CHARMM Force Field Parameter Development for Thioester and Acyl-phosphate Functional Groups

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Ongoing work in our laboratory seeks to understand whether the presence of reaction intermediates in enzyme active sites modulates the conformational energetics of mobile loops during catalytic turnover (*1*). The recent determination of a series of X-ray crystallographic "snapshots" of the enzyme formyl-CoA:oxalate CoA transferase (FRC) at various steps of the catalytic mechanism provides a unique starting point for computational investigations of this biophysical problem (*2*). This poster will present recent work aimed at obtaining optimized CHARMM force field parameters for thioester functionality, which are essential for future efforts employing the OSRW methodology (*3*) for computing conformational free energies. In addition, optimized force field parameters for acyl-phosphates, another important class of reactive intermediates in enzyme-catalyzed reactions, will be reported.

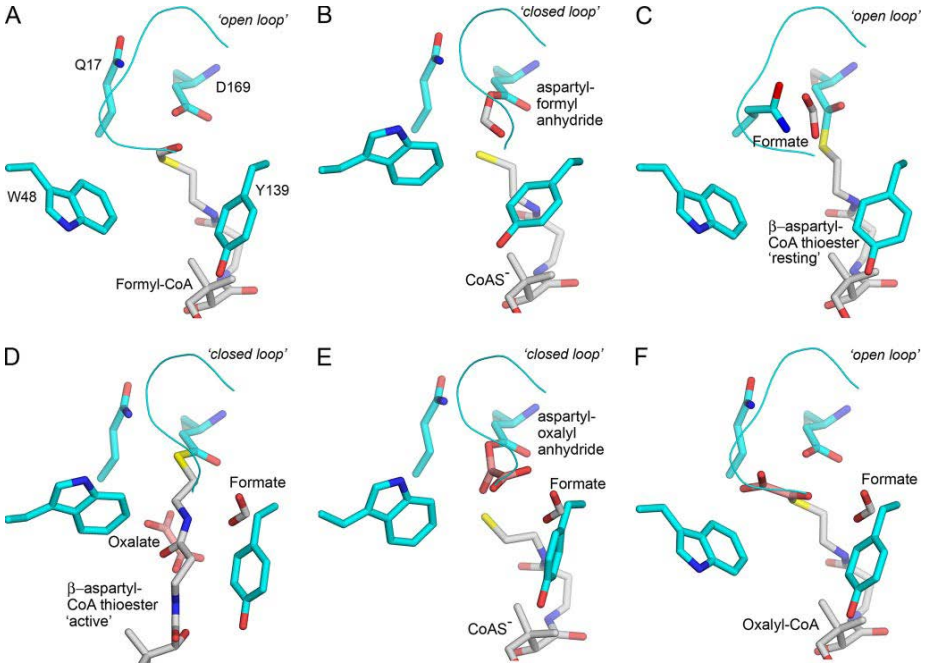

Figure: Crystallographic "snapshots" of the reaction catalyzed by *Oxalobacter formigenes* FRC.

References

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3. Zheng, L., Chen, M. and Yang, W. (2008) *Proc. Natl. Acad. Sci., USA* **105**, 20227-20232.

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