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Magnetically Enhanced Microflow Cytometer for Bead- and Cell-based Immunoaffinity Measurements in Whole Blood Samples

Scientific thesis for the attainment of the academic degree
Master of Science (M.Sc.)
of the Department of Electrical and Computer Engineering
at the Technical University of Munich.

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Contents

1. Theoretical Prequisites

The main measurement principle by a GMR (Giant Magneto Resistance)-Sensor has been already described and characterized exhaustively by Helou [1], Reisbeck [2] and Brenner [3]. Therefore, this theoretical part will focus on (bio-)physical aspects of a cell rolling motion inside a microfluidic channel and surface modification chemistry.

1.1. Microfluidics

The main experiments of this work were carried out in microfluidic environments, which exhibit favorable properties compared to common turbulent systems. From a fluid-mechanical standpoint, shrinking the scales makes interfacial as well as electrokinetic phenomena much more significant, and reduces the importance of pressure and gravity.[4] However, electodynamics, chemistry and fluid dynamics are incetricably intertwined, so that fluid flow can create electric fields (and vice versa), with a degree of coupling driven by the surface chemistry. Many of the resulting phenomena arise or can explained by Cauchy-Momentum equation (eq. 1.2) an the resulting Navier-Stokes equation (eq. 1.3).

$$\nabla \cdot \mathbf{u} = 0 \tag{1.1}$$

$$\rho \frac{\partial \mathbf{u}}{\partial t} + \rho \mathbf{u} \cdot \nabla \mathbf{u} = \nabla \cdot \boldsymbol{\tau} + \sum_i \mathbf{f}_i \tag{1.2}$$

$$\rho \frac{\partial \mathbf{u}}{\partial t} + \rho \mathbf{u} \cdot \nabla \mathbf{u} = -\nabla p + \eta \nabla^2 \mathbf{u} + \sum_i \mathbf{f}_i \tag{1.3}$$

conservation of mass, momentum reynolds number

1.1.1. Flow Field inside Microchannels

The foremost characteristic of a microchannel is the laminar flow behavior, which causes deterministic pathlines, and is described by the reynolds number.

$$Re \ = \ \frac{2\rho|\overline{u}|l}{\eta} \tag{1.4}$$

Navier-Stokes-Approximation for Hagen-Poiseuille

1.1.2. Particles in Microfluidics

Stokes Drag Force Gravity Electro-static interaction Magnetic Force Friction Interface-Forces

1.1.3.

1.2. Surface Chemistry

1.2.1. Silane Chemistry

1.2.2. Carbodiimide Crosslinker Chemistry

EDC-NHS-Activation sulfo-NHS vs. NHS

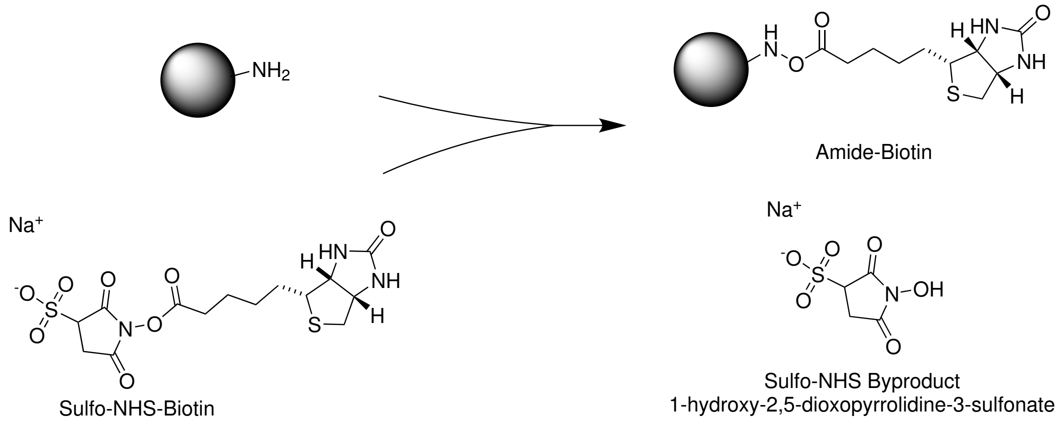

Figure 1 TestSvg

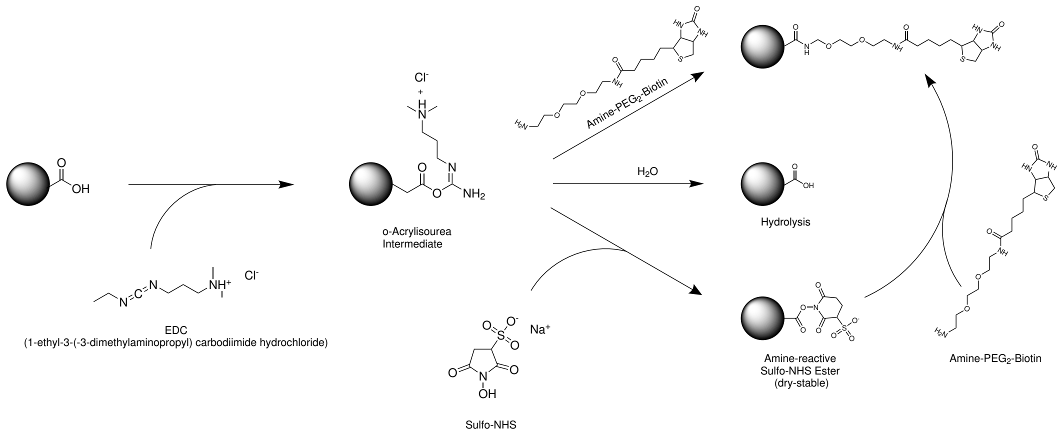

Figure 2 TestSvg

1.2.3. Microscopic Particle Surface Physics

1.2.4. The Biotin-Avidin-System

1.3. MRCyte

Short intro over MRCyte Foto of setup with arrows to necessary parts Microscope Stages PEEK holder Helmholtz coils Kepco MFLI DAQ

1.3.1. Focusing Structures

test,test Loss because of reduced velocity and magnetic drag

1.3.2. GMR

Different produced GMR stacks Wheatstone Bridge setup Magnet alignment

1.3.3. Electrical Circuit

Ground PCB Stacked PCBs with spacer

1.3.4. Electronic Readout

test,test

Hysteresis Alignment

test,test

Single GMR

test,test

Dual GMR

one MFLI supplies both at same freuqency. Aux Trigger tested, but no advantage.

List of Abbreviations

Symbols

τ - surface stress tensor

η - dynamic viscosity

ρ - density

$\sum_i \mathbf{f}_i$ - body forces

A

AAF - Artificial Anti-Ferromagnet

AcOH - Acetic Acid

AFM - Anti-Ferromagnetism

APTES - (3-aminopropyl)triethoxysilane

D

diH_2O - deionized water

E

EDC - 1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide

EtOH - Ethanol

F

FM - Ferrimagnetism

FWHM - Full Width at Half Maximum

G

GMR - Giant Magneto Resistance

GUI - Graphical User Interface

H

H_2O_2 - Hydrogen Peroxide

H_2SO_4 - Sulfuric Acid

HCl - Hydrochloric Acid

HF - Hydrofluoric Acid

I

IPA - Isopropanol..

M

MACS - MACS running buffer..

MeOH - Methanol..

MES - 2-(N-morpholino)ethanesulfonic Acid...

MNP - Magnetic Nanoparticle..

N

N_2 - Nitrogen Gas...

NFM - non-ferro-magnetic...

NHS - N-hydroxysuccinimide..

O

O_2 - Oxygen Gas...

P

PAA - Poly(acrylic) Acid...

PBS - Phosphate Buffered Saline...

PCB - Printed Circuit Board...

PDMS - Poly(dimethyl siloxane)..

Piranha - H_2O_2:H_2SO_4...

PM - Paramagnetism...

S

SiN - Silicon Nitride...

SMA - Styrene Maleic Anhydride..

SPM - Superparamagnetism...

U

u - flow field..

µF - Microfluidic...

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Bibliography

[1] M. Helou, “Magnetic flow cytometry,” PhD Thesis, 2014.

[2] M. Reisbeck, “Integration und quantitative analyse in der magnetischen durchflusszytometrie,” PhD Thesis, 2019.

[3] J. Brenner, “Superparamagnetic nanoparticles in picoliter droplets for measurements with spin valves,” Bachelor Thesis, 2018.

[4] B. Kirby, *Micro- and Nanoscale Fluid Mechanics*. 2010, ISBN: 9780511760723. DOI: 10.1017/cbo9780511760723.

[5] A. P. Guimarães, *Principles of Nanomagnetism*. Springer International Publishing, 2017. DOI: 10.1007/978-3-319-59409-5.

[6] micromod Partikeltechnologie GmbH, *Technical data sheet - nanomag®-d-spio 50nm*, 2018.

[7] M. J. Owen and P. J. Smith, “Plasma treatment of polydimethylsiloxane,” *Journal of Adhesion Science and Technology*, vol. 8, no. 10, pp. 1063–1075, 1994. DOI: 10.1163/156856194X00942.

[8] C.-G. Stefanita, *Magnetism*. Springer Berlin Heidelberg, 2012. DOI: 10.1007/978-3-642-22977-0.

[9] K. H. J. Buschow and F. R. de Boer, *Physics of Magnetism and Magnetic Materials*. Springer US, 2003. DOI: 10.1007/b100503.

[10] G. C. Papaefthymiou, “Nanoparticle magnetism,” *Nano Today*, vol. 4, no. 5, pp. 438–447, Oct. 2009. DOI: 10.1016/j.nantod.2009.08.006.

[11] P. Gravesen, J. Branebjerg, and O. S. Jensen, “Microfluidics-a review,” *Journal of Micromechanics and Microengineering*, vol. 3, no. 4, pp. 168–182, Dec. 1993. DOI: 10.1088/0960-1317/3/4/002.

[12] W. J. Dressick, C. S. Dulcey, J. H. Georger, G. S. Calabrese, and J. M. Calvert, “Covalent binding of pd catalysts to ligating self-assembled monolayer films for selective electroless metal deposition,” *Journal of the Electrochemical Society*, vol. 141, no. 1, pp. 210–220, 1994, ISSN: 0013-4651. DOI: 10.1149/1.2054686.

[13] K. C. Andree, A. M. Barradas, A. T. Nguyen, A. Mentink, I. Stojanovic, J. Baggerman, J. van Dalum, C. J. van Rijn, and L. W. Terstappen, “Capture of tumor cells on anti-epcam-functionalized poly(acrylic acid)-coated surfaces,” *ACS Appl*

Mater Interfaces, vol. 8, no. 23, pp. 14 349–56, 2016, ISSN: 1944-8252 (Electronic) 1944-8244 (Linking). DOI: 10.1021/acsami.6b01241.

[14] R. Hicsanmaz, “Setup and assessment of laser lithography for the fabrication and integration of biosensor and microfluidic devices,” Technical University Munich, 2020.

Statement

I declare that I have authored this thesis independently, that I have not used other than the declared sources / resources, and that I have explicitly marked all material which has been quoted either literally or by content from the used sources.

Munich, December 4th, 2020, Signature