

Crystallization of High-Quality Proteins using Microfluidic Devices

Ilya Avros, Hansen Pan, Jack Yakoub, Mohammed Bah, Jonathan Fey, Charles Maldarelli,
Jing Fan

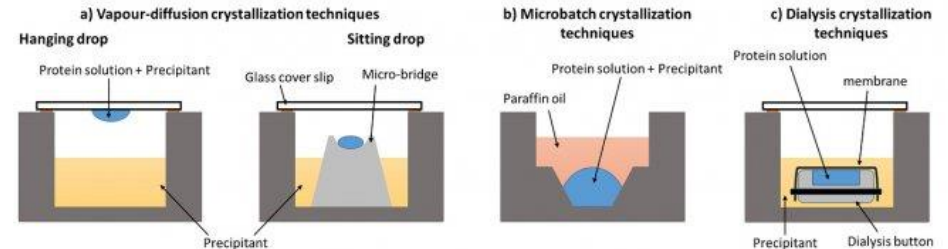
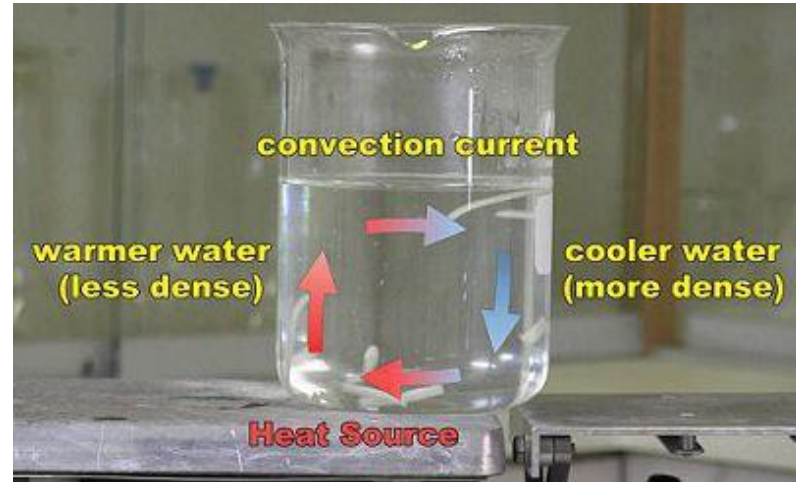


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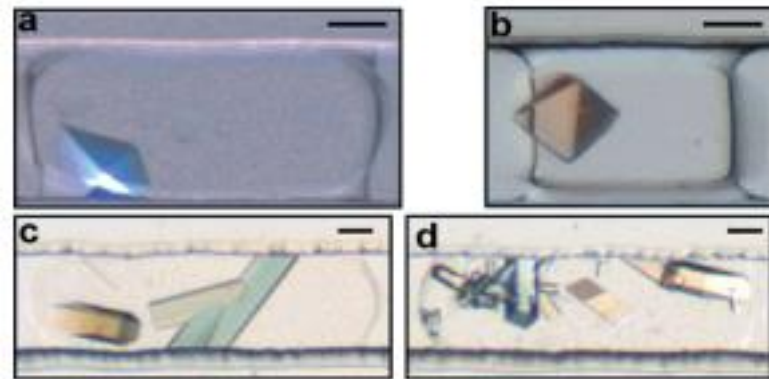
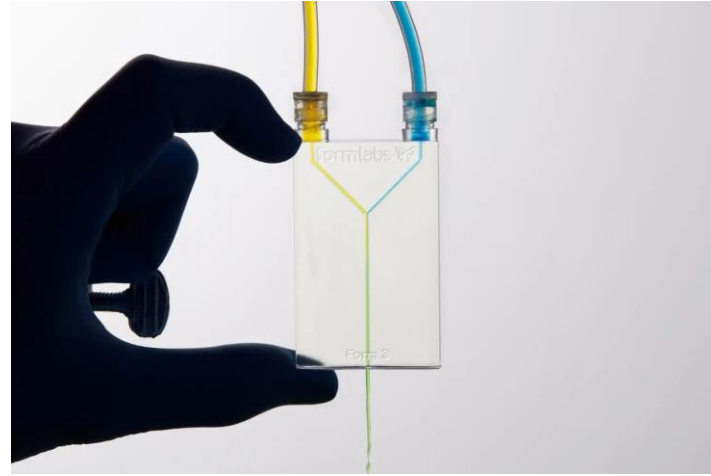
Introduction

- Increased interest by the pharmaceutical industry for reproducible methods for growing large, high-purity protein crystals.
- Current batch based methods of growing protein crystals are inefficient.
 - Influence of convection.
 - Expensive Materials.
 - Relatively low yield of ideal crystals for therapeutic applications.



Microfluidic Approach

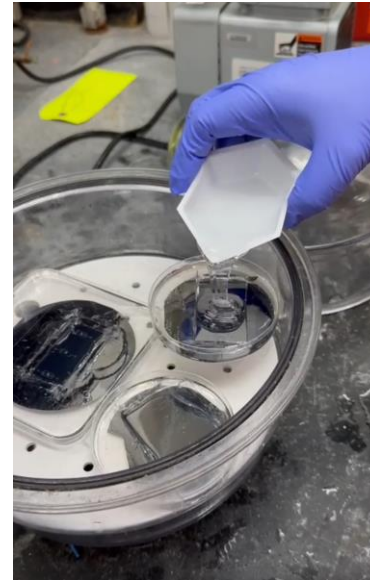
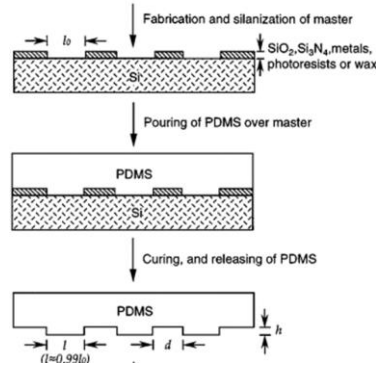
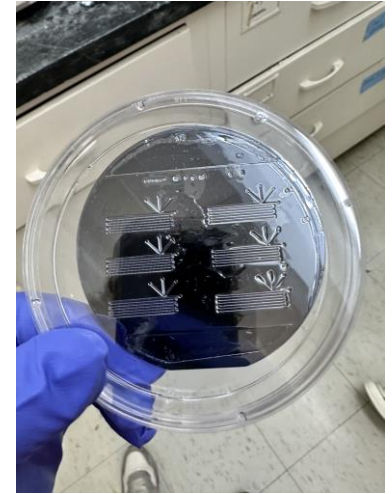
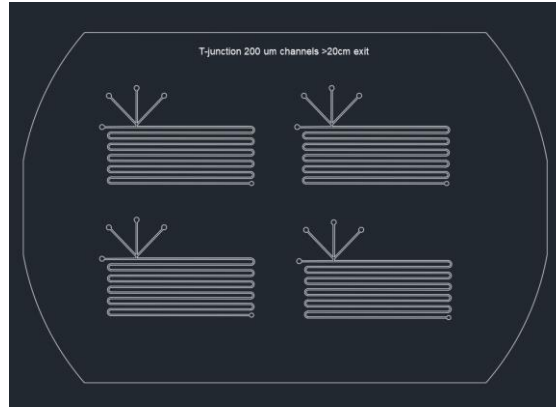
- Microfluidic approach allows for a higher degree of control.
 - Microgravity environment.
 - Minimized Reynolds number.
 - Concentration gradient.
 - Less material wastage.



Materials/Manufacturing

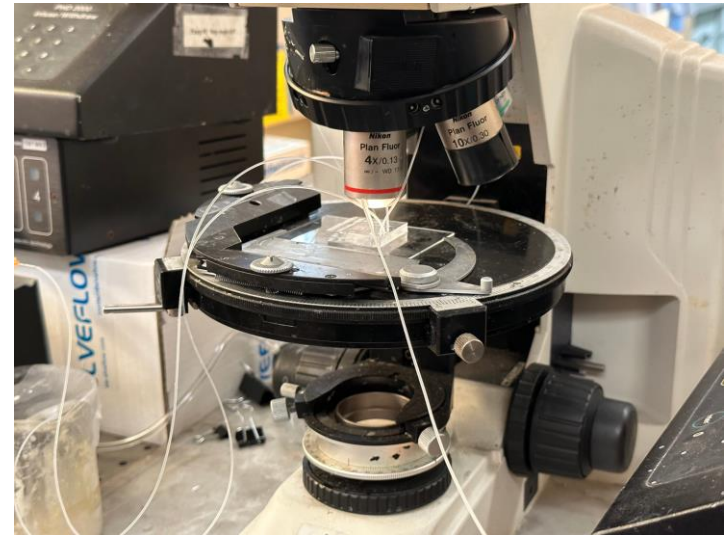
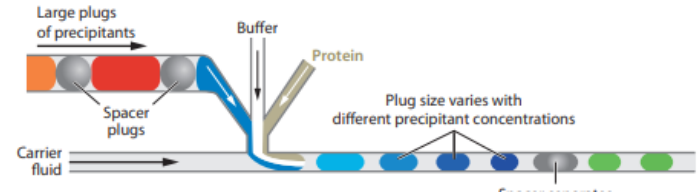
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- AutoCAD drawings.
- Soft Lithography with minor modifications.
 - Outsourced production of UV masks.
 - Lamination using 200 micron photoresist films.
- PDMS based devices.
 - Plasma binding to glass slides
- Channels treated with Aquapell.



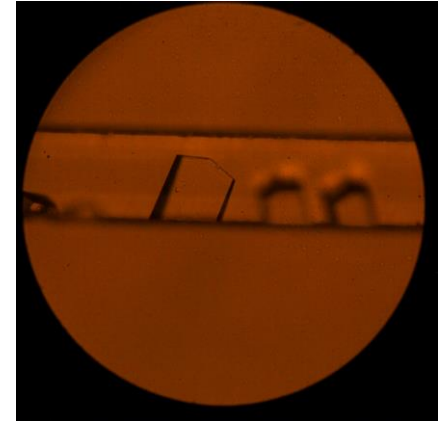
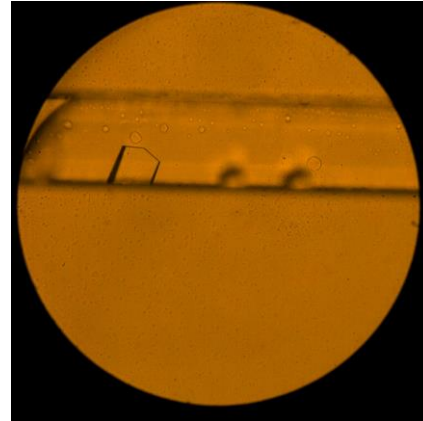
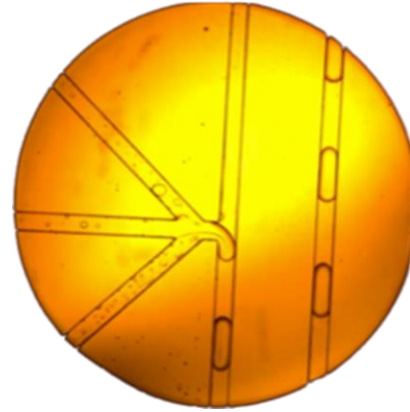
Experimental Testing

- Dispersed Phase:
 - Hen Egg-White Lysozyme dissolved in deionized water: 105 mg/ml.
 - NaCl: 1.5M dissolved in deionized water.
 - Titration of 3M Sodium Acetate Trihydrate with 99% acetic acid: pH 4.5.
- Continuous Phase:
 - Hydrofluoroether (HFE) oil with 2% w/w fluorosurfactant.



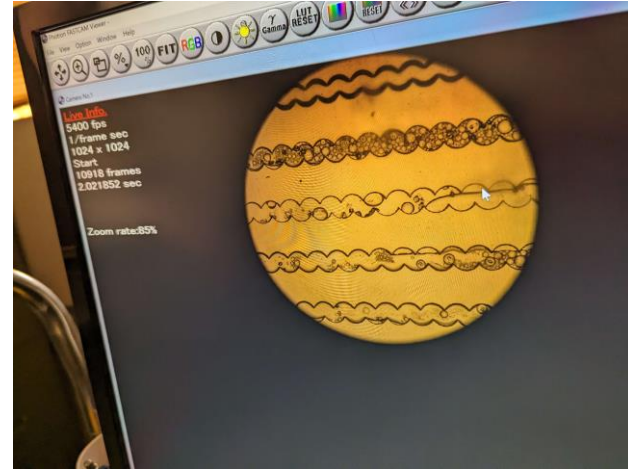
Results

- Dispersed phase flow rate:
 - 500 $\mu\text{L/hr}$.
 - Total: 1500 $\mu\text{L/hr}$.
- Continuous phase flow rate:
 - 2500 $\mu\text{L/hr}$.
- Monodispersed generation of droplets.
- Crystallization observed over 6-day period.
 - Nucleation approximately 24 hours after droplet generation.
 - Further crystal growth observed 5 days later.



Future Directions

- Improved sealing of stored droplets.
 - Evaporation of continuous phase.
 - Coalescence of aqueous droplets.
- Backflow into inlet channels.
- Collection of data.
 - Impractical methodology for monitoring several devices.



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