

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

*Subtitle*

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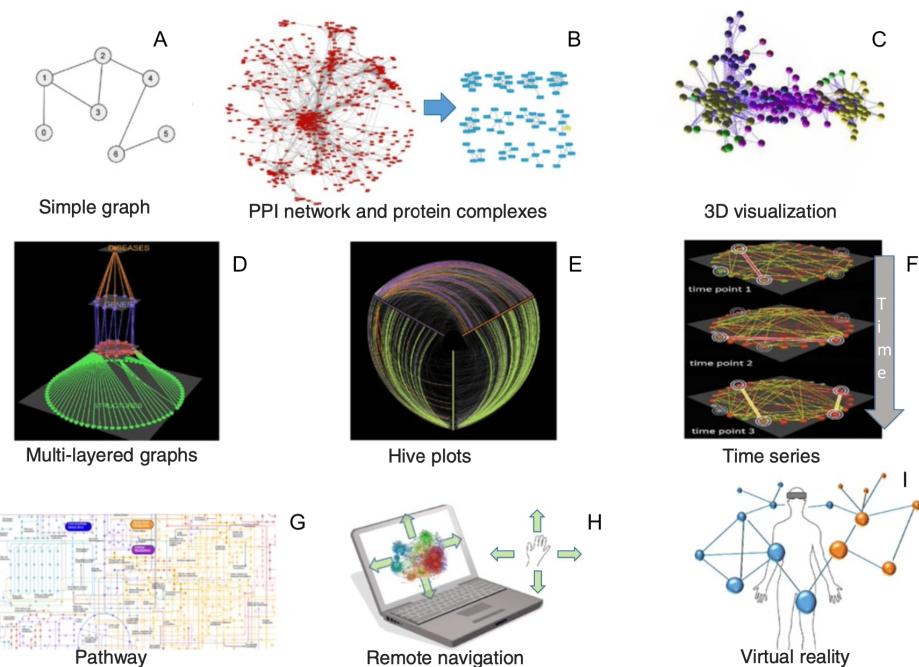
## Introduction

### 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[7]. 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. 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[14].

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[10].

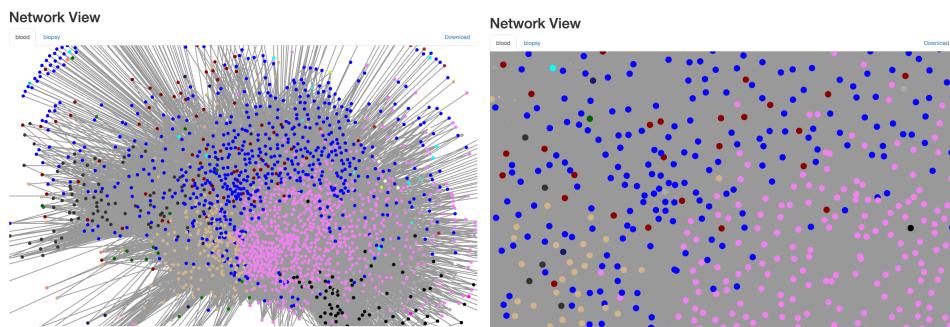
Virtual reality (VR) is still a field under exploration and that can be of great help in network analysis. VR can be very powerful because it takes advantage of the way the human being perceives and analysis things. We as human beings have a great ability to discover patterns, however we are biologically 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 [6][12][3], biology[13][11] and neuroscience[1][8], 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[5] 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[4] 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 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.



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

### **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.

### **1.5 Outline**

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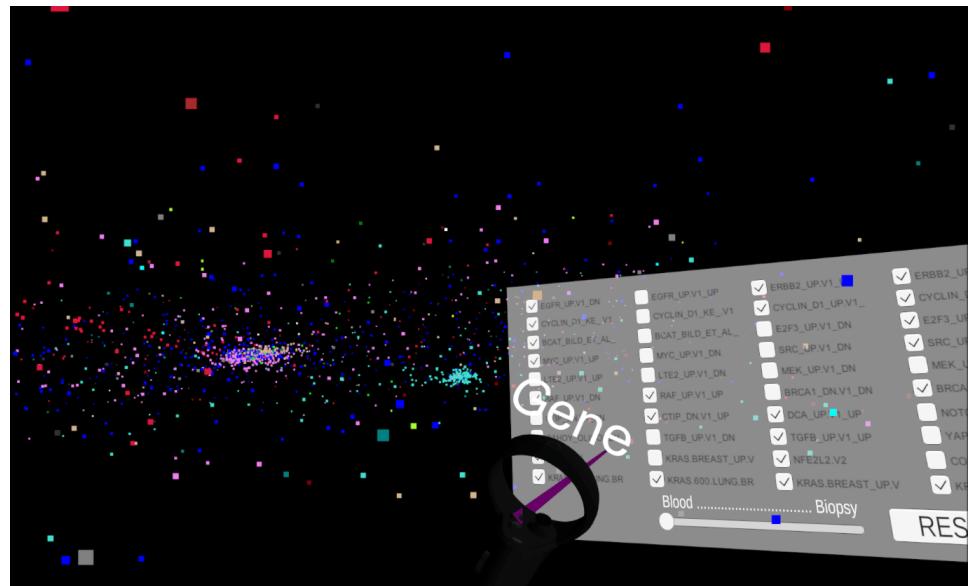
## **BigNet VR**

BigNet VR is a virtual reality application for the interactive visualization of large-scale networks in a 3D space. The networks are represented using nodes and connections between them. In order to explore the data, the user can walk around, scale the network, move it around, filter the nodes using a 2D interface and also interact with the nodes to get more information about them. In Figure 2.1 we can see an example of the application running.

BigNet VR works with a dataset that contains the information of the nodes and relationships of the network. This dataset needs to be obtained from an external source or application. Once we have our dataset we can load it to the application and then run BigNet VR using a Head Mounted Display or HMD for VR. Finally we can explore the network and interact with it to visualize the dataset in a VR experience.

The implementation of BigNet VR is done in Unity, a cross-platform game engine. This engine is used for a wide range of applications, especially for the development of videogames in 3D and 2D, VR applications and engineering solutions. The programming language used to develop the application inside Unity is C#. We also used VRTK, a VR toolkit to build VR solutions in Unity. As for the VR hardware, we used an Oculus Quest headset. This type of headset is an all-in-one HMD, which means that it doesn't need to be connected to a PC to run an application, it can be run inside the hardware of the headset itself. However during the development process, the headset needs to be connected to the PC and the application can be run directly from Unity.

For this chapter we will use dataset examples from MiXT to illustrate the concepts in this chapter. MiXT is a web application that is used for the visualization of bioinformatic data[5][4] and the datasets used here contain genetic information about a woman with breast cancer. There are in total 2 datasets, the first one is from a blood sample and the second one is from the tumor sample. In Figure 2.1 we can see an example of the application running using the blood dataset from MiXT.

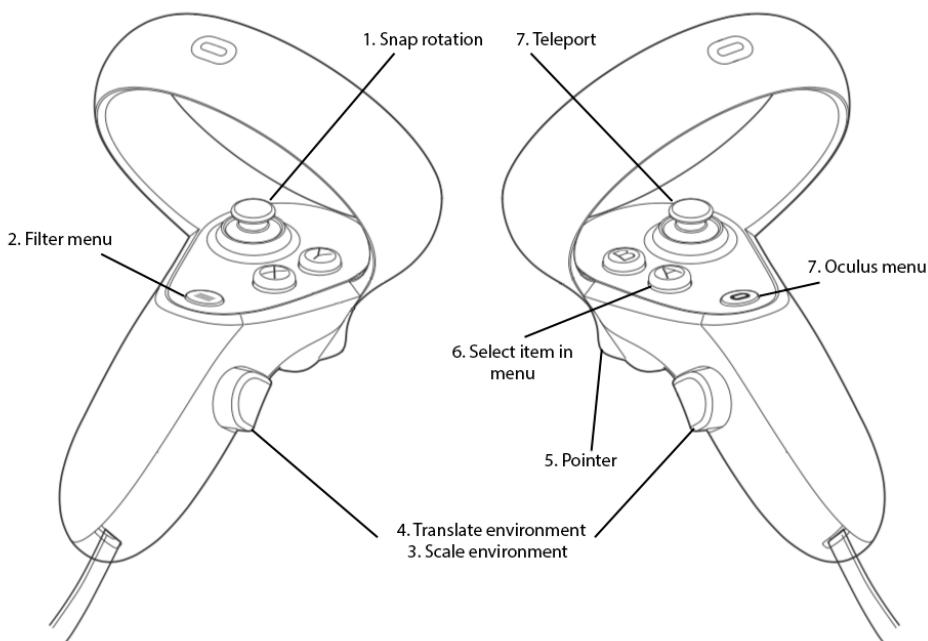


**Figure 2.1:** BigNet VR. Example of the application running on a Oculus Quest.

## 2.1 Visualization and interaction with the network

Virtual reality headsets offer a rich immersive experience. It's not only about immersing the user into a 3D environment, but also giving the user the possibility to interact with the environment itself. This makes it possible to build complex VR applications where the user can do almost anything in a virtual world. Some examples of what it is possible to do in a VR application are moving around by teleporting to a different spot, grabbing objects, interact with the environment, 2D interfaces and menus and interact with them, etc. In this section we will explain the techniques that we have implemented to visualize and interact with the network. These techniques correspond to how the user can move around in the network and how the user can manipulate it.

Oculus Quest is an all-in-one VR headset and so it doesn't need a PC nor wires to run the applications. Apart from the headset it comes with 2 controllers, one for each hand. These controllers have inputs as buttons, thumbsticks and triggers that can be used to activate actions in the VR application. We have used some of these inputs available in the controllers in BigNet VR and mapped them to different actions that allow the user interact with the network and the environment. In Figure 2.2 we can see which action correspond each input from the controllers. We will explain now the different methods that we use in BigNet VR to visualize the data.



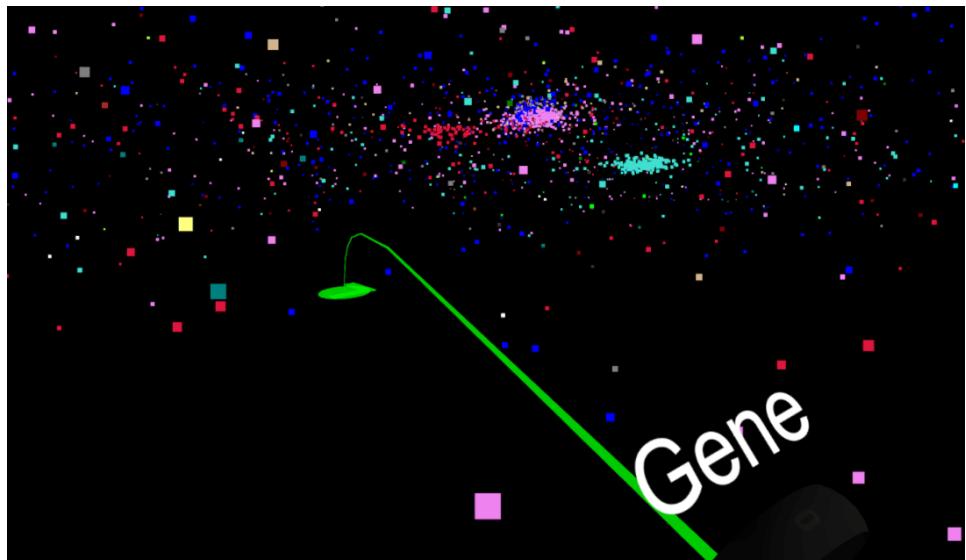
**Figure 2.2:** Mapping of the Oculus Quest controllers for the different actions implemented in BigNet VR. 1. Snap rotation. 2. Filter menu. 3. Scale environment. 4. Translate environment. 5. Pointer. 6. Select item in menu. 7. Oculus menu. 7. Teleport. Adapted figure from Oculus developer's page[9].

### 2.1.1 Locomotion

Locomotion is one of the most important ways of interaction in virtual reality experiences. It can be defined as a self-propelled movement in virtual environments. Even though moving around is not the main goal in most of VR applications, it is an important aspect for the user's perspective in order to move the user's viewpoint in the virtual world and navigate around this world.

Locomotion can have an strong influence in the user's experience. A poorly designed locomotion technique can reduce the user's immersion and even introduce motion sickness, which is related to the movement that the locomotion technique produces. HMDs like Oculus Quest allow the users to control the position and the orientation of the viewpoint by moving their heads and walking. However large virtual environments such as BigNet VR needs a big physical tracked area which cannot be covered by just walking around. It is for this reason that we need to use a locomotion technique that makes it possible to move around without the having to walk[2].

The locomotion technique that we use in BigNet VR is called teleportation. It consists in choosing a spot on the floor were we want to teleport to. To do this the user has to move forward the thumbstick from the right controller (see "7. Teleport" from Figure 2.2). In addition it is possible to choose which direction the user will face once the teleportation is done. To do this we just need to rotate the same thumbstick to the desired direction. Once the user releases the thumbstick, a black flash will show followed by the new position. This black flash is very important when implementing some techniques because it prevents from producing motion sickness and disorientation.



**Figure 2.3:** Teleportation technique. The user can use the joystick from the right controller to teleport to a different spot. To choose the spot a parabolic arc will appear.

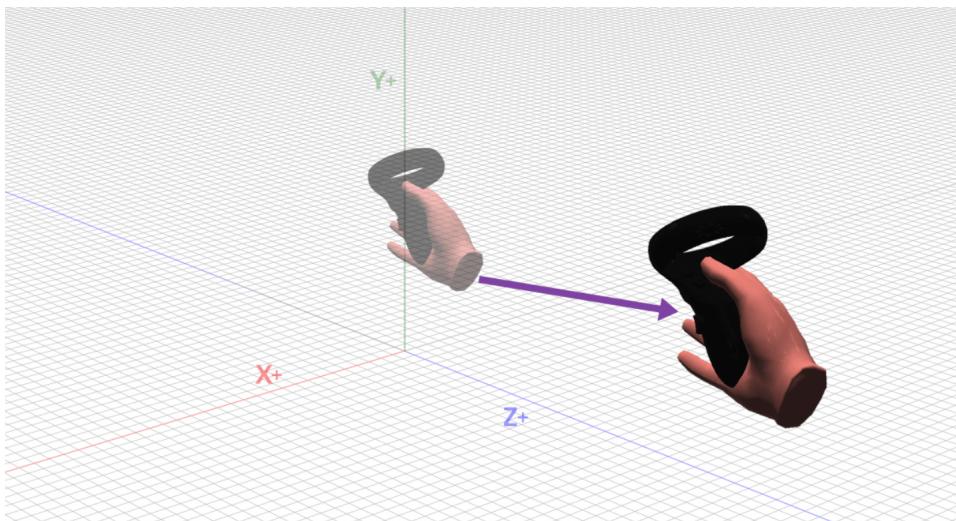
In Figure 2.3 we can see an example of how the teleportation technique is used in BigNet VR. As we can see, a parabolic arc is shown as if we are throwing an object to the spot where we want to teleport. A round green circle is also shown on the floor on the place where we will teleport. This includes also an

arrow, indicating the direction that we will face once we are teleported.

In addition to the teleportation, we have also added the possibility to rotate to the left or to the right so that the user doesn't need to move to see around. This action is triggered using the thumbstick on the left hand (See 1. Snap rotation in 2.2). By moving the thumbstick to the left side, the camera will rotate  $45^\circ$  to the left side, and  $45^\circ$  to the right side if the user moves it to the right side. A black transition is also used before the rotation happens to avoid motion sickness.

### 2.1.2 Translation of the network

By teleporting to different places in the environment we allow the user see the network from different perspectives. However it is also interesting being able to move the network and specially move in a precise way so that the user has more control over it. The user might for instance be able to see the network or a specific node or cluster from above or also from below. To do this we have implemented a functionality to translate the network to wherever we want.



**Figure 2.4:** Translation of the network functionality. The user holds the translation button on the Oculus controller and moves the hand to the direction where he or she wants the network to translate.

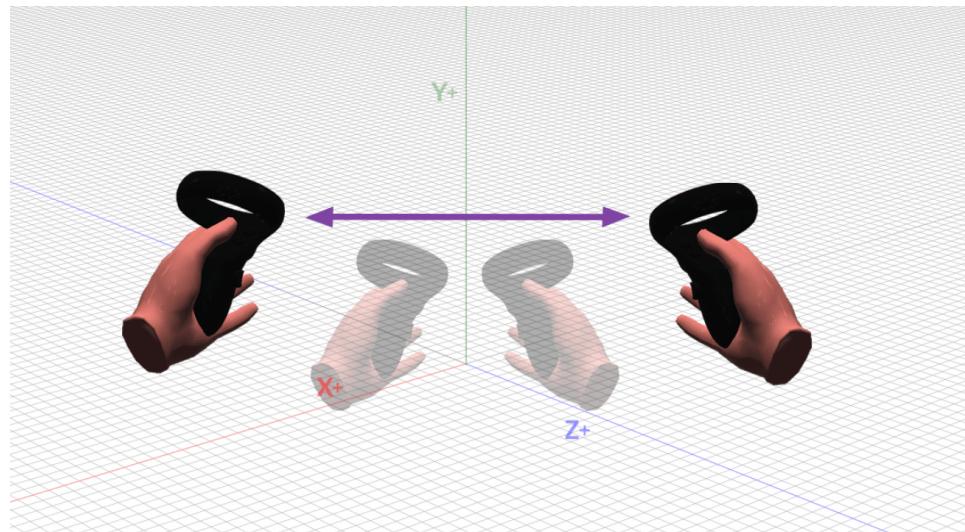
In order to translate the network in BigNet VR, the user just needs to press on the "4. Translate environment" hand trigger from the right controller as shown in 2.2. Then the user needs to keep holding this trigger down and move the hand to the direction to which the user wants the network to move to. This

intuitive approach feels like we are just pulling from a rope connected to the network and we just move it to the direction we want.

### 2.1.3 Zooming in the network

When exploring a big network with hundreds of nodes, sometimes the information can be too crowded. In our example dataset that we use in BigNet VR, there are some clusters of nodes that have too many nodes close to each other and it gets very hard to visualize them properly. A way to cope with this problem is for instance by "zooming" in the part of the network that we want to explore better. We implement then a scaling functionality that makes the network bigger or smaller and so simulating a zooming action.

The way we implemented the zooming functionality in BigNet VR is by using the hand triggers with the name "3. Scale environment" shown in Figure 2.2. In the first place the user needs to press and hold this trigger from both right and left controllers and then the user needs to expand or contract the arms, as if we were stretching out or contracting the network itself. This is also an intuitive action to do since the user might think that we are actually stretching the network with the hands.



**Figure 2.5:** Zooming in the network functionality. The user can hold the scaling buttons on the Oculus controller to make the network bigger or smaller. In this example if we stretch our hands outside, the network will expand.

In Figure 2.5 we can see a visual example of how the zooming works using the Oculus controllers. In this example the user is stretching the hands out in order to make the network bigger. The user starts in an initial position, then holds

the zooming triggers from both controllers and then moves the hands out. If we wanted to make the network smaller we would do the opposite action, by contracting the hands to the inside.

#### 2.1.4 Interaction with the nodes

BigNet VR provides also detailed information about the data that is being displayed. The user can interact with the nodes of the network to obtain information about each of them. In our example, the nodes represent genes and the user might be interested in knowing which gene name corresponds to a specific node. The action that we need to do to obtain the name of the gene is to point at the node that we are interested in and press the "5. pointer" index trigger on the right controller (see 2.2). When we press this trigger, a laser pointer will appear from the virtual controller in BigNet VR. When we point to a specific node with the pointer, we will get the name of that gene node that will be displayed in a rendered text.

[User figure showing how the pointer works and explain it. This part of the implementation needs to be improved.]

#### 2.1.5 Node relationships

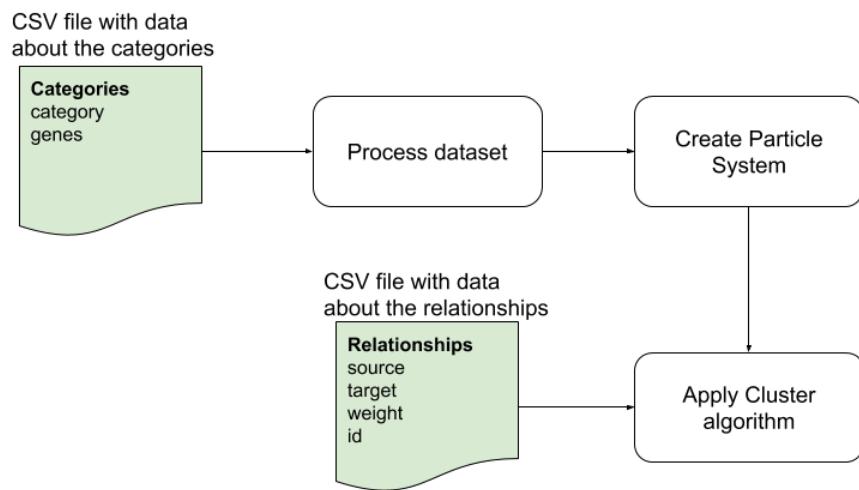
Finally, our dataset has information about the relationships between the nodes. BigNet VR is implemented to show also this information. There can be many relationships in the dataset so that's why we don't show them all of them at the same time, but only those of the nodes who are closed to the user. The way that these relationships are represented is with lines between one to another node. These lines disappear once the user moves away from the nodes.

[User figure showing how the relationships are shown in the application and explain the example. This part of the implementation needs to be improved.]

## 2.2 Building the network

To build the network, BigNet VR uses datasets that have been created from an external source. The datasets have to be in CSV format and we need 2 datasets in total in order to build the network. The first one contains the information about the categories and the nodes that belong to each category. The second dataset has information about the relationships between each of the nodes.

The following diagram in Figure 2.6 explains in a general way, what steps we follow to build the network in Unity. We start with the 2 datasets described before, containing the data for the network. We start processing the dataset with the categories and use this data to build a particle system object in unity. Each particle from the particle system corresponds to a node. We also add to each particle a color, which is related to the category that the particle belongs to. Finally we apply a cluster algorithm using the data from the dataset with information about the relationships.



**Figure 2.6:** Diagram explaining how the network is built in Unity.

Following our bioinformatic network example, in Table 2.1 and Table 2.2 we show an extract of how the datasets look like. Table 2.1 has the data about the nodes or genes in this case and the category to which each node belongs to. This categories are named by colors and these color names will be used by BigNet VR to color each particle of the particle system. Then in Table 2.2 we have the information about the relationships. This dataset can be very extend because row of the CSV file corresponds to a relationship between 2 nodes or genes in this case and one gene can be connected to many other nodes.

| category   | genes                                           |
|------------|-------------------------------------------------|
| brown      | ARHGAP30 FERMT3 ARHGAP25 CD53 PLEK IRF8 DOCK2   |
| cyan       | SAFB MOB3A RAB35 ABR ASCC2 CDC37 ANKFY1 GLTSCR1 |
| darkgrey   | RAB40C ZNF213 ZNF263 PIGQ RHBDF1 RAB11FIP3      |
| darkorange | TCEB1 MRPL13 ENY2 MTERF3 UBE2W WDYHV1           |

**Table 2.1:** Fragment of the dataset with the categories and the genes belonging to each category from the biopsy sample.

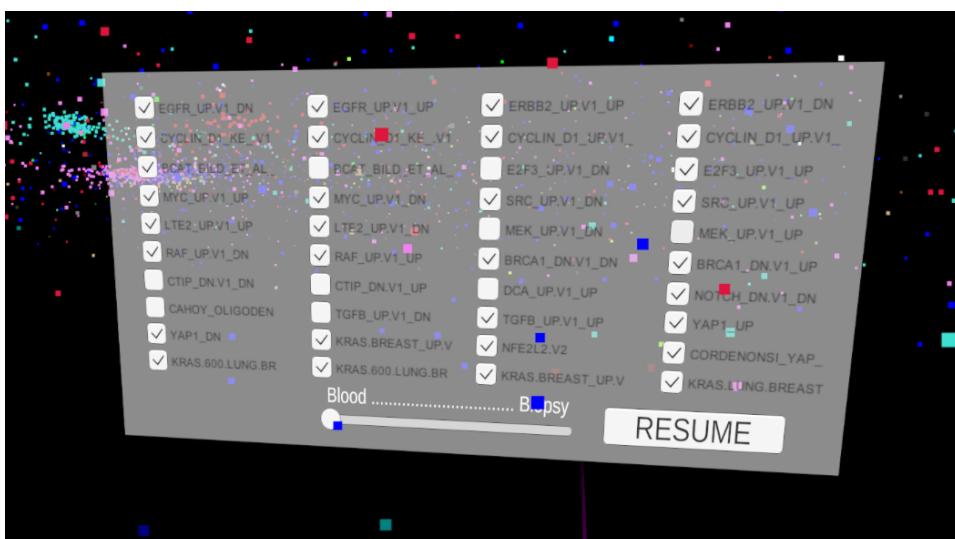
| source | target | weight            | id          |
|--------|--------|-------------------|-------------|
| AAMP   | ARGLU1 | 0.102486209330144 | AAMP-ARGLU1 |
| ACADM  | FOXN2  | 0.107506881676173 | ACADM-FOXN2 |
| ACADM  | MBNL1  | 0.12269622045714  | ACADM-MBNL1 |
| ACADM  | PPM1B  | 0.103496640767895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

**Table 2.2:** Fragment of the dataset used to build the network relationships of the blood sample.

## 2.3 Filtering information in the network

Another feature that BigNet VR uses to handle improve the visualization of networks is a filtering menu. When we have huge amounts of data in large networks, it is sometimes necessary to show less or more data. By filtering the nodes we can visualize only the part that we are interesting in.

We have built a 2 dimensional menu in Unity, see Figure 2.7, to filter the data in our example network. We use checkboxes for the filtering. From a starting point, all the boxes are checked, and if the user wants to hide a part from the visualization it is done by unchecking the box. To show the filtering menu we need to press on the menu button from the left controller, see the "2. Filter menu" in Figure 2.2. The to check or uncheck the boxes we need to use the A button from the right controller, also named after "6. Select item" in 2.2.



**Figure 2.7:** Filtering menu in BigNet VR.

## 2.4 Switching dataset

Finally BigNet VR has also the possibility to switch from one dataset to a different one. This can be done in the filtering menu by pressing the menu button from the left controller and there we can see a slider UI element as in Figure 2.7 which we can move to the right or to the left in order to change the dataset that is being visualized. When we switch the dataset, the filters are also reset to their default state, so all of them will be checked. In our bioinformatic example we can switch from the blood dataset to the biopsy one.

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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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## Evaluation and discussion

Questions to answer in the evaluation chapter:

1. How big can the graph be so that it is comfortable visualizing the network?  
What is comfortable? Number of FPS? How can we scale the graph? By adding nodes and spread them around, by adding more interconnexions? Should the experiment split in several parts? Scaling, filtering, moving around, etc. What is the performance by using Oculus Link and the performance using just the Quest hardware? -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. How is this way of visualizing the graph better by using VR?  
We are researchging the technology and the test with actual users is for future work.
3. In what way can the application and the visualization of the graph be improved?  
Argue in the discussion part.



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## **Conclusion and future work**



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