PERSPECTIVES

The Heartbeat: Evidence and Presupposition from Days of Yore and Far Yonder

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For the Most High knows all that may be known,
and He looks into the signs of the age.
He declares what has been and what is to be,
and he reveals the tracks of hidden things.
- Book of Sirach

INTRODUCTION

Let we, who are supposed experts of the heart and know that there's a tiny node at the roof of the right atrium that fires impulses automatically to the demand of the body with nary our care or intent, pause for a moment to appreciate what it took for our forefathers to put us in this position of knowledge; and, by the same awareness, be humbled to realize that there's a lot more beyond what we know and understand.

Voluminous scientific evidence gathered from ages and from all corners of the world have revealed so much information in attempt to search for the anatomic, physiologic, down to embryogenic fundamentals of the cardiac electrical system to answer the question: *"How is one heartbeat formed?"*

How is the conduction system configured?

After fertilization, the immediately busy blastocyst travels from the ampulla of the fallopian tube to be imbedded in the endometrium while cell division continues along the way. Along with it, a trophoblast develops as an essential component of the placenta to begin feeding the growing embryo. All these happen within 6 days after the honeymoon.[1]

At about 3 weeks, a day after the fusion of the heart tubes – lo and behold - the heart begins to beat. [2-4] Initially asynchronous, because the conduction system is yet to be fully developed, the resolute primitive heart becomes the first functioning organ determined to bring the embryo to maturity in a most precarious environment. This officially marks the beginning of life in the mortal body, though some are to believe that the soul preceded this.

Here is an oversimplified version of how the electrical system develops over the course of embryogenesis, occurring after the looping process is completed. As it goes, there are 3 germ layers of the embryo, namely the ectoderm, mesoderm, and endoderm. From the middle mesoderm, progenitor cells destined to become myocytes, further differentiate into working myocardial cells or specialized electrical cells.[5]

Those cells found in the caudal tube of the right sinus venosus organize themselves to be the eventual sinus node. It is not settled whether the sinus node develops with the incorporation of the sinus venosus into the atrium or that it is already formed even before the merging.[6-8] Regardless, it is strategic that this occurs in the atrium right at the entrance of the superior vena cava.

Meanwhile, from another site, the atrioventricular node and the His Bundle evolve at the base of the outflow tract. [7-8] And then somehow, the electrical cells of the entire conduction system are miraculously connected, touching every myocyte of the heart, with not one spared.

Where are these structures found?

Once upon a time, our ancestral physiologists were divided in thought, with one group believing that the heart muscle provided itself with the stimulus to beat the heart, while another argued that an external stimulus did the job.[8-10] In the midst of this century-long “myogenic vs neurogenic” debate, some mavericks took the initiative to locate its possible source.

In the early 1839, Jan Evangelista Purkinje serendipitously found a gelatinous network of fibers in the subendocardium, unbeknownst to him of what its function was.[8-10] The realization that there indeed might exist an electrical system within the muscular heart did not come to fore until Gaskell’s curious scrutiny in 1880 pinpointed a very specific start of the impulse originating from the vicinity of the sinus venosus.[8-10] Up until then, no one had the slightest inkling of a possible specialized electrical structure.

But, alas, localizing the sites of the electrical system did not come easy. Independent searches were launched over centuries to situate the source of stimuli that rhythmically beat the heart. Disconnected parts were separately found before a completed map of the conduction system was finally assembled. Interestingly, the campaign unearthed discoveries that oddly took the retrograde route to connect the whole structure.

It began with an eye-opening moment in 1893 when a bundle connecting the atria and the ventricles was discovered by Wilhelm His, Jr. near the tricuspid valve.[8-12] This bundle divided into right and left branches terminating at the network found earlier and gave purpose to the previous finding of Jan Evangelista Purkinje about half a century before.

More than a decade later in 1906, Sunao Tawara discovered a “complex Knoten” tissue atop the bundle described earlier by Wilhelm His,[8-10] which set aright the thinking that there indeed was a specialized tissue made by the Maker imbedded in the thick of the muscle. However, this still did not connect with Gaskell’s “start” of the heartbeat.

Ironically, it was the elusive sinus node, which was last to be discovered in the entire conduction system. For many years, raiders in search for the coveted map had to remain content with an incomplete chart, perhaps imagining invisible bridges that connected within the myocardium. Later that same year,

Figure 1. “Figuring the Divine Design”. Pencil and ink on paper depicting electrophysiologists of yore unraveling mysteries. Original art work from the author.

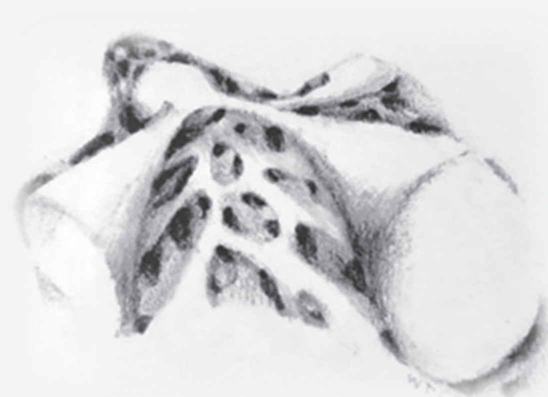

Figure 2. ”The Sieve” from HEART: Sketches in Eden, 02 August 2007. Pencil drawing on paper depicting the AV node, His Bundle, Right and Left Bundle Branches, as imagined (not anatomically accurate) by the artist.

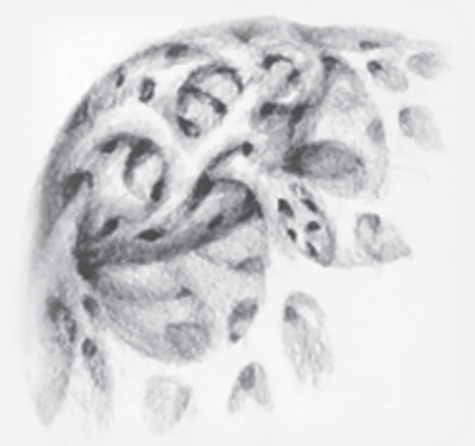

Figure 3. "The Springwell" from HEART: Sketches in Eden, 02 August 2007. Pencil drawing on paper depicting the sinus node, as imagined (not anatomically accurate) by the artist.

Keith and Flack unearthed a node that resembled the familiar "knoten" found by Tawara,[8-10] but this time in the region where Gaskell had described the source of the impulse a quarter of a century before them.

Finally, the origin of the impulse and where it spreads through the heart with a complete itinerary of its journey, from start to end, was established by the collaboration of evidences and careful presuppositions, put together from days of yore and from far yonder.

How do they work?

As the electrical landscape was being drawn and mapped out, another big quest was underway. Cellular and clinical electrophysiologists wanted to know the properties of the newfound electrical system. They began developing various techniques to probe the mysterious electricity occurring in the heart.

Cellular electrophysiologists impaled microelectrodes into single cardiac cells to record the dynamics of the electricity in the form of a "monophasic action potential". [13-14] And with the "voltage clamp" technique,[14-16] changes in conductance and currents timed with opening and closing of channels for ions to cross the cell membrane were eventually elucidated.

Two types of deflections, namely the slow and fast channel dependent action potentials (Figure 4), with various phases were described and identified from different parts of the conduction system.[14] A barrage of papers with more evidence formed the basis of how the electricity works inside the heart.

Clinical electrophysiologists, on the other hand, developed surface and intracardiac electrograms to track the course taken by the impulse. The invention of ECG by Willem Einthoven in 1901 opened more ways to study the impulse from the surface.[8] Half a century later, audacious electrophysiologists passed electrodes into the heart to record localized electrograms in more specific locations.[17]

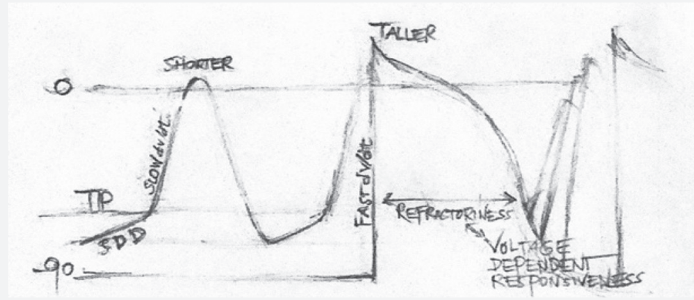

Figure 4. "The Slow and Fast Channel Dependent Action Potentials" modified from figure in the book The Art of ECG, The Crucible Workshop 2021. Pen and ink drawing on paper (not from recordings) describing features of action potentials from slow and fast channel dependent cells, from depolarization to repolarization and their refractoriness.

Together, the cellular and the clinical electrophysiologists reconstructed the meticulously designed system painstakingly executed by our Maker. One after another, wonders of the cardiac electrical system were brought to light on how a mysterious impulse is formed and navigated through the heart to accomplish its mission of producing a heartbeat.

Finally, A Coherent Compiled Story

It is reassuring to know that the electrical system of the heart is all organized and stationed in their designated positions with fail-safe and back-up mechanisms, rehearsed and tested, long before it is delivered to the outside world. From uncountable pieces of a puzzle, we have a synthesized groundwork of what is behind the making of a heartbeat. Below is an oversimplified storyline for a background sewn for us, the proclaimed stewards of the heart.

"From one of many "P" cells inside the strategically situated sinus node - an electrical impulse is born, not at all by our doing, but given as a Divine Gift. Intracellular recording would show spontaneous diastolic depolarization to be responsible for the automaticity of these slow-channel dependent cells.[18] Once the membrane potential reaches threshold, a propagated response is produced resulting in an impulse to be reckoned with.[18]

Underlying this feat is a complexity of ion movements crossing the highly selective and picky semipermeable membrane only He can make. It involves the decay of delayed rectifier K^+ current[18-21] along with activation of various so-called "funny" inward currents of slow Na^+ and Ca^+ ions.[18-22] Thus far, this is what we know to be responsible for the most mysterious self-depolarization that ushers in life. Surely, there is more beyond understanding.

Three factors regulate the rate of this impulse generation inside the sinus node: these are the slope of the diastolic depolarization (SDD), the maximum diastolic potential (MDP)

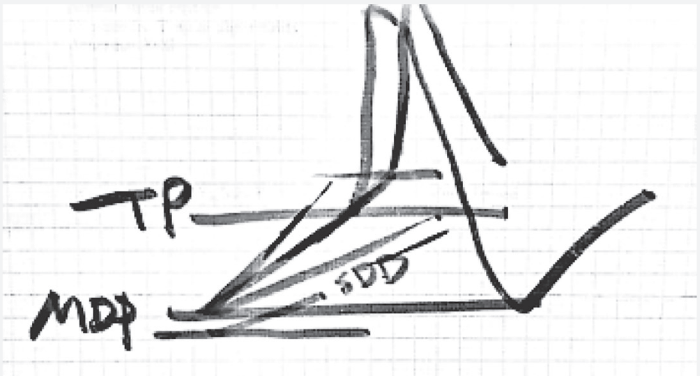

Figure 5. "Determinants of Rate of Impulse Generation". Original artwork from the author. Ink on paper demonstrating the 3 factors that determine impulse generation, namely: MDP (maximum diastolic potential); TP (threshold potential); and SDD (spontaneous diastolic depolarization with different rate of rise of Phase 4.

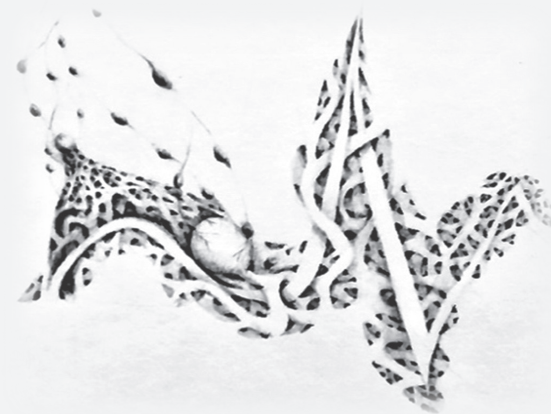

Figure 6. "The Impulse Path", from the book The Art of ECG, The Crucible Workshop 2021. Pencil on paper depicting the path taken by the impulse from sinus node to the rest of the conduction system as it writes the PQRST.

from where it starts, and the threshold potential (TP) for it to reach (Figure 5).[14,21,23] Each one of these are altered accordingly to the modulation of the sympathetic and the parasympathetic influence by the richly innervated autonomic nervous system.[14,21,24] As a result, a beat-to-beat interval change of impulse discharge varies instantaneously, according to the body's need and demand at every millimoment throughout life.

Once formed, the impulse then leaves its home. Departing the confines of the sinus node, it touches and excites the fast-channel dependent cells awaiting outside ~~at~~ the internodal tracts and continue to spread radially to the atrial Purkinje system. Eventually, every atrial myocyte is sequentially stimulated to effect an organized contraction. It is important to note that the impulse leaving the sinus node is not a guaranteed success as it has to negotiate through the sino-atrial junction and has been shown to sometimes fail.[14,18]

Widespread and multi-directed in the atria but unable to traverse down because the entire perimeter is effectively insulated from the ventricles, the impulse then converges at the base of the right atrium near the tricuspid valve. Here it finds the only accessible conduit. This time, it proceeds at a deliberately moderate pace through a compact AV node, which is packed with slow-channel dependent cells for three very important reasons and purposes.[25]

Firstly, by virtue of its unhurried rate of rise and smaller amplitude of phase 0, the slow channel-dependent cells retard the conduction of the impulse getting through. In effect, an intended delay of ventricular activation results in a favorable AV sequential contraction for best hemodynamics.[22,25]

Secondly, the extended refractoriness, which is beyond voltage recovery, makes it prone for decremental conduction and block. This is intended to sieve unreasonably rapid atrial impulses, like atrial fibrillation, to protect the ventricle.[25]

Lastly, and there might be more reasons to discover later, the slow channel-cells come with automaticity although with slower spontaneous diastolic depolarization. In the event of lack of impulses due to failure of sinus node production or conduction, these cells rise to the occasion and take over pacing the ventricle, like a dependable spare.[25]

Having negotiated through the AV node, the impulse emerges out to confront the vast ventricular horizon. It then resumes full speed and swoops down unimpeded through the sea of countless fast-channel dependent cells that lie in wait, beginning at the main avenue of the His Bundle, then reaching the bifurcation and divides into the right and left bundle branches.[25]

In no time, that very impulse that started as a small spark in the sinus node is all over the array of Purkinje fibers penetrating into each of the working myocytes to the very periphery. With inexplicable and precise sequence of activation of one cell after another, a perfectly choreographed ventricular contraction is produced for a heartbeat to sustain life for the next few minutes.

Not only did our Maker gift us with the impulse and paved the path for it, but to protect us, He made certain that each cardiac cell goes through a required period of refractoriness after depolarization before regaining responsiveness [25]. Because of this, the impulse can only advance forward, unable to turn back to the refractory cells behind its trail until it reaches the last working myocyte. Having done its singular mission to provide one purposed heartbeat, the impulse then disintegrates. And, the heart prays for the gift of the next impulse.

Postscript

As questions are being answered, more are raised that we can never get to the bottom of. Whatever we have thus far unearthed is just superficial of an unfathomable mystery. Our inquisitive but inchoate human mind must know to leave the unanswerable to faith and instead ask: why is so much ado given to all the complexities that began from the very beginning when the fateful sperm fertilized the anointed egg, just to give us the gift of a Heartbeat? The answer I believe is an Unreasonable Love wanting to give life, that we hardly deserve. Thank you, God!

Note: Dr William T. Chua is a cardiac electrophysiologist and the honorary founding president of the Philippine Heart Rhythm Society. He is a Fellow of the Philippine Heart Association-Philippine College of Cardiology and a former editor-in-chief of the Philippine Journal of Cardiology. He is also an artist and has held local and international exhibitions of his paintings and sculptures centering on the heart as the subject.

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“Now faith is the assurance of things hoped for, the conviction of things not seen.”
– Hebrews 11:1