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A Bistable Field Model of Cancer Dynamics

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Abstract. Cancer spread is a dynamical process occurring not only in time but also in space which, for solid tumors at least, can be modeled quantitatively by reaction and diffusion equations with a bistable behavior: tumor cell colonization happens in a portion of tissue and propagates, but in some cases the process is stopped. Such a cancer proliferation/extintion dynamics is obtained in many mathematical models as a limit of complicated interacting biological fields. In this article we present a very basic model of cancer proliferation adopting the *bistable* equation for a single tumor cell dynamics. The reaction-diffusion theory is numerically and analytically studied and then extended in order to take into account dispersal effects in cancer progression in analogy with ecological models based on the porous medium equation. Possible implications of this approach for explanation and prediction of tumor development on the lines of existing studies on brain cancer progression are discussed. The potential role of continuum models in connecting the two predominant interpretative theories about cancer, once formalized in appropriate mathematical terms, is discussed.

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1 Introduction

The quantitative description of the form development in living beings is a central problem in Biology. The process of animal growth, or morphogenesis, occurs in Nature in a variety of shapes and patterns which seem to have typical regularities, as pointed out one century ago by Darcy Thompson in his classical work "On Growth and Form" [1]. Some biological populations of fungi and amoebae appear aggregated in complicated structures which often have a spiralling shape, but spirals of action potential are experimentally observed also in cardiac cell tissues and even in neural ones [2–5]. In plants complicated morphogenetic processes occur in the developmental process of *kinetic phyllotaxis* [6]. Finally it's worthwhile to notice that spiral waves appear not only in biological systems but also in unanimated ones as the chemical reactions of Zhabotinsky-Belousov type or the gaseous eddies in the atmosphere [4]. All of these different phenomenologies are seen as non-equilibrium thermodynamical processes which can be subject to complicated bifurcations in their dissipative dynamics [7–9] and which can be mathematically described, provided specific technical *caveats* regarding the validity of the continuum hypothesis, by systems of equations of Reaction-Diffusion (RD) class [4]. This type of partial differential equations have represented historically and still represents today a proper tool to deal with non-equilibrium chemical dynamics in fact (in particular when phenomena like oscillations, waves, pattern formation and turbulence occur). Alan Turing in the Fifties formulated an elegant theory for animal coats and morphogenesis using RD equations [10], so it appeared plausible to extend his successful theory to cancer growth processes whose understanding represents still today a major challenge for Biology [11]. Cancer is commonly believed to be a disease that begins at the cellular level. Its development is related with somatic mutations which are transferred from a cell to its progeny, bypassing controls of the immune system and being responsible then for the neoplastic phenotype. Therefore the initiation of cancer is mainly seen as a mutation that involves a set of regulatory genes [12], which either enhance or inhibit malignant properties.

On the other hand, tissues are relatively ordered complex structures which generate forces due to the adhesion between cells, the adhesion between cells and the extracellular matrix that surrounds them and the global property of the tissue itself. These interactions together with biochemical and electrical signals, contribute to the shape of the tissue and can even determine the cellular fate [3]. Cell-to-cell and/or tissue-to-tissue communication represent fundamental aspects which contribute to tissue organization then and their failure can generate cancer [13, 14]. Specific substances (morphostats) analogous to Turing morphogen fields drive this communication: their local concentrations in particular influence the phenotype of neighboring regions of tissue around the specific cell taken in considerations. Some substances which have the properties of the morphostats have been recently identified [15] but it is still unclear their hierarchy, and in particular the way in which they promote carcinogenetic processes. One can interpret these results using the most diffused paradigm in cancer dynamics, the Somatic Mutation Theory (or SMT) which proposes that successive DNA mutations in a single cell cause cancer cell