# Screening approaches that explore chemical space in order to identify suitable starting conditions for structure determination by cryoEM or other methods

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Protein structure determination by cryoEM requires expensive equipment that has low throughput. It is therefore wasteful to examine samples that can be shown in advance to be aggregated, since such samples are unlikely to be suitable for structure determination by any method. It may, however, be possible to break up aggregated samples by adding low concentrations of additives such as denaturants, detergents, osmolytes, etc. This study used a high-throughput screening approach to explore chemical space with premixed screens using several biophysical methods, focusing on dynamic light scattering (DLS), differential scanning fluorimetry (DSF) and circular dichroism (CD). DLS was found to be particularly suitable for additive screening because 96 conditions could be explored with as little as 10 µL of protein solution, and screens could be run automatically e.g. overnight.

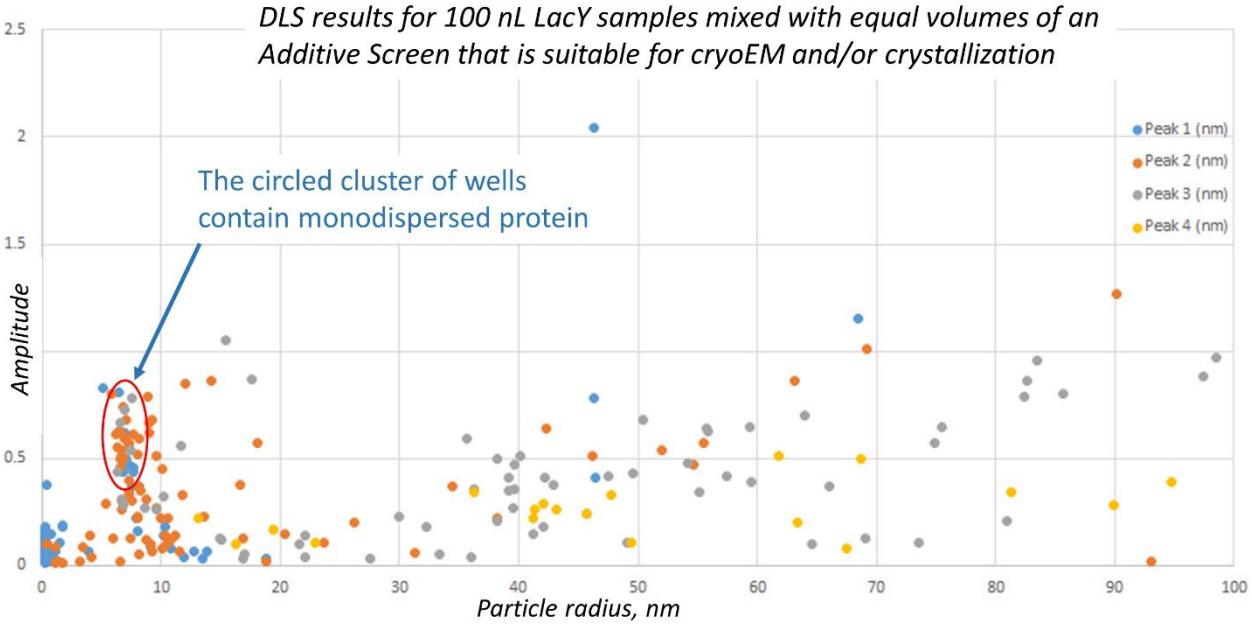


Figure 1