University of Groningen

Folding and replication in complex dynamic molecular networks

Liu, Bin

DOI:
[10.33612/diss.99784510](https://doi.org/10.33612/diss.99784510)

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:
2019

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

Citation for published version (APA):
Liu, B. (2019). *Folding and replication in complex dynamic molecular networks*. [Thesis fully internal (DIV), University of Groningen]. University of Groningen. <https://doi.org/10.33612/diss.99784510>

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.

Folding and Replication in Complex Dynamic Molecular Networks

Bin Liu

The work described in this thesis was carried out at the Stratingh Institute for Chemistry, University of Groningen, The Netherlands.

This work was financially supported by the European Research Council (ERC) and Zernike Dieptestrategie.

Printed by ProefschriftMaken, The Netherlands.

ISBN: 978-94-034-2086-8 (print)

ISBN: 978-94-034-2085-1 (e-book)

university of
 groningen

Folding and Replication in Complex Dynamic Molecular Networks

PhD thesis

to obtain the degree of PhD at the
University of Groningen
on the authority of the
Rector Magnificus Prof. C. Wijmenga
and in accordance with
the decision by the College of Deans.

This thesis will be defended in public on

Tuesday 29 October 2019 at 12.45 hours

by

Bin Liu

born on 22 July 1988
in Chongqing, China

Supervisors

Prof. S. Otto

Prof. G. Roelfes

Assessment Committee

Prof. G. Guichard

Prof. L. Brunsveld

Prof. W. Browne

Contents

Chapter 1 Folding and Replication in Complex Chemical Systems	1
1.1 Systems chemistry and the <i>de-novo</i> synthesis of life	2
1.2 Synthetic folded structures - foldamers	4
1.2.1 Aliphatic peptide foldamers	4
1.2.2 Aromatic foldamers	6
1.2.3 Aliphatic and aromatic hybrid foldamers	8
1.3 Synthetic self-replicating systems	8
1.3.1 DNA-based self-replicating systems	10
1.3.2 RNA-based self-replicating systems	11
1.3.3 Peptide-based self-replicating systems	12
1.3.4. Non-biological self-replicating systems	13
1.4 Dynamic combinatorial chemistry	15
1.4.1 Folding in DCLs	16
1.4.2 Emergence of self-replicators from DCLs	18
1.5 Aim and outline	21
1.6 References	23
Chapter 2 Complex Molecules that Fold like Proteins Can Emerge Spontaneously	27
2.1 Introduction	28
2.2 Results and discussion	29
2.2.1 Design and synthesis of building blocks	29
2.2.2 Formation of complex folded structures from DCLs	29
2.2.3 Structure characterization of foldamer	31
2.2.4 Unfolding and refolding	34
2.2.5 Building block modification	35
2.3. Conclusion	36
2.4. Experimental section	37
2.4.1 General methods	37
2.4.2 Synthesis and characterization of building blocks	39
2.7 References	59
Chapter 3 Dynamic Combinatorial Foldamers	61
3.1 Introduction	62
3.2 Results and Discussion	63

3.2.1 Design and synthesis of building blocks	63
3.2.2 Emergence of complex peptide foldamers	64
3.2.3 Characterization of the foldamers	65
3.2.4 Unfolding and refolding of the foldamers.....	70
3.2.5 Effect of the solvent environment on the formation of foldamers	72
3.3 Conclusions.....	72
3.4. Acknowledgements	73
3.5. Experimental section	74
3.5.1 General methods.....	74
3.5.2 Synthesis and characterization of building blocks	76
3.6 References	100
Chapter 4 Dynamic Peptide Nucleic Acid Self-Replicators	103
4.1. Introduction.....	104
4.2. Results and discussion	106
4.2.1. Emergence of nucleobase-peptide self-replicators	106
4.2.2. Cross-catalysis between nucleobase containing self-replicators	111
4.2.3. Importance of the nucleobase	114
4.3. Emergence of PNAs based replicators	115
4.3.1 Emergence of amino acid functionalized PNA replicators	115
4.3.2 Cation-introduced guanine based supramolecular assembly	118
4.4. Conclusion	119
4.5. Acknowledgements	119
4.6. Experimental section	120
4.6.1 General methods.....	120
4.6.2 Synthesis and characterization of building blocks	123
4.6.3 Appendix.....	131
4.6.4 UPLC and UPLC-MS analysis	135
4.9 References	188
Chapter 5 Self-replication Promotes the Formation of Complex Folded Structures.....	189
5.1 Introduction.....	190
5.2 Results and discussion	191
5.2.1 Self-sorting of a self-replicator and a foldamer	191
5.2.3 Ratio effects.....	195
5.2.4 Transient self-replication.....	197

5.3 Conclusion	199
5.4. Experimental section	200
5.4.1 General methods	200
5.4.2 Appendix	202
5.4.2 UPLC and UPLC-MS Analyses	206
5.5 References	212
Chapter 6 Overview and Perspectives	215
6.1 Overview	215
6.2 Perspectives	216
Summary	219
Samenvatting	223
Acknowledgements	227