## Voltage across a hydrogel: A new perspective on cell's membrane potential and its implications for early embryogenesis.

Two general features characterize each healthy cell: its ability to maintain an ion concentration gradient across the cell membrane and its ability to generate an electric potential difference between the cytosol and the extracellular fluid. Inside of a cell the concentration of potassium ions  $(K^+)$  is much higher than that of sodium ions  $(Na^+)$ , while the situation is reversed outside of the cell. It is recognized that the difference in ion concentrations is maintained by energy consuming pumps located in the cell's membrane. Another associated theory is that of membrane channels, which allow ions to move through the membrane down their concentration gradients, but at different rates. Because  $K^+$  ions move out of the cell at a faster rate than  $Na^+$  ions penetrate in, a difference in voltage across the cell membrane is created. This results in a negative voltage of a cell with respect to its outside. The magnitude of this voltage, called resting membrane potential, defines physiological state and function of the cell.

Different resting membrane potential is characteristic for different cells' types. Plastic (undergoing changes and fast division), embryonic, steam, but also cancerous cells have less negative potential than terminally differentiated cells. So, if we can affect membrane potential, we can possibly control cell's performance. It is very intriguing idea to find a specific space, determined by some physico-chemical parameters (e.g. pH, CO<sub>2</sub>, infrared radiation, electrolytes), for each cell type. Then adjusting those parameters could allow shifting cells from one state to the other. In fact, it has already been shown that by changing resting potential it is possible to reversibly block cell division. Having in mind that e.g. cancerous cells have specific potential that determines their proliferative ability, affecting voltage could hamper their spreading. Then, adjusting resting potential can affect regenerative properties of different tissues or organs, by stimulating division of respective cells. As already suggested by other studies, control of electric potential could become very useful tool in medicine.

Our study in particular will focus on the effect of gel-like characteristics of the cell on its electric properties. Ionic pumps and channels, now assumed to be solely responsible for generating membrane potential, are highly sophisticated biological machineries using metabolic energy to function. In fact, since early days of introducing of membrane theory, there have been some concerns, that cell cannot produce enough energy to support their work. And there have been experiments showing that cell can maintain its electric properties even without an intact cell membrane. This is because cell cannot be treated simply as a bag of aqueous solution enclosed by a membrane, without which its content would leak and mix with the surrounding fluid. Cell is in fact a gel-like body maintaining its integrity even when membrane continuity is affected. And gels have many well-studied properties, some of which resemble fundamental features of living cells. For example, many gels generate negative electric potential. And in fact, it has been already shown that gelatinous components of a cell can create voltage without the input from membrane-based pumps and channels.

We are used to think of any properties of a cell as resulting exclusively from biological processes. But there is also chemistry and physics of different states of matter, e.g. gels, that applies also to biological world and at cellular level. While ionic pumps and channels, definitely play their role in fine-tuning of electric potential, it seems plausible that cell does not have to expend its energy on simply maintaining potential at its resting value. Cell's intrinsic gel-like state may support the latter feature. Based on these considerations, we would like to create abiotic, gel-based model of membrane potential generation. We can use this model to study effects of specific stimuli – CO<sub>2</sub> (respiratory gas), infrared (metabolic heat) and mechanic deformation - on electric potential. Model's predictions can be verified in systems involving living cells. We will start from algal cells and proceed toward animal embryos. Control of membrane potential can be very useful tool for emerging applications in medicine founded on bioelectrical, rather than biochemical, communication. In our work, we will first focus on the role of membrane potential in embryogenesis, the first and fundamental process in organism development. At this stage continuous exchange of information, also by bioelectrical signaling, is absolutely crucial for proper cell division and differentiation.