TAGUCHI METHOD FOR PARTIAL DIFFERENTIAL EQUATIONS WITH APPLICATION IN TUMOR GROWTH

M. Ilea[1], M. Turnea[1], M. Rotariu[2], D. Arotăriței[2], Marilena Popescu[2]
University of Medicine and Pharmacy“Grigore T. Popa”- Iasi
1. Faculty of Medical Bioengineering
2. Secondary School of Baltati, Iasi

TAGUCHI METHOD FOR PARTIAL DIFFERENTIAL EQUATIONS WITH APPLICATION IN TUMOR GROWTH (Abstract): The growth of tumors is a highly complex process. To describe this process, mathematical models are needed. A variety of partial differential mathematical models for tumor growth have been developed and studied. Most of those models are based on the reaction–diffusion equations and mass conservation law. A variety of modeling strategies have been developed, each focusing on tumor growth. **Material and methods**: Systems of time-dependent partial differential equations occur in many branches of applied mathematics. The vast majority of mathematical models in tumor growth are formulated in terms of partial differential equations. We propose a mathematical model for the interactions between these three cancer cell populations. The Taguchi methods are widely used by quality engineering scientists to compare the effects of multiple variables, together with their interactions, with a simple and manageable experimental design. In Taguchi’s design of experiments, variation is more interesting to study than the average. **Results:** First, Taguchi methods are utilized to search for the significant factors and the optimal level combination of parameters. Except the three parameters levels, other factors levels other factors levels would not be considered. Second, cutting parameters namely, cutting speed, depth of cut, and feed rate are designed using the Taguchi method. Finally, the adequacy of the developed mathematical model is proved by ANOVA. According to the results of ANOVA, since the percentage contribution of the combined error is as small. **Conclusions:** Many mathematical models can be quantitatively characterized by partial differential equations. The use of MATLAB and Taguchi method in this article illustrates the important role of informatics in research in mathematical modeling. The study of tumor growth cells is an exciting and important topic in cancer research and will profit considerably from theoretical input. Interpret these results to be a permanent collaboration between math’s and medical oncologists. **Keywords:** TUMOR GROWTH, DIFFERENTIAL EQUATIONS, TAGUCHI METHOD, NUMERICAL MODELING

Cancer is a generic name given to a group of malignant cells that have lost their specialization and normal control growth. This group of malignant cells can be regarded as a nonlinear dynamic system self-organized in time and space. Mathematical modeling is a process by which a real world problem is described by a mathematical formulation. Mathematical modeling of avascular tumors can be seen as the first step in building models for tumors in later stages (1, 2). Taguchi methods consist of 3 phases: designing the experiment, running and analyzing, and confirming and validating the assumptions (3, 4).

MATERIAL AND METHODS

The model is based on a set of partial differential equations with form:

$$\begin{cases} \frac{\partial u}{\partial t} = \frac{\partial}{\partial x}[\frac{u}{u+v}\frac{\partial}{\partial x}(u+v)] + g(c)u(1-u-v) - f(c)u. \\ \frac{\partial v}{\partial t} = \frac{\partial}{\partial x}[\frac{v}{u+v}\frac{\partial}{\partial x}(u+v)] + f(c)u - h(c)v \\ \frac{\partial w}{\partial t} = h(c)v \\ c = \frac{c_1[1-\alpha(u+v+w)]}{\beta+u}, \beta = \frac{k_1}{k_2} \end{cases}$$

Where are denoted by:

$u(x,t), b(x,t), v(x,t), w(x,t)$ the cell densities for the proliferating, quiescent, necrotic cells and concentration of some nutrients (1),(2). In this stage, Taguchi methods were used to find the optimal parameters combination. Taguchi (4) has envisaged a new method of conducting the design of experiments which are based on well defined guidelines. This method uses a special set of arrays called orthogonal arrays. These standard arrays stipulate the way of conducting the minimal number of experiments which could give the full information of all the factors that affect the performance parameter. The table I shows an L^{16} orthogonal array (3). There are totally 16 experiments to be conducted and each experiment is based on the combination of level values as shown in the table. The third experiment is conducted by keeping the independent design variable 1 at level 1, variable 2 at level 3, and variable 3 at level 3.

TABLE I
Layout of L^{16} orthogonal array.
Taguchi's orthogonal arrays are highly fractional orthogonal designs

Exp. No.	Parameter 1	Parameter 2	Parameter 3
1	1	1	1
2	1	2	2
3	1	3	3
4	1	4	4
5	2	1	2
6	2	2	1
7	2	3	4
8	2	4	3
9	3	1	3
10	3	2	4
11	3	3	1
12	3	4	2
13	4	1	4
14	4	2	3
15	4	3	2
16	4	4	1

The relationship between one column and another is arranged so that factor for each level within one column, each level within any other column occur an equal number of times as well. These designs can be used to estimate main effects using only a few experimental runs.

There are totally 16 experiments to be conducted and each experiment is based on the combination of level values as shown in the table II. The third experiment is conducted by keeping the independent design variable 1 at level 1, variable 2 at level 3, and variable 3 at level 3.The additive assumption implies that the individual or main effects of the independent variables on performance parameter are separable, but the model assumes that there exist no cross product interactions among the individual factors (4). Furthermore, each factor can be assigned a significance weight to denote its importance in affecting the end result of the experiment.

TABLE II
Experimental data for Taguchi method

Tests	α	k_1	k_2
1	0.5	0.08	115
2	0.5	0.092	120.5
3	0.5	0.105	127
4	0.5	0.121	133
5	0.63	0.08	120.5
6	0.63	0.092	115
7	0.63	0.105	133
8	0.63	0.121	127
9	0.78	0.08	127
10	0.78	0.092	133
11	0.78	0.105	115
12	0.78	0.121	120.5
13	0.97	0.08	133
14	0.97	0.092	127
15	0.97	0.105	120.5
16	0.97	0.121	115

RESULTS

The design of the experiments has an effect on the number of experiments required. Taguchi’s experimental approach was applied to design the experiments using the three parameters of this study .The results of the 16 experiments of Taguchi's L^{16} series, were analyzed in order to determine the mean effect of each factor. These results suggest that the method of Taguchi's optimization approach remarkable rapid tumor growth. A major finding of the study was that the Taguchi methods predicted the combination of factors that results in the lowest survival of the malignant cells. The experimental results indicate that the proposed mathematical models suggested could adequately describe the performance indicators within the limits of the factors that are being investigated. After the simulation model using different values of the three parameters α,k_1 and k_2 are obtained following fig. 1.

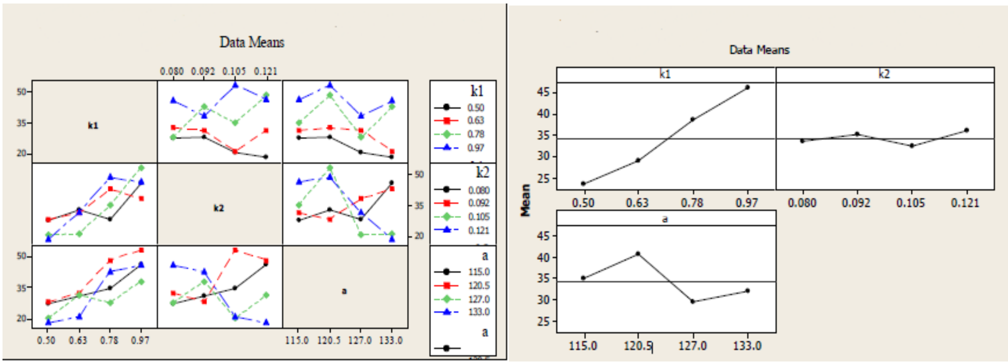

Fig. 1. The results of L^{16}.

Each experiment run was done in triplicate and repeated three times, the mean values were calculated and the results were expressed as mean. The adequacy of the predictive model was verified using ANOVA at 95% confidence level. The ANOVA revealed that feed is the most significant factor influencing the response variables investigated. The first step in the optimization process is to determine the ratio for the entire experiments test. The percentage contribution of each control factor is employed to measure the corresponding effect on the quality characteristic. In this experiment, Taguchi's graphical approach is used to plot the "marginal means" of each level of each factor and "pick the winner" to determine the best setting for each control factor. An advantage of the Taguchi method is that it emphasizes a mean performance characteristic value close to the target value rather than a value within certain specification limits.

CONCLUSIONS

In this paper we presented a partial differential equations model of avascular tumor growth which consists of proliferating, quiescent and necrotic cells and includes chemo taxis interactions and nutrient diffusion. The use of Taguchi method in this article illustrates the important role of informatics in research in mathematical modeling. A major finding of the study was that the Taguchi methods predicted the combination of factors that results in the lowest survival of the malignant cells. We have presented this method in systems of partial differential equations, which is integration based. For model systems have been chosen to demonstrate the validity of this method. We have seen that this method is relatively simple and therefore requires very little computational time. The study of avascular tumor growth cells is an exciting and important topic in cancer research and will profit considerably from theoretical input.

REFERENCES

1. Orme M.E., Chaplain M.A.J., A mathematical Model of Vascular Tumor Growth and Invasion, *Mathematical and Computer Modelling*,1996; 23: 43-60.
2. Sherratt J.A., Mark A. J, A new mathematical model for avascular tumor growth, *J Mathem Biol*, 2001; 43: 291- 312.
3. Ranjit K. R., Design of experiments using the Taguchi Method, John Wiley & Sons, 2001.
4. Taguchi G., Clausing Don, *Robust Quality*, Harvard Business Review, 1990.