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Review article

A biophysical approach to cancer dynamics: Quantum chaos and energy turbulence

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ABSTRACT

Cancer is a term used to define a collective set of rapidly evolving cells with immortalized replication, altered epimetabolomes and patterns of longevity. Identifying a common signaling cascade to target all cancers has been a major obstacle in medicine. A quantum dynamic framework has been established to explain mutation theory, biological energy landscapes, cell communication patterns and the cancer interactome under the influence of quantum chaos. Quantum tunneling in mutagenesis, vacuum energy field dynamics, and cytoskeletal networks in tumor morphogenesis have revealed the applicability for description of cancer dynamics, which is discussed with a brief account of endogenous hallucinogens, bioelectromagnetism and water fluctuations. A holistic model of mathematical oncology has been provided to identify key signaling pathways required for the phenotypic reprogramming of cancer through an epigenetic landscape. The paper will also serve as a mathematical guide to understand the cancer interactome by interlinking theoretical and experimental oncology. A multi-dimensional model of quantum evolution by adaptive selection has been established for cancer biology.

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1. Introduction

Cancer is defined as the malignant transformation of tissues characterized by abnormal cell division through the accumulation of unrepaired driver mutations and self-sufficient growth signals. It is a highly complex biosystem that rapidly adapts to its environment, where a single tumor can have hundreds of mutated genes. Due to tumor heterogeneity, personalized pharmacogenomics must be approached as each cancer has a unique signaling identity or a reprogramming cascade for all cancers must be identified.

On a systemic level, cancer is a disease with patient-specific cell-surface biomarkers and gene expression profiles. However, at a cellular basis, cancer cells outperform normal cells in terms of survival pathways and longevity. Hereby, I will establish the mathematical foundations for the understanding of cancer evolution as a coherent feedback system between the genome, epigenome and the cell-cell/cell-matrix interactome, from which a proteomic landscape will be constructed for reprogramming cancer cells to mutually coexist with non-cancerous cells (i.e. phenotype reversal). To understand these processes, we must explore tumorigenesis and cancer progression under a quantum dynamical framework.

Evolution is currently seen as the variation in the genetics of biological populations over time. However, epigenetic evolution and acquisition of epimutations (genetically non-inheritable changes that determines cell phenotype and gene expression patterns) is not accounted for Darwinian models. The mechanisms by which

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transgenerational epigenetic memory can be transmitted to successive generations, especially over a large period of time must be investigated to understand cancer evolution. More importantly, we must validate whether these on/off gene expression states can be described as quantum states (i.e. qubits). With currently existing experimental evidence and theoretical models, I propose the following hypothesis: *The evolution of cancer cells through quantum selective adaptations to the environment.*

The hallmarks of cancers such as unlimited replication, reprogrammed respirasome, apoptosis evasion, angiogenesis, insensitivity to anti-growth signals, contact inhibition, rewired metabolic cascades, immune system hijacking, etc. have been established by Hanahan and Weinberg (2011). Cancers can selectively over-express or down-regulate protein complexes (ex: cell surface adhesion molecules, membrane proteins, transport molecules, epigenetic factors, enzymes, ion channels, receptors and growth factors), secretory vesicles, exosomes, ribosomes, and lipids depending on their survival needs, adapted mutations and epigenetic changes (Weinberg, 2007). Even amidst aerobic conditions (ample oxygen supply), most cancer cells express hypoxia inducing signaling pathways and the Warburg effect (glycolysis) as an evolutionary strategy to enhance their survival/longevity and proliferation. The excess lactate production allows faster incorporation of carbon into cell biomass and fuels rapid cell division. The suppression of oxidative phosphorylation may help cancer cells evade apoptotic pathways and ageing (energy depletion).

One critical step in oncogenesis involves the up-regulation or reactivation of telomerase in order to overcome the Hayflick limit. Approximately 85–90% of all tumor biopsies are telomerase positive. Although the remainder lack detectable enzyme activity, they can maintain telomere length by ALT (alternate lengthening of telomeres). Furthermore, Cancer stem cells and embryonic stem cells have a depolarized plasma membrane potential in order to proliferate easily and alter their morphogenesis (cytoskeleton) constantly (i.e. regenerative stem cell potency).

Cancers evolve by tissue microenvironment co-dependent phenotype selection. In principle, since cancer cells have a stronger resonant cell-matrix coupling strength than healthy cells (*environmental dominance*), it is inferred that they can selectively adapt the epigenetic landscape of their microenvironment in favor of their survival cues. According to the proposed model, the temporal evolution of cancer cells' quantum-adaptive energy (epigenetic) landscapes determine morphogenetic plasticity and differentiation through the signaling network dynamics of a *perturbation* (mutation) induced *shift* in the underlying pilot wave potential Q. As a result of the altered phenotypic landscape, selective evolutionary properties such as hyper-proliferation and metastatic invasion are acquired by cancer cells via coupling with the energy fields of the tumor microenvironment.

The coupling strength of cell–cell and cell-matrix interactions can be measured using techniques such as force spectroscopy and Bio-AFM (atomic force microscopy) although it varies from cell to cell depending on the environment and measurement context (ex: focal adhesions, cytoskeletal proteins, integrin mediated forces, cell type, etc.). At thermal scales, fluid dynamical models and Boltzmann distributions elucidate cancer dynamics. However, in contrast to the widely held scientific paradigm, the energy dynamics of cancer cells (signaling pathways and information flow) display equivalent topological flux patterns at all orders of magnitude whether at quantum or physiological scales. Mathematically, the energy turbulences of epigenetic landscapes modeling cancer evolution are indistinguishable from the quantum fluctuations governing cosmic inflation.

Empirical evidence asserts that the metastatic potential and cancer cell properties (proliferation, longevity, etc.) are a result of the altered fluid dynamics of cancer's developmental (epigenetic) landscape. Cancer cells quickly adapt to environmental changes and reorganize their morphology by continuously updating their cell–cell and cell-matrix coupling strengths (chaotic adhesion profile). In theory, these matrix-coupling dynamics can be studied as physiological quantum phenomena by modeling the cancer system as a Bose-Einstein condensate and by measuring the changes in the cytoskeletal-bioelectric field potential or transcriptome-epigenome flux rates.

Epigenetic memory transfer determines cell phenotype and stem cell-lineage specification. The epigenetic modifications determining cancer stem cell reprogramming and the tumor microenvironment's epigenetic reprogramming circuitry have been discussed by many. Epigenetic reprogramming can reset the rate of biological ageing clocks (Rando and Chang, 2012). Altering the DNA methylation patterns alone can lead to stable phenotypic reprogramming of cancer cells (Blancafort et al., 2013). Cell phenotype is the product of an inherited genotype and the many microenvironmental influences (epigenome). Natural Selection (NS) non-randomly selects phenotypes within populations (Reece et al., 2010). The morphological plasticity of cells is governed by the epigenome whereby selective mutations can enhance reproductive success and survival as seen in cancer cells. As cancer cells rapidly divide (altered chronobiology), new mutations that confer selective advantages for microenvironmental adaptation and reproductive success are acquired in subsequent populations.

Apart from covalent post-translational modifications (ex: acetylation, methylation, phosphorylation), extracellular matrix components, cytoskeletal remodeling factors, cell surface adhesion molecules, internal membrane proteins, enzymes, etc. dynamically repress or activate chromatin sites for transcription. For instance, the nuclear lamina interaction with chromatin is essential for normal tissue-specific transcription of certain genes. Hence, nuclear lamina should comprise of epigenetic regulation. By definition, all genetically non-inheritable changes contributing to the cell phenotype that modifies its gene expression and regulation is an epigenetic process/modification (Fig. 1). For instance, glycosylation is proposed as a quantum biological mechanism (Lauc et al., 2014). In argument, epigenetic inheritance can be interpreted as biochemical Lamarckism (Wintrebert, 1962). However, the principal query is whether these epigenetic alterations are macroscopic (biomolecular) quantum systems (i.e. superposition of histone modifications, wave-particle behavior of nucleosome interactions, quantum tunneling of epigenetic signals, etc.)?

Quantum wave effects occur in proteomics. Quantum vibrational free energies of many enzyme complexes such as isomerase and dehydrogenase reactions have been validated. Luo and Lu (2011) verified that the quantum transition between conformational torsion states of polypeptides determines its temperature-dependent protein folding. Quantum coherence in physiological time scales has been well documented. Quantum effects such as the superposition principle and wave-particle duality in photosynthesis cascades (excitons of the chromophores and energy transport complexes), the magnetoreception of birds (quantum entanglement of retinal photoreceptors with the electron spin of Earth's magnetic field) and the olfactory receptors have been experimentally established (Arndt et al., 2009; Lambert et al., 2012; Mohseni et al., 2014).

Schoenlein et al. (1991) validated that vision is a quantum process whereby photon signals are converted to action potentials. The femtosecond isomerisation of rhodopsin via photon interaction is clear evidence to biological quantum information processing. Additionally, quantum wave effects occur in the electron/proton transfers of protein complexes. Electron transfer is gated by environmental energy fluctuations. In theory, oxidative phosphorylation, proton gradients and mitochondrial-metabolome energy transduction should exhibit the quantum phenomena observed in