

A digital tool for three-dimensional visualization and annotation in Anatomy and Embryology learning

Jon-Jatsu Azkue

*Department of Neurosciences, School of Medicine and Dentistry,
University of the Basque Country, Leioa, Bizkaia, Spain*

SUMMARY

Mental representation and proper understanding of the three-dimensional structure of the human body is commonly challenging to the learner. Advances in computing science hold promise to significantly contribute to scientific visualization, including three-dimensional visualization of anatomical structures. This paper describes the implementation of a computer application designed for addressing two major aspects of anatomy education, namely (i) effective three-dimensional visualization for classroom or laboratory demonstration, and (ii) exploration and annotation for personal, self-directed learning. The digital tool presented here relies on a polygon mesh surface rendering technique to represent anatomical scenes which the user can navigate by translating or rotating the viewing direction. A stereoscopic, anaglyph view mode is also provided to increase depth perception within the scene. Colouring and opacity change operations enable the user to modify the appearance of rendered models, which also can be removed and retrieved as needed during the session. All changes to the scene can be saved to file and retrieved at a later time. The graphical and textual annotation features included in this application enable the user to enrich structural information in the anatomical scene with personal input. An overview is provided of potential uses of this tool in anatomy and embryology learning.

Key words: Anatomy – Teaching – Computer-assisted teaching – Medical education – Gross anatomy – Three-dimensional visualization

INTRODUCTION

Learning anatomy is essentially a three-dimensional endeavour. In the anatomy lab, cadaver dissection and the analysis of prosected specimens remains a straightforward and powerful approach to demonstrate and learn the three-dimensional structure and relevant spatial relationships in a number of body regions and organs. When dealing with small and intricate structures, resorting to physical models and high-quality graphic renditions is often preferred. For instance, structures contained in the middle and inner ear, terminal branches of cranial nerves, or certain brain nuclei and pathways are commonly recognized as difficult structures to successfully demonstrate by dissection (Nicholson et al., 2006; Bowen et al., 2007; Estevez et al., 2010; Yeung et al., 2011). In addition, an illustrative example of the difficulty to generate a mental representation of anatomical three-dimensional structure may be found in the developing human embryo, where spatial details often pose considerable difficulty to the teacher to graphically represent and quite a challenge for the learners to understand in its full complexity (Kakusho et al., 2001; Mizuta et al., 2002; Abdulla et al., 2004; Garcia et al., 2012; Yamada et al., 2006, 2012). Over the last decades, the advancement of clinical imaging and computing technologies has made available a variety of visualization tech-

Corresponding author: Jon-Jatsu Azkue. Department of Neurosciences, School of Medicine and Dentistry, University of the Basque Country, Barrio Sarriena s/n, E-48940 Leioa, Bizkaia, Spain Tel: +34 94601 8379 . E-mail: jonjatsu.azkue@ehu.es

Submitted: 20 November, 2012. *Accepted:* 27 March, 2013.

niques that have opened up a new view for anatomical information and education. Alone or in combination with a variety of computer-based media, three-dimensional visualizations are becoming widely used tools in medical instruction today (Rochford, 1985; Garg et al., 2001; Henn et al., 2002; Risucci et al., 2002; Wanzel et al., 2003; Keehner et al., 2004; Huk, 2006; Temkin et al., 2006; Guillot et al., 2007; Gangata, 2008; Silen et al., 2008; Perry 2007; Crossingham et al., 2009; Hilbelink, 2009; Hoyek et al., 2009; Petersson et al., 2009). In most three-dimensional viewing software applications, data visualization typically relies on scene rendering techniques that include surface rendering, volume rendering or planar rendering, alone or in combination. Surface rendering is based on reflection of scene lights on multiple small interconnected triangles that collectively shape the external surface of a three-dimensional structure. In contrast, in volume rendering techniques polygon extraction is not required and the volumetric dataset is directly rendered according to predefined colour and transparency transfer functions. Finally, planar rendering corresponds to standard visualization of tomographic sections in axial, frontal and sagittal views. An evident benefit of anatomical 3D models is the ability to render the spatial relationships between structures. This is expected to improve the acquisition of spatial knowledge, hereby contributing to overcome difficulty both mentally transposing a two-dimensional image onto a three-dimensional patient and identifying structures in the living body as required in clinical examination (Heylings, 2002), although optimal contexts and uses for this approach remain to be established (Henn et al., 2002; Huk, 2006; Perry et al., 2007; Hilbelink, 2009; Petersson et al., 2009; Price and Lee, 2010). In addition, digital didactic material can also provide interaction, in contrast to textbook diagrams and photographs, and 3D presentation of material can improve learning by increasing a learner's immersion, interest and motivation (Dalgarno and Lee, 2010). In recent years, biomedical educational institutions all over Europe are facing a shift in teaching methodologies within the new Bologna paradigm that entails a transition from lecture-based, traditional didactic instruction to the use of active learning methodologies encouraging independent thought, teamwork, and life-long learning. In addition, the hours devoted to dissection and anatomy teaching are declining from the medical curriculum (Aziz et al., 2002; Parker, 2002) and in many institutions there has been a loss of staff in anatomy that are skilled in teaching the subject (Heylings, 2002). This has prompted considerable debate as to the best methods of teaching anatomy in an efficient and cost-effective manner (James et al., 2004). In this changing context, a variety of complementary

methods have been proposed to address these new needs in anatomical teaching and training both for the educator and the student (Verhoeven et al., 2002; McLachlan et al., 2004; McLachlan and Patten, 2006). Among other approaches, computer-based resources and particularly three-dimensional representations of the human body hold promise to become a useful, cost-effective adjunct to other resources employed in anatomical teaching (Aziz et al., 2002; Older, 2004; Shaffer, 2004; Patten, 2007).

This proof-of-concept paper describes the implementation of a digital tool devised to address two central aspects of anatomy education, namely (i) effective three-dimensional visualization for classroom or laboratory demonstration, and (ii) exploration and annotation for personal, self-directed learning. The potentialities of this tool are discussed.

MATERIALS AND METHODS

Three-dimensional rendering

For the purposes of the present work, a polygon surface mesh rendering procedure was chosen for several reasons. First, surface rendering can be less demanding in computational terms than volume rendering, provided that a trade-off is reached between elimination of superfluous triangles and preservation of an adequate level of spatial detail. Second, surface meshes acquire a solid appearance when rendered, and thus their resemblance to body constituents such as bones, viscera or blood vessels is relatively simple to achieve. Finally, surface rendering allows the user to easily modify the rendering features (i.e. colour and opacity level) of any model of the scene individually, rather than to the whole scene.

The viewing application reported on here was implemented by using libraries from the Visualization Toolkit package (VTK; <http://www.vtk.org>). The VTK is an open-source software project devoted to scientific visualization (Schroeder et al., 1998) that has been used for a variety of medical visualization applications (Palombi et al., 2006; Rosset et al., 2004; Burgielski et al., 2002). The visualization pipeline in VTK typically includes creating or importing the models, mapping their visualization properties, and laying them out as actors in the scene to be finally rendered. In standard VTK-based applications, the rendering window allows the user to interact with the elements comprising the 3D scene by mouse clicking and dragging, for example to zoom in or out, to displace the viewing camera within the scene, or to rotate the models.

Interface layout and user controls

The user interface and controls were constructed here using the Java JDK 1.7 (Sun Microsystems Inc.) and the Swing Application Framework. A compiled version of VTK with the Java wrapping for different computer platforms (MS® Windows (TM), MAC OS (TM), or GNU Linux) was used.

Test model generation

Three-dimensional polygon surface meshes can be generated either by 3D modelling from geometric primitives or via segmentation of stacked sectional data. The latter is often preferred for generating anatomically accurate and realistic meshes, since this procedure ensures the preservation of relative positions and anatomical accuracy of three-dimensional relationships among the segmented elements. The term segmentation refers to subdivision of an image into its constituent parts. In particular, the contours of the desired structures within the global dataset can be outlined manually, semi-automatically or automatically throughout the dataset, so three-dimensional surface meshes of selected elements can be computed from outlined contours.

In this work, 3D models were generated from three different data sources and procedures. Stacked optical projection tomography data (Sharpe et al., 2002) of a human embryo at the Carnegie Stage 12 (26th post-ovulatory day approximately) were used; these were generated and distributed as part of the HUDSEN atlas project (<http://www.hudsen.org>, Kerwin et al. 2010). The external surface of this embryo was segmented automatically from transverse sections by using the 3D Slicer software version 3.6.3 (<http://www.slicer.org>), whereas the neural tube, the heart, part of the primitive gut, the arterial and venous systems, and particularly the early aortic arches were manually seg-

mented by using the itk-SNAP software version 2.2.0 (Yushkevich et al., 2006). A four-somite embryo at the Carnegie Stage 9 (ca. 20 post-fertilization days) was modelled by using Blender v 2.63 software (<http://www.blender.org>), based on sectional data from the Virtual Human Embryo Project website (<http://virtualhumanembryo.lsuhsu.edu/>).

Finally, osseous labyrinth, middle ear ossicles and tympanic membrane were adapted from Virtual Reality Model Language (vrml) files made available from the Auditory Mechanics Laboratory at the Department of BioMedical Engineering, McGill University (Montreal, Canada).

RESULTS

A simple computer application was implemented here for visualization and annotation of three-dimensional anatomical scenes. The user interface consists of a main visualization panel, a set of controls that support operations to the models featured in the scene, a table listing the names of loaded models, and a menu bar including standard file- and application operations (Fig. 1). The interface is highly intuitive and user-friendly, and has a steep learning curve. The implemented application was named *Anatorama*, highlighting the ability this software application provides to *visualize* anatomy. The core application can be distributed with a portable Java (TM) runtime engine (Java Portable 7) for execution on a flash drive device.

Navigating scenes and customizing scene configuration

User interactions include navigation of the scene and modification of the rendering proper-

Fig. 1. Layout of the *Anatorama* application's user interface. **1.** Main viewing panel where the anatomical scene is to be rendered. **2.** Model table to list all models loaded into memory and rendered in the viewing panel. **3.** File and session operation menu bar, including a *Scene components* menu for selecting and loading the 3D model files comprising the scene, a *Session* menu for saving and loading set configuration files, and a *Help* menu for user's reference. **4.** Set of controls for colouring and opacity level operations, for capturing still pictures of the rendered scene, as well as for enabling stereoscopic anaglyph view mode.

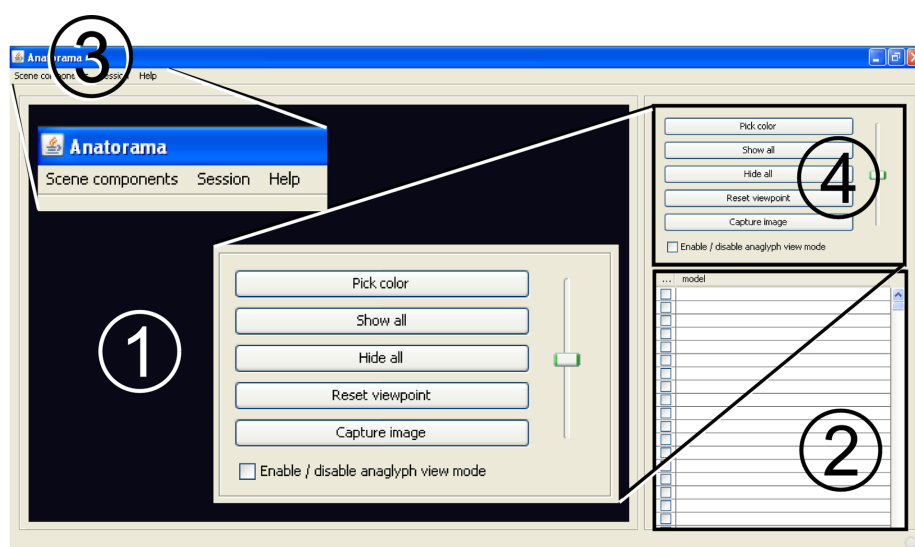


Fig. 2. Captures of lateral and posterior views (A and B, respectively) of a 3D scene containing featuring the left bony labyrinth, middle ear ossicles and tympanic membrane. The tympanic membrane has been rendered translucent in A, in order to expose ear ossicles and the stapes footplate apposed to the oval window. 1. Tympanic membrane. 2. Umbo of tympanic membrane. 3. Neck of malleus. 4. Lateral process of malleus. 5. Head of malleus. 6. Body of incus. 7. Short limb of incus. 8. Long limb of incus. 9. Lenticular process of incus and head of stapes. 10. Limbs of stapes. 11. Lateral semicircular canal. 12. Posterior semicircular canal. 13. Anterior semicircular canal. 14. Cochlea.

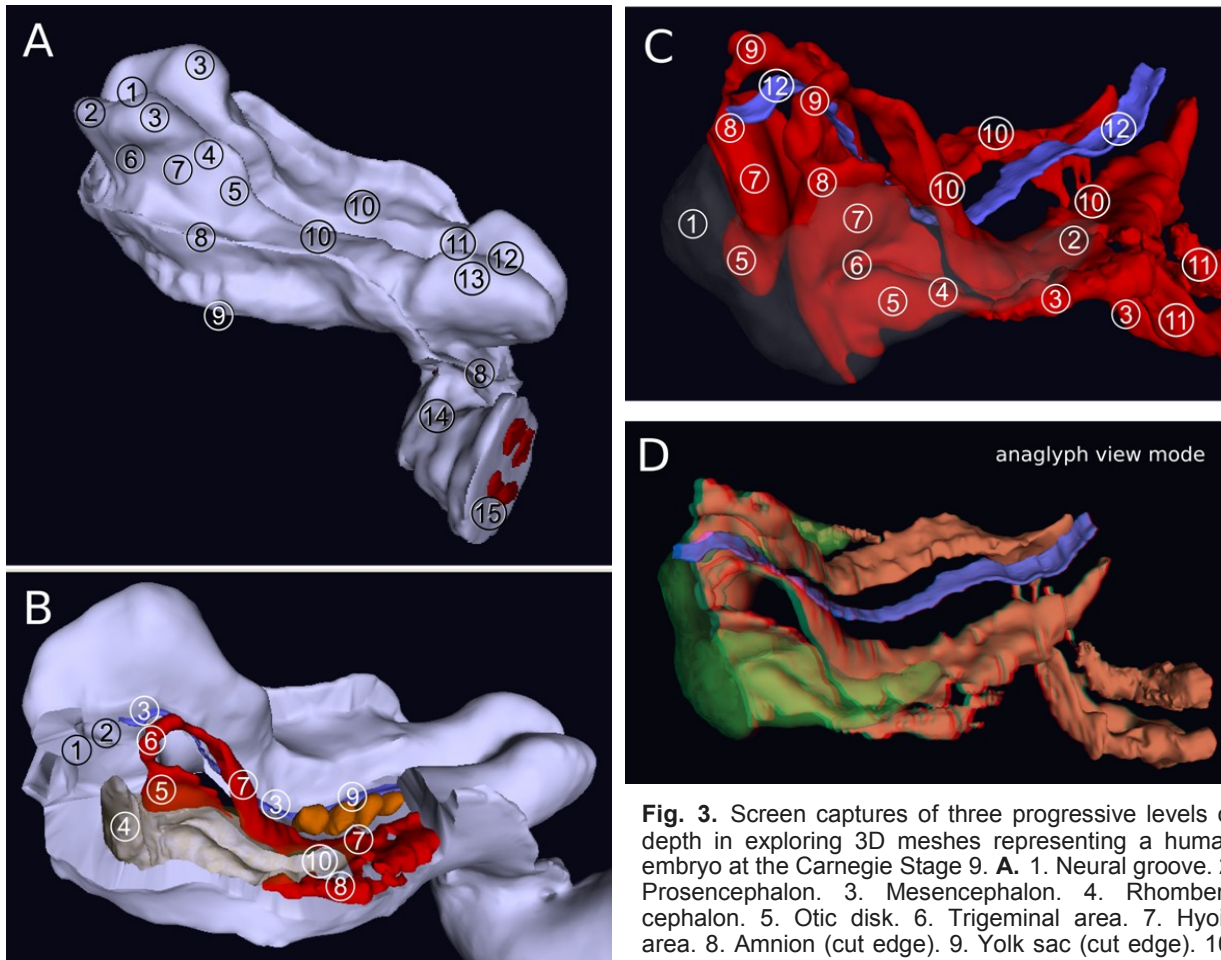
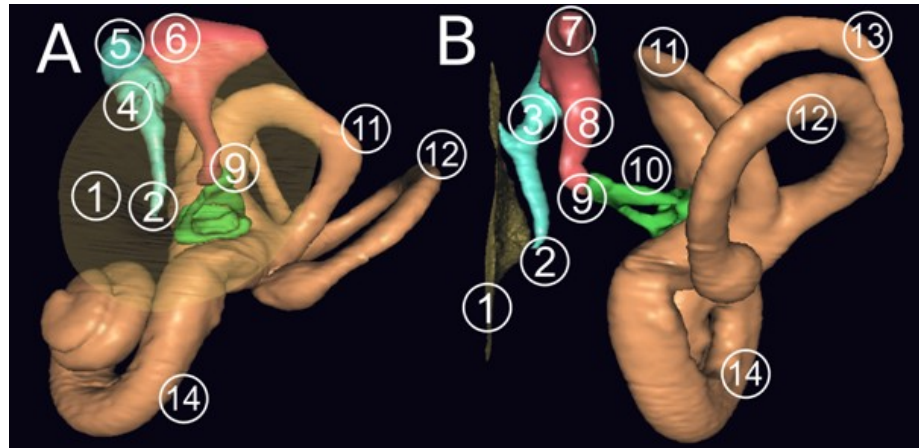


Fig. 3. Screen captures of three progressive levels of depth in exploring 3D meshes representing a human embryo at the Carnegie Stage 9. **A.** 1. Neural groove. 2. Prosencephalon. 3. Mesencephalon. 4. Rhombencephalon. 5. Otic disk. 6. Trigeminal area. 7. Hyoid area. 8. Amnion (cut edge). 9. Yolk sac (cut edge). 10. Surface ectoderm overlying somites. 11. Primitive node. 12. Primitive streak. 13. Caudal eminence. 14. Connecting stalk. 15. Umbilical vessels. **B.** 1. Oropharyngeal membrane. 2. Developing pharynx. 3. Notochordal plate. 4. Pericardial cavity (bottom). 5. Conoventricular region. 6. First aortic arch. 7. Dorsal aorta. 8. Vitelline veins. 9. Somites 1 through 4. 10. Caudal coelomic cavity. **C.** 1. Pericardial cavity (translucent). 2. Caudal coelomic cavity (translucent). 3. Vitelline veins. 4. Sinus venosus. 5. Atrium. 6. Atrio-ventricular junction. 7. Ventricular region. 8. Conal region. 9. First aortic arch. 10. Dorsal aorta. 11. Umbilical vessels. 12. Notochordal plate. **D.** Similar view to C in stereoscopic, anaglyph view mode.

12. Primitive streak. 13. Caudal eminence. 14. Connecting stalk. 15. Umbilical vessels. **B.** 1. Oropharyngeal membrane. 2. Developing pharynx. 3. Notochordal plate. 4. Pericardial cavity (bottom). 5. Conoventricular region. 6. First aortic arch. 7. Dorsal aorta. 8. Vitelline veins. 9. Somites 1 through 4. 10. Caudal coelomic cavity. **C.** 1. Pericardial cavity (translucent). 2. Caudal coelomic cavity (translucent). 3. Vitelline veins. 4. Sinus venosus. 5. Atrium. 6. Atrio-ventricular junction. 7. Ventricular region. 8. Conal region. 9. First aortic arch. 10. Dorsal aorta. 11. Umbilical vessels. 12. Notochordal plate. **D.** Similar view to C in stereoscopic, anaglyph view mode.

ties (i.e. colour and opacity) of the models within the scene. The navigation mode chosen here was camera-mode, i.e. the one in which mouse clicking and dragging affects the viewer's position rather than the models'. This mode of scene navigation allows for zooming in and out the scene, displacing the viewpoint across the frontal plane, and rotation around the models to explore the scene in different viewing directions. Upon loading the surface models into memory, the anatomical scene is rendered in the viewing panel, and the names of all featured models are listed in the model table. Interaction of the user with the anatomical scene can then commence. For example, double-clicking the left mouse button on any model within the viewing panel will remove it from

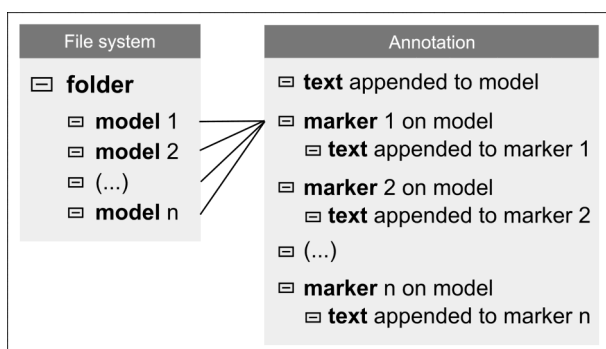


Fig. 4. General organization of the 3D surface files (*models*) and the graphical and textual annotation features. All surface model files are opened from a single containing folder. Each model can be attached a piece of text as an annotation (textual annotation), as well as one or more bright green spheres termed here as *markers* (graphical annotation). Each marker can be itself also labelled textually, so the user's input ends up enriching the scene with custom, personal information.

the scene, whereas double-clicking on its name will either remove it or bring it back to scene depending on its previous state. In addition, the models can all be removed or rendered back at once by clicking on the appropriate buttons on the panel.

All models loaded are first rendered in a neutral colour and completely opaque by default, and any changes to their rendering properties should be made either individually by using the appropriate set of controls, or collectively by loading a previously saved *set* file (cf. below). To select an individual model for colouring or opacity operations, the user can click the left mouse button either on the model itself in the rendered scene or on the model's name in the list. The colouring operation consists of applying an arbitrary colour that can be selected from a menu in a pop-up window (Red-Green-Blue or Hue-Saturation-Brightness colour dimensions, or palette colour). This allows the user to visually classify homologous structures with conventional (e.g. bright red for arteries, blue for veins, white or marble for bones, etc) or any desired colour codes, as well as to highlight any structure in a different colour. The opacity changing operation is used to apply any arbitrary level of translucency to a model, so its presence can be obscured and all structures lying behind exposed. Using opacities wisely allows the user to effectively highlight and demonstrate the relative positions of internal or tightly packed structures. Examples of colour and transparency changes to anatomical scenes are provided in Figs. 2, 3 and 5. A check-box within the control panel permits the user to view the scene in stereoscopic, anaglyph mode (Fig. 3), and any



Fig. 5. Captures of 3D meshes representing a human embryo at the Carnegie Stage 12. **A.** Low magnification view of the embryo's body. The opacity level of the embryo's external surface has been lowered in A in order to expose a number of structures inside the body. 1. Heart. 2. A. Arterial system. 2. Venous system. 3. Primitive gut. 4. Connecting stalk. 5. Folding neural tube. 6. Optic vesicle. 7. Auditive vesicle. **B.** Graphical annotation on the arterial system in a close-up view of the developing aortic arches. Markers have been placed in A to pinpoint a few relevant structures. 1. Left first aortic arch. 2. Left second aortic arch. 3. Left third aortic arch. 4. Aortic sac. 5. Truncus arteriosus. 6. Left atrium. 7. Left dorsal aorta. 8. Left common cardinal vein. 9. Left anterior cardinal vein. 10. Left posterior cardinal vein. A pop-up window prompting the user for text input is shown corresponding to marker number 6.

rendered image in the viewing panel can be captured and saved to file.

Textual and graphical annotation

A primary objective in designing this digital tool was to provide the user with the ability to make annotations on the anatomical scene. This feature was deemed important to promote an active engagement of the user and to integrate the learner's input. To this end, two mechanisms – termed here *model annotation* and *marker annotation* – were devised (fig. 4). Model annotation refers to linking a text label to any model in the scene. Thus, double-clicking the right mouse button on any model within the scene will bring up a text box for textual user-input, which can be retrieved later on during the session or saved to file as needed. In addition, *markers* are bright green spheres that the user can place arbitrarily as graphical annotations anywhere on the surface on a model to highlight specific locations (Fig. 5). Also markers can be labelled with textual annotations (Fig. 5). The combination of graphical and textual annotations allows the user to enrich the scene with personal input.

Saving and loading annotations and scene configurations

All changes applied by the user to a scene, including modifications to the rendering properties of the models and graphical and textual annotations, can be saved to *set* files for further use. Moreover, by previously generating different *set* files for a particular scene, the user will be able to load a variety of rendering configurations as needed, even radically different ones. This resource maximizes the versatility of each scene, which can be customized to fit specific visualization needs or to include textual information in varying teaching and learning contexts (see below).

DISCUSSION

This paper is a proof of concept demonstration of how a simple software application for 3D visualization and annotation can become a useful tool in the educational setting.

Three-dimensional scenes in both the classroom and the anatomy lab

An obvious advantage of anatomical 3D models is the ability to demonstrate the spatial relationships between structures. During classroom presentations, some items such as the spatial structure of morphogenetic changes of the human embryo or the connecting pathways between certain brain regions are usually hard to represent

graphically on the blackboard or by projected illustrations, and often histological material or schematics diagrams are required for further demonstration. In these contexts, three-dimensional representation by using a digital tool such as the one reported on in this paper can represent a valuable adjunct to conventional media. According to specific demonstration needs, instructors can edit in different possible ways the rendering properties of the surface models comprising the scene, and save these changes to different *set* files so the desired scene appearances can be loaded directly from file as needed during classroom presentations. All necessary files (application files, Java runtime environment, 3D model files, and *set* files) can be brought to the classroom computer on a flash drive, since *Anatorama* can be executed directly on this device without installation.

The anatomy lab is also a learning context that can benefit from a computer application for 3D visualization (Campbell et al., 2001; Doubleday et al., 2011). Three-dimensional computer visualization can provide a virtual-dissection-like approach that can compare favourably to cadaver dissection when minute and intricate structures are dealt with. For example, investigators have proposed 3D visualization technologies as a viable adjunct to conventional media for the study of cranial nerves (Yeung et al., 2011), inner and middle ear (Nicholson et al., 2006; Venail et al., 2010), lymph nodes (Qatarneh et al., 2006), or a developing viscus (Abid et al., 2010). In addition, when time devoted to dissections is restricted and access to cadavers is limited or cost-prohibitive (American Association of Colleges of Nursing, 2003), computer exploration of virtual specimens represents an affordable and highly cost-effective educational resource.

Finally, the image capture feature in *Anatorama* can be used to generate still pictures of anatomical scenes that can serve specific demonstration needs. High quality anatomical illustrations are not inexpensive, and the generation of appropriate iconography poses a limitation to the production of learning materials in the academic setting. In this sense, a promising strategy to attain photo-realistic quality and to produce high-end anatomic illustrations by capturing rendered 3D scenes would be the addition of a texture mapping feature in future versions of this software.

Self-directed learning

The capacity to think and work independently is central to active learning methodologies in the new Bologna paradigm. Several features of *Anatorama* can be considered as supporting self-directed learning. Firstly, it enables the learner

not only to navigate the scene but also to actively manipulate the appearance of any anatomical model at her/his own pace. For example, the orderly removal of superficial anatomical structures to progressively expose deeply located ones is comparable to a simulated cadaver dissection experience. Interestingly, during the computer simulation the learner will be able to restore any removed model or to start over. The immersion experience can be further intensified by enabling the anaglyph view mode, which creates a stereoscopic effect by encoding each eye's image using filters of different (red and cyan) colours (fig. 3D). This approach has long been used in printed form in the context of anatomy teaching and learning (Cunningham, 1909; Basset, 1962; Prentice et al., 1977), and also more recently in digital media (Nogueira et al., 2008; Trelease, 1998; Nguyen and Wilson, 2009). Importantly, the learner here should be able to use the same digital models presented in the classroom or in the anatomy lab, as well as appropriate *set* files, for individual in-depth study. Secondly, the textual and graphical annotation features in *Anatorama* enable both the learner and the teacher to enrich the structural information with personal notes. Thus, *set* files can be generated to contain custom information for personal study or for one's records. Thirdly, the appropriate management of *set* files that storage annotation information poses new scenarios for information sharing among learners, as well as for collaborative work. For example, *set* files can be shared over the Internet and developed collaboratively. In addition, if *Anatorama* is devised as a learning tool for specific tasks or assignments, information annotated by the learner, saved to a *set* file and sent over to the instructor can be used for evaluation in the way of a learner portfolio. Finally, while this software application can be used without sequential format, i.e. with no specified beginning and end, three-dimensional exploration and annotation can be conceived as structured learning activities if more directive teaching styles are adopted, by providing supplementary learning materials or instructions for sequential exploration. *Anatorama* also can be effectively used in tutorials, as well as in e-learning or blended learning contexts (Pereira et al., 2007).

Limitations and future directions

A limitation of computer rendition of body structures as three-dimensional surface meshes is that these may appear stiff, textureless and unrealistic. For example, fibre orientation will be missing if a surface mesh representing a muscle is rendered in a uniform, synthetic colour. In addition, the textures of fasciae and intervening connective tissue can be difficult to reproduce realis-

tically.

Texture mapping, i.e. the addition of pixel information to the mesh surfaces, can overcome these limitations and provide surface meshes with photo-realistic quality and higher resemblance to biological tissue. However, this technique is rather demanding in computational terms and should thus be used wisely. Secondly, generating anatomical 3D surface meshes by segmentation requires specialized anatomic knowledge and may be a time-consuming task, which poses a limitation to a more generalized use of 3D visualization techniques in the teaching of human anatomy. Generation of high-quality anatomical surface models should be seen as a research contribution and regarded as an academic merit, much the same as other forms of scientific illustration such as didactic drawing, as long suggested by others (Krstic, 1993). Ideally, generated meshes should be peer-reviewed for anatomic accuracy and educational relevance, and made available to the anatomy teaching community as educational assets. A repository of contributed material would be best viewed as a community resource, where datasets, generated meshes, and even *set* files may be shared for open use by teachers and learners alike.

In future works, the convenience of including additional features such as texture mapping, volume rendering or planar viewing capabilities may be considered for specific learning contexts as needed. In addition, hierarchies that define relationships among body parts, e.g. *part of*, *tributary of*, *branch of*, etc., may be included in the organizational structure of the models. It is important to emphasise, nevertheless, that although this digital tool can be used in a variety of different ways as discussed above, its usefulness in the teaching of anatomy and embryology will need to be empirically evaluated and validated for specific curricular contents and learning contexts.

REFERENCES

- ABDULLA R, BLEW GA, HOLTERMAN MJ (2004) Cardiovascular embryology. *Pediatr Cardiol*, 25: 191-200.
- ABID B, HENTATI N, CHEVALLIER JM, GHORBEL A, DELMAS V, DOUARD R (2010) Traditional versus three-dimensional teaching of peritoneal embryogenesis: a comparative prospective study. *Surg Radiol Anat*, 32: 647-652.
- AMERICAN ASSOCIATION OF COLLEGES OF NURSING (2003) *Faculty shortages in baccalaureate and graduate nursing programs: scope of the problem and strategies for expanding the supply (White paper)*. AACN, Washington DC.
- AZIZ MA, MCKENZIE JC, WILSON JS, COWIE RJ,

- AYENI SA, DUNN BK (2002) The human cadaver in the age of biomedical informatics. *Anat Rec*, 269: 20-32.
- BASSETT D (1962) A Stereoscopic Atlas of Human Anatomy. Sawyer, Portland, Oregon.
- BOWEN LI, GU L, PENGFEI H (2007) Construction of a three dimensional anatomical brain atlas. *Proceedings of 21st International Congress and Exhibition of Computer Assisted Radiology and Surgery. CARS'07*, Berlin.
- BURGIELSKI Z, JANSEN T, VON RYMON-LIPINSKI B, HANSSSEN N, KEEVE E (2002) Julius-a software framework for computer-aided-surgery. *Biomed Tech (Berl)*, 47 Suppl 1 (Pt 1): 101-103.
- CAMPBELL B, ROSSE C, BRINKLEY JF (2001) The Virtual Anatomy Lab: a hands-on anatomy learning environment. *Stud Health Technol Inform*, 81: 85-87.
- CROSSINGHAM JL, JENKINSON J, WOOLRIDGE N, GALLINGER S, TAIT GA, MOULTON CA (2009) Interpreting three-dimensional structures from two-dimensional images: A web-based interactive 3D teaching model of surgical liver anatomy. *HPB (Oxford)*, 11: 523-528.
- CUNNINGHAM DJ (1909) Stereoscopic Studies of Anatomy. Imperial Pub. Co., New York.
- DALGARNO B, LEE MJW (2010) What are the learning affordances of 3-D virtual environments? *Br J Educ Technol*, 41: 10-32.
- DOUBLEDAY EG, O'LOUGHLIN VD, DOUBLEDAY AF (2011) The virtual anatomy laboratory: usability testing to improve an online learning resource for anatomy education. *Anat Sci Educ*, 4: 318-326.
- ESTEVEZ ME, LINDGREN KA, BERGETHON PR (2010) A novel three-dimensional tool for teaching human neuroanatomy. *Anat Sci Educ*, 3: 309-317.
- GANGATA H (2008) An innovative approach to supplement the teaching of the spatial gross anatomy relationships of muscles to undergraduates in health sciences. *Clin Anat*, 21: 339-347.
- GARCIA LG, PACHECO DA, DE SOUSA RL, SANTOS RS, BRUNE FHR (2012) EMBRIO – a 3D software for learning Embryology. *Int Proc Econ Dev Res*, 41: 73-78.
- GARG AX, NORMAN G, SPEROTABLE L (2001) How medical students learn spatial anatomy. *Lancet*, 357: 363-364.
- GUILLOT A, CHAMPELY S, BATIER C, THIRIET P, COLLET C (2007) Relationship between spatial abilities, mental rotation and functional anatomy learning. *Adv Health Sci Educ Theory Pract*, 12: 491-507.
- HENN J, LEMOLE M, FERREIRA M, GONZALEZ F, SCHORNAK M, PREUL M, SPETZLER R (2002) Interactive stereoscopic virtual reality: A new tool for neurosurgical education. *J Neurosurg*, 96: 144-149.
- HILBELINK A J (2009) A measure of the effectiveness of incorporating 3D human anatomy into an online undergraduate laboratory. *Br J Educ Technol*, 40: 664-672.
- HEYLINGS DJ (2002) Anatomy 1999–2000: the curriculum, who teaches it and how? *Med Educ*, 36: 702–710.
- HOYEK N, COLLET C, RASTELLO O, FARGIER P, THIRIET P, GUILLOT A (2009) Enhancement of mental rotation abilities and its effect on anatomy learning. *Teach Learn Med*, 21: 201-206.
- HUK T (2006) Who benefits from learning with 3D models? The case of spatial ability. *J Comp Assist Learn*, 22: 392-404.
- JAMES D, PURKAYASTHA S, PARASKEVAS P, SHAFIQ O, DARZI A, ATHANASIOU T (2004) Anatomy: the future teaching of undergraduates. *Hosp Med*, 65: 681-685.
- KAKUSHO K, MIZUTA S, MINEKURA Y, MINOH M, NAKATSU T, SHIOTA K (2001) Illustrating human development by computer graphics for education in Embryology. *Proceedings of the International Conference on Computers in Education*. IEEE Computer Society Washington, Washington DC, pp 412-415.
- KEEHNER M, TENDICK F, MENG MW, ANWAR HP, HEGARTY M, STOLLER ML, DUH QY (2004) Spatial ability, experience, and skill in laparoscopic surgery. *Am J Surgery*, 188: 71-75.
- KERWIN J, YANG Y, MERCHAN P, SARMA S, THOMPSON J, WANG X, SANDOVAL J, PUELLES L, BALDOCK R, LINDSAY S (2010) The HUDSEN Atlas: a three-dimensional (3D) spatial framework for studying gene expression in the developing human brain. *J Anat*, 217: 289-299.
- KRSTIC R (1993) A didactic drawing in morphological sciences is a form of scientific research. *An Anat*, 39: 161-164.
- MCLACHLAN JC, BLIGH J, BRADLEY P, SEARLE J (2004) Teaching anatomy without cadavers. *Med Educ*, 38: 418-424.
- MCLACHLAN JC, PATTEN D (2006) Anatomy teaching: ghosts of the past, present and future. *Med Educ*, 40: 243-253.
- MIZUTA S, KAKUSHO K, MINEKURA Y, MINOH M, NAKATSU T, SHIOTA K (2002) Construction and application of 3D model sequence to illustrate the development of human embryo. *Proc SPIE/ Medical Imaging*, 4681: 732-741.
- NGUYEN N, WILSON TD (2009) A head in virtual reality: Development of a dynamic head and neck model. *Anat Sci Educ*, 2: 294-301.
- NICHOLSON DT, CHALK C, FUNNELL WRJ, DANIEL SJ (2006) A randomized controlled study of a computer-generated three-dimensional model for teaching ear anatomy. *Med Educ*, 40: 1081-1087.
- NOGUEIRA JF JR, BARAÚNA FILHO I, HERMANN DR, GARCÍA STAMM R, SOLFERINI SILVA ML, CASSOL STAMM A (2008) Stereoscopic tridimensional images of the anatomy of the temporal bone: acquisition and demonstration. *Intl Arch Otorhinolaryngol* 12: 105-110.
- OLDER J (2004) Anatomy: a must for teaching the next generation. *Surgeon*, 2: 79-90.
- PARKER LM (2002) Anatomical dissection: Why are we cutting it out? Dissection in undergraduate teach-

- ing. *ANZ J Surg*, 72: 910-912.
- PALOMBI O, SHIN JW, WATSON C, PAXINOS G (2006) Neuroanatomical affiliation visualization-interface system. *Neuroinformatics*, 4: 299-317.
- PATTEN D (2007) What lies beneath: the use of three-dimensional projection in living anatomy teaching. *Clin Teach*, 4: 10-14.
- PEREIRA JA, PLEGUEZUELOS E, MERÍ A, MOLINAROS A, MOLINA-TOMÁS MC, MASDEU C (2007) Effectiveness of using blended learning strategies for teaching and learning human anatomy. *Med Educ*, 41: 189-195.
- PERRY J, KUEHN D, LANGLOIS R (2007) Teaching anatomy and physiology using computer-based, stereoscopic images. *J Coll Sci Teach*, 36: 18-23.
- PETERSSON H, SINKVIST D, WANG C, SMEDBY Ö (2009) Web-based interactive 3D visualization as a tool for improved anatomy learning. *Anat Sci Educ*, 2: 61-68.
- PRENTICE ED, METCALF WK, QUINN TH, SHARP JG, JENSEN RH, HOLYOKE EA (1977) Stereoscopic anatomy: evaluation of a new teaching system in human gross anatomy. *J Med Educ*, 52: 758-763.
- PRICE A, LEE H-S (2010) The effect of two-dimensional and stereoscopic presentation on middle school students' performance of spatial cognition tasks. *J Sci Educ Techn*, 19: 90-103.
- QATARNEH SM, KIRICUTA I-C, BRAHME A, TIEDE U, LIND BK (2006) Three-dimensional atlas of lymph node topography based on the visible human data set. *Anat Rec*, 289B: 98-111.
- RISUCCI DA (2002) Visual spatial perception and surgical competence. *Am J Surgery*, 184: 291-295.
- ROCHFORD K (1985) Spatial learning disabilities and underachievement among university anatomy students. *Med Educ*, 19: 13-26.
- ROSSET A, SPADOLA L, RATIB O (2004) OsiriX: an open-source software for navigating in multidimensional DICOM images. *J Digit Imaging*, 17: 205-216.
- SCHROEDER W, MARTIN K, LORENSEN B (1998) *The Visualization Toolkit An Object-Oriented Approach To 3D Graphics*, 2nd ed. Prentice-Hall, Old Tappan, NJ.
- SHAFFER K (2004) Teaching anatomy in the digital world. *N Engl J Med*, 351: 1279-1281.
- SHARPE J, AHLGREN U, PERRY P, HILL B, ROSS A, HECKSHER-SØRENSEN J, BALDOCK R, DAVIDSON D (2002) Optical projection tomography as a tool for 3D microscopy and gene expression studies. *Science*, 296: 541-545.
- SILEN C, WIRELL S, KVIST J, NYLANDER E, SMEDBY O (2008) Advanced 3D visualization in student-centred medical education. *Med Teach*, 30: e115-124.
- TEMKIN B, ACOSTA E, MALVANKAR A, VAIDYANATH S (2006) An interactive three-dimensional virtual body structures system for anatomical training over the internet. *Clin Anat*, 19: 267-274.
- TRELEASE RB (1998) The Virtual Anatomy Practical: a stereoscopic 3D interactive multimedia computer examination program. *Clin Anat*, 11: 89-94.
- VENAIL F, DEVEZE A, LALLEMANT B, GUEVARA N, MONDAIN M (2010) Enhancement of temporal bone anatomy learning with computer 3D rendered imaging softwares. *Med Teach*, 32: e282-e288.
- VERHOEVEN BH, VERWIJNEN GM, SCHERPBIER AJ, VAN DER VLEUTEN CP (2002) Growth of medical knowledge. *Med Educ*, 36: 711-717.
- WANZEL KR, HAMSTRA SJ, CAMINITI MF, ANASTAKIS DJ, GROBER ED, REZNICK RK (2003) Visual-spatial ability correlates with efficiency of hand motion and successful surgical performance. *Surgery*, 134: 750-757.
- YAMADA S, NAKASHIMA T, HIROSE A, YONEYAMA A, TAKEDA T, TAKAKUWA T (2012) Developmental Anatomy of the Human Embryo – 3D-Imaging and analytical techniques. In: Yamada S, Takakuwa T (ed), *The Human Embryo*, InTech. Available from: <http://www.intechopen.com/books/the-human-embryo/developmental-anatomy-of-the-human-embryo-3d-imaging-and-analytical-techniques> (accessed Nov 10, 2012).
- YAMADA S, UWABE C, NAKATSU-KOMATSU T, MINEKURA Y, IWAKURA M, MOTOKI T, NISHIMIYA K, IYAMA M, KAKUSHO K, MINOH M, MIZUTA S, MATSUDA T, MATSUDA Y, HAISHI T, KOSE K, FUJII S, SHIOTA K (2006) Graphic and movie illustrations of human prenatal development and their application to embryological education based on the human embryo specimens in the Kyoto collection. *Dev Dyn*, 235: 468-477.
- YEUNG JC, FUNG K, WILSON TD (2011) Development of a computer-assisted cranial nerve simulation from the Visible Human dataset. *Anat Sci Educ*, 4: 92-97.
- YUSHKEVICH PA, PIVEN J, HAZLETT HC, SMITH RG, HO S, GEE JC, GERIG G (2006) User-guided 3D active contour segmentation of anatomical structures: Significantly improved efficiency and reliability. *Neuroimage*, 31: 1116-1128.