

University of Groningen

Molecular motors in new media

Lubbe, Anouk Sophia

IMPORTANT NOTE: You are advised to consult the publisher's version (publisher's PDF) if you wish to cite from it. Please check the document version below.

Document Version

Publisher's PDF, also known as Version of record

Publication date:
2017

[Link to publication in University of Groningen/UMCG research database](#)

Citation for published version (APA):

Lubbe, A. S. (2017). *Molecular motors in new media*. Rijksuniversiteit Groningen.

Copyright

Other than for strictly personal use, it is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), unless the work is under an open content license (like Creative Commons).

The publication may also be distributed here under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license. More information can be found on the University of Groningen website: <https://www.rug.nl/library/open-access/self-archiving-pure/taverne-amendment>.

Take-down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

Downloaded from the University of Groningen/UMCG research database (Pure): <http://www.rug.nl/research/portal>. For technical reasons the number of authors shown on this cover page is limited to 10 maximum.

Molecular Motors in New Media

Anouk Sophia Lubbe

Molecular Motors in New Media

Anouk Sophia Lubbe
PhD Thesis
University of Groningen

ISBN: 978-94-034-0090-7 (printed version)
978-94-034-0000-6 (electronic version)
Print: Ipkamp Drukkers B.V., Enschede, the Netherlands

Cover illustration by Emanuelle van den Broek. Cover design by Jos Kistemaker.

The work described in this thesis was carried out at the Stratingh Institute for Chemistry, in compliance with the requirements of the Graduate School of Science (Faculty of Science and Engineering, University of Groningen).



**university of
groningen**

**faculty of science
and engineering**

The work was financially supported by the Royal Netherlands Academy of Arts and Sciences (KNAW).



K O N I N K L I J K E N E D E R L A N D S E
A K A D E M I E V A N W E T E N S C H A P P E N



rijksuniversiteit
groningen

Molecular Motors in New Media

Proefschrift

ter verkrijging van de graad van doctor aan de
Rijksuniversiteit Groningen
op gezag van de
rector magnificus prof. dr. E. Sterken
en volgens besluit van het College voor Promoties.

De openbare verdediging zal plaatsvinden op

vrijdag 24 november 2017 om 16.15 uur

door

Anouk Sophia Lubbe

geboren op 26 januari 1988
te Groningen

Promotor

Prof. dr. B. L. Feringa

Copromotor

Dr. W. C. Szymanski

Beoordelingscommissie

Prof. dr. ir. A. J. Minnaard

Prof. dr. J. G. Roelfes

Prof. dr. J. Andréasson

Table of Contents

Chapter 1: Photoregulation of Oligonucleotide Structure and Function	1
1.1 Introduction	2
<i>1.1.1 Overview of photoswitches used for oligonucleotide regulation</i>	<i>3</i>
<i>1.1.1.1 Azobenzenes</i>	<i>3</i>
<i>1.1.1.2 Stilbenes</i>	<i>4</i>
<i>1.1.1.3 Diarylethenes</i>	<i>4</i>
<i>1.1.1.4 Spiropyrans</i>	<i>5</i>
<i>1.1.2 Overview of the photoswitch incorporation strategies</i>	<i>5</i>
<i>1.1.3 Analytical methods</i>	<i>7</i>
1.2 Molecular photoswitches as nucleoside surrogates	8
<i>1.2.1 Design</i>	<i>9</i>
<i>1.2.2 Computational studies</i>	<i>10</i>
<i>1.2.3 Photochemistry of azobenzenes as nucleoside surrogates</i>	<i>11</i>
<i>1.2.4 Effect of azobenzenes on duplex stability</i>	<i>13</i>
<i>1.2.5 Alternative molecular photoswitches for use as nucleoside surrogates</i>	<i>15</i>
<i>1.2.6 Biological applications</i>	<i>16</i>
<i>1.2.6.1 Transcription</i>	<i>16</i>
<i>1.2.6.2 Strand displacement at physiological temperature</i>	<i>17</i>
<i>1.2.6.3 DNA ligation and cleavage</i>	<i>18</i>
<i>1.2.7 Oligonucleotides for nanotechnology and materials</i>	<i>20</i>
<i>1.2.7.1 Photoswitchable annealing</i>	<i>21</i>
<i>1.2.7.2 Cargo release</i>	<i>21</i>
<i>1.2.7.3 DNA walkers</i>	<i>23</i>
<i>1.2.8 Concluding remarks</i>	<i>24</i>
1.3 Molecular photoswitches attached to nucleosides	25
<i>1.3.1 Design</i>	<i>25</i>
<i>1.3.2 Interactions between oligonucleotides and attached molecular photoswitches</i>	<i>27</i>
<i>1.3.3 Photochemistry of molecular photoswitches attached to nucleosides</i>	<i>28</i>
<i>1.3.4 Effect of photoswitches attached to nucleosides on duplex stability</i>	<i>29</i>
<i>1.3.5 Concluding remarks.</i>	<i>29</i>
1.4 Photochromic nucleosides	29
<i>1.4.1 Concluding remarks</i>	<i>31</i>

Table of Contents

<i>1.5 Photoswitches as phosphate backbone linkers</i>	31
1.5.1 Design	32
1.5.2 Computational studies	33
1.5.3 Photochemistry of molecular photoswitches as phosphate backbone linkers	34
1.5.4 Influence on hairpin stability	35
1.5.5 Applications of oligonucleotides with molecular photoswitches introduced as phosphate backbone linkers	35
1.5.6 Concluding remarks	36
<i>1.6 Noncovalent interactions between oligonucleotides and molecular photoswitches</i>	36
1.6.1 Design	37
1.6.2 Photochemistry of photoswitches complexed to oligonucleotides	40
1.6.3 Influence of supramolecular binding of photoswitches on duplex stability	42
1.6.4 Oligonucleotide condensation	43
1.6.5 Other applications for molecular photoswitches complexed to oligonucleotides	46
1.6.6 Concluding remarks	46
<i>1.7 End-capping of oligonucleotides with molecular photoswitches.</i>	47
1.7.1 Concluding remarks	48
<i>1.8 Summary and outlook</i>	49
<i>1.9 Aim of this research and thesis outline</i>	51
<i>1.10 References</i>	52
Chapter 2: Photoswitching of DNA Hybridization using a Molecular Motor	59
<i>2.1 Introduction</i>	60
<i>2.2 Computational-aided molecular design of the linker</i>	63
<i>2.3 Synthesis of the molecular motor-based linker</i>	64
<i>2.4 Analysis of the motor-based linker</i>	66
2.4.1 ^1H NMR analysis	66
2.4.2 UV-vis analysis	68
2.4.3 Kinetic analysis	68
<i>2.5 DNA synthesis</i>	69
<i>2.6 Melting temperature analysis</i>	70
<i>2.7 DNA photochemistry</i>	71
<i>2.8 Molecular Dynamics</i>	75
<i>2.9 Conclusions</i>	76
<i>2.10 Experimental procedures and acknowledgements</i>	77
<i>2.11 References</i>	83

Chapter 3: Light Actuated Morphological Change in Organic Microcrystals	85
3.1 Introduction	86
3.2 Synthesis	88
3.3 Analysis of photochemical properties of motor 3.3	88
3.3.1 NMR analysis	88
3.3.2 UV-vis analysis	91
3.3.3 Kinetic analysis	93
3.4 CPD formation	93
3.5 TEM experiments	94
3.6 Conclusions	97
3.7 Experimental procedures and acknowledgements	98
3.8 References	99
Chapter 4: Molecular Motors in Aqueous Environments	103
4.1 Introduction	104
4.2 Water-soluble molecular motors	105
4.2.1 Design	105
4.2.2 Synthesis	106
4.2.3 Analysis of motor 4.1	107
4.2.3.1 ^1H NMR analysis	107
4.2.3.2 UV-vis spectroscopy	108
4.2.4 Analysis of motor 4.2	108
4.2.4.1 ^1H NMR analysis	108
4.2.4.2 UV-vis spectroscopy	110
4.2.4.3 Circular dichroism spectroscopy	111
4.2.4.4 Nile Red fluorescence assay	111
4.2.4.5 Synthesis and analysis of a model compound for studying the possible decomposition pathway	112
4.2.4.6 UV-vis spectroscopy under varying atmospheres	113
4.2.4.7 UV-vis spectroscopy over a pH range	114
4.2.4.8 Identification of potential degradation products	116
4.2.5 DNA binding assays	117
4.3 Motor rotation in micelles	118
4.3.1 UV-vis spectroscopy	118
4.3.2 Kinetic analysis	120
4.3.3 Viscosity measurements	121
4.3.4 Fatigue resistance	122
4.3.5 UV-vis spectroscopy over a pH range	122
4.4 Conclusions	124
4.5 Experimental procedures and acknowledgements	125
4.6 References	129

Table of Contents

Chapter 5: Towards Photoswitchable Chemotherapy Agents	131
5.1 General introduction	132
5.2 Photoswitchable <i>cisplatin</i> derivatives	132
5.2.1 Design and synthesis	133
5.2.2 NMR analysis of rotary cycle	135
5.2.3 DNA-binding assay	137
5.3 Photoswitchable colchicine derivatives	137
5.3.1 Synthesis	138
5.3.2 UV-vis analysis	141
5.3.3 NMR analysis	143
5.3.4 Glutathione reduction	143
5.3.5 Water solubility	144
5.4 Conclusions and outlook	145
5.5 Experimental procedures and acknowledgements	145
5.6 References	150
Chapter 6: Solvent Effects on the Thermal Isomerization of a Rotary Molecular Motor	153
6.1 Introduction	154
6.2 Choice of molecular motor probe	156
6.3 Results	157
6.3.1 Polar solvents	161
6.3.2 Polar solvents II and alcohols	163
6.3.3 Aromatic solvents	164
6.3.4 Cycloalkanes and branched alkanes	166
6.4 Correlation of rate to other solvent effects.	166
6.5 Statistical analysis	171
6.6 Conclusions	174
6.7 Experimental procedures and acknowledgements	175
6.8 References	176
Summary	179
Samenvatting	183
List of Publications	189
Acknowledgements	191

