Projecte de Treball Fi de Màster (TFM)

Màster en Modelització Computacional Atomística i Multiescala en Física, Química i Bioquímica
UB/UPC

Títol	**Investigant els efectes del tampó en l'estabilitat de les PETases amb simulacions de dinàmica molecular.**
Title	**Investigating buffer effects on the stability of PETases with molecular dynamics simulations**

Director	**Francesco Colizzi**
Departament	**Chemical Biology**
Universitat	**IQAC-CSIC**
Tutor[1]	**Iberio de Pinho Ribeiro Moreira**

Curs	**2023-24**

Summary[2]

Single-use plastics like Poly(ethylene terephthalate) (PET) are extensively used but poorly recycled, leading to environmental pollution. Enzymatic biodegradation presents a cost-effective and selective solution to plastic waste. This proposal originates from the observation that some PET-degrading enzymes, such as the one called PHL7, are effective only at high concentrations of potassium phosphate buffer, greatly limiting their application beyond laboratory settings. The aim of the research will be to use molecular dynamics simulations and their analysis to characterize the molecular determinants of this behavior. Overall, the student will contribute to the Lab's overarching objective of characterizing and engineering PETase variants through advanced molecular simulations and deep-learning-based design, aiming to effectively degrade various types of PET.

Keywords[3] protein dynamics, molecular dynamics simulations, thermal stability, protein design

Breu descripció del projecte[4]

General Objective: The research will focus on exploring the molecular determinants underlying the buffer concentration-dependent stability of the PET-degrading enzyme PHL7 (C. Sonnendecker et al., ChemSusChem 2022, 15, e202101062). The investigation will involve conducting and analyzing molecular dynamics simulations using advanced tools.

Work Plan delivered in different Tasks(T):

Literature Review-T1: Review of scientific literature related to PETases and PHL7, in particular. Understanding the scientific problem and generating initial hypotheses on how to model the system.

Structural Modeling-T2: Use of specialized software for structural modeling of the system of interest and generation of the related force-field parameters (AMBERff with GAFF parameters for the buffer), as well as familiarization with CHARMM-GUI. Construction of atomistic models of the protein embedded in water, containing both high and low concentrations of the potassium phosphate buffer. The X-ray crystal structure of PHL7 will be used as reference (P.K. Richter et al., Nature Communications 2022, 14, 1905)

Molecular Dynamics Simulations-T3: Application of molecular dynamics techniques using software such as GROMACS and PLUMED (M. Bonomi et al., Nature Methods 2019). Execution of simulations to study the behavior and dynamics of the protein at different concentration of the buffer.

Development of Analysis Tools-T4: Creation of analysis tools using PLUMED or scripts based, for example, on dimensionality reduction, clustering, principal component analysis. These tools shall allow for effective and efficient analysis and visualization of simulation results, and the identification of possible region of the protein interacting with the buffer.

Discussion and interpretation of the results-T5: The overall results will be critically analyzed, presented at internal group meeting and discussed with our experimental collaborators at the University of Leipzig.

Writing the Final Report-T6: Drafting a final report following the style of a scientific article. The report will include an introduction to the scientific question, a detailed description of the methods used, the results obtained and their interpretation, as well as the conclusions and potential implications of the research.

For a tentative schedule see the chronogram below.

[1]Si el director no és un professor de la UB o e la UPC, caldrà assignar un tutor del TFM que designarà la Comissió Coordinadora del Màster.
[2]Aquest "summary" és el que apareixerà a la futura pàgina web dedicada al TFM. Procureu que sigui concís i entenedor (máx. 10 línies).
[3]Aquestes "keywords" no només són les que apareixeran al web sinó que ajudaran la Comissió Coordinadora del Màster a **assignar el projecte a un àrea concreta**.
[4]Procureu ser concisos però proporcioneu prou informació per tal que l'estudiant i la Comissió Coordinadora del Màster es facin una idea prou acurada de en què consistirà el treball. **Indiqueu 3-6 publicacions de referència en la descripció del projecte per donar una idea dels fonament, metodologia, objectius, etc.**

Competències addicionals[5] (opcional)

i) Gain proficiency in analyzing and visualizing simulation data using statistical analysis techniques, data visualization tools, and scripting languages like Python. This skill will be valuable for extracting meaningful insights from the simulation data and communicating the findings effectively to both technical and non-technical audiences. ii) Develop project management skills by coordinating and organizing various tasks, timelines, and resources throughout the research process. Learn to prioritize tasks, set goals, and allocate resources effectively to ensure timely completion of the project. This skill will be valuable for future endeavors in academia or industry, where efficient project management is essential for success.

Tasques a desenvolupar[6]		Cronograma (setmanes)																
Tasca	Descripció	01	02	03	04	05	06	07	08	09	10	11	12	13	14	15	16	17	18
T01	Bibliography and Literature review	X	X	X	X					X	X	X	X						
T02	System set-up			X	X	X													
T03	MD simulations production					X	X	X	X										
T04	MD simulations analysis								X	X	X	X	X	X					
T05	Discussion and interpretation of the results												X	X	X				
T06	Writing the Final Report and Presentation Preparation														X	X	X	X	X

Observacions i comentaris

Per a la realització del treball pròpiament dit es preveu una dedicació d'unes quatre hores diàries durant cinc dies a la setmana, amb la opció de modificació de l'horari per poder adaptar-se millor a l'horari acadèmic de l'estudiant.

COMENTARI: Recordeu que el TFM son 18 ECTS=18*25=450 hores de dedicació de l'estudiant (un 20% han de ser tutelades pel director). Calculeu 18-20 setmanes de març a juny (inclosos) per fer totes les tasques (inclosa la redacció de la memòria).

COLIZZI FRANCESCO - Y4519328A

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Date: 2024.02.13 01:53:54 +01'00'

Signatura (el director del TFM)

Signatura (el tutor del TFM, si s'escau)

[4] Enumereu breument qualsevol competència addicional a les competències genèriques enumerades en el Pla Docent del TFM (opcional).
[5] Feu servir només les línies que calgui. Escolliu-les de manera que donin una idea aproximada de en què consistirà el treball i la seva distribució temporal.