[P12] Developing probabilistic restraint optimization protocols for comparative modelling in MODELLER

Evgeni Grazhdankin[1], Karen Culotta, Cédric Gageat, Henri Xhaard[1]

[1]*Faculty of Pharmacy, Division of Pharmaceutical Chemistry and Technology, University of Helsinki, P.O. Box 56, FIN-00014 Helsinki, Finland*

We have developed a framework for comparative modelling on top of MODELLER [1], which extends exploration of spatial restraints and the conformational space. Restraints are optimized by diverse protocols in a model-creation-restraint-evaluation feedback loop (figure 1) using probabilistic graphs, heuristic optimization algorithms and quantitative quality gauges. The framework is written in Python, and restraints operationalized with a relational PostgreSQL database. The performance of the method is evaluated for its ability to reconstruct GPCR structures.
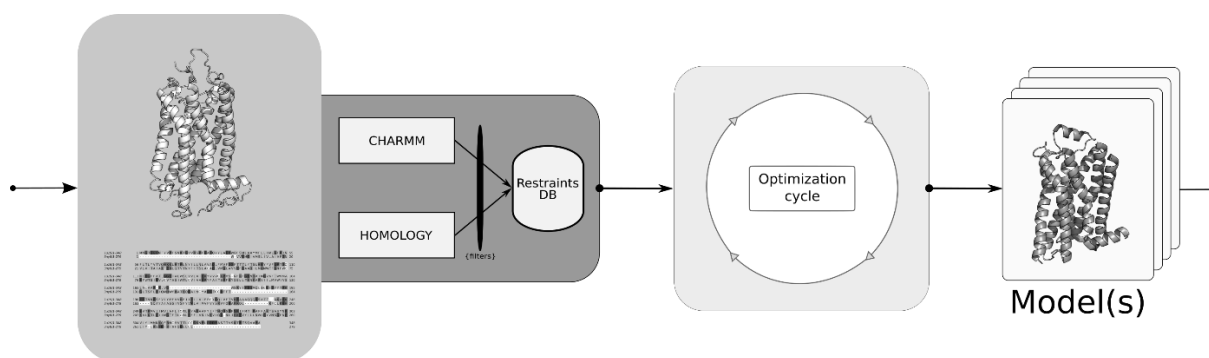

Figure 1 Initialization and the modeling cycle. Input consists of a template and the sequence alignment to the target. Restraints are created by MODELLER and stratified into CHARMM and homology types. In addition to these restraints, we create custom restraints, which are then subjected to the optimization protocols.

Bibliography:

[1] A Šali and TL Blundell. 1993. "Comparative Protein Modelling by Satisfaction of Spatial Restraints" *Journal of Molecular Biology* 234(3): 779–815.