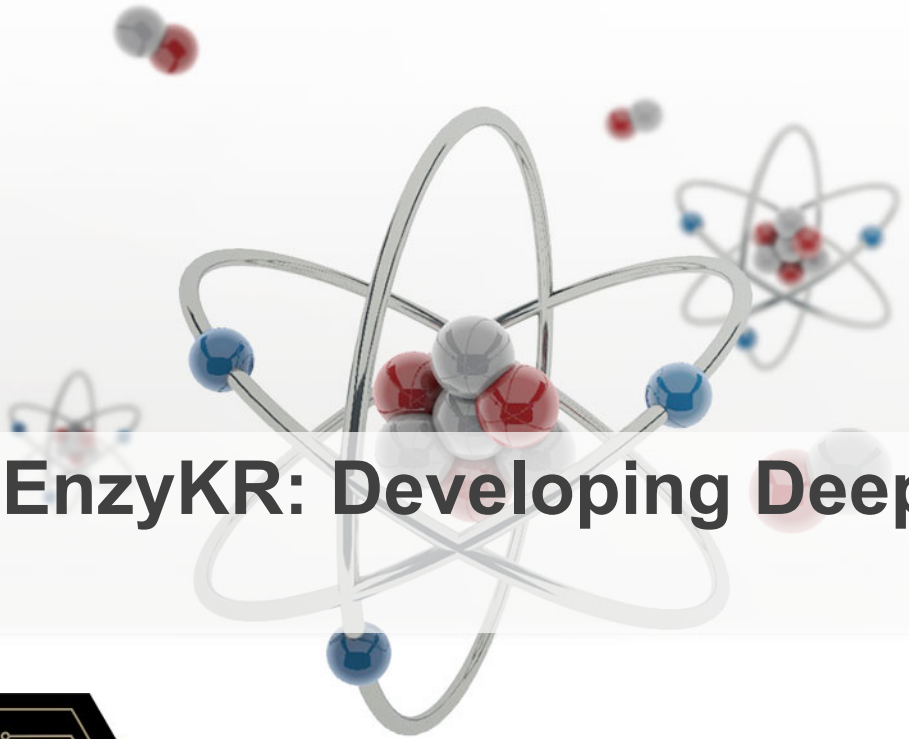

EnzyKR: Developing Deep Learning Framework for Kinetic Resolution

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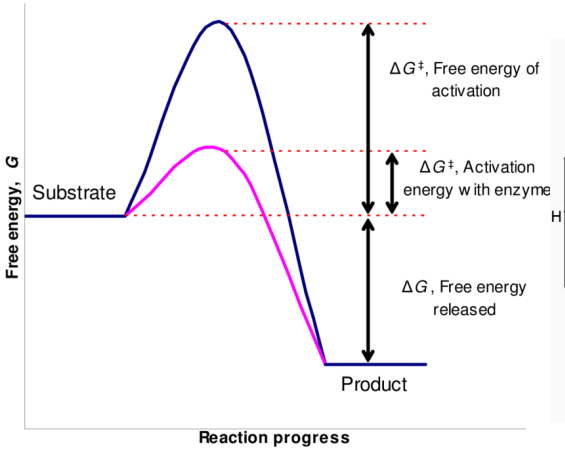
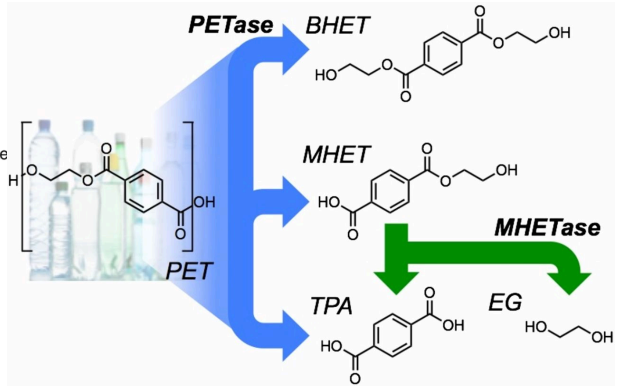
Department of Chemistry
Vanderbilt University

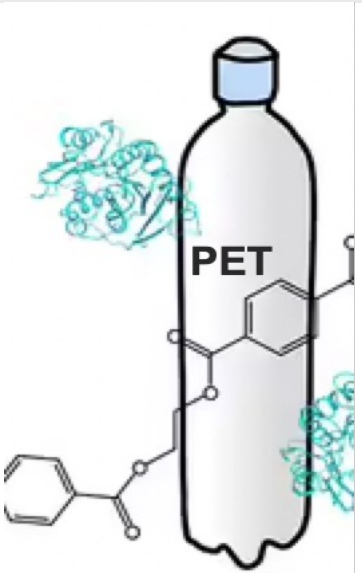
Background: Enzyme Engineering

Enzymes are curial in Pharmaceutical and Envi ronment Engineering such as PET degradation and anti-biotics syntheses

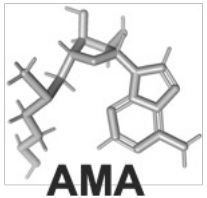
Enzymes can make the biocatalytic reaction easier by reducing the reaction activation free energy







1JRL



6ANE

David, Allan E. Immobilization of enzymes on nanoporous, silica co mposites. University of Maryland, College Park, 2004.

Motivation: Activation free energy prediction

Rational design

Directed evolution

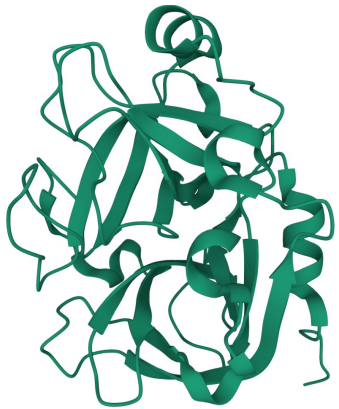
Virtual Ranking

3R3U

Fluoroacetate dehalogenase

Enzyme

modification



Functions

modification

Catalytic Reaction Rate

Substrate Selectivity

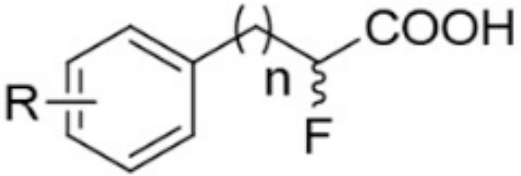
Enzyme stability

Activation free energy modification

How can we predict the activation free energy chirality preference?

O, Gabriel, et al. Physical Chemistry Chemical Physics 18.19 (2016): 13346-13356

Catalytic reaction

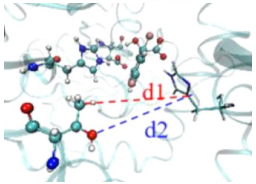


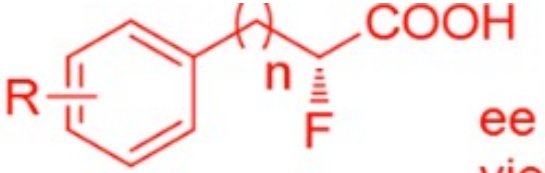
1a-1j

n= 0, R = H, 2-F, 2-Cl, 4-F,
4-Cl, 4-Br, 4-CF_3,
2,4-2F, 3,5-2F;
n = 1, R=H

RPA1163

WT, W185N
or W185T

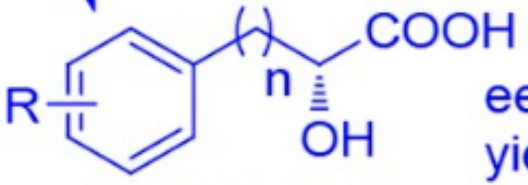




(*R*)-2a-2j

ee ≥ 97%,
yield ≈ 1 g

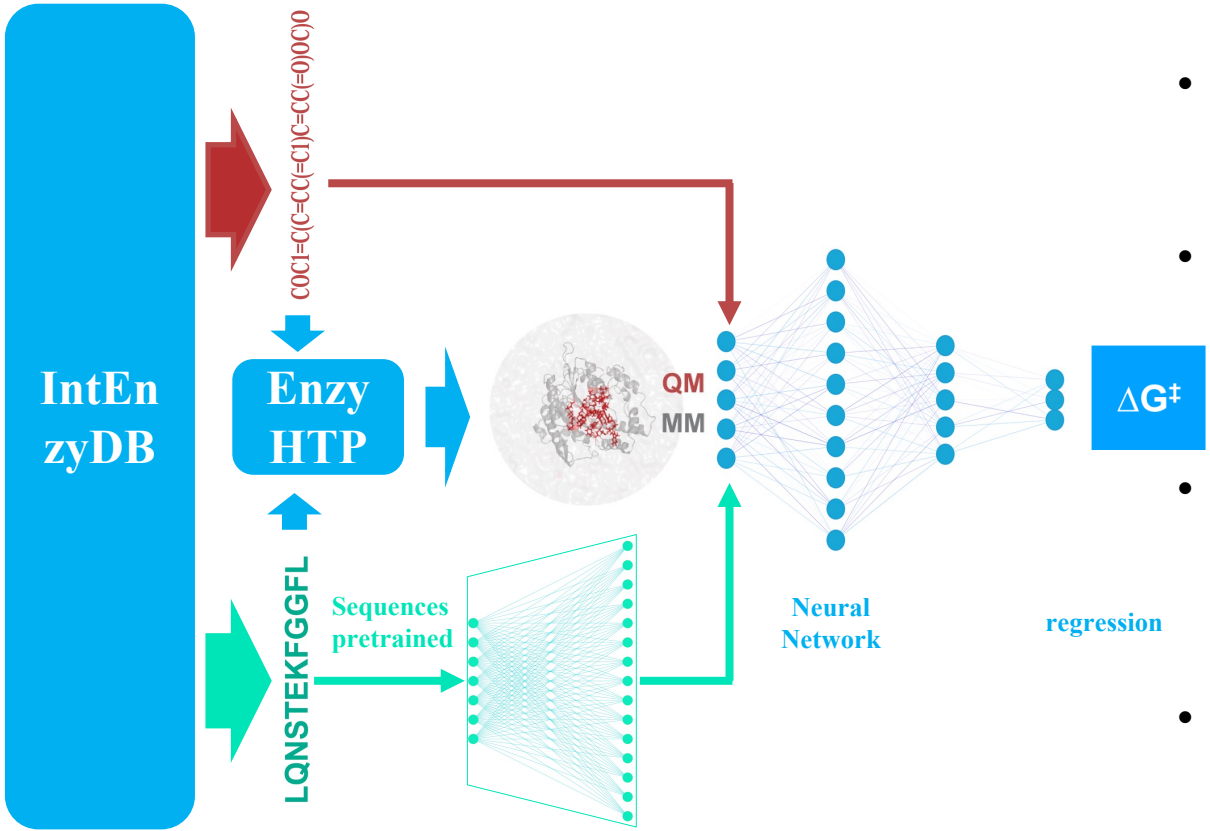
+



(*R*)-3a-3j

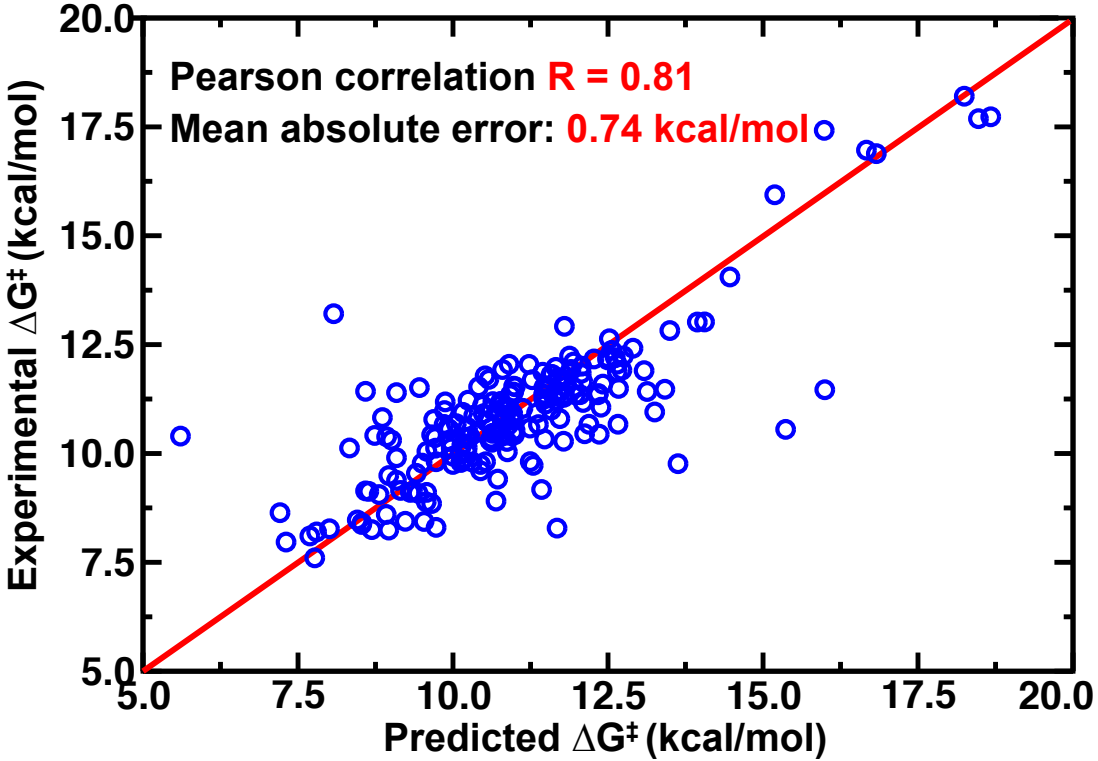
ee ≥ 99%,
yield ≈ 1 g

Solution: Neural networks



- High quality energy annotation
- High Throughput feature generations
- High performance deep learning model capacity
- Well aligned substrate-enzyme

Results - Regressor



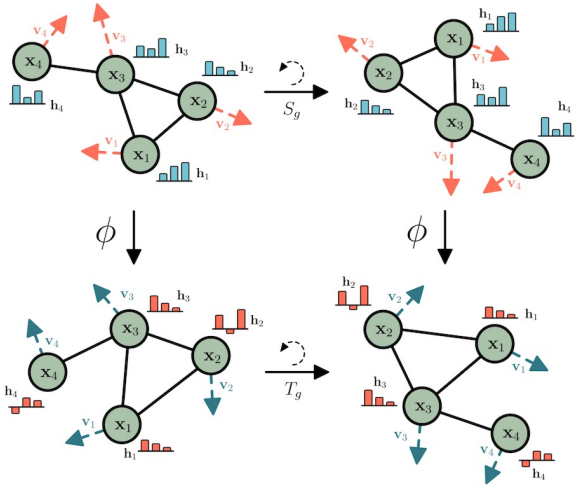
Regressor results show robustness to different frames of MD trajectory

Prelim Result: chirality results (no further updated)

result_without_3DGNN_KDR_prediction_R&S_updated

dg kcal/mol	EnzyKD preference	S-1a alpha- fluorocarboxylic	R-1a alpha-fluorocarboxylic acids	Arxiv paper - preference	S-1a alpha-fluorocarboxylic	R-1a alpha-fluorocarboxylic
a	3.4593	11.2612	14.7205	0.4014	11.4737	11.8751
b	2.0945	11.0534	13.1479	0.1038	13.7924	13.8962
c	2.4577	12.3519	14.8096	0.2466	12.9638	13.2104
d	1.4249	12.8753	14.3002	-0.1335	12.2788	12.1453
e	1.6527	12.2234	13.8761	-0.2550	13.6902	13.4352
f	2.2317	13.0021	15.2338	0.1205	13.1173	13.2378
g	4.5247	12.2767	16.8014	-0.1270	12.5798	12.4528
h	5.6941	10.9494	16.6435	0.1570	13.6160	13.7730
i	2.7167	10.6812	13.3979	0.5158	11.3365	11.8523
dg kcal/mol	EnzyKD preference	S-1a halohydrin	R-1a halohydrin	Arxiv paper - preference	S-1a halohydrin	R-1a halohydrin
j	1.1274	15.1103	16.2377	0.1704	11.2672	11.4376
k	-1.5459	16.6074	15.0615	-0.6611	14.1953	13.5342
i	2.554	15.0352	17.5892	0.6216	12.1569	12.7785
m	2.1191	15.9837	18.1028	0.576	11.9865	12.5625
n	0.7454	14.1329	14.8783	-0.5019	15.1397	14.6378
o	3.9119	12.5772	16.4891	0.873	11.9798	12.8528
r	2.313	13.6094	15.9224	1.357	12.416	13.7730
q	-2.5289	16.9286	14.3997	0.5158	11.3365	11.8523
r	2.9046	13.8741	16.7787	-0.8061	14.7824	13.9763

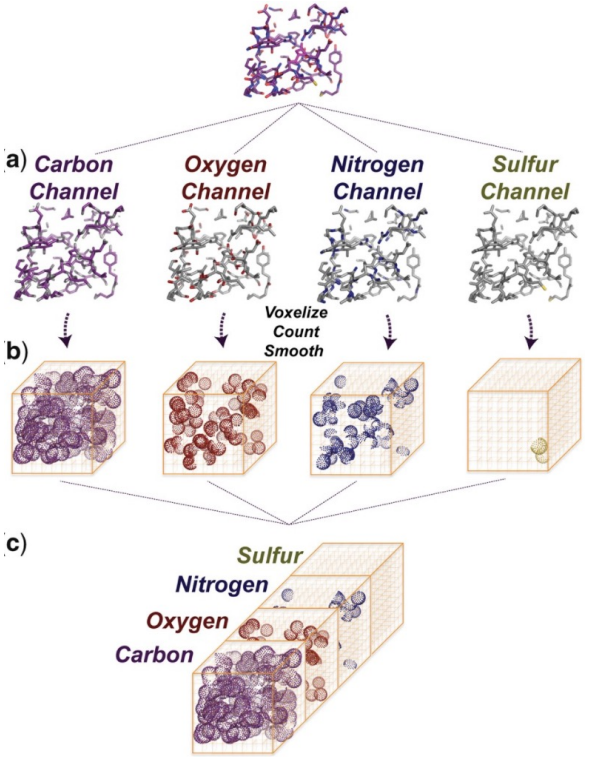
Futures: 3D GNN and coordinates embedding



Pretrained Embedding

Voxel Embedding
Low-N substrates

ΔG‡



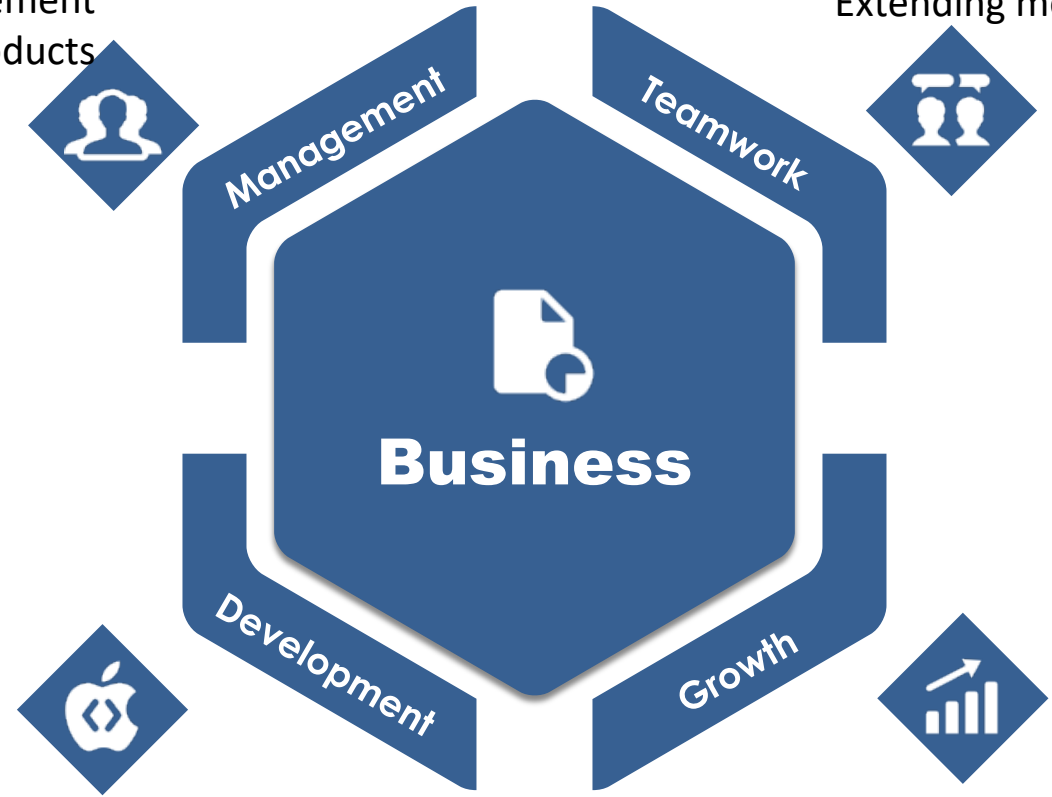
MD trajectory & Products chirality?

Torng, W., et al. (2019). Bioinformatics, 35(9), 1503-1512.

EnzyKR: Business Development Plan

Obtaining a good management team for Sales the products

Extending more experimental users

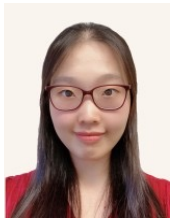


Obtaining better performance models

Developing our pipeline more efficient

Acknowledgement

Data science team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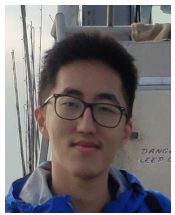
Anvita Gollu

Computational chemistry team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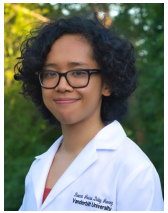
Matthew Tremblay


Reecan Juarez

Group Photo

Funding source

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