





Tutorial on DeerAnalysis & MMM

epr.ethz.ch/software.html





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DeerAnalysis 2019

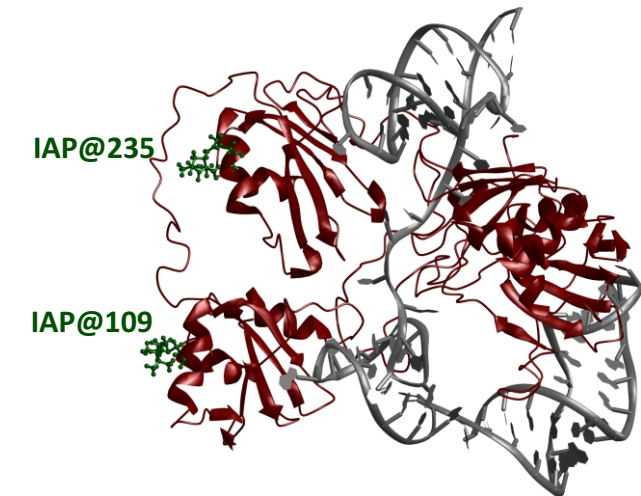
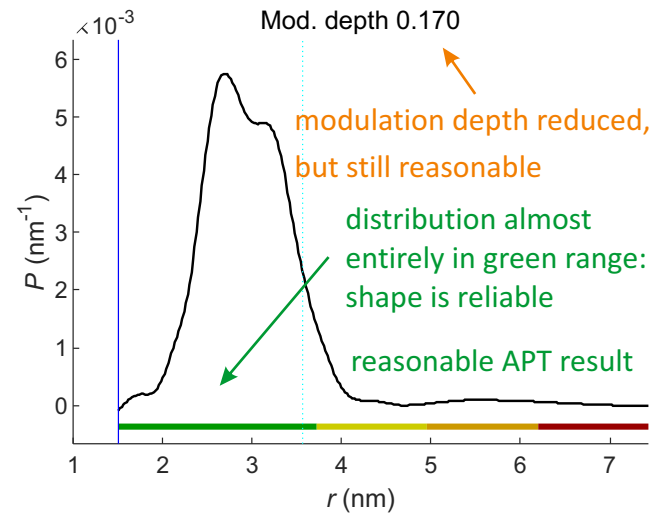
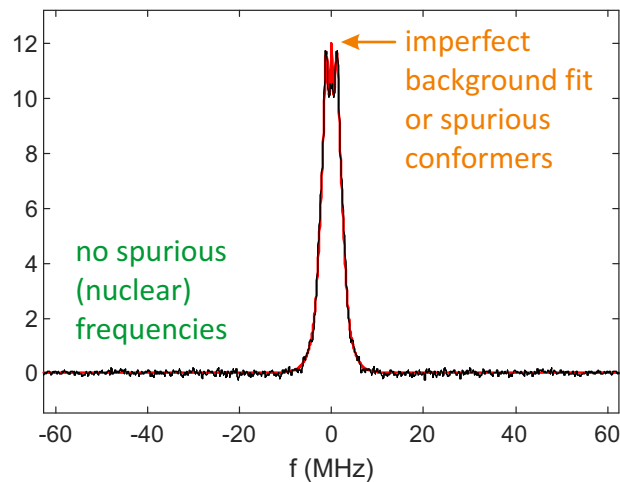
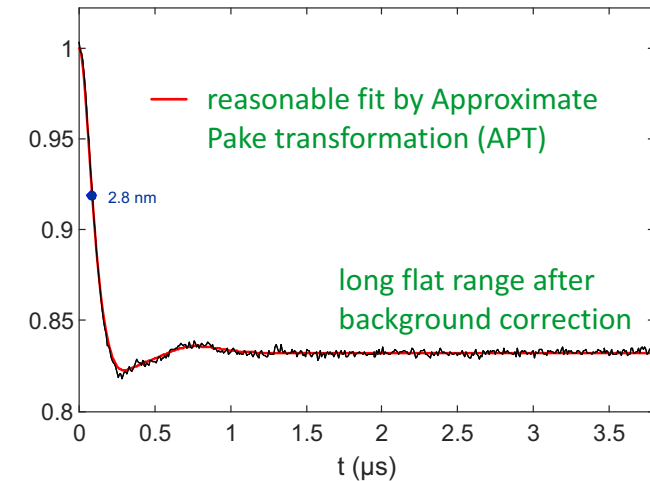
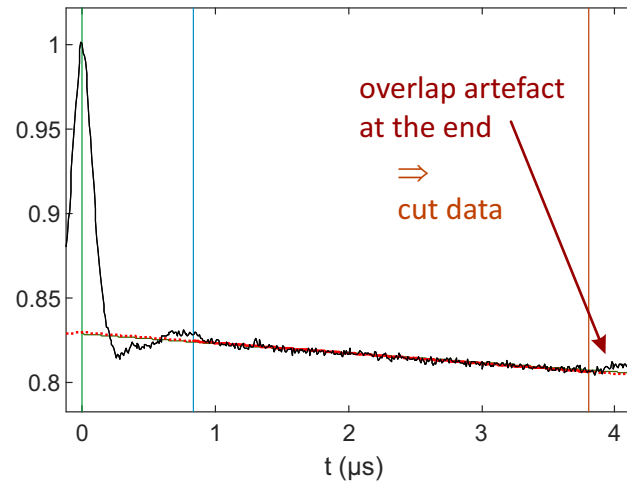
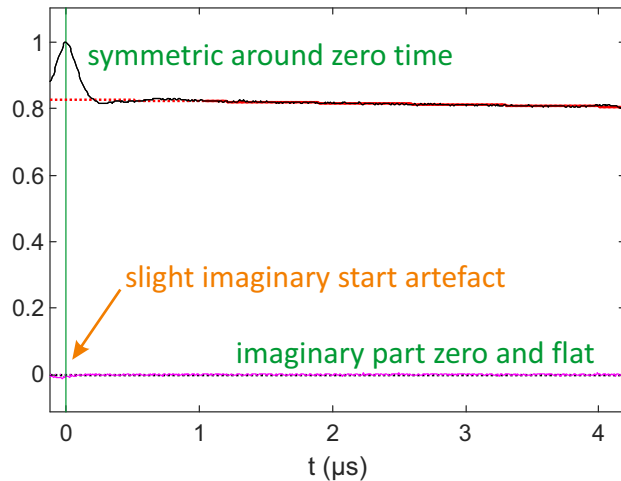
-  Checking data quality
-  Modes of background correction
-  Tikhonov regularization & DEERNet
-  Validation tool

MMM 2018.2

-  Spin labeling/localization
-  Elastic network modelling
-  Flexible domain (ensemble model)
-  RigiFlex

High data quality

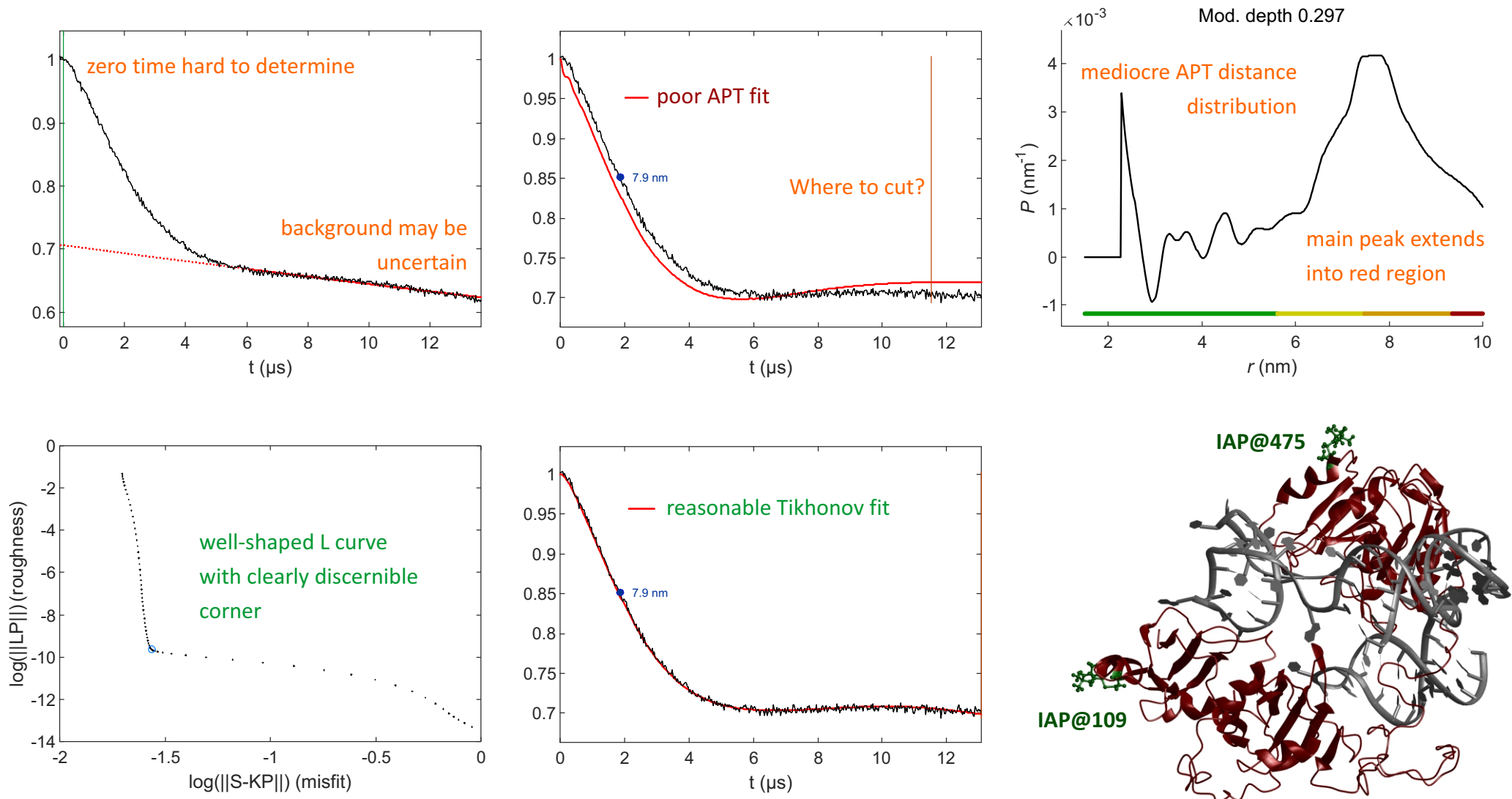
Double mutant T109C/Q235C of PTBP1 in complex with EMCV-IRES DtoF



Data courtesy CHRISTOPH GMEINER

Limited data quality

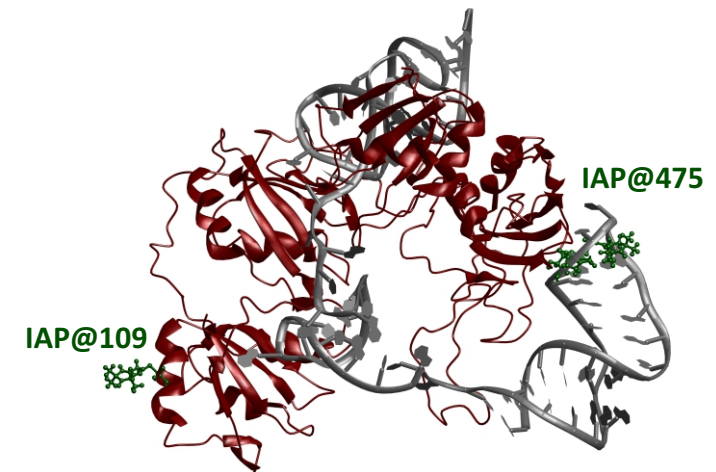
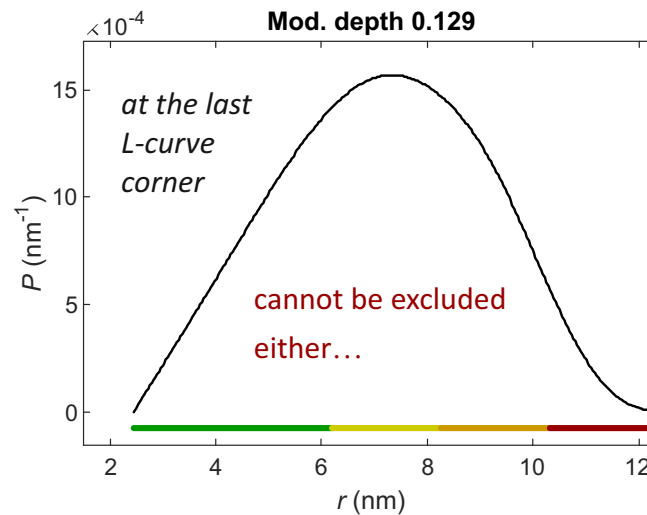
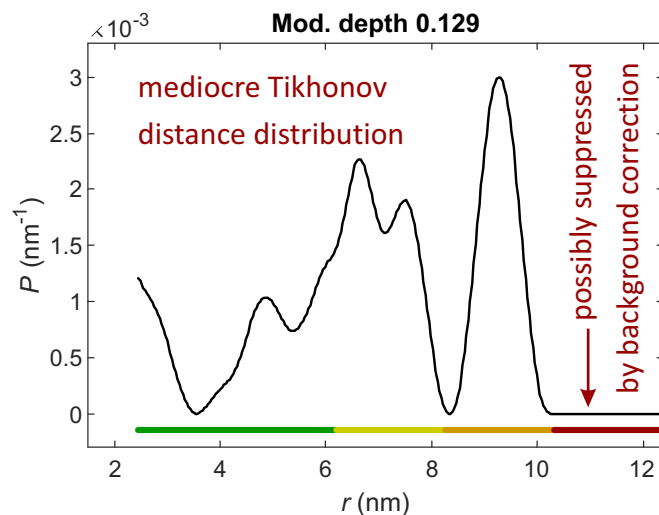
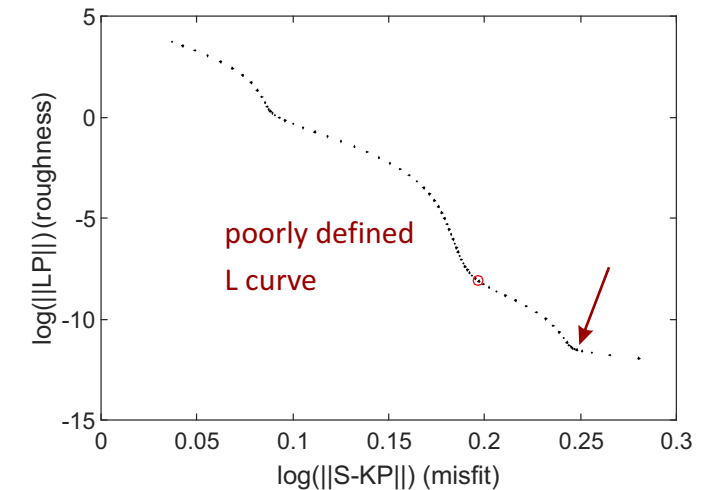
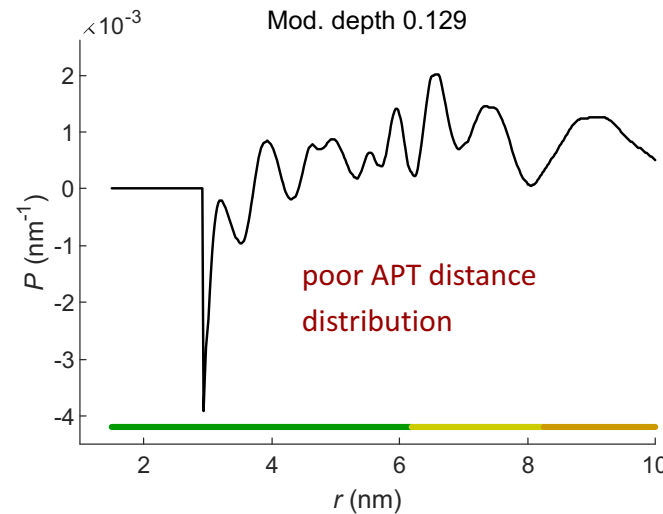
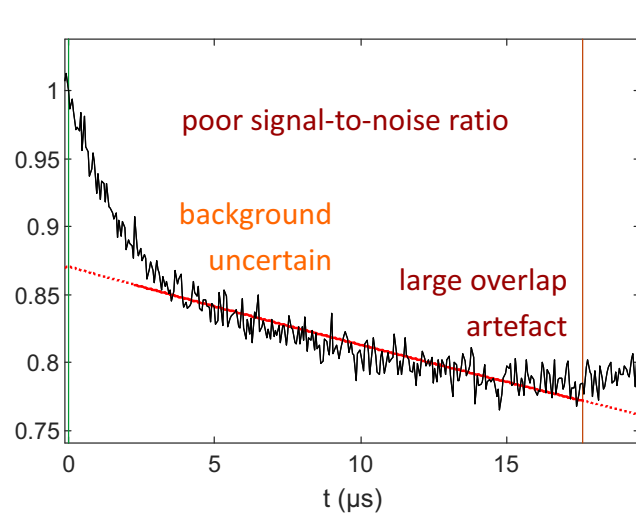
Double mutant T109C/S475C of PTBP1 in complex with EMCV-IRES DtoF



Data courtesy CHRISTOPH GMEINER

Rather poor data quality

Double mutant T109C of PTBP1/ U304 of EMCV-IRES DtoF



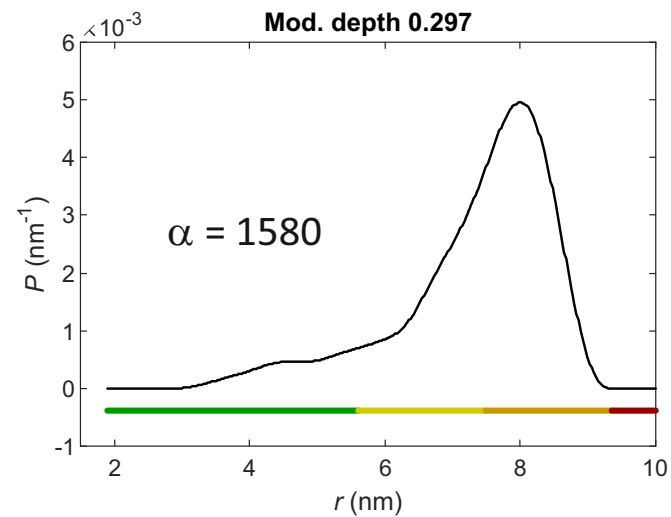
Data courtesy CHRISTOPH GMEINER

Dependence of the distance distribution* on background model

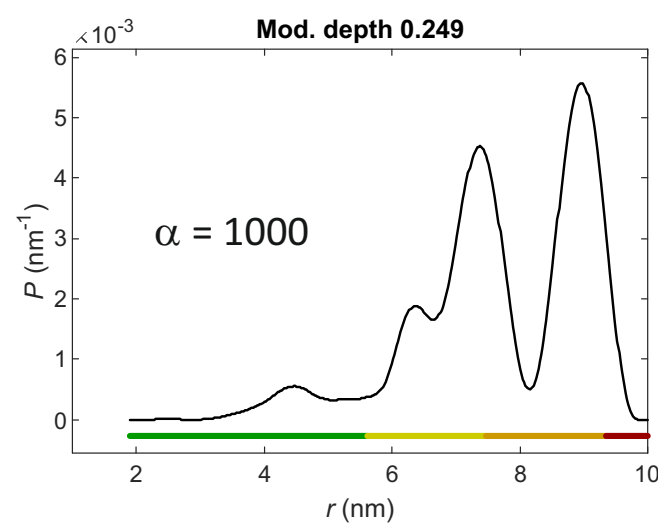
*Tikhonov regularization with L-curve corner selection

Double mutant T109C/S475C of PTBP1 in complex with EMCV-IRES DtoF

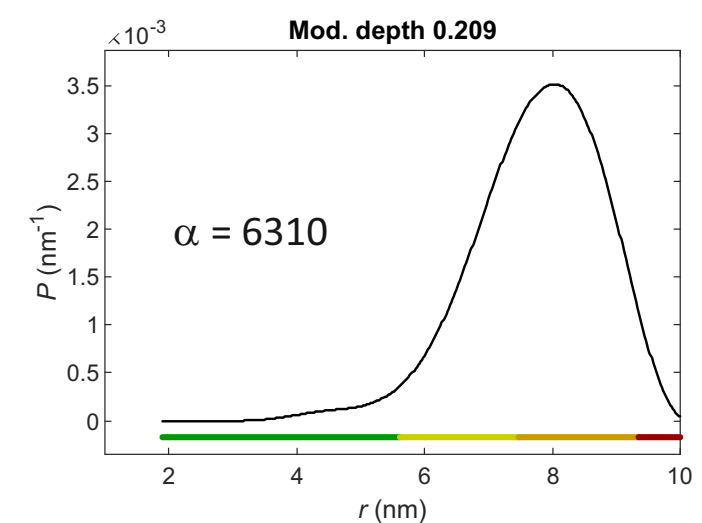
Fit in optimized range



Form-factor based fit

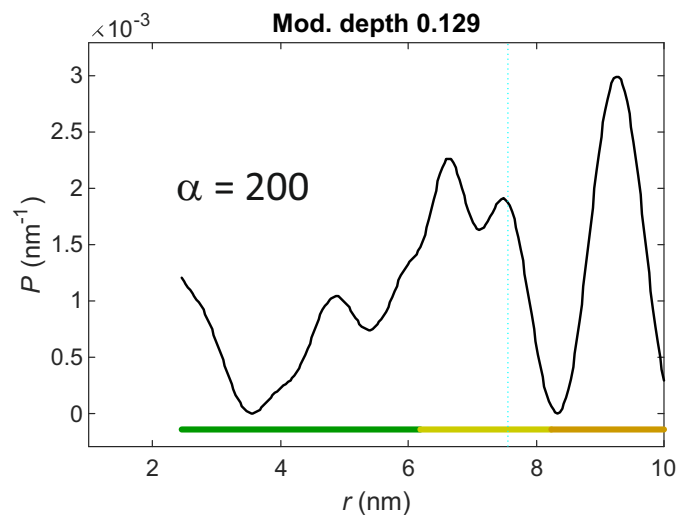


DEERNet background

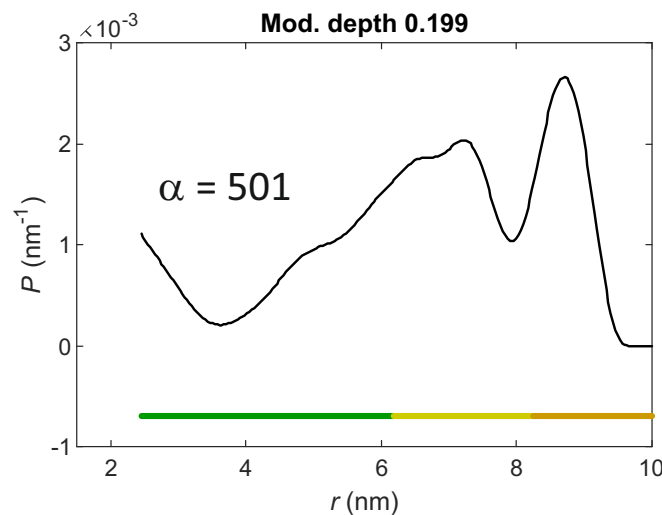


Double mutant T109C of PTBP1/ U304 of EMCV-IRES DtoF

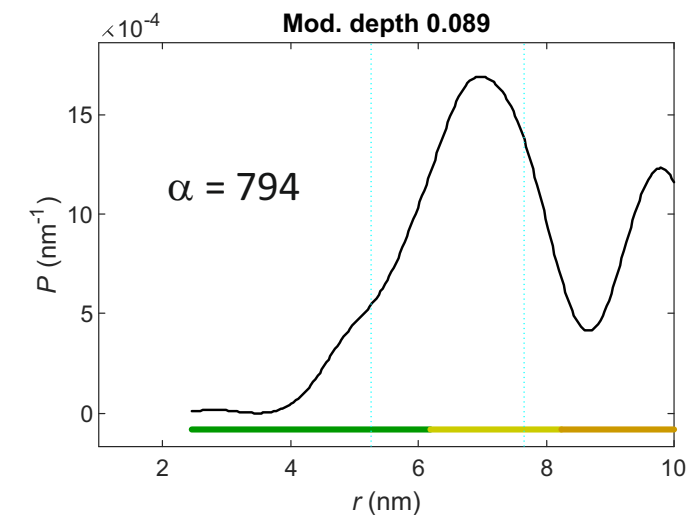
Fit in optimized range



Form-factor based fit



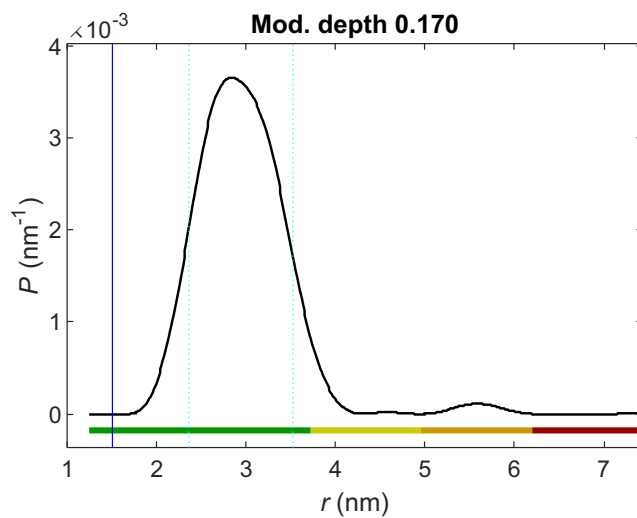
DEERNet background



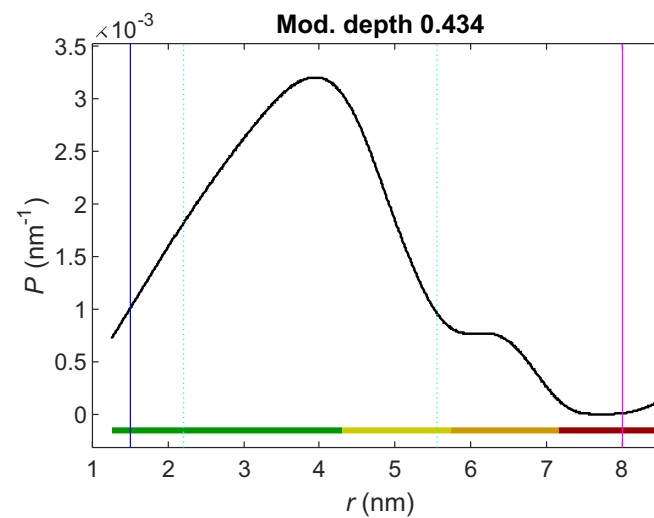
Tikhonov regularization versus DEERNet

Tikhonov regularization

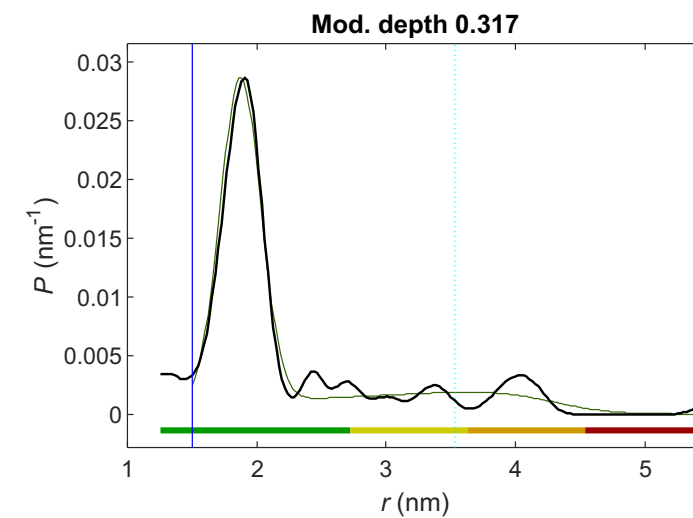
T109C/Q235C PTBP1/EMCV-IRES DtoF



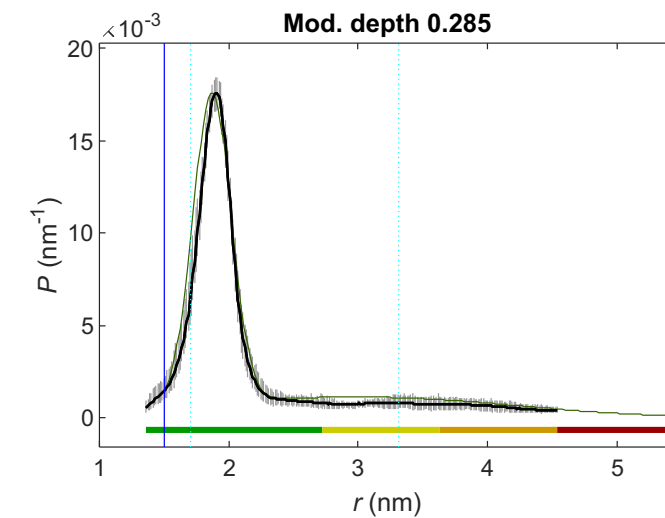
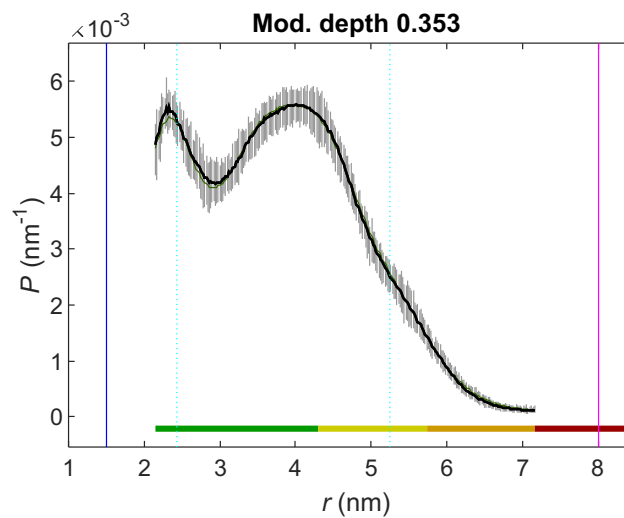
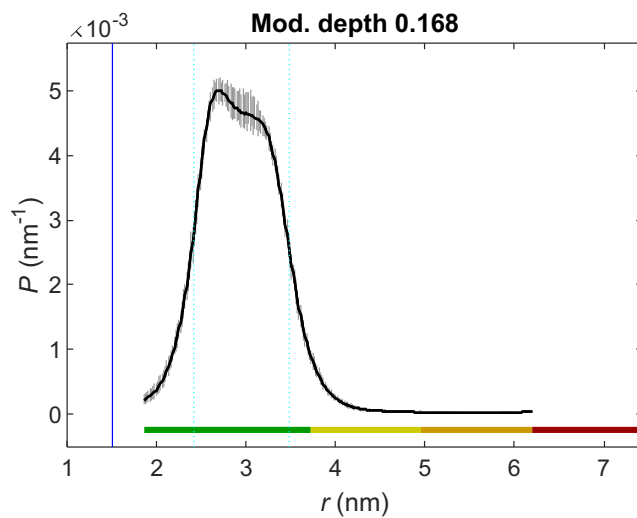
S3C/S34C in N-terminal loop of LHCII



Biradicals on spherical gold nanoparticles



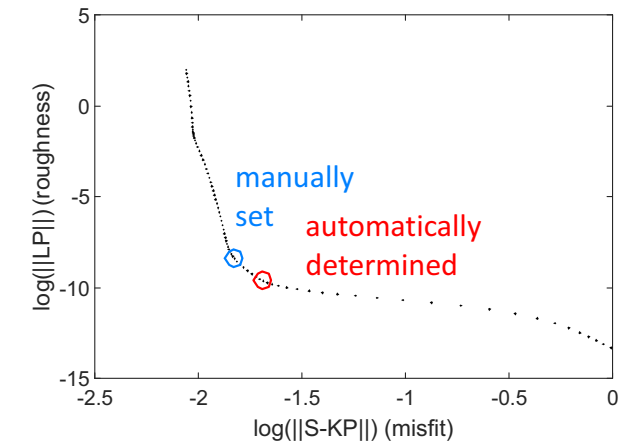
Neuronal network



Validation of results: High-quality data

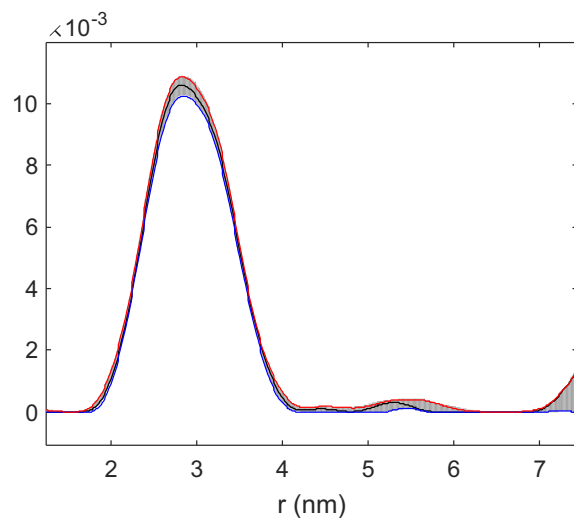
Double mutant T109C/Q235C of PTBP1 in complex with EMCV-IRES DtoF

<input checked="" type="checkbox"/> White noise	0.001487	Level: 1.5	Trial number: 10
<input checked="" type="checkbox"/> Background start	Min: 8.400000e+	Max: 2.520000e+	Trial number: 11
<input type="checkbox"/> Background dim.	Min: 2.00	Max: 3.00	Trial number: 1
<input type="checkbox"/> Background density	Min: 0.3000	Max: 1.2000	Trial number: 1
<input type="checkbox"/> Modulation depth	Min: 0.100	Max: 0.350	Trial number: 1



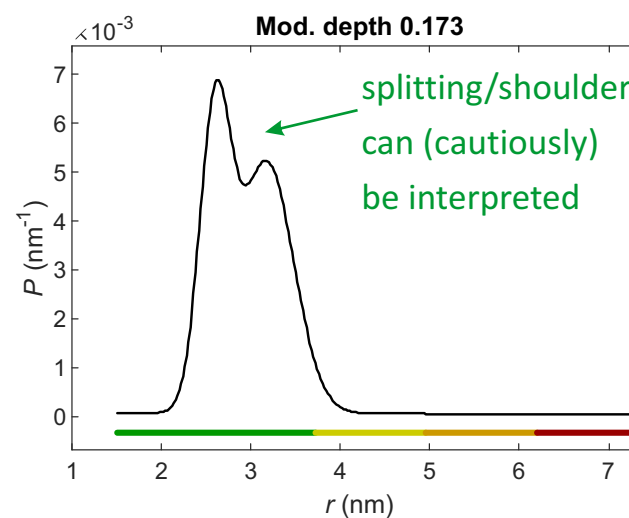
Tikhonov regularization validated
(automatically determined L-corner)

rmsd 0.001487



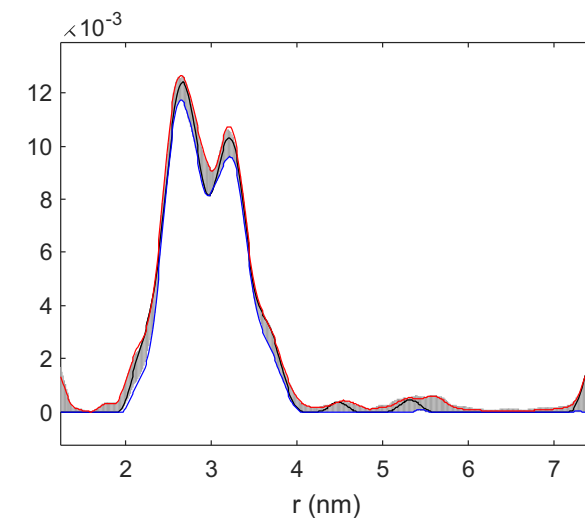
Fit by three Gaussians

rmsd 0.001281



Tikhonov regularization validated
(manually set L-corner)

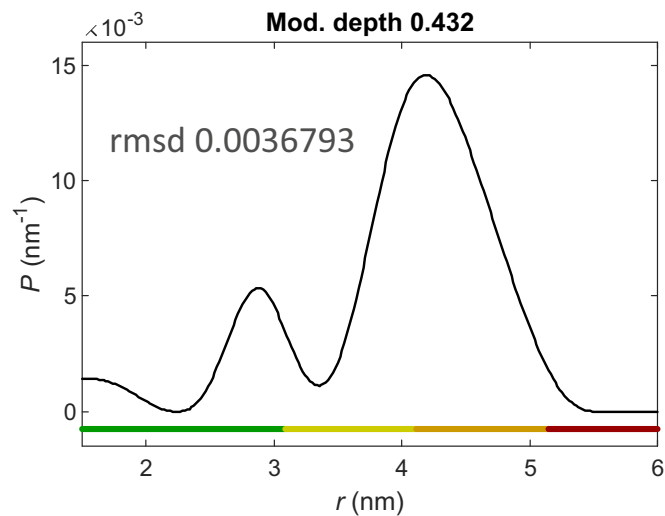
rmsd 0.001267



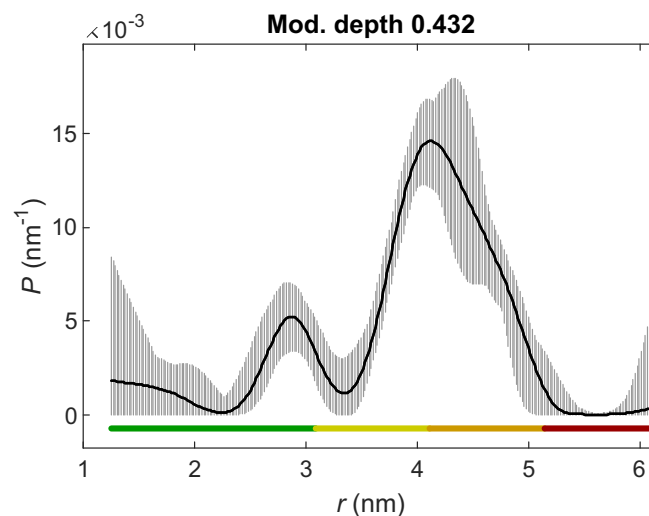
Validation of results: Low-quality data

Double mutant S106C/S160C in heterogeneous trimers of LHCI

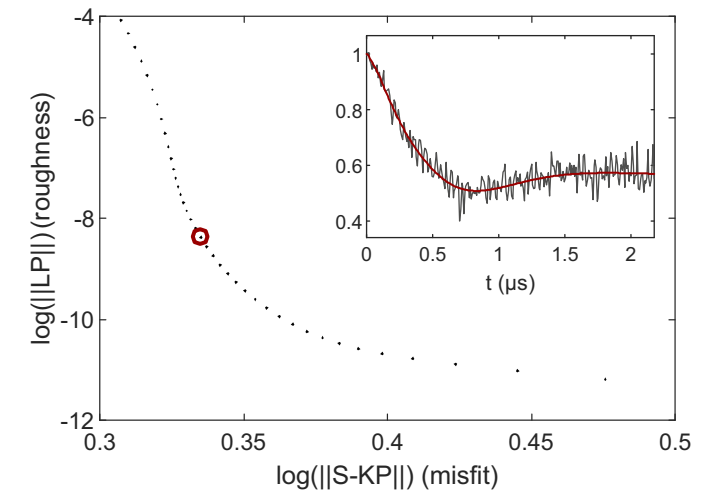
Tikhonov regularization (DEERNet bckg.)



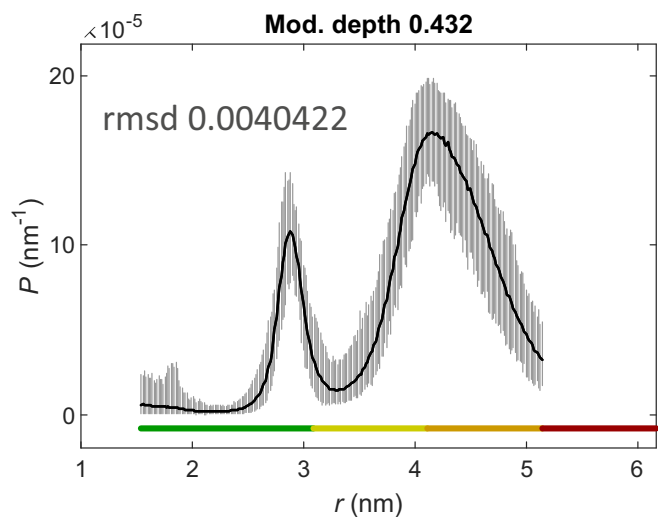
Tikhonov validation



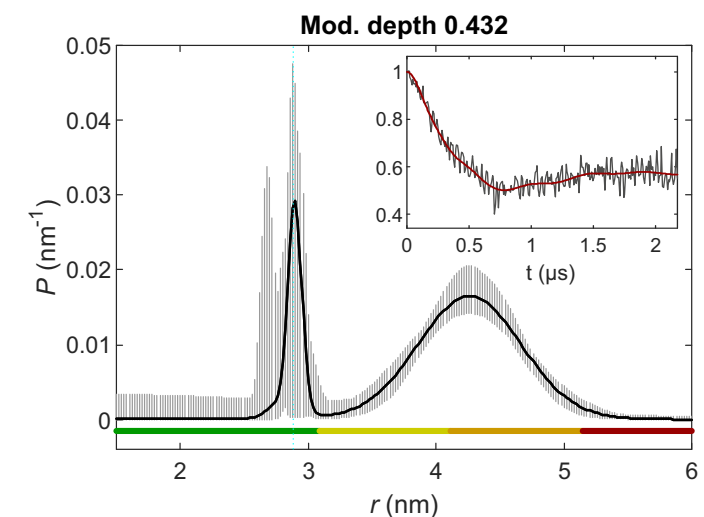
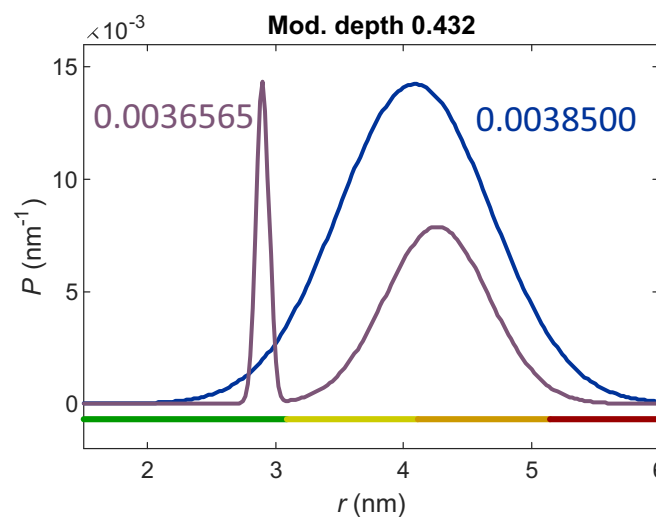
Tikhonov L curve (optimum α by GCV)



Second opinion: DEERNet



Third opinion: 1 & 2 Gaussians (DEERNet bckg.)



We now break for a commercial. Stay tuned..



Coming from the Stoll and Jeschke labs,
by Luis Fábregas Ibáñez

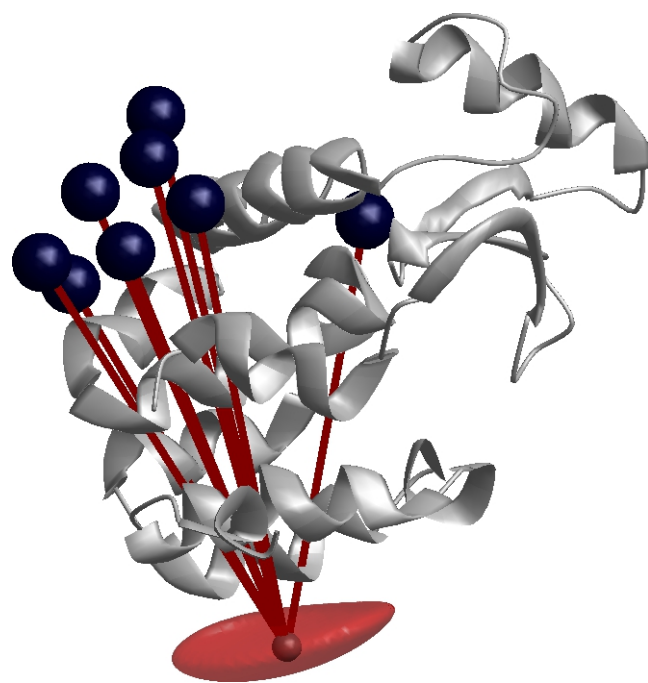
The engine of next DeerAnalysis

- API (application programming interface) implemented as Matlab toolbox
- several regularization techniques & multi-Gauss fitting & any parametric model
- flexible global fitting
- flexible validation
- Open Source on GitHub



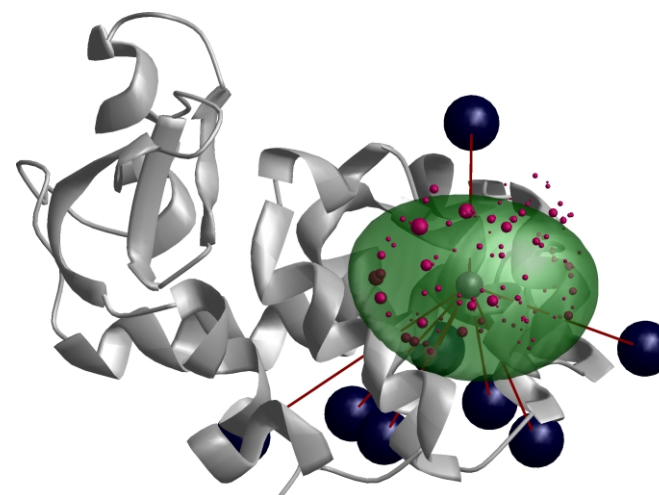
Localization and rotamer library modelling

Localization of residue 131 in T4 Lysozyme
(8 distance restraints from literature/ C. Altenbach)



131 (predicted)

Comparison to rotamer model of label distribution

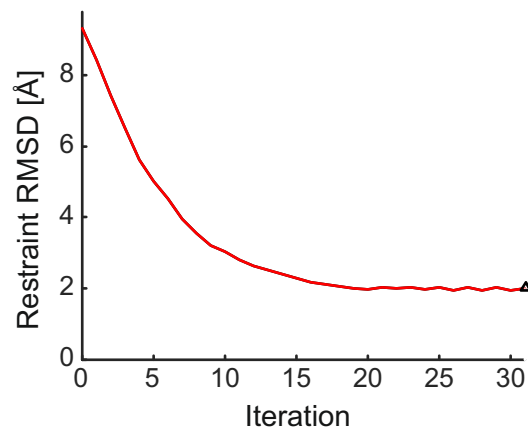


Conformational change by elastic network modeling

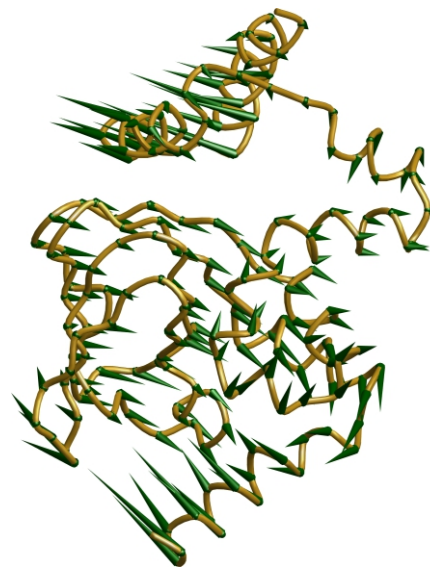
Apo form of the HCN ion channel (6 distance restraints from literature)

M. C. PULJUNG, H. A. DEBERGA, W. N. ZAGOTTA, S. STOLL,
PNAS **2014**, *111*, 9816-9821

Restraint rmsd decreases - but not to zero!



Motion display with cones



Motion display by coil superposition



G. JESCHKE, *Protein Science* **2018**, *27*, 76-85; worked examples in Supplementary Information

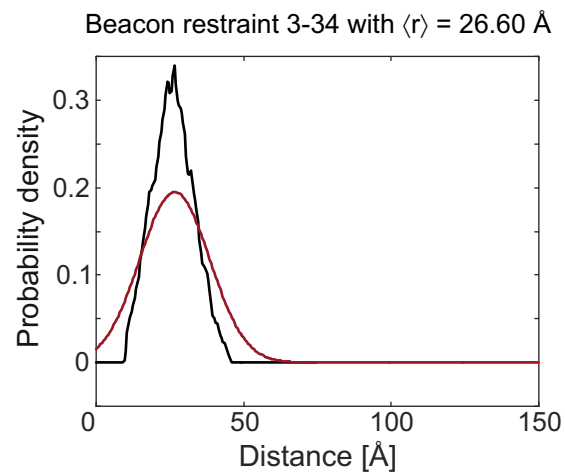
Ensemble model of a flexible peptide section

Residues 3-13 of trimeric LHCII

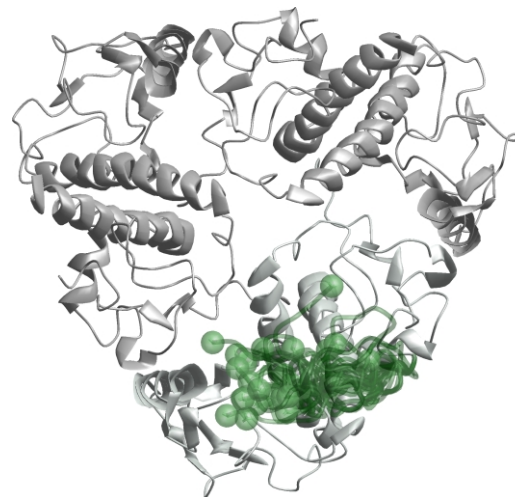
(13 distance restraints, 7 bilayer depth restraints)

N. FEHR, C. DIETZ, Y. POLYHACH, T. VON HAGENS, G. JESCHKE, H. PAULSEN,
J. Biol. Chem. **2015**, *290*, 26007-20 (2015)

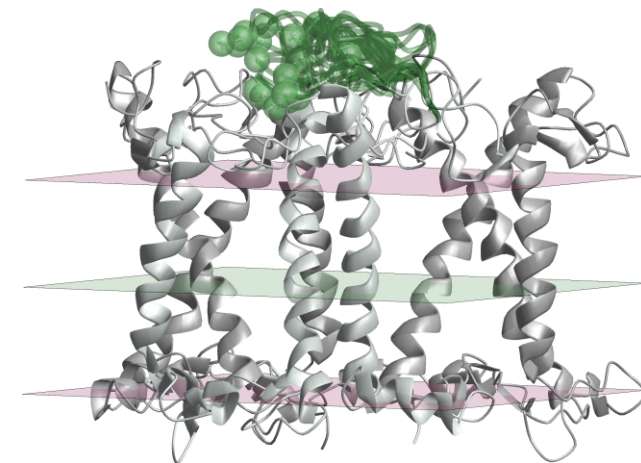
Example for restraint fitting



View perpendicular to bilayer



View in bilayer plane



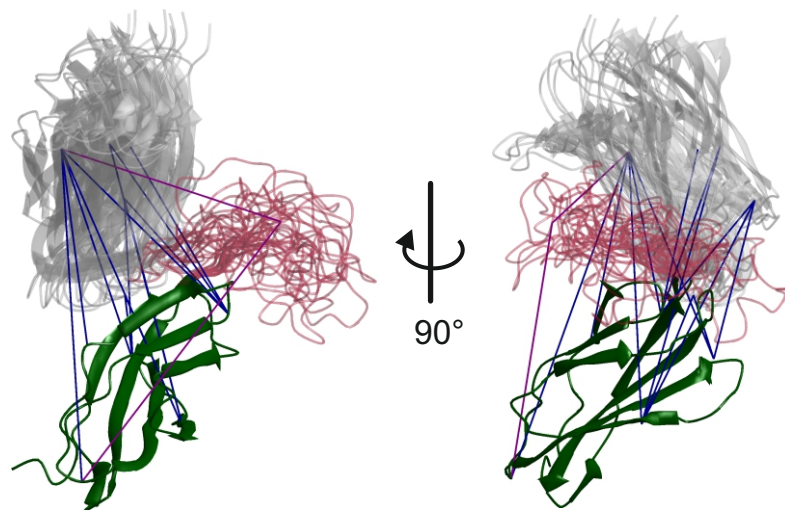
G. JESCHKE, *Protein Science* **2018**, *27*, 76-85; worked examples in Supplementary Information

RigiFlex modeling of FnIII-3,4 domains of integrin $\alpha 6/\beta 4$

11 distance restraints between rigid bodies, 2 restraints to flexible linker

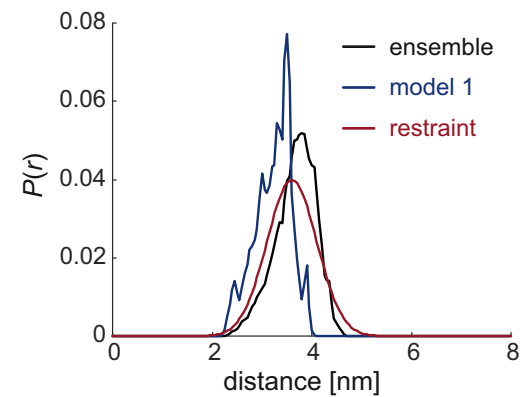
Data:

N. ALONSO-GARCÍA, I. GARCÍA-RUBIO, J. A. MANSO, R. M. BUEY, H. URIEN,
A. SONNENBERG, G. JESCHKE, J. M. DE PEREDA, *Acta Cryst. D* **2015**, *71*, 969-985



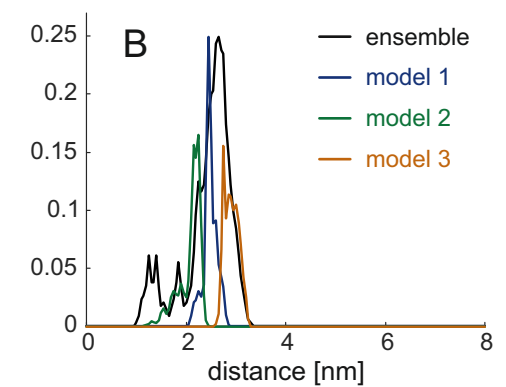
Actual restraint

1472(FnIII-3)-1626(FnIII-4)



Potential restraint

1472(FnIII-3)-1598(FnIII-4)



G. JESCHKE, *Protein Science* **2018**, *27*, 76-85; worked examples in Supplementary Information