



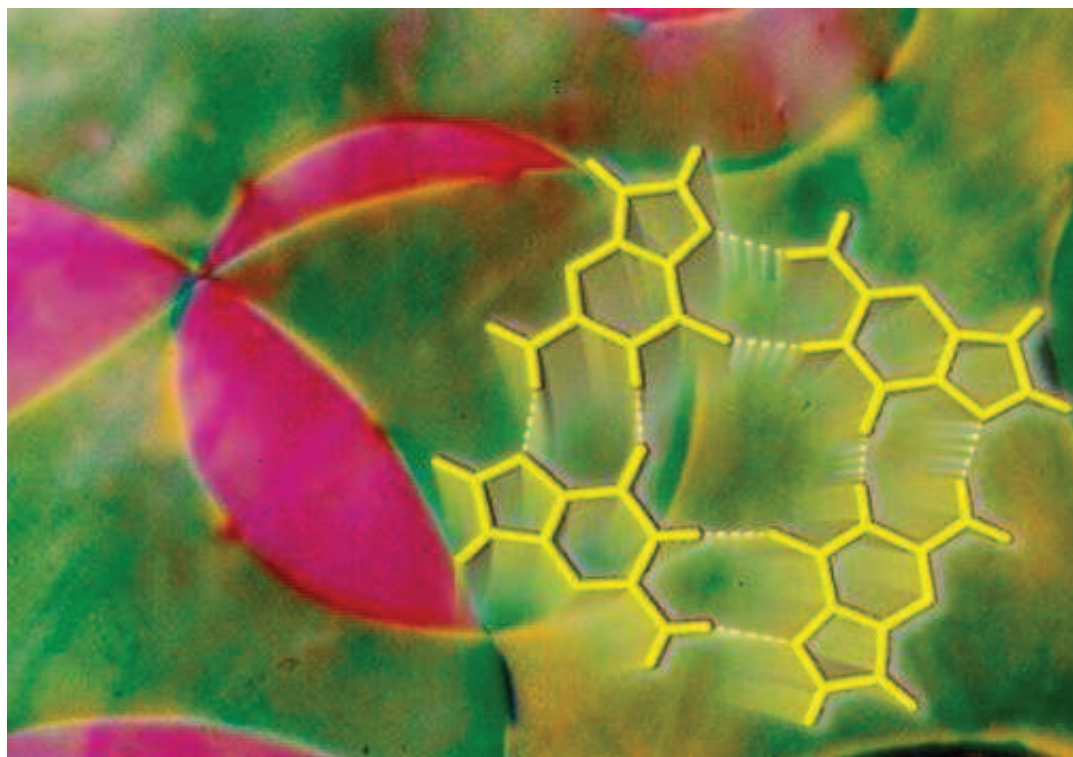
**RESEARCH CONFERENCES**

# Self-Assembly of Guanosine Derivatives: From Biological Systems to Nanotechnological Applications

Universitätszentrum Obergurgl (Ötz Valley, near Innsbruck) • Austria  
20-25 June 2009

Chair: **Gian Piero Spada**, University of Bologna, IT  
Co-Chairs: **Irena Drevensek-Olenik**, University of Ljubljana, SI;  
**Lea Spindler**, University of Maribor, SI

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## Conference Highlights

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*Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)*

In September 2006 the ESF Exploratory Workshop "Self-assembly of guanosine derivatives: from quadruplex DNA to biomolecular devices" was organised by I. Drevenšek-Olenik, P. Mariani and L. Spindler in Bled, Slovenia. At the workshop several new collaborations were established and future research directions were set. Moreover, the need of the community for a large-scale meeting was recognized with a special emphasis on young researchers actively taking part in it. Those objectives were followed when the ESF Research Conference "Self-assembly of guanosine derivatives: From Biological Systems to Nanotechnological Applications" was held in Obergurgl, Austria in June 2009. The conference was chaired by Prof. G. P. Spada from Bologna, Italy and co-chaired by I. Drevenšek-Olenik and L. Spindler from Slovenia. The meeting was funded by ESF in partnership with Fonds zur Förderung der wissenschaftlichen Forschung in Österreich (FWF) and the Leopold-Franzens-Universität Innsbruck (LFUI).

Guanosine molecules show a remarkable ability to self-assemble into highly complex patterns, the so called G-quadruplexes. Recently the applicative value of these self-assembled structures was recognized in several different fields ranging from molecular electronics to oncology. The conference merged scientists from many different fields like physics, biophysics, supramolecular chemistry, biochemistry, molecular biology and nanotechnology. The conference had a total of 75 attendees and the most recent scientific progress in the field was communicated by 17 invited speakers, 21 selected short talks and 24 poster presentations. At the conference a recently established European network on guanosine-self assembly (COST Action MP0802) was introduced. This initiative will further promote guanosine-based research on a European level by exchange of expertise and knowledge in the following years.

I hereby authorize ESF – and the conference partners to use the information contained in the above section on 'Conference Highlights' in their communication on the scheme.

# Scientific Report

## Executive Summary

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(2 pages max)

The ESF Research Conference "Self-assembly of Guanosine Derivatives: From Biological Systems to Nanotechnological Applications" covered the topic of G-based materials from their very fundamentals all the way to nanotechnological and biological applications. Three scientific sessions represented the most different branches of the field: Session 1 – *Synthesis and supramolecular structures*, Session 2 – *Biological systems*, and Session 3 - *Charge transfer and ionic effects (with nanotechnological implications)*. It was demonstrated that guanosine-based self-assembled structures possess large potential that connects biological with the technical world. The importance of G-quadruplex structures in vivo (discussed mainly in Session 2) has required development of a comprehensive knowledge of the structural and folding properties of the G-rich DNA regions (discussed mainly in Session 1). In addition, many recent successful demonstrations of applications of the G-based materials in areas ranging from medical chemistry to molecular nanotechnology and biotechnology require a rapid progress of the interdisciplinary expertise on the topic (discussed mainly in Session 3).

The conference had a total of 75 attendees, of which 17 were invited speakers, 21 young researchers had selected short talks and 24 posters were presented. The participation of young researchers was especially encouraged (73% of participants – excluding invited) and a good gender balance (51% of female participants – excluding invited) was achieved.

At the Round Table a recently established European network on guanosine-self assembly (COST Action MP0802) was introduced. This initiative will promote guanosine-based research on a European level by exchange of expertise and knowledge in the following years. At the Round Table also future research directions were set and future meetings on guanosine self-assembly were agreed and announced.

## Scientific Content of the Conference

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(1 page min.)

- Summary of the conference sessions focusing on the scientific highlights
- Assessment of the results and their potential impact on future research or applications

The work of the Conference was divided in three scientific sessions presenting different aspects of the self-assembly of guanosine derivatives although the content of several talks could not be strictly confined in a single session.

**Session 1** was dedicated to the *Synthesis and supramolecular structures*. The key-lectures were given by the 7 invited speakers of this session. (i) **Gang Wu** (Kingston, CA) presented some historical perspectives of the 5'-GMP self-assembly story and described his recent findings regarding 5'-GMP self-assembled structures in neutral solution, the role of alkali metal ion binding, and new results on the structure of the acidic 5'-GMP gel. (ii) **Mihai Barboiu** (Montellier, FR) reported synthetic routes for preparing self-organized systems from guanine and other nucleobases which have been "frozen", through the sol-gel process, in a solid state matrix, as a straightforward approach for the design of a novel class of nanomaterials. (iii) **Koji Araki** (Tokyo, JP) described how to design hydrogen bond-directed supramolecular materials of guanosine derivatives either one-dimensional (tape), or bi-dimensional (sheet), or 3-D (lamella) and finally supramolecular vesicles. (iv) **Nada Spackova** (Brno, CZ) presented a theoretical out in-depth characterization of the loop topology of a telomeric quadruplex using MD simulations with the main purpose was testing of the capability of the MD simulation technique to describe G-DNA loop

topologies, which represent a very challenging task for computational methods. (v) **Mateus Webba da Silva** (Colerain, UK) discussed how, in order to realize programmed build up of DNA objects, devices, and materials, a systematization of the principles at the basis of control of the assembly process is necessary. He demonstrated the design, and control of self-assembly, of novel quadruplex topologies through the use of a rational axiomatic approach based on the two-state disposition of the glycosidic bond angle. (vi) **Anh Tuan Phan** (Singapore, SG) presented his structural study on various G-quadruplex topologies formed by biologically important DNA and RNA sequences and showed that while G-quadruplex structures formed by human telomeric DNA are diverse (six different intramolecular G-quadruplex structures observed for human telomeric DNA sequences were discussed), those formed by human telomeric RNA sequences are more conserved. (vii) **Paolo Samorì** (Strasbourg, FR) discussed the reasons why, given the possibility to functionalize the guanosines in the side-chains, they appear as ideal building blocks for the fabrication of complex architectures with a controlled high rigidity, thus paving the way towards their future use for scaffolding, i.e. to locate functional units in pre-programmed positions; in his lecture he reviewed results on the 2D self-assembly of various guanosine derivatives and showed how ordered guanosines 1D H-bonded architectures can be used to control the 2D patterning of oligo-thiophenes at surfaces. In the Session 1, eight **short-talks** covered different aspects from computational and experimental analysis of G-quadruplex formation, stability and function (J. Huppert, Cambridge, UK) to multifolding of putative sequences (L. Payet, Cambridge, UK), to control of the assembly with synthetic receptors (A. Marsh, Coventry, UK), to design of quadruplex topologies with high stability (Nason Hessari, Colerain, UK), to time resolved spectroscopies (A. Banyasz, Gif-sur-Yvette, FR), to solid state NMR (A. Webber, Warwick, UK), to Langmuir-Blodgett formation (M. Devetak, Ljubljana, SI) and, finally, to the effect of 8-substitution in the guanosine self-assembly (J. M. Rivera, Puerto Rico, US).

**Session 2 was dedicated to *Biological systems*.** The key-lectures were given by the 6 invited speakers of this session. (i) **Jean-Louis Mergny** (Paris, FR) spoke on the “rules” that govern the formation of these intramolecular G-quadruplex structures and determine their stabilities. (ii) **Rosa Di Felice** (Modena, IT) discussed the QM simulation of G-quadruplex and their electronic properties. (iii) **Shozeb Haider** (London, UK) reported on a molecular model for drug binding to tandem repeats of human telomeric G-quadruplexes. (iv) **Nancy Maizels** (Seattle, US) discussed the function of G4 in the human genome and in particular the chromosomal domains with high potential to form G4 DNA (the telomeres, the ribosomal DNA, and the immunoglobulin class switch regions) were considered. (v) **Antonio Randazzo** (Naples, IT) discussed the G-quadruplex-drug binding: most of the reported G-quadruplex binding agents bind to DNA by interacting with the wide  $\pi$ -stacking surface of the G-tetrads at the edges of the quadruplex; in contrast to this mode, groove-binding modes are characterized by a very different specificity with an higher extent of selectivity. (vi) **Paula Bates** (Louisville, US) presented her investigations on the mechanism and therapeutic potential of guanine-rich oligodeoxynucleotides as novel treatments for cancer and the development of an unmodified 26-base oligodeoxynucleotide, which has cancer-selective antiproliferative activity against a wide range of malignant cell types. In the Session 2, six **short-talks** covered different aspects from the chaperon role of polymers for G-quadruplex formation (R. Moriyama, Fukuoka-shi, JP) to the use of a peptidic scaffold as a topological template that can direct the intramolecular assembly of covalently attached oligonucleotides into a parallel G-quadruplex (E. Defranq, Grenoble, FR), to recognition of G-quadruplex in a gene promoter (Wan Chi Lam, Coleraine, UK), to interactions between porphyrins and Human telomeric G-quadruplex (B. Pagano, Salerno, IT), to the synthesis and characterization of G-rich oligonucleotides as potential anti-HIV agents (D. Montesarchio, Naples, IT) and, finally, to interactions between anticancer drugs and the G-quadruplex structure of the Human telomeric DNA (I. Manet, Bologna, IT).

**Session 3** was dedicated to *Charge transfer and ionic effects (and nanotech implications)*. The key-lectures were given by the 4 invited speakers of this session. (i) **Jeffery Davis** (College Park, US) discussed the use of lipophilic guanosine derivatives that combine both “molecular recognition” and “membrane soluble” features for the development of synthetic ion channels. (ii) **Janez Plavec** (Ljubljana, IS) Discussed the role of cations in stabilization of G-quartets and how formation, stability and structural details of G-quadruplexes are dependent on cation species and cation concentration: cation localisation and movement can be inferred by NMR. (iii) **Alexander Kotlyar** (Tel Aviv, IL) described the synthesis and properties of novel long G4-nanowires. (iv) **Ross Rinaldi** (Lecce, IT) reported on nanotechnological strategies to fabricate electronic devices based on guanosines; self assembled mono layers were produced by physisorption or chemisorption by cast deposition and slow solvent evaporation.

In the Session 3, seven **short-talks** covered different aspects from the electronic structure of DNA assemblies complexated with transition metal ions (G. Brancolini, Modena, IT) to the role coulombic interactions in regulation G-quadruplex self-assembly (D. Gonzalez, Madrid, SP), to electrical conductivity of Origami DNA (V. Linko, Jyvaskyla, FI), to contractile electrical switch made of DNA (D. Sen, Burmaby, CA), to the use of guanosine gel for aligning carbon nanotube (L. McGown, Troy, US), to the investigation of guanosine self-assembly with electrochemical AFM (A.-M. Chiorchea, Coimbra, PT) and, finally, to the self-assembly of 5'-GMP on the surface (K. Kunstelj, Ljubljana, SI).

On the occasion of the **two poster sessions**, 24 communications were presented.

As a summary of the scientific contributions it emerges that Guanosine-based self-assembled structures possess large potential that connects biological with the technical world. The importance of G-quadruplex structures in vivo (discussed mainly in Session 2) has required development of a comprehensive knowledge of the structural and folding properties of the G-rich DNA regions (discussed mainly in Session 1). In addition, many recent successful demonstrations of applications of the G-based materials in areas ranging from medical chemistry to molecular nanotechnology and biotechnology require a rapid progress of the interdisciplinary expertise on the topic (discussed mainly in Session 3).

The Conference was really interdisciplinary and scientists from very different backgrounds (chemists, physicists, biologists, engineers) met and joined their expertises. It should be appreciated, from the scientific point of view, the participation of many young people (73% of participants – excluding invited) indicating that the Conference topics will have a next future development. Also the perfect gender balance (51% of female participants – excluding invited) should be stressed.

The geographic origin of the participants appear to be a bit unbalanced (44% from IT, 15% from UK, 12% from SI, 10% from FR), however it should be noticed that Italy has the highest number of research groups active in Guanosine self-assembly (as confirmed by the participation to the COST Action MP802 on a very similar topic).

## Forward Look

(1 page min.)

- Assessment of the results
- Contribution to the future direction of the field – identification of issues in the 5-10 years & timeframe
- Identification of emerging topics

The conference created a stimulating environment for scientific discussions, exchange of ideas and establishing of new collaborations. It successfully followed the ESF Exploratory Workshop held in Bled, Slovenia in September 2006. Since then, several new trends in the field appeared and were covered during this meeting.

A forward look and future activities of the community were presented at the **Round Table**. The recently established European network on guanosine self-assembly (**COST Action MP0802** "Self-assembled guanosine structures for molecular electronic devices") was introduced by Action Chair L. Spindler from University of Maribor and J. Stefan Institute, Slovenia. The Action started in November 2008 and many attendees to this meeting are already actively participating in it. The conference enabled new candidates to realize this opportunity and join the Action (J Huppert, UK; E. Defrancq, FR; A Mash, UK; O Ryazanova, UA). **Internet pages** covering the guanosine structures - from very basic information to all updates on future activities - were presented by two young and ambitious webmasters: Dr. Shozeb Haider from London School of Pharmacy, UK (<http://www.g4net.org/home.html>) and Dr. Julian Huppert from University of Cambridge, UK (<http://www.quadruplex.org/>).

A highly interesting future event was presented by Prof. Antonio Randazzo from University of Naples, Italy. He will organise a **Training School** with the title "Fundamentals of guanosine assembly and quadruplex formation" in scope of the COST Action MP0802. The school will be held in Ischia, Italy on 27-29 October 2009. Many students and postdocs attending the ESF Conference were in this way informed about this school and decided to use this unique opportunity. Several speakers from this conference will give lectures at the school (J Davies, US; JL Mergny, FR; D. Montesarchio, IT; J. Plavec, SI; A. Randazzo, IT; GP Spada, IT; M Webba Da Silva.

**Future meetings** were also discussed and agreed between the interested organisers during this conference:

- European meeting of the guanosine community in London in September 2010 hosted by S. Haider from London School of Pharmacy, UK.
- 3rd International Quadruplex Meeting in Naples in 2011 hosted by A. Randazzo from University of Naples, IT.
- 4th International Quadruplex Meeting in Singapore in 2013 hosted by Anh Tuan Phan from Nanyang Technological University, Singapore.

This great interest in organising future meetings clearly shows that the guanosine assemblies are a hot topic and new advances in the field can be expected. Major interest is focused on possible applications of guanosine-based structures in molecular biology (the formation and role of G-quadruplexes *in vivo* in the genome), oncology (as possible anti-cancer therapeutic agents) and nanotechnology (as molecular wires, templates for nanocircuits, hybrid electronic devices).

▪ Is there a need for a foresight-type initiative?

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## Atmosphere and Infrastructure

▪ *The reaction of the participants to the location and the organization, including networking, and any other relevant comments*

The conference was held in the beautiful setting of Ötz Valley in Austria. The University Centre Obergurgl did great services in accommodation, meals and lecture halls. The isolated setting helped keeping the attendees together and promoted fruitful discussions. Walking paths around Obergurgl were an ideal place for spending leisure time. The ESF Secretary Mrs. Judith Sabaton was very helpful and took care that everything ran smoothly on-site. All the participants left the meeting with very positive impressions.