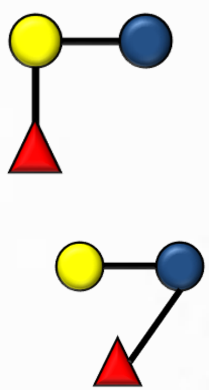
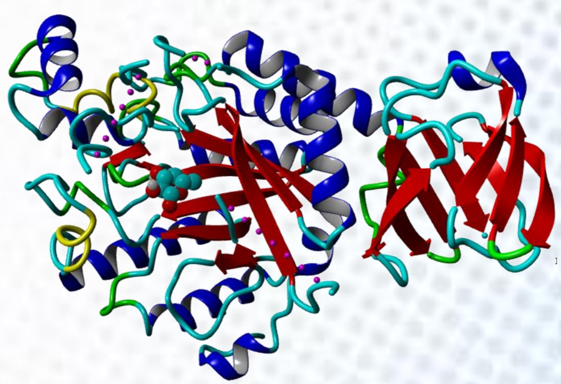
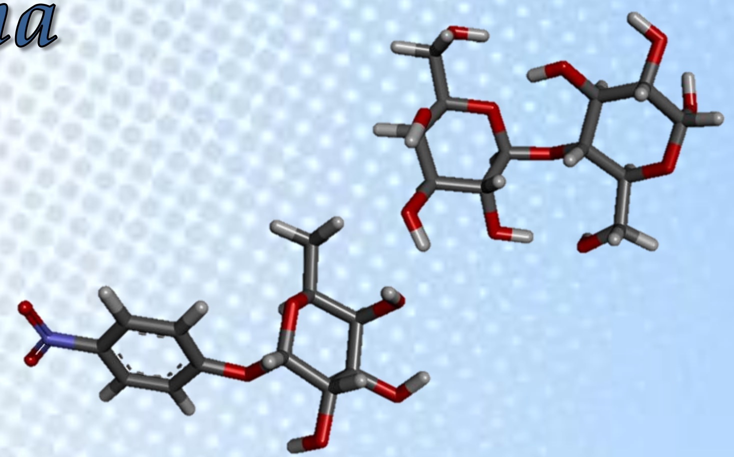
ECSOC 24
The 24th International Electronic Conference on Synthetic Organic Chemistry
15 Nov–15 Dec 2020

An *in silico* approach to enzymatic synthesis of fucooligosaccharides using α-L-fucosidase from *Thermotoga maritima*







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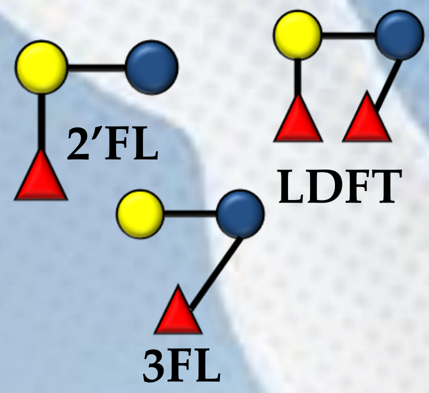
INTRODUCTION



Fucooligosaccharides (FucOS) = main oligosaccharide group in human milk

Immunomodulatory

Prebiotic

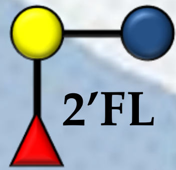
FucOS abundance respect to total oligosaccharides: <u>65-77%</u>

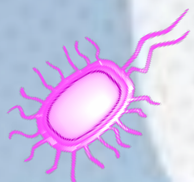
Antiviral

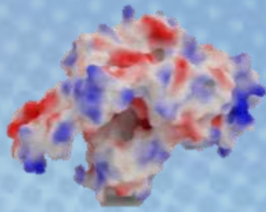
FucOS abundance respect to total oligosaccharides: <u>~1%</u>

Cognitive enhancer

INTRODUCTION



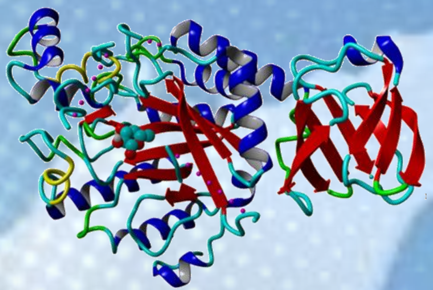




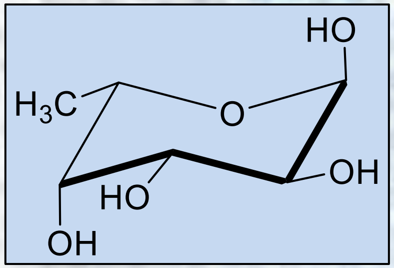
Enzymatic synthesis as potential alternative

Synthetic production by fermentation process

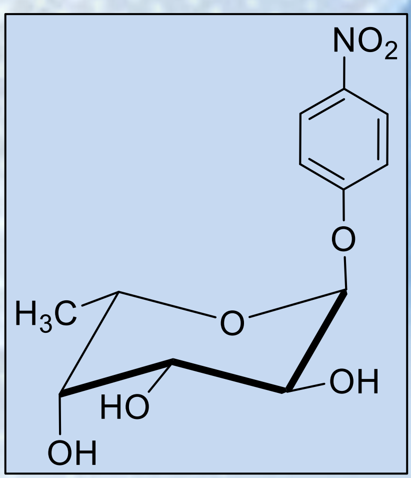
α-L-fucosidase from *Thermotoga maritima* as power catalyst



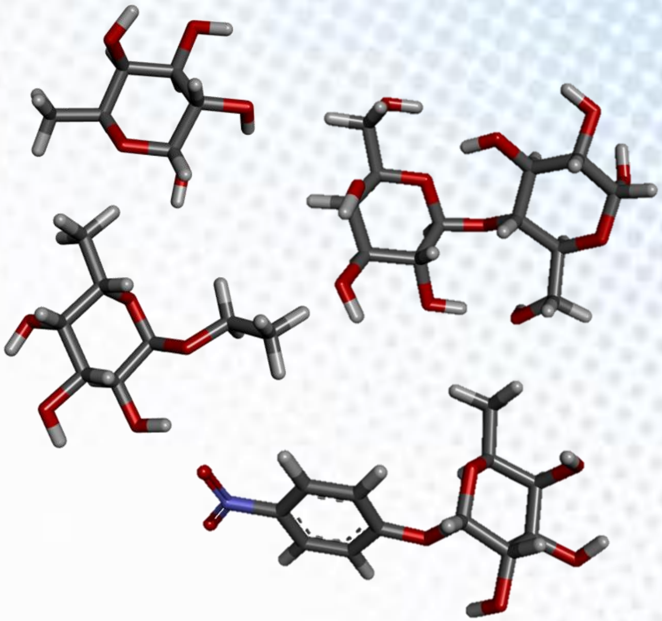
Alternatives are highly desirable



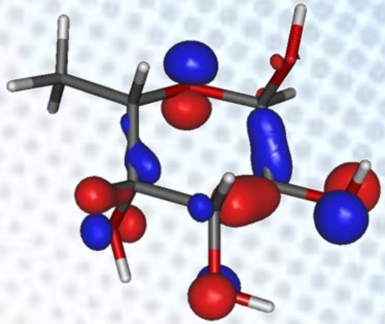
Few substrates options for the α-L-fucosidase



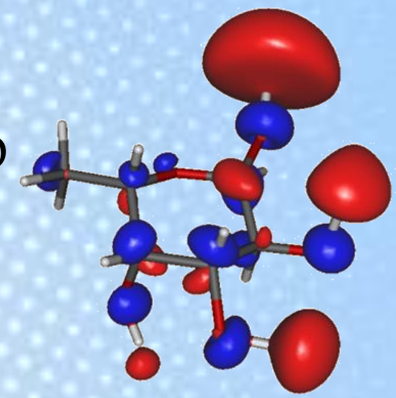
METHODS



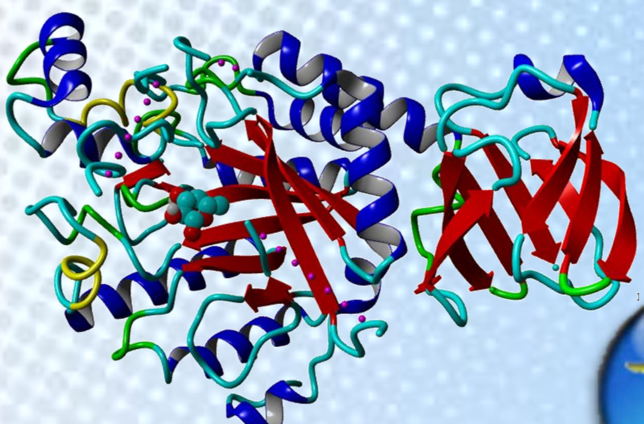
Geometry optimization of α/β- fucose, ethyl-fucose, pNP-fucose and lactos by DFT at B3LYP/6-311++G(2d,2p)



HOMO-LUMO descriptors



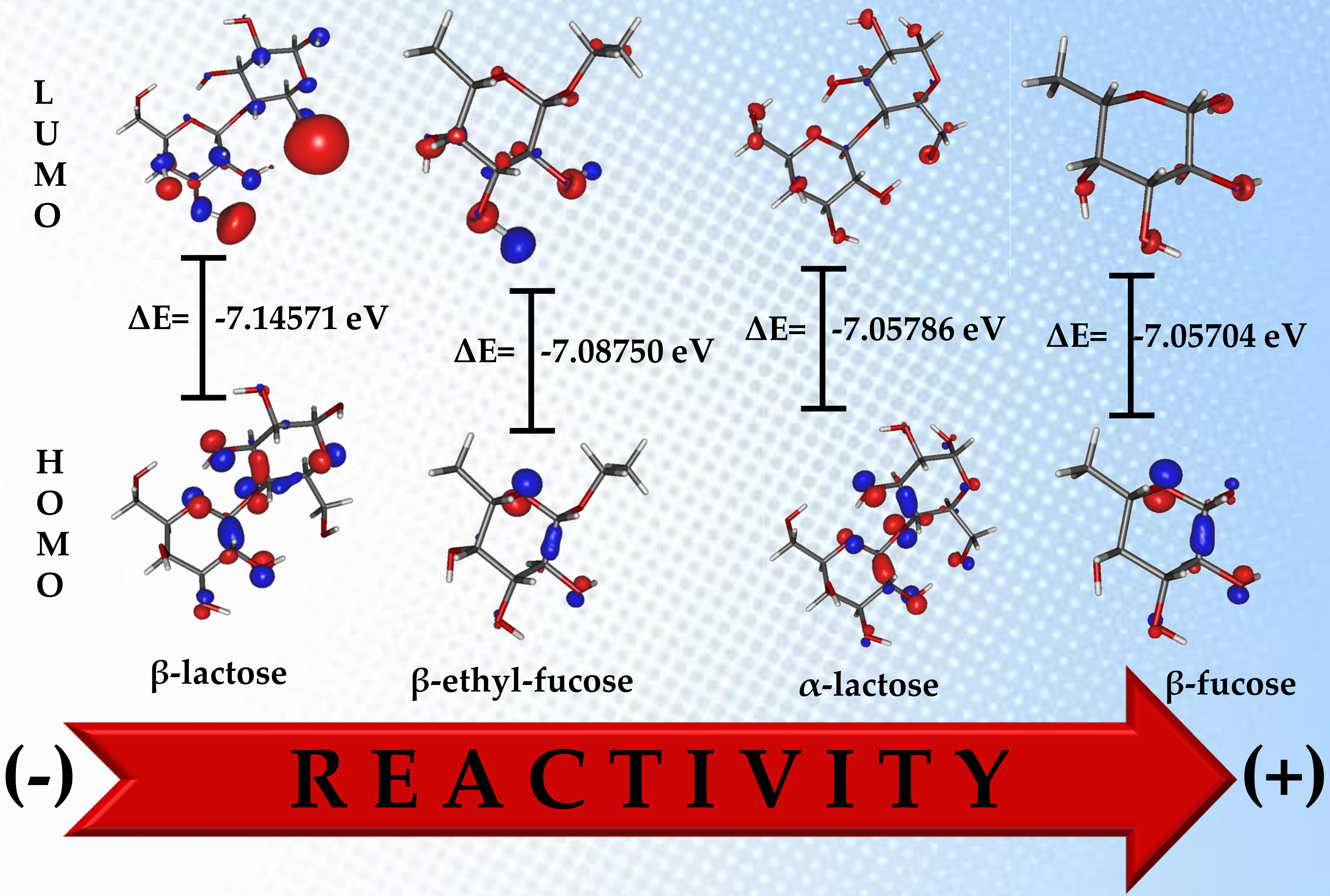
Molecular docking by Autodock VINA with PyRx software



<u>Hydrolysis processes</u>**:** Single docking among fucosyl donors and enzyme

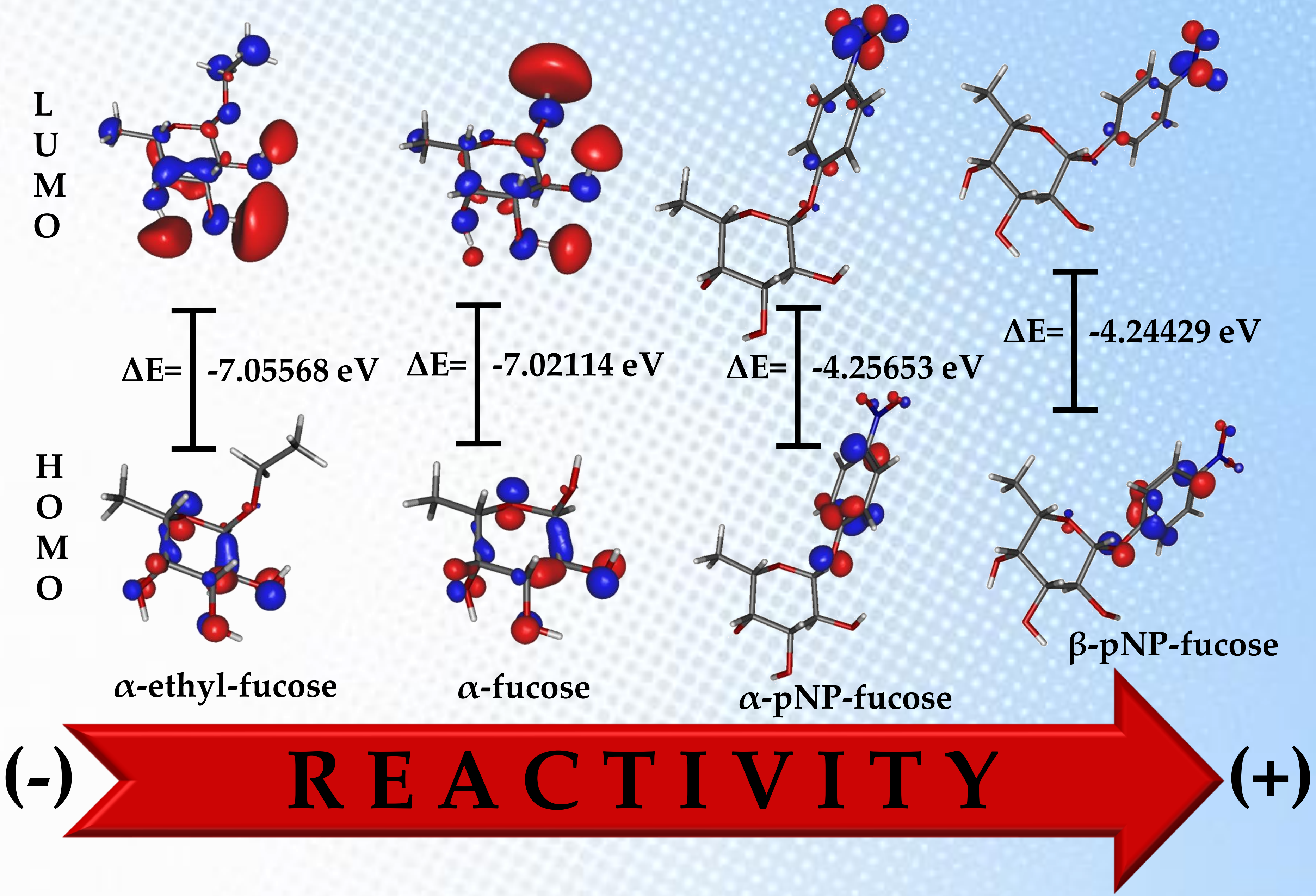
<u>Transfucosylation process</u>**:** Sequential docking to form β-fucose/enzyme complex and then docking with lactose

RESULTS

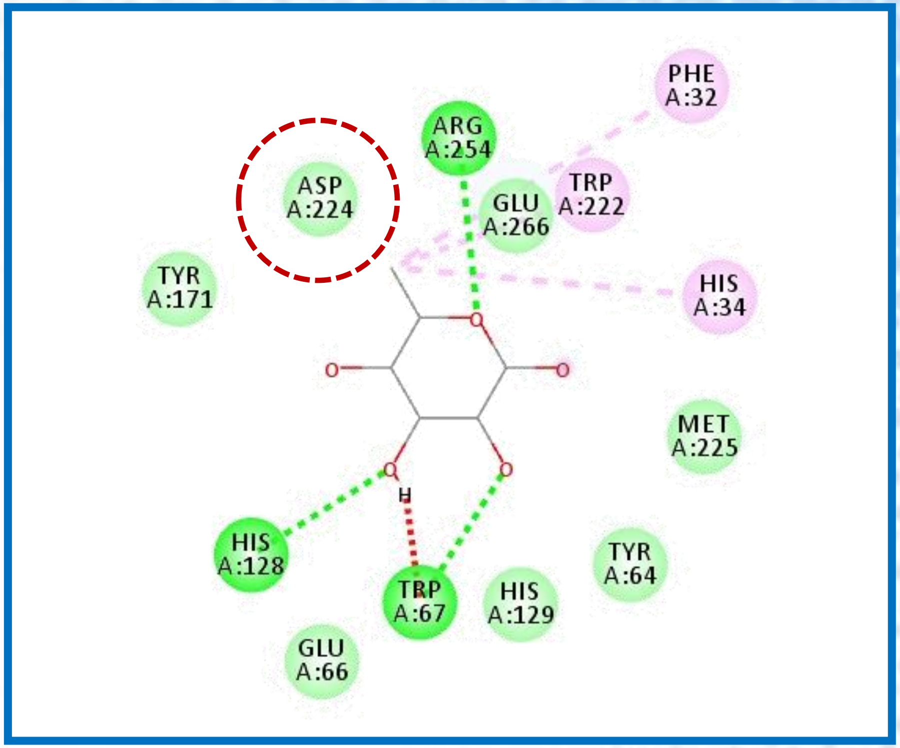


LUMO
HOMO
ΔE= -7.14571 eV
ΔE= -7.08750 eV
ΔE= -7.05786 eV
ΔE= -7.05704 eV
β-lactose
β-ethyl-fucose
α-lactose
β-fucose
(-)
REACTIVITY
(+)

RESULTS

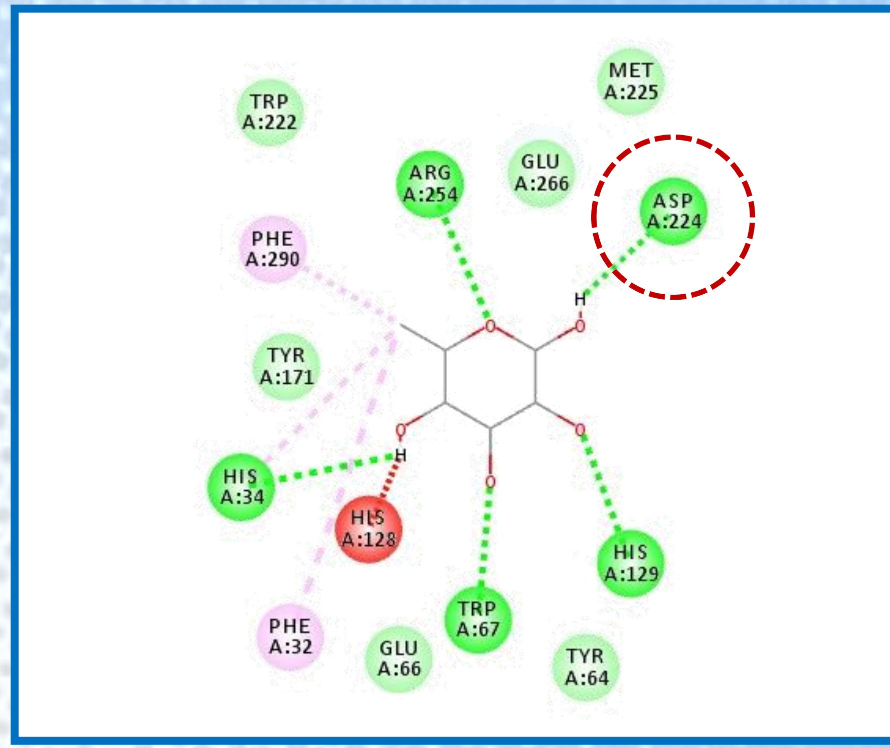

LUMO
HOMO
ΔE= -7.05568 eV
ΔE= -7.02114 eV
ΔE= -4.25653 eV
ΔE= -4.24429 eV
α-ethyl-fucose
α-fucose
α-pNP-fucose
β-pNP-fucose
(-)
REACTIVITY
(+)

RESULTS



α-fucose

Coupling energy: -6.0 kcal·mol^{-1}



β-fucose

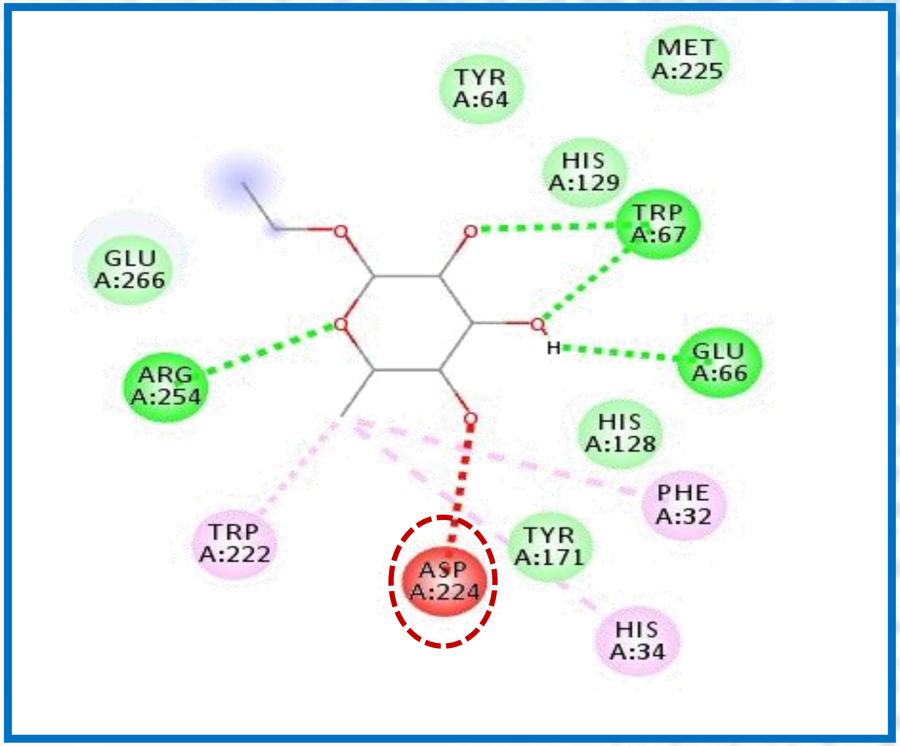
Coupling energy: -6.3 kcal·mol^{-1}

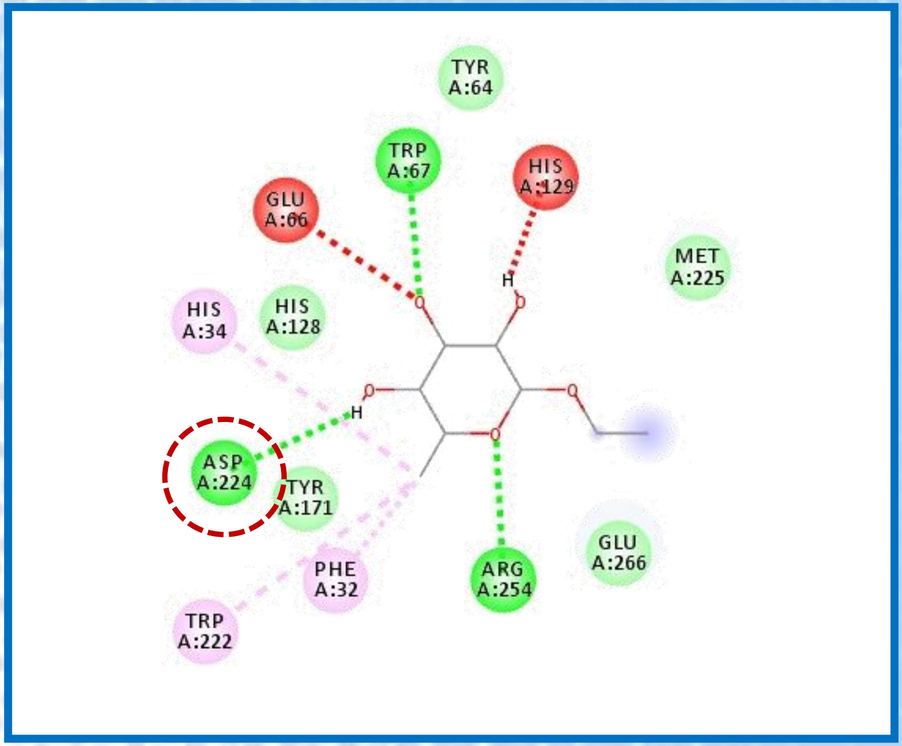
Interactions

- van der Waals
- Conventional Hydrogen Bond
- Pi-Anion
- Pi-Pi T-shaped
- Pi-Alkyl
- Unfavorable

DOCKING FOR HYDROLYSIS

RESULTS



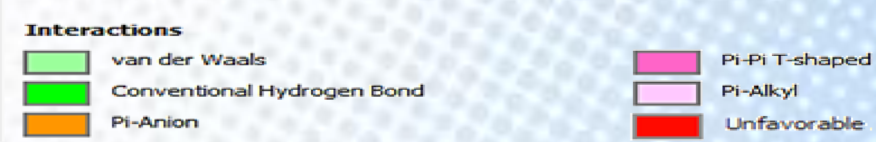


***α*-ethyl-fucose**

Coupling energy: -5.5 kcal·mol^{-1}

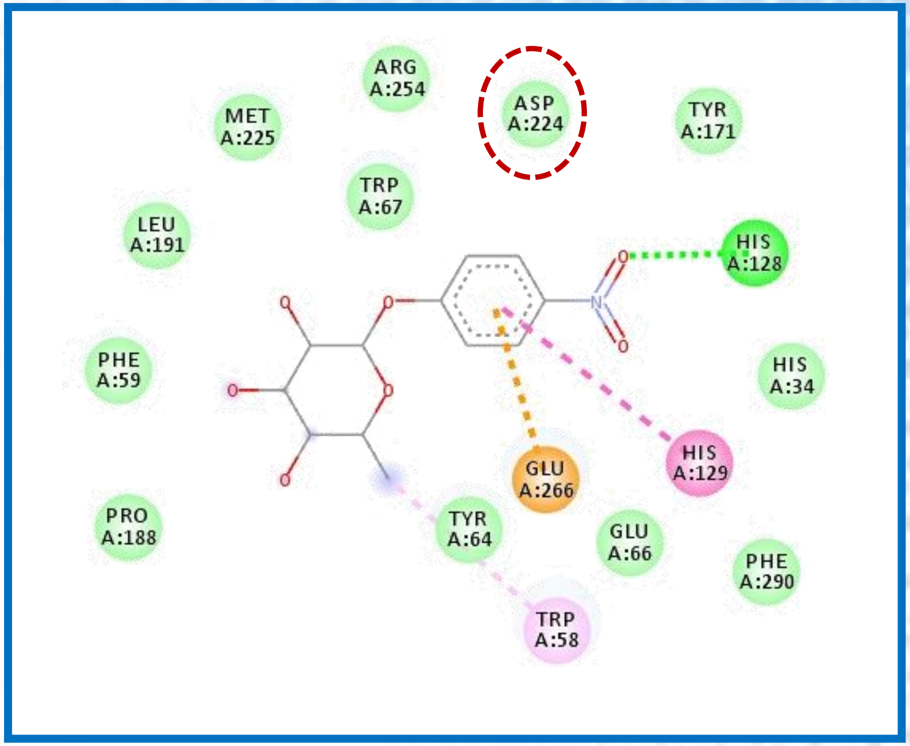
***β*-ethyl-fucose**

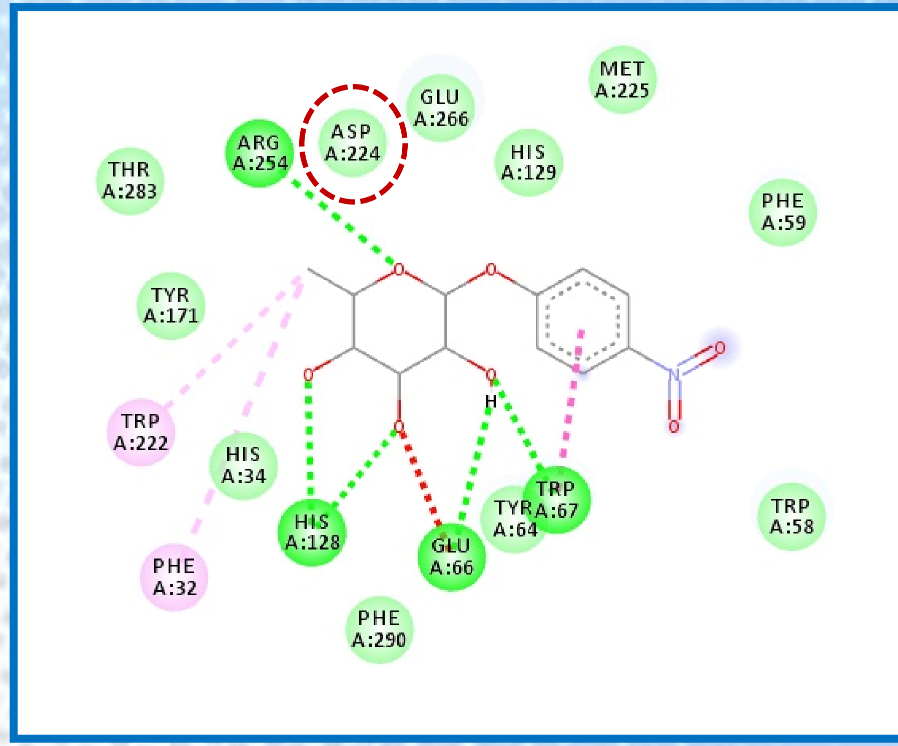
Coupling energy: -5.8 kcal·mol^{-1}



DOCKING FOR HYDROLYSIS

RESULTS



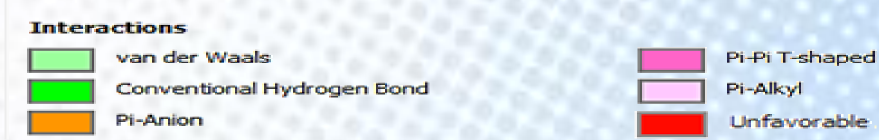


α-pNP-fucose

Coupling energy: -5.9 kcal·mol^{-1}

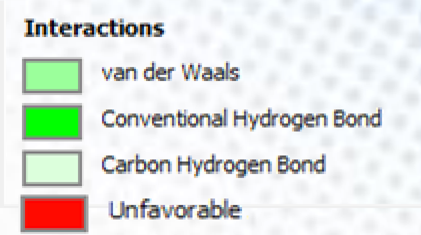
β-pNP-fucose

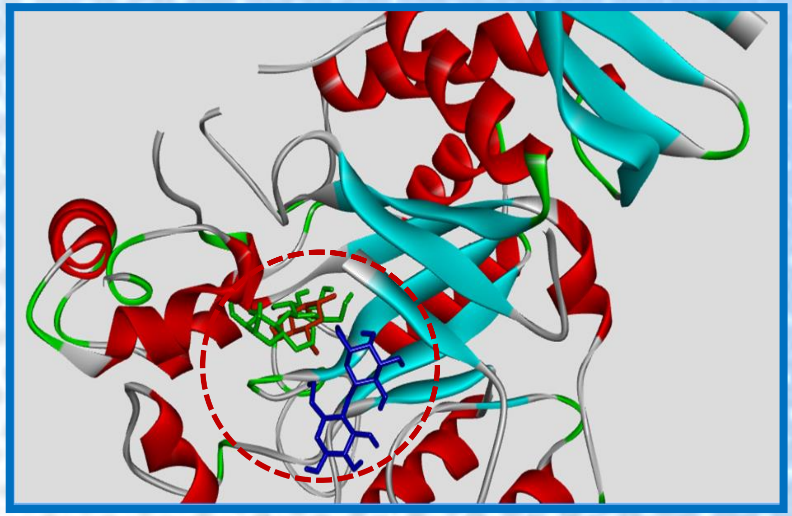
Coupling energy: -6.4 kcal·mol^{-1}



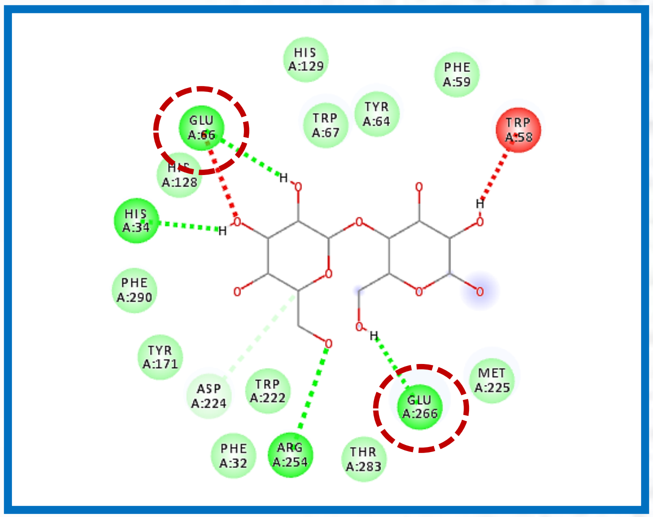
DOCKING FOR HYDROLYSIS

RESULTS

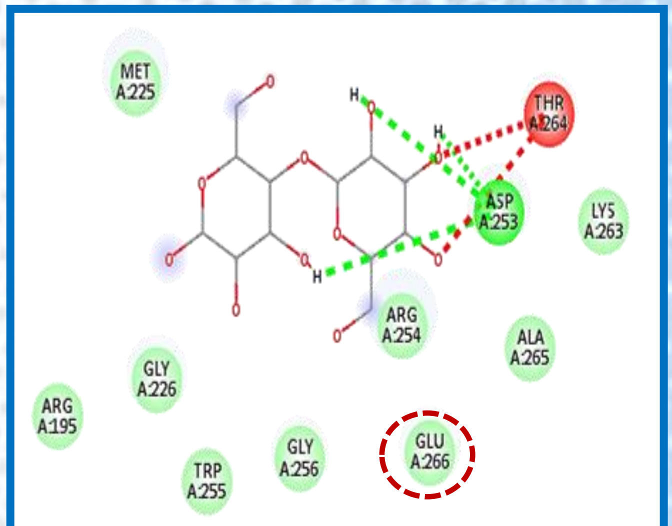




β-Fucose
α-Lactose
β-Lactose



α-lactosa
Coupling energy: -5.7 kcal·mol^{-1}

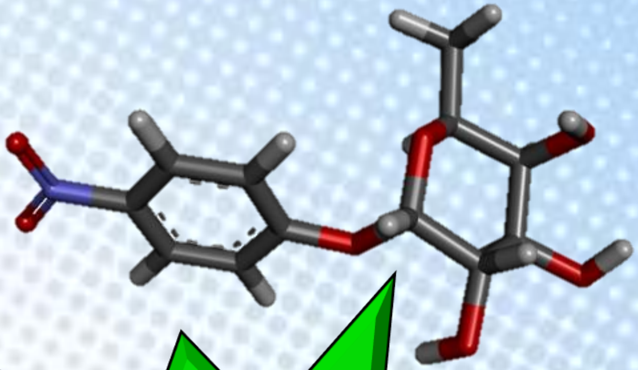


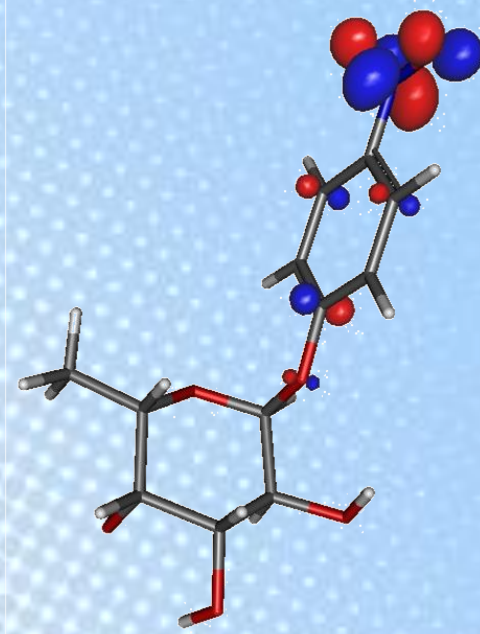
β-lactose
Coupling energy: -5.8 kcal·mol^{-1}

DOCKING FOR TRANSFUCOSYLATION

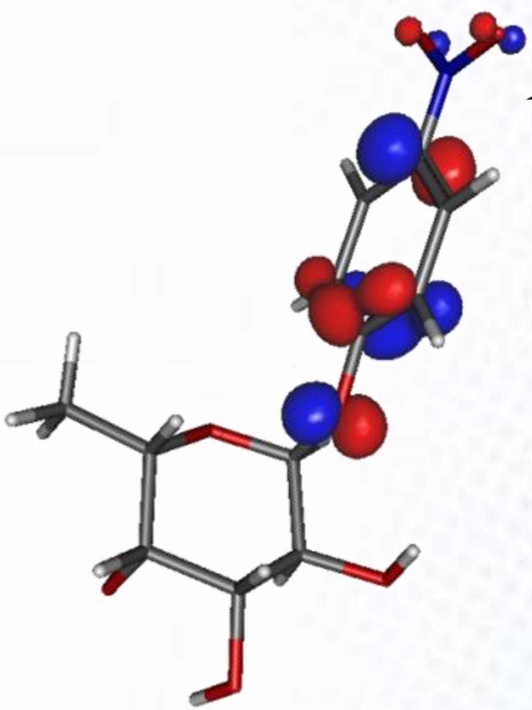
CONCLUSIONS

In silico insights here obtained





Next generation fucosyl transfer agents



Reactivity similar to pNP-fucose but with lower toxicity