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Peer Review

Review of: "Modelling Skeletal Muscle Motor Unit Recruitment Contributions to Contractile Function: Part 3 - Substrate Oxidation of Phosphagen, Lipid, and Carbohydrate Metabolism"

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This manuscript presents an ambitious and technically detailed computational model integrating motor unit recruitment, fibre-type–specific ATP turnover, and substrate oxidation pathways (phosphagen, glycolytic, and mitochondrial carbohydrate and lipid metabolism) in the vastus lateralis, offering a novel attempt to bridge contractile mechanics with cellular bioenergetics. A major strength is the systematic extension of prior Parts 1 and 2 into substrate-level flux estimates across varying contraction frequencies, recruitment fractions, and genetic ST–FT distributions, generating physiologically interpretable patterns such as increased glycolytic and phosphagen dependence with fast-twitch recruitment and greater fatty acid oxidation at lower intensities. The effort to compare modeled outputs with classical human exercise studies (e.g., Romijn, Coggan) is commendable and partially supports physiological plausibility. However, the model relies heavily on assumed nonlinear proportional contributions of metabolic pathways (Equations 1–20) that are not empirically derived from fibre-type–specific in vivo data, which substantially limits validation; many parameter choices appear theoretically constructed rather than experimentally constrained, and no sensitivity analysis is provided to test robustness. Additionally, some modeled peak values (e.g., lactate production and CK-AK turnover) exceed commonly reported physiological measurements, and while the authors provide theoretical justification, these discrepancies underscore the need for stronger validation or uncertainty quantification. Overall, the study is innovative and conceptually valuable for hypothesis generation in muscle physiology, but its

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conclusions should be interpreted cautiously due to its dependence on theoretical proportionality functions and assumptions that are difficult to experimentally verify with current technology.

Declarations

Potential competing interests: No potential competing interests to declare.