Poster

A Joint X-ray/cryo-EM platform for fragment-based drug discovery

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Fragment-based drug discovery (FBDD) [1] is now a widely used technique for developing potent and selective small-molecule binders to macromolecular targets. FBDD comprises probing the molecular surface of macromolecules with a library of low-molecular weight ligands to characterise protein-ligand interactions. This information is exploited throughout the drug development cycle to inform ligand design. Astex has developed its proprietary Pyramid+ platform to enable automated cryo-EM and X-ray structure determinations for fragment screening campaigns.

Considering the high number of experiments and structures needed for FBDD, it is imperative that experimental data are recorded in a central repository and made available to all scientists. From its inception, Astex has provided a web-based interface and a computational backend to support protein crystallisation, data collection and structure determination activities. More recently, the platform capabilities have been extended to support cryo-EM workflows.

Here we outline computational aspects of the Pyramid+ process, presenting the workflow from X-ray/cryo-EM data collection to final structure.

[1] Davies, T.G., Tickle, I.J. (2011). *Fragment Screening Using X-Ray Crystallography.* In: Davies, T., Hyvönen, M. (eds) *Fragment-Based Drug Discovery and X-Ray Crystallography. Topics in Current Chemistry*, **vol 317**. Springer, Berlin, Heidelberg.