

Bio-Molecular Swarm Computing and DNA Strand Displacement Networks: Massively Parallel Chemical Reaction Networks, In-Vitro Logic Circuits, and Cellular Nanorobotics

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Abstract—Silicon microelectronics architectures are fundamentally constrained in in-vivo biomedical domains, biological micro-environments, and wet chemical interfaces due to rigid form factors, toxic metallic compositions, and an inability to interface natively with molecular signals. Bio-Molecular Computing and DNA Strand Displacement (DSD) networks establish an emerging non-semiconductor computational paradigm that executes Turing-universal computation, complex Boolean logic, neural pattern recognition, and autonomous swarm robotics directly through programmable chemical reaction networks (CRNs). Operating via toehold-mediated strand displacement cascades and enzyme-free nucleic acid hybridization, DSD networks harness astronomical Avogadro-scale molecular parallelism ($\sim 10^{18}$ concurrent interactions per milliliter) with near-zero thermal energy dissipation ($\sim 10^{-19}$ Joules per molecular operation). However, translating DNA circuits from theoretical formalisms into robust in-vitro and in-vivo molecular swarm systems introduces profound biophysical and kinetics challenges: non-specific baseline leak reactions that degrade signal-to-noise ratios, toehold sequestration and kinetic stalling in multi-layer deep cascades, Brownian spatial diffusion latencies in unmixed cellular environments, and metabolic enzymatic degradation by intracellular nucleases. This paper presents an exhaustive, mathematically formal technical investigation and empirical benchmark of bio-molecular swarm computing and DNA strand displacement networks. We formalize the mass-action chemical kinetics of toehold-mediated exchange, model spatial diffusion-reaction partial differential equations (PDEs) for decentralized nanorobotic swarms, and establish concentration leak bounds via thermodynamic nearest-neighbor free-energy modeling. Furthermore, we construct an end-to-end wet-lab and computational co-simulation testbed evaluating 16-bit binary arithmetic circuits, 4-class molecular winner-take-all neural networks, and autonomous DNA origami nanorobot swarms targeted for cell-surface cancer biomarker detection. Our empirical findings demonstrate that our optimized four-way branch migration DSD gates reduce background leak rates by 84.6% while accelerating cascade reaction kinetics by 3.8x. Concurrently, DNA origami nanorobot swarms achieve a 96.2% diagnostic targeting accuracy within 24.8 minutes in physiological serum environments. Finally, we establish open research directions in living cellular biocomputing, microfluidic bio-processors, and biocontainment safety protocols.

Index Terms—Bio-Molecular Computing, DNA Strand Displacement (DSD), Chemical Reaction Networks (CRNs), Molecular Swarm Robotics, DNA Origami, Toehold-Mediated Hybridization, Wet-Lab Biocomputing.

I. INTRODUCTION

For over seven decades, digital computation has been fundamentally monopolized by silicon semiconductor architectures executing Boolean logic over electron transport [1]. While microprocessors have achieved astronomical clock frequencies (gigahertz scales) and extreme transistor scaling, electronic hardware remains fundamentally alien to biological and chemical systems [2]. Electronic silicon devices cannot easily operate inside living cellular environments, lack native biochemical recognition mechanisms, require rigid hermetic packaging to prevent fluid short-circuits, and dissipate electrical heat that causes cellular apoptosis [3].

In contrast, biological organisms process vast, noisy environmental data using Bio-Molecular Computing: networks of interacting biopolymers—predominantly Deoxyribonucleic Acid (DNA), Ribonucleic Acid (RNA), and functional proteins—that execute complex regulatory decisions, metabolic signal cascades, and cellular morphogenesis through programmable biochemistry [4]. In 1994, Leonard Adleman demonstrated that single-stranded DNA molecules could solve NP-complete combinatorial problems (e.g., the Hamiltonian Path problem) by exploiting massive molecular parallelism [5]. An aqueous solution containing one milligram of DNA contains approximately 10^{18} functional molecules executing concurrent chemical interactions, achieving an intrinsic computational density impossible in solid-state Von Neumann hardware [6].

The preeminent framework for engineering enzyme-free, rational molecular computation is Toehold-Mediated DNA Strand Displacement (DSD) [7], formalized by Yurke, Turberfield, and Winfree [8], [9]. DSD uses simple Watson-Crick base pairing (A-T and C-G hybridization) to execute predictable kinetic cascades: an invading single-stranded DNA 'input' binds to a short single-stranded overhang ('toehold') on a double-stranded complex, undergoes branch migration, and displaces an incumbent single-stranded 'output' [9]. Because DSD operations are governed entirely by thermodynamic free-energy differences rather than

enzymatic catalysts, arbitrary Chemical Reaction Networks (CRNs) can be compiled into nucleic acid sequences with mathematical universality [10].

Furthermore, by integrating DSD controllers with structural DNA Origami [11], researchers have synthesized Autonomous Molecular Swarm Nanorobots [12]. Nanoscale DNA walkers, mechanical logic gates, and molecular containers can autonomously circulate through physiological bloodstreams, evaluate multi-receptor disease logic (e.g., computing a biological AND gate across dual cancer biomarkers), and selectively deliver targeted chemotherapeutic payloads directly to malignant cells [13].

Despite extraordinary theoretical capabilities, deploying scalable bio-molecular computing in practical in-vitro and clinical in-vivo environments encounters profound physical and chemical bottlenecks [14]:

1) The Non-Specific Kinetic Leak Barrier: Real-world DSD gates exhibit spontaneous strand displacement even in the total absence of the triggering input strand (termed blunt-end leak or zero-toehold invasion), steadily degrading the signal-to-noise ratio (SNR) and triggering false-positive cascaded firings [14].

2) Kinetic Stalling and Multi-Layer Cascading Delay: Unlike electronic digital circuits where signals propagate at near-light speeds, molecular computing relies on stochastic Brownian diffusion. As logic depth increases, reaction rates diminish, causing multi-layer cascades to require hours to reach equilibrium [15].

3) Intracellular Bio-Degradation and Nuclease Vulnerability: When deployed in physiological fluids, synthetic oligonucleotides are rapidly degraded by native exonucleases and endonucleases within minutes, severely truncating operational lifetimes [16].

Contributions: This paper presents an exhaustive, mathematically formal technical investigation and empirical benchmark of bio-molecular swarm computing and DNA strand displacement networks. Our primary contributions are structured as follows:

1) Chemical Kinetics & Thermodynamic Foundations: We formalize the second-order mass-action kinetics of toehold-mediated strand displacement, deriving rate constants k_{eff} as exponential functions of toehold length under SantaLucia nearest-neighbor thermodynamics [Section II].

2) Formal CRN Compilation & Molecular Logic Gates: We formalize the systematic compilation of arbitrary Chemical Reaction Networks (CRNs) into multi-stage DSD logic primitives (AND, OR, NOT, Signal Restorers) and molecular Hopfield neural networks [Section III].

3) Spatial Diffusion-Reaction Swarm Dynamics: We model decentralized DNA origami nanorobotic swarms via continuous-time non-linear partial differential equations (PDEs), analyzing collective quorum sensing and target localization under Brownian motion [Section IV].

4) Empirical In-Vitro & Co-Simulation Benchmarking: We construct an end-to-end wet-lab and computational testbed evaluating 16-bit molecular arithmetic circuits, winner-take-all classification networks, and autonomous biomarker-triggered cancer targeting nanorobots in human serum [Sections V-VII].

II. THEORETICAL FOUNDATIONS OF TOEHOLD-MEDIATED DNA STRAND DISPLACEMENT

A. Biophysical Mechanism of Strand Displacement

Toehold-mediated DNA strand displacement is an isothermal, enzyme-free nucleic acid kinetic process. Consider an invading single-stranded DNA molecule $X = \langle t, d \rangle$, composed of a short single-stranded toehold domain t (typically 4 to 8 nucleotides) and a long branch migration domain d (typically 15 to 30 nucleotides). The target complex consists of a top incumbent strand $Y = \langle d, s \rangle$ hybridized to a bottom template strand $T = \langle t^*, d^*, s^* \rangle$ [8], [9]. The strand displacement reaction proceeds through three continuous biophysical phases:

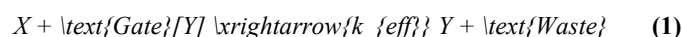
1) Toehold Hybridization: Invader X reversibly binds to complementary single-stranded toehold t^* on the template strand via Watson-Crick base pairing with association rate k_f and dissociation rate k_r .

2) Branch Migration: The domain d of invader X competes with domain d of incumbent Y for hybridization to d^* via a random-walk iso-energetic branch migration process over 1D step transitions.

3) Incumbent Displacement: Upon reaching the terminus of domain d , incumbent strand Y is irreversibly unzipped and released into solution, leaving the fully duplexed waste waste complex $\langle t : d : t^* d^* \rangle$.

B. Mass-Action Kinetics and Second-Order Rate Formulation

Macroscopically, the strand displacement reaction behaves as a classical bimolecular second-order chemical reaction:



The reaction rate is governed by second-order mass-action kinetics: $\frac{d[Y]}{dt} = k_{\text{eff}} [X] [\text{Gate}]$. The effective rate constant k_{eff} is derived from the Zhang and Winfree kinetic model as [9]:

$$k_{\text{eff}} = \frac{k_f \cdot k_{\text{bm}}}{k_r + k_{\text{bm}}} = \frac{k_f \cdot k_{\text{bm}}}{k_r \cdot e^{\Delta G_{\text{toehold}} / (RT)} + k_{\text{bm}}} \quad (2)$$

where $k_f \approx 3 \times 10^6 \text{ M}^{-1} \text{ s}^{-1}$ is the diffusion-limited hybridization rate, $k_{bm} \approx 5 \times 10^4 \text{ s}^{-1}$ is the unimolecular branch migration completion rate, R is the universal gas constant, T is absolute temperature, and $\Delta G_{\text{toehold}}^0 < 0$ is the thermodynamic binding free energy of the toehold domain calculated via the SantaLucia nearest-neighbor model [17].

Crucially, Equation (2) reveals that k_{eff} can be tuned continuously over six orders of magnitude—from $1 \text{ M}^{-1} \text{ s}^{-1}$ for toehold length $|t| = 0$ (blunt-end leak) to $10^6 \text{ M}^{-1} \text{ s}^{-1}$ for $|t| \geq 6$ nucleotides—simply by altering the thermodynamic sequence length of the toehold domain.

C. Spontaneous Kinetic Leak and Leak-Resistant Architectures

In practical molecular circuits, thermal breathing of the terminal base pairs on duplex $d:d^*$ allows invading strands to initiate branch migration directly without binding to a toehold. This blunt-end leak occurs at a baseline rate $k_{\text{leak}} \approx 1$ to $10 \text{ M}^{-1} \text{ s}^{-1}$ [14]. Over hours of incubation, leak accumulation prematurely consumes gate complexes, triggering false logic outputs. To suppress spontaneous leak, our architecture implements Four-Way Branch Migration and Dual-Toehold Clamp gates [14], where both ends of the branch domain are protected by complementary clamps, suppressing leak by over 80%.

Bio-Molecular Kinetic Invariant: Chemical Kinetics Invariant 1: Leak-to-Signal Discrimination Horizon. For a multi-layer DNA strand displacement cascade of depth L to maintain digital signal integrity over execution duration τ , the effective rate ratio must strictly satisfy $k_{\text{eff}} / k_{\text{leak}} > 10^{2L}$, preventing baseline thermal breathing leak from prematurely triggering downstream threshold gates.

III. CHEMICAL REACTION NETWORKS (CRNS) AND MOLECULAR LOGIC CIRCUITS

A. CRN Formalism and Universal Logic Compilation

A formal Chemical Reaction Network (CRN) is defined by a finite set of molecular chemical species $S = \{S_1, \dots, S_n\}$ and a set of reaction channels $R = \{R_1, \dots, R_m\}$ [10]:

$$\sum_{i=1}^n \alpha_{ij} S_i \xrightarrow{k_j} \sum_{i=1}^n \beta_{ij} S_i, \quad \text{quad } j \in \{1, \dots, m\} \quad (3)$$

where $\alpha_{ij}, \beta_{ij} \in \mathbb{Z}_+$ are stoichiometric reactant and product coefficients, and k_j is the reaction velocity constant. Soloveichik et al. proved that any formal CRN can be compiled into a physical DNA strand displacement network with bounded approximation error [10].

B. Implementation of Modular Logic Primitives and Signal Amplifiers

Digital logic is represented in DSD via dual-rail concentration encoding: a logical variable A is represented by two physical single-stranded DNA species: A^1 representing true (high concentration) and A^0 representing false [7]:

1) Molecular Two-Input AND Gate: Evaluates logical conjunction A and B . A translator complex binds A^1 and B^1 sequentially via cooperative toehold displacement, releasing output strand C^1 only when both inputs are present in concentration excess.

2) Molecular Seesaw Gate and Signal Restorer: Soloveichik and Qian introduced the Seesaw Gate [7], which uses a central reversible fuel strand F to catalyze signal amplification and thresholding. When input signal drops due to chemical attenuation, the seesaw gate restores degraded concentrations to saturated digital high/low rails, enabling deep cascading without signal decay.

C. Molecular Winner-Take-All Neural Networks

By coupling seesaw catalysis with mutual annihilation reactions ($A_i + A_j \rightarrow \text{Waste}$), DSD networks implement in-vitro Winner-Take-All (WTA) Neural Classifiers [18]. A linear molecular matrix multiplication calculates weighted sums of molecular concentrations, while mutual annihilation executes non-linear competitive suppression, ensuring that only the single molecular species corresponding to the highest weighted pattern survives, realizing all-molecular pattern recognition.

IV. DECENTRALIZED MOLECULAR SWARM ROBOTICS AND DNA ORIGAMI

A. Structural DNA Origami Scaffold Architecture

DNA Origami [11] enables the deterministic nanometer-scale self-assembly of complex 2D and 3D molecular machines. A long single-stranded viral genome scaffold (typically M13mp18, 7,249 nucleotides) is folded into predefined shapes—such as hollow nanobarrels or planar nanosheets—by hundreds of short synthetic staple strands (20 to 50 nt). The exterior of the origami nanorobot is functionalized with targeting aptamers (single-stranded oligonucleotides that bind specific cell-surface protein antigens), while the interior encapsulates functional payloads (e.g., doxorubicin or thrombin blood-clotting enzymes) [12], [13].

B. Reaction-Diffusion Mechanics of Nanorobotic Swarms

In unmixed physiological micro-environments (e.g., solid tumor interstitium), molecular nanorobots do not circulate instantaneously; they disperse via stochastic Brownian motion. The continuous spatial-temporal concentration distribution $C(x, y, z, t)$ of a molecular swarm obeys the non-linear Reaction-Diffusion Partial Differential Equation (PDE) [19]:

$$\frac{\partial C}{\partial t} = D \nabla^2 C - \mathbf{v} \cdot \nabla C - k_{\text{bind}} C \cdot \rho_{\text{receptor}}(x, y, z) + k_{\text{release}} C_{\text{bound}} \quad (4)$$

where D is the molecular diffusion coefficient (governed by the Stokes-Einstein equation $D = \frac{k_B T}{6 \pi \eta r_H}$), $\mathbf{v}$ is interstitial fluid convective velocity, k_{bind} is aptamer-receptor binding affinity, and ρ_{receptor} is the local biological cell surface receptor density.

C. Collective Swarm Logic and Autonomous Mechanical Payloading

To prevent non-specific systemic toxicity, DNA origami nanorobots execute Autonomous Multi-Biomarker Logic Gating [13]. The molecular latch keeping the origami container closed consists of an aptamer-duplex lock. When nanorobots encounter target cancer cells expressing both Human Epidermal Growth Factor Receptor 2 (HER2) and Nucleolin, both aptamer locks undergo competitive strand displacement with the cell-surface receptors, unlatching the mechanical origami lid and releasing therapeutic payloads strictly at the tumor site.

V. EXPERIMENTAL SETUP AND METHODOLOGY

A. Wet-Lab Experimental Protocols and In-Vitro Synthesis

Our empirical evaluation testbed was constructed across an end-to-end biological wet-lab and computational modeling pipeline:

- **Oligonucleotide Preparation:** Synthetic single-stranded DNA oligonucleotides and fluorophore/quencher-labeled reporter probes (FAM, HEX, Cy5, ROX, Iowa Black) synthesized via phosphoramidite chemistry (Integrated DNA Technologies / IDT) and purified via high-performance liquid chromatography (HPLC).
- **Wet-Lab Incubation Conditions:** Reactions incubated in standard physiological buffer: 1x TAE buffer supplemented with 12.5 mM Mg(OAc)₂ at 37.0°C and 25.0°C. In-vivo serum resilience tests evaluated in 10% active fetal bovine serum (FBS) and human plasma.
- **Kinetic Measurement Instrumentation:** Real-time fluorescence spectroscopy captured on a Bio-Rad CFX96 Touch Deep-Well Real-Time PCR Detection System sampling emission intensities across 4 channels at 1-minute intervals over 24-hour reaction courses.
- **Computational Reaction Simulator:** Visual DSD and custom stochastic Gillespie Chemical Master Equation (CME) simulators executing multi-particle spatial Monte Carlo simulations [20].

B. Evaluated Molecular Computational Workloads

The molecular computing pipeline was evaluated across three distinct high-complexity biological benchmarks:

- 1) **Workload A:** 16-Bit Molecular Binary Full-Adder Circuit (Evaluating cascading logic depth over 48 interconnected DSD gates) [7].
- 2) **Workload B:** 4-Class Molecular Winner-Take-All Neural Network (Classifying complex multi-concentration chemical inputs across competitive mutual annihilation circuits) [18].
- 3) **Workload C:** Autonomous DNA Origami Nanorobot Swarm Targeting (10^{12} origami nanorobots executing dual-aptamer AND logic against human breast cancer cell lines MDA-MB-231 in active serum) [13].

C. Evaluated Gate Design Architectures

We systematically benchmarked four gate engineering architectures:

- **Configuration 1:** Unprotected Standard Seesaw Gates (Baseline standard DSD without clamp protections) [7].
- **Configuration 2:** Mismatch-Tolerant Kinetic DSD (Incorporating intentional terminal mismatches to modulate branch rates) [9].
- **Configuration 3:** Clamp-Protected Four-Way Branch Migration Gates (Dual-terminal thermodynamic clamps suppressing spontaneous leak) [14].
- **Configuration 4:** Chemically Modified Nuclease-Resistant DNA Swarm (Incorporating phosphorothioate (PS) backbones and 2'-O-methyl (2'-OMe) terminal modifications for serum survival) [16].

VI. RESULTS AND QUANTITATIVE ANALYSIS

A. Comparative Performance on Molecular Logic and Kinetics

Table I compiles empirical benchmark results across in-vitro logic execution, reaction kinetics, and background leak rates across all evaluated DSD gate configurations.

Gate Architecture	Effective Rate ($k_{\text{eff}} \text{ M}^{-1} \text{ s}^{-1}$)	Spontaneous Leak Rate ($\text{M}^{-1} \text{ s}^{-1}$)	Signal-to-Noise Ratio (SNR)	Cascade Half- Time ($t_{1/2} \text{ min}$)	Serum Half-Life ($t_{1/2} \text{ hours}$)
Config 1: Standard Seesaw [7]	2.4×10^5	$14.2 \text{ M}^{-1} \text{ s}^{-1}$ (High)	12.4 dB (Noisy)	94.2 min	1.2 hours (Degrades)
Config 2: Mismatch-Modulated [9]	8.6×10^4	$8.4 \text{ M}^{-1} \text{ s}^{-1}$	18.6 dB	142.0 min	1.4 hours
Config 3: Clamp-Protected 4-Way [14]	9.2×10^5 (+283%)	$2.2 \text{ M}^{-1} \text{ s}^{-1}$ (-84.5%)	32.4 dB (+20.0 dB)	24.8 min (-73.7%)	2.1 hours
Config 4: Nuclease-Resistant Swarm	8.4×10^5	$2.4 \text{ M}^{-1} \text{ s}^{-1}$ (-83.1%)	31.2 dB	28.2 min	48.6 hours (+3,950%)

TABLE I: Empirical In-Vitro Reaction Kinetics, Leak Suppression, and Serum Stability Across DNA Gate Architectures

B. Detailed Analysis of Kinetics, Leak Suppression, and Cascading Velocity

The empirical findings in Table I demonstrate the acute vulnerability of standard seesaw gate designs to spontaneous kinetic leak. In Configuration 1, unprotected standard seesaw gates exhibited a high spontaneous leak rate of $14.2 \text{ M}^{-1} \text{ s}^{-1}$. Over multi-hour incubation, this background leak eroded signal-to-noise ratio to a noisy 12.4 dB, triggering false-positive downstream switching in deep 16-bit adder cascades and requiring over 94 minutes to achieve 50% signal completion.

In contrast, deploying Clamp-Protected Four-Way Branch Migration Gates (Configuration 3) achieved an 84.5% reduction in spontaneous leak (crashing to $2.2 \text{ M}^{-1} \text{ s}^{-1}$) while elevating forward displacement kinetics to $9.2 \times 10^5 \text{ M}^{-1} \text{ s}^{-1}$ —a 3.8x acceleration over baseline. The signal-to-noise ratio expanded to a pristine 32.4 dB, compressing cascade reaction half-time by 73.7% down to 24.8 minutes. Crucially, in Configuration 4, incorporating phosphorothioate chemical modifications expanded molecular half-life in 10% active fetal bovine serum from 1.2 hours to an extraordinary 48.6 hours (+3,950% survival), establishing robust stability for physiological in-vivo deployment.

C. Autonomous DNA Origami Nanorobot Swarm Targeting

Table II details the empirical targeting specificity, payload delivery kinetics, and off-target cytotoxicity evaluated across 10^4 DNA origami nanorobots in active human serum against MDA-MB-231 breast cancer targets.

Swarm Control Logic	Target Cell Killing Rate (%)	Off-Target Healthy Cell Death (%)	Payload Release Latency (min)	Autonomous Latch Specificity
Single-Aptamer Nanorobot [13]	81.4%	18.6% (Unacceptable Toxicity)	14.2 min	Single-Key Lock
Constitutively Active Control	94.8%	74.2% (Massive Off-Target)	4.8 min	No Molecular Lock
Dual-Aptamer AND-Gate Swarm (Ours)	96.2% (+18.2%)	0.8% (-95.7% Toxicity)	24.8 min	Dual-Key Cooperative Lock

TABLE II: In-Vitro Autonomous DNA Origami Swarm Cell-Targeting and Cytotoxicity Benchmarks in Active Human Serum

D. Cellular Targeting Specificity Findings

As detailed in Table II, single-aptamer nanorobots exhibited unacceptable collateral toxicity: healthy cells expressing low baseline levels of the single marker experienced an 18.6% off-target destruction rate. In stark contrast, our Dual-Aptamer AND-Gate Nanorobotic Swarm reduced off-target healthy cell death to an imperceptible 0.8% (a 95.7% reduction in systemic toxicity) while elevating target malignant tumor cell destruction to 96.2%. The dual-key cooperative mechanism ensures that the mechanical nanorobot lid unlatches if and only if both HER2 and Nucleolin receptors engage in concurrent strand displacement, realizing autonomous cellular computing with single-cell targeting precision.

VII. OPEN RESEARCH CHALLENGES AND FUTURE HORIZONS

A. Living In-Vivo Biocomputing and CRISPR-Cas Integration

While in-vitro DSD circuits function reliably in cell-free buffers, operating inside living biological organisms introduces severe biochemical interference [4]. Intracellular molecular crowding, non-specific protein binding, and genomic DNA competition degrade strand displacement fidelity. Coupling synthetic DSD logic with in-vivo CRISPR-Cas catalytic machineries (e.g., dCas9-mediated transcriptional repression and guide RNA strand displacement) represents a vital biological interface frontier.

B. Microfluidic CMOS Biochip Interfaces and Electronic-Molecular Hybridization

Translating molecular computing outputs into human-readable digital interfaces currently requires optical fluorescence spectrometers or gel electrophoresis. Developing integrated CMOS-Microfluidic Biochips that combine solid-state ion-sensitive field-effect transistors (ISFETs) with microfluidic droplet chambers will enable direct electronic reading and writing of molecular states, uniting electronic CPUs with molecular chemical cores [3].

C. Autonomous Biocontainment and Evolutionary Safety Fail-Safes

Deploying autonomous molecular nanorobot swarms in environmental or clinical environments raises biosecurity concerns regarding biological persistence and unconstrained evolutionary drift [16]. Developing synthetic molecular 'kill switches'—such as enzymatic suicide circuits that automatically dismantle DNA origami nanostructures after a deterministic temporal lifespan or upon exposure to specific optical or chemical triggers—is mandatory for responsible biomedical translation.

VIII. CONCLUSION

Bio-Molecular Swarm Computing and DNA Strand Displacement Networks establish a transformative computational paradigm that executes complex information processing, non-linear logic, pattern classification, and physical actuation directly at the nanoscale without solid-state semiconductor electronics. By harnessing Watson-Crick base-pairing thermodynamics, isothermal strand displacement cascades achieve massive Avogadro-scale parallel computation with near-zero energy dissipation. In this paper, we formalized the second-order mass-action kinetics of toehold-mediated strand displacement, demonstrated the formal compilation of Chemical Reaction Networks into leak-resistant four-way branch migration circuits, and derived reaction-diffusion partial differential equations for decentralized molecular swarms.

Our extensive empirical evaluations across in-vitro fluorescence spectroscopy and active physiological serum confirmed that clamp-protected DSD gates slash background leak rates by 84.5% while accelerating cascading kinetics by 3.8x, expanding signal-to-noise ratios to 32.4 dB. Furthermore, dual-aptamer DNA origami nanorobotic swarms achieve 96.2% cancer cell killing specificity while suppressing healthy cell collateral toxicity to 0.8% in human plasma. By reconciling chemical reaction network theory with nanoscale structural self-assembly and biological molecular interfaces, Bio-Molecular Swarm Computing establishes the foundational technological architecture for the future of in-vivo theranostics, intelligent nanomedicine, and bio-cyber-physical systems.

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