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Investigation of protein-ligand interactions

Yoshinori Hirano[1] hirano@riken.jp
Noriaki Okimoto[1] okimoto@riken.jp
Makoto Taiji[1] taiji@riken.jp

[1] Laboratory for Computational Molecular Design, Computational Biology Research Core Quantitative Biology Center (QBiC), RIKEN, Hyogo, 651-0047, Japan

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Finding therapeutic drugs is challenging matter. Many methodologies have been applied to this matter (*i.e.* drug design). In addition to the experimental techniques, various computational approaches are utilized at the different stages of drug design. In the early stage, compound libraries are screened in order to increase potential compounds. Due to select the compound from the huge number of compounds in relatively short time, molecular docking methods are routinely used. The molecular docking has already proven to be a successful virtual screening tool for several target proteins, but it is less reliable because the calculation of binding free energy between target protein and ligand is not so accurate. The problems with molecular docking have been widely mooted: protein dynamics and solvation effects are ignored, the energy functions are inaccurate, and so on. Therefore more effective computational method is necessary for rational drug design.

Molecular dynamics (MD) simulations can treat both proteins and ligands in a flexible manner, directly estimate the effect of explicit water molecules, and provide more accurate binding affinity, although their computational costs and times are significantly greater than those of molecular docking. We report an effective method for computational screening; this method is a combination of molecular docking and molecular dynamics simulations. The proposed method showed a higher and more stable enrichment performance than the molecular docking method used alone. We will use quantum chemical (QC) calculations as final filter of drug screening.

[1] Okimoto N. *et al.*, PLoS Comput Biol 5(10): e1000528.