(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

MS.02.5

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 Cα 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

MS.03.1

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 (Aβ) 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 Aβ (16-20). Aβ 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 βAβAKLVFF [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 Aβ (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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Keywords: peptide, gel, SAXS

MS.03.2

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

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Molecular gels formed by the self-assembly of small molecules in organic or aqueous solvents have attracted widespread attention. It is known that a common factor in all gels is the presence of a network formed by fibrous assemblies. This talk will attempt to classify molecular gels into two distinct classes based on the nature of these assemblies. In many gels, the fibers have a crystalline packing, and often the crystal structure of the fibers (in a xerogel) is identical to that of the molecules in their solid crystal. It is argued that these crystalline gels are analogous to many fibrous structures found in biology, notably the amyloid plaques that have been implicated in neurodegenerative diseases. In other gels, the fibers are completely amorphous, and in these cases, the fibers are analogous to assemblies of amphiphilic molecules such as micelles. It is further argued that these amorphous fibers are comparable to filamentous structures found in the cytoskeleton of every biological cell. Crystalline and amorphous fibers (and their gels) also show distinct properties in terms of both their structural responses (e.g., via scattering techniques) as well as in their mechanical and rheological properties.

S.R. Raghavan, *Langmuir*, **2009**, *25*, 8382.

MS.03.3

Dynamic covalent molecular gelators: in control of soft matter properties by dynamic covalent chemistry

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The self-assembly of small molecules, polymers, proteins, nanoparticles and colloids under thermodynamic equilibrium conditions has been a powerful approach for the construction of a variety of structures of nano- to micrometer dimensions, like vesicles, capsules, and nanotubules. Despite these advances, the permanent nature of these synthetic self-assembled structures does not compare well to the complex spatiotemporally confined self-assembly processes seen in natural systems, which for instance allow the dynamic compartmentalization of incompatible processes, responsiveness, and self-healing. It remains a challenge to develop systems in which equilibrium and kinetics of self-assembly can be independently controlled.

In our research we focus on molecular approaches which allow independent control over interaction strength and dynamics of the self-assembling building blocks [1], [2]: (i) the development of dynamic covalent gelators, leading to new supramolecular assemblies with unprecedented control of the dynamic properties, (ii) dynamic and reversible conjugated polymers, allowing easy processing in water, and (iii) dissipative self-assembly driven by a chemical fuel [3]. I will discuss the background of our approaches together with recent results, and will suggest how dynamic self-assembling systems may lead to the next generation responsive, nanostructured or self-healing materials.

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MS.03.4

The relationship between crystallisation and gel formation in low molecular weight gelators

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Crystallisation and gel formation of low molecular weight gelators (LMWGs) are inherently related as can be witnessed by many researchers the world over [1]. We shall present results on crystallisation within LMWGs and the conversion of LWMG gels into crystals. These results will help to rationalise the relationship between gel and crystal formation.

The use of the gel matrix to control crystallisation is a well known procedure. However, LMWGs have been scarcely looked at as the gel former in this crystallisation technique. We therefore aimed, and now shall present, the control of pharmaceutical polymorphism and morphology by testing a series of LWMGs [2]. Due to their reversible physical nature, in our case using anion tuning of gelation [3,4], LMWG crystallisation may represent an exciting new addition to the crystal growth tool kit.

Many researchers have noted that many LMWGs tend to convert from a gel to a crystalline material [5]. This process is often used to help determine the structure of the gel forming solid. We shall also present our take on this "phase" change and the possible applications of this phenomenon in the context of controlling crystallisation and the lack of crystallisation leading to stable gels. By influencing assembly and disassembly of the gel components, which is related to the underlying structure, the stability in relation to the gel to crystal transformation can be controlled. As a result of this knowledge, we are able to show post-assembly modification of a LMWG at the interface of the solid and liquid phases.

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MS.03.5

New insights into the polymerization and structural mechanisms of the polydiacetylene DCHD: an X-ray/MEM study

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