THE USE OF A HANDS-ON MODEL IN LEARNING THE REGULATION OF AN INDUCIBLE OPERON AND THE DEVELOPMENT OF A GENE REGULATION CONCEPT INVENTORY

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A Thesis Submitted in Partial Fulfillment of the Requirements for the Degree of Master of Science in Biology at Middle Tennessee State University

August 2015

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ACKNOWLEDGMENTS

I would like to give special thanks to Drs. Jeffrey Leblond, Steven Wright, and Mohammed Salem for allowing me to interact with their students, Dr. Matt Elrod-Erickson for sharing his *lac* operon expertise and Dr. Sarah Bergemann for reviewing the proposal for this thesis. Thank you to Angelique Troelstrup for her expert help with statistical analysis. Thank you to the genetics teaching assistants Jacob Crigler, Katherine Sampuda, Paola Molina, and Penny Carroll for their help in implementing the hands-on activity and collecting data. I would also like to express my gratitude to my friends and fellow graduate students Rayne Leonard, Jon Ashley, Sarah Kirkpatrick, Ali Jordan-Foster, and Alyssa Hoekstra for piloting my activity and providing infinitely helpful feedback. And last, but certainly not least, I would like to thank my husband and our two pups and my family for their continued love and support.

ABSTRACT

A central concept in genetics is the regulation of gene expression. Inducible gene expression is often taught in undergraduate biology courses using the *lac* operon of *Escherichia coli* (*E. coli*). With national calls for reform in undergraduate biology education and a body of literature that supports the use of active learning techniques including hands-on learning and analogies we were motivated to develop a hands-on analogous model of the *lac* operon. The model was developed over two iterations and was administered to genetics students. To determine the model's worth as a learning tool a concept inventory (CI) was developed using rigorous protocols. Concept inventories are valuable tools which can be used to assess students' understanding of a topic and pinpoint commonly held misconceptions as well as the value of educational tools. Through in-class testing (n =115) the *lac* operon concept inventory (LOCI) was demonstrated to be valid, predictive, and reliable (α coefficient = 0.994). LOCI scores for students who participated in the hands-on activity (n = 67) were 7.5% higher (t = -2.281, $P < 0.05$) than students who did not (n = 62). Use of the model is also supported by student feedback from two surveys. This study provides an effective activity that aids students' understanding of the lac operon. We were able to determine the efficacy of the activity and identify misconceptions held by students about the lac operon because of the use of a valid and reliable CI.

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CHAPTER I: BACKGROUND AND PURPOSE

An understanding of biological sciences is increasingly important for society. It informs views on healthcare, educational curricula, climate change, and food sources. Together with nationwide calls for more graduates with degrees in science, technology, engineering and math (STEM) it is becoming even more important to examine how college biology is taught (PCAST, 2012).

In 2011 the American Association for the Advancement of Science published a report with support from the National Science Foundation entitled *Vision and Change in Undergraduate Biology Education: A Call to Action* (2011). *Vision and Change* attempts to tackle the issues in college biology education that have arisen from contemporary biology curricula lagging behind modern breakthroughs in biology and the increasingly interdisciplinary nature of biology research. This report explores the ever growing disconnect between instruction in science courses and the actual practice of science. The authors note that oftentimes science courses are taught in a manner where instructors are purveyors of information and that rote memorization of disconnected facts are required for exams. Instead, *Vision and Change* advocates for curricula that use facts to promote a deeper understanding of core biological concepts and teaching styles that are student-centered and in which the instructor is actively following students' progress in the practice of science rather than the cataloging of facts (AAAS, 2011).

1.1 Active Learning

Among many other topics, this report discusses instructional approaches that align with how biology is currently practiced and supported by disciplinary-based education research. The report strongly endorses student-centered instruction and advocates the use of multiple modes of instruction in addition to traditional lecture (AAAS, 2011). Traditional teaching practices focus on an instructor-centered classroom with students passively listening and taking notes; while active learning is any type of student-centered classroom technique that engages students in the process of learning by asking them to participate in classroom activities, discussion, answering questions, etc. These activities not only engage students but more accurately reflect the practice of science. Biologists ask questions, conduct experiments to answer those questions, and discuss their findings with peers. Active learning has been shown to maximize learning and performance in undergraduate STEM courses (Freeman, 2014).

In their 2014 paper, Freeman, et al. set out to empirically determine whether or not active learning increases exam scores and decreases failure rates in STEM courses. They were motivated to perform their investigation because in the United States, the President's Council of Advisors on Science and Technology had called for a 33% increase in bachelor's degrees in STEM fields and specifically endorsed instructional methods supported by research (PCAST, 2012). Their review of 225 separate studies concluded that students who engaged in active learning, when compared to students

taught only by traditional lecture methods, showed a 55% decrease in failure rates in STEM courses. Their study also showed that on identical/equivalent examinations, concept inventories, and other assessments, students who engaged in active learning showed an increase in performance of about one standard deviation above students only taught by traditional means (Freeman, 2014).

Active learning is generally described as any instructional method which requires students to engage in meaningful activities and think about what they are doing (Prince, 2004). Types of active learning can include, but are not limited to: problem or case-based learning, group work (collaborative or cooperative), peer instruction of many kinds, inquiry-based learning, and discover-based learning (Michael and Modell, 2003). Active learning methods are often techniques in which students work to solve problems individually or in groups (peer learning) and are either being assessed together (collaborative learning) or individually (cooperative learning) (Prince, 2004; Michael, 2006). In college level biology, this type of student-centered learning has been shown to be advantageous over traditional teacher-centered lectures in student understanding and performance on science literacy assessments, graded course work, and assessment questionnaires. (Brickman, 2009; Burrowes, 2003; Lord 1997).

Discovery-based learning, which is one type of active learning, involves learning by doing and which focuses on learning concepts rather than unrelated facts. In discovery-based learning content is inseparable from the processes being learned (Michael, 2006). Guided discovery is a type of discovery-based learning in which the instructor provides necessary information for learners to complete a task and assists students during the

activity. It has been demonstrated to be more effective than pure discovery in which students learn through unstructured exploration (Mayer, 2004).

1.2 Hands-On Learning and Analogies

One type of active discovery-based learning employs the use of hands-on activities. Studies have shown that regular use of hands-on activities enhances both achievement and motivation in the classroom (Freedman, 1997; Schaal, 2005; Gerstner, 2010). Hands-on or manipulative models employ physical models to be handled in some way by the learner to enhance his or her understanding of a particular concept. Manipulative models have been used successfully to learn basic science at the elementary school level through college level biology, chemistry, and physics (Gerstner, 2010; Haglund, 2012; Lin, 2013). Specifically in biology, hands-on models have been successful in teaching certain concepts in evolution, genetics, and introductory biology (Witfield, 2008; Seipelt, 2006; Mathis, 1979). For example, paper models of cells have been used to learn mitosis and meiosis (Mathis, 1979).

Hands-on models can range in their form and function. One form can be a literal representation of something such as a model of an enlarged cell. However, when representing something more abstract, a model representing the analog can be used (Duit, 1991). An analogy is an association or comparison of similarities between two things based on their structures or functions for the purposes of explanation (Glynn, 2006). The familiar concept is referred to as the analog while the new concept is the target (Glynn,

2006; Duit, 1991). Analogous models are often a means of illustrating or demonstrating an analogy with parts of the model representing the target or analog. In this instance, the analogy is what makes the use of a model possible (Duit, 1991). Therefore, a hands-on model can be used as an analog to aid a student's understanding of a target concept. Comparisons between the analog and target are made as a way of explaining or describing the target through links or attributes that are similar between the target and analog (Glynn, 1995; Glynn, 2006). Analogies can be quite varied in their structure, but do share some common elements, including introduction of the target, review of the analog, identification of linkages between and the similarity between target and analog, inconsistencies of target and analog, and conclusions of the analogical model (Oliva, Axcarate & Navarrete 2007; Glynn, 2007; Glynn, 2008). Uncommon features can include whether the analogy is planned or not, the degree to which the analog is scientific and abstract, and who initiates the analogy (Oliva, Axcarate & Navarrete, 2007).

Analogies are frequently used as a means of explanation both in and outside of the classroom. Historically, analogies have been used by scientists to explain their discoveries and have been a source of inspiration shaping the thinking of researchers (Glynn, 2008). Many empirical studies have explored the value of analogies as instructional tools. In physics, several papers have concluded that analogies provide an effective means of learning new concepts and may in some cases, be better than teaching without analogies (Duit, 1991; Brown and Clement, 1989; Podolefsky and Finkelstein, 2007). In biology, the use of analogies has been shown to be effective in teaching courses such as introductory biology, biochemistry and genetics and specific concepts like

evolution, genetic mutations, glycolysis and genotype-phenotype relationships (Orgill, 2007; Marcelos, 2012; Seipelt-Thiemann, 2012; Seipelt, 2006; Stavrianeas, 2005).

The idea and logic integrating both the hands-on and analogous model are consistent with the constructivist view of learning. Constructivism approaches learning as a process by which each learner engages with concepts and integrates them within their own prior knowledge scaffold (Glasersfeld, 1989; Lord, 1997). Analogies of this type provide both cognitive and tactile experiences allowing the learner to map new ideas and concepts using multiple modes. This study provides not only a learning activity that is at the intersection of hands-on and analogous learning but also provides a rigorous assessment of its efficacy, which has yet to be well-established in the literature.

1.3 Methods of Assessing Teaching Techniques

In order to draw any comparisons between teaching techniques or assess their value, a tool is needed to measure or assess students' understanding. These tools, also outlined in *Vision and Change*, can come in many forms ranging in their ease of implementation and their efficacy in accurately capturing student understanding. These learning assessments can range from true/false questions to research papers synthesized by students.

The method chosen for this study is a concept inventory (CI). Concept inventories are easy to administer to large numbers of students and the data provided by a CI is easily quantified and analyzed. A growing body of validated CIs have been published ranging from broad general introductory biology inventories to more narrow inventories dealing

with specific concepts such as meiosis (D'Avanzo, 2008; Kalas, 2013). Concept inventories are traditionally composed of multiple-choice items in which the distractors contain common misconceptions held by students (D'Avanzo, 2008). This design helps educators not only identify which concepts students have mastered but also pinpoint common areas of confusion during the learning process. The distractors are chosen intentionally through careful assessment design protocols (Knight, 2010). The wording of CI questions is also given careful consideration to ensure that the language used is appropriate.

Both the validity of the distractors and item wording are usually derived from student responses to open ended questions and validation from experts in the field (Knight, 2010). These factors make CIs useful and reliable tools for assessing what students know. In fact, in her 2013 follow up to *Vision and Change*, D'Avanzo (2013) suggests that a body of CIs be used as a means of providing data as evidence to biology department faculty members supporting the use of active learning and student-centered course design. An emphasis was placed on the importance that active learning exercises be carefully designed for specific concepts (D'Avanzo, 2013).

1.4 Purpose

One such topic, gene regulation, is identified as an important concept to the overarching principles laid out as being fundamental to meeting the goals of the five core concepts established by *Vision and Change* (AAAS, 2014). Given the importance of the

topic of gene regulation and that biology students have been shown to struggle with genetics concepts that require critical thinking, we were motivated to investigate a better way to teach students concepts relating to gene regulation using the *lac* operon and to assess their learning of this difficult topic (Cavallo, 1996; Lewis, 2000). Indeed, a key concept to the understanding of the broad fields of genetics and cell biology is the regulation of gene expression. There are a wide range of mechanisms that cells use to control whether or not genes are transcribed, when genes are transcribed, and to increase or decrease the quantity of certain proteins based on the cell's needs. One of the best understood examples of gene regulation is the inducible *lac* operon *E. coli*.

Regulation of the *lac* operon was first described by François Jacob and Jacques Monod. Their research demonstrated how enzyme quantities can be controlled directly at the level of transcription (Jacob and Monod, 1961). For their discoveries, Jacob and Monod were awarded the Nobel Prize for Physiology or Medicine in 1965. Their discoveries gave rise to a large sub-discipline within molecular biology devoted to the understanding of genetic regulation and have become well established in the curriculum of undergraduate genetics and microbiology courses. The *lac* operon teaches students a transcriptional regulatory system that, if understood, serves as a base for the understanding other and more complicated systems of gene regulation. Further, well described mutations to the *lac* operon are used teach students how mutant alleles cause phenotypic differences.

Upper division and graduate level courses explore this topic in greater detail and an understanding of this system is needed to comprehend more complex laboratory

techniques such as blue-white screening and molecular cloning (Cronan, 1988). In addition, regulation of gene expression is an important feature of many biomedical, environmental, and pharmaceutical research and development endeavors. For example, human insulin, which is used by diabetics is currently produced in bacteria using bacterial gene regulatory regions in control of the human insulin gene (Walsh, 2005).

The primary goal of this study was to investigate the usefulness of an analogous hands-on model in learning the regulation of an inducible system, the *lac* operon. An analogous hands-on model was the chosen method of instruction based on the body of literature supporting the educational benefits of active learning and the use of models and analogies. The hypothesis was that the model would promote better conceptual understanding of 1) the components of the operon, 2) how environmental conditions influence the expression of genes, and 3) how specific mutations affect the operon's regulation.

CHAPTER II: METHODOLOGIES

2.1 Creating a Gene Regulation Concept Inventory

Study Context and Participants

This study was conducted between May 2014 and March 2015 at a large Southeastern public university of 22,000 undergraduates where the average age of students is 23 years, the average ACT score is 22.3, he student body is roughly 53% female, and 79% are on financial aid (MTSU, 2014). Participants were students registered in microbiology or genetics (n = 299) during the 3 semester. Participants enrolled in the microbiology course are typically freshman or sophomores while students in the genetics course are typically sophomores or above. The study was conducted using ethical protocols for human subjects and was approved by the Internal Review Board at MTSU (IRB 15-025). Only data from those students who gave informed consent were included in this study.

Concept Inventory Design

A valid and reliable tool to measure student learning regarding prokaryotic gene regulation could not be located despite examination of current literature and location of some biology CIs for the model and activity (D'Avanzo, 2008; Kalas, 2013; Knight, 2010). Utilizing a rigorous protocol for concept inventory design a validated and reliable concept inventory was developed as part of this research study (Table 1). First, using a

backward instructional design, the following student learning objectives were established: After instruction, students were expected to be able to:

1. Identify, and understand the role of, each structure and component of the *lac* operon
2. When given particular cellular conditions, accurately predict whether or not gene expression will occur and
3. When given particular mutations to the *lac* operon, predict affected outcomes of gene expression.

Table 1. Concept Inventory Generation Workflow. The steps used in developing a gene regulation concept inventory including the purpose for each step, manner in which data was collected, and sample size for each step.

Step	Purpose	Sample Size (n)	Feedback Type
1. Learning objectives established and initial Questions Developed (Spring 2014)			Expert review of questions
2. Piloting 1st iteration (Maymester and Summer Session 1 2014)	Identify misconceptions (distractors) and clarity of questions	22, 18	Short written responses, class discussion
3. Piloting 2nd, MC iteration (Summer Session 2 2014)	Wording/phrasing of questions and answer choices	23	One on one interviews
4. In class testing (Fall 2014)	Item analysis , validity, and reliability	100, 15	In class administration of 12 MC questions

Using items from previous educational resources as a guide, twelve open-ended short answer items were carefully designed as a pilot inventory aligned with the learning objectives. These items were then reviewed by three experts in the field (biology department faculty members) to ensure readability, representativeness, and content validity of the items aligned with the learning objectives. On Friday May 16, 2014 this open-ended item set was initially given to a section of microbiology students (n = 22) as a means to catalogue common student misconceptions related to the learning objectives. Students were instructed to answer, in writing, the items with as much detail as possible. In addition, they were asked to provide feedback on the items themselves in order to help clarify the wording. This provided additional face validity to the items. Following administration of the pilot inventory, the items were discussed with the class as a group to receive additional verbal feedback regarding clarity of the item wording. However, the initial validation of the pilot instrument was difficult as the students appeared unmotivated to provide feedback in the discussion and the written items were not thoroughly answered.

Following the experience with the first group of students, the pilot inventory was then given to a second group of students in order to collect more rigorous data. These items were administered again on June 24, 2014 with the same instructions, to a second microbiology class of n = 18 students with the added incentive of extra credit for thoroughly answering each item. More rigorous data was collected during this administration and was added to the initial data for analysis.

Having received sufficient feedback, one prominent misconception held by students was identified, the mistaken belief that the *lac* repressor protein binds to the promoter of the *lac* operon. These groups also held misconceptions regarding whether or not the repressor protein is active in the absence of lactose. Several students said "no" and stated in their reasoning that this was so the cell can save energy. This indicated that students misunderstood that the function of the active repressor is to prevent transcription, which saves energy. These microbiology students struggled with the questions regarding mutations because they were not specifically taught about the mutations in class. However, several students were able to use their understanding of the operon to correctly determine the answers to those specific questions. The questions on which these students performed poorly involved the third learning objective, about what would happen in a mutant cell if a wild-type copy of the mutated gene were introduced.

Using identified misconceptions from the first two groups of students on the first pilot iteration of the CI, twelve multiple choice items were developed which aligned with the established learning objectives. Word choices used by the students were identified and used when constructing the items and answer choices. For example, the term promoter was used as an answer choice for item 1 instead of *lacP*.

During the second validating iteration, the revised multiple-choice LOCI was administered to students from a genetics course (n = 23) during the week of July 31, 2014. To do this, an administration procedure was followed similar to Kalas et al. (2013) in their design of a meiosis CI. I met with individual students in this sample outside of

class, had them answer the LOCI verbally while talking out their reasoning as they answered each item. Using this feedback the wording of item 5 was adjusted from "Is mRNA transcribed from the *lac* operon when lactose is present in the cell? Why or why not?" to "Is mRNA transcribed from the *lac* operon when lactose is present and glucose is not present in the cell? Why or why not?" After revisions, it was not necessary to discard any of the twelve questions. It should also be noted that during these interviews students expressed a misconceptions about the operator and promotor of the operon.

Item Analysis

The revised LOCI (Table 2) was given to a larger sample of $n = 115$ genetics students from two different sections of genetics, one honors section ($n = 15$) during the fall 2014 semester and another general genetics section ($n = 100$) during the last week of the spring semester of 2015. All participants were awarded extra credit for answering the LOCI. Initially students' responses were converted to 1-4, correlating to answer choices A-D. A frequency distribution was created for each item and it's distractors (See Appendix B for correct answer choices and distractors) that showed how often each answer choice was selected, which indicated the most commonly selected answer and to identified commonly selected distractors.

Table 2. *Lac* Operon Concept Inventory Questions. The twelve multiple-choice items of the LOCI. Each item corresponds to one of the learning objectives.

Learning Objective	Item
lac Operon Structures/Components	This information is being withheld to maintain the integrity of the concept inventory. The CI items can be obtained by verified instructors from: Dr. Rebecca Seipelt-Thiemann, Rebecca.Seipelt@mtsu.edu.
Predicting Outcomes	
Mutations	

Item analysis for each item on the LOCI was conducted including index of difficulty, item discrimination index, and the point-biserial correlation as described by Kalas *et al*. (2013). The index of difficulty is the portion of students who selected an incorrect answer and is used to determine if particular items are appropriate for the group based on their current level of understanding of the topic. When items difficulty is too high or too low, construct validity is threatened.

$$P = \frac{N_1}{N}$$

N_1 is the number of correct responses while N is the total number of responses. Students' raw answers were then converted to a score of either 1 for a correct answer or 0 for an incorrect answer for each item on the CI. The index of difficulty was calculated by finding the proportion of students who gave the correct answer for each item. The index of difficulty in this context indicates how challenging a particular item is and ranges from 0.00 (very easy item) to 1.0 (very difficult item). Experts suggest a range of 0.60 to 0.80 as optimal when constructing multiple choice items (Kubiszyn & Borich, 2003).

The discrimination index and the point-biserial correlation both compare a student's score for an individual item to how well they performed on the overall assessment. The discrimination index was found by first ordering students' answers by performance on the entire inventory. The responses were then divided into the top 27% (31 total) of performers and bottom 27% (31 total) of performers. Then for each item, the number of students who answered incorrectly in the bottom 27% were subtracted from the number

of students who answered correctly in the top 27%. This number was then divided by the total number of students in either group, 31.

$$D = \frac{N_H - N_L}{31}$$

Where N_H is the number of students in the high scoring group who answered the item correctly and N_L is the number students in the low scoring group who answered the item correctly. The discrimination index values range from -1.0 to +1.0 where +1.0 is the best possible outcome. A value of +1.0 would indicate that every student in the top performing group answered the item correctly whereas a value of -1.0 would indicate that every student in the bottom performing group answered the item correctly. Both of these indices indicate if an item (or assessment) is appropriately differentiating (or discriminating) between low- and high-knowledge students. For example, if generally high-performing students are consistently getting a particular item incorrect than that item is not appropriately discriminating students with high conceptual understanding from those with low conceptual understanding and content validity as well as reliability of the assessment are threatened.

A point-biserial correlation was calculated between the score on each question and the score on the remaining 11 questions as follows:

$$r_{pbs} = \frac{\bar{X}_1 - \bar{X}}{\sigma_x}\sqrt{\frac{P}{1-P}}$$

Where $\bar{X}_1$ is the mean total score of students who answered the item correctly, $\bar{X}$ is the mean total score of the whole sample, σ_x is the standard deviation of the total score of the whole sample and P is the difficulty index of the item. Point-biserial correlations will be positive if the item is discriminating students well and negative if the item is poorly discriminating students. The qualitative meaning of the index is similar to that of the discrimination index noted above. The values for correlation range between 0.0 and 1.0. Item difficulty and item discrimination are closely tied to one another.

Additionally, a coefficient alpha was calculated to determine the internal reliability of the LOCI. Where:

$$\alpha = \frac{k}{k-1}\left(1 - \frac{\sum_{i-1}^{k} P_i Q_i}{\sigma^2 x}\right)$$

k is the number of items, where σ_X^2 is the variance of the observed total test scores, where P_i is the proportion scoring 1 on item *i*, and $Q_i = 1 - P_i$.

2.2 The Model and Student Activity

Model Development

Development of the hands-on model, went through several steps. The first iteration of the model was a locking box that contained sets of instructions inside which were to be used by students to assemble Legos that would be analogous to proteins. In this model the lock and key were analogous to the repressor protein and inducer. The latch on which the

lock was placed was analogous to the operator. The instructions on the inside of the box were analogous to structural genes. The activity was administered with oral instructions and a set of notecards for each box that had cellular conditions written on them. This first iteration of the model was constructed and piloted with a class of honors genetics students.

During its implementation, a couple of issues with this version of the model became apparent. First, without specific instructions to guide students through the activity, students jumped to the end conclusion of whether or not to build Lego proteins without considering the regulatory steps in between. Students opened the box once, removed the instructions and pushed the rest of it aside for the remainder of the activity. This experience made it clear that more detailed instructions would be necessary to encourage students to actively engage with the regulatory process that the activity was meant to teach them. There was also a practical issue regarding the size of the box. They were large and it was difficult to move them around, even in a small class.

A new design was devised which assimilated many of the original analogy ideas, but used a locking journal design in place of the box (Figure 1). This model is made up of analogous components as follows: a lockable journal with written instructions for assembling Legos representing the operon and its structural genes, a lock representing the repressor protein, and a key representing the inducer. The loop the lock attaches to represents the operator, while reading the instructions is analogous to transcription, and assembling the Legos per the manual's instructions is analogous to translation.

a.

Analog	Target
Locking Instruction Manual	*lac* Operon
Loop for Lock	Operator
Title Page	Promoter
Lock	Repressor
Key	Inducer (Allolactose)
Instructions for Assembling Legos	Structural Genes
Assembled Legos	β-Galactosidase, Permease, Transacetylase

b.

Figure 1. ***Lac* Operon Analogy Components.** a. The *lac* operon model analogs and targets. b. The *lac* operon hands-on model components.

This model solves the issues of the original model. Since it is small, it is easy to transport to a classroom and within the classroom and is more easily handled by students. Also, since the instructions are attached to the book, students must interact with the regulatory analogs to complete the activity. In this way, students are forced to confront what the model is intended to teach them.

Implementing the Model and Activity

Permission was granted by the genetics course instructor to implement the activity with the seven laboratory sections of genetics for the spring 2015 semester. There were a total of seven lab sections taught by assigned graduate teaching assistants (GTAs). Each of the seven lab sections were designated as either treatment or comparison sections. Three of the four lab instructors taught two sections so, in order to control for differences in the instructors themselves, one of their sections was designated a comparison group while the other was classified as treatment group. One GTA only taught a single section and this section was designated a treatment group. In order to determine a baseline for comparison of initial participant conceptual understanding, every student was asked to answer the LOCI before being taught about gene regulation that semester. To control from potential prior knowledge, participants were also asked if they were repeating genetics or had any previous knowledge of the *lac* operon. A total of $n = 121$ students responded to the LOCI and survey questions. Additionally, these students also gave their informed consent to have their data included in this study.

Every lab section was given a short lecture covering the *lac* operon during the week of March 23, 2015. The genetics GTAs were given a set of instructions on how to teach the *lac* operon and what specifically to cover (Appendix B) in an attempt to ensure each class was taught in the same manner and no pertinent material was excluded. The instruction included a three minute video explaining the normal regulation of the *lac* operon followed by a description of the common mutations effecting lac operon function by the lab instructor.

The following week, students in the comparison lab sections were given the LOCI to answer with no additional instruction. The treatment lab sections participated in the hands-on activity and then answered the LOCI. Each student was awarded five points for a quiz grade for answering the LOCI and an additional 0.5 point for each item they answered correctly.

Each treatment lab section was subdivided into groups of four and occasionally a group of three or five was necessary based upon the number of students in attendance. Each group was given one *lac* operon model and one worksheet with instructions. Per the worksheet instructions, each member of the group was given a specific job: 1) worksheet reader 2) Lego assembler 3) key keeper 4) *lac* instruction manual reader. This kept each member of the group actively engaged in the activity and is supported by research in appropriate collaborative group instruction. In part one of the activity, the groups determined if specified cellular conditions (presence of a certain sugar) allowed them to use the key to remove the lock, open the manual, read the instructions, and assemble the Legos. In the second part of the exercise students explored various mutations affecting

the *lac* operon. They were asked to determine which of the components of the manual would be affected and relate that to how the mutation changes the circumstances under which the genes of the *lac* operon are transcribed.

Once the groups completed parts 1 and 2 of the activity, the author led them in a group discussion of the exercise. We discussed the correct results from parts 1 and 2 and then discussed induced partial diploids and the potential for complementation in each of the mutations. The students were then asked to answer the LOCI to determine if the use of the analogy aided in learning prokaryotic gene regulation.

Post Assessment and Surveys

The week following the activity implementation, two different surveys were administered to the study participants to determine if students who were in the treatment group found the hands-on activity to be helpful and if so, in what way. Each instructor was given a small number of surveys (2-6) to give to students in their treatment sections. The GTAs were instructed to use a random number generator to select students from their class roster to give the survey to. However, these instructions may have not been followed in every class so there is no way to completely rule out a response bias. These surveys asked students to describe what ideas/facts aligned with each learning objective that the activity helped them understand. This survey also asked what aspects of the activity they found to be helpful if at all.

A second survey was made available to all students to answer online (Table 3). This survey listed all of *lac* operon teaching resources that were available to the students and

asked students to rank each one, separately, on scale from 1 to 5 regarding how useful they were to learning. They were also given an N/A option for teaching resources that they did not use.

Table 3. Summary of Survey Questions Made Available to Students Online. Six total instructional tools used were rated from 1 – 5. N/A was an available choice for students who did not utilize a tool.

Instructional Tool	Ratings Choices					
YouTube video	1 – Not Helpful	2	3 – Somewhat Helpful	4	5 – Extremely Helpful	N/A
In-class lecture	1 – Not Helpful	2	3 – Somewhat Helpful	4	5 – Extremely Helpful	N/A
Hand-out from Instructor	1 – Not Helpful	2	3 – Somewhat Helpful	4	5 – Extremely Helpful	N/A
Textbook	1 – Not Helpful	2	3 – Somewhat Helpful	4	5 – Extremely Helpful	N/A
Hands-on Activity	1 – Not Helpful	2	3 – Somewhat Helpful	4	5 – Extremely Helpful	N/A
Previous Instruction	1 – Not Helpful	2	3 – Somewhat Helpful	4	5 – Extremely Helpful	N/A

CHAPTER III: FINDINGS

Gene regulation is an important biological concept. An analogous hands-on model was developed to aid in learning the *lac* operon. However no CI-style assessment tool was available to utilize in testing this model of prokaryotic gene regulation. The LOCI was developed and tested. It was found to be reliable, predictive and valid. The model was then tested in genetics laboratory sections. To test its efficacy the LOCI was administered to both treatment and comparison groups to determine their conceptual understanding of the *lac* operon. Two surveys were used to determine how students viewed the usefulness of the model and other instructional techniques.

3.1 Concept Inventory

Development of the LOCI began with determining learning objectives and writing 12 questions representing these objectives, which were piloted with microbiology students who gave short written answers. From these answers, initial common misconceptions were identified along with wording that students were comfortable using in answers. Then 12 multiple choice items were written and given to genetics students to answer in a one-on-one interview. The wording for questions and answer choices were clarified, where needed (Tables 1 and 2). Finally, the LOCI was given for in-class testing with two genetics sections (n =100, n =15). The data from this group was then analyzed for difficulty, reliability, and discriminatory power (Table 4).

Table 4. Difficulty, Reliability, and Discriminatory Power of the LOCI Items. The learning objectives and statistics associated with each of the twelve LOCI items is shown. The Difficulty Index is the proportion of students who answered the item correctly. The discrimination index indicates an item's ability to distinguish between high performing students and low performing students. The point biserial correlation compares how students performed on an individual item to their total score giving a measure of single-item reliability. The coefficient is a measure of internal reliability of the LOCI as a whole.

Learning Objective	Question	Index of Difficulty	Discrimination Index	Point-Biserial Correlation
Knowledge of operon structure and its Components	1	0.42	0.19	0.36
	2	0.77	0.42	0.44
	3	0.55	0.12	0.32
	4	0.40	0.48	0.43
Predicting outcomes of various cellular conditions	5	0.46	0.45	0.34
	6	0.34	0.48	0.40
Understanding the effects of known mutations	7	0.54	0.65	0.54
	8	0.42	0.56	0.53
	9	0.49	0.52	0.44
	10	0.30	0.23	0.32
	11	0.46	0.42	0.42
	12	0.50	0.55	0.47
α coefficient = 0.994				

Item Analysis

The Difficulty Index is a measure that ranges between 0 and 1 and is the proportion of students who answered the item correctly. The Difficulty Index of one item was above 0.7, three fell between 0.5 and 0.7, while seven items fell between 0.3 and 0.5. This suggests that the items cover an appropriate range of difficulties with the majority falling into the moderately difficult category (Adams, 2011; Kalas, 2013) (Table 4). The Discrimination Index measures the ability of an item to distinguish between high and low performing students. The Discrimination Index for the majority of the items was ≥ 0.3 (except items 1, 3, and 10) with a mean discrimination index = 0.42. This indicates that most items have the ability to distinguish between high performing students and low performing students (Ding, 2006). The Point-Biserial Correlation compares how students performed on a particular question to how they performed on the rest of the items giving a measure of single-item reliability. The point biseral coefficient of all items fell above the recommended value of ≥ 0.2 (Ding, 2006) (Table 4).

Finally, the coefficient alpha, which is a measure of internal reliability, was found to be 0.994 suggesting a very high internal reliability of the LOCI as a whole. This value is extremely high but given that the scope of the LOCI is quite narrow it does not seem unreasonable.

Misconceptions Identified

Through the item analysis, misconceptions were identified on several items (Figure 2), which were similar to those identified in the pilot iterations of the LOCI. The most prominent of these was the mistaken belief that the *lac* repressor binds to the promoter, not the operator, as evidenced by students choosing this answer 37.4% of the time from item 1. The frequency distribution for item 6 showed many students (29.6%) had a mistaken belief that the repressor is activated by the inducer. Another 22.6% of students incorrectly believed that lactose activates the repressor. Item 10 was another poorly understood item, where 31.3% of students believed that introducing a wild-type copy of *lacI* into a cell with a supper-repressor (*lacI*^{s}) would rescue a wild-type phenotype while 30.4% correctly answered that it would not. This may indicate that students hold a mistaken belief that when another gene is introduced into a cell on a plasmid that it replaces the existing gene.

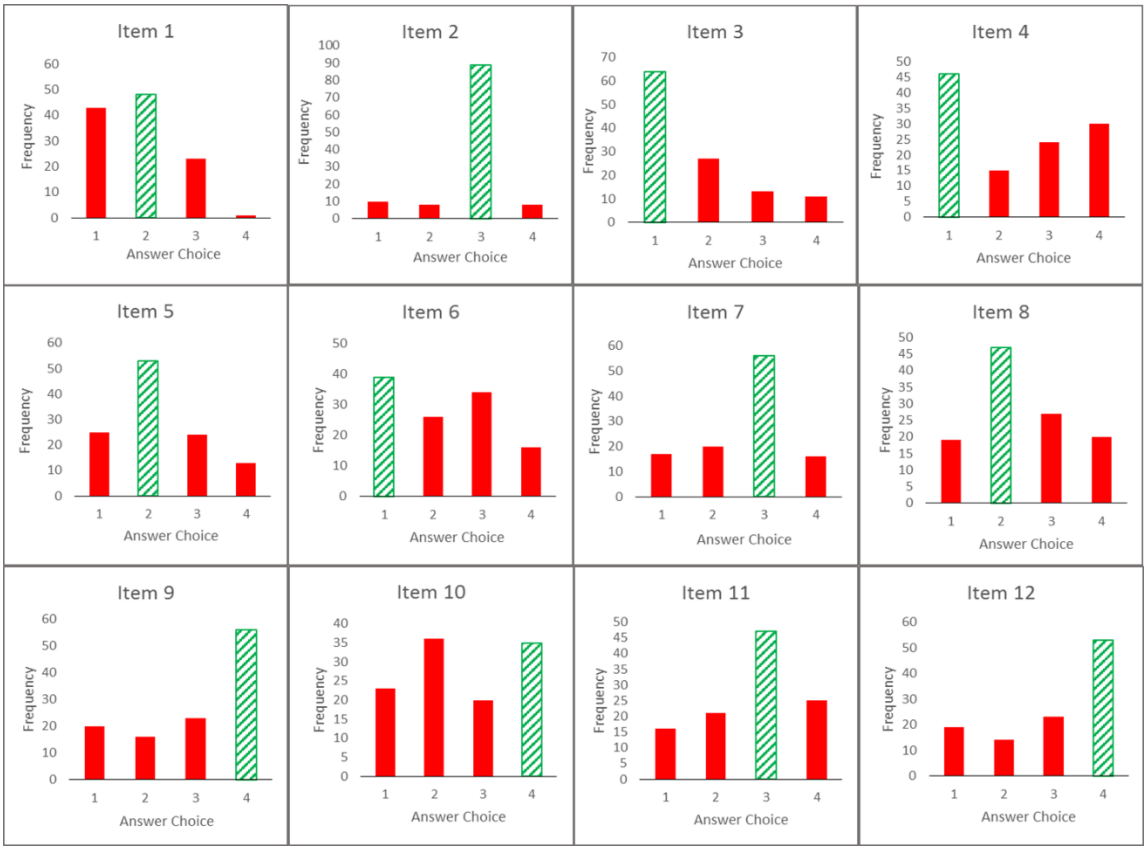

Figure 2. **Frequency Distributions for Each Item of the CI.** The frequency of the correct answer choice is shown in green (hash marks) and the distractors in red from in-class testing (*n* =115) of the CI. Data from items 1 and 10 both show commonly held misconceptions in this group of students while items 6 shows a poorly understood concept. Data from item 2 indicates an idea that was well understood by this group of students.

Observations

The results of item analysis and reliability testing show that the LOCI covers a broad range of difficulty, has the ability to discriminate between high performing and low performing students and is very reliable. Overall, students performed poorly on the LOCI after instruction. The average score for all participants was 5.65 out of 12 or 47.1% indicating that generally these students struggled with this concept. This lends support to the need for additional or improved instructional techniques to help students gain more understanding of this complicated regulatory system. The misconceptions that were identified can provide instructors with insight into student thinking to better inform their approaches. For example, knowing that students have confusion over the location to which the repressor protein binds, instructors can construct appropriate hands-on or visual activities which cause students to confront this misconception, as well as the other common misconceptions.

3.2 LOCI and Survey Results from Hands-on Activity

With the LOCI, a comparison could be drawn between traditional lecture alone and the addition of an active learning approach to learning the *lac* operon. A hands-on analogous model and accompanying worksheet were developed and administered to seven genetics laboratory sections. Roughly half of the lab sections were designated as comparison

groups and were taught about the *lac* operon using traditional methods while the other half also participated in the hands-on activity. Upon completion of their respective treatments, each group's knowledge gain was assessed by the LOCI.

LOCI Scores following the hands-on actvity

It was determined that no mean differences existed between the two treatment groups on the pre-test LOCI scores (t = -0.333, $P \geq 0.05$). In fact, the data strongly suggests that students' answer choices were based on chance or guesses. The pre-assessment survey questions indicated only 1 student out of 47 in the treatment group and 3 out of 56 students in the comparison group had learned about the *lac* operon before this study. Furthermore, the Z-score for the treatment and comparison groups were 0.35 and 0.31 respectively, indicating that the correct answers that were chosen by students were likely the result of the 25% chance of guessing the correct answer out of four possible answer choices. With this quantitative support for the limited validity of the pre-test administration, it was determined that it would be more descriptive of the sample to set aside the pre-test data when analyzing the post-test scores.

The comparison and treatment groups' CI mean scores (Table 5) were compared and it was found that the treatment group's scores ($\bar{X}$ = 7.88) were significantly higher, about 7.5%, than the comparison group's ($\bar{X}$ = 6.98) (t = -2.281, P <0.05). An examination of students' individual item responses (Figure 3) indicated that for a majority of the LOCI items, students in the treatment group selected the correct answer choice more frequently

Table 5. Mean, Median, Range, and Standard Error of LOCI Scores. Descriptive statistics calculated for the treatment (n = 67) and comparison (n = 62) groups after learning the *lac* operon.

Group	Mean	Median	Range	Standard Error
Experimental (n=67)	7.88	8	10	0.26
Control (n=62)	6.98	7	11	0.29

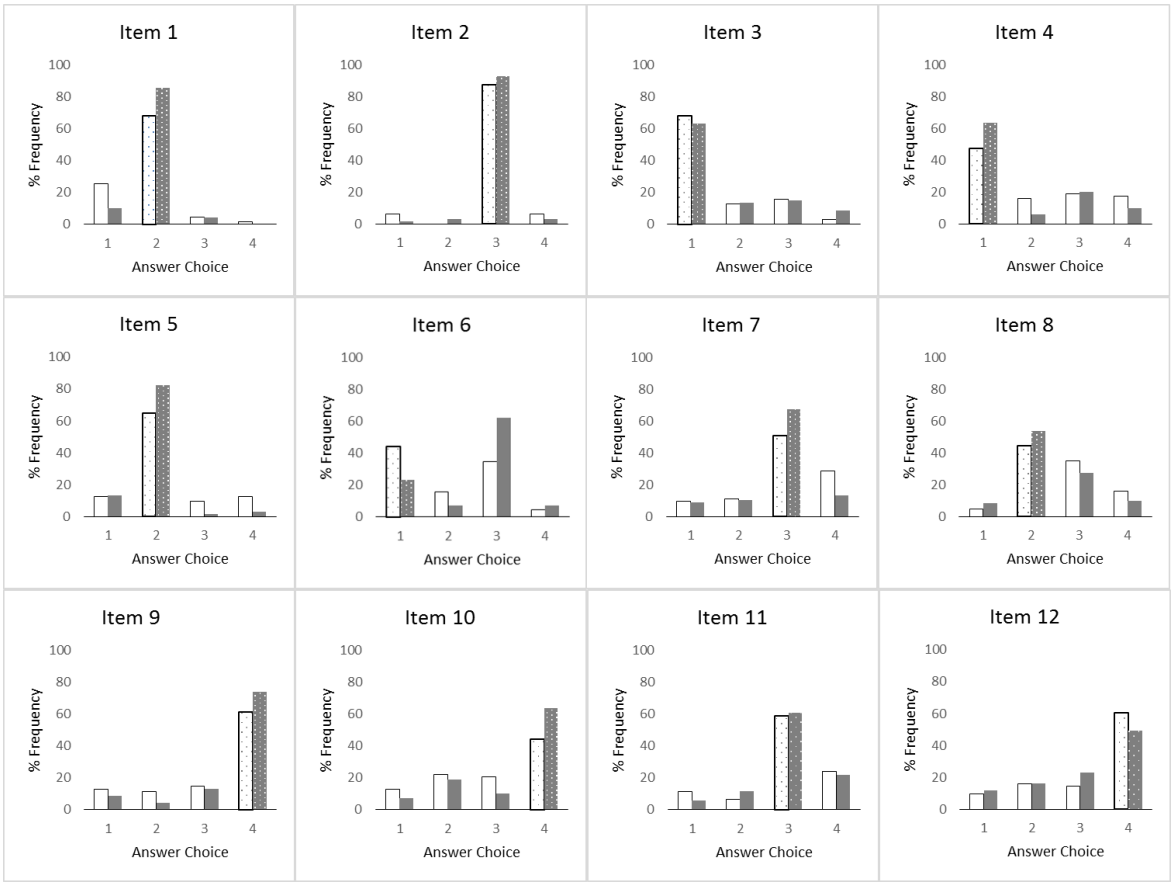

Figure 3. Percent Frequency Distributions of LOCI Answer Choices Comparing Treatment and Comparison Groups. Answers from the comparison group are shown in white and answers from the treatment group in gray. The patterned bars indicate the correct answer choice for each item.

than the comparison. Students in the treatment group showed a greater than 15% increase in selecting the correct answer over students in the comparison group on items 1, 4, 5, 7, and 10. By comparison, one distractor was substantially selected for items 1 and 7 in the comparison group only. Higher distractor selection proportion in the comparison group suggests that the active, hands-on modeling activity helps with addressing misconceptions related to items 1 and 7. One distractor was substantially selected for items 6 and 8 in both groups suggesting that a misconception remains. However, the proportion of the treatment group selecting the distractor was actually higher for item 6 than the comparison group. Therefore, it appears that the activity may have pushed students towards a misconception for item 6. Also, students in the comparison group selected the correct answers on item 3 and 12 more frequently than the treatment group, but both groups selected the correct answer, rather than any particular distractors, in overwhelming numbers.

Survey Responses

The students' LOCI scores provide a means of comparing levels of understanding between treatments groups. However, on their own, the scores do not provide an assessment of how helpful the hands-on analogous model was to students in comparison to other tools. In order to draw any conclusion about the utility of the hands-on model it needs to be established the mean difference in LOCI scores was not simply due to students spending a little extra time with the material.

Two surveys were constructed to gain additional feedback from the students regarding the activity specifically. They were asked to complete an online survey in which they assigned a score from 1 to 5 for the different learning tools that were available to them for the *lac* operon. A more comprehensive open-ended survey was also given to the treatment sections asking them to describe how, if at all, the activity helped them with each learning objective.

A total of 49 students responded (38%) to the online survey (Figure 4). From this data, a percentage was calculated for each instructional tool in which responses which ranged from 3 to 5 (somewhat helpful to extremely helpful). When calculating this percentage the "N/A" responses were excluded from each instructional tools' total. Of the tools available, 97.8% of the respondents found the YouTube video helpful while 97.9% found the lecture instruction helpful. In addition, 88.2% rated the hands-on model activity to be helpful. By comparison, 73.5% and 50% of students rated their textbooks and previous instruction, respectively, as helpful. This suggests that most students in the treatment sections did find the activity, specifically, to be helpful and, at the very least, did not inhibit the students' understanding of the *lac* operon.

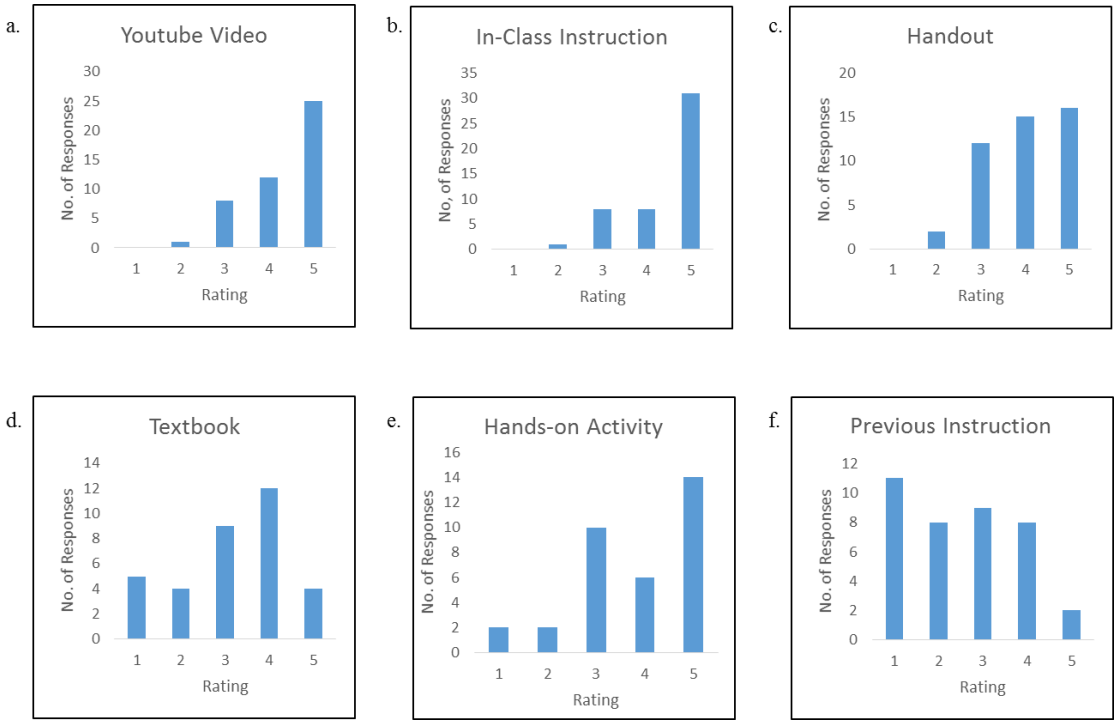

Figure 4. Frequency Distributions of Instructional Tool Rankings. The number of respondents ranking a particular tool is shown on the y-axis (n = 49). a. Youtube video. b. In-class instruction. c. Handout. d. Textbook. e. Hands-on activity. f. Previous instruction. The hands-on activity was generally rated well along with in-class instruction and a YouTube video. Text book and previous instruction were not rated as high

Generally, the students' responses to the open-ended survey were positive and indicated that the activity was able to address and help students with the three different learning objectives for which the LOCI was designed. Students had strong positive feedback regarding how the activity helped with the first learning objective. One student said, "I like the whole lock and key thing to help understand the repressor," while another said, "I understand it better after the activity. I am a very hands-on and visual learner. It was good to have something to relate [the structures and components of the *lac* operon] to," while yet another student said, "it makes sense when you can have a physical model to operate in the same way that something else does."

The responses concerning the helpfulness of the activity in regard to the second learning objective were more varied. One student indicated that the model was unnecessary for this objective since you only need to know what sugar is present. However another student said, "The discussion helped more with this part because we were able to say what we knew would happen and then show it with the [model]" indicating that group discussion in combination with the model was the way in which the activity helped them with this objective. On the other hand, a different student said, "I enjoyed building the proteins. After seeing the visualizing the proteins, it made more sense to me."

Responses regarding the third learning objective were also generally positive and indicated a preference for having a hands-on model. Several respondents said that they understood the mutations better by having the parts of the model to visualize for each

mutation. One student said, “It helped me remember what mutations did what. By visualizing it, it made so much more sense,” and another student said, “the activity helped me what each mutation did by comparing them to parts of the model.” Another student gave this response: “The discussion and notes we had done before class helped with this because we could help each other remember what mutations did what and the objects [of the model] helped to reinforce that.”

Lastly, the students gave overall feedback on which aspect of the activity, as a whole, were helpful to them. One student said, “The visual representation of each component helped because I am a visual learner. The discussion helped some but the diary, lock, key, Legos, etc. helped the most because it simplifies the subject. It’s easy to comprehend that when the book was locked that it couldn’t be read just like in the *lac* operon.” Another student responded that, “I am a very visual learner but I also talk my way through things so being able to see it and touch it and talk to my group about it really helped my understanding of the *lac* operon.”

Interestingly, one of the survey respondents seemed to have missed the previous week’s instruction or did not understand it. This led to some interesting comments on these survey questions. In regard to each learning objective this person said, “With no previous understanding of what a *lac* operon even is, I understood what the activity was attempting to teach me, but I should have read about it first.” And in response to the last question asking generally what aspects the activity helped with this student said, “The concept of being able to or not being able to open the book to access the information to

make a protein was good and probably very helpful for hands-on learners." Finally, even though the value of the hands-on activity was being assessed with this survey, one student indicated that he/she much preferred the YouTube video as an instructional tool.

CHAPTER IV: DISCUSSION

The purpose of this study was to examine the efficacy of a hands-on analogous model in learning the *lac* operon. In order to assess the value of this activity, a valid and reliable CI was constructed. The data showed that students who participated in the activity scored higher on the LOCI than students who only learned the *lac* operon by traditional lecture. Students that had the opportunity to participate in the activity selected the correct responses over the distractors more often that the comparison group for 9 of the 12 CI items (Figure 3). Of the three remaining items, one (item 12) shows a higher proportion of correct answers in the comparison group compared to the treatment group, but no particular distractor was selected more than any other and not to a high extent in either group. The other two items (6 and 8) showed misconceptions are present in both groups and remain following the activity. Of these two items, the data for item 6 shows participation in the activity may have increased a misconception as indicated by students in the treatment group selecting a distractor more often than the comparison group. Any further revision to the activity will necessarily involve investigating and addressing these misconceptions. In addition, anyone teaching the concept of gene regulation would be wise to address misconceptions relating to these items in his/her teaching. Student interviews, similar to those used in the LOCI design, could be utilized to learn how these misconceptions are being formed. Information from the interviews could then be used to implement changes to how the information is introduced in lecture or to the activity described in this thesis. This analysis of the hands-on analogy was only possible because

a valid and reliable concept inventory was generated specifically for this study, but will be made available to the biology education community.

4.1 Use of CIs and Application of LOCI

In recent years, concept inventories have been recognized for their value to educators as tools for assessing student learning and to inform instructional methods (Knight, 2010). Education research benefits from the increasing use of CIs by providing a source of hard data for analysis. Often, educational studies describe an instructional methodology and provide anecdotal evidence for their efficacy without descriptive statistics to support their conclusions. Concept inventories can, in part, aid in filling this void in education research. With a repository of CIs available, researchers could adapt and apply them to their educational studies which would result in more powerful and valid inferences being drawn based on data.

Adding to an existing body of CIs, the LOCI provides an inventory which covers inducible gene expression which was not previously available. The LOCI will be available for future use by biology instructors. Since creating a CI is time and labor intensive, having the LOCI accessible provides a method for researchers and instructors to collect data that can be incredibly informative without necessitating that a CI be written and validated for each study. It can be used to examine students' understanding of the *lac* operon and/or in the continued exploration of active learning techniques applied to learning the *lac* operon. For example, in his 2015 paper, Robert Cooper outlined a comprehensive approach to teaching five "big idea" biology concepts with

operon models. The paper provides the ideas and activities, but does not provide assessment to support that the approaches are educationally beneficial. The LOCI could be implemented in classes being taught as described to examine how well students understand the big ideas using operons and whether or not they have any widely held misconceptions. The results from the LOCI could then provide instructors with tangible data to support or refute the use of Cooper's approach, therefore, potentially broadening the impact of his paper. These types of data either from CIs or other forms of assessments, are crucial to advancing the use of evidence-based, active learning techniques and support education research and the broader discourse in the literature.

4.2 Implications for Active Learning, Hands-on Learning, and Analogous Models

The additional element of providing evidence for validity and usefulness for a learning activity allows instructors to make an informed choice about an activity. Students who participated in this hands-on activity outperformed students who learned about the *lac* operon through passive techniques alone by 7.5% on the LOCI. The difference is both positive and statistically significant. Therefore, the gain in understanding following the activity indicated that the activity was positively associated with learning prokaryotic gene regulation. Further, using this data, along with the students' survey responses, it can be concluded that the analogous hands-on model and activity is helpful to students when learning the *lac* operon. Taken together, the data suggest that an approach that combines multiple methods of instruction, combining active and passive learning, to be more

effective and helpful to students who are learning the *lac* operon than lecture alone. This is in agreement with the conclusions reached by Freeman, *et al.* (2014) in their review of 225 educational studies. This also aligns with the recommendations laid out in "Vision and Change" which endorsed approaches that added active learning techniques to traditional lecture.

In addition to supporting the use of active learning, this study further supports the use of hands-on models to learn difficult and abstract concepts that exist at a small scale, termed the microcosm scale by Niebert and Gropengiesser (2015). Indeed, they provide evidence that understanding starts at the mesocosm (medium-scale) dimension and that students should be provided opportunities to bring macrocosmic (big-scale dimension) and microcosmic (small-scale dimension) concepts into the world that is experienced by students through the use of metaphor and analogy (Niebert and Gropengiesser, 2015). The hands-on approach used in this activity forced students in this study to engage and interact with the microcosm-level structures and processes being learned. It also provided an object for them to see and manipulate that they could then compare to something too small and complicated to view directly. Studies have previously shown that hands-on models are effective tools for science instruction across age/level of expertise groups and scientific disciplines (Gerstner, 2010; Haglund, 2012; Lin, 2013). The *lac* operon model joins other micro- and macrocosm-level models which have been used to teach other biology concepts including but certainly not limited to introductory biology concepts, evolution, genetic mutations, DNA structure, symbiosis, cell membrane structure, and the

difference between genomic and plasmid DNA (Witfield, 2008; Seipelt, 2006; Mathis, 1979; Altiparmak, 2009; Miller, 1998).

The active learning technique employed in this study was that of a hands-on analogous model. At the heart of this study was the idea that students would be able to learn and understand the concept of gene regulation better by analogy using items familiar to students. For example, by telling students that the lac repressor is like a lock, they were able to make the connection between something previously foreign to them and something simple that they were all familiar with. The use of analogies to communicate new concepts is a natural and intuitive way to learn. By making the analog, or familiar concept, something very simple makes understanding the target, or new concept, easier to grasp and less intimidating. Carefully constructed analogies have been shown to be effective tools in biology instruction by facilitating learning and problem solving. (Venville, 1997; Glynn, 1989; Duit, 1991).

4.3 Extensions to the Activity

Not only can analogous hands-on models aid in learning the concept of interest, they can be extended in numerous directions by instructors or students. Instruction of the *lac* operon falls into a larger discussion of gene regulation which takes place in genetics, microbiology, molecular genetics and biochemistry courses. The *lac* operon is one specific method, among others, that has evolved which allows organisms to control the

expression of genes through differential protein function, co-factor binding, and steric hindrance. In addition to learning the theory related to gene regulation, the activity and model can be paired with instruction on laboratory techniques. For example, blue-white screening takes advantage of *lac*Z, one of the structural genes of the *lac* operon as a quick phenotypic screen for successful cloning. Molecular cloning is another technique that can take advantage of inducible promoters, such as the *lac* promoter, to give researchers the ability to control when a target gene is expressed to learn more about the function of a gene or genes in the same metabolic pathway or to augment gene expression, among others. These techniques have broad applications in the biomedical field like gene therapy and the production of certain proteins such as insulin and clotting factors (Walsh, 2005; Pipe, 2005). The model and activity also have the potential to be used to teach additional systems of gene regulation. The *trp* operon, a repressible system, could be demonstrated as an extension of the *lac* operon activity. Eukaryotic gene regulation, including regulation that takes place via mechanisms like chromatin modification, transcription factor dimerization, and competitive binding of regulatory factors would also be natural extensions. These could be modeled by the students or instructor as a follow-up to the use of the *lac* operon analogous model.

4.4 Peer Learning

Analogies, like the one described in this study, have previously been demonstrated to be valuable in teaching biological concepts in biochemistry, introductory biology, and genetics (Orgill, 2007; Marcelos, 2012; Seipelt-Thiemann, 2012; Seipelt, 2006). However, the success of the *lac* operon model activity may not solely be due to the use of analogy in learning gene regulation. I initially set out to craft an analogy to the *lac* operon which developed into a model that eventually became a group learning activity. The structure of the final version of the activity employs peer discussion. Directed discussion in small groups gives students the opportunity to practice talking about and engaging with the material they are learning. In their 2005 paper, Knight and Wood showed that students in courses which include group discussion, including clicker questions, have been shown to demonstrate higher learning gains than those taught by traditional lecture (Knight and Wood, 2005). Similarly, Smith *et al*. (2009), demonstrated that when answering clicker questions, small group discussion can result in a correct answer being determined by a group in which no individuals knew the correct answer before discussion. Having a group member who knew that answer to start with was unnecessary (Smith, 2009). This study also supports the value of learning using peer learning. On survey responses, some students indicated that they found this aspect of the activity to be particularly helpful to their understanding of the *lac* operon.

4.5 Challenges

Active learning strategies which employ group discussion and analogous models have been shown to be effective by this and other studies and are included among promoted strategies of instruction (Tanner, 2015; AAAS, 2011). Despite reports like *Vision and Change* calling for biology instructors to adopt more active learning techniques into their courses, widespread change has yet to be achieved (NRC, 2012; Tagg, 2012). Biology faculty members have indicated, among other factors, that they felt ill-equipped to enact these changes due to a lack of sufficient training (Brownell and Tanner, 2015). By providing ready to use activities like the *lac* operon activity, we can better equip instructors to use active learning resources that target difficult concepts to learn. Another way to remove barriers to these changes is to provide biology faculty members with empirical evidence that these activities are valuable and tools that improve conceptual understanding which are worth their and their students' time. In her 2013 follow-up to *Vision and Change* D'Avanzo calls for educators to take advantage of the existing body of CIs to provide evidence of program efficacy. She suggests that learning gains calculated by using CIs be tied to one or more of the 5 conceptual areas laid out in *Vision and Change* and that this data be presented to faculty members to influence their development of course design (D'Avanzo, 2013). In summary, this study addresses the barriers to change noted above by providing the means of gathering evidence, the evidence, and an assessed, hands-on analogic activity for teaching the valuable and far-reaching concept of gene regulation.

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APPENDICES

APPENDIX A: IRB Approval

8/25/2014

Investigator(s): Katherine Stefanski, Dr. Rebecca Seipelt-Thiemann

Department: Biology

Investigator(s) Email Address: kms8y@mtmail.mtsu.edu; rebecca.seipelt@mtsu.edu

Protocol Title: The Use of a Hands-On Model in Learning the Regulation of an Inducible Operon

Protocol Number: #15-025

Dear Investigator(s),

Your study has been designated to be exempt. The exemption is pursuant to 45 CFR 46.101(b)(1) Evaluation/Comparison of Instructional Strategies/ Curricula.

We will contact you annually on the status of your project. If it is completed, we will close it out of our system. You do not need to complete a progress report and you will not need to complete a final report. It is important to note that your study is approved for the life of the project and does not have an expiration date.

The following changes must be reported to the Office of Compliance before they are initiated:

• Adding new subject population

• Adding a new investigator

• Adding new procedures (e.g., new survey; new questions to your survey)

• A change in funding source

• Any change that makes the study no longer eligible for exemption.

The following changes do not need to be reported to the Office of Compliance:
• Editorial or administrative revisions to the consent or other study documents

• Increasing or decreasing the number of subjects from your proposed population

If you encounter any serious unanticipated problems to participants, or if you have any questions as you conduct your research, please do not hesitate to contact us.

Sincerely,

Lauren K. Qualls, Graduate Assistant

Office of Compliance

615-494-8918

3/25/2015

Investigator(s): Katherine Stefanski, Rebecca Seipelt-Thiemann

Department: Biology

Protocol Title: The Use of a Hands-
On Model in Learning the Regulation of an Inducible Operon

Protocol Number: #15-025

Dear Investigator(s):

I have reviewed your research proposal identified above and your requested cha nges. I approve of the following change:

- Use of the post-
concept inventory as lab quiz grade (students receive 5 full points for taking it, but also can receive additional ½ bonus point for every correctly answered ques tion)

Please note that any unanticipated harms to participants or adverse events must be reported to the Office of Compliance at (615)494-
8918 or compliance@mtsu.edu. Any change to the protocol must be submitted to the IRB before implementing this change.

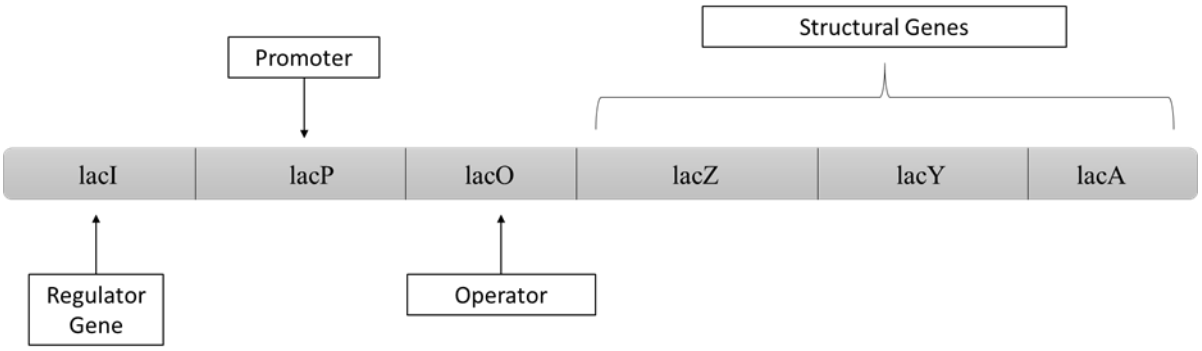
According to MTSU Policy, a researcher is definied as anyone who works with data or has contact with participants. Anyone meeting this definition needs to b e listed on the protocol and needs to complete the online training. If you add re searchers to an approved project, please forward an updated list of researchers t o the Office of Compliance before they begin to work on the project.

Sincerely,

Office of Compliance

Middle Tennessee State University

APPENDIX B: Instructions to Genetics GTAs



1. Short youtube video will instruct students on the normal functions of the lac operon (3 min)
   https://www.youtube.com/watch?v=h5p05aFzWdA

2. You will need to describe 3 mutations:
   a. *lacI*$^{-}$ - this is a loss of function mutation in the gene which encodes the regulatory protein. In cells with this mutation, no functional regulatory protein is produced leading to continuous transcription of the lac genes regardless of the presence of lactose.
   b. *lacI*^{S} – this mutation creates a "super repressor" which is incapable of being bound by allolactose. Cells with this mutation have a repressor protein continuously bound to the Operator thereby preventing transcription regardless of the presence of lactose.
   c. *lacO*^{C} – this is mutation in the operator which prevents the operator from being bound by the repressor. Cells with this mutation will continuously transcribe the lac genes.

3. Induced partial diploids
   a. Inserting wildtype copies of each genes into cells with mutations
   b. Inserting a copy of *lacI* into a *lacI*$^{-}$ mutant: normal function would be rescued
   c. Inserting a copy of *lacI* into a *lacI*^{S} mutant: no change
   d. Inserting a copy of *lacO* into a *lacO*^{C} mutant: no change

APPENDIX C: LOCI

For purposes of maintaining the integrity of the items of LOCI it is not being included here. The LOCI can be obtained by verified instructors from Dr. Rebecca Seipelt-Thiemann at Rebecca.Seipelt@mtsu.edu or Katherine Stefanski at k.m.smith726@gmail.com.

APPENDIX D: Hand-on Model Worksheet

Hands-on *lac* Operon Model Activity:

Complete the following activity in groups of 4-5 using the *lac* operon model with the following components.

***lac* Operon** – *lac* Instruction Manual

Operator – where the lock attaches

***lac* Repressor** – lock

Inducer (allolactose) – Key

Structural Genes (*lacZ*, *lacY*, *lacA*) – instructions for assembling Legos

Proteins (β-galactosidase, permease, transacetylase) – assembled Legos

Each group member should be assigned a task: 1) Worksheet Reader- reads aloud instructions and questions from this worksheet

2) Lego Assembler – Assembles Lego proteins per the instructions from the manual

3) Key keeper – holds on to the key and ONLY gives the key to the manual reader IF conditions are right

4) *lac* Instruction Manual Reader – if able, opens the manual and reads out the Lego assembly instructions to the Lego Assembler

Part 1. Examine the function of the *lac* operon in wild type cells: If the conditions are correct, open the manual and follow the directions for building Lego proteins.

1. No lactose is present in the cell.

    a. Are you able to use the key to remove the lock?

    b. Are you able to access the directions and assemble the Lego proteins?

    c. Under this condition does *E. coli* express the genes of the *lac* operon?

2. Lactose is present while glucose is not present.

a. Are you able to use the key to remove the lock?

b. Are you able to access the directions and assemble the Lego proteins?

c. Under this condition does *E. coli* express the genes of the *lac* operon?

Part 2. Examine the effects of different mutations on the function of the *lac* operon. If you can, open the manual and assemble the Lego proteins.

1. *lacI* is the gene that encodes for the repressor, in a $lacI^-$ (loss of function) mutant:

a. What feature of the model would be altered with this mutation and in what way?

b. Can the Legos be assembled?

c. Under what conditions (glucose or lactose) will *E. coli* with this mutation express the genes of the *lac* operon?

2. $lacI^S$ is a mutation that encodes for a "super repressor" that will not bind the inducer.

a. What feature of the model would be altered with this mutation and in what way?

b. Can the Legos be assembled?

c. Under what conditions (glucose or lacose) will *E. coli* with this mutation express the *lac* operon?

3. *lacO* is the gene that encodes for the operator. $lacO^C$ is a mutation that causes the operator to be unable to be bound by the repressor.

a. What feature of the model would be altered and in what way?

b. Can the Legos be assembled?

c. Under what conditions (glucose or lactose) will *E. coli* with this mutation express the *lac* operon?

Part 3. Discuss as a class your findings from Parts 1 and 2 then discuss what would happen if a wild-type copy of each mutated gene were inserted into each mutant.

APPENDIX E: *Lac* Operon Activity Survey

By answering these questions I certify that I understand that I am participating in a research study and that my anonymous answers may be included in the study.

1. Did you find the hands-on lac operon activity helpful to your understanding of the *lac* operon? If so, Why?

2. If you found the hands-on *lac* operon activity helpful, please indicate which of the following objectives the activity helped you most with. Please describe in as much detail as possible which ideas/concepts the activity helped you with under each learning objective.

    a. Identifying and understanding the role of each structure (For example, the operator, repressor protein, ect.) of the *lac* operon in gene expression.

    b. Accurately predicting whether or not gene expression will occur in a wild-type cell when given particular cellular conditions (i.e. the presence of a specific sugar).

    c. When given a particular mutation ($lacI^-$, $lacI^S$, $lacO^C$) to the *lac* operon predicting the outcomes of gene expression.

3. If you can, please describe which aspects of the activity helped you understand the *lac* operon best. Ect.