Modeling cardiac propagation

Outline

- Cardiac propagation.
- The bidomain concept.
- Derivation of the bidomain model from assumptions on the cell membrane and basic electromagnetic relations.
- A model for the surrounding body.
- Reduction to a monodomain model.

Cardiac propagation

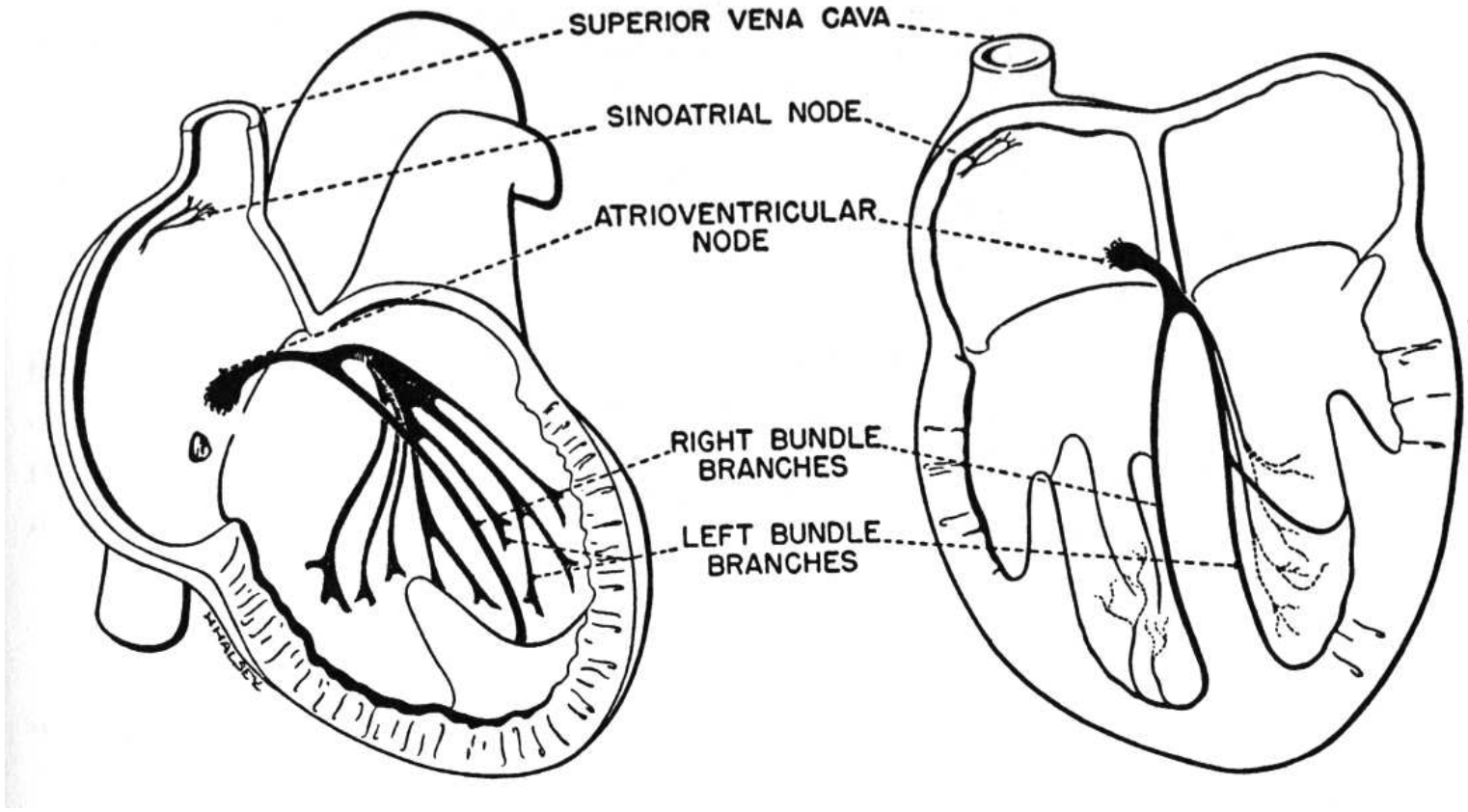
Cardiac cells has two properties and corresponding function

- Excitable $\rightarrow$ Propagates the AP
- Contractive $\rightarrow$ Pumps blood

Furthermore, the arrival of an AP triggers contraction. Cell to cell coupling. Two types:

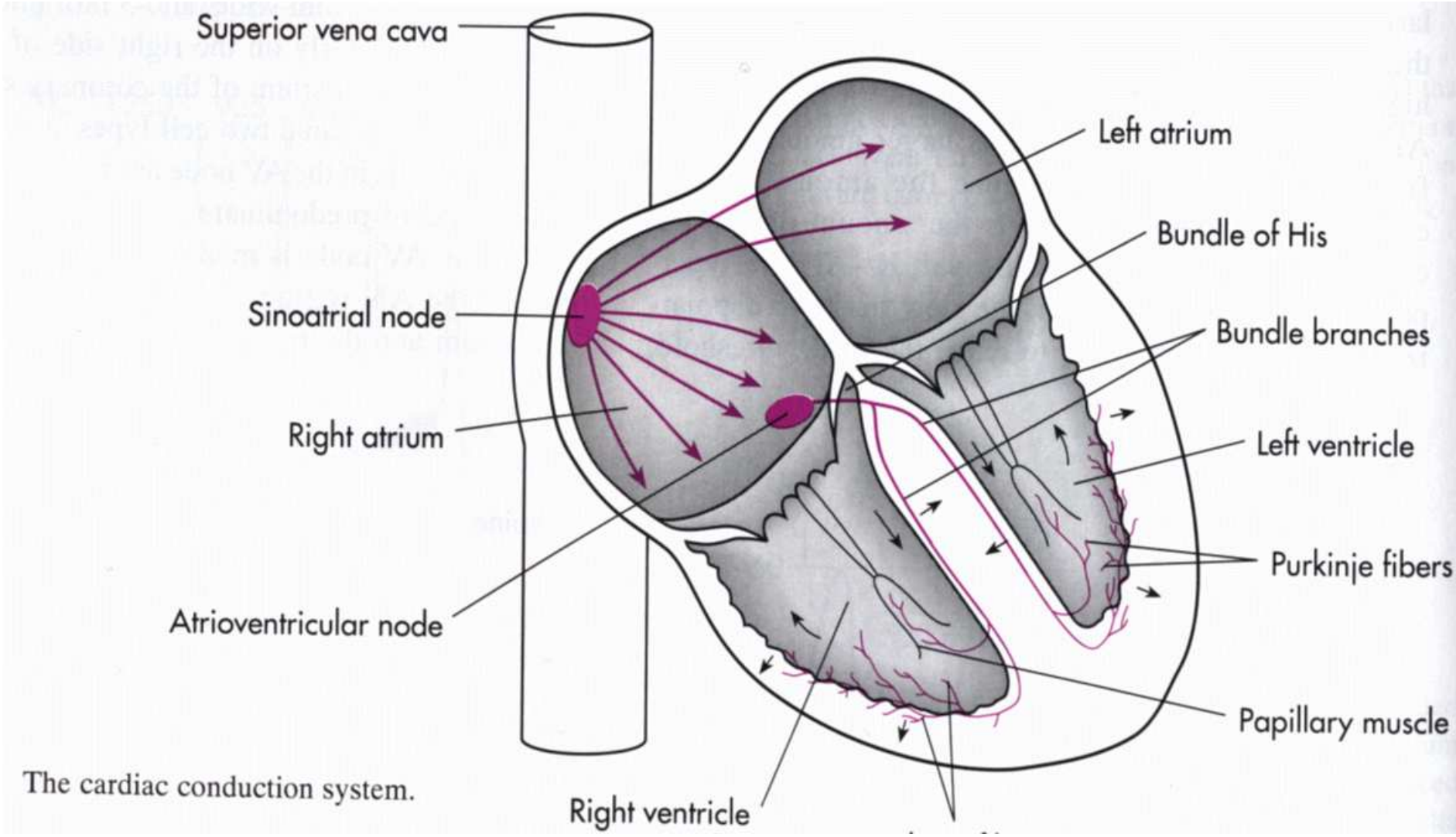
- Tight junctions: Transfer mechanical energy
- Gap junctions: Inter cellular channels where ions can flow

The conduction system



Cardiac propagation

- Electrical signal initiated in the sinoatrial node (SA node).
- The action potential propagates the atria, which are insulated from the ventricles by a septum of non-excitable cells.
- The signal is conducted to the ventricles through the atrioventricular node (AV-node), located at the base of the atria.
- Conduction through the AV-node is fairly slow, but from there the action potential enters the so-called bundle of HIS, made up of fast-conducting Purkinje fibers.



The cardiac conduction system.

- The Purkinje fibers spread in a tree-like branching, ending on the endocardiac surface of the ventricles.
- Muscle cells are stimulated at the end of the Purkinje fibers, and the action potential spreads through the muscle tissue.
- The electrical propagation in the heart is both one-dimensional (along the purkinje fibers) and three-dimensional (in the muscle tissue).

Modelling propagation in heart tissue

- Because of the large number of cells, it is impossible to model the tissue by modeling each individual cell.
- The cells are connected, and the heart may be seen as consisting of two continuous spaces, the intracellular and the extracellular domain.
- The geometries of the two domains are too complex to be represented accurately.

The bidomain concept

- Instead of accurately modeling the geometry of the two domains, they are assumed to be overlapping, both filling the complete volume of the heart muscle.
- Hence, every point in the myocardium lies in both the intracellular and the extracellular domain.

Basic equations

Maxwells equations states that

$$\nabla \times E + \dot{B} = 0$$

where E and B are the strength of the electrical and magnetic field, respectively. Since $\dot{B}$ denotes the time derivative of the magnetic field, if the fields are stationary we have.

$$\nabla \times E = 0$$

The quasi-static condition

Although the electrical and magnetic fields resulting from cardiac activity are not stationary, the variations are fairly slow. We may therefore assume that the fields are stationary, an assumption called the “quasi-static condition”. As above, we have

$$\nabla \times E = 0,$$

which means that the field E may be written as

$$E = -\nabla u$$

for some potential function u.

Current

In a conducting body, the electrical current is given by

$$J = ME,$$

where M is the conductivity of the medium. With the definition of E given above, the current is given by

$$J = -M\nabla u\,.$$

- Following the bidomain concept introduced above, we introduce two electrical potentials:

  Intracellular potential u_i

  Extracellular potential u_e

- Since every point in the heart muscle lies in both the extracellular and intracellular domain, both u_i and u_e are defined in every point.

The currents in the two domains are given by

$$\begin{aligned} J_i &= -M_i \nabla u_i, \\ J_e &= -M_e \nabla u_e, \end{aligned}$$

and if we assume no accumulation of charge, the total current entering a small volume must equal the total current leaving the volume. This gives

$$\int_{\partial V} (J_i + J_e) \cdot n ds = 0$$

Since the volume V is arbitrarily chosen, this may be written as

$$\nabla \cdot (J_i + J_e) = 0$$

Inserting the expressions for the currents, we get

$$\nabla \cdot (-M_i \nabla u_i) + \nabla \cdot (-M_e \nabla u_e) = 0$$

(This equation states that all current leaving one domain must enter the other domain.)

- The two domains are separated by the cell membrane. Hence, all current going from one domain to the other must cross the cell membrane. We have

$$-\nabla \cdot (-M_i \nabla u_i) = \nabla \cdot (-M_e \nabla u_e) = I_m$$

We have previously modeled the membrane current I_m as the sum of a capacitive current and an ionic current. However, that current was measured per membrane area, while we are now interested in the current per volume. The current per volume is achieved by multiplying with a scale factor χ, which is the ratio of cell membrane surface to cell volume.

$$I_m = \chi(C_m \frac{\partial V}{\partial t} + I_{\text{ion}}),$$

where V is the transmembrane potential.

To summarize, we now have two relations for the unknown potentials u_i and u_e:

$$\nabla \cdot (M_i \nabla u_i) = \chi C_m \frac{\partial V}{\partial t} + \chi I_{\text{ion}}$$

and

$$\nabla \cdot (M_i \nabla u_i) + \nabla \cdot (M_e \nabla u_e) = 0$$

We see that we have three unknown potentials u_i, u_e and V, and only two equations. But V is defined as the difference between the intracellular end the extracellular potential, and this may be used to eliminate one of the unknowns.

We have $V = u_i - u_e$, or $u_i = u_e + V$. Inserting this into the two equations, we get

$$\begin{aligned} \nabla \cdot (M_i \nabla (V + u_e)) &= \chi C_m \frac{\partial V}{\partial t} + \chi I_{\text{ion}} \\ \nabla \cdot (M_i \nabla (V + u_e)) + \nabla \cdot (M_e \nabla u_e) &= 0 \end{aligned}$$

These equations may be rewritten as

$$\begin{aligned} \nabla \cdot (M_i \nabla V) + \nabla \cdot (M_i \nabla u_e) &= \chi C_m \frac{\partial V}{\partial t} + \chi I_{\text{ion}} \\ \nabla \cdot (M_i \nabla V) + \nabla \cdot ((M_i + M_e) \nabla u_e) &= 0 \end{aligned}$$

This is the standard formulation of the bidomain model.

Potential in the surrounding body

- The tissue surrounding the heart is mostly non-excitable, meaning that the cells do not actively change their electric properties.
- The body surrounding the heart may hence be modeled as a passive conductor.

Extracardiac potential u_o

- Introducing the extracardiac potential u_o, and using the arguments presented above, we derive the equation

$$\nabla \cdot (M_o \nabla u_o) = 0,$$

where M_o is the (averaged) conductivity of the tissue.

Boundary conditions

- To complete the mathematical model, we need boundary conditions for V and u_e on the heart surface, and for u_o on the surface of the heart and the surface of the body.
- It is natural to assume that the body is insulated from its surroundings, implying that no current leaves the body.
- This gives the condition

$$n \cdot (M_o \nabla u_o) = 0$$

on the body surface.

- At the heart surface, the normal component of the current in the heart must be equal to the normal component of the current in the surrounding body

$$n \cdot (J_i + J_e) = n \cdot J_o,$$

where n is the outward unit normal of the surface of the heart.

- Inserting expressions for J_i, J_e, and J_o in terms of u_e, v, and u_o gives

$$n \cdot (M_i \nabla v + (M_i + M_e) \nabla u_e) = n \cdot (M_o \nabla u_o). \qquad (1)$$

- This condition is not sufficient. We need to make additional assumptions about the coupling between the heart and the body.
- Several choices of boundary conditions exist for this coupling.
- A common assumption is that the intracellular domain is insulated from the tissue surrounding the heart, while the extracellular domain connects directly to the surrounding tissue.
- This implies that at the heart surface the extracellular potential must equal the extracardiac potential

$$u_e = u_o \tag{2}$$

- The assumption that the intracellular domain is completely insulated implies that the normal component of the intracellular potential must be zero on the heart surface

$$n \cdot J_i = 0.$$

Writing this in terms of u_e and v gives

$$n \cdot (M_i \nabla v + M_i \nabla u_e) = 0, \tag{3}$$

- We insert this expression into (1) to get

$$n \cdot (M_e \nabla u_e) = n \cdot (M_o \nabla u_o). \tag{4}$$

- The 3 boundary conditions at the heart surface are (2), (3), (4).

The complete model

$$
\begin{aligned}
\frac{\partial s}{\partial t} &= F(v,s) && x \in H \\
\chi C_m \frac{\partial V}{\partial t} + \chi I_{\mathsf{ion}}(V,s) &= \nabla \cdot (M_i \nabla V) + \nabla \cdot (M_i \nabla u_e) && x \in H \\
\nabla \cdot ((M_i + M_e) \nabla u_e) &= -\nabla \cdot (M_i \nabla V) && x \in H
\end{aligned}
$$

$$
\begin{aligned}
u_e &= u_o && x \in \partial H \\
n \cdot (M_i \nabla v + M_i \nabla u_e) &= 0 && x \in \partial H \\
n \cdot (M_e \nabla u_e) &= n \cdot (M_o \nabla u_o) && x \in \partial H
\end{aligned}
$$

$$
\begin{aligned}
\nabla \cdot (M_o \nabla u_o) &= 0 && x \in T \\
n \cdot (M_o \nabla u_o) &= 0 && x \in \partial T
\end{aligned}
$$

Reduction to a monodomain model

- The bidomain model is a very complex system of equations.
- Many (most) simulations are based on a simpler monodomain equation.
- The derivation of the monodomain model is based on the assumption of equal anisotropy ratios:

$$M_e = \lambda M_i$$

With this simplification, the bidomain equations may be written as

$$\begin{aligned} \chi C_m \frac{\partial v}{\partial t} + \chi I_{\text{ion}}(v, s) &= \nabla \cdot (M_i \nabla v) + \nabla \cdot (M_i \nabla u_e) \\ \nabla \cdot (M_i (1 + \lambda) \nabla u_e) &= -\nabla \cdot (M_i \nabla v) \end{aligned}$$

The second equation gives

$$\nabla \cdot (M_i \nabla u_e) = -\frac{1}{1+\lambda} \nabla \cdot (M_i \nabla v),$$

and if we insert this into the first equation we get

$$\chi C_m \frac{\partial v}{\partial t} + \chi I_{\text{ion}}(v, s) = \nabla \cdot (M_i \nabla v) - \frac{1}{1+\lambda} \nabla \cdot (M_i \nabla v)$$

Finally, we get

$$\chi C_m \frac{\partial v}{\partial t} + \chi I_{\text{ion}}(v, s) = \frac{\lambda}{1+\lambda} \nabla \cdot (M_i \nabla v)$$

A problem with the monodomain model is that it can not be coupled directly to a surrounding body. Reproduction of ECG signals hence require additional computations.

Conclusions

- Because of the excitability of cardiac cells, a simple volume-conductor model is not sufficient for modeling the heart muscle.
- By conceptually dividing the tissue into extracellular and intracellular domains, we are able to construct a mathematical model which describes signal propagation in the excitable tissue.
- By making a (non-physiological) assumption, the complex model may be reduced to a simpler monodomain model.