REPORT DOCUMENTATION PAGE

Form Approved OMB NO. 0704-0188

The public reporting burden for this collection of information is estimated to average 1 hour per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggesstions for reducing this burden, to Washington Headquarters Services, Directorate for Information Operations and Reports, 1215 Jefferson Davis Highway, Suite 1204, Arlington VA, 22202-4302. Respondents should be aware that notwithstanding any other provision of law, no person shall be subject to any oenalty for failing to comply with a collection of information if it does not display a currently valid OMB control number.
PLEASE DO NOT RETURN YOUR FORM TO THE ABOVE ADDRESS.

1. REPORT DATE (DD-MM-YYYY)	2. REPORT TYPE	3. DATES COVERED (From - To)
29-08-2007	Technical Report	1-Sep-2006 - 1-Nov-2006

4. TITLE AND SUBTITLE
Recent Advances in supramolecular assemblies with nucleic acids

5a. CONTRACT NUMBER
W911NF-06-1-0286

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER
611102

6. AUTHORS
Philippe Barthelemy

5d. PROJECT NUMBER

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAMES AND ADDRESSES
Inst Nat Sante et laRecherche Medicale
101 Rude De Tolbiac

75013 -

8. PERFORMING ORGANIZATION REPORT NUMBER

9. SPONSORING/MONITORING AGENCY NAME(S) AND ADDRESS(ES)
U.S. Army Research Office
P.O. Box 12211
Research Triangle Park, NC 27709-2211

10. SPONSOR/MONITOR'S ACRONYM(S)
ARO

11. SPONSOR/MONITOR'S REPORT NUMBER(S)
49737-CH-CF.2

12. DISTRIBUTION AVAILIBILITY STATEMENT
Approved for public release; Federal purpose rights

13. SUPPLEMENTARY NOTES
The views, opinions and/or findings contained in this report are those of the author(s) and should not contrued as an official Department of the Army position, policy or decision, unless so designated by other documentation.

14. ABSTRACT
The workshop entitled “Recent Advances in Supramolecular Assemblies with Nucleic Acids” was held in Bordeaux, France 16th-17th of October 2006. This event was organized at the "European Institute of Chemistry and Biology (IECB)”, with a financial support coming from the ARO.

15. SUBJECT TERMS
conference proceeding "Recent Advances in supramolecular assemblies with nucleic acids" (workshop)

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	15. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Philippe Barthelemy
U	U	U	UU		19b. TELEPHONE NUMBER 335-575-7485

Report Title

Conference proceeding and certification
"Recent Advances in Supramolecular Assemblies with Nucleic Acids"

ABSTRACT

The workshop entitled “Recent Advances in Supramolecular Assemblies with Nucleic Acids” was held in Bordeaux, France 16th-17th of October 2006. This event was organized at the "European Institute of Chemistry and Biology (IECB)”, with a financial support coming from the ARO.

MASTER COPY: PLEASE KEEP THIS "MEMORANDUM OF TRANSMITTAL" BLANK FOR REPRODUCTION PURPOSES. WHEN REPORTS ARE GENERATED UNDER THE ARO SPONSORSHIP, FORWARD A COMPLETED COPY OF THIS FORM WITH EACH REPORT SHIPMENT TO THE ARO. THIS WILL ASSURE PROPER IDENTIFICATION. NOT TO BE USED FOR INTERIM PROGRESS REPORTS; SEE PAGE 2 FOR INTERIM PROGRESS REPORT INSTRUCTIONS.

MEMORANDUM OF TRANSMITTAL

U.S. Army Research Office
ATTN: AMSRL-RO-BI (TR)
P.O. Box 12211
Research Triangle Park, NC 27709-2211

☐ Reprint (Orig + 2 copies)
☑ Technical Report (Orig + 2 copies)
☐ Manuscript (1 copy)
☐ Final Progress Report (Orig + 2 copies)
☐ Related Materials, Abstracts, Theses (1 copy)

CONTRACT/GRANT NUMBER: W911NF-06-0286

REPORT TITLE: Workshop on
Recent Advances in Supramolecular Assemblies with Nucleic Acids

is forwarded for your information.

SUBMITTED FOR PUBLICATION TO (applicable only if report is manuscript):

Sincerely,
Philippe Barthélémy

REPORT

Workshop on
Recent Advances in Supramolecular Assemblies with Nucleic Acids

European Institute of Chemistry and Biology (IECB)

Bordeaux, France 16th-17th of October 2006

The workshop entitled “Recent Advances in Supramolecular Assemblies with Nucleic Acids” was held in Bordeaux, France 16th-17th of October 2006. This event was organized at the "*European Institute of Chemistry and Biology (IECB)”*, with a financial support coming from the ARO.

During this workshop a special attention was devoted to the following four topics:

- *1- Hybrid amphiphile-nucleic acid structures.* The recent progress achieved in the synthesis and of supramolecular self-assemblies that mimic the molecular recognition functionalities found with nucleic acids. This topic will include hybrid bio-inspired molecules bearing both nucleic acid and amphiphilic moieties.

- *2- Nucleic acids transport.* Artificial systems currently developed to carry nucleic acids into cells using a synthetic supramolecular assembly. Transport of double strand RNA (siRNA, miRNA), and single strand RNA and/or DNA aptamers.

- *3- Biomaterials derived from nucleic acid.* Soft materials using bio-macromolecules are finding applications in areas ranging from drug delivery technology to nanofabrication.

- *4- Functional supramolecular systems*. Functional devices that use the intrinsic nature of these biomolecules (nano-switch properties of aptamers, nanoengines, detection devices…).

These four aspects were discussed during seven sessions including sixteen lectures:

All presentations were discussed in group discussions. The schedule and the organization selected for this meeting was appropriate to induce deep scientific exchanges and new collaborations.

This meeting highlighted the potential of DNA supramolecular assemblies in the following areas; nucleic acids transport, functional supramolecular systems, hybrid structures and biomaterials derived from nucleic acid biomolecules. The information collected should familiarize the ARO with the latest important developments in supramolecular chemistry involving nucleic acids.

Certification and conference proceedings are enclosed to this report.

INSERM U386 - Modulation Artificielle des Gènes Eucaryotes

Institut Fédératif de Recherche Pathologies Infectieuses et cancers

Prof Philippe Barthélémy
INSERM U386
Université Victor Segalen Bordeaux 2
146 rue Léo Saignat Bat. 3A, 1er étage
33076 Bordeaux cedex, France
barthelemy@bordeaux.inserm.fr
Tel 33 (0)5 57 57 48 53, Fax 33 (0)5 57 57 10 15

Workshop on
Recent Advances in
Supramolecular Assemblies with Nucleic Acids
European Institute of Chemistry and Biology (IECB)
Bordeaux, France 16th-17th of October 2006

I certify that funds provided by the Army research office under the grant W911NF-06-0286 were expended in accordance with the provisions of the grant and that required conference conference proceeding have been delivered to the Army Research Office

Philippe Barthélémy

Modulation Artificielle des Gènes Eucaryotes
INSERM U386
Université Victor Segalen Bordeaux 2
146 rue Léo Saignat - Bât. 3A, 1er étage
33076 Bordeaux cedex (France)
Tél. (33) 05 5757 1014 // Fax (33) 05 5757 1015

Recent Advances in Supramolecular Assemblies with Nucleic Acids

Inserm
Institut national
de la santé et de la recherche médicale

Université Victor Segalen Bordeaux 2

European Institute of Chemistry and Biology (IECB)

SCIENCE TO SHAPE THE FUTURE OF THE ARMY · ARMY RESEARCH OFFICE · 1951

REGION AQUITAINE

Bordeaux, France 16th-17th of October 2006

© Office de Tourisme de Bordeaux / F. POINCET

Workshop Committee:

Philippe Barthélémy
Mark Grinstaff
Jean Herscovici
Chad Immoos
Arnaud Gissot

sfc Société française de Chimie

In Cell art

I- Forewords

Dear Colleagues,

In the spring of 2004, a group of scientists assembled in Avignon, Provence, south of France for a meeting entitled "*DNA supramolecular assemblies*". Different experts in the field of nucleic acids came to the "*City of Popes*" from all around the word to share ideas on this exciting area of research. It was an interdisciplinary meeting that included the participation of chemists, physicists and biologists. All the communications presented in Avignon highlighted the fascinating properties of this genetic material in terms of supramolecular systems. Since 2004, new exciting developments in this very active field of research have been reported offering to scientists new perspectives.

The 16th and 17th of October 2006, a second meeting on the fascinating supramolecular systems involving nucleic acids molecules and/or derivatives will be held at the European Institute of Chemistry and Biology (*IECB*) in Bordeaux. This workshop will include again academic scientists from all over the world. The invited speakers will give presentations on the most advanced aspects of their research on "*Supramolecular assemblies with nucleic acids*". The different scientific themes will include the following four topics:

1- Hybrid amphiphile-nucleic acid structures.
2- Nucleic acids transport.
3- Biomaterials derived from nucleic acid.
4- Functional supramolecular systems.

The organizing committee warmly thanks the sponsors for supporting this project.
Dear invited speakers and participants, we wish you a pleasant stay in Bordeaux.

Bienvenue à tous !

Philippe Barthélémy

II- Program

Monday October 16th (Morning)

9:00-9:30 Registration – IECB

9:30-10:00 Stephen J. Lee, U.S. Army Research Office, Research Triangle Park, (USA)

"Introductory Remarks"

Session I, *Nucleic acids transport*
Chairman: Jean Herscovici

10:00-10h30 Mark Grinstaff, Dept of Biomed. Eng & Chemistry, Boston University (USA)

"New Functional Transfection Reagents for Gene Delivery"

10:30-11:00 Bruno Pitard, Faculté de Médecine de Nantes (France)

"Synthetic nanovectors for in vitro and in vivo intracellular delivery of nucleic acids"

11:00-11:30 Break, Posters (IECB)

Session II, *Nucleic acids transport*
Chairman Mark Grinstaff

11:30-12:00 Suzie H. Pun, University of Washington, Department of Bioengineering (USA)
"Localized gene delivery mediated by synthetic materials"

12:00-12:30 Guy Zuber, Faculté de Pharmacie de Strasbourg, Illkirch (France)

"Cationic oligonucleotide-peptide conjugates with aggregating properties enter efficiently into cells while maintaining hybridization properties and enzymatic recognition"

12:30-3:00 Lunch break, posters (IECB)

Monday October 16th (Afternoon)

Session III, *Nucleic acids transport*
Chairman

3:00-3:30 Jean Herscovici, Ecole Nationale Supérieure de Chimie de Paris (France)

"Lipopolythioureas: a New Efficient Non Cationic System for Gene Delivery"

3:30-4:00 Pierre Vierling, Université de Nice Sophia Antipolis, Parc Valrose (France)

"Synthetic viruses for gene delivery"

4:00-4:30 Break, Posters (IECB)

Session IV, *Functional supramolecular systems.*
Chairman

4:30-5:00 Chad Immoos, California Polytechnic State University (USA)

"Development of Conformationally-Gated Electrochemical Gene Detection: The Hairpin and Wrap Assays"

5:00-5:30 Eugen Stulz, University of Southampton, School of Chemistry (UK)

"Porphyrin-DNA: towards nanoscale multifunctional molecules"

5:30-6:00 Krishna Ganesh, National Chemical Laboratory, Maharashtra (India)

"Supramolecular recognition of DNA by modified PNA and gold nanoparticles"

Tuesday October 17th (Morning)

9:00-9:30 Peter Walde, ETH Zürich (Switzerland)

"The possible roles of surfactant assemblies for the origin of life"

Session V, *Supramolecular systems*
Chairman: Chad Immoos

9:30-10:00 Chengde Mao, Purdue University, Dept of Chemistry, West Lafayette (USA)

"Self-assembly of DNA nanostructures"

10:00-10:30 Ivan Huc, Institut Européen de Chimie Biologie (IECB), Bordeaux (France)

"Artificial Double Helical Architectures"

10.30-11:00 Break, Posters (IECB)

Session VI, *Hybrid structures*
Chairman

11:00-11:30 Debora Berti, Universita' degli Studi di Firenze (Italy)

"Phospholipids membranes decorated by cholesterol-based oligonucleotides as addressable soft nanostructures"

11:30-12:00 Peter Strazewski, Université Claude Bernard Lyon 1 (France)

"Synthesis and atomic force imaging of amphiphilic peptidyl-RNA conjugates"

12:00 Lunch break

Tuesday October 17th (Afternoon)

Session VII, *Biomaterials derived from nucleic acid*
Chairman

3:00-3:30 Dan Luo, Dept of Biol. and Environ. Engineering, Cornell University, NY (USA)

"Nucleic Acid Engineering: Using DNA as a Generic instead of a Genetic Material"

3:30-4:00 Cécile Zakri, Centre de Recherche Paul Pascal (CRPP), Bordeaux (France)

"Carbon nanotube dispersion and assembly: an interest for biomaterials?"

4:00 Group Discussion, Future directions

III- Book of Abstracts

Carla A. H. Prata,[1] Yougen Li,[2] Dan Luo,[2] Thomas J. McIntosh,[3] Philippe Barthélémy,[4] and **Mark W. Grinstaff[1]***

"New Functional Transfection Reagents for Gene Delivery"

[1] Departments of Biomedical Engineering and Chemistry, Boston University, Boston MA 02215.
[2] Department of Biological and Environmental Engineering, Cornell University, Ithaca, NY, 14853.
[3] Department of Cell Biology, Duke University Medical Center, Durham, NC, 27710.
[4] Université Victor Segalen Bordeaux 2, France.

Abstract : Delivering a gene to a cell is widely performed in research laboratories and in vivo gene therapy holds promise for the cure of genetic diseases. However the efficiency of this transfection process is low, and thus functional delivery systems are being explored, that respond to local stimuli, to increase cellular uptake of the DNA and protein expression. Herein, we describe the synthesis, characterization, and transfection activity of a series of functional transfection reagents. These reagents alter their electrostatic interactions with DNA to release the nucleic acids within the cell.

Bruno Pitard, INSERM, Université de Nantes (France)

"Synthetic nanovectors for in vitro and in vivo intracellular delivery of nucleic acids"

Abstract : One major approach in non-viral gene therapy is based on complexes formed by electrostatic interactions between negatively charged DNA and cationic molecules. A variety of cationic vectors, such as cationic lipids or cationic polymers, have been synthesized. Polyplexes and lipoplexes consisting of highly ordered structures of DNA molecules trapped within positively charged supramolecular assemblies have clearly demonstrated their transfection efficiency *in vitro*. However, aggregation in tissues fluids, toxicity and low *in vivo* efficiency have thus far hampered their clinical use. Therefore a need remains for developing new vectors with alternative molecular structures. With this goal in mind, we have examined the potential of amphiphilic block copolymers to promote gene delivery *in vivo*.

Suzie H. Pun, University of Washington (USA)

"Localized gene delivery mediated by synthetic materials"

Abstract : Localized gene delivery has important applications such as tissue engineering, drug delivery and functional genomics. For example, gene delivery vehicles can be integrated with implanted biomedical devices to improve integration with host tissue or incorporated in tissue engineering scaffolds to promote functional tissue growth. Several design considerations exist for optimal application of this technology. The delivery vehicles should be combined with the delivery substrate without compromising delivery efficiency. In addition, the ability to spatially and temporally control of transgene expression is desirable. In this talk, I will summarize our recent efforts toward developing polymeric materials for localized gene delivery.

Guy Zuber, Faculté de Pharmacie de Strasbourg (France)

"Cationic oligonucleotide-peptide conjugates with aggregating properties enter efficiently into cells while maintaining hybridization properties and enzymatic recognition"

Abstract : Oligonucleotide delivery is a crucial issue for therapeutical purposes and is often addressed by conjugation to short cationic peptides although with controversial results. Experiences accumulated in gene delivery indicate that the most efficient synthetic delivery systems are based on cationic molecules that interact with the macromolecules to form assemblies with overall cationic-charged surface. These aggregates in turn anchor to the external face of cell plasma membranes by electrostatic interactions with proteoglycans, are engulfed into intracellular compartments (endosomes and lysosomes) and are eventually liberated into the cytosol. However, shortening the nucleic acid segment ca. hundredfold weakens electrostatic cohesion of the complexes which no longer withstand competition with larger polyanions present in biological fluids or at cell surfaces. One solution for exploiting this efficient pathway is to covalently link the oligonucleotide to a cationic chain that is longer than the oligonucleotide. We therefore conjugated a 15 mer anionic oligonucleotide to a cationic peptide in order to obtain a diblock compound with an overall positive charge with aggregation properties. These microaggregates were efficiently internalized in cells via the expeditious pathway used by commercial gene delivery systems. Moreover, stability of the duplex formed with the complementary sequence increased without inhibiting oligonucleotide enzyme recognition as shown by the properties of the conjugate to prime chain elongation by Taq DNA polymerase in a linear amplification/sequencing process. Altogether, these properties open novel perspectives for oligonucleotide applications without the use of delivery systems involving formulation of the nucleic acid.

Jean Herscovici, Ecole Nationale Supérieure de Chimie de Paris (France)

"Lipopolythioureas: a New Efficient Non Cationic System for Gene Delivery"

Abstract : Cationic lipids have been widely studied for gene delivery to cells. In vivo these systems encounter problems with serum stability, cell internalisation and endosomal escape. Modification or shielding of the liposome surface helps to inhibit non-specific interaction with blood components and enables an extended circulation of the vectors after systemic administration. Our strategy to efficiently deliver gene to cell was to study the possibility to use non cationic liposome.

Thiourea is one of the best hydrogen-bond donors, due to the relatively acidic NH protons, and the ability to form two bonds per function. Moreover, thiourea moieties selectively bind to dihydrogenphosphate via multitopic hydrogen bonding, giving stronger complexes with $H_2PO_4^-$ than any synthetic neutral receptor known so far. These data prompted us to prepare new vectors based on hydrogen-bond interaction with DNA and build around three- and di-thiourea scaffolds. The thiourea vector showed a good ability to associate DNA and to increase its circulation time in the blood stream.

Lipopolythioureas were evaluated for their in-vitro and in-vivo transfection activity. Variation of hydrophobic anchor size and linker has also been investigated. All the compounds with logP < 6.4 could be formulated without helper lipid. On the other hand derivative with logP higher that this value yielded also small particles when formulated with DPPC. Lipolythiourea liposomes were evaluated for in vitro transfection activity against B16 cell line. It was found that several compounds transfect cells with the same level of efficiency as cationic lipids in the presence of serum. Intratumoral transfection was also investigated and various mixtures of thioureas led to good efficiency with a low toxicity.

Pierre Vierling, LCMBA, UMR 6001 CNRS, Université de Nice Sophia-Antipolis (France)

"Synthetic viruses for gene delivery"

Abstract: Non-viral gene delivery systems based on (poly)cationic lipids/liposomes or polymers (respectively, lipoplexes or polyplexes) have become very promising novel forms of medicine. Although the gene expression levels obtained with these systems are transient and lower than with viral vectors, they present several advantages including low-cost and large-scale production, safety, and capacity to deliver large gene fragments. However, there is still a need for the development of gene delivery systems with improved and original properties. Progress in this field requires the development of "synthetic viruses", which allow specific organ and cell targeting and efficient gene expression. The presentation is dedicated to our efforts aimed at improving these issues. It is focussed on the synthetic systems that were developed in our laboratory, which include (i) acridine-Nuclear Localisation Signal (NLS) peptide conjugates as DNA intercalating and NLS-labelling agent for improving gene nuclear import and expression of lipoplexes and polyplexes, (ii) highly fluorinated, polycationic and dimerisable thiol detergents as condensing agents of DNA into small-sized, cationic monomolecular DNA nanoparticles for improving their extra- and intra-cellular diffusion and facilitating their tumor accumulation due to the enhanced permeation and retention (EPR) effect (also known as passive targeting), and (iii) targeted vectors deriving from these monomolecular DNA nanoparticles for the specific transfection of folate-expressing cancer cells and of tumor cells associated to angiogenesis.

Chad E. Immoos[1], Leon Sheynkman[1], Patricia Bailey[1], Aliyah Lakha[1], Stephen Lee[2], and Mark W. Grinstaff[3].

"Development of Conformationally-Gated Electrochemical Gene Detection: The Hairpin and Wrap Assays"

[1] *Department of Chemistry and Biochemistry, California Polytechnic State University, San Luis Obispo, CA 93407, USA*
[2] *Army Research Office, Research Triangle Park, NC 27709, USA*
[3] *Departments of Chemistry and Biomedical Engineering, Boston University, 590 Commonwealth Ave., Boston, MA 02215, USA*

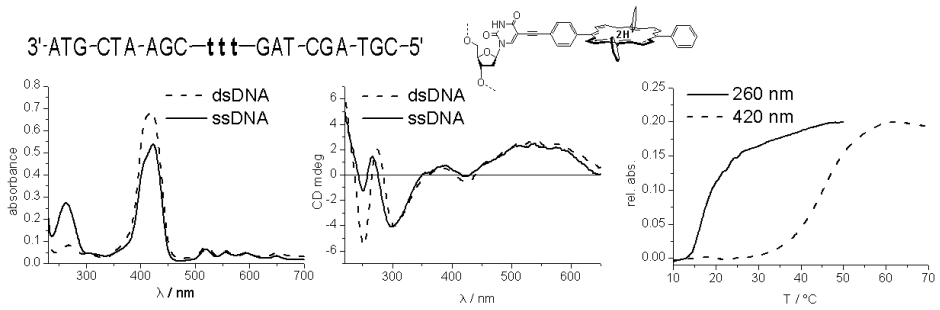
Abstract : Identifying specific nucleic acid sequences of viral or bacterial pathogens, hereditary diseases, or genetic abnormalities is of widespread interest in the areas of medicine, biotechnology, and homeland security. We are interested in developing electrochemical DNA sensors where electron-transfer dynamics are altered as a consequence of large structural/conformational changes upon hybridization with the target DNA strand. For these studies, oligodeoxynucleotides were synthesized containing electroactive probes. Significant effort has been made in our lab to develop methods for the site-specific labeling of oligodeoxynucleotides. Two conformationally-gated electrochemical detection systems will be described. In the first system, to afford significant structural rearrangement of the electroactive DNA, we have selected a DNA stem-loop sequence, with the loop DNA sequence complementary to a specific DNA target. This detection platform can be altered to provide different modes of detection, and the electrochemical signal is shown to be highly dependent upon hybridization with target DNA, consistent with a stem-loop to duplex transition. In the second system, two strands of ssDNA, a capture and probe strand, are linked together via a flexible polyethylene glycol (PEG) spacer to afford an ABA triblock macromolecule which is then immobilized on an electrode surface. The tethered probe strand contains a 5'-terminal ferrocene for electrochemical detection. Upon addition of target DNA the electrochemical signal increases, consistent with the tethered probe strand hybridizing near the electrode surface. Both of these new reagentless approaches provide advantages over conventional DNA sandwich assays.

Imenne Bouamaied,[a] Leslie-Anne Fendt,[a] and **Eugen Stulz**[a,b]

"Porphyrin-DNA: towards nanoscale multifunctional molecules"

[a] *University of Basel, Department of Chemistry, St. Johanns-Ring 19, 4056 Basel, Switzerland*
[b] *University of Southampton, School of Chemistry, Highfield, Southampton, Hants, SO17 1BJ, UK*

Abstract : Recently, DNA has become attractive as a supramolecular scaffold to produce nanoscaled entities. The dsDNA is suitable to specifically connect nano particles, in DNA chip technology and nanolithography, to create nanomechanical devices or to construct protein arrays and nanowires. Nucleobases themselves have been substituted to create functional DNA, e.g. for directly positioning reactive groups in the major groove for further derivatisation.
Here, we present a general synthetic route to porphyrinyl—nucleosides[1] and their subsequent site specific incorporation into short oligonucleotides and DNA to create multiporphyrin arrays.[2] The mixed porphyrin tetranucleotide arrays show induced energy transfer between the chromophores ,which is evidenced by the altered emission spectra as compared to the spectra of both the individual building blocks and the homoporphyrin systems. In the DNA strands, up to eleven consecutive porphyrins could be incorporated. The porphyrin modification induces a thermodynamic destabilisation of about 6.5°C per porphyrin. The absorbances of the porphyrin arrays show a significantly broadened peak at around 420 nm (characteristic porphyrin absorption) indicating electronic interactions in the arrays. Both the melting profile at 420 nm and CD spectroscopy show that the hydrophobic π-systems of the porphyrin induce a structure stabilisation in the single strand which is different from the unmodified DNA. In the duplexes, however, the α-helical structure is retained.



[1] I. Bouamaied, E. Stulz, *SYNLETT* **2004**, 1579-1583.
[2] I. Bouamaied, L.-A. Fendt, M. Wiesner, D. Häussinger, N. Amiot, S. Thöni, E. Stulz, *Pure Appl. Chem.* **2006**, in press; I. Bouamaied, E. Stulz, *Chimia* **2005**, *59*, 101-104.

K.N.Ganesh, IISER, Pune (India)

"Supramolecular recognition of DNA by modified PNA and gold nanoparticles"

Abstract : The principles of molecular recognition of DNA by a complement of itself, drugs, proteins and other modified nucleic acids have not only physico-chemical interest, but also have significance for practical applications. A variety of non-covalent molecular forces mediate such recognition and structural modulation of such forces lead to tuning the specificity and strength of such interactions. We have been studying specificity of DNA/RNA complementation by peptide nucleic acids (PNAs) rationally modified by conformational constraining of its backbone and introduction of chirality. These studies have lead to introduction of selectivity and discrimination in binding of DNA and RNA by modified PNAs. We have also devised protocols for generating nanoassemblies from DNA and gold nanoparticles by electrostatic encapsulation rather than the standard thiolation strategy. The results have implications for devising DNA/PNA templated assemblies of nanoparticles towards function.

References:

1. K. N. Ganesh and V. A. Kumar, Conformationally constrained PNA analogs: Structural evolution towards DNA/RNA binding selectivity, *Acc. Chem. Res.* **2005**, *38*, 404-412.
2. T. Govindaraju, V. A. Kumar and K. N. Ganesh, (SR/RS)-cyclohexanyl PNAs: Conformationally preorganised PNA analogues with unprecedented preference for duplex formation with RNA, *J. Am. Chem. Soc.* **2005**, *127*, 4144-4145.
3. Gourishankar, S. Shukla, K. N.Ganesh, M. Sastry, Isothermal titration calorimetry on binding of DNA bases and PNA-base monomers to gold nanoparticles, J. Amer. Chem. Soc. **2004**, 126, 13186-13187.
4. A. Gourishankar, S. Shukla, R. Pasricha, K.N.Ganesh, and M.Sastry, *Curr. Appl. Phys.* **2005**, *5*, 102-107.

Peter Walde, Department of Materials, ETH, Zürich (Switzerland)

"The possible roles of surfactant assemblies for the origin of life"

Abstract : A large number of surfactants are chemically simple compounds that may be obtained under presumably prebiotic conditions. Surfactant assemblies are self-organized polymolecular aggregates of surfactants, in the simplest case micelles, vesicles, hexagonal and cubic phases. It may be that these different types of surfactant assemblies have played various, so-far underestimated important roles in the processes that led to the formation of the first living systems.

Although nucleic acids are key players in the formation of cells as we know them today (RNA world hypothesis), it is still unclear how RNA could have been formed under prebiotic conditions. Surfactants with their self-organizing properties may have assisted, controlled and compartimentalized some of the chemical reactions that eventually led to the formation of molecules like RNA. Therefore, surfactants were possibly very important in prebiotic times in the sense that they may have been involved in different physical and chemical processes that finally led to a transformation of non-living matter to the first cellular form(s) of life.

There are many examples that illustrate the different roles and potential roles of surfactant assemblies in different research areas outside of the field of the origin of life, most importantly in investigations of contemporary living systems, in nanotechnology applications, and in the development of drug delivery systems. Concepts and ideas behind many of these applications may have relevance also in connection to the different unsolved problems in understanding the origin of life.

Literature: Walde P. *Origins Life Evol. Biospheres* **2006**, *36*, 109-150.

Chengde Mao, Purdue University, West Lafayette (USA)

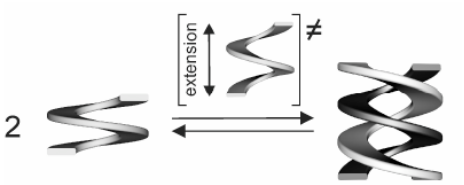
"Self-assembly of DNA nanostructures"

Abstract : Structural control at the nanometer scale is key to the development of nanotechnology. Supramolecular self-assembly is one promising approach to achieve this goal. Among many self-assembly molecular systems, DNA stands out as one of the best choices. Because DNA is the universal genetic materials, its structure and physical/chemical properties have been extensively studied, and a rich array of manipulation tools have been developed. DNA has excellent molecular recognition capability. Its structure can be precisely predicted. And branched DNA motifs have also been constructed. Combining all these factors together, DNA-based nanostructures have been rapidly developed. Here, the discussion focuses on the recent development of DNA nanostructures in my group: (1) static structures, (2) dynamic structures, and (3) conversion of DNA structures into metallic structures.

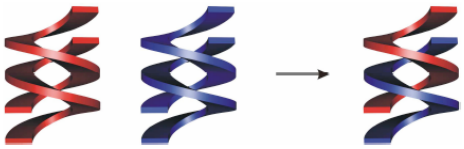
Ivan Huc, IECB, Bordeaux (France)

"Artificial Double Helical Architectures"

Abstract : Chemists have exploited the ability of nucleic acids to form sequence selective double stranded hybrids and turned it into an incredibly powerful tool to direct chemical synthesis[1] and to create well-defined discrete nanoarchitectures and two-dimensional patterns.[2] This lecture will focus not on nucleic acids but on artificial oligomeric molecules that also possess the ability to hybridize into double stranded helical structures and that may potentially find similar applications. Specifically, the folding of oligoamides of aromatic amines and acids into single helical conformation and the spring-like extension of these single helices to form double helices will be discussed.



The structures of these double stranded architectures have been characterized in solution and in the solid state.[3] The strength of hybridization shows unexpected dependencies on oligomer length,[4] and is also strongly influenced by peripheral residues.[5] Specific functions allow to promote cross-hybridization at the expense of homodimerization.[6]



[1] X. Li, D. R. Liu, *Angew. Chem. Int. Ed.* **2004**, *43*,4848; T. M. Snyder, D. R. Liu, *Angew. Chem. Int. Ed.* **2005**, *44*, 7379.
[2] N. C. Seeman, *Angew. Chem. Int. Ed.* **1998**, *37*, 3220; P. W. K. Rothemund, A. Ekani-Nkodo, N. Papadakis, A. Kumar, D. K. Fygenson, E. Winfree, *J. Am. Chem. Soc.* **2004**, *126*, 16344; M. Endo, N. C. Seeman, T. Majima, *Angew. Chem. Int. Ed.* **2005**, *44*, 6074; A. Y. Koyfman, G. Braun, S. Magonov, A. Chworos, N. O. Reich, L. Jaeger, *J. Am. Chem. Soc.* **2005**, *127*, 11886; S. H. Park, C. Pistol, S. J. Ahn, J. H. Reif, A. R. Lebeck, C. Dwyer, T. H. LaBean, *Angew. Chem. Int. Ed.* **2006**, *45*, 735.
[3] V. Berl, I. Huc, R. Khoury, M. J. Krische, J.-M. Lehn, *Nature* **2000**, *407*, 720; V. Berl, I. Huc, R. Khoury, J.-M. Lehn, *Chem. Eur. J.* **2001**, *7*, 2810.
[4] H. Jiang, V. Maurizot, I. Huc, *Tetrahedron* **2004**, *60*, 10029
[5] D. Haldar, H. Jiang, J.-M. Léger, I. Huc, *Angew. Chem. Int. Ed.* **2006**, *45*, in press.
[6] C. Dolain, C. Zhan, J.-M. Léger, I. Huc, *J. Am. Chem. Soc.* **2005**, *127*, 2400; C. Zhan, J.-M. Léger, I. Huc, *Angew. Chem. Int. Ed.* **2006**, *45*, in press.

Debora Berti, University of Florence (Italy)

"Phospholipids membranes decorated by cholesterol-based oligonucleotides as addressable soft nanostructures"

Abstract : The development of programmable assemblies for the the precise spatial arrangement of components at the molecular scale remains a major goal for nanoscience. DNA-mediated assembly initially suggested by Seeman,[1] is one of the most promising approaches for the supramolecular 'bottom-up' engineering of artificial nanostructured devices.
Mirkin and co-workers[2] have reported on the DNA-directed immobilization of gold nanoparticles to form supramolecular surface architecture. More challenging is the anchoring of oligonucleotides to soft surfaces such as phospholipid bilayers.
Cholesterol-based oligonucleotides are very promising building block molecules towards bottom-up design of nanoarrays on lipid surfaces, thanks their molecular recognition properties (selectivity) and the relative rigidity of their duplex form. In this contribution we report on the incorporation of cholesterol-TEG-ss-DNA-10mers and cholesterol-TEG-ss-DNA-18mers in lipid membranes through spontaneous anchoring of the cholesterol units in the hydrophobic environment. The incorporation and hybridization of cholesterol–based DNA molecules in POPC liposomes has been monitored by means of Dynamic Light Scattering, SAXS and Fluorescence Correlation Spectroscopy experiments.
Cholesterol-PEG-DNA affinity for supported lipid membranes has been studied by Quartz Crystal Microbalance Finally the orientation of DNA molecules anchored into the lipid surface have been investigated by UV-linear dichroism experiments that show an opposite sign signal between the ss-strand and duplex form indicating a change in the orientation of the base transition moments (hence of the base rings) with respect to the lipid surface.

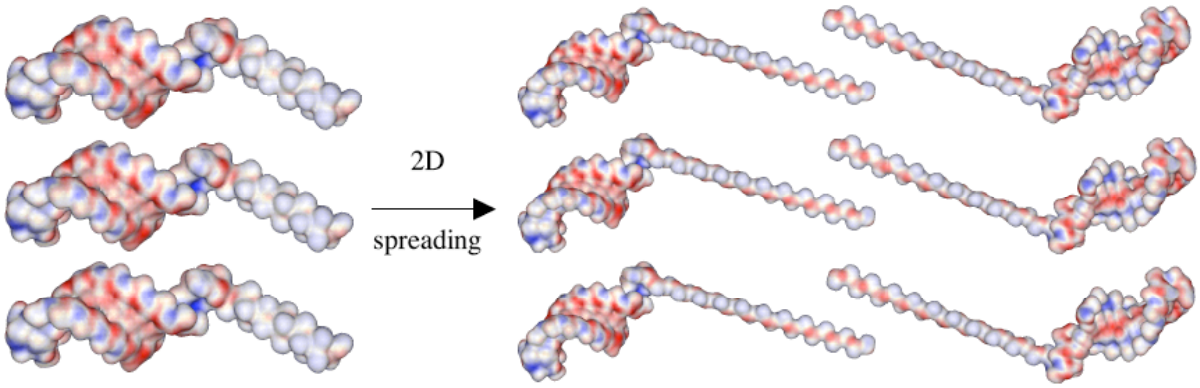
[1] Seeman NC: Nucleic acid junctions and lattices. *J Theor Biol* **1982**, *99*, 237-247.
[2] Taton TA, Mucic RC, Mirkin CA, Letsinger RL: The DNA-mediated formation of supramolecular mono- and multilayered nanoparticle structures. *J Am Chem Soc* **2000**, *122*, 6305-6306.
[3] Pfeiffer, I.; Höök, F., *J. Am. Chem. Soc.* **2004**, *126*, 10224-10225.

Adina Lazar,[1] Anthony W.Coleman,[1] Silvia Terenzi,[2] **Peter Strazewski**[3]

"Synthesis and atomic force imaging of amphiphilic peptidyl-RNA conjugates"

[1] Assemblages Moléculaires d'Intérêt Biologique (UMR 5086) IBCP, Lyon, France
[2] Laboratoire de Chimie Physique des Polymères et Membranes, EPFL, Switzerland
[3] *Laboratoire de Synthèse de Biomolécules, Bât. Eugène Chevreul, Domaine Scientifique de la Doua, 43 boulevard du 11 novembre 1918, 69622 Villeurbanne Cedex, France*
Email : pierre.strazewski@univ-lyon1.fr

Abstract : Peptidyl transfer RNA are key molecules for the biosynthesis of proteins taking place in ribosomes. Amphiphilic peptidyl-RNA are likely to have played an important role at the origin of RNA-controlled peptide synthesis that could have taken place in lipidic bilayer vesicles in some early version of modern translation from the genetic code to functional proteins. Lipophilic peptides would have served as primordial molecular anchoring devices that enabled their RNA carriers to be transiently immobilized, compartmentalized and thus highly concentrated on or in liposomes. In the absence of lipids synthetic amphiphilic 3'-peptidyl-RNA conjugates, molecules that mimic natural peptidyl-transfer RNA, are capable of self-assembling as vesicles in diluted aqueous solutions. In these molecules, the oligomeric folded RNA chain forms the polar 'head group', while suitable helix forming peptides form the hydrophobic group. Here we report on the solid support synthesis, the secondary structure analysis[‡] and the AFM imaging[§] of 3'-peptidyl-RNAs consisting of one 22-meric RNA seven base pair-hairpin mimicking the acceptor stem sequence of a tRNA connected through an amide linkage to a variety of lipophilic up to 22-meric peptides. Alanine, leucine and in some examples glutamic acid residues were chosen for our constructs. We observed the formation of vesicles of several hundred nanometers diameter and of thick (~21 nm) supported bilayers by peptidyl-RNA on optical glass surfaces. Their strong amphiphilicity drives the conjugates to aggregate into nanovesicles and, upon concentration and 2D spreading on a glass surface, into exceptionally regular and flat supported bilayers. The structure and a model of one peptidyl-RNA molecule used in this study, $Ala_{21}RNA_{22}$, is most consistent with the flat and relatively robust bilayers of the size and homogeneicity measured by AFM if a rearrangement from the α-helical conformation of the peptide, as was spectroscopically observed in solution, into β-sheets within the layered structure is assumed.



Such bilayers are the first ones observed that do not contain lipids or cholesterol. We shall use these conjugates to investigate their insertion into liposomes. Peptidyl-RNA bearing a peptide sequence capable of forming pores in bacterial membranes have the potential for

antibiotic activity. The same compounds bear supramolecular properties that may be of interest in their application as biodegradable nano materials.

‡ S. Terenzi, E. Biala, N.Q. Nguyen-Trung, P. Strazewski, “Amphiphilic 3’-Peptidyl-RNA Conjugates” *Angew. Chem.* **2003**, *42*, 3015-3018; *Angew. Chem. Int. Ed.* **2003**, *42*, 2909-2912.
§ A. Lazar, A.W. Coleman, S. Terenzi, P. Strazewski, “Observation of the Formation of Supported Bilayers by Amphiphilic Peptidyl-RNA” *Chem. Comm.* **2006**, *(1)*, 63-65.

Dan Luo, Dept. of Biological and Environmental Engineering, Cornell University, NY (USA)

"Nucleic Acid Engineering: Using DNA as a Generic instead of a Genetic Material"

Abstract : Our research focuses on engineering DNA as a generic instead of a genetic material. By taking advantages of the amazing chemical, physical, and biological properties of DNA and by utilizing a myriad of DNA manipulating enzymes, we have employed DNA as a true polymer. However, unlike chemical polymers which have linear, branched, networked, and dendritic structures, almost all DNA has only linear (or circular) architectures. To realistically use DNA as a polymeric material, we have created branched, networked, and dendritic DNA as additional material building blocks; many of them were inspired by pioneering work of Seeman and his group. These DNA materials are water soluble, biocompatible, biodegradable and most importantly monodisperse and anisotropic and have provided us with an enlarged tool box of designer hybrid materials for complex nano-architectures as well as novel functionalities. In essence we have created DNA-based "tinker-toys" for construction of new materials. A few examples of nucleic acid engineered materials are discussed in this talk; they include DNA-dendrimers, DNA nano-buckyballs, DNA-based nanobarcode systems, DNA hydrogels, DNA liposomes, and in particular, a cell-free, protein producing DNA hydrogel. These examples not only illustrate the concept that DNA can be utilized as a generic, designer material but also demonstrate the power of nucleic acid engineered materials as a link between biology and materials sciences and engineering. New properties and applications are expected from nucleic acid engineered materials.

Cécile Zakri, CRPP, Bordeaux (France)

"Carbon nanotube dispersion and assembly : an interest for biomaterials ? "

Abstract : Carbon nanotubes are considered as promising materials for a variety of applications, including new biomaterials and biomedical devices. Unfortunately, as produced nanotubes are under the form of a light and disordered powder. Processing nanotubes in macroscopic forms of practical use is a major challenge, to open the route towards applications.

We will first present a short review of carbon nanotube interactions with different biomolecules, and their utilities in processing and assembling nanotubes. Then we will describe the efficiency of different dispersants and the effect of several dispersing conditions on carbon nanotubes suspensions. We will particularly emphasize the use of denatured DNA to prepare concentrated and liquid crystalline suspension of nanotubes [1]. Such ordered phases could serve for the synthesis of oriented scaffolds for the directed growth of living cells.

The second part of the presentation will deal with the properties of nanotube micro-fibers obtained by a particle coagulation spinning process [2]. This process allows the fabrication of continuous assemblies of oriented nanotubes. After thermal treatments, the nanotube microfibers can be used as microelectrodes and micro-actuators. Another distinctive and interesting property of nanotube micro-fibers concerns their excellent toughness. The values of toughness can reach 55 J/gr for less than 10% strain [3]. In spite of the early stage of this research, the mechanical performances compare already very well with industrial high toughness fibers like Kevlar® which have been optimized over the last decades. That is why we believe that further improvements could soon lead significant advances for the development of new biomaterials.

[1] S. Badaire et al., *Adv. Mat.* **2005**.
[2] B. Vigolo et al., *Science* **2000**.
[3] P. Miaudet et al., *Nano Letters* **2005**.

IV- Participants:

Name	Contact Information
Philippe Barthélémy	INSERM U386, Université Victor Segalen Bordeaux 2, 146 rue Léo Saignat Bat. 3A, 33076 Bordeaux cedex, France *Email : barthelemy@bordeaux.inserm.fr*
Jennifer Becker	US Army Research Office, PO Box 12211, Research Triangle Park, NC 27709-2211, USA *Email : jennifer.j.becker@us.army.mil*
Debora Berti	Department of Chemistry and CSGI, University of Florence, Via della Lastruccia 3, 50019, Sesto Fiorentino, Firenze, Italy *Email : debora.berti@.unifi.it*
Michel Camplo	Lab. Matériaux Moléculaires et Biomatériaux, Fac. Sciences Luminy, case 901, 163, Av. de luminy, 13288 Marseille Cedex 09, France *Email : camplo@luminy.univ-mrs.fr*
Frédéric Dallemer	Laboratoire BioSciences FRE3005 CNRS, Université Paul Cézanne-Aix-Marseille 3, Case 432, Avenue Escadrille Normandie-Niémen, 13397 Marseille cedex 20, France *Email : frederic.dallemer@univ-cezanne.fr*
Krishna Ganesh	National Chemical Laboratory and Indian Institute of Science Education and Research (IISER), Dr Homibabha Road, Pune 411008, India *Email : kn.ganesh@ncl.res.in*
Arnaud Gissot	INSERM U386, Université Victor Segalen Bordeaux 2, 146 rue Léo Saignat Bat. 3A, 33076 Bordeaux cedex, France *Email : gissot@bordeaux.inserm.fr*
Frédéric Godde	Institut Européen de Chimie et Biologie, 2 rue Robert Escarpit, 33607 Pessac, France *Email : f.godde@iecb.u-bordeaux.fr*
Mark Grinstaff	Departments of Biomedical Engineering and Chemistry, Boston University, Boston MA 02215, USA *Email: mgrin@bu.edu*

Name	Contact Information
Jean Herscovici	Unité de Pharmacologie Chimique et Génétique, UMR 8151/U640, Synthèse Organique, Imagerie et Electrochimie, ENSCP 11 rue Pierre et Marie Curie 75231 Paris Cedex, France *Email : jean-herscovici@enscp.fr*
Ivan Huc	Institut Européen de Chimie et Biologie, 2 rue Robert Escarpit, 33607 Pessac, France *Email : i.huc@iecb.u-bordeaux.fr*
Chad Immoos	Department of Chemistry and Biochemistry, California Polytechnic State University, San Luis Obispo, CA 93407, USA *Email : cimmoos@calpoly.edu*
Jennifer Kelley	US Army Research Office, PO Box 12211, Research Triangle Park, NC 27709-2211, USA *Email : jenny.kelley@arl.army.mil*
Stephen Lee	US Army Research Office, PO Box 12211, Research Triangle Park, NC 27709-2211, USA *Email : stephen.lee2@us.army.mil*
Dan Luo	Dept. of Biological and Environmental Engineering, Cornell University, 226 Riley-Robb, Ithaca, New York 14853-5701, USA *Email : DL79@cornell.edu*
Chengde Mao	Purdue University, Department of Chemistry, West Lafayette, Indiana 47907, USA *Email : mao@purdue.edu*
Patrick Midoux	Centre de Biophysique Moléculaire CNRS UPR4301, rue Charles Sadron, 45071 Orléans cedex 2 *Email : midoux@cnrs-orleans.fr*
Laetitia De Jong-Moreau	"Biodiversité et Environnement", Case 18, Université de Provence, 3 place Victor Hugo , 13331 Marseille Cedex 3, France *Email : laetitia.moreau@up.univ-mrs.fr*
Xavier Moreau	"Biodiversité et Environnement", Case 18, Université de Provence, 3 place Victor Hugo , 13331 Marseille Cedex 3, France *Email : xavier.moreau@up.univ-mrs.fr*

Name	Contact Information
Laurence Navailles	Centre de Recherche Paul Pascal, 115, Avenue Albert Schweitzer 33600 Pessac, France *Email : navailles@crpp-bordeaux.cnrs.fr*
Reiko Oda	Institut Européen de Chimie et Biologie, 2 rue Robert Escarpit, 33607 Pessac, France *Email : r.oda@iecb.u-bordeaux.fr*
Bruno Pitard	Inserm U533, «Physiopathologie et pharmacologie cellulaires et moléculaires» Faculté de Médecine de Nantes, 1 rue Gaston Veil, 44000 Nantes, France *Email : bruno.pitard@nantes.inserm.fr*
Suzie Pun	University of Washington, Department of Bioengineering, Box 355061, Seattle, WA 98195, USA *Email : spun@u.washington.edu*
Peter Strazewski	Laboratoire de Synthèse de Biomolécules, Bât. Eugène Chevreul, Domaine Scientifique de la Doua, 43 boulevard du 11 novembre 1918, 69622 Villeurbanne Cedex, France *Email : pierre.strazewski@univ-lyon1.fr*
Eugen Stulz	University of Southampton, School of Chemistry, Highfield, Southampton, Hants, SO17 1BJ, UK *Email : est@soton.ac.uk*
Pierre Vierling	Laboratoire de Chimie des Molécules Bioactives et des Arômes, UMR 6001 CNRS, Université de Nice Sophia Antipolis, Parc Valrose, 06108 Nice Cedex 2, France *Email : Pierre.VIERLING@unice.fr*
Peter Walde	ETH, HCI F 501, Department of Materials, Wolfgang-Pauli-Strasse 10, CH-8093 Zurich, Switzerland *Email : peter.walde@mat.ethz.ch*

Name	Contact Information
Cécile Zakri	Centre de Recherche Paul Pascal, 115, Avenue Albert Schweitzer 33600 Pessac, France *Email : zakri@crpp-bordeaux.cnrs.fr*
Guy Zuber	Laboratoire de Chimie Génétique, CNRS UMR 7175-LC1- Faculté de Pharmacie, Université Louis Pasteur, Strasbourg I, 74 route du Rhin, BP 60024, 67401 Illkirch Cedex, France *Email : zuber@bioorga.u-strasbg.fr*