$\text{Na}^+ + \text{K}^+$ -stimulated adenosine triphosphatase (Inturrisi, 1969b) of ox brain, and at one-tenth the concentration also stimulates the calcium pump at much lower concentrations than does K^+ .

When Ca^{2+} uptake is taking place at a decreased rate in the absence of K^+ many barbiturates and phenothiazines have a stimulatory effect. Amylo-barbitone is the most active of the barbiturates, Ca^{2+} uptake being increased by about 300% at 2mM concentration. Chlorpromazine is the most potent of the phenothiazines, being active at about one-thousandth the concentration of K^+ (Duggan, 1971). At a K^+ concentration optimum for Ca^{2+} uptake all the barbiturates and phenothiazines decrease Ca^{2+} transport, in agreement with previous reports (Balzer, Makinose & Hasselbach, 1968; Azzone, Azzi, Rossi & Milic, 1966). It is considered that the stabilizing effect of barbiturates and phenothiazines on biological membranes generally is mediated by this mechanism whereby the displacement of Ca^{2+} from membrane binding sites, the basis of membrane labilization, is diminished. Chlorpromazine has been shown to decrease the leakage of L-aspartate aminotransferase (EC 2.6.1.1) from hypoxic heart to the control value (Langslet, 1971).

Rabbit muscle microsomal fraction has been concentrated and separated from mitochondria on a sucrose density gradient in a BXIV zonal rotor and re-run on a shallower sucrose density gradient. Sealed vesicles with a high rate of Ca^{2+} uptake and low associated adenosine triphosphatase activity were obtained. The distributions of NAD nucleosidase (EC 3.2.2.5), NADH-cytochrome c reductase (EC 1.6.2.1), adenosine triphosphatase (EC 3.6.1.4) and AMP deaminase (EC 3.5.4.6) are sufficiently different to show that some sub-fractionation of the muscle microsomal fraction has been achieved by this technique.

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- Azzone, G. F., Azzi, A., Rossi, C. & Milic, G. (1966). *Biochem. Z.* **345**, 322.
 Balzer, H., Makinose, M. & Hasselbach, W. (1968). *Arch. exp. Path. Pharmac.* **259**, 151.
 Duggan, P. F. (1971). *Eur. J. Pharmac.* **13**, 381.
 Ebashi, S. & Endo, M. (1968). *Prog. Biophys. molec. Biol.* **18**, 123.
 Ebashi, S., Endo, M. & Ohtsuki, I. (1969). *Q. Rev. Biophys.* **2**, 351.
 Ebashi, S. & Lipmann, F. (1962). *J. Cell Biol.* **14**, 389.
 Langslet, A. (1971). *Eur. J. Pharmac.* **13**, 292.
 Lee, K. S., Tanaka, K. & Yu, K. S. (1965). *J. Physiol., Lond.*, **179**, 456.
 Martonosi, A. & Feretos, R. (1964). *J. biol. Chem.* **239**, 648.
 Inturrisi, C. E. (1969a). *Biochim. biophys. Acta*, **173**, 567.

- Inturrisi, C. E. (1969b). *Biochim. biophys. Acta*, **178**, 630.
 Pedersen, C. J. (1968). *Fedn Proc. Fedn Am. Socs exp. Biol.* **27**, 1305.

Structural Changes during Muscle Contraction

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There has been general agreement for some time now that contraction in striated muscle is brought about by a process in which actin and myosin filaments are forcibly caused to slide past each other. It is also agreed by many people that the most likely way in which the sliding force is developed is by a cyclical chemical and mechanical interaction taking place at cross-bridges between the two types of filaments.

More recent X-ray evidence (Huxley & Brown, 1967; Huxley, 1968, 1969) has indicated that cross-bridge movement depends essentially on an active change in the effective angle of attachment of the heads of the myosin molecules to the actin monomers in the actin filaments. Other evidence indicates that it is the attachment process itself that is blocked by the regulatory protein system (tropomyosin and troponin) in a relaxed muscle. Electron-microscopic studies (Moore, Huxley & DeRosier, 1970) utilizing the three-dimensional reconstruction technique have analysed the structural details of this attachment in the 'rigor' configuration, which probably corresponds to the end of the working stroke in an actively contracting muscle, and have shown that the bridges are tilted in the expected direction. Further studies by J. Spudich & H. E. Huxley (unpublished work) have applied the same technique to a study of the location of the regulatory proteins in the thin filaments; these results will be described, together with recent X-ray diffraction studies on contracting muscles that show evidence for a substantial structural rearrangement in the thin filaments on activation. The latter may represent a change in position of tropomyosin, making possible the attachment of a myosin head carrying ATP (or its split products), in the configuration corresponding to the beginning of the working stroke, an attachment that is apparently blocked by tropomyosin plus troponin in the relaxed muscle.

- Huxley, H. E. (1968). *J. molec. Biol.* **37**, 507.
 Huxley, H. E. (1969). *Science, N.Y.*, **164**, 1356.
 Huxley, H. E. & Brown, W. (1967). *J. molec. Biol.* **30**, 383.
 Moore, P. B., Huxley, H. E. & DeRosier, D. J. (1970). *J. molec. Biol.* **50**, 279.