

# Multiscale numerical modeling of the spherically symmetric cryosurgery problem

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**Abstract.** The work is concerned with the numerical studying of the cryogenic biotissue destruction by a spherically symmetric tip. The multiscale bioheat transfer model is used for the describing of the biological solutions crystallization features. An explicit finite volume based approximation is applied for the numerical modeling of the processes taking place during the cryosurgery. The phase averaging method is applied as an computationally economic approach for the numerical modeling of the problem under study.

## 1. Introduction

During the last decades the cryosurgery methods has been considerably developed and has become a competitive approach for human cancer treatment. In the light of introduction of computer technologies into the wide range of science-based applications, nowadays, the prediction of the cryosurgery results is one of the actual problems of the computational medicine. The cryosurgical treatment is known to be based on the tissue necrosis effect. The last one is caused by the ice ball propagation from the tips of cryoneedles in the tissue to treat. However, the describing of the freezing interface evolution in terms of the classical Stephan problem for the phase change of the first kind meets a valuable difficulties because of the peculiarities of physical processes in the bio-tissues which take place under the cryogenic treatment on the cell scale.

## 2. Multiscale model of the cryogenic bioheat transfer

Let us consider the problem of the cryogenic bio-tissue destruction by a spherical cryotip with the radius  $R_0$ . The main peculiarity of the propagation of the freezing interface is the blurring of the last one in some temperature interval depending on the intensity of cryogenic impact, i.e. local freezing speed. In particular, the cell dehydration process caused by the occurring of the difference between the osmotically pressures from different sides of the cell membrane may become even negligible comparing with an intracellular ice nucleation. It is caused by the exponential reduction of the membrane permeability:

$$L_p = L_{pg} \exp \left[ -\frac{E_{lp}}{R} \left( \frac{1}{T} - \frac{1}{T_r} \right) \right]. \quad (1)$$



In current work for the cell dehydration process a model, obtained by Mazur [1] for the dynamics of the unfrozen intracellular water volume  $V_w$ , was used:

$$\frac{\partial V_w(T, t)}{\partial t} = -\frac{L_p A R T}{\nu_w} \left( \ln \left[ \frac{V_w - V_b}{(V_w - V_b) + \phi \nu_w n_s} \right] - \frac{L}{R} \left[ \frac{1}{T_r} - \frac{1}{T} \right] \right) \quad (2)$$

The intracellular ice nucleation speed  $\frac{dN}{dt}$  is assumed to be described in the following manner [2, 3]:

$$\frac{dN}{dt} = IN(V_w - V_b), \quad (3)$$

where  $I$  is the coefficient of the nucleation speed, satisfying the following equalities:

$$\begin{aligned} I &= \Omega(T) \exp \left( -\frac{\kappa}{\delta T^2 T^3} \right), \delta T = (T_r - T), \\ \Omega &= \Omega_0 \left( \frac{T}{T_r} \right)^2 \left( \frac{\eta_0}{\eta(T)} \right). \end{aligned} \quad (4)$$

Here  $\eta$  has sense of the viscosity and can be directly calculated:

$$\eta = 0.139 \cdot 10^{-3} \left[ \frac{T}{225} - 1 \right]^{-1.64}. \quad (5)$$

The extracellular ice nucleation can be described well by the temperature dependance of liquid phase fraction  $\Lambda_{ec}$  for NaCl solution:

$$\Lambda_{ec}(T) = \begin{cases} 1 & T \geq 272.62K \\ \max(\frac{0.53}{273.15-T}, b_e) & T < 272.62 \end{cases} \quad (6)$$

On this way the fraction of unfrozen water  $\Lambda$  can be estimated in the form:

$$\Lambda = f_{ic}\Lambda_{ic} + f_{ec}\Lambda_{ec}, \quad f_{ic,ec} = Const \quad (7)$$

Here  $f_{ic}, f_{ec}$  are the corresponding mass fractions and  $\Lambda_{ic} = V_w/V_0$ , where  $V_0$  is the intracellular water volume under the normal conditions. Using the mass conservation law and introducing functions  $X = V_w/V_0$  and  $Y = V_{ice}/V_0$  for the intracellular ice one can obtain the governing system for the phase content of the cell, which in appropriate notation can be deduced to the form:

$$\frac{\partial X}{\partial t} = F(X, Y, T), \quad \frac{\partial Y}{\partial t} = G(X, Y, T) \quad (8)$$

Taking into account the mentioned above, it seems naturally to demand from macroscopic characteristics of heat capacity and thermal conductivity (which is known for fully unfrozen and frozen states) to be the functions of water content of the tissue. In this paper we assume that on the macroscopic scale the heat transfer can be described by the Pennes model [4]. In this way the problem under study can be written in following manner:

$$\begin{aligned} \bar{C} \frac{\partial T}{\partial t} &= \frac{1}{r^2} \frac{\partial}{\partial r} \left( r^2 \bar{k}(T) \frac{\partial T}{\partial r} \right) + \rho_b \omega_b C_b (T_b - T) + q_{met} - \rho L \frac{\partial \Lambda}{\partial t}, \\ T(R_0, t) &= \Phi(t), \quad \left. \frac{\partial T}{\partial r} \right|_{r=L} = 0, \quad t > 0, \quad L > r > R_0, \end{aligned} \quad (9)$$

where  $\Phi(t)$  is the temperature of the cryotip surface neighborhood and the macroscopic characteristics are assumed as the weighted functions of the known values:

$$\begin{aligned}\overline{C}(T) &= [f_{ic}\alpha_{fr} + f_{ec}\beta_{fr}]C_{fr}(T) + [f_{ic}\alpha_{unfr} + f_{ec}\beta_{unfr}]C_{unfr}(T), \\ \overline{k}(T) &= f_{ic}\alpha_{fr} + f_{ec}\beta_{fr}]k_{fr}(T) + [f_{ic}\alpha_{unfr} + f_{ec}\beta_{unfr}]k_{unfr}(T), \\ \frac{\partial X}{\partial t} &= F(X, Y, T), \quad \frac{\partial Y}{\partial t} = G(X, Y, T), \quad \Lambda = (f_{ic}X + f_{ec}\Lambda_{ec})\rho_w L, \\ \alpha_{fr} &= \frac{1 - X}{1 - V_b/V_0}, \quad \alpha_{unfr} = \frac{X - V_b/V_0}{1 - V_b/V_0}, \quad \beta_{fr} = \frac{1 - \Lambda_{ec}}{1 - b_e}, \quad \beta_{unfr} = \frac{\Lambda_{ec} - b_e}{1 - b_e}.\end{aligned}\tag{10}$$

The condition  $\frac{\partial T}{\partial r}|_{r=L} = 0$  means the considered computational domain to be of spherical layer form with outer border enough distant from the cryotip surface.

For the numerical modeling of the thermal processes around the cryotip's working surface an explicit finite volume scheme was used. Introducing a computational mesh  $\omega_{h_1, h_2}$ :

$$\begin{aligned}\omega_{h_1, h_2}^{\tau_M} &= [r_i : r_0 = R_0, r_N = L, r_i = r_{i-1} + h_i, i = \overline{1, N_r}] \\ t^n : t^0 &= 0, t^N = T, t^j = t^{j-1} + \tau_M, j = \overline{1, N}], \\ h_1 &= \min_i h_i, \quad h_2 = \max_i h_i\end{aligned}\tag{11}$$

and defining a half step nodes  $r_{i+1/2} = (r_{i+1} + r_i)/2$  one can integrate (9) upon the spherical layer enclosed by  $r_{i\pm 1/2}$  and obtain the following scheme:

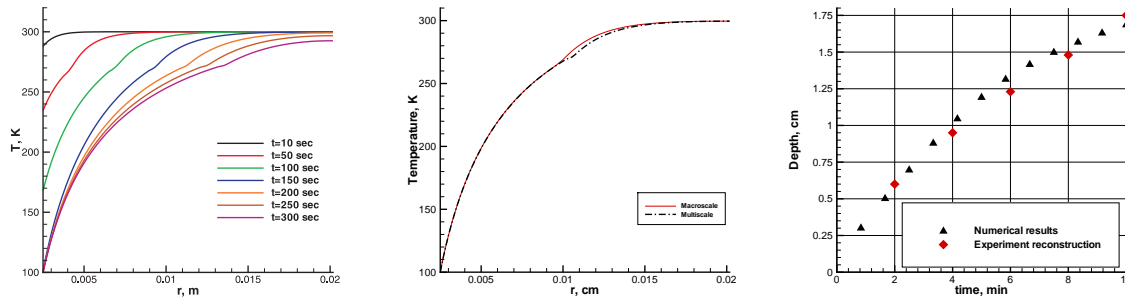
$$\begin{aligned}V_i \frac{T_i^{n+1} - T_i^n}{\tau_M} &= \frac{4\pi}{\overline{C}_i^n} \left[ (r_{i+\frac{1}{2}})^2 \overline{k}_{i+\frac{1}{2}}^n \frac{T_{i+1}^n - T_i^n}{r_{i+1} - r_i} - (r_{i-\frac{1}{2}})^2 \overline{k}_{i-\frac{1}{2}}^n \frac{T_i^n - T_{i-1}^n}{r_i - r_{i-1}} \right] + \\ &+ \rho_b \omega_b C_b (T_b - T_i^n) V_i + q_{met} V_i - \rho L \frac{\Lambda_i^n - \Lambda_i^{n-1}}{\tau_M}, \\ V_i &= \frac{4\pi}{3} \left[ (r_{i+\frac{1}{2}})^3 - (r_{i-\frac{1}{2}})^3 \right], \\ \overline{k}_{i+\frac{1}{2}}^n &= (\overline{k}_i^n + \overline{k}_{i+1}^n) / 2.\end{aligned}\tag{12}$$

The semi-implicit Euler-Cauchy scheme was applied to evaluate the microscopic tissue parameters in each computational cell. During the numerical experiments the cryotip with working surface radius  $R_0 = 0.0025\text{m}$  and temperature  $\Phi(t) = \max(300 - At, 100)K$  with  $A = 80K/\text{min}$  was considered. The results of numerical computation for the evolution of the temperature profile in the tissue are shown on Fig.1 (left).

Unfortunately, the multiscale model is not applicable for practicing surgeons to obtain the prognosis of cryosurgery because of its computational economy even for the one dimensional reduction of the problem under study. Yet, it can be successfully used for the carrying out the scientific research of the cryogenic processes in bio-tissues.

In order to avoid the computational difficulties, arising when the multi-scale model is applied, and to save the consideration of the cryogenic processes on the cell scale the phase-averaged method can be used. This approach supposes the introduction of the biparametric family of an enthalpy models:

$$\begin{aligned}C(T; T_\alpha, T^*) \frac{\partial T}{\partial t} &= \frac{1}{r^2} \frac{\partial}{\partial r} r^2 \overline{k}(T; T_\alpha, T^*) \frac{\partial T}{\partial r} + \rho_b \omega_b C_b (T_b - T), \\ t > 0, L > r > R_0.\end{aligned}\tag{13}$$



**Figure 1.** Left: the multiscale model based numerical results for the temperature profile evolution. Center: Comparison of the results obtained by multi-scale and phase-averaged model. Right: The dependence of the freezing zone propagation depth on the freezing time. Comparison of the numerical results with the experimental data reconstruction

Here the macroscopic parameters are determined by the interpolation equalities:

$$\begin{aligned} \bar{k}(T; T_\alpha, T^*) &= \begin{cases} k_1(T), & T \leq T_\alpha \\ k_1(T_\alpha) + \frac{k_2 - k_1(T_\alpha)}{T^* - T_\alpha}(T - T_\alpha), & T_\alpha < T < T^* \\ k_2, & T \geq T^* \end{cases} \\ \bar{C}(T; T_\alpha, T^*) &= \begin{cases} C_1(T), & T \leq T_\alpha \\ \frac{\rho L}{T_c - T_\alpha} + \frac{T^* - T_\alpha}{T_c - T_\alpha} C_1(T_\alpha) + \frac{T_c - T^*}{T_c - T_\alpha} C_2, & T_\alpha < T < T_c \\ C_2, & T \geq T_c \end{cases} \end{aligned} \quad (14)$$

In this way the parameters of the phase averaging are the lower temperature of the phase change  $T_\alpha$  and  $T^*$ , which has sense of the normalized phase change temperature in terms of the Stefan problem. The upper phase change temperature is assumed to be known value  $T_c = 273K$ . The numerical experiments have shown the possibility of choosing the averaging parameters which give the 98% agreement with the multiscale model based results. To validate the developed cryosurgery modeling tool the dependence of the freezing region propagation depth on the time was calculated and compared with the experimental data [5] for 3mm cryotip in the chicken breast (See Fig.1, Right). The discrepancy in the results was less than 5%.

### 3. Discussion

Although the multiscale model takes into account the features of the cryogenic processes on the cell scale its application in the medical practice meets the valuable difficulties caused by its computational cost. The phase-averaging approach has not got this disadvantage and can easily applied for the multidimensional problems [6], but it needs the knowing of the averaging parameters values.

It should be mentioned that the most of the cryosurgery protocols can be characterized by enough common thermal regimes. So, if the number of cryotips in the tissue to treat is not big (3-4) and their sizes are much lesser of the tumor tissue characteristic sizes ( $\sim 2 - 4\text{mm}$  versus  $\sim 3 - 4\text{cm}$ ), the following values for the averaging parameters can be taken:  $T_\alpha = 265K$ ,  $T^* = 269K$ .

#### 4. Conclusion

The problem of the cryogenic biotissue destruction by a spherically symmetric tip was numerically studied. The multiscale bioheat transfer model was used for the describing of the biological solutions crystallization features. An explicit finite volume based approximation was applied for the numerical modeling of the processes taking place during the cryosurgery. The evolution of the temperature profile in the neighborhood of the cryotip surface was computed. The phase averaging method was applied as an computationally economic approach for the numerical modeling of the problem under study. The comparison between the multi-scale model and averaged model with the experimental data has shown the applicability of the proposed methods for the prediction of the cryosurgery results and carrying out the research of the cryogenic processes in living tissues.

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