

# DEVELOPMENT OF SARCOMERE LENGTH NON-UNIFORMITY DURING LENGTHENING CONTRACTIONS OF PERMEABILIZED SINGLE MUSCLE FIBERS FROM RAT

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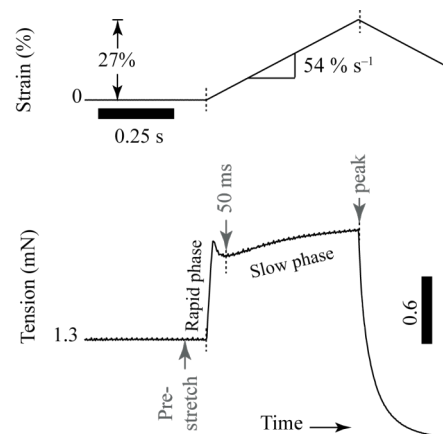
## INTRODUCTION

Structural damage is evident by electron microscopy (Macpherson et al. 1997) immediately following stretches of maximally activated skeletal muscle fibers ('lengthening contractions'). The damage is localized within single sarcomeres or small groups of sarcomeres that appear to be distributed randomly among the intact sarcomeres. Steady-state models of muscle contraction predict that, when maximally activated fibers are lengthened, longer sarcomeres stretch more than shorter sarcomeres (Morgan, 1990), increasing the likelihood that the longer sarcomeres will become damaged by over-stretch. We tested the hypotheses that: (1) regions of activated fibers that contain sarcomeres at longer lengths prior to a lengthening contraction undergo greater increases in the lengths of sarcomeres ( $L_s$ ) during the lengthening contraction, and (2) the non-uniform lengthening behavior takes place during the slow phase of the tension rise that accompanies the stretch.

## MATERIALS AND METHODS

To test the hypotheses, we used a laser diffraction technique (Panchangam et al. 2006, 2008) to make rapid measurements ( $500 \text{ s}^{-1}$ ) of the  $L_s$  in 20 contiguous regions of permeabilized single fiber segments ('fibers') undergoing lengthening contractions with a strain of 27 % and a strain rate of  $54 \% \text{ s}^{-1}$  (Figure 1). Stretches were initiated at mean  $L_s$  of  $2.54 \pm 0.12 \mu\text{m}$ . Sixteen (16) fibers, obtained from the *soleus* muscles of adult male rats, were used in the study. Measurements of  $L_s$  were obtained 50 ms

before (pre-stretch), 50 ms after and at the peak of the stretch (Figure 1). Relative pre-stretch  $L_s$  was computed as the ratio of pre-stretch  $L_s$  to the fiber mean for each region of the fiber. Similarly, the increase in  $L_s$  and the relative increase in  $L_s$ , defined as the ratio of increase in  $L_s$  to the mean  $L_s$  increase, were computed at both 50 ms after onset and at the peak of the stretch.

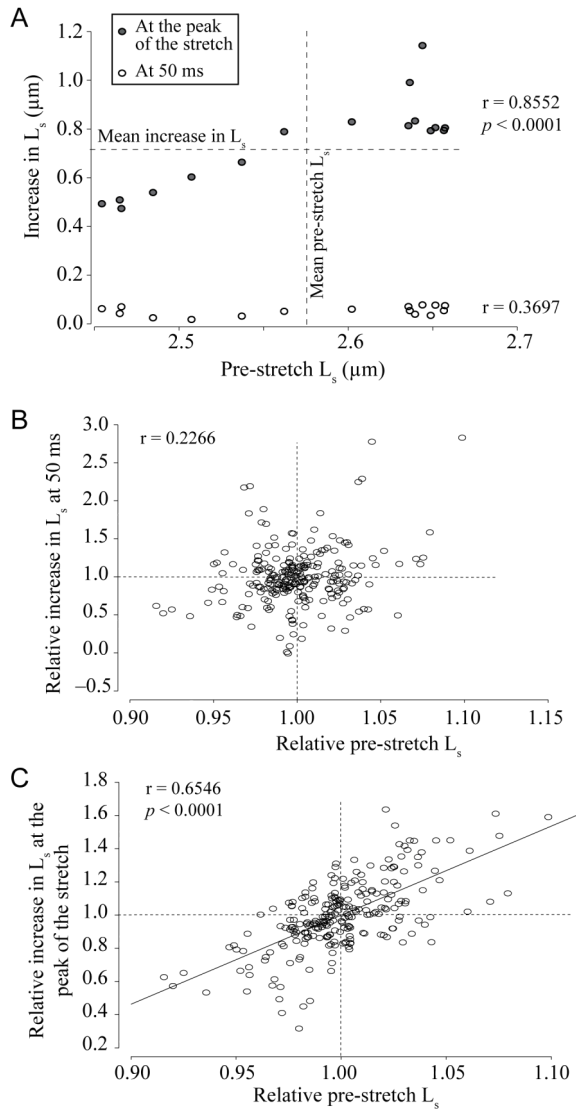


**Figure 1.** Tension response (bottom) of a fiber to a lengthening contraction with a strain of 27% (top).

## RESULTS

The data from a representative fiber are shown in Figure 2A and suggest a correlation between the pre-stretch  $L_s$  and increase in  $L_s$  during the stretch, but the relationship did not develop until after the first 50 ms of the stretch. Data pooled from all 16 fibers are presented in Figure 2B&C. The relationship between relative increase in  $L_s$  at 50 ms and relative pre-stretch  $L_s$  showed no correlation (Figure 2B), indicating no systematic growth in  $L_s$  non-uniformity during this phase. In

contrast, the relative increase in  $L_s$  at the peak of the stretch correlated with relative pre-stretch  $L_s$  (Figure 2C).



**Figure 2.** A. Data from a representative fiber. B & C. Relationship between relative increase in  $L_s$  and relative pre-stretch  $L_s$ .

## DISCUSSION

The results show that non-uniformity in  $L_s$  increases during a lengthening contraction as regions of single permeabilized fibers containing longer sarcomeres undergo a greater increase in  $L_s$  during the stretch. The correlation between relative pre-stretch  $L_s$  and relative increase in  $L_s$  developed during the

slow phase of tension increase with stretch, not during the rapid phase.

For a sarcomere operating at lengths longer than the optimum, continued increase of tension with stretch cannot be explained by static properties of activated muscle. Morgan (1990) explained the increase by incorporating  $L_s$  non-uniformities into his computer models and proposed that, during activated stretches, some weak sarcomeres undergo a rapid transition to long lengths where filament overlap is lost and the sarcomere becomes permanently damaged. The results of the present study support the contention that the slow increase in force during stretch is accompanied by a growth of  $L_s$  non-uniformity. However, because laser diffraction measurements reflect the average behavior of a large number of sarcomeres within the illuminated volume, the hypothesis that a small number of individual sarcomeres are undergoing rapid elongation cannot be tested using this technique.

## SUMMARY

The findings support the hypothesis that sarcomeres operating at longer lengths stretch more during a lengthening contraction, and that development of non-uniformity in  $L_s$  during a lengthening contraction coincides with the slow phase of the force increase.

## REFERENCES

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## ACKNOWLEDGMENTS

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