Modelling of cardiac cross-bridge cycling during ischemia

Mario Uhrin[1], Andrej Klic[1] and Ivan Valent[2]

[1] Department of Pharmacology and Toxicology, Faculty of Pharmacy
Comenius University, Bratislava, Slovakia

[2] Department of Physical and Theoretical Chemistry, Faculty of Nat. Sciences
Comenius University, Bratislava, Slovakia

Contact: klic1@uniba.sk

Introduction

Pri nahlom preruseni dodavky kyslika nastanu metabolicke zmeny, ktore spravadza hromadenie urcitych metabolitov. Tieto metabolity ovplyvnuju silu maju urcity vplyv na silu kontrakcie v srdcovych bunkach a preto sme sa rozhodli vykonat analyzu citlivosti, ktora by rozhodla, ktore z parametrov maju vyznamny vplyv na silu. Upravili a rozsirili sme myofilamentovy model od uja Rajsa (ref 1).

In sudden oxygen delivery cut-off, the metabolical changes occurs, which have direct impact on cycle of heart muscle contraction. The concentrations of ATP and creatine-phosphate are quickly decreasing and cummulation of ADP, phospates and protons occurs. The cell metabolism decreases and switches to anaerobic regime. Ions like calcium and sodium are cummulating in cell, which can lead as far as to infarct, the apoptosis.

Our work discusses the contractile cyrcle (crossbridge), affected by metabolites acummulating during oxygen deficiency, the ischemia. Metabolites like phosphates and protons are acummulating during ischemia and are directly interferring with the crossbridge cycle, which manifestates as decrease in myocardial contractile force.

Theory

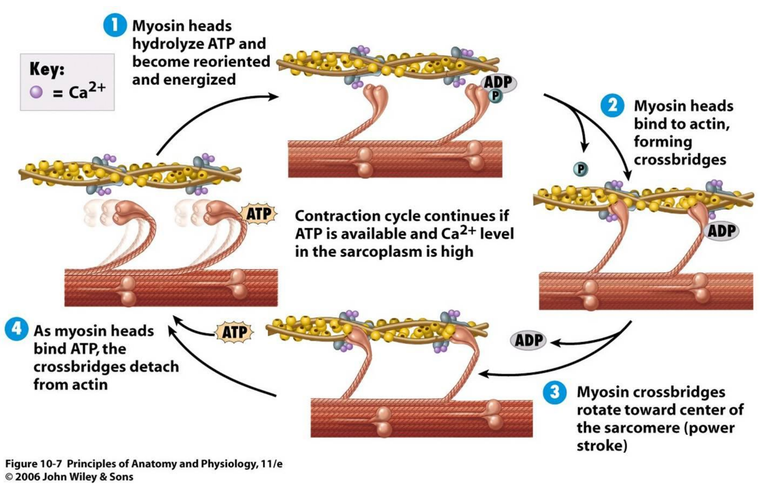

Figure 1: Figure caption

Methods and Implementation

Base model [Tran, 2010], implemented in CellML was exported as Python code. Our model is using the the mean-field approximations implemented as set of ODEs. The numerical analysis was performed using VODE integrator with BDF method from the Python SciPy package. Resulting data were visualised with the ggplot2 plotting system supplied in R programming language distribution.

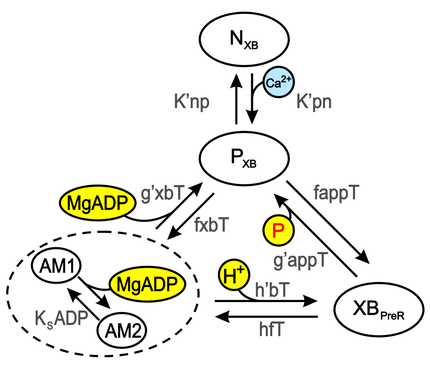

Figure 2: Figure caption

Results

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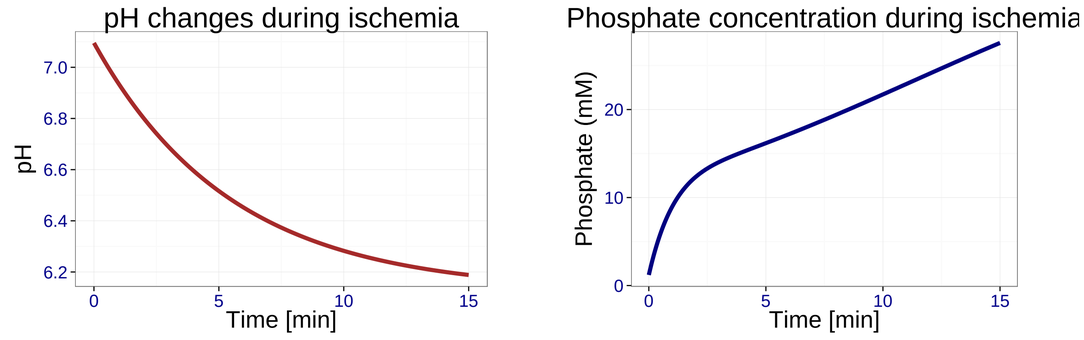

Figure 3: Zmen

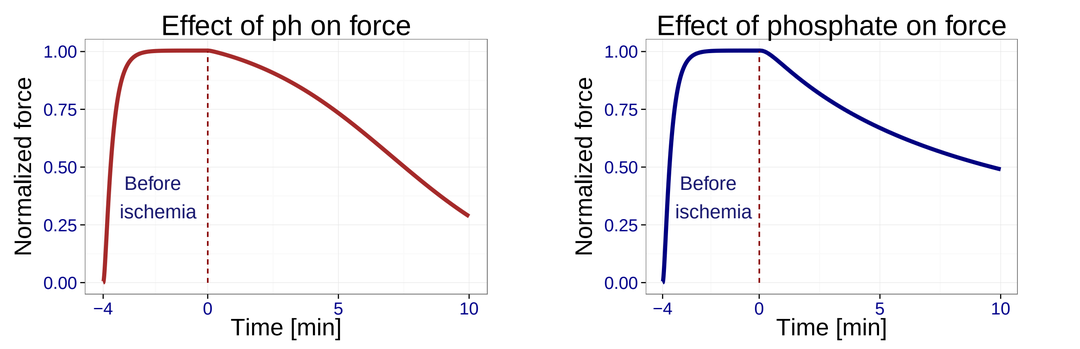

Figure 4: Figure caption

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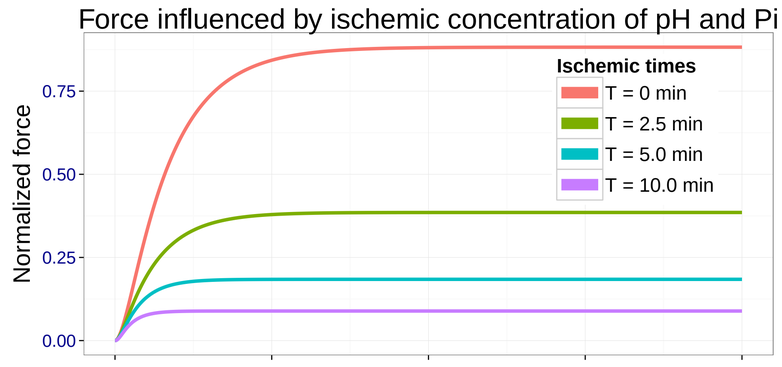

Figure 5: Figure caption

Conclusions

- Sensitivity analysis ukazala, ze pH a Pi maju najvacsi vplyv na znizenie sily kontrakcie.
- During 10 minutes of ischemia force rapidly decrease to 10%, co je v sulade s experimentalnymi datami (Terkildsen ref 3)

Forthcoming Research

V buducich vyskumoch chceme rozsirit nas model o nove parametre, ktore suvisia s mitochodnrialnou dysfunckou. Tieto patologicke stavy suvisia skor s hypoxiou a jemnejsimi zmenami metabolitov v case. Okrem toho planujeme upravit regulaciu vapnika s napojenim na ionove kanaly a ryanodinove receptory.

References

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K. Tran, N. P. Smith, D. S. Loiselle, and E. J. Crampin. *Biophys J.*, **98(2):**267-376, 2010.
J. R. Terkildsen, E. J. Crampin, et all. *Am J Physiol Heart Circ Physiol*, **293(5):**H3036-H3045, 2007.

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