Multi-scale Model of Respiration during Exercise

HAIYING ZHOU[1], NICOLA LAI[1], GERALD M. SAIDEL[1], AND MARCO E. CABRERA[1-3]

Departments of Biomedical Engineering[1], Pediatrics[2], and Physiology and Biophysics[3], Case Western Reserve University, Cleveland, Ohio 44106, USA

ABSTRACT: The regulation of pulmonary oxygen uptake (VO_2) during exercise depends on the imposed energy demand, as well as on the dynamics of blood flow, ventilation, oxygen exchange across membranes and oxygen utilization in contracting muscles. Pulmonary VO_2 dynamics, as measured at the mouth using indirect calorimetry (IC), is typically used to investigate the metabolic processes that control cellular respiration in the working skeletal muscles. On the other hand, muscle oxygenation, as measured using near-infrared spectroscopy (NIRS), provides quantitative information on the dynamic balance between oxygen delivery and oxygen consumption at the microvascular level. To gain quantitative understanding of the regulation of VO_2 at the cellular, tissue and whole-body level, a multi-scale computational model that links O_2 transport and cellular metabolism in skeletal muscle was developed. The model incorporates mechanisms of oxygen transport from the airway opening to the cell, as well as the phosphagenic and oxidative pathways of ATP synthesis in the tissue-cells.

A multi-organ model of gas exchange and a skeletal muscle model of oxygen transport and metabolism were combined here with experimental measurements of ventilation during exercise to predict muscle oxygenation and pulmonary VO_2 dynamics. Simulated and measured pulmonary VO_2 dynamics were in good agreement. Moreover, muscle oxygen consumption dynamics during moderate intensity exercise is significantly faster than muscle and pulmonary oxygen uptake dynamics. Manipulation of parameter values related to kinetics, perfusion, diffusion, and ventilation at each scale, suggests that the extent of relative effect on the dynamics of variables at a higher scale is greater the lower the scale at which the parameter is being manipulated. The study demonstrates the potential usefulness of a multiscale model of oxygen transport and metabolism as a tool to investigate the regulation of cellular and tissue processes, under various stress conditions, e.g. hypoxia/hyperoxia and exercise.

KEYWORDS: Simulations, Modeling, Oxygen transport, Energy metabolism, O_2 Uptake

Address for correspondence: Marco E. Cabrera, PhD, Department of Pediatrics, Case Western Reserve University, Cleveland, OH 44106-6011, USA. Tel: 216-844-5085; Fax: 216-844-5478,
E-mail: Marco.Cabrera@cwru.edu