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種別(和文)	要約
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Computational Study of *Candida antarctica* Lipase B: Lid Dynamics and Substrate Binding

Background

- *Candida antarctica* lipase B (CALB) is one of the most popular lipases used in academia and industry¹.
- The lid region of CALB controls the substrate entry to the active site.
- The lid region transition from the close conformation to the open conformation when interacts with hydrophobic surface (interfacial activation).²
- CALB reaction with triglycerides is slower than reaction with diglycerides and monoglycerides.³

Goals

- Understand the effect of hydrophobic surface on the conformational dynamics of CALB. Tricaprylin was chosen as a triglyceride model.
- Predict the complex structure of CALB and tricaprylin.

Computational Methods

- CALB in water (CALB/W) and CALB on the water/tricaprylin interface (CALB/I) system were prepared.
- The free energy surface (FES) describing the lid region conformational dynamics was constructed using Parallel Cascade Selection Molecular Dynamics (PaCS-MD)⁴ and the Markov State Model (MSM) methods.
- CALB/tricaprylin complex structures and interactions were predicted using molecular docking with AutoDock Vina and molecular dynamics simulations.

Main Results

- Based on the FESs, CALB prefers the close and semi-open conformations in CALB/W and CALB/I, respectively.
- Tricaprylin conformation in the CALB active site can be classified into three states: full binding, transition, and initial binding states.
- The full binding state is more stable when the terminal ester bond interacts with the active site than when the central ester bond interacts with the active site.
- Initial binding happens mostly with CALB in the semi-open conformation, which is the most preferable conformation in CALB/I, while the full binding can happen with CALB in the close, semi-open, and open conformations.

Future Works

- Investigate the binding mechanism from the fully dissociated state.
- Investigate the reactions and subsequent product release.

References

1. Ortiz, C. et al. Novozym 435: the “perfect” lipase immobilized biocatalyst? *Catal Sci Technol* 9, 2380–2420 (2019).
2. Zisis, T. et al. Interfacial Activation of *Candida antarctica* Lipase B: Combined Evidence from Experiment and Simulation. *Biochemistry* 54, 5969–5979 (2015).
3. Fedosov, S. N. et al. Kinetic model of biodiesel production using immobilized lipase *Candida antarctica* lipase B. *J Mol Catal B Enzym* 85–86, 156–168 (2013).
4. Harada, R. & Kitao, A. Parallel cascade selection molecular dynamics (PaCS-MD) to generate conformational transition pathway. *J Chem Phys* 139, 035103 (2013).