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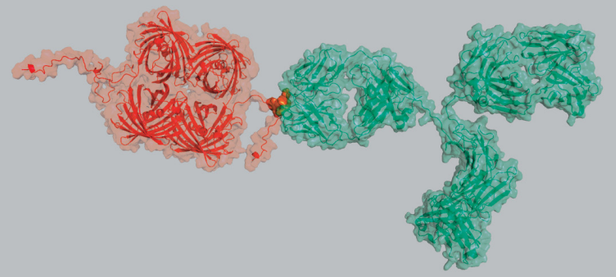
FRAUNHOFER INSTITUTE FOR MOLECULAR BIOLOGY
AND APPLIED ECOLOGY IME



CONSULTING AND EXPRESSION SCREENING,
PROTEIN PURIFICATION, PROCESS MODELING

BIOPROCESS ENGINEERING

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Purified fluorescent protein produced in trangenic tobacco
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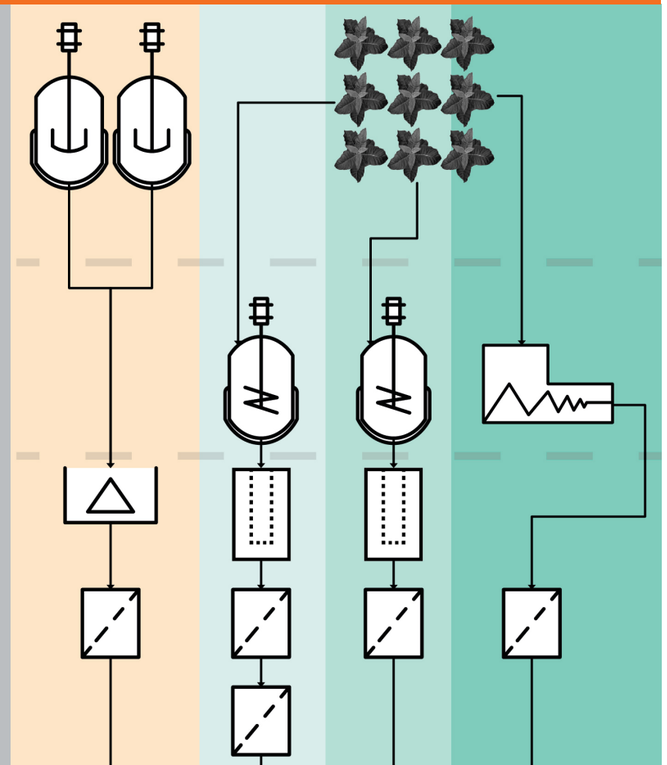

Key research and development services

- Development of cost-efficient expression and purification processes for biopharmaceuticals in less than six weeks
- Identification of manufacturable product variants from pools of several thousand candidates
- Bioprocess overhaul to reduce running costs and increase revenue while considering device and product-related specifications
- Quality analysis of bioprocesses and corresponding models for improved compliance with quality-by-design requirements

Everything starts with your brilliant idea

Biotechnology is a key 21st century technology. As such, biotechnological products are already changing our lives, for example as active pharmaceutical ingredients (APIs) in new medicines that facilitate the treatment of challening

Recombinant protein ligand with monoclonal antibody
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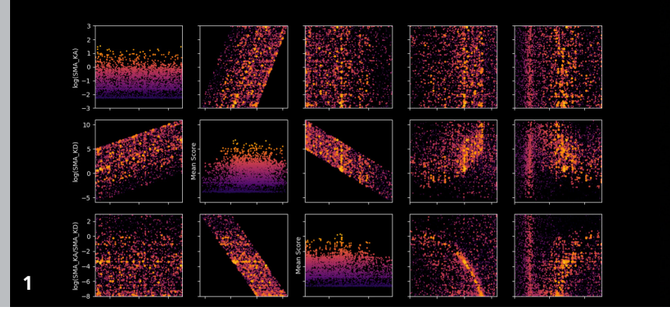

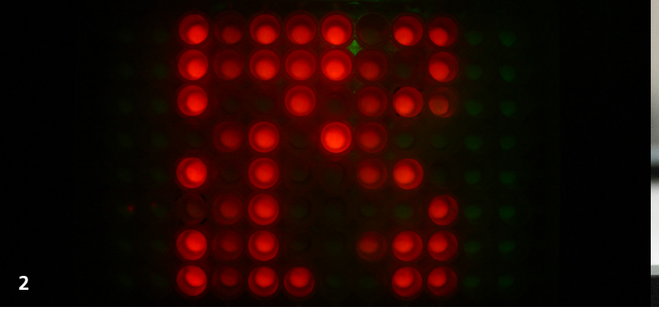

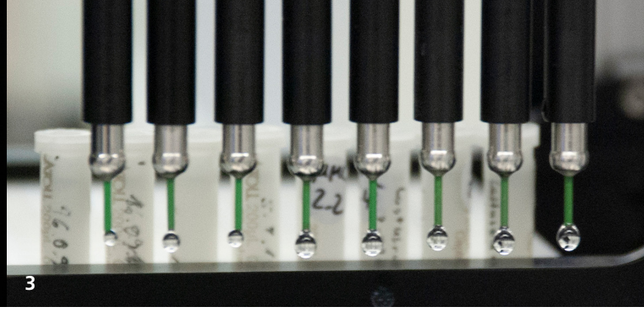

diseases such as cancer. Biopharmaceuticals now account for 30 percent of all new medicines approved by the regulatory authorities, but before any such medicines enter the market, they must undergo an extensive development process. Although such processes may involve different steps and unit operations, they all trace back to a common origin: A brilliant idea for a new API. Today recombinant DNA can be used routinely in even the smallest laboratories and the associated costs have fallen dramatically. Tremendous creative and intellectual potential has therefore been unleashed, enabling not only major pharmaceutical companies but also academic research groups, start-ups as well as small and medium enterprises (SMEs) to fuel the development pipeline with their own ideas. The challenge is to get an active, safe and cost-efficient product to the market quickly.

We accelerate your biotechnology research towards clinical trials

If you have an idea, the Department of Bioprocess Engineering (BPE) at the Fraunhofer Institute for Molecular Biology and Applied Ecology IME offers a partnership to transform the idea into a product candidate and a matching scalable production process. Why would you need a partner? Because time is of the essence and we can help to save you some. As an API developer you belong to an elite group requiring product design and proof of concept studies, but many organizational, regulatory and technical questions are likely to arise before manufacturing can begin. For example, the milligram to gram quantities of API required for characterization and preclinical testing can be difficult to produce within several weeks in typical molecular biology laboratories and even dedicated research laboratories.

The Fraunhofer IME's comprehensive expertise as a contract research organization and our consulting services covering gene design, process development and modeling can therefore provide valuable assets. As an application-driven, non-for-profit organization, we offer the highest degree of flexibility, ranging from small specific optimization or feasibility studies to complete process development strategies spanning gene design, expression system selection and optimization, downstream process development, scale up and process models that can be used to support a quality by design (QbD) approach. Process and product development activities can thus be condensed to a couple of weeks, saving you time and the costs of process, data and technology handling, and reducing the time to market for your product. You will also benefit from our highly motivated and experienced senior scientists, engineers and technicians, who are permanent members of our project teams.

1 Parameter determination for chromatography models
© Fraunhofer IME | R. Jäpel.

Applied research for your process and product development

Recombinant protein production technology has benefited from the development of new 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 gene and protein, the quantity and quality of product required, downstream processing issues, and regulatory and intellectual property issues that might arise in the future. Only then can the most appropriate production strategy be selected.

The Fraunhofer IME Department Bioprocess Engineering has established an automated and integrated platform facilitating the screening of gene variants encoding protein-based APIs using our proprietary plant-cell-pack (PCP) and cell-free systems as well as customer-selected expression hosts including bacteria, yeast, and mammalian cell lines like CHO. The system allows a translation from gene to pilot-scale protein production in less than 4 weeks. It is combined with parallelized chromatographic purification and protein analytics such as capillary electrophoresis on the same device. All operations can be conducted in safety level 1 and 2 environments according to the german regulations for GMOs. The experiments are typically built around a design-of-experiments (DoE) strategy that provides rich information, and the generation of descriptive models for the complex influences of different process parameters, which in turn facilitates rapid process optimization.

This approach is complemented by mechanistic models describing protein expression and chromatographic purification, allowing many conditions to be screened in silico. The most beneficial conditions can then be tested and confirmed using the HTS platform before the process is scaled-up, supporting a quality-by-design (QbD) approach recommended by the regulatory authorities. We therefore encourage you to challenge our current capacities as we push your product forward to market!

2 Plant cell packs expressing recombinant protein
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3 Parallelized protein purification using an automated system
© Fraunhofer IME | B. Orthen.