

# Biomolecular Information Processing Systems: Design, Optimization and Applications

Evgeny Katz and Vladimir Privman

Department of Chemistry and Biomolecular Science and  
Department of Physics  
Clarkson University, Potsdam NY 13699, USA

Joseph Wang

Department of NanoEngineering, University of California  
San Diego, La Jolla, California 92093, USA

## I. INTRODUCTION

Biomolecular computing is an emerging field of unconventional computing that attempts to process information with biomolecules and biological objects using digital logic. We review enzymatic systems which involve biocatalytic reactions utilized for information processing (biocomputing) [1]. Extensive ongoing research in biocomputing, mimicking Boolean logic gates has been motivated by potential applications in biotechnology and medicine. Furthermore, novel sensor concepts [2] have been contemplated with multiple inputs processed biochemically before the final output is coupled to transducing “smart-material” electrodes and other systems [3,4]. These applications have warranted recent emphasis on *networking* of biocomputing gates. First few-gate networks have been experimentally realized [5], including coupling, for instance, to signal-responsive electrodes for signal readout [6]. In order to achieve scalable, stable network design and functioning, considerations of noise propagation and control have been initiated as a new research direction [7]. Optimization of single enzyme-based gates for avoiding analog noise amplification has been explored, as were certain network-optimization concepts. We review and exemplify these developments, as well as offer an outlook for possible future research foci. The latter include design and uses of non-Boolean network elements, e.g., filters [8], as well as other developments motivated by potential novel sensor and biotechnology applications.

We also overview recent advances in biomedical applications of enzyme-based logic systems, particularly for the analysis of pathophysiological conditions associated with various injuries [9]. Novel biosensors digitally processing multiple biomarker signals produce a final output in the form of YES/NO response through Boolean logic networks composed of biomolecular systems. The biocomputing approach applied to biosensors leads to a high-fidelity biosensing compared to traditional single-analyte sensing devices. By processing complex patterns of multiple physiological biomarkers, such multi-signal digital biosensors should have a profound impact on the rapid diagnosis and treatment of diseases, and particularly can provide timely detection and alert of medical emergencies (along with immediate therapeutic intervention). The novel biosensing concept has been exemplified with the systems for logic analysis of various injuries, including soft

tissue injury, traumatic brain injury, liver injury, abdominal trauma, hemorrhagic shock and oxidative stress [10].

## REFERENCES

- [1] E. Katz and V. Privman, “Enzyme-based logic systems for information processing,” *Chem. Soc. Rev.* 2010, 39, 1835-1857.
- [2] J. Wang and E. Katz, “Digital biosensors with built-in logic for biomedical applications –Biosensors based on biocomputing concept,” *Anal. Bioanal. Chem.* 2010, 398, 1591-1603.
- [3] M. Krämer, M. Pita, J. Zhou, M. Ornatska, A. Poghossian, M.J. Schöning and E. Katz, “Coupling of biocomputing systems with electronic chips: Electronic interface for transduction of biochemical information,” *J. Phys. Chem. C* 2009, 113, 2573-2579.
- [4] E. Katz and M. Pita, “Biofuel cells controlled by logically processed biochemical signals: Towards physiologically regulated bioelectronic devices. (Concept paper),” *Chem. Eur. J.* 2009, 15, 12554-12564.
- [5] V. Privman, M.A. Arugula, J. Halánek, M. Pita and E. Katz, “Network analysis of biochemical logic for noise reduction and stability: A system of three coupled enzymatic AND gates,” *J. Phys. Chem. B* 2009, 113, 5301-5310.
- [6] M. Privman, T.K. Tam, M. Pita and E. Katz, “Switchable electrode controlled by enzyme logic network system: Approaching physiologically regulated bioelectronics,” *J. Am. Chem. Soc.* 2009, 131, 1314-1321.
- [7] V. Privman, G. Strack, D. Solenov, M. Pita and E. Katz, “Optimization of enzymatic biochemical logic for noise reduction and scalability: How many biocomputing gates can be interconnected in a circuit?” *J. Phys. Chem. B* 2008, 112, 11777-11784.
- [8] V. Privman, J. Halánek, M.A. Arugula, D. Melnikov, V. Bocharova and E. Katz, “Biochemical filter with sigmoidal response: Increasing the complexity of biomolecular logic,” *J. Phys. Chem. B* 2010, 114, 14103-14109.
- [9] J. Halánek, V. Bocharova, S. Chinnapareddy, J.R. Windmiller, G. Strack, M.-C. Chuang, J. Zhou, P. Santhosh, G.V. Ramirez, M.A. Arugula, J. Wang and E. Katz, “Multi-enzyme logic network architectures for assessing injuries: Digital processing of biomarkers,” *Molecular Biosystems* 2010, 6, 2554-2560.
- [10] J. Halánek, J.R. Windmiller, J. Zhou, M.-C. Chuang, P. Santhosh, G. Strack, M.A. Arugula, S. Chinnapareddy, V. Bocharova, J. Wang and E. Katz, “Multiplexing of injury codes for the parallel operation of enzyme logic gates,” *Analyst* 2010, 135, 2249-2259.