Intenso Newsletter 2/2015

This project has received funding from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement n° 312004.

Editorial:

We are proud to present the second newsletter of the Intenso project. In the first newsletter we have introduced Aqueous Two Phase Systems (ATPS). This time, we have asked our partner Proxcys to shortly explain the HP-RFC (High Performance Radial Flow Chromatography) technology they are focussing on. We have also interviewed the project coordinator to hear more about his motivation to carry out this international project. We hope that we have selected interesting topics for you.

Interview with the coordinator about his motivation for this project

Dear Prof Dr. Fernandéz Lahore (MFL), you are the coordinator of the FP 7 project Intenso. Could you please introduce yourself shortly?

MFL: I am a Biochemist by education that has specialised in Bioprocess Technology. I have been active in this field for the last 25 years. Currently, I am Professor of Biochemical Engineering at Jacobs University in Bremen, Germany. The main focus of my research is the downstream processing of biologicals (DSP).

What was your main motivation to conceptualize and propose this project?

MFL: As a downstream processing specialist it has become more and more apparent during the last decade that this fundamental aspect of process biotechnology is not progressing at the same pace that fermentation or cell-culture technology are. We are still using processes that, while fine and innovative at the time of their conceptualization, are now outdated and do not reflect the current scientific state of the art. This has led to a serious bottleneck in biotechnological processes, both from the purely technical and also from the economic point of view. If you realize that downstream processes account for up to 70-85% of the overall processing costs, it becomes readily apparent that there is a whole scientific sector that will eventually yield huge dividends when it comes to cost, process time, usage of materials and waste management. Realizing this, it was very clear to me that a project utilizing the newest and most promising alternatives to the established downstream processing purification trains would be just the thing to considerably advance biotechnology as a whole. Finding the right partners form industry and academia to build the perfect consortium to tackle the challenges of providing better integration, meaning less distinct purification steps, and intensification, meaning higher yield and purity, seemed to me the most logical way of approaching the task for better DSP technology.

What was the rationale behind the 4 pillar structure? Why did you include these specific technologies?

MFL: Right from the early concept stages of the project it became clear that Intenso would have to be more than the exploration and development of just one technology. We selected technologies that were either new, for example the functionalised fibres, or whose potential had never been fully tapped, as is the case for EBA (expanded bed adsorption): If we combine that with the new classes of biomolecules that are in the pipeline, things like VLP or mRNA therapeutics, that cannot be properly purified by todays standard methods at all, it is clear that a broad approach is the only sensible way to provide a benefit to the participants, the companies working in biotechnology and of course the end-user as well.

What are the main challenges of the project?

MFL: Predicated on the vast and divergent capabilities required due to the technical sophistication of the Intenso project, it was necessary to find the very best companies and academic institutions in their respective fields. We anticipated in the beginning that getting such a diverse group to cooperate and share information would be a daunting tasks, but it turns out that the partners have begun to work together very well right at the start of the project. This common understanding and the culture of mutual respect will prover invaluable when it comes to the biggest technical challenge of the project: integrating the results into a horizontal demonstrator in the pilot, i.e., 40 L plus, scale.

Can you please describe your main tasks?

MFL: Besides of being the coordinator of the Intenso project, we study the suitability and performance of second-generation EBA adsorbents; evaluate the efficacy and the integration potential of EBA, and the control of deleterious biomass-adsorbent interactions. This will help to establish this new technology in the industrial landscape.

The technologies developed in the project seem to compete with one another at first glance. Is this causing problems within the project, i.e. by developing economical "rivals" in the same framework?

MFL: The different downstream methods used in the project show the best results for different products. This allows choosing an appropriate downstream processing method optimising the production cost. Moreover, we are observing the emergence of natural product-technology niches, as well as a synergistic dovetailing of several technologies to yield integrated downstream processing schemes.

How do you think will the Intenso project impact the future of the downstream processing industry?

MFL: Intenso will enable the downstreaming industry to produce and enlarge variety of bio-products utilising less production steps for reaching a better product final quality. In this way, the project will enable the biochemical industry to become more competitive in terms of both quality and cost.

What economic results do you expect?

MFL: We hope that Intenso will enable the participating SMEs to use more effective production methods and in this way withstand the competition of international operating enterprises. We also hope to help SMEs increase their European presence and to increase their business.

Thank you for your time giving us this interview.

Proxcys explanation of the High Performance Radial Flow Chromatography (HP-RFC)

Intensification of purification is one of the key attributes of the Proxcys technology. The Intenso project challenged us to apply and/or combine the Proxcys technology with an array of queries from a variety of organizations. This type of multifocal interaction always results in fresh and inspiring concepts or market ideas. Initially we were highly surprised how easy the Direct Capture approach could be adapted to robustly process enormously high cell density of CHO feedstock in our Radial Flow packed bed column. Unlike the general opinion that cell densities of 60 million CHO cells per ml

would immediately block the packed bed columns, in Radial Flow format we could prove contrary by processing this dense feedstock into a result that was plain amazing. Contrary to our expectation we experienced major difficulty in combining the ideas of a hybrid TFF with Monolytic adsorber technology, pairing the separating power of TFF to remove particles with the selectivity of a highly efficient monolytic adsorber to isolate the precious protein. We encountered unexpected difficulties and bottlenecks, but finally the first tests of the prototype 'BiAxcys column', are showing promising results. Further development of both solutions "Direct Capture" and "BiAxcys" are now being intensified and the ideas are channeled towards the conception of new, sustainable solutions in targeted market applications, including continuous processing.

Proxcys is a privately held independent company, located in the Netherlands, and its primary focus is on the development and manufacturing of innovative High Performance Radial Flow Columns, smart Pack & Run stations and innovative ancillary equipment solutions.
Radial Flow Chromatography (RFC) is an efficient, low pressure downstream processing technology for bio-molecule fractionation. Most of Proxcys' equipment is custom engineered and purpose-designed creating the best fit for the process at hand.

RFC columns are easy to pack, gentle to the resin and gentle to the processed proteins. Yet the throughput of the systems is very high and therefore this technology will result in a reduced CapEx and Opex. This is the main reason Proxcys equipment is extremely popular in the human plasma-industry to fractionate highly sensitive clotting factors like Factor VIII, factor IX, fibrinogen and immunoglobulin. These proteins need to be isolated rapidly but will denature immediately on mechanical strain. The awareness of these attributes is the reason of the expansion of the technology in the Biopharmaceutical production of recombinant products. Recent studies have clearly positioned the High Performance RFC technology as a "must have" in the processing of functional food proteins, an expanding and demanding market with economical restrictions. Low cost isolation of anti-bodies from milk should open the door to a reduction in the use of antibiotics in bio-industry, creating a sustainable solution to counter the adverse effects of current pharming practices. The fields of application are very diverse and with an initiative like Intenso further enhanced. The multi-disciplinary professionals are providing interesting discussions, views, market demands and developments. Additional to the main goal of the project, the diversity of applications presented, the insights and contacts are extremely valuable to a small SME like ours.

More information about the project can be found on our website: http://intensoproject.eu/

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