

UNDERSTANDING DLS DATA

To assess the reliability of screening hits, it is good practice to verify that compounds are soluble and do not aggregate at concentrations where they are found active (a recurring source of artefacts). Dynamic light scattering (DLS) can be used to measure compound aggregation and solubility. This is typically conducted on compounds of interest (i.e. hit candidates), not on the full chemical library.

As a rule of thumb, compounds should be soluble and should not aggregate at concentrations that are double the K_D value measured by SPR, in the buffer used in the SPR experiment (minus detergent – detergent scatters light).

The laser goes through each well of plated compounds, and its power is decreased if a compound precipitates in the well, leading to < 100% laser power.

Compound aggregates scatter the laser, resulting in an increase in scattering (counts per second) with increasing compound concentration.

HOW TO USE THIS DATA

Cross-reference SPR data (or other activity data) with DLS data for all hits. Consider a red flag if

- Laser power is < 100% at concentration < 2 x K_D value
- Laser intensity increases with concentration at concentration ranges < 2 x K_D value

More details are available in <https://doi.org/10.1021/acs.jmedchem.1c01547>