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Novel concepts for efficient and predictable membrane separation in continuous cell retention and downstream processing

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Novel Concepts for Efficient and Predictable Membrane Separation in Continuous Cell Retention and Downstream Processing

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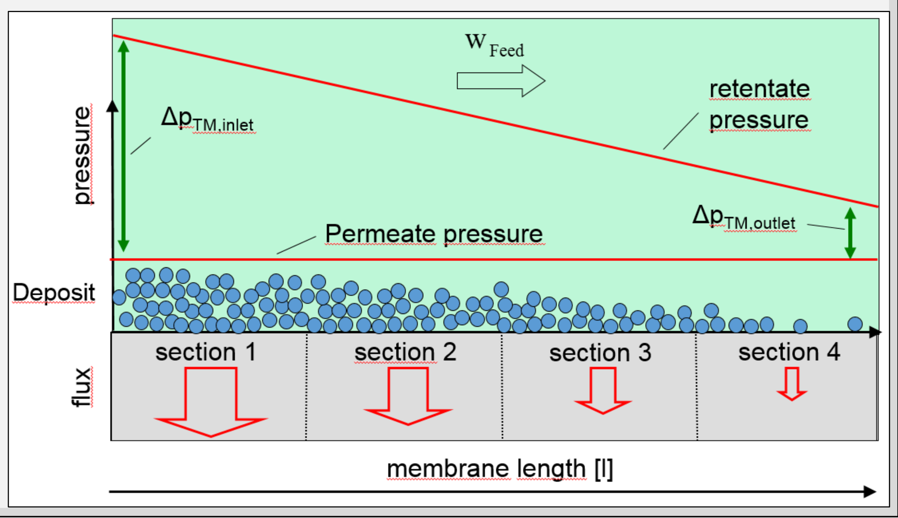
Motivation, Objective & Methodology

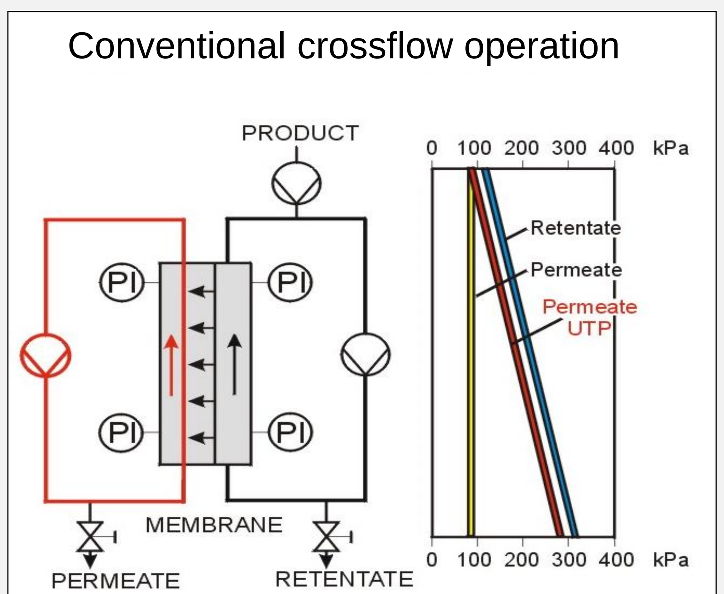
- In bioprocess engineering the retained biogenic polymers and other material form an undefined deposited layer on membrane surfaces with strong, but unpredictable and time dependent impact on permeability, process stability/ efficiency.
- A deeper understanding of deposit formation & systems to minimize its effect are required, esp. for conti-operations.
- This study reports on tools and results for a better understanding of deposit formation on membrane surfaces as a function of time and membrane length.



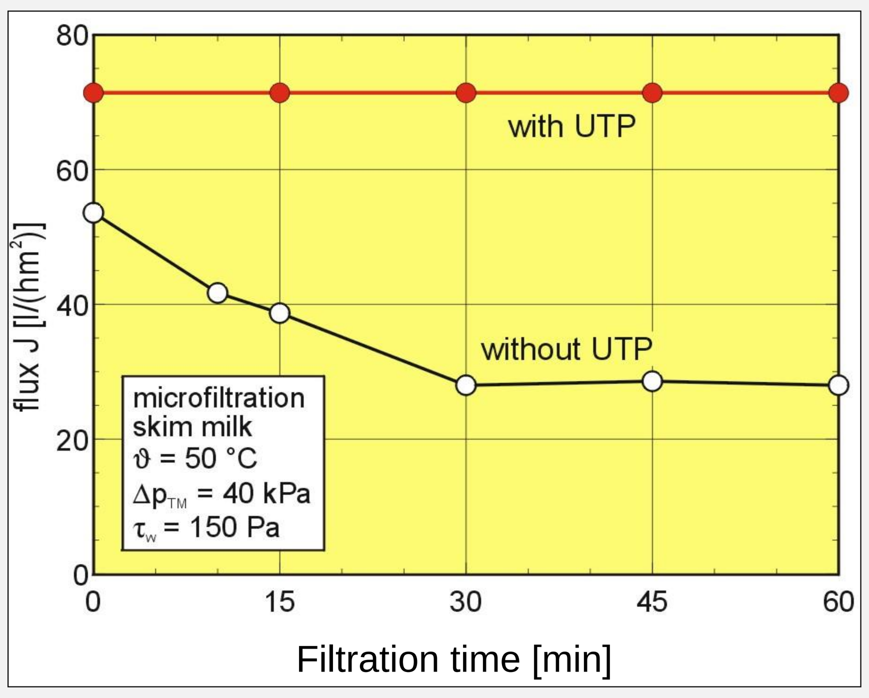
- The aim is membrane process intensification by minimizing the effect of deposit formation, increasing flux and permeation of target substances as a function of operation time and uniform performance within the module.
- Various module types (tubular and spiralwound (SWM), processing modes and membrane materials (Ceramic and polymeric) are compared.
- Segmented industrially sized novel module concepts were assessed by measuring flux and permeation of target molecules.
- Analytical tools were developed to assess deposit formation within a module as a function of spacer geometry, position and processing conditions.

Membrane/Module concepts

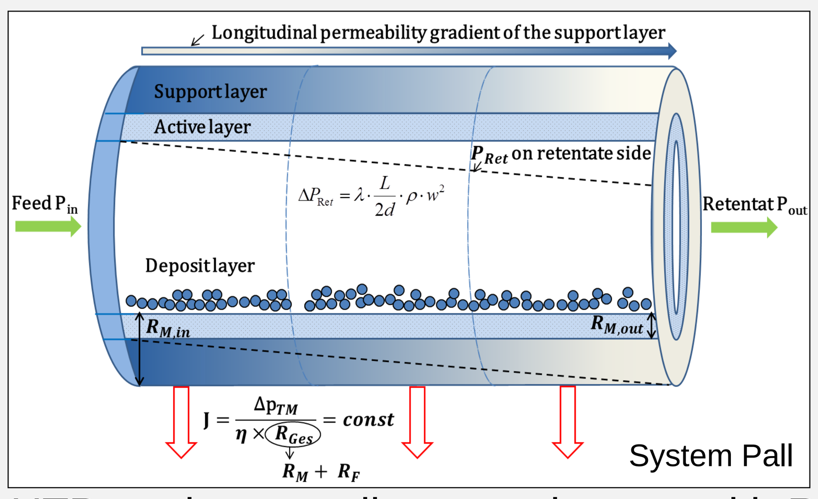
Isoflux system I: Uniform Transmembrane Pressure

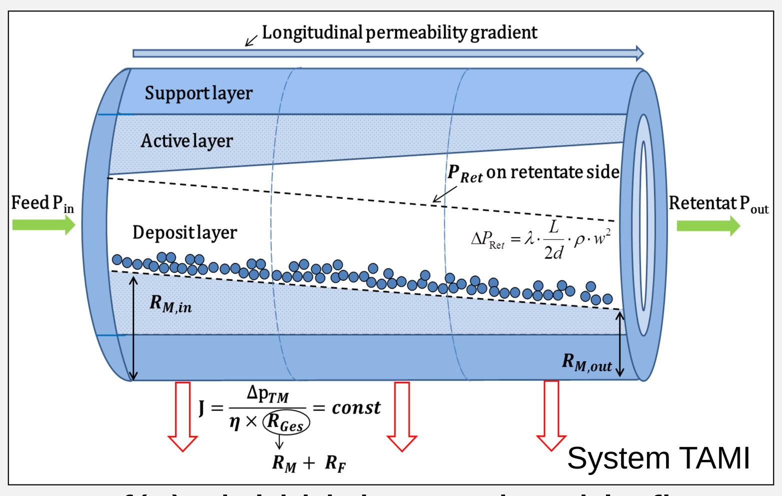


Uniform Transmembrane Pressure (UTP) mode



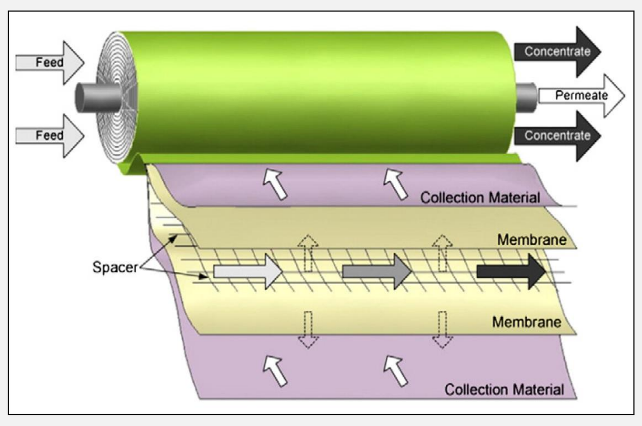
Isoflux systems II: `Gradient´ Membranes



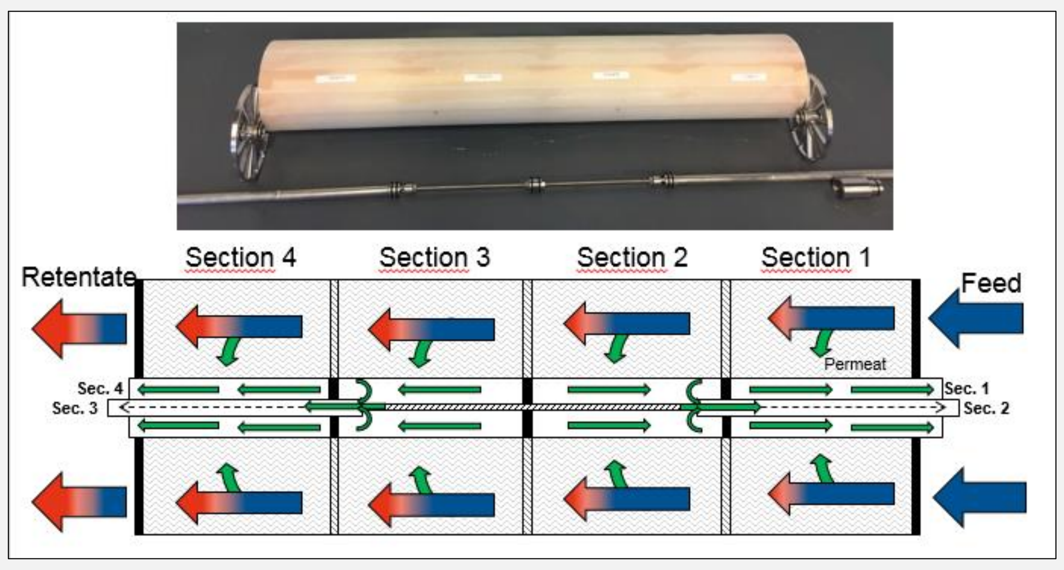


UTP mode or gradient membranes with $R_{Mem} = f(L)$ yield higher and stable flux by better control of deposit formation along the flow path.

Segmented/Un-segmented modules

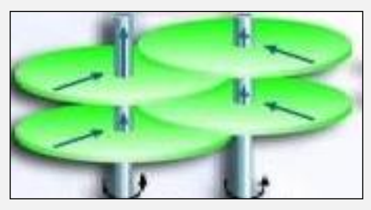


- Segmented membrane prototypes were constructed, both for ceramic tubular membranes (not shown) and SWM polymeric membranes.
- Thus, the effect of membrane length on deposit formation and permeation could be studied.



Dynamic Cross Flow (DCF) membranes

System GEA (Membraflow) Aalen/Oelde, Germany

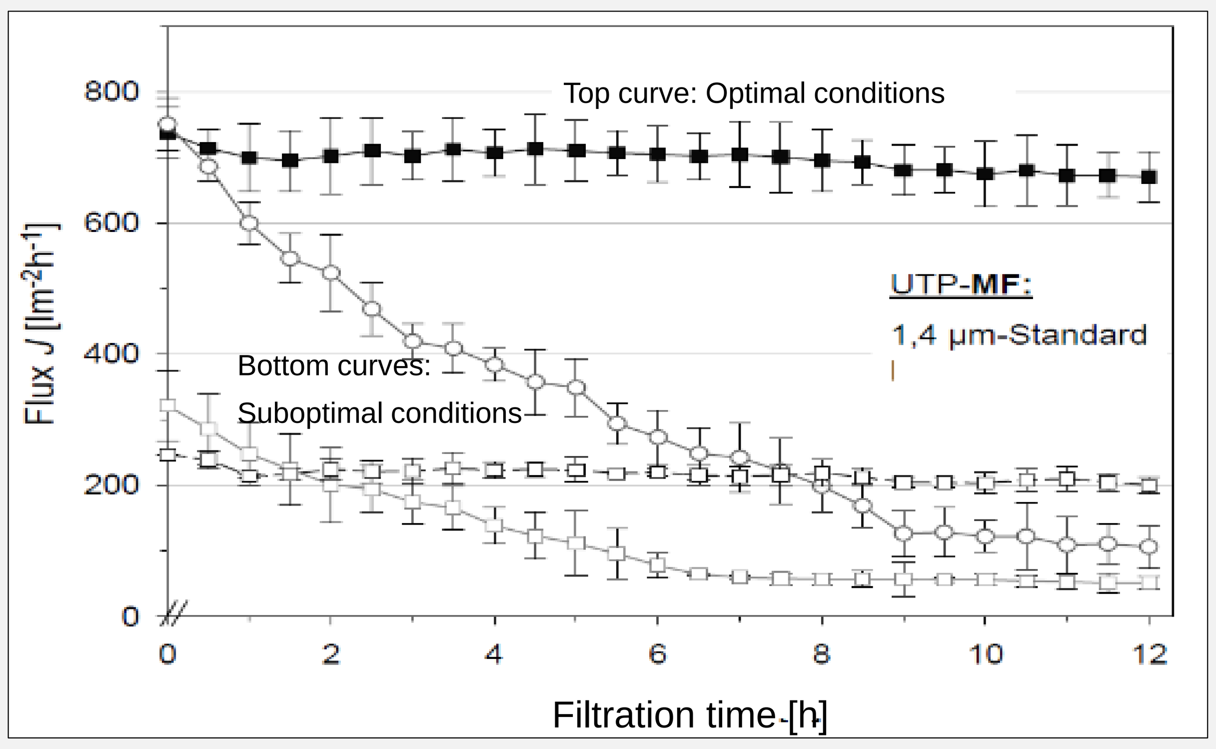


Principle of DCF for NF/UF/MF applications

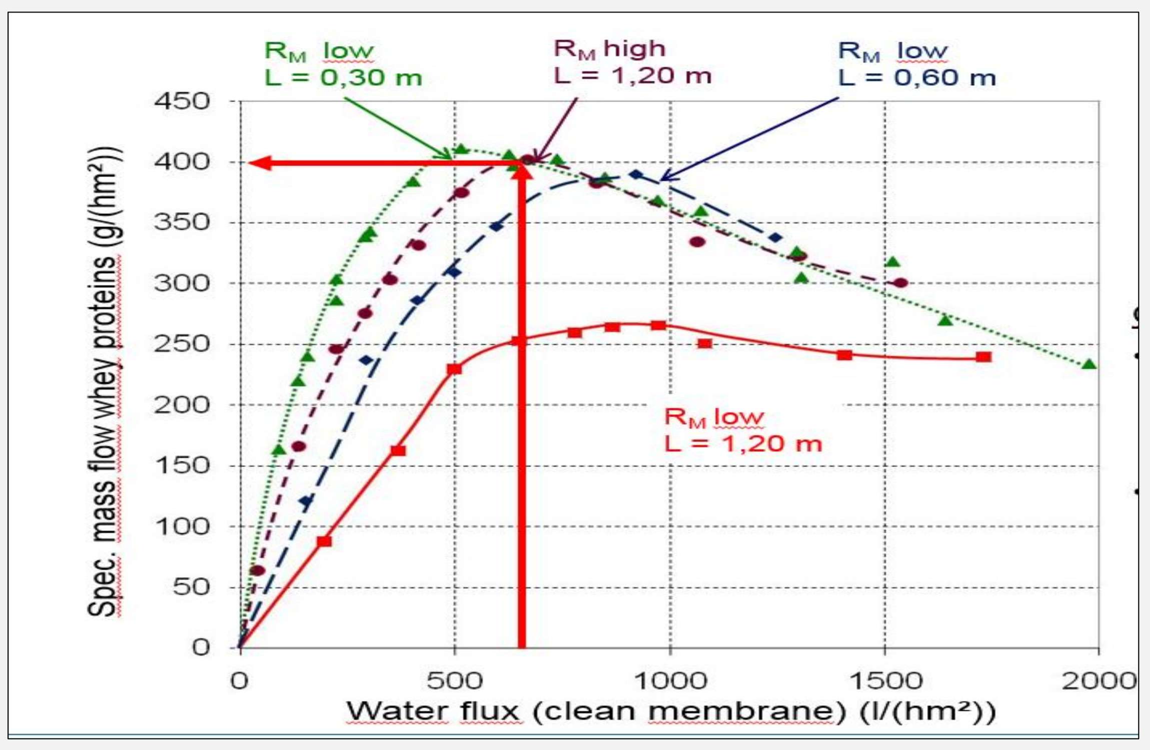
System KMPT Vierkirchen, Germany

DCF systems work with rotating membranes, thus creating high wall shear stresses and minimizing deposit formation, while volume throughput can be low and concentration high.

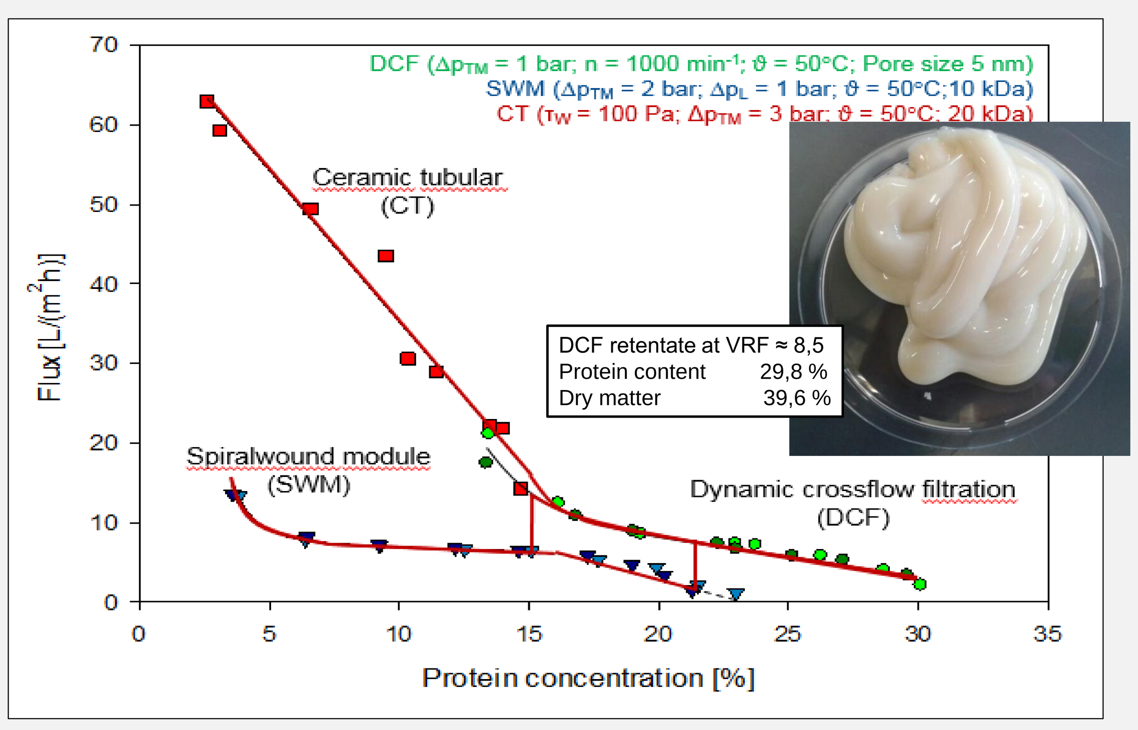
Results & Conclusions



UTP mode reduces deposit formation and stabilizes flux

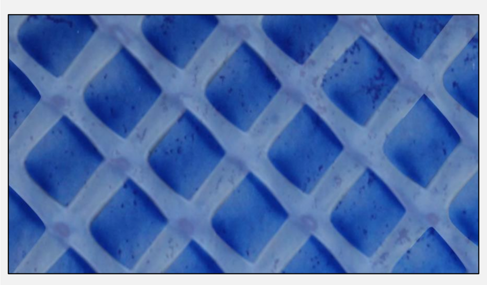


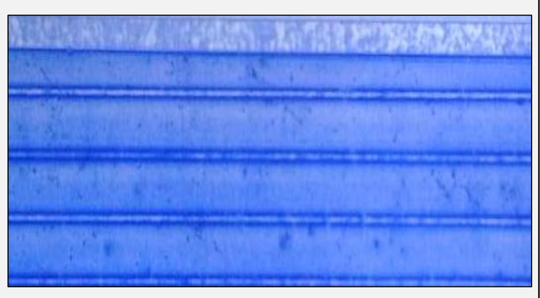
High R_{Mem} (same cut-off) enhances target protein permeation



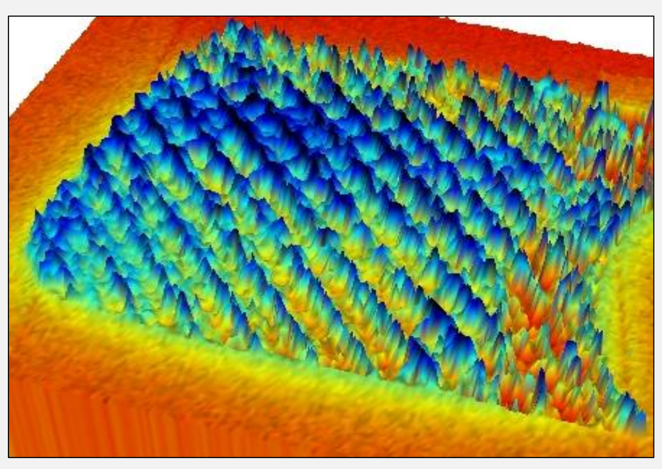
DCF can achieve and cope with very high concentration

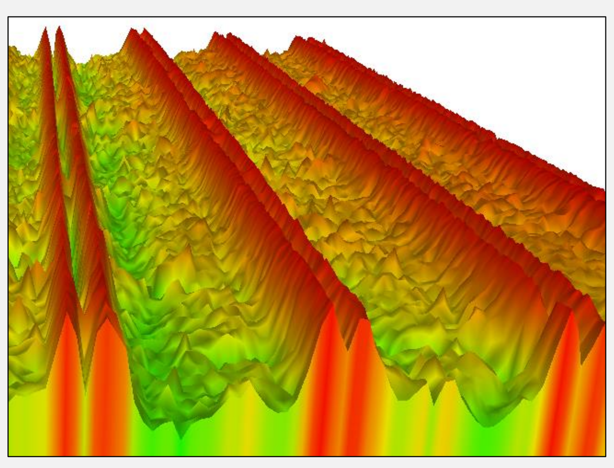
Analytical assessment of deposit formation within a module





- Amount and distribution of deposited protein material assessed using SDS-PAGE techniques.
- The effect of spacer shape and fluid dynamics thus became obvious.
- Results are useful for validation of simulation results and to further optimize module/spacer geometries.





Conclusions

- Based on selected results presented, novel membrane concepts appear to be candidates for stable bioprocess operation with cell retention and/or protein separation. Validation for pharmaceutical biotech processes is required.
- Novel modules and processing modes both yield options for process intensification by minimizing deposit formation.
- New insights gained in this work are important for continuous operation of biological processes, where high flux and a defined, stable permeation/low retention of target substances over long periods are key.
- Benchmarking results and methodology for process optimization between food process and bioprocess engineering could result in higher overall bioprocess productivities by avoiding of operational bottlenecks.

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