[W2] Linking DNA structure and sequencing using model based learning

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Such is the iconic status of DNA in modern life that we are used to seeing the double helix depicted in sculptures and paintings. In 2003 a set of UK postage stamps celebrated 50 years since the discovery of this structure, and in the same year DNA even graced the two pound coin. For students of biological disciplines, however, it is important that their understanding of this pivotal molecule runs rather deeper than this. Experience shows that some of the fundamental principles involved in the molecular biology of DNA are actually quite difficult for students to grasp when taught via either conventional lectures or practical classes. Successful acquisition of such knowledge is, however, crucial for the comprehension of more complex DNA processes.

This workshop will offer the opportunity to participate in two interlinked 'hands-on' tutorials that have been designed to increase students' understanding of both DNA structure and the importance of this structural knowledge in strategically significant technologies such as DNA sequencing. We also offer an evaluation of the exercise when piloted with second-year undergraduates at the University of Leicester.

In the first tutorial, a semi-space-filling atomic model of a DNA molecule (purchased from Spiring Enterprises Ltd.; www.molymod.com) is used to conceptualise a number of issues related to the basic atomic structure of the double-helix. In addition, each student pair was given an atomic model of one of the four DNA building blocks (a 'nucleotide', consisting of one of the four 'DNA bases', one sugar group and one phosphate group). Physical handling of these semi-space-filling models helped the students to distinguish the bases, to visualise the interaction between bases and to understand the rules governing DNA base pairing. The directional nature of DNA strands and the double helical structure of DNA (including the major and minor grooves) are easily seen when using these models. The tutorial on DNA structure culminates with the opportunity to 'read' the DNA sequence of the model and subsequently build a replica 'mini-DNA model', using simplified and stylised DNA models (also purchased from Spiring Enterprises). Having to build the replica model reiterates the basic principles of DNA base pairing and DNA structure.

The second tutorial comprises a sequencing scenario to simulate the dideoxy method of DNA sequencing (Sanger *et al*., 1977) using 'pop-it' beads (purchased from Philip Harris Education; www.findel-education.co.uk) as DNA building blocks, to determine the sequence of a short stretch of DNA. A similar, but less sophisticated, activity was described a few years ago (Roels and Vranckx, 2002) which involved large numbers of paper letters and was based upon generating 'ladders' of radioactively-labelled nucleotides, a process that has been superseded by the use of fluorescently-labelled bases (Glazer and Mathies, 1997). In our activity, students act as DNA polymerase (Taq)

Figure 1: University of Leicester students participating in the DNA structure (left) and DNA sequencing (right) tutorial sessions.

to 'synthesise' short DNA products by making 'copies' of a provided nine-base-pair template sequence. To 'copy' this sequence a DNA primer is selected (represented by a 5-bead pop-it chain) and then further bases are added onto this primer, following the base-pairing rules learnt in the DNA structure tutorial session. Beads of different colours are provided in four bags. The majority of beads in each bag are pink these represent 'normal' bases (i.e. deoxy nucleoside triphosphates, dNTPs). One out of every seven beads in each bag is of a different colour and represents the 'terminating' bases, which are dideoxy nucleoside triphosphates (ddNTPs) that lack the hydroxyl group necessary for the connection of additional bases. If a 'normal' base is selected this is added to the chain and 'synthesis' continues. However, if a 'terminating' base is selected further bases cannot be linked to the chain. When twenty such chains have been produced these are sorted by size (simulating electrophoresis). Subsequently, the sequence of bases is 'read' by looking at the coloured beads terminating each chain, from shortest to longest. This section of the tutorial provides a useful scenario to visualise the complex process of DNA sequencing.

One of the great assets of these tutorials is their visual and 'hands-on' nature, which enhances students' spatial thinking. For instance, it became clear that students find the concept of the double helix difficult to grasp, until they can see (and touch) one in the DNA model. Another great strength of these tutorial sessions is that they are conducted in combination. To fully comprehend the process of DNA sequencing it is crucial to have clear appreciation of DNA as a molecule. Running the tutorials in succession provided the students with a visual blueprint of the DNA structure that could then be used seamlessly in the second tutorial.

We designed these tutorials to complement information already covered in a second-year undergraduate module (through a number of lectures and laboratory- and computer-based practical sessions), describing general molecular biology techniques and their application for addressing problems relating to genome research. However, the nature of these tutorials is such that they lend themselves perfectly to be adapted and simplified to explain and address the basic principles of the DNA double helix in the classroom in a fun and relatively inexpensive way.

Evaluation

Relevant knowledge acquired by University of Leicester second-year undergraduate students was tested by means of a simple questionnaire immediately pre- and post-tutorial, and again, without prior notification to the students, five weeks later. A clear post-tutorial improvement of understanding of the subject was noted, both in the questionnaire scores, as well as from the students' own perception — to quote for instance: '*It helped me to understand the structure. When I handled the model it really helped me to understand'*. and '*It made how [DNA] sequencing works clearer, I was quite confused before*'. In addition, there was a clear indication of the enhancement of student learning — to quote for instance: '*It was an enjoyable way to give us a greater understanding of the subject*' and '*It helped me understand the process with an element of fun. Working in groups with coloured beads is more fun than listening to a lecturer talk'*. Furthermore, the effect of these tutorials on students' performance in summative assessments is being evaluated.

References

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