NAVRNA:
Visualization – Exploration – Editing of RNA

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ABSTRACT

In this paper we describe NAVRNA, an interactive system that enables biologists or researchers in bioinformatics to visualize, explore and edit RNA molecules. The key characteristics of NAVRNA are (1) to exploit multiple display surfaces (2) to enable the manipulation of both the 2D view of RNA called secondary structure, as well as the 3D view of RNA called tertiary structure while maintaining consistency between the two views, (3) to enable co-located synchronous collaborative manipulation of the RNA structures and (4) to provide two-handed interaction techniques for navigating and editing RNA structures and in particular a two-handed technique for bending the structure.

Categories and Subject Descriptors

H.5.2 [**Information Interfaces And Presentation**] User Interfaces - *Graphical user interfaces, Interaction styles, User-centered design*. I.3.6 [**Computer Graphics**] Methodology and Techniques - *Interaction techniques*.

General Terms

Design, Human Factors, Algorithms.

Keywords

Visualization, RNA structure, Tabletop display, Distributed display environment, Two-handed interaction.

1. INTRODUCTION

NAVRNA is an interactive system for visualizing, exploring and editing RNA molecules. RNA is a ribonucleic acid transcribed from DNA (deoxyribonucleic acid) that serves as the template for translation of genes into proteins. The structure of RNA is often studied based on three different graphical representations as shown in Figure 1: (1) The primary structure comprises the linear string of amino acids also called bases. RNA is primarily made up of four different bases: Adenine, Cytosine, Guanine and Uracil. It is usually represented as a string (Figure 1-a) in the alphabet {A, C, G, U}. (2) The secondary structure is a 2D representation that is a simplification of a more complex three- dimensional folding. Figure 1-b represents the usual display of an RNA secondary structure. The secondary structure is created when some amino acids in the sequence bond to others, forming a two-dimensional structure. (3) The tertiary structure corresponds to the geometric form that the RNA adopts in space as shown in Figure 1-c. The secondary structure corresponds to an unfold view of the 3D geometric form of RNA: as a consequence, all bases are visible, but close bases in tertiary structure can appear far in the secondary structure.

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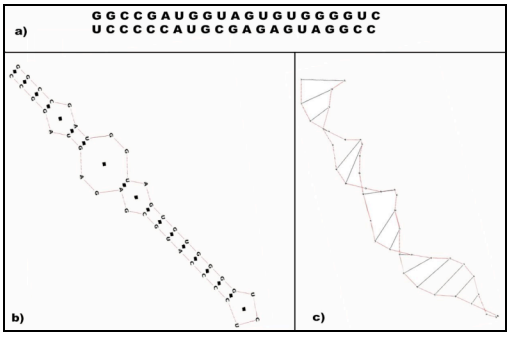

Figure 1: Three representations of RNA using a small number of bases. a) The primary structure. b) The secondary structure (2D) and c), the tertiary structure (3D). These representations are created from the RNA file: 1A51.pdb (Protein Data Bank: http://www.rcsb.org/pdb).

When studying RNA, biologists use these representations. In particular before dedicated visualization tools such as S2S [6] were developed, the biologists used to draw the secondary structure by hand. It is therefore important to respect the visual constraints used by biologists: for example stems, hairpins, internal and multibranch loops should be displayed the same way they would be drawn by hand since they constitute key patterns for the biologists' studies. NAVRNA is an interactive system for manipulating these different graphical representations of RNA.

In this paper, we first focus on the key issues that guided the design of NAVRNA and briefly introduce its design process. We then describe the underlying hardware and software platform and present the designed interaction techniques. We conclude the presentation of NAVRNA by comparing it with existing tools.

2. DESIGN PROCESS AND ISSUES

As part of a multidisciplinary project that includes combinatorists, biologists, researchers in bioinformatics as well as in HCI, we had the opportunities to focus on the biologists' activities and tasks. For identifying the requirements, we did not fully perform a real task analysis (i.e., explanation by the biologists of her/his relevant work phases, away from the work setting) or a complete activity analysis (i.e., observation and video recording of the activity of the biologists on site). Nevertheless for supporting the iterative design with biologists, we developed scenarios as storyboards (work scenarios) that described the system to be developed. Figure 2 presents some snapshots of such storyboards that were presented to biologists during the design. The results of this

collaboration with biologists prompted us to focus on the following issues for the design of the NAVRNA system:

Multiple views: On the one hand, the size of manipulated data space and the occlusion due to the folding up of the molecule in space make study directly on the tertiary structure difficult. On the other hand, although the secondary structure can be graphically manipulated by the users, such a 2D representation does not fully convey how the RNA functions and interacts with its environment. The two views are therefore complementary and visual consistency must be maintained at all time.

Exploration: In order to explore the molecules, efficient interaction techniques must be designed for translating, zooming and rotating the structures.

Editing: Editing tools of the secondary structure are useful for adding or deleting bases as well as edges. Moreover, deformation of the secondary structure can be used for transforming the 2D representation to a known pattern as well as for making two RNA chains that are close in the tertiary structure, close within the 2D representation.

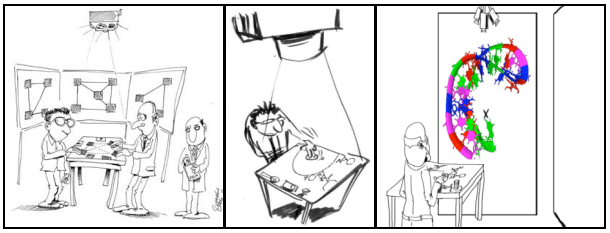

Figure 2: Some snapshots of storyboards to present design solutions to biologists. For example, the left snapshot presents an augmented office where biologists work collaboratively on RNA representations.

We did not address in NAVRNA tasks of comparing and aligning RNA secondary structures, that have been extensively studied [2]. In [5], an interactive tool is defined for comparing RNA secondary structures, where different alignment algorithms can be plugged in. Such important tasks of secondary structure comparison can be the focus of further work for extending the NAVRNA system.

The NAVRNA system focuses on the above listed design issues with a high level of interactivity in spite of the size of data manipulated. Its design has been discussed with biologists based on storyboards. In the following sections, we present its hardware and software underlying platform and the developed interaction techniques.

3. NAVRNA

3.1 Hardware Setup

NAVRNA defines a distributed display environment made of (1) a table on which the secondary structure is projected by a video projector fixed on top of the table and (2) a whiteboard on the wall on which the tertiary structure is projected by a second video projector (Figure 3). The NAVRNA distributed display environment enables co-located synchronous collaborative manipulation of the RNA structures by several biologists. Interaction on the table is based on the magic table [3] and consists of the manipulation of tokens that are tracked by a vision-based mechanism. A tracking video camera is therefore fixed on top of the table, whose field of view is set to encompass the entire projected image on the table.

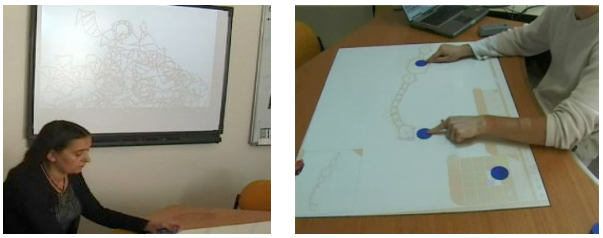

Figure 3: NAVRNA distributed display environment and two-handed interaction on the table.

3.2 Software Platform

For interaction on the table, we reused the tracking mechanism of the magic table [3]. The salient properties of the magic table in the context of NAVRNA are to allow multiple users to simultaneously interact with two hands as shown in Figures 3 and 4. In this version of the magic table, tokens are all the same, and their blue color facilitates the tracking mechanism. We plan in the near future to experiment with a new version of the magic table that is based on finger tracking instead of using tokens [10].

For drawing the secondary structure as well as the tertiary structure, we reuse the Tulip toolkit dedicated to large graph visualization [1] and its extensions for pdb files. We start by loading a pdb file (Protein Data Bank: http://www.rcsb.org/pdb), then Tulip displays the tertiary structure as well as the automatically derived corresponding secondary structure [2].

The interactive system NAVRNA is developed in C and C++. It is built on GLUT, the OpenGL Utility Toolkit. NAVRNA runs on Linux platform on a laptop with a 2 GHz Pentium 4 processor, and a NVIDIA GeForce FX Go 5200 graphic card with 64 MB of memory.

3.3 Interaction Techniques

We now describe the main interactive techniques developed in NAVRNA according to the three key design issues exposed above: visualization, exploration and editing.

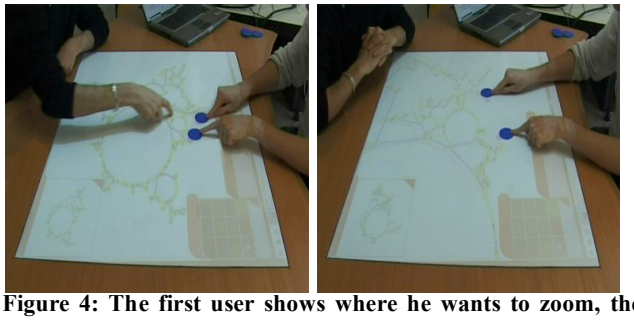

Figure 4: The first user shows where he wants to zoom, the second user is rotating and zooming the RNA representation with two hands. The distance between the two tokens defines the zoom factor.

3.3.1 Visualization

The NAVRNA distributed display environment enables the biologists to visualize both the secondary and tertiary structures. One starts by opening an RNA pdb file and the two structures are displayed.

On top of the secondary structure projected on the table, the biologists can manipulate a transparent window with two hands for specifying a zone that will be highlighted on the 3D tertiary structure displayed on the whiteboard. On the whiteboard, the

complete 3D molecule is displayed with some parts highlighted. When the biologists rotate the secondary structure on the table, the tertiary structure is rotated accordingly. But when the biologists translate or zoom the secondary structure displayed on the table, it has no effect on the display of the tertiary structure because biologists always want to keep a global 3D view. In this configuration where the secondary structure is projected on the table and the tertiary structure on the whiteboard, the table is designed as a tool to explore the tertiary structure projected on the whiteboard by highlighting parts of it and by allowing rotation. Nevertheless, it is possible to modify the configuration so that the tertiary structure is projected on the table and the secondary structure on the whiteboard.

More generally, the software architecture of NAVRNA according to the PAC-Amodeus [11] software architecture model enables us to easily add or remove views and interaction surfaces. Moreover, we have developed a meta-User Interface (meta-UI) on a PDA for managing the views that is not yet fully integrated in NAVRNA. Figure 5 presents the interface for managing the views among multiple interactive surfaces, including the table and the wall, by direct manipulation on the PDA.

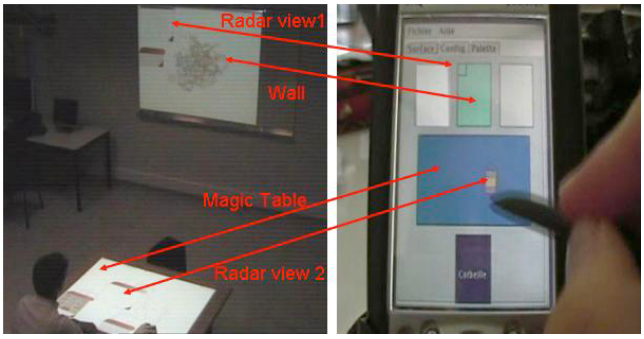

Figure 5: Meta-User Interface on a PDA for managing the views among multiple surfaces.

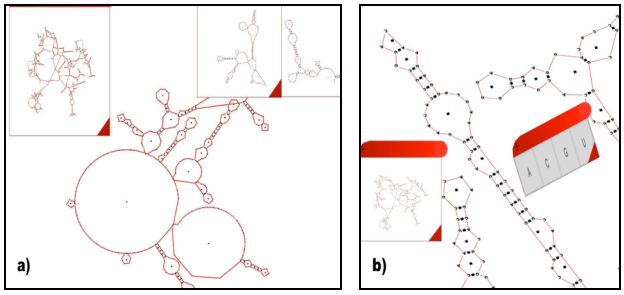

Figure 6: a) Projected tabletop display: overview on the left and two windows on the right where selected parts of the secondary structure are copied. b) ToolGlass for editing the structure.

Finally when the secondary structure is displayed on the table, an overview is also displayed (Figure 6-a). Moreover it is possible to select a part of the secondary structure to be kept apart in a separate window called copy-window. Several copy-windows can be created as shown in Figure 6-a.

3.3.2 Exploration

For exploring the structure, one single mode enables pan-zoom-rotate actions. This mode is selected by putting a token on the corresponding button of a palette shown in Figure 7. Pan, zoom and rotate actions are then performed on the structure displayed on the table by moving tokens (Figure 4). Such actions play a key role in NAVRNA for rapidly exploring the visualized structures but also for helping the collaboration around the table: Indeed orientation plays a major role in comprehension, coordination and communication [8].

With one hand, a panning action can be performed by sliding a token. With two hands, the biologists can zoom and rotate the view displayed on the table in a continuous gesture without switching mode. This exploration metaphor is similar to a technique described in [9]. For example for zooming, the distance between the two tokens defines the zoom factor. It is called the "stretch and squeeze" metaphor in [7]: Pulling one's hands apart stretches the structure (to get more detail: zoom in) while pushing one's hands together squeezes the structure (to get a more global view: zoom out). If the user is dragging the two tokens in the same direction, a compound panning action is performed. As a consequence by continuously manipulating two tokens, the user can perform pan-zoom-rotate actions without tool switching: such two-handed interaction encourages rapid exploration of the visualized secondary and tertiary structures as well as collaboration amongst the biologists.

3.3.3 Editing

For changing or adding a base within the secondary structure the biologist uses a toolglass [9] that contains four tools corresponding to the four amino acids (A, C, G, U), as shown in Figure 6-b. With the non-dominant hand, the biologist is moving the toolglass by sliding a token and with the dominant hand is putting a token on the selected acid. Such single action will result in the creation or modification of a base at the location under the corresponding acid button. Moreover, the biologist can create and delete edges. For example for deleting an edge, the biologist slides a token across the edge. Partial visual consistency is maintained between the secondary and tertiary structures while editing on the table. Bases and edges are coherent within the two views. Nevertheless it is important to note that the modification of a single base may imply a complete reconfiguration of the tertiary structure that we do not address in NAVRNA: this is a complex process called prediction of RNA folding that is currently being studied.

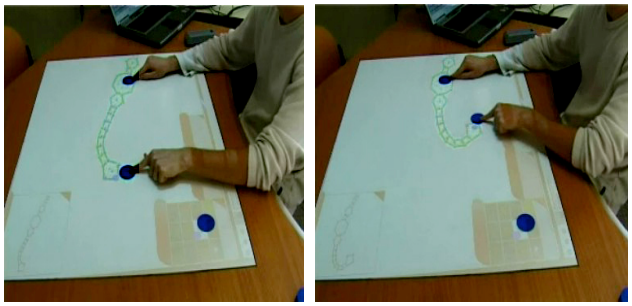

Figure 7: Bending an RNA branch.

Finally we have developed an efficient collaborative and interactive technique for bending the secondary structure. Such action has no effect on the tertiary structure. As explained in Section 2, deformation of the secondary structure is first useful when the biologists want to modify the automatic 2D representation for coming back to a known drawing. In addition it may help to understand the overall structure by putting next to each other RNA chains that are close in the tertiary structure. For deforming the structure, the biologists attach tokens to RNA

chains. By sliding the tokens the whole structure is deformed as shown in Figure 7: each token applies a force for deformation that is propagated until the location of another token. More than two tokens can be used so that the deformation can be performed by multiple users. The deformation algorithm respects the visual constraints such as the coherency of edge size and form of internal/multibranch loops. A special effort has been exercised to guarantee performance and high level of interactivity while writing the bending algorithm since several thousands of bases can be manipulated at a given time: the developed algorithm is O(n) in time, n being the number of manipulated bases.

4. RELATED WORK

Several tools have been developed for manipulating RNA. We distinguish two classes of systems: the virtual environments and the GUI tools.

First, virtual environments for molecular visualization and modeling can be used in a CAVE, with a head-mounted display or on screen with a data glove for navigation [4]. Several studies focus on collaborative virtual environment as well as force feedback based on molecular dynamics simulators. The key point of these tools is that the biologist is immersed within the 3D structure to be explored. We adopted another approach in NAVRNA by maintaining the biologists in the real world enabling them to take notes for example and by augmenting their physical environment.

Second several GUI tools for visualizing and manipulating RNA exist. They are all based on WIMP interfaces. While some of the tools are dedicated to visualize secondary structures, some of them focus on the exploration of tertiary structures. S2S [6] is an attempt to define a unified framework in which a user can easily display, manipulate and interconnect heterogeneous RNA data such as multiple sequence alignments, secondary and tertiary structures. Such tools offer more advanced functions in comparison with NAVRNA such as alignment of RNA secondary structures as well as complex algorithms for deriving the tertiary structure from a secondary structure (RNA structure prediction). Indeed in NAVRNA we focused on the interactive visualization techniques for exploring and editing the RNA structures. For example in S2S only the last helix selected within the secondary structure is highlighted within the tertiary structure. In NAVRNA we allow the user to select an area that can contain several helices and loops. Moreover the user can also select an area of interest within the tertiary structure, an action that is not possible in S2S. For exploring the structure using S2S, the user must always shift between modes (pan, zoom and rotate) and rotation is not continuous but step by step (5 degrees rotation step) as opposed to NAVRNA that allows continuous mode (Only one mode for pan-zoom-rotate) exploration of the structure with two-handed interaction. Finally, NAVRNA is the first collaborative and interactive tool capable of efficiently bending the secondary structure. Our system is then complementary to these tools: we could integrate the functions of S2S for example within the interaction framework defined by NAVRNA.

5. FUTURE WORK

Before enriching NAVRNA with new functions such as secondary structure comparison, we plan to perform experimental evaluation of NAVRNA with biologists. In particular we would like to examine how they collaborate around the table and the whiteboard. In addition we would like to further study two-handed interaction techniques on the table for manipulating the 3D tertiary structure displayed on the whiteboard.

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