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**RESEARCH CONFERENCES**

ESF-EMBO Research Conference

# Molecular Bioenergetics of Cyanobacteria: From Cell to Community

Hotel Eden Roc, Sant Feliu de Guixols (Costa Brava) • Spain

10-15 April 2011

Chair : Cheng-Cai Zhang, Université d'Aix-Marseille II and CNRS, FR

Co-Chairs: Elke Dittmann, University of Potsdam, DE
Conrad Mullineaux, Queen Mary University of London, UK

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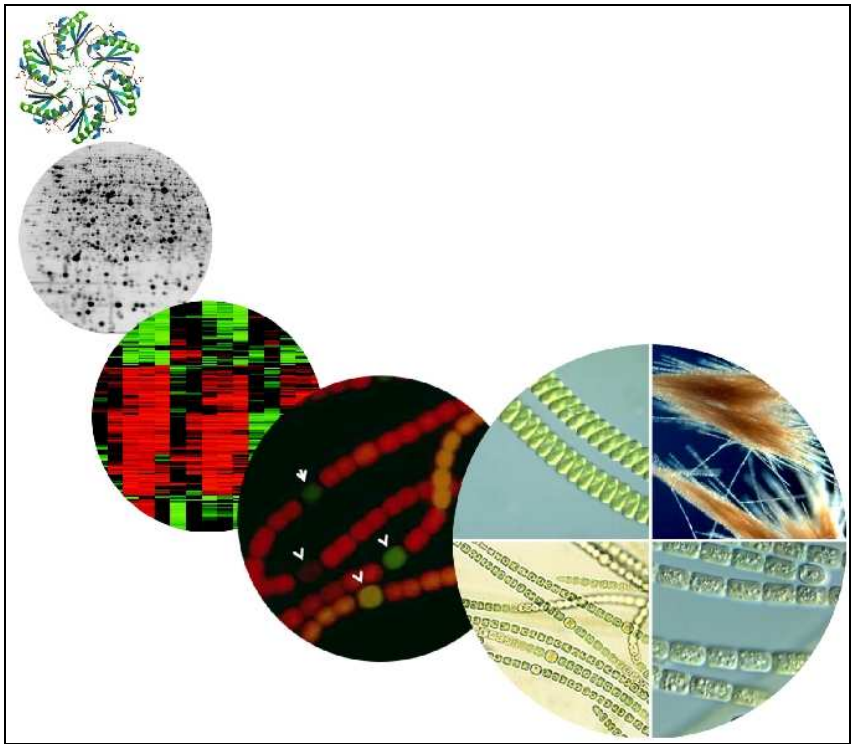
**Highlights & Scientific Report**



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## Conference Highlights

*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)*

The activities of cyanobacteria, also known as blue-green algae, shaped extensively the evolutionary landscape of both living organisms and our planet. Cyanobacteria first appeared on the earth around 2.5 billions years ago, if not earlier, and they were the first organisms to emit oxygen through their photosynthetic activity, which made possible the appearance of the ozone layer, and all other organisms using oxygen as electron acceptor. They are also ancestors of chloroplasts and major contributors of genetic resources during the evolution of plants.

Today, cyanobacteria still constitute important primary producers, in particular in the ocean environments around the globe (see a movie at http://www.youtube.com/watch?v=wAsNzQ2RDqM), thriving in environments where nutrients are scarce. This is possible because cyanobacteria use water as electron donor, sunlight as energy, and minerals as building blocks. Thus these organisms constitute important resources for future sustainable production of bioenergy, secondary metabolites for drug development, and for our basic understanding on the evolutionary history of both life and the Earth.

The research conference is the sixth among a series of conferences started in 1999 under the title of “Molecular Bioenergetics of Cyanobacteria”. Each of them focused on a particular topic, highlighting recent progress in the area of cyanobacterial research. The latest conference focused on the impressive progress of our understanding on the cellular structure of cyanobacteria, their multicellular behaviors both at the level of an organism and the level of community composed of cyanobacteria and other organisms in the natural environment. 130 young and senior scientists from Europe, America and Asia attended this conference.

The appearance of multicellular cyanobacteria very early during evolution marked an important milestone in the evolution of living organisms. How different cells talk to each other and exchange various compounds has been largely a mystery for a long time. Recent advances in cell biology, combined with imaging and molecular genetics enabled us not only to visualize fine cellular structures allowing filamentous cyanobacteria to exchange carbon or nitrogen sources but also to test the function of these structures. Several presentations and posters showed important progress on these topics.

Impressive progress is also being made on cyanobacterial genomics. Currently, 37 cyanobacterial genomes are already listed in the CyanoBase databank, and most importantly, 50 more cyanobacterial genomes, representing cyanobacterial lineages not covered by previous genome sequencing, are being sequenced. One talk summarized the progress of this effort. These new data will offer an important tool for our understanding on the physiology and environmental adaptation of cyanobacteria. Many cyanobacteria live in community with other bacteria or even in symbiosis with plants or animals. Comparative genomics, bioinformatics analysis and in situ measurement of the activities are starting to give us information on the important steps during evolution allowing free-living cyanobacteria to establish close relationships to other organisms, and even became an integral part like a chloroplast in plants.

Finally, one of the goals of a high-level research conference is to allow researchers to exchange ideas though contact and discussions. In this regard, this research conference was really outstanding as measured by strong interaction between speakers and the audience, as well as the extensive discussion during the two poster sessions. Each talk was followed by lively, open, constructive and long discussions. This was made possible by allowing a flexible period of time in each session under the control of the experienced session chairs.

The forward-looking discussion session at the end of the conference was an opportunity to highlight the challenge of European research on cyanobacteria, proposed future directions and tools allowing European research to stay at the forefront of international research on the use of cyanobacteria for bioenergy development, environmental protection and identification of useful drugs for pharmaceutical industry.

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Scientific Report

## Executive Summary

*(2 pages max)*

We used several mail lists to reach various researchers in the world interested in the major topics of the conference. These lists include members attending the European or American workshops on cyanobacteria, and the ISPP (International symposium of photosynthetic prokaryotes) symposium. The conference was also announced at other meeting where one of the chair/co-chairs attended. 18 invited speakers accepted to come, a few others declined because of the conflicts with invitations. Those invited speakers are all leading scientists in the field of cyanobacterial research. Among them, 7 of them are females, 3 from the US, and 1 from China.
In addition to the invited speakers, we received 131 applicants, and 110 attended the conference. 133 abstracts were received.
Overall 10 sessions were organized, including two poster sessions, two round-table discussion sessions, and 6 sessions of presentation by both invited speakers and those giving short talks selected among the applicants. In addition to the 18 invited talks each lasting 30 min, 23 short talks with each lasting 15 min were selected from the applicants, and more than 90 posters were displayed during the two poster sessions.
The conference was praised by a number of attendees as among the most successful scientific meetings they ever participated in. Several major factors contributed to this success: 1) very high quality talks; 2) extensive exchanges and discussions following each talk and during the poster sessions; 3) shared interests of scientists on common themes yet using multi-disciplinary approaches such as molecular genetics, structural biology, bioinformatics, genomics, and mathematic modeling. The lively discussion during each session was made possible by planning fewer short talks, but leaving at least 30 min flexible time in the hands of the session chair to allow extensive discussion. A large number of people from the audience participated in such discussion, including young scientists.

## Scientific Content of the Conference

*(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*

Session 1: “stress” and metabolism in the lab and the environment. This session included 3 invited talks. M. Hagemann presented the new results on the characterization of a glycolate oxidase, so far found only in plants, as an important player in photorespiratory metabolism. The cyanobacterial counterpart has both common and distinct features as compared to its counterpart in green algae and higher plant. Interestingly, this metabolic pathway is required for O2 scavenging during N2 fixation in heterocyst-forming cyanobacteria, a process highly sensitive to oxygen. These data provide an additional mechanism allowing the oxygen-sensitive nitrogenase to function properly. A. Latifi summarized their studies on an important gene cluster, highly conserved in cyanobacteria, that regulates oxidative stress response. Many cyanobacteria can synthesize various toxins, which are a major environmental concern worldwide; however, the biological function of such toxins remained poorly understood. A. Kaplan showed evidence that the cyanobacterium *Aphanizomenon ovalisporum* may use the hepatotoxin cylindrospermopsin as inter-species signal for phosphate acquisition, while the group of E. Dittmann presented data indicating that the other important hepatotoxin microcystin may bind to proteins and be involved oxidative stress response.

Session 2. Cyanobacteria as multicellular mechanisms. This session included 4 invited speakers and 4 short talks. A number of posters also deal with related topics. Under diazotrophic growth conditions, heterocyst-forming filamentous cyanobacteria rely on two different cell types on

carbon and nitrogen fixation, in vegetative cells and heterocysts, respectively. This multicellular life style must rely on inter-cellular exchanges of nutrients for filament growth. Following the pioneering work in 2008 by Mullineaux and colleagues establishing the existence of channels located at the intercellular junctions allowing rapid exchanges of small molecules from cell to cell, important progress was reported during the conference. AmiC2, a cell-wall amidase, may play a role in the establishment of the intercellular channels, possibly by locally remodeling the peptidoglycan layer at the cell-cell junction. A poster from Mullineaux's group indicates that various signals regulate the opening and closing of the channels. Both tomographic and electron microscopic images suggest the outer membrane is continuous along the filament, but proteins as small as 15 kDa can not cross cell junctions through the periplasmic space. The nature of such barriers remains unknown but the best candidate may be the peptidoglycan layer that covers the entire cytoplasmic membrane of each cells. The major function of the continuous outer membrane is to ensure filament integrity, an important element for multicellular growth. Heterocyst differentiation is under the control of HetR. While the HetR function has been well characterized by molecular and biochemical analyses, it resisted so far to crystallographic studies for years. Finally, R. Haselkorn reported the first data on HetR structure. Exciting discoveries are ahead on this research topic.

Session 3. The circadian clock and cell biology. This session included 3 invited talks and 3 short talks. Cyanobacteria, at least some of them, have a unique feature among prokaryotes in possessing a circadian clock allowing cells to modulate the entire activities on the basis of daily rhythm. S. Golden reported the latest discovery of a new cell cycle element under the control of the clock, that is cell division. A. Wilde reported astonishing data showing that by simply expressing a cyanobacterial light receptor makes *E. coli* light-sensitive in their motility. F. Chauvat compared the cell-division machinery from cyanobacteria to that of other model organisms such as *E. coli* and *B. subtilis*, and established *Synechocystis* PCC 6803 as a model organism for the regulation of cell division of spherical bacteria. Cyanobacteria possess three different membrane systems: outer membrane, cytoplasmic membrane, and thylakoid membrane. E. Schleiff explored the features of outer membrane and its function, while L. Liu from Mullineaux's group presented a cell biology approach to study the dynamics and localization of respiratory protein complexes.

Session 4. How relevant is laboratory-based photosynthesis research to the real world? This session included three invited talks and three short talks. Whereas light is the energy source for photosynthetic organisms such as cyanobacteria, excessive light leads to oxidative stress and damages cellular machinery. D. Kirilovsky's group has characterized a protein, OCP (orange carotenoid protein) as a major component for excess energy dissipation. The new data presented at the conference detailed the mechanism of OCP action, modulated by light activation and interaction with a key component of the phycobilisome. Furthermore, a new component has been identified, FRP (fluorescence recovery protein) completing the cycle of fluorescence loss and recovery during the photoprotective mechanism.

Session 5. Adaptation to environment. This session included 3 invited talks and 4 short talks. Some cyanobacteria can establish stable symbiotic relationships to plants. The endosymbiosis theory suggests that the invasion of an ancient cyanobacterium with an eukaryote led to the evolution of chloroplasts. B. Bergman's group used comparative genomics to study the symbiotic relationship between a cyanobacterium *Anabaena* strain with the water fern *Azolla*. The genome of the cyanobacterial partner is found to be at a stage of extensive gene erosion, a process that appears to be still continuing, but genes involved in functions required for plant growth (such as $N_2$ fixation) are well preserved. Such symbiotic relationship may offer a nice opportunity to study cyanobacterial and plant co-evolution. L. Stal presented data on how environmental factors affect the activity of cyanobacteria in microbial mats, complex communities established by cyanobacteria and also other bacteria. Cyanobacteria, such as the tiny *Prochlorococcus* species, are important players in the marine environment. Genomic studies reported by C. Steglich suggest that non-

coding RNAs play important roles in the physiology of these cyanobacteria. In addition, extensive anti-sense transcriptional activities were detected; the function of such activities was debated. Several talks, by J-F Humbert, W. Hess and others, also reported the biodiversity and genetic dynamics of either the freshwater bloom-forming cyanobacteria, or the chl-d containing cyanobacteria found in coastal areas.

Session 6. Systems biology and integrated approaches. This session included 2 invited talks and 5 short talks. The speakers used very diverse approaches for the understanding of cyanobacterial regulation, including structural biology, genetics, modeling and genomic studies. P. Shih reported the first analysis of the 50 cyanobacterial genomes that are sequenced at the DOE and the Pasteur Institute. These new genomic resources, once released, will constitute important tools for cyanobacterial research. Several groups (C. Zhou, JL Llacer, A. Contreas) reported their new findings on the nitrogen control in cyanobacteria. Two structures of NtcA, an important control element in nitrogen metabolism as well as heterocyst development, have been resolved, together with the structure of PII and PipX as well as their complexes.

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- *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*

1. **State-of-the-Art**

· Current state of research in the area

The use of multiple approaches to tackle scientific problems in cyanobacterial research becomes more and more evident. This has led to important progress on our understanding on the basic processes of bioenergetics in model organisms, the cell biology and heterocyst development, and multi-levels of interactions (cell-cell, cell-host, cell-environments). The availability of increasing amounts of genomic data, together with the new approaches, helps to unravel new regulation pathways (anti-sense RNA, regulatory RNA, global control), as well as giving insight into the evolution of cyanobacteria and other photosynthetic organisms.

· Likely advances in the near future

Several presentations started to use synthetic biology approaches for metabolic engineering in cyanobacteria. The start of synthetic biology, combined with new techniques (NanoSIMS, deep sequencing, omics techniques) for basic research as well as the use of cyanobacteria for potential application in environmental protection and bioenergy etc. The extraordinary developments in environmental research related to cyanobacteria, made possible by in situ detection and measurement and metagenomics, will certainly continue.

**2. Scientific Challenges**

· Major knowledge gaps and potential “hot topics″, as well as lines of research less likely to move the topic forward

Cell biology, environmental biology, and bioenergy research will be likely to dominate our research in the near future. However, such studies are hampered by the lack of genetic tools on most cyanobacterial strains and the lack of fast-growing species better suitable for generating large biomass for potential application. Furthermore, the uncertainty surrounding the best known

cyanobacterial culture collection (Pasteur Culture Collection) will be potentially disruptive to the community as this collection continues to serve as the best resource center available to the community.

· Assessment of the impact of future advances on the research agenda
The potential of cyanobacterial research for basic understanding of biological processes as well as in various applications is well recognized. The rapid advances in these research areas will likely to provide new data for treatment of harmful cyanobacterial blooms, production of various products for energy or drugs, etc. The multiple approaches increasingly used by the research community will also provide an important platform for the training and exchanges of young scientists around Europe.

· European strengths and weakness in the research topic
-Strength:
Critical mass of scientists involved in aspects of cyanobacterial research;
Strong interactions among the scientists
Complementarities in approaches ranging from modeling to genomics and basic biochemistry.

-Weakness:
Relatively few European projects supporting cyanobacterial research
Requirement for more data sharing, mining, and integration
Little involvement of private sector in comparison to America and Asia.

**3. Impact and Follow-up**

· Recommendations for actions required to achieve the goals
Bring institutional support in line with the relevance of cyanobacterial research to the areas of bioenergy, environmental protection, and understanding of basic mechanisms some of which are unique among bacteria (multiple membrane systems and their biogenesis, circadian rhythm, $O_2$-evolving photosynthesis..).
Encourage better interaction with the private sector and risk-taking.

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

Yes. The researchers present at the conference felt strongly the need to continue this very successful meeting series, by identifying key new elements that are likely to make strong impact in the future. The two co-chairs, Elke Dittmann and Conrad Mullineaux, will lead this role in continuing to interact with the scientific community in these tasks.
In addition, we felt the need to better structure the scientific research community in Europe. A European Society for cyanobacterial research was discussed, and Prof. B. Bergman agreed to take the leading role with the help of other researchers in different European countries. This organization will help us to have a better visibility and attract better funding to support European research on these organisms.

## Atmosphere and Infrastructure

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

There was extremely positive reaction from the attendees for both the atmosphere and the infrastructure. In each session we reserved about 30 min flexible time that could be used by the chair person of the session to stimulate discussions. The strong interaction, and long period of discussion following each talk made this meeting truly outstanding and highly successful.

The infrastructure makes for a relaxed atmosphere allowing easy scientific exchange. The quality of service was excellent, and the personnel very nice.

We also acknowledge the highly efficient and professional help of Jean Kelly, whose effort and organizational skill were key elements for the success of this conference.

**Sensitive and Confidential Information**

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**Date & Author**:

**21st April 2011, Cheng-Cai Zhang, Elke Dittmann, and Conrad Mullineaux**