Genomics Analogy Model for Educators (GAME): VELCRO® Analogy Model to Enable the Learning of DNA Arrays for Visually Impaired and Blind Students

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Abstract

Although members of the general public have often heard of the terms *genetic engineering* and, more recently, genomics, they typically have little to no knowledge about these topics, and in some cases are confused about basic concepts in these areas. There is currently a need for teaching models to explain concepts behind genomics. Additionally, almost nothing exists for teaching the visually impaired and blind about genomics. The purpose of the Genomics Analogy Model for Educators (GAME) approach is to convey the basic concepts of genomics to students using analogies and inexpensive materials that students encounter in their daily lives. In recent articles, we have introduced the GAME approach with several of its components. In this article, we present the concept that a VELCRO® analogy model could be used to enable learning of the concepts of DNA microarrays for both fully-sighted and potentially visually impaired students. Classroom activities using VELCRO® are proposed as a teaching module to explain how DNA microarrays work. In summary, differentially shaped VELCRO® pieces fixed to a solid base are used to represent the array and the complementary pieces of VELCRO® are used to represent the cDNA. Students can use this approach, for example, to explore expression patterns of "genes" (actually the mRNA from these genes) between experimental groups. We term this teaching approach the VELCRO® Analogy Model (VAM).

Introduction

Genomics is arguably one of the most important scientific advances of the 20th and 21st centuries. The sequencing of the human genome has (i) laid the foundation for development of new generations of drugs, (ii) led to the development of novel diagnostic techniques, and (iii) provided the foundation for new approaches to preventive medicine. In order for medical professionals (i.e., doctors, nurses, and dieticians) to effectively discuss and utilize the benefits of these new technologies, there is a need for the general public to have a greater knowledge of genomics (Collins, 2004; Gilbride & White, 2000; Jenkins & Collins, 2003; McInernery, 2002). Whole genome arrays support a technology already impacting our understanding of the expression of genes associated with, among other things, diseases, plant-insect interactions, and pesticide resistance (Carvalho, Ouwerkerk, Meijer, & Ylstra, 2004; Pedra, McIntyre, Scharf, & Pittendrigh, 2004; Schmidt, Voelckel, Hartl, Schmidt, & Baldwin, 2005). Although efforts are underway to teach microarrays in high schools, time and money are certainly two limitations associated with bringing this information to the classroom in an effective fashion (Campbell et al., 2006).

The scientific, ethical, social, and legal ramifications of these new genomics technologies will impact almost every individual in our society at some point in their life. For example, in the United States, genomics-related technologies have the potential to play an important role in an individual's ability to obtain health insurance coverage (Carnovale & Clanton 2002; Collins & McKusick, 2001), medical therapy, and neonatal health. Thus, one could argue that there is a need to better educate the general public on the topic of genomics, so that proper debate can occur on how these technologies will ultimately impact our society.

Students, and individuals in the general public, who are knowledgeable of the ideas and processes involved in genomics will be better equipped to understand the scientific and social issues brought up in the public arena by these new technologies (Corn, Pittendrigh, & Orvis, 2004; Marbach-Ad, 2001). This knowledge will further aid in decision-making regarding scientific topics they will undoubtedly encounter in their lives (e.g., genetically modified organisms). Lewis and Wood-Robinson (2000) gave an account of the lack of knowledge and limited understanding on the part of high school students about key biological and genetic concepts. They observed that confusion occurred in the students, beginning with the most basic concepts in molecular biology: (i) Structures such as cells, chromosomes, and genes, and (ii) the relationships between these structures (Marbach-Ad, 2001). This indicates that there is disparity between public understanding of genetics and genomics when compared to the level of knowledge needed for informed public debate. For this gap to be narrowed, it is extremely important that more adequate models for teaching genomics become available for teachers.

The general public, as well as students, are not homogenous groups; there is a great diversity of students with different learning needs and abilities. For example, in the 1990's there were an estimated 20-30,000 pre-college-aged 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). This is not surprising, as genomics education for the general public is a recent phenomenon (Campbell et al., 2006; Corn et al., 2004; Genome BC, 2008; Kirkpatrick, Orvis, & Pittendrigh, 2002).

In order for students, and particularly learners with special needs, to comprehend topics such as genomics and genetics, the foundation must be laid for the understanding of rudimentary concepts in molecular biology. The Genomics Analogy Model for Educators (GAME) approach is intended 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. The intent of the GAME approach is to introduce the various concepts of genomics in simple analogies prior to teaching students the technical terms associated with this area of 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, Pittendrigh, & Orvis, 2006). This strategy relies on the colors of the Lego® blocks in order to explain sequencing, making it a good approach for the fully sighted; however, this strategy would be inappropriate for completely blind students. We have recently adapted the LAM for visually impaired students, by adding distinct textures to each colored Lego® block so that the students can learn sequencing through both the feel and color of the blocks (Butler, Bello, York, Orvis, & Pittendrigh, in press).

The next step in this GAME teaching process is to introduce the concepts behind DNA microarrays. Briefly, DNA microarrays involve placing numerous genes from the tissue of a whole organism on a "chip" (or array) and examining the resulting presence of cDNA to determine the expression levels of many genes at once. Such an approach could be used to teach the concepts of microarrays to high school level students. These genes might originate from organisms, individual cells, or cell cultures. The concepts in microarrays can be easily adapted to the GAME approach, providing instructors with an opportunity to use readily understandable concepts and inexpensive items that can be purchased at most department stores.

Here we present the concept that VELCRO® can be used in the GAME approach for enabling the learning of DNA microarrays for both fully sighted and potentially visually impaired students. There are several aspects to the VELCRO® array model (VAM) that should make it useful across a variety of classroom environments: (i) VECLRO® is inexpensive and is easily accessible in most department stores; (ii) the "arrays" for the classroom are easy to put together; and (iii) it provides a hands-on teaching approach that allows students to both look at and manipulate the arrays.

Briefly, the rough side of the VELCRO® is cut into different shapes and these are affixed onto a solid surface. This constitutes the "VELCRO® chip," which is analogous to a DNA chip. The fuzzy side VELCRO® shapes represent the different genes (actually cDNA; see Purdue University [2008b] for the dowloadable document explaining the details of cDNA) that will be tested for expression patterns. Different numbers of fuzzy VELCRO® shapes can be made to represent the cDNA that will be hybridized to the "VELCRO® chips" in order to determine the expression levels of the "genes" in question. To the authors' knowledge, this represents the first publication on enabling learning of "DNA arrays" for the visually impaired and blind. Of course, for visually enabled learners, one can simply use a piece of paper with the shapes drawn on it for the array and cut-out pieces of paper (in the respective shapes) can be used as the cDNA. A downloadable lesson plan for this later approach is available at Purdue University (2008b).

VELCRO® Analogy Model

Most of the cells in our body contain the same basic genetic materials (the genome) (notable exceptions include red blood cells and gametes), but different cells express different sets of genes at different levels, depending on the cell's purpose. Each cell is controlled ("instructed") by a different combination of genes to maintain and, in many cases, to replace itself. However, there are many different types of cells in our bodies, from our hair to our fingernails, skin, and eyes. As a result, while each cell may have the same genome, the genes it uses to become a skin cell are different than the genes it expresses to be a hair cell. One way of examining the differences in the genes being expressed in different cells is to use DNA microarrays. The microarray allows us to look at the genome of any cell and to see what genes the cell is using and how often, and, in some cases, what genes are not being used. Not only could we learn what genes are responsible for the difference in a skin cell and a hair cell, we could also learn more about diseases such as cancer, ALS, lupus, and other auto-immune diseases. A cancerous cell(s), which is functioning "incorrectly," could be compared with non-cancerous cells in the body that are functioning "properly." Discovering which genes are involved in making the cells cancerous would allow researchers or clinicians early and accurate diagnoses of cancer in patients and possibly provide target sites for the development of compounds to control or cure the cancerous cells.

DNA chips are being used in a variety of scientific fields including molecular genetics, biochemistry, agronomy, entomology, animal science, evolutionary biology, medicine, and a variety of other fields of biology. These chips typically contain copies of many genes (or all the genes), typically from a single species, placed on a glass or plastic slide. Some of the copies of these genes are built on the base material (the chip) through a lithography approach and representative bases for each gene occur at a specific spot. In other cases, substantial portions of each of the genes (reverse-transcribed RNA that is turned into the more stable cDNA or copy DNA) are placed on the chip. These are called cDNA microarrays and are often placed on glass slides.

The VELCRO® Analogy Model (VAM) is intended to introduce students to the basic concepts behind cDNA microarrays that are fundamental to many of the scientific discoveries being made. This approach can be used for both sighted and visually impaired students. In contrast to actually performing oligoarray or cDNA microarray experiments, the VAM will not require expensive equipment or chemicals. In addition, another innate problem with actually performing an array experiment is that it is "visual" in nature and it would be virtually impossible to adapt this process to the needs of blind students. Instead, the same principles can be taught with the VELCRO® Analogy Model, where each VECLRO® shape represents a gene that has been placed on the "chip."

The VAM is intended to clarify the process of how scientists determine the expression levels of mRNA in an organism, tissue, or cell using "DNA arrays." The VAM can be used to clarify several concepts involved in DNA arrays. These include (i) reverse transcription of the mRNA to cDNA for the sample material that is being tested, (ii) complementation between the DNA on the array and cDNA that is hybridized to the array, and (iii) how the arrays are used to determine differential expression of genes between the different treatments.

Reverse Transcription and Complementation

When messenger RNA (mRNA) is extracted from the cells of the organism that is the subject of an experiment, copies of the mRNA must be made. While the number of mRNA present in a cell is used to determine which genes are being used, mRNA is highly unstable, and it cannot be manipulated on a DNA array (Boyer, 1999). Instead, a stable complimentary copy is made, which is called cDNA. Because the copy, or cDNA, is complimentary, each base in the mRNA strand is copied into its matching base pair in a cDNA strand. The bases C (cytosine) and G (guanine) pair together, as do the bases A (adenine) and T (thymine), where T is used instead of U (uracil) in the cDNA strand. Consequently, if the RNA has a C base in the strand, the cDNA will have a G at that same position in the cDNA strand. If the RNA has a G at the spot then the cDNA will have a C. If the mRNA has an A at a spot, then the cDNA will have a T. If the mRNA has the RNA equivalent of T (called U), then the cDNA will have an A at the spot. This builds on concepts that we explain in our lesson plan #3 of the G.A.M.E. website (Purdue University, 2008a).

One can demonstrate why mRNA is unstable and must be copied into cDNA by using rough VELCO® that is not attached to the "array" board. First, one can explain to the students that the mRNA is equivalent to the rough side of the VELCRO® with a piece of felt attached to the back of it. This extra component added on the back of the rough VELCRO® represents the one extra OH (oxygen and hydrogen) group found on the backbone, or mRNA. This extra OH group is one of the reasons mRNA is much more unstable than DNA; RNA can actually use this OH group to tear itself apart.

Thus, in order to measure the expression of a gene, RNA must be turned into a more stable material, such as DNA. We call this cDNA, where the *c* stands for *copy*. In our analogy, the rough side of VELCRO® can be cut out in a circle, star, square, or triangle (Figure 1, left side). Each different shape represents a different "gene" (or more precisely, mRNA transcript from the gene). One can have the students imagine that this first rough-sided VELCRO® represents mRNA and is inherently unstable. Consequently, one must make stable, complimentary copies of the fuzzy-sided VELCO® pieces in the exact same shape as the "mRNA rough" VELCRO®. This is the cDNA copy of the mRNA for a given gene. These cDNA fuzzy sided VELCRO® pieces will be used to interact with the rough-sided DNA that will be on the "DNA VELCRO® arrays." For every mRNA of a given gene, a single copy of cDNA will be made (Figure 2).

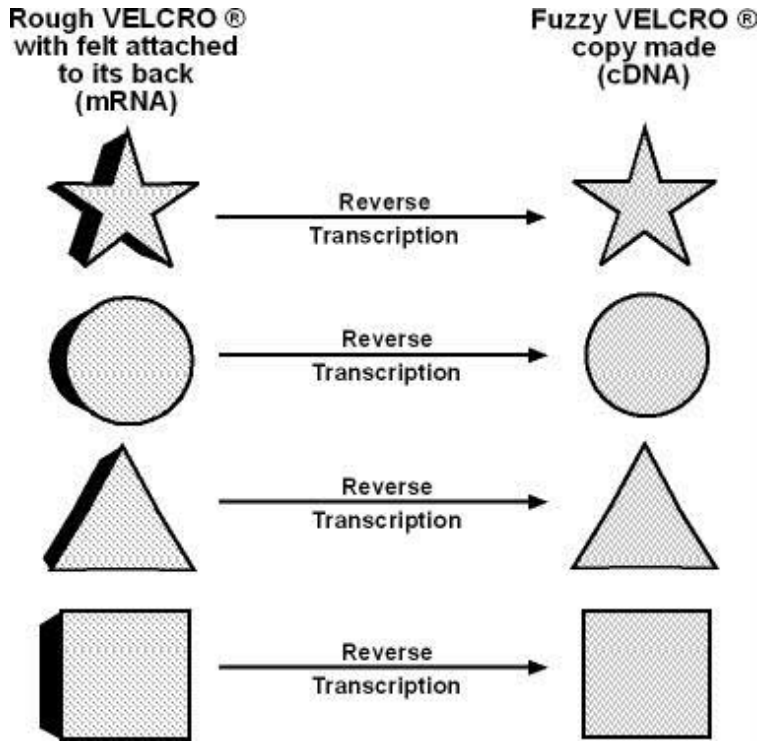

Figure 1. Reverse transcription of mRNA to cDNA analogy. Hooked VELCRO® with velvet on the back of the material represents mRNA. Each shape represents mRNA coded for by four separate genes. A "copy" is made of each mRNA (shape of VELCRO®) with the fuzzy side of VELCRO® and this "stable copy is "cDNA." Thus, a copy DNA or cDNA is made from the mRNA using a reverse transcriptase enzyme.

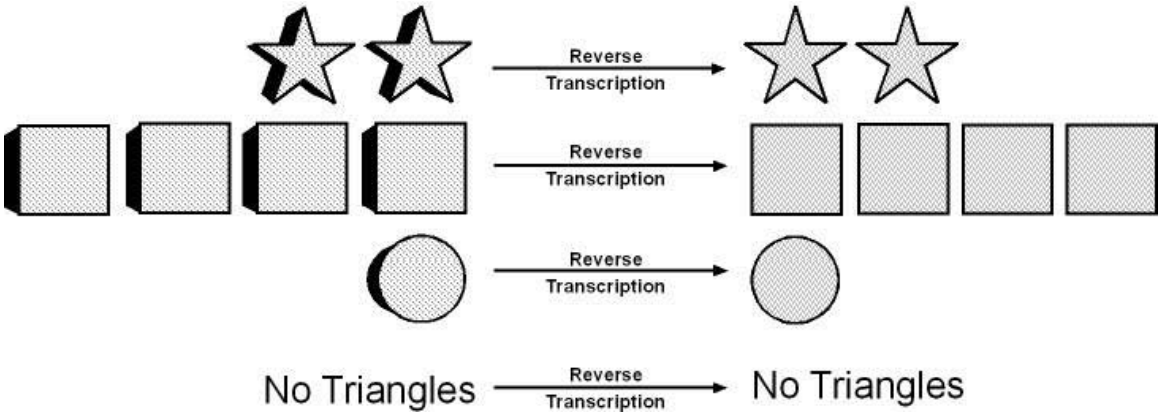

Figure 2. For every mRNA there is a cDNA made during reverse transcription. Thus, if there were two "star gene" mRNAs, then there would be two star cDNAs reverse transcribed. If there were four "square gene" mRNAs, then there would be four square cDNAs reverse transcribed. If there was one "circle gene" mRNA, then there would be one circle cDNA reverse transcribed. Also, if there were no "triangle gene" mRNAs, then there would be no triangle cDNAs reverse transcribed.

The actual "VECLRO® arrays" can be created with two pieces of wood or plastic to explain the concept behind DNA arrays. Both "VECLRO® arrays" will have identical copies of the rough side of the VELCRO® shapes (Figure 3). For simplicity, both boards could have five copies of each of the four shapes, each set of shapes located in each of the four corners of the "array."

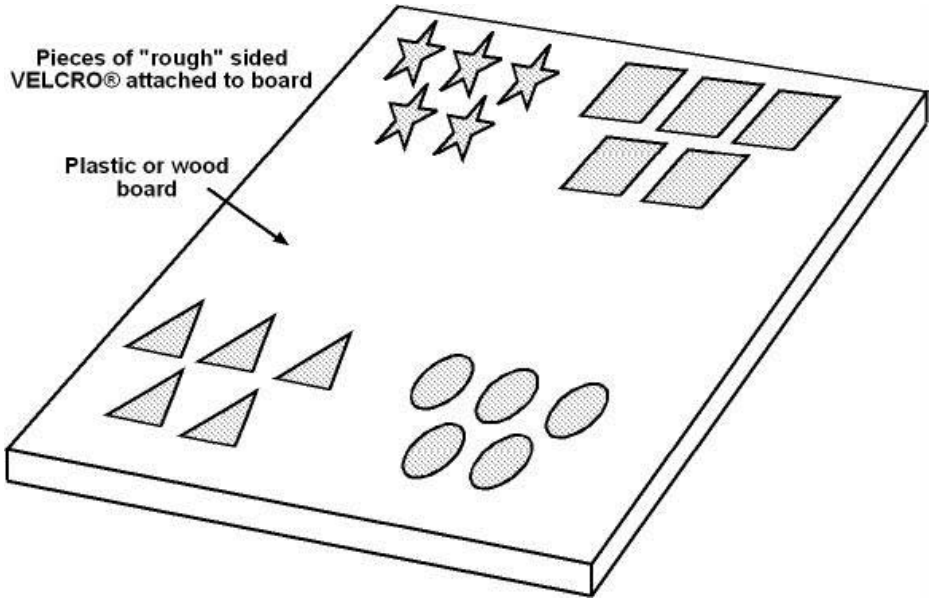

Figure 3. VELCRO® analogy model (VAM) for explaining the concept underlying cDNA arrays ("chips"). Hook sided VELCRO® shapes are attached to a solid square base (e.g., a wood board or plastic sheet). The solid square base represents the material that the cDNAs are "printed on," or bound to, in order to create the array. For each shape, five copies of the given shape are placed on a respective corner of the wooden board or plastic sheet. They are attached to the solid base such that their hook side faces away from the base.

One of the two arrays will be used to bind the cDNA from the "control" organism (Figure 4, left side). The second array will be used to bind the cDNA from the "treatment" organism (Figure 4, right side). In the example given in Figure 5, we see that in the control and treatment organism there were equal numbers of stars. Thus, the genes showed no difference in expression (constitutively expressed). The organisms in the treated group expressed fewer squares than in the control group, meaning the "square genes" are under-transcribed. The organisms in the treated group expressed more triangles than in the control group. Consequently, the "triangle genes" were over-transcribed. The organisms in the treated group expressed more circles than the control group, which had no circles group. Thus, the "triangle genes" were over-transcribed, where the circles were absent in the control group and present in the treatment group. Over-transcribing a gene may allow an organism to do things that it normally cannot. For example, some insects over-transcribe certain genes in order to become resistant to insecticides (Pedra et al., 2004).

A-T and G-C Content and its Influence on how Tightly Complimentary Strands Will Bind

In a separate lesson, VELCRO® can also be used to explain how the GC and AT content of the DNA will influence how tightly the complimentary strands interact. The two bases G and C have three hydrogen bond interactions, whereas A and T have only two hydrogen bonds. This means it

takes more energy to pull apart G and C than it does to pull apart A and T, because more bonds must be broken in a G-C bond than in an A-T bond. VECLRO® can be used to explain this concept in terms of the energy required to pull apart A-T or G-C rich strands of DNA. VELCRO® comes in several forms; some forms have weak interactions so that the two compliments are easy to pull apart (VELCRO® "Soft and Flexible") and other forms are very difficult to pull apart (VELCRO® "Industrial Strength"). The A-T rich DNA is analogous to the Soft and Flexible VELCRO® and the G-C rich DNA is analogous to the Industrial Strength VELCRO®. Thus, it takes more energy to pull apart strands of complimentary DNA that is G-C rich than strands that are A-T rich. In this example, the students can be told that Soft and Flexible VELCRO® represents A-T interactions, while they are pulling the VELCRO® strands apart. The same can also be done for Industrial Strength VELCRO® in explaining that G-C interactions bind the complimentary strands together more tightly.

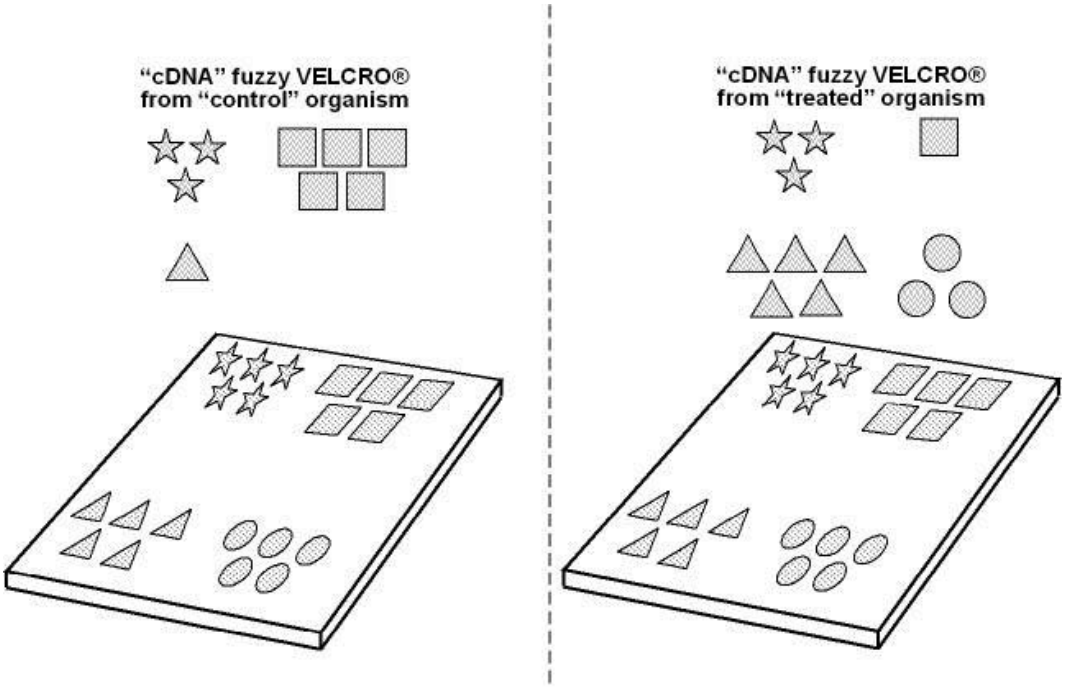

Figure 4. One can now compare the expression levels between a control group (untreated organisms, left side) and the treated group (right side). The students can actually perform an experiment to determine expression level differences between the control and treated organisms, to determine the impact of the treatment on expression levels of the four different "genes." The fuzzy VELCRO® representing the cDNA from the control organism is placed beside the array (left side). The fuzzy VELCRO® representing the cDNA from the treated organism is placed beside the second array (right side).

Discussion

Instructional media has shown great potential in its capacity to enhance the quality of learning experiences for students (Williams, 1998). Classroom evaluations of other components of the GAME teaching strategy have already been performed (Rothhaar et al., 2006) and have shown that the approach is an effective teaching tool for genomics. Specifically, a LEGO® analogy model was used to explain how genes are sequenced (Kirkpatrick et al., 2002). This model has

been adapted for use with the visually impaired (Butler et al., in press). To date, classroom testing (Rothhaar et al., 2006) of the LEGO® analogy model with sighted students revealed a positive impact on the learning of ninth- and tenth-grade students. However, the adaptation suggested by Butler et al. remains to be tested in the classroom.

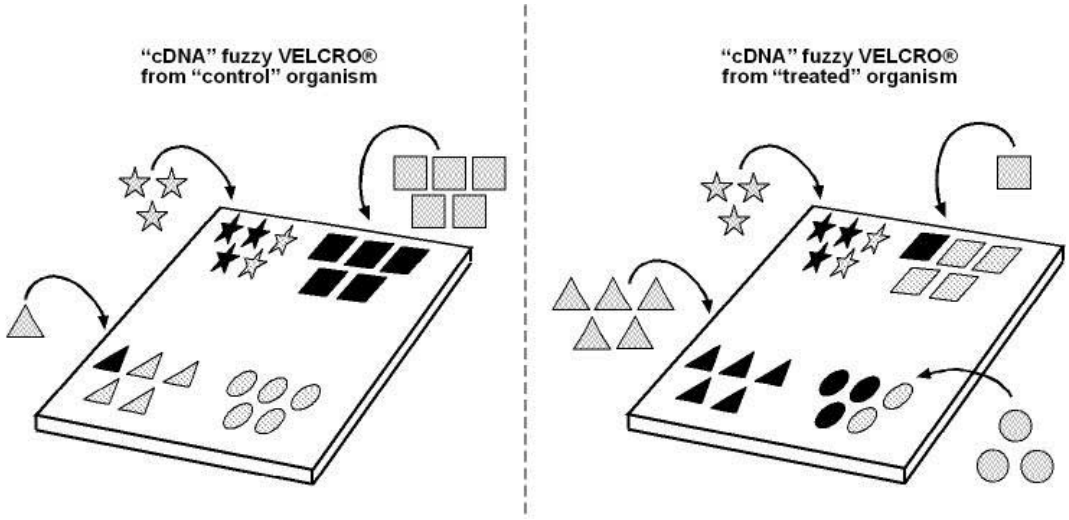

Figure 5. The students attach ("hybridize") the fuzzy VELCRO® "cDNA" to the respective arrays. They can then compare the numbers of "cDNAs" that have been bound to each array. From this they can compare expression level differences of "mRNA" between the control (left side) and treatment (right side) groups.

In this article, we present how VELCRO® can be used in separate teaching lessons to (i) explain cDNA microarrays and (ii) influence how tightly complimentary strands of DNA will interact. Such a teaching strategy is adaptable for use with both sighted and visually impaired high school students. It is possible to distinguish between the genes not only by shape, but also by color, which has the potential to assist both groups of learners. Unless a student is completely blind, color is still an important learning tool. For example, seventh-grade students with some level of sight immediately took note of colors and when given choices of materials, chose to use colored materials (R. Radavich, personal observation, April 27, 2005).

Visually impaired children often have difficulties forming complete mental pictures of objects and processes, which may be due to second-hand descriptions, and limited first-hand exploration. For example, a student may know a chick is a baby chicken, but if they were given a baby chick to handle, they would not know what it was (Gough, 1978). Children with diminished levels of sight often have difficulties discerning details, and are left with an overall picture, including shapes and sizes and colors, but lack details that may be very important when trying to form an understanding of scientific information such as biological processes. Visually impaired learners not only make use of their existing sight, but often rely heavily on other modalities, such as hearing, touch, taste, and smell to help complete their mental images (Anderson, 1984; Corley & Pring, 1996). As a result, multi-sensory learning has been extremely successful in bridging the gaps in understanding with visually impaired learners (Pring, 1989).

Currently, the most common practice to accommodate visually impaired students into mainstream K-12 classrooms and college level courses has been to provide them with the same text book as

the fully-sighted students, but in large print or translated into Braille (S. Wilder, personal communication, January 14, 2005). The difficulties for visually impaired learners arise when graphics are tied to lessons. The current strategy for learning is to transform the graphics into a simple, tactile representation using raised and textured lines. However, these tactile graphics have limitations when applied to complex images, and can easily confuse students when too much detail is added to the drawings (Hinton & Ayres, 1987; Watson & Johnston, 2004).

The limitations of tactile graphics can be overcome by using hands-on models. These models can be manipulated by students, and altered by the teacher for each student as materials progress or needs arise. The VELCRO® Analogy Model utilizes the best aspects of hands-on teaching by allowing the students to touch and examine, as well as manipulate, the "DNA array" they are learning about. The model itself, coupled with the analogies, teaches about DNA microarrays via a conceptually and tactilely simple process.

Shapes, colors, and textures incorporated into the VAM model makes it no less valuable for fully sighted children. When designing and teaching materials, researchers and teachers have stressed that the strategies used to teach visually impaired students are also excellent when teaching fully-sighted students (Lee & Groom, 1996; Watson & Johnston, 2004; Womble & Walker, 2001). By incorporating multiple senses in this teaching model, it makes the concepts more accessible to all students.

Analogies can have both strengths and weaknesses, and Appendix A contains a guide to help those who may decide to use the VELCRO® Analogy Model to enable the learning of DNA arrays. 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. For example, which aspects of teaching with this model may give rise to misconceptions and how can instructors avoid such problems? Ultimately, the development of teaching tools for genomics and molecular biology will be a first step towards helping the 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.

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Appendix A

A Guide for Teaching With the VELCRO® Analogy Model

Concept

Explanation of microarrays using shapes that represent the expression patterns of specific gene transcripts. We also discuss how this concept can be adapted for the visually impaired.

Students

Students (sometimes even at the university level) are not prepared to understand the concept of microarrays. They are often familiar with the concepts of genes, DNA, and RNA, but not with the concept of how these come together in microarray technologies.

Analogy 1

Reverse transcription of mRNA to cDNA. The hooked VELCRO® with velvet on the back of the material represents mRNA. Each shape represents mRNA coded for by four separate genes. A "copy" is made of each mRNA (shape of VELCRO®) with the fuzzy side of VELCRO® and this "stable copy" is "cDNA." Thus, a copy DNA, or cDNA, is made from the mRNA using a reverse transcriptase enzyme.

Analogy 2

The number of cDNAs is representative of the level of mRNA in the system. For example, if there (i) were two "star gene" mRNAs, then there would be two star cDNAs reverse transcribed; (ii) were four "square gene" mRNAs, then there would be four square cDNAs reverse transcribed; (iii) was one "circle gene" mRNA, then there would be one circle cDNA reverse transcribed; and (iv) were no "triangle gene" mRNAs, then there would be no triangle cDNAs reverse transcribed.

Analogy 3

Concept of the microarray. Hook-sided VELCRO® shapes are attached to a solid square base. The fuzzy VELCRO® shapes representing the cDNAs are then placed with the hook-sided VELCRO® shapes on the solid base to simulate hybridization.

Analogy 4

Weaker VELCO® can be used to demonstrate AT interactions and stronger VELCO® can be used to demonstrate CG interactions.

LIKES - Mapping the Analogy to the Target

Analogy 1: Reverse Transcription

- Explains that the reverse transcribed cDNA is a copy of the mRNA.

Analogy 2: Numbers of cDNAs

- Explains the basic concept of reverse transcription.

Analogy 3: Concept of the Microarray

- Explains the concept that DNA is attached to a solid base and cDNAs hybridize with the respective DNA located on the microarray.
- Explains the concept that microarrays can be used to compare transcription level differences between two separate groups (e.g., different treatments, tissues, time points, etc.).

Analogy 4: Strength of AT and CG Interactions

- DNA-DNA interacting strands with high CG content take more energy to separate than ones with high AT content.

UNLIKES - Where the Analogies Break Down

Analogy 1: Reverse Transcription

- Analogy does not explain CG and AT complimentary relationships in the process of reverse transcription.

Analogy 2: Numbers of cDNAs

- Does not explain that there may be thousands, or tens of thousands (or greater), of transcripts.

Analogy 3: Concept of the Microarray

- Does not explicitly demonstrate that microarrays often involve hundreds, thousands, or even tens of thousands of genes.
- The differences in genes, as well as their resultant mRNA and cDNA, are not due to shape differences, but due to differences in the sequence combinations of A, G, C, and T.
- Does not explain cross-hybridization that may occur between closely related genes.
- Does not explain than in some micoarrays (e.g., oligoarrays) only part of the cDNA interacts with the sequence on the array.

Analogy 4: Strength of AT and CG Interactions

- DNA rarely contains only CG or AT, but is typically a mixture of these bases. Strands with higher CG content take more energy to separate than strands with low CG content (i.e., high AT content).