

**Table S6**, parameter settings for the simulations of post exercise recovery dynamics (Figure 6)

*Control dataset*

| <b>Model configuration</b>                  | <b>Parameter name</b>                                   |  |                            |  |   |   |
|---|---|--|----------------------------|--|---|---|
|   | ATPase demand flux (mmol (L cell water) <sup>-1</sup> ) | Mitochondrial volume (mL mito / mL cell) | End exercise pH (unitless) | Cr <sub>tot</sub> (mmol (L cell water) <sup>-1</sup> ) | Pi initial (mmol (L cell water) <sup>-1</sup> ) | $\lambda$ (mM s <sup>-1</sup> pH unit <sup>-1</sup> ) |
| Original model                              | 0.90  | 0.056                                    | 6.65                       | 41.2   | 4.0   | 0.33  |
| Model configuration 1 (substrate feedback)  | 0.90  | 0.056                                    | 6.65                       | 41.2   | 4.0   | 0.33  |
| Model configuration 2 (parallel activation) | 0.90  | 0.056                                    | 6.65                       | 41.2   | 4.0   | 0.12  |

*Athlete dataset*

| <b>Model configuration</b>                  | <b>Parameter name</b>                                   |  |                            |  |   |   |
|---|---|--|----------------------------|--|---|---|
|   | ATPase demand flux (mmol (L cell water) <sup>-1</sup> ) | Mitochondrial volume (mL mito / mL cell) | End exercise pH (unitless) | Cr <sub>tot</sub> (mmol (L cell water) <sup>-1</sup> ) | Pi initial (mmol (L cell water) <sup>-1</sup> ) | $\lambda$ (mM s <sup>-1</sup> pH unit <sup>-1</sup> ) |
| Original model                              | 1.1   | 0.085                                    | 6.95                       | 38.2   | 4.0   | 1.33  |
| Model configuration 1 (substrate feedback)  | 1.1   | 0.085                                    | 6.95                       | 38.2   | 4.0   | 1.33  |
| Model configuration 2 (parallel activation) | 1.1   | 0.080                                    | 6.95                       | 38.2   | 4.0   | 1.33  |

*Subject with sedentary lifestyle dataset*

| <b>Model configuration</b> | <b>Parameter name</b> |  |  |  |  |  |
|----------------------------|-----------------------|--|--|--|--|--|
|----------------------------|-----------------------|--|--|--|--|--|

|   | ATPase demand flux (mmol (L cell water) <sup>-1</sup> ) | Mitochondrial volume (mL mito / mL cell) | End exercise pH (unitless) | Cr <sub>tot</sub> (mmol (L cell water) <sup>-1</sup> ) | Pi initial (mmol (L cell water) <sup>-1</sup> ) | $\lambda$ (mM s <sup>-1</sup> pH unit <sup>-1</sup> ) |
|---|---|--|----------------------------|--|---|---|
| Original model                              | 0.35  | 0.0235                                   | 6.70                       | 47.0   | 4.0   | 0.1   |
| Model configuration 1 (substrate feedback)  | 0.35  | 0.0235                                   | 6.70                       | 47.0   | 4.0   | 0.1   |
| Model configuration 2 (parallel activation) | 0.42  | 0.030                                    | 6.70                       | 47.0   | 4.0   | 0.017   |