PROCANINT: An Agent-Based Model to TreatProstate Cancer

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Abstract

In recent years a lot of clinical trials have been carried out to analyze the effectiveness of interventions used to cure cancer.Creating the exact environmental conditions to test and analyze the interventions has been a major challenge so far. Hereby to improve the ways of giving the intervention, we propose a computational agent based model called PROCANINT in our paper which can be used as a reference for successively carrying various clinical trials on prostate cancer patients to treat the cancer. Safety & efficacy of drug to be given to a patient for treating cancer can be analysed and modified accordingly.The model serves as platform to compare different drugs impact on prostate cancer and improvement of tumour reduction assessed by reduction of prostate specific antigen. Computer simulations enable one to perform several 'what-if 'analyses cost effectively.

1. Introduction

Agentscan be defined to be autonomous, problem-solving computational entities capable of effective operation in dynamic and open environments [2][3]. Agents are often deployed in environments in which they interact, and maybe cooperate, with other agents (including both people and software)that have possibly conflicting aimsautonomy decentralizes decision making and therefore greatly simplifies the implementation of the whole system's control. Since each agent decides by itself when to act and what action to perform, there is no need for a complex centralizeddecision making entity.

Agent can make the best decisions in the shortest time and the negative impact of environmental factors. Main features of agents include:

i) Autonomy*:* It improves the power of decision-making and performance independently without supervisory and external Control of the agent.

ii) Mental mechanisms: Realization of Goal Mechanisms in agent.

iii) Adaptability: Agents are compatibles to the dynamic environmental changes to adjust their activities.

iv)Concurrency: multi tasking of an agent.

v) Cooperation: There are some methods that agents can cooperate with the other agents to achieve the goals.

vi)Reactive: this feature gives the early reactive abilities to agent against environmental changes.

vii) Benefit: It gives the agent perseverance to get to the new goals.

viii) Communications: Protocols and mechanisms for identifying agent's mutual-reaction.

ix) Sociality: It gives the agent the ability to interact with other agents. GAIA, MaSE methodologies areindependently to accomplish the task instead of its users.Such standard agent-oriented methods in Production of Intelligent complex software systems are used in Distributed systems.

Cancer begins when cells in a part of the body start togrow out of control. There are many kinds of cancer, but they all start because of this out-of-control growth of abnormal cells[1].Cancer cell growth is different from normal cell growth. Instead of dying, cancer cells keep on growing and form new cancer cells. These cancer cells can grow into (invade) other tissues, something that normal cells cannot do. Being able to grow out of control and invade other tissues is what makes a cell a cancer cell. In most cases the cancer cells form a tumor.When cancer cells get into the bloodstream or lymph vessels, they can travel to other parts of the body. There they begin to grow and form new tumors that replace normal tissue. This process is called*metastasis.*Prostrate is a gland found only in males.Prostrate contains cells that make some of the fluid (semen) that protects and nourishes the sperm. There are several types of cells in the prostrate but nearly all prostrate cancers start in the gland cells.This kind of cancer is known as adenocarcinoma.Someprostrate cancers can grow and spread quickly. Prostatecancer progression depends on the complex interactions between testosterone, its active meta but nearly all prostate cancers start in the gland cells. This kind of cancer is known as *adenocarcinoma*. Some prostate cancers can grow and

spread quickly. Prostate cancer progression depends in part on the complex interactions between testosterone, its active metabolite DHT, and androgen receptors.

In our paper we are focusing on developing an agent based model to treat prostatecancer.We are considering two main agents in our model. They are Testosterone and Testosterone Blocking Drug. These agents are described in System Model section.

1.1 Prostate Epithelial Cell Behaviour

The working of the testosterone on prostrate epithelial cells can be illustrated as follows.

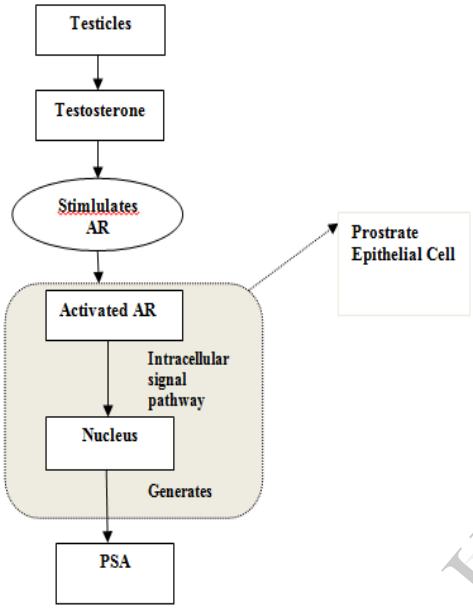

Figure 1. Action before drug intake

Testosterone is a hormone that controls the development and growth of the sexual organs, including the prostate gland. This testosterone stimulates the androgen receptors present in the prostate epithelial cells. These receptors generate intracellular signal pathway to the nucleus. The nucleus then uses this information to produce a protein called PSA (Prostate Specific Antigen) and is one of the main factors which pave the way to cell division and proliferation. The increased level of PSA indicates more number of cells which may be cancerous or non-cancerous and chances of prostate cancer are high. In a metastatic setting, the first line of treatment is blocking actions of testosterone.Oneof the effective ways to treat prostatecancer is throughHormone therapy [2].Hormone therapy is treatment to stop your body from producing the male hormone testosterone. Prostate cancer cells rely on testosterone to help them grow. Cutting off the supply of hormones may cause cancer cells to die or to grow more slowly. Hormone therapy options include:

i) Medications that stop your body from producing testosterone*:* Medications known as luteinizing hormone-releasing hormone (LH-RH) agonists prevent the testicles from receiving messages to make testosterone. Drugs typically used in this type of hormone therapy include leuprolide (Lupron, Eligard), histrelin (Vantas).etc

ii) Medications that block testosterone from reaching cancer cells: Medications known as anti-androgens prevent testosterone from reaching your cancer cells. Examples include bicalutamide (Casodex).

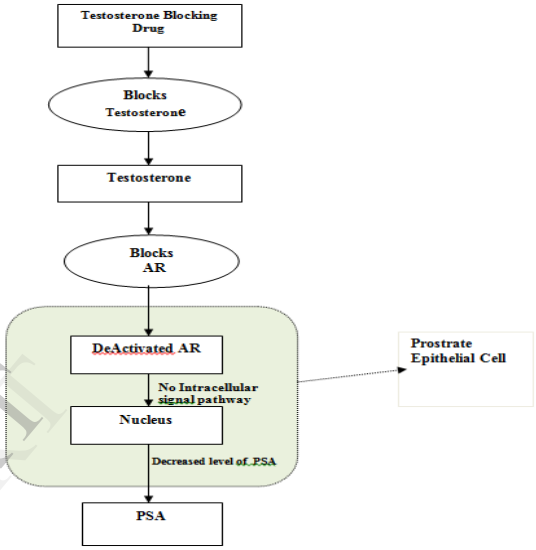

Figure 2: Action after testosterone blocking drug intake

This figure mainly shows the change in behavior of the testosterone on receiving the drug dosage.

The testosterone blocking drug blocks testosterone which then blocks Androgen Receptors and deactivates androgen receptor. There is no intracellular signal pathway to the nucleus.Hence nucleus generates very less PSA thus preventing cell division. The drug concentrations can be varied accordingly by noting down the decrease in PSA levels thus killing all the prostrate cells and eliminating prostate cancer.This entire process can be initially simulated using an agent based model and simulated results can be used as a reference for future research.

1.2. Agent Oriented Software Engineering

Agent-oriented software engineering is based on agent. The main goal of agent-oriented software engineering is to create methodology, tools and facilities for simple preparation and maintenance of the agent-based software. Due to the fact that object-oriented software engineering is unable to response the requirement of the agent-based software ,an urgent need of a new engineering coordinated to the view of agent, arose. That caused agent-oriented software engineering development out of the object-oriented software

engineering. The appearance of agent technologycaused a revolution in the software industry and hashad great advantages, such as autonomy, interaction, Knowledge base and intelligence. Thus Agent can be considered as an abstraction level of software [5].

In general it can be assumed that Agent software engineering having the characteristics inherited from the Object software engineering is able to do thingsindependently to accomplish the task instead of its users.

Agent Oriented Software Engineering is not only for "agent system..The agent abstractions, the methodologies, and the tools of AOSE suit such software systems.Agent Oriented Software Engineering is suitable for a wide class of scenarios and applications! Agents' "artificial Intelligence" features may be important but are not central Agent Oriented Software Engineeringmay sometimes be too "high-level" for simple complex systems.Appears to be applicable to a very wide range of distributed computing applications.

2. System Model

Here in our proposed system we are considering two main agents. Both the agents are autonomous and have their own roles and responsibilities

i) *Testosterone blocking Drug*

ii)*Testosterone*

i) Testosterone: This agent interacts with the external factors and is responsible for either simulating the Androgen receptor in normal scenario or blocking the Androgen receptor on effect of the Testosterone blocking drug acting on it.This behavior depicts the autonomous and dynamic behavior of an agent.

ii.Testosterone blocking drug:This drug on varying the concentration expressed in mg/ml can be used to block the testosterone thus decreasing the PSA levels.This interaction between the agents depicts the sociality,benefit and cooperation behavior of an agent in dynamic environment.

Our model consists of the following packages and classes.

i).*Model*: This is the main controller class responsible for controlling the entire *simulation* activity. This class interacts with the scheduler and has a role of increasing or decreasing the *testosterone* levels depending considering age as factor. This has a main attribute called *testosteronelevel*and 2 other attributes called*highrat*e and *lowrate* used to categorize the testosterone levels.

ii) *Agent: This* is an*abstract* class which acts a reference for the 2 sub classes *1.Testosterone2Drug.*

iii) *Testosterone:* This is an agent class which has an attribute called *concentration* expressed in ng/ml responsible for simulating the Androgen receptor present in the prostrate epithelial cell. Further it has an operation called *action.* This operation can be either simulating the androgen receptor or blocking the androgen receptor depending on the context.

iv) *Drug:* This is another agent class which has attributes such as *concentration,mechanism* and *adverseeffects*.The administration of drug dosage is controlled by a class called *DrugConcentrationControlle*r. The Drug class has the action of acting on testosterone and blocking it.

v) *DrugConcentrationController*: This is the controller class for controlling the drug dosage to be administered. This class has attributes such as *time* and *dosageadministered*. This class in turn interacts with scheduler.

vi)Cells: The default attributes of a cell are position, orientation, and volume.Further this abstract class has attributes such as *AndrogenReceptor*and *Nucleus* which are used for the protein generation process

vii) *AndrogenReceptor*: This class is responsible for generating the intracellular signal pathway to the Nucleus. It has an operation called *generatesignalpathway*

viii) Nucleus: This class is responsible for generating the protein called PSA (Prostate Specific Antigen) whose levels determine the cell division. It has an operation called *generatePSA.*

ix)*PSAMeasurementUnit*:This class is responsible for measuring the PSA generated by nucleus which thus can act as a reference for the comparison of PSA levels with different drug dosage intake.

x) *Scheduler*: The entire activity is monitored by a scheduler which has attributes such as *starttim*e and *endtime* to monitor the simulation activities

The model and the related class diagram can be illustrated as shown in figure. This figure depicts both theMain classes used as well as the packages in which they are located. Further the interactions between these classes are also shown in the subsequent figure.

The class diagram also shows the inheritance, dependency and ownership between the classes.

2.1 Architecture of PROCANINT

The architecture of PROCANINT includes the system model as shown in figure 3 and the class diagram [4] shown in Figure. 4

Prostate cancer prevention is the main objective of our proposed model. Preventive steps involve the interaction between the two agents Testosterone and TestosteroneBlockingDrug. This entire activity is monitored by a scheduler.On startup, testosteronecontoller will feed the testosterone levels in ng/ml and theDrugConcentrationController will feed the Testosterone blocking drug dosage to the system. The testosterone blocking drug dosage in ng/ml is given as the input to Testosterone agent.. The drug dosage parameter which is present in the Testosteone Blocking Drug agent interacts with the testosteronelevel parameter of the the Testosterone agent,thus reducing testosterone levels.Testosterone agent blocks the AndrogenReceptors contained in the ProstrateEpithelialcell.TheAndrogenReceptor class and Nucleus class are contained within The ProstrateEpthilial cell class. The intracellular signal pathway parameter contained within the ProstrateEpithelial cell gets blocked. Thus the PSA levels generated by the nucleus class will be reduced. The generated PSA levels after drug administration is measured using PSAMeasureUnit. The output of our model is the reduced PSA level which we obtain by simulation.Later we compare the simulated results with the result obtained from clinical trials,and correspondingly we modify the drug dosage input levels to be fed to the system. We define suitable methods in all the classes to support every functionality described.This simulation activity is carried out recursively ,eventually blocking the testosterone levels.

System Model can be represented as follows

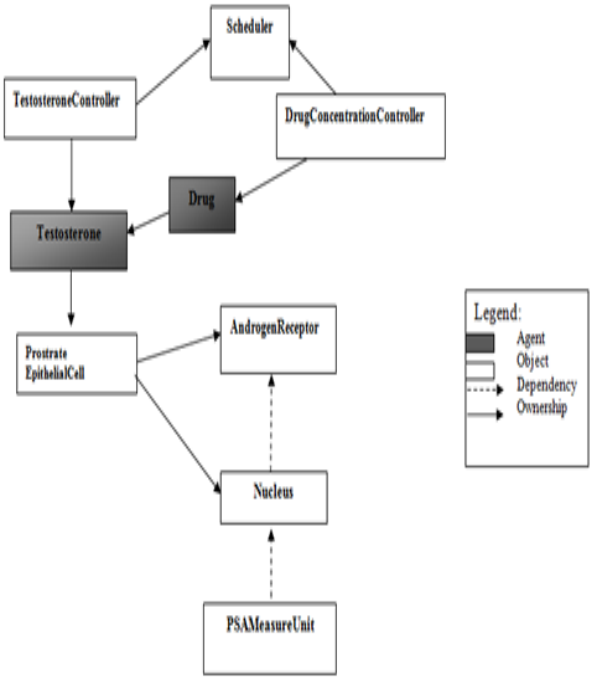

Figure 3: Architecture of PROCANINT: Ownership and dependency relationship

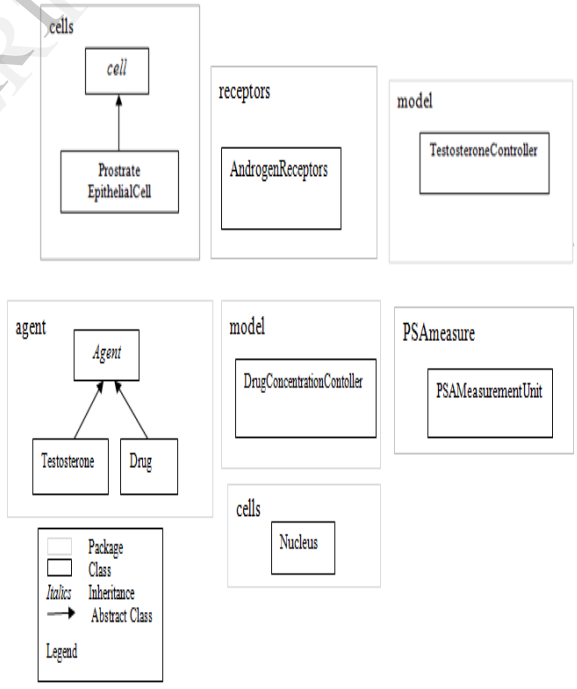

Figure 4.Architecture of PROCANINT:A class diagram showing dependencies and inheritance grouped in packages.

2.2Parameters to be used in PROCANINT model.

The parameters to be used are Drug Concentration (mg/ml) and PSA Level (ng/ml).Below table shows the drug concentration and the corresponding PSA level readings according to the data obtained from various clinical trials. The table gives information about the age of the patient,the current PSA level,the drug concentration administered per day and the clinical PSA level after drug intake.All these details are obtained through clinical trials. We use this information i.e., age of a patient, drug concentration administered per day as input to our proposed system model and the predicted PSA level which is the output of the system is be compared with clinical PSA level obtained from patients. Based on the results which will be obtained after simulation a graph of number of week over PSA level can be plotted. Thus providing us with further information regarding drug concentration which is to be administeredto the patient for further treatment.

2.3Software

We are planning to build PROCANINT using the agent-based Repast framework(Collier and Sallach, 2001, http://repast.sourceforge.net). Owing to its implementation in Java, Repast is platform independent,web-compatible and allows integration across a variety of languages.In particular, Repast provides the software apparatus for creating,running, displaying and collecting data from an agent-based simulation.It also has libraries for handling complex interactions between agents.

Table 1: Readings of PSA level from clinical trials

Patients	Age	Current PSA Level (ng/ml)	Drug concentration (mg/ml) per day	Clinical PSA Level (ng/ml) After Drug Intake
P 1	63	20	150	10
			300	8
			450	5
P 2	67	60	150	30
			300	20
			450	10
P3	75	90	150	85
			300	75
			450	65
P 4	77	1000	150	800
			300	700
			450	600

3. Future work

As mentioned in the introduction the model attempts to reduce the PSA level through proper testosterone blocking drug, thus curing prostate cancer. This model can be improved by integrating new mechanisms of drug treatment and compare the results obtained through various trials.

4. Conclusions

In this paper, we presented the design ideas behind *PROCANINT*, an agent based model to cureprostate cancer.This model offers a platform for effective mathematical simulation of targeted chemotherapy. New drugs can be developed to arrest cell division and multiplication by acting it various targets. Same model can be extended to other types of cancers.

5. References

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