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Using the Mitochondrial ETC to Effectively Illustrate Protein Structure and Function

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Various elements of protein structure and function are taught throughout biology and biochemistry programs. Learning outcomes range from describing the primary structure to as advanced as explaining molecular details of structure-function relationships and mechanisms. Students often experience two-dimensional representations of proteins in textbooks and lectures; however, they are usually unable to use these images to grasp the spatial concepts being explained. In this workshop, we will look at multiple ways of overcoming this disconnect. In conjunction, we use molecular models, LEGO® bricks and the protein visualisation software PyMOL to experience the wonder of the electron transport chain. Participants visualise ETC complexes with PyMOL and generate videos to explain mechanics and protein features. Using specific examples of complex I (NADH dehydrogenase) and complex V (ATP synthase) from the ETC to demonstrate various concepts and construct physical models in the session using molecular models and LEGO® bricks. Specifically, secondary structure, non-covalent interactions, metal ion coordination, reaction mechanism and conformation change. To reinforce the importance of these features, we link each feature to the function of these essential proteins. The workshop is targeted at those teaching protein structure/function to both majors and non-majors.

Keywords: protein function, protein structure, electron transport chain, models

Introduction

The objective of this practical activity is to provide students with an opportunity to explore some of the structural features of proteins from the electron transport chain. Even though the activity presented was used at the advanced level of a biochemistry course focused on Mitochondrial Bioenergetics, the content of the activity can be applied to any biochemistry or cell biology course. The level of the activity can be appropriately scaled based on the learning objectives of the course. The models generated and shown were used in the course for hands on demonstration; however, with sufficient time in the lab session, students can generate models as part of their assessment.

Why the Electron Transport Chain?

The electron transport chain (ETC) is a concept taught widely in several biology and biochemistry courses. ETC content can be found in courses from the introductory level to advanced level courses. Therefore, the features of this complex assortment of proteins can easily vary in degree of complexity from a straightforward explanation of function to detailed surveys of the chemiosmotic theory. Interestingly, because of the features of the chain, it is possible to explain several biological concepts related to proteins structure and function. For instance, the ETC may be used to describe the idea of protein-protein interactions, similarly secondary structure or even metal ion interaction may be explained depending on the example used by the instructor.

Materials

The PyMOL software from Schrodinger LLC. is needed for each student. The software can be downloaded at **http://pymol.org/educational.**

The following interlocking brick sets as produced by LEGO® were used: Large Creative Brick Box (#10698)- A fair selection of 790 bricks, this box should be able to provide enough basic as well as specialized bricks for explaining concepts to a class of 10 students. For more complex concepts or more creative cohorts of students, more bricks might be needed. Bricks, Bricks, Bricks (#10717)- This is a large selection of bricks (1500) that can easily supplement a medium or large creative box for use in the classroom. This box offers multiple colors and

several “standard” bricks as well as a few special bricks. Bricks and Gears (#10712)- This selection is small (240) but ideal if you are considering incorporating motion or movement into anything you are building or considering asking students to build. The special bricks in this set are designed for modelling and constructing moving models. Also, it comes with a wide selection of tyres and circular bricks.

Notes for the Instructor

PyMOL Environment

At first glance, the PyMOL environment may seem complicated, however, for most of the operations we need to carry out, it will be sufficient to be familiar with the panel located at the right of the PyMOL window. Using one of the five buttons, it is possible to perform a plethora of functions to the protein displayed. The buttons are as follows A- Action, S- Show, H- Hide, L- Label, C- Colour. Once clicked, each of these will lead to several options that relate to the main operation for which the button was named. For example, the way the protein can be illustrated can be changed by selecting the ‘show as’ option in the S tab. It is worthwhile to ask students to view a tutorial video on PyMOL use before the class. Several such video can be found on various video-sharing platforms.

ETC Features

As mentioned the ETC has multiple examples that can be used to illustrate protein structure and function. Features of the chain that are essential for the function of both complexes I and V are excellent for illustrating these relationships. For instance, in complex I, the once perceived rare pi helix, along with the help of a specialized channel, links the electron transport (hydrophilic) portion of complex I to the proton translocating region (hydrophobic portion). This function is facilitated through a domino effect like motion, causing multiple half channels to open and protons to reach the other side of the membrane. In addition to pi helices, the proton half channels of complex I are excellent examples of structure giving rise to function. This can be illustrated with LEGO® bricks, in particular, mutations can also be illustrated with LEGO® bricks by blocking the path of proton translocation.

Similarly, in complex V the rotation of the c ring with the stationary F1 portion of the protein is a difficult concept for several students to grasp. Constructing a model of complex V that facilitates rotation in one portion of the molecule, while the F1 portion remains stationary is crucial for highlighting this point. Relating the model to the structure of the protein in PyMOL, or animated videos, begins to concrete for students the mechanism of movement in the mitochondrial membrane. The brick selection from the Bricks and Gears set are particularly useful for this.

Mission, Review Process & Disclaimer

The Association for Biology Laboratory Education (ABLE) was founded in 1979 to promote information exchange among university and college educators actively concerned with teaching biology in a laboratory setting. The focus of ABLE is to improve the undergraduate biology laboratory experience by promoting the development and dissemination of interesting, innovative, and reliable laboratory exercises. For more information about ABLE, please visit **http://www.ableweb.org/.**

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