Genomics Analogy Model for Educators (GAME): Fuzzy DNA Model to Enable the Learning of Gene Sequencing by Visually-Impaired and Blind Students

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Abstract

Much of the general population is aware of terms such as biotechnology, genetic engineering, and genomics. However, there is a lack of understanding concerning these fields among many secondary school students. Few teaching models exist to explain concepts behind genomics and even less are available for teaching the visually impaired and blind. The purpose of the Genomics Analogy Model for Educators (GAME) tutorial is to enable an understanding of the fundamental aspects of genomics. The GAME tutorials use simple analogies to convey scientific information. Recent articles have introduced the GAME approach and two of its components: (1) An explanation of sequencing technology using Lego® blocks (the Lego® analogy model [LAM]), and (2) use of a small town analogy model to explain cellular biology. In this article, we present the concept that the Lego® analogy model can be adapted to enable learning of the concepts of sequencing for visually-impaired and blind students. Textured Lego® blocks, combined with classroom physical activities, are proposed as a teaching module to explain gene sequencing. We term this teaching approach the *Fu*zzy *D*NA *Mo*del (FUDMO).

Genomics is becoming one of the most important scientific advances of the 21st Century. Genomics technologies have already transformed biological, biochemical, and medical research. The sequencing of the human genome has laid the foundation for the development of new drugs and new diagnostic techniques, and will undoubtedly play a major role in the future of preventive medicine. In order for medical professionals, including doctors, nurses, and dieticians, to effectively deliver the benefits of these new technologies, a more thorough public knowledge of gene sequencing is needed (Collins, 2004; Gilbride & White, 2000; Jenkins & Collins, 2003; McInernery, 2002).

Although the development of these new technologies may primarily occur in the realm of the scientific and biotechnology communities, the social and legal ramifications of these genomics approaches will impact every individual in our society. For example, DNA technology has been used extensively in legal cases (Cohen, 1995; Garrison, 2004). In the foreseeable future, genomics-related technologies have the potential to play an influential role in health-related insurance coverage (Carnovale & Clanton, 2002; Collins & McKusick, 2001). Thus, there is an urgent need to better educate the general public on the topic of genomics in order to facilitate proper debate on how these technologies will shape our society.

Individuals who are familiarized with the ideas and processes involved in biology, genetics, and genomics will certainly be better equipped to understand the scientific issues of genomics brought up in the public arena (Corn, Pittendrigh, & Orvis, 2004; Marbach-Ad, 2001). A greater understanding of concepts in molecular biology will facilitate the general population to more effectively participate in meaningful discussions. This will further aid in decision-making regarding genomics-related topics they will undoubtedly encounter in their lives, such as medical testing. Lewis and Wood-Robinson (2000) documented the lack of knowledge and limited understanding on the part of high school students with regard to key concepts in biology and

genetics. They observed that confusion occurred in the students beginning with the most basic concepts in molecular biology: (1) Structures such as cells and chromosomes, as well as genes, and (2) the relationships between these structures (Kirkpatrick, Orvis, & Pittendrigh, 2002; Marbach-Ad, 2001). Thus, there is disparity between public understanding of genetics and genomics when compared to that needed for informed public debate. For this gap to be narrowed, it is extremely important that more adequate genomics teaching models become available for teachers.

The general public and students do not constitute an homogenous group; there is a great diversity of students with different learning needs and abilities. For example, in the 1990's there was an estimated 20,000 to 30,000 pre-college blind and visually-impaired students in the United States (Kumagai, 1995). To date, there are a limited number of teaching tools for general science education for this group of learners and to the authors' knowledge very little currently exists in the area of genomics education for the visually impaired and blind (Erwin, Perkins, & Ayala, 2001; Hinton & Hinton, 1999; Kumagai, 1995; Monaghan, 2004; Pranoti, 2001).

In order for students, and especially learners with special needs, to comprehend topics such as genomics and genetics, the groundwork has to be laid with the understanding of rudimentary concepts in molecular biology. The Genomics Analogy Model for Educators (GAME) approach aims to enable learning in the area of molecular biology by using everyday concepts and materials, such as a town, a library, Lego® blocks, and factories to represent scientific terminology and relationships (Corn et al., 2004; Kirkpatrick et al., 2002; Purdue University, 2008; Rothhaar, Pittendrigh, & Orvis, 2006). The intent of the GAME approach is to introduce the various concepts of genomics prior to teaching students the technical terms associated with this area of molecular biology. One of the modules in the GAME approach is the Lego® Analogy Model (LAM), which uses common Lego® blocks to explain how genes are sequenced (Kirkpatrick et al., 2002). Classroom testing of this approach has demonstrated that this analogy model increases student understanding of sequencing (Rothhaar et al., 2006). This strategy relies on the colors of the Lego® blocks in order to explain sequencing, making it a good approach for the visually able. However, this strategy is inappropriate for visually-impaired students.

In this paper we adapt the LAM approach to enable the understanding of concepts of sequencing in visually-impaired and blind students. Lego® blocks with four different textures are proposed for use in the lesson. One of these textures is "fuzzy" (VELCRO®), and hence the use of the term *fuzzy DNA* in the title of the lesson. The other three textures include a smooth surface, a plastic package bubble surface (bubbles), and a velvet surface. To the authors' knowledge, this represents the first publication on enabling learning of genomics for the blind.

Fuzzy DNA Model (FUDMO) for Enabling Learning of Gene Sequencing by Visually-Impaired and Blind Students

Sequencing is used in several scientific fields including molecular genetics, biochemistry, agronomy, entomology, animal science, evolutionary biology, medicine, and a diversity of other fields of biology. Additionally, electrophoresis is (1) a tool used for gene sequencing and (2) a broadly used technique in molecular biology. For example, sequencing can be particularly helpful in forensic science where it is used to examine human DNA that is used as evidence in criminal cases. The *Fu*zzy *D*NA *Mo*del (FUDMO) is intended to introduce to visually-impaired and blind students a concept that is fundamental to many of the scientific breakthroughs being made. In contrast to actually performing electrophoresis, the FUDMO will not require expensive equipment or chemicals. In addition, another innate problem with actually performing electrophoresis in the

classroom is that it is visual in nature and it would be virtually impossible to adapt this process to the needs of the blind or visually impaired. Instead, the same principles can be taught with the before-mentioned textured Lego® blocks, where each texture represents one of the four bases used in gene sequences.

The FUDMO is intended to clarify the process of genetic sequencing. One major problem with explaining sequencing is that there are layers of concepts involved in this process (Kirkpatrick et al., 2002). These include (1) termination reactions, (2) copying a complement, not an exact copy of the sequence (complementation), and (3) the numbers of hydrogen bonds that exist between G-C and A-T bases. Combining all aspects of sequencing at once is too complex for the majority of students and the basic points of the concept at hand may ultimately be missed (Kirkpatrick et al., 2002). Thus, in the FUDMO model one should begin with a tutorial that describes the concept of termination reactions and follow this with an explanation of electrophoresis (for separation of the different lengths of DNA) using a classroom activity that involves physical movement of students individually or in groups through a room. Later tutorials could easily build on these more complex issues. The basic idea of termination reactions can be explained to the students by using differentially-textured Lego® blocks, where some of the blocks have their tops smoothed off (shaved off), so no more blocks can be added to the stack.

There are four different chemical bases (*A*denosine, *C*ytosine, *T*hiamine, and *G*uanidine) that can make up the sequence of a gene, just as there are four differently-textured blocks in the FUDMO. Genetic sequencing is the chemical process of identifying the order of the DNA bases. When a gene is copied in a cell or in a test tube, each base is added one after another by an enzyme called DNA polymerase, exactly as one would add a Lego® block on top of a previous Lego® block (Figures 1 and 2, both adapted from Kirkpatrick et al., 2002). When one removes the connectors (the tops) of these Lego® blocks (Figure 3a, right hand side), then another block can no longer be added to the top of the Lego® block stack (Figure 4). In sequencing reactions, dideoxy terminators (Figure 3b) perform the same function as do flat-topped Lego® blocks in the Fuzzy DNA Model (Figure 3a). Once a flat-topped Lego® is added to the top of a Lego® stack, no more bases can be added to the gene sequence. For clarity, direct discussions on base pairing and complementary DNA strands used for replication should be omitted from this initial tutorial. However, these topics can be discussed after the initial presentations of gene sequencing and electrophoresis.

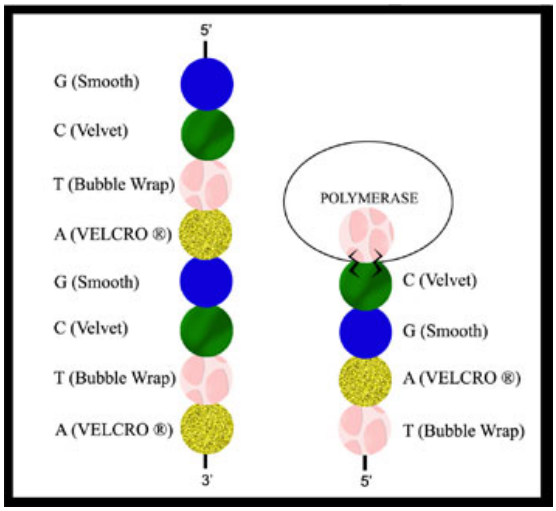


Figure 1. Molecular biology of how DNA strands are copied by polymerase enzymes. On the left-hand side is the template strand running 5-prime to 3-prime. On the right-hand side the strand is copied in the 5-prime to 3-prime in the other direction. Complimentary bases are added to the copied strand: (1) A compliments with T, and (2) C with G. Each of the bases are also shown corresponding to the textures that are used on the Lego® blocks to help introduce the analogy.

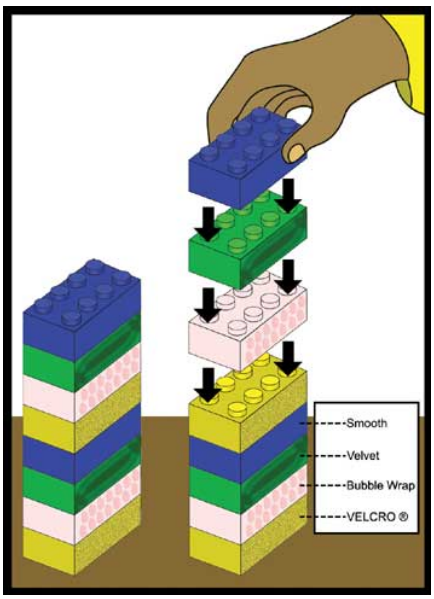
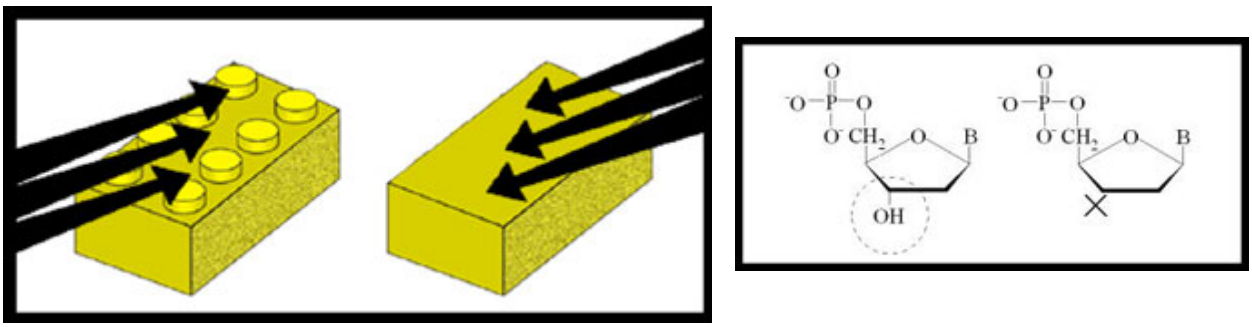


Figure 2. In the FUDMO we have blocks that have one of four textures, with each texture representing a separate base in the DNA strand. We do not complicate the situation with the explanation that the copy is a complimentary copy. Instead, we make a direct copy of the first series of blocks.

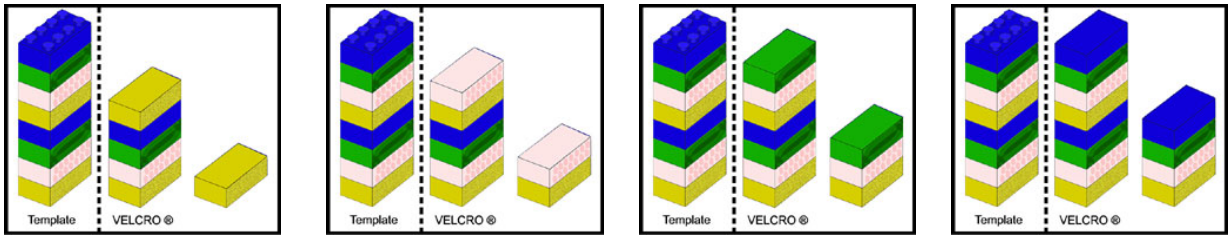


(a) (b)

Figure 3. Lego® blocks lacking their tops (3a, right-hand side) are an analogy for dideoxy terminators used in sequencing (3b, right-hand side). When the –OH group occurs at the 3rd carbon (given in the dashed circle of 3b, left-hand side), other bases can be added to the DNA strand after this base has been added. This is analogous to a Lego® block with its top connectors (3a, left-hand side). When the –OH no longer exists (it is replaced with an –H) on 3rd carbon (3b, right-hand side), then one has a dideoxy terminator nucleotide. This is just like a Lego® block with no top connectors on it (3a, right-hand side). When this dideoxy terminator, or the block without the top, are respectively added to a DNA strand or a Lego® stack, nothing else can be added. Thus, the reaction, or Lego® stack, is terminated. In 3b, the *B* stands for Base (A or T or G or C). In the FUDMO, A, T, G, and C are represented by different textures.

Explaining Electrophoresis

It will also be necessary to explain how the different sized stacks of blocks (DNA) are physically separated in order to determine the sequence of the blocks. DNA has a negative charge and DNA can be pulled towards a positive charge, just like two magnets with opposite poles will attract. If one puts a large and a small piece of DNA in an agarose gel, and a positive charge is applied, then the small piece of DNA is pulled through the agarose gel faster than the larger piece of DNA.



(a) (b) (c) (d)

Figure 4. When a "dideoxy terminator" Lego® block (a block with a top shaved off) is placed on the Lego® block stack, one can no longer add more blocks. On the left side of the dashed lines in Figures 4a, 4b, 4c, and 4d are the template strands and on the right side are the terminated sequences for each of the textured blocks. In (a), no more blocks can be added in the places where VELCRO® blocks occur. Thus, where the VELCRO® blocks exist in the "sequence," the Lego® stacks will "terminate" (the first and fifth blocks in the stack). In (b), the stacks terminate at the second and sixth blocks, where the bubble wrap textured blocks occur in the sequence. In (c), the stacks terminate at the third and seventh blocks, where the velvet textured blocks occur in the sequence. In (d), the stacks terminate at the fourth and eighth blocks, where the smooth blocks occur in the sequence.

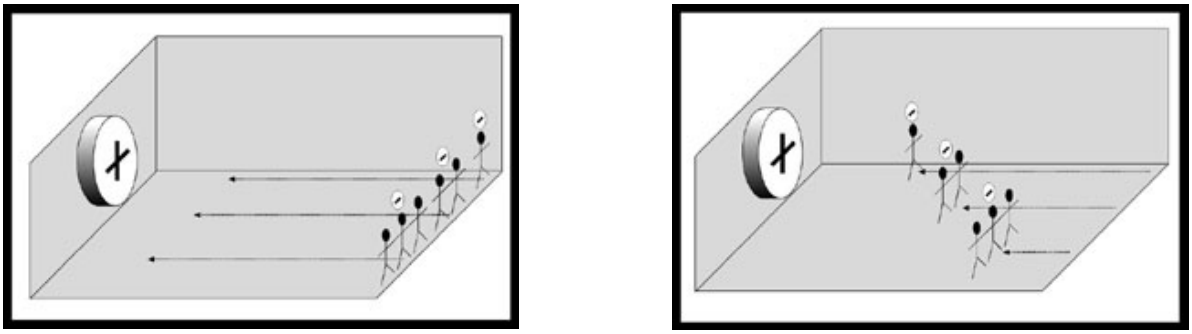
Small and large Lego® stacks (like DNA) are like an individual student and multiple students arm-in-arm (or holding hands), respectively, walking across a classroom (Figure 5). It must be emphasized to the students that DNA is negatively charged. The students can then be told to imagine that, just like DNA, they are also negatively charged. They then further imagine that a giant positive charge pulls them to the other end of the room. It will be much easier for an individual student to walk across a classroom than a group of students holding hands, especially if there are (imagined) obstacles in the room. It can be explained to the students that the more obstacles in the students' path (such obstacles are not shown in Figure 5), the more difficult it will be to cross the room, especially for the group comprising 3 students holding hands. During a certain time interval, the single student can be taken across the room rapidly while a group of students will move slower and be taken only partially across the room. It is not suggested that actual objects are placed in the path of the students.

Students will be told that an agarose, or polyacrylamide, gel is like a room full of obstacles. A very thick gel (high percentage agarose or polyacrylamide) is like a room with several obstacles. If there are too many obstacles in the classroom, it will be difficult for even the smaller groups (or single student) to get through the room. If there are too few obstacles (a low percent agarose, or polyacrylamide, gel) then everyone, even the biggest groups, can get through very rapidly. Thus, having enough objects (the right percent of agarose or polyacrylamide in the gel) and running the experiment for the right amount of time will allow for the best separation of different sizes of students holding hands (i.e., stacks of blocks or sizes of DNA).

As shown in Figure 5b, it is then explained to the students that a single student will be the first to get to the other side of the classroom, with the 2 students together some distance behind, the group of 3 students further behind, and so on (i.e., the group with the longest chain of students will have traveled the least distance across the classroom in a given time). This is exactly how the different lengths of DNA are separated by electrophoresis.

The stacks of Lego® blocks can then be separated out in a pattern that explains how different sizes of DNA are separated out in an electrophoresis gel (Figure 6a). In the first lane of the sequencing gel, one would run the stacks of blocks that have terminating Lego® blocks for the VELCRO®

surface. This will tell us where all the VELCRO®-surfaced blocks are occurring. In the second lane one would run Lego® blocks with the bubble-wrap-terminating blocks (blocks with their tops shaved off), in order to determine where the bubble-wrap blocks are in the stack. The same can be done with the velvet and smooth blocks, respectively, in the third and fourth lanes (Figure 6b).



(a) (b)

Figure 5. (a) Students can be lined up at one end of the room. The line can comprise a single student, two students holding hands, and three students holding hands. Students can be told to imagine they are negatively charged and that a giant positive charge exists at the other end of the room. The students can also be told to imagine that there are obstacles in the room. Thus, the more students holding hands, the more difficult it will be for them to cross the room, especially if there are (imagined) obstacles in their path. (b) A single student can be taken more paces forward in a given allotment of time than two or three students holding hands. This demonstrates to the student that shorter stacks of Lego® blocks (or short strands of DNA) will run faster in a sequencing gel than larger Lego® block stacks (or longer strands of DNA).

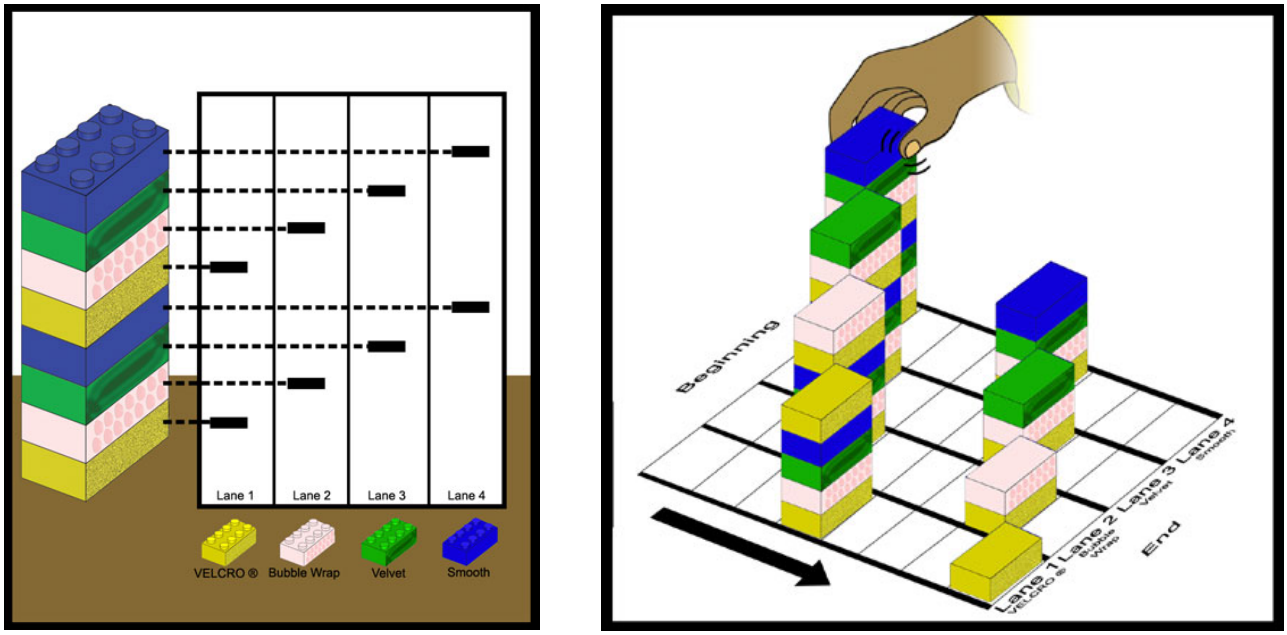
From this, we can determine the sequence of the blocks, just as one can determine the sequence of a gene using electrophoresis. A tray explaining the final position of the blocks in the gel can be given to the students for them to feel where each stack will be located. By going over this stack of blocks with the instructor they can determine the original sequence of blocks (Figure 6).

Discussion

Instructional media has shown great potential in its capacity to enhance the quality of learning experiences for students (Williams, 1998). Classroom evaluations of the LAM approach, for visually-able students, have already been performed (Rothhaar et al., 2006) and have shown that LAM is an effective teaching tool for genomics. However, enabling learning with analogies has its limitations and care must be taken by the instructor to explicitly define the attributes shared between the target concepts and the analogy (Harrison & Treagust, 1993; Treagust, Harrison, & Venville, 1998) (Appendix A). Also, issues that do not map out between these two domains should also be determined to prevent misinformation being conveyed through the analogies (Harrison & Treagust, 1993; Treagust et al., 1998).

The Fuzzy DNA model is an extension of the LAM concept and is intended to improve and expand opportunities for visually-impaired students in the areas of biology, genetics, and genomics. Although the basic concepts are in place for the development of this instructional approach, further work with instructors of the blind and visually impaired will help to define revisions that will be needed to make this model as effective as possible. Ultimately, the development of teaching tools for genomics and molecular biology will be a first step towards

helping visually-impaired and blind students participate in the discussions and debates that will occur in the near future over the impacts of genomics on our society.



(a) (b)

Figure 6. (a) It can be explained to the students that when the "terminated" stacks of Lego® blocks are run in four separate lanes, one can then determine the series of blocks that occur, just like one would read a sequencing gel in order to determine a gene sequence. (b) A stack of blocks can be created, such that the students can run their hands over an example of how the blocks (*i.e.*, DNA) would separate out in a sequencing gel. Starting at the top (or bottom), one can read out the sequence from the distance the stack of blocks ran in the electrophoresis reaction. From this the students can actually determine the "sequence" of the blocks.

Acknowledgments

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Appendix A

Enabling the Learning of Gene Sequencing for Visually-Impaired and Blind Students

Concept

Use textured Lego® blocks, coupled with physical activities, to explain the concept of how genes are sequenced using dideoxy terminator sequencing reactions and gel electrophoresis. This approach can be used to explain the aforementioned concepts to visually-impaired and blind students.

Students

Students at the high school and university levels are often not prepared to understand the concept of gene sequencing. Few teaching tools exist for enabling the learning of such concepts for visually-impaired and blind students.

Analogy 1

The four bases C, G, A, and T are represented by Lego® blocks with four different textures. Each texture also has a corresponding color to the block (which can help students with partial sight and also help the teacher keep track of the materials).

Analogy 2

The dideoxy terminators C, G, A, or T are represented by textured Lego® blocks with their tops removed.

Analogy 3

Students use a physical classroom activity to enable the learning of the concept of electrophoresis. Specially, students move from one end of the classroom to the other in varying-sized groups to simulate short and longer DNA sequences.

LIKES - Mapping the Analogy to the Target

Analogy 1: Four Separate Bases (G, A, T, and C) Represented by Four Differentially-Textured Lego® Blocks

- DNA is made up of four separate bases.
- The G, A, T, and C bases do interconnect to form DNA sequences.

Analogy 2: Lego® Blocks With Their Tops Removed Represent Dideoxy Terminators and These are Used to Terminate the Sequencing Reactions

- Dideoxy terminators are unable to "connect" with the next base due to their inability to form bonds, much like two Lego® blocks interconnecting.
- Dideoxy terminators, like Lego® blocks with their tops removed, stop any further bases (blocks) from being added to the sequence.

Analogy 3: Explanation of Electrophoresis by Having the Students Move From One End of the Room to the Other, Either Individually or in Varying-Sized Groups, to Represent Different-Sized Pieces of DNA

- Smaller groups, like smaller pieces of DNA, will move more quickly.
- Separation of sizes of DNA and groups of students can be demonstrated.

UNLIKES - Where the Analogies Break Down

Analogy 1: Four Separate Bases (G, A, T, and C) Represented by Four Differentially-Textured Lego® Blocks

- G, A, T, and C bases are structurally more complicated than a simple Lego® block.
- Differences between G, A, T, and C bases are not due to texture differences, but to structural differences. In contrast, in the analogy, the blocks differ in texture, not in structure.

Analogy 2: Lego® Blocks With Their Tops Removed Represent Dideoxy Terminators and These are Used to Terminate the Sequencing Reactions

- The analogy does not easily explain the concept of complimentary strands of DNA during the sequencing reactions.
- Tops of the Lego® involve many contact points with the next block and in DNA there is a single covalent bond that is formed when each base is added to the existing DNA sequence.

Analogy 3: Explanation of Electrophoresis by Having the Students Move From one End of the Room to the Other, Either Individually or in Varying-Sized Groups, to Represent Different-Sized Pieces of DNA

- Having students move through the room must be controlled, since there is no significant "resistance" experienced by the students, as pieces of DNA would encounter as they move through a gel.
- DNA is negatively charged and moves through the gel due to a positive charge; the students do not move through the classroom due to charge.