Construction and manipulation of DNA tiles in free space

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ABSTRACT

Virtual reality (VR) systems are used to create, display, and interact with virtual objects in space. They create an illusion of reality in 3-dimensions (3D) by providing a specific collection of technologies such as head mounted 3D displays, Glove input devices and audio systems. The goal of the research project was to develop a tangible and user-friendly 3D interface for spatial construction and manipulation of a virtual object, namely, a DNA tiled network. A DNA tiled network is composed of DNA tiles, or double crossover DNA (DX) molecules in space. This interface has been implemented on a VR system situated in the multi-res lab at Caltech. It allows the users to create DNA tiles by letting them place DNA molecules in 3-dimensinal space and join them using specialized tools. Once individual tiles are created in the space, they can be connected together to form a network of DNA tiles.

DNA tiles shape the foundation for research in the field of DNA based computation. This research project aims at being significant to researchers in this field by offering them a virtual interface to manipulate DNA tiled structures and hence aid their search for stable and robust DNA tiled structures.

INTRODUCTION

The project involved working on a Virtual Reality system [1] developed by Steven Schkolne, a graduate student and member of the multi-res modeling group, led by Prof. Peter Schröder. The interface for this system has been implemented using a 3D semi-immersive computer. The user can create objects in front of the computer screen by tracing them with hand or by using special tools designed for the purpose. Glasses worn by the user enable him to view 3D images, and a head-tracking mechanism controls what is projected. Projection of the images in the 3D space allows users to interact with the objects and at the same time touch and remodel them in the interactive environment. The users can load different objects into the 3D environment by incorporating the required code into the system.

Such VR systems can be conveniently used to model biological molecules by constructing them as virtual objects, and displaying them in the system. This could provide a useful platform for studying molecular structures and exploring diverse structural possibilities. This research project explores one such possibility in the field of DNA nano-technology by attempting to create spatial structures, which can be of possible use in the field of DNA based computation.

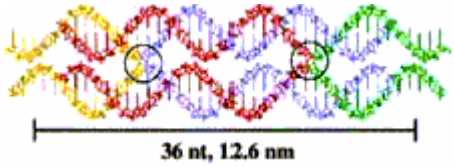

Figure 1: DNA tile or a Double Crossover DNA molecule: *The circular regions represent the crossover regions in between the red and green and, yellow and purple strands. The strands (yellow and green), which stick out on both sides, are called sticky ends.*

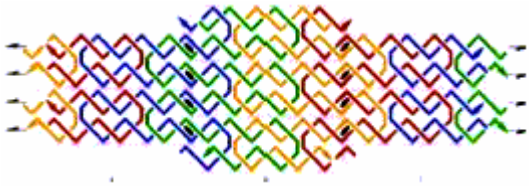

Figure 2: DNA tiled network made from individual DNA tiles: *The sticky ends from different tiles combine together to form a network of DNA tiles. Once can see sticky ends from DNA tiles sticking out on all sides in the above figure.*

DNA networks offer an immense potential in the field of DNA computation, i.e., the use of skillfully designed DNA structures to carry out scientific computation. DNA has been shown to have significant advantages over conventional electronic computing techniques that could allow a DNA- based computer to solve difficult computational problems in a reasonable time[2]. The technique for building such computers is still in a developmental stage. DNA designers are continuing their search for suitable DNA structures which could help in building a DNA-based computer.

The process of designing new DNA structures poses several challenges. First, it is not possible to physically interact with DNA molecules owing to their extremely small size. Second, drawing these complex structures on paper proves to be insufficient, since it lacks important structural details. Even some of the traditional 2D interfaces prove to be insufficient, since they restrict 3-dimensional structures to a 2 dimensional space, thus not providing enough scope for creativity and exploration. All the above shortcomings can be overcome by developing a 3D interface for DNA design. This project attempts to help in this design process by initiating the development of a 3D interactive interface for constructing, manipulating and combining DNA molecules to form DNA networks.

Using this interface, DNA molecules comprised of single strands and/or double strands (fig. 5) can be displayed and placed arbitrarily in space using the physical *Tongs* (fig. 3, 8a, 8b). Furthermore, these molecules can be joined together to form a DNA tile (fig.1) by using the *Ray Gun* (fig. 4, 6, 7). These tiles can be put together to form a network using the *Ray Gun* as well. This interface offers the options for changing and experimenting with the DNA structures at any stage of construction.

TOOLS USED

Virtual objects are displayed in front of the 3D-immersive computer provided by the system [1] .The position, structure and orientation of the objects are manipulated with the help of numerous hardware tools provided with the system [1]. The two tools, which were used in this research project, are the *Tongs* (fig. 3) and the *Ray Gun* (fig. 4).

***Tongs*:** The system provides the user with two pairs of sensed tongs [4], which are used to displace objects in space (fig. 3). Physical motion of these tongs regulates the spatial displacement of the objects. This tool was of prime importance in the project since it helped in achieving desired arrangement of DNA molecules in space.

Figure 3: Tongs: *The tong can have three states:*
a. Open (top): in this state the tong is idle and the sensors are not activated.
b. Weakly closed: in this state (middle one), the tong can be used in two modes: to move single DNA molecule by selecting any base, or to move several molecules together by grabbing on to free space.
c. Tightly pressed: in this state (bottom), a menu is displayed that enables the mode for the tong.

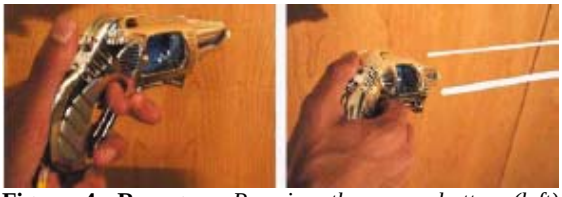

Figure 4: Ray gun: *Pressing the menu button (left) displays the options for drawing hydrogen bonds (thick line) and phosphate bonds.*

Ray Gun: This is a hardware tool (fig.4) provided with the system [1], which was originally designed to join bases in DNA molecules by creating hydrogen or phosphate bonds between them [4]. In the new interface, this tool serves the purpose of joining different DNA molecules by joining the respective bases.

METHODS

This 3D interface has been designed and implemented in an object-oriented manner using C++ and the utilities offered by the open GL graphics library. The underlying code was written following a strict hierarchical pattern of classes. These classes contain the code required to construct and display different constituents of a DNA tiled network

A DNA tile is made up of multiple DNA strands. In such a structure, two different helices are connected together at the crossover points (the circled regions of fig. 1), and the single strands from double helices extend to form the sticky ends. Displaying a tile required the functionality to display double helices, sticky ends and the connection or crossover points between different bases.

Creation of DNA Double-Helix

A new double helix class was implemented in order to handle all DNA manipulations at the molecular level. Originally, such manipulations in the system were handled at the level of bases only [3] due to the absence of a double helix class. This implementation simplified simultaneous interactions with multiple DNA double helices making it possible for the user to enforce structural and positional changes at a higher level, namely, the molecular level.

The double helix class has been implemented in accordance with the molecular restraints and structure of a DNA molecule. This class inherits data declarations and functions from a lower level 'Base' class. Helices can be drawn in space by providing the class constructor with desired forward and backward strands as arguments. Functions were written for twisting and stretching a DNA double helix, in order to add more functionality to the class. This class was made compatible with the hardware tongs. As a result, the tongs can detect and select different bases on a double helix whenever they are brought sufficiently close to any base on a helix (fig. 8a, 8b). The helix molecule can be dragged in the desired direction by holding on to the selected base, or by simply holding on to space, and by moving the tongs in any direction.

Construction of Sticky ends

In order to represent the sticky ends of a DNA tile, a new 'Single Strand' class was implemented. Using this class, single strands in the forward/backward direction can be drawn by providing the class constructor with the desired strand and a Boolean variable representing the direction of the strand. This class was also made compatible with the hardware tongs, so that every base on a single strand can be detected and selected by the hardware tongs. The tongs can be used to move the single strand in the desired direction. Hence, Sticky

ends can be constructed by calling the single strand constructor with the appropriate arguments.

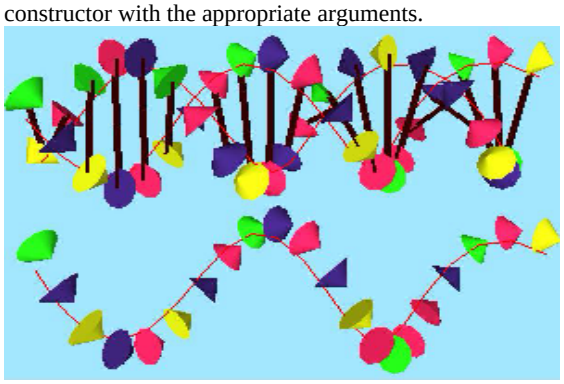

Figure 5: Construction of DNA molecules: *A Double Helix and single strand displayed in the system environment. The cones on the molecules represent the bases.*

Putting helices and sticky ends together

In a DNA Tile, the double helices are connected together at the crossover points. The crossover points in this interface are represented by drawing phosphate bonds (fig. 6,7) between two helix molecules. Similarly, the bases from the sticky ends in a DNA tile are hydrogen bonded to the bases in their corresponding double helix molecules.

In order to construct hydrogen or phosphate bonds in space, two previously written classes were used. A phosphate/hydrogen bond between two bases can be drawn by providing the appropriate class constructor with the physical pointers to those bases.

Saving and Retrieving Structures

Different constituents of a DNA tile should be displayed in the system environment simultaneously so that they can be connected together to form the tile. This necessitated the ability to save DNA structures and parts, such as double helices, single strands/sticky ends, and the bonds, and load them during execution time. Therefore, 'Save' and 'Open' functions supporting XML format were implemented for these structures.

While a structure is being displayed in the execution window, it can be saved by selecting the 'save' option from the file menu. Similarly, it is possible to load and display previously saved structures in the system by selecting the 'Import' command from the file menu and selecting one file at a time. Multiple objects loaded into the system in this manner are saved by maintaining a list of all objects in space and calling the appropriate save function for every object in the list whenever the 'save' option is selected from the file menu. A similar approach was applied to load a file comprised of different DNA components.

Ray gun: Putting elements together

The interface provides the user with the facility to join bases using phosphate or hydrogen bonds. This was made possible with the help of the *Ray Gun*, which is a hardware tool built in the system. The hardware gun can be used to join different objects together by pointing it at the desired objects. For example, it can be used to join two bases by pointing at them one after another. A ray emerges from the *Ray Gun*, which becomes attached to an object when it reaches sufficiently close to the object.

The task of joining DNA molecules required interfacing all the DNA classes with the hardware gun so that the gun can detect these objects in 3D. In order to accomplish this, some changes were made in the *Ray Gun* class so that the gun can form both hydrogen and phosphate bonds between the bases. Functions were written in the double helix and single strand classes so as to make these structures and their constituent bases gun-detectable. Consequently, bases from different molecules (single strands or double helices) can be joined together by using hydrogen bonds or phosphate bonds.

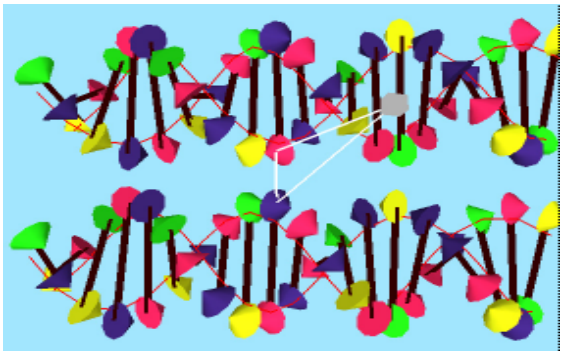

Figure 6: Before formation of phosphate bond: *Two double helices are being connected by using the Ray Gun. A triangle shape visible between the two bases implies the formation of phosphate bond.*

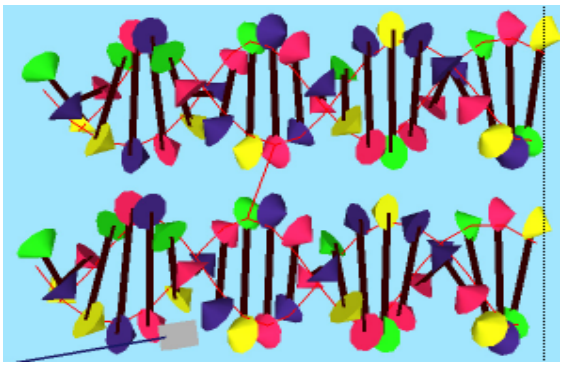

Figure 7: After formation of phosphate bond: *Red colored phosphate bond can be seen between the two helix molecules*

Construction of Tiles and Networks

After the functionality for joining bases was implemented, bases from different molecules could be joined together using the *Ray Gun* to represent the crossover points (phosphate bonds) in a DX molecule leading to the construction of a DNA tile (fig. 10), or double crossover DNA molecules in space. Construction of tiles enabled the construction of networks, since the interface allows the sticky ends from different tiles to be joined together using hydrogen from using the *Ray Gun*.

Figure 8(a): Interaction with tongs: *Pressing the tong's menu displays the two modes: the yellow cone mode (described first in fig. 3b) and the purple circle mode described second in fig. 3b).*

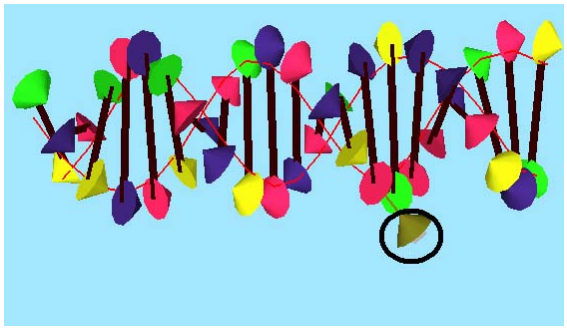

Figure 8(b): Interaction with tongs: *Tong in the yellow cone mode can be seen connected to a base in the molecule.*

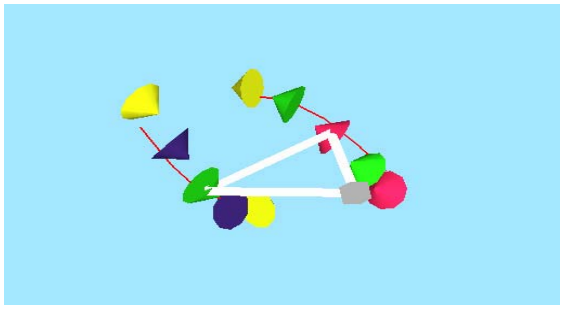

Figure 9 (a): Before formation of hydrogen bond: *Two bases from different single strands being connected by using the Ray Gun. A triangle shape visible between the two bases implies the formation of hydrogen bond.*

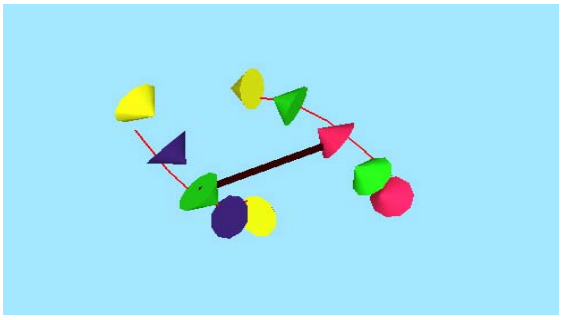

Figure 9 (b): After formation of hydrogen bond: *Black colored thick hydrogen bond can be seen between the two selected bases.*

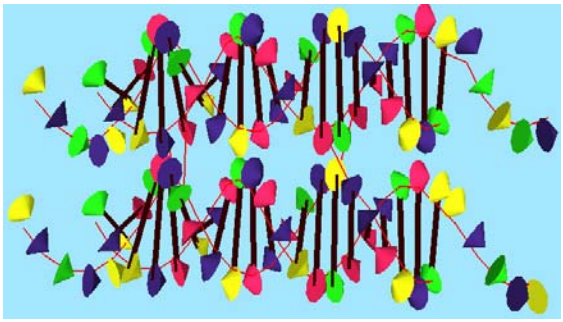

Figure 10: A DNA tile: *A DNA tile constructed from joining double helices with each other and corresponding sticky ends.*

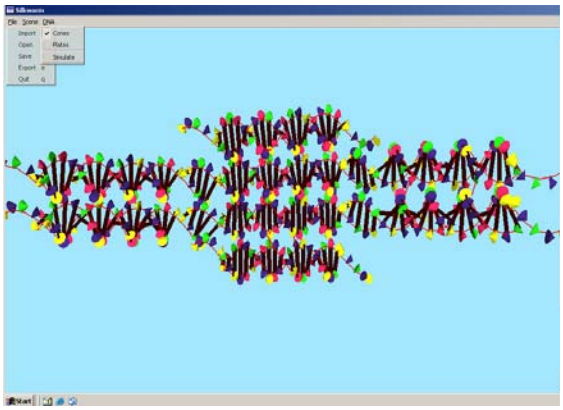

Figure 11: A DNA network: *DNA network constructed from joining several DNA tiles*

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