Surface **M**odification of **P**oly(dimethylsiloxane) (**PDMS**) for **M**icrofluidic **D**evices

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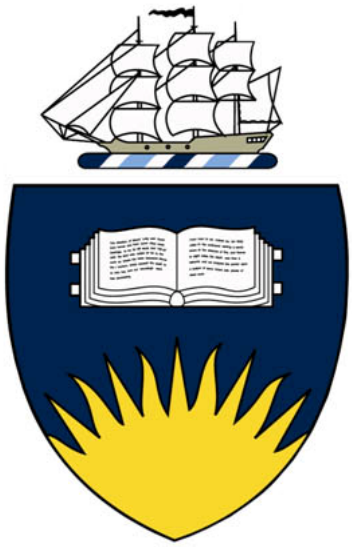

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TABLE OF CONTENTS

ABSTRACT

Poly(dimethylsiloxane) (PDMS) is a popular material for microfluidic devices due to its relatively low cost, ease of fabrication, oxygen permeability and optical transmission characteristics. However, its highly hydrophobic surface is still the main factor limiting its wide application, in particular as a material for biointerfaces. This being the case, surface modification to tailor surface properties is required to render PDMS more practical for microfluidic applications.

This thesis focuses on three different PDMS surface modification techniques, including 1) thermal assisted hydrosilylation; 2) self-assembled molecule (SAM) assisted templating and 3) a combination of Soxhlet-extraction and plasma treatment. The modified PDMS surfaces were then used for a series of analytical applications, including DNA hybridization and cocaine detection. Finally, the fabrication of native and surface modified PDMS-based microfluidic devices is also presented. The content in each chapter is outlined in the following.

In Chapter 1, a comprehensive review of recent research regarding PDMS surface modification techniques is presented, including gas-phase processes, wet-chemical methods and the combination of gas-phase and wet-chemical methods. In addition, topographical and chemically patterned PDMS is discussed, as well as examples of the application of modified PDMS surfaces in microfluidics.

Chapter 2 is the methodology chapter, which describes the three PDMS surface modification techniques used in this thesis. It also describes the fabrication process involved in the making of PDMS-based microfluidic devices. Moreover, details of the surface characterization techniques used for the analysis of the PDMS surfaces are described. These techniques include water contact angle (WCA) measurements, Fourier transform infrared-attenuated total reflection (FTIR-ATR) spectroscopy, X-ray photoelectron spectroscopy (XPS), atomic force microscopy (AFM), streaming zeta-potential analysis, electroosmotic flow (EOF) measurements and fluorescence microscopy. Experimental details for the experiments involving DNA hybridization on

modified PDMS are also described.

In Chapter 3, we report on a cheap, easy and highly repeatable PDMS surface modification method by heating pre-cured PDMS with a thin film of undecylenic acid (UDA) at 80 ºC in an oven. A hydrosilylation reaction between the UDA and the PDMS curing agent was induced during heating. The results showed the modified PDMS surfaces became more hydrophilic compared to native PDMS and showed a more or less constant WCA for up to 30 d storage in air. In addition, the stability of the modified PDMS surface was further improved by reducing the weight ratio of PDMS base and curing agent from 10:1 to 5:1.

In Chapter 4, we present a chemical modification strategy for PDMS by curing a mixture of 2 wt % UDA in PDMS prepolymer on a pretreated gold coated glass slide. The pretreatment of the gold slide was achieved by coating the gold with a self-assembled monolayer of 3-mercaptopropionic acid (MPA). During curing of the UDA/PDMS prepolymer on the MPA/gold coated slide the hydrophilic UDA carboxyl moieties diffuse towards the hydrophilic MPA carboxyl moieties on the gold surface. This diffusion of UDA within the PDMS prepolymer to the surface is a direct result of surface energy minimization. Once completely cured, the PDMS was peeled off the gold substrate, thereby exposing the interfacial carboxyl groups. These groups were then available for subsequent attachment of 5'-amino-terminated oligonucleotides *via* amide linkages. Finally, fluorescently tagged complementary oligonucleotides were successfully hybridized to this surface, as determined by fluorescence microscopy.

In Chapter 5, the surface modification of PDMS was carried out by using a 2-step plasma modification with Ar followed by acrylic acid (AAc). The stability of the modified PDMS surface was further improved by Soxhlet-extracting the PDMS with hexane prior to plasma treatment. 5´-amino-terminated oligonucleotides were covalently attached to the PAAc modified PDMS surface *via* carbodiimide coupling. Results show that the covalently tethered oligonucleotides can successfully capture fluorescein-labeled complementary oligonucleotides *via* hybridization, which were visualized using fluorescence microscopy.

In Chapter 6, we report on an optical aptamer sensor for cocaine detection by first using minor groove binder based energy transfer (MBET) technique. First, a

carboxyl-functionalized PDMS was prepared using SAM assisted templating as described in Chapter 4. A cocaine sensor was then fabricated on this carboxyl-functionalized PDMS surface by covalently immobilizing DNA aptamers *via* amide linkages. The cocaine sensitive fluorescein isothiocyanate (FITC)-labeled aptamer underwent a conformational change from partial single-stranded DNA to a double stranded T-junction in the presence of the target. The DNA minor groove binder Hoechst 33342 selectively bound to the double stranded T-junction, bringing the dye within the Förster radius of FITC. This process initiated MBET, thereby reporting on the presence of cocaine. In addition, this aptamer sensor was also implemented for cocaine detection in solution.

In Chapter 7, the fabrication of microfluidic devices based on the native PDMS and/or the modified PDMS is described. First standard soft-lithography was used to produce PDMS microchannels. Then, the sealing of the microchannels was achieved with the assistance of thermal treatment or an O_2 plasma. Finally, for the modified PDMS-based devices, the presence of reactive carboxyl groups from the initial UDA or AAc plasma treatment were verified by the immobilization of Lucifer Yellow CH dye in modified PDMS microchannels.

In Chapter 8, an overall comparison between the three different PDMS surface modification methods is provided and the future perspectives are outlined.

DECLARATION

I certify that this thesis does not incorporate without acknowledgment any material previously submitted for a degree or diploma in any university; and that to the best of my knowledge and belief it does not contain any material previously published or written by another person except where due reference is made in the text.

Signed  Date 29/11/2012

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LIST OF PUBLICATION

Papers arising from Chapter 1

1. Zhou, J. W., Ellis, A. V., Voelcker, N. H., Recent developments in poly(dimethylsiloxane) surface modification for microfluidic devices. *Electrophoresis* 2010, *31,* 2-16. http://onlinelibrary.wiley.com/doi/10.1002/elps.200900475/abstract

2. Zhou, J. W., Khodakov, D. A., Ellis, A. V., Voelcker, N. H., Surface modification for PDMS-based microfluidic devices. *Electrophoresis* 2012, *33,* 89-104. http://onlinelibrary.wiley.com/doi/10.1002/elps.201100482/abstract

Papers arising from Chapter 3

3. Zhou, J. W., McInnes, S. J. P., Mutalib Md Jani, A., Ellis, A. V., Voelcker, N. H., One-step surface modification of poly(dimethylsiloxane) by undecylenic acid. *Proceedings of SPIE* 2008, *7267 (726719)*, 1-10. http://spie.org/x648.html?product_id=810101

Papers arising from Chapter 4

4. Zhou, J. W., Voelcker, N. H., Ellis, A. V., Simple surface modification of poly(dimethylsiloxane) for DNA hybridization. *Biomicrofluidics* 2010, *4*, 046504. http://bmf.aip.org/resource/1/biomgb/v4/i4/p046504_s1

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6. Zhou, J. W., Ellis, A. V., Voelcker, N. H., Poly(dimethylsiloxane) surface modification by plasma treatment for DNA hybridization applications. *Journal of Nanoscience and Nanotechnology* 2010, *10,* 7266-7270. http://www.ingentaconnect.com/content/asp/jnn/2010/00000010/00000011/art00061

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Other papers

8. Mutalib Md Jani, A., Zhou, J. W., Nussio, M. R., Losic, D., Shapter, J. G., Voelcker, N. H., Pore spanning lipid bilayers on silanised nanoporous alumina membranes. *Proceedings of SPIE* 2008, *7267 (2670T)*, 1-10.

LIST OF ABBREVIATIONS

AA	ascorbic acid
AAc	acrylic acid
AAm	acrylamide
AFM	atomic force microscope
AHPCS	allylhydridopolycarbosilane
Ala	alanine
AMPS	2-acrylamido-2-methyl-1-propanesulfonic acid
4-AP	4-aminophenol
AP	alkaline phosphatase
APDMES	3-aminopropyldimethylethoxysilane
APTES	3-aminopropyltriethoxysilane
APTMS	3-aminopropyltrimethoxysilane
Arg	arginine
Asn	asparagine
Asp	aspartic acid
ATRP	atom transfer radical polymerization
BAS	1-butyl-3-methylimidazolium dodecanesulfonate
BGE	background electrolyte
$BMImBF_4$	1-butyl-3-methylimidazolium tetrafluoroborate
BODIPY® FL CASE	*N*-(4,4-difluoro-5,7-dimethyl-4-bora-3a,4a-diaza-s-indacen e-3propionyl)cysteic acid, succinimidyl ester
BP	benzophenone
BSA	bovine serum albumin
CAD	computer-aided design
CE	capillary electrophoresis
CEC	capillary electrochromatography
Chit	chitosan
COMOSS	collocated monolith support structure
CPTCS	3-chloropropyltrichlorosilane

CTMS	chlorotrimethylsilane
CVD	chemical vapor deposition
Cys	cysteine
3D	three dimensional
DA	dapamin
DBA	dobuamine
DDAB	didodecyldimethylammoniumbromide
DDM	n-Dodecyl-β-D-maltoside
DNA	deoxyribonucleic acid
DOC	sodium deoxycholate
dsDNA	double stranded deoxyribonucleic acid
ECM	extracellular matrix
EDAC	*N*-(3-dimethylaminopropyl)-*N´*-ethylcarbodiimide hydrochloride
EDTA	ethylenediaminetetraacetic acid
μ_{eo}	electroosmotic mobility
EOF	electroosmotic flow
EP	epinephrine
ERα	estrogen receptor α
FAM	6-carboxyfluorescein
FITC	fluorescein isothiocyanate
FRET	fluorescence resonance energy transfer
FTIR-ATR	Fourier transform infrared-attenuated total reflection
Gln	glutamine
Glu	glutamic acid
Gly	glycine
GMA	glycidyl methacrylate
GPTMS	3-glycidoxypropyltrimethoxysilane
HA	hyaluronic acid
HEPES	4-(2-hydroxyethyl)-1-piperazineethanesulfonic acid
His	histidine
HPGs	hyperbranched polyglycerols
h-PSMA	hydrolyzed poly(styrene-*co*-maleic anhydride)

HQ	hydroquinone
HSA	human serum albumin
5-HT	5-hydroxytryptamine
Ig	immunoglobulin
Ile	isoleucine
IPA	isopropyl alcohol
LBL	layer-by-layer
LPEI	linear polyethyleneimine
Lys	lysine
MA	maleic anhydride
MAAc	methacrylic acid
MALDI	matrix-assisted laser desorption/ionization
MBET	minor groove binder based energy transfer
Met	methionine
2-MP	2-mercaptopyridine
MPA	3-mercaptopropionic acid
mPEG	methyl-poly(ethylene glycol)
MPTMS	3-mercaptopropyltrimethoxysilane
MS	mass spectrometry
NHS	*N*-hydroxysuccinimide
O/W	oil-in-water
PA	phosphatidic acid
PAAc	poly(acrylic acid)
PAAm	Poly(acrylamide)
PAH	poly(aromatic hydrocarbon)
PAS	poly(4-aminostyrene)
PBS	phosphate buffered saline
PDDA	poly (diallyldimethylammonium chloride)
P(DMA-*co*-GMA)	poly(dimethylacrylamide-*co*-glycidyl methacrylate)
PDMS	poly(dimethylsiloxane)
PE	poly(ethylene)
PEG	poly(ethylene glycol)
PEGMEM	poly(ethylene glycol) methyl ether methacrylate

PEI	poly(ethyleneimine)
PEMEA	propylene glycol methyl ether acetate
PEMs	polyelectrolyte multilayers
PEO	poly(ethylene oxide)
PGA	poly(L-glutamic acid)
PGMA	poly(glycidyl methacrylate)
Phe	phenylalanine
PHMA	poly(hydromethylsiloxane)
PLLA	poly(L-lactic acid)
PMAAc	poly(methacrylic acid)
PNIPAAm	poly [*N*-isopropyl acrylamide]
P(NIPAAm-*co*-AAc)	poly(*N*-isopropyl acrylamide-*co*-acrylic acid)
p-PDA	p-phenylenediamine
PPEGMA	poly(poly(ethylene glycol)methacrylate)
PPO	poly(propylene oxide)
Pro	proline
PSCA	prostate stem cell antigenv
PSS	poly(sodium 4-styrenesulfonate)
PTX	paclitaxel
PVA	poly(vinyl alcohol)
PVA-*g*-GMA	poly(vinyl alcohol)-*g*-glycidyl methacrylate
PVC	poly(vinyl chloride)
PVP	poly(vinylpyrrolidone)
PVP-*g*-GMA	Poly(vinylpyrrolidone)-*g*-glycidyl methacrylate
QD	quantum dot
RB	rhodamine B
RGDS	Arg-Gly-Asp-Ser
RMS	root mean square
RSD	relative standard deviation
SAMs	self-assembled monolayers
SDS	sodium dodecyl sulfate
SELEX	systematic evolution of ligands by exponential enrichment
Ser	serine

SP-PCRs	solid phase-polymerase chain reactions
STB	sodium tetraborate
TAPS	*N*-tris(hydroxymethyl)methyl-3-aminopropanesulfonic acid
TBE	Tris-borate-EDTA
TEOS	tetraethyl orthosilicate
TFOS	trichloro(1H, 1H, 2H, 2H-perfluorooctyl)silane
Thr	threonine
TOF	time of flight
Tris	tris(hydroxymethyl)aminomethane
Try	tryptophan
TTE	Tris-TAPS-EDTA
Tyr	tyrosine
UDA	undecylenic acid
UV	ultraviolet
UVO	ultraviolet/ozone
Val	valine
WCA	water contact angle
W/O	water-in-oil
W/O/O	water-in-oil-in-oil
W/O/W	water-in-oil-in-water
XPS	x-ray photoelectron spectroscopy

LIST OF FIGURES

LIST OF SCHEMES

LIST OF TABLES