A Survey and Classification of Visualisation in Multiscale Biomedical Applications

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Abstract

The MSV project aims to survey current best practice in multiscale visualisation and to construct a software toolkit which will make multiscale techniques readily accessible to biomedical researchers and clinicians. In this paper, current methods for multiscale data visualisation in several domains are reviewed, and a novel classification of multiscale techniques for biomedical applications by function is proposed. The classification will form the basis of a design menu and toolkit for multiscale visualisation.

1. Introduction

The term "multiscale visualisation" generally implies that an image or scene contains detail over a range of scales that exceeds the resolution of the display or the human eye. The term encompasses a wide variety of types of data and the techniques required to visualise it; for example, the multiscale may be spatial or temporal; data may be a single image, a multi-object scene, or perhaps a high-resolution graph; and techniques may be required to deal with occlusions, ill-conditioning, levels-of-detail and scene navigation.

Domains such as medical visualisation, architecture and urban design, geospatial scanning, astrophysics, biochemistry and abstract data analysis are regularly producing massive datasets containing features that are many orders of magnitude apart in scale.

The MSV project [1], part of the European Commission Virtual Physiological Human (VPH) programme [2,3], aims to survey current best practice in multiscale visualisation and to construct a software toolkit which will make multiscale techniques readily accessible, particularly to biomedical researchers.

The best known multiscale visualisations are Google Maps and Google Earth [4], in which the dataset consists of the whole planet, from the entire globe down to street level. The challenges of navigation in a multiscale cartographic environment have been addressed in detail in McCrae *et al*. [5,6], including the automatic sensing of the current scale, and the provision of widgets to assist with global orientation.

Astrophysical data and simulations can generate very large datasets comprising an enormous range of scales; multiscale visualisation techniques such as Adaptive Mesh Refinement [7] and the compression of distances using log scales are well-established in tools such as the World in Miniature [8], AMUSE [9] and Uniview [10].

The biomedical field has seen a rapid increase in the size and complexity of datasets, creating challenges in usability, visual analysis and standardisation [11]. Biological data visualisation covers a broad range of scales, from whole organisms to macromolecules, where even genes and proteins are themselves multiscale structures. Akkiraju *et al*. [12] used immersive virtual reality to explore protein structure in multiscale. Nielsen *et al*. [13] presented a multiscale tool called VISTA for comparing genomes. However, despite numerous calls for multiscale visualisation in the biomedical field [14] there has so far been little demand from applications, outside the fields of protein visualisation and genomics, for the kind of interactive multiscale views that are now common in cartography and astrophysics. Multiscale visualisations have been presented for the lung [15] and for blood flow [16], but thus far these examples are few, and there is no equivalent to Google Earth for the human body. One reason is the poor availability of medical data: integrated datasets are difficult and expensive to produce, and time-consuming to publish; another is the lack of accessible visualisation tools for multiscale problems. Auer *et al*. [17] questioned whether it was worthwhile to collect multiscale data without having the means to visualise it adequately. In fact, as we will show in Section 2, a wide variety of methods do exist, but only as isolated bespoke solutions; the effort required to reproduce them is prohibitive for most research projects. One such application, which is one of several exemplar projects in MSV, is the blood-clotting protein fibrin [18], the structure and dynamics of which are hierarchical and require simultaneous visualisation to achieve an understanding of how the different scale levels interact.

In the following section, we present a brief survey of the functional components of a multiscale visualisation and the techniques available for each. We then discuss some design considerations for multiscale visualisation and draw conclusions about approaches to adopt.

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DOI 10.1109/IV.2012.95

2. Multiscale techniques

A wide variety of techniques are in current use in multiscale visualisation. We propose that almost all of these techniques can be grouped under the following headings, according to the function which they perform in the visualisation:

- handling of large data
- interaction mode
- representation of sub-scale data
- magnification of sub-scale data
- level of detail (LoD)
- global context
- numerical precision
- temporal multiscale.

2.1 Handling of large data

Datasets larger than 1-3 GB might not fit into the RAM of a typical PC, nor into the 1GB memory of a typical GPU. Data which exceeds the size of the memory must be stored on slower media, and loaded into the graphics pipeline as required. Most solutions to this use a class of technique called bricking (also variously called blocking or chunking), in which the data is stored out-of-core in a form optimised for efficient retrieval. Other techniques involve the precomputing of visibility from different viewpoints, in order to avoid loading data which is occluded or outside the viewing frustrum; LoD management, in which data is loaded at a resolution proportional to the current region of interest [19]; prefetching, in which data are loaded on-the-fly in anticipation of it being required; and rendering objects such as distant scenery as images.

Surveys of methods for out-of-core handling of large datasets can be found in [20-23]. Biomedical examples of large datasets include the well-known Visible Human Male and Female, at 15 and 40 GB respectively [24], and a 55 GB cryo-image of a whole mouse [25].

2.2 Interaction mode

Two common modes in which a user interacts with the graphical display of a spatial scene are scene-in-hand and fly-through [5, 26]. Scene-in-hand is widely used when interacting with graphical objects on a desktop display: the user visualises the object from the outside and manipulates it using the mouse. Fly-through interaction is used in the street level visualisation of Google maps [4]: the metaphor is that of the user being immersed in the scene and walking or flying through it. The user might move about between pre-defined targets or have unconstrained movement in the form of flight controls. Fly-through interaction is well-suited for large, complex scenes, such as cities, where the scene is so much larger than the scale of the user that the scene-in-hand metaphor cannot be sustained. A form of fly-through interaction frequently used in medicine is virtual endoscopy [27, 28], in which the colon, lung and blood vessels are visualised and navigated from the inside. Figure 1 shows a dual-scale visualisation of a virtual colonoscopy.

Issues in the navigation of such structures are path planning [27, 28], collision detection and seeing into occluded corners.

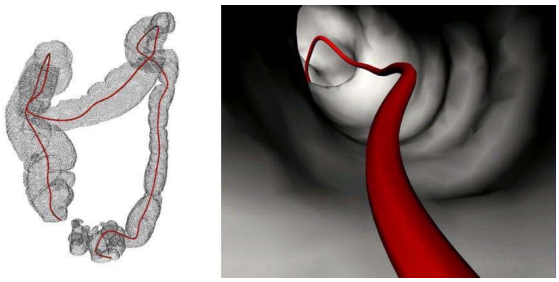

Figure 1. Virtual colonoscopy on two scales, showing global context with path planning and virtual fly-through. Images courtesy of [28], © IEEE 2001.

2.3 Representation of sub-scale data

The representation of embedded sub-scale targets in a scene is an important consideration.

One method is to use small placeholder tokens to indicate data which is too small to resolve; for example, McFarlane *et al.* [29] presented a femur visualisation containing nested images of the bone structure, in which sub-scale data was represented by small click-and-zoom cubes (Figure 2). Thurmond *et al.* [30] used hyperlinks to mark sub-scale datasets in geological outcrops; hyperlinks provide a convenient method for embedding data in scenes, and are particularly useful for calling up textual metadata and related files, but they are a rather crude and disorientating method of navigating between objects. The main disadvantage of using placeholder tokens is occlusion: in cluttered scenes, or with visualisation styles such as isosurfaces and direct volume rendering, the tokens can be hidden behind or within larger objects.

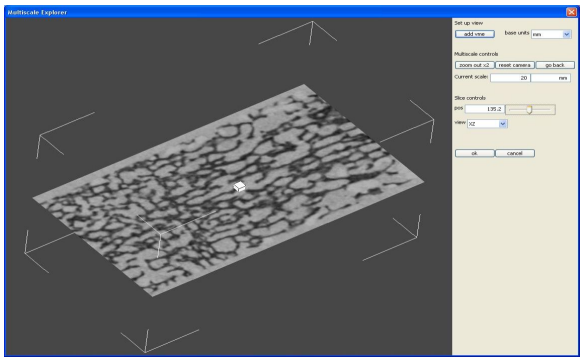

Figure 2. Micro-CT image (20mm) of the trabecular structure of a human femur, with click-and-zoom placeholder token marking location of embedded nano-CT image (0.8mm) Image courtesy of [29], © IEEE 2008.

Another method of indicating sub-scale data is to use call-outs. In visualisation and illustration, a call-out is an annotation that is associated with a point in an image and

connected to the point by means of a pointer. This could be a text label connected to an image feature by a line or arrow, a flag, or even a speech balloon. Call-outs are also a powerful way to magnify data, and this will be discussed further in the next section. For marking the presence of sub-scale data, call-outs have an advantage because they can be placed where they are visible, beyond the clutter and occlusions of the scene.

In scenes consisting of a single large image, such as the Visible Human [24], where there are no pre-defined targets, the user may define their own subvolumes of interest as they navigate the scene. One such method, which might be termed "crop-and-zoom", was used in [19]: the user advanced into the data by using a bounding box widget to define a volume-of-interest, followed by cropping and zooming in on the sub-volume.

In very complex scenes, the scene structure might have to be navigated using GUI panels which are external to the scene. Zomit [31], a click-and-zoom interface with a rich set of navigation tools, including a hierarchical data tree, has been employed in diverse applications such as library navigation and genomics.

2.4 Magnification of sub-scale data

Indicating the presence and location of target data in a scene is only half the story; the subscale data must also be magnified, which can be achieved in various ways.

The most common approach to magnifying data is with a zoom interaction, usually initiated by a click on the target, as in [4] or [29]. Ideally, the zoom should be slow, allowing users to see what is happening and where they are heading. Thus the familiar click-and-zoom interaction can be regarded as a composite of two techniques: placeholder tokens to indicate the targets and a zoom to magnify them.

Another method for magnification is lensing. A lens is a magnified region of an image or scene, located in the scene at the point being magnified. Lenses provide magnification of detail which is in-place and therefore retains the position and context in the global view. Lenses are normally used in 2D visualizations, though some work has been done to extend them into 3D [32, 33]. Figure 3 shows a frog heart magnified by a 3D lens.

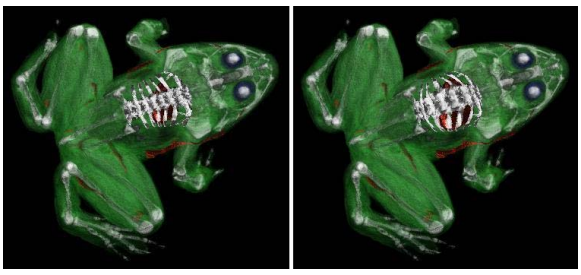

Figure 3. Volume rendered image of frog, showing heart magnified by 3D lens. Image courtesy of [33], © IEEE 2005.

Callouts have already been discussed as a means of indicating the location of sub-scale data, but they are also an important means of magnification. In multiscale illustration, a magnifying call-out is an enlarged sub-region, expanded out of the parent image and magnified into a new image. Callouts are most often seen in static illustrations but they have also been used interactively. ExoVis [34] used magnifying call-outs for interactive 3D visualisation of medical data, allowing a subvolume to be pulled out of the image and magnified into a new image, with pointers connecting it to the corresponding region in the original (Figure 4). This is an excellent way of viewing sub-scale detail and global position at the same time, since the whole path through the scales is visible and located at each step. The ability to view two or more scales simultaneously is also potentially powerful, especially if the data is time-varying. A disadvantage is that it is extravagant with screen space, since each change in scale requires a new image, but this is not an insurmountable problem as two images can easily be displayed on a split screen without much loss of size, and more could be accommodated, given suitable management of the screen space.

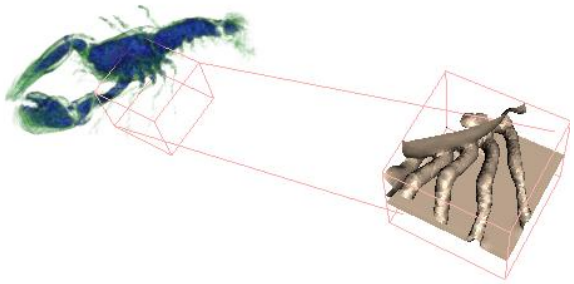

Figure 4. Visualisation in ExoVis, showing volume of interest magnified by call-out. Image courtesy of [34], © AK Peters 2003.

A visually striking form of magnification was recently presented in [35]. By use of non-linear ray-tracing, multiscale detail was pulled seamlessly out of the target image with increasing magnification, in the manner of a continuous call-out, or a stretched lens. The results were remarkable in terms of illustrative rendering, though difficult to interpret quantitatively, and too computationally expensive for real-time rendering.

2.5 Level-of-detail

All multiscale visualisations must consider what to do about the Level of Detail (LoD) that is to be rendered at a particular scale. Does the data need to be resampled, redrawn or relabelled at different scales? Should data too small to be seen be marked by a placeholder, redrawn to suit the scale, or simply allowed to vanish? In its simplest form, LoD might simply consist of modifying the resolution of an image to avoid processing voxels that are too small to be resolved. More complex examples can be found in fields such as cartography, in which a large body of algorithms exists describing how features should be added, deleted and redrawn at different scales in order to preserve properties such as connectivity [36]; and in genomics, in which the

semantic requirements of the visualisation are highly scale-dependent [37, 38].

Long thin objects in the form of collections of fibres are a special case in multiscale visualisation. They occur in medical images of brains and muscles, in vector and tensor field visualisations, and in diagrams of interconnected items and densely connected edge graphs [39]. The problem of visualising fibrous connections at multiresolution is so important that it has its own LoD technique, called bundling. This is analogous to the way in which electric wires are merged into bundles along shared paths, fanning out at the ends to connect distinct endpoints. The technique is important in visualising the complex connections of brain fibres [40-42]. Figure 5 shows bundling of fibres in the brain.

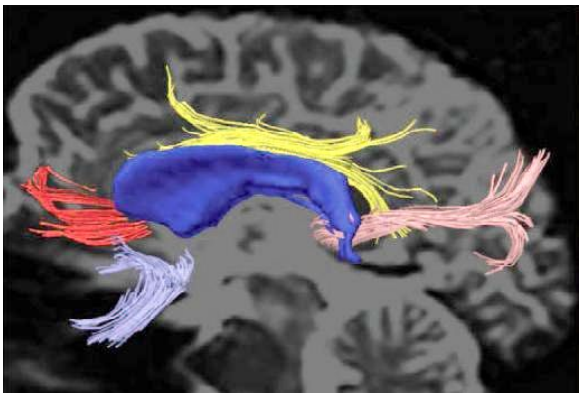

Figure 5. Bundling of DTI fibres in the human brain. Image courtesy of [41], © IEEE 2009

2.6 Global context

It can be difficult for users to orient themselves (i.e. understand their pose and location) in cluttered multiscale scenes. Navigating large scenes requires the user to obtain both detailed content and sufficient context information, exploring small details and changing scale without losing track of the global context. Interaction in a large scene can be considered as two tasks – moving and wayfinding [43]. The main ways in which users move around a scene are: target-based motion, in which the user selects an object and moves directly towards it; path-based, in which the user moves along a pre-planned and landmarked path, as when following a road in Google Streetview [4]; steering-based, in which the user steers towards a target and (probably) change the scale when it is reached; and map-based, in which the user manipulates their position from an external map or hierarchical representation of the scene. McCrae *et al.* [6] used a wide variety of widgets, such as radars and maps, placed within the scene to aid navigation in a large cartographic environment. A click-and-zoom interface called Zomit [31], provided a rich set of navigational tools, including pop-up pie menus, context and history overlays and a scene hierarchy. Context is very important in virtual endoscopy, which has already been discussed in Section 2.2. Lin *et al.* [28] used a split screen to show the endoscope view in one half and a control panel with the global position in the other; the camera could be moved in either view, using the mouse or the control panel.

2.7 Numerical precision

Numerical precision problems can arise in multiscale datasets when small objects are located far from the origin in a much larger world coordinate system. Such problems in a large cartographic scene were reported by [5], when attempting to visualise small objects in a coordinate system with a fixed origin at the centre of the Earth; the ill-conditioning was removed by locating objects relative to a local, mobile origin.

The range of scales in cartography is dwarfed by that in astrophysics, which can cover 40 orders of magnitude, from nuclear physics to the observable universe. Power scaled coordinates [44] provide an elegant solution to the precision problem, with the homogenous coordinate, already present as the fourth component of all graphics coordinates, being used to carry the exponent of the spatial scale. Objects can be viewed at their own spatial scale simply by setting the exponent to unity.

The risk of precision problems depends on the underlying floating point representation. A 4-byte float typically has 6-7 significant digits; an 8-byte double has 15-16. Many applications, particularly those including biomolecular simulations, could exceed the single-precision limit. The double-precision limit is unlikely to be breached, except in extreme astrophysical applications. Thus, the use of double precision is a simple method of avoiding ill-conditioning, provided it is supported by the underlying software and target hardware, including the GPU.

2.8 Temporal multiscale

Data may be multiscale in time as well as space, in that the data contains features of interest at a range of timescales. Even if we exclude biochemistry, the human body undergoes processes at timescales ranging from milliseconds to decades. The electrical activity of the human body, as measured by electromyography (EMG), electrocardiography (ECG) and electroencephalography (EEG), is a rich source of temporal multiscale data. A temporal multiscale view of EMG data of a muscle was presented in [45], showing features at timescales of 2s, 200ms and 20ms. The graph of the electrical data was coupled with an animated spatial view of the electrical activity in the muscle. A temporal zoom expanded the time-axis of the graph to show the activity on that scale, while the corresponding spatial animation was slowed down in order to be visible to the user.

Lenses are a popular technique for time-series data, since they work well in 1D and retain the global context of the magnified region [46, 47]. Figure 6 shows a signal magnified by a temporal lens.

Because time is one-dimensional, selecting the time of interest and the timescale is relatively simple compared with the spatial case. However, unlike spatial data, the sampling frequency of time data can be very high, with the scales of interest somewhere between the highest and lowest frequencies. Wavelets [48] have been

used to assist the user in locating the times and timescales of interest in the data. Another important factor is that time data is often periodic, in which case it may be necessary to select and track small periodic or recurring features over longer timescales [47].

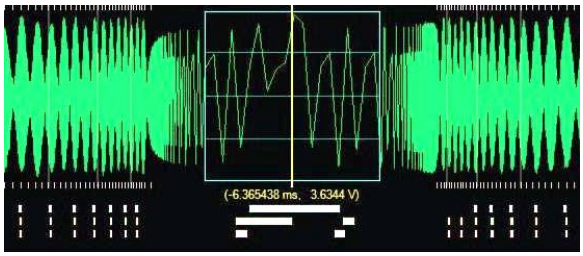

Figure 6. Time series lensing using the SignalLens system, showing magnification and context of a small section of an electrical signal. Marks below the signal indicate the locations of tracked features. Image courtesy of [47], © IEEE 2010.

3. Design considerations for multiscale

There are many multiscale techniques, almost all of which perform one of the functions listed in Section 2. It is notable that the multiscale techniques described here are all add-ons, to be integrated into a scene *after* the user has selected the basic visualisation style. None of these techniques is a visualisation style in its own right; they are ways of navigating datasets in multiscale, but do not introduce new ways of presenting the data. It is also notable that all of the functional components have more than one possible solution, so that our grouping of techniques by function forms not only a classification but also a basic design menu from which the visualisation developer may select techniques.

A detailed analysis of the relative merits of each technique is beyond the scope of this report. However, the choice is broadly influenced by the following:

- data type and visualisation style (surface, volume, plane, vector field, etc.)
- interaction style (scene-in-hand, fly-through)
- quantitative properties of data (range of scales, size of data, number of targets, amount of occlusion, periodicity, fibrous structure, ill-conditioning, etc.).

4. Conclusions

Multiscale visualisation is widely used in cartography and astrophysics but, with the exception of genomics, has received less attention in the biomedical field, largely because of the difficulty and expense of creating high-resolution datasets, and the bespoke nature of current solutions.

Multiscale techniques are not visualisation styles in their own right, in the manner of volumes, surfaces, slices or streamlines; they provide additional navigation features which are integrated into a view after the visualisation style has been decided by the user.

There are many multiscale techniques, most of which perform one of eight functions: handling large data, interaction mode, representing sub-scale data, magnifying sub-scale data, level of detail, global context, numerical precision and temporal techniques. These functional groups form both a classification and a design menu for developers.

Visualisation design consists of choosing a technique for each functional component, and depends on the data type, visualisation style, interaction style and various properties inherent in the data.

For most applications, multiscale visualisation does not require new techniques, but rather a new unified approach. Currently it takes a great deal of research and programming effort to create a multiscale visualisation for an application, but with suitable guidelines to provide an infrastructure for design, and a software library that supports a range of multiscale methods, multiscale visualisation will become more accessible, and many more problems will become amenable to solution.

Acknowledgement

This work was partially supported by the Virtual Physiological Human Programme of the European Commission under the MSV project (FP7 #248032).

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