F}(X^*, Y^*)$.*

Remark 7

- *To obtain the uniqueness of the optimal solution we can use similar assumption about sufficiently small final time T as e.g. in (Belmiloudi, 2005).*
- *If we assume in addition that the operator c, d, e, r and κ are twice differentiable, we can also derive the uniqueness result by proving the strict convexity of the functional $\mathcal{P}_Y$ and the strict convexity of the functional $\mathcal{R}_X$, which are equivalent to showing*

  $$\Psi_Y''(\epsilon) > 0 \textit{ and } \Phi_X''(\epsilon) < 0 \quad \forall \epsilon \in [0,1],$$

  where $\Psi(\epsilon) = \mathcal{J}(\epsilon X + (1-\epsilon)\overline{X}, Y)$, $\Phi(\epsilon) = \mathcal{J}(X, \epsilon Y + (1-\epsilon)\overline{Y})$, for $X, \overline{X}$ given in $\mathcal{U}_{ad}$ and $Y, \overline{Y}$ given in $\mathcal{V}_{ad}$. More precisely,

  "If the coefficients α, β are sufficiently large, i.e. if there exists (α_L, β_L) such that $\alpha \geq \alpha_l \geq \alpha_L$ and $\beta \geq \beta_l \geq \beta_L$, then the robust control problem admits one unique solution."

- *According to the previous results, we can deduce that*

  "If there exists (α_L, β_L) such that $\alpha \geq \alpha_l \geq \alpha_L$ and $\beta \geq \beta_l \geq \beta_L$, or if the final time T is sufficiently small, $\alpha \geq \alpha_l$ and $\beta \geq \beta_l$, then the robust control problem admits one unique solution."

In order to solve the saddle problem (27) it is necessary to derive the gradient $\mathcal{J}'(X, Y)$ of the cost functional $\mathcal{J}$ with respect to the control-disturbance (X, Y). To this end, let us introduce the directional derivative $\mathcal{J}'(X,Y).(H,K)$, where $X=(p,\xi)$, $Y=(\varphi,\eta,\pi)$, $H=(\mathfrak{y},\mathfrak{h})$ and $K=(\psi,\mathfrak{e},\mathfrak{z})$ by

$$\begin{aligned}\mathcal{J}'(X,Y).(H,K) &= \frac{d}{d\mathfrak{s}}\mathcal{J}(X+\mathfrak{s}H,Y+\mathfrak{s}K)|_{\mathfrak{s}=0}\\ &= a\iint_Q((\gamma u+\delta p)-\mathfrak{m}_{obs})(\gamma w+\delta\mathfrak{y})\,dxdt\\ &\quad +b\int_\Omega(\int_0^T\tilde{\mathcal{H}}(t,u(.,t))\,dt-D_{obs})(\int_0^T\tilde{\mathcal{H}}'(t,u(.,t))w\,dt)\,dx\\ &\quad +\alpha(n_1\iint_Q p\mathfrak{y}\,dxdt+n_2\iint_Q\xi\mathfrak{h}\,dxdt)\\ &\quad -\beta(m_1\int_\Omega\varphi\psi\,dx+m_2\iint_Q\eta\mathfrak{e}\,dxdt+m_3\iint_\Sigma\pi\mathfrak{z}\,d\Gamma dt),\end{aligned} \tag{32}$$

where $w=\mathcal{F}'(X,Y).(H,K)$ is the solution of the sensitivity problem (6.2) and $\tilde{\mathcal{H}}'$ is the differential of $\tilde{\mathcal{H}}$ at the second variable u.

Remark 8 *Since $\tilde{\mathcal{H}}(t,u)=\mathcal{H}(t,U+u)-\mathcal{H}(t,U)$ then $\tilde{\mathcal{H}}'(t,u)=\mathcal{H}'(t,U+u)$. Consequently, for example in the case of Arrhenius model, we have that $\tilde{\mathcal{H}}'(t,u)=\dfrac{E}{R(U+u)^2}\mathcal{H}(t,U+u)$.*

It is clear from (32) that the main difficulty is the simplification of the directional derivative $\mathcal{J}'(X,Y).(H,K)$, which requires the introduction of the adjoint (or dual problem) to the sensitivity state corresponding to the direct problem (25). The adjoint model and the evaluation of the gradient of $\mathcal{J}$ are given in the next section.

6.3 Adjoint model and gradient

Let $\tilde{u}$ be a sufficiently regular function such that $\tilde{u}(T)=0$. Multiplying the first part of (29) by $\tilde{u}$ and integrating with respect to space and time, and using Green's formula, we obtain according to the second part of (29) (the boundary condition) that (since $c(\varphi)$ is independent on time)

$$\begin{aligned}&\iint_Q -c(\varphi)\frac{\partial\tilde{u}}{\partial t}w\,dxdt+\int_\Omega(c(\varphi)(\tilde{u}(T)w(T)-\tilde{u}(0)w(0))\,dx\\ &\quad+\iint_\Sigma(qw+\lambda(x)L'(u)w-\mathfrak{z})\tilde{u}\,d\Gamma dt+\iint_\Sigma\kappa(\varphi,u)\nabla\tilde{u}.\mathbf{n}w\,d\Gamma dt\\ &\quad+\iint_Q(\frac{\partial\kappa}{\partial\varphi}(\varphi,u)\psi+\frac{\partial\kappa}{\partial u}(\varphi,u)w)\nabla U_1.\nabla\tilde{u}\,dxdt-\iint_Q div(\kappa(\varphi,u)\nabla\tilde{u})w\,dxdt\\ &\quad+\iint_Q d(\varphi)K_v(w)\tilde{u}\,dxdt+\iint_Q e(\varphi)P_1\tilde{u}w\,dxdt\\ &\qquad=-\iint_Q(e'(\varphi)P_1V_a+c'(\varphi)\frac{\partial U_1}{\partial t}+d'(\varphi)K_v(U_1)-r'(\varphi)G_1)\psi\tilde{u}\,dxdt\\ &\qquad\quad-\iint_Q e(\varphi)V_a\tilde{u}\mathfrak{y}\,dxdt+\iint_Q r(\varphi)\tilde{u}\mathfrak{e}\,dxdt+\iint_Q\tilde{u}\mathfrak{h}\,dxdt.\end{aligned} \tag{33}$$

According to (18) we can deduce that

$$\iint_Q d(\varphi)K_v(w)\tilde{u}\,dxdt=\iint_Q K_v^*(d(\varphi)\tilde{u})w dx+\iint_\Sigma d(\varphi)\tilde{u}\vec{\vartheta}.\mathbf{n}w\,d\Gamma dt. \tag{34}$$

Since $\tilde{u}(T) = 0$, $w(0) = 0$ and according to (34), we obtain (since ψ is independent on time)

$$\begin{aligned}
&\int\int_Q \left(-c(\varphi)\frac{\partial \tilde{u}}{\partial t} - div(\kappa(\varphi,u)\nabla\tilde{u}) + K_v^*(d(\varphi)\tilde{u}) + e(\varphi)P_1\tilde{u} + \frac{\partial\kappa}{\partial u}(\varphi,u)\nabla U_1.\nabla\tilde{u} \right) w\, dxdt \\
&\quad + \int\int_\Sigma (q\tilde{u} + \lambda(x)L'(u)\tilde{u} + \kappa(\varphi,u)\nabla\tilde{u}.\mathbf{n} + d(\varphi)\tilde{u}\vec{\vartheta}.\mathbf{n}) w\, d\Gamma dt \\
&\quad = -\int_\Omega \left(\int_0^T (e'(\varphi)P_1V_a + c'(\varphi)\frac{\partial U_1}{\partial t} + d'(\varphi)K_v(U_1) - r'(\varphi)G_1)\tilde{u}dt \right) \psi\, dx \\
&\qquad - \int_\Omega \left(\int_0^T \frac{\partial\kappa}{\partial\varphi}(\varphi,u)\nabla U_1.\nabla\tilde{u}dt \right) \psi\, dx \\
&\qquad - \int\int_Q e(\varphi)V_a\tilde{u}\mathfrak{y}\, dxdt + \int\int_Q r(\varphi)\tilde{u}\mathfrak{e}\, dxdt + \int\int_Q \tilde{u}\mathfrak{h}\, dxdt + \int\int_\Sigma \mathfrak{z}\tilde{u}\, d\Gamma dt.
\end{aligned} \tag{35}$$

In order to simplify the problem (35), we assume that $\tilde{u}$ satisfies the following so-called adjoint problem (with initial value given at final time T)

$$\left\{\begin{aligned}
&-c(\varphi)\frac{\partial\tilde{u}}{\partial t} - div(\kappa(\varphi,u)\nabla\tilde{u}) + K_v^*(d(\varphi)\tilde{u}) + e(\varphi)P_1\tilde{u} + \frac{\partial\kappa}{\partial u}(\varphi,u)\nabla U_1.\nabla\tilde{u} \\
&\qquad + a\gamma(\gamma u + \delta p - \mathfrak{m}_{obs}) + b(\int_0^T \tilde{\mathcal{H}}(t,u(.,t))\, dt - D_{obs})\tilde{\mathcal{H}}'(.,u) = 0 \quad in \ \mathcal{Q}, \\
&\text{subjected to the boundary condition} \\
&-\kappa(\varphi,u)\nabla\tilde{u}.\mathbf{n} = q\tilde{u} + \lambda(x)L'(u)\tilde{u} + d(\varphi)\tilde{u}\vec{\vartheta}.\mathbf{n} \quad in \ \Sigma, \\
&\text{and the final condition} \\
&\tilde{u}(T) = 0 \ \ in \ \ \Omega.
\end{aligned}\right. \tag{36}$$

Remark 9

1. *We point out that : if the function $\tilde{\mathcal{H}}$ is a Carathéodory function from $\mathbb{R} \times \mathbb{R}$ into $\mathbb{R}^+$ and $\tilde{\mathcal{H}}(t,.)$ is Lipschitz, differentiable, bounded function and its partial derivative is Lipschitz and bounded function (for almost all $t \in (0,T)$), the adjoint problem (36), which is backward in time, can be transformed into an initial-boundary value problem by the time transformation $t := T - t$, which allows to employ similar argument as in the proof of Theorem 1 for the existence of a unique solution $\tilde{u}$ of (36) for a sufficiently regular data. So, we omit the details.*
2. *In the sequel we denote by $\mathcal{F}^\perp(X,Y) = \tilde{u}$ the solution of the adjoint problem (36) corresponding to the direct solution $u = \mathcal{F}(X,Y)$.*

Using the system (36), the problem (35) becomes

$$\begin{aligned}
&\int\int_Q - \left(a\gamma(\gamma u + \delta p - \mathfrak{m}_{obs}) + b(\int_0^T \tilde{\mathcal{H}}(t,u(.,t))\, dt - D_{obs})\tilde{\mathcal{H}}'(.,u) \right) w\, dxdt \\
&\quad = -\int_\Omega \left(\int_0^T (e'(\varphi)P_1V_a + c'(\varphi)\frac{\partial U_1}{\partial t} + d'(\varphi)K_v(U_1) - r'(\varphi)G_1)\tilde{u}dt \right) \psi\, dx \\
&\qquad - \int_\Omega \left(\int_0^T \frac{\partial\kappa}{\partial\varphi}(\varphi,u)\nabla U_1.\nabla\tilde{u}dt \right) \psi\, dx \\
&\qquad - \int\int_Q e(\varphi)V_a\tilde{u}\mathfrak{y}\, dxdt + \int\int_Q r(\varphi)\tilde{u}\mathfrak{e}\, dxdt + \int\int_Q \tilde{u}\mathfrak{h}\, dxdt + \int\int_\Sigma \mathfrak{z}\tilde{u}\, d\Gamma dt.
\end{aligned} \tag{37}$$

According to the expression (32) of $\mathcal{J}'(X,Y)$ we can deduce that

$$\begin{aligned}
\mathcal{J}'(X,Y).(H,K) &= \frac{\partial \mathcal{J}}{\partial X}(X,Y).H + \frac{\partial \mathcal{J}}{\partial Y}(X,Y).K \\
&= \iint_{\mathcal{Q}} (e(\varphi)V_a\tilde{u} + \alpha n_1 p + a\delta(\gamma u + \delta p - \mathfrak{m}_{obs}))\mathfrak{y}\, dxdt + \iint_{\mathcal{Q}} (n_2\xi - \tilde{u})\mathfrak{h}\, dxdt \\
&\quad + \int_{\Omega} (\mathcal{E}(\varphi, U_1, \tilde{u}) - \beta m_1 \varphi)\psi\, dx - \iint_{\mathcal{Q}} (r(\varphi)\tilde{u} + \beta m_2 \eta)\mathfrak{e}\, dxdt \\
&\quad - \iint_{\Sigma} (\tilde{u} + \beta m_3 \pi)\mathfrak{z}\, d\Gamma dt,
\end{aligned} \tag{38}$$

where

$$\begin{aligned}
\mathcal{E}(\varphi, U_1, \tilde{u}) = \int_0^T (e'(\varphi)P_1 V_a + c'(\varphi)\frac{\partial U_1}{\partial t} + d'(\varphi)K_v(U_1) - r'(\varphi)G_1)\tilde{u}dt \\
+ \int_0^T \frac{\partial \kappa}{\partial \varphi}(\varphi, u)\nabla U_1.\nabla \tilde{u}dt.
\end{aligned} \tag{39}$$

Consequently the gradient of $\mathcal{J}$ at point (X,Y), in weak sense, is

$$\begin{aligned}
\frac{\partial \mathcal{J}}{\partial X}(X,Y) &= \begin{pmatrix} e(\varphi)V_a\tilde{u} + \alpha n_1 p + a\delta(\gamma u + \delta p - \mathfrak{m}_{obs}) \\ n_2\xi - \tilde{u} \end{pmatrix}, \\
\frac{\partial \mathcal{J}}{\partial Y}(X,Y) &= \begin{pmatrix} \mathcal{E}(\varphi, U_1, \tilde{u}) - \beta m_1 \varphi \\ -(r(\varphi)\tilde{u} + \beta m_2 \eta) \\ -(\tilde{u} + \beta m_3 \pi) \end{pmatrix}.
\end{aligned} \tag{40}$$

We next wish to show the appropriate first-order necessary optimality conditions of the saddle point (X^*, Y^*) of the functional $\mathcal{J}$, by using the characterization (30).

6.4 First-order optimality conditions

Let $(X^*, Y^*) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$ and $u^* \in \mathcal{Z}$ be an optimal solution such that (X^*, Y^*) is a saddle point of $\mathcal{J}$ and $u^* = \mathcal{F}(X^*, Y^*)$ is the solution of (22). Then according to (30) and the expression (38) of $\mathcal{J}'$ we can deduce that, for all $(X,Y) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$

$$\begin{aligned}
\frac{\partial \mathcal{J}}{\partial X}(X^*, Y^*).(X - X^*) &= \iint_{\mathcal{Q}} (e(\varphi^*)V_a^*\tilde{u}^* + \alpha n_1 p^* + a\delta(\gamma u^* + \delta p^* - \mathfrak{m}_{obs}))(p - p^*)dxdt \\
&\quad + \iint_{\mathcal{Q}} (n_2\xi^* - \tilde{u}^*)(\xi - \xi^*)\, dxdt \geq 0 \\
\frac{\partial \mathcal{J}}{\partial Y}(X^*, Y^*).(Y - Y^*) &= \int_{\Omega} (\mathcal{E}(\varphi^*, U_1^*, \tilde{u}^*) - \beta m_1 \varphi^*)(\varphi - \varphi^*)\, dx \\
&\quad - \iint_{\mathcal{Q}} (r(\varphi^*)\tilde{u}^* + \beta m_2 \eta^*)(\eta - \eta^*)\, dxdt \\
&\quad - \iint_{\Sigma} (\tilde{u}^* + \beta m_3 \pi^*)(\pi - \pi^*)\, d\Gamma dt \leq 0
\end{aligned} \tag{41}$$

where $U_1^* = u^* + U$, $P_1^* = p^* + P$, $V_a^* = u^* - w_a$, $G_1^* = \eta^* - g$ and $\tilde{u}^* = \mathcal{F}^{\perp}(X^*, Y^*)$ is the solution of the adjoint problem (36).

6.5 Optimization procedure

By using the successive resolutions of both the direct problem and the adjoint problem, we can therefore calculate the gradient of the objective function relative to the control-disturbance functions X and Y. Once the gradient of the objective function $\mathcal{J}$, $\nabla\mathcal{J}$, is known, we can seek a saddle point of $\mathcal{J}$. For a given observation $(\mathfrak{m}_{obs}, D_{obs})$ for the outline temperature and thermal damage, the optimization algorithm is summarized in Table 1.

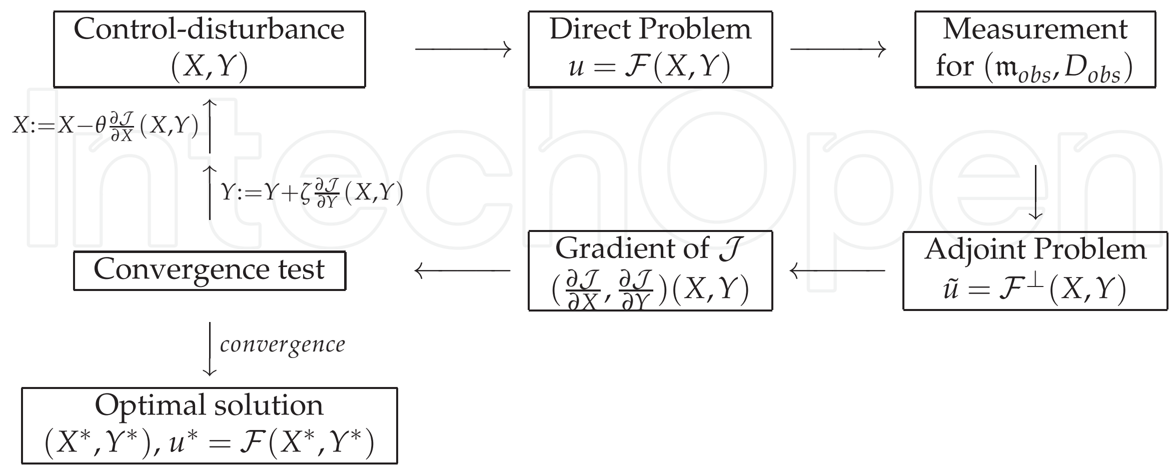


Table 1. Optimization algorithm : $\mathcal{J}$ is optimized until some convergence criteria are attained.

7. Finite number of measurements and different tissues

7.1 Finite number of measurements

In many situations, we can measure the online temperature $\mathfrak{m}_{obs}$ and the thermal damage D_{obs} in only some points in space-time domain. Let now some points be in $\Omega \times (0,T)$ where we assume that we can measure $(\mathfrak{m}_{obs}, D_{obs})$. Let $x_i \in \Omega, i = 1, \cdots l$ such that $x_i \neq x_j$ if $i \neq j$, $0 < t_1 < t_2 < \cdots < T$, and assume that we measure quantity ϵ_{ij} and $\mathfrak{d}_i$ which are meant to be the value of the functions $(\gamma u + \delta p)$ at point (x_i, t_j) and $\int_0^T \tilde{\mathcal{H}}(t, u(.,t))dt$ at point x_i denoted by $M(x_i, t_j)$, for $i = 1, \ldots, l$ and $j = 1, \ldots, N$ and $D(x_i)$, for $i = 1, \ldots, l$, respectively. Let $(\Omega_i)_{i=1,l}$ be a sequence of disjointed small ball in Ω such that $x_i \in \Omega_i$, $\forall i = 1, \ldots, l$. Let $(I_j)_{j=1,N}$ be also a sequence of disjoint intervals in $(0,T)$ such that $t_j \in I_j$, $\forall j = 1, \ldots, N$. We introduce the following average operators over the domains Ω_i and $\mathcal{Q}_{ij} = \Omega_i \times I_j$ (for $i = 1, \ldots, l$, $j = 1, \ldots, N$) by

$$< v >_{ij} = \frac{1}{meas(\mathcal{Q}_{ij})} \int_{\mathcal{Q}_{ij}} v(x,t)dxdt \ \text{ and } \ < v >_i = \frac{1}{meas(\Omega_i)} \int_{\Omega_i} v(x)dx,$$

respectively, and we propose the following cost function ($(X,Y) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$)

$$\begin{aligned} \mathcal{J}(X,Y) = & \frac{a}{2} \sum_{i=1,l} \sum_{j=1,N} |< M >_{ij} - \epsilon_{ij}|^2 + \frac{b}{2} \sum_{i=1,l} |< D >_i - \mathfrak{d}_i|^2 \\ & + \frac{\alpha}{2} \| \mathcal{N}X \|^2_{L^2(\mathcal{Q}) \times L^2(\mathcal{Q})} - \frac{\beta}{2} \| \mathcal{M}Y \|^2_{L^2(\Omega) \times L^2(\mathcal{Q}) \times L^2(\Sigma)} . \end{aligned} \tag{42}$$

Let χ_D be the usual characteristic function of a domain D i.e. $\chi_D = 1$ on D, and 0 outside of D. Let $\mathcal{L}_T : L^2(\mathcal{Q}) \longrightarrow L^2(\mathcal{Q})$ and $\mathcal{L}_D : L^2(\Omega) \longrightarrow L^2(\Omega)$ be defined by ($\forall v \in L^2(\mathcal{Q})$ and $w \in L^2(\Omega)$)

$$\mathcal{L}_T(v) = \sum_{i=1,l} \sum_{j=1,N} \frac{1}{meas(\mathcal{Q}_{ij})} \chi_{\mathcal{Q}_{ij}} < v >_{ij}, \ \ \mathcal{L}_D(w) = \sum_{i=1,l} \frac{1}{meas(\Omega_i)} \chi_{\Omega_i} < w >_i \tag{43}$$

and

$$\epsilon = \sum_{i=1,l}\sum_{j=1,N} \frac{1}{meas(\mathcal{Q}_{ij})}\chi_{\mathcal{Q}_{ij}}\epsilon_{ij}, \ \ \mathfrak{d} = \sum_{i=1,l} \frac{1}{meas(\Omega_i)}\chi_{\Omega_i}\mathfrak{d}_i. \tag{44}$$

By using the same technique as in the proof of the results of the previous section, we can prove the existence theorem of the control problem and obtain necessary optimality conditions as follows.

For α and β sufficiently large there exists an optimal solution $(X^*, Y^*) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$ and $u^* \in \mathcal{Z}$ such that (X^*, Y^*) is a saddle point of $\mathcal{J}$ and $u^* = \mathcal{F}(X^*, Y^*)$ is the solution of (25). Moreover, the optimal solution (X^*, Y^*) is characterized by (for all $(X, Y) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$)

$$\begin{aligned}\frac{\partial \mathcal{J}}{\partial X}(X^*, Y^*).(X - X^*) = &\iint_{\mathcal{Q}} (e(\varphi^*)V_a^*\tilde{u}^* + \alpha n_1 p^* + a\delta(\mathcal{L}_T(M^*) - \epsilon))(p - p^*)dxdt \\ &+ \iint_{\mathcal{Q}} (n_2\xi^* - \tilde{u}^*)(\xi - \xi^*)\, dxdt \geq 0 \\ \frac{\partial \mathcal{J}}{\partial Y}(X^*, Y^*).(Y - Y^*) = &\int_{\Omega} (\mathcal{E}(\varphi^*, U_1^*, \tilde{u}^*) - \beta m_1\varphi^*)(\varphi - \varphi^*)\, dx \\ &- \iint_{\mathcal{Q}} (r(\varphi^*)\tilde{u}^* + \beta m_2\eta^*)(\eta - \eta^*)\, dxdt \\ &- \iint_{\Sigma} (\tilde{u}^* + \beta m_3\pi^*)(\pi - \pi^*)\, d\Gamma dt \leq 0\end{aligned}$$

where $U_1^* = u^* + U$, $P_1^* = p^* + P$, $V_a^* = u^* - w_a$, $G_1^* = \eta^* - g$, $\mathcal{E}$ is given in (39) and $\tilde{u}^* = \mathcal{F}^{\perp}(X^*, Y^*)$ is the solution of the following adjoint problem

$$\begin{aligned}-c(\varphi^*)\frac{\partial \tilde{u}^*}{\partial t} - div(\kappa(\varphi^*, u^*)\nabla\tilde{u}^*) + K_v^*(d(\varphi^*)\tilde{u}^*) + e(\varphi^*)P_1\tilde{u}^* + \frac{\partial \kappa}{\partial u}(\varphi^*, u^*)\nabla U_1^*.\nabla\tilde{u}^* \\ + a\gamma(\mathcal{L}_T(M^*) - \epsilon) + b(\mathcal{L}_D(D^*) - \mathfrak{d})\tilde{\mathcal{H}}'(., u^*) = 0 \quad in \ \ \mathcal{Q},\end{aligned}$$

subjected to the boundary condition

$$-\kappa(\varphi^*, u^*)\nabla\tilde{u}^*.\mathbf{n} = q\tilde{u}^* + \lambda(x)L'(u^*)\tilde{u}^* + d(\varphi^*)\tilde{u}^*\vec{\vartheta}.\mathbf{n} \quad in \ \ \Sigma,$$

and the final condition

$$\tilde{u}(T) = 0 \ \ in \ \ \Omega.$$

7.2 Union of finite number of different tissue types

Suppose now that the body is constituted by different tissue types which occupy finitely many disjointed subdomains Ω_i, $i = 1, ..., N_D$, of Ω, such that $\overline{\Omega} = \bigcup_{i=1,N_D}\overline{\Omega}_i$. Moreover we assume that the perfusion acts continuously according to the temperature in each domain Ω_i and discontinuously at tissue boundaries. We propose the following cost function

$$\begin{aligned}\mathcal{J}(X, Y) = \frac{a}{2} \parallel (\gamma u + \delta p) - \mathfrak{m}_{obs} \parallel^2_{L^2(\mathcal{Q})} + \frac{b}{2} \parallel \int_0^T \tilde{\mathcal{H}}(t, u(., t))dt - D_{obs} \parallel^2_{L^2(\Omega)} \\ + \frac{\alpha}{2} \parallel \mathcal{N}X \parallel^2_{L^2(0,T,\mathcal{R})\times L^2(\mathcal{Q})} - \frac{\beta}{2} \parallel \mathcal{M}Y \parallel^2_{L^2(\Omega)\times L^2(\mathcal{Q})\times L^2(\Sigma)}\end{aligned}$$

where $(X, Y) \in \tilde{\mathcal{U}}_{ad} \times \mathcal{V}_{ad}$, $\tilde{\mathcal{U}}_{ad} = (L^2(0, T, \mathcal{R}) \cap D_1) \times \mathcal{K}_1$ and $\mathcal{R}$ is the Hilbert space

$$\{v \in L^2(\Omega), |v \in H^1(\Omega_i), \ for \ i = 1, ..., N_D\}$$

equipped with the following norm and its corresponding scalar product:

$$\| v \|_{\mathcal{R}} = \Big(\sum_{i=1,N_D} (\alpha_1 \| v \|^2_{L^2(\Omega_i)} + \alpha_2 \| \nabla v \|^2_{L^2(\Omega_i)}) \Big)^{1/2},$$

$$< v, w >_{\mathcal{R}} = \sum_{i=1,N_D} \Big(\alpha_1 \int_{\Omega_i} vw \, d\Omega_i + \alpha_2 \int_{\Omega_i} \nabla v . \nabla w \, d\Omega_i \Big),$$

with the fixed constants $\alpha_i > 0$ for $i = 1, 2$.
Let the linear operator $\Lambda : L^2(\Omega) \longrightarrow \mathcal{R}$ be defined by $(\forall v \in L^2(\Omega))$ $\pi = \Lambda(v)$ is the solution of

$$\begin{aligned} -\alpha_2 \Delta \pi_i + \alpha_1 \pi_i = v|_{\Omega_i}, \;\; in \; \Omega_i \\ \frac{\partial \pi_i}{\partial n} = 0 \;\; on \; \partial\Omega_i, \end{aligned} \tag{45}$$

where $\pi_i = \pi$, *a.e. in* Ω_i and $v|_{\Omega_i}$ denotes the restriction of v on the subdomain Ω_i, for $i = 1, ..., N_D$.
By using the same technique as in the previous section, we can derived the existence of an optimal solution and its necessary optimality conditions as follows.

For α and β sufficiently large there exists an optimal solution $(X^*, Y^*) \in \tilde{\mathcal{U}}_{ad} \times \mathcal{V}_{ad}$ and $u^* \in \mathcal{Z}$ such that (X^*, Y^*) is a saddle point of $\mathcal{J}$ and $u^* = \mathcal{F}(X^*, Y^*)$ is the solution of (25). Moreover, the optimal solution (X^*, Y^*) is characterized by (for all $(X, Y) \in \tilde{\mathcal{U}}_{ad} \times \mathcal{V}_{ad}$)

$$\begin{aligned} \frac{\partial \mathcal{J}}{\partial X}(X^*, Y^*).(X - X^*) = & \int_0^T < \Lambda(e(\varphi^*) V_a^* \tilde{u}^* + \alpha n_1 p^* + a\delta(M^* - \mathfrak{m}_{obs})), p - p^* >_{\mathcal{R}} dt \\ & + \iint_{\mathcal{Q}} (n_2 \xi^* - \tilde{u}^*)(\xi - \xi^*) \, dxdt \geq 0 \\ \frac{\partial \mathcal{J}}{\partial Y}(X^*, Y^*).(Y - Y^*) = & \int_{\Omega} (\mathcal{E}(\varphi^*, U_1^*, \tilde{u}^*) - \beta m_1 \varphi^*)(\varphi - \varphi^*) \, dx \\ & - \iint_{\mathcal{Q}} (r(\varphi^*) \tilde{u}^* + \beta m_2 \eta^*)(\eta - \eta^*) \, dxdt \\ & - \iint_{\Sigma} (\tilde{u}^* + \beta m_3 \pi^*)(\pi - \pi^*) \, d\Gamma dt \leq 0 \end{aligned}$$

where $U_1^* = u^* + U$, $P_1^* = p^* + P$, $V_a^* = u^* - w_a$, $G_1^* = \eta^* - g$, $M^* = \gamma u^* + \delta p^*$, $\mathcal{E}$ is given in (39) and $\tilde{u}^* = \mathcal{F}^{\perp}(X^*, Y^*)$ is the solution of the following adjoint problem

$$\begin{aligned} -c(\varphi^*) \frac{\partial \tilde{u}^*}{\partial t} - div(\kappa(\varphi^*, u^*) \nabla \tilde{u^*}) + K_v^*(d(\varphi^*) \tilde{u}^*) + e(\varphi^*) P_1 \tilde{u}^* + \frac{\partial \kappa}{\partial u}(\varphi^*, u^*) \nabla U_1^* . \nabla \tilde{u}^* \\ + a\gamma(M^* - \mathfrak{m}_{obs}) + b(D^* - D_{obs}) \tilde{\mathcal{H}}'(., u^*) = 0 \quad in \;\; \mathcal{Q}, \end{aligned}$$

subjected to the boundary condition

$$-\kappa(\varphi^*, u^*) \nabla \tilde{u}^* . \mathbf{n} = q \tilde{u}^* + \lambda(x) L'(u^*) \tilde{u}^* + d(\varphi^*) \tilde{u}^* \vec{\vartheta} . \mathbf{n} \quad in \;\; \Sigma,$$

and the final condition

$$\tilde{u}(T) = 0 \;\; in \;\; \Omega,$$

where $D^* = \displaystyle\int_0^T \tilde{\mathcal{H}}(t, u^*(., t)) dt.$

Remark 10 *We can also combine the results of this paragraph with the results of the previous paragraph, by replacing the first term of the function* $\mathcal{J}$ *as in (42),* (M, D) *by* $(\mathcal{L}_T(M), \mathcal{L}_D(D))$ *and* $(\mathfrak{m}_{obs}, D_{obs})$ *by* $(\epsilon, \mathfrak{d})$ *(see (43) and (44), respectively).*

8. Stochastic robust control

In this section, we present formally a sketch of an extension of our robust control approach to the stochastic process. Consider then a complete probability space $\mathcal{T} = (\mathcal{D}, \mathfrak{F}, \mathcal{P})$, with $\mathcal{D}$ the sample space of elementary events, $\mathfrak{F}$ the minimal $\sigma - algebra$ of $\mathcal{D}$ and $\mathcal{P}$ a probability measure. In this context, a real-valued space-time stochastic process $v(x,t)$ with a known probability distribution can be written as a function $v(x,t;\mathfrak{f})$, where $\mathfrak{f}$ denotes the dependence on elementary events i.e. the process v can be interpreted as a function that maps each point $(x,t,\mathfrak{f}) \in (\mathcal{Q}, \mathcal{D})$ to a corresponding point $v(x,t;\mathfrak{f})$ according to the probability measure. For more details on the representation of random variables and stochastic processes see e.g. (Loeve, 1977; Prato & Zabczyk, 1992).

Assume that the stabilization and regulation process are with random temperature distribution, data, controls, disturbances and measurement. Then the perturbation problem with random corresponding to (25) can be written as

$$\begin{aligned} c(\varphi;\mathfrak{f})\frac{\partial u}{\partial t} &- div(\kappa(\varphi,u;\mathfrak{f})\nabla u) + e(\varphi;\mathfrak{f})(p(x,t;\mathfrak{f}) + P(x,t;\mathfrak{f}))(u - w_a(x,t;\mathfrak{f})) \\ &+ d(\varphi;\mathfrak{f})K_v(u) = div((\kappa(\varphi,u;\mathfrak{f}) - \kappa(0,0;\mathfrak{f}))\nabla U) + r(\varphi;\mathfrak{f})\eta(x,t;\mathfrak{f}) + \xi(x,t;\mathfrak{f}) \\ &\qquad - (c(\varphi;\mathfrak{f}) - c(0;\mathfrak{f}))\frac{\partial U}{\partial t} + e(0;\mathfrak{f})Pv_a(x,t;\mathfrak{f}) \\ &\qquad - (d(\varphi;\mathfrak{f}) - d(0;\mathfrak{f}))K_v(U) \\ &\qquad + (r(\varphi;\mathfrak{f}) - r(0;\mathfrak{f}))g(x,t;\mathfrak{f}) \ \ in \ \ \mathcal{Q} \times \mathcal{D}, \end{aligned}$$

subjected to the boundary condition (46)

$$\begin{aligned} (\kappa(\varphi,u;\mathfrak{f})\nabla u).\mathbf{n} = &-((\kappa(\varphi,u;\mathfrak{f}) - \kappa(0,0;\mathfrak{f}))\nabla U).\mathbf{n} - q(u - u_b(x,t;\mathfrak{f})) \\ &- \lambda(x)(L(u) - L^b(u_b(x,t;\mathfrak{f}))) + \pi(x,t;\mathfrak{f}) \ \ in \ \ \Sigma \times \mathcal{D}, \end{aligned}$$

and the initial condition

$$u(x,0;\mathfrak{f}) = u_0(x;\mathfrak{f}) \ \ in \ \ \Omega \times \mathcal{D}.$$

We propose the following cost function

$$\begin{aligned} \mathcal{J}(X,Y) = &\frac{a}{2}\int_{\mathcal{D}} \| (\gamma u(.\,;\mathfrak{f}) + \delta p(.\,;\mathfrak{f})) - \mathfrak{m}_{obs}(.\,;\mathfrak{f}) \|^2_{L^2(\mathcal{Q})} \, d\mathcal{P} \\ &+ \frac{b}{2}\int_{\mathcal{D}} \| \int_0^T \tilde{\mathcal{H}}(t,u(.,t);\mathfrak{f})dt - D_{obs}(.\,;\mathfrak{f}) \|^2_{L^2(\Omega)} \, d\mathcal{P} \\ &+ \frac{\alpha}{2}\int_{\mathcal{D}} \| \mathcal{N}X(.\,;\mathfrak{f}) \|^2_{L^2(0,T,\mathcal{R}) \times L^2(\mathcal{Q})} \, d\mathcal{P} - \frac{\beta}{2}\int_{\mathcal{D}} \| \mathcal{M}Y(.\,;\mathfrak{f}) \|^2_{L^2(\Omega) \times L^2(\mathcal{Q}) \times L^2(\Sigma)} \, d\mathcal{P}, \end{aligned}$$

where $(X,Y) \in \tilde{\mathcal{U}}_{ad} \times \tilde{\mathcal{V}}_{ad}$, with $\tilde{\mathcal{U}}_{ad} = L^2(\mathcal{D};\mathcal{U}_{ad})$ and $\tilde{\mathcal{V}}_{ad} = L^2(\mathcal{D};\mathcal{V}_{ad})$, and $\int_{\mathcal{D}} .\, d\mathcal{P}$ is an integral with respect to the probability space $\mathcal{T}$.

If we assume that, for α and β sufficiently large, there exists an optimal solution $(X^*,Y^*) \in \tilde{\mathcal{U}}_{ad} \times \tilde{\mathcal{V}}_{ad}$ and $u^* \in L^2(\mathcal{D};\mathcal{Z})$ such that (X^*,Y^*) is a saddle point of $\mathcal{J}$ and $u^* = \mathcal{F}(X^*,Y^*)$ is the solution of (46), we can obtain, in the same way as to derive the necessary optimality conditions (41), the following result.

The optimal solution (X^*,Y^*) is characterized by (for all $(X,Y) \in \tilde{\mathcal{U}}_{ad} \times \tilde{\mathcal{V}}_{ad}$)

$$\frac{\partial \mathcal{J}}{\partial X}(X^*,Y^*).(X-X^*) = \int_{\mathcal{D}} (\iint_{\mathcal{Q}} (e(\varphi^*;\mathfrak{f})V_a^*\tilde{u}^* + \alpha n_1 p^* + a\delta(M^* - \mathfrak{m}_{obs}))(p-p^*)\, dxdt)d\mathcal{P}$$
$$+ \int_{\mathcal{D}} (\iint_{\mathcal{Q}} (n_2\xi^* - \tilde{u}^*)(\xi - \xi^*)\, dxdt)d\mathcal{P} \geq 0$$
$$\frac{\partial \mathcal{J}}{\partial Y}(X^*,Y^*).(Y-Y^*) = \int_{\mathcal{D}} \int_{\Omega} (\mathcal{E}_P(\varphi^*,U_1^*,\tilde{u}^*) - \beta m_1\varphi^*)(\varphi - \varphi^*)\, dx)d\mathcal{P}$$
$$- \int_{\mathcal{D}} (\iint_{\mathcal{Q}} (r(\varphi^*;\mathfrak{f})\tilde{u}^* + \beta m_2\eta^*)(\eta - \eta^*)\, dxdt)d\mathcal{P}$$
$$- \int_{\mathcal{D}} (\iint_{\Sigma} (\tilde{u}^* + \beta m_3\pi^*)(\pi - \pi^*)\, d\Gamma dt)d\mathcal{P} \leq 0$$

where $U_1^*(x,t;\mathfrak{f}) = u^* + U$, $P_1^*(x,t;\mathfrak{f}) = p^* + P$, $V_a^*(x,t;\mathfrak{f}) = u^* - w_a$, $G_1^*(x,t;\mathfrak{f}) = \eta^* - g$, $M^*(x,t;\mathfrak{f}) = \gamma u^* + \delta p^*$ and

$$\mathcal{E}_P(\varphi^*,U_1^*,\tilde{u}^*) = \int_0^T (e'(\varphi^*;\mathfrak{f})P_1^*V_a^* + c'(\varphi^*;\mathfrak{f})\frac{\partial U_1^*}{\partial t} + d'(\varphi^*;\mathfrak{f})K_v(U_1^*) - r'(\varphi^*;\mathfrak{f})G_1^*)\tilde{u}^* dt$$
$$+ \int_0^T \frac{\partial \kappa}{\partial \varphi}(\varphi^*,u^*;\mathfrak{f})\nabla U_1^*.\nabla \tilde{u}^* dt,$$

with $\tilde{u}^*(x,t;\mathfrak{f}) = \mathcal{F}^{\perp}(X^*,Y^*)$ the solution of the following adjoint problem

$$-c(\varphi^*;\mathfrak{f})\frac{\partial \tilde{u}^*}{\partial t} - div(\kappa(\varphi^*,u^*;\mathfrak{f})\nabla \tilde{u^*}) + K_v^*(d(\varphi^*;\mathfrak{f})\tilde{u}^*)$$
$$+e(\varphi^*;\mathfrak{f})P_1^*\tilde{u}^* + \frac{\partial \kappa}{\partial u}(\varphi^*,u^*;\mathfrak{f})\nabla U_1^*.\nabla \tilde{u}^*$$
$$+a\gamma(M^* - \mathfrak{m}_{obs}(.\,;\mathfrak{f})) + b(D^* - D_{obs}(.\,;\mathfrak{f}))\tilde{\mathcal{H}}'(.,u^*;\mathfrak{f}) = 0 \quad in \ \mathcal{Q} \times \mathcal{D},$$

subjected to the boundary condition

$$-\kappa(\varphi^*,u^*;\mathfrak{f})\nabla \tilde{u}^*.\mathbf{n} = q\tilde{u}^* + \lambda(x)L'(u^*;\mathfrak{f})\tilde{u}^* + d(\varphi^*;\mathfrak{f})\tilde{u}^*\vec{\vartheta}.\mathbf{n} \quad in \ \Sigma \times \mathcal{D},$$

and the final condition

$$\tilde{u}(x,T;\mathfrak{f}) = 0 \ \ in \ \ \Omega \times \mathcal{D},$$

where $D^*(x;\mathfrak{f}) = \int_0^T \tilde{\mathcal{H}}(t,u^*(x,t;\mathfrak{f});\mathfrak{f})dt.$

9. Radiation transport and coagulation process

In this section, we present formally the stabilization and regulation of the thermotherapy (by e.g. minimally invasive microwave or laser-induced thermal therapies) and radiation transport. During the treatment, the power energy provided by, for example, the laser or microwave, heats up the tumor to produce a coagulated region including the target cancer cells. As progression of tissue coagulation, physical properties of the tissue change, so, it is necessary to control the variation of the coagulated region.

9.1 Formulation and perturbation problem

We denote by Θ (which measures the fraction of native tissue) the concentration of living cells C which satisfy the relation (10) and we assume that the initial distribution of native tissue is given by $\Theta(x,t=0)=\Theta_0(x)$. So, the state Θ satisfies the following Cauchy equation (for a.e. $x\in\Omega$)

$$\begin{aligned} &\frac{\partial\Theta}{\partial t}(x,t)=\mathcal{H}(t,U(x,t))\Theta(x,t) \ \ in \ \ (0,T) \\ &\Theta(x,t=0)=\Theta_0(x), \end{aligned} \tag{47}$$

where U is the temperature distribution.
We assume also that the sum of absorbed laser radiation, f, is given by

$$f(x,t)=\aleph(\theta(x,t),x)\Phi(x,t). \tag{48}$$

Here Φ ($W.m^{-2}$) is the irradiance and $\aleph=\aleph_a-\mathcal{B}$ where $\aleph_a$ is the absorption coefficient and $\mathcal{B}$ is the Planck emission function for the material. Then, according to (48), the problem (4) becomes

$$\begin{aligned} c(\phi,x)\frac{\partial U}{\partial t}&=div(\kappa(\phi,U,x)\nabla U)-e(\phi,x)P(x,t)(U-U_a)\\ &\quad -d(\phi,x)K_v(U)+r(\phi,x)g(x,t)+\aleph(\theta(x,t),x)\Phi(x,t) \ \ \ in \ \ \mathcal{Q}, \end{aligned}$$

subjected to the boundary condition

$$\begin{aligned} (\kappa(\phi,U,x)\nabla U).\mathbf{n}&=-q(x,t)(U-U_b)\\ &\quad -\lambda(x)(L(U)-L(U_b))+h(x,t) \ \ \ in \ \ \Sigma, \end{aligned} \tag{49}$$

and the initial condition

$$U(x,0)=U_0(x) \ \ in \ \ \Omega.$$

The irradiance Φ, which corresponds to the radiation transport through the tissue, can be described by the following stationary diffusion equation (Niemz, 2002) (which is an approximation of more general radiation transport equation (Ishimaru, 1978; Pomraning, 1973))

$$-div(\mathfrak{X}(\Theta,x)\nabla\Phi)+\aleph(\Theta,x)\Phi=0 \ \ in \ \ \Omega,$$

under the boundary conditions

$$\begin{aligned} &-\mathfrak{X}(\Theta,x)\nabla\Phi.\mathbf{n}+\mathfrak{s}\Phi=\mathfrak{J} \quad in \ \ \Gamma_r,\\ &-\mathfrak{X}(\Theta,x)\nabla\Phi.\mathbf{n}+\mathfrak{s}\Phi=0 \quad in \ \ \Gamma_{nr}, \end{aligned} \tag{50}$$

where $\mathfrak{s}$ is a fixed constant, $\mathfrak{J}$ is the power of the applied laser source and $\Gamma=\Gamma_r\cup\Gamma_{nr}$ such that $\Gamma_r\cap\Gamma_{nr}=\emptyset$. Boundary Γ_r denotes the boundary through which radiation is emmitted and Γ_{nr} denotes the other boundary of the domain.
In the sequel, we assume that $\mathfrak{X}$ and $\aleph$ satisfy similar hypotheses as (**H1**)-(**H3**) and, for simplicity, we denote the values $\aleph(\Theta,.)$, $\mathfrak{X}(\Theta,.)$ and $\mathcal{H}(.,U)$ by $\aleph(\Theta)$, $\mathfrak{X}(\Theta)$ and $\mathcal{H}(U)$, respectively. In this context, we can formulate the perturbation problem as follows. We assume that (U,Φ,Θ) satisfies the problem (49),(47), (50) with data $(U_0,P,\phi,g,h,U_a,U_b,\Theta_0,\mathfrak{J})$ and $(U+u,\Phi+\Psi,\Theta+\theta)$ satisfies problem (49),(47), (50) with

data $(U_0 + u_0, P + p, \phi + \varphi, g + \eta, h + \pi, U_a + u_a, U_b + u_b, \Theta_0 + \theta_0, \mathfrak{J} + \xi)$. Hence we consider the following systems (for a given (U, Φ, Θ) sufficiently regular) as follows.

Perturbation of the transient bioheat transfer type problem

$$
\begin{aligned}
c(\phi+\varphi)\frac{\partial u}{\partial t} - div(\kappa(\phi+\varphi, U+u)\nabla u) - div((\kappa(\phi+\varphi, U+u) - \kappa(\phi, U))\nabla U)\\
= -e(\phi+\varphi)(p+P)(u-u_a) - d(\phi+\varphi)K_v(u) + r(\phi+\varphi)\eta + \aleph(\Theta+\theta)\Psi\\
-(c(\phi+\varphi) - c(\phi))\frac{\partial U}{\partial t} - (e(\varphi+\phi)(p+P) - e(\phi)P)(U-U_a)\\
-(d(\varphi+\phi) - d(\phi))K_v(U) + (r(\varphi+\phi) - r(\phi))g\\
+(\aleph(\Theta+\theta) - \aleph(\Theta))\Phi \quad in \;\; \mathcal{Q},
\end{aligned}
$$

subjected to the boundary condition (51)

$$
\begin{aligned}
\kappa(\phi+\varphi, U+u)\nabla u.\mathbf{n} + (\kappa(\phi+\varphi, U+u) - \kappa(\phi, U))\nabla U.\mathbf{n} = -q(u-u_b)\\
-\lambda(x)((L(U+u) - L(U)) - (L(U_b+u_b) - L(U_b))) + \pi \quad in \;\; \Sigma,
\end{aligned}
$$

and the initial condition

$$u(0) = u_0 \;\; in \;\; \Omega.$$

Perturbation of the coagulated region type model

$$
\begin{aligned}
&\frac{\partial \theta}{\partial t} = \mathcal{H}(U+u)\theta + (\mathcal{H}(U+u) - \mathcal{H}(U))\Theta \;\; in \;\; (0,T),\\
&\theta(., t=0) = \theta_0.
\end{aligned}
\tag{52}
$$

Perturbation of the radiation transport type problem

$$
\begin{aligned}
-div(\mathfrak{X}(\Theta+\theta)\nabla\Psi) - div((\mathfrak{X}(\Theta+\theta) - \mathfrak{X}(\Theta))\nabla\Phi) + \aleph(\Theta+\theta)\Psi\\
= -(\aleph(\Theta+\theta) - \aleph(\Theta))\Phi \;\; in \;\; \Omega,
\end{aligned}
$$

under the boundary condition (53)

$$
\begin{aligned}
-\mathfrak{X}(\Theta+\theta)\nabla\Psi.\mathbf{n} - (\mathfrak{X}(\Theta+\theta) - \mathfrak{X}(\Theta))\nabla\Phi.\mathbf{n} + \mathfrak{s}\Psi = \xi \quad in \;\; \Gamma_r,\\
-\mathfrak{X}(\Theta+\theta)\nabla\Psi.\mathbf{n} - (\mathfrak{X}(\Theta+\theta) - \mathfrak{X}(\Theta))\nabla\Phi.\mathbf{n} + \mathfrak{s}\Psi = 0 \quad in \;\; \Gamma_{nr}.
\end{aligned}
$$

If we set : $\tilde{L}(u) = L(U+u) - L(U)$, $\tilde{L}^b(u_b) = L(U_b+u_b) - L(U_b)$, $\tilde{\mathcal{H}}(u) = \mathcal{H}(U+u)$, $\tilde{\mathfrak{X}}(\theta) = \mathfrak{X}(\Theta+\theta)$, $\tilde{\aleph}(\theta) = \aleph(\Theta+\theta)$, $\tilde{\kappa}(\varphi, u) = \kappa(\phi+\varphi, U+u)$, and $\tilde{\beta}(\varphi) = \beta(\phi+\varphi)$, where the function β plays the role of c, d, e or r, then System (51),(52), (53) reduces to

$$
\begin{aligned}
\tilde{c}(\varphi)\frac{\partial u}{\partial t} - div(\tilde{\kappa}(\varphi, u)\nabla u) + \tilde{e}(\varphi)(p+P)(u-w_a) + \tilde{d}(\varphi)K_v(u)\\
= div((\tilde{\kappa}(\varphi, u) - \tilde{\kappa}(0,0))\nabla U) + \tilde{r}(\varphi)\eta + \tilde{\aleph}(\theta)\Psi\\
-(\tilde{c}(\varphi) - \tilde{c}(0))\frac{\partial U}{\partial t} + \tilde{e}(0)Pv_a - (\tilde{d}(\varphi) - \tilde{d}(0))K_v(U)\\
+(\tilde{r}(\varphi) - \tilde{r}(0))g + (\tilde{\aleph}(\theta) - \tilde{\aleph}(0))\Phi \quad in \;\; \mathcal{Q},
\end{aligned}
\tag{54}
$$

subjected to the boundary condition

$$\begin{aligned}&\tilde{\kappa}(\varphi,u)\nabla u.\mathbf{n}+(\tilde{\kappa}(\varphi,u)-\tilde{\kappa}(0,0))\nabla U.\mathbf{n}\\&\qquad=-q(u-u_b)-\lambda(x)(\tilde{L}(u)-\tilde{L}^b(u_b))+\pi\quad in\ \ \Sigma,\end{aligned}$$

and the initial condition

$$u(0)=u_0\ \ in\ \ \Omega,$$

$$\begin{aligned}&\frac{\partial\theta}{\partial t}=\tilde{\mathcal{H}}(u)\theta+(\tilde{\mathcal{H}}(u)-\tilde{\mathcal{H}}(0))\Theta\ \ in\ \ (0,T),\\&\theta(.,t=0)=\theta_0\end{aligned}\tag{55}$$

and

$$\begin{aligned}&-div(\tilde{\mathfrak{X}}(\theta)\nabla\Psi)-div((\tilde{\mathfrak{X}}(\theta)-\tilde{\mathfrak{X}}(0))\nabla\Phi)+\tilde{\aleph}(\theta)\Psi\\&\qquad=-(\tilde{\aleph}(\theta)-\tilde{\aleph}(0))\Phi\ \ in\ \ \Omega,\end{aligned}$$

under the boundary conditions (56)

$$\begin{aligned}&-\tilde{\mathfrak{X}}(\theta)\nabla\Psi.\mathbf{n}-(\tilde{\mathfrak{X}}(\theta)-\tilde{\mathfrak{X}}(0))\nabla\Phi.\mathbf{n}+\mathfrak{s}\Psi=\xi\quad in\ \ \Gamma_r,\\&-\tilde{\mathfrak{X}}(\theta)\nabla\Psi.\mathbf{n}-(\tilde{\mathfrak{X}}(\theta)-\tilde{\mathfrak{X}}(0))\nabla\Phi.\mathbf{n}+\mathfrak{s}\Psi=0\quad in\ \ \Gamma_{nr},\end{aligned}$$

where $v_a=U-U_a$ and $w_a=u_a-v_a$.
For simplicity of future reference, we omit the " ˜ " on $\tilde{\mathfrak{X}}$,$\tilde{\aleph}$, $\tilde{L}$, $\tilde{L}^b$, $\tilde{c}$,$\tilde{d}$,$\tilde{e}$,$\tilde{r}$ and $\tilde{\kappa}$ for the system (54),(55), (56).

9.2 Robust control problem

Similarly as in the section 6, the problem is to find the best admissible perfusion function p and power of the applied laser source ξ in the presence of the worst disturbance in the porosity function φ, in the evaporation term π and in the metabolic heat generation type term η. We then suppose that the control is in $X=(p,\xi)$ and the disturbance is in $Y=(\varphi,\eta,\pi)$. Therefore, the function (u,θ,Ψ) is assumed to be related to the disturbance Y and control X through the problem (54),(55), (56) under the pointwise constraints (26).
Let $\mathcal{K}_1$ be convex, closed, non-empty and bounded subset of $L^2(\Sigma_r)$, $\mathcal{K}_2$ be convex, closed, non-empty and bounded subset of $L^2(\mathcal{Q})$ and $\mathcal{K}_3$ be convex, closed, non-empty and bounded subset of $L^2(\Sigma)$. The studied control problem is to find a saddle point of the cost function $\mathcal{J}$ which measures the distance between the known observation $\mathfrak{m}_{obs}$, corresponding to the online temperature control via radiometric temperature measurement system and the prognostic variables $\gamma u+\delta p$. Then we propose the following cost

$$\begin{aligned}\mathcal{J}(X,Y)=&\frac{a}{2}\parallel(\gamma u+\delta p)-\mathfrak{m}_{obs}\parallel^2_{L^2(\mathcal{Q})}+\frac{\alpha}{2}\parallel\mathcal{N}X\parallel^2_{L^2(\mathcal{Q})\times L^2(\Sigma_r)}\\&-\frac{\beta}{2}\parallel\mathcal{M}Y\parallel^2_{L^2(\Omega)\times L^2(\mathcal{Q})\times L^2(\Sigma)}\end{aligned}\tag{57}$$

where $a>0$, $\alpha>0$, $\beta>0$, the matrix $\mathcal{N}=diag(\sqrt{n_1},\sqrt{n_2})$ and $\mathcal{M}=diag(\sqrt{m_1},\sqrt{m_2},\sqrt{m_3})$, are predefined nonnegative weights such that $n_1+n_2\neq0$ and $m_1+m_2+m_3\neq0$, $\mathcal{U}_{ad}=$

$D_1 \times \mathcal{K}_1$, $\mathcal{V}_{ad} = D_2 \times \mathcal{K}_2 \times \mathcal{K}_3$ and $\mathfrak{m}_{obs}$ is the target. The parameters γ, δ are positive with space-time dependent entries and are in $L^\infty(\overline{Q})$. Let us introduce the operator solution $\mathcal{F}$ which maps the source term $(X,Y) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$ of (54),(55), (56) into the corresponding solution $(u,\theta,\Psi) = \mathcal{F}(X,Y)$. We suppose that the operator solution $\mathcal{F}$ is continuously differentiable (in weak sense) on $\mathcal{U}_{ad} \times \mathcal{V}_{ad}$ and its derivative (at point $(X,Y) = (p,\xi,\varphi,\eta,\pi)$) $\mathcal{F}'(X,Y) : (H,K) = (\mathfrak{y},\mathfrak{h},\psi,\mathfrak{e},\mathfrak{z}) \in L^\infty(Q) \times L^2(\Sigma_r) \times L^\infty(\Omega) \times L^2(Q) \times L^2(\Sigma) \longrightarrow (w,\varpi,\Pi) = \mathcal{F}'(X,Y).(H,K) = \lim_{\epsilon \longrightarrow 0} \frac{\mathcal{F}(X+\epsilon H, Y+\epsilon K)}{\epsilon}$, where $(X+\epsilon H, Y+\epsilon K) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$, is such that $(w,\varpi,\Pi) = \frac{\partial \mathcal{F}}{\partial X}(X,Y)H + \frac{\partial \mathcal{F}}{\partial Y}(X,Y)K$ is the unique weak solution of the following system

$$\begin{aligned} c(\varphi)\frac{\partial w}{\partial t} - div(\kappa(\varphi,u)\nabla w) - div((\frac{\partial \kappa}{\partial \varphi}(\varphi,u)\psi + \frac{\partial \kappa}{\partial u}(\varphi,u)w)\nabla U_1) + d(\varphi)K_v(w) \\ +e(\varphi)P_1 w + e'(\varphi)\psi P_1 V_a + e(\varphi)\mathfrak{y} V_a + d'(\varphi)\psi K_v(U_1) \\ = -c'(\varphi)\frac{\partial U_1}{\partial t}\psi + r'(\varphi)\psi G_1 + r(\varphi)\mathfrak{e} + \aleph'(\theta)\varpi\Phi_1 + \aleph(\theta)\Pi \quad in \;\; Q, \end{aligned}$$

subjected to the boundary condition

$$\begin{aligned} (\kappa(\varphi,u)\nabla w).\mathbf{n} = -((\frac{\partial \kappa}{\partial \varphi}(\varphi,u)\psi + \frac{\partial \kappa}{\partial u}(\varphi,u)w)\nabla U_1).\mathbf{n} \\ -qw - \lambda(x)L'(u)w + \mathfrak{z} \quad in \;\; \Sigma, \end{aligned} \tag{58}$$

and the initial condition

$$w(0) = 0 \;\; in \;\; \Omega,$$

$$\begin{aligned} \frac{\partial \varpi}{\partial t} = \mathcal{H}'(u)w\Theta_1 + \mathcal{H}(u)\varpi \;\; in \;\; (0,T), \\ \varpi(0) = 0 \end{aligned} \tag{59}$$

and

$$-div(\mathfrak{X}(\theta)\nabla\Pi) - div(\mathfrak{X}'(\theta)\varpi\nabla\Phi_1) + \aleph'(\theta)\varpi\Phi_1 + \aleph(\theta)\Pi = 0 \;\; in \;\; \Omega,$$

under the boundary condition

$$\begin{aligned} -\mathfrak{X}(\theta)\nabla\Pi.\mathbf{n} - \mathfrak{X}'(\theta)\varpi\nabla\Phi_1.\mathbf{n} + \mathfrak{s}\Pi = \mathfrak{h} \quad in \;\; \Gamma_r, \\ -\mathfrak{X}(\theta)\nabla\Pi.\mathbf{n} - \mathfrak{X}'(\theta)\varpi\nabla\Phi_1.\mathbf{n} + \mathfrak{s}\Pi = 0 \quad in \;\; \Gamma_{nr}, \end{aligned} \tag{60}$$

where $(u,\theta,\Psi) = \mathcal{F}(X,Y)$, $U_1 = u + U$, $\Theta_1 = \Theta + \theta$, $\Phi_1 = \Psi + \Phi$, $P_1 = p + P$, $V_a = u - w_a$ and $G_1 = \eta - g$. Moreover the derivative of $\mathcal{J}$ is given by

$$\begin{aligned} \mathcal{J}'(X,Y).(H,K) &= \frac{d}{d\lambda}\mathcal{J}(X+\lambda H, Y+\lambda K)|_{\lambda=0} \\ &= a\iint_Q ((\gamma u + \delta p) - \mathfrak{m}_{obs})(\gamma w + \delta\mathfrak{y})\, dxdt \\ &\quad +\alpha(n_1 \iint_Q p\mathfrak{y}\, dxdt + n_2 \iint_{\Sigma_r} \xi\mathfrak{h}\, d\Gamma dt) \\ &\quad -\beta(m_1 \int_\Omega \varphi\psi\, dx + m_2 \iint_Q \eta\mathfrak{e}\, dxdt + m_3 \iint_\Sigma \pi\mathfrak{z}\, d\Gamma dt), \end{aligned} \tag{61}$$

where $(w,\varpi,\Pi) = \mathcal{F}'(X,Y).(H,K)$.

We assume that, for α and β sufficiently large, there exists an optimal solution $(X^*,Y^*) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$ and (u^*,θ^*,Ψ^*) such that (X^*,Y^*) is a saddle point of $\mathcal{J}$ and $(u^*,\theta^*,\Psi^*) = \mathcal{F}(X^*,Y^*)$ is the solution of (54),(55), (56). In order to derive the necessary optimality conditions for the optimal solution (X^*,Y^*), we start by calculating the gradient of the cost $\mathcal{J}$. For this, consider a sufficiently regular function $(\tilde{u},\tilde{\theta},\tilde{\Phi})$ such that $(\tilde{u},\tilde{\theta})(T) = (0,0)$. Multiplying the system (58),(59) and (60) by $(\tilde{u},\tilde{\theta},\tilde{\Phi})$, respectively and integrating with respect to space and time, and using Green's formula, we obtain according to the boundary and initial conditions, and the relation (34) that (similarly as to obtain the relation (35))

$$\begin{aligned}
&\int\int_{\mathcal{Q}}\Big(-c(\varphi)\frac{\partial\tilde{u}}{\partial t} - div(\kappa(\varphi,u)\nabla\tilde{u}) + K_v^*(d(\varphi)\tilde{u}) + e(\varphi)P_1\tilde{u} + \frac{\partial\kappa}{\partial u}(\varphi,u)\nabla U_1.\nabla\tilde{u}\Big)\, w\, dxdt \\
&\quad + \int\int_{\Sigma}(q\tilde{u} + \lambda(x)L'(u)\tilde{u} + \kappa(\varphi,u)\nabla\tilde{u}.\mathbf{n} + d(\varphi)\tilde{u}\vec{\vartheta}.\mathbf{n})w\, d\Gamma dt \\
&\quad = -\int_{\Omega}\Big(\int_0^T (e'(\varphi)P_1V_a + c'(\varphi)\frac{\partial U_1}{\partial t} + d'(\varphi)K_v(U_1) - r'(\varphi)G_1)\tilde{u}dt\Big)\,\psi\, dx \\
&\quad - \int_{\Omega}\Big(\int_0^T \frac{\partial\kappa}{\partial\varphi}(\varphi,u)\nabla U_1.\nabla\tilde{u}dt\Big)\,\psi\, dx \\
&\quad - \int\int_{\mathcal{Q}} e(\varphi)V_a\tilde{u}\mathfrak{y}\, dxdt + \int\int_{\mathcal{Q}} r(\varphi)\tilde{u}\mathfrak{e}\, dxdt + \int\int_{\Sigma}\mathfrak{z}\tilde{u}\, d\Gamma dt \\
&\quad + \int\int_{\mathcal{Q}}(\tilde{u}\aleph'(\theta)\Phi_1)\varpi\, dxdt + \int\int_{\mathcal{Q}}(\tilde{u}\aleph(\theta))\Pi\, dxdt,
\end{aligned} \tag{62}$$

$$\int_0^T(-\frac{\partial\tilde{\theta}}{\partial t} - \mathcal{H}(u)\tilde{\theta})\varpi\, dt = \int_0^T(\mathcal{H}'(u)\tilde{\theta}\Theta_1)w\, dt \tag{63}$$

and

$$\begin{aligned}
&\int_{\Omega}(-div(\mathfrak{X}(\theta)\nabla\tilde{\Phi}) + \aleph(\theta)\tilde{\Phi})\Pi\, dx + \int_{\Gamma}(\mathfrak{X}(\theta)\nabla\tilde{\Phi}.\mathbf{n} - \mathfrak{s}\tilde{\Phi})\Pi\, d\Gamma \\
&\qquad + \int_{\Gamma_r}\mathfrak{h}\tilde{\Phi}\, d\Gamma + \int_{\Omega}(\mathfrak{X}'(\theta)\nabla\Phi_1\nabla\tilde{\Phi} + \aleph'(\theta)\tilde{\Phi}\Phi_1)\varpi\, dx = 0.
\end{aligned} \tag{64}$$

To simplify the relations (62), (63) and (64), we assume that $(\tilde{u},\tilde{\Phi},\tilde{\theta})$ satisfies the following adjoint system

$$\begin{aligned}
&-c(\varphi)\frac{\partial\tilde{u}}{\partial t} - div(\kappa(\varphi,u)\nabla\tilde{u}) + K_v^*(d(\varphi)\tilde{u}) + e(\varphi)P_1\tilde{u} + \frac{\partial\kappa}{\partial u}(\varphi,u)\nabla U_1.\nabla\tilde{u} \\
&\qquad + a\gamma(\gamma u + \delta p - \mathfrak{m}_{obs}) + \mathcal{H}'(u)\tilde{\theta}\Theta_1 = 0 \quad in \ \mathcal{Q}, \\
&\text{subjected to the boundary condition} \\
&-\kappa(\varphi,u)\nabla\tilde{u}.\mathbf{n} = q\tilde{u} + \lambda(x)L'(u)\tilde{u} + d(\varphi)\tilde{u}\vec{\vartheta}.\mathbf{n} \quad in \ \Sigma, \\
&\text{and the final condition} \\
&\tilde{u}(T) = 0 \ \ in \ \ \Omega,
\end{aligned} \tag{65}$$

$$\begin{aligned}
&-\frac{\partial\tilde{\theta}}{\partial t} = \mathcal{H}(u)\tilde{\theta} + \tilde{u}\aleph'(\theta)\Phi_1 + \mathfrak{X}'(\theta)\nabla\Phi_1\nabla\tilde{\Phi} + \aleph'(\theta)\tilde{\Phi}\Phi_1 \ \ in \ \ (0,T) \\
&\tilde{\theta}(T) = 0
\end{aligned} \tag{66}$$

and

$$
\begin{aligned}
&-div(\mathfrak{X}(\theta)\nabla\tilde{\Phi}) + \aleph(\theta)\tilde{\Phi} + \tilde{u}\aleph(\theta) = 0 \;\; in \;\; \Omega, \\
&\text{under the boundary condition} \\
&-\mathfrak{X}(\theta)\nabla\tilde{\Phi}.\mathbf{n} + \mathfrak{s}\tilde{\Phi} = 0 \quad in \;\; \Gamma.
\end{aligned}
\tag{67}
$$

Using the system (36), the problem (35) becomes

$$
\begin{aligned}
&\int\!\!\int_Q - \big(a\gamma(\gamma u + \delta p - \mathfrak{m}_{obs}) + \mathcal{H}'(u)\tilde{\theta}\Theta_1\big)\, w\, dxdt \\
&\quad = -\int_\Omega \Big(\int_0^T (e'(\varphi)P_1 V_a + c'(\varphi)\frac{\partial U_1}{\partial t} + d'(\varphi)K_v(U_1) - r'(\varphi)G_1)\tilde{u}dt \Big)\, \psi\, dx \\
&\qquad - \int_\Omega \Big(\int_0^T \frac{\partial \kappa}{\partial \varphi}(\varphi,u)\nabla U_1.\nabla\tilde{u}dt \Big)\, \psi\, dx \\
&\qquad - \int\!\!\int_Q e(\varphi)V_a\tilde{u}\mathfrak{y}\, dxdt + \int\!\!\int_Q r(\varphi)\tilde{u}\mathfrak{e}\, dxdt + \int\!\!\int_\Sigma \mathfrak{z}\tilde{u}\, d\Gamma dt \\
&\qquad + \int\!\!\int_Q (\tilde{u}\aleph'(\theta)\Phi_1)\varpi\, dxdt + \int\!\!\int_Q (\tilde{u}\aleph(\theta))\Pi\, dxdt,
\end{aligned}
\tag{68}
$$

$$
-\int_0^T (\mathcal{H}'(u)\tilde{\theta}\Theta_1)w\, dt + \int_0^T (\tilde{u}\aleph'(\theta)\Phi_1)\varpi\, dt = -\int_0^T (\mathfrak{X}'(\theta)\nabla\Phi_1\nabla\tilde{\Phi} + \aleph'(\theta)\tilde{\Phi}\Phi_1)\varpi\, dt,
$$

$$
\int_\Omega (\tilde{u}\aleph(\theta))\Pi\, dx = \int_{\Gamma_r} \mathfrak{h}\tilde{\Phi}\, d\Gamma + \int_\Omega (\mathfrak{X}'(\theta)\nabla\Phi_1\nabla\tilde{\Phi} + \aleph'(\theta)\tilde{\Phi}\Phi_1)\varpi\, dx.
$$

Integrating by time the third part of (68) and by space the second part (68), and adding the first part, the second part and the third part of (68), we can deduce that

$$
\begin{aligned}
&-\int\!\!\int_Q a\gamma(\gamma u + \delta p - \mathfrak{m}_{obs})w\, dxdt \\
&\quad = -\int_\Omega \Big(\int_0^T (e'(\varphi)P_1 V_a + c'(\varphi)\frac{\partial U_1}{\partial t} + d'(\varphi)K_v(U_1) - r'(\varphi)G_1)\tilde{u}dt \Big)\, \psi\, dx \\
&\qquad - \int_\Omega \Big(\int_0^T \frac{\partial \kappa}{\partial \varphi}(\varphi,u)\nabla U_1.\nabla\tilde{u}dt \Big)\, \psi\, dx \\
&\qquad - \int\!\!\int_Q e(\varphi)V_a\tilde{u}\mathfrak{y}\, dxdt + \int\!\!\int_Q r(\varphi)\tilde{u}\mathfrak{e}\, dxdt + \int\!\!\int_\Sigma \mathfrak{z}\tilde{u}\, d\Gamma dt + \int_{\Gamma_r} \mathfrak{h}\tilde{\Phi}\, d\Gamma.
\end{aligned}
\tag{69}
$$

According to the expression (61) of $\mathcal{J}'(X,Y)$ we can deduce that

$$
\begin{aligned}
&\mathcal{J}'(X,Y).(H,K) = \frac{\partial \mathcal{J}}{\partial X}(X,Y).H + \frac{\partial \mathcal{J}}{\partial Y}(X,Y).K \\
&\quad = \int\!\!\int_Q (e(\varphi)V_a\tilde{u} + \alpha n_1 p + a\delta(\gamma u + \delta p - \mathfrak{m}_{obs}))\mathfrak{y}\, dxdt + \int\!\!\int_{\Sigma_r} (n_2\xi - \tilde{\Phi})\mathfrak{h}\, dxdt \\
&\qquad + \int_\Omega (\mathcal{E}(\varphi,U_1,\tilde{u}) - \beta m_1\varphi)\psi\, dx - \int\!\!\int_Q (r(\varphi)\tilde{u} + \beta m_2\eta)\mathfrak{e}\, dxdt \\
&\qquad - \int\!\!\int_\Sigma (\tilde{u} + \beta m_3\pi)\mathfrak{z}\, d\Gamma dt,
\end{aligned}
\tag{70}
$$

where

$$
\begin{aligned}
\mathcal{E}(\varphi,U_1,\tilde{u}) = &\int_0^T (e'(\varphi)P_1 V_a + c'(\varphi)\frac{\partial U_1}{\partial t} + d'(\varphi)K_v(U_1) - r'(\varphi)G_1)\tilde{u}dt \\
&+ \int_0^T \frac{\partial \kappa}{\partial \varphi}(\varphi,u)\nabla U_1.\nabla\tilde{u}dt.
\end{aligned}
\tag{71}
$$

Consequently the gradient of $\mathcal{J}$ at point (X,Y), in weak sense, is

$$\frac{\partial \mathcal{J}}{\partial X}(X,Y) = \begin{pmatrix} e(\varphi)V_a\tilde{u} + \alpha n_1 p + a\delta(\gamma u + \delta p - \mathfrak{m}_{obs}) \\ n_2\xi - \tilde{\Phi} \end{pmatrix},$$

$$\frac{\partial \mathcal{J}}{\partial Y}(X,Y) = \begin{pmatrix} \mathcal{E}(\varphi, U_1, \tilde{u}) - \beta m_1 \varphi \\ -(r(\varphi)\tilde{u} + \beta m_2 \eta) \\ -(\tilde{u} + \beta m_3 \pi) \end{pmatrix}. \tag{72}$$

We can now give the first-order optimality conditions for the robust control problem as follows.

The optimal solution (X^*,Y^*) is characterized by (for all $(X,Y) \in \mathcal{U}_{ad} \times \mathcal{V}_{ad}$)

$$\begin{aligned}
\frac{\partial \mathcal{J}}{\partial X}(X^*,Y^*).(X-X^*) = & \int\int_Q (e(\varphi^*)V_a^*\tilde{u}^* + \alpha n_1 p^* + a\delta(M^* - \mathfrak{m}_{obs}))(p - p^*)\, dxdt \\
& + \int\int_{\Sigma_r} (n_2\xi^* - \tilde{\Phi}^*)(\xi - \xi^*)\, d\Gamma dt \geq 0 \\
\frac{\partial \mathcal{J}}{\partial Y}(X^*,Y^*).(Y-Y^*) = & \int_\Omega (\mathcal{E}(\varphi^*, U_1^*, \tilde{u}^*) - \beta m_1 \varphi^*)(\varphi - \varphi^*)\, dx \\
& - \int\int_Q (r(\varphi^*)\tilde{u}^* + \beta m_2 \eta^*)(\eta - \eta^*)\, dxdt \\
& - \int\int_\Sigma (\tilde{u}^* + \beta m_3 \pi^*)(\pi - \pi^*)\, d\Gamma dt \leq 0
\end{aligned}$$

where $(u^*, \theta^*, \Psi^*) = \mathcal{F}(X^*,Y^*)$, $U_1^* = u^* + U$, $\Theta_1^* = \Theta + \theta^*$, $\Phi_1^* = \Psi^* + \Phi$, $P_1^* = p^* + P$, $V_a^* = u^* - w_a$ and $G_1^* = \eta^* - g$, $M^*(x,t) = \gamma u^* + \delta p^*$ and $(\tilde{u}^*, \tilde{\theta}^*, \tilde{\Phi}^*) = \mathcal{F}^\perp(X^*,Y^*)$ is the solution of the adjoint problem (65),(66),(67).

Remark 11 *We can apply easily our stochastic robust control approach developed in the section 8 to the problem of coagulation process analyzed in the present section.*

To help the interested reader with the transition from theory to implementation, we also discuss some optimization strategies in order to solve the robust control problems, by using the adjoint model.

10. Minimax optimization algorithms and conclusion

We present algorithms where the descent direction is calculated by using the adjoint variables, particularly by choosing an admissible step size. The descent method is formulated in terms of the continuous variable such is independent of a specific discretization. The methods are valid for the continuous as well as random processes.

10.1 Gradient algorithm

The gradient algorithm for the resolution of treated saddle point problems is given by:
for k=1,..., (iteration index) we denote by (X_k, Y_k) the numerical approximation of the control-disturbance at the *kth* iteration of the algorithm.

(*Step*1) Initialization: (X_0, Y_0) (given initial guess).

(*Step*2) Resolution of the direct problem where the source term is (X_k, Y_k), gives $\mathcal{F}(X_k, Y_k)$.

(*Step*3) Resolution of the adjoint problem (based on $(X_k, Y_k, \mathcal{F}(X_k, Y_k))$, gives $\mathcal{F}^{\perp}(X_k, Y_k)$,

(*Step*4) Gradient of $\mathcal{J}$ at (X_k, Y_k):

$$(\mathbf{GJ})\begin{cases} c_k \overset{def}{=} \dfrac{\partial \mathcal{J}}{\partial X}(X_k, Y_k), \\ \\ d_k \overset{def}{=} \dfrac{\partial \mathcal{J}}{\partial Y}(X_k, Y_k), \\ \\ G_k = (c_k, d_k). \end{cases}$$

(*Step*5) Determine X_{k+1}: $X_{k+1} = X_k - \gamma_k c_k$,

(*Step*6) Determine Y_{k+1}: $X_{k+1} = Y_k + \delta_k d_k$,
where $0 < m \leq \gamma_k, \delta \leq M$ are the sequences of step lengths.

(*Step*7) If the gradient is sufficiently small: end; else set $k := k + 1$ and goto (*Step*2).
Optimal Solution: $(X, Y) = (X_k, Y_k)$.

The convergence of the algorithm depends on the second Fréchet derivative of $\mathcal{J}$ (i.e. m, M depend on the second Fréchet derivative of $\mathcal{J}$) see e.g. (Ciarlet, 1989).

In order to obtain an algorithm which is numerically efficient, the best choice of γ_k, δ_k will be the result of a line minimization and maximization algorithm, respectively. Otherwise, at each iteration step k of the previous algorithm, we solve the one-dimensional optimization problem of the parameters γ_k and δ_k:

$$\begin{aligned} \gamma_k &= \min_{\lambda > 0} \mathcal{J}(X_k - \lambda c_k, Y_k), \\ \delta_k &= \min_{\lambda > 0} \mathcal{J}(X_k, Y_k + \lambda d_k), \end{aligned} \tag{73}$$

To derive an approximation for a pair (γ_k, δ_k) we can use a purely heuristic approach, for example, by taking $\gamma_k = min(1, \| c_k \|_{\infty}^{-1})$ and $\delta_k = min(1, \| d_k \|_{\infty}^{-1})$ or by using the linearization of $\mathcal{F}(X_k - \lambda c_k, Y_k)$ at X_k and $\mathcal{F}(X_k, Y_k - \lambda d_k)$ at Y_k by

$$\mathcal{F}(X_k - \lambda c_k, Y_k) \approx \mathcal{F}(X_k, Y_k) - \lambda \frac{\partial \mathcal{F}}{\partial X}(X_k, Y_k).c_k, \;\; \mathcal{F}(X_k, Y_k + \lambda d_k) \approx \mathcal{F}(X_k, Y_k) - \lambda \frac{\partial \mathcal{F}}{\partial Y}(X_k, Y_k).d_k,$$

where $\dfrac{\partial \mathcal{F}}{\partial X}(X_k, Y_k).c_k = \mathcal{F}'(X_k, Y_k).(c_k, 0)$ and $\dfrac{\partial \mathcal{F}}{\partial Y}(X_k, Y_k).d_k = \mathcal{F}'(X_k, Y_k).(0, d_k)$ are solutions of the sensitivity problem. According to the previous approximation, we can approximate the problem (73) by

$$\gamma_k = \min_{\lambda > 0} H(\lambda), \;\; \delta_k = \min_{\lambda > 0} R(\lambda), \tag{74}$$

where the functions H and R are polynomial functions of the degree 2 (since the functional $\mathcal{J}$ is quadratic), then the problem (74) can be solved exactly. Consequently, we obtain explicitly the value of the parameter λ_k.

10.2 Conjugate gradient algorithm:

Another strategy to solve numerically the treated saddle point problems, is to use a Conjugate Gradient type algorithm (CG-algorithm) combined with the Wolfe-Powell line search procedure for computing admissible step-sizes along the descent direction. The advantage of this method, compared to the gradient method, is that it performs a soft reset whenever the GC search direction yields no significant progress. In general, the method has the following form:

$$D_k = Dz = \begin{cases} -G_k \;\; for \;\; k = 0, \\ \\ -G_k + \xi_{k-1} D_{k-1} \;\; for \;\; k \geq 1, \end{cases}$$

$$z_{k+1} = z_k + \lambda_k D_k$$

where G_k denotes the gradient of the functional to be optimized at point z_k, λ_k is a step length obtained by a line search, D_k is the search direction and ξ_k is a constant. Several varieties of this method differ in the way of selecting ξ_k . Some well-known formula for ξ_k are given by Fletcher-Reeves, Polak-Ribière, Hestenes-Stiefel and Dai-Yuan.

The GC-algorithm for the resolution of the considered saddle point problems is given by: for k=1,..., (iteration index) we denote by (X_k, Y_k) the numerical approximation of the control-disturbance at the kth iteration of the algorithm.

($Step$1) Initialization: (X_0, Y_0) (given), $\xi_{-1} = 0$, $\eta_{-1} = 0$ and $C_{-1} = 0$, $D_{-1} = 0$,

($Step$2) Resolution of the direct problem where the source term is (X_0, Y_0), gives $\mathcal{F}(X_0, Y_0)$,

($Step$3) Resolution of the adjoint problem (based on (X_0, u_0)), gives $\mathcal{F}^{\perp}(X_0, Y_0)$,

($Step$4) Gradient of $\mathcal{J}$ at (X_0, Y_0), the vector (c_0, d_0) is given by the system (GJ),

($Step$5) Determine the direction: $C_0 = -c_0$, $D_0 = -d_0$

($Step$6) Determine (X_1, Y_1): $X_1 = X_0 + \lambda_0 C_0$, $Y_1 = Y_0 - \delta_0 D_0$

($Step$7) Resolution of the direct problem where the source term is (X_k, Y_k), gives $\mathcal{F}(X_k, Y_k)$,

($Step$8) Resolution of the adjoint problem (based on (X_k, Y_k), gives $\mathcal{F}^{\perp}(X_k, Y_k)$,

($Step$9) Gradient of $\mathcal{J}$ at (X_k, Y_k), the vector (c_k, d_k) is given by the system (GJ),

($Step$10) Determine (ξ_{k-1}, η_{k-1}) by one of the following expressions:

$$\xi_{k-1} = \frac{\| c_k \|^2_{U_{ad}}}{\| c_{k-1} \|^2_{U_{ad}}}, \; \eta_{k-1} = \frac{\| d_k \|^2_{V_{ad}}}{\| d_{k-1} \|^2_{V_{ad}}}$$

(Fletcher-Reeves),

$\xi_{k-1} = \dfrac{< c_k - c_{k-1}, c_k >_{U_{ad}}}{\| c_{k-1} \|^2_{U_{ad}}}$, $\eta_{k-1} = \dfrac{< d_k - d_{k-1}, d_k >_{V_{ad}}}{\| d_{k-1} \|^2_{V_{ad}}}$
(Polak-Ribière),
$\xi_{k-1} = \dfrac{< c_k, c_k - c_{k-1} >_{U_{ad}}}{< C_{k-1}, c_k - c_{k-1} >_{U_{ad}}}$, $\eta_{k-1} = \dfrac{< d_k, d_k - d_{k-1} >_{V_{ad}}}{< D_{k-1}, d_k - d_{k-1} >_{V_{ad}}}$
(Hestenes-Stiefel),
$\xi_{k-1} = \dfrac{\| c_k \|^2_{U_{ad}}}{< C_{k-1}, c_k - c_{k-1} >_{U_{ad}}}$, $\eta_{k-1} = \dfrac{\| d_k \|^2_{V_{ad}}}{< D_{k-1}, d_k - d_{k-1} >_{V_{ad}}}$
(Dai-Yuan),

(*Step*11) Determine the direction: $C_k = -c_k + \xi_{k-1} C_{k-1}$, $D_k = -d_k + \eta_{k-1} D_{k-1}$,

(*Step*12) Determine (X_{k+1}, Y_{k+1}): $X_{k+1} = X_k + \lambda_k C_k$, $Y_{k+1} = Y_k - \delta_k D_k$,
where $0 < m \leq \lambda_k, \delta_k \leq M$ are the sequences of step lengths,

(*Step*13) If the gradient is sufficiently small (convergence): end; else set $k := k + 1$ and goto (*Step*7).

Optimal Solution: $(X, Y) = (X_k, Y_k)$.

Remark 12

1. *After derived the gradient $\mathcal{J}'$ of the cost functional $\mathcal{J}$, by using the adjoint model corresponding to the sensitivity state corresponding to the direct problem, we can use any other classical optimization strategies (see e.g (Gill et al., 1981)) to solve the robust/minimax control problems considered in this chapter.*
2. *For the discrete problem, the direct, sensitivity and adjoint problems can be discretized by a combination of Galerkin and the finite element methods for the space discretization and the classical first-order Euler method for the time discretization (see e.g. Chapter 9 of (Belmiloudi, 2008)).*

10.3 Conclusion

In ultrasound surgery, the best strategy to destroy the cancerous tissues is based on the rise in the temperature at the cytotoxic level (because the tumors are highly dependent on the temperature). Thus, in the clinical treatment of the tumors, it is very important to have enough complete knowledge about the behavior of the temperature in tissues. The mathematical models that we have used in this present work take account on the physical and thermal properties of the living tissues, in order to show the effects of living body exposure to variety energy sources (e.g. microwave and laser heating) on the thermal states of biological tissues.
For predicting and acting on the temperature distribution, we have discussed stabilization identification and regulation processes with and without randomness in data, parameters and, boundary and initial conditions, in order to reconstitute simultaneously the blood perfusion rate and the porosity parameter from MRI measurements (which are the desired online temperature distributions and thermal damages). In this context, we have considered two types of system of equations: a generalized form of the nonlinear transient bioheat transfer systems with nonlinear boundary conditions **(GNTB)** and the system (GNTB) coupled with a nonlinear radiation transport equation and a model of coagulation process.
The existence of the solution of the governing nonlinear system of equations is established and the Lipschitz continuity of the map solution is obtained. The differentiability and some

properties of the map solution are derived. Afterwards, robust control problems have been formulated. Under suitable hypotheses, it is shown that one has existence of an optimal solution, and the appropriate necessary optimality conditions for an optimal solution are derived. These conditions are obtained in a Lagrangian form. Some numerical methods, combining the obtained optimal necessary conditions and gradient-iterative algorithms, are presented in order to solve the robust control problems. We can apply the developed technic to other systems which couple the system **(GNTB)** with other processes, e.g. with a model calculating the SAR distribution in tissue during thermotherapy from the electrical potential as follows (Maxwell-type equation):

$$\begin{aligned} \nabla \times B &= \kappa_c E + J_{source}, \\ \nabla \times E &= -i\omega\mu_c B, \end{aligned} \tag{75}$$

where $i^2 = -1$, $\kappa_c = \sigma + i\omega$ is the complex admittance, σ is the electrical conductivity, μ_c is the magnetic permeability type, J_{source} is the current density, E is the complex electric field vector, B is the complex magnetic field vector. The heat source term f can be taking as

$$f = SAR = \frac{1}{2}\sigma \mid E \mid^2 .$$

To derived the SAR distribution requires complex approach that is not discussed here : reader may refer e.g. to (Belmiloudi, 2006), for details on application complex robust control approach .

It is clear that we can consider other observations, controls and/or disturbances (which can appear in the boundary condition or in the state system) and we obtain similar results by using similar technique as used in this work (see (Belmiloudi, 2008)).

11. References

Adams, R. A. (1975). *Sobolev spaces,* Academic Press, New-York.

Arkin, H.; Holm, K.R.; Chen, M.M. & Bottje, W.G. (1986). Thermal pulse decay method for simultaneous measurement of local thermal conductivity and blood perfusion: A theoritical Analysis, *J. Biomech. Eng.*, 108, (1986), 208-214.

Atkins, P.W. (1982). *Physical chemistry,* Oxford University Press.

Belmiloudi, A. (2005). Nonlinear optimal control problems of degenerate parabolic equations with logistic time-varying delays of convolution type. *Nonlinear Anal.,* 63, (2005), 1126-1152.

Belmiloudi, A. (2006). Robust control problems of vortex dynamics in superconducting films with Ginzburg-Landau complex systems. *Abstr. Appl. Anal.,* 1-43, (2006) (Article ID 26724).

Belmiloudi, A. (2006). On some control problems for heat transfer systems in perfused biological tissues. *Wseas Translations on System,* 5, (2006), 17-25.

Belmiloudi, A. (2007). Analysis of the impact of nonlinear heat transfer laws on temperature distribution in irradiated biological tissues: Mathematical models and optimal controls. *J. Dynam. Control Systems,* 108, (2007), 217-254.

Belmiloudi, A. (2008). *Stabilization, optimal and robust control. Theory and applications in biological and physical sciences,* Communications and Control Engineering. Springer, London.

Belmiloudi, A. (2010). Parameter identification problems and analysis of the impact of porous media in biofluid heat transfer in biological tissues during thermal therapy. *Nonlinear Analysis: Real World Applications,* 11, (2010), 1345-1363.

Bohm, M.; Kremer, J. & Louis, A.K. (1993). Efficient algorithm for computing optimal control of antennas in hyperthermia. *Surveys Math. Indust.*, 3, (1993), 233-251.

Charney, C.K. (1992). Mathematical models of bioheat transfer. *Adv. Heat Trans.*, 22, (1992), 19-155.

Chato, J.C. (1980). Heat transfer to blood vessels. *J. Biomech. Eng.*, 102, (1980), 110-118.

Chen, M.M. & Holmes, K.R. (1980). Microvascular contributions in tissue heat transfer. *Annals N.Y. Acad. Sci.*, 335, (1980), 137-150.

Chen, M.M. & Holmes, K.R. (1980). In vivo tissue thermal conductivity and local blood perfusion measured with heat pulse-decay method. *Adv. Bioeng.*, (1980), 113-115.

Ciarlet, P.G. (1989). *Introduction to numerical linear algebra and optimization,* Cambridge Press.

Delfour, M.C.; Payre, C. & Zelesio, J.P. (1987). Approximation of nonlinear problems associated with radiating bodies in space. *SIAM J. Numer. Anal*, 24 (1987), 1077-1094.

Deuflhard, P. & Seebass, M. (1998). Adaptive multilevel FEM as decisive tools in clinical cancer therapy hyperthermia. *Konrad-Zuse-Zentrum fur informationstechnikl, Berlin Takustr.*, 7, (1998), D-14195 Berlin.

Ekeland, I. & Temam, R. (1976). *Convex analysis and variational problems,* North-Holland, Amsterdam.

Feng, Y.; Oden, J.T. & Rylander, M.N. (2008). A two-State cell damage model under hyperthermic conditions: theory and in vitro experiments. *J. Biomech. Engrg.*, 130, (2008), 1-10.

Gilbarg, D. & Trudinger, N.S. (1983). *Elliptic partial differential equations of second order*, Springer, Berlin.

Gill, P.E.; Murray, W. & Wright, M.H. (1981). *Pratical Optimization,* Academic Press, San Diago.

Hadamard, J. (1923). *Lectures on Cauchy problem in linear differential equations,* Yale University Press, New Haven, CT.

He, X. & Bischof, J. (2003). Quantification of temperature and injury response in thermal therapy and cryosurgery. *Crit. Rev. Biomed. Eng.*, 31, (2003), 355-421.

Henriques Jr, F.C. (1947). Studies of thermal injury: V. The predictability and the significance of thermally induced rate process leading to irreversible epidermal injury. *Arch. Pathol.*, 43, (1947), 489-502.

Hill, J. & Pincombe, A. (1992). Some similarity temperature profiles for the microwave heating of a half-space. *J. Austral. Math. Sco. Ser. B,* 33, (1992), 290-320.

Hirst, D.G. (1989). Tumor blood flow modification therapeutic benifit: is this approach ready for clinical application? In: *Review. GrayLaboratory 1989 Annual Report.* Michael B and Hance M (eds). Cancer Research Campaign, London, (1989), 14-17.

Hutchinson, E.; Dahleh, M.A. & Hynynen, K. (1998). The feasibility of MRI Feedback Control for Intracavitary Phased Array Hyperthermia Treatments. *Int. J. Hyperthermia,* 14, (1998), 39-56.

Ishimaru, A. (1978). *Waves propagation and scattering in random media*, Vol. I, Academic Press, New York.

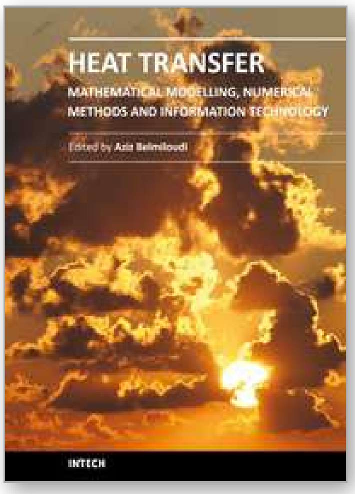
Khaled, A.R.A. & Vafai, K. (2003). The role of porous media in modeling flow and heat transfer in biological tissues. *Int. J. Heat. Mass transfer,* 46, (2003), 4989-5003.

Köhler, T.; Maass, P.; Wust, P. & Seebass, M. (2001). A fast algorithm to find optimal controls of multiantenna applicators in regional hyperthermia. *Phys. Med. Biol.*, 46, (2001), 2503-2514.

Kowalski, M.E. & Jin, J.M. (2004). Model-based optimization of phased arrays for electromagnetic hyperthermia. *IEEE Trans. Microwave Theory Tech.*, 52, (2004),

1964-1977.
Lions, J.L. (1961). *Equations differentielles operationnelles,* Springer-Verlag, New York.
Lions, J.L. & Magenes, E. (1968). *Problèmes aux limites non homogènes et applications,* Tome 1&2, Dunod, Paris.
Liu, J.; Zhu, L. & Xu, X.L. (2000). Studies on three-dimensional temperature transients in the canine prostate during transurethal microwave thermal therapy. *ASME J. Biomech. Eng.,* 122, (2000), 372-379.
Loève, M. (1977). *Probability theory*, Springer-Verlage, Berlin.
Marchant, T. & Lui, B. (2001). On the heating of a two-dimensional slab in a microwave cavity: aprature effects. *ANZIAM J.,* 43, (2001), 137-148.
Martin, G.T.; Bowman, H.F. & Newman, W.H. (1992). Basic element method for computing the temperature field during hyperthermia therapy planning. *Adv. bio. Heat Mass Transf.,* 23, (1992), 75-80.
Malinen, M.; Duncan, S.; Huttunen, T. & Kaipio, J. (2006). Feedforward and feedback control of ultrasound surgery. *Appl. Numer. Math.,* 56, (2006), 55-79 .
Niemz, M. (2002). *Laser-tissue Interactions. Fundamentals and Applications,* Springer, Berlin.
Pennes, H.H. (1948). Analysis of tissue and arterial blood temperatures in the resting human forearm. *J. Appl. Phys.,* 1, (1948), 93-122 (and 85, (1998), 5-34).
Pincombe, A.H. & Smyth, N.F. (1991). Microwave heating of materials with low conductivity. *Proc. R. Soc., A,* 433, (1991) ,479-498.
Pomraning, G. C. (1973). *The Equations of Radiation Hydrodynamics,* Pergamon, Oxford.
Prato, G.Da. & Zabczyk, J. (1992). *Stochastic equations in infinite dimension*, University Press, Cambridge.
Seip, R. & Ebbini, E.S. (1995). Studies on three-dimensional temperature response to heating fields using diagnostic ultrasound. *IEEE Trans. Biomed. Eng.,* 42, (1995), 828-839.
Shih, T.C.; Kou, H.S. & Lin, W.L. (2002). Effect of effective tissue conductivity on thermal dose distributions on living tissue with directional blood flow during thermal therapy, *Inter. Comm. Heat Mass transfer,* 29, (2002), 115-126.
Skinner, M.G.; Iizuka, M.N.; Kolios, M.C. & Sherar, M.D. (1998). A theoretical comparison of energy sources-microwave, ultrasound and laser-for interstitial thermal therapy. *Phys. Med. Biol.,* 43, (1998), 3535-3547.
Sturesson, C. & Andersson-Engels, S. (1995). A mathematical model for predicting the temperature distribution in laser-induced hyperthermia. Experimental evaluation and applications. *Phys. Med. Biol.,* 40, (1995), 2037-2052.
Tropea, B.I. & Lee, R.C. (1992). Thermal injury kinetics in electrical trauma. *J. Biomech. Eng.,* 114, (1992), 241-250.
Valvano, J.W. et al. (1984). An isolated rat liver model for the evaluation of thermal techniques to measure perfusion. *J. Biomech. Eng.,* 106, (1984), 187-191.
Vanne, A. & Hynynen, K. (2003). MRI feedback temperature control for focused ultrasound surgery. *Phys. Med. Biol.,* 48, (2003), 31-43.
Weinbaum, S. & Jiji, L.M. (1985). A two simplified bioheat equation for the effect of blood flow on average tissue temperature. *J. Biomech. Eng.,* 107, (1985) , 131-139.
Wissler, E.H. (1998). Pennes' 1948 paper revisited. *J. Appl. Phys.,* 85, (1998), 35-41.
Xu, L.; Zhu, L. & Holmes, K. (1998). Blood perfusion measurements in the canine prostate during transurethral hyperthermia. *Ann. New York Acad. Sci.,* 858, (1998), 21-29.
Zhang, J.; Sandison, G.; Murthy, J. & Xu, L. (2005). Numerical simulation for heat transfer in prostate cancer cryosurgery. *J. Biomech. Eng.,* 127, (2005), 279-293.

Zhou, J. & Liu, J. (2004). Numerical study on 3d light and heat transfer in biological tissue with large blood vessels during laser-induced thermotherapy. *Numer. Heat Transfer A*, 45, (2004), 415-449.



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Over the past few decades there has been a prolific increase in research and development in area of heat transfer, heat exchangers and their associated technologies. This book is a collection of current research in the above mentioned areas and describes modelling, numerical methods, simulation and information technology with modern ideas and methods to analyse and enhance heat transfer for single and multiphase systems. The topics considered include various basic concepts of heat transfer, the fundamental modes of heat transfer (namely conduction, convection and radiation), thermophysical properties, computational methodologies, control, stabilization and optimization problems, condensation, boiling and freezing, with many real-world problems and important modern applications. The book is divided in four sections : "Inverse, Stabilization and Optimization Problems", "Numerical Methods and Calculations", "Heat Transfer in Mini/Micro Systems", "Energy Transfer and Solid Materials", and each section discusses various issues, methods and applications in accordance with the subjects. The combination of fundamental approach with many important practical applications of current interest will make this book of interest to researchers, scientists, engineers and graduate students in many disciplines, who make use of mathematical modelling, inverse problems, implementation of recently developed numerical methods in this multidisciplinary field as well as to experimental and theoretical researchers in the field of heat and mass transfer.