# Guide for Instructors for The Facts of Life: Mitosis animation

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Introduction: This Guide accompanies the teaching animation video *The Facts of Life: Mitosis (make this a link)*. A second animation, *The Facts of Life: Meiosis* is also available with a similar Guide for Instructors. Both the animations and the guides are available at www.usefulgenetics.com/mitosis-and-meiosis-resources, along with a short slide deck introducing the pair-pull-part strategy used by both mitosis and meiosis. These materials are also accompanied by an open-access article describing our concerns about how mitosis and meiosis are currently taught and our ideas for improvements (*Addressing biology's memorization problem: Resources for mitosis and meiosis*, P. Kalas and R. J. Redfield, Submitted May 2022. A pdf is available at http://www.usefulgenetics.com/mitosis-resources.)

Understanding mitosis is an essential component of a biology education, since this is the fundamental mechanism by which eukaryotic organisms grow and reproduce. Although animations are very helpful tools for understanding processes, most mitosis animations focus on the stages and terminology traditionally emphasized in static instructional materials, and many contain significant 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 molecular events that underly chromosome interactions and movements.

This animation is different. It is designed to encourage students to think about mitosis as a series of processes that evolved to solve cell-division problems. Students are first shown a simplified version of mitosis, followed by a series of segments introduced by 'Why...?' and 'How...?' questions about the underlying mechanisms. To prevent students from defaulting to memorization, the animation does not directly tell them the answers; instead they must infer the answers from what they observe in the explanatory simulation that follows each question.

This animation may appear simple or even naïve, since the technique is stop-motion and candies are used to represent chromosomes and other cellular components,. However, because it incorporates the molecular processes underlying the chromosome behaviours it actually takes students far beyond the content of other mitosis animations. Because we have found genetics jargon to be an obstacle to learning rather than an aid, the animation does not introduce any terminology; there is no voice-over, and nothing is labeled. We recommend that instructors introduce only those terms they consider essential and use plain English descriptions for everything else.

**Ways to use this animation:** Although anyone 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. It also can be used as background preparation for a class on meiosis, especially one that will use our Meiosis animation.

• Emphasize the strategy, shared with meiosis: Mitosis has evolved a very elegant 'pair-pull-part strategy to ensure that each daughter cell gets a complete set of chromosomes. Before mitosis, as each chromosome is replicated, the sister chromatids are tied together with loops of protein ('cohesin) along their lengths. They remain tied through the first stages of mitosis, when fibers attach to the chromatids and pull on them. Once persistent tension on the fibers signals that all the chromatid pairs have bidirectional attachment, the loops are cut all at once

and the pairs separate. 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. (Meiosis adapts this strategy for distribution of homologous chromosomes, typically tying these together by crossovers.) 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.

- Before class: Assign the animation as preparation for a class on mitosis (or meiosis), together with a set of questions that students should try to answer (these need not be the questions posed in the animation), then debrief them while they rewatch the specific segments in class. Alternatively, students could be given the task of writing down all the questions they have about the animation, as well as one thing they have learned from it, and these could be addressed in class.
- **During class:** Show the animation, one segment at a time, 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, before debriefing them.
- After class: If students need to learn specific terminology, they could be given a list or glossary of technical terms and ask them to associate these with specific items and events in the animation.

## **Technical issues:**

- Some events in the animation happen quite quickly; the animation can be slowed down using YouTube's 'settings' controls.
- 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 its learning goals, optional terminology, and lists of questions that instructors and students might raise (with suggested answers).

Segment, Time and Content	Goals, Terminology and Questions for students
<b>Time:</b> 0:13–0:38	Goals: This segment is intended to help students recall some basics they may have already
First a simplified view of mitosis	learned about mitosis and to trigger their questions.
This segment shows a cell containing six condensed chromosomes, each consisting	<b>Optional terminology:</b> chromosome, chromatid, diploid, allele, prophase, metaphase anaphase, telophase, homologous, maternal, paternal.
of two replicated DNAs. The condensed	Questions students could be asked:
chromosomes move to the center of the	1. Why is each chromosome represented by two Twizzlers? What does each single Twizzler
cell and then synchronously separate into	represent? (Answer: Each Twizzler represents a single double-stranded DNA molecule and its

Segment, Time and Content	Goals, Terminology and Questions for students
two chromosomes that move into the daughter cells. For simplicity other components are omitted (nucleus, spindle fibers, centrosomes, kinetochores).	<ul> <li>accompanying chromatin proteins. Each chromosome consists of two Twizzlers because its DNA has been replicated.</li> <li>What do the different chromosome colours (red, blue and orange) represent? (Answer: Chromosomes with different sets of genes.)</li> <li>Why are the red, blue and orange chromosomes different lengths? (Answer: The chromosomes they represent have different numbers of base pairs and genes.)</li> <li>Why are there two chromosomes of each colour (two blue, two red and two orange)? What's the difference between the two? (Answer: These are the two 'homologous' chromosomes, one inherited from Mom and one from Dad. Their DNA sequences are very similar but not identical; they have different versions of some genes.)</li> <li>Why do some chromosomes have yellow stripes and some green stripes? (Answer: the stripe colours indicate different gene versions (different variants or alleles) on homologous chromosomes inherited from Mom and Dad respectively.)</li> <li>Questions students might ask:</li> <li>Why are the chromosome versions from Mom and Dad described as 'homologous'? (Answer: As you probably already learned in evolutionary biology, features that are similar in 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.)</li> </ul>
<b>Time:</b> 0:39–0:54	<b>Goals:</b> This segment exists to let the student know that the simple view of mitosis they've just seen is incomplete, and that the animation is going to raise and address a series of 'How' and
Easy, right? But do you know	'Why' questions.
<ul> <li>Why cells need mitosis?</li> <li>How they prepare for it?</li> </ul>	Questions students could be asked:
<ul> <li>How the pairs of replicated DNAs get to the center of the cell?</li> <li>What holds the pairs together and how they come apart?</li> </ul>	If students have already studied mitosis in an earlier course, Instructors could have them try to answer the questions on the left before they watch the rest of the animation.
To find out, watch what happens in each segment.	

## Goals, Terminology and Questions for students

#### Time: 0:55-1:38

### Why do cells need mitosis?

This segment first shows an imaginary cell dividing without mitosis, and then a cell dividing with mitosis exactly as in the initial segment. In the division without mitosis the newly-replicated DNAs are not paired and thus do not become evenly distributed in the daughter cells, which form 'sad' faces to indicate that they are defective. After both cells have divided the animation shows each pair of daughter cells with their chromosomes aligned to make the discrepancies clear. **Goals:** Students should realize that the daughter cells will be defective unless the chromosomes have been correctly distributed, and that mitosis includes specific steps to ensure that both daughter cells have complete sets of chromosomes. Students should be able to explain why the cell keeps the replicated DNAs together until the actual division begins.

#### Optional terminology: diploid, aneuploid

This would be a good place to teach the pair-then-separate strategy, and show the slides (also available at www.usefulgenetics.com).

## Questions students could be asked:

After the first (without mitosis) division the instructor could ask students:

- 1. What is wrong with the daughter cells from this division without mitosis? (Answer: the two daughter cells are not genetically identical each other or to the parent cell; each has too many copies of some chromosome and too few or none of others. They both lack some genes needed for a functional cell.
  - One cell has all the blue chromosomes; the other has none.
  - One cell has three orange chromosomes; the other has one.
  - One cell has both red chromosomes with green gene versions, the other has both red chromosomes with yellow gene versions.
- 2. Would the identical errors always occur in every division without mitosis? (If ten cells identical to the cell in the animation divided without mitosis, would all of them produce the same chromosome combinations? (*Answer: No, because the chromosome positions in a dividing cell are random, daughter cells from independent divisions will have different combinations of chromosomes.*)
- 3. How should the chromosomes have been distributed, so that both daughter cells are identical to the parent cell? (*Answer: Each cell needs to have two of each colour of chromosome, one with green stripes and one with yellow stripes.*)

After the second cell divides (with mitosis) the instructor could ask students:

**1.** What causes the different outcomes of the two cell divisions you've just seen? (*Answer: In the first version the sister chromatids are separate and drift randomly in the cell. In the second version the sister chromatids appear together. They stay together as they move to* 

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	<ul> <li>the center of the cell, and then the chromatids in each pair separate as the cell begins to divide.)</li> <li>2. Another way to ask the same question: If the cell divisions were not labelled, how would you know that one division used mitosis and the other didn't?</li> </ul>
	Questions students might ask:
	1. Could a division that didn't use mitosis still produce cells with the correct chromosomes?? (Answer: Yes, this could happen by chance. How often this would happen depends on how many different chromosomes the species has (the more chromosomes that need to be partitioned by chance, the rarer correct partitioning will be.)
<b>Time:</b> 1:39–2:44	<b>Goals:</b> Students should learn that cells prepare for mitosis by (1) replicating their chromosomal DNAs and (2) tying the replicated DNAs together with loops of a string-like protein.
How do cells prepare for mitosis?	
The scene starts with an interphase cell; chromosomes in the nucleus are unreplicated and uncondensed (shown as licorice laces, not Twizzlers). The camera zooms in on a replication fork with a green DNA polymerase. The daughter DNAs (the sister chromatids) become tied together with loops of string as they emerge from the DNA polymerase. Note that, in the first view, the DNA	<ul> <li>Optional terminology: DNA polymerase, replication fork, sister chromatid, cohesin</li> <li>Questions students could be asked: <ol> <li>What is happening here? (Answer: DNA is being replicated. This is 'S phase'.)</li> <li>Where in the scene is the parent DNA? (Answer: On the upper right.)</li> <li>Where in the scene are the replicated DNAs? (Answer: At the lower left.)</li> <li>What happens to the replicated DNAs after they leave the polymerase? (Answer: They get tied together with loops of string.)</li> <li>What do you think the loops of string represent? (Answer: protein loops that hold the replicated DNAs together.)</li> <li>What would happen at cell division if the replicated DNAs were not tied together?</li> </ol> </li> </ul>
polymerase (green circle) is stationary, and the DNA moves from right to left. In the extreme close-up view, the DNA is stationary and the polymerase moves from left to right. The difference is just a matter of perspective, but some students may benefit from an explanation. At the end, the camera zooms back out to a view of the nucleus with sister	<ul> <li>(Answer: It would be like the division without mitosis: chromosomes would move at random and daughter cells would often have incorrect sets of chromosomes.)</li> <li>7. At the end of the segment, why are both Twizzlers in each pair the same colour, with the same coloured stripes? (Answer: because they represent identical DNA copies produced by DNA replication.)</li> <li>Questions students might ask:         <ol> <li>Is this the only replication fork in the cell (the only place where DNA is being replicated, and the only DNA polymerase)? (Answer: No, replication of each chromosome simultaneously occurs at many different sites along its DNA.)</li> </ol></li></ul>

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chromatids tied together with string. The DNA condenses into chromosomes, which we see as pairs of Twizzlers held together with white rubber-band loops.	2. Do the loops that tie the DNAs together form at specific locations? (Answer: To a first approximation their locations are random, but they are influenced by features of chromatin organization.)
<b>Time:</b> 2:45–3:41 <i>How do the pairs of replicated DNAs get</i>	<b>Goals:</b> Many students may already know that fibers originating at the poles of the cell attach to the chromosomes at their centromeres/kinetochores and pull them towards the center.
to the center of the cell?	The more subtle points for students to learn here are:
The pairs of condensed sister chromatids initially drift around. A red knob (a 'kinetochore') appears on each sister, and orange disks ('centrosomes') appear at the cell poles. Fibers grow from the centrosomes in towards the chromosomes. First the camera focuses on the pair of red sisters with green stripes. The end of a fiber connects to one knob, pulls briefly and lets go. Then the end of another fiber connects to the other knob,	<ol> <li>That stable attachment of a fiber to a kinetochore depends on the fiber experiencing tension. If nothing is pulling the chromosome in the opposite direction, the fiber detaches because it is not under tension. This dependence ensures that the two sister chromatids in each pair become stably attached to fibers from opposite poles.</li> <li>That this tension is made possible by the cohesin loops that hold the pairs of chromatids together.</li> <li>That movement of chromosomes towards the cell center is caused by a tug-of-war between the oppositely directed fibers pulling on each chromatid.</li> <li>Optional terminology: prophase, metaphase, spindle, spindle fiber, centriole, centrosome, centromere, kinetochore.</li> </ol>
pulls briefly and lets go. Finally, each fiber connects to a knob, and both pull in opposite directions. Then the knobs and connection points turn orange and the connections persist.	<ul> <li>Questions students could be asked:</li> <li>1. What are the red knobs on the replicated DNAs for? (<i>Answer: they're the attachment points for the fibers.</i>)</li> <li>2. What are the fibers for? (Answer: They pull on the knobs and thus on the sister chromatids.)</li> <li>3. Why do you think the fibers sometimes attach and then let go? (<i>Answer: They let go if</i></li> </ul>
The same things are happening to the other pairs in the background. The focus shifts to the blue sister	<ul> <li>nothing is pulling back in the opposite direction.)</li> <li>4. The connections between the pairs of replicated DNAs and the fibers eventually turn orange.</li> <li>When does this happen and what do you think it signifies? (Answer: The change to orange only happens when two fibers have both attached to the pair of replicated DNAs and are</li> </ul>
chromatid pair with yellow stripes. It similarly makes several unstable single	pulling in opposite directions. The colour change signifies that the attachment has stabilized because it is under tension.)
connections before two fibers become attached to the knobs on both sides.	<ol> <li>Why don't the sister chromatid pairs come apart when the fibers pull on them? (Answer: Because they're held together by the white loops.)</li> </ol>

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	6. Why do the pairs of replicated DNAs end up near the middle of the cell? (Answer: because they're being pulled in both directions, like in a tug-of-war.)
	<ul> <li>Questions students might ask:</li> <li>1. How does tension on the fibers stabilize their attachments to the kinetochores? (Answer: The force generated by the tension physically changes the conformation of the kinetochore proteins responsible for binding to the fibers.)</li> </ul>
Time: 3:42–4:15 How do the replicated DNAs come apart? First we see the sister chromatid pairs being pulled back and forth by the fibers. Then many tiny scissors appear at the upper right, move onto the chromosomes and cut the white loops, allowing the chromatids to be pulled apart by their oppositely oriented fibers.	<ul> <li>Goals: Students should understand that the pairs of replicated DNAs can't come apart until the protein loops are cut open. As soon as this happens, the ongoing pulling by the fibers causes the replicated DNAs to separately move towards the two poles. (This time-lapse video from 1956 clearly shows the separation event in a real cell: http://www.cellimagelibrary.org/images/11952.)</li> <li>Optional terminology: separase (the enzyme that cuts the cohesin loops).</li> <li>Questions students could be asked: <ol> <li>What do you think the white loops represent? (Answer: protein loops that hold the replicated DNAs together.)</li> <li>What do you think the scissors represent? (Answer: an enzyme that cuts the protein loops.)</li> <li>What would happen at cell division if the loops of protein weren't cut? (Answer: the cell couldn't divide because the pairs of replicated DNAs couldn't separate. Or, the daughter cells would have incorrect sets of chromosomes, with duplicates of some and none of others.)</li> </ol> </li> </ul>
Time: 4:16–5:04 <i>How do the scissors know when to act?</i> This segment begins like the previous one, but at the upper right we see the tiny scissors being held back by a yellow rope; nearby is a supervisor with a large pair of scissors. The focus shifts to the other side of the cell, where we see an inspector with a clipboard. The inspector then inspects the fiber connections of each	<b>Goals:</b> Students should learn that before the cell begins to divide it carefully checks the chromosomes for correct attachment of fibers coming from both poles of the cell. The scissors are not activated until all the attachments are correct. This is called the 'mitosis checkpoint'. <b>Optional terminology:</b> mitosis checkpoint.
	<ul> <li>Questions students could be asked:</li> <li>1. What is the inspector checking for? (<i>Answer: He's checking that each replicated DNA is stably connected to a fiber, and that the two sister DNAs in each chromosome are being pulled in opposite directions.</i>)</li> <li>2. Why does he wait beside the blue chromosome pair with yellow bands? (<i>Answer: Because at first its replicated DNAs are not stably connected to fibers.</i>)</li> </ul>

Segment, Time and Content	Goals, Terminology and Questions for students
chromatid pair in turn, giving each a green check mark. The blue chromatid pair with yellow stripes is slow to attach to fibers, and the inspector waits until the connections stabilize and turn orange. He then signals to the supervisor, who cuts the rope and releases the scissors. The scissors then move onto the chromosomes and cut the white loops, allowing the chromatids to be pulled apart by their oppositely oriented fibers.	<ol> <li>What would happen if the scissors acted before this pair of replicated DNAs was stably attached to fibers? (Answer: The pairs of replicated DNAs would come apart before the cell was ready to divide. The fibers would let go because they were no longer under tension. The replicated DNAs would drift around and might end up in the wrong daughter cells.)</li> <li>Questions students might ask:         <ol> <li>How long will the attachment inspector wait? (I don't know.)</li> <li>What happens if the inspector doesn't</li> <li>Does the inspector sometimes make mistakes? (Yes, especially if only a single chromosome is not correctly attached to fibers, the inspector will sometimes allow mitosis to proceed.)</li> </ol> </li> </ol>
Time: 5:05–6:43 sec Once again, with the details This segment knits together all the new information into one complete mitosis, starting with unreplicated DNA and ending with two daughter cells, each with the same diploid chromosomes as the parent cell had.	<ul> <li>Goals: Students should now view mitosis as a process, not as a series of stages. Ideally, they will realize that, by tying the replicated DNAs together and requiring tension for stable fiber attachment, the cell is able to accurately separate each pair of replicated DNAs and ensure that the daughter cells each have the same) chromosomes as the parental cell.</li> <li>Questions students could be asked: <ol> <li>Would mitosis work if the replicated DNAs were not initially tied together? Why or why not? (Answer: No, because the pairs of replicated DNAs could not be stably attached to oppositely oriented fibers and separated into the two daughter cells.)</li> <li>Would mitosis work if the cell had only one set of chromosomes (e.g., one orange, one red, one blue)? (Answer: Yes, mitosis doesn't care how similar or different the chromosomes are to each other.)</li> </ol> </li> </ul>
<b>Time:</b> 6:44–6:50 At the very end of mitosis the chromosomes in the daughter cells again arrange themselves into 'happy faces'.	<ul> <li>Goal: This image is to remind students that the overall goal of mitosis is to give daughter cells complete sets of the parental cell's chromosomes.</li> <li>Questions students could be asked:         <ol> <li>Why are these cells happy? (Answer: Because they have complete sets of chromosomes.)</li> </ol> </li> <li>Questions students might ask:</li> </ul>

Segment, Time and Content	Goals, Terminology and Questions for students
	<ol> <li>How are we supposed to learn the right answers, when the animation doesn't tell us them? (Answer: Each question is answered by the events in the animation segment following it. You should check your interpretation with other students and with what you're taught in class.)</li> <li>How are we supposed to learn the terminology, when the animation has no labels and no voice-over? (Answer: At this stage of your biology studies you don't need to learn most of mitosis' specialized terminology. Then the instructor should explain how this course will handle terminology.)</li> </ol>