ed with movement and intensity of use⁸.

One way of proceeding is to measure the underlying structure of movement which such spaces imply and use these 'movements' to condition the environmental baseline. For example, Hillier and Hanson^{9,10} have developed ways in which the syntax or rules that determine the configuration of such space can be detected through the identification of the most significant lines of sight. These 'axial' lines and their relative connectivity to one another are highly correlated with movement¹¹. They suggest an underlying structure to urban space that is determined by the complexity of buildings or rooms which bound the space.

The syntax based on such lines might be used to condition the environmental variables in the active-walker model, which in turn determine the potential for walking at different points within the space. Further developments for more structured kinds of vehicular traffic at the micro-spatial scale suggest themselves. Traffic prediction along streets is difficult and the macro-models rarely hold up. Active-walker models might be used to embed such macro-predictions into a local geometric context, picking up data on environmental conditions which have no meaning at more macro levels where conventional traffic models operate.

There is a wealth of possible applications and extensions of such models, not only to human but to animal populations, and to social as well as physical spaces. These models naturally extend to problems where the goal is to optimize, to design 'best' paths, as is characteristic of many planning problems where the task is to design high-quality urban environments. □

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Membrane fusion

Bridging the gap by AAA ATPases

Tony Rowe and William E. Balch

Membrane fusion is central to a number of tightly regulated events, including vesicle transport, the maintenance of subcellular compartments, and the disassembly and reassembly of organelles during cell division. Targeting and fusion of transport vesicles¹ requires many membrane-bound and cytosolic factors, and much attention has been paid to the ATPase, *N*-ethylmaleimide-sensitive factor (NSF) and its functional partners — the soluble NSF attachment proteins (SNAPs), and SNAP receptors (SNAREs).

NSF belongs to a growing family of proteins known as the AAA-type ATPases, which are implicated in a diverse array of activities including intracellular membrane dynamics². All of the AAA-type proteins contain one or two copies of a 200-amino-acid ATPase module that is essential for ATP binding and hydrolysis. One member of this family — the product of the yeast cell-cycle gene *CDC48* — is involved in the fusion of endoplasmic reticulum and nuclear membranes³. The rat homologue of *Cdc48p* is p97, and this protein is involved in the reassembly of Golgi cisternae after cell division^{4,5}.

Although much is known about the binding partners for the NSF, the factors that

interact with the other AAA-type ATPases are unknown. But on page 75 of this issue, Kondo *et al.*⁶ report that they have identified an accessory factor, called p47, which is required for p97-dependent membrane fusion *in vitro*. They find that p47 forms a stable cytosolic complex with p97, at a stoichiometry of one trimer of p47 per hexamer of p97. Furthermore, the active cytosolic component that is required for membrane assembly is the p97/p47 complex, rather than p97 alone as was previously suggested³⁻⁵.

When examined by electron microscopy, the p97/p47 complex shows a barrel-shaped structure containing a central channel that is ringed by the p47 trimer. This structural organization is very similar to NSF and other members of the AAA-type ATPase family, including molecular chaperones, indicating that they may share similar modes of action. Although the sequence of p47 is unrelated to the SNAPs, it is homologous to yeast Shp1p, which is a protein of unknown function that is required for normal cell growth. So Shp1p is probably the cytosolic binding partner for *Cdc48p*.

With the discovery of p47 by Kondo *et al.*, the molecular details of p97-dependent fusion can now be addressed. For instance,

what is the role of p47? Is it an 'adaptor' protein that mediates the binding of p97 to a membrane-bound receptor(s) — in the same way as SNAPs recruit NSF? And at what step of the membrane targeting/fusion pathway does the p97/p47 complex act? This question is relevant to the debate over the mechanism of NSF action⁷: whereas the original proposal of the SNARE hypothesis was that NSF could promote fusion following membrane docking, recent results indicate that NSF is needed at a pre-docking (or 'priming') step^{7,8}. So NSF, p97 and related AAA-type ATPases may coordinate the protein-protein interactions that mediate membrane priming and targeting⁷, and analysis of the p97/p47-mediated pathway could help to resolve this issue.

Another potentially common feature of membrane-recognition events that involve AAA-type ATPases is the Rab family of GTPases. These proteins are required for many NSF-dependent steps, leading to the homotypic assembly of organelles (that is, fusion of 'like' membranes)^{9,10}, and heterotypic fusion (vesicular transport between different compartments)¹. So are these Rab proteins necessary for the function, in membrane dynamics, of other AAA-type ATPases such as p97? Consistent with this possibility, a Rab GTPase is required for the homotypic assembly of mammalian endo-

Figure 1 Members of the AAA-type family of ATPases are involved in the membrane dynamics of subcellular compartments. Many of them, such as *N*-ethylmaleimide-sensitive factor (NSF) and yeast *Cdc48p*, have accessory factors. The accessory factor for the rat homologue of *Cdc48p*, p97, has now been found by Kondo *et al.*⁶. p97 forms a complex with this accessory factor (p47), and the p97/p47 complex forms the active cytosolic component for membrane assembly. AAA-type ATPases are required for homotypic events (that is, between 'like' membranes) involved in the assembly and maintenance of different compartments (X and Y), and vesicular trafficking between these compartments. The membrane-recognition events that are controlled by these proteins and their accessory factors may involve an evolutionarily conserved mechanism.

plasmic reticulum cisternae — a process that involves an unknown AAA-type ATPase¹¹.

Even more intriguing is the identity of the membrane-bound p97/p47 receptors. Are they related to the SNARE proteins that are involved in Rab-dependent NSF/SNAP-mediated membrane recognition? If so, AAA-type ATPases may be central to priming the assembly of different membrane-targeting protein complexes.

Why does the cell use distinct, but related, AAA-type ATPases in membrane dynamics? Both NSF and p97 are necessary for reassembly of the Golgi apparatus — NSF seems to mediate the initial heterotypic recognition of small vesicles, whereas p97 promotes the subsequent homotypic-recognition events that lead to the formation of cisternae^{4,5}. Moreover, two AAA-type ATPases (the *PAS1* and *PAS5* gene products²) are required for peroxisome biogenesis in yeast. So the maintenance of subcellular compartments may, in general, involve both homotypic and heterotypic membrane recognition and fusion events, which probably require the activity of diverse AAA-type ATPases (Fig. 1). Given the importance of p97 in the reassembly of the Golgi stack during mitosis, it will be interesting to see whether it, and possibly other, members of the AAA-type ATPase family are regulated in a cell-cycle-dependent manner.

The members of the AAA-type family of ATPases that are involved in membrane

dynamics seem to have ancient origins. Archaeobacteria — cells that lack internal membranes — contain a homologue for p97, suggesting an ancestral role in the fusion events that accompany cell division. Many members of the family could have evolved with the emergence of compartmentalized cells. They may use a subset of structurally and functionally related accessory proteins, and a common molecular mechanism, to promote membrane recognition. But for now, the identification of the p97/p47 complex by Kondo *et al.*⁶ represents an important step towards working out the general principles of how the AAA-type ATPases act. □

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Chemistry

Oddly ordinary seaborgium

Ron Lougheed

The correct position of new elements in the periodic table is not a trivial matter. We understand the periodic table in terms of the filling of electron shells — a process that would seem to be entirely predictable. But relativistic effects can make the heaviest elements, notably rutherfordium and hahnium¹, behave in unexpected ways. Now, working with just seven atoms, Schädel *et al.* on page 55 of this issue² have extended chemistry to element 106 (seaborgium). They place it firmly in group 6, under tungsten and molybdenum (Fig. 1), raising the question of why it behaves in such a conventional way.

In this region, from the actinides on, one cannot predict properties by simple extrapolation of the periodic table. The high charges on these large atomic nuclei mean that the electrons are tightly bound, orbiting at relativistic velocities (a substantial fraction of the speed of light). And in many cases valence electron levels are close, and their order can be swapped by relatively small effects. Electrons with low angular momentum (in the *s* and *p_{1/2}* shells) overlap the nucleus strongly enough to be drawn into tighter orbits, partly by relativistic effects. That

screens the nucleus electrostatically from other electrons with higher angular momentum, whose orbits consequently expand.

Relativistic effects can even be important in lighter elements — for example, they explain the stability of the +1 oxidation state in thallium — but because these effects increase as the square of the nuclear charge, the greatest effect is expected in the heaviest elements. It isn't easy to predict what will happen, though: the heaviest-known group-5 element hahnium behaves more like the actinide protactinium and the lighter group-5 element niobium than its closest homologue tantalum³; so tantalum could be considered the oddest member of group 5.

If seaborgium is a conventional group-6 element, its properties will be similar to those of tungsten or molybdenum, its lighter homologues; and it could also have some properties similar to those of uranium. Schädel and colleagues have shown by gas chromatography that seaborgium forms volatile oxyhalides similar to the group-6 elements², and by liquid chromatography experiments, using nitric acid and dilute hydrofluoric acid, that it forms neutral

or anionic species similar to the group-6 elements, but not cationic species like uranium. There is no guarantee that other chemical species containing seaborgium won't have more peculiar chemistry — the relativistic effects may be different for different molecular orbitals — but for now the periodic table is firm.

The practicalities of chemistry on these elements are daunting. Chemists have to work with short-lived radionuclides and very low production rates, so experiments must be performed quickly and still efficiently separate the desired nuclide from similar products. Any chemistry that depends on complexes containing two or more of the studied atoms must be avoided, because of the one-atom-at-a-time nature of these experiments — just three daughter decay chains were observed in 5,000 solution-chemistry experiments on seaborgium, for example — and direct measurement of the large number of atoms needed to measure physical properties is impossible. Even though the chemistry of single atoms should be identical to that of a large number, additional experiments with radioactive tracers are usually made to confirm this expectation. Finally, materials or chemicals that act as trapping agents, as many precipitates do, must usually be avoided. (An exception is the clever chemistry⁴ that showed the group-5 element hahnium to be like niobium and protactinium, by its absorption on glass from solution in nitric acid.)

The short-lived man-made elements are produced by charged-particle accelerators, instead of the classical techniques that separate elements from natural materials, nuclear-explosion debris or reactor materials. The particle beam is aimed at a thin target, from which the reaction products emerge at high speed. They are then usually transported in a gas jet to the chemical apparatus in seconds, and separated by gas or liquid chromatography, or solvent extraction.

The subsequent decay, usually by α -particle emission or spontaneous fission, is

1	2	3	4	5	6	7
Rb 37	Sr 38	Y 39	Zr 40	Nb 41	Mo 42	Tc 43
Cs 55	Ba 56	La 57	Hf 72	Ta 73	W 74	Re 75
Fr 87	Ra 88	Ac 89	Rf 104	Ha 105	Sg 106	Ns 107
Actinides			Th 90	Pa 91	U 92	Np 93
Lanthanides			Ce 58	Pr 59	Nd 60	Pm 61

Figure 1 Part of the periodic table, including the early actinides, and the three latest elements to have their chemistry analysed: rutherfordium (104); hahnium (105); and now seaborgium (106).