A Proposed Mathematical Model of Tumor Growth and Host Consciousness

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Abstract
In this paper a mathematical model for tumor growth based on a Boltzmann-type equation is formulated. The tumor growth factor is defined and the tumor cell density is calculated. It is shown that tumor evolution strongly depends on the growth factor $k$. For $k<0.5$ tumor density oscillates and the tumor is in the “hesitate” state. For $k>0.5$ the tumor loses the oscillatory character and grows abruptly and emits cells to the host body. We argue that the oscillation of tumor density creates tumor waves which can be coined as tumor conscious waves. The tumor waves “inform” host consciousness.

Key Words: Tumor, conscious, tumor waves, growth factor, density

1. Introduction
Since 2002, cancer has become the leading cause of death for Americans between the ages of 40 and 74 (Jemal, 2005). However, the overall effectiveness of therapeutic cancer treatments is only 50%. Understanding tumor biology and developing a prognostic tool could therefore have immediate impact on the lives of millions of people diagnosed with cancer. There is growing recognition that achieving an integrative understanding of molecules, cells, tissues, and organs is the next major frontier of biomedical science. Because of the inherent complexity of real biological systems, the development and analysis of computational models based directly on experimental data is necessary to achieve this understanding.

Tumor development is very complex and dynamic. Primary malignant tumors arise from small nodes of cells that have lost, or ceased to respond to, normal growth regulatory mechanisms through mutations and/or altered gene expression (Sutherland, 1988). This genetic instability causes continued malignant alterations, resulting in a biologically complex tumor. However, all tumors start from a relatively simple, avascular stage of growth, with nutrient supply by diffusion from the surrounding tissue. The restricted supply of critical nutrients, such as oxygen and glucose, results in marked gradients within the cell mass. The tumor cells respond through both induced alterations in physiology and metabolism, and through altered gene and protein expression (Marusic, 1994), leading to the secretion of a wide variety of angiogenic factors.

Angiogenesis (formation of new blood vessels from existing blood vessels) is necessary for subsequent tumor expansion. Angiogenic growth factors generated by tumor cells diffuse into the nearby tissue and bind to specific receptors on the endothelial cells of nearby pre-existing blood vessels. The endothelial cells become activated; they proliferate and migrate towards the tumor, generating blood vessel tubes that connect to
form blood vessel loops that can circulate blood. With the new supply system, the tumor will renew growth at a much faster rate. Cells can invade the surrounding tissue and use their new blood supply as highways to travel to other parts of the body. Members of the vascular endothelial growth factor (VEGF) family are known to have a predominant role in angiogenesis.

Physicists have long been at the forefront of cancer diagnosis and treatment, having pioneered the use of x-rays and radiation therapy. In the contemporary initiative, the US National Cancer Institute’s conviction that physicists bring unique conceptual insights that could augment the more traditional approaches to cancer research is very appealing.

In this paper we present the first attempt to consider the tumor cancer as the physical medium with some sort of memory.

2. Consciousness of cancer cells
Cancer is pervasive among all organisms in which adult cells proliferate. There is Darwinian explanation of cancer insidiousness which is based on the fact that all life on Earth was originally single-celled. Each cell had a basic imperative: replicate, replicate, replicate. However, the emergence of multicellular organisms about 550 million years ago required individual cells to cooperate by subordinating their own selfish genetic agenda to that of the organism as a whole. So when an embryo develops, identical stern cells progressively differentiate into specialized cells that differ from organ to organ.

If a cell does not respond properly to the regulatory signals of the organism it may go reproducing in an uncontrolled way, forming a tumor specific to the organ in which it arises. A key hallmark of cancer is that it can also grow in an organ where it does not belong: for example a prostate cancer cell may grow in a lymph mode. This spreading and invasion processes is called “metastasis”. Metastatic cells may lie dormant for many years in foreign organs evading the body’s immune system while retaining their potency. Healthy cells, in contrast, soon die if they are transported beyond their rightful organ.

In some respect, the self centered nature of cancer cells is a reversion to an ancient pre-multicellular lifestyle. Nevertheless cancer cells do co-operate to a certain extent. For example tumors create their own new bloody supply, a phenomenon called angiogenesis by co-opting the body’s normal wound healing functions. Cancer cells are therefore neither rogue “selfish cells,” nor do they display the collective discipline of organism with fully differentiated organs. They fall somewhere in between perhaps resembling an early form of loosely organized cell colonies. In other words the cancer tumor remember the early state of existence, it has a memory which have been erased in healthy cells.

The proliferation of the tumor cells is described by the diffusion processes (Jamal, 2005). The standard diffusion equation is based on the Fourier law in which all memory of the initial state is erased. Simply speaking, the diffusion equation does not have time reversal symmetry, i.e., if the function $f(x,t)$ is the solution of Fourier equation, $f(x,-t)$ is not.

Let us consider one-dimensional transport “particles”, e.g., cancer cells. These cells however may move only to the right or to the left on the line road. Moving cells may interact with the fixed host body cells the probabilities of such collisions and their expected results being specified. All particles will be of the same kind, with the same energy and other physical specifications distinguishable only by their direction (Cf. Appendix for details of the mathematical model for tumor growth.)

Let us define:

\[ u(z,t) = \text{expected density of cells at } z \text{ and at time } t \text{ moving to the right}, \]
\[ v(z,t) = \text{expected density of cells at } z \text{ and at time } t \text{ moving to the left}. \]

Furthermore, let

\[ \delta(z) = \text{probability of collision occurring between a fixed scattering centrum and a cell moving between } z \text{ and } z + \Delta. \]

Suppose that a collision might result in the disappearance of the moving cell without new particle appearing. Such a phenomenon is called absorption. Or the
moving particle may be reversed in direction or back-scattered. We shall agreeing that in each collision at \( z \) an expected total of \( F(z) \) cells arises moving in the direction of the original cell, \( B(z) \) arise going in the opposite direction.

In the stationary state transport phenomena \( \frac{dF(z,t)}{dt} = \frac{dB(z,t)}{dt} = 0 \) and \( d\delta(z,t)/dt = 0 \). In that case we denote \( F(z) = F(z,t) = B(z) = k(z) \) and master equation for tumor evolution can be written as can be written as

\[
\frac{du}{dz} = \delta(z)(k-1)u(z) + \delta(z)kv(z),
\]

(1)

\[
-\frac{dv}{dz} = \delta(z)k(z)u(z) + \delta(z)(k(z)-1)v(z)
\]

Formula (1) describes the evolution of the cell aggregation- tumor. The development of the tumor strongly depends on the coefficient \( k \). In the following we will call \( k \)-the growth coefficient. The solutions of the model equation for the density of cancer cell has the form:

\[
\begin{align*}
\rho(z,t) &= u(z,t) + v(z,t) \\
\rho(z) &= \frac{2qe^{\frac{(f(a)-f(0))}{1+\beta e^{\frac{f(a)-f(0)}{\alpha}}}}}{1+\beta e^{\frac{f(a)-f(0)}{\alpha}}} \left[ \frac{(1-2k)^2}{(1-2k)^2 -(k-1)} \right] \cosh \left[ \frac{\beta}{(1-2k)^2 -(k-1)} \right] \\
&+ \frac{k-1}{(1-2k)^2 -(k-1)} \sinh \left[ \frac{\beta}{(1-2k)^2 -(k-1)} \right],
\end{align*}
\]

(2)

\[
\begin{align*}
u(z) &= \frac{2qe^{\frac{(f(a)-f(0))}{1+\beta e^{\frac{f(a)-f(0)}{\alpha}}}}}{1+\beta e^{\frac{f(a)-f(0)}{\alpha}}} \left[ \frac{1}{(1-2k)^2 +(k-1)} \right] \sinh \left[ \frac{\beta}{(1-2k)^2 +(k-1)} \right],
\end{align*}
\]

and

\[
\begin{align*}
u(z) &= \frac{2qe^{\frac{(f(a)-f(0))}{1+\beta e^{\frac{f(a)-f(0)}{\alpha}}}}}{1+\beta e^{\frac{f(a)-f(0)}{\alpha}}} \left[ \frac{(1-2k)^2}{(1-2k)^2 -(k-1)} \right] \cosh \left[ \frac{\beta}{(1-2k)^2 -(k-1)} \right] \\
&- \frac{1}{(1-2k)^2 -(k-1)} \sinh \left[ \frac{\beta}{(1-2k)^2 -(k-1)} \right].
\end{align*}
\]

(3)

Is the density of the tumor cells? The results of the calculations are presented in Figures 1 and 2. For \( k<0.5 \) the density of the cell oscillate, Figure 1a and 2a. On the other hand for \( k>0.5 \) the cell density grows exponentially, Figure 2a and 2b.

For \( k<0.5 \) the cell aggregation emits the wave with length \( \lambda = 8^{-1} = \text{size of the tumor} \). For \( k=0.5 \) the cancer development has singularity \( \rho \rightarrow \infty \). The first stage \( k<0.5 \) we will call the “hesitation” period in which tumor send the “information” waves to the host body. The response of the host depends on its willingness to cooperate with cancer. For \( k<0.5 \) the response of the host is negative and tumor is stable. For \( k>0.5 \) the angiogenesis starts – the host cooperates with tumor and tumor grows abruptly.

It seems that the first “hesitation” stage is the information exchange tumor→host→tumor and vice versa. Next, through the singularity point \( k=0.5 \) the cancer obtain the information, go and metastasis process starts.

From the therapeutic point of view the most important result of the paper is the description of the “information-conscious” waves in the host body.
3. Conclusions

In this paper we argue that the cancer tumor evolution can be described as the process which strongly depends on the growth factor \( k \), defined in the paper. For \( k < 0.5 \) tumor is stable with oscillatory cells density behavior. For \( k > 0.5 \) the tumor grows exponentially. For the moment the tumor wave emission was not observed. It seems that the observation of the emitted waves can be an important therapeutic tool for the description of the cancer status. Stopping the emission of these waves is the signature of the invasive evolution of the tumor. It seems that the host is informed by emitted waves of the existence of the tumor and its evolution. We can speculate on the same sort of tumor consciousness which can influence the host consciousness. In that case we can anticipate the correlation of the tumor growth and psychic state of the host. It is interesting to note that in paper by Erica K. Sloan and others (Sloan, 2010) the role of the neuroendoctrine activation in cancer propagation is described and investigated.

Appendix

The model equations

Let us define:

\[
\begin{align*}
  u(z,t) &= \text{expected density of cells at } z \text{ and at time } t \text{ moving to the right}, \\
  v(z,t) &= \text{expected density of cells at } z \text{ and at time } t \text{ moving to the left}.
\end{align*}
\]

Furthermore, let

\[
\delta(x) = \text{probability of collision occurring between a fixed scattering centre and a cell moving between } z \text{ and } z + \Delta.
\]

Suppose that a collision might result in the disappearance of the moving cell without new particle appearing. Such a phenomenon is called absorption. Or the moving particle may be reversed in direction or back-scattered. We shall agreeing that in each collision at \( z \) an expected total of \( F(z) \) cells arises moving in the direction of the original cell, \( B(z) \) arise going in the opposite direction.

The expected total number of right-moving cells \( z_i \leq z \leq z_f \) at time \( t \) is

\[
\int_{z_i}^{z_f} u(z,t)dz , \tag{1}
\]
while the total number of cell passing $z$ to the right in the time interval $t_1 \leq t \leq t_2$ is

$$w \int_{t_1}^{t_2} u(z,t)dt,$$

(2)

where $w$ is the particles speed.

Consider the cell moving to the right and passing $z + \Delta$ in the time interval $t_1 + \frac{\Delta}{w} \leq t \leq t_2 + \frac{\Delta}{w}$:

$$w \int_{t_1 + \frac{\Delta}{w}}^{t_2 + \frac{\Delta}{w}} u(z + \Delta, t')dt' = w \int_{t_1}^{t_2} u(z + \Delta, t') \left( \frac{\Delta}{w} \right) dt'.$$

(3)

These can arise from cells which passed $z$ in the time interval $t_1 \leq t \leq t_2$ and came through $(z, z + \Delta)$ without collision

$$w \int_{t_1}^{t_2} (1 - \delta(z, t'))u(z,t')dt'$$

(4)

plus contributions from collisions in the interval $(z, z + \Delta)$. The right-moving cells interacting in $(z, z + \Delta)$ produce in the time $t_1$ to $t_2$,

$$w \int_{t_1}^{t_2} \Delta \delta(z, t')F(z, t')u(z,t')dt'$$

(5)

cells to the right, while the left moving ones give:

$$w \int_{t_1}^{t_2} \Delta \delta(z, t')B(z, t')u(z,t')dt'.$$

(6)

Thus

$$w \int_{t_1}^{t_2} u(z + \Delta, t') \left( \frac{\Delta}{w} \right) dt' = w \int_{t_1}^{t_2} u(z,t')dt' + w \Delta \int_{t_1}^{t_2} \delta(z, t')(F(z, t') - 1)u(z,t')dt'$$

$$+ w \Delta \int_{t_1}^{t_2} \delta(z, t')B(z, t')u(z,t')dt'.$$

(7)

Now, we can write:

$$u\left(z + \Delta, t' + \frac{\Delta}{w}\right) = u(z,t') + \left( \frac{\partial u}{\partial z} \right)(z,t') + \left( \frac{1}{w} \right) \left( \frac{\partial u}{\partial t} \right)(z,t') \Delta$$

(8)

to get

$$\int_{t_1}^{t_2} \left( \frac{\partial u}{\partial z} \right)(z,t') dt' + \frac{1}{w} \int_{t_1}^{t_2} \left( \frac{\partial u}{\partial t} \right)(z,t') dt' = \int_{t_1}^{t_2} \delta(z, t')((F(z, t') - 1)u(z,t') + B(z, t')v(z,t'))dt'.$$

(9)

On letting $\Delta \to 0$ and differentiating with respect to $t_2$ we find

$$\frac{\partial u}{\partial z} + \frac{1}{w} \frac{\partial u}{\partial t} = \delta(z,t)(F(z,t) - 1)u(z,t) + \delta(z,t)B(z,t)v(z,t).$$

(10)

In a like manner

$$-\frac{\partial v}{\partial z} + \frac{1}{w} \frac{\partial v}{\partial t} = \delta(z,t)B(z,t)u(z,t) + \delta(z,t)(F(z,t) - 1)v(z,t).$$

(11)
The system of partial differential equations of hyperbolic type (10-11) is the Boltzmann equation for one dimensional transport phenomena (Kozlowski and Marciak-Kozlowska, 2009)

Let us define the total density for cells, $\rho(z,t)$

$$\rho(z,t) = u(z,t) + v(z,t)$$

and density of cells current

$$j(z,t) = w(u(z,t) - v(z,t)).$$

Considering equations (10-13) one obtains

$$\frac{\partial \rho}{\partial z} + \frac{1}{w^2} \frac{\partial j}{\partial t} = \delta (z,t)u(z,t)(F(z,t) - B(z,t) - 1) + \delta (z,t)v(z,t)(B(z,t) - F(z,t) + 1).$$

Equation (14) can be written as

$$\frac{\partial \rho}{\partial z} + \frac{1}{w^2} \frac{\partial j}{\partial t} = \frac{\delta (z,t)u(z,t)(F(z,t) - B(z,t) - 1)}{w}$$

or

$$j = \frac{w}{\delta (z,t)(F(z,t) - B(z,t) - 1)} \frac{\partial \rho}{\partial z} + \frac{1}{w \delta (z,t)(F(z,t) - B(z,t) - 1)} \frac{\partial j}{\partial t}.$$  \hspace{1cm} (15)

Denoting, $D$, diffusion coefficient

$$D = -\frac{w}{\delta (z,t)(F(z,t) - B(z,t) - 1)}$$

and $\tau$, relaxation time

$$\tau = \frac{1}{w \delta (z,t)(1 - F(z,t) - B(z,t))}$$

equation (10) takes the form

$$j = -D \frac{\partial \rho}{\partial z} - \tau \frac{\partial j}{\partial t}. $$  \hspace{1cm} (18)

Equation (18) is the Cattaneo’s type equation and is the generalization of the Fourier equation (Kozlowski and Marciak-Kozlowska, 2009). Now in a like manner we obtain from equation (15 –18)

$$\frac{1}{w} \frac{\partial j}{\partial z} + \frac{1}{w} \frac{\partial \rho}{\partial t} = \delta (z,t)u(z,t)(F(z,t) - 1 + B(z,t))$$

$$+ \delta (z,t)v(z,t)(B(z,t) + F(z,t) - 1)$$

or

$$\frac{\partial j}{\partial z} + \frac{\partial \rho}{\partial t} = 0.$$  \hspace{1cm} (20)

Equation (20) describes the conservation of cells in the transport processes.

Considering equations (19) and (20) for the constant $D$ and $\tau$ the hyperbolic Heaviside equation is obtained:

$$\tau \frac{\partial^2 \rho}{\partial t^2} + \frac{\partial \rho}{\partial t} = D \frac{\partial^2 \rho}{\partial z^2}.$$  \hspace{1cm} (21)

where $\tau$ is the relaxation time

In the stationary state transport phenomena $dF(z,t)/dt = dB(z,t)/dt = 0$ and $d\delta(z,t)/dt = 0$. In that case we denote $F(z,t) = F(z) = B(z,t) = B(z) = k(z)$ and equation (18) and (19) can be written as
\[ \frac{du}{dz} = \delta(z)(k-1)u(z) + \delta(z)kv(z), \]
\[ -\frac{dv}{dz} = \delta(z)k(z)u(z) + \delta(z)(k(z)-1)v(z) \]  

with diffusion coefficient
\[ D = \frac{w}{\delta(z)} \]  
and relaxation time
\[ \tau(z) = \frac{1}{w\delta(z)(1-2k(z))}. \]

The system of equations (22) can be written as
\[ \frac{d^2u}{dz^2} + \frac{1}{\delta z} \frac{d}{dz} \left[ \frac{\delta}{\delta k} \frac{du}{dz} + \frac{d\delta}{dz} \right] = 0, \]
\[ \frac{du}{dz} = \delta(k-1)u + \delta kv(z). \]

Equation (26) after differentiation has the form
\[ \frac{d^2u}{dz^2} + f(z)u + g(z)u(z) = 0, \]
where
\[ f(z) = -\frac{1}{\delta} \left( \frac{\delta k}{dz} + \frac{d\delta}{dz} \right), \]
\[ g(z) = \delta^2(z)(2k-1) - \frac{\delta k}{dz}. \]

For the constant absorption rate we put
\[ k(z) = k = \text{constant} = \frac{1}{2}. \]

In that case
\[ f(z) = -\frac{1}{\delta} \frac{d\delta}{dz}, \]
\[ g(z) = \delta^2(z)(2k-1). \]

With functions \( f(z) \) and \( g(z) \) the general solution of the equation (2.30) has the form
\[ u(z) = C_1 e^{(1-2k)z^2} \int_{dz}^{z} \delta(z) dz + C_2 e^{-(1-2k)z^2} \int_{dz}^{z} \delta(z) dz. \]

In the subsequent we will consider the solution of the equation (28) with \( f(z) \) and \( g(z) \) described by (30) for Cauchy condition:
\[ u(0) = q, \quad v(0) = 0. \]

Boundary condition (31) describes the generation of the heat carriers (by illuminating the left end of the strand with laser pulses) with velocity \( q \) heat carrier per second.

The solution has the form:
\[
\begin{align*}
 u(z) &= \frac{2q\epsilon}{1 + \beta\epsilon^2} \left[ \cosh[f(z) - f(a)] - \frac{(1-2k)^2}{1-2k^2} \sinh[f(z) - f(a)] \right] \\
 &\quad + \frac{k}{(1-2k)^2 - (k-1)} \int_0^{(1-2k)^2} \delta dz, \\
 f(0) &= \left(1 - 2k\right)^2 \int_0^{(1-2k)^2} \delta dz, \\
 f(a) &= \left(1 - 2k\right)^2 \int_a^{(1-2k)^2} \delta dz, \\
 \beta &= \frac{(1-2k)^2 + (k-1)}{(1-2k)^2 - (k-1)}.
\end{align*}
\]

where

\[
\begin{align*}
 f(z) &= \left(1 - 2k\right)^2 \int_0^z \delta dz, \\
 f(0) &= \left(1 - 2k\right)^2 \int_0^0 \delta dz, \\
 f(a) &= \left(1 - 2k\right)^2 \int_a^a \delta dz, \\
 \beta &= \frac{(1-2k)^2 + (k-1)}{(1-2k)^2 - (k-1)}.
\end{align*}
\]

Considering formulae (12), (13) and (33) we obtain for the density, \( \rho(z) \) and current density \( j(z) \).

\[
\begin{align*}
 j(z) &= \frac{2q\epsilon}{1 + \beta\epsilon^2} \left[ \cosh[f(z) - f(a)] - \frac{(1-2k)^2}{1-2k^2} \sinh[f(z) - f(a)] \right] \\
 &\quad - \frac{1}{1-2k} \int_0^{(1-2k)^2} \delta dz.
\end{align*}
\]

and

\[
\begin{align*}
 q &= \frac{2q\epsilon}{1 + \beta\epsilon^2} \left[ \cosh[f(z) - f(a)] - \frac{(1-2k)^2}{1-2k^2} \sinh[f(z) - f(a)] \right] \\
 &\quad - \frac{1}{1-2k} \int_0^{(1-2k)^2} \delta dz.
\end{align*}
\]

Equations (34) and (35) fulfill the generalized Fourier relation

\[
\begin{align*}
 j &= \frac{\partial \rho}{\partial z}, \\
 D &= \frac{W}{\delta(z)},
\end{align*}
\]

where \( D \) denotes the diffusion coefficient.

Analogously we define the generalized diffusion velocity \( v_D(z) \)

\[
\begin{align*}
 v_D(z) &= \frac{\delta^2}{m(z)} \left[ \frac{(1-2k)^2}{1-2k^2} \cosh[f(z) - f(a)] - \frac{(1-2k)^2}{1-2k^2} \sinh[f(z) - f(a)] \right] \\
 &\quad + \frac{1}{1-2k^2} \int_0^{(1-2k)^2} \delta dz.
\end{align*}
\]

Assuming constant cross section for heat carriers scattering \( \delta(z) = \delta_o \) we obtain from formula (33).
\[ f(z) = (1 - 2k)^2 z, \]
\[ f(0) = 0, \]
\[ f(a) = (1 - 2k)^2 a \]

and for density \( \rho(z) \) and current density \( j(z) \)

\[
j(z) = \frac{2qwe^{-(1-2k)^2a\delta}}{1 + \beta e^{-(1-2k)^2a\delta}} \left[ \frac{\frac{1}{(1-2k)^2}}{(2k-1)^2(x-a)\delta} \cosh \left( \frac{2k-1}{(1-2k)^2} (x-a)\delta \right) \right] \]
\[
- \frac{\frac{1}{(1-2k)^2}}{(2k-1)^2(x-a)\delta} \sinh \left( \frac{2k-1}{(1-2k)^2} (x-a)\delta \right),
\]

\[
\rho(z) = \frac{2qe^{-(1-2k)^2a\delta}}{1 + \beta e^{-(1-2k)^2a\delta}} \left[ \frac{\frac{1}{(1-2k)^2}}{(2k-1)^2(x-a)\delta} \cosh \left( \frac{2k-1}{(1-2k)^2} (x-a)\delta \right) \right] \]
\[
- \frac{\frac{1}{(1-2k)^2}}{(2k-1)^2(x-a)\delta} \sinh \left( \frac{2k-1}{(1-2k)^2} (x-a)\delta \right).
\]

Formulae (39) and (40) describe the kinetic of the growth of the cell aggregation-tumor. The development of the tumor strongly depends on the coefficient \( k \). In the following we will call \( k \)-the growth coefficient. For \( k < 0.5 \) the density of the cell oscillates, Figure 1a, 2a. On the other hand for \( k > 0.5 \) the cell density grows exponentially, Figure 2a, 2b.

References
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