Fitzhugh-Nagumo Proposal (Addendum 1)

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1 Model Coupling

1.1 Coupled Oscillators

Starting with the Fitzhugh Nagumo model equivalent

$$\frac{dV}{dt} = V(\alpha + V)(1 - V) - W + z \tag{1}$$
$$\frac{dW}{dt} = \beta V - cW \tag{2}$$

We connect connect oscillators with a gap junctional current ($I_g = G_g(\Delta V)$). For a population of n oscillators Ω, with members $\omega_i; i \in \mathbf{N}; 1 \leq i \leq n$. If ω_i is connected to $x; x \subset \Omega$, then the gap junctional current to ω_i is $\sum_x G_{x,i}(V_i - V_x)$

In the case of 2 oscillators (A and B)

$$\frac{dV_A}{dt} = V(\alpha + V_A)(1 - V_A) - W_A + G_g(V_A - V_B) + z_A \tag{3}$$
$$\frac{dV_B}{dt} = V(\alpha + V_B)(1 - V_B) - W_B + G_g(V_B - V_A) + z_B \tag{4}$$
$$\frac{dW_A}{dt} = \beta V_A - cW_A \tag{5}$$
$$\frac{dW_B}{dt} = \beta V_B - cW_B \tag{6}$$

1.2 Diseased States

For the coupled oscillators representing cardiac myocytes (eq. 3-6), as the cells die through an apoptotic pathway, a fraction of their gap junctions $\nu \in [0, 1]$ will be destroyed, through cell decay.

In order to model disease, each myocyte will have a corresponding ν term, such that

$$\frac{dV_A}{dt} = V(\alpha + V_A)(1 - V_A) - W_A + (1 - \nu_A)G_g(V_A - V_B) + z_A \tag{7}$$
$$\frac{dV_B}{dt} = V(\alpha + V_B)(1 - V_B) - W_B + (1 - \nu_B)G_g(V_B - V_A) + z_B \tag{8}$$

With increasing ν, the cell becomes less responsive to its coupled partners

1.3 Disease Progression

In order to model disease progressing over time, we need to model the progression of ν. Since apoptosis is unidirectional (once started it will not end). We can model ν as assymptotically stable to one, and unstable at 0.

$$\frac{d\nu}{dt} = \gamma\nu(\nu - 1); \gamma<0 \tag{9}$$

Which fits the biological model, with controllable rate γ