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Web-based volume slicer for 3D electron-microscopy data from EMDB

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ABSTRACT

We describe the functionality and design of the Volume slicer – a web-based slice viewer for EMDB entries. This tool uniquely provides the facility to view slices from 3D EM reconstructions along the three orthogonal axes and to rapidly switch between them and navigate through the volume. We have employed multiple rounds of user-experience testing with members of the EM community to ensure that the interface is easy and intuitive to use and the information provided is relevant. The impetus to develop the Volume slicer has been calls from the EM community to provide web-based interactive visualisation of 2D slice data. This would be useful for quick initial checks of the quality of a reconstruction. Again in response to calls from the community, we plan to further develop the Volume slicer into a fully-fledged Volume browser that provides integrated visualisation of EMDB and PDB entries from the molecular to the cellular scale.

1. Introduction

Over the past decade cryo-electron microscopy and electron tomography have become increasingly important tools in the arsenal of structural biology. Traditionally, these techniques complemented the more established approaches of X-ray crystallography and Nuclear Magnetic Resonance (NMR) spectroscopy by allowing larger structures, pleomorphic structures and structures in the cellular context to be studied albeit at poorer resolutions but without the need for crystals or high concentrations. Recent technological advances such as the introduction of direct electron detectors have revolutionised the field and led to the *de novo* determination of large complexes at near-atomic resolution, further underpinning the importance of these techniques for structural biology (Bai et al., 2015).

The Electron Microscopy Data Bank (EMDB) archive (Tagari et al., 2002) was established at the European Bioinformatics Institute (EBI) in 2002 and is the authoritative source for 3DEM data. Against the backdrop of technological advances, EMDB has experienced rapid growth and now contains over 3400 structures derived from a range of 3DEM techniques including single-particle reconstruction, helical reconstruction, tomography and electron crystallography (http://pdbe.org/emdb). The data archived in EMDB finds many uses. 3D reconstructions can be viewed in conjunction with published results to further analyse or corroborate claims made by the authors. They may be used to boot-strap single-particle image processing, compared with similar structures to examine structural changes, and fitted into reconstructions of larger structures such as cellular tomograms to further aid in their interpretation. They can be used for teaching and training purposes and by methods developers to refine, test or implement new algorithms.

The Protein Data Bank in Europe (PDBe; (Velankar et al., 2016)) currently provides a wide range of web-based services for searching (EMSearch – http://pdbe.org/emsearch, EMStats – http://pdbe.org/emstats; (Gutmanas et al., 2014)), and validating and visualising EMDB data (visual analysis pages, volume viewer, slice viewer; (Gutmanas et al., 2014; Lagerstedt et al., 2013)). Key to PDBe's mission of "*Bringing structure to biology*" is the development of web-based resources that make it easier for expert and non-expert users alike to access and exploit structural data in EMDB, and to integrate it with data from other structural archives, such as the PDB, and with other bioinformatics resources (Gutmanas et al., 2013). PDBe engages regularly with relevant user communities to

Abbreviations: CSS, Cascading Style Sheets; DOM, Document Object Model; EMDB, Electron Microscopy Data Bank; EBI, European Bioinformatics Institute; NMR, Nuclear Magnetic Resonance; OME, Open Microscopy Environment; OMERO, OME Remote Objects; PDB, Protein Data Bank; PDBe, Protein Data Bank in Europe; SVG, Scaled Vector Graphics; 3DEM, Three-Dimensional Electron Microscopy.

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understand their needs and requirements with regards to archiving and resources for structural data. Notably, PDBe has organised several expert workshops in recent years to focus on specific issues including "*Data-Management Challenges in 3D Electron Microscopy*" (Patwardhan et al., 2012) and "*A 3D Cellular Context for the Macromolecular World*" (Patwardhan et al., 2014). These community interactions have identified a need for improved interactive visualisation of 2D slice images from 3D maps. Viewing individual slices provides a very simple means for users to assess the quality of maps and details of the processing such as the use of masking. Hitherto the EMDB slice viewer was the only web-based tool available for this purpose but it was restricted in that it was only available for tomograms in EMDB (which represent a minority of the entries) and only allowed viewing of slices in one direction (Lagerstedt et al., 2013). We have now developed a "Volume slicer" web service, which is available for all EMDB entries and allows for interactive visualisation of 2D slices in three orthogonal directions. In this paper we describe the design and implementation of, and future prospects for the Volume slicer.

2. User's perspective

The Volume slicer is available for all EMDB entries from URLs of the form http://pdbe.org/EMD-####/3dslice (where EMD-#### is an EMDB accession code, e.g., EMD-2363), Fig. 1a. The Volume slicer can be used to examine the definition of structures in detail providing, for instance, more information on artefacts and resolution variation within a structure, Fig. 1b. The Volume slicer consists of a main viewing panel showing a 2D slice from the 3D map, a 3D navigation cube and thumbnail images for orientation and navigation, *min* and *max* density range sliders with a density histogram, and summary information about the entry. The image in the main viewing panel can be zoomed by using the slider to the right of the image; left clicking on a point will re-centre the view on that point if possible given the chosen zoom level. The 3D cube shows the location of the slice being examined in the main viewing panel as a rectangle. The three sliders or input boxes can be used to move the rectangle and will update the slice shown in the main viewing panel. Selecting one of the three radio buttons in the thumbnail panel changes the active viewing direction. The area shown in the main viewing panel is highlighted in orange in the thumbnail panels; the area can be changed with a left-mouse click on the thumbnail images.

3. Design overview

Web-based visualisation resources for EMDB provide easy, quick and convenient views of the data without requiring the EM

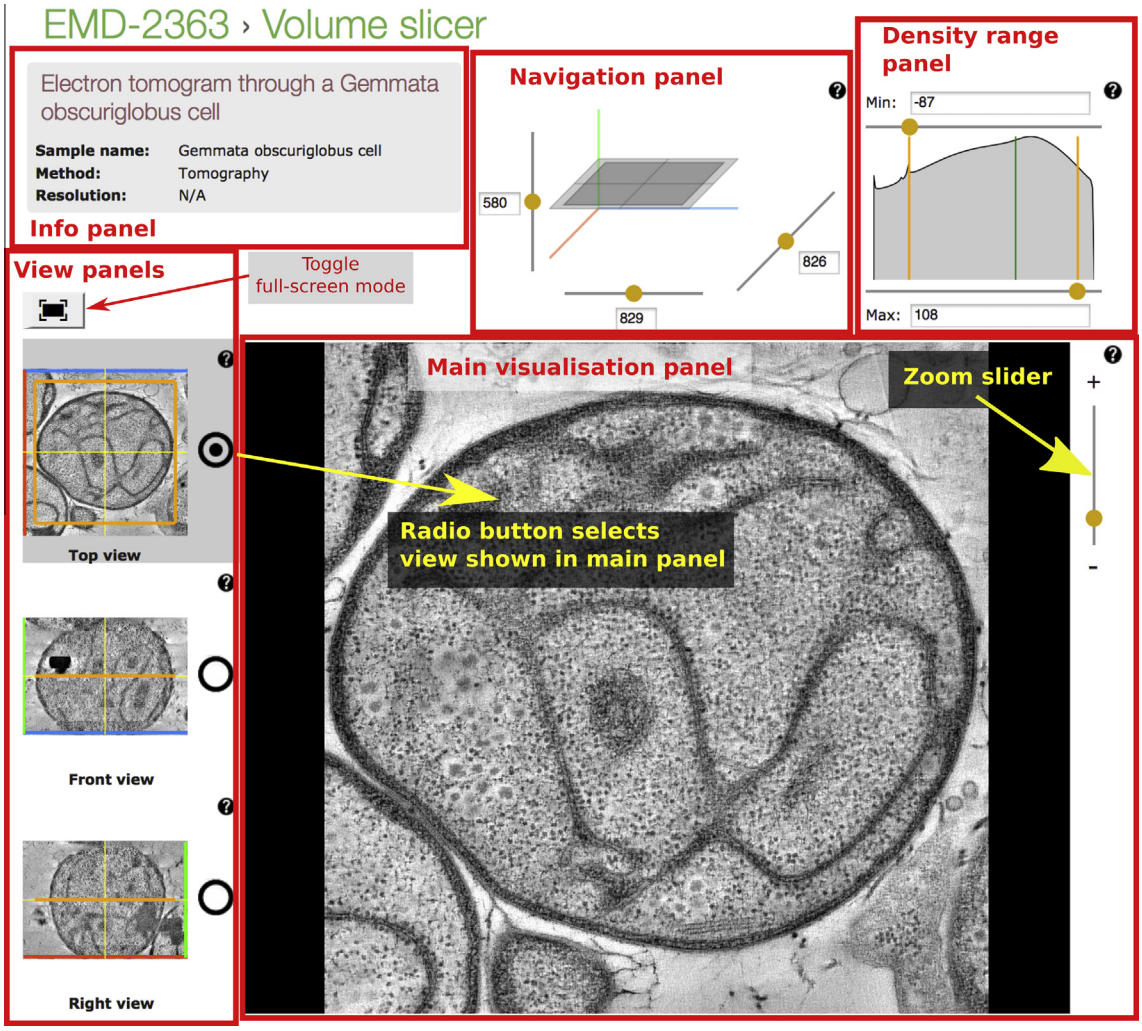

Fig. 1a. The Volume slicer page for EMD-2363 (pdbe.org/emd-2363/3dslice; (Santarella-Mellwig et al., 2013)). The navigation panel and view panels can be used to change the slice shown in the main visualisation panel. The three view panels show orthogonal slices from the 3D volume centred at the origin of the plane shown in the navigation panel. The radio buttons can be used to change the active view orientation shown in the main panel. Full-screen mode can be toggled using the button above the view panels. The density-range panel shows the density histogram for the volume and the *min* and *max* sliders allow the mapping to the display grey scale range to be adjusted.