Handbook of Single-Cell Technologies

Tuhin Subhra Santra • Fan-Gang Tseng
Editors

Handbook of Single-Cell Technologies

With 296 Figures and 38 Tables

Springer

Editors
Tuhin Subhra Santra
Department of Engineering Design
Indian Institute of Technology Madras
Chennai, India

Fan-Gang Tseng
Department of Engineering and System Science
National Tsing Hua University
Hsinchu, Taiwan

ISBN 978-981-10-8952-7 ISBN 978-981-10-8953-4 (eBook)
ISBN 978-981-10-8954-1 (print and electronic bundle)
https://doi.org/10.1007/978-981-10-8953-4

This Springer imprint is published by the registered company Springer Nature Singapore Pte Ltd, part of Springer Nature.
The registered company address is: 152 Beach Road, #21-01/04 Gateway East, Singapore 189721, Singapore

Preface

The cell is the fundamental unit of biological organisms. It plays a significant role in coordinating with each other to perform systemic functions. Numerous bioanalytical techniques depend on the whole sample's analysis while performing a study on bio-entities existing in a very low concentration. Thus, the outcome of the study reflects merely an average. Though the approach is best suited for whole bio-samples (blood, saliva, urine, and other bodily fluids), where quantity is not a limiting factor, there is also increasing need for extreme small-quantity sample analysis on the single cell or subcellular level. Such needs in the case of limited number of cells, for example, circulating tumor cells (CTCs), early-stage embryos or rare cells, or even when differences among the cells in the cell population, are of interest. Despite the apparent synchrony in cellular systems, single cell analysis (SCA) is important due to its capability to reveal the environmental and developmental changes in the chemical content of individual cell. The fundamental principle of cell biology is cellular heterogeneity that arises from stochastic expression of genes, proteins, and metabolites. Thus, the natural cellular heterogeneity is manifested not only in the structure and composition of cells but also in their functionality. SCA plays an important role in the system biology, where the interactions of molecular components are studied at different molecular levels, from genome to cellular functions. Individual cell or cell organelle analysis can reveal an effect of different life conditions, surrounding environment on the genome, cell cycle, and also transcriptome, proteome, peptidome, metabolome, etc. In this respect, single-cell-omics promote system biology to investigate cellular heterogeneities and their reasons.

Initial basic techniques mainly focus on single modalities, such as DNA sequence, RNA expression, or chromatin accessibility. These technologies have yielded transformative insights into cellular development and diversity. But the cellular segregation is driven by methodological convenience and limits the ability to derive a deep understanding of the relationship between biomolecules in single cell. To understand these interactions is the key to derive deep understanding of the cellular state and remains a challenge for the field of SCA. Moreover, the availability and scale of the data sets are rapidly growing, which requires new computational methods for normalization and joint analysis across samples, even for the presence of significant batch effects or interindividual variation. Approximately, 5 years ago, flow cytometry, patch-clamping electrophysiology methods, fluorescence in situ

hybridization, and enzyme-linked immunospot assays were among few single cell molecular analysis tools available. From a given cell, most of these methods could analyze only between 1 and 3 molecules, while multicolor flow cytometry has been successful in capturing approximately 12 cell surface protein markers. This scenario is rapidly changing. Recently, single-cell sequencing technologies have been mainly led by the recent advances observed in the field of molecular biology, microfluidics, and nanotechnology. Several new technologies have emerged for the comprehensive analysis of single molecules. Some single cell methods are capable to assay about >40 secreted proteins, elements of phosphoprotein signaling pathways, and large number of cell surface markers. Even single cells genome can be analyzed at high coverage or focused, whereas transcriptome at sparse coverage at moderate or high cell statistics.

In the last two decades, due to the rapid development of sophisticated micro-/nanofluidic devices, we now have Bio-MEMS, Lab on a Chip (LOC), and micro total analysis systems (μTAS) that enable more complex manipulations of chemicals and biological agents in fluidic environments. Microfluidics methods enable single cell or molecular analysis correlated with measurement of cellular functionality. These devices permit single cell analysis within custom environment, highly controlled, or even allow nondestructive cell analysis to identify cell of interest, for example, B cells producing specific antibodies to be harvested for further use. In situ RNA profiling via sequential hybridization and proteomic analysis via ion beam profiling are the two recent tissue staining methods. These techniques enable single cell analysis within fixed and intact tissues, with multiplexing level that significantly exceeds traditional immunohistochemical staining methods. Thus, generate new types of data and which has been integrated with new computational tools. With these novel devices, technology has become a pioneer in omics analysis and an integral part of medical biotechnology, such as diagnostics, prognostics, and cancer therapy.

This book comprises eight parts broadly covering several aspects of single cell analysis using different technologies. **Part one** emphasizes in detail about single cell therapy and analysis using different physical methods such as optoporation or photoporation, mechanoporation, electroporation, and microinjection. Most of these techniques use micro-/nanofluidic devices to induce different physical energy such as optical, electrical, and mechanical stress. These energies can deform cellular membrane, create hydrophilic transient membrane pores, deliver exogenous biomolecules into cells, and perform different cellular analysis. **Part two** broadly covers micro-/nanofluidic devices design, fabrication, and their operation for cellular analysis. The devices not only perform single cell manipulation, separation, isolation, cultivation, and lysis, but also electrical, mechanical, and biochemical characterization and analysis. **Part three** covers different chemical methods for single cell analysis. The part covers in detail about liposome-mediated molecular delivery into cells, antibody discovery using single cell analysis, and antibody discovery for detection, diagnosis, and treatment of infectious diseases. Moreover, this part demonstrates high-throughput screening of antigen-specific antibody-secreting cells and secreted molecules from individual cells. This can offer a valid approach

towards understanding and treatment of various diseases, disorders, and syndromes. **Part four** elaborates in detail about single cell genomics, proteomics, transcriptomics, and high-throughput transcriptome sequencing. **Part five** demonstrates single cell analysis in system biology and biocatalysis and covers the adult bovine intervertebral disc model system, which anatomically and histologically reflects the situation in human. The primary cell lineages were repeatedly isolated from the annulus fibrosus and the nucleus pulposus tissues of bovine intervertebral disc, and the isolation was typically heterogeneous in culture. Moreover, the part covers rapid cell process, with a focus on receptor signal transduction within the cell membrane. Also, it covers how large-scale single cell assays provide an efficient route for the identification of biocatalysts with novel or improved function.

Part six broadly discusses single cell adhesion in cancer progression, single cell technologies for cancer therapy, analytical tool for single cancer cell analysis, and transmembrane receptor dynamics as biophysical markers for cancer cells analysis.

Part seven briefly emphasizes flow cytometry-based high-throughput single cell electrical characterization and single cell cytometry for the application in biology and medicine.

Part eight discusses spectrum analysis, methods, targets, imaging, and applications. The part broadly covers single cell electrophysiology, analytical techniques for single cell study in microbiology, microwave and mechanical resonators for sensing and sizing of single cells, molecular force spectroscopy to measure the physiological function of cell adhesion, mass spectrometry for single cell analysis, micro-tweezers and force microscopy techniques for single cell mechanobiological analysis, acoustic tweezers for single cell manipulation, and **single cell pull down for characterization of protein complexes.**

We hope this book will be fascinating to the readers, especially undergraduate and graduate students, and it will be efficient for scientists in academic and industrial research who are performing various aspects of single cell analysis.

Chennai, India — Tuhin Subhra Santra
Hsinchu, Taiwan — Fan-Gang Tseng
November 2021 — Editors

Contents

About the Editors

Tuhin Subhra Santra is Assistant Professor in the Department of Engineering Design at the Indian Institute of Technology Madras, India, from July 2016. He was a tenure track "Honorary Visiting Professor" at National Tsing Hua University" Taiwan from 2108 to 2020, and he was a "Visiting Professor" at the University of Cambridge, UK, in 2019. Dr. Santra received his Ph.D. degree in Bio-Nano Electro Mechanical Systems (Bio-NEMS) from National Tsing Hua University (NTHU), Taiwan, in 2013. Dr. Santra was a Postdoctoral Researcher at the California NanoSystems Institute (CNSI), University of California, Los Angeles (UCLA), USA, from 2015 to 2016. His main research areas are Bio-NEMS, MEMS, single cell technology, single molecule detection, biomedical micro-/nano devices, nanomedicine, etc. Currently, Dr. Santra is serving as a Guest Editor for Cells, Micromachines, MDPI Journals and Frontiers of Bioengineering and Biotechnology. He served as a Guest Editor for *Cells*, MDPI, in 2020; *International Journal of Molecular Sciences* (IJMS) in 2018, 2017, and 2015; *Sensors* in 2016; *Molecules* in 2016; and *Micromachines* in 2020 and 2013, among others. He was conference chair and committee member of IEEE-NEMS in 2017, 2020 and 2021.

Dr. Santra has received many honors and awards such as "DBT/Wellcome Trust India Alliance Fellowship" in 2018, Honorary Research Fellow from National Tsing Hua University, Taiwan, in 2018, Bharat Bikas Award in 2017, IEEE-NEMS best conference paper award in 2014, a silver medal from Vidyasagar University in 2004, etc. He is Editor of the book entitled *Nanomaterials and Their Biomedical Applications* by

Springer Nature, Singapore, in 2021; *Microfluidics and Bio-NEMS: Devices and Applications* by Jenny Stanford Publisher, Singapore, in 2020; and *Essential of Single Cell Analysis* Springer, Germany, in 2016, among others. He published more than 6 books, 35 SCI journals, 20 book chapters, 15 US/Taiwan/Indian patents, and 20 international conference proceedings in his research field.

Dr. Fan-Gang (kevin) Tseng received his Ph.D. degree in Mechanical Engineering from UCLA, USA, in 1998. He joined Engineering and System Department of National Tsing Hua University in 1999 and advanced to Professor in 2006. He was the Chairman of ESS Department in NTHU (2010–2013), Associate Vice President for Global Affair in NTHU (2013), a Visiting Scholar of Koch Institute of Integrated Cancer Research in MIT USA (2014–2015), and the Dean of Nuclear Science College in NTHU (2016–2017). He is currently a distinguished professor of ESS Department as well as NEMS I., and the Vice President for R&D at NTHU (2017–present), as well as a Research Fellow with Academia Sinica Taiwan (2006–present). He was elected an ASME fellow in 2014. His research interests are in the fields of BioNEMS, biosensors, micro-fluidics, tissue chips, and fuel cells. He received 60 patents, wrote 8 book chapters, and published more than 260 SCI journal papers and 400 conference technical papers. He has received several awards, including Shakelton Scholar, twice National Innovation Award, twice Outstanding in Research Award, and Mr. Wu, Da-Yo Memorial Award from MOST, Taiwan, and more than20 best papers and other awards in various international conferences and competitions. He is among the editorial board of several journals including *IJMS*, *Cells*, *Micromachines*, and *Applied Science*, and also the general co-chair for MicroTas 2018 and a board member of CBMS from 2018 to 2022.

Contributors

Mohd Ridzuan Ahmad Micro-Nano System Engineering Research Group, Division of Control and Mechatronics Engineering, School of Electrical Engineering, Faculty of Engineering, Universiti Teknologi Malaysia, Skudai, Johor, Malaysia

Pranav Ambhorkar School of Engineering, University of British Columbia, Kelowna, BC, Canada

Dian Anggraini Division of Materials Science, Nara Institute of Science and Technology, Nara, Japan

Apratim Bajpai Department of Mechanical and Aerospace Engineering, New York University, New York, NY, USA

Saumendra Bajpai Applied Mechanics, Biomedical Division, Indian Institute of Technology Madras, Chennai, Tamilnadu, India

Maniraj Bhagawati Institute of Molecular Cell Biology, University of Münster, Münster, Germany

Rohit Bhardwaj Department of Mechanical Engineering, Toyohashi University of Technology, Toyohashi, Japan

Katherine Bohn Department of Infectious Diseases and Immunology, College of Veterinary Medicine, University of Florida, Gainesville, FL, USA

Jolien Breukers Department of Biosystems – Biosensors Group, KU Leuven, Leuven, Belgium

O. T. M. Bucheli ETH Laboratory for Functional Immune Repertoire Analysis, Institute of Pharmaceutical Sciences, D-CHAB, ETH Zürich, Zürich, Switzerland

Anna Sanchez Calle Division of Molecular and Cellular Medicine, National Cancer Center Research Institute, Tokyo, Japan

Bruno P. A. Cammue Centre of Microbial and Plant Genetics, KU Leuven, Leuven, Belgium

VIB Center for Plant Systems Biology, Ghent, Belgium

Hao-Chen Chang Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli, Taiwan

Tissue Engineering and Regenerative Medicine, National Chung Hsing University, Taichung, Taiwan

Hwan-You Chang Department of Medical Science, National Tsing Hua University, Hsinchu, Taiwan

Chih-Wei Chen Department of Molecular and Cellular Biology, National Tsing Hua University, Hsinchu, Taiwan

Deyong Chen State Key Laboratory of Transducer Technology, Institute of Electronics, Chinese Academy of Sciences, Beijing, People's Republic of China

University of Chinese Academy of Sciences, Beijing, People's Republic of China

Jian Chen State Key Laboratory of Transducer Technology, Institute of Electronics, Chinese Academy of Sciences, Beijing, People's Republic of China

University of Chinese Academy of Sciences, Beijing, People's Republic of China

Weiqiang Chen Department of Biomedical Engineering, New York University, New York, NY, USA

Department of Mechanical and Aerospace Engineering, New York University, New York, NY, USA

Yu-Chih Chen Department of Electrical Engineering and Computer Science, University of Michigan, Ann Arbor, MI, USA

Forbes Institute for Cancer Discovery, University of Michigan, Ann Arbor, MI, USA

Ya-Yu Chiang Department of Mechanical Engineering, National Chung Hsing University, Taichung, Taiwan

Yehyun Choi Department of Electrical Engineering and Computer Science, University of Michigan, Ann Arbor, MI, USA

Jing Ding Department of Mechanical and Nuclear Engineering, Kansas State University, Manhattan, KS, USA

Sayan Deb Dutta Department of Biosystems Engineering, The Institute of Forest Science, Kangwon National University, Chuncheon, Republic of Korea

K. Eyer ETH Laboratory for Functional Immune Repertoire Analysis, Institute of Pharmaceutical Sciences, D-CHAB, ETH Zürich, Zürich, Switzerland

Laboratoire de Colloïdes et Matériaux Divisés (LCMD), ESPCI Paris, PSL Université, Paris, France

Shih-Kang Fan Department of Mechanical and Nuclear Engineering, Kansas State University, Manhattan, KS, USA

Keya Ganguly Department of Biosystems Engineering, Kangwon National University, Chuncheon, Republic of Korea

Reya Ganguly Chungnam National University, Daejeon, Republic of Korea

Fabrice Gielen University of Exeter, Living Systems Institute, University of Exeter, Exeter, UK

Lanqi Gong Department of Biomedical Engineering, New York University, New York, NY, USA

Harsh Gupta Department of Mechanical Engineering, Toyohashi University of Technology, Toyohashi, Japan

M. Selim Hanay Department of Mechanical Engineering, Bilkent University, Ankara, Turkey

Institute of Materials Science and Nanotechnology (UNAM), Bilkent University, Ankara, Turkey

Althea Henderson Department of Biology, Clarkson University, Potsdam, NY, USA

Sara Horta Laboratory for Thrombosis Research, IRF Life Sciences, KU Leuven Campus Kulak Kortrijk, Kortrijk, Belgium

Yoichiroh Hosokawa Division of Materials Science, Nara Institute of Science and Technology, Nara, Japan

Chia-Hsien Hsu Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli, Taiwan

Institute of Nanoengineering and Microsystems, National Tsing Hua University, Hsinchu, Taiwan

Tissue Engineering and Regenerative Medicine, National Chung Hsing University, Taichung, Taiwan

Geng-Ming Hu Department of Physics, National Taiwan Normal University, Taipei, Taiwan

Myat Noe Hsu Singapore-MIT Alliance for Research and Technology, Singapore, Singapore

Shen Hu School of Dentistry, Jonsson Comprehensive Cancer Center, University of California, Los Angeles (UCLA), Los Angeles, CA, USA

Tony Jun Huang Department of Mechanical Engineering and Material Science, Duke University, Durham, NC, USA

Satoshi Ihida Development Group, Display Device Company, Sharp Corporation, Tokyo, Japan

Seungwon Jung Department of Electrical Engineering and Computer Science, University of Michigan, Ann Arbor, MI, USA

Srabani Kar Department of Engineering Design, Indian Institute of Technology Madras, Chennai, India

Department of Electrical Engineering, University of Cambridge, Cambridge, UK

Tomoji Kawai The Institute of Scientific and Industrial Research, Osaka University, Ibaraki, Japan

Keekyoung Kim Department of Mechanical and Manufacturing Engineering, Schulich School of Engineering, University of Calgary, Calgary, AB, Canada

Biomedical Engineering Graduate Program, University of Calgary, Calgary, AB, Canada

Mirae Kim Department of Biomedical Engineering, The University of Texas at Austin, Austin, TX, USA

Peter Koltay Laboratory for MEMS Applications, Department of Microsystems Engineering-IMTEK, University of Freiburg, Freiburg, Germany

Petra Kraus Department of Biology, Clarkson University, Potsdam, NY, USA

Amogh Kumar Department of Engineering Design, Indian Institute of Technology Madras, Chennai, India

Hitendra Kumar School of Engineering, University of British Columbia, Kelowna, BC, Canada

Ching-Te Kuo Department of Mechanical and Electro-Mechanical Engineering, National Sun Yat-sen University, Kaohsiung, Taiwan

Jeroen Lammertyn Department of Biosystems – Biosensors Group, KU Leuven, Leuven, Belgium

Chang-Soo Lee Chungnam National University, Daejeon, Republic of Korea

Hsinyu Lee Department of Life Science, National Taiwan University, Taipei, Taiwan

Victor Daniel Lee Bio-Gen Inc., Tegucigalpa, Honduras

Kangning Li Department of Biology, Clarkson University, Potsdam, NY, USA

Ming Li School of Engineering, Macquarie University, Sydney, Australia

Shunbo Li College of Optoelectronic Engineering, Chongqing University, Chongqing, China

Zehao Li College of Life Sciences, Beijing University of Chemical Technology, Beijing, China

Hongyan Liang State Key Laboratory of Transducer Technology, Institute of Electronics, Chinese Academy of Sciences, Beijing, People's Republic of China

University of Chinese Academy of Sciences, Beijing, People's Republic of China

Ki-Taek Lim Department of Biosystems Engineering, The Institute of Forest Science, Kangwon National University, Chuncheon, Republic of Korea

Hung-Yu Lin NeuroSky, Inc., San Jose, CA, USA

Weikang Nicholas Lin Department of Biomedical Engineering, National University of Singapore, Singapore, Singapore

Hsin-Yi Liu Department of Pharmacy, Hsinchu National Military Hospital, Hsinchu, Taiwan

Yen-Liang Liu Master Program for Biomedical Engineering, China Medical University, Taichung, Taiwan

Research Center for Cancer Biology, China Medical University, Taichung, Taiwan

Thomas Lufkin Department of Biology, Clarkson University, Potsdam, NY, USA

Hima Manoj Department of Engineering Design, Indian Institute of Technology Madras, Chennai, India

Muhammad Asraf Mansor Micro-Nano System Engineering Research Group, Division of Control and Mechatronics Engineering, School of Electrical Engineering, Faculty of Engineering, Universiti Teknologi Malaysia, Skudai, Johor, Malaysia

Pu-Wei Mao Genomics Research Center, Academia Sinica, Taipei, Taiwan

Ninad Mehendale Department of Biosciences and Bioengineering, Indian Institute of Technology Bombay, Mumbai, Maharashtra, India

L. Mohan Department of Engineering Design, Indian Institute of Technology Madras, Chennai, India

Renee-Tyler Tan Morales Department of Biomedical Engineering, New York University, New York, NY, USA

Muniesh Muthaiyan Shanmugam Department of Life Science, National Tsing Hua University, Hsinchu, Taiwan

Buck Institute for Research on Aging, Novato, CA, USA

Moeto Nagai Department of Mechanical Engineering, Toyohashi University of Technology, Toyohashi, Japan

Cuong Q. Nguyen Department of Infectious Diseases and Immunology, College of Veterinary Medicine, University of Florida, Gainesville, FL, USA

Department of Oral Biology, College of Dentistry, University of Florida, Gainesville, FL, USA

Center of Orphaned Autoimmune Diseases, University of Florida, Gainesville, FL, USA

Zhonghua Ni School of Mechanical Engineering, and Jiangsu Key Laboratory for Design and Manufacture of Micro-Nano Biomedical Instruments, Southeast University, Nanjing, China

Takahiro Ochiya Division of Molecular and Cellular Medicine, National Cancer Center Research Institute, Tokyo, Japan

Institute of Medical Science, Tokyo Medical University, Tokyo, Japan

Nobutoshi Ota Center for Biosystems Dynamics Research (BDR), RIKEN, Osaka, Japan

Adem Ozcelik Department of Mechanical Engineering, Aydin Adnan Menderes University, Aydin, Turkey

Gaurav Pandey Department of Mechanical Engineering, Toyohashi University of Technology, Toyohashi, Japan

Shilpi Pandey Department of Biosciences and Bioengineering, Indian Institute of Technology Bombay, Mumbai, Maharashtra, India

Long Pang College of Basic Medical Science, The Shaanxi Key Laboratory of Brain Disorders, Xi'an Medical University, Xi'an, China

Dinesh K. Patel Department of Biosystems Engineering, The Institute of Forest Science, Kangwon National University, Chuncheon, Republic of Korea

Debjani Paul Department of Biosciences and Bioengineering, Indian Institute of Technology Bombay, Mumbai, Maharashtra, India

Jih-Hou Peh BSL3 core facility Laboratory, National University of Singapore, Singapore, Singapore

Michael Philippi Department of Biology/Chemistry, University of Osnabrück, Osnabrück, Germany

Center for Cellular Nanoanalytics (CellNanOs), University of Osnabrück, Osnabrück, Germany

Marta Prieto-Vila Division of Molecular and Cellular Medicine, National Cancer Center Research Institute, Tokyo, Japan

Evgeny Puchkov All-Russian Collection of Microorganisms, G.K. Skryabin Institute of Biochemistry and Physiology of Microorganisms of the Russian Academy of Sciences, Pushchino Center for Biological Research of the Russian Academy of Sciences, Pushchino, Russia

Weiyi Qian Department of Mechanical and Aerospace Engineering, New York University, New York, NY, USA

Privita Edwina Rayappan George Edwin Applied Mechanics, Biomedical Division, Indian Institute of Technology Madras, Chennai, Tamilnadu, India

Julian Riba Laboratory for MEMS Applications, Department of Microsystems Engineering-IMTEK, University of Freiburg, Freiburg, Germany

Sangjin Ryu Department of Mechanical and Materials Engineering, University of Nebraska-Lincoln, Lincoln, NE, USA

Nebraska Center for Materials and Nanoscience, University of Nebraska-Lincoln, Lincoln, NE, USA

Mahmoud Ahmed Sakr School of Engineering, University of British Columbia, Kelowna, BC, Canada

Tuhin Subhra Santra Department of Engineering Design, Indian Institute of Technology Madras, Chennai, India

Brianna L. Schroeder Department of Infectious Diseases and Immunology, College of Veterinary Medicine, University of Florida, Gainesville, FL, USA

Touyana Semenova Department of Infectious Diseases and Immunology, College of Veterinary Medicine, University of Florida, Gainesville, FL, USA

Faruk Azam Shaik Institute of Industrial Science, The University of Tokyo, Tokyo, Japan

University of Lille, Lille, France

Yigang Shen Center for Biosystems Dynamics Research (BDR), RIKEN, Osaka, Japan

Takayuki Shibata Department of Mechanical Engineering, Toyohashi University of Technology, Toyohashi, Japan

Ashwini Shinde Department of Engineering Design, Indian Institute of Technology Madras, Chennai, India

Pallavi Shinde Department of Engineering Design, Indian Institute of Technology Madras, Chennai, India

I. Sigvaldadóttir ETH Laboratory for Functional Immune Repertoire Analysis, Institute of Pharmaceutical Sciences, D-CHAB, ETH Zürich, Zürich, Switzerland

Darren Sipes Department of Biology, Clarkson University, Potsdam, NY, USA

Caroline Struyfs Centre of Microbial and Plant Genetics, KU Leuven, Leuven, Belgium

VIB Center for Plant Systems Biology, Ghent, Belgium

Shantanu Sur Department of Biology, Clarkson University, Potsdam, NY, USA

Hiroaki Suzuki Faculty of Science and Engineering, Chuo University, Tokyo, Japan

Ryou-u Takahashi Department of Cellular and Molecular Biology, Hiroshima University, Higashihiroshima, Japan

Huiwen Tan State Key Laboratory of Transducer Technology, Institute of Electronics, Chinese Academy of Sciences, Beijing, People's Republic of China

University of Chinese Academy of Sciences, Beijing, People's Republic of China

Yo Tanaka Center for Biosystems Dynamics Research (BDR), RIKEN, Osaka, Japan

Zirui Matthew Tay Singapore Immunology Network, Agency for Science, Technology and Research, Singapore, Singapore

Karin Thevissen Centre of Microbial and Plant Genetics, KU Leuven, Leuven, Belgium

Agnes Tixier-Mita Institute of Industrial Science, The University of Tokyo, Tokyo, Japan

Jie Tong Department of Mechanical and Aerospace Engineering, New York University, New York, NY, USA

Hiroshi Toshiyoshi Institute of Industrial Science, The University of Tokyo, Tokyo, Japan

Chia-Hung Dylan Tsai Department of Mechanical Engineering, National Chiao Tung University, Hsinchu, Taiwan

Fan-Gang Tseng Department of Engineering and System Science, National Tsing Hua University, Hsinchu, Taiwan

Mamiko Tsugane Faculty of Science and Engineering, Chuo University, Tokyo, Japan

Japan Society for the Promotion of Science (JSPS), Tokyo, Japan

Makusu Tsutsui The Institute of Scientific and Industrial Research, Osaka University, Ibaraki, Japan

Karen Vanhoorelbeke Laboratory for Thrombosis Research, IRF Life Sciences, KU Leuven Campus Kulak Kortrijk, Kortrijk, Belgium

Lara Varden Department of Biology, Clarkson University, Potsdam, NY, USA

Alexandria Voigt Department of Infectious Diseases and Immunology, College of Veterinary Medicine, University of Florida, Gainesville, FL, USA

Junbo Wang State Key Laboratory of Transducer Technology, Institute of Electronics, Chinese Academy of Sciences, Beijing, People's Republic of China

University of Chinese Academy of Sciences, Beijing, People's Republic of China

Takashi Washio The Institute of Scientific and Industrial Research, Osaka University, Ibaraki, Japan

Shih-Chung Wei Department of Biomedical Engineering, National University of Singapore, Singapore, Singapore

Richard Witas Department of Oral Biology, College of Dentistry, University of Florida, Gainesville, FL, USA

Min-Hsien Wu Graduate Institute of Biochemical and Biomedical Engineering, Chang Gung University, Taoyuan City, Taiwan

Nan Xiang School of Mechanical Engineering, and Jiangsu Key Laboratory for Design and Manufacture of Micro-Nano Biomedical Instruments, Southeast University, Nanjing, China

Xiangdong Xu School of Dentistry, Jonsson Comprehensive Cancer Center, University of California, Los Angeles (UCLA), Los Angeles, CA, USA

School of Public Health, Hebei Medical University, Shijiazhuang, China

Yaxiaer Yalikun Division of Materials Science, Nara Institute of Science and Technology, Nara, Japan

Center for Biosystems Dynamics Research (BDR), RIKEN, Osaka, Japan

Yusuke Yamamoto Division of Molecular and Cellular Medicine, National Cancer Center Research Institute, Tokyo, Japan

Takeshi Yanagida Institute for Materials Chemistry and Engineering, Kyushu University, Kasuga, Japan

Chuan-Feng Yeh Institute of Biomedical Engineering and Nanomedicine, National Health Research Institutes, Miaoli, Taiwan

Institute of Nanoengineering and Microsystems, National Tsing Hua University, Hsinchu, Taiwan

Rachel Yerden Department of Biology, Clarkson University, Potsdam, NY, USA

Euisik Yoon Department of Electrical Engineering and Computer Science, University of Michigan, Ann Arbor, MI, USA

Department of Biomedical Engineering, University of Michigan, Ann Arbor, MI, USA

Center for Nanomedicine, Institute for Basic Science (IBS) and Graduate Program of Nano Biomedical Engineering (Nano BME), Advanced Science Institute, Yonsei University, Seoul, South Korea

Changjiang You Department of Biology/Chemistry, University of Osnabrück, Osnabrück, Germany

Center for Cellular Nanoanalytics (CellNanOs), University of Osnabrück, Osnabrück, Germany

College of Life Sciences, Beijing University of Chemical Technology, Beijing, China

Mingde Zheng Nokia Bell Laboratories, Murray Hill, NJ, USA

Stefan Zimmermann Laboratory for MEMS Applications, Department of Microsystems Engineering-IMTEK, University of Freiburg, Freiburg, Germany