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Advances in Trainable Molecular Algorithms for Biological Computing with DNA

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***Abstract*—The integration of trainable molecular algorithms within biological computing frameworks using DNA represents a transformative advance in unconventional computing paradigms. By leveraging the inherent parallelism, high storage density, and biochemical specificity of DNA molecules, these systems enable the execution of computational processes that transcend traditional silicon-based architectures. This work explores recent advances in the design and implementation of DNA-based learning systems capable of performing logical operations, adaptive decision-making, and basic machine learning tasks in biochemical environments. Additionally, the main challenges in the field are addressed, including kinetic unpredictability, molecular noise propagation, limited scalability, and constraints in the interface between molecular and electronic systems. Finally, future perspectives on the training of molecular algorithms are discussed, such as programmable biochemical networks, adaptive molecular memory, and the development of biochemical compilation toolchains. These advances pave the way toward autonomous and intelligent molecular systems with applications in biosensing, therapeutic diagnostics, and next-generation hybrid computing architectures.**

***Keywords*—molecular algorithms, trainable systems, synthetic biology, biochemical logic, bio-hybrid computing, adaptive molecular networks, unconventional computing, nanoscale learning, intelligent biomolecular systems.**

I. Introduction

In recent decades, DNA-based molecular computing has emerged as a promising alternative to traditional electronic paradigms, offering massive parallel processing, minimal energy consumption, and natural integration with biological systems [1]–[3]. Within this framework, trainable molecular algorithms represent an emerging frontier that enables the implementation of adaptive learning mechanisms at the molecular level [4], [5]. Trainable molecular algorithms are those implemented in biochemical systems that can adapt or modify themselves based on experience or environmental conditions. Unlike traditional molecular systems that execute rigidly encoded instructions, these algorithms are capable of modifying their internal parameters, such as reactant concentrations, structural states, or enzymatic configurations, in response to external signals or previous outcomes [4]–[6]. Different approaches have been proposed to materialize this idea. One of them is the use of DNA strand displacement systems, which allow the construction of reconfigurable logic gates and reaction networks controlled by sequence programming [7], [8]. Moreover, these mechanisms have been used to implement artificial neural structures such as molecular perceptrons, capable of performing basic classification tasks through molecular adjustment of "synaptic weights" [9]. Complementarily, the use of trainable dimerization reaction networks has been explored, allowing the evolution of biochemical response patterns through adaptive optimization, simulating learning processes at the molecular level [4].

A more advanced approach involves the emulation of complex neuronal models, such as discontinuous activation neurons, through the assembly of molecular systems capable of generating controlled discrete signals, similar to the activation spikes in biological neural networks [10]–[12]. These developments open the door to new forms of artificial intelligence implemented directly in biochemical environments, with potential to operate in contexts inaccessible to conventional electronic systems, such as intracellular environments or soft biological matrices [13].

The potential benefits of these models include distributed computing in biological environments, molecular sensors with learning capability, personalized medical treatments based on local processing of biological information, and biohybrid devices that integrate chemical processing with adaptive decision-making [6], [14]. However, challenges such as scalability, processing speed, tolerance to biological noise, and integration with external electronic platforms remain [7], [15].

This article presents a general review of the main advances between 2015 and 2025 in the field of trainable molecular algorithms for DNA-based biological computing. The most representative approaches, implementation strategies, and relevant demonstration experiments are compiled. The objective is to offer a consolidated view of this emerging area, identifying current contributions, limitations, and future projections in the context of intelligent biological computing.

II. Fundamentals of Molecular Computing with DNA

DNA molecular computing is a paradigm that leverages the physicochemical properties of nucleic acids to perform information processing tasks. Unlike conventional electronic

systems, DNA computing relies on chemical reactions primarily hybridization, strand displacement, and enzymatic modifications to encode and manipulate data at the nanoscale [1], [15].

DNA molecules store information in the sequence of their nucleotide bases (A, T, C, G), enabling massive parallelism and high data density [2]. A typical DNA computing process consists of several fundamental stages, which are described in Figure 1.

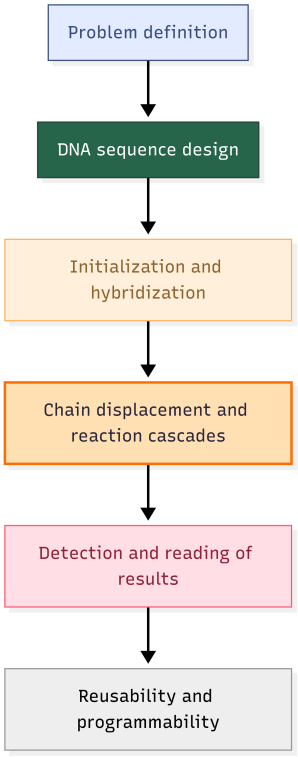

Fig. 1: Basic process flow of molecular DNA computation.

The first step in the workflow consists of problem encoding, in which the computational task to be solved is translated into a set of specific DNA sequences. Each logical variable, state, or operation is associated with an oligonucleotide designed to hybridize exclusively with its complementary counterpart. This encoding is essential to ensure that subsequent biochemical reactions faithfully reflect the logic of the desired algorithm [15]. Based on this foundation, the process advances to the design of DNA sequences, a stage where nucleotide strands are selected and optimized. The aim here is to maximize hybridization specificity, minimize undesired secondary structures, and control binding energies. Proper design reduces cross-reactions and improves the robustness of the entire molecular system [1], [7].

With the sequences defined, the process proceeds to initialization and hybridization, where synthesized strands are mixed in a controlled biochemical environment. Thanks to Watson–Crick base pairing, the target sequences selectively bind, giving rise to intermediate complexes that represent logical states of the system. This phase establishes the initial configuration upon which subsequent reactions will operate [1], [6].

Next, the process continues with strand displacement and reaction cascades, through mechanisms of *toehold-mediated strand displacement*. At this stage, auxiliary oligonucleotides displace previously hybridized fragments, activating or deactivating molecular logic gates. The concatenation of multiple displacement events generates reaction networks capable of executing complex sequential or parallel operations [5], [7], [8].

Once the computational phase is completed, result detection and reading are carried out. The reaction products are identified using techniques such as fluorescent markers, gel electrophoresis, or quantitative PCR. The released or modified strands correspond to the system's final responses, allowing the interpretation of the solution to the original problem [10], [13].

Finally, the stage of reusability and programmability explores how to reset or reconfigure the system for new computations. Through DNA origami techniques and reprogrammable self-assembly, it is possible to disassemble molecular complexes and regenerate active components, increasing modularity and extending the lifespan of biochemical computing devices [6], [9].

This approach offers unique advantages such as massive parallelism, biocompatibility, and integration with living systems, although challenges such as errors, reaction speed, and scalability remain [7], [15].

III. Trainable Molecular Algorithms

Trainable molecular algorithms represent an evolution in the design of biochemical systems capable of adaptation. Unlike traditional static DNA algorithms, these systems have the ability to modify their behavior through internal mechanisms that respond to chemical signals or experimental feedback. This section presents a concise overview of the main reported architectures, the training mechanisms employed, and representative examples that have demonstrated experimental or computational feasibility.

A. Representative Designs and Architectures

In the development of trainable molecular algorithms, one of the most widespread approaches is based on adaptive logic gates through DNA strand displacement. In these systems, regulatory oligonucleotides interact with specific inputs to dynamically modify the gate topology, so that the implemented logic (e.g., AND, OR, or NOT) is reconfigured according to molecular concentrations or external signals [7]. This reconfiguration capability forms the basis for designing reaction networks that adjust their behavior without the need to resynthesize the entire circuit.

A second group of architectures implements molecular perceptrons, inspired by artificial neurons, where "synapses" are emulated by catalytic oligonucleotides or exonucleases that regulate the weight of each input. By varying the concentration

of these reagents or enzymatic activity, the system adjusts its firing threshold, allowing the classification of binary signals directly in an aqueous medium [9]. These perceptrons have demonstrated the ability to learn basic classification tasks after chemically controlled training phases. Meanwhile, adaptive dimerization networks exploit dimer association and dissociation reactions to evolve response parameters. Through cycles of hybridization and stochastic rupture, these models emulate biochemical reinforcement processes, where input patterns favor the stabilization of optimal molecular configurations [4]. At a more complex level, spiking neuron-type models use DNA assemblies that generate discrete signal spikes, analogous to neuronal action potentials, achieving architectures capable of processing temporal information according to spike-timing-dependent training protocols [10].

Finally, enzymatic adjustment mechanisms constitute a complementary strategy, in which specific catalytic pathways modulate the system output based on a chemically measured error. By employing enzymes that degrade or extend DNA strands according to the difference between the desired and obtained signal, molecular feedback loops are implemented that progressively optimize the algorithm's performance [5]. These architectures offer a high degree of control and have been validated under laboratory conditions, demonstrating the feasibility of direct chemical learning. Table I presents a comparison of the most relevant trainable molecular algorithms reported in the literature between 2015 and 2025, emphasizing their training and implementation mechanisms.

IV. Results and Discussion

A. Recent Advances and Applications

The analysis of the 20 selected articles (Table II) reveals a notable concentration of scientific output in America, Europe, and Asia. The United States leads with 9 publications (45% of the total), accumulating 537 citations in total. It is followed by China with 5 articles and 310 citations, the United Kingdom with 2 papers and 250 citations, Germany with 1 article and 20 citations, Spain with 1 article and 14 citations, South Korea with 1 article and 40 citations, and the Netherlands with 1 article and 27 citations. Regarding methodologies and algorithms, approaches based on molecular neural networks stand out: winner-take-all networks (Cherry *et al.*) [16], molecular perceptrons [9], and chemically emulated spiking neurons [10] concentrate much of the interest. Simultaneously, programmable logic via strand displacement remains fundamental for designing reconfigurable gates [7], while DNA strand displacement enables complex circuit design [17] and the scaling of digital storage [1]. The most cited works, Cherry *et al.* (250 citations), Chen *et al.* (130 citations), and Buterez (120 citations) indicate a clear preference for hybrid architectures combining principles of classical artificial intelligence with biocomputing [1], [7], [16]. Additionally, emerging trends include DNA-based reinforcement agents [18], supervised learning in displacement networks [19], and enzymatic feedback mechanisms [20]. This statistical and thematic overview underscores the predominance of the United States and China in the development of trainable molecular algorithms, the dominance of molecular neural models, and the growing integration of deep learning techniques and programmable chemical control. These advances lay the groundwork for future applications in intelligent biosensing, personalized therapies, and biohybrid devices with in situ learning capabilities.

B. Challenges and Future Perspectives

Despite recent advances in the design and implementation of trainable molecular algorithms using DNA as a computational substrate, the field faces fundamental technical challenges that limit its scalability, reliability, and applicability in real-world environments. One of the main bottlenecks lies in the kinetics of biochemical reactions, which imposes severe constraints in terms of computational latency and parallelization capacity. Hybridization, dissociation, and degradation rates in DNA systems are not easily controllable and can be affected by physicochemical parameters such as temperature, pH, ionic concentration, or enzymatic contaminants, complicating the reproducibility of computational results.

Another critical challenge is the formal modeling of the dynamics of trainable DNA systems. Unlike conventional algorithms, where control structures and data are discrete and deterministic, molecular systems are governed by reaction equations and stochastic processes. This necessitates the development of hybrid formal languages that integrate models of chemical automata, biochemical reaction networks, molecular logic, and machine learning. Additionally, the training of these systems remains rudimentary: current methods, based on evolutionary optimization or molecular reinforcement learning, suffer from high computational complexity and low experimental efficiency, hindering scaling to high-level learning tasks.

The information storage capacity of DNA structures is theoretically high, but their manipulation for input/output processes, writing, and reading remains slow, costly, and error-prone, especially in dynamic contexts. The lack of robust bioelectronic interfaces that enable seamless interaction between digital and molecular modules further limits practical integration in hybrid systems. Additionally, cross-contamination, undesired DNA degradation, and nonlinear effects from multiple simultaneous reactions introduce high levels of molecular noise, compromising computational fidelity.

Regarding future perspectives, the design of self-trainable molecular systems is anticipated to be catalyzed by the convergence of synthetic biology, quantum computing, and deep learning. The creation of molecular architectures inspired by deep neural networks is projected, where the encoding of synaptic weights, activation functions, and backpropagation processes can be implemented through hybridization logic and enzymatic control, giving rise to trainable molecular neurons. Additionally, the implementation of in vitro structural learning systems is foreseen, in which reconfigurable DNA structures can adaptively modify their topology according to environmental stimuli, forming the basis of contextual molecular intelligence.

TABLE I: Summary of Trainable Molecular Algorithms in DNA

Model	Main Approach	Training Mechanism	Implementation	Reference
Molecular perceptron with λ-exonuclease	Binary pattern classification	Enzymatic adjustment of molecular weights	Experimental	[9]
Trainable dimerization networks	Adaptive chemical evolution	Stochastic reinforcement-based optimization	Simulation	[4]
Molecular spiking neuron	Neuro-inspired discrete spike signaling	Structural modulation of molecular signals	Experimental	[10]
Trainable logic gate with strand displacement	Adaptable logical molecular computing	Gate reconfiguration via strand displacement	Experimental	[7]
Weight-dependent enzyme learning	Chemical output adjustment	Enzymatic regulation based on measured error	Partial experimental	[5]
DNA-based WTA neural network	Pattern recognition via molecular input competition	Molecular input competition	Experimental	[16]
Adaptive circuits with strand displacement	Supervised molecular learning	Concentration gradient-based adjustment	Simulated and experimental	[19]
Reprogrammable self-assembly with origami	Reconfigurable modular molecular computing	Activation by trigger strands	Experimental	[6]
Programmable chemical controllers	Sequential biochemical control systems	Regulated biochemical networks	Experimental	[21]
DNA deep network design	Self-designed neural architectures via evolution	Computational topology evolution	Simulation	[15]

TABLE II: Recent Advances and Applications in Trainable Molecular Algorithms. Number of Citations (NC) from Google Scholar, accessed July 2025.

Article	Research Objective	Algorithm Used	Year	Country	NC
[16]	Scale efficient pattern recognition with DNA-based WTA neural networks.	Winner-take-all neural networks	2018	USA	250
[7]	Translate complex logic networks into programmable strand displacement devices.	Logic programming for nucleic acid devices	2018	UK	130
[1]	Improve DNA hybridization prediction for large-scale digital storage.	Deep learning for hybridization prediction	2021	UK	120
[22]	Program DNA reaction networks for intracellular logic-based cell recognition.	Programmable intracellular DNA biocomputing circuits	2019	China	91
[10]	Emulate a spiking neuron using DNA origami molecular systems experimentally.	Spiking neuron emulation	2021	USA	90
[15]	Design deep neural network architectures via DNA computing algorithms.	DNA computing structure learning	2018	China	75
[23]	Develop trainable DNA aptamers for multiplexed biosensing applications.	DNA aptamer-functionalized field-effect transistors	2020	USA	69
[8]	Build reliable 8-bit molecular adders and subtractors via strand displacement.	DNA strand displacement adder/subtractor	2018	China	60
[4]	Evaluate trainable dimerization networks as adaptive chemical classifiers.	Evolutionary chemical learning	2025	USA	45
[5]	Propose an enzymatic weight update algorithm in molecular learning systems.	Enzymatic weight update	2019	South Korea	40
[24]	Assist with deep learning in DNA nanostructure design for molecular computing.	Deep learning–based DNA origami detection and characterization via CNN	2022	USA	28
[25]	Create adaptive molecular circuits via programmable enzyme-driven reaction networks.	Automated design of programmable enzyme-driven DNA circuits	2015	Netherlands	27
[17]	Analog computation by DNA strand displacement circuits.	DNA strand displacement for analog computation	2016	USA	22
[13]	Develop molecular classifiers for biochemical signal classification tasks.	Molecular classification networks	2023	Germany	20
[26]	Evolutionarily optimize DNA computing circuits for performance.	Multi-objective evolutionary design of DNA libraries for computation	2018	Spain	14
[9]	Implement a programmable molecular perceptron using λ-exonuclease enzyme.	Molecular perceptron	2024	USA	10
[20]	Implement enzyme-controlled DNA neural network (neuron model with feedback via DNAzymes).	DNAzyme-regulated molecular neuron	2021	China	5
[18]	Design regulatory DNA sequences with reinforcement learning fine-tuning.	Regulatory DNA sequence design via reinforcement learning (TACO)	2025	USA	1
[27]	Create multistable reaction networks with dynamic learning behavior.	Programmable DNA reaction networks using allosteric hairpins	2023	China	0
[28]	Implement three-state logic computation by activating DNA origami strands.	Three-state logic gates activated by DNA origami	2024	USA	0

At the tool level, molecular hardware description languages (HDL-DNA) and biochemical compilers are being developed to enable the transition from algorithms written in high-level languages to executable reactions in in vitro systems. The use of microfluidic platforms, automated oligonucleotide synthesis, and high-throughput sequencing will allow increasingly agile training-execution cycles. In parallel, advances in optical reading technologies, field-effect transistor-based biosensing (bio-FETs), and nanopores will enable the establishment of bio-cyberphysical communication interfaces, necessary for the deployment of autonomous cyber-biological systems. In summary, a future generation of trainable molecular algorithms with capabilities for self-organization, distributed learning, and evolutionary adaptation is envisioned, which will be able to operate in a decentralized manner in applications such as intelligent biosensing, targeted therapies with intracellular computational logic, and biochemical decision-making networks. However, the transition to this paradigm requires a profound reconfiguration of computational design, from logical and mathematical foundations to experimental validation and verification methods, as well as the establishment of specific ethical and regulatory frameworks for living computational systems.

V. Conclusion

Advances in trainable molecular algorithms applied to biological computing with DNA represent a fundamental milestone in the convergence between synthetic biology and computer science. This approach proposes a paradigm shift by using biomolecules as the physical substrate for computation, enabling massive parallel processing, adaptability, and direct integration with living systems. Despite significant technical challenges such as low processing speed, reaction design complexity, biochemical noise, and limited scalability, the field is rapidly evolving thanks to the development of molecular modeling tools, automated DNA synthesis and sequencing platforms, and hybrid computational frameworks. The possibility of implementing trainable logic in molecular systems opens new pathways for disruptive applications in intelligent biosensing, personalized medicine, adaptive biotechnology, and biohybrid devices. In this context, trainable algorithms will not only redefine the notion of computation from a biophysical perspective but also drive the emergence of autonomous systems with learning, self-organization, and decision-making capabilities in complex biological environments. Consolidating this vision will require an interdisciplinary approach, as well as the development of standards, predictive design platforms, and a robust ethical framework to ensure the safety and sustainability of these emerging technologies.

References

[1] A. Buterez, "Scaling up dna digital data storage by efficiently predicting dna hybridisation using deep learning," *Nature Communications*, vol. 12, p. 1054, 2021.

[2] C. Limbachiya and S. Jain, "The art of dna strings: Sixteen years of dna coding theory," *ACM Computing Surveys*, vol. 49, pp. 1–39, 2016.

[3] L. Qian and E. Winfree, "Dna molecule provides a computing machine with both data and fuel," *Proceedings of the National Academy of Sciences*, vol. 108, pp. E616–E624, 2011.

[4] A. V. Tkachenko, B. M. Mognetti, and S. Maslov, "Evolutionary chemical learning in dimerization networks," *bioRxiv*, 2025, preprint. [Online]. Available: https://www.arxiv.org/abs/2506.14006

[5] S. Baek *et al.*, "Enzymatic weight update algorithm for dna-based molecular learning," *Biosystems*, vol. 182, pp. 1–10, 2019.

[6] D. Woods *et al.*, "Diverse and robust molecular algorithms using reprogrammable dna self-assembly," *Nature Chemistry*, vol. 11, pp. 249–258, 2019.

[7] Y. Chen, N. Dalchau, D. Soloveichik, and G. Seelig, "A logic programming language for computational nucleic acid devices," *Nature Chemistry*, vol. 10, pp. 139–148, 2018.

[8] D. Han and C. Zhou, "8-bit adder and subtractor with domain label based on dna strand displacement," *IEEE Transactions on Nanotechnology*, vol. 17, pp. 928–935, 2018.

[9] W. Zhang *et al.*, "Arbitrary digital dna computing: A programmable molecular perceptron using -exonuclease," *ACS Synthetic Biology*, 2024, in press.

[10] G. Seelig, D. Soloveichik, and E. Winfree, "Programming molecular systems to emulate a learning spiking neuron," *Nature Nanotechnology*, vol. 16, pp. 730–738, 2021.

[11] B. Cabarle *et al.*, "Spiking neural p systems with scheduled synapses," *Neural Processing Letters*, vol. 46, pp. 331–349, 2017.

[12] ——, "Spiking neural p systems with colored spikes," *Journal of Cellular Automata*, vol. 14, pp. 305–324, 2019.

[13] M. Kieffer *et al.*, "Molecular computation for molecular classification," *Nature Machine Intelligence*, vol. 5, pp. 224–232, 2023.

[14] M. Liu *et al.*, "Dna-based molecular machines," *Chemical Reviews*, vol. 119, pp. 10 612–10 635, 2019.

[15] Y. Zhong *et al.*, "Structure learning of deep networks via dna computing algorithm," *IEEE Access*, vol. 6, pp. 38 230–38 240, 2018.

[16] K. M. Cherry and L. Qian, "Scaling up molecular pattern recognition with dna-based winner-take-all neural networks," *Nature*, vol. 559, pp. 370–376, 2018.

[17] T. Song, S. Garg, R. Mokhtar, H. Bui, and J. Reif, "Analog computation by dna strand displacement circuits," *ACS Synthetic Biology*, vol. 5, no. 8, pp. 898–912, 2016, pMID: 27363950. [Online]. Available: https://doi.org/10.1021/acssynbio.6b00144

[18] Z. Yang, B. Su, C. Cao, and J.-R. Wen, "Regulatory dna sequence design with reinforcement learning," *arXiv preprint arXiv:2503.07981*, 2025.

[19] M. R. Lakin and D. Stefanovic, "Supervised learning in adaptive dna strand displacement networks," *ACS Synthetic Biology*, vol. 5, pp. 885–895, 2016.

[20] C. Chen, R. Wu, and B. Wang, "Development of a neuron model based on dnazyme regulation," *RSC advances*, vol. 11, no. 17, pp. 9985–9994, 2021.

[21] N. Srinivas, J. Parkin, G. Seelig, E. Winfree, and D. Soloveichik, "Programmable chemical controllers made from dna," *Nature Nanotechnology*, vol. 12, pp. 601–607, 2017.

[22] X. Gong, J. Wei, J. Liu, R. Li, X. Liu, and F. Wang, "Programmable intracellular dna biocomputing circuits for reliable cell recognitions," *Chemical science*, vol. 10, no. 10, pp. 2989–2997, 2019.

[23] Q. Liu, C. Zhao, M. Chen, Y. Liu, Z. Zhao, F. Wu, Z. Li, P. S. Weiss, A. M. Andrews, and C. Zhou, "Flexible multiplexed in2o3 nanoribbon aptamer-field-effect transistors for biosensing," *Iscience*, vol. 23, no. 9, 2020.

[24] M. Chiriboga, C. M. Green, D. A. Hastman, D. Mathur, Q. Wei, S. A. Díaz, I. L. Medintz, and R. Veneziano, "Rapid dna origami nanostructure detection and classification using the yolov5 deep convolutional neural network," *Scientific reports*, vol. 12, no. 1, p. 3871, 2022.

[25] H. W. Van Roekel, L. H. Meijer, S. Masroor, Z. C. Felix Garza, A. Estévez-Torres, Y. Rondelez, A. Zagaris, M. A. Peletier, P. A. Hilbers, and T. F. de Greef, "Automated design of programmable enzyme-driven dna circuits," *ACS synthetic biology*, vol. 4, no. 6, pp. 735–745, 2015.

[26] J. M. Chaves-González and J. Martínez-Gil, "An efficient design for a multi-objective evolutionary algorithm to generate dna libraries suitable for computation," *Interdisciplinary Sciences: Computational Life Sciences*, vol. 11, no. 3, pp. 542–558, 2019.

[27] R. Qin, S. Cui, X. Zhang, P. Shi, S. Zhou, and B. Wang, "Programming dna reaction networks using allosteric dna hairpins," *Biomolecules*, vol. 13, no. 3, p. 481, 2023.

[28] K. Wang, Q. Huang, M. R. Elshaer, B. Knorr, P. Chaikin, and G. Zhu, "Tri-state logic computation by activating dna origami chains," *Nanoscale*, vol. 16, no. 25, pp. 11 991–11 998, 2024.