

## Design of bioreactor – in situ product separation hybrid system for natural compounds production

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### Highlights

- Hybrid system for 2-phenylethanol bioproduction was developed.
- Bioreactor combined with membrane based solvent extraction module.
- High efficiency of hybrid system compared to classical batch fermentation.
- Mathematical models verified by experiments.

### 1. Introduction

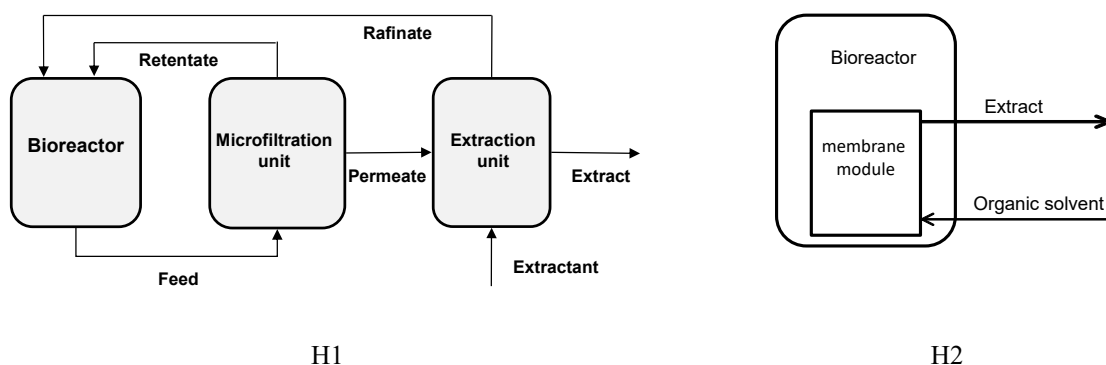
In the past decade, strong academic and industrial interest was devoted to hybrid reactive – separation systems. Integration of reaction and separation steps into one operation unit can save raw materials, as well as capital and operational costs. There are no general rules for a design of an optimal hybrid system for the given process [1].

In the presented paper, the design of a hybrid system for biocatalytic synthesis of natural aroma – 2-phenylethanol, is discussed. The product exhibits high toxicity against a production strain, and to prolong the production cycle and to increase the efficiency of the process, its continual removal from fermentation broth can be achieved by extraction using membrane separation in a hybrid system consisting of a batch bioreactor and an extractive membrane module. This model system was studied in cooperation with a small company in Slovakia producing food additives, which defined its interest accordingly:

- possible use of a hybrid system, using membrane module for continuous removal of 2-PEA from the fermentation broth,
- as a result, 2-phenylethanol was concentrated in an organic solvent.

### 2. Methods

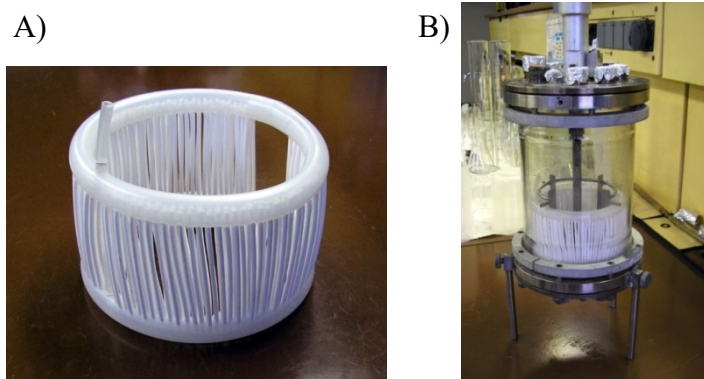
Taking into account the requirements of the production company, two different hybrid systems were proposed (Figure 1). Advantage of the system in Fig. 1A is that it can be built by commercial membrane modules (which have sufficient surface area) and it is independent on the type of the bioreactor used for the production. Disadvantage of this system is the intensive fouling of the microfiltration membrane at high biomass concentration [2].



**Figure 1.** Two studied hybrid systems. H1) Bioreactor connected with a microfiltration membrane module, extraction of 2-PEA is done in an external hollow fibre module; H2) bioreactor with an immersed membrane module.

In the second hybrid system, problems with microfiltration membrane fouling can be avoided employing an immersed membrane module for the extraction; however, the type of such a module is strongly dependent on the construction and size of the bioreactor and it is practically not possible to find a suitable module on the market. Because the omission of microfiltration could prolong the bioproduction in comparison with the first discussed hybrid system, a custom immersed membrane module was proposed and the final membrane was constructed in our laboratory from the commercially available hollow fibre membrane (hydrophobic hollow fibers Accurel® PP S6/2 purchased from MEMBRANA GmbH, Wuppertal, Germany, see Fig. 2.) [3]. As the extractant, pentane was selected.

Distillation was selected as the best way for extraction solvent regeneration from 2-PEA. The distillation has to be very effective to achieve high driving force for the 2-PEA mass transfer from the fermentation broth to the extraction solvent. All proposed systems were tested experimentally and described by appropriate mathematical models.



**Figure 2.** A) Membrane hollow fibre module, B) laboratory stirred tank reactor with an immersed membrane module.

**Table 1.** Comparison of 2-PEA productivity for different studied systems.

| System | Time of one batch cycle [h] | Average volumetric rate [g/L/h] | Average volumetric rate [g/L/h] |
|--------|-----------------------------|---------------------------------|---------------------------------|
|        | exp                         | exp                             | calc                            |
| Batch  | 26                          | 0.16                            | 0.12                            |
| H1     | 72                          | 0.16                            | 0.20                            |
| H2     | 72                          | 0.27                            | 0.28                            |

Continuous product removal led to higher average volumetric reaction rate (see Table 1). Mathematical model of the hybrid system can sufficiently predict the course of the extractive bioproduction and thus can be a helpful tool for further optimization or scale-up of the process.

#### 4. Conclusions

Differences between the proposed configurations of hybrid systems were studied by mathematical modeling and simulation and compared with a classical batch system. The used mathematical models were verified by experiments which proved that they describe the studied systems with acceptable accuracy and can be used for the design, optimization and scale-up of real systems. Simulations have shown that hybrid system H2 with an immersed membrane module in the bioreactor provides the highest productivity in a long time operation. The concept of the proposed hybrid system seems very suitable for biotransformation processes where in-situ product removal is necessary for efficiency improvement, which enables its future scale-up and optimization.

#### Acknowledgements

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#### References

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#### Keywords

Bioreactor, product inhibition, hybrid system, mathematical modeling.

### 3. Results and discussion

The proposed hybrid system consisting of a bioreactor and an immersed membrane module for the membrane extraction seems to be a very suitable device for in situ PEA removal from the fermentation medium. Contact of the biomass with the membrane module during the extraction experiments did not cause any fouling of the membrane and the biomass had no influence on the PEA extraction kinetics or on the PEA partition coefficient.