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Simply InGEN(E)ious! How Creative DNA Modeling Can Enrich Classic Hands-On Experimentation†

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Innovative 21st-century methods for teaching biology should provide both content knowledge and diverse scientific competencies. The Curriculum Guidelines of the American Society for Microbiology highlight the importance of developing scientific thinking skills, which include the abilities to formulate hypotheses, to communicate fundamental concepts effectively, and to analyze and interpret experimental results. Additionally, contemporary science education should enhance creativity and collaboration as key student assets in its bid to overcome negative perceptions and learning difficulties. In recent years, the expanding movement for so-called "STEAM" approaches (science, technology, engineering, arts, and math) has increased in STEM curricula. The movement seeks to integrate the arts into science classes to transfer enthusiasm, support individual self-sufficiency, and encourage creative solutions. To meet all these demands, we developed an inquiry-based approach that actively engages students in hands- and minds-on activities on the topic of "decoding the DNA structure" in an outreach laboratory. Since teaching abstract molecular phenomena is a challenge in biology classes, we combine classical experimental tasks (DNA isolation, gel electrophoresis) with creative modeling. The experiments are linked by the modeling phase: immersed in the story of the discovery of the DNA structure, our participants independently construct a DNA model from a box filled with inexpensive craft supplies (e.g., glue, straws, pipe cleaners, beads). After initial pilot testing, the implementation of our approach clearly produced short- and mid-term learning effects among the students, providing a successful example of a STEAM-based approach in a laboratory setting.

INTRODUCTION

The transmission of genetic information from DNA to gene actions within an organism, within families, and within populations of organisms over many generations is a frequent subject of classroom lessons. The broad and dynamic field of genetics can even be considered a form of information science, in which discoveries are continually advancing our understanding of many other life sciences as well (1).

The discovery of DNA structure in 1953 was an important milestone for molecular genetics, as two young researchers, James Watson and Francis Crick, won the race against other groups in successfully decoding DNA's double helix (2). Without completing their own experiments, they managed to correctly interpret the complex X-ray crystallography work pioneered by Rosalind Franklin and Maurice Wilkins (3). After discussion and mental modeling based on Watson and Crick's suspicions regarding a helical DNA structure, they built a physical DNA model. Built from simple shining metal plates to weld together the atoms, the scientists conceived a model which connected the X-ray data with the laws of stereochemistry (4). The groundbreaking work of Watson, Crick, and Wilkins was honored by the awarding of the Nobel Prize in Physiology or Medicine in 1962.

The importance of the topic for fundamental knowledge acquisition in genetics and biology in general is indisputable. However, a common problem seems to be transmitting a proper understanding of the three genetics concepts—DNA, gene, and chromosome—in the classroom (5). As visual presentation is assumed to be essential in this setting, model-based learning may provide a bridge between abstract scientific theory and real-world experience, especially when direct observation is difficult (6, 7). A key factor for successful model construction is individual creativity, incorporating a process of sensitization and development of innovative solutions (8). It is further expected that cultivating

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creativity in science as an auxiliary skill might help the development of individual self-efficacy and foster greater motivation in science education (9).

We designed a student-centered laboratory activity that combines creative modeling with experimental work, offering an innovative way to link abstract scientific theory and practical experiences. Our hands-on approach provides scaffolds that actively involve students and support them to independently conduct experiments, create a protocol using their observations, and build a DNA model. The recently published research used to accompany our approach confirms that students demonstrate significant short-term (directly after participation) and mid-term (6 weeks after participation) gains in knowledge compared with a test–retest group. Correlating the quality of the models built to the cognitive achievement and creativity of the tested students, we found that female students in particular tend to benefit from this new artistically inspired laboratory activity (10).

Intended audience

The laboratory activities outlined in this paper are intended for high school students (ninth graders) in biology in the context of genetics. The hands-on modeling phase itself may be extended or modified for use in higher grades in molecular biology with the addition of focused material regarding molecular interactions.

Learning time

Our inquiry-based laboratory module requires 4.5 hours consisting of five phases (maximum of 60 min each). The time required for the individual learning activities is shown in Figure 1. The DNA modeling can also be done independently within a classroom session.

Prerequisite student knowledge

The activities presented here are suitable for beginners in genetics. Nonetheless, some general skills from science classes are helpful in managing content and practical tasks. For the experiments, students should be capable of using basic laboratory materials (e.g., pipettes, beakers, test tubes). Furthermore, students should be able to make experimental observations appropriately and to derive substantiated interpretations from experimental observations. The workbook supplied (Appendix 2) provides them with templates according to the standard formatting of a scientific report. Successful DNA modeling can benefit from previous student experiences in developing scientific models, e.g., students have been introduced and guided by the teacher in other molecular contexts (model of a cell or a protein, etc.). Additionally, basic craft skills could be helpful for an appealing implementation of students' ideas.

Learning objectives

Upon completion of this activity, students will be able to:

1. Perform and describe selected gene technology laboratory techniques, as well as understand their purpose (e.g., micropipetting, agarose gel electrophoresis)
2. Name, describe, and explain selected aspects of DNA structure (e.g., possible base pairings, components of the DNA backbone, electrophoretic separation of DNA molecules based on phosphate [5])
3. Engage actively in class sessions by collaborating with classmates to elaborate, draw, evaluate, and/or critique models of their creative work and identify, describe, and reorganize key elements of DNA structure during modeling (e.g., cohesion of

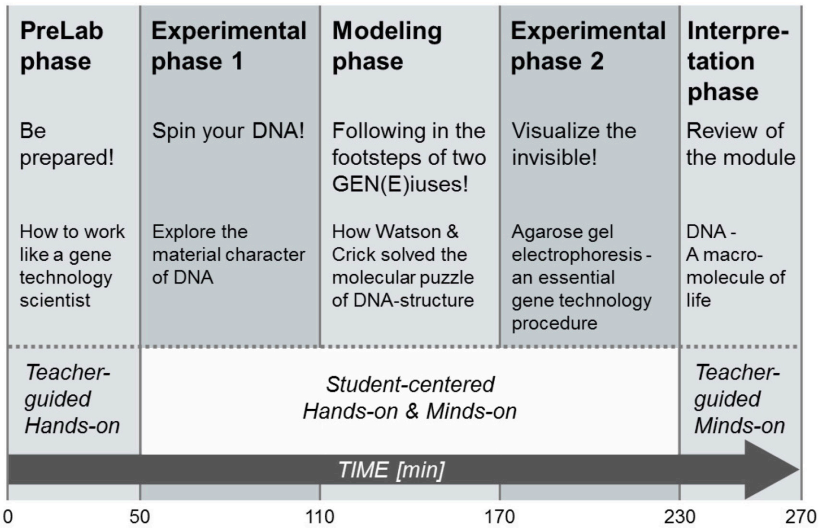

FIGURE 1. Schedule and learning activities of the laboratory module "Simply inGEN(E)ious! DNA as a carrier of genetic information."

the two DNA strands by hydrogen bonds, spatial structure of DNA as a right-handed double-helix)
4. Evaluate the importance of creativity in the scientific process using the example of the discovery of the DNA structure
5. Be familiar with the safe handling of human samples at biosafety level 2 (BSL2) using Biosafety in Microbiological and Biomedical Laboratories (BMBL) safety guidelines

The content-oriented learning objectives can be assessed with the cognitive knowledge questionnaire (laboratory activities and learning content of the model phase; Appendix 1), and the models can be evaluated by a category system to assess the model quality with regard to key elements of DNA structure (10). In order to evaluate students' ideas on the importance of creativity in the scientific process, students can write short reflections after completing the activity. For assessment of the BMBL safety guidelines, the teacher should check orally that the students have understood them, before performing the experiments.

PROCEDURE

Materials

The materials needed for the experiments (outlined in Appendix 2) are to be provided on the laboratory benches, and DNA modeling kits are to be distributed to the participants after the first experiment (Fig. 2). A separate gel station with two electrophoresis chambers sufficient for a maximum of eight DNA samples is recommended (e.g., ThermoScientific Owl EasyCast B1A mini gel electrophoresis systems). Larger laboratory devices (centrifuge, water bath) can be used by several groups of students. We developed and implemented the activity with two students per group. In small classes it would be possible for students to work on their own.

Notes for instructor preparation

The preparation of this learning activity takes about 2 hours. It is advisable to set up the laboratory benches beforehand with the necessary equipment. Table 1 gives details of the materials required for the experiments. Other general equipment used by the entire class during this activity is summarized in Table 2. Table 3 shows the preparation and quantities of the required reagents and chemicals and gives information about recipes and storage conditions where necessary.

Student instructions and sample models

A workbook (Appendix 2) allows students to work independently throughout the hands-on activities, with information, instructions for the experiment, and upcoming challenges. In order to foster comprehension of the individual steps and the roles of the applied chemicals, participants should answer the relevant questions in the workbook during the experimentation. Based on the students' initial hypotheses that DNA seems invisible to the naked eye after a short introduction by the teacher about a real crime case, they isolate DNA threads from oral mucosal membrane cells in the first classic experiment, a process leading to the rejection of their earlier assumption. The second experiment demonstrates the molecular character of the DNA structure during gel electrophoresis.

The creative modeling phase is the key activity of our module. It connects the two experiments and provides the theoretical basis for further understanding of the experimental findings. According to the students' level of understanding, they follow the footsteps of Watson and Crick in solving the molecular puzzle of DNA structure. In preparation, our participants read an abridged version of the

FIGURE 2. Example of a DNA-modeling box with various inexpensive craft supplies.

TABLE 1.
Preparation for students' laboratory benches (each bench is prepared for 4 students, or 2 pairs).

Quantity	(Shared) Equipment and Source
2	Signs with group number
1	Discard/waste jar (lettered)
3	Boxes with rubber gloves (size S, M, L)
1	Stack of paper towels
1	Plastic tub for devices to be rinsed after laboratory activities
4	Waterproof pens
4	Pens
2	(Digital) chronometers (e.g., Fisher brand)
2	Student workbooks (Appendix 2)
2	DNA-modeling boxes (see Fig. 2)
2	One-way drinking cups (foodsafe)
1	Water bottle (foodsafe) with distilled water
2	Small beakers with color solution (e.g., water with blue food coloring or ink) and empty white Eppendorf tube
4	Plastic Pasteur pipettes (3 ml; sterile sealed)
2	Pipette pumps (e.g., Karter Scientific Labware Manufacturing)
2	Snap-cap vials (20 ml; clean and dry) (e.g., Resch Glas)
2	Tweezers (clean and dry)
2	Black placemats (e.g., laminated color paper)
1	Centrifuge
1	Linear pipettor stand with 6 micropipettes (two 1,000 μl, two 200 μl, two 20 μl) (e.g., Eppendorf)
2	Racks with pipette tips in two sizes (sterilized; e.g., blue and yellow)
1	Rack filled with Eppendorf tubes (all sterilized; filled with adequate reagents: 2 white, 2 green, 2 blue, 2 red; and 6 closed, empty Eppendorf tubes marked with "1, 2, 3" for each group) (see Table 3 for filling)
1	Styrofoam box with ice cubes (ice bath) for storing the isopropyl alcohol snap-cap vial (P) and 2 Eppendorf tubes with isopropyl alcohol (yellow)

original letter Francis Crick wrote to his 12-year-old son in 1953 (Appendix 3). After reading, students are to answer comprehension questions in the workbook. In the process of formulating their answers, they internalize essential background information as they mentally begin their model building. DNA modeling kits containing a variety of craft materials (e.g., glue, scissors, straws, pipe cleaners, beads, cardboard, and markers) to help them construct a physical model. To foster problem-solving as well as communication skills, students work collaboratively. To consider the scope and limitations of their models, students have to compare their models' elements with the previously answered comprehension questions by making a labeled sketch. Finally, they compare their work with an unlabeled commercially available school model of the DNA structure and evaluate similarities and differences (Appendix 4). Impressions of the modeling phase are shown in Figure 3.

Faculty instructions

In this activity, short teacher-guided instructions connect the student-centered experimental subunits with the hands-on DNA modeling. The teacher supervises from the background, provides guidance during the hands-on components, and answers students' questions on request.

The first experimental phase can be introduced with the report of a hypothetical crime. In this context the teacher emphasizes the organization levels of genetic material (cell, chromosome, DNA, gene) and explains important experimental steps for the isolation of DNA from oral mucosal

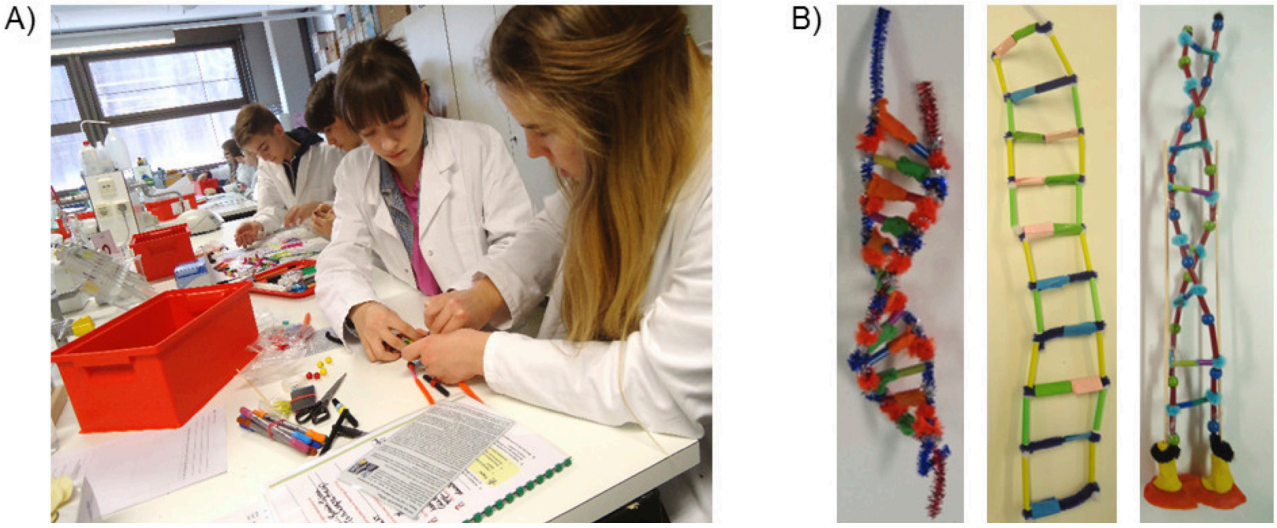

FIGURE 3. Impressions of the modeling phase: A) Students working on their models. B) Examples of constructed DNA models.

cells. After the teacher has given a brief historical summary of pioneering discoveries around DNA (e.g., *Proving That DNA Is the Substance That Contains the Genetic Information*, by Oswald T. Avery, in 1944), the participans read a text on the history of DNA research, following which they begin working on their models. After the students complete their model work, the teacher presents a poster with step-by-step information on the workings of gel electrophoresis. Different sections on the poster give short summaries on important theoretical background information, as well as practical instructions to successfully conduct the second experiment (Appendix 5). Leading questions are discussed with the students to emphasize the most relevant steps. During the interpretation phase, the teacher presents the experimental results of the gel electrophoresis to the class using a slide or poster as the findings, and possible sources of error are analyzed and discussed (e.g., *Describe and compare the experimental results for the different DNA samples*; *Specify possible sources of error that led to deviations in the experimental results*). The results can then be compared with the conclusions drawn from the first experiment, as well as with the finished models. Finally, the teacher gives a conclusive summary on DNA, presented as a macromolecule of life encoding the genetic information of all species.

TABLE 2.
General preparation in the laboratory for one class in the required order.

Quantity	Shared Equipment for One Class (up to 30 Students)
2	Standard water baths filled with distilled water (50°C)
15	Chilled, graduated pipettes (volume min. 10 ml; stored in the freezer until students need them)
1	Magnetic board (for the instruction poster "Gel electrophoresis" with removable magnet applications
2	Standard heating plates
1	Scales
2	Heat-resistant gloves
1	Roll of aluminum foil
2	Erlenmeyer flasks to prepare the agarose gel
2	Electrophoresis chambers with gel combs
1	Power supply for electrophoresis with 4 suitable power cables
1	Erlenmeyer flask with TBE electrophoresis buffer solution (1 L, to flood both electrophoresis chambers)

TABLE 3.
Preparation and quantities of reagents and chemicals for the experiments.

Reagents and Chemicals (with recipes and storage conditions if necessary)	Unit Quantity (per student pair)	Total Quantity Per Class (for 15 student pairs)
Water with blue food coloring or ink	3 ml	45 ml
Lysis buffer Recipe: • 27 ml H_2O • 3 ml dish soap or detergent • 0.9 g NaCl Mix ingredients by stirring and store at room temperature.	2 ml	30 ml
Standard mild detergent (e.g., Woolite Gentle Cycle Liquid Laundry Detergent) (purchased)	Five drops with the Pasteur pipette	10 ml
Isopropyl alcohol (2-propanol; Bio Reagent for molecular biology, > 99.5%); for better experimental results store in the fridge and for DNA sample processing (store in yellow Eppendorf tubes on ice)	5 ml 100 µl	75 ml 1,500 µl
Certified Molecular Biology Agarose (Bio-Rad)	350 g	700 g (two groups prepare this for the entire class)
Electrophoresis buffer (Tris-borate-EDTA buffer; BioReagent, suitable for electrophoresis; 1% concentrate) (e.g., Sigma-Aldrich) and for DNA-Sample processing (store in blue Eppendorf tubes)	50 ml (for agarose suspension) + 450 ml (for flooding the electrophoresis chambers) 150 µl	1 L (for two agarose gel preparations) 3,000 µl
SYBR Green I (Nucleic acid gel stain; 10,000 x in DMSO; store in freezer and let thaw just before boiling agarose solution; wear rubber gloves) (Sigma-Aldrich)	5 µl	10 µl (for two agarose gel preparations)
5x Nucleic acid sample loading buffer for DNA-sample processing (store in red Eppendorf tubes)	5 µl	75 µl
DNA size standard Recipe: • 2 µL EZ Load 1 kB Molecular Ruler (80 µg/ml) • 2 µL 5x Nucleic acid sample loading buffer • 6 µL H_2O (PCR Reagent) Mix solution by pipetting up and down and then centrifuge the solution shortly (14.5 rpm)	10 µl	40 µl (in the two outer wells per each agarose plate)

Suggestions for determining student learning

Formative assessment during the lab day includes teacher-guided in-class discussions, a review of the completed workbooks (Appendix 2; for suggested solutions see Appendix 4), and monitoring by the teacher during the lab work. For the self-evaluation of the DNA models, a comparison of students' models with an adequate commercial school model is recommended (see Appendix 4, p. 9). The pupils can recognize important features of the DNA structure on the picture and quickly check them on their own models (e.g., cohesion of the two DNA strands by hydrogen bonds, possible base pairings). For a more precise and detailed evaluation of cognitive achievement during laboratory and modeling, we provide a questionnaire to test the knowledge of the participants (Appendix 1), as well as a category system the teacher can use to assess the model quality once the learning activity is completed (10). The category system for evaluating the DNA models includes five analysis sectors (e.g., Bases, Primary structure) and grades the resulting models regarding the concrete representations and structural characteristics using sum scores (e.g., analysis sector BA1: 1 point for "symbolized bases" or 2 points for "symbolized and qualified bases"; max. 19 points).

Safety issues

The activity does involve human saliva that should be handled at BSL2 according to the BMBL guidelines given by the CDC (Centers for Disease Control and Prevention) (11). The lab day starts with mandatory safety instruction in which students are initially familiarized with the laboratory rules prescribed by the ASM Biosafety Guidelines (12; e.g., wearing safety goggles and gloves is mandatory, food and

drinks are not allowed) as well as crucial behaviors in case of an emergency (e.g., the way to the nearest fire escape and the use of the eye wash units). Prior to entering the laboratory, students get lab coats which they are to wear during the experiments. Gloves are placed on the middle of the tables and are to be used during the experiments in order to avoid direct contact with human saliva and contamination of the DNA samples. The saliva samples are bleached with 10% bleach for 24 hours before discarding. Additionally, personal protection when handling SYBR Green as a possible mutagen requires gloves and safety goggles for the teacher.

To prevent learning difficulties and injuries caused by lack of experience with lab work, we orient the students with an introductory pre-laboratory phase (13). In this teacher-centered phase, students are initially familiarized with the laboratory equipment and essential scientific techniques (micropipetting, decanting, and centrifugation) are presented. Students have time to ask questions about the safety instructions, and the laboratory supervisor or assistants check whether students follow them during the lab activities. As micropipetting is one of the most relevant working techniques in gene technology labs, it is a major part of the pre-lab orientation.

DISCUSSION

Field testing

As requested by the Genetics Education Outreach Network (14), many outreach programs have been developed to offer authentic learning experiences and compensate for the limitations of time and resources within classroom settings. Our activity is in line with these programs and was conceived and implemented as field trips for students to the university with the intent of providing hands-on experience with conducting lab experiments. The contents of the lesson were modulated to follow the guidelines set by the Bavarian high school syllabus (15). In our pilot lessons, all interventions were implemented by the same instructor and the same tutor, guiding participants through lab safety, the pre-laboratory phase, all main phases, the lab investigation, and concluding with analysis and assessment. Students always worked in pairs. In gaining experience from such pilot lessons, we were able to optimize the module's elements.

In spring 2017, six classes across five different high schools (Gymnasium) in the German state of Bavaria participated in the pilot lessons. Due to space and material resource limitations in the lab, our classes have ranged in size from 20 to a maximum of 34 students. Data were collected from 114 ninth graders (40.87% female; age 14.45 ± 0.69 years [novices]). To control for the effect of repeated measurement, a test–retest sample was also taken from a comparator group of high school students in (n = 39; 100.00% female; age 14.69 ± 0.57 years) who completed the knowledge questionnaire without having participated in the module or receiving any instruction on the topic during data collection.

Throughout the lab day, students were actively engaged in the prescribed activities: they trained with hands-on work in the lab, organized and wrote protocols for their experimental investigations, discussed their findings with peers, and thoughtfully answered the given questions. During modeling, we observed that the artistic aspect of working with craft materials positively attracted learners' attention and enhanced motivation. One reason might be that students had no restrictions in presenting information and could act more creatively than in traditional model-supported approaches (16). At the same, time they managed to visualize and connect the theoretical dimensions of the experiment (17), which helped them understand the links between the different taxonomic levels in gene theory.

Evidence of student learning

From an observer perspective, we can report positive feedback from the students; in particular, the practical work in the laboratory, the handling of materials, and the creative modeling tasks were enthusiastically perceived, as evidenced by active participation in class discussions about the experiments and DNA models. To assess the lesson as planned, we used in our recently published study (10) a quasi-experimental design to measure cognitive achievement (Fig. 4), in which we additionally observed the level of individual creativity in post-test evaluations, as well as heeding the quality of the students' models after lab day. Appendix 1 contains the applied multiple-choice knowledge questionnaire. Selected results of the complete module as well as results on the content of the model phase are presented in Table 4 and show that the modelers achieved significant

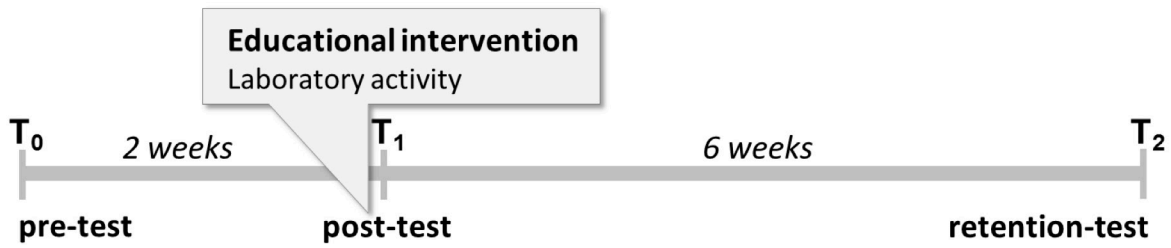

FIGURE 4. Quasi-experimental design of the study with regard to cognitive achievement.

TABLE 4.
Selected results of the assessed cognitive achievement.[a]

Parameter	Knowledge (Sum Score)			Inner-Group Comparison	
	Pre-Test (T_0)[b]	Post-Test (T_1)[c]	Retention Test (T_2)[d]	Chi-square (2)	*p*
$Mdn_{test–retest}$ (*n*=39) Complete module (max. 30 points)	5.00	4.64	4.38	—	ns[e]
$Mdn_{modelers}$ (*n*=114) Complete module (max. 30 points)	10.30	20.20	16.80	180.013	<0.001
Modeling phase (max. 18 points)	5.72	12.43	10.09	177.837	<0.001

[a]The multiple choice test (Appendix 1) consisted of 30 items of varying difficulty: 18 covering the contents of the modeling phase and 12 the laboratory activities. Every item offered four response options, only one of which was correct (max. 30 points).
[b]Pre-test (T_0): 2 weeks before.
[c]Post-test (T_1): immediately after.
[d]Retention-test (T_2): 6 weeks after participation.
[e]ns = not significant

improvement in their short- and mid-term knowledge of the subject. As modeling and creativity are both seen as key factors for science education, we examined relations between model quality scores, individual knowledge, and creativity. While both genders showed similar levels of creativity (Table 5), there was no general correlation between creativity and the quality of the models. Nonetheless, it is to be noted that relative to the male students, the female students produced better-structured models in general, and correlations between creativity and model quality are revealed with their cognitive achievement (Spearman's correlation coefficient $r_s < 0.338$ [$p < 0.05$] > 0.469 [$p < 0.01$]). For male students, neither creativity nor model quality correlated with their cognitive performance (10). We therefore recommend that the use of model work in biology lessons be increased in order to improve the clarity of content and maintain motivation among the students. Female students, in particular, seem to benefit from our STEAM-inspired activity, which offers a new, creative, and artistic approach in the classroom.

Possible modifications

Depending on the amount of time available, we suggest an additional pre-modeling phase to foster the development of modeling skills. Taking the approach introduced in the *Model of Modeling* by Justi and Gilbert (18), such an introductory lesson is aimed at allowing teachers to orient their students in essential lab skills, including data interpretation, consolidation of ideas, and the development of mental modeling. To add a competitive dimension to the lessons, teachers may ask the students to present their DNA models in a small exhibition and/or give out awards for the most accurate models in a classroom competition.

Further modifications for upper-level biology and microbiology courses could integrate additional layers

TABLE 5.
Selected results of the activity's assessment regarding model quality and creativity (10).

Assessment	Median Score (*n*)		Between-Group Comparison		
	Women (47)	Men (67)	*U*	z	*p*
Model quality [max. 19 points]	15.58	13.50	1,094.00	–2.79	0.005
Creativity subscale "act"	2.32	2.39	1,486.50	–0.51	ns[a]
Creativity subscale "flow"	2.33	2.21	1,450.50	–0.72	ns

[a] ns = not significant

of complexity, extending the lesson to incorporate the molecular and atomic structures of DNA. An example of such a lesson could involve students exploring, comparing, and evaluating their models vis-à-vis an interactive three-dimension molecule viewer (19).

CONCLUSION

Our gene technology module combines creative modeling with hands-on experimentation to be conducted in a cooperative learning environment. The targeted educational goals, which follow the Next Generation Science Standards (20), would be easy to realize within regular science classes. As our intervention is inquiry-based, students develop and use models to explain their own experimental results and to solve tasks during the lessons. In the course of the lesson, they come into contact with core ideas such as the inheritance of traits. Finally, we also attempted in the course of our lessons to implement the guidelines laid out in the NGSS *Structure and Function*. During modeling and experimentation, the students investigated the structure of DNA from different perspectives and accumulated their findings to extrapolate its functions.

We conclude that the processes of lab experiments benefit from the addition of modeling assignments, and the two complement each other in providing students with paths of learning and comprehension within the complex field of genetics. After participation, the benefits to students' short- and mid-term retained knowledge were evident. The support provided by DNA modeling in the comprehension of fundamental scientific ideas was particularly notable in the case of female students (10).

SUPPLEMENTAL MATERIALS

Appendix 1: Evaluation instrument (multiple-choice questionnaire)
Appendix 2: Student workbook
Appendix 3: Info text DNA structure, "Following in the Footsteps of Watson and Crick"
Appendix 4: Suggested solutions for student workbook (teacher version) and DNA model evaluation
Appendix 5: Instruction poster, "Gel electrophoresis," with applications

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