UNIWERSYTET WARSZAWSKI

CeNT CENTRUM NOWYCH TECHNOLOGII

invites to a seminar by

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Efficient sampling and optimization on manifolds for macromolecular docking

17th of July (Wednesday) 2019 at 12.30 p.m.

Venue: Centre of New Technologies, Banacha 2C, Lecture Hall 0142 (Ground floor)

Host: dr hab. Joanna Sułkowska

Three-dimensional structure prediction of macromolecular interaction complex is an important component in small molecular and biologics drug discovery. The search space includes the 6D rotational/translational space of mutual rigid body orientations of receptor and ligand, as well as additional degrees of freedom that represent the flexibility of the two molecules. Solving this problem requires detailed sampling and optimization of an energy-based scoring function.

Since the energy function has a large number of local minima separated by high barriers, the minimization problem is extremely challenging. The search space includes the 6D rotational/translational space as well as additional degrees of freedom that represent the flexibility of the macromolecules and is a manifold. Here we present effective approaches for different steps of docking protocols, which effectively use manifold geometry to significantly speed up the search. Specifically we will describe Fast Manifold Fourier Transform (FMFT) approach for effective global grid based sampling for macromolecular docking, and local and medium range optimization using exponential map parametrization for docking refinement. The methods described above have been blindly validated in international docking competitions CAPRI (protein docking) and D3R (protein-ligand docking) and were among the best performers in both.