Towards Advanced Interactive Visualization for Virtual Atlases

Noeska N. Smit and Stefan Bruckner

Abstract An atlas is generally defined as a bound collection of tables, charts or illustrations describing a phenomenon. In an anatomical atlas for example, a collection of representative illustrations and text describes anatomy for the purpose of communicating anatomical knowledge. The atlas serves as reference frame for comparing and integrating data from different sources by spatially or semantically relating collections of drawings, imaging data, and/or text. In the field of medical image processing, atlas information is often constructed from a collection of regions of interest, which are based on medical images that are annotated by domain experts. Such an atlas may be employed for example for automatic segmentation of medical imaging data. The combination of interactive visualization techniques with atlas information opens up new possibilities for content creation, curation, and navigation in virtual atlases. With interactive visualization of atlas information, students are able to inspect and explore anatomical atlases in ways that were not possible with the traditional method of presenting anatomical atlases in book format, such as viewing the illustrations from other viewpoints. With advanced interaction techniques, it becomes possible to query the data that forms the basis for the atlas, thus empowering researchers to access a wealth of information in new ways. So far, atlas-based visualization has been employed for mainly medical education, as well as biological research. In this survey, we provide an overview of current digital biomedical atlas tasks and applications and summarize relevant visualization techniques. We discuss recent approaches for providing next-generation visual interfaces to navigate atlas data that go beyond common text-based search and hierarchical lists. Finally, we reflect on open challenges and opportunities for the next steps in interactive atlas visualization. **Keywords**: biomedical visualization, virtual atlases, interactive visualization, atlases, visualization

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1 Introduction

Since the 16th century, the word 'atlas' has been used to describe a collection of geographical maps. In the medical context, an atlas of human anatomy refers to a collection of illustration and descriptive text that captures knowledge on the morphological structure of the human body. An example of such an atlas is Netter's Atlas of Human Anatomy (Netter, 2017), which depicts the human body in hand-painted illustrations, annotated radiological images, and quick look-up tables. The main aim of such an atlas is to improve the understanding of anatomy and how it applies to medicine. Anatomical atlases are an important reference in both medical education as well as in clinical practice, providing information on shape, position, and structural relations.

With the advent of increased computing power, it became feasible to construct virtual atlases. These virtual atlases can be used in the traditional sense, as a digital collection of texts and illustrations, but also enable more advanced representations of human anatomy, for instance by constructing virtual three-dimensional reference models of standard anatomy. Such models allow for additional interaction techniques, such as rotation, zooming, and showing and hiding structures, which were not possible with traditional illustrations. The digital nature of such atlases offers several advantages over the traditional printed atlases. First, this opens up for additional content creation methods, above the limitations of printed materials, such as 3D reconstruction. Second, virtual atlases allow for novel methods of content curation, where additions to the atlas can be made continuously. Finally, virtual atlas information can be combined with complex (visual) querying techniques, empowering researchers to access a wealth of information via simple interactions.

These advantages have given rise to the creation of a multitude of diverse virtual atlases in the biomedical domain, for example the Allen Brain Atlas (Jones et al., 2009), the DigiMouse atlas (Dogdas et al., 2007), and an atlas of the adult human brain transcriptome (Hawrylycz et al., 2012). For an overview of atlases in developmental biology, please refer to the survey of online atlases and gene expression resources for model organisms by Clarkson (2016). Given the wealth of virtual atlases now available, there is an opportunity to employ advanced visualization and interaction techniques that go beyond traditional atlas-use as a static reference collection.

In this work, we present a characterization of tasks and applications within the context of virtual biomedical atlases. Subsequently, we provide an overview of advanced visualization techniques that are applicable to atlas visualization, followed by a description of potential interaction and navigation strategies. We briefly describe relevant technology which enables interactive atlas visualization and conclude with an outlook on open challenges and opportunities. Our aim with this work is twofold; we seek to raise awareness among atlas curators of advanced data analysis and visualization techniques, and we hope to highlight open research questions and challenges in atlas visualization for visualization researchers.

2 Biomedical Atlas Tasks and Applications

There is a wide variety of tasks and application areas that virtual atlases may support. A well-known application originating from the traditional use of the anatomical atlas, is to use a virtual atlas for educational purposes. Preim and Saalfeld (2018) presented a comprehensive survey on virtual human anatomy education systems. While the authors do not explicitly focus on virtual atlases in this survey, they do mention that most of the virtual anatomy systems were described as a digital atlas. The authors characterize the sources of spatial information that may be collected in such an educational digital atlas as (commercial) 3D models, radiological imaging data, cadaver data, and segmentations. The Virtual Surgical Pelvis for example consists of cadaver data, segmentations, 3D models, and knowledge from histological analysis, and was so far mainly employed as an educational resource (Smit et al., 2016). There are also commercial platforms available aimed at anatomy education via a web-interface. Examples are the Biodigital Human (Qualter et al., 2012) and ZygoteBody (Kelc, 2012). Typically the 3D models are developed in house and as such protected intellectual property, but Zygote also sells their assets.

In addition to education, a virtual atlas may also support data analysis and image processing. An example of this is to use an atlas dataset for image segmentation, for instance in segmentation of MR brain scans (Cabezas et al., 2011). Through registration of the atlas to an unseen dataset, the unseen dataset can be segmented based on the mapped atlas information. This approach can also be modified to to work with multiple atlases (Aljabar et al., 2009). When registering an atlas to patient-specific imaging data, it may be used to construct patient-specific models for treatment planning purposes (Smit et al., 2017) (see Figure 1).

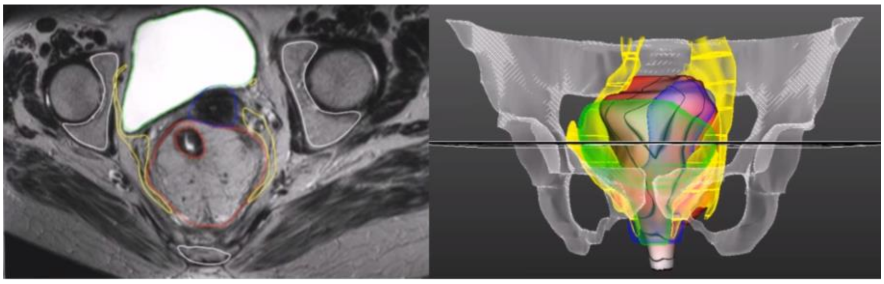

Fig. 1 The Virtual Surgical Pelvis atlas is mapped to a patient-specific MRI scan (left), allowing for the creation of patient-specific models (right) (Smit et al., 2017).

Generally, the atlas is used to transfer knowledge to an unseen dataset, however, the reverse is also possible. By registering additional datasets to a virtual atlas, an atlas may be further enriched with additional information. For example, by registering patient-specific information to the atlas, pathology such as a tumor can be visualized with the atlas as an anatomical reference (Kikinis et al., 1996). The atlas space may also be used as a common frame of reference, for instance to bring gene activity imaging data together in an idealized expert-defined atlas (Walter et al., 2010).

Virtual atlas information can also be employed for simulation and prediction. An atlas dataset can form a basis for biomechanical simulations, for instance to compensate brain shift (Dumpuri et al., 2007).

Furthermore, virtual atlases may be used for consolidation and summarization of research data. The adult human brain transcriptome atlas (Hawrylycz et al., 2012) is an example of such an atlas that caters to researchers as a baseline for studies of (ab)normal human brain function. The Allen Human Brain Atlas (Shen et al., 2012) similarly aims to boost brain research by bringing together structure, function, and gene expression data.

In addition to these diverse tasks that virtual atlases may support, there is a wide range of types of application domains that are supported. On the medical side, a virtual atlas may describe anatomy, physiology, pathology, variation, development, or a mixture of multiple aspects. In the biological domain, digital atlases also vary from describing gene expression, neural circuitry, cell types, to development.

3 Visualization Techniques

When virtual atlas data features a spatial aspect, there are many standard and advanced visualization techniques that can be employed to visualize this data efficiently. In the survey by Clarkson (2016), an overview of common design patterns for graphic representation of anatomy is presented.

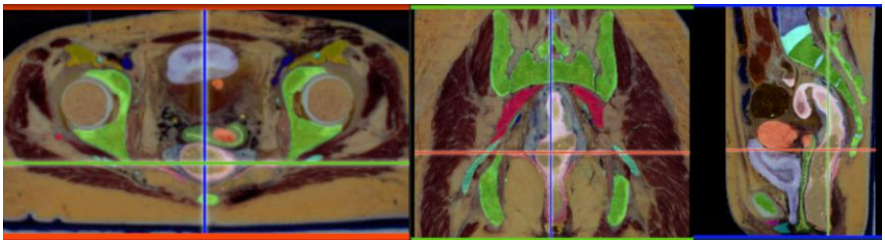

Fig. 2 A 2D slice-based visualization of the Virtual Surgical Pelvis atlas visualized in the browser showing cryosection and segmentation information (Smit et al., 2016). The axial (red outline), coronal (green outline), and sagittal (blue outline) plane are visible. Slices can be selected by moving the crosshair in one of the views, which updates the other views to the slices indicated by color-coordinated lines.

3.1 Standard Visualization Techniques

There are two standard visualization techniques that are currently regularly employed for virtual atlas-data: 2D slice-based visualization and 3D surface visualization.

In 2D slice-based visualization, a 3D volume is sectioned in the axial, coronal, or sagittal plane, and presented as a collection of 2D images. A single slicing direction may be presented, or a combination of all three orthogonal views can be employed. An example of the latter is visible in Figure 2. Here, to navigate through the stack of slices, users can drag a crosshair around to control the two other views indicated by the colored lines. The Allen Brain Reference Atlases, such as the Human Brain Atlas (Hawrylycz et al., 2012), also offer a slice-based view, but they offer a single anatomical plane and visualize the slices next to each other in juxtaposition. A slider is then used to navigate to slices of interest. It is also possible to pick arbitrary slicing directions, a feature which is available for instance in the eMouseAtlas (Armit et al., 2012). This makes complicates the interaction by adding three degrees of freedom (pitch, yaw, roll) to select an appropriate slicing plane, but can be essential if the subject of interest is not aligned with the standard orthogonal planes.

When the atlas features 3D models, they can be shown in a surface visualization. In Figure 3, we see the Virtual Surgical Pelvis atlas in a 3D surface visualization. Here, the surfaces feature textures which employ colors that are either representative for tissue color, or standard in anatomy communication. Such an anatomical standard is to use red for arteries, blue for veins, and yellow for nerves. The textures themselves are meant to communicate the type of tissue that is visualized, for instance with a veined appearance for the organs, and a striped appearance for the musculature. The Allen Mouse Brain Connectivity Atlas (Oh et al., 2014) is also visualized in a surface visualization in the browser: the Allen Brain Explorer. However, here the structures are not textured, and the colors are varying in hue in such a way that structure classes are visually separable, and groups of similar structures can easily be identified.

Many of the more comprehensive virtual atlases feature an aggregation of multiple datasets. In such cases, a summarization visualization can be used to provide an overview of the fused information. For instance, a representative average of the atlas

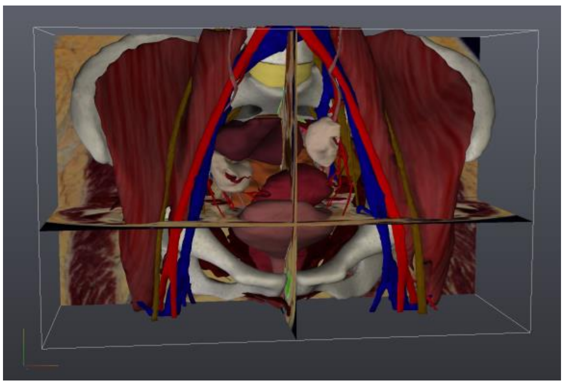

Fig. 3 A 3D surface visualization of the Virtual Surgical Pelvis atlas visualized in the browser (Smit et al., 2016). The slice planes from Figure 2 are also visible in the 3D surface view for reference.

dataset can be presented for navigation purposes, as is visible in the AFQ-Browser tool (Yeatman et al., 2018). Here, a general 3D models of major fiber tracts are presented to the user for selection of bundles of interest.

3.2 Advanced Visualization Techniques

In addition to standard visualization techniques, more recent visualization research presents novel techniques that have good potential for interactive atlas visualization yet are currently under-explored.

The cumbersome task of creating 3D models may be avoided by direct visualization of volumetric data using a volume rendering approach. Direct volume rendering (Levoy, 1988) is currently not employed very often in atlas visualization but can be a highly effective way of visualizing volumetric data without the need for generating explicit surface models. One advantage of directly visualizing the volumetric data is that the full three-dimensional information can be represented. While previously considered to be prohibitively expensive, advances in the performance of Graphics Processing Units (GPUs) have lead to the availability of advanced volume rendering techniques even on low-end systems. For instance, a direct volume rendering approach is used in the BrainGazer project (Bruckner et al., 2009) to render volumetric confocal microscopy data. As discussed in the comprehensive survey by Jönsson et al. (Jönsson et al., 2014), in recent years a number of interactive volume rendering methods that can even incorporate global illumination effects such as ambient occlusion (Hernell et al., 2010), multiple scattering (Kniss et al., 2003), or refraction (Magnus and Bruckner, 2018), have been presented. While such methods can be utilized to generate visually appealing results, they may not necessarily be ideally suited for the purpose of visualizing atlas data.

In *illustrative visualization*, on the other hand, rendering techniques are inspired by scientific illustrations. Here, the focus is not on rendering structures as realistically as possible, but rather on adapting the visual representation in such a way that essential information is emphasized. This reduces visual clutter, which can become an issue in comprehensive virtual atlases that feature a multitude of structures. The challenge of reproducing the clarity and aesthetic quality of traditional illustrations such as those found in medical textbooks has been one of the main drivers in illustrative visualization, and several sophisticated techniques for the visualization of surface and volume data have been developed (see Figure 4). One way to classify these methods is according to the level of abstraction that individual approaches operate on.

Low-level abstraction techniques tend to focus on the appearance of structures and include approaches that aim to reproduce particular artistic styles.

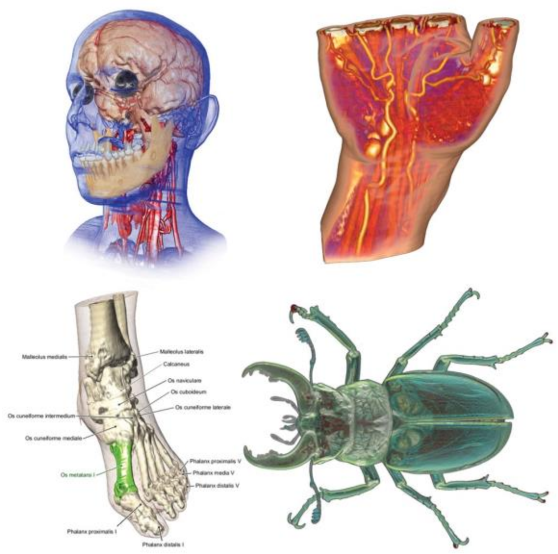

Fig. 4 Examples for illustrative visualization techniques for different types of volumetric data available in the VolumeShop framework (Bruckner and Gröller, 2005).

Lawonn et al. (2018) present a comprehensive survey on illustrative visualization for 3D surface models, in which they categorize techniques into silhouettes and contours, feature lines, hatching, stippling, and shading. Likewise, for volumetric data several powerful methods for mimicking various rendering styles including stippling (Lu et al., 2002), line drawing (Burns et al., 2005), and many other artistic techniques, have been developed. Style transfer functions (Bruckner and Gröller, 2007), for instance, enable the specification of object appearance based on the image of a sphere shaded in the desired manner. *High-level abstraction techniques*, on the other hand, are concerned with what is visible and recognizable in the scene. This class of methods, also referred to as *smart visibility* (Viola and Gröller, 2005), aims to reveal otherwise hidden or poorly visible objects by selectively displacing or altering the visual prominence of occluding structures. Examples include approaches such as cutaways and ghosting (Feiner and Seligmann, 1992; Bruckner et al., 2006; Diepstraten et al., 2003), where an occluding object is removed or its opacity is reduced, or exploded views (Bruckner and Gröller, 2006; Li et al., 2008). Viola and Isenberg (2018) further expand on the idea of abstraction in illustrative visualization.

A concept closely related to abstraction is the notion of *focus+context*, where both low-level and high-level abstraction techniques are employed in order to emphasize particular structures (e.g., the results of a current selection or query) while still presenting them in relation to their surroundings. Focus+context approaches typically employ the concept of an importance function (Viola et al., 2005) to characterize the relevance of an object or region. Such importance functions have been, for instance, used to steer interactive cutaways (Krüger et al., 2006), close-ups (Taerum et al., 2006), peel-aways (Correa et al., 2006), or lenses (Tominski et al., 2017). For biomedical data, the importance function is typically defined based on a geometric region in the data or by a segmentation mask. More advanced ideas aim to provide fine-grained control over the mapping of data attributes to visual styles. Rautek et al. (2007), for instance, presented a system based on fuzzy-logic, which allows users to formulate rules for data and illustration semantics, while Svakhine et al. (2005) proposed the use of multi-level motifs that encapsulate domain knowledge of illustration styles. While such approaches could potentially enable a more tailored experience, the difficulty of specifying and maintaining appropriate rule bases has to date prevented the widespread adoption of these methods.

In the context of atlas visualization, illustrative abstraction may be a suitable approach to visualize information at different scales. In an exploratory user study, Kuß et al. (2010) evaluated the use of different illustrative enhancements for the visualization of filament-surface relationships in 3D brain models. They conclude that the best results are achieved using a combination of line coloring and intersection glyph display. Swoboda et al. (2017) make heavy use of abstraction in the information and interaction design of their neuronal atlas interface. In collaboration with artists, they propose a highly reduced spatial visualization in order to avoid visual clutter. Additional information is presented in the form of glyphs which also convey quantitative information and are used as a central interaction element to provide details on demand.

In *uncertainty visualization*, uncertainty in the data coming from a variety of sources is visually communicated in order to give a faithful representation of the underlying data. Potter et al. (2012) present a taxonomy of uncertainty visualization approaches. In the context of atlas visualization, uncertainty visualization techniques may be employed to visually encode variability, for instance when visualizing a statistical atlas of bone anatomy (Chintalapani et al., 2007). While approaches such as average volumes are frequently used to characterize variation, more advanced techniques may be beneficial. Raj et al. (2016), for example, evaluated the use of 3D contour boxplots in the construction and analysis of anatomical atlases and showed that they provide superior information about shape variability.

Comparative visualization deals with the challenge of making visual comparisons of data. Approaches for comparative visualization in general are categorized into juxtaposition, superposition and explicit encodings (Gleicher et al., 2011). In juxtaposition, visualizations are placed side by side, while in superposition visualizations are placed on top of each other. In explicit encoding, the difference between the datasets are explicitly visualized. With respect to atlas visualization, a comparison between multiple selections of atlas data is often desirable. In the AFQ-Browser tool (Yeatman et al., 2018) for example, comparisons of cohort selections are made by a combination of juxtaposition for multiple fiber tract selections, and superposition to display individual cohort members. Kim et al. (2017) provide an extensive survey of comparative visualization techniques for spatial data.

4 Interaction and Navigation Strategies

To access the wealth of information virtual atlases offer, good interaction and navigation strategies are essential. Clarkson (2016) offers a comprehensive overview of textual and graphical design patterns for querying gene expression databases.

Hierarchical navigation techniques are often employed to browse atlas information. Typically, this is presented in a nested list, where groups of structures or individual structures can be selected and deselected. Examples of such hierarchical navigation tools are visible in both the Online Anatomical Human web application (Smit et al., 2016) and the The Allen Mouse Brain Connectivity Atlas (Oh et al., 2014) visualized in the Allen Brain Explorer. Selections via hierarchical menus can be used to make structures visible or invisible, or to retrieve more detailed information on the selection. A benefit of using a hierarchical list is that groups may be collapsed or unfolded such that the user can pick an appropriate level of detail for his/her investigation. In cases where there is no underlying hierarchy in the items or there is only a limited number of items, a list may be offered instead as a compact representation.

In addition to querying via hierarchical or list menus, text-based search can be a powerful addition for information retrieval. This is especially useful when combined with auto-completion to suggest search terms that may be relevant based on the textual input so far. A combination of a hierarchical menu and text-based search can be especially powerful when the amount of structures and groups of structures are very large.

Rather than searching explicitly for specific information, similarity search can be used to find information that is either semantically or spatially close to selected information. This can be an additional strategy to navigate large amounts of data, as well as to navigate to additional resources linked from the atlas. Appropriate similarity criteria need to be decided upon when offering such a search feature. An example of such a criterion could be spatial proximity.

Besides the more traditional textual search and navigation strategies, visual queries can be an intuitive way to search directly from within a visualization. An straight-forward example of this is querying a structure by clicking on it in a graphical representation. Smit et al. (2012) also allow atlas querying via a selection sphere. A 3D sphere can be placed in the surface visualization, and all information present inside the sphere, for instance anatomical landmarks and related literature, will be retrieved. In addition to providing traditional search and browsing facilities, BrainGazer (Bruckner et al., 2009) allows for several types of interactive visual queries based on distance and structural information, and subsequent work extended this approach to support more advanced shape-based object retrieval (Trapp et al., 2013).

5 Technology

To enable storage and querying of virtual atlas information, the technology stack must be chosen to adequately handle the specific requirements an atlas may have. There is a plethora of database technologies available, and the best fit depends on the atlas specifics. When at the start of the data acquisition the type and characteristics of the data are already known, a traditional relational database may be a good fit. If, however, it is not yet possible to state the exact format of the data that will be a part of the atlas in advance, a so-called schema-less database may be employed, which is considered a promising for clinical data storage (Lee et al., 2013).

Another technology decision must made with respect to designing the atlas interface as a desktop application, for the Web, or as a combination of the two. While traditionally desktop applications were needed to utilize the advanced graphics processing power, currently many web-technologies have become available that allow for interactive visualization in the browser. Examples of this are the WebGL standard, which now allows for volume rendering in the browser (Congote et al., 2011), and the Three.js framework (Danchilla,2012). Yeatman et al. (2018), the authors of the AFQBrowser tool, argue that browser-based tools will be increasingly employed for highdimensional data exploration, scientific communication, data aggregation across labs, and data publication. Commercial tools such as the Biodigital Human (Qualter et al., 2012) platform currently also allow content API access as well as a mobile SDK to support mobile- and web-developers.

6 Open Challenges and Opportunities

There are still many open challenges and opportunities for interactive atlas visualization. These challenges and opportunities lie both on the side of atlas creators, as well on the side of visualization researchers. For atlas creators, it may be worthwhile to employ more advanced data analysis and visualization techniques, while for visualization researchers, there are open research challenges that atlases present which require the development of new methods.

As the volume, variety, and complexity of data to be represented in atlases constantly increases, novel solutions for efficient and effective exploration are needed. Visual analytics defined as "the science of analytical reasoning facilitated by visual interactive interfaces" (Thomas and Cook, 2006) has grown out of the fields of information visualization and scientific visualization in computer science with a specific focus on enabling the analysis of large amounts of heterogeneous data, integrating techniques from visualization, interaction, and automatic data analysis. It is characterized by a strong emphasis on enabling the formulation and validation of hypotheses, facilitated by a combination of human knowledge and intellect with automated techniques. Interactive visualization acts as a high-throughput channel used to make this human-machine interface as efficient as possible. Partly due to its origins in U.S. national security, visual analytics research has mostly focused on abstract data (Cammarano et al., 2007), i.e., points located in a high-dimensional space without any particular a-priori preferences among the dimensions.

The aim of interactive visual analysis is to provide users with insight into the meaning of the data. Using multiple, interactively linked views of the same data set allows the user to productively combine different aspects of the available information. The visual information-seeking-mantra – overview first, filter, zoom in, details on demand – as defined by Shneiderman (1996), is frequently used as a guiding principle. Weaver (2004) showed that the use of multiple linked views can assist the analysis of complex phenomena but requires careful coordination. The concept of linking and brushing allows the user to select an area or parameter range of interest by interactively placing selections on a rendering. Other views and interactions are linked to the selections and focus on information related to the selected subset. Hauser (2006) states that as soon as a notion of interest in some subset of the data is established, we can visualize the selection in full detail while reducing the amount of visual information about the remaining data. One example for the power of visual analytics in the context of medical data visualization is the work of Termeer et al. (2007), who present an interactive system for the investigation of cardiac models augmented with patient-specific late enhancement MRI data. In the context of atlas data, we believe that similar interactive analysis mechanisms could greatly expand the power and flexibility of existing interfaces. As atlas data is becoming richer and more heterogeneous, the analysis and visualization of such data also becomes more challenging. In future interactive atlas visualization platforms, it could therefore be worthwhile to provide data science facilities and tools directly integrated into an interactive visual analysis interface, such that these large and heterogeneous datasets can be analyzed and visualized more effectively. Examples of such techniques are clustering (Xu and Wunsch, 2005) and dimensionality reduction (Van Der Maaten et al., 2009). Providing data science tools could provide more insight into the complex data sets that an atlas may constitute and may lift the purpose of an atlas from use as a descriptive resource to use as a research tool.

Furthermore, as the curation of atlas data takes place at multiple scales, all the way from the organism level to detailed DNA acquisitions, and in multiple domains, interlinking across these scales and domains would be an interesting avenue for visualization research, extending upon the notion of seamless transitions between visual representations (Miao et al., 2018).

Many of the current atlas interfaces are set up in such a way that there is a general 3D model visible, and additional information can be retrieved via hierarchical menus. Interactive visualization of variation and distributions within data collections is currently under-explored. While the AFQ-Browser (Yeatman et al., 2018), features tractography information from a cohort, the mean and variation are not explicitly visualized. The uncertainty visualization techniques described in Section 3.2 could play a crucial role here to showcase variability and distribution.

In recent years, more and more emphasis has been placed on the advantages of open science. By having platforms and data openly available, there is an increase in transparency and reproducibility, which facilitates a more efficient scientific process (Molloy, 2011). In this light, many of the atlases are also freely available, as for instance the atlases of the Allen institute are. To further strengthen such initiatives, providing standardization of atlas formats would allow easier integration and exchange of information between different initiatives worldwide.

With the movement towards open access of publicly funded research data, there are now a multitude of publicly available datasets. These data collections are often stored in larger repositories dedicated to a specific theme, such as for example the Cancer Imaging Archive (Clark et al., 2013). It would further enrich atlases if they could integrate stronger links to these general data repositories and specifically to closely related datasets within such repositories.

7 Conclusion

We have presented an overview of digital biomedical atlas tasks and applications along with relevant visualization and interaction techniques for interactive atlas visualization. There are still many challenges and research opportunities for both atlas developers and visualization researchers alike. We hope that this chapter can form a solid foundation and reference for both of these target audiences to further advance the field towards advanced interactive visualization for virtual atlases.

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References

Aljabar P, Heckemann RA, Hammers A, Hajnal JV, Rueckert D (2009) Multi-atlas based segmentation of brain images: atlas selection and its effect on accuracy. Neuroimage 46(3):726–738, DOI 10.1016/j.neuroimage.2009.02.018

Armit C, Venkataraman S, Richardson L, Stevenson P, Moss J, Graham L, Ross A, Yang Y, Burton N, Rao J, et al. (2012) eMouseAtlas, EMAGE, and the spatial dimension of the transcriptome. Mammalian genome 23(9-10):514–524, DOI 10.1007/s00335-012-9407-1

Bruckner S, Gröller ME (2005) VolumeShop: An interactive system for direct volume illustration. In: Proceedings of IEEE Visualization, pp 671–678, DOI 10.1109/VISUAL.2005.1532856

Bruckner S, Gröller ME (2006) Exploded views for volume data. IEEE Transactions on Visualization and Computer Graphics 12(5):1077–1084, DOI 10.1109/TVCG.2006.140

Bruckner S, Gröller ME (2007) Style transfer functions for illustrative volume rendering. Computer Graphics Forum 26(3):715–724, DOI 10.1111/j.14678659.2007.01095.x

Bruckner S, Grimm S, Kanitsar A, Gröller ME (2006) Illustrative context-preserving exploration of volume data. IEEE Transactions on Visualization and Computer Graphics 12(6):1559–1569, DOI 10.1109/TVCG.2006.96

Bruckner S, Soltészová V, Groller E, Hladuvka J, Buhler K, Jai YY, Dickson BJ (2009) Braingazer - visual queries for neurobiology research. IEEE Transactions on Visualization and Computer Graphics 15(6):1497–1504, DOI 10.1109/TVCG.2009.121

Burns M, Klawe J, Rusinkiewicz S, Finkelstein A, DeCarlo D (2005) Line drawings from volume data. ACM Transactions on Graphics 24(3):512–518, DOI 10.1145/1073204.1073222

Cabezas M, Oliver A, Lladó X, Freixenet J, Cuadra MB (2011) A review of atlasbased segmentation for magnetic resonance brain images. Computer methods and programs in biomedicine 104(3):e158–e177, DOI 10.1016/j.cmpb.2011.07.015

Cammarano M, Dong X, Chan B, Klingner J, Talbot J, Halevey A, Hanrahan P (2007) Visualization of heterogeneous data. IEEE Transactions on Visualization and Computer Graphics 13(6):1200–1207, DOI 10.1109/TVCG.2007.70617

Chintalapani G, Ellingsen LM, Sadowsky O, Prince JL, Taylor RH (2007) Statistical atlases of bone anatomy: construction, iterative improvement and validation. In: International Conference on Medical Image Computing and Computer-Assisted Intervention, Springer, pp 499–506, DOI 10.1007/978-3-540-75757-3_61

Clark K, Vendt B, Smith K, Freymann J, Kirby J, Koppel P, Moore S, Phillips S, Maffitt D, Pringle M, et al. (2013) The Cancer Imaging Archive (TCIA): maintaining and operating a public information repository. Journal of digital imaging 26(6):1045–1057, DOI 10.1007/s10278-013-9622-7"

Clarkson MD (2016) Representation of anatomy in online atlases and databases: a survey and collection of patterns for interface design. BMC Developmental Biology 16(1):18, DOI 10.1186/s12861-016-0116-y

Congote J, Segura A, Kabongo L, Moreno A, Posada J, Ruiz O (2011) Interactive visualization of volumetric data with WebGL in real-time. In: Proceedings of the 16th International Conference on 3D Web Technology, ACM, pp 137–146, DOI 10.1145/2010425.2010449

Correa C, Silver D, Chen M (2006) Feature aligned volume manipulation for illustration and visualization. IEEE Transactions on Visualization and Computer Graphics 12(5):1069–1076, DOI 10.1109/TVCG.2006.144

Danchilla B (2012) Three.js framework. In: Beginning WebGL for HTML5, Springer, pp 173–203, DOI 10.1007/978-1-4302-3997-0_7

Diepstraten J, Weiskopf D, Ertl T (2003) Interactive cutaway illustrations. Computer Graphics Forum 22(3):523–532, DOI 10.1111/1467-8659.t01-3-00700

Dogdas B, Stout D, Chatziioannou AF, Leahy RM (2007) Digimouse: a 3D whole body mouse atlas from CT and cryosection data. Physics in Medicine & Biology 52(3):577, DOI 10.1088/0031-9155/52/3/003

Dumpuri P, Thompson RC, Dawant BM, Cao A, Miga MI (2007) An atlas-based method to compensate for brain shift: Preliminary results. Medical Image Analysis 11(2):128–145, DOI 10.1016/j.media.2006.11.002

Feiner SK, Seligmann DD (1992) Cutaways and ghosting: satisfying visibility constraints in dynamic 3D illustrations. The Visual Computer 8(5):292–302, DOI 10.1007/BF01897116

Gleicher M, Albers D, Walker R, Jusufi I, Hansen CD, Roberts JC (2011) Visual comparison for information visualization. Information Visualization 10(4):289– 309, DOI 10.1177/1473871611416549

Hauser H (2006) Generalizing Focus+Context Visualization, Springer, pp 305–327. DOI 10.1007/3-540-30790-7_18

Hawrylycz MJ, Lein ES, Guillozet-Bongaarts AL, Shen EH, Ng L, Miller JA, Van De Lagemaat LN, Smith KA, Ebbert A, Riley ZL, et al. (2012) An anatomically comprehensive atlas of the adult human brain transcriptome. Nature 489(7416):391, DOI 10.1038/nature11405

Hernell F, Ljung P, Ynnerman A (2010) Local ambient occlusion in direct volume rendering. IEEE Transactions on Visualization and Computer Graphics 16(4):548–559, DOI 10.1109/TVCG.2009.45

Jones AR, Overly CC, Sunkin SM (2009) The Allen brain atlas: 5 years and beyond. Nature Reviews Neuroscience 10(11):821, DOI 10.1038/nrn2722

Jönsson D, Sundén E, Ynnerman A, Ropinski T (2014) A survey of volumetric illumination techniques for interactive volume rendering. Computer Graphics Forum 33(1):27–51, DOI 10.1111/cgf.12252

Kelc R (2012) Zygote Body: A new interactive 3-dimensional didactical tool for teaching anatomy. WebmedCentral ANATOMY 2012;3(1):WMC002903 DOI 10.9754/journal.wmc.2012.002889

Kikinis R, Shenton ME, Iosifescu DV, McCarley RW, Saiviroonporn P, Hokama HH, Robatino A, Metcalf D, Wible CG, Portas CM, et al. (1996) A digital brain atlas for surgical planning, model-driven segmentation, and teaching. IEEE Transactions on Visualization and Computer Graphics 2(3):232–241, DOI 10.1109/2945.537306

Kim K, Carlis JV, Keefe DF (2017) Comparison techniques utilized in spatial 3D and 4D data visualizations: A survey and future directions. Computers & Graphics 67:138–147, DOI 10.1016/j.cag.2017.05.005

Kniss J, Premoze S, Hansen C, Shirley P, McPherson A (2003) A model for volume lighting and modeling. IEEE Transactions on Visualization and Computer Graphics 9(2):150–162, DOI 10.1109/TVCG.2003.1196003

Krüger J, Schneider J, Westermann R (2006) Clearview: An interactive context preserving hotspot visualization technique. IEEE Transactions on Visualization and Computer Graphics 12(5):941–948, DOI 10.1109/TVCG.2006.124

Kuß A, Gensel M, Meyer B, Dercksen VJ, Prohaska S (2010) Effective techniques to visualize filament-surface relationships. Computer Graphics Forum 29:1003 – 1012, DOI 10.1111/j.1467-8659.2009.01703

Lawonn K, Viola I, Preim B, Isenberg T (2018) A survey of surface-based illustrative rendering for visualization. Computer Graphics Forum DOI 0.1111/cgf.13322

Lee KKY, Tang WC, Choi KS (2013) Alternatives to relational database: comparison of NoSQL and XML approaches for clinical data storage. Computer methods and programs in biomedicine 110(1):99–109, DOI 10.1016/j.cmpb.2012.10.018

Levoy M (1988) Display of surfaces from volume data. IEEE Computer Graphics and Applications 8(3):29–37, DOI 10.1109/38.511

Li W, Agrawala M, Curless B, Salesin D (2008) Automated generation of interactive 3D exploded view diagrams. ACM Transactions on Graphics 27(3):101:1–101:7, DOI 10.1145/1360612.1360700

Lu A, Morris CJ, Ebert DS, Rheingans P, Hansen C (2002) Non-photorealistic volume rendering using stippling techniques. In: Proceedings of IEEE Visualization, pp 211–218, DOI 10.1109/VISUAL.2002.1183777

Magnus JG, Bruckner S (2018) Interactive dynamic volume illumination with refraction and caustics. IEEE Transactions on Visualization and Computer Graphics 24(1):984–993, DOI 10.1109/TVCG.2017.2744438

Miao H, De Llano E, Isenberg T, Gröller ME, Barišić I, Viola I (2018) DimSUM: Dimension and scale unifying map for visual abstraction of DNA origami structures. Computer Graphics Forum 37(3):403–413, DOI 10.1111/cgf.13429

Molloy JC (2011) The open knowledge foundation: open data means better science. PLoS biology 9(12):e1001195, DOI 10.1371/journal.pbio.1001195

Netter FH (2017) Atlas of Human Anatomy E-Book. Elsevier Health Sciences

Oh SW, Harris JA, Ng L, Winslow B, Cain N, Mihalas S, Wang Q, Lau C, Kuan L, Henry AM, et al. (2014) A mesoscale connectome of the mouse brain. Nature 508(7495):207, DOI 10.1038/nature13186

Potter K, Rosen P, Johnson CR (2012) From quantification to visualization: A taxonomy of uncertainty visualization approaches. In: Uncertainty Quantification in Scientific Computing, Springer, pp 226–249, DOI 10.1007/978-3-642-326776_15

Preim B, Saalfeld P (2018) A survey of virtual human anatomy education systems. Computers & Graphics 71:132–153, DOI 10.1016/j.cag.2018.01.005

Qualter J, Sculli F, Oliker A, Napier Z, Lee S, Garcia J, Frenkel S, Harnik V, Triola M (2012) The biodigital human: a web-based 3D platform for medical visualization and education. Studies in health technology and informatics 173:359–361, DOI 10.3233/978-1-61499-022-2-359

Raj M, Mirzargar M, Preston JS, Kirby RM, Whitaker RT (2016) Evaluating shape alignment via ensemble visualization. IEEE Computer Graphics and Applications 36(3):60–71, DOI 10.1109/MCG.2015.70

Rautek P, Bruckner S, Gröller E (2007) Semantic layers for illustrative volume rendering. IEEE Transactions on Visualization and Computer Graphics 13(6):1336– 1343, DOI 10.1109/TVCG.2007.70591

Shen EH, Overly CC, Jones AR (2012) The Allen Human Brain Atlas: comprehensive gene expression mapping of the human brain. Trends in neurosciences 35(12):711– 714, DOI 10.1016/j.tins.2012.09.005

Shneiderman B (1996) The eyes have it: A task by data type taxonomy for information visualizations. In: Proceedings of the IEEE Symposium on Visual Languages, pp 336–343, DOI 10.1109/VL.1996.545307

Smit N, Kraima A, Jansma D, de Ruiter M, Botha C (2012) A unified representation for the model-based visualization of heterogeneous anatomy data. In: EuroVis Short Papers, pp 85–89, DOI 10.2312/PE/EuroVisShort/EuroVisShort2012/085089

Smit N, Hofstede CW, Kraima A, Jansma D, deRuiter M, Eisemann E, Vilanova A (2016) The Online Anatomical Human: web-based anatomy education. In: Proceedings of the 37th Annual Conference of the European Association for Computer Graphics: Education Papers, Eurographics Association, pp 37–40, DOI 10.2312/eged.20161025

Smit N, Lawonn K, Kraima A, DeRuiter M, Sokooti H, Bruckner S, Eisemann E, Vilanova A (2017) Pelvis: Atlas-based surgical planning for oncological pelvic surgery. IEEE

Transactions on Visualization and Computer Graphics 23(1):741– 750, DOI 10.1109/TVCG.2016.2598826

Svakhine N, Ebert DS, Stredney D (2005) Illustration motifs for effective medical volume illustration. IEEE Computer Graphics and Applications 25(3):31–39,DOI 10.1109/MCG.2005.60

Swoboda N, Moosburner J, Bruckner S, Yu JY, Dickson BJ, Bühler K (2017) Visualization and quantification for interactive analysis of neural connectivity in drosophila. Computer Graphics Forum 36(1):160–171, DOI 10.1111/cgf.12792

Taerum T, Sousa MC, Samavati F, Chan S, Mitchell JR (2006) Real-time super resolution contextual close-up of clinical volumetric data. In: Proceedings of EuroVis, pp 347–354, DOI 10.2312/VisSym/EuroVis06/347-354

Termeer M, Bescós JO, Breeuwer M, Vilanova A, Gerritsen F, Gröller E (2007) CoViCAD: Comprehensive visualization of coronary artery disease. IEEE Transactions on Visualization and Computer Graphics 13(6):1632–1639, DOI 10.1109/TVCG.2007.70550

Thomas JJ, Cook KA (2006) A visual analytics agenda. IEEE Computer Graphics and Applications 26(1):10–13, DOI 10.1109/MCG.2006.5

Tominski C, Gladisch S, Kister U, Dachselt R, Schumann H (2017) Interactive lenses for visualization: An extended survey. Computer Graphics Forum 36(6):173–200, DOI 10.1111/cgf.12871

Trapp M, Schulze F, Bühler K, Liu T, Dickson BJ (2013) 3D object retrieval in an atlas of neuronal structures. The Visual Computer 29(12):1363–1373, DOI 10.1007/s00371-013-0871-8

Van Der Maaten L, Postma E, Van den Herik J (2009) Dimensionality reduction: a comparative review. J Mach Learn Res 10:66–71, DOI 10.1.1.112.5472

Viola I, Gröller E (2005) Smart visibility in visualization. In: Computational Aesthetics, pp 209–216, DOI 10.2312/COMPAESTH/COMPAESTH05/209-216

Viola I, Isenberg T (2018) Pondering the concept of abstraction in (illustrative) visualization. IEEE Transactions on Visualization and Computer Graphics 24(9):2573–2588, DOI 10.1109/TVCG.2017.2747545

Viola I, Kanitsar A, Gröller ME (2005) Importance-driven feature enhancement in volume visualization. IEEE Transactions on Visualization and Computer Graphics 11(4):408–418, DOI 10.1109/TVCG.2005.62

Walter T, Shattuck DW, Baldock R, Bastin ME, Carpenter AE, Duce S, Ellenberg J, Fraser A, Hamilton N, Pieper S, et al. (2010) Visualization of image data from cells to organisms. Nature methods 7(3s):S26, DOI 10.1038/nmeth.1431

Weaver C (2004) Building highly-coordinated visualizations in improvise. In: Proceedings of IEEE InfoVis, pp 159–166, DOI 10.1109/INFVIS.2004.12

Xu R, Wunsch D (2005) Survey of clustering algorithms. IEEE Transactions on neural networks 16(3):645–678, DOI 10.1109/TNN.2005.845141

Yeatman JD, Richie-Halford A, Smith JK, Keshavan A, Rokem A (2018) A browserbased tool for visualization and analysis of diffusion MRI data. Nature communications 9(1):940, DOI 10.1038/s41467-018-03297-7