Exploration

Ethanol Treatment of Cancer & Model of Cancer Growth Wave ("Consciousness")

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Abstract

Scientists have known for some time that ethanol can kill cancer cells, but several limitations held it back from becoming a broadly used treatment. A team at Duke University has recently developed a new type of ethanol solution that can be injected directly into a variety of tumors to potentially offer a new, safe, and cheap form of cancer treatment. In this paper the mathematical model for tumor growth, based on Boltzmann type equation is formulated. The tumor growth factor is defined. The tumor cells density is calculated. It is shown that the tumor evolution strongly depends on the growth factor k. For k<0.5 tumor density oscillate and tumor is in the " hesitate" state. For k>0.5 tumor lost the oscillatory character and grows abruptly and emits cells to the host body. We argue that the oscillation of the density of tumor crates the tumor waves which can be coined as the tumor conscious waves. The tumor waves "inform" host consciousness. We argue that ethanol influenced the consciousness of tumor and reset the interaction of tumor –host consciousness. The ethanol injected to cancer tumor preumbly change the growth factor k.

Keyword: Tumor, conscious, tumor waves, growth factor, density

1. Ethanol treatment

Scientists have known for some time that ethanol can kill cancer cells, but several limitations held it back from becoming a broadly used treatment. A team at Duke University has recently developed a new type of ethanol solution that can be injected directly into a variety of tumors to potentially offer a new, safe, and cheap form of cancer treatment. [Murhard R., 2017]

Ethanol ablation is a form of cancer therapy where ethanol is injected directly into a tumor. It is currently used only for some types of liver and thyroid cancers and the treatment is notoriously limited because of the need to use large volumes of ethanol that can damage surrounding tissue. This means it is primarily only effective for tumors surrounded by a fibrous capsule that can contain the ethanol.

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Researchers at Duke University have overcome these limitations by developing a solution that mixes ethanol with ethyl cellulose. This novel solution turns into a gel when injected into a tumor, allowing it to remain concentrated at the site of injection. The team studied the effects of the new ethanol treatment in hamsters with induced cheek cancers. A control group was established and its tumors were injected with pure ethanol. Positive results were identified only when large volumes of ethanol were used, and even then only four of 12 treated tumors regressed completely after eight days. The ethanol gel group, on the other hand, displayed rather extraordinary results. After eight days all seven tumors treated with the ethanol gel had completely disappeared.

The Duke University team is clear in pointing out this is still just an early proof-of-concept trial with a very small sample size, but the results are encouraging. One of the primary outcomes suggested by the research is an ability to increase cancer treatments offered in the developing world. While this kind of ethanol ablation may be just as effective as tumor removal by surgery, it is significantly easier and cheaper, allowing for simple, non-surgical treatments for those in areas that lack effective medical resources.The treatment could also prove useful for a variety of other tumors, from some breast cancers to cervical precancerous lesions.

Since 2002, cancer has become the leading cause of death for Americans between the ages of 40 and 74 (Jemal,2005). But the overall effectiveness of cancer therapeutic treatments is only 50%. Understanding the 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 simpler, 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 both through 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 the conviction that physicists bring unique conceptual insights that could augment the more traditional approaches to cancer research is very appealing.

2. Consciousness of the 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 millions years ago required individual cells to co-operate 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 as we know all memory of the

initial state is erased. Simply speaking diffusion equation has not 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 the one-dimensional transport "particles", eg.cancer cells. These cells however may move only to the right or to the left on the rod. 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.

Let us define:

$u(z,t)$ = expected density of cells at z and at time t moving to the right,
$v(z,t)$ = expected density of cells at z and at time t moving to the left.

Furthermore, let

$\delta(z)$ = probability of collision occurring between a fixed scattering centrum and a cell moving between z 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 $z_1 \le z \le z_2$ at time t is

$$\int_{z_1}^{z_2} u(z,t)dz, \tag{2.6}$$

while the total number of cell passing z to the right in the time interval $t_1 \le t \le t_2$ is

$$w\int_{t_1}^{t_2} u(z,t)dt, \tag{2.7}$$

where w is the particles speed.

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

$$w\int_{t_1+\Delta/w}^{t_2+\Delta/w} u(z+\Delta,t')dt' = w\int_{t_1}^{t_2} u\left(z+\Delta,t'+\frac{\Delta}{w}\right)dt'. \tag{2.8}$$

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

$$w\int_{t_1}^{t_2}(1-\Delta\delta(z,t'))u(z,t')dt' \tag{2.9}$$

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,

$$w\int_{t_1}^{t_2}\Delta\delta(z,t')F(z,t')u(z,t')dt' \tag{2.10}$$

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

$$w\int_{t_1}^{t_2}\Delta\delta(z,t')B(z,t')v(z,t')dt'. \tag{2.11}$$

Thus

$$\begin{aligned} w\int_{t_1}^{t_2}u\left(z+\Delta,t'+\frac{\Delta}{w}\right)dt' = w\int_{t_1}^{t_2}u(z,t')dt' + w\Delta\int_{t_1}^{t_2}\delta(z,t')(F(z,t')-1)u(z,t')dt' \\ +w\Delta\int_{t_1}^{t_2}\delta(z,t')B(z,t')v(z,t')dt'. \end{aligned} \tag{2.12}$$

Now, we can write:

$$u\left(z+\Delta,t'+\frac{\Delta}{w}\right)=u(z,t')+\left(\frac{\partial u}{\partial z}(z,t')+\frac{1}{w}\frac{\partial u}{\partial t}(z,t')\right)\Delta \tag{2.13}$$

to get

$$\int_{t_1}^{t_2}\left(\frac{\partial u}{\partial z}(z,t')\right)+\frac{1}{w}\frac{\partial u}{\partial t}(z,t')dt' = \int_{t_1}^{t_2}\delta(z,t')((F(z,t')-1)u(z,t')+B(z,t')v(z,t'))dt'. \tag{2.14}$$

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

$$\frac{\partial u}{\partial z}+\frac{1}{w}\frac{\partial u}{\partial t}=\delta(z,t)(F(z,t)-1)u(z,t)+\delta(z,t)B(z,t)v(z,t). \tag{2.15}$$

In a like manner

$$-\frac{\partial v}{\partial z}+\frac{1}{w}\frac{\partial v}{\partial t}=\delta(z,t)B(z,t)u(z,t)+\delta(z,t)(F(z,t)-1)v(z,t). \tag{2.16}$$

The system of partial differential equations of hyperbolic type (2.15, 2.16) is the Boltzmann equation for one dimensional transport phenomena (Kozlowski, Marciak-Kozlowska,2009) Let us define the total density for cells, $\rho(z,t)$

$$\rho(z,t)=u(z,t)+v(z,t) \tag{2.17}$$

and density of cells current

$$j(z,t) = w(u(z,t) - v(z,t)). \tag{2.18}$$

Considering equations (2.15 – 2.18) one obtains

$$\frac{\partial \rho}{\partial z} + \frac{1}{w^2}\frac{\partial j}{\partial t} = \delta(z,t)u(z,t)(F(z,t) - B(z,t) - 1) + \delta(z,t)v(z,t)(B(z,t) - F(z,t) + 1). \tag{2.19}$$

Equation (2.19) can be written as

$$\frac{\partial \rho}{\partial z} + \frac{1}{w^2}\frac{\partial j}{\partial t} = \frac{\delta(z,t)(F(z,t) - B(z,t) - 1)\, j}{w} \tag{2.20}$$

or

$$j = \frac{w}{\delta(z,t)(F(z,t) - B(z,t) - 1)}\frac{\partial \rho}{\partial z} + \frac{1}{w\delta(z,t)(F(z,t) - B(z,t) - 1)}\frac{\partial j}{\partial t}. \tag{2.21}$$

Denoting, D, diffusion coefficient

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

and τ, relaxation time

$$\tau = \frac{1}{w\delta(z,t)(1 - F(z,t) - B(z,t))} \tag{2.22}$$

equation (2.21) takes the form

$$j = -D\frac{\partial \rho}{\partial z} - \tau\frac{\partial j}{\partial t}. \tag{2.23}$$

Equation (2.23) is the Cattaneo's type equation and is the generalization of the Fourier equation (Kozlowski,Marciak-Kozlowska,2009). Now in a like manner we obtain from equation (2.15 – 2.18)

$$\frac{1}{w}\frac{\partial j}{\partial z} + \frac{1}{w}\frac{\partial \rho}{\partial t} = \delta(z,t)u(z,t)(F(z,t) - 1 + B(z,t)) + \delta(z,t)v(z,t)(B(z,t) + F(z,t) - 1)) \tag{2.24}$$

or

$$\frac{\partial j}{\partial z} + \frac{\partial \rho}{\partial t} = 0. \tag{2.25}$$

Equation (2.25) describes the conservation of cells in the transport processes.

Considering equations (2.23) and (2.25) for the constant D and τ the hyperbolic Heaviside equation is obtained:

$$\tau\frac{\partial^2 \rho}{\partial t^2} + \frac{\partial \rho}{\partial t} = D\frac{\partial^2 \rho}{\partial z^2}. \tag{2.26}$$

where τ 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 (2.10) and (2.11) can be written as

$$\begin{aligned} \frac{du}{dz} &= \delta(z)(k-1)u(z) + \delta(z)kv(z), \\ -\frac{dv}{dz} &= \delta(z)k(z)u(z) + \delta(z)(k(z)-1)v(z) \end{aligned} \tag{2.27}$$

with diffusion coefficient

$$D = \frac{w}{\delta(z)} \tag{2.28}$$

and relaxation time

$$\tau(z) = \frac{1}{w\delta(z)(1-2k(z))}. \tag{2.29}$$

The system of equations (2.27) can be written as

$$\frac{d^2u}{dz^2} - \frac{\frac{d}{dz}(\delta k)}{\delta k}\frac{du}{dz} + u\left[\delta^2(2k-1) + \frac{d\delta}{dz}(1-k) + \frac{\delta(k-1)}{\delta k}\frac{d(\delta k)}{dz}\right] = 0, \tag{2.30}$$

$$\frac{du}{dz} = \delta(k-1)u + \delta kv(z). \tag{2.31}$$

Equation (2.30) after differentiation has the form

$$\frac{d^2u}{dz^2} + f(z)\frac{du}{dz} + g(z)u(z) = 0, \tag{2.32}$$

where

$$\begin{aligned} f(z) &= -\frac{1}{\delta}\left(\frac{\delta}{k}\frac{dk}{dz} + \frac{d\delta}{dz}\right), \\ g(z) &= \delta^2(z)(2k-1) - \frac{\delta}{k}\frac{dk}{dz}. \end{aligned} \tag{2.33}$$

For the constant absorption rate we put

$$k(z) = k = \text{constant} \neq \frac{1}{2}.$$

In that case

$$\begin{aligned} f(z) &= -\frac{1}{\delta}\frac{d\delta}{dz}, \\ g(z) &= \delta^2(z)(zk-1). \end{aligned} \tag{2.34}$$

With functions $f(z)$ and $g(z)$ the general solution of the equation (2.30) has the form

$$u(z) = C_1 e^{(1-2k)^{1/2}\int \delta dz} + C_2 e^{-(1-2k)^{1/2}\int \delta dz}. \tag{2.35}$$

In the subsequent we will consider the solution of the equation (2.32) with $f(z)$ and $g(z)$ described by (2.34) for Cauchy condition:

$$u(0) = q, \quad v(a) = 0. \tag{2.36}$$

Boundary condition (2.36) 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:

$$\begin{aligned} u(z) &= \frac{2qe^{[f(0)-f(a)]}}{1+\beta e^{2[f(0)-f(a)]}}\left[\frac{(1-2k)^{\frac{1}{2}}}{(1-2k)^{\frac{1}{2}}-(k-1)}\right]\cosh\left[f(x)-f(a)\right] \\ &\quad + \frac{k-1}{(1-2k)^{\frac{1}{2}}-(k-1)}\sinh\left[f(x)-f(a)\right], \\ u(z) &= \frac{2qe^{(f(0)-f(a))}}{1+\beta e^{2[f(0)-f(a)]}}\left[\frac{(1-2k)^{\frac{1}{2}}+(k-1)}{k}\sinh\left[f(x)-f(a)\right]\right], \end{aligned} \tag{2.37}$$

where

$$\begin{aligned} f(z) &= (1-2k)^{\frac{1}{2}}\int \delta dz, \\ f(0) &= (1-2k)^{\frac{1}{2}}\left[\int \delta dz\right]_0, \\ f(a) &= (1-2k)^{\frac{1}{2}}\left[\int \delta dz\right]_a, \\ \beta &= \frac{(1-2k)^{\frac{1}{2}}+(k-1)}{(1-2k)^{\frac{1}{2}}-(k-1)}. \end{aligned} \tag{2.38}$$

Considering formulae (2.17), (2.18) and (2.37) we obtain for the density, $\rho(z)$ and current density $j(z)$.

$$j(z)=\frac{2qwe^{[f(0)-f(a)]}}{1+\beta e^{2[f(0)-f(a)]}}\left[\begin{array}{c}\dfrac{(1-2k)^{\frac{1}{2}}}{(1-2k)^{\frac{1}{2}}-(k-1)}\cosh\left[f(z)-f(a)\right]\\ -\dfrac{1-2k}{(1-2k)^{\frac{1}{2}}-(k-1)}\sinh\left[f(z)-f(a)\right]\end{array}\right] \tag{2.39}$$

and

$$q=\frac{2qe^{[f(0)-f(a)]}}{1+\beta e^{2[f(0)-f(a)]}}\left[\begin{array}{c}\dfrac{(1-2k)^{\frac{1}{2}}}{(1-2k)^{\frac{1}{2}}-(k-1)}\cosh\left[f(z)-f(a)\right]\\ -\dfrac{1}{(1-2k)^{\frac{1}{2}}-(k-1)}\sinh\left[f(z)-f(a)\right]\end{array}\right]. \tag{2.40}$$

Equations (2.39) and (2.40) fulfill the generalized Fourier relation

$$j=-\frac{w}{\delta(z)}\frac{\partial\rho}{\partial z},\qquad D=\frac{W}{\delta(z)}, \tag{2.41}$$

where D denotes the diffusion coefficient.

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

$$v_D(z)=\frac{j(z)}{n(z)}=\frac{w(1-2k)^{\frac{1}{2}}\left[\cosh\left[f(z)-f(a)\right]-(1-2k)^{\frac{1}{2}}\sinh\left[f(x)-f(a)\right]\right]}{(1-2k)^{\frac{1}{2}}\cosh\left[f(x)-f(a)\right]-\sinh\left[f(x)-f(a)\right]}. \tag{2.42}$$

Assuming constant cross section for heat carriers scattering $\delta(z)=\delta_o$ we obtain from formula (2.38)

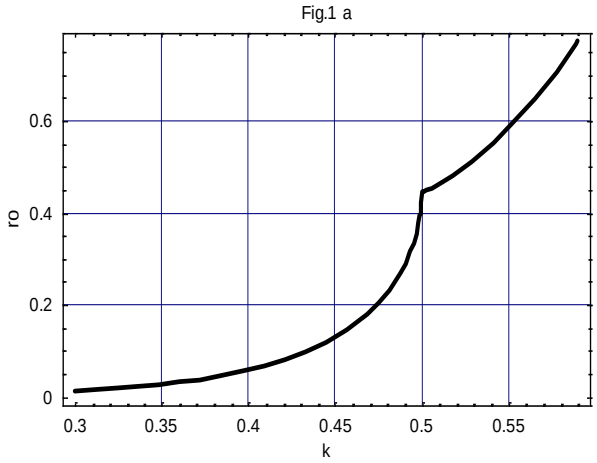
$$\begin{aligned}&f(z)=(1-2k)^{\frac{1}{2}}z,\\ &f(0)=0,\\ &f(a)=(1-2k)^{\frac{1}{2}}a\end{aligned} \tag{2.43}$$

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

$$\begin{aligned}j(z)=\frac{2qwe^{-(1-2k)^{\frac{1}{2}}a\delta}}{1+\beta e^{-(1-2k)^{\frac{1}{2}}a\delta}}&\left[\frac{(1-2k)^{\frac{1}{2}}}{(1-2k)^{\frac{1}{2}}-(k-1)}\cosh\left[(2k-1)^{\frac{1}{2}}(x-a)\delta\right]\right.\\ &\left.-\frac{(1-2k)}{(1-2k)^{\frac{1}{2}}-(k-1)}\sinh\left[(2k-1)^{\frac{1}{2}}(x-a)\delta\right]\right],\end{aligned} \tag{2.44}$$

$$\rho(z)=\frac{2qe^{-(1-2k)^{\frac{1}{2}}a\delta}}{1+\beta e^{-(1-2k)^{\frac{1}{2}}a\delta}}\left[\frac{(1-2k)^{\frac{1}{2}}}{(1-2k)^{\frac{1}{2}}-(k-1)}\cosh\left[(2k-1)^{\frac{1}{2}\delta}(x-a)\right]\right.$$
$$\left.-\frac{1}{(1-2k)^{\frac{1}{2}}-(k-1)}\sinh\left[(2k-1)^{\frac{1}{2}}(x-a)\delta\right]\right]. \qquad (2.45)$$

Formulae (2.44) and (2.45) 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 oscillate, Fig.1a, 2a. On the other hand for *k>0.5* the cell density grows exponentially, Fig. 2a, 2b.



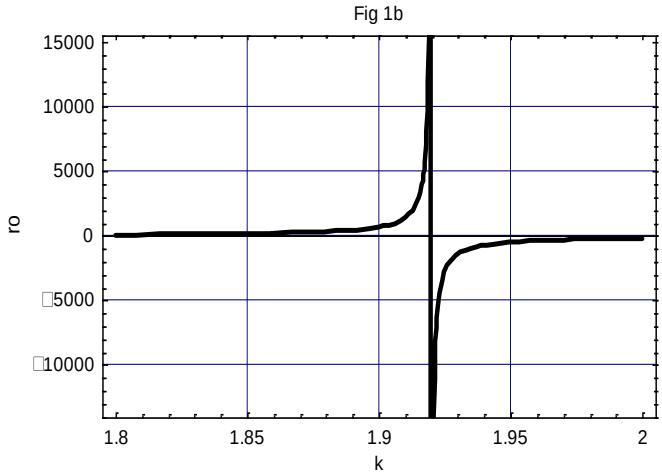


Fig.1a Cells density, formula (2.45) as the function of the growth factor k, for x=3 um, a=1 um. **Fig.1b**, the same as in Fig 1 a but for k>0.5

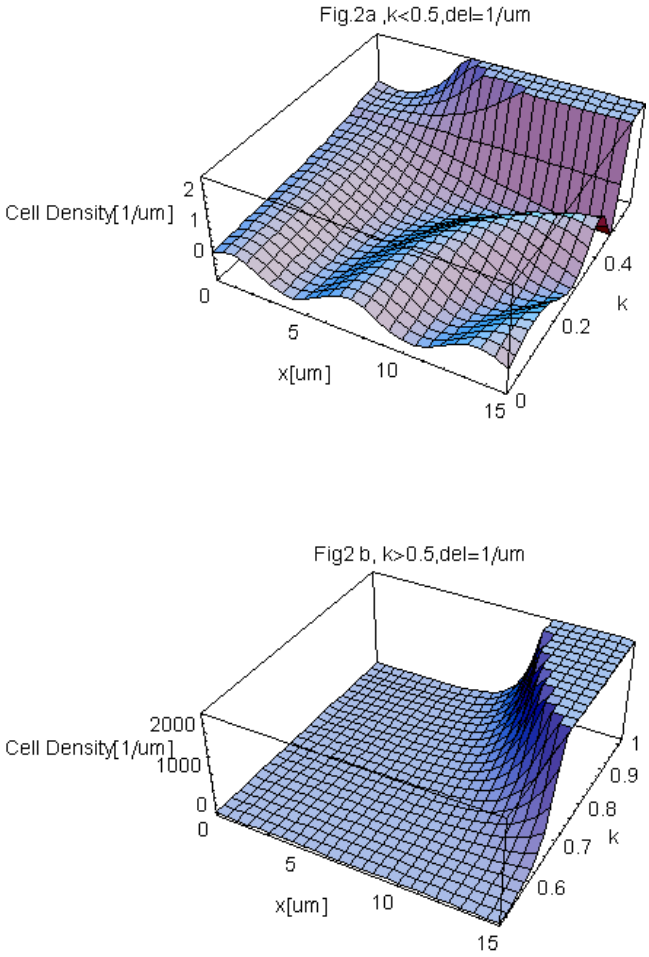


Fig.2a Cells density, formula (2.45) as the function of x and growth factor k, for k<0.5, a=10 um. **Fig. 2b** the same as in Fig 2a but for k>0.5

For k<0.5 the cell aggregation emits the wave with length λ= size of the tumor. For *k=0.5* the cancer development has a cusp. Fig1 a. For k=1.91 density of the tumor cells has a singularity. For *k<0.5* the density of the cell oscillate, Fig.2 a, a. On the other hand for *k>0.5* the cell density grows exponentially, Fig. 2 b.

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 the willing 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 exchange the information tumor→ host→ tumor and *vice versa*. Next , through the singularity point *k=1.9 , for x=3 um* 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 behavior of the cells density. 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 important therapeutic tool for the description of the cancer status. The stop of the emission of the waves is the signature of the invasive evolution of the tumor. It seems that host is informed by emitted waves on the existence of the tumor and its evolution. We can suspect of 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 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

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