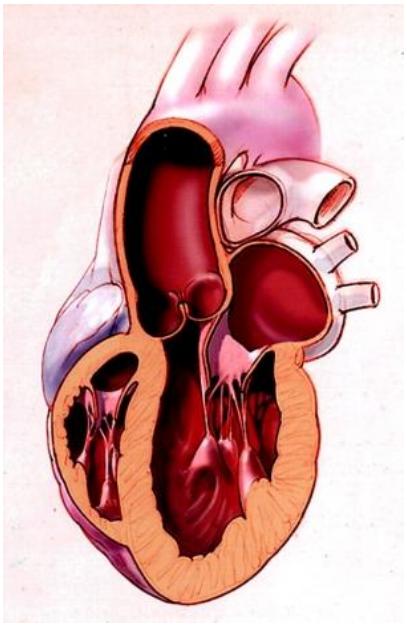
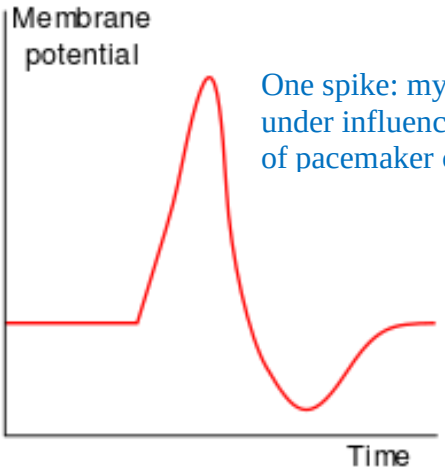
Research (What is it about?)	**Biochemistry of heart failure**
UNN authors	*Shilnikov A.*
We find (The result)	By highly detailed mathematical model of mouse ventricular myocytes we disclose the key mechanisms underlying the continual transition towards a state of heart failure. We show that the slow component of the fast Na^+ current is a key determining factor for the onset of bursting activity in mouse ventricular myocytes.
Abstract	Elementary electro-chemical model of heart muscle cell (***ventricular myocytes***) describes the dynamics of its action potential as a result of summing the fast Na^+ and slow Ca^{2+} currents through selectively penetrable membrane, which is possessed of ***trigger*** features, under influence of electrical signals of pacemaker cells. This model in principle can't describe many actually observed processes in myocytes, pathological ***arrhythmia*** in particular, which leads to heart failure. Real biochemistry of myocytes is much more complicated than the above described model. Large amounts of experimental data on cell processes and their parameters have been accumulated so far. They differ not only for different types but sometimes for different genetic lines of the same type, mouse for example: wild type (WT) and transgenic (TG) mice. We have constructed a complex mathematical model of ventricular myocytes which takes into consideration ***all*** known electrochemical processes with experimentally measured parameters as for WT so for TG mice. The unknown mathematical parameters have been reconstructed by ***Markov modeling process*** on the basis of known experimental data. This model includes 40 first order ordinary differential equations which are solved by forth order Runge-Kutta method for two types of ***stimulation protocols***. The first one is the standard protocol, which stimulates cardiac cells with a sequence of small pulses of current with pulse duration 1 ms (periodic stimulation). The second protocol using constant stimulus currents (steady-state stimulation). In the latter case, the model becomes an autonomous dynamical system with rich and complex dynamics compared to mouse ventricular myocytes at the standard protocol. It is shown that under the steady-state current stimulation depending on its value along with the regular mode of action potential (spiking activity) the irregular mode (bursting activity) it may occur. It is proved that the ***slow component of the fast Na^+ current*** through the membrane is the key biochemical factor of this arrhythmia.

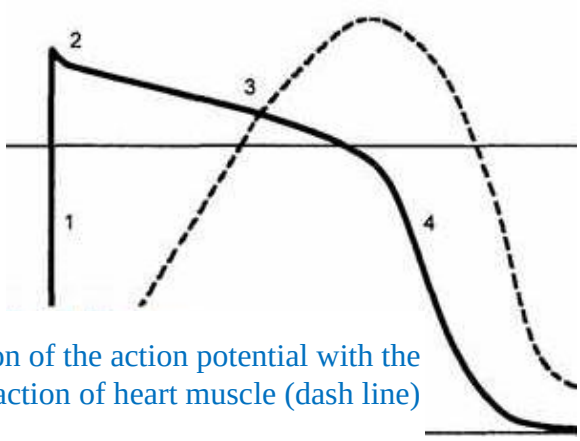
Representative articles 2017-2018, quartiles	1. *Bondarenko V.E, Shilnikov A.L.* Bursting dynamics in the normal and failing hearts. Sci. Reports. **7:**5927 (2017).	Q1
	Q-index (Qi) for the result	**4**
	high blue	

In collaboration	Georgia State University, Atlanta, GA 30303 USA



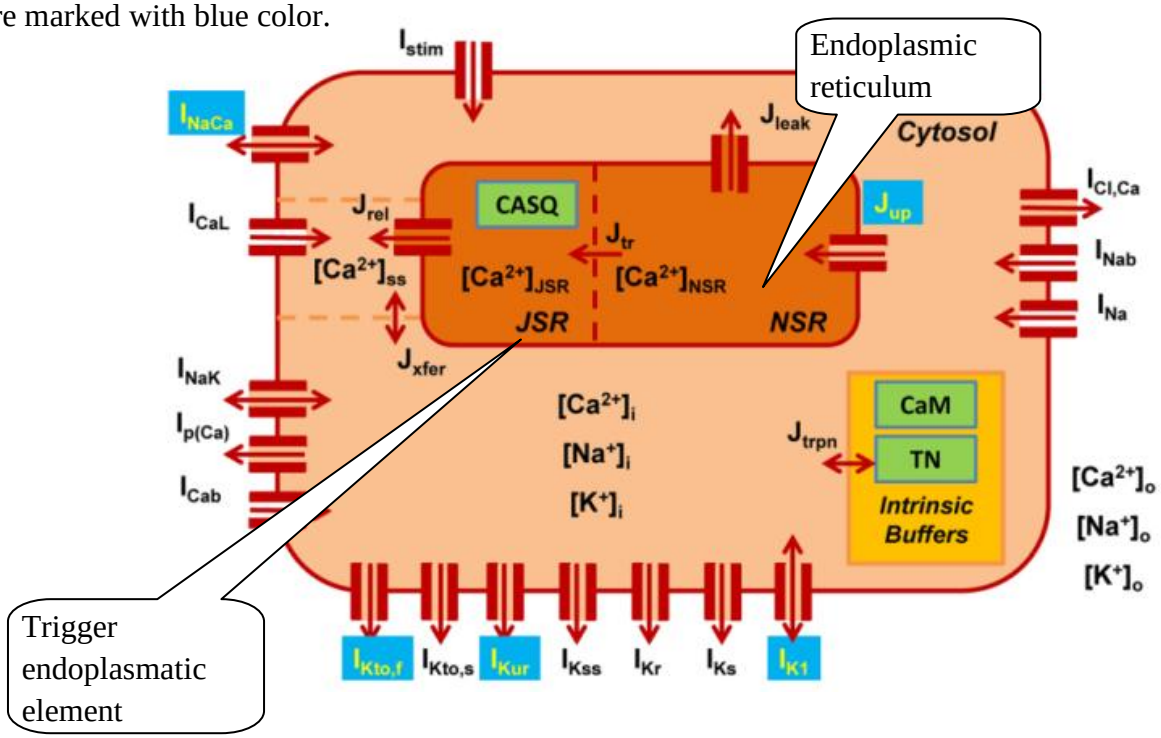


One spike: myocytes action potential under influence of electrical signal of pacemaker cells.



Collation of the action potential with the contraction of heart muscle (dash line)

Schematic diagram of the mouse ventricular myocyte model that includes ionic currents Ca^{2+}, Na^{+}, K^{+} (**I**) and Ca^{2+} fluxes (**J**). The differences between WT and TG mice are marked with blue color.



An example of myocytes bursting activity under the steady-state current stimulation.