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Microfluidic Protein Crystallography

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Due to their impressive economies of scale and unique mass transport properties microfluidic devices have become viable technologies for nano-volume protein crystallization screening and growth. In particular, soft microfluidic devices based on multilayer soft lithography (MSL) have been successfully applied to systematic protein solubility studies and efficient nanoliter volume screening by free interface diffusion. While these systems have proven highly effective in identifying crystallization conditions for a large number challenging crystallization targets, realizing the full potential of microscale crystallization requires complementary technologies for crystal optimization and harvesting. In this talk I will briefly review previous studies of protein phase space mapping and crystallization screening, and will present recent work on a microfluidic device which provides a link between chip-based nanoliter volume crystallization screening and structure analysis through “kinetic optimization” of crystallization reactions and direct in situ structure determination. Using this device we demonstrate control over crystal quality, reliable scale-up from nanoliter volume reactions, facile harvesting and cryo-protectant screening, and protein structure determination at atomic resolution from data collected in-chip.