The metabolism of adenosinetriphosphate (ATP) in skeletal muscle can be considered from two aspects. On the one hand there are anaerobic and aerobic systems concerned with the production of the high-energy phosphate bonds of ATP, whereas on the other hand this chemical energy is converted into mechanical work in the highly specialized contractile system. These phases in ATP metabolism show precise intracellular localization. Anaerobically the ATP is produced by soluble enzyme systems in the sarcoplasm, whereas the main aerobic source of supply is to be found in the mitochondria, the large granular components of skeletal muscle (Chappell & Perry 1952, 1953). The mechanism of aerobic ATP production in muscle follows the general pattern which has already been demonstrated in other tissues such as liver, but the utilization of ATP by the myofibrils is a process which is characteristic of muscle.

It is generally conceded that the energy required for contraction is derived from the splitting of ATP. Within the skeletal muscle cell there are two main sites of adenosinetriphosphatase (ATPase) activity, namely, the myofibrils (Perry 1951) and the lipoprotein granules of the sarcoplasm (Perry 1952a). The ATPase of the granules is dominantly magnesium activated, and although the role of this enzyme in intracellular function is not at all clear, that associated with the mitochondria may be in some way concerned with the phosphorylating function of these particles. Certainly the ATPase activity of granules with oxidative activity which can be isolated from pigeon breast muscle (Chappell & Perry 1953) is very similar to that of mitochondria obtained from liver.

The other important ATPase of the skeletal muscle cell is associated with the myofibrils. It is closely related to the myosin component of these structures and likewise shows calcium activation, but the enzyme can be activated by magnesium when the ionic conditions are such that this cation inhibits the ATPase activity of myosin and actomyosin. Presumably the myofibrillar ATPase is the site of the conversion of chemical energy of ATP into mechanical work.

For the splitting of high-energy phosphate bonds to take place at the myofibril it must be supplied with high-energy phosphate which has been transported from the sites of aerobic and anaerobic production. It seems unlikely that free ATP is in contact with the myofibrils in relaxed muscle, for when myofibrils isolated from rabbit skeletal muscle are treated with low concentrations of ATP they rapidly shorten anisodimensionally to one-third to one-fourth of their original length, a change which must be closely related to the contractile process. Muscle cytoplasm contains ATP in a concentration adequate to bring about this shortening, but in relaxed muscle this ATP is in some way rendered ineffective so far as shortening of the myofibril is concerned. Disorganization of the muscle cytoplasm, such as is induced by the freezing and subsequent thawing of whole muscle, allows
the ATP to act *in situ* on the myofibrils with the result that the irreversible shortening of thaw rigor takes place (Perry 1950).

Certain features of the isolated myofibril throw some light on the way in which the myofibril may be supplied with energy-rich phosphate without the direct participation of the bulk of the intracellular ATP. Myofibrils which have been isolated free from granules and soluble components of the cell contain nucleotide, mainly in the form of adenosinediphosphate (ADP) tightly bound to their structure (Perry 1952b). This nucleotide, probably associated with the actin component, is remarkably constant in amount in isolated rabbit myofibrils and is in some way rendered inaccessible to enzymes such as myokinase and ATPase which are abundant in skeletal muscle, and which readily break down ADP when it is added to muscle homogenates. Nevertheless, in the presence of an enzyme found in the aqueous extract of muscle acetone powder, this bound ADP may act as acceptor for the phosphate of creatine phosphate. When myofibrils, muscle enzyme, creatine phosphate and magnesium are incubated together, creatine and phosphate are liberated and the myofibrils shorten in the same way as they do on the addition of ATP. A possible enzymic mechanism for the system is illustrated in figure 20.*

![Figure 20](http://rspb.royalsocietypublishing.org/content.figures/1855-rspb-122-606-fig20.large.jpg)

In the presence of the enzyme and creatine phosphate the bound ADP is phosphorylated to ATP, which is instantly hydrolyzed by the myofibrillar ATPase to reform ADP, and inorganic phosphate is liberated. The bound ADP acts simply as a phosphate carrier undergoing successive phosphorylation and dephosphorylation, and although present in low concentration it can bring about an appreciable breakdown of creatine phosphate by this catalytic function. So far it has not been possible to decide whether the shortening of the myofibril takes place immediately the ADP is phosphorylated to ATP or whether it is a direct consequence of the subsequent splitting of ATP.

*Note added in proof.* The results of investigations carried out since this communication was presented have necessitated a modification in this hypothesis, see Perry (1954).
Adenosinetriphosphate metabolism in skeletal muscle

The enzyme in the acetone powder extract of muscle that catalyzes the transfer of phosphate from creatine phosphate to the myofibril is of sarcoplasmic origin and might be expected to be creatine phosphokinase. Although preliminary investigation indicates considerable similarities between the two enzymes there are some anomalies. For example, creatine phosphokinase purified by the method of Banga (1943) usually has little ability to catalyze creatine phosphate breakdown in the myofibrillar system.

The system described indicates a mechanism for the supply of energy-rich phosphate to the myofibril. Shortening of the myofibril \textit{in vivo} is mediated not by free movement of ATP in the sarcoplasm, but rather by direct phosphorylation of the ADP which is closely associated with the protein components of the myofibril.

References (Perry)

Perry, S. V. 1950 \textit{J. Gen. Physiol.} 33, 563.
Perry, S. V. 1952b \textit{Biochem. J.} 51, 495.

Cell morphology and the organization of enzymatic systems in cytoplasm

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[Plate 18]

Introduction

The past development of biological sciences demonstrates that any significant advance, is the result of technical progress, or follows the application of new methods borrowed from other fields. One may wonder what credit would have remained attached to the wise writings of Claude Bernard if he had not been guided, in some of his inquiries, by a tool as simple as the reaction between iodine and glycogen.

A slight improvement in the resolving power of microscopic lenses, brought about around the year 1827 by Amici, who succeeded in correcting the optical aberrations of the early microscopes, terminated a deadlock that had lasted for nearly one hundred and fifty years. Cells were seen, and almost immediately recognized as the basic units of living matter. In the next hundred and ten years or so, exploration of the interior of the cell itself was mostly confined to microscopical observation. All the morphological elements of the cell that could be seen by means of the microscope were discovered and, for good measure, some artifacts such as the