# A Modified Fitzhugh-Nagumo Model that Reproduces the Action Potential and Dynamics of the Ten Tusscher *et. al* Cardiac Model in Tissue

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## Abstract

*The two-variable Fitzhugh-Nagumo (FHN) model is widely used due to its simplicity; however, it lacks many of the dynamics observed in cardiac experiments that can be reproduced by complex ionic cell models, such as the 19-variable Ten Tusscher et. al (TNNP) model. We aim to parameterize a modified version of the FHN model that reproduces the dynamics in space of more complex cardiac cell models. We combined a series of modifications that previously were applied to the FHN model – mainly, the addition of a nullcline at zero voltage for the fast variable, that eliminates the hyperpolarization of the traditional FHN model and the modification of the slow nullcline from linear to quadratic, which allows alternans behavior and a better fit to experiments and other models. This new model is fitted using particle swarm optimization (PSO) to fit the action potential for a large number of pacing periods so that the restitution of the action potential is matched between the two models. We created a modified FHN model that matches most of the AP shape of the TNNP model for a large range of periods and dynamics in space. This model allows for faster proof of concept investigations that can then help guide the more time-consuming simulations with complex ionic models.*

## 1. Introduction

The 19-variable Ten Tusscher *et. al* (TNNP) model [1] is one of the most commonly used models for detailed electrophysiological studies as it enables researchers to reproduce many detailed properties of a single human ventricular cell resulting from ionic currents and intracellular calcium dynamics, and is able to exhibit properties of the wave propagation in human ventricular tissue such as the action potential duration (APD) and conduction velocity (CV) restitutions. However it can be very computationally demanding for large scale studies, such as those which simulate 3D ventricles.

In the realm of more simplistic models, the FHN model — a valuable precursor to more complex models — stands out due to its wide application in many studies of nerve, heart and excitable media in general. However, it is deficient compared to focused cardiac models due to its simplicity, which includes the lack of "spike-and-dome"morphology of the cardiac action potential that appears in some types of cardiac cells such as epicardium and mid-miocardium. Perhaps more importantly, it cannot study the effects of drugs or mutations that interact with ion channels and FHN was not designed to fit experimental data or other numerical models.

However recent improvements on the FHN model such as those shown by Eq (1) have been made in order to more accurately describe the cardiac action potential and to enable the model to be fitted to experimental data [2]. With these modifications, even when the FHN model can not directly reproduce specific cardiac cell effects, it can be fitted to data resulting from changes to the ion channels. The resulting fit can perform preliminary exploratory studies of various hypotheses, that are far less computational intensive, before using the more complex models for validation of these studies.

$$\begin{aligned} \frac{\partial u}{\partial t} &= D\nabla^2 u + \mu u(1-u)(u-\alpha) - vu \\ \frac{\partial v}{\partial t} &= \epsilon((\beta - u)(u-\gamma) - \delta v - \theta) \end{aligned} \tag{1}$$

This manuscript provides a blueprint for mapping the modified FHN model, Eqn (1), to the TNNP model. By doing so, we have created a parameter set which closely reproduces the APD restitution curve as well as the general shape of the action potential for the TNNP model. This parameterization allows for faster computational investigation of cardiac cells and tissues before embarking with the use of the more complex ionic cell models.

## 2. Methods

Two-dimensional TNNP simulations were run on an altered version of the code constructed by Abuzar Kaboudian in WebGL [3–5], which creates a spiral wave in tissue in accordance with the TNNP model. The alterations made allowed us to pace in a single cell, pace in tissue, record conduction velocity, and pace in the presence of an obstacle such as scar tissue. Additionally, we modified the code to record the action potential signal at a chosen probed point as a function of time.

The properties of the action potential (AP) morphologies and restitution curves were meticulously matched using the PSO (particle swarm optimization) [6] algorithm for several action potentials at different pacing frequencies. The PSO algorithm is derivative of swarming behavior seen in a flock of birds [7]. The algorithm works by beginning with a random set of initial conditions, in our case, initial voltages and searching for the global best fit to the data given. Each particle, or data point has both a best individual voltage and a best global voltage to track. Movements of these particles are guided by their best individual and global voltages as described by Zhang et. al. [8].

We supplied this algorithm with simulated data from the TNNP model. Once a fit is obtained, a new set of initial conditions are obtained and the fit is repeated recursively for increased accuracy. The PSO program we used employed increments of 32 iterations at a time. We then compared the modified FHN model to the original TNNP data fed into the algorithm. To ensure a good fit for cardiac tissue, we used data from multiple cycle lengths in our PSO algorithm.

After a fit was created by PSO it was tested in single cell pacing to see if the fit's single cell restitution curve at 75% fit the TNNP model. Once a match was found here, we simulated the fit in WebGL, using Kaboudian's library and TNNP code as a reference [3–5]. The action potentials of both the FHN fit and the TNNP fit were recorded and compared. Once a fit passed these stages, the CV and action potential of a plane wave were recorded in both TNNP and the FHN fit. This allowed us to make a restitution curve of the conduction velocity. This allowed for appropriate adjustments to be made to the model parameters in order to replicate the TNNP CV, spiral wave behavior, and scar tissue reaction.

## 3. Results

The resulting fit can be seen in Equation 2:

$$\begin{aligned}\frac{\partial u}{\partial t} &= D\nabla^2 u + 1.475u(1-u)(u-0.203) - vu \\ \frac{\partial v}{\partial t} &= 0.005((1.63-u)(u-0.325) - 1.403v + 0.095)\end{aligned} \tag{2}$$

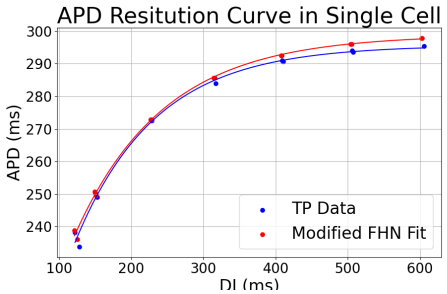


Figure 1. The single cell restitution curve of the TNNP and the modified FHN models.

The fit was made by PSO to match the restitution curve and AP shape in a single cardiac cell of the TNNP model as seen in Figure 1. The particular parameters that made this fit a good in tissue candidate were $\alpha$, $\beta$, $\mu$, and $\gamma$. These values correlate directly (except for $\alpha$ which correlates inversely) with the APD in tissue and the CV. Since the TNNP model has a larger action potential than typically seen in the FHN model and a faster conduction velocity, it was critical to match these variable with initial conditions starting at their maximum (or in the case of $\alpha$ the minimum) allowed values. The in-tissue results of the fit can be seen in Figures 4 and 5.

The accurate in-tissue results obtained by the fit allowed us to find the appropriate diffusion and time scale to allow the modified FHN model to mimic the TNNP model. While doing this we wanted to ensure that our solution for propagation was the same and did not crash our simulation. To obtain both results we scaled the diffusion constant, $D$, up by a factor of 9 and the $dt$ down by a factor of $\frac{1}{9}$. This allowed for us to effectively zoom in on the correct scale of the modified HFN model so its variable speeds could match that of the TNNP model.

This resulted in the CV restitution curve seen in Figure 6 and the spiral wave seen in Figure 3. For the spiral wave the modified FHN model has a rotation period of approximately $252ms$ while the TNNP model has a rotation period of approximately $231ms$.

Additionally, the new fit for TNNP was tested around scar tissue to ensure the model behaved the same as the TNNP model. The resulting test can be seen in Figure 7. The same characteristic double arch pattern seen in the TNNP model by Costa et. el. [9] and Figure 8 is seen in Figure 7. Furthermore, we included a representation of the

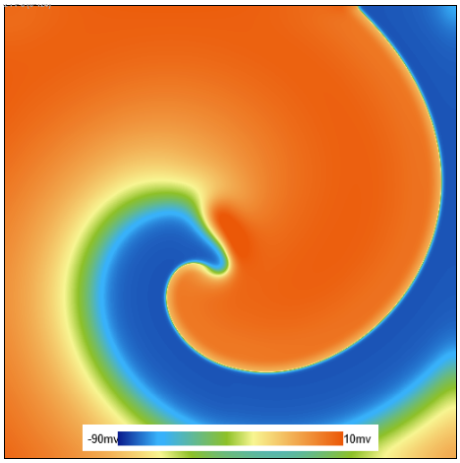


Figure 2. A spiral wave in the TNNP model.

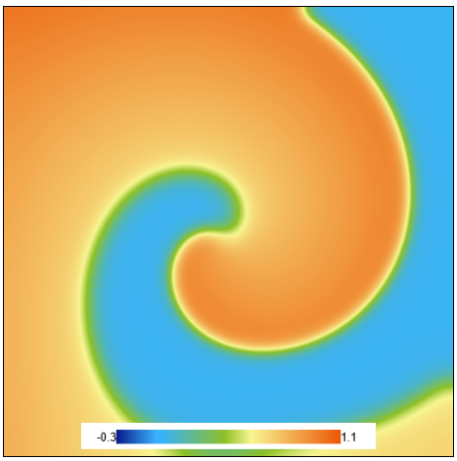


Figure 3. A spiral wave in the modified FHN model.

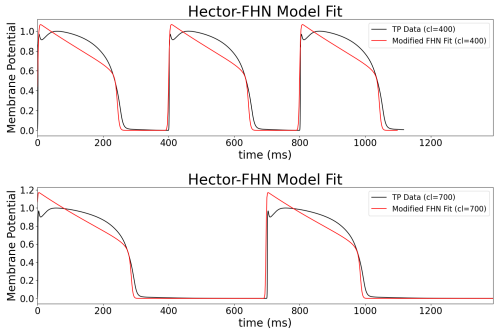


Figure 4. The in-tissue action potential of the TNNP and modified FHN models at a cycle length of $400ms$ (top) and $700ms$ (bottom).

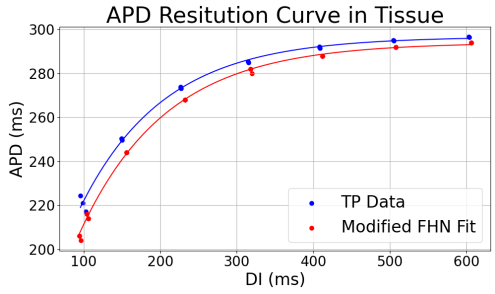


Figure 5. The in-tissue restitution curve of the TNNP and the modified FHN models.

boarder zone to demonstrate that the action potential behaved the same in the boarder zone as well. The boarder zone in a naturally occurring regime of tissue around a scar where the APD is reduced by a damping coefficient, $\rho$. Here we use $\rho = 0.5$ as a proof of concept that the modified FHN fit will behave similarly to the TNNP. Within

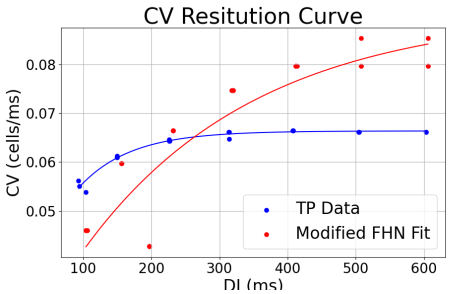


Figure 6. The conduction velocity restitution curve of the TNNP and the modified FHN models.

the boarder zone we are able to see the triangulation of the action potential in both models. We used the same ratios for the dimensions of our tissue and boundary zone as the study done by Costa et. al. [9].

## 4. Discussion

The modified FHN fit has strengths and limitations. It can be used to replicate the action potential of the TNNP model, ensuring that the fit makes a good restitution curve. However, the fit goes into conductance block at a cycle length of $300ms$, where as the TNNP goes into conduction block at a cycle length of $320ms$. Both the fit and the TNNP model show bifurcation at a cycle length of $320ms$ in tissue and $360ms$ in single cell. The fit is additionally able to recreate the spiral wave dynamics seen in the TNNP model as well as respond similarly to scar tissue.

The fitted modified FHN model is far from perfect though. Due to the massive reduction in information on the ion channels that is inherit with the FHN model, the fit cannot perfectly imitate the TNNP model. The main limitation of the modified FHN fit is the CV restitution. As

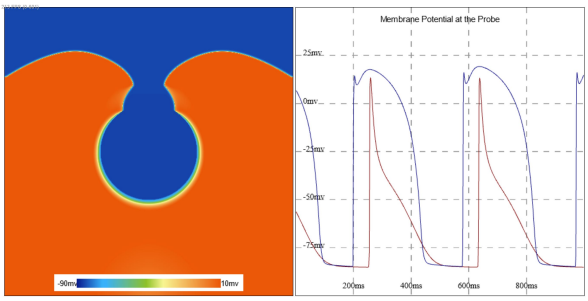


Figure 7. The TNNP model propogating around scar tissue. Two probes are station, one far away from the scar tissue in the lower right corner (blue) and one inside the boarder zone (red). The scar tissue is set up as an insulator forcing the diffusion coefficient to be 0 and the voltage to be at resting membrane potential.

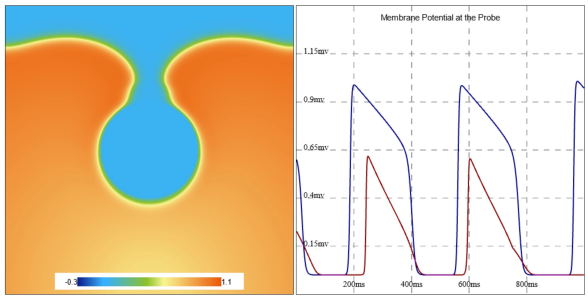


Figure 8. The modified FHN fit propogating around scar tissue. The same two probes were set up as in the TNNP model. This model clearly demonstrates both the warping of the action potential wave as it passes through the boarder zone and the double arch dynamics of the wave as it passes aroud the scar tissue that are seen in the TNNP model.

seen in Figure 6, the CV of the TNNP model has a shallow slope and large fluctuations. The modified FHN fit on the other hand has smaller fluctuations, but a significantly steeper slope. Further more, with our particular fit, the alternans are more pronounced in the TNNP model than in the modified FHN model.

Some interesting dynamics to try with the modified FHN fit that we did not have time for would be to vary the different ion channels in the TNNP model and see which of the FHN parameters correspond to said variations. This would allow for precursor computations of the FHN model to be run in order to test hypotheses before a detailed investigation is made.

## 5. Conclusion

The TNNP fit of the modified FHN equations discussed in this paper is capable of replicating the action potential shape and restitution in single cell and tissue dynamics. In tissue, the fit is limited by its conduction velocity, but can mimic the remaining dynamics of spiral waves. The fit responds similarly to the TNNP model around scar tissue and within the boarder zone.

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