
Preface

The development of PCR, which enables extremely small amounts of DNA to be amplified, led to the rapid development of a multiplicity of analytical procedures to utilize this new resource for analysis of genetic variation and for the detection of disease causing mutations. The advent of capillary electrophoresis (CE), with its power to separate and analyze very small amounts of DNA, has also stimulated researchers to develop analytical procedures for the CE format. The advantages of CE in terms of speed and reproducibility of analysis are manifold. Further, the high sensitivity of detection, and the ability to increase sample throughput with parallel analysis, has led to the creation of a full range of analysis of DNA molecules, from modified DNA-adducts and single-strand oligonucleotides through to PCR-amplified DNA fragments and whole chromosomes. *Capillary Electrophoresis of Nucleic Acids* focuses on such analytical protocols, which can be used for detection and analysis of mutations and modification, from precise DNA loci through to entire genomes of organisms. Important practical considerations for CE, such as the choice of separation media, electrophoresis conditions, and the influence of buffer additives and dyes on DNA mobility, are discussed in several key chapters and within particular applications. The use of CE for the analysis of drug–DNA interactions and for examination of the metabolism of therapeutic oligonucleotides and modified nucleosides illustrate the burgeoning applications of CE for the analysis of a wide range of medical and molecular diagnostic problems. The study of interactions between nucleic acids and diverse ligands by CE is also a new and rapidly developing area. Microanalytical devices, which include capillary electrophoretic separations, have resulted from the fusion of semiconductor devices and microdiagnostic analysis. Several seminal papers on the application of microchip-based capillary electrophoresis for genotyping and DNA sequence determination signal the revolution that is occurring in both capillary electrophoresis and laboratory analysis.

Capillary Electrophoresis of Nucleic Acids comprises two volumes divided into twelve parts, each part containing chapters that address particular general goals, or experimental approaches. Broadly, Volume I addresses instrumentation, signal detection, and the capillary environment, as well as the integration of mass spectrometry and CE for the analysis of small oligonucleotides and

modified nucleotides. Volume II broadly addresses techniques for high-throughput analysis of DNA fragments of less than 1 kb, employing SNP detection, mutation detection, DNA sequencing methods, and DNA-ligand interactions.

Volume I

Volume I, Part I presents basic CE instrumentation and the theoretical background to the separation of DNA by CE. The choice of different modes of CE and detection systems, the characteristics of sieving matrices, sample preparation, and quantitation of measurement are emphasized. DNA sequencing by CE is discussed. Methods for the manufacture of microchip devices are illustrated.

Volume I, Part II presents important factors, such as choice of capillary coatings and separation media, which offer new possibilities for separations. The theoretical background for the selection and composition of sieving polymers for optimal separation is illustrated.

Volume I, Part III presents choices of separation media and the CE environment for size-based (fragment length) separations of DNAs. Emphasis is made on new co-polymer matrix materials and liquid agaroses.

Volume I, Part IV discusses the fast separations of large DNA molecules and chromosomes, using pulsed-field capillary electrophoresis formats. Methods of collection of separated CE fractions for the analysis of supercoiled DNAs are also presented.

Volume I, Part V presents practical choices for the analysis of small therapeutic oligonucleotides, nucleosides, ribonucleotides, and DNA metabolism products by CE. Practical applications for the control of quality of nucleotides and oligonucleotides are illustrated.

Volume I, Part VI presents choices for the sensitive CE analysis of nucleotides and DNA metabolism products arising from environmental and cellular damage through disease. Practical applications of mass spectrometry and capillary zone electrophoresis for the detection of oncogenic change are also presented.

Volume II

Volume II, Part I presents practical considerations necessary for very rapid and accurate separations of linear DNAs by CE using short capillaries. SNUPE, heteroduplex analysis, ARMS analysis of DNA, and SSCP analysis.

Volume II, Part III details various modes of genotyping by CE. Particular emphasis is given to the use of multiplex separations. The techniques include parallel analysis of multiple simple repeat loci in human and CE analysis

of gene markers following degenerate oligonucleotide amplification from single cells. Methods for the application of chemical cleavage of mismatched DNA for mutation detection are illustrated.

Volume II, Part IV presents techniques for the quantitative estimation of gene expression using CE. Both quantitative RT-PCR and differential display analyses are highlighted.

Volume II, Part V presents practical choices of separation media and the capillary electrophoresis environment for DNA sequencing by CE. Rapid sequencing at elevated temperature and sequencing on micro- and array-CE devices are discussed. Methods for sequencing with selective primers are also illustrated.

Volume II, Part VI presents the analysis of DNA protein and DNA ligand interactions using CE. Techniques discussed include mobility shift assays and capillar affinity-gel electrophoresis.

Keith Mitchelson
Jing Cheng



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Mitchelson, K.R.; Cheng, J. (Eds.)

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