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Impulse Delay in the Cardiac Conduction System

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Abstract- The physiology or otherwise of blood circulation is predicated on the electrical conduction of the heart. As a rule electrical impulse suffusing the cardiac cells, just like all time-dependent phenomena, transmits with a modicum of time delay. Such delay may be physiological (benign) or pathological; the later is seen as a cardiac liability. This paper treated impulse conduction delay in the cardiac system. A set of matrices resulting from the graph theoretic description of the conduction system was generated and fitted into a continuous time invariant state-space delay equation, and a state-transition matrix solution was sought. An input control-based minimization scheme by which ensuing deleteriousness of pathological delay could be assuaged was proposed.

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Impulse Delay in the Cardiac Conduction System

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Abstract- The physiology or otherwise of blood circulation is predicated on the electrical conduction of the heart. As a rule electrical impulse suffusing the cardiac cells, just like all time-dependent phenomena, transmits with a modicum of time delay. Such delay may be physiological (benign) or pathological; the later is seen as a cardiac liability. This paper treated impulse conduction delay in the cardiac system. A set of matrices resulting from the graph theoretic description of the conduction system was generated and fitted into a continuous time invariant state-space delay equation, and a state-transition matrix solution was sought. An input control-based minimization scheme by which ensuing deleteriousness of pathological delay could be assuaged was proposed.

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I. Introduction

Impulse transmission is a notable neuronal and cardiac occurrence. In fine, the overall vivacity of animated cells is attributable to a balanced electrical impulse budget. The cardiac conduction system (CCS) is a network of bio-electric process. In effect, the impulse under consideration is electrical. The physiology of blood circulation is based on the electrical conduction of the heart. As a rule, electrical phenomena bear on bio-electric structures, and therefore the similitudes of electrical events bring to bear on the cardiac cells. Beck[1] was right: *The reason a heart beats is simple: electricity.* It is no secret that ionic concentration gradient constitutes a major source of bio-electric impulse drive around cells. Basically, all time-based events such as electrical impulse have some element of time delay. Delays are a crucial element of physiological phenomena. This can only be said about benign or a physiological delay. In neurology such delay may be normal in axonal conduction time when an action potential (AP) travels from an active site near the neuronal soma to the axon terminals [2,3].Such conduction delays may be created by several different factors, such as variation in membrane time constants, number of synapses, and some associated length scales[4]. In pharmacokinetics drug delivery experiences normal equilibration delay between pharmacologic response and plasma drug concentrations [5]. In the cardiac conduction system (CCS), the onset of each phase of AP is preceded by a benign impulse transmission delay. This is the refractory period of the AP. However, while cell-to-cell benign delays are recorded within transmission time (such as seen during impulse transmission at atrioventricular (AV) junction so as to enhance full contraction of the a trial chambers [6,7]), pathological delays are observable in the event of cardiac anomalies. From the aforesaid, pathological delay is noticeable either during refractoriness or (at any region) during transmission or at both times. It is of note that

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despite their so called bad reputation [8, 9], physiological delay may have a stabilizing effect. Minimizing conduction delays is evidently beneficial since hurried conduction is, more or less, a cardiac liability. Pathological delays are implicated in a group of deleterious cardiac events.

Dynamics of electric networks with spatially distributed delays have been recently studied in the past [10, 11]. In [9] the critical point at which time delay is beneficial in a communication network was analysed in terms of a linear-quadratic performance measure. In a rather non-specific treatment of any physical system, Chen and Zhang [12] considered two types of delayed impulses: the destabilizing delayed impulses and the stabilizing delayed impulses. In a more precise analysis Saleh *et al* [13] studied failures in transmission systems of electric power networks. The study showed the effect of a single line failure of electric flow on the other lines. This is similar to any arc/nodal transmission failure in the cardiac conduction system. The graph theoretic analysis employed in the work was no less desirable. The CCS is, to all intents and purposes analogous to electrical networks discussed. Since the input and output of the system obeys Ohm's law, (see [7]), their relationship may be represented by a linear proportionality. Therefore the control of the system may be of a linear control type.

II. Model of Network Topology

The CCS network system was treated in [7].This section draws largely from it for some details on the present work. Consider the conduction schematic (Fig.1) below.

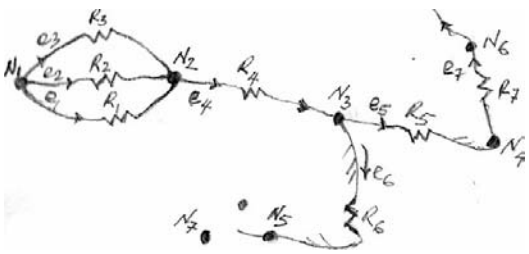

Fig. 1: Schematic of the CCS nodes (N_i), arcs (e_i) and resistors (R_i)

The nodes $N_1, N_2,\ldots,N_n$ are specified as follows: the SAN,N_1;the AVN,N_2; the point of bifurcation of the bundle of His,N_3; the left bundle branch, N_5; the right bundle branch, N_6.

The network constraints associated with the conduction system are the branch (edge) constraints, arising from Kirchhoff's Current Law (KCL),and the non-element based topological constraints, arising from Voltage Law (KVL). In the cardiac network the arcs have the semblance of electric wires, and therefore they have specific resistance. The linear relationship between current (I) and voltage (V) is expressed on the network by *Ohm's law*.

In a node where branch currents $x_1, \ldots, x_n$ enter (i.e. the currents are a form of input to the inactive nodes), Kirchhoff's current law (KCL) gives the total current as

$$x_1 + \cdots + x_n = 0. \tag{1}$$

Similarly, by Kirchhoff's voltage law (KVL)

$$v_1 + \cdots + v_n = 0. \tag{2}$$

Ref
9. Jean-Pierre Richard, Linear time delay systems: Some recent advances and open problems, www.elsevier.com/locate/ifac

where v_i denote the voltage drop in the circuit. The CCS is a structure with many nodes and many circuits. It requires the application of KCL and the KVL, together with Ohm's law for the network equations.

a) Potential difference across edges

The edges (arcs)of cardiac network, analogous to an electric wire, has an Ohmic resistance. Let r_0 be a voltage source, and let $R_1, \ldots, R_7$ be resistances (see fig.1). The potential difference, v_i, across each of the resistances measured across each arc, e_i is:

$$\begin{aligned} v_1 &= N_1\text{-}N_2 \quad v_3 = N_1\text{-}N_2 \quad v_5 = N_3\text{-}N_4 \\ v_2 &= N_1\text{-}N_2\, v_4 = N_2\text{-}N_3\, v_6 = N_3\text{-}N_5 \\ v_7 &= N_4\text{-}N_{6,} \end{aligned} \tag{3}$$

where, in the above, N_i (i=1,2,…,6) represents the nodes. (It shall be noted that there is infinite number of in-degree nodes N_j in the CCS that satisfy $d^-(N_i)=0$. For any arc e_j dispensing from the Purkinje fibre and any infinitely large number of nodes N_∞, $d^-(N_\infty)=0$.).

The vector form of (3) gives

$$\begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \\ v_7 \end{bmatrix} = \begin{bmatrix} 1 & -1 & 0 & 0 & 0 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & 0 & -1 & 0 \\ 0 & 0 & 0 & 1 & 0 & -1 \end{bmatrix} \begin{bmatrix} N_1 \\ N_2 \\ N_3 \\ N_4 \\ N_5 \\ N_6 \end{bmatrix} \tag{4}$$

Take N_2 as the reference node. The incidence matrix the CCS, with N_2 grounded, is [7]

$$\mathrm{B} = \begin{array}{c} \begin{matrix} e_1 & e_2 & e_3 & e_4 & e_5 & e_6 & e_7 \end{matrix} \\ \begin{pmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 \end{pmatrix} \end{array} \begin{matrix} N_1 \\ N_3 \\ N_4 \\ N_5 \\ N_6 \end{matrix} \tag{5}$$

where e_i are the edges.With N_2 as the reference node we have, from (5)

$$\begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \\ v_7 \end{bmatrix} = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 \\ 0 & 1 & 0 & -1 & 0 \\ 0 & 0 & 1 & 0 & -1 \end{pmatrix} \begin{pmatrix} N_1 \\ N_3 \\ N_4 \\ N_5 \\ N_6 \end{pmatrix}, \tag{6}$$

which is of the vector form

Ref

7. Nzerem F. E. and Ugorji H.C.,Cardiac conduction system: the graph theoretic approach, J. Math. Comput. Sci. 9 (2019), No. 3, 303-326 https://doi.org/10.28919/jmcs/4027

$$v = DN. \tag{7}$$

In (6), D is the matrix network's connectivity matrix.

Ohm's Law "$I = V/R$" is now used in relating the current to voltage drop across each resistor. At each of the resistors Ohm's Law gives,

$$x_j = v_j/R_j, \qquad j = 1, \ldots, 7. \tag{8}$$

with the matrix-vector form

$$\begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_6 \\ x_7 \end{bmatrix} = \begin{pmatrix} 1/R_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1/R_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1/R_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1/R_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1/R_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1/R_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1/R_7 \end{pmatrix} \begin{pmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \\ v_7 \end{pmatrix}. \tag{9}$$

The above has the matrix equation

$$x = Kv. \tag{10}$$

The matrix K describes the physics of the network. By KCL we get

$$\begin{pmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_6 \\ x_7 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}. \tag{11}$$

i.e.

$$D^T x = 0. \tag{12}$$

III. CCS Conduction Delay

A typical electrical conduction through the cardiac muscle takes ananticipated pathway. It travels from the sinoatrial node to the AVN and gets to the *bundle of His*. It then travels to the left and right bundle branches until it eventually terminates in the *Purkinje fibres*. As usual with cardiac electrophysiology, conduction travels from left to right, basically stimulating the left bundle, and left ventricle first. AV nodal blocks may well have an inherent delayed firing or a restriction to firing down the Purkinje system and consequently may cause bradycardias and hypo-perfusion to essential organs. Pathological delay in the conduction pathway is always implicated in bundle branch blocks. Clinical studies posit that patients' underlying aetiology who present with branch blocks may be determined to a high degree [14].

The diseases of the CCS (such as MI, pulmonary HTN, digoxin toxicity, etc.) are often precipitated by conduction delays. In the event of blockage of either bundle branch the electrical impulse travels directly from one cardiac myocyte to the other. The journey takes a much slower process than traveling via the ordinary low-resistance pathways. This pathophysiology prolongs the conduction time through the ventricles, resulting in widening of the QRS complex (¿ 120 m/sec).This QRS complex is the electrical impulse spreading through the ventricles, indicative of ventricular

Ref

14. Restivo A., Haughey M., MD and Chrisina H.D.O: Edited by Julianne Jung, Conduction Abnormalities, *https://www.saem.org/group-electrocardiogram-(ecg)-rhythm-recognition.*

depolarization. A study of CCS impulse delay is essential to clinical intervention. It is not unusual, however that a system could be unstable without delay, and could be stable with some delay. A careful distinction should therefore be made between essential (benign) delay and a pathological delay.

Many conducting bioelectric mediums have distributed resistances, capacitances, batteries, and extends continuously [15], the CCS may well be modelled as a system with distributed impulse delays. As treated in [16], the nodes are current sources and sinks. The main actors of the conduction system are the SAN, AVN, His bundle branches (HBB), Purkinje's fibres together with their conduction paths (edges). Any pathological conduction delay into an i-th node results in delay to subsequent nodes. The question of stabilising such delay by employing clinical intervention as a control input is one that requires attention.

a) Conduction impulse function

We assume a linear the spatial-temporal system under consideration. The CCS transmission is marked by an extremely short duration, and thus, the pulse may be seen to approximate an impulse. True impulse functions may be a wishful thinking in nature. However, its bio-physiological approximation may be found in very high velocity vascular pulse waves, blood vessel spasm, and spasmy muscular tetanisation, not to exclude the CCS in the main. The CCS conduction pathways may, in the limit, be approximated to rectangles. Thus, we conceive of a rectangular pulse function - a *unit pulse* function $\delta_T(t)$, of duration T, which has a constant amplitude $1/T$ over its range:

$$\delta_T(t) = \begin{cases} 0 & \text{for } t \le 0 \\ 1/T & 0 < t \le T \\ 0 & \text{for } t > 0 \end{cases} \tag{13}$$

Take the limit of the unit pulse $\delta_T(t)$ as the duration T approaches zero:

$$\delta(t) = \lim_{T \to 0} \delta_T(t) \quad . \tag{14}$$

The limiting form of many functions may be used to approximate the impulse. Any impulse occurring at some $t = a$is $\delta(t-a)$.

b) Impulse-response causality

Now, consider the continuous-time bio-electrical system (here, the CCS) with input $x(t)$, and the associated response $y(t)$, at a nodal point of interest. We suppose that the system is momentarily at rest, that is all initial conditions are zero at time $t = 0$. This condition corresponds to the resting phase after ionic depolarization.

Let the continuous input function $x(t)$ be approximated by a *staircase* function [23] $\hat{x}(t) \approx x(t)$, consisting of a series of piecewise constant sections each of an arbitrary fixed duration, T, where

$$\hat{x}_T(t) = x(nT) \qquad \text{for} \quad nT \le t \le (n+1)T \qquad \forall n, \tag{15}$$

and thus,

$$x(t) = lim\hat{x}_T(t) \tag{16}$$

The totality of non-overlapping delayed pulses, $p_n(t)$, each of which is with duration T, as represented by the staircase approximation $\hat{x}_T(t)$ is

$$\hat{x}_T(t) = \sum_{-\infty}^{\infty} p_n(t) \tag{17}$$

where

$$p_n(t) = \begin{cases} x(nT) & nT \le t < (n+1)T \\ 0 & \text{elsewhere} \end{cases} . \tag{18}$$

If each component pulse $p_n(t)$ is written in terms of a delayed unit pulse $\delta_T(t)$ we get

$$p_n(t) = x(nT)\delta_T(t - nT)\,T, \tag{19}$$

andtherefore (17) reads:

$$\hat{x}_T(t) = \sum_{n=-\infty}^{\infty} x(nT)\delta_T(t-nT)T \ . \tag{20}$$

Suppose $q_T(t)$ is the system response to the impulse $\delta_T(t)$. For a linear and time-invariant system, the response to a delayed unit pulse, happening at time nT, is tantamount to a delayed form of the pulse response:

$$y_n(t) = q_T(t - nT). \tag{21}$$

The superposition of the sum of the responses to all of the component weighted pulses in (20) is given by

$$\hat{y}_T(t) = \sum_{n=-\infty}^{\infty} x(nT)q_T(t-nT)T \tag{22}$$

For the system being considered the pulse response $qT(t)$ is zero for time $t<0$, and forthcoming input components do not add to the sum. Therefore the upper limit of the summation may read:

$$\hat{y}_T(t) = \sum_{n=-\infty}^{N} x(nT)q_T(t-nT)T \ \text{ for } NT \le t<(N+1)T. \tag{23}$$

The above encodes the system response to the said staircase approximation of the input in terms of the system pulse response $qT(t)$. Let T become very small, and let $nT = \tau$, $T = d\tau$, and take $lim\delta_T(t) = \delta(t)$ as $T \to 0$, then we have :

$$y_T(t) = \lim_{T\to 0} \sum_{n=-\infty}^{N} x(nT)q_T(t-nT)T \tag{24}$$

Equation (24) above yields the convolution or super position integral,

$$\int_{-\infty}^{t} x(\tau)q(t-\tau)d\tau = x(t) \otimes q(t) \tag{25}$$

where $q(t)$ is encodes the system *impulse response,*

$$q(t) = \lim_{T \to 0} q_T(t) \tag{26}$$

Equation (19) shows that the system is totally characterized by its response to the impulse function $\delta(t)$, since the forced response to any arbitrary input $x(t)$ may becomputed from knowledge of the impulse response alone.

Now consider the CCS topology (Fig.1).The SAN-AVN impulse is a parallel arrangement shown in Fig.2 below.

Fig. 2: Schematic of SAN-AVN current (I)and resistors (R) in parallel

The non-delayed impulse response, $q(t)$ of the arrangement within this section of the CCS, with state delay, is

$$q(t) = x(t-\tau) \otimes (q_1(t) + q_2(t) + q_3(t)) \tag{27}$$

The series connection has the response,

$$q(t) = x(t-\tau) \otimes (q_1(t) \otimes q_2(t) \otimes \ldots q_n(t)), \tag{28}$$

and as found along the *His bundle branch* (HBB) that contains R_5 and R_7,

$$q(t)_{HBB} = x(t-\tau) \otimes [q_1(t) \otimes q_2(t)] = [x(t-\tau) \otimes q_1(t)] \otimes q_2(t). \tag{29}$$

c) Conduction delay equation

To begin with, we take a look at the delay systems with multiple point wise incommensurate delay equation given by

$$\dot{x}(t) = A_0 x(t) + \sum_{k=1}^{m} A_k x(t-\tau_k), \quad \tau_{k\geq 0}, \tag{30}$$

where the delays τ_k may possibly be independent of each other. A special case is the system with single delay (viewing all delays as multiples of a single one) is the continuous time-invariant state-space equation of the form

$$\dot{x}(t) = A_0 x(t) + A_1 x(t-\tau), \tag{31}$$

with the initial condition of the form

$$x_t = \varphi, \tag{32}$$

where A_0 is the system matrix and A_1 is the system matrix for the state delay, both of which are given $\mathbb{R}^{m\times n}$ constant matrices; $x \epsilon \mathbb{R}^n$, is the state of the system.

Special note: Matrices arising from applicable systems are largely non-square ($\mathbb{R}^{m\times n}$, $m \neq n$). Those generated and considered here are non-square, except otherwise indicated. Therefore, each matrix here is presupposed Moore-Penrose invertible. Details on Moore-Penrose pseudoinverse of matrices may be found in [17, 18] and in profuse literatures. *The beauty of non-square systems is their less amenability to modelling errors*[19].

We relate equation (31) with the conduction matrix already generate by letting D^{T} (in (12)) = A_0, and A_1 can be obtained from the description of the delay. Let us, painstakingly, construct a prototype of A_1this way: Consider Fig. 1, and assume here that impulse conduction delay is observed from N_3 (corresponding to the *His bundle branch*); the delay has a cascading effect on the spectrum of subsequent nodes and edges. Let

$$A_1 = a_{ij} = \begin{cases} 1 & \text{if } N_i \text{ is a terminal node of } e_j, \text{ with conduction delay} \\ -1 & \text{if } N_i \text{ is an initial node of } e_j, \text{without conduction delay} \\ 0 & \text{otherwise} \end{cases}. \quad (33)$$

We ground$N_3$to get the state delay matrix

$$A_1 = \begin{pmatrix} -1 & -1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix}. \quad (34)$$

With this, a particular case of, the delay equation (31) takes the form

$$\dot{x}(t) = \begin{pmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 \end{pmatrix} x(t) + \begin{pmatrix} -1 & -1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1 \end{pmatrix} x(t-\tau) \quad (35)$$

Note that A_1 so obtained defines a region where multiple delay is experienced, which includes the considered point of initial delay.

i. *State-transition matrix solution*

Using (31) or (35) we set the following Cauchy problem:

$$\begin{aligned} \dot{x}(t) &= A_0 x(t) + A_1 x(t-\tau) + g(t), \quad t \geq 0 \\ x(t) &= \varphi(t), \quad -\tau \leq t \leq 0, \end{aligned} \quad (36)$$

where $x(t) = (x_1(t), x_2(t), \ldots, x_n)^{T}$is a vector of states of the system, $g(t) = (g_1(t), \ldots, g_n(t))^{T}$is a function that denotes disturbance signal, A_0, A_1 are constant matrices $\tau > 0$ is a constant delay. The state-transition matrix equation, with the ideal disturbance response $g(t) = 0$ (since disturbance acts on controller output), is

$$\dot{X}(t) = AX(t) + AX(t-\tau), \quad t \geq 0 \quad (37)$$

with the initial condition

$$X(t) = I, \quad -\tau \leq t \leq 0, \quad (38)$$

where I is the identity matrix. The solution of (37) with (38) is of the form [28]

$$X_{k+1}(t) = e^{A_0(t-k\tau)} X_k(k\tau) + \int_{k\tau}^{t} e^{A_0(t-s)} A_1(s-\tau) ds, \quad (39)$$

with $X_k(t)$ is defined on the interval $(k-1)\tau \leq t \leq k\tau$, $k = 0, 1, \ldots$

Ref

28. Baštinec J., Piddubna G., Solution of matrix linear delayed system. In XXIX International Colloquium on the Management on the Educational Process aimed at current issues in science, education and creative thinking development. Brno. 2011. p. 51 - 60.

It was shown in [28] that the fundamental solution matrix of equation (37) with identity initial conditions (38) has the form

$$X_0 = \begin{cases} \Phi, & -\infty \le t < -\tau \\ I, & -\tau \le t < 0 \\ e^{A_0 t} + g_1(t), & 0 \le t \le \tau \\ e^{A_0 t} + eA^0(t-\tau) g_1(\tau) + g_2(\tau), & \tau \le t \le 2\tau \\ \dots & \\ \sum_{m=0}^{k-1} e^{A_0(t-m\tau)} g_m(m\tau) + g_k(t), & (k-1)\tau \le t < k \\ & k = 3, 4, \dots \end{cases} \tag{40}$$

where Φ is the zero matrix and

$$g_p(t) = \sum_{\sum i_j = 1}^{p} \prod_{j=p}^{1} \left(\sum_{k_j=0}^{\infty} A_0^{k_j} A_1^{i_j} \right) \frac{(t-(p-1)\tau)^{K(p)}}{K(p)!} \prod_{s=p-1}^{1} \frac{\tau^{(1-i_{s+1})K(s)}}{(1-i_{s+1})!},$$

$$i_p = 1, i_j \in \{0, 1\}.$$

IV. Input Control

In this section we will study the possibility of optimizing a *control* that would keep the transmission of impulse within reasonable physiological window, or mitigate the deleteriousness of pathological time delay. If the control is drug-based, then there is an associated equilibration delay which does not constitute a component of the impulse delay.

Let Z be the state space of an impulsive system and U the set of control functions. Let $u \in U$ be the control function. $z \in Z$: $z = z(z_0, u, t)$ is a vector depicting the state of the system at the instant t, with the initial state $z_0 = z(t_0)$. Let X denote a subspace of Z and $x = x(z_0, u, t)$ be the projection of the state vector $z(z_0, u, t)$ onto X.

Definition 1. The state z_0 is said to be controllable in the class U if there exist such control $u \in U$ and the number T, $t_0 \le T \le \infty$ such that $z(z_0, u, T) = 0$.

If every state $z_0 \in Z$ of an impulsive system is controllable, then the system is said to be controllable.

Consider the Cauchy problem

$$\begin{aligned} &\dot{x}(t) = A_0 x(t) + A_1 x(t-\tau) + Bu(t), \quad t \in [0, T], \quad T < \infty, \\ &x(0) = x_0, \quad x(t) = \varphi(t), \quad -\tau \le t < 0, \end{aligned} \tag{41}$$

where $x = (x_1(t), \dots, x_n(t))^{\mathrm{T}}$ is a vector, $x \in X$, $u(t) = (u_1(t), \dots, u_r(t))^{\mathrm{T}}$ is the control function, $u \in U$. U is the set of piecewise-continuous functions and A_0, A_1, B are constant matrices of appropriate dimensions, $\tau > 0$ is as defined.

The state space Z of this system is the set of n-dimensional functions

$$\{x(\xi), \quad t - \tau \le \xi \le t\}, \tag{42}$$

And the initial state z_0 of the system (41) is determined by conditions

$$z_0 = \{x(\xi) = \varphi(\xi), \quad -\tau \le \xi < 0, \quad x(0) = x_0\}. \tag{43}$$

Ref

28. Baˇstinec J., Piddubna G., Solution of matrix linear delayed system. In XXIX International Colloquium on the Management on the Educational Process aimed at current issues in science, education and creative thinking development. Brno. 2011. p. 51 - 60.

In accordance with (38) the system (41) is controllable if there exists a control $u \in U$ such that $x(t) \equiv 0, T\text{-}\tau \leq t \leq T; T < \infty$.

Lemma1 [see 30] If the linear system with delay (41) is controllable in the interval $\in[(k-1), k\tau]$, then rank $(R_k) = n$, where R_k is the augmented matrix given by

$$R_k = \{B \quad e^{-A_0\tau}A_1B \quad e^{-2A_0\tau}A_1^2B \quad \ldots \quad e^{-(k-1)A_0\tau}A_1^{k-1}B\}. \tag{44}$$

A control may be constructed for the control problem with delay (41). Let Q be an augmented matrix satisfying

$$Q = \{B \quad A_0B \;\; A_1B \;\; A_0^2B \;\; (A_0A_1 + A_1A_0)B \;\; A_1^2B \;\; A_0^3B(A_0^2A_1 + A_0A_1A_0 + A_1A_0^2)B \ldots A_0^{n-1}A_1^pB\} \tag{45}$$

For controllability of the delay system (41) it is sufficient that for $(p-1)\tau \leq t \leq p\tau$, with rank$(Q) = n$ [31].

With the sufficient conditions for controllability employed for:det$(Q) = n$, for $t_1 \geq (k-1)\tau$w here the matrix Q was defined in (45) the control function can takes the form [30]

$$u(\eta) = \left[X_0(t_1 - \tau - \eta)B\right]^T \left[\int_0^{t_1} X_0(t_1 - \tau - \zeta)BB^T\left[X0(_1 - \tau - \zeta)\right]^T d\zeta\right]^{-1} \lambda, \quad 0 \leq \eta \leq t_1$$

where

$$\lambda = x_1 - X_0(t_1)\varphi(-\tau) - \int_{-\tau}^{0} X_0(t_1 - \tau - \zeta)\varphi'(\zeta)d\zeta, \tag{46}$$

And X_0 is the fundamental matrix of solutions (40) on time interval $t \geq (k-1)\tau$.

Consider, for a state feedback control, the linear time-delay system with both state and input delays given by

$$\dot{x}(t) = A_0x(t) + A_1x(t-\tau) + B_0u(t-\tau_1), \quad t \geq t_0, \tag{47}$$

where $u(t)$ is the control input and B_0 is the input matrix and τ_1 is the input delay. The pair A_0, B_0 are assumed controllable. The case with no control input delay is

$$\dot{x}(t) = A_0x(t) + A_1x(t-\tau) + B_0u(t), \quad t \geq t_0, \tag{48}$$

Suppose there exists a bounded Lipschitz continuous function,

$$\mathrm{f} : \square^{\mathrm{n}} \times U \to \square^{\mathrm{n}}, \tag{49}$$

with U as compact subset of $\square^m$, say.

The delay equation (48) maybe put in the form

$$\left.\begin{aligned} \dot{\mathrm{x}}(s) &= \mathrm{f}(\mathrm{x}(s), \mathrm{u}(s)) \qquad (t-\tau < s < t_f) \\ \mathrm{x}(t-\tau) &= \boldsymbol{x} \end{aligned}\right\}, \tag{50}$$

where

$t\text{-}\tau \geq 0$ is a given initial time,

$t_f > 0$ is a fixed terminal time,

$x \in \mathcal{R}^n$ is a prescribed initial point,

$\mathrm{u}(.) \in U$ is the *control*.

$\mathrm{x}(s)$ is the state of the system at time s

Ref
31. GannaPiddubna, Controllability Criterion for Linear Delayed Differential Equation,The Sixth International Workshop on Differential Equations and Applications, September 11-14, 2013

Each solution $x_i(.)$, (i =1, 2, 3,…,n) of (50) evolves at some succeeding time $t_i > t$-σ in the prescribed time interval. For any set of controls $u_i(.)$ (i =1, 2, 3,…,n), the set of permissible controls reads

$$U \square \{u:[t-\sigma, t_f] \to U \,|u(.) \text{ is measurable}\}. \tag{51}$$

Each permissible control has its degree of optimality. Since

$$|f(x,c)| \le C, \quad |f(x,c)-f(y,c)| \le C|x-y| \qquad (x, y \in \square^n, c \in U), \tag{52}$$

for some constant C, then for each control $u(.) \in U$ equation (50) has a unique Lipschitz continuous solution $x(.) = x^{u(.)}(.)$ on the time interval [t-σ, t_f]. The equation (50) may be solved *a.e.* on $t-\sigma < s < t_f$. We seek a control $u^*(.)$, for $x \in \square^n$ and $t-\tau \in (t-\sigma, t_f)$, among all other permissible controls which minimizes the impulse delay (as in our present case) functional

$$G_{x,t-\tau}[u(.)] = \int_{t-\tau}^{t_f} \chi(x(s),u(s))ds + \omega(x(t_f)), \tag{53}$$

where $x(.) = x^{u(.)}(.)$ is the solution of (50) and

$$\chi : \square^n \times U \to \square, \qquad \omega : \square^n \to \square$$

are given functions. From expenditure-based control systems, χ could be considered as the *running cost per unit time* and ωthe *terminal cost*. From the physiological perspective, χ could be seen as the cost of minimizing or mitigating impulse delay per unit time, andωis the terminal effect of mitigating the delay. Any least cost $V(x, t-\tau)$ is such that

$$V(x,t-\tau) = \inf_{u(.)\in U} G_{x,t}[u(.)] \quad (x \in \square^n, \quad t-\tau \in [t-\sigma, t_f]). \tag{54}$$

V. Optimality Criterion

First we state, without proof, the following:

Theorem 1 (Optimal controller (see [32]). Suppose that u(t-τ), t-τ ϵ [t-σ, t_f] minimizes*

$$G[u(.),x,t-\sigma] = \int_{t-\sigma}^{t_f} \chi(x(s),u(s))ds + \omega(x(t_f)), \tag{55}$$

subject to $x^*(t-\sigma) = x$ and $x^*(t-\sigma)$ is the related state trajectory. Let the minimum delay attained by $u^*(t-\tau)$ be:

$$G^*(x,t-\sigma) = \arg \min_{u(\beta),\beta\in[t-\sigma,t_f]} G(u(.),x^*,t-\sigma,t_f). \tag{56}$$

Then, for any t-τ∈[t-σ, t_f], the restriction of $u^*(\beta)$ optimal over the sub-interval [t-τ,t_f] minimizes

$$G[u(.),x(t-\tau),] = \int_{t-\tau}^{t_f} \chi(x(s),u(s))ds + \omega(x(t_f)),$$

subject to the initial condition $x(t-\tau) = x^*(t-\tau)$; u^* is optimal over [t-τ, t_f].

For the purpose of optimality the *value function* $V(x, t\text{-}\tau)$ shall be considered. In what follows, we fix $x\in\mathbb{R}^n$, $t\text{-}\sigma\leq t\text{-}\tau< t_f$

Theorem 2 (Optimality (see Lawrence [33]). For each $\sigma > 0$ sufficiently small that $t-(\tau-\sigma)\leq t_f$,

$$V(\boldsymbol{x},t\text{-}\tau)=\inf_{\mathbf{u}(.)\in U}\int_{t-\tau}^{t-(\tau-\sigma)}\chi[\mathrm{x}(s)+\mathrm{u}(s)]ds+V(\mathrm{x}(t-(\tau-\sigma)),t-(\tau-\sigma))], \tag{57}$$

where $\mathrm{x}(.)=\mathrm{x}^{\mathrm{u}(.)}(.)$ is the solution of (50) for the control $\mathrm{u}(.)$.

Proof. Let $u_1(.)$ be any chosen control. We set an ODE analogous to (50) in the form

$$\left.\begin{aligned}\dot{\mathrm{x}}_1(s)&=\mathrm{f}(\mathrm{x}_1(s),\mathrm{u}_1(s))ds\quad(t-\tau<s<t-(\tau-\sigma))\\ \mathrm{x}_1(t-\tau)&=x.\end{aligned}\right\} \tag{58}$$

For a fixed $\varepsilon > 0$ choose $\mathrm{u}_2(.)\in U$ so that

$$V(\mathrm{x}_1(t-(\tau-\sigma)),t-(\tau-\sigma))+\varepsilon\geq\int_{\tau-(\tau-\sigma)}^{t_f}g(\mathrm{x}_2(s),\mathrm{u}_2(s))ds+\omega(\mathbf{x}_2(t_f)), \tag{59}$$

where

$$\left.\begin{aligned}\dot{\mathrm{x}}_2(s)&=\mathrm{f}(\mathrm{x}_2(s),\mathrm{u}_2(s)\quad(t-(\tau-\sigma)<s<t_f)\\ \mathrm{x}_2(t-(\tau-\sigma))&=\mathrm{x}_1(t-(\tau-\sigma)).\end{aligned}\right\} \tag{60}$$

Describe the control

$$\mathrm{u}_3(s):=\begin{cases}\mathrm{u}_1(s) & \text{if } t-\tau\leq s<t-(\tau-\sigma)\\ \mathrm{u}_2(s) & \text{if } t-(\tau-\sigma)\leq s\leq t_f,\end{cases} \tag{61}$$

and let

$$\left.\begin{aligned}\dot{\mathrm{x}}_3(s)&=\mathrm{f}(\mathrm{x}_2(s),\mathrm{u}_2(s)\quad(t-\tau<s<t_f)\\ \mathrm{x}_3(t-\tau)&=x.\end{aligned}\right\} \tag{62}$$

The uniqueness of solutions of the equation (50) enables us to write

$$\mathrm{x}_3(s)=\begin{cases}\{\mathrm{x}_1(s) & \text{if } t-\tau\leq s\leq t-(\tau-\sigma)\\ \mathrm{x}_2(s) & \text{if } \mathrm{t}-(\tau-\sigma)\leq s\leq t_f\end{cases}. \tag{63}$$

By definition (54) we have

$$\begin{aligned}V(\boldsymbol{x},t-\tau)&\leq G_{x,t-\tau}[\mathrm{u}_3(.)]\\ &=\int_{t-\tau}^{t_f}g(\mathrm{x}_3(s),\mathrm{u}_3(s))ds+\omega(\mathrm{x}_3(t_f))\\ &=\int_{t-\tau}^{t-(\tau-\sigma)}g(\mathrm{x}_1(s),\mathrm{u}_1(s))ds+\int_{t-(\tau-\sigma)}^{t_f}g(\mathrm{x}(s),\mathrm{u}_2(s))ds+\omega(\mathrm{x}(t_f))\\ &\leq\int_{t-\tau}^{t-(\tau-\sigma)}g(\mathrm{x}_{\mathbf{1}}(s),\mathrm{u}_{\mathbf{1}}(s))ds+V(\mathrm{x}_1(t-(\tau-\sigma)),t-(\tau-\sigma))+\varepsilon,\end{aligned} \tag{64}$$

where the last inequality above resultsfrom (59). Since $u_1(.) \in U$ was arbitrarily chosen we infer that

$$V(\boldsymbol{x}, t-\tau) \leq \inf_{u(.)\in U} \left\{ \int_{t-\tau}^{t-(\tau-\sigma)} g(\mathrm{x}(s), \mathrm{u}(s)) ds + V(\mathrm{x}(t-(\tau-\sigma)), t-(\tau-\sigma)) \right\} + \varepsilon . \tag{65}$$

Continuing, choose $u_4(.)$, for a fixed $\varepsilon > 0$, such that

$$V(x, t-\tau) + \varepsilon \geq \int_{t-\tau}^{t_f} g(\mathrm{x}_4(s), \mathrm{u}_4(s)) ds + \omega(\mathrm{x}_4(t_f)), \tag{66}$$

where

$$\left.\begin{aligned} \dot{\mathrm{x}}_4(s) &= \mathrm{f}(\mathrm{x}_4(s), \mathrm{u}_4(s) \quad (t-\tau < s < t_f) \\ \mathrm{x}_4(t-\tau) &= x. \end{aligned}\right\} \tag{67}$$

From (54) we have

$$V(\mathrm{x}_4(t-(\tau-\sigma)), t-(\tau-\sigma)) + \varepsilon \leq \int_{t-(\tau-\sigma)}^{t_f} g(\mathrm{x}_4(s), \mathrm{u}_4(s)) ds + \omega(\mathrm{x}_4(t_f)), \tag{68}$$

and thus

$$V(\boldsymbol{x}, t-\tau) + \varepsilon \geq \inf_{\boldsymbol{u}(.)\in U} \left\{ \int_{t-\tau}^{t-(\tau-\sigma)} g(\mathbf{x}(s), \boldsymbol{u}(s)) ds + V(\mathbf{x}(t-(\tau-\sigma)), t-(\tau-\sigma)) \right\}, \tag{69}$$

noting that $\mathrm{x}(.) = \mathrm{x}^{\mathrm{u}(.)}(.)$ solves (50). Thus, (69) and (65) complete the proof of (57)

a) Multiple Time Delays

Let us return to the case with multiple time delays is described by equation (30)

$$\begin{aligned} \dot{x}(t) &= A_0 x(t) + \sum_{k=1}^{m} A_k x(t-\tau_k), \quad \tau_{k\geq 0} \\ x(t) &= \varphi(t), \ t \in [-\tau, 0], \end{aligned} \tag{70}$$

where $\tau = \max\{\tau_k : k = 1,2,\ldots,m\}$, $A_k \in M^{n\times n}$ are constant matrices. $\varphi(t) \in C([-\tau, 0], \mathbb{R}^n)$. Here $C([-\tau, 0], \mathbb{R}^n)$ represents the Banach space of all piecewise continuous vector-valued functions mapping $[-\tau, 0]$ into $\mathbb{R}^n$. The goal here is to convert the system with multiple time delays to a stable system with single time-delay. When this is done, the multiple time delay case may be handled as a single delay system, as was done in Ordokhani *et al.*[37].

Consider the system (70).Convert the matrices, A_k, k=1,2,..., $m$to diagonal form and subtract γ>0 from each diagonal entry. Pick the matrix with maximum norm and designate it by $M\gamma$ and denote the remaining matrix is by $A\gamma$. Using (70) we have

$$\begin{aligned} \dot{x}(t) &= A_0 x(t) + (M_\gamma + mA_\gamma) x(t-\tau), \quad t \in \mathbb{R}^+ \\ x(t) &= \varphi(t), \quad t \in [-\tau, 0], \end{aligned} \tag{71}$$

where the matrix functions A_0, ($M\gamma$+$mA\gamma$) are constant matrices. The system (71) is the conversion of the system with multiple time delays (70) to a system with single time-delay.

b) Stability criterion

Lemma 2[38] *The system (70) is said to be exponentially stable with decay rate* α, *if there is a function* ζ: $\mathbb{R}^n \to \mathbb{R}^n$ *such that for each* $\varphi(t) \in C([-\tau, 0], \mathbb{R}^n)$ *the solution* $x(t,\varphi)$ *of the system satisfies* $\|x(t,\varphi)\| \leq \zeta(\|A\|)e^{-\alpha t}$, $\forall t \in \mathbb{R}^+$.

Lemma3 [37] System (70) is uniformly asymptotically stable independent of delay if

$$\mu(A_0) + \sum_{k=1}^{m} \|A_k\| < 0. \tag{72}$$

The stability of the system (71) can be seen from the time delay system described by (70). Change the matrices A_k, k=1,2,..., , m, are to diagonal form and subtract $\gamma > 0$ from each diagonal entry. Assume the stability of the system with multiple time delay (70) satisfies (72). Now, transform the system with multiple time delays to a stable system with single time-delay (71). Since

$$\|M_\gamma + mN_\gamma\| \leq \|M_\gamma\| + m\|N_\gamma\| < \|M_{1\gamma}\| + \|M_{2\gamma}\| + \ldots + \|M_{m\gamma}\| + m\|N_\gamma\|, \tag{73}$$

By Theorem 1? we get

$$\mu(A_0) + \|M_\gamma + mN_\gamma\| < \mu(A_0) + \sum_{r=1}^{m} \|A_r\| = \mu(A_0) + \sum_{r=1}^{m} \|M_{r\gamma} + mN_\gamma\| < 0\,. \tag{74}$$

Therefore system (71) is uniformly asymptotically stable independent of delay.

Theorem 3: The system (71) is exponentially stable with decay rate α, *if there exists symmetric and positive-definite matrices* $P > 0$ and $Q > 0$ *such*

$$\begin{pmatrix} -I & \tau e^{\alpha\tau} A^T \\ \tau e^{\alpha\tau} A & -I \end{pmatrix} < 0 \tag{75}$$

$$\begin{pmatrix} \hat{A}^T P + P\hat{A} + \tau Q & \tau e^{\alpha\tau} \hat{A}^T PA \\ \tau e^{\alpha\tau} A^T P\hat{A} & -\tau Q \end{pmatrix} < 0 \tag{76}$$

where $\hat{A} = A_0 + A_1 e^{\alpha\tau}$.

The inequalities (75) and (76) are *linear matrix inequalities* (LMIs). This is in line with the standard Riccati equation

$$PA_0 + A_0^T P + PA_1 Q^{-1} A_1^T P + Q + R = 0 \tag{77}$$

consisting of triple matrices P, Q, R assumed to be positive definite, and where in the present case A_0 and A_1 are Moore-Penrose invertible [18, 19, 20]). Therefore:

Theorem 4: The time-delay system (70, 71) *is asymptotically stable for any* $\alpha \geq 0$ *if there exist matrices* $P > 0$, $Q > 0$ *and* R *such that*

$$\begin{bmatrix} A_0 P + PA_0^T + \alpha Q & A_1 P \\ PA_1^T & -\alpha Q \end{bmatrix} < 0 \tag{78}$$

Let ρ be a positive scalar such that

Ref
38. Ren F., Cao J., "Novel ∝ -stability criterion of linear systems with multiple time delays", J. Comput. Math. Appl. 181, 2006, 282-290.

$$Q = \frac{1}{\rho} A_1^T P A_1 . \tag{79}$$

Then the Riccati equation (77) reduces to the Sylvester equation

$$A_0^T P + P A_0 \frac{1}{\rho} A_1^T P A_1 + \rho A_1 + R = 0 \quad . \tag{80}$$

The sufficient conditions for Riccati Stability is given by the following Lemma:

Lemma 4[26] *Iffor some ρ¿0, the matrix* $M = (A_0 + \frac{\rho}{2} I) \otimes I + I \otimes (A_0 + \frac{\rho}{2} I) + \frac{1}{\rho} A_1 \otimes A_1$ *is Hurwitz, then the pair* (A_0, A_1) *is Riccati stable.*

c) Stabilization of delayed system

Now suppose (as in Theorem 4) that there exists a scalar $\alpha > 0$, and asymmetric matrix P such that

$$\begin{bmatrix} A_0 P + P A_0^T + \alpha P & A_1 P \\ P A_1^T & -\alpha P \end{bmatrix} < 0 \tag{81}$$

for which (70,71) is asymptotically stable [27]. Consider, for stabilization, the linear time-delay system (48)

$$\dot{x}(t) = A_0 x(t) + A_1 x(t-\tau) + B_0 u(t), \quad t \geq t_0, \tag{82}$$

We seek a state feedback controller of the form

$$u(t) = K_0 x(t) + K_1 x(t-\tau) \tag{83}$$

such that the closed loop system

$$\dot{x}(t) = (A_0 + BK_0) x(t) + (A_1 + BK_1) x(t-\tau) \tag{84}$$

is stable independent of delay. Using (81) we have to satisfy

$$\begin{pmatrix} (A_0 + BK_0)P + P(A_0 + BK_0)^T + \alpha P & (A_1 + BK_1)P \\ P((A_1 + BK_1)^T & -\alpha P \end{pmatrix} < 0 . \tag{85}$$

Using the variable transformation

$$V_0 = K_0 P$$
$$V_1 = K_1 P$$

Equation (85) becomes

$$\begin{pmatrix} A_0 P + B V_0 + P A_0^T + V_0^T B^T + \alpha P & A_1 P + B V_1 \\ ((A_1 P + B V_1)^T & -\alpha P \end{pmatrix} < 0 . \tag{85}$$

The knowledge of V_0, V_1 and the other determiners in (85) will supply the computational scheme for the inequality (85).

VI. Discussion and Summary

Delay is obviously triggered in a system by the presence of a time lag between the control action and its stimulus on the system. In the same way, delay occurs in an observable way if substantial measurement processing time is taken into account. The

Ref

27. Keqin G., Vladimir L. K., Jie C., (2013), Stability of Time-Delay Systems, Springer-Verlag

CCS is a sequence of electrical impulse-based cardiac activation. Physiological delays in the CCS are observable during the following events [34]:

(i) The *SAN* produces action potentials which diffuse through the atria via cell-to-cell conduction at a rate of about 0.5 m/sec.

(ii) The AVN slows the impulse conduction considerably to about 0.05 m/sec in order to allow satisfactory time for complete a trial depolarization and contraction.

(iii) The left and right bundle branches transmit impulses at a speedy velocity of about 2 m/sec.

(iv) A trial activation ends within about 0.09 sec after SAN firing. After a delay at the AV node, the septum becomes activated (about 0.16 sec). The entire ventricular mass is activated by about 0.23 sec.

Any further delay arising in any of the conduction times above may be considered a pathological event. Notably, the system may be fraught with multiple delay, depending on the source or aetiology of the delay. Any delay arising from the SAN or AVN is most likely to induce a cascading multiple delay. This work considered delays arising from *His bundle branch* delay. Electrical input delay to the His bundle nodal point has the effect of delayed depolarization of all other surrogates in the conduction grid. This is a case of multiple system delay. A typical example of system delay is the *QT prolongation* in which ventricular repolarisation is delayed. This pathophysiology is observed when the heart muscle takes abnormally long time to recharge between beats. Undue *QT* prolongation is implicated in tachycardias such as *Torsades de Pointes* (TdP) [35, 36], (meaning *twisting of the peaks,* as seen in undulated complexes or twist around an EKG baseline). TdP patients may have a heart rate of 200 to 250 beats/minute as against the physiologic 60 to 100bpm range. Such patients may present with palpitations or syncope [35]. There is the need to assuage pathological delay in the CCS if the culprit cannot be censored. To do this, a critical input control stabilizing measure is put into effect. Here the input control measure by means of therapeutics, preferably by drug regimented delivery is suggested. In the clinical sense, if an initial therapy s_b at time t_0 say, could be successfully regulated to meet therapeutic gains *up to approximately a final time* t_f at which the adverse effect, if any, of the final therapy $s_b(t_f)$ will be ineffectual, then a condition is *controllable*. Put succinctly, a clinical condition is *controllable* if it responds favourably to a target treatment. Such therapies are, in mathematical esoteric, the *input sequence* u_n*, which transfers* $s_b(t_0)$ *to* $s_b(t_f)$ *for some initial and finite time,* t_0 *and* t_f respectively. If the response holds, then the next goal is to seek a control for which it is at optimal. *If the state equation (41) (or the pair [A, B]) is non-controllable then it is pathologically unstable, and therefore defies clinical remedy.*

A notable point of this discussion is the understanding that non-square matrices are rife in application, albeit sparse in relation to the preponderance of square matrices in literature. A judicious use of the singular value decomposition (SVD) ensures that each matrix $A \in \mathbb{R}^{m \times n}$ can be decomposed into $A = U \Sigma V^T$, where $U \in \mathbb{R}^{m \times m}$ and $V \in \mathbb{R}^{n \times n}$ are orthogonal matrices and $\Sigma \in \mathbb{R}^{m \times n}$ is a diagonal matrix with nonnegative entries, which are singular values of A.

We saw that there is a general system response $q(t)$ to any impulse given in(25)

$$\int_{-\infty}^{t} x(\tau) q(t-\tau) d\tau = x(t) \otimes q(t) .$$

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

This response, when considered in the context of the optimal control, in line with the limit of integration, takes the form

$$\int_{t-\tau}^{t-(\tau-\sigma)} x(t-\tau)q(t-\tau)d\tau = x(t)\otimes q(t)$$

But since a positive outcome is desired, the system response may possibly have no time delay; so we have

$$\int_{t-\tau}^{t-(\tau-\sigma)} q(t)x(t-\tau)d\tau = x(t)\otimes q(t)\,.$$

At the His bundle branch (HBB) that contains R_5 and R_7 the quantity $q(t)$, is given by

$$q(t)_{HBB} = x(t-\tau)\otimes[q_1(t)\otimes q_2(t)] = [x(t-\tau)\otimes q_1(t)]\otimes q_2(t)$$

Conflicts of Interest

None.

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