

# Adaptation of Muscle Size and Force by Mechanical Stimuli

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## Background

*In vivo*, mechanical loading of muscle by immobilization at extended length causes hypertrophy and an increase in the number of sarcomeres in series [1]. Mechanical loading may affect muscle protein turnover directly or indirectly by stimulating the expression of insulin-like growth factor 1 (IGF-1) [2], which is an autocrine anabolic factor in muscle. However, the mechanical stimulus for adaptation and induction of IGF-1 expression is not well known. Skeletal muscle finite element models have shown that strain distributions are likely to occur *in vivo* due to epimuscular myofascial force transmission [3]. The aim of this study was to investigate effects of high muscle fiber strain *per se* on hypertrophy, adaptation of the number of sarcomeres in series and IGF-1 expression and to compare sarcomere strain distributions in isolated muscle fibers *in vitro* with those *in vivo*.

## Methods

To test the effects of high muscle fiber strain, single muscle fibers (with basal lamina and endomysium) were dissected from m. iliofibularis of *Xenopus laevis* and attached to a force transducer in a culture chamber (20 °C). Isolated fibers were cultured in a serum-free medium either at passive slack length (mean sarcomere length 2.3 μm) or at extended lengths (12% over slack “high strain”) for 10 to 24 days. Before and after culture, fiber cross-sectional area (CSA) and the number of sarcomeres in series were determined [4]. After culture, IGF-1 mRNA expression in the muscle fibers was determined using in situ hybridization. Serial sarcomere strain distributions within the isolated muscle fibers were analyzed using laser diffraction. Sarcomere strain distributions within a muscle in its natural context of connective tissue were investigated using a 3D Finite element model of a rat EDL with epimuscular connections to surrounding tissues [3].

## Results

During culture, tetanic force of fibers cultured at passive slack length (n=5) remained unchanged. For fibers cultured at high strain, tetanic force decreased by 1.4±0.2% (mean±SEM, n=5) per day. For both conditions, CSA and number of sarcomeres remained constant. IGF-1 mRNA expression levels in fibers cultured at high strain did not differ from those cultured at slack length. These results are in contrast to the effects of immobilization of muscle *in vivo* at an extended length. The coefficient of variation of sarcomere lengths within extended isolated muscle fibers was <5%. At extended muscle lengths, the finite element model predicts a higher coefficient of variation of sarcomere lengths within the muscle fibers.

## Conclusions

We conclude that the lack of adaptation in isolated muscle fibers is accompanied by a smaller variation of sarcomere length along the cultured muscle fiber. The possibility exists that *in vivo* adaptation of muscle fiber size is regulated by local mechanical stimuli that vary along the muscle fiber length

## References

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