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When Invading, Cancer Cells Do Not Divide: A Geometric (Symmetry-Based) Explanation of an Empirical Observation

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When Invading, Cancer Cell Do Not Divide: A Geometric (Symmetry-Based) Explanation of an Empirical Observation

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Abstract

In general, malignant tumors are known to grow fast, cancer cells that form these tumors divide and spread around. Tumors also experience the process of metastasis, when cancer cells invade neighboring organs. A recent experiment has shown that, contrary to the previous assumptions, when cancer cells are invading, they stop dividing. In this paper, we provide a geometric explanation for this empirical phenomenon.

1 Formulation of the Problem

What is cancer and how it is usually treated: a brief reminder. In a nutshell, cancer is when some cells in the body start dividing uncontrollably. As a result, we have a growing mass of such defective cells – a tumor – which, if untreated, is usually fatal for the patient.

Many other illnesses – e.g., many bacterial infections – are caused by an exponential growth of corresponding cells. However, in such diseases, the dividing cells are alien to the body and thus, the immune system is actively fighting against the proliferation of these cells. In contrast, cancer cells are minor modifications of the cells that form the patient's body; the difference between the cancer cells and the healthy cells is so small that it does not trigger the immune system response – and, as a result, if untreated, cancer tumors grow exponentially.

The fact that cancer cells are similar to healthy ones not only makes it difficult for the body to fight cancer, it also makes it difficult to come up with good treatments for cancer.

Typically, a cancer treatment targets cells that are dividing too much. While such a treatment is aimed at cancer cells, because of the similarity between the cancer and healthy cells, this treatment also harms nearby healthy cells as well.

As a result, cancer treatment is usually effective only when the cancer cells are concentrated in one reasonably small location in the body. In such situations, an (inevitable) damage to healthy cells in this (relatively small) part of the body is not fatal for the patient.

The situation is much worse in metastatis, when cancer cells have spread to many locations within the body. In such situations, the prognosis is often bad: we cannot apply the usual cancer treatment to all these locations, since the resulting damage to healthy cells in all these locations may also be fatal.

A recent discovery. A recent empirical study (see, e.g., [1, 5]) showed that when the cancer cells invade new organs, they stop dividing.

This discovery is important for cancer treatment. This empirical discovery is very important, since cancer cells are usually detected by their fast division. The above result means that when a cancer cells is in the process of invading a new organ, it is not affected by the current cancer treatments. In other words, while the current cancer treatments help fight the cancer cells in their original organ, they do not prevent these cells from metastasis – and metastasis is what usually kills the patient.

Thus, to prevent metastasis, new methods are needed for detecting and destroying invading cancer cells.

The empirical fact is important, but how do we explain it? At this moment, there is no convincing explanation for the above empirical phenomenon.

In this paper, we show that geometric analysis can provide such an explanation.

2 Geometric Analysis of the Problem

Original (pre-cancer) state of an organ. The tissue within an organ is reasonable homogeneous: if we shift from one location to another or rotate, we will not see much of the difference. Similarly, if we re-scale the tissue, it will still look approximately the same.

In other words, the original organ is (locally) invariant with respect to shifts, rotations, and scalings ($\vec{x} \to \lambda \cdot \vec{x}$).

From the geometric viewpoint, cancer is a symmetry violation. Cancer does not immediately appear at all the locations of the organ, it only appears at some of the locations. As a result, if we shift from a cancer location to a non-cancer location, the tissue changes.

In other words, with the appearance of cancer, the organ is no longer invariant with respect to all the shifts, i.e., we have what physicists call *symmetry violation*.

What physics can teach us about symmetry violations. According to physics, while it is possible to go directly from a highly symmetric state to a state with no symmetries, such transitions are highly improbable. In general, the more symmetries are preserves, the more probable the transition. Thus,

in most cases, we first go to the state with the largest number of remaining symmetries. Similarly, from a solid state, we usually first go to a fluid state, and only then to gas – although in some cases, a solid can directly turn into gas; see, e.g., [2].

What are the resulting geometric shapes? We start with the group G_0 generated by all shifts, rotations, and scalings. After a symmetry violation, the state is invariant with respect to only some of these transformations, i.e., with respect to some proper subgroup G of the original symmetry group G_0.

If we have cancer cells at some location x, then, due to symmetry of the resulting configuration, we should have cancer cells also at every point $g(x)$ corresponding to transformations $g \in G$. Thus, the set of all cancer locations contains, with each point x, the whole orbit $G(x) \stackrel{\text{def}}{=} \{g(x) : g \in G\}$.

So, to describe all possible shapes, we must describe the orbits of all the proper subgroups G of the largest possible dimension.

Such orbits have already been classified, let us use it. The full description of all the orbits of subgroups of the group G_0 is already known; see, e.g., [3, 4]. Let us use this known classification to describe the orbits of the most symmetric (and thus, the most probable) groups. This will allow us to describe the most probably shapes of cancer-affected regions.

Resulting shapes of cancer configurations. The largest possible subgroups are 4-dimensional (= 4-parametric) ones. There are three types of orbits corresponding to such groups:

- a single *point*, which is invariant with respect to 3 rotations and scaling,
- a *plane*, which is invariant with respect to 2 shifts (in this plane), rotation (in this plane), and scaling, and
- a *half-space*, which is invariant with respect to 2 shifts in the boundary plane, rotation in the boundary plane, and scaling.

So, the starting point of cancer configuration must have one of these shapes.

The half-space means that cancer has immediately affected half of the organ. This may be possible for some cancers, but most cancers start small.

Similarly, a plane means that the cancer has immediately spread to the whole surface – e.g., to a large skin area in case of melanoma. Again, this may be possible, but this is not a typical start of a cancer.

For describing typical cancers, the only remaining shape is a point, which means that the cancer starts with one location.

As cancer progresses, symmetry decreases further, from a 4-dimensional symmetry group to smaller subgroups. As we have mentioned, the most probable transitions are to the largest possible proper subgroups, i.e., in this case, to 3-dimensional subgroups. There are two geometric shapes corresponding to 3-dimensional symmetry groups G:

- a *sphere*, which is invariant with respect to 3 rotations, and

- a *straight line*, which is invariant with respect to shifts along the line, rotations around this line, and scaling.

So, we conclude that once the cancer emerged at some location, it will spread either to a spherical (ball) shape, or to a linear shape.

Seemingly natural interpretation. In cancer terms, a spherical shape seems to correspond to tumor growth in all directions, while a linear shape seems to correspond to invasion.

Let us check that this is indeed the case.

How are different shapes related to the dynamical picture: a symmetry-based analysis. Our interest is to describe when cancer cells invade neighboring tissues, i.e., when we see a movement in a certain direction.

In the case of a sphere, once we add a direction, for the resulting configuration of a shape and a direction, only one symmetry remains: rotations around the direction. Thus, in case of a spherical shape – corresponding to tumor growth – invasion requires symmetry violations and is, thus, highly improbable.

On the other hand, for a linear shape, if the direction of the invasion coincides with the direction of the shape, all symmetries remain in place. So, in this case, there is no symmetry-based reason why there will be no invasion.

Conclusion. Our geometric analysis shows that in the tumor growth stage – when the shape of the tumor corresponds to a ball – invasion is highly improbable, while invasion is quite possible for the linear shape.

In other words, our geometric analysis shows that in most cases, when cancer cells invade the neighboring organs, in the process of invasion they stop the usual dividing-and-spreading-around behavior – which is exactly what the new research has observed. So, we have indeed come up with a geometric explanation for the observed behavior.

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