

Dissertation

Sensors and Actuators for Single Particles and Cells

ausgeführt zum Zwecke der Erlangung des
akademischen Grades eines Doktors der technischen
Wissenschaften von

Stefan Kostner

eingereicht an der Technischen Universität Wien
Fakultät für Elektrotechnik und Informationstechnik

2009

The research presented in this thesis was carried out at the Industrial Sensor Systems group of the Institute of Sensor and Actuator Systems, Vienna University of Technology, Austria.

Erstbegutachter Univ.-Prof. Dr. Michael J. Vellekoop
Vienna University of Technology, Vienna, Austria

Zweitbegutachter Univ.-Prof. Dr. Andreas Hierlemann
ETH Zürich, Basel, Switzerland

Schriftenreihe des Instituts für Sensor- und Aktuatorssysteme
Technische Universität Wien

Stefan Kostner

Sensors and Actuators for Single Particles and Cells

Shaker Verlag
Aachen 2010

Bibliographic information published by the Deutsche Nationalbibliothek

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

Zugl.: Wien, TU, Diss., 2009

Copyright Shaker Verlag 2010

All rights reserved. No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without the prior permission of the publishers.

Printed in Germany.

ISBN 978-3-8322-8838-9

ISSN 1866-1181

Shaker Verlag GmbH • P.O. BOX 101818 • D-52018 Aachen

Phone: 0049/2407/9596-0 • Telefax: 0049/2407/9596-9

Internet: www.shaker.de • e-mail: info@shaker.de

Contents

Nomenclature	ix
0.1 List of Abbreviations	ix
0.2 List of Symbols	ix
0.3 List of Variables	x
1 Introduction	1
1.1 Aspects of on-chip cell detection and analysis	4
1.2 Some remarks on the theory of microfluidics	6
1.3 Outline	8
2 Microfluidic Interfacing and Fabrication Technologies	11
2.1 Fabrication Technology	11
2.1.1 Single layer fluidic device	13
2.1.2 Double layer fluidic device	15
2.2 Microfluidic interfacing and sample introduction	15
3 Optical Sensors for Single Cells	21
3.1 Integrated Projection Cytometer	27
3.1.1 Sensor Principle	27
3.1.2 Simulation	30
3.1.3 Experimental Setup	34
3.1.4 Measurement Results	36
3.1.5 Discussion	39
3.1.6 Conclusions	39
3.2 Cytometer based on a DVD Pickup Head	41
3.2.1 Sensor Principle	42
3.2.2 Experimental Setup	46
3.2.3 Measurement Results	48
3.2.4 Conclusions	50

4 Impedance Sensor for Single Particles	53
4.1 Introduction	53
4.2 Theory of the Coulter counter	57
4.3 Detection Principle	58
4.4 Simulation of the focusing unit	60
4.5 Experimental Setup	65
4.5.1 Chip Fabrication	65
4.5.2 Electrical Readout	67
4.6 Measurement Results	69
4.7 Discussion and Conclusions	71
5 Dielectrophoresis based Separators	73
5.1 Introduction	73
5.2 Theory	76
5.3 Separation based on dielectrophoresis retention	80
5.4 Separation based on lateral DEP	84
5.5 Separation based on lateral DEP guiding	86
5.5.1 Separation Principle	86
5.5.2 Trajectory Simulation	88
5.5.3 Chip fabrication	92
5.5.4 Experimental Setup	92
5.5.5 Sample Preparation	93
5.5.6 Particle Detection Software	94
5.5.7 Experimental Results	94
5.5.8 Discussion	96
5.6 Conclusions	98
6 Conclusions and Outlook	99
6.1 The sensor systems	99
6.2 Cell and particle actuation	101
6.3 Comparison to conventional cytometers	101
6.4 Comments on device fabrication	102
6.5 Further research and industrial relevance	102
Acknowledgements	105
List of Publications	107
Bibliography	111

Summary	119
Kurzfassung	121
About the Author	123

Nomenclature

0.1 List of Abbreviations

Symbol	Description
APC	automatic power control
CCD	charge coupled device
CHO	Chinese hamster ovary
CMOS	complementary metal oxide
DEP	dielectrophoresis
DVD	digital versatile disc
FACS	fluorescent activated cell sorting
FEM	finite element model
nDEP	negative dielectrophoresis
PBS	phosphate buffered saline
PCB	printed circuit board
pDEP	positive dielectrophoresis
PMT	photomultiplier tube
SU-8	epoxy-based negative photoresist
VCM	voice coil motor

0.2 List of Symbols

Constant	Description	Unit
ε	relative permittivity	-

Constant	Description	Unit
ε_0	vacuum permittivity	$8.854 \cdot 10^{-12}$ F/m
σ	conductivity	S/m
$\Re[x]$	real part of a number x	

0.3 List of Variables

Symbol	Description	Unit
K	Clausius Mossotti factor	-
\mathbf{F}_{DEP}	dielectrophoretic force (vector)	N
R	particle radius	m
$E_{0,\text{RMS}}$	absolute value of the electric field (RMS)	V/m
$\underline{K}(\omega)$	complex Clausius Mossotti function	-
ε	complex permittivity	
f	frequency	Hz
\mathbf{F}_{drag}	drag force on a particle (vector)	N
η	viscosity	Pa·s
m	mass	kg
\mathbf{v}_l	local liquid velocity	m/s
\mathbf{v}_p	particle velocity	m/s
x, y, z	coordinates	m
$v_{p,x}, v_{p,y}, v_{p,z}$	velocity components	m/s
n	refractive index	-
κ	absorption coefficient	-
$\tilde{n} = n - j\kappa$	complex refractive index	-
λ	optical wavelength	m
FE	focus error signal	-
