Calculation of NMR spin-spin couplings for intrinsically disordered proteins: a prospective tool to facilitate experimental NMR studies.

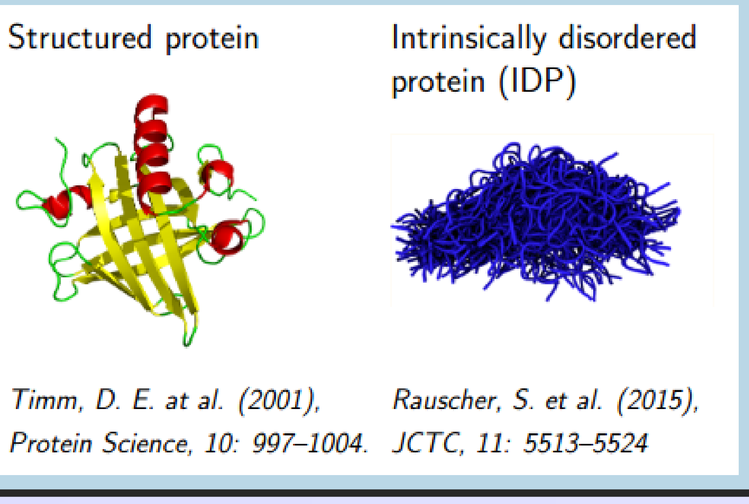
[1]*Amina* Gaffour, [2]*Krishnendu* Bera , [1]*J.* Pavlíková přecechtělová

[1]*Faculty* of Pharmacy in Hradec Králové, Charles University, Akademika Heyrovského 1203, 500 05 Hradec Králové, CZ

[2]*CEITEC*, Masaryk University, Kamenice 753/5,625 00 Brno, CZ

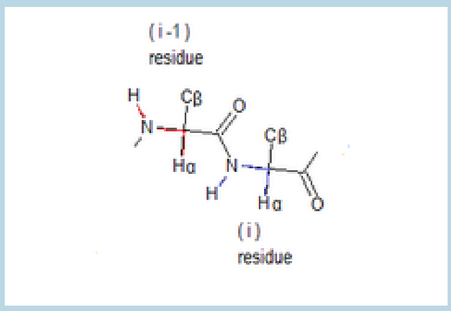
Introduction

Intrinsically disordered proteins (IDPs) are identified by polypeptide chains that do not have a stable single well-defined structure.



J-couplings predictions

The prediction of J-couplings for IDPs builds on empirically parameterized Karplus equations. Alternatively, quantum mechanics (QM) can be applied if the empirical parametrization is prevented by the lack of training experimental data. We design a computational protocol that combines the molecular dynamics (MD) calculations with density functional (DFT) calculations along with fragmentation techniques.

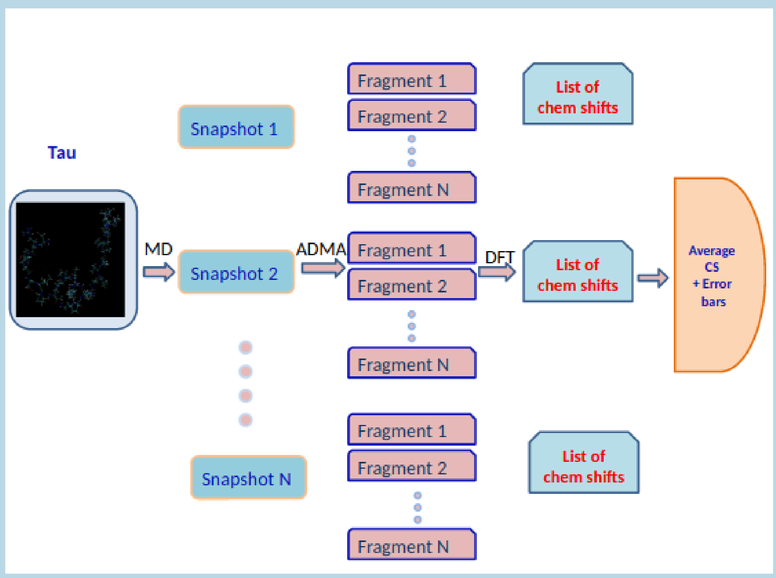


$$3_H^{J\ N} - H_{(Hz)}(1)$$

$$J_{KL} = J_{KL}^{DSO} + J_{KL}^{PSO} + J_{KL}^{FC} + J_{KL}^{SD} \qquad (2)$$

Method

Graphical representation of the project's methodology simplified to the three primary computational tools employed – MD/ADMA/DFT.



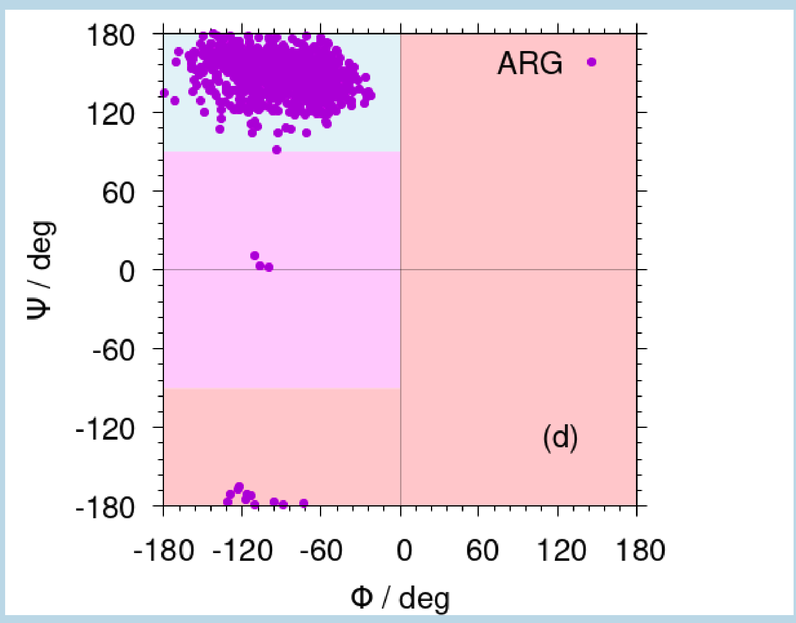
Acknowledgements

This research is supported by the Charles University Grant Agency (GA UK). The computational resources necessary for this project are secured from MetaCentrum and supported by the Ministry of Education, Youth and Sports of the Czech Republic through the e-INFRA CZ (ID:90140).

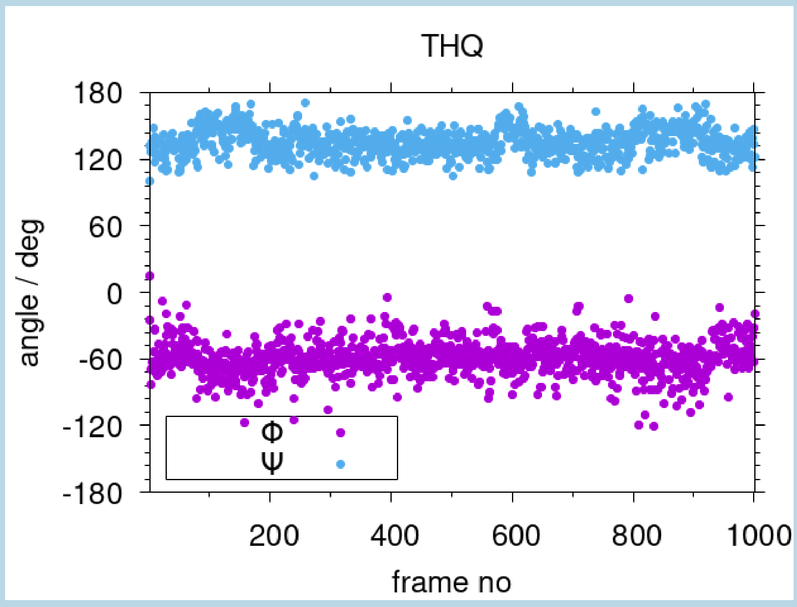
Results

We used a 31-amino acid (AA) fragment of the Tau protein (residues 210-240). We are calculating its apo- as well as its phosphorylated form . The phosphorylated Tau fragment includes 4 phosphorylated AAs: 1 phosphorylated serine (pS)and 3 phosphorylated threonines (pT).
Apo Tau: SRTPSLPTPPTREPKKVAVVRTPPKSPSSAK
Phosphorylated Tau : SR(pT)PSLP(pT)PPTREPKKVAVVR(pT)PPK(pS)PSSAK

Ramachandran plots for some amino acids:



Time dependence plots:



MD calculation results: