The significance of variable passive compliance in smooth muscle

ANYONE CONTEMPLATING dynamic roentgenograms of hollow viscera must be impressed that the length changes in the smooth muscles that comprise their walls are larger than the threefold range produced by skeletal muscle having a fixed filament array (1), and studies of muscles isolated from these viscera confirm very long functional ranges. Urinary bladder muscle, for example, has been shown to generate force over a greater than sevenfold length range (10), and airway smooth muscle has been shown to have a nearly flat length-force relationship over a threefold length range (5). But these extensive length ranges in airway smooth muscle are disputed by other studies using the same tissue and similar methods that found shorter functional length ranges (3, 7). The study by Speich et al. (8) in this issue of the Journal of Applied Physiology offers a likely explanation for these differences.

Mechanical studies of whole striated muscle usually begin with a measurement of the relationship between muscle length and active force to determine the length ($L_0$) where developed force is maximum, and this length is then used as a reference. In maximally activated frog skeletal muscle near 0°C, $L_0$ correlates with the optimum overlap of actin filaments with cross bridges on thick filaments (1), giving a structural rationale for the choice, although the force peak does not always correlate with optimal overlap of the contractile elements (6). By contrast, most smooth muscles do not produce a well-defined force peak, and some other length reference must be used. Often it is defined by a parameter of the passive length-force curve, such as the length where passive force is some percentage of the active force. Speich et al. (8) now show that passive tension in urinary bladder muscle is highly dynamic. In an earlier study (9), these authors showed that this muscle exhibits strain softening; i.e., elongation of the unstimulated muscle reduces passive tension at lengths shorter than the maximum reached during the stretch. Intuitively, such behavior is expected and might be considered as “getting the kinks out” (or, more scientifically, that manipulation during dissection produces localized contractures that are reversed by stretch). Today, the same investigators present the much more striking results, and which conclusions, are correct. The present study suggests a mechanism for the transient relief provided by deep inspiration during bronchoconstriction (4): stretching the bronchiolar muscle resets its resting length. At a basic level, they have profound implications for the interpretation of mechanical studies of smooth muscle and are likely to explain the different active length-force curves reported by different laboratories.

Major practical lessons from the present study are that the passive length-force curve of smooth muscle cannot be assumed to be static and that the reliability and reproducibility of a reference length based on a passive curve must be tested under each condition where it is used. This raises the immediate question of what length can be used as a reliable reference. Thankfully, the authors offer some guidance. Their passive length-force curves show substantial hysteresis, with the curve produced during successive stretches lying well above that produced during successive releases. They attribute this hysteresis to strain softening of a variable passive elastic component that is distinct from a separate, static parallel elastic component. Ideally, passive length-tension relationships should be measured and other mechanical studies done after the tension in the variable component has been reduced to zero by repetitive strain softening.

The reference length would then be defined by a parameter of the passive length-tension relationship of the static parallel elastic component alone.

Another practical issue is distinguishing active force from passive tension in the presence of passive tension. Often, active force is measured simply as the force increase during stimulation, but, in the presence of passive tension, such measurements fail to account for the transfer of load from passive to active elements during force generation. All isolated muscles have some compliant elements in series with the contractile elements. As a minimum, these series elastic elements include crushed tissue or tendons where the preparation is gripped and the apparatus itself (force transducer, hooks, clips, etc.). During force development, these elements elongate, allowing the parallel elastic elements to shorten, and this shortening reduces the tension in the parallel elements, transferring it to the contractile elements. This load transfer can be estimated and active force measurements corrected accordingly (5), but often the issue is avoided by working at short lengths where the correction is small and considered insignificant. Thus most length-force studies avoid lengths where tension in the unstimulated muscle is high and rising steeply.

A final practical issue, not fully addressed by the authors, is the use of contractures to study the active muscle. They mention that submaximal activation does not increase resting tension in the unstimulated muscle, and their example of submaximal activation is the “spontaneous rhythmic tone” seen in the preparation. As described below, it would be helpful to know if other forms of activation, such as brief tetani, also fail to stimulate increases in resting tension.

All of these practical issues become important when comparing active length-force studies. For example, our own experiments with tracheal muscle using brief (12 s) tetani show that muscles could be stretched with very little resistance by at least 40% (5) and sometimes by 100% (2) from the length where rest tension was 1–2% of developed force. Nearly constant force over a threefold length range beginning below the length where rest tension is zero and strong length dependence of velocity and stiffness over the same length range were taken as strong evidence of plastic adaptations of the filament lattice that placed more contractile filaments in series at longer lengths. By contrast, other experiments (3, 7) using KCl or acetylcholine contractures lasting up to 10 min showed that muscles could not be stretched from the length where developed force was maximal without encountering substantial resting tension, and in one instance (7), these results were interpreted as showing that filament lattice plasticity is much more limited than previously concluded. Such disparate results and conclusions often lead to the unfortunate question of which results, and which conclusions, are correct. The present study is very relevant to this issue because it suggests that the disparities in the different studies would be explained if the structures that resist passive stretch were restored by long...
contractures but not by brief tetani. It also suggests experiments that should be done by anyone using sustained contrac-

tures to test the plasticity hypothesis, and it seems likely that such experiments could resolve the present question of which conditions are necessary to demonstrate plasticity. We are grateful to the authors for providing this timely discovery.

REFERENCES


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