

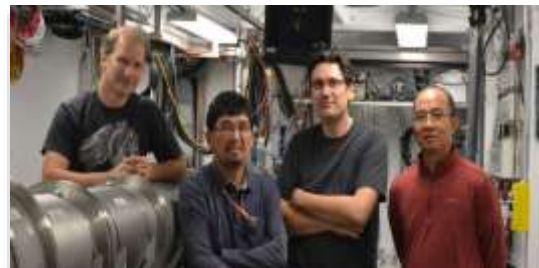
BL4-2: biological Small Angle X-ray Scattering

SAXS instrument at BL4-2



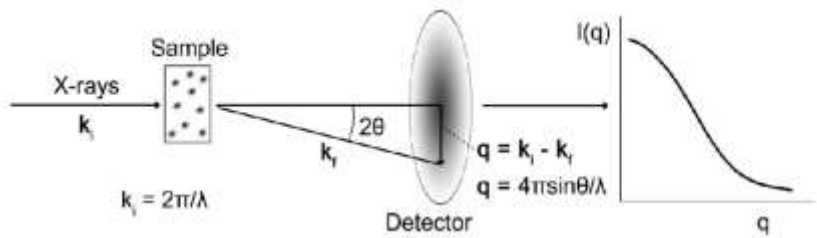
pinhole camera with variable flight path length for optimizing experimental setup

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



Thomas Weiss Ivan Rajkovic
Tutomu Matsui Ping Liu

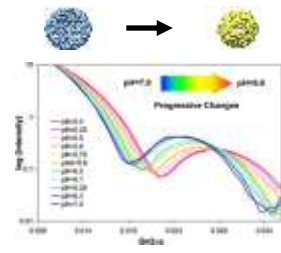
SAXS of biological macromolecules:



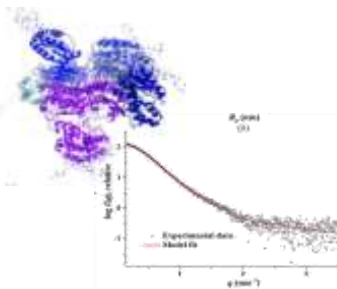
- molecules in solution: complete orientational average
- average of 2D detector image around beam
- data is essentially 1-dimensional

→ 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)



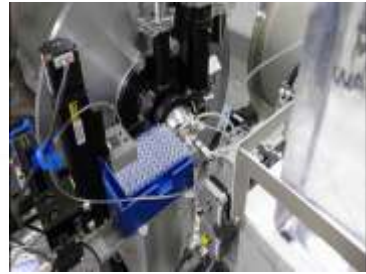
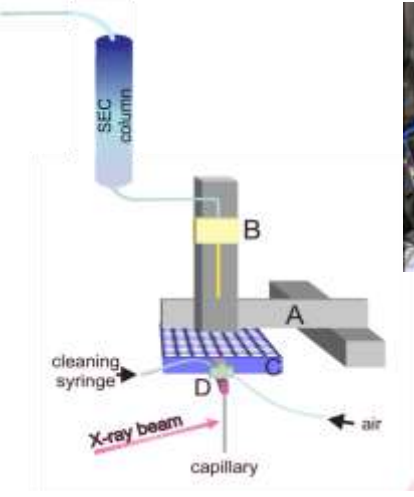
Virus Maturation



Dengue Virus NS5 flexibility

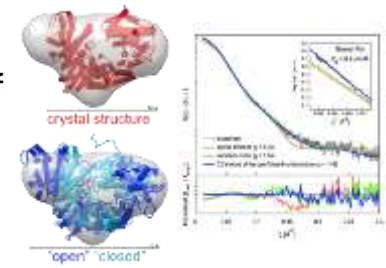
Automated solution SAXS methods

Autosampler and chromatography coupled data collection



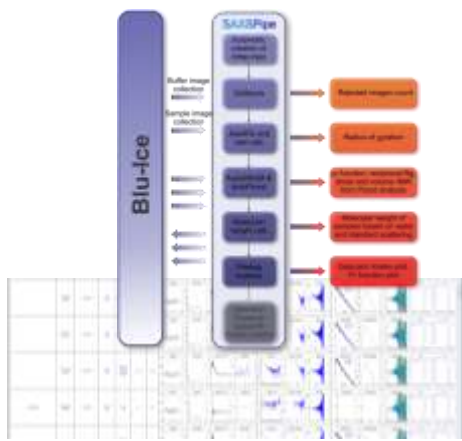
Autosampler hardware including SEC setup

- 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



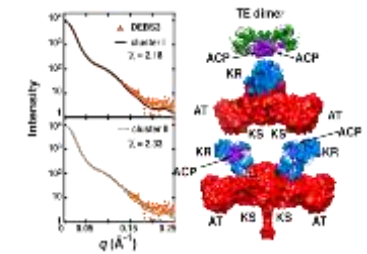
SAXS modelling of NUP192

data pipelines for processing

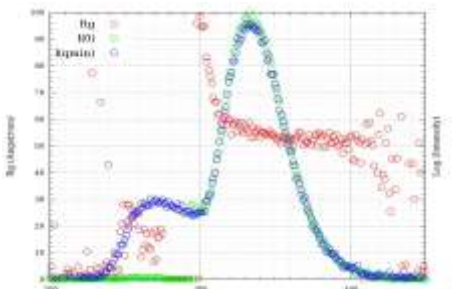


Schematic of data analysis pipeline and output table

- 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 data and model of DEBS complex



SAXS elution diagram created by SECPIPE

Recent Covid related research at BL4-2

Collaboration lead by Gerard Wong at UCLA



Gerard Wong



Jaime De Anda

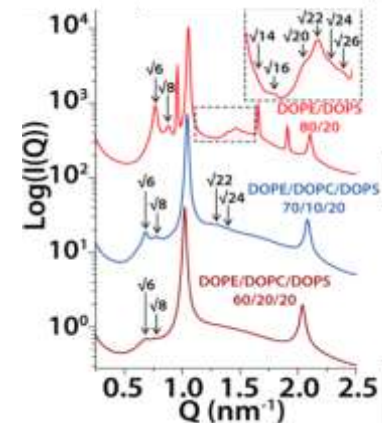


Yue Zhang

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



Representative SAXS data showing the effect of induced membrane curvature due to interaction with peptides

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