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Automated collection and screening capabilities at the Australian Synchrotron MX beamlines)

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Fragment screening using synchrotron macromolecular crystallography is one of the most common approaches for identifying binding sites and binding mechanisms of small organic drug molecules to protein targets and is a well-established approach to initial lead identification and drug discovery. ANSTO's Australian Synchrotron houses the two most powerful and advanced instruments in the field of protein crystallography in Australia, with the Macromolecular (MX1) and Microfocus (MX2) Crystallography Beamlines (soon to be joined by MX3) being the cornerstone of structure-based ligand design for local and international researchers. However, even when using synchrotron beamlines for data collection, the time consuming nature of acquiring and processing the data and analysing the structures of the 100's to 1000's of models involved in a fragment screening campaign results in primary screening remaining outside the repertoire of most laboratories. Recognising the need for such a national capability, the MX Beamlines are developing on-site fragment screening capabilities at the Australian Synchrotron.

Developments in our automation capabilities include: automated sample centering and initial screening for diffraction, automated data acquisition (including mounting, crystal location, centering, data collection). A processing and refinement pipeline, utilising code developed at the Australia Synchrotron, has been used to solve structures and identify ligands in over 100 datasets in less than 30 min, indicating the throughput possible with our modular framework.