Relative acceleration approach in the study on cardiac electric signal propagation

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Harmonia mundi in the heart

To gaze up from the ruins of the oppressive present towards the stars is to recognize the *indestructible world of laws*, to strengthen faith in reason, to realize the ‘harmonia mundi’ that transfuses all phenomena, and that never has been, nor will be, disturbed, by Hermann Weyl, 1919.

Hermann Weyl, 1885-1955
Introducing the HEART

• 72 beat per minute, 2.5 billion times in average
• Probability for beat = 100%
• Electrical signal -> contraction
  -> Pumping oxygenated blood
• Heart model
  = Electricity (Electro-diffusion + bio-chemistry)
  + Mechanics(contraction) + Elasticity (elastic tissue property) + Fluids (oxygenated blood flow)
• One of the hardest Mathematical and Computational models
How electric signal propagates
What is the electric signal?

- All-or-nothing non-decrement traveling wave.
- No conservational laws of energy, momentum, charges.
- Ex) Collision of two waves = canceling out.
- Refractory area (In-excitile region right behind signal).
The FitzHugh-Nagumo model

\[ \frac{\partial u}{\partial t} = \nabla \cdot (d\nabla u) + F(u, v) \]

\[ \frac{\partial v}{\partial t} = G(u, v) \]

\( u \) : Membrane potential difference, the activator
\( v \) : Ion channel openness or refractoriness, the inhibitor

\( F(u,v) \) and \( G(u,v) \) are chosen for the van der Pol a relaxation oscillator
Analogy in nature, Forest Fire

1. Energy is **not** conserved (Otherwise, a match could be the most dangerous weapon !)

2. Temperature of the fire does **not** depend on the **distance** from the origin, but depend on the **media**.
Cardiac cell (myocardial cell)

Intracellular pathways

Ion channels

Cardiac cell

Intracellular space

Extracellular space
Electromagnetic field in the microscopic cardiac cells

\[ \nabla \cdot d^i = \rho^i, \quad \nabla \times h^i = j^i + \frac{\partial d^i}{\partial t} \]

\[ \nabla \cdot b^i = 0, \quad \nabla \times e^i + \frac{\partial b^i}{\partial t} = 0 \]

At Intracellular space

\[ \nabla \cdot d^e = \rho^e, \quad \nabla \times h^e = j^e + \frac{\partial d^e}{\partial t} \]

\[ \nabla \cdot b^e = 0, \quad \nabla \times e^e + \frac{\partial b^e}{\partial t} = 0 \]

At Extracellular space

\[ \rho^i + \rho^e = \text{const.}, \quad j^i + j^e = 0 \quad \text{in } \Omega^i \cup \Omega^e \]
Microscopic To Macroscopic

Collecting several cells + Averaging the quantities

\[
\bar{d}^i = D^i, \bar{h}^i = H^i \quad \bar{d}^i = D^i, \bar{h}^i = H^i
\]

\[
\bar{b}^i = B^i, \bar{e}^i = E^i \quad \bar{b}^i = B^i, \bar{e}^i = E^i
\]
Electromagnetic field in the macroscopic cardiac cells

\[ \nabla \cdot D^i = \rho^i, \quad \nabla \times H^i = J^i + \frac{\partial D^i}{\partial t} \]

\[ \nabla \cdot B^i = 0, \quad \nabla \times E^i + \frac{\partial B^i}{\partial t} = 0 \]

\[ \nabla \cdot D^e = \rho^e, \quad \nabla \times H^e = J^e + \frac{\partial D^e}{\partial t} \]

\[ \nabla \cdot B^e = 0, \quad \nabla \times E^e + \frac{\partial B^e}{\partial t} = 0 \]

\[ \rho^i + \rho^e = \text{const.}, \quad J^i + J^e = 0, \quad \text{in } \Omega \]

Macroscopic extracellular and Macroscopic Intracellular spaces can not be separated by boundaries

-> In the same space, there are two different equations
Introducing Bi-domain

• **Each point** in the macroscopic domain represents **two points** in the extracellular and intracellular space.

• Energy and charges are **conserved in bi-domains**.

• Intracellular space is only our concern, then energy and charges are **not conserved in one domain**.

• Diffusion-reaction system, or the relaxation oscillator in biology, only exists in bi-domain because it requires an **external energy source**.
Anisotropy in the heart

- Cable-like, cylindrical, 100 um long and 15um
- Cardiac tissue is **anisotropic**, with wave speeds that differ substantially depending on their direction.
- 0.5 m/s along fibers and about 0.17 m/s transverse the fibers.
Anisotropy in physics

• d: Diffusion tensor, variable coefficient

\[ \nabla \cdot (d \nabla \phi) \]

• Anisotropic direction = characteristics line.
• A little misplacement leads to the shock of waves.
• Related to the way the heart is folded for mechanical contraction.

• Difficulty 1: Heart consist of multiple layers with different angle of anisotropy.
• Difficulty 2: Anisotropy lies in curved surfaces.
Summary of the properties of cardiac electric signal propagation

(1) In **Bi-domain** where none of conservation laws holds.

(2) **Anisotropy** is everywhere.

(3) 3D shape is smooth, but non-uniform with **various curvature**.
How atrial fibrillation (AF) happens?

- Normal propagation starts from a point and converges to a point.
- AF only happens when the propagation deviates from its original track and comes back to excite cardiac tissue again (Reentry)
- Reentry requires unidirectional pathway.
Clinical observations and conjectures

• The role of PVs on AF:
  - Arrhythmogenic substrate of the Pulmonary Veins Assessed by High-Resolution Optical Mapping, Circulation 2003, by R. Arora et al.

• Observations and theories of AF:
  - New ideas about atrial fibrillation 50 years on, Nature 2002, by S. Nattel
  - Atrial Remodeling and Atrial Fibrillation: Mechanisms and Implications, Circulation 2008, by S. Nattel et al
  - Rotors and Spiral waves in Atrial Fibrillation, J. Cardiovasc Electrophysiol 2003, by J. Jalife
  - Circulation movement in rabbit atrial muscle as a mechanism of tachycardia. III. The “leading circle” concept: a new model of circus movement in cardiac tissue without the involvement of an anatomical obstable, Circ. Res. 1977, by M.A. Allessie et al.

• Structures of left atrium and PVs:
  - The importance of Atrial Structure and Fibers, Clinical Anatomy 2009, by S. Y. Ho
  - The structure and components of the atrial chambers, Europace 2007, by R. H. Anderson
Blocking Pulmonary Veins by lesions

A surgical procedure is to insert a catheter through the vein into the atrium and to burn cardiac cells around the PV to prevent the self-initiators around the PVs.
Theories of electrophysiology in the heart

• Regarded as a kind of nerve system.
• Quick transfer from ODE to PDE.
• Analogous jump from a 1D cable to multidimensional space.
• Alternative is the Kinematics approach (1990s~): Study of the wave front to find the critical curvature to find $K^* > K$ in

$$\frac{\partial K}{\partial \ell} \left( \int_0^\ell KV \, d\xi + C \right) + \frac{\partial K}{\partial t} + K^2 V + \frac{\partial^2 V}{\partial \ell^2} = -\Gamma V$$
Inspirations for relative acceleration approach

Rule of games:
(1) Excited person has 3L of water.
(2) Given 1L of water, an excitable person get 2L more water and get excited.
(3) A player wins if it has more children than the competitor.
(4) Game stops if any one of the column can not receive 1L.
Hypothesis and Proposition

• Hypothesis: If the relative acceleration of cardiac excitation propagation becomes sufficiently large, then the propagation stops.

• Proposition: If the following is sufficiently large, then the propagation stops

\[
- \frac{1}{E} \left[ \frac{\partial E}{\partial n} \frac{\partial v^i}{\partial \lambda} + \frac{\partial G}{\partial n} v^i + G \frac{\partial v^i}{\partial n} + \frac{\partial (cv^i)}{\partial n} \right]
\]

where,

\[
E = \sum_{k=1}^{2} (\Lambda_k)^2 d^k g^{kk} \quad G = \sum_{k=1}^{2} \frac{1}{\sqrt{g}} \frac{\partial (\sqrt{g} \Lambda_k d^k g^{kk})}{\partial x^k}
\]
Diffusion-Reaction Tensor

• A DR-tensor, is obtained as

\[ C^k = d^k \Lambda_k g^{kk} \]

Anisotropic coefficient \( \times \) Propagational direction \( \times \) the conjugate metric tensor for 3D geometric shape

• Definition of geometry:
  • (1) \( d^k \) : type of media.
  • (2) \( \Lambda_k \) : Location of SAN and surface 2D geometries.
  • (3) \( g^{kk} \) : 3D shape.

• Large variation of the tensor means the break-up of the wave
Definition of geometry in electrophysiology

• Geometry = the combination of the followings:
  1) Location of the starting point
  2) Conducting properties of the media
  3) 3D shape of the heart
-> Geometry is taken in the sense of the Field theory.

• Electric signal only depends on geometry.
• Electric signal has negligible kinetic energy.
• Heart works 100% according to its design.
• Analogous to the light as a signal
Applying to the PVs

\[ + \quad d^\theta \quad 4 \times \]
Various Anisotropy on the PV

A shape of PV junction

Circumferential anisotropy

Longitudinal anisotropy (Perez-Lugones et al, 2003)
LA-PV tracts

- Activation in SR
- Generator of ectopics, AT, AF (and AFI)
- Isolation by LA-PV ostial ablation
- PV triggering seen more frequently in wider tracts
Construct a model

Left anisotropy

Right anisotropy

Scar tissue

Point-initialized
Modelling of Re-entrance on a spherical shell with a PV-like column

1) Normal condition

T=0, Front  T=10, Front  T=20, Back  T=25, Back

2) Deteriorated myocardial cells on the PVs

Multiple reentrant waves  Overdrive suppression

T=20, Back  T=22, Back  T=37, Front  T=100, Front
Consequences

1. Unidirectional pathways are the PVs with weakened anisotropy toward which the wave approaches with an oblique angle due to some other factors, for example, the presence of scar tissue, the change of SAN, etc.

2. Cardiac excitation propagation can be represented as the Field of the trajectories.

3. Implying the existence of the Field tensor.

4. Something is moving along the trajectory.
Analogies from light propagation

• In the early 1900s, light propagates by the medium, called the Aether.

• The Field theory replaced the concept of Aether, not because Aether is proved to be real, but because Aether is not required any more.

• This research can be regarded as making the cardiac tissue redundant from the analysis and establishing a field for cardiac signal propagation.

• Interesting to see that the field can exist without any conservation laws.
What is actually moving in electric signal propagation?

\[ K^+, Cl^- (out) \]

\[ Ca^+, K^+ (out) \]

\[ Na^+ (in) \]

Stimulating moving body consist of many stimulation particles that lower the resting potential to initiate cardiac action potential. Ex) For forest fire, it is equivalent to a group of particles of high-temperature to initiate fire on a unburned tree.
Stimulating moving body

- Intracellular pathways
- Intracellular space
- Extracellular space
- Cardiac cell
- Ion channels
- $p_s$
- $B_s$
- $v_0$

From Ion Channel

$v$

$v_0$
Maxwell’s equations in the universe vs. Maxwell’s equations in the heart

<table>
<thead>
<tr>
<th>Maxwell’s equations</th>
<th>in the universe</th>
<th>in the heart</th>
</tr>
</thead>
<tbody>
<tr>
<td>How to propagate</td>
<td>Ray</td>
<td>Diffusion</td>
</tr>
<tr>
<td>Gauge choice</td>
<td>( \nabla \cdot A + \frac{1}{c^2} \frac{\partial \Phi}{\partial t} = 0 )</td>
<td>( \nabla \cdot A + \Phi = 0 )</td>
</tr>
<tr>
<td>Gauge function</td>
<td>( \nabla^2 \Lambda - \frac{1}{c^2} \frac{\partial^2 \Lambda}{\partial t^2} = 0 )</td>
<td>( \nabla^2 \Lambda - \frac{\partial \Lambda}{\partial t} = 0 )</td>
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</tbody>
</table>
Diffusion-reaction equations from Maxwell’s equations

• The diffusion-reaction equations are one projection of Maxwell’s equations in bi-domain, so E and B are under-determined.

• The normal heart is designed to generate the minimum degree of the magnetic field (conjecture 1).

• Increasing magnetic field in the specific area of the heart may mean AF (conjecture 2).

• It may explain why the external electric shock can resuscitate temporarily non-moving heart after CPR or can cure AF temporarily.
Thank you for attention!

Now I know I've got a heart, 'cause it's breaking

(Tin Woodsman in The Wizard of Oz)