

# Computational modelling identifies impact of subtle anatomical variation on skeletal muscle local calcium dynamics

**Citation for published version (APA):**

Groenendaal, W., Riel, van, N. A. W., Jeneson, J. A. L., Eikelder, ten, H. M. M., Nicolay, K., & Hilbers, P. A. J. (2008). Computational modelling identifies impact of subtle anatomical variation on skeletal muscle local calcium dynamics. In *Experimental biology 2008, San Diego California* (pp. 756.11-). (FASEB Journal : The Journal of the Federation of American Societies for Experimental Biology; Vol. 22). FASEB.

**Document status and date:**

Published: 01/01/2008

**Document Version:**

Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

**Please check the document version of this publication:**

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

**General rights**

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

[www.tue.nl/taverne](http://www.tue.nl/taverne)

**Take down policy**

If you believe that this document breaches copyright please contact us at:

[openaccess@tue.nl](mailto:openaccess@tue.nl)

providing details and we will investigate your claim.

(*The FASEB Journal*. 2008;22:756.11.)  
© 2008 FASEB

---

756.11

## Computational modelling identifies impact of subtle anatomical variation on skeletal muscle local calcium dynamics

Willemijn Groenendaal, Natal van Riel, Jeroen Jeneson, Huub ten Eikelder, Klaas Nicolay and Peter Hilbers

Biomedical Engineering, Eindhoven University of Technology, Eindhoven, Netherlands

### ABSTRACT

Calcium is the main regulator of skeletal muscle metabolic activity. The question has been addressed whether the highly structured spatial organization of sites of Ca<sup>2+</sup> release, uptake and action in skeletal muscle substantially impacts the dynamics of cytosolic Ca<sup>2+</sup> handling and thereby the physiology of the cell. Hereto, the spatiotemporal dynamics of the free calcium distribution in a fast-twitch muscle sarcomere was studied using a reaction-diffusion computational model.

The model was based on the model of Baylor and Hollingworth (*J Gen Physiol*. 1998 112:297-316), but was adapted to handle local calcium dynamics in mouse EDL fast twitch muscle at 35°C. Furthermore, the Ca<sup>2+</sup> mass balance was closed by adding a mathematical representation of the sarcoplasmic reticulum. Experimental calcium time courses (high time resolution, but spatially averaged) obtained under physiological conditions (35°C, 125 Hz stimulation frequency) were used for model validation.

The model showed that subtle changes in sarcomere microstructure influenced the local calcium concentration. Furthermore, local calcium concentration sensed by mitochondria was higher than average calcium concentration and also above the activation constant of the mitochondria, whereas the local concentration was not. Furthermore, the free Ca<sup>2+</sup> concentration was higher at the positions with troponin C than without troponin C.