Available online at http://scik.org

J. Math. Comput. Sci. 9 (2019), No. 3, 303-326

https://doi.org/10.28919/jmcs/4027

ISSN: 1927-5307

CARDIAC CONDUCTION SYSTEM: THE GRAPH THEORETIC APPROACH

NZEREM FRANCIS EGENTI*, AND UGORJI HYCINTH CHIMEZIE

Department of Mathematics and Statistics, University of Port Harcourt, Choba, Nigeria

Abstract: Cardiac conduction system (CCS) describes the mode of transmission of ionic current through the cardiac myocytes. An unperturbed conduction system is required for the integrity of blood flow and for the prevention of cardiac events. In keeping with the CCS as an electrical system, this paper treated the ionic current as an electrical circuit flow with nodal and conducting structures. This is not novel. What may be unique and appealing is the graph theoretic method by which the work is couched. As electric current is a directed flow, directed graph (digraph) theory was used in the conduction system schematics, which in turn aided the resulting matrix analysis. Make no mistake, this work does not model the electrical behaviour of the components of the CCS. In a bid to have an insight into the patho-physiology inherent in the system, the concept of efficiency (of the CCS) was discussed using the nodal and conducting structures. Reasonable clues suggest that undue resistance to flow may be culpable in cardiac events.

Keywords: circuit; source and sink; matrix; efficiency; patho-physiology.

2010 AMS Subject Classification: 94C15, 62P10,47N70.

1. Introduction

The cardio-vascular system, consisting of the heart and the vasculature, is specialized in the circulation of blood about the entire body. Circulation ensures that essential nutriments and therapeutic substances are delivered to various parts of the body. The heart is a special blood pump. The filling and ejection of blood in and out of its chambers are better explained by the systolic and

*Corresponding author

E-mail address: frankjournals@yahoo.com

Received February 10, 2019

diastolic components of blood pressure. In order to play the invaluable role of circulating blood, the heart must be electrically activated. The (human) heart requires a power source for its electrical energy needs. The cardiac conduction system (CCS) encompasses all processes that induce a 'spark' for the cell membranes to begin to change the flow of ions, giving effect to cardiac action potential (AP).

Electrical charge on cells, including the myocytes, is induced by ions rather than electrons [1]. The prominent ions that saturate the myocytes are the sodium ion (Na^+), calcium ion (Ca^{2+}), potassium ion (K^+). The presence of these ions enables the heart to create electrical impulses. The route the impulses take are controlled as they are caused to travel via specialised conduction nodes and pathways. The conduction system consists of five elements [2, 3, 4]: the sino-atrial node (SAN), the atrio-ventricular node (AVN), the bundle of His, the left and right bundle branches, the Purkinje fibres, all of which are linked by the conduction pathways. Electrical flow in the system is characterized by a source-sink process. The sequence of the conduction system is described as follows: The pacemaker cells of the SAN initiate electrical impulses that spread out through the atria by a sequence of cell to cell depolarization. (Unlike atrial and ventricular cells, pacemaker cells in the SAN have no resting phase; they have pacemaker potential that induces depolarization automaticity at the end of each action potential.) The right atrium is depolarized and electrical activity exits the right atrium through Bachman's Bundle and the AVN. The left atrium starts depolarizing at the entry of Bachman's Bundle on the left atrial septum. The signal travels all over the atrium terminating on the left lateral wall, and propagation reaches to the lateral wall from both the posterior and anterior walls. (There are no excitable cells on the lateral wall to transmit the electrical activity forward. Therefore, signal ends and left atrial depolarization is complete.) Rapid activation through Bachman's Bundle precedes the activation of the AVN. After depolarization of the atria, the electrical activity passes through the AVN. The slow conducting node cardiomyocytes of the AVN delay the impulses at atrioventricular (AV) junction. This delay is induced in order to give time for full contraction of the atrial chambers so that blood can be pumped across the AV valves preceding ventricular contraction [3]. After the AV delay, the impulse is transmitted to the ventricular bundle branches through the AV (His) bundle. The ventricular bundle branches split into left and right subdivisions on each side of the ventricular septum and terminate into a network of Purkinje fibres. Then electrical impulses are transferred from the Purkinje fibre network to activate the papillary muscles near the apex of the ventricles. This induces the

ventricular depolarization from apex to base, maximizing cardiac output. As the electrical signal gets to the base it runs out of excitable tissue. This completes a single cardiac cycle.

Refractoriness prevents a single heart beat from continually triggering myocardial cells to depolarize over and over. Individual cell gets refractory to exterior stimulus during phases 1-3 of the action potential. Under physiological condition, the cardiac cells do not respond to electrical activity until it reaches the quiescent period in phase 4 of the action potential. Thus, a single heart beat is stopped from repeatedly propagating. Cardiac myocytes are connected end to end to another by intercalated disk, with adjoining gap junction. The gap junctions provide low resistance to action potentials which spread between abutting myocytes.

In what follows, the CCS is given a mathematical outlook. Graph theory has been used enormously in various situations, including flow networks [6, 7, 8, 9, 10]. In Waterman [11] the graphical representation of RNA (a linear polymer of nucleotides found in the cytoplasm of a cell) primary/secondary network is developed. Kim *et al* [12] applied graph partitioning for the analysis of RNA modularity. It has been used widely as a mathematical tool in brain network analysis [13, 14, 15]. Keijo [16] provided a piece on graph theory worthy of reading. In this paper the pattern of CCS is described by means of mathematical graph theory.

2. Some relevant network terminologies

A few pertinent definitions and lingoes, among other things that are of interest to this work are presented below. More of the lingoes may also be seen as required in this work.

Definition 1. In network parlance, a graph $G = (\mathcal{V}, \mathcal{E})$ is a pair of sets $(\mathcal{V}, \mathcal{E})$ where $\mathcal{V}$ is the set of vertices (or nodes) and $\mathcal{E}$ is the set of edges (or arcs) between pairs of nodes (see Keijo [16]) .

A finite directed graph (digraph), G, consists of a set of vertices or nodes, $\mathcal{V}(G)$;

$$\mathcal{V}(G) = \{v_1, v_2, \ldots, v_n\}, \tag{1}$$

together with an edge set, $\varepsilon(G) \subseteq \mathcal{V}(G) \times \mathcal{V}(G)$. If v_l and v_m are two vertices connected by an edge (v_l, v_m), then two vertices v_l and v_m are *end vertices* of the edge (v_l, v_m). In a digraph the elements of E are ordered pairs. Thus the arcs (v_l, v_m) and (v_m, v_l) are in opposite directions.

Definition 2. The *degree* of the node v, written as $d(v)$, is the number of edges connecting the node with all other nodes, with v as an end node.

(Note, as an appendage to the above definition, that a loop counts twice and parallel edges give separate contributions.)

Definition 3. A *walk* on the graph $G = (\mathcal{V}, \mathcal{E})$ is a *trail* if any edge is traversed at most once.

Definition 4. A *trail* is a path if any vertex is visited at most once except possibly the initial and terminal vertices when they are the same; a closed path is a circuit.

If there are no loops and there is at most one path between any two given vertices of the graph G, then G is said to be circuitless. The proof of this may be found in Keijo [16].

Definition 5. The *out-degree* of the node v_l is the number of arcs leaving it (denoted $d^+(v_l)$) and the *in-degree* of v_l is the number of arcs going into it (denoted $d^-(v_l)$).

Definition 6. A *directed* graph with at least one directed circuit is said to be cyclic. It is acyclic otherwise

Definition 7. The *adjacency matrix* of a directed graph G is number of arcs that come out of vertex v_i and go into vertex v_j. That is to say that if $D = (d_{ij})$ is the adjacency matrix of G, then

$$d_{ij} = \text{number of arcs that come out of vertex } v_i \text{ and go into vertex } v_j. \quad (2)$$

2.1 The cardiac network

Electrical current is a directed flow. We therefore represent the cardiac conduction network by a directed graph (digraph), $G = (\mathcal{V}, \mathcal{E})$. The diagram (Fig. 1) below is the CCS. Fig.2 is extracted from Fig. 1. It is used for the node-edge analysis of the CCS.

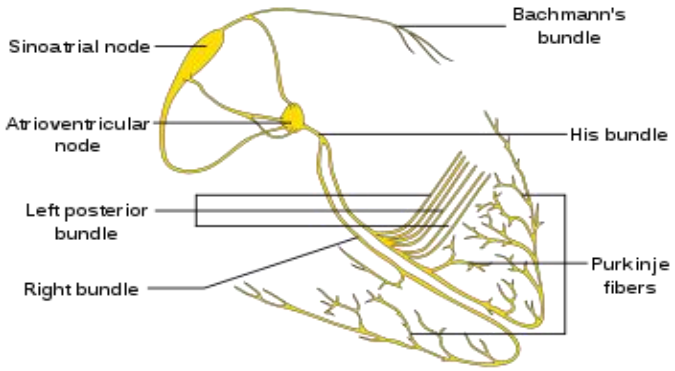

Fig.1 Electrical conduction system of the heart [17]

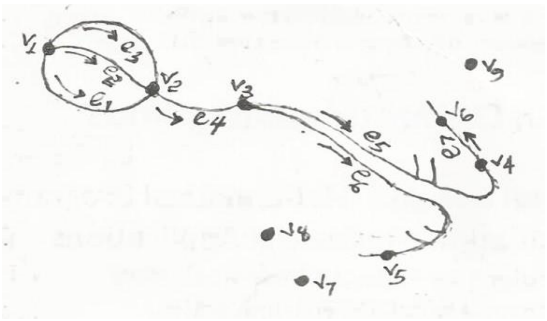

Fig.2 Node-edge schematic of the CCS

In Fig. 2 the arcs (edges) and the nodes are represented by e_i (i = 1, 2, …,7) and v_i (i = 1, 2 ,…, 7) respectively. The SAN is denoted v_1; the AVN is denoted v_2; the point of bifurcation of the bundle of His is denoted v_3; the left bundle branch is denoted by v_5; the right bundle branch is denoted by v_6. Each of the bundle branches has attachment to the Purkinje fibres, and these fibres have infinitely many minute branches and nodes. Since electrical current is a directed flow, arrow heads were used to indicate flow direction, as shown.

2.1.1 Adjacency matrix of CCS

There are some salient assumptions to be made before the construction of the adjacency matrix, and other matrices of the CCS: (i).The arc connecting each node set is *rectifiable*. (ii).There are infinitely many in-degree nodes v_i that satisfy $d^-(v_i) = 0$ (see definition (2.5)). (iii).For any arc e_j issuing from the Purkinje fibre and any infinitely large number of nodes v_∞,

$$d^{-}(v_{\infty}) = 0 \tag{3}$$

The adjacency matrix of the CCS is now constructed using Fig. 2 and definition (2.7) or equation (2). The require matrix is

$$A = \begin{array}{c} \begin{matrix} v_1 & v_2 & v_3 & v_4 & v_5 & v_6 \end{matrix} \\ \begin{pmatrix} 0 & 0 & 0 & 0 & 0 & 0 \\ 3 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \end{pmatrix} \begin{matrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \end{matrix} \end{array} \tag{4}$$

In the above table each v_i on the row indicates the initial vertex (node) of an arc e_j while each v_j on the column indicates the terminal vertex of the arc. The node v_1 corresponds to the SAN. The SAN recruits autonomous impulse that is essential for cardiac action potential. It acts as a source [22], and since it has a zero *in-degree*, it cannot be a sink. It is readily seen from Fig. 2 that, for the SAN,

$$d^{-}(v_1) = 0 \quad \text{and} \quad d^{+}(v_1) \cong 3\ . \tag{5}$$

For any isolated node $v_{k,}$

$$d^{+}(v_k) = 0 \quad \text{and} \quad d^{-}(v_8) = 0\ . \tag{6}$$

Thus, each v_k is not on the conduction system. There are infinitely many such nodes that are not on the CCS. Therefore, the minimum degree of the CCS is zero, i.e. $\delta(G_{CCS}) = 0$.

2.1.2 The incidence matrices

The flow pattern of the CCS may be described by means of the incident matrix. If $B = (b_{ij})$ is the all-vertex incidence matrix, then the matrix elements are obtained from the definition

$$b_{ij} = \begin{cases} 1 \text{ if } v_i \text{ is the initial vertex of } e_j \\ -1 \text{ if } v_i \text{ is the terminal vertex of } e_j \\ 0 \quad \text{otherwise.} \end{cases} . \tag{7}$$

Thus,

$$b_{ij} = \begin{array}{c} \begin{matrix} e_1 & e_2 & e_3 & e_4 & e_5 & e_6 & e_7 \end{matrix} \\ \begin{pmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ -1 & -1 & -1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 \end{pmatrix} \end{array} \begin{matrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \end{matrix} \tag{8}$$

As mentioned earlier, there are infinitely many in-degree nodes v_k that satisfy $d^-(v_r) = 0$. The zero row may be removed from the all-vertex incidence matrix, as was done here, without any loss to details.

2.2 Circuit matrix of G_{CCS}

A circuit matrix may be generated from the SAN-AVN intermodal pathways (see Fig.2) as shown in Fig.3 below.

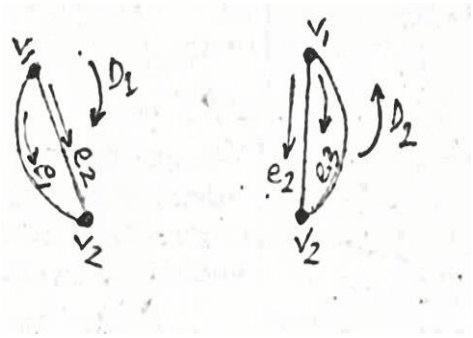

Fig.3 SAN-AVN intermodal pathways

Give each of the circuits D_1 and D_2 an arbitrary orientation so as to define the circuit matrix. The circuit matrix is $D = (d_{ij})$, where

$$d_{ij} = \begin{cases} 1 & \text{if the arc } e_j \text{ is in the circuit } D_i \text{ and they in the same direction} \\ -1 & \text{if the arc } e_j \text{ is in the circuit } D_i \text{ and they are in the opposite direction} \\ 0 & \text{otherwise} \end{cases} \tag{9}$$

The matrix is shown below

$$d_{ij} = \begin{array}{c} \begin{matrix} e_1 & e_2 & e_3 \end{matrix} \\ \begin{pmatrix} -1 & 1 & 0 \\ 0 & 1 & -1 \end{pmatrix} \end{array} \begin{matrix} D_1 \\ D_2 \end{matrix} . \tag{10}$$

3. Electrical Conductivity of Tissues

A frequently occurring problem in bioelectric theory is the calculation of the potential distribution, $\Phi(V)$, all through a volume conductor. The calculation of the scalar potential, Φ, is crucial to cardiac pacing and defibrillation. Plonsey [26] assumed Φ to be quasi-static since it frequently changes slowly enough in bioelectric problems. Under such consideration, capacitive and inductive effects are ignored. In considering electrical current through volume conductors flow is better explained as a gradient of continuous distribution rather than a specific pathway [27]. In the quasi-static assumption under consideration, the continuity equation states that the divergence,$\nabla\bullet$, of the current density, **J** (A/m^2), is equal to the applied or endogenous source of electrical current, S (A/m^3)

$$\nabla\bullet\mathbf{J} = S. \tag{11}$$

In the absence of source in any region, S is zero. In such case amounting to no divergence of **J** the law of conservation of current is often invoked in analysing electrical circuits. The property of a volume conductor requires a linear relationship between the current density and the electric field, **E** (V/m), in line with Ohm's Law,

$$\mathbf{J} = \sigma\mathbf{E} , \tag{12}$$

where σ is the electrical conductivity (S/m). The quantity $\sigma\mathbf{E}$ is often denoted as the *return current*. It is necessary to avoid accumulation of charges as a result of the source current. The electric field and the gradient, ∇, of the potential are related by

$$\mathbf{E} = -\nabla\Phi. \tag{13}$$

Thus,

$$\mathbf{J} = -\sigma\nabla\Phi . \tag{14}$$

.

A general volume conductor may describe a region of volume, Ω, which has conductivity, σ, and permittivity, ε, in which there exists a source current, I_{Vol} , where the subscript signifies per-unit volume. The solution to a volume conductor problem involves finding expressions for the electric, *E*, and potential, Φ , fields everywhere within the prescribed volume, Ω, and/or on one of the bounded surfaces, Γ_i . The current sources, I_{Vol}, derive from bio-excitable cells experiencing an activation process. In cardiac tissue activation can be considered as the process in which cells undergo rapid depolarization. Here the movement of ions across the cell membrane lead to inactivation of electrical charges and a drop in potential. The depolarization process causes a propagation of excitation waves to move through the myocardium. This work does not treat the volume conductor problem, but garners the essentials of conductors since the cardiac tissues are reckoned as one.

3.1 CCS resistive network

This section will dwell on the CCS as an analogue to electrical network. Fig. 4 below is a schematic of the CCS resistive network consisting of seven resistors, R_1, R_2, R_3, …, R_7.

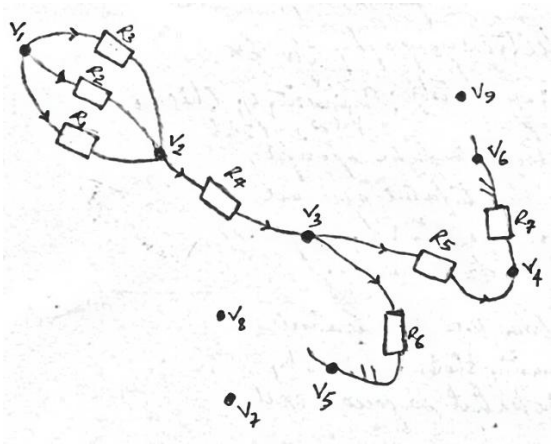

Fig. 4 CCS resistive network

The topology* of the CCS shows to wit:

(i) The resistors R_1, R_2, R_3, corresponding to the arcs e_1, e_2, e_3 within the SAN and AVN, as shown in Figs. 2 and 4, and excised as Fig. 5 below are in parallel arrangement.

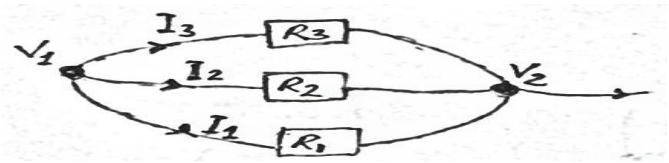

Fig. 5 Schematic of SAN-AVN resistors in parallel.

(ii) e_4, e_5, e_6 together with v_3 is a *claw* (a star topology with 3 edges) with source point of e_5 and e_6 at v_3, as shown in Fig.6 below. The proximal resistors along each of the bifurcating arcs are R_5 and R_6.

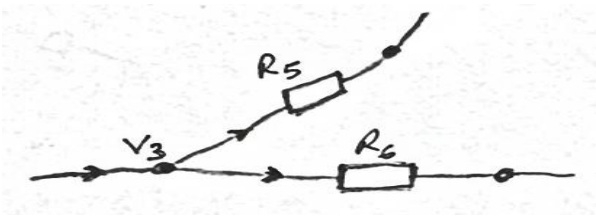

Fig.6 Resistor arrangement of His Bundle branch

(iii) The resistor R_5 is in series arrangement with R_7.

(* Topology here treats neither the physical layout of components in a circuit, nor their positions on a circuit diagram; it only treats the connections that exist between the components.) From known simple circuit law, resistors in parallel arrangement have same *voltage* rating, and resistors in series arrangement have same current rating. Therefore, R_1, R_2, R_3 are isopotential; R_5, R_7 have same current.

In the connected digraph G_{CCS} *circulation* is define as a function

$$h: F \rightarrow R \tag{15}$$

which fulfils the conservation condition at each vertex (see Bondy and Murty [20]):

$$h^{+}(v) = h^{-}(v), \quad \forall v \in \mathcal{V} \tag{16}$$

Since G_{CCS} is an electrical network, the above equation describes a circulation of currents in G_{CCS}. Therefore, one may write a matrix representation of the form

$$\mathbf{H}\boldsymbol{h} = \mathbf{0} \tag{17}$$

where **H** is the $n \times m$ incidence matrix of G_{CCS} and **0** the $n \times 1$ zero-vector.

3.2 Topological constraints

Each network may be characterized by a set of network constraints. Two types of network constraints that apply are the branch constraints, also called branch (edge) equations or element equations and the non-element based topological constraints, arising from Kirchhoff's Current Law (KCL) and Voltage Law (KVL). In a resistive electrical network each wire has a specific resistance. In the cardiac network each of the arcs is seen as a virtual wire. Therefore, it has a specific resistance. To that effect, *Ohm's law* will bring to bear on the network. By this law, the

voltage drop V between the ends of each wire is given by the equation $V=IR$, where I is the current in the wire and R its resistance. If a function on the arc set F of the graph $G_{CCS} := G_{CCS}(v_l, v_m)$ is both an (v_l, v_m)-flow and a tension, then it is called a *current flow* in G_{CCS} from v_l to v_m.

Consider one node in which branch currents $x_1, \ldots, x_n$ enter. By Kirchhoff's current law (KCL), the sum of all branch current entering a node equals zero. Thus,

$$x_1 + \cdots + x_n = 0. \tag{18}$$

Similarly, by Kirchhoff's voltage law (KVL)

$$u_1 + \cdots + u_n = 0. \tag{19}$$

where u_i represent the voltage drop in the circuit. In a multi-nodal and multi-circuit structure, as considered presently, the equations for the network are to be derived. To do this, the KCL and the KVL are to be applied together with Ohm's law.

3.2 Voltage drop across resistive edges

Since each of the arcs (edges) of the cardiac network is seen as a wire with some Ohmic resistance, the voltage drop, $u_1, u_2, \ldots, u_7$ may be calculated. Assume there is a voltage source r_0, and there are resistances $R_1, \ldots, R_7$. The voltage drop, u_i, across each of the resistances is measured across each corresponding arc, e_i as:

$$\begin{aligned} u_1 &= v_1 - v_2 & u_5 &= v_3 - v_4 \\ u_2 &= v_1 - v_2 & u_6 &= v_3 - v_5 \\ u_3 &= v_1 - v_2 & u_7 &= v_4 - v_6 \\ u_4 &= v_2 - v_3 \end{aligned} \tag{20}$$

The vector form gives

$$\begin{bmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \\ u_6 \\ u_7 \end{bmatrix} = \begin{bmatrix} 1 & -1 & 0 & 0 & 0 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 \\ 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 & 0 \\ 0 & 0 & 1 & -1 & 0 & 0 \\ 0 & 0 & 1 & 0 & -1 & 0 \\ 0 & 0 & 0 & 1 & 0 & -1 \end{bmatrix} \begin{bmatrix} v_1 \\ v_2 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \end{bmatrix} \tag{21}$$

Take v_2 as the reference (*ground*) node. Therefore the incidence matrix of *B* reduces to the matrix C = c_{ij}, given by

$$c_{ij} = \begin{array}{c} \begin{matrix} e_1 & e_2 & e_3 & e_4 & e_5 & e_6 & e_7 \end{matrix} \\ \begin{pmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 \end{pmatrix} \begin{matrix} v_1 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \end{matrix} \end{array} \tag{21 b}$$

Since v_2 is the reference (grounded) node we have, from (21)

$$\begin{bmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \\ u_6 \\ u_7 \end{bmatrix} = \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 \\ 0 & 1 & 0 & -1 & 0 \\ 0 & 0 & 1 & 0 & -1 \end{pmatrix} \begin{pmatrix} v_1 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \end{pmatrix}, \tag{22}$$

which is denoted in vector form by

$$\mathbf{u = Dv}. \tag{23}$$

The matrix D encodes network's connectivity.

Use Ohm's Law to relate the voltage drop across each resistor to current. We now use provision of Ohm's law to seek the current "*I*," noting that "*I = V/R*". (Note that this equation is a version of **J** = σ**E,** equation (12).) Therefore, at each of the resistors Ohm's Law gives,

$$x_j = u_j/R_j, \qquad j = 1, \ldots, 7. \tag{24}$$

The matrix-vector form is

$$\begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_6 \\ x_7 \end{bmatrix} = \begin{pmatrix} 1/R_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1/R_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1/R_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1/R_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1/R_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1/R_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1/R_7 \end{pmatrix} \begin{pmatrix} u_1 \\ u_2 \\ u_3 \\ u_4 \\ u_5 \\ u_6 \\ u_7 \end{pmatrix}. \tag{25}$$

Denote the above matrix equation as

$$\mathbf{x = Ku}\ . \tag{26}$$

In the above, **K** depicts the physics of the network. The application of KCL yields the matrix-vector product:

$$\begin{pmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 \end{pmatrix} \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_6 \\ x_7 \end{pmatrix} = \begin{pmatrix} 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}\ . \tag{27}$$

The above has the form

$$\mathbf{D^T x = 0.} \tag{28}$$

(Observe that $\mathbf{D}^T = C$)

Insert (**x = Ku**) for **x** into (28) above to get

$$\mathbf{D}^T\mathbf{Ku} = \mathbf{0}. \tag{29}$$

Take the existence of a constant voltage source, r_0, at which the network is at equilibrium, into account, such that

$$\mathbf{u} = \mathbf{r} - \mathbf{Dv}. \tag{30}$$

Then

$$\mathbf{D}^T\mathbf{Ku} = \mathbf{D}^T\mathbf{K(r - Dv)}.$$

Thus,

$$\mathbf{D}^T\mathbf{KDv} = \mathbf{f}, \tag{31}$$

where $\mathbf{f} = \mathbf{D}^T\mathbf{Kr}$. The vector **f** denotes the vector of current sources. It is a representation of the network's stimuli.

3.2.1 System of equations for v_i

This section seeks the potential at each node of the system.

First compute D^TK:

$$\mathbf{D}^{\mathrm{T}}\mathbf{K} = \begin{pmatrix} 1 & 1 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 0 & -1 & 0 & 1 \\ 0 & 0 & 0 & 0 & 0 & -1 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1 \end{pmatrix} \begin{pmatrix} 1/R_1 & 0 & 0 & 0 & 0 & 0 & 0 \\ 0 & 1/R_2 & 0 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1/R_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 1/R_4 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1/R_5 & 0 & 0 \\ 0 & 0 & 0 & 0 & 0 & 1/R_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & 1/R_7 \end{pmatrix}$$

$$= \begin{pmatrix} 1/R_1 & 1/R_2 & 1/R_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1/R_4 & 1/R_5 & 1/R_6 & 0 \\ 0 & 0 & 0 & 0 & -1/R_5 & 0 & 1/R_7 \\ 0 & 0 & 0 & 0 & 0 & -1/R_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1/R_7 \end{pmatrix}. \qquad (32)$$

Next is the matrix $\mathbf{(D^TK)D}$. Now compute:

$$\mathbf{(D}^{\mathrm{T}}\mathbf{K)D} = \begin{pmatrix} 1/R_1 & 1/R_2 & 1/R_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1/R_4 & 1/R_5 & 1/R_6 & 0 \\ 0 & 0 & 0 & 0 & -1/R_5 & 0 & 1/R_7 \\ 0 & 0 & 0 & 0 & 0 & -1/R_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1/R_7 \end{pmatrix} \begin{pmatrix} 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 1 & 0 & 0 & 0 & 0 \\ 0 & -1 & 0 & 0 & 0 \\ 0 & 1 & -1 & 0 & 0 \\ 0 & 1 & 0 & -1 & 0 \\ 0 & 0 & 1 & 0 & -1 \end{pmatrix}$$

$$= \begin{pmatrix} 1/R_1 + 1/R_2 + 1/R_3 & 0 & 0 & 0 & 0 \\ 0 & 1/R_4 + 1/R_5 + 1/R_6 & -1/R_5 & -1/R_6 & 0 \\ 0 & -1/R_5 & 1/R_5 + 1/R_7 & 0 & -1/R_7 \\ 0 & -1/R_6 & 0 & 1/R_6 & 0 \\ 0 & 0 & -1/R_7 & 0 & 1/R_7 \end{pmatrix}. \qquad (33)$$

$\mathbf{(D^TK)D}$ is a symmetric matrix whose inverse, when applied to **f**, furnishes the vector of potentials v_i, if R_i are known.

Next, evaluate the vector **f**:

$$\mathbf{f} = \left(\mathbf{D}^T\mathbf{K}\right)\mathbf{r} = \begin{pmatrix} 1/R_1 & 1/R_2 & 1/R_3 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & -1/R_4 & 1/R_5 & 1/R_6 & 0 \\ 0 & 0 & 0 & 0 & -1/R_5 & 0 & 1/R_7 \\ 0 & 0 & 0 & 0 & 0 & -1/R_6 & 0 \\ 0 & 0 & 0 & 0 & 0 & 0 & -1/R_7 \end{pmatrix} \begin{pmatrix} r_0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} = \begin{pmatrix} r_0/R_1 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}. \tag{34}$$

Apply $\mathbf{(D^TK)D}$ to **f**

$$\begin{pmatrix} 1/R_1+1/R_2+1/R_3 & 0 & 0 & 0 & 0 \\ 0 & 1/R_4+1/R_5+1/R_6 & -1/R_5 & -1/R_6 & 0 \\ 0 & -1/R_5 & 1/R_5+1/R_7 & 0 & -1/R_7 \\ 0 & -1/R_6 & 0 & 1/R_6 & 0 \\ 0 & 0 & -1/R_7 & 0 & 1/R_7 \end{pmatrix} \begin{pmatrix} v_1 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \end{pmatrix} = \begin{pmatrix} r_0/R_1 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix} \tag{35}$$

If each of the quantities $R_1, R_2, \ldots, R_7$ is known, then $v_1, v_3, \ldots, v_6$ may be determined.

Suppose, for instance, that all resistors have the same (?) value, R Ohms. If we clear $1/R$ terms, the above equation becomes

$$\begin{pmatrix} 3 & 0 & 0 & 0 & 0 \\ 0 & 3 & -1 & -1 & 0 \\ 0 & -1 & 2 & 0 & -1 \\ 0 & -1 & 0 & 1 & 0 \\ 0 & 0 & -1 & 0 & 1 \end{pmatrix} \begin{pmatrix} v_1 \\ v_3 \\ v_4 \\ v_5 \\ v_6 \end{pmatrix} = \begin{pmatrix} r_0 \\ 0 \\ 0 \\ 0 \\ 0 \end{pmatrix}. \tag{36}$$

Now it is easy to solve for v_i. (The thought of assuming that all resistors have the same value is, however perceivable, physiologically untenable. Therefore, the system of equations derivable from the above matrix equation would only furnish ideal nodal potentials.)

Certainly, the potential at $v_1, v_2, \ldots, v_7$ depend on two factors- the voltage source, r_0, and the relative strength of the resistors. The potentials must decay with distance from the voltage source.

3.3 G_{CCS} Centrality and efficiency

The centrality concept is a measure the importance of nodes in a graph network. Here our graph is the G_{CCS} whose nodes are not interconnected. Centrality may be from the standpoint of the impact of a node on other nodes. Following [18], let v^* be the node with highest degree centrality in G. Let $X := (Y, Z)$ be the $|Y|$ node connected graph that maximizes the quantity (with y^* being the node with highest degree centrality in X):

$$R = \sum_{j=1}^{|Y|} \left[C_D(y^*) - C_D(y_j) \right], \tag{37}$$

where $C_D(.)$ is the centrality degree of a given node. Therefore, the *degree centralization* of the graph G is

$$C_D(G) = \frac{\sum_{i=1}^{|V|} \left[C_D(v^*) - C_D(v_i) \right]}{Q} \tag{38}$$

Q is maximized when the graph X contains one central node to which all other nodes are connected. For any graph G,

$$C_D(G) = \frac{\sum_{i=1}^{|V|} \left[C_D(v^*) - C_D(v_i) \right]}{|V|^2 - 3|V| + 2} \tag{39}$$

Degree centrality is the most widely used measure of centrality. It uses the degree of a node to explain the importance of the node in a given network. In the brain network it is said to measure the impact of the brain region on other adjacent brain regions [15]. In the CCS network analysis, the degree centrality of a cardiac nodal cell shall measure the influence of the nodal cell on other nodal cells. In the CCS we have, for the SAN,

$$d^{+}(v_1) = 0 \quad \text{and} \quad d^{-}(v_1) = 3,$$

.

and for the AVN,

$$d^{+}(v_2) = 3 \quad \text{and} \quad d^{-}(v_2) = 1. \tag{40}$$

The HIS bundle has

$$d^{+}(v_3) = 1 \quad \text{and} \quad d^{-}(v_3) = 2. \tag{41}$$

3.3.1 The SAN is most central

The niggardly *in-degree* of the SAN, $d^{+}(v_1) = 0$ may not be construed as a lesser degree of importance. In conduction system the *out-degree* is of immense importance. An *out-degree* node acts as a source while an in-degree node acts as a sink. In CCS architecture, a sink remains quiescent until the transmission of impulse from an abutting source. By the conservation law, each sink is also a source. However the SAN is never a sink, save when seen as a sink to itself as it is the first to absorb the self-generated impulse. In physiological state it generates and transmits the current required to activate all quiescent cells. Analogous to the closeness centrality measure of a brain region [23], the closeness centrality of a CCS node will measure the indirect impact of a node on other nodes. In fine, the closeness centrality of the SAN is accentuated by its impulse-generation which other CCS components utilize. There are some salient points about the SAN:

(i). It has a large out-degree in order to mitigate the impact of the enormous ionic current it generates, being a voltage source, and also to drive the atria.

(ii). In the CCS network it has no need for an *in-degree* since, in virtue of its automaticity, it has no resting phase; only quiescent cells have such needs.

(iii) It is so generous to the AVN: The SAN, with its niggardly *in-degree*, $d^{+}(v_1) = 0$, bequeaths three out-degree arcs to the AVN. Therefore, it hands to it (AVN) a substantial amount of impulse that guarantee less degree of gap-junctional resistance in the vicinity of the abutting cell.

The global efficiency and local efficiency of the CCS are, in the main, linked to the nodal efficiency. The former is a measure of the ability of all the conducting facilities to maintain the integrity of the ionic current. Local efficiency is a measure of the ability of fault tolerance in a prescribed vicinity on the network (see Achard and Bullmore [19]). The CCS global efficiency is tenable in physiological states. Such states are only evinced by cardio-vascular parameters which are not discussed here.

3.4 When local efficiency is wanting

The physics of the CCS will be more of the analytic concern here, though without prejudice to the biology. The malfunctioning of a node indicates that local efficiency is compromised. Individual nodes must be locally efficient in order to maintain the integrity of the CCS. If the SAN malfunctions, it may be unable to control the heart rate (60-100bpm). Weak impulse transmission to the AVN may follow. At times it is within context to surmise that high pathway (edge) resistance may be implicated. Take a look at the SAN (v_1)- AVN (v_2) pathways consisting of R_1, R_2, R_3 in parallel. A single unreciprocated equivalent resistor representing the three resistors is

$$\frac{\prod_{i=1}^{3} R_i}{\sum_{i=1}^{3} R_i} = \frac{R_1 R_2 R_3}{R_1 + R_2 + R_3} = R_{123}\,. \tag{42}$$

The use of Ohm's law gives

$$I = \frac{V}{R_{123}} = V \frac{\sum_{i=1}^{3} R_i}{\prod_{i=1}^{3} R_i} \tag{43}$$

Observe that

$$\lim_{R_{123}\to 0}\left(V\frac{\sum_{i=1}^{3}R_i}{\prod_{i=1}^{3}R_i}\right)=\infty,\quad \text{and}\quad \lim_{R_{123}\to \infty}\left(V\frac{\sum_{i=1}^{3}R_i}{\prod_{i=1}^{3}R_i}\right)=0\,. \tag{44}$$

From (44) above, the current supply, I , to AVN gets infinitely large as resistance, R_{123} weakens progressively, and current supply, I, plummets as resistance, R_{123} increases progressively. Each of these cases diminishes local efficiency. As R_{123} weakens, current supply to the AVN becomes excessive and incommodious. On the other hand, a progressive increase in R_{123} leads to a drip or sluggish supply of current to the AVN. Therefore, the SAN may not transmit generated impulse within physiological time constraint (sinoatrial conduction time (SACT)).This is a mark of sinoatrial dysfunction (SND). In turn, SND may induce the development of re-entrant circuits which may be prodromal to atrial fibrillation [24, 25].

In the event of SAN failure, the AVN becomes the *ectopic* pacemaker of the heart. The cells of the AV node are called the *secondary pacemaker*, normally discharging at about 40-60 bpm [25].
AVN efficiency may be impaired when partial or complete block in the transmission of electrical impulses from the atria to the ventricles, known as *heart bloc*, occurs. This is an ominous case of very high resistant e_4 pathway. The next in the cardiac electrical conducting system is the *Bundle of His*, consisting of the left and right branches. This bundle, together with the *Purkinje fibres* fire spontaneous action potential at a rate of 30-40 beats per minute [25]. Each of them has its peculiar patho-physiological event(s) to which pathway resistances are liable.

4. Summary and discussion

The cardiac conduction system is the electrical conduction system of the heart which transmits electrical signals generated typically by the sinoatrial node to induce contraction of the heart muscle. It is a virtual electric circuit whose conduction pathways have the similitude of electric cables with resistances. The use of graph theory in analysing networks, which include the CCS, is a judicious mathematical enterprise. Since electrical flow is a directed flow, any representative graph must be a directed graph (digragh). In dealing with the CCS, the nodes and arcs which

characterise graphs were defined. The nodes are essentially the ionic current sources and sinks, to wit SAN, AVN, Bundle of His, Purkinje fibres. There are infinite nodes of zero degree as well. The arcs (edges) are the conduction pathways already described. The graph theoretic approach made the matrix method of analysis an endearing tool. The concept of centrality showed that the SAN is the epicentre of the CCS, all else being equal. The concept of (local) efficiency explained the deleterious effects of nodal and/or edge dysfunction.

It is agreed that the CCS describes cardiac electrical system involving ionic current; it is a fact that the conduction mechanism drives blood flow. Some salient questions are: (From the nodal point of view) (i) Are the CCS nodes actually similar to electrical nodes? (ii) If yes, then what problems do electrical nodes pose? (iii) Are those problems tractable? From the arc point of view (i) Can the material component of the arc(s) of each segment of the CCS be ascertained? (ii) Is the resistivity of each arc measurable (iii) What are the endogenous and exogenous factors that possibly affect the resistivity of the arcs?

Answers to these questions can guide suggestions/actions that may provide solutions to many cardiovascular events due to poor conduction system. It seems worthwhile to take a more than cursory look at the Bundle of His branches. If we do, we conjecture nature's endowment to humankind: the *claw* topology gives the following benefits:

(i) The breakdown of one connection may not affect the benefits which beneficiary cardiac components derive from the other connection. Thus, one bundle branch may keep the system alive in the event of malfunctionality of a sister branch, though it may not be maximally efficient.

(ii) Prosthetic intermodal pathways may be introduced along any axis of a bundle branch with minimal deleteriousness in exigent situations. This presupposes a clear knowledge of the conductivity/resistivity of both the failing and prosthetic pathways.

(iii) Claws are believed to work well under heavy loading [28]. Thus neither series nor parallel arrangement may be a better impulse driver of the quiescent cells along the bundle branches.

However, we should not lose sight of the fact that the nodal point is a *single point of failure* for the sub-circuit.

Conflict of Interests

The authors declare that there is no conflict of interests.

REFERENCES

[1] R. Maex, Mathematical models of excitability in Biological membranes, cells and network Encyclopaedia of Life Support Systems (EOLSS), www.eolss.net/sample-chapters/c02/E6-188-06-00.pdf.

[2] Cardiac Conduction System, https://www.nottingham.ac.uk/nursing/practice/resources/cardiology/function/conduction.php

[3] H. Jan van Weerd and V. M. Christoffels, The formation and function of the cardiac conduction system, Development 143(2016), 197-210.

[4] J.H. Cathy and T.B.Craig, Specification of the Cardiac Conduction System by transcription factors, Circ Res., 105(7)(2009) 620–630.

[5] R. Nicolas, G. Celso and S. B. Murilo, Structure and function in flow networks, Europhysics Letters, Volume 101(2013), 68001.

[6] R.Nicol ás, G. Celso and S. B. Murilo, Understanding information transmission in complex networks, arXiv:1705.05287 [nlin.AO]

[7] W. Wen-Xu and L. Ying-Cheng, Abnormal cascading on complex networks, Phys. Rev. 80(2009), 036109.

[8] K. Ahuja Ravindra, L. Magnanti Thomas and B. Orlin James, Network Flows: Theory, Algorithms, and Applications (Prentice-Hall, NJ) 1993.

[9] A. P. Georgios, S. Maria, N. M. Charalampos, G S. Theodoros, K. Sophia, A. Jan, S. Reinhard, and G B. Pantelis, Using graph theory to analyze biological networks, BioData Min. 4(2011), 10.

[10] S.H Yook, H Jeong, A.L. Barabasi, Modeling the Internet's large-scale topology. Proc. Natl Acad. Sci. 99 (2002), 13382-13386.

[11] M.S. Waterman, Secondary Structure of Single-Stranded Nucleic Acids. Adv. Math. Suppl. Stud. 1(1978), 167–212.

[12] K Namhee., Zhe Zheng, E. Shereef, S. Tamar, RNA Graph Partitioning for the discovery of RNA modularity: A novel application of graph partition algorithm to Biology, PloS one 9.9 (2014): e106074.

[13] A. Zalesky, L. Cocchi, A. Fornito, M. M. Murray, and E. Bullmore, Connectivity differences in brain networks, NeuroImage, 60(2012), 1055–1062.

[14] D. Mears and H. B. Pollard, Network science and the human brain:Using graph theory to understand the brain and one of its hubs, the amygdala,in health and disease, J. Neurosci. Res. 94 (2016), 590–605.

[15] Jin Liu, Min Li, Yi Pan, Wei Lan, Ruiqing and Jianxin Wang, Complex brain network analysis and its applcations to brain disorders: A survey, Complexity, 2017 (2017), Article ID 8362741.

[16] Keijo Ruohonen, Graph theory, math.tut.fi/~ruohonen/GT_English.pdf (2013)

[17] Electrical conduction system of the heart, https://en.wikipedia.org/wiki/Electrical_conduction_system_of_the_heart

[18] Centrality, *https://en.wikipedia.org/wiki/Centrality*

[19] S. Achard and E. Bullmore, Efficiency and cost of economical brain functional networks, PLoS Comput. Biol. 3 (2007), e17.

[20] J.A. Bondy and USR Murty, Graph theory, Springer. (2008).

[21] C. Thomassen, (1990). Resistances and currents in infinite electrical networks. J. *Combin. Theory Ser. B* **49**, 87–102.

[22] F. E. Nzerem, H. C. Ugorji, Cardiac Electrophysiology: The sinoatrial node in focus, Mathematics Letters**,** 4 (4) (2018), 59-66.

[23] M. A. Beauchamp, "An improved index of centrality," Behavioural Science,10(1965), 161–163.

[24] P Sanders,J.B. Morton, PM Kistler et al.Electrophysiological and electro anatomic characterization of the atria in sinus node disease: evidence of diffuse atrial remodeling. Circulation. 109(2004),1514–22.

[25] Moinuddin Choudhury, Mark R Boyett and Gwilym M Morris , Biology of the sinusnode and its disease, Arrhythm Electrophysiol Rev. 4(1) (2015), 28–34.

[26] R. Plonsey, Bioelectric Phenomena, McGraw-Hill, New York. (1969).

[27] Gerald E. Loeb and Carl Gans, Electromyography for experimentalists, University of Chicago Press. (1986)

[28] Star network, https://en.wikipedia.org/wiki/Star_network