chemical doping and magnetic-field measurements to very low temperatures. Chemical doping, however, introduces inhomogeneities in the material that might easily confuse the interpretation of experiments. But in this case the results for the germanium-doped material overlap convincingly with those of the pure compound. This overlap is by no means a foregone conclusion: magnetic field and chemical (or here, size) doping are not in general interchangeable. But the singular nature of the quantum critical point is revealed in these measurements: the mass of the 'dressed' electrons diverges towards infinity.

The temperature dependence of physical properties, in particular how these quantities scale with an exponent of temperature, is a useful diagnostic close to the quantum critical point. This scaling behaviour — of specific heat, electrical resistivity and magnetic susceptibility — is used in attempts to model quantum critical behaviour, and to describe the physics of the fluctuations. Custers *et al.*[2] have uncovered a linear temperature-dependence of electrical resistivity over a remarkably large range, from 10 mK to 10 K (as shown in Fig. 1 on page 524). Moreover, the new data reveal that, as the temperature changes and the system moves away from the quantum critical point, temperature is the only energy scale necessary to describe the evolution. Similarly, when the magnetic field is varied, that quantity sets the energy scale for variations in the material's properties.

There is obvious danger in drawing conclusions from such power-law fits, which can only be suggestive, but our modern understanding requires that if there is a critical point, there should be scaling. Theoretical work[5,6] has shown that it is reasonable to think of quantum phase transitions as classical phase transitions in higher dimensions, but the question remains whether the highly developed scaling concepts of classical critical phenomena can be simply borrowed here.

The measurements made by Custers *et al.*[2] show just how strongly the phase diagrams of heavy-fermion materials are organized by their singularities, the quantum critical points. The goal is to understand the nature of this organization at a deeper level; the dream is that some essentially new ground state may be found in the quantum-critical-point regime. ■

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Cell biology

Moving inside membranes

Katsuyoshi Mihara

The mechanism that inserts proteins into the membranes of cellular organelles was thought to be well understood. But studies in yeast reveal that this process is sometimes more complicated than had been suspected.

Rather like the organs of the human body, the 'organelles' of plant, animal and yeast cells are specialized compartments that fulfil specific functions. Each organelle is bounded by a lipid membrane, which contains 'translocase complexes' that ferry proteins from outside the compartment to the inside. But organelle membranes are more than just barriers; besides the translocase complexes, they contain many other proteins, which often adopt intricate configurations within the membrane itself. The prevailing view is that these proteins are sorted and assembled in the membrane by the same translocase complex that transports proteins across the membrane to the organelle interior. But on page 565 of this issue, Wiedemann *et al.*[1] report an unexpected finding from their studies in yeast mitochondria. They show that additional machinery, besides the translocase complex, is required to sort and assemble mitochondrial outer-membrane proteins that have a complicated conformation — including the translocase proteins themselves.

Mitochondria, the powerhouses of the cell, are bounded by not one, but two membranes. Some mitochondrial proteins reside in one of these membranes, some occur in the space between the membranes, and yet others are at the heart of the mitochondrion (Fig. 1, overleaf). All of these proteins are synthesized as precursor proteins (preproteins) inside the cell and are shuttled across the membranes by TOM and TIM complexes — preprotein translocases of the outer and inner membranes, respectively[2]. The TOM complex forms a channel in the outer membrane, called the general insertion pore, through which nearly all mitochondrial preproteins pass. The channel is made by the protein Tom40. This protein chain spans the membrane many times, forming an intricate pore-shaped structure. The entire TOM complex, however, is composed of many

100 YEARS AGO

The additions to the Zoological Society's Gardens during the past week include a Sooty Mangabey (*Cercocebus fuliginosus*) from West Africa, presented by Mrs. Watkins; a Ring-tailed Lemur (*Lemur catta*) from Madagascar, presented by Mr. H. P. Jacques; a Suricate (*Suricata tetradactyla*) from South Africa, presented by Captain C. P. Harvey; two Kinkajous (*Cercoleptes caudivolvulus*) from South America, presented by Miss C. Wallace Dunlop; a Himalayan Whistling Thrush (*Myiophoneus temmincki*), a Blue-winged Siva (*Siva cyanouroptera*), a Lesser Blue-winged Pitta (*Pitta cyanoptera*) from the Himalayas, presented by Mr. E. W. Harper; … two Wanderoo Monkeys (*Macacus silenus*) from Malabar, a Common Crowned Pigeon (*Goura coronata*), a Sclater's Crowned Pigeon (*Goura sclateri*) from New Guinea… two Indian Rollers (*Coracias indica*), three Pond Herons (*Ardeola grayi*), five Scarlet-backed Flower-peckers (*Dicaeum cruentatum*), two Two-banded Monitors (*Varanus salvator*) from India, deposited.
From *Nature* 30 July 1903.

50 YEARS AGO

***Traité de zoologie* Anatomie, systématique, biologie. Publié sous la direction de Prof. Pierre-P. Grassé. Tome 1, Fascicule 1: Phylogénie; protozoaires, généralités; flagellés. (Paris: Masson et Cie., 1952.) 9,600 francs. This is another volume of the now well-known "Traité de Zoologie", issued under the editorship of Prof. Pierre-P. Grassé, of the Sorbonne. While the seventh to appear, it is in fact the first fascicle of the first volume of the series and is in every way worthy of its predecessors. Its 1,071 pages are provided with 829 illustrations (there is no Fig. 285), 694 in line-drawings, 116 in half-tone from wash drawings, 18 in half-tone of photographs and 1 in line and colour… The present volume deals only with the general introductory matters and the sub-phylum Flagellata. The introductory accounts of the structure, physiology, nuclear behaviour, life-cycle and biology of the various categories form a valuable part of the work. Under the systematics of each class there is, wherever possible, a section dealing with its fossil members, a reminder of the present interest in microfossils. It is regrettable that the exigencies of the times are reflected in the price, for this highly commendable book should be readily accessible to every zoologist.**
From *Nature* 1 August 1953.

different Tom proteins, which together have a relative molecular mass of 400,000 (400K).

But how are the mature TOM complexes themselves assembled and inserted into the membrane? Some details were already known. Newly synthesized Tom40 precursor protein is recognized by the import receptor Tom20 and is then shuttled across the outer membrane through pre-existing TOM channels. The assembly of new translocases then occurs through two intermediate structures[3]. First, the pore-forming Tom40 preprotein assembles with Tom5 to form a 250K intermediate complex (intermediate I), which is associated with the inner surface of the outer membrane. Second, this complex rearranges into a 100K structure (intermediate II), concomitant with the integration of Tom40 into the membrane. This step is followed by the sequential addition of several other Tom proteins to form the mature TOM complex[3].

In the new study, Wiedemann *et al.*[1] asked whether a protein called Mas37 was involved in the assembly of TOM complexes. This protein was first identified during the screening of yeast mutants defective in phospholipid metabolism, but mutation of the Mas37 gene has many other adverse effects on mitochondrial function[4]. Although Mas37 is not part of the mature 400K translocase, it is found on the outer mitochondrial membrane and has been proposed to act as a preprotein receptor. But its precise involvement in the assembly of TOM has been unclear[5]. To investigate this, Wiedemann *et al.* tracked the Tom40 preprotein after import into yeast mitochondria lacking Mas37. They found that the formation of TOM intermediates I and II, as well as mature TOM, was blocked in these cells. Strikingly, however, the import and assembly of preproteins destined for inner mitochondrial sub-compartments were unaffected.

Wiedemann *et al.* next examined whether Mas37 was involved in the assembly of other outer-membrane proteins besides Tom40. They found that assembly of the proteins porin and Mdm10 — which have complicated structures that span the outer membrane many times — was inhibited in Mas37-deficient yeast cells, but that simpler outer-membrane proteins were assembled as normal. These results suggest that Mas37 only participates in the assembly and integration of outer-membrane proteins that have complicated conformations.

Could Mas37 be a component of the TOM assembly intermediates I or II? The authors found that anti-Mas37 antibodies bound to intermediate I, but not to intermediate II or mature TOM, suggesting that Mas37 is indeed an integral part of the 250K intermediate I complex. In support of this finding, Tom40 accumulated within a structure of around 210K in the absence of Mas37 (which, as its name suggests, has a relative molecular mass of 37K). Furthermore, in the absence of Tom40, Mas37 was found in a 210K complex that was distinct from the mature TOM complex. The authors conclude that the 210K structure containing Mas37 is a complex that makes up the bulk of intermediate I, and that also recruits certain proteins destined for the outer membrane, such as Tom40. They call this complex SAM, because it appears to be necessary for the correct sorting and assembly of outer-membrane proteins.

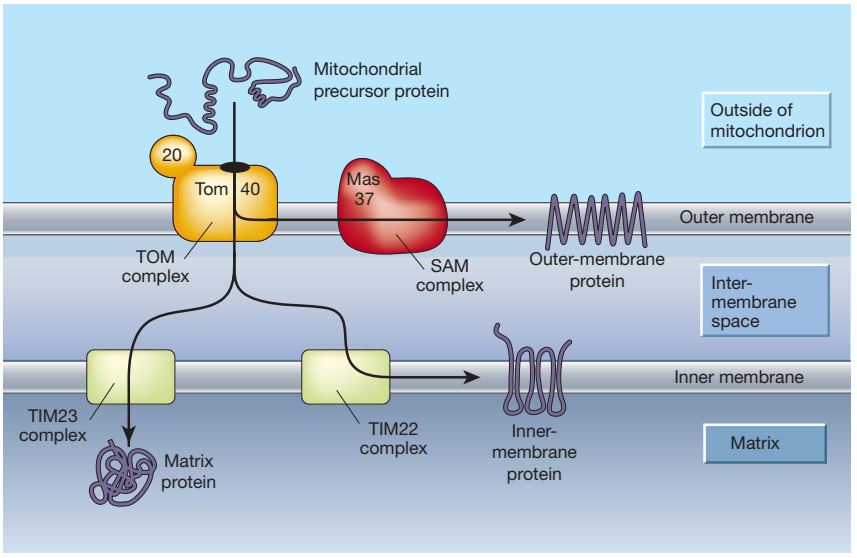

Figure 1 **Sorting and assembly pathways of mitochondrial precursor proteins. All mitochondrial preproteins are recognized by import receptors (Tom20 is the major import receptor) and are then imported through the translocase of the outer mitochondrial membrane (TOM complex). Preproteins destined for the inside of the mitochondrion (the matrix) are then shuttled through the inner membrane by the TIM23 complex, whereas those destined for the inner membrane are transferred across the intermembrane space to the TIM22 complex, through which they are inserted into the membrane. Wiedemann *et al.*[1] have found that outer-membrane proteins with a complicated topology pass through the TOM complex, then become integrated in the membrane with the assistance of a separate sorting and assembly complex (SAM).**

These findings suggest that outer-membrane preproteins are imported through TOM, then recognized and assembled by SAM. In the case of Tom40, when SAM recognizes and assembles this protein, the resulting complex makes up intermediate I. To confirm that Tom40 was initially imported through the TOM channel, Wiedemann *et al.* saturated pre-existing TOM channels with a preprotein destined for the inside of the mitochondrion, and then tried to import Tom40 preprotein. They found that the assembly of the SAM–Tom40 complex (intermediate I) was blocked, indicating that Tom40 does need to be transported through the TOM channel before it is handed over to SAM.

Wiedemann and colleagues' results change our views on the sorting and assembly of proteins in the organelle membrane. It had generally been assumed that the sorting of membrane proteins always occurred within the translocation machinery itself. Wiedemann *et al.* show that in the mitochondrial outer membrane this is not the case. Instead, although all mitochondrial precursor proteins initially pass through the translocation channel, some proteins destined for the outer membrane are subsequently recruited by the SAM complex, which helps them to integrate into the membrane and attain their correct conformation (Fig. 1).

So far, this finding is restricted to mitochondrial outer-membrane proteins that have complicated conformations. It remains to be seen whether the protein translocases of other organelles[6,7] also possess distinct sorting and assembly machinery for inserting complex proteins into the membrane. Perhaps there are unique mechanisms operating in the membranes of other organelles that are as yet unidentified. How the TOM or SAM complex discriminates between preproteins for the outer membrane and those for other mitochondrial subcompartments is another unanswered question. Dissecting the molecular cues that underlie this process should be the next goal. ■

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