

## Lambratu Rahman

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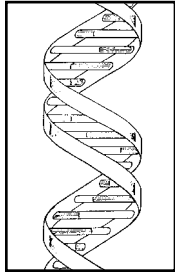
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**Lambratu Rahman**  
**Biochemist & Molecular Biologist**



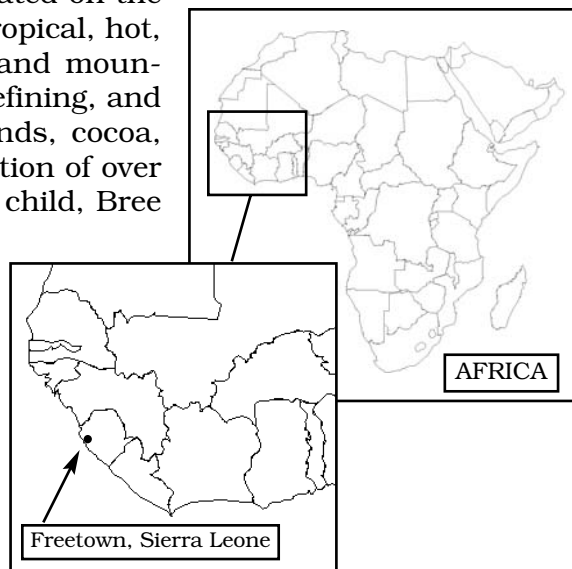
*Unit developed by*  
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## Who is Lambratu Rahman?

Lambratu (or “Bree” as she is known to her family and friends) Rahman was born and grew up in the capital city of Freetown in Sierra Leone, located on the western coastline of Africa. Sierra Leone’s climate is tropical, hot, and humid, with swampy land along the coastline and mountains to the east. Its main industries are mining, oil refining, and light manufacturing, and it exports primarily diamonds, cocoa, coffee, and palm kernel oil. The country has a population of over 4.7 million, and the official language is English. As a child, Bree enjoyed going to the beach and shopping with her family in the marketplaces in downtown Freetown. But her special love was reading, and one of her favorite things to read was comic books.



In school, Bree was on an academic track. In the education system in Sierra Leone, students are directed toward the academic track early in their school years; this means that they will attend college when they complete their schooling. Bree loved chemistry and biology when she took them during her high school years. Throughout her precollege work she continued to love reading and she also enjoyed writing.

## How did Bree decide to come to the United States from Africa?

Bree attended Fourahbay College, part of the University of Sierra Leone. She majored in biology and chemistry and took honors courses in zoology. She made many friends during college and enjoyed attending parties. After graduating from college, she came to the United States to visit. Bree’s friend, Ijatu, wanted to attend Howard University in Washington, DC. At the same time, the President of Sierra Leone was visiting the U.S., and Bree and Ijatu were invited to attend a reception in his honor. The Mayor of the District of Columbia was also there. During the reception a Howard University staff person talked to Bree and Ijatu about the University and about doing graduate studies there. Both of them decided they wanted to go to graduate school at Howard University. Bree was already sure that she wanted to work in biochemistry.



During her first year at Howard, Bree and the other new graduate students had a chance to spend a few weeks in each biochemistry faculty member’s laboratory. She became especially interested in working with Dr. Carolyn Broome. Bree felt that Dr. Broome came across as a wonderful teacher and mentor and that she “knew what she wanted and how to get it done.” Bree found that they approached biochemistry problems very similarly.

## Strong influences developed her interest in biochemistry

Bree feels that her biology and chemistry professors in college were strong influences in developing her interest in biochemistry. They pointed out the “why” and “how” of chemical and biological processes; these were the questions that Bree found fascinating. She was also influenced by the work she did during a summer externship at a research company. Bree worked at Life Technologies, Inc. (LTI) during the summer of 1994 after she completed her master’s

degree at Howard University. LTI makes molecular biology products, including restriction enzymes. Bree says that Larry Mertz, who supervised her work at LTI, encouraged her to go ahead and complete her doctoral degree because it would give her greater freedom and allow her to take on more responsibilities, so she could do the kind of work that she wants to do.

Bree has also had tremendous support from her family for her studies. Several members of her family had attended college, but she is the first in her family to attend graduate school and work toward a Ph.D. Her family is very proud of her accomplishments.

### **What kind of research does Bree conduct?**

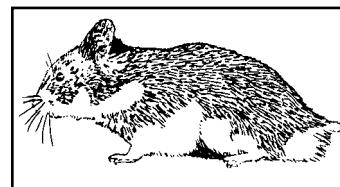
In her research, Bree looks at *mutations* (or changes) in the DNA found inside mitochondria in the cell. For a number of years, scientists have known that the genetic material DNA is found in the mitochondria as well as in the nucleus of animal cells. This DNA codes for proteins, which are important to the function of the mitochondria. Mitochondria are the “powerhouses” of the cell, producing special molecules that are used throughout the cell to release energy. This energy is used to do work within the cell.



Bree looks at a specific mutation found in the DNA in mitochondria from hamster lung cells. The cells are grown in cell culture dishes. She is trying to find out precisely where the mutation is located within the DNA. When that segment of DNA is translated into the corresponding protein, Bree wants to know how the mutation in the DNA affects the function of the protein. Earlier research has shown that the mutations cause decreases in the production of proteins within the mitochondria. Several human diseases are related to defects in mitochondrial DNA.

These include diseases affecting muscles and the central nervous system. Specifically, the mutation can lead to heart failure, stroke, kidney failure, diabetes, Alzheimer’s disease, and *myoclonic epilepsy*, a disease related to defective muscle fibers.

To learn about the mutations, Bree uses animal cells grown in culture, in this case, lung cells from a particular type of hamster. These cells serve as a model for human cells and provide complex information that computer models cannot. She also uses many advanced research techniques in her work, such as finding information in the database of human gene information on the Internet and doing Northern and Southern “blots” to learn more about the DNA fragments used in her experiments. One of these “blotting” methods is also used to perform DNA fingerprinting in criminal trials.



### **What kind of impact will her research have on people?**

Bree especially enjoys seeing the results of her experiments, being able to see new findings that prove or disprove her hypothesis. She is excited that her work is part of the overall progress of scientific understanding. Her work builds on the findings of other scientists, and tomorrow’s scientists will use her work to advance human understanding even further. Bree

feels that her research will have important impacts on human health. She says, “If we can figure out how inherited mitochondrial diseases work — pinpoint the gene, test for it, and in the future, target the defective gene for correction — we can help people who are affected by these diseases.”

### **A busy schedule to juggle**

As a graduate student, Bree admits that her studies and research require hard work. She says it’s hard to juggle a social life during graduate school because she often works on weekends. Bree knows that, in graduate school, working harder means you’ll probably graduate sooner. Graduate students often have flexible hours, but, for Bree, a typical weekday usually starts about 9:30 A.M. She plans her experiments for the day and reviews them with Dr. Broome. She does her experiments, attends scientific seminars where she hears other researchers present their work, and attends biweekly laboratory



meetings where all members in her laboratory group review their research findings. At this point, Bree has finished taking all of her classroom courses, so she can concentrate on her research full-time. Her day ends at about 6:00 P.M. unless she has an experiment that is running late.

Bree does manage to set some time aside for relaxation. She has a good friend, Mbalu, whom she says, “...makes me take a break now and then.” She likes basketball and enjoys all kinds of music, from rap to jazz to classical. She also enjoys traveling, whether to see family in New Jersey or to visit friends in London, as she did earlier this year. As part of her graduate work, she presented her research at meetings in California, the District of Columbia, and New Orleans this year. She is also at the point in her graduate work where she is thinking about where she would like to work in the future. She is looking at the types of research careers available in industry, government, and universities. She knows that each type of position has different things to offer!

### **Bree’s advice on becoming a scientist**

Bree offers some advice for students, “Don’t just accept everything. Find out how things happen and why. How is your food digested? Who figures out what happens when people are sick? How does a medication work? Don’t shut down your imagination and curiosity and don’t accept the everyday as routine. Always question ‘Why?’” She also encourages students not to buy into stereotypes about scientists: “Scientists are not nerds. Science is hard work — there’s no denying that. But you can be a scientist and still be anything else you want to be in your personal life.”

## SUGGESTIONS FOR TEACHERS

### ACTIVITY #1: DNA Fingerprinting Simulation

**Purpose**

To develop an understanding of the DNA fingerprinting process via a simulation activity.

**Objectives**

- 1) To improve understanding of DNA sequencing restriction enzymes, electrophoresis, and fingerprinting.
- 2) To improve measuring and graphing skills.

**Materials**

*Per student*

- 1.5 m strip of adding machine tape (or other narrow paper strip)
- metric ruler
- scissors
- graph paper

*Per group of four students*

- 1.5-2.0 m sheet of bulletin board paper (any color except black)
- masking or cellophane tape
- graph paper

**Before You Begin**

- 1) Cut strips of adding machine tape and sheets of bulletin board paper.
- 2) Prepare sheets of bulletin board paper as “gels” as shown below:

Lane 1	Lane 2	Lane 3	Lane 4	Line Marker
				6
				5
				4
				3
				2
				1
				Starting Wells

- 3) Assign the initial development of the DNA strips (*steps 1, 2, and 3* on the student handout) as homework.
- 4) In your introduction to the lab, you may want to explain the major points of DNA fingerprinting and gel electrophoresis; some general information is summarized in the Resource Sheet, “An Overview of DNA Fingerprinting,” on page 276.
- 5) Groups of four students work on a single gel. Each student should have his or her own lane. Students work together to “run” the gel.
- 6) Each student should prepare a graph, or “photograph,” of their group’s gel. Do this as a group activity if you prefer.
- 7) If desired, individual students or groups can write answers to the “Questions to Consider” in the student activity pages.

**Safety Considerations**

None.

**Questions to Ask**

- See the “Questions to Consider” in the student activity pages.
- What errors could occur that would affect the final DNA fingerprint? (Examples: DNA not replicated well in all samples; DNA broken into pieces physically or chemically during processing; gel is uneven in thickness; electrical current is not applied evenly to whole gel; and/or standards are contaminated).

**Where to Go From Here**

- Do *Activity #2*, “Finding the Mutation.”
- Conduct a crime investigation using the DNA fingerprints your class has already developed as described in Nunley (1996). (See “References and Resources.”)
- Do a laboratory or demonstration of a real DNA extraction and/or electrophoresis.
- Interview a researcher who uses DNA fingerprinting in his/her research and/or invite a lawyer (possibly from the county prosecutor’s office) to discuss the use of DNA fingerprinting in court trials.

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**Ideas for Assessment**

- Ask students to turn in their graphs and answers to “Questions to Consider” as an individual or group project. This can also be expanded to a full laboratory report, if desired.
- *Activity #2*, “Finding the Mutation,” can be used as an assessment tool if students are already familiar with experimental design.

**References and Resources**✓ *On related activities:*

The Genentech Access Excellence website at <http://www.gene.com/ae> has a wealth of teacher-developed activities, including many on DNA fingerprinting.

Nunley, K. F. (March 1996). Making DNA fingerprints. *The Science Teacher*, p. 32-35.

Rasmussen, A. M., & Matheson, R. H., III. (1990). *A Sourcebook of Biotechnology Activities*. National Association of Biology Teachers, 11250 Roger Bacon Drive, #19, Reston, VA 22090.

✓ *Other resources:*

The Howard Hughes Medical Institute, 4000 Jones Bridge Road, Chevy Chase, MD 20815-6789, (301) 215-8855, offers several free booklets on human development, genetics, and blood, including *Blazing a Genetic Trail*, *From Egg to Adult*, and *Blood: Bearer of Life and Death*.

✓ *Photo credit:*

Photos on page 269, 272, and 273 courtesy of Marsha Matyas, The American Physiological Society, Bethesda, MD.

## Resource Sheet

### *An Overview of DNA Fingerprinting*

#### What Is DNA Fingerprinting?

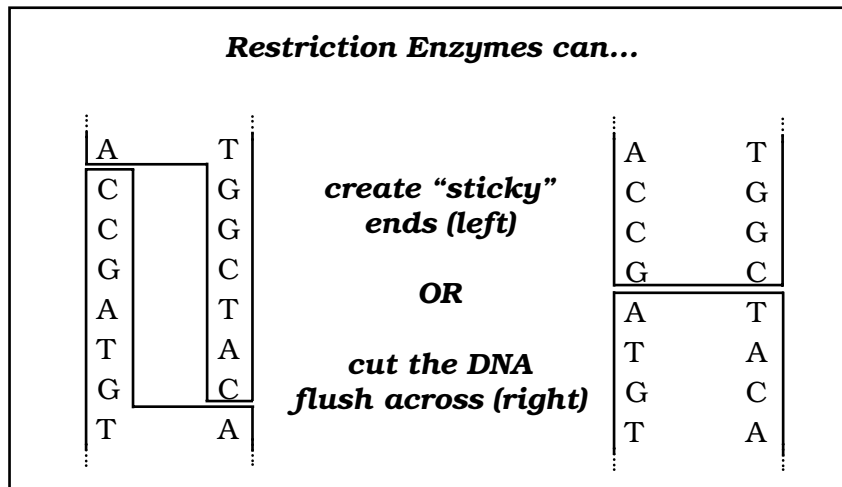
DNA fingerprinting is a procedure often used in research laboratories. It is useful in exploring a variety of biological structures and processes, including genetic mutations, the evolution of various species, and sequencing genes. Researchers often refer to the technique as Southern blots or Northern blots, depending upon the specific procedure used.

#### Preparing the DNA

In general, DNA is isolated from an animal or plant tissue by breaking open the cells and nuclei to release the DNA. The DNA is then mixed with specific chemicals, allowing lone strands of the DNA to be twirled around a glass rod and removed from the solution. If only a small amount of tissue is available, the DNA may need to be replicated, using enzymes called *reverse transcriptases*.

#### Cutting the DNA into Fragments

Special enzymes called *restriction endonucleases* are used to cut the DNA into fragments. Each enzyme cuts the DNA in places where there are specific patterns in the DNA sequence, that is, a specific sequence of nucleotide bases. There are two general types of these enzymes. One type cuts the DNA so that it has “sticky” ends (see below). This is very useful for inserting a gene into a chromosome. The other type makes a straight cut across the DNA. One or more enzymes may be used in preparing the DNA.



#### Separating the Fragments

DNA fragments are put into small wells at the end of a special slab of gel. This gel feels and looks like soft gelatin and is often held between two layers of glass or plastic. Electrodes are connected to the two ends of the gel, and a low electrical current is run down the lanes. What happens to the DNA fragments? The fragments are moved toward

*(continued)*

*(continued)*

the positive electrode by the electrical currents because the DNA, being an acid, has an overall negative charge.

However, the fragments aren't moving through air, but through a meshwork of gel pieces. Imagine you are trying to swim from one end of a pool to the other in one minute. In your way are many layers of fish netting. Some of the holes in the netting are large enough for you to swim through, but many are not. In the lane on your left is a walrus twice your size in width and in the lane on your right is an otter, which is much smaller than you. If you are all capable of swimming at the same speed, who will get the furthest down the pool in one minute?

The otter will easily find holes to swim through while you search for holes large enough to fit through. The walrus has an even more difficult time. The otter will go furthest, followed by you. The walrus may have great difficulty making any headway at all.

The same thing happens in the gel. Pieces of DNA must move through the meshwork formed by the gel. The larger the piece of DNA, the more slowly it will move through the gel. When the gel is stained, the result is a series of visible bands across the lane, representing DNA fragments of various sizes. The width of the band indicates the number of fragments found there.

Researchers can determine the size of the fragments in each band by using one lane to run a set of DNA fragments of known sizes, called "standards." They create a type of ruler along the edge of each DNA fingerprint.

### **How Are DNA Fingerprints Used?**

- In a court case, the DNA of the suspect might be compared with the DNA extracted from skin cells found under the fingernails of an assault victim who scratched his attacker. If the patterns do not match, it is highly unlikely that the suspect is the attacker.
- A researcher is examining the evolution of several species of birds. She uses DNA fingerprints to explore how similar each species is to the other. The results help her develop an evolutionary tree for the bird species.
- A team of biochemists believe they have identified the specific enzyme that is missing in persons who have a disease that causes the breakdown of muscle tissue. They look for information provided by the Human Genome Project that is working to determine the nucleotide sequence for the entire human genome, that is, the sequence of genes making up each human chromosome. With this information, they think they know the site where the genetic code for the enzyme is located. By comparing DNA fragments from that part of the genome from persons with and without the disease, researchers can take one more step toward confirming the cause of the disease and, possibly, a cure.

## ACTIVITY #1: DNA Fingerprinting Simulation



Recently, there has been extensive media coverage of DNA “fingerprinting.” Although we are most likely to hear about DNA fingerprinting when it is used as evidence in court, it is used far more widely as a powerful research tool by scientists. This simulation activity will help you discover how DNA fingerprinting is done.

### Materials

- 1.5 meter strip of adding machine paper
- pencil or pen
- metric ruler
- scissors

### Procedure

1. Along the left side of your strip of paper, make a small mark every 2.4 cm (see Figure 1).
2. Write a random series of nitrogen bases (A, T, C, G) along the left side of the strip as shown in Figure 1. Write 4 bases every 2.4 cm, as shown. Be sure to keep mixing up the order of bases. (Draw slips of paper from a bag if desired). You should have a total of about 250 bases when you are done.
3. Along the right side of the paper, write the complementary strand of DNA bases as shown in Figure 2. Remember that A bonds with T, and C bonds with G.
4. Next, use a restriction enzyme to cut your DNA into pieces. Restriction enzymes cut the DNA at a point where they find a specific series of nucleotide bases.

### NOTE:

*Nitrogen bases are the building blocks that make up DNA*

*A=Adenosine  
T=Thymine  
C=Cytosine  
G=Guanine*

The enzyme you will use makes a flush cut after the sequence “AT” starting at the 3’ end (Figure 3). With scissors, cut across the paper strip wherever you see this AT sequence along the left side of your paper. Make the cut after the AT sequence.

*(continued)*

(continued)

You should have several pieces of “DNA” and are now ready to place them on an “electrophoresis gel” and create a fingerprint of your DNA. Your instructor has set up large sheets of paper to represent a sheet of electrophoresis gel. In the research laboratory, this gel is like a slab of soft gelatin between two sheets of glass or plastic. Each gel has several lanes, like lanes on a track or in a pool. Each lane has a starting well.

5. Place your DNA pieces in the starting well of ONE lane; you’ll be sharing your gel with three other students.
6. Move each strip of DNA along the gel using the following guidelines:

Length of Piece of Paper	Number of Base Pairs	Move to Line Marker
0 to 2.0 cm	1-3	6
2.1 to 4.0 cm	4-6	5
4.1 to 6.0 cm	7-10	4
6.1 to 10.0 cm	11-16	3
10.1 to 14.0 cm	17-23	2
14.1 to 20.0 cm	24-33	1
Larger than 20.0 cm	More than 33	Leave in starting well

Don’t pile segments on top of each other. Instead, lay them side-by-side above the line so you can tell how many segments moved to a particular spot.

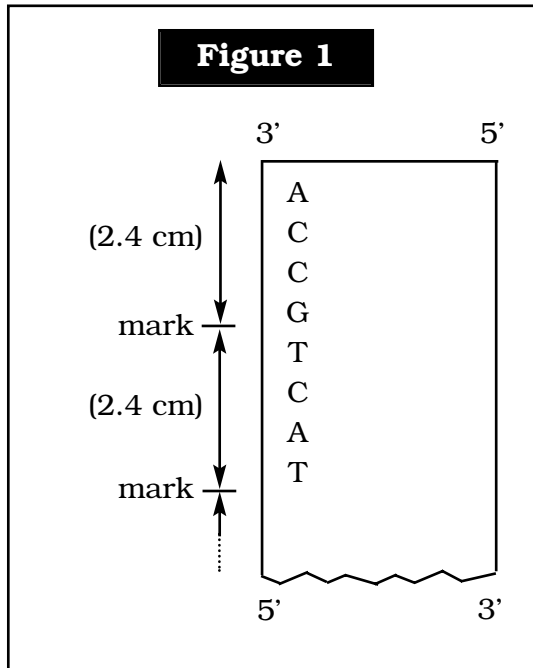
7. In the laboratory, scientists stain and photograph their gels. When all of the students working on your gel are finished, you will make a graph to record your gel. Use the graph paper provided. Color one row for each strip found at each line marker. For example, if you moved three strips of DNA to line marker 2, you would color in three rows of your lane at line marker two on your graph paper. Be sure to do the graphs for the other lanes that were on your gel, showing the findings for other students in your group.



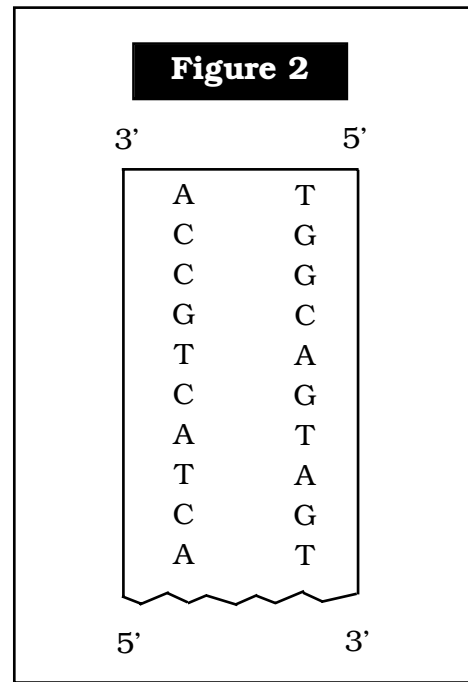


**Figures 1-3**

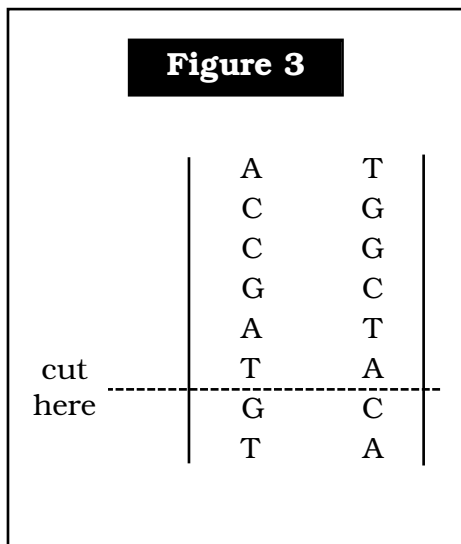
**Figure 1**



**Figure 2**



**Figure 3**

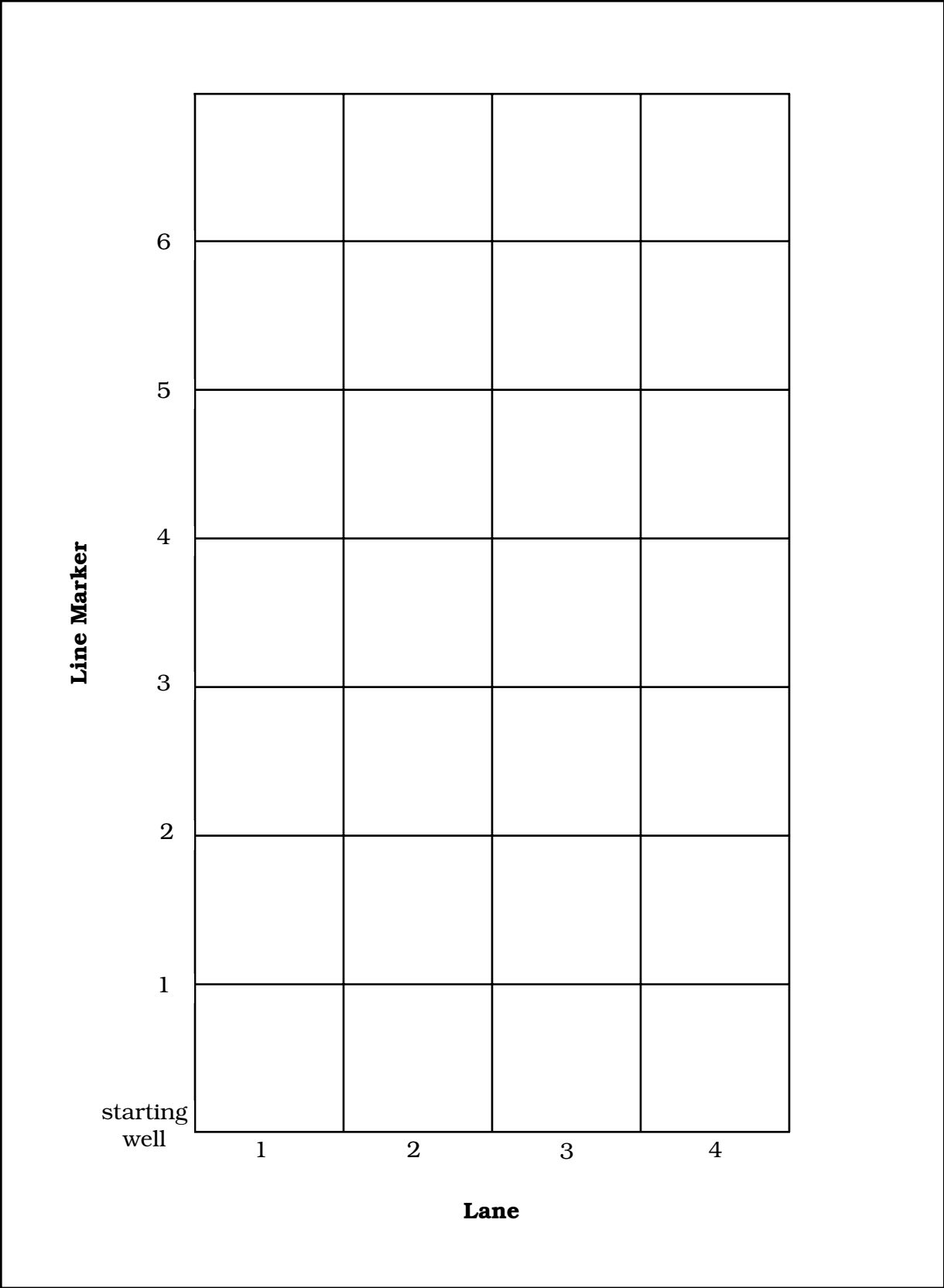


### Questions to Consider

1. Why do smaller pieces move further than larger pieces?
2. In this simulation, you are the force moving pieces along the gel. In a real electrophoresis, what is the force used to move the DNA through the gel?
3. Look at your completed graph. Do the patterns in each lane look the same? Does each band have the same width? Are there bands at each line marker? Note three differences between your bands and the other bands on your gel.
4. If you repeated this experiment again with the same sequence of DNA, would you get the same pattern of bands? Why or why not?
5. Similarly, if we collect a sample of DNA from a person's cells now and a year from now, would we get the same pattern each time? Why or why not?
6. Would a DNA fingerprint from a sample of your white blood cells match a fingerprint from a sample of your muscle tissue?
7. Would a DNA fingerprint from two different humans be completely different? Would they be identical? How about fingerprints from two different species such as a frog and a human?



**Graph**



## SUGGESTIONS FOR TEACHERS

### ACTIVITY #2: Finding the Mutation

#### Purpose

To strengthen students' skills in developing hypotheses, designing experiments, and analyzing results, especially using DNA fingerprinting as a research tool.

#### Objectives

- 1) To design and conduct an experiment using a DNA fingerprinting simulation technique.
- 2) To improve graphing and measuring skills.
- 3) To improve data analysis skills.
- 4) To improve experimental design skills.

#### Materials

*Per group of one to four students*

- 1-3 strips (1.5 m each) of adding machine paper (or other narrow paper)
- metric ruler
- 1.5-2.0 m sheet of bulletin board paper (any color except black)
- masking or cellophane tape
- scissors
- graph paper

#### Before You Begin

- 1) Cut strips of adding machine tape and sheets of bulletin board paper.
- 2) Decide how to divide students into groups for the activity.

#### Safety Considerations

None.

#### Questions to Ask

- What was your reason for selecting the restriction enzymes you used?
- What do the bands on your gels suggest about the samples?
- Did some enzymes give you better results than others? If you were using real DNA, could you tell this ahead of time?
- See also "Questions to Ask" in the student activity pages for *Activity #1*.

#### Where to Go From Here

- Do a laboratory or demonstration of a real

DNA extraction and/or electrophoresis.

- Interview a researcher who uses DNA fingerprinting in his/her research and/or invite a lawyer (possibly from the county prosecutor's office) to discuss the use of DNA fingerprinting in court trials.
- Teams of students can explore and develop a poster or presentation on different genetic diseases. Each team should answer the following questions: What are the symptoms of this disease? Who is most at risk for developing the disease? Has the gene which causes the disease been identified? How is the disease treated? How is research contributing to our understanding of the disease or its cure?

#### Ideas for Assessment

- Students' initial experimental design and their final laboratory reports can serve as assessment tools.
- Teams of students can provide verbal reports to the class on their findings.

#### References and Resources

See listing at end of *Activity #1*, "Suggestions for Teachers."

## ACTIVITY #2: Finding the Mutation

### The Problem

You are spending your summer working with Bree Rahman and her laboratory group on identifying the gene that relates to a defective enzyme in mouse cells grown in culture flasks.

You have isolated some DNA fragments from the section of the chromosome where you think the mutation(s) are. You gathered these fragments from two normal animals and from one animal with the defective enzyme. Now you must prove that you have really isolated the portion of DNA where the mutation(s) lie.

### Your Mission

Use your DNA fingerprinting simulation technique, the DNA fragments from the three samples provided on the following page, and the restriction enzymes listed below to design and carry out a simulated experiment to determine whether or not you have isolated the segment of DNA which contains one or more mutations. Remember — you can replicate the DNA strands and run multiple tests using various enzymes, if desired.

### Materials

- DNA samples
- restriction enzymes A, B, and C
- scissors
- tape
- paper strips
- pen or pencil
- metric ruler
- graph paper
- large sheets of paper to use as gels

### NOTE:

*Enzymes  
(reading from  
3' end of DNA)*

*A cuts after "AT"  
B cuts after "CAG"  
C cuts after "CG"*



### Procedure

1. Work with one to three other students, as directed by your teacher.
2. Brainstorm with your group to discuss how you want to approach the problem.
3. Design your experiment, using the form on the following page. Be sure to write out your purpose and hypotheses, what your procedures will be, and the materials you will need. Be sure your experimental design allows you to answer the “Questions to Consider” below.
4. Before you do the simulated experiment, review your experimental design with your teacher.
5. Perform your experiment.
6. Prepare a report on your experimental design and your findings. Be sure to include the following: purpose, hypothesis, materials, procedures, results, conclusions, and further research needed.

### Questions to Consider

1. Which enzyme(s) did you select to use? Explain why you made these choices and how you plan to use the enzymes.
2. What is your “control” in this experiment?
3. What conclusions can you draw from your findings? Justify each conclusion by referring to your data.
4. What other experiments would you want to do to explore this further?



**NOTE:** *Show your plan to your instructor before you execute it!*

**Experimental Design**

Describe how you plan to do your experiment:

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Purpose:

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Prepare a graph paper for your experiment.

**Conclusions**

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**DNA Sequences****DNA sample from normal animal #1**

AGGTCGTATCCACTGACGAGGTATATACCAGACTCGGAACTTACAGGACATGACAT  
ATGGCATCTTCAGAATCTTCAGAATGGCACAAGTTCAGCTCTGCGCAGATGCCATA  
TTCGTACAGACACTCGGCCTCGACCGACATACAGAACCTCGGCCTCGAGGACAATC  
AGCACGATCACGAGCGTCACGATCAGATGAGCGTCACGAGTCAGCAATCACGAGC  
GTCACGATCAGCACGATCAGATCAGAT

**DNA sample from normal animal #2**

TACGTCGTATCCGTCGCGAGATCATACCGGACTCGGAACTTACAGGATGACATCAA  
TCGGCATCTTCAGAATGTTTCAGAATCGCACAGGTTTCAGCTCTGCGCACAATGCCAT  
ATCCAGTACAGACACTCGGCCTCGACCGAAGCATTACAGAACGTCGGCCTCGAGGA  
TGAGCACATCAGGAGCGTCACGATTCAGATTGCAGCGTCACGTCAATCCACGAGCG  
TCACGATTCAGCACGATGCAGATAT

**DNA sample from animal with defective enzyme**

AGGTCGTATCCACTGACGAGGTATATACCAGACTCGGAACTTACAGGACATGACAA  
ATGGCTTCTTCAGAATCTTCAGAATGGCACAAGTTCAGCTCTGCGCAGATGCCAAA  
TTCGTACAGACACTCGGCCTCGACCGACAAACAGAACCTCGGCCTCGAGGACAATC  
AGCACGATCACGAGCGTCACGATCAGATGAGCGTCACGAGTCAGCAATCACGAGC  
GTCACGATCAGCACGATCAGATCAGAT



