# TONUS IN UNSTRIATED MUSCLE

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Tonus in unstriated muscle has been variously explained. It has been ascribed to a catch mechanism (Grutzner, 1904; Von Uexkull, 1912) to increase in viscosity (Bayliss, 1928; Winton, 1930; Bozler, 1931; Singh, 1938 *a* and other papers).

No single explanation of tonus can suffice, as there are distinctly two kinds of tone. Many observers have shown that tone diminishes in the absence of oxygen, while others have shown that there is no increase in the oxygen usage during contraction. Parnas (1910) made experiments which show that in the bivalve mollusc no increase in metabolism is to be detected during the contraction. Bethe (1911) investigated the question in another way and confirmed the views of Parnas.

The metabolism of the mammalina plain muscle in the relaxed and the tonic states has been directly compared by Lovatt Evans (1923): he found that there was no increase in the oxygen usage of the tissue when it was brought into the tonically contracted state by the use of drugs such as histamine, but on the contrary rather less oxygen was used; this was accounted for by the fact that the tonic muscle was shorter and therefore exposed less surface than relaxed muscle; a similar diminution in oxygen usage was seen when the muscle was shortened by reduction of its load. Singh and Rao (1940) however found in the thin flat muscle of the frog stomach that extension decreased the oxygen consumption; they found that the oxygen consumption decreased during the isometric contraction and increased during inhibition. Singh (1938 *a*) found that life is not necessary for the slow tonic relaxation of the plain muscle.

In the present research an attempt has been made to elucidate the mechanism of tonus in the unstriated muscle.

## Tonus with Oxygen Usage

This is an ordinary contraction dependent upon the oxygen supply. It is due to ions in the saline as it is antagonised by increase of osmotic pressure. It has the following characteristics: it has superadded sponta-

neous contractions or the muscle relaxes spontaneously periodically (Singh, 1942); inhibition is facilitated.

The relation between tone and inhibition is shown by the following experiments. The stimulating power of the ions varies in the order

$$Cl < Br < NO_3 < I < SCN < CN.$$

Using the guineapig uterus, replacement of the chlorides of the saline with bromide increases tone as well as inhibition. The same may happen with nitrate, but with iodide and thiocyanate tone decreases. The explanation is given in the previous paper (Singh, 1945 *a*).

This kind of tone develops in steps from relaxed condition of the muscle. On the top of the tonic contraction, spontaneous contractions are superadded. It is antagonistic to electrical excitation, the sensitivity to which can be increased by increasing the osmotic pressure of the saline. The excitatory action of the substances is decreased while their inhibitory action is increased; the reason for this is given in another paper (Narayana and Singh, 1944). A substance may affect the inhibition produced by another substance by producing an antagonistic or potentiating inhibition or by changing tone. Thus in the guineapig uterus (Singh, 1945 *b*) small concentrations of potassium decrease the adrenaline inhibition by a direct antagonistic action; larger concentrations increase it by increasing tone, and still larger concentrations decrease it by greatly increasing tone.

The above tone is excited by stretch and often a constant length appears to act as stimulus, preventing the muscle from elongating. In this way I have seen a muscle kept at practically constant length for four hours automatically.

## Tonus without Oxygen Usage

To explain the holding power of the unstriated muscle a "catch" or "ratchet" mechanism has been suggested (Grutzner, 1904; Von Uexkull, 1912). There is some evidence for such a mechanism. Often the movements of the muscle in one direction appears facilitated but retarded in the opposite direction (see Fig. 9 of Singh, 1938 *b*; Fig. 6 of Singh, 1943 *b*). The assymetric stretch and release curves also suggest a similar mechanism (Singh, 1938 *c*).

The action of distilled water on unstriated muscle (Singh, 1944) supports the above view. When the frog stomach muscle is placed in distilled water, it elongates actively. This elongation may amount to 200% of the original length and cannot be accounted for by mere expansion due to gain of water by the muscle. It occurs in living as well as dead muscle, so that it appears to be a property of the myosin molecules. It also supports the view that

muscular contraction is due to folding of myosin molecules as elongation will then be due to opposite action.

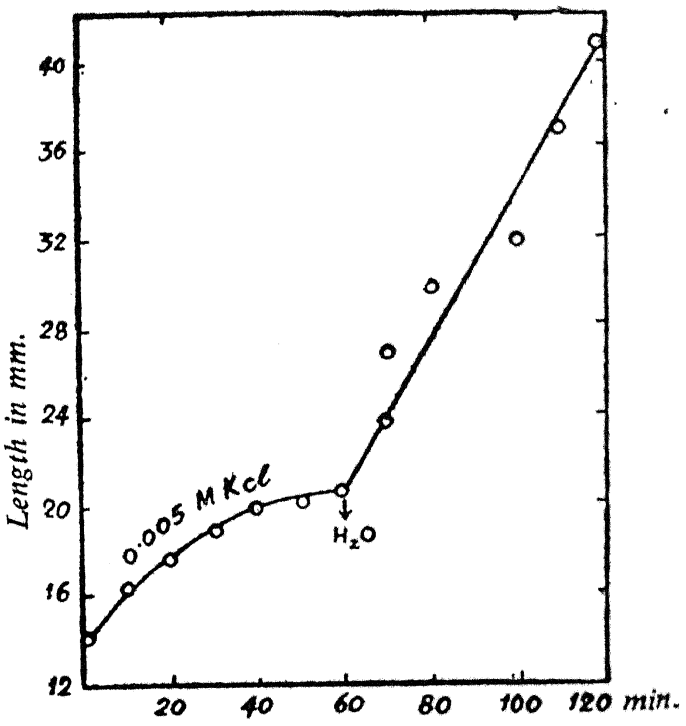


FIG. 1. Frog stomach. Effect of KCl on elongation

The addition of the ions to the water checks the elongation (Fig. 1). There is no significant difference between the actions of sodium and potassium chlorides; calcium chloride has a more potent action (Table I).

TABLE I

*Effect of* 0·01 *M salts on the elongation of the frog stomach*

| Time in minutes | NaCl mm. | KCl mm. | $CaCl_2$ mm. |
|---|---|---|---|
| 0 | 18·0 | 16·0 | 18·0 |
| 10 | 20·0 | 18·2 | 20·1 |
| 20 | 23·0 | 20·0 | 22·0 |
| 30 | 24·5 | 22·0 | 21·0 |
| 40 | 26·0 | 23·0 | 22·5 |
| 50 | 27·5 | 26·5 | 23·0 |
| 60 | 29·0 | 28·0 | 24·5 |
| 70 | 32·0 | 28·0 | 24·5 |
| 16 hours | 39·0 | 34·0 | 27·0 |

The nearest approach to the physiological saline in which the muscle elongates significantly consists of 9 c.c. of 0·112 M KCl, 4 c.c. of 0·073 M $CaCl_2$, 5 c.c. of M/15 sodium phosphate at pH 7, 7 c.c. of 0·112 M NaCl, and water upto 100 c.c. (Table II).

TABLE II

*Effect of mixtures of salts on elongation of frog stomach*

| Time in minutes | Number of muscles | | |
|---|---|---|---|
| | 1 | 2 | 3 |
| 0 | 17·0 | 19·0 | 17·0 |
| 10 | 19·0 | 21·5 | 20·0 |
| 20 | 20·0 | 22·5 | 21·5 |
| 30 | 20·5 | 23·0 | 21·5 |
| 40 | 20·5 | 23·0 | 22·0 |
| 50 | 21·0 | 23·0 | 22·0 |
| 60 | 20·5 | 23·0 | 22·5 |
| 16 hours | 24·0 | 27·0 | 27·5 |

In doing the above experiments three narrow strips were cut transversely from the middle of the stomach, as the pieces from the pyloric and cardiac ends behaved irregularly. The narrower the piece the greater the elongation as the opposing force becomes less. One could see the separation of the longitudinal fibres by the elongating forces.

The cause of elongation must be opposite that of contraction. Distilled water would dilute the muscle contents, so that some constituents normally present in the muscle in combination with myosin is diminished in concentration and the forces of electrostatic attraction which it gives rise to are lessened, or the water molecules have the opposite effect. The substance responsible for the shortening of myosin is probably some ion, as shown by the action of ions on dead muscle (Singh, 1943 *c*). It is probably sodium (Singh, 1938 *a*, 1945 *a*); it must be a stable substance, otherwise energy will be required continuously during contraction.

An electrostatic system would give rise to a catch mechanism, but as mentioned, movement in direction of attraction will be facilitated but retarded in the opposite direction. This view fits in with the modern conception of the intimate nature of the muscular contraction as being due to folding of myosin molecules and suggests a common mechanism for tonic as well as twitch contractions; they have some common properties (Singh, 1946).

If substances combining with myosin (M) to produce tonic contraction be designated as T, and that to produce twitch or quick contraction be Q, then the compound MT would result in tonic contraction and MQ in twitch contraction. The chief difference between MT and MQ will be that the former will be a stable and the latter an unstable compound (Singh, 1943 *c*). The former will therefore not require a continuous increase in metabolism.

The instability of Q may be due to the fact that it may be continuously destroyed, an acetylcholine-like substance may be produced which is destroyed by an enzyme, or that Q may be simultaneously resynthesised into its former origin. Q may be adenosinediphosphate which is resynthesised into adenosinetriphosphate. T must be a stable compound.

Q and T appear to be mutually exclusive as shown by the fact that twitch and tone are antagonistic. Thus unstriated muscle may relax before it contracts, and so also striated muscle (Sandow, 1945).

There is probably a T acceptor C and a Q acceptor D. The formula for the twitch contraction would be

$$MT + C = M + CT$$
$$M + QD = MQ + D$$
$$MT + C + QD = MQ + D + CT$$

or it may be $$MT + Q = MQ + T$$

D may be phosphate. T may be sodium as unstriated muscle is richer in sodium than striated muscle (Singh, 1938 *a*, 1945), and C is probably protein.

The above explains many of the tonic and twitch phenomena in unstriated muscle. The increase in viscosity found in the tonic contractions is probably a result and not the cause of them (Singh, 1938 *a*). MQ is accompanied by increase in viscosity (Gasser and Hill, 1942), so also MT (Singh, 1943 *a*). But if the viscosity of MQ is less than that of MT, then during twitch, the viscosity will descrease, as found by Winton (Singh, 1943 *a*).

The normal contractions of the unstriated muscle are probably mixtures of two to a varying degree ($xMT + yMQ$) where $x$ and $y$ are variables. If MQ predominates during contraction, then the oxygen consumption will increase, but if MT predominates, then it will decrease.

## Summary and Conclusion

No single explanation of tonus in unstriated muscle can suffice as there are two kinds of tonic contractions, one with and the other without oxygen usage. The former is akin to ordinary contraction and the latter to some structural change in muscle. It is suggested that in tonic contractions without oxygen usage, myosin forms a stable compound with some ions in the muscle fibres, while in twitch such a compound is unstable. The two factors which combine with myosin to form the contractible compounds of tonic and twitch contractions respectively are mutually exclusive in their combination with myosin; this explains many tonic and twitch phenomena in unstriated muscle.

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