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Fouling mitigation in membrane based perfusion systems by oscillating tangential flow

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Fouling Mitigation and Hydrodynamic Characterization of Membrane based Perfusion Systems (XCell™ ATF)

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Background

- Fouling is a major drawback of membrane processes
  - Deposit layers lead to reduced flux and filtration efficiency
  - Permeation of target molecules changes
- Cell retention device using alternating tangential flow (ATF) are applied, but mechanisms appear not to be fully understood
- High residence times influence cell viability

Hypothesis

- Alternating stress due to oscillating tangential flow can mitigate deposit layer formation, thus enhancing flux, permeation and filtration efficiency.
- Residence times can be minimized by optimizing cycle time and tangential flow velocity
- Residence times depend on particle properties

Experimental setup

The filtration plant and model suspension

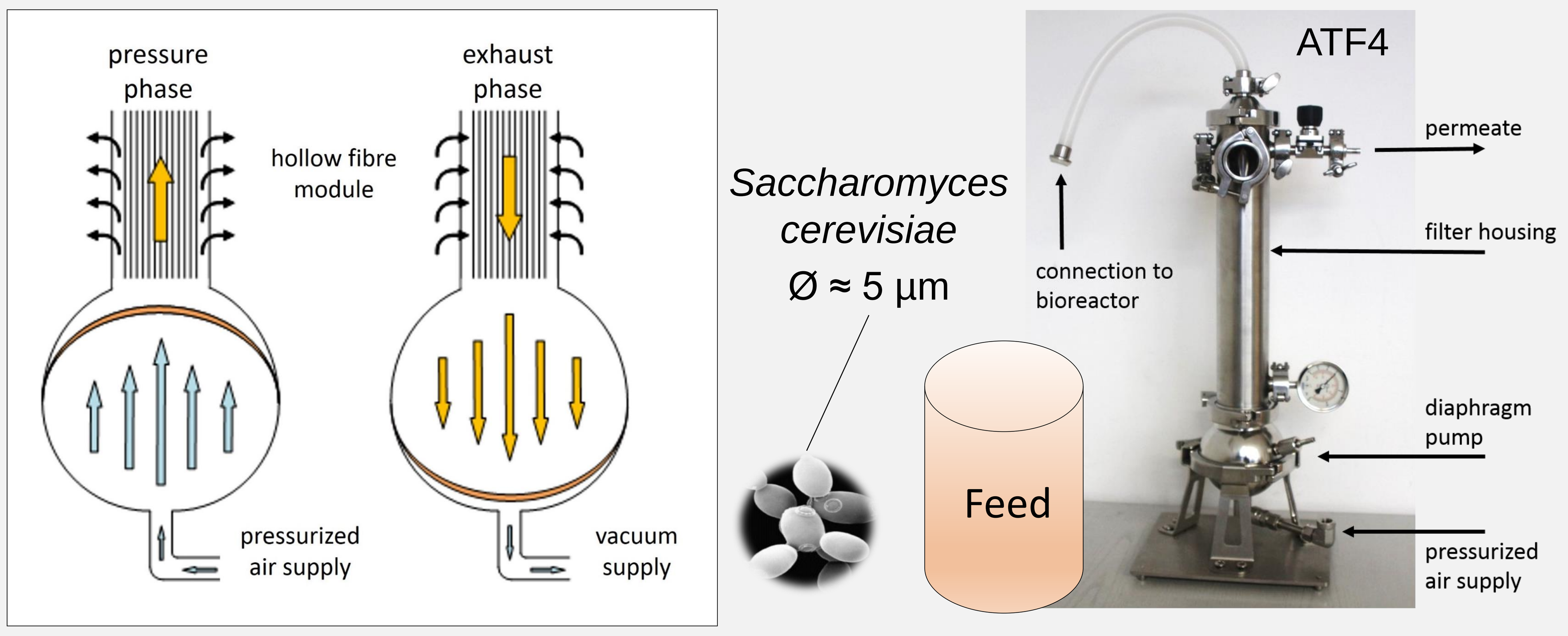


Fig. 1: Alternating tangential flow induced by a diaphragm pumps

- Diaphragm pump at the end of the filter is air pressure driven
- After full inflation/deflation phases are switched
- Permeate is removed by a peristaltic pump

Results

Particle accumulation in the diaphragm dead space

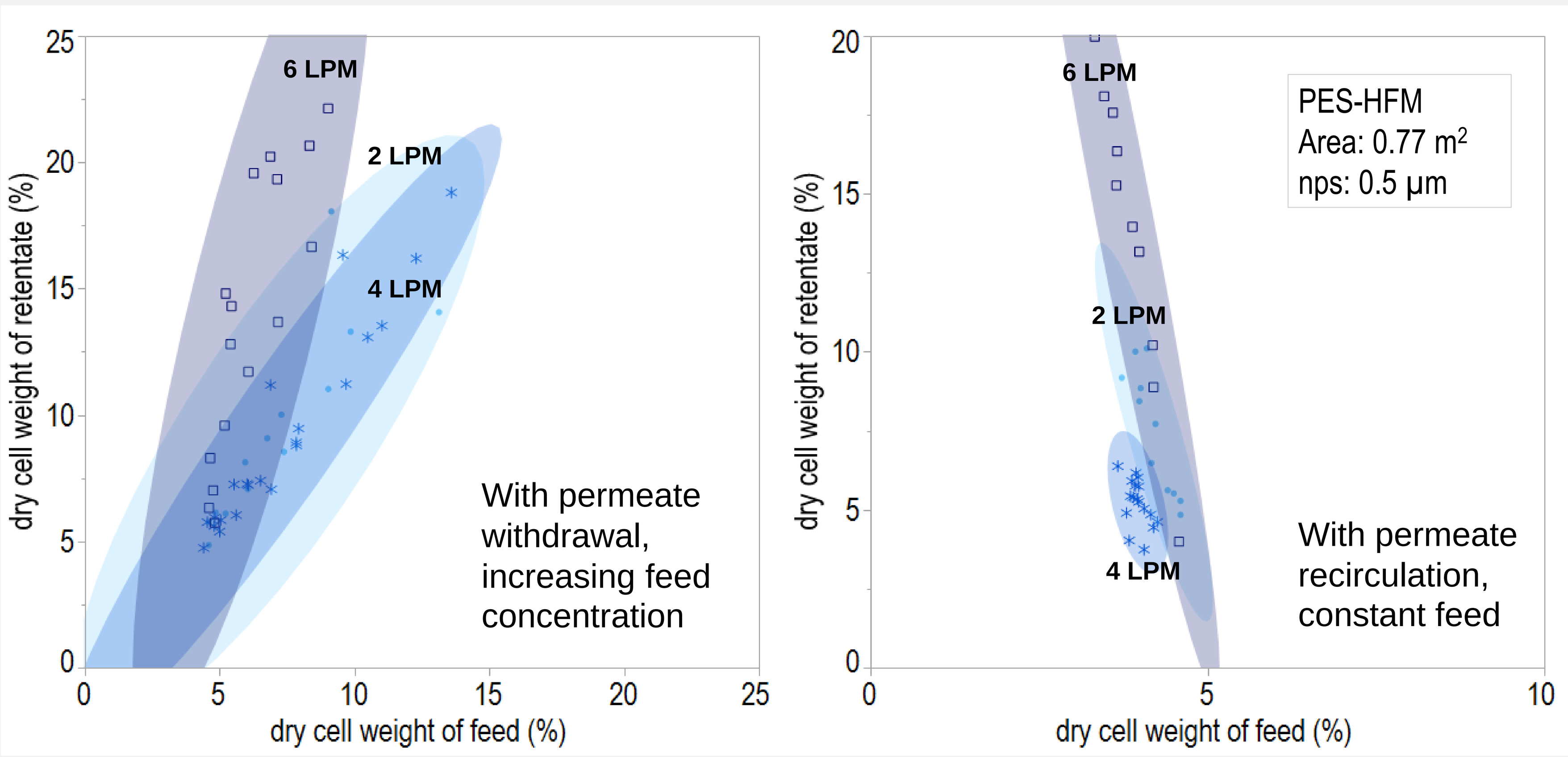
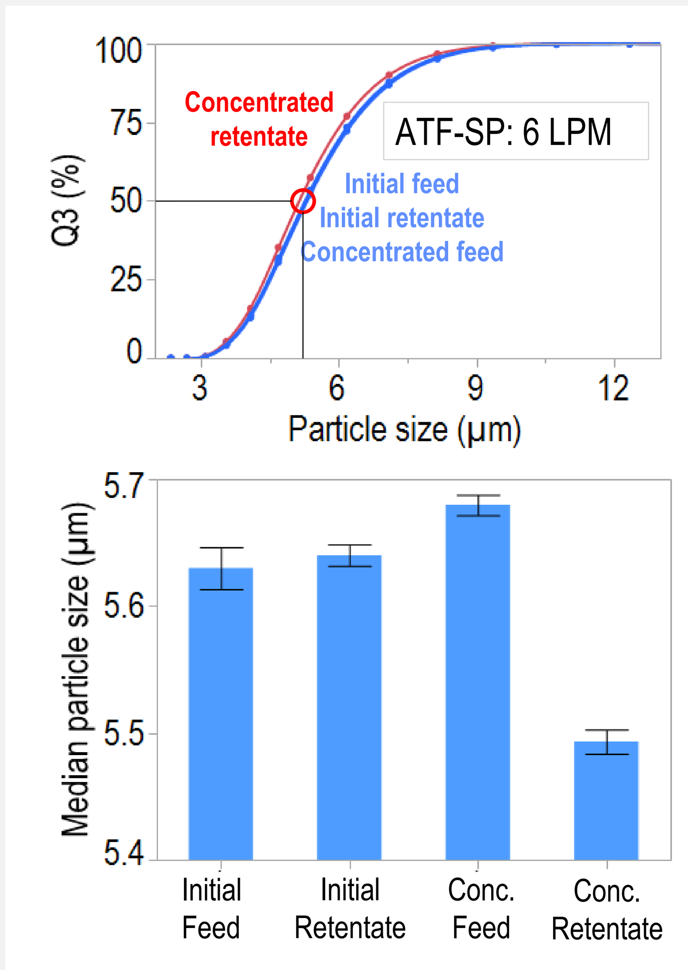


Fig. 2: Dry cell weight of retentate compared to the feed



- Particles accumulate in the diaphragm dead space and HFM
- Accumulation depends on the alternating tangential flow
- Medium flow rates are favorable in terms of cells' residence time within the perfusion device
- Particle size distribution indicates that smaller particles are enriched in the diaphragm dead space
- Hydrodynamic lift forces increase with particle size, they can thus better remove cells from the HFM

Fig. 3: Particle size distribution of accumulated particles compared to the initial feed

Principal component analysis of pressure data from both phases

- Transmembrane pressures increase with increasing flux
- Tangential flow velocity during exhaust phase has higher influence on pressure data than during pressure phase
- Settings with unfavorable conditions regarding particle accumulation can be identified by the first principal component
- Settings with similar tangential flow velocity during pressure phase behave similarly, independent from pressure phase settings

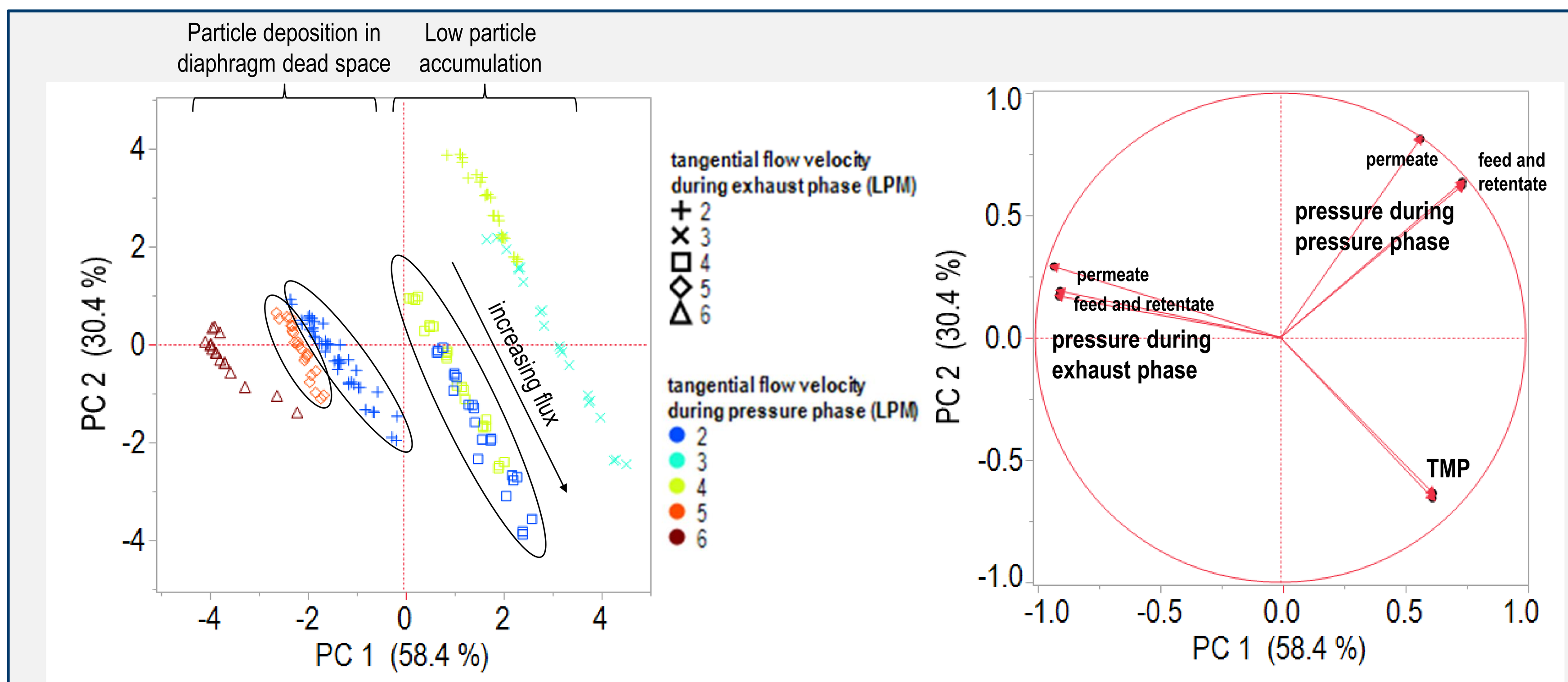


Fig. 4: Principal component analysis of yeast filtration with varying tangential flow velocity and flux. The permeate was recycled to the feed to obtain constant conditions.

Conclusion

The choice of tangential flow velocity …

- … highly influences particle deposition and residence time within the follow fiber module and therefore can establish unfavorable conditions (e.g. starving of cells)
- … enhances particle flush out if high tangential flow velocity during pressure phase is chosen
- … during the exhaust phase mainly influences the transmembrane pressure

Perspectives

Evaluating the impact of alternating stress on fouling

with different flow patterns, process variables and particles sizes

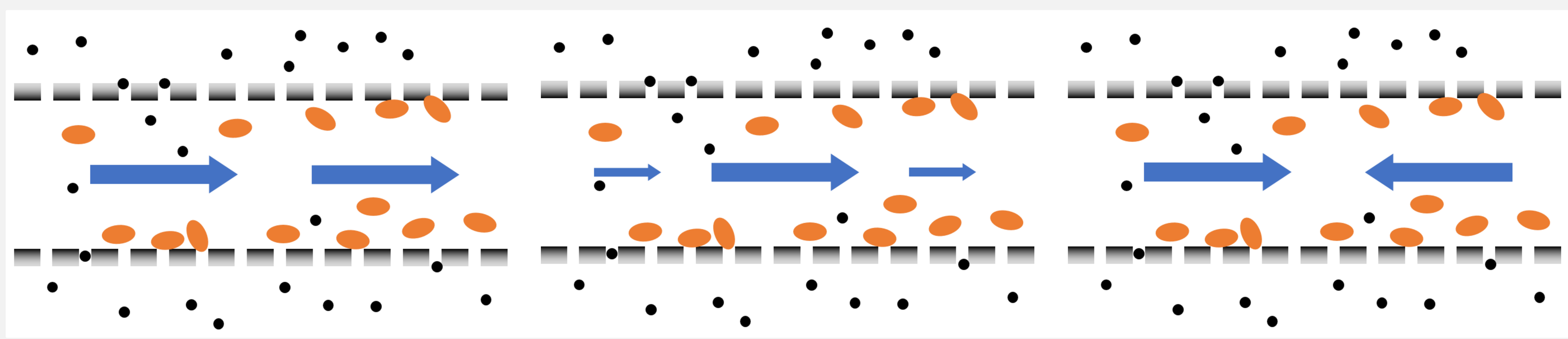


Fig. 5: Options for flow modes: Steady flow (std. crossflow as control), pulsating forward flow, and alternating tangential flow (w/o deadspace)

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