A Mechanism for QRS Amplitude Alternans in Electrocardiograms and the Initiation of Spatiotemporal Chaos

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(Dated: August 1, 2016)

It is widely believed that the life-threatening transition to chaotic fibrillation occurs via spiral-wave breakup (SWB) that is preceded by spatio-temporal dispersion of refractoriness due to alternations in the duration of the cardiac action potential (AP). However, recent clinical and experimental evidence suggests that other characteristics of the AP may contribute to, and perhaps drive this dangerous dynamical instability. To identify the relative roles of AP characteristics, we performed experiments in rabbit hearts under conditions to minimize AP duration dynamics which unmasked pronounced AP amplitude alternans just before the onset of fibrillation. We used a simplified AP ionic cell model to derive a return map and a stability condition that elucidates a novel underlying mechanism for AP alternans and SWB. We found that inactivation of the sodium current is key to develop amplitude alternans which is directly connected to conduction block and initiation of arrhythmias. Simulations in 2D in which AP Amplitude (APA) led to SWB confirm our hypothesis. Our results suggest novel approaches for preventing the dangerous transition to fibrillation.

I. SUPPLEMENTARY MATERIALS

Due to lack of space, we will write the parameter values for the two 2-variable models in this document.

A. Model 1

The equations for the minimum Model 1 are

$$\begin{aligned} I_{Na} &= \begin{cases} -h(V-V_C)(1-V)/\tau_{Na}, & V \geq V_C\text{mV} \\ 0, & \text{otherwise} \end{cases} \\ I_K &= \begin{cases} 1/\tau_{K1}, & V \geq V_C\text{mV} \\ V/\tau_{K2}, & \text{otherwise} \end{cases} \\ \frac{dh}{dt} &= \begin{cases} -h/\tau_h^+, & V \geq V_C\text{mV} \\ (1-h)/\tau_h^-, & \text{otherwise} \end{cases} \\ \tau_h^- &= \begin{cases} \tau_{h1}^-, & V \leq V_h\text{mV} \\ \tau_{h2}^-, & \text{otherwise} \end{cases} \end{aligned} \tag{1}$$

PARAMETER TABLE FOR MODEL 1

The following table gives the values for Model 1,

τ_{Na}	0.572	τ_{k1}	450
τ_{k2}	120	τ_h^+	7
τ_{h1}^-	580	τ_{h2}^-	1280
V_C	0.13	V_h	0.04

B. Model 2

Model two, which is also a 2-variable model, has slightly more complex structure as to reproduce additionally the experimentally measured membrane voltage from rabbit hearts perfused with low calcium Tyrode's solution.

The equations for model 2 are where:

$$\begin{aligned} I_{Na} &= g_{Na} m_\infty^3 h (V - E_{Na}) \\ I_k &= \begin{cases} I_{k1}, & V > -65\text{mV} \\ I_{k2}V + I_{k3}, & \text{otherwise} \end{cases} \\ \alpha_h &= \alpha_1 e^{\alpha_2(V+\alpha_3)} \\ \beta_h &= \beta_1/(e^{\beta_2(V+\beta_3)}+1) \\ h_\infty &= \alpha_h/(\alpha_h+\beta_h) \\ m_\infty &= \begin{cases} e^{\mu_1 V} + \mu_2 e^{\mu_3 V}, & V \geq -83\text{mV} \\ 0, & \text{otherwise} \end{cases} \\ \tau_h' &= \begin{cases} \tau_1 V + \tau_2 & V \leq -67\text{mV} \\ \tau_3 V + \tau_4 & -67\text{mV} < V \leq -40\text{mV} \\ \tau_5 & -40\text{mV} < V \leq 5\text{mV} \\ \tau_6 & \text{otherwise} \end{cases} \\ \frac{dh}{dt} &= \left\{ \frac{h_\infty - h}{\tau_h'} \right. \\ \frac{dV}{dt} &= \begin{cases} -I_{na} - I_k + I_{stim}, & V \geq -84\text{mV} \\ V = -84, & \text{otherwise} \end{cases} \end{aligned} \tag{2}$$

PARAMETER TABLE FOR MODEL 2

The following table gives the values for Model 2. Images relating to Model 2 appear in the entire paper in most figures,

α_1	0.126	α_2	-0.25
α_3	77	μ_1	$4.5 \cdot 10^{-5}$
μ_2	$-9 \cdot 10^{-4}$	μ_3	-0.083
β_1	1.7	β_2	-0.082
β_3	22.5	τ_1	109.848
τ_2	9257.576	τ_3	-69.217
τ_4	-2743.182	τ_5	20.2
τ_6	37.879	E_{Na}	50
I_{k1}	0.396	I_{k2}	0.0135
I_{k3}	1.155	g_{Na}	0.0792