Tangible BioNets: Multi-Surface and Tangible Interactions for Exploring Structural Features of Biological Networks

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Biological networks analysis has become a systematic and large-scale phenomenon. Most biological systems are often difficult to interpret due to the complexity of relationships and structural features. Moreover, existing primarily web-based interfaces for biological networks analysis often have limitations in usability as well as in supporting high-level reasoning and collaboration. Interactive surfaces coupled with tangible interactions offer opportunities to improve the comparison and analysis of large biological networks, which can aid researchers in making hypotheses and forming insights. We present Tangible BioNets, an active tangible and multi-surface system that allows users with diverse expertise to explore and understand the structural and functional aspects of biological organisms individually or collaboratively. The system was designed through an iterative co-design process and facilitates the exploration of biological network topology, catalyzing the generation of new insights. We describe a first informal evaluation with expert users and discuss considerations for designing tangible and multi-surface systems for large biological datasets.¹

CCS Concepts: • **Human-centered computing~Collaborative interaction** • **Human-centered computing~Interaction techniques** • **Human-centered computing~Interaction design process and methods** • **Human-centered computing~Visualization application domains** • **Human-centered computing~Scientific visualization** • *Human-centered computing~User interface design* • *Human-centered computing~User centered design* • *Human-centered computing~Visual analytics*

KEYWORDS

Tangible interaction; multi-surface interaction; interactive tabletops; interactive wall; active tangibles; biological networks; visualization; exploration; collaboration;

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1 INTRODUCTION

Biological networks analysis has become a systematic and large-scale phenomenon. Researchers working in this area investigate gene interactions in different organisms in order to gain insights into the functional and evolutionary connections among genes such as the resiliency of a network, how information flows through a network, and what is the effect of a disruption on a network. These insights are crucial for determining essential genes in cellular life. However, challenges in the analysis of gene interactions arise due to the large number of genes, which increases the complexity of how to efficiently and effectively discover and understand their structural features in order to gain deeper insights into the organizational principles of biological networks. As a result, computational methods and visualization tools have become central components of biological networks analysis. These methods and tools intend to describe relations within complex systems and play a key role in understanding cellular functions. Some of these efforts are focused on reconstructing the biological network topology by using existing features from signal processing, mathematics, and physics, and relating them to cellular organization. However, based on the interdisciplinary nature of this research, these features are difficult to follow and understand. Therefore, much of the reconstruction methods have been developed based on unreal topological features that are borrowed from engineering fields. Moreover, nowadays researchers from different disciplines are increasingly doing computational biology research in larger groups [14]. However, they lack tools for collaboratively surveying and gathering evidence to confirm the meaningfulness of identified features among an interdisciplinary team of researchers. The difficulty of understanding large biological networks is additionally complicated by the significant limitations that the existing, often web-based, tools have in terms of usability and persistence of data and views [8,29], as well as in terms of support for high-level reasoning and collaboration [20,24].

In recent years, there has been a growing interest in the use of tangible and embodied interaction (TEI) techniques and large tabletop/wall displays to facilitate problem solving and understanding around large genomic datasets [24,27]. Tangible and tabletop interfaces have proved to be effective in supporting collaboration, distributed cognition, and reflection [27], making them good candidates for enhancing research and discovery around large biological datasets. However, while TEI approaches have potential benefits for working with big biological datasets, Shaer et al. [24] outlined some of the broad challenges of designing for computational biology, including the diversity of users, the scale of the data, and the heterogeneity of the datasets, as well as potential areas where further interaction research is needed. Some potential research directions included handling scale and complexity in TEI systems, representing and transforming between multiple scales and types of data, highlighting connections between multiple forms of evidence, and supporting discovery and learning for diverse users, among others. As suggested by Shaer et al. [24], furthering this research may be best approached: 1) with initial small steps that address specific problems, and then investigating how the designed visualization and interaction methods can be generalized, and 2) by building collaborations between TEI and genomics researchers in order to help move both fields forward together.

In this spirit, our work aims to further the research agenda described by Shaer et al. [24] within the specific context of biological networks analysis through an interdisciplinary collaboration between three biomedical engineering (BME) researchers with experience in bioinformatics tools, an electrical and computer engineer, and four human computer interaction (HCI) researchers with expertise in tangible and wall/tabletop interaction methods. Together, we investigate how multi-display environments coupled with TEI techniques can be used to support learning and discovery in the analysis and reconstruction of gene interaction networks. Given the complex and interdisciplinary nature of biological networks analysis, our work looks specifically at: 1) how tangible interactions on and off an interactive tabletop surface can

support search and comparison within the data, 2) how multiple displays at different scales can support visualization and comparison of large networks and multiple forms of related evidence, and 3) how the system and interactions can be designed to support collaboration among researchers from various backgrounds. We follow an iterative co-design and research through design process in which BME experts on the team use the system to work on networks reconstruction while the system is iteratively designed and developed by the whole team. In this model, the system is tested continuously throughout the design process. All design decisions and revisions are informed by the practices and needs of BME experts, and are discussed as a group prior to implementation.

In this paper, we present the first complete version of the Tangible BioNets system, which is the result of the above-described design process. In the following sections we describe the related work and background context for our research. Then, we elaborate on our design process and goals, and describe the design and implementation of the Tangible BioNets system. We also present the results of a first informal evaluation with external expert users, discuss design considerations that stem from both the co-design process and informal evaluation, and conclude with an outlook on future directions.

2 RELATED WORKS

2.1 Biological Data Visualization

Biological and health sciences have become important players in the meta-data world. Recently, biological databases have expanded by collecting various types of genetic and clinical factors such as gene and protein interactions. Also, GUI visualization techniques have been emphasized in the understanding and accessibility of these complex biological data. A comprehensive review done by Pavlopoulos et al. [22] provides a selection of effective and common genome and systems biology visualization tools and discusses their limitations and the importance of using the advances from HCI and the gaming industry to make strong interactions with big biological data. One of the limitations is that current visualization tools are focused only on visualizing data, rather than on exploring relationships and making interpretable comparisons between different structural features of data [12]. Also, current tools focus largely on single user interaction and do not provide platforms for collaborative exploration [16,17].

2.2 TEI for Computational Biology

TEIs hold the promise of overcoming some of the limitations of biology visualization tools outlined above. Megren and et al. [1] have shown that users found patterns in data visualization tasks faster on tangible user interfaces than with only multi-touch screens. Shaer et al. [24] have described the challenges of using TEIs for the study of genomic data and have also suggested potential solutions to those challenges for the TEI community. In particular, the paper proposes the use of tangible interaction techniques and large surfaces as a means of facilitating the manipulation and investigation of large and complex datasets.

In recent years, a few TEI and/or tabletop systems have been developed that partially address the challenges defined by Shaer et al. [24]. A multi-touch tabletop interface named G-nome Surfer [25] was designed to browse gene expression data. However, G-nome Surfer was designed for non-experts and does not support tangible interaction. Its focus is more on learning of biological concepts rather than on the exploration and analysis of data and direct comparison of information by experts. A tangible museum exhibit, SynFlo [21], facilitates engagement in a bio-design activity by using passive tangibles as well as active tangibles, programmable physical objects with integrated display, sensing, or actuation technologies [27]. SynFlo invites collaboration between children, students, and parents, and is focused on teaching

synthetic biology concepts in an informal learning environment rather than on exploration and investigation by experts. In addition, Eugenie [13] is a multi-touch and tangible interface for searching big biological datasets. The system uses tangible interactions to form queries and explore 3,000 biological parts. Eugenie's limitations include restricted table space and users' lack of understanding of the designed interactions. A vocabulary of user-defined gestures for interacting with active tangibles to manipulate large datasets that was defined by Valdes et al. [27] serves as inspiration for our work. However, the study did not address collaborative exploration scenarios, and interactions for comparing datasets were not considered.

Most closely related to our work, Sparse Tangibles [3] was a system for collaborative gene network exploration of a database of organisms. It employed an interactive tabletop and custom active tangibles to assist expert users in better understanding experimentally extracted gene interactions. The system provided an interface to explore genes and proteins on different organisms, and used stacking of active tangibles to apply an agreement score filter to show how much each genetic interaction can be trusted based its number of related published papers. In contrast to Sparse Tangibles, our Tangible BioNets system provides access to large-scale genetic interaction datasets, implements algorithms for extracting sixty defined network structural features, and allows comparison of different networks and features on large displays. In addition, Tangible BioNets is a multi-platform system that includes an interactive tabletop, active tangibles, an interactive Wall (iWall) and several mobile devices.

2.3 Large Interactive Displays for Scientific Visualization

Researchers have also studied the effects of display size on various tasks (such as productivity, navigation, user performance improvement, perception, etc.) based on the observations of real uses of a wall display (see e.g., [4,6,10,30]). Although these studies show the benefits of multiple displays, most of them use traditional desktop settings where users sit in front of a large display with no physical interaction. Liu et al. [19] highlight the usage of multiple displays as a wall to address visualization, search, sense-making, and data manipulation tasks. They observed that multiple displays gain a sizable advantage by displaying more information and enhancing peripheral awareness as the tasks become more difficult. In addition, the large-scale wall provides a virtual workspace where meaning is encoded in the spatial relationship between data, the wall, and the user [2]. There is a need to extend this type of research to support data exploration and collaborative work, where multiple users could track and compare various aspects of the data and have the chance to share and clarify their own prior knowledge with their colleagues. This encouraged us to design and develop the Tangible BioNets platform to provide a deeper understanding of biological networks in which structural features can be deployed, assessed, and validated by users from different backgrounds.

3 CONTEXT: GENETIC NETWORKS DESIGN

Gene interactions have been investigated in different organisms to reveal insight into functional and evolutionary connections among genes based on their produced proteins [18,28]. Network analysis and modeling define gene networks as a set of nodes (genes or their produced proteins) and edges forming linkages between them (interactions). Network scientists often represent a network through its adjacency matrix. When there is information regarding the direction of gene interactions and the importance of these interactions (represented with a weight value), it is possible to define four adjacency matrices (binary directed, binary undirected, weighted directed, weighted undirected). This simplification makes it easier for scientists to extract local and global structural features, resulting in improved insight into the processes driving the growth and response of living organisms [5]. Evidence gathering, by examining the structural features among various biological systems, can help to identify

functional groups interactively with or without prior knowledge of the biological systems' processes.

The challenge is that many structural features of networks are abstractly defined in mathematics. In modeling biological systems like gene interaction networks, researchers from different fields such as biology, biomedical engineering, and mathematics, integrate these features into the models they build in order to gain insight into the functioning of the biological systems. However, it is not clear if these structural features that are defined abstractly in mathematics are valid when applied to biological networks, and there is currently no easy way for researchers to test this. As a result, when these structural features are used in biological modeling, it is unclear whether the models are accurate and whether they can be used to provide any valid insights. What is needed, then, is a way for researchers to explore and compare the structural features of networks that are defined in mathematics on various biological networks in order to understand whether or not they are valid. Given the interdisciplinary nature of this problem, which brings together expertise from biology, mathematics and engineering, what is further needed is a collaborative system that can allow researchers from different disciplines to work together to develop an understanding of the structural features from mathematics as they are applied to different biological networks.

4 DESIGN PROCESS AND GOALS

We follow an iterative co-design and research through design methodology to design and develop the Tangible BioNets system. Our broad goal is to investigate how multi-display environments coupled with TEI techniques can be designed to support biological networks analysis, thereby advancing both the HCI/TEI and computational biology fields, as described by Shaer et al. [24]. Our team includes the ultimate users of the system: three BME researchers with engineering and biology backgrounds and one electrical/computer engineer, all of whom were involved throughout the design and development process of Tangible BioNets. We developed the collaborative interaction and visualization techniques in support of specific scenarios that these expert co-designers (a.k.a. users) were working on. We analyzed their needs and began to iteratively design and develop prototypes to support their needs. They in turn worked with these prototypes at each step of the process and provided feedback about whether and how well the designs met their needs, what features and interactions were needed, as well as the specific way in which these features and interactions were designed and implemented. To this end, our whole team met on a weekly basis in order to assess current progress based on system use, make design decisions, and decide on next steps for improving and refining the design.

Our BME co-designers work with the BioGrid database, an online database of gene interactions in 60 organisms [26], with the intention of developing novel and robust methodologies that integrate the structural features of gene interaction networks in their models. Based on the domain problem described in section 3 above, the key requirements for the tool were identified as: 1) provide a means for researchers to familiarize themselves with the concepts of different structural features as they are applied to individual networks, 2) provide a means for researchers to get a better understanding of the same feature as it is applied to networks of different sizes, 3) explore the similarity or dissimilarity of different features as they are applied to one or more biological networks, and 4) to provide a common space to share and juxtapose users' understanding of biological network topologies. This means providing support for navigating and selecting biological organism networks and structural features, as well as support for both single network/feature investigation and multiple network/feature comparison. Additionally, given the interdisciplinary and collaborative nature of biological networks analysis, the tool needs to support collaborative interactions by multiple users.

Based on these requirements and informed by the literature discussed above, we set out to investigate: 1) how tangible interactions on and off an interactive tabletop surface can support

search and comparison within the data, 2) how multiple displays at different scales can support visualization and comparison of large networks and multiple forms of related evidence, and 3) how the system and interactions can be designed to support collaboration among researchers from different backgrounds. According to this, and with the research agenda outlined by [24] in mind, we formulated the following set of design goals:

G1: Provide multiple entry points for search, comparison and filtering of the data.

Prior work has shown that tangibles perform significantly better than touch interactions when users need to apply basic manipulation tasks and require a large number of attempts in a closed-loop feedback process in order to gain insights [9]. The same study also showed that touch interactions perform notably better in terms of time and number of actions in conditions that require multiple exploration and selection operations. We decided to use a combination of touch and tangible interactions on an interactive tabletop surface to leverage the advantages of both approaches. We use active tangibles based on a design by East et al. called “actibles” [11]. The actibles were selected as they provide an integrated display screen, LED feedback, and support for both on and off the table interactions. This allows for multiple entry points into the dataset, as well as a persistent presence that is visible to all users at once.

G2: Provide support for visualization and comparison of large biological networks.

Prior works have shown that large high-resolution displays are beneficial for sense-making [2] and knowledge discovery [23] when dealing with large amounts of data. We decided to use a large interactive wall display for visualizing and comparing multiple gene interaction networks at the same time. The large wall display was selected given the large size of the gene interaction networks, which can have as many as 20,000 gene interactions that need to be displayed at once, and our BME co-designers often needed to display and compare several networks at the same time.

G3: Provide support for additional detailed analyses of the data. Mobile devices, in conjunction with large displays can support detail and context interactions [7] that are ideal for collaborative tasks. We decided to use separate smaller interactive displays to allow for additional analyses and visualizations of the gene interaction networks and their structural features. Mobile devices such as tablets were selected, as they offer a form factor that can be easily moved around. They can thus serve as separate mobile windows into the data, allowing users to walk around with them as they investigate the larger-scale views of the networks on the interactive wall-display. Additionally, using small separate displays for certain information saves screen real-estate on the table and wall displays.

5 TANGIBLE BIONETS

Tangible BioNets employs tangible and tabletop interactions coupled with visualizations on both large and small displays to allow users to browse, select, compare and analyze gene interaction networks and various structural features. Active tangible interactions both on and off the table are used as a means to navigate the data, and make selections and comparisons. We use the actibles [11] for this purpose, which support tangible interactions including bumping, stacking and shaking. The actibles also support touch input, e.g. tap and swipe, and graphical feedback on their small display screen, as well as visual feedback via their ring of colored LEDs. A large interactive wall display (the 55-foot iWall in our lab) is used to visualize selected networks and structural features. Additional small displays such as tablets or smartphones are used for deeper analysis of the networks and selected structural features (see Figure 1). We provide an overview of the system and interaction techniques, then illustrate the system’s functionality with a user interaction scenario, and lastly describe the designed interactions in detail.

Fig. 1. System overview. Interactive wall: to represent the organisms and structural features; Active tangibles: to control the exploration process; Interactive Tabletop: to select organisms and structural features; Tablets: to display the structural features which are not applicable on the network (on the interactive wall).

5.1 Overview of System and Interaction Techniques

The BME researchers work with two main elements in their analyses. First, they need to choose the specific organism network(s) they want to work with from the BioGrid database, and next they need to select which structural features they want to test on the selected networks. Users also need to be able to compare multiple organism networks with the same or different structural features applied, and analyze the effects of the applied structural features. As described above, our design was informed by prior work as well as by the needs of the BME researchers. During our co-design process, we iteratively prototyped and refined the system features and interactions based on input and feedback from the BME researchers. Here we describe the final system and interactions techniques.

We use the actibles as tangible handles to hold organisms and structural features, as users can easily assign one or more actible(s) to different organism networks or structural features, and make use of these in subsequent comparisons. The actibles are manipulated on an interactive table, which provides additional screen space for exploring and selecting organism networks and structural features. Per our key requirements and in order to meet our design goals, we designed the system around a core set of basic interactions with the actibles and tabletop. These are accompanied by visualizations on the iWall and any connected mobile devices. These core interactions are illustrated in Figure 2: (a) swiping/touching on an actible's screen, (b) touching on the tabletop, (c) bumping an actible to a specific side of another actible, and (d) stacking an actible on top of another actible. Conceptually, these basic interactions fulfill different task goals. Touch interactions (see Figure 2(a&b)) are used to browse and select organisms and structural features, bumping interactions (see Figure 2(c)) are used for single organism interactions, and stacking interactions (see Figure 2(d)) are used for multi-organism interactions.

We created three modes to navigate on the active tangible menu: Organisms Space (OS) (see Figure 2(a)(i)), Structural Features Space (SFS) (see Figure 2(a)(ii)), and Networks Workspace

(NW) (see Figure 2(a)(iii)). The user can swipe and select different modes based on their needs. This interaction is familiar from mobile devices and helps make the user's experience as fluid as possible. The OS and SFS modes support the selection of organism networks and structural features. When an actible is assigned to OS or SFS mode, specific organisms or structural features can be selected using the donut menu that appears around the actible when it is placed on the table (see Figure 2(b)). In contrast, the NW mode supports comparison and analysis. When an actible assigned to NW mode is placed on the table, it will have four empty containers around it, and four corresponding empty containers will be displayed on iWall (see Figure 2(a)(iii)). Note that our design uses four containers for the Networks Workspace because of the four-sided "squircular" design and sensor layout of the actibles [11]. The inside walls of the actible's case house magnets and Hall effect sensors to detect adjacency interactions (bumping, neighboring, and stacking). Having only four containers was not perceived as a limitation by the BME researchers, who felt that this was a sufficient number for them to work with. They also preferred the simple mapping of one side to one container over having additional containers per side, along with additional interactions to select between them.

Fig. 2. Tangible BioNets consists of four core interactions: (a) swiping and touching to select the mode on an actible, (b) selecting organisms or features by touching the tabletop menu around an actible, (c) bumping an actible to a specific side of a container actible to visualize or apply features to single organisms, and (d) stacking an actible on top of another actible to perform operations on multiple organisms or features.

Bumping interactions are used to copy individual organisms into the containers of a NW actible and the corresponding networks are then visualized on the iWall in the corresponding container and color (see Figure 2(c)(i)). Bumping interactions are also used to apply structural features to individual organisms in specific containers, which updates the visualization on the iWall and any connected mobile devices (see Figure 2(c)(ii)). Stacking interactions are used to copy the same organism to all containers of a NW actible (see Figure 2(d)(i)), to apply a selected feature to multiple different organisms stored in a NW actible (see Figure 2(d)(ii)), or to copy a set of organisms from one NW actible to another (see Figure 2(d)(iii)). These interactions are described in more detail in section 5.3.

5.2 User Interaction Scenario

This scenario is based on the domain problem and key requirements described above. It is intended to illustrate how two users work with the Tangible BioNets system. Emily and Jasjit are investigating the concepts of structural features on genetic networks. Each of them has their own tablet. Typically, they work by performing independent analyses of the networks and then coming together to discuss their observations. With Tangible BioNets, they can perform their analyses in a hands-on manner, together or in parallel, and discuss them immediately. This supports the formation of insights by allowing them to get a more accurate understanding of the biological networks topology, and to develop a shared conceptual model of similarity or dissimilarity within the structural features of these networks in real time. This 3-step scenario describes part of their work process with Tangible BioNets, in which they visualize a set of four genetic networks, *E. coli*, HIV, *Danio rerio*, *Rattus norvegicus*. Step 1) to be familiar with the concept of each feature; Step 2) to get a better understanding of the feature applied to networks of different sizes; and Step 3) to explore similarity or dissimilarity of the features.

Step 1: Emily and Jasjit each place an actible on the interactive table and swipe to select the Organisms Space (OS) mode. A donut menu of organism networks is shown around each actible, and the network and its type can be selected by tapping on the screen. Emily and Jasjit select the *E. coli* and HIV networks, respectively, and then specify the network type to be “binary directed”. Emily places a third actible on the table and selects the Networks Workspace (NW) mode. Four empty containers are displayed around the actible, and four corresponding empty containers are shown on the iWall. These containers can hold selected organisms. Emily bumps her OS actible to the NW actible in the direction to copy *E. coli* to the first empty container on the iWall, while Jasjit copies HIV to the third empty container. The *E. coli* and HIV networks are visualized on the iWall in the first and third containers. Emily and Jasjit then select and copy the *Danio rerio* and *Rattus norvegicus* networks to the second and fourth containers on the iWall. Next, they want to test structural features on their selected networks. By switching their first actibles to the Structural Features Space (SFS) mode, they select a feature category (Network-based) and then a feature of interest (Betweenness for Emily, Eigen Space for Jasjit). They apply these features to their organism networks by bumping the actible to the sides of the NW actible holding their networks. They see the plots for Eigen Space on their tablets, as well as the achieved outcomes of Betweenness for each gene on the relevant networks on the iWall. This is visualized by changing the size of nodes based on the outcome values. Emily and Jasjit now inspect the visualizations and discuss the effects of the different features.

Step 2: Emily and Jasjit use their first actible and select four networks of different sizes like in the first step and copy them to four empty containers by bumping their first actible to different sides of the NW actible. Next, Emily selects the Eigen Space feature with her first actible and stacks it on top of the NW actible. In this way, the Eigen Space feature is applied to all selected organisms at the same time and becomes visible on tablet screen as four different interactive plots. Emily and Jasjit now observe and discuss the effects of applying the same feature to different sized networks.

Step 3: Emily uses one actible to select NW mode and another actible to select the E.coli organism. She stacks her E.coli actible on the NW one. This copies the E.coli organism into all containers of the NW actible, and the corresponding network is shown in all containers on the iWall. Jasjit and Emily then each select two different structural features and bump each of them to one of the containers holding the E.coli organism. This applies four different structural features to the same organism, allowing Emily and Jasjit to inspect the changes in nodes/links on the iWall as well as corresponding plots on their tablets. This helps them discuss and understand the similarities and dissimilarities among the selected structural features.

Jasjit uses his first actible and selects four networks like in the first step and copies them to the NW actible to display them on the iWall. Emily places her first NW actible on the table and stacks the second actible, which now holds the four selected networks, onto her first actible. This copies the selected networks into her actible and also duplicates them on the iWall, which now displays eight networks. Jasjit and Emily want to compare the Clustering Coefficient and Eigen Centrality features to see if there is any correlation between them on networks with different sizes. They now have two NW actibles, each containing the four selected organisms. They use Jasjit's first actible two times. Emily selects Clustering Coefficient and stacks it on one NW actible, which applies this feature to four networks on the iWall. Jasjit then picks the Eigen Centrality feature and stacks it onto the other NW actible to apply it to the other four networks. Jasjit and Emily now observe and discuss the effects of these two features on the same set of four networks.

5.3 Detailed Description of Designed Interactions

We provide a detailed description of the interactions that were designed to support: 1) browsing and selection of networks and structural features, and 2) comparison and analysis of networks with different structural features applied. The description is accompanied by photos of the Tangible BioNets system in action.

5.3.1 Browsing and Selection

Selecting Organism Networks: When an actible in Organisms Space (OS) mode is placed on and moved around the table, the organism selection menu is shown around it. Rotating the actible causes the menu to rotate as well. This donut-shaped menu is divided into 60 segments based on the number of organisms available in the BioGrid database. Each segment is labeled based on an organism's name (see Figure 3(a)). To select an organism, users tap the corresponding on-table segment. The system then brings up a secondary donut menu of all available network types for the selected organism: Binary Directed (BD), Binary Un-directed (BU), Weighted Directed (WD), Weighted Un-directed (WU) (see Figure 3(b)). Once the network type is selected, the actible's screen shows the organism name and network type; additionally, the actible's LED ring changes color to reflect the color of the selected organism's segment (see Figure 3(c)). The donut menu disappears when the actible is lifted from the table and reappears when placed back on the table. The user is also able to select multiple networks using the same actible. Any selection made will overwrite the previous one. The Networks Workspace mode discussed later supports comparison of multiple organism networks on the iWall and mobile displays. While the donut menu works well for the current set of 60 organisms that are available in the BioGrid database, in its current form it would not scale well to a much larger number of organisms. This can be addressed in future implementations, for example by categorizing the organisms by species, and allowing a user to first select the species in a first layer of the donut-menu, and then the specific organism within that species in a secondary menu. This grouping approach with secondary menu is currently used for the structural features described next.

Selecting Structural Features: When an actible in Structural Features Space (SFS) mode is placed on the table, the structural feature selection menu is shown around it. Selecting structural features is similar to selecting organisms. In SFS mode, the donut menu shows categories of structural features named based on the principal components of the networks they

affect: Node-based, Linked-based, and Network-based features (see Figure 3(d)). After selecting one of the feature types, all the features of that type are displayed in a secondary donut menu around the actile (see Figure 3(e)). After selecting the feature, its name is displayed on the actile's screen and the LED ring color mirrors the selected feature's color (see Figure 3(f)).

Fig. 3. (a) The OS tabletop menu, with all BioGRID organisms displayed in a donut menu. (b) When an organism is selected, its network types, such as “binary directed” are shown in a secondary menu. (c) When the network type is selected, the actile's LEDs take on the color of the selected organism. (d) The SFS tabletop menu. Feature categories are initially shown in a donut menu around the actile. (e) When a category is selected, features of that category are shown in a secondary donut menu. (f) When a feature is selected, the actile's LEDs take on the color of the selected feature.

5.3.2 Comparison and Analysis

Visualizing Organism Networks: The Networks Workspace (NW) mode allows users to visualize selected organisms on the iWall and explore the effects of different features. When the user selects the NW mode, four empty containers appear both on the iWall and on the tabletop as segments of a donut menu around the tangible. These containers remain empty until they are filled by a selected organism. To copy an organism to a specific container segment of the NW actile, a user bumps an actile in OS mode with an organism selected to the desired container's side of the NW actile. The organism's network is visualized in that container segment's corresponding container on the iWall as a force-directed network (see Figure 4). Also, the donut segment and LEDs on that side of the tangible take on the color of the copied organism, as does the corresponding iWall container. This color-coding helps users connect organisms selected on the actibles and tabletop with the visualizations shown on the iWall. Attempting to copy a new organism to a container that already houses an organism will simply overwrite that organism.

Applying Structural Features: A structural feature can be applied to an organism network by bumping an actile in SFS mode with a given feature selected to the side of the actile in NW mode that contains that organism network. Applying any feature to any organism prompts the iWall and any connected mobile devices (e.g., tablets or smartphones) to display the outcome of the features on the organisms of interest (see Figure 5). The results of applying a feature on a network on the iWall can manifest visual changes in the nodes and edges (such as increasing or

Fig. 4. iWall network visualizations. If an actible is in NW mode, its four containers are shown on the iWall. Any organisms that have been copied to containers around the actible are visualized as force-directed networks in corresponding containers on the iWall.

decreasing node radius, changing color, etc.). This function allows users to familiarize themselves with complex features on biological networks, and explore meaningful structures in

Fig. 5. Results of applying features to networks are shown on the iWall and a connected tablet. Results that target nodes or links are shown in the iWall container, whereas figures (e.g. plots, charts) produced by the feature are shown on the tablet.

these networks. Moreover, when a feature is applied to an organism, its color is reflected into the LEDs on the corresponding side of the active tangible, as well as onto the edge of the corresponding container on the iWall. This color-coding allows users to more easily see which features have been applied to the different networks visualized on the iWall. Note that the choice of colors was discussed with the BME researchers during our co-design process, and we opted for colors that are sufficiently distinct from one another both on the wall/table displays and on the LEDs of the actives, and that would also maintain good visibility of the networks shown on the wall.

Comparing Structural Features on Organisms: An important part of network analyses involves: (a) comparing a certain feature on multiple organisms to gather evidence to confirm the universality of that feature across gene interaction networks, and (b) discovering relationships between the topological features of gene interaction networks.

(a) Surveying universality of a structural feature: Users can compare a structural feature across several organisms by stacking the active assigned to that feature on top of the tangible in NW mode (see Figure 6). The stacking interaction is a quick way to apply the selected feature to all organisms stored in the NW active at once. In this way, users are able to make valuable comparisons by selecting networks of different sizes and observing the effects of a given feature on these different organisms at once.

Fig. 6. Stacking a selected feature onto an active in NW mode applies the feature to all organisms, with the outside ring reflecting the feature color.

(b) Surveying relationships between features: Users can investigate the similarities or differences between structural features on the same set of organisms. To do this, an active in NW mode that contains up to four organisms is first stacked on top of another active in NW mode in order to duplicate them. The NW active on the bottom thus receives a copy of the top active's organisms with any applied features removed, and four additional containers are displayed on the iWall representing the copied set of organisms. This can be repeated on additional actives to kickstart the process of feature comparison across a consistent set of organisms. After duplication, actives in SFS mode can be used to select each of the features of interest independently and then stacked onto the duplicated sets in

NW mode to quickly apply the different features to the consistent organism sets (see Figure 7). With each of the features affecting the network components visually in different ways, comparison of the feature effects becomes rapidly apparent and deductions about the meaning of the features and their relationships to one another in genetic networks can be made.

Fig. 7. Stacking two actives in NW mode copies all organism data from the top active into the bottom one. Top image: before stacking, the four containers on the iWall corresponding to the empty NW active are empty. Bottom image: after stacking the NW active containing four organisms onto the empty NW active as shown in the inset, the four empty containers now contain the same four organisms, but without any applied features.

6 TECHNICAL IMPLEMENTATION

Tangible BioNets is a primarily web-based platform made using front-end web development tools such as HTML, CSS, and JavaScript. Back-end tools such as Node.js and MATLAB scripts handle, process, and transfer project data. We decided on a Web-based solution for several reasons: (i) almost all current devices provide HTML/JavaScript support, which makes our system as platform independent as possible; (ii) there are numerous open source JavaScript libraries available, which eases software development; and (iii) it requires the least amount of client-side tools, and can run solely on a web browser.

Figure 8 summarizes the system's technical implementation, which generally follows the model-view-controller (MVC) design pattern. The MVC paradigm ensures that all interactable surfaces (views) get updated from the same data at the same time, so they cannot be showing conflicting "versions" of the data. We describe the implementation of the system components, including the active tangibles (actives), the interactive wall/tabletop, the mobile devices, the communication processes, and the system engine.

Fig. 8. A schematic of system architecture.

6.1 Actibles

Actibles [11] (Figure 8(d)) are hand-held devices that support tangible interactions both on and off interactive tables. Through both custom and proprietary hardware, actibles enable rapid application development by enabling the use of web technologies, such as HTML and JavaScript. The custom hardware of the actibles enables the use of tangible controls in Tangible BioNets via neighboring actions (i.e. bumping or stacking of two actibles) and physical motion (i.e. shaking). Actibles interact with other devices in Tangible BioNets in two ways. First, they feature a fiducial marker detectable by the 3-tile tabletop to enable positional tracking. Second, they connect to a central Node.js2 server over a Wi-Fi module to communicate data to other devices on the network. Technical details about the actibles design can be found in the work published by East et al. [11].

6.2 Interactive Wall/Tabletop

The interactive 12-tile wall (Figure 8(c)) and 3-tile tabletop (Figure 8(b)) used in Tangible BioNets consist of fifteen MultiTaction Cell Ultra-Thin Bezel (MT553UTB) displays³. The MT553UTB is a 55-Inch High Definition LCD display that features several built-in infrared cameras for touch and marker detection. Each display has its own internal computer running Linux. It includes a Hybrid Tracking Engine⁴ that allows for several interaction methods such as

²<https://nodejs.org/>

³<https://www.multitaction.com/>

⁴<https://cornerstone.multitouch.fi/sites/default/files/generated-content/taction-guide/adjustingtracking.html>

multi-finger touch, hold, drag, as well as fiducial marker tracking using the MultiTaction Codice markers⁵.

The interactive wall and tabletop are connected to two computers running Windows 10. A web browser is used to open the HTML5/JavaScript web-pages of the Tangible BioNets system, which display the wall and tabletop visualizations and menus. The system uses two libraries, D3.js and Paper.js. D3 is used for tabletop menus, as well as for network force simulation data. Paper.js uses the node and link data created by D3 to populate an HTML5 canvas with container-bound networks.

6.3 Mobile Devices

In our system, mobile devices that are equipped with Wi-Fi or cellular access, touch-screen interface, and wireless operation such as iPad2 and iPhone6 Plus are used for visualization of and interaction with the obtained figures (e.g. plots, charts) from applying the structural features. We use mobile devices because their size and weight allows them to be carried in one hand and manipulated with the other hand and their battery powers the device for several hours. Hence users can easily carry the figures around with them and inspect them at the same time as they inspect the network visualizations on the iWall.

6.4 Communications

To communicate between devices, a Node.js server is used in conjunction with Socket.IO, a JavaScript library that allows for real-time bidirectional communication between devices via web-browsers. When a device-based event such as a tap or swipe occurs on a device, Socket.IO broadcasts a message, which is received by the central Node.js server. Data is centralized to the server, and Socket.IO functions primarily to update clients of any changes, allowing data to remain consistent across the devices. This is also the case for TUIO positioning data; events created by MultiTaction cells are combined together on the central Node.js server, to which all other clients in the system listen.

6.5 System Engine

The system engine (Figure 8(a)) is centralized on the system's primary server; the model is stored as data in a .mat format (Figure 8(a)(i)), and the controller is implemented as a Node.js server (Figure 8 (a)(ii)) in parallel with a MATLAB looping script (Figure 8(a)(iii)) that provides the system with additional processing libraries. The hot-loading of data directly from the server's file system into MATLAB's workspace for processing removes latency from fetching external resources, and MATLAB's direct TCP connection with Node.js provides an interface for all other devices to have access to the processed information. Alternatively, MATLAB can "send" processed information through the local file system, but the TCP connection is extensible in that the MATLAB server could be run on a separate, more powerful, computer while still granting the Node.js server the processed data.

The tabletop, iWall, actibles, and mobile devices (Figure 8 (b), (c), (d) and (e), respectively) are all views that respond to user events, which get sent directly to the Node.js server through the Socket.io protocol. The primary server hosts an ad-hoc network over Wi-Fi that facilitates this view-to-controller communication. The Node.js server stores the working state of all actibles and clients, and updates all of the views depending on the users' interactions. All views are implemented as HTML5 web pages, which are hosted by the Node.js server.

⁵<https://www.multitaction.com/products/codice>

In theory, the MVC pattern mentioned above allows the system's information to be distributed to any of the views. However, because each of the views have varying usable real estate, decisions were made by the BME co-designers to distribute information according to its scale and functional contexts. For example, networks were visualized on the iWall because its larger size fits the scale of the network data, which would be impractical to view on an actible or mobile device. In contrast, plots and charts that are related to the networks are shown on the mobile devices since they require less screen real-estate but the researchers sometimes want to pick them up and take them with them (similar to graphs printed on paper) as they inspect the larger network visualizations on the wall.

7 EVALUATION

7.1 Results from the Co-Design Process

Our BME team members have used Tangible BioNets for understanding, exploring, and interpreting structural features in biological networks throughout the design and development process. We describe one example insight that served both to inform the design, as well as to iteratively test the designed interactions in a realistic use case.

The BME team members were using a stability criterion in their modeling as it is defined for the continuous domain in the control systems field (e.g., if the real parts of eigenvalues are in the left-hand plane, the system is stable). During the exploration of this feature on different biological networks using Tangible BioNets, they revealed evidence that the eigenvalue distribution of these networks follows a circle shape around the origin axis in the complex plane, which overturned their previous assumption. To this end, one of the team members made a new insight and suggested checking the definition of the stability criterion for discrete systems (e.g., a system is asymptotically stable if all its eigenvalues are located in the unit circle of the complex plane). Interestingly, it was a much better match with the obtained evidence and the BME team members utilized the discrete definition of stability criterion in their gene network reconstruction algorithm. Tangible BioNets was integral in this discovery, which would have been much more difficult to achieve in other tools for several reasons.

First, the ability to do two different types of comparisons was especially important and is difficult to achieve in existing tools. This includes applying one structural feature to several networks and applying several structural features to the same network. We discussed various options for performing these comparisons, such as selecting features from menus on the table, wall, actible or mobile device, and decided on tangible interactions for comparisons based on input from our BME users. The Networks Workspace (NW) actible combined with tangible interactions such as stacking and bumping simplified the process of making comparisons by providing physical actions as shortcuts to complex but often-used functions that might otherwise be buried in menus (e.g. duplicating sets of organisms, applying a structural feature to multiple organisms).

Second, existing tools provide no support for side-by-side comparison of multiple networks; this requires going back and forth between different windows/views. In this respect the large wall display proved useful, as the BME users were more easily able to analyze the similarities and differences between various networks and structural features. Also, the large displays made it easy for multiple users to observe and discuss the networks together.

Third, viewing other outputs of applied features (e.g., histograms) in parallel to changes shown on the networks was important for analyses. We discussed different options for presenting these outputs, such as on the wall adjacent to the networks, or on the tabletop surface, and collectively settled on the use of mobile devices for this purpose. The mobile devices allow users to focus in on different sets of outputs on their smaller screens, and users can also walk around with them in order to examine the details next to the broader context of the visualizations on the wall.

7.2 External Expert Feedback

We conducted a first informal evaluation with six experts from the biological research field in order to gain feedback on the Tangible BioNets system. The experts were from an applied genomics and cell biology department and were familiar with biological data and network science. Upon arrival, they were introduced to the system components, including the interactive wall/tabletop and active tangibles and we asked them to use their own mobile devices. Next, the participants were asked to assemble around the table and the overall concept and interactions of the Tangible BioNets system were presented to the group. They were then seated in the common area and we invited two users at a time to interact with the system. Finally, they were all assembled as a group and were asked to provide their feedback about the system in a focus group format.

The session lasted about two hours and the participants were compensated \$10 for their time. In contrast to our BME team members, they did not get the chance to use the system for their own tasks, but they helped to provide a broader perspective about the system's applicability and usefulness to other kinds of problems in the field. The majority of the participants said they interact with genetic networks in an Excel file format. Only one of them was using this data in the form of a network. They found this interactive visualization to be unique, and all of them mentioned that the system has the potential to enhance sense-making, collaborative exploration, and hypothesis formation. We briefly summarize their feedback here.

Tangible Interactions: All participants found that the bumping and stacking gestures could simplify the comparison of organisms and the exploration of features. They especially appreciated the ability to take a copy of all selected organisms by stacking. They found this useful for comparing and finding the potential relationships between features. Two users were able to collaboratively find a reverse relationship between two selected structural features that they applied on 4 selected organisms at the same time. They asked us to check the defined equations of those features to see if their hypothesis was right or not.

Visual Feedback: All participants appreciated the LED feedback and the syncing of the same color across the active tangibles, tabletop and iWall. In terms of using the color feedback around container frames to track the applied features, four of them agreed that this interaction was useful when two users are collaborating because they could more easily identify their own selected features. The other two mentioned that when they selected features they had similar colors, and they were thus confused about their applied feature. They suggested fixing this by distinguishing the color spectrum better or by adding additional signs or flags. They also noted that, given this improvement to the system, the ability to compare and distinguish different features would be one of the strongest aspects of the system.

Interdisciplinary Collaboration: All participants felt that the system could help to create a common language between users with different backgrounds. Four participants felt that the system is helpful for learning and understanding complicated mathematical concepts of biological networks for users with different levels of knowledge. The other two felt that users should have a good background in network science before using this platform. But all of them thought this platform creates a higher level of engagement and allows users to discover complex concepts, and enhances their learning process.

Broader Applicability: One participant mentioned that she has some colleagues who encountered invalid constraints when they were using reconstruction methods and she was surprised how this platform, by using comparison query, could help to avoid applying non-approved structural features to the modeling. Another participant suggested expanding the system by developing an interactive module to see the equation related to each structural feature and to allow the users to modify this equation and apply the modified one as a new feature to the selected organisms. After this comment, another participant suggested adding modeling as a module to this platform and allowing users to utilize different databases (such as

gene expression data) to apply the modified definition of features and visualize predicted networks to compare it with the consensus.

8 DISCUSSION

Based on our team's combined expertise in TEI and computational biology and a research agenda laid out by Shaer et al. [24], we set out to investigate: 1) how tangible interactions on and off an interactive tabletop surface can support search and comparison within the data, 2) how multiple displays at different scales can support visualization and comparison of large networks and multiple forms of related evidence, and 3) how the system and interactions can be designed to support collaboration among researchers from different backgrounds. We provide preliminary design considerations on these three points.

8.1 Tangible Interactions for Large Datasets

The tangible interactions were both desired by our BME co-designers and appreciated by our external experts. Through our iterative design process, we found that when working with large datasets, tangible interactions can serve as shortcuts to complex but often-used functions. For example, our BME co-designers much preferred a stacking gesture over a menu selection.

The size of biological datasets has been noted as a challenge for tangible interaction design [24]. A related challenge that emerged for us was deciding which parts of the data should be assigned to the tangibles, which is important for designers to consider from the outset. This decision can be aided by analyzing existing workflows and extracting key components. In our initial analysis of the BME co-designers' workflow, we found that they need to make two main high-level selections: organism networks and structural features. This served as a starting point for determining how to organize the tangible interactions and assigning modes to our tangibles. However, these two modes were not enough, and as we delved into the approaches for making comparisons, we realized there was a need for a "container" tangible that could house multiple selected networks at once. The container concept is not new in tangible interaction design (see e.g., [15]), but is especially useful when working with large datasets.

Another consideration is whether to use dedicated tangibles for different functions (e.g. organisms vs. structural features in our case), or to allow users to re-assign the function of a tangible. We opted for the latter approach to maintain flexibility and reduce the number of tangibles required. By allowing users to re-assign tangibles, a set of three tangibles is sufficient to allow for complex physical interactions between tangibles such as stacking and bumping.

8.2 Multi-Scale and Multi-Display Visualization

Visualizations at multiple scales proved to be an essential aspect of our system. One of the challenges of working with large biological networks is having enough screen real-estate to be able to view a single complete network, let alone to be able to view multiple complete networks side-by-side. The large wall display proved essential for this. However, the large display was not enough on its own. As is well established within the information visualization field, effective visualizations must provide not only the broader context, but also alternate views with more focused or detailed information on demand (see e.g., [8]). In our case, given the need to make comparisons across multiple networks, it proved useful to provide the more detailed outputs such as histograms on mobile devices that could be moved around and would not clutter the network visualizations, which also reflected the applied structural features (e.g., through color and size of nodes and edges).

Another important consideration in using multiple displays is ensuring that users can easily relate what they are seeing on them. We used color-coding for this purpose. The colors of selected organisms or structural features were reflected not only by the LED ring on the actibles, but also onto the containers on the iWall. Nevertheless, some of our external experts

found that some of the colors were too similar, which resulted in confusion. Refining the color design and also investigating other approaches for clarifying the relationship between information presented on different displays is something to further consider in future.

8.3 Supporting Interdisciplinary Collaboration

The analysis of biological networks is an interdisciplinary field that draws on knowledge and approaches from different disciplines including biology, engineering, mathematics, and physics. In this respect, having multiple disciplinary viewpoints engaged in the design process was critical. Indeed, our BME co-designers themselves came from different backgrounds, and as part of the co-design process we worked to create interactions and visualizations that would help them create a shared mental model of the networks they were investigating. Design considerations include the legibility of the visualization, for example carefully considering how size, color, placement, movement, etc. reflect information as well as changes within the visualized networks. It is also important to consider how multiple users work at the platform, either together or in parallel. Providing multiple tangible handles, large shared displays, as well as the ability to use personal mobile devices provides flexibility for users to shift fluidly between collaborative work and discussion of observations, and individual explorations and analyses.

We also found a tension between the need to present concepts in a manner simple enough to be understood by users from different backgrounds (e.g., those with a deep understanding of mathematics vs. not), yet at the same time complex enough to be able to support in-depth analyses. Indeed, this tension was reflected in the feedback from external experts; some felt the system was useful for users with different levels of knowledge, while others felt the system required a solid knowledge of network science.

9 CONCLUSION AND FUTURE WORK

We presented Tangible BioNets, a multi-surface and tangible interaction system for supporting expert users (e.g., engineers, biologists) in analyzing biological networks and their structure. The system was designed through an iterative co-design process centered around real use cases, which has already yielded a novel insight about the eigenvalue distribution of biological networks for our BME team members. An informal study with six biologists found that the platform has the potential to enhance understanding of complex concepts, as well as collaborative exploration and hypothesis formation. Based on the findings from our co-design process and informal study, we discussed preliminary design considerations for tangible interactions with large biological datasets, multi-display/multi-scale visualizations of these data sets, and supporting interdisciplinary collaboration. In particular, these design considerations point to the kinds of questions designers need to think about when building tools to support sense-making around large biological datasets. Important design choices include: when to use tangibles and how to assign them to specific interactions or parts of the data; how to most effectively use screen real-estate across multiple displays; and how to best support multiple users working together around the data. Although it is too preliminary to generalize, our findings point to three design strategies that may be effective for collaborative interfaces for large biological networks. First, offering only a small number of tangibles that can be re-assigned to different functions appears to be sufficient for complex interactions with the data, and provides users with a high degree of control over the environment. Second, distributing visualizations (e.g. network visualization vs. histograms) to different configurations/sizes of displays while giving users clear cues to relate between the different views may be an effective approach for navigating and inspecting large networks. Implementing an engine that uses patterns (such as model-view-controller) that are focused on event-based user interaction and data-centralization supports this strategy. Third, supporting interactions through multiple tangible handles and touch on large displays, as well as personal devices, appears to provide

users with the flexibility to shift between collaborative and individual explorations and analyses. As a next step, we aim to conduct a more formal user study in order to better understand these design choices and how they affect work on specific network exploration and analysis tasks. Other next steps include refinements to our system such as improved color-coding, as well as further investigation into how Tangible BioNets can be used (and further generalized) for tackling real-world problems in biological networks analysis.

Given that existing tools for biological network analysis are limited, e.g. most of our external experts use Excel to work with gene networks, there is much room for improvement. An important question is how to design tools that will be used by the computational biology community. Prior work has suggested that starting with specific problems that can later be generalized, as well as increasing collaboration between TEI researchers and computational biologists, are important paths forward for both fields [24]. We have taken these points as core aspects of our design approach and hope that our work can inspire further investigation into HCI/TEI design for computational biology.

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