The amazing world of biophysics and the connection between sarcomere length non-uniformities and residual force enhancement.

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- Title: Force enhancement after stretch of isolated myofbrils is increased by sarcomere length non uniformities
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In the world of biophysics the amount of force produced by a muscle fiber is dictated by length. Which has given rise to the very well known force-length relation. This relation was discovered many decades ago, and has since been reproduced in many other laboratories. However when a muscle fiber is stretched while activated through contractions, the steady state force, the balance between the centripetal force, and the attractive coulomb force, stabilizes at a level than that produced during isothermal contractions at the corresponding length. This phenomenon is known as the residual force enhancement, and can still not be explained by force-length relation. This has left biophysicists baffled on how residual force enhancement works. In recent times however, one of the most accepted explanations for the residual force enhancement is the development of the sarcomere length non-uniformities, within a myofibril during activation and after stretching through contractions. This paper specifically looks at the effects of sarcomere length non-uniformities on the residual force enhancement by inducing sarcomere length non-uniformities in isolated myofibrils, and if here was a connection between sarcomere length non-uniformities and residual force enhancement.

To prove the connection researchers; Ricarda M. Haeger and Dilson E. Rassier from the McGrill University in Montreal, QC, Canada, first had to conduct experiments on muscle fibers. The specific muscle fibers they tested came from rabbits. All samples were acquired in compliance with the McGill Animal Care Committee and the Canadian Council on Animal care. The samples were then placed in a 50/50 rigor/general solution, which is a simple solution used to preserve the muscle fiber before being used in the experiments. Then using two glass micro needles the muscle fibers were lifted from the surface of the chamber to better identify the key proteins they were experimenting with. This specific protein is known as a myofibril, a filament that contains the contractile elements of the cardiomyocyte,the machinery or motor that drives contraction and relaxation of the muscle. And the myofibril is made up of several sarcomeres, the basic contractile unit of muscle fiber, which is the main focus of the study. The myofibrils were adjusted so that the nominal average sarcomere length was 2.8 micrometers, which is about as small as an individual strand of a spider's web.

The myofibril then went through into a solution that would induce activation through contractions, similar to how you contract your arm to flex your bicep but on a microscale. After the initial fast activations the researchers steadied the contractions at 15 seconds before the surrounding solution was switched to a relaxing solution. After the two controlled contractions, the sarcomere length was reduced by 20 percent. During the activation the myofibril stretched 20 percent its total length at a speed of 0.3 micrometers/ second. After that myofibrils were treated with a high ionic strength solution administered by the micro-perfusion system. The researchers then, through a novel lab technique, were able to successfully target one select sarcomere to deplete the A-band. Which is the dark region within a sarcomere that contains thick myosin filaments responsible for generating force during muscle contraction. Since the researchers were successful in inactivating the A-band in a myofibril, through a mirco-prefusion system will target a single sarcomere inactivation. They were now able to test to see if there was a connection between sarcomere length non-uniformities and residual force enhancement.

From that experiment Haeger, and Rassier were able to determine results like: contractile properties, such as, strength speed and velocity, in a single myofibril. They were then able to compare; before and after localized treatment of a single sarcomere with a high ionic strength solution. Isometric forces were the result of the experiment. Myofibrils treated with high ionic strength solution will show higher levels of stretch in contractions with active stretch then in controlled groups through isometric contractions. The residual force enhancement was then compared in both the active and inactive sarcomere to find another result that was: the inactive sarcomere decreased force after depletion of the A-band, but the residual force enhancement following stretch was larger than that observed on untreated myofibrils. The inactivation of one sarcomere within the myofibril test led to a significant increase in the residual force enhancement. Lastly, to prove the connection between sarcomere length non-uniformity and residual force enhancement, sarcomere length dispersion was calculated in each myofibril. Control myofibrils showed an average sarcomere length dispersion of 0.21 micrometers at rest, and the dispersion increased slightly during the contraction to 0.22 micrometers. Sarcomere length dispersion was significantly higher once one sarcomere was inactivated with values of 0.33 micrometers and 0.34 micrometers for relaxed and contracted states. This shows a close relationship between the increase in sarcomere length dispersion and the residual force enhancement.

Overall by using this novel technique, Haeger, and Rassier were able to introduce targeted sarcomere non-uniformity in a myofibril. And directly compare its effect on force production before and after stretch through contractions.Through their experiments they were able to conclude: residual force enhancement after stretch was observed in all myofibrils tested. The activation of a selected sarcomere increased both sarcomere length dispersion and the level of residual force enhancement. And there is a close relationship between the increase in sarcomere length dispersion and the residual force enhancement. These results also matched that of other laborites as well as a range of values in the literature cited in the study. Now that a connection between sarcomere length non-uniformity and residual force enhancement has been shown biophysicists are one step closer to understanding the mechanics of the body.

Haeger, R. M., Rassier, D. E. (2020). Force enhancement after stretch of isolated myofibrils is increased by sarcomere length non-uniformities. Scientific reports, 10(1), 21590.