

# Application of Statistical-Thermal Coupling Analysis to Identify Residue-Residue Interaction Networks that Facilitate Coupled-Domain Dynamics in Methionyl-tRNA Synthetases

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Methionyl-tRNA synthetase (MetRS) is a modular protein that catalyzes covalent attachment of methionine to the 3'-end of the tRNA<sup>Met</sup>. It is known that the coupling of distant domain dynamics is a pre-requisite for catalysis in modular proteins. Recent studies conducted in our lab have also demonstrated that networks of evolutionarily and dynamically-coupled residues promote coupled-domain dynamics.<sup>1,2</sup> In the present study, the interaction networks fostering coupled-domain motions in *Escherichia coli* MetRS have been identified by using bioinformatics and molecular simulation studies. Specifically, the Statistical Thermal Coupling Analysis (STCA) method that integrates the information of dynamic coupling of residues with their evolutionary features (conserved and coevolved) has been employed. Herein, we will present the methods and some preliminary results that include the identification of several residue-residue interaction pathways and their characterizations using *in silico* mutations.

## References

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- (2) Johnson, J. M.; Sanford, B. L.; Strom, A. M.; Tadayon, S. N.; Lehman, B. P.; Zirbes, A. M.; Bhattacharyya, S.; Musier-Forsyth, K.; Hati, S. *Biochemistry* **2013**, *52*, 4399.