

## **Virtual Reality for the visualization of high-dimensional relationships in bioinformatics**

*Subtitle*

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## Introduction

### 1.1 Background

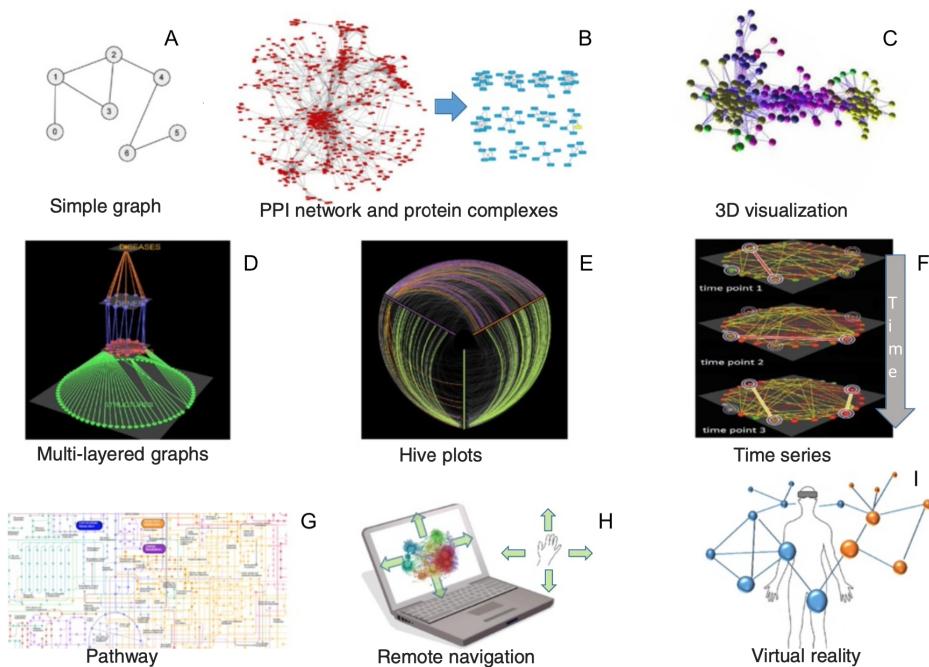
Technological advancement has revolutionized the field of genomics, which has led to a cost-effective generation of big amounts of sequence data. The sequencing of the first human genome (2002) took around 13 years and cost over \$3 million to complete. Nowadays we can resequence a human genome for \$1000 and can generate more than 320 genomes per week[6]. This technological innovation leads to the accumulation of vast quantities of genomic data, posing a tremendous challenge to scientists for effective mining of data to explain a phenomenon of interest[12]. New ways of analysing the produced data have been therefore necessary in order to discover interesting patterns and make the most out of it. No matter how much resources we use into extracting the data if we don't get anything interesting out of it.

Some of the main problems that researchers face when analysing genomic data are information overload, data interconnectivity and high dimensionality. Visualization is one way of facing this problems. For this reason it is very important to implement efficient visualization technologies that can lead to find new patterns and the extraction of good conclusions of the data.

In the field of system biology there are usually network representations where the nodes or bioentities are connected to each other, where these edges represent associations. Because of the improvements in technology, these networks can increase dramatically in size and complexity. We need therefore better

visualization systems and more efficient algorithms for the analysis of the data.

In 1.1 we can see a representation of the evolution for visualization of networks in system biology. From simple graphs in 2 dimensions, to 3D representations and nowadays also visualizations in virtual reality where we can interact directly with the data itself.



**Figure 1.1:** Visualization for network biology. a A simple drawing of an undirected unweighted graph. b A 2D representation of a yeast protein-protein interaction network visualized in Cytoscape (left) and potential protein complexes 3D identified by the MCL algorithm from that network (right). c A 3D view of a protein-protein interaction network visualized by BiolayoutExpress. d A multilayered network integrating different types of data visualized by Arena3D. e A hive plot view of a network in which nodes are mapped to and positioned on radially distributed linear axes. f Visualization of network changes over time. g Part of lung cancer pathway visualized by iPath. h Remote navigation and control of networks by hand gestures. i Integration and control of 3D networks using VR devices. Figure adapted[8].

Virtual reality (VR) is still a field under exploration and that can be of great help in network analysis. VR can be very powerful because it takes advantage of the way the human being perceives and analyzes things. We as human beings have a great ability to discover patterns, however we are biologically optimized to see the world and the patterns in 3 dimensions. VR is one of the best ways then for better discovery in spatial dimensions. It has been demonstrated that

VR help scientists work more effectively in fields like medicine [5][10][2], biology[11][9] and neuroscience[1][7], to cite some examples.

## 1.2 Challenges and research problem

This project focus mainly on solving the problem of visualization of high dimensional data from the MIxT project by using virtual reality. Furthermore the application allows the user to interact with the network created from the data in the virtual environment. It also allows the user compare the blood and biopsy networks at the same time in order to finde relationship, which wasn't possible in the MIxT web application as this only allows the user to visualize one network at a time.

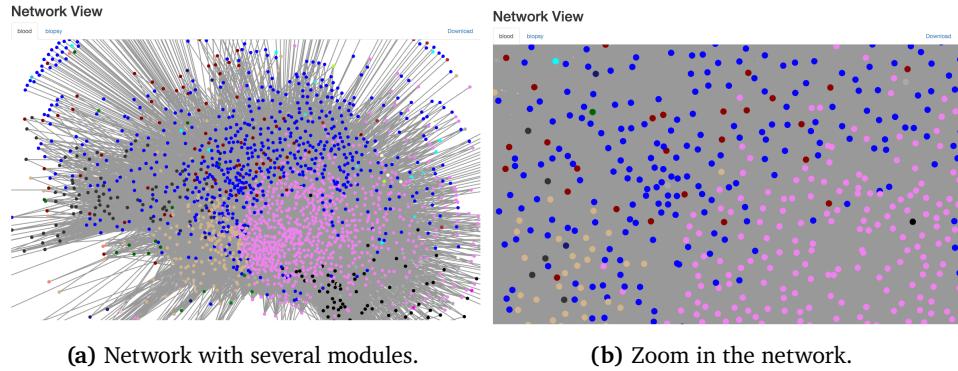
MIxT[4] is a web application for bioinformaticians. Among other tools, it offers a network visualization of genes which are represented as nodes in the network and where the edges represent statistically significant correlation in expression between two nodes. This tool was used in a study[3] that identifies genes and pathways in the primary tumor that are tightly linked to genes and pathways in the systemic response of a patient with breast cancer. When exploring a network in MIxT, it can be hard to understand the data and its relationships because there is too much data. This problem is easy to occur when there are too many node and edges. In figure 1.2 we can see an example of the network visualization from MIxT. As we can see in Figure 1.2a, there are many nodes and relationships among them and when we zoom in in the network, it becomes very difficult to understand the data and the relationships as shown in in Figure 1.2b.

The network is also in 2-dimensions and what we propose in this project is to use a virtual reality 3d visualization in order to cope better with this problem.

## 1.3 Proposed solution

## 1.4 Significance and Contribution

This project contributes in the exploration of the possibilities that Virtual Reality offers for visualization of big data in bioinformatics.



**Figure 1.2:** Network view of the MIxT application where nodes represent genes and the modules are represented by colors. Relationships are represented by grey lines that connect a gene with another one.

## 1.5 Outline

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## Bioinformatics in VR

This section will be dedicated to aspects about VR development and visualization of a gene network in VR. I will cover softwares used for VR development and aspects to take into account in VR like frameworks used, hardware, common problems in VR like locomotion. Talk also about clustering.

### 2.1 VR

#### 2.1.1 Software and frameworks for VR development

Unity3D<sup>1</sup> and Unreal Engine<sup>2</sup> are two popular programs for development of videogames and also virtual reality games and applications. They offer integrations for Oculus Quest and other VR devices in the market. In addition, Oculus Quest offers a development mode that can be activated once the glasses are connected to the PC. In this way the VR application can be tested directly on the VR device.

Virtual Reality development can also be done for the browser. WebVR<sup>3</sup> is an open specification that makes it possible to experience VR in the browser, no

1. <https://unity.com>
2. <https://www.unrealengine.com>
3. <https://webvr.info>

matter what VR device is used. We can find many web frameworks to build VR applications for the web that are based on WebVR. Some of these frameworks are A-frame<sup>4</sup>, React360<sup>5</sup> and three.js<sup>6</sup>.

### 2.1.2 Locomotion and ergonomics

- Physical movement
- Script movement
- Avatar movement
- Steering motion
- World pulling
- Teleports

### 2.1.3 Clustering analysis

Cluster analysis is used to classify objects or cases into relative groups called clusters. Unlike supervised machine learning techniques, in cluster analysis, there is no prior information about the group or cluster membership for any of the objects. We can find many clustering approaches, two of the most commonly used ones are k-means and DBSCAN.

The k-means algorithm starts by choosing k random centers which can be manually set. Then the data points are assigned to the closest center based on their Euclidean distance.

DBSCAN (Density-Based Spatial Clustering of Applications with Noise) is another algorithm that is based on the density of the data points. The algorithm identifies clusters and expands them by scanning neighborhoods. If it cannot find any points to add, it simply moves on to a new point hoping it will find a new cluster.

4. <https://aframe.io>

5. <https://facebook.github.io/react-360>

6. <https://threejs.org>

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## Related work

I will focus in this chapter on VR applications found in the literature for the visualization of bioinformatic data.

### 3.1 BioVR

### 3.2 CellexaVR

### 3.3 BigTop



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## MIxT VR

MIxT VR is a virtual reality application developed in Unity for the interactive visualization of a network of genes and their significant co-expression relationships between them. The genes nodes in the network and are represented as squared dots and the relationships are represented with lines between them. In Figure 4.1 we can see an example of the application running.

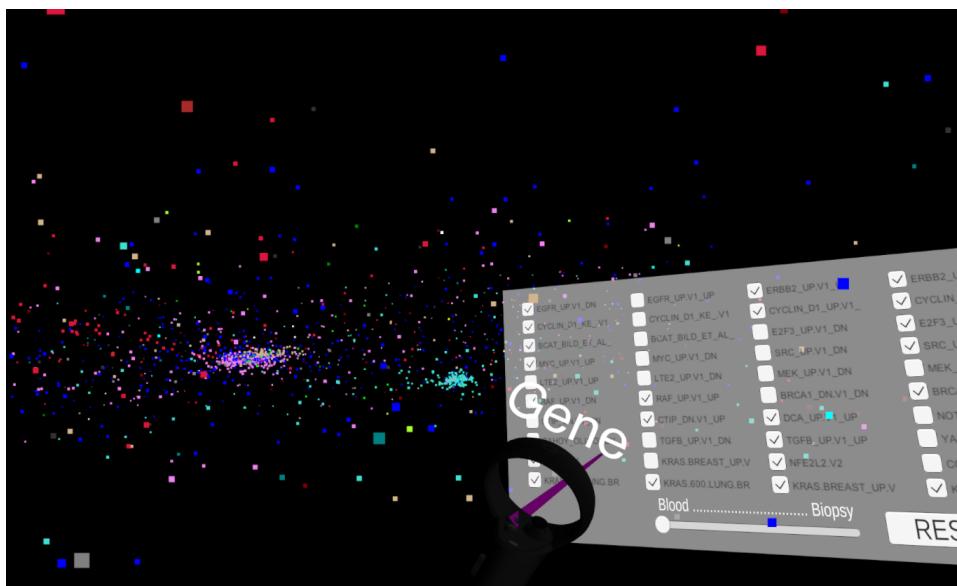


Figure 4.1: MIxT VR. Example of the application running on a Oculus Quest.

In order to explore the network, several features have been implemented with the purpose of enhance the experience of the visualization process. For example the user has the possibility to move around the network by teleporting to a different place. It is also possible to translate the network and scale it, allowing the user have a better view of the data. The user can also point at a node using the controller to show the name corresponding to that gene or node. Another feature is about entering into a menu where the user can filter the network according to gene sets that represent signatures of cellular pathways which are often dis-regulated in cancer. And finally it is possible also to switch the network from a blood dataset to a biopsy dataset and viceversa.

The datasets that are used for data visualization are the same ones that are used in the MiXt web application[4]. These datasets contain genetic information about a woman with breast cancer. The first one is a dataset from a blood sample and the second one is from the tumor.

## 4.1 Creation of the network in a 3D space

category	genes
brown	ARHGAP30 FERMT3 ARHGAP25 CD53 PLEK IRF8 DOCK2
cyan	SAFB MOB3A RAB35 ABR ASCC2 CDC37 ANKFY1 GLTSCR1
darkgrey	RAB40C ZNF213 ZNF263 PIGQ RHBDL1 RAB11FIP3
darkorange	TCEB1 MRPL13 ENY2 MTERF3 UBE2W WDYHV1

**Table 4.1:** Fragment of the dataset with the categories and the genes belonging to each category from the biopsy sample.

source	target	weight	id
AAMP	ARGLU1	0.102486209330144	AAMP-ARGLU1
ACADM	FOXN2	0.107506881676173	ACADM-FOXN2
ACADM	MBNL1	0.12269622045714	ACADM-MBNL1
ACADM	PPM1B	0.103496640767895	ACADM-PPM1B

**Table 4.2:** Fragment of the dataset used to build the network relationships of the blood sample.

## 4.2 Visualization of the network

In this section I will write about the VR techniques used to visualize the network in a good way.

#### **4.2.1 Locomotion**

How the player can move around the environment.

#### **4.2.2 Network manipulation**

Translation and scaling of the network for better visualization.

### **4.3 Filtering information in the network**

How the network is filtered.



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## Evaluation and discussion

Questions to answer in the evaluation chapter:

1. What is the performance of the Oculus Quest while using the application?  
We can use the Unity GPU Profiler for Oculus Quest and Go in order to see the performance.  
See: Getting Started w/ The Unity GPU Profiler for Oculus Quest and Go
2. Is there any performance issues when manipulating the graph? Like rotating, scaling, translation, filtering and changing the graph.  
We can use the Unity GPU Profiler for Oculus Quest and Go in order to see the performance.  
See: Getting Started w/ The Unity GPU Profiler for Oculus Quest and Go
3. How is this way of visualizing the graph better by using VR?  
Questionnaire for Bioinformaticians.
4. In what way can the application and the visualization of the graph be improved?  
Questionnaire for Bioinformaticians.



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## **Conclusion and future work**



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