**A Parsimonious Model of the Rabbit Action Potential Elucidates the Minimal Physiological Requirements for Alternans and Spiral Wave Breakup**

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**SUPPLEMENTARY MATERIAL**

1. Cell versus tissue (propagation) dynamic I-V curves
2. Parameter sensitivity analysis
3. Comparison with previous experimental results
4. Movie legends
5. Cell versus tissue (propagation) dynamic I-V curves

We fit the dynamic I-V curves of single cells (Fig. 1B) and from the whole heart during propagation to fifth order polynomials with R2 = 0.99 and R2 = 0.97, respectively. These fits are shown in **Figure A** (myocyte: solid line; tissue; dashed line) along with their 95% confidence intervals (corresponding thin lines).



**Figure A**

1. Parameter sensitivity analysis for “Parsimonious Rabbit “(PR) model

We performed two parameter sensitivity analyses. First we quantified the effect of varying eight parameters on eight quantities of interest (QOIs) as shown as an 8x8 matrix in **Table A**. Second, we also characterized the effect of repolarization parameters  and  on certain cell and tissue-level behavior by running simulations while varying them to cover the entire “physiological range” for all mammals (see **Figures B & C**).

We choose the following eight QOIs (2 cellular, 0D, and 6 corresponding to propagation, 1D): , , , , , , , and , where  is conduction velocity, ,  is the time interval between the maximum and minima of , and  is % recovery of at RT=0.8 ms[1]. Specifically, we adjusted each parameter individually by ±0.5% and computed the corresponding % change in each QOI; the corresponding 8x8 matrix is provided in **Table A**. Here we list the combinations that had an “amplifying” effect (i.e, > 1% change in QOI): : , ,; : , , ; :, ; : , ,; :  , ; : , , ; : , .  parameters and had the largest effect on model predictions; recall that  influences the voltage dependence of the inactivation time constant (see Eqn, (6)); the % change in 7/8 QOI were smaller when was modified in  (Eqn. (5)) but not in  (Eqn. (6)) as seen in **Table A**. This highlights the important role of the *voltage dependence* of  (not so much its scaling). It should be noted that in many cases the representation of in HH models is extrapolated an order of magnitude near  where data is especially sparse (see Fig. 1D in Ref #[2]; Fig. S1E. in Ref[3]).

Table S1: Parameter sensitivity matrix for PMR model

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **QOI ->**  **parameter** |  |  |  |  |  |  |  |  |
|  | 0.663 | 0.379 | 0.585 | 0.558 | 0.287 | 0.661 | -0.355 | 0.108 |
|  | **1.106** | 0.352 | 0.523 | 0.600 | 0.870 | **1.055** | -0.709 | 0.233 |
|  | 0.057 | -0.016 | 0.036 | 0.016 | 0.020 | 0.081 | -0.177 | 0.050 |
|  | -0.444 | -0.100 | -0.524 | -0.272 | -0.321 | -0.693 | 0.532 | 0.086 |
|  | **-2.944** | **-3.010** | **-1.823** | **-4.131** | **-1.018** | **-2.36** | 0.887 | **-6.706** |
|  | 0.451 | **2.086** | 0.070 | **3.023** | 0.207 | 0.486 | 0.00 | 0.240 |
|  | 0.413 | 0.651 | 0.146 | 0.840 | 0.109 | 0.254 | -0.177 | -0.340 |
|  | **2.377** | **8.627** | 0.817 | **12.537** | **1.08** | **2.539** | -0.354 | 0.639 |

% change in QOI for a 1% change in parameter

We considered the two reversal potentials ( and) as “environmental parameters” because they are determined by the temperature and ion concentrations inside and outside the cell, and did not include them in the above analysis.

We also characterized the effect of repolarization parameters  and  on certain cell and tissue-level behavior for our new PR model by running simulations while varying them over the entire “physiological range” for all mammals: reported values of  range from 0.1 to 0.5 mS/F and the range of values chosen, 0.03  0.05 mV-1 as shown in **Figure B**. Over this range, the values of action potential duration () vary between 23 and 516 ms (**Figure C**) and ranges from to -6.1 to -0.74 μA/cm2 (data not shown), while the depolarization properties change very little (**Fig.B**). Hence, this choice of  and  encompasses a large range of repolarization behavior. Example action potentials are shown in **Fig. C**. We performed this analysis to determine if coupling our ionic model to our phenomenological  model would adversely affect the ability of the cell model to reproduce the cellular depolarization process that the model was designed to reproduce.



 

 



**Figure B**



**Figure C**

1. Comparison with previous experimental results

Table B. Selected Experimental Results: Adult New Zealand rabbit (temperature: 36±1 C)

|  |  |  |  |
| --- | --- | --- | --- |
| **QOI** | **Unit** | **PR**  **value** | **values from literature: mean**± **SEM (BCL) [citation #]** |
| myocyte (M) |  |  | Microelectrode recordings |
|  |  | -83 | -84.6 ± 0.5 [4]; -82.8 ± 0.7 [5]; -82.7 ± 0.4 [6]; -82.4 ± 0.6 [7]; -81.4 ± 1.3 [8]; -81.3 ± 0.2 [9]; -81 ± 2 [10]; -78.8 ± 2 [11] |
|  |  | 117 | 114 ± 1 [7]; 117 ± 4 [4]; 121 ± 3 [11]; }; 122 ± 8 [8];  127 ± 1 [6]; 127 ± 3 [10] |
|  |  | 233 | 113 ± 8 [7]; 146 ± 18 [4]; 309 ± 11 [5]; 395 ± 21 [6] |
| tissue (T) |  |  | floating microelectrode and extracellular mapping (CV) |
|  |  | -83 | -85 ± 1 [12]; -83 ± 1 [13]; -82 ± 1 [14];  -81.7 ± 0.6 [15]; -81 ± 3 [16] |
|  |  | 107 | -95 ± 1 [13]; 106 ± 2 [16]; 118 ± 2 mV [12]; 120 ± 2 [14] |
|  |  | 55 | 50 ± 6 (300) [17]; 55 ± 0.3 (250) [18];  61 ± 2 (350) [19]; 67 ± 4 (250) [15] |

\* NOT comprehensive

RMP: resting membrane potential

APA: action potential amplitude

CV: conduction velocity

1. Movie legends

**Gray\_Fig6\_gk3\_b045\_2d.avi**. Spiral wave dynamics  and .

**Gray\_Fig6\_gk5\_b035\_2d.avi**. Spiral wave dynamics  and .

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