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Teaching meiosis with the DNA triangle framework: A classroom activity that changes how students think about chromosomes

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Abstract

Many biology students struggle to learn about the process of meiosis and have particular difficulty understanding the molecular basis of crossing over and the importance of homologous pairing for proper segregation. To help students overcome these challenges, we designed an activity that uses a newly developed Chromosome Connections Kit® from 3-D Molecular Designs to allow learners to explore meiosis at the molecular level. We took a backwards design approach in constructing an effective classroom activity. We developed evidence-based learning objectives and designed a crossing over activity that targets students' misconceptions and key concepts about meiosis. Assessment questions were designed based on the learning objectives and common student misconceptions. The activity consists of three parts: an interactive introductory video, a model-based activity, and reflection questions. The activity was first beta-tested with a small number of students and revised based on feedback. The revised activity was deployed in a mid-level Cell and Molecular Biology course. Analysis of pre-/post-assessment data from students who completed the activity ($n = 83$) showed strong learning gains on concepts related to ploidy, homology, segregation, and the mechanism and purpose of crossing over. Additionally, students who participated in the activity outperformed nonparticipants on a Genetics assessment about meiosis the following semester.

KEYWORDS

active learning, assessment of educational activities, molecular biology, student conceptual and reasoning difficulties

1 | INTRODUCTION

Getting students to understand the process of meiosis is a common struggle for undergraduate biology instructors.

College students are often bored or frustrated when presented with information about meiosis in their classrooms because they (mistakenly) think they already have solid knowledge about this subject. Since typical instruction

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about meiosis often begins in middle school, is repeated in high school, and then again in college Introductory Biology, and yet again in Cell Biology and Genetics courses, it is not surprising that students are tired of reading, seeing, and/or hearing about this process. Contrary to what many students may think about their own mastery of the subject, the biology education literature provides ample evidence that students hold numerous misconceptions, incomplete and/or incorrect ideas about this process. $1-9$ When students do not have deep knowledge about the underlying reasons and concepts linked with meiosis, it hinders their ability to master future concepts in genetics and evolution. We have focused much of our research on understanding how learners conceptualize meiosis and how their mental models of this process differ from that of experts.^{10,11} One of the most important differences between experts and novices is that experts rely on molecular level knowledge about DNA when they describe certain concepts related to meiosis, learners do not.

The underlying processes that drive meiosis (i.e., meiotic recombination) are not directly observable, so instructional materials usually rely on simplified drawings to help learners visualize what is happening within a cell. Biology experts, who have both content knowledge and visual literacy skills, can create and decipher visual representations to communicate, ask, and answer questions.^{12–} ¹⁴ Learners, on the other hand, do not have the experience or the visual literacy skills of experts^{15–18} and may not learn as much from static textbook images as instructors would hope. Bolstered by previous research findings about the deficiencies of traditional textbooks in illustrating the molecular level of meiotic processes, $11,19$ we posit that students struggle to understand meiosis because they see (when looking at textbook images as well as when picturing the process in their minds) chromosomes in a twodimensional way—usually as red or blue blob-like structures. Chromosomes, however, are incredibly complex molecules of DNA and protein. DNA encodes genetic information in both a concrete (sequence of nucleotide bases) and an abstract way (regulatory regions of genes influence expression, which can influence phenotype). The DNA helix and nucleotide bases cannot be visualized directly and yet, the nucleotide sequence promotes or represses molecular level interactions that drive expression and chromosome behavior. Macroscopic level chromosome structures also present problems for learners; experts understand why and how chromosomes can be one or two-DNA molecules, but students get confused as to what counts as a chromosome and where the structures originated from. To be proficient at understanding meiosis one must integrate three levels of DNA knowledge (molecular, chromosomal, and informational) into their mental model. Experts can do this readily, but students cannot.

The DNA Triangle framework is an established model that serves to reconcile and integrate these three different levels of DNA into one cogent mental model.¹¹ The corners of the triangle represent each of the three levels of DNA that must be conceptualized when teaching or learning about a process such as meiosis. The chromosomal (C) level describes the structure of chromosomes (with and without sister chromatids), identification of chromosomes by banding pattern and centromere location, representations of chromatin packing, and counting chromosomes. The informational (I) level describes how DNA encodes genetic information, such as genes or alleles, protein-coding regions, or regulatory information. Lastly, the molecular (M) level describes the chemistry and nucleotide sequence of DNA. Unfortunately, collegelevel biology textbooks typically describe (by the text as well as the visual representations) important concepts like ploidy, homology, and segregation at only the chromosomal level.11,19 Typical models or activities designed to help students learn meiosis often involve manipulatives such as pool noodles, pop-beads, or socks. $7,20,21$ While a hands-on "active-engagement" approach is certainly better than a straight lecture, $22-24$ most models fall short because they mainly focus on the chromosomal level and only hint at the informational level. A classic example is a pop-bead kit in which students build pairs of "homologous chromosomes" with red or blue beads. Color (blue or red beads) represent origin (paternal or maternal) but the lack of nucleotide sequence and molecular level structure encourages students to only focus on superficial aspects such as length and size of "homologous" chromosomes. Beads often represent different genes with different colors representing different alleles, but this model focuses mainly on the chromosome structure, which is highly problematic for several reasons. The scale is completely nonsensical (if there are 12 beads on the chromosomes, do chromosomes only contain 12 genes?) and alleles are versions of genes, which are sequences of nucleotides. The beads look more like a protein than they do DNA. In addition, all of the beads on a chromosome are identical, which makes it confusing as to what an "allele" actually is. Lastly, students are encouraged to exchange red and blue beads to mimic the results of crossing over, but there is no instructional cue or information presented on how that process actually works.

Out of all the parts of meiosis, the process of crossing over for proper chromosome segregation is likely the most mysterious to students.7,25 Most textbooks illustrate the process of crossing over (meiotic recombination) and resolution very poorly. Many textbook illustrations simply show a pair of homologous chromosomes, one red and one blue, lined up side-by-side (no physical interaction) and do not show individual strands of DNA nor 46 WEIGHT ET AL.

how they invade and combine with a complementary strand on a non-sister chromatid.¹⁹ Hand-held models such as pop-bead chromosomes show crossing over by exchanging red and blue beads on non-sister chromatids; this model serves to strengthen a common misconception or misunderstanding about crossing over, namely that chromatid pieces simply break off and exchange places.

The process of crossing over (meiotic recombination) is essential for proper chromosome alignment and segregation, and failure to maintain the integrity of this process has severe consequences for a cell. The basic mechanisms that drive meiotic recombination arise from the double-strand break repair pathway,²⁶ a process that is of critical importance in numerous molecular and genetics topics. Yet the underlying molecular nature of the crossing-over process is rarely described or illustrated in undergraduate biology textbooks, especially introductory levels.^{11,19} Molecular-level interactions that drive cellular processes cannot be directly visualized and, thus, may be "black boxes" for the novice student trying to comprehend these processes. We hypothesized that revealing the molecular level would help students understand how and why homologous DNA sequence drives the process of crossing over and why it is essential for proper segregation.

With the advancement of three-dimensional (3D) printing and other educational technologies, it is now possible to bring physical models of biomolecules (DNA, RNA, and proteins) into the undergraduate classroom.²⁷⁻³⁰ Physical models provide opportunities for students to compare and revise their own mental models of scientific phenomena³¹ and have been shown to produce increased learning gains compared to other active learning strategies.32 Thus, we set out to design an activity to explicitly reveal the molecular level to help students visualize homology and the process of crossing over. Following evidence-based practice, we wanted the activity to require the students to construct their own understanding of the process through the manipulation of physical models. $30,32$

2 | DEVELOPMENT OF THE MODEL

The Center for BioMolecular Modeling (CBM) is a grantsfunded instructional materials development laboratory that focuses on developing tactile materials to explore challenging concepts at the molecular level. The CBM offers a number of professional development opportunities for high school and college educators who provide input on which concepts are difficult for students to grasp. As part of an NIH-SEPA grant focusing on genome editing, educator colleagues identified mitosis and meiosis as challenging topics to teach. Many existing tools focus on the movement of chromosomes during cell division (a cytological view), and some make the connection between alleles and chromosomes. But none of the cell division models made the connection between chromosomes and nucleotides (a molecular perspective). Discussions with LKW and DLN regarding student misconceptions, along with the DNA Triangle framework 11 guided the design of foam chromosome models that allow for a "zoom in" on the chromosome to reveal that it contains double-stranded DNA (see Figure 1). The modularity of the foam models allows for the exploration of cell division (mitosis and meiosis) at both the cytological and molecular scales, thereby solidifying the connection between DNA and chromosomes. The kits went through several iterations of field-testing in high school and college classrooms, and educator feedback guided final model designs. Red and blue (signifying maternal and paternal origin) foam pieces fit together like puzzle pieces, to build chromosomes at the macroscopic/chromosomal level and nucleotide pieces (also red or blue) to allow learners to appreciate the molecular structure and sequence of chromosomes. The nucleotide sequences embedded within the chromosome allow for the exploration of advanced topics, including the molecular mechanism of crossing over and the creation of a Holliday junction. They can also be used to explore chromosomal aberrations and recombination repair of damaged DNA. These kits are now produced by and available from 3D Molecular Designs as the Chromosome Connections Kit© and are also available for loan from the MSOE Model Lending Library ([https://cbm.](https://cbm.msoe.edu/lendingLibrary) [msoe.edu/lendingLibrary](https://cbm.msoe.edu/lendingLibrary)).

3 | METHODS

Following the three main steps in backwards design identify desired results, determine acceptable evidence, plan learning experiences, and instruction 33 —we developed the activity and assessment materials to ensure that the assessment, activities, and learning objectives (LOs) were in alignment. The process was iterative. For example, as we crafted the LOs we also considered assessment questions and what, specifically, students would do with the models in class.

3.1 | Development of learning objectives

Using the literature and our own teaching experiences we drafted a set of LOs. As we developed the assessment and activities, we continued to refine the LOs for improved clarity and readability. Table 1 lists the LOs,

FIGURE 1 The crossing over activity is based on the Chromosome Kit® from 3D molecular designs. It contains foam pieces that interlock and can be used to build chromosomes. (a) Red and blue pieces can be used to represent maternal and paternal chromosomes. Inserts allow for demonstration of "zooming in" to the sequence level, where individual nucleotides can be added. (b) The three types of parts are put together to show the sequence similarity of homologous chromosomes

TABLE 1 Learning objectives were developed based on research about student misconceptions and naïve ideas about meiosis

references, and examples of common novice idea/ misconceptions that helped informed each one.

3.2 | Development of assessment

Guided by the LOs a series of multiple select assessment questions (i.e., "select all that apply") were developed. Four answer choices were created for each question stem and between 1 and 4 answer choices were correct for each question. Questions and answer choices (both correct and incorrect) were mapped back to the LOs and questions were revised to ensure coverage of all LOs. With the exception of LO4, all objectives aligned with both correct and incorrect answer choices. The assessment is included as a Data S1.

3.3 | Development of the activity

D.L.N. and L.K.W. collaborated with the team at the CBM on early model prototypes. The starting point for

the model was the paper chromosomes described in Reference 25, which was then transitioned to a more manipulable and durable foam structure. The basic concept of the design was to create a model that allowed for users to zoom in (to M level) and out (to C level) and to incorporate allelic differences (I level) in order to bring all parts of the DNA Triangle together. This allows users to manipulate chromosomes to show large-scale movements (C level) but also to get insight into how similar homologues are (M level), how the process of crossing over works (M level), and the genetic outcomes (I level). Once the model was fully developed, the research team worked with the model to develop LOs and conceptualize how students would move the model pieces around to accomplish the LOs. Step by step instructions were developed and revised. The activity was given to four beta-testers, who explained their thinking while following instructions and manipulating the models. Their experiences revealed confusing steps/language and the fact that the activity was too long for one in-class setting. In the second major revision, the activity was divided into three parts, one of which included a video. Table 2 provides a

TABLE 2 Description of the activity and alignment with the DNA triangle framework (key concepts of meiosis and levels of DNA)

Abbreviations: C, chromosomal; I, informational; M, molecular.

FIGURE 2 During the crossing over activity students construct a Holliday junction. (a) Students are able to model strand invasion during crossing over. Red and blue represent different parental origins, and the homologous chromosomes base-pair with each other. (b) The model allows for a 3D representation of the Holliday junction that connects all four strands. The model represents new DNA synthesis with gray nucleotides. (c) This is the same structure as shown in panel (b) but flattened. Yellow and green dots placed on the model (white arrows) indicate where the homologous sequences differ, so that students can track recombination of alleles

synopsis of the activity (all three parts) and how they align with levels of DNA as described in the DNA Triangle framework. Figure 2 shows students constructing a Holliday junction with the model. Assessments and the activity are available as Data S1.

3.4 | Implementation of activity

The crossing over activity was tested in a second-year Cell and Molecular Biology majors-level course at a large, private institution in the Northeast. Students enrolled in this course were biology, biochemistry, or other biologyrelated majors or were pursuing their minor or concentration in biology. All completed a year of introductory biology before enrollment in this course. There were three identical lecture sections of this course taught by two different instructors (author L.K.W. was one of the instructors but administered the model-based activity in all three sections for this study). One week prior to the implementation of Part I of the activity, students completed the multiple select pre-assessment given in an online format. Students were awarded homework points for their participation and "best effort" but scores were not shared nor were questions discussed. During class, students completed Part I of the crossing over activity. After class was complete, students watched a short review video on their own (Part II of the activity) before coming to the subsequent class to complete Part III of the activity. Of 93 students enrolled in the course,

83 completed the pretest, posttest, and all parts of the activity. Figure 3 provides an overview of the student populations included in this study.

3.5 | Analysis of assessment data

Pre and posttests from students who completed the crossing over activity ($n = 83$) were analyzed two ways. We calculated pre- and post-scores for each student based on whole question and also partial responses. This dual scoring strategy (whole question and partial or "fractional") has been utilized in other studies such as References 35,36. For whole question analysis, students got credit for each question they answered perfectly correct (selecting all correct choices and not selecting any incorrect choices). The percentage of each question students answered correctly was calculated for partial answer scores. We also analyzed assessment data based on LOs. Table 3 illustrates the alignment of LOs with correct and incorrect answer choices. Normalized learning gains for each LO were calculated using (post-pre)/(1-pre). We also calculated the percent change in selection of correct answers or incorrect answers on pretest compared with posttest for each LO.

To investigate longer-term impacts on learning, we analyzed student performance on a meiosis-related question that appeared on a Genetics in-class exam 5 weeks into the semester, after all students had reviewed meiosis. Genetics is a course that students take after Cell and

FIGURE 3 Data for this study was drawn from two populations. First, pre-/post-scores were calculated from 83 students enrolled in a cell and molecular biology class, who completed all parts of the model-based activity and pre/posttests. A subset of the 83 students enrolled the following semester in a Genetics class. The second analysis compared the 15 students exposed to the model to 19 students who had not been exposed to the model. Two students in Genetics had partial experience with the model and were excluded from the analysis

Learning objective	Students will be able to:	Correct	Incorrect	Average normalized learning gain
LO ₁	Correctly predict chromosome number at any stage of meiosis.	1b, 1d, 2a, 2b	1a, 1c, 9c	0.2875
LO2	Correctly count chromosomes and chromatids at all stages of meiosis.	4a, 4b, 4c, 4d	2c, 3b	0.3309
LO ₃	Identify the basis of homology.	5c	5a, 5b, 5d	0.1172
LO ₄	Describe the process of crossing over at the molecular level.	6a, 6b, 6c, 6d		0.4914
LO ₅	Correctly outline three major steps of meiosis.	3a, 8c, 9d	3c, 3d	0.4422
LO ₆	Describe possible outcomes of crossing over.	8a, 8b	8d	0.3788
LO ₇	Explain why crossing over is necessary for homologous chromosomes to segregate properly.	7a, 7c, 7d	7b, 10d	0.4860
LO ₈	Apply their knowledge on ploidy in distinguishing the types of cells that result after both stages of meiosis.	9a	2d, 9b	0.3400
LO ₉	Correctly identify where crossing over occurs in meiosis.	10c	10a, 10b	0.4691

TABLE 3 Alignment of learning objectives with correct and incorrect answer choices from the multiple select assessment

Note: Average normalized learning gains for each learning objective were also calculated.

Molecular Biology, although not always in the next consecutive semester. Thus, about half of the students enrolled in Genetics had used the model when it was first introduced the previous semester and half had taken the course earlier, without the model. Thirty-six students were enrolled in the course. The instructor of the Genetics course (author D.L.N.) did not have prior knowledge as to which students had used the model previously. In the exam question, students were presented with illustrations of various cells containing replicated or unreplicated chromosomes and asked to determine the total number of chromosomes, number of homologous pairs, and number of double-stranded DNA molecules, and to

decide whether each was haploid or diploid and whether or not replication had already taken place. They were also asked to place alleles on one diagram to indicate a triple heterozygote where one pair was linked, and to predict the gametes produced by that individual. After the exams were all graded, co-author L.K.W. looked at the class-list and sorted the 36 students enrolled in the Genetics course. Nineteen of the students were not exposed to the model ($N = 19$, "controls") and 15 students were exposed to the model ($N = 15$, "cases"). Two students did not fit into either category because these students had only completed half of the model-based activity in Cell and Molecular. These two students,

therefore, were not included in the analysis because they had partial exposure but did not complete the entire activity as intended. Median scores and effect size for each group were calculated.

4 | RESULTS

4.1 | Pre and posttesting reveals learning

Analysis of the pre and post-assessment scores strongly suggests students learned as a result of using the crossing-over model. The median score on the pretest assessment was a 61.63%, which improved to a 72.72% on the posttest (Figure 4).

The multiple select nature of the assessment improves the validity of the assessment, as students cannot use typical "game playing" strategies to identify just one correct answer choice. Students must evaluate each answer choice as being correct or incorrect which also increases the difficulty of the assessment. The multiple select formats allow students to be both partially incorrect and partially correct at once, which offers instructors and researchers a more complete picture of student understanding compared to a standard forced-choice assessment.^{36,37} We found that students make learning gains on all LOs (Table 3), with particularly strong gains on LO4, LO7, and LO9. Students made the smallest gains on LO3, to "Identify the basis of homology." Deeper analysis into the responses reveals the vast majority of students (89%) correctly recognize choice 5c that "Both chromosomes of the pair have similar DNA sequence" on the posttest but they do not easily stop choosing 5a and 5b, which are "both chromosomes of the pair have the same

FIGURE 4 Students ($N = 83$) made significant improvements on their posttest scores, suggesting they gained knowledge on the learning objectives aligned with the activity

alleles" and "both chromosomes of the pair are similar in length". While choices 5a and 5b are not untrue statements, they are not the underlying basis of homology.

As the pre-/post-assessment followed a multiple select format we were able to calculate the percent change in selection of correct and incorrect answers on post compared to pre, aligned by each LO. As demonstrated by Figure 5, students selected more correct choices and fewer incorrect choices after engaging in the crossing over activity. The pattern varied somewhat by LO, but students improved on all objectives in the postassessment analysis. This outcome is especially pronounced in LO7 (Students will be able to explain why crossing over is necessary for homologous chromosomes to segregate properly), which was a major focus of the activity. Since there were no incorrect answer options for LO4, only the increase in correct responses could be calculated.

4.2 | Long-term effects

To asses any long-term impacts of the crossing over activity, we analyzed data from a genetics exam question given the following semester. The Cell and Molecular course is a pre-requirement for Genetics, but students do no always take Genetics immediately after Cell and Molecular Biology. Of the students enrolled in the Genetics course, 15 students did the crossing over activity and 19 students did not (they had completed the Cell and Molecular Biology course in a previous term). As illustrated by Figure 6, students who had previously used the model outperformed students who did not. Students who

FIGURE 5 Students ($N = 83$) chose more correct options and fewer incorrect options on the posttest compared to the pretest for every learning objective (note that there were no incorrect options offered for LO4). The bar graph shows the change in the percentage of correct answers (positive change, more correct answers selected) and incorrect answers (negative change, fewer wrong answers selected) in the posttest compared with the pretest

FIGURE 6 Students who had completed the three-part activity $(N = 15)$ outperformed students who did not $(N = 19)$ on a meiosisrelate question in a follow-up Genetics course

used the model (cases) had a mean score of eight (of 10) points while students who did not (controls) had a mean score of 6.1. Effect size was calculated at 0.9939, which shows an extremely strong relationship between exposure to the model and exam question performance.³⁸

5 | DISCUSSION

Visualizing the molecular level of DNA and seeing its relationship to the other levels are key to understanding the behavior of chromosomes (and the genetic consequences) during the process of meiosis. Traditional classroom activities and textbook illustrations of meiosis focus almost exclusively on the chromosomal and informational level and fail to incorporate the molecular level.19,39 Students are exposed to these same sets of teaching materials time and time again and are rarely challenged to think about the underlying molecular processes that drive chromosomal behavior. We designed our novel set of materials using the DNA Triangle framework as a guide to help students "see" the underlying molecular structure (nucleotide sequence) of homologous chromosomes and explore how sequence similarity drives the process of crossing over. The dynamic, 3D model also allows students to build the physical interaction of homologous chromosomes during crossing-over. This physical interaction is essential for proper chromosome alignment and eventual chromosome segregation; a fact that is not made clear to them with most other teaching approaches. Data analysis of pre-/post-assessment strongly suggests this crossing-over activity is an effective tool for learning. Because we did not have a control group of students who did not complete the activity but also completed pre/posttesting, we cannot rule out that students may have learned these concepts on their own and/or during some other part of the class. However, the quasi-random study of a subset of students who went on to a Genetics course compared to a control group who never experienced the activity supports our argument that the model-based activity was the element that improved learning.

Although the Chromosome Kit is available to borrow from the MSOE CBM Lending library [\(https://cbm.msoe.](https://cbm.msoe.edu/lendingLibrary/) [edu/lendingLibrary/\)](https://cbm.msoe.edu/lendingLibrary/), not all instructors will want to or will be able to use the kit and our three-part activity in their classrooms. Regardless, we feel there are still valuable ideas that instructors can use from our study, as discussed below.

5.1 | Implications for teaching

Our current study illustrates how important it is to let students "see" the molecular level of DNA; especially when learning about molecular processes that depend on the underlying nucleotide sequence. For instance, the concept of homology is rooted in the molecular level so we strongly suggest instructors use something other than standard textbook-like illustrations that depict homologous chromosomes as cartoonish red and blue chromosomes.¹⁹ Such illustrations direct students to focus on the color and size and shape of the chromosomes rather than the underlying sequence similarity. As a result, many students are unaware of the molecular basis of homology. The partial DNA sequences we provided for a maternal and paternal homologous pair (Data S1) may be a good way to illustrate the concept without using the kit-based model.

The process of crossing over is both familiar but also confusing to the typical biology student. Most students will remember that crossing over happens in meiosis, but the molecular details of the process are missing from students' mental models.¹¹ Most textbooks give little detail about the process and, instead, show the product of crossing over with cartoonish red and blue chromosomes that have "swapped" pieces. We argue that these figures are misleading, as they seem to show a piece from a "red" chromosome breaking off and fusing with a "blue" chromosome. The process of crossing over becomes much less mysterious to students when they can see a single paternal strand base-pair with a complementary maternal strand. If the kit-based model that we described here is not possible to bring into class, a paper-based model may be a useful alternative for instructors.²⁵

Explicitly bringing in the molecular level of DNA does not begin and end with the process of meiosis. Many processes are facilitated by complementary base-pairing such as DNA repair pathways (homologous recombination after double-strand break), hairpin loop-mediated transcriptional termination, and even tRNA:mRNA binding during translation. Molecular biology experts can "see" (in their mental models) nucleotides and the interactions that depend on precise nucleotide sequences, but learners (novices) cannot. Thus, when teaching topics in Molecular Biology we encourage instructors to find ways to make the molecular level visible to their students.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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