

Peer Review

Review of: "The LIME Framework: A Novel Conceptual NIRS Approach for Quantifying Muscle Metabolic Flexibility via Mitochondrial Oxidative Efficiency"

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This manuscript presents a well-articulated commentary proposing the LIME framework, a NIRS-based conceptual approach to assess local muscle metabolic flexibility using k_{HHb}-derived indices (LIME_{Lip}, LIME_{Carb}, and LIME_{Flex}).

The rationale is physiologically plausible, clearly described, and timely, but the framework remains entirely hypothetical. The main concerns relate to the need for clearer justification of k_{HHb} as a surrogate of mitochondrial oxidative capacity, more rigorous treatment of vascular and adipose-related confounders, and greater precision in articulating the proposed mechanistic pathway linking substrate utilization, CO₂/H⁺ production, and HHb recovery kinetics.

While formal validation is appropriately deferred for future studies, the manuscript would benefit from a more concrete validation roadmap, clearer statistical expectations, explicit acknowledgment of device and muscle-selection limitations, and a stronger discussion of alternative interpretations.

Minor suggestions focus on refining protocol timing, muscle choice justification, and signal origin considerations to further strengthen clarity and credibility.

Declarations

Potential competing interests: No potential competing interests to declare.