Statistical Design of Biomedical Devices and Systems

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Abstract. The aim of this article is to explore the use of statistical design in biomedical engineering applications. These techniques are not extensively used in this discipline possibly due to the current content of most curriculum. They may however be very valuable in optimizing the performance of biomedical devices and systems. We first review the two major methods of statistical design, namely the Taguchi Robust Design and the Response Surface Methodology. Examples of applications are given from other disciplines and in particular electronic engineering. We then explore statistical design experiences in biomedical engineering. Examples from imaging equipment design are described. It is shown that lesion detectability can be increased significantly and therefore misses be reduced. The effectiveness and efficiency advantages of these methods with respect to classical experimentation methods for system optimization are also outlined.

1 Introduction

Statistical design has been used as part of the general quality improvement initiatives in diverse industries in order to obtain high quality and robust products and processes that reduce errors, accidents and related loss. The two widely used statistical design methods, namely the Taguchi Method and the Response Surface Methodology (RSM) have received wide attention in industries from electronic engineering to chemistry [1,2] especially in the context of the six sigma quality programs that aim to to reduce errors in processes and products to a level of (3.4 defects per million) , or equivalently to 99.99966% defect free systems [4]. This program has been adopted in many industries and recently in medical care [5,6].

In product or process design, one usually does not have an analytical form that describes the quality characteristics as a function of the design parameters. This naturally leads us to consider experimentation for design optimization. Classical experimentation schemes are based on changing one parameter while keeping the others constant. With this scheme however, the optimum cannot be located in a reliable and efficient manner in a multiparameter context. Furthermore interaction between design parameters cannot be established. Another potential problem is to keep the statistical measurement error at a low level. Both the Taguchi method and the Response Surface Methodology are based on experimental design principles, developed by Fisher in 1920's initially for agricultural applications [7,8]. He introduced the Factorial Experiments and then Fractional Factorial Designs where a process can be studied without trying all the parameter combinations. This leads to efficient experimental designs where very few experiments are run. An ANOVA analysis is then performed to check if the main effects and interactions are statistically significant.

Taguchi quality engineering has been developed to extend these techniques in order to design robust systems that exhibit low sensitivity to statistical variation in the environment and internal components. Another related scheme named the Response Surface Method is used in order to find precise optimum levels by fitting mathematical models to experimental results and uses a variety of standard optimization methods to arrive at an optimum.

One difficulty with experimentation is the practicality and cost effectiveness encountered in many applications that require expensive and complex equipment as well as quality metrics that estimate human performance such as lesion detectability figures on radiological images. Monte Carlo simulation has been developed for many such applications in order to alleviate this difficulty. Another major difficulty is the computer simulation of human organs. Realistic anthropomorphic phantoms are now been developed for imaging studies.

Statistical design methods such as the design of experiments including Taguchi Robust Engineering and Response Surface Methodology can further enhance these developments by offering a scheme for optimizing system performance in an efficient manner in that the number of experiments is kept at a minimum while the optimization can encompass a great number of formulations that can include multiple objectives as well as constraints. In RSM, a propagation of error term is utilized to simultaneously reduce the sensitivity to variation in noise factors.

A vast literature exists that describe the application of statistical design techniques to various engineering systems. Integrated circuit design and power circuits reliability optimization are among the pioneering work in the electrical engineering field. Few work has been conducted in the implementation of these methods in biomedical engineering.

In the following a short description of these two methods are first given. Then a survey of recent statistical design applications in a representative industry, namely electronic engineering and then in biomedical engineering is presented. Finally new developments are discussed and conclusions drawn.

2 Statistical design methods

2.1 Taguchi quality engineering

The Taguchi method developed by Dr. Genichi Taguchi [2,9,10], uses experimental design specifically to improve engineering products and processes and is intended to be used for improving performance while reducing cost and variance in order to obtain robust products under statistical uncertainties in the components and environment. He introduced the notion of loss-to-society which incorporates a penalty for the variance in products (Fig. 1). He advocates that the unnecessary variation in products may not only cause that the quality characteristic exceeds the specification limits but also create losses such as repeat work or lack of satisfaction for the entire society even when the products are within specifications.

He then elaborates the concept of signal-to-noise borrowed from electrical engineering in order to express an objective function describing both performance and variance. The objective is to maximize this S/N ratio in order to obtain the operating conditions that will give the best performance and the minimum variance despite the mentioned uncertainties. Taguchi defines three S/N ratios for different cases.

Nominal the best

$$n = 10 \text{ Log10 } \frac{\text{square of mean of measurements}}{\text{variance of measurements}} \qquad (1)$$

Larger the better

$$n = -10 \text{ Log10 } [\text{MSS of reciprocal of measurements}] \qquad (2)$$

Smaller the better

$$n = -10 \text{ Log10 } [\text{ MSS of measurements }] \qquad (3)$$

He then resorts to orthogonal arrays which are used to study the effects of design factors and their interaction with noise factors (mainly environmental factors and uncertainties in components). The proper orthogonal array is selected according to the number of factors and effects to be studied.

The next step is the procedure to follow for finding the lowest cost design that delivers the best quality, namely the best performance and the least variation.

The Taguchi approach has allowed a large number of engineers to apply process improvement in a practical way. It however does not offer any sequential approach to experimentation and its basic philosophy and method has been complemented by modern approaches that offer higher experimental efficiency.

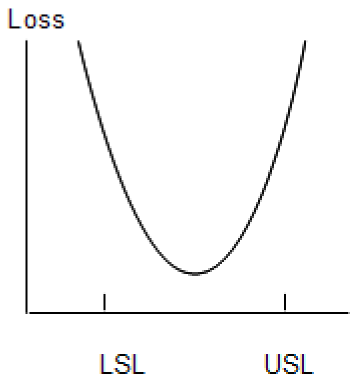

Fig. 1. The loss function.

2.2 Response Surface Model for process improvement

Taguchi methods allow one to investigate a process based on one large experimental set-up. In response surface methodology, a sequential experimentation scheme is used by iteratively and systematically approaching the precise optimum. The objective is to express an output response variable as a function of the design parameters:

$$y = f(x1, x2) + e \tag{4}$$

In the beginning a screening experiment is used to single out the most important factors to be used in the next experiments. A first order model is used with a factorial design to determine the direction of a steepest descent optimization (Fig 2). This is repeated until we are close to the optimum where a more elaborate model such as a central composite design is used for a higher order model fit [11,12].

RSM offers tremendous advantages such as being able to systematically move to the optimum, to investigate the response surface shape and use more efficient designs. Furthermore, robust designs can be obtained by the use of error of propagation in the objective function to be optimized.

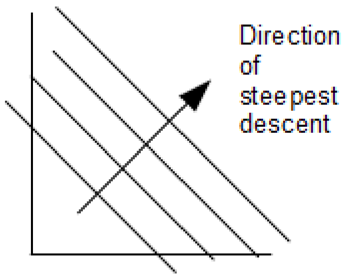

Fig. 2. The steepest ascent method

3. Survey of statistical design applications

3.1 Design of electronic circuits

Statistical design has been extensively used in electronic circuit design, and in particular in order to build robustness to statistical variations of the parameters due to technological processes and aging [1,2]. A MOS VLSI statistical circuit design techniques and examples are given in [13]. In [14], The design of reliable integrated circuits is characterized as a significant current challenge that is likely to remain relevant for all circuit designs. In [15], multi-objective robust parameter design goal is pursued for a microwave circuit. An achievement of 97 % in the manufactures of a microwave amplifier is reported. Another interesting example has been the use of Response Surface Methodology to planar transformer winding design [16]. Design of experiments for the reliable operation of electronics in automotive applications is presented in [17] where variation in internal and external factors are modeled. The proposed methods have been applied to a window lifting automotive system. In these and similar studies a high rate of success is demonstrated in maximizing the reliability and minimizing the costs.

3.2. Statistical design in biomedical engineering

Although these techniques have been widely used by many fields such as mechanical engineering, chemical engineering, biochemistry and electronics as illustrated above, not much work has been reported in the literature in the area of biomedical engineering. A few applications have been published such as the robust design of a finger probe in non- invasive in total haemoglobin monitor [18]. The Taguchi method has been applied to biomechanical analysis by using a case study of a cervical ring cage optimization in [19]. In another interesting application [20], a broadband transducer design problem is solved using statistical design of experiments.

In the area of complex medical imaging systems, design optimization present unique challenges. Since patients are difficult or impossible to use for optimization studies geometric or anthropomorphic phantoms are being developed. The difficulty in experimentation with real systems led to the development of a number of notable Monte Carlo Simulation Packages. Another difficulty is the quantification of image quality for use in optimization. The well known Rose model and more recently developed model observers such as the channelized Hotelling observers have been used successfully in many such optimization projects.

The contribution of the work in [21] is the introduction of the new experimentation strategies borrowed from the Taguchi and RSM techniques allowing a very high efficiency and reliability in finding the optimum with respect to conventional experimentation schemes. Furthermore, it is possible to study interactions through these methods and we may obtain robust designs against variations in the environment or internal components.

In [22], the effects of acquisition parameters on lesion detectability and their interaction for a breast scintigraphy system has been investigated using experimental design. In [23] a breast scintigraphy collimator is designed using RSM, and Monte Carlo Simulation. A second order model fit is achieved using Monte Carlo Simulations in a three dimensional region determined from specifications (hole length, hole width and wall septa) of existing collimators and then optimization performed It is shown that a significant improvement in detectability can be achieved for a worst case lesion.

4 Discussion and conclusions

In this paper, the statistical design concepts and methods have been presented with the purpose of drawing attention to the use of these methods for obtaining defect free processes and devices in the biomedical field. These set of techniques can be used in research where the aim is to study the effect of multiple design or control parameters and their interactions on a response variable, allowing us to obtain a high level of efficiency in experimentation. Considering that experiments or even simulations are often expensive and extremely time consuming in many cases, efficient optimization methods become an important advantage. We prefer to use the Taguchi method for the initial screening experiments while RSM has been proven to be extremely practical and effective for subsequent optimization due to its sequential nature.

Various successful examples have been presented which includes recent work on the optimization of a scintigraphic imaging system with significant improvements in lesion detectability, which results in fewer misses in patient studies.

There is no doubt that the presented and similar statistical design methods will play a uniquely important role in achieving high quality and robust designs of biomedical devices and processes. Changes in the biomedical engineering curriculum may be necessary to accommodate these new goals. In medicine, each increase in performance and reliability such as diagnostic performance has a very large impact on human life. For that reason, all losses should be minimized and these methods will provide improvements in almost any biomedical device or system.

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