pulse width, frequency, and voltage. Once optimal settings are selected, the amount of liquid delivered is constant and thus every spot is identical. By varying the number of drops per spot, the spot diameter and/or amount of material can be altered. Any kind of nucleic acids (oligonucleotides, genomic DNA, cDNA, and RNA) and in principle, almost any kind of solution may be spotted with this technique. Therefore, piezo-based sample delivery can be used for a wide range of applications, e.g., proteomics and combinatorial chemistry. Moreover, because of the active pumps, enough liquid for the production of thousands of arrays can be aspirated at once thereby reducing production time and interarray variances.

4. GENE EXPRESSION PROFILING—PRACTICAL CONSIDERATIONS

It has already been discussed that various types of microarray formats exist. Although it is not discussed in this review, we wish to point out that microarrays are also used for SNP detection and genotyping (6,7). When applying microarray technologies, the crucial question is: which microarray configuration fits best for a given research program? In the following, the utility of microarrays for: gene discovery, "genome-wide" expression patterns (transcriptome analysis), functional analysis of new genes, drug validation, and pharmaco- and toxicogenomics are discussed.

The importance of gene discovery lies in the identification of gene expression profiles and its correlation with the biological states of cells, tissues, and organs during disease or upon drug treatment. This enables the identification of new drug targets and a molecular medicine-based understanding of disease. For example, Alizadeh et al. (8) reported the identification of tumor-specific expression patterns in hematopoietic (lymphoid) cells. In gene discovery programs, it is essential to simultaneously study as many genes as possible, but this requires a profound understanding of the genome. In the foreseeable future, the genomes of common laboratory animals will be unraveled and reliable cross-species comparisons (human and animal) and predictions of biological responses will thus become possible.

In gene discovery programs, an approximate expression intensity of a given gene is sufficient, so that it does not make a great difference if the arrays are membrane- or glass-based. Currently, various arrays are available for the large-scale/genome-wide study of human, model organism, or bacterial genes. It should be noted that every cDNA which is on an off-the-shelf array has been cloned and presumably sequenced before. In consequence, this means that (i) the array hybridization is more precisely termed function or expression discovery than gene discovery and (ii) most of the genes are not low copy number genes. The only way to find truly new (and patentable) genes is to generate new libraries or to use one of the numerous alternative techniques, such as serial analysis of gene expression, SAGE (9), suppression