

Integrative computational modeling of calcium handling and cardiac arrhythmias

Citation for published version (APA):

Sutanto, H. (2021). *Integrative computational modeling of calcium handling and cardiac arrhythmias*. Maastricht University. <https://doi.org/10.26481/dis.20210115hs>

Document status and date:

Published: 01/01/2021

DOI:

[10.26481/dis.20210115hs](https://doi.org/10.26481/dis.20210115hs)

Document Version:

Publisher's PDF, also known as Version of record

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.umlib.nl/taverne-license

Take down policy

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

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

Propositions

1. Cardiomyocyte calcium handling is the key determinant of excitation-contraction coupling in the heart and its dysregulation is strongly associated with cardiac arrhythmias (Chapters 1 and 2).
2. The subcellular distribution of cardiac ryanodine receptors modulates proarrhythmic cardiomyocyte calcium handling abnormalities independent of total protein expression or single-channel function (Chapter 3).
3. Calcium-dependent regulation of cardiac potassium channels can modulate arrhythmogenesis through the inhibition of triggered activity and stabilization of reentrant arrhythmias (Chapter 5).
4. The proarrhythmic effects of excessive alcohol or drug-induced ion-channel and calcium-handling abnormalities depend on both the underlying structural remodeling and acute electrophysiological conditions modulated by the autonomic nervous systems and electrolyte disturbances, explaining the dynamic occurrence of cardiac arrhythmias (Chapters 6 and 8).
5. Due to its complex interplay with major regulating proteins, cardiomyocyte calcium handling serves as a potential therapeutic target for cardiac arrhythmias.
6. Integrative clinical, experimental and computational studies provide a better understanding on the determinants, precipitating factors and pathophysiology of complex cardiac arrhythmias.
7. Multiscale computational modeling has undergone significant development in the past 80 years and is now able to provide novel mechanistic insights and assist both bench and bedside cardiac electrophysiology.
8. MANTA is a freely available educational tool to improve understanding of the complex cellular effects of antiarrhythmic drugs by employing the perfect control and observability of computational modeling.
9. All models are imperfect, but they are nonetheless useful. (adapted from a quote by George P. Box)
10. With four parameters I can fit an elephant, and with five I can make him wiggle his trunk, but even with thousands of parameters, I cannot make him alive. (adapted from a quote by John von Neumann)
11. *“Science cannot solve the mystery of nature. And that is because, in the last analysis, we ourselves are a part of the mystery that we are trying to solve.”* – Max Planck