

W0400

Advances in Instrumentation for Automated Combinatorial Crystallization Screening. B.W. Segelke, T.P. Lakin, D. Toppani, Biology and Biotechnology Program, Lawrence Livermore National Laboratory, Livermore CA 94551, M. Cornett, J. Johnson, D. Martin, Innovadyne Technologies, Inc. Santa Rosa, CA.

By considering crystal screening as a sampling problem, we have previously demonstrated the inherent efficiency of stochastic combinatorial screening for crystallization. Though stochastic combinatorial screening is efficient, it has been challenging to automate. Robotic liquid handling instruments are generally designed for high throughput mother-daughter transfers or for lower throughput, though versatile, re-arraying. A newly developed, non-contact liquid handling instrument equipped with 96+8 independently actuated tips (Screenmaker) holds the promise of delivering the speed and versatility required to make high-throughput, on the fly, stochastic combinatorial screening practical. The independent actuation enables “any source any destination” liquid handling. The instrument also maintains high precision over a broad range of volumes and viscosities, delivering the necessary versatility for the types, concentrations, and ratios of components used in custom combinatorial screens. We are currently working to generate performance parameters for the full set of reagents we use and to integrate our CRYSTOOL design engine with the instrument, to pass instructions and performance parameters for aspirate/dispense operations to the instrument at run-time. This will fully enable stochastic combinatorial screening. Stock reagents arrayed in 96-well deep well blocks are aspirated simultaneously and dispensed in the random order and volume prescribed by worklists generated by the design engine. The same instrument can also be used for rapid setup of crystallization experiments from pre-made screens or for the setup of grid optimization screens.

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