POLITECNICO DI TORINO
Repository ISTITUZIONALE

Biosensors for Biomolecular Computing: a Review and Future Perspectives

Original
Biosensors for Biomolecular Computing: a Review and Future Perspectives / Aiassa, S.; Terracciano, R.; Carrara, S.; Demarchi, D.. - In: BIONANOSCIENCE. - ISSN 2191-1630. - 10:3(2020), pp. 554-563. [10.1007/s12668-020-00764-8]

Availability:
This version is available at: 11583/2841331 since: 2020-07-25T15:15:40Z

Publisher:
Springer

Published
DOI:10.1007/s12668-020-00764-8

Terms of use:

This article is made available under terms and conditions as specified in the corresponding bibliographic description in the repository

Publisher copyright
Springer postprint/Author's Accepted Manuscript

This version of the article has been accepted for publication, after peer review (when applicable) and is subject to Springer Nature's AM terms of use, but is not the Version of Record and does not reflect post-acceptance improvements, or any corrections. The Version of Record is available online at: http://dx.doi.org/10.1007/s12668-020-00764-8

(Article begins on next page)

24 April 2024

Biosensors for Biomolecular Computing: A Review and Future Perspectives

Simone Aiassa[12] · Rossana Terracciano[13] · Sandro Carrara[2] · Danilo Demarchi[1]

Abstract Biomolecular computing is the field of engineering where computation, storage, communication, and coding are obtained by exploiting interactions between biomolecules, especially DNA, RNA, and enzymes. They are a promising solution in a long-term vision, bringing huge parallelism and negligible power consumption. Despite significant efforts in taking advantage of the massive computational power of biomolecules, many issues are still open along the way for considering biomolecular circuits as an alternative or a complement to competing with Complementary Metal–Oxide–Semiconductor (CMOS) architectures. According to the Von Neumann architecture, computing systems are composed of a central processing unit, a storage unit, Input and Output (I/O). I/O operations are crucial to drive and read the computing core and to interface it to other devices. In emerging technologies, the complexity-overhead and the bottleneck of I/O systems are usually limiting factors. While computing units and memories based on biomolecular systems have been successfully presented in literature, the published I/O operations are still based on laboratory equipment without a real development of integrated I/O. Biosensors are suitable devices for transducing biomolecular interactions by converting them into electrical signals. In this work, we explore the latest advancements in biomolecular computing, as well as in biosensors, with focus on technology suitable to provide the required and still missing I/O devices. Therefore, our goal is to picture out the present and future perspectives about DNA, RNA, and enzymatic-based computing according to the progression in its I/O technologies, and to understand how the field of biosensors contributes to the research beyond CMOS.

Keywords Biomolecular · Biosensing · DNA computing · Enzyme computing · Ribocomputing

Corresponding author: S. Aiassa (simone.aiassa@polito.it)

[1]Department of Electronics and Telecommunications, Politecnico di Torino, Turin 10129, Italy.

[2]Integrated Systems Laboratory, École Polytechnique Fédérale de Lausanne, Lausanne 1015, Switzerland.

[3]Department of Nanomedicine, Houston Methodist Research Institute, Houston, TX 77030, USA.

1 Introduction

Complementary Metal–Oxide–Semiconductor (CMOS) technologies present some challenges to address the request for further increasing of computational power as well as related miniaturization and power consumption. Beyond CMOS, several completely new paradigms are emerging to extend over the current limit the processing speed, the size, or the energy consumption [1,2]. Breakthrough ideas in processing, data storage, communication, and encryption resulted in several areas of unconventional computing [3]. For examples, quantum technologies [4, 5], molecular computing [6–8], memristive computing [9], and magnetic circuits [10,11]. One of the approaches, already proposed more than twenty years ago, proposes the use of biomolecules as unit blocks to create processing, storing and coding systems. This discipline is called biomolecular computing [12], not to be confused with computational biology, where the focus is to propose new computer science algorithms helping in biological studies [13].

Biomolecules offer three main promising intrinsic characteristics: massive parallelism, abundance in nature, and self-assembly capabilities [12]. Nature developed several mechanisms to allow massive communication in a noisy environment with intrinsically balanced loads, leading to parallelism in order to avoid processing bottlenecks. Biomolecules are abundant since they constitute the basis of life, and they show self-assembly mechanism, hence, their physical implementation is simpler than the actual fabrication process of CMOS [12, 14]. Despite their exceptional properties, biomolecular computing still presents open issues, e.g., limitations due to the complexity of the biomolecular paradigm, especially at system level [15].

So far, the Von Neumann architecture has been proven to be the best architecture for developing computing systems. As displayed in Fig. 1a, this architecture is featuring an input device, a central processing unit, a memory unit, and an output device [16]. Similarly, Fig. 1b displays the architecture for a complete biomolecular computing complete system to be interfaced to already existing technologies. On it, the input is realized by converting the electrical input information into biological or biochemical stimuli. The biomolecular-computing core is again the central processor unit, while the information is stored in a biomolecular-memory instead of a CMOS memory. As output device, a biosensor converts back the energy/information from the biological/biochemical format into an electrical signal to produce a final output suitable for the next incoming block in the computing and communication chain.

Considering the current limits in CMOS technology, researchers are now mainly focusing on developing new computing cores and new storage units. Meanwhile, the Input and Output (I/O) of the system is essential to evaluate the capability, the feasibility, and the performance of any new technology. The overhead in complexity related to the I/O devices highly contributes to the success or the failure of any emerging technology [17]. In practice, the I/O devices must be accessible by currently-existing interface devices, and they must not down set the advantages of the proposed computing-cores. For example, defective I/O devices may limit the bandwidth, increasing the size of the complete architecture, or increasing the total power consumption of the resulting system.

In biomolecular systems, the output devices are composed by a biosensor, which translates the biochemical information in an electric signal. Today, the I/O operations of biomolecular architectures are usually obtained with bulky and costly laboratory instrumentation with the only scope of validating the core. On the other hand, the field of biosensors for molecular detection has dramatically increased in sensing performance and, at the same time, in reducing devices-size [18]. The birth of the field of BioCMOS [19] has paved the road for a new generation of fully integrated biosensors, which could now be the base of output technologies for biomolecular computing devices as well.

In this review, we analyze the latest advancement in biomolecular computing to understand how to integrate central processing units and memories with biosensors, assuring the development of complete systems of biomolecular computing, capable to interface other most conventional electronic systems. Section 2 presents biomolecular computing cores and memories. Section 3 shows new biosensing technologies with a focus on integrated solutions that can be fruitfully used as output devices. Finally, Section 4 describes the possible forthcoming path in biomolecular computing, from current approaches to future perspective.

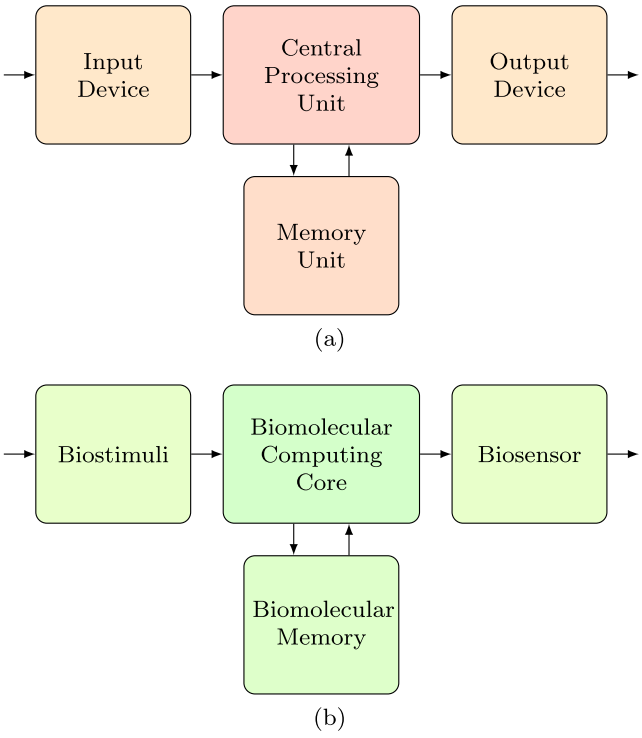

Fig. 1 Standard Von Neumann architecture (a) and a biomolecular computing system (b). Both architectures are composed by I/O, core, and memory.

2 Biomolecular Computing and Storage

Numerous are the mechanism provided by nature that can be exploited to use a molecule as a logic gate, a computational block, a cryptography key, or a memory cell. An exhaustive and detailed description of all the possible related techniques is out of the scope of this review. Instead, this work provides an overview to demonstrate advantages in building central processing units through biomolecules (see Fig. 1). Three main types of biomolecular computing had shown good results: DNA (Section 2.1), RNA (Section 2.2), and Enzyme (Section 2.3). Then, we briefly review them in terms of their complexity, size, and different mechanism of performing the core operations.

2.1 DNA Computing

DNA (DeoxyriboNucleic Acid) encodes the amino acid sequence, their primary structure, and their interactions. DNA is a double-stranded sequence of 4 nucleotides: adenine (A), guanine (G), cytosine (C) and thymine (T), where the pairs G and C, A and T are complementary base pairs. These four bases encode all the information required for life [20], similarly as a byte encodes a character using ones or zeros in digital architectures. Considering the intrinsic properties of DNA, this structure contains itself the element required for computing. Indeed, every DNA sequence has a natural complement, due to its double-stranded nature, and DNA mimics all the other Boolean operations through enzymes which can denature, replicate and anneal the DNA biomolecules. Moreover, the DNA structure allows high parallelism because enzymes can work on multiple DNA sequences [21]. Since the distance between nucleotides is around 0.35 nm, the DNA molecule presents a high data density promoting it to be a highly efficient storage unit.

In 1994, L. Adleman presented a solution to the well-known-in-computation travelling-salesman problem using DNA and exploiting its properties [22]. Since then, DNA has become a reference in biomolecular computing, and several studies had explored several aspects and challenges about computing as based on DNA. Numerous review papers and books may be considered for details about this research (E.g. [20,21,23]). Here, in the following, we just review the main features that allow the exploitation of DNA in biomolecular computing.

DNA was assembled to build up universal DNA logic gates performing Boolean operations, and even to build up more complex digital architectures [24, 25]. Using single DNA strands as inputs and leveraging on the complementarity between nucleotides, logic gates called Molecular Beacon Units (MBU) had been proposed [26]. DNA based XOR logic gates, AND logic gates, and half adder relying on the DNA strand displacement reaction have been proposed [27]. Modular electrochemical logic gates were implemented through DNA polymerization/nicking machines, for example, single-strand DNA prevented or started the DNA polymerization/nicking to synthesize as output G-quadruplex sequences [28]. A reversible Feynman gate leveraging on the interaction between graphene oxide and DNA has been proposed [29]. G-quadruplexes inputs, interacting with hairpin-modified gold nanoparticles, linked to magnetic particles in developing DNA-based arithmetic operations [30]. Moreover, hairpin-based gates, with the simple addition of extractors, are renewable to maintain such a consistent performance of biomolecular circuits during time [31]. A DNA nanotripod-graphene oxide platform was realized with three-input majority gates, multiple elementary logic gates, and combinatorial gates, assembling multiple DNA probes, massively simplifying the assembly of the gates too [32]. Domain-based encoders have been developed with differential information of four homologous oligonucleotides [33].

One of the most promising fields of application of DNA computing is storage. DNA stores a considerable quantity of digital information, for example, encapsulating the DNA in an inorganic matrix [34, 35], with a density up to three orders of magnitude higher than CMOS [36]. Random-access memories were implemented with several primers that enable individual recovery of different files stored within DNA sequences [37]. The first patents on DNA memories appeared in 2019 [38, 39], proving the industrial interest on this approach. DNA storage in living cells opens instead of the possibility of new frontiers, where the cellular history and environment variation were directly logged inside biological cells [40, 41].

DNA molecules were used as carriers for high-density information [42] and data transmission error correction [43]. The most catching results using DNA in communication is the increase of security, as due to the slow diffusivity of the molecules. The DNA cryptography is a new field of study, where the properties of the strand are applied to encrypt information in a new, faster, and highly secure way [44]. For example, encryption of keys in DNA microdots raises cost and effort to hackers well beyond traditional digital protections [45]. Polymerase Chain Reaction (PCR) technique was adopted to secure images [46], and DNA encoding provided a solution to the problem of security flaws in the Internet of Things (IoT) [47].

2.2 RNA Computing and Ribocomputing

RNA (Ribonucleic Acid) is another building block of biomolecular computer circuits. RNA is a polymeric molecule naturally coding and decoding genes' expression [48]. In the year 2000, RNA was introduced as the optimal molecule for solving propositional logic problems [49], as an alternative to DNA proposed to the very same aim [22]. Nowadays, set of logic circuits are proposed as synthetically produced inside living mammalian cells [50], and in escherichia coli cells as well [51], by using microRNA. Similarly to DNA, RNA showed high capability in encryption techniques, for both text-messages [52] and images [53].

The term Ribocomputing appeared quite recently, as the best of our knowledge, only in 2016 [54]. Ribo-

computing devices were defined as circuits to compute complex logic operations in living cells. Ribocomputing leverages on a new class of synthetic RNA called toehold switches [55], which mimics messenger RNAs whose transport information from the DNA to protein translators [56]. The synthetic usage of toehold switches brought to logic gates (NOT or AND) in a single layer, without delays and reduced diffusion-mediated signal losses [57].

2.3 Enzyme-Based Computing

In enzyme-based computing, a complete logic set of operations was defined digitalizing a chemical reaction in two levels of concentrations of chemical substances. For example, the absence of reacting species can be considered as a logic state 0, while the presence of that species as logic state 1. In particular, enzyme-based computing represented the two logic states through low molecular weight substrates at two different concentration levels. The enzymes convert substrates into products in biocatalyzed-reaction, so performing the computing [58]. Katz published in 2019 a book about enzyme-based computing [59], which exhaustively covers the field. Just a few examples of enzyme-based computing are presented here.

Similarly to DNA computing, various Boolean operations have been mapped by through of enzyme-catalyzed reactions [60–62]. For example, NOT [63] ports were built directly on a semiconductor transducer, while NXOR were created controlling the biocatalytic reaction by varying the pH of the input signals [64]. Enzymatic reaction cascades half-adders and a half-subtractors have also been realized by assembling more logic gates [65].

The logic capability of enzymes was directly linked in-situ with biological targets of biosensors. In this way, it is possible to create real intelligent biosensors with embedded logic, like in [66], where a personal glucose meter was designed using enzymes based logic blocks. In 2015, a universal interface between enzymatic and DNA computing had been presented [67], fostering the possibility of a system capable of leveraging independently on both the technologies.

3 Biosensors

Section 2 introduced the advantages of biomolecular computing core and biomolecular memories in comparison to CMOS central processing units and memory units, and Section 2 presents today approaches in building those components. Concerning Fig.1, the I/O devices are still mostly missing in many of the biomolecular architectures proposed so far by the literature. In any biomolecular computation, the input devices are typically composed by stimuli, e.g., electrical or optical, while the output devices need to be a biosensor. The term biosensor refers here to a variety of systems able to detect or measure biological compounds for monitoring concentrations of biomolecules, typically for applications in medicine [68], environment monitoring [69], or in production-control or quality-control in industry [70]. In this work, we focus on sensing technologies for DNA, RNA, enzyme, and molecules produced by their interactions, which are the main molecules exploited in biomolecular computing.

Section 3.1 shows the considered biological probes and the techniques to measure target molecules. Moreover, since biomolecular computing requires maintaining scalable size and feasible fabrication, this review focuses mainly on the field of BioCMOS [19], which is presented in Section 3.2 along with the architectures and technologies for the related electronic read-outs.

3.1 Sensing Bioprobes

Biosensors provide low-cost, efficient, and easy-to-use devices for fast measure and monitoring of patients [71–73]. Several techniques can be implemented to convert the biological information into an electrical signal, leveraging on electrochemical reaction or displacement of charge. As well as patients' metabolism, most of the biomolecular computing approaches exploited catalytic reactions, molecular aggregation, and other chemical interactions to assure information transfer, processing and storing. Hence, metabolites, amino acids, peptides, and proteins are just some of the possible products that biomolecular computing is interested in. All these compounds are detectable and, in some cases, also measurable by through probe functionalization. If the detection is done with the correct electrochemical technique, it may be implemented with CMOS technologies for easy and integrated transduction to electrical signals [19]. In literature, several reviews described these techniques in detail; here, we briefly highlight some of the more recent advancement in biosensing technology.

Much work has been done on metabolites sensing, and it was possible to identify human pathogen through real-time in vitro metabolites detection [74]. For example, a composite modified glassy carbon electrode was proposed to determine the presence of an amino acid essential in neuroregulation (Tryptophan) [75]. Electrochemical methods allow the detection of beta-amyloid peptides and aggregates [76], and peptides were used

to functionalize the sensor surfaces to detect antibodies [77]. Electrochemical Impedance Spectroscopy (EIS) is used to evaluate binding interactions among peptides and proteins [78]. In Microelectromechanical Systems (MEMS) technologies, assay system based sensor helps in rapid analysis of C-reactive proteins [79]. MEMS are indeed a significant breakthrough because they enable fast detection of several biomarkers [80, 81]. MicroRNAs gained consideration due to their importance in early-stage diagnosis [82]. Today, several options exist for detecting microRNAs through simple and integrated technologies [83, 84]. Electrochemical biosensors target DNA sequences or mutated genes as related to several disease [85]. The DNA is also detected by considering the interactions at the nanoscale [86]. For example, a DNA sensor through was developed by exploiting redox activity on graphene electrodes [87], while nanoparticles carbon nanotubes showed excellent detection potential on DNA as well [88]. DNA-mediated charge transport chemistry is considered for the displacement of charges among molecules according to the base pair affinity in the DNA-strand [89, 90], and this allowed the development of DNA impedance-based sensors [91,92]. Finally, G-quadruplex is exploited in electrochemical biosensors because their response is particularly sensitive to the DNA structural changes biosensors in the evaluation of molecules, proteins, and cells, with increased selectivity and sensitivity [93].

3.2 BioCMOS Interfaces

The development of integrated CMOS interfaces is growing at a similar speed than biosensors and probe technologies. Merging different transducing mechanisms to CMOS read-out electronics, several integrated biosensing devices have been developed to enhance decentralized point-of-care diagnostic [94,95]. The lab-on-chip technology paved the road in terms of low-cost and high-throughput analysis of biomolecules [96]. Both chip size and power-consumption are scaling down significantly, pushing down as well the implantable sensing technologies [97]. Several different solutions for implementing highly integrated fully autonomous systems for biosensing have been proposed, for example, integrated potentiostat for amperometric measurment [98, 99] and also implantable dust size chip [100] or extremely miniaturized DNA readers [101, 102]. Electrode arrays [103] or also nanogap-based arrays [104–109] are interesting to the scope, since their driving, in term of both sampling and transmission, is a real challenge for more efficient output detectors for applications in biomolecular computers. Fortunately, fully integrated neuromorphic chips have been proposed to manage the interface to such complex array [110]. At the same time, the integration of micro-nano electrodes promoted highly dense electrochemical sensing techniques [111].

4 Biomolecular Output Units

In the field of biomolecular computing, much effort was spent on developing new methods for computation, processing, and storing, as summarized in Section 2. Considering the actual readiness level of this technology, the focus at the system level has been not surprisingly too-low so far. Recent reviews on biomolecular computing even do not mention about the inter-connectivity of the system while just focus on the computational units and methods [20, 21, 55, 59]. Nevertheless, if the final aim is to develop a complete device, then the system interconnection to the computing core has to be taken into account. For this reason, we will describe in next Section 4.1 the current approaches for developing output devices for biomolecular systems, while in Section 4.2, we will draw some possible future perspectives about.

4.1 Current Approaches

Any biomolecular system requires an output device as depicted in Fig. 1. Currently, the output devices are provided by laboratory instruments, methods, and procedures that covert biochemical information from the biomolecular computing core into an electrical signal. To this aim, colorimetry [112, 113], fluorescence [114], chemiluminescence [115,116], electrochemiluminescence [117], and electrochemistry [28, 64] are usually used. However, these methods are not necessarily translatable in an easy manner into integrated systems for real applications of biomolecular computing. For example, fluorescence sensing is used in DNA nanodevices due to the sensitive and quantitative nature of the read-out. However, DNA sensing with modified fluorophores is usually too-highly expensive for low-cost applications and requires complex photodetector systems. Easy and label-free detection has been exploited with reduced cost for computing technology, but still keeping the same read-out complexity [118]. Excitation light at a given wavelength activated DNA devices, while the light is also a useful carrier to transport e communicate the information [119].

On the other hand, electrical transducers are better links to the BioCMOS paradigm, since easy electrical detection was demonstrated in label-free operation applied to a DNA and nanopore system in droplet network [120], including electrochemical logic gates by integrated read-outs [28]. Cyclic Voltammetry (CV) am-

Table 1 State of the art of biomolecular computing, focusing on output sensing method and its integration.

Implemented technology	Computing method	Output method	Reference
Logic gate, adder	DNA	Fluorescence	[27]
Logic gate	DNA	Electrochemical	[28]
Logic gate	DNA	Fluorescence	[29]
Logic gate	DNA	Fluorescence	[30]
Logic gate	DNA	Fluorescence	[31]
Logic gate	DNA	Fluorescence	[32]
Memory	DNA	Fluorescence	[35]
Data transmission	DNA	Fluorescence	[43]
Encryption	DNA	N/A	[44]
Logic gate	RNA	Fluorescence	[50]
Logic gate	RNA	Fluorescence	[51]
Encryption	RNA	N/A	[53]
Logic gate	RNA	Fluorescence	[56]
Logic gate	RNA	Fluorescence	[57]
Logic gate	Enzyme	Chemiluminescence	[58]
Logic gate	Enzyme	Electrochemical	[63]
Logic gate	Enzyme	Chemiluminescence, electrochemical	[64]
Adder	Enzyme	Chemiluminescence	[65]
Logic gate	DNA	Colorimetry	[112]
Logic gate	DNA	Colorimetry	[113]
Logic gate	DNA	Fluorescence	[114]
Logic gate	DNA	Chemiluminescence	[115]
Logic gate	DNA	Chemiluminescence	[116]
Logic gate	DNA	Electrochemiluminescence	[117]
Logic gate	DNA	Fluorescence	[118]
Logic gate	DNA	Fluorescence	[119]
Logic gate	DNA	Electrochemical	[120]
Logic gate, encoder, decoder	DNA	Electrochemical	[121]

perometric techniques were also implemented as read-outs in designing of logic gates [121]. Table 1 presents a summary of the sensing techniques adopted so far in literature by recent works about biomolecular computing. None of those works, however, shows a system integration between the computing core and the output devices. All the cases require still external laboratory instrumentation. Moreover, in Table 1 just a small portion of the biosensing techniques used in literature appears, meaning that there is still unexplored room for several more unexploited possibilities.

4.2 Future Perspective

An endless number of possibilities may easily extend the limit of current systems for output conversion by exploiting the many biosensing technologies not yet proposed so far for applications to biomolecular architectures. It is possible to fit already existing biosensor in the proximity of biomolecular core or memory. For most of the measurement techniques used today, and briefly presented in Section 4.1, solutions already exist to move from laboratory instrumentation to integrated devices. In the near future, the interaction of DNA at nanoscale may be used to interrogate the output of individual MBU. DNA detection label-free systems may provide small, efficient, and low cost approaches for reading vast arrays of DNA memories. G-quadruplex electrochemical biosensors may contribute to the development of G-quadruplex DNA-based arithmetic processor. Meanwhile, logic outputs of catalyzed reaction in enzymatic processors may be read-out by electrochemical biosensors. MicroRNAs sensor and microRNAs logic gates may perform computation directly inside living cells returning kind of living computer. In BioCMOS, the biomolecular-interface is straightly in contact with a CMOS reader. Therefore, integrated design is an excellent opportunity for taking advantages of biomolecular technologies and enlarge capability and power of CMOS computing since the logic output of the biomolecular computation will be then directly read in the usual form of electrical signals as well as in CMOS computation. Extensive arrays of biosensors directly embedded in neuromorphic chips will then allow simultaneous direct detection of numerous biochemical reactions, fostering the possibility of programmable biomolecular devices. Forthcoming biosensor systems will start to reach performance that will reduce power, area, and delay overhead, which is nowadays limiting the application of biomolecular processor. Moreover, the complexity will drastically scale down to provide lower cost as well.

5 Conclusion

The biomolecular computing is attempting to broadening the horizon well beyond CMOS approach, but the complexity overhead as related to interactions among biomolecules is still an obstacle to its success. We presented in this paper the efforts done by the research community for building computing architectures based on biomolecular solutions, and discussed what is still missing with respect to the current state-of-the-art in literature. We pointed out that I/O technology is often left unaddressed in the present research in the field. Meanwhile, biosensors are the most natural input/output devices for biomolecular computing systems, having already shown their high power, reliability, and capabilities in other fields of application. We envisioned a future path that may overcome the present limitations of the I/O systems in biomolecular computing by reviewing both biomolecular computing-cores/memories and biosensing technologies. In this path, biosensor and bio-nano-technology may largely contribute to the development of better devices with higher data density, lower power consumption, increased processing speed, reduced cost, and lower environmental impact.

6 Declaration

Funding This work is supported by Politecnico di Torino and Compagnia di San Paolo under the initiative "Joint research projects with top universities"

References

1. Hutchby, J. A., Bourianoff, G. I., Zhirnov, V. V., & Brewer, J. E. (2002), Extending the road beyond CMOS, *IEEE Circuits and Devices Magazine*, *18*(2), 28–41.
2. Rotolo, D., Hicks, D., & Martin, B. R. (2015), What is an emerging technology?, *Research Policy*, *44*(10), 1827–1843.
3. Katz, E. (2015), Biocomputing—tools, aims, perspectives, *Current Opinion in Biotechnology*, *34*, 202–208.
4. Preskill, J. (2018), Quantum computing in the NISQ era and beyond, *Quantum*, *2*, 79.
5. Shalf, J. (2020), The future of computing beyond Moore's law, *Philosophical Transactions of the Royal Society A*, *378*(2166), 20190061.
6. Pulimeno, A., Graziano, M., Demarchi, D., & Piccinini, G. (2012), Towards a molecular QCA wire: simulation of write-in and read-out systems, *Solid-State Electronics*, *77*, 101–107.
7. Pulimeno, A., Graziano, M., Sanginario, A., Cauda, V., Demarchi, D., & Piccinini, G. (2013), Bis-ferrocene molecular QCA Wire: Ab initio simulations of fabrication driven fault tolerance, *IEEE Transactions on Nanotechnology*, *12*(4), 498–507.
8. Ardesi, Y., Gnoli, L., Graziano, M., & Piccinini, G. (2019), Bistable propagation of monostable molecules in molecular field-coupled nanocomputing, *2019 15th Conference on Ph.D Research in Microelectronics and Electronics (PRIME)*, 225–228.
9. Ielmini, D. & Wong, H.-S. P. (2018), In-memory computing with resistive switching devices, *Nature Electronics*, *1*(6), 333–343.
10. Riente, F., Garlando, U., Turvani, G., Vacca, M., Ruo Roch, M., & Graziano, M. (2017), MagCAD: Tool for the design of 3-D magnetic circuits, *IEEE Journal on Exploratory Solid-State Computational Devices and Circuits*, *3*, 65–73.
11. Garlando, U., Riente, F., Turvani, G., Ferrara, A., Santoro, G., Vacca, M., & Graziano, M. (2018), Architectural exploration of perpendicular nano magnetic logic based circuits, *Integration*, *63*, 275–282.
12. Garzon, M. H. & Deaton, R. J. (1999), Biomolecular computing and programming, *IEEE Transactions on Evolutionary Computation*, *3*(3), 236–250.
13. Angermueller, C., Pärnamaa, T., Parts, L., & Stegle, O. (2016), Deep learning for computational biology, *Molecular Systems Biology*, *12*(7).
14. Drakopoulos, G., Tsolis, D., Stefani, A., & Mylonas, P. (2018), The biomolecular computation paradigm: A survey in massive biological computation, *Artificial Intelligence Applications and Innovations*, Iliadis, L., Maglogiannis, I., & Plagianakos, V., Eds.
15. Amos, M., Gibbons, A., & Dunne, P. E. (1997), The complexity and viability of DNA, *Biocomputing and Emergent Computation: Proceedings of BCEC97*.
16. Von Neumann, J. (1993), First draft of a report on the EDVAC, *IEEE Annals of the History of Computing*, *15*(4), 27–75.
17. Markov, I. L. (2014), Limits on fundamental limits to computation, *Nature*, *512*(7513), 147–154.
18. Vigneshvar, S., Sudhakumari, C., Senthilkumaran, B., & Prakash, H. (2016), Recent advances in biosensor technology for potential applications – An overview, *Frontiers in Bioengineering and Biotechnology*, *4*, 11.
19. Carrara, S. (2012)Springer New York, 1–258.
20. Pisanti, N. (1998), DNA computing: a survey, *Bulletin of the EATCS*, *64*, 188–216.
21. Ezziane, Z. (2005), DNA computing: applications and challenges, *Nanotechnology*, *17*(2), R27.
22. Adleman, L. M. (1994), Molecular computation of solutions to combinatorial problems, *Science*, 1021–1024.
23. Păun, G., Rozenberg, G., & Salomaa, A. (1998)Springer Berlin Heidelberg.
24. De Silva, A. P. (2001), Unconventional computing: A boolean chemical perspective, *Wiley Encyclopedia of Electrical and Electronics Engineering*, 1–11.
25. de Silva, A. P.Royal Society of ChemistryCambridge. [Online]. Available: http://ebook.rsc.org/?DOI=10.1039/9781849733021
26. Thabit, Q. Q. & Al-Saffar, A. A. (2019), DNA-strand molecular beacon optical processor, *Heliyon*, *5*(9), e02389.
27. Li, W., Zhang, F., Yan, H., & Liu, Y. (2016), DNA based arithmetic function: a half adder based on DNA strand displacement, *Nanoscale*, *8*(6), 3775–3784.
28. Ge, L., Wang, W., Sun, X., Hou, T., & Li, F. (2016), Versatile and programmable DNA logic gates on universal and label-free homogeneous electrochemical platform, *Analytical Chemistry*, *88*(19), 9691–9698.

29. Zhou, C., Wang, K., Fan, D., Wu, C., Liu, D., Liu, Y., & Wang, E. (2015), An enzyme-free and DNA-based Feynman gate for logically reversible operation, *Chemical Communications*, *51*(51), 10 284–10 286.
30. Zhang, S., Wang, K., Huang, C., & Sun, T. (2015), Reconfigurable and resettable arithmetic logic units based on magnetic beads and DNA, *Nanoscale*, *7*(48), 20 749–20 756.
31. Eshra, A., Shah, S., Song, T., & Reif, J. (2019), Renewable DNA hairpin-based logic circuits, *IEEE Transactions on Nanotechnology*, *18*, 252–259.
32. He, K., Yang, H., Wang, L., Guan, J., Wu, M., He, H., Gunasekaran, S., Wang, X., Wang, Q., & Xu, X. (2019), A universal platform for multiple logic operations based on self-assembled a DNA tripod and graphene oxide, *Chemical Engineering Journal*, *368*, 877–887.
33. Zhong, W., Tang, W., Fan, J., Zhang, J., Zhou, X., & Liu, Y. (2018), A domain-based DNA circuit for smart single-nucleotide variant identification, *Chemical Communications*, *54*(11), 1311–1314.
34. Grass, R. N., Heckel, R., Puddu, M., Paunescu, D., & Stark, W. J. (2015), Robust chemical preservation of digital information on DNA in silica with error-correcting codes, *Angewandte Chemie International Edition*, *54*(8), 2552–2555.
35. Ceze, L., Nivala, J., & Strauss, K. (2019), Molecular digital data storage using DNA, *Nature Reviews Genetics*, *20*(8), 456–466.
36. Extance, A. (2016), How DNA could store all the world's data, *Nature*, *537*(7618).
37. Organick, L., Ang, S. D., Chen, Y.-J., Lopez, R., Yekhanin, S., Makarychev, K., Racz, M. Z., Kamath, G., Gopalan, P., Nguyen, B. *et al.* (2018), Random access in large-scale DNA data storage, *Nature Biotechnology*, *36*(3), 242.
38. Erlich, Y., Efficient encoding of data for storage in polymers such as dna, united States Patent 946 16/032, Jan 17, 2019.
39. Su, X., Wu, K., & Tayebi, N., Data storage based on encoded DNA sequences, united States Patent 022 15/929, Feb 14, 2019.
40. Tang, W. & Liu, D. R. (2018), Rewritable multi-event analog recording in bacterial and mammalian cells, *Science*, *360*(6385), eaap8992.
41. Sheth, R. U. & Wang, H. H. (2018), DNA-based memory devices for recording cellular events, *Nature Reviews Genetics*, *19*(11), 718–732.
42. Furubayashi, T., Nakano, T., Eckford, A., Okaie, Y., & Yomo, T. (2016), Packet fragmentation and reassembly in molecular communication, *IEEE Transactions on NanoBioscience*, *15*(3), 284–288.
43. Fan, D., Wang, E., & Dong, S. (2017), Exploiting polydopamine nanospheres to DNA computing: a simple, enzyme-free and g-quadruplex-free dna parity generator/checker for error detection during data transmission, *ACS Applied Materials & Interfaces*, *9*(2), 1322–1330.
44. Malhotra, M. *et al.* (2019), DNA cryptography: A novel approach for data security using flower pollination algorithm, *Available at SSRN 3358159*.
45. Chaudhary, H. & Bhatnagar, V. (2014), Hybrid approach for secure communication of data using chemical DNA, *2014 5th International Conference - Confluence The Next Generation Information Technology Summit (Confluence)*, 967–971.
46. Vinotha, P. & Jose, D. (2019), VLSI implementation of image encryption using DNA cryptography, *Intelligent Communication Technologies and Virtual Mobile Networks*, 190–198.
47. Barman, P. & Saha, B. (2019), Dna encoded elliptic curve cryptography system for IoT security, *International Journal of Computational Intelligence & IoT*, *2*(2).
48. Jacob, F. & Monod, J. (1961), Genetic regulatory mechanisms in the synthesis of proteins, *Journal of Molecular Biology*, *3*(3), 318–356.
49. Faulhammer, D., Cukras, A. R., Lipton, R. J., & Landweber, L. F. (2000), Molecular computation: RNA solutions to chess problems, *Proceedings of the National Academy of Sciences*, *97*(4), 1385–1389.
50. Matsuura, S., Ono, H., Kawasaki, S., Kuang, Y., Fujita, Y., & Saito, H. (2018), Synthetic RNA-based logic computation in mammalian cells, *Nature communications*, *9*(1), 4847.
51. Wei, Z., Fu, W., Liu, Q., Jing, H., Jin, C., Chen, Y., Xia, W., Zhu, X., & Xu, D. (2019), Construction of boolean logic gates based on dual-vector circuits of multiple gene regulatory elements, *Molecular Genetics and Genomics*, *294*(2), 277–286.
52. Krishna, B. M., Khan, H., & Madhumati, G. (2018), Reconfigurable pseudo biotic key encryption mechanism for cryptography applications, *International Journal of Engineering & Technology*, *7*(1.5), 62–70.
53. Mahmud, M., Lee, M., Choi, J.-Y. *et al.* (2020), Evolutionary-based image encryption using RNA codons truth table, *Optics & Laser Technology*, *121*, 105818.
54. Green, A. A., Kim, J., Ma, D., Silver, P. A., Collins, J. J., & Yin, P. (2016), Ribocomputing devices for sophisticated in vivo logic computation, *Proceedings of the 3rd ACM International Conference on Nanoscale Computing and Communication*, 11.
55. Kim, J., Yin, P., & Green, A. A. (2018), Ribocomputing: Cellular logic computation using RNA devices, *Biochemistry*, *57*(6), 883–885.
56. Green, A. A., Silver, P. A., Collins, J. J., & Yin, P. (2014), Toehold switches: de-novo-designed regulators of gene expression, *Cell*, *159*(4), 925–939.
57. Green, A. A., Kim, J., Ma, D., Silver, P. A., Collins, J. J., & Yin, P. (2017), Complex cellular logic computation using ribocomputing devices, *Nature*, *548*(7665), 117.
58. Katz, E. (2017), Enzyme-based logic gates and networks with output signals analyzed by various methods, *ChemPhysChem*, *18*(13), 1688–1713.
59. Katz, E. (2019)Wiley-VCH Verlag GmbH & Co., 422.
60. Baron, R., Lioubashevski, O., Katz, E., Niazov, T., & Willner, I. (2006), Logic gates and elementary computing by enzymes, *The Journal of Physical Chemistry A*, *110*(27), 8548–8553.
61. Huang, Y., Pu, F., Ren, J., & Qu, X. (2017), Artificial enzyme-based logic operations to mimic an intracellular enzyme-participated redox balance system, *Chemistry–A European Journal*, *23*(38), 9156–9161.
62. Katz, E., Poghossian, A., & Schöning, M. J. (2017), Enzyme-based logic gates and circuits-analytical applications and interfacing with electronics, *Analytical and Bioanalytical Chemistry*, *409*(1), 81–94.
63. Honarvarfard, E., Gamella, M., Poghossian, A., Schöning, M. J., & Katz, E. (2017), An enzyme-based reversible controlled NOT (CNOT) logic gate operating on a semiconductor transducer, *Applied Materials Today*, *9*, 266–270.

64. Filipov, Y., Bollella, P., & Katz, E. (2019), Not-XOR (NXOR) logic gate realized with enzyme-catalyzed reactions: Optical and electrochemical signal transduction, *ChemPhysChem*, *20*(16), 2082–2092.
65. Fratto, B. E., Lewer, J. M., & Katz, E. (2016), An enzyme-based half-adder and half-subtractor with a modular design, *ChemPhysChem*, *17*(14), 2210–2217.
66. Zhang, J. & Lu, Y. (2018), Biocomputing for portable, resettable, and quantitative point-of-care diagnostics: Making the glucose meter a logic-gate responsive device for measuring many clinically relevant targets, *Angewandte Chemie International Edition*, *57*(31), 9702–9706.
67. Mailloux, S., Gerasimova, Y. V., Guz, N., Kolpashchikov, D. M., & Katz, E. (2015), Bridging the two worlds: a universal interface between enzymatic and DNA computing systems, *Angewandte Chemie International Edition*, *54*(22), 6562–6566.
68. Aiassa, S., Carrara, S., & Demarchi, D. (2019), Optimized sampling rate for voltammetry-based electrochemical sensing in wearable and iot applications, *IEEE Sensors Letters*, *3*(6), 1–4.
69. Cuartero, M., Crespo, G., Cherubini, T., Pankratova, N., Confalonieri, F., Massa, F., Tercier-Waeber, M.-L., Abdou, M., Schäfer, J., & Bakker, E. (2018), In situ detection of macronutrients and chloride in seawater by submersible electrochemical sensors, *Analytical Chemistry*, *90*(7), 4702–4710.
70. Meshram, B., Agrawal, A., Adil, S., Ranvir, S., & Sande, K. (2018), Biosensor and its application in food and dairy industry: A review, *International Journal of Current Microbiology and Applied Sciences*, *7*, 3305–3324.
71. Shafiee, A., Ghadiri, E., Kassis, J., & Atala, A. (2019), Nanosensors for therapeutic drug monitoring: implications for transplantation, *Nanomedicine*, *14*(20), 2735–2747.
72. Aiassa, S., Stradolini, F., Tuoheti, A., Carrara, S., & Demarchi, D. (2019), Quasi-digital biosensor-interface for a portable pen to monitor anaesthetics delivery, *2019 15th Conference on Ph.D Research in Microelectronics and Electronics (PRIME)*, 265–268.
73. Malpartida-Cardenas, K., Miscourides, N., Rodriguez-Manzano, J., Yu, L.-S., Moser, N., Baum, J., & Georgiou, P. (2019), Quantitative and rapid plasmodium falciparum malaria diagnosis and artemisinin-resistance detection using a cmos lab-on-chip platform, *Biosensors and Bioelectronics*, *145*, 111678.
74. Simoska, O., Sans, M., Fitzpatrick, M. D., Crittenden, C. M., Eberlin, L. S., Shear, J. B., & Stevenson, K. J. (2018), Real-time electrochemical detection of pseudomonas aeruginosa phenazine metabolites using transparent carbon ultramicroelectrode arrays, *ACS Sensors*, *4*(1), 170–179.
75. He, Q., Tian, Y., Wu, Y., Liu, J., Li, G., Deng, P., & Chen, D. (2019), Electrochemical sensor for rapid and sensitive detection of tryptophan by a cu2o nanoparticles-coated reduced graphene oxide nanocomposite, *Biomolecules*, *9*(5), 176.
76. La, M., Chen, C., Xia, X., & Zhou, J. Z. B. (2019), Electrochemical, photoelectrochemical and electrochemiluminescent biosensors for the detection of beta-amyloid peptides and their aggregates, *International Journal of Electrochemical Science*, *14*, 5547–5562.
77. Puiu, M., Idili, A., Moscone, D., Ricci, F., & Bala, C. (2014), A modular electrochemical peptide-based sensor for antibody detection, *Chemical Communications*, *50*(64), 8962–8965.
78. Lim, J. M., Kim, J. H., Ryu, M. Y., Cho, C. H., Park, T. J., & Park, J. P. (2018), An electrochemical peptide sensor for detection of dengue fever biomarker NS1, *Analytica Chimica Acta*, *1026*, 109–116.
79. Guo, L., Yang, Z., Zhi, S., Feng, Z., Lei, C., & Zhou, Y. (2018), A sensitive and innovative detection method for rapid c-reactive proteins analysis based on a microfluxgate sensor system, *PloS One*, *13*(3), e0194631.
80. Carrara, S., Sacchetto, D., Doucey, M.-A., Baj-Rossi, C., De Micheli, G., & Leblebici, Y. (2012), Memristive-biosensors: A new detection method by using nanofabricated memristors, *Sensors and Actuators B: Chemical*, *171*, 449–457.
81. Tzouvadaki, I., Jolly, P., Lu, X., Ingebrandt, S., De Micheli, G., Estrela, P., & Carrara, S. (2016), Label-free ultrasensitive memristive aptasensor, *Nano Letters*, *16*(7), 4472–4476.
82. Kilic, T., Erdem, A., Ozsoz, M., & Carrara, S. (2018), microRNA biosensors: opportunities and challenges among conventional and commercially available techniques, *Biosensors and Bioelectronics*, *99*, 525–546.
83. Qiu, X.-Y., Zhu, L.-Y., Zhu, C.-S., Ma, J.-X., Hou, T., Wu, X.-M., Xie, S.-S., Min, L., Tan, D.-A., Zhang, D.-Y. *et al.* (2018), Highly effective and low-cost microRNA detection with CRISPR-Cas9, *ACS Synthetic Biology*, *7*(3), 807–813.
84. Eksin, E., Bikkarolla, S. K., Erdem, A., & Papakonstantinou, P. (2018), Chitosan/nitrogen doped reduced graphene oxide modified biosensor for impedimetric detection of microRNA, *Electroanalysis*, *30*(3), 551–560.
85. Drummond, T. G., Hill, M. G., & Barton, J. K. (2003), Electrochemical DNA sensors, *Nature Biotechnology*, *21*(10), 1192.
86. Ferapontova, E. E. (2018), DNA electrochemistry and electrochemical sensors for nucleic acids, *Annual Review of Analytical Chemistry*, *11*, 197–218.
87. Yang, T., Chen, H., Qiu, Z., Yu, R., Luo, S., Li, W., & Jiao, K. (2018), Direct electrochemical vibrio DNA sensing adopting highly stable graphene–flavin mononucleotide aqueous dispersion modified interface, *ACS Applied Materials & Interfaces*, *10*(5), 4540–4547.
88. Lee, J., Morita, M., Takemura, K., & Park, E. Y. (2018), A multi-functional gold/iron-oxide nanoparticle-cnt hybrid nanomaterial as virus DNA sensing platform, *Biosensors and Bioelectronics*, *102*, 425–431.
89. Zwang, T. J., Tse, E. C. M., & Barton, J. K. (2018), Sensing DNA through DNA charge transport, *ACS Chemical Biology*, *13*(7), 1799–1809.
90. Carrara, S., Benini, L., Bhalla, V., Stagni, C., Ferretti, A., Cavallini, A., Riccò, B., & Samorì, B. (2009), New insights for using self-assembly materials to improve the detection stability in label-free dna-chip and immuno-sensors, *Biosensors and Bioelectronics*, *24*(12), 3425–3429.
91. Teengam, P., Siangproh, W., Tuantranont, A., Vilaivan, T., Chailapakul, O., & Henry, C. S. (2018), Electrochemical impedance-based dna sensor using pyrrolidinyl peptide nucleic acids for tuberculosis detection, *Analytica Chimica Acta*, *1044*, 102–109.
92. Zangeneh, M. M., Norouzi, H., Mahmoudi, M., Goicoechea, H. C., & Jalalvand, A. R. (2019), Fabrication of a novel impedimetric biosensor for label free detection of DNA damage induced by doxorubicin, *International Journal of Biological Macromolecules*, *124*, 963–971.

93. Chiorcea-Paquim, A.-M., Eritja, R., & Oliveira-Brett, A. M. (2018), Electrochemical and AFM characterization of G-quadruplex electrochemical biosensors and applications, *Journal of Nucleic Acids*, *2018*.
94. Lei, K.-M., Mak, P.-I., Law, M.-K., & Martins, R. P. (2018), State-of-the-art CMOS in vitro diagnostic devices, *Handheld Total Chemical and Biological Analysis Systems*. Springer, 2018, 11–39.
95. Hassibi, A., Wood, N., & Manickam, A. (2018), CMOS biochips: Challenges and opportunities, *2018 IEEE Custom Integrated Circuits Conference (CICC)*, 1–7.
96. Wu, J., Dong, M., Rigatto, C., Liu, Y., & Lin, F. (2018), Lab-on-chip technology for chronic disease diagnosis, *NPJ Digital Medicine*, *1*(1), 1–11.
97. Baj-Rossi, C., Cavallini, A., Kilinc, E. G., Stradolini, F., Rezzonico Jost, T., Proietti, M., De Micheli, G., Grassi, F., Dehollain, C., & Carrara, S. (2016), In-vivo validation of fully implantable multi-panel devices for remote monitoring of metabolism, *IEEE Transactions on Biomedical Circuits and Systems*, *10*(5), 955–962.
98. Tan, X., Chen, S., Xiao, Z., Chen, F., & Wang, J. (2015), A low power potentiostat for implantable glucose sensor tag, *2015 IEEE 11th International Conference on ASIC (ASICON)*, 1–4.
99. Zuo, L., Islam, S. K., Mahbub, I., & Quaiyum, F. (2015), A low-power 1-V potentiostat for glucose sensors, *IEEE Transactions on Circuits and Systems II: Express Briefs*, *62*(2), 204–208.
100. Carrara, S. & Georgiou, P. (2018), Body dust: Miniaturized highly-integrated low power sensing for remotely powered drinkable CMOS bioelectronics, *arXiv preprint arXiv:1805.05840*.
101. Toumazou, C., Shepherd, L. M., Reed, S. C., Chen, G. I., Patel, A., Garner, D. M., Wang, C.-J. A., Ou, C.-P., Amin-Desai, K., Athanasiou, P. *et al.* (2013), Simultaneous DNA amplification and detection using a pH-sensing semiconductor system, *Nature methods*, *10*(7), 641.
102. Stagni, C., Guiducci, C., Benini, L., Riccò, B., Carrara, S., Samorí, B., Paulus, C., Schienle, M., Augustyniak, M., & Thewes, R. (2006), CMOS DNA sensor array with integrated A/D conversion based on label-free capacitance measurement, *IEEE Journal of Solid-State Circuits*, *41*(12), 2956–2964.
103. Manickam, A., You, K., Wood, N., Pei, L., Liu, Y., Singh, R., Gamini, N., McDermott, M. W., Shahrjerdi, D., Kuimelis, R. G., & Hassibi, A. (2019), A CMOS electrochemical biochip with 32 × 32 three-electrode voltammetry pixels, *IEEE Journal of Solid-State Circuits*, *54*(11), 2980–2990.
104. Chen, X., Guo, Z., Yang, G. M., Li, J., Li, M. Q., Liu, J. H., & Huang, X. J. (2010), Electrical nanogap devices for biosensing, *Materials Today*, *13*(11), 28–41.
105. Motto, P., Crepaldi, M., Piccinini, G., & Demarchi, D. (2014), NanoCube: A low-cost, modular, and high-performance embedded system for adaptive fabrication and characterization of nanogaps, *IEEE Transactions on Nanotechnology*, *13*(2), 322–334.
106. Bonanno, A., Sanginario, A., Marasso, S. L., Miccoli, B., Bejtka, K., Benetto, S., & Demarchi, D. (2016), A multipurpose CMOS platform for nanosensing, *Sensors (Switzerland)*, *16*(12).
107. Miccoli, B., Cauda, V., Bonanno, A., Sanginario, A., Bejtka, K., Bella, F., Fontana, M., & Demarchi, D. (2016), One-Dimensional ZnO/Gold Junction for Simultaneous and Versatile Multisensing Measurements, *Scientific Reports*, *6*(1), 1–10.
108. Ghobaei Namhil, Z., Kemp, C., Verrelli, E., Iles, A., Pamme, N., Adawi, A. M., & Kemp, N. T. (2019), A label-free aptamer-based nanogap capacitive biosensor with greatly diminished electrode polarization effects, *Physical Chemistry Chemical Physics*, *21*(2), 681–691.
109. Shim, J. S., Rust, M. J., & Ahn, C. H. (2013), A large area nano-gap interdigitated electrode array on a polymer substrate as a disposable nano-biosensor, *Journal of Micromechanics and Microengineering*, *23*(3), 035002. [Online]. Available: https://iopscience.iop.org/article/10.1088/0960-1317/23/3/035002
110. Tripathi, P., Moser, N., & Georgiou, P. (2019), A neuron-based isfet array architecture with spatial sensor compensation, *2019 IEEE International Symposium on Circuits and Systems (ISCAS)*, 1–5.
111. Tedjo, W. & Chen, T. (2019), An integrated biosensor system with a high-density microelectrode array for real-time electrochemical imaging, *IEEE Transactions on Biomedical Circuits and Systems*.
112. Wang, C., Cheng, N., Zhu, L., Xu, Y., Huang, K., Zhu, P., Zhu, S., Fu, W., & Xu, W. (2017), Colorimetric biosensor based on a DNAzyme primer and its application in logic gate operations for DNA screening, *Analytica Chimica Acta*, *987*, 111–117.
113. Hu, Z., Jian, J., Hua, Y., Yang, D., Gao, Y., You, J., Wang, Z., Chang, Y., Yuan, K., Bao, Z. *et al.* (2018), DNA colorimetric logic gate in microfluidic chip based on unmodified gold nanoparticles and molecular recognition, *Sensors and Actuators B: Chemical*, *273*, 559–565.
114. Gao, R.-R., Shi, S., Zhu, Y., Huang, H.-L., & Yao, T.-M. (2016), A RET-supported logic gate combinatorial library to enable modeling and implementation of intelligent logic functions, *Chemical Science*, *7*(3), 1853–1861.
115. Hun, X., Meng, Y., Wang, S., Mei, Z., & Luo, X. (2017), Concatenated logic gates by amplified chemiluminescence of hemin/g-quadruplex dnazyme based on a nonlinear hybridization chain reaction, *Sensors and Actuators B: Chemical*, *246*, 734–739.
116. Yan, Y., Yue, S., Zhao, T., Luo, B., & Bi, S. (2017), Exonuclease-assisted target recycling amplification for label-free chemiluminescence assay and molecular logic operations, *Chemical Communications*, *53*(90), 12 201–12 204.
117. Lian, W., Yu, X., Wang, L., & Liu, H. (2015), Biomacromolecular logic devices based on simultaneous electrocatalytic and electrochemiluminescence responses of Ru (bpy) 32+ at molecularly imprinted polymer film electrodes, *The Journal of Physical Chemistry C*, *119*(34), 20 003–20 010.
118. Bader, A. & Cockroft, S. L. (2018), Simultaneous G-quadruplex DNA logic, *Chemistry–A European Journal*, *24*(19), 4820–4824.
119. Tam, D. Y., Dai, Z., Chan, M. S., Liu, L. S., Cheung, M. C., Bolze, F., Tin, C., & Lo, P. K. (2016), A reversible DNA logic gate platform operated by one-and two-photon excitations, *Angewandte Chemie International Edition*, *55*(1), 164–168.
120. Yasuga, H., Kawano, R., Takinoue, M., Tsuji, Y., Osaki, T., Kamiya, K., Miki, N., & Takeuchi, S. (2016), Logic gate operation by dna translocation through biological nanopores, *PLoS One*, *11*(2), e0149667.
121. Liu, S., Li, M., Yu, X., Li, C.-Z., & Liu, H. (2015), Biomacromolecular logic gate, encoder/decoder and keypad lock based on DNA damage with electrochemiluminescence and electrochemical signals as outputs, *Chemical Communications*, *51*(67), 13 185–13 188.