

Spectral analysis of hypoxia-induced calcium waves in working rat heart reveal local hypercontracts as subcellular sources for damped high-frequency oscillations

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ABSTRACT Spectral analysis of hypoxia-induced calcium waves in isolated rat heart on the subcellular level reveal local hypercontraction sites as sources for high-frequency oscillations.

Key words: calcium waves, calcium overloading, cardiomyocytes, myocardium, ischemia, arrhythmia

INTRODUCTION

An intracellular accumulation of Ca²⁺ caused by a failure of the ATP-dependent mechanisms known to be the key events in myocardial damage during ischemia (1–3). In the process of damage progression functional myocardial tissue becomes Ca²⁺-overloaded and then lost functionality with the properties of Ca²⁺ waves changing progressively over time (4, 5). Now it is well acknowledged that Ca²⁺-overloaded cardiomyocytes are essential substrate for arrhythmias and contractile failure, especially in acute myocardial infarct.

Ca²⁺ dynamics at the border zones between the infarcted and non-infarcted myocardium is considered to be a key element for arrhythmogenesis (6). In this study, we applied the method of confocal microscopy and carried out a frequency analysis of calcium oscillations in cardiomyocytes from border zone between the necrotic and healthy myocardium. For optical registration of calcium waves. (7) Thanks for using Overleaf to write your article. Your introduction goes here! Some examples of commonly used commands and features are listed below, to help you get started. Leave a blank line between blocks of text to start a new paragraph—use \\ for separating tabular rows or hard line-breaks only. Abbreviations should be defined in the text at first mention.

Please also take note of the \section*{...} titles in this template: they are the required sections in a regular research Article manuscript.

In particular, the main text of regular Articles and Computational Tools manuscripts must be structured with the following sections: **Introduction, Materials and Methods, Results, Discussion (or Results and Discussion), Conclusion.**

Theoretical manuscripts may include just a **Methods** section and do not require **Materials**.

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MATERIALS AND METHODS

Capitalize trade names and give manufacturers' full names and addresses (city and state).

Sectioning commands

Use `\section*{...}` and `\subsection*{...}` to create first- and second-level headings. Sed ut perspiciatis unde omnis iste natus error sit voluptatem accusantium doloremque laudantium, totam rem aperiam, eaque ipsa quae ab illo inventore veritatis et quasi architecto beatae vitae dicta sunt explicabo.

Figures and Tables

Use the `table` and `tabular` commands for basic tables — see Table 1, for example. [TablesGenerator.com](#) is a handy tool for designing tables and generating the \LaTeX `tabular` code, which you can copy and paste into your article here.

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In addition, you can use `\ref{...}` and `\label{...}` commands for cross-references.

Table 1: An example table

Code	Item	Quantity
W1	Widgets ^a	42
G35	Gadgets	13 ^b

^a This is a table note.
^b This is another table note.

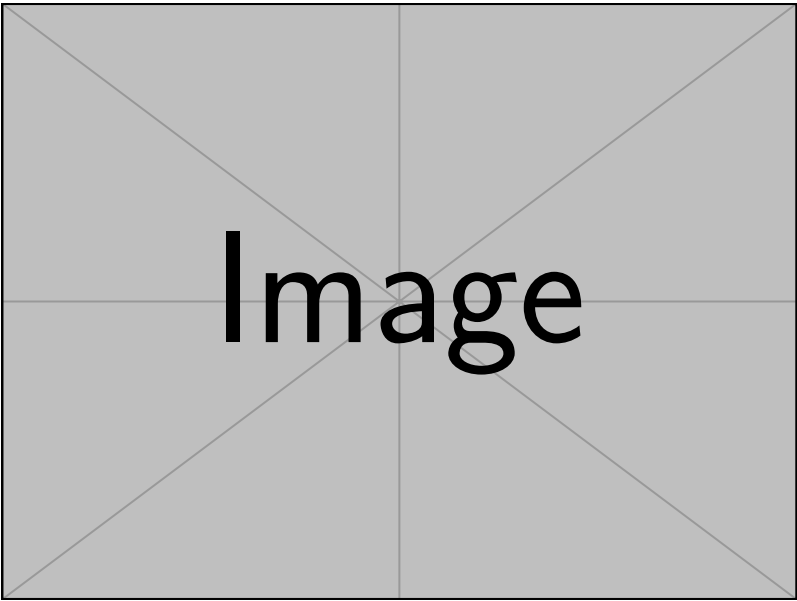


Figure 1: A figure example.

RESULTS

\LaTeX is great at typesetting mathematics:

Let X_1, X_2, \dots, X_n be a sequence of independent and identically distributed random variables with $E[X_i] = \mu$ and $\text{Var}[X_i] = \sigma^2 < \infty$, and let

$$S_n = \frac{X_1 + X_2 + \dots + X_n}{n} = \frac{1}{n} \sum_i^n X_i \tag{1}$$

denote their mean. Then as n approaches infinity, the random variables $\sqrt{n}(S_n - \mu)$ converge in distribution to a normal $\mathcal{N}(0, \sigma^2)$. Thus concludes the explanation about Eq. 1.

You can make lists with automatic numbering ...

1. Like this,
 2. and like this.
- ... or bullet points ...

- Like this,
- and like this.

... or with words and descriptions ...

Word Definition

Concept Explanation

Idea Text

An example quotation:

Lorem ipsum dolor sit amet, consectetur adipiscing elit, sed do eiusmod tempor incididunt ut labore et dolore magna aliqua. Ut enim ad minim veniam, quis nostrud exercitation ullamco laboris nisi ut aliquip ex ea commodo consequat.

DISCUSSION

L^AT_EX formats citations and references automatically using the bibliography records in your .bib file, which you can edit via the project menu. Use the `\cite` command to insert a citation, like this: (8) Multiple citations can be given as (9–11). You can use either BibTeX or biblatex; see the following subsections.

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Using bibtex

This is the default. Specify your .bib file with `\bibliography{sample}` (the extension is unnecessary) near the end of your manuscript, where you want the references list to appear.

Using biblatex

Pass the `biblatex` option to the `\documentclass` declaration, then specify your .bib file name in the *preamble*: `\addbibresources{sample.bib}` (the extension is necessary). Write `\printbibliography` near the end of your manuscript where you want the references to appear.

CONCLUSION

Sed ut perspiciatis unde omnis iste natus error sit voluptatem accusantium doloremque laudantium, totam rem aperiam, eaque ipsa quae ab illo inventore veritatis et quasi architecto beatae vitae dicta sunt explicabo.

AUTHOR CONTRIBUTIONS

Author2 designed the research. Author1 carried out all simulations, analyzed the data. Author1 and Author2 wrote the article.

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REFERENCES

1. Shen, A. C., and R. B. Jennings, 1972. Myocardial calcium and magnesium in acute ischemic injury. *The American journal of pathology* 67:417.
2. Shen, A. C., and R. B. Jennings, 1972. Kinetics of calcium accumulation in acute myocardial ischemic injury. *The American journal of pathology* 67:441.
3. Nayler, W. G., 1981. The role of calcium in the ischemic myocardium. *The American journal of pathology* 102:262.
4. Minamikawa, T., S. H. Cody, and D. A. Williams, 1997. In situ visualization of spontaneous calcium waves within perfused whole rat heart by confocal imaging. *American Journal of Physiology-Heart and Circulatory Physiology* 272:H236–H243.
5. Hama, T., A. Takahashi, A. Ichihara, and T. Takamatsu, 1998. Real time in situ confocal imaging of calcium wave in the perfused whole heart of the rat. *Cellular signalling* 10:331–337.
6. Takamatsu, T., 2008. Arrhythmogenic substrates in myocardial infarct. *Pathology international* 58:533–543.
7. Matsuura, R., S. Miyagawa, S. Fukushima, T. Goto, A. Harada, Y. Shimozaaki, K. Yamaki, S. Sanami, J. Kikuta, M. Ishii, et al., 2018. Intravital imaging with two-photon microscopy reveals cellular dynamics in the ischemia-reperfused rat heart. *Scientific reports* 8:15991.
8. Chen, K. C., and C. Nicholson, 2000. Changes in brain cell shape create residual extracellular space volume and explain tortuosity behavior during osmotic challenge 97.
9. Stiles, J. R., and T. M. Bartol, 2001. Monte Carlo methods for simulating realistic synaptic microphysiology using MCell. In E. D. Schutter, editor, *Computational Neuroscience: Realistic Modeling for Experimentalists*, CRC Press, Boca Raton, 87–127.
10. el Kareh, A. W., S. L. Braunstein, and T. W. Secomb, 1993. Effect of cell arrangement and interstitial volume fraction on the diffusivity of monoclonal antibodies in tissue. *Biophys. J.* 64:1638–1646.
11. Callaghan, P. T., 1991. *Principles of Nuclear Magnetic Resonance Microscopy*. Clarendon Press, Oxford, first edition.

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