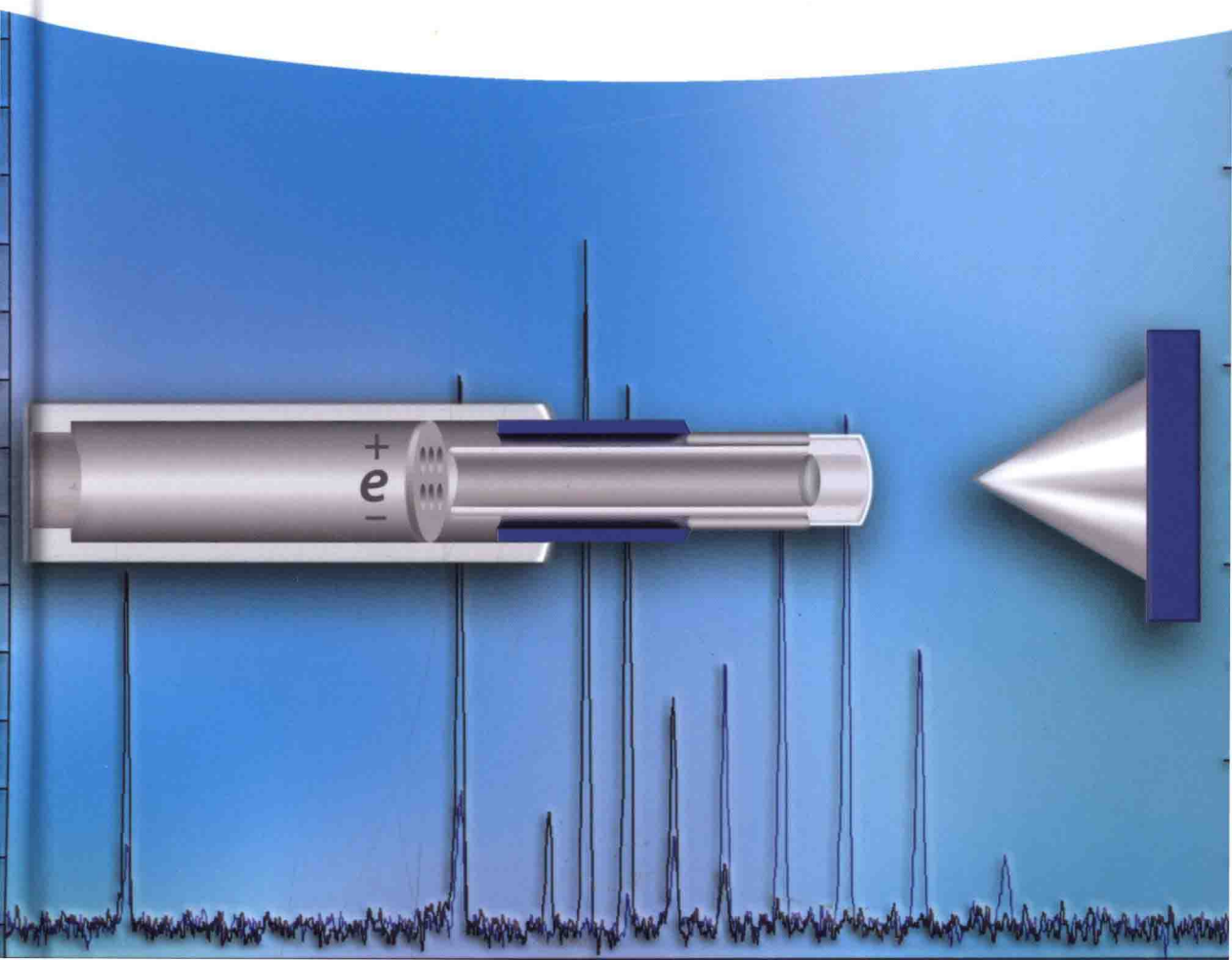


Edited by  
Yiyang Dong

# Direct Analysis in Real Time Mass Spectrometry

Principles and Practices of DART-MS



**D**ART-MS is a relatively new, but very fast evolving technology. The book provides an introduction to the technique and includes a thorough discussion of the ionization mechanism as well as sampling and analyte enrichment strategies. Due to its versatility of the technique, DART-MS is an important analytical technique in many fields. The book includes applications in agro-products analysis, clinical and pharmacological analysis as well as environmental contaminants analysis.



***Yiyang Dong** is director of Food Safety & Risk Assessment Laboratory and full professor of chemistry at Beijing University of Chemical Technology (BUCT) in Beijing, China. Having obtained his PhD from Peking University in 1998 and pursued a postdoctoral position in the University of Tokyo, Japan in 2011, he spent most of his career working for Chinese Academy of Inspection and Quarantine before taking up his present appointment at BUCT. He authored over 100 scientific publications in analytical and bio-analytical fields using capillary electrophoresis, liquid chromatography, microfluidics and biosensors with mass spectrometric identification. He is frequently invited as peer reviewer for journals such as Biosensors and Bioelectronics, Analyst, Analytical Methods, and Journal of Molecular Recognition.*

**Dong (Ed.)**

**Direct Analysis in Real Time  
Mass Spectrometry**

**WILEY**

# **Direct Analysis in Real Time Mass Spectrometry**

Principles and Practices of DART-MS

*Edited by Yiyang Dong*

**WILEY-VCH**

## Editor

### **Prof. Yiyang Dong**

Beijing University of Chemical  
Technology  
College of Life Science and Technology  
No.15 Beisanhuan East Road  
Chaoyang District  
100029 Beijing  
China

■ All books published by **Wiley-VCH** are carefully produced. Nevertheless, authors, editors, and publisher do not warrant the information contained in these books, including this book, to be free of errors. Readers are advised to keep in mind that statements, data, illustrations, procedural details or other items may inadvertently be inaccurate.

**Library of Congress Card No.:** applied for

### **British Library Cataloguing-in-Publication Data**

A catalogue record for this book is available from the British Library.

### **Bibliographic information published by the Deutsche Nationalbibliothek**

The Deutsche Nationalbibliothek lists this publication in the Deutsche Nationalbibliografie; detailed bibliographic data are available on the Internet at <<http://dnb.d-nb.de>>.

© 2018 Wiley-VCH Verlag GmbH & Co. KGaA, Boschstr. 12, 69469 Weinheim, Germany

All rights reserved (including those of translation into other languages). No part of this book may be reproduced in any form – by photoprinting, microfilm, or any other means – nor transmitted or translated into a machine language without written permission from the publishers. Registered names, trademarks, etc. used in this book, even when not specifically marked as such, are not to be considered unprotected by law.

**Print ISBN:** 978-3-527-34184-9

**ePDF ISBN:** 978-3-527-80373-6

**ePub ISBN:** 978-3-527-80371-2

**Mobi ISBN:** 978-3-527-80372-9

**oBook ISBN:** 978-3-527-80370-5

**Cover Design** Adam-Design, Weinheim, Germany

**Typesetting** SPi Global, Chennai, India

**Printing and Binding** C.O.S. Printers Pte Ltd  
Singapore

Printed on acid-free paper

10 9 8 7 6 5 4 3 2 1

**Direct Analysis in Real Time Mass Spectrometry**



*I dedicate this book to my beloved parents, Yuante Tung and Shuchen Hsu.  
I am best endowed with your love, goodness, honesty, wisdom, endeavors, and  
perseverance; for that, thank you so much.*







## Preface

All the authors who have contributed to this book have tried to describe that direct analysis in real time (DART), as a representative ambient ionization technique initiated by Penning ionization of atmosphere or electron emission from surfaces, has developed into a potential analytical tool from a mechanistic perspective for various applications.

In Chapter 1, the evolution of mass spectrometry and its role in contemporary analytical chemistry have been reviewed, desorption/ionization in mass spectrometry is discussed, and ambient ionization and DART are briefly introduced. In Chapter 2, the principle of DART and ionization mechanisms are well depicted.

In Chapter 3, to overcome DART limitations in terms of sample uniformity, ionization energy and efficiency, sample preparation and analyte-enrichment strategies are provided. In Chapter 4, parameters that influence DART-MS performance are summarized to optimize and quantitate analytes with improved sensitivity and accuracy. To further extend analytical capabilities, interfacing TLC, GC, HPLC, CE, SPR, and IMS with DART-MS has been realized and summarized in Chapter 5 systematically.

Abundant DART-MS applications for foods/agro-products, industrial chemicals, environmental contaminants, pharmaceuticals, clinical/pharmacological analysis, natural phytochemical research, and relevant DART-MS reports are comprehensively presented in Chapters 6–12, respectively. In Chapter 13, inherent limitations of DART-MS are thoroughly investigated. In addition, comparisons for DART with other ambient ion sources are made. Furthermore, some prospective applications, such as DART with high resolution MS, instrumental automation and miniaturization, surface scanning and imaging, and so on, are rather promising and encouraging.

I hope both analytical experts and novice investigators will find this book very useful, and acknowledge all the authors who have contributed to this book with great appreciation thereof.

Oct 8th, 2017  
Beijing University of Chemical Technology  
China

*Yiyang Dong*



## About the Editor



*Yiyang Dong, PhD*

**Yiyang Dong** obtained his bachelor's degree in Chemistry in 1989 from the East China Normal University where he acquired knowledge in fundamental analytical chemistry and mass spectrometry; then he went on to pursue his postgraduate study at the Nankai University and got his master's degree in liquid chromatography. In 1995, he went to the Peking University to investigate capillary electrophoresis for chiral separation and obtained a doctorate of philosophy in separation science in 1998. He also carried out postdoctoral research at Prof. Kitamori's laboratory in the University of Tokyo, Japan, to study microfluidics and related miniaturized bioanalytical techniques and tried to hyphenate these frontier techniques with mass spectrometry (MS) for various analytical applications later.

In early 2012, Dong joined the Beijing University of Chemical Technology (BUCT) as a full professor of Chemistry through a talent program and set up a research laboratory for food safety analysis and risk assessment, where he developed mass spectrometric and several facile bioanalytical methodologies for fast identification of small molecular adulterants, additives, and functional ingredients in various food matrices. It was here that his interest in direct analysis in real time (DART) and other ambient ionization strategies began with a cooperatively gelivable investigator Professor Wei Yong from the Chinese Academy of Inspection and Quarantine (CAIQ).

This research interest continued when Dong's graduate students Tianyang Guo and Pingping Fang began to participate in relevant DART research projects. Recent years have witnessed a broad utilization of DART in various research fields to introduce DART with representative analytical applications; he is therefore pleased to be the editor of this book on MS and feels happy to share with the audience the state of the art.



## Contents

Preface *xv*

About the Editor *xvii*

|          |  |           |
|----------|--|-----------|
| <b>1</b> | <b>Introduction of Mass Spectrometry and Ambient Ionization Techniques</b>                 | <b>1</b>  |
|          | <i>Yiyang Dong, Jiahui Liu, and Tianyang Guo</i>   |           |
| 1.1      | Evolution of Analytical Chemistry and Its Challenges in the Twenty-First Century           | 1         |
| 1.2      | Historical Overview of Mass Spectrometry and Its Role in Contemporary Analytical Chemistry | 5         |
| 1.3      | Desorption/Ionization in Mass Spectrometry   | 12        |
| 1.3.1    | Electronic Ionization (EI)   | 13        |
| 1.3.2    | Chemical Ionization (CI)   | 14        |
| 1.3.3    | Fast Atom/Ion Bombardment Ionization (FAB)   | 15        |
| 1.3.4    | Electrospray Ionization (ESI)  | 16        |
| 1.3.5    | Matrix Assisted Laser Desorption/Ionization (MALDI)  | 18        |
| 1.3.6    | Field Desorption (FD) or Field Ionization (FI)   | 19        |
| 1.3.7    | Plasma Desorption (PD) (ICP, LTP, DART)  | 19        |
| 1.4      | Ambient Ionization and Direct Analysis in Real Time  | 21        |
| 1.4.1    | Ambient Ionization   | 21        |
| 1.4.2    | Direct Analysis in Real Time   | 24        |
| 1.4.2.1  | Mechanisms   | 24        |
| 1.4.2.2  | Parameters   | 27        |
| 1.4.2.3  | Devices  | 29        |
|          | References   | 30        |
| <b>2</b> | <b>DART Mass Spectrometry: Principle and Ionization Facilities</b>                         | <b>43</b> |
|          | <i>David Rondeau</i>   |           |
| 2.1      | Introduction   | 43        |
| 2.2      | Metastable Gas Stream Formation  | 43        |
| 2.3      | Ionization Mechanisms in Positive DART   | 45        |
| 2.3.1    | Generation of Primary Ions by Ambient Air Ionization                                       | 46        |
| 2.3.2    | Formation of the Protonated Molecules  | 50        |

|          |   |           |
|----------|---|-----------|
| 2.3.3    | Formation of the Ammonium Adducts                                   | 54        |
| 2.3.4    | Formation of the Radical Cations and Their Fragments                | 55        |
| 2.3.5    | Matrix Effects in DART Due to Sample Solvents                       | 59        |
| 2.4      | Ionization Mechanisms in Negative DART                              | 65        |
| 2.4.1    | Generation of Primary Ions by Ambient Air Ionization                | 65        |
| 2.4.2    | Formation of Deprotonated Molecules                                 | 68        |
| 2.4.3    | Formation of Radical Anions   | 69        |
| 2.4.4    | Formation of Anionic Adducts  | 70        |
| 2.5      | Some Parameters Affecting the DART Mass Spectra                     | 71        |
| 2.5.1    | Substitution of Helium by Nitrogen or Argon                         | 71        |
| 2.5.2    | The Temperature of the Gas Stream                                   | 75        |
| 2.5.3    | The Internal Energy of Ions in DART-MS                              | 76        |
| 2.6      | Conclusion  | 78        |
|          | References  | 78        |
| <b>3</b> | <b>Sampling and Analyte Enrichment Strategies for DART-MS</b>       | <b>81</b> |
|          | <i>Wen Ma, Xianjiang Li, and Huwei Liu</i>                          |           |
| 3.1      | Dilution Strategy for Sticky Sample Analysis                        | 81        |
| 3.2      | Purification Strategy for Eliminating the Matrix Interference       | 82        |
| 3.2.1    | Liquid Phase Extraction   | 82        |
| 3.2.2    | Solid Phase Extraction (SPE)  | 86        |
| 3.2.3    | Solid Phase Microextraction (SPME)                                  | 87        |
| 3.3      | Derivatization Strategy to Decrease Polarity and Enhance Volatility | 89        |
| 3.4      | Conclusions   | 91        |
|          | References  | 91        |
| <b>4</b> | <b>Optimization of DART and Mass Spectrometric Parameters</b>       | <b>97</b> |
|          | <i>Guohua Wu and Wushuang Li</i>                                    |           |
| 4.1      | Introduction  | 97        |
| 4.2      | Effect of Working Gas Type, Gas Flow Rate, and Its Temperature      | 98        |
| 4.2.1    | Gas Type  | 98        |
| 4.2.2    | Gas Flow Rate   | 99        |
| 4.2.3    | The Working Gas Temperature of DART Ionization Source               | 100       |
| 4.3      | Effects of Grid Electrode Voltage and Sampling Speed                | 102       |
| 4.3.1    | Effect of Grid Electrode Voltage                                    | 102       |
| 4.3.2    | Effect of Sampling Speed  | 103       |
| 4.4      | Effect of the Sampling Mode   | 104       |
| 4.4.1    | Sampling Methods  | 104       |
| 4.4.2    | Position and Angle of the DART Ion Source                           | 105       |
| 4.5      | Effect of Ion Mode  | 106       |
| 4.6      | Effect of Solvent Type and Reagents                                 | 108       |
| 4.7      | Summary   | 109       |
|          | References  | 109       |

|              |  |                |
|--------------|--|----------------|
| <b>5</b>     | <b>Interfacing DART to Extend Analytical Capabilities</b>                            | <b>115</b>     |
|              | <i>Yiding Zhang, Shuting Xu, and Yu Bai</i>  |                |
| 5.1          | Introduction   | 115            |
| 5.2          | Interfacing DART with Different Separation Techniques                                | 116            |
| 5.2.1        | Solid Samples  | 116            |
| 5.2.2        | Gaseous Samples  | 118            |
| 5.2.3        | Liquid Samples   | 119            |
| 5.2.3.1      | Liquid Chromatography  | 119            |
| 5.2.3.2      | Capillary Electrophoresis  | 123            |
| 5.3          | Techniques of Interfacing DART with Other Analytical Techniques                      | 125            |
| 5.3.1        | Surface Plasmon Resonance  | 125            |
| 5.3.2        | Ion Mobility Spectrometry  | 126            |
| 5.4          | Conclusion and Perspectives  | 129            |
|              | References   | 129            |
| <br><b>6</b> | <br><b>Application of DART-MS in Foods and Agro-Products Analysis</b>                | <br><b>133</b> |
|              | <i>Canping Pan and Lei Wang</i>  |                |
| 6.1          | Introduction   | 133            |
| 6.2          | Applications of DART-MS in Agriculture and Food Science                              | 134            |
| 6.2.1        | DART-MS in Pesticide Residue Analysis  | 134            |
| 6.2.1.1      | Fast Screening Purposes  | 134            |
| 6.2.1.2      | Screening Highly Hazardous Pesticides in Agrochemical Formulations                   | 140            |
| 6.2.1.3      | Quantitative MRM Residue Method  | 147            |
| 6.2.2        | Veterinary Drug Residue Detection  | 148            |
| 6.2.3        | Fast Detection of Melamine in Milk   | 149            |
| 6.2.4        | Detection of Mycotoxins in Cereals   | 150            |
| 6.2.5        | Food Component Rapid Analysis  | 151            |
| 6.2.6        | Contaminations in Food Contact Materials (FCMs)                                      | 156            |
| 6.3          | Conclusion   | 156            |
|              | References   | 157            |
| <br><b>7</b> | <br><b>Application of DART-MS for Industrial Chemical Analysis</b>                   | <br><b>163</b> |
|              | <i>Qiang Ma</i>  |                |
| 7.1          | Application on Household Items   | 163            |
| 7.1.1        | Polydimethylsiloxane (PDMS) Analysis in Articles for Daily Use                       | 163            |
| 7.1.2        | Identification of Sulfides in Drywall  | 165            |
| 7.1.3        | Phosphoric Acid Esters Screening in Aqueous Samples                                  | 168            |
| 7.2          | Application on Food Packaging Safety and Quality Control                             | 172            |
| 7.2.1        | Identification of PDMS in Food Packaging Materials                                   | 172            |
| 7.2.2        | Identification of Polymer Additives in Food and Food Packaging                       | 175            |
| 7.2.3        | Identification of Residue Primary Aromatic Amines (PAAs) in Food Packaging Materials | 176            |
| 7.3          | Application on Pharmaceutical Products   | 177            |
| 7.3.1        | Toxic Glycols Identification   | 177            |



|          |  |            |
|----------|--|------------|
| 7.3.2    | Identification of Active Ingredients in Chinese Herbal Medicines   | 179        |
| 7.4      | Application on Cosmetics Quality Control   | 182        |
| 7.4.1    | Screening of Glucocorticoids Illegal Addition  | 182        |
| 7.5      | Application on Other Industrial Chemical Fields  | 184        |
| 7.5.1    | Ink Discrimination on Questioned Document  | 184        |
| 7.5.2    | Ionic Liquids Identification   | 189        |
| 7.6      | Conclusions  | 190        |
|          | References   | 190        |
| <b>8</b> | <b>Application of Direct Analysis in Real Time Coupled to Mass Spectrometry (DART-MS) for the Analysis of Environmental Contaminants</b> | <b>193</b> |
|          | <i>Maxime C. Bridoux and Sébastien Schramm</i>   |            |
| 8.1      | Introduction   | 193        |
| 8.2      | Screening and Quantitative Analysis of Pesticides  | 194        |
| 8.3      | Flame Retardants DART-MS Analysis  | 204        |
| 8.3.1    | Organophosphorus Flame Retardants (OPFRs)  | 204        |
| 8.3.2    | Brominated Flame Retardants (BFRs)   | 207        |
| 8.4      | Use of DART-MS for the Analysis of Personal Care Products (PCPs)   | 210        |
| 8.4.1    | Screening of Organic UV Filters in Water   | 210        |
| 8.4.2    | Screening of Phthalic Acid Diesters  | 211        |
| 8.4.3    | HPLC-DART-MS Analysis of Parabens  | 211        |
| 8.5      | Use of DART-MS for the Analysis of Aerosols  | 212        |
| 8.5.1    | Online DART for Aerosols Analysis  | 212        |
| 8.5.2    | Offline DART Methods   | 213        |
| 8.5.3    | Advantages and Limitations of DART-MS for Aerosols Characterization  | 213        |
| 8.6      | Miscellaneous Environmental Application of DART-MS   | 214        |
| 8.7      | Conclusions  | 215        |
|          | References   | 216        |
| <b>9</b> | <b>Application of DART-MS in Clinical and Pharmacological Analysis</b>   | <b>223</b> |
|          | <i>Yue Li</i>  |            |
| 9.1      | Introduction   | 223        |
| 9.2      | Sample Preparation   | 224        |
| 9.3      | Applications of DART-MS  | 225        |
| 9.3.1    | Rapid Determination of Small Organic Compounds in Biological Samples   | 225        |
| 9.3.1.1  | Analysis of a Bitter Herbal Medicine <i>Gentiana scabra</i> Root Extract   | 225        |
| 9.3.1.2  | Simultaneous Determination of 3-Chlorotyrosine and 3-Nitrotyrosine in Human Plasma   | 226        |
| 9.3.1.3  | Rapid Screening for Methamphetamine, 3,4-Methylene-dioxymethamphetamine, and Their Metabolites in Urine                                  | 227        |