

A MULTI-DISCIPLINARY RESEARCH AND TEACHING PROGRAM IN BIOMEDICAL ENGINEERING FOR DISCOVERY AND UNDERSTANDING OF CELL COMMUNICATION

Stuart Tobet, Charles Henry, Michael DeMiranda, Thomas Chen

School of Biomedical Engineering, Colorado State University, Fort Collins, CO, USA

This project provides an innovative program for developing a new generation of scientists in biomedical science and engineering that are trans-disciplinary in their training, better equipped for multilevel communication across ages (GK-12) and fields (e.g., industry interaction), and finally prepared to take leadership roles for scientific inquiry and progress into the 21st century. The research component consists of activities in sensing, modeling, and understanding how molecules move and the functions of multi-cellular tissues and organ systems in response to external chemical and physical stimuli through intercellular communication. The research project focuses on studying the release of key molecules of intercellular communication in brain, pituitary, and gonads and their effects on cell behavior. Additional project components also examine ways in which such data can be modeled and interpreted for maximum understanding of complex processes. Among the molecules of interest, there are major advantages for biosensor technologies that are amenable to electrochemical detection. (e.g., 1). The project is particularly interested in the detection of molecular gradients in extracellular space that are essential for the development of tissue and organ systems as well as marking the response to external chemical and physical stimuli (2, 3). Such gradients are difficult to detect because molecules released into extracellular space are not readily fixable in space by the vast majority of histological methods (4). Advanced silicon technology is being used to build dense biosensor arrays with the resolution of single cells, and that can operate at high frequencies to achieve sufficient temporal resolution to visualize molecules released to communicate between cells.

The results of the microscopic approach must be interrogated using state of the art techniques of data and image analysis. Using in vitro slice preparations from developing mammalian embryos, there are multiple patterns of cell migration in different brain regions (e.g., 5, 6, 7), including significant cell mixing, and the identification of apparent boundaries. The number of different fluorophores useful for cellular level imaging has exploded over the last 10 years. Visual imaging is being combined with electrochemical methods to yield synergisms in molecular information processing. Micro-sized biosensor arrays will allow the detection of small currents with micron resolution, and yield chemical data to complement optical methods. The broad impact of the program is three-fold: 1) the research is critical for continued understanding and advances in fundamental questions facing biology and medicine; 2) it provides a broad framework for incorporating biomedical engineering research in K-12 STEM (Science, Technology, Engineering, and Math) curriculum; and 3) it demonstrates the power of broad partnerships between universities, K-12 education districts, local industry, and international collaboration on improving graduate and K-12 education.

Supported by NSF DGE-0841259.

References

1. Liu Y, Vickers JA, Henry CS. Simple and sensitive electrode design for microchip electrophoresis/electrochemistry. *Anal Chem* 2004; 76: 1513–7.
2. Wolpert L. One hundred years of positional information. *Trends Genet* 1996; 12(9): 359–64.
3. Gurdon JB, Bourillot PY. Morphogen gradient interpretation. *Nature* 2001; 413(6858): 797–803.
4. Tobet S, Henderson R, Whiting P, Sieghart W. Special relationship of gamma-aminobutyric acid to the ventromedial nucleus of the hypothalamus during embryonic development. *J Comp Neurol* 1999; 405: 88–98.
5. Bless E, Walker H, Yu K, et al. Live view of gonadotropin-releasing hormone containing neuron migration. *Endocrinology* 2005; 146: 463–8. [*cell movement video available from Journal Website*].
6. Knoll JG, Wolfe CA, Tobet SA. Estrogen modulates neuronal movements within the developing preoptic area-anterior hypothalamus. *Eur J Neurosci* 2007; 26:1091–9.
7. McClellan KM, Calver AR, Tobet SA. GABAB receptors role in cell migration and positioning within the ventromedial nucleus of the hypothalamus. *Neuroscience* 2008; 151: 1119–31.