NATURE|Vol 466|26 August 2010

that the particle could be found there.

The second effect, called electron correlation in the quantum-chemical literature[7], describes the fascinating way in which electrons and holes tend to coordinate their motions to minimize repulsions. For example, two electrons might move in such a fashion that they avoid crossing paths. The complexity of this problem scales steeply with the number of particles involved. Although current investigations into many-body effects provide an important first step to understanding how groups of carriers interact collectively, they cannot quantify the average Coulomb repulsions and attractions relative to how these are modified by correlations in multiparticle motions.

There are many reasons to investigate how electrons (and holes) interact[8]. For instance, chemical structure–property relationships that govern the nonlinear response of organic molecules to light depend on the energy of multiexciton states relative to singly excited states[9]. The factors dictating electron–hole binding in organic solar cells are also under intense investigation now. The challenge in this area is that electrons and holes in organic materials interact much more strongly than those in semiconductors such as GaAs or silicon because of the low dielectric constant of organic materials. Dissociating the carriers efficiently to produce electricity is therefore a much harder task in organic solar cells than in conventional silicon ones.

Predicting chemical reactivity is another salient example. Mean-field models in chemistry — that is, theories based on molecular-orbital energies, symmetries and shapes — have been enormously successful in predicting electronic structure, explaining reactivity and qualitatively describing spectroscopy. To a significant extent, for example, our understanding of chemical reactivity is guided by Pauling's electronegativity scale; electrons move from electron-rich to electron-poor regions of reactants. However, the correlated motions of electrons in molecules are significant. Can we use this correlated response of electrons to promote efficient, concerted chemical change? Elucidating these kinds of quantum-mechanical details in condensed-matter physics would be transformative and have far-reaching consequences. ■

Gregory D. Scholes is in the Department of Chemistry and the Center for Quantum Information and Quantum Control, University of Toronto, Toronto, Ontario M5S 3H6, Canada.
e-mail: gscholes@chem.utoronto.ca

1. Koch, S. W., Kira, M., Khitrova, G. & Gibbs, H. M. *Nature Mater.* **5,** 523–531 (2006).
2. Turner, D. B. & Nelson, K. A. *Nature* **466,** 1089–1092 (2010).
3. Axt, V. M. & Kuhn, T. *Rep. Prog. Phys.* **67,** 433–512 (2004).
4. Chemla, D. S. & Shah, J. *Nature* **411,** 549–557 (2001).
5. Li, X., Zhang, T., Borca, C. N. & Cundiff, S. T. *Phys. Rev. Lett.* **96,** 057406 (2006).
6. Karaiskaj, D. *et al. Phys. Rev. Lett.* **104,** 117401 (2010).
7. Wilson, S. *Electron Correlation in Molecules* (Oxford Univ. Press, 1984).
8. Kim, J., Mukamel, S. & Scholes, G. D. *Acc. Chem. Res.* **42,** 1375–1384 (2009).
9. Albota, M. *et al. Science* **281,** 1653–1656 (1998).

STRUCTURAL BIOLOGY

Conservation in vesicle coats

Stephen C. Harrison and Tomas Kirchhausen

Coat proteins of vesicles involved in intracellular membrane trafficking have closely related molecular architectures. The structure of COPI extends known similarities, and strengthens the case for a common evolutionary origin.

Vesicles that transport cargo between intracellular compartments bud from the membrane of one compartment and fuse with the membrane of its target compartment. Vesiculation requires the introduction of local curvature into a lipid bilayer, typically by assembly of a closed protein shell — the coat — linked specifically to membrane-anchored proteins. Previous work has revealed some noteworthy similarities among coat proteins from different routes for membrane traffic. Reporting in *Cell*, Lee and Goldberg[1] now describe the structures of components of coat-protein I (COPI)-coated vesicles. Their results clarify the characteristics required of a protein assembly that vesiculates membranes.

Three routes for membrane traffic, conserved in their molecular components from yeast to human, are of particular physiological interest. Clathrin-coated vesicles transport cargo from the cell membrane to endosomes, and between endosomes and the trans-Golgi network[2]. COPII-coated vesicles export newly synthesized proteins from the endoplasmic reticulum[3]. COPI-coated vesicles carry retrograde cargo between compartments of the Golgi apparatus[4]. The structures and assembly properties of clathrin[5] and COPII[6] components have revealed some noteworthy similarities between the two and suggested common evolutionary origins. Lee and Goldberg's data extend the pattern of similarities to COPI.

Clathrin is a trimer, with three molecular 'legs' radiating from a compact hub in a configuration known as a triskelion (Fig. 1a). The tip of each leg consists of the amino-terminal domain of the clathrin polypeptide chain, together with a β-propeller fold consisting of 'WD40' repeats. The legs themselves are α-helical zigzags, known as α-solenoids because of the (irregular) superhelical packing of their α-helices. Repeats of this kind generate stiff but still-compliant structures, which allow the formation of large-scale bends from small, energetically negligible, local perturbations in successive helix–helix contacts.

Clathrin triskelions assemble into open lattices, in which each leg extends around three lattice edges (Fig. 1b). Gentle bending of the legs allows the generation, from uniform components that make essentially identical local contacts, of lattices with a triskelion hub at each vertex but with a considerable range of diameters. The amino-terminal domains

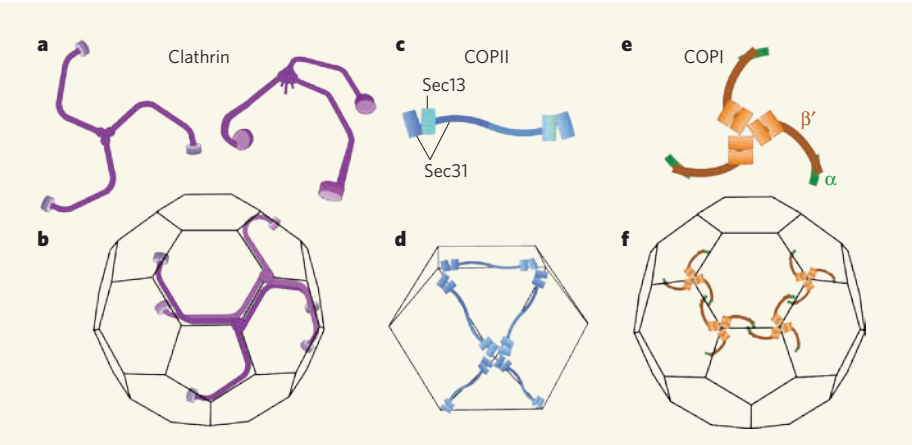

Figure 1 | Schematic representation of coat proteins and their assemblies. The basic structural elements of the assembly units of clathrin, COPII and COPI are α-solenoids (thick, curving lines) and β-propellers (cylinders). **a**, Two views of a clathrin triskelion. The N-terminal, β-propeller domains are at the tips of the legs. **b**, Packing of triskelions in an icosahedral clathrin coat, one of many lattices formed by clathrin[5]. There is a triskelion at each vertex, but only two are shown. **c**, The dimeric Sec31/Sec13 complex forms the coat of COPII vesicles[6]. The N-terminal, β-propeller domain of Sec31 is at the tip of the rod-like complex. A C-terminal segment of Sec31 is not present in the structure shown. **d**, Packing of Sec31/Sec13 in a COPII cuboctahedral lattice. The Sec31 β-propellers pack around the four-coordinated vertices[6,7]. **e**, Lee and Goldberg[1] report the crystal structure of the COPI assembly unit, a complex of the N-terminal half of the β′-chain and a central segment of the α-chain. **f**, The authors propose this model for the lattice of a COPI coat. Although the COPI triskelion is present in their crystal structure, the lattice symmetry and packing of triskelions within the lattice are speculative. The lattices are shown roughly to scale; the outer diameter of the clathrin coat in **b** is about 90 nm.

project inwards to contact membrane-associated adaptor proteins, which in turn recruit the cargo proteins.

COPII is a set of four proteins organized as two heterodimers: the Sec31/Sec13 pair generates the lattice of a coat; and the Sec23/Sec24 dimer is the cargo adaptor. Sec13 is a WD40 β-propeller. Sec31 also has an amino-terminal β-propeller, followed by an α-solenoid, rather like clathrin. Unlike clathrin, however, the β-propellers of these proteins form the vertices. Previous work[6,7] has shown how the assembly unit of COPII, composed mainly of Sec31 plus Sec13, can generate a set of symmetrical lattices in which four edges converge on a two-fold symmetrical vertex (Fig. 1c,d). Variability in the curvature of the α-solenoid elements can allow for variable diameters of the COPII coat, to accommodate cargoes of various sizes. The carboxy-terminal half of Sec31, which recruits Sec23/Sec24, projects flexibly inward, towards the membrane.

COPI is a complex of seven proteins: α-, β-, β′-, γ-, δ-, ε- and ζ-COP. Of these, three — α-, β′- and ε-COP — make up a stable, shell-forming heterotrimer, and the remaining four form a complex similar to heterotetrameric clathrin adaptors. Lee and Goldberg[1] have determined crystal structures of an αβ′-subcomplex; it consists of most of the β′-chain (two tandem WD40 β-propellers followed by an α-solenoid) and a central fragment of the α-chain (a further α-solenoidal segment). This basic unit makes a triskelion-like trimer, with the dual β-propellers of β′-COP at its centre and the overlapping, antiparallel α-solenoids of the α- and β′-chains radiating outwards (Fig. 1e). The amino-terminal part of α-COP, which is missing from the structure, includes a further predicted β-propeller; a continuation of the legs, therefore, will place such a domain at their tips, just as in clathrin.

The authors (and another team[8]) also report the structure of the carboxy-terminal part of α-COP in complex with ε-COP: the two polypeptide chains form an intertwined, α-solenoid handshake. This subcomplex is linked to the αβ′-subcomplex by a flexible α-chain segment, and a plausible suggestion is that it projects inwards from the αβ′-lattice to recruit the βγδζ-adaptor complex. COPI vesicles seen by electron microscopy of thin-sectioned cells seem to be relatively uniform in diameter[9], so the range of lattice diameters to which the COPI αβ′-triskelions must adapt may be relatively small. Lee and Goldberg propose a model for such a lattice, with an αβ′-triskelion at each vertex and with postulated two-fold contacts between such triskelions at the middle of each edge (Fig. 1f). Whether this model is correct can be verified by analysis of isolated or reconstituted COPI coats by electron cryomicroscopy or tomography.

Lee and Goldberg's results show that clathrin, COPI and COPII have certain architectural principles in common; these include the structural motifs that contribute to the shell and the characteristics of the linkage between the coat and the membrane. The conservation of α-solenoid and β-propeller substructures between these three coat proteins is probably also a sign of their common evolutionary origin. The combination seems unlikely to be coincidental, even though the roles of the β-propeller components vary among the different coat proteins. A reason for the evolutionary persistence of the α-solenoid could be its suitability for creating lattices of variable diameter. A clearer view of potential missing links may be necessary to establish a common origin with confidence.

The same α-solenoid and β-propeller substructures (including Sec13 itself) make up a large part of another membrane-curving assembly (the scaffold of the nuclear pore[10]), which may also have been derived from the common vesicle-coat precursor. The nuclear pore has a fixed geometry, however, and the α-solenoids of nuclear porin proteins curve back on themselves to form a more rigid structure than the completely extended legs of a clathrin triskelion.

The flexible tethers that link the COP coats and clathrin to adaptor components make minimal demands on the organization of the vesicle and thus allow for a wide selection of protein and lipid cargo. The relatively open lattices of all three types of coat allow access to the underlying membrane and accommodate variable projections from its cytoplasmic surface. The clathrin lattice is so open that it does not constrict the 'neck' of the budding vesicle tightly enough to drive fission; it recruits a large protein called dynamin, which has GTPase-enzyme activity, to finish the job[11].

There is one further, noteworthy, common principle of vesicle-coat biochemistry. A reversible assembly–disassembly cycle that allows reuse of the coat components requires the input of free energy. COPI, COPII and clathrin coats meet this requirement by harnessing hydrolysis of the nucleotides GTP and ATP. Assembly and release of COPI and COPII are linked to the GTP-hydrolysis cycle of a small GTPase enzyme — Arf1 in the case of COPI[12] and Sar1 in the case of COPII[13]. COPI is itself a crucial component of the Arf-GTPase activating complex[14]. Clathrin recruits the Hsc70 ATPase, which dissociates the coat after dynamin has pinched off the internal vesicle[15]. The unified picture of carrier-vesicle properties that derives both from these parallels and from the recent structural studies of COPI components[1] enhances the likelihood that analysis of one transport system will inform characterization of the others. ■

Stephen C. Harrison is in the Department of Biological Chemistry and Molecular Pharmacology and the Howard Hughes Medical Institute, and Tomas Kirchhausen is at the Immune Disease Institute and the Department of Cell Biology, Harvard Medical School, Boston, Massachusetts 02115, USA.
e-mail: harrison@crystal.harvard.edu

1. Lee, C. & Goldberg, J. *Cell* **142,** 123–132 (2010).
2. Goldstein, J. L., Anderson, R. G. W. & Brown, M. S. *Nature* **279,** 679–685 (1979).
3. Barlowe, C. *et al. Cell* **77,** 895–907 (1994).
4. Waters, M. G., Serafini, T. & Rothman, J. E. *Nature* **349,** 248–251 (1991).
5. Fotin, A. *et al. Nature* **432,** 573–579 (2004).
6. Fath, S., Mancias, J. D., Bi, X. & Goldberg, J. *Cell* **129,** 1325–1336 (2007).
7. Stagg, S. M. *et al. Cell* **134,** 474–484 (2008).
8. Hsia, K.-C. & Hoelz, A. *Proc. Natl Acad. Sci. USA* **107,** 11271–11276 (2010).
9. Orci, L., Glick, B. S. & Rothman, J. E. *Cell* **46,** 171–184 (1986).
10. Brohawn, S. G., Leksa, N. C., Spear, E. D., Rajashankar, K. R. & Schwartz, T. U. *Science* **322,** 1369–1373 (2008).
11. van der Bliek, A. M. & Meyerowitz, E. M. *Nature* **351,** 411–414 (1991).
12. Serafini, T. *et al. Cell* **67,** 239–253 (1981).
13. Matsuoka, K. *et al. Cell* **93,** 263–275 (1998).
14. Goldberg, J. *Cell* **100,** 671–679 (2000).
15. Chappell, T. G. *et al. Cell* **45,** 3–13 (1986).

ASTROPHYSICS

Making black holes from scratch

Marta Volonteri

The means by which supermassive black holes form and grow have remained largely unclear. Numerical simulations show that the collision of massive galaxies can naturally lead to the creation of these objects.

Black holes are objects in which the pull of gravity is so strong that nothing — not even light — can escape. However, they are far from being 'invisible': they can be detected through the effect they have on their surroundings. Stellar-mass black holes have long been known to exist and to be the evolutionary end point of massive stars. But we now have evidence of another class of black hole, termed supermassive black holes (SMBHs). These have masses of millions, or even billions, of solar masses, and inhabit the centres of galaxies. A black hole of four million solar masses is thought to sit at the centre of the Milky Way. Stars in the Galactic Centre move 'too fast' to be explained solely by the gravitational potential generated by the Galaxy's luminous matter: a massive dark object must be lurking in the depths of the Galaxy, masterminding the movement of its puppet stars. Although the existence of SMBHs can be inferred in nearby and distant galaxies, the way in which they form is still largely mysterious.