results in propagation of the impulse along the muscle fibres and activation of the contractile apparatus. In mammalian skeletal muscle the endplate has a diameter of 20–60 μm, but its surface area is increased by infolding of the postsynaptic membrane. The acetylcholine receptor in normal muscle is confined almost exclusively to the endplate, as has been shown autoradiographically by labelling with the specific and irreversible blocking agent α-bungarotoxin (α-Bgt) (Lee, Tseng and Chiu, *Nature*, **215**, 1177; 1967; Barnard *et al.*, *Nature*, **234**, 207; 1971). Recent estimates of receptor sites suggest a density of $2–4 \times 10^4\ \mu m^{-2}$ (Fertuck and Salpeter, *Proc. natn. Acad. Sci. U.S.A.*, **71**, 1376; 1974; Porter and Barnard, *J. Membrane Biol.*, **20**, 31; 1975). When the nerve to a muscle is cut, acetylcholine sensitivity begins to appear over the entire surface of the muscle fibre and reaches a maximum in 2–3 weeks, only declining as reinnervation takes place (Axelsson and Thesleff, *J. Physiol., Lond.*, **147**, 178; 1959; Miledi, *J. Physiol., Lond.*, **151**, 241; 1960). Radioactively labelled α-Bgt binding again follows this closely: binding increases 20-fold overall (Miledi and Potter, *Nature*, **233**, 599; 1971), but the density of extrajunctional sites, at peak $600\ \mu m^{-2}$ (Fambrough, *J. gen. Physiol.*, **64**, 468; 1974), never approaches that at the endplate itself. Despite the translation freedom found for many membrane-bound proteins the normal endplate receptors remain discretely localised—even after denervation and degeneration of the nerve ending.

What makes the endplate so stable? Berg and Hall (*Science*, **184**, 473; 1974) labelled rat denervated diaphragm with ^{125}I-α-Bgt *in vivo*, removed the muscles and cultured them for 24 hours. They found that the extrajunctional radioactivity declined with a half life of 8 h, whereas there was only a marginal reduction in endplate labelling during that time. The rate of ^{125}I loss was reduced considerably by metabolic or protein synthesis inhibitors, indicating that little of it was due to reversibility of the toxin–receptor complex. Radioactivity recovered from the medium was mostly degraded toxin, although native toxin added to the culture was not broken down. They concluded that the extrajunctional toxin–receptor complex was being metabolised considerably faster than the endplate complex. Chang and Huang (*Nature*, **253**, 643; 1975) confirmed these findings, but they left the ^{3}H-α-Bgt-labelled diaphragms *in situ* for several days before removing them. They found that the turnover of endplate receptors had a half life of about 7.5 days which could be shortened by conditions which are known to increase the synthesis of new receptor, such as denervation performed at the same time as labelling. Their value for the half life of extrajunctional receptors in rats denervated 9 days previously was 19 hours, somewhat longer than Berg and Hall found in rats which had been denervated 5 days previously.

Does this different turnover reflect differences in the receptor molecules themselves, or in their mode of incorporation into the membrane? Several reports suggest that the two classes of receptor in intact muscle are not identical—with respect to their sensitivity to cholinergic antagonists (Beranek and Vyskocil, *J. Physiol., Lond.*, **188**, 53; 1967 and Lapa *et al.*, *Exp. Neurol.*, **43**, 375; 1974) and their acetylcholine noise spectra (Katz and Miledi, *J. Physiol., Lond.*, **224**, 665; 1972). On the other hand, using detergent-solubilised receptors, Chiu *et al.* (*Biochem. Biophys. Res. Commun.*, **51**, 205; 1973) showed that both receptors had the same apparent molecular weight on gel filtration; and Alper *et al.* (*FEBS Lett.* **48**, 130; 1974) found very similar 'protection constants' for several cholinergic ligands with respect to α-Bgt binding.

Many of the α-Bgt binding studies have been done on the intact rat diaphragm but this has certain disadvantages since one is dealing with a slowly diffusing polypeptide which makes kinetic analysis difficult. In *Biochemistry* (**13**, 5522; 1974), Almon, Andrew and Appel report some interesting results with Triton-solubilised receptors from rat leg muscles. They show ^{125}I-α-Bgt binding isotherms for normal and denervation-induced receptors. In both cases they find that the binding follows that predicted for a homogenous ligand interacting with a single class of independent sites. They find, however, that the toxin has a 10-fold higher affinity constant in denervated muscle extracts. More important, prolonged exposure to 1% Triton X-100 changes the toxin's affinity for the normal receptors to that found for the extrajunctional ones, although the number of sites remains the same.

Until now, the separate purification of the two types of muscle receptor has seemed a formidable task, because of the very low yield obtainable from normal muscle. Nevertheless, in the Abstracts of the Biophysical Society (*Biophys. J.*, **15**, 332a; 1975) Brockes and Hall report the purification, by affinity chromatography, of normal and denervation-induced receptors from rat diaphragm. Apparently, the two receptors are both glycoproteins and indistinguishable on gel-filtration and zone centrifugation. But they do exhibit some differences in affinity for α-Bgt and sensitivity to D-tubocurarine, and show separate peaks on isoelectric focusing.

At present it looks as if the normal and denervation-induced receptors are not very different, at least in macromolecular terms. The very high density of receptors on the postsynaptic endplate membrane makes interactions between them seem a possible explanation for the lower rate of turnover and other differences observed *in situ*. There is, however, no evidence that the solubilised endplate receptors are aggregates of the less densely packed extrajunctional ones. On the contrary, the results of Almon *et al.* suggest that other hydrophobic components could interact with the receptors in the membrane-bound state, and survive to some extent in mixed Triton micelles on

A hundred years ago

The third paper was by Mr B. Tower, on a method of obtaining motive power from wave motion. He said that this inquiry originated with Mr Deverell, who came home from the antipodes for the purpose of promulgating it. Mr Deverell's proposition was to suspend a heavy weight on board a ship by means of springs, and to obtain motive power by the oscillation of this weight through a distance not more than the height of the waves. It however appeared to Mr Tower that since the centrifugal force of wave motion in a vertical direction is alternately added to and subtracted from, the force of gravity thereby causing a virtual variation of the intensity of that force, the question might be broadly stated as follows:—

Supposing the force of gravity to vary in intensity at regular intervals, that is, to become alternately greater and less than its normal amount, what is the best means to obtain the maximum amount of energy from a given weight oscillating under the influence of these variations?

. . . Now, as energy or power is defined as force moving through distance, it is clear that the quantity of energy or power to be obtained by this system will depend on the distance through which this weight is caused to move during each successive variation of gravity. . .

The first experiments Mr Tower made with a model apparatus constructed on these principles showed him that the best arrangement would be to put a weight on the end of a revolving arm, whereby the centrifugal force of the wave motion might be utilised as well as the rising and falling motion.

from *Nature*, **11**, 410; March 25, 1875.