Teaching comparative metabolism using a graphic computer model, Virtual Tissue

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The systems approach to teaching and understanding metabolism promotes a functional understanding of metabolite flow through pathways at the enzymatic, cellular, tissue, and whole body levels. However, most courses are taught from a reductionist point of view (5) in which the focus is on enzymatic regulation at a few “key” points in a pathway in the liver and/or muscle. A few general comments are made on how regulation is affected by metabolic anomalies such as diabetes, etc. Students get very little exposure to how pathways function in different tissues and how these tissues function together to support whole body metabolism. Changes in metabolism in tissues and the whole body due to changes in physiological state are discussed very little, and students are left drawing pathways with very little understanding of how the pathway fits into whole body metabolism. Conversely, by building on knowledge of enzyme regulation and tissue function, the systems approach offers a teaching method that is inquiry based and promotes a functional understanding of metabolism at many levels (1, 6).

Central to using a systems approach to teach metabolism is putting together information on the integration of metabolism between tissues in a way that allows both professors and students a reference point to delve into metabolism at different levels of integration. For that purpose, a graphic computer model of metabolism called the Virtual Tissue model was created. The goal of this article is to describe how the Virtual Tissue model can be used to teach metabolism using a systems approach.

Design Goals of the Virtual Tissue Model

Models can serve as repositories of information or as interactive, active learning tools (3, 7). The Virtual Tissue model was intended to be used as both. Specifically, the graphic program was designed to 1) show the integration of metabolism from chemical structures, enzymes, cellular pathways, and tissues to the whole body; 2) apply knowledge of regulation to understand changes in metabolism with different physiological states; 3) serve as a reference for structures, metabolic diagrams, and energy transactions; and 4) function as an interactive computer tool for comparing metabolic states and self-testing. The design of the program promotes thinking of whole body metabolism as a system because navigation between integration levels is simple and changes in a physiological state alter interactions at each integration level.

The Virtual Tissue program has been used in an upper-division nutritional biochemistry course (ABI 103) as a reference for students. It is a source of metabolic diagrams that can be used in lecture and blank diagrams that students can use to test themselves and enable students to sum ATP use and creation across pathways (2). In an upper-division course on lactation (ANS 124), the program is used in a laboratory to compare metabolic states to illustrate how metabolism changes in the liver, adipose, and muscle support lactation in humans and ruminants. Students choose from a sample list of questions and compare diagrams to answer a metabolic question in a laboratory report. In this way, student exploration of metabolism is self-paced and inquiry based. The laboratory handout is shown in Fig. 1. The handout and sample study questions are also available from the website where the model can be downloaded at http://www.vmtrc.ucdavis.edu/metabolic/.

Description of the Virtual Tissue Model Program

Computer programs have been used in teaching with mixed results (4). Models are most useful in teaching when they are easy for students to use and understand (8). The software is stable, navigation is simple, and model results do not require much explanation. The Virtual Tissue model was designed to be self-explanatory and self-enclosed. Figure 2 shows the opening screen. Buttons within the graphic program expand integration layers to go more in depth into metabolism, and different metabolic states are selected from a drop-down menu (“Choose Physiologic State”). Nutrient transport between tissues is shown for the current physiological state. Explanations of any button, arrow (enzyme), or abbreviation appear by hovering the cursor over the item in question. Within the tissue cell diagrams (Fig. 3), relative changes in substrate levels are indicated by color changes: blue is decreased, green is no change, and red is increase. Pressing the metabolite button shows the structure of the metabolite, and energy transactions can be toggled on or off using the “View Energy” menu. The successful use of any new technology is dependent on design and introduction of technology to the students. When used in the lactation course laboratory or introduced in the nutritional biochemistry lecture, 10–15 min of lecture are used to show the model and explain how it is used. This program is designed to need minimal explanation so that the majority of laboratory or classroom time can be spent exploring metabolic system changes.

Assessment of Student Attitudes and Perceptions

Because the model can function as a reference tool and its use was optional, it is difficult to assess the impact of the Virtual Tissue model on student learning. However, at the end
of each course, student assessments and suggestions for program improvement were collected. Based on suggestions made by students on the evaluation forms, the model developed over 2 yr to its present form. Students from both courses (nutritional biochemistry and lactation) were given an evaluation form at the end of the quarter (Fig. 4) and asked to evaluate the models based on the presentation of the subject matter by the models, efficient organization of model content and program manipulation, and the technical ease of using the models. A total of 110 and 300 students were registered, and 69 and 296 evaluations were received for the lactation and nutritional biochemistry courses, respectively. In the nutritional biochemistry course, the program was used as a reference; in the lactation course, the program was used in the laboratory. Results from each course evaluations are shown in Table 1.

Responses listed on the evaluations were similar for both courses. The majority of students spent between 0 and 20 min learning the program (75% and 61% in nutritional biology and lactation, respectively), and students in nutritional biochemistry spent 30–60 min using the program (61%). Comments indicated that there was considerable variability in the reports by students as to how long it took to download, install, and

### Integration of Tissue Metabolism during Lactation

**OBJECTIVE:** To gain an understanding of metabolism relating to lactation by examining a particular aspect in depth.

**METHODS:** The Virtual Tissue program (VirTiss) shows changes in liver, adipose, muscle and mammary metabolic pathways with changes in physiological states. Familiarize yourself with the basic principles and directions of metabolism in different tissues using the program. Then select a question to answer in your lab report from the following list:

1. What is the importance of NADPH to the mammary gland and how does its source differ between ruminants and nonruminants?
2. How do milk fat precursors differ between ruminants and nonruminants?
3. What are the fates of cytoplasmic and mitochondrial AcCoA? How are they different in ruminants and nonruminants?
4. What appears to be the predisposing factor for ruminant ketosis (look at ruminant liver and ruminant adipose)? What substrate would you increase to cure it and why?
5. How is the overall flow of glucose and fatty acids between tissues affected by ketosis?
6. Write your own question — but see me first!

**LAB REPORT:** Answer one of the above questions in 1-2 pages typed and double spaced not including diagrams or drawings. Please list your question at the top of the report.

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**Fig. 1.** Handout for the laboratory using the Virtual Tissue model.

**Fig. 2.** Opening screen of the Virtual Tissue model showing overall metabolite flow between tissues and the selection menu for physiological states.
**EVALUATION FORM FOR VIRTUAL TISSUE MODEL**

If you did not use any of the tissue models during ABI 103 or ANS 124 please do not fill out this evaluation form.

Please circle your response

1. How much time did you spend using the programs in this course?
   - NEVER  
   - LESS THAN 30 MIN  
   - 30 MIN - 1 HOUR  
   - MORE THAN 1 HOUR

2. How useful were the programs to learning concepts in the course?
   - NOT USEFUL  
   - SOMEWHAT USEFUL  
   - USEFUL  
   - VERY USEFUL

3. How long did it take you to figure out how to use the programs?
   - LESS THAN 5 MIN  
   - 5-10 MIN  
   - 10-20 MIN  
   - 30-60 MIN  
   - GREATER THAN 60 MIN

4. Did the programs help you integrate material presented in class?
   - NO  
   - SOMEWHAT  
   - YES

5. Do you think you understand metabolic regulation and the integration of pathways better as a result of the programs?
   - NO  
   - SOMEWHAT  
   - YES

Please include any additional comments or suggestions about the programs in the space below.
learn how to use the models. Individuals that were very proficient with the computer had no problem downloading and running the program. Most students also thought that the model was somewhat useful (54% and 42%) or useful (34% and 32%) in understanding the course concepts and helped somewhat to integrate (54% and 61%) and understand metabolic regulation and pathway integration (55% and 46%) in nutritional biology and lactation, respectively. Students that identified themselves as visual learners in the comments section also tended to consider the program more useful. Suggestions for improving the Virtual Tissue program included adding structures, adding another layer to integrate metabolism beyond individual organs (including a color key), allowing more than one window for a given organ to be visible at once, and showing energy costs associated with the pathways. In response to these suggestions, we added pop-up windows of chemical structures and explanations of abbreviations and enzymes, a key that remains in the master window, and added the opening window, which shows metabolite flow between tissues. Positive comments stated that the models helped the student gain an appreciation for the overall map of metabolism in the specific organs and tissues and that they were able to “see” how physiological changes altered metabolism in those tissues and organs.

Table 1. Results of student evaluations for the Virtual Tissue program from the nutritional biochemistry and lactation courses

<table>
<thead>
<tr>
<th>Question</th>
<th>Nutritional Biochemistry Course</th>
<th>Lactation Course</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. How much time did you spend using the programs in this course?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 min</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>&lt;30 min</td>
<td>56</td>
<td></td>
</tr>
<tr>
<td>30–60 min</td>
<td>183</td>
<td></td>
</tr>
<tr>
<td>&gt;60 min</td>
<td>54</td>
<td></td>
</tr>
<tr>
<td>2. How useful were the programs to learning the concepts in the course?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not useful</td>
<td>25</td>
<td>11</td>
</tr>
<tr>
<td>Somewhat useful</td>
<td>160</td>
<td>28</td>
</tr>
<tr>
<td>Useful</td>
<td>101</td>
<td>21</td>
</tr>
<tr>
<td>Very useful</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>3. How long did it take you to figure out how to use the programs?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5 min</td>
<td>41</td>
<td>17</td>
</tr>
<tr>
<td>5–10 min</td>
<td>90</td>
<td>27</td>
</tr>
<tr>
<td>10–20 min</td>
<td>92</td>
<td>17</td>
</tr>
<tr>
<td>30–60 min</td>
<td>48</td>
<td>8</td>
</tr>
<tr>
<td>&gt;60 min</td>
<td>25</td>
<td>7</td>
</tr>
<tr>
<td>4. Did the programs help you integrate the material presented in class?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>27</td>
<td>12</td>
</tr>
<tr>
<td>Somewhat</td>
<td>158</td>
<td>42</td>
</tr>
<tr>
<td>Yes</td>
<td>105</td>
<td>15</td>
</tr>
<tr>
<td>5. Do you think you understand metabolic regulation and the integration of pathways better as a result of the programs?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>72</td>
<td>21</td>
</tr>
<tr>
<td>Somewhat</td>
<td>160</td>
<td>32</td>
</tr>
<tr>
<td>Yes</td>
<td>59</td>
<td>16</td>
</tr>
</tbody>
</table>

Values are numbers of responses. See Fig. 4 for the evaluation form.

Discussion

In general, students appreciated the importance of learning metabolism from a systems perspective. The most positive comments indicated that they were able to integrate lecture material at the whole body, tissue, and pathway levels more effectively with the Virtual Tissue model. The addition of more detail on enzyme regulation and quantification of pathways would improve the usefulness of the model. At present, enzyme regulation is not explicitly represented in the model program other than being able to compare metabolite levels in different physiological states. We are currently examining ways of incorporating regulation. In addition, we are currently working on computational models of liver, adipose, and muscle metabolism that could be incorporated into the Virtual Tissue program. Examples of liver and adipose models (1) are available at http://www.vmtrc.ucdavis.edu/metabolic/. These models quantify metabolic pathway intermediates and can be used to predict radiolabeled carbon distribution using different labeled carbon substrates. The models could be included in the Virtual Tissue program in an abbreviated form.

Conclusions

Using a systems approach to teach metabolism provides students with a greater depth of understanding into how tissues function together in different physiological states. Traditional sources of information such as pathway charts are good representations of chemical structures and pathways but do not provide information as to what processes are occurring in tissues and how processes change in different states. The Virtual Tissue graphic model program was created with a systems perspective to represent the integration of metabolic processes from the structural, enzymatic level to whole body metabolic interactions. The model has been used successfully as a reference tool and in an interactive laboratory setting to foster inquiry into metabolic processes. Students have benefited from incorporating the systems approach into teaching metabolism using the Virtual Tissue program by increasing their ability to integrate information.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

REFERENCES