COMPUTATIONAL STRATEGIES FOR NMOSD AND MOGAD: MOLECULAR MODELING AND SIMULATIONS

Prof. Dr. João Marcos Brandet[1]

[1]Mitglied of the Deutsche Gesellschaft für Neurologie/Deutsche Physikalische Gesellschaft

INTRODUCTION

NMOSD and MOGAD are autoimmune disorders where autoantibodies target AQP4 and (MOG), respectively. This study integrates computational chemistry, nuclear physics methodologies, and immunology tools to explore innovative therapeutic strategies, focusing on advanced molecular modeling and immune system simulations.

RESULTS

AQP4 Analysis: Identified S63, Y250, R261 as primary autoantibody binding sites. Structural destabilization linked to disrupted hydrogen bonding.

MOG Conformational Plasticity: F77, Y104 residues showed significant solvent accessibility shifts upon autoantibody interaction, exposing hydrophobic regions.

Quantum Mechanical Insights: Localized electron density shifts alter electrostatic properties, enhancing binding affinity.
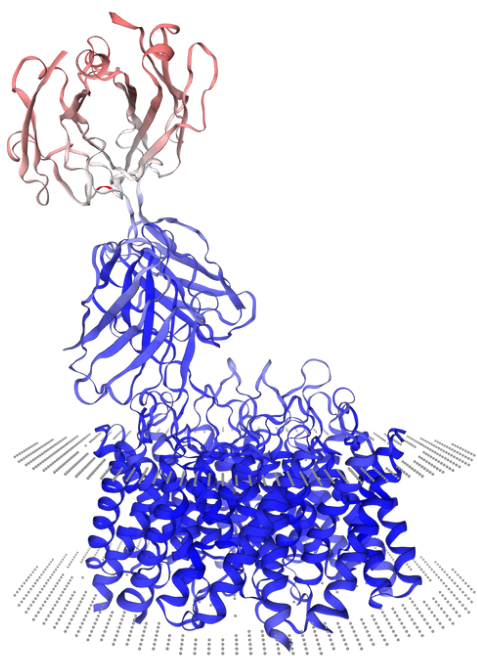

Figure I. Structure of human AQP4 with a pathogenic autoantibody- rAB 58
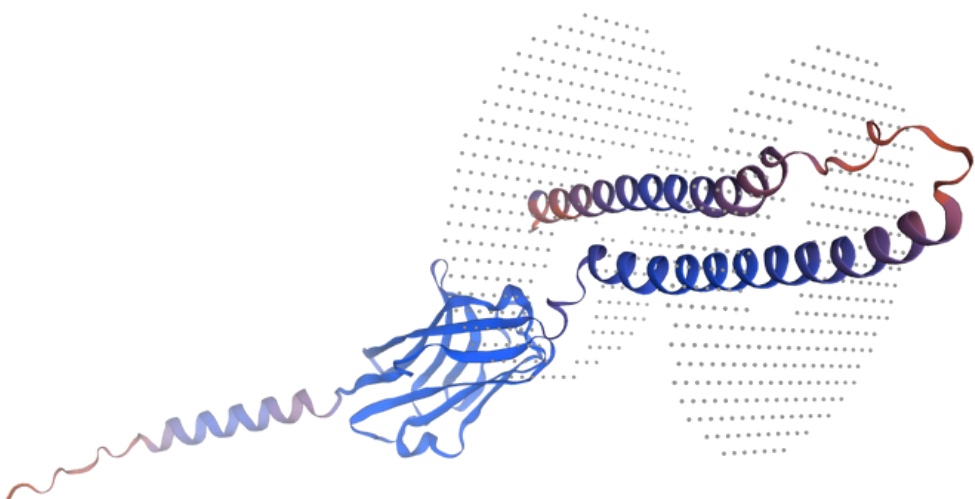**Credits:** João Marcos Brandet

Figure II. MOG by Nuclear Physics
Credits: João Marcos Brandet

METHODOLOGY

Molecular Modeling
- Utilized quantum and classical approaches for structural analysis.
- Software: PyMOL, VMD, Swiss-PdbViewer, ICM-Browser.
- Density Functional Theory (DFT) and Hartree-Fock approximations for electronic properties and binding affinity calculations.
- Molecular dynamics simulations: GROMACS, LAMMPS.

Immune System Simulations
- Platforms: C-ImmSim, Simmune.
- Data integration: Transcriptomic analysis (DESeq, GOseq) for cytokine signaling, T-cell activation, and immune tolerance predictions.

DISCUSSION

The computational approach presented in this study offers a novel perspective on NMOSD and MOGAD by integrating quantum mechanics, molecular dynamics, and immunological simulations. The identification of key binding sites and electrostatic alterations provides a foundation for future therapeutic developments. These findings emphasize the importance of multidisciplinary methodologies in advancing autoimmune disorder research.

LITERATURE

Huda S, Whittam D, Bhojak M, et al. Neuromyelitis optica spectrum disorders[J]. Clin Med (Lond), 2019, 19(2): 169-176.

Wu Y, Zhong L, Geng J. Neuromyelitis optica spectrum disorder: Pathogenesis, treatment, and experimental models[J]. Mult Scler Relat Disord, 2019, 27: 412-418.

Corbali O, Chitnis T. Pathophysiology of myelin oligodendrocyte glycoprotein antibody disease. Front Neurol. 2023 Feb 28;14:1137998.

European Charcot Foundation   DGN   DPG