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Biomolecular Computing: From Unconventional Computing to “Smart” Biosensors and Actuators – Editorial Introduction

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Chemical computing [1] as a subarea of unconventional computing [2] has achieved tremendous development in the past two decades, driven mostly by the idea of making revolutionary changes in computing technology. While the conventional silicon-based electronic technology comes to the physical limit of miniaturization [3], chemical systems might operate at the level of single molecules, bringing information processing systems from the present microsize to novel nanosize [4]. Even more importantly, chemical systems can perform massively parallel computational operations with involvement of as many as 10^{23} molecules, resulting in a speed of information processing presently impossible in silicon-based computers [5]. Motivated by these ideas from computer science, chemists designed sophisticated switchable molecules and supramolecular complexes to perform logic operations and mimic computing systems [6]. Complex chemical reactions with unusual kinetics (e.g., oscillating diffusional systems – Belousov–Zhabotinsky reactions) [7] were suggested as media performing computing operations [8]. Extensive research in the area of reaction–diffusion computing systems [9] resulted in the formulation of conceptually novel circuits performing information processing with the use of subexcitable chemical media [10]. Novel conceptual approaches required for the usage of new chemical ‘‘hardware’’ were designed, resulting in algorithms potentially capable of solving ‘‘hard-to-solve’’ computational problems, thus demonstrating potential advantages of the novel unconventional chemical computing systems over classic silicon-based systems. The present state of the art of the unconventional chemical computing was summarized in the recent Wiley-VCH book: ‘‘*Molecular and Supramolecular Information Processing: From Molecular Switches to Logic Systems*,’’ E. Katz – Editor.

It should be noted, however, that chemical systems designed for information processing usually suffer from two major problems: (i) They are very difficult to prepare – in other words – the synthetic processes required for their preparation are so complex that only a few laboratories are able to prepare and study the switchable molecules operating as the chemical computing ‘‘hardware.’’ This problem is technical rather than conceptual, and it could be solved at the present level of technology if the molecular computing elements find real applications. (ii) The main challenge in further development of chemical information processing systems is

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scaling up their complexity assembling individual logic gates in logic networks [11]. Impressive results have recently been achieved in this direction [6]. Combination of chemical logic gates in small groups or networks resulted in simple computing devices performing basic arithmetic operations such as half-adder/half-subtractor or full-adder/full-subtractor [12]. Integration of several functional units in a molecular structure resulted in multisignal responses to stimuli of various chemical or physical natures, thus allowing different logic operations or even simple arithmetic functions to be performed within a single multifunctional molecule [13]. Despite the progress achieved, assembling complex systems from individual chemical components is very limited and presently achieved only for very small networks incomparable with silicon-based electronic chips. The chemical computing units performing logic operations [6] and functioning as auxiliary ''devices'' (e.g., memory units [14], multiplexers/demultiplexers [15]) are very difficult for integration in functional networks. In other words, each chemical unit might be a perfect computing element, but the integration of this element with other similar elements for their concerted operation is extremely difficult. The difficulty in the interconnectivity of chemical elements in computing networks mostly originates from incompatibility of the chemical input and output signals. The product of the preceding chemical reaction frequently cannot be used as a reagent for the following chemical step. Even more problematic is the use of chemical switchable systems activated by physical signals (such as light [16], magnetic [17] or electrical field [18]) since these signals operating as inputs cannot be reproduced by the chemical reactions and cannot be used for interconnecting several chemical steps in a functional network. This is already a conceptual problem that limits the practical application of chemical systems, keeping them mostly at the level of single units, being scientific ''toys'' rather than practical devices. It is not surprising that these kinds of molecules were not used by Nature in living systems, where interconnectivity between chemical steps is critically important for their concerted operation, being the base of life.

Many of the problems hardly addressable by synthetic chemical systems can be solved naturally by utilization of biomolecular systems [19, 20]. The emerging research field of biocomputing, based on application of biomolecular systems for processing chemical information, has achieved higher complexity of information processing while using much simpler chemical tools, because of the natural specificity and compatibility of biomolecules [21]. Different biomolecular tools, including proteins/enzymes [20, 22], DNA [19, 23], RNA [24], and whole cells [25], were used to assemble computing systems processing biochemical information. Arithmetic functions, for example, full-adder, were realized using RNA as the information processing biomolecular tool [26]. Deoxyribozymes with various catalytic abilities toward DNA assemblies were applied to extend the computing options provided by DNA-based systems [27]. RNA-based computing systems exploit the biological regulatory functions of RNA in cells, thus allowing operation of cells as ''biocomputers'' programed by artificially designed biomolecular ensembles [28]. Recently pioneered DNA molecules with biocatalytic properties mimicking enzyme functions, called *DNAzymes* [29], were extensively used to carry out logic operations [30]. These briefly mentioned biomolecular computing systems represent a rapidly developing research field, and they are already covered by comprehensive review articles, for example,on DNA [31], RNA [32], and DNAzyme [33] biocomputing.

The present book summarizes the diverse subareas of biomolecular computing including (i) various aspects of protein/enzyme information processing systems – Chapters 2–7 (ii) DNA/RNA-based computing systems – Chapters 8–13; (iii) application of whole biological (mostly microbial) cells for biocomputing – Chapters 14–16; as well as (iv) general computational aspects of biomolecular computing – Chapter 17. Chapter 18 offers conclusions and perspectives for the biomolecular computing research area summarized by the Editor.

The variety of the systems described in the book and their possible applications are really impressive. While some of the biochemical systems, particularly represented by DNA computing, follow the general trend of unconventional computing, pretending to bring up novel computational chemical "devices" and algorithms competing with conventional silicon-based computers [34], other systems, mostly represented by enzyme-based assemblies, are directed to "noncomputational" applications, which are more related to "smart" biosensors [35] and bioactuators [36]. Biomolecular systems can perform various automata operations [37], particularly illustrated by the tic-tac-toe game [38]. Much more complex robotic functions of biocomputing systems are also feasible [39]. However, the main expected shorter term practical benefit of biomolecular computing systems is their ability to process biochemical information received in the form of chemical inputs directly from biological systems, offering the possibility to operate in biological environments [40], for biomedical/diagnostic [35] and homeland security applications [41]. Biomolecular logic gates and their networks can recognize various biomarkers associated with diseases [42] or injuries [43] and generate a biomedical conclusion in the binary form "YES"/"NO" upon logic processing of the biomarker concentration patterns. The produced binary output can be extended to a chemical actuation resulting in drug release or bioelectronic system activation controlled by logic conclusions derived from the information processed by biomolecular systems [44]. This research direction will certainly result in tremendous contribution to future personalized medicine [45]. Biochemical systems activated by several chemical input signals processed via logic circuitry implemented in the biochemical assembly can activate/inactivate various bioelectronic devices [46], for example, electrodes [47], biofuel cells [48], and field-effect transistors [49] (Figure 1.1), thus contributing to the next level of sophistication of bioelectronics [50] (Figure 1.2). Chemical signal processing through biocatalytic or biorecognition reactions might be applicable in information security systems performing encoding and encrypting operations as well as providing hiding of information in steganography applications [51] (Figure 1.3). Biocomputing systems can also be used as a part of signal-responsive "smart" materials with functions controlled by logically processed biochemical signals. Various nanostructured materials, including switchable membranes [52]

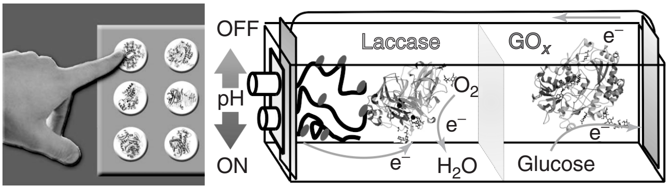

Figure 1.1 A cartoon illustrating biocomputing control over a switchable biofuel cell producing electrical power on demand upon receiving signals processed through an enzyme-based logic system (see [48] for details).

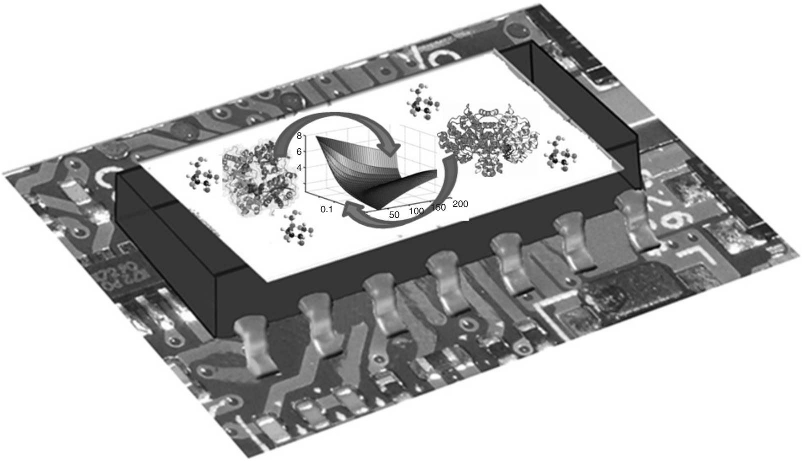

Figure 1.2 An artistic vision of the integration of biomolecular systems with bioelectronic devices (see [46] for details).

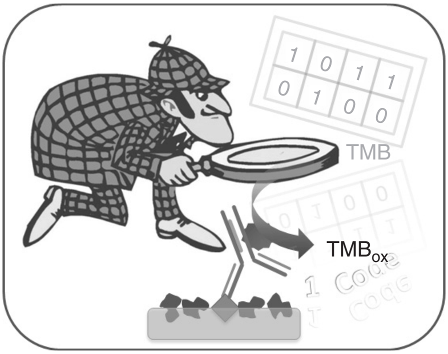

Figure 1.3 A cartoon outlining application of a biorecognition information processing system for data security, encoding, and steganography (see [51c] for details).

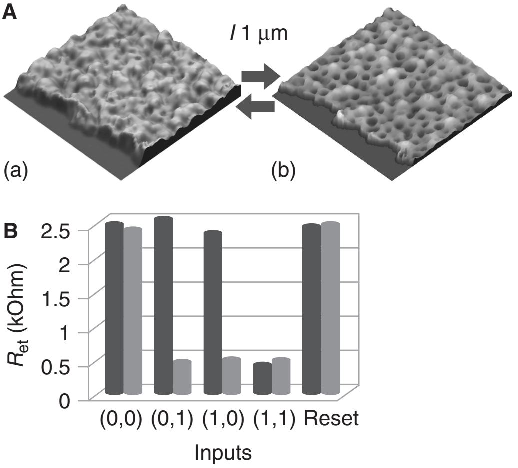

Figure 1.4 The signal-responsive membrane associated with an indium tin oxide (ITO) electrode and coupled with the enzyme-based AND (dark gray bars)/OR (light gray bars) logic gates. (A) Atomic force microscope (AFM) topographic images (10×10 μm^2) of the membrane with closed (a) and open (b) pores. (B) The electron transfer resistance, R_{et}, of the switchable interface derived from the impedance spectroscopy measurements obtained upon different combinations of the input signals. (Adapted from 52, with permission; Copyright American Chemical Society, 2009.)

(Figure 1.4), can benefit from built-in logic implemented via biocomputing gates and networks [52, 53].

The variety of systems inspired by biology and their possible applications are really unlimited, and the combination of computer science, biomolecular science, material science, and electronics will result in novel scientific and technological advances in this multidimensional research area. The present book aims at summarizing the achievements in this rapidly developing multifaceted research area providing background for further progress and helping in understanding of various aspects in this complex scientific field.

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