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Map quest

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Structure determination by electron microscopy (EM) has become an essential tool in structural biology. The power of this approach comes from its ability to obtain three-dimensional structural information for macromolecular complexes as well as virus particles, the cell and beyond, whether they are static or dynamic entities. As such, it provides views of the changing shapes of biological molecules or systems as they function. The resolution of EM structures ranges from tens of ångstroms to near-atomic resolution. However, even the electron density maps of low- to medium-resolution EM structures can provide a wealth of information when high-resolution structures determined by X-ray crystallography or NMR are fitted into them. Thus, the deposition of three-dimensional EM maps into an independently curated, publicly -accessible database would complement and add to the value of the existing database of high-resolution structures.

The EM data base (EMDB) at the European Bioinformatics Institute (EBI) was established to do just that. EMDB accepts three-dimensional EM maps, issues accession codes and annotates the data. Currently, there are close to 200 entries in the database. Users can search the database through a simple interface, view a snapshot of the structure and download the data, if they are released by the authors. EBI recognizes the importance of preserving three-dimensional EM maps and has made a long-term commitment to the operation of this database.

With a public repository in place, approximately three years ago the editors of *Nature Structural Biology* looked into whether the time was right to establish a policy requiring deposition of three-dimensional EM maps as a condition of publication. We contacted several researchers in the community for feedback. The consensus at the time was that deposition would be a good step, but there were a number of issues that needed to be ironed out.

First, there were some technical issues. Different groups had been developing software programs for analyzing EM images and reconstructing structures. If the parameters used by the programs differed, validating the deposited data would be difficult and a common set of data standards would be essential to address this problem. Second, to make the database a useful resource for the broader scientific community, easily accessible viewing programs would be necessary. A third issue raised at the time was that EMDB only hosts the density maps, whereas the coordinates that are generated by fitting and adjusting high-resolution structures into the three-dimensional maps are deposited into the Protein Data Bank (PDB) managed by the Worldwide PDB (http://www.wwpdb.org), a partnership of structural data centers in Europe, Japan and the US (see the correspondence published in the October 2003 issue of *Nature Structural Biology*). A mechanism is needed to link these intimately related entries in the two separate databases. Finally, there was a general concern about how to handle data release. The availability of the three-dimensional EM map of a macromolecular complex can potentially help others (read: competitors) solve the structure of the same complex, perhaps at a better resolution. Thus, many researchers wanted to put a hold on their data for a while so that they could enjoy the spoils of their hard work for at least some time without having to look over their shoulders. This followed the precedent set for high-resolution structural data, which while deposited in the PDB could be held without being released for up to one year. Because of these issues, we decided to encourage deposition, rather than making mandatory deposition a condition of publication.

We are now revisiting these issues and find that progress has been made. For example, through a series of workshops in Europe and the US, a set of common definitions for three-dimensional EM has been established. There are many software packages that can view the EM maps, as they are in standard X-ray electron density map format. In particular, for those who want to do more than just view EM maps, such as fitting structures into the map, a powerful program called Chimera (http://www.cgl.ucsf.edu/chimera), developed at the University of California, San Francisco, is free for noncommercial use. For more casual users, EBI is currently developing a desktop Java-based viewer, which parallels several applications that are used to view high-resolution structures in the PDB, such as FirstGlance in Jmol (see Editorial in the February 2006 issue of *Nature Structural & Molecular Biology*). In addition, there is an effort to obtain funding to accelerate the building of the computational infrastructure to make it possible to deposit EM maps and fitted coordinates (if available) to both EMDB and the PDB in a one-stop shop within the framework of the Worldwide PDB.

Given that a functional permanent EM database is available, that there is willingness on the part of the community to participate and that the previous concerns of the community are being addressed, it is curious that many of the recent EM structures, including some published in *Nature Structural & Molecular Biology*, are absent from the database. We are again considering requiring the deposition of three-dimensional EM maps as a condition of publication. But before taking such a step, we need to hear from you. To make this quick, easy and as painless as possible, we have set up an online survey (http://www.nature.com/nsmb/em_survey). We hope to hear from many of you, and we'll get back to you later in the year with the results. ■