Modelling the AV Electric Potential of the Cardiac Cycle

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We use a simplified mathematical model to reproduce the periodic changes of the electric potential in the atrioventricular node. The model is used to recreate both regular and irregular heartbeat patterns based on variation of model parameters and input signals from the sinoatrial node, including the Wenckebach phenomenon and the second-degree block.

I. INTRODUCTION

Understanding the cardiac cycle is integral to the diagnosis and treatment of irregular heart conditions. For centuries, perhaps one of the most useful tools for such diagnoses has been a person's pulse, an indication of their heartbeat and consequently their cardiac health. Heart rate is often measured in beats per minute (bpm) and the average adult has a rate between 60 - 100 bpm [1]. In a simplistic model of a heart, the rate at which your heart beats is controlled by two mechanisms: the sinoatrial (SA) node and the atrioventricular (AV) node.

The SA node is the heart's biological pacemaker; it sets the pace at which the heart beats by sending regular pulses to the AV node. The AV node discriminates the acceptance of pulses through a decaying electric potential, where if the potential is sufficiently low, the AV node accepts the pulse and the heart beats through contraction of the Purkinje fibres.

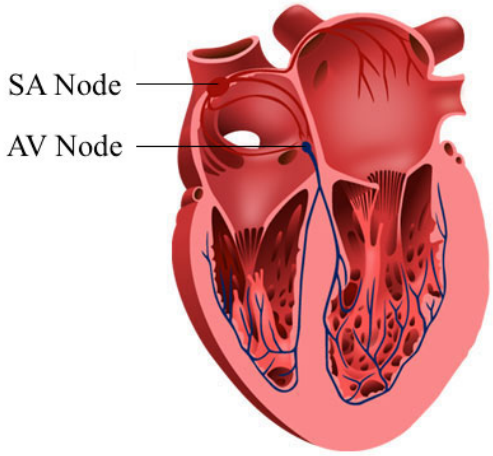

FIG. 1: The locations of the SA and AV nodes, adapted from the University of Southern California, Department of Surgery (http://www.surgery.usc.edu/cvti/z-glossary-avnodeablation.html)

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People have been trying to mathematically model this process since at least the 1960's. One of the earliest successful models is the FitzHugh model (also known as the FitzHugh-Nagumon or FHN model), which modelled the electrical impulses across nerve membranes [2]. This model was based on a cubic excitation model, included the recovery of the membrane, and stimulus applied from surrounding cells, generally defined as

$$\begin{aligned} \frac{dv}{dt} &= v(v-a)(1-v) - w + I_{stim}, \\ \frac{dw}{dt} &= b(v - \gamma w), \end{aligned} \tag{1}$$

where v, w, and I_{stim} are the potential, recovery, and stimulus, respectively, while a, b, and γ are model parameters. Since the development of this model, many others have been developed that improve the realism and explore many cardiological phenomena more accurately [3]. Modern models take into account the complex movement of ions and their associated potential across the membrane, as well as interactions with other neurons within the neurological network. The goal of this report was to develop a simplified model and analyze it's effectiveness in reproducing biological phenomenon. The phenomena in question include the Wenckebach phenomenon (Mobitz Type I), where the heart will miss beats periodically in between a series of regular beats in an $X : X-1$ ratio of SA pulses to conducted pulses. Mobitz Type I blocking is caused by progressive fatigue of the AV node cells leading to increasing delay between conducted pulses before a pulse is blocked[4]. 2:1 Mobitz II block is a condition where the AV node rejects every other pulse received from the SA node in a 2:1 ratio. 2:1 Mobitz II block results from SA pulses entering the AV node during the refractory period [5]. These biological phenomena should both arise through variation of parameters in a system that produces regular heart beats.

II. FORMULATION

We assume the electric potential of the AV node decays exponentially. Noting that the AV node experiences a fatigue due to repeated strain from incoming pulses [6], one possible formulation for the electric potential can be created from a system of differential equations:

$$\begin{aligned} \frac{dv}{dt} &= -\alpha\left(1-\frac{w}{w+1}\right)v, \\ \frac{dw}{dt} &= \beta v - \gamma w, \end{aligned} \tag{2}$$

where v is the electric potential, w is the fatigue, t is the time, and α, β, $\gamma > 0$ are parameters. The first equation in Eq. 2 was constructed from the exponential decay, but the coefficient

$$\left(1-\frac{w}{w+1}\right)$$

was borrowed from continuum damage mechanics [7]. The presence of this term ensures that as the fatigue increases, the rate at which the potential decreases is reduced, effectively increasing the refractory period of the AV node. It is not difficult to see that as the fatigue increases this term reduces to ∼0. The second equation in Eq. 2 ensures that the rate at which the fatigue increases is affected by the current potential of the AV node but because this is a biological system that can recover, there is a recovery dictated by the current fatigue and γ. High potentials thus cause the fatigue to increase at a faster rate determined by β, but the recovery will eventually reduce the fatigue back to a low value. One can infer with this information that the parameters are indicative of a person's health (for example, a higher γ will ensure a faster recovery time).

Because the AV node requires incoming pulses from the SA node, those must be modelled as well. We've assumed that the incoming pulses maintain a constant frequency, and require a pulse-like shape, thus any well-behaved periodic function $f(\omega, t)$ will suffice. This was arbitrarily chosen as

$$f(\omega, t) = \sin(\omega t) \tag{3}$$

where ω is the frequency (in rad s^{-1}) of the incoming pulse. In reality, the SA node does not send pulses at constant frequencies and strengths but with more of a chaotic behaviour to allow for quick reactions of changes to environment [8]. This model restricts this value to a constant 80 bpm.

The model takes into account thresholds that both the AV potential and the SA potential must meet in order for the AV node to accept a pulse, i.e. the AV potential must be below some threshold η_{AV} and the SA potential must be above a different threshold η_{SA}. Only if these conditions are met will the AV node accept a pulse and the heart will beat. The time between the last heartbeat and when the AV node is below the threshold is known as the refractory period.

III. RESULTS

The method required numerical solutions to a system of differential equations, so the Runge-Kutta method was chosen for its robustness and simplicity. Iterative analysis allowed for increase of the AV potential if threshold conditions were met. Implemented using Matlab (see the appendix for scripts), variation of the parameters generated Figures 2, 3, and 4 (vertical lines represent peaks of the SA node pulses to view the changes between SA pulse frequency and heartbeat frequency).

IV. DISCUSSION

The resulting figures demonstrated the expected behaviours. Figure 2 demonstrated the behaviour of a "healthy" heart, where the incoming pulses from the SA node always aligned with the decaying potential in such a way that the frequency of heartbeats always matched the frequency of the SA node. Every incoming pulse remains outside outside of the refractory period of the AV node, thus every pulse is conducted.

Figure 3 exhibits the Wenckebach phenomenon. The heart beats normally most of the time, but occasionally misses a pulse (indicated by a gap between pulses). Careful examination of the decaying potential finds that this occurs due to the buildup of fatigue within the AV node, which extends the refractory period after each successive beat. Eventually, the refractory period extends past the incoming SA pulse, rejecting the pulse and allowing the AV node to recover longer, reducing the fatigue. Interestingly, we find this behaviour has a periodicity based on the input parameters. The example given demonstrates a relatively short period of 1 missed beat per 3.75 s, but other variations gave examples at much lower frequencies (such as one miss per minute).

Figure 4 presents the final phenomenon, the 2:1 Mobitz block. Though heartbeats occur at regular intervals, only half of the incoming SA pulses are accepted because every other SA pulse enters the AV node during the refractory period. The ratio of pulses entering from the SA node to the number of accepted pulses is 2:1, but variation of the parameters, particularly the frequency, can generate other ratios, such as 3:2 and 4:3.

Qualitative sensitivity analysis of the parameters α, β, γ, and ω yielded interesting results. Utilizing the one-at-a-time (OAT) sensitivity analysis, the plots in Figures 5, 6, 7, and 8 revealed the changes in conducting ratio (the ratio of successful heartbeats to incoming SA pulses) with the changes in the parameter. The key feature in each of these plots is where the slope of the graph becomes 0, i.e. a flat line, specifically at a counting ratio of 1. This means that the number of beats is equal to the number of incoming pulses, what is considered a normal heartbeat and where we have defined a stable heartbeart.

The thresholds η_{AV} and η_{SA} produced predicted behaviours and their sensitivity plots can be seen in the

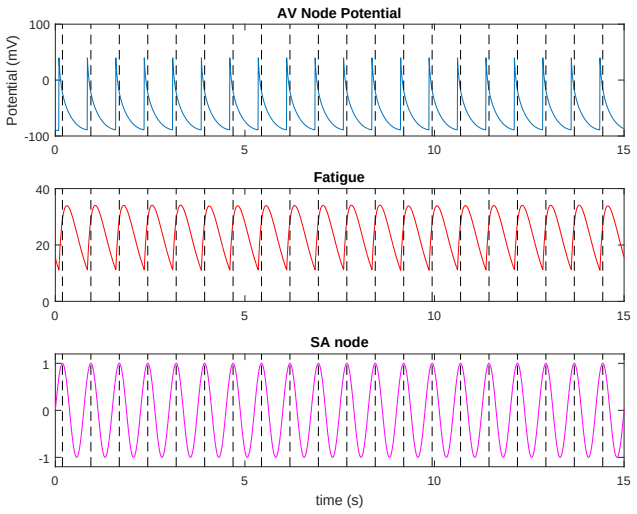

FIG. 2: Normal beating of the heart, with parameters $\alpha = 154$, $\beta = 3$, and $\gamma = 3.50$. Incoming pulses from the SA node align well with the increase in potential of the AV node, outside of the refractory period. The fatigue behaves periodically, recovering similarly between successive beats.

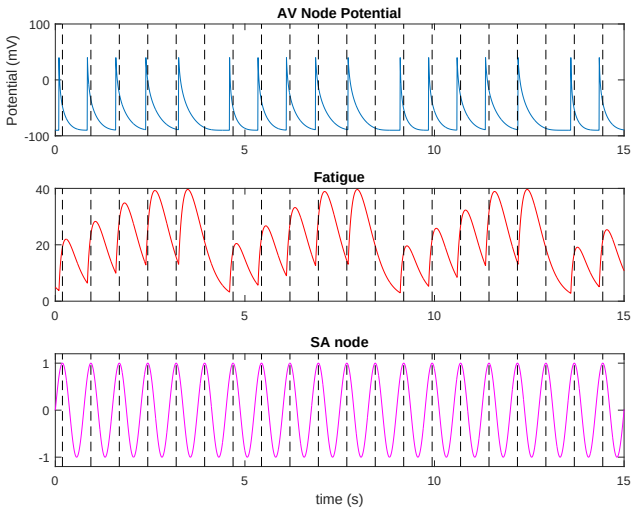

FIG. 3: An example of the Wenckebach phenomenon, with parameters $\alpha = 154$, $\beta = 3$, and $\gamma = 3$. Incoming pulses from the SA node move closer to the refractory period with each successful heartbeat, until the period is surpassed (such as at $\sim$4 s). Until this missed beat, the fatigue continues to increase, lengthening the refractory period.

appendix. Note that areas of plots with stabilities above a ratio of 1 are possible, but these are considered biological extremes. In this case, the AV node is accepting the same SA node multiple times due to a quick exponential decay which, though mathematically possible, is not likely in a real heart.

The model is useful for demonstrating the problems posed, and allows for individual variation. Regular heart-

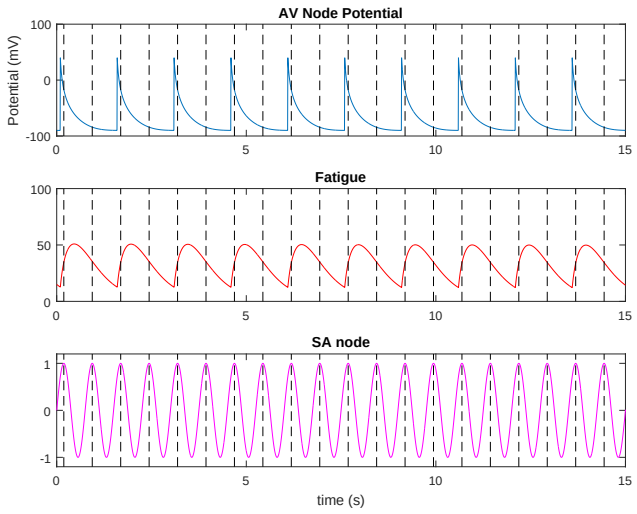

FIG. 4: An example of the second-degree block, with parameters $\alpha = 154$, $\beta = 3$, and $\gamma = 1.75$. Every other incoming SA pulse arrives during the refractory period, causing the AV node to effectively reject half of the pulses. Similarly to the normal heartbeat, the fatigue recovers effectively between beats.

beats, the Wenckebach phenomenon, and the second-degree block were all successfully emulated through alterations of parameters, but not without limitation. Each outcome was highly dependent on frequency, thus the responses for a particular set of parameters changed drastically for another frequency. The potential model was representative of an individual cell, not the collective effort of an entire node or organ. Dependence on neighbouring cells would improve accuracy.

Furthermore, the model fails to recreate an integral feature of the body: adaptation. As mentioned, real hearts do not behave linearly with time; chaotic variations in frequency, recovery rates, nutrition, hydration, and many other factors influence the performance of cardiovascular cells. The parameters, assume constant in this model, would be governed by other external factors and change with time. Fully accurate models would adjust for perturbations in these factors to accurately simulate the mammalian heartbeat.

V. CONCLUSIONS

This model took relied upon a system of differential equations to model both regular and irregular heartbeat patterns, successfully demonstrating normal heartbeats, the Wenckebach phenomenon, and 2:1 Mobitz block. The model is able to demonstrate the progressive fatigue of the AV cells causing pulses to be rejected by the AV node. Lack of recovery time causes fatigue to increase progressively until the AV node rejects a pulse (the Wenckebach phenomenon). The recovery rate of a cell may be so

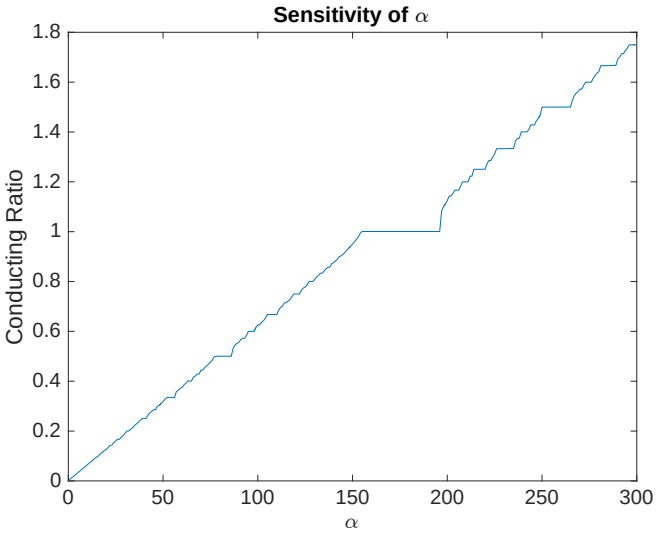

FIG. 5: The sensitivity of α. Stability occurs at $\alpha \approx 150-200$. Small stable areas occur outside of these values, but none are as wide.

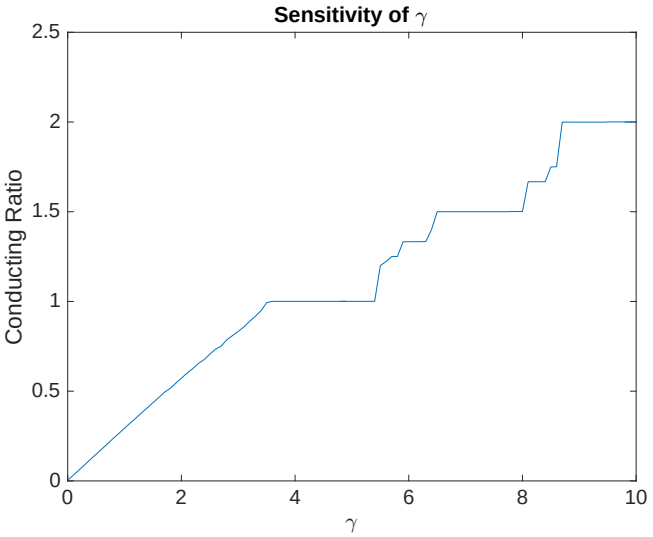

FIG. 7: The sensitivity of γ. Stability occurs at $\gamma \approx 3.5-5.5$. There seems to be a linear increase in the count ratio before these values, indicative of the influence of recovery on the AV node.

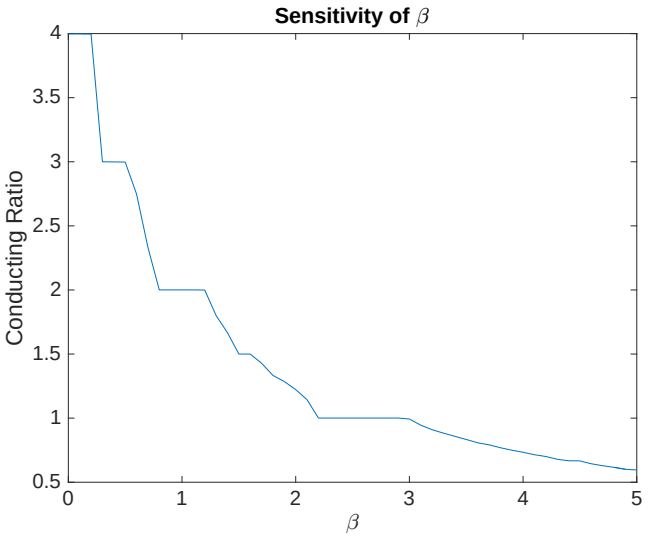

FIG. 6: The sensitivity of β. Stability occurs at $\beta \approx 2.2-3$. Few noticeable stabilities occur beyond these values, but the succeeding trend is that of decay.

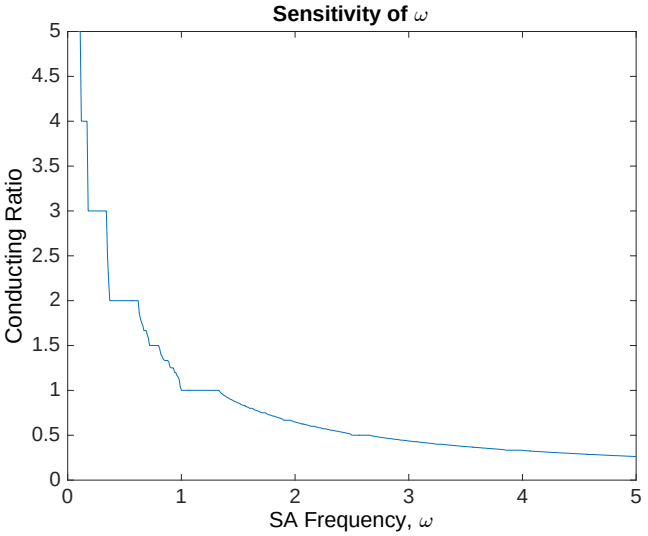

FIG. 8: The sensitivity of ω. Stability occurs at $\omega \approx 1-1.3$. Larger values give a noticeable decay. Low frequencies generate multiple beats per SA pulse due to a large SA pulse width.

small that half of all incoming SA pulses are rejected (2:1 block) due to arriving during the refractory period, though higher orders of blocking can also occur.

The model faces shortcomings, most notably with chaotic variability real cells produce, but has merit as a simplistic device for predicting heartbeats given a regular SA node frequency. The values of the parameters within the model can be indicative of one's cardiovascular health in regards to the ability to recover from and manage fatigue.

VI. APPENDIX

SA and AV threshold sensitivities are shown below, as well as the Matlab script for the AV node. Figure 11 demonstrates the scripts process.

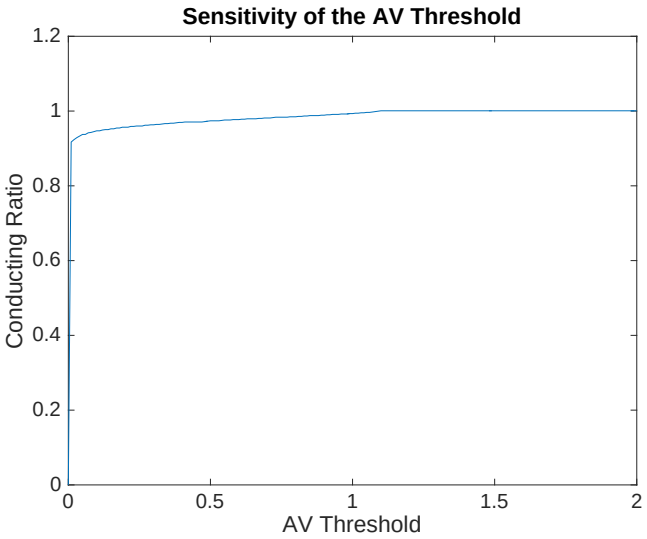

FIG. 9: The sensitivity of the AV threshold. Larger values meet the decaying exponential earlier, but due to the fast decaying nature of the model, suitably small thresholds did not change the outcome significantly.

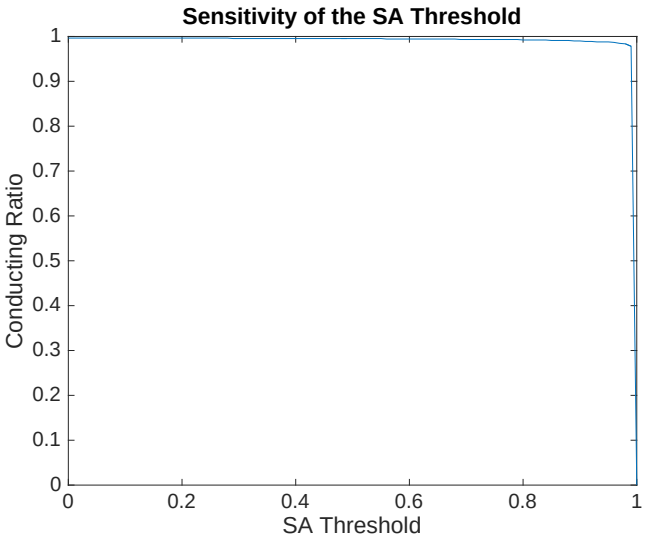

FIG. 10: The sensitivity of SA threshold. Similar to the sensitivity of the AV threshold, this parameter was required to be less than 1 to accept a pulse from the sine wave. Too low of values (near 0) cause the height and width of the pulse to be less effective in determining the outcome whereas high values (near 1) caused a sudden decrease in pulse conduction.

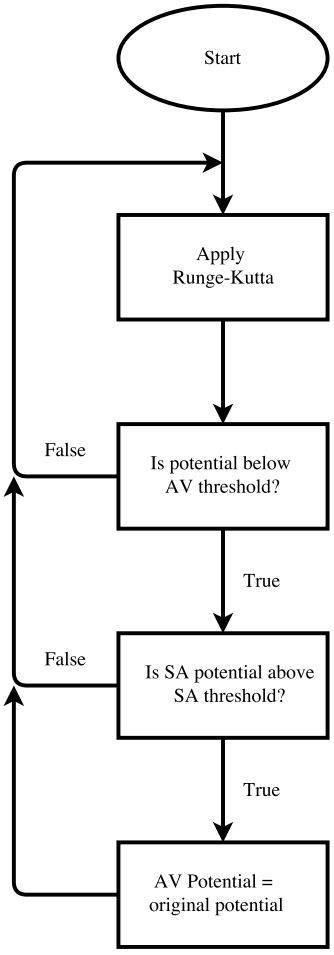

FIG. 11: Computational process of the Matlab script, taking advantage of the iterative Runge-Kutta method.

```
function out = AV(tSpace, param)
    % takes as an input a vector 'tSpace' and object 'param':
    % 'tSpace' is the vector of time values to solve for. tSpace must be
    % uniform.
    % 'param' must define the constants a,b,y,freq,SAthresh,AVthresh, and
    % pulseStrength.
    %%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%%
    % AV outputs an object containing 3 properties:
    % 'v' is the vector containing the solution for the AV potential.
    % 'w' is the vector containing the solution for the fatigue.
    % 'pulses' is an integer which counts the total number of pulses
    % conducted by the AV node.

    SAthresh = param.SAthresh; % minimum SA node threshold to conduct a pulse.
    AVthresh = param.AVthresh; % maximum AV node threshold to conduct a pulse.
    pulseStrength = param.pulseStrength; % potential jump when a pulse is conducted.
    a = param.a;                         %alpha constant.
    b = param.b;                         %beta constant.
    y = param.y;                         %omega constant.
    freq = param.freq;                   %frequency of SA node.
    h = tSpace(2) - tSpace(1);           %time step size.

    out.v = zeros(length(tSpace),1); % instantiate the v and w vectors.
    out.w = zeros(length(tSpace),1);
    out.v(1) = 0;                    % initial conditions for the
    out.w(1) = 0;                    % the v and w vectors.
    out.pulses = 0;                  % initialize the pulse counter

    f = @(t,v,w) -a*(1-w/(w+1))*v;       % equation for v prime.
    g = @(t,v,w) b*(v)-y*w;              % equation for w prime.
    SA = @(t,freq) sin(freq*2*pi*t);     % equation the describes the SA node.


    for i=1:(length(tSpace)-1)           %Runge Kutta
        t =  tSpace(i);

        k0 = h*f(t, out.v(i), out.w(i));
        l0 = h*g(t, out.v(i), out.w(i));
        k1 = h*f(t+0.5*h, out.v(i)+0.5*k0, out.w(i)+0.5*l0);
        l1 = h*g(t+0.5*h, out.v(i)+0.5*k0, out.w(i)+0.5*l0);
        l2 = h*g(t+0.5*h, out.v(i)+0.5*k1, out.w(i)+0.5*l1);
        k2 = h*f(t+0.5*h, out.v(i)+0.5*k1, out.w(i)+0.5*l1);
        l3 = h*g(t+h, out.v(i)+k2, out.w(i)+l2);
        k3 = h*f(t+h, out.v(i)+k2, out.w(i)+l2);

        out.v(i+1) = out.v(i) + 1.0/6 * (k0 + 2*k1 + 2*k2 + k3);
        out.w(i+1) = out.w(i) + 1.0/6 * (l0 + 2*l1 + 2*l2 + l3);

        if out.v(i)<AVthresh && SA(h*i, freq)>SAthresh % pulse conditional.
            out.v(i+1) = pulseStrength;               % depolarize the AV node
                                                      % potential.
            out.pulses =  out.pulses + 1;             % count the conducted pulses.
        end
    end
end
```

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