

**CELLULAR ELECTROPHYSIOLOGY: FROM ION CHANNELS TO  
ARRHYTHMIAS. ELECTROPHARMACOLOGY APPLIED TO  
ELECTROCARDIOGRAM AND FUNCTIONAL PROPERTIES OF CARDIAC  
CELLS**

Andrés Ricardo Pérez Riera

Chief of Electro-Vectorcardiography Sector of the ABC School of Medicine – ABC  
Foundation – Santo André – São Paulo, Brazil

"Science is to create in the absence of models, and to seek the knowledge of  
truths, even though relative, since they are the steps in discovering the absolute  
truth – not influenced by friendship, politics and gratefulness."

Radi Macrúz

If we put both ends or electrodes (A and B) of a galvanometer (device that records the difference of potential between two points) outside a cardiac cell in rest or polarized (Figure 1), we observe that the needle of the mentioned device does not move (it points to zero). The same will occur if we leave both ends within the cell (Figure 2).

Finally, if we introduce one end inside and the other one outside of the cell, we will observe that the galvanometer needle moves pointing the difference of potential between the positive external medium (+) and the negative intracellular one (-).

Figures 1 to 3

REPRESENTATION OF TRANSMEMBRANE POTENTIAL IN REST IN FAST CARDIAC CELLS AND ITS MEASUREMENT WITH A GALVANOMETER

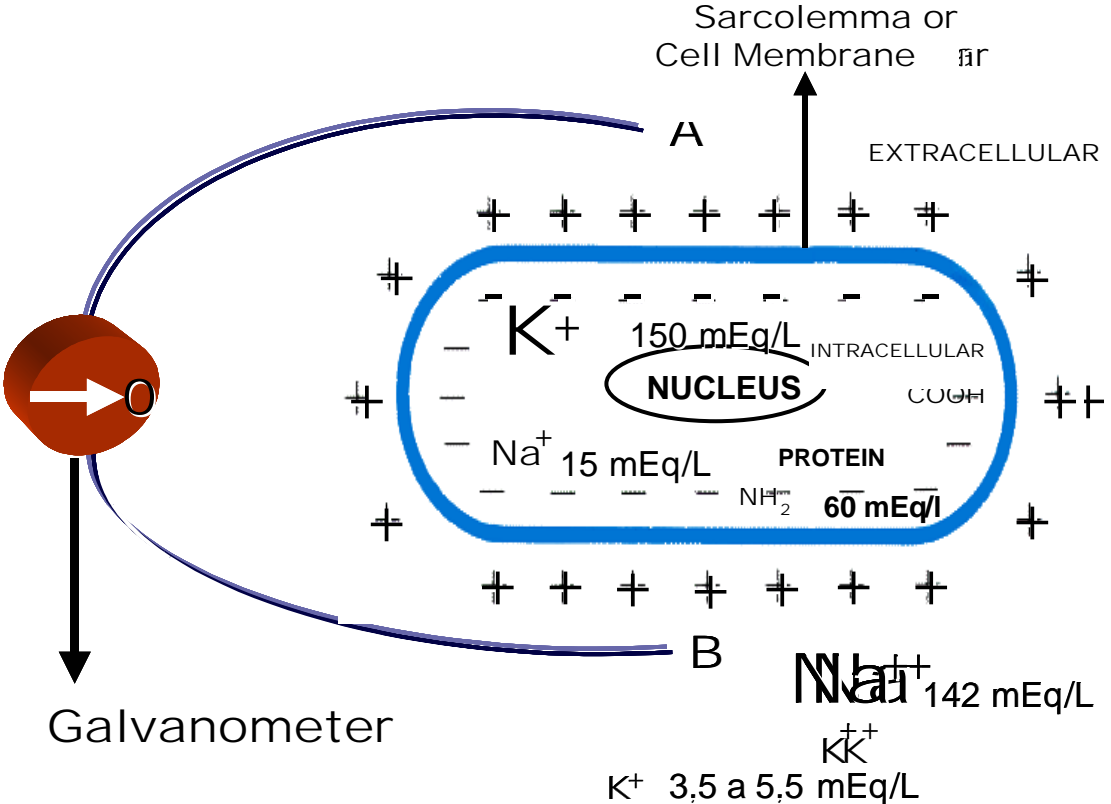


Figure 2

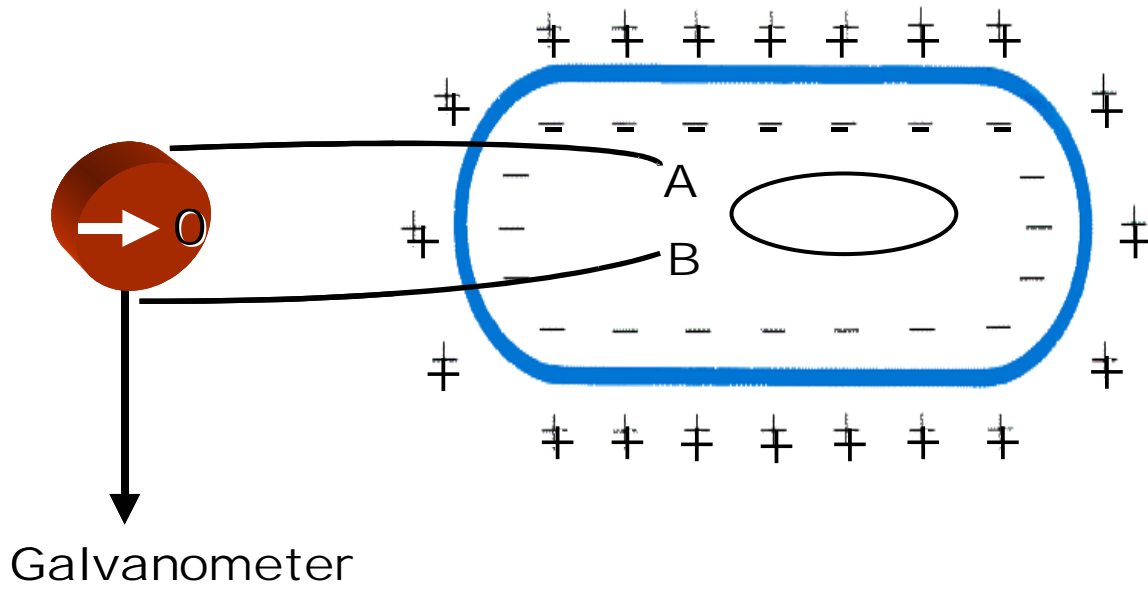
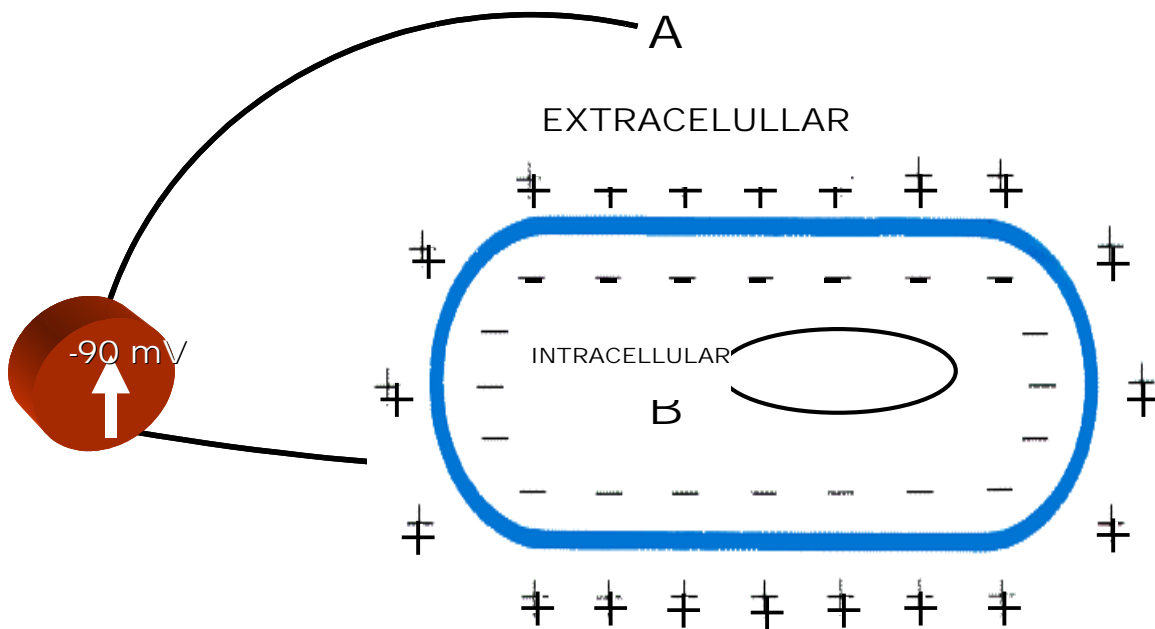


Figure 3



- 90 mV = DTP represents the difference of potential existing in rest between the extracellular medium (+) and the intracellular one (-), known as Diastolic Transmembrane Potential.

The difference of the potential existing in the diastole that is translated into the balance between the intracellular and the extracellular medium, with predominance of positive charges in the exterior and negative in the interior, is known as Diastatic Resting Transmembrane Potential (DTP), the value of which is variable according to the cell we are studying. Thus, if the fiber in study belongs to the His-Purkinje conduction system, internodal bundles, atrial muscle or contractile cells, the DTP will be very negative, around  $-80$  mV to  $-100$  mV; while if it was of the sinus node, the atrio-nodal and nodal region of the AV node, or near the atrioventricular valves, it will be less negative, approximately  $-55$  to  $-70$  mV<sup>1</sup>.

The conclusion is that there are two cell categories in the heart, according to the level of DTP:

- 1) Fast fibers: those with very negative DTP;
- 2) Slow fibers: those with less negative DTP.

Both, when stimulated or autostimulated, reveal a different action potential (AP) profile.

The action potential (AP) may be defined as the fast change in the electrical potential of the cell, from negative in the interior to positive, and returning to the starting point. The AP has then, two major phases: the one of depolarization (phase zero) and the one of repolarization (phases one, two, three and four), since in the slow fibers the 1,2 phase disappears.

#### I) AP of rapid fibers

In the action potential of the fast fibers there are five phases:

Phase zero or of depolarization;

Phase one or of initial fast repolarization;

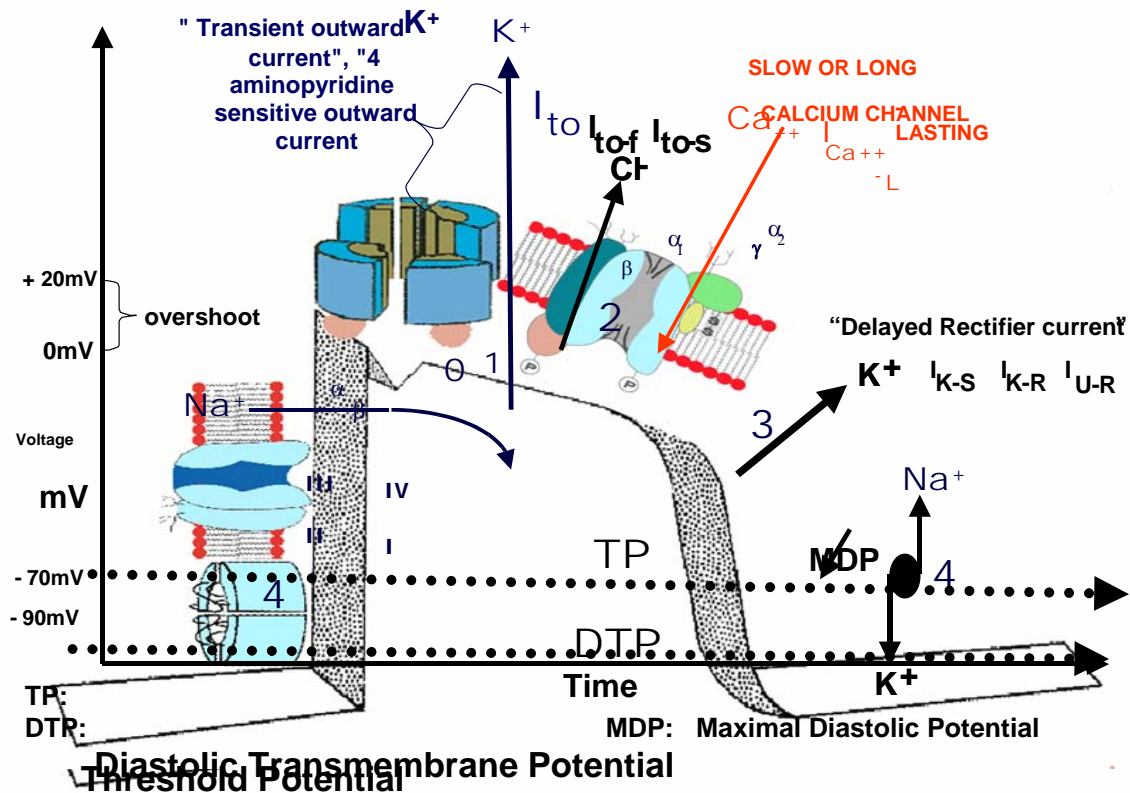
Phase two or of dome or plateau;

Phase three or of final repolarization, and

Phase four, of diastolic or resting potential, which could be:

- a) With spontaneous diastolic depolarization: automatic fibers, and
- b) Without diastolic depolarization or non-automatic<sup>2</sup>.

**Figure 4**  
**OUTLINE OF THE FIVE PHASES OF AP OF FAST FIBERS**



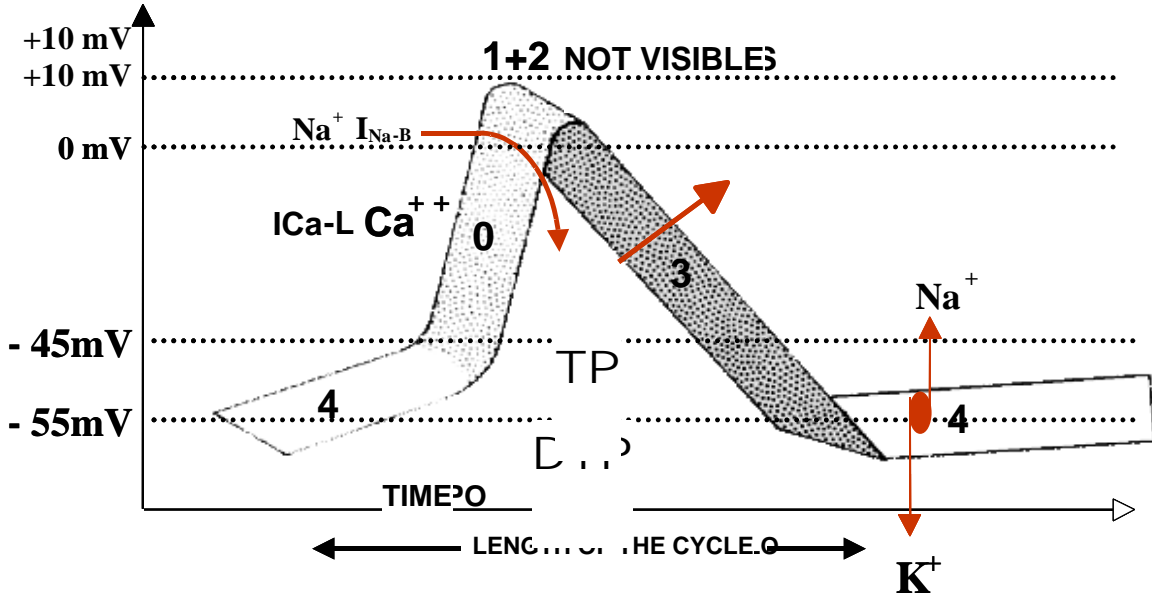
II) AP of slow fibers

In the slow fibers, the AP is characterized by presenting:

- 1) Slightly negative DTP: - 55 to -70 mV
- 2) Phase zero of small amplitude (65 mV and 70 mV, which conditions a very slow conduction velocity: 0.4 to 1 m/s), and inversion of polarity absent or in its maximal value, is of up to +15 mV (overshoot), mainly due to the slow inflow of Ca<sup>2+</sup> (upstroke) (I<sub>Ca<sup>2+</sup>-L</sub>), and secondarily of Na<sup>+</sup> by a channel called I<sub>NaB</sub>, what differentiates it from the fast Na<sup>+</sup> channel (I<sub>Na</sub>); is independent from voltage, and may be blocked by Ca<sup>2+</sup> antagonists, manganese, cobalt, and nickel;
- 3) Phases one and two are not recognizable (absence of phase one with notch and plateau);
- 4) Phase four, ascending (automatic) with higher slope in the SA node of the cells and slightly lower in the AV node cells;
- 5) AP duration: 100 to 300 ms.

**Figure 5**  
**AP OF SLOW FIBERS**

(Found in the sinus node, atrio-nodal and nodal region of the AV node, and mitral-tricuspid rings)



**Table 1**

## Differences between fast and slow fibers

	<b>Fast</b>	<b>Slow</b>
Location:	Myocardial contractile cells, ventricular myocardium, internodal bundles, His bundle and Purkinje branches and arborizations.	Sinus node, AV node, and mitral-tricuspid rings.
Kinetics	Fast.	Slow.
Phase zero	Fast and wide: 110 mV.	Slow and narrow: 70 mV.
Blockers of phase zero	Tetrodotoxin (TTX) and Class I antiarrhythmic agents	Calcium antagonists, manganese, cobalt and nickel.
Phase one	Notch present.	Not visible.
Phase two	Horizontal: "plateau".	Not visible.
DTP	- 90 mV.	- 55 mV.
TP	- 70 mV.	- 45 mV.
Overshoot	+20 mV.	It could be absent or up to +15.
Type of response	All or nothing.	It depends on the intensity
Dromotropism	500 to 4000 m/s.	0.4 to 1m/s.

There are in the heart, several types of cells with individual electrophysiological and electropharmacological properties and AP with particular characteristics:

## ELECTROPHYSIOLOGICAL CLASSIFICATION OF CARDIAC CELLS

### **A) Automatic or with spontaneous diastolic depolarization**

1) Sinoatrial node (SA) cells: in this structure there are three types of cells, with only these being automatic: nodal or P cells. The transitional and atrial myocardial ones, also found within the SA node, are not automatic.

1 A) P or nodal cells

2 B) Transitional or T cells;

3 C) Atrial myocardial cells

2) Atrioventricular (AV) node cells

3) His-Purkinje system cells

### **B) Non-automatic**

3) Atrial myocardial contractile cells

4) Ventricular myocardial contractile cells:

- subepicardial

- subendocardial

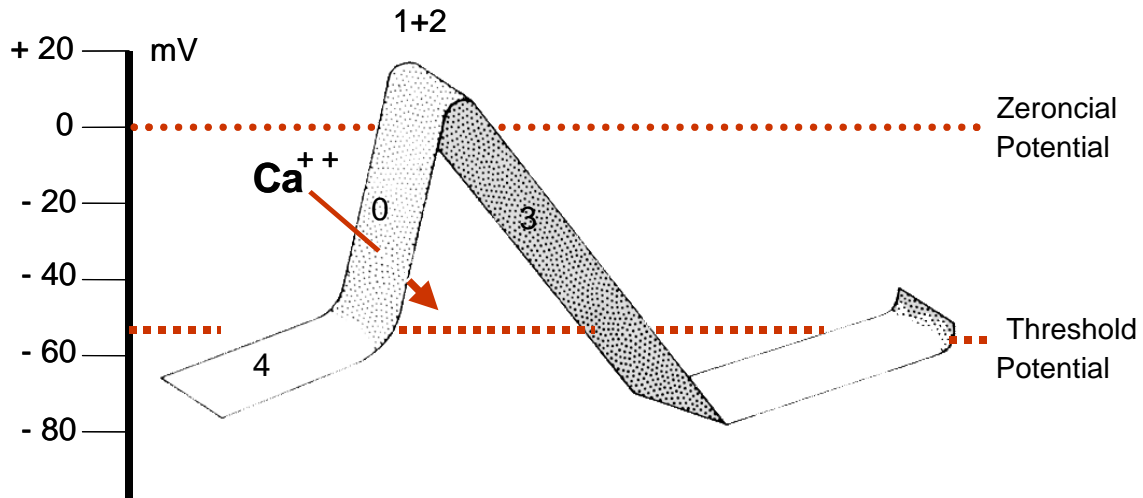
- mid-myocardium

α) contractile

β) "M" cells

**Figure 6**  
CELLULAR CHARACTERISTICS OF THE PROFILE OF AP IN THE DIFFERENT  
CARDIAC CELLS

I) Characteristics of the cells of the SA node from Keith and Flak and AP



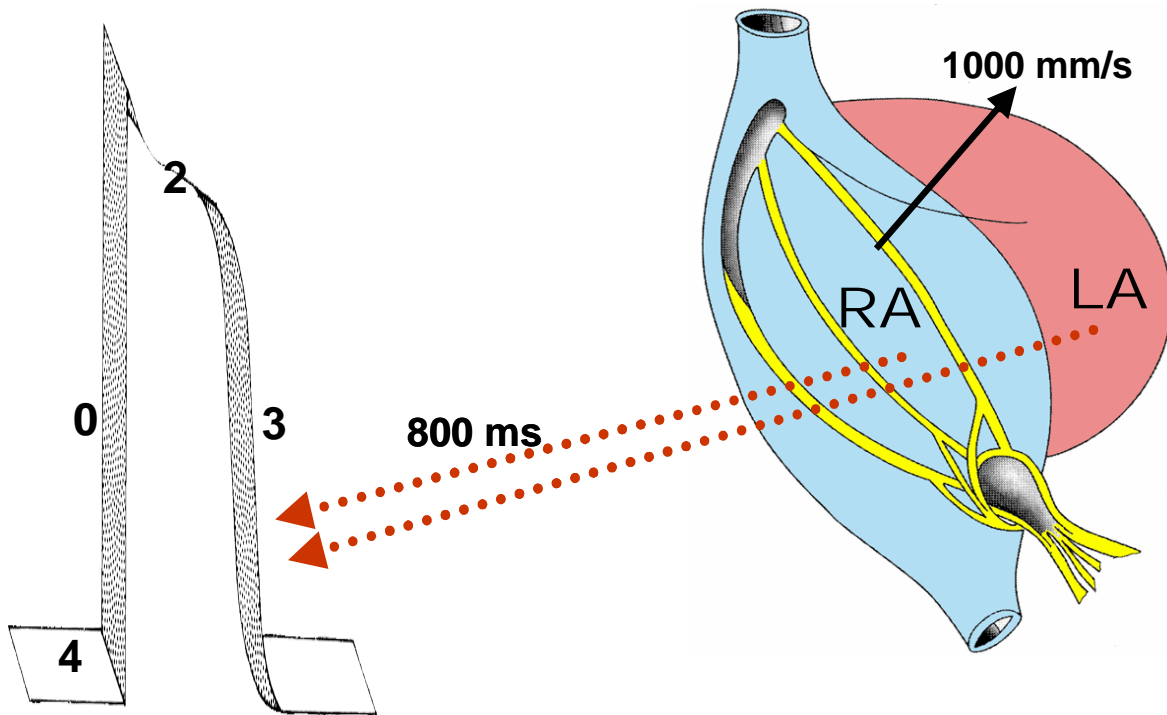
"P" cells: small, ovoid, cytoplasm poor in glycogen, (pale) without myofibrils, rudimentary T system with aspect of primitive cells. The name P derives from the fact they are:

- a) Pale (little glycogen in cytoplasm);
- b) Pacemaker cells;
- c) Primitive of the heart in phylogeny

Characteristics of AP: little negative resting potential; phase zero: low amplitude and dependent on slow inflow of  $\text{Ca}^{2+}$ ; they do not possess plateau (absence of phases 1 and 2); very slow dromotropism: 2 to 5 mm/s in the central region and 7 to 11 mm/s in the borders by absence of GAP junction<sup>3</sup>; phase 4 with marked slope: the greatest automatism, rhythmicity or diastolic depolarization of the organ. The channels involved in phase 4 of diastolic depolarization are: in the initial part, the  $I_f$  channel, activated by negative hyperpolarization of the membrane, and which enables a  $\text{K}^+$  inflow current or "pacemaker current;" acetylcholine-activated inward rectifying current, which produces hyperpolarization and stimulated bradycardia and the  $I_{\text{CA}2+-\text{L}}$  channel<sup>4-5</sup>.

**Figure 7**

II) Characteristics of atrial contractile cardiomyocytes and AP<sup>6</sup>.



Characteristics of cells: Size: 20  $\mu\text{m}$  to 50  $\mu\text{m}$  of length, and 10 to 30 of diameter (large); elliptic morphology; nucleus/nuclei: central; volume 500  $\mu\text{m}^3$ ; rare or absent T tubules; bundles of atrial tissue separated by large areas of collagen.