Blow-up singular dynamics in breast cancer metabolism

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Abstract. Cancer cells have an altered metabolism, which results in specific kinetics of the heat localization and coherent pattern formation. Modified nonlinear Pennes equation was used for the modeling of the metabolic temperature dynamics. The numerical experiments were conducted in order to identify the tissue metabolic reactions in terms of multiscale correlation parameters (spatial invariants) as the characteristics of globally convergent dynamics of blow-up collective modes and the cancer precursor.

1. Introduction
Heat transfer in biological systems plays an important role in different physiological processes because it affects the temperature and its spatial distribution in tissues [1]. It is known, that temperature dynamics within the living tissue may be used as a physical factor of progressing disease [2]. For example, breast cancer is usually associated with the skin temperature fluctuations overlying the tumor area [3]. Consequently, the analysis of thermal behavior in biological materials is important for understanding of biological processes and for several clinical applications [4] in the combination of experimental study and realistic models reflecting biologically based metabolic scenario of tissue evolution.

Infrared thermography is one of the methods which is used for investigation of thermal behavior in the human body. Thus, the work [5] considers the use of thermography to describe thermal pattern when orofacial pain. The application thermography for various medical fields is discussed in the work [6].

Pennes equation is the most commonly used for mathematical modeling of heat processes in the human organism [7]. This equation had been introduced in the work [8] for tissue temperature distributions of forearm. The dimensionless forms of Pennes equation for cylindrical and spherical coordinates were derived in [1, 9]. Parabolic and hyperbolic Pennes equations were applied for the modeling of transient temperature of the human eye in [10].

Infrared thermography and mathematical modeling can also be used for the study of the surface temperature pattern in the breast cancer [3, 11]. The study of the temperature fluctuation correlation properties from thermography data was conducted in the work [12] by wavelet transform maximum modulus (WTMM) method to establish the monofractal temperature dynamics for breast cancer tissue. Results of this method for one of the patients with cancerous breast and healthy volunteer are depicted in
the Fig. 1. Results of 3D-analysis of the temperature distribution of cancerous breasts, mathematical modeling of static and dynamic thermography is presented in the papers [13, 14].

This research represents the mathematical model for describing thermal behavior of breast tissue metabolism with the possible link of the spatial-temporal correlations in the blow-up heat dynamics and the cancer precursors.

**Figure 1.** Result of the use of WTMM method. A. Thermogram of cancerous breast for patient. B. Thermogram of opposite breast for same patient. C. Thermogram of right breast for healthy volunteer. D. Averaged scaling exponents. All thermograms were segmented into 8 x 8 pixel² squares. Red squares correspond to monofractal temperature dynamics, blue squares correspond to multifractal dynamics and white squares are no scaling. Scaling exponents were calculated in each squares and averaged over all squares. Red line corresponds to cancerous breast, black line corresponds to opposite breast for same patient and green line corresponds to healthy volunteer [12]
2. Temperature dynamics in cancer breast

The term cancer marks a group of disorders associated with dysregulated cell growth resulting in tumor formation, invasion into neighbouring tissues and spread to other parts of body. Some of common types of cancer originate in the breast, lung, skin and others organs [7]. Breast cancer is the most type of cancer in the world [12]. Because cancers vary so widely in their histologic features and physiological properties, the development of the non-invasive infrared scanning of tissue and the tumor diagnosis represents both fundamental and clinical interests [11].

There are differences in an energy consumption of normal and cancer tissue with local temperature changes [2]. Temperature and thermal conductivity, which directly depends on local blood flow, are much higher for the cancer breast that reflects the local metabolism leading to local heat generation [11]. An altered metabolism is observed also in cancer cells [15]. This metabolism is associated with critical dynamics of structural transformation in ensembles of biomolecules and results in specific kinetics of the heat distribution and correlated behavior of the heat localization areas. The surface thermal pattern of a breast, which related to metabolism and vascularization within the underlying tissues, may be changed as a result of pathological processes [11]. The correspondence of structural transformation to self-organized scenario could be experimentally observed in tissue by the analysis of temperature fluctuation series [16].

We use the nonlinear Pennes equation in order to design model of breast cancer metabolism, and describe temperature dynamics on the breast surface. The boundary problem reads:

\[
\rho c \frac{\partial T}{\partial t} = k \frac{\partial^2 T}{\partial x^2} + \alpha_k c_v (T_e - T) + Q_c \exp\left(-\frac{E}{RT}\right),
\]

\(T(0,x) = T_e\),

\( \frac{\partial T(t,0)}{\partial x} = 0\),

\(-k \frac{\partial T(t,r)}{\partial x} = h(T(t,r) - T_e)\).

The last term of equation (1) is the metabolic heat source in the form of the activation law [17]. The physical meaning of parameters in (1) – (4) problem is discussed in [18], where the nonlinear Pennes equation in the dimensionless form is considered. The modified nonlinear Pennes equation (5) combined with initial (6) and boundary conditions (7) – (8) was represented in the form [18]:

\[
\frac{\partial \theta}{\partial t} = \frac{\partial^2 \theta}{\partial \xi^2} + \alpha(1 - \theta) + \gamma \exp(\nu \theta),
\]

\(\theta(0,\xi) = \theta_0\),

\( \frac{\partial \theta(t,0)}{\partial \xi} = 0\),

\( \frac{\partial \theta(t,1)}{\partial \xi} = -Bi \cdot \theta(t,1)\).

Here \(t\) is a dimensionless time, \(\alpha, \gamma\) and \(\nu\) is dimensionless parameters. The solution of the boundary problem (5) – (8) revealed the existence of the blow-up solution for the developed stage of the heat localization for corresponding values of \(\alpha, \gamma\) and \(\nu\) parameters. Numerical methods for the solution of boundary problem in the presence of the blow-up regimes are discussed in [19, 20].

The dimensionless parameters in (5)-(6) were determined as

\[
\alpha(t) = \frac{\gamma(t) - \alpha_1}{29}.
\]
Here \( y_1, y_2, y_3 \) are the solutions of the Rössler system (12) – (17); \( a_1, a_2, a_3 \) is the coordinate of the global minimum for \( y_1, y_2, y_3 \). This form for \( \alpha, \gamma, \nu \) was chosen in order to obtain temporal solutions, which will be similar on temperature fluctuations. The Rössler system is a system of three non-linear ordinary differential equations that generate a regime of chaotic oscillation, and may be written as [21, 22]

\[
\begin{align*}
\dot{y}_1 &= -(y_2 + y_3), \\
\dot{y}_2 &= y_1 + 0.15y_2, \\
\dot{y}_3 &= 0.2 + y_3(y_1 - 10).
\end{align*}
\]

\(^{(12)}^{(13)}^{(14)}\)

\[
y_1(0) = -8, \\
y_2(0) = -8, \\
y_3(0) = -8.
\]

\(^{(15)}^{(16)}^{(17)}\)

3. Results

The (5) – (8) problem under (9) – (11) conditions, \( \theta_0 = 0 \) and \( Bi = 3.95 \) was solved. Results of problems solution are shown in Fig 2.

\[
\gamma(t) = \frac{y_2(t) - a_2}{27},
\]

\(^{(10)}\)

\[
\nu(t) = \frac{y_3(t) - a_3}{38}.
\]

\(^{(11)}\)

\[
\alpha(t) = \frac{y_1(t) - a_1}{15},
\]

\(^{(18)}\)

\[
\gamma(t) = \frac{y_3(t) - a_3}{10}.
\]

\(^{(19)}\)

**Figure 2.** Solution of (5) – (8) problem under (9) – (11) conditions. (a) Spatial temperature distribution at different time moments. (b) Temperature fluctuation series on surface breast. No blow-up solution.

It is seen that spatial temperature distribution has a gradual decreasing for temperature values under approaching to breast surface at any time moment. Temporal distributions look like a random temporal signal. For modified parameters (9) – (11) in the form
\[ \nu(t) = \frac{y_1(t) - a_1}{18}. \]  

(20)

results of the solution of (5) – (8) are depicted in the Fig 3.

![Figure 3](image)

**Figure 3.** Solution of (5) – (8) problem under (18) – (20) conditions. (a) Spatial temperature distribution at different time moments. (b) Temporal temperature distribution on surface breast. Blow-up solution

A drastic temperature rise at some point of spatial distribution is observed under (18) – (20) conditions. The transition from fluctuations to gradually temperature rise is observed for temporal distribution in this case that is characteristic for temporal behavior of system “attracting” to the blow-up singular dynamics. Blow-up modes are characterized by the similarity of nonlinear kinetics and spatial localization. These regularities should be established by comparison with experiment as precursor of qualitative metabolism changes.

The subjection of the entire system to this dynamics can be considered as the precursor of the tissue metabolic response on the cancer progression [18]. The results of modeling for both statements demonstrate the ability of this approach to distinguish the thermal behavior of cancerous and normal breast.

### 4. Conclusion

The authors used the nonlinear modified Pennes equation in order to describe the qualitative changes in the metabolism dynamics of normal and cancerous breast tissue. The qualitative difference in the metabolisms is associated with the subjection of the entire system dynamics to the blow-up singular solutions of temperature pattern corresponding to the critical stages of tumor evolution. This approach may be applied for the description of real breast heat kinetics in order to distinguish the nonlinear temperature dynamics of cancerous and normal breast.

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