

# Cancer is a nonlinear structural disorder caused by stress

## Abstract

There are two major types of organization in the body: organization in space and organization in time. Strong or prolonged stress influences the organization in time because it creates large delays - the body needs to stop its habitual work and mobilize for response to the stressor. In some individuals these delays lead to temporal disorder of the biorhythms of the genetically inherited weak organ manifested as functional or chronic disease. In other individuals (as we shall see in this article) the long term presence of electrically charged neurotransmitters secreted during prolonged stress creates electrical gradients, which lead to synthesis of electrically charged, but chemically distorted neurotransmitters. These nonlinear electrical distortions make it impossible for the cells to bind normally, which leads to the structural disorder, called malignancy. Cancer in its last stage 'malignancy' is 'a jumbled mass of cells instead of useful architecture, which multiply senselessly'. This article explains for the first time how stress, with the nonlinear distortions it creates, leads to the structural disorder called cancer. Nonlinear mathematical model is offered to describe the nonlinear distortions; it is based on the system theory used for neuronal networks and the areas flooded with electrically charged and chemically distorted neurotransmitters are considered neuronal pools. Words: 205

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## Cancer

In the last stage of cancer called malignancy, the cells grow fast and out of control. In a normal growing tissue culture cells stop growing when they meet and cell touches cell. This was called contact inhibition. The contact inhibition in a cancerous tissue is missing.<sup>1</sup> The famous Szent-Gyorgyi said: "Normal cells stop growing when growth is needed no more, while the cancer cells multiply senselessly".<sup>2</sup> This indicates changed metabolism. It was found experimentally that the cellular membranes of cancerous cells are strongly negative.<sup>3</sup> The excessive negative electric charges on the surface of cancerous cells will make them repulse each other instead of attract. This explains why cancerous cells are more easily detached from their neighbors and why they don't bind to each other. How does the negative electric charges on the surface of cancerous cells relate to their changed metabolism? Metabolism and electric charges are closely related<sup>4</sup> because the enzymes ruling the cellular metabolism and the hormones ruling the body metabolism are activated by ions. Thus, negative membrane charges on the surface of the cells mean wrong ionic fluxes through the membrane, which result in changed metabolism within the cells.

## Cancer and stress

Almost everybody knows that stress causes cancer, but we do not know how. We will try to explain in this article how stress causes cancer with the nonlinear changes it creates in the body.

## Mechanism of structural disordering by strong or prolonged stress

When exposed to strong stressor or prolonged stressors, the

body mobilizes for response - to fight or flight, adapt or resist. The mobilization reaction is called stress. The first step of the mobilization reaction for response to a stressor is called alarm signal, and during it neurotransmitters are released. They are "emergency" substances stored at the junctions of neurons ready to be released when stressors are present.<sup>5</sup>

"Neurotransmitters are electrically charged substances, released by one neuron, that act upon another neuron (a muscle or a gland) and alter its electrical state of activity".<sup>7</sup> Therefore, when exposed to strong or prolonged stressors, the cells around the neuronal junctions, called synapses, will be imbedded in the released electrically charged neurotransmitters for a long time. This without doubt will induce inappropriate electric charges in the membranes of adjacent cells. The membrane electric charges play essential role in the structural order of cells. When the cells have proper electric charges, they join in a proper way, and communicate in a proper way with appropriate ionic exchange. When the membrane electrical charges are changed beyond a critical level, the cells will not be able to bind properly anymore and the final result will be "a jumbled mass instead of useful architecture".<sup>2</sup> But until the critical level of accumulated electrically charged neurotransmitters is reached, the cells will remain normal. Dramatically changed membrane charges will make the proper communications among the cells impossible. The improper communication among the cells will lead to improper ionic exchange between them, which will lead to metabolic changes in the cells (because ions activate both - the enzymes and the hormones). The further damage from the nonlinear electrical distortions will be explained in § 6. However, this is only part of the problem called malignancy.

## Stress also weakens the immune systems

Our immune system has two large subdivisions: body immune system, called also humoral immune system (HIS), and local cellular immune systems (CIS), whose role is to suppress the mutant cells and cancer viruses and not allow them to multiply. Stress weakens both of them.<sup>5</sup> *The suppression of mutant cells by the cellular immune system (CIS) is a collective effort of all cells.* The permanent presence of electrically charged neurotransmitters during prolonged stress disintegrates the cells. Then the CIS can no longer efficiently suppress the mutant cells and cancer viruses, they start multiplying, and this starts the malignancy called cancer. *Malignancy itself is a fast process. However, if the weakening of CIS by stressors is considered, which takes years, cancer is a slow process, just like chronic diseases ('chronic' means 'slow').* Cancer should include the weakening of CIS by stressors, which take years, because this is what made the start of malignancy possible.

We know that the weakening of CIS and HIS takes years from the experiments of Dr. Halberg, who showed that years before the malignancy started the rhythm of body temperature changed from 24hours to 20hours and in some cases even to 8hours.<sup>8</sup> These two, and other changed rhythms, could and should be used for early detection of oncoming cancer, which will allow early and easy cure. If we would only start paying attention to these changes, maybe malignancy can be prevented. Dr. Frank Halberg observed skin arrhythmic mitosis in the ears of animals with implanted cancerous tumors long before the tumors would appear.<sup>8</sup> Hence *arrhythmic mitosis in the ears signals oncoming malignancy.* This could and should also be used for early detection of oncoming cancer. The present approach to cancer is: we wait until the malignancy starts and then we are looking for cure, trying to integrate the disintegrated cells. *We influence the system too late and that is why the cure is so difficult; cancer needs preventive measures.*

## Cancer is a disease of mal adaptation to stressors

Experiments showed that *two groups of animals exposed to the same carcinogenic agent, reacted differently when one of the groups was exposed to stressors, and the other was not.* In the control group not exposed to stressors, cancer was developed by only 27% of the animals, while in the group exposed to stressors the cancer was 62%.<sup>7</sup> Obviously carcinogenic agents when combined with stress bring more than 2times (2times) more cancer. Since the carcinogenic agent is also a stressor, cancer is obviously more frequent when the body must adapt to more than one stressor. Therefore, the disease *cancer should be considered a failure of the body to adapt adequately when more than one stressor is present for a long time. Selye called it maladaptation to stressors.*<sup>5</sup> Why did the body fail? When the body is exposed to a series of stressors, acting within relatively short time intervals (less than 2-3days), their nonspecific effects (characterized with secretion of neurotransmitters and hormones) accumulate because it takes 2 to 3days for the hormones and neurotransmitters emitted during stress to be washed away and excreted from the body completely.<sup>9</sup> If a second and third stressors strike before the body is back to norm, the amount of newly depleted hormones and neurotransmitters would be summed up with the residual amounts of the first stressor. This accumulation is what brings the body to the ultimate stress, which an organ can tolerate, and fails the adapting mechanisms. Which of the organs will fail depends on genetic predisposition. *A person with genetic predisposition to chronic disease, when exposed to prolonged stress, will develop a functional (chronic) disease.* His

weak organ with weakest biorhythm integration will be the first to experience biorhythm dissociation under stress and suffer functional (chronic) disease. *A person with a genetic predisposition to cancer, when exposed to prolonged stress, will develop cancer.* Please, pay attention! Cancer is with a genetic predisposition just like the chronic diseases!<sup>10-12</sup> If the stomach was the genetically inherited weak organ with weakest structural organization, prolonged stress will result in stomach cancer and its cells will turn into a "jumbled mass of cells". By analogy with the functional ultimate stress after which a functional disease appears, we can introduce a structural ultimate stress, after which cancer (structural disorder) appears.

## Ultimate stress or the limit of stress endurance role of stress sensitivity

The *level of ultimate stress*, which an organ can endure before becoming cancerous, depends on the stress sensitivity of the individual, which is measured with the amount of neurotransmitters released per unit stressor per unit time. It depends on the neuro hormonal balance of the individual. Since sensitivity means more neurotransmitters released per unit stressor, *fewer stressors will fail the CIS of sensitive individuals, and they will face malignancy earlier.* In the research of Wickramasekera,<sup>13</sup> there are three basic categories of people with three different levels of sensitivity to stress, pain, etc. - high, average and low. He found that stress sensitivity correlates with hypnotic abilities, which also could be: high, average, or low. Systematic measurements of neurotransmitters are necessary to find the correlations between type of neuro hormonal balance, hypnotic ability, and stress. Wickramasekera<sup>13</sup> claims that emotional individuals have an unusually long attention span and superior sensory and objective memory. These people are extremely creative and have the ability to process information outside of their own awareness. Such highly emotional individuals will have a lot of neurotransmitters of excitation (glutamates) released in their body at each excitation.

Since clinical observations show that the emotional people are most frequent victims of stress-related diseases, somatic disorders, and cancer, this means that for them not only the amount of the released neurotransmitters of excitation (glutamates) is high, the amount of the released stress neurotransmitters adrenaline and noradrenalin is also high. It seems that if somebody is highly emotional, he is also highly sensitive to stress. In the next paragraphs, we are going to discuss how the presently used treatments for cancer, such as X-rays and surgery, restore the structure of the malignant cells and add order to the disordered malignant cells.

## X-ray treatments add order

Dr. Halberg found that after X-ray treatment the biorhythm of cell division in cancerous tissue was closer to 24-hour, with only a few signs of fast division.<sup>8</sup> This means that the x-rays somehow time-shifted the biorhythms of cell division back to normal. Thus, after X-ray treatment not only did the cancerous tissue look structurally more ordered and normal, as if the X-rays added the missing order and the missing binding energy among the cells, the biorhythms' organization in time (called temporal organization) determining the function of the organ, was also better after X-rays' treatment. The X-rays, like any other stressor, have a nonspecific effect on the body because the mobilization reaction for response to stressors is the same for all stressors. However, X-rays also have effect specific for X-ray treatment. How much the cellular order has improved from the nonspecific stimulation effect of the X-rays and how much from their

specific effect, we still don't know, but such knowledge would help tremendously in the search for new treatments for cancer. We are just starting to understand the role of stress proteins,<sup>14</sup> which were first discovered in burn injuries, but turned out to be stress nonspecific. They are found in each endangered cell and are obviously an indelible component of the mobilization reaction called stress. The understanding of their role is expected to offer new alternative cures of cancer. More knowledge on stress-proteins and the nonspecific effects of other stressors would help us deal better with cancer by offering combinations of treatments with fewer side effects.

### Similarity of re growing and cancerous tissues

It turned out that when the body is wounded, accidentally cut, or surgically cut, the cells dedifferentiate to assure fast re growth and fast healing. They are no longer tissue specific, but transformed into primitive undifferentiated cells, which grow and multiply faster and are free to move into the wound. This metamorphosis allows fast re growth of cuts and fast healing. In the process of wound healing, the movement of the dedifferentiated cells is ruled by a negative electric current called current of re growth, which starts at the cut (for details see next section). In the case of cancer, during prolonged stress the long-term presence of electrically charged neurotransmitters had transformed the cells around the synapses into dedifferentiated fast growing cells, but there is no current to control the growth. As a result the cancerous cells multiply senselessly, taking all the nutrients circulating in the blood, when the healthy part of the body gets what is left over. The cancer disseminates and grows, while the host wastes away and dies.

### Surgical cut below malignancy restores both long and short range correlations among cells

Long time ago F. Seilern-Aspang and O. Cratochwil found that if a surgical cut was done below the place of skin cancer induced with chemicals, this added an organizing, regulating force, which re-differentiated the cancerous cells and turned them into normal cells.<sup>1</sup> This surgical cut added to the cancerous tissues the missing current of re growth. A similar experiment was done by M. Rose, who implanted frog kidney tumor on the limbs of a salamander. Even when the malignancy has spread to other places, when the surgical cut was under the primary tumor, the healing of the cut converted all cancerous cells into normal tissue.<sup>1</sup> The current of re growth rules the re growth, which starts at the cut line and runs back along the nerve.<sup>15</sup> *Initially, it was assumed that this current is what turns the cancerous tissue into normal*, which initiated an avalanche of experiments trying to imitate the current of re growth.

Scientists used direct current, pulsed direct current, or different kinds of electric, magnetic, or electromagnetic fields.<sup>15</sup> Some experimenters reported a positive impact on cancer, but the effect was not persistent - while in some cases the positive effect was there, in other cases it was missing. Obviously, the current of re growth and its electromagnetic field are not the only things that are missing in a cancerous tissue. As said, the cancerous cells have abnormal metabolism and membrane charges. That is why it is not possible to turn cancerous cells into normal by just imitating the nerve electromagnetic field or by using electric current. If cancer surgeries proved that surgical cut below the malignancy turned the cancerous cells into normal, it was because the surgical cut induced not only a current of re growth. It created an army of normal cells of re growth, which through contact with the dedifferentiated cancerous cells induced proper electric charges on their

surface. This induced proper ionic fluxes through the membranes of the cancerous cells, which restored their metabolism. Then, ruled by the current of re growth, the normal cells formed a normal tissue. This explains why the cancerous cells wouldn't turn into normal by only simulating the current of re growth. The current of re growth rules the long-range order of the cells, and in a cancerous tissue the short-range order is also missing. Once the short-range order is restored by contact with normal cells of re growth, the long-range order, ruled by the current of re growth, will restore the cellular structure not only around the surgical cut, but also in far spread malignancies. It is like an avalanche. Once the process of restoration has started, it will not stop until all cancerous cells are turned into normal. This raises questions: "Are there other ways, besides a surgical cut through or below the malignancy that can normalize the metabolism of cancerous cells?" Suss R et al.,<sup>16</sup> claimed that the structure of cancerous tissue could be restored, if some cancerous cells are pulled out and after prolonged shacking injected back. More studies are necessary.

### Nonlinear distortions

A cut below the malignancy not only creates an army of normal growing cells, which through contact with the cancerous cells turns them into normal, the disordered biorhythms of the cancerous cells become tamed and synchronized as those of the normal cells. The cancerous cells through contact with normal cells were entrained to become normal. Since entrainment<sup>17</sup> is specific only for nonlinearly related units, *the cells in a normal tissue must be related in a nonlinear way*. If the cells in a normal tissue are related nonlinearly, *only nonlinear distortions can destroy existing cellular order*. Therefore, the electrical gradients created by electrically charged neurotransmitters accumulated during strong or prolonged stress must be nonlinear and strong enough to destroy the existing nonlinear connection among the cells and turn the normal cells into "jumbled mass", i.e. cancerous cells.

It was found experimentally that electromagnetic fields lead to synthesis of chemically distorted neurotransmitters.<sup>18</sup> If so, the electromagnetic fields and gradients, which the electrically charged neurotransmitters (NTs) create around the nerves' junctions during strong or prolonged stress, can be expected to make impossible further synthesis of normal electrically charged neurotransmitters. They will be chemically distorted and this will lead to even heavier nonlinear distortions, which will destroy the short-range order of the cells and bring malignancy. Nonlinear changes can also be expected in the nerve transmissions and the nerve electromagnetic fields, which rules the long-range alignment of the cells. *Thus, prolonged stress destroys both short- and long-range order of the cells through the nonlinear electric distortions it creates*. If malignancy results from nonlinear distortions, the mathematical description of the onset of cancer would require nonlinear equations.

### Nonlinear mathematical model

*During prolonged stress, the areas around the synapses will be flooded with electrically charged neurotransmitters for a long time. Let us consider them as neuronal pools. The nonlinear integration of these neuronal pools could be explained by the system theory.*<sup>19</sup> When applied to a system of neuronal pools, the system theory gives the following nonlinear expression for the output electric potential:

$$v_j(t) = v_j(0) + \int K_{ji}(x_i(t'), t, t') dt' \quad (1)$$

where  $K_{ji}$  is the nonlinear kernel of interaction of two adjacent neuronal pools  $i$  and  $j$  ( $x_i$  - input current of excitation). According to Miller<sup>20</sup> the linear system, which corresponds to the nonlinear equation (1), has a solution

$$z(t) = f(t) + \int g(t-t')z(t')dt'. \tag{2}$$

This is a linear Volterra integral equation, which can be expressed in terms of a resolvent  $R(t-t')$  and a function  $f(t')$ ,

$$z(t) = f(t) - \int R(t-t')f(t')dt'. \tag{3}$$

The resolvent  $R$ , corresponding to a continuous matrix kernel  $g$ , is:

$$R(t) = -g(t) + \int g(t-t')R(t')dt'. \tag{4}$$

A simple condition (on the resolvent  $R$  of the linear system) is sufficient to guarantee asymptotic stability of the steady states of the nonlinear system.

$$\lim \int R(t) dt = \sim It$$

In the neighborhood of the steady state  $v$  of the system, the roots of the characteristic equation determine the stability

$$g^*(k) = \exp(-kt) g(t) dt \tag{5}$$

where  $g^*(k) = \exp(-kt) g(t) dt$  is the Laplace transform of the kernel  $g$ .

The equation (2) is linear because the nonlinear kernel  $K_{ij}(x_i(t'), t, t')$  has been replaced with a linear one

$$g_{ij}(t) = u_{ij}'(v_j)h_{ij}(t). \tag{6}$$

Here  $h_{ij}(t)$  has the meaning of a weight function. It describes the distribution of  $v_j$  around the average  $v_j$ , with a normalization condition

$$\int |h_{ij}(t)| dt = 1, \quad u_{ij}'(j) \geq 0, \tag{7}$$

which implies, as a condition for stability.

$$|h_{ij}(k)| \leq 1, \quad \text{if } Re k \leq 0 \tag{7'}$$

Unstable stationary solutions can be used to describe the regions of attraction of stable states. A natural question arises: With time which of the constant states will exhibit a global excitation or global inhibition?

The system theory has a theorem<sup>19</sup> stating: A local excitation of sufficient strength will spread out to a global constant excitation, i.e.  $\lim v(s,t) = 1$  for all  $s$  if  $T_j(v_j) = x_j$ . As stated, each highly stress-sensitive individual will have a larger amount of adrenaline and noradrenalin released at each neuro synaptic junction. Such individual will achieve state of global mobilization fast, i.e. his energy to fight or flight, adapt or resist the stressor will increase fast. Since the neuronal pools are related in a nonlinear way, the distance among them will be bridged long before their borders will reach each other. Recent research on doped organic polymers shows that they become conductors when doped (with iodine or bromine). The doping increases the in homogeneity of the sample because the dopant accumulates at the places of structural imperfection, which become conducting, and the

semiconducting organic polymer becomes conducting long before the borders of these conducting areas reach each other. This leads to changes in the characteristic frequencies of the sample.

Thus, one can see from doping how the increased in homogeneity of a sample leads to changes in its characteristic frequencies.<sup>20</sup> This makes us believe that, just like the doping, the flooding with neurotransmitters, which are electrically charged, will increase the electrical in homogeneity, which will lead to changes in frequency characteristics. Let us now introduce a conversion function  $T_j(v_j) = x_j$  (where  $v$  is the potential,  $x$  - the frequency for area  $j$ ), which will allow us instead of potential representation (2)

$$v_j = v_{j0} + u_{ji}(v_i) * h_{ji} + u_{jj}(v_j) * h_{jj} \tag{8}$$

to use frequency  $x_j$ -representation:

$$x_j = T_j(v_j + S_{ji}(x_i) * h_{ji} + S_{jj}(x_j) * h_{jj}). \tag{9}$$

$S_{ji}(x_i) * h_{ji} = \int S_{ji}(x_i(t'))h_{ji}(t-t')dt'$ , where  $S_{ji}$  is the average generator potential produced in  $j$  by  $x_i$ . The third term reflects self-inhibition.

The potential representation (8) can be written in a new form after substitution  $u_{ji} = S_{ji} \circ T_i$

$$v_j = v_{j0} + S_{ji} \circ T_i(x_i) * h_{ji} + S_{jj} \circ T_j(v_j) * h_{jj}, \tag{10}$$

where  $u_{jj}$  and  $u_{ji}$  are monotone increasing, nonnegative, and bounded functions.

Further modifications of equation (8) transform it to a form formally identical with Fitzhugh-Nagumo equations,<sup>19</sup> which have solutions of the type wave-trains and traveling-pulse solutions.<sup>19</sup>

## Conclusion

Selye's experiments showed that the same stress causes different chronic diseases in different individuals and cancer in others (Selye). Obviously, genetic predisposition determines would strong or prolonged stress result in a functional (chronic) disease of an organ or cancer. Cancer is with genetic predisposition.<sup>10,12</sup> *Stress-sensitive individuals would secrete larger amounts of electrically charged neurotransmitters per unit stress. For them, this would create larger electrical gradients leading to synthesis of chemically distorted neurotransmitters, which would make normal binding among cells impossible.* Once the cells are disconnected and disorganized, they cannot defend themselves because the cellular defense is a collective event. The cellular immune system (CIS) would no longer be able to suppress the mutant cells and cancer viruses and they would start multiplying, which would initiate malignancy.<sup>21</sup>

*Since cancer is a cellular order destroyed by prolonged stress, the disease cancer should include the weakening of the CIS by stressors, which takes years and makes the start of malignancy possible. If the changes in CIS are considered, cancer is a slow disease. If the changes in CIS are monitored, the appearance of cancer could be predicted and cancer could be prevented. Research shows that many changes in the body, such as: body temperature rhythm, rhythm of skin mitosis, etc., precede the malignancy and signal its oncoming.* When we learn

to understand these signals, we will *be able to predict and prevent cancer*. We shouldn't wait until the malignancy starts and then try to restore the destroyed cellular organization; it is too late. Presently, cancer (malignancy) is treated with radiation (X-rays or gamma rays) and surgery. As shown in §4 and §6 they normalize the structure of the cancerous tissue. *Surgical cut below the malignancy (see §6) was found to turn all cancerous cells into normal ones even in the far spread areas*. As underlined, surgery restores both the short-range order of the cells and the long-range order of the cells ruled by the current of re growth. If the scientists were not able to turn cancerous cells into normal by just imitating the current of re growth, it was because the current of re growth can normalize only the long-range order of the cells. Since cancerous tissue lacks short-range order as well, which can be restored only through contacts with normal re-growing cells, only surgical cut can normalize cancerous cells.

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## Conflict of interest

Author declares that there is no conflict of interest.

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