Networking Activity within the framework of the EUROCORES Programme
"Synthetic Biology: Engineering Complex Biological Systems"

"Global Challenges – Opportunities for Nanotechnology"
Final report

Venue: Venice International University**,** San Servolo/Venice, Italy

Date: 15-18 April, 2013

Number of participants: 67, thereof 57 junior scientists (PhD students and postdocs) from different disciplines and internationally recruited. Nine participants were PI or project members within the EUROCORES Programme „Synthetic Biology: Engineering Complex Biological Systems".

Organizers: Prof. Hermann E. Gaub, Prof. Dr. Christoph Gerber, Prof. Dr. Daniel J. Müller, Dr. Susanne Hennig (Managing Director CeNS)

Senior participants/advisors/teachers:

Proffs. Gerd Binnig (Nobel laureate, Munich), Hermann E. Gaub (Munich), Christoph Gerber (Basel), Jean-Marie Lehn (Nobel laureate, Strasbourg), Daniel J. Müller (Zurich), Adi Scheidemann (Zurich), and Viola Vogel (Zurich).

Summary

As a key technology of this century, nanotechnology and –engineering will play a leading role in the development of solutions for our global challenges. The upcoming threatening problems, which in turn pose rewarding research opportunities, will engross our next generation of scientists. The SNI Basel, the Center for NanoScience Munich, and the Department of Biosystems Science and Engineering at the ETH Zürich made a joint effort to address this urgent issue by inviting junior scientists to Venice International University for an intense four-day workshop. The junior scientists were recruited internationally and from very different disciplines (nanotechnology, molecular and cell biological engineering, microengineering, biotechnology, and medicine). In addition, a concise expert team was invited to substantiate the discussions. Two nobel laureates, Jean-Marie Lehn and Gerd Binnig, Viola Vogel (the former US presidential advisor on nanotechnology) and Adi Scheidemann, a nanotechnology entrepreneur, helped with detailed knowledge and know-how.

The first part of this meeting was to foster the awareness for the globes' status by an analysis through this group of junior scientists from all continents. In the next round, the junior researchers identified key problems, where nanotechnology and nano- and bioengineering can help: energy production, storage and distribution; health; environment; food & water; and new materials as a topic overlapping with the former ones. The last and possibly most important part was that the researchers formed interdisciplinary networks in which they worked out detailed concepts how the most urgent global challenges can be targeted using nanotechnology and bioengineering.

Since any change requires internationally consorted efforts, the initiation of a network amongst those scientists, which will sculpture our scientific and technological future, seemed essential. This was the second goal of this workshop, which was supported by creating an interactive WIKI-based platform for further networking and exchange of ideas between the participants. In addition, a summary of all ideas and results obtained by the interdisciplinary groups is currently in preparation and will be published in a booklet "Global challenges – opportunities for nanotechnology".

Final Programme

"Global Challenges - Opportunities for Nanotechnology"

Sunday, April 14	Time	Monday, April 15	Time	Tuesday, April 16	Time	Wednesday, April 17	Time	Thursday, April 18
	08:00	Breakfast	08:00	Breakfast	08:00	Breakfast	08:00	Breakfast
	08:30	Registration/ Poster Mounting Group A						
	09:00	Welcome & introduction	09:00	Organizational details	09:00	Wrap-up: Identification of Challenges	09:00	Results / Conclusions / Summary for policy makers
	09:30	Participants' short presentations (3 min) - Group A	09:30	Group Discussions: Identify Global Challenges	09:30	Group Discussions: How can Nanotechnology help?		
	10:30	Poster session Group A & Coffee						
	12:00	Short presentations Group B					12:00	Lunch/Departure
Arrival at San Servolo Dinner possible until 9 pm Opening times reception: 24 hours/day		Lunch (13:00-14:30)						
	13:00	Poster Mounting Group B (Group C - please hand over your poster at the conference office!)	13:00	Lunch	13:00	Lunch (13:00-14:30)		
	14:30	Poster session Group B & Coffee		Informal discussions	14:30	Group Discussions: How can Nanotechnology help?		
	16:00	Short presentations Group C						
	17:00	Poster session Group C			17:00	Wrap-up		
	18:30	Some time with J.-M. Lehn (Nobel laureate)						
	19:30	Welcome reception			19:00	Buffet Dinner		

Scientific Content

On the first day of the workshop, all junior participants presented themselves and their research topics with a 3-minute short presentation and in the subsequent poster sessions. In the evening, the junior participants had the chance to discuss with Nobel laureate Jean-Marie Lehn about science, but also career decisions, passion for science or the importance of luck.
The second day continued with round table discussions to identify and evaluate global challenges. The eight tables with eight participants each mixed again after 30 minutes discussions, while a "wisdom keeper" kept the knowledge of the table. The challenges identified were then ranked by the each table again, according to criteria defined by the junior researchers (urgency, global impact, sustainability, costs and nanotechnological potential). The conclusions of all tables were presented by the "wisdom keepers". In a next wrap-up, all participants agreed on a list of challenges identified as most important and with a potential for nano- and biotechnological solutions: food & water; energy production, storage and distribution; health; environment; and new materials as a topic overlapping with the other topics.

On day three, interdisciplinary teams were formed, consisting of 5 to 8 participants. Each team took advantage of their diverse expertise. They discussed potential solutions and worked out more detailed concepts of how a certain challenges can be targeted using nanotechnology and –engineering. The participants put forward new ideas in an interactive fashion that eventually should lead to an international network. Valuable possible projects in the different identified areas have been established. Three examples are given here:

(a) Disposable multiplex bio-sensing array for POC diagnosis

Current sensors are usually composed of one bio-interface and one transducer. Here we propose a novel approach that will bring bio-sensing to another level. The combination of two or more transducing elements used simultaneously to probe a nano-structured bio-interface will improve the reliability and specificity of the sensor and enable the detection of a wide variety of diseases.

Key advantages: A dual transducer sensor will probe the bio-interface with two independent methods, increasing reliability. It will also enable the detection of contaminants or non-specific interaction (see scenario 1 below) and enable diagnosis of "conformational diseases" such as Alzheimer's, Parkinson's, and Creutzfeld-Jakob's, etc. (see scenario 2 below). The bio-interface of the sensors will be nanostructured to increase specificity and improve sensitivity (in the case of an acoustic transducer). The bio-interface will also be selected so as to minimize the impact of the epigenetical differences among patients.

Scenario 1: A gravimetric sensor cannot differentiate a non-specifically bound large molecule from specifically bound target analytes of total equivalent mass. However assuming both have different sizes and shapes, it will be possible to differentiate them using a complementary technique such as Surface Plasmon Resonance (SPR) that measures the surface coverage or resonators that measure hydrodynamic properties of the analytes.

Scenario 2: Conformational diseases (Alzheimer's, Parkinson's, and Creutzfeld-Jakob's, etc.) are difficult to diagnose. Indeed, in addition to being able to detect a specific protein, one should also be able to determine if it is misfolded or not. It is obvious that in those cases a gravimetric or surface coverage transducer alone could not differentiate misfolded from wild-type proteins. Resonators whose responses depend on the interaction between the analyte and the surrounding fluids (hydrodynamics) are better suited, however the models are quite complicated and it is currently impossible to differentiate a homogenous layer of misfolded protein from a heterogenous layer of wild type proteins. Models could be used quite reliably however provided that one parameter, such as the mass, is fixed. This could be achieved using a complementary gravimetric sensor.

Sensing platform: Our plan is to design a smart, integrated device with exchangeable and disposable cartridges. The cartridges will be disease-specific or region-specific, i.e. they will be sensitive to biomarkers specific to a chosen disease or to multiple diseases prolific in the target region (e.g. HIV, malaria, and TB in Africa). Each cartridge will consist of an array of sensors, including a reference sensor to compensate for any signal drift (due to temperature, evaporation etc) and to take into consideration the non-specific interaction. Each sensor will use the same transducer platform, while the bio-interface will be chosen and functionalized to bind the appropriate molecules. This will result in a single, simple to use device for the detection of various diseases. The cartridges, made of silicon, will be mass-produced using conventional micro-fabrication techniques and will feature electronics for the readout and/or actuation through CMOS integration. It will therefore result in a low cost disposable device. The planar sensors could easily be interfaced with a microfluidics circuit to integrate further functions. Two potential sensor designs are presented below:

Design 1: The transducer platform will combine Surface Acoustic Wave (SAW) and Surface Plasmon Resonance (SPR) measurements on a single device. The SAW technique will provide information about the evolution of the mass and viscoelastic properties of the film formed on the surface, which

can be then be related to the binding of analytes, while SPR will probe surface coverage. Impedance measurement could also be easily implemented in parallel.

A nano-imprinting technique will be used to create a bio-interface suitable for detecting small molecules. By using a layer of gold nano-particles functionalized with molecules which were electro-polymerized in the presence of molecules similar to the target analyte, a shape and size specific binding site will be created. To detect proteins or nucleic acids, a nanostructured interface incorporating antibodies, aptamers or peptide nucleic acids (PNA) will be used. The structure will be designed to increase the available bio-interface area and thus minimize the time of detection needed to bind a bio-analyte.

Design 2: The transducer will consist of a silicon membrane that can be used in deflection or resonant mode. The deflection mode can be measured piezo-resistively and does not require actuation. This will enable the measurement of mass changes on the membrane. The resonant mode requires electrostatic actuation (DC bias and AC) and a capacitive or piezo-resistive output can be measured. This mode will provide information about the mass and viscoelastic properties of the binding analytes. The Solid On Liquid Deposition (SOLID) technique will be used to prevent fluid flowing between the electrode and the membrane. Impedance measurement could also be easily implemented in parallel for the analysis of the desired analyte.

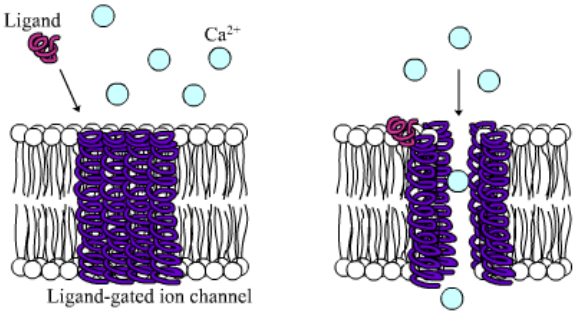
A nanostructured bio-interface will be functionalized with antibodies, peptide nucleic acids (PNA) or aptamers to target specific bio-markers. This sensor platform could be used for detection of bio-markers in air or liquid.

(b) Highly sensitive bio-sensor based on trans-membrane proteins

Some bio-markers (analytes) are found in very low concentration in biological fluids. Current sensors usually make use of amplification (for nucleic acid based sensors) or concentration methods to detect such bio-markers. However those methods can be time consuming and are often complicated and expensive. Drawing inspiration from life science, a novel bio-mimetic sensing platform is proposed where a molecule (e.g. protein) can trigger an avalanche of events on the other side of a synthetic membrane when coupled to the appropriate trans-membrane protein. The sensor would detect the events triggered by the interaction of the target analyte with an engineered trans-membrane protein.

Key advantages: A single molecule could trigger an avalanche of events that could be easy to detect by conventional sensors. By analogy, it is easier to “detect” an open door than the key that was used to open it.

Sensing platform: The platform could be a micro-fluidic device comprising a channel with side chambers. The biological fluid of interest would flow in the main channel and a synthetic membrane with engineered trans-membrane protein receptor would separate the main channel from the small compartments. When the analyte of interest couples to the trans-membrane protein, it triggers an avalanche that can be detected by the sensors in the chambers. The example of a ligand-gated ion channel is shown below.



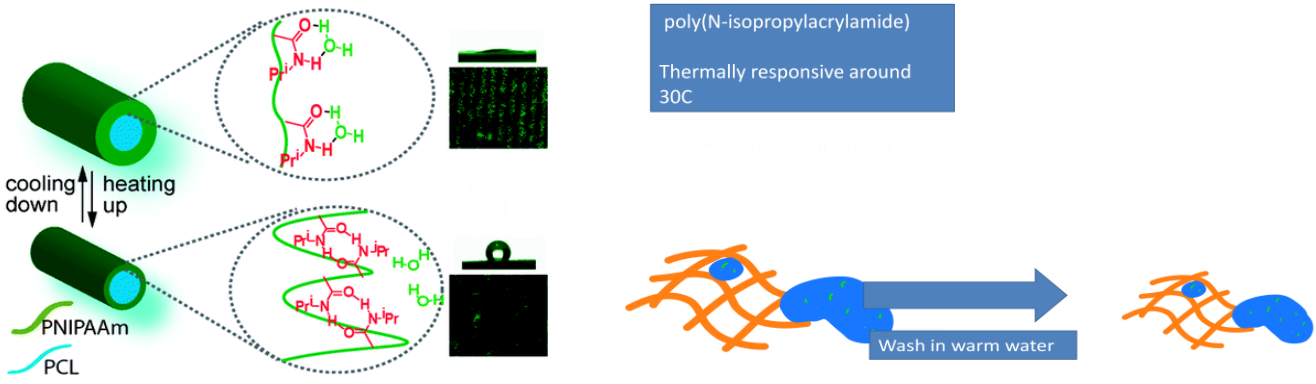
source: Wikipedia

Another approach could be to use vesicles with trans-membrane proteins. They would be mixed with the biological fluid of interest in a single channel and the coupling of the protein of interest would trigger an avalanche of events inside the vesicle, which could be detected by impedance measurement for example.

(c) Reusable, Self-cleaning, Antibacterial Materials

The aim of this project is to create an intelligent material with the following properties:

- Innate antibacterial properties in the passive fibre.
- Switchable 'intelligent' properties that change upon an external stimulus.
- Using electrospinning to create a large amount of nano-designed materials in a relatively fast, up-scalable way.



Where is this useful:

- Areas where more sophisticated or expensive cleaning apparatus (ie autoclave, industrial washing machines) are not available.
- No harsh cleaning chemicals are needed, no run off into the environment.
- Reusable textiles for use in medical services means there is less medical waste to dispose of, and easier for a clean environment no matter where you are.

Assessment of the results and impact of the event on the EUROCORES programme

The EUROSYNBIO call for proposals included 4 research topics, three of which focused on basic and applied sciences ("System assembly and molecular and cellular complexity in a context of Darwinian evolution"; "Computational design tools" and "The biosystems design laboratory") and one focused on the social context. The "Global challenges" workshop was as a unique opportunity to fulfill the EuroSYNBIO objectives by bringing EuroSYNBIO young researchers as well as well-renowned experts to focus and to address the existing and upcoming global challenges from different disciplines. These scientific disciplines are nanotechnology, molecular and cell biological engineering, micro-engineering, biotechnology, and medicine. It also was an ideal venue for presenting the progress in this field and disseminating the work of the NANOCELL, SynDiv, SYNAPTA, SynMet and SYNMOD Collaborative Research Projects. The international participants of the workshop learned from the participating young EUROSYNBIO researchers about newest achievements in synthetic biology, and young EUROSYNBIO researchers formed networks with young experts from all over the world, crossing disciplines to develop new (technology and engineering) strategies towards targeting global challenges. This networking was a major goal of this workshop and was supported by creating an interactive WIKI-based platform for future exchange of ideas between the participants even after the workshop.
In addition, a summary of all ideas and results obtained by the interdisciplinary groups is currently in preparation and will be published in a booklet "Global challenges – opportunities for nanotechnology". The booklet will provide a comprehensive overview of the major global challenges and how to address these challenges by combining nanotechnology with molecular and cell biological engineering, synthetic biology, microengineering, biotechnology, and/or medicine. This brochure is written and in close collaboration with the workshop participants and will be distributed to international stakeholders.

Last but not least, the feedback of the participants was enthusiastic, as illustrated by the following quote from a participant from Sweden:
"From the lovely location, to the thought-provoking questions and discussions, to the encouragement of the eminent scientists who served as experts and advisors, it was certainly a week that we will not soon forget. We went home enthused about the possibility that our work can be used to tackle the challenges ahead and that there are others who also share the same hopes. We also are happy to have had the opportunity to open up more lines of communication between other PhD students and postdocs for future collaborations. Last week, we gave a short overview of the workshop concerting the overall format and the problems and solutions to our coworkers here in Lund. The audience was very interested and we continued the discussions started in Venice. There was also interest in the possibility to organize a similar type of workshop here in the future."

List of speakers and participants

Title	Name	First Name	Organization
	Allegri	Sergio	EPF Lausanne
Dr	Aponte-Santamaria	Camilo Andres	Heidelberg Institute for Theoretical Studies
	Awad Sarhan	Wesam	The American University in Cairo
	Beane	Gary	The University of Melbourne
Prof	Binnig	Gerd	Definiens, München
	Box	Stuart	University of Bristol
	Brzezinka	Grzegorz	Jagiellonian University
	Ceylan	Hakan	Bilkent University, UNAM
	Charmet	Jérôme	University of Cambridge
	Chhaya	Mohit	Queensland University of Technology
	Churnside	Allison	University of Colorado
Dr	Dabkowska	Aleksandra	Lund University
	Di Paolo	Diana	University of Oxford
	Fichtl	Bernhard	Augsburg University
	Fischer	Audrey	Universität Basel
	Frølich	Simon	iNANO, Aarhus University
Prof	Gaub	Hermann	LMU Munich
Dr	Gelmi	Amy	Linköping University
Prof	Gerber	Christoph	Universität Basel
Dr	Golub	Eyal	The Hebrew University, Jerusalem
	Gould	Oliver	University of Bristol
	Grønborg Sørensen	Signe	iNANO, Aarhus University
	Günzburger	Gino	Universität Basel
Dr	Hafaid	Imen	National Institute of Applied Science and Technology, INSAT
Dr	Hennig	Susanne	CeNS, LMU Munich
	Hol	Felix	Delft University of Technology
	Jia	Dewei	University of Oxford
	Kappeler	Natascha	London Centre for Nanotechnology
	Kershaw	Rebecca	University of Cambridge
	Khudiyev	Tural	Bilkent University, UNAM
	Kleylein	Claudia	CeNS, LMU Munich
	Kolmer	Marek	Jagiellonian University
	Komatsuzaki	Akihito	QBiC, RIKEN, Japan
	Kretschmer	Simon	MPI of Biochemistry, Martinsried
	Lard	Mercy	Lund University
Prof	Lehn	Jean-Marie	Laboratoire de Chimie Supra-moléculaire (ISIS), Strasbourg
Dr	Liao	Hsien-Shun	Academia Sinica
	Liu	Kai	Tsinghua University
Dr	Lopez-Ayon	Monserratt	McGill University
	Luelf	Henning	University of Strasbourg, ISIS
	Malinowska	Klara	LMU Munich, CeNS
Dr	Meehan	David	Trinity College Dublin, CRANN
	Mickler	Frauke	LMU Munich

Title	Name	First Name	Organization
	Milles	Lukas	LMU Munich, CeNS
Dr	Miszta	Przemyslaw	University of Warsaw
	Modena	Mario	MPI for Biophysical Chemistry, Göttingen
	Mohr	Manuel A.	ETH Zürich
Prof	Müller	Daniel	ETH Zürich
	Odermatt	Pascal	EPF Lausanne
	Oertle	Philipp	SNI Basel
	Patricio	Beatriz	IBCCF / UFRJ
	Persson	Henrik	Lund University
	Pfadler	Thomas	University of Konstanz
	Pfreundschuh	Moritz	ETH Zürich
	Purcell-Milton	Finn	Trinity College Dublin
	Ricci	Maria	EPF Lausanne
Dr	Scheidemann	Adi	NanoScan
	Schlegel	Kristina	London Centre for Nanotechnology
	Sekhavati	Farzad	LMU München
	Serdiuk	Tetiana	ETH Zürich
	Shen	Jie-Pan	Academia Sinica Taiwan
Dr	Taylor	Alex	Medical Research Council
	Turbé	Valérian	London Centre for Nanotechnology
Prof	Vogel	Viola	ETH Zürich
Dr	Walder	Rob	National Institute of Standards and Technology, JILA
Dr	Wilner	Ofer	University of Oxford
	Zhang	Tao	LMU Munich