biological specimens by the alternative chemical fixation and cryoprotection techniques normally used by electron microscopists. One example of this, from the work of Heuser and Salpeter, is the striking differences in appearance and aggregation state of the intramembrane particles on the P and E fracture faces of *Torpedo* postsynaptic membranes when freeze-fractured after quick-freezing and after glutaraldehyde fixation, glycerination and Freon freezing. Other examples of such artefacts, which are important in assessing current theories of membrane fusion, come from the studies which Chandler and Heuser (*op. cit.* 1979) have made of cortical granule exocytosis in fertilised sea urchin eggs. In this work, the authors used the quick-freeze technique to capture stages in the 'cortical reaction' which originates from the point of entry of the sperm and which within 30 s sweeps across the entire surface of the egg. This process starts with the explosive exocytosis of the cortical granules, causing the characteristic elevation of the vitelline layer, and is followed by an elaboration of microvilli and subsequent membrane recovery by coated vesicle endocytosis. Chandler and Heuser found that freeze-fracture replicas of eggs fixed with glutaraldehyde and cryoprotected with glycerol before freezing displayed forms of interaction between the granule membrane and the plasma membrane, including particle-free single-bilayer membrane diaphragms formed from apposed fusing membranes, which looked identical to those described by other investigators and proposed as essential intermediates in the process of membrane fusion (see *News and Views* **272**, 16; 1978). However such membrane interactions were never found in eggs which had been quick-frozen without glycerination, even after glutaraldehyde fixation. The authors review other recent literature reporting lability of aldehyde-fixed membranes and glycerol-induced membrane changes, and conclude that many of the postulated 'intermediate stages' in fusion are in fact artefacts resulting from the lack of complete stabilisation of lipid bilayers by aldehyde fixation, exacerbated by the dehydrating effects of glycerol. This is further discussed by Chandler in a forthcoming book entitled *Freeze-fracture: Methods, Artifacts and Interpretations* (eds Rash & Hudson, Raven Press, New York). Since glutaraldehyde does not affect most membrane lipids, such lability is not unreasonable, but the question remains as to what chemical changes have already occurred in those membranes to permit such artefacts to develop only in situations where membrane fusion is imminently likely to occur.

The quick-freezing method instantaneously samples one particular moment in a biological process, and avoids the accumulation of intermediate stages which sometimes happens during slow death aldehyde fixation. As Chandler and Heuser were not able to detect preliminary fusion stages in their quick-frozen fertilised eggs, before seeing fused granules open to the extracellular space, they concluded that such stages could last no longer than 5 ms. An understanding of the molecular events which initiate membrane fusion thus seems as elusive as ever! □

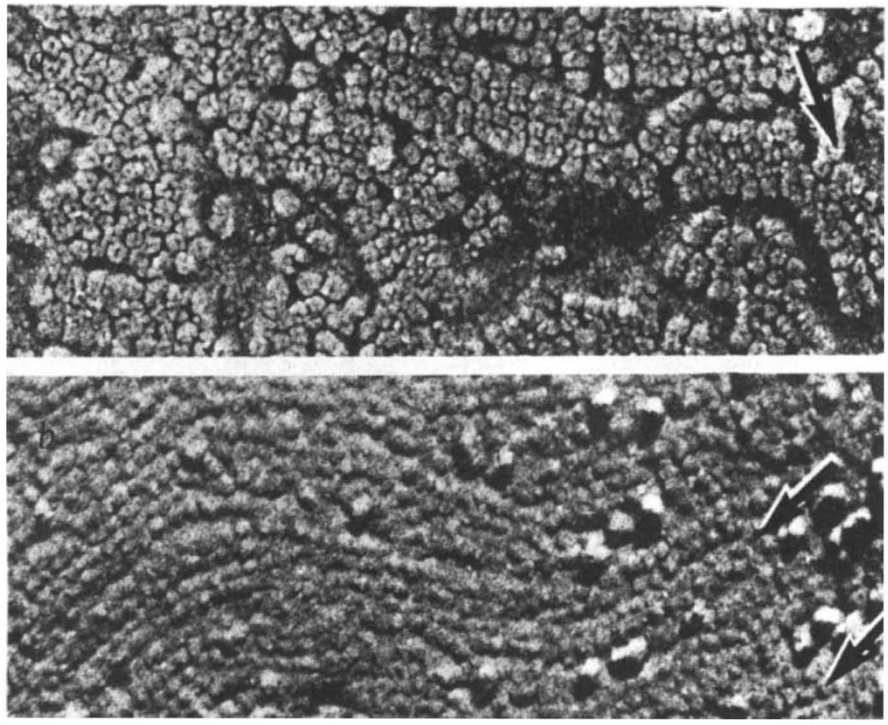


Fig. 2 *a*, Characteristic view of the pattern of grouping of surface projections seen on deep-etched postsynaptic membrane fragments. The most obvious pattern is rows four abreast, with many breaks and curves (arrow). × 270,000; so 3 mm ≃ 10 nm. *b*, Unidirectional shadow-casting of an unetched E face of the postsynaptic membrane, exposed by fracturing intact, quick-frozen tissue, which illustrates that the shallow bumps seen on this surface also group into curvilinear rows, most often two or four abreast (arrows), like the surface projections in Fig. 2a × 270,000; so 3 mm ≃ 10 nm.

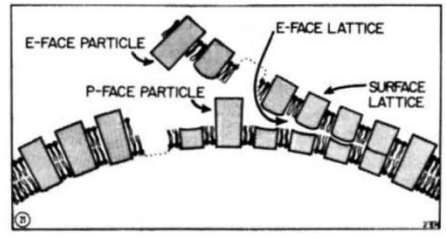
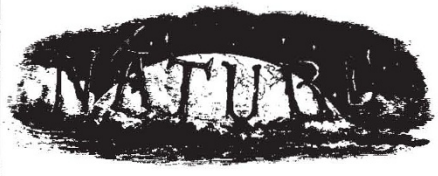


Fig. 3 Diagram illustrating, first, how cleavage of intramembrane receptor molecules could generate the match between the E face lattice and the surface lattice of projections that is observed in etched *Torpedo* post-synaptic membrane; and second, how extraction of whole receptors from one leaflet or the other could generate the large intramembrane particles which also characterise this membrane.



100 years ago

The *Hannoversche Courier* announces that Leibnitz's long-lost calculating machine has been recovered. Leibnitz invented and constructed this machine in 1672, during his stay in Paris. It can add, subtract, divide and multiply and was the wonder of the time. This machine became the property of the Hanover public library, but long ago disappeared from among its treasures. All that was known about its disappearance was that it had once been sent to an instrument maker at Göttingen to be repaired. It has now turned up again in the Göttingen library.

It is only about a year since we gave some account (Nature, vol. xviii. p. 361) of the railway bridge which spans the Firth of Tay at Dundee, and on Sunday it was the scene of one of the most terrible railway accidents on record. With the details of this sad occurrence our readers are no doubt familiar; for accurate information as to the prime cause we must await the searching inquiry which will no doubt be instituted. The structure appears to have been subjected to the most rigid tests before being opened to traffic, but we fear there must have been more than one screw loose somewhere. Upwards of 3,000 feet of the high girders are reported to have been swept away. One conjecture is that the train had got well upon the girders when a gust of greater strength had caught the structure. There would thus be, in addition to the ordinary vibration of the train, an enormous lateral pressure from the wind.

From *Nature* **21**, Jan. 1, 214; 1880.