Reaction-Diffusion Model of Energy Transfer During Mitochondrial Respiration in Heart Cells

Catherine Lloyd

Table of Contents

Model Structure

Traditionally the conceptual framework of cellular energy metabolism has been based on the assumption that the reactions involved are at equilibrium. However, this assumption is based on little experimental evidence, and the experiments that have been carried out have all been in resting muscle - where the equilibrium assumption is more likely to be met. More recently this assumption of equilibrium has been analysed using mathematical models of compartmentalised energy transfer, and these studies have shown that the assumption is not totally valid. In a pumping heart, the creatine kinase (CK) reaction is out of equilibrium for most of the contraction cycle.

This observation led to two questions:

1. 1) For which reactions, if any, is the assumption of equilibrium reasonable? and
2. 2) Do concentration gradients exist for metabolites, and how steep are these gradients?

Understanding these two points is important to the understanding of the intracellular factors which regulate the rate of mitochondrial oxidative phosphorylation in the heart cells *in vivo*.

In the 2000 Vendelin *et al.* publication described here, the authors develop a mathematical model that describes quantitatively the experimental data on how the rate of oxygen consumption and the metabolic state of the working isolated perfused rat heart depend on workload over its physiological range (see Figure 1 below). They use the model of Aliev and Saks (1997) as a foundation, and then supplement this with the model of oxidative phosphorylation by Korzeniewski and Froncisz (1991, 1998), in order to account for the changes in mitochondrial membrane potential and to calculate the rates of oxygen consumption for different workloads.

Model simulation results suggest that the assumption of reaction equilibrium for phosphocreatine, creatine, and ATP diffusion in the intracellular bulk water phase is acceptable. However, due to the nonequilibrium state of the CK reaction, intracellular ADP concentration gradients exist. Together with changes in inorganic phosphate (Pi) concentration, localised changes in ADP concentration (oscillations) are thought to be a major component of the metabolic feedback signal for regulation of respiration in muscle cells.

The model has been described here in CellML (the raw CellML description of the Vendelin *et al.* 2000 model can be downloaded in various formats as described in the section "Download This Model").

The complete original paper reference is cited below:

Regulation of mitochondrial respiration in heart cells analyzed by reaction-diffusion model of energy transfer [http://ajpcell.physiology.org/cgi/content/abstract/278/4/C747], Marko Vendelin, Olav Kongas, and Valdur Saks, 2000, *American Journal of Physiology* [http://ajpcell.physiology.org/], 278, C747-C764. (Full text (HTML) [http://ajpcell.physiology.org/cgi/content/full/278/4/C747] and PDF [http://ajpcell.physiology.org/cgi/reprint/278/4/C747.pdf] versions of the article are available on the *American Journal of Physiology* website.) PubMed ID: 10751324 [http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retrieve&db=PubMed&list_uids=10751324&dopt=Abstract]

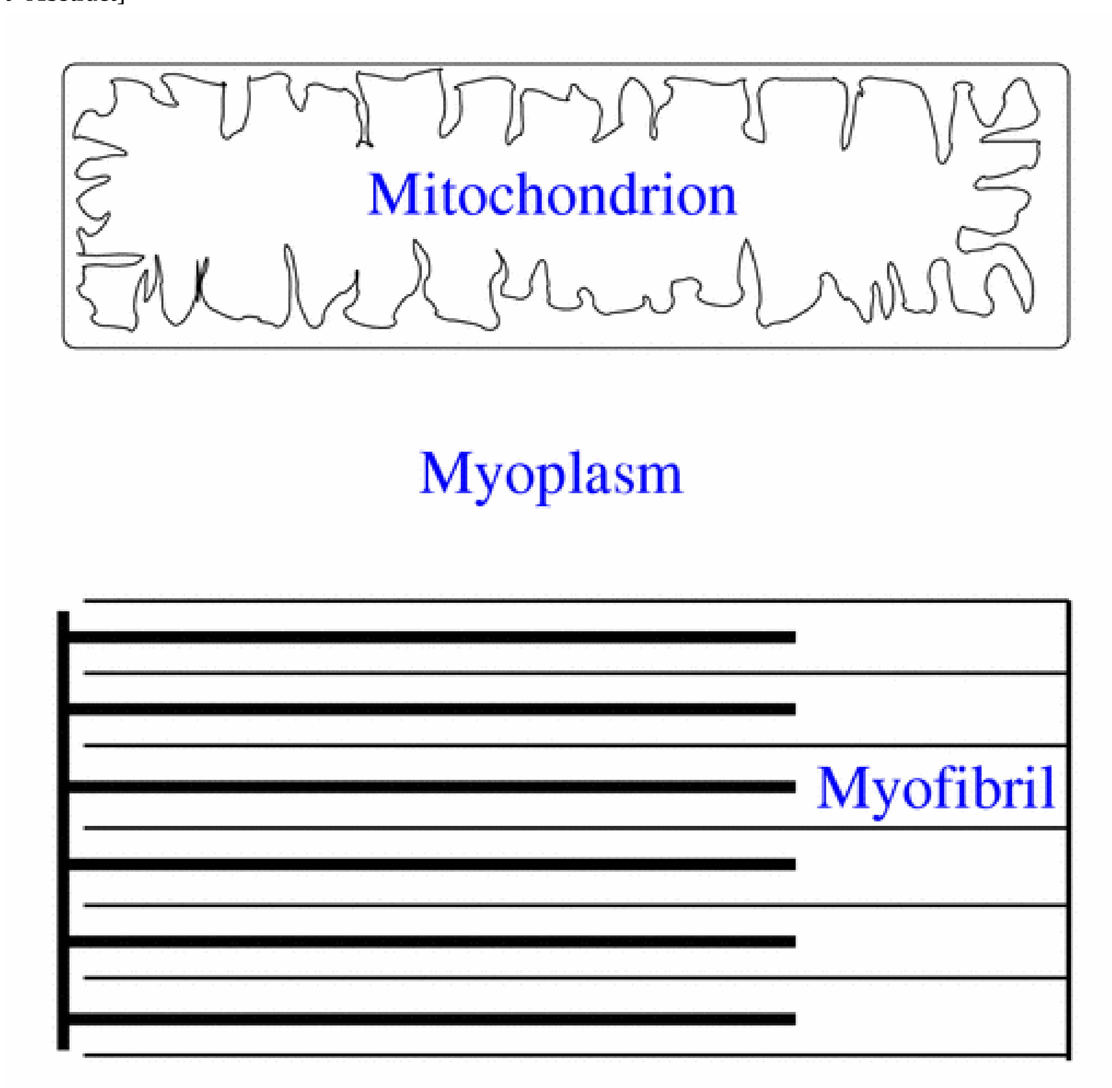

Figure 1. Scheme of the two-dimensional compartmentalised energy transfer model of cardiac cells: the components of the model. The total diffusion pathway is 1.2 micrometres, including the outer mitochondrial membrane, the layer of myoplasm and the myofibril. Creatine kinase (CK) and myosin magnesium ATPase activities are distributed non-uniformly along the myofibril.

Download This Model

- vendelin_model_2000.xml [../models/vendelin_model_2000.xml] — the raw XML.
- vendelin_model_2000.html [../models/vendelin_model_2000.html] — an HTML version for browsing online.
- vendelin_model_2000.pdf [../models/vendelin_model_2000.pdf] — a PDF version suitable for printing.
- cellml_vendelin_model_2000.tar.gz [../downloads/cellml_vendelin_model_2000.tar.gz] — a gzipped tarball with the XML and this documentation.

- vendelin_model_2000_maths.pdf [../maths_pdf/vendelin_model_2000_maths.pdf] — a PDF of the equations described in the model generated directly from the CellML description using the MathML Renderer [../../public/tools/index.html].