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Automation of Hanging Drop Protein Crystallization: Experiences and Implications for Crystallization Screening Strategies. Joel Bard, Kristine Svenson, Mark Johnson, Rajiv Chopra, Lydia Mosyak, Will Somers, Structural Biology and Computational Chemistry, Wyeth Research, 85 Bolton St. Cambridge, MA 02140.

The acquisition of diffraction quality protein crystals remains the biggest bottleneck in most structure determination projects. One must examine a large, multidimensional chemical space as efficiently as possible in order to maximize the chance of finding crystallization conditions with a given amount of available protein. Automation can improve the success of this search in at least two ways. First, by relieving the tedium of setting up crystallization experiments by hand, automation can encourage a more thorough examination of crystallization space. Second, since automated dispensers can accurately dispense smaller volumes than can be dispensed by hand, more conditions can be examined with a given volume of protein stock. We have been using an automated system for the design and execution of hanging drop crystallization experiments for the last two years. The system includes robots for the preparation of solutions, setup of hanging drops, and automated imaging, as well as a new software package (RoCKS) for managing all phases of the crystallization process. This system has been used to set up over 6000 trays for both screening and optimization. The automated system has allowed us to more than double the number of conditions typically screened for each project. We have also been able to support more drug development projects without increasing staff. In developing our automation platform we have dealt with a number of interesting problems both in ensuring that the hardware functions as desired and in finding laboratory practices that allow us to take full advantage of the automated systems.