(chaperonin containing TCP-1, or TRiC) is a 1-MDa oligomer that is built by two rings comprising eight different 60-kDa subunits. This chaperonin regulates the folding of important proteins including actin, α-tubulin and β-tubulin. We used an electron density map at 5.5 Å resolution to reconstruct CCT, which showed a substrate in the inner cavities of both rings. Here we present the crystal structure of the open conformation of this nanomachine in complex with tubulin, providing information about the mechanism by which it aids tubulin folding. The structure showed that the substrate interacts with loops in the apical and equatorial domains of CCT. The organization of the ATP-binding pockets suggests that the substrate is stretched inside the cavity. Our data provide the basis for understanding the function of this chaperonin.

I.G. Muñoz, H. Yébenes, M. Zhou, P. Mesa, M. Serna, A.Y. Park, E. Bragado-Nilsson, A. Beloso, G. de Cárcer, M. Malumbres, C.V. Robinson, J.M. Valpuesta, and G. Montoya. *Nature Structural & Molecular Biology* **2011**, *18*, 14-9.

Keywords: macromolecular complex, chaperonin, tubulin

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Pattern recognition for modeling in very low resolution density maps

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We present a novel method for the interpretation of low-resolution maps, which does not rely on any map segmentation or knowledge about the position of the individual structural fragments. The structures of the fragments should be known in advance.

3D structural studies of macromolecular complexes often yield data to only very low resolution (cryo EM/X-ray Crystallography). The interpretation of such data usually starts with the segmentation of the map (e.g., with Watershed algorithm), which does not always give satisfactory results (over-segmentation/incorrect structural borders). Overall, docking of known structures currently requires a lot of human expert knowledge and interaction so that an automated procedure is a highly desirable.

We use 3rd order moment invariants, chirality, skewness and kurtosis of the density to identify regions in density maps of macromolecular complexes that match the corresponding regions in the known structures of the constituting fragments. Finally the structures of the fragments are placed into the map. The used features give a concise but comprehensive description of 3D objects in only a few numerical values, providing convenient means for fast search through a large amount of 3D data. The method has been tested on calculated structure factors for large macromolecular complexes (genotoxin and GroEL) with 10 or 15 Å high-resolution limit. The individual subunits were fitted in the low-resolution density maps with an average r.m.s.d. on C α atoms of 2 Å. New results obtained for interpretation of EM data will also be presented.

Since the last decade there have been many attempts to develop reliable 3D map segmentation algorithms with varying success, in order to reduce the complexity of the challenging task of low-resolution density map interpretation. The method presented here does not require a map segmentation step and provides accurate results without human interaction in reasonable time, due to the use of sophisticated pattern recognition algorithms. Implementation of real-space refinement procedures is expected to improve the results even further.

Keywords: low_resolution, macromolecular_modelling, novel_ algorithms

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Structure and self-assembly of amyloid peptide-based hydrogelators

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There has been great interest recently in the fibrillisation of peptides, especially the amyloid beta (A β) peptide which is involved in diseases such as Alzheimer's [1]. We have recently commenced a study of the self-assembly of peptides and peptide copolymers based on a fragment KLVFF, corresponding to the core region of A β (16-20). A β self-assembly is driven by inter-molecular β -sheet self-assembly into fibrils. A primary objective of our work is to identify fragments that bind to amyloid fibrils and disrupt fibrillisation (aggregation inhibitors based on self-recognition elements [2]). We are also interested in peptides and peptide/polymer conjugates as hydro- and organo-gelators. I will present results on the self-assembly of peptides such as AAKLVFF [3], [4] and PEGylated diblock copolymers of these peptides [5], [6]. Self-assembly, using techniques including SAXS, SANS and fibre diffraction, is studied in water for hydrophilic peptides and peptide copolymers and in organic solvents for hydrophobic peptides. Gelation at higher concentration is also discussed. Peptide AAKLVFF is the subject of detailed studies (FTIR, CD, NMR, molecular dynamics simulations) of its self-assembly into nanotubes in methanol and twisted fibrils in water [4], [7]. Very recently we have discovered a novel twisted ribbon fibril structure by adding β_2-amino acids to the N terminus of KLVFF to give β A β AKLVFF [8], and the fascinating structural properties of this will be discussed. We have recently examined the binding of this peptide to the amyloid β peptide A β (1-42), as part of a project to develop aggregation inhibitors, which may be useful in the treatment of amyloid disease [9]. In addition, we have found that a PEGylated version of this peptide forms spherical micelles in aqueous solution, pointing to the ability to modulate the self-assembled structure by introduction of amphiphilicity [10]. The enzymatic cleavage (using α-chymotrypsin) of the peptide from the PEG3000 chain (between phenylalanine residues) leads to release of unassociated peptide monomers [10]. This nanocontainer delivery and release system could be useful in therapeutic applications. As another example, we have investigated the self-assembly of a novel peptide amphiphile (PA) Matrixyl, with collagen-stimulating properties [11]. It forms self-assembled tape-like structures in aqueous solution. These can be dispersed into amyloid-like fibrils by use of the anionic surfactant SDS.

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Crystalline vs Amorphous molecular gels: two distinct classes of self-assembled structures with unique biological connections

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