

opportunity

Neutron scattering and simulations reveal the dynamics of protein complexes
- but this method is practically inaccessible to most bio scientists

challenge

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ESS DMSC meets DTU and UCPH

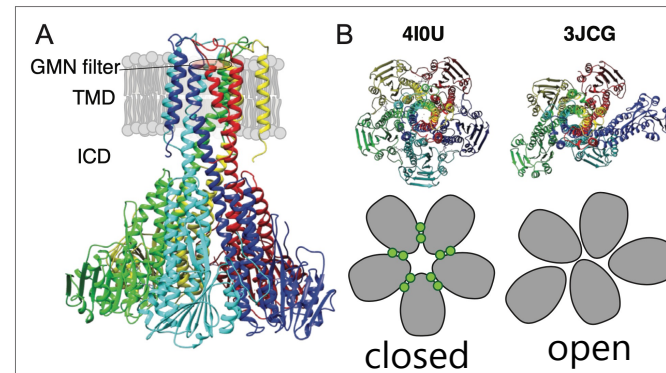
UNIVERSITY OF COPENHAGEN



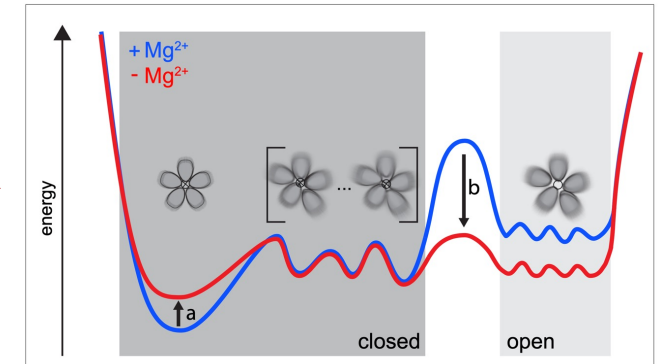
opportunity

- X-ray crystallography
- Electron microscopy
- Small-angle X-ray scattering (SAXS)
- Small-angle neutron scattering (SANS)

Membrane protein structural complexity:

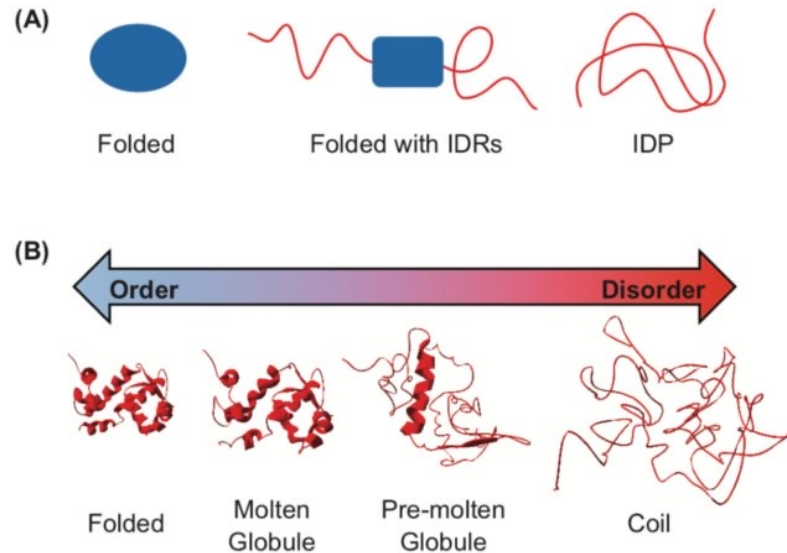


CorA magnesium transporter

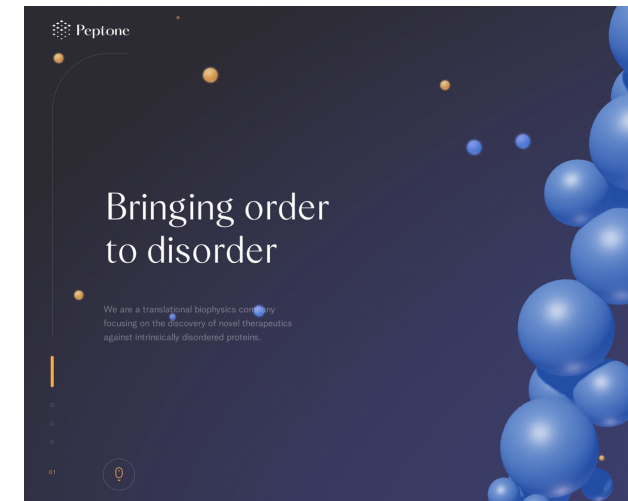


Johansen et al 2020, eLife 11:e71887

Intrinsically disordered proteins or regions (IDPs or IDRs)



Watson and Stott 2019, Essays in Biochem 63:EBC20180068

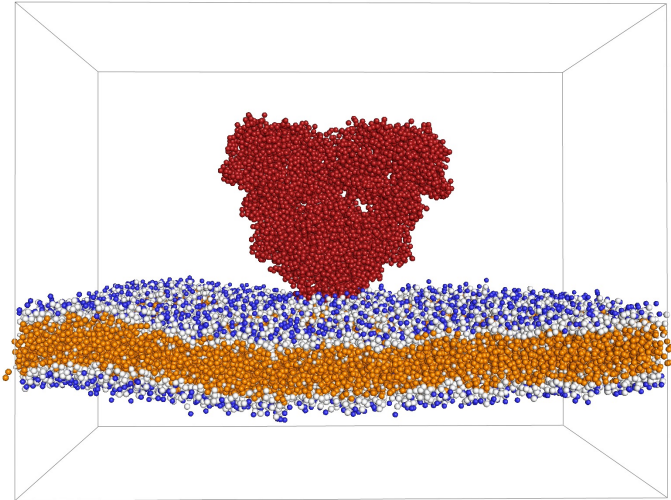


<https://peptone.io> (5.10.2023)

New type of drug target?

opportunity

Molecular Dynamics Simulation of GluA2 receptor

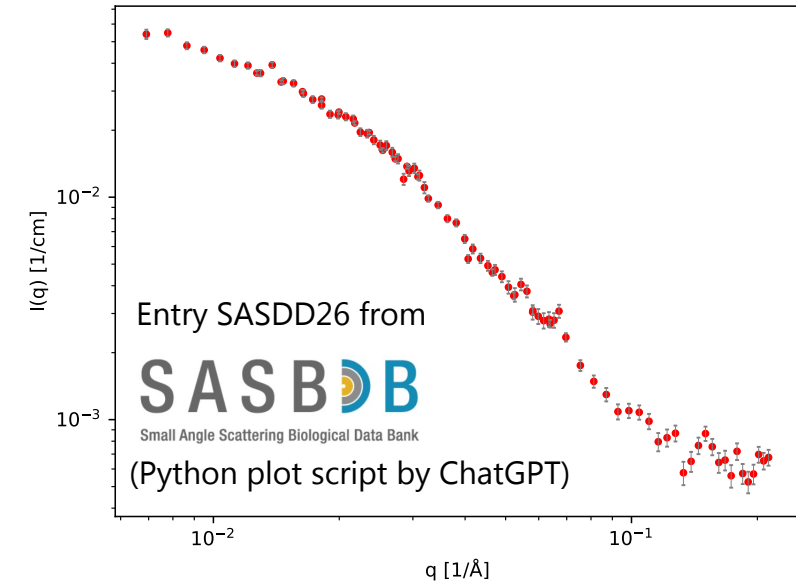


- Atomic details
- Dynamics
- Needs verification

AND
Good models to calculate
SAXS/SANS from MD



SANS measurement of GluA2 receptor



- Low resolution
- Time/ensemble average
- Indirect: needs a model
- Many possible solutions!

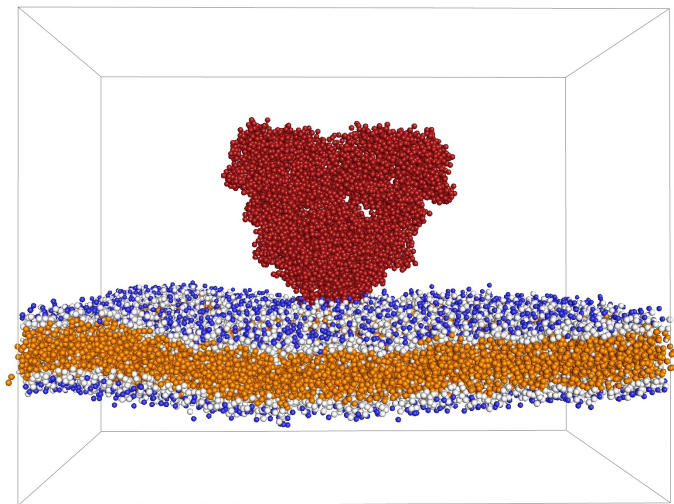
Strategies for obtaining consistency

- 1) SAXS/SANS in MD as energy term
- 2) Unbiased MD -> reweight trajectory

[Change the simulation as little as possible]

opportunity

Molecular Dynamics Simulation of GluA2 receptor

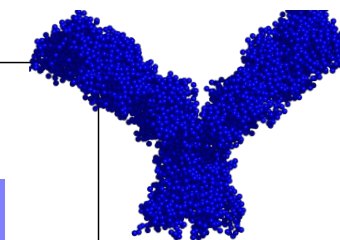
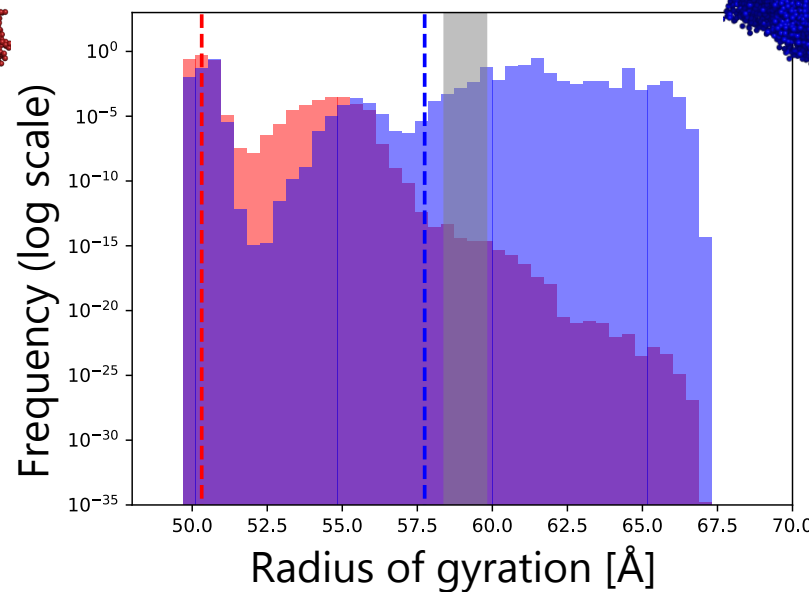
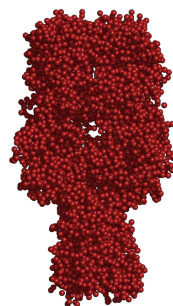
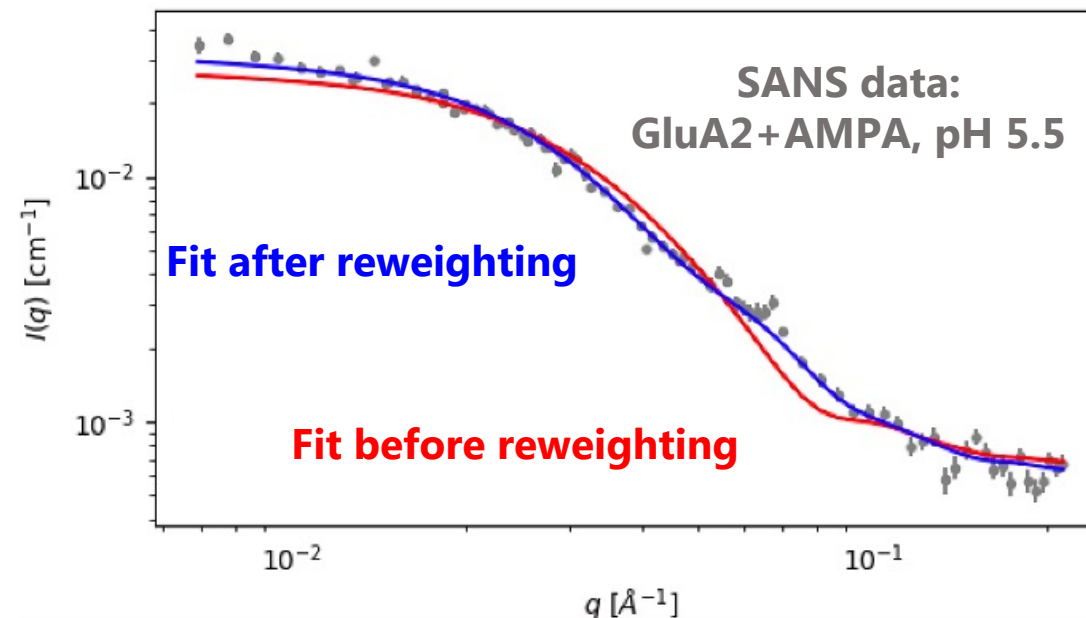


- Atomic details
- Dynamics
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Towards consistency

- 1) SAXS/SANS in MD as energy term
- 2) Unbiased MD -> reweight trajectory

[Change the simulation as little as possible]

Reweighted ensemble
qualitatively consistent
with EM

challenge

complex setup of MD simulations
lack of GUI

```
mark@linux-desktop: /tmp/tutorial
File Edit View Search Terminal Help
Setting up tree (1.7.0-5) ...
Processing triggers for man-db (2.8.3-2) ...
mark@linux-desktop:/tmp/tutorial$ tree
.
├── another
│   └── combined.txt
├── dir1
├── dir2
│   ├── dir3
│   │   ├── test_1.txt
│   │   ├── test_2.txt
│   │   └── test_3.txt
│   ├── dir4
│   │   └── dir5
│   │       └── dir6
├── folder
└── output.txt

8 directories, 5 files
mark@linux-desktop:/tmp/tutorial$
```

- Making MD+SAXS/SANS accessible to more bioscientists
- Ensure validity of results

Example of solution

The screenshot displays the WAXSiS web interface. At the top, the logo 'WAXSiS' is shown, with a small candle icon replacing the 'i'. A text box explains: 'WAXSiS in Solvent (WAXSiS) computes small- and wide-angle X-ray scattering curves based on explicit-solvent all-atom molecular dynamics simulations.' Below this is a 'Learn More' button. The navigation bar includes 'Home', 'Help', 'About', 'Contact', and 'Links'. A status bar indicates 'Jobs in Queue: 0'.

Below the navigation bar, a message states: 'Jobs can be submitted by entering a PDB ID, uploading a PDB file (max 20 MB), or uploading trajectory files. PDB files may have 300 to 40000 heavy atoms.'

The main content area features three green buttons: 'PDB ID', 'PDB File', and 'Trajectory'. Below these, a text prompt says 'Please select one of the above options.' There are input fields for 'Email Address (Optional)' and 'Confirm Email Address'. A message states 'Job will be submitted using default options.' with a 'Review Options' link. A 'Submit Job' button is at the bottom.

To the right, a diagram labeled 'B' illustrates the simulation setup. It shows a 3D box containing a protein (red and yellow) and water (pink dots). An arrow points down to a yellow molecular surface representation, and another arrow points down to a large, detailed molecular model with a yellow surface and a dense packing of atoms (red, blue, green, and grey).