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Conference Report

Olten Meeting 2013 – Bioinformatics and Bioprocess Engineering

Elsbeth Heinzelmann, Journalist science + technology

Abstract: 'Make Changes!' was the theme of the Olten Meeting 2013, which took place on 29 November 2013, where expert speakers from Swiss academia and abroad introduced new and innovative concepts in the domain of bioinformatics and bioprocess engineering. Representatives of science and companies took the opportunity to exchange ideas and to establish new contacts across the border.

Keywords: Accelerating bioprocess development · Bacterial bioplastics · Microencapsulation · Polyhydroxyalkanoates (PHA) · Protein structure modelling

With *bioinformatics* we use computer technology to manage and analyze biological information. It allows us to gather, store, analyze and integrate biological and genetic information and to apply it to, for example, gene-based drug discovery and development.

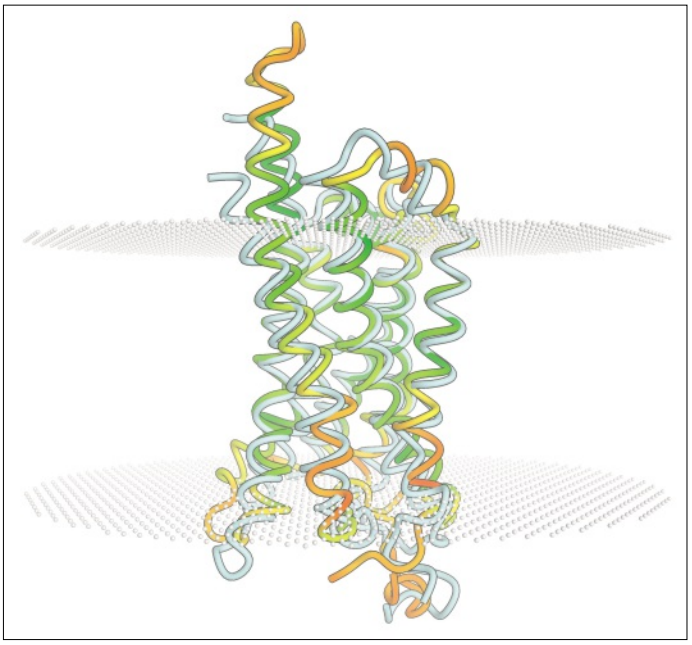
How to Access Structural Information for Proteins

One important aspect of bioinformatics is protein structure modelling, the area of expertise of ***Torsten Schwede***, associate professor for structural bioinformatics at the Biozentrum of the University of Basel and the SIB Swiss Institute of Bioinformatics. For him, knowing a protein's three-dimensional structure is crucial to understanding its biological function at the molecular level. But despite advances in experimental protein structure determination, there is still no experimental structural information available for the majority of protein sequences resulting from large-scale genome sequencing and metagenomics projects. In order to fill this gap, different computational methods for predicting the structure of proteins have been developed. They differ in their computational complexity, the range of proteins that they can be applied to, and also the accuracy and reliability of resulting models. New horizons have been opened by SWISS-MODEL. This server for automated comparative modelling of 3D protein structures provides several levels of user interaction with its web interface. In the automated mode, an amino acid sequence of a protein is submitted to build a 3D model. The steps of template selection, alignment and model building are completely automated. In the alignment mode, the modelling process is based on a user-defined target-template alignment. Complex modelling tasks can be handled with the project mode using *DeepView*, an integrated sequence to-structure workbench. All models are accompanied by a detailed modelling report. "The reliability of SWISS-MODEL is continuously evaluated and developed to improve the successful implementation of expert knowledge into an easy-to-use server."

(*http://swissmodel.expasy.org*)

Another comprehensive resource for protein structure and model information is the Protein Model Portal (PMP). It fosters the effective use of 3D molecular models in biomedical research by providing convenient and comprehensive access to structural information for proteins. "Both experimental structures and theoretical models for a protein of interest can be searched simultaneously and analyzed for structural variability", explains Torsten Schwede. PMP offers the opportunity to apply consistent assessment and validation criteria to the complete set of structural models available for proteins. "PMP is an open project, so new methods developed by the community can be contributed to PMP, for example new modelling servers for creating homology models and model quality estimation servers for model validation."

(*http://www.proteinmodelportal.org*)



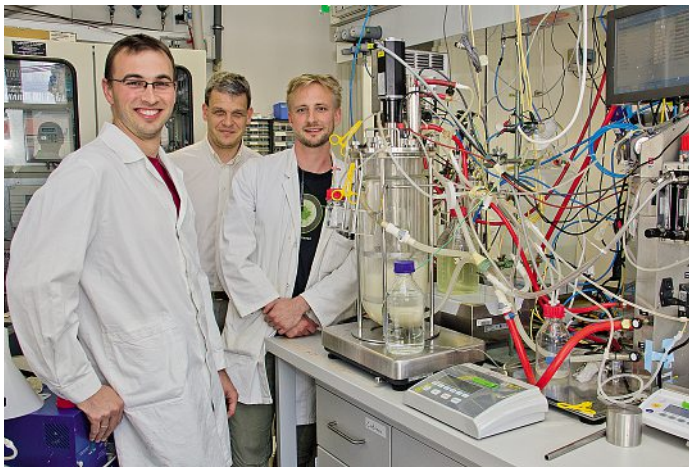
G-protein coupled receptor: in grey the crystallographically solute structure and – in color – a model. The color gradient corresponds to a predicted quality score. The cell membrane is represented with white balls. (Copyright University of Basel)

Open up New Horizons with Bioprocess Technology

With bioprocess technology we intend to convert renewable materials to generate novel products. The spectrum expands from research and development through to manufacturing new value-added biomaterials like fuels, food, feed, pharmaceuticals and nutraceuticals.

An interesting approach for accelerating bioprocess development was demonstrated by ***Christoph Herwig***, Professor of Bioprocess Technology at the Vienna University of Technology. According to the Global Biotechnology Market Research Report of April 2013, the global recession tempered the demand for non-essential health products in the last five years. But despite these factors, industry growth is forecast to continue skyrocketing in the next five-year period. Robust and scalable bioprocesses are prerequisites for product safety and economic efficiency in the production of biomolecules in 'red' and 'white' biotechnology. Furthermore, the optimization of the processes is essential, for instance to compete with biosimilars. The focus is on a '50%/2×'

Researchers at the Institut für Verfahrenstechnik, Umwelttechnik und Technische Biowissenschaften at the Vienna University of Technology have developed a method of obtaining information much faster than before with the aid of metabolism of micro-organisms which increases productivity. (Copyright Vienna University of Technology)



The researchers at the Vienna University of Technology (from left to right: Christian Dietsch, Christoph Herwig, and Oliver Spadiut) expose microorganisms' changing dynamic conditions to learn more about their metabolism. Much to their surprise, the generated stress increases the efficiency of the microorganisms substantially. (Copyright Vienna University of Technology)

approach: reduce process development time by 50% and achieve a 2-fold increase in productivity.

The current trend to accomplish these tasks is in line with Quality by Design (QbD) principles. However, the current interpretation of QbD is based on statistical approaches and therefore cannot reach the objectives of process optimization and the scalable and synergistic usable process understanding. "We suggest a mechanistic understanding of the processes as successfully completed in other market segments", explains Christoph Herwig. In his view, the central issue is physiology, the perspective from the cell, which allows a systematic analysis of the biological system and therewith a predictive control of the process by mechanistic and predictive modelling and optimum control. According to the scientist, this approach could solve future impediments in bioprocesses. "The challenge of the future is the development of generic methods and their tailored implementation in the industrial environment. In order to meet this challenge, we have to make available university education, interdisciplinarity and appropriate software."

You can find the full article on *www.researchgate.net*

Training and Research go Hand-in-hand

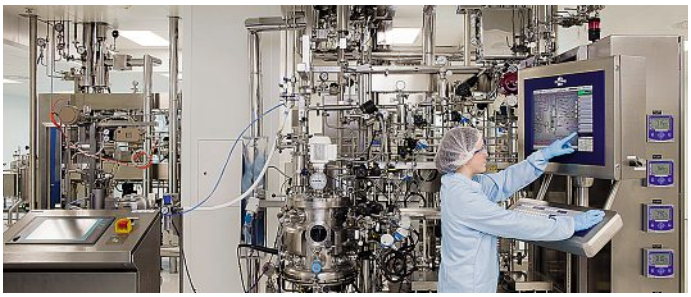
An emphasis on education, especially in training, is laid down at the National Institute for Bioprocessing Research & Training (NIBRT) of the Dublin City University. It's a 'one stop shop' for the bioprocessing industry's training requirements, offering an effective way to keep up with best practices and recent advancements in industry, while also bringing invaluable knowledge and resources to their companies. They range from operator courses through to senior management training and can be delivered in a variety of formats to suit each client's situation. "Our aim is to deliver holistic training programs in a realistic GMP simulated, operational manufacturing environment", points out ***Ian W. Marison***, Professor at and Head of the School of Biotechnology. Innovative partnerships have been established for example with the Swiss Endress+Hauser or the US based Waters Cooperation to develop a comprehensive solution to complex glycan analysis that combines NIBRT's novel GlycoBase 3+ database with the unique capabilities of ACQUITY UPLC System and their application-optimized Glycan Separation Technology chemistries for HILIC-UPLC separations.

One of Ian Marison's specialist areas is Process Analytical

Upstream processing suite at the National Institute for Bioprocessing Research & Training (NIBRT) in Dublin, showing a completely controlled 150-litre perfusion bioreactor. (Copyright NIBRT)

Technology for the online monitoring and controlling of high cell density cultures. Microencapsulation offers a unique potential for high cell density, high productivity mammalian cell cultures. The process involves the complete envelopment of a pre-selected core material within defined porous or impermeable membrane using various techniques to realize miniature particles. However, for successful exploitation there is the need for microcapsules of defined size, properties and mechanical stability. With a custom-developed Vibrating-Nozzle Jet, a laminar flow jet break-up technique, Ian Marison and his crew produced alginate beads without any defined core in the size range of 150 µm to 2 mm and a deviation of ±1.5%. Their capsules – for instance liquid-core microcapsules used for drug recovery – range between 200 µm and 2 mm with a deviation of ± 2.5%.

The reasons for encapsulating a material are manifold: "The encapsulation gives protection and stabilization", states Ian Marison, co-founder of the Swiss Inotech Bioencapsulation AG. "The capsules offer enhanced flow properties and a sustained, controlled or timed release, can be transported to specific sites. They show improved organoleptic properties and enable the usage of liquids as extraction devices." And he adds, in order to take the wind out of the sails of his critics: "The capsules are not



Fill-finish of therapeutic protein-based drug substances at the Irish National Institute for Bioprocessing Research & Training (NIBRT). (Copyright NIBRT)

Upstream processing suite at the National Institute for Bioprocessing Research & Training (NIBRT) in Dublin, showing two completely controlled 150-litre perfusion bioreactors (left of image) and harvest vessel (on right of image). (Copyright NIBRT)

limited to any one area – they are essentially micro-reactors with controlled properties."

www.nibrt.ie

Plastics from Bacteria

The idea of developing plastics synthesized by bacteria is receiving growing attention due to rising oil prices and plastic waste being an environmental problem with a global impact. About 280 million tons of petrol-based and yet cheap plastics will be produced worldwide in 2014. The consumption in Switzerland is about 1 million tons, of which 650,000 tons are incinerated each year. For ***Manfred Zinn***, Professor in Biotechnology, specializing in bioprocess design and biomaterials at the HES-SO Valais in Sion, possible alternatives are polyhydroxyalkanoates (PHA), bacteria-synthesized, intracellularly accumulated polyesters from sugars as well as fatty acids.

"Our idea is to replace traditional carbon substrates – sugars and fatty acids – with cheap, non-food competitive alternatives from Valais", explains the scientist. He and his colleagues at the Institute of Life Technologies at HES-SO Valais investigate therefore pomace – the residue obtained after pressing and distillation – of native fruits such as apricots, cherries, and grapes. In the case of wine waste especially, promising results were achieved for producing PHA by bacterial fermentation. "PHA is interesting for producing PHA by bacterial fermentation", comments Manfred Zinn. "Its material properties can be adjusted to produce different products such as adhesives (glue), elastomers (hydrophobic coatings) and thermoplasts (solid products)."

Fed-batch cultivation of *Pseudomonas putida* for the production of polyhydroxyalkanoates. (Picture photo-genic.ch)

Modern process analytical technology is essential for the biosynthesis of novel generation polyhydroxyalkanoates. (Picture photo-genic.ch)

Safety first! The recently established fermentation infrastructure enables the safe handling of bioprocesses with dangerous gases (CO, CO_2 and H_2). (Picture photo-genic.ch)

Another brainwave is to establish an integrated processing technology for the efficient synthesis of cost-effective commercial new biopolymers by fermenting Syngas generated from the pyrolysis of very complex feedstocks. "We focus on the integration of innovative physico-chemical, biochemical, downstream and synthetic technologies to produce a wide range of new biopolymers, based on a number of novel and mutually synergis-

tic production methods", says Manfred Zinn. Being part of the SYNPOL project sponsored by the 7th framework program of the EU, his team and 13 other partners from industry and academia are looking for novel ways of valorizing organic wastes and raw materials for the production of biopolymers in a single integrated process.

www.hevs.ch; *www.synpol.org*

An Optimistic Look into the Future

At the end of the event, Daniel Gygax, President of biotechnet Switzerland, highlighted the chances given by the new partnership of the Swiss Biotech Association and the biotechnet Switzerland linking their R&D and their activities related to the knowledge and technology transfer within the NTN Swiss Biotech™. This National Thematic Network covers all relevant competences across the entire value generation chain from innovation to product development and commercialization. Initial positive reactions include the 16 new memberships, new CTI projects up to CHF 2.8 million and the successful development and internationalization of the TEDD competence center in Tissue Engineering for Drug Development.

www.biotechnet.ch

A novel generation of bacterial biopolyesters are more transparent and exhibit enhanced material properties. (Picture photo-genic.ch)

For further information, please contact Dr. ***Daniel Gygax***, Professor of Bioanalytics at the FHNW School of Life Sciences and President of biotechnet. E-mail: daniel.gygax@fhnw.ch

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