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Advances in Biochemical Engineering / Biotechnology

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In references Advances in Biochemical Engineering/Biotechnology is abbreviated as *Adv Biochem Engin/Biotechnol* as a journal.

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http://link.springer-ny.com/series/abe/

ISSN 0724-6145
ISBN 3-540-43215-9
Springer-Verlag Berlin Heidelberg New York

Library of Congress Catalog Card Number 72-152360

Springer-Verlag Berlin Heidelberg New York
a member of BertelsmannSpringer Science+Business Media GmbH

http://www.springer.de

Printed in Germany

Typesetting: Fotosatz-Service Köhler GmbH, Würzburg
Cover: E. Kirchner, Heidelberg

Printed on acid-free paper SPIN: 10846806 02/3020mh – 5 4 3 2 1 0

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Preface

DNA-chip analysis has come a long way since the first official gathering of scientists working in this field, which took place in Moscow in 1991, comprising about 50 scientists from Europe and the USA. Then, the initial aim was the development of a technology for high-throughput sequencing of the human genome, named sequencing by hybridisation. The field soon diversified, however, in terms of methodology and application. Nowadays, DNA-microarrays seem to be a common commodity in biological sciences. The complexity hidden behind the apparent ease of such studies, however, is highlighted by the fact that it took about ten years of technology development – and persuasion – before the methodology really took off. Also, at closer scrutiny one realises that many problems still need to be resolved and only relatively limited inquiries have been attempted so far considering the potentially possible. Nevertheless, even these experiments have produced data on a scale beyond imagination for most people in biology a few years ago and for many even today. Even the data sets originating from large-scale sequencing are dwarfed by the quantity of information from chip-based analyses. Thus, DNA-microarray technology will be the true herald of change in biology. Having developed earlier from a descriptive to an analytical science, biology will split in future into an experimental and a theoretical branch, similar to what happened in physics quite a long time ago.

This change in biology is no better represented than by the authors of this book, who took part in bringing about this shift in emphasis. They are well-known experts in the field, many – like Edwin Southern, Hans Lehrach, Radoje Drmanac, Pavel Pevzner and Charles Cantor – have been actively pursuing array technology for more than a decade. Rather than pondering on the good old times, however, they demonstrate the continuous development in both technology and application areas and elucidate some critical points that need to be considered, when performing microarray analyses.

The first article, by Pavel Pevzner and co-workers, informs on aspects of designing DNA-arrays, which is not a trivial undertaking, although rarely discussed. Even at this level of array-based analysis – right at the start rather than the end – informatics is required in order to deal with the inherent complexity.

Such a design phase is followed by the actual production process. Although by no means the sole procedure for doing so, photolithographically controlled in situ synthesis is currently the best advanced technique for large-scale chip production with a high degree of reproducibility. Glen McGall and Fred Christians report on the procedures involved, some future developments and applications.

Muhammad Sohail and Edwin Southern describe in their contribution a different process for the creation of oligonucleotide arrays. Subsequently, they used the arrays in the screening for effective antisense reagents. This study is fascinating because of its impact on the understanding of interactions between nucleic acids, an interesting research area even after 50 years of structural DNA analysis, and in view of its practical implications for applications in biotechnology and molecular medicine.

Hubert Köster, Charles Cantor and co-workers combine two high-throughput techniques – arrays with detection by mass spectrometry – for genotyping analyses. With the existence of about 1.5 million publicly known single nucleotide polymorphisms (SNPs), the exploration of this resource is a major challenge in the effort of translating basic genomics into applied, medically relevant molecular genetics.

The work of Radoje Drmanac extends the objective of genotyping analyses and, at the same time, returns to the origin of DNA-chip analysis by pursuing 'sequencing by hybridisation', which is nothing short of performing a SNP analysis for each and every nucleotide of a given DNA-fragment. He reports recent achievements and deliberates on the exciting opportunities of this methodology.

The text of Holger Eickhoff and colleagues already reaches beyond the mere DNA-chip by reporting on procedures that extend strongly into the field of proteomics, thus linking the two areas. Only by such measures, carried out experimentally as well as in silico, the complexity of functions in cellular systems will eventually be unravelled.

Considering how array analyses are performed, it is only natural that a contribution on bioinformatics tools and databases should come at the end of the list. Its position does not reflect its importance, however. As a matter of fact, all preparatory work going into the production of the nice looking, colourful pictures from DNA-arrays is a useless squander unless it is assessed and presented in a way that makes the data accessible to human interpretation. Currently, much of the data produced on microarrays is actually wasted. Transcriptional profiling studies, for example, usually concentrate on few, specific biological aspects and ignore much else contained in the very set of raw data. This information could be useful for other studies, if only one could access it. For the purpose of going back to results for entirely different analytical purposes, central databases with appropriately designed and standardised procedures, as well as a common ontology, are essential. Alvis Brazma and colleagues have been instrumental in getting such efforts started.

Overall, the various articles provide a good mix, covering many, although not all, aspects of microarray-based analysis, the latter no longer achievable in a single book, for the days of the Moscow meeting in 1991 are long past and the breadth of the field has expanded enormously both in terms of its technical aspects and the variety of potential applications. Nevertheless, I hope the picture is comprehensive enough for understanding the basics, elaborate enough to inform in detail on certain aspects and speculative enough to stimulate further developments.

Heidelberg, May 2002 Jörg D. Hoheisel

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