

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

Subtitle

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1

Introduction

It is very cheap nowadays to produce data and many people are doing it due to technological advancement. Just as an example, in the field of genomics, the sequencing of the first human genome (2002) took around 13 years and cost over \$3 million to complete. Now we can sequence hundreds of genomes in a few days[10]. This leads to the accumulation of vast quantities of genomic data, which can be used for new scientific discoveries, diagnose of rare diseases, etc. However we still need a human expert to visually inspect the data to find new signals and discover interesting patterns or to set a diagnosis. No matter how much resources we use into extracting the data if we don't get anything interesting out of it[25]. Therefore there is a great need for new and better tools to support this task.

Some of the main problems that researchers face when analysing genomic data are information overload, data interconnectivity and high dimensionality. One way to deal with all this data is to invent novel analysis. However we still need visual inspection of the data, so the information overload still remains as an important challenge and this is what we attempt to solve. 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. Networks can increase dramatically in size and complexity and this is due to computational power to create very large networks, scientific knowledge about large networks and the big amounts of data that we have to

analyze. We need therefore better visualization systems for the analysis and inspection of these networks.

In Figure 1.1 we can see a representation of the evolution for visualization of networks in system biology. Before the computers, networks were represented in 2 dimensions and they were static representations that lacked interactivity, see Figure 1.1 A. With the computer era and the advancement in computer graphics, 3D representations were possible, with the addition of interactivity with the network (See Figure 1.1 C). As computer science progressed, there was a big improvement in visualization and also new technologies emerged like virtual reality, which has a huge potential with regards to the interactivity (Figure 1.1 I).



Figure 1.1: Visualization for network biology. a Undirected unweighted graph showing co-expression relationship between genes. 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 network of genes showing co-expression relationships. d A multilayered network integrating different types of data visualized by Arena3D. e A hive plot view of a network where nodes are mapped to and positioned on radially distributed linear axes. f Visualization of network changes over time. g Static picture showing part of lung cancer pathway. h Navigation of networks using hand gestures. i Integration and control of 3D networks using VR devices. Figure adapted[14].

We believe that virtual reality (VR) can offer new possibilities for visual inspec-

tion in large networks. Even though VR is still a field under exploration, it has been demonstrated that it help scientists work more effectively in fields like medicine [9][23][3], biology[24][19] and neuroscience[1][11], to cite some examples. VR can be very powerful because it takes advantage of the way the human being perceives and analysis things. We have a great ability to discover patterns, however we are biologically optimized to see the world and the patterns in 3 dimensions. Some of the advantages that VR has over non-VR approaches are the following:

1. Visualization of the network in a 3D space.
2. Possibility to move around the virtual environment and visualize the network from different perspectives as in real life.
3. Interaction with the the environment by using controllers and our virtual hands in the virtual world.

We have implemented a virtual reality application for the visualization of 3-dimensional networks of data. We have used up-to-date virtual reality techniques that we think it improves the visualization of this type of data structures. The techniques that we have used consist in: the exploration of the network by moving around the virtual space, making it easier for the user to see the network from different angles; interaction with the network and nodes to comprehend better the data that is being visualized; and the use of 2-dimensional user interfaces to filter and have more control of the data.

What did we learn... [Write when the evaluation is finished].

Thesis statement: *Virtual reality techniques can improve the visualization and interactivity of data networks.*

1.1 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[7] 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[6] 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.



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.

1.2 Proposed solution

1.3 Significance and contribution

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

1.4 Outline



2

BigNet VR

BigNet VR is a virtual reality application for the interactive visualization of gene networks in a 3D space. The network is represented using nodes and edges between them. In order to explore and visualize the data in BigNet VR, the user can for example walk around the 3D environment, zoom in the network, translate it to other places, filter the visible nodes using a user interface and also obtain detailed information about the nodes.

BigNet VR loads the data from local files with the information about the nodes and relationships. Then the network is built using the data and clustered using an algorithm. Finally the user can explore it and interact with it using the VR headset and controllers.

We implemented BigNet VR in Unity, a cross-platform game engine. This software is used for a wide range of applications, especially for the development of videogames in 3D and 2D, VR applications and engineering solutions. We used C# as the main programming language to develop the application in Unity. 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 has its own hardware to run the applications although this can be more limited than the hardware from a PC. Also during the development process I used a cable and Oculus Link, a software to connect Oculus Quest to the PC, to run the application and test it directly from Unity on the Oculus Quest, without having to load it to the headset. This was from

great help during the development process.

We have chosen two datasets from MIxT to develop BigNet VR. MIxT is a web application that is used for exploring and comparing bioinformatic data[7][6]; and the data visualization is an important part of the process. The datasets used here contain genetic information about a woman with breast cancer. There are in total 2 tissues; the first one is from a blood sample and the second one is from tumor tissue. In Figure 2.1 we can see an example of BigNet VR running using the blood dataset from MIxT. We will now go in deep with how we implemented BigNet VR.

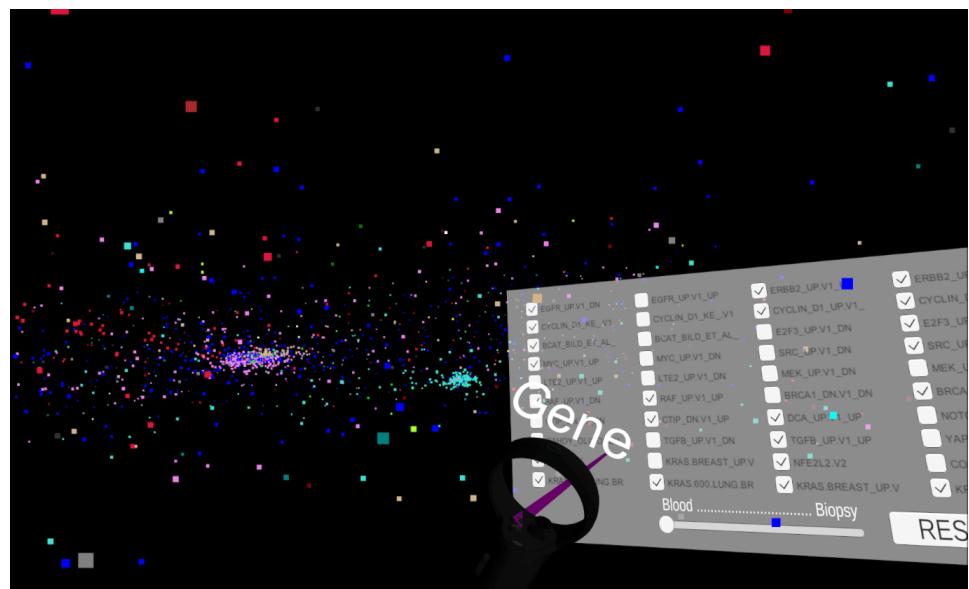


Figure 2.1: BigNet VR. Example of the application running on a Oculus Quest.

2.1 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 virtual reality is for example moving around, grabbing objects, interact with the environment using your hands or virtual tools, like pushing a button, 2D interfaces and menus, etc. In this section we will explain the techniques that we have implemented to visualize and interact with the network and make the most of VR.

The interation and the visualization also depends on the VR technoloy used. We use Oculus Quest in this project, an all-in-one VR headset that 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 actions correspond to each input from the controllers. We will briefly explain now what these actions consist of: 1. Snap rotation: It allows the user to instantly rotate to the right or to the left 45°; 2. Filter menu: The user can filter the nodes of the network according to a filtering algorithm used in BigNet VR; 3. Translate network: The network can be translated or moved to other positions in the scene; 4. Scale network: The network can be scaled or "zoomed"; 5. Select node: The user can select a node in order to get more information about it; 6. Select item in menu: It allows the user interact with the menu, for instance to filter the nodes by enabling or disabling the checkboxes from the filtering menu; 7. Oculus menu: It opens the menu from oculus and pauses BigNet VR; 8. Teleport: It teleports the user to another position on the floor of the VR scene.

As for the use of the Oculus Quest HMD (Head Mounted Display), this is placed in the head and it has a belt that is used to adjust the headset to the head. This will help the user feel more comfortable while wearing the HMD. Another important aspect that we have taken into account in BigNet VR is that the user can use the application and explore the network by sitting on a chair. This is possible thanks to the locomotion techniques implemented that allows the user to move around with the controllers. We will go into more detail later in this chapter about this.

We will explain now in the following subsections the different interaction techniques that we have used and also what benefits they bring for the visualization and interaction of the network.

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 the virtual world. 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 it.

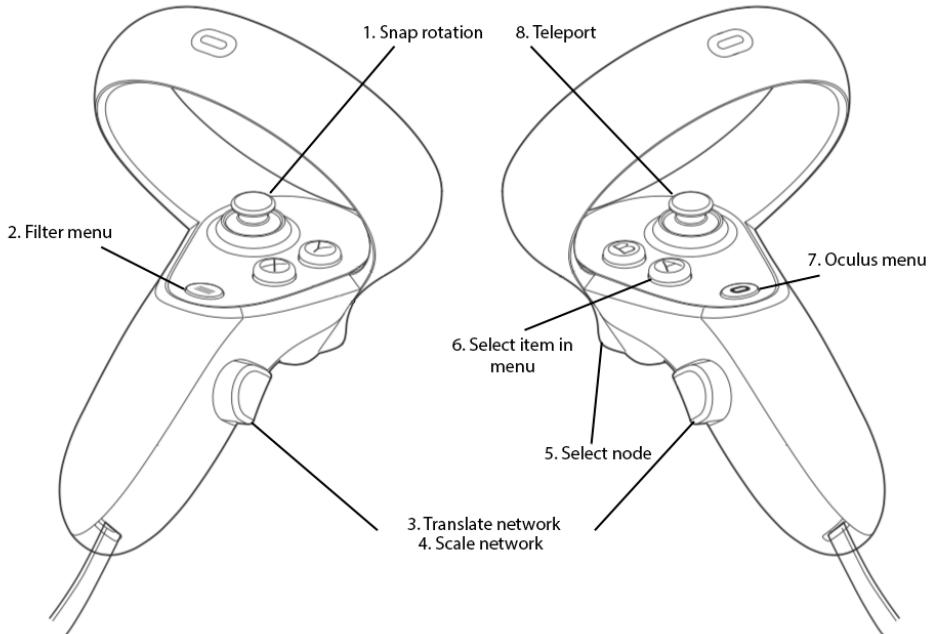


Figure 2.2: Mapping of the Oculus Quest controllers for the different actions implemented in BigNet VR: 1. Snap rotation. 2. Filter menu. 3. Scale environment. 4. Translate environment. 5. Pointer. 6. Select item in menu. 7. Oculus menu. 8. Teleport. Adapted figure from Oculus developer's page[13].

Locomotion can have a 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 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 need 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 having to walk around in the physical world[2].

The locomotion technique that we use in BigNet VR is called teleportation. It consists in choosing a spot on the floor where we want to teleport to. To do this the user has to move forward the thumbstick from the right controller (see "8. Teleport" from Figure 2.2). In addition it is possible to choose which direction the user will face once the teleportation is completed. 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 be followed by the new position in the space. This black flash is very important when implementing some of the locomotion techniques because it prevents from producing motion sickness.

and disorientation. Without the black flash, the transition to the new position would be too abrupt and it may disorient the user.

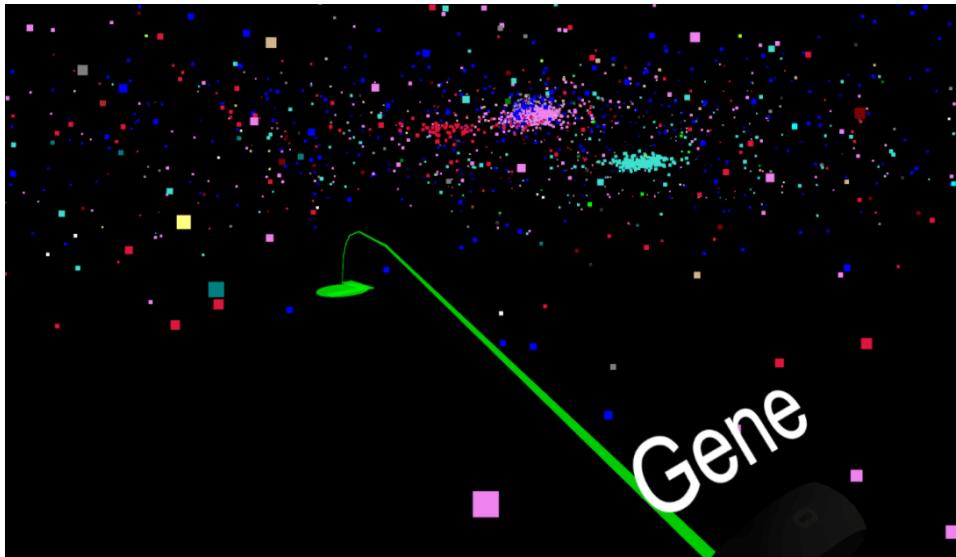


Figure 2.3: Teleportation technique. The user can use the joystick from the right controller to teleport to a different spot. To choose the spot a parabolic arc will appear.

In Figure 2.3 we can see an example of how the teleportation technique is used in BigNet VR. A parabolic arc is created in the 3D space with a circle representing the spot where we are going to teleport to. It can be seen as if we are throwing an object to the spot where we want to teleport to. The green circle includes also an arrow, indicating the direction that we will face once we are teleported.

In addition to the teleportation, it is also possible to rotate to the left or to the right with the Oculus controllers so that the user doesn't have to rotate the head to look around in the scene. This action is triggered using the thumbstick on the left hand (See 1. Snap rotation in Figure 2.2). By moving the thumbstick to the left side, the camera will rotate 45° to the left side, and 45° to the right side if the user moves it to the right side. A black transition is also used in this case before the rotation happens to avoid motion sickness, for the same reason as in the teleportation technique.

2.1.2 Translation of the network

By teleporting to different places in the environment we allow the user visualize the network from different perspectives. However it is also interesting to be

able to move the network and specially move it in a precise way so that the user has more control over what it is being visualized. 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 in the 3D space.

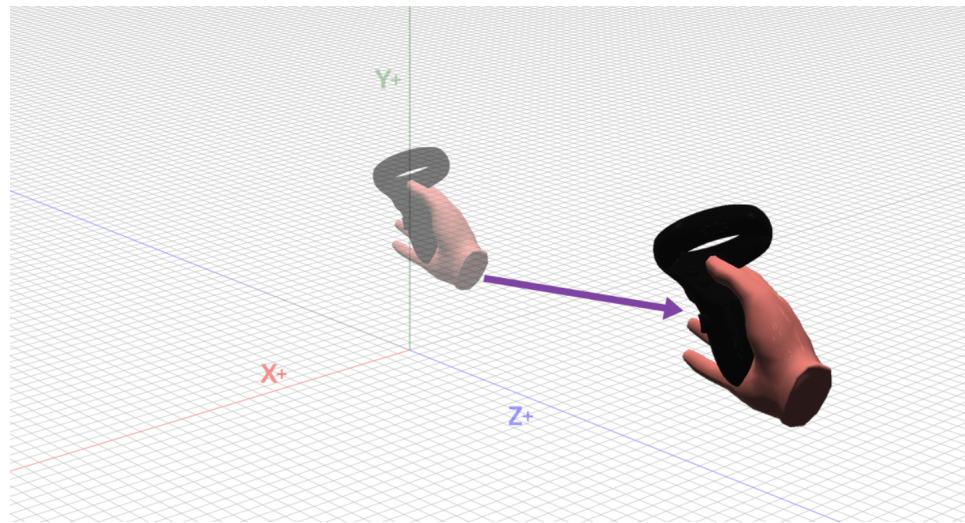


Figure 2.4: Translation of the network functionality. The user holds the translation button on the Oculus controller and moves the hand to the direction where he or she wants the network to translate.

To translate the network in BigNet VR, the user needs to press on the hand trigger from the right controller (see "3. Translate network" in Figure 2.2). Then the user needs to keep holding this trigger down and move the hand to the direction to which we want the network to move to. This intuitive approach feels like we are just pulling from a rope tied 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 and several clusters, 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.

The way we implemented the zooming functionality in BigNet VR is by using

the hand triggers with the name "4. Scale network" (see the reference in Figure 2.2). In the first place the user needs to press and hold these triggers from both controllers and then we need 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.

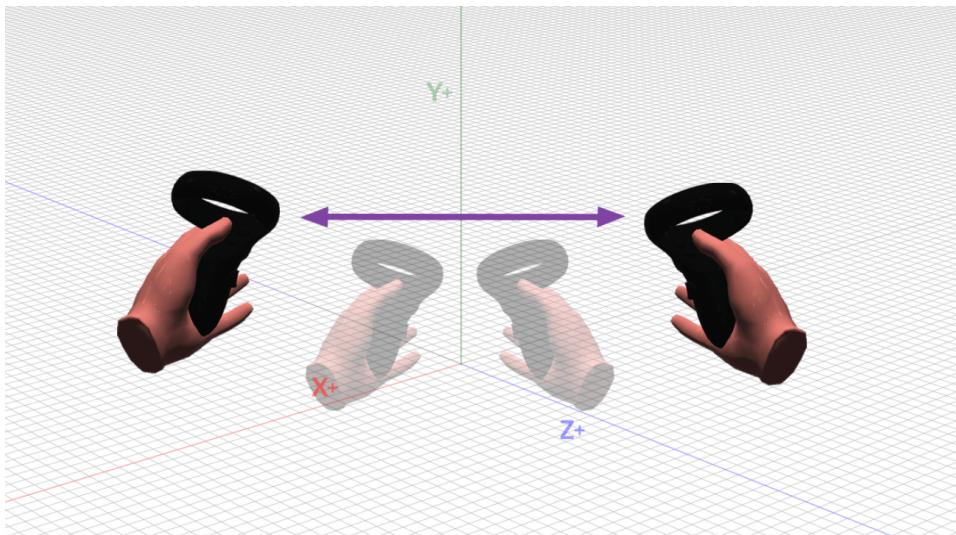


Figure 2.5: Zooming in the network functionality. The user can hold the scaling buttons on the Oculus controller to make the network bigger or smaller. In this example if we stretch our hands outside, the network will expand.

In Figure 2.5 there is 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 a intial 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 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 get close with the right controller to the node that we are interested in and press the "5. Select node" index trigger on the right controller (see Figure 2.2). When we press this trigger, we can select a node from the network. By selecting a node,

we will get the name of that gene node that will be displayed in a rendered text and we will also visualize the edges from this node to other nodes. The node is selected with an algorithm that searches for the node closest to our right controller.

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. Because there can be too many relationships in the dataset, we don't show them all at the same time. Therefore we can only see those of the node that the user has selected. The way that these relationships are represented is with lines between the nodes.

2.2 Scalable network in Unity and data structures

BigNet VR uses files from an external source with data that will be used to be the network. The first file contains the information about the nodes and what category the node belongs to; The second one has information about the relationships between each of the nodes. As for the content of the files look like, in Table 2.1 and Table 2.2 we show an extract from them. Originally the files are in CSV format. CSV[4] stands for Comma-Separated Values where each record is located on a separate line within the file, delimited by a line break. In addition, each record can contain one or more fields, separated by commas.

For our example we represent the extract from the CSV files using tables, which are more illustrative. Table 2.1 contains an extract from the file with information about the genes and the categories to which each gene belongs to. Here each row is a category and as we can see, the second cell contains all the gene names for that specific category. These categories are named by colors and these color names will be used by BigNet VR to color each node from the network. As for the second table, Table 2.2, this one shows an extract with the information about the relationships between the genes. This file can be very large since each row in the CSV file corresponds to a relationship between two genes and one gene can be related with multiple genes. For instance one of the CSV files that BigNet VR uses to build the relationships contains almost 90k lines.

The following diagram shown in Figure 2.6 schematizes the steps that we follow

category	genes
brown	ARHGAP30 FERMT3 ARHGAP25 CD53 PLEK IRF8 DOCK2
cyan	SAFB MOB3A RAB35 ABR ASCC2 CDC37 ANKFY1 GLTSCR1
darkgrey	RAB40C ZNF213 ZNF263 PIGQ RHDF1 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.

to build the network in Unity. We start with the 2 CSV files described before, containing the data about the nodes and the relationships. We process these CSV files in order to store the data in data structures in BigNet VR. During the process of storing this data we also apply a clustering algorithm that will set the correct position for each node in the network. After doing this we can easily access the information about the nodes, their position, color and to which nodes they are related to in order to draw the edges. Finally the network is created using a particle system as we will explain later.

Now that we know how sources of information to build the network in BigNet VR, let's take a look at how the network itself is represented in Unity and what algorithms and data structures we use for that. These will have an impact in the scalability of the network and therefore it's important to choose a good solution. We have three elements from the network that have more weight in its scalability: the nodes, the edges and the cluster algorithm used. We are going to explain each of them in more detail now.

The nodes in BigNet VR are represented using a particle system. In Unity a particle system[16] is defined an array of particle objects. Each particle is a defined structure in Unity that contains properties like the life duration of the particle, start color, start size or position in the 3D space. Particle systems in Unity are very useful to render some special effects like fire, steam, fireworks or projectiles. They are also very powerful because they give plenty of control to the developer over the particles. In BigNet VR we take advantage of this, allowing us to structure the network in the way we want. Usually particles have a lifetime, which means that for instance they can start in a position with

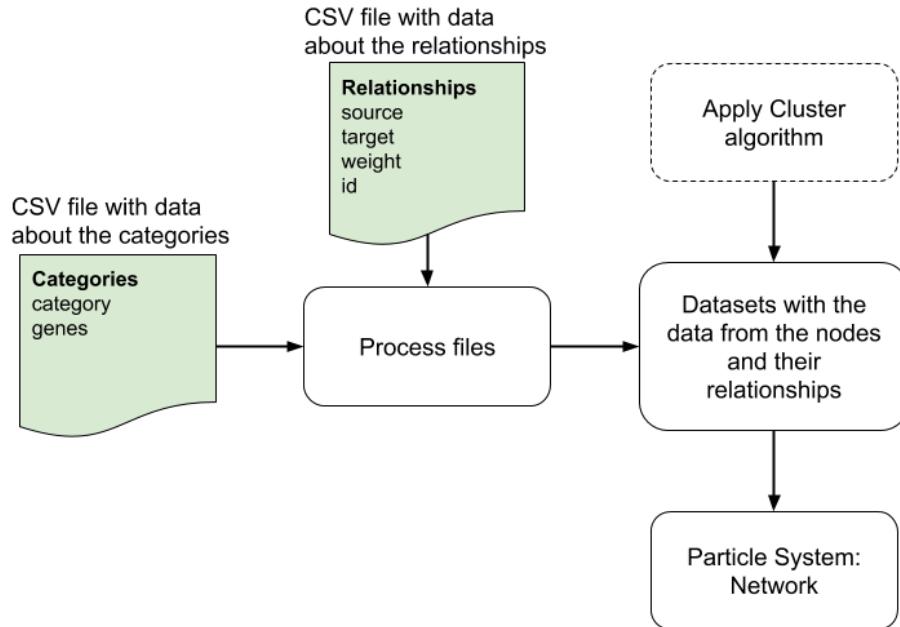


Figure 2.6: Diagram: steps for the creation of the network from the 2 CSV files.

a particular colour and finish or disappear after a few seconds in a different position and colour. However in BigNet VR the particles are static and have a very long lifetime, giving the perception that the network is a rigid structure. As for the way the particles are rendered, a 2-dimensional square is shown in the scene for each particle or node. Finally, in order to store the information of each node or particle we have a dictionary object in BigNet VR that looks like this:

```
private Dictionary<string, ParticleSystem.Particle> particles;
```

A dictionary in C# is a data structure that contains a set of keys and each key has a single associated value. In our case the key corresponds to the name of the node, the name of the genes in this case, and the value is a particle object.

The edges between the nodes are represented with 2-dimensional lines in BigNet VR. A line in Unity is created with a Line Render component[15]. These lines are very flexible and can be used to draw anything from a straight line to a spiral. They also have properties like color, texture mode, possibility to have different widths along the line, etc. In our case we want to render straight lines, so we need to know the start and the end points where the line will be rendered. This information is taken from the CSV file with the edges information where

we can see which nodes are connected to each other. To store the information about this we also use a Dictionary, where the key is the name of a node and the value is a list with all the nodes to which this node is connected to. This looks like this in C#:

```
private Dictionary<string, List<string>> edges;
```

Showing all the edges at the same time in BigNet VR would make it very hard to visualize the network. For this reason we show only the edges of the node that the user has selected. Also, in BigNet VR the edges are shown dynamically, meaning that they are created everytime the user selects a node. When the user selects a different node, the current edges are removed and a new set of edges are rendered for the new node. This process can be a bit CPU-consuming in Unity. Everytime an edge has to be rendered an edge object is instantiated with the CreateInstance method from Unity. The edge object in the scene from what is called a prefab in Unity. A prefab[17] is basically a reusable asset, which in our cause is the line with some defines properties like the width and the colour.

The algorithm used to cluster the nodes in the network is another important aspect that can influence in the scalability. In BigNet VR we use a linear algorithm that clusters the nodes in the 3d space depending on the module where they belong too. In this way the user can visualize each module as single clusters with a distinct colour per cluster.

2.3 Other features of BigNet VR

BigNet VR provides some features that help in the process of visualization and interaction with the network. They have a complementary purpose and they don't influence much in the scalability of the system.

2.3.1 Filtering information in the network

Another feature that BigNet VR uses to 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

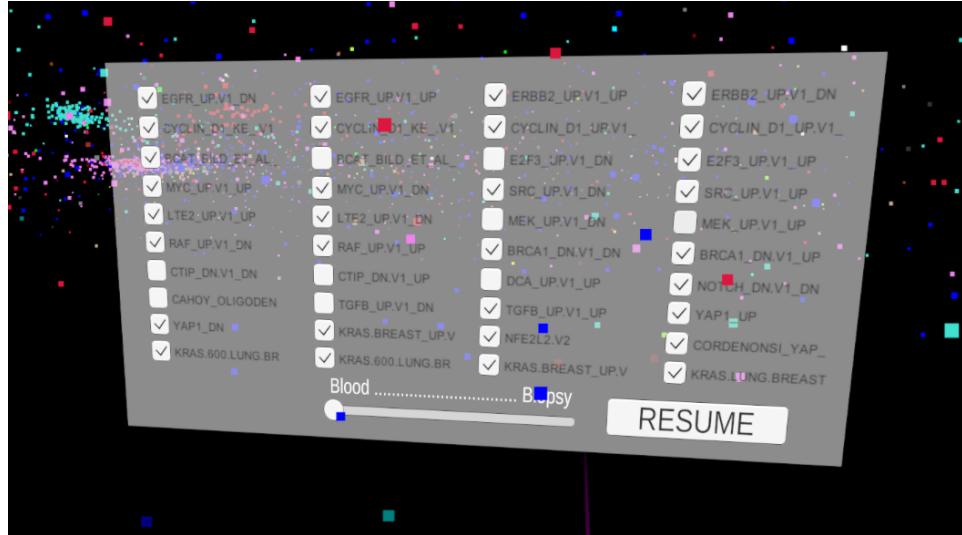


Figure 2.7: Filtering menu in BigNet VR.

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, named "6. Select item", see Figure 2.2.

2.3.2 Switching dataset

Finally BigNet VR has also the possibility to switch between networks. 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 switch 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 example we can switch from the blood network to the biopsy one.

2.4 Implementation details

Unity (version 2018.4.10f1[20]) is the software that was used to build the system. It is a multi-platform game engine. It is known to be easy to use and for having a big community of creators and asset designers[8]. Even though it is intuitive to use, it also has a low-level access for developers. As for Virtual Reality, Unity has been up-to-date with the new VR technologies thanks to professionals and amateurs in this area who have built integrations for Unity. In our case, our

device is an Oculus Quest, and for this reason we use the Oculus integration for Unity[21]. In addition we have used VRTK, a collection of ascripts and assets that help build VR solutions[22]. Finally, the programming language used in Unity to implement the system is C#.

2.5 Architecture and design

The architecture for BigNet VR is very simple since it is an offline application that runs on an Oculus Quest or on a machine with Unity. As we can see in Figure 2.8, the system is divided in three parts. The main part is the Unity application, or BigNet VR where we process everything like loading the CSV files, creating the network, applying the cluster algorithm to the nodes, interactions using the VR hardware, etc. As for the data, they come from external files and they have to be manually imported into the Unity application, where they will be processed when running BigNet VR. Finally there is the client, which is the Oculus Quest headset where we run the application. Here the user can visualize the network and use the controllers to interact with it. As the figure shows the Oculus Quest can be connected to the PC itself using an Oculus Link which is basically a high-quality USB 3 C to C or USB A to C cable with proven performance[12]. This allows the user run BigNet VR on the PC. Another possibility is also load BigNet VR into the Oculus Quest and run it there without any cable or PC.

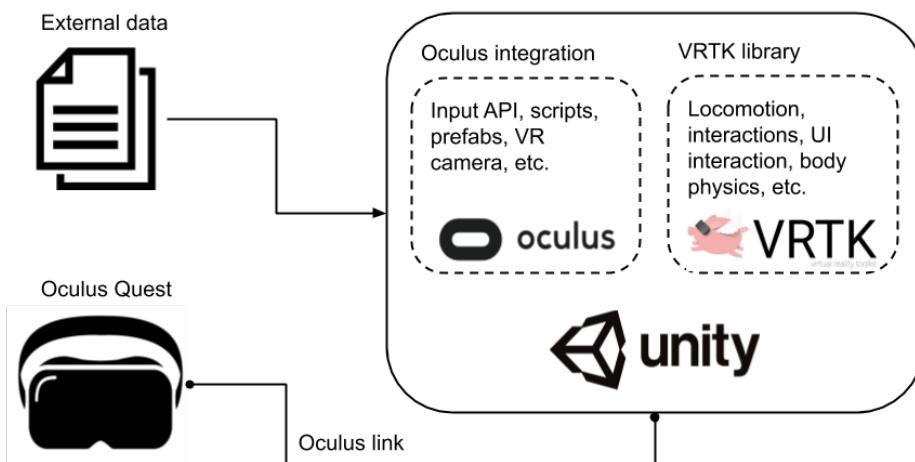


Figure 2.8: Architecture and design of BigNet VR.

Todo: Write about the design and technologies used in BigNet VR like Unity, VRTK, etc and discuss why they were used instead of others.

/3

Visualizing MIxT in VR

What is MIxT used for? And how would users do it in VR? How the MIxT application is implemented in BigNet VR and what it does. What are typical network characteristics for this (type of) application? Size, clusters, edges, connectivity, etc?

/ 4

Related work

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

4.1 BioVR

4.2 CellexaVR

4.3 BigTop

/ 5

Evaluation and discussion

BigNet VR has been built to explore biological networks that contain genetic information from human beings. We have used two networks from MiXT where we applied several VR techniques to build a visualization system. In this chapter we want to evaluate this system focusing on scalability and performance problems. Since we are visualizing networks with genetic information using VR, we want to know if the system that we built can be used for any size of this type of networks. As part of the evaluation process, we designed a list of questions that we will try to answer along this chapter. These questions are:

1. For which interactions do we achieve the recommended FPS (72) when scaling the network?
2. What characteristics of the network influence the scalability?
3. What is the performance by using Oculus Link and the performance using just the Quest hardware?
4. How do users perceive the interaction of the network?

Question one is based on the Oculus' performance guidelines[18], that say that an application should meet the following.

- 72 FPS for Oculus Quest (required by Oculus).

- 50-100 draw calls per frame.
- 50,000-100,000 triangles or vertices per frame.

As for the second question, we want to know what characteristics influence the scalability of the network and the visualization system. Some elements of the network have more impact in the performance than others. To keep it simple, we will evaluate the impact in the performance done by the following elements, that are the most important for the visualization: number of nodes, number of lines and number of clusters.

We will also evaluate the performance of the application being run in the Oculus Quest hardware and also in a PC, using the Oculus Link cable that connects the headset to the machine. The hardware of the Oculus Quest is not as powerful as the one of the machine that was used for the development. We would like to know if the performance is good in both the machine and the headset.

Finally, as the last question says, we want to know how the users perceive the interaction and visualization of the network. We will evaluate this with a qualitative method with a demo of the application using the MIxT network and also an interview.

5.1 Experimentation plan

An experimentation plan was designed to ensure that the experiments are consistent and that they can be repeated several times getting realistic measurements. We take into consideration the following aspects for our experiments:

1. Scalability for different interactions.
2. Network characteristics.
3. Bottlenecks.
4. User study.
5. Hardware and software specification.

There are some elements of the network that influence more in the scalability and performance of the system. In Table /reftab:network-elements we describe

these elements.

Element	Description
Clusters	description for clusters
Nodes	Represented as 2D squares in the space. The position is calculated when creating the clusters.
Lines	They represent relationships between the nodes. Everytime a node is selected, line objects are added to the scene.

Table 5.1: Elements of the network that have influence in the scalability.

We ran the experiments in a machine with Windows 10. In Table 5.2 we can see some of the hardware specification from the machine used:

Machine specification	
Processor	Intel(R) Xeon(R) CPU E3-1275 v6 @ 2.80GHz 3.79 GHz
RAM memory	64.0 GB
System type	64-bit Operating System

Table 5.2: Machine specification.

Since the GPU is important in this type of applications, we show the specs of the GPU used in Table 5.3.

GPU specification	
Adapter type	NVIDIA GeForce GTX 1080 Ti
Chip Type	GeForce GTX 1080 Ti
DAC Type	Integrated RAMDAC
Available memory	45025 MB

Table 5.3: GPU specification.

As for the VR headset hardware, we used a Oculus Quest. In Table 5.4 we can see the hardware specifications for this type of headset.

The experiments were run in Unity, the same software that was used for the development. The version of Unity used for the experiments is 2018.4.10f1. Also Vulkan is used as the graphic API.

A test scene was built in order to test the network and the scalability of it. A random network is built and we test how comfortable it is to navigate through it. This is measured by the FPS rate.

Oculus Quest specifications	
Panel Type	Dual OLED 1600x1440
Supported Refresh Rate	72Hz
Tracking	Inside out, 6DOF
CPU	Qualcomm® Snapdragon 835
GPU	Qualcomm® Adreno™ 540 GPU
Memory	4GB total

Table 5.4: Oculus Quest specifications.

VR profiling is a technique used to get an overview of the performance of our application. This is usually done in order to find bottlenecks so that we can eliminate them and improve the application's performance.

To profile the application we used the built-in profiler in Unity, the software used for the development. The Unity Profiler gives information about per-frame CPU and GPU performance metrics.

5.2 Performance of the system

5.3 Scalability of the network

Creating the lines for relationships.

5.4 Demo and interview

One of the questions that we asked ourselves during the evaluation process was about the comfortability of using BigNext VR to explore a biological network. This is an important aspect when building VR applications. Some of the aspects to take into account are for instance the motion sickness or the intuitiveness. In order to evaluate this we made a questionnaire for bioinformaticians that would test the application. Unfortunately, due to the Covid-19 situation [5], we were not able to carry out the questionnaire with people. The reason is because it wasn't possible to test BigNet VR with people on a single Oculus Quest device without avoiding the social distancing rules. We estimated to have around 10 participants with knowledge in bioinformatics to test the application. With this number of participants we could have made some statistics and obtained feedback for future improvement.

The following questionnaire is divided in four sections; a general section about VR headsets, a section about comfortability exploring the network using BigNet VR, a section about the different actions in BigNet VR and finally a section about feedback.

To complete the questionnaire, the teste has to indicate the level of agreement or disagreement with each of the statements, mark yes or no when it is asked and in the feedback section reply the questions with constructive feedback if possible.

Questionnaire section 1: VR headsets.

1. Have you ever used a VR headset before?
Yes / No
2. Have you ever used a Oculus Quest headset before?
Yes / No
3. I feel comfortable using a VR headset.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
4. I feel comfortable using the Oculus Quest headset.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree

Questionnaire section 2: Comfortability exploring a biological network with BigNet VR.

1. I feel comfortable moving around the virtual environment using the teleport functionality.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
2. I feel comfortable rotating to any direction.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
3. I feel comfortable visualizing the network by moving my head.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
4. I feel comfortable selecting the nodes to visualize the relationships.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
5. I feel comfortable moving the network to the position that I want.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree

6. I feel comfortable scaling the network.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
7. I feel comfortable using the UI menu to filter the data from the network.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree

Questionnaire section 3: Performing different actions in BigNet VR to explore the biological network.

1. It is intuitive to manipulate the network using the controllers.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
2. The different actions in the controllers are easy to learn and remember.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
3. I can move the network to any position that I want.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
4. I can scale the network to any size that I want.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
5. I can select any node that I want.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
6. I can easily visualize the relationships of any node.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree
7. I can easily filter the data by using the UI menu.
Strongly agree / Agree / Neutral / Disagree / Strongly Disagree

Questionnaire section 4: Feedback.

1. Did you experience any difficulties exploring the biological network? If so, indicate which ones.
Yes / No
2. Is there anything that could be improved for the visualization of biological data in BigNet VR? If so, write your suggestions.
Yes / No
3. Write any feedback and comments that you have about the exploration of biological networks with BigNet VR.

/ 6

Conclusion and future work

In this section we will conclude the thesis and describe what we can do to improve the project and the future work.

6.1 Future work

Bibliography

- [1] Corey J. Bohil, Bradly Alicea, and Frank A. Biocca. “Virtual reality in neuroscience research and therapy.” In: *Nature Reviews Neuroscience* 12.12 (2011), 752–762. DOI: 10.1038/nrn3122.
- [2] Evren Bozgeyikli et al. “Point & Teleport Locomotion Technique for Virtual Reality.” In: *Proceedings of the 2016 Annual Symposium on Computer-Human Interaction in Play - CHI PLAY 16* (2016). DOI: 10.1145/2967934.2968105.
- [3] “Commentary on Rose, F.D., Brooks, B.M., & Rizzo, A.A., Virtual Reality in Brain Damage Rehabilitation: Review.” In: *CyberPsychology & Behavior* 8.3 (2005), 263–271. DOI: 10.1089/cpb.2005.8.263.
- [4] *Common Format and MIME Type for Comma-Separated Values (CSV) Files*. URL: <https://tools.ietf.org/html/rfc4180>.
- [5] *Coronavirus*. URL: <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.
- [6] Vanessa Dumeaux et al. “Interactions between the tumor and the blood systemic response of breast cancer patients.” In: *PLOS Computational Biology* 13.9 (2017). DOI: 10.1371/journal.pcbi.1005680.
- [7] Bjørn Fjukstad et al. “Building Applications for Interactive Data Exploration in Systems Biology.” In: *Proceedings of the 8th ACM International Conference on Bioinformatics, Computational Biology, and Health Informatics - ACM-BCB 17* (2017). DOI: 10.1145/3107411.3107481.
- [8] Jason Jerald et al. “Developing virtual reality applications with Unity.” In: *2014 IEEE Virtual Reality (VR)* (2014). DOI: 10.1109/vr.2014.6802117.
- [9] KE. Laver et al. “Virtual reality for stroke rehabilitation.” In: *Cochrane Database of Systematic Reviews* 11 (2017). ISSN: 1465-1858. DOI: 10.1002/14651858.CD008349.pub4. URL: <https://doi.org/10.1002/14651858.CD008349.pub4>.
- [10] Mike May. “LIFE SCIENCE TECHNOLOGIES: Big biological impacts from big data.” In: *Science* 344.6189 (2014), pp. 1298–1300. ISSN: 0036-8075. DOI: 10.1126/science.344.6189.1298. eprint: <https://science.sciencemag.org/content/344/6189/1298>. URL: <https://science.sciencemag.org/content/344/6189/1298>.
- [11] Matthias Minderer et al. “Virtual reality explored.” In: *Nature* 533.7603 (2016), 324–325. DOI: 10.1038/nature17899.

- [12] *Oculus Link Compatibility*. URL: <https://support.oculus.com/444256562873335/>.
- [13] *OVRInput*. URL: <https://developer.oculus.com/documentation/unity/unity-ovrinput/>.
- [14] Georgios A. Pavlopoulos et al. “Visualizing genome and systems biology: technologies, tools, implementation techniques and trends, past, present and future.” In: *GigaScience* 4.1 (2015). DOI: 10.1186/s13742-015-0077-2.
- [15] Unity Technologies. *Line Renderer*. URL: <https://docs.unity3d.com/Manual/class-LineRenderer.html>.
- [16] Unity Technologies. *ParticleSystem*. URL: <https://docs.unity3d.com/ScriptReference/ParticleSystem.html>.
- [17] Unity Technologies. *Prefabs*. URL: <https://docs.unity3d.com/Manual/Prefabs.html>.
- [18] *Testing and Performance Analysis*. URL: <https://developer.oculus.com/documentation/unity/unity-perf/?device=QUEST>.
- [19] David A. Thorley-Lawson, Karen A. Duca, and Michael Shapiro. “Epstein-Barr virus: a paradigm for persistent infection – for real and in virtual reality.” In: *Trends in Immunology* 29.4 (2008), 195–201. DOI: 10.1016/j.it.2008.01.006.
- [20] *Unity 2018.4.10*. URL: <https://unity3d.com/unity/whats-new/2018.4.10>.
- [21] *Unity Integration*. URL: <https://developer.oculus.com/downloads/package/unity-integration/1.29.0/>.
- [22] *Welcome to VRTK · VRTK - Virtual Reality Toolkit*. URL: <https://vrtoolkit.readme.io/docs/summary>.
- [23] James Xia et al. “Three-dimensional virtual-reality surgical planning and soft-tissue prediction for orthognathic surgery.” In: *IEEE Transactions on Information Technology in Biomedicine* 5.2 (2001), 97–107. DOI: 10.1109/4233.924800.
- [24] Yuting Yang et al. “Integration of metabolic networks and gene expression in virtual reality.” In: *Bioinformatics* 21.18 (July 2005), pp. 3645–3650. ISSN: 1367-4803. DOI: 10.1093/bioinformatics/bti581. eprint: <http://oup.prod.sis.lan/bioinformatics/article-pdf/21/18/3645/520673/bti581.pdf>. URL: <https://doi.org/10.1093/bioinformatics/bti581>.
- [25] Jimmy F. Zhang et al. “BioVR: a platform for virtual reality assisted biological data integration and visualization.” In: *BMC Bioinformatics* 20.1 (2019). DOI: 10.1186/s12859-019-2666-z.

