e-ISSN: 2349-9745
p-ISSN: 2393-8161

Scientific Journal Impact Factor (SJIF): 1.711

International Journal of Modern Trends in Engineering and Research

www.ijmter.com

2D CAT Based Modeling of Tumour Growth and Drug Transport

Kalyani Bodake[1], S.P.Sonavane[2]

[1]*Department of Computer Science and Engineering, WCE,Sangli*
[2]*Department of Information Technology , WCE,Sangli*

Abstract—The transition of normal cells in the tissue that leads into tumour and spreads throughout depending upon its behavioural conditions is a complex biological process studied through the use of both in vivo and in vitro experimentation. Mathematical models provide the approach by using a controlled environment in which a system can be described quantitatively. This can also yield data which predicts the behaviour of cells and likely medical conditions after thorough analysis by the modeller. In an effort to study the characteristics that increase cell fitness, the paper presents a 2D Cellular Automaton model that uses computer simulation to describe the invasion of healthy tissue by cancer cells. The growth process is simulated and it was found that movement of cells affects tumour growth rate. It was also found that the relative distance of the tumour initiation area from neighbouring vessels influences the growth of tumour. The model and the simulation software developed thus can be used to understand the dynamics of early tumour growth and to explore various hypotheses of tumour growth relevant to drug delivery in chemotherapy. Importantly, this approach highlights that vessel displacement should not be neglected in tumour growth models. The paper thus presents two models i.e cancer growth model and drug transport model for tumour growth and treatment that will help to diagnose the early tumour growth. Though cancer is uncurable;early and quick detection of cancer will help doctors in better way by suggesting quick remedial action against it.

Keywords- Cellular Automata, Hybrid CA, Tumour Growth ,Drug Transport, Von Neumann Neighborhood ,In-silico model

I. INTRODUCTION

Cancer is a disease which has threatened the world due to its unusual behavioural properties that it exhibits. The reason is cancer cells display characteristic traits acquired in a step-wise manner .That is why it had been difficult to evaluate whether the tumour is malignant or non malignant.Tumour growth is a complex phenomenon that integrates genetic, biochemical, chemical and mechanical processes. While modelling tumour growth is one of the most active areas of research within the computational biology community; much work which remains to be done in order to produce clinically relevant and predictive models. One obstacle that must be overcome is the intrinsic multiple scale nature of tumour growth. It involves processes occurring over a variety of time and length scales: from the tissue scale to intra-cellular processes.

Models for tumour growth can be continuous, discrete or hybrid. Continuous models are based on the use of partial differential equations or stochastic methods and treat the tumour as a (homogeneous or inhomogeneous) continuum surrounded by advancing boundaries. These models actually calculate the velocity and direction of the various tumour boundary points under conditions imposed by the flow of oxygen, nutrients and drugs [1]. In discrete models, the area occupied by the

tumour and its environment is divided into small equal areas, thus forming a discrete lattice and the growth process follows the local rules. In this case, tumour growth emerges as a result of the collective behavior of the processes that takes place in each of these areas. Hybrid models combine the discrete models with the solution of partial differential equations on the discrete lattice of these models. In a cellular automaton modeling, researchers are required to set an initial configuration, design a cell dynamics to be the cellular's rule and follow cellular's rule iteratively for each time step [2]. The proposed CA based computerized model investigates the early tumour growth where each cell is taken as an individual and independent entity. The model determines how different sub clones behave in a heterogeneous microenvironment. It simulates the drug transport by calculating the partial pressure of oxygen (pO2) and measuring the available drug concentration inside the solid tumour at cellular level. The ultimate objective is to develop an in-silico model that can facilitate the drug discovery process by streamlining preclinical drug development.[1].Simulations carried out in such a way thus allow researchers to test medical conditions that are difficult to observe through in vivo and in vitro experimentation.[8].

II . CELLULAR AUTOMATA[CA]

Cellular Automata are called as "Systems of Finite Automata" means "Deterministic Finite Automata"(DFA) and are given in a lattice arrangement. The Concept of CA was developed by Von Neumann with the purpose of obtained models of biological reproduction. Now a day's Cellular Automata has become very popular because of its diverse function and utility as a discrete modal for many processes .Cellular Automata includes an array of cells each of which can be in one of a finite number of possible states, updated synchronously in discrete time steps, according to a local identical interaction state transition function .The state of a cell at the next time step is determined by the current states of a surrounding neighborhood of cells .

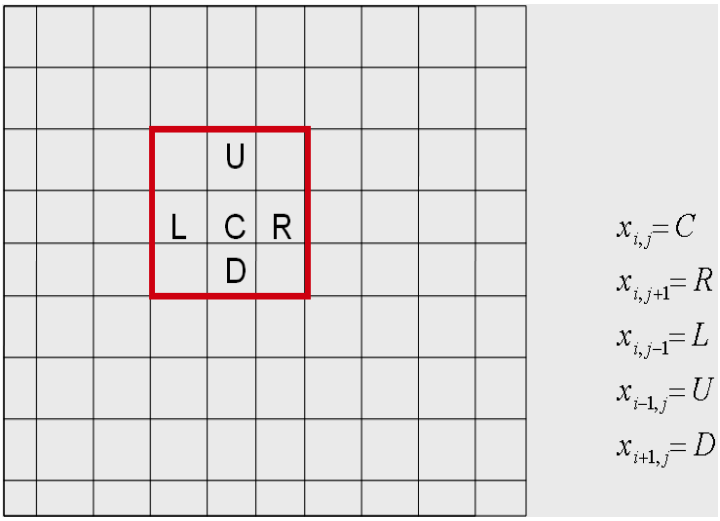

Fig 1: The grid is a discretization of a slice of tissue

Thus, CA finds most of its applications in complex biological systems to demonstrate the independent behaviour of the cells in body that changes according to the varying CA rules.CA is parallelizable .It is suitable for a hierarchical ,multigrid approach. In CA, diffusion can be modelled locally. CA is useful for incorporating tissue heterogeneity and for simplifying computations. However ,CA has its disadvantage as it will be difficult to analyaze the actual period of division for every individual cell as all cell have same period of division.It might be the case cells that undergo the proliferation belong to independent surrounding tissue. This is one of the difficult task to evaluate the time taken by individual cell to undergo cell division.

III. LITERATURE SURVEY

A number of mathematical models have coupled tumor growth with immune system dynamics. Usually, these models are fully deterministic, comprised of a series of ordinary or partial differential equations (ODEs or PDEs) describing the dynamics of, for example, tumor cells, host cells, and immune cells.Mathematical modeling of solid tumour growth provides an opportunity for cancer specialists to interact and explore the dynamic behavior of tumour and its response to therapy. Enderling et.al.measured the tumour growth using ordinary differential equations [7] and a study used partial differential equations [PDE] to observe the tumour development [5].The hybrid CA–PDE modeling approach has been successfully used in the past to model tumor growth, chemotherapeutic treatment and the effects of vascularization on tumor growth.The first work using CA in cancer modeling was done by ditching and vogelsaenger[4]who used it to investigate the effects of radiotherapy. Many attempts have been made to model dynamics of tumour growth and its invasion and some of the attempts are also been made to model for bio reductive drug transport .Majority of modeling approaches have considered all cancer cells to share the same properties. However, the computerised model discussing the behaviour of drug inside the solid tumour has not yet completed.

IV. FLOWCHART

Fig 2a and 2b discusses the tumour growth model and drug transport model which are supposed to be developed in the laboratory. The tumour behavior is guessed with the help of feed forward neural network and is demonstrated using CA model.

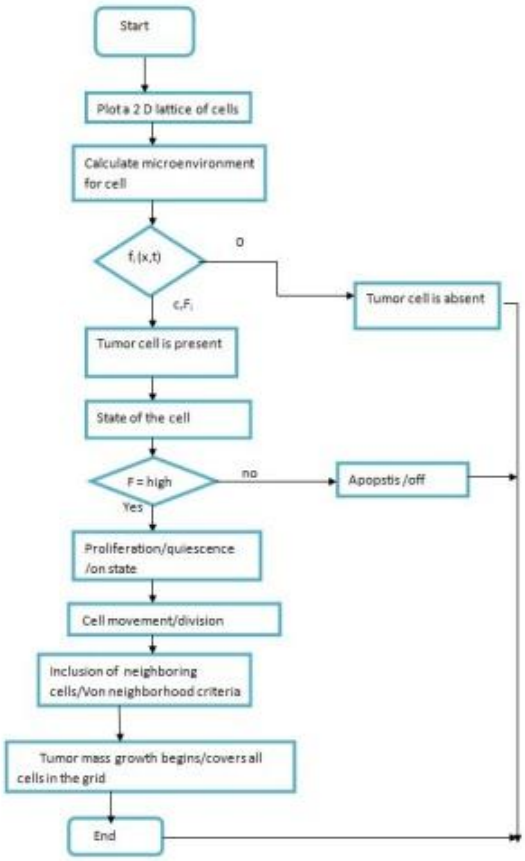

Fig 2a:- Tumour Growth Model

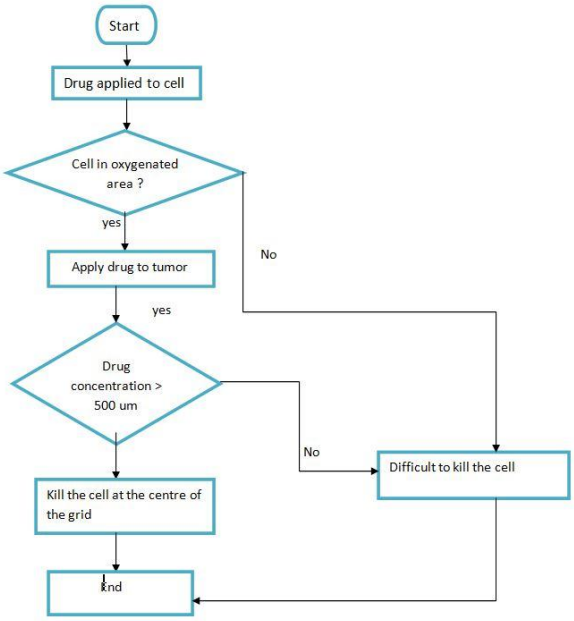

Fig 2b :- Drug Transport Model

V. PROPOSED METHODOLOGY

5.1 Tumour Growth Model

The flowchart for the tumour growth model is as shown above (fig 2a).Tumour growth model begins with the growth of tumour on the square domain Ω = [0,L] * [0,L] where L is the length of the each side of the domain. The spatial domain represents a two-dimensional patch of tissue that is supplied with nutrients by blood vessels that occupy the y = 0 and y = L boundaries. Each grid point is independent from the others and has local amount of chemicals and independent behavioural characteristics. Tumour growth process is initialized from few cells at the centre of the grid. Blood vessel surrounds tumour mass as source of nutrients. The proposed models explores the behavior of every tumour cell and its interaction with the neighbours representing the Von Neumann Neighborhood. The PDE system defines the nutrients consumption or production for the cell at every time instance. Considering the term fi(x,t) as the production or consumption function of cell at a specific position x and at time t can be explained as,

$f_i(x,t) = 0$ ……..no tumor cell is at that grid point

cr_i F(x)…… grid point is located by the tumor cell which is the production or consumption rate

F(x) is the energy consumed by the cell at the grid element x. Depending on the energy consumed by the cell, cell state is classified as proliferating /quiescence /apoptosis state. .In terms of CA, cell either becomes active/inactive or on/off.

5.2 Drug Transport Model

This model e proposed explores the behavioral properties of the drug by its transport through the multicellular layers of the tumor cells and its effect over each tumour cell. The effect of drug depends upon the amount of the drug delivered to the tumor cell as well as the oxygen concentration .Cells in well oxygenated area are difficult to kill even with a appropriate drug concentration .Hence in some cases the drug is combined with the radiotherapy or chemotherapy treatment.

VI. SIMULATION AND RESULTS

Simulation and computations are performed in MATLAB 2013.Neural network is designed for the purpose of classification of the values generated as the result of the neural network response. Base Conditions assumed for designing the neural network is as given:

- Input values provided to nodes in the neural network designed are predicted and calculated from the weight matrices
- Values for target response [T(x)] and modulation strength[k] are model specific[1]
- Model design considers cell neighbours ,oxygen, hydrogen and glucose as the inputs for the node
- Output of the network is the node with the highest network response

Functional parameters assumed for designing the neural network are as follows :-

1. Net = newff ([0 1;0 1 ; 0 1],[6, 1],{‘logsig’, ’logsig’})
   //creation of feed forward neural network.
2. Input =[];
   // Input to the neural network
3. net.trainParam = Nan function
   net = train(net, input, target) // To train the network.

4. output = sim (net, Input) //output of the network.
5. net. IW{1,1} net. LW{2,1}
   // to examine the weights of the neural network
6. net. Layers{1}.size = 6
   //number of neurons in the hidden layer

Neural Network Design :-

Input Values :- [-2 0 1 0.5 0 0 ; 0 -2 0 0 -2 0 ; 0 0 0 0 0 -2 ; 0 0 0 0 0 0.5]

Input to the neural network is the columns of matrices with the above given values. Fig 3a is the neural network designed using nntool. Fig 3b is the 6 by 4 matrix of the values generated between the input and the hidden layer.

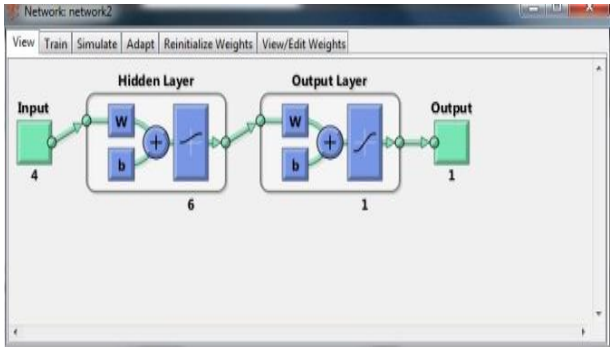

Fig 3a :- Neural Network for tumour microenvironment [Matlab 2013a]

4.3706	-4.8853	6.0234	3.8500
11.5279	0.2672	9.1483	4.2092
-4.6305	5.8937	3.8980	1.9989
2.1061	4.7727	-4.4960	-4.5539
2.6458	-5.8541	-1.3092	5.9623
-3.3540	4.7797	4.2225	4.4080

Fig 3 b : output from input layer to hidden layer

Following are the values generated as the calculation between the hidden and the output layer

Step I :

-9.1701 -0.9234 -0.8157 -9.8737 11.7694 5.8906

Step II :

-3.2534 -7.6123 13.3648 10.5514 -4.6476 1.5018

Step III :

-9.8538 -1.4366 12.9636 1.8334 0.8114 -9.8726

Step IV :

0.2311 3.0165 -13.2754 1.3925 8.0604 11.4189

Step V :

6.6646 -9.1252 -4.7868 9.2854 3

Fig 4 : Output values for neural network

The results are the response of the neural network. Value encircled is the node with the highest response which is responsible for the movement and thus for the tumour growth. Figures show sample results to demonstrate the spatiotemporal distribution of cells starting from a single cell which is considered as a seed. Cell population is plotted as a function of time by counting the number of cells at each time evolution.

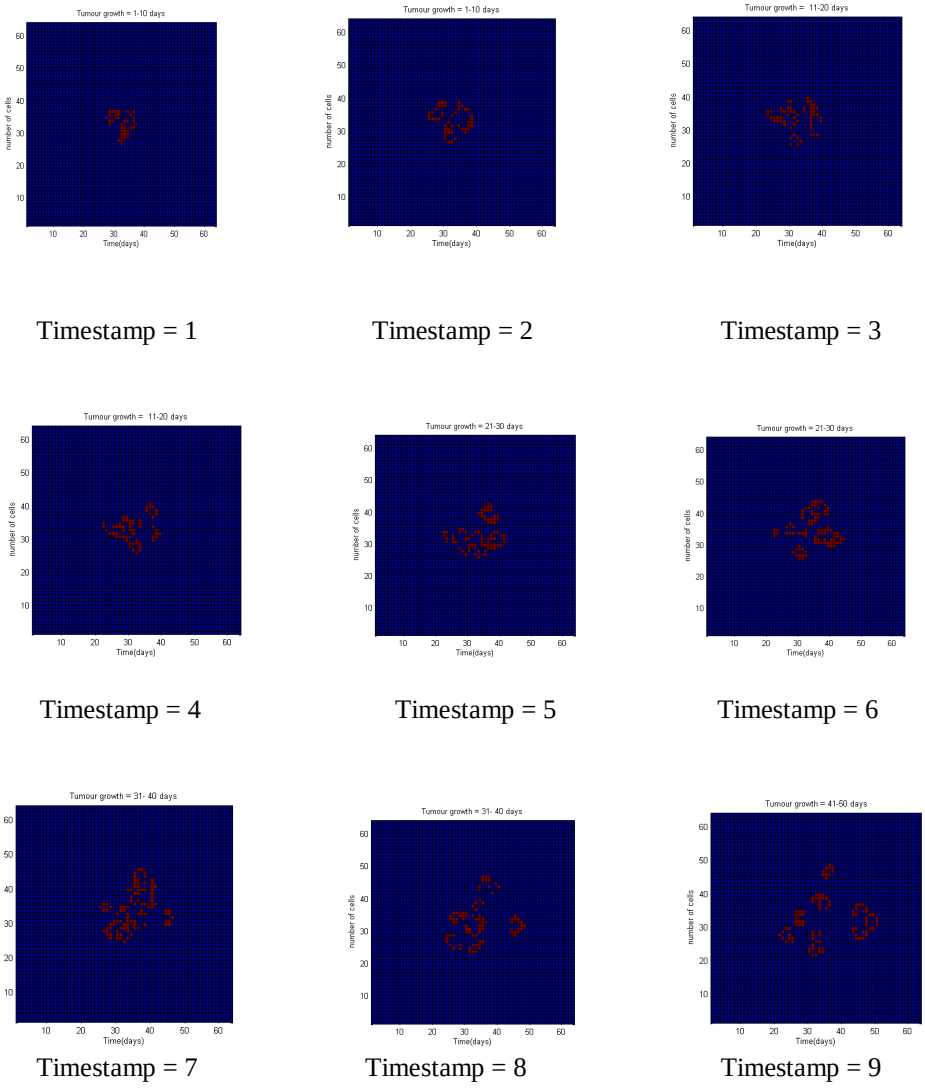

Fig 5: Result for daywise growth of tumour -CA based Modeling

Results shows that more migratory the cell, more are the chances of tumor growth even though proliferation rates remain unchanged. Invasion time is defined as the number of time steps it takes for the each lattice site in the host tissue to be occupied by a tumor cell. The CA model demonstrated allows us to quantify the proportion of each cell type within a simulated tumor as a function of parameters responsible for tumor growth. The laboratory work is progressing towards the development of the drug transport model which is helpful for further detailed tumour behavioral analysis.

REFERENCES

1. Nabila Kazmi, M.A.Hossain,Roger M.Philips "A Hybrid Cellular-Automaton Model of solid Tumor Growth and Bio reductive Drug Transport "IEEE/ ACM Transactions on computational Biology and Bio Informatics vol.9 no.6, p.1-14, November 2012
2. Boondirek, Ankana and Triampo, Wannapong and Nuttavut, Narin" A Review of Cellular Automata Models of tumor growth "vol 5 no.51, 2010
3. Hatzikirou, Haralambos and Deutsch, Andreas "Cellular automata as microscopic models of cell migration in heterogeneous environments " Proc. Elsevier , vol 59,no 7 ,2008
4. Mallet, Daniel G and De Pillis, Lisette G " A cellular automata model of tumor--immune system interactions" Journal of Theoretical Biology, vol 239,no 3 2006
5. P. Gerlee and A.R.A. Anderson "An Evolutionary Hybrid Cellular Automaton Model of Solid Tumour Growth " J. Theoretical Biology, vol. 246,no 4, pp. 583-603, 2007
6. Alarcon, T and Byrne, HM and Maini, PK "Towards whole-organ modelling of tumour growth " Progress in biophysics and molecular biology, vol 85, no 2, 2004
7. Phan, Dustin D and Lowengrub, JS," A Discrete Cellular Automaton Model Demonstrates Cell Motility Increases Fitness in Solid Tumors " The UCI Undergraduate Research Journal,2010

