



RESEARCH CONFERENCES

ESF-EMBO Symposium

Bacterial Networks *bacnet13*

16-21 March 2013

Polonia Castle in Pultusk, Poland

Chaired by Prof. Regine Hengge, Freie Universität Berlin (DE)

Co-Chaired by Prof. Victor Sourjik, University of Heidelberg (DE)

<http://www.esf.org/conferences/13410>

Highlights & Scientific Report

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)

Since the 90s of last century the biannual *Bacterial Networks Conference* or shortly *BacNet* has been the most important meeting point and show case at the interface of molecular microbiology and bacterial systems biology in Europe. By focusing on the architecture, function and dynamics of bacterial regulatory networks, BacNet presents and discusses the key topics required to understand the molecular structure and function of bacteria, their role in pathogenesis and ecology as well as their use in biotechnology and synthetic biology. *BacNet13* impressively demonstrated that understanding bacterial regulatory networks requires interdisciplinary approaches that combine molecular biology, biochemistry and structural biology with the latest microscopy developments to visualize dynamic cellular processes, single-molecule analyses, whole cell (–omics) approaches, quantitative description and mathematical modelling. Moreover, it showed how current biotechnology, in particular synthetic biology as the engineering science of the future, can profit from our understanding of and ability to recombine the modules of cellular regulatory networks of bacteria.

The session on 'Networks in bacterial stress responses and environmental adaptation' made it amply clear that regulatory networks can only be understood if our knowledge on transcriptional regulation is integrated with insight into regulation at the RNA level and regulated proteolysis. 'Bacterial biofilm formation' highlighted the role of the ubiquitous biofilm-promoting nucleotide second messenger cyclic-di-GMP (a recurrent theme throughout the entire conference) and the control of the spatial architecture of bacterial biofilms. Also in the analysis of 'Bacterial motility and chemotaxis' spatio-temporal aspects as well as questions of robustness of signaling were addressed. 'Bacterial development' is now being unravelled in striking molecular detail in model organisms such as *Caulobacter*, *Streptomyces* and myxobacteria. Presentations on 'Bacterial communication, sociality and competition' highlighted the rapid evolution within biofilms and complex multispecies and/or host environments. The session on 'Cell shape, polarity and division' demonstrated the power of novel high-throughput approaches as well as single-molecule analysis and high resolution microscopy. 'Systems biology and modeling' and 'Synthetic biology' were an eye-opener to understanding the quantitative behaviour of stress response networks, readdressed regulatory behaviour of bacteria observed 50 years ago but never understood, and demonstrated how bacterial cell extracts will be converted to in-vitro factories for metabolic intermediates of medical or biotechnological interest or how engineered bacteria will be used as sensors for environmental pollutants.

In addition to these strictly scientific sessions, *BacNet13* also provided a novel highlight – a 'Science&Society' session focussing on 'Creative experiments at the interface of science and the arts'. A major topic was the generation, use and impact of images both in historic and contemporary science as seen by an art historian, who also used *BacNet13* as an opportunity for 'field research'. The second speaker presented her work in 'artistic research' which aims at generating knowledge by subjective interventions with nature. Finally, a DNA artist showed how he uses electrophoresis as an artistic medium to demonstrate the social impact of contemporary genetics. This session turned out to be extremely thought-provoking and generated intense and lasting discussions. In the final discussion this *Science&Society* session found enthusiastic support also for future *BacNet* conferences.

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

(2 pages max)

BacNet13 had a total of 164 participants (representing the absolute highest number that Pultusk Castle could handle, which meant that approximately 20 participants had to lodge in another nearby hotel). Besides the invited speakers, these participants were chosen among the 197 applicants (based scientific interest and quality of poster abstracts). 46 % of the participants were females. The fact that the *BacNet* conference had moved from Sant Feliu in Spain (where it had taken place several times in the past) to the current location in Pultusk in Poland resulted in a slight shift in the nationality of participants, with fewer Americans but more researchers from Asia, in particular from India, participating.

BacNet13 featured 21 invited and 20 short scientific talks (in 8 scientific sessions), and 3 interdisciplinary invited talks of broader content (in the *Science&Society* session). 19 of the 44 speakers were female (43 %), with the numbers of females among invited speakers and short talk speakers being 9/34 (38 %) and 10/20 (50 %), respectively. 12 of 44 speakers were young investigators/early stage researchers (27 %; defined by an age of below 36 years), with even 5 of the 21 invited scientific speakers being young investigators (23 %).

134 posters were presented in three well attended evening poster sessions. Three poster prizes were sponsored by *Nature Reviews Microbiology*, whose editor-in-chief Sheilagh Molloy attended the entire conference. The poster prizes were awarded to Felix Hol (Delft University), Panis Gael (Université de Genève) and Susan Schlimpert (Max-Planck-Institute for Terrestrial Microbiology).

Besides the budget jointly provided by ESF and EMBO, *BacNet13* was also funded by:

- (i) the *EMBO Young Investigator Programme* supporting the invited talk by Rut Carballido-Lopez (INRA, Jouy-en-Josas; unfortunately, however, the speaker could not attend the conference due to sudden illness)
- (ii) the *Society for General Microbiology* supporting 4 speakers from the UK (with up to £ 2.000)
- (iii) the *Ernst Schering Foundation* (Berlin) supporting the 3 speakers of the *Science&Society* session (with up to € 5.000)

Scientific Content of the Conference

(1 page min.)

▪ Summary of the conference sessions focusing on the scientific highlights

In molecular microbiology, research on regulatory networks in bacteria is currently focusing on a number of different physiological contexts such as stress responses, environmental adaptation and survival of bacteria, biofilm formation (with its practical implications in medicine and technology), motility and chemotaxis (the latter as the perhaps best understood signal transduction system), development and morphogenesis, communication in microbial communities, the generation of cell shape and macroscopic morphological patterns in bacterial communities and cell division. While bacterial systems biology provides a quantitative and whole genome/cell perspective, contemporary synthetic biology makes use of our knowledge of bacterial regulatory networks and circuits to generate new applications in biotechnology. Some selected highlights from the sessions were the following:

'Networks in bacterial stress responses and environmental adaptation':

This session presented an integrative perspective on bacterial regulatory networks by combining a recently discovered key example of transcriptional control, i.e. the general stress response in alpha-proteobacteria (Julia Vorholt), with a completely novel translational control mechanism dependent on Elongation factor EF-P (Kisten Jung) and a novel system that links thermotolerance and the oxidative stress response with regulation by proteolysis (Kürsad Turgay).

'Bacterial biofilm formation':

This session highlighted the role of the ubiquitous biofilm-promoting nucleotide second messenger cyclic-di-GMP and control of the spatial architecture of biofilms of *E. coli* (Regine Hengge) and the complex role of a two-component system in biofilm formation of *Bacillus subtilis* (Nicola Stanley-Wall).

'Bacterial motility and chemotaxis':

Novel insights into the phenomenon of bacterial gliding motility (Tam Mignot) as well as into the complex mechanisms of spatio-temporal control of chromosomes and chemosensory proteins in *Rhodobacter* were presented, with the latter also providing a striking example of the use of cell biology technology in bacterial genetics (Judy Armitage). Finally, the

question of robustness of chemotactic signaling was addressed by elucidating how the *E. coli* chemotactic system elegantly compensates for temperature effects (Victor Sourjik).

'Bacterial development':

Using *Caulobacter* as a model organism, development of cell polarity and asymmetric cell division into two different cell types was shown to completely depend on the temporal and spatial control of the second messenger c-di-GMP (Urs Jenal), yet to be highly redundantly controlled (Sean Murray). A spectacular presentation showed how the predatory bacterium *Bdellovibrio bacteriovorus* invades and develops inside the periplasm of prey *E. coli* cells which are completely deconstructed during this process (Liz Sockett). A new molecular partner switching mechanism based on two-component regulators was shown to be crucial for *Streptomyces* development (Mark Buttner) and yet another novel second messenger, c-di-AMP, was found to be even essential in *B. subtilis* (Jörg Stülke).

'Bacterial communication, sociality and competition':

In this session on bacterial 'sociobiology', highlights were the evolution of competition versus cooperation in biofilms (Kevin Foster) and the report of lysogenic phages that also react to quorum sensing by their host bacteria (Sine Lo Svenningsen).

'Bacterial cell shape, polarity and division':

The power of novel high-throughput approaches was exemplified in recent work on cell envelope signaling in *E. coli* (Christina Pesavento speaking on behalf of Athasios Typas). The role of ser/thr kinases in the control of *Streptococcus* cell wall synthesis provided a striking example of the complexity of prokaryotic morphogenesis control machineries (Christophe Grangeasse). State-of-the-art fluorescent single-molecule analysis and high resolution microscopy allowed to demonstrate in vivo that SMC proteins move along the chromosomal DNA (Peter Graumann).

'Bacterial systems biology: quantitative network analysis and modeling':

This session presented a general strategy to convert cellular extracts of appropriately engineered strains into 'in-vitro synthetic factories' by insulating desired production pathways using triggered proteolysis of disturbing enzymes (Sven Panke). Another highlight was a quantitative analysis of the general stress response in *B. subtilis* using time-lapse microscopy of fluorescent reporter strains, which showed this response to occur in frequency-modulated stochastic or single deterministic pulses depending on the nature of the input signal (James Locke). By showing that keto-acids are key signals, the old riddle of how the nitrogen supply can affect catabolite control was resolved (Terence Hwa).

'Synthetic biology: rewiring bacterial regulatory networks':

Using a microfluidic device, drastic population heterogeneity in the reaction to changing environmental conditions was demonstrated (Sander Tans). Finally, custom-tailoring of a sensory-regulatory system for environmental pollutants was shown by modifying the effector-sensing XylR transcription factor, its cognate promoter regions and improving signal-to-noise ratio (Victor de Lorenzo).

'Science & Society: Creative experiments at the interface of science and the arts':

The subject was introduced with a historic account of the relationship between natural history/science and the arts as well as by pointing out current trends such as an ever increasing importance of images in science, 'artistic research' and modern biology as a source for new artistic tools and topics, which e.g. has led to 'Bio-Art' and numerous connections between synthetic biology and the arts (Regine Hengge). A key issue of the session was visualization in science, pointing out the unresolvable conflict between complex images of scientific objects and the epistemological ideal of objectivity, with images not only illustrating but shaping the object they show as well as our ideas and concepts (Horst Bredekamp). This also resulted in a lively discussion about the unspoken rules (if any) of visualization of data and concepts/models used by the scientists that make up the BacNet community. The second presentation showed an artist's work in and with nature, which revealed striking parallels between the convergence of engineering and nature, as it is now common in synthetic biology (Ursula Damm). Finally, the social impact of contemporary genetics, with its deterministic view focused on 'DNA' as a metaphor for the 'code of life', was addressed in examples of artistic work that uses DNA (literally in electrophoresis devices) as a material and medium (Paul Vanouse).

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

In an overall assessments of *BacNet13* – taking into account multiple feedback given by large numbers of participants – one clearly has to refer to the outstanding scientific quality of nearly all the presentations. In particular, also several of the short talks selected from the poster application abstracts were of a quality that will certainly place these young researchers on the map of European microbiology.

BacNet Conferences have been instrumental and will remain so for the generation and highly successful maintenance of a thriving and well-connected European community of molecular microbiologists, bacterial systems and synthetic biologists. It is also obvious that highly successful and ambitious young researchers, who have done their postdoctoral work in the US, consider their talks at *BacNet* as their points of entry into this European scientific community. Examples on *BacNet13* were Athanasios Typas (EMBL) or James Locke (Cambridge), who both recently returned to Europe, or Kristina Jonas (MIT) who is about to come back.

The very high quality of research presented at *BacNet13* – which was at least on an equal level with that of many Gordon Research Conferences in the US (e.g. *GRC on Microbial Stress Responses*) – probably also reflects the fact that the funding situation, especially for basic research, meanwhile seems better in Europe than in the US. It is also likely that several years after its introduction, funding by the European Research Council (ERC) begins to have an impact on scientific progress and excellence also in molecular microbiology and bacterial systems biology (several of the speakers, e.g. Regine Hengge, Urs Jenal and Victor Sourjik have ERC Advanced Grants, and a substantial number of posters came from ERC-funded groups, as e.g. that of Uri Alon, who unfortunately had to cancel his attendance and thus also his talk for personal reasons).

With respect to scientific topics, a number of emerging trends could be observed at *BacNet13*. In particular, these were:

(i) The growing importance of the *spatial organization* of regulatory networks – networks seem to ‘go 3D’ at all levels of resolution. This applies to single cells, in which many of the components of regulatory networks can be found at specific locations such as the poles or the midplane of the cell. Also the determination of cell shape has become an intriguing topic for investigation. Moreover, the spatial structure of cellular communities, i.e. biofilm microanatomy and differentiation into distinct physiological strata and regions, is becoming a hot topic that will also address the question how complex morphological pattern form at the macroscopic level. This trend reflects the introduction of cell biology technology and high resolution microscopy into molecular microbiology (actually this is rather a re-introduction, since gene fusion technology was originally developed by molecular microbiology in the 70ies and 80ies of last century).

(ii) *Evolutionary aspects* are clearly becoming ever more important. On the one hand, this relies on microbial genomics based on the availability of (soon) thousands of genome sequences. On the other hand, this is a consequence of the small size and fast growth of microbes, which allows to follow evolution *in vitro* in real-time. In particular, evolutionary aspects are being studied within the context of biofilms and complex microbial communities in general, with special emphasis on the evolution of communication, cooperativity and mutualism under highly competitive conditions and adaptation to complex environments as e.g. within hosts.

(iii) Another trend clearly observable on *BacNet13* is a *merging of classical molecular microbiology and bacterial systems biology*. Thus, quantitative analysis and mathematical modeling of regulatory networks very often is no longer separate from the molecular analysis of a system, but join in rather early during the projects and in presentations become just an integral part. On the other hand, a consensus seems to evolve that the collection of large scale –omics data alone (until recently popularized as ‘non-hypothesis-driven research’) will not lead ‘automatically’ to progress in our understanding of the complex regulatory networks that underly all microbial life functions – after all, it is a long way from data to knowledge to insight, which clearly requires creative hypothesis making on the basis of the treasure trove of data that –omics approaches provide us with.

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

No – what is required is the continuation of the *BacNet* series of conferences as a focus for scientific community building and maintenance and as the most important place for the exchange of knowledge and fostering novel collaborations in European molecular and systems microbiology.

Business Meeting Outcomes

- Election of the Organizing Committee of the next conference
- Identified Topics
- Next Steps

The forward-looking session was chaired by Victor Sourjik (as the Vice-Chair of *BacNet13* and future Chair of *BacNet15*). The following topics were discussed or dealt with:

Julia Vorholt (ETH Zürich) was elected as a Vice-Chair for *BacNet15*.

The Forward Looking plenary discussion confirmed that *BacNet13* was a full success. The balanced coverage of topics related to understanding of bacterial networks was highly praised by the attendees, and no criticism of the scientific program has been raised during the discussion. It was a clear consensus that the program has very well covered the new developments in the field, from molecular foundations of the cellular processes to the quantitative analysis of the higher-order control of the cellular networks in bacteria to the efforts of designing novel cellular networks. Also the newly introduced 'Science and Society' session resonated very well with the audience and it was clearly supported as an integral part of the future conferences.

The only discussion points for potential improvement raised by participants during the session were related to the schedule. One suggestion was to allocate even more time to informal discussions among participants, to further foster the exchange of ideas and increase the potential for developing new joint project. This could be achieved by extending the coffee breaks, from 30 to 45 minutes, at the expense of a minor shortening of the lunch break. An alternative would be reducing the duration of the sessions, but the ensuing discussion clearly showed that the number of the talks should not be reduced. The number and balance of invited and short talks during the conference was just right to ensure a broad coverage of different topics and also to enable both leaders in the field and young scientists to present their work.

Another discussed suggestion was to shorten the conference by one day, at the expense of abandoning a free afternoon at the fourth day of the conference and with adding scientific sessions at the days of arrival and departure. However, this proposal was not supported by the majority of participants, since such shortening would reduce the number of presented topics and shorten the time for informal discussions. It was agreed, however, that scheduling a Keynote Lecture before the dinner at the evening of the first day of arrival might be beneficial.

A third discussed proposal was to extend the time during which individual posters are presented, from one to at least two days. This was generally supported by most of the participants, but has to be clarified with the conference venue regarding the capacities. A further suggestion of moving the posters into the conference room was rejected because of the logistical difficulties.

One proposal that was strongly favored by most participants was to hold the conference at a slightly later time point, for example in May, which would allow a better use of the outsider areas of the venue for informal communication.

In respect to the future directions and emerging topics in the field, it was clear that the conference was already at the forefront of the current developments, which will continue and burgeon in the following decade. These topics include bacterial cell biology, signal transduction, stress responses, cell-cell communication and biofilm development, as well as systems and synthetic biology. Nevertheless, some of the areas will be expanded and added in the future conferences:

- *Environmental sensing by bacteria in the context of global cell regulatory networks.* The rapid development of this area is empowered by recent dramatic advances in the methods of genome- and proteome-wide analysis. By following changes in expression of most genes and proteins in a cell population, these techniques allow a global view of the overall cellular regulation upon changes in the environmental conditions. Further related and very promising developments reside in the field of metabolomics, which should in the near future allow quantification of hundreds of metabolites, and thus understanding the overall changes in the metabolic networks upon changing environmental conditions. Combined with quantitative computational modeling, such system-level analysis promises a much more comprehensive understanding of the regulatory networks that allow bacterial cells to optimally adjust their functions to the environment, including the environment within the host organism in case of pathogenic and commensal bacteria.
- *Second messenger signaling in bacteria.* Although examples of second messenger signaling (such as cAMP or ppGpp) in bacteria are known for decades, the extent of this mode of signaling is only becoming clear now, with several novel second messengers (c-di-GMP, c-di-AMP) being identified recently. The importance of these messengers in the global regulation of gene expression during life-style transitions is already recognized, but the regulatory mechanisms are still to be elucidated.
- *Analysis of bacterial communities.* It became clear over the last years that most bacteria in the nature do not exist as individual cells but rather as microbial communities. These communities can be composed of either one or of multiple species, with such examples as surface-attached biofilms or metabolically interdependent

species that share common environmental niche (e.g., human gut). The development and dynamics of these communities depends upon the sophisticated but currently poorly understood intra- and inter-species signal exchange. Understanding the spatial-temporal structure of these communities, the composition of species and the underlying signal exchange is one of the most important emerging topics in the field.

- *Design of synthetic intra- and intercellular networks.* With their comparatively modest complexity and the ease of genetic manipulation, bacteria provide ideal model systems for the emerging field of synthetic biology. Currently, there are multiple ongoing efforts to design novel functional modules within the cells, as well as synthetic multicellular systems that promise novel and exciting results.

With respect to the *Science & Society* session, participants enthusiastically supported such a session also for the future. The lively discussion of future topics for the Science and Society session yielded several areas of interest:

- Science communication & new media: how to best communicate science to a non-scientific community, also using new means of communication
- Philosophical and ethical aspects of biology, for example in relation to synthetic biology
- History of microbiology
- Perception of life science/scientists in the public and in the media/literature

These topics will be considered for presentations and/or plenary discussions at the *Science & Society* session during the upcoming meetings.

Based on the outcome of this forward-looking session, Victor Sourjik (Chair) and Julia Vorholt (Vice-Chair) will submit a proposal for the *BacNet15* conference to ESF in September 2013.

Atmosphere and Infrastructure

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

During the forward-looking session as well as in a lot of personal feedback during and after the conference, participants expressed their enthusiasm about Pultusk Castle as a meeting place (despite the extremely cold weather – actually snow storms in the middle of March!). This included the room situation, the excellent food, management and service – only internet service in the rooms may be improved somewhat. Moreover, participants were very satisfied with the highly professional and efficient organization by ESF and local representatives.

The social atmosphere during the conference was friendly, inclusive for everybody with intensive communication also between established and young researchers and not 'cliquish' at all. Informal networking among the participants was greatly facilitated by the familiar atmosphere in the dining places as well as by the presence of a large and pleasant bar area right next to the poster room located in one of the nicest parts of historic Pultusk Castle.

Two female participants (one an invited speaker) actually brought along their babies and husbands (to take care of the babies). This was entirely smoothly integrated into the daily routine of the conference and provided for great role models for the younger female scientists demonstrating the compatibility of science and family obligations.

Sensitive and Confidential Information

This report will be submitted to the relevant ESF Standing Committees for review.

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Date & Author:

April 14, 2013 Regine Hengge (Chair of *BacNet13*)