Multimodal Approach for Natural Biomedical Multi-scale Exploration

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Abstract. Pathologies which simultaneously involve different spatial scales are often difficult to understand. Biomedical data from different modalities and spatio-temporal scales needs to be combined to obtain an understandable representation for its examination. Despite of requests to improve the exploration of multi-scale biomedical data, no major progress has been made in terms of a common strategy combining the state of art in visualization and interaction. This work presents a multimodal approach for a natural biomedical multi-scale exploration. The synergy of a multi-layered visualization environment based on spatial scales with hand gestures and haptic interfaces opens new perspectives for a natural data manipulation.

1 Introduction

An in-depth analysis of a human pathology usually needs a large diversity of data from different medical specialties. This data, acquired from different acquisition modalities, is distributed over multiple spatial scales. The data extracted from such acquisitions has not only different spatial dimensions, but also diverse visualization properties. Therefore, the presentation and exploration of this plethora of information quickly becomes complex for a multidisciplinary group of specialists working on the biomedical case.

For instance, consider the study of diseases affecting the musculoskeletal articulation, such as osteoarthritis of the knee joint. Biomechanical engineers, radiologists and tissue engineers contribute with their data and expertise. The gathered datasets contain gait pattern analyses (behavior scale), MRI and CT images of the knee joint (organic scale) and chondrocytes death analyses of the meniscus (cellular scale), among others. Some of these are presented as 3D models, other through InfoVis representations, such as graphs or diagrams.

Since disease features propagate across different spatial scales, information sources from the entire range of scales and their known relationships need to be explored for a complete analysis of such disease. However, conventional techniques of visualization and interaction by themselves do not constitute an effective tool for the analysis of the complete collection of data.

In the example above, phenomena at the cellular scale, such as anabolic/catabolic reactivation, propagate upwards through organic scales, affecting the cartilage thickness of the meniscus, and finally causing an alteration in gait pattern.

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A quantitative and qualitative analysis of the impact of such influences is currently not possible. Generally, experts use isolated systems allowing only the exploration of features involving a concrete specialty and scale but not the complete picture. Moreover, the existing multimodal exploratory systems are based on traditional standard interfaces, which do not allow a flexible exploration of multi-scale data. Therefore, specialists lack of an exploratory environment to efficiently support the analysis of causality across evidences from different scales.

This work describes an approach for a natural biomedical multi-scale exploration. The proposed approach is based on multimodal visualization and interaction. It makes use of a multi-layered visualization, in which data acquired from different modalities belonging to different spatial scales can be manipulated with a multimodal interaction method. This involves a synergy of hand gestures, haptic interfaces and traditional means of human machine communication. For the storage, rendering and interaction of many large datasets, distributed computing techniques are involved. We evaluate and discuss the principal aspects of the proposed approach comparing it with traditional methods.

2 Motivation of Work

Recent projects [1,2] allow a collaborative investigation of the human body or other biological complex systems as a whole. These approaches help to observe and quantify natural processes occurring at various spatio-temporal scales, solving concrete multidisciplinary biomedical problems. However, the current level of integration of visualization encompassing all information of the process under study, still needs to be improved [3]. In such scenarios, a large amount and variety of data has to be explored. Therefore, methods of interaction with the content requires also adaptation and extension.

Our approach towards an exploration environment of biomedical data makes strong use of Virtual Reality (VR) techniques, such as 3D stereographic visualization and gesture interaction. Most acquired biomedical data has a 3D representation, i.e. volumetric objects. The most natural and intuitive way to interact with real objects is to look at them from different sides, move closer or just turn them around with the hand. In our approach we try to mimic these natural strategies to allow an intuitive and user friendly data space exploration.

2.1 Previous Work in Biomedical Multi-scale Exploration

Challenges of biomedical multi-scale visualization are due to the variety of data formats, a massive amount of information and diverse levels of abstraction [4]. First, biomedical data of a concrete domain is acquired by a broad range of acquisition modalities which must be merged within the same spatial reference system (e.g. CT and MRI in anatomical analysis). However, a visualization which improves the understanding of each spatial scale is not enough. For a multi-scale exploration the importance lies in coupling the spatial scales.

In the last decade, many authors called for efforts to improve the exploration of biological data [5], especially in terms of improved visualization techniques able to deal with the complete range of possible biological data types [3]. Some of the authors emphasized the advantage of multidisciplinary approaches in an integrated visualization [6,7], forming alliances not only across biomedical domains but also between the visualization (InfoVis and SciVis) communities [8].

Indeed, recent projects [1,2] indicate that the interplay of domains of science across spatial scales is beneficial for a complete analysis of a biological phenomenon. This approach provides scientists with new knowledge that would have not been possible without multi-scale visualizations. The *MSV Project* [9] focuses to cover the inadequacy of interactive visualization paradigms for biomedical multi-scale data. The use of placeholders as a Level of Detail (LoD) approach allows the navigation across CT scans at different scales. The *Multimod Application Framework (MAF)* [10] provides support of biomedical time-varying data, allowing for instance an analysis of human motion [11].

Nevertheless, the aforementioned projects show that no major advances in terms of visualization have been made to facilitate scientists' tasks in the multi-scale biomedical exploration. In some exploratory systems, small scale data does not have visibility in large scale view, avoiding a global view [9]. Other systems provides a standard graphical user interface (GUI), composed of a set of opaque windows and dialog boxes, to configure viewports. This, however, does not provide a simple method for a transition between scales [10]. Moreover, in most of the current systems the multiscalar exploration is even more difficult because they do not provide sufficient semantic means to visually understand internal relations between datasets [12].

Regarding interaction, until recently, hand gesture interface realizations were expensive and used to struggle with several problems: high latency, computationally intensive computer vision algorithms and uncomfortable work area for the user [13]. Constant technological growth lowered price barriers and allowed people to access cheap and high quality interfaces, opening new perspectives for elaborated systems for medical imaging exploration. As result, many new applications of hand gestures in the medical field have emerged [14].

Hand gestures try to replace mouse interaction by mimicking it and following the same interaction strategy (simple pointing, dragging, etc.) [15]. Nevertheless, replacing the mouse completely can lead to lack of interaction tangibility [16]. Therefore hand gestures are not ready to replace the mouse alone. This leads to propose integrated interfaces, allowing for an intuitive and natural biomedical data exploration [17].

2.2 Proposed Approach to Improve the Exploration of Biomedical Data

Our approach is based on the datasets as the main actors of visualization and interaction (Table 1). Each dataset from a different acquisition modality is displayed as an independent entity, called *node*. Nodes are distributed in a *multi-layered 3D workspace* with spatial connections, allowing for a direct exploration of all the data. Node features and their dependencies are encoded in an underlying ontology. This ontology captures all of the important aspects of a set of multi-scale datasets and provides semantic means to identify relevant items during the exploration, e.g. relations between evidences in a multiscalar pathology [12]. Overlaying and perceptual cues in the relations between such nodes enrich the understanding of the complete collection of data.

The *multimodal interaction* approach proposed in this paper is realized with a focus on natural 3D interaction. Two-dimensional mouse interaction is replaced as a primary method of interaction by hand gestures. The exploration of the datasets is performed through operations on the nodes, and several actions can be performed by grasping and moving (e.g. combining two complementary datasets). In order to fill the gap between tangibility of traditional interfaces (mouse, keyboard) and gesture interaction (which gives no sensory feedback), we introduce the haptic device as an auxiliary interface. The user can perform natural gestures and experience physical feedback from the 3D workspace.

The presentation of all datasets in a single view might not always be feasible, due to their large size and limitations of the system memory. In order to overcome this issue we use a *distributed rendering* scheme. Since a single machine is sufficiently performant to render at least a complete biomedical volume DICOM file, we do not consider traditional approaches for distributed rendering [18]. Instead, we composite the visualization scene from several datasets rendered on different machines.

The proposed exploratory system is intended to be usable by a broad group of users with expertise in several disciplines working collaboratively on the same scenario. Therefore, it is imperative to address issues of multi-platform design and scalability, as well as to foresee problems concerning transferring large amounts of data through the Internet (caching, streaming).

3 Methodology

3.1 Architecture

The central part of the system architecture is the *exploratory environment*. It is realized in a form of a thin-client based on the Unity3D software framework [19]. Unity is well known for its lightweightness, modularity and extendability, which allow to address multi-platform and scalability challenges.

The exploratory environment accesses various network resources in order to provide the visualization environment (Section 3.2) and the multimodal interaction (Section 3.3) to the user. Consequently, the system can remain scalable with respect to an increasing number of simultaneous users as well as with respect to the complexity of multi-scale datasets.

The visualization and interaction pipeline is described in Fig. 1. The first actor in the process of visualizing data is the *metadata database* with underlying ontology [12]. The metadata database provides a list of data *nodes* (each representing data from a single acquisition) together with the corresponding location of such preprocessed resources in the *data repository*, which stores frequently large datasets.

Table 1. Conventional approaches ([9]-[15]) and proposed approach for exploration of multi-scale biomedical data

Exploration features	Conventional approaches	Proposed approach
Representation of datasets based on	Tree list structure	Nodes displaying datasets
Visualization scenario	Flat desktop	3D workspace
Focus and Context technique	Preserving spatial dimensions (placeholders)	Multilayered workspace with non-linear depth
Superposition of datasets	Overlapping	Overlaying
Visual semantic means among datasets	None: inferred by the experience of users	Visual links thanks to an underlying ontology
Means of interaction	Mouse and keyboard	Hand gesture and haptic devices
Interaction paradigm	GUI 2D interaction	Multi-modal natural 3D interaction
Objects of interaction	Commands on the GUI	Gestures on the nodes

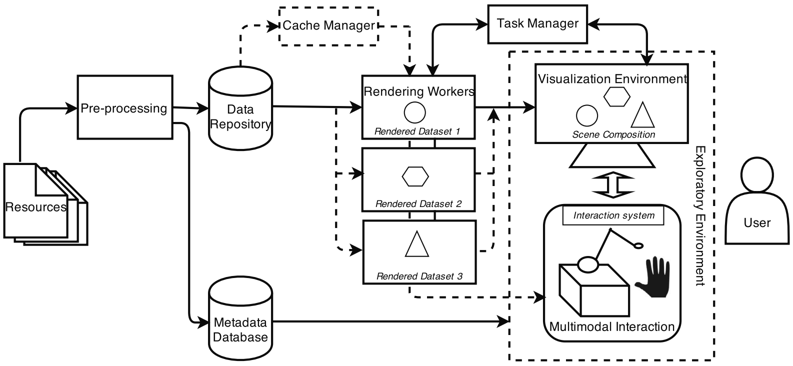

Fig. 1. Visualization and interaction pipeline of the proposed approach

The composition of the visualization scene is based on a distributed rendering strategy. In order to display *nodes* obtained from the database, *the visualization environment* connects to a *rendering worker* entity, which acts as an active proxy between the client and the data repository. The rendering worker renders the dataset and sends it to the scene. Thanks to that, the processing power needed to visualize complex and large datasets can be parallelized between different rendering workers, running on different machines. The *task manager* monitors the use of rendering workers' resources and load-balances rendering requests from the visualization environment.

Data repositories can be spread geographically. In this case, data is cached as close to the rendering workers as possible thanks to the *cache manager*. These entities store data that was already requested by rendering workers before. Data is stored within the limit of the local area network, in the way similar to web proxy servers.

Rendering workers can support different types of rendering. The *3D worker* is based on VTK [20], which supports rendering of 3D file formats (VTK, STL, DICOM). The *InfoVis worker* is based on the Chromium [21] HTML rendering engine which allows to render interactive InfoVis content by using the InfoVis toolkit [22].

The *multimodal interaction* is provided by the *interaction system*, which constitutes a part of the exploratory environment and is described in detail in the Section 3.3.

3.2 Visualization Environment

The visualization scene consists of a 3D multi-layered environment with nodes connected through visual links (Fig. 2). Each node is classified according to the spatial range of the acquired dataset and its suitability for presentation by a SciVis or InfoVis technique. Such parameters, stored in the metadata database, define the visualization properties of the nodes on the scene [12].

The *layers*, distinguished by their z-order, are *focus*, *context* and *background*. They group the nodes with the same spatial scale. These nodes, including 2D, 3D or InfoVis contents, allow for a consistent representation. *Focus* constitutes the main scale of interest of the user. Datasets with InfoVis and SciVis suitabilities are linked and visualized on the foreground. *Context* is placed behind and aims to provide context to the data on the focus layer with data coming from a contiguous spatial scale. Only main SciVis datasets are presented and these are spatially aligned with the Focus layer. *Background* is the last layer, and completes the general view across all the spatial ranges. The most representative SciVis dataset node is presented by using the call-out technique, alleviating the differences in the order of magnitude of data.

Visual links between nodes represent semantic relations across datasets, provided by the underlying ontology of the metadata database. These visual cues can take different forms, including arrows and region of interest markers. Visual cues play an important role in the presentation of hierarchy among the disease features in a multiscalar pathology.

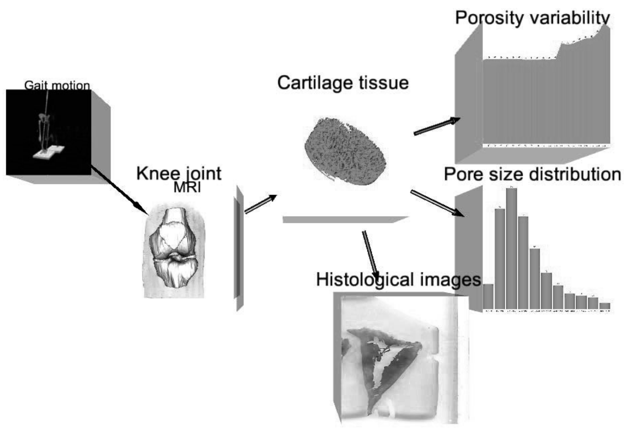

Fig. 2. Visualization environment. Example of a multiscalar set of datasets (patient-specific knee joint from cellular, organic and behavior scales) placed on *focus* (knee joint, 3D reconstruction of micro-CT scan of cartilage of meniscus, graphs associated, and histological images of meniscus), *context* (MRI of knee) and *background* (gait motion analysis) layers.

3.3 Multimodal Interaction

Multimodal interaction is an approach to integrate interfaces with different interaction qualities, similarly to the way humans communicate. This approach includes various scenarios and subsequent interfaces e.g.: (i) manipulating the objects with hands through hand gesture device, (ii) being able to feel underlying structures through force feedback loop of a haptic device, (iii) ultimately using traditional means of interaction like mouse and keyboard. The architecture of the interaction system (Fig. 3a) follows the modular principle of the overall system in order to decouple any of the interfaces from the exploratory environment (Fig. 3b) if necessary without loosing its major functionality.

The following sections describe the implemented methods on the multimodal interaction.

Hand Gestures. The Leap Motion high-speed infrared depth camera was chosen due to its low-latency processing and low price [23]. Leap Motion provides basic hand tracking algorithms bundled with its driver processing stack. Network-based access is a core functionality of this stack, enabling the use of this interface also on mobile devices without capabilities to run a full version of computer vision tracking algorithms. Leap Motion is especially suited for hand tracking in a working area adjusted to a user sitting in front of the screen. All implemented gestures were designed according to this assumption.

Different gestures include: *(i) Grasping and moving* nodes around together with their corresponding layer. *(ii) Two-hand stretching/compressing* nodes allowing to expand/shrink them for a detailed/general observation. *(iii) Pinching with two fingers* to changes a node's internal features, like rotating a 3D model or changing the speed of a temporal dataset. *(iv) Waving hands horizontally* to clean the central part of the 3D workspace, by moving all nodes to the edges.

Haptics. For haptic interaction a SensAble Phantom Premium 1.5 device is used. However the use of another device is possible since the interaction system makes use of the framework library H3DAPI [24], which supports other haptic devices and manufacturers as well.

Communication between the interaction system and the Phantom device is performed via a network using a H3DAPI-based server working on an individual machine. This is a requirement of haptic interfaces due to the need of high rate control updates and high computational power [25]. The interaction system needs to take care to synchronize the position of the haptic probe and the scene geometry with the haptic interface machine. The H3DAPI framework handles haptic rendering of individual 3D datasets on the haptic machine (connecting directly to the data repository or the cache manager).

Traditional Input. The interaction system still accepts basic input from mouse and keyboard, although the system design emphasizes supporting novel interaction scenarios. This duality creates a perfect opportunity for the analysis of comfort factors between conventional and modern interface techniques as described in the following section.

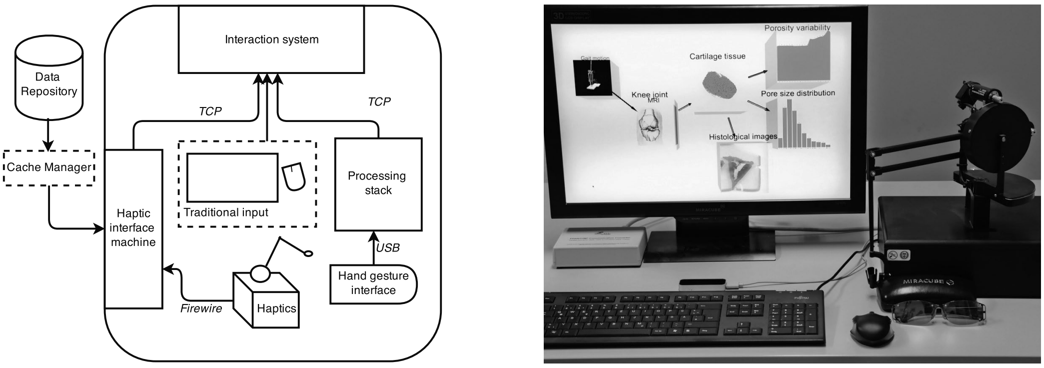

Fig. 3. (a) Multi-modal interaction architecture (b) Proposed exploratory environment

4 Evaluation

A controlled experiment was conducted in order to compare the major visualization and interaction features of our proposed approach with the conventional methods (Table 1). Hand gesture interaction, as the primary method from our multimodal strategy, was chosen to be compared with the mouse interaction. The tasks under evaluation were related to the exploration of a complete patient-specific knee joint dataset.

Subjects. The experiment population was composed of 13 volunteers (aged 20 to 31, 9 males, 4 females, without visual deficiencies). The participants were members of the groups addressed in the design of the system, involving users from the fields of computer graphics, physics and biomechanical engineering.

Evaluation setup. The visualization environment was run on a MacBook Pro computer with external Miracube Full HD 16:10 passive stereoscopic display. Regarding interaction, the hand gesture tracking was provided by the Leap Motion device, and the Razer Orochi gaming grade device was used for the mouse input. The test was conducted under stable artificial light conditions.

Protocol. There are 9 scenarios designed to evaluate each pair of the features, defined in Table 2. Each scenario is evaluated twice, using a condition associated first with feature A and then with feature B, other conditions remain unchanged during each scenario. All these 18 cases, in a random sequence different for each participant, are performed using the mouse and repeated with the Leap Motion device. All the participants performed the same set of 36 tasks.

During each scenario participants were asked to perform tasks related to the exploration of multiscalar data of the knee joint. Every scenario was composed of a maximum of 8 nodes containing patient-specific knee joint datasets from the behavior, organic and cellular scales (as shown in the Fig. 2) which had different visualization properties, described in the Table 2. Prior to the evaluation users were trained on two example tasks, in order to learn how to manipulate the nodes with both methods of interaction. Users were observed for the full duration of experiment. After performing each task, participants gave comfort score - an integer between 0 and 10 (0 - uncomfortable; 10 - comfortable). After completing all tasks, users answered a written questionnaire in order to assess their comfort with concrete visualization properties.

Table 2. Description of scenarios and evaluated features (X indicates the pair of features under evaluation)

Cond.	Features		Scenarios								
	Feature A	Feature B	S1	S2	S3	S4	S5	S6	S7	S8	S9
1	File tree list	Datasets displayed in nodes	X	B	B	B	B	B	B	B	B
2	Rectangle nodes	Circle nodes	A	X	A	A	B	B	A	B	B
3	Opaque nodes	Semi-transparent	B	A	X	B	B	A	B	B	B
4	Flat workspace	Multi-layered workspace (max. 3 layers)	B	B	B	X	B	B	A	B	B
5	Linear depth scale and placeholders	Non-linear depth scale	B	B	B	B	X	B	B	B	B
6	3D Monoscopic	3D Stereoscopic	B	A	B	B	B	X	A	A	B
7	Separated SciVis and InfoVis views	Linked views of SciVis and InfoVis	X	A	A	A	B	B	X	X	A
8	Only description of each node	Visual (semantic) links between nodes	A	A	A	A	A	A	A	X	A
9	Manual alignment of nodes	Guided alignment of nodes	A	A	B	A	A	B	B	B	X

Task of the scenario S1. Indicate the maximum value of the bar chart. S2. Find zone in the cartilage. S3. Find color of the MRI of the leg. S4. Find the leg which belongs to the knee system. S5. Find the color of the cartilage of meniscus S6. Indicate the action performed in the gait motion dataset S7. Indicate the maximum value of variation during the gait motion S8. Find the dataset which might be influenced by a problem on the knee system S9. Fuse the knee system with the MRI dataset. **Questions on written formulaire** Indicate preference between: Q1. File tree list / Nodes containing datasets. Q2. Cube / Sphere as shape of the node for exploration of SciVis data Q3. Cube / Sphere as shape of the node for exploration of InfoVis data Q4. Opacity / Transparency of nodes Q5. Arrows / No arrows between nodes **Datasets** Gait motion analysis (video), Knee joint (DICOM, VTK), histology of meniscus (HQ images), cartilage of meniscus (3D reconstruction of micro-CT scan) and graphs associated (InfoVis)

Data Analysis and Discussion. The results obtained during the experiment were preprocessed in order to obtain a trinary user preference value. This preference value was calculated for each pair of cases individually from visualization and interaction perspectives. Visualization preference was calculated by pairing cases with the same scenario and interaction methods and opposite condition under test. Similarly, interaction preference was calculated by pairing cases with the same scenario and condition under test and opposite interaction method. In order to determine the preference value, the following rule was used: if scores from the two cases have the same value then there is *no preference* else preference was chosen in favor of the case with higher score.

Figure 4 presents the distribution of preferences, based on evaluated conditions (visualization) and performed scenarios (interaction). Figure 4a shows that users preferred the proposed visualization for most of the conditions (8 out of 9) rather than conventional approaches. The preference is even more visible in the conditions 1, 4, 5 and 9 in which users found appealing the idea of (1) displaying all relevant datasets, (4) multi-layered workspace, (5) non-linear depth scale and (9) computer supported manipulation of datasets. The results also reveals that there is a susceptible lower preference for (6) 3D stereoscopic presentation of

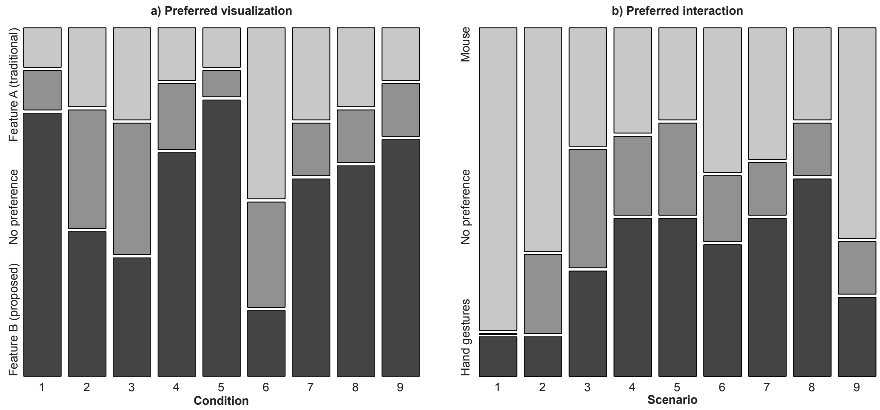

Fig. 4. Distribution of user preference related to: a) visualization b) interaction

content. This might be attributed to the passive polarized stereoscopic technology display used during the experiment. Since this display has narrow vertical viewing angles, the users could have changed their body posture after initial calibration, causing visual discomfort and affecting the preference values. In terms of interaction (Fig. 4b) results show that users do not have one preferred method of interaction. The results from scenarios 4, 5, 7 and 8 suggest that hand gesture interface was the users' first choice in the tasks based on node manipulation, where the advantage of direct 3D gestures manipulation is clear. The results from other scenarios, either show no clear preferences (scenario 3 and 6), or tend to favor traditional mean of interaction (scenario 1, 2 and 9).

From the written questionnaire, almost all users preferred nodes displaying datasets than a tree list structure (75%), the cube was preferred as a node representation figure for InfoVis exploration (80%) and for manipulation of 3D SciVis models (70%). The qualitative analysis showed that users opt more for a opaque node (64%) than for transparent ones. Arrows between nodes helped to facilitate to understand the scene (92%). The observation of the experiment revealed that the arrows were more useful for the users with no previous knowledge in the concrete scale. The absence of arrows showed how their action was based on spatial proximity or experience. In terms of interaction, it was observed that users' skills in gesture control improved between each task. Although the impact of this effect was mitigated by randomization of the case sequence order, the learning curve could still lower the overall score attributed to hand gestures.

5 Conclusions and Future Plans

The proposed exploratory environment supports the analysis of pathologies of multi-scale nature. The visualization allows for the presentation of a complete set of multiscalar datasets as individual nodes in a single view. Visually indicating semantic connections between the nodes is essential in order to understand relations of the contained datasets. The multimodal interaction allows users to feel and manipulate 3D objects in a natural and intuitive manner.

Referring to the example of the Introduction, this tool allows a multidisciplinary team of experts to explore the entire range of datatypes related to osteoarthritis. The proposed interactions allow, for instance, an intuitive and thereby fast observation of the relevant datasets. Visualization helps to observe spatially the relationships among datasets, e.g. the propagation of the cartilage degradation evidenced in each dataset.

The evaluation of the visualization environment revealed that our proposed features had major acceptance among the study participants. This involves a multilayered workspace, with non-linear depth scale, which contains datasets in cube nodes. In terms of interaction, no clear preference for interaction method shows that users tend to adapt and be pragmatic in their choices. It is good that participants were not bound to the traditional way of thinking about interaction and therefore profited three-dimensional gestures interaction in the situations that the gestures provide the highest gain. It is also important to note that although participants were "experts" in using mouse, their prior experience with gesture based interfaces was limited.

Our future work is based on improving the features of the visualization and interaction system. In terms of visualization, next steps will handle customized visual links according to the nature of dataset, and the occlusion avoidance of nodes. A higher level of integration between visualization and interaction, e.g. by the introduction of additional visual feedback for each interaction scenario, might lower the user confusion while performing more complex gestures. Analysing different variants of hand gestures and their influence on comfort, as well as focusing on multimodal scenarios involving more input methods are also interesting for further investigation.

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