

## SHORT COMMUNICATIONS

### A SUGGESTION CONCERNING THE PRESSURE-INDUCED CONTRACTION OF MUSCLE\*

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Ebbecke (1914) observed that hydrostatic pressures of a few hundred atmospheres can cause contractions in striated muscle without any additional stimulus. Cattell (1936) has reviewed a number of later investigations of this effect. A series of experiments by Deüticke and Ebbecke (1937) established that the chemical processes accompanying the contraction are the same as those occurring in normal contraction.

It is interesting to examine this effect in the light of Riseman and Kirkwood's (1948) suggested mechanism of muscle contraction. According to this model extended muscle is held in that state by the electrostatic repulsions between similarly charged groups ( $-\text{HPO}_4^-$ ) in the myosin or actomyosin molecule. Contraction occurs when these charges are removed by dephosphorylation to produce inorganic phosphate ions. Riseman and Kirkwood estimated the increment  $\Delta E$  in elastic modulus of the molecule due to the presence of  $n$  charges of the same sign and of magnitude  $e$ , at equal distances  $L$  throughout the molecule. It is :

$$\Delta E = -\frac{8}{3} \frac{N \rho n^2 e^2}{M D_e L}, \dots \dots \dots (1)$$

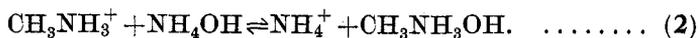
where  $D_e$  is the effective dielectric constant,  $N$  is Avogadro's number,  $M$  is the molecular weight of the structural unit, and  $\rho$  is the density of the structure. If  $n$  is assumed to be constant the only quantity in (1) which is significantly altered by pressure is  $D_e$ . It is known from the measurements of Kyropoulos (1926) that the dielectric constant of water is increased 2.8 per cent. by a pressure of 500 atm. A similar change can be expected in  $D_e$  and this would lead to a decrease in  $\Delta E$  and to contraction of the molecule against a constant stress. But this effect alone is hardly sufficient to explain the magnitude (*c.* 10 per cent.) of the observed contractions. Furthermore it requires a nearly instantaneous and reversible response to pressure changes, neither of which is generally found.

It seems necessary therefore to assume that the number of charged groups  $n$ , and consequently their spacing  $L$ , may be affected by pressure. This could happen if the extent or rate of the dephosphorylation process were dependent

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upon the pressure and in this case the response of the system to changes in pressure need be neither instantaneous nor reversible. The dephosphorylation of myosin produces a small inorganic (phosphate) ion from a large organic ion. In this Laboratory it has been shown (Buchanan and Hamann 1953) both theoretically and experimentally that the free energy of small ions in solution is decreased more by pressure than that of large ions: this means that an equilibrium between small and large ions is displaced in favour of the small ions at high pressures. Table 1 shows our experimental results for the equilibrium:



In this table

$$K = \frac{a_{\text{NH}_4^+} a_{\text{CH}_3\text{NH}_2\text{OH}}}{a_{\text{CH}_3\text{NH}_3^+} a_{\text{NH}_4\text{OH}}}$$

is the equilibrium constant, the  $a$ 's being activities.

TABLE 1  
EQUILIBRIUM CONSTANTS  $K$  FOR REACTION (2)

Pressure (atm)	1	1000	2000	3000
25 °C	0.0418	0.0433	0.0475	0.0524
45 °C	0.0484	0.0520	0.0561	0.0598

A similar but greater effect is to be expected in the dephosphorylation of an extended myosin chain. A circumstance which accords with these views is that the hydrolyses of large organic phosphate molecules occur with a decrease in volume (Meyerhof and Möhle 1933), that is,

$$\Delta V = -RT \left( \frac{\partial \log K}{\partial p} \right)_{T,c}$$

is negative and so pressure aids the hydrolyses.

It seems likely then, that the pressure-contraction arises in part from the increase in dielectric constant of the medium and in part from the assistance which pressure gives to the dephosphorylation of a charged molecular unit.

#### References

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