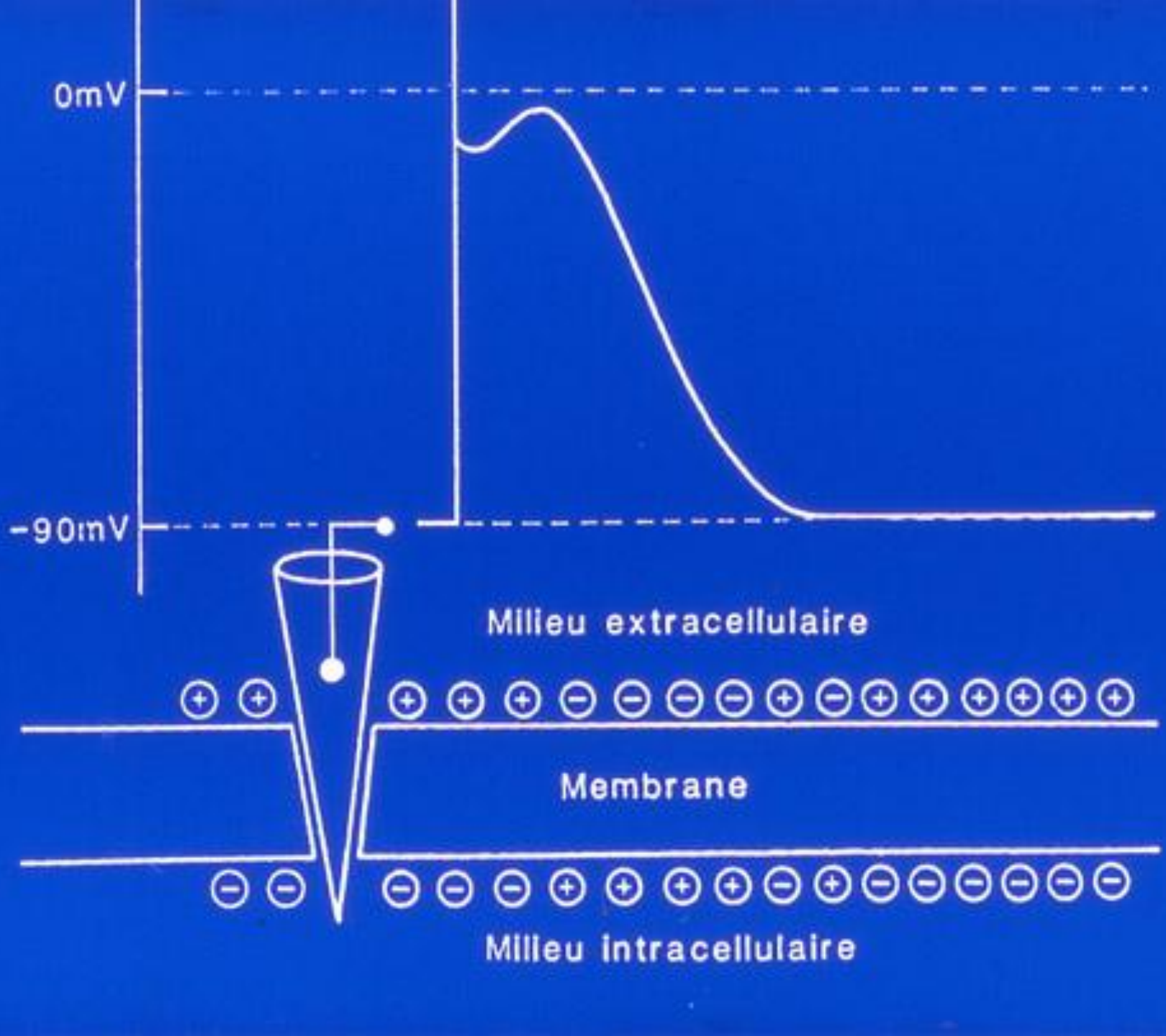
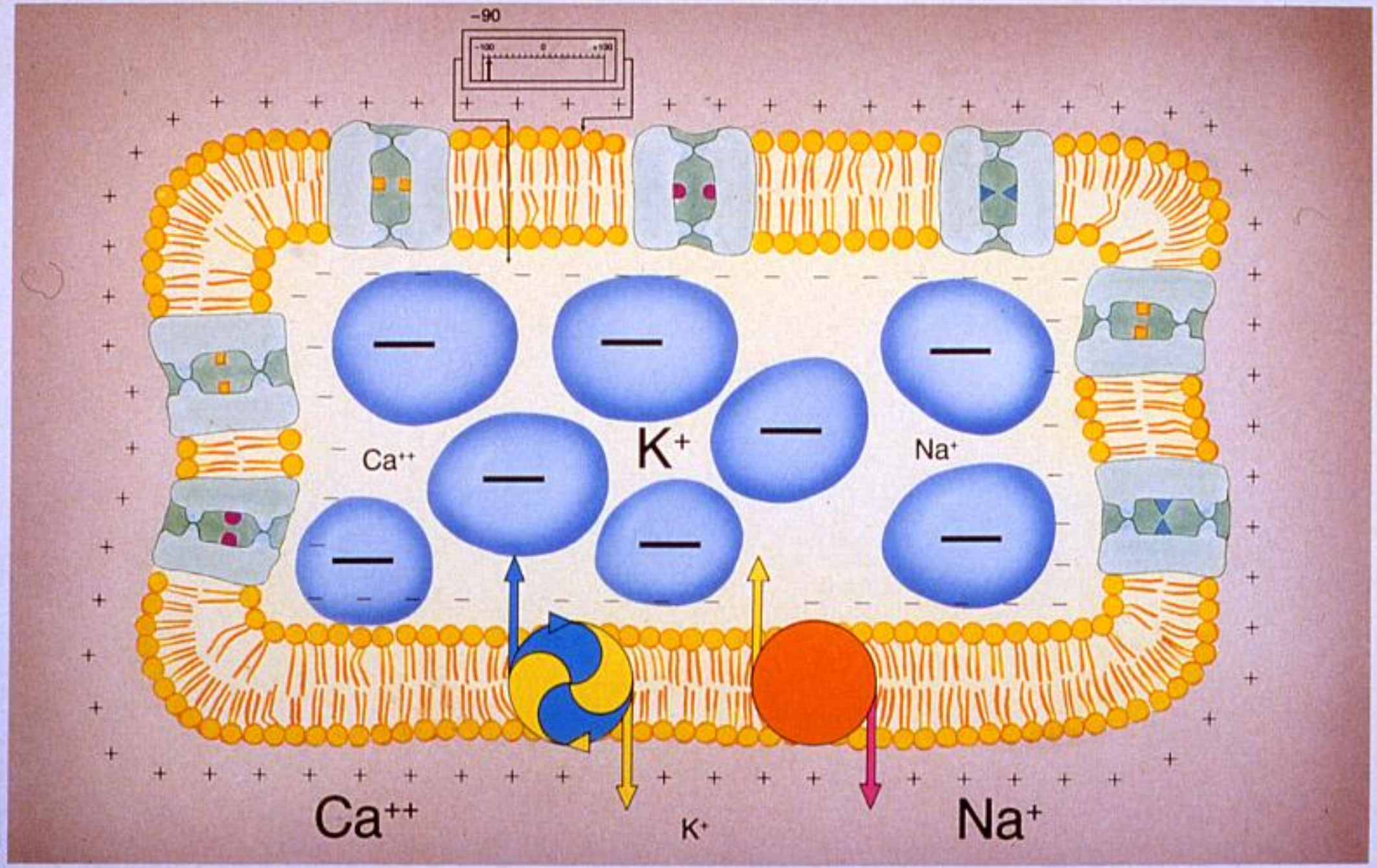
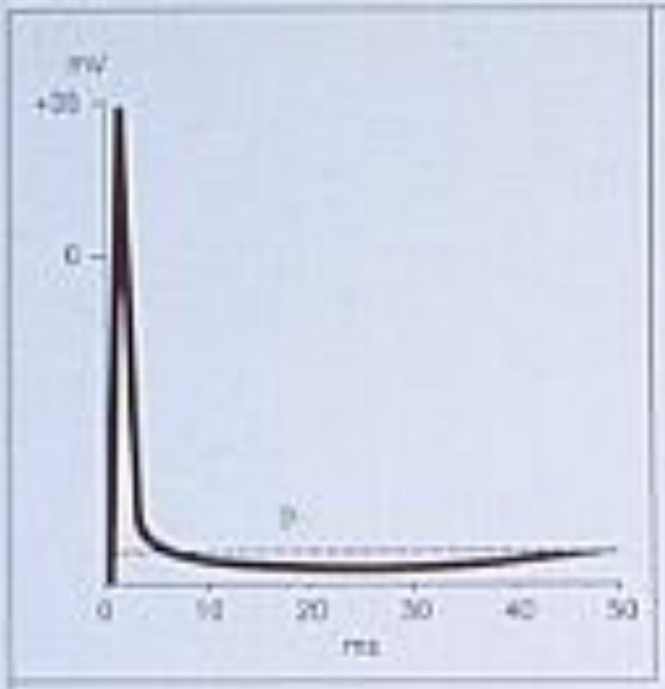

0mV
-90mV
Milieu extracellulaire
Membrane
Milieu intracellulaire

The membrane potential

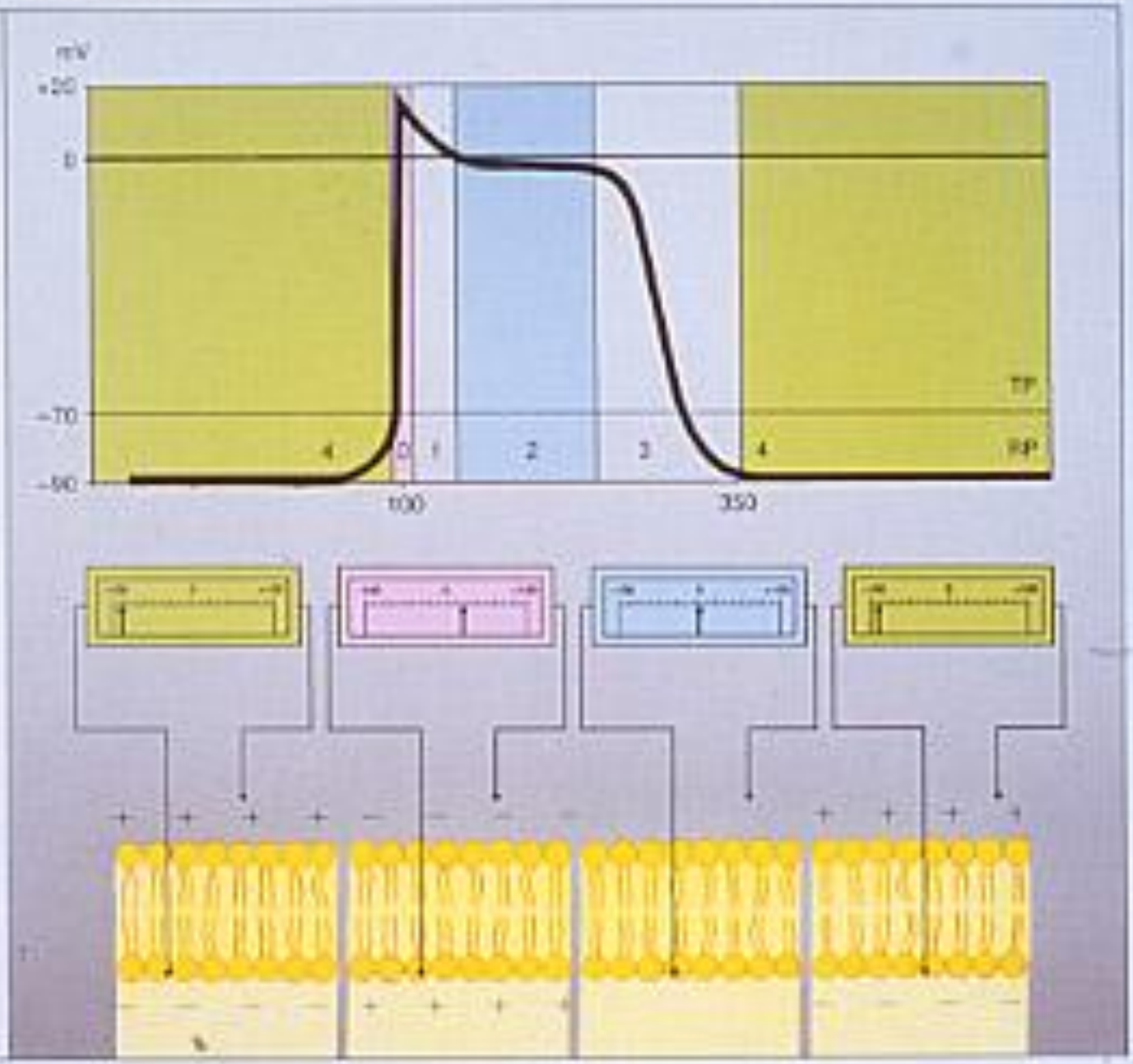


Action potentials

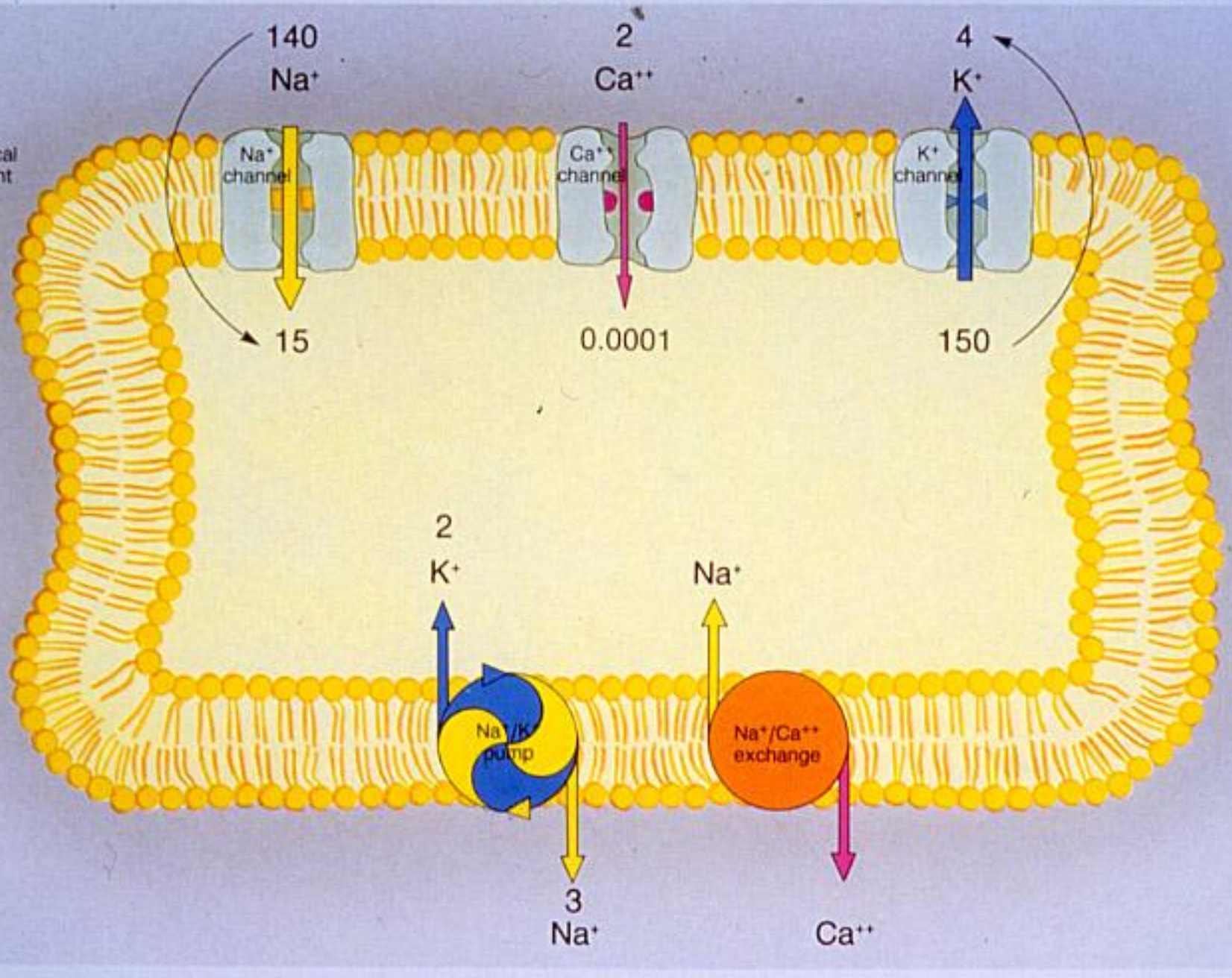
Skeletal muscle



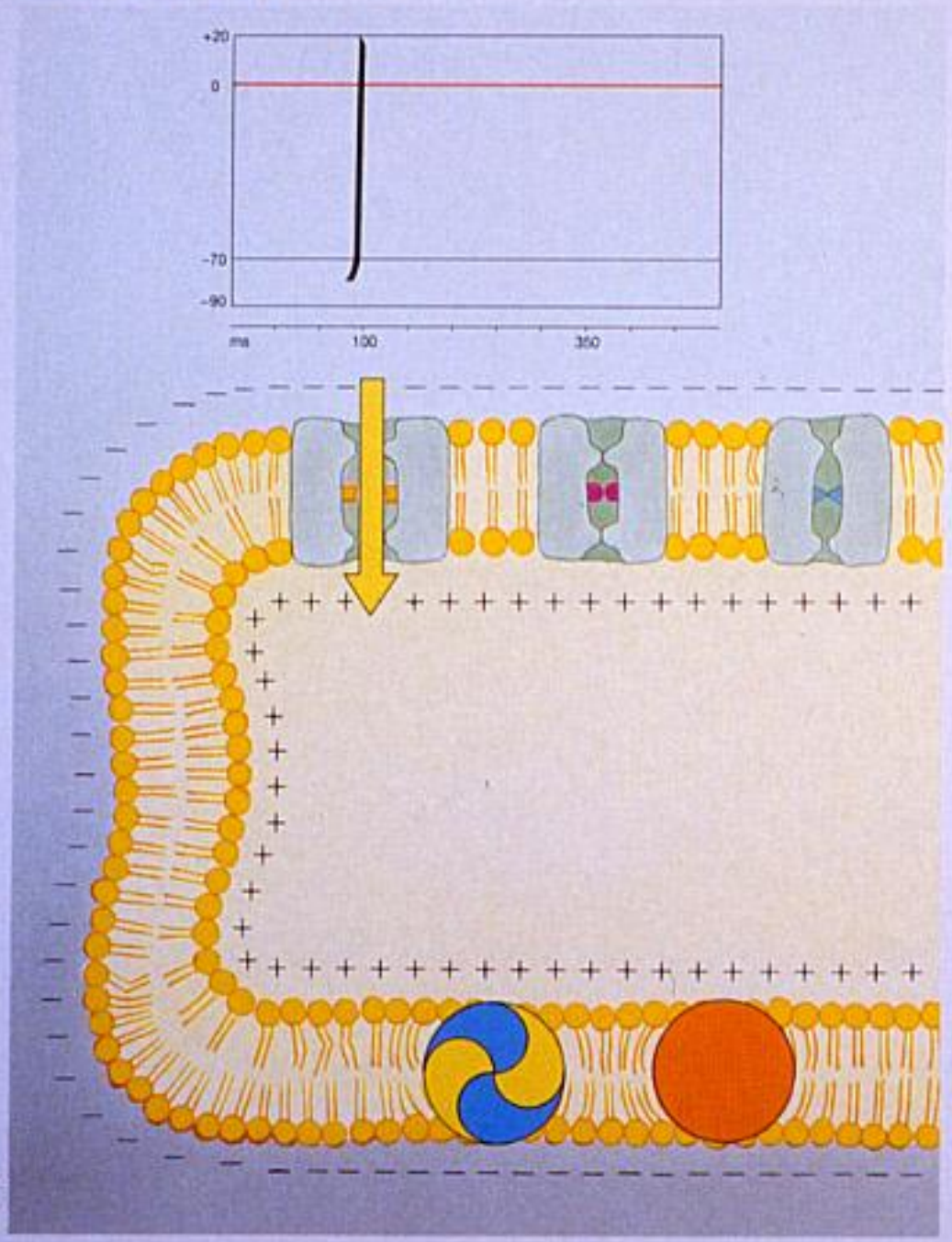
Cardiac muscle

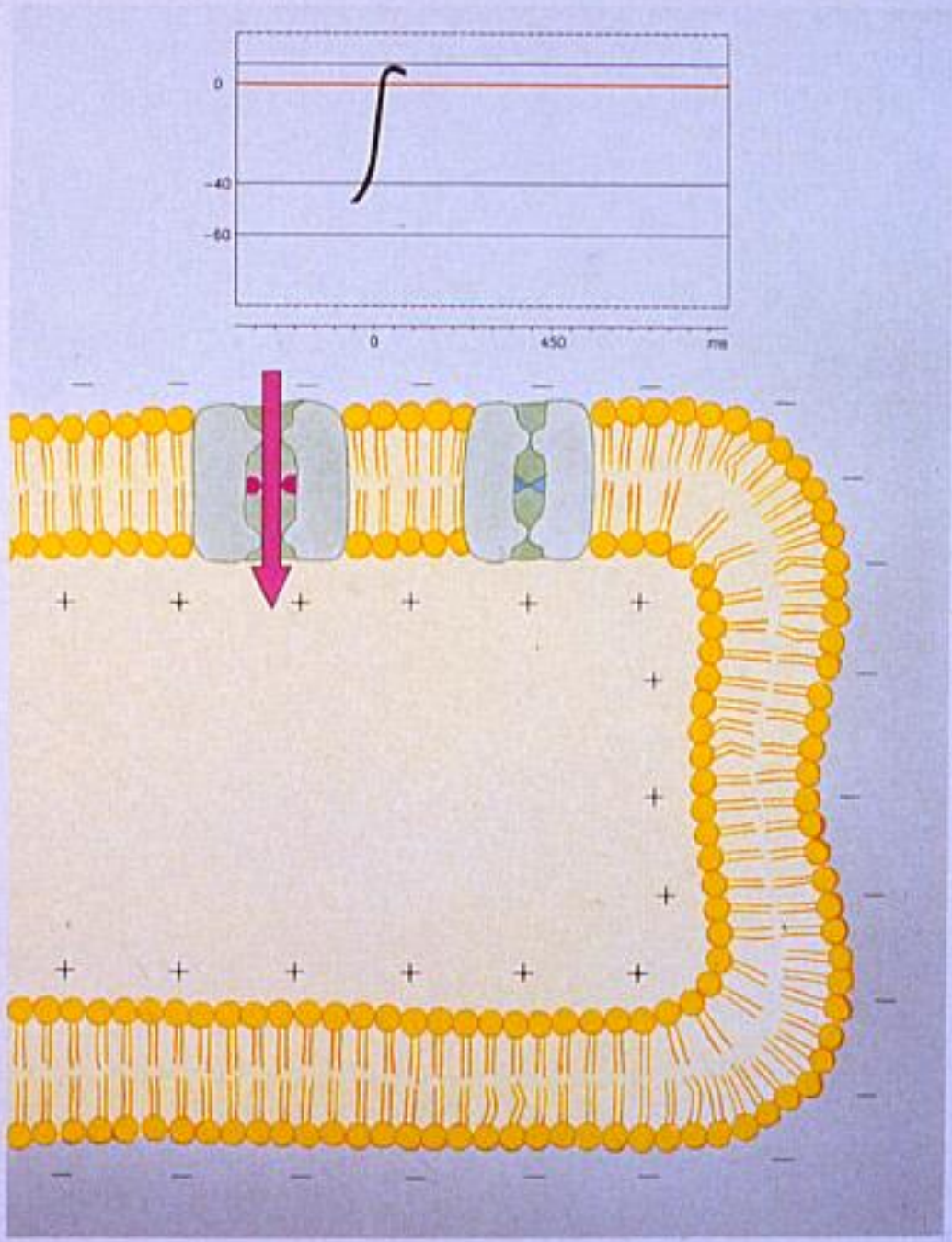


The cardiac cell

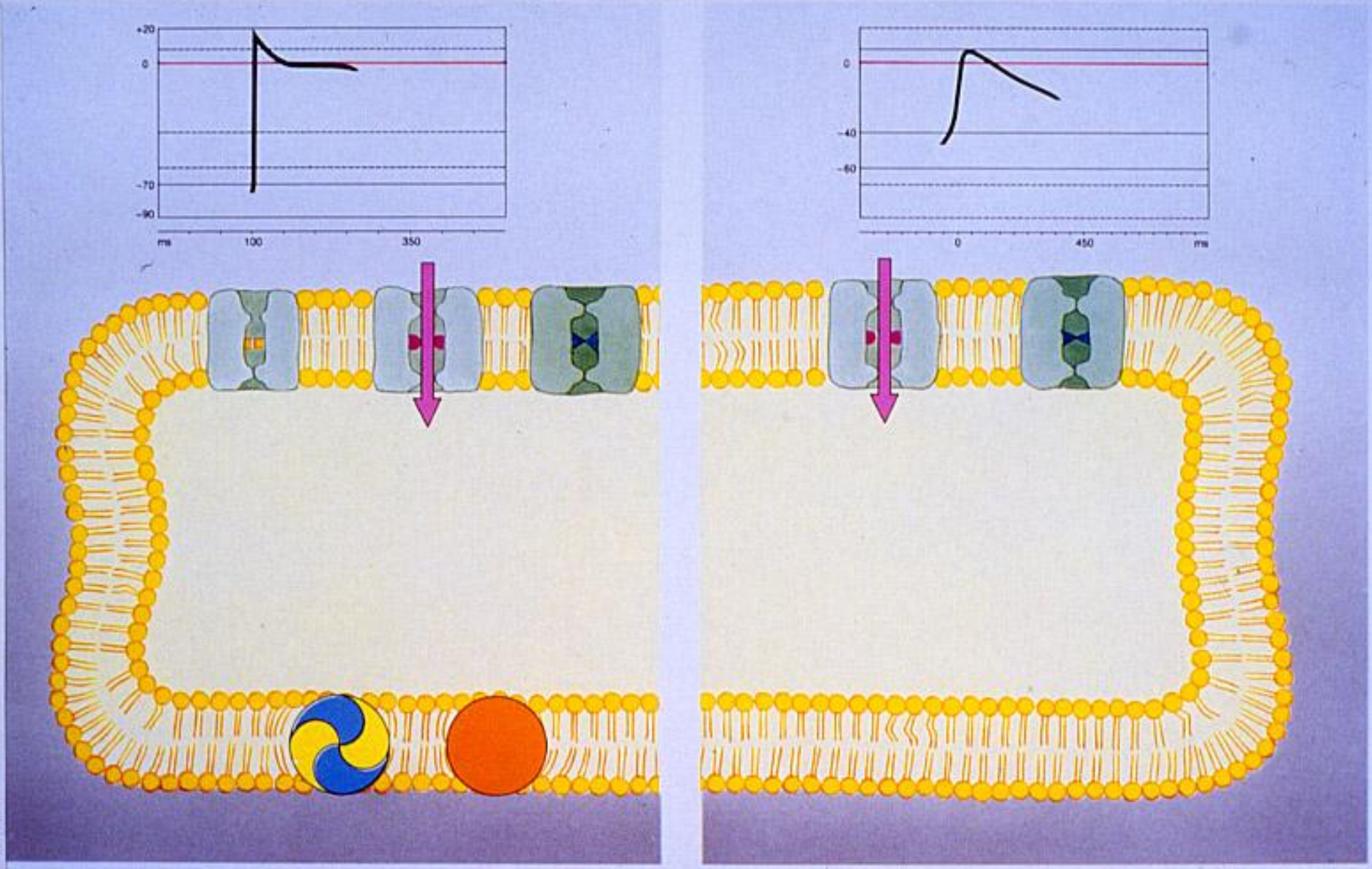


Ionic currents in phase 0

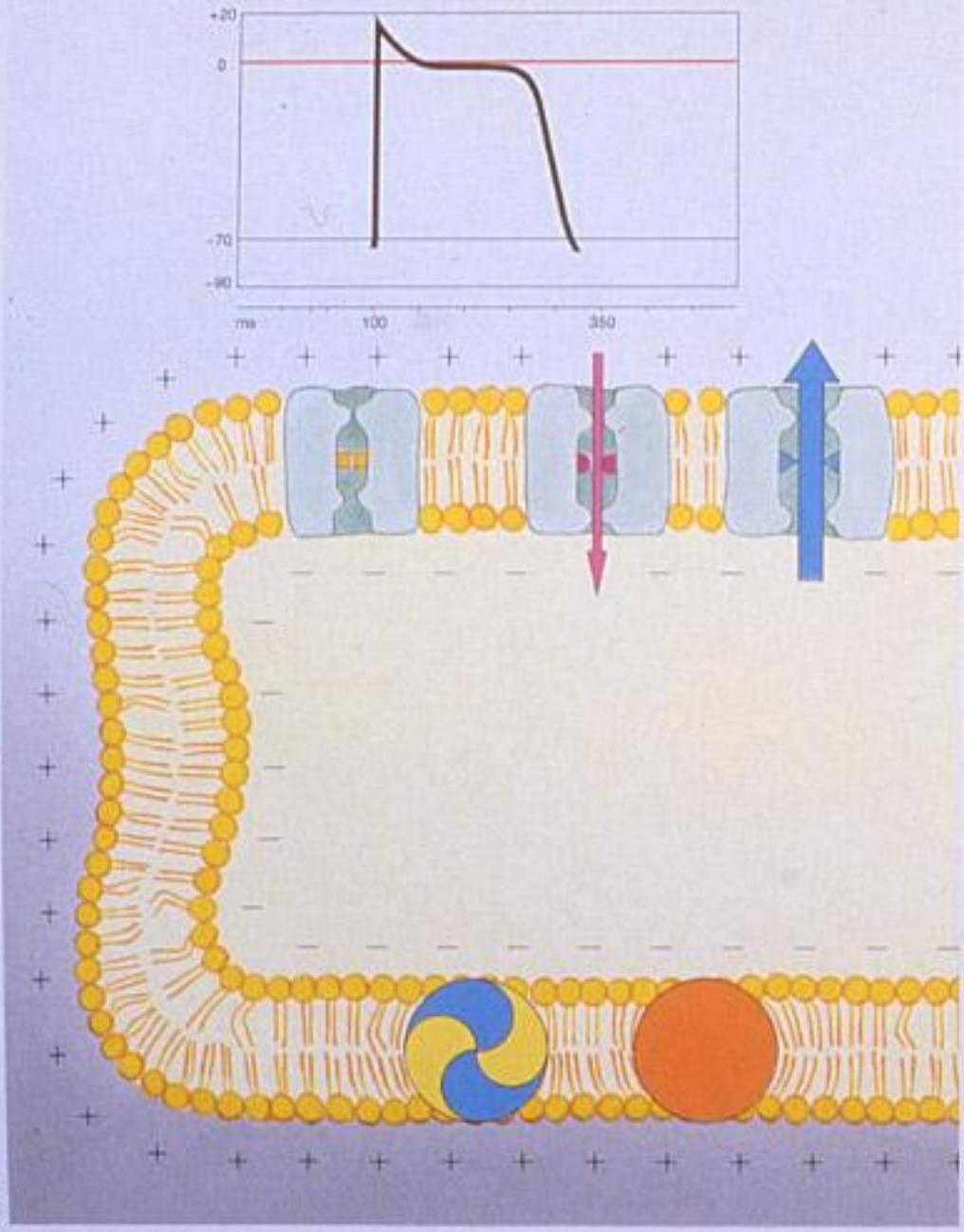


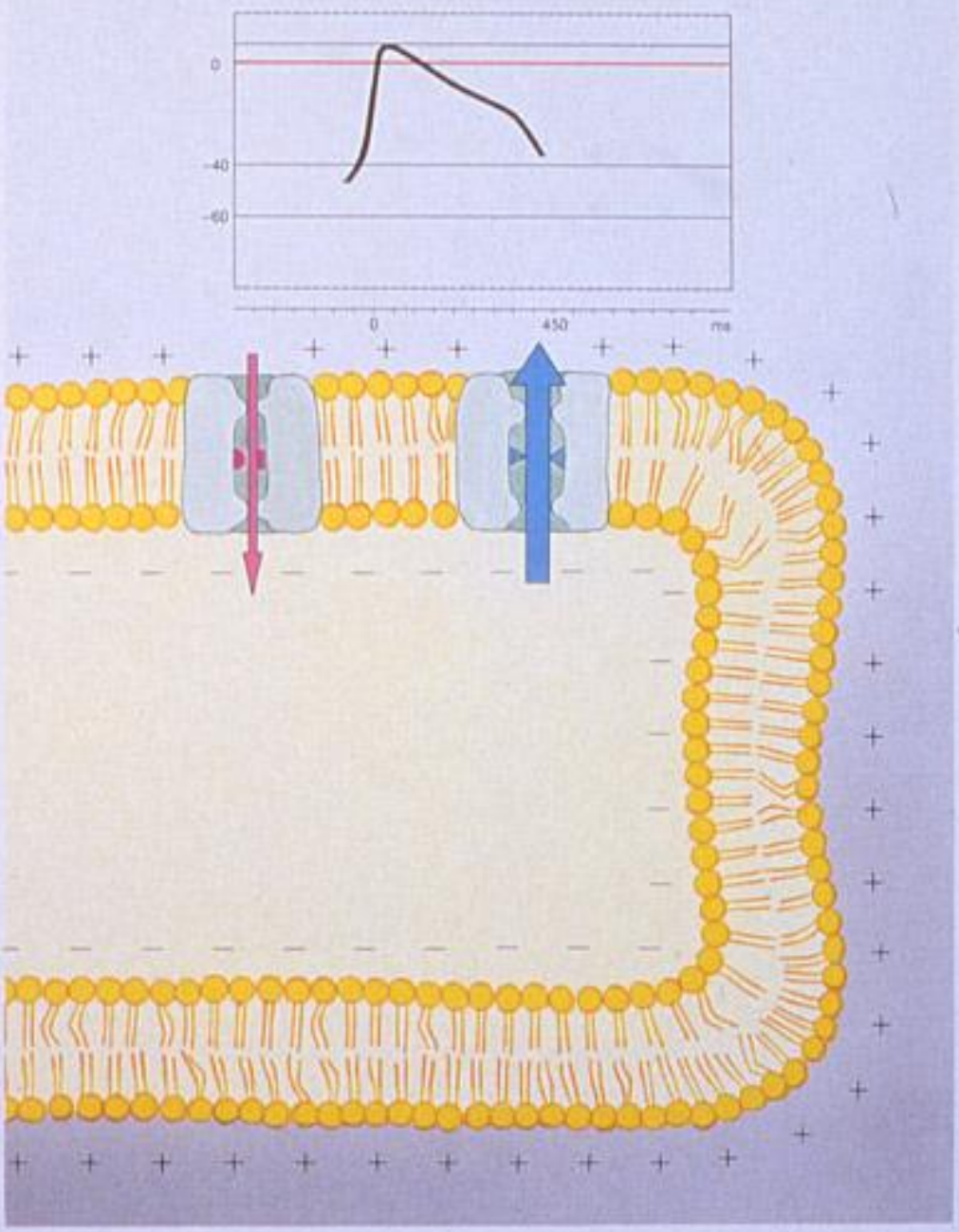


Ionic currents in phase 2

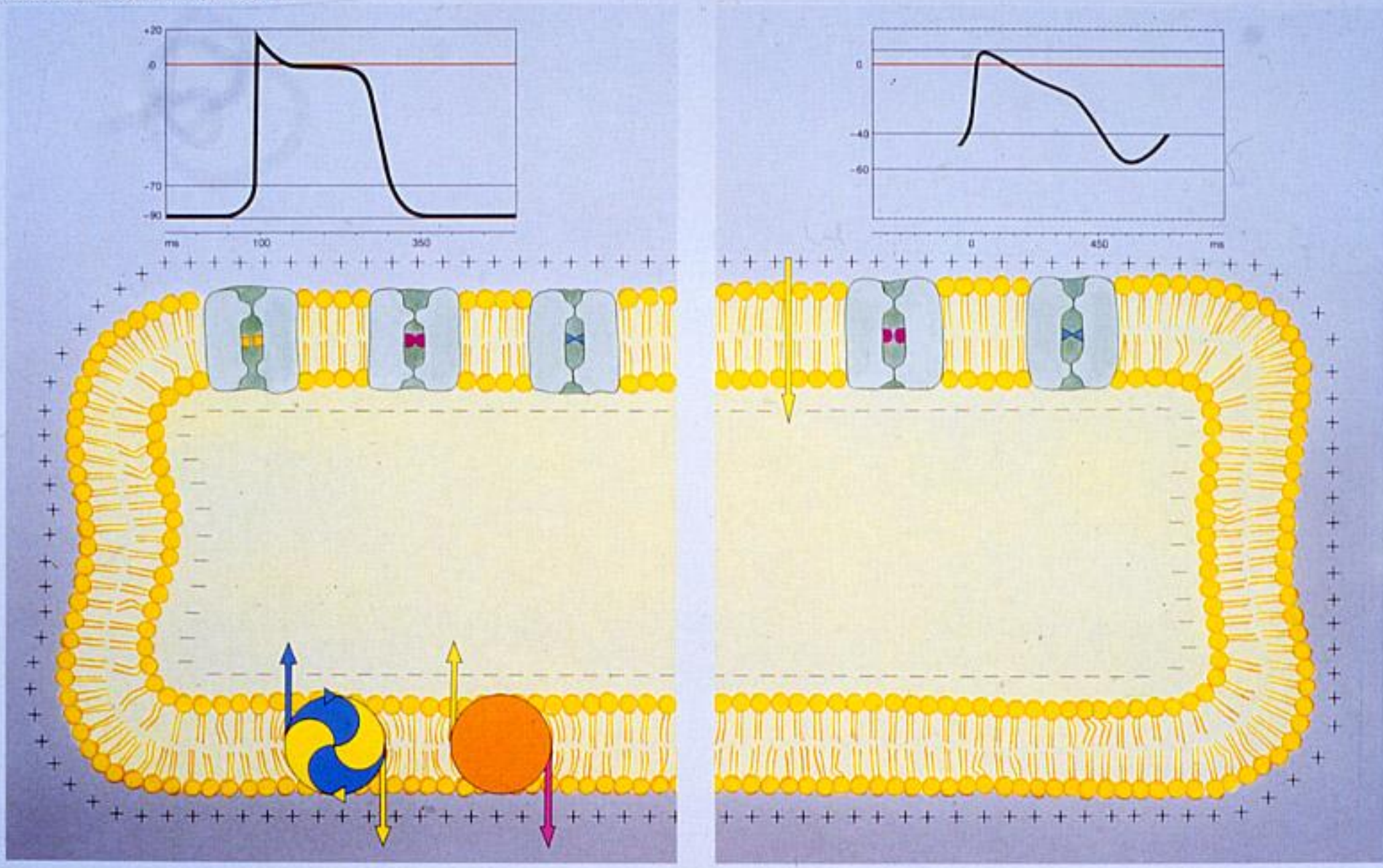


Ionic currents in phase 3





Active transport in phase 4



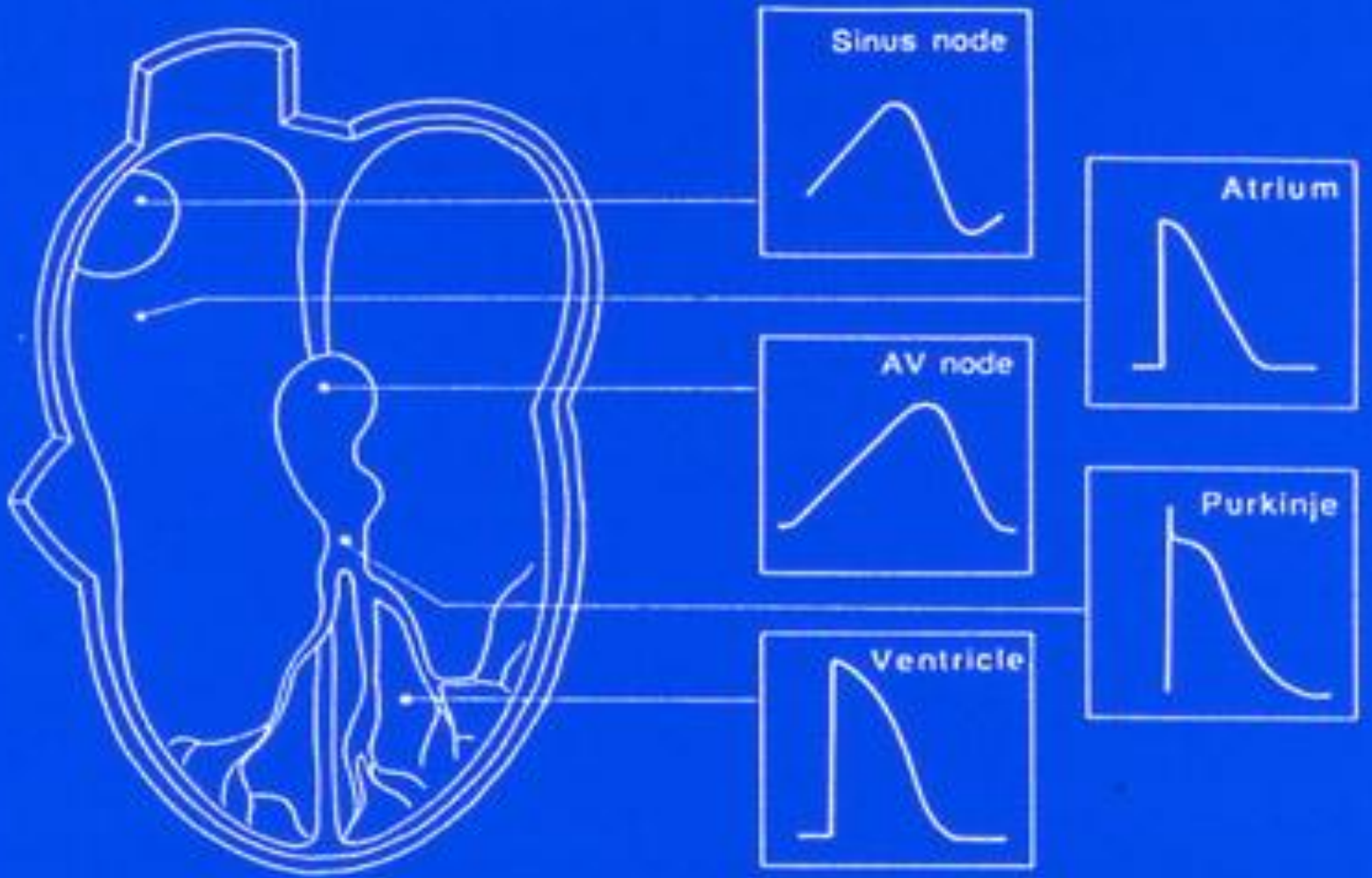
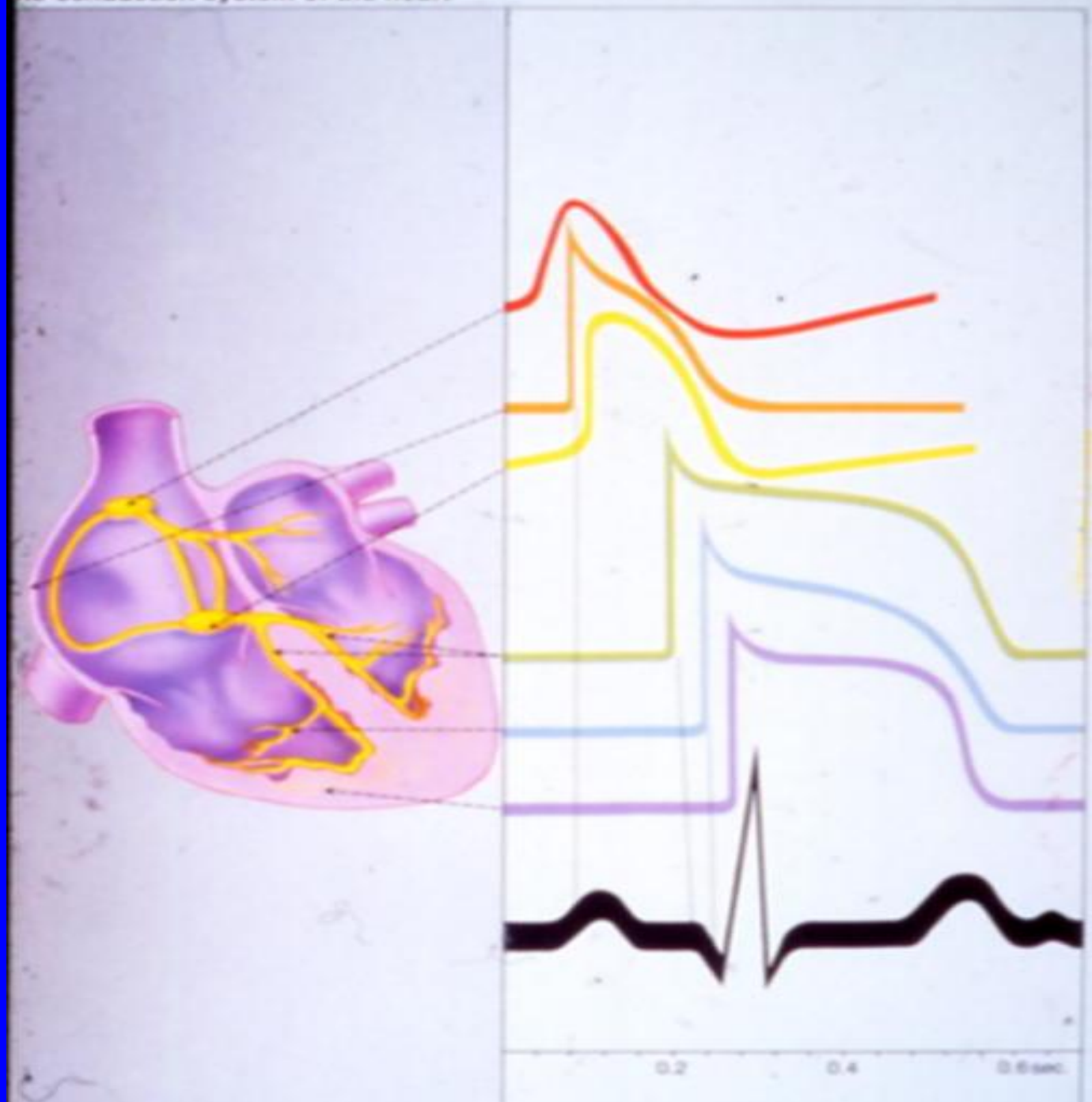


Fig. 3.2 Different morphologies of cardiac cell action potentials.

J.Y. Le Heuzey and P. Puech, Electrophysiological principles of arrhythmias in C. Wren and R.W.F. Campbell Eds, Paediatric cardiac arrhythmias, 1996

he conduction system of the heart



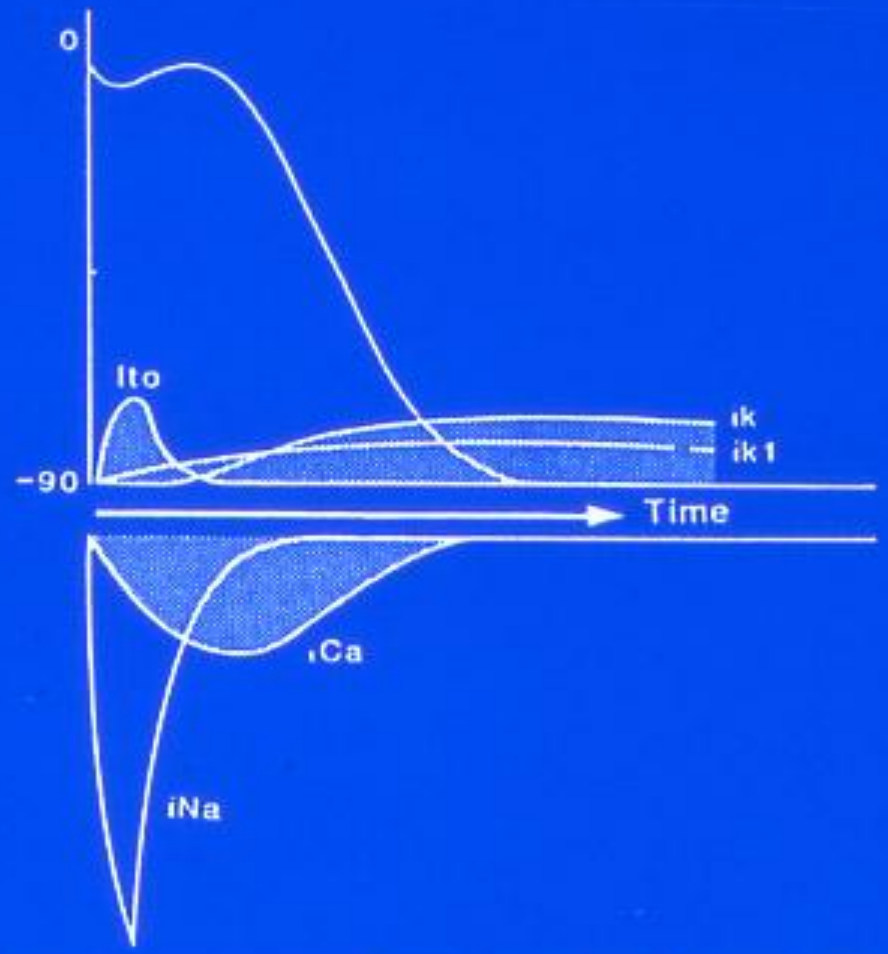
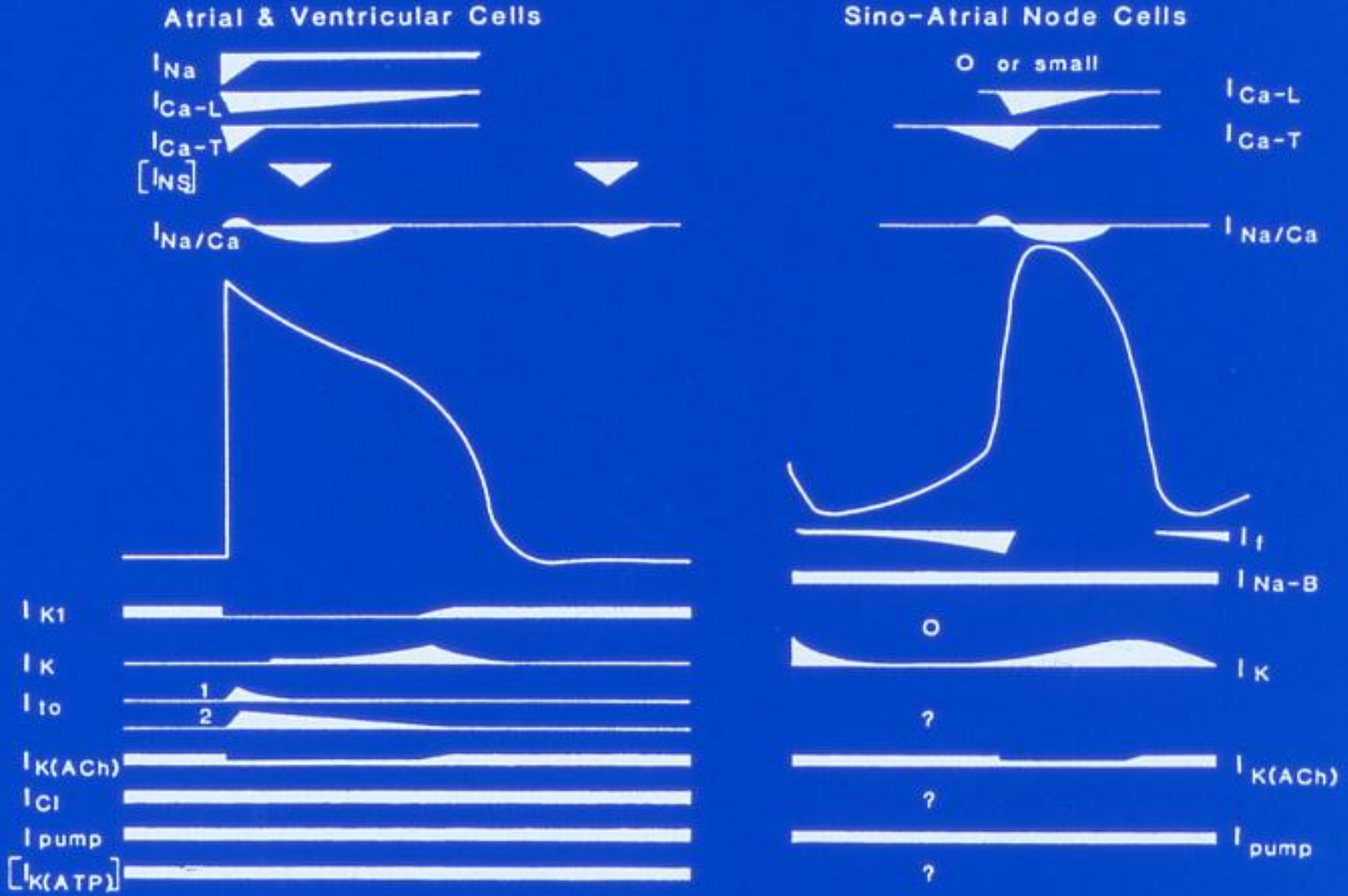


Fig. 3.4 Different ionic currents responsible for the cell electrical activity. Upward (or outward) currents are repolarizing and downward (or inward) currents are depolarizing.

J.Y. Le Heuzey and P. Puech, Electrophysiological principles of arrhythmias in C. Wren and R.W.F. Campbell Eds, Paediatric cardiac arrhythmias, 1996


Atrial & Ventricular Cells
I_{Na}
I_{Ca-L}
I_{Ca-T}
$[I_{NS}]$
$I_{Na/Ca}$
I_{K1}
I_K
I_{to}
1
2
$I_{K(ACh)}$
I_{Cl}
I_{pump}
$[I_{K(ATP)}]$
Sino-Atrial Node Cells
0 or small
I_{Ca-L}
I_{Ca-T}
$I_{Na/Ca}$
I_f
I_{Na-B}
0
I_K
?
$I_{K(ACh)}$
?
I_{pump}
?

Different refractory periods in myocardial cells

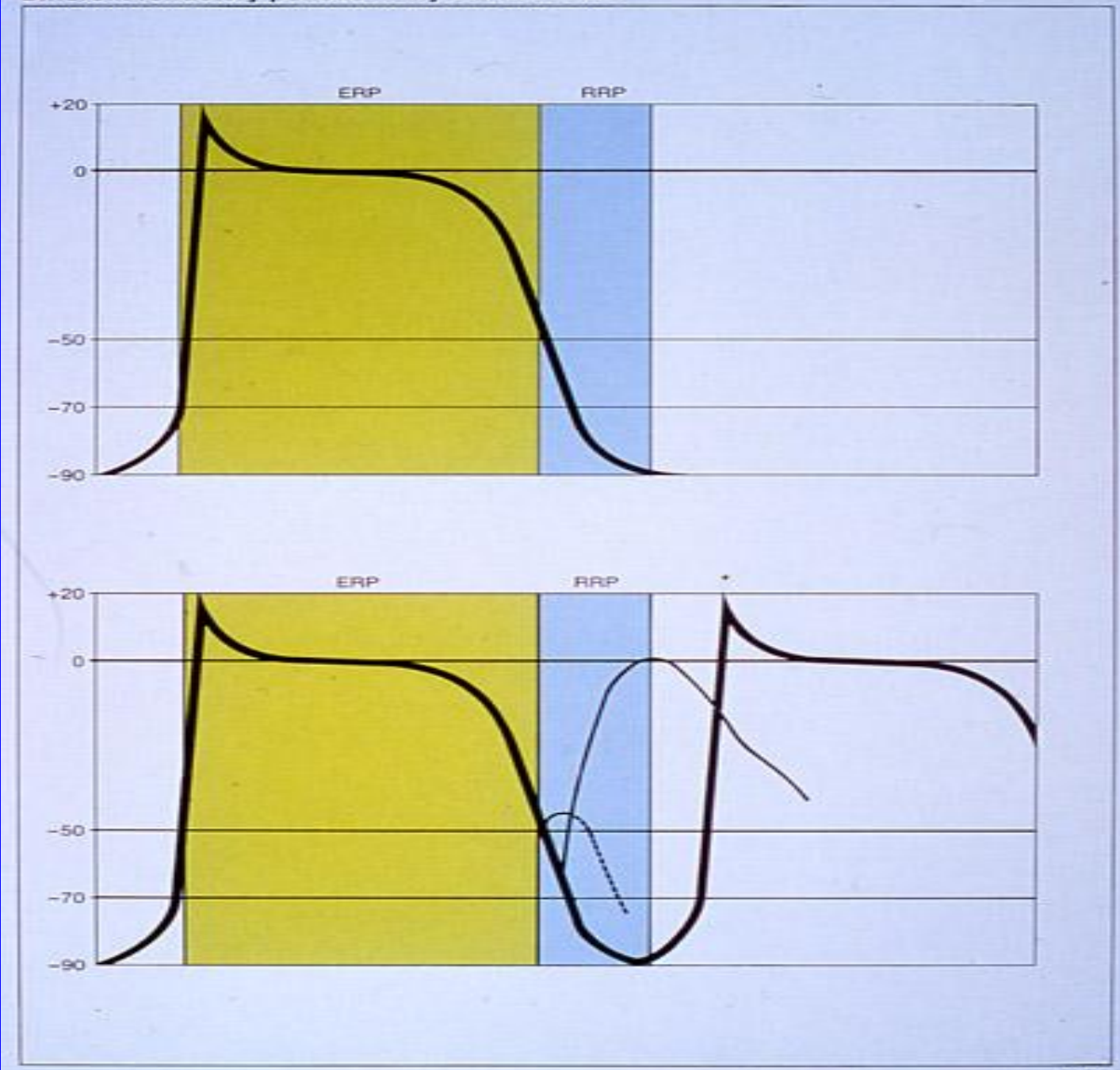


TABLE 11. Resting Potentials (or Maximal Diastolic Potentials) and Maximal Upstroke Velocities (dV/dt_{max}) of Different Cardiac Tissues

Cardiac Tissues	Resting or Maximum Diastolic Potential (mV)	Authors	dV/dt_{max} V/s	Authors
SA node	−50 to −60 −55 to −60 (Rhesus monkey)	Cranefield (1975) Fleckenstein (1963 b)	2 to 3	Brooks and Lu (1972)
Atrium	−78 (Rabbit) −80 to −90 (Guinea pig) −85 (Dog)	West (1955) Fleckenstein (1963b) Hoffman and Suckling (1952)	340 (dog)	Trautwein and Schmidt (1960)
AV node (N cells)	−53 (Dog)	Sano (1976)	6.7	Paes de Carvalho
Purkinje fibers	−96 (Dog) −85 (Rhesus monkey)	Trautwein and Zink (1952) Kotowski, Antoni, Vahlenkamp and Fleckenstein (1961)	400 (guinea pig, cat, rhesus monkey)	Tritthart, Grundy, Haastert, and Herbst (1972)
Ventricle (papillary muscles)	−85 (Dog) −88 (Cat) −90 (Rhesus monkey) −78 (Guinea pig)	Hoffman and Suckling (1952) Trautwein, Gottstein, and Dudel (1954) Antoni and Engstfeld (1961) Engstfeld, Antoni, and Fleckenstein (1961)	170 to 180 (guinea pig, cat, rhesus monkey)	Tritthart, Grundy, Haastert, and Herbst (1972)

TABLE 12. Normal Conduction Velocities in Different Cardiac Tissues

Cardiac Tissues	Velocity (cm/sec)	Species	Authors
SA node	2–6	Rabbit	Sano and Yamagishi (1965)
Atrium	80	Rabbit	Sano and Yamagishi (1965)
	50–100	Rabbit	Paes de Carvalho, de Mello, and Hoffman (1959)
	90–120	Dog	Goodman, van der Steen, and van Dam (1971)
	80	Dog	Hogan and Davis (1971)
AV node (N cells)	2–5	Cow	van der Kooi, Durrer, van Dam, and van der Tweel (1956)
		Dog	Scher, Rodriguez, Liikane and Young (1959)
			Alanis, Lopez, Mandoki, and Pilar (1959)
		Rabbit	Pruitt and Essex (1960)
His bundle (and branches)	100–150	Different Species	Sano (1976)
Purkinje fibers	200	Dog	Draper & Weidmann (1951)
	80	Rhesus monkey	Antoni and Zerweck (1967)
Ventricle (papillary muscle)	60	Rhesus monkey	Antoni and Zerweck (1967)

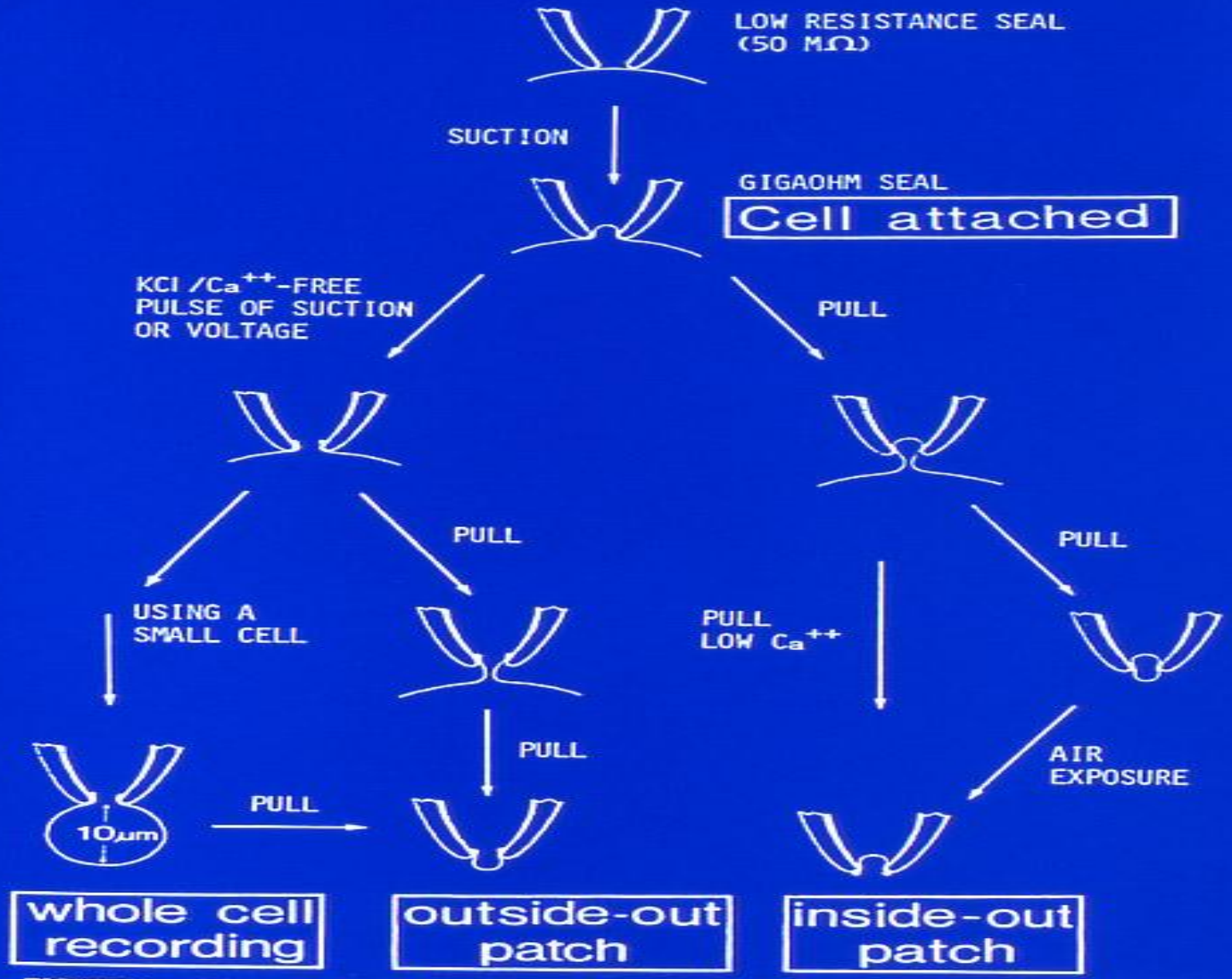
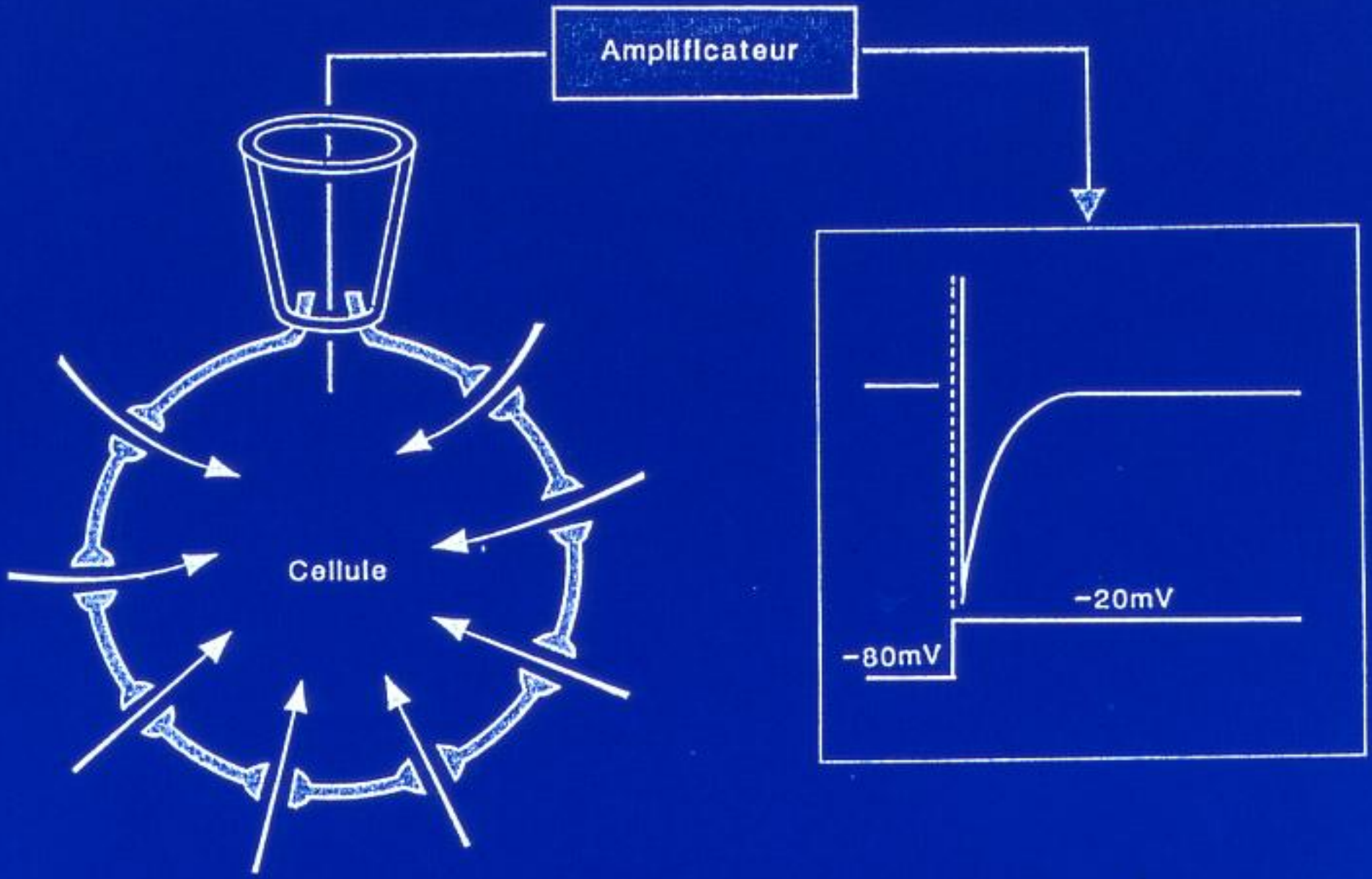
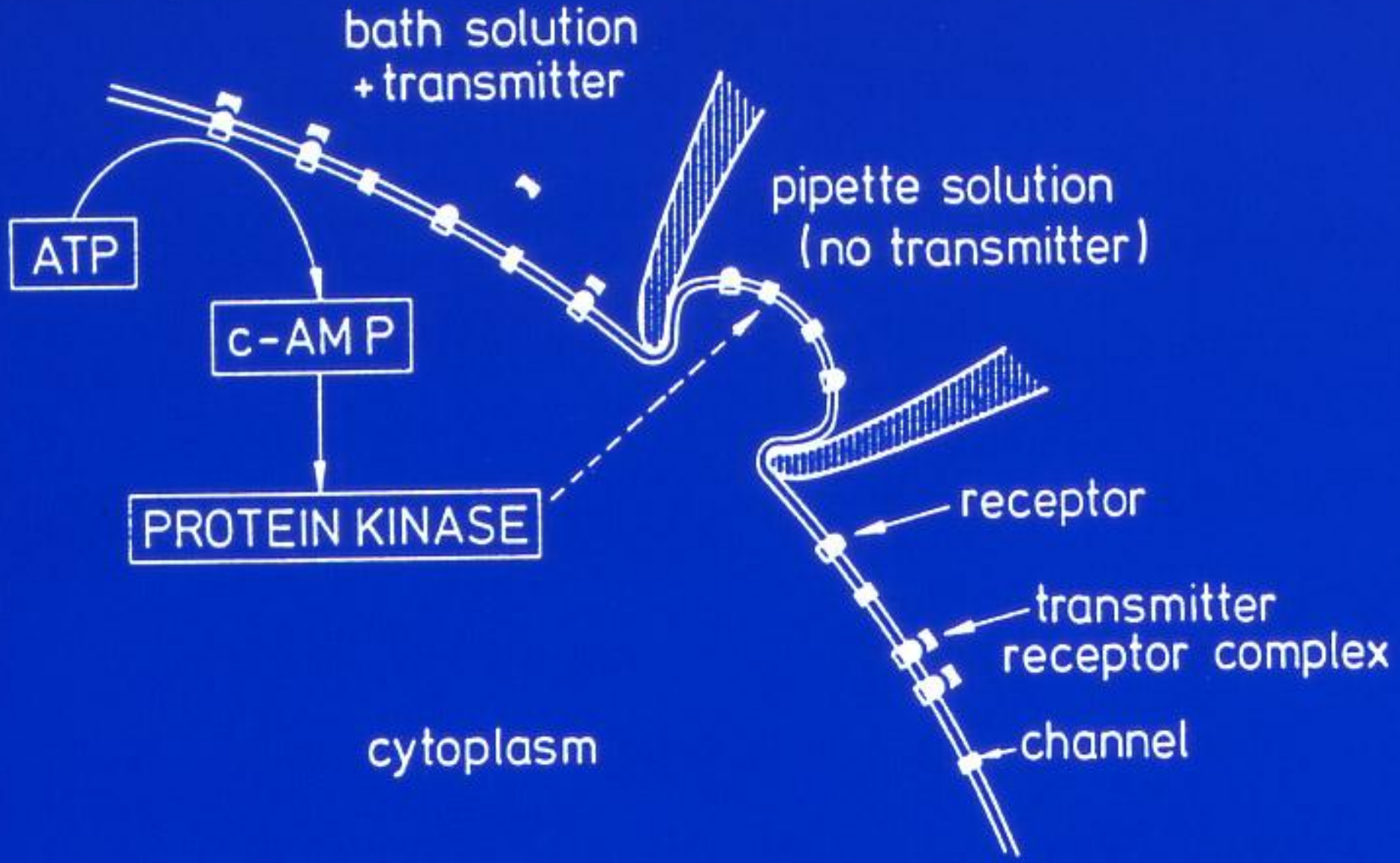
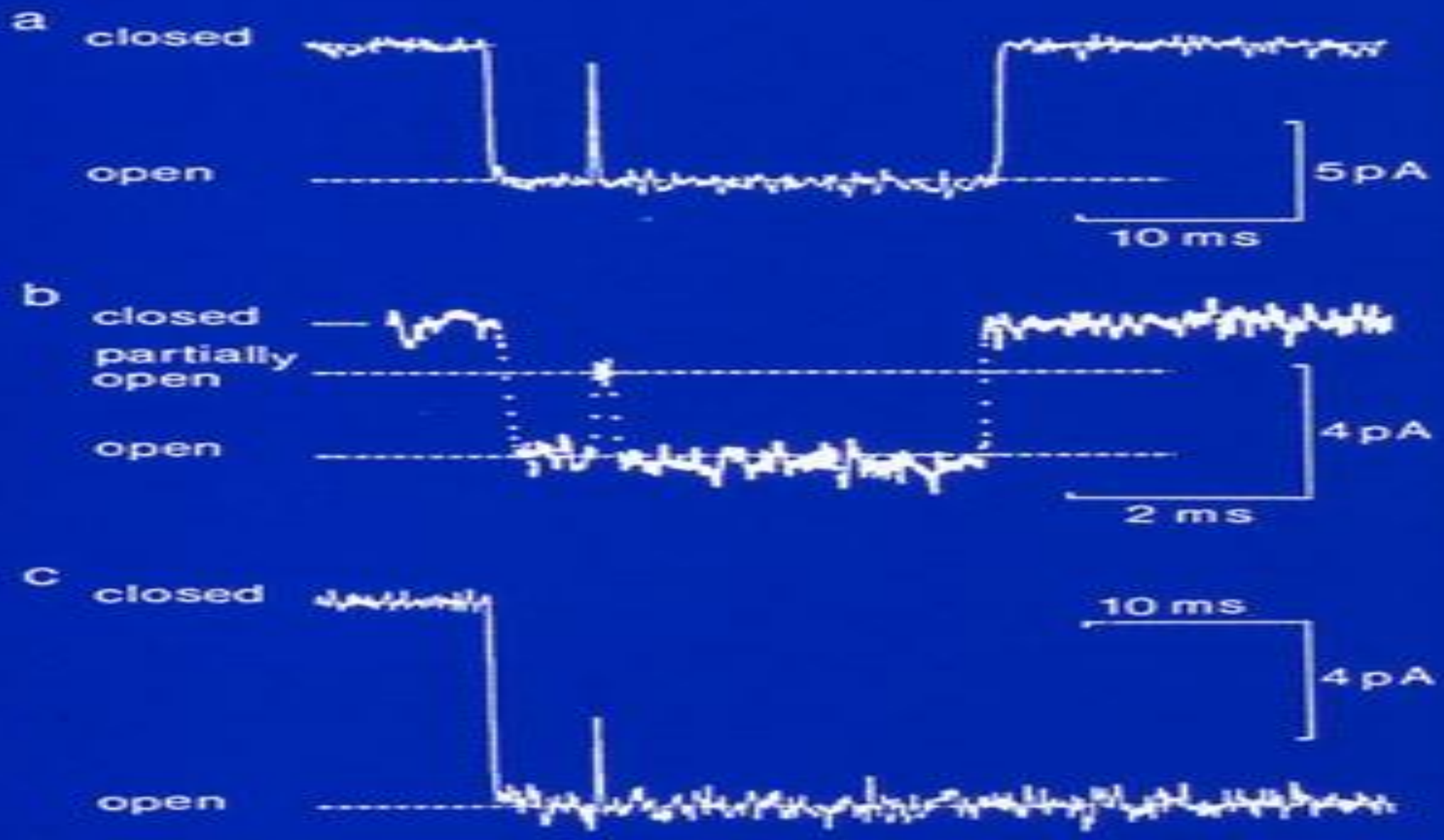
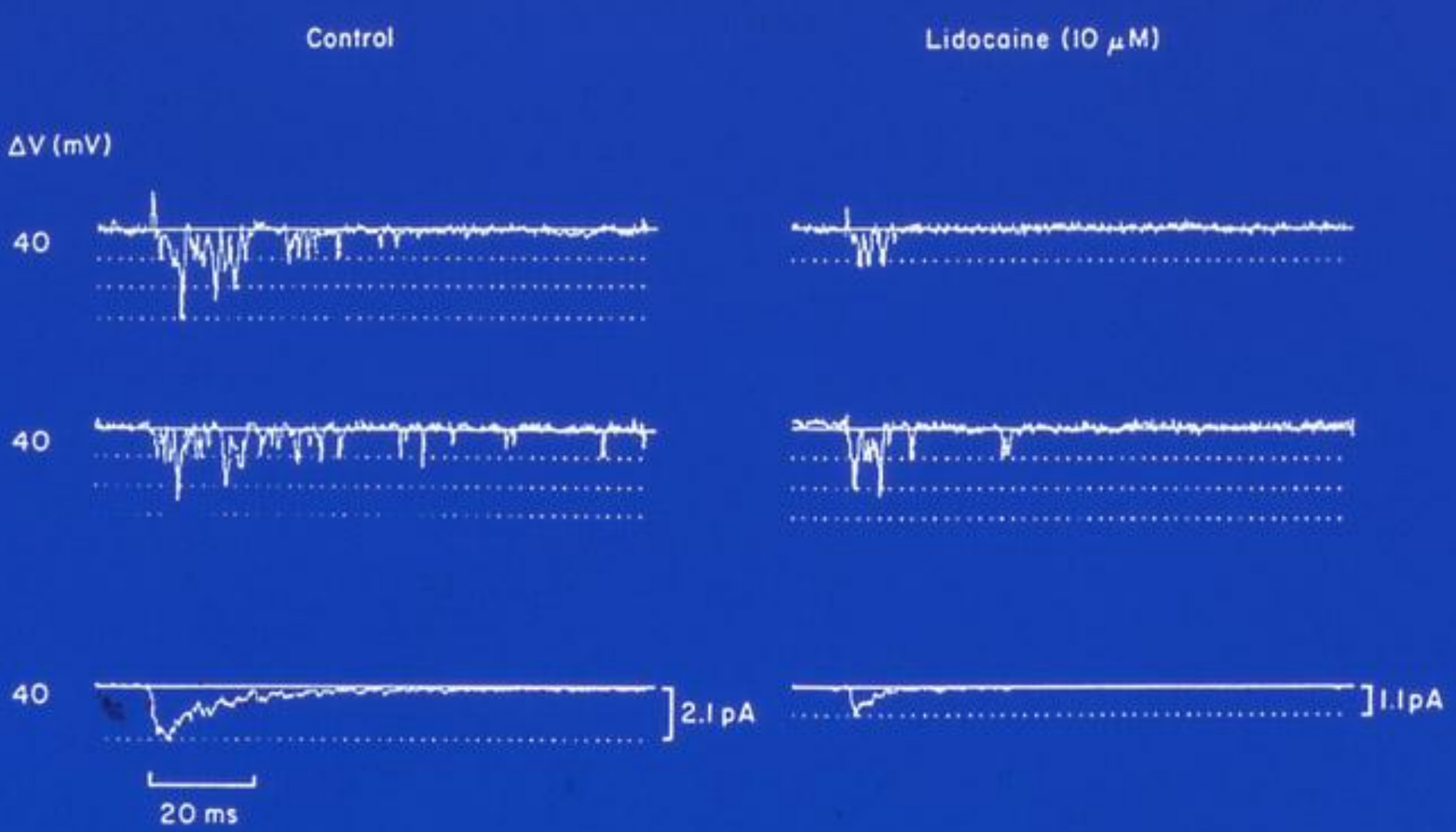


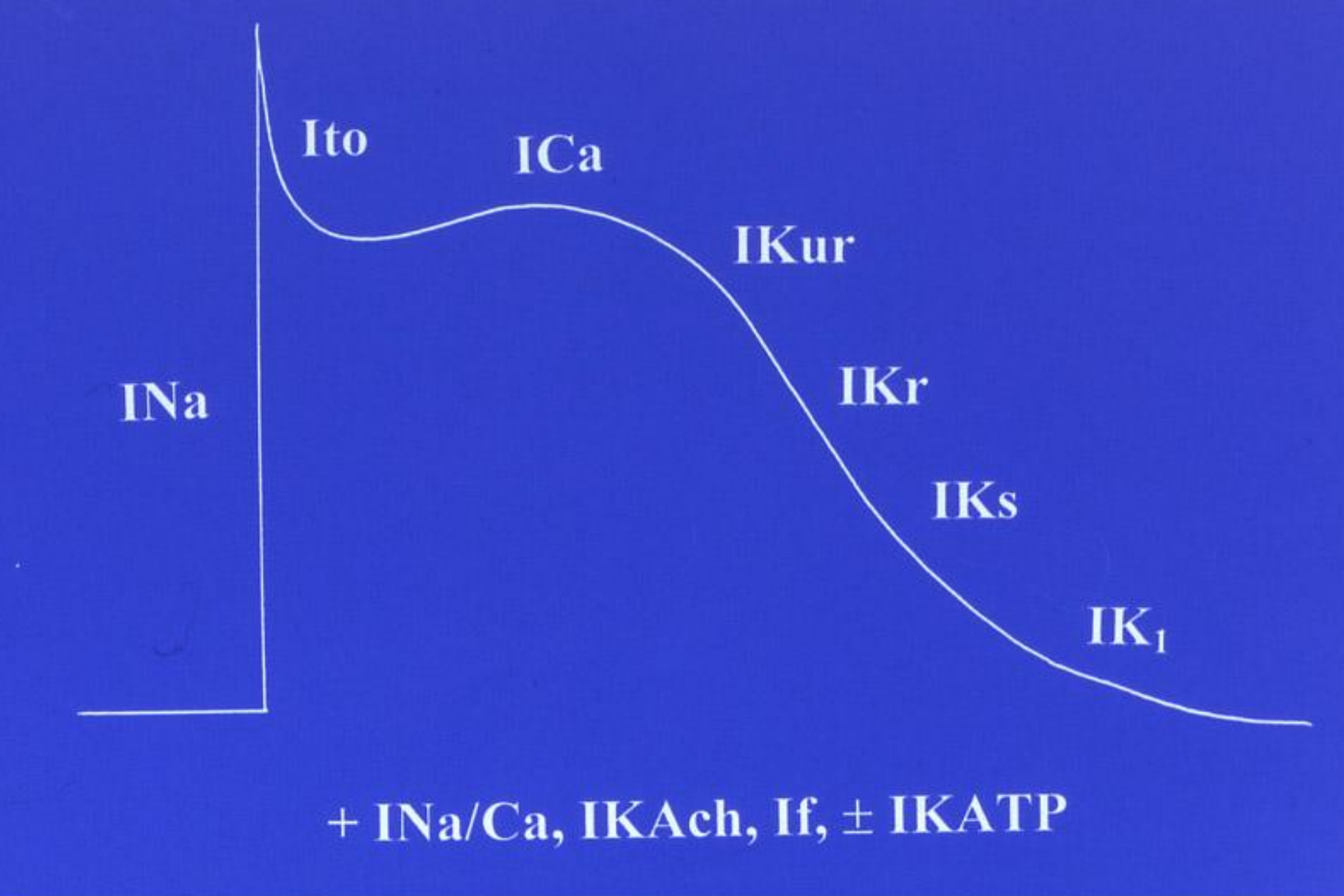
FIGURE 1. Schematic illustration of the different configurations of the patch clamp and of the manipulations that lead to them. From Hamill et al (32), by permission of Springer-Verlag. Heidelberg.


Amplificateur
Cellule
-20mV
-80mV


bath solution
+ transmitter
pipette solution
(no transmitter)
ATP
c-AMP
PROTEIN KINASE
receptor
transmitter
receptor complex
channel
cytoplasm


a
closed
open
5pA
10 ms
b
closed
partially open
open
4pA
2 ms
c
closed
open
10 ms
4pA


Control
Lidocaine (10 μM)
ΔV (mV)
40
40
40
2.1 pA
1.1 pA
20 ms


Ito
ICa
IKur
IKr
IKs
INa
IK1
+ INa/Ca, IKAch, If, ± IKATP

SODIUM CURRENT

- Inhibition of sodium current reduces automaticity and slows conduction
- Greater inhibition in diseased tissues and during tachycardia
- Problem of inotropism depression and ventricular proarrhythmia especially during acute ischaemia

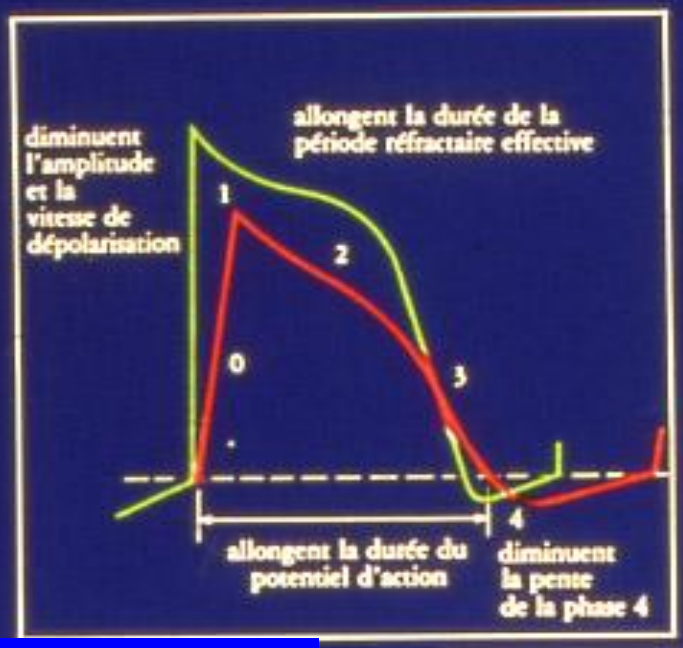
CALCIUM CURRENTS

- L type : . conduction in SA and AV node
  . electromechanical coupling
  . target of Diltiazem and Verapamil

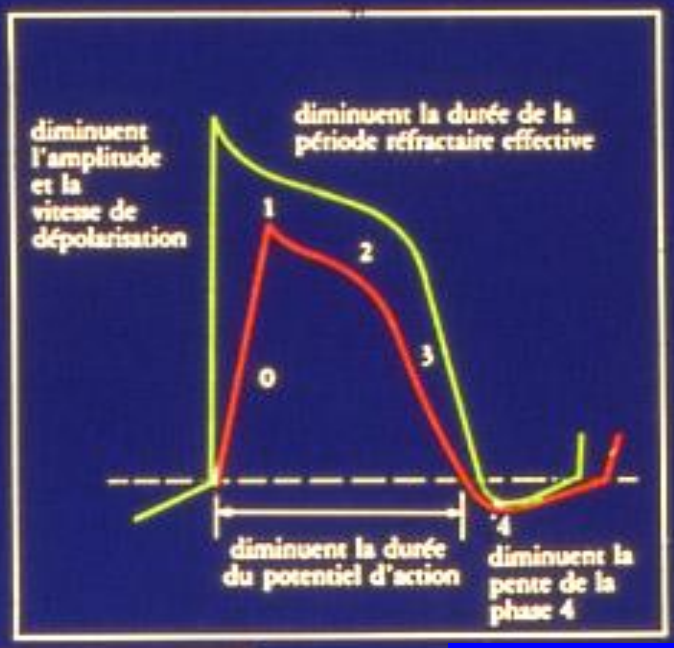
- T type : . present in SA node and atrium
  . role in automaticity of SA node
  . target of Mibefradil

MOLECULAR BIOLOGY OF POTASSIUM CHANNELS

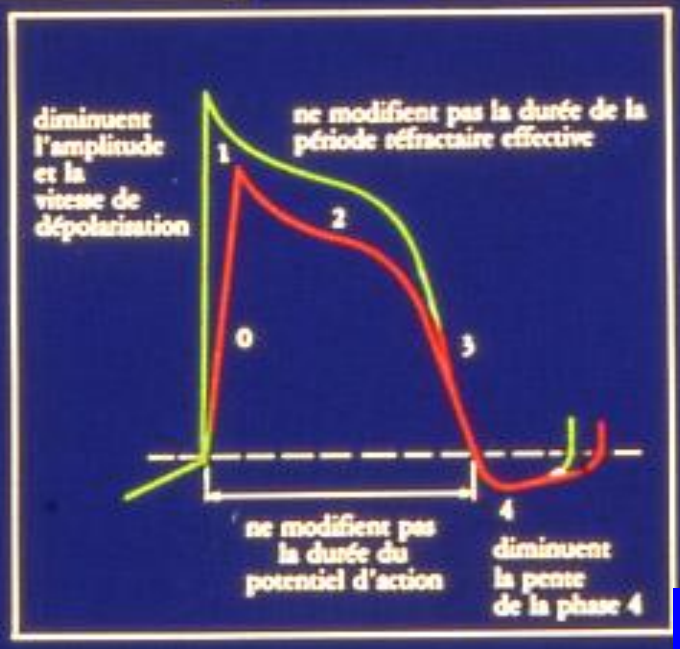
- Molecular structures largely identified for most potassium currents : Ikr, Iks, Ikur, IkAch, IkATP, Ik1
- Potential insights into disease and arrhythmia mechanisms
- Explanations of class III proarrhythmia



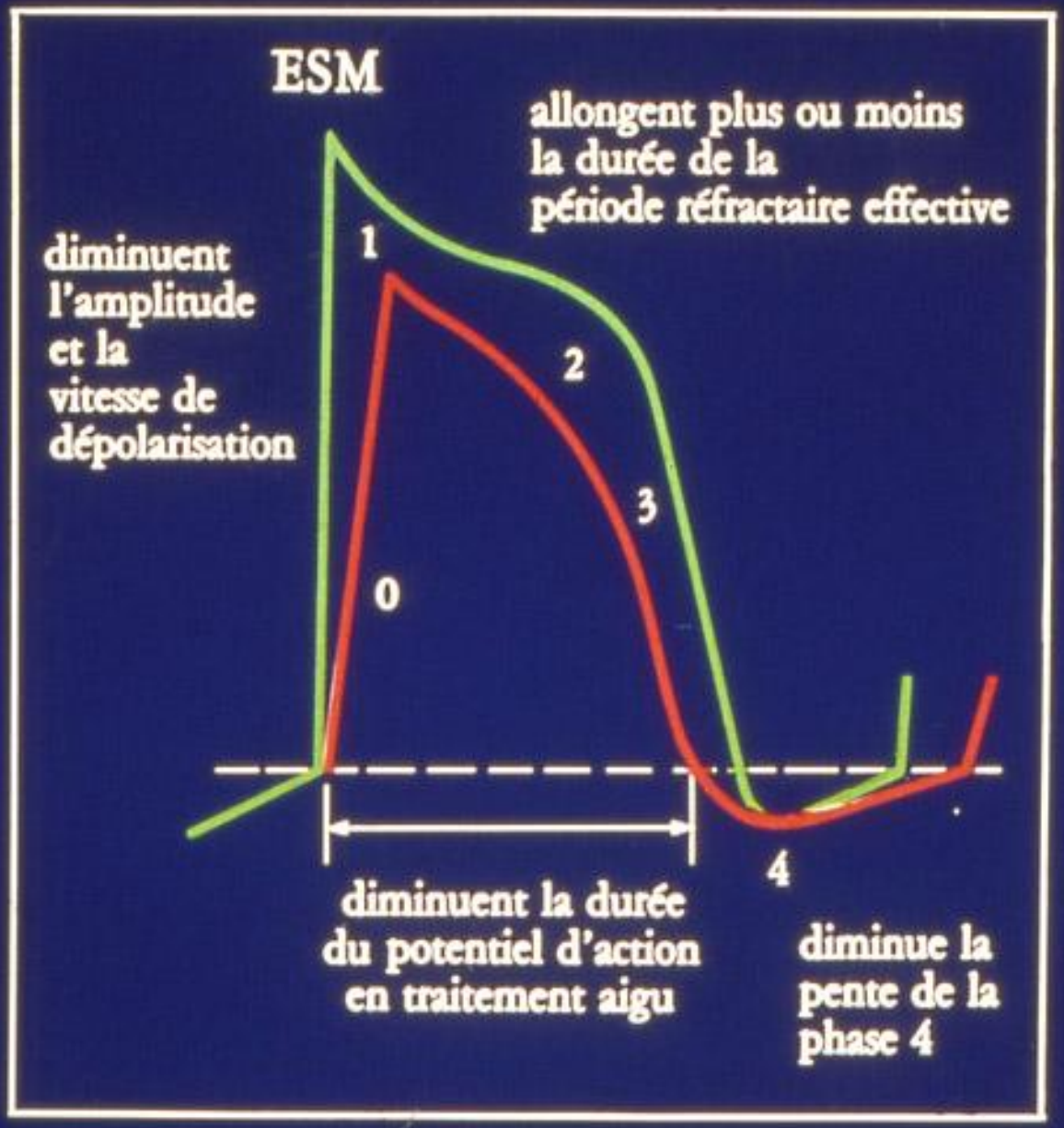
Classe Ia



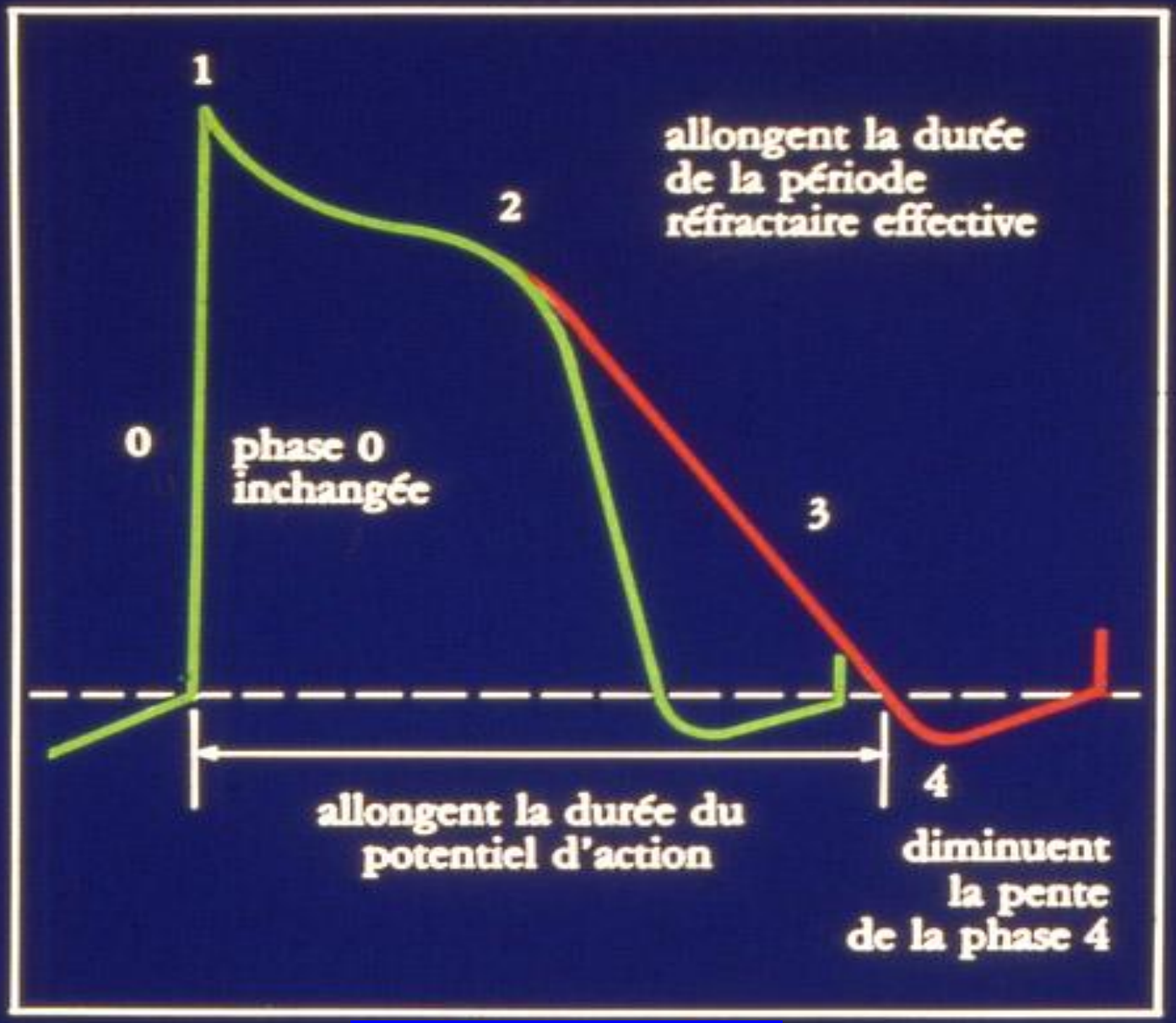
Classe Ib



Classe Ic


ESM
allongent plus ou moins
la durée de la
période réfractaire effective
diminuent
l'amplitude
et la
vitesse de
dépolarisation
1
2
3
0
4
diminuent la durée
du potentiel d'action
en traitement aigu
diminue la
pente de la
phase 4

Classe II


1
2
allongent la durée
de la période
réfractaire effective
0
phase 0
inchangée
3
4
allongent la durée du
potentiel d'action
diminuent
la pente
de la phase 4

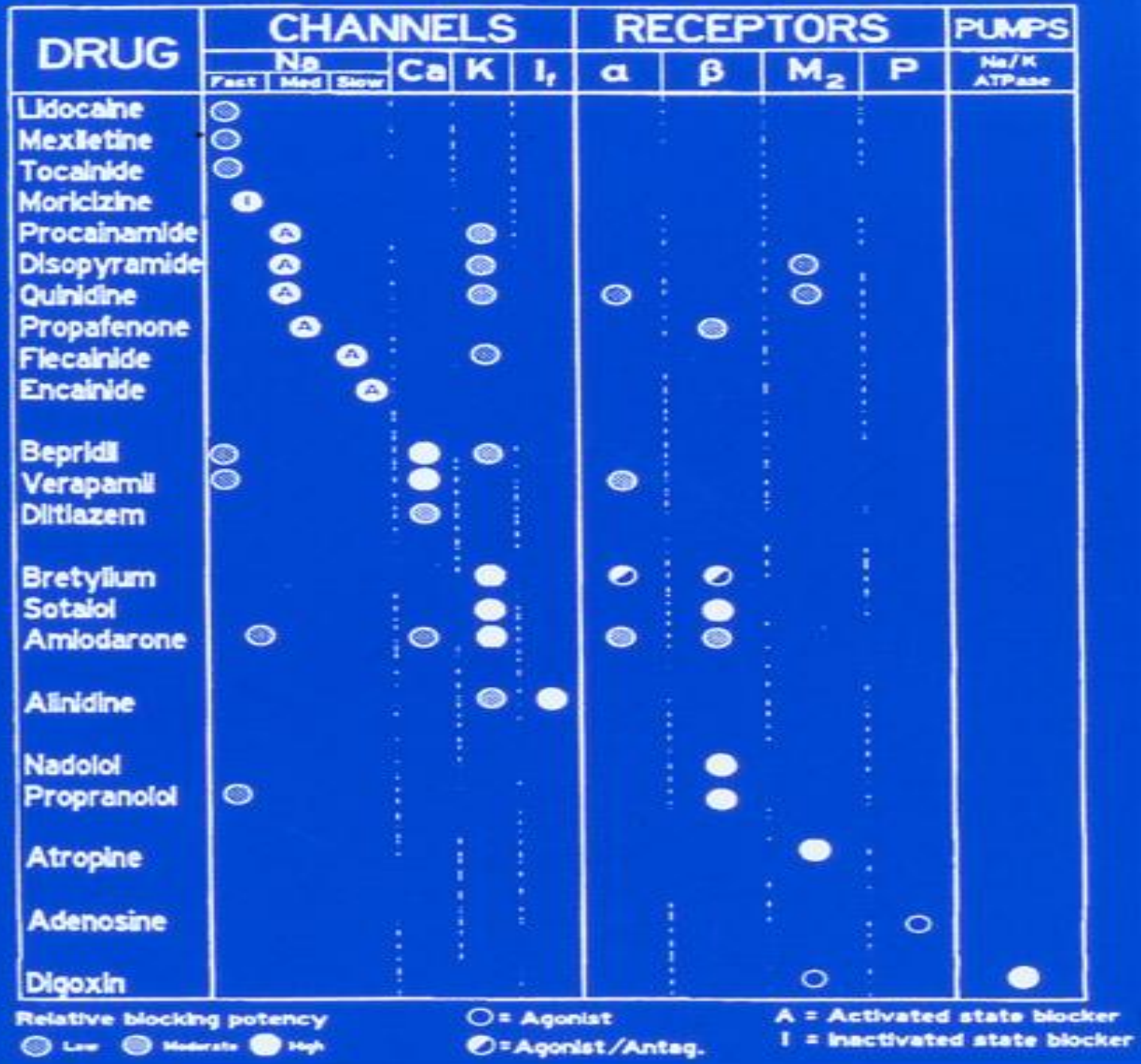
Classe III


1
diminuent la durée du potentiel d'action (en diminuant la durée de la phase 2)
allongent la période réfractaire effective
2
0
phase 0 inchangée
3
4
diminuent la durée du potentiel d'action sur les fibres à réponse rapide
diminuent la pente de la phase 4

Classe IV

	Class IIIa	Class IIIb
Repolarization prolongation	Increases in tachycardia	Increases in bradycardia
Prevention of arrhythmias	+	+++
Suppression of arrhythmias	+++	+
Induction of torsades de pointes	+	+++
	None Amiodarone (I + II + III + IV) ?	D Sotalol Dofetilide ... "pure" class III

→ Azimilide (Ikr + Iks) ?


DRUG
CHANNELS
Na
Fast
Med
Slow
Ca
K
I_f
RECEPTORS
α
β
M_2
P
PUMPS
Na/K ATPase
Lidocaine
Mexiletine
Tocainide
Moricizine
Procainamide
Disopyramide
Quinidine
Propafenone
Flecainide
Encainide
Bepridil
Verapamil
Diltiazem
Bretylium
Sotalol
Amiodarone
Alinidine
Nadolol
Propranolol
Atropine
Adenosine
Digoxin
A
I
Relative blocking potency
Low
Moderate
High
= Agonist
= Agonist/Antag.
A = Activated state blocker
I = Inactivated state blocker