BL4-2: biological Small Angle X-ray Scattering

SAXS instrument at BL4-2

- automated data collection
- remotely accessible (using Blulce control)
- open for COVID research during SIP

pinhole camera with variable flight path length for optimizing experimental setup

SAXS of biological macromolecules:

- molecules in solution: complete orientational average
- average of 2D detector image around beam
- data is essentially 1-dimensional
- reduction in structural resolution

- SAXS provides unique structural and dynamic information
  - no crystals needed
  - physiological conditions
- Flexible and unstructured proteins
- Time-resolved: proteins/virus at work (millisecond time scale)
- large protein complexes
- virus and virus particles (maturation events, interaction of viral proteins with host cell)
Automated solution SAXS methods

**Autosampler and chromatography coupled data collection**

- Data collection including background measurements (buffer) and cleaning of capillary cell **fully automated**
- **Remotely accessible** through dedicated BluIce tab
- Hardware can be coupled to chromatography instrument for **in-situ sample purification** (SEC-SAXS)
- Switch between Autosampler and SEC-SAXS data collection mode can be done remotely via BluIce

**Data pipelines for processing**

- A customized software pipeline **automatically processes and analyzes** the collected data in real-time
- The pipeline creates an **overview table** summarizing the results for each sample
- In SEC-SAXS mode the pipeline continuously extracts basic parameters ($R_g, I_0$) during the sample elution creating a **SAXS based elution diagram**
SAXS on non fluid and viscous samples

**data collection using capillaries**
- using regular thin-walled X-ray capillaries
- temperature controlled **multi capillary holder** for up to 30 capillaries at a time
- **sample microscope** for selection of exact position to be probed by X-ray beam
- 150 sample position can be stored and **automatically measured**
- **Full remote control** through dedicated BluIce tab
- data analysis pipeline for **real-time data reduction** gives immediate feedback on the current measurement

**High-throughput fixed target sample plates**
- flat sample plates with fixed positions for 96 samples at a time (same format as 96-well plates)
- **temperature controlled** sample holder
- exact position of samples in the wells can be specified
- **Automated data collection** of all samples in the plate (< 10min)

- data reduction and analysis pipeline for **real-time evaluation** of data
Recent Covid related research at BL4-2

Collaboration lead by Gerard Wong at UCLA

Central Hypothesis:
Some humans are allergic to parts of the SARS-CoV2 proteome

• BioSAXS is used for probing changes in membrane curvature induced by the virus - one of the key factors during infection - and how it can be modified (prevent infection) by added compounds

• Combination of multiple techniques, including machine-learning classifiers to select candidate peptides for experiments

Specific questions
• Why is COVID-19 so pro-inflammatory? SARS-CoV-2 derived peptides organize innate immune ligands for amplified inflammation

• Cell death from SARS-CoV-2 derived peptides and why are bats more resistant to COVID-19 acute inflammation

• Demonstration of suppression of SARS-CoV-2 infection by inhibiting viral membrane remodeling (and why bats are good at this...)

Data collection stats
• 100% remote data collection
• using capillaries
• 391 samples measured
• Some at multiple distances