Biocomputing — tools, aims, perspectives

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Biomolecular systems for information processing have recently received great attention in the general framework of unconventional computing. While DNA biocomputing systems have been studied by many researchers and have already reached a high level of complexity, enzyme-based cascades mimicking Boolean logic operations are a relatively new subfield that is rapidly progressing. The present paper reviews recent progress in the enzyme-based information processing systems and suggests applications in biosensing, rather than computation. Specific examples of enzyme-based logic systems are discussed to introduce readers to this rapidly developing research area.

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Introduction

Computer technology presently based on silicon-materials and binary algorithms is coming to the end of its exponential development, being limited by further component-miniaturization and speed of their operation. Conceptually novel ideas to breakthrough to another level of information processing technology are needed in order to maintain its fast progress. The quest for novel ideas in information processing resulted in several directions in the general area of unconventional computing [1], including research in quantum computing and biologically inspired molecular computing. While molecular computing [2•,3•,4•] is generally motivated by mimicking natural biological information processing, the tools used are not necessarily based on biological systems and often employ synthetic molecules with signal-controlled properties. Synthetic molecular systems [5] and nano-species [6•] have been designed to mimic operation of Boolean logic gates and have demonstrated basic arithmetic functions and memory units. Despite the great progress that molecular computing has achieved in the last decade

[7,8], the major challenge in further development of molecular computing systems is the limit to their complexity [9]. A new advance in development of molecular information systems has been achieved with the use of biomolecular species [10••,11], borrowing some ideas from systems biology [12], which is devoted to the study of biological information processing. The first demonstration of computational processes performed by DNA molecules to solve some combinatorial problems [13] was recently extended to the use of various biomolecular systems based on DNA/RNA [14••,15,16], oligopeptides [17], proteins [18], enzymes [19••] and even whole biological cells [20,21] for mimicking various information processing steps, Figure 1. One of the obvious advantages of biomolecular systems is their ability to integrate in complex reacting processes mimicking multi-step information processing networks; indeed, their operation in biological environments complementing natural biological processes has been demonstrated [22]. Multi-step biochemical cascades mimicking electronic circuitries have demonstrated the ability to perform simple arithmetic operations [23–25], play games [26] and make multi-choice logic decisions [27].

Developing novel functionalities, that can supplement electronics and are achievable in biomolecular systems is the most challenging goal of this research [28,29]. These systems are still far away from the natural information processing in cells, but already much greater in complexity than pure synthetic molecular systems. The present paper is a short overview of the biomolecular information processing systems ('biocomputing' systems for brevity), mostly exemplified by the systems based on the enzyme catalyzed reactions. The paper concentrates on enzyme-based biocomputing systems because of personal research preferences of the author. It should be also noted that presently there are very few reviews on the enzyme-based biocomputing [19••], while other biocomputing systems, particularly based on DNA/RNA molecules [11,14••,15,16], have been extensively reviewed recently by other authors.

Logic gates based on enzyme reactions

Rapid progress in enzyme-based information processing systems has resulted in the design of biocatalytic cascades mimicking various Boolean logic gates [19••], including AND [30–34], OR [33,35], NAND [36], NOR [34,36], CNOT [37], XOR [33,34,38,39], INHIBIT [33,34], Identity [34] and Inverter [34] gates. In order to digitalize chemical processes the reacting species considered as logic input signals were applied at two levels of their concentrations: their physical absence (zero concentration) was

Figure 1
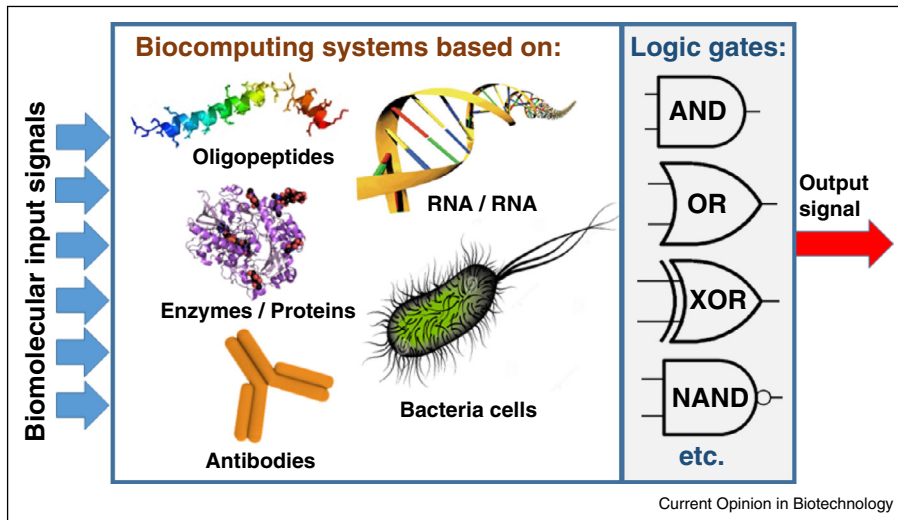
Biocomputing systems based on various biomolecular/biological species can process multiple chemical input signals and generate an output signal according to different logic implemented in the systems.

defined as logic **0** input, while logic **1** input was defined as experimentally optimized and conveniently high concentration, thus allowing significant separation in the produced output signals when inputs **0** or **1** were applied in different combinations. Figure 2 exemplifies two Boolean logic gates based on enzymatic reactions. An OR logic gate, Figure 2a,

Figure 2
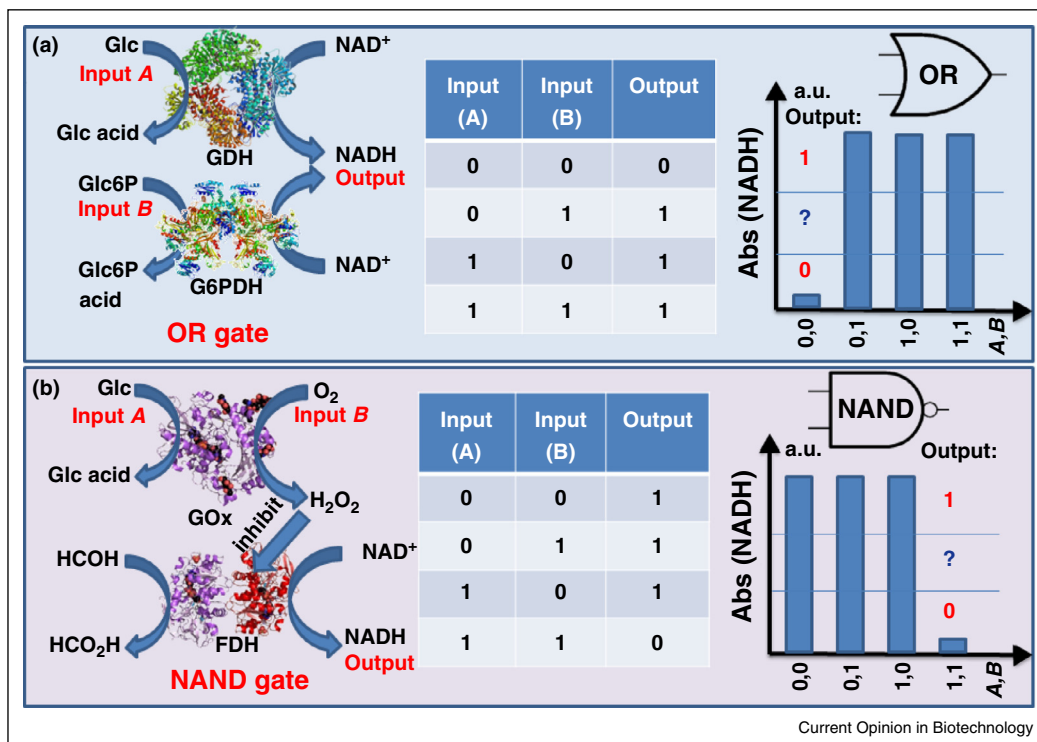
Enzyme-based biocomputing systems mimicking OR **(a)** and NAND **(b)** logic gates. The corresponding truth tables and schematic bar-charts for the optically read output signals obtained for various combinations of input signals are also shown. The horizontal lines in the bar-charts correspond to the thresholds separating logic **0**, **?** (undefined) and logic **1** output values. The following abbreviations are used: Glc acid = gluconic acid, Glc6P acid = 6-phosphogluconic acid. All other abbreviations and processes are explained in the text.