Construction of optimal designs for estimating the treatment×cell line interaction effect in two-colour cDNA microarray experiments

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With the quick growth of biotechnology during the last decades, medical research interest in genetic causes for the development of certain diseases (like diabetes, breast cancer and Parkinson's disease) gained tremendously in importance. The conduct of gene expression analyses using two-colour cDNA microarray experiments [1] is aimed at identifying candidate genes that can be made accountable for the genesis of a certain disease or the mutation of a benign into a malignant tumour.

Using statistically efficient designs for two-colour cDNA microarray experiments increases the precision of the statistical analysis of the gene expression data generated by those experiments. Landgrebe et al [2] proposed a gene-specific fixed effects linear model for statistical evaluation of the log ratios calculated from the gene expression values measured in the experiments.

In this talk we will consider a specific three-factorial layout of the experiments with N microarrays, two colours, $K \geq 2$ cell lines and $L \geq 2$ treatments.
We will present ϕ_p-optimal block designs for estimating the linear contrast related to the treatment×cell line interaction term of the Landgrebe model. We adopt modified versions of the generalized equivalence theorems suggested by Pukelsheim [3] to proof optimality. We demonstrate the interesting result that the solution of the optimization problem depends on the relation between the number of treatments and the number of cell lines used. The independency of this solution from the optimality criterion chosen can be interpreted as robustness characteristic.

For practical purposes, the optimality results obtained can be transferred into direct recommendations for the choice of an efficient design for a concrete experiment with given numbers of microarrays, treatments and cell lines.

References

[1] Brown, P.O., Botstein, D. (1999). Exploring the new world of the genome with DNA microarrays. Nature Genetics 21 (1): 10-14.

[2] Landgrebe J., Bretz F., Brunner E. (2006). Efficient design and analysis of two colour factorial microarray experiments. Computational Statistics and Data Analysis 50: 499-517.

[3] Pukelsheim F. (1972). Optimal Design of Experiments. Wiley, New York.