An Open-Source Platform for the Automated Optical Analysis of Multi-Well Crystallisation Plates

T. Smith, M. Probert, M. Hall

School of Natural and Environmental Sciences, Bedson Building, Newcastle University, NE1 7RU, Newcastle Upon Tyne

t.smith7@newcastle.ac.uk

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Parallel crystallisation experiments provide users with the ability to probe a large and diverse volume of the chemical space of a small molecule quickly and, in the case of the high throughput ENaCt technique, with very little starting material. However, performing a large number of crystallisations in parallel creates a new problem, namely analysis. Under the ENaCt scheme, crystallisations are performed in 96-well plates, and each well is optically analysed using polarisation microscopy. This process requires an operator to spend significant quantities of time using a manual microscope – time which could better be spent elsewhere.

Some commercial products exist to solve this problem. Fully automated plate readers with integrated plate hotels are available, but are mainly pitched at the biological and protein crystallography sectors. These instruments are both large and expensive, putting them far outside the reach of small laboratories who are uninterested in their biologically relevant capabilities, such as UV imaging. On the other end of the spectrum, there exist traditional optical microscopes with programmable translation stages. These save on both space requirement and cost by re-using equipment a laboratory is likely to already have. Translation stages are an unrefined solution – they require both manual programming and manual operation of the other components of the microscope (zoom, focus, and optionally an attached camera) - as well as other support hardware like power supplies and interface adaptors.

By reusing hardware designed for the hobby-grade 3D printer & computer numerical control (CNC) mill markets, it is possible to build an all-in-one automated optical microscope with custom control software to enable users of all technical ability to quickly image plates with a high degree of accuracy and reliability. Based on a design by Bohm et al.[2,3] we present an automated optical microscope suitable for interrogating the crystallisation outcomes for small molecules, and show its use as part of the ENaCt parallel crystallisation pipeline.


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