GERMAN NETWORK FOR BIOINFORMATICS INFRASTRUCTURE

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BioData

EnzymeStructures: Supporting Structure-Driven Molecular Life Science Research in BRENDA

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Short description of the project

The EnzymeStructures project is geared to make structural data of proteins accessible and usable to life scientists. The previous project phase was used to establish the ProteinsPlus web service internationally and to integrate manifold tools and functionalities based on structural data provided by the Protein Data Bank (PDB). The tools are focused on binding sites and interactions with small molecules like substrates, co-factors and inhibitors.

https://proteins.plus

ProteinsPlus offers an intuitive and easily understandable user interface and can be used by all life scientists without restrictions. We established a RESTful service that enables the integration of ProteinsPlus in other web services as well as in graphical programming interfaces like KNIME. Additionally, ProteinsPlus functionality has been integrated in the BRENDA database.

In the current project phase, we aim at finalizing prototypic software packages in order to integrate them as ProteinsPlus tools. Also continuous training activities in terms of video tutorials, summer schools and training courses will be part of our efforts.

Progress report

RESTful service

- Each tool accessible via a REST API
- KNIME node available for each tool as application example

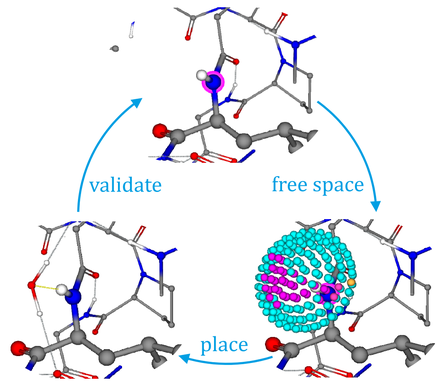
WarPP places water molecules in ligand binding sites of a given PDB file

- Potential water positions are generated for free interaction directions
- Sophisticated numerical optimization and clustering produces stable water positions
- Iterative use for creating waters with stable water-water interactions

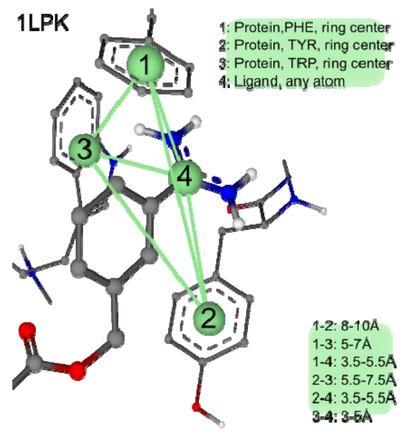
GeoMine* - textual, numerical and 3D searching with full chemical awareness in collections of protein-ligand interfaces

- Tailor-made geometric index allow arbitrary geometry queries in molecular interfaces
- Multi-threaded PostgreSQL database for close to interactive use

* Alpha version available at https://geomine.zbh.uni-hamburg.de



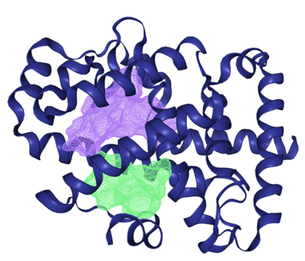
WarPP – prediction of favorable water positions in active sites



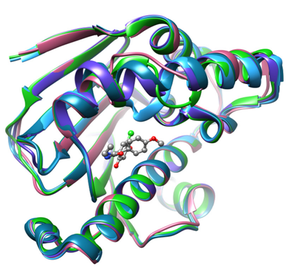
GeoMine – web-based geometric search in protein structures

de.NBI services

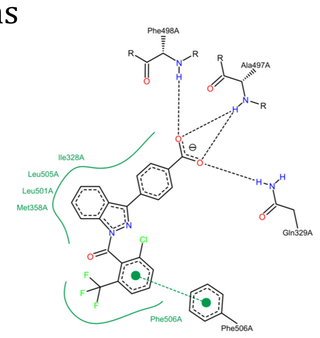
- Protoss – hydrogen bond network optimization
- DoGSiteScorer – identify protein binding sites and predict their druggability
- EDIA & StructureProfiler – structure validation using electron density and structural criteria
- PoseView – 2D visualization of protein-ligand interactions
- SIENA – binding site superpositioning and ensemble generation
- METALizer – determination of metal coordination geometry
- HyPPI – prediction of protein-protein interactions



Active and allosteric site of transcription factor RPRγt (PDBid: 5c4o)



Ensemble of HSP90 structures



Transcription factor RPRγt complex (PDBid: 5c4o)

de.NBI Training and education

- Workshop: “Protein Structure Fundamentals: Searching – Analyzing – Modeling”
  - At the Center for Bioinformatics in Hamburg (ZBH)
  - Covered Topics: BRENDA, ProteinsPlus and KNIME
  - Focus on protein function and related interactions to small molecules.
  - Workshop was fully booked
  - Above-average evaluation results
- New Tutorial videos on Proteins*Plus* website
  - How does my protein interact with its ligands?
  - Where do I find druggable binding sites in my protein?
  - Is my crystal structure suitable for docking?
  - Am I looking at a protein-protein interaction or just at a crystal artifact?

General information on the project

No. of staff paid from de.NBI grant: 1 FTE

- Katrin Schöning-Stierand (since 07/2019)
- Rainer Fährrolfes
- Eva Nittinger (until 08/2019)

Other staff involved

- Matthias Rarey - Supervision
- Konrad Diedrich, Joel Graef, Martin Poppinger – GeoMine Development
- Gerd Embruch – Server administration
- Several undergraduate assistants

Publications

Proteins*Plus:*

- Schöning-Stierand, K .; et al. (2020). Nucleic Acids Research, submitted.
- Fährrolfes, R.; et al. (2017). Nucleic Acids Research, 45:W337-W343.

Selected publications of de.NBI services:

- Nittinger, E., et al. (2018). J. Chem. Inf. Model., 58(8), 1625-1637. (WarPP)
- Inhester, T. et al. (2017). J. Chem. Inf. Model., 57(2), 148-158. (GeoMine)
- Volkamer, A., et al. (2012). J. Chem. Inf. Model., 52(2):360-372. (DoGSiteScorer)
- Meyder, A., et al. (2017). J. Chem. Inf. Model., 57(10): 2437-2447. (EDIA)
- Stierand, K., et al. (2006). Bioinformatics, 22(14):1710-1716. (PoseView)
- Bietz, S.; Rarey, M. (2016). J. Chem. Inf. Model., 56(1):248-59. (SIENA)

GEFÖRDERT VOM
Bundesministerium für Bildung und Forschung
Projektträger Jülich Forschungszentrum Jülich