

Mammalian cell cultivation techniques

Summary

Biotherapeutics, such as monoclonal antibodies (mAbs) and vaccines, belong to the most rapidly growing biotechnological products and are most often manufactured with mammalian, in particular Chinese hamster ovary (CHO), cell lines (Figure 1). Nowadays the production cell lines, which are mainly suspension cells, are cultivated in chemically defined (CD) culture medium. The production bioreactor of choice is a reusable or single-use stirred system, the size of which has decreased over the past 10 years due to increasing product titers.

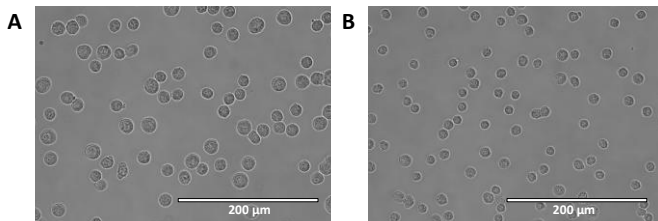


Figure 1: A) Secreted alkaline phosphatase (SEAP) expressing CHO XM 111-10 cells (CCOS 837) and B) CHO DP-12 (ATCC 12445) grown in serum-free and CD medium in shake flasks. These model cell lines are used in our labs for training and comparative studies.

Research and services

Our range of research and services include:

- Development of cell banking procedures based on cryobags
- Cell line screening in cooperation with cell line developers
- Adaptions to serum-free and CD media, as well as medium optimizations in cooperation with medium companies
- Upstream process developments up to 200 L working volume
- Qualification of cell culture bioreactors and peripheral equipment (bioengineering and biological studies)

We also provide customized training courses for companies focusing on these topics.

Collaboration opportunities

During the past 25 years we have developed upstreaming for both stable and transient mammalian cell-based production processes up to pilot scale. We have carried out research and service projects in cooperation with companies such as Hoffmann-La Roche, NovImmune, Bavarian Nordisc, Berna Biotech, Medica Zurich, Cytos Biotechnology, Cell Culture Technologies and Gibco Invitrogen. In addition, we closely cooperate with different well-known bioreactor manufacturers (e.g., Sartorius Stedim Biotech, GE Healthcare, Eppendorf, Finesse Solutions) and also in-house specialists who support us in relation to downstreaming.

Research group leader contact

Prof. Dr.-Ing. Regine Eibl
Group Leader for Cell Cultivation Techniques
Institute of Chemistry and Biotechnology
Zurich University of Applied Sciences (ZHAW)
Phone: +41 (0)58 934 5713
E-Mail: regine.eibl@zhaw.ch
Group Website: <http://www.zhaw.ch/icbt/bioverfahrenstechnik>

Vision and activities

We are familiar with all the usual techniques required to develop and scale-up efficient upstream production processes for mammalian cells growing in suspension as well as on microcarriers. Our vision is to realize process development (cell line screening, medium optimization, parameter scouting), to generate preclinical sample material, and to perform the scale-up as quickly and safely as possible, and with no more experiments than required. To realize this, we consider both bioengineering and cell biological aspects and apply Design of Experiment approaches. Our labs are well-equipped with orbitally shaken high-throughput systems, such as the BioLector for investigations at mL-scale. In addition, wave-mixed and stirred cell culture bioreactors from different suppliers are available up to pilot scale, and are most often operated in fed-batch mode. We also have experience of upstream perfusion development based on tangential flow filtration systems (Figure 2). Control of cell and product quality is carried out with automatic cell counting (Cedex HiRes, NucleoCounter) as well as media and product analyzers such as the BioProfile, the Cedex Bio and the BLtz.



Figure 2: Experimental set-up of an upstream perfusion process executed in Sartorius Stedim's BIOSTAT STR 50L with a hollow fiber cartridge from GE Healthcare in our lab.

Selected publications

- Disposable bioreactors for inoculum production and protein expression. R. Eibl *et al.*, In: Animal cell biotechnology: Methods and protocols, methods in molecular biology. Vol. 1104, Humana Press, 2014
- Investigations on mechanical stress caused to CHO suspension cells by standard and single-use pumps. K. Blaschczok *et al.*, *Chemie Ingenieur Technik*, 2013
- Combining single-use stirred bioreactor with standard cross-flow technology in biphasic protein production processes at pilot scale. K. Blaschczok *et al.*, *Engineering in Life Sciences*, 2013
- Cell and tissue reaction engineering, R. Eibl *et al.*, Springer, 2009

European cooperation contact

Dr. Agnes Zoller
Scientific Officer for European Research and Innovation
Institute of Chemistry and Biotechnology
Zurich University of Applied Sciences (ZHAW)
Phone: +41 (0)58 934 5295
E-Mail: agnes.zoller@zhaw.ch
Website: <http://www.zhaw.ch/icbt/europeancooperations>