

**MS44-1-10 Implementation of a crystallographic fragment screening pipeline at the Swiss Light Source
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Abstract

In recent years, fragment-based drug discovery (FBDD) has emerged as a viable strategy to develop lead compounds against protein targets. The “start small, elaborate efficiently” directive that defines FBDD stands in contrast to more traditional high-throughput drug discovery campaigns. FBDD has been used successfully in both industry and academics, delivering several drugs to the clinic with many more candidates currently in clinical trials. One of the most useful and informative techniques for FBDD is X-ray crystallography, employed most effectively as a primary screen to detect the binding of fragment hits to protein target sites, while simultaneously elucidating binding pose and identifying possibilities for fragment development.

In recent years, technological advances at macromolecular crystallography beamlines in terms of instrumentation, beam intensity, and robotics have enabled the development of dedicated platforms at synchrotron sources for FBDD using X-ray crystallography. Here, we report the development of the Fast Fragment and Compound Screening (FFCS) platform at the Swiss Light Source (SLS): an integrated pipeline for crystal soaking, handling, and data collection, which allows crystallography-based screening of protein crystals against hundreds of fragments and compounds.

References

Kaminski, J. W., Vera, L., Stegmann, D., Vering, J., Eris, D., Smith, K. M. L., Huang, C.-Y., Meier, N., Steuber, J., Wang, M., Fritz, G., Wojdyla, J. A. & Sharpe, M. E. (2022). Acta Cryst. D78, 328-336.