Towards the Virtual Screening Technique: Trends and Updates

The problem of computational affinity estimation has grown as computers became a powerful tool of today science. It is hardly to find any modern investigation that is not aided with computational models. However demands of scientists expand even faster than microelectronic industry capabilities. Numerous computational clusters help to facilitate bio- and pharmacological projects. Nevertheless the numbers of projects that require rigorous computations are growing. To deal with this problem researches worldwide have to use in their projects less accurate but computationally faster theoretical methods. That is why new, more efficient and faster algorithms are of great importance in modern bioscience.

Mathematical modeling in biology is a problem often related to interactions estimation between a biomolecular target and small molecule compounds. The knowledge of such interactions permits us to interrupt certain processes in cells and, for example, to impede such a devastating disease as cancer. For this reason a lot of efforts are concentrated on designing of better models and algorithms for high-throughput virtual screening technique.

One of the leading Ukrainian companies, OTAVA Ltd., started developing its own virtual screening system in 2004 [1-3]. The project was started as an attempt to incorporate entropy change that occurs during ligand-receptor binding into virtual screening protocol. Initially this project was restricted to model entropy change in harmonic oscillation approximation. As such model is extremely related to quality of potential energy calculations. OTAVA's scientists have designed a universal polarizable force field to achieve reasonable entropy change accounting (on the basis of unique empirical charges definition scheme). Spanning entropies with traditional enthalpy calculations for free energy of binding prediction showed some lack in accuracy. It was significantly improved with addition of ligands desolvation free energy which was calculated with our modified GBSA method (up to 0.95 regression coefficient with experimentally derived data).

Further testing of the improved virtual screening system showed strong dependence of its efficiency on nearest environmental water molecules that are usually ignored in the field of high-throughput virtual screening. To implement fast but accurate water position finding, a new algorithm of molecular docking code was proposed by OTAVA' scientists and its utilization is on the way in our laboratories.

List of selected publications by OTAVA's scientists:

[1] O.Ya. Yakovenko, A.A. Oliferenko, V.G. Bdzhola, V.A. Palyulin, N.S. Zefirov. **Kirchhoff atomic charges fitted to multipole**

moments: implementation for a virtual screening system. *J. Comput. Chem.* **2008**, *29*, 1332.

[2] Yakovenko O.Ya., Olifirenko A.A., Golub A.G, Bdzhola V.G., Yarmoluk S.M. **The new method of distribution integrals evaluationsfor high throughput virtual screening**. *Ukrainica Bioorganica Acta* - **2007.** – Vol. 5, No. 1. – P. 52-62.

[3] Yakovenko O.Ya., Golub A.G., Bdzhola V.G., Yarmoluk S.M. **Application of distribution function of rotation and transla_tion degrees of freedom for CK2 inhibitors K_i estimation**. *Ukrainica Bioorganica Acta* - **2006.** – Vol. 4, No. 2. – P. 47-55.

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