R&D field: Life science

Docking simulation of protein and drug

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- Developer
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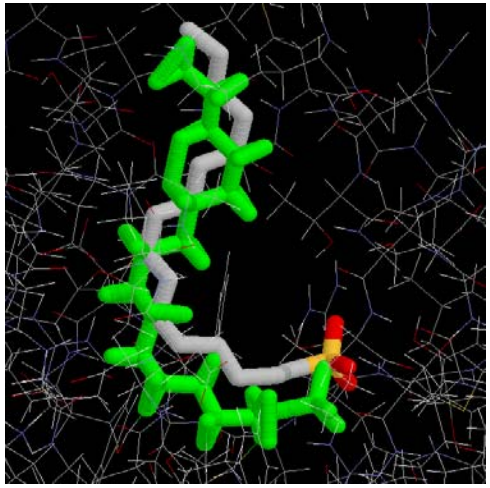
- Abstract
  - Search of candidate compound for drug based on docking simulation between several millions of commercially available chemical compounds and target proteins and estimation of complex structures and their binding energy.
  - Determination of interaction between proteins and chemical compounds with classical force fields for hydrophobic, Coulomb interaction and etc.
- Algorithm
  - Search of complex structure between proteins and chemical compounds with the geometric hashing method for global search and the steepest descent method for local search (interaction is estimated with the grid potential).
  - Serial computation with Fortran90.
- Current computation size
  - Lattice points of the grid potential: 60x60x60.
  - One million of chemical compounds x 100 of target proteins (serial computation).
  - Memory 0.2 GB (one node) and disk 0.5 TB.
- Future computation size in 2010
  - Computation time is 30 times for one docking simulation (10-15 % increase of accuracy) and the number of chemical compounds is 100 times, totally 3,000 times.
  - Memory 1 TB and disk 50 TB.



Estimated (green) and experimentally measured (CPK colors) structures of a low-molecular ligand bound to a protein receptor pocket.

- Expected results
  - To estimate between the all commercially available chemical compounds and 1,000 typical proteins, 100 times of the current computation is necessary. To increase accuracy by 10-15 %, 30 times of computation is necessary for each docking simulation.
  - The obtained data will be used for drug search ranging from protein with known three-dimensional structure to protein with unknown structure such as membrane protein. We will decrease development time by increasing efficiency several dozens time compared to drug search with the random-screening experiment.
- Reference
  - “Classification of chemical compounds by protein-compound docking for use in designing a focused library”, Y. Fukunishi, Y. Mikami, K. Takedomi, M. Yamanouchi, H. Shima, H. Nakamura, Journal of Medicinal Chemistry, 49, 523-533 (2006).