

ocean and the atmosphere, and is a central mechanism of oceanic control of climate. They constitute a repository for heat, fresh water and gases such as carbon dioxide, all of which are exchanged at the ocean–atmosphere interface. On the largest scale, the water masses spread and fill the ocean basins. These huge bodies of water are also the engines of large-scale ocean circulation, one that is primarily driven by so-called North Atlantic Deep Water (NADW). As its name suggests, this is water that forms at high latitudes in the North Atlantic, sinks to depth and flows southwards.

Since the initial recognition of this circulation², oceanographers have busied themselves with finding out how NADW is resupplied to the Northern Hemisphere. A complex pattern of circulation pathways has become evident, with the Southern Ocean (Fig. 1) apparently having an important role in the production and interchange of water masses^{3,4}. Subantarctic Mode Water (SAMW) is a large water mass created by exchange of heat and fresh water with the atmosphere over much of the Southern Ocean. It sinks below the ocean surface^{5,6} and moves northwards at depths of about 200–600 m. These regions of the Southern Ocean can be thought of as windows to the deep ocean that allow water of particular heat, freshwater and nutrient content to enter the subsurface ocean.

The surface regions where SAMW is formed are characterized by low levels of silicic acid and high concentrations of nitrate. Sarmiento *et al.*¹ apply a newly designed 'conservative' tracer that captures this nutrient signature as a characteristic of SAMW. Their analysis of its distribution shows that SAMW reaches most of the world's upper ocean — that is, much of the global marine environment receives nutrients from the surface of the Southern Ocean. Another water mass, known as North Pacific Intermediate Water, has a subordinate role only: its nutrient delivery is limited to the upper ocean of the North Pacific.

Sarmiento *et al.*¹ also performed several computational experiments. They used a model of the global ocean that couples physical and biological processes, and came up with a reason why diatoms, a major component of the phytoplankton, do not reach their full productive potential in much of the global ocean. By varying the strength of the nutrient source in their models, Sarmiento *et al.* found that the ratio of silicic acid to nitrate in SAMW is less than ideal for diatom growth, and is therefore a primary cause of diatoms' widespread low productivity.

The conclusion that a physical process, and one operating in only a tiny part of the world's oceans, has such a huge influence on productivity is startling in itself. But there are more lessons to be learned from the new work¹.

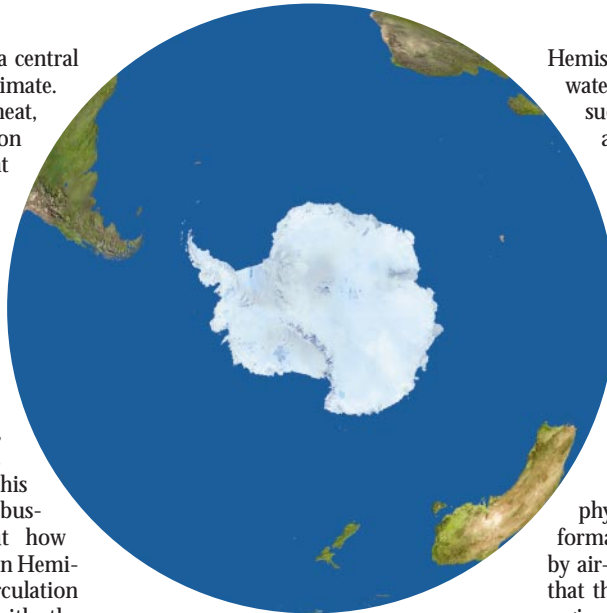


Figure 1 Well connected. The Southern Ocean surrounds Antarctica but has a global influence on marine productivity.

First, use of the new tracer as a diagnostic tool allows further insight into the dynamics of present-day ocean circulation. In particular, it has revealed that Antarctic surface water, driven northwards by the winds, contributes to the characteristics of SAMW. This finding supports earlier studies of this water mass^{5,7} and highlights the more general point that models of the climate system have to capture accurately the physical processes through which water masses form.

Second, the simulations identify a possible deficiency in representing mixing processes in the North Pacific. Models of the climate system may have to include the possible effect of tides on water-mass formation globally, which in turn has implications for the global influence exercised by the outflow characteristics of NADW.

Third, the SAMW pathway does more than provide nutrients for the upper branch of the ocean circulation. In the Southern

Hemisphere it also supplies heat and fresh water to the thermocline — the layer of sudden temperature change that occurs at varying depth below the surface and effectively separates the upper, productive part of the ocean from the deeper waters. The authors do not stress this point, but it is highly topical, given its bearing on our understanding of climate variability in the tropics. At the moment there is vigorous debate over the question of oceanic 'teleconnection' of high and mid-latitudes with low latitudes, which may drive year-to-year climate variability in the tropics⁸.

As to the climate connection, the physical processes that lead to water-mass formation in the Southern Ocean are driven by air–sea interactions. The indications are that the Southern Ocean is one of the few regions of the global ocean where the atmospheric consequences of climate change enter the ocean⁹. Any perturbation of the formation of SAMW, and subsequently of ocean circulation, is likely to have a dramatic impact on global marine productivity. That will affect the levels of carbon dioxide in the atmosphere, which in turn are linked to global temperature changes¹⁰. The overall conclusion is that the Southern Ocean has as powerful an influence on climate change as the North Atlantic. Difficult though it may be, it would pay to monitor conditions there. ■

Joachim Ribbe is in the Department of Biological and Physical Sciences, University of Southern Queensland, Toowoomba, Queensland 4350, Australia.

e-mail: Joachim.Ribbe@usq.edu.au

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Cell biology

Shape-shifting protein channel

Jordi Benach and John F. Hunt

Newly made proteins are moved across cellular membranes through a protein channel. The crystal structure of this channel is now revealed and confirms expectations that it must change shape to allow proteins to pass.

All cellular proteins are synthesized in the body of the cell, the cytosol. But many of them must then be transported through phospholipid membranes to reach their final destinations, which might be intracellular compartments or even, following secretion, outside the cell^{1–5}. The

molecular mechanism of this 'translocation' process has been the subject of elegant biochemical^{1,4–9}, genetic³ and biophysical^{10–12} studies. This body of work has shown that the main secretion pathway in all kingdoms of life involves a heterotrimeric protein complex, or translocase^{4,5}, which forms a

Atmospheric pollution

The veil of two cities

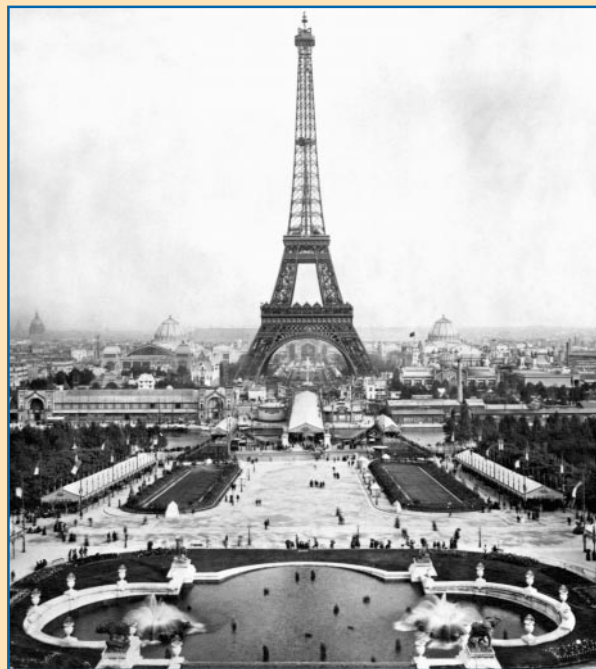
In 1752, Benjamin Franklin sent a metal key on its famous kite flight to demonstrate the electrical nature of lightning. The study of atmospheric electricity subsequently burgeoned, and writing in *Atmospheric Environment* (37, 5319–5324; 2003) R. G. Harrison and K. L. Aplin describe how they have mined records of one aspect of later historical research. They show that electrical measurements made at the Eiffel Tower in the 1890s can be used to estimate the levels of Parisian smoke pollution at that time.

The atmosphere's electrical system results from a combination of thunderstorm activity and the slight ionization of air. The upshot is an electrical potential difference between the ionosphere (at an altitude of some 60 km and more) and the Earth's surface, which causes a small current to flow. The potential gradient close to the ground is an indicator of the electrical state of the atmosphere, and in the nineteenth century it was commonly measured in several European cities.

In clean air, the potential gradient has a distinctive diurnal cycle known as the Carnegie curve. Local aerosol pollution alters this

gradient. So if that effect can be separated from the influence of the global electrical circuit at atmospherically clean sites, it becomes possible to infer pollution levels from potential-gradient measurements. But that is easier said than done.

To analyse electrical measurements made at the top of the Eiffel Tower, Harrison and Aplin applied a relationship between smoke pollution and potential gradient that had emerged from their earlier historical study for Kew, near London, using data from 1863. But they also needed an absolute calibration that was specific for Paris. For this, the authors conducted a modelling study that enabled them to identify the time of day when the top of the Eiffel Tower was in clean air and when it was in the urban boundary layer — the atmospheric layer affected by urban pollution. At times when the tower was in clean air, the observed electrical variations can be attributed to the Carnegie curve alone, allowing an absolute calibration of the electrical data based on the tabulated Carnegie values. At times when it was in the urban boundary



layer, the higher potential gradient signals the presence of smoke pollution.

The approach allowed Harrison and Aplin to estimate smoke pollution at both the top and the bottom of the Eiffel Tower in the 1890s. They calculate that pollution at ground level had an autumnal daily peak of $60 \pm 30 \mu\text{g m}^{-3}$. Their

earlier study gives a value of $170 \pm 50 \mu\text{g m}^{-3}$ for London. In the 1860s the UK Clean Air Act lay almost 100 years in the future. So in the late nineteenth century it is likely that, as a place to live, Paris had the edge over its English counterpart in more than just cancan and cabaret. **Juliane Mössinger**

tightly controlled conduit that allows newly made proteins to pass through membranes before the proteins fold into their functional shape.

On page 36 of this issue, van den Berg and colleagues¹³ present the X-ray crystal structure of the translocase (the SecY $\text{E}\beta$ complex) from the single-celled archaeon *Methanococcus jannaschii*, providing an initial view of the atomic architecture of this universally conserved channel. This structure could be considered the latest triumph of genomics, because the choice of the best translocase for structure determination was made on the basis of empirical examination of the expression, purification and crystallization properties of a range of translocases from organisms with fully sequenced genomes.

Almost 30 years ago, as a corollary to his 'signal hypothesis', Günter Blobel^{1,2} proposed that the translocation of proteins across membranes would occur through a proteinaceous channel of the kind now crystallized. Blobel's research at that time had shown that newly made proteins ('preproteins') that are

targeted for export from the cytosol have an extension at one end, called a signal peptide, that is removed during passage through the membrane¹. The hypothesis proposed that different types of extension would function as signals, directing newly made proteins to different membrane-bounded compartments^{1,2}, and the importance of this insight was rapidly accepted. The proposal that protein translocation occurs through a protein channel remained controversial for some time, until later experiments^{3–7,10} confirmed it.

Ion channels have received considerable attention because they show remarkable specificity in allowing one kind of ion through while preventing the passage of very similar molecular species. The protein-translocation channel faces what could be considered a more daunting task, in that it must allow the passage of chemically and sterically varied substrates — representing any segment from a translocating protein — without compromising the permeability barrier of the membrane^{2,4–6,11}. Blobel's original answer to this conundrum was that

translocation would occur at the same time that the protein was being made¹ (co-translationally), with a tight seal between the protein-synthesis machinery (ribosomes) and the pore of the translocation channel maintaining osmotic integrity. But biochemical studies have shown that translocation occurs at least partially post-translationally^{4–7}, and cryo-electron-microscopic studies show a gap of some 15 Å separating the ribosomal exit site from the translocase in detergent-solubilized samples performing co-translational translocation¹⁰ (as in Fig. 1, overleaf). So the pore of the channel seems likely to have variable but controlled conformational properties, expanding just enough to accommodate larger protein segments without compromising the integrity of the osmotic seal.

The crystal structure of the SecY $\text{E}\beta$ channel presented by van den Berg *et al.*¹³ provides an initial atomic-level glimpse of this shape-shifting channel. The authors advance structural arguments to support the hypothesis that the channel's pore is located at the centre of a single SecY $\text{E}\beta$ heterotrimer.

Previous work had found that biochemically well-characterized translocases, such as that from *Escherichia coli*, purify as higher-order multimers^{4,5,10}, which led to the suggestion that the pore would be located at the interface between several heterotrimers. This possibility was supported by biophysical studies suggesting that the pore is too large to be accommodated in a single heterotrimer¹¹. Although these observations suggest that several heterotrimers might fuse to form a larger channel under certain circumstances, the hypothesis that individual heterotrimers are active in protein translocation is supported by biochemical studies of the *E. coli* complex⁸.

The SecYE β structure¹³ seems to be in a closed state — not surprisingly, given that the complex was crystallized in the absence of a preprotein substrate. With support from biochemical and genetic results, van den Berg *et al.* propose that a short α -helix (a canonical structural feature in proteins) that plugs the exit from the channel will move out of the way during protein translocation. But removal of this plug would expose a pore whose molecular surface, at its narrowest point, has a diameter of only 3 Å (Fig. 1). The minimal requirement for channel function would be the ability to pass an arbitrary preprotein segment in an extended conformation, which would have a maximal width of around 12 Å. Moreover, several observations suggest that the channel can accommodate larger transport substrates, including α -helices destined to adopt a transmembrane conformation^{2,5,9}, which have a diameter of some 14 Å. So the channel must dynamically expand and contract in a way that is coordinated with the passage of preprotein segments.

Surprisingly, van den Berg *et al.* find that the limiting constriction — the 3-Å pore in the channel — is lined by a ring of inflexible isoleucine amino acids. This suggests that the inferred dynamic resizing of the channel must be mediated by diaphragm-like movements of the constituent transmembrane α -helices of the SecYE β heterotrimer, rather than by changes in side-chain conformation. Movements of the α -helices in SecYE β that are considerably larger than those that allow preprotein passage are also inferred from evidence that hydrophobic transmembrane α -helices in translocating preproteins can be released directly into the membrane bilayer when their presence is sensed in the translocation channel⁹. Van den Berg *et al.* propose a pathway for this sideways release, involving disruption of the interface between two pseudosymmetric halves of the SecY subunit of SecYE β , leading to opening of the central channel to the membrane.

Future experiments will need to explore how these inferred conformational changes are controlled by, and coupled to, preprotein translocation. In addition to regulation by

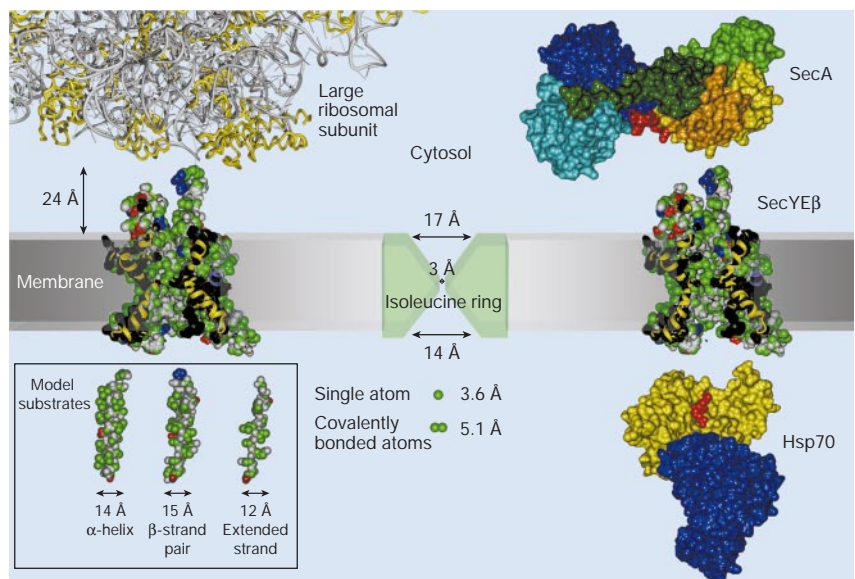


Figure 1 The SecYE β channel¹³, with some of its binding partners and model substrates shown at the same scale. The channel transports newly made proteins across cell membranes. Two cut-away views through its centre are shown at left and right, with the α -helix that blocks the exit channel moved into the proposed 'open' position¹³. Hydrophobic amino-acid side chains are in green, acidic groups in red, basic groups in blue, and other atoms in grey; yellow ribbons denote α -helices of SecY inside the surface. Space-filling representations of model substrates use the same colours. The channel's molecular dimensions are shown in the middle. The large ribosomal subunit synthesizes proteins; RNA is in grey and the subunit's protein backbone in yellow, with its exit channel positioned roughly as seen in ref. 10. A surface representation of an Hsp70 protein related to BIP shows the peptide-binding domain in yellow, bound peptide in red and ATP-hydrolysing domain in blue (with relative orientation roughly as in ref. 14); BIP prevents preproteins from slipping back into the channel. A surface representation of SecA from *Bacillus subtilis* shows the first (blue) and second (cyan) ATP/ADP-binding folds, amino-terminal (yellow) and carboxy-terminal (orange) preprotein-crosslinking domains, scaffold domain (dark green), wing domain (light green), and carboxy-terminal linker (red)¹⁵. This protein helps to push preproteins into the channel. The figure was created with DINO¹⁶. Protein Data Bank accession numbers are available from us on request.

translocating transmembrane α -helices, van den Berg *et al.* propose a model in which the channel's dynamics are modulated directly by the signal peptide of the preprotein being transported. Some of the required conformational changes could also be coupled to the protonmotive force (a transmembrane gradient in hydrogen-ion concentration and/or electrical potential), which enhances the efficiency of protein translocation in bacteria⁶.

Both these possibilities need to be addressed, as does the manner in which the channel is regulated by its known protein partners (Fig. 1). In bacteria, for instance, the SecA protein uses energy from ATP hydrolysis to push preprotein segments through the channel^{4,6,7}. How does the binding of SecA to the channel's cytosolic surface control the expansion and contraction that allows preproteins to pass while maintaining osmotic integrity? Finally, in eukaryotic (nucleated) cells, the Hsp70-family chaperone BIP is believed to act like a ratchet that prevents translocated preprotein segments from slipping back into the channel. Given that BIP and the channel interact¹², BIP might also regulate channel dynamics. The crystal

structure of the SecYE β channel¹³ will allow mechanistic issues such as these to be addressed with greater structural specificity and sophistication. ■

Jordi Benach and John F. Hunt are in the Department of Biological Sciences, 702A Fairchild Center, MC2434, Columbia University, New York, New York 10027, USA.

e-mail: hunt@sid.bio.columbia.edu

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