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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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The manuscript **"Modelling Skeletal Muscle Motor Unit Recruitment Contributions to Contractile Function: Part 3 – Substrate Oxidation of Phosphagen, Lipid, and Carbohydrate Metabolism"** presents an advanced computational framework aimed at integrating motor unit recruitment dynamics with fibre type–specific substrate oxidation during skeletal muscle contraction. The study demonstrates strong theoretical integration by combining previously developed ATP turnover models with nonlinear metabolic pathway modelling, providing a detailed multi-scale simulation linking contractile physiology and muscle bioenergetics. The incorporation of genetic motor unit proportion variability and contraction frequency analysis represents a valuable contribution to exercise physiology modelling and offers potential relevance for sports science and neuromuscular disease research. However, several methodological limitations reduce the overall scientific robustness. A major concern is that many pathway proportionality functions were constructed using theoretical assumptions rather than experimentally validated fibre-specific metabolic data, which introduces potential uncertainty and model dependency. Additionally, model validation against direct experimental measurements remains limited, and comparisons with prior studies require multiple physiological conversion assumptions that may affect accuracy. The model also assumes constant metabolic efficiency and neglects dynamic contractile failure and intracellular metabolic regulatory mechanisms, which may limit physiological realism at higher intensities. Greater sensitivity analysis, uncertainty quantification, and clearer differentiation between evidence-based parameters and theoretical estimations would strengthen the

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study's reliability. Overall, the article offers a sophisticated and innovative modelling approach that advances understanding of motor unit–specific metabolic function but would benefit from further experimental validation and refinement of physiological assumptions.

Declarations

Potential competing interests: No potential competing interests to declare.