



Fraunhofer

IME

**FRAUNHOFER INSTITUTE FOR MOLECULAR BIOLOGY
AND APPLIED ECOLOGY IME**

**INTEGRATED
PRODUCTION
PLATFORMS
PROCESS DEVELOPMENT**





PerkinElmer Janus BioTX Pro automated liquid handling station

- 2 x 40-L (30-L working volume) stainless steel stirred tank reactors (Applikon) for high-cell-density microbial culture or plant cell culture

Downstream processing hardware

- Janus BioTX Pro liquid handling station for HT DSP screening in Atoll columns
- Pall Filtron ProVario3 benchtop and Sartorius alpha cross-flow filtration systems
- North Carolina SRT Model 10 pilot-scale cross-flow filtration system
- Äkta Explorer 10 XT
- Äkta Purifier 100
- 2 x Äkta Purifier 10
- 2 x Äkta FPLC
- 4 x Äkta Pure
- Index, Fineline and XK columns
- Äkta Bioprocess Standard 6 mm chromatography controller
- Malvern Zetasizer and additional sensor for process characterization



Process scale extraction of recombinant proteins from plant biomass

RESEARCH MOTIVATION

Recombinant proteins are widely used in the life sciences and reliable production options are required. Researchers may need proteins for characterization, animal experiments or for analytical or diagnostic tests. At some stage, it will always be necessary to scale up production and develop a reproducible process.

Integrated approach

Recombinant protein production technology has benefited from the development of novel vectors, expression hosts and cultivation strategies. Despite progress with specific proteins, it is widely recognized that generic protocols do not exist and process development is necessary on a case-by-case basis. Contemporary protein production processes are integrated from the earliest R&D stages by considering the properties of the gene and protein, the quantity and quality of protein required, downstream processing issues, and any regulatory and intellectual property issues that might arise in the future. Only then can the most appropriate strategy be selected. Maintaining and operating fermentation and downstream processing suites is too costly for most biotech research groups and SMEs because equipment is expensive and skilled personnel



5 gram purified red fluorescent protein

are scarce. Dedicated and experienced recombinant protein production units offering rapid, expert and cost-effective services can solve these challenges. The Fraunhofer IME Department of Integrated Production Platforms has produced more than 100 different recombinant proteins in bacteria, yeast, plant and animal cell cultures, and whole plants over the last 10 years, and has the expertise to tackle the most challenging processes.

Contract protein production

Protein production at the Fraunhofer IME often begins with consulting services to determine the best:

- Expression systems
- Vector designs
- Gene cloning strategies
- High-throughput expression and purification approaches.

Alternatively, if an expression strategy has already been selected, process development can start when the integrity of the protein product is verified. High-throughput screening (HTS) systems such as the BioLector Pro can be used to screen host strains and media. High-cell-density fed-batch processes are available with nine stirred-tank bioreactors in the multi-purpose production facility for scale-up experiments and production. Fermentation



Upstream process development and plant suspension cell cultures using 1-1.5L stirred-tank bioreactors

broth or plant material then enters the recovery steps (homogenization/cell disruption/separation/flocculation/filtration) and the proteins are then purified using a process-specific combination of unit operations such as AEX, CEX, IMAC, Protein A and gel filtration chromatography. HTS systems such as the Janus BioTX Pro workstation are available for automated small-scale optimization before process scale-up. Quality control can include a combination of standard protein analytics (Coomassie staining, western blots, ELISA, UV/vis, Bradford method) or more sophisticated approaches (BiaCore, calorimetry, mass spectroscopy, AAA, FACS) using our in-house facilities.

Bioreactor hardware

- BioLector Pro for HT USP screening under controlled conditions
- 4 x 3-L (2 L working volume) autoclavable glass stirred-tank reactors (Applikon) for microbial culture, plant cell culture or hybridoma perfusion culture
- 1 x 7-L (5 L working volume) autoclavable glass stirred-tank reactors (Applikon) for plant cell culture or hybridoma perfusion culture
- 2 x 7-L (5-L working volume) stainless steel stirred tank reactors (Applikon) for high-cell-density microbial culture or plant cell culture

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