UNDERSTANDING THE UNPREDICTABILITY OF CANCER USING CHAOS THEORY AND MODERN ART TECHNIQUES

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See <www.mitpressjournals.org/toc/leon/49/1> for supplemental files associated with this issue.

Submitted: 5 November 2014

Abstract

The unpredictability of cancer poses a threat to personalized cures. Although cancer is studied as a chaotic system, the shape of its unpredictability, known as the strange attractor, is unclear. In this article, the author discusses a conceptual model, building on the strange attractor in cancer phase space. Using techniques of cubism, the author defines the 10-dimensional phase space and then, using an abstract expressionist approach, represents the strange attractor, which twists and turns in multi dimensions, indicating the unpredictability of cancer. This conceptual model motivates the identification of specific experiments for a system-level understanding of cancer.

Keywords: cancer, unpredictability, chaos, strange attractor, phase space, hallmarks of cancer, single-cell variability, cubism, abstract expressionism

Introduction

Cancer remains the second leading cause of death in the United States [1]. The variability within and among patient tumors creates a major challenge to the study and cure of some types of cancer [2]. Recent studies have been directed towards understanding this variability at the single-cell level for some tumor attributes [3]. However, technologies are not well developed to study all attributes of tumors in single cells. In this scenario, as a cancer researcher and a fine artist, I seek to design a general, cognitive model of the unpredictability of cancer. Such a model would present a novel perspective of cancer variability.

Cancer as a Chaotic System

There is an uncanny similarity between the progression of a chaotic system and that of cancer. The unpredictability of a chaotic system comes from the missing information gathered over an iterative process [4]. In cancer, similar events occur via genetic and epigenetic changes gathered over many cell divisions. Additionally, both emergence of chaotic systems and cancer progression are step-wise processes initiated by stress events [5]. This suggests we may study cancer as a chaotic system.

What properties of chaotic systems could we employ to study cancer? The shape to which the trajectory of a chaotic system is attracted over time is called a strange attractor [4]. The parameter space in which such trajectory is calculated is called a phase space [4]. Earlier studies on tumor growth in its phase space with four parameters have observed a chaotic strange attractor [6,7]. However, the shape of the strange attractor in high-dimensional phase space is unclear. Such understanding is necessary, as it would provide information about the behavior of a malignant tumor over time. Without considering all the biological attributes for building a phase space, the strange attractor of cancer cannot be clearly understood.

High-Dimensional Cancer Phase Space

To build a high-dimensional cancer phase space I employed the concept of 10 distinct biological attributes shared by all types of tumors, known as the hallmarks of cancer [8]. Interestingly, there could be variability within and among tumors in each of these attributes [9]. Traditionally, the value of an attribute can be represented along a linear axis. But, in order to consider variability of those attributes, an additional dimension is required. Hence, in cancer phase space I represented these attributes using two-dimensional planes instead of one-dimensional lines. The variability within a population of cancer cells can be studied as more than one subpopulation [2] (Fig. 1). Over the process of progression, this variability may alter, as certain subpopulations may grow faster than the others, taking over the whole population. This suggests that the two-dimensional planes may not be uniform over time. Depending on how many subpopulations exist at a given time, the width of the plane varies over time. Essentially, we need to paint multiple non-uniform dimensions in two dimensions.

How do we represent 10 non-uniform dimensions in a two-dimensional painting? For this purpose, I used techniques from cubism. In cubism, subjects are analyzed, deconstructed and reassembled in an abstract form [10]. Instead of depicting a subject from a single viewpoint, the subject is studied and represented from multiple viewpoints. This technique allows the representation of a subject in a greater context and in higher dimensions. Hence, the 10 non-uniform dimensions representing 10 hallmarks of cancer can be painted in an abstract form using cubism. I built a cancer phase space representing a 10-dimensional space in two dimensions, using acrylic on paper (see online supplemental images).

Strange Attractor in Cancer Phase Space

How do we paint the path to which a cancer cell’s trajectory will be attracted in its phase space (strange attractor of cancer)? Experimental data are not available on all 10 hallmarks of any kind of cancer at the single-cell level over time. Hence, computational data plotting is not achievable yet. Nonetheless, we know that the missing information in a chaotic system traces out its unpredictability via multiple iterations. The shape it traces out is the strange attractor [4]. In the case of cancer, the unpredictability arises due to the unavailability of data over
many cell divisions. This suggests the strange attractor of cancer may depict its uncertainty.

How do we represent the uncertainty of cancer using an abstract shape? For this purpose, I employed visualization techniques from quantum mechanics. The uncertainty or probability of finding electrons in any region of an atom is represented by atomic orbitals [11] in quantum mechanics. The atomic orbitals are indicated by cloud-like shapes. The specific shape can also be shown by a contour map. In this case, negative and positive values for the contour of atomic orbitals are indicated by dashed and solid lines, respectively [11]. The probability density in phase space of an evolving chaotic system is depicted as a cloud-like shape in literature [12]. Hence, to depict the strange attractor of cancer we can use a cloud-like shape painted with solid and dashed lines that twist and turn in the cancer phase space (see Fig. 1 and supplemental figures). In such a cancer space, normal healthy cells can only reside at the center where all the planes meet. Highly dividing cancer cells are known to have higher energy metabolism than normal cells [5]. Hence, I represented the high energy of cancer cells using warm colors in the final image of the strange attractor. To capture the dynamics of the strange attractor in a static painting, I have used multiple colors instead of a monochrome.

In general, the above conceptual model of cancer's unpredictability does not depict objective reality. The assumptions I made about understanding the behavior of cancer as a chaotic system cannot be validated with objective data at this point. On the contrary, this is a subjective response aroused in a cancer biologist and a fine artist from my understanding of cancer and chaos theory. Hence, I categorize this work as abstract expressionism [13]. However, the motivation for generating such artwork is not entirely autotelic. I believe this conceptual model will motivate specific experiments. One such experiment can be the development of a preclinical animal model of cancer where single-cell data on all the hallmarks of cancer can be collected as the cancer progresses. Such an experimental model can be used to identify the parameters for each of these 10 hallmarks of cancer, to represent them by differential equations and to solve them to find the shape of the strange attractor.

**Conclusion**

I propose a cognitive model of the unpredictability of cancer using principles from chaos theory. In general, what should be entailed in a successful art-science model is not well defined, let alone in a specific case of cancer art. However, a new model should put forth an idea or perspective that allows oncologists to consider a problem or concept in a novel or modified way. My model proposes a new idea that all the hallmarks of cancer are important to study at the single-cell level. Additionally, this model puts forward ideas of utilizing principles of complex systems to study a tumor.

As a cancer-based art project, the idea of this painting can be extended into a linear or full round sculpture. It is known that tumor cells can interact among themselves and with the microenvironment [6]. Hence, it would also be interesting to utilize interactive media art techniques to document the responses from the audience given a choice of altering the values of the 10 hallmarks of cancer during cancer progression.

**Methods**

I created paintings of both phase spaces and strange attractors using acrylic on paper. I created the first impression of the strange attractor on paper using a cotton thread dipped into acrylic paint. Later I painted the details using a paintbrush. Both paintings were scanned and saved as image files. The cool colors of the strange attractor were inverted to warm colors using Picasa photo editor. Both images were opened as layers on Adobe illustrator with the strange attractor on top. The raster images were converted to vector objects using the live trace and expand functions. The background of the strange attractor painting was selected and deleted to superimpose the strange attractor on the phase space. The superimposed layers were exported as single image file (see online supplemental text).

**Glossary**

*Phase space*—The space in which all the possible states of a system are represented over time.

*Strange attractor*—The shape to which the trajectory of the chaotic system is attracted.

*Hallmarks of cancer*—Ten biological attributes shared by all types of cancer. They include sustaining proliferative signaling, evading growth suppressors, avoiding immune destruction, enabling replicative immortality, tumor-promoting inflammation, activating invasion and metastasis, inducing angiogenesis, genome instability and mutation, resisting cell death, and deregulating cellular energetics.

*Cancer progression*—A stepwise process of healthy cells transforming into malignant tumor. The steps include hyperplasia, dysplasia, carcinoma in situ and malignant tumor.

*Subpopulation*—A fraction of the total population of cancer cells which may have different biological properties than the other cells in the population.

*Atomic orbital*—A mathematical function that describes the wave-like behavior of either one electron or a pair of electrons in an atom. This function can be used to calculate the probability of finding any electron of an atom in any specific region around the atom's nucleus.

*Contour map*—A projection of a high-dimensional object on lower dimensions.

*Microenvironment*—The cellular and stromal environment surrounding a tumor.

**Acknowledgment**

I acknowledge Caroline Shaw Ometz for useful discussions.

**References and Notes**

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