Memprot & Dadimodo: programs for modeling the detergent belt in solubilized membrane protein complexes & re-orienting domains of multi-domain proteins

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Membrane proteins participate in many critical cellular processes, including apoptosis, drug import/export and cell division, and are thus very important for biomedical research. Despite their importance, the research on membrane proteins is hampered by insufficient understanding of methods used to solubilize them, like detergent micelles, detergent bicelles or polymer/detergent nanodiscs. Moreover, the ability to model the solubilizing agent around a transmembrane protein is often necessary for further investigations of the protein itself. Therefore, to facilitate research into structure of solubilizing agents (alone and in complex with membrane proteins), the program Memprot[1] was developed in SWING beamline. Memprot builds a low resolution model of the solubilizing agent belt that surrounds a protein of known atomic coordinates by trying to fit the experimental SAXS scattering curve of the complex. The initial version of Memprot could be used to model a corona of single detergent around a protein. Recent developments in new versions of Memprot include, among others:

- Models of detergent bicelles and detergent/polymer nanodiscs
- Adaptive Shape Algorithms which allow for deformation of detergent corona based on the shape of the trans-membrane region of the protein
- Parallelization with MPI and code optimizations

Based on a genetic algorithm, the program Dadimodo is meant to "refine" the 3D structure of a multi-domain protein complex against SAXS experimental data, the degrees of freedom being the backbone dihedral angles of the protein flexible fragments. A complete (all-atoms) structure representation is used with energy control for every newly generated model so as to prevent steric clashes and converge to a physically feasible structure. The program takes its roots from [2, 3]. The new version offers an automated analysis of the structure topology (fixed vs. variable parts of the structure) which extends the applicability of the software to a larger class of topologies and opens its use to a larger community of users. Moreover, the presented update allows for a better exploration of the search space at the advanced evolution stage thanks to an adaptive mechanism of decreasing the amplitude of the conformation changes. In terms of implementation, the calculation is speeded up as a result of parallel execution enabled through the DEAP package [4]. Dadimodo addresses domain re-orientation of both soluble proteins and membrane proteins with a belt modeled using Memprot. Since last year Dadimodo has been made available to the research community as a web application [5].

References

[1]. J. Pérez, A. Koutsioubas, Memprot: a program to model the detergent corona around a membrane protein based on SEC–SAXS data, Acta Crystallographica Section D, 2015, 71, 86-93.

[2] G. Evrard, F. Mareuil, F. Bontems, C. Sizun, and J. Pérez (2011), DADIMODO: a program for refining the structure of multidomain proteins and complexes against small-angle scattering data and NMR-derived restraints. Journal of Applied Crystallography 44, 1264–1271.

[3] F. Mareuil, C. Sizun, J. Pérez, M. Schoenauer, JY. Lallemand, and F. Bontems (2007). A simple genetic algorithm for the optimization of multidomain protein homology models driven by NMR residual dipolar coupling and small angle X-ray scattering data. Eur. Biophys J 37(1), 95–104.

[4] Félix-Antoine Fortin, François-Michel De Rainville, Marc-André Gardner, Marc Parizeau, and Christian Gagné (2012). DEAP: Evolutionary Algorithms Made Easy. J. Mach.Learn. Res. 13, 1 (2012), 2171–2175.

[5] O. Roudenko, A. Thureau and J. Pérez (2018) Dadimodo: Refining Atomic Models of Multi-Domain Proteins against SAXS Data, https://dadimodo.synchrotron-soleil.fr