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Biochemical Engineering – A Competence of Our New Universities of Applied Sciences

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Abstract. The missions of the recently founded Swiss Universities of Applied Sciences are schematically sketched, and the activities within Biochemical Engineering at these institutions are highlighted. Special attention is paid to the coordination of activities and networking. As an example, the way of the 'Zürcher Hochschule Winterthur' is depicted in more detail.

Introduction

Seven Universities of Applied Sciences have been recently founded in Switzerland. They have four decisive, general missions:

- education: diploma curricula
- postgraduate training
- applied research & development
- networking: (inter)national relations and services

The teaching mission refers to full diploma curricula. Usually, these curricula span three years of theoretical and practical courses plus a diploma work extending over three to six months.

In addition, post graduate curricula spanning 800 lessons or more, including a final diploma work, are planned. Postgraduate courses are shorter and are not honoured with a diploma; they span *ca.* 200 lessons. Furthermore the Universities of Applied Sciences offer training courses of less than 70 lessons, which are usually not confined to the post-graduate level. All types of educative actions at the Universities of Applied Sciences are aimed at providing a ratio of science to engineering of approximately 1:2.

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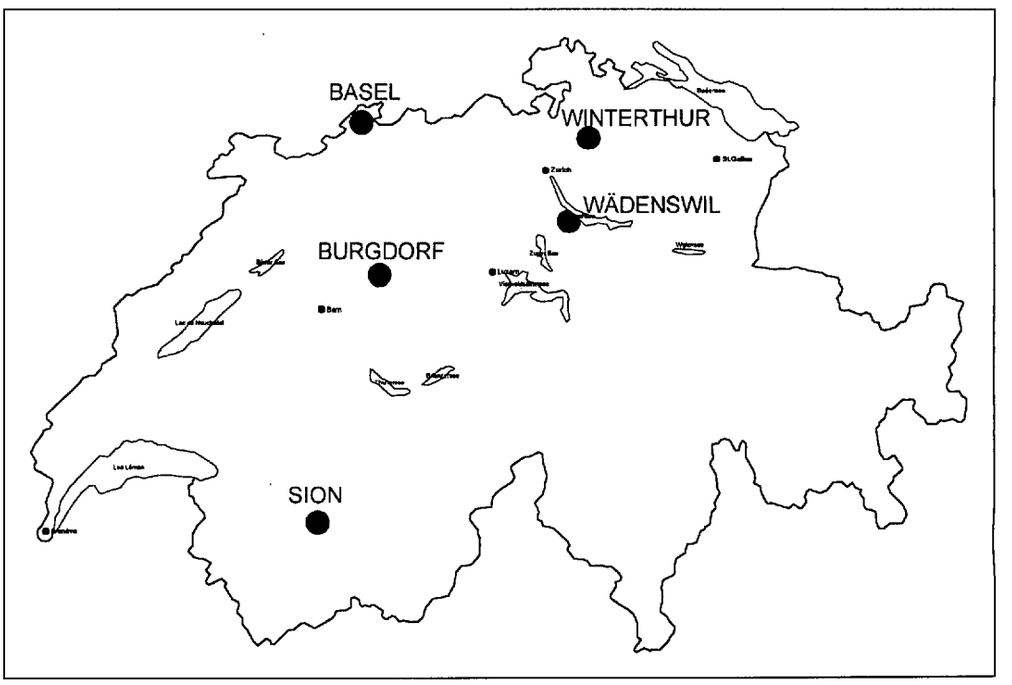

Fig. 1. *Location of Universities of Applied Sciences with significant activities in biochemical engineering*

Biochemical Engineering is an Applied Discipline

Biochemical engineering requires a profound knowledge of biology, chemistry, and engineering. Traditionally, biochemical engineering included mainly applied microbiology and fermentation technology. In the past few years, however, the focus in biotechnology moved more and more to molecular and cell biology, thus rendering biochemical engineering less attractive, especially in the purely science-oriented universities. This development is recognized worldwide. The European Federation of Biotechnology, for instance, reacted by founding a Section of Biochemical Engineering Science. In Switzerland, this gave rise to biochemical engineering acitivites at some Universities of Applied Sciences (*Fig. 1*).

However, this development was reasonably natural: it emerged from different starting points at the different sites. In Winterthur and Muttenz, it was a logical and mandatory extension of chemistry. In Wädenswil and Sion, it emerged from food engineering, and in Burgdorf, it arose primarily from chemical engineering. In other words, new tools are used to achieve old(er) goals more effectively and sustainably.

The general objectives identified within biochemical engineering, not biotechnology in its full breadth, are sketched in *Fig. 2*, separated according to the already established competences and the desired expansions and extensions.

The site-specific bioengineering topics addressed in teaching at the distinct places are, in short:

Muttenz:
- chemical, pharmaceutical, and biotechnological developments
- biotransformations (stereospecific reductions)

Sion:
- integration of biotechnology into food technology
- industrial fermentations
- enzyme technology
- molecular-biological methods in food analysis

Wädenswil:
- applied biotechnology
- biotechnological processes for production and waste treatment on the laboratory and pilot scale (furthermore, Wädenswil is active in the molecular-biological disciplines as well)

Winterthur:
- biochemical engineering
- (technical) biochemistry and biocatalysis
- process monitoring, analysis, and sensors
- downstream processing and process integration

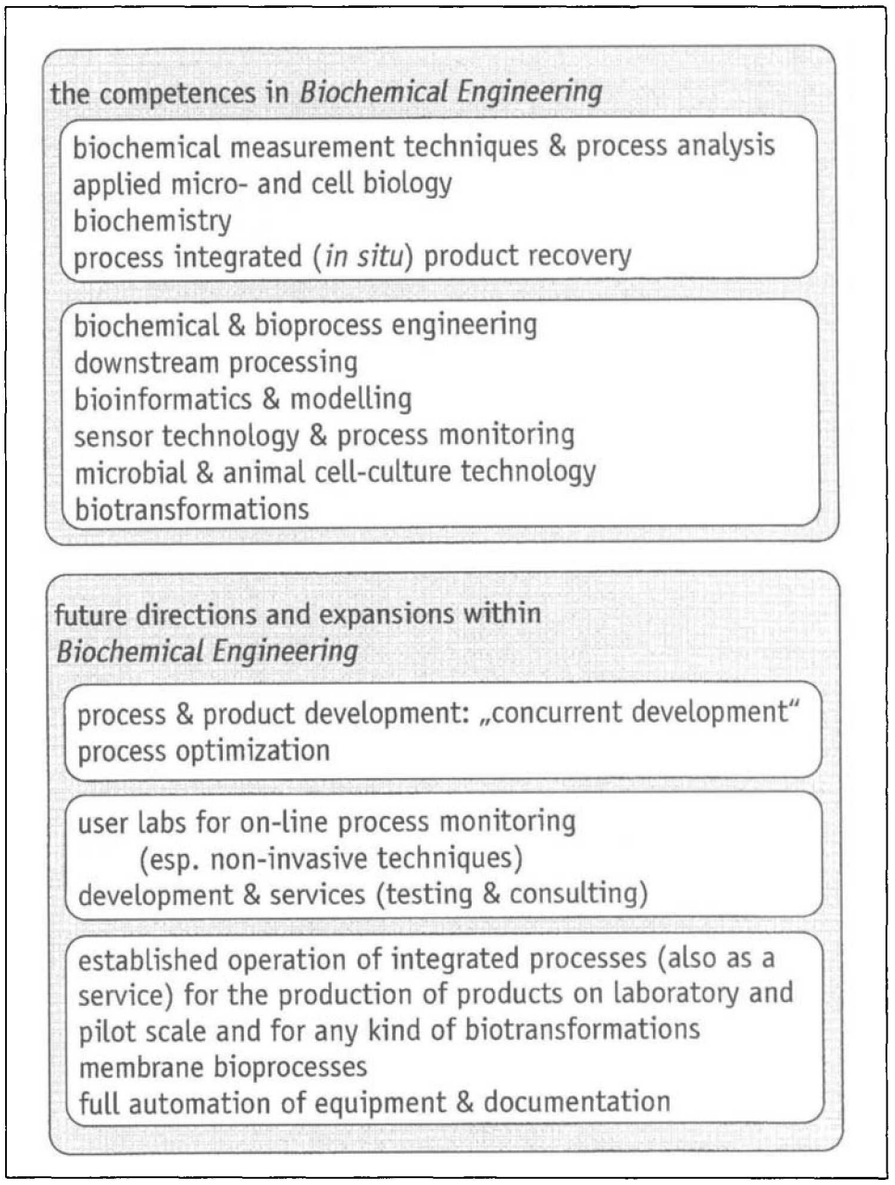

Fig. 2. *The general objectives of importance for Universities of Applied Sciences identified within biochemical engineering; established activities on top, targeted expansions below*

The Mission 'Education'

Besides the ETH Zürich and the participation of the University of Basel in the trinational curriculum in biotechnology, there is – among the universities of applied sciences – only Wädenswil that offers a distinct curriculum in biotechnology. All other universities have decided to act in a different way, extendeding existing curricula of chemistry, engineering, or food engineering with the necessary modules. They promote either chemists or engineers who have an in-depth training in biodisciplines on top of their basic skills.

Winterthur, for instance, offers an optional curriculum within the curriculum 'chemistry' which is called 'biological chemistry'. This reflects specific requirements of the current job market. Both the HSW in Wädenswil and the ZHW in Winterthur are members of one University of Applied Sciences, namely the 'Zürcher Fachhochschule'. Their curricula in biotechnology and chemistry are coordinated; some common and distinct characteristics are sketched in the *Table*. This particular coordination is part of a coordination framework organized by the Swiss Coordination Committee for Biotechnology (SKB) for the entire country and on any level of education.

The Mission 'Applied Research and Development (aR&D)'

In the predecessors of today's Universities of Applied Sciences, research was a tolerated freedom, but now, aR&D is a mandatory mission. There is a significant number of activities already established, yet, the new situation certainly needs further development and extension. Networks are currently being built or extended, both on a national and an international level. Cooperations with small and medium enterprises are specifically encouraged and supported by the federation, especially by the Commission of Technology and Innovation (CTI). What they request is 'equivalence but distinctness' of the aR&D-projects.

A National Competence Network is *in statu nascendi*

Its current members are:
- Zürcher Hochschule Winterthur, **Z:W**
- Hochschule Wädenswil
- Fachhochschule beider Basel, Muttenz
- Hochschule für Technik und Architektur, Burgdorf
- Hochschule für Technik Wallis, Sion
- several cooperation partners from academia and industry, both national and international

Its missions are:
- post-graduate education
- aR&D, especially compound projects
- technology transfer
- services

Table. *Some Common and Some Distinct Characteristics of the two Locally Distant Parts of the 'Fachhochschule Zürich'*

HSW	Z:W
'biotechnology'	'biological chemistry'
micro- & cell biology	biochemistry
molecular biology	biocatalysis
biopharmaceutical technology	process monitoring, analysis, sensors
bioprocess technology	downstream processing
quality assurance	process integration quality assurance

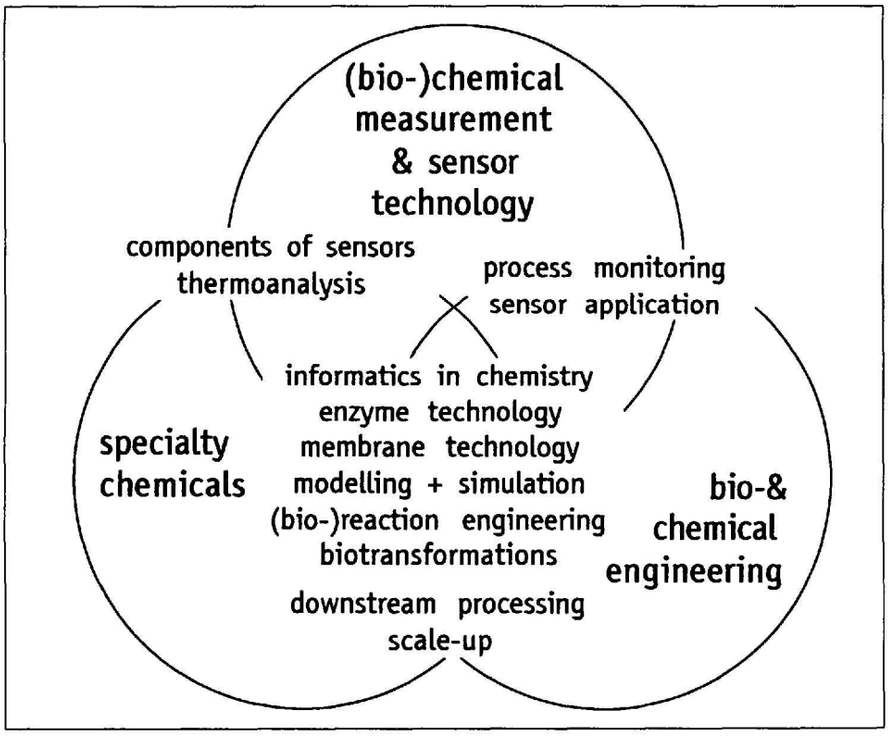

Fig. 3. Internal organization of the department of chemistry of the ZHW in three competence groups for aR&D; they are well coordinated, interlinked, and cooperating: specialty chemicals [1], (bio-)chemical measurement and sensor technology [2], and bio- and chemical engineering [3]. The most important links between the individual groups are indicated.

One Paradigm — the Z:W

The Organization of the University

The **Z:W** is organized in seven departments, five technical ones (including the department of chemistry), one for economy and management and one for linguistics and humanities, thus facilitating
- projects involving more than one department
- transdisciplinary curricula such as 'data analysis & process design'
- ethical awareness in engineering
- communication of problems and solutions

The department of chemistry hosts the biochemical engineering branch.

The Organization of the Department of Chemistry

The department of chemistry of the **Z:W** is organized in three well-coordinated competence groups (*Fig. 3*), thus facilitating integrated projects and problem solving.

Current aR&D Projects in Biochemical Engineering in the Department of Chemistry

The following list of projects gives an impression of the fields of activity. It must be clearly stated that all of these projects are in tight cooperation with industrial partners, small, medium or large enterprises, and all aim at the missions mentioned above. Some of the projects are confidential. A few selected examples will be shortly described below.
- gas transfer to biosuspensions
  - air trap reactor
  - small-bubble reactor
- bio-scrubber for VOCs
- tissue engineering
- animal cells: optimizing engineering aspects
- continuous extraction
- enzyme membrane reactor
- kinetic resolution of stereoisomers
- integrated lactate removal during LTA-production
- aldolases, nitrilases, decarboxylases
- microelectrodes and microreactors for analyses
- ameliorization of (waste) by-products

The small-bubble reactor is a patented version of a high-performance low-cost aeration system that achieves, under appropriate hydrodynamic operating conditions, volumetric mass-transfer coefficients of greater than 1 s^{-1}. It consists of a sintered tube through which the gas enters the liquid stream. The bubbles are sheared

off by the liquid quasi *in statu nascendi*; this exploits the energy input at the site where it is required, and small bubbles are generated. The stream of the dispersion is further controlled by either a draft tube or static mixers. The aeration device is useful for biosuspensions that are free of fibres and insensitive to gas bubbles. If mounted appropriately, it can substitute a mechanical mixing device.

Contrary to this, the air trap reactor is useful for bubble- and shear-sensitive biosuspensions. The patented trick is the amplification of a single, continuous gas-liquid interface by stacking the air traps in a bioreactor (*Fig. 4*). Comparative cultivations of animal cells showed that a high oxygen partial pressure can be maintained while the air or oxygen supply can be reduced by a factor of 20 or more with respect to a sparger- or surface-aerated system, which usually also suffers from oxygen limitation at higher cell densities.

This reactor princple, in a slightly modified form, is also useful and very efficient for liquid-liquid extraction when the formation of an emulsion is undesirable.

aF&E is not an isolated activity, it is to a great extent transferred into the teaching mission which can be best illustrated by the following (nonexhaustive) list of recent diploma theses that have been conducted in the biochemical engineering field at **ZHW**, all of them in cooperation with one or more industrial partners:

- microbial production of 2-phenylethanol from L-phenylalanin
- production of an amino-acid decarboxylase
- production of lipoteichoic acid
- improvement of the cell density of *Streptococcus* sp.
- microbial production of (*R*)- and (*S*)-isomers using whole cells
- elaboration of an enzyme test for HIV-RT and RNase H
- expression and isolation of the enzyme HIV-RT
- influence of precultivation methods on antibody production
- FIA for glucose monitoring
- recalcitrant materials during biological degradation
- monitoring of aerobic biological degradation
- 2-cyano-*N*-Boc-D-tryptophane as an important synthon for the production of a drug
- peptide aldehydes as interesting pharmacological substances
- production and characterization of phosphorylated peptides pursuing a solid-phase strategy

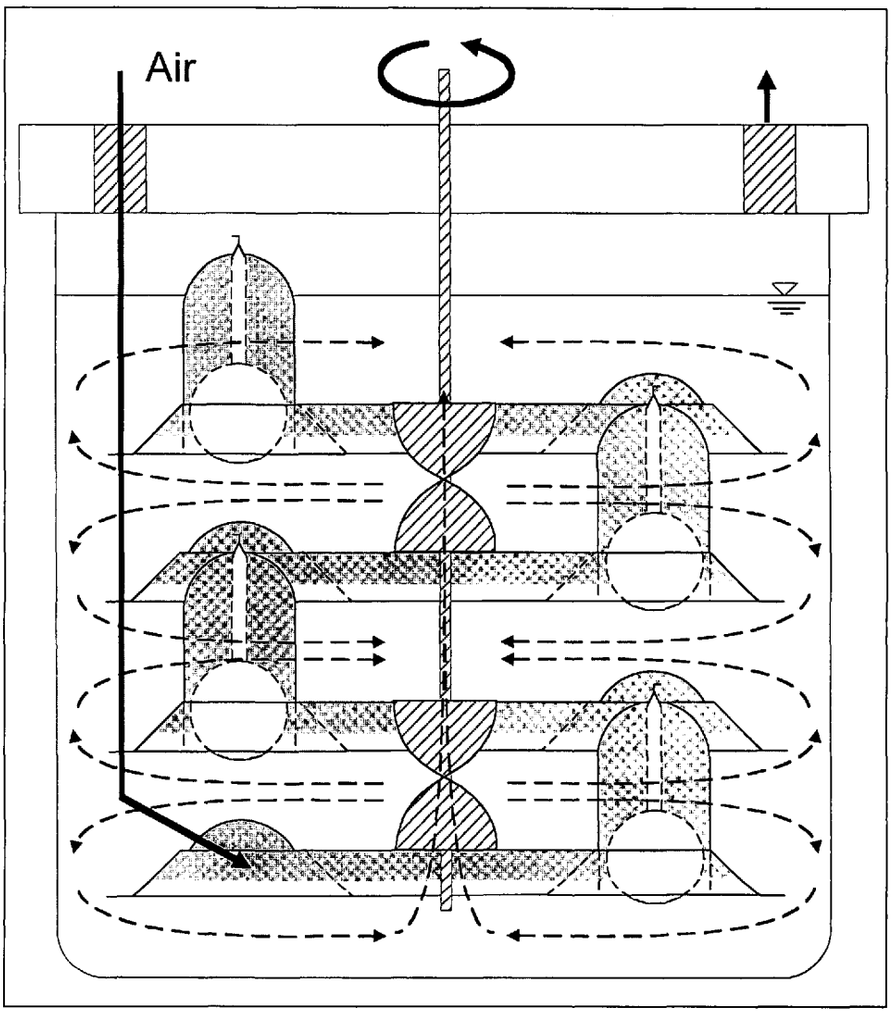

Fig. 4. *Schematic representation of the air-trap technology.* The stacked air traps are half-toruses, interconnected by self-regulating floating valves. The continuous 'submerged' gas phase is drawn in grey. A central helical stirrer (hatched) is used for both renewal of the gas-liquid interface and for achieving axial as well as radial mixing as required (dashed arrow-lines).

- non-proteinogenic α-amino acids: synthesis of 4-fluoro-L-phenylalanine
- optimization of a continuous extractor
- concentration using a hair-pin counter-current membrane principle
- waste-water treatment with a rotor filter

We are optimistically looking forward to a constructive contribution of the Swiss Universities of Applied Sciences to a prosperous development of biochemical engineering in Switzerland for the benefit of quality of life.

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