opportunity

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

challenge

Andreas Haahr Larsen
Department of Neuroscience

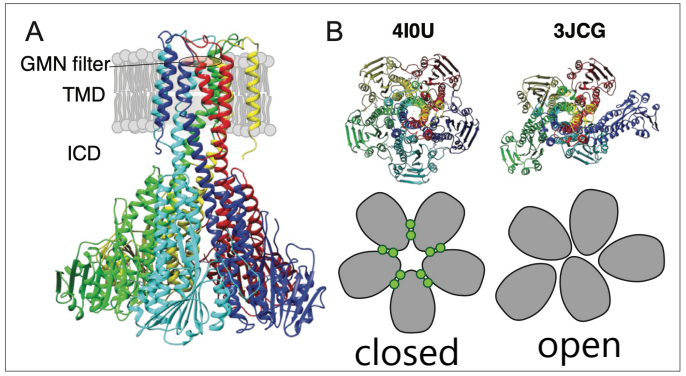
ESS DMSC meets DTU and UCPH

UNIVERSITY OF COPENHAGEN

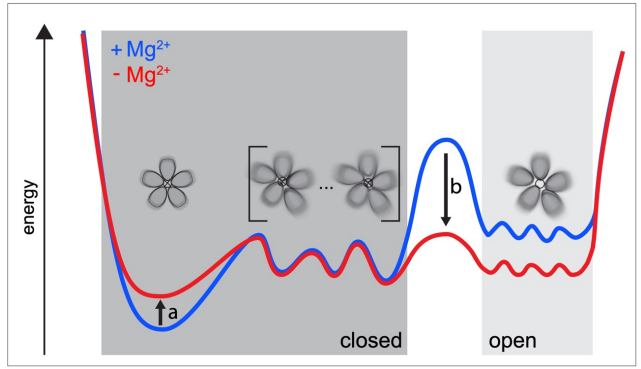
opportunity

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

Membrane protein structural complexity:

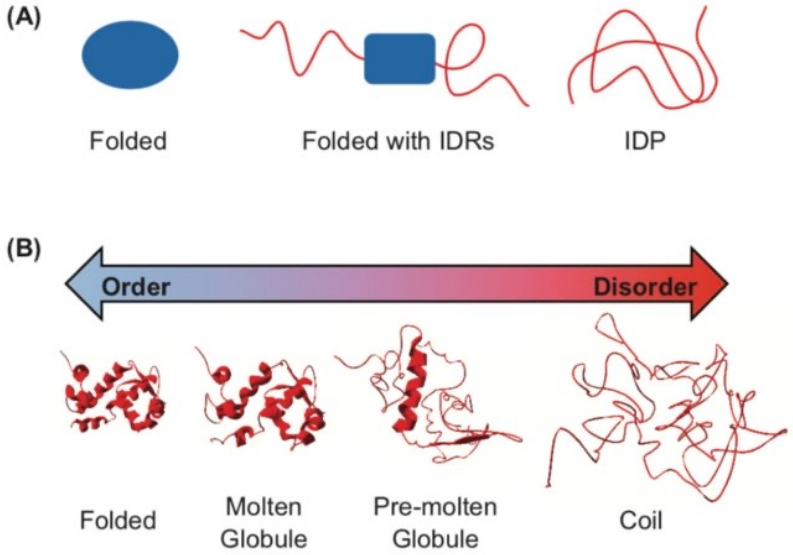


CorA magnesium transporter

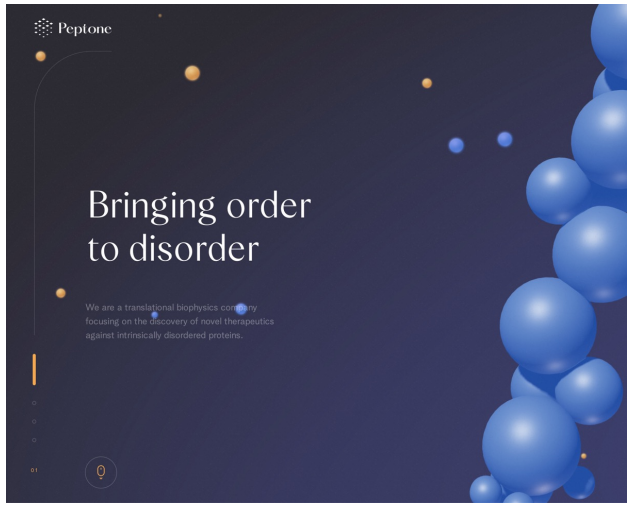


Johansen et al 2020, eLife 11:e71887

Intrinsically disordered proteins or regions (IDPs or IDRs)



Watson and Stott 2019, Essays in Biochem 63:EBC20180068

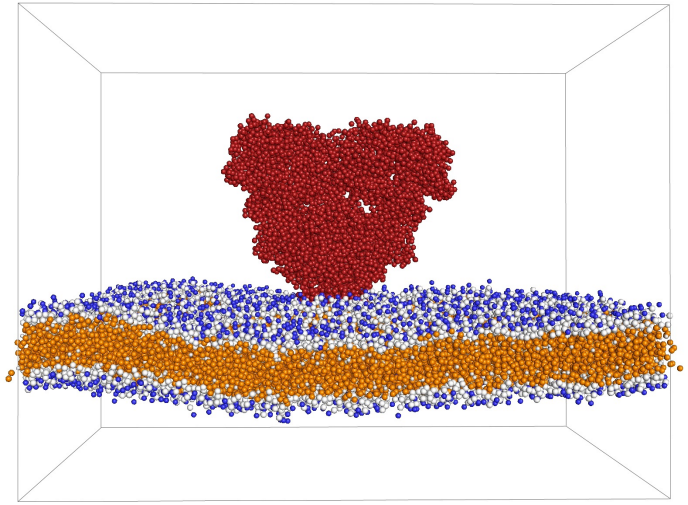


https:/peptone.io (5.10.2023)

New type of drug target?

opportunity

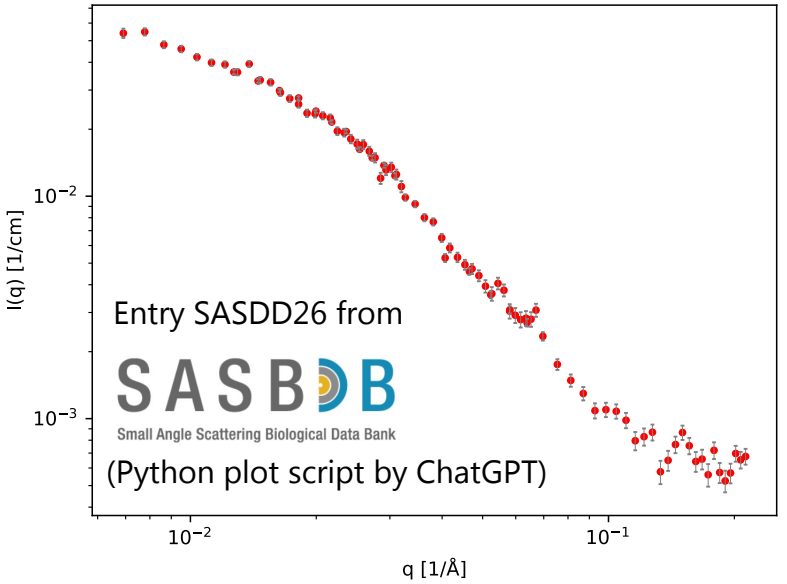
Molecular Dynamics Simulation of GluA2 receptor



- 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

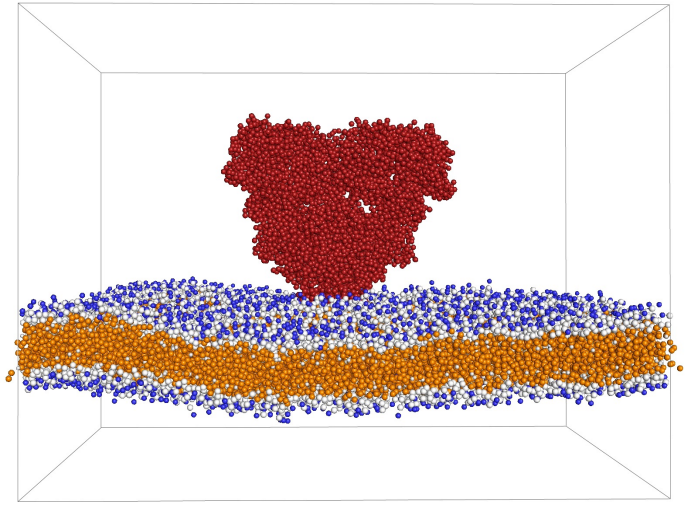
2) Unbiased MD -> reweight trajectory

[Change the simulation as little as possible]

Example: Reweigting MD using SAXS/SANS

opportunity

Molecular Dynamics Simulation of GluA2 receptor



- Atomic details
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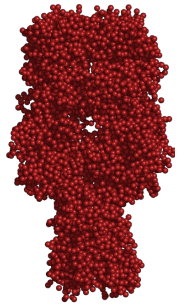
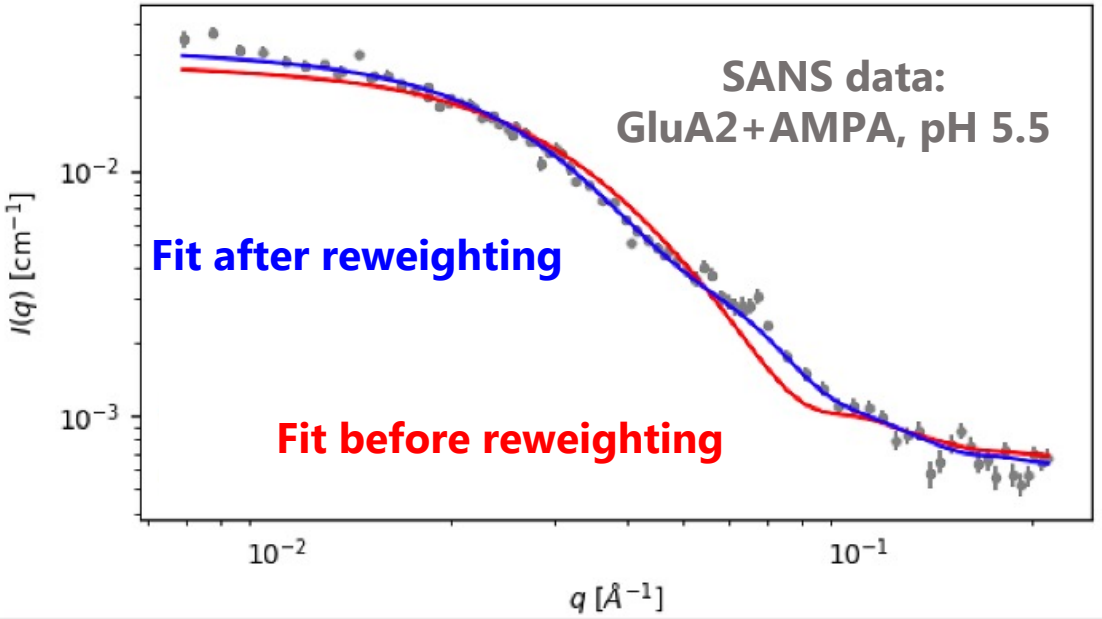
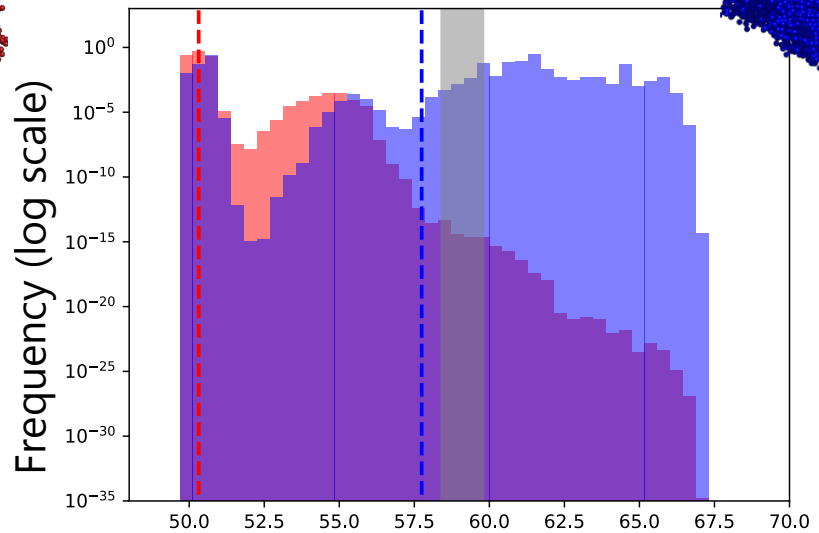
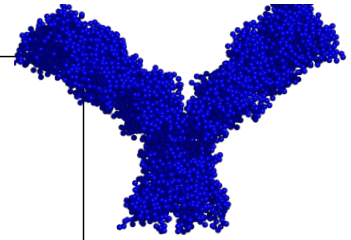








Reweighted ensemble qualitatively consistent with EM

Towards consistency

1) SAXS/SANS in MD as energy term

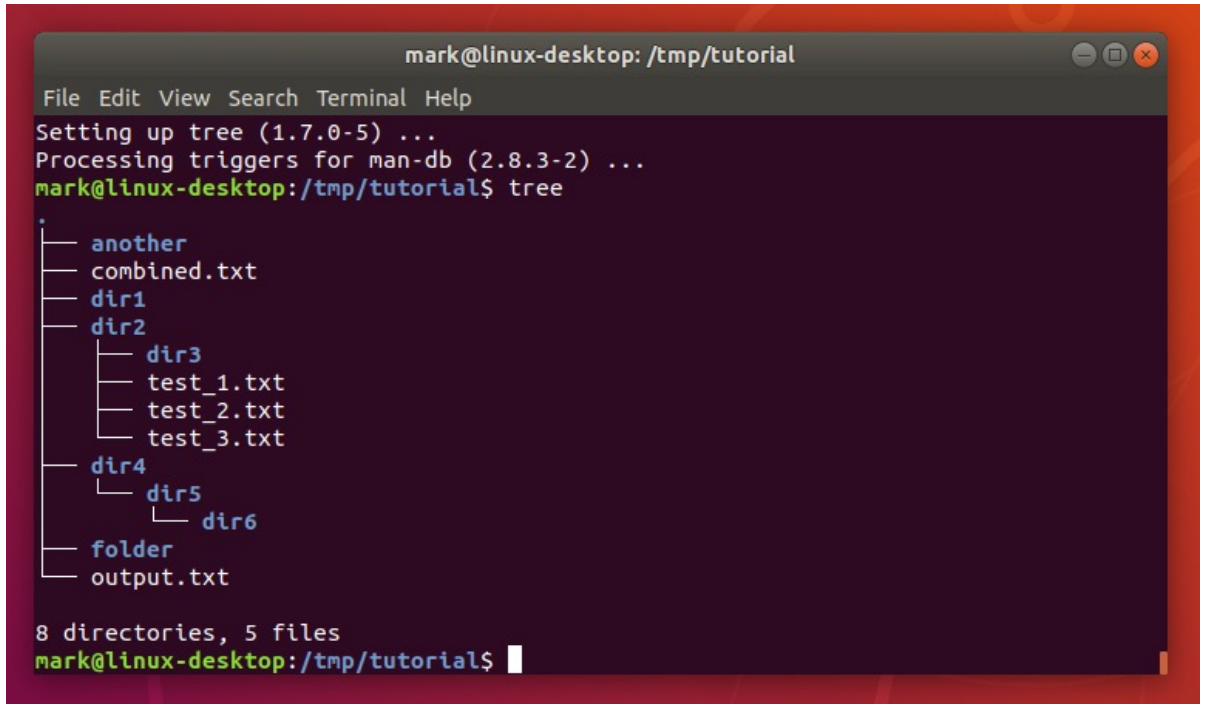
2) Unbiased MD -> reweight trajectory

[Change the simulation as little as possible]

Larsen, Perozzo et al. unpublished

challenge

complex setup of MD simulations
lack of GUI



Example of solution

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

Knight and Hub, 2015, Nucl Acid Res 43: 225