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Commentary

Considering Taguchi method as a feature selection method in agent-based models of cancer disease: A mini-review

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Abstract

Cancer biology involves complex dynamics and interactions between cells and the tissue environment. Mathematical modeling and computer simulation can provide a powerful instrument for considering this complexity. Agent-based modeling is a particular discrete hybrid modeling method. Because of their ability to model heterogeneity of cancerous tumors, this modeling has particular importance. For proposing this kind of model need important features. In this mini-review we consider Taguchi method in features selection and its applications in cancer biology.

Keywords: Computational cancer modeling, Agent-based models, Multi-agent systems, Features selection

Introduction

Cancer is a disease that still causes the death of many people in the world. Cancer is a most complicated disease and there are many factors involved in getting it [1]. Therefore, accurate knowledge of the dynamics of this disease is essential. Traditional *in vitro* and *in vivo* approaches do not provide a global view on cancer disease, and sometimes they cannot produce a significant understanding of it. On the other hand, *in silico* models have more capacity for integration and are increasingly used in oncology. In the recent decade, mathematical models of cancer have become widely used, and most of these models cover the dynamics of cancer. These models are also considered a suitable platform for developing and promoting theories of control and stability [2-4]. A mathematical model with the ability to predict how a cancerous tumor will grow and spread can be used to develop treatments tailored to different types of cancer. The latest theory in the world considers stem cells to be the source of cancers. Tumors involve a heterogeneous population whose ability to grow and metastasize to a small population of stem cells. Therefore, advances in specific therapies that target is cancer stem cells raise hopes in cancer patients [5]. The problem is the lack of knowledge about the behavior of cancerous tumors. The stem cell hypothesis explains that tumors arise from a small number of cells with properties such as self-renewal and the ability to differentiate to other cells (tumor's non-stem cells), which act much like body's stem cells [6]. If we have a systematic and mathematical view of cancer treatment, we need accurate modeling. In other words, system identification is essential. Therefore, models of cancer stem cells propose valuable insights into cancer biology [7]. One of the techniques in dealing with cancer and consideration its various behaviors to find the correct and low-complication treatments is to use mathematical models. Some of them include understanding the dynamics of tumor growth [8]. For designing a mathematical model that can explain cancer stem cells growth process exactly, we need the features that influence on this process. There are some papers that proposed a model which includes several important cellular features. Norton et al. [9] proposed an agent-based stochastic model of breast cancer metastatic seeding. Their model includes several important cellular features such as stem cell symmetric and asymmetric division, migration, cellular quiescence, senescence, apoptosis, and cell division cycles. It also includes external features such as stem cell seeding frequency and location. Enderling et. al developed an individual cell-based computer model for considering the interaction of cancer stem cells and their non stem progeny to study early tumor dynamics. They showed the effect of three basic features of tumor growth. These features are cell proliferation, migration, and death [10]. In another work in 2009, Enderling and co-workers proposed an agent-based model with basic rules for three features that have influence on control and definition spatial and temporal tumor growth dynamics in tumor development [11]. Pcleszczuk et al. proposed a computational model *in silico* of growth and evolution according to the cancer stem cells hypothesis [12]. They tracked four traits: migration rate, apoptosis, symmetric cancer stem cell division, and cancer cell proliferation potential. Authors found that cell proliferation potential is the strongest regulator of tumor growth. Increasing proliferation potential yields a larger population of non-stem cancer cells that compete with CSCs (cancer stem cells) in space and inhibit these cells to symmetric division. They also found that traits rise from centers of growing tumors in the form of rays, and this causes tumor heterogeneity. Brown et al. proposed an innovative multi-agent approach for cancer modeling [13]. In their research modeled two teams of cancerous and healthy cells. These two teams are different, and agents in interaction with the environment must learn the optimal policy. They are modeled with a decentralized Markov decision process. **Table 1** shows the features of this model.

Malekian and her coworkers modeled the gap junction communication by using evolutionary game theory [14]. The main goal of this model is to illustrate the gap junction role in early-stage cancers. They consider ductal carcinoma *in situ*. The model showed the role of gap junction communication in reducing tumor growth and the ability of multi-agent learning methods to cancer modeling.

In this section, we consider some agent-based models and features that author selected for proposing models. As we see in the previous works in the field of cancer mathematical modeling, selecting important and effective features on tumor growth is so important. Also, there are more features that effect on tumor growth. Therefore, the existence of a method that helps in choosing the most effective features will be valuable. There are more feature selection methods that used in cancer diagnosis, classification tumors as a malignant or benign tumor and so on [15]. Lagzian et. al for the first time used Taguchi method to get the most effective features of the six important features that influence on cancer stem cells growth. They used the Taguchi results for proposing an agent-based model of cancer stem cells growth process.

In the next section, first we explain a brief history of Taguchi method and its applications and then answer this main question: why the Taguchi method can be a suitable features selection method in cancer computational model?

Discussions

Taguchi method

The Taguchi method of quality control is an approach to engineering that emphasizes the roles of research and development (R&D), and product design and development in reducing the occurrence of defects and failures in manufactured goods. The Taguchi method is a powerful tool for designing and optimizing a system's performance [17-21]. For this reason, it has been considered in a wide range of industrial systems because it can reduce their cost by reducing the number of necessary tests. The Taguchi method is a combination of sophisticated mathematical and statistical techniques used in academic and industrial studies. By using this method, optimal conditions are achieved with minimal experimentation. These conditions are characterized by changes in the signal to the noise ratio (S / N). In the following, the conditions that have a greater S / N ratio are considered optimal settings.

This technique has seven phases, as shown in **Figure 1**, determining the functions that must be optimized, determine the

Table 1. Features of Brown et al. model.

Modeled population	agents design	environment	perception	control	communication
Cancerous and healthy cells	heterogeneous	semi-dynamic	visible	decentralized	limited

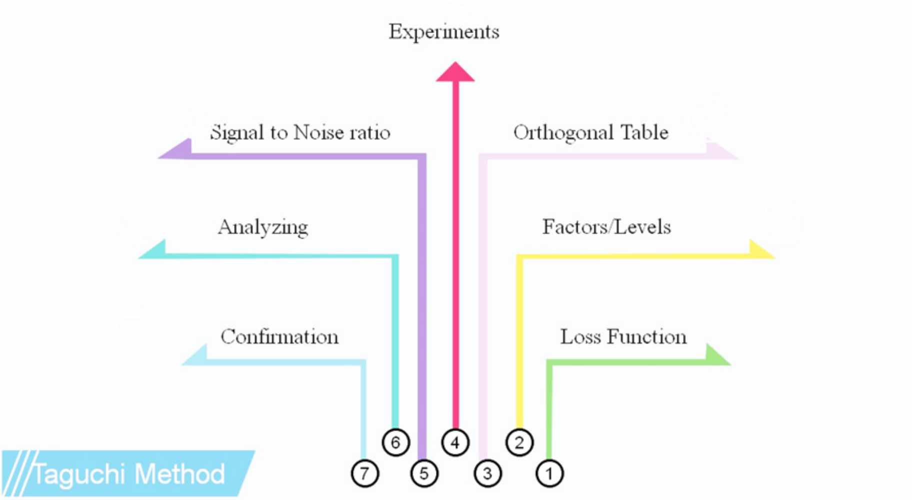

Figure 1. Taguchi method procedure.

control factors and their levels, select the S / N ratio and select parameters associated with optimal conditions, data analysis, and output prediction in optimal mode, and the last stage that tests the confirmation test.

Aims and findings

In this section we focus on reference [16] and talk about its ideas and aims. Authors want to propose a precisely agent-based model for cancer stem cell growth process. Based on the work done in computational models of cancer disease, agent-based models are so suitable models for considering tumor dynamics and cancer stem cells growth process [review article in this field]. The stem cell hypothesis said that tumor progress belongs to a small population of cancer cells that named stem cells [9]. These cancer cells remain in human body even after remedy and then return and causes cancer metastasis and tumor progression. It is worth noting that cancer stem cells' behavior is stochastic. Therefore, the position of model that can predict this behavior is empty yet. There are some notes that show some reasons of this loss as following:

1- Complexity and stochastically behavior of cancer cells specially cancer stem cells

2- Weakness of computational modeling methods in modeling more variables or agents

3- Unusual behaviors of cancer cells in reality that models cannot predict them

Therefore, all models are wrong but some of them are useful [22]. In order to achieve a more accurate and usable model, select effective features on tumor growth process is very important. Lagzian et. al have two views on cancerous tumor: the first one is that the tumor is a multi-agent system with two agents namely cancer stem cells and cancer non-stem cells, and the second one is that the tumor is a system or factory that produces cancer cells. As a factory, products have some features that determines the extent of their production. This is important to say that the main goal of Lagzian and co-workers is to propose an agent-based model for cancer stem cells growth process and control it [16].

In order to achieve this goal, Lagzian et. al [16] collected features from previous work in this field and used Taguchi method for considering the effect of this features on cancer stem cells and tumor growth process. The advantages of this method are as following:

1- In engineering, this method focuses on design and development to produce efficient and reliable products. Therefore in cancer biology we can use this method in order to consider the conditions that influence the tumor growth and determine their impact with high probability.

2- In this method manufacturing process has less importance than designed experiments and try to eliminate variances of products before production. With a systematic view of a cancerous tumor as a black box, this method can be useful.

3- The important notes of this method are considering disadvantages and side effects of products, and quality of a product is measured according to changes and deviations in performance. This tip can help to propose a treatment plan.

4- This is a practical and straightforward method which considers all possible modes for selecting features and determines the best and most practical arrangement.

Conclusion

In this mini-review we focus on Lagzian et. al [16] and consider the aims and ideas of authors in using Taguchi method for feature selection and then proposed an agent-based model for cancer stem cells growth process. Computational modeling in the field of biology is constantly being updated and improved, especially researchers and specialists try to gain a progressive mathematical model that can help them to better understanding of tumor growth process and any kind of cancer disease. The use of different statistical and mathematical methods can considerably help in this field.

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