In recent years, fragment-based drug discovery (FBDD) has revolutionized the development of potent lead compounds against protein targets. This “start small, elaborate efficiently” approach promises to address many deficiencies of traditional medicinal chemistry. It has been used successfully by industry and academics, delivering several drugs to the clinic, and many more to late-stage clinical trials. Probably the most useful and informative technique 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 poise 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.

In this presentation I will talk about the development of the Fast Fragment and Compound Screening (FFCS) platform at the Swiss Light Source (SLS), an integrated next-generation pipeline for crystal soaking, handling, and data collection, which allows crystallography-based screening of protein crystals against hundreds of fragments and compounds\(^1\,^2\).