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Article

Mutation-Based Learning to Improve Student Autonomy and Scientific Inquiry Skills in a Large Genetics Laboratory Course

Jinlu Wu

Department of Biological Sciences, Faculty of Life Science, National University of Singapore, Singapore 117543

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Laboratory education can play a vital role in developing a learner's autonomy and scientific inquiry skills. In an innovative, mutation-based learning (MBL) approach, students were instructed to redesign a teacher-designed standard experimental protocol by a "mutation" method in a molecular genetics laboratory course. Students could choose to delete, add, reverse, or replace certain steps of the standard protocol to explore questions of interest to them in a given experimental scenario. They wrote experimental proposals to address their rationales and hypotheses for the "mutations"; conducted experiments in parallel, according to both standard and mutated protocols; and then compared and analyzed results to write individual lab reports. Various autonomy-supportive measures were provided in the entire experimental process. Analyses of student work and feedback suggest that students using the MBL approach 1) spend more time discussing experiments, 2) use more scientific inquiry skills, and 3) find the increased autonomy afforded by MBL more enjoyable than do students following regimented instructions in a conventional "cookbook"-style laboratory. Furthermore, the MBL approach does not incur an obvious increase in labor and financial costs, which makes it feasible for easy adaptation and implementation in a large class.

INTRODUCTION

Laboratory education plays various roles in developing students' interests, scientific inquiry skills, and understanding and application of scientific concepts learned in lecture. It is believed that appropriate exposure to practical work is an essential component of any bioscience degree (Hofstein and Lunetta, 2004; Hofstein and Mamlok-Naaman, 2007). However, laboratory work is expensive; once a laboratory has been set up, it leaves little room for changes, due to budget and labor constraints. A direct consequence of this limitation is a "cookbook" approach widely used in laboratory teaching. In this approach, students often simply go through the motions of laboratory work in a series of cookbook-style activities. Furthermore, experiments are repeated for many batches of students and are guaranteed to produce expected results. The very stringent protocol and highly predictable results reduce student autonomy, curiosity, and motivation. Thus, the effectiveness of this conventional cookbook-style laboratory education has often been questioned (White, 1996; Adams, 2009).

It is widely accepted that giving learners autonomy increases motivation (Sierens *et al.*, 2009). According to the self-determination theory, when the three basic psychological needs of autonomy, competence, and relatedness are met, intrinsic motivation is enhanced, leading to autonomous internalization of behaviors of initial extrinsic origin (Ryan and Deci, 2000; Wichmann, 2011). The needs for autonomy, competence, and relatedness refer to the experience of behavior as volitional and reflectively self-endorsed, effectively enacted, and intimately connected to others, respectively (Katz and Assor, 2007; Niemiec and Ryan, 2009; Van den Broeck *et al.*, 2010). The need for autonomy is particularly important in promoting intrinsic motivation (Ryan and Deci, 2000). Autonomy-supportive teaching has been demonstrated to

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Address correspondence to: Jinlu Wu (dbswjl@nus.edu.sg).

enhance student intrinsic motivation and ownership and to promote a more enduring psychological investment in deep-level thinking (Sheldon, 1995; Chan, 2001; Stefanou *et al.*, 2004; Katz and Assor, 2007; Furtak and Kunter, 2012). Autonomy support can be manifested in at least three different ways (Stefanou *et al.*, 2004): organizational (developing rules, latitude over rate of progress, selecting due dates for assignments), procedural (choosing the appropriate media to present ideas and results), and cognitive autonomy supports (justifying an argument, generating one's own solutions, evaluating ideas and results). The cognitive autonomy support is the most critical, leading to psychological investment in learning. However, in many traditional laboratory exercises, no deviation is allowed, and no choice is offered to support student autonomy in the design and performance of experiments.

To achieve efficient laboratory teaching and learning, extensive exploration of reformed pedagogical approaches has been undertaken. The project-based laboratory was used to develop initiative and innovation (Cioc *et al.*, 2009) and to improve students' skills in critical thinking and analysis (Treacy *et al.*, 2011). In addition, the inquiry-based laboratory was used to enhance students' understanding and engagement in experimental design (Hofstein and Lunetta, 2004; Howard and Miskowski, 2005; Bugarcic *et al.*, 2012); to increase student excitement about and motivation for engaging in research (Knutson *et al.*, 2010); and to promote curiosity, creativity, and critical thinking (Zion and Sadeh 2007; Casotti *et al.*, 2008; Moskovitz and Kellogg, 2011). The research-based laboratory was also shown to bring about greater learning investment in and excitement about the experiment when compared with non–research-based projects (Brame *et al.*, 2008). It provided students with immense benefits over traditional laboratory experiences, and even over inquiry-based laboratory experiences (Weaver *et al.*, 2008; Brownell *et al.*, 2012). Many derivatives and hybrids have originated from the three approaches, such as guided-inquiry learning (Spiro and Knisely, 2008) and investigative and cooperative learning (Seifert *et al.*, 2009), as well as integrated teaching and research (Kloser *et al.*, 2011). These approaches offer varying levels and forms of autonomy supports for students' cognitive engagement and learning motivation. However, giving students autonomy to carry out experiments that interest them creates many challenges and a heavy workload for technical and support staff, particularly in large classes. It is generally agreed that increased benefits for students run parallel to increased difficulties for implementation from cookbook-style to project-based, inquiry-based, and research-based laboratories (Oliver-Hoyo *et al*. 2004; Roehrig and Luft, 2004; Weaver *et al.*, 2008; Furtak and Kunter, 2012). The difficulties largely stem from logistics and little incentive for faculty to dedicate much time to teaching (Anderson *et al.*, 2011; Kloser *et al.*, 2011).

Therefore, continuing efforts must be dedicated to developing new pedagogic strategies that increase student autonomy but also remain feasible for educators constrained by large class sizes and modest budgets. In this study, we applied the concept of gene mutation from genetics to transform a cookbook-based molecular genetics lab exercise into a hypothesis-based inquiry science lab. In this new approach, students enjoy the freedom to "mutate" teacher-designed experiments to test their hypotheses and interpret experimental data in a written report. We prefer the word "mutate" to "alter" because the different types of mutations in genetics generate constructive ideas on how an experiment can be redesigned. In this approach, which we named "mutation-based learning" (MBL), we aim to enhance learner autonomy and scientific inquiry skills. The feedback from different batches of students over three semesters shows that this innovative approach has successfully improved student engagement and motivation. The MBL approach also provides a new venue for students to develop their scientific inquiry skills by studying case scenarios as scientists do. Furthermore, the implementation of MBL does not incur significant increase of labor and financial costs, thus making it practical.

METHODS

Module and Laboratory Contents

This study involved a first-year undergraduate module in molecular genetics, which is required for life sciences majors in the Faculty of Science at the National University of Singapore (NUS). The module is taught over 65 h and consists of lectures (36 h), tutorials (15 h), and laboratory sessions (14 h) within one semester. Class sizes varied between 200 and 280 students. The module contents include three parts. The first part covers DNA structure; replication; and gene transcription, translation, and regulation. The second part focuses on cell division; chromosome transmission and organization; and gene transfer, mapping, and recombination. The last part deals with Mendelian and population genetics at the molecular level. Each part, which is taught by a different lecturer, has a continuous assessment component contributing 15% to a student's final module score.

The laboratory contents include genomic DNA extraction and agarose gel electrophoresis (practical one, abbreviated as P-one), plasmid DNA purification and transformation (P-two), and basic bacterial manipulation (P-three). P-one and P-three were carried out with a conventional cookbook approach, while P-two was conducted using the innovative MBL approach. Both approaches are explained in the following section. P-two was chosen for MBL because it started in the third week, while P-one and P-three commenced in the first week. This allowed students more time to know their classmates before forming groups and to familiarize themselves with the laboratory equipment and requirements for the MBL approach. The laboratory contents are widely connected with the second part of the lecture contents, such as genome organization and gene transfer and recombination. The assessment of laboratories contributes 10% to student's final module score. This 10% is further divided into three parts: 2% for proposal writing, 2% for laboratory performance, and 6% for laboratory reports.

Conventional Cookbook Approach versus Mutation-Based Learning Approach

With the cookbook-style approach, a teacher-designed, step-by-step protocol (see standard protocol in the Supplemental Material) and related references were distributed to students at the beginning of each semester. Students were asked to read the materials before they attended the lab session. During practical sessions, students carried out experiments in pairs, strictly following the protocol and teaching assistants' (TAs) guidance.

Table 1. Autonomy supports in the MBL approach

Category of autonomy	Student's self-determined activities
Organizational autonomy	• Form a group (relatedness support is needed here) • Decide when/where to discuss their project • Decide their roles in the project, such as uploading materials, communications with TAs, editing proposal, etc. • Decide when to prepare additional reagents and to collect extra data if needed
Procedural autonomy	• Develop their own experimental protocol • Make a time plan for additional experimental activities • Learn required experimental skills from TA (competence support also needed) • Perform experiments collaboratively as planned
Cognitive autonomy	• Look for relevant references and provide literature review • Identify a question of interest to the group • Make a hypothesis based on the experimental contents (case scenario) [Permission to proceed required at this point] • Collect data on a group decision • Individually process, present, and interpret data • Write an individual report

In the MBL approach, students were also given the standard protocol, but they were asked to look for references and to "mutate" the standard protocol with a written proposal to explain the rationale for their mutations. The method to mutate an experimental protocol is conceptually similar to the method used for gene mutations. Students could mutate the experiments by: deleting certain experimental steps in the standard protocol (namely deletion mutation), adding extra steps (insertion mutation), reversing the order of experimental steps (reverse mutation), or replacing certain steps (substitute mutation). TAs and instructors subsequently assessed students' mutated protocols and proposals. Freedom for students to develop and implement their proposals was usually granted, unless there were safety concerns and logistical difficulties. During the scheduled lab sessions, students in groups of four performed the P-two in parallel, following both standard and mutated protocols. Additional time needed in the lab (e.g., for preparation of additional buffer or extra efforts for data collection) was available by appointment. After the lab session, the students could share, compare, analyze, and discuss their results in a group, but they were required to write individual reports.

All students experienced the two approaches, which enables comparison of each individuals' learning experiences via questionnaires. However, they carried out different experiments using different approaches. It is not educationally effective to ask students to repeatedly perform the same experiments via the two approaches. Logistically, it would be very difficult to have half of the class doing cookbook style, while the other half is using the MBL approach during a week of laboratory sessions. It would also be unfair to subject the students to a "controlled" cookbook approach as soon as any indication that the MBL approach is better arises. Thus, quantitative comparisons of student scores from the two lab approaches in the laboratory were not present.

Student Autonomy Supports in the MBL Approach

Various choices were offered in P-two to support student autonomy. The three categories of autonomy supports proposed for classroom teaching by Stefanou *et al*. (2004) were adopted but redefined in the context of laboratory activities (Table 1).

Assessment Rubrics

Proposal of Mutation. Students were asked to submit their proposals 1 wk before the first lab session for P-two. The proposal was limited to two pages and was evaluated by TAs. Students' competence in formulating hypotheses and reasoning was the main consideration for assessment among many scoring points (Table 2). A maximum of 8 points was given to a group proposal submitted by four students. Depending on the level of individual contribution to the proposal, the students would then decide how to share out the total points assigned by the TA among the group members. When an individual contributed more to the proposal, he or she would be entitled to a larger portion of the total points. This exercise simulates the delicate collaborative and recognition behavior that research scientists engage in on a regular basis. The TA and/or instructor would help to make a final decision regarding the point distribution only when an agreement could not be reached among the group members.

Implementation of Proposed Mutation. Students' performance during the lab session was monitored and evaluated. Each TA guided a group of 16–24 students, demonstrating technique skills and explaining key principles underlying the experiments, while instructors provided short overviews of important concepts and overall supervision for the entire class to encourage active participation and learning. TAs evaluated the performance of each student for each lab session based on the following rubrics, with major emphasis on student participation and conscientiousness (Table 3).

Laboratory Report. Students were instructed to write a laboratory report within four pages consisting of introduction, materials and methods, results, and discussion sections. Experimental results were shared among the group members, but each member had to write an individual report to ensure everyone was trained in scientific report writing. As they were first-year students, detailed instructions on writing a scientific report were given during a special tutorial. Their reports should present a clear comparison between the experiments conducted according to standard protocols (control) and mutated protocols (experimental group). Students had to submit soft copies of their reports to an online folder before the deadline. A 50% deduction was applied to any student

Table 2. Assessment rubrics for student proposals

Proposal content	Student goals/desired outcomes	Score points	Lose points
Introduction (40%)	1. Search and read relevant references and identify questions by themselves, showing enhanced cognitive autonomy 2. Produce well-specified goals and objectives for the mutations, showing independent thought and ownership of learning Example: A mutation is to substitute a circular plasmid with a linearized plasmid.	Briefly review the relationship of plasmid conformation and transformation efficiency; explain interest in a particular mutation and its significance and connection to the module/previous knowledge • Methods commonly used for DNA delivery, references cited • Concept of transformation efficiency and the factors affecting the efficiency, references cited • Why the substitution is of interest	Unpersuasive, disjointed, or unclear reasoning Fails to use references and/or previous knowledge Lacks or supplies an insufficient or wrong description of the following: • The concept of transformation efficiency • Factors affecting transformation efficiency • Rationale for the substitute mutation • References
Hypothesis (10%)	1. Learn how to ask a scientific question and write a scientific hypothesis 2. Foster curiosity and creativity, enhance cognitive autonomy The example continued:	Has scientific merit; is testable and provable Well-phrased intellectual guess A hypothesis being similar to the following: • Linearized plasmid DNA leads to lower transformation efficiency compared with circular plasmid via heat shock method	Irrelevant or uninteresting, impracticable, not testable or falsifiable Poor hypothesis, as in the following: • Linearized plasmid is cleaved by bacterial enzymes (without subsequent test to prove it) • Linearized plasmid takes longer time to enter bacterial cells, leading to lower transformation efficiency (it is difficult to measure the time and the hypothesis is therefore not testable)
Prediction (10%)	1. Learn how to set controls and minimize the variables 2. Appreciate that reductionisms (i.e., reduce the complexity of testing) play an extremely significant role in scientific inquiry The example continued:	Expected outcomes if experiments are done Preferably, only one variable is tested A prediction tells the dependent and independent variables, being similar to the following: • If the same amount of plasmid used (controlled variable), linearized plasmid leads to fewer colonies than the circular plasmid does	Outcome unknown or immeasurable or not observable, unclear what to be tested, no proper control • Different molar amount of plasmid used (although the same volume of plasmid preparation used) • Different delivery methods used, such as heat shock method for circular plasmid, while electroporation for linearized plasmid • Different buffers used (more than one variable)
Mutated protocol and needed materials (20%)	1. Develop student competence and know-how/experimental skills 2. Learn how to plan their experiments timely and logistically, ensure experiments are feasible 3. Enhance organization and procedural autonomy The example continued:	Clearly list what is required and highlight the mutated steps; the experiments, hypothesis and protocols agree with each other • Enzyme (e.g., *Eco*RI) required for linearizing the plasmid • A miniscale DNA purification kit required to purify the DNA • A set of agarose gels to examine the cleavage, etc.	Incomplete list of materials needed or the list does not match the needs, incoherence of protocol changes • Without quality check after cleavage • A wrong enzyme chosen • Protocol incomplete or scientifically wrong • Plasmid amount not equal in two experiments
Planned data collection and analysis (20%)	1. Plan experiments in a coherent manner, so the data can be meaningful to verify the hypothesis 2. Think critically to define the controlled variables 3. Enhance cognitive autonomy The example continued:	Determine data to be collected and analysis to be conducted Any additional efforts to collect data • Measure the plasmid purity and quantity • Electrophoresis to check the efficiency of linearization • Count the number of colonies • Compare transformation efficiency	Data are not useful for validation of prediction, or required data are not collected Without or insufficient • Data to show the plasmid was linearized • Data to show the amount and purity of plasmid used • Data to show the transformation efficiency

Table 3. Assessment rubrics of student performance in the laboratory

Performance	Goals/desired outcomes	Score points	Lose points
Safety (20%)	Be familiar with safety rules, knowing that safety issues are paramount and cannot be compromised under any circumstances	Comply with safety rules and wear proper protection attire Handle toxic chemicals and sort wastes properly	Wear improper attire such as slippers and shorts Discard wastes wrongly Exhibit risk-taking behavior
On-schedule (20%)	Enhance organization autonomy, self-discipline, and teamwork attitudes	Arrive on time and manage to finish planned experiments efficiently	No clear working plan Late Unable to complete experiments within time frame
Conduct (60%)	Enhance procedural autonomy and competence in skills Develop interpersonal skills, such as being collaborative, peer teaching, negotiation, and collaboration	Know what to do Engaged and collaborative Appropriate use of equipment and apparatus Conscientious Take notes	Play mobile devices Chit-chat Rash, careless, mishandle materials No participation and data collection

report submitted before a late submission deadline (within 2 d past the set deadline), and reports were not accepted at all after the late submission deadline. TAs were instructed to base their assessment of the reports mainly on critical thinking and logical reasoning, so not much emphasis was placed on the experimental results per se. To avoid bias, a TA did not mark the reports from students who were under his or her supervision.

Report scores were classified under five categories: introduction (10%), materials and methods (5%), results (40%), discussion (40%), and other (5%). The percentage for each category differed slightly in each semester. A report score was the sum of the points that a student earned in the five categories. The average of the report score was calculated by dividing the total scores of all reports by the total number of student submissions. The percentage scored for each category was also calculated by dividing points earned by students by the maximum points of the respective category. Report marking rubrics with an example are shown in Table 4.

Feedback Collection. Anonymous Likert questionnaires were administered to all participants after the entire lab course using forms 1 (Table 5) and 2 (Table 6). Form 1 was used for the first trial during semester 2 in the academic year 2010–2011 (abbreviated as AY1011). Form 2, which had additional questions, was used to achieve direct measurement of students' learning and engagement in AY1112 semesters 1 and 2. Students were instructed to make a comparison between the mutated (P-two) and the conventional experimental work (P-one and P-three) in the same course. In addition, students were also encouraged to write comments on the module website or to send feedback to TAs and instructors by email.

Both forms 1 and 2 adopt the 5-point Likert scale to assess different levels of efforts/satisfaction of the students, from the lowest to the highest: strongly disagree (1 point), disagree (2 points), undecided (3 points), agree (4 points), and strongly agree (5 points). The sum score for each question in the survey form 2 was calculated with the formula: sum score = $\sum(nL \times L)$, where L is the Likert level (1–5) and nL is the number of respondents at the corresponding Likert level. The "difference of sum scores" was calculated for each question by subtracting the sum score for the cookbook-based approach from the sum score for the MBL approach. The average score of a question was calculated by dividing the sum score by the total number of respondents ($n = 320$). A paired two-tailed Student's t test was used for statistical analysis of 320 individual scores from the two approaches. $P < 0.001$ was considered as the significance level after a Bonferroni correction via the formula $1 - (1 - \alpha)^{1/n}$, in which α is 0.01 and $n = 13$ (total number of survey questions in Table 6).

In addition, one 5-point Likert questionnaire (form 3 in the Supplemental Material) was used to collect students' evaluations of TAs. It provided a measurement of TAs' capabilities in implementing the teaching strategy and in providing students with competence and relatedness support in addition to autonomy support.

RESULTS

Students' Proposal

The students designed a number of mutations of P-two and conducted the mutated P-two in many different ways. In contrast, the entire class performed the same experiments in P-one and P-three, following the standard protocols. Representative mutations that appeared in a few groups' proposals are listed in data 2 (Supplemental Material) to reflect different levels of engagement and intellectual and scientific inquiry skills in a large class.

TAs assessed the proposals according to the marking rubrics prepared by the instructors. Ambiguous points during the marking process were settled by the instructors and communicated to all TAs by email to minimize variations. Considering this is a first-year undergraduate module, most proposals were approved and granted high scores, although some were not scientifically sound. Less than 10% of proposals were turned down and subject to revision. Rejected proposals were mostly due to dramatic changes of the standard protocol, resulting in too many variables and untestable conditions. In the P-two scenario, plasmid extraction and

Table 4. Scoring rubrics of laboratory reports

Content	Goals/desired outcomes	Score points	Lose points
Introduction (10%)	1. Promote extensive reading of relevant references 2. Generate curiosity about "what I want to know" 3. Correlate known knowledge to unknown area The example in Table 2 continued:	Be consistent with the Introduction of the proposal Provide the most salient background closely related to the proposed mutation • Comprehensive review of mechanisms of heat shock transformation • More information about factors affecting transformation efficiency, especially as related to DNA conformation	Inconsistent with the proposal No references cited Irrelevant materials used, such as • Horizontal gene transfer • Relationship of transformation and spread of antibiotic-resistant bacterial strains • Bacterial pathogenicity/virulence
Materials and methods (5%)	1. Emphasis on communicative purpose, being aware that there is no need to repeat something well known among audience 2. Be sufficient to allow the experiments to be repeated 3. Be technically competent The example continued:	Be brief and consistent with the proposed alteration of standard protocol Highlight "the mutated part" Avoid redundancy with the content in the lab manual [This differs from published scientific reports.] • As simple as one sentence for plasmid extraction: "Plasmid was extracted using a High-Speed Plasmid Mini Kit (Geneaid Biotech) according to the manufacturer's manual." • An equal amount of linearized and circular plasmid was used to transform *E. coli* cells by a heat shock method	Copy and paste the details from lab manual and proposal A long and wordy comparison of standard and mutated protocols • List experimental steps like a cookbook-style manual • List buffers, reagents, and required volumes already shown in the laboratory manual • Wrong information about the plasmid extraction kit, competent cells, and plasmid used
Results (40%)	1. Learn how to process and present data scientifically 2. High standard of scientific integrity, being aware of data misconduct, such as fabrication, manipulation, and falsification 3. Maintain originality and avoid plagiarism 4. comparing and contrasting especially crucial in MBL The example continued:	High clarity and in logical order Contents precise and consistent in figures, tables, legend, and text • Plasmid concentrations and qualities obtained from different experimental designs • Gel photos showing linearized plasmid • Number of colonies obtained from different designs • Transformation efficiency under different conditions • Analysis to show differences of results between different designs	Fabricating or selecting data with bias Presenting raw data without organization and processing Inconsistent or disorganized Redundant • Supply no or only partial results • Cover or ignore unexpected results • Data presented in a messy way • Lack or give insufficient description of table or figure • Without analysis, only number is presented • Redundant figures and tables
Discussion (40%)	1. Compare, evaluate, and interpret the results critically 2. Logic is clear and the statement convincing	Critically and scientifically interpret outcomes from mutated and standard protocols Comprehensive explanation of unexpected results Conclusion drawn based on data	Discussion does not lead to a conclusion or correlate to the proposal and the results Simply repeat introduction, results, a principle, or a theory without personal insights given

(*Continued*)

Table 4. Continued

Content	Goals/desired outcomes	Score points	Lose points
	3. Synthesize or create new information or ideas for further study The example continued:	• Discuss how the ratio of plasmid amount to the number of competent cells affects the transformation efficiency • Interpret the different transformation efficiencies resulting from circular and linear plasmid • Predict what are the possible factors leading to the differences; references must be cited in support • Explain factors causing the errors or deviations from the results expected, such as efficiency of enzyme cleavage, plasmid purity, etc.	Overreached conclusion, such as: • Irrelevant: e.g., importance of "mutated" experiment to study genetics, how the plasmid contributed to the antibiotic's resistance • Goes beyond published and/or experimental data, too much speculation, e.g., plasmid interacts with some unknown proteins, affecting the transformation efficiency • Reiterate principles without correlation to the results
Others (5%)	1. A paper must be presentable and readable 2. Encourage creativity	References in a unified format Presentable figures and tables Paper is easy to read Bonus (maximum of 5 points) for creativity	References not well organized Figures and tables wrong size, alignment, and/or position Poor grammar and spelling errors

transformation, we did not expect students to make significant findings. However, the references, questions, hypotheses, and mutated protocols in students' proposals demonstrated that their autonomy and inquiry skills were enhanced.

In addition, we seldom encountered difficulties when supporting proposed mutated experiments, because the substituted mutations only needed additional materials that usually consisted of very common chemicals. Logistical support required for other types of mutations are the same as those in a cookbook-style approach.

Lab Performance

Based on the TAs' observation, students were much more serious when doing P-two than they were when doing P-one and P-three. Students were very conscientious and spent a longer time completing experiments in MBL than they had anticipated. This was especially common when they prepared the reagents. They were not practically proficient in calculating molar concentration, adjusting pH, and weighing very small amounts (e.g., in milligrams or micrograms) of chemicals, although they were often amazed at advanced infrastructures and instruments. How plasmid DNA could be transferred into bacterial cells by such a short heat shock process often triggered contemplation. They collaborated as a team and engaged in experimenting. They were impressed by their observation of DNA bands on the UV trans-illuminator, gel electrophoresis, and measurement of plasmid DNA concentration and quality by NanoDrop. Different colors of colonies from *Escherichia coli* cells with and without plasmid (pUC18) made the relationship between genotype and phenotype distinct for them, thus reinforcing the relatedness with lecture content. The students also observed safety rules and were able to keep paper and electronic records of experimental steps, observations, and data. Only a small cadre of students (~1%) showed any reluctance in spending additional time on the mutated experiments.

Table 5. Survey form 1 used for students to compare the mutation-based approach with the conventional cookbook approach in semester 2 of AY1011

Survey questions	Student number[a]					% of (5 + 4)	% of (2 + 1)
	5	4	3	2	1		
Q1: The mutation approach is more challenging and stimulating.	57	147	52	5	2	77.6	2.7
Q2: The mutation approach enhances a sense of ownership for my learning.	59	143	55	4	2	76.8	2.3
Q3: The mutation approach gives me freedom to test my own idea/hypothesis.	74	149	34	4	2	84.8	2.3
Q4: The mutation approach enhances my interest in molecular genetics lab.	44	147	62	7	3	72.6	3.8
Q5: The mutation approach improves my critical-thinking skills.	51	160	47	4	1	80.2	1.9
Q6: The mutation approach improves my ability to communicate and work with teammates.	55	164	42	2	0	83.3	0.8
Q7: Overall, mutation-based learning is more effective.	**55**	**156**	**48**	**4**	**0**	**80.2**	**1.5**

[a]The scores from 5 to 1 represent different agreement levels: strongly agree, agree, neutral, disagree, and strongly disagree, respectively. At the right side of each question, it shows the student numbers at different levels of agreement. The % of (5 + 4) represents the percentage of students in "agree and strongly agree"; the % of (2 + 1) represents the percentage of students in "disagree and strongly disagree."

Table 6. Survey form 2 used for students to compare the MBL approach with the conventional cookbook approach in semesters 1 and 2 of AY1112

	MBL approach[a]					Cookbook-style approach[a]					
Survey questions	5	4	3	2	1	5	4	3	2	1	Difference of sum scores[b]
Q1: I make efforts to understand the experimental design before the lab.	75	186	50	8	1	64	181	60	14	1	33
Q2: I look for additional materials related to the experimental contents.	51	161	68	38	2	29	106	127	49	9	124
Q3: I am eager to try the experiments.	86	177	50	7	0	72	160	81	7	0	45
Q4: I am curious to know what will happen to the experiments.	114	172	29	4	1	85	161	68	5	1	70
Q5: I discuss the experiments before the lab class.	51	119	85	54	11	27	94	113	68	18	101
Q6: I discuss the experiments after the lab class.	67	161	70	20	2	49	136	103	27	5	74
Q7: The exercise in the molecular genetics lab is challenging and stimulating.	73	175	64	6	2	44	157	108	7	3	79
Q8: It enhances a sense of ownership/responsibility for my learning.	86	168	58	7	1	48	152	104	14	2	101
Q9: It gives freedom to test my own idea/hypothesis.	110	148	57	3	2	41	123	122	29	5	195
Q10: It enhances my interests at molecular genetics/biology lab.	79	168	65	6	2	55	151	99	14	1	71
Q11: It improves my critical-thinking skills.	80	179	57	3	1	52	153	101	14	0	91
Q12: It improves my ability to communicate and work with teammates.	93	170	53	3	1	68	157	84	11	0	69
Q13: Overall, learning in the lab is effective.	**90**	**192**	**35**	**2**	**1**	**66**	**179**	**71**	**4**	**0**	**61**

[a]The number of students at different levels of agreement to the questions; the scores from 5 to 1 represent strongly agree, agree, neutral, disagree, and strongly disagree, respectively.

[b]Sum score = $\sum(nL \times L)$, where L is the Likert level (1–5) and nL is the number of respondents at the corresponding Likert level. The difference of sum scores was calculated for each question by subtracting the sum score for the cookbook-based approach from the score for the MBL approach.

In addition, the students were impressed with TAs competences in technical skills and knowledge, giving TAs an average score of 4.4 out of 5 (data 3 in the Supplemental Material), indicating satisfaction with the competence support from TAs. Overall, the MBL laboratory not only provides autonomy support, but also competence and relatedness support. One quote from a student follows:

> The "mutations" introduced by virtue of modifying experimental protocol were very innovative and interesting. Though there were constraints on the kind of "mutations" we could implement, we were really required to think hard about the consequences of each action, rather than just mindlessly follow a protocol and answer some questions thereafter. I believe this kind of thinking is beneficial to our development as scientists or even science students, as it is necessary for us to practice how to make hypotheses and carry out experiments to determine the final result.

Lab Reports

Reports were first scrutinized through the Turnitin program for plagiarism detection. Before we conducted MBL, we had identified a few cases (<1%) in the previous years in which students copied a classmate's or a senior's report. Further investigation revealed that a plagiarism offender often made an excuse that he or she referred to but did not copy another report of a student who had done the exactly same experiments. After the implementation of MBL, no plagiarism was identified. The average score of the lab reports was 82 out of 100 in the three semesters. As for the average scoring percentages of the five categories in the report marking rubrics, they were 85, 90, 88, 81, and 90% for the introduction, materials and methods, results, discussions and others, respectively.

Feedback from Students

A survey using form 1 was administered after the first trial of MBL. All feedback was manually inspected. The number of students at different levels of agreement with the seven survey questions is supplied in Table 5. A substantial proportion of students (72.6–84.8%) were of the same mind (strongly agreed or agreed) that MBL was better than the cookbook-style learning for all seven questions in form 1. In contrast, only 0.8–3.8% of students thought otherwise (disagreed and strongly disagreed). The highest satisfaction was given to question 3 (Q3), regarding the freedom of idea testing, while the lowest went to Q4, which was about interest enhancement.

Encouraged by the promising results from AY1011 (Table 5), MBL was deployed in the following two semesters in AY1112. A total of 188 and 171 survey forms were gathered after the laboratory course in semesters 1 and 2, respectively. After a manual check to remove partially filled and illegible forms, 156 and 164 forms, representing 77 and 61% of student cohorts in semesters 1 and 2, respectively, were used for data collection and analysis. The total number of students who strongly agreed and agreed with all 13 questions were larger when students carried out P-two via MBL than the number of students who did the experiments via the conventional approach in the two semesters (P-one and P-three; Table 6). The greater difference between the total scores of MBL and conventional learning was associated with Q2, Q5, Q8, and Q9, with different scores of 124, 101, 101, and 195, respectively. The smaller difference appeared to be related to Q1 and Q3 (Table 6). The differences between the learning activities in the two approaches are summarized in Table 7.

The different levels of agreement from "strongly disagree" to "strongly agree" were assigned a score from one to five. The average feedback score for each question was calculated over two semesters ($n = 320$; Figure 1). The highest scores

Table 7. Learning activities in conventional cookbook-style and MBL approaches

Conventional cookbook-style learning approach	MBL approach
Prelab	
Spend little effort to understand lab contents	Make effort to redesign/mutate experiments, including reference review, group discussion, proposal writing, and preparation of chemicals and buffers
In lab	
Follow standard instructions, conduct experiments in an orderly manner without deviations, get anticipated results for most experiments, and learn technique skills and underlying principles	Conduct experiments facilitated by teaching assistants, experience uncertainties and a sense of ownership, get various and sometimes unanticipated results, learn additional technique skills/knowledge by doing
Postlab	
Individually process data and write a report, reiterate underlying principles in their own words	Share and discuss results with group members, compare and analyze results from different approaches, cope with unanticipated data, re-examine experimental design, write a report (as an individual, not as part of a group), form a conclusion to support or falsify a hypothesis

for both approaches were given to Q4, regarding curiosity (4.23 in MBL vs. 4.02 in the conventional approach), while the lowest scores (3.45 vs. 3.14) were given to Q5, regarding the efforts spent to discuss experiments before the lab class. The scores for the overall effectiveness of laboratory learning (Q13) were 4.15 versus 3.96. Statistical analysis showed the average scores for 11 survey questions are significantly higher ($P < 0.001$) for the MBL approach than for the conventional approach. The feedback scores from only two survey questions (Q1 and Q7) did not lead to such significance ($P > 0.001$).

DISCUSSION

A gene mutation is a change in the DNA sequence that may be beneficial, detrimental, or have no effect on an organism. Well-designed gene mutation has been an important approach for studying gene function in biology. We expected that a well-designed "mutation of experimental design" could be used to explore scientific questions underlying each experimental scenario by following an authentic inquiry process. In the MBL approach, students enjoy autonomy in identifying questions that interest them, formulating hypotheses, designing experiments, collecting data, and writing reports. They learn and improve their inquiry skills by practicing. TAs and instructors act as facilitators and "Sherpa guides," providing autonomous support and encouraging students to take ownership for their own learning.

Various studies have shown that intrinsic motivation is linked with active and engaged behaviors (Ryan and Deci, 2000; Furtak and Kunter, 2012). Based on our survey (form 2), students were generally interested in the laboratory course (Q3) and curious about their experimental outcomes (Q4), but they were not motivated and did not pursue active learning, as reflected by the relatively low average scores of Q2 and Q5. They neither extensively sought additional information nor discussed the experiments before the class. This might have arisen from insufficient support of student autonomy and ownership of learning as suggested by low scores of Q8 and Q9 in the conventional laboratory approach. These

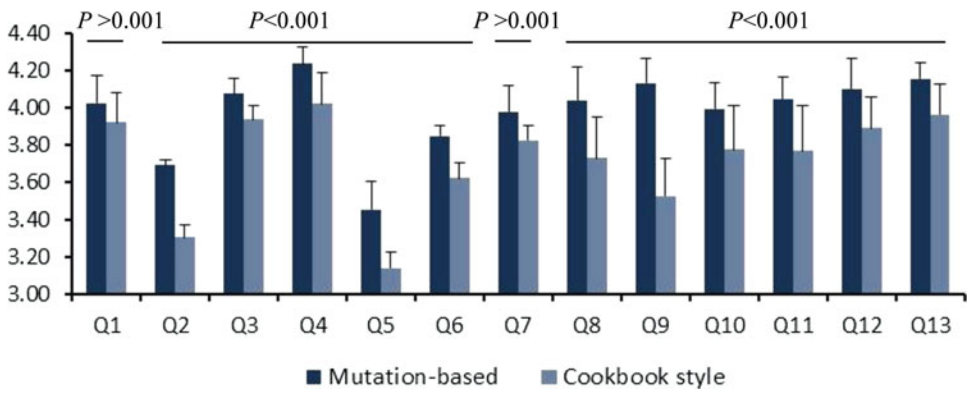

Figure 1. The average feedback scores with standard deviations of 13 questions in form 2 (Table 6). The average score was calculated from student feedback over two semesters ($n = 320$, representing 68% of the entire student cohort). All feedback scores from the MBL approach (dark blue columns) are higher than these from the conventional (light blue columns) laboratory approach. A higher score represents a higher level of agreement with the assessed questions and a higher level of satisfaction with laboratory learning. A paired two-tailed Student's t test was used for statistical analysis of 320 individual scores from the two approaches. $P < 0.001$ was adapted as significance level after Bonferroni correction via the formula $1 - (1 - \alpha)^{1/n}$, in which $\alpha = 0.01$ and $n = 13$ (total number of survey questions in Table 6).

scores improved significantly through MBL, as evidenced by significantly higher scores of Q2, Q5, Q8, and Q9 (Table 6 and Figure 1). The active and engaged behaviors, such as reading additional references and discussing experiments with peers and TAs, manifest intrinsic motivational development, which is usually correlated to higher learning achievements (Elliot, 1999; Russell and French, 2002; Niemiec and Ryan, 2009). To foster stronger self-motivated and independent learning further, we may need to examine other factors, such as creating more attractive experimental scenarios (Katz and Assor, 2007) and adopting new grading methods for the module (Shim and Ryan, 2005).

Systematic analysis of students' reports revealed that students were able to make critical comparison of experimental data from both teacher-designed and mutated protocols. Their reports adopted the same format for papers in scientific journals. They generally wrote well, with an average score of 82 points out of 100. The scoring percentages for introduction (85%), materials and methods (90%), results (88%), and discussion (81%) show that students faced more challenges in writing the introduction and discussion sections. The difficulty in writing these two sections is a common challenge for scientists. The overall high scores may indicate that students are capable of writing reports in a scientific journal format if they have genuine experimental scenarios and data.

Importantly, the greatest difference of total scores was generated from Q9 (Table 6), which indicates that students were highly satisfied with the freedom to test their own hypotheses in the MBL. This freedom is critical for enhancing autonomy and ownership of learning. A great number of diverse mutations and hypotheses demonstrate various interests, understanding, and creative-thinking skills among students (data 2 in the Supplemental Material). This diversity and the broad choices are different than project-, inquiry-, and research-based laboratory exercises, in which available projects are usually limited and designed for a small class size (Weaver *et al*., 2008).

The students' proposals were very diverse. Some proposals in MBL were creative, innovative, and scientifically sound. Others were driven by curiosity, because students doubted what is stated in the textbook. Some students ventured to make new findings, while others were very conservative in securing a set of data for reporting. Not surprisingly, some students made illogical hypotheses. In high school or conventional laboratories, students are usually misled by "foolproof" experiments that make science appear to be straightforward and always yielding anticipated results. In contrast, MBL allowed students to know the complexity of science research and nature of science by doing. Students were nudged or motivated to look for references, discuss with group members, and interpret both anticipated and unanticipated results. All these processes eventually provide the requisite training in scientific inquiry skills.

All students knew that the standard protocol had been optimized and worked well for experimental purposes. Some students turned their focus to understanding the science behind the each experimental step. Their mutations were proposed to verify the importance of the particular step or the function of chemicals. Nevertheless, a comparison of results from different approaches is still helpful to improve their critical-thinking skills and understanding of experimental principles (Spiro and Knisely, 2008). Overall, only a small percentage of proposals were put forward to improve the experimental design, and very few led to potential improvement of the standard protocols, such as using plasmid mass instead of volume to optimize transformation efficiency.

In addition to promoting student autonomy, the MBL approach provides opportunities for teaching scientific integrity. During student consultation, a substantial number of students did not get the data they expected. Most of these unanticipated data were derived from students ventures in innovation or improvement of the standard protocol. They felt confused and did not know how to deal with the unanticipated or conflicting data. Some were liable to take a shortcut, simply choosing the data supporting their hypotheses and forgoing those unanticipated data, so finishing their reports became easy. Some even intended to modify the data to make them appear better. To ensure scientific integrity, we repeatedly reminded students to record all data without bias during all lab sessions, not to group their data into "bad" and "good" categories, and not to copy data from others. They were encouraged to organize and interpret the data critically and to prepare their reports independently. We highlight the value of learning from both successes and failures, and reward such learning in assessment by focusing on critical analysis and logical interpretation of results rather than on data alone. This may promote a better attitude toward science. Because the students made various mutations, the final report from each student was unique. This is distinctly different from the outcomes of the conventional laboratory, in which all students conduct the exact same experiments. In other words, MBL prevents students from a "copy-and-paste" approach at the onset of their experiments; instead, unique proposals are raised by autonomous learners.

In summary, while the conventional cookbook style and recently reformed approaches work in many ways to achieve certain pedagogic goals, the MBL approach supports student autonomy to acquire scientific inquiry skills and fosters intrinsic motivation and a sense of ownership of learning. It engages students in many of the same activities and thinking processes used by scientists. It is similar to an authentic inquiry process in which questions are not defined, experiments are not predesigned, and data are not provided to students (Buck *et al*., 2008). However, MBL has a few distinguishing features. First, it provides a reference (teacher-designed experiment) to explicitly guide students in designing experiments of interest to them. Second, the concept of gene mutation also encourages constructive ideas on how students can redesign the experiment. Third, students collect real data from comparable experiments to practice scientific writing. Fourth, logistical cost is limited. Finally, MBL can be implemented in large experimental classes. While some features may pare down complete autonomy, MBL offers competence support that is beneficial for first-year undergraduate students in their acquisition of scientific inquiry skills.

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