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Biochemical engineering's grand adventure

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ABSTRACT

Building on the recent revolution in molecular biology, enabling a wealth of bio-product innovations made from renewable feedstocks, the biotechnology field is in a transition phase to bring the products to the market. This requires a shift from natural sciences to engineering sciences with first conception of new, efficient large-scale bioprocess designs, followed by implementation of the most promising design in practice. Inspired by a former publication by O. Levenspiel in 1988, an outline is presented of main challenges that the field of biochemical engineering is currently facing, in a context of major global sustainability trends. The critical stage is the conceptual design phase. Issues can best be addressed and overcome by adopting an attitude where one begins with the end in mind. This applies to three principal components: 1. the bioprocess value chain, where the product specifications and downstream purification schemes should be set before defining the upstream sections, 2. the time perspective, starting in the future assuming that feedstock and product-market combinations are already in place and then going back to today, and 3. the scale of operation, where the industrial operation sets the boundaries for all lab-scale research and development, and not *vice versa*. In this way, and ideal process is defined taking constraints from anticipated manufacturing into account. For illustration, three bioprocess design examples are provided, that show how new, ideal conceptual designs can be generated. These also make clear that the engineering sciences are undergoing a revolution, where bio-based approaches replace fossil routes, and gross simplification is replaced by highly detailed computational methods. For biochemical processes, lifeline modeling frameworks are highlighted as powerful means to reconcile the competing needs for high speed and high quality in biochemical engineering, both in the design and implementation stages, thereby enabling significant growth of the bio-based economy.

1. Introduction

It was 30 years ago today that prof. Octave Levenspiel conceived his Danckwerts memorial lecture, entitled: Chemical Engineering's Grand Adventure. There he reasoned that:

1. chemical engineering is a two-step affair, i.e. first conceiving a process scheme and then making it real
2. the first step is the most important step in the development of a process
3. chemical engineers are generally focusing on the second step
4. more attention is needed for the first step, both in academic education programs and in industrial practice.

This lecture and related article in Chemical Engineering Science (Levenspiel, 1988) has inspired a whole generation of chemical engineers to come with better process designs for novel products wanted by man. Now, with the fruits from molecular biology breakthroughs ready for harvesting, and the bio-based economy in surge, it is a good moment to reiterate his ideas, and project them onto the contemporary status and direction of the field of biochemical engineering.

The mission and essence of biochemical engineering is to deliver products that are desired by humanity, from processes where microorganisms, enzymes and/or cell lines convert renewable feedstocks, or intermediates derived from them, into added-value products in a chain of operations. Similar to chemical engineering, also biochemical engineering is a two-step activity: first conceiving a design, and then putting it into reality.

Abbreviations: BD, 1,3-butadiene; BDO, 1,4-butanediol; CFD, computational fluid dynamics; EJ, exa Joule; kT, kilotonnes; MT, million tonnes; PBS, poly butylene succinate; PDO, 1,3-propanediol.

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Nomenclature

Symbol

a	anabolic
c	number of carbon atoms in 1 molecule C-source
C	concentration [mol/m^3]
C*	solubility [mol/m^3]
F	flow rate [kg/h]
k_La	mass transfer coefficient [h^{-1}]
M	broth mass [kg]
m	maintenance rate [mol/mol$_x$ h]
N	number of moles [mol]
P	pressure [bar]
q	biomass specific reaction rate [mol/mol$_x$ h]
R	reaction rate [mol/h]
R	gas constant [8.314 J/mol K]
T	temperature [°C]
V	volume [l, m^3]
y	partial pressure [mol/mol]
γ	degree of reduction of 1 molecule C-source
μ	specific growth rate [h^{-1}]

Superscript

max	maximum, without involvement of O_2

Subscript

c, CO_2	carbon dioxide
e	ethanol
G	Gibbs energy
h	protons
m	liquid
N	total gas
n	nitrogen source
o, O_2	oxygen
s	substrate (mostly glucose)
p	product
Q	heat
w	water
x	biomass

We can also acknowledge that the second part of this activity is something that has traditionally received most attention, and has resulted in global total markets for liquid biofuels, other bio-energy products (biogas, bioelectricity), food and food ingredients, feed and feed products (dairy, meat), bio-materials, and other products made in thousands of large-scale factories harnessing the power of biology.

In order to meet the requirements for the assumed growth of the bio-based markets, maintaining the products at high quality and affordable for consumers and in parallel meeting targets to limit poverty and climate change, and as well satisfy other global macro-trends, it is questionable whether the current state-of-the-art in biochemical engineering will be adequate. Instead, new practical unit operations, contacting schemes and biocatalysts need to be designed and then implemented. This creative or inventive step and the need for adequate training of the next generation of biochemical engineers will be one of the main challenges, and topic of discussion in this overview.

2. Bioprocess design

Bioprocess design is in the classical way executed from the perspective of where one starts, i.e. with the raw materials, with the experimental set-up and conditions in the lab, and with the market and technology knowledge of today. However understandable from the point of view of the engineer, this approach is inherently slow because merely based on trial-and-error and incremental steps forward, and therefore not adequate to meet ambitious goals and aggressive timelines. For better, representative design results, it is advised to revise the perspective in all these three dimensions: start with the product, the future market situation and the large scale (see Fig. 1). In brief, begin with the end in mind. This retro design philosophy will now be further elaborated in three examples.

2.1. Reversing the bioprocess value chain

A bioprocess can be depicted as a sequence of operations, run at industrial large scale, where renewable feedstock is converted and purified into a final form that meets the specifications of the client or user. Zooming in on the whole chain, it is clear that there are alternating steps of conversion to rearrange the molecular bonds, and separation to get rid of the co-products (either 'waste' or a compound that can be separately valorized) of the reaction. Usually, it is presented as a linear path from feedstock to product. However, for the design purpose it is better to start from the perspective of the final product, see Fig. 2.

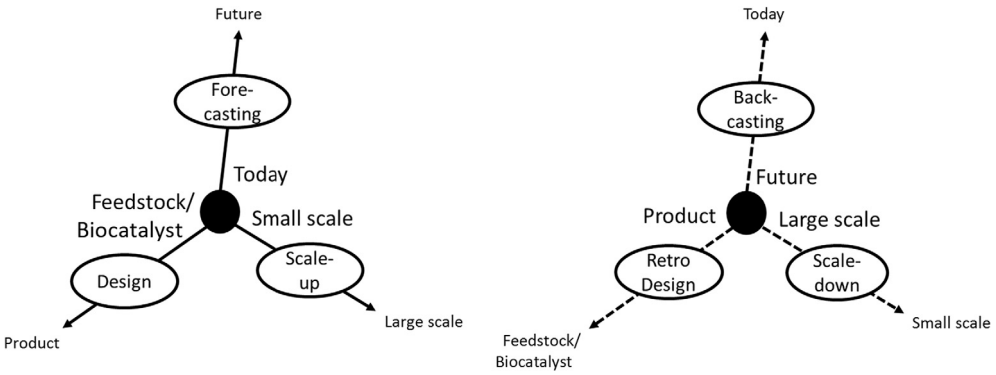

Fig. 1. Left: traditional approach in bioprocess design. Right: recommended view on bioprocess design, with a reversed perspective in three dimensions. This turns value chain design into retro design, forecasting into backcasting and scale-up into scale-down.

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