ANALYSIS OF MICROARRAYS INCORPORATING ADJUSTMENTS FOR SPATIAL EFFECTS

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SUMMARY
Various models were used to extract spatial effects from microarray data. Large discrepancies between the rankings of genes for the different methods were found, due to the roughness of the signal. Models assuming separability and autocorrelation did not perform as well as wavelets because the data were fractal in dimension, so assumptions underlying those models were violated.
Keywords: Microarray, spatial effects, wavelet, fractal.

INTRODUCTION
Microarray technology is becoming increasingly available to animal scientists to estimate expression levels of genes in biological processes. Intensity bias, dye bias and spatial bias can all influence the estimated expression level of genes if they are not included in the model or considered in the design of the experiment. This may result in inefficient allocation of resources in subsequent studies. This paper is concerned with spatial bias. Spatial trends can accumulate in the various stages of a microarray experiment. The final intensity reading of each spot is the result of a complex process involving array fabrication, sample preparation, cDNA synthesis and labeling, hybridization and microarray quantification. There are many possible causes for spatial trends on a slide within each step of a microarray experiment, not all of which are fully understood. The sources of variation in a microarray slide may not act continuously, so may be fractal and discontinuous in dimension.

Several authors have considered models to account for spatial bias involving autocorrelation (Burgueno *et al*. 2005, Baird *et al.* 2004). Models involving autocorrelation and splines assume separability (Adler 1981). Such methods rely on the data having an integer fractal dimension. When this condition is violated they may not be as efficient as other methods of removing spatial dependencies such as wavelet decomposition. This paper compares the efficiency of four methods in removing spatial dependencies from a murine microarray experiment.

MATERIALS AND METHODS
Data. The data used in this study came from cDNA extracted from mice livers in experiments conducted by Harry Noyes at The University of Liverpool. The treatments applied to the microarray were determined by strain of mice, challenge, replicate and time and these factors were unbalanced. Two types of mice were used, AJ and C57BL6. The mice were further divided into two challenges.

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