

METHODS IN MOLECULAR BIOLOGY

Series Editor

John M. Walker

School of Life and Medical Sciences

University of Hertfordshire

Hatfield, Hertfordshire, AL10 9AB, UK

For further volumes:

<http://www.springer.com/series/7651>

Clinical Applications of Capillary Electrophoresis

Methods and Protocols

Second Edition

Edited by

Terry M. Phillips

*Department of Pharmaceutics School of Pharmacy, Virginia Commonwealth University
Richmond, VA, USA*

Department of Pharmaceutics, Virginia Commonwealth University, Washington, DC, USA

 **Humana Press**

Editor

Terry M. Phillips
Department of Pharmaceutics
School of Pharmacy
Virginia Commonwealth University
Richmond, VA, USA

Department of Pharmaceutics
Virginia Commonwealth University
Washington, DC, USA

ISSN 1064-3745 ISSN 1940-6029 (electronic)
Methods in Molecular Biology
ISBN 978-1-4939-9212-6 ISBN 978-1-4939-9213-3 (eBook)
<https://doi.org/10.1007/978-1-4939-9213-3>

Library of Congress Control Number: 2019933290

© Springer Science+Business Media, LLC, part of Springer Nature 2019

This work is subject to copyright. All rights are reserved by the Publisher, whether the whole or part of the material is concerned, specifically the rights of translation, reprinting, reuse of illustrations, recitation, broadcasting, reproduction on microfilms or in any other physical way, and transmission or information storage and retrieval, electronic adaptation, computer software, or by similar or dissimilar methodology now known or hereafter developed.

The use of general descriptive names, registered names, trademarks, service marks, etc. in this publication does not imply, even in the absence of a specific statement, that such names are exempt from the relevant protective laws and regulations and therefore free for general use.

The publisher, the authors, and the editors are safe to assume that the advice and information in this book are believed to be true and accurate at the date of publication. Neither the publisher nor the authors or the editors give a warranty, express or implied, with respect to the material contained herein or for any errors or omissions that may have been made. The publisher remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Cover illustration: This image represents detection of neuropeptides in human cerebral spinal fluid. Cover Image courtesy of Dr. Terry M. Phillips.

This Humana Press imprint is published by the registered company Springer Science+Business Media, LLC part of Springer Nature.

The registered company address is: 233 Spring Street, New York, NY 10013, U.S.A.

Preface

It is over 30 years since I purchased my first capillary electrophoresis (CE) instrument with the purpose of applying it to clinical analysis, and since that time, it has been very gratifying to see the increased use of this versatile technique in clinically relevant studies. CE is a rapid technique capable of performing complex analyses of a number of different molecular species ranging from small inorganic ions to large nucleic acid fragments and proteins. Perhaps the greatest attribute of this technique is its consumption of minute samples (from 1 μL and less). This coupled with extreme sensitivity, depending upon the type of detector, has led to CE being applied to numerous different fields ranging from analytical chemistry and pharmaceutical analysis to molecular biology and proteomics.

The past two decades have shown an increase in CE applications, especially in the clinical sciences where there has been a need for the introduction of rapid, accurate technologies capable of measuring specific analytes in complex biological matrices. CE is a powerful and often rapid tool for performing such analyses, being capable of measuring a number of different molecular species. CE is becoming established as a useful tool in clinical medicine due to several factors, namely, its small sample requirement, low reagent costs, and—depending upon the detection system (LIF, electrochemical, or mass spectrometers)—high sensitivity. Additionally, many CE analyses can be rapidly performed: a strong advantage in diagnostic situations where time can be of the essence. Further, new trends in chip-based CE systems offer clinical analysis, further reduction in sample consumption, and faster analyses. These factors are essential when performing analyses on pediatric or neonatal samples. CE is now replacing many enzyme-based immunoassays because of the less likelihood of false positive and fast turnaround time. Previously published work has also indicated that CE immunoassays on fluids extracted from tissue biopsy samples can aid pathological diagnosis by adding biochemical measurements to the classical histopathology. CE and MCE have been applied to a number of different clinical fields including clinical chemistry, drug analysis and monitoring, endocrinology, hematology, bacteriology and virology, analysis of genetic disorders, pediatric and neonatal analysis, immunology and immunoassays, urology, and nephrology.

The 19 papers that comprise this book are divided into seven parts starting with an overview of the application of CE to clinical analysis; this will be followed by the second part, which is dedicated to applications in clinical chemistry and small molecule analysis. Part three will give an example of application in drug analysis, and part four will give a further example of CE applied to metabolomics. Part five will give examples of application in pediatrics, and part six will deal with CE analysis on oncology. Finally part seven will give an example of CE analysis in virology.

In conclusion, it is intended that this book will provide a valuable source of information on the application of CE to the many different aspects of clinical medicine. The techniques described may even stimulate new research in the clinical sciences. It is hoped that the book will become a resource not only for clinical chemists but also physicians and scientists, alike, who wish to apply these techniques to diagnosis and clinical research. The techniques outlined in this book will also be useful to biomedical researchers looking for new ways to analyze small biological samples or precious archival samples at a sophisticated level.

As editor of this book, I would like to express my sincere thanks to all of the authors for their valuable contributions and the referees for their generous gift of their time and expertise in evaluating these chapters. Further, I would like to especially thank Professor John Walker, the editor-in-chief of the series, for his continuous support during the preparation of this issue. My thanks also extend to the staff members of Springer who have performed a wonderful job in producing this book.

Washington, DC, USA

Terry M. Phillips

Contents

<i>Preface</i>	<i>v</i>
<i>Contributors</i>	<i>xi</i>

PART I OVERVIEW

1 An Overview of CE in Clinical Analysis	3
<i>David S. Hage</i>	

PART II APPLICATIONS IN CLINICAL CHEMISTRY

2 Rapid and Sensitive Determination of Branched-Chain Amino Acids in Human Plasma by Capillary Electrophoresis with Contactless Conductivity Detection for Physiological Studies	15
<i>Petr Tůma</i>	
3 Monitorization of α 1-Acid Glycoprotein Deglycosylation Using SU-8 Microchips Electrophoresis with LIF Detection	25
<i>María del Mar Barrios-Romero, Agustín G. Crevillén, Angel Puerta, Mercedes de Frutos, and José Carlos Díez-Masa</i>	
4 Glycoform Analysis of Alpha ₁ -Acid Glycoprotein by Capillary Electrophoresis Using Electrophoretic Injection	41
<i>Chenhua Zhang, William Clarke, and David S. Hage</i>	
5 On-Line Immunoaffinity Solid-Phase Extraction Capillary Electrophoresis-Mass Spectrometry for the Analysis of Serum Transthyretin	57
<i>Roger Pero-Gascon, Laura Pont, Victoria Sanz-Nebot, and Fernando Benavente</i>	
6 Measurement of Neutral and Sialylated IgG N-Glycome at Asn-297 by CE-LIF to Assess Hypogalactosylation in Rheumatoid Arthritis	77
<i>Christian Schwedler and Véronique Blanchard</i>	
7 The Control of Glucose and Lactate Levels in Nutrient Medium After Cell Incubation and in Microdialysates of Human Adipose Tissue by Capillary Electrophoresis with Contactless Conductivity Detection	95
<i>Petr Tůma</i>	
8 Flow-Induced Dispersion Analysis (FIDA) for Protein Quantification and Characterization	109
<i>Morten E. Pedersen, Jesper Østergaard, and Henrik Jensen</i>	

PART III APPLICATION IN DRUG ANALYSIS

- 9 A Chiral Generic Strategy for Enantioseparation of Acidic and Basic Drugs Using Short End Injection Capillary Electrophoresis: Application to Design of Experiment 127
Hassan Y. Aboul-Encin and Ahmed M. Abdel-Megied

PART IV APPLICATION IN METABOLOMICS

- 10 New Advances for Newborn Screening of Inborn Errors of Metabolism by Capillary Electrophoresis-Mass Spectrometry (CE-MS) 139
Meera Shanmuganathan and Philip Britz-McKibbin
- 11 Capillary Electrophoresis-Mass Spectrometry for Metabolic Profiling of Biomass-Limited Sample 165
Wei Zhang, Thomas Hankemeier, and Rawi Ramautar

PART V APPLICATIONS IN PAEDIATRICS

- 12 Device Fabrication and Fluorescent Labeling of Preterm Birth Biomarkers for Microchip Electrophoresis 175
Anna V. Nielsen and Adam T. Woolley
- 13 Analysis of Inflammatory Mediators in Newborn Dried Blood Spot Samples by Chip-Based Immunoaffinity Capillary Electrophoresis 185
Terry M. Phillips and Edward F. Wellner
- 14 Triplet-Repeat Primed PCR and Capillary Electrophoresis for Characterizing the Fragile X Mental Retardation 1 CGG Repeat Hyperexpansions 199
Indhu-Shree Rajan-Babu and Samuel S. Chong

PART VI APPLICATIONS IN ONCOLOGY

- 15 A Capillary Electrophoresis UV Detection-Based Method for Global Genomic DNA Methylation Assessment in Human Whole Blood 213
Angelo Zinellu, Elisabetta Sotgiu, Salvatore Sotgia, and Ciriaco Carru
- 16 Capillary Electrophoresis Analysis of Prostate-Specific Antigen (PSA) 221
Noemi Farina-Gomez, Diana Navarro-Calderon, Angel Puerta, Monica Gonzalez, José Carlos Diez-Masa, and Mercedes de Frutos
- 17 Prostate Protein N-Glycosylation Profiling by Means of DNA Sequencer-Assisted Fluorophore-Assisted Carbohydrate Electrophoresis 235
Tijl Vermassen, Nico Callewaert, Sylvie Rottey, and Joris R. Delanghe
- 18 Aptamer-Based Microchip Electrophoresis Assays for Amplification Detection of Carcinoembryonic Antigen 251
Shulin Zhao

PART VII APPLICATION IN VIROLOGY

19 Highly Sensitive SDS Capillary Gel Electrophoresis with Sample Stacking Requiring Only Nanograms of Adeno-Associated Virus Capsid Proteins..... 263
Chao-Xuan Zhang and Michael M. Meagher

Index 271

Contributors

- AHMED M. ABDEL-MEGIED • *Pharmaceutical Analytical Chemistry Department, Faculty of Pharmacy and Pharmaceutical Manufacturing, Kafrelsheikh University, Kafrelsheikh City, Egypt*
- HASSAN Y. ABOUL-ENEIN • *Pharmaceutical and Medicinal Chemistry Department, Pharmaceutical and Drug Industries Research Division, National Research Center, Dokki, Cairo, Egypt*
- FERNANDO BENAVENTE • *Department of Chemical Engineering and Analytical Chemistry, Institute for Research on Nutrition and Food Safety (INSA-UB), University of Barcelona, Barcelona, Spain*
- VÉRONIQUE BLANCHARD • *Charité—Universitätsmedizin Berlin, Campus Virchow Klinikum, Institut für Laboratoriumsmedizin, Klinische Chemie und Pathobiochemie, Berlin, Germany*
- PHILIP BRITZ-McKIBBIN • *Department of Chemistry and Chemical Biology, McMaster University, Hamilton, ON, Canada*
- NICO CALLEWAERT • *Center for Medical Biotechnology, VIB, Ghent, Belgium*
- CIRIACO CARRU • *Department of Biomedical Sciences, University of Sassari, Sassari, Italy*
- SAMUEL S. CHONG • *Department of Pediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore; Khoo Teck Puat—National University Children's Medical Institute, National University Health System, Singapore, Singapore; Department of Laboratory Medicine, National University Hospital, Singapore, Singapore*
- WILLIAM CLARKE • *Johns Hopkins University School of Medicine, Baltimore, MD, USA*
- AGUSTÍN G. CREVILLÉN • *Institute of Organic Chemistry (IQOG-CSIC), Madrid, Spain; Science Faculty—UNED, Madrid, Spain*
- MERCEDES DE FRUTOS • *Institute of Organic Chemistry (IQOG-CSIC), Madrid, Spain*
- JORIS R. DELANGHE • *Department of Clinical Chemistry, Microbiology and Immunology, Ghent University, Ghent, Belgium*
- MARÍA DEL MAR BARRIOS-ROMERO • *Institute of Organic Chemistry (IQOG-CSIC), Madrid, Spain*
- JOSÉ CARLOS DIEZ-MASA • *Institute of Organic Chemistry (IQOG-CSIC), Madrid, Spain*
- NOEMI FARINA-GOMEZ • *Institute of Organic Chemistry (IQOG-CSIC), Madrid, Spain*
- MONICA GONZALEZ • *Institute of Organic Chemistry (IQOG-CSIC), Madrid, Spain*
- DAVID S. HAGE • *Department of Chemistry, University of Nebraska, Lincoln, NE, USA*
- THOMAS HANKEMEIER • *Biomedical Microscale Analytics, Leiden Academic Center for Drug Research, Leiden University, Leiden, The Netherlands*
- HENRIK JENSEN • *FIDA-Tech Aps, C/O University of Copenhagen, Copenhagen, Denmark; Department of Pharmacy, University of Copenhagen, Copenhagen, Denmark*
- MICHAEL M. MEAGHER • *Department of Therapeutics Production and Quality, St. Jude Children's Research Hospital, Memphis, TN, USA*
- DIANA NAVARRO-CALDERON • *Institute of Organic Chemistry (IQOG-CSIC), Madrid, Spain*
- ANNA V. NIELSEN • *Department of Chemistry and Biochemistry, Brigham Young University, Provo, UT, USA*
- JESPER ØSTERGAARD • *FIDA-Tech Aps, C/O University of Copenhagen, Copenhagen, Denmark; Department of Pharmacy, University of Copenhagen, Copenhagen, Denmark*

- MORTEN E. PEDERSEN • *FIDA-Tech Aps, C/O University of Copenhagen, Copenhagen, Denmark*
- ROGER PERO-GASCON • *Department of Chemical Engineering and Analytical Chemistry, Institute for Research on Nutrition and Food Safety (INSA-UB), University of Barcelona, Barcelona, Spain*
- TERRY M. PHILLIPS • *Department of Pharmaceutics, School of Pharmacy, Virginia Commonwealth University, Richmond, VA, USA; Department of Pharmaceutics, VCU, Washington, DC, USA*
- LAURA PONT • *Department of Chemical Engineering and Analytical Chemistry, Institute for Research on Nutrition and Food Safety (INSA-UB), University of Barcelona, Barcelona, Spain*
- ANGEL PUERTA • *Institute of Organic Chemistry (IQOG-CSIC), Madrid, Spain*
- INDHU-SHREE RAJAN-BABU • *Department of Pediatrics, Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore; Department of Medical Genetics, The University of British Columbia, Vancouver, BC, Canada*
- RAWI RAMAUTAR • *Biomedical Microscale Analytics, Leiden Academic Center for Drug Research, Leiden University, Leiden, The Netherlands*
- SYLVIE ROTTEY • *Department of Medical Oncology, Ghent University Hospital, Ghent, Belgium; Drug Research Unit Ghent, Ghent University Hospital, Ghent, Belgium*
- VICTORIA SANZ-NEBOT • *Department of Chemical Engineering and Analytical Chemistry, Institute for Research on Nutrition and Food Safety (INSA-UB), University of Barcelona, Barcelona, Spain*
- CHRISTIAN SCHWEDLER • *Charité—Universitätsmedizin Berlin, Campus Virchow Klinikum, Institut für Laboratoriumsmedizin, Klinische Chemie und Pathobiochemie, Berlin, Germany*
- MEERA SHANMUGANATHAN • *Department of Chemistry and Chemical Biology, McMaster University, Hamilton, ON, Canada*
- SALVATORE SOTGIA • *Department of Biomedical Sciences, University of Sassari, Sassari, Italy*
- ELISABETTA SOTGIU • *Department of Biomedical Sciences, University of Sassari, Sassari, Italy*
- PETR TŮMA • *Department of Hygiene, Third Faculty of Medicine, Charles University, Prague, Czech Republic*
- TIJL VERMASSEN • *Department of Medical Oncology, Ghent University Hospital, Ghent, Belgium; Drug Research Unit Ghent, Ghent University Hospital, Ghent, Belgium*
- EDWARD F. WELLNER • *National Institute of Bioimaging and Bioengineering, National Institutes of Health, Bethesda, MD, USA*
- ADAM T. WOOLLEY • *Department of Chemistry and Biochemistry, Brigham Young University, Provo, UT, USA*
- CHAO-XUAN ZHANG • *Department of Therapeutics Production and Quality, St. Jude Children's Research Hospital, Memphis, TN, USA*
- CHENHUA ZHANG • *Department of Chemistry, University of Nebraska, Lincoln, NE, USA*
- WEI ZHANG • *Biomedical Microscale Analytics, Leiden Academic Center for Drug Research, Leiden University, Leiden, The Netherlands*
- SHULIN ZHAO • *Key Laboratory for the Chemistry and Molecular Engineering of Medicinal Resources, College of Chemistry and Pharmacy, Guangxi Normal University, Guilin, China*
- ANGELO ZINELLU • *Department of Biomedical Sciences, University of Sassari, Sassari, Italy*