PROJECT SUMMARY

Bioelectronics has a double meaning in scientific literature. On the one hand, as a branch of basic biophysical sciences, it deals with electric phenomena appearing on any organization level of living systems (A). On the other hand, as a recently developed discipline of information technological science, it explores the potential of biological materials for application in molecular electronics (B). In both disciplines, interfaces between structural units play a crucial role. Our main goal is to develop novel experimental methods based on integrated micro- and nanotechnological platforms, as well as theoretical models, to study biological interfaces, and utilize them in both branches of bioelectronics. Besides its impact on basic biophysical science, this research is expected to have various applications in molecular electronics.

BACKGROUND OF THE STUDY

A) Electric signals associated to membrane transport processes

Electric phenomena, ubiquitous in living systems, carry a lot of information about basic physiological processes that are inaccessible to other techniques (e.g., ECG or EEG). All they can be traced back to the cellular level, namely to membrane-coupled signal- and energy transduction processes. The importance of methodological developments aiming at the detection of the associated electric signals is underpinned, e.g., by the Nobel Prize given for the patch clamp technique (Neher and Sackmann, 1991).

However, application of the most commonly used microelectrode methods to the investigation of transmembrane ionic currents often fails due to technical limitations, while alternative optical techniques still suffer from fundamental sensitivity and time resolution problems. Active pump currents, therefore, are still measured on suspensions of cell organelles or cells by macroelectrode methods, in whose elaboration our institute in Szeged played a determining role. The generalization of one of our techniques allowed the detection of intramolecular electric signals in all the three spatial dimensions.

B) Protein-based integrated optical switching

Since the start of integrated electronics, the expansion of development has been described by “Moore’s law”: the density (performance) of integrated electronic circuits doubles about every 1.8 years. While this “law” has remained proven valid for a remarkable period of 30 years, there is a general perception that the evolutionary development has reached a limit. It is agreed that future development needs revolutionary new principles. Presently, all possible candidates are explored in the search for new routes. Molecular electronics combined with optical data processing is regarded as being among the most promising emerging alternative technologies. Coupling of optical data-processing devices with microelectronics, as well as sensory functions, is one of the biggest challenges in molecular electronics.
Suitable nonlinear optical (NLO) materials with high stability and sensitivity are being intensively researched. In addition to organic and inorganic crystals, biological molecules have also been considered for use in optoelectronics, among which bR has generated the most interest.

RELEVANT RESEARCH IN THE HOST LABORATORY

A) Recent developments in nanotechnology offer the opportunity of a natural extension of our techniques to the investigation of interfaces of single cells or cellular monolayers forming biological barriers. In line with this, we have measured electric signals associated to the signal transduction processes of the phototaxis of Chlamydomonas cells by a modified light gradient method. Comparing the signals detected with and without a pre-orienting light, it was possible to separate signal components generated in different regions of the plasma membrane (eye spot, flagellae). The method represents an ideal tool for in vivo testing point mutants of the visual pigment of Chlamydomonas, „Channelrhodopsin”, that plays a key role in a whole new branch of neuro-electrophysiological applications (optogenetics).

Besides proceeding with the topics above, we are going to utilize our expertise to establish various lab-on-a-chip measuring platforms for the investigation of the active and passive electric properties of living cells and endothelial tissues, combined with a microscopic control. Endothelial membranes play a role analogous to cell membranes on a higher level of hierarchy, hence they may serve as an ideal model system to investigate the primary processes associated with inflammation and related diseases. The research is going to be carried out in cooperation with the group of Prof. Mária Deli (Lab of Neurobiology).

B) We suggested the application of this protein as an active, programmable nonlinear optical material in all-optical integrated circuits, and demonstrated the first integrated optical switching by bR, with a switching speed of ca. 1 μs. Based on these findings, a USA patent [Light-driven integrated optical device (US 6,956,984 B2)] was registered in 2005. Later on, we improved the switching time to ca. 10 ns, still behind the state of the art (some 100ps). Eventually, using the picosecond BR-K and the subpicosecond BR-I transitions, we have recently demonstrated switching speeds increased by several orders of magnitude, to subpicosecond switching times, well beyond the present state of the art. This superior performance brings biomaterials to the frontline of modern photonic technology.

A novel, all-optical biosensor was also created using a thin bacteriorhodopsin film of unique nonlinear optical properties as an active element of the device. The passive part of the sensor consisted of an integrated optical Mach-Zehnder interferometer produced by the direct laser writing technique. After a thorough optical test, the sensor was successfully applied to detect protein-protein interactions (antigen-antibody reactions).

In addition to its impact on basic biophysical science, we expect our Bioelectronics research to have various applications in molecular electronics and medical diagnostics.

SPECIFIC AIMS

The PhD studies will focus on the investigation of electric (and optical) properties of biological barriers (represented by cell- or monocellular membranes) occurring on various levels of organization in living organisms, as well as on seeking for possible optoelectronic applications. Relevant methodological developments will be of special interest.
MATERIAL AND METHODS

- Preparation of microfluidical, optical and microelectronic structures, and performing electric and optical measurements to investigate biological barriers. Relevant techniques: photopolymerization, soft lithography, metal coating of surfaces.
- Preparation and cultivation of proteins (bacteriorhodopsin, photoactive yellow protein), cells (e.g., Chlamydomonas, E. coli, blood cells) or monacellular membranes (of endothelial and epithelial cells), respectively.

SUGGESTED READINGS

Vsevolodov NN: Biomolecular Electronics, Birkhauser, Boston (2011)

SNAPSHOTS FROM THE HOST LABORATORY

Significant publications

Representative recent research grants
„Fénnyel gerjeszthető membránok bioelektronikája” (NKTA-OTKA, 2009-2013)
„Impulzuslézerek alkalmazása a biofotonikában” (TÁMOP, 2012-2014)

Some of the latest students in the laboratory
Fábián L, Ph.D., (2013), „Integrated optical applications of bacteriorhodopsin”
Czeller T, B.Sc., 2013-2014, „Miniaturized biotechnological tool for the investigation of monacellular membranes”
Petneházi A, B.Sc., 2013-2014; „Effect of medium flow on the structure and function brain endothelial membranes”
Mathesz A, Ph.D., 2011-recent; title to be announced
Kincses A, Ph.D., 2012-recent; title to be announced
Újvárosi A, B.Sc., 2014-recent; title to be announced
Szombati A, B.Sc., 2014-recent; title to be announced
Krekic Sz, B.Sc., 2013-recent; title to be announced
Volosin M, B.Sc., 2014-recent; title to be announced