additional 'cancel' button enables any reading to be aborted and the counters to be re-set to the initial condition.

The mean respiratory interval obtained with 50 untreated mice was 281 ± 4.96 ms (mean ± s.e. mean). This corresponds to a mean respiratory rate of 213/minute. For most purposes pre- and post-drug respiratory intervals are recorded and it is therefore not necessary to convert the respiratory interval to a rate/minute.

Simultaneous recording of electrical and mechanical activity from intestinal and vascular smooth muscle

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The simultaneous measurement of mechanical and intracellular electrical activity of smooth muscle is difficult because the cells are small and easily damaged during microelectrode impalement. Mechanical activity may increase cellular damage and also result in electrode displacement.

A method for the long-term recording of mechanical and intracellular electrical activity has been described by Golenhofen & v. Loh (1970). With this technique, the section of the preparation to be impaled is stretched to limit movement whilst the remainder is held under normal tension and this allows continuous recordings of up to 60 min to be made (Golenhofen & Weston, 1975). However, a limitation of this method is that once the preparation is attached to its holder, no further adjustment of the degree of stretch can be made. Modified holders for intestinal and vascular smooth muscle have now been developed to overcome this limitation (Figure 1).

The conical holder (Figure 1a) was developed primarily for use in portal vein and is inserted into the hepatic end of the vessel. The vein is then removed from the animal and placed in Krebs solution at 37°C. The tissue is observed under a binocular microscope and if movement in the region to be impaled is visible, the degree of stretch can be increased by turning the screw (s) until movement is reduced. Finally, the tissue is tied to the holder at the groove (g) using fine thread. The other holder (Figure 1b) is designed for use with flat sheets of muscle e.g. guinea-pig taenia coli. Here the tissue is tied to the holder and subsequent adjustment of stretch made again by adjustment of screws (s).

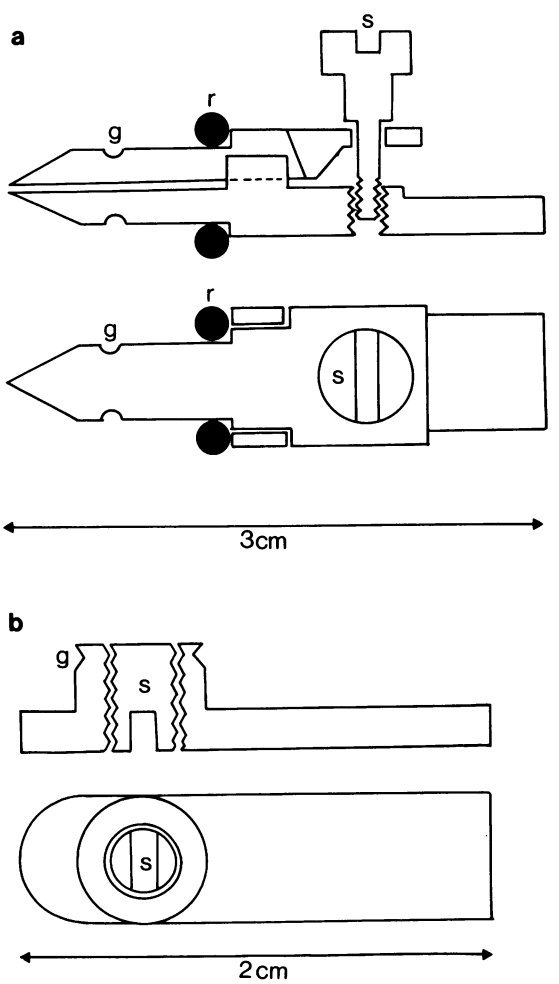

Figure 1 Tissue holders for the simultaneous recording of mechanical activity and transmembrane potential of smooth muscle cells. s=screws for adjustment of tissue stretch, r=rubber ring holding jaws of cone closed, g=grooves to accommodate tissue-fixing thread.

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The influence of the baseline on the size of pharmacological responses: a theoretical model

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It is frequently observed that the size of the response to a given dose of an agonist changes if a shift in the baseline activity of the test system occurs (e.g. Trendelenburg, 1974). A theoretical model is presented which describes how the position of the baseline may influence the relationship between biological stimulus (Stephenson, 1956) and effect (Figure 1).

Situation 1

Let us assume that agonist A is a full agonist which needs to activate all the receptors to produce its maximum effect (E_{1max}), i.e. there are no spare receptors in the system. In this case $E_1 = S_1$ (where E_1 is the effect and S_1 is the stimulus in the presence of a given concentration of A). Let us further assume that $E_{1max} = r_1$ (where r_1 is the possible range of effect within the system).

Situation 2

Let us assume that the baseline is shifted over a range a, and thus the range of observable effect is reduced ($r_2 = r_1 - a$). In this situation $S_{2max} > E_{2max}$, indicating the presence of functionally spare receptors in the system. Let us further assume that the shift in the baseline was due to a given concentration of drug B which acts at separate, but functionally synergistic receptors compared to the receptors activated by drug A. Thus the equation suggested by Ariëns, Simonis & van Rossum (1964) to describe functional synergism is applicable:

$$Q = E_1 + a - E_1 \frac{a}{E_{1max}} \quad (1)$$

where Q is the effect in Situation 2 measured from the baseline in Situation 1. Using the baseline in Situation 2 as a basis of reference:

$$Q = E_2 - a \quad (2)$$

$$E_1 = S_1 = S_2 \quad (3)$$

$$a = S_{2max} - E_{2max} \quad (4)$$

Substituting Q from eq. (2), E_1 from eq. (3) and a from eq. (4), eq. (1) becomes

$$E_2 = S_2 - S_2 \frac{S_{2max} - E_{2max}}{S_{2max}} \quad (5)$$