Implementing SANS Analysis Models for Concentrated Protein Solutions

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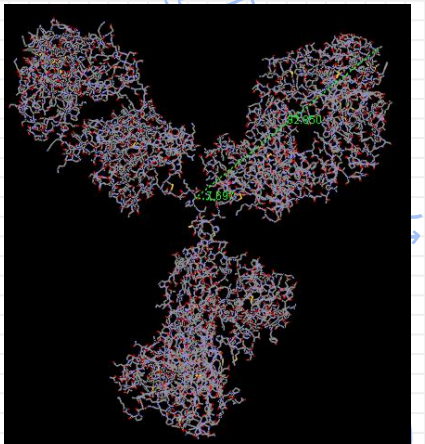
Background:

- My project develops software to supplement and improve Sasview, particularly in investigating the properties of proteins
  - There are many different focuses and parts to the project
  - Main goal is to develop fit models for Sasview
- By comparing SANS data to these models, size and interactions between proteins are revealed
- Important in cases such as pharmaceuticals
  - Protein-protein structure and interactions are essential to their applications.

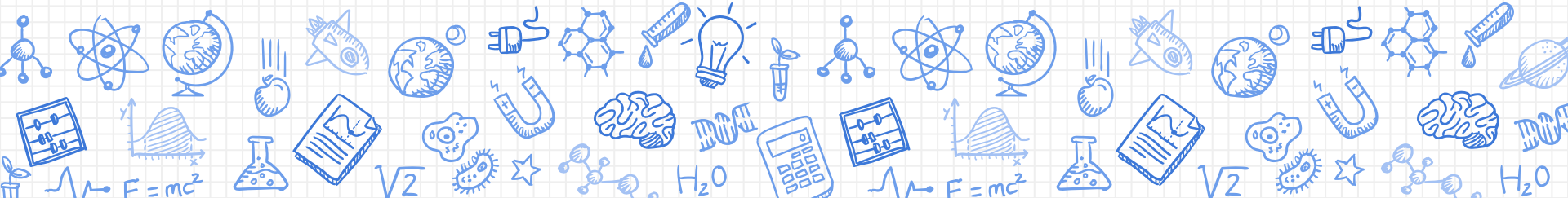


NIST MAB Protein

Special thanks to Dr. Christina Bergonzo for providing the MD Simulation files

Brief Overview:

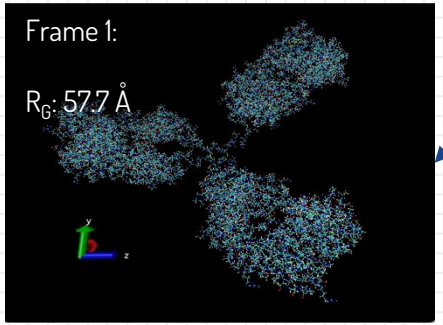
Radius of Gyration (R_G) // Scattering Pattern ($I(Q)$) // Beta Q ($\beta(Q)$)

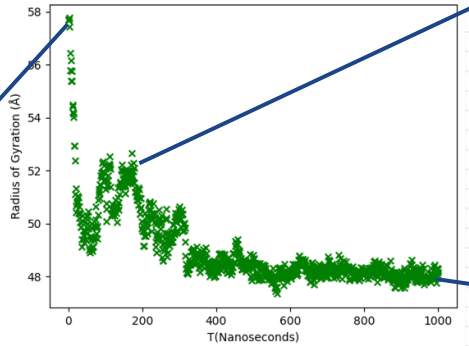


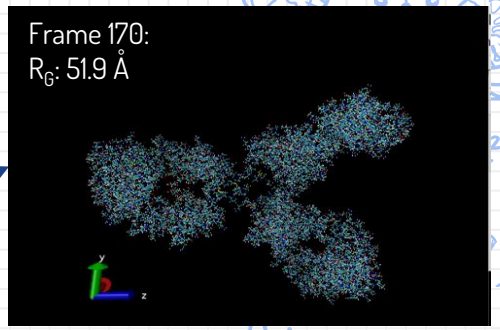
Radius of Gyration: R_G

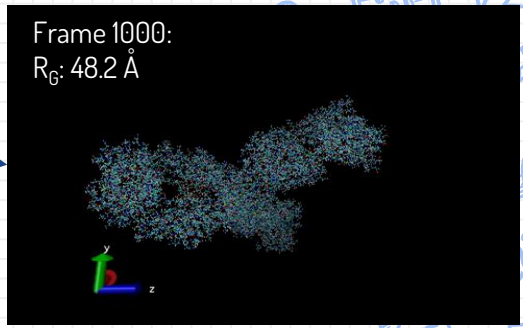
- Size of the molecule (unit: Angstrom (Å), 0.1 nanometer or 10^{-10} meters)
- Used for calculating other properties as well
- R_G is the average distance of all the atoms in the molecule from the center of mass.
  - A smaller R_G means a more compact protein
- We can calculate it with Mass or Scattering Length Density (SLD)

$$R_g^2 = \frac{\sum_i m_i (\vec{r}_i - \vec{r}_c)^2}{\sum_i m_i} = \frac{\sum_i m_i \vec{r}_{i,c}^{\,2}}{\sum_i m_i}$$





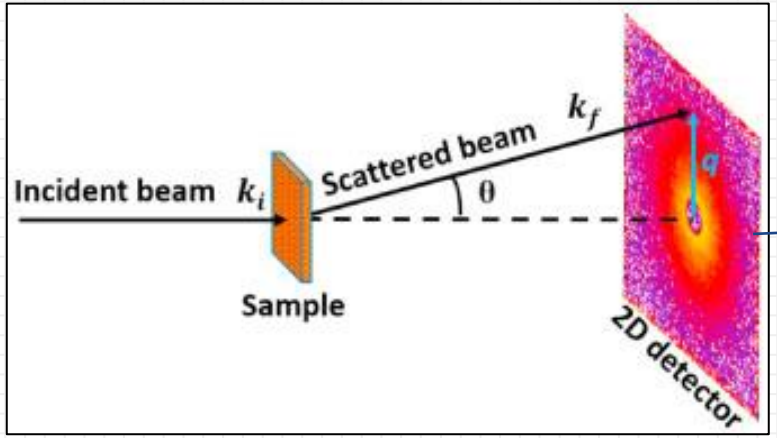


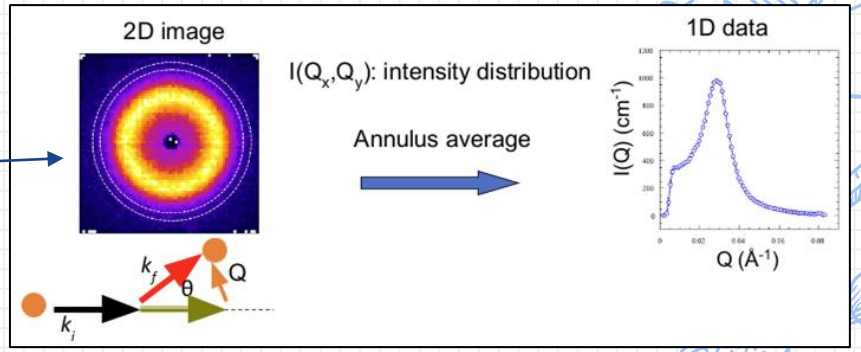


Trajectory A: Protein change over time

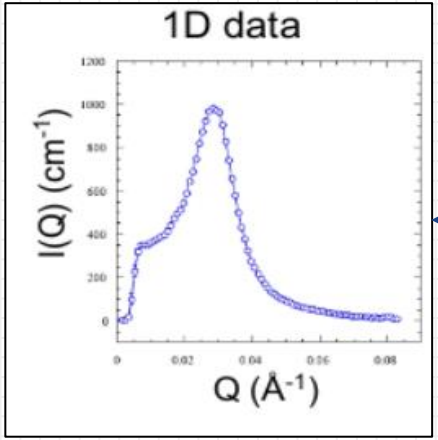
Scattering Pattern: I(Q)

- I(Q) is the 1D scattering pattern obtained from averaging 2D scattering data
  - Essential to understanding interactions between proteins through SANS
  - Dependent on Q (Angle)
  - We can find I(Q) either experimentally through physical scattering in real space (see below) or theoretically through calculations (next slide)

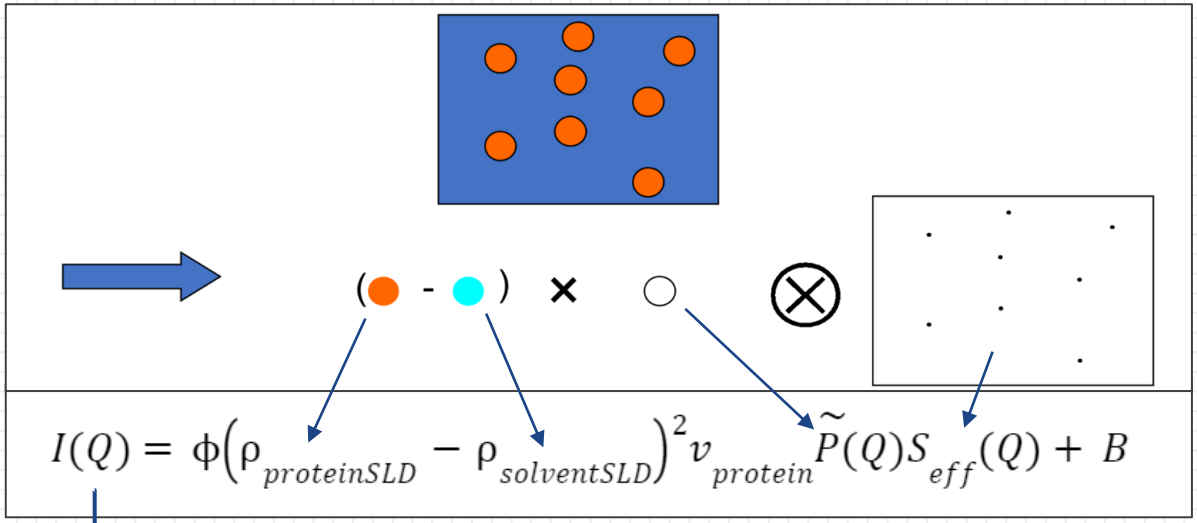




Scattering Pattern: I(Q)



- I(Q) can be also be calculated (see equation)
- This allows us to compare the experimental and calculated I(Q) to ascertain various properties of the sample.
  - More details later



φ - Scale

ρ - Scattering Length Density; effective size of interaction field, related to probability of scattering

v - Volume

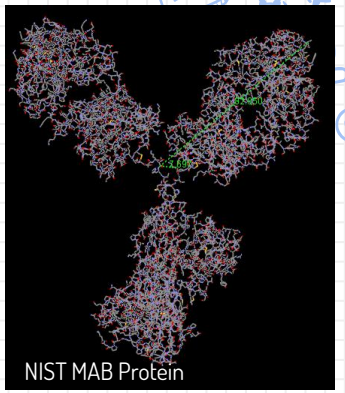
$\tilde{P}(Q)$ - Normalized Form Factor; Particle Shape

$S_{eff}(Q)$ - Effective Structure Factor; Protein Location & Interaction

B - Background

Beta Q: β(Q)

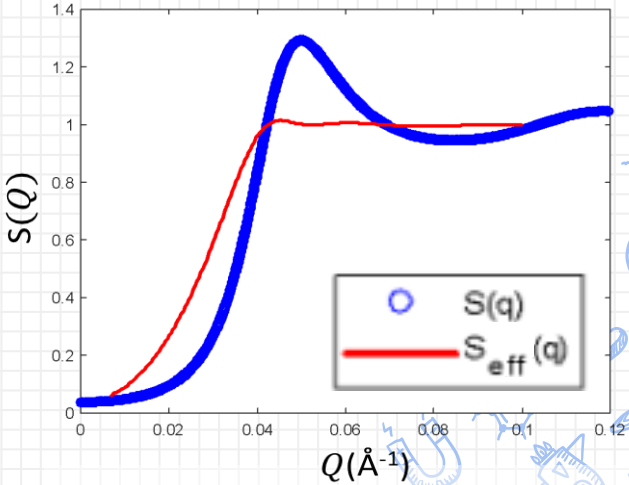
- Beta Q is a correction factor that accounts for the **orientation and interaction between proteins** in solution
- I(Q) (SANS Scattering pattern) is calculated with $S_{eff}(Q)$
  - Results from the experiments is $S_{eff}(Q)$ rather than S(Q)
  - S(Q) assumes a spherical shape (β(Q) of 1)
  - β(Q) is used to transform S(Q) to $S_{eff}(Q)$
- It is important to calculate the Effective Structure factor to accurately obtain the Scattering patterns



$$I(Q) = \Phi\left(\rho_{proteinSLD} - \rho_{solventSLD}\right)^2 v_{protein} \widetilde{P}(Q) S_{eff}(Q) + B$$

$$S_{eff}(Q) = 1 + \beta(Q)(S(Q) - 1)$$

$$\beta(Q) = \frac{\langle F(Q^-)\rangle^2}{\langle F^2(Q^-)\rangle} = \frac{\langle F(Q^-)\rangle^2}{P_A(Q)}$$



The effect of the static beta approximation

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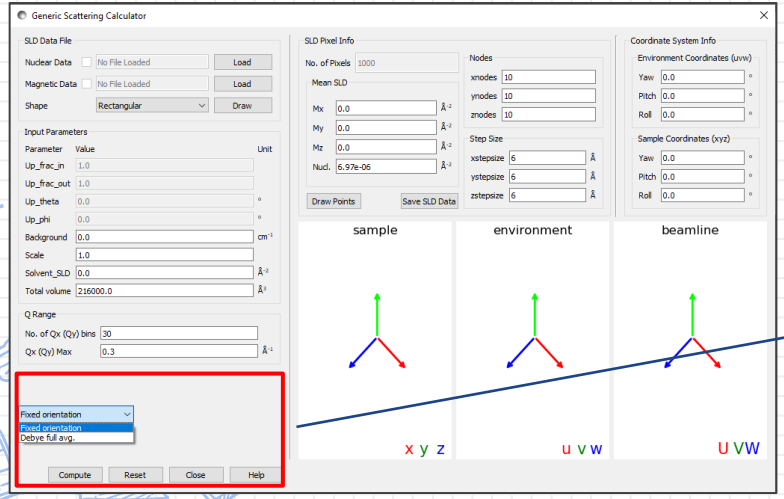
Project 1: R_G and β(Q)

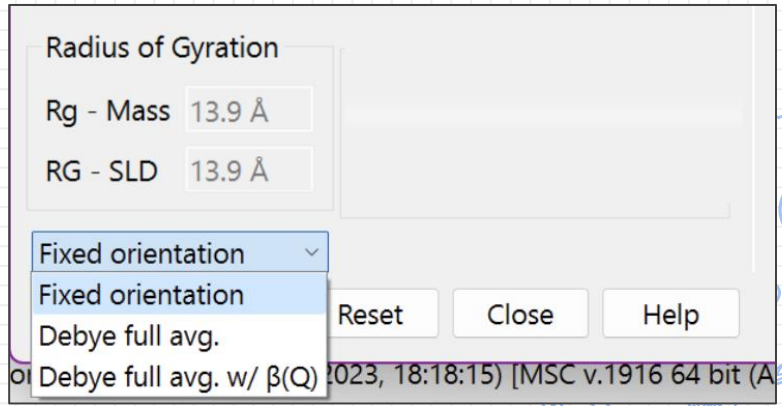
2	ATOM	1	N	ASP	X	1	29.350	18.970	134.130	0.00	0.00
3	ATOM	2	H1	ASP	X	1	29.580	19.450	134.990	0.00	0.00
4	ATOM	3	H2	ASP	X	1	30.210	18.550	133.810	0.00	0.00
5	ATOM	4	H3	ASP	X	1	28.670	18.240	134.290	0.00	0.00
6	ATOM	5	CA	ASP	X	1	28.810	19.950	133.150	0.00	0.00
7	ATOM	6	HA	ASP	X	1	27.860	20.210	133.610	0.00	0.00
8	ATOM	7	CB	ASP	X	1	29.590	21.270	133.050	0.00	0.00
9	ATOM	8	HB2	ASP	X	1	29.020	22.000	132.480	0.00	0.00

PDB file example

- Calculate R_G and β(Q) from Nuclear data (PDB Files)
- Integration into the Generic Scattering Calculator of Sasview to make it more accessible
- Involves revamping the GUI as well as working in the backend to properly integrate features.



Before



After

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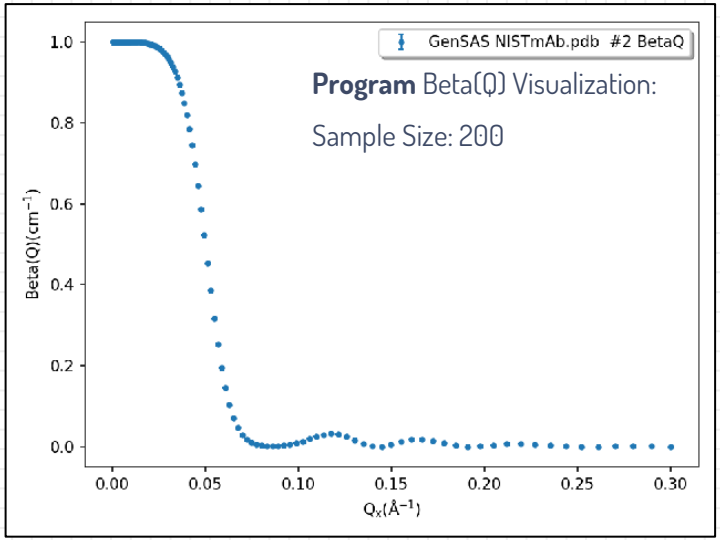
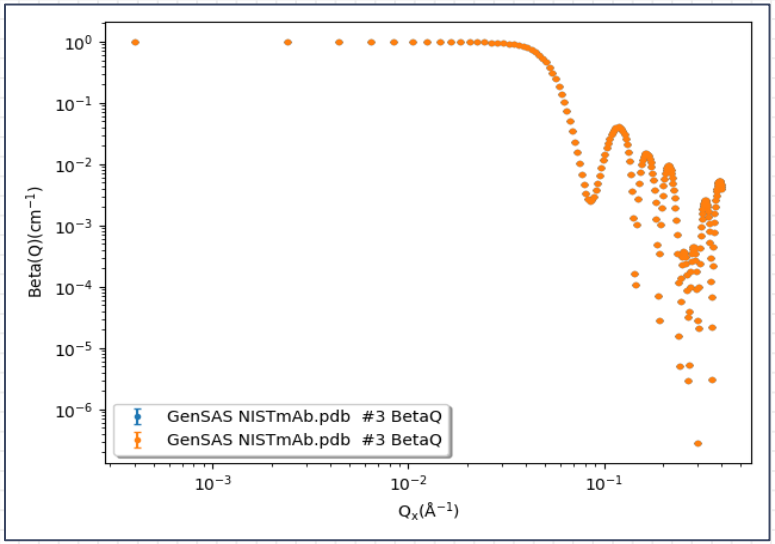
Generated β(Q)

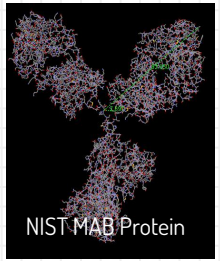


Separate Program Visualization



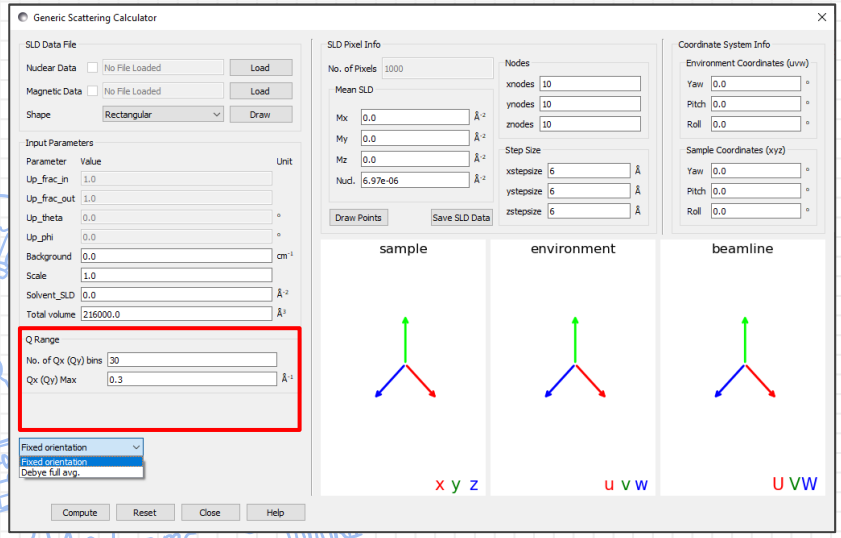
Post-Sasview Integration

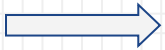
Notice how the separate program visualization has a linear spacing between the points and is plotted on a linear scale. In contrast, the Sasview program has linear spacing, but is plotted on a log scale.

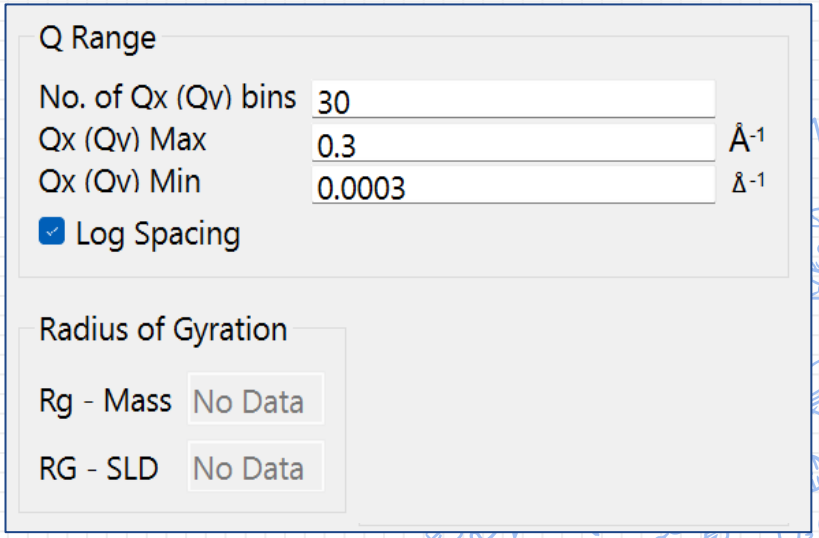


Project 2: Adjusting Q Spacing

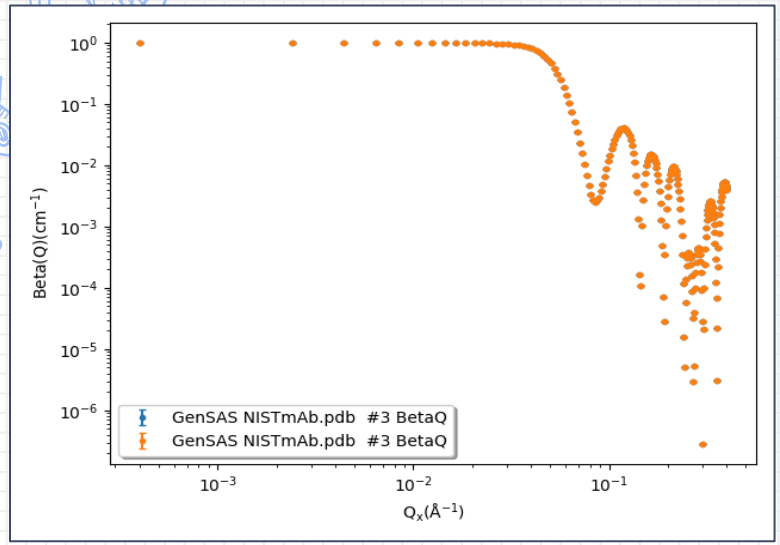
- Sasview utilizes linear spacing between points, but is plotted on a log scale.
- At times, log spacing is more useful than linear spacing
- Adjust the program to allow the user to choose between linear and log spacing.
- Allow User to set a QMinimum as well
  - Default set to .001 * QMax in the past



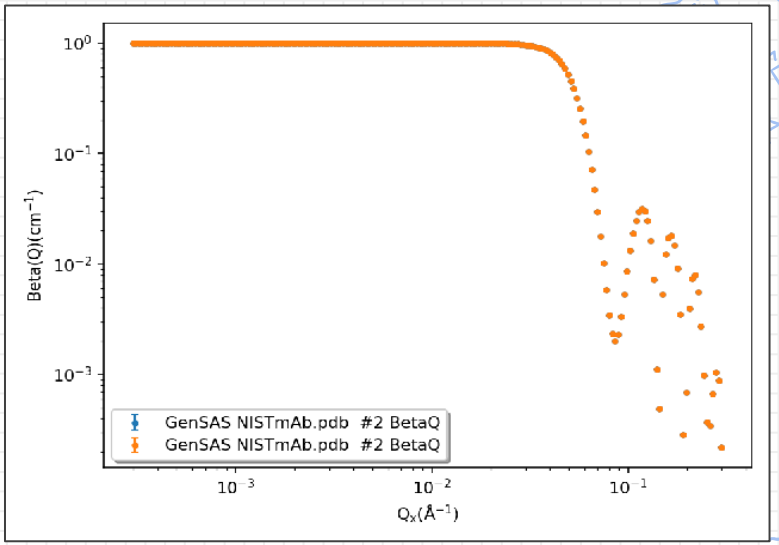




Linear vs Log Spacing



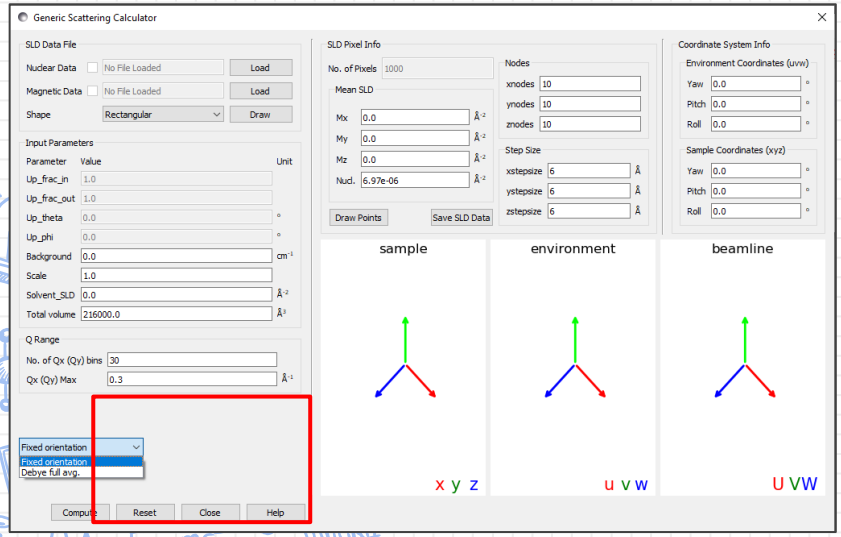
Linear Spacing, Log Scale

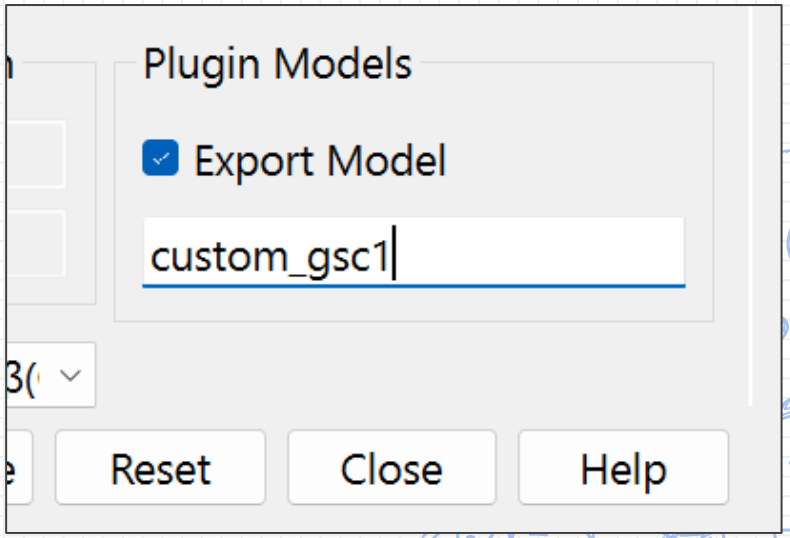


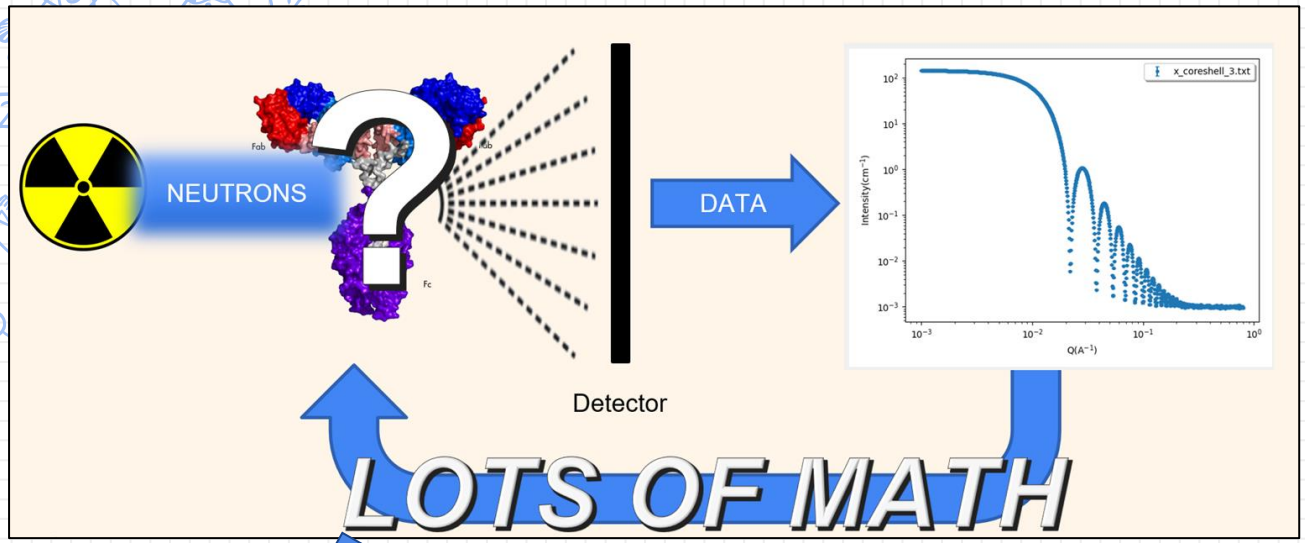
Log Spacing, Log Scale

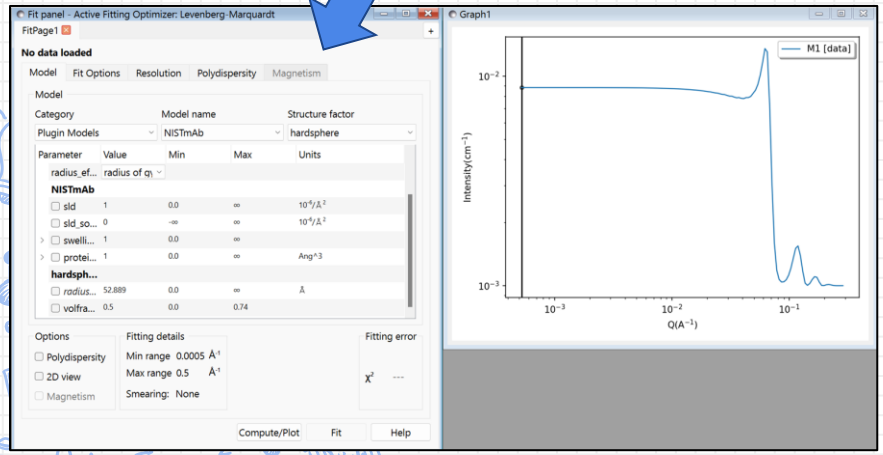
Project 3: Adding Custom Fit Models in the GSC

- Adding Custom Fit Models into the Generic Scattering Calculator of Sasview
- Takes the protein that has been imported and builds a custom plugin model to calculate and interpolate I(Q).
- Simulates the scattering pattern the protein would produce.
- Now able to fit data to **obtain interaction information** from PDB files in Sasview

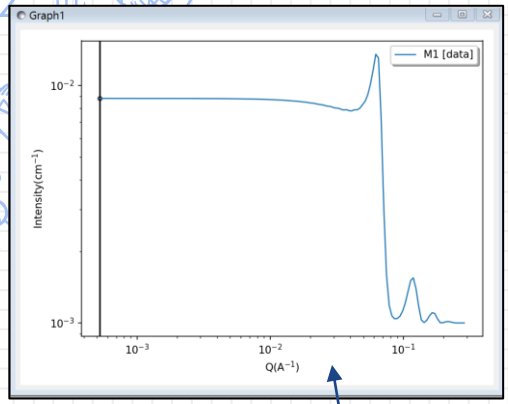


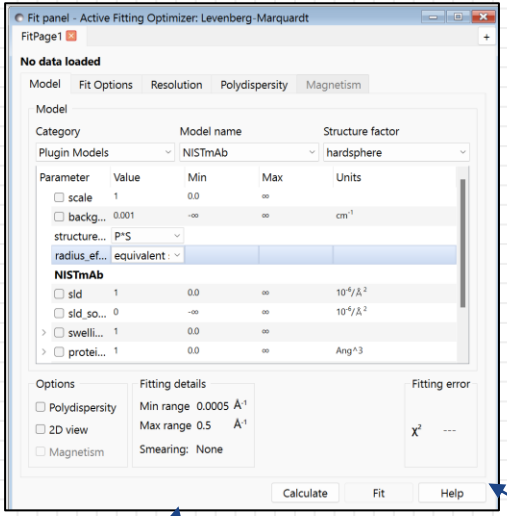


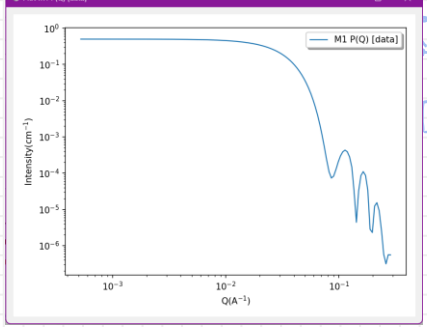


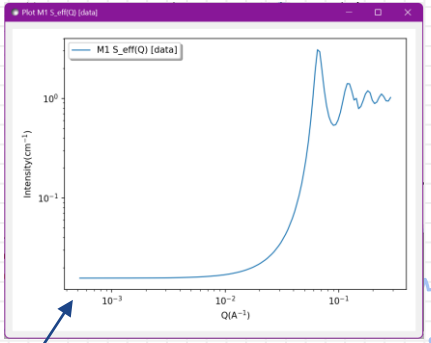


- Simulate the scattering pattern of the protein with our calculated plugin model
- Work backwards by adjusting parameters of the protein minimize the differences (residuals) between the experimental and simulated data.
- Derive meaningful structural information and gain insights into the properties



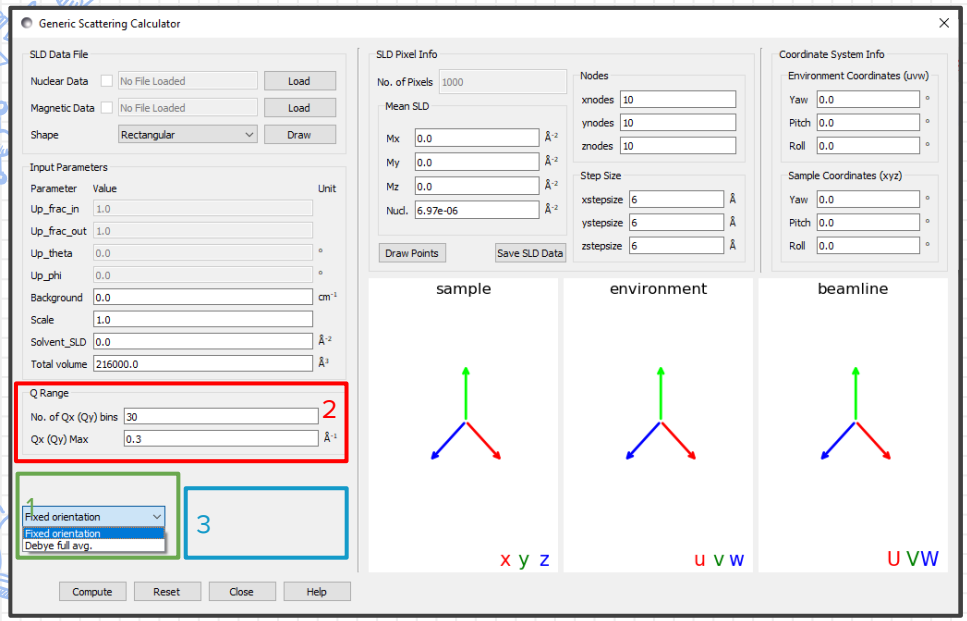






$$I(Q) = \phi\left(\rho_{proteinSLD} - \rho_{solventSLD}\right)^2 v_{protein} \tilde{P}(Q) S_{eff}(Q) + B$$

All Changes: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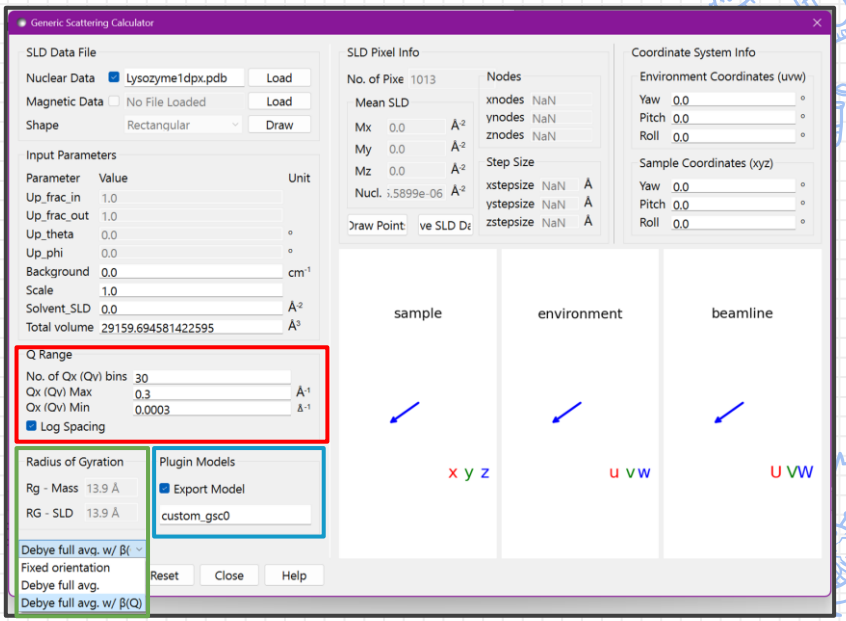
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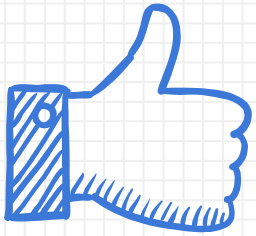

THANKS!

Any questions?