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1965–1969	Chemistry studies at the University of Vienna
1969–1970	Diploma, Technical University Braunschweig
1970–1974	Ph.D., Max-Planck-Institut für Experimentelle Medizin, Göttingen and Max-Planck-Institut für Biophysikalische Chemie, Göttingen
1974–1976	Research Fellow of the Jane Coffin Child's Memorial Fund for Medical Research, Harvard University, Boston, MA
1976–1978	Research Fellow, Department of Biochemistry and Molecular Biology, Harvard University, Boston, MA
1978–1987	Head of a research group at the EMBL, Heidelberg, Germany
1987–1994	Head of Department Genome Analysis at the ICRF, London, UK
1994–present	Director at the Max-Planck-Institut für Molekulare Genetik, Berlin
1995–present	Head of the Resource Center in the German Human Genome Project

Honors

1993	Fellow of the American Association for the Advancement of Science

DNA and protein analysis on arrays

Biological processes depend on complex interactions between many genes and gene products. To understand the role of a single gene or gene product in this network, many different types of information will be needed (gene and mRNA sequences, expression patterns at the RNA and protein level, protein-protein interactions, protein structure, phenotype information and so on). Understanding of the entire process, or even characterizing biological states in the characterization of disease processes, will therefore require much of this information for most or all of the genes of the organisms. Array techniques are inherently highly parallel, and can be easily miniaturized, and therefore offer in many cases the most appropriate technical solution to achieve the data rates required for these applications. We have therefore developed and used array-based analysis techniques for close to 15 years. A number of current developments to enable high-throughput and highly parallel hybridization or protein-based analysis will be described.

We are using a non-redundant clone set consisting of 36,000 clones based on the clustering of 700,000 EST sequences from the IMAGE consortium. This library (p950) has been established and rearrayed in collaboration with the divisions of Annemarie Poustka and Martin Vingron at the German Cancer Research Center (DKFZ) in Heidelberg. The library is maintained in the Resource Center of the German Genome project, which is distributing high-density filters and clones. Clones are PCR amplified and bound covalently to glass. Typically 19,200 gene fragments are immobilized as duplicates on each slide. Analyses are being carried out by hybridizing of labelled human tissue RNAs to an array of the selected 36,000 human gene fragments. Images from healthy and disease tissues are compared and analysed for spot recognition and spot quantification with an image analysis package developed in-house.

To extend the highly parallel analysis made possible by array techniques to protein analysis, cDNA libraries are now routinely cloned into expression vectors, permitting direct expression of the corresponding proteins. HIS-tagged and expressed proteins were immobilized as lysates or as purified proteins as arrays on membranes or glass, where they allow to study protein-protein and protein-DNA interactions.

To allow a further miniaturization of the DNA or protein arrays, we have adopted a highly parallel piezoelectronic drop-on-demand technology. We have implemented a multihead piezo-jet microarraying system, able to aspirate biological samples out of microtitreplates. A linear 16-way and a 4 x 4 nozzle multihead permit the construction of large microarrays on a variety of surfaces.

Because the spot density obtained by these systems is more than 4,000 clones per cm^2, we have developed higher-resolution detection systems based on a laser scanning principle. The detection system scans areas of 22 x 22 cm with 20-µm resolution for two colours at a sensitivity of less than 1 attomole fluorescent dye per spot. The system is used for RNA expression and SNP analysis.