Sanger sequencing – a hands-on simulation

Resource Justification

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Synopsis

This hands-on simulation teaches the Sanger (dideoxy) method of DNA sequencing. In the process of carrying out the exercise, students confront DNA synthesis as it relates to chemical structure and the stochastic nature of biological processes. The exercise is designed for an introductory undergraduate genetics course for biology majors. The exercise can be completed in around 90-minutes, which can be broken up into a 50-minute period for the simulation and a follow-up 50-minute (or less) period for discussion. This follow-up could also take place in a Teaching Assistant (TA) led section. The exercise involves interactions between student pairs and the entire class. There is an accompanying student handout.

Introduction

Sanger sequencing is an important technique: it revolutionized the field of Genetics and is still in wide use today. Sanger sequencing is a powerful pedagogical tool well-suited for inducing multiple "aha" moments: in achieving a deep understanding of the technique, students gain a better understanding of DNA and nucleotide structure, DNA synthesis, the stochastic nature of biological processes, the utility of visible chemical modifications (in this case, fluorescent dyes), gel electrophoresis, and the connection between a physical molecule and the information it contains. Sanger sequencing is beautiful: a truly elegant method that can bring a deep sense of satisfaction when it is fully understood.

Because it incorporates many different concepts, Sanger sequencing is a fairly complicated topic to learn. It is also difficult to fully comprehend from words and pictures. In this exercise, students act out the dynamic processes of DNA synthesis and gel electrophoresis, forcing them to think deeply about what is happening and discover for themselves the essence of the process. Other good exercises have been designed to teach Sanger sequencing (DiGiuseppe 2003, Kosinski 2003) and are also worth considering. The simulation presented here provides a more accurate representation of how Sanger sequencing is carried out today than these earlier exercises, and should be more successful at providing students with the skills to evaluate current sequencing data.

Approach/Method

This exercise centers on a simulation in which students act out the synthesis and electrophoresis steps of Sanger sequencing. They are guided through the simulation by the instructor and a student handout is provided to support their learning. During and after the simulation, the students are prompted to discuss concepts with each other to develop their communication skills and solidify their understanding. They are also asked to evaluate actual sequencing data and consider how various scenarios might affect the data produced. Detailed instructions are provided in the "Background and Guidelines for Instructor" document.

Justification

Because students are required to act out the processes of synthesis and electrophoresis, they will discover for themselves what will happen during these processes. This leads to stronger comprehension and retention than if they are told what will happen. Students find the experience satisfying because they gain a deep understanding of the process and are able to appreciate its elegance and beauty. Furthermore, they often unmask misconceptions they harbored about fundamental concepts such as DNA replication, electrophoresis, and DNA structure. The simulation also provides effective understanding of another important and confusing biological concept – that of a stochastic process (random nucleotide incorporation yields chains of varying lengths, but with a large enough sample size, this random process will generate results that are consistent). The exercise is also structured to help students develop their communication and data analysis skills.

References

DiGiuseppe, M. 2003. Additional Activity: Sanger Dideoxy Sequencing: A Simulation Activity. In: *Nelson Biology 12.* Nelson Thomson Learning, Toronto.

Kosinski, R. 2003. A simulation of the Sanger (dideoxy) method for sequencing DNA. In: Tested studies for laboratory teaching, Vol. 24 (M. A. O' Donnell, editor). Proceedings of the 24th Workshop/Conference of the Association for Biology Laboratory Education (ABLE).