

Supporting Information

Protein Conformational Landscapes and Catalysis. Influence of active site conformations in the reaction catalyzed by L-Lactate Dehydrogenase.

Katarzyna Świderek,^{*,1,2} Iñaki Tuñon¹, Sergio Martí,³ and Vicent Moliner^{*,3}

1. Departament de Química Física, Universitat de València, 46100 Burjassot, (Spain)

2. Institute of Applied Radiation Chemistry, Lodz University of Technology, 90-924 Lodz, (Poland)

3. Departament de Química Física i Analítica, Universitat Jaume I, 12071 Castelló (Spain)

Corresponding Authors

*E-mail: katarzyna.swiderek@uv.es. Fax: (+34) 963544564

*E-mail: moliner@uji.es. Fax: (+34) 964728066

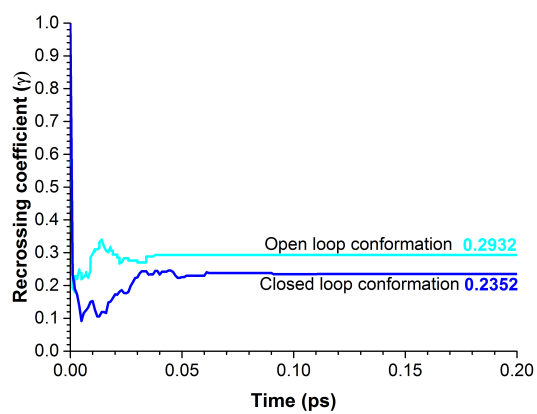


Figure S1. Time-dependent evolution of the recrossing transmission coefficients, $\gamma(t)$, obtained for both conformations of the enzyme at 300 K.

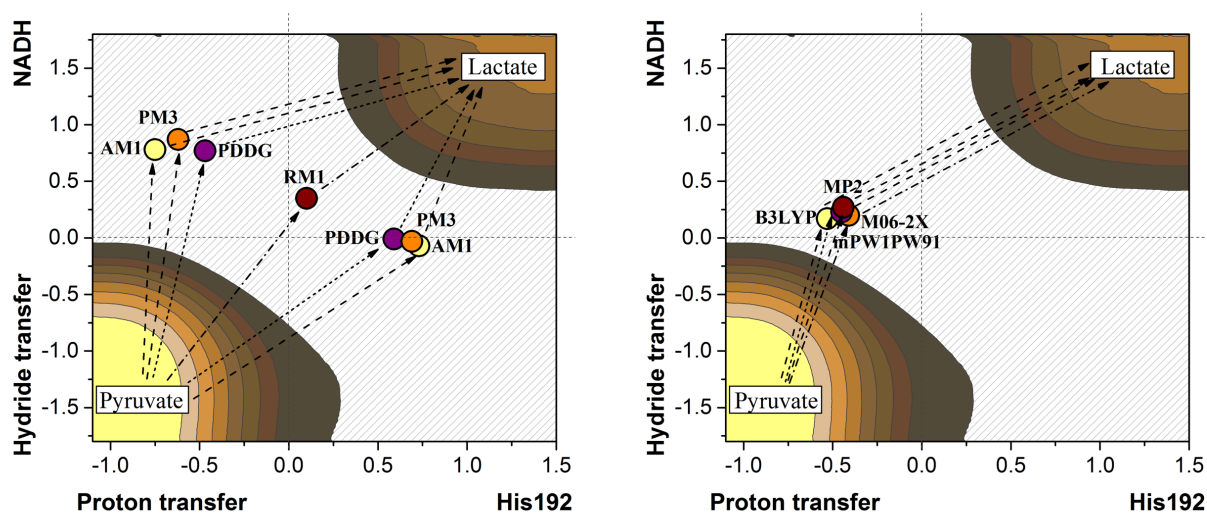


Figure S2. Summary of TS localized in the closed active site at different level of QM theory during QM/MM calculations. On left semiempirical (AM1 – yellow, PM3 – orange, PDDG/PM3 – purple, RM1 – brown), on right DFT and ab initio methods (B3LYP – yellow, M06-2X – orange, mPW1PW91 – purple, MP2 – brown). The reaction coordinate for the hydride transfer is defined as the the anti-symmetric combination of the distances between the transferring hydride-ion and the donor ($C4_{\text{Nic}}$) and the acceptor ($C2_{\text{pyr}}$) atoms. For the proton transfer the reaction coordinate is defined as the difference in the distance of the bonds between the transferring proton and the donor (N_{His}) and the acceptor (O_{pyr})

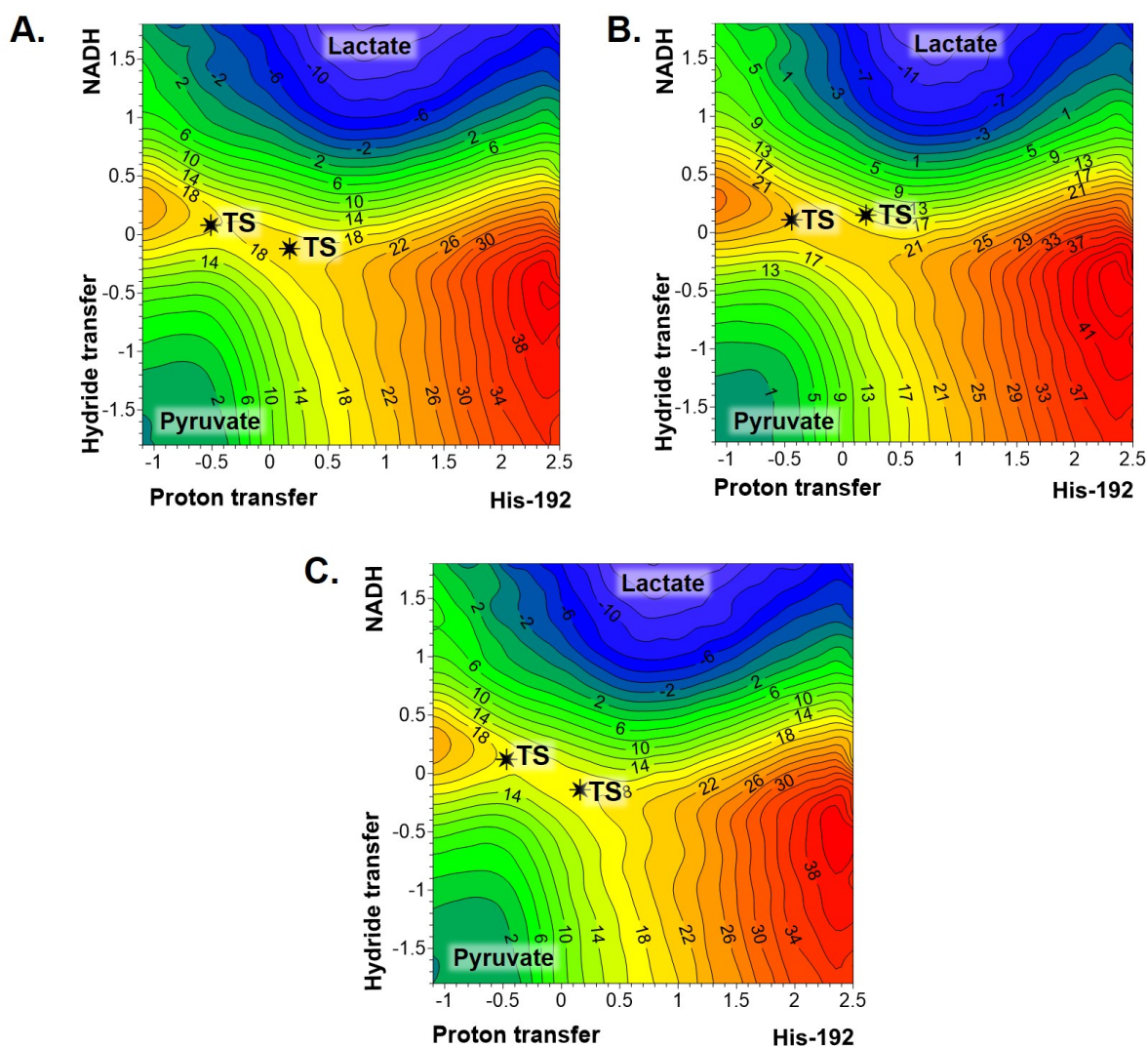


Figure S3. RM1/MM free energy surfaces, computed as 2D PMFs, with spline corrections at: A) B3LYP/MM; B) M06-2X/MM; and C) mPW1PW91/MM level of theory for the pyruvate to lactate transformation catalysed by LDH with open loop conformation. Values of isoenergetic contour lines are reported in $\text{kcal}\cdot\text{mol}^{-1}$, and distances in Å. Black stars indicate the position of TSs localized on the PESs at the corresponding levels of theory.

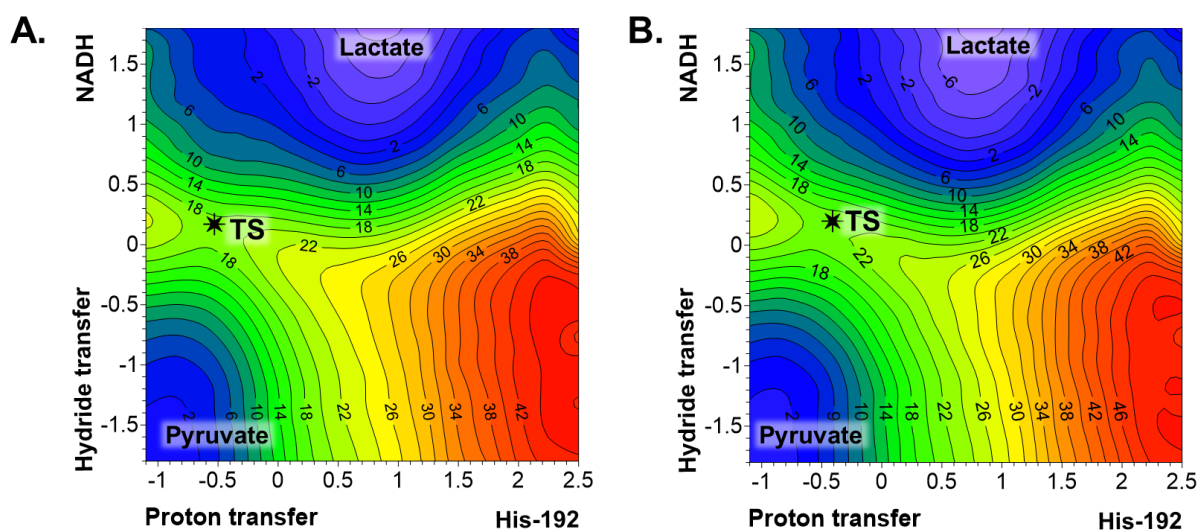


Figure S4. AM1/MM free energy surfaces, computed as 2D PMFs, with spline corrections at: A) B3LYP/MM; and B) M06-2X/MM level of theory for the pyruvate to lactate transformation catalysed by LDH with closed loop conformation. Values of isoenergetical contour lines are reported in $\text{kcal}\cdot\text{mol}^{-1}$, and distances in \AA . Black stars indicate the position of TSs localized on the PESs at the corresponding levels of theory.

Table S1. Sum of ChelpG atomic charges on His192, Pyruvate and NADH species (in a.u.) computed in reactant complex (RC), TS and product complex (PC) at M06-2X/MM level for the open and closed loop conformation

	RC	TS	PC
Open loop conformation			
imidazole ring of His192	1.020	0.625	0.312
pyruvate	-1.164	-1.634	-1.271
nicotinamide ring of NADH	0.145	0.506	0.959
Closed loop conformation			
imidazole ring of His192	1.004	0.612	0.060
pyruvate	-1.096	-1.510	-1.102
nicotinamide ring of NADH	0.093	0.551	1.042