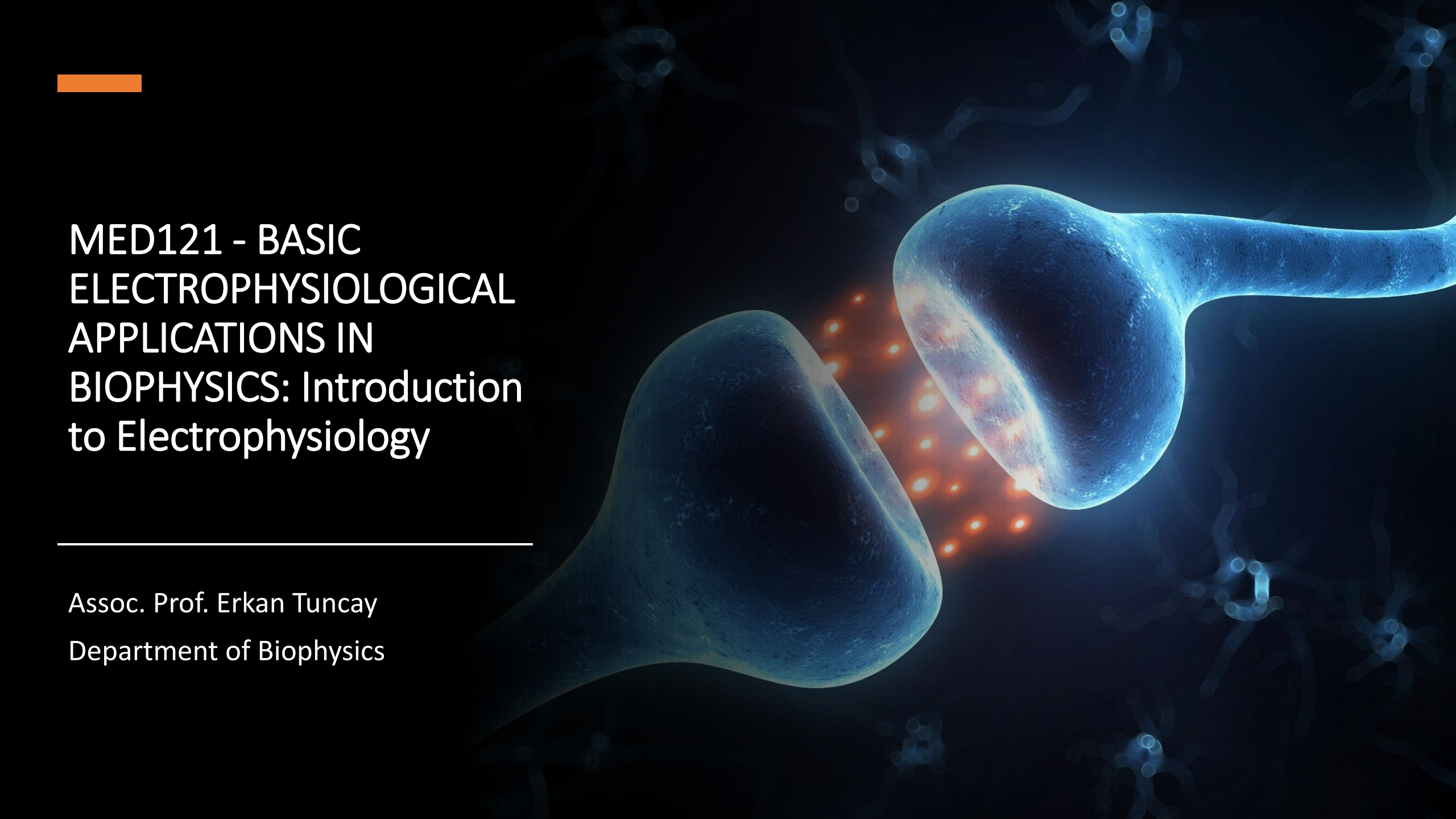
MED121 - BASIC ELECTROPHYSIOLOGICAL APPLICATIONS IN BIOPHYSICS: Introduction to Electrophysiology



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Department of Biophysics

Outline:

- Course details
- Learning activity
- What is Electrophysiology?
- Brief information about electrophysiological methods

Course details

The basic and clinical science research in several of the laboratories in the universities and the institutes makes extensive use of single-cell electrophysiological methods.

The scope of this course is to

- learn basic electrophysiological methods and applications,
- the importance of academic studies,
- how basic science research is carried out in the universities and institutes
- writing a scientific article and publishing processes.

Learning Activity

- Presentation
- Homework, journal club
- Interactive sessions through Zoom, Slack or other applications

Weekly subject distribution

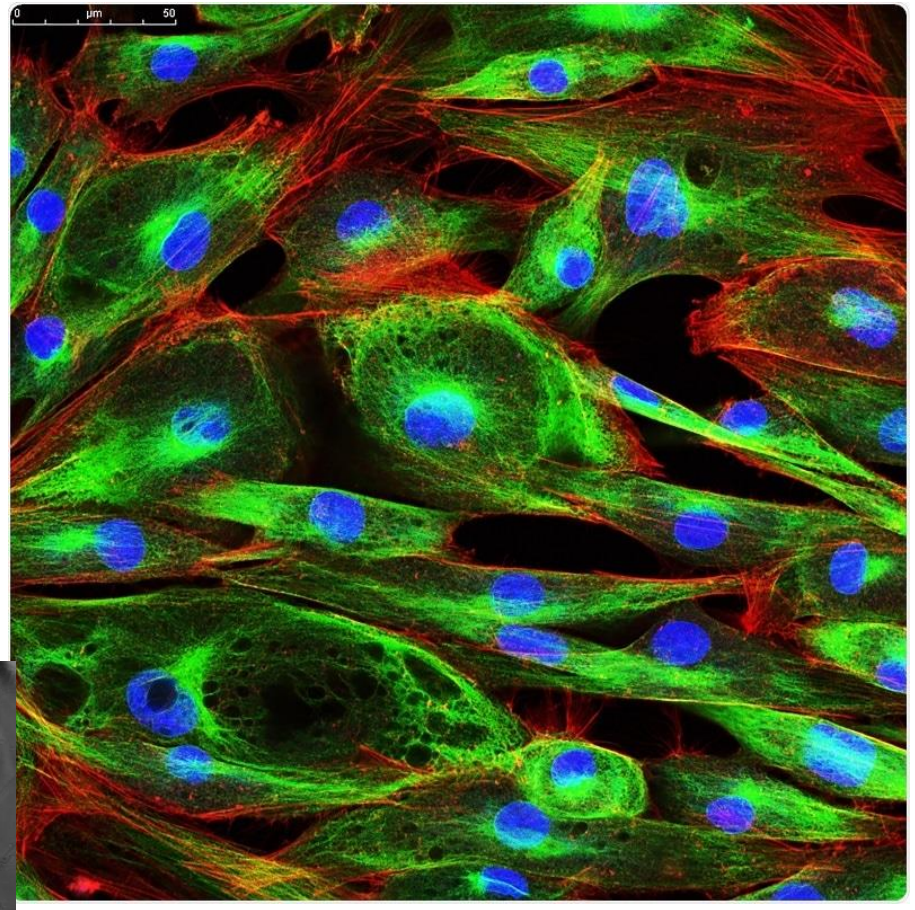
- 1. week: Introduction to Electrophysiology
- 2. week: Basic Electrophysiological Methods
- 3. week: Cardiac Electrophysiology
- 4. week: Cell culture techniques
- 5. week: Study design in cell culture
- 6. week: Patch-Clamp technique-I
- 7. week: Patch-Clamp technique-II

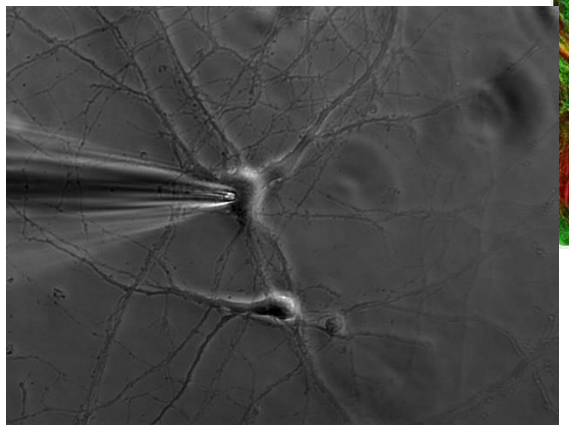
Weekly subject distribution

- 8. week: Basic Imaging Techniques
- 9. week: Basic Imaging Applications, Techniques and Image analyzes in Electrophysiology-I
- 10. week: Basic Imaging Applications, Techniques and Image analyzes in Electrophysiology-II
- 11. week: Cardiac muscle contraction recordings and analysis-I
- 12. week: Cardiac muscle contraction recordings and analysis-II
- 13. week: Electrophysiological application in clinics
- **14. week: Interpretation of scientific article (journal club)**

What is Electrophysiology?

- Electrophysiology is a field of research that deals with the electrical properties of cells and biological tissues. Using various stimulation techniques along with a selection of quality equipment and setup design can give rise to a wealth of applications in electrophysiology.





What is Electrophysiology?

- Electrophysiology studies are a direct way to measure neuronal function, detect pathological functional abnormalities and analyze changes in spontaneous and evoked electrical signals in response to therapeutics or disease modeling. Up- or down-regulation of synaptic transmission can shed light on cellular and network mechanisms of numerous CNS diseases, including yet not limited to Alzheimer's disease, Parkinson's disease, Autism, and Pain.

How will electrophysiology studies help our research?

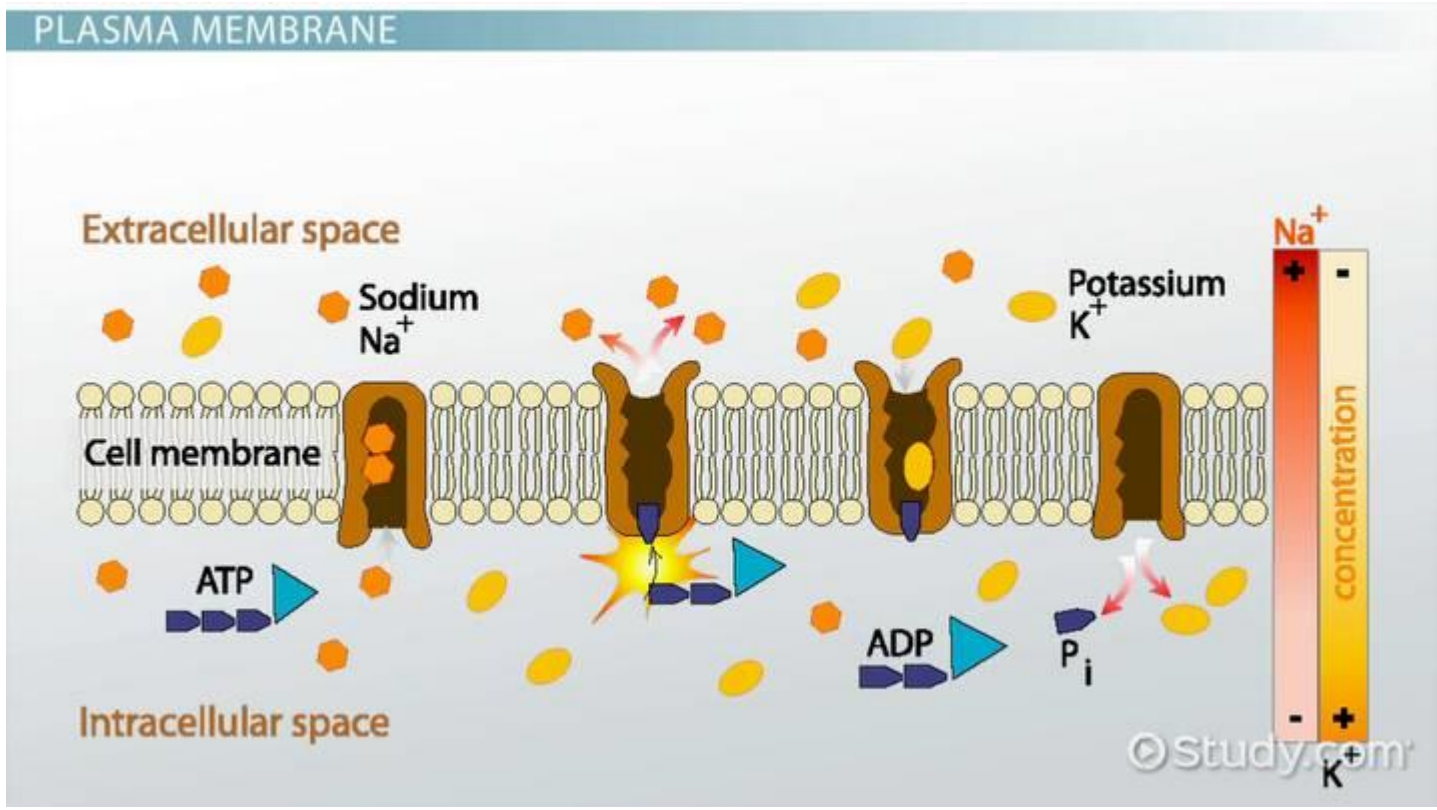
- Your compound can be evaluated *in vivo* or *in vitro* under the most physiologically relevant conditions to probe mechanisms of action questions addressed at probing the effects on specific neurons, receptors, ion channels or neurotransmitter systems. Electrophysiology studies can provide functional abnormalities of neuronal circuitry in genetic or pharmacological models of CNS disorders such as Alzheimer's disease, Parkinson's disease, Huntington's disease, epilepsy, ataxia, schizophrenia and other psychiatric disorders.

What kind of information do you get from electrophysiology studies?

- Electrophysiological recordings directly measure endogenous neural function. Spontaneous or evoked electrical events generated by individual neurons or large neuronal populations reflect voltage changes from ligand gated ion channels. These voltage changes tell us important features about a single neuron or neuronal population derived from various endpoints related to amplitude, frequency and waveform morphology.

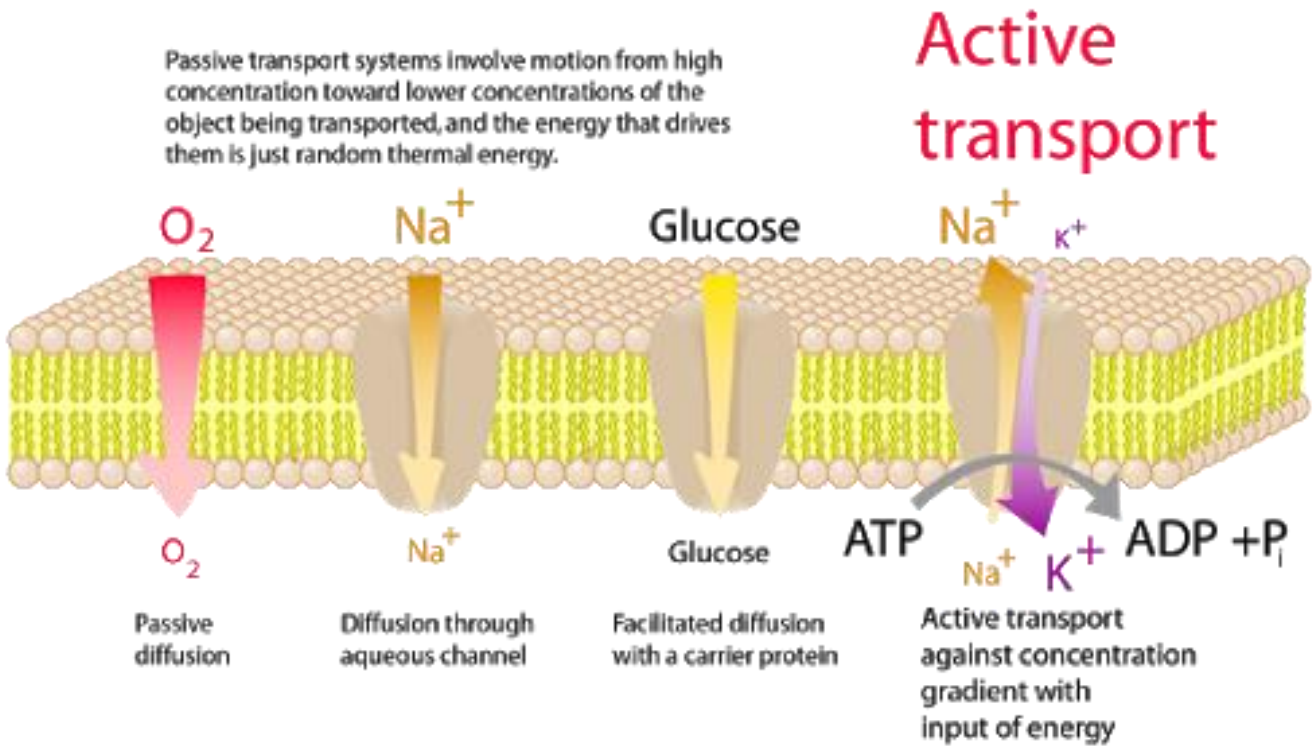
Electrical properties of cells

- A cell derives its electrical properties mostly from the electrical properties of its membrane. A membrane, in turn, acquires its properties from its lipids and proteins, such as ion channels and transporters.



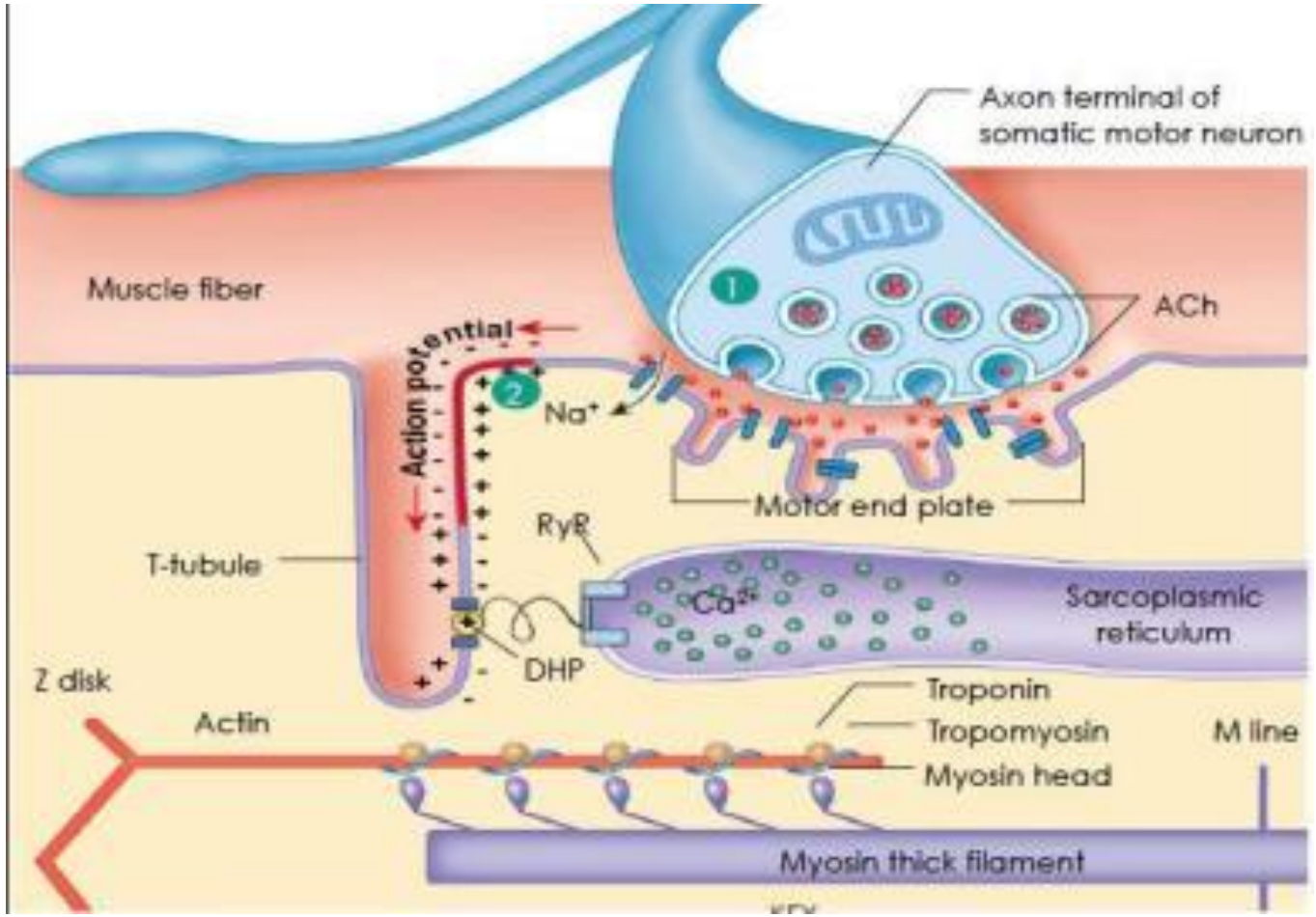
Electrical properties of cells

- Transmembrane proteins allows ions to cross the membrane. This happens in varios ways
  - Passive diffusion
  - Active diffusion
  - Facilitated diffusion



Electrical properties of cells

- The action potential describes the molecular basis of electrical activity within the cells.
- Neurons communicate with each other via electrical events called ‘action potentials’ and chemical neurotransmitters. At the junction between two neurons (synapse), an action potential causes neighbouring neuron to release a chemical neurotransmitter.



Basic Electrophysiological Methods

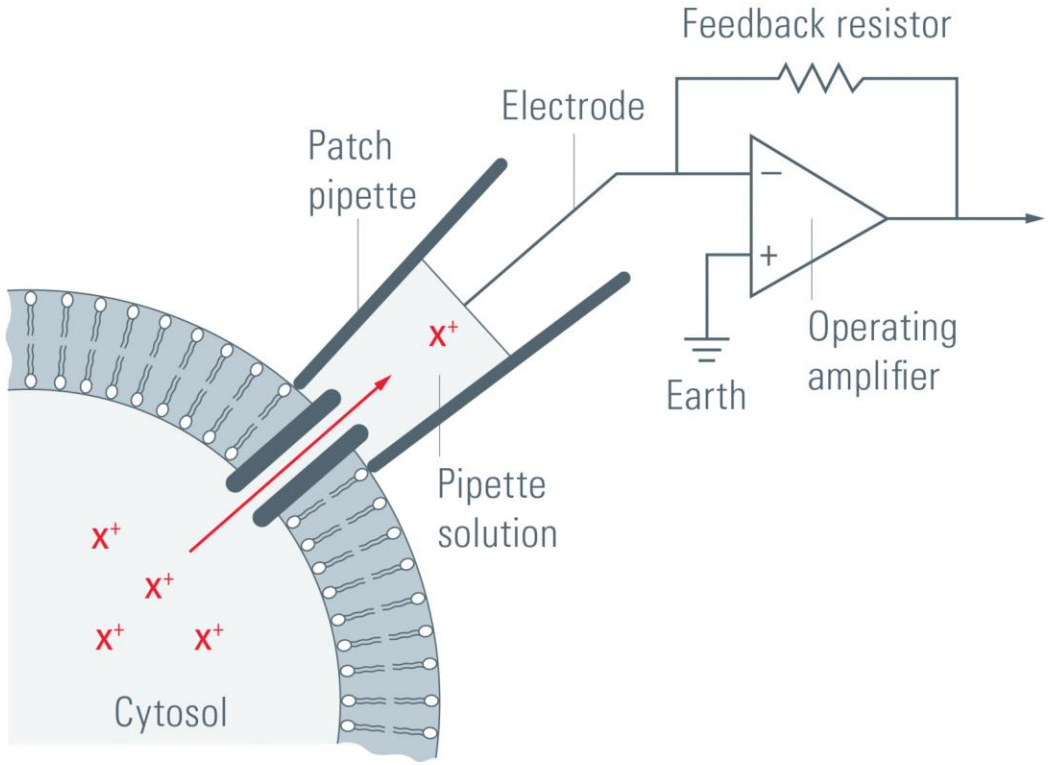
- Electrophysiological techniques commonly used for the study of ionic currents and the ion channels that mediate them. These techniques include electroencephalograms (EEGs), electrocardiograms (ECGs), single- and multiunit extracellular recording, multielectrode arrays, transepithelial recording, impedance measurements, and current-clamp, voltage-clamp, patch-clamp, and lipid bilayer recording.

Patch Clamp Electrophysiology

- Patch-clamp **electrophysiology** provides the highest resolution recordings from a single neuron down to a single channel. Physiological and pharmacological questions can be answered using this technique to understand mechanisms of action. Patch clamp is performed both *in vitro* and *in vivo* to evaluate compound effects on single proteins and receptors. These electrophysiology studies are routinely used to evaluate mechanism of action, disease modeling and high throughput **ion channel screening for hit discovery** in **neurodegeneration**, **pain**, **seizure** and psychiatric disorders.

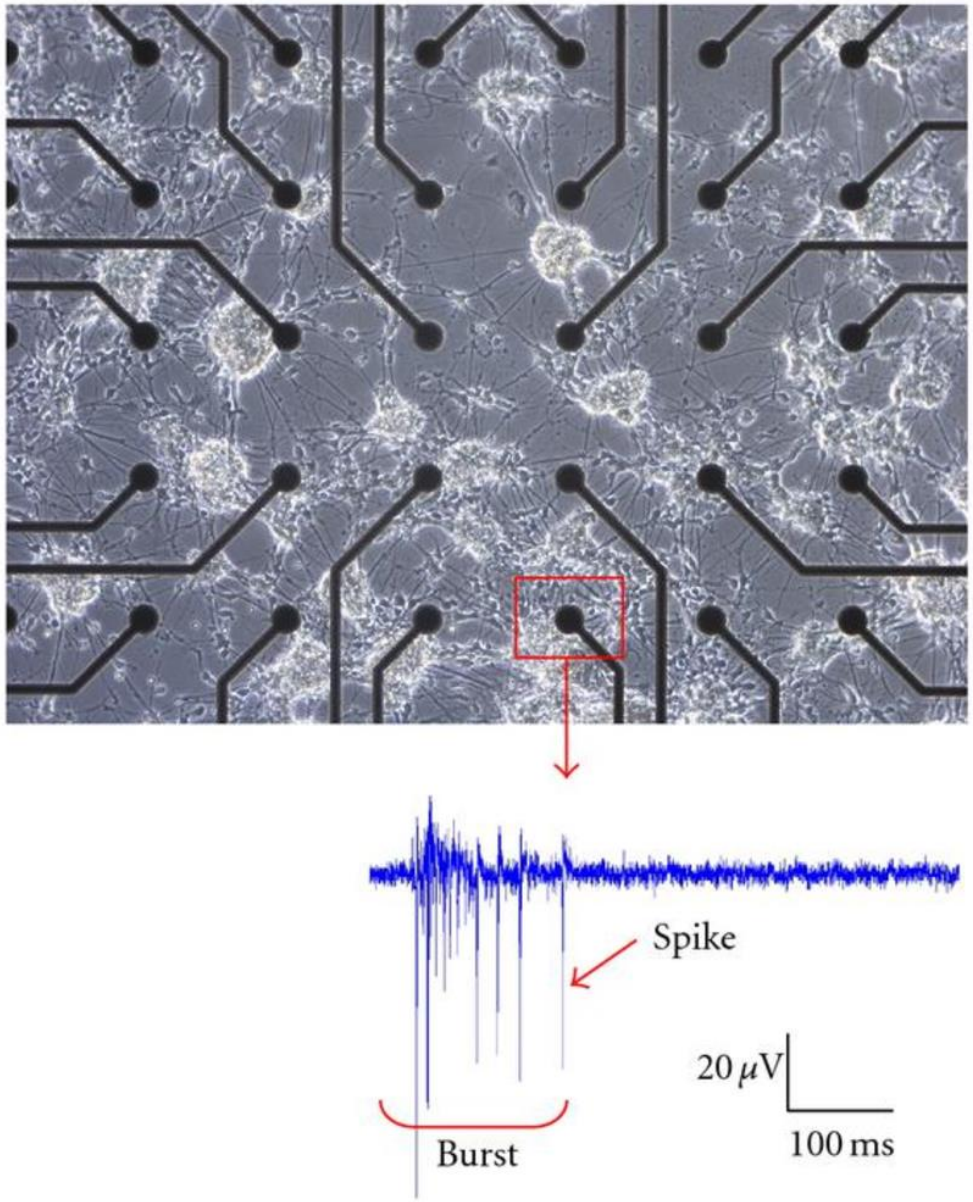
The Patch-Clamp Technique

- The patch-clamp technique allows the investigation of a small set or even single ion channels. It is thus of special interest in the research of excitable cells such as neurons, cardiomyocytes and muscle fibers.



Multielectrode Array

- Multielectrode array is an array of microscopic electrodes distributed over a small surface area. They are spaced to cover the center of a single or multi-well. Multielectrode array recordings enable high throughput field potential recordings of brain slices, dissociated tissues, organoids, spheroids or 2-D neuronal cell culture.
- **The arrays are suitable for laboratory and for acute or chronic animal studies. Fabricated on flexible polyimide using advanced materials and thin-film processing techniques, the arrays provide unmatched design flexibility, optimum electrode properties, and long-term in vitro and in vivo stability.**



Antonio Novellino and José-Manuel Zaldívar; 2010

Determination of the electrophysiological properties of iPSC-derived Atrial and Ventricular Cardiomyocytes by using the Microelectrode Array

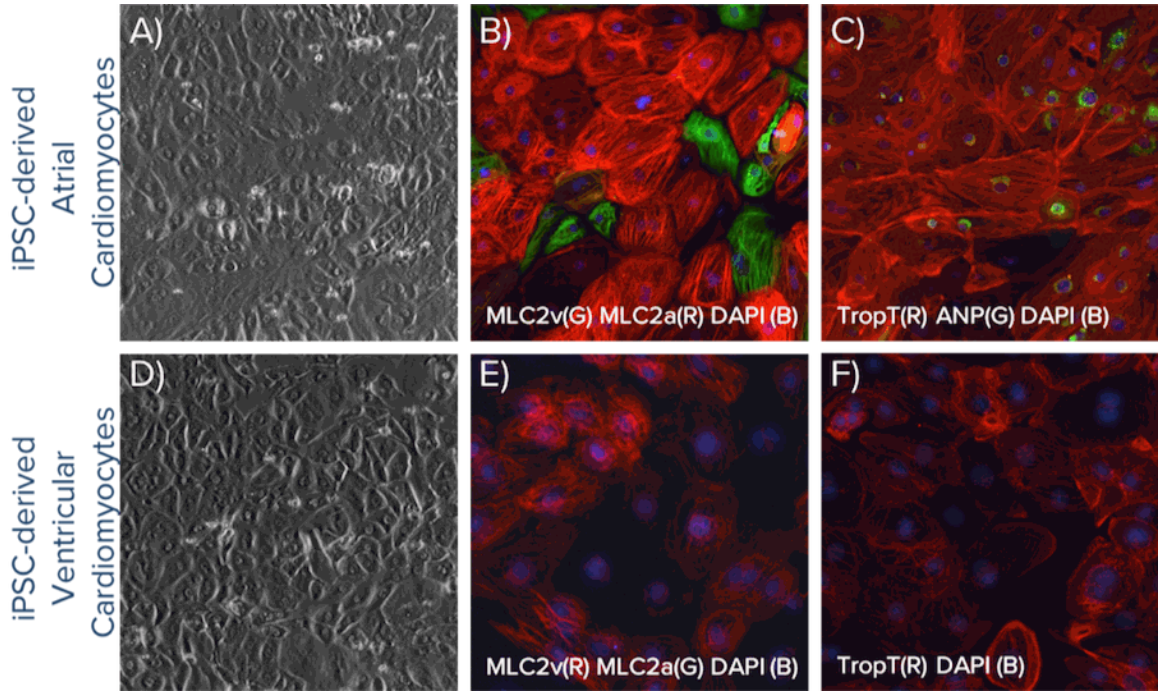
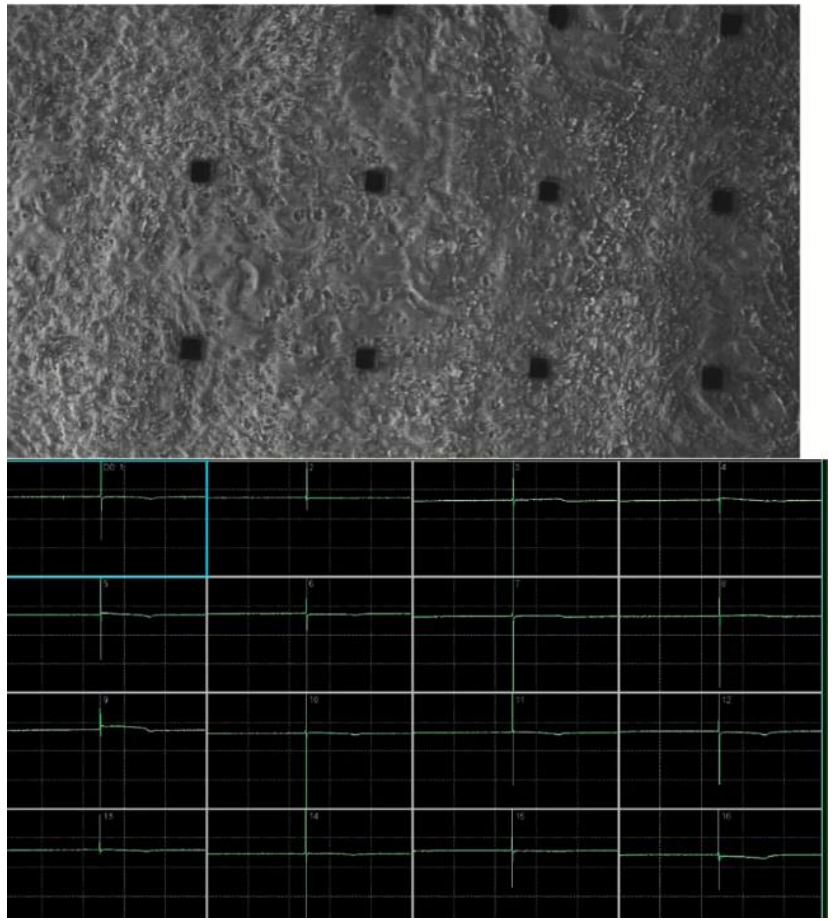


Figure 1: Phase contrast (A & D) and immunocytochemistry (B, C, E & F) images of Human iPSC-derived Atrial and Ventricular Cardiomyocytes after 8 days of culture express typical morphology and express the expected cardiac markers MLC2a (B), MLC2v (E) Troponin T and ANP (C & F).

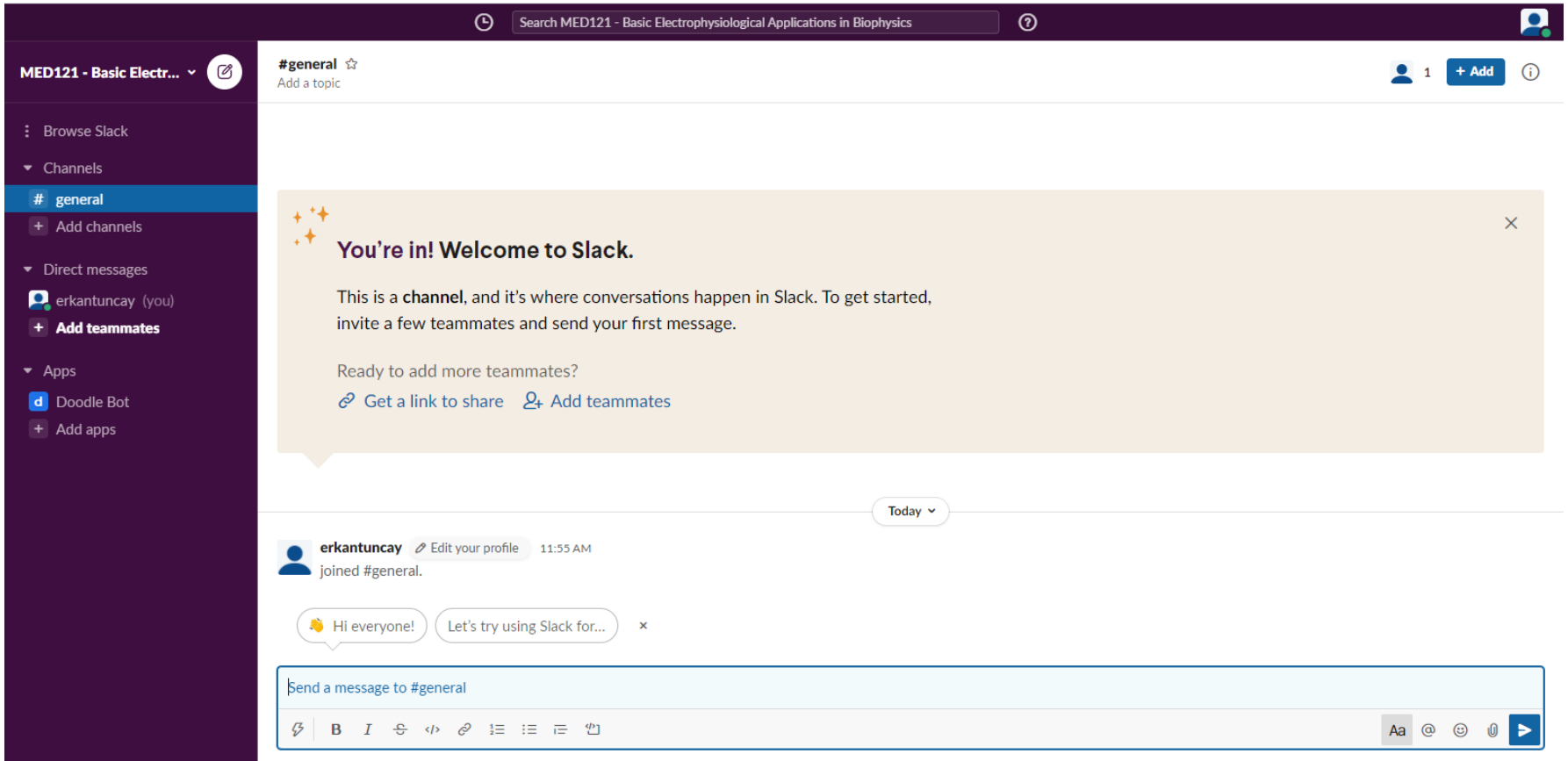


Representative beat rate recorded from Human iPSC-derived Atrial Cardiomyocytes using an Alpha MED Presto MEA platform.

Interactive sessions

Slack account for general and scientific discussions:

- https://join.slack.com/t/newworkspace-h7r7587/shared_invite/zt-hxwtgzlg-TmgLvqbF2Qd82aZxoLRr1Q



References:

- Biyofizik; Prof. Dr. Ferit Pehlivan
- Hücre Elektrofizyolojisi ve Görüntülemenin Temelleri; Prof. Dr. Nuhan Puralı
- Ion channels of Excitable Membranes; Bertil Hille
- Fluorescence microscopy, B. Herman
- Scientific articles related to electrophysiology

What is Confocal Imaging?

- https://www.azolifesciences.com/article/What-is-Confocal-Imaging.aspx

- https://www.youtube.com/watch?v=drykDg5p0O4