

# Some Considerations for the Design of Microarray Experiments

*John H. Maindonald, Yvonne E. Pittelkow and Susan R. Wilson*

## Abstract

Issues relevant for the design of gene expression experiments using spotted cDNA microarrays and gene chip microarrays are overviewed. Emphasis is placed on the uses of replication, and on the importance of identifying major sources of variation.

**Keywords:** microarrays; oligonucleotide; design of experiments; variability; replication; gene expression

## 1 Introduction

Microarrays are new and evolving technologies that enable large numbers of genes, up to the order of tens of thousands, to be evaluated simultaneously. Our aim is to give a brief overview of principles of experimental design, and to comment on their application to microarray experiments. A major theme is that, for purposes of design, the different sources of variation in gene expression are not well understood.

The objective of a microarray experiment might be to investigate genes which are differentially up or down regulated in cells between, say, a control group and cells which have undergone some treatment, or between cells of animals of different genetic background (*e.g.*, control mice compared to knockout mice) or between cells in healthy tissue and diseased tissues, or between cells at different time points (*e.g.*, developmental biology). Many studies search for genes that have similar expression profiles, often in an attempt to determine genes involved in biological pathways, or in development, or genes involved in regulatory functions. The focus would then be on the analysis of dependency structure. Time course experiments may investigate how the pattern of expression or relative expression changes over the cycle of cell division, or following administration of a drug. Finally, interest may be in estimation of gene expression levels.

The primary goal of the experiment should be clear, as this gives focus to the investigation, desirable even if a major part of the analysis will be a general search for interesting patterns of expression. Many experiments have multiple aims; these must be prioritized. Both in its scale and in the processes that are under investigation, the