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Open peer review and authors' responses Mitochondrial respiratory function in living cells

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Reviewer 1: Brian Irving
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Manuscript reviewed 2025-04-22: *Only major points included.*

Reviewer 1

The use of the term "oxidative capacity" to refer to maximal oxygen consumption in the uncoupled state may be confusing, particularly given its typical physiological association with coupled respiration (e.g., VO_2max). Why not refer consistently to this state as "ET capacity"?

Authors

Thank you for highlighting the importance for further clarification, to more explicitly contrast OXPHOS capacity from oxidative capacity.

Changes made:

- In the bullet point of the summary added: '.., in contrast to the capacity of oxidative phosphorylation (OXPHOS capacity).
- Added clarification in Section 1.1:
  "The oxidative capacity *E* — in contrast to OXPHOS capacity *P* — .."
  "Oxidative capacity (*E*) is obtained under non-physiological conditions when respiration is decoupled from ATP production."

Reviewer 1

Lactate is referred to as a waste product, but it is no longer considered such in modern bioenergetics.

Authors

You are absolutely correct that lactate may not be a waste product. I have revised the relevant sentence to express more clearly the dual fate of lactate.

Changes made:

- Revised text in Section 1 to read:
  "Catabolism is the breakdown of nutrients to smaller metabolites that are either discharged as waste products or utilized as building blocks required for biosynthesis (anabolism) and growth."

Further edits in the text:

- Abstract: Added 'to improve human performance': Measuring cell respiration helps assess mitochondrial bioenergetic function to improve human performance, detect potential defects, ..
- Introduction: changed 'respiratory' to 'ventilatory'.
- Instead of changing 20 % to 21 % oxygen in air, I added 'wet air' to clarify why it is not 21 %.