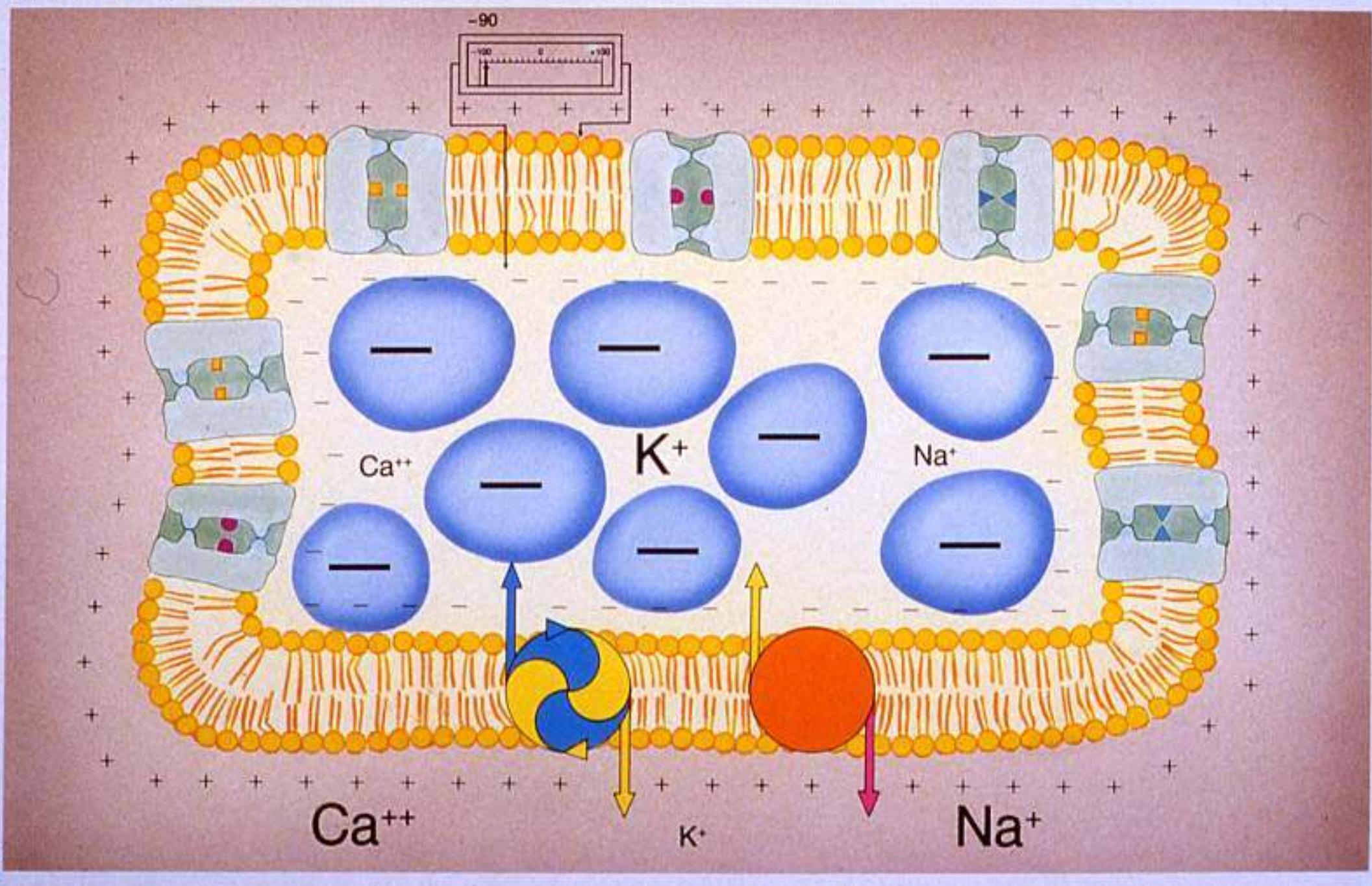
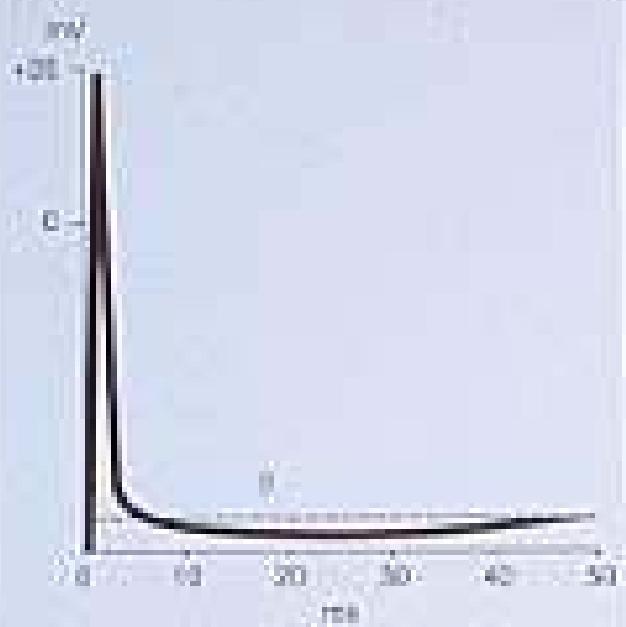


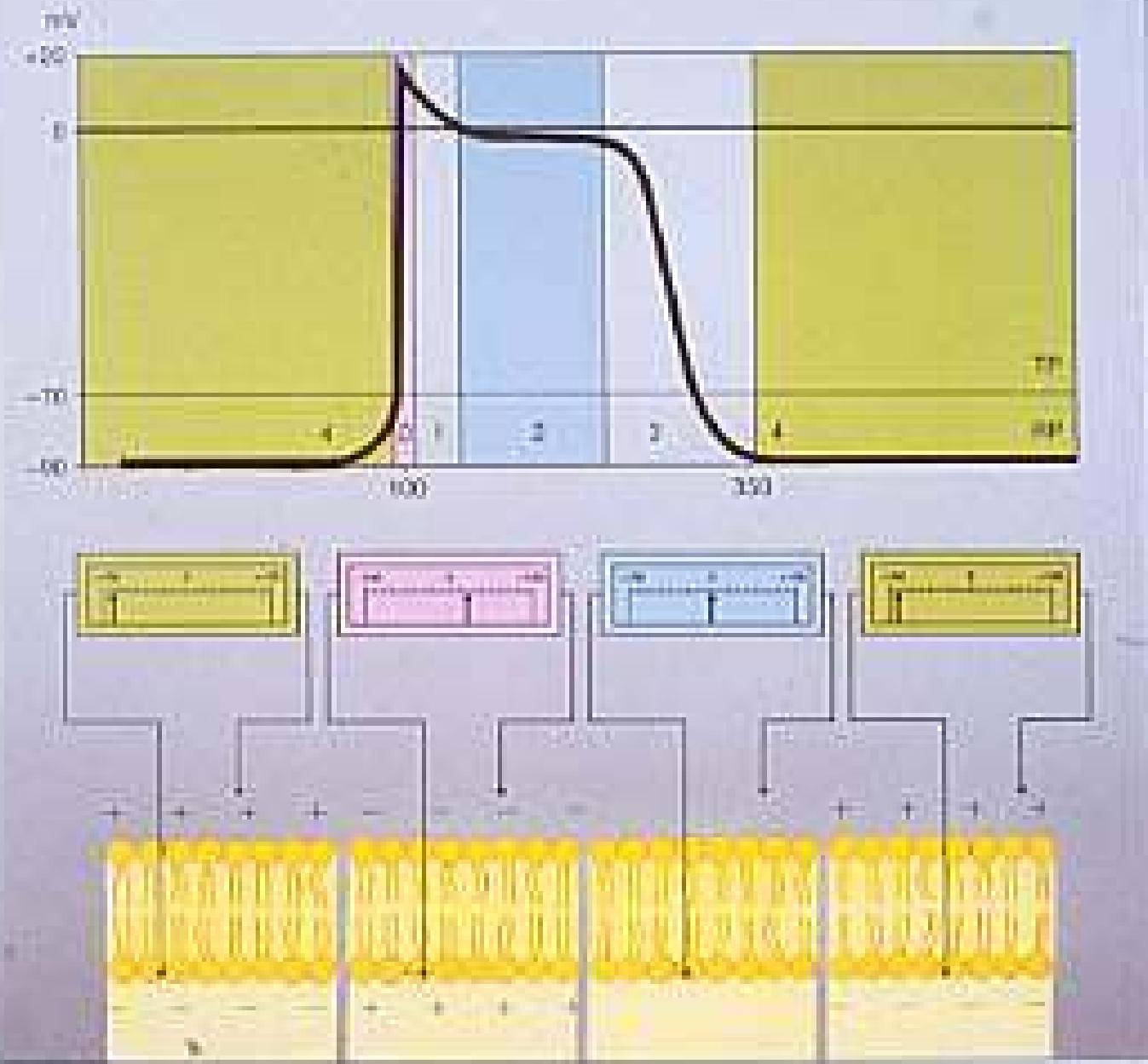
The membrane potential



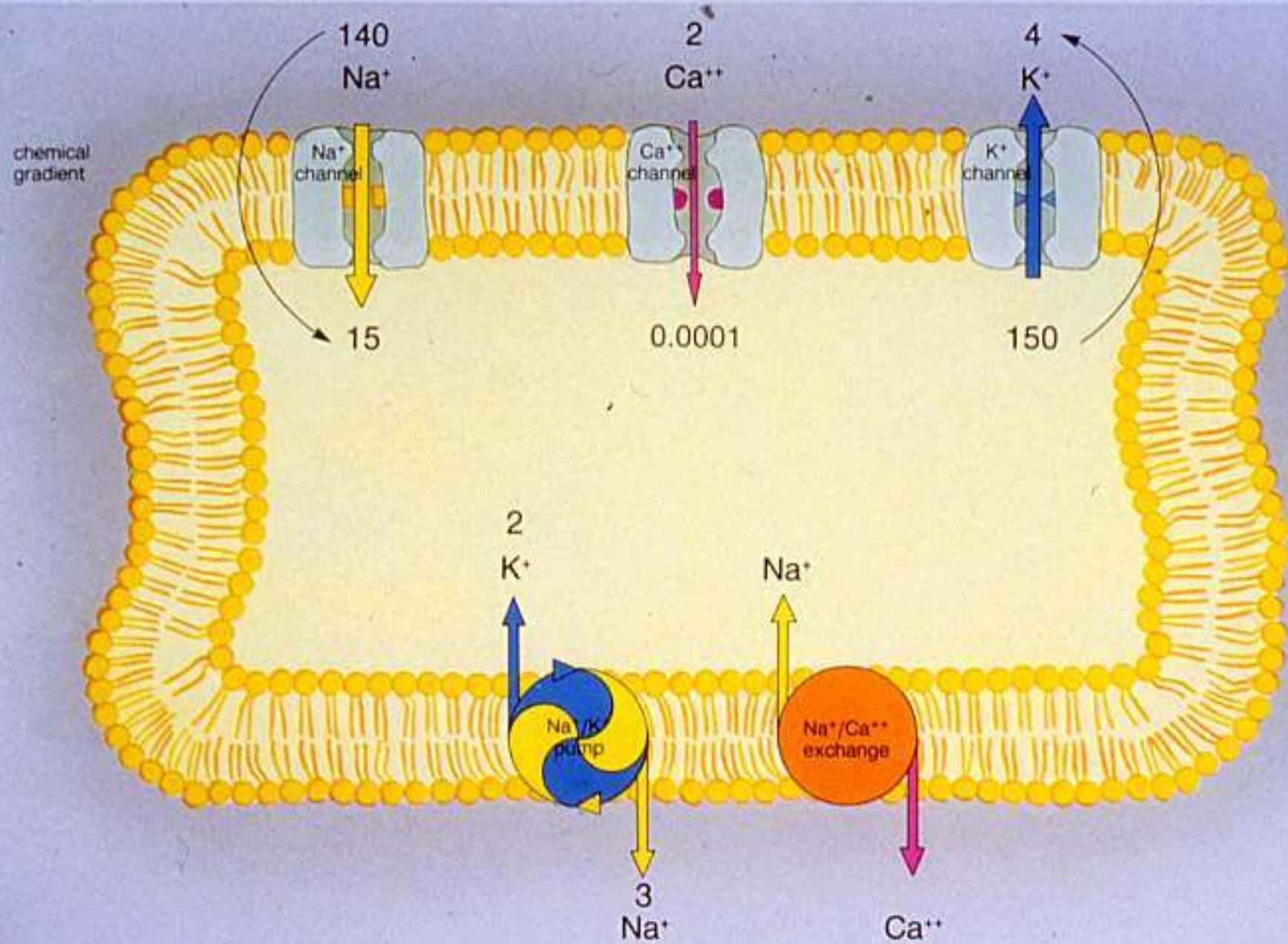
Action potentials
skeletal muscle



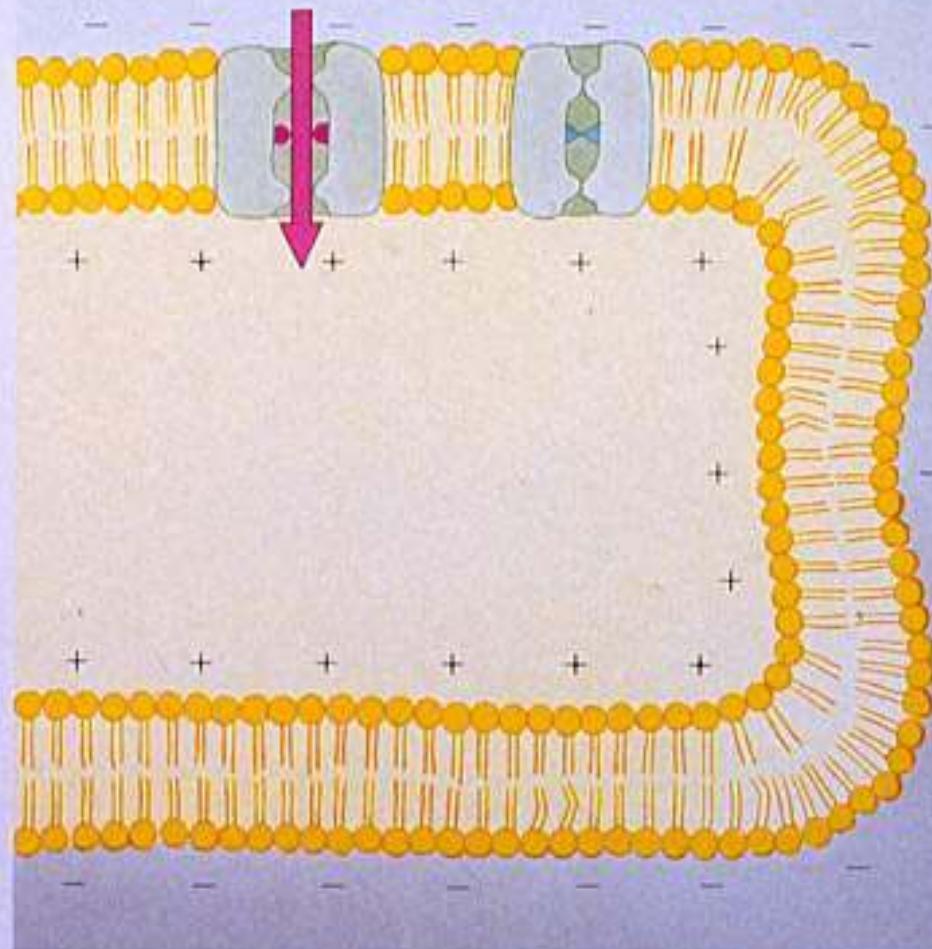
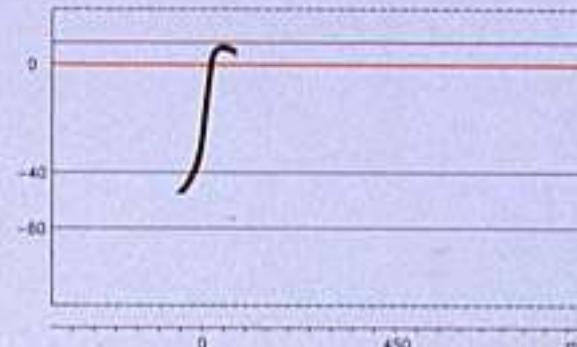
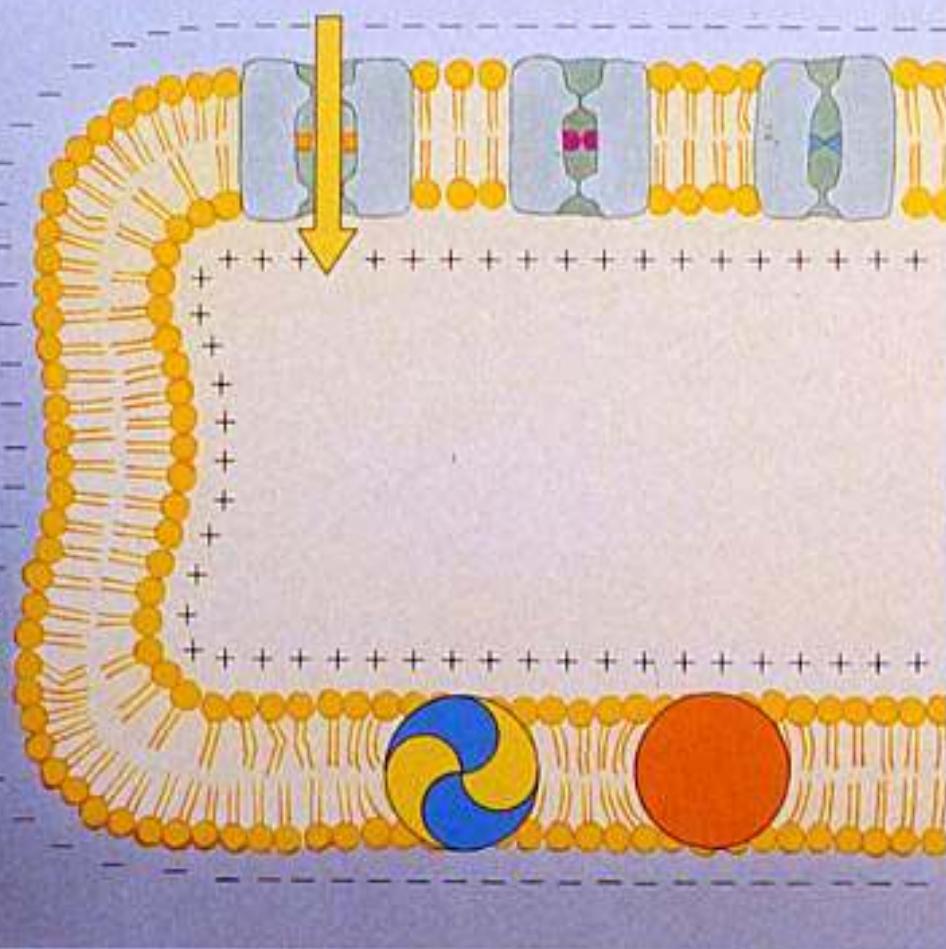
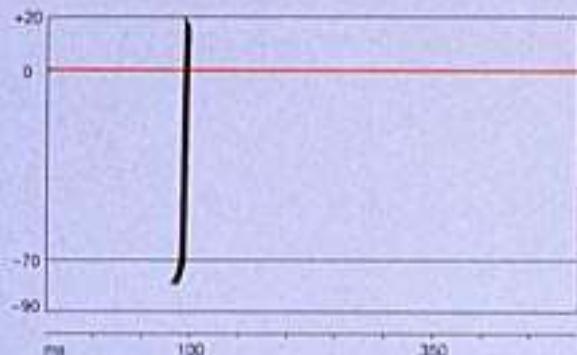
Cardiac muscle



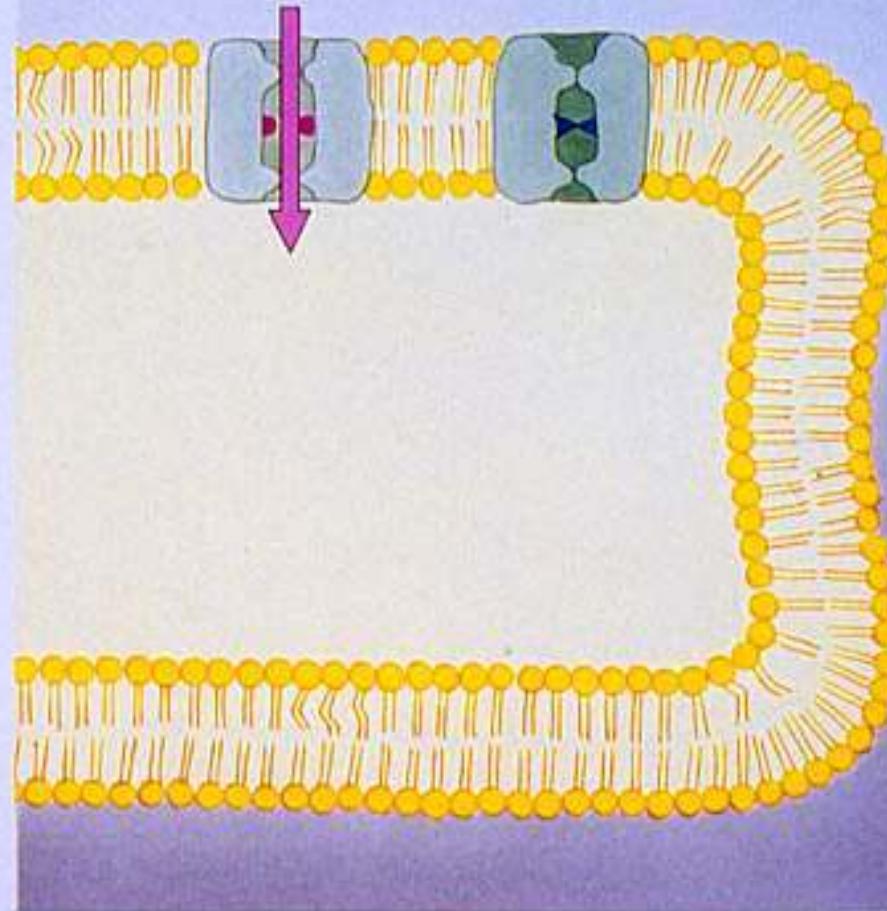
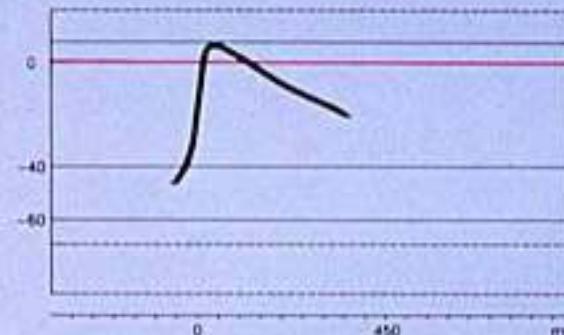
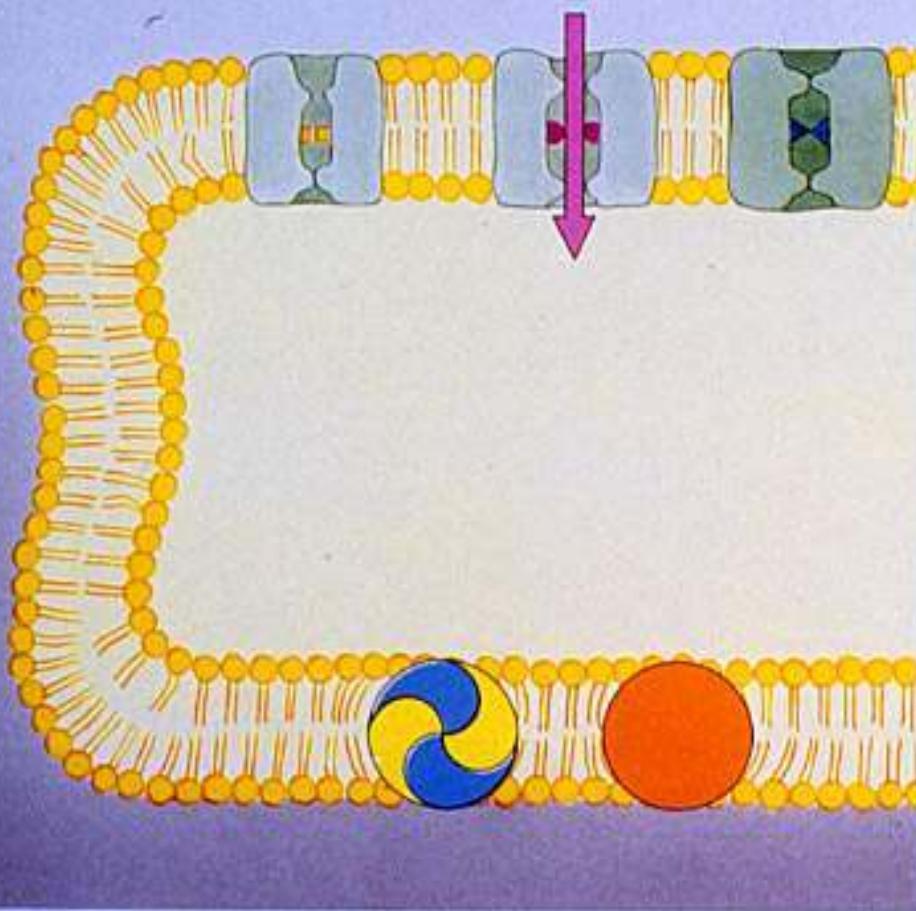
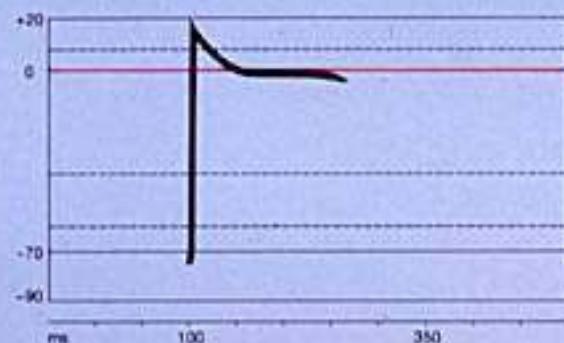
The cardiac cell



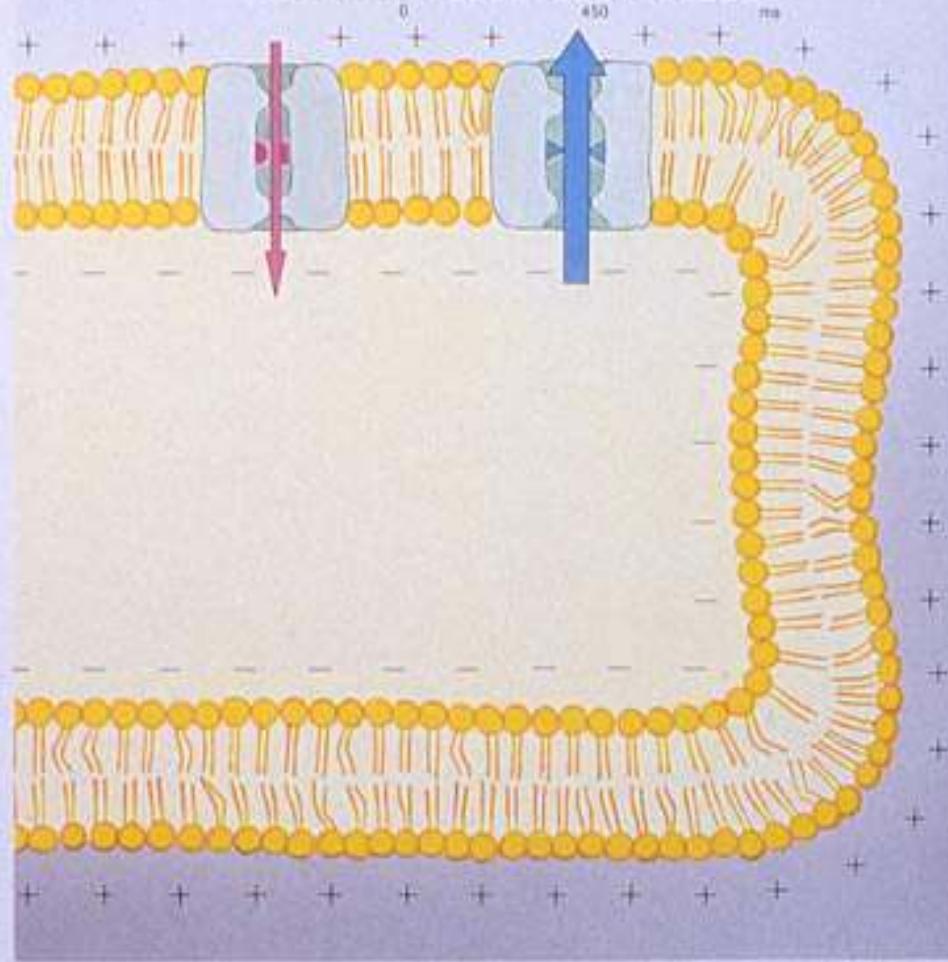
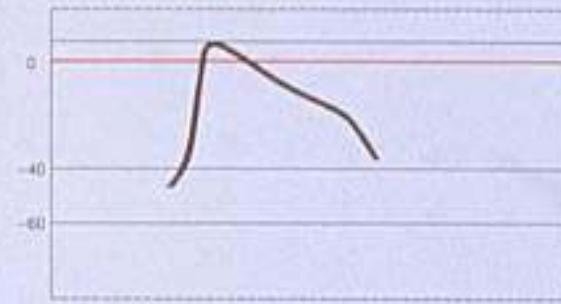
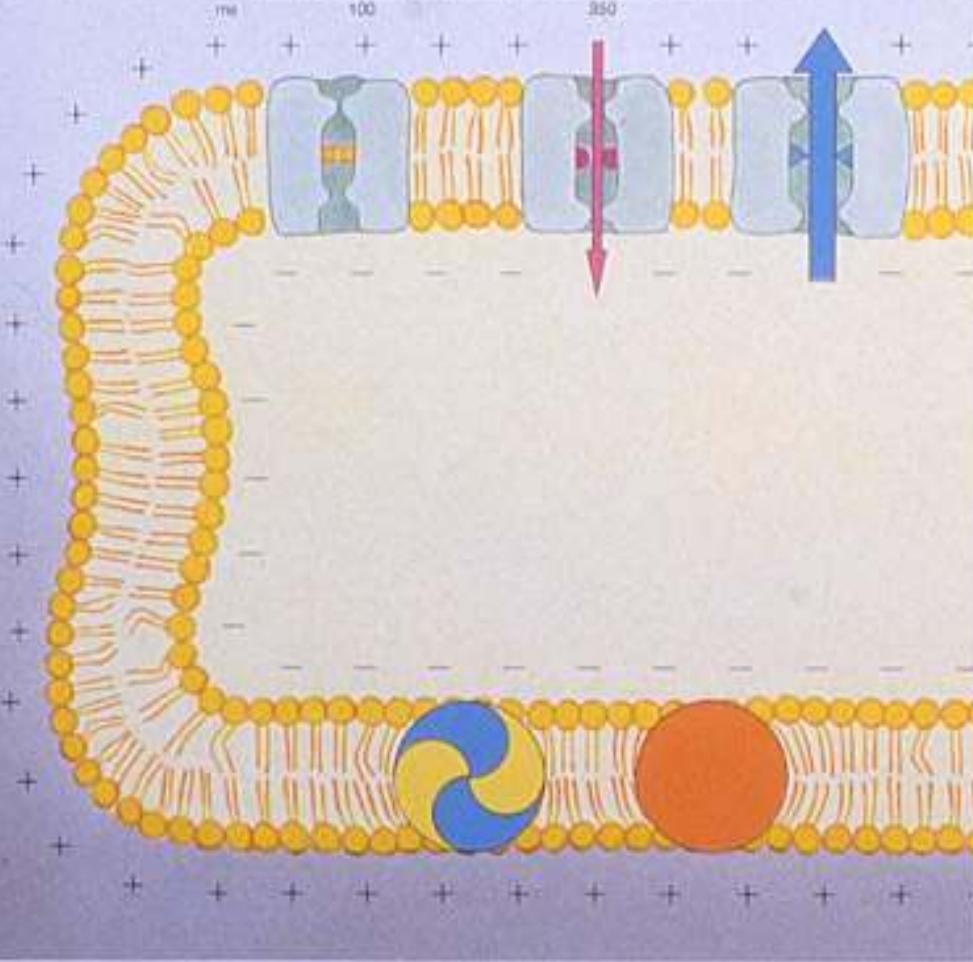
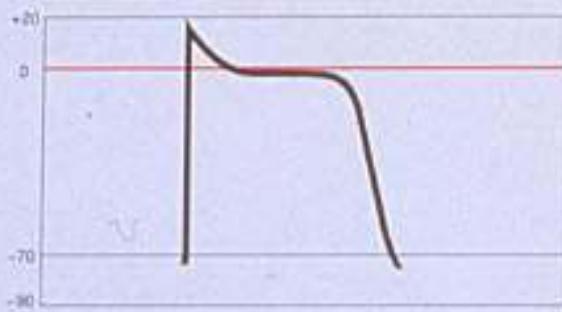
Ionic currents in phase 0



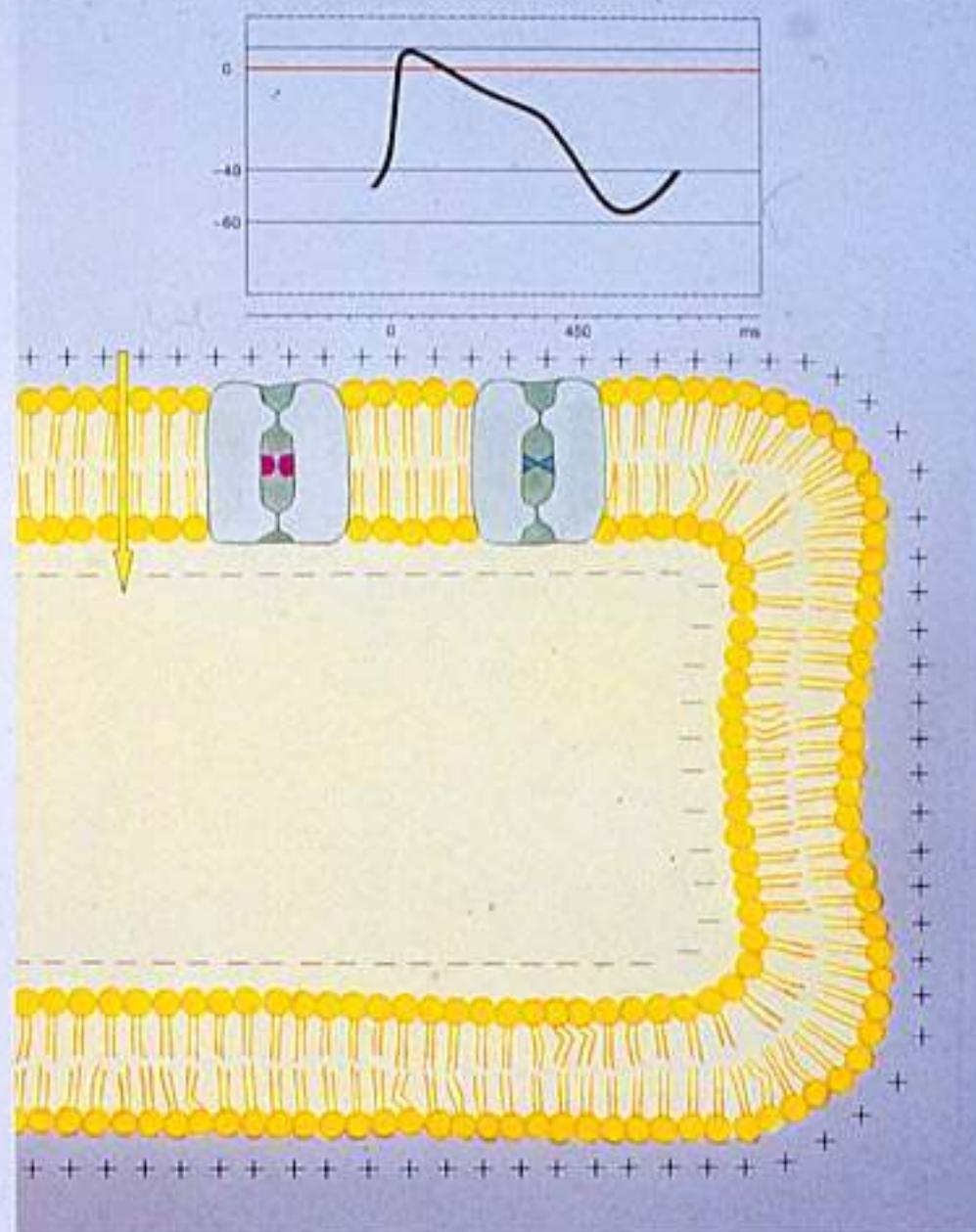
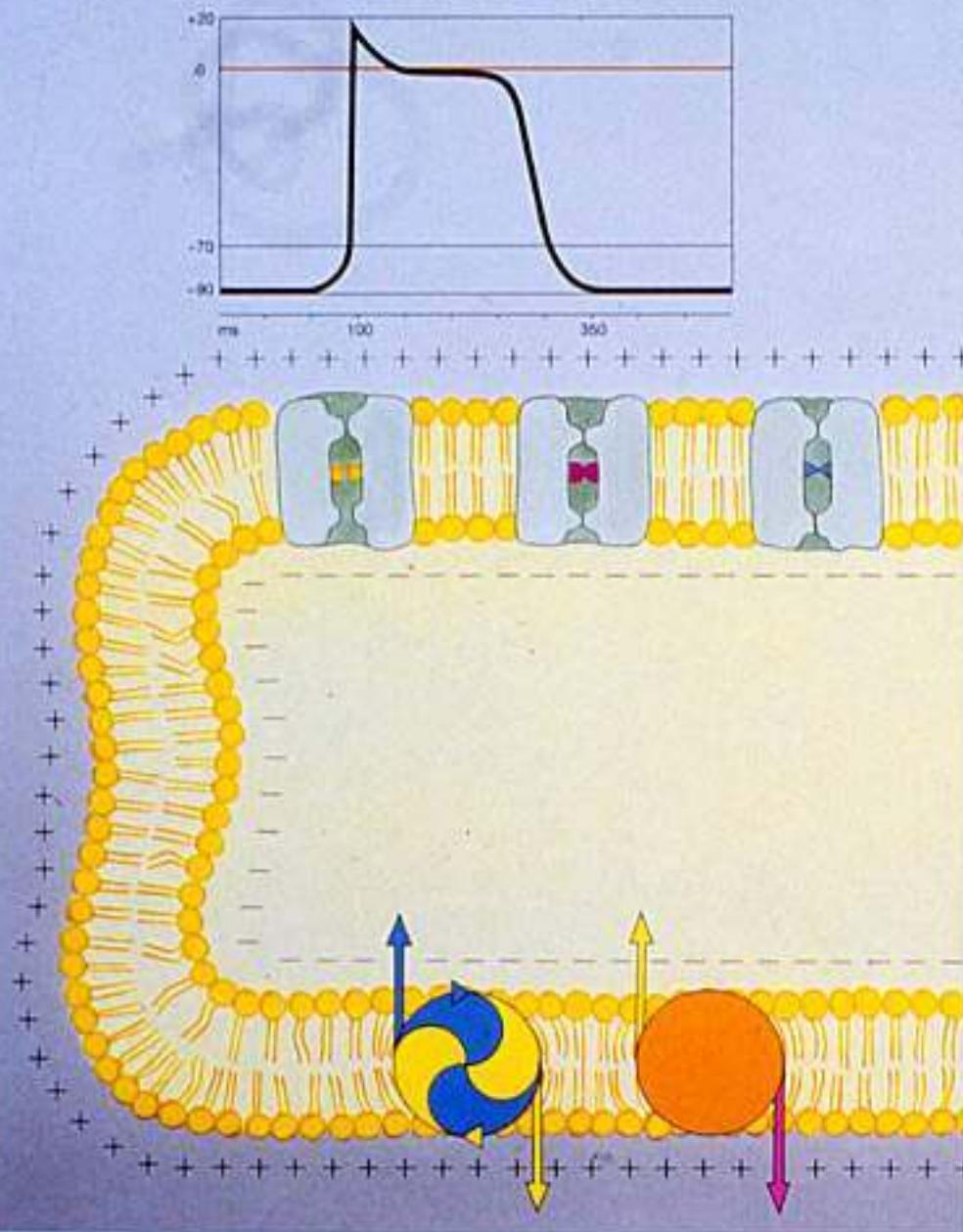
Ionic currents in phase 2



Ionic currents in phase 3



Active transport in phase 4



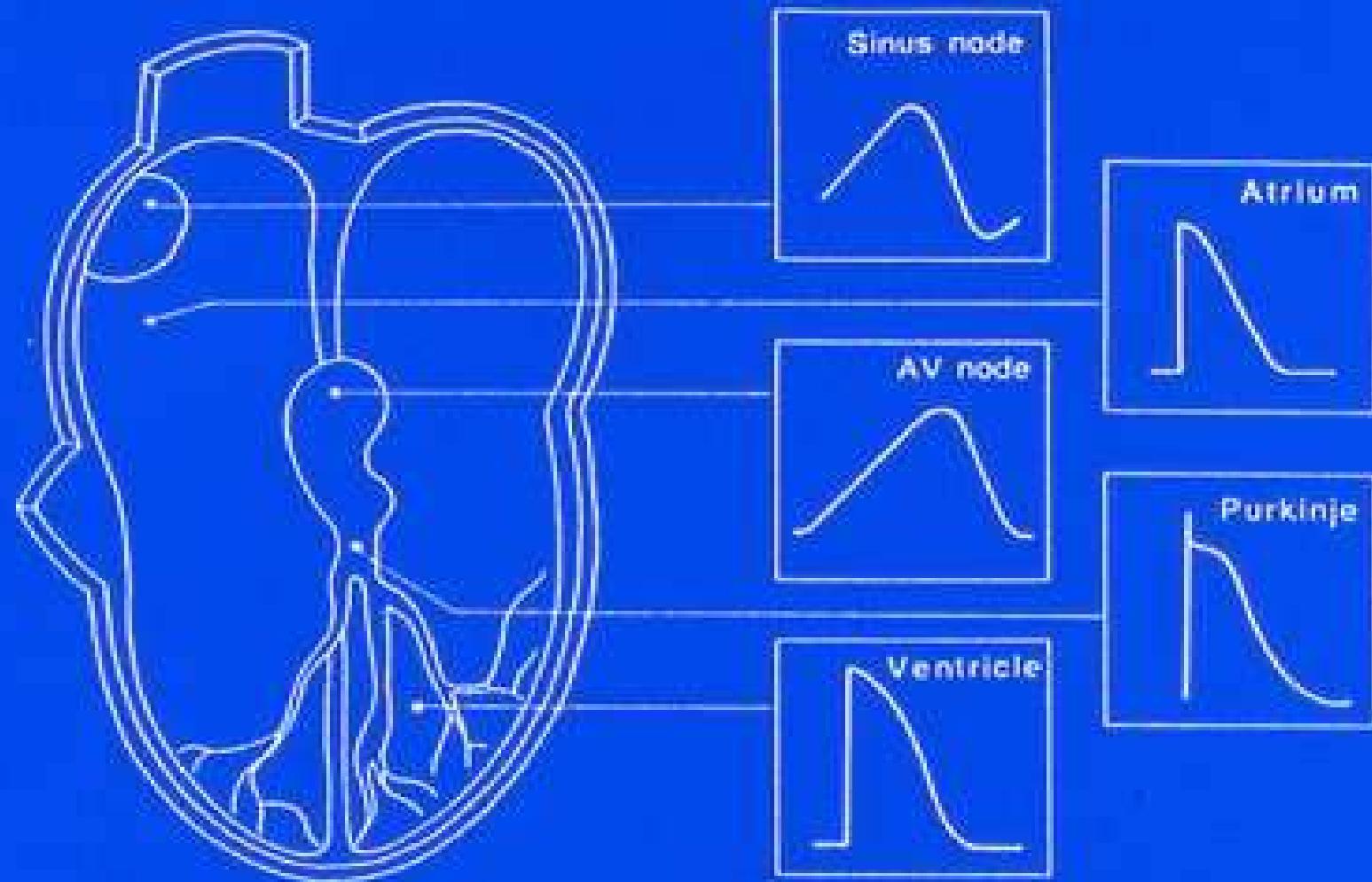
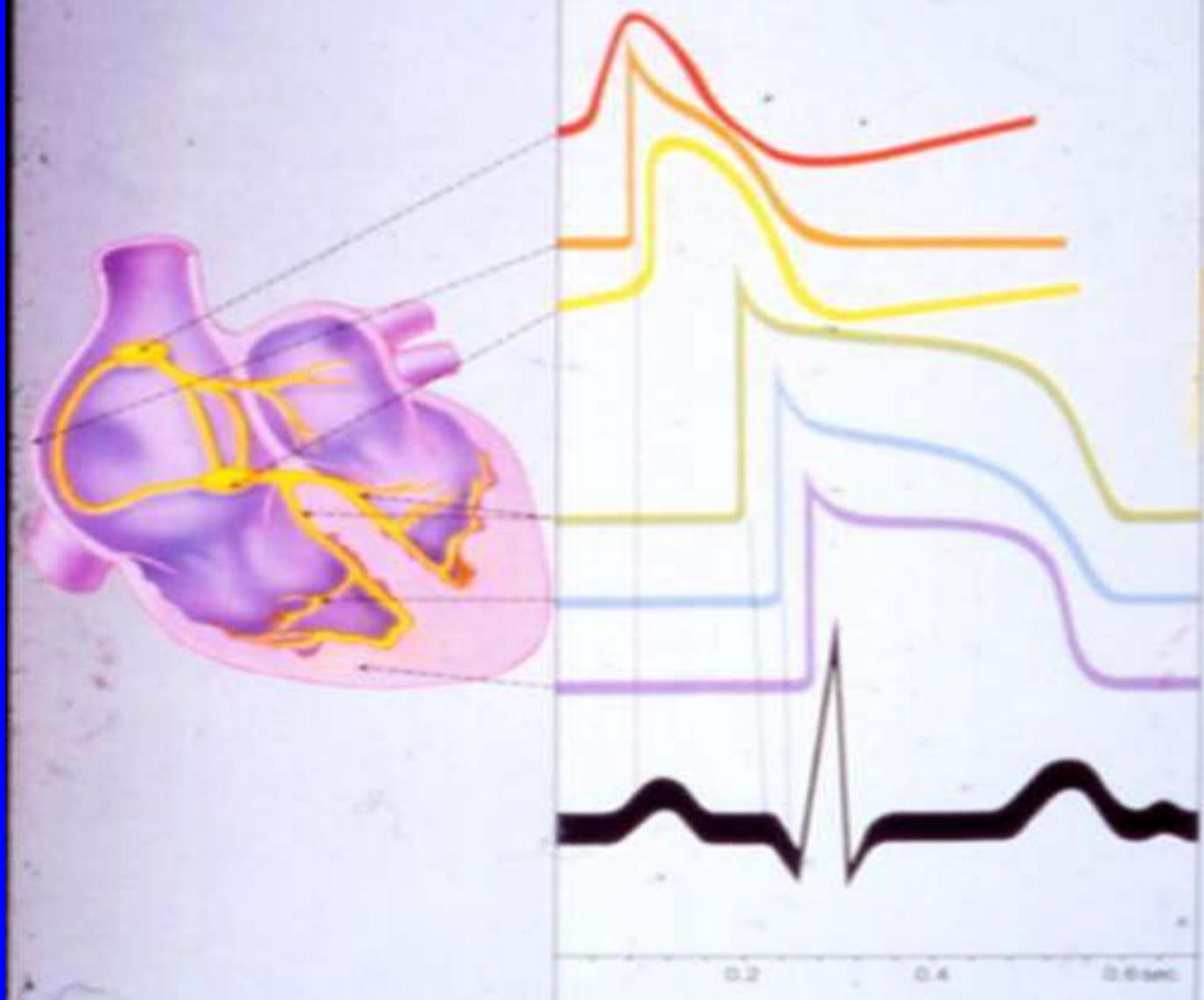


Fig. 3.2 Different morphologies of cardiac cell action potentials.

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

The conduction system of the heart



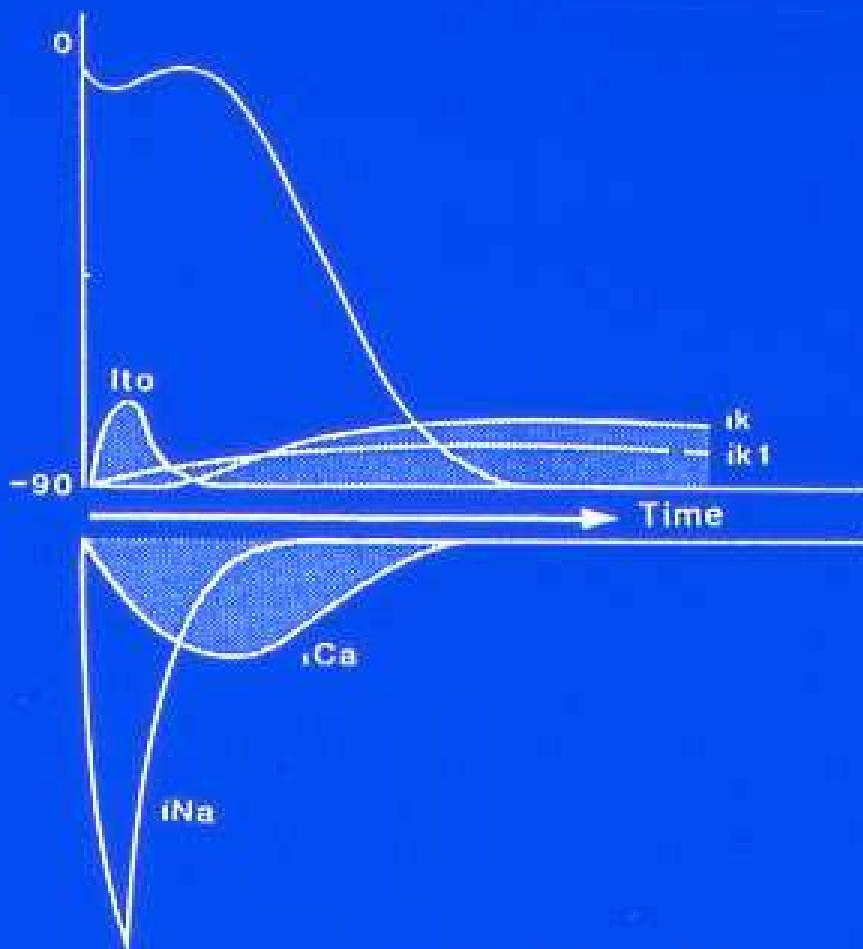
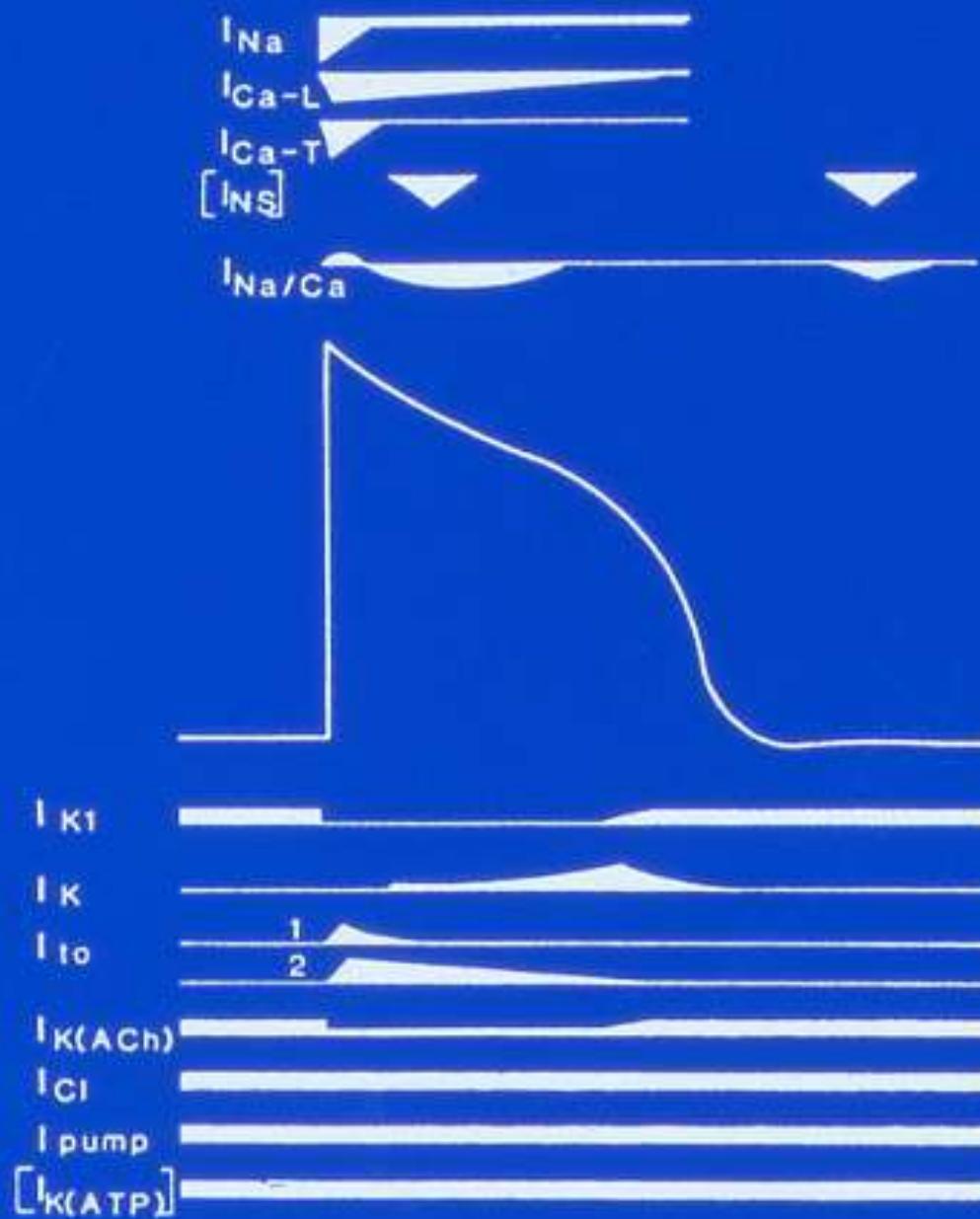


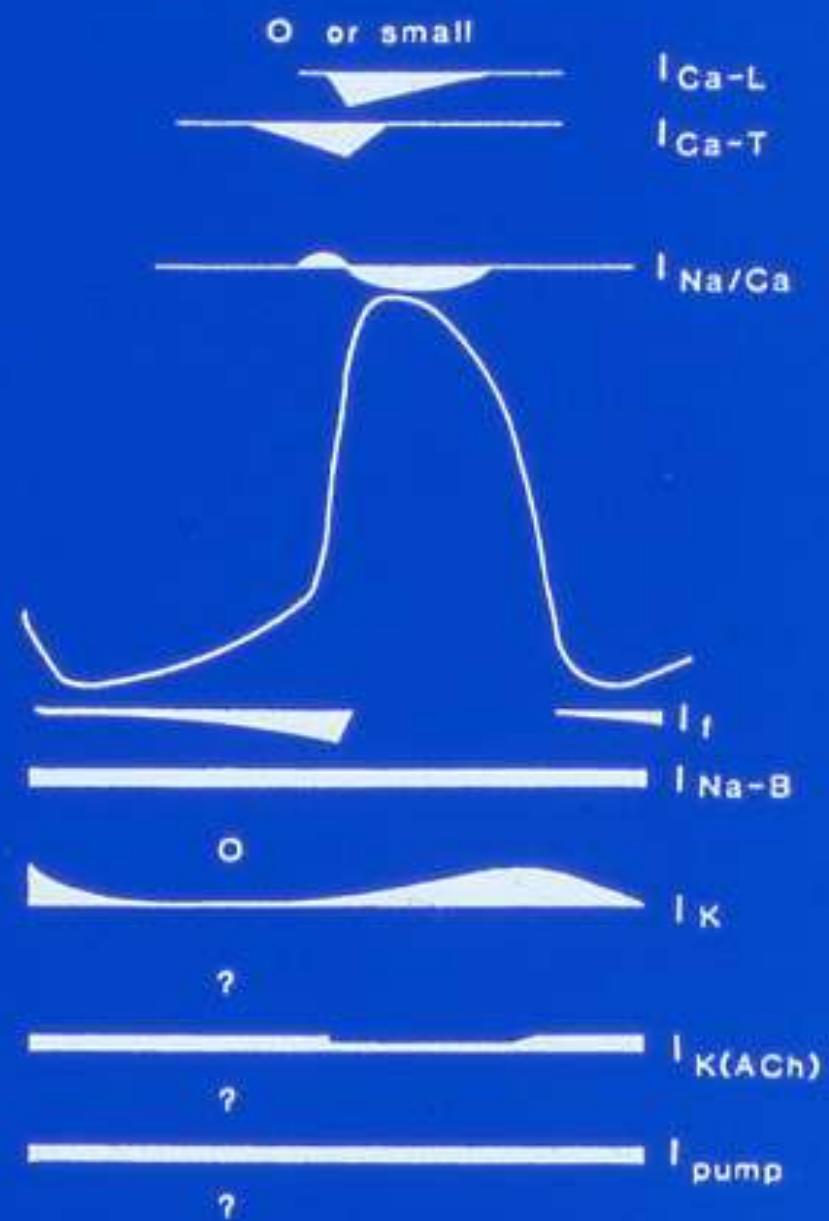
Fig. 3.4 Different ionic currents responsible for the cell electrical activity. Upward (or outward) currents are repolarizing and downward (or inward) currents are depolarizing.

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



Sino-Atrial Node Cells



Different refractory periods in myocardial cells

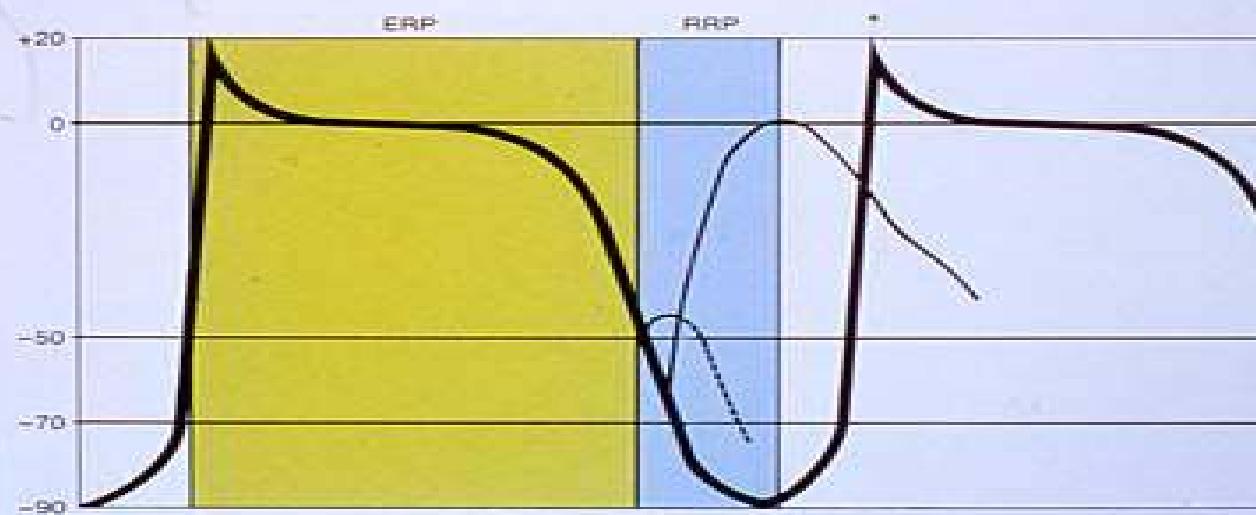
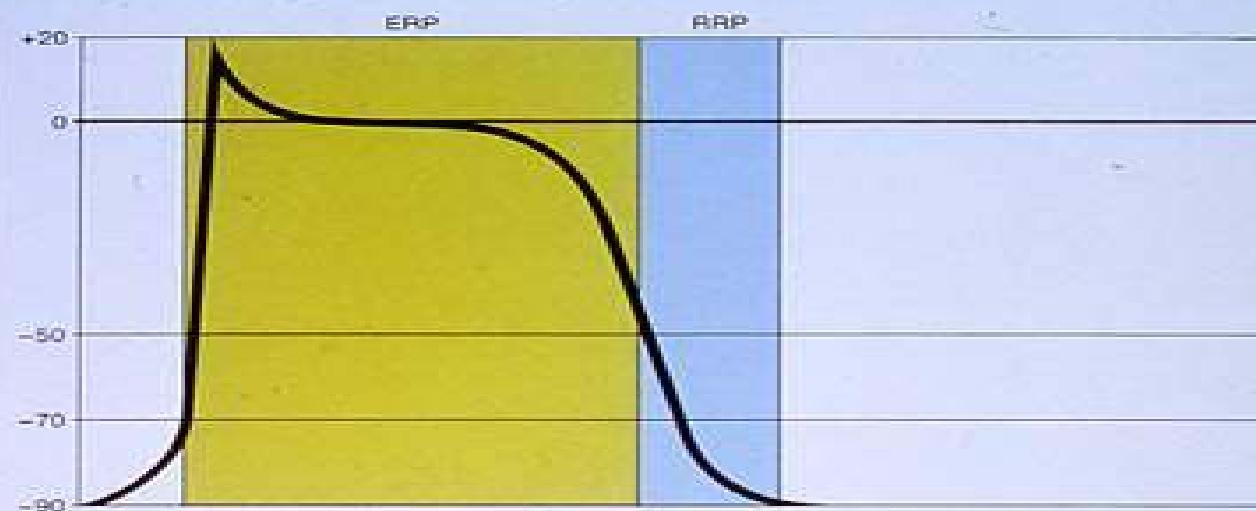


TABLE II. Resting Potentials (or Maximal Diastolic Potentials) and Maximal Upstroke Velocities (dV/dt_{max}) of Different Cardiac Tissues

| 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) |
| His bundle (and branches) | 100-150 | Rabbit Different Species | Pruitt and Essex (1960) Sano (1976) |
| Purkinje fibers | 200 | Dog | Draper & Weidmann (1951) |
| | 80 | Rhesus monkey | Antoni and Zerweck (1967) |
| Ventricle (papil- lary muscle) | 60 | Rhesus monkey | Antoni and Zerweck (1967) |

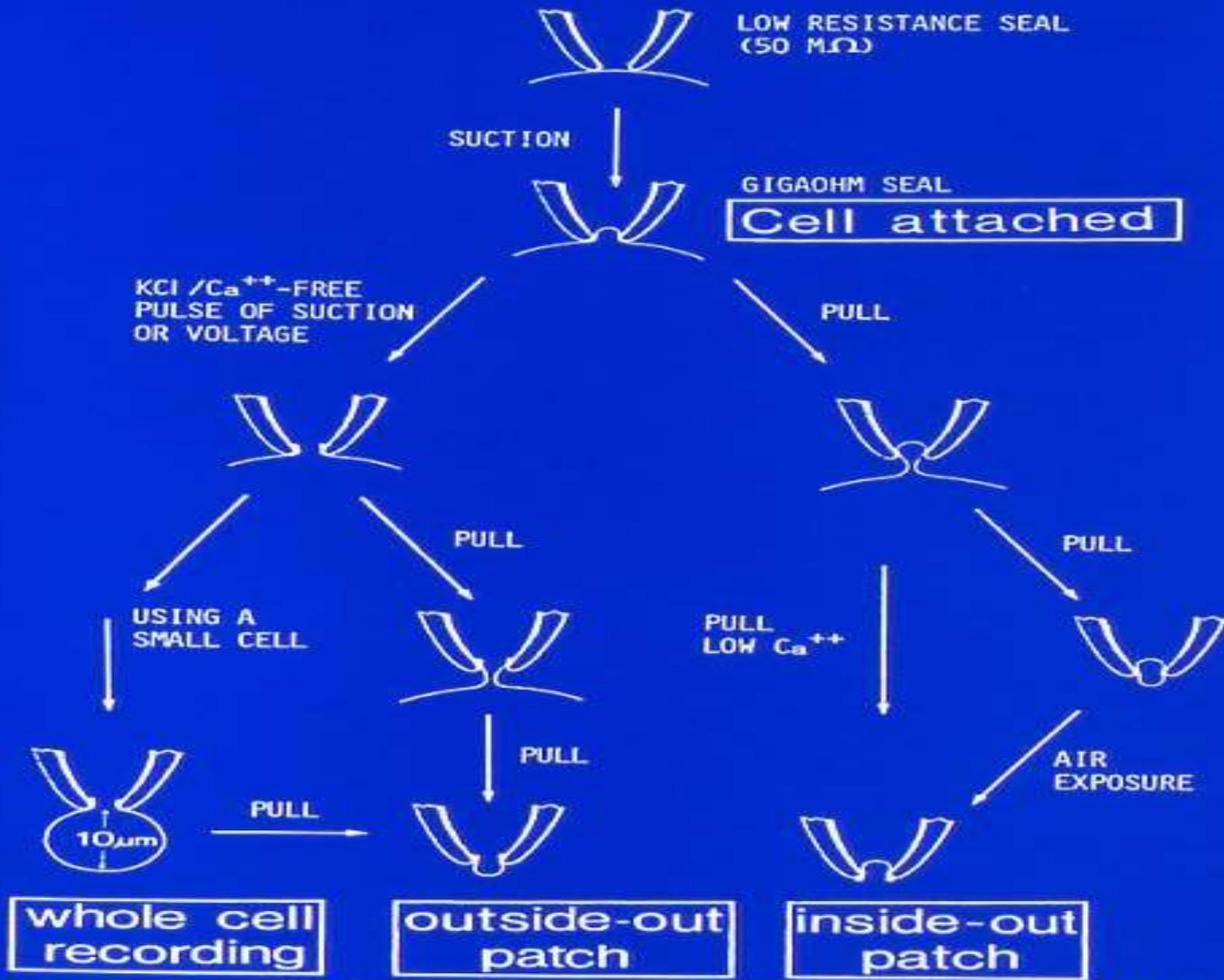
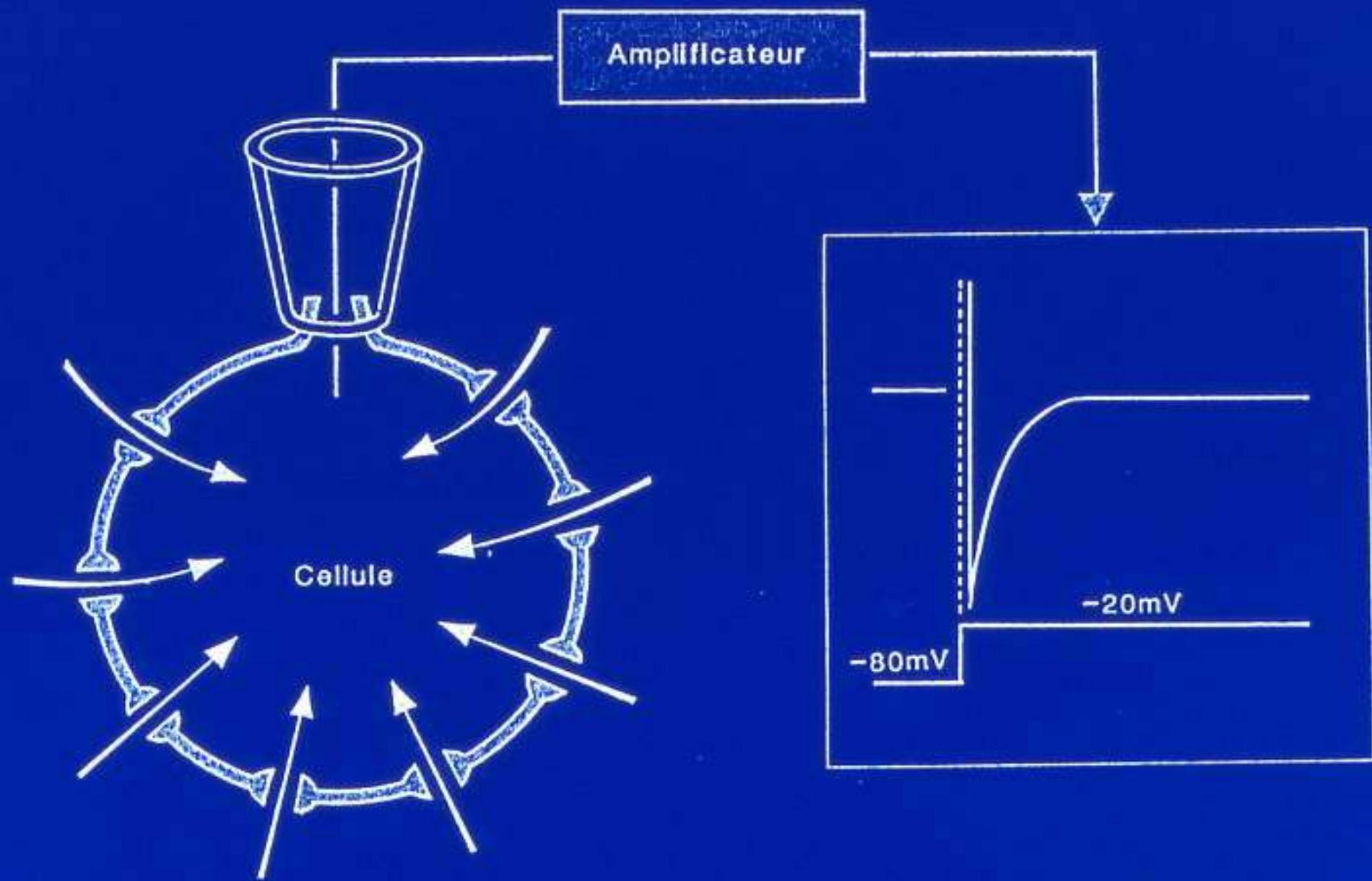
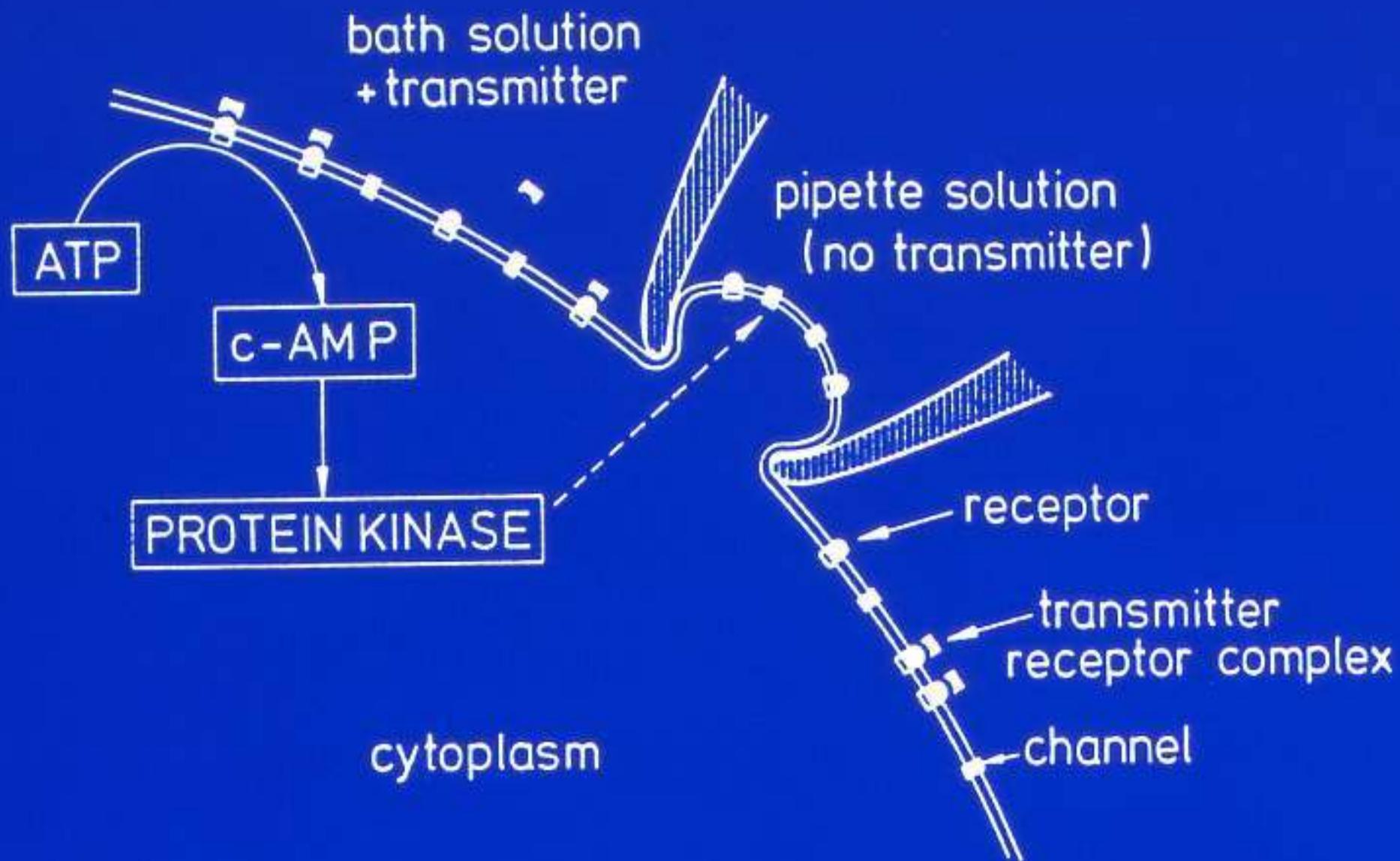
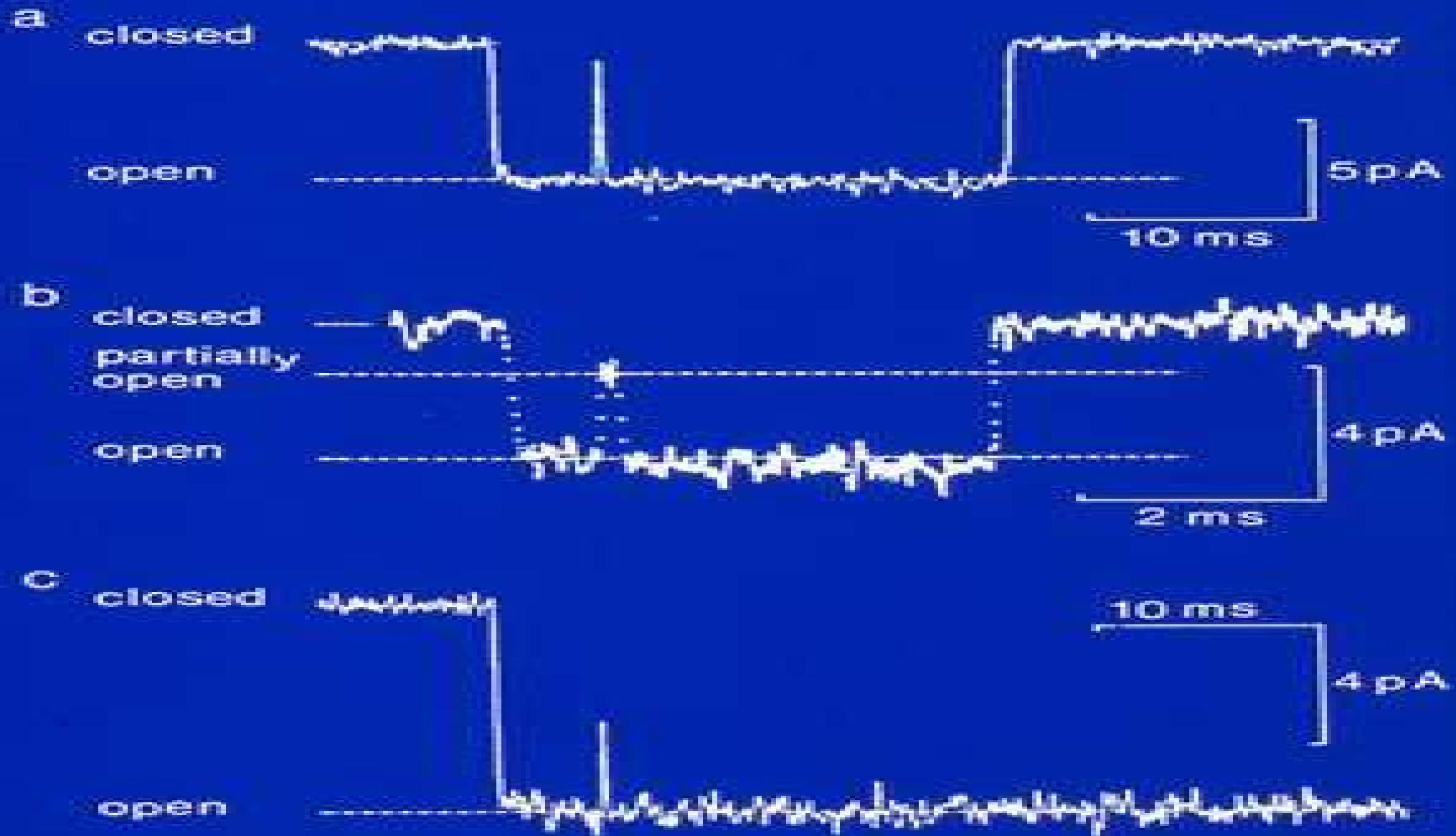
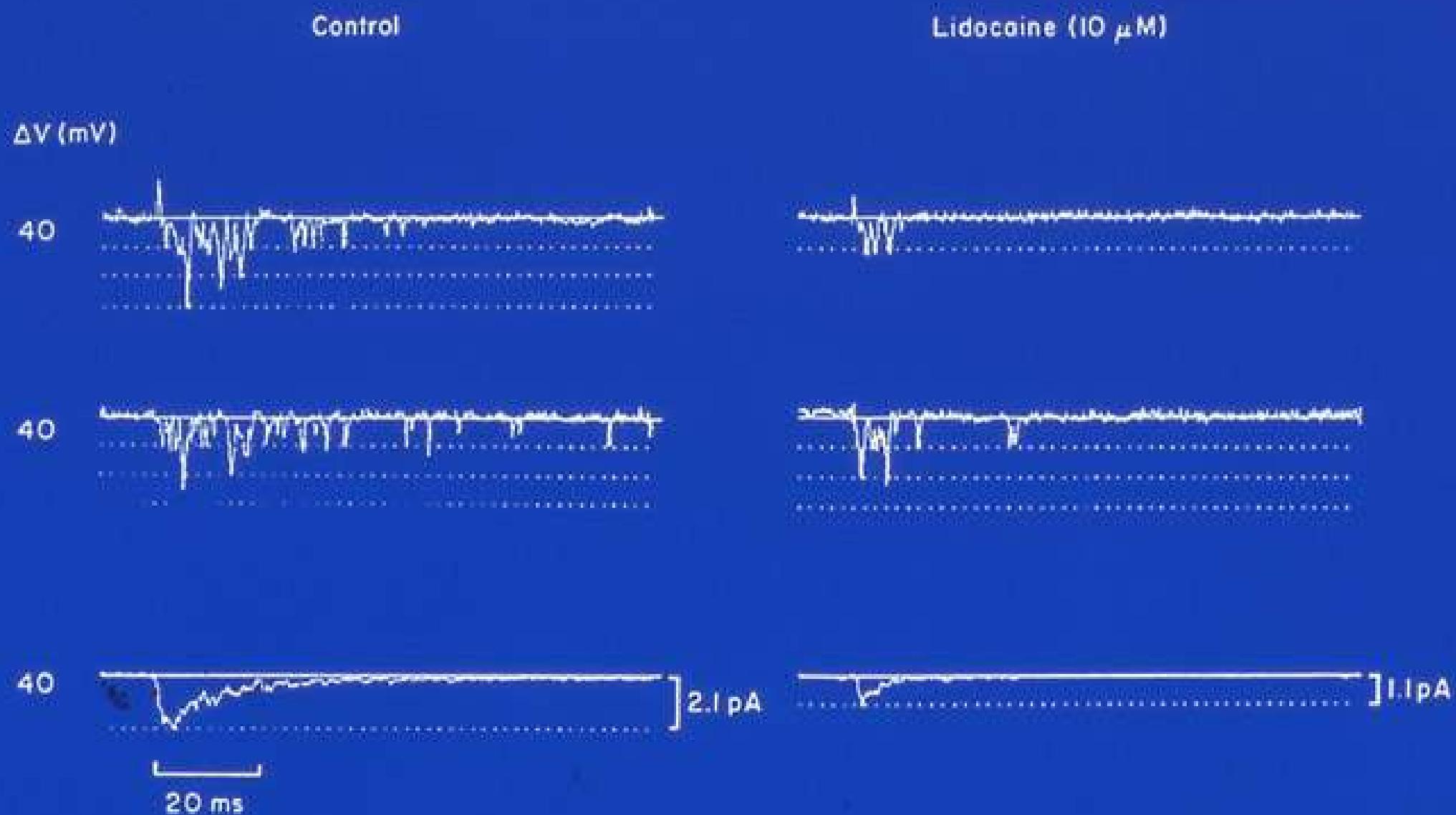


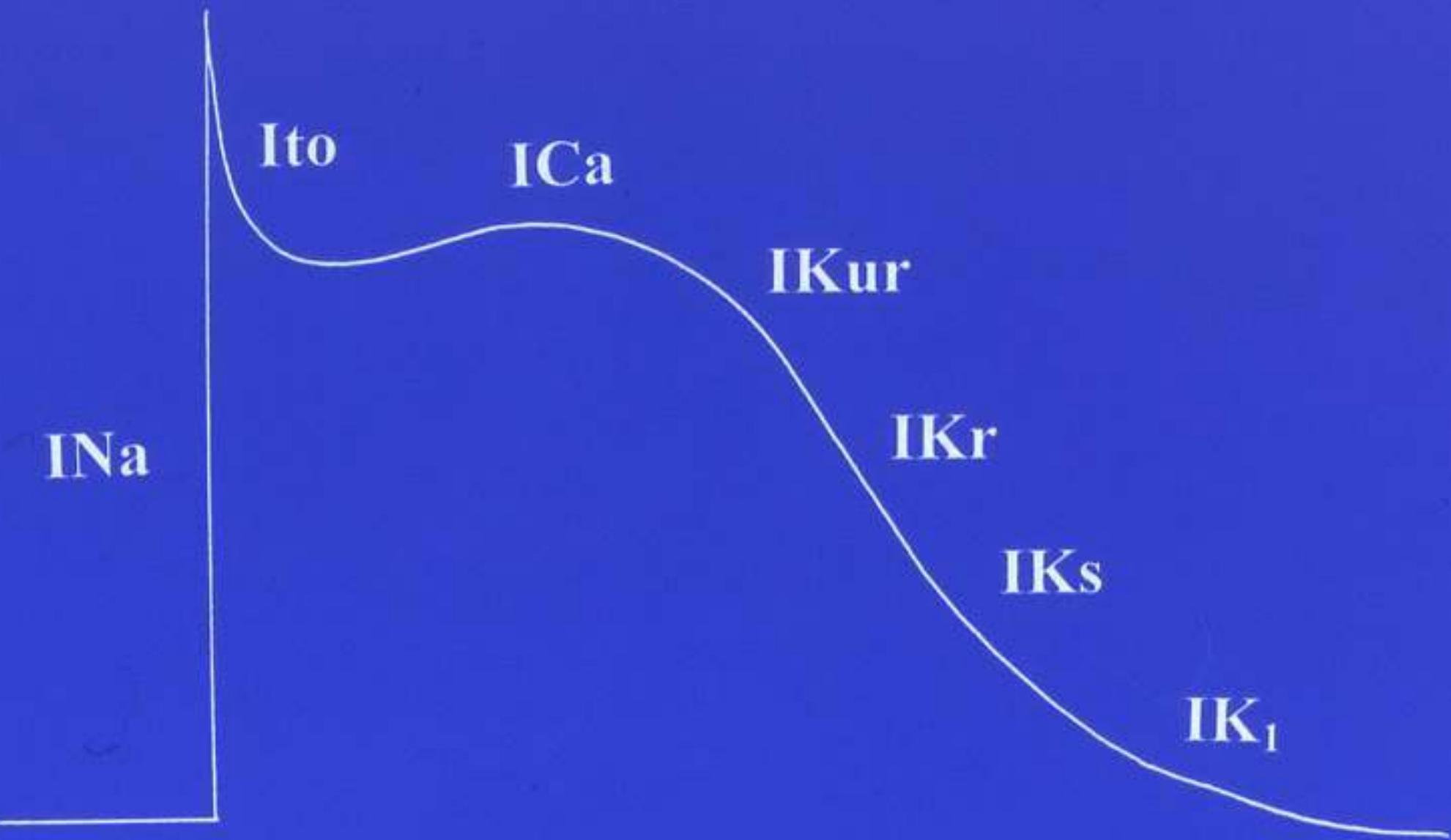
FIGURE 1. Schematic illustration of the different configurations of the patch clamp and of the manipulations that lead to them. From Hamill et al (32), by permission of Springer-Verlag, Heidelberg.











+ INa/Ca , $IKAch$, If , \pm $IKATP$

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

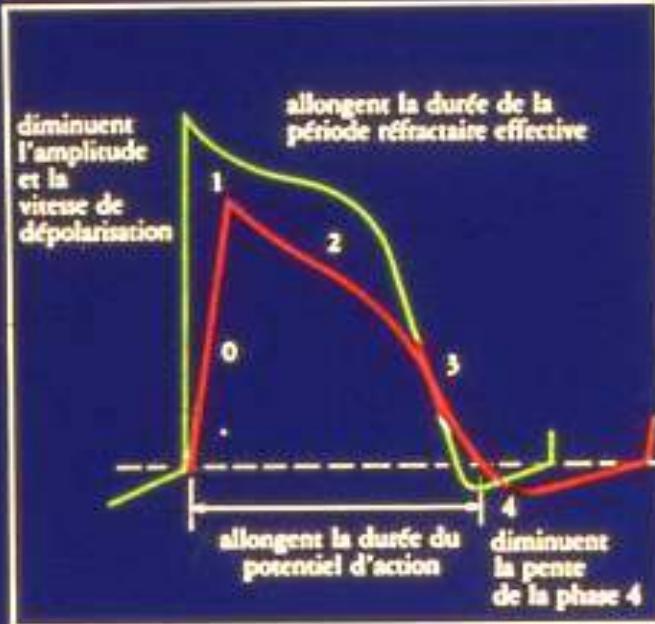
CALCIUM CURRENTS

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

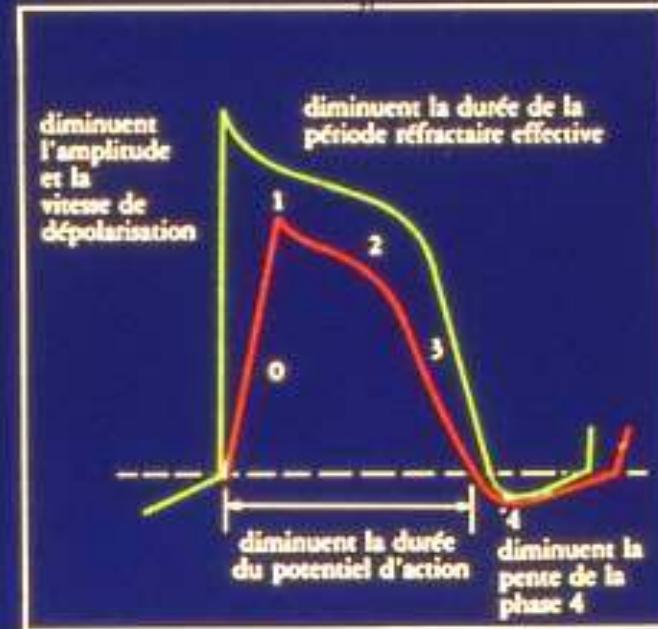
- **T type :**
 - . present in SA node and atrium
 - . role in **automaticity** of SA node
 - . target of Mibebradil

MOLECULAR BIOLOGY OF POTASSIUM CHANNELS

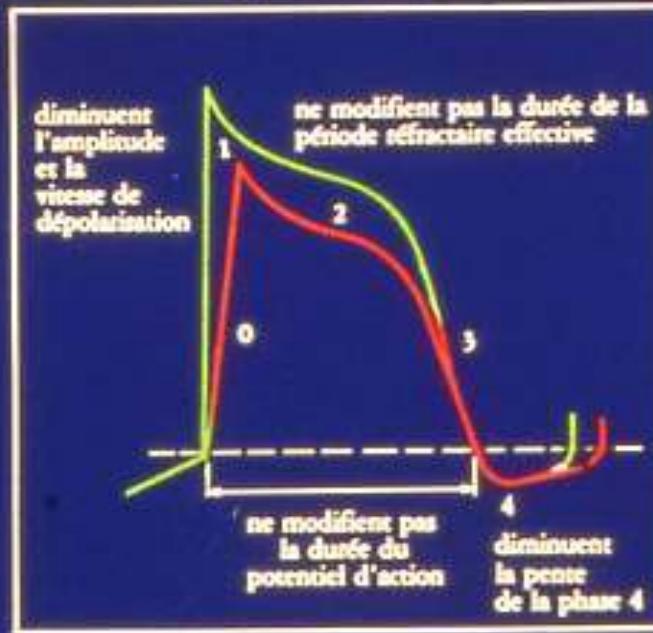
- Molecular structures largely Identified for most potassium currents : Ikr, Iks, Ikur, IkAch, IkATP, Ik1
- Potential insights into disease and arrhythmia mechanisms
- Explanations of class III proarrhythmia



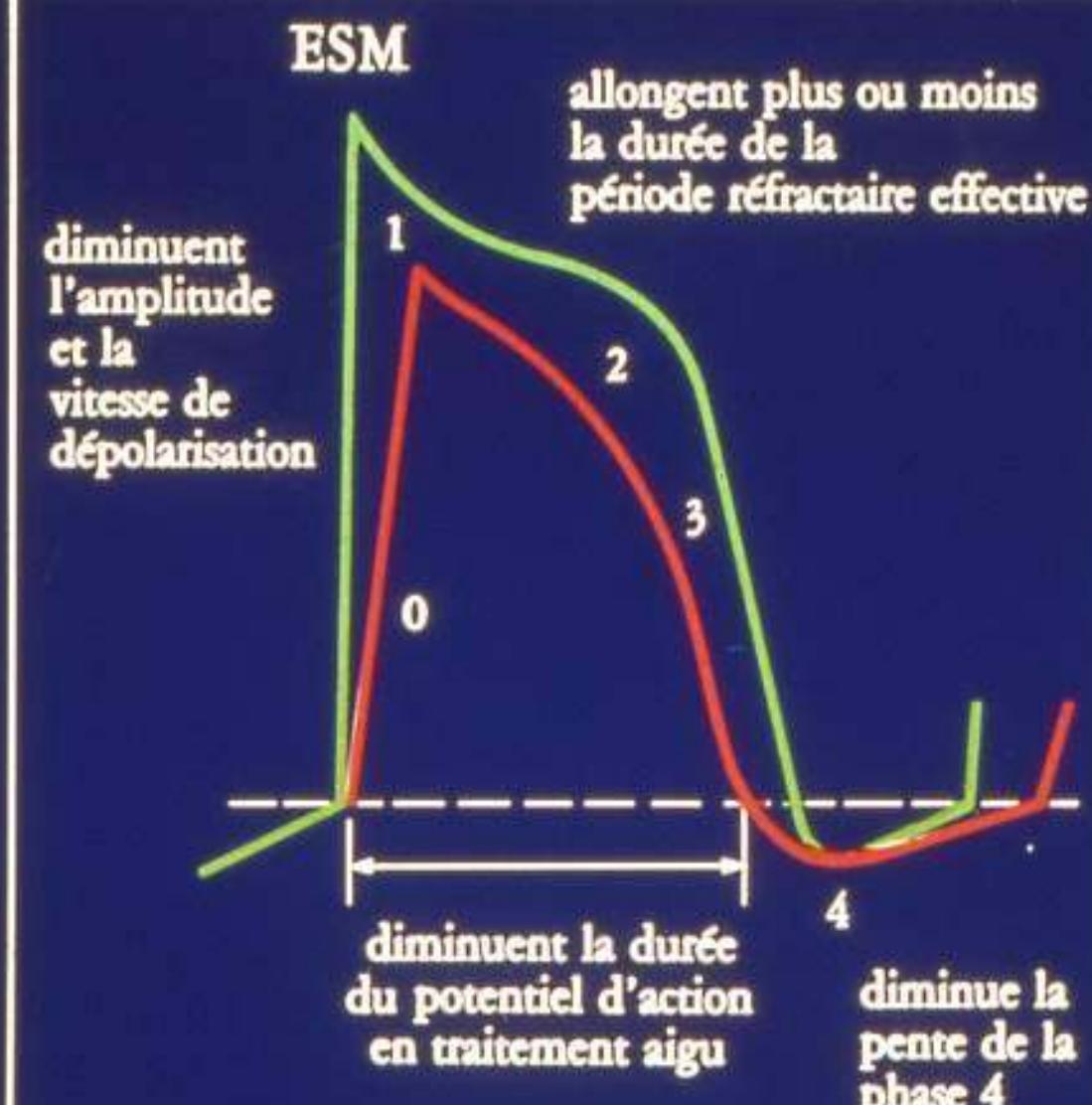
Classe Ia



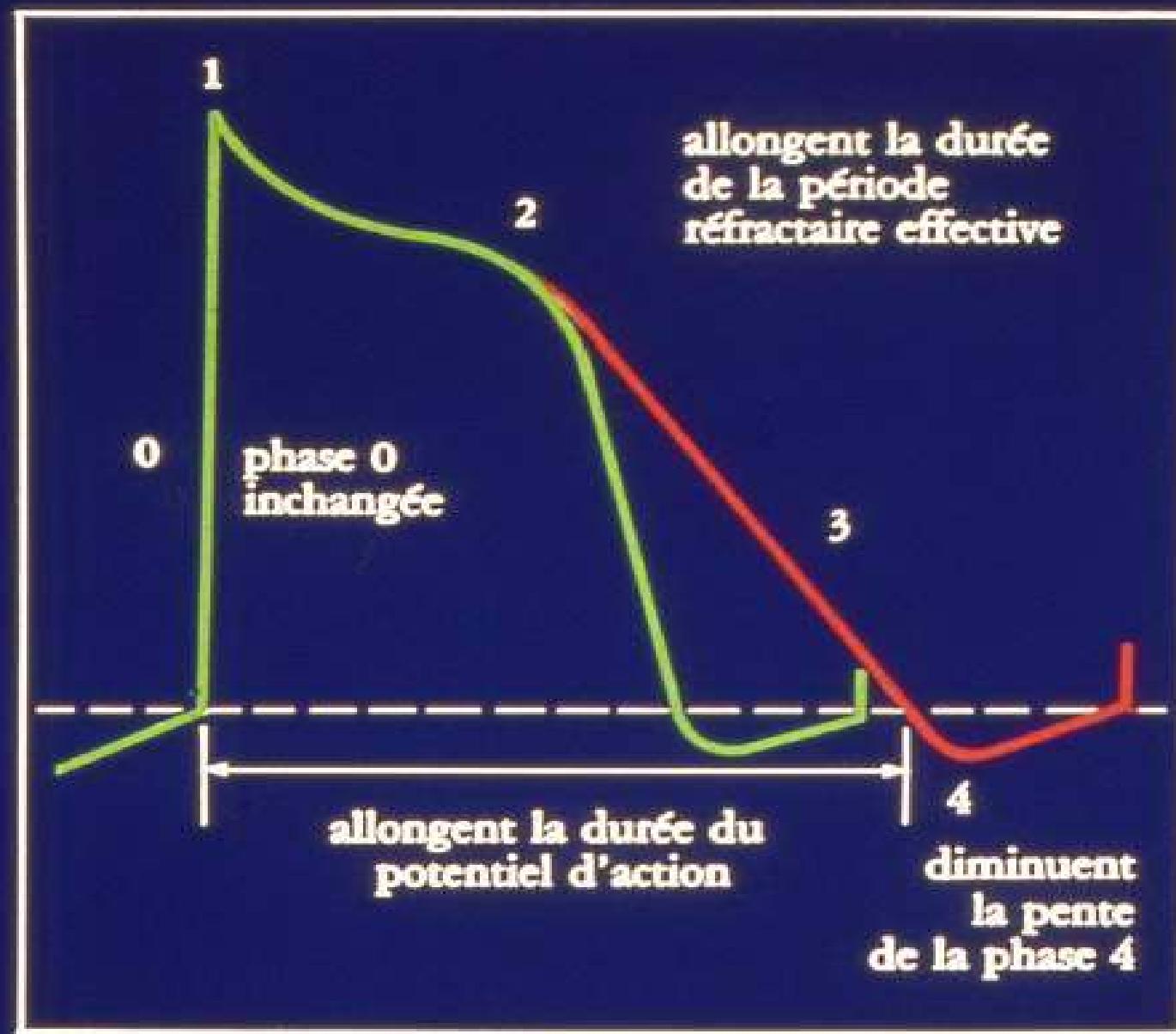
Classe Ib



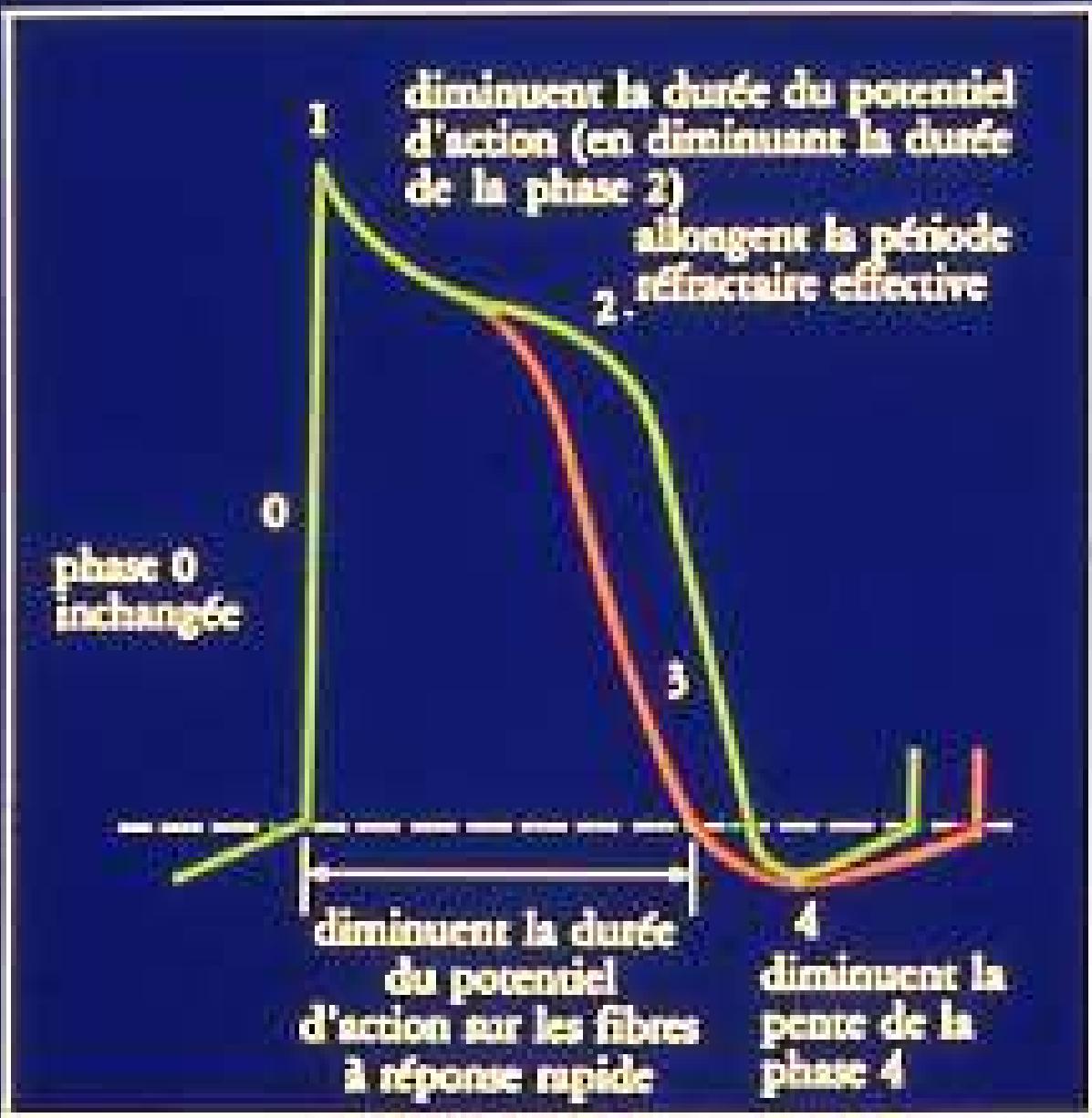
Classe Ic



Classe II



Classe III



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 | | | | RECEPTORS | | | | PUMPS |
|--------------|------------|------------|----|---|----------------|---|---|----------------|-------|
| | No Fast | Na Slow | Ca | K | I _r | α | β | M ₂ | |
| Lidocaine | ○ | | | | | | | | |
| Mexiletine | ○ | | | | | | | | |
| Tocainide | ○ | | | | | | | | |
| Moricizine | ● | | | | | | | | |
| Procainamide | ○ | | | | ○ | | | | |
| Disopyramide | ○ | | | | ○ | | | | |
| Quinidine | ○ | | | | ○ | | | ○ | |
| Propafenone | ○ | | | | ○ | | | | |
| Flecainide | | ○ | | | ○ | | | | |
| Encainide | | ○ | | | ○ | | | | |
| Bepридil | ○ | | | | ○ | | | | |
| Verapamil | ○ | | | | ○ | | | | |
| Diltiazem | | ○ | | | ○ | | | | |
| Bretylium | | | | | ○ | | | | |
| Sotalol | | | | | ○ | | | | |
| Amiodarone | ○ | | | | ○ | | | | |
| Alinidine | | | | | ○ | | | | |
| Nadolol | | | | | | ○ | | | |
| Propranolol | ○ | | | | | ○ | | | |
| Atropine | | | | | | | ○ | | |
| Adenosine | | | | | | | | ○ | |
| Digoxin | | | | | | | | | ○ |

Relative blocking potency

○ = Low ○ = Moderate ● = High

○ = Agonist

○ = Agonist/Antag.

● = Activated state blocker

○ = Inactivated state blocker

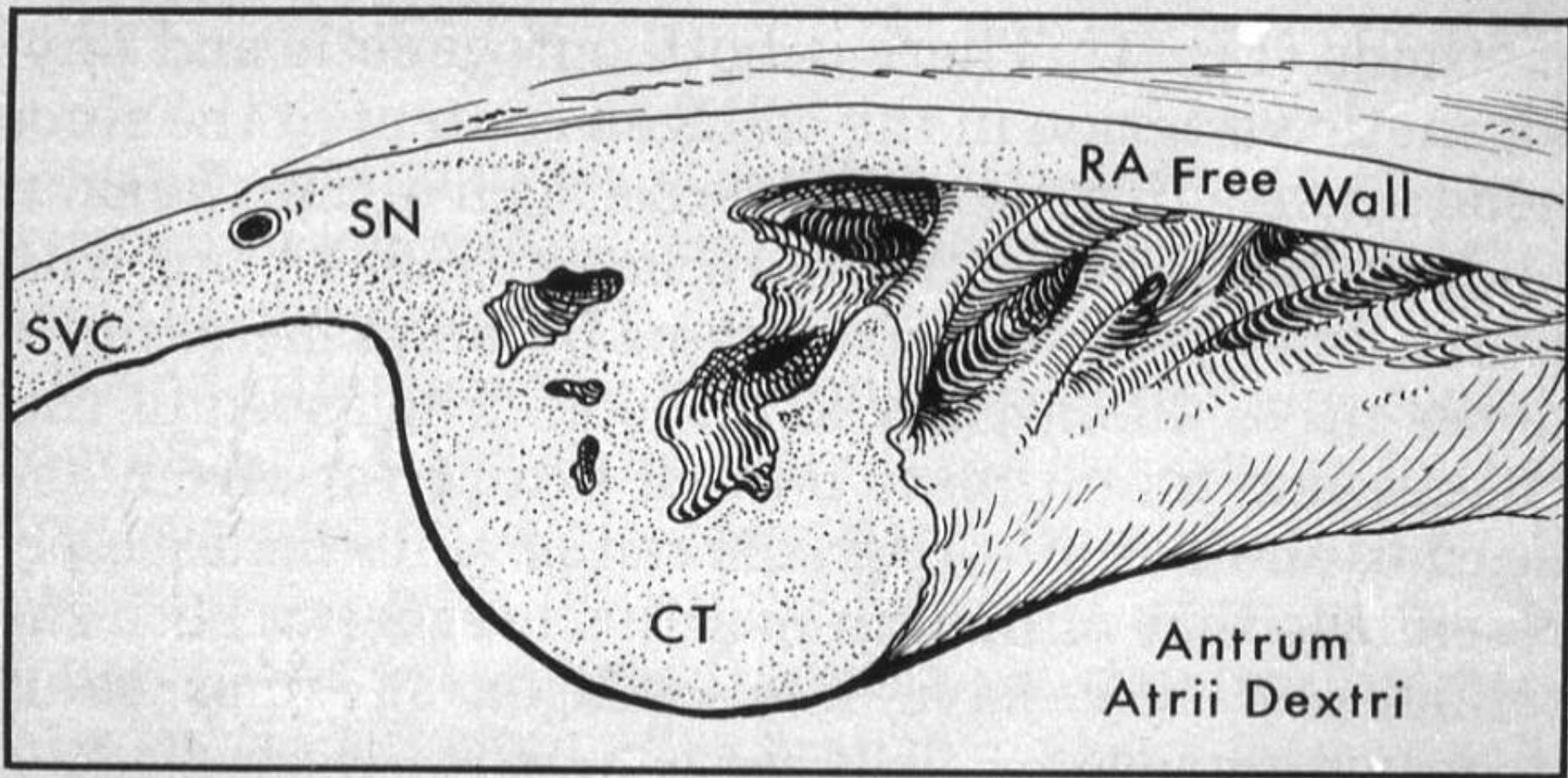
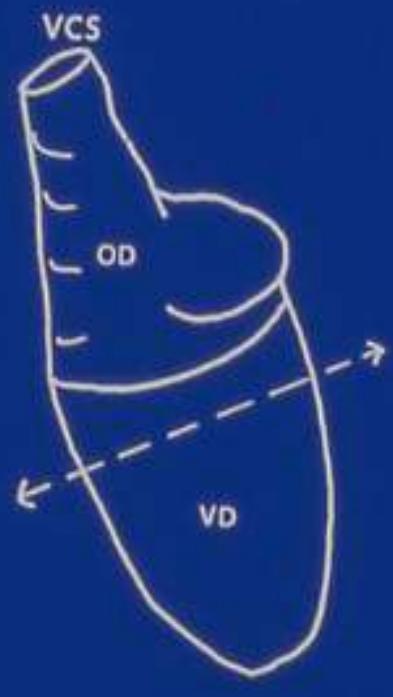


FIGURE 4. Drawing showing the normal endocardial recesses of the antrum atrii dextri between the free wall of the right atrium (RA) and body of crista terminalis (CT), which has been cut across. SN = sinus node; SVC = superior vena cava.



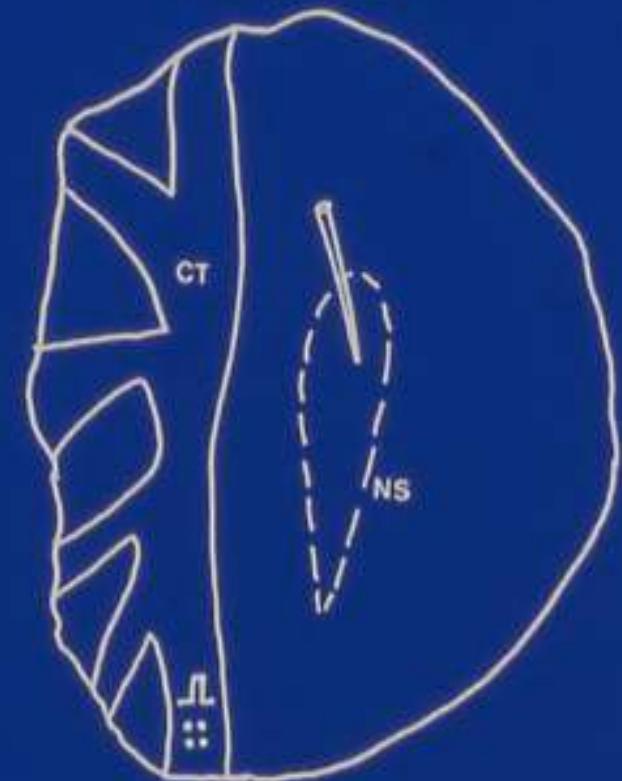
1

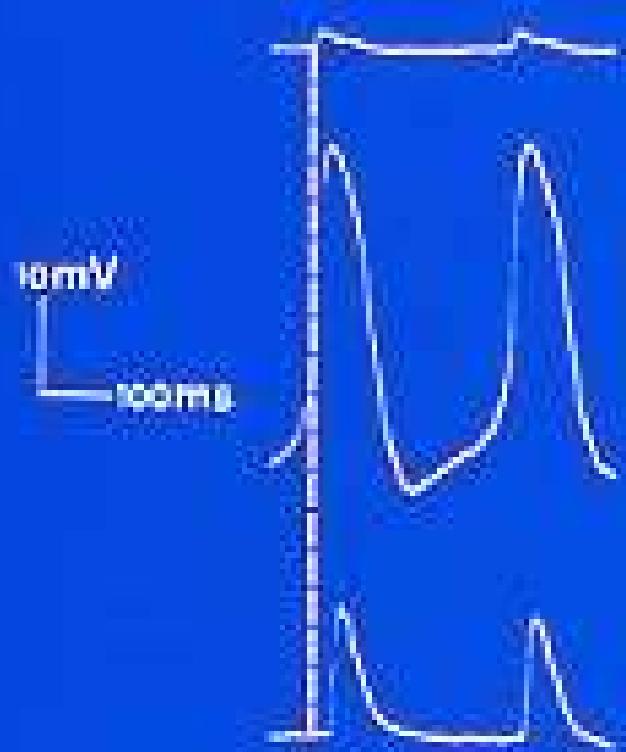


2



3



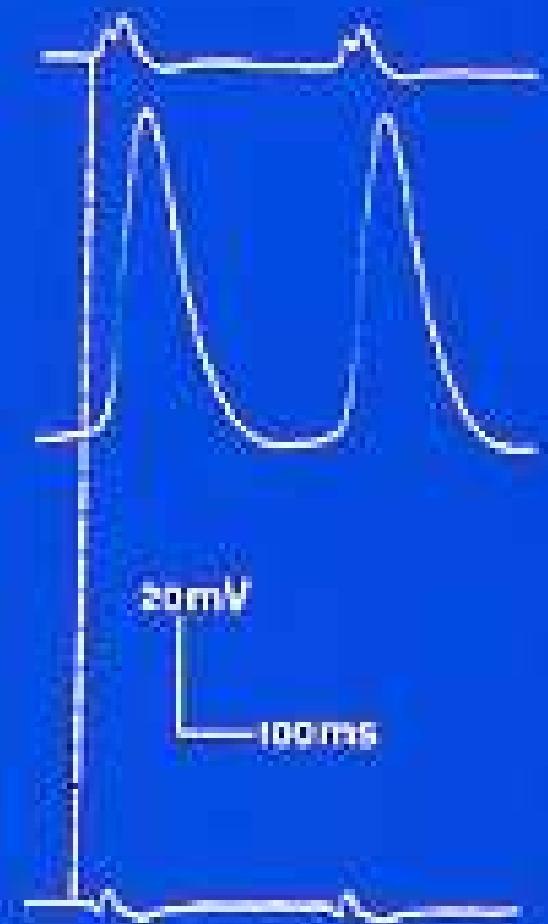


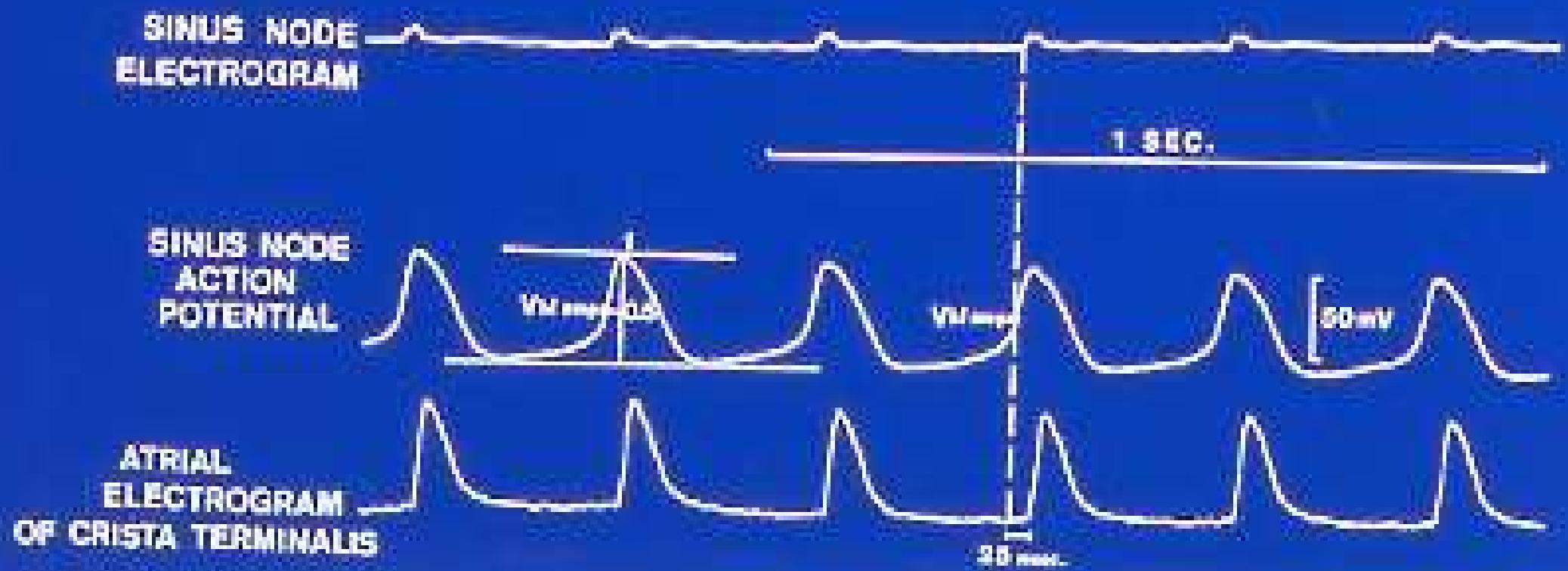
ELECTROGRAMME
SINUSAL

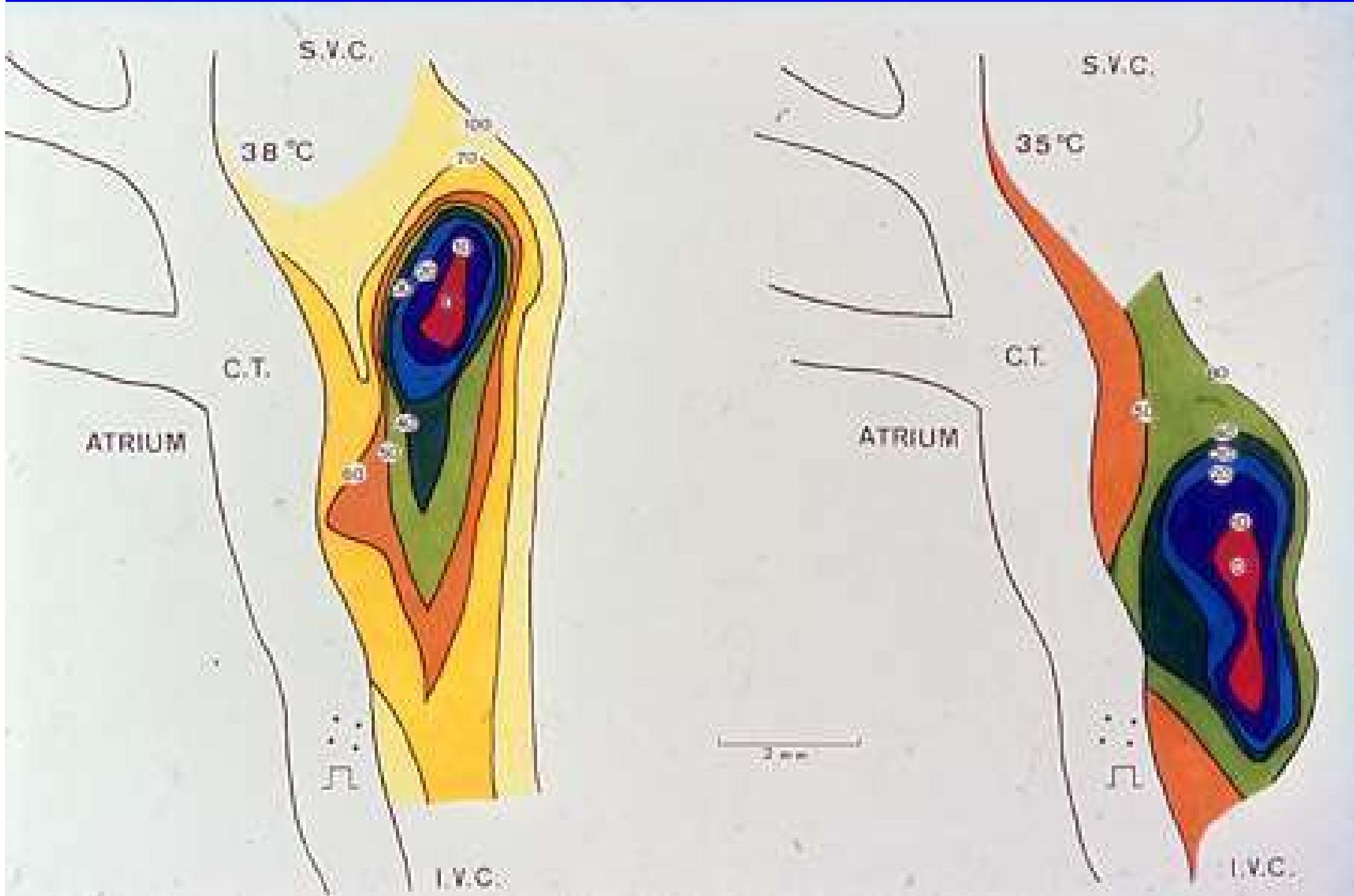
RA. PACEMAKER
LATENT

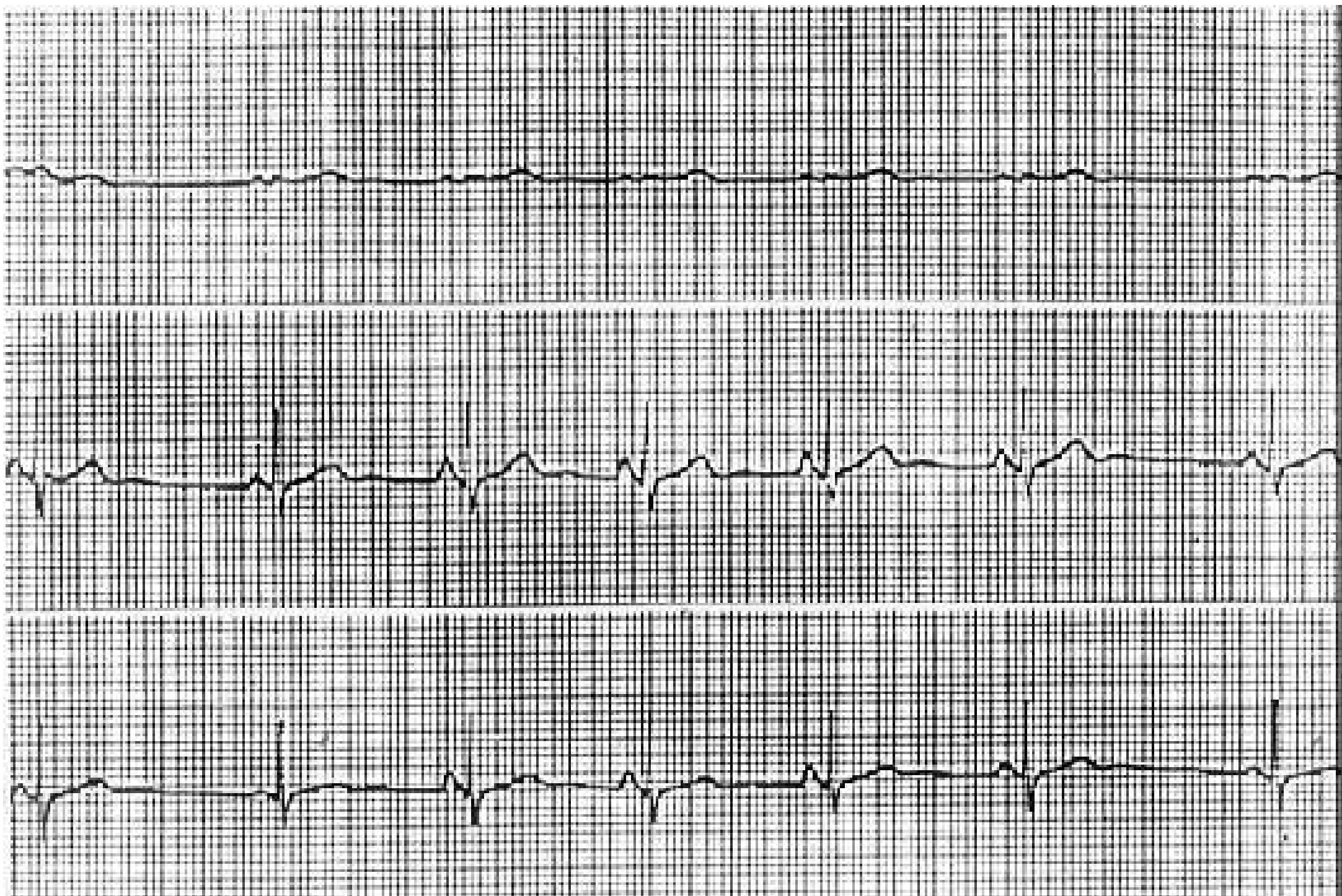
RA. PACEMAKER
DOMINANT

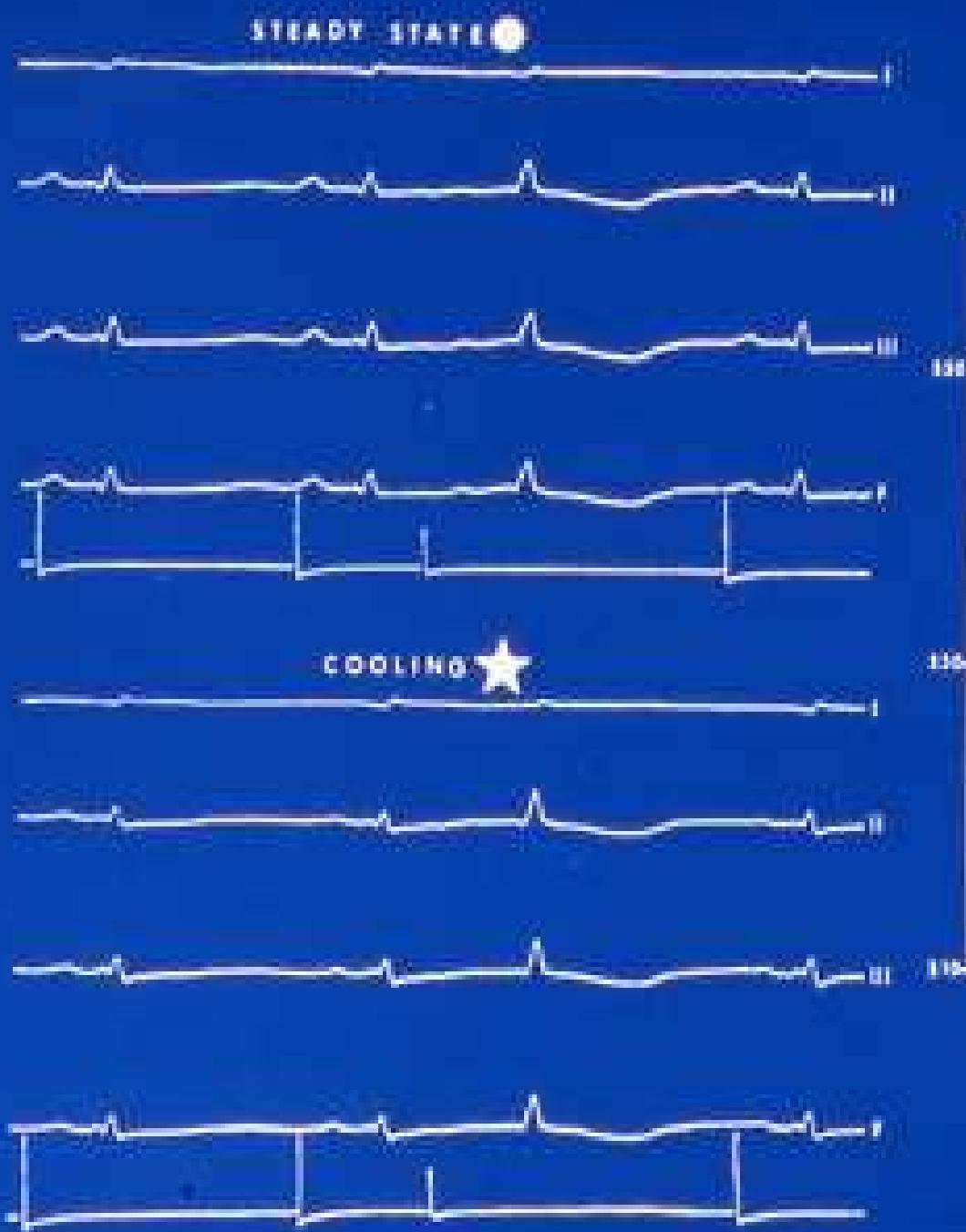
ECGOLOGRAMME
(CRISTA TERMINALIS)











A₂A₃ ms

150

$$\begin{aligned}a &= 0.97 \\b &= 382.4 \\r &= 0.96 \\p &< 0.01\end{aligned}$$



A₁A₁ ms

100

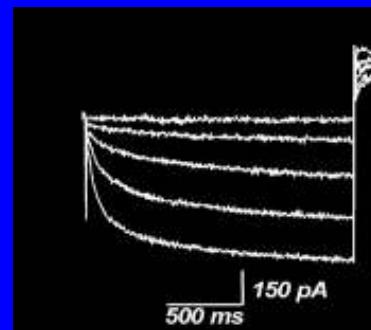
200

| AUTEURS | FACTEURS PROVOQUANT LE DEPLACEMENT | MISE EN EVIDENCE |
|---------------------|--|--------------------|
| Meek et Eyster 1914 | Sti. vagale, refroidissement, élévation K+ | Cœur chien in situ |
| Lewis 1914 | Stimulation vagale | Cœur chien in situ |
| West 1955 | Acétylcholine | Sinus isolé lapin |
| Katoh 1964 | Acétylcholine, sti. Vagale | Cœur chien in situ |
| Toda 1968 | Sti. Sympathique, noradrénaline | Sinus isolé lapin |
| Lu 1970 | Elévation K + | Sinus isolé lapin |
| Goldberg 1975 | Sti. vagale, sti. sympathique, noradrénaline | Cœur chien in situ |
| Bouman 1978 | Sti. vagale, refroidissement, baisse Ca++ | Sinus isolé lapin |

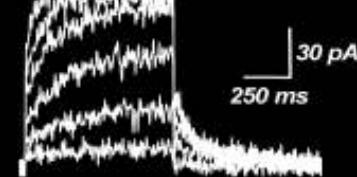
La cellule sinusale de souris est un nouveau modèle d'étude de l'activité pace-maker cardiaque



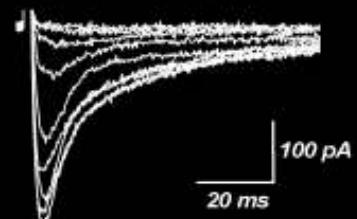
Courant I_f



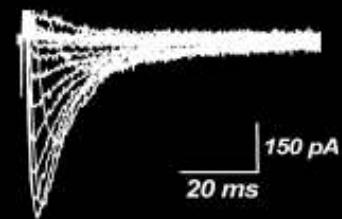
Courant K^+ (I_{Kr})



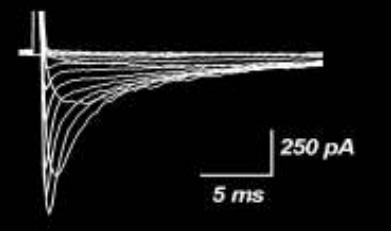
Courant Ca^{2+} type L



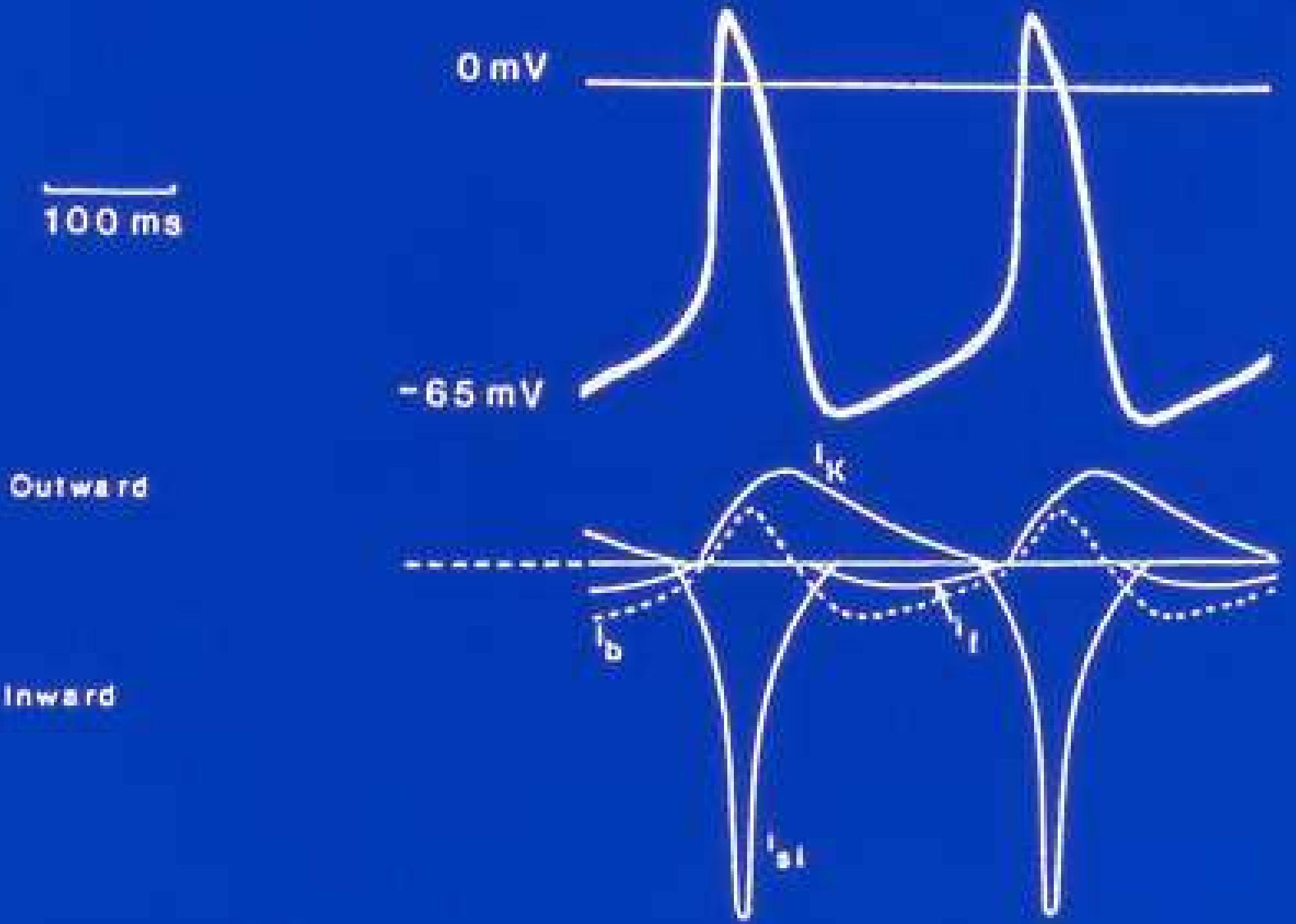
Courant Ca^{2+} type T

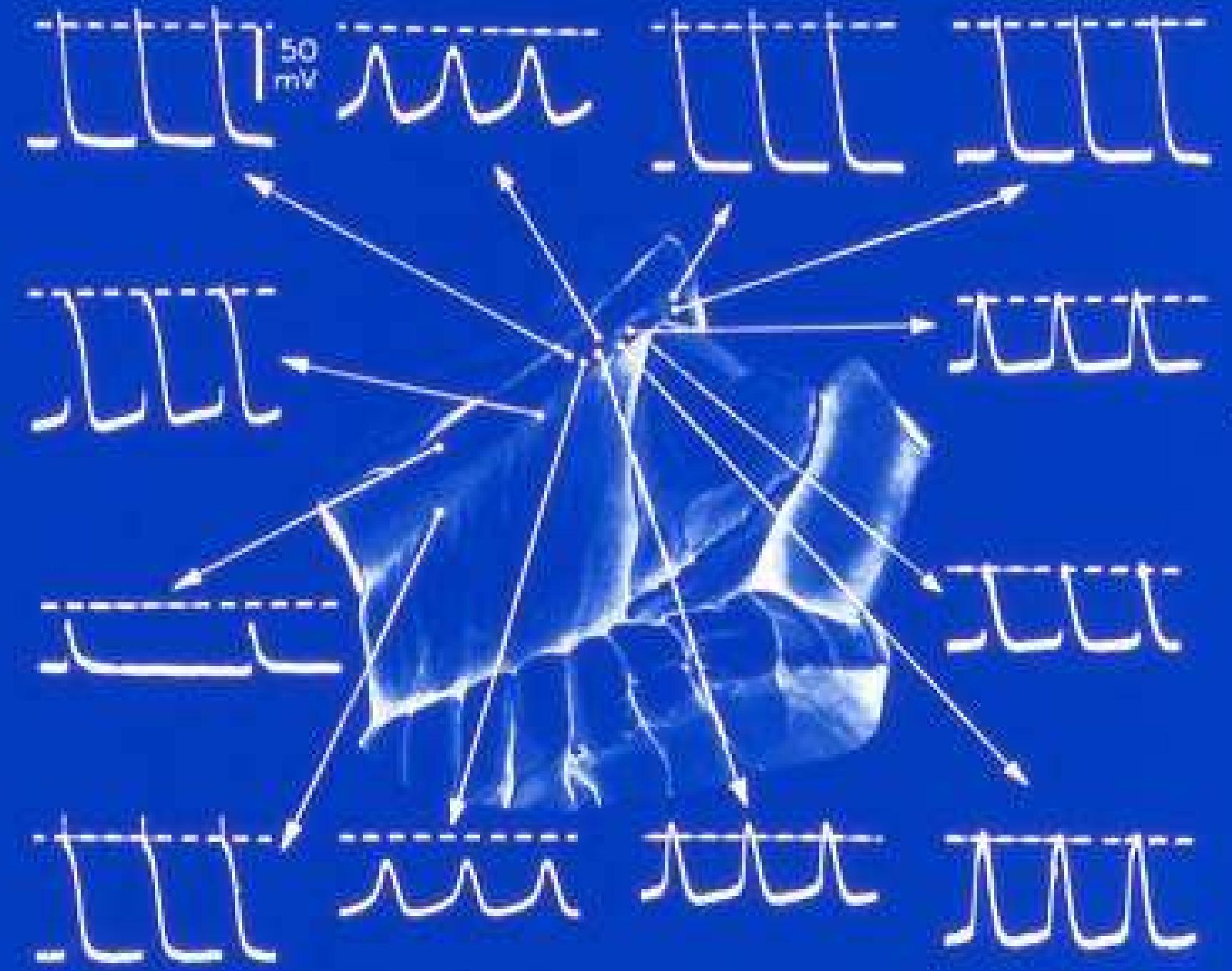


Courant Na^+ (I_{Na})

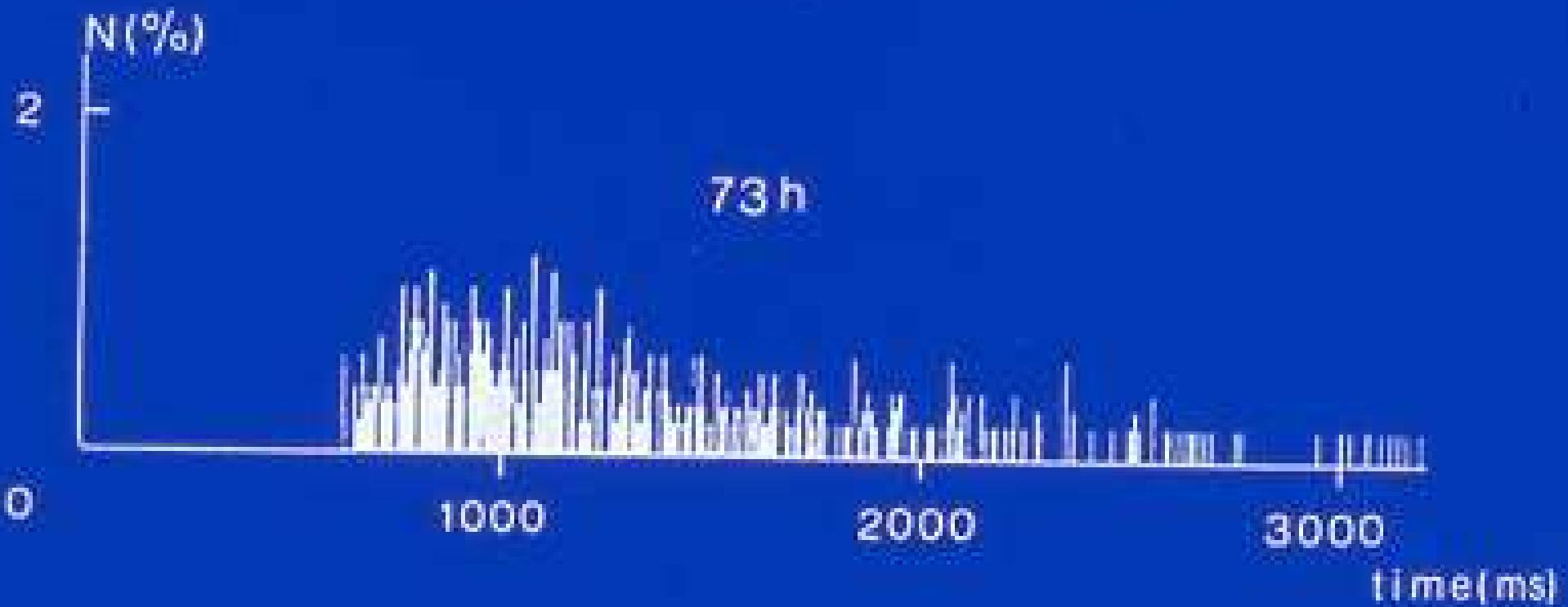


Mangoni et Nargeot, Cardiovasc Res 2001

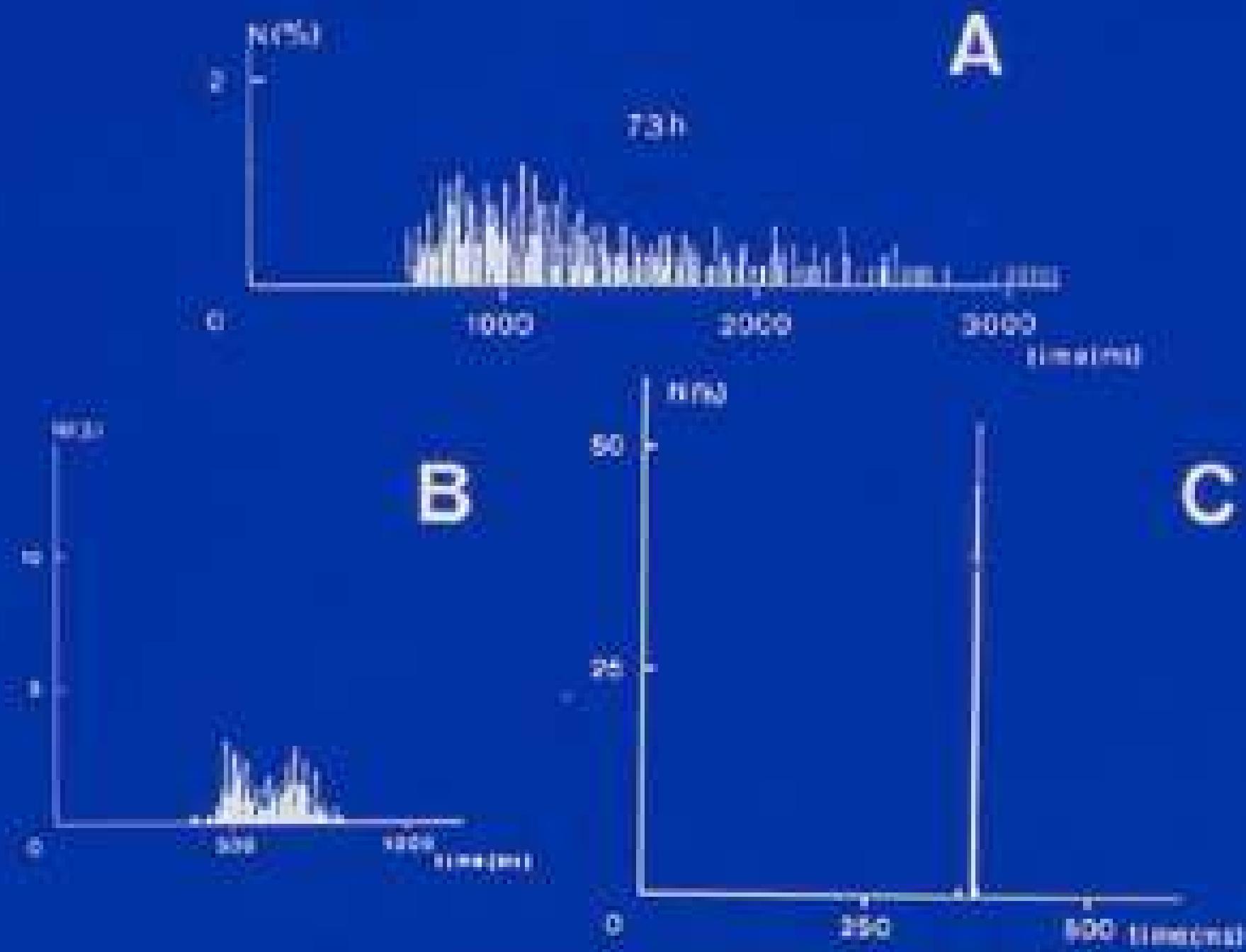


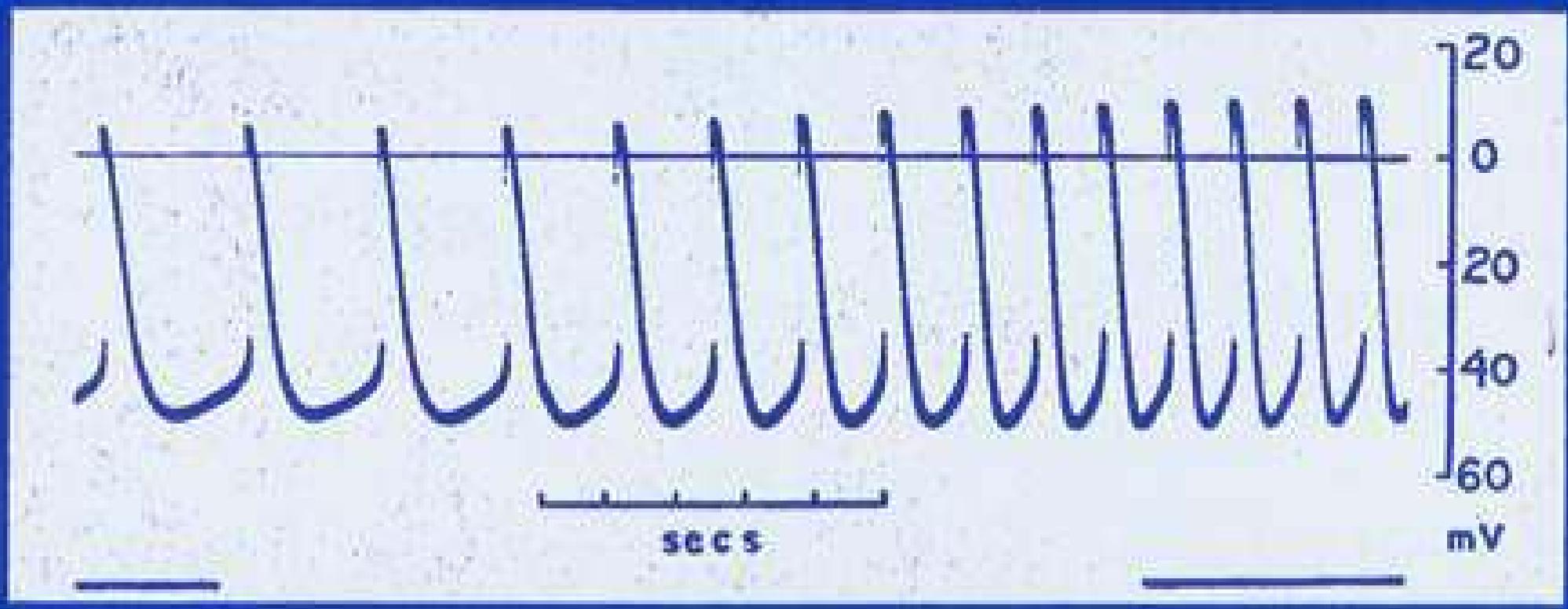


50
mV



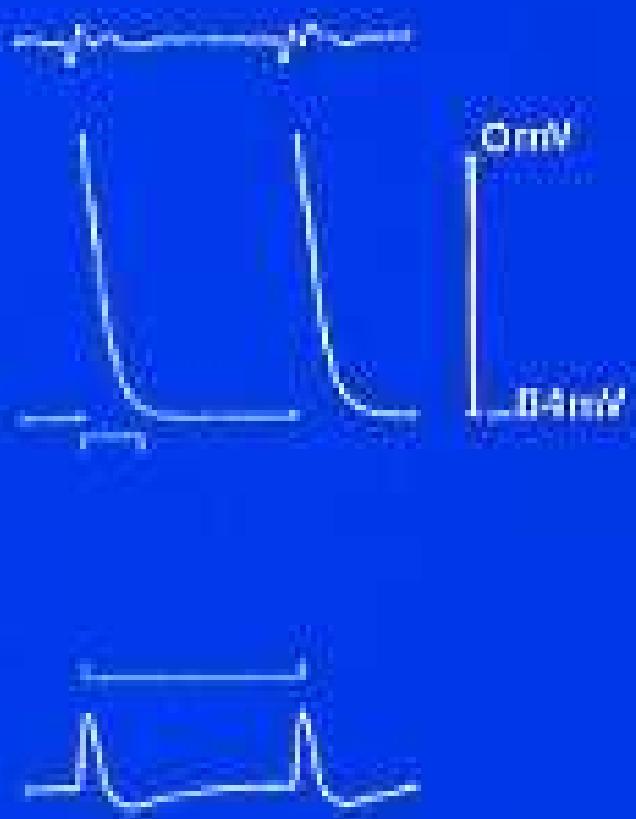
CELLULE ISOLEE
= PHENOMENES STOCHASTIQUES
(DE σΤΟΧΑΣΤΙΚΟΥ, DEVIN)



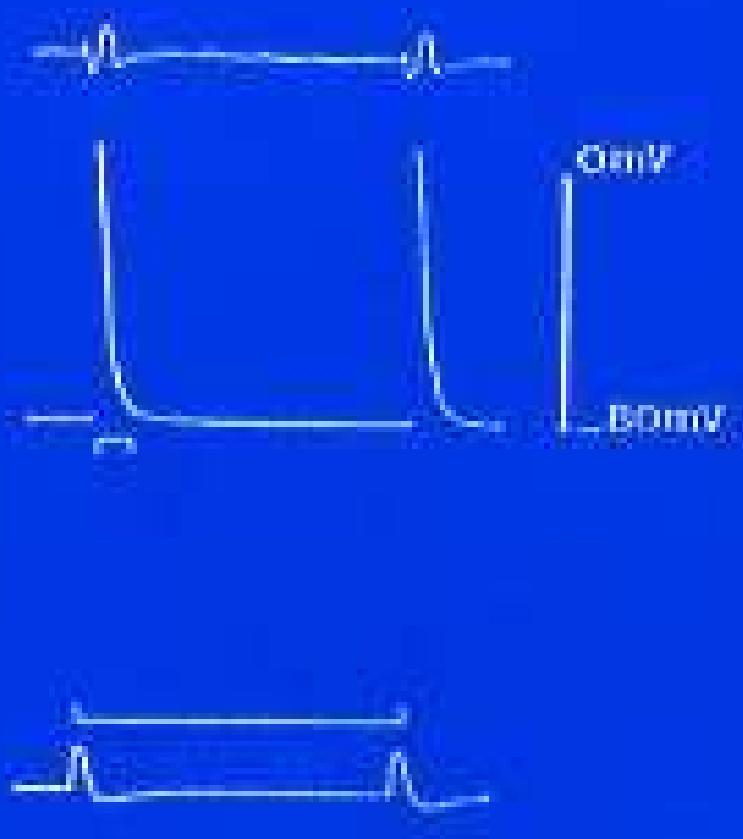


Hutter et al., 1956

CONTROL



Ach 1.4×10^{-5} M



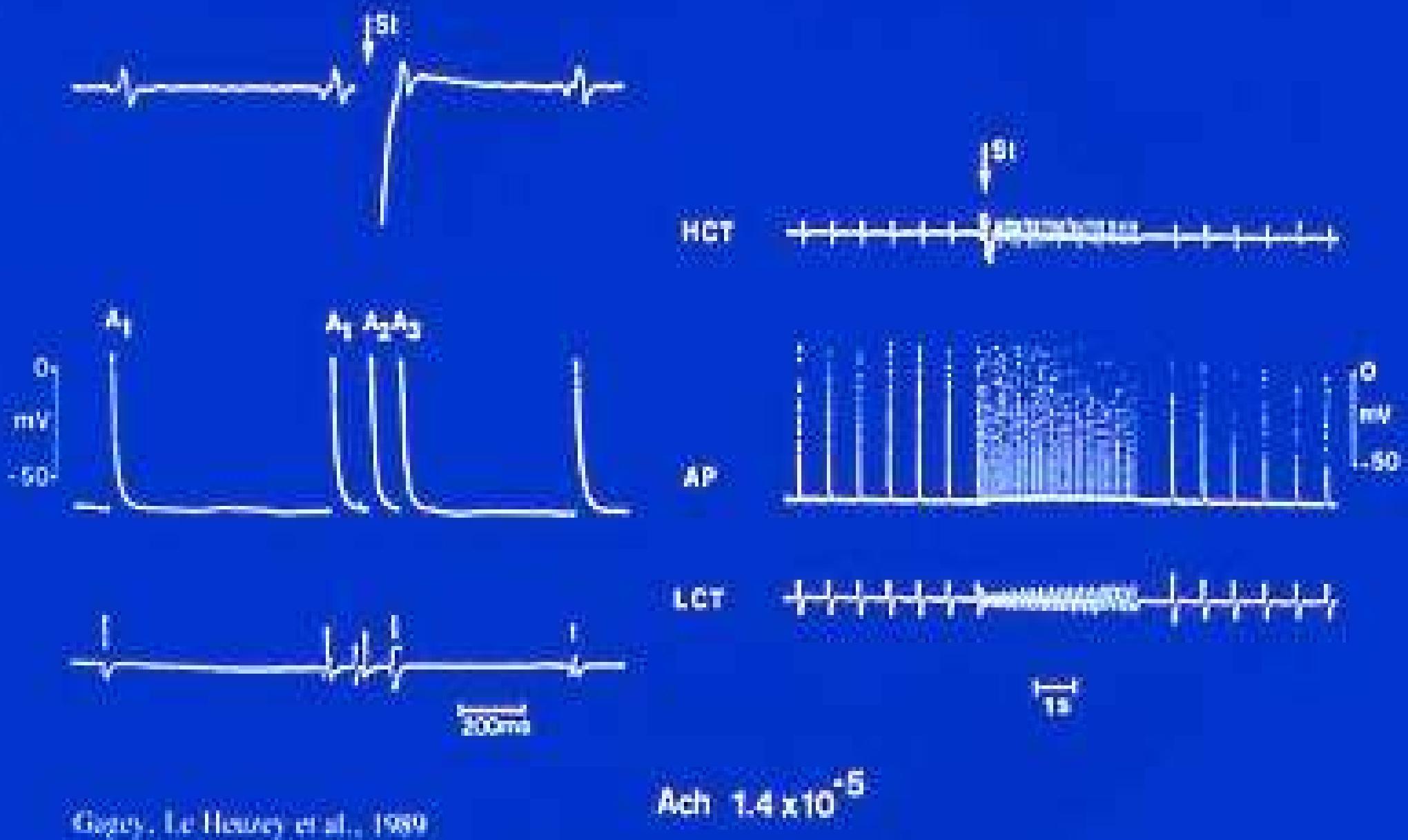
HCT

AP

LCT

200ms

Gagey, Le Henzey et al., 1989



Gagey, Le Houeyg et al., 1989

CIRCUS MOVEMENT

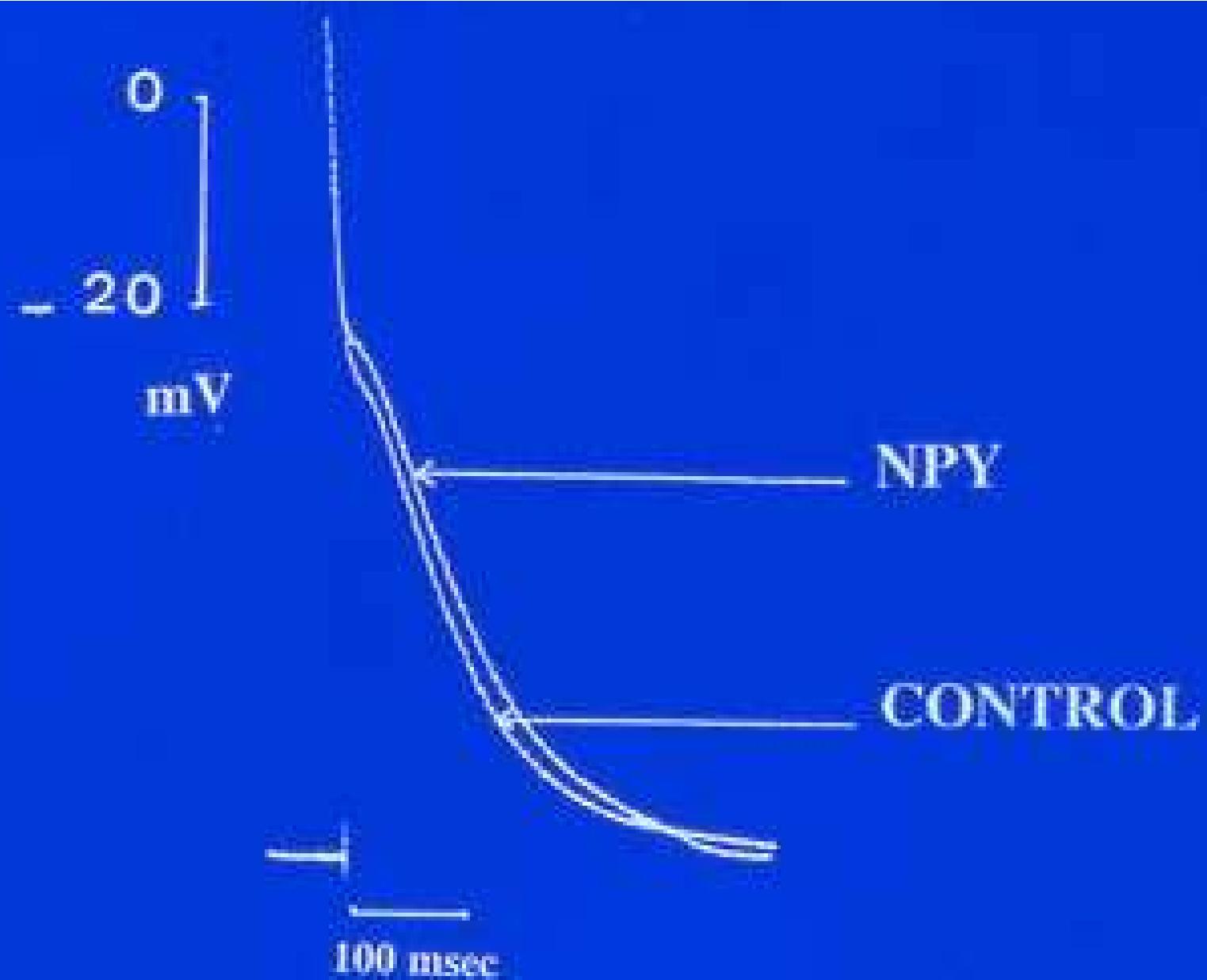
Anatomically determined
(Mines, 1913)



Functionally determined
(Allessie et al. 1977)

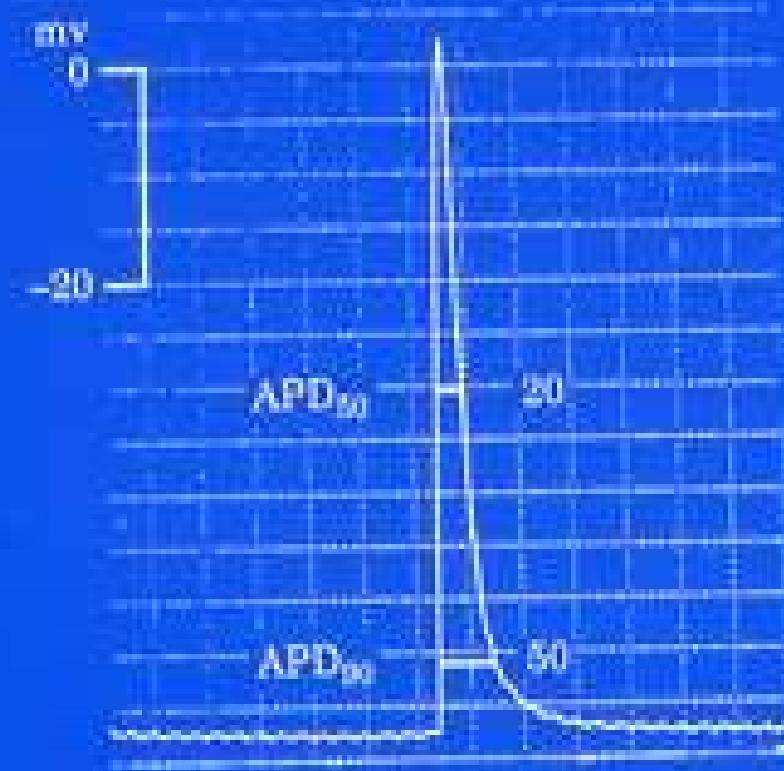


$$WL = RP \times CV$$

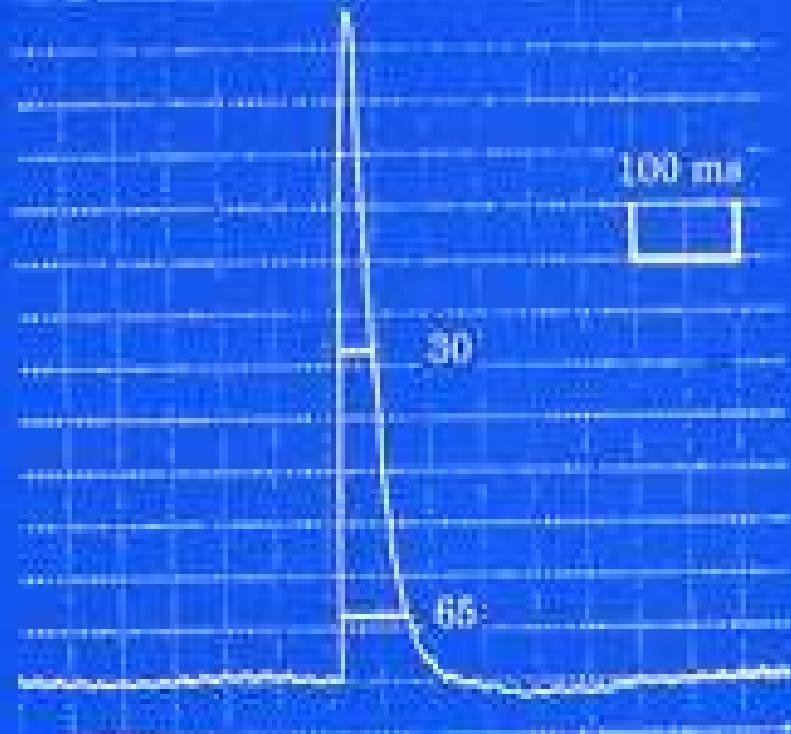


Dinanian, Le Heuzey et al., 1992

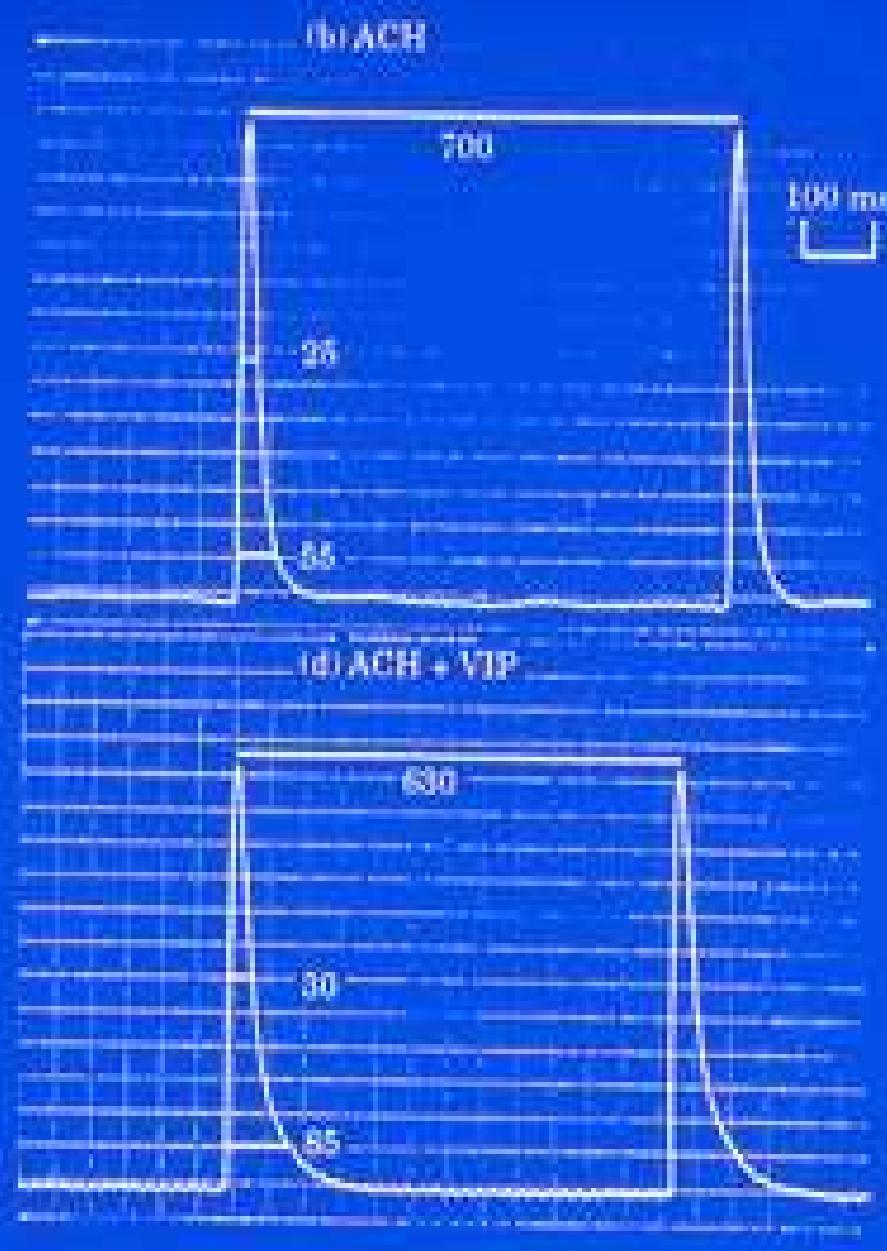
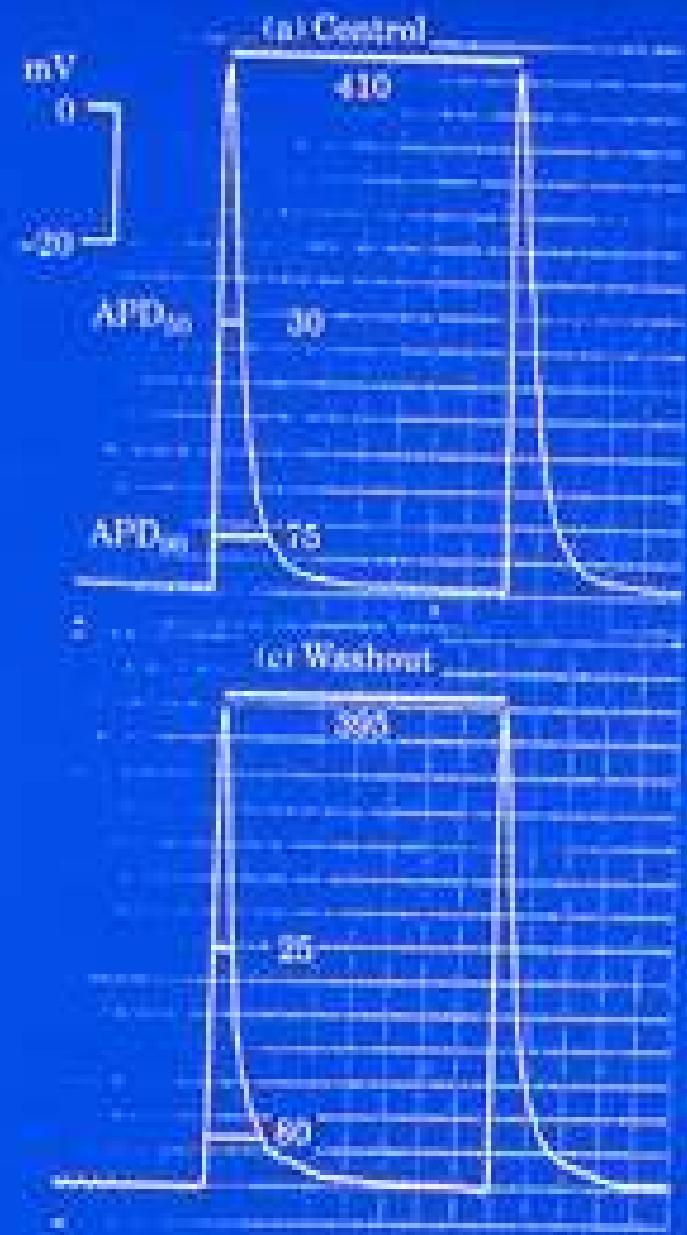
Control



VIP 10⁻⁷ M



Halimi, Le Heuzey et al., 1997



Halimi, Le Houzey et al., 1997

CONTROL

ACh 1.4×10^{-6} M

ACh + VIP

SURFACE
ELECTRODE

AP

Si

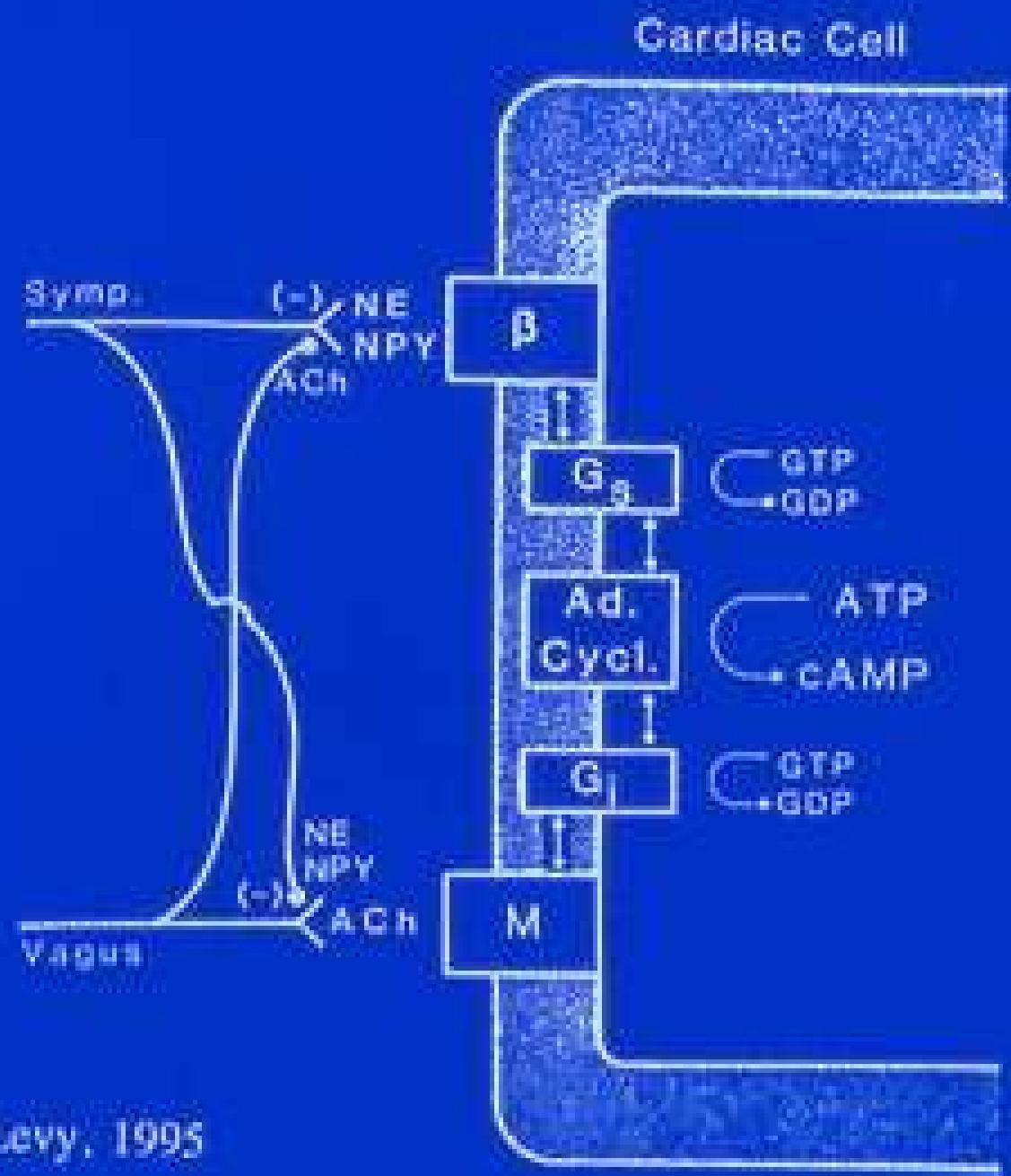
Si

0.4 sec



Si

Jalali, Le Bouzey et al., 1997

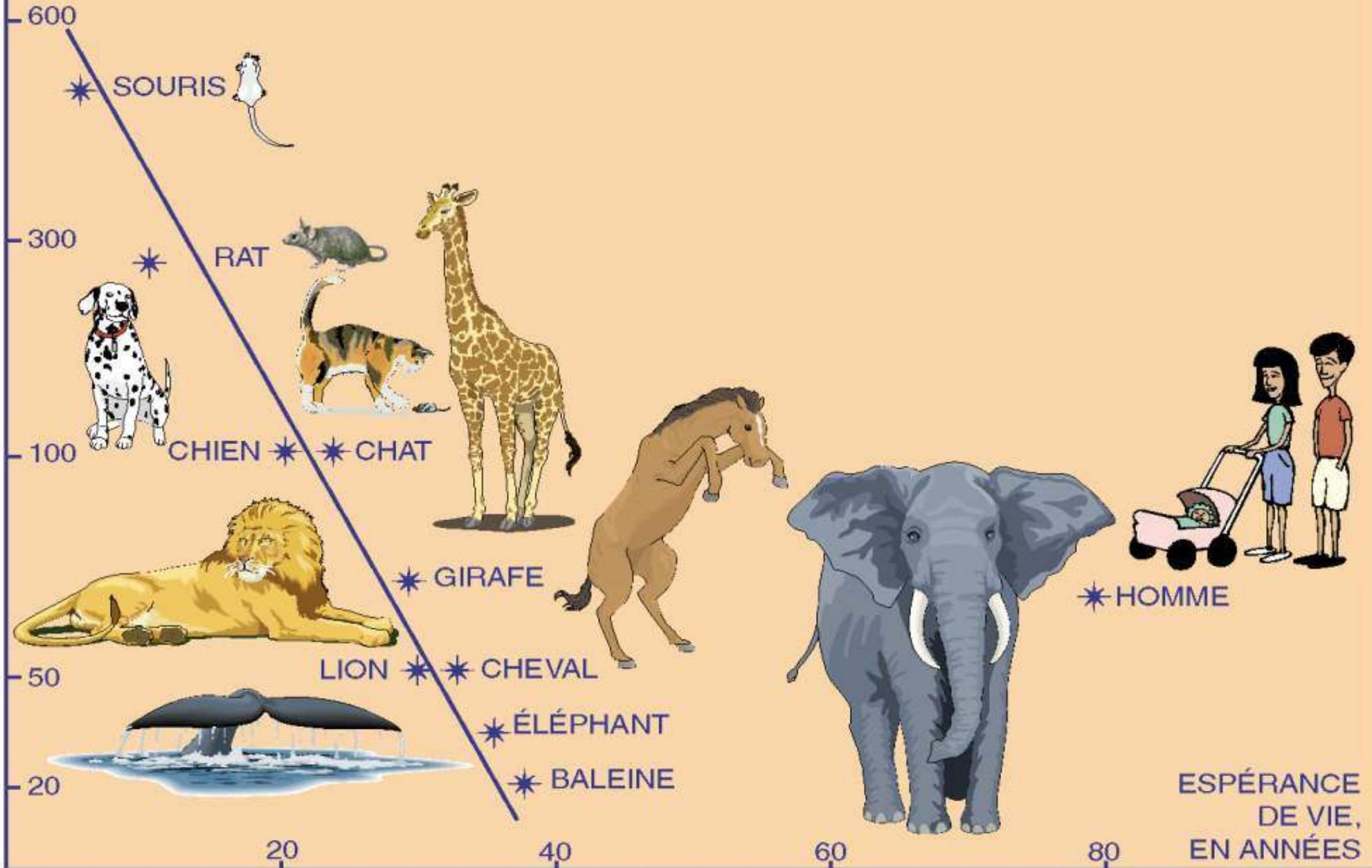


Levy, 1995

NEUROPEPTIDES

- Opioids
 - enkephalins
 - endorphins
 - dynorphin
- Neurotensin
- Substance P and tachykinins
- Angiotensin
- Vasopressin and oxytocin
- Somatostatin
- Cholecystokinin (CCK)
- **Neuropeptide Y (NPY)**
- Thyrotropin-releasing hormone (TRH)
- **Vaso intestinal peptide (VIP)**
- Calcitonin gene-related peptide (CGRP)
- **Corticotrophin-releasing factor (CRF)**

FRÉQUENCE CARDIAQUE EN BATTEMENTS PAR MINUTE



« The brain is my second favorite organ »

Woody Allen

