Structure Discovery Using an Integrated Microfluidic Crystallization System

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Use of the three-dimensional structures of biological macromolecules is now a key component of many research programs. Identifying conditions for the growth of diffraction quality crystals of target proteins remains one of the main bottlenecks in structure determination. The TOPAZ™ system provides a rapid and efficient path to structure through the use of *integrated fluidic circuits* (IFCs), which enable the routine setup of sub-nanoliter crystallization experiments. IFCs are miniaturized fluidic devices that control the precise metering of fluid through the use of integrated valves controlling the flow between interconnected channels and chambers. Crystallization in TOPAZ IFCs is effected through microfluidic free-interface diffusion (μFID). μFID provides a complementary approach to crystallization by traditional methods, such as vapor diffusion.

Data will be presented describing evaluation studies carried out at academic and pharmaceutical customer sites. These studies include comparisons of screening experiments carried out using the TOPAZ system and vapor diffusion on a variety of samples. Results from screening experiments demonstrate the highly reproducible reagent distribution and crystallization behavior within experiments conducted using TOPAZ IFCs. Paths for successful translation of sub-nanoliter crystallization hits to larger-scale diffraction-quality crystals will also be discussed, including examples from experiments carried out at Fluidigm and independently at customer sites.

The presentation will also discuss ongoing product development at Fluidigm, highlighting paths for future additions and improvements to the TOPAZ system.