Rapid microfluidic osmotic compression of proteins to establish equations of state and phase diagrams

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Understanding protein-protein interactions is essential for predicting and controlling the phase behavior of biomolecular systems, with direct implications for protein formulation, stability, and crystallization. However, stabilizing proteins in solution or, conversely, promoting their crystallization remains largely empirical.
Here, we will show how to design a microfluidic chip integrating a PEGDA hydrogel membrane synthesized in situ to perform osmotic compression experiments on small proteins. Compared to a previous design for larger colloids [1,2], these new membranes imply a smaller cutoff and a larger surface area. Different designs of membrane shape will be discussed.
Equations of state (osmotic pressure Vs. concentration) can be measured by fluorescence or Raman spectroscopy, for fixed pH and chemical potential of ions. These parameters are fixed precisely by maintaining a continuous thermodynamic equilibrium between the reservoir and the dispersion through the membrane. Changing the composition of this flowing reservoir can be performed in real time to observe the immediate response of the dispersion. A proof of concept is proposed with the well-known lysozyme protein.

Keywords:
microfluidics, membrane,
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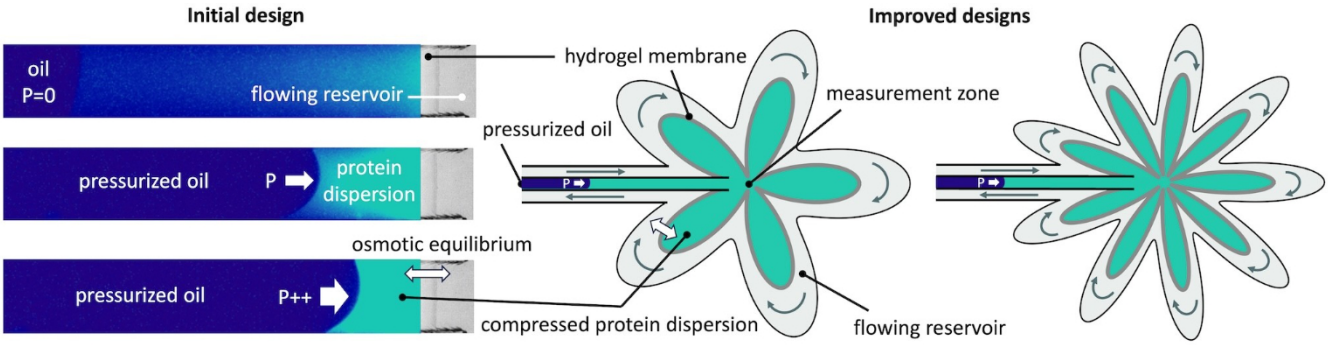

Initial design (left) with a flat membrane synthesized across a straight channel and improved designs (center and right) with a membrane and flowing reservoir geometry optimized to accelerated osmotic compression

References:

[1] C. Keita. Y. Hallez. J. B. Salmon. Physical Review E. 2021.
[2] D. Radajewski. P. Roblin. P. Bacchin. M. Meireles. Y. Hallez. Lab on a Chip. 2025.