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Inter-filament spacing mediates calcium binding to troponin: a simple geometric-mechanistic model explains the shift of force-length maxima with muscle activation. (English)

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Summary: The maximum of a muscle fiber's force-length curve (FLC) shifts to shorter lengths as muscle activation increases. State-of-the-art muscle models cannot explain the mechanistic basis for this shift, which is therefore either omitted or added ad hoc in a descriptive manner. A more theoretical approach developed by Hatze, who had particularly modeled the process of muscle activation, does predict this shift but can be shown to consist of multiple mathematical attempts that are all inconsistent with their common assertion: to represent local volume constancy. What mechanism may underlie the experimentally well-known shift has thus remained unclear. We work out here that the simple assumption of sarcomere volume constancy can, first of all, indeed explain the shift in the activity-Ca^{2+} relation as a function of sarcomere length by the enforcement of a decrease in inter-filament spacing that must occur as sarcomere length increases. We show that physiological data of this shift are consistent with a simply linear dependency of troponin (volumetric) density on sarcomere length. Further incorporating filament overlap as a second, independent mechanism, we can moreover reproduce, by means of a single master equation, an entire set of measured FLCs from literature, which testify shifts in their maxima at different levels of activation. We conclude that both phenomena, the shift in activity-Ca^{2+} relations with length and the shift in the maxima of FLCs with Ca^{2+}, can be explained by the superposition of two mechanisms immediately connected to the same sarcomere state variable *length*: filament overlap and inter-filament spacing.

MSC:

92C30 Physiology (general)
92C10 Biomechanics
92C40 Biochemistry, molecular biology

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