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A course-based undergraduate research experience to illustrate the early stages of the drug discovery process

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Abstract

We have implemented at the University of Málaga (Spain) a new course-based undergraduate research experience (CURE) to involve undergraduate students of Science in a real-world scientific problem. Within the topic "Let's find acetylcholinesterase inhibitors as new drug candidates for the treatment of Alzheimer's", students have been engaged into the early stages of the drug discovery process. Working in groups of 4–5 persons, they have searched information in databases, proposed solutions to the driving question and designed protocols to carry them out in vitro and in silico. Overall, the implementation of this experience has been very satisfactory in terms of academic performance and students' perception. This article reports a session from the virtual international 2021 IUBMB/ASBMB workshop, "Teaching Science on Big Data".

KEYWORDS

acetylcholinesterase inhibitors, CURE, drug discovery process

1 | INTRODUCTION

Simulation of a real-world scientific problem may help to engage undergraduate students of Science degrees in more authentic experiences.[1–3] In this context, we have implemented at the University of Málaga (Spain) a new course-based undergraduate research experience (CURE) which aims to be a practical introduction into the early stages of the drug discovery process. Within the subject "Pharmacological Biochemistry", 4th year-Biochemistry undergraduate students have undergone this experience, in which the laboratory work has been just a part of a more complete practical project, aiming to answer the meaningful question "Let's find acetylcholinesterase inhibitors as new drug candidates for the treatment of Alzheimer's." Working in groups of 4–5 persons, students have replicated situations resembling the real-life scenario that can be found by a professional worker of the Medicinal Chemistry area, and they have tried to apply their knowledge to solve specific problems. After searching for information in the bibliographic databases, students proposed solutions to the driving question and designed protocols to carry them out in vitro and in silico. By means of the in vitro studies, they were trained in operational issues such as the acquisition of reagents, method fine-tuning and experimental validation in the laboratory, and got hands-on experience of the process of identifying acetylcholinesterase inhibitors in a blind screening. In silico studies were devoted to characterize the interaction of drug

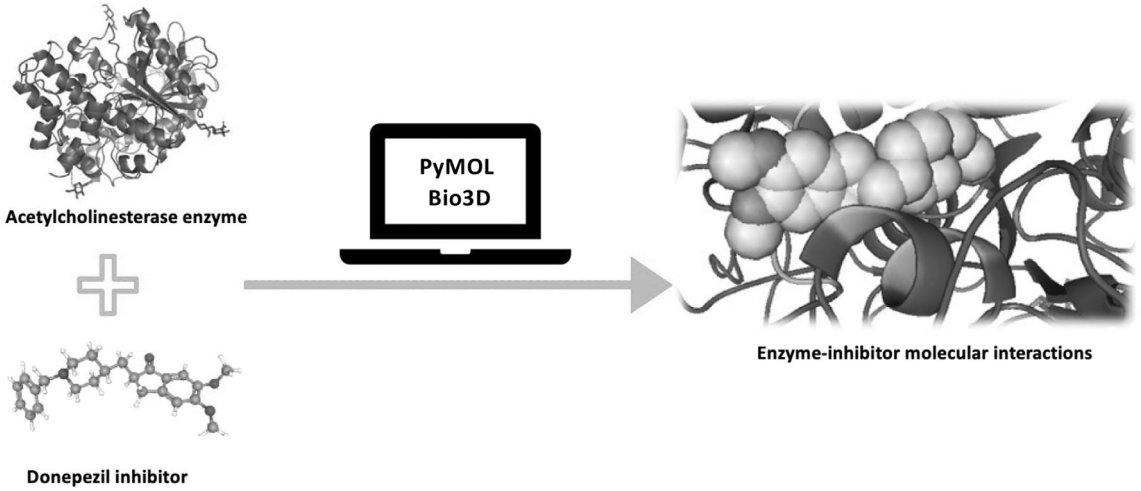

FIGURE 1 *T. californica* acetylcholinesterase, donepezil inhibitor, enzyme-inhibitor molecular interactions using PyMol and Bio3D

candidates with the molecular target (*E. electricus* acetylcholinesterase, used in the in vitro assay), and to predict their inhibitory activity on the human enzyme, by studying the alignment of *Electrophorus electricus*, *Torpedo californica*, and *Homo sapiens*. Finally, students had to summarize their results and present their conclusions to a diverse audience. This was done in an autonomous way, working in groups and under the supervision and guide of educators.

2 | EXPERIMENTAL OVERVIEW

Working into small groups of four or five students, and under the guidance of the responsible teacher, in the role of the facilitator, the groups independently carried out the different CURE activities. First, each group chose its specific name and worked as an independent "laboratory" that received a letter exposing the question "Let's find acetylcholinesterase inhibitors as new drug candidates for the treatment of Alzheimer's." Then, they performed a bibliographic search about Alzheimer's disease and the current therapies, and the instructor explained in class the basis of the drug discovery process and the strategies for the blind screening of enzyme inhibitors. Afterward, students searched information about the most suitable method for the detection of new acetylcholinesterase inhibitors, and wrote a first report summarizing their findings and the commercial inquiry for the reagents and the instrumentation required. During the laboratory activities phase, students designed the experimental protocol, did the corresponding calculations to prepare reagents, went to the lab to optimize their experimental protocol and performed the blind screening assay, being able to identify an inhibitor of the enzymatic activity of acetylcholinesterase among a group of unlabeled compounds provided by the instructor.

Once the in vitro part of this CURE was performed, students focused on the in silico studies. To this end, the instructor introduced them in the rationale of the drug design using computational techniques, so that they could get familiar with the informatics tools of statistical computing language R (PyMol—https://pymol.org—a molecular visualization software, and Bio3D—http://bio3d.ucsd.edu—a software for the modeling and analysis of the structures). Working autonomously in small groups, students solved the following tasks (Figure 1): (i) Workflow and scheme of the working hypothesis; (ii) modeling and representation of the acetylcholine binding site in the acetylcholinesterase from *T. californica*; (iii) modeling and representation of the binding site of an inhibitor in *T. californica* acetylcholinesterase; (iv) modeling and representation of the structural alignment of *T. californica* acetylcholinesterase and human acetylcholinesterase. In order to support students in their in silico laboratory activities, biweekly tutorial sessions were established by the instructor to encourage them to actively share their bioinformatics results and discuss their concerns and the difficulties found throughout this phase.

At the end of the CURE, students prepared both a final report and an oral presentation about the different stages of the project and the results obtained.

3 | STUDENTS' RESULTS

Students' achievement of the learning goals was rated from 0 (absent) to 5 (excellent) by 2–4 instructors, being very satisfactory and obtaining the mean score of 4.7.

Overall, students' responses revealed that this experience was innovative with respect to those used in other subjects of the degree, they found that working in groups was efficient, and acknowledged that this experience allowed them to understand how a laboratory protocol is designed and how to approach similar situations in their future professional career.

4 | CONCLUSIONS

This CURE has helped students to develop skills related to the treatment of information and digital competence by using open-source big data applications, the learning to learn competence, or the competence in autonomy and personal initiative. Many of these skills have an intrinsic relationship with the future development of students as professionals in technical, scientific, or academic positions. Our results indicate that the implementation of this experience has been very satisfactory, in terms of academic performance and students' perception.

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