

The 2DSA-CG-MC models for each detection method are overlaid with the corresponding raw data for comparison in Supplemental Figures S1-4. The fit quality is indicated by how closely the modeled data (red) overlays the raw data (yellow), with a lower root mean square deviation (RMSD) value indicating better agreement. The residuals, which show the differences between the modeled and raw data, are expected to be randomly distributed.

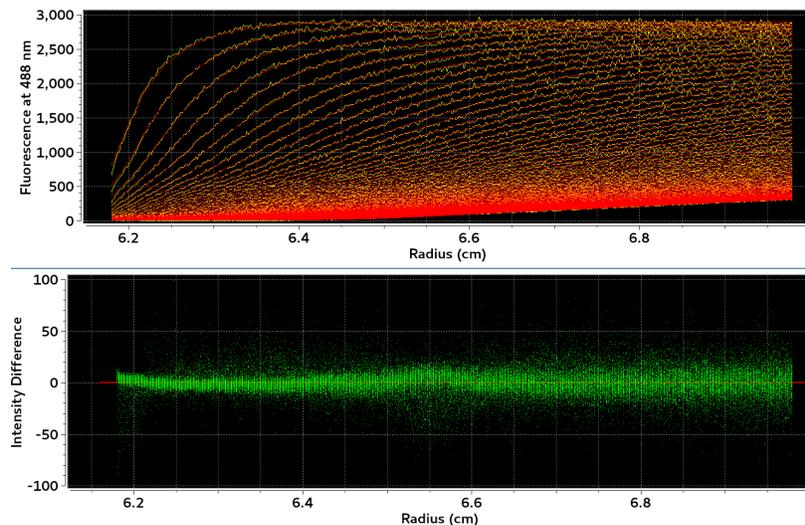


Figure S1: 2DSA-CG-MC overlay of the AcoRL-600 (1.78 mg/mL) measured using fluorescence at 488 nm. The fit yielded an RMSD of 11.56, an SNR of 242, and residuals randomly distributed within ± 50 intensity counts.

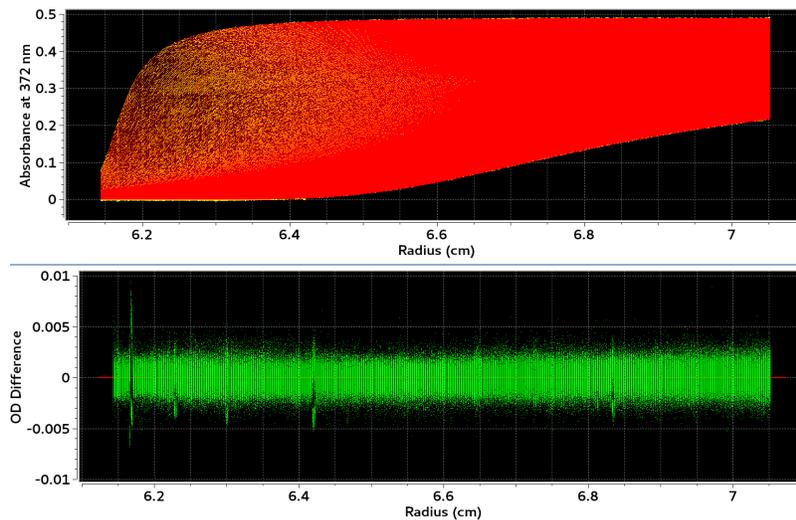


Figure S2: 2DSA-CG-MC overlay of the AcoRL-600 (1.78 mg/mL) measured by absorbance at 372 nm. The fit yielded an RMSD of $1.133 \cdot 10^{-3}$, an SNR of 424, and residuals randomly distributed within ± 0.005 OD.

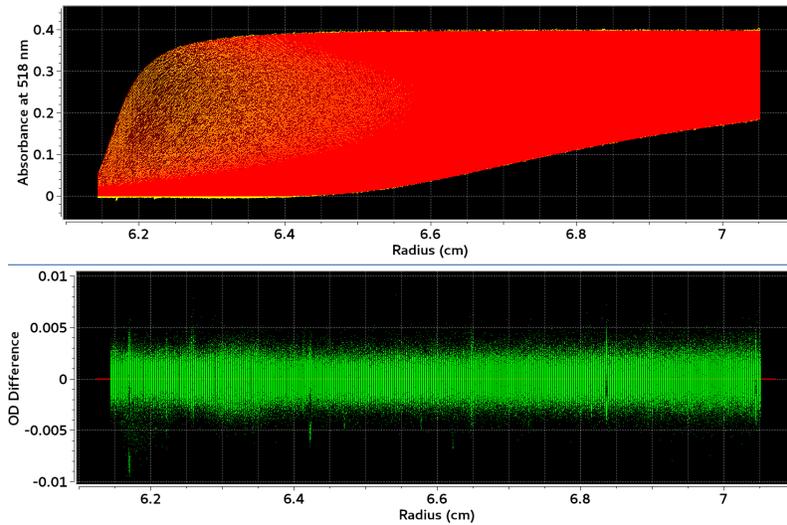


Figure S3: 2DSA-CG-MC overlay of the AcoRL-600 (1.78 mg/mL) measured by absorbance at 518 nm. The fit yielded an RMSD of $1.361 \cdot 10^{-3}$, an SNR of 294, and residuals randomly distributed within ± 0.005 OD.

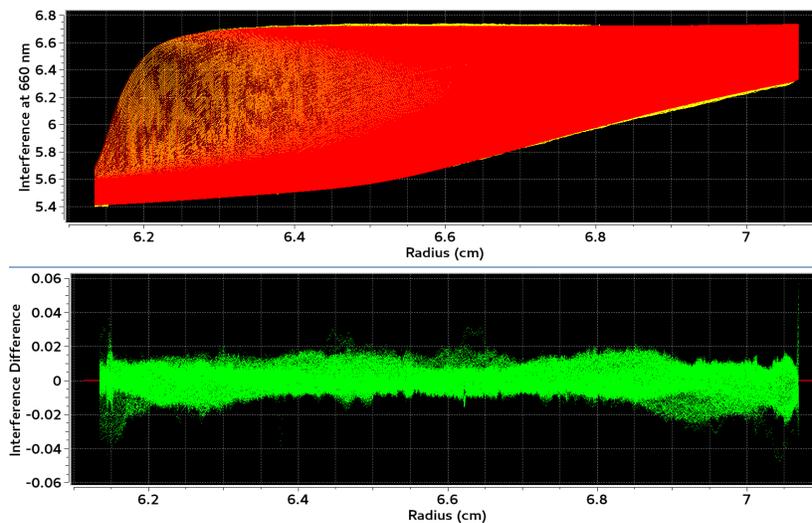


Figure S4: 2DSA-CG-MC overlay of AcoRL-600 (1.78 mg/mL) measured by Rayleigh interference at 660 nm. The fit yielded an RMSD of $7.084 \cdot 10^{-3}$ and an SNR of 184. The presence of non-random residual features is considered less concerning due to the heightened sensitivity of Rayleigh interference optics compared to absorbance optics.