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BAYESIAN PARAMETER ESTIMATION IN THE BIOHEAT TRANSFER EQUATION

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Abstract. *In this work we applied the Markov Chain Monte Carlo method for the estimation of parameters appearing in Pennes' equation of bioheat transfer. The inverse problem of parameter estimation was solved with simulated transient temperature measurements. A one-dimensional test case was used to explore the capabilities of the MCMC method for bioheat transfer problems. The analysis of the sensitivity coefficients was performed in order to examine the linear dependence and low sensitivity of the model parameters. The direct problem was verified against a commercial code and the results of the inverse problem are presented for the detection of skin tumors.*

Keywords: *inverse problems, MCMC, Pennes' Equation, tumor*

1. INTRODUCTION

A classical model for bioheat transfer was proposed by Pennes (1948), which involves the heat transferred to a tissue from the blood and the metabolic heat rate as source terms in the heat conduction equation. Although some extended forms of the Pennes' equation were presented in the literature, its classical form is still applied in many cases nowadays. Extensions of Pennes' model for the mathematical modeling of the human thermal system were presented, for example, by (Stolwijk, 1971; Gagge, 1973; Gordon, 1974; Charny, 1992; Wissler, 1998; Werner and Buse, 1988; Fiala *et al.*, 2001). These models are based on physical laws for heat transfer from the core organs to the body surface. In almost all human organs (except bones and epidermis) metabolic heat is produced (Severens, 2008). Each organ of the human body has different thermophysical parameters (Fiala, 1998; Holmes, 2000). Temperature of the body skin depends on the environmental conditions, such as the ambient temperature, the thermal convection and radiation to the surroundings. Despite this very complicated heat transfer processes, the human body is kept at practically constant core temperature, normally between 36.5°C and 37.1°C, by active thermoregulation (Fiala, 1998). With respect to the skin, its mean temperature varies from 33.0°C to 34.5°C for men, and from 32.2°C to 35.0°C for women. Local skin temperature is variable over the body, in the range from 32.0°C to 35.5°C (Hardy and Stolwijk, 1966).

A situation different from that of normal cells is observed when a tumor exists. Tumors are not connected with a central regulation system and their cells have different thermophysical parameters. As an example, blood perfusion coefficient might be 50 times higher in a tumor than in a healthy tissue, while metabolic heat generation might be 65 times higher (Das and Mishra, 2013). If a tumor has a proper size and is located in a favorable location, it can be detected by a thermography imaging system. Some benefits of using thermography in the early stages of tumor growth are widely described in Kateb *et al.* (2009).

An important stage of tumor detection, however, is related to the estimate of bioheat equation parameters, based on thermography and inverse analysis. Many authors tried to estimate the tissue parameters using numerical analysis (Yuan *et al.*, 2012, Das *et al.*, 2014) or thermography images (Agnelli *et al.*, 2011; Bezerra *et al.*, 2013). Das *et al.* (2013) estimated the size and position of the tumor in a tissue by using an inverse methodology. For the detection of surface tumors, however, the variation of the temperature at the skin surface usually is very small, with fluctuations around 0.55°C or even 0.0077°C (Das *et al.*, 2013). Such small differences make the detection process very difficult. Souza *et al.* (2014) performed an inverse determination of blood perfusion coefficient, with good results. The effective thermal conductivity and the volumetric heat capacity of a living tissue were simultaneously estimated by Huang and Huang (2007). Figueiredo and Guimarães (2015) used the sequential function specification method for estimating location and

metabolic heat generation of a 6 cm tissue (1D problem) containing a breast tumor. Umadevi *et al*. (2011) used the MCMC method for estimating the position, size and temperature of a tumor.

In this work, we apply the Markov Chain Monte Carlo (MCMC) Method with the Metropolis-Hastings (M–H) algorithm to identify parameters appearing in a one dimensional bioheat transfer problem, involving a single tissue. The main advantage of such technique is the fact that prior information about the model parameters can be modeled and taken into account for the inverse problem analysis, together with the measurements.

Bioheat transfer is modelled in terms of Pennes' equation. Simulated temperature measurements are used for the solution of the present inverse problem. The sensitivity coefficients with respect to the different parameters are examined, in order to detect small sensitivity and linear dependency among the parameters.

2. DIRECT PROBLEM

The one-dimensional case analyzed here is a representation of a skin layer located at the thigh of a human body. Simulated transient temperature measurements are taken on the skin surface. The medium is considered as a slab of thickness *L*, with the internal surface subjected to a constant temperature T_a (the arterial blood temperature). The other surface is exposed to the ambient, at a temperature T_∞. Heat is transferred from the skin surface to the surrounding medium by convection and linearized radiation, with a heat transfer coefficient h. It is considered that the surface of the skin is initially in thermal equilibrium with a cold body, to generate a perturbation in the temperature, at time $t = 0$.

The heat transfer in a living tissue is thus described by the classical Pennes' equation:

$$\rho_t c_t \frac{\partial T}{\partial t} = \frac{\partial}{\partial x}\left(k_t \frac{\partial T}{\partial x}\right) + \omega_b \rho_b c_b (T_a - T) + \dot{q}_m \qquad \text{in } 0 < x < L \qquad \text{for } t > 0 \tag{1}$$

where T is the temperature of the tissue, T_a is the temperature of the arterial blood, ρ_t, c_t, k_t are the density, specific heat, and thermal conductivity of the tissue, respectively, ω_b is the blood perfusion rate of the tissue, ρ_b, c_b are the density and specific heat of the blood, respectively, and $\dot{q}_m$ represents a constant and uniform metabolic heat generation rate. The boundary and initial conditions are expressed as:

$$T = T_a \qquad \text{at } x = 0 \qquad \text{for } t > 0 \tag{2.a}$$

$$k_t \frac{\partial T}{\partial x} + hT = hT_\infty \qquad \text{at } x = L \qquad \text{for } t > 0 \tag{2.b}$$

$$T = F(x) \qquad \text{in } 0 < x < L \qquad \text{for } t = 0 \tag{3}$$

In this paper, the thermal parameters for the thigh are considered constant during the whole process. Their values, presented in Tab. 1, were taken from Fiala (1998) and Das and Mishra (2013).

Table 1. Input data used in this problem (Fiala, 1998; Das and Mishra, 2013)

No.	Variable	Value	Unit	No.	Variable	Value	Unit
1.	L	5	mm	8.	ρ_t	1085	$kg \cdot m^{-3}$
2.	T_a	37	°C	9.	c_t	3680	J/kg·K
3.	h	5	$W \cdot m^{-1}K^{-1}$	10.	k_t	0.47	$W \cdot m^{-1}K^{-1}$
4.	T_∞	23	°C	11.	$\dot{q}_m$	368	$W \cdot m^{3}$
5.	ω_b	1.05	$L \cdot s^{-1} \cdot m^{-3}$	12,	$\omega_{b\ tumor}$	50	$L \cdot s^{-1} \cdot m^{-3}$
6.	ρ_b	1060	$kg \cdot m^{-3}$	13.	$\dot{q}_{m\ tumor}$	29 000	$W \cdot m^{3}$
7.	c_b	3617	J/kg·K	14.	τ	250	s

The initial condition is assumed as a linear variation from $T_a = 37$°C at $x = 0$ to 1°C at the skin surface, $x = L$.

In the direct problem, all parameters appearing in equations (1-3) are considered as known; the objective of the direct problem is to determine the transient temperature variation in the skin layer. The solution of the direct problem was computed using the fully implicit Finite Volume Method, which was implemented in the MATLAB, (2014) platform. A grid independency analysis was made and 24 volumes were chosen to represent the spatial domain. A time step equal to 0.05 second was chosen, for a total time of 250 seconds. The code was verified against another numerical solution obtained with the ANSYS package, (2014).

3. INVERSE PROBLEM

The inverse problem examined here aims at estimating the parameters appearing in Eq. (1) by using transient temperature measurements taken at the surface x=0. The inverse problem is recast as statistical inference in the Bayesian framework of statistics. In order to obtain a solution for the inverse problem, in the form of a posterior

probability density, the likelihood function (which is the conditional probability of the measurements given the unknown parameters) and the prior model for the parameters, are necessary. The posterior probability distribution is a model of the conditional probability distribution of the unknown parameters given the measurements. The likelihood incorporates the measurements and their related uncertainties, while the prior is a model for the unknowns, that reflects all the uncertainty of the parameters before the measurements are available. All of those data can be combined, using Bayes' theorem (Kaipio and Somersalo, 2004; Beck and Arnold, 1977; Calvetii and Sormesalo, 2007), to calculate the posterior distribution. The Bayes' theorem is the formal mechanism that allows combining the new information (measurements) with the previously available information (prior). If **P** (parameters) and **Y** (measurements) are continuous random variables, the following equation can be written:

$$\pi(\mathbf{P}|\mathbf{Y}) = \frac{\pi(\mathbf{P},\mathbf{Y})}{\pi(\mathbf{Y})} \tag{4}$$

where, the conditional density of the random variable **P**, given a value of the random variable **Y** is the joint density of **P** and **Y** divided by the marginal density of **Y**, where:

$$\pi(\mathbf{Y}) = \int_{R^N} \pi(\mathbf{P},\mathbf{Y}) d\mathbf{P} \tag{5}$$

where R^N is N–dimensional space.

The joint density $\pi(\mathbf{P},\mathbf{Y})$ is not generally known, but it can be written in terms of the likelihood and the prior as:

$$\pi(\mathbf{P},\mathbf{Y}) = \pi(\mathbf{Y}|\mathbf{P})\pi(\mathbf{P}) \tag{6}$$

By substituting Eq.(6) into Eq.(4) we then obtain Bayes' theorem, which is given by:

$$\pi_{posterior}(\mathbf{P}) = \pi(\mathbf{P}|\mathbf{Y}) = \frac{\pi(\mathbf{Y}|\mathbf{P})\pi(\mathbf{P})}{\pi(\mathbf{Y})} \tag{7}$$

where $\pi_{posterior}(\mathbf{P})$ is the posterior probability density, $\pi(\mathbf{P})$ is the prior density, $\pi(\mathbf{Y}|\mathbf{P})$ is the likelihood function and $\pi(\mathbf{Y})$ is the marginal probability density of the measurements, which plays the role of a normalizing constant.

In this work, a prior density model in the form of a truncated Gaussian distribution was assumed. For a single parameter P_j, truncated by P_{min} and P_{max}, the truncated Gaussian prior with mean μ_j and variance $\sigma_j^2, P_j \sim N(\mu_j, \sigma_j^2)$, is given by:

$$\pi(P_j) = \left[-\frac{1}{2}\frac{(P_j - \mu_j)^2}{{\sigma_j}^2}\right] \qquad \text{for } P_{min} \le P_j \le P_{max} \tag{8.a}$$

$$\pi(P_j) = 0 \qquad \text{for } P_j < P_{min} \text{ or } P_j > P_{max} \tag{8.b}$$

Since the computation of $\pi(\mathbf{Y})$ with Eq. (5) is in general difficult, and usually not needed for a practical calculations, Bayes' theorem is commonly written as:

$$\pi_{posterior}(\mathbf{P}) = \pi(\mathbf{P}|\mathbf{Y}) \propto \pi(\mathbf{Y}|\mathbf{P})\pi(\mathbf{P}) \tag{9}$$

For those cases that the posterior is not analytical and/or numerical integrations required for estimates are not practical, Markov Chain Monte Carlo methods appears as practical tool for the solution of the inverse problem (Kaipio and Somersalo, 2004; Calvetii and Sormesalo, 2007). One disadvantage on the application of MCMC methods is the large computational time required.

The most common MCMC algorithm is the Metropolis-Hastings (M-H) (Metropolis *et al*., 1953; Hastings, 1970; Lee, 2004; Winkler, 2003; Kaipio and Somersalo, 2004; Orlande *et al*., 2011; Orlande, 2012; Orlande *et al*., 2014). The M-H algorithm draws samples from a candidate density, such as in the acceptance-rejection sampling method.

The M–H algorithm draws samples from a candidate density, such as in acceptance-rejection sampling and is used to generate samples from a density $p(\boldsymbol{P}) = \tilde{p}(\boldsymbol{P})/K$, where the normalizing constant K might be unknown. Instead of sampling form $p(\boldsymbol{P})$, assume that there exists a candidate density $h(\boldsymbol{P})$ that is easy to simulate samples form, where $p(\boldsymbol{P}) \le c\, h(\boldsymbol{P})$ and c is constant. To obtain a random variable $\widehat{\boldsymbol{P}}$ from density $p(\boldsymbol{P})$ with the acceptance rejection method (Lee, 2004) can be done by the following steps:

1. Generate a random variable $\boldsymbol{P}^*$ from the density $h(\boldsymbol{P})$;
2. Generate a random value $U \sim U(0,1)$ which is uniformly distributed in (0,1);
3. If $U \leq \tilde{p}(\boldsymbol{P})/c\, h(\boldsymbol{P})$, let $\widehat{\boldsymbol{P}} = \boldsymbol{P}^*$. Otherwise, back to step 1.

The selection of a candidate proposal distribution $\left(\mathbf{P}^*|\mathbf{P}^{(t)}\right)$, which is used to draw a new candidate state $\mathbf{P}^*$ given the current state $\mathbf{P}^{(t)}$ of the Markov chain, should be the first step of the implementation M-H algorithm.

A random walk proposal was used in this work, given by

$$P_j^* = P_j^{(t)} + w_j(2r - 1) \tag{10}$$

where r is a random number with uniform distribution in $(0,1)$, that is, $r \sim U(0,1)$, while w_j is the maximum variation for the parameter P_j.

Simulated temperature measurements were utilized in this paper, which were obtained as:

$$\mathbf{Y} = \mathbf{T}_{\boldsymbol{dir}} + \mathbf{r}_{randn}\sigma_{meas} \tag{11}$$

where $\mathbf{Y}$ is the vector of simulated measured temperatures, $\mathbf{T}_{\boldsymbol{dir}}$ is the vector of exact temperatures obtained from the direct problem solution with known parameters, and $\mathbf{r}_{randn}$ is the vector of normally distributed uncorrelated random numbers, with zero means and constant standard deviations σ_{meas}.

A crucial step in the inverse problem of parameter estimation is the analysis of the sensitivity coefficients. Parameters that are linearly dependent or have small sensitivity with respect to the measurements cannot be identified (Ozisik and Orlande, 2000). In this paper, since the parameters have different orders of magnitude, it is more appropriate to use the reduced sensitivity coefficients, defined as:

$$J_{P_j} = P_j \frac{\partial T}{\partial P_j} \tag{12}$$

where $P_j, j = 1, \ldots, N$, are the unknown parameters.

4. RESULTS AND DISCUSSIONS

The analysis of equation Eq.(1) clearly shows that it is not possible to estimate all 7 parameters (ω_b, ρ_b, c_b, ρ_t, c_t, k_t, $\dot{q}_m$), because some of them are linearly dependent, that is, they do not appear in the formulation independently, but as a group of parameters. Therefore, the following groups of parameters were analyzed: $A = (\rho_t\, c_t)$; $B = k_t$; $C = (\omega_b\, \rho_b\, c_b)$; $D = \dot{q}_m$. The linear dependence could be easily recognized by displaying their ratio (in example $z = B/A$) for each point as a function of the time $f(\tau) = z$.

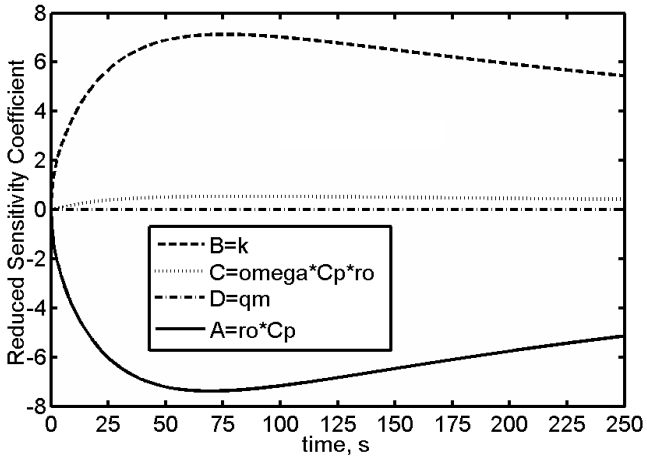

Figure 1. Sensitivity analysis for heathy skin tissue.

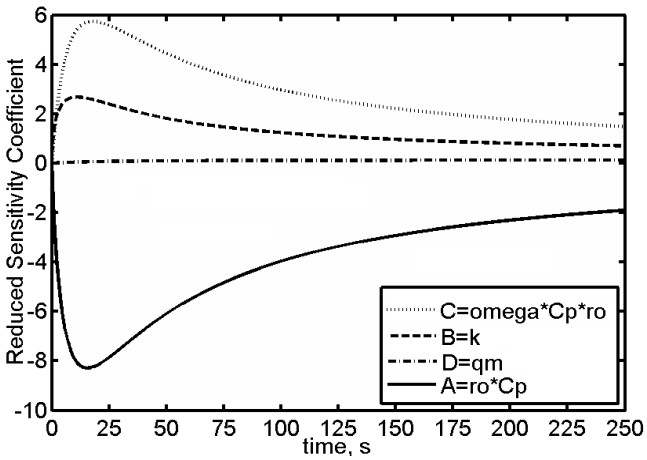

Figure 2. Sensitivity analysis for tumorous skin tissue.

Figures 1 and 2 present the sensitivity coefficients with respect to the above parameters, as a function of time, for healthy and tumorous tissues, respectively. As it can be observed in Fig.1, the magnitude of the sensitivity coefficient with respect to D is very small for a healthy tissue; hence, the estimation of this parameter is difficult in this case. Similarly, the magnitude of the sensitivity coefficient of this parameter is very small for the case of a tumorous tissue (see Fig. 2). The magnitude of the sensitivity coefficient with respect to the parameter C for the healthy tissue (Fig.1) is also very small. For the healthy tissue, parameters A and B are linearly dependent. Such is also the case for the

tumorous tissue, where parameter C is also linearly dependent with respect to parameters A and B (Fig.2). Therefore, the analysis of the sensitivity coefficients shows that the conditions are appropriate for the estimation of parameter C, for both healthy and tumorous tissues, provided that informative priors are provided for the other parameters. Nevertheless, we note in figures 1 and 2 that parameter D does not influence the temperature variation at x=0, even for the very different values assumed for this parameter in the sensitivity analysis (see Table 1).

We now proceed to the estimation of parameters, aiming at the identification of a cancerous tissue. After the analysis of figure 2, we seek to accomplish this objective through the estimation of parameter C. Therefore, informative priors will be used for parameters A and B, in order to handle their linear dependence, that is, such parameters would need to be measured prior to the experiment proposed in this work. Since parameter D does not significantly influence the temperature at the surface of the skin where measurements are taken, it is also considered with a non-informative prior for the application of the Markov Chain Monte Carlo method. The priors used for the results presented below are shown in table 2. The values presented in this table, as well as for the results presented below, are relative to the exact values of the tumorous tissue.

Table 2. Values specified for the truncated Gaussian priors

Parameter	μ_i	σ_i	$P_{min,j}$	$P_{max,j}$
C	0.021	0.01	0	1.2
D	0.0126	0.01	0	1.2

The Markov chains were started at the values of the healthy tissues, and 40000 states were simulated. Two different levels of measurement errors were used in the inverse analysis, involving standard deviations of 0.01°C and 0.1°C. In the following analysis measurements were simulated, as well as theirs errors. Although accuracy 0.01°C is not possible to reach and was taking into account only for tests, however value 0.1°C is possible to keep for a thermocouple, especially that the temperature range is not too wide, and occurs between 0°C to 36°C. The results obtained for the estimated means and standard deviations for parameters C and D, after the chains have reached equilibrium with burn-in periods of 20000 states, are presented in Table 3.

We note in table 3 that both parameters C and D were accurately estimated when measurements with small uncertainties were used in the inverse analysis, despite the fact that the sensitivity coefficients of parameter D was quite small. The Markov chains after the burn-in period and the histograms of the respective marginal posterior distributions for this case are presented by figures 3 and 4, respectively.

The marginal posteriors are Gaussian, but the uncertainties in the estimated parameter D are relatively larger than those for the parameter C, as a result of the small magnitude of the sensitivity coefficient for D. Such a fact becomes more apparent when the parameters are estimated with measurements with a larger standard deviation, where only the parameter C could be accurately estimated (see table 3). Anyhow, the value estimated for the parameter D is much larger than that of the healthy tissue, where the Markov chain was started. Hence, the estimation of both C and D strongly suggest that the tissue is tumorous, which is indeed the case.

The Markov chains for the case with a larger standard deviation is presented in figures 5.a,b, which shows convergence after about 10000 states. It is interesting to note in these figures that the chain for the parameter C immediately increases from the initial guess (value for the healthy tissue) to the exact value of the tumorous tissue. On the other hand, the Markov chain for the parameter D remains around its initial value and only starts to increase after the chain for C has converged. Such behavior is also due to the small magnitude of the sensitivity coefficient for the parameter D.

For the sake of brevity, the estimation of parameters C and D for the healthy tissue are not presented in this paper, but they were accurately recovered when the chains were started at their mean values.

Table 3. Results for cases with tumor.

σ_{meas} (°C)	C_{est}/C_{exact}	$SD(C_{est}/C_{exact})$	D_{est}/D_{exact}	$SD(D_{est}/D_{exact})$
0.01	1.00200	0.000141	0.9677	0.0016
0.1	1.02290	0.000516	0.1550	0.0082

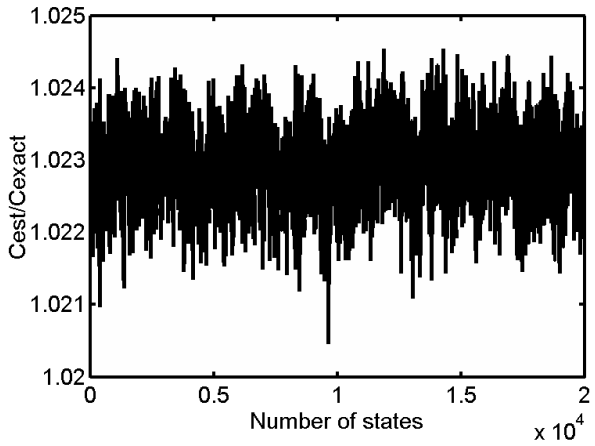

Fig.3.a. Markov chain for parameter C (σ = 0.1°C).

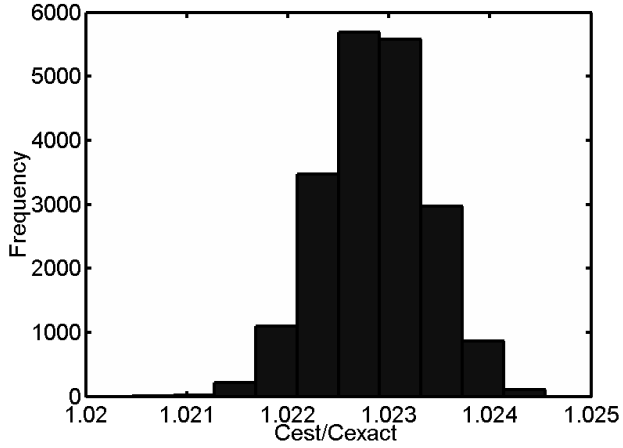

Fig.3.b. Marginal posterior for parameter C (σ = 0.1°C).

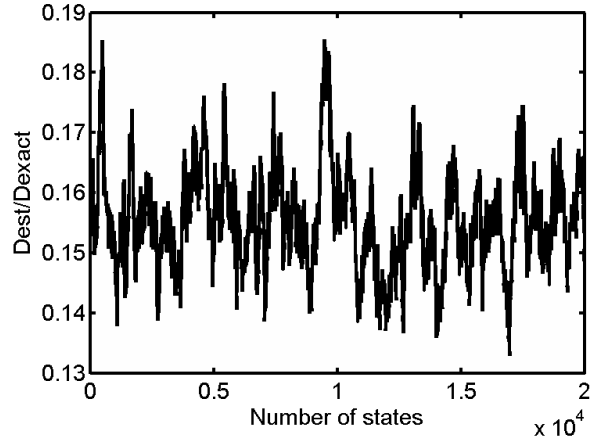

Figure 4.a Markov chain for parameter D (σ= 0.1°C).

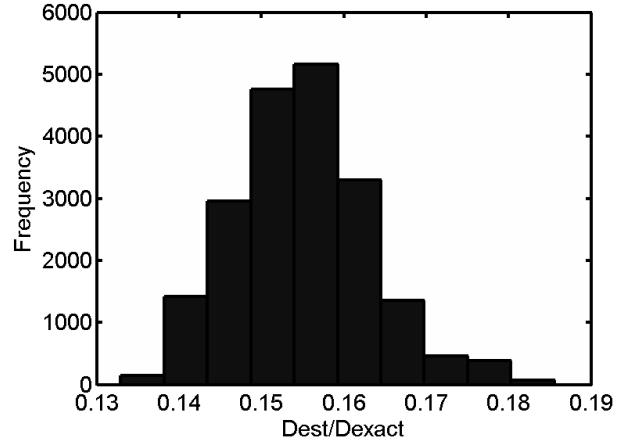

Figure 4.b Marginal posterior for parameter D (σ= 0.1°C).

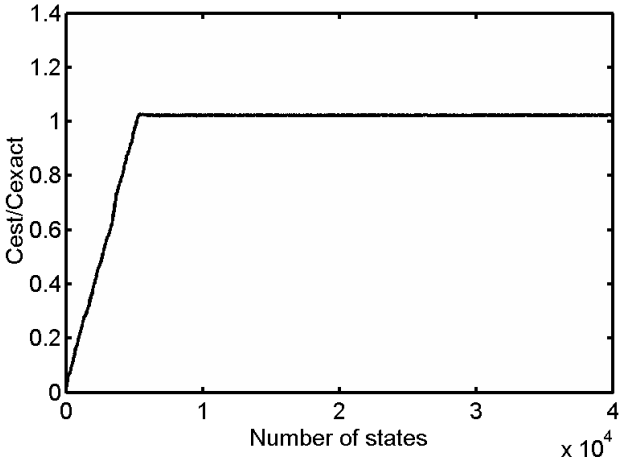

Figure 5.a Markov chain for parameter C (σ = 0.1°C).

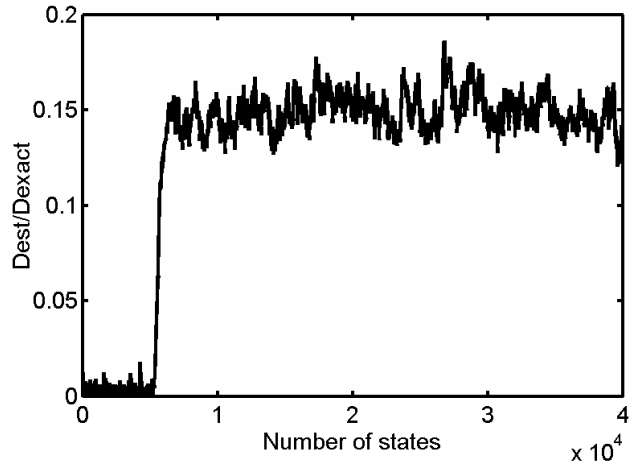

Figure 5.b Markov chain for parameters D (σ = 0.1°C).

5. CONCLUSIONS

This paper dealt with the solution of an inverse parameter estimation problem in bioheat transfer, aiming at the detection of cancer in a skin layer. The experiment under analysis involves the cooling of the surface of the skin and monitoring of its temperature during re-heating caused by perfusion, metabolism and surface convective/radiative heat transfer. Results obtained with simulated transient measurements show that estimates of parameters associated to the perfusion rate and to the metabolic heat generation rate could characterize a cancerous tissue, even by starting the Markov chains at the values of healthy tissues. More realistic cases involving a multidimensional problem and surface temperature measurements with an infrared camera are currently being undertaken.

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