Artists’ Article

Exploring 4D Image Sets Of Early Heart Development Using Gesture And An Immersive, Spatial Operating Environment

John Carpenter and Rusty Lansford

John Carpenter (artist, designer, educator), HRL Laboratories, LLC, 3011 Malibu Canyon Rd, Malibu, CA 90265 (Formerly Oblong Industries). Department of Cinematic Arts, University of Southern California, Los Angeles, CA 90089, USA. Email: johnbcarpenter@gmail.com. Web Address: http://johnbcarpenter.com, http://instagram.com/johnbcarpenter.com.

Rusty Lansford, Ph.D., Department of Radiology and Developmental Neuroscience Program, Saban Research Institute, Children’s Hospital Los Angeles, Los Angeles, CA 90027, USA. Department of Radiology, Keck School of Medicine, University of Southern California, Los Angeles, CA 90033, USA. Email: lansford@usc.edu. ORCID ID: 0000-0002-2159-3699

© ISAST
Manuscript Received 9 April 2020

Abstract:
Scientists today can collect more data than they can perceive using traditional visualization methods. New technologies and sensors allow researchers to gather dynamic, complex multi-dimensional data sets—all of which must be carefully studied to reveal their hidden patterns and narratives. The authors have utilized an immersive platform to design a new visualization for real-time, intuitive, spatial manipulations of time-based volumetric data sets via a wand-based gestural interface. The resulting work resolves microscopic tissue structures at a human scale in a room-based pixel space, facilitating research, discovery, and in-person teaching and collaboration.

BIG DATA

“Scientists collect more data than humans can actually perceive” (see Kremers [1]). In the era of big data, there exists a critical need for new perspectives, tools, and techniques to visualize, filter, interpret, and share high-dimensional image datasets—including those gathered through vital microscopy, magnetic resolution imaging, and computer-assisted tomography. The authors aimed to develop a custom software-based, room-scaled, gesture-driven visualization tool that enables the exploration of individual cells en masse in the developing heart. The resulting work captures the dynamic geometries and spatial complexities of both the cells, and the evolving tissue structures, and provides an intuitive means for retrospective analysis and exploration at a human scale.

ART, SCI + TECH

While there are many examples of artists working with scientists to create “tools for conveying complex information in a comprehensible form” via an “expanded artistic language and iterative design process” (Samsel [2]); this research is largely modeled on David Kremers’ work applying paint brushstrokes to diffusion tensor imaging of mouse spinal cords (Laidlaw [3]). This work was more than a data visualization tool, it is an example of reciprocal technology transfer
between the artist and the lab: both groups were empowered by aligned interests and intersections of knowledge, technique, and technology (Lynch [4]).

LAGERSTROEMIA INDICA

The research for this paper began over coffee and a discussion about an upcoming art installation: Carpenter was developing an interactive, software-based work that tracked viewers’ movements through a garden, and projected their data as emergent forms---evocative of blooming Lagerstroemia indica---onto nearby walls (Figure 01, Carpenter [5]). A 3D depth sensor installed in the garden generated point cloud data that was visualized as a series of stylized trails (amongst other visuals), and their representation was evocative of heart assembly data being collected in the Lansford lab. This inspired the authors to explore whether similar techniques could be applied to understanding cellular movements in the nascent heart.

+4D IMAGE SETS OF QUAIL HEART ASSEMBLY

The Lansford lab uses Japanese quail to explore the molecular and cellular events of early embryogenesis because the process occurs within an egg, allowing for continuous observation of the developing organism (Sato and Lansford [6]). Similarities in genetic mechanisms and morphology (four-chambered hearts) allow scientists to study avians as a model for early heart formation---and disease---in humans.

To study how cardiac progenitor cells (CPCs) assemble during heart formation, Lansford used transgenic Japanese quail [Tg(PGKp.H2B-chFP; TIE1p.H2B-eYFP)] embryo that genetically express mCherry fluorescent protein (chFP) within the nuclei of all cells (Huss [7]) and also express yellow fluorescent proteins (eYFP) in nuclei cells that have differentiated into endothelial cells (EC) (Sato [8]) (Figure 02). Image sets were acquired through multispectral 4D (xyzt) confocal microscopy and quantitative analysis (Huss [7]; Benazeraf [9]) to record and analyze the behavioral history of populations of live CPCs in vivo with subcellular resolution.

All cells in the transgenic quail embryos contain a detectable fluorescent label, so the image sets can reveal information for thousands of cells moving across hundreds of time points in 3D space (Figure 02) (details in Supplementary data, Movie 1). Typical parameters obtained from image sets include nuclear perimeter, volume, and mean pixel intensity; however, determining other measurements including cell motility (e.g. velocity, direction, persistence), rates and orientations of cell division, and daughter cell and tissue-specific cell movements (Lodish [10]) first requires the identification of individual cells across time points and frames. To accomplish this, Lansford’s lab used Bitplane’s Imaris (software for 3D and 4D analysis) to quantitate changing cell behaviors at ~460,000 cell locations linked across time to form ~78,000 movement tracks throughout the heart.

At this point, visual inspection of the original image set and its analysis typically occurs on a standard lab computer monitor. However, it is often challenging to comprehend the complexities of a dynamic volumetric structure like the heart on a monitor. Lansford sought to immerse himself within the data to explore new perspectives that might better inform our understanding of
cardiogenesis; and ultimately seeks to use this research to gain more insight into how and why hearts sometimes abnormally form, resulting in congenital heart defects.

**IMMERSIVE VISUALIZATION**

The Electronic Visualization Laboratory (EVL) at the University of Illinois at Chicago is an early pioneer in CAVE-based research (Marai [11]). Their work with the CAVE and CAVE2 systems helped to establish “immersive environments can augment [a] humans’ ability to analyze and make sense of large and multifaceted datasets.” In the authors’ experience, the additional space created by expansive pixel surfaces also enables collaborative exploration of the data at a familiar scale (Figure 03, 06), and peripheral pixels enhance the immersive effect and offer vantage points for *serendipitous discovery*: while navigating the data, the authors often found an interesting cell path or pattern that had previously eluded observation. By presenting the data at a human scale, the authors aim to provide an intuitive framework for interacting with spatially complex cellular movements.

While other capable systems exist, the work in this paper relies on Oblong’s g-speak spatial operating environment (SOE) as the platform provides a framework for writing custom software for spatial datasets and distributed, scalable, multi-user, multi-screen, multi-device applications. This paper is not intended as an endorsement of a particular software platform, but instead aims to share some of the advantages of working with gesture, an SOE, and immersive physical screen-based installations. The authors would like to note that other promising platform work is being done in Unreal Engine 4 and Unity3D, both of which have a large and active community and a variety of deployment options for immersive technologies (e.g. Unity is the customizable framework used in the CAVE2 system).

The g-speak framework is a custom software platform written in C++ that provides classes for manipulating objects in 3D space (translation, rotation), reading in and working with common data formats, and applying custom GLSL shaders. The platform also handles deployment to physical installations and the required scene graph and projection matrices for those setups (and since the software is written for space, the same application can run on multiple hardware setups with little to no adaptation). In the author’s experience, different installations can create varied experiences of the data: the immersion room provides better spatial context while exploring tracks, while the display wall helps to generate a sense of the overall cellular movements (Figure 03).

The most useful aspect of the platform is that it syncing virtual and physical spaces through a shared origin in the physical world (Figure 04) that results in “all scene graph objects hav[ing] real-world positioning, sizing, and orientations” (Oblong [12]). This calibration ties input from the physical world directly into the virtual environment. These conveniences help to allow the developer to focus on visualization work, instead of the typical technical hurdles involved in immersive installations.

Data from Imaris was read into the authors’ custom software as several comma-separated value (csv) files. The YFP expressing endothelial cells (ECs)---which define the internal tissues in the heart---were given a brighter yellow hue to draw user attention, and the color was slightly ramped (red to green) to visually encode collection time (Figure 05). In addition to providing an
impression of the cell movements *en masse*, these variations also helped to distinguish structures in the forming heart. Custom GLSL line and point shaders provide time-based animation effects and depth-based atmospheric cues—a technique that is especially important for conveying a sense of immersion.

**GESTURE AND VISUALIZATION**

While the screen-based surfaces expand the visual workspace, gesture-based navigation provides an intuitive means to access and utilize those pixels. As discussed by Shin, Tsap, and Goldgof, gesture recognition systems are prime candidates for “developing interactive settings for exploring large data sets in an intuitive environment” (Shin [13]).

Gesture can also help to aid collaboration and communication by conveying user intention to others in the space both through the physical act of pointing, and the virtual UI feedback of the software. Furthermore, the authors’ software can be controlled simultaneously by multiple users, allowing for collaborative exploration within the space: one user can rotate the visualization while the other translates the data; or one user can select and zoom into an ROI while the other manipulates time. Allowing multiple users to control the system necessitates dialogue, and the gesture-based controls facilitate the discussion as users intuitively navigate the dataset to support their perspective.

While many interactions are currently thought of as gesture—from touch screen interaction (multi-finger swipes) to handheld devices and VR controllers to stereo cameras, 3D sensors, and Vicon system hand and body tracking—in Carpenter’s experience at Oblong (Carpenter [14]), room-based installations are best driven by spatial input devices (like the ultrasonic wand) and 3D sensors (like the Kinect in concert with gesture recognition pipelines). The authors have found that device-based interactions are ideal for larger, room-based collaborative installations because they provide precise navigation and high fidelity data streams even in *groups of people*, and they are less susceptible to some of the current technological hurdles of 3D sensors like limited tracking areas, occlusion and consistent user identification (though the technology is rapidly evolving and the new Microsoft Kinect Azure seems to have potentially solved several of these issues).

Work at the EVL, “further points to the benefits of embodied navigation in the context of large spatial datasets” (Marai [11]). The ultrasonic wand (via a grid of ultrasonic emitters in the ceiling, and an array of microphones in the wand) provides a continuous stream of data at 60-70 frames per second that includes the wand position, orientation, and button states. These readings can be used to determine the users’ positions and interactions within the system. The sample rate and fidelity is significant because the responsiveness helps to sustain the illusion that the user is experiencing a haptic connection to the virtual system.

Regardless of the sensing device, the authors believe that gesture is an ideal candidate for the navigation of complex multidimensional data sets because both are intrinsically spatial (Carpenter [15]). Furthermore, it is often the most intuitive means for addressing all of the pixels in a space. This is particularly relevant when moving data from one side of a room to another—
an action that would be less spatially direct with a 2D input device like a mouse, and inconvenient with interfaces like a touch screen.

GESTURAL INTERFACE

When the system is translated or rotated, a three-ringed UI element (shape similar to a gyroscope) unfurls at the center of the system to indicate the axis of translation and rotation. Pointing at the data brings up a secondary smaller “selector” UI element and hover information that reveals cell and track ID, along with the precise location (in µm) and general time (in minutes) of each point. The user can also select a region of interest (ROI), which adds an additional 3D bounding box to the system to filter the data (Figure 08a). This box restricts the visualized cell movements to those that pass through it, provides a precise location reference, and offers a framework for further analysis (scrubbing through time).

ROIs → RETROSPECTIVE ANALYSIS

A primary goal of this research is to determine where specific CPCs originate and end, and what their fate is after differentiating. To accomplish this, the authors created an interface that allows for both the manipulation of time (through a time scrub gesture), and the nimble selection of regions of interest (ROIs) within the developing heart field (through a pointing-based gesture) (Figure 07, 08b+c). Software settings allow the user to highlight tracks that migrate to, from, or through a selected ROI, and time scrub explores the temporal movements of the subset of cells. To maintain context, unselected tissues and cell tracks were ghosted and not entirely faded out. The system can also be translated (pushed back) in space to gain a sense of the selected region’s relationship to the overall data set or pulled closer to explore the movements of the tracks. This ability to seamlessly explore the data from multiple perspectives allows for a critical spatial understanding of the cellular movements and behaviors (Figure 08).

The approach provides new tools for the identification of cellular origins for different tissue regions. Visualizing the paths and origins of cell migration is important for developmental biologists because it aids in the understanding the factors that influence tissue growth. Furthermore, the ability to fluidly navigate this data enhances researchers’ ability to properly identify samples and individual cell tracks for further study (via software readouts of selected track and cell IDs).

AR/MR/VR

The authors acknowledge the field of immersive visualization is rapidly evolving and that there are other exciting technologies under development—foremost among them augmented reality (AR), mixed reality (MR) and virtual reality (VR). A key benefit of these setups when compared to large screen-based systems is that the hardware is more accessible to both developers and researchers due to reduced costs and ease of transportation (Donalek [16]). While the authors are interested in these other technologies, current work focuses on room and screen-based immersive environments for their scale and architectural grounding (which helps to reduce disorientation in the authors’ experience), the social and collaborative benefits, and simply because the authors had regular access to these systems.
CONCLUSION

This paper offers support for gesture-based immersive research to better visualize and process complex spatial datasets in the sciences, and posits that coordinated SOEs and interfaces are essential for the navigation of virtual, room-scaled data environments. This work has helped to reveal the choreography of cardiac progenitor cells (CPC) proliferation, migration, and differentiation as they form the nascent heart. Future explorations aim to develop the software into a system for comparative analysis between healthy and diseased samples. The authors are also interested in using this system as a foundation for future visualization techniques exploring other high-dimensional datasets, such as gene expression across tissues.

As new scientific technologies increase the number of parameters that can be measured in each cell, large scale immersive systems and the gestural interfaces will be essential for understanding multi-dimensional datasets and the patterns and narratives within them. Regardless of the development platform and sensing technologies, gesture creates an intuitive way to spatially navigate and manipulate data sets, and an SOE can offer a platform for calibrating physical and virtual spaces. This research is an initial step towards a real-time, gesture-based immersive navigation tool for exploring cell migration in the developing heart, though the authors believe that the techniques discussed could also apply to other large complex data sets including those generated through magnetic resonance imaging (MRI), Computer-assisted tomography (CT), Cryo-Electron microscopy and light-sheet microscopy.

ACKNOWLEDGMENTS
The authors would like to thank John Underkoffler and Oblong Industries, David Kremers (California Institute of Technology), and Scott Fraser and Russ Jacobs (University of Southern California) whose research, support, and friendship helped to inspire this work. Additionally, Jennifer Yang (California Institute of Technology) for collecting the heart data.

REFERENCES AND NOTES


