Dear Erich,

these are my comments to the manuscript version 44. Comments are under the screenshot.


Page 1: wrong spelling

powerhouses of the cell contain the coenzyme ubiquinone and cytochrome b, c, a,a3 redox systems, and ATP synthase or alternative oxidases, ion transporters including proton pumps, mi-

Page 6: delete and

1. Introduction

Every study of mitochondrial function and disease is faced with Evolution, Age, Gender and sex, Lifestyle, and Environment (EAGLE) as essential background conditions characteriz-

Page 4: delete and sex

ria are largely maintained. The plasma membrane separates the cytosol, nucleus and organelles (the intracellular compartment) from the environment of the cell. The plasma membrane con-

Page 9: delete of the cell.

Reprogramming mitochondrial pathways may be considered as a switch of gears (stoichiome-

Page 11: add of

Until page 25 – all definitions are clear, the manuscript is readable and understandable.

The understandability is difficult from page 26, the real problem to understand starts for me on page 28. The Table 5 and explanations in Table 5 legend are confusing.

**Table 5. Power, exergy, force, flow, and advancement.**

<table>
<thead>
<tr>
<th>Expression</th>
<th>Symbol</th>
<th>Definition</th>
<th>Unit</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power</td>
<td>$P_p$</td>
<td>$P_p = I_{tr} \cdot F_{tr} = \partial G \cdot \partial t$</td>
<td>W=J·s⁻¹</td>
<td>Eq. 4</td>
</tr>
<tr>
<td>Force, isomorphic</td>
<td>$F_{tr}$</td>
<td>$F_{tr} = \partial G \cdot \partial \theta_{tr}$</td>
<td>J·X⁻¹</td>
<td>Eq. 5</td>
</tr>
</tbody>
</table>

Eq. 5: $\partial G$ is the partial Gibbs energy change (exergy) in the advancement of transformation $\text{tr}$.

Page 28: add consistency to table Eq. 5 and explanation Eq. 5 (tr)
**Number concentration, \( C_{\text{NX}} \):** The experimental *number concentration* of sample in the case of cells or animals, e.g., nematodes is \( C_{\text{NX}} = \frac{N_X V}{V} \) [cell L\(^{-1}\)]. where \( N_X \) is the number of cells or organisms in the chamber (Table 6).

**Flow per sample entity, \( I_{X,02} \):** A special case of normalization is encountered in respiratory studies with permeabilized (or intact) cells. If respiration is expressed per cell, the \( O_2 \) flow per measurement system is replaced by the \( O_2 \) flow per cell, \( I_{\text{cell,02}} \) (Table 6). \( O_2 \) flow can be calculated from volume-specific \( O_2 \) flux, \( J_{V,02} \) [nmol s\(^{-1}\)s\(^{-1}\) L\(^{-1}\)] (per \( V \) of the measurement chamber [L]), divided by the number concentration of cells, \( C_{\text{Nce}} = \frac{N_{ce} V}{V} \) [cell L\(^{-1}\)], where \( N_{ce} \) is the cell number concentration.

Page 38: The term *number concentration* is very strange. **Cell number concentration is more understandable.** But anyway - it is just concentration of cells in the chamber.

Expression of respiration in amol s\(^{-1}\).cell\(^{-1}\) looks fine for me.