

Mechanism of chemical reactions in the active site of aspartate *N*-acetyltransferase NAT8L revealed by molecular modeling

Igor V. Polyakov, Maria G. Khrenova, Bella L. Grigorenko and Alexander V. Nemukhin

The model of NAT8L with the reactants, aspartate and acetyl-CoA.

The left part in Figure S1 illustrates the secondary structure of NAT8L consistent with the experimental ^{S1} and computational ^{S2} studies. Two catalytic regions, incorporating amino acid residues 80-118 and 149-302, are separated by the membrane-associated region 119-148. The right part shows a view on the reactants, aspartate and acetyl-CoA, in the enzyme active site and the side chains of amino acid residues, which surround the reacting area.

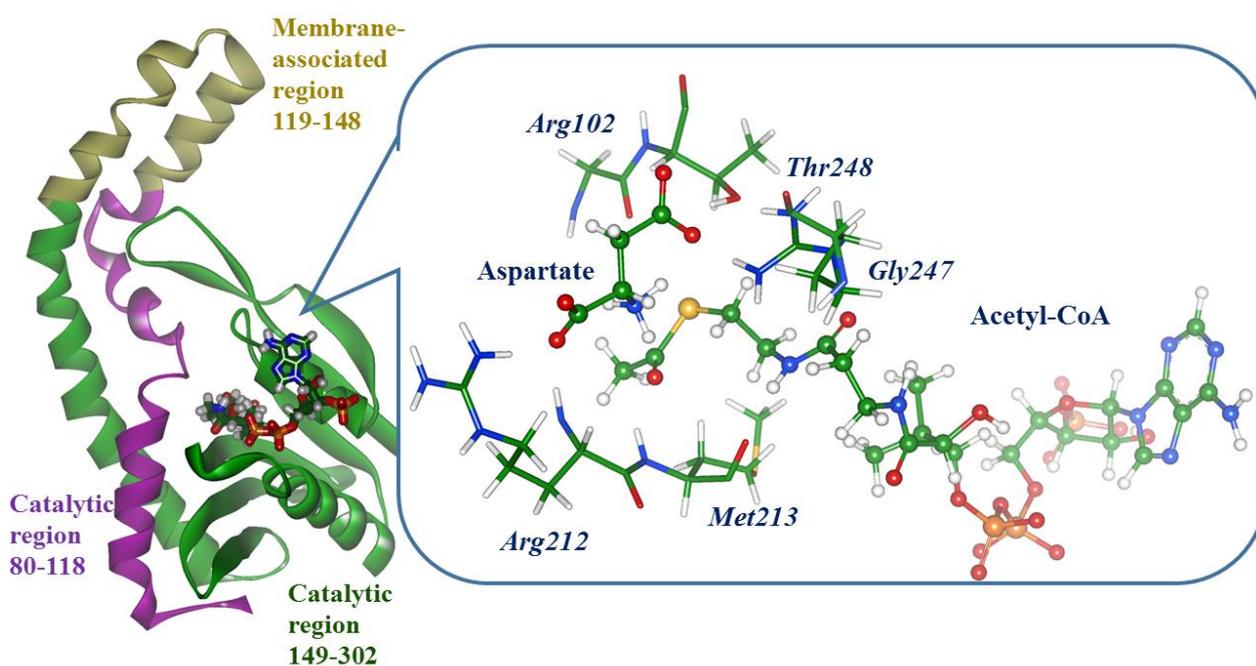


Figure S1. Left - 3D structure of NAT8L and the reactants, aspartate and acetyl-CoA, shown in sticks. Right – a view on the active site. Carbon atoms are colored in green, oxygen in red, nitrogen in blue, phosphorus in orange, sulfur in yellow, hydrogen in white.

Step 1: REAC → REAC*.

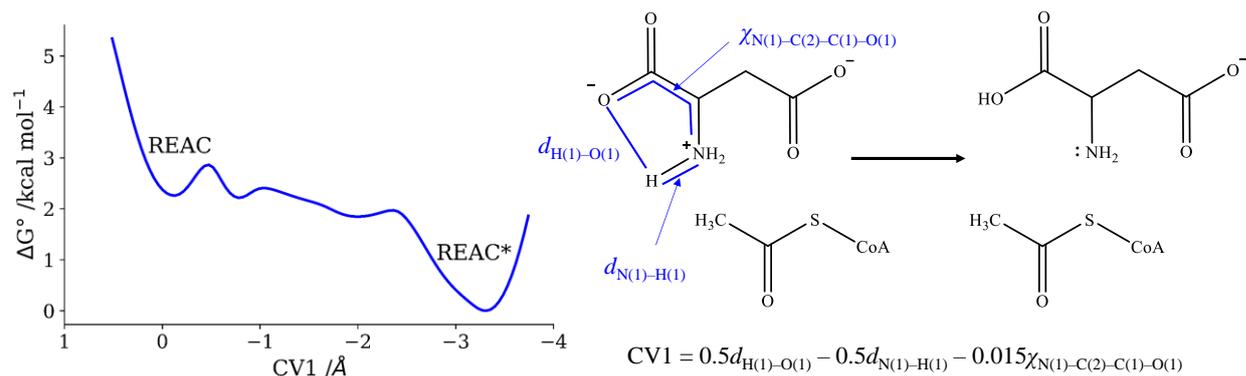


Figure S2. Computed Gibbs energy profile for the step REAC → REAC*.

Step 2: REAC* → INT1.

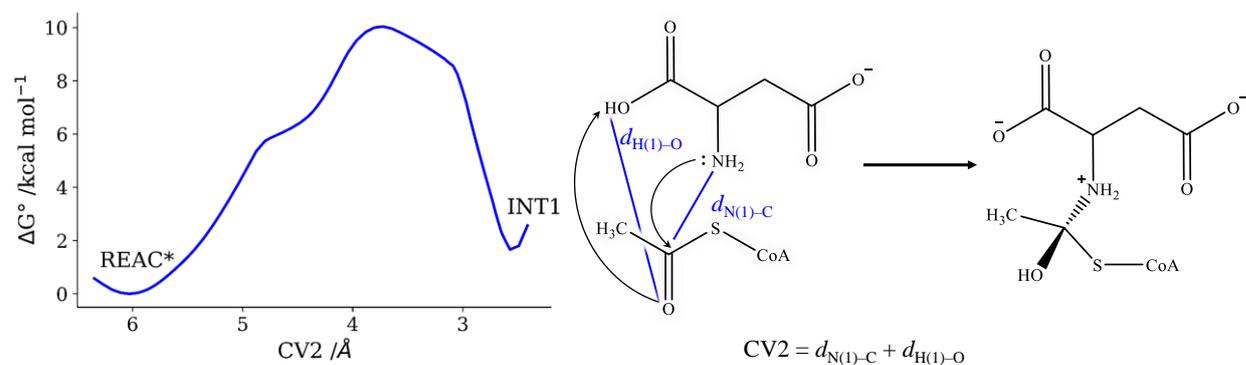


Figure S3. Computed Gibbs energy profile for the step REAC* → INT1.

Step 3: INT1 → INT2.

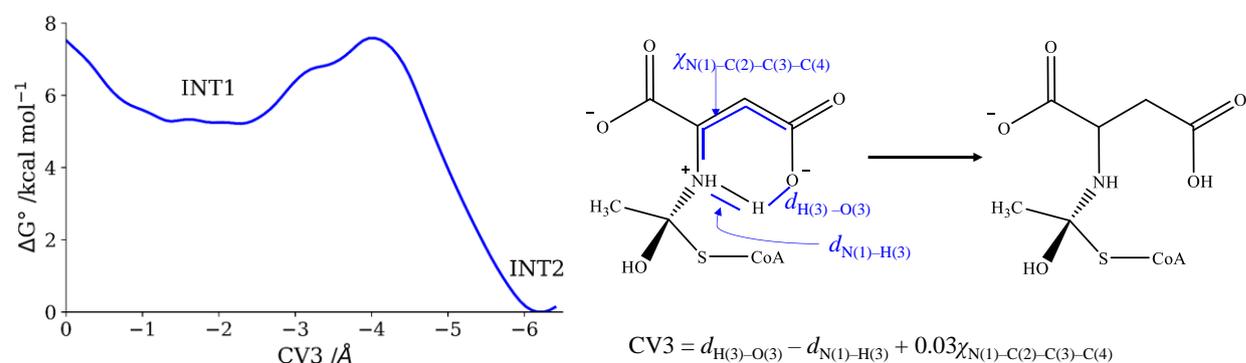


Figure S4. Computed Gibbs energy profile for the step INT1 → INT2.

Step 4: INT2 → PROD.

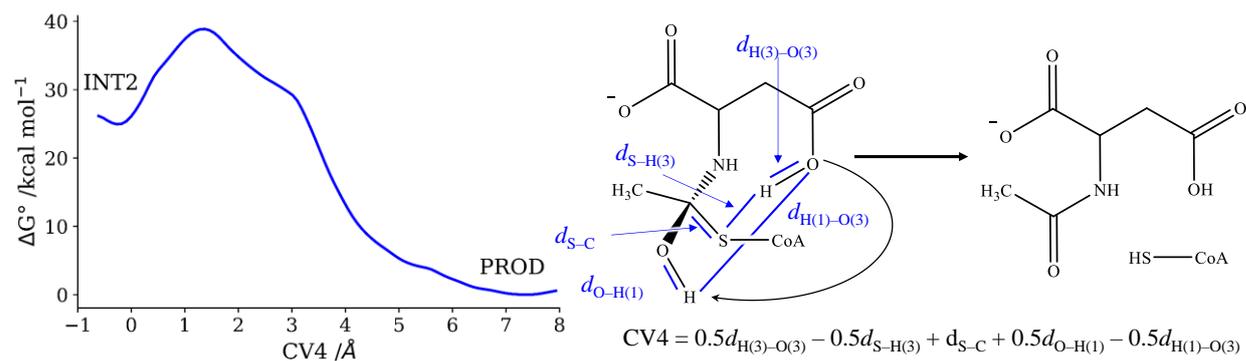


Figure S5. Computed Gibbs energy profile for the step INT2 → PROD.

References

- S1 G. Tahay, E. Wiame, D. Tyteca, P. J. Courtoy, and E. Van Schaftingen, *Biochem. J.*, 2012, **441**, 105.
- S2 V. Polyakov, A. E. Kniga, B. L. Grigorenko and A. V. Nemukhin, *ACS Chem. Neurosci.*, 2020, **11**, 2296.