



Supplementary Materials for

Engaging Students in Molecular Biology via Case-Based Learning

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Materials and Methods
Full References

Using *Case It!* materials in classes

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Overview of the Case It! project

Case It! is an NSF-supported project to develop a framework for collaborative case-based learning in molecular biology using interactive computer simulations. *Case It v6.06* is an open-ended simulation that reads any nucleotide or amino acid sequence file, and includes methods for analyzing DNA and proteins. These methods include restriction digestion and mapping, polymerase chain reaction (PCR), DNA electrophoresis, Southern blotting and dot blotting, microarray analysis, protein electrophoresis, Western blotting, and ELISA. Detailed tutorials that describe the various features and the steps for using them can be accessed from the Case It home page (www.caseitproject.org). The download includes the simulation as well as all of the sequences necessary to run the cases described on the web site. The case descriptions can be viewed from the Cases menu of the Case It home page and downloaded as a pdf file. An instructor's manual that includes the keys to the cases and additional background information is available by contacting mark.s.berglund@uwrf.edu.

Version 6 of the software has new features including automated loading for gels, blots, and ELISAs. Bioinformatics capabilities (sequence alignment, tree building) have been added via integration with MEGA software (5). Several cases have bioinformatics extensions that utilize these new features (11).

Case It software can be downloaded from the Case It web site (www.caseitproject.org/download-2/) at no cost to educators. MEGA software must be downloaded and registered separately from the MEGA web site, www.megasoftware.net (also free of charge). Contact mark.s.berglund@uwrf.edu for additional information concerning the project.

Suggestions for Class Use of Case It!

Most of the cases currently available were developed for use in introductory undergraduate biology classes to help students address concepts and issues in molecular biology, but they can be adapted to a variety of educational settings. These cases guide students through the analysis steps and then provide focused questions to prompt interpretation and application of the results.

Each case description includes the case scenario and instructions for analyzing the case, as well as background information and discussion questions. Students first read the background information provided and gather additional information from online sources (e.g., <http://www.cdc.gov/>). They then carry out the analysis, interpret results, and discuss the significance of scientific and social issues raised by the case. Alternatively, instructors can edit the cases to add or omit information as appropriate for the backgrounds of students and the course objectives. Students may be asked to:

- Focus on the ethical and social issues raised by the analysis and the decision-making process involved
- Take on a particular role, e.g., genetic counselor or family member, and present the case interpretation from that perspective (see below for more details).
- Develop hypotheses about the results, based on background information about the molecular biology in the case, before running the analysis
- Start with the case analysis and results, then carry out their own research to obtain information necessary to interpret the case

In addition to using cases and sequences provided with the simulation, instructors may develop their own cases using DNA sequences obtained from [GenBank](#) or elsewhere. Sequences, restriction enzyme sites, probes, primers and antibodies are all read by the simulation as editable text files. Students in more advanced biology courses can be assigned to develop new cases. These student-designed cases can then be subjected to peer review, and used by students in introductory courses.

Presentation of case results

Students can present their case analyses in a variety of formats, including

- Conventional lab reports, where students insert images from the simulation, write an interpretation, answer the questions, and/or extend the analysis with additional research
- Presentation to the class, as individuals or groups, displaying the images from the software while providing interpretations and background information
- Posters with images and text, which can be printed and used in a poster session where students interact in person to ask questions about the cases
- Online poster sessions or other online presentations.

Role-playing and online communication

With the human genetic disease, cancer, and infectious disease cases, we have had particular success when students interact online, taking on different roles as they analyze and discuss the case results (4). Students work in teams using the Case It simulation to analyze samples in the case, then present their results in web-based format. We previously used a custom system that generated web pages with associated discussion boards (called the *Case It Launch Pad*), but a wiki system provides the same features (for an example, see <http://caseitconferencing.wikispaces.org>). Any online system that allows students to upload images and text and communicate interactively could be used to accomplish these steps.

1. Playing the role of a lab technician, students use the Case It simulation to analyze DNA or protein samples. Images from the simulation are saved and posted to a web page, along with background information and an interpretation of the results.
2. Students play the role of a genetics or health counselor as they compose a statement to the patient or family.
3. While interacting online, students switch between roles when they ask and answer questions. For example, when students visit other web pages they play the role of patients/family members in the case, whereas when responding to questions about their own web pages they play the role of genetic/health counselors. It is possible to do something similar in person rather than online, but in our experience students prefer the anonymity of online communications because they can be more open in their answers and it is easier to assume roles. An online format also gives them more time to reflect and gather information before responding.

Example of class implementation: Huntington's disease case with online role playing

Overview: This document provides more detail on classroom implementation of genetic disease cases using the Huntington's disease (HD) case as an example (see IBI essay). These cases have been used in Introductory Biology courses for non-majors at the University of Wisconsin-River Falls, as part of a genetics unit. Each team of students chooses or is assigned one of the genetic disease cases. There are 8 different genetic disease cases, each with three case scenarios, for a total of 24 case scenarios.

Students review the background information for their disease, read the case scenario, and use the *Case It* software to run PCR and gel electrophoresis on samples representing individuals described in the case scenarios. They export their results as image files and upload them to a web page along with a summary of the background information. They interpret results and include this interpretation in a statement to the person or family in the case (posted on their web page along with the images). Students are told that this statement is the first thing they would say to person or families in the case entering their online 'office', so they need to write it tactfully. Students read other team's web pages and use a discussion board to pose questions to the authors in the role of the people in the case. They respond to questions about their own web page in the role of a health care professional.

Biology content: This particular exercise helps students understand inheritance patterns, DNA structure, the nature of mutations, and techniques used to detect mutations (e.g. PCR, restriction enzyme digestion, Southern blot). Note that the original Huntington's disease case uses Southern blotting, but sequences for a PCR-based version are also included with the download.

Class time required: One to three lab sessions are required, depending on how much work students do outside of class time. We have used one two-hour lab period to demonstrate the software and allow students to run and analyze at least one of their case scenarios, a second lab period for web page preparation, and a third to give students time for synchronous discussions with their peers in the same lab section. We also ask students to post messages for asynchronous discussions with students in other lab sections, or at other institutions.

Students can independently download the simulation and access web pages and discussion boards, so part of the activity can be assigned to complete outside of class. However, we have found that discussion is considerably enhanced if class time is devoted to synchronous discussions within the same lab section, as students become much more engaged in conversing with their peers and considerably more data can be gathered for assessment purposes.

Preparation:

- Download *Case It* software from www.caseitproject.org and determine how it will be distributed to the students. It can be installed on the server for a computer lab, copied onto flash drives or to a class web site for downloading, or students can download it themselves. The folder extracted from the downloaded zipped file includes the *Case It v6.06* executable file, which requires no further installation and no administrative access on lab computers when run from a flash drive (this is the way we run *Case It v6.06* at workshops).
- If you wish to have students perform sequence alignment of the PCR products (to demonstrate the variable number of triplet nucleotide repeats in the Huntington's gene), it will be necessary to install MEGA software (5). MEGA is downloaded . See the tutorial on the Case It web site for instructions to download and install MEGA. Not all of the genetic disease cases have a sequence analysis component, so it might not be necessary for all students to have MEGA installed, and you may opt to use this feature as a demonstration. Note that *Case It v6.06* works with either MEGA 4 or MEGA 5.
- Become familiar with the software features that will be used in class. There are tutorials available on the *Case It!* web site, including video screencast tutorials for PCR and gel electrophoresis. An instructor's manual with keys to cases and additional background information is available by contacting mark.s.bergland@uwr.edu.

- Determine teams and how cases will be assigned. Two students per team works well in our experience. We have both members of the team conduct the analysis and set up the web page, but then have team members conference independently when role-playing. Students prefer this method, and that way we know who is contributing to the discussions and can assign credit accordingly.
- Set up the web page system for sharing results and discussion. An example of how this could be set up for a class is provided at <http://caseitconferencing.wikispaces.com>. Wikispaces (<http://www.wikispaces.com>) offers free full-service wikis for education, but there are other options. Any system allowing students to upload images and text could be used, providing it also allows for communication via discussion boards.

Wikispaces allows you to upload a spreadsheet with usernames, passwords and email addresses to quickly set up accounts for the class and send students login information automatically. Wikispaces also recently added a “Projects” feature that allows you to set up teams that will each have a page to edit. Each page includes a discussion board. Access to pages can be restricted to teams while they are building them, then released to the class for review and discussion.

- Determine discussion assignments, i.e. which other web pages students will view, asking questions of students who constructed those pages. We have found that it is better to make assignments rather than let students choose which cases to view, so that each team receives roughly the same number of questions. One way to do this is to number the teams, and assign Team 1 to view web pages for Teams 2 and 3; Team 2 to view web pages for Teams 3 and 4, etc.

Classroom activity:

1. We recommend that the instructor first demonstrate *Case It v6.06* using an example case. Alternatively, students can be directed to view the tutorials on the Case It web site. However, a demonstration allows the instructor to model data analysis and interpretation. As an example, here is how the Huntington’s disease case can be presented:

Give an overview of Huntington’s disease (from www.caseitproject.org > Cases): Huntington’s disease is a neurodegenerative disorder characterized by motor, cognitive, and emotional symptoms. The age of onset for symptoms is generally 30-50 years. The genetic basis of the disease is an amplification in a gene with an (as yet) unknown function. A triplet (CAG) is repeated 20-50 times in asymptomatic individuals; having more than 50 repeats is associated with disease symptoms. Huntington’s disease is considered a dominant disorder, since one copy of the amplified gene appears to be sufficient to cause disease symptoms. This amplification can be detected by restriction enzyme digestion and Southern blot analysis, since the size of the fragment bound by the probe is increased as a result of the amplification of the triplet repeat. Alternatively, PCR can be used to isolate the region containing the triplet repeats; the relative size of the repeat region can be determined by running the PCR products on a gel.

Present a scenario (Case A): Susan is a 23-year-old whose father, age 55, and paternal aunt, age 61, have been diagnosed with Huntington’s chorea. A paternal uncle, age 66, appears to be unaffected by the disease. Susan wants to know if she inherited the mutated gene from her father so that she can prepare for that future if necessary. She arranges to undergo DNA testing for Huntington’s disease. Her 17-year old brother, John, also decides to be tested after talking with Susan.

Run the analysis: Use the HD primers to run PCR on the following DNA samples:

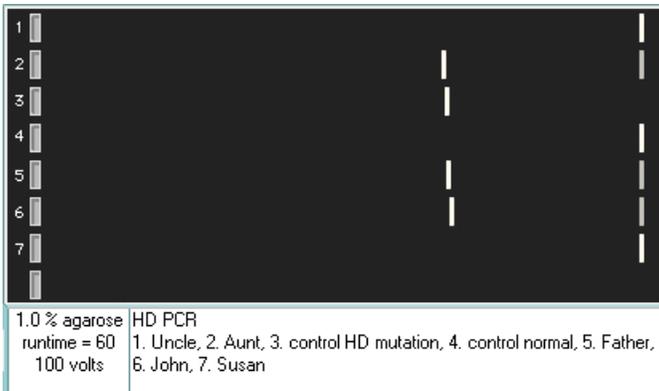
Susan (patient)
 Father (affected)
 Aunt (affected)
 Uncle (unaffected)

John (brother)
 Control DNA with HD mutation
 Control DNA, normal (without HD mutation)

The procedure to run PCR in the Case It simulation is as follows:

(Note: For a real-time demonstration, see video tutorials at www.caseitproject.org):

- Open the DNA sample files and then open the HD primers file. The files will appear in the "Opened & Processed" window.
- Select all of the DNA samples and click the Run button. New files corresponding to the PCR products for each sample will appear in the "Opened & Processed" window.
- Select all of the PCR projects and use the Quick Load/Run button to load them into the gel and run the gel. Staining the gel using the UV photograph option yields the following result, which can be saved as a .jpg file:



d. Suggested discussion questions:

- 1) What conclusions can you draw from these results? What is the status of each individual?

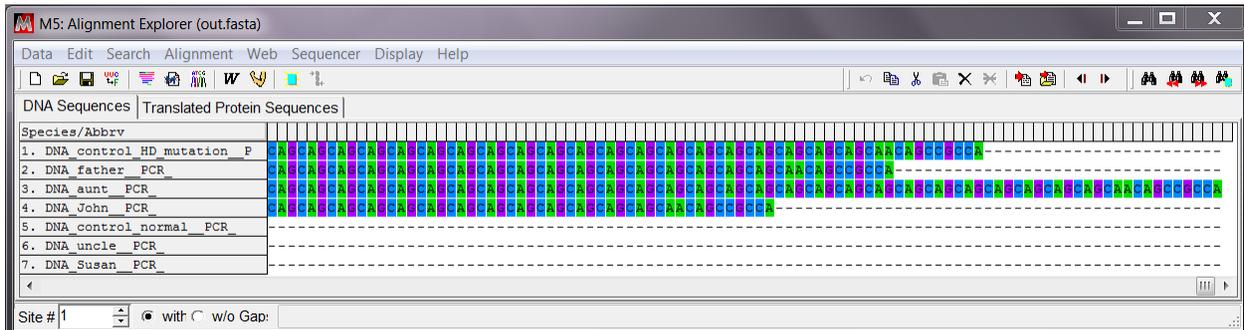
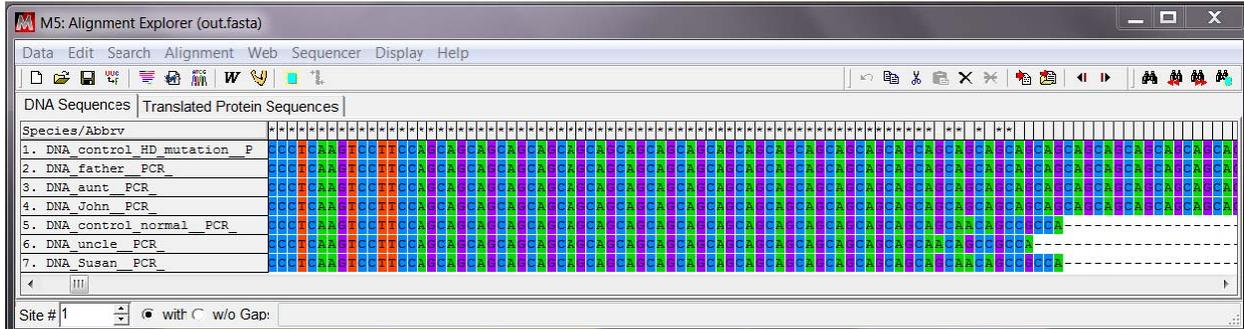
Since the mutation is dominant, heterozygous individuals will be affected.

- Lane 1: uncle - homozygous normal (unaffected)
- Lane 2: aunt - heterozygous (affected)
- Lane 3: control HD mutation – larger band only
- Lane 4: control normal – smaller band only
- Lane 5: father - heterozygous (affected)
- Lane 6: John (brother) - heterozygous (affected)
- Lane 7: Susan - homozygous normal (unaffected)

- 2) What is the molecular basis of this disease, and why does this result in the pattern observed on the gel?

The mutation is amplification of a triplet repeat (CAG). The PCR products from the samples containing the mutation are larger because there are more repeats, and fragment sizes vary because each individual has a different number of repeats. This can be demonstrated by aligning the sequences of the PCR products:

- Clicking on a band in the gel will display the sequence of that DNA in the lower window of the Data Screen.
- From the Analyze menu, select Export sequence to add the selected sequence to the Export window.
- Once all of the sequences have been exported, use the Analyze menu to align the sequences. This will open MEGA software to display the alignment:



- How would you counsel Susan and her brother based on the results of the test? Recall that Susan talked John into taking the test, and he is the one that tested positive for the mutation.
- What issues are raised by this type of testing? For example:
 - Should someone with a family history of HD be required to undergo testing? Should they have children if they test positive, or if they have not been tested?
 - Should the results of such tests be made available to insurance companies? to potential employers? to potential mates?
 - Should someone as young as John be tested?
- After the above demonstration (with students following along on their computers), students read the background information and scenario for their case. Additional time may be provided for students to conduct additional research into the genetic condition and the nature of the mutation and inheritance.
- Teams of students use the simulation to run samples according to instructions. For this step the students are in the role of "lab technician". Results are saved as .jpg images (gels are labeled prior to saving). Note that the .jpg suffix must be part of the filename if the image is to save properly.

4. Students prepare web pages, entering text and uploading images. We have used the following outline, which could be set up as a template on the wiki:
 - a. Disease background, symptoms
 - b. Molecular biology of the disease
 - c. Description of laboratory procedure
 - d. Presentation of results
 - e. Interpretation of results
 - f. Statement to persons in the case (diagnosis, suggestions for treatment, etc.)
 - g. Ethical issues associated with the case
 - h. References
5. Students are assigned to view another team's web pages, read the information, and post questions in the role of one of the people in the case. They should identify their role when asking questions. We recommend that this be assigned as an individual activity rather than having the team pose questions, as it is easier to give credit and students become more involved personally in the interactions.
6. Authors of web pages respond to questions in the role of a health care professional. This can be an individual or team effort (i.e. team members consult before posting their answers). We tell students that they can consult with team members, but that they should give their own responses to questions, as a "second opinion". That way they can put their own interpretation on a response, rather than rely on a team member to frame a joint response.

Assessment: The web pages can be assessed for content, and discussions assessed for number and/or quality of messages (6). A sample rubric for evaluating the web posters is shown below.

Rubric for evaluating web posters

Molecular Biology of the disease: Quality of Information 1 2 3 4

Major inaccuracies	Some inaccuracies	Correct basic information	Correct information and some in-depth investigation is apparent
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Symptoms and treatments: Quality of Information 1 2 3 4

Major inaccuracies	Some inaccuracies	Correct basic information	Correct information and some in-depth investigation is apparent
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Laboratory procedure: Quality of Information 1 2 3 4

Major inaccuracies	Some inaccuracies	Correct basic information	Correct information and some in-depth investigation is apparent
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Accuracy of results (based images of gels, blots, etc.) from simulation 1 2 3 4

Image is missing	Image indicates procedure not done properly	Image indicates slight problems with procedure Not all images are present or labeled properly	Image indicates procedure done correctly and labeled properly
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Interpretation of results 1 2 3 4

No interpretation	Some inaccurate interpretation	Slight misconception of meaning of results	Understanding and clear interpretation of results
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Statement to persons in case (e.g. family members) 1 2 3 4 5

No diagnosis or counsel given	Gives poor/vague counsel	Correct diagnosis but offers no counsel for persons in case	Correct diagnosis & some counsel for persons in case	Correct diagnosis & detailed counsel for persons in case
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Ethical issues 1 2 3

No ethical issues mentioned	Issues mentioned, but not relevant to case or do not show much thought	Identifies pertinent ethical issues, evidence of thought
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References 1 2 3

No references included	References included, but incomplete and/or not cited in page	Complete references included and cited in page
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Grammar, spelling 1 2 3

Many organizational, spelling or grammatical errors	Some problems with organization, spelling or grammar	Good organization of information, few spelling or grammatical errors
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Individual contribution to project 1 2 3

Did not contribute to team effort	Some contributions to team effort	Fulfilled all team obligations
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References and Notes

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