ABSTRACT

Statistical design of experiments (DOE) is an experimental strategy to fit specific relationships between outcomes(s), often called response(s) of a process or system and a number of associated control (input) variables, often called factors. DOE used for the purpose of response surface modeling are called response surface designs (RSD). Response surfaces in several fields including chemical, biotechnology processes are adequately modeled by the first, second and partially mixed third order models in qualitative, quantitative factors. At the beginning of the response surface methodology (RSM) for modeling and optimization, the surface within the design area is assumed to be approximately linear, that is, a hyperplane. The additional centre points are used to check for curvature. If the curvature is found to be statistically significant, the design should be upgraded into a second order design, allowing building of a quadratic model. The replicate experiments are used to estimate the mean experimental error, and for testing model adequacy, i.e. the lack of fit in the model. Designs for fitting first-degree models are called first-order designs and those for fitting second-degree models are referred to as second-order designs.

Many a designs have been tried and tested exclusively as the first order designs, as the second order designs or as serving both the purposes. The most commonly used first-order designs are $2^k$ factorial and their regular fractions ($k$ is the number of control variables), Plackett Burman designs, and simplex designs and, the second-order designs are the $3^k$ factorial, the Box Behnken and the central composite designs. In both the cases, while the former two can readily be used for qualitative and quantitative factors, the latter ones have uses only for experiments in quantitative factors. Another class of first and second order designs requiring less number of runs includes Koshal (1933)$^{32}$, Hartley (1959)$^{26}$, Westlake (1965)$^{54}$, Roquemore (1976)$^{50}$, Draper (1985)$^{18}$, Draper and Lin (1990)$^{23}$, Oehlert and Whitcomb (2002)$^{43}$, Angelopoulos et al. (2009)$^6$ and Nguyen and Lin (2011)$^{42}$ work. They gave small size composite designs by selecting appropriate and minimized set of runs for the factorial portion for fitting second order response surface model. However, they are not meant for experiments with qualitative
factors. The class of response surface designs involving qualitative and quantitative factors have mainly been constructed by Draper and John (1988)\textsuperscript{21} and Wu and Ding (1998)\textsuperscript{55}. Among several response surface designs, the composite form designs like the central composite design (CCD) have found maximum applications, for they satisfy most of the good design criteria.

Number of research articles has been published in this area but still several problems in response surface designs exist for experiments with, qualitative and quantitative factors, practical limits on the region of interest and region of operability, and those with cost and precision constraints have scope for improvement.

Most generally, a process consists of quantitative and qualitative variables or factors which may be influenced by nuisance or noise factors. It is desirable at the time of screening that, we do not miss any interaction between a qualitative and a quantitative factor. This is most likely to happen with saturated designs because of complex aliasing among factorial effects. Chapter 2 revisit the two levels irregular fractions. Among the irregular fractions of $2^k$ factorials, the $3.2^{k-m}$ fractions have greater practical value because their alias patterns are known. Based on alias pattern, the variances and covariances of all estimable factorial effects can be known hence also A-efficiency of design. A new criterion called efficient estimation capacity (EEC) index is introduced to assess designs of $3.2^{k-m}$ fraction of a $2^k$ factorial which is simply a count generated from alias pattern. It serves as surrogate for identifying the most A-efficient design among the designs having equal number of runs. Higher the EEC index, higher the A-efficiency, that is lower the variance and covariance of $3.2^{k-m}$ design for interaction model. This index has opened up comparison among $3.2^{k-m}$ fractions of variable resolutions between resolutions II to IV. The role of EEC index as compared to other assessment criteria for irregular factorial designs namely A-, df-efficiency, generalized resolution and minimum moment aberration has been discussed. A design with lower EEC index would be df-efficient, while a design with moderate EEC index would be MMA design. Further it is shown that, some $3.2^{k-m}$ designs having resolution III or less, possess special properties. The chapter presents two new $3.2^{k-m}$ designs for $(k, m)=$(5, 2),
(6, 3) of practical importance. The resulting 24 run design in six factors allowing estimation of all MEs and 14 TFI s provide useful alternative to the Rechtschaffner (1967) saturated design.

At the time of optimization, most quantitative factors are studied at five levels including two extreme levels. Then to accommodate some qualitative factors at two/three levels, replicated CCD are employed, but they require too many experimental runs. In chapter 3, a structured method of construction for obtaining small, balanced, efficient, optimal and near rotatable RSDs is given for fitting second order response surface model (SORSM) to experiments asymmetrical in some quantitative and qualitative factors. Most of our RSDs allow experimenters to perform lack of fit test. This will protect experimenters from missing any useful mixed third order effects. A further goal of this work is to construct RSDs which can achieve desirable targets for the expected response, such as predictions with the least prediction variance. The RSDs presented for asymmetric quantitative factors are either $G$-optimal or they contain an internal spherical design region which is $G$-optimal. The RSDs in quantitative and qualitative factors while being $D$-efficient with a lower limit of 50% possess competency to estimate some mixed third order effects. Cases of our RSDs having at least two, five level factors and multiple two/three level quantitative, qualitative factors, in total 3 to 6 factors have been studied exhaustively for rotatability, optimality and prediction capability criteria. The same exhaustive assessment can be done for $k > 6$ factors.

In the context of composite designs, especially the CCDs, three formula based values of alpha, namely, rotatable-, spherical-, and practical- alpha have been suggested. The practical alpha provides axial points that are less extreme than those given by the spherical alpha, but it cuts down the design region considerably and hence hampers the prediction variance properties. In chapter 4, the new formula for alpha that balances nicely on both the aspects called practically efficient alpha is introduced. Interestingly, for small size composite designs, the practically efficient alpha values are close to the corresponding rotatable alpha values. It ensures desirable prediction variance and other properties, as well as sets axial points within the region of interest/operability by setting them at adequate distance from the factorial points. Tables mainly featuring variety
of choices of alpha values for the five well acclaimed composite designs, CCD, SCD, MinResV, designs of Draper and Lin (1990)\textsuperscript{23}, and of Angelopoulos et al. (2009)\textsuperscript{6} in 3 to 9 factors are given. Alpha values rendering composite designs to be $D$-optimal are also provided. The performance of these useful second order response surface designs (SORSDs) have also been compared for some additional user-friendly values of alpha, restricted to have only one decimal point. For fair comparisons, both, the numerical and graphical assessments of composite designs are made in terms of rotatability, $D$-, $G$- efficiencies, and FDS plots for various alpha values. It is found that, in particular for 7 to 9 factors, the Minimum Resolution V based composite designs with practically efficient alpha can replace the CCDs with alpha below 2.

The second order response surface designs are widely used for scientific experimentations. However, the number of design runs and value of alpha for axial runs often become impractical when the number of factors is more than 5. In chapter 5, the five equi-spaced levels ($\pm \alpha/2, \pm \alpha, 0$) composite designs ($\alpha > 2$) are given as a new alternative to rotatable/ spherical CCD along with optimal CCDs for experiments in 4 to 10 factors. It is shown that the central composite design (CCDs) and Minimum resolution V composite design (Min-ResV) in five equi-spaced levels ($\pm 1.1, \pm 2.2, 0$) are $D$-(efficient) optimal in the class of CCDs and MinResV composite designs, having various alpha ($> 2$) levels. It is also shown that smaller alpha values with equi-spaced levels in CCD do not affect rotatability to a large extent but enhance the desirable properties of designs. Taking smaller alpha values with slightly elevated factorial levels not only retain rotatability but also provide economical alternative to spherical/ rotatable CCD and MinResV designs. The comparison of the three classes of composite designs, CCD, MinResV designs and SBCCD, in terms of numerical measures, $D$-efficiency, rotatability measure $Q^*$, and $G$-efficiencies for five different radii ($r$) of prediction regions of interest is given. The catalogue of design statistics in 4 to 10 factors is given for ready reference.

We have written MATLAB code for most of the computations done in this thesis and also used commercial software Design-Expert 9, MINTAB 14 and, MATHEMATICA 9.0 for few computations.