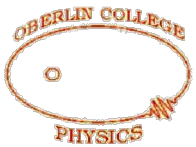
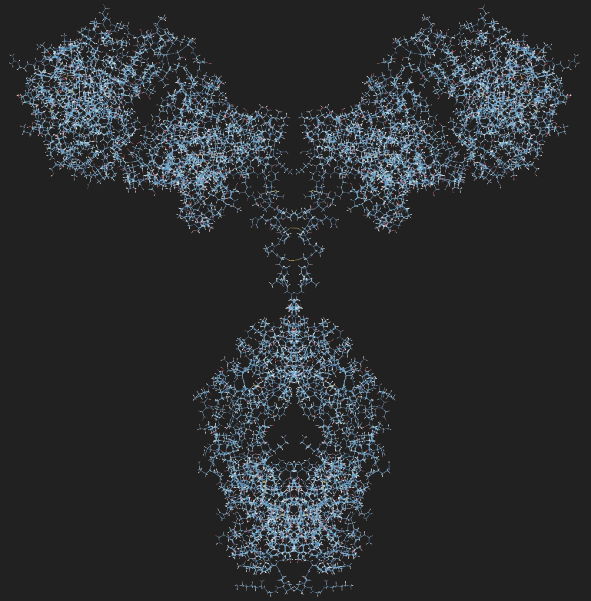
SASCalc Periodic Boundary Conditions

Ian Hunt-Isaak, Joseph E. Curtis, Steven C. Howell



Why are concentrated proteins so viscous?

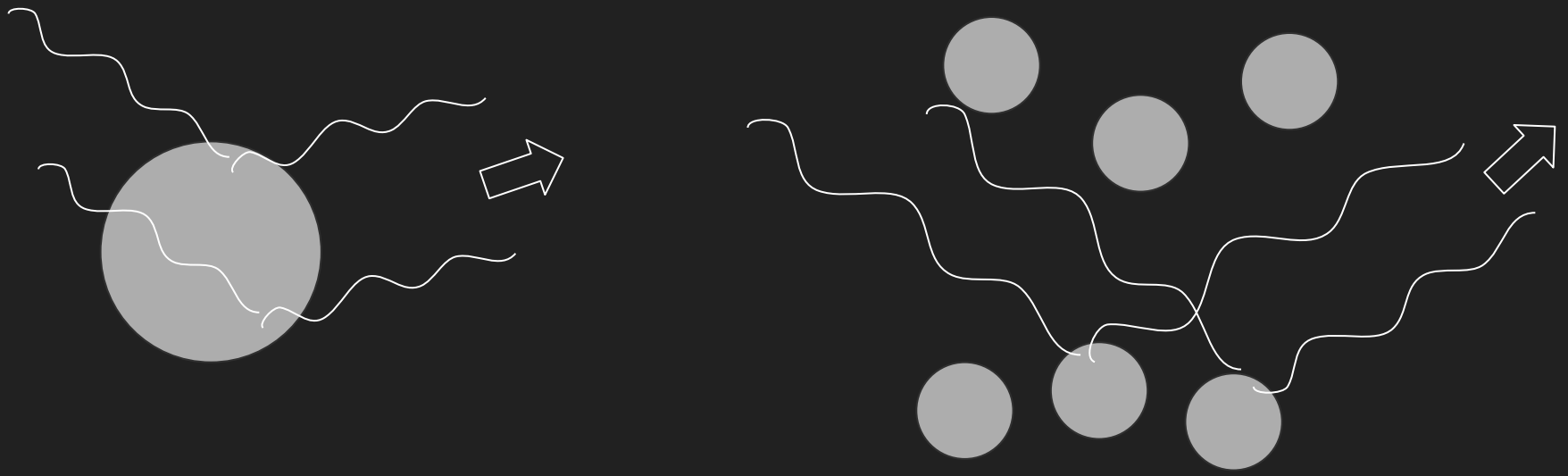


https://openclipart.org/image/2400px/svg_to_png/205886/remigho-syringe.png

Small-Angle Scattering (SAS) Measures

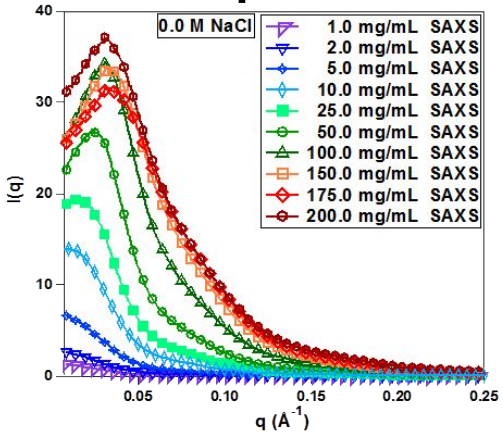
Form factor

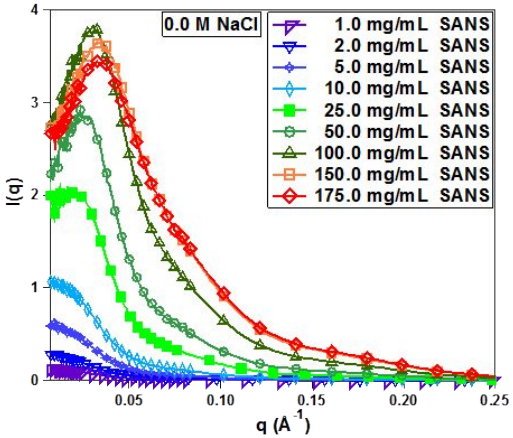
Structure factor



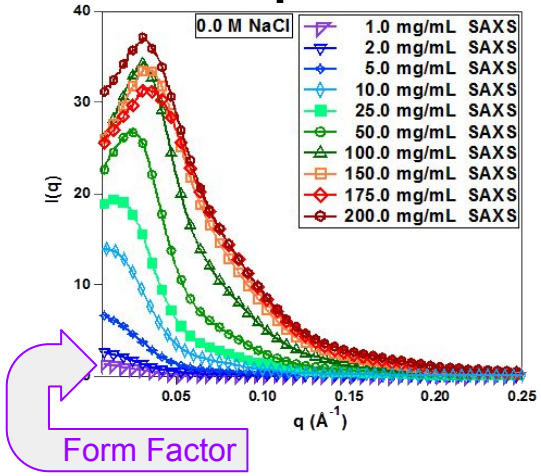
$$I(Q) = P(Q)S(Q)$$

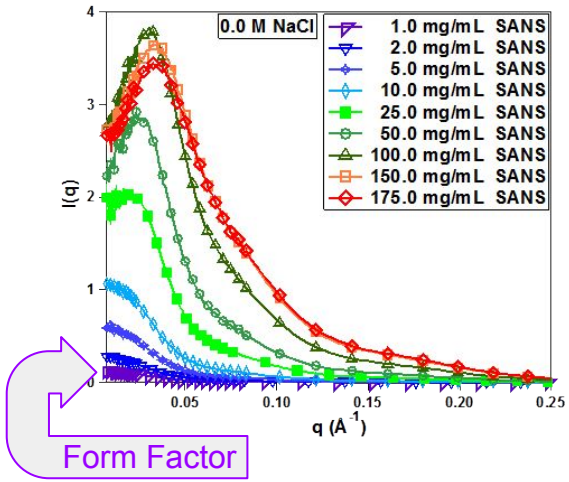
SAS measures protein interactions



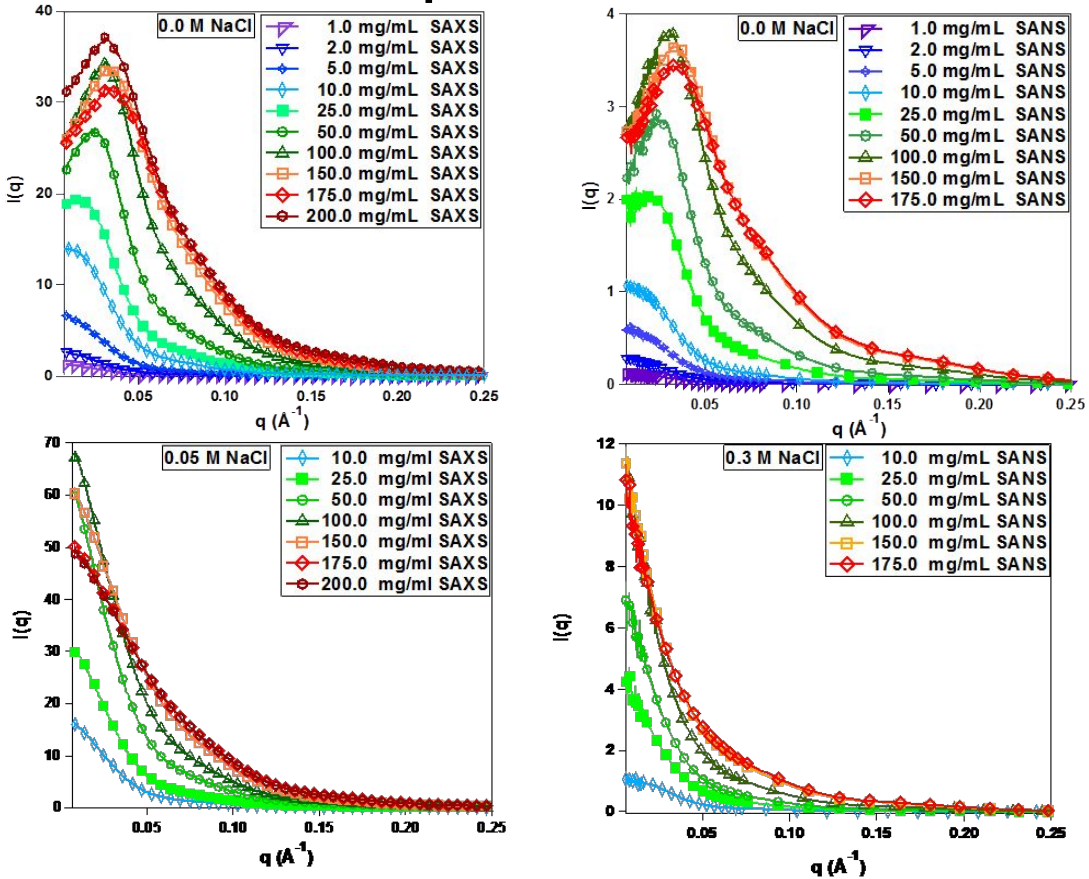


SAS measures protein interactions



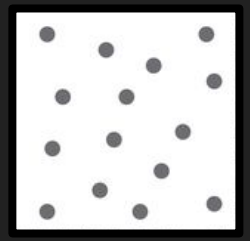


Co-solutes modulate protein interactions



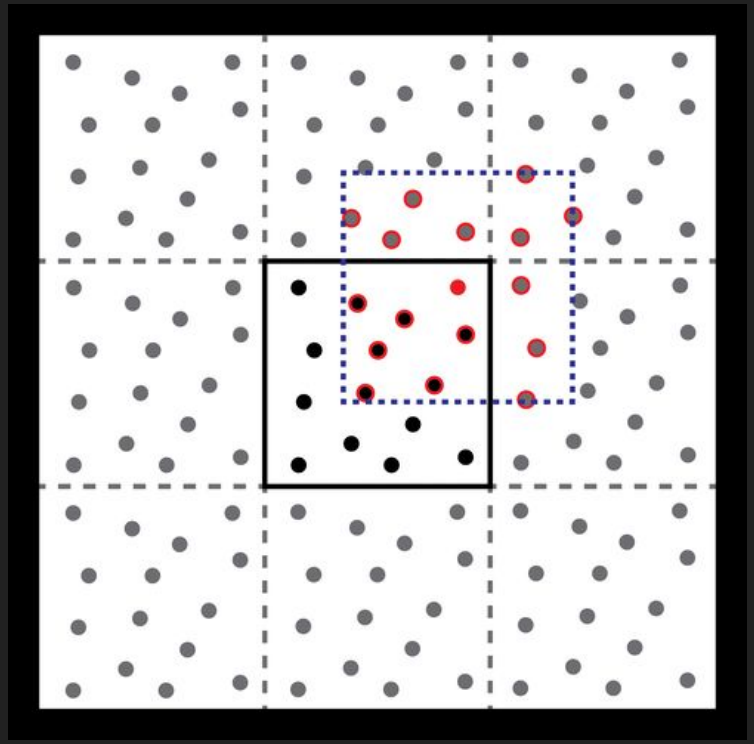
Change in scattering is not dominated by P (q) or S(q) alone.

Molecular Simulation



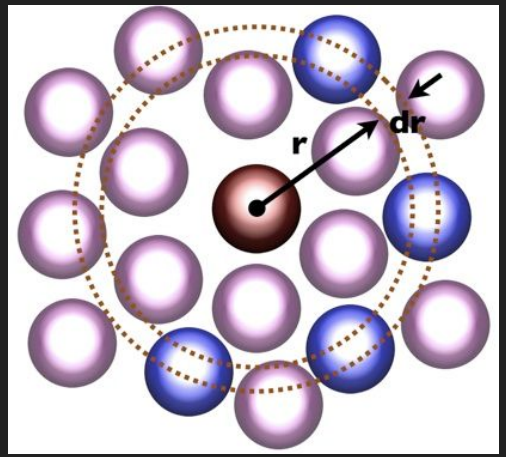
http://nmschneider.com/blog/2014/5/9/nearest-image-for-particle-simulations-in-matlab

Molecular Simulation



http://nmschneider.com/blog/2014/5/9/nearest-image-for-particle-simulations-in-matlab

Fourier Transform: g(r) → S(Q)

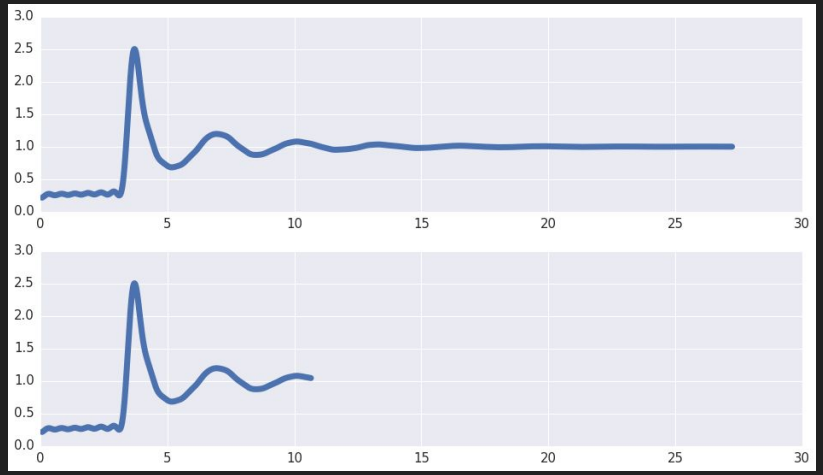


$$S(Q) = 1 + 4\pi\rho\frac{1}{q}\int (g(r) - 1) \cdot r \sin(qr) dr$$

- Limited to spherical systems

Finite size effects

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

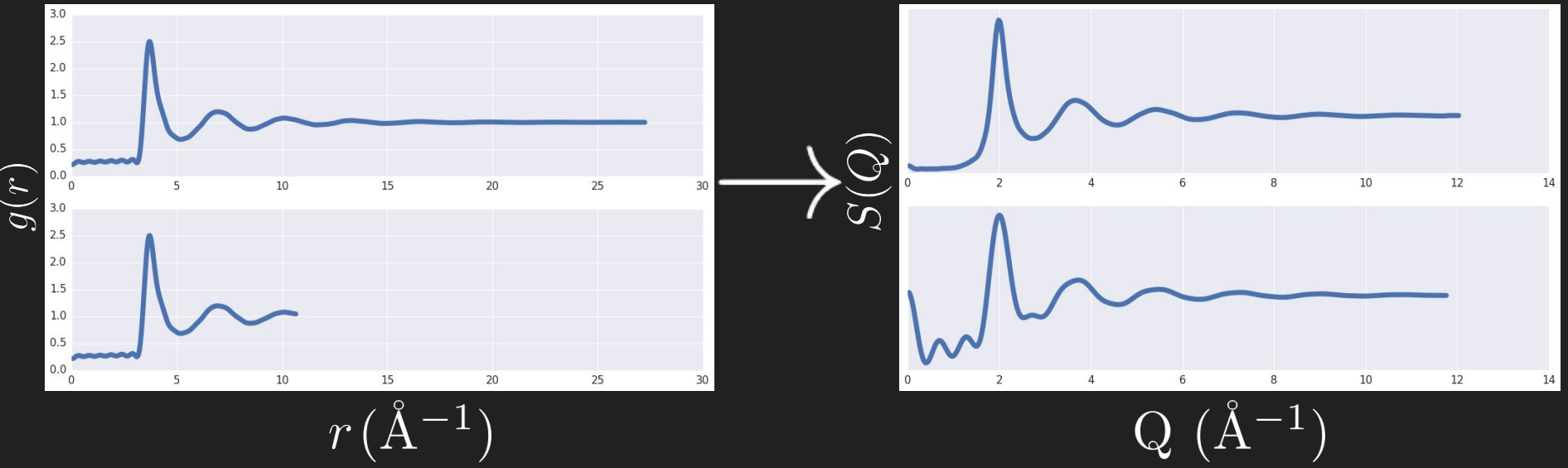


$g(r)$

$r\,(\mathrm{\AA}^{-1})$

Finite size effects

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



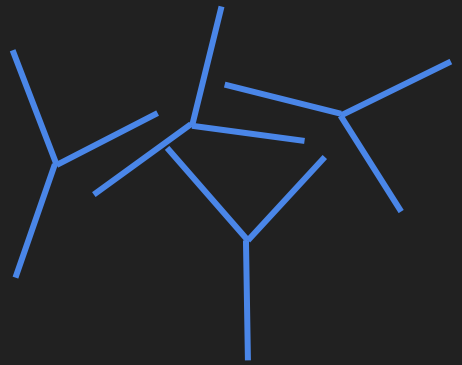
Desired Features of Calculator

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

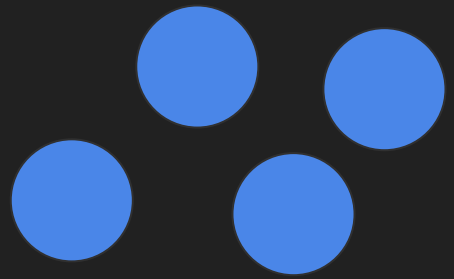
Debye Formula

$$I(q) = \sum_{j=1}^{N} \sum_{k=1}^{N} f_i(q) f_j(q) \frac{\sin(q r_{ij})}{q r_{ij}}$$

Not universally applicable:



vs

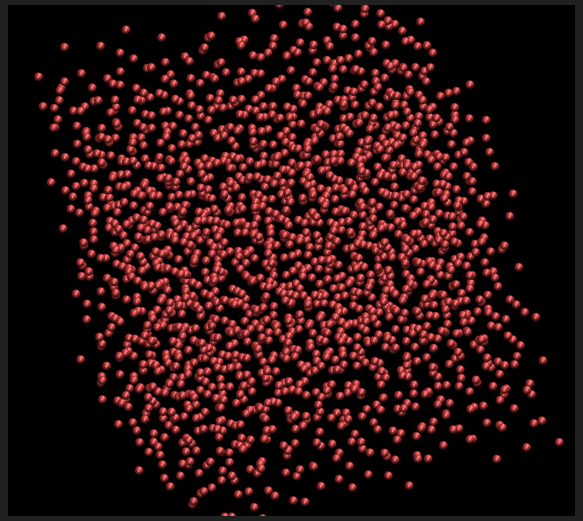


Explicit Fourier Transform

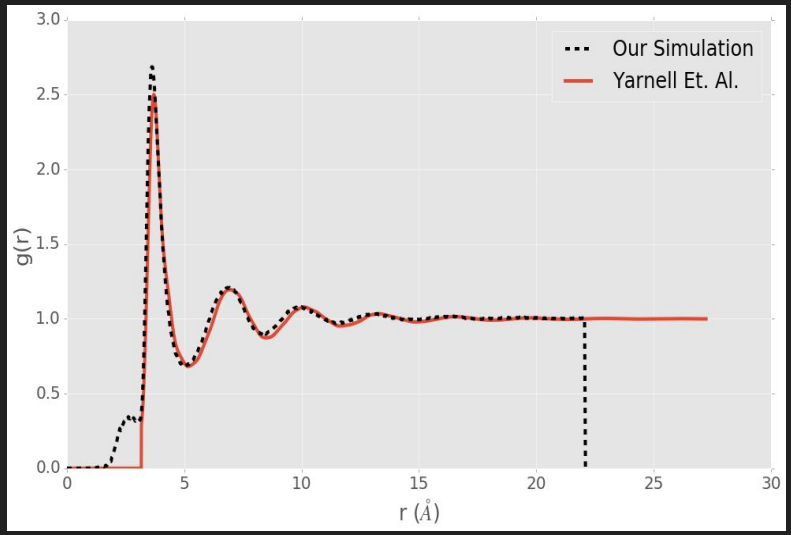
- Most general
  - Contains P(Q) and S(Q)

$$I(q) = I_1(q)\langle \sum_{j=1}^{N}\sum_{k=1}^{N} e^{-i\boldsymbol{qr}_{jk}} \rangle = I_1(q)\langle \sum_{j=1}^{N}\sum_{k=1}^{N} \sin \boldsymbol{qr}_{jk} \rangle$$

First Test System - Lennard Jones Particles



Verify Radial Distribution of Simulation

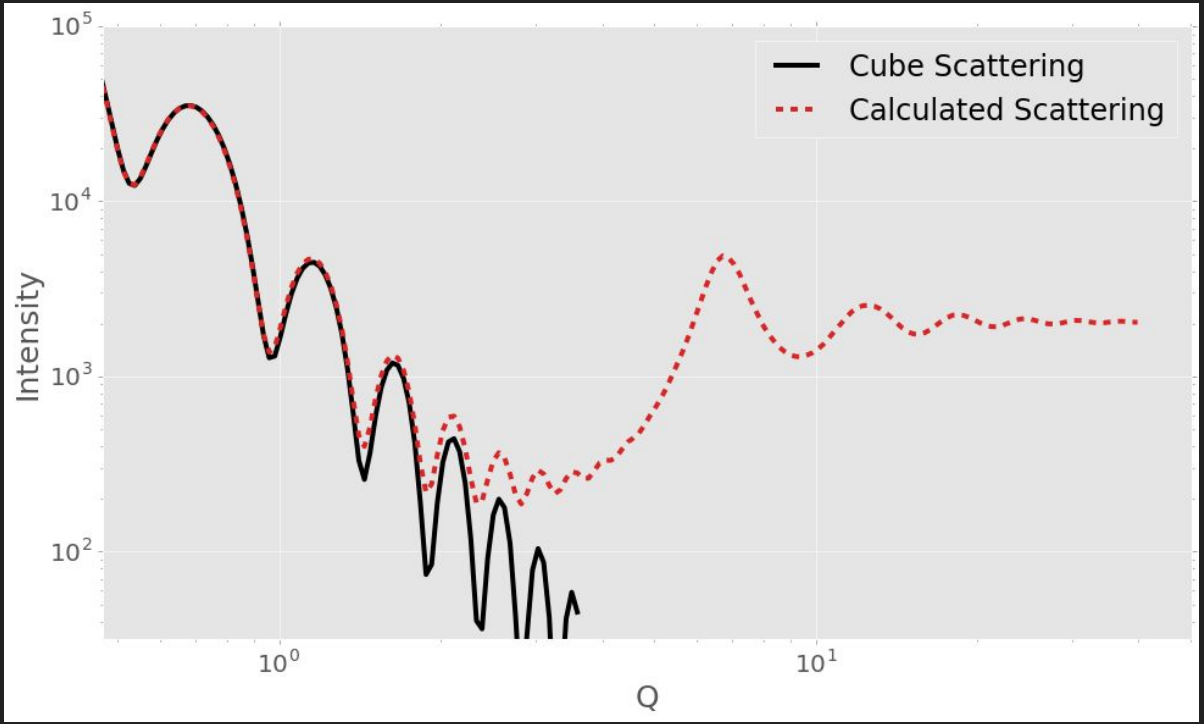


Radial Distribution Function for Liquid Argon at 85 K - Yarnell, et al.

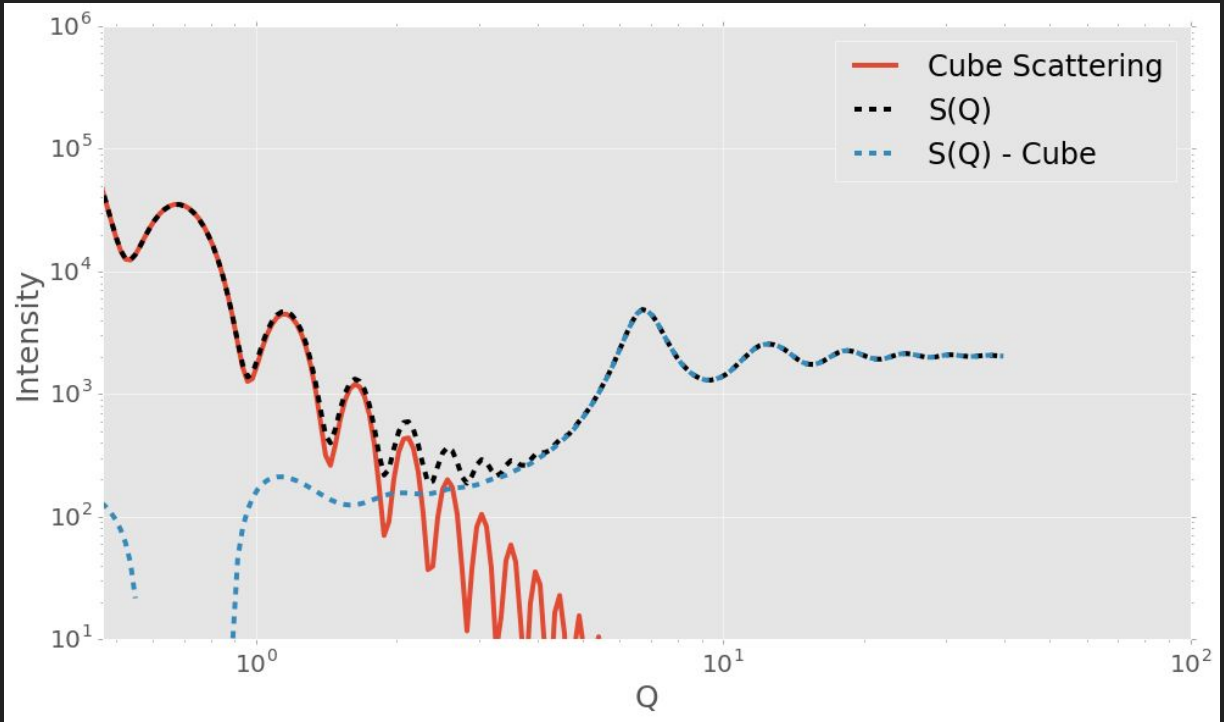
Solution

- Fancy Stat Mech - g(r)
  - Limited to spherical systems
- Bigger Box
  - Num Atoms ~ (Box Length)^3
- Calculate Box scattering and remove

Removing Box Effects

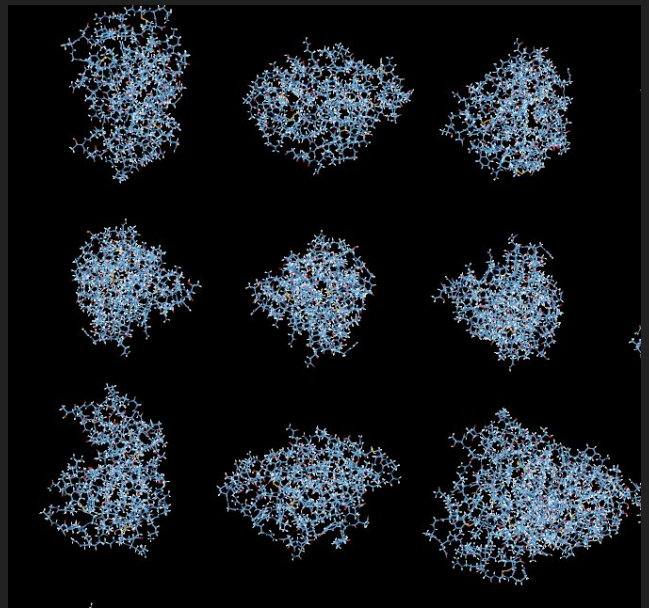


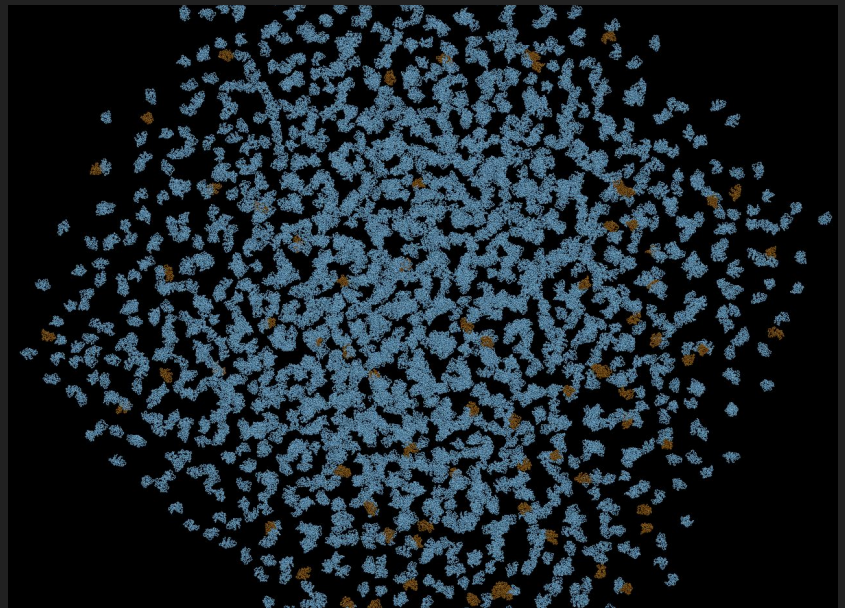
Removing Box Effects



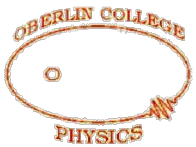
Next Steps

- Apply this to a periodic box of proteins (lysozyme, mAb)
- Automate algorithm to subtract box effects
- Parallelize using GPUs





Thank you!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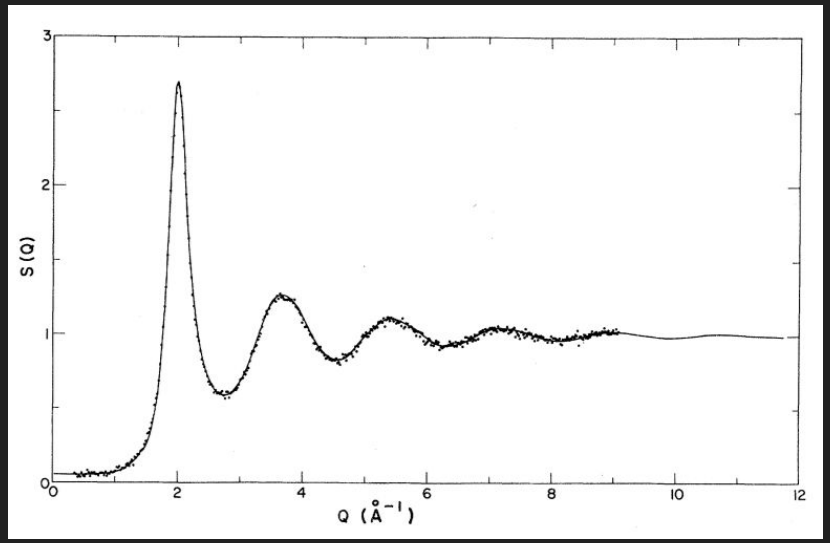
Neutron Research

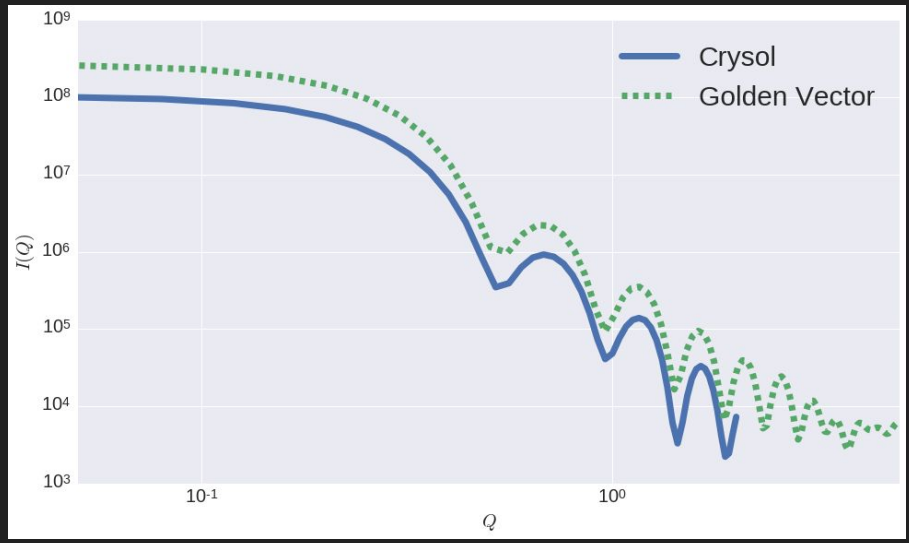
Backup Slides

Existing Calculators

Experiment



Simulation



Watch out S(Q) ≠ I(Q).

S(Q) via Fourier Transform

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

$$h(r) = g(r) - 1$$

$$S(Q) = \frac{1}{1 - \widetilde{h}(q)}$$

Sascalc - Golden Vector

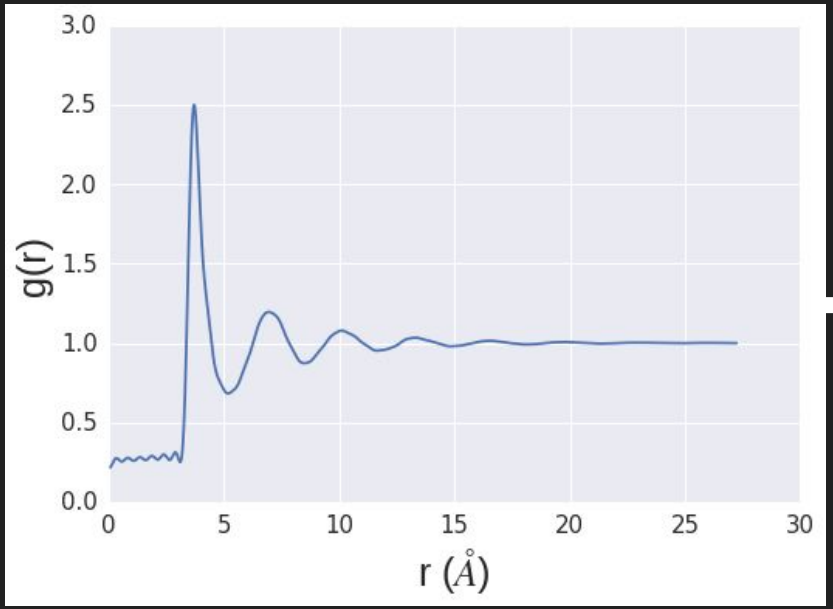
$$I(\mathbf{q}) = \left[\sum_j^N b_j \cos(\mathbf{q}\cdot\mathbf{r}_j)\right]^2 + \left[\sum_j^N b_j \sin(\mathbf{q}\cdot\mathbf{r}_j)\right]^2$$

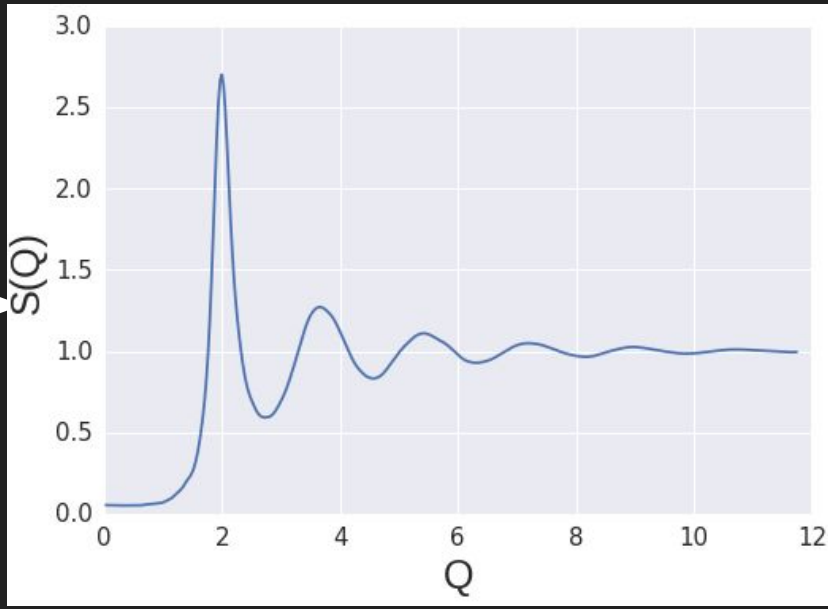
- Multiple Molecules?
- Separation of S and P?

Two questions:

- Can Extract S?
- Periodic Boundary Conditions effects?

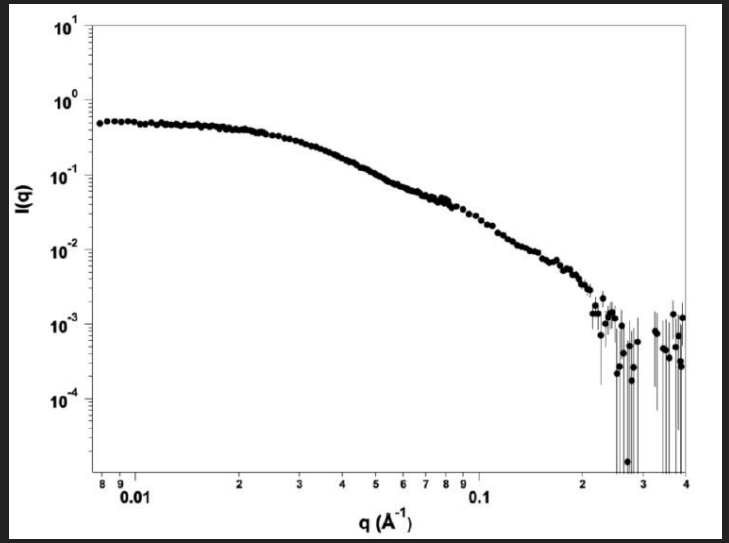
$$\int_0^\infty (g(r) - 1) \cdot r \sin(qr) dr$$



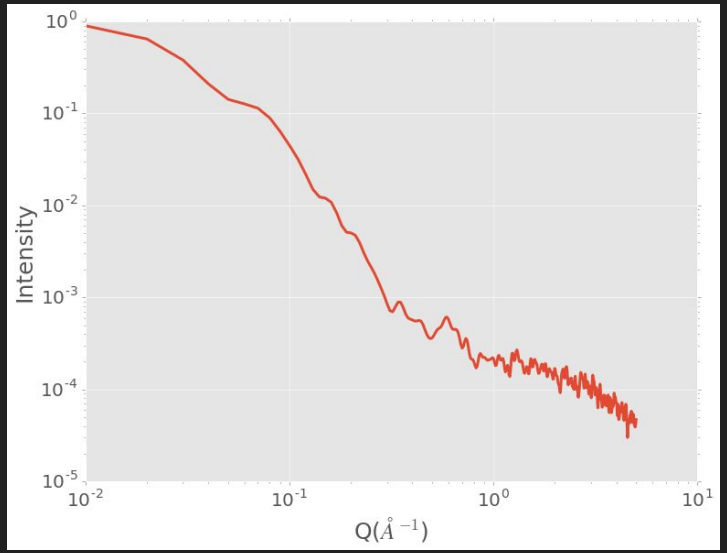


How do we study?

Experiment



Simulation

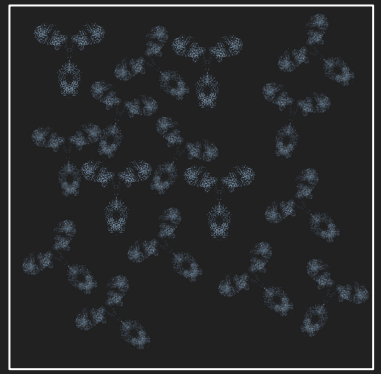


Small-Angle Neutron Scattering Study of a Monoclonal Antibody Using Free-Energy Constraints. Clark Et. Al (2013)

Current Limitations

	10 mg/ml	100 mg/ml
Of Medical interest?	YES	YES
Can we calculate Scattering?	YES	NO (somewhat)

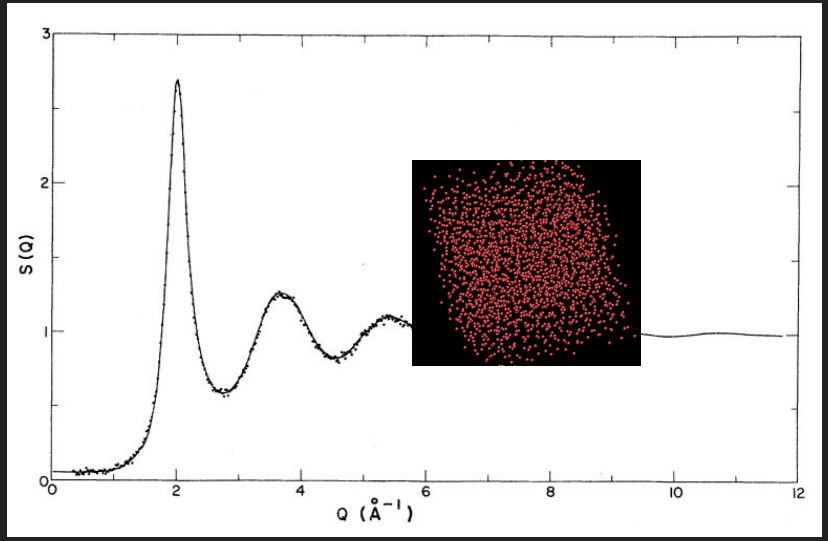
Simulation Boxes:



Methods to Calculate S(Q)

- Pair Distance Distribution
- Debye Formula
- Explicit Fourier Transform

First Test System - Lennard Jones Particles



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

Verify Pair Distance Distribution of Simulation