Why are concentrated proteins so viscous?
Small-Angle Scattering (SAS) Measures
Form factor

\[ I(Q) = P(Q)S(Q) \]

Structure factor
SAS measures protein interactions
SAS measures protein interactions
Co-solutes modulate protein interactions

Change in scattering is not dominated by $P(q)$ or $S(q)$ alone.
Molecular Simulation

Fourier Transform: \( g(r) \rightarrow S(Q) \)

\[
S(Q) = 1 + 4\pi \rho \frac{1}{q} \int (g(r) - 1) \cdot r \sin(qr) \, dr
\]

- Limited to spherical systems
Finite size effects

\[ S(Q) = 1 + 4\pi \rho \frac{1}{q} \int (g(r) - 1) \cdot r \sin(qr) dr \]
Finite size effects

\[ S(Q) = 1 + 4\pi \rho \frac{1}{q} \int (g(r) - 1) \cdot r \sin(qr) \, dr \]
Desired Features of Calculator

- Simultaneously calculate both $P(Q)$ and $S(Q)$
- Avoid finite size effects
- Fast
Debye Formula

\[ I(q) = \sum_{j=1}^{N} \sum_{k=1}^{N} f_i(q) f_j(q) \frac{\sin(qr_{ij})}{qr_{ij}} \]

Not universally applicable:

vs
Explicit Fourier Transform

- Most general
  - Contains $P(Q)$ and $S(Q)$

\[
I(q) = I_1(q)\left\langle \sum_{j=1}^{N} \sum_{k=1}^{N} e^{-iqr_{jk}} \right\rangle = I_1(q)\left\langle \sum_{j=1}^{N} \sum_{k=1}^{N} \sin qr_{jk} \right\rangle
\]
Verify Radial Distribution of Simulation

Solution

- Fancy Stat Mech - $g(r)$
  - Limited to spherical systems
- Bigger Box
  - Num Atoms $\sim (\text{Box Length})^3$
- Calculate Box scattering and remove
Removing Box Effects
Removing Box Effects

![Graph showing intensity vs. Q for Cube Scattering, S(Q), and S(Q) - Cube.](image-url)
Next Steps

- Apply this to a periodic box of proteins (lysozyme, mAb)
- Automate algorithm to subtract box effects
- Parallelize using GPUs
Thank you!
Backup Slides
Existing Calculators

Watch out $S(Q) \neq I(Q)$.
S(Q) via Fourier Transform

- g(r) simple to calculate
- Can extend g(r) to large r

\[ h(r) = g(r) - 1 \]

\[ S(Q) = \frac{1}{1 - \tilde{h}(q)} \]
Sascalc - Golden Vector

\[ I(q) = \left[ \sum_{j}^{N} b_j \cos(q \cdot r_j) \right]^2 + \left[ \sum_{j}^{N} b_j \sin(q \cdot r_j) \right]^2 \]

- Multiple Molecules?
- Separation of S and P?

Two questions:

- Can Extract S?
- Periodic Boundary Conditions effects?
\[ \int_0^\infty (g(r) - 1) \cdot r \sin(qr) \, dr \]
How do we study?

Experiment

Simulation

# Current Limitations

<table>
<thead>
<tr>
<th></th>
<th>10 mg/ml</th>
<th>100 mg/ml</th>
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</thead>
<tbody>
<tr>
<td>Of Medical interest?</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Can we calculate Scattering?</td>
<td>YES</td>
<td>NO (somewhat)</td>
</tr>
</tbody>
</table>

Simulation Boxes:
Methods to Calculate $S(Q)$

- Pair Distance Distribution
- Debye Formula
- Explicit Fourier Transform
First Test System - Lennard Jones Particles

Verify Pair Distance Distribution of Simulation

Taken from Structure Factor and radial Distribution Function for Liquid Argon at 85 K - Yarnell, Et. al.