Molluscs transport oxygen with hemocyanin, a supermolecule composed of homologous functional units (FUs). Molluscan hemocyanin is a decamer or multidecamer of approximately 330–450 kDa, which results in a molecular mass of larger than 3.3 MDa. Therefore, molluscan hemocyanin is one of the largest known proteins. We have determined the crystal structure of 3.8 MDa molluscan hemocyanin at 3.0 Å resolution (Fig. 1). This is the first atomic-resolution structure of molluscan hemocyanin, which is superior to previously reported cryo-electron microscopy (EM) structures with regards to accuracy of the structure and the discussions (Fig. 2). The structure which we determined allows conclusive elucidation of the hierarchical assembly manner of 80 FUs with D5 symmetry, which explains the functional relevance of carbohydrates to the decameric assembly. Furthermore, the coordination geometry around the oxygen-binding site of all FUs was revealed.

Fig. 1 Crystal structure of squid hemocyanin

Fig. 2 Electron density surrounding the oxygen binding site
blue: 2Fo-Fc map, red: anomalous difference Fourier map of Cu