The following handle holds various files of this Leiden University dissertation: http://hdl.handle.net/1887/67391

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Appendix

LETTER BY HOUSTON ET AL REGARDING ARTICLE, “LOCALIZED OPTOGENETIC TARGETING OF ROTORS IN ATRIAL CARDIOMYOCYTE MONOLAYERS”

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TO THE EDITOR

We read with great interest the article by Feola and colleagues on investigating the mechanisms of rotor-guided ablation through optogenetic stimulation in monolayers of neonatal rat atrial cardiomyocytes. The authors optically map single stable rotors which could be reliably initiated in their homogeneous monolayers, and report on the success rate of different light ablation approaches to terminate the rotors by localized conduction block.

We previously studied similar rotor activity using high spatiotemporal resolution optical mapping in monolayers of functionally homogeneous atrial murine cells (HL1-6 myocytes). At similar mapping resolutions to this work, we also observe apparent spiral waves characteristic of rotor theory. Upon mapping the cores of our rotors at higher single-cell resolution (2.6x2.6μm per pixel), we found that the activity was instead driven by microreentry around lines of conduction block/slowing with lengths 200-800μm (http://wwwf.imperial.ac.uk/imedia/content/view/6049. Houston C, MRes, Dupont E, PhD, unpublished data, 2017). These lengths correlate with the regularity of the macro spiral wave, and contrast the view that the cores are round areas of excitable but unexcited cells as rotor theory postulates. Although a different functionally homogeneous biological model, we expect that similar microreentrant mechanisms drive the activity in this study.

The authors reported that their light-based S1-S2 protocol was reliable in initiating stable rotor activity at predetermined locations. Have the authors used their technique to study the core of rotors at higher resolution? In-silico studies of spiral waves in nraCMC monolayers suggest that microscopic heterogeneity is necessary for stable rotors. Our results similarly suggest that microscopic heterogeneity in electrical coupling or cell volume may lead to particular sites being susceptible to microreentry. If this is the case, we would expect rotors to reappear in the same location and with similar dynamics following termination. Was an attempt made to reinitiate a rotor using the same protocol following previous rotor termination? Do new rotors present the same spatial and temporal characteristics observed prior to termination?

Lastly, we would like to commend the authors for using a two-dimensional model of reduced complexity in studying the mechanisms of rotor-guided ablation; we fully support the application of biological models in laying foundations for future research across the translational spectrum.

DISCLOSURES

None.
REFERENCES


