Instructors Guide for The Facts of Life: Meiosis animation

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General Introduction: This Guide accompanies the teaching animation video *The Facts of Life: Meiosis*. A second animation, *The Facts of Life: Mitosis*, is also available, with a similar Guide for Instructors. Both animations and guides are available at <u>www.usefulgenetics.com/mitosis-and-meiosis-resources</u>, along with a slide deck explaining the shared strategy of these divisions. Accompanying all these materials is an open-access article describing our concerns about how mitosis and meiosis are currently taught and our ideas for improvements (*Tackling biology's memorization problem: resources for mitosis and meiosis*; P. Kalas and R. J. Redfield, submitted July 2022. A pdf is available at <u>usefulgenetics.com</u>.)

Understanding mitosis and meiosis is essential to a biology education, since these are the fundamental mechanisms by which eukaryotic cells and organisms reproduce. Although animations are in principle very helpful tools for understanding biological processes, most mitosis and meiosis animations focus on the named stages traditionally emphasized in static instructional materials and thus unwittingly encourage rote memorization; many also contain serious errors. A more general problem is that, in both textbooks and animations, the level of explanation has not advanced since the early days of light microscopy, neglecting the now well-understood molecular events underlying chromosome interactions and movements.

Our Mitosis and Meiosis animations are different, being designed to encourage students to think about these processes as solutions to cell-division problems. In each animation, students first see a simplified version of the process, and then a series of segments introduced by 'Why...?' and 'How...? questions about the underlying mechanisms. To prevent students from defaulting to memorization, the animations do not directly provide the answers; instead students must infer the answers from what they observe in the simulations that follow each question.

As an introduction to this and the Mitosis animation, we have also provided an accompanying set of editable PowerPoint slides that can be used to introduce students to the 'pair-pull-part' strategy used by both cell-division processes (available at <u>usefulgenetics.com</u>).

This animation may appear simple or even naive; the animation technique is stop-motion and candies are used to represent chromosomes and other cellular components. However, because it illustrates the molecular processes underlying the chromosome behaviours, it actually takes students well beyond the content of other meiosis animations. Our emphasis is genetic, focusing on what happens to the DNA rather than on the many proteins that drive the processes. In designing the animations we chose not to introduce any terminology (there is no voice-over, and nothing is labeled), because we have found genetics jargon to be an obstacle to learning rather than an aid. We provide terminology lists below, and recommend that instructors introduce only those technical terms they consider essential, using plain English descriptions for everything else.

Ways to use this animation: Although students can easily can find this animation on YouTube, it will be much more effective with guidance from an instructor. Since it has been designed to require only a very basic biology background, it should be useful in a wide range of educational settings, from an enrichment resource for high school students to a refresher for students entering genetics or cell biology graduate programs.

- Emphasize the strategy, shared with mitosis: Mitosis and meiosis share a very elegant 'pair-pull-part strategy to ensure that each daughter cell gets one complete set of chromosomes. First as each chromosome is replicated, the sister chromatids are tied together with loops of protein ('cohesin) along their lengths. Homologous chromosomes are then identified and tied together by crossovers. They remain tied through the first stages of meiosis I, when fibers attach to the chromatids and pull on them. Once persistent tension on the fibers signals that all the homologous pairs have bidirectional attachment, the loops of cohesin in the chromatid arms are cut all at once, which allows the homologs to separate. In meiosis II, sister chromatids are initially held together by the cohesin loops in their centromeric regions. This strategy greatly simplifies chromosome distribution, since the dividing cells do not need to identify and track individual chromosomes or check the contents of the daughter cells. We provide a set of PowerPoint slides to illustrate this strategy for both mitosis and meiosis. Depending on the instructor's goals, these slides could be shown to students before or after they watch the mitosis animation.
- As preparation for a lecture or tutorial on meiosis: Provide students with a set of questions to answer before class, then watch the specific segments in class and discuss the answers. Alternatively, students could be given the task of writing down all the questions they have about meiosis, as well as one thing they have learned from the animation, and their questions could be addressed in class.
- **During a class on meiosis:** Show the animation, asking students to answer each question before and/or after its explanatory segment. Or have groups of students watch the animation together in class and answer questions on a worksheet, then debrief.
- As homework after a class on meiosis: Students could be asked to write out answers to the questions posed in the animation. Since the animation avoids introducing any genetics terminology, students could be given a glossary of technical terms which they are asked to associate with specific items and events in the animation.

Technical issues:

- The animation can be slowed down using YouTube's 'settings' controls.
- Some events in the animation happen quite quickly; students will probably need to pause some segments and rewatch them, perhaps several times.
- The audio should be turned off for classroom use.

The table below provides a description of each segment of the animation, with learning goals and lists of questions that instructors and students might raise, and suggested answers. Many of these questions can also be adapted for assessment of student learning in the classroom and in both open-book and closed book tests.

Segment, Time and Heading or Question	Goals and Questions for Students
	different organisms are said to be homologous if they are similar because the organisms have descended from a common ancestor. In the same way, the various versions of each chromosome in a species are similar because they are all descended from the same ancestral chromosome.)
 Time: 0:50-1:07 Maybe you already learned this, but do you know: How mitosis works? Why we also need meiosis? How cells must prepare for meiosis? How crossovers happen? To learn the answers to these and other questions, watch what happens in each animation segment. 	 Goal: This brief segment exists mainly to motivate students, since many will have been badly taught about meiosis in earlier courses. It also prepares them for the upcoming questions and explanatory segments. (The word 'mitosis' is in red because it's so easily misread as 'meiosis'.) Questions students could be asked: Try to answer the questions this segment poses. (Before or after watching the 'simplified' segment) Explain meiosis to your neighbour. Students could be given strips of coloured paper to use as model chromosomes in their explanations. What does meiosis accomplish that mitosis doesn't?
Time: 1:07-2:11 Why should I first learn how mitosis works? This segment shows a student at a computer, about to start watching this animation, and deciding that she already understands mitosis and doesn't need to first watch the mitosis animation. But as she watches the meiosis animation she realizes that meiosis uses many processes that also function in mitosis. She clicks on a link that takes her to the mitosis animation, and students are	Goal: Many students mistakenly believe that they already understand mitosis (and even meiosis). However, although they may have been previously taught about mitosis in high school or college biology courses, that material is likely to have been superficial and their retention to have been poor. Even those students who correctly remember what they were taught about mitosis will often lack the deeper understanding needed as the foundation to understanding meiosis. Our mitosis animation is designed to remedy this deficiency. To understand how meiosis works, students need to know that immediately after replication sister chromatids are tied together with protein loops (cohesins) and that they stay tied together until the loops are cut when the cell is ready to separate the chromosomes. They also need to know that spindle fibers won't stably attach to kinetochores unless they feel tension from the pulling of oppositely oriented fibers (like a tug of war). If they don't know these things students should watch the mitosis animation before watching the meiosis animation, preferably with guidance from their instructor. Note that watching some other animation of mitosis will not suffice, since most of these are much too simple and often contain errors.

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directed to a similar link in this real animation.	This is an appropriate place to show the PowerPoint slides explaining the 'pair-pull-separate' strategy shared by mitosis and meiosis.
	 Questions for students: 1. Did you go back and watch the mitosis animation? If yes, what did you relearn, and what did you learn for the first time?
 Time: 2:12-3:40 Why do we need meiosis? This segment shows A pastoral scene with pairs of animals, flowers, bees and worms. Meiosis in a female rabbit, producing an oocyte arrested at the end of Meiosis I Meiosis in a male rabbit, producing four sperm Copulation by all the animals Fertilization of the female rabbit's oocyte by a sperm. The pairs of animals again, now with their offspring. 	 Goal: Students should recognize that meiosis is essential for our reproduction and determines our genetic inheritance. They should know that meiosis is more complicated in females than in males, but the level of detail taught will depend on the course. Optional terminology: sexual reproduction, gametes, sperm, egg, meiotic arrest, pollen, ovule, fertilization Questions students could be asked: 'Why do we need meiosis?' (Answer: Humans need meiosis because, like most other animals and plants, we are diploid organisms that reproduce sexually. Meiosis produces the specialized haploid gametes (egg and sperm cells) whose fusion creates the next diploid generation.) Why do we (biology students) need to learn how meiosis works? (Answer: This is the process that determines which gene versions you inherited from each of your parents, and which versions you will pass on to your children. Errors in meiosis are responsible for many medical problems.) When is meiosis happening in the animals in the animation? In the flowering plants? (Answer: In the adult male animals it's happening all the time. In the females it begins before birth but pauses until adulthood. In the flowering plants it happens when pollen and ovules are produced as the flower develops, before the seeds form. Where is meiosis happening in the animals? In the flowering plants? (Answer: In the testes and ovaries of the animals, and in the ovules and stamens of the flowers.)
	Questions students might ask: 1. Why does the egg cell: a. already have its chromosomes paired up when we first see it? b. pause after completing MI, and not restart MII until the sperm attaches to it? c. put one set of its MI chromosomes into a little cell?

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	d. put one set of its MII chromosomes into a tiny cell?
	Students may not have learned about meiosis-specific processes in females. Female mammals produce egg cells before they are born, and these cells arrest at metaphase I. When the egg matures before fertilization it completes MI and discards one set of replicated chromosomes (both sister chromatids) into the 'first polar body. It then pauses meiosis until a sperm arrives, when it completes MII and discard a final set of unreplicated chromosomes into the 'second polar body'.
	Note: Ambitious students may want a deeper explanation, asking why plants and animals have evolved to reproduce by sexual reproduction. A simplified explanation is that offspring benefit by having different combinations of alleles than their parents did. For a more detailed discussion see this <u>Wikipedia</u> article.
Time: 3:41-4:05	Goal: Students should realize that the same-colour Twizzlers represent homologous
What do the coloured bands on the chromosomes represent?	chromosomes. These chromosomes have the same genes, but many of these genes are present as different versions ('alleles'). The orange and yellow bands on the chromosomes represent a few of these genes, with yellow indicating the paternal versions and orange the maternal
A sperm with yellow-banded	versions.
chromosomes fertilizes an egg with orange-banded chromosomes.	Optional terminology: sister chromatids, homologous chromosomes, genes, alleles
	 Questions students could be asked: What do the coloured bands on the chromosomes represent? (Answer: The orange and yellow bands represent the different versions of genes (alleles) inherited from the mother (in the egg) and father (in the sperm).) Do all the orange bands represent the same gene? (Answer: No, the bands at different positions on the chromosomes represent different genes.) Do the yellow bands represent different genes than the orange bands? (Answer: No, they represent different versions of the same genes. Are the orange and yellow bands in different locations on their chromosomes? (Answer: No, they're at the same positions. For every orange band there's a corresponding yellow band at the homologous position on a same-coloured chromosome.
	Questions students might ask:

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	 Are there only two versions of each gene? (Answer: No. Each individual can only have two alleles (and these can sometimes be the same version), but most populations of individuals have at least several different versions of each gene. Are the two alleles from Mom and Dad always different versions? (Answer: No, sometimes by chance the alleles inherited from Mom and Dad are identical.
Time: 4:06-7:36 How do cells prepare for meiosis? Four sub-questions:	Goal: To teach students about the important events in meiosis that occur before the condensed chromosomes become visible. (Traditionally, only the DNA replication step has been taught.) By the end of the animation (not by the end of this segment), students should be able to explain why each of these steps is essential for meiosis.
 Does the DNA replicate? The camera first shows a pile of laces 	Optional terminology: DNA polymerase, sister chromatids, homologs, base pairs, Spo11 (the nuclease that makes the initial cut) double-strand break, single strand of DNA
 representing uncondensed chromatin of the chromosomes. It then zooms in on a replication fork of a red chromosome with green alleles. 2. What holds the replicated DNAs together? Intertwined strands of red licorice represent the two strands of the DNA. We see the newly synthesized chromatid pairs being tied together with loops of string, representing molecules of the cohesin protein. Some loops are blue – we will later see that these are close to the centromeres. 3. How do the chromosomes search for and recognize their homologs? a. A nuclease (orange ring) cuts both strands of a chromatid. Halves of the nuclease initially bind to the DNA-strand ends on each side of the 	 Nuclease that makes the initial cut) double-strand break, single strand of DNA Questions students could be asked: What has happened in each step? What does the pile of laces seen at the beginning represent? (Answer: Uncondensed molecules of double-stranded DNA in the nucleus.) Why does the DNA need to be replicated? (Answer: This seemingly simple question has a complicated answer. In principle a diploid cell with unreplicated chromosomes could produce two haploid gametes by a single division (a hypothetical 'one-step meiosis'). But the homologs would still need to pair up and stay together until the cell divided, and the process would not necessarily be simpler than the 'two-step' meiosis we know. This and other unresolved issues about the evolution of meiosis are discussed in these open-access articles: https://doi.org/10.1534/genetics.108.099762 Why do the replicated DNAs need to be tied together? (Answer: As explained in the 'pair-pull-separate' slides, this attachment is what holds the homologous chromosomes together at metaphase.) Why do the single strand ends feel around on other DNAs? (Answer: they are seeking strands that can base-pair with them. Only the homologous positions in homologous chromosomes can do this (since pairing with a sister chromatid is not allowed).)

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chromatid that they are already base-paired to.	Notes: Many incorrect diagrams and animations show the chromatid arms beyond the crossover point moving over to be with their homologs (as in the right-hand panel of the figure. Because this would not generate recombinant chromosomes, these erroneous Illustrations typically also contain a second error, showing the crossover point not breaking arejoining until the homologs separate at Anaphase I. Unless your students are quite advanced, do not expect them to remember exactly how conduction site into a crossover, since even explave difficulty keeping this straight. 	and
Time: 7:37-8:08	Goal: Students should learn that every chromosome pair gets <i>at least</i> one crossover in meio but that some get more than one. Multiple crossovers are more likely in longer chromosom	
Does every chromosome pair get one crossover?	Optional terminology: crossover, chromatids	103.
This segment shows an array of homologous chromosome pairs, from very short to very long, each with at least one crossover. Then a number appears above each pair, corresponding to its number of crossovers. All the short pairs, and some of the longer ones, have a single crossover. But some of the longer ones have two or three crossovers, mostly involving different combinations of chromatids.	 Questions students could be asked: Does each chromosome pair get only one crossover? (Answer: No, pairs of short chromosomes have only one crossover but pairs of longer chromosomes usually have more.) Do some chromosome pairs get no crossover? (Narrow answer: Every chromosome pairs shown in the animation has at least one crossover. Broader answer: No, the number crossovers is regulated to ensure that each chromosome pair gets at least one. Would something go wrong if a chromosome pair had no crossover? (Answer: Yes. T homologous chromosomes would not be held together and, because there would be r tension, their kinetochores would not stably attach to opposing fibers. 	pair of The

Segment, Time and Heading or Question	Goals and Questions for Students
	 4. When a crossover occurs, how many chromatids have new combinations of alleles? (Answer: Each crossover changes connections in two of the four chromatids in the paired homologs.) 5. When a chromosome has two or three crossovers, are they all between the same two chromatids? (Answer: No, multiple crossovers on the same chromosome often involve different combinations of chromatids.) 6. Can some chromosomes have more than three crossovers? (Answer: Yes, long chromosomes can have even more crossovers, but having too many crossovers will also make separation difficult because of how entangled the chromatids will be.)
	 Questions students might ask: 1. How is the number of crossovers regulated? (<i>Answer: When a crossover forms, its structure inhibits nearby interaction sites from becoming crossovers.</i>) 2. Does the cell regulate which combinations of chromatids are used for each crossover, when there are multiple crossovers on the same chromosome? (<i>Answer: No, the choice of chromatid partners appears to be random.</i>)
	Note: The rule that all homolog pairs must have at least one crossover is not universal. The best- known exception is male fruit flies, which use cohesin-like proteins instead of crossovers to tie the homologs together after they have identified their partners by base pairing.
Time: 8:09-9:21	Goal: Students should identify the similarities and differences between how chromosomes
What holds the pairs of sisters or homologs together? And how do they	separate in Mitosis, Meiosis I and Meiosis II, especially the essential role of tension on the fibers, created by the cohesins and crossovers.
come apart?	Optional terminology: meiosis I, meiosis II, metaphase, cell division checkpoint, spindle fibers, bidirectional/bipolar attachment, cohesin, separase,
This segment shows three panels, labelled Mitosis, Meiosis I and Meiosis II.	This is another appropriate place to show the PowerPoint slides explaining the 'pair-pull-separate'
Each panel's chromosomes complete	strategy shared by mitosis and meiosis, if they have not been shown previously.
their separation in turn:	Questions students could be asked:
Mitosis panel: A pair of sister chromatids with spindle fibers attached to their small yellow kinetochores are held together by white cohesin loops. The	 What happens in each panel? What are the inspectors checking for in each panel? (Answer: for secure attachment of the fibers to the kinetochores, which depends on tension caused by bidirectional ('bipolar')

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Inspector (representing the Spindle Assembly Checkpoint) confirms that fibers are stably attached to the sister chromatids and pulling them in both directions, and signals to the scissors (representing the enzyme separase) to begin cutting the white cohesin loops, allowing the sisters to separate. Meiosis I panel: This shows a pair of homologs, each with two sister chromatids held together by loops of	 attachment of the fibers to chromatids/chromosomes that are being held together by cohesins. 3. What happens when the white loops are cut in Meiosis I? (Answer: the arms of the sister chromatids can separate, but not their centromere regions. This lets the arms of the homologs separate beyond the crossover point, and thus lets the homologs separate while the sister chromatids remain attached at their centromere regions. 4. What happens when the blue loops are cut in Meiosis II? (Answer: the sister chromatids can separate completely.) 5. What would happen if the blue loops were cut in Meiosis I, along with the white loops? (Answer: The siter chromatids would be separated before Meiosis I began, so the fibers wouldn't form stable attachments.)
white and blue cohesins). The inspector checks the fiber connections, and a zoomed-in view shows that the one crossover prevents the homologs from separating, because the chromatid arms beyond the crossover point are still tied to each other by white cohesins. Cutting the white cohesins then allows the arms beyond the crossover points to separate from their sisters and thus allows the homologs to completely separate. The blue cohesins around the kinetochores remain uncut and still hold the sister pairs together.	 Questions students might ask: 1. In Meiosis I, why don't the scissors cut the blue loops around the centromeres? (Answer: In Meiosis I these loops (cohesin proteins) are protected by a special protein that's removed before Meiosis II.) 2. What's the difference between Mitosis and Meiosis II? (Answer: Genetically a lot: The daughter cells in Meiosis II are haploid and many of their chromosome segments contain new combinations of the parental alleles. But mechanistically there's not much difference.)
Meiosis II panel: Two chromatids, with spindle fibers attached to their small yellow kinetochores as in mitosis, are held together by the blue cohesin loops near their kinetochores. One chromatid	

arm is a cross-over product from the other homolog. After the inspector approves the fiber attachments, the

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scissors appear and cut the blue cohesin loops, allowing the chromatids to separate.	
Time: 9:22-12:37 One more time, with the details This segment knits together all the steps shown in previous segments, giving a full view of meiosis.	 Goal: To show meiosis as a continuous process, and to help students remember and integrate what they have learned. Questions students could be asked: In Meiosis II (time: 12:19-12:27), why does the Inspector initially give one pair of chromosomes a red 'X' rather than a green checkmark? (<i>Answer: because that pair is not yet properly connected to spindle fibers.</i> Only one of its two kinetochores has a fiber connected to it. Would meiosis work if the replicated DNAs were not initially tied together by cohesin loops? Why or why not? (<i>Answer: No, because the pairs of replicated DNAs could not be stably attached to oppositely oriented fibers and separated into the two daughter cells.</i>) Would meiosis work if the cell had only one set of chromosomes (<i>e.g.,</i> one orange, one red, one blue)? (<i>Answer: No, unlike mitosis, meiosis can't happen to haploid cells.</i>) What components of the meiosis machinery are also used in mitosis? What ones are not? Are some components of the mitosis machinery not used in meiosis? Consider two identical diploid cells that have exactly the same crossovers in Meiosis I. Will they produce genetically identical gametes? (<i>Answer: Probably not, because their chromosomes can line up in different orientations in both Meiosis I and Meiosis II.</i>) We have developed a number of multiple-choice problems that test students' ability to predict the genotypes of gametes produced by meiosis. These are available on the Useful Genetics site (www.usefulgenetics.com/mitosis-and-meiosis-resources.)