Massively Parallel All-Optical Cardiac Electrophysiology

Professor Emilia Entcheva
Department of Biomedical Engineering, George Washington University, Washington DC, USA

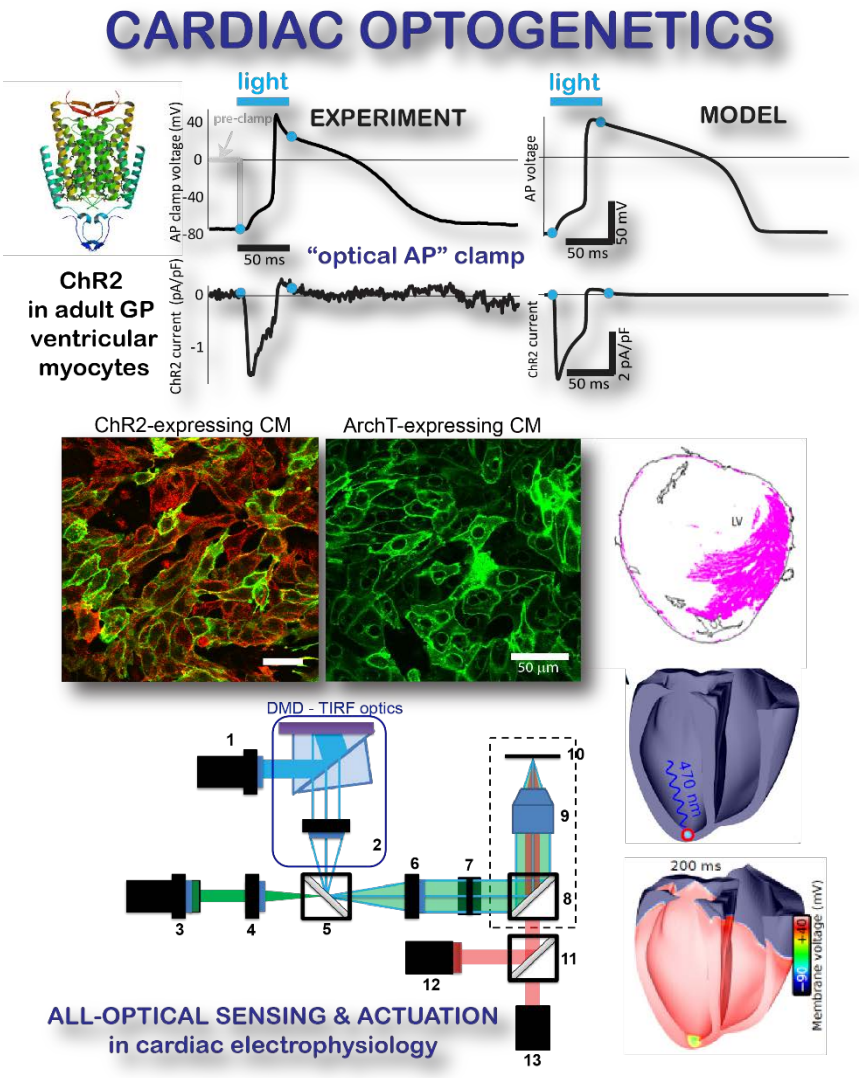
Abstract

Optical targeting (stimulation or recording) allows distributed parallel access to thousands and even millions of cells and locations at the same time, and within the tissue setting; optical targeting is high-throughput by nature. In this talk, I will discuss and demonstrate the combination of optogenetic stimulation with optical imaging of electrical activity in cardiomyocytes, i.e. the realization of "all-optical electrophysiology" in a high-throughput manner (HTS). Examples will include demonstration of cardiac "wave steering" by light and the use of a new fully-automated all-optical HTS platform (OptoDyCE) for drug screening using patient-derived cardiomyocytes (iPS-CMs).

Bio

Dr. Emilia Entcheva is a Professor of Biomedical Engineering at George Washington University; she recently moved her laboratory to Washington DC, after 15 years as faculty at Stony Brook University. She directs the Cardiac Optogenetics and Optical Imaging Laboratory. Her research group has contributed to the development of new tools for optical mapping of cardiac excitation, computational modeling of cardiac electrophysiology, as well as innovative techniques to engineering cardiac tissue and its functional characterization using lab-on-a-chip platforms. Since 2010, her group has spearheaded efforts in shaping a new field, cardiac optogenetics (the genetically-mediated light sensitization of cardiac cells and tissue), and the development of highly-parallel all-optical cardiac electrophysiology. These developments open new possibilities for mechanistic studies in cardiac arrhythmias using "live tissue simulations" and "wave control" by light; importantly, they offer for the first time the opportunity for high-throughput cardiac cell electrophysiology as a much desired tool in (personalized) cardiotoxicity screening and in drug development.

Images:


CARDIAC OPTOGENETICS
light
EXPERIMENT
light
MODEL
pre-clamp
AP clamp voltage (mV)
40
0
-40
-80
50 ms
AP voltage
50 mV
50 ms
"optical AP" clamp
ChR2
in adult GP
ventricular
myocytes
ChR2 current (pA/pF)
0
-1
ChR2 current
2 pA/pF
50 ms
ChR2-expressing CM
ArchT-expressing CM
50 µm
LV
DMD - TIRF optics
1
2
3
4
5
6
7
8
9
10
11
12
13
470 nm
200 ms
Membrane voltage (mV)
ALL-OPTICAL SENSING & ACTUATION
in cardiac electrophysiology