

Cardiac action potential and underlying ionic currents:

methods, physiology and selected pathologies

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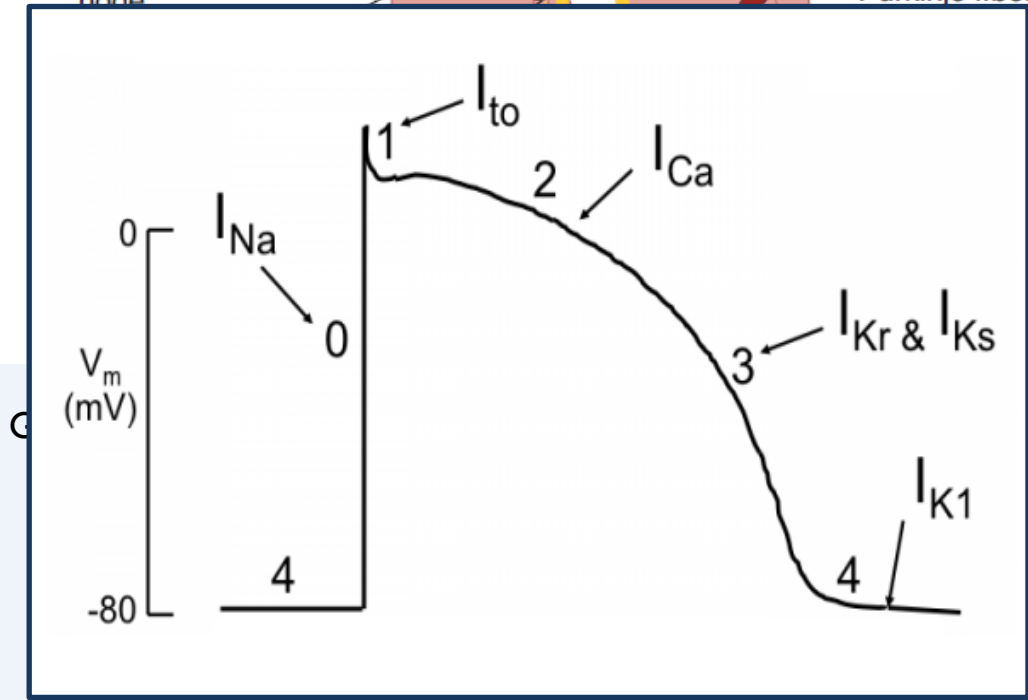
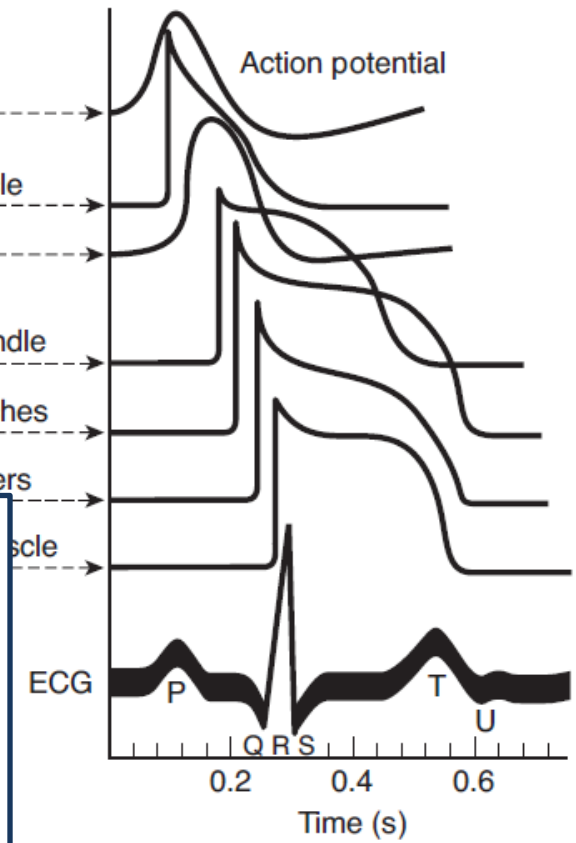
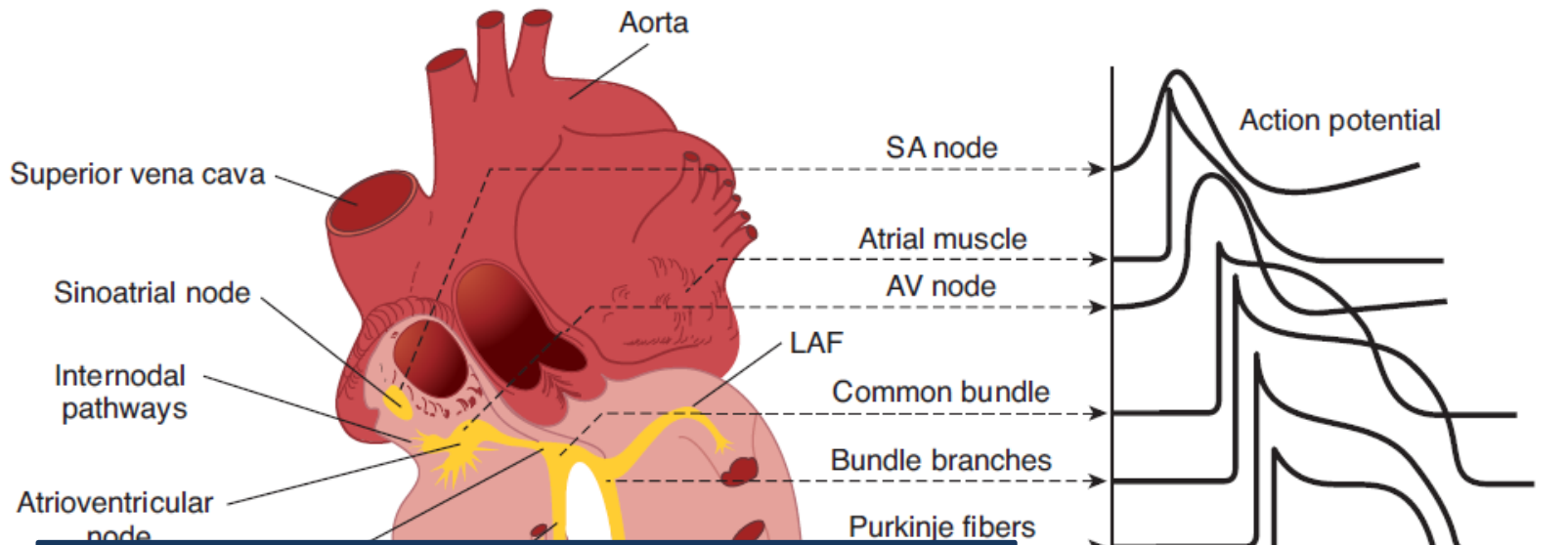
Assoc. Prof. MUDr. Milena Šimurdová, CSc.

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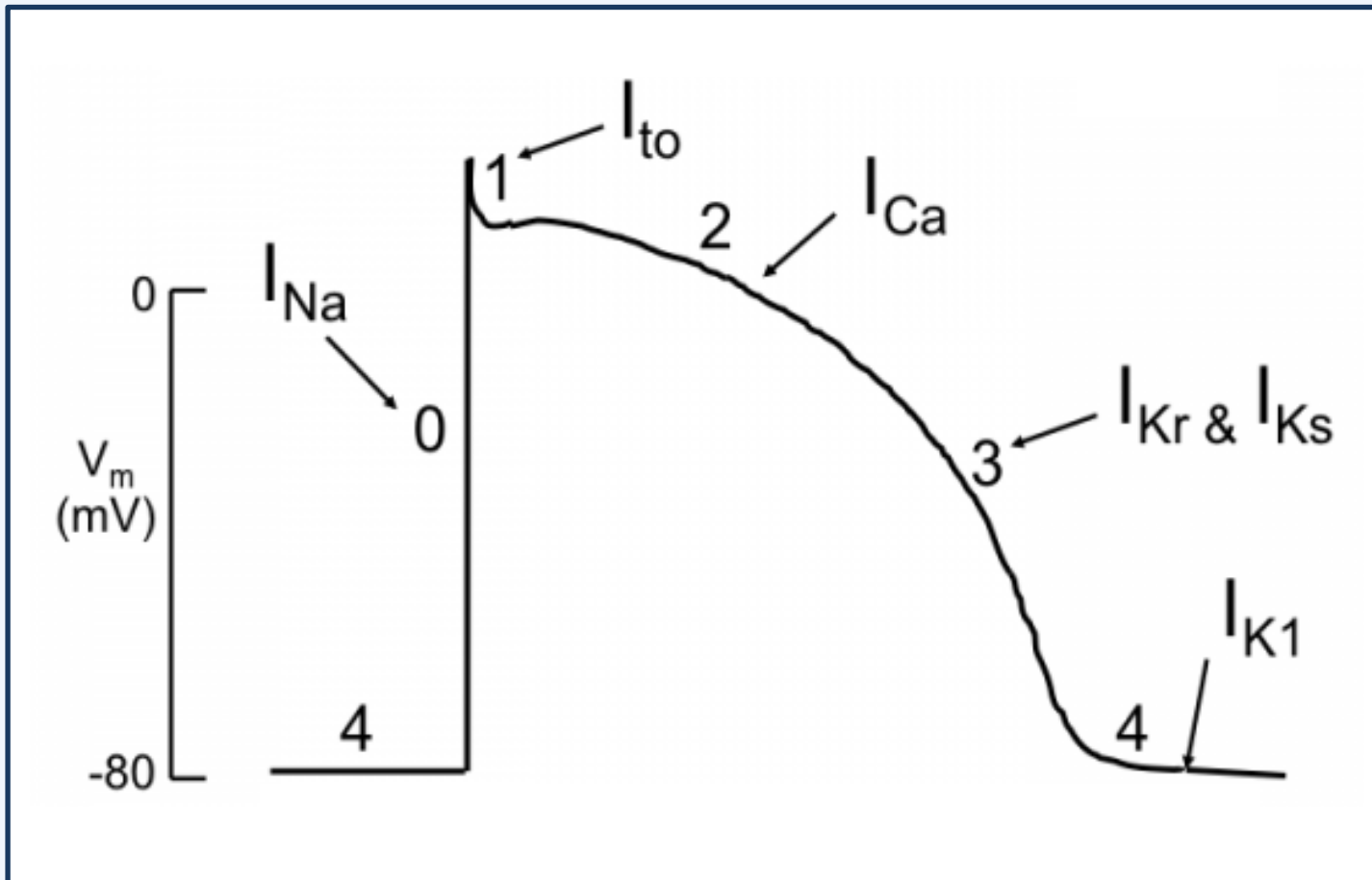
Selected Lessons from Physiology



[http://tmedweb.tulane.edu/tmedwiki/doku.php/intro to the heart cardiac electrophysiology](http://tmedweb.tulane.edu/tmedwiki/doku.php/intro%20to%20the%20heart%20cardiac%20electrophysiology)

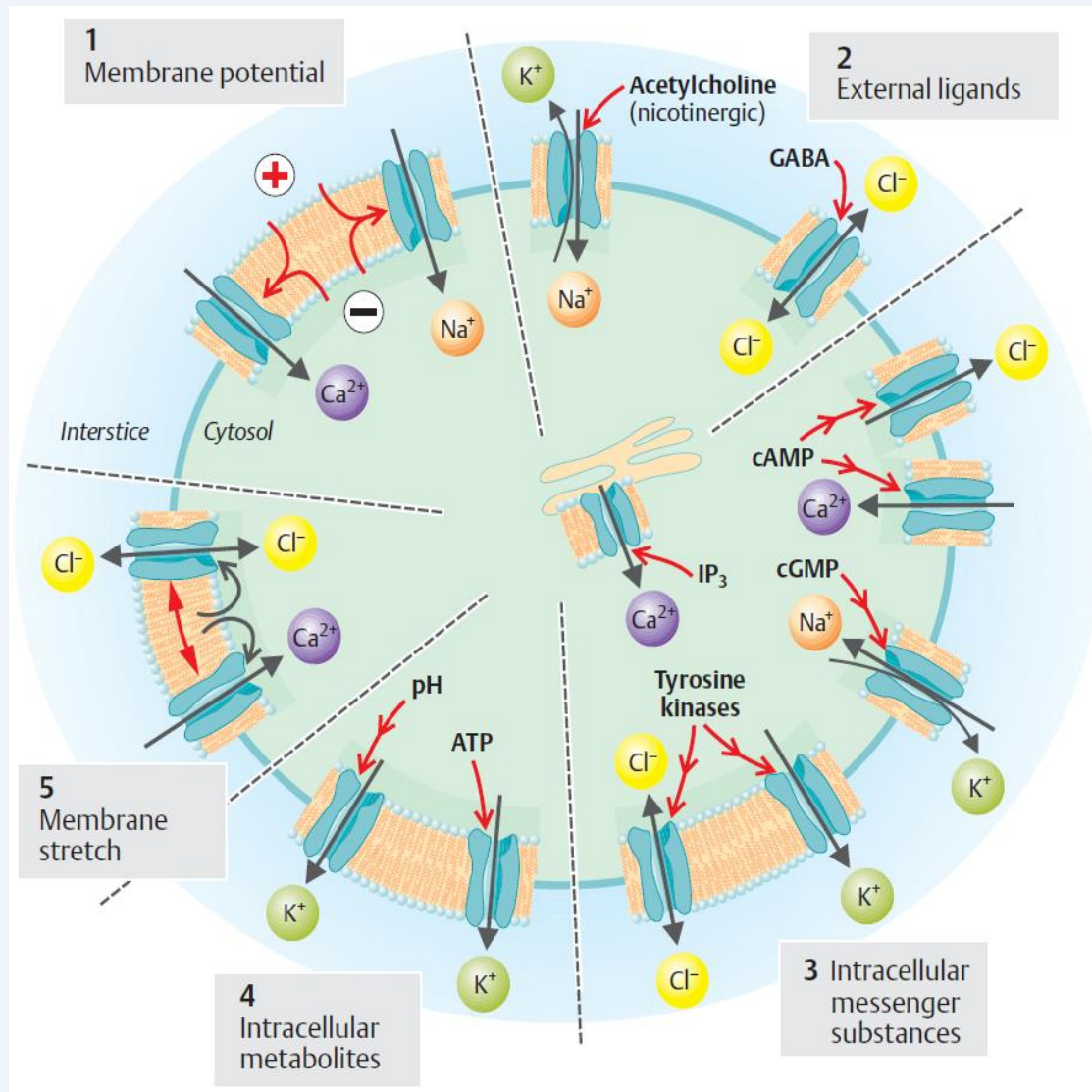


Ionic Base of Action Potential

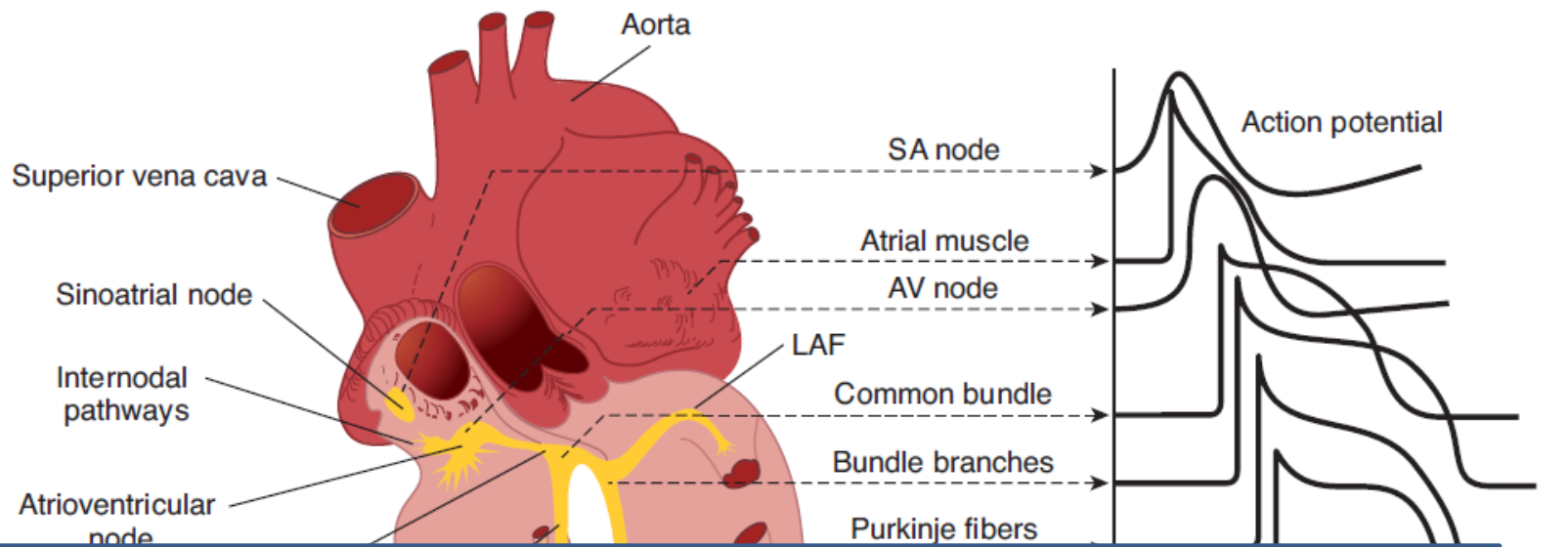


[http://tmedweb.tulane.edu/tmedwiki/doku.php/intro to the heart cardiac electrophysiology](http://tmedweb.tulane.edu/tmedwiki/doku.php/intro%20to%20the%20heart%20cardiac%20electrophysiology)

Ionic Channels



Despopoulos, Color Atlas of Physiology © 2003



Impact of Knowledge on Electrical Properties of Cardiac Cells for Clinical Medicine

- Inherited Arrhythmogenic Syndromes
- Acquired Arrhythmogenic Syndromes
 - on a base of other primary cardiac diseases
 - side effects of drugs
 - effects of other substances including addictive drugs
- Sudden Cardiac Death
- Mechanisms of Action of Antiarrhythmic Drugs

Electrophysiological Methods in Cardiology

- 1) Whole organism (ECG)**
- 2) Isolated heart (Langendorff)**
- 3) Multicellular cardiac samples**
- 4) Isolated cardiomyocytes**
- 5) Single membrane channels**

Zipes D. a Jalife J. (2003)

Cardiac Electrophysiology: From Cell To Bedside

Electrophysiological Methods in Cardiology

- 1) Whole organism (ECG)
- 2) Isolated heart (Langendorff)

measured quantity: voltage (V)

potential difference φ between two points
of a volume conductor
(*outside the cells*)

$$V = \varphi_2 - \varphi_1$$

Electrophysiological Methods in Cardiology

- 1) Whole organism (ECG)**
- 2) Isolated heart (Langendorff)**

Recorded signals

represent a sum of contributions of electrical activities of individual cells of the organ during propagation of excitation.

Electrophysiological Methods in Cardiology

- 1) Whole organism (ECG)**
- 2) Isolated heart (Langendorff)**
- 3) Multicellular cardiac samples**
- 4) Isolated cardiomyocytes**
- 5) Single membrane channels**

Zipes D. a Jalife J. (2003)

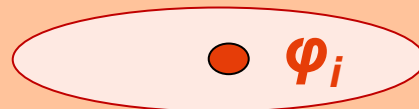
Cardiac Electrophysiology: From Cell To Bedside

Electrophysiological Methods in Cardiology

- 3) Multicellular cardiac samples
- 4) Isolated cardiomyocytes
- 5) Single membrane channels

measured quantities: 1) membrane voltage (V)

potential difference between the extra- and intracellular medium (*across the cellular membrane*)

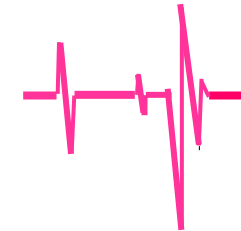
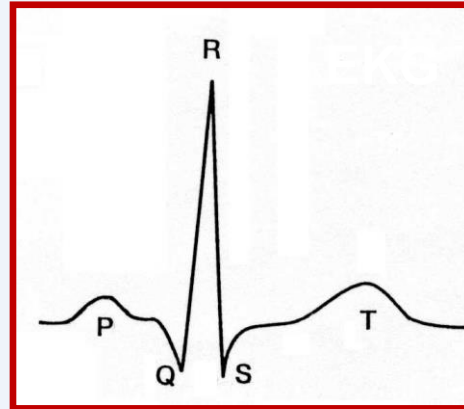
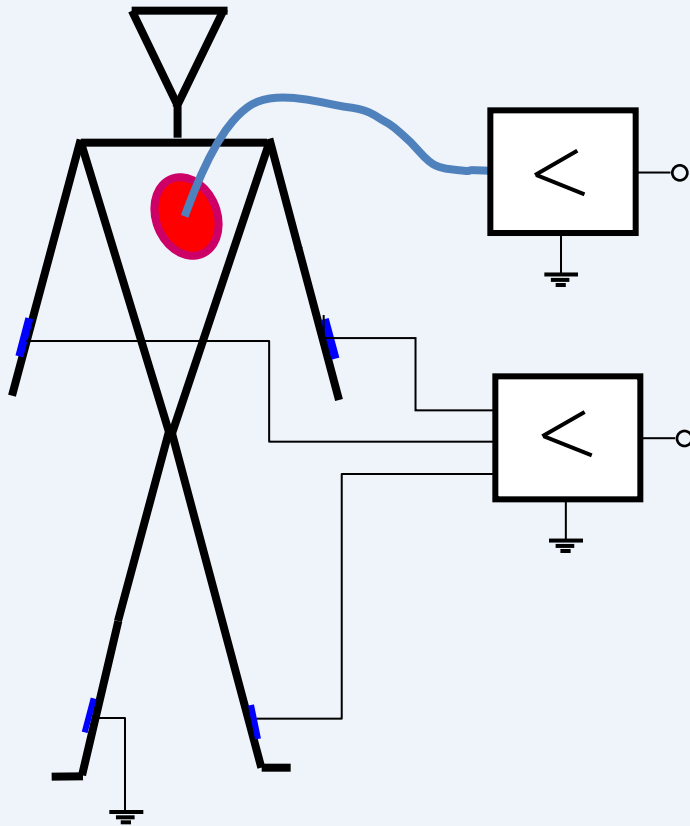


$$V = \varphi_i - \varphi_e$$

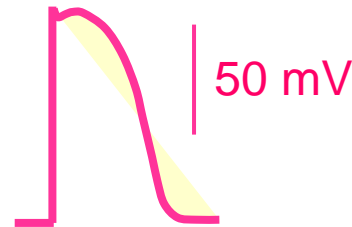
measured quantities : 2) membrane current (I)

BASIC PRINCIPLES OF MEASUREMENTS ON VARIOUS LEVELS OF ORGANISM

LEVEL OF WHOLE ORGANISM



**His bundle
electrogram**



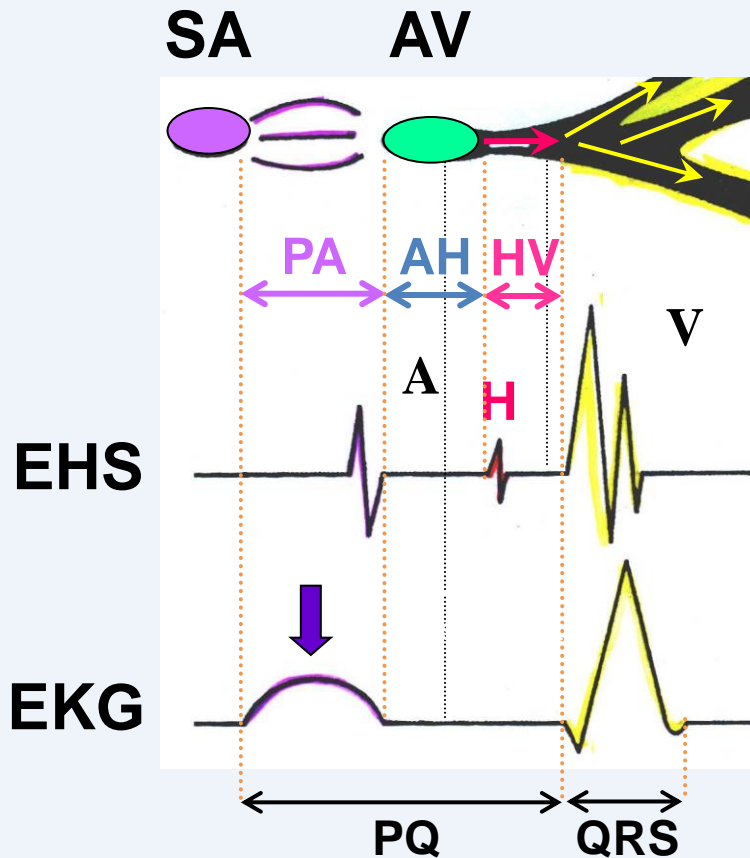
MAP
(**M**ONOPHASIC
ACTION **P**OENTIAL)

suction electrode

recorded quantity: VOLTAGE (*as the potential difference*)

method: surface and intracardial recording electrodes

His bundle electrogram



PA

conduction time of atrial excitation

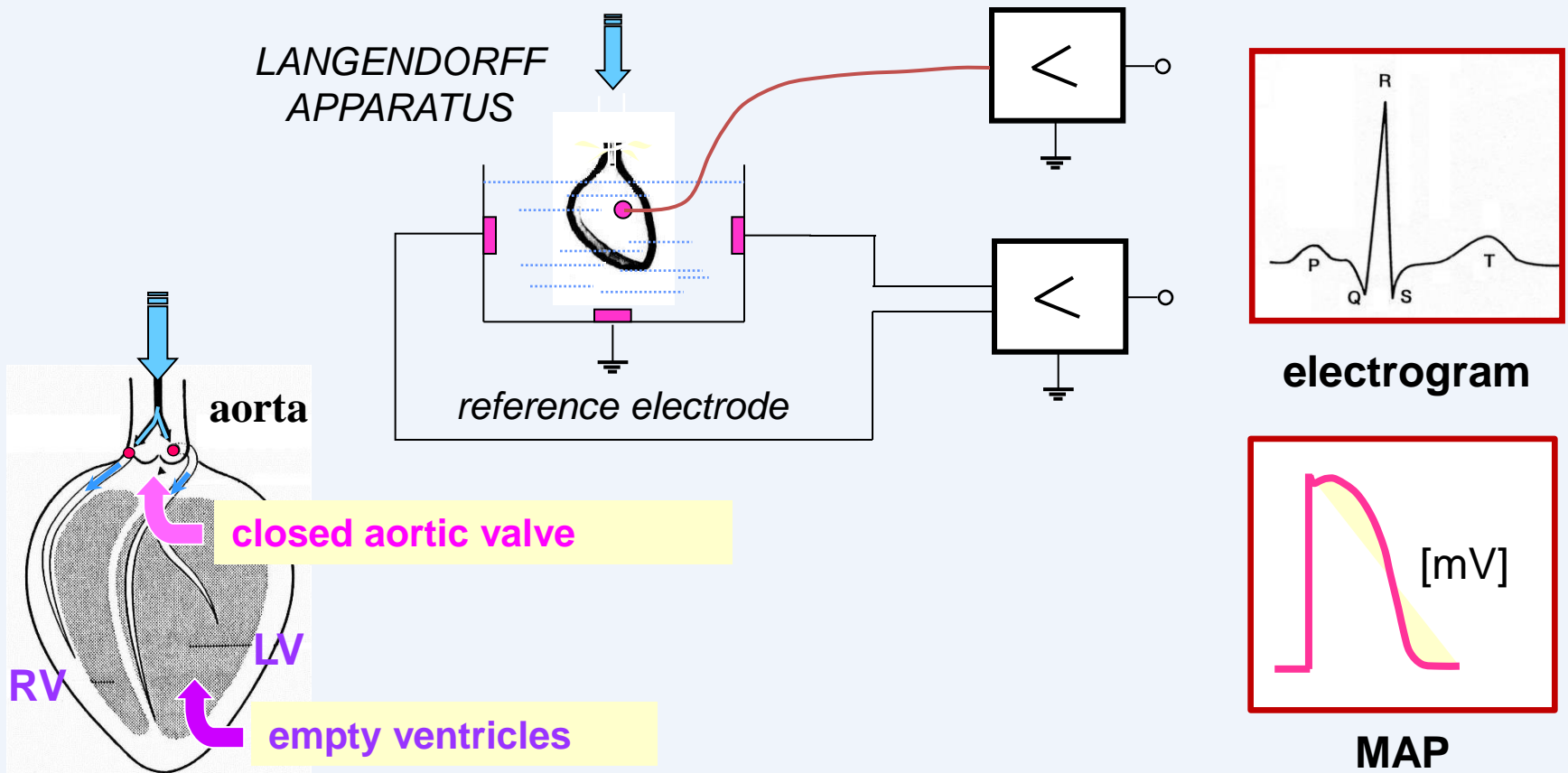
AH

conduction time of excitation through AV node

HV

conduction time of excitation through the bundle of His

LEVEL OF ISOLATED ORGAN

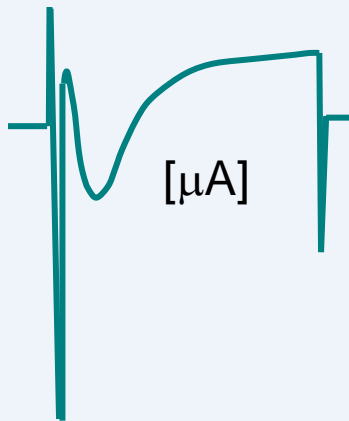


recorded quantity: **VOLTAGE** (as the potential difference)

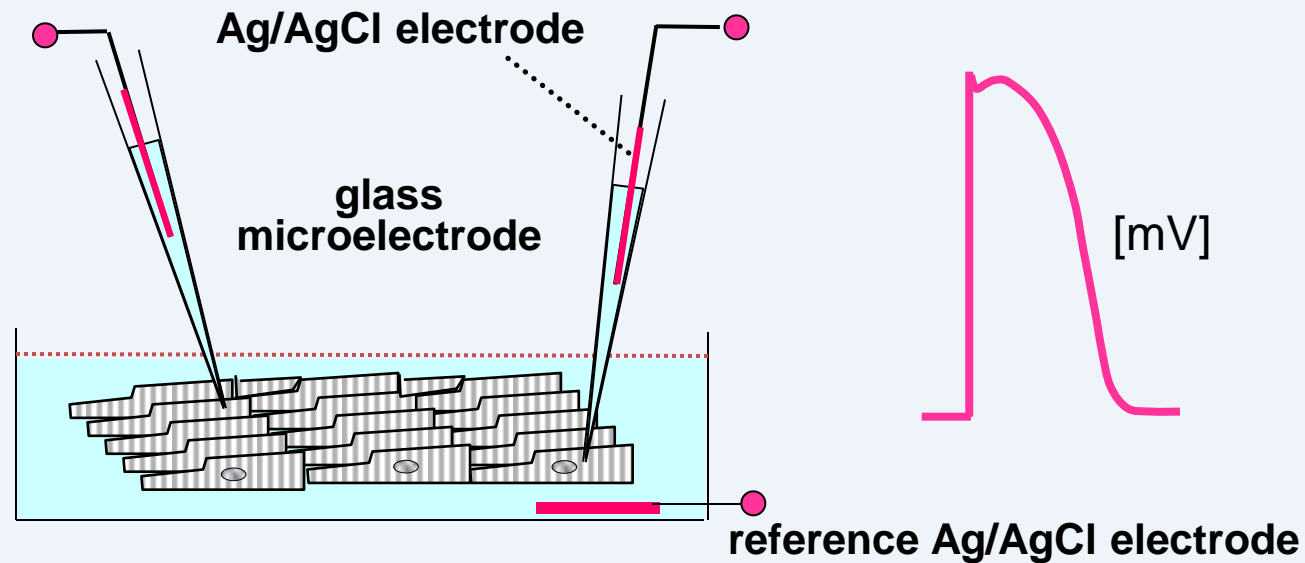
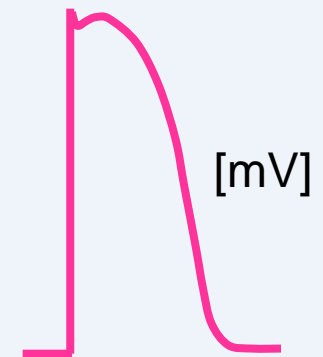
method: **electrodes embedded in walls of the bath or the epicardial suction electrode**

MULTICELLULAR CARDIAC SAMPLES

membrane currents



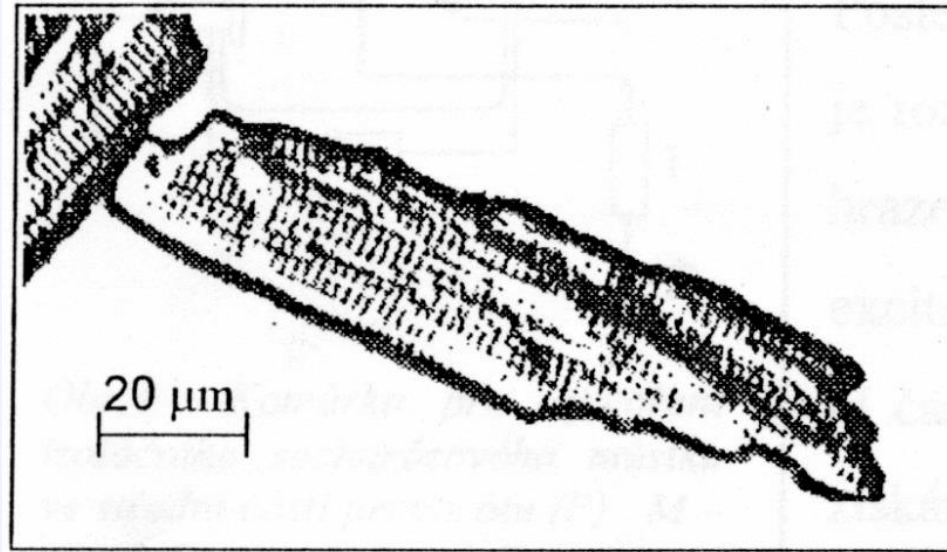
membrane voltage



recorded quantities: **membrane voltage**
membrane currents

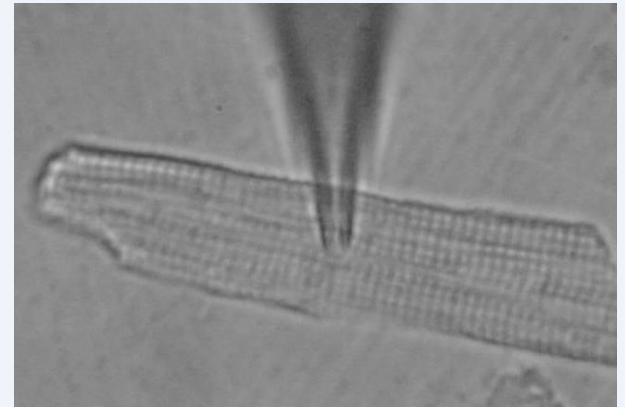
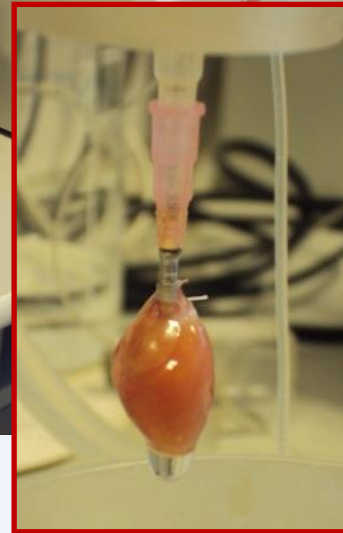
methods: **glass microelectrodes** 
'current clamp' mode of stimulation
'voltage clamp' mode of stimulation

TWO ELECTROPHYSIOLOGICAL METHODS BASED ON ISOLATION OF CARDIOMYOCYTES



CELLULAR ELECTROPHYSIOLOGY

ENZYMATIC ISOLATION OF CARDIOMYOCYTES



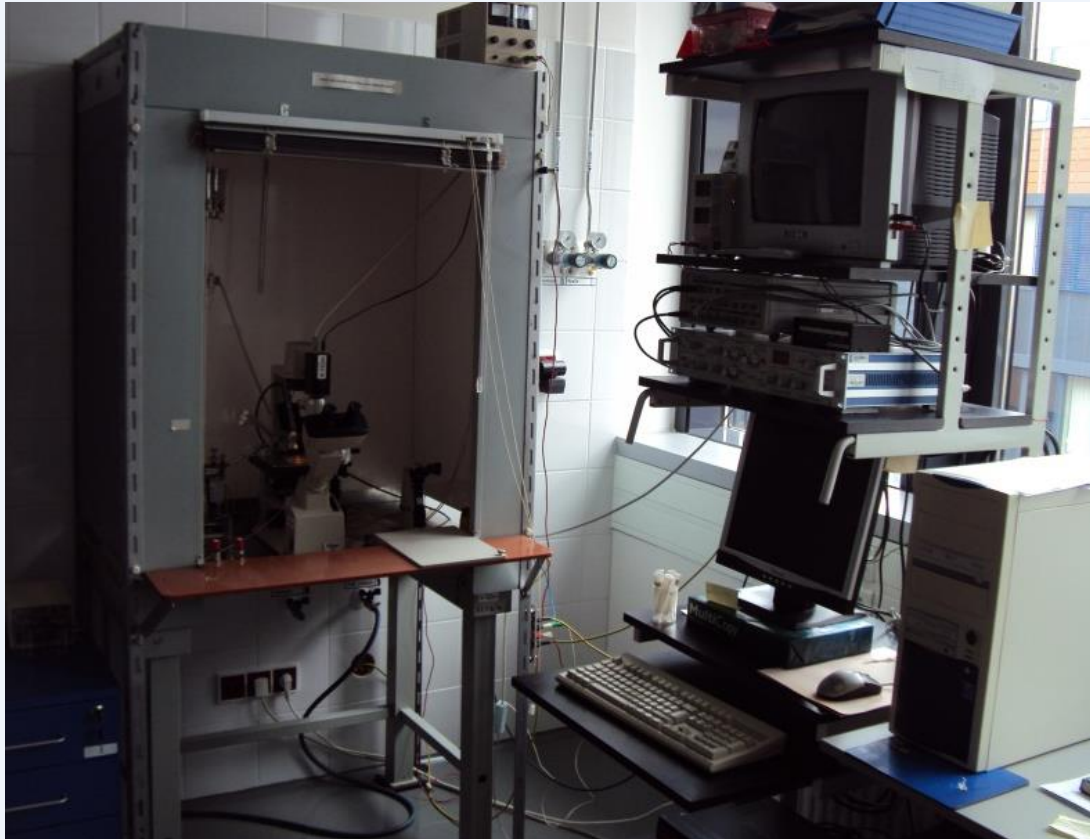
**SUCCESSFUL DISSOCIATION
OF CARDIAC TISSUE RESULTS IN ...**



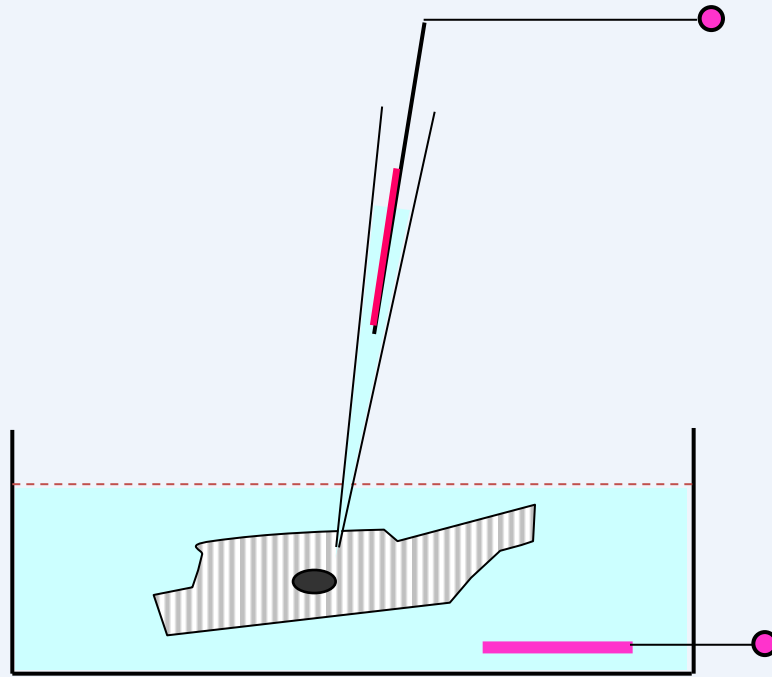
**SUFFICIENT FRACTION OF
VIABLE, FUNCTIONALLY UNDAMAGED CELLS
RESPONDING TO ELECTRICAL STIMULATION BY :**

- **CONTRACTION**
- **CHARACTERISTIC ELECTRICAL ACTIVITY
(ACTION POTENTIAL and MEMBRANE CURRENTS)**

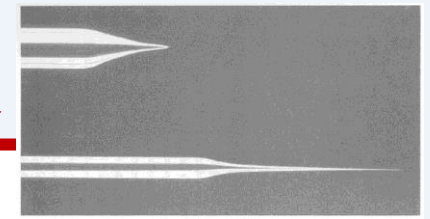
ISOLATED CARDIOMYOCYTES



ISOLATED CARDIOMYOCYTES

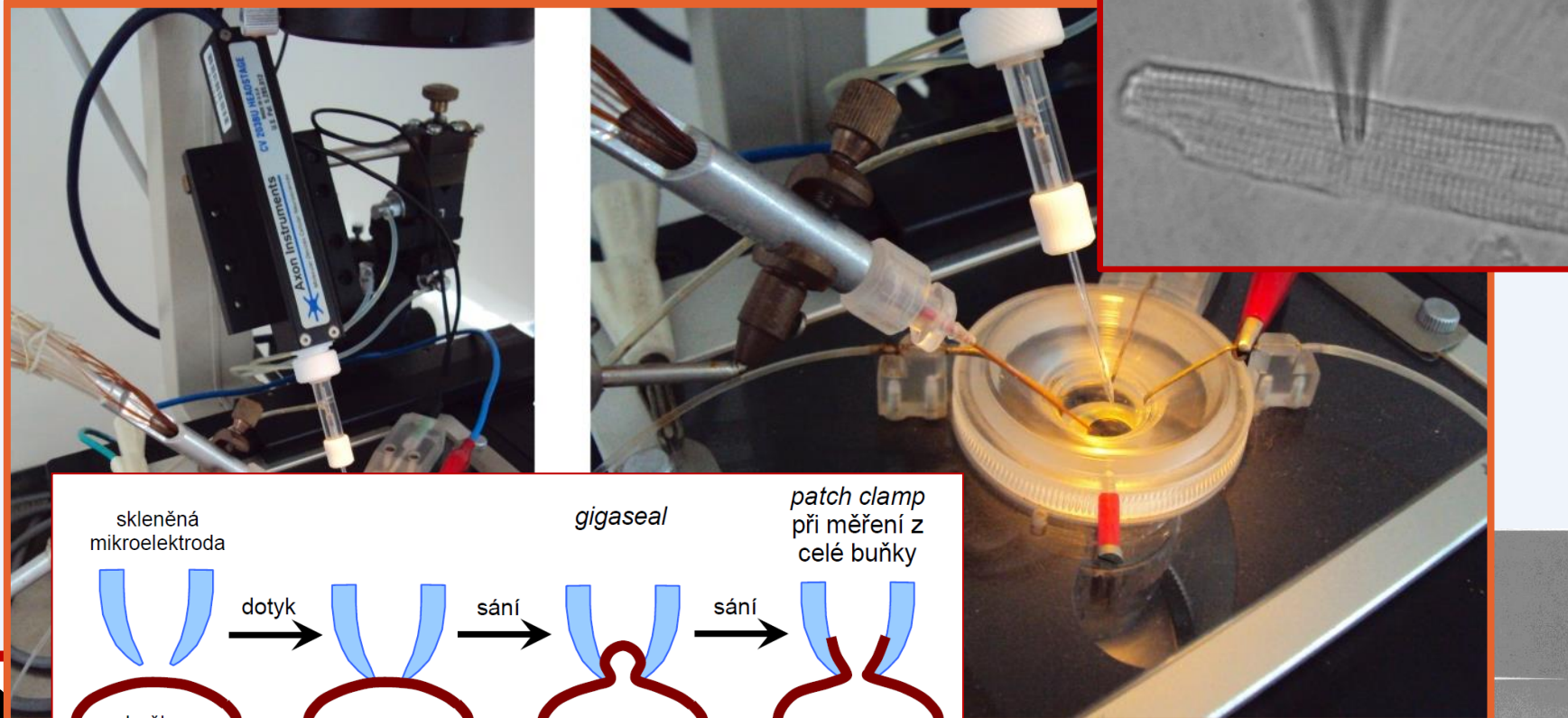


methods: **glass microelectrodes**

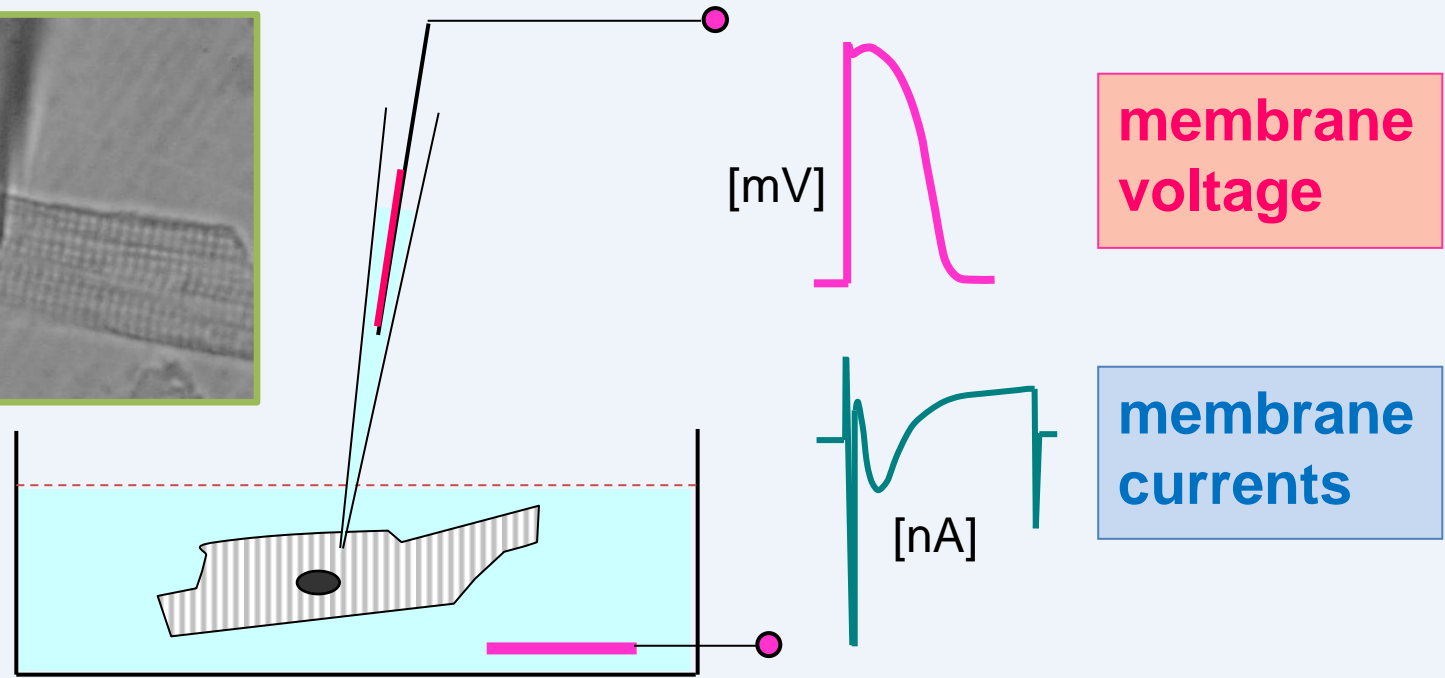
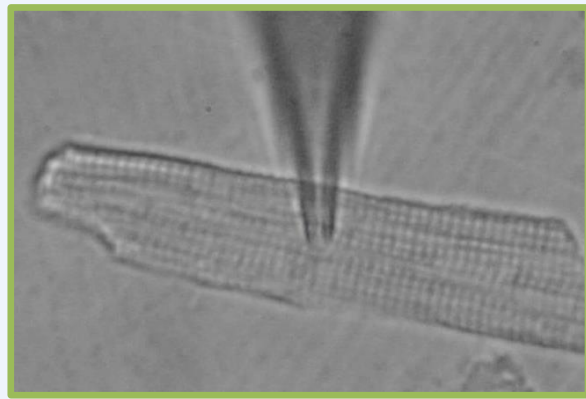


ISOLATED CARDIOMYOCYTES

Technika *patch clamp* při měření z celé buňky
(*whole cell patch clamp technique*)



ISOLATED CARDIOMYOCYTES

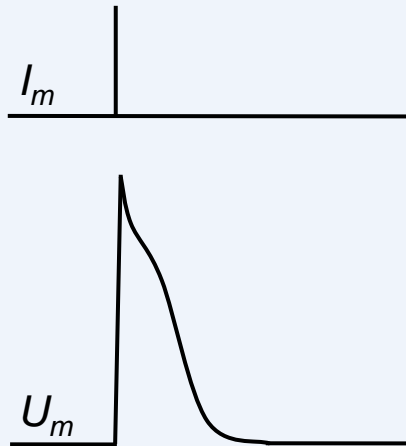


recorded quantities: **membrane voltage**
membrane currents

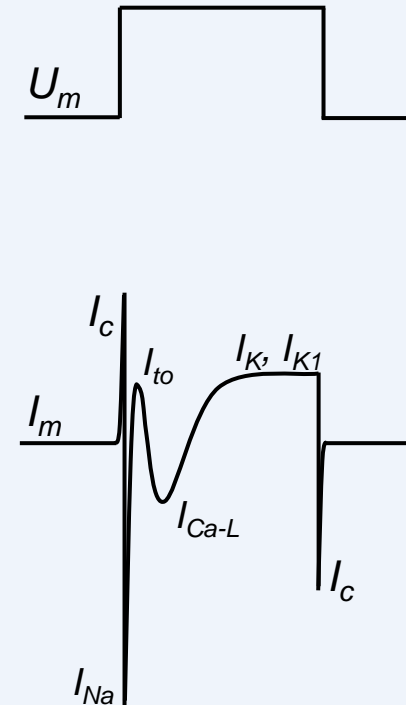
methods: **glass microelectrodes** 
'current clamp' mode of stimulation
'voltage clamp' mode of stimulation

ISOLATED CARDIOMYOCYTES

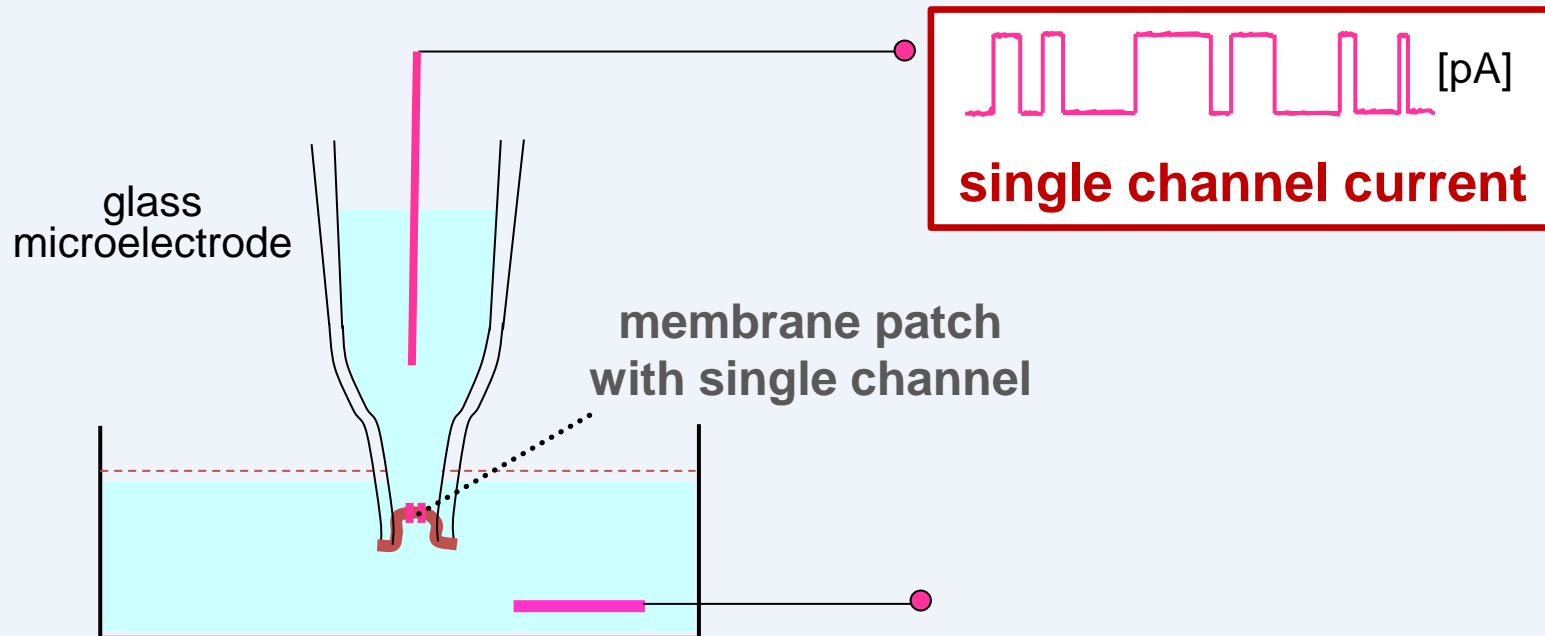
current clamp mode
of stimulation



voltage clamp mode
of stimulation



SINGLE MEMBRANE CHANNELS (molecular level)



recorded quantity: **current flowing through single channel**
in response to imposed voltage pulse

methods: **glass microelectrode**
'patch clamp' in single channel arrangement
(membrane located inside the tip of microelectrode)

Possibilities of Use of These Techniques

Analysis of **electrical properties** of cardiomyocytes **under physiological and pathological conditions**

Analysis of changes of electrical properties of cardiomyocytes under **the effect of drugs**

Methods of Analysis of Electrophysiological Properties of Cardiac Cells

Whole cell patch clamp technique

