# PathSim Visualizer: an Information-Rich Virtual Environment Framework for Systems Biology

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#### ABSTRACT

Increasingly, biology researchers and medical practitioners are using computational tools to model and analyze dynamic systems across scales from the macro to the cellular to the biochemical level. We are using Information-Rich Virtual Environments (IRVEs) to display the results of biological simulations, and to allow users to interact with those simulations. While simulation architectures, algorithms, and processing power have enjoyed continuous optimization to date, the user interfaces to these applications have not. The problems of designing such IRVE interfaces arise from the requirement that a variety of spatial and abstract information must be integrated into one coherent experience for the user. This paper explores the design and development issues encountered in our implementation of a bioinformatics application, PathSim (Pathogen Simulation). Specifically, we describe the information and interaction issues in building a front-end tool to visually analyze the results of an agent-based immunology simulation. Finally, we present custom scenegraph objects and consider candidate functionality for future standards components.

# **Categories and Subject Descriptors**

D.3.3 [**Programming Languages**]: Language Constructs and Features – *abstract data types, polymorphism, control structures.* 

#### **General Terms**

Design, Human Factors, Standardization, Languages.

#### Keywords

Virtual Environments, Bioinformatics, Information Visualization

#### **1. INTRODUCTION**

The emerging paradigm of digital biology is providing

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researchers with new computational tools for modeling and analysis. The multi-disciplinary field of Bioinformatics has advanced the application of new simulation techniques, algorithms, and data modeling to biological systems across genomics, proteomics, metabolomics, immunology, and epidemiology. Not only are the systems complex, spanning multiple scales and factors, but they also generate massive quantities of data. This data is heterogeneous, meaning it consists of spatial, temporal, and abstract types, each with its own structure. Temporal and abstract information may be related to spatial, biological structures such as cells, tissues, organs, and systems for example. This data may also be distributed across a variety of local and remote machines and application servers.

For effective scientific visual analysis, researchers and clinicians need integrated access to this variety of information resources and consequently, improved systems for the management and presentation of this data. We have been working with medical and bioinformatics researchers to design and develop nextgeneration interfaces to explore and understand biological data such as models, simulations, and their references. PathSim Visualizer takes the approach of displaying 3D anatomy (spatial information) in an interactive virtual environment (temporal information) that is annotated and enhanced with a variety of abstract information about the anatomy. This abstract information may include text, numbers, hyperlinks, graphs, videos or audio resources referring to some object, world, or user state. We have described the principal interface design challenges for this class of problem and proposed the term 'Information Rich Virtual Environments' (IRVEs)[Bowman et al. 20031

We are applying the usability engineering process [Rosson & Carroll 2002] to develop a visualization tool for in silico immunology simulations. In silico experiments are useful when clinical data is difficult or expensive to collect, or when experiments are too dangerous or unethical to perform in vivo. Once a biology simulation model is validated and tuned to known data, such simulations can help researchers test 'what if ...' hypothesis and develop interesting experimental questions for further investigation and investment.

The PathSim Project [Duca et al. 2004] simulates pathogen and host interaction with an agent-based computer model built from current biomedical knowledge. In PathSim, systems biology investigators are concerned with different infection behaviors as they are related to various systems and parts of the anatomy over time. PathSim simulations may run on large servers or clusters, but the results must accessible to researchers on desktop machines across the network.

Our work has been iterative, gathering user requirements, designing and implementing the interface framework, and refining it through user evaluations. This paper enumerates the problems and tradeoffs we encountered in building the prototype system for PathSim Visualizer and provides the rationale and details behind our design solutions. These solutions involve encapsulating physical scales and information behaviors into custom scenegraph objects that manage scale, timeseries, and information visualizations for in silico research and analysis. We believe the work presented in this paper highlights current deficiencies and opportunities for standards-based 3D information environments.

#### 2. RELATED WORK

In our work, we are developing *information-rich* virtual environments (IRVEs) [Bowman et al. 2003]. In a nutshell, IRVEs are a combination of traditional virtual environments and information visualization. Whereas virtual environments typically contain information that would be perceptible in the physical world (such as geometry, colors, textures, lighting), IRVEs enhance the perceptual experience with representation(s) of related abstract information. This combination of perceptual and abstract information is typical for data generated for biomedical research and by biological simulation systems such as PathSim.

IRVEs share a great deal in common with Augmented Reality (AR) [e.g. Hoellerer et al. 1999; Bell et al. 2001]. AR applications enhance the physical world with additional information, much of it abstract, while IRVEs enhance the virtual world with abstract information. The key difference between IRVEs and AR, however, is that IRVEs are purely synthetic, which gives them much more flexibility. Information objects in an IRVE can be perfectly registered with the world, and realistic objects in an IRVE can be animated, moved, scaled, and manipulated by the user at a distance, for example.

The goal of the IRVE research agenda is to understand how media designers can disambiguate perceptual stimuli and enable users to accurately form concepts about and mental models of the phenomena they perceive. By taking account of how humans build their cognitive models and what perceptual predispositions and biases are in play, designers can take steps to minimize or leverage their effect. This line of inquiry has been termed the 'inverse problem of design' by Joseph Goguen [2000] and 'Information Psychophysics' by Colin Ware [2003]. The research and analysis we present here is couched in a framework for understanding user activities and requirements known as user-centered and scenario-based design [Rosson & Carroll 2002].

While PathSim has obvious medical applications, it goes much further than that. It may also serve as a basic research tool for life scientists working on a range of questions and a teaching tool that could find application from grades K-12 all the way to professional medical training. The value and need for such tools have long been recognized [Farrell & Zappulla 1989; KlingPetersen et al. 1999]. It has been shown that conceptual learning can be aided by features of VEs such as: their spatial, 3-dimensional aspect, their support for users to change their frames of reference, and the inclusion of multi-sensory cues [Salzman et al. 1999]. This is compelling evidence for the value of VEs as experiental learning tools and for concept acquisition during the development of a user's mental model.

The NYU School of Medicine [Bogart et al. 2001] for example, has published a number of anatomy courseware modules in VRML that provide an IRVE interface to detailed models of the human head. The Open Virtual Reality Testbed Group at the National Institute of Standards and Technology has produced AnthroGloss [Ressler 2003], which is an IRVE Anthropometric Landmark Glossary in VRML. We combine referenced elements and adaptations of these models to provide users with context as they explore PathSim simulation results.

Systems biology researchers have begun to use modern computing power to simulate the immune system using generalized cellular automata [i.e. Celada & Seiden 1992; Bernaschi et al. 2000; Grilo et al. 2001; Puzone et al. 2002]. These simulations use probabilistic or deterministic rules to govern the interaction of automata on some lattice or in some grid space. There is a broad range of implementation details concerning the simulation that cannot be covered here. These are principally concerned with the nature and evaluation of the rules governing agent interaction. However, the PathSim system is unique in that the agents (Virions, B-cells, T-cells, etc.) may number in the millions  $(10^8)$  and they travel and interact on a micro-scale 3D mesh that approximates average human anatomy.

In biotechnology, there are a number of groups that have defined XML-based languages for describing systems and data relating to biology. The Physiome project has specified AnatML, FieldML, and CellML [Physiome 2003] which describe finite element geometry, spatially varying fields, and mathematical cellular models respectively. Systems Biology Markup Language [SBML 2003] allows the flexible representation for models of biochemical reaction networks. These languages are considered as future integration targets for the PathSim simulation architecture as it becomes more developed and robust.

#### **3. SYSTEM DESIGN**

To provide access to a broad range of users, the PathSim simulation engine is run on a server or High-Performance Computing (HPC) system, but provides setup and visualization facilities through a web-based front end (Figure 1).

Through user interviews and the scenarios generated in the design process, we discovered a set of fundamental activities and goals that users may expect the system to support. The setup activities are presented in a 2D webform interface and include: configuring anatomy parameters, defining agent interaction rules, defining an infection scenario, and setting the simulation parameters such as time interval and duration. User activities for results analysis include: determining the overall behavior of the agent populations during infection, identifying areas of high agent activity (hot-spots), and drilling down to observe agent states and dynamics on local levels.



Figure 1: PathSim Architecture

We applied Hierarchical Task Analysis [Diaper 1989] to the generated list of end-user activities, and enumerated the subtasks and artifacts required for each to be accomplished. To understand the details of user interactions across the scales of information and space, we developed a 'Task-Action Grammar' [Payne & Greene 1986] for each task that allowed us to consider the command lexicon and keep the operational rules simplecombinations of navigation, selection, and manipulation interactions had to operate consistently across scales and data views.

From an information design perspective, we then employed a 'Task-Knowledge Structure' analysis [Sutcliffe & Faraday 1994], which concentrates on user task and resource analysis to formalize an entity-relationship model. This model enables the effective design of multimedia interfaces and information presentation – i.e. what media resources the user needs visual access to when. This is an important technique for IRVE design as it intends to formally identify items that need user attention and minimize perceptual overload and interference per task.

As we have mentioned, the variety and volume of data to be displayed by PathSim Visualizer required a rational design approach. Multiple meshes, and the simulation results on those meshes had to be accounted for. In IRVE terms, we had to address: where the enhancing information was located, how it was associated to an object or location, and how dense and aggregated it was depending on the viewed scale.

A variety of user controls are required within the PathSim IRVE for navigation, selection, and manipulation. Navigation requires not only both spatial and temporal agency in the context of the virtual environment, but also the steerage of views of abstract information. Each anatomical structure has scalar properties and descriptions, and users may require overview and detail information of different objects or levels simultaneously; scene logics and selection interfaces aid users in fulfilling this requirement. In addition, manipulation user interfaces can be advantageous for temporal indexing (e.g. a slider).

#### 3.1 Multi-scale Spatial Information

PathSim simulations run on anatomical meshes that are generated to a hierarchical archive according to current clinical knowledge. Each point in the mesh represents a certain type and volume of tissue where agent interactions (hosts/pathogens) can take place. We have modeled the lymphatic tissue (especially tonsils), blood circulation, and lymphatic drainage of the Waldeyers' Ring from the macroscopic level to the microscopic level. The Waldeyer's Ring is a collection of lymphoid tissue encircling the top of the esophagus.

The anatomical description is hierarchical XML and distributed across a number of referenced files. The fundamental unit is a hexagonal section of tonsiliar tissue modeled to include mesh points representing: the tonsil surface, reticulated epithelium, mantle zone, and germinal center. Figure 2 (color plate) shows a visualization of the unit anatomical mesh with spheres representing the location of mesh points and white lines representing the possible travel paths for agents. Blood from the circulation system enters the tissue through the High-Epithelial Venule (HEV) and lymph is drained into the lymphatic system from the mantle zone. Figure 3 (color plate) shows a labeled example of how unit tissues are arranged to approximate the lymphatic tissue of the tonsils.

Users can generate interconnected lattices of the unit and tonsil mesh by supplying the tonsil's surface area dimensions. After the main tonsils of the Waldeyer's ring are defined, another type of tissue (diffuse lymphatic) is instantiated to connect them. The relation of all tonsil and connective tissues is described in a macro-level tissue file that defines the simulation environment. Any subsequent processing and visualization is based on references to this hierarchical simulation mesh.

PathSim Visualizer manages an integrated information environment across multiple scales. Users have a number of firstperson spatial navigation options including free-navigational modes such as: fly, pan, turn, and examine. This empowers users to explore the system, zooming in and out of anatomical structures as desired. Expert users can employ control keys for quick mode changes. To aid wayfinding, certain structures persist across scales (serving as landmarks). In addition, the result space is navigable by predefined viewpoints, which can be visited sequentially or randomly through menu activation. This guarantees that all content can be accessible, and users can recover from any disorientation.

PathSim Visualizer manages macro and micro scale result visualizations using proximity-based filtering and scene logic Scripts. As users approach a given anatomical structure, the micro-scale meshes and results are loaded and synchronized to the time on the users' Heads-Up-Display (HUD). Figure 4 shows a macro-scale view of the Waldeyer's ring simulation environment in context. Figures 5-8 (see color plate) show a typical zooming sequence.



Figure 4: The generated Waldeyer's Ring tissue anatomy; skull model [Bogart et al., 2001] shown for reference

### **3.2 Abstract Information**

There is a variety of abstract information that may be relevant to a researcher investigating a digital biology simulation through PathSim. This information may be represented graphically or numerically within the virtual environment:

•Lymphocyte/Virus populations for the system •Lymphocyte/Virus populations per local region or unit •Annotations, hyperlinks, and references about the structure or process being evaluated

The PathSim Visualizer implements custom software objects to manage, layout, and display this abstract information in the context of the virtual environment. These are described in detail in Section 5.

From a design standpoint, there are at least four possibilities for locating information annotations based on what coordinate system they are relative to. These are: world-fixed, display-fixed, user-fixed, and object-fixed locations [Feiner et. al. 1993; Bowman et al. 2003]. Information may be associated to a particular object in the world, which is termed as 'object-fixed'. Alternatively, the information may be associated to a location in the world, which is termed 'world-fixed'. If the annotation travels with the user regardless of their navigational actions, this is classified as 'user-fixed'; if persistently located relative to the display, its is termed 'display-fixed'.

PathSim Visualizer displays abstract information related to the simulation in user, world, and object fixed locations. PathSim Visualizer gives the user a Heads-Up-Display where system variables and global state are displayed. This HUD functions as a read-out and control panel, travelling with the user throughout the environment. Information displays in the environment aggregate data from smaller scales into suitable, object-fixed visual representations at larger scales (figures 5 - 8). This overview-plus-detail helps investigators explore and understand the dynamics of the system:

•HUD- animated bar-graph for system's global population

•Agent Views – Color coding of anatomy by agent type; logarithmic scale to regional total

•**Toggle Population Display** – animated bar-graph or numerical encoding for a given structure; the bar-graph is normalized to show the region's population in proportion to the global population.

•Links – hyperlinked websites, resources, and references may be rendered in additional windows (display-fixed locations)

# 3.3 Temporal Information

PathSim Visualizer also renders the dynamic temporal aspect for the abstract and spatial information- how that information changes over time. Through processing components (Visualization Generators), simulation data is transformed into sequencer and interpolator animations. Animation data is used to drive anatomical coloring, as well as global and local population graphs and numerical read-outs.

Investigators into dynamical systems such as the immune system need capable controls to manage and index the temporal dimension: coarse enough to find a maximum population value in a month of simulated infection time and fine-grained enough to examine behavior at 15 intervals. PathSim Visualizer synchronizes data across scales through a familiar DVD interface that gives both step-wise and continuous time control (adapted from NPS SAVAGE archive [2003]). Figure 6 shows a microscale view of the infection, synchronized to the time controller on the HUD.

# 4. SYSTEM IMPLEMENTATION

Users can configure, run, and view PathSim simulations remotely over the web. The mesh description, simulation code, simulation parameters, and results all reside on the server in structured directories and files. The Visualization Generators of PathSim are a set of Perl scripts that process the simulation output files, composing and writing a set of directories and VRML files on the server. One principal challenge (addressed in this paper) is the management and transformation of PathSim simulation results to information-rich objects and scenegraphs that include the anatomical mesh.

Raw simulation results are written into unique files on the server that correspond to the hierarchy of the mesh description files. The results files contain time-stamped population numbers for each agent and each anatomical region at that scale. Visualization Generator scripts read the simulation result files and compute color, string, and float animation values for each region at that scale. Color and float information for each agent type population is normalized to the maximum value achieved during the course of the simulation. Numeric population values absolute and converted to strings for display as field-value pair text. These values are composed into VRML nodes and syntax and the result files saved on the server for viewing.

Currently, the PathSim Visualizer output runs fully on desktop workstations using standards-based formats such as XML, X3D, and VRML. While we have successfully demonstrated our information display aspects in Head Mounted Displays (HMDs), elumens Domes, and the CAVE, our future work is to extend the system's interactive capabilities to immersive display and input devices. For future versions, we will continue to apply the usercentered design process to identify human-computer interaction issues and visualization features for biomedical IRVE toolkits like PathSim.

## 5. SCENEGRAPH OBJECTS

## 5.1 Nested Scales

A crucial requirement for PathSim Visualizer is the capacity to explore simulation results across the macro and micro scales. This presented some interesting scenegraph challenges. Not only did we have to manage a large volume of simulation data for multiple anatomical regions, but also maintain application performance, rendering speed, and interface continuity. For example, the HUD interface should follow the user uninterrupted by zooming and scale changes; the controls on the HUD (such as the DVD Time Controller) must maintain event links to the environment no matter what scale or model is loaded.

The HUD interface is loaded from the top-level file, which also contains ProximitySensors and Scripts to manage scene and state information. In the top-level file, a WorldGroup Group is defined that contains macro-scale models such as the body, skull. The visualization processing scripts wrap each scale model of anatomy and result animations in a PROTO declaration. There is one set\_fraction eventIn on the PROTO interface that is processed by a TimeManager Script. Within the Prototype declaration of each scale, the TimeManager script is connected to all sequencers and interpolaters that animate at that scale. This keeps event management encapsulated across scales and allows models to be loaded and connected to the environment easily.

As users zoom into the head and neck area and the Waldeyer's ring becomes visible, the simulation results are loaded into the WorldGroup using a Browser.createVRMLFromString method. The string is an EXTERNPROTO definition and an instance. Routes between the DVD controller and the new scene are added in order to link the scene to user global time. Similarly, as users zoom into specific anatomical structures (i.e. the tonsils), the appropriate detail geometry and simulation results are loaded into the WorldGroup as an EXTERNPROTO instance and Routes are added.

## 5.2 Semantic Objects

Recently in our IRVE research, we have implemented a set of IRVE behaviors encapsulated as Semantic Objects for VR scenegraphs [Bowman et al. 2003; Polys & Bowman 2003]. Semantic Objects are a conceptual and programmatic abstraction of spatial objects in the visual space of the IRVE that carry associated information along with their geometric and appearance information. Thus, information layout locations for Semantic Objects can all be described as object-fixed. The advantages of defining annotation information and display behaviors along with the objects are: display behaviors are in the scenegraph and operate independently of the display's size and resolution, and no central 'layout manager' is needed. This has made it possible to deploy Semantic Objects and their related information display objects across desktops, HMDs, Domes, and theoretically a CAVE as well.

## 5.2.1 Information Panels

Our currently defined objects for the display of associated abstract information are: unstructured text, text as field-value pairs, bar-graphs, images, movies, or audio clips. For example, the exposed functionality of the text annotation panels allows authors to specify values along each of the VRML attributes (i.e. font family, style, color etc.). In order to aid text legibility across a wide variety of scenes, text panels may be instantiated with or without a label background whose color and transparency may be specified. The text's background is automatically sized to the number of lines and characters in the MFString. Unstructured text panels are organized simply by the semantics of the Text {String []} field.

However, one common use for text annotations is to display an object's name and its attributes such as field-value pairs. We implemented a structured text panel that allows authors to specify a title, a set of field\_names, and a set of field\_values. Since each text string is an exposedField, textual content can be dynamically updated. Each of these parameters on text display objects gives IRVE designers flexibility to define the visual characteristics of text labels or field/value pairs across a range of environments.

In many applications, text or numeric detail has to be managed to reduce crowding and distraction in the interface. To reduce cognitive load in PathSim Visualizer, we also implemented a color-coded population bar-graph where users can get a quick, qualitative understanding of the agent populations in a certain location. To support details-on-demand, users can click the bargraph to toggle the information display to a field-value pair text panel for the agent populations.

#### 5.2.2 Layout Behaviors

There are a number of principal parameters on Semantic Objects. First, separate 'level of detail' groups can be defined for the object geometry and the annotation information (e.g. a panel); this insures the capability for designers to aggregate referring information independent of the object's levels of detail. Second, a Semantic object's abstract information display may or may not be explicitly associated to the geometry by way of the Gestalt connectedness principle (such as a drawn line) or implicitly by the Gestalt proximity principle [Ware 2000].

Third, the scaling of the annotation group is a function of user visibility and proximity with options for constant size, periodically sized, or smoothly sized. Preliminary evaluations on the dynamic sizing of information panels have shown that the smooth scaling technique can confound the user's normal depth cues and thus constant or periodic sizing may be preferable. Finally, our abstract display objects act as true 3D Billboards insuring legibility from any viewing angle. This combined functionality can aid authors in mitigating the aggregation, association, density and tradeoffs in IRVE design.

We also implemented a set of Semantic Objects that vary the spatial location of the information panel relative to the object. The display location of the annotation is a function of the user's position and viewing angle to the object. We defined 3 layout techniques in order to aid association and prevent occlusion in the enhanced scene: the relative orthogonal, the bounding prism, and the bounding prism plus flocking [Bowman et al. 2003; Polys

& Bowman 2003]. While Semantic Objects' information display is always a function of user's proximity and angle, we also built a version that renders the information group only when the user toggle-selects the object. This final feature is used to pop-up (or hide) information panels for secondary anatomical structures.

## 5.3 MFSequencers

In order to drive data to the various visualization components in PathSim Visualizer, we wrote a set of Sequencer nodes that derive their interface from the abstract *X3DSequencer* node type. These nodes output discrete, multi-fielded events along a timeline. We introduced the integer field batch in order to specify how many values are in the eventOut array. Consequently, the number of keyValues must be evenly divisible by the batch value. We have implemented the MFStringSequencer and MFFloatSequencer to drive data to abstract information display objects such as text panels and bar-graphs. The multi-fielded string and float keyValues are populated from the simulation results during the visualization processing.

In a given simulation run, the duration and time intervals for evaluation are the same for all objects' Sequencer and Interpolator animations. In order to keep the resulting file size down, the processing script first writes a file containing the animation prototype declarations, each with the same key field. When the processing script instantiates the animation node into the result files, all that need be specified is the keyValue.

# 5.4 Heads Up Display

Finally, we defined a generic Heads-Up-Display (HUD) for userfixed controls and abstract information. We used a simple ProximitySensor setup, routing position and orientation to the HUD parent. The HUD can take a set of children and an offset that specifies the distance from the user's bound ViewPoint. While extremely useful for maintaining the visibility of overview information and system controls, the HUD in this implementation has some drawbacks. Most importantly are the facts that the HUD is rendered with the rest of the scene and browsers vary on where they implement the near clipping plane. In cases where users have zoomed into very small scales, objects may actually come between the user and the HUD geometry.

## 6. SUMMARY and FUTURE WORK

Through the PathSim project, we have implemented a number of custom information and interaction objects to meet the requirements of Systems Biologists to explore multi-scale, heterogeneous information. These scenegraph objects attempt to resolve tradeoffs on the dimensions of the IRVE design space [Bowman et al. 2003]. The PathSim information features are classified by the IRVE design space in Table 1. In the process of implementing these objects to meet our usability requirements, we have discovered deficiencies and opportunities in current Web3D standards languages.

In our formative evaluations, each of the scenegraph objects described in Section 5 (Nested Scales, Semantic Objects, MFSequencers, and Heads-Up-Display) has been identified as distinct and usable in our application across a range of platforms including desktops, HMDs, and Domes. Some of the

functionality, as implemented in VRML/X3D, has known limitations (such as the HUD clipping problem).

Table 1: PathSim Design Features and IRVE DesignDimensions (S=Spatial, V= Visual; E= Explicit, I=Implicit)

Information Feature	Information Location	Information Association	Information Aggregation
Agent Population View: Information panel per object/unit	Object-fixed	SE, VE	Low
Agent Population View: Information panel per region	World-fixed	SE, VI	High
Agent Population View: Information panel for system (global)	User-fixed	SI, VI	Highest
Time Read- out and Controller	User-fixed	SI, VI	Low
Links & References	Display- fixed	SI, VI	High

In IRVEs, there are at least three principal possibilities for how abstract information is related to perceptual information:

- Abstract information varies continuously across the space
- Abstract information is embedded/associated with points/regions in spatial data
- The structures of the spatial data and the structured abstract data are mutually interlinked

The first is a technique widely used in scientific visualization or visualization of population/census data. If the abstract data is structured by the spatial data, the data values are a function of the space. In PathSim, the color animations per anatomy and the nested scales fall into this category. The multi-fielded Sequencer nodes fit easily into X3D paradigm and could be candidate nodes for future standardization; the Nested Scales functionality is addressed by new X3D capabilities such as IMPORT/EXPORT where Inlined worlds can communicate events with their parent world.

The second relation can take the form of visual items (pop-up labels, hyperlinks) where the abstract data is related to localized objects in the space. For example, a text description of an organ of the human anatomy or the numerical description of an atom or molecule. This functionality, as defined in our Semantic Objects, provides high-level user interface behaviors that may not be best implemented in the current X3D paradigm. In conjunction with the X3D Specification Working Group, we are developing future standards components as a foundation to address these interface requirements. These include the Annotation Component and the Compositing Component (in progress).

A proposed Annotation Component for example, would provide better support for the functionality we encapsulate in Semantic Objects. In the proposed component, associated information lives as geometry in a coordinate space parallel to the display surface; there is a reference point, an offset, and a connection point that can be connected by a lead line.

While some browsers can support 'Overlays' or rendering 'Layers' (Xj3D [2004] and BitManagement [2004] respectively), the interoperability problem can only be solved through improvement of the standard. A Compositing Component would allow more sophisticated author control over rendering (i.e. Z-order, clipping, etc). This would improve support for Heads-Up-Displays, which are common in applications, but awkward between browsers.

The third IRVE relation - where the abstract data and spatial data each have a structure of their own should also be common. In fact, there are many information visualizations applications that we might like to integrate with the virtual environment. Through PathSim, we can see this would mean extending our concept of Information Panels to define 'Application Surfaces' where the windows of other analytic tools can be mapped to a pickable 3D surface. This seems most appropriate to pursue in the Compositing component interface.

Such functionality is extremely desirable, especially when the application and content is loaded into an immersive system. Previously, we have implemented display-fixed prototypes using the DIVERSE tookit [2004] and XWindows for a molecular IRVE application in the CAVE [Polys et al. 2004]. Further work in this vein must address and resolve operating system, software, and hardware architectures for a generalized way of embedding windowed applications in virtual environments.

Future work includes further exploring and optimizing these object/information behaviors through formal usability evaluations and proposing them as future standardization components for X3D. For PathSim Visualizer, we intend further integration of information resources such as published biochemical and cellular models, new multi-scale data and visualization architectures, and interface improvements such as analytic tools and indexing through the abstract data. Future bioinformatics research will involve using PathSim with other anatomical models, mesh generation techniques, and pathogen agents.

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