Computer Model of Cancer development

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ABSTRACT

Cancer development is a very complex process due to the fact that a wide range of factors could contribute to the development of cancer. Factor that can lead to the development of cancer can range from oxygen free radicals to micronutrient deficiencies, mutation of signaling network, increased cell division, overweight and so on. Technical advances have always played a key role in improving our ability to understand disease development and treatment. Computer modeling of cancer development can provide an unprecedented opportunity to study cancer. Simulation and analysis of the model will provide us with understanding of the interaction of factors that are contributing to the development of cancer. However the exponential growth in the volume of experimental information available makes it difficult for researchers to assemble the details. To overcome this problem we propose the use of mathematical applications and modeling tools to model, simulate and analyze the process of cancer development. In this paper as a first step toward integration of factors leading to cancer development, we propose a Colored Petri Net model of the factors leading to cancer development and their effects at molecular, cellular, organ, system and clinical phenotypic levels.

INTRODUCTION

Despite the abundance of attention that the cancer study has attracted, it continues to be one of the leading diseases, cause of death and source of morbidity in adults [2]. The incidence of cancer increases with advancing age. Tumor evolution is a very complex process, involving many different phenomena, which occur at different scales. Not all tumors are malignant (cancerous) tumors; however a benign (non cancerous) tumor can progress to a malignant tumor under certain conditions. Based on available data one could say that cancer is an example of a complex, robust system [3], [4]. To a large extent, the plasticity and adaptability exhibited by tumors are due to their internal instabilities [5]. In this research paper we use modeling techniques and mathematical approaches to model, simulate and analyze the process of cancer development. Since a detailed model requires a huge number of data and empirical results that can be assembled over a long period of time, this paper presents a high level view of the cancer development process by using a compact model of it. More detailed models and extensive analysis of the process require further experiments and data mining that we are planning to accomplish in the future.

As a modeling tool we propose to use Colored Petri Nets (CPN) tools to model and simulate cancer development at the nuclear or molecular level, cellular level, tissue level, and system level.

A detailed Petri net model requires intense theoretical review of the available experimental data, which is out of the scope of this paper. However in this research we will use some of the available experimental data to develop a compact model of the process of cancer development. A compact model of cancer development can be extended to a detailed model, and a detailed model could help us in cancer diagnosis and treatment.

COLORED PETRI NETS (CPNs)

Colored Petri Nets is a graphical oriented language for design specification, simulation and verification of systems [1]. One of the strengths of CPN is its combination of Petri nets notions and programming language concept that resulted in a number of useful modeling features such as: Petri Nets support synchronization, communication with other modeling tools, and resource sharing; programming language describes data and data manipulations. CPN models are validated by means of simulation and verified by means of state spaces and place invariants. Since CPN models are dynamic they allow researchers to execute the model, change variables and investigate different scenarios.

CPN models provide a framework for the design, specification, validation, simulation and verification of

systems [6]. In contrast to most specification languages, Petri nets are state and action oriented and at the same time provide an explicit description of both the states and the actions. This enables researcher to determine whether to concentrate on state or action at any given time. A Petri net graph has two types of nodes - place and transition (see figure 1). The places, drawn as ellipses or circles, represent the sates of CPNs. A rectangle represents a transition (events, activities, actions, operations). In a Petri nets graph every place has a capacity and every arc has a weight. This allows multiple tokens to reside in a place, thus enabling researcher to model a very complex behavior such as cancer development or other biological and molecular processes. In high-level Petri Nets such as CPNs, tokens have a color that enables them to hold complex information. Furthermore time delays at an interval or variable can be associated with transitions and/or places. CPNs have an industrial strength modeling language as well as well founded theoretical practice for systems of the size and complexity found at molecular, cellular and system levels.

Colored Petri Net tools allow analysts to model, analyze, edit, simulate, verify, validate, specify and implement a very complex process.

Tokens are data objects (class instances). An action associated to each transition, when the transition fires its action is performed in order to compute the output token(s) and perform external actions (e.g., tool invocations).

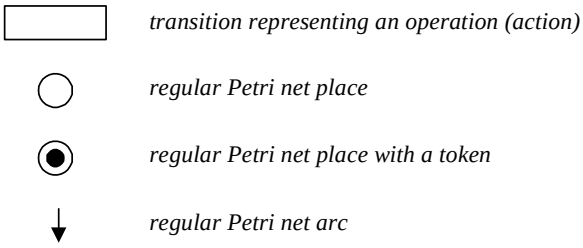

Figure 1: Legend of Petri nets

The following are few examples that illustrate Petri nets model of different processes such as sequential, parallel, conditional and synchronous (see figure 2):

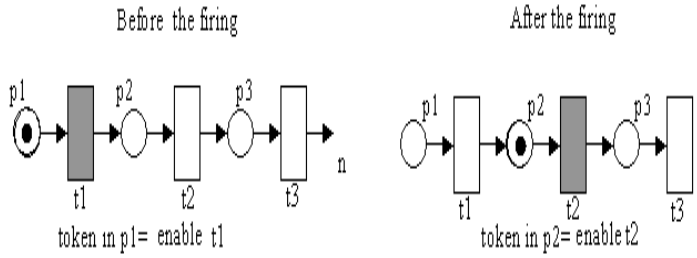

Figure 2: An example of sequential net

In order for operation "t1" to be performed, a token (in the case of cancer development it could be a condition that triggers genetic change) is needed in the input place "p1". A transition firing automatically removes as many tokens from all the transition input places as the weight of the connecting arcs; inserts as many tokens in all the transition output places as the weight of the connecting arcs.

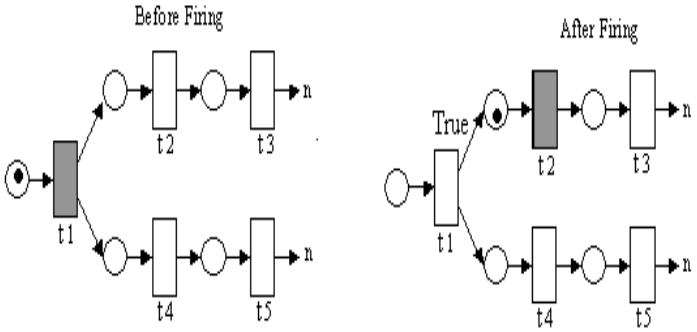

Figure 3: An example of parallel net

Non-determinist events occur in situation such as conflict, choice or decision. If the condition for transition "t1" is right than either "t2", or "t3", or both "t3" and "t2" transition will be enabled. Either one of the two competing operations or both of the operations can be performed. For instance Stem cell that undergoes mitotic division could either terminally differentiate or continue as a stem cells.

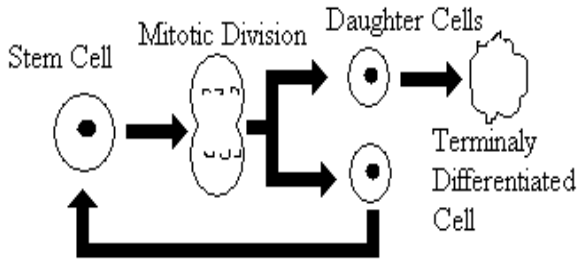

Figure 4: Differentiation of stem cell

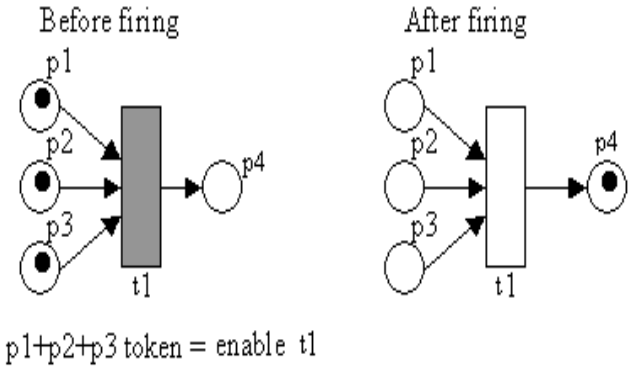

Figure 5: An example of Synchronization and Concurrency net

In a synchronization and concurrency a transition is enabled only after a token is fired from place 1 “p1”, place 2 “p2” and place3 “p3”. Once the required numbers of token are present in place 4 “p4”, place 4 could enable one or number of other transitions.

COMPACT MODEL OF CANCER DEVELOPMENT

Cancer is predominantly a disease of aging. The incidence of cancer increases dramatically with age. This epidemiological data suggest that over the period of time we acquire genetic mutations that lead to nuclear and cellular changes.

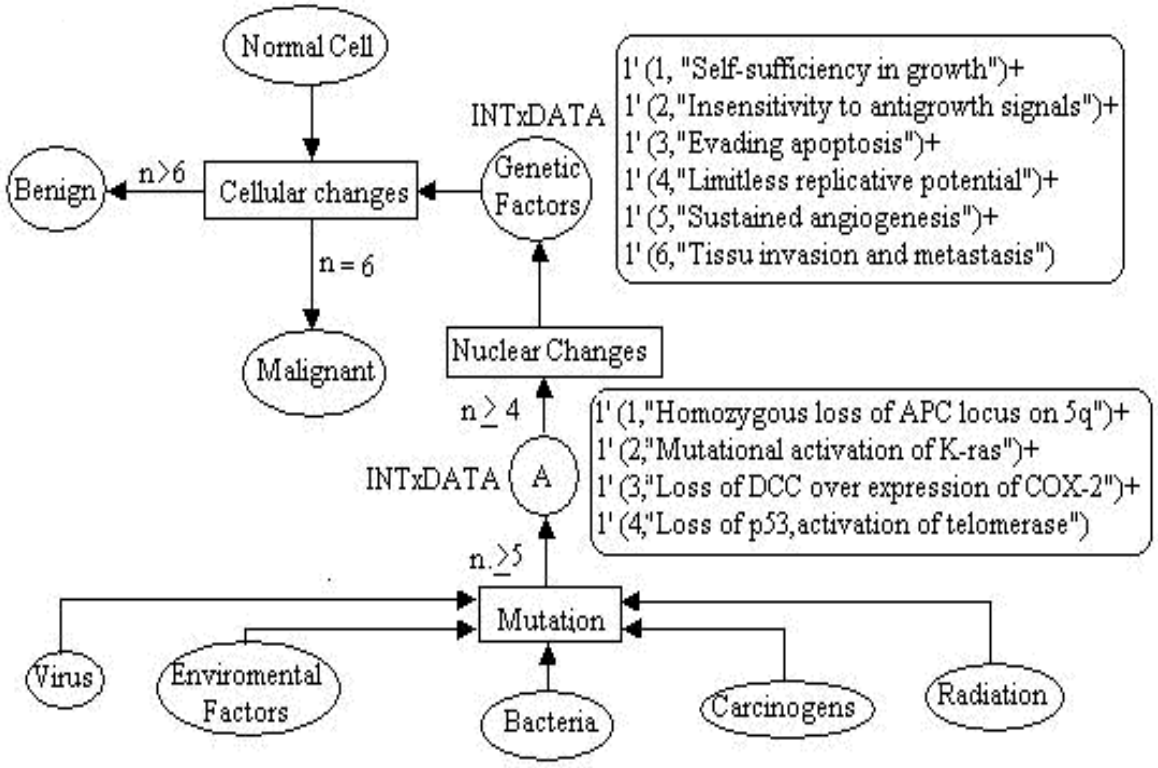

Figure 6. Compact model of the cancer development. NormCell = Normal Cell, AbnormCell = Abnormal cell

As it is shown in figure 6 above, the “genetic factor” state is integrated with six data type tokens. Each token is associated with a data type that is described in the box next to the state.

As it can be seen from the above diagram a normal cell could either lead to a malignant tumor or benign tumor. It will become malignant tumor only if “n=6”. If any of the initial marking are not true (n ‹ 6) than the cell will become a benign tumor.

CONCLUSION

The main purpose of this paper was to model the process of cancer development using colored Petri net tools. This methodology helps formalization, modeling and simulation of the cancer development. Even though it was out of the scope of this paper to include all the models and results, however we presented part of the results here.

Two areas can benefit from such a methodology that has been presented in this paper: research institutions could use cancer development models for early detection, prevention, diagnosis and treatment. Educational institutions could use the model as an instructional technology tool to visualize the process of cancer development. Number of science educators feel that the computer simulation offers tremendous potential for the enhancement of the teaching and learning science concept. The pursuit of computer simulations in an educational context is worthwhile for several reasons. Simulations potentially offer students opportunities to explore physical or biological situations that may be impossible, too expensive, difficult, or time-consuming to accomplish with actual laboratory or real-life experiences (animal dissection or frictionless environments). Even if real-life exploration is feasible, such experimentation can be supplemented by simulations that offer students the opportunity to explore a wider range of variables more rapidly. Such simulated experiences potentially can be used to confront alternative conceptions, produce disequilibration and with appropriate scaffolded instruction, lead students to a new accommodation. In addition to being safe, convenient and controllable, simulations may encourage students to participate actively in learning activities. Researchers could use this preliminary results to develop more advanced models of cancer development. The models could serve as a useful tool in diagnosis, prevention and treatment of cancer. As indicated earlier, simulation is the use of a powerful tool, the computer, to emulate or replicate an object in a real or imagined world

FUTURE RESEARCH

As a future research it is planed to model analyzing and simulating a detailed model of cancer development at cellular, sub-cellular and molecular levels.

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