Supporting Information Available: Movies illustrating the device in operation. This material is via the Internet at http://www.elsie.brandeis.edu/Protein_Site01/microfluidics.html .

Acknowledgments: SF acknowledges support from the NSF Major Research Instrumentation program, DMR-0420921, the NIH-NIGMS, R21 PA-03-1000, and the CIMS at Harvard University (now the Center for Nanoscale Science).

REFERENCES:

Bergfors, T. 2003. Seeds to crystals. *J. Struct. Biol.* 142: 66-76.

Berland, C.R., Thurston, G.M., Kondo, M., Broide, M.L., Pande, J., Ogun, O., and Benedek, G.B. 1992. Solid liquid-phase boundaries of lens protein solutions. *Proc. Natl. Acad. Sci*. 89: 1214-1218.

Chayen, N.E. 2004. Turning protein crystallisation from an art into a science. *Curr. Op. Struct. Biol.* 14: 577-583.

Chayen, N.E. 2005. Methods for separating nucleation and growth in protein crystallisation. *Prog. Biophys. Mol. Biol*. 88: 329-337.

Debenedetti, P.G. 1996. Metastable liquids: Concepts and principles, Princeton University Press, Princeton, NJ, pp. 411.

Hansen, C.L., Skordalakes, E., Berger, J.M., and Quake, S.R. 2002. A robust and scalable microfluidic metering method that allows protein crystal growth by free interface diffusion. *Proc. Natl. Acad. Sci*. 99: 16531-16536.

Hansen, C.L., Sommer, M.O.A., and Quake, S.R. 2004. Systematic investigation of protein phase behavior with a microfluidic formulator. *Proc. Natl. Acad. Sci.* 101: 14431-14436.

Lee, S.S.J., and Cudney, R. 2004. A modified microdialysis button for use in protein crystallization. *J. Appl. Cryst.* 37: 504-505.

McPherson, A. 1999. Crystallization of biological macromolecules. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, pp. 586.

Muschol, M., and Rosenberger, F. 1997. Liquid-liquid phase separation in supersaturated lysozyme solutions and associated precipitate formation/crystallization. *J. Chem. Phys.* 107: 1953-1962.

Randall, G.C., and Doyle, P.S. 2005. Permeation-driven flow in poly(dimethylsiloxane) microfluidic devices. *Proc. Natl. Acad. Sci.* 102: 10813-10818.

Smith, H.W., and Delucas, L.J. 1991. A method for programmable control of reservoir concentrations for protein crystal growth. *J. Cryst. Growth* 110: 137-141.

Squires, T.M., and Quake, S.R. 2005. Microfluidics: Fluid physics at the nanoliter scale. *Rev. Modern Physics* 77: 977-1026.

Watson, J.M., and Baron, M.G. 1995. Precise static and dynamic permeation measurements using a continuous-flow vacuum cell. *J. Membrane Sci.* 106: 259-268.

Zheng, B., Gerdts, C.J., and Ismagilov, R.F. 2005. Using nanoliter plugs in microfluidics to facilitate and understand protein crystallization. *Curr. Op. Struct. Biol.* 15: 548-555.

Zheng, B., Roach, L.S., and Ismagilov, R.F. 2003. Screening of protein crystallization conditions on a microfluidic chip using nanoliter-size droplets. *JACS* 125: 11170-11171.

Figures

Figure 1. (a) Plan view of the Phase Chip. One reservoir (red) located underneath 100 wells (green circles) is shown here. There are five such sections on the chip. (b) Vertical section of a storage well, channel, reservoir and dialysis membrane. The device is constructed from two PDMS layers and subsequently sealed together (Squires and Quake 2005). In the upper, thick (5 mm) layer, there are flow channels and storage wells. In the lower, thin (40 μm) layer, there is a reservoir, sealed by a 15 μm thick PDMS membrane, The reservoir is formed by spin coating a 40 μm thick layer PDMS over a 25 μm high photoresist mold (Squires and Quake 2005). (c) Photographs of surface tension guided storage of aqueous drops into rectangular wells, without a reservoir. (d-f) Protein crystallization with reversible dialysis. The photographs are of a single 300 μm diameter circular well that contains protein solution.