A computational study on the catalytic mechanism of Pdx2: a glutaminase containing the Cys-His-Glu triad

André F. Pina[1,2]*, Sérgio F. Sousa[1,2], and Nuno M.F.S.A. Cerqueira[1,2]

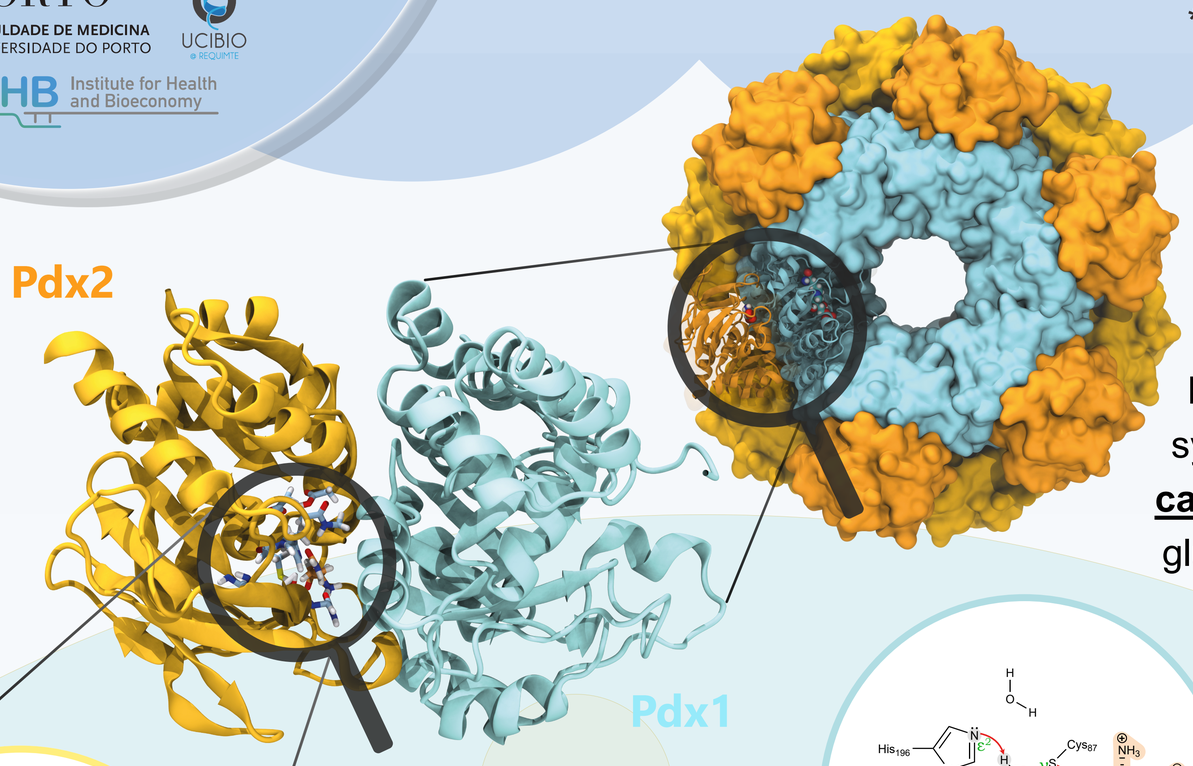
[1] Associate Laboratory i4HB – Institute for Health and Bioeconomy, Faculty of Medicine, University of Porto, 4200-319 Porto, Portugal

[2] UCIBIO – Applied Molecular Biosciences Unit, BioSIM – Department of Biomedicine, Faculty of Medicine, University of Porto, 4200-319 Porto, Portugal

* apina@med.up.pt in/andrefpina @andrefpina

Biomolecular SIMulations Research Group

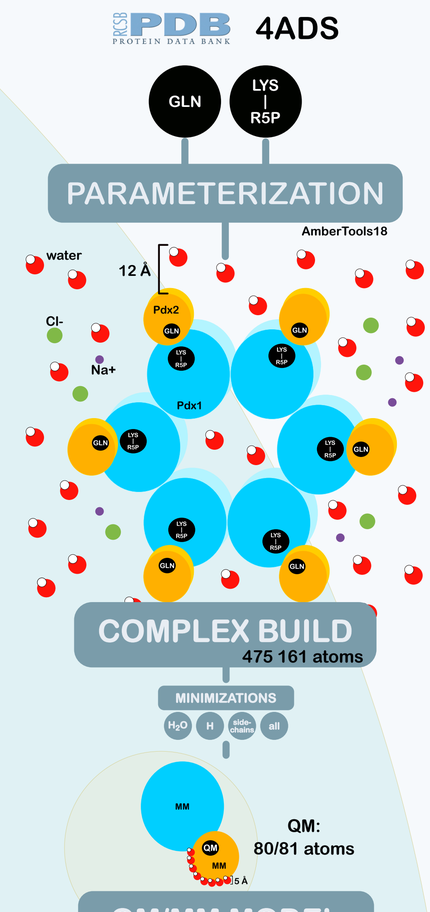
info@biosim.pt www.biosim.pt



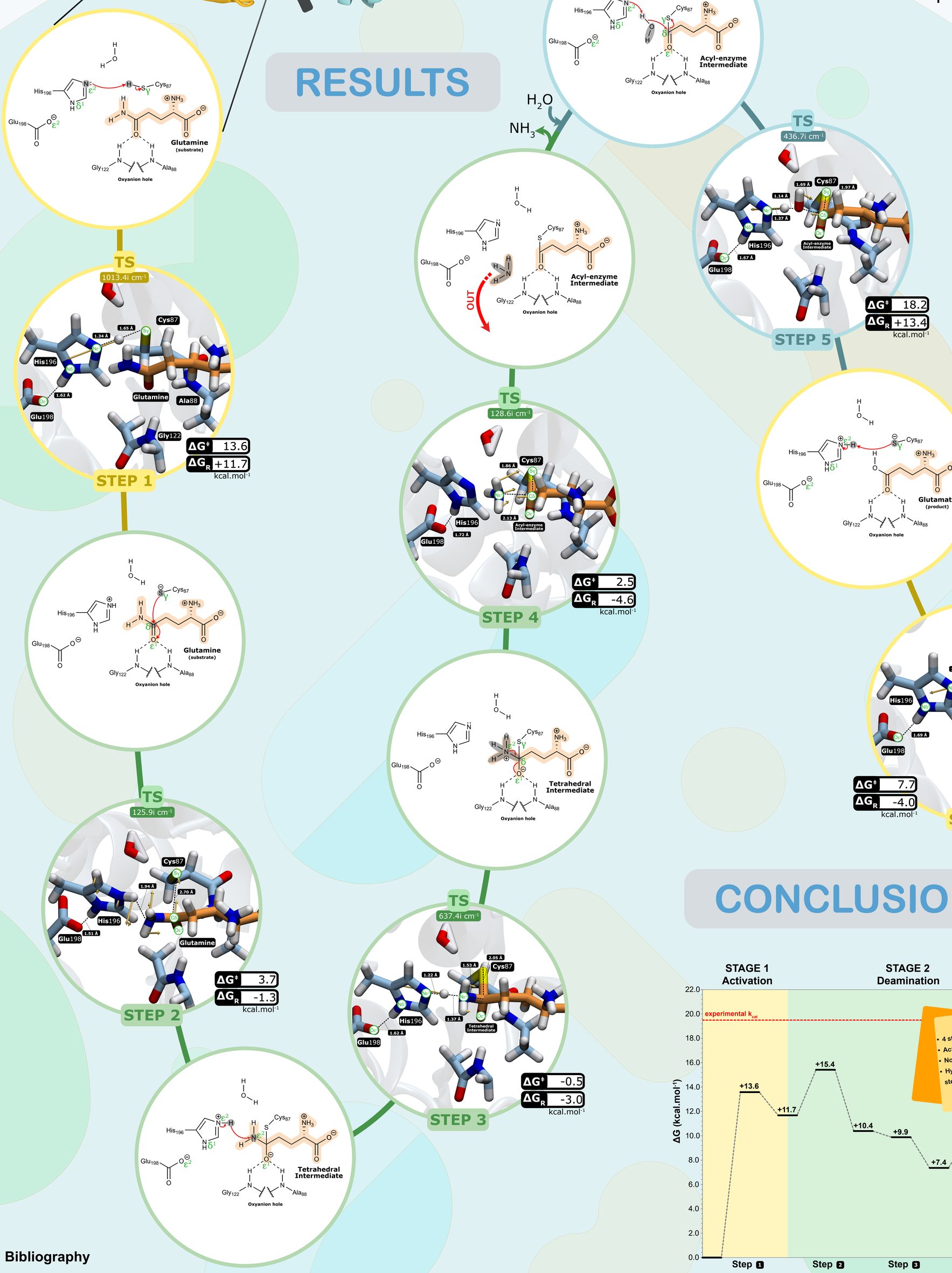
INTRODUCTION

Pdx2, the glutaminase subunit of the pyridoxal 5'-phosphate (PLP) synthase, is a key enzyme in the synthesis of PLP. It employs a **non-canonical Cys-His-Glu triad** to catalyze the deamination of glutamine to glutamate and ammonia – the source of the nitrogen of PLP. For this reason, Pdx2 is considered a novel and promising drug target against diseases such as Malaria and Tuberculosis, whose pathogens rely on this enzyme to obtain PLP.

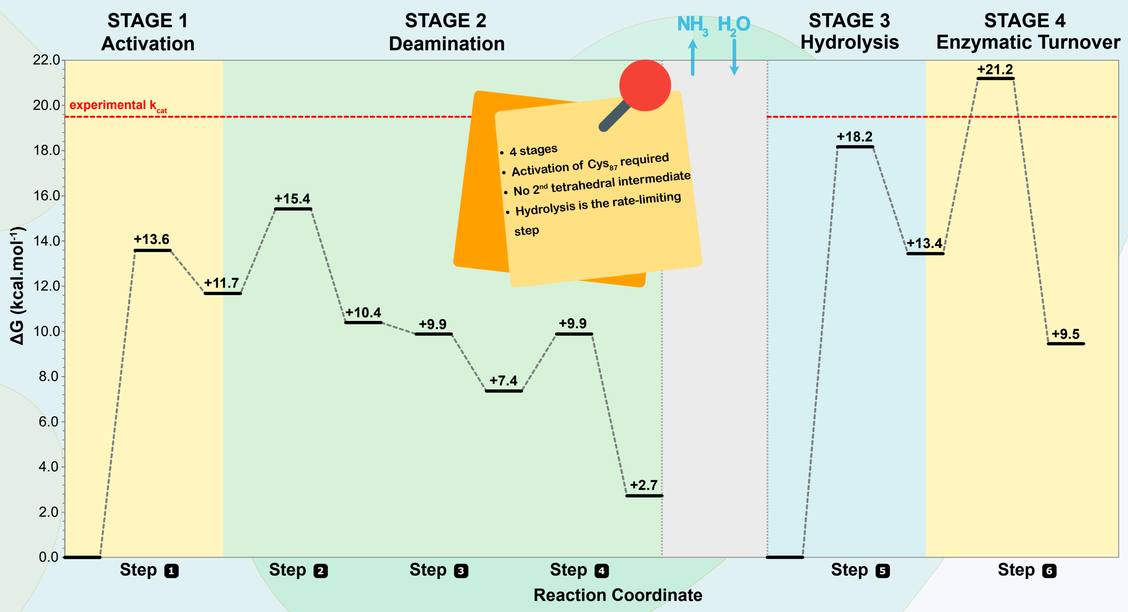
METHODS



RESULTS



CONCLUSION



Bibliography

Pina, A.F., Sousa, S.F. and Cerqueira, N.M.F.S.A. (2021), The Catalytic Mechanism of Pdx2 Glutaminase Driven by a Cys-His-Glu Triad: A Computational Study. ChemBioChem. DOI: 10.1002/cbic.202100555

This work was supported by the Applied Molecular Biosciences Unit — UCIBIO and Associate Laboratory i4HB, which are financed by national funds from FCT (UIDP/04378/2020, UIDB/04378/2020, and LA/P/0140/2020). This work was also partially supported by the PTDC/QUI-QFI/31689/2017 project financed by FCT. AFP acknowledges FCT for his PhD grant SFRH/BD/136594/2018 and SS for grant 2020.01423.CEECIND. Some of the calculations were produced with the support of INCD funded by FCT and FEDER under the projects 01/SAICT/2016 number 022153, CPCA/A00/7140/2020, and CPCA/A00/7145/2020.