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Optimizing Impulse Controlin a Bio-Cell flow

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Abstract
Biological systems have their share of observable impulsive phenomena. Impulses that arise from electrical conduction are a major source of activation (depolarization and repolarization) of the cell membrane.Here the atrioventricular node (AVN) membrane is treated as a similitude of a resistor-capacitor (RC) circuit with a lag in impulse transmission.This lag is often implicated in cardiac events. The question of optimizing the control of pathological impulse delay in the AVN relates to the sequence of interventionsthat would make treatment effectual. If the delay is from an external voltage source (the sinoatrial node, SAN), what control could enhance the AVN depolarization? If repolarization is delayed at the AVN, then what control would assuage firing and recovery? The most striking concern should be the choice of a permissible control-the bulwark of this work. This choice may be sanguinely chosen is by making an apt diagnosis of the assailing condition.
Keywords: *electrical conduction, biological membrane, delayed impulse, Hamilton-Jacobi-type PDE, optimal control.*

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I. INTRODUCTION

Impulse phenomena are observable in varieties of biological, physical, and economical evolution processes that are characterized by a sudden change of state at some time instants. In each system, the impulse scenario may be such with a natural (normal) delay.Delay is often inevitable in a system state, the control input, or the measurement, as numerous processes have time delay characteristics in their dynamics.In noticeable delays other than natural (here called 'pathological'), deleterious impacts may bring to bear on the system. Delayed impulses, therefore may be *stabilizing*,as the case with normal or induced delay and *destabilizing*[1, 2, 3], as the case with pathological delay. Yang *et al.*[3], and numerous literature [4,5,6] noted that the impending evolution of the system state of a time delay system often depends not only on its currentvalue, but also on its previous values. In essence, the evolution of the system state may be largely a *non-Markovian* process.A study of the control of impulse of non-Markovian process was done by Djehiche*et al.*[7] and Jönsson[8].In present times there is a mounting interest in the concept of impulsive dynamical systems on account of their applications to numerous problems arising incontrol technology, communications, electrical engineering, biology and medicine, among others [9,10,11]. InStamov*et al.* [11] an impulsive delayed reaction-diffusion model applied in biology was studied with the view to enhancing optimal control of epidemic models. In Bro *et al.*[12] a closed-form Laguerre-domain demonstration of discrete linear time-invariant systems with constant input time delay is generated and used in identifying the pharmacokinetics of a drug (levodopa) from plasma concentration information from a single dose response.

Delayed impulse prevalent in all systems, especially biological systems elicit worries if it fails to be a stabilizing type. For instance, the delay in the transmission of action potential from the sinoatrial node (SAN) to the AVN is considered a deep concern. Regarding the impulses of the cardiac conduction system, the following apply [13,14]:

(i)The SAN produces action potentials (AP), which spread through the atria by cell-to-cell conduction at a rate of about 0.5 m/sec.
(ii)The AVN *delaysthe impulse* conduction significantly to about 0.05 m/secto allow adequate time for complete atrial depolarization and contraction.
(iii)The left and right HIS bundle branchestransmit impulses at a speedy velocity of about 2 m/sec.
(iv) Atrial activation ends within 0.09 sec after SAN firing. After an *impulse delay* at the AVN, the septum becomes activated (for about0.16 sec). The entire ventricular massis activated within 0.23 sec.

Studied show that the region between atrium and AVN, which has the slowest conduction velocity (0.05 m/see.) has the lowest safety factor (see Scher*et al*. [15]). Moreover the conduction barrier between atrial and nodal cells (see Choi and Salama [16]) may be implicated in precarious impulse delay-mediated cardiac

events.The movement of ions across cell membranes causes the systematic depolarization and repolarizationof the cell membranes of the heart muscles. In effect, contraction of the heart muscle cellsis enhanced. During the cardiac conduction phase,a wave of excitation spreads out from the SAN through the atria along specialized conduction channels;this activates the AVN. The AVN delays impulses by about0.09s ensure that the atria have ejected their blood into the ventricles prior to the ventricular contraction, and also insulates the ventricles from excessively fast rate response to atrial arrhythmias[17]. A very crucial idiosyncratic property of the AV node is *decremental conduction*[18] in which a slower rate of conduction is associated with a higher frequencyof node stimulation. By this the AVN averts rapid conduction to the ventricle in the events of rapid atrial rhythms, such as atrial fibrillation or atrial flutter. It is of note that the AVN hasa normal intrinsic firing rate of 40-60bpm [19].Naturally, the AVN cell membrane is seen to possess some parameters attributive of an electrical circuit. Thus, one may conceive of cell membrane resistance (MR) and capacitance (MC) and admire how cell membranes form nature's definitive stretchable resistor–capacitor network, asbyBrosseau and Sabri [20].

The question of stability impulse delay systems (IDSs) and impulsive stabilization of delay systems requires a careful investigation. Some works, including those by Li [**21**], Vadivoo*etal*., [22], and Wu [23] have therefore been done in this regard.In Nzerem and Ugorji [14] the prospect of optimizing a control that would keep impulse transmission within reasonable physiological window or alleviate the deleteriousness of pathological time delay was explored.**In this work the impulse delay in the AVN is considered.** (**ADD More**)

II. CELL ELECTRICAL CONDUCTION

The way the AVN conducts the electrical impulses, the likelyimpact of previous impulses and the time intervals between the impulses are, to say the least, uncertain.The *impulse response* of the system is its output that corresponds to a given input (impulse). Being a dynamical system, it is time dependent.An impulse response function has frequencies content, therefore theimpulse response describes the response of a linear time-invariant system for all frequencies.A linear, time-invariant (LTI) system is entirely characterized by its impulseresponse [24].For an easier analysis, the method of impulse responses is often supplanted by the use transfer functions. The latter was applied by Van der Tweel [25] in describing the AVN conduction.

2.1 Impulse function

In Nzerem and Ugorji [14] conduction pathways were approximated to rectangles. Therefore, there was a conception of a rectangular pulse function - a unit pulse function $\delta_\tau(t)$ of duration T, with a constant amplitude $1/T$ over the range

$$\delta_T(t) = \begin{cases} 0 & \text{for } t \le 0 \\ 1/T & 0 < t \le T \\ 0 & t > 0 \end{cases} \quad (1)$$

As the duration T approaches zero, one finds that $\delta_T(t)$ approximates to $\delta(t)$, the impulse function. Suppose $x(t)$ is the electrical input and $y(t)$ is the associated response. The former may have originated for the SAN, while the latter is give off from the AVN membrane. By approximating $x(t)$ by a *staircase* function [26].

$$\hat{x}_T(t) = x(nT) \qquad \text{for } nT \le T \le (n+1)T \quad \forall n \qquad (2)$$

and

$$x_T(t) = \lim_{T \to 0} \hat{x}_T(t) \quad (3)$$

An ensemble of non-coinciding delayed pulses, $p_n(t)$, with duration T approximated by $\hat{x}_T(t)$ is

$$\hat{x}_T(t) = \sum_{-\infty}^{\infty} p_n(t) \quad (4)$$

where

$$p_n(t) = \begin{cases} x(nT) & nT \le t \le (n+1)T \\ 0 & \text{elsewhere} \end{cases} . \qquad (5)$$

The sum of all unit pulse gives

$$\hat{x}_T(t) = \sum_{n=-\infty}^{\infty} x(nt)\delta_T(t - nT)T \quad (6)$$

Considering an LTI system, the response of each delayed unit pulse at time nTsynchronize with the response

$y_n(t) = \gamma_T(t - nT),$ (7)

Where $\gamma_T(t)$ encodes the system response to the impulse (input), $\delta_T(t)$. $\gamma_T(t)$ being the impulse response of the (LTI) system means that if $\delta(t)$ is the input to the system when it is initially at rest, then the at some time *t* is $\gamma_T(t)$ .Therefore, the response associated with the pulse (6) is

$\hat{y}_T(t) = \sum_{n=-\infty}^{\infty} x(nt)\gamma_T(t - nT)T \cdot$ (8)

In the limit,

$y_T(t) = \lim_{T \to 0} \sum_{n=-\infty}^{\infty} x(nt)\gamma_T(t - nT)T.$ (9)

By convolution,

$\int_{-\infty}^{t} x(t)\gamma(t - \xi)d\xi = \int_{-\infty}^{t} x(t - \xi)\gamma(\xi)d\xi = x(t) * \gamma(t)$ (10)

It is noteworthy that delayed impulse has an associated delayed response. Thus,

$\int_{-\infty}^{t} x(t - \xi)\gamma(t - \xi)d\xi = x(t) * \gamma(t)$

2.1.2 *Impulse response*

Biological cells consist of very conductive aqueous electrolytes separated by very thin, low conductivity membranes. The cell membrane may be modelled in electrostatics as a capacitor that may be charged when an electric field is applied across the membrane. As already indicated, in the cardiac conduction system,the SAN produces AP, which spread through the atria by cell-to-cell conduction and the AVN delays the impulse conduction to allow adequate time for complete atrial depolarization and contraction. It is assumed here that the integrity of the SAN action potentials is maintained, and the SAN is an external source of AP. We conceive of a RC circuit composed of the AVN membrane as seen in in Fig.1.

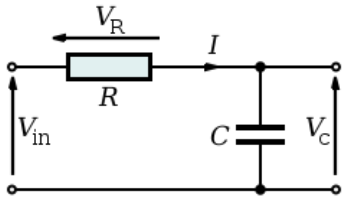

Figure 1. Series RC circuit:The current in the circuit, *I*,

the voltage across the resistor, V_R and the voltage across
the capacitor, V_C are shown.*https://en.wikipedia.org › wiki › RC_circuit*

In the conduction system vis-à-vis the electrical circuit, repolarizationimplies open switch (i.e. **current does not flow through**the circuit**)**.This holds at each cycle of depolarization. Therefore, depolarization entails the switch closure (A closed switch delivers a direct (low resistance) path for current flows.). The voltage and current adjustment to the current conditions as a switch closes.In the event of asudden change,a step response is induced. Such a change may well occur either in the event of an abnormally fast or delayed impulse propagation. A step response may therefore be a forced response, which is away from a natural response. As the system adjusts to the forced impulse, anatural response ensues.The over-all response of a circuit is equal to the superposition ofthe forced and natural responses.

Assume that a cycle of depolarization has occurred. Now the AVN will providea source-free response, which entails the discharge of the capacitor through a resistor in series with it.The time-dependent voltage across the capacitor can be found by using Kirchhoff's current law (KCL). Noting that the current through the resistor is equal in magnitude, but opposite in sign, to the time derivative of the stored charge on the membrane capacitor, the ensuing linear differential equation is

$C\frac{dV_C}{dt} + \frac{V_C}{R} = 0$ (11)

The above equation underscores the natural response of the circuit.The solution to the equation (3) is

$V_C(t)\big|_{Nat} = V_0 e^{-\frac{t}{RC}}$, (12)

wherethe subscript '*Nat*' on the left-hand side indicates that $V_C(t)$ is evaluated as the natural response, and $V_0$is the membrane capacitor voltage at time $t = 0$. Assume now that the AVN membrane capacitor is at a fully discharged state (full repolarization)and switched open over a long time and it is closed at a time $t = 0$. Therefore, this initial condition reads [27]

$$V_C(0^-) = V_0 = V = V_C(0^+) \quad (13)$$

whenthe circuit is switched open at $t = 0^-$ since there is no instantaneous of voltage across the capacitor.
The AVN consists of the compact portion and a region of transitional cells; the later constitute a sort of bridge between the working and nodal myocardium, and gather electrical information from the atrial walls, transmitting same to the AVN [28]. Membrane electrical models may be described by a parallel-plate capacitor composed of two identical plates whose capacitance is [20]

$$C_m = \frac{\varepsilon_o \varepsilon_m}{d_m}\left[1 + o\left(\frac{\log\left(\sqrt{A_m}/d_m\right)}{2\sqrt{A_m}/d_m}\right)\right], \quad (14)$$

whereA_{m} is the thickness of the plate (with $d_{m=}\ A_m$), and the subscripted ε refer to some permittivity parameter. From the foregoing, ionic flow through the AVN may be described by a circuit comprising a one-loop resistor and capacitor (i.e. RC circuit) without an external voltage source.

When the circuit is closed at $t \geq 0$, voltage source is introduced in the circuit.Kirchhoff's voltage law (KVL) applies to the circuit, which yields the equation

$$C\frac{dV_C}{dt} = \frac{V^* - V_C}{R}, \quad (15)$$

Where V*encodes the steady-state response. The solution of (6) is

$$V_C(t)\Big|_{Forced} = V^*(1 - e^{-\frac{t}{RC}}) \quad (16)$$

where the subscript 'Forced' on the left-hand side indicates that $V_C(t)$ is evaluated as theforced response. The forced response to any arbitrary impulse may be computed from knowledge of the impulse response alone.The total response is the superposition of (4) and (7), which reads

$$V_C(t) = V^* + (V_0 - V^*)e^{-\frac{t}{RC}} \quad (17)$$

Consider the AVN membrane circuit presented as a series RC circuit in Fig.1. The voltage across the capacitor is

$$V_{C_m}(\eta) = \frac{1}{1 + RC_m\eta}V_{in}(\eta), \quad (18)$$

and the voltage across the resistor reads

$$V_R(\eta) = \frac{RC_m\eta}{1 + RC_m\eta}V_{in}(\eta), \quad (19)$$

And the current in the circuit is

$$I(\eta) = \frac{C_m\eta}{1 + RC_m\eta}V_{in}(\eta), \quad (20)$$

where$\eta = \sigma + j\omega$ is the complex frequency; σ encodes the exponential decay constant, and ω is the sinusoidal angular frequency.
The respective transfer functions from the input voltage to the voltage across the capacitor and the resistor are

$$H_c(\eta) = \frac{1}{1 + RC\eta},$$

and (21 a,b)

$$H_R(\eta) = \frac{RC\eta}{1 + RC\eta}$$

Taking the inverse Laplace transform of the corresponding transfer function furnished the impulse response function. The impulse response for the capacitor voltage reads

$h_c(t) = \frac{1}{\tau} e^{-\frac{t}{\tau}} u(t),$ (22)

where$u(t)$ is the Heaviside step function and $\tau = RC$ is the time constant.Correspondingly, the impulse response for the resistor voltage reads

$h_R(t) = \delta(t) - \frac{1}{\tau} e^{-\frac{t}{\tau}} u(t),$ (23)

where$\delta(t)$ is the Dirac delta function.

The superposition of the natural and forced response (4) and (7) yielded (8)

$V_C(t) = V^* + (V_0 - V^*) e^{-\frac{t}{RC}}$. (24)

III. IMPULSE DELAY AND CONTROL

Suppose there was a single time-delay to the process. Differentiate equation (24) w.r.t. *t* and supplant dV_C/dt by a system state dx/dt to get the form

$$\begin{cases} \dot{x}(t) = M_0 x(t) + M_1 x(t-\tau) + v(t), & t \geq 0 \\ x(t) = \lambda(t), & -\tau \leq t \leq 0. \end{cases} \quad (25a,b)$$

Equations (25) above describes the state transition matrix delay equation,where $M_0$and $M_1$are derived constant matrices of appropriate dimensions whose components relate to-V_0/RC andV^*/RC respectively.

Introduce the output controller. The state-transition matrix equation at $v(t) = 0$ is

$$\begin{cases} \dot{X}(t) = M_0 X(t) + M_1 X(t-\tau), & t \geq 0, \\ X(t) = I, & -\tau \leq t \leq 0 \end{cases} \quad (26)$$

where$I$ is the identity matrix. The solution of (26) is of the form

$$X_{r+1}(t) = e^{M_0(t-r\tau)} X_r(r\tau) + \int_{r\tau}^{t} e^{M_0(t-s)} M_1(s-\tau) ds, \quad X_r(t) \in \{(r-1)\tau \leq t \leq r\tau\} \quad (27)$$

Seek an optimal control that aims at keeping delayed impulse within physiological window or alleviate harmful effect of undue time delay. Suppose$Z$ encodes the state space of the system, and K the set of all control functions.

Let $u \in K$be the control function, and$z \in Z$: $\mathbf{z} = \mathbf{z}(z_0, u, t)$ is a vector describing the state of the system at the instant t, withthe initial state $z_0 = z(t_0)$. Let Xindicate a subspace of $S$and $\mathbf{x} = \mathbf{x}(z_0, u, t)$ be the projection of the state vector $z(z_0, u, t)$ onto X. The state z_0 is assumed controllable in the class K if there exist a control $u \in K$ and the number N, in the range $t_0 \leq T \leq \infty$ such that $\mathbf{z}(z_0, u, T) = 0$. The entire system is controllable if each $z_0 \in Z$ is controllable.

Now, employ an input controller to the system in the form

$$\begin{cases} \dot{x}(t) = M_0 x(t) + M_1 x(t-\tau) + Bu(t), & t \in [0,T], T < \infty \\ x(0) = x_0, \quad x(t) = \lambda(t), & -\tau \leq t < 0. \end{cases} \quad (28)$$

where $\mathbf{x} = (\mathbf{x_1}(t), ..., \mathbf{x_n}(t))^T$ is a vector, $\mathbf{x} \in X$, $\mathbf{u}(t) = (\mathbf{u_1}(t), ..., \mathbf{u_r}(t))^T$ is the control function, $u \in K$. $K$is the set of piecewise-continuous functions and M_0, M_1, B are constant matrices of appropriate dimensions. The state space Z of this system is the set

$$\{x(\alpha), \quad -\tau \leq \alpha \leq t\} . \quad (29)$$

The initial state z_0 of the system (28) is determined by

$$z_0 = \{x(\alpha) = \lambda(\alpha), \quad -\tau \leq \alpha \leq t, \; x(0) = x_0\} . \quad (30)$$

The system (28) is controllable if a control $\mathbf{u} \in K$ exists suchthat $x(t) \equiv 0, T-\tau \leq t \leq T; T < \infty$.

The state feedback control below consists the linear time-delay in both state and input by,

$$\dot{x}(t) = M_0 x(t) + M_1 x(t-\tau) + B_0 u(t-\tau_1),\ t \geq t_0 \quad (31)$$

where $\mathbf{u}(t)$ is the control input and B is the input matrix and τ_1 is the input delay. The pair M_0, B_0 are assumed controllable. The equation (31) may take the form

$$\begin{cases} \dot{\mathbf{x}}(h) = \mathbf{f}(\mathbf{x}(h), \mathbf{u}(h)) & (t-\tau < h < t_f \\ \mathbf{x}(t-\tau) = x \end{cases} \quad (32)$$

where $\mathbf{f}$ is a bounded Lipschitz continuous functionsuch that

$$\mathbf{f} : \mathbb{R}^n \times K \to \mathbb{R}^n, \quad (33)$$

$K$is a compact subset of $\mathbb{R}^m$, say.In equation (32): $t-\tau \geq 0$ is an initial time (with delay τ),$tf > 0$ encodes a fixed terminal time, $\mathbf{x} \in \mathbb{R}^n$ is a prescribed initial point, $\mathbf{u}(.) \in K$represents the control. $\mathbf{x}(h)$ encodes the state of the system at time h.Let

$$K := \{\mathbf{u} : [0, t_f] \to K \mid \mathbf{u}(.) \text{ is measurable}\} \quad (34)$$

encode the set of admissible controls. For each control $\mathbf{u}(.)$, the equation (32) has a unique, Lipschitz continuous solution $\mathbf{x}(.) = \mathbf{x}^{\mathbf{u}(.)}(.)$ in the interval $[t-\tau, t_f]$. We note that $\mathbf{x}(.)$ encodes the response of the system to the control $u(.)$, and $\mathbf{x}(h)$ encodes the state of the system at time h. The aim is to find a control that minimizes the system time delay. The question is: what is the cost criterion? For each admissible control, define a *cost functional*

$$C_{x,t}[\mathbf{u}(.)] := \int_{t-\tau}^{t_f} r(\mathbf{x}(h), \mathbf{u}(h)dh + l(\mathbf{x}(t_f)) \quad (35)$$

where

$$r : \mathbb{R}^n \times K \to \mathbb{R},\ l : \mathbb{R}^n \to \mathbb{R}$$

denotes some prescribed functions. In equation **(**35**)***r* and *l* denote the respective *running cost per unit time* and *terminal cost*. The problem is to find a control **u***(.) which maximizes (35) among all other admissible controls, noting that $x \in \mathbb{R}^n$ and $0 \leq t-\tau \leq t_f$. Now, the *value function*takes the form

$$v(x, t-\tau) := \inf_{\mathbf{u}(.) \in K} C_{x,t-\tau}[\mathbf{u}(.)] \quad (x \in \mathbb{R}^n, 0 \leq t-\tau \leq t_f) \cdot \quad (36)$$

What are the connotations *costs* in the context of the bio-cell flow? What connotes the *running costper unit time*? In the business climate, "they are the cost of resources used by an organization just to maintain its existence" [29]. Of course, it has every semblance of money.In the bio-cell in question, this cost involves all it takes to *depolarize a membrane within a permissible time interval.*In essence, the membrane appurtenances, which include the arc and nodal structures, must maintain the integrity of flow. Where delay is inevitable,(much as the inherent role of the AVN is to delay the cardiac impulse [30],a(pathological) delay in conduction through the AVNproducesa prolonged PR interval, known as first-degree AV block), such cost has to be reasonably minimized. As to the *terminal cost*, there is the compellingneed to ensure a secure repolarization. Therefore, the goal of optimal control is to minimize the deleterious impact of delayed impulses by maximizing intervention.

The outline is:Given that $v(x, t)$ in (36) is the least cost, begin at x (position)at time t and observe the behaviour of $v$as x and t vary. The control problem (32), (35) will be embedded into a bigger class of all suchproblems as x and t vary. In doing this, $v$is shown to solve a Hamilton-Jacobi-type PDE, and a solution in effect assists in the creation of an optimal feedback control. This erudite pattern was developed by Evans [31] in approaching a dynamic programming problem and it is the bastion of the control applied here.

Henceforth let $x \in \mathbb{R}^n,\ 0 \leq t-\tau \leq t_f$ be fixed. The optimality criterion is detailed by the following:

Theorem 1(modified from[31]). Given each r so small that $t-\tau+r \le t_f$we get

$$v(x,t-\tau) = \inf_{\mathbf{u}(.)\in K} \left\{ \int_{t-\tau}^{t-\tau+r} r(\mathbf{x}(h), \mathbf{u}(h))dh + v(\mathbf{x}(t-\tau+h), t-\tau+h \right\}, \quad (37)$$

in which $\mathbf{x}(.) = \mathbf{x}^{\mathbf{u}(.)}(.)$ solves (32) for the control $\mathbf{u}(.)$.

Proof. Chooseany permissible control $\mathbf{u}_1(.) \in K$ and solve

$$\begin{cases} \dot{\mathbf{x}}_1(h) = \mathbf{f}(\mathbf{x}_1(h), \mathbf{u}_1(h)) & (t-\tau < h < t_f \quad (38) \\ \mathbf{x}_1(t-\tau) = x. \end{cases}$$

Now fix $\varepsilon > 0$ and choose $\mathbf{u}_2(.) \in K$To find that

$$v((\mathbf{x}_1(t-\tau+r), t-\tau+r) + \varepsilon \ge \int_{t-\tau+r}^{t_f} r(\mathbf{x}_2(h), \mathbf{u}_2(h)dh + l(\mathbf{x}_2(t_f)), \quad (39)$$

Where

$$\begin{cases} \dot{\mathbf{x}}_2(h) = \mathbf{f}(\mathbf{x}_2(h), \mathbf{u}_2(h)) & (t-\tau < h < t_f \quad (40) \\ \mathbf{x}_2(t-\tau+r) = \mathbf{x}_1(t-\tau+r). \end{cases}$$

Introduce the control

$$u_3(h) := \begin{cases} \mathbf{u}_1(h) & \text{if} \quad t-\tau \le h < t-\tau+r \\ \mathbf{u}_2(h) & \text{if} \quad t-\tau+r \le h \le t_f \end{cases}, \quad (41)$$

And let

$$\begin{cases} \dot{\mathbf{x}}_3(h) = \mathbf{f}(\mathbf{x}_3(h), \mathbf{u}_3(h)) & (t-\tau < h < t_f \quad (42) \\ \mathbf{x}_3(t-\tau) = \mathbf{x}. \end{cases}$$

The uniqueness of solutions of (34) impels us to write

$$\mathbf{x}_3(h) := \begin{cases} \mathbf{x}_1(h) & \text{if} \quad t-\tau \le h < t-\tau+r \\ \mathbf{x}_2(h) & \text{if} \quad t-\tau+r \le h \le t_f. \end{cases} \quad (43)$$

Therefore, from (38) we have

$$\begin{aligned} v(x,t-\tau) &\le C_{x,t}[\mathbf{u}_3(.)] \quad (44) \\ &= \int_{t-\tau}^{t_f} r(\mathbf{x}_3(h), \mathbf{u}_3(h)dh + l(\mathbf{x}_3(t_f)) \\ &= \int_{t-\tau}^{t-\tau+r} r(\mathbf{x}_1(h), \mathbf{u}_1(h)dh + \int_{t-\tau+r}^{t_f} r(\mathbf{x}_2(h), \mathbf{u}_2(h)dh + l(\mathbf{x}_2(t_f)) \\ &\le \int_{t-\tau}^{t-\tau+r} r(\mathbf{x}_1(h), \mathbf{u}_1(h) + v(\mathbf{x}_1(t-\tau+h), (t-\tau+h) + \varepsilon, \end{aligned}$$

Where the last inequality is a consequence of (42). The arbitrariness of $\mathbf{u}_1(.)$ informs us to conclude that

$$v(x,t-\tau) \le \inf_{\mathbf{u}(.)\in K} \left\{ \int_{t-\tau}^{t-\tau+r} r(\mathbf{x}(h), \mathbf{u}(h))dh + v(\mathbf{x}(t-\tau+h), t-\tau+h \right\} + \varepsilon \quad (45)$$

$\mathbf{x}(.) = \mathbf{x}^{\mathbf{u}(.)}(.)$ solving (32).

Fix $\varepsilon > 0$, again and choose a controller $\mathbf{u}_4(.) \in K$ so that

$$v(\mathbf{x}, t-\tau) + \varepsilon \ge \int_{t-\tau}^{t_f} r(\mathbf{x}_4(h), \mathbf{u}_4(h)dh + l(\mathbf{x}_4(t_f)), \quad (46)$$

Where

$$\begin{cases} \dot{\mathbf{x}}_4(h) = \mathbf{f}(\mathbf{x}_4(h), \mathbf{u}_4(h)) & (t-\tau < h < t_f \quad (47) \\ \mathbf{x}_4(t-\tau) = \mathbf{x}. \end{cases}$$

From (38) we see that

$$v((\mathbf{x}_4(t-\tau+r), t-\tau+r) \le \int_{t-\tau+r}^{t_f} r(\mathbf{x}_4(h), \mathbf{u}_4(h)dh + l(\mathbf{x}_4(t_f)). \quad (48)$$

Thus,

$$v(x,t-\tau) + \varepsilon \ge \inf_{\mathbf{u}(.)\in K} \left\{ \int_{t-\tau}^{t-\tau+r} r(\mathbf{x}(h), \mathbf{u}(h))dh + v(\mathbf{x}(t-\tau+h), t-\tau+h) \right\},$$

$\mathbf{x}(.) = \mathbf{x}^{\mathbf{u}(.)}(.)$ solving (32). The inequality (48) and (45) complete the proof of (39) ■

IV. SUMMARY AND CONCLUSION

Impulses are evolution processes that are characterized by a sudden change of state at some time instants. Biological systems have their share of observable impulsive phenomena. Impulses that arise from electrical conductionare a major source of activation of the cell membrane.Here impulse is delivered to the AVN, which is a major player in the cardiac conduction system.Oftentimes the impulse scenario may be such with a natural (normal) delay, typical of the AVN, which is also inevitable in some system state, the control input, or the measurement, as numerous processes have time delay characteristics in their dynamics. The debilitating pathological delay is a matter of concern. Another issue of concern is how a system responds to the latter concern. The crux of the evolving issue is to seek a measure that would assuage the impact of the impulse delay. Towardshandling this, the delayed electrical impulse was transformed into a Hamilton-Jacobi type equation, whose solution is known in the design of an optimal feedback control.

What then is the gain derivable from the latter? The question of optimizing the control of pathological impulse delay in the AVN concerns the sequence of intervention in which treatment would be effectual. If the delay is from an external voltage source (the sinoatrial node, SAN), what control could enhance the AVN depolarization? If repolarization is delayed at the AVN, then firing and recovery is a target for control. The most striking concern should be the choice of a *permissible* control. This choice may be sanguinely chosen is by making an apt diagnosis of the assailing condition.

REFERNCES

[1]. K. Gu, V. Kharitonov and J. Chen, Stability of Time-Delay Systems, Boston, MA, USA: Birkhauser, 2003.

[2]. X. Li and X. Fu, Effect of leakage time-varying delay on stability of nonlinear differential Systems, Journal of the Franklin Institute, 350 (2013) 1335–1344.

[3]. X. Yanga, X. Lia,, Q.Xic and P.Duana, Review of stability and stabilization for impulsive delayed systems Mathematical Biosciences and Engineering,15(6), (2018) 1495–1515, doi:10.3934/mbe.2018069

[4]. Y. Li, H. Li, X. Ding and G. Zhao, Leader-follower consensus of multi-agent systems with time delays over finite fields, IEEE Transactions on Cybernetics, (2018) 1–6.

[5]. X. Song, J. H. Park and X. Yan, Linear estimation for measurement-delay systems with periodic coefficients and multiplicative noise, IEEE Transactions on Automatic Control, 62(2017) 4124–4130.

[6]. Wu_Hua Chen and Wei Xing Zheng, The effect of delayed impulses on stability of impulsive time-delay systems, Proceedings of the 18th World Congress the International Federation of Automatic Control, Milano(Italy), August28-September 2, 2011.

[7]. B.Djehiche, S.Hamad`ene, and I.Hdhiri, Stochastic Impulse Control of Non-Markovian Processes, Article in Applied Mathematics & Optimization, July 2008DOI: 10.1007/S00245-009-9070-4 · Source: arXiv

[8]. J. Jönsson, A Probabilistic Approach to Non-Markovian Impulse Control, Doctoral Dissertation, Department of Physics and Electrical Engineering Engineering,Linnaeus University, Växjö, 2022, https://www.diva-portal.org/smash/get/diva2:1640331/FULLTEXT01.pdf

[9]. W. He, F. Qian and J. Cao, Pinning-controlled synchronization of delayed neural networkswith distributed-delay coupling via impulsive control, Neural Networks, 85 (2017) 1–9.

[10]. L. Lee, Y. Liu, J. Liang and X. Cai, Finite time stability of nonlinear impulsive systems andits applications in sampled-data systems, ISA Transactions, 57 (2015) 172–178.

[11]. G. Stamov, I.Stamova, andC.Spirova, Impulsive Reaction-Diffusion Delayed Models in Biology: Integral Manifolds Approach. Entropy 2021, 23, 1631. https://doi.org/10.3390/e23121631

[12]. V. Bro, A. Medvedev, R.Ushirobira. Laguerre-domain Modeling and Identification of Linear Discrete-time Delay Systems. IFAC 2020 - 21st IFAC World Congress, Jul 2020, Berlin, Germany. hal-02887957

[13]. E. K. Richard, Normal Impulse Conduction [in Cardiovascular physiology concepts], https://www.cvphysiology.com/Arrhythmias/A003

[14]. F.E.Nzerem andH.C.Ugorji, Impulse Delay in the Cardiac Conduction SystemGlobal Journal of Science Frontier Research: F, Mathematics & Decision Science, 20(3), (2020)29-47.

[15]. A. M. Scher, M. I. Rodriguez, J. Liikane, and A. C. Young, The Mechanism of Atrioventricular Conduction, Circulation Research, (8)(1959) 54-61.

[16]. B-R Choi and G. Salama Optical mapping of atrioventricular node reveals a conduction barrier between atrial and nodal cells, Am. J. Physiol. 274 (Heart Circ.Physiol. 43): H829–H845, 1998

[17]. H. H.Gray, K.D. Dawkins, I.A. Simpson and J. M. Morgan,Lecture Notes on Cardiology. Boston: BlackwellScience,(2002).

[18]. E.Patterson, B.J.Scherlag, (October).Decremental conduction in the posterior and anterior AV nodal inputs,Journal of Interventional Cardiac Electrophysiology. **7** (2)(2002) 137–48.

[19]. D. C. Sweeney, T. A. Douglas, and R. V. Davalos, Characterization of cell membrane permeability in vitro. Part II: Computational model of electroporation-mediated membrane transport, Technol. Cancer Res. Treat. 17, (2018)1–13.

[20]. C. Brosseau and E. Sabri, Resistor–capacitor modeling of the cell membrane: A multiphysics analysisJ. Appl. Phys. 129, 011101 (2021),doi: 10.1063/5.0033608.

[21]. X. Li, New results on global exponential stabilization of impulsive functional differentialequations with infinite delays or finite delays, Nonlinear Analysis: Real World Applications,11 (2010) 4194–4201.

[22]. B. Vadivoo, R. Ramachandran, J. Cao, H. Zhang and X. Li, Controllability analysis of non-linear neutral-type fractional-order differential systems with state delay and impulsive effects,International Journal of Control, Automation and Systems, 16 (2018) 659–669.

[23]. Q. Wu, J. Zhou and L. Xiang, Global exponential stability of impulsive differential equations with any time delays, Applied Mathematics Letters, 23 (2010), 143–147.

[24]. Wikipedia contributors. (2021, November 17). Impulse response. In Wikipedia, The Free Encyclopedia. Retrieved 21:20, March 9, 2022, from https://en.wikipedia.org/w/index.php?title=Impulse_response&oldid=1055712736

[25]. I. Van der Tweel , J . N. Herbschleb and F. L. Meijler, A transfer function model for AV conductionin the human heart, Automedica.4, (1983) 251-256.

[26]. The Dirac Delta Function and Convolution, web.mit.edu›www ›Handouts ›Convolution

[27]. RC Circuit Analysis: Series, Parallel, Equations & Transfer Function, https://www.electrical4u.com › rc-circuit-analysis
[28]. D. T. Edmonds, Electricity and Magnetism in Biological Systems, Oxford University Press, 2001
[29]. Wikipedia contributors. (2021, September 4). Operating cost. In Wikipedia, The Free Encyclopedia. Retrieved 22:20,April 3,2022,from https://en.wikipedia.org/w/index.php?title=Operating_cost& oldid=1042404511
[30]. D. Sánchez-Quintanaa and S. Y. Hob, Anatomy of Cardiac Nodes and Atrioventricular Specialized Conduction System, Revisit Espanola de Cardiologia 56(11) (2003) 1085-1092.
[31]. L. C. Evans Partial Differential Equations (2^{nd} ed.), American Mathematical Society, Rhode Island,(1997).