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An In Silico Hexagonal Model of Myocardial Fibrillation

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1. Introduction

The overarching goal of computational studies in this area is to aid detection and treatment of cardiac arrhythmia. This project aims to achieve a better understanding of how structural heterogeneity in the coupling space of a hexagonal lattice affects charge propagation and the induction of continuous activity (CA). Results from this project will aid future similar studies.

This aim was achieved through the development of a model that simulates the beating of the heart via the propagation of charge on a discrete 2D hexagonal lattice [1]. We vary the model parameters to get results about how the induction of continuous activity is affected by changes in local coupling space.

2. Key Definitions

Continuous activity (CA) – Our lattice-based equivalent of Fibrillation. It exhibits as self-sustaining activation across a portion of the lattice. A lattice in this state is shown in Fig. 1.

Reentrant circuit – A complete circuit (contains a cell from each phase) of cells which are continuously activated. A key driver behind CA.

Percolation – A wavefront percolates if it can travel the entire width of the lattice and activate at least one edge cell .

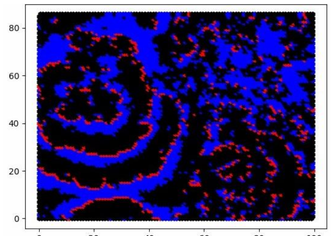


Fig 1: A lattice showing continuous activity

3. The model

The model is made up of a discrete lattice of hexagonal unit cells. Each cell is identical with bonds to all its neighbours. These bonds are filled with some pre-determined probability. Charge is instigated in all the cells on the left-most boundary and passes through the lattice according to a set of rules described in Fig. 2. When a cell receives charge, it has a probability to activate based on how much charge it receives. The activation function is shown in Fig. 3. In images of the model, activated sites are displayed in red, resting sites in blue and refractory sites in black.

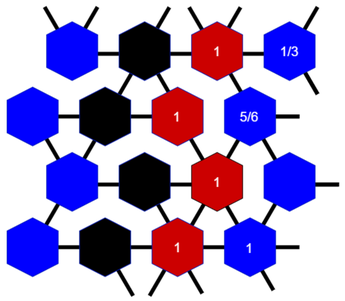


Fig 2: Example of charge propagation rules in our model. When activated (red), a cell passes on a total of *1* charge split between its applicable neighbours.

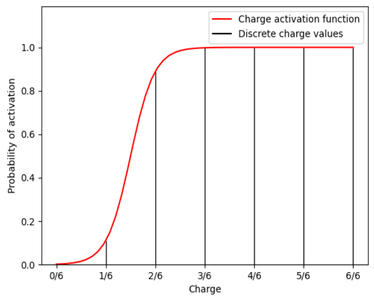


Fig 3: The sigmoid activation function sampled at the discrete charge values regularly seen on a hexagonal lattice.

References

[1] Ciacci A, Falkenberg M, Manani K, Evans T, Peters N, Christensen K. Understanding the transition from paroxysmal to persistent atrial fibrillation. Physical Review Research. 2020;2(2).

[2] Christensen K, Manani K, Peters N. Simple Model for Identifying Critical Regions in Atrial Fibrillation. Physical Review Letters. 2015;114(2).

4. The Lattice

We implemented our model on a 100 cell by 100 cell hexagonal lattice structure. We have enforced a cylindrical geometry within our lattice, i.e. continuous in the $\hat{y}$ direction and discontinuous in the $\hat{x}$ direction. This geometry removes any edge effects that would occur, and allows us to properly analyse the propagation of activation wavefronts through the lattice.

The introduction and management of structural heterogeneity is pivotal for our investigations. We decided to use the following 2D sinusoid to generate our coupling space:

$$\frac{\text{Amplitude}}{2} \times \left[\sin\left(\text{A}\frac{2\pi x}{\text{width}}\right) + \sin\left(\text{A}\frac{2\pi y}{\text{height}}\right)\right] + \text{ Offset}$$

where *x* and *y* are the cartesian coordinates of the position on the lattice and *A* is the frequency of the sinusoid. We have enforced periodic boundary conditions in the *x* and *y* plane to ensure our spaces are repeatable and comparable. *A* can also be thought of as the number of maxima of one of the 1D sinusoids which have been superposed.

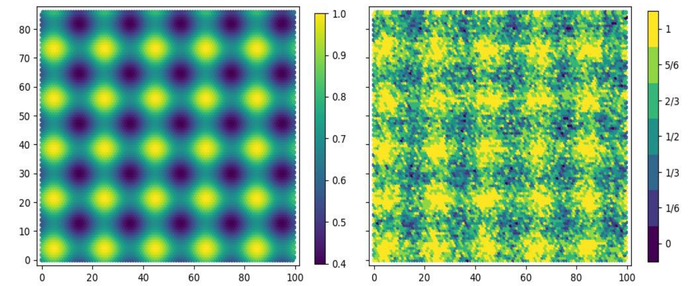


Fig 4: The coupling space (left) and a corresponding sample (right). Offset = 0.7, Amplitude = 0.3, A = 5. The colour bar indicates the coupling fraction at a given site (i.e. 1 = fully coupled).

For each realisation of our model, the probability of a bond existing between two lattice sites is measured by sampling the 2D sinusoid at the position of the midpoint of the bond. This results in a stochastic sample of our coupling space and allows us to generate many different architectures for the same space; an example of which is shown in Fig. 4.

5. Phase Space

We investigated the probability of inducing CA for various lattice conditions by changing the offset, amplitude and *A* of the coupling space.

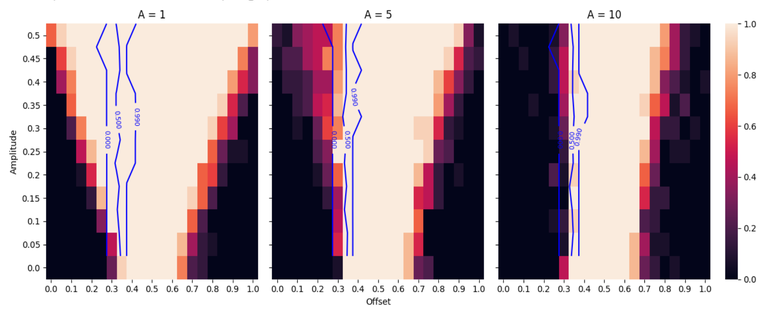


Fig 5: Phase spaces in offset and amplitude for varying *A*. The colours in the colour bar correspond to the fraction of simulations that resulted in CA. The blue contours represent the fraction of simulations that percolated.

As *A* Increases, two main changes occur. The left triangle below the percolation threshold disappears. This is because the regions of higher coupling get smaller and are therefore no longer able to sustain activity. The right triangle, starting at an offset of 0.7, begins to recede. The reasoning behind this is linked to the roughness of the wavefronts.

6. Induction Locations

With a focus on areas in the phase space where CA was induced over 99% of the time (i.e. offset = 0.5, amplitude = 0.2), we investigated the dependence of CA induction probability on the position within the lattice, for a range of *A* values. Fig. 6 shows the result of these investigations for *A =1* and *A = 5*.

As seen in Fig. 6, CA is more likely to be induced in locations which have a lower value of local coupling. This is because there is a higher probability that the wavefront can form a reentrant circuit, which are a known driver of CA and have been observed in our system. This highlights the regions which should be targeted for ablation-based treatment methods.

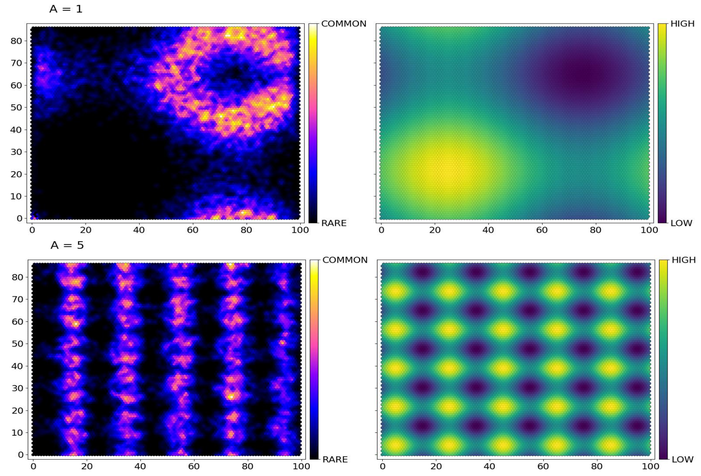
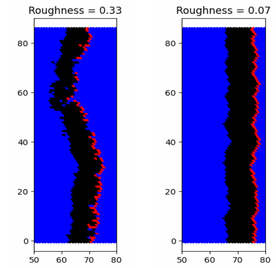


Fig 6: Heatmaps of the position in the lattice where CA is most likely to be induced (left) and its corresponding coupling space (right). For *A = 1* and *A = 5*. A bilateral filter has been applied to the heat maps.

7. Roughness of the Wavefront



For CA to be induced in the lattice, the wavefront must break up and a reentrant circuit form. We attempt to quantify the level at which the wavefront has broken up and attach a probability of CA forming from this. To do this, we measure the 'roughness' of the wavefront which is found using the standard deviation of the *x* position of all activated sites, divided by the number of activated sites. The hypothesis is that the larger the roughness of the surface, the higher the probability that CA will be induced.

Fig 7: Wavefronts with varying roughness and stability.

8. Conclusion

We have successfully implemented our model to study the impact of structural heterogeneity on the charge dynamics in a hexagonal lattice. We have highlighted regions in our coupling phase space which are more sensitive to inducing CA, and have identified regions on the lattice which are prone to inducing CA.

We aim to further investigate the implications of the roughness of the wavefront and its effects on the inducibility of CA. Moreover, the dependence of the Induction Locations on other model parameters (e.g. offset, amplitude) needs to be investigated. In general, using a complexity science approach to study the critical behaviour behind cardiac arrythmias can help us to qualitatively understand the phenomena [2] – this model is a further step to achieve those goals.