

Conferencia: Dynamic Expression of Multivalency

Sebastien Ulrich



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Mousseron (IBMM),
Ecole Nationale Supérieure de
Chimie de Montpellier
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France**

11/05/17

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EXECUTIVE SUMMARY

Sébastien Ulrich carried out his PhD under the guidance of Pr. Jean-Marie Lehn at ISIS, Strasbourg, France, developing molecular switches for controlling dynamic combinatorial libraries. He subsequently joined the groups of Pr. Harry L. Anderson (Oxford University, UK) as an EPSRC fellow and of Pr. Eric T. Kool (Stanford University, CA, USA) as a Fulbright fellow. In 2011 he was awarded an ANR starting grant and joined the group of Pr. Pascal Dumy, first in Grenoble, then at IBMM in Montpellier, France where he was promoted to a permanent CNRS research position in 2012. He was named Junior Distinguished member of the French Chemical Society in 2014 and was rewarded the bronze medal by the CNRS in 2017.

His current research interests lie at the interface of supramolecular chemistry and bioorganic chemistry, and focus in particular on the design and study of dynamic self-assembled systems and multivalent recognition systems for biological applications such as nucleic acids delivery and enzyme inhibition.

RESEARCH TOPICS: [SUPRAMOLECULAR BIOORGANIC CHEMISTRY](#)

Self-assembly: supramolecular hybrid DNA-small molecules nanostructures, peptide-based nanostructures

Dynamic chemistry: dynamic covalent polymers, dynamic combinatorial chemistry

Multivalency: self-assembled approaches applied to biomolecular recognition and transport

SCIENTIFIC OUTCOMES

25 publications in peer-reviewed scientific journals (average IF 5.95; 295 citations; H-factor: 10)
 33 oral communications (14 invited) and 17 poster presentations at national and international conferences

FIVE MOST REPRESENTATIVE SCIENTIFIC PUBLICATIONS

- 5) Bioactive clusters promoting cell penetration and nucleic acids complexation for drug and gene delivery applications: from designed to self-assembled and responsive systems, E. Bartolami, C. Bouillon, P. Dumy, S. Ulrich, *Chem. Commun.*, **2016**, 52, 4257-4273
- 4) Dynamic expression of DNA complexation with self-assembled biomolecular clusters, E. Bartolami, Y. Bessin, V. Gervais, P. Dumy, S. Ulrich, *Angew. Chem. Int. Ed.*, **2015**, 54 (35), 10183-10187
- 3) Probing the importance of π -stacking interactions in DNA-templated self-assembly of bisfunctionalized guanidinium compounds, D. Paolantoni, J. Rubio-Magnieto, S. Cantel, J. Martinez, P. Dumy, M. Surin, S. Ulrich, *Chem. Commun.*, **2014**, 50 (91), 14257-14260
- 2) Degradable Hybrid Materials Based on Cationic Acylhydrazone Dynamic Covalent Polymers Promote DNA Complexation through Multivalent Interactions, C. Bouillon, D. Paolantoni, J. C. Rote, Y. Bessin, L. W. Peterson, P. Dumy, S. Ulrich, *Chem. Eur. J.*, **2014**, 20 (45), 14705-14714
- 1) Probing Secondary Interactions in Biomolecular Recognition by Dynamic Combinatorial Chemistry, S. Ulrich, P. Dumy, *Chem. Commun.*, **2014**, 50 (44), 5810-5825

WORK EXPERIENCES

2016/10-present	Chargé de Recherche CNRS CR1, IBMM , Montpellier, France
2012/09-2016/09	Chargé de Recherche CNRS CR2, IBMM , Montpellier, France
2011/09-2012/09	R&D Project leader, CNRS/Université Joseph Fourier, DCM , Pr. P. Dumy , Grenoble, France
2010/01-2011/07	Post-doctoral research associate and Fulbright fellow, Pr. E. T. Kool , Stanford University, CA, USA
2009/01-2010/01	Post-doctoral research assistant, Pr. H. L. Anderson , Oxford University, Oxford, UK
2008/10-2008/12	Research and teaching assistant (ATER) at the Collège de France , Paris, France
2005/10-2008/09	Ph.D. , Laboratory of Supramolecular Chemistry, Pr. J.-M. Lehn , ISIS, Strasbourg, France

EDUCATION

2016	Habilitation	H.D.R., Université de Montpellier, Montpellier, France
2005-2008	Ph.D.	Laboratory of Supramolecular Chemistry, I.S.I.S., Strasbourg, France Supervisor: Prof. J.-M. Lehn
2004-2005	M.Sc.	D.E.A., <i>summa cum laude</i> , Molecular and Supramolecular Organic Chemistry University of Strasbourg, Strasbourg, France
2002-2005	M.Sc.	Ingénieur E.C.P.M. (European School of Chemistry, Polymers and Materials), Strasbourg, France

RESPONSIBILITIES

2016-	Associate Editor at RSC Advances
2015-	Elected member of the French Chemical Society Languedoc-Roussillon section
2015-	Selected participant in COST action CM1304
2012-	Peer reviewer for <i>Nature Comm.</i> , <i>Angew. Chem.</i> , <i>Chem. Commun.</i> , <i>Chem. Sci.</i> , <i>Org. Biomol. Chem.</i> , <i>Bonconj. Chem.</i> , <i>New J. Chem.</i> , <i>Biomaterials</i> , <i>Polym. Chem.</i>
2012-	Member of the selection committee of the Franco-American Fulbright Commission

RESEARCH GRANTS AND FELLOWSHIPS

2016-2017	Co-laureate, LabEx CheMISyst Master support
2016-2017	Co-laureate, Hubert Curien program "Polonium 2016"
2016	Co-laureate, LabEx CheMISyst Master support
2015-2017	Laureate of the research call, LabEx CheMISyst program, 70 k€
2015	Laureate, LabEx CheMISyst Master support
2014-2015	Participant in a project funded by La Ligue contre le Cancer, 15 k€
2012-2015	Participant in LabEx CheMISyst program, 100 k€
2011-2015	ANR Starting Grant (PDOC DynEnON), 520 k€
2009-2010	Fulbright fellowship, Franco-American Commission for Educational Exchange (1 year)
2009	EPSRC research fellow (1 year)

TEACHING ACTIVITIES

Since 2012	Supervision of 3 post-doctoral researchers, 3 PhD students, 5 graduates and 15 undergraduates
2016-2017	Organic chemistry (30 h TD + 16 h TP), Université de Montpellier
2015-2016	Organic chemistry (51 h TD + 28 h TP), Université de Montpellier
2014-2015	Organic chemistry (39 h TD + 28 h TP), Université de Montpellier
2013-2014	Organic chemistry (80 h TD + 30 h TP), Université de Montpellier
2013-	Tutoring « découverte du monde de la recherche », ENSCM
2012-2013	Organic chemistry (21 h TD + 45 h TP), Université de Montpellier
2011-2012	Organic chemistry (14 h TP), Université Joseph Fourier, Grenoble, France
2009-2010	Organic chemistry (5 h TD), Oxford University, UK

AWARDS

2017	CNRS Bronze Medal
2014	Junior Distinguished member of the French Chemical Society
2009	PhD prize from the French Chemical Society (SCF-DCO)
2009	PhD award "Le Monde de la Recherche Universitaire"
2009	PhD prize from the Scientific Council of the University of Strasbourg

LIST OF SCIENTIFIC PUBLICATIONS

- 25) Auto-assemblage dynamique de clusters cationiques pour la complexation et la vectorisation d'acides nucléiques. E. Bartolami,* S. Ulrich,* P. Dumy, *L'Actualité Chimique*, **2017**, in press
- 24) Effective Access to Multivalent Inhibitors of Carbonic Anhydrases Promoted by Peptide Bioconjugation. N. Kanfar, M. Tanc, P. Dumy, C. T. Supuran, S. Ulrich,* J.-Y. Winum,* *Chem. Eur. J.*, **2017**, in press
- 23) Functional interplay between NTP leaving group and base pair recognition during RNA polymerase II nucleotide incorporation revealed by methylene substitution. C. S. Hwang, L. Xu, W. Wang, S. Ulrich, L. Zhang, J. Chong, J. H. Shin, X. Huang, E. T. Kool, C. E. McKenna,* D. Wang,* *Nucl. Acids Res.*, **2016**, *44* (8), 3820-3828
- 22) Bioactive clusters promoting cell penetration and nucleic acids complexation for drug and gene delivery applications: from designed to self-assembled and responsive systems. E. Bartolami, C. Bouillon, P. Dumy, S. Ulrich,* *Chem. Commun.*, **2016**, *52*, 4257-4273
- 21) A metal-free synthetic approach to peptide-based iminosugar clusters as novel multivalent glycosidase inhibitors. R. Zelli, E. Bartolami, J.-F. Longevial, Y. Bessin, P. Dumy, A. Marra,* S. Ulrich,* *RSC Adv.*, **2016**, *6*, 2210-2216
- 20) Emerging trends in enzyme inhibition by multivalent nanoconstructs. N. Kanfar, E. Bartolami, R. Zelli, A. Marra, J.-Y. Winum,* S. Ulrich,* P. Dumy, *Org. Biomol. Chem.*, **2015**, *13*, 9894-9906
- 19) Multivalent DNA recognition by self-assembled clusters: deciphering structural effects by fragments screening and evaluation as siRNA vectors. E. Bartolami, Y. Bessin, N. Bettache, M. Gary-Bobo, M. Garcia, P. Dumy, S. Ulrich,* *Org. Biomol. Chem.*, **2015**, *13*, 9427-9438
- 18) Dynamic expression of DNA complexation with self-assembled biomolecular clusters. E. Bartolami, Y. Bessin, V. Gervais, P. Dumy, S. Ulrich,* *Angew. Chem. Int. Ed.*, **2015**, *54* (35), 10183-10187
- 17) Fluorescent silica nanoparticles with multivalent inhibitory effects towards carbonic anhydrases. N. Touisni, N. Kanfar, S. Ulrich, P. Dumy, C.T. Supuran, A. Mehdi, J.-Y. Winum,* *Chem. Eur. J.*, **2015**, *21* (29), 10306-10309
- 16) Synthesis of α -PNA containing a functionalized triazine as nucleobase analogue. E. Bartolami, A. Gilles, P. Dumy, S. Ulrich,* *Tetrahedron Lett.*, **2015**, *56* (18), 2319-2323
- 15) A Dynamic Combinatorial Approach for Identifying Side Groups that Stabilize DNA-Templated Supramolecular Self-Assemblies. D. Paolantoni, S. Cantel, P. Dumy, S. Ulrich,* *Int. J. Mol. Sci.*, **2015**, *16*, 3609-3625
- 14) Probing the importance of π -stacking interactions in DNA-templated self-assembly of bisfunctionalized guanidinium compounds. D. Paolantoni, J. Rubio-Magnieto, S. Cantel, J. Martinez, P. Dumy, M. Surin,* S. Ulrich,* *Chem. Commun.*, **2014**, *50*, 14257-14260

- 13) Degradable Hybrid Materials Based on Cationic Acylhydrazone Dynamic Covalent Polymers Promote DNA Complexation through Multivalent Interactions. C. Bouillon, D. Paolantoni, J. C. Rote, Y. Bessin, L. W. Peterson, P. Dumy, S. Ulrich,* *Chem. Eur. J.*, **2014**, *20* (45), 14705-14714
- 12) Probing Secondary Interactions in Biomolecular Recognition by Dynamic Combinatorial Chemistry. S. Ulrich,* P. Dumy,* *Chem. Commun.*, **2014**, *50* (44), 5810-5825
- 11) Theoretical and Structural Analysis of Long C–C Bonds in the Adducts of Polycyanoethylene and Anthracene Derivatives and their Connection to the Reversibility of Diels–Alder Reactions. A. K. H. Hirsch, P. Reutenauer, M. Le Moignan, S. Ulrich, P. J. Boul, J. M. Harrowfield, P. D. Jarowski, J.-M. Lehn, *Chem. Eur. J.*, **2014**, *20* (4), 1073-1080
- 10) Oxime Ligation: a Chemoselective Click-Type Reaction for Accessing Multifunctional Biomolecular Constructs. S. Ulrich, D. Boturyn, A. Marra, O. Renaudet, P. Dumy, *Chem. Eur. J.*, **2014**, *20* (1), 34-41
- 9) Engineering of biomolecules for sensing and imaging applications. S. Ulrich,* P. Dumy,* D. Boturyn, O. Renaudet, *J. Drug Del. Sci. Tech.*, **2013**, *23* (1), 5-15
- 8) Biodistribution and Pharmacokinetic Studies of a Porphyrin Dimer Photosensitizer (Oxdime) by Fluorescence Imaging and Spectroscopy in Mice Bearing Xenograft Tumors. M. Khurana, S. Ulrich, A. Kim, Y. Moriyama, G. Natchev, M. K. Akens, H. L. Anderson, B. C. Wilson, *Photochem. Photobiol.*, **2012**, *88*, 1531-1538
- 7) Dissecting Chemical Interactions Governing RNA Polymerase II Transcriptional Fidelity. M. W. Kellinger, S. Ulrich, J. Chong, E. T. Kool, D. Wang, *J. Am. Chem. Soc.*, **2012**, *134*, 8231-8240
- 6) Importance of Steric Effects on the Efficiency and Fidelity of Transcription by T7 RNA Polymerase. S. Ulrich, E. T. Kool, *Biochemistry*, **2011**, *50* (47), 10343-10349.
- 5) Metallo-controlled Dynamic Molecular Tweezers: Design, Synthesis, and Self-assembly by Metal-ion Coordination. S. Ulrich, A. Petitjean, J.-M. Lehn, *Eur. J. Inorg. Chem.*, **2010**, *13*, 1913-1928
- 4) Adaptation and Optical Signal Generation in a Constitutional Dynamic Network. S. Ulrich, J.-M. Lehn, *Chem. Eur. J.*, **2009**, *15*, 5640-5645
- 3) Adaptation to Shape Switching by Component Selection in a Constitutional Dynamic System. S. Ulrich, J.-M. Lehn, *J. Am. Chem. Soc.*, **2009**, *131*, 5546-5559
- 2) Reversible Constitutional Switching between Macrocycles and Polymers Induced by Shape Change in a Dynamic Covalent System. S. Ulrich, E. Buhler, J.-M. Lehn, *New. J. Chem.*, **2009**, *33*, 271-292
- 1) Reversible Switching between Macrocyclic and Polymeric States by Morphological Control in a Constitutional Dynamic System. S. Ulrich, J.-M. Lehn, *Angew. Chem. Int. Ed.*, **2008**, *47*, 2240-2243

DYNAMIC EXPRESSION OF MULTIVALENCY

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Our research is directed toward the generation of smart bioactive systems for drug and gene delivery applications. We are particularly interested in harnessing the power of multivalency in order to achieve effective biomolecular recognition of nucleic acids. Our approach rests on the implementation of controlled self-assembly processes for endowing a responsive and adaptive behavior to self-synthesizing chemical systems. In this talk, we will present three examples where we used dynamic covalent chemistry for generating dynamic materials (peptide-based clusters, biopolymers) that express, in a controlled manner, multivalent recognition of nucleic acids. We will show that these systems are adaptive and responsive to physico-chemical stimuli, thereby opening new avenues for the generation of “smart” gene delivery vectors.

References

- C. Bouillon, D. Paolantoni, J. C. Rote, Y. Bessin, L. W. Peterson, P. Dumy, S. Ulrich, *Chem. Eur. J.*, **2014**, 20 (45), 14705-14714
S. Ulrich, D. Boturyn, A. Marra, O. Renaudet, P. Dumy, *Chem. Eur. J.*, **2014**, 20 (1), 34-41
E. Bartolami, Y. Bessin, V. Gervais, P. Dumy, S. Ulrich, *Angew. Chem. Int. Ed.*, **2015**, 54 (35), 10183-10187
E. Bartolami, Y. Bessin, N. Bettache, M. Gary-Bobo, M. Garcia, P. Dumy, S. Ulrich, *Org. Biomol. Chem.*, **2015**, 13, 9427-9438
E. Bartolami, C. Bouillon, P. Dumy, S. Ulrich, *Chem. Commun.*, **2016**, 52, 4257-4273