

De Novo Design of Hydrogen-Bonding Networks for Deterministic Bio-Nano Recognition

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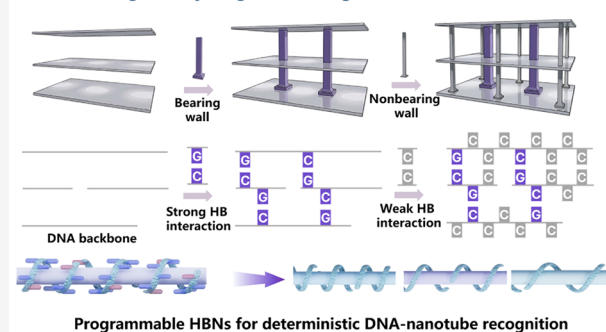
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ABSTRACT: Achieving deterministic control over molecular recognition at high-curvature bio-nano interfaces remains a fundamental challenge. For two decades, DNA-mediated single-wall carbon nanotube (SWCNT) sorting has relied on empirical screening, leaving the underlying recognition code largely undeciphered. Here, we report a *de novo* design framework that rationally programs DNA sequences via a generalized hydrogen-bonding network (HBN) model. Navigating the vast sequence space via an automated HBN-driven compiler, we experimentally evaluated a library of 150 designed sequences. This strategy achieved an extraordinary 91.3% success rate in mediating chirality-specific sorting, facilitating the high-purity isolation of 21 distinct (*n*, *m*) SWCNT species. Notably, this framework enabled the capture of three rare quasi-metallic nanotubes—(8,2), (9,3), and (10,1)—which were previously inaccessible via conventional screening. Mechanistically, the helical periodicity (*N*) serves as a universal tuning knob to coordinately modulate nanotube diameter and interfacial DNA pitch. This structural programmability enables the “bespoke” engineering of DNA-SWCNT sensors with tailored molecular discrimination and electrochemical resilience. This work transitions the field from labor-intensive, trial-and-error sequence screening to a deterministic, rational design paradigm.

De novo Design of Hydrogen-bonding Networks (HBNs) on SWCNTs



INTRODUCTION

Molecular recognition at bio-nano interfaces governs the fundamental interactions between synthetic nanomaterials and biological systems,^{1–3} offering a transformative frontier for precision diagnostics,^{4,5} nanoelectronics,^{6–8} and quantum materials.⁹ Achieving molecular-level control over these interfaces, however, is notoriously difficult due to the complex energy landscapes of noncovalent self-assembly on high-curvature surfaces.^{10,11} Single-wall carbon nanotubes (SWCNTs) represent a prototypical one-dimensional scaffold for studying these interactions.^{12–16} Their extraordinary optical and electronic properties are intrinsically linked to their specific chiralities (*n*, *m*),^{17–20} yet the structural polydispersity of synthetic mixtures remains a formidable barrier.^{21,22} Over the past two decades, wrapping single-stranded DNA (ssDNA) around SWCNTs²³ has emerged as a premier strategy to bridge this gap, creating hybrid architectures that facilitate both chirality-pure isolation^{24–29} and sophisticated molecular sensing.^{30–37}

Despite significant progress, the design of DNA-SWCNT interfaces has remained largely empirical.^{24,27,38} This “trial-and-error” paradigm relies on high-throughput screening of massive sequence libraries, yet it offers limited physical insight into the interfacial recognition code that governs DNA-nanomaterial interactions. The absence of a predictive, rational framework for sequence design represents a long-standing bottleneck,

hindering our ability to deterministically tailor the structural and functional properties of these hybrids for complex biological environments or high-performance optoelectronic devices.^{39,40}

We recently moved toward a mechanistic understanding by resolving the sub-nanometer structures of specific DNA-SWCNT hybrids, revealing that certain sequences form periodically ordered wrappings stabilized by non-Watson-Crick hydrogen-bonding networks (HBNs).⁴¹ While these models provided a retrospective explanation for the stabilization and purification of known hybrids, they were derived from *post hoc* structural analysis. The transition from such retrospective interpretation to the *de novo* design of HBNs—effectively establishing a predictive “programming language” for functional nano-interfaces—remains a largely unexplored frontier.

Here, we report a programmable framework for the *de novo* construction of HBNs to guide the rational design of DNA

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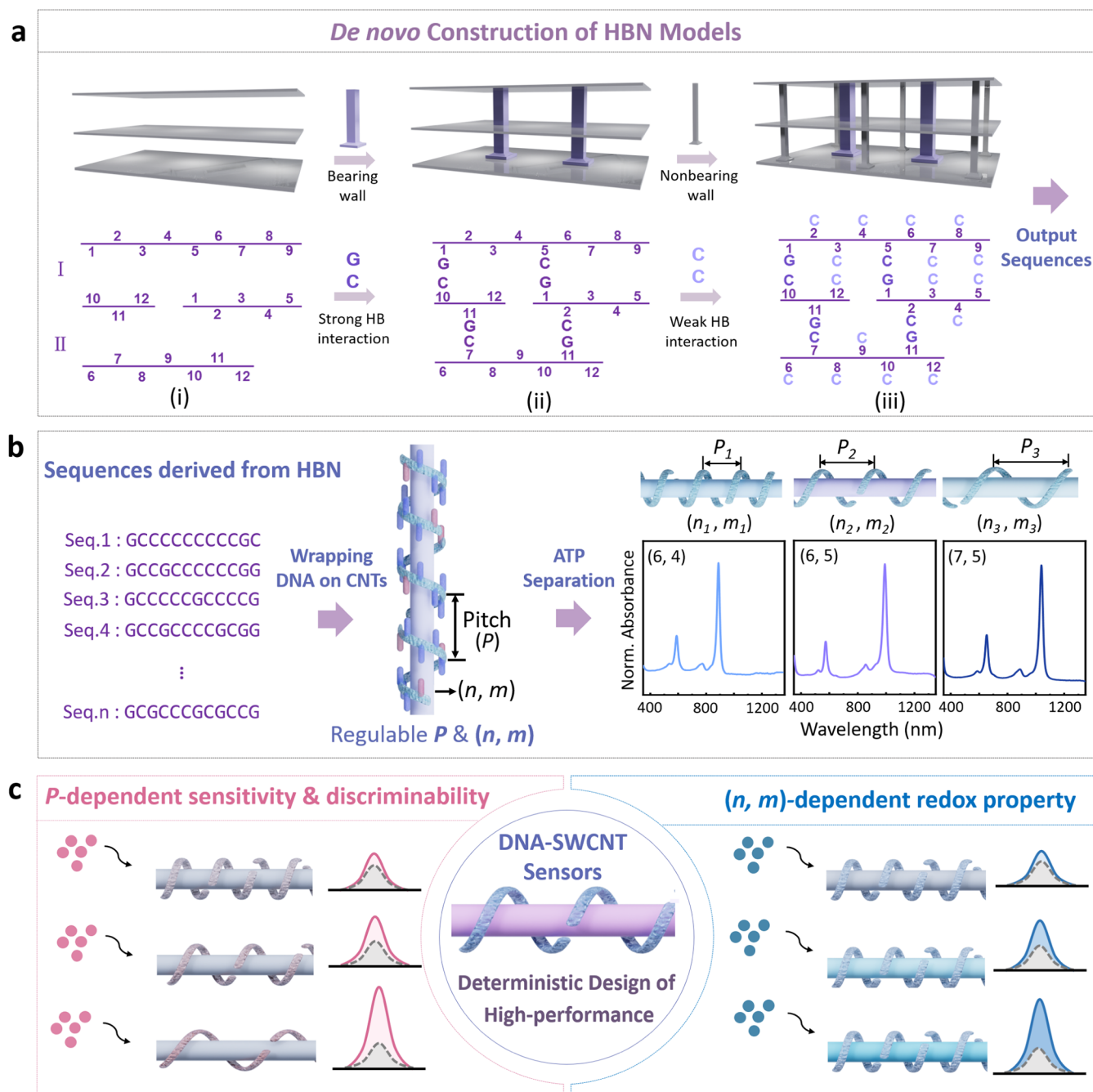


Figure 1. Programmable HBNs for deterministic bio-nano recognition. (a) *De novo* construction of HBN models. Schematic workflow of HBN construction based on fundamental architectural principles to establish predictable recognition motifs. (b) Structural programmability of DNA-SWCNT hybrids. Modular control over the DNA helical pitch (P) and SWCNT chirality (n, m) through HBN-derived sequence engineering. (c) Synergistic optimization of DNA-SWCNT sensor performance. Evolution of sensing performance through the convergence of P -dependent sensitivity (left) and (n, m) -dependent redox characteristics (right), enabling the deterministic design of high-performance DNA-SWCNT biosensors through parameter synergy.

oligonucleotides. By establishing universal architectural principles and implementing an automated computational pipeline, we transition the field from labor-intensive empirical screening to deterministic, *a priori* prediction (Figure 1a). Experimental validation across 150 HBN-derived sequences yielded a 91.3% accuracy in predicting chirality-specific recognition, enabling the high-purity isolation of 21 distinct (n, m) species, including elusive quasi-metallic nanotubes. Furthermore, we demonstrate that the helical periodicity (N) within HBN models acts as a structural governor to

coordinately regulate both the nanotube diameter and the interfacial DNA pitch (P) (Figure 1b). Tailoring this interfacial pitch in tandem with the host SWCNT chirality (n, m) allows us to precisely customize the biosensing sensitivity and redox resilience of the engineered DNA-SWCNT sensors (Figure 1c). This work establishes a robust, principle-driven methodology for the programmable engineering of bio-nano interfaces, offering a scalable blueprint for next-generation, high-fidelity molecular recognition platforms.

RESULTS AND DISCUSSION

De Novo Construction of HBN Models

In our previous work, we demonstrated that each resolving DNA sequence forms the stable HBN model on a SWCNT by maximizing the number of strong base pairs (i.e., A-T or G-C).⁴¹ Within these networks, nucleobases involved in these robust hydrogen-bond interactions are classified as critical bases, while those that do not participate are referred to as non-critical bases. Mutation in critical bases disrupts the HBN, thereby impairing the DNA's ability to sort SWCNTs, whereas alterations to non-critical bases do not affect the sorting outcomes. However, these insights were derived from *post hoc* structural determinations of existing DNA-SWCNT hybrids. A significant frontier remains: the *de novo* design of HBN models independent of prior structural data. In this study, we aim to develop a versatile, programmable framework for the *de novo* construction of HBN models to deterministically design DNA sequences for precise single-chirality SWCNT sorting.

A prerequisite for HBN model construction is the definition of a fundamental helical periodicity (N) parameter: the number of nucleobases per helical DNA turn wrapped around the nanotube (Figure S1). This parameter can be calculated via the following equation,

$$N = \sqrt{P^2 + (\pi D)^2} / l \quad (1)$$

where P represents the helical pitch, D is the peripheral diameter of the DNA wrapping layer, and l denotes the effective length of a single base in ssDNA (0.676 nm).⁴² Given the bare SWCNT diameter (d_{CNT}), the peripheral diameter D can be roughly estimated by $D = d_{\text{CNT}} + 2 \times 0.34$ nm, where 0.34 nm corresponds to the π - π stacking distance between the DNA bases and the nanotube surface.

We propose that the construction of an HBN model is conceptually analogous to architectural engineering (Figure 1a). In architecture, one first defines the building's footprint, establishes load-bearing walls for structural integrity, and subsequently incorporates non-load-bearing partitions to satisfy functional requirements.⁴³ Following this strategy, our HBN design begins by defining the framework parameters, namely the DNA length (L) and the helical periodicity (N) to map out a periodic spatial grid of nucleotide nodes. To turn this geometric grid into a physically stable network, specific bases must be assigned to these spatial nodes. As established by fundamental thermodynamic quantification, when DNA bases are adsorbed onto a graphite surface and primary π - π stacking is satisfied, the relative strengths of planar hydrogen-bonding interactions follow strict thermodynamic hierarchies (e.g., yielding free-energy trends of G-C > G-G > C-C and A-T > A-A > T-T).⁴⁴ Rooted in this quantitative basis, strong hydrogen-bonding (HB) units (G-C or A-T pairs) are positioned at critical nodes to function as "load-bearing walls", ensuring the overall structural stability. Subsequently, weak HB units (C-C or T-T pairs) are utilized in non-critical positions as "non-load-bearing partitions" to provide auxiliary connectivity and conformational flexibility, completing a functional HBN.

Given that GC-rich sequences exhibit superior sorting performance compared to those with other base compositions,⁴⁵ this study primarily focuses on the GC composition. To explicitly demonstrate these foundational design principles, building an HBN sequence can be conceptualized as a step-by-step constraint satisfaction process (Figure 1a and Figure S2).

Taking a 12-base DNA sequence ($L = 12$) with $N = 9$ as a representative model, the framework parameters are first established to define the periodic topological grid (Figure 1a–i). It is important to emphasize that these structural parameters can be adjusted within the physical and experimental boundary conditions (Table 1, with detailed rationales provided in the Supporting Information).

Table 1. Summary of Structural Parameters and Boundary Settings for HBN Design

Symbol	Parameter Name	Definition	Boundary
N	Helical Periodicity	Number of nucleobases per helical turn on SWCNT	$9 \leq N < L$
L	Sequence Length	Number of nucleobases per DNA sequence	$10 \leq L \leq 30$
G or A Counts	Strong-Base Count	Number of G or A bases per sequence	$\leq L/2$

Within this periodic framework, the assignment and placement of nucleobases follow a strict constraint-propagation mechanism. For instance, assigning the first G to any available node (e.g., position 1) immediately dictates local steric constraints due to HBN periodicity. Specifically, its coupled spatial coordinates (e.g., positions 5 and 10) are strictly prohibited from accommodating additional G bases to prevent forbidden G-G clashes, and are consequently designated as C bases. Selecting a subsequent available position for another G (e.g., position 11) similarly propagates local constraints across its interconnected coordinates. It is important to note that these initial G assignments represent just one permutation example; the G bases can be iteratively placed at any other nonconflicting positions.

Under this periodic topology, two adjacent DNA strands form the minimum repeating unit, establishing four robust G-C base pairs: intrastrand pairs 1G-10C (strand I) and 2C-11G (strand II), alongside inter-strand pairs 5C-11G and 11G-7C (Figure 1a–ii). These strong G-C pairs provide the rigid structural scaffolding, while the remaining unassigned interstitial positions are filled with C to form weak C-C pairs for structural connectivity (Figure 1a–iii). This rule-governed, iterative construction eventually yields a fully HBN-compliant target sequence, such as GCCCCCCCCCCG (12-2G-1-11). By applying these constraint rules across all valid permutations, one can systematically generate the complete library of compliant sequences (e.g., yielding exactly 376 sequences for $L = 12$ and $N = 9$, as detailed in the following section).

To synthesize these topological rules into a systematic methodology, the *de novo* design process is governed by three primary architectural principles that guarantee rationality, rigor, and efficiency. First, the structural parameters L and N are determined within the established physical and experimental boundary conditions aforementioned, with the guanine count restricted to $G \leq L/2$ to prevent oversaturation. Second, within the constraint-satisfaction framework, guanine bases are sequentially assigned to available nodes to form strong G-C base pairs. Each assignment acts as a localized constraint that deterministically dictates the placement of C bases at coupled coordinates, while unassigned interstitial positions are filled with weak C-C pairs. Third, G-G pairings are systematically excluded within the helical wrapping framework to eliminate forbidden steric clashes that would destabilize the periodic structures. By integrating these principles, the design frame-

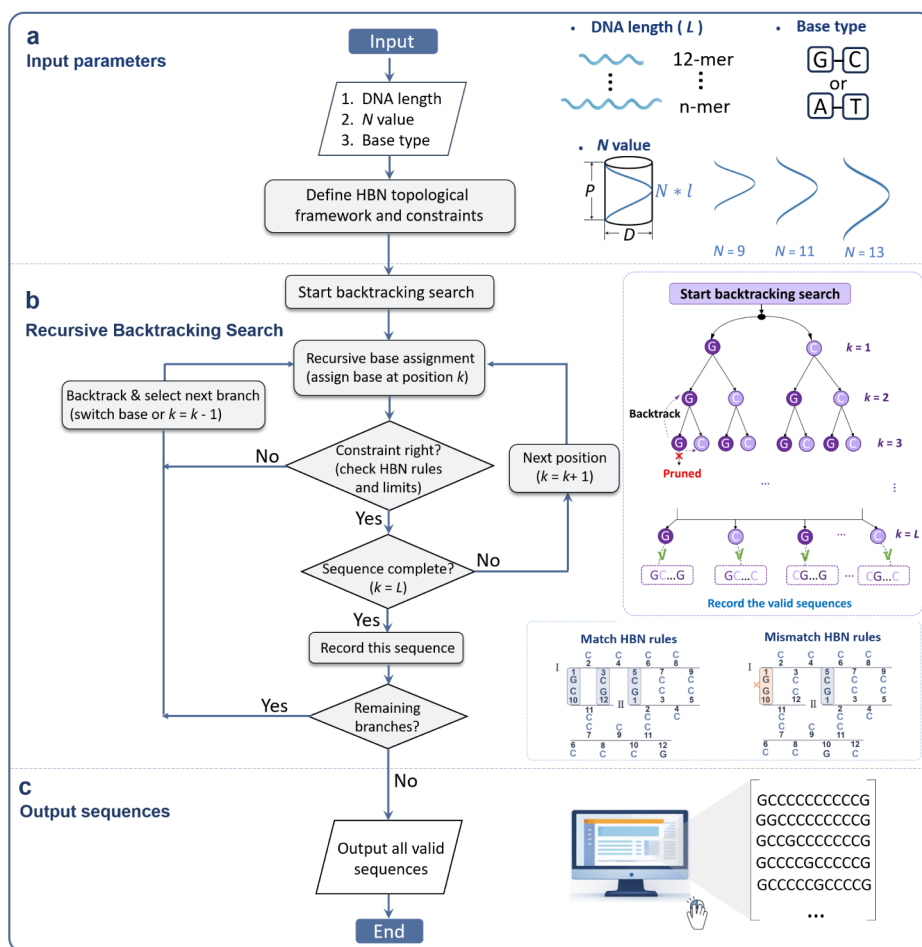


Figure 2. Automated design workflow for DNA sequences conforming to HBN models. (a) Input parameters: defining fundamental geometric and structural constraints, including DNA length (L), helical periodicity (N) and base system type. (b) Algorithmic execution of the recursive backtracking search with constraint pruning: Candidate bases (G/C or A/T) are recursively assigned at position k ($k = 1, 2, \dots, L$). Sequences violating HBN topological rules or physical limits trigger instant constraint pruning, prompting the algorithm to backtrack ($k = k - 1$) and switch to unvisited branches. Fully assembled valid sequences ($k = L$) are systematically recorded into the target candidate ensemble. (c) Output sequences: Collection and export of valid DNA sequences.

work ensures the deterministic generation of highly stable, conflict-free DNA sequences, thereby establishing a rigorous foundation for downstream experimental validation.

It should be noted that the G-G exclusion rule represents a specific boundary condition of our current helical-based framework⁴¹—derived directly from structure-resolved conformations—rather than a universal denial of G-G functionality. Recent literature has revealed that the DNA-SWCNT interface can exhibit remarkable structural diversity, including non-helical geometries such as ring-like structures.^{46,47} Consequently, sequences containing G-G motifs might still operate effectively by adopting alternative non-helical conformations that bypass the steric clashes inherent to a rigid helical wrap. This structural plasticity represents an intriguing direction for future framework expansion.

Automated Compiler for HBN Construction

Despite the conceptual clarity of the HBN design rules, translating these principles into functional sequences presents a challenge due to the combinatorial complexity and the coupling of multivariable constraints. The construction of an HBN is inherently a high-dimensional constraint problem; even a single nucleotide substitution can exert a disproportionate impact on the global thermodynamic stability and

structural integrity of the DNA-SWCNT hybrid. Consequently, manual design is ill-suited for navigating this vast sequence space to identify global optima or to balance competing structural requirements. In this context, automated algorithms offer a superior alternative, enabling the rapid screening and rigorous evaluation of vast sequence libraries while minimizing human bias and ensuring precise structural control.

To facilitate the broad implementation of our design protocol, we developed the DNA-HBN Compiler,⁴⁸ a Python-based computational tool providing a streamlined pipeline for HBN-compliant sequence generation (Figure 2). As illustrated in Figure 2a, users first input primary structural parameters including DNA length (L), the helical periodicity (N), and preferred nucleobase compositions to establish the HBN framework.

To efficiently navigate the combinatorial space of DNA sequences of length L while circumventing the exponential complexity barrier (2^L), the compiler employs a recursive backtracking algorithm with constraint pruning (Figure 2b). Specifically, it generates sequences via a step-by-step decision process, systematically evaluating and assigning candidate nucleotides (e.g., G or C) one position at a time, starting

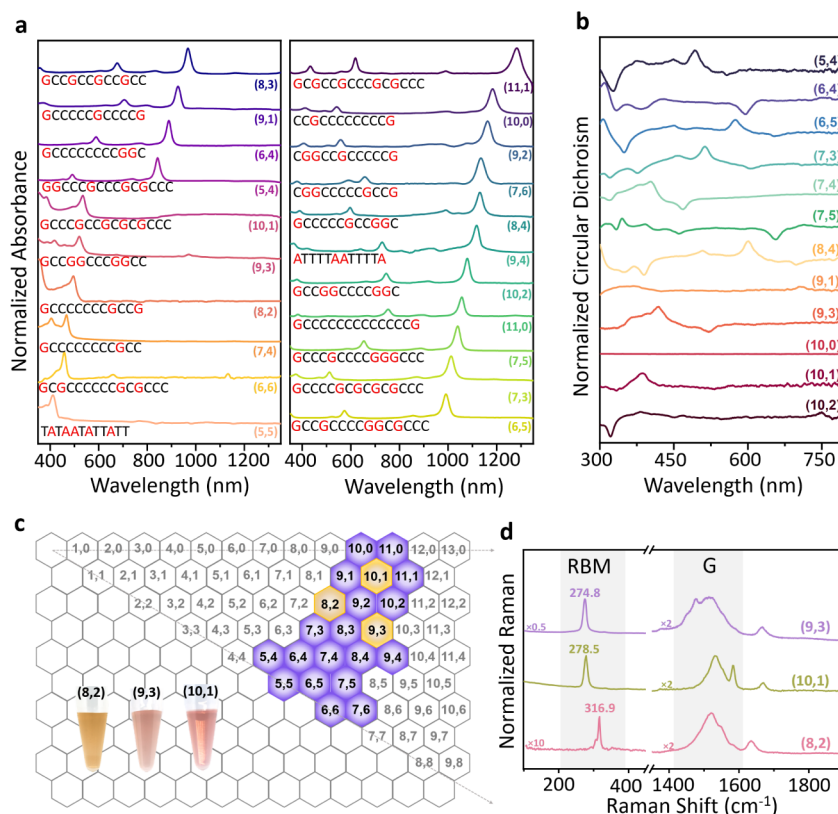


Figure 3. Comprehensive optical characterization of single-chirality SWCNTs isolated via HBN-directed sequence design. (a) Optical absorption spectra of 21 distinct single-chirality SWCNT species, each isolated using its respective HBN-derived sequence. Spectra are normalized to the E_{11} transition for comparative clarity. (b) CD spectra of 12 representative single-chirality SWCNT species, normalized to the E_{22} (semiconducting) or M_{11} (metallic) transition. The corresponding raw CD data are provided in Figure S5. (c) Distribution of isolated SWCNT species across the (n, m) chirality landscape. The map highlights the diversity of species successfully sorted by the HBN framework; inset photographs show concentrated aqueous solutions of (8,2), (9,3) and (10,1) species, demonstrating distinct excitonic colors. (d) Raman characterization of purified (8,2), (9,3) and (10,1) species (532 nm excitation). Intensities are normalized to the G-band.

from the 5'-terminus ($k = 1$). Immediately following each assignment, this addition is screened against predefined HBN design rules and physical constraints, such as enforcing guanine count limits and avoiding G-G steric clashes.

If the candidate base assignment at position k satisfies all currently evaluable HBN and base-composition constraints (Match), the algorithm recursively proceeds to position $k + 1$. Conversely, detecting a constraint violation at position k (Mismatch) triggers immediate constraint pruning, halting further depth extension along that invalid subtree. The algorithm then attempts an alternative base assignment at position k ; if no valid candidate remains, it backtracks to position $k - 1$ to explore alternative branches. Upon reaching the full sequence length ($k = L$), the valid candidate is recorded into the target ensemble, and backtracking continues until the search space is completely exhausted. By evaluating constraints at shallow depths ($k \ll L$), this approach drastically reduces computational complexity compared to an exhaustive search while guaranteeing complete coverage of the valid candidate ensemble.

Finally, as depicted in Figure 2c, the valid sequences are systematically compiled and exported into user-friendly formats, including HBN structural visualizations and structured datasets. This high-throughput workflow seamlessly couples physicochemical design rules with algorithmic execution, transforming complex HBN modeling into a robust, automated process for the rapid generation of *de novo* DNA sequence

libraries tailored for downstream SWCNT chirality recognition. To ensure computational reproducibility, the recursive pseudocode for this framework is provided in the SI (Algorithm S1). The DNA-HBN Compiler is freely available for download and direct use via the website provided in ref 48.

Experimental Validation of HBN-Derived Sequences for SWCNT Sorting

To experimentally validate the efficacy of our HBN-derived sequences, we employed the aqueous two-phase (ATP) extraction technique to isolate single-chirality SWCNTs from commercial SG6Si raw nanotubes (Figure S3).^{26–29} We systematically evaluated a library of 140 HBN-derived GC-rich oligonucleotides, spanning diverse structural topologies: 12-base sequences with $N = 9$ and $N = 11$, alongside 15-base sequences with $N = 13$ (Table S1 and Figures S6–S75). Remarkably, 128 of these rationally designed sequences successfully isolated at least one specific (n, m) species, representing a success rate of 128/140 (91.4%) in identifying effective resolving sequences. Importantly, our HBN design framework is inherently adaptable to AT-rich oligonucleotides. To demonstrate the versatility and broad sequence scope of this methodology, we designed and experimentally evaluated 10 AT-rich sequences. As summarized in Table S2, 9 of these candidates achieved high-purity, single-chirality SWCNT sorting (Figures S76–S80), confirming that our HBN design rules are robustly applicable across diverse nucleobase compositions.

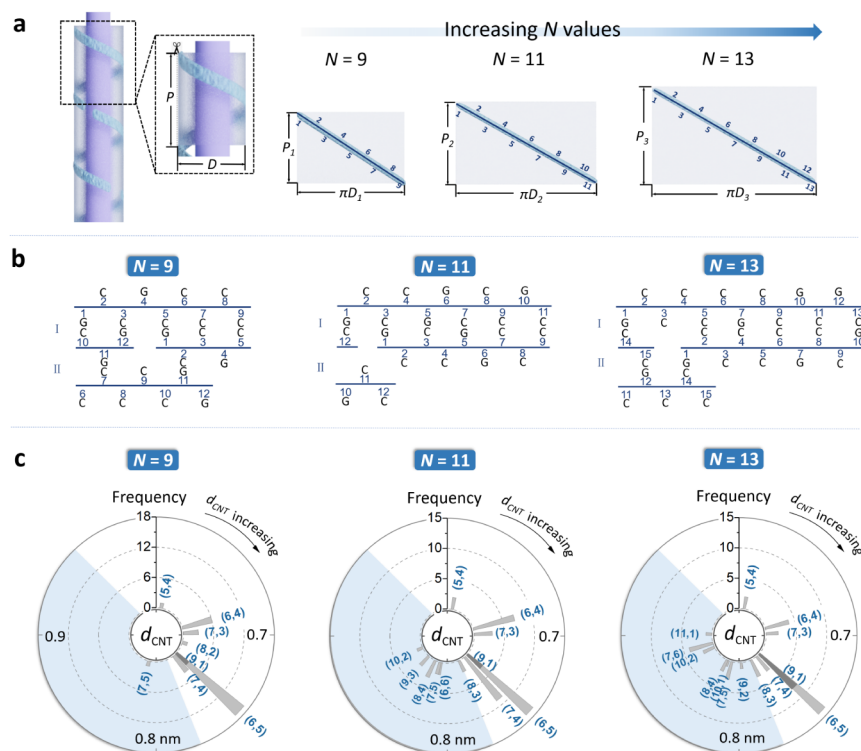


Figure 4. HBN-directed SWCNT diameter tuning via N parameter modulation. (a) Schematic and unrolled views of DNA-SWCNT hybrids, illustrating how the helical periodicity parameter ($N = 9, 11, 13$) governs the spatial trajectory and footprint of the DNA backbone on the nanotube surface. (b) Representative HBN models corresponding to various N values, showing the structural evolution of the DNA motifs. (c) Statistical ensemble analysis of sorted SWCNT diameters as a function of the N parameter. The shaded regions indicate the population of species with $d_{\text{CNT}} > 0.78$ nm (referencing the average diameter of SG6Si). The data demonstrate a systematic and predictable shift toward larger-diameter SWCNTs as N increases from 9 to 13, validating the HBN-directed diameter-tuning strategy.

The comprehensive isolation results, supported by absorption spectra for all 150 sequences (Figures S6–S80 and Tables S1–S2), demonstrate the accuracy of the HBN models. Among these 150 sequences, 137 acted as resolving sequences (an overall success rate of 91.3%), outperforming conventional empirical screening ($\sim 10\%$) by nearly an order of magnitude.²⁷ It should be noted that the remaining 13 sequences (8.7%) primarily exhibited low sorting selectivity—yielding multi-chirality mixtures—rather than a complete failure to interact with SWCNTs. This is likely attributed to the deliberately fixed macroscopic thermodynamic parameters (e.g., salt and polymer concentrations) in our standard ATP protocols, which were rigidly controlled across all runs to isolate sequence-dependent effects and eliminate confounding experimental variables.

To further benchmark the efficiency and cost-effectiveness of our framework against data-driven methods, we conducted a direct quantitative comparison with recent state-of-the-art machine learning (ML) workflows (Table S3). While emerging ML models can achieve high screening efficiencies,^{45,49,50} they remain inherently tethered to massive, experimentally derived pre-training datasets—requiring hundreds of DNA sequences to be synthesized and screened *a priori* at substantial temporal and financial expense. Bound by restricted sequence spaces and protocol-specific conditions, such data-driven predictions serve primarily as domain-limited prioritization tools rather than universal predictors of DNA-SWCNT recognition. Conversely, our HBN strategy circumvents the need for training datasets entirely, operating as a *de novo* rational design framework guided by structural and thermodynamic heuristics. By directly

translating fundamental interfacial hydrogen-bonding principles into 150 candidate sequences, the HBN compiler achieved an extraordinary 91.3% accuracy rate. This approach bypasses the resource-intensive pre-screening and iterative validation loops typical of conventional ML workflows, streamlining high-fidelity SWCNT sorting.

Through this high-efficiency screening, these effective sequences yielded 21 distinct single-chirality SWCNT species, as confirmed by UV-Vis-NIR absorption spectroscopy (Figure 3a). These species encompass a broad electronic diversity, including semiconducting (e.g., (6,5), (9,1)), quasi-metallic (e.g., (7,4), (8,2)), and armchair-like metallic (e.g., (5,5), (6,6)) nanotubes. Circular dichroism (CD) spectra further established the high enantiomeric purity of the sorted samples, showcasing the chiroptical selectivity of the HBN-directed SWCNT sorting (Figure 3b and Figure S5).

Beyond the high purity of individual species, analysis of the (n, m) distribution reveals that the sorted species are clustered within specific regions of the chirality map (Figure 3c). Notably, our method successfully captured three rare quasi-metallic species—(8,2), (9,3) and (10,1)—which exist in extremely low abundance in the raw material and have remained largely elusive in previous literature (highlighted in orange, Figure 3c). The structural and chiral purity of these rare species were rigorously verified via Raman spectroscopy (Figure 3d). All three isolated species exhibit a characteristic asymmetric G-band, which serves as a spectroscopic hallmark of their metallic electronic structure.⁵¹ The observed asymmetry of the overall G-band envelope fundamentally originates from the asymmetric broadening of the lower-

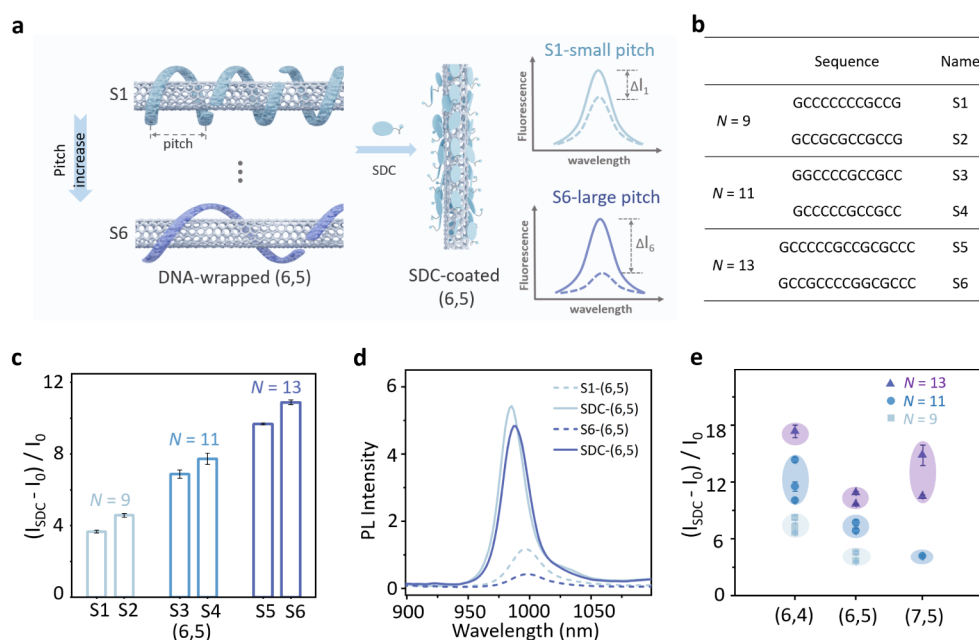


Figure 5. HBN-directed DNA helical pitch tuning. (a) Schematic of HBN-directed wrapping on (6,5) SWCNTs and subsequent displacement by SDC. Variations in DNA pitch dictate surface coverage, affecting the magnitude of PL enhancement upon SDC treatment. (b) Six representative HBN-directed DNA sequences for (6,5) at varying N values. (c) Relative PL intensity change, $(I_{\text{SDC}} - I_0)/I_0$, for the six DNA-(6,5) hybrids after SDC displacement. (d) PL spectra of S1-(6,5) and S6-(6,5) before and after SDC displacement. (e) Summary plot for relative PL enhancement for DNA-(6,4), DNA-(6,5), and DNA-(7,5) at different N values, demonstrating the generality of the pitch-tuning strategy across different chiralities.

frequency G^- peak. In metallic SWCNTs, strong coupling of this mode to an electronic continuum gives rise to a broad Breit-Wigner-Fano (BWF) lineshape, whereas the higher-frequency G^+ component retains a relatively narrow Lorentzian profile. Furthermore, the observation of single, sharp radial breathing mode (RBM) peaks at 274.8 cm^{-1} for (9,3), 278.5 cm^{-1} for (10,1), and 316.9 cm^{-1} for (8,2) matches theoretical predictions for these specific tubes, providing unambiguous evidence of their high-purity isolation.⁵²

Programmable Modulation Of DNA-SWCNT Structural Parameters

The optical and sensing profiles of DNA-SWCNT hybrids are fundamentally dictated by two structural determinants: the CNT diameter (d_{CNT})⁵³ and the DNA helical pitch (P).⁴¹ While d_{CNT} governs the intrinsic electronic bandgap⁵⁴ and redox potential⁵⁵ of the nanotube, P determines the degree of surface coverage; specifically, a larger P increases the solvent-accessible surface area, whereas a smaller P signifies more dense DNA packing.⁵⁶ Despite their importance, the simultaneous and deterministic control of these parameters remains a formidable challenge. We address this by demonstrating that both d_{CNT} and P can be regulated through HBN-driven sequence design, where the helical periodicity (N) serves as a universal tuning knob.

According to eq 1, N encapsulates the geometric coupling between the P and the D . We therefore hypothesized that N could be utilized to modulate the structural landscape of the hybrids (Figure 4a). To test this, we constructed HBN models with three distinct N values (9, 11, and 13), employing 12-base sequences for $N = 9$, 11 and 15-base sequences for $N = 13$ (Figure 4b). Using the DNA-HBN Compiler, we navigated large GC-rich sequence libraries (376 for $N = 9$ and 11; 4245 for $N = 13$) conforming to these models.

A critical technical challenge in HBN design is that some sequences may coincidentally satisfy multiple N models. To ensure precise N -value locking and eliminate structural ambiguity, we implemented a “negative design” rule based on G-G pairing conflicts. For instance, in an $N = 9$ model (12-base DNA), positioning G at both the 1st and 12th positions creates a forbidden G-G clash specifically within the $N = 11$ framework (Figure S82). This represents one of 11 algorithmically valid positional combinations for $N = 11$ exclusion (Figure S81). Similar geometric exclusion strategies were employed to uniquely lock sequences for the $N = 11$ and $N = 13$ models, the detailed methodologies of which are provided in the Supporting Information (Figures S83–S84). By applying these exclusivity criteria, we successfully identified sequences uniquely designated for $N = 9$ (32 sequences, Table S4), $N = 11$ (40 sequences, Table S5), and $N = 13$ (42 sequences, Table S6), ensuring a rigorous one-to-one mapping between the HBN model and the resulting hybrid structures. This sequence screening process was automated using a custom-developed program; its graphical user interface (GUI) and operational guidelines are detailed in Figure S85.

The experimental SWCNT sorting results of these sequences, visualized via radial frequency distributions (Figure 4c), reveal a systematic correlation between N and d_{CNT} . Using the average diameter of SG65i (0.78 nm) as a benchmark,⁵⁷ we observed that $N = 9$ predominantly favored small-diameter species such as (6,4) and (6,5). As N increased to 11, the affinity for larger nanotubes ($d_{\text{CNT}} > 0.78\text{ nm}$) significantly rose, a trend that culminated at $N = 13$, where 15 frequencies of distinct large-diameter species were identified, including (7,6) and (11,1) which were absent at lower N values. This consistent bathochromic-like shift in the diameter distribution validates that the N parameter effectively governs the chirality-selective recognition of the HBN framework.

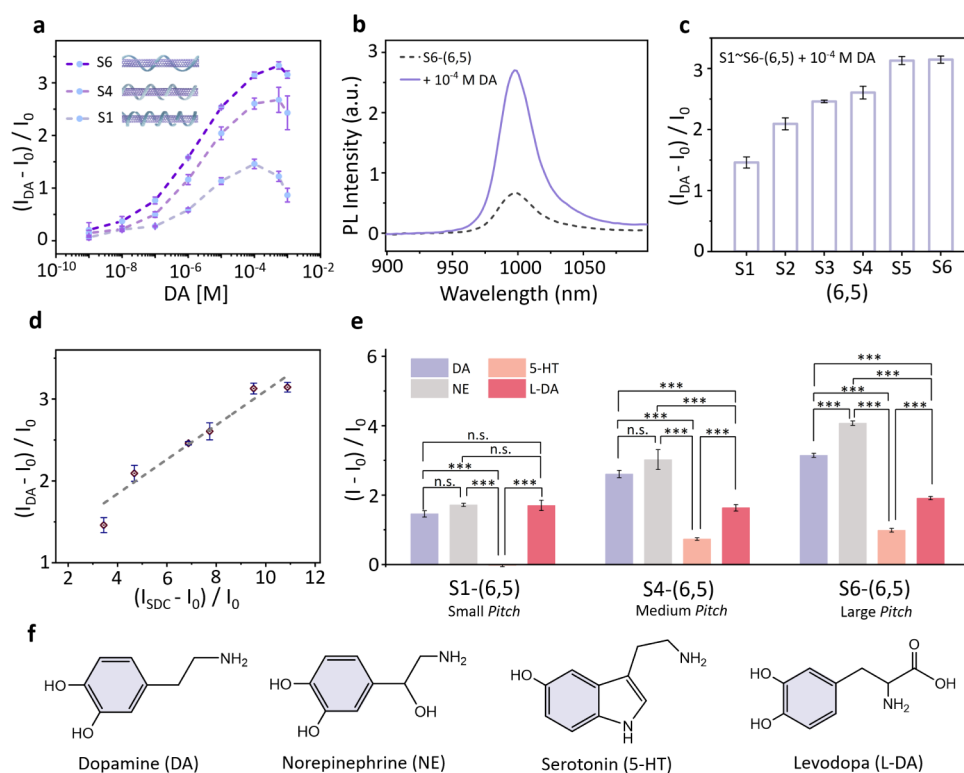


Figure 6. Pitch-mediated DNA-SWCNT biosensing performance. (a) Photoluminescence (PL) response profiles of three representative DNA-(6,5) sensors (S1, S4, and S6) toward varying concentrations of dopamine (DA). I_0 and I_{DA} denote the PL intensity before and after DA addition, respectively. (b) Representative PL enhancement spectra of the S6-(6,5) sensor upon exposure to 10^{-4} M DA. (c) Comparison of relative PL intensity changes across six DNA-(6,5) sensors at 10^{-4} M DA. (d) Correlation between SDC-induced PL variation and the corresponding DA sensitivity for six DNA-(6,5) sensors. (e) Differential sensing profiles of selected DNA-(6,5) sensors toward four distinct neurotransmitters (10^{-4} M). Error bars represent the standard deviation from three independent replicates. Statistical significance is denoted as * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$; n.s. denotes no statistical significance. (f) Chemical structures of the investigated neurotransmitters.

Beyond diameter tuning, we investigated whether N could modulate the DNA pitch (P) for a fixed chirality. For a constant d_{CNT} , eq 1 predicts that P must increase with N . We probed this “pitch-tuning” effect using sodium deoxycholate (SDC)-mediated displacement assays (Figure 5a). As a potent surfactant, SDC can completely displace the noncovalently wrapped DNA oligomers from the nanotube surface, restructuring the interfacial dielectric environment and thereby enhancing the intrinsic photoluminescence (PL) profiles. The relative PL enhancement upon SDC addition, $\Delta I/I_0 = (I_{SDC} - I_0)/I_0$, serves as a high-sensitivity indicator of the initial DNA packing density and surface accessibility.^{41,58,59} Taking the DNA-(6,5) hybrid as a model system, we systematically screened six HBN-derived sequences across $N = 9, 11$, and 13 (Figure 5b). The $\Delta I/I_0$ values exhibited a clear positive correlation with N (Figure 5c, Figures S89–S91 and Table S7), increasing monotonically from 3.66 for S1 ($N = 9$) to 10.89 for S6 ($N = 13$) (Figure 5d). This trend was consistently reproduced in (6,4) and (7,5) species (Figure 5e, Figures S92–S96 and Tables S8–S9), confirming that a larger N facilitates an increased helical pitch and enhanced SWCNT surface exposure. While the PL enhancement of DNA-(6,5) hybrids is strongly dependent on N values due to the pitch-mediated modulation, minor PL variations were observed within the same N group. These deviations are likely attributable to subtle molecular-level conformational fluctuations and the inherent structural flexibility of the DNA wrapping; nevertheless, the overarching programmable trend remains robust and predictive.

Pitch-Mediated Modulation of Molecular Sensing Properties

The variations in P values within DNA-SWCNT hybrids fundamentally reshape the molecular recognition interface, offering a versatile platform for the deterministic fine-tuning of biosensing properties. As rigorously validated by our recent high-resolution AFM and cryo-EM observations,⁴¹ tuning the DNA helical pitch directly governs the analyte-mediated optical responsiveness and subsequent target recognition capabilities. To systematically assess the influence of P values on biosensing responsiveness, we evaluated the sensing response of DNA-(6,5) hybrids toward neurotransmitters, starting with dopamine (DA).³² Upon the addition of DA, we observed a concentration-dependent enhancement in PL intensity (Figure 6a). Notably, the DA sensitivity, defined as $(I_{DA} - I_0)/I_0$, exhibited a pronounced sequence-dependence among the (6,5) hybrids. For instance, at 10^{-4} M DA, the PL enhancement factors for S1-(6,5), S4-(6,5), and S6-(6,5) were 1.46, 2.46, and 3.15, respectively (Figure 6b–c and Figure S97). Since the SWCNT chirality remains constant in these hybrids, the divergent sensing magnitudes must be primarily attributed to the programmable variations in DNA pitch.

To rigorously correlate interfacial structure with sensing performance, we plotted the DA-induced PL changes against the SDC-induced displacement magnitude, which serves as a robust structural proxy for P (Figure 6d). This analysis revealed a strong linear correlation, confirming that DNA pitch fundamentally dictates analyte sensitivity. To verify the

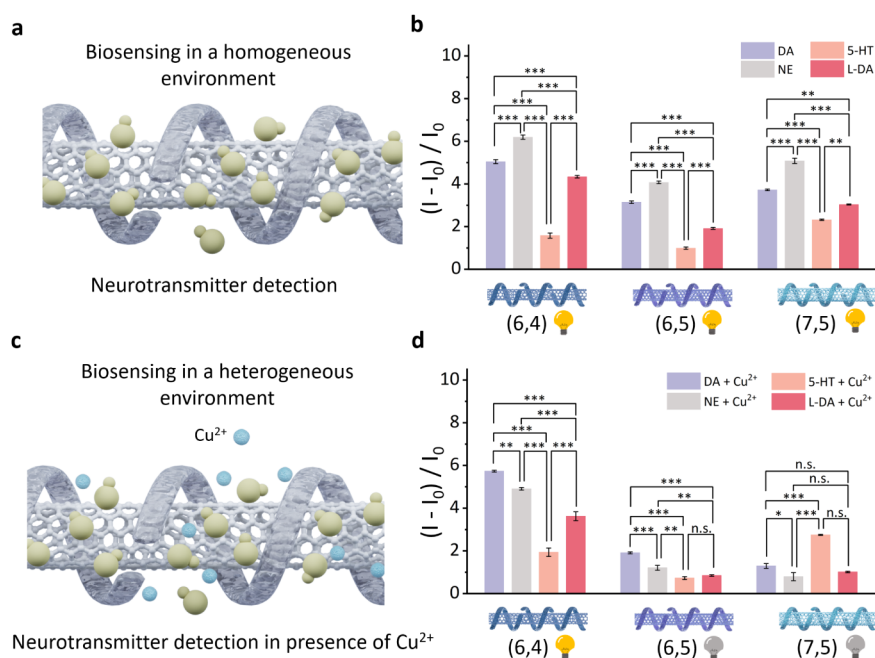


Figure 7. SWCNT chirality-governed biosensing in homogeneous and heterogeneous chemical environments. (a) Schematic of molecular sensing in a homogeneous chemical environment dominated strictly by steric excluded volume effects (e.g., neurotransmitter detection). (b) Differential sensing profiles of three chirality-specific sensors—utilizing (6,4), (6,5) and (7,5) species—toward a panel of four neurotransmitters (10^{-4} M). Within this homogeneous matrix, all three sensors exhibit robust, cross-reactive analyte discrimination. (c) Schematic illustration of molecular sensing in a heterogeneous chemical environment where competitive redox-active interactions (e.g., mediated by Cu^{2+} ions) and steric excluded volume effects operate concurrently at the bio-nano interface. (d) Differential sensing performance of the corresponding sensors toward the four neurotransmitters (10^{-4} M) under Cu^{2+} -induced chemical perturbation. In this heterogeneous matrix, only the (6,4)-based sensor retains effective analyte discrimination, demonstrating that the optical response is heavily modulated by the intrinsic electronic band structure and redox potential of the host nanotube.

universality of this behavior, we extended our analysis to other representative neurotransmitters (Figure 6f and Figure S98). Both norepinephrine (NE) and serotonin (5-HT) display strong linear correlations akin to DA. We attribute this universal pitch-dependent behavior to a synergistic interfacial docking and excluded-volume mechanism.^{60–62} Physically, a larger DNA pitch creates a more expansive solvent-accessible surface area, providing more “unoccupied” interfacial pockets.⁴¹ Chemically, for analytes enriched with hydroxyl and amino groups (DA, NE, 5-HT), their recognition is firmly governed by specific hydrogen-bonding interactions with the DNA wrapper within these pockets.^{63,64} The subsequent adsorption of these molecules effectively displaces fluorescence-quenching species (e.g., water and dissolved oxygen), yielding a substantial PL enhancement that scales proportionally with the structural porosity. In contrast, levodopa (L-DA) does not conform to this linear trend (Figure S98c). The additional carboxyl group in L-DA likely introduces electrostatic repulsion with the negatively charged DNA phosphate backbone alongside structural steric hindrance. Collectively, these factors disrupt the hydrogen-bonding docking, decoupling the optical response of L-DA from the structural porosity.

Beyond sensitivity, the DNA pitch also critically influences the molecular discrimination capacity of the sensors. We compared the differential sensing profiles of S1-(6,5), S4-(6,5), and S6-(6,5)—representing a gradient of increasing P —against four neurotransmitters. The small-pitch S1-(6,5) sensor exhibited muted and indistinguishable responses across the analytes, rendering it incapable of effective discrimination (Figure 6e and Figures S99–101). As P increased, S4-(6,5) showed enhanced sensitivity, yet still failed to clearly

differentiate between the structurally similar DA and NE. In contrast, the large-pitch S6-(6,5) sensor achieved full resolution and significant discrimination among all four neurotransmitters. This pitch-regulated sensing performance underscores the power of the HBN-driven design: it enables the “bespoke” engineering of nano-bio interfaces, providing a systematic route toward sophisticated, high-performance molecular recognition platforms.

Chirality-Dependent Sensing in Chemically Heterogeneous Environments

While the preceding findings underscore the role of DNA pitch in tailoring molecular recognition, this mechanism primarily addresses sensing governed by excluded volume effects upon analyte adsorption.^{2,65} In practical applications, DNA-SWCNT sensors often encounter a second, concurrent mechanism: charge or electron transfer.^{53,66,67} In such scenarios, the intrinsic electronic bandgap and redox potential of the SWCNTs—properties intrinsically linked to chirality—become the dominant determinants of performance. To engineer robust sensors for complex biological matrices, it is therefore imperative to leverage the HBN framework to select chiralities that optimize both steric accessibility and electronic band structure.

To isolate the influence of chirality from interfacial structure, we selected three DNA-SWCNT hybrids: $(\text{GCCC})_2\text{G}_2\text{C}_2$ -(6,4), $(\text{GCC})_2\text{C}_2\text{G}(\text{GC})_2\text{C}_2$ -(6,5), and $\text{GC}_3\text{GC}_2(\text{GC})_3\text{C}_2$ -(7,5). These hybrids were specifically chosen for their near-identical SDC-induced displacement magnitudes ($\Delta I/I_0 \sim 10.5$), effectively neutralizing the impact of DNA pitch as a variable (Figure S102). In a homogeneous environment

containing neurotransmitters only, all three sensors exhibited high responsiveness and exceptional discrimination among DA, NE, 5-HT, and L-DA (Figure 7a–b and Figures S103–S104), as the sensing was dominated by the steric-driven exclusion of quenchers.

To simulate a more challenging heterogeneous environment, we introduced Cu^{2+} ions as a redox-active species into the system (Figure 7c).⁵³ Unlike neurotransmitters, the interaction between Cu^{2+} and nanotubes is governed by redox-mediated quenching. Our results revealed a stark, diameter-dependent divergence in sensing robustness. Under Cu^{2+} interference, the (7,5) sensor (largest diameter) suffered a drastic loss in fluorescence and failed to discriminate among the four neurotransmitters. The intermediate-diameter (6,5) sensor also showed compromised performance, losing the ability to distinguish between 5-HT and L-DA. In contrast, the small-diameter (6,4) sensor remained remarkably resilient, maintaining both its optical signal and its full discriminative power (Figure 7d and Figures S105–107).

This trend is fundamentally rooted in the chirality-dependent electrochemical landscape of SWCNTs: smaller-diameter tubes possess larger bandgaps and higher reduction potentials,^{55,60} making them thermodynamically more resistant to oxidation by Cu^{2+} . Conversely, larger-diameter tubes are more susceptible to redox-induced quenching, which obscures the subtle signal changes induced by neurotransmitter binding. These findings demonstrate that SWCNT chirality acts as a critical filter for anti-interference, where the HBN-directed design allows us to navigate the trade-off between sensitivity and environmental robustness.

Taken together, by integrating HBN-driven sequence design with chirality selection, we have established a dual-parameter optimization strategy. Tuning the DNA pitch enables the customization of interfacial fingerprints for specific analytes, while manipulating SWCNT chirality fortifies the electrochemical resilience of the sensor in complex backgrounds. This synergistic approach provides a robust methodology for the deterministic design of high-performance, next-generation nano-biosensors (Figure 1c).

CONCLUSIONS

In summary, we have established a programmable, *de novo* design framework for constructing DNA-SWCNT hybrids with deterministic structural and functional properties. By conceptualizing the HBN as an architectural blueprint, this work transitions the field from empirical, trial-and-error sequence screening to a rational, *de novo* design-driven engineering paradigm. Empowered by the automated DNA-HBN Compiler, this methodology achieved an unprecedented 91.3% success rate in resolving DNA sequence design, facilitating the high-purity isolation of 21 distinct (*n*, *m*) species—including rare quasi-metallic nanotubes that were previously elusive.

Beyond high-fidelity sorting, our work identifies the helical periodicity (*N*) as a universal design descriptor that orchestrates the simultaneous modulation of nanotube diameter (d_{CNT}) and helical pitch (*P*). We demonstrate that *N* not only governs chirality-selective recognition but also defines the solvent-accessible landscape of the resulting hybrids. This structural programmability translates directly into tailored biosensing performance: while the DNA pitch determines the molecular recognition capacity in matrices dominated by steric excluded volume effects, the intrinsic electronic structure of the selected (*n*, *m*) species dictates the

redox resilience and signal transduction in electrochemically active environments. By synergizing programmable DNA pitch with chirality selection, our framework provides a deterministic platform for nano-interface engineering. This methodology opens new avenues for the rational optimization of bio-nano hybrids across diverse chemical and biological contexts, laying a robust foundation for next-generation molecular electronics and biosensing platforms with unmatched specificity and environmental resilience.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/jacs.6c11726>.

Detailed experimental procedures, HBN design principles and computational workflow, designed DNA sequence libraries, spectroscopic characterization and chirality assignment of separated DNA-SWCNTs, sensing measurements and analyses, and additional separation and characterization data (PDF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

- (1) Nel, A. E.; Mädler, L.; Velegol, D.; Xia, T.; Hoek, E. M. V.; Somasundaran, P.; Klaessig, F.; Castranova, V.; Thompson, M. Understanding Biophysicochemical Interactions at the Nano–Bio Interface. *Nat. Mater.* **2009**, *8*, 543–557.
- (2) Zhang, J.; Landry, M. P.; Barone, P. W.; Kim, J.-H.; Lin, S.; Ulissi, Z. W.; Lin, D.; Mu, B.; Boghossian, A. A.; Hilmer, A. J.; Rwei, A.; Hinkley, A. C.; Kruss, S.; Shandell, M. A.; Nair, N.; Blake, S.; Şen, F.; Şen, S.; Croy, R. G.; Li, D.; Yum, K.; Ahn, J.-H.; Jin, H.; Heller, D. A.; Essigmann, J. M.; Blankschtein, D.; Strano, M. S. Molecular Recognition Using Corona Phase Complexes Made of Synthetic Polymers Adsorbed on Carbon Nanotubes. *Nat. Nanotechnol.* **2013**, *8*, 959–968.
- (3) Yang, X.; Tsai, C.-T.; Yang, Y.; Zhang, W.; You, H.; Forró, C.; Pasca, S. P.; Cui, B. Nano-Bio Interfaces for Electrical and Biochemical Signal Transduction. *Nat. Rev. Bioeng.* **2026**, *4*, 250–268.
- (4) Kim, M.; Chen, C.; Wang, P.; Mulvey, J. J.; Yang, Y.; Wun, C.; Antman-Passig, M.; Luo, H.-B.; Cho, S.; Long-Roche, K.; Ramanathan, L. V.; Jagota, A.; Zheng, M.; Wang, Y.; Heller, D. A. Detection of Ovarian Cancer via the Spectral Fingerprinting of Quantum-Defect-Modified Carbon Nanotubes in Serum by Machine Learning. *Nat. Biomed. Eng.* **2022**, *6*, 267–275.
- (5) Howes, P. D.; Chandrawati, R.; Stevens, M. M. Colloidal Nanoparticles as Advanced Biological Sensors. *Science* **2014**, *346* (6205), 1247390.
- (6) Keren, K.; Berman, R. S.; Buchstab, E.; Sivan, U.; Braun, E. DNA-Templated Carbon Nanotube Field-Effect Transistor. *Science* **2003**, *302*, 1380–1382.
- (7) Allen, B. L.; Kichambare, P. D.; Star, A. Carbon Nanotube Field-effect-transistor-based Biosensors. *Adv. Mater.* **2007**, *19*, 1439–1451.
- (8) Maune, H. T.; Han, S.; Barish, R. D.; Bockrath, M.; Goddard, W. A., III; Rothmund, P. W. K.; Winfree, E. Self-Assembly of Carbon Nanotubes into Two-Dimensional Geometries Using DNA Origami Templates. *Nat. Nanotechnol.* **2010**, *5* (1), 61–66.
- (9) Piao, Y.; Meany, B.; Powell, L. R.; Valley, N.; Kwon, H.; Schatz, G. C.; Wang, Y. Brightening of Carbon Nanotube Photoluminescence through the Incorporation of Sp³ Defects. *Nat. Chem.* **2013**, *5*, 840–845.
- (10) Mahmoudi, M.; Lynch, I.; Ejtehadi, M. R.; Monopoli, M. P.; Bombelli, F. B.; Laurent, S. Protein–nanoparticle Interactions: Opportunities and Challenges. *Chem. Rev.* **2011**, *111*, 5610–5637.
- (11) Lundqvist, M.; Stigler, J.; Elia, G.; Lynch, I.; Cedervall, T.; Dawson, K. A. Nanoparticle Size and Surface Properties Determine the Protein Corona with Possible Implications for Biological Impacts. *Proc. Natl. Acad. Sci. U. S. A.* **2008**, *105*, 14265–14270.
- (12) Barone, P. W.; Baik, S.; Heller, D. A.; Strano, M. S. Near-Infrared Optical Sensors Based on Single-Walled Carbon Nanotubes. *Nat. Mater.* **2005**, *4*, 86–92.
- (13) Heller, D. A.; Jeng, E. S.; Yeung, T.-K.; Martinez, B. M.; Moll, A. E.; Gastala, J. B.; Strano, M. S. Optical Detection of DNA Conformational Polymorphism on Single-Walled Carbon Nanotubes. *Science* **2006**, *311*, 508–511.
- (14) Landry, M. P.; Ando, H.; Chen, A. Y.; Cao, J.; Kottadiel, V. I.; Chio, L.; Yang, D.; Dong, J.; Lu, T. K.; Strano, M. S. Single-Molecule Detection of Protein Efflux from Microorganisms Using Fluorescent Single-Walled Carbon Nanotube Sensor Arrays. *Nat. Nanotechnol.* **2017**, *12*, 368–377.
- (15) Gillen, A. J.; Boghossian, A. A. Non-Covalent Methods of Engineering Optical Sensors Based on Single-Walled Carbon Nanotubes. *Front. Chem.* **2019**, *7*, 612.
- (16) Schroeder, V.; Savagatrup, S.; He, M.; Lin, S.; Swager, T. M. Carbon Nanotube Chemical Sensors. *Chem. Rev.* **2019**, *119*, 599–663.
- (17) Bachilo, S. M.; Strano, M. S.; Kittrell, C.; Hauge, R. H.; Smalley, R. E.; Weisman, R. B. Structure-Assigned Optical Spectra of Single-Walled Carbon Nanotubes. *Science* **2002**, *298*, 2361–2366.
- (18) Weisman, R. B.; Bachilo, S. M. Dependence of Optical Transition Energies on Structure for Single-Walled Carbon Nanotubes in Aqueous Suspension: An Empirical Kataura Plot. *Nano Lett.* **2003**, *3*, 1235–1238.
- (19) Yang, F.; Wang, M.; Zhang, D.; Yang, J.; Zheng, M.; Li, Y. Chirality Pure Carbon Nanotubes: Growth, Sorting, and Characterization. *Chem. Rev.* **2020**, *120*, 2693–2758.
- (20) Li, Y.; Zhao, X.-K.; Wu, J.; Zhu, L.; Tian, S.; Feng, Y.; Zhang, Z.; Xu, C.-Q.; Lin, Z. Inverse Design of Guanine-Defects in Carbon Nanotubes for High-Resolution Emission Tuning. *Sci. Adv.* **2026**, *12* (28), No. eae8922.
- (21) De Volder, M. F. L.; Tawfick, S. H.; Baughman, R. H.; Hart, A. J. Carbon Nanotubes: Present and Future Commercial Applications. *Science* **2013**, *339*, 535–539.
- (22) Yang, F.; Wang, X.; Zhang, D.; Yang, J.; Luo, D.; Xu, Z.; Wei, J.; Wang, J.-Q.; Xu, Z.; Peng, F.; Li, X.; Li, R.; Li, Y.; Li, M.; Bai, X.; Ding, F.; Li, Y. Chirality-Specific Growth of Single-Walled Carbon Nanotubes on Solid Alloy Catalysts. *Nature* **2014**, *510*, 522–524.
- (23) Zheng, M.; Jagota, A.; Semke, E. D.; Diner, B. A.; Mclean, R. S.; Lustig, S. R.; Richardson, R. E.; Tassi, N. G. DNA-Assisted Dispersion and Separation of Carbon Nanotubes. *Nat. Mater.* **2003**, *2*, 338–342.
- (24) Ao, G.; Khripin, C. Y.; Zheng, M. DNA-Controlled Partition of Carbon Nanotubes in Polymer Aqueous Two-Phase Systems. *J. Am. Chem. Soc.* **2014**, *136*, 10383–10392.
- (25) Tu, X.; Manohar, S.; Jagota, A.; Zheng, M. DNA Sequence Motifs for Structure-Specific Recognition and Separation of Carbon Nanotubes. *Nature* **2009**, *460*, 250–253.
- (26) Khripin, C. Y.; Fagan, J. A.; Zheng, M. Spontaneous Partition of Carbon Nanotubes in Polymer-Modified Aqueous Phases. *J. Am. Chem. Soc.* **2013**, *135*, 6822–6825.
- (27) Ao, G.; Streit, J. K.; Fagan, J. A.; Zheng, M. Differentiating Left- and Right-Handed Carbon Nanotubes by DNA. *J. Am. Chem. Soc.* **2016**, *138*, 16677–16685.
- (28) Lyu, M.; Meany, B.; Yang, J.; Li, Y.; Zheng, M. Toward Complete Resolution of DNA/Carbon Nanotube Hybrids by Aqueous Two-Phase Systems. *J. Am. Chem. Soc.* **2019**, *141*, 20177–20186.

- (29) Lyu, M.; Li, C.; Liu, Y.; Li, Y.; Zheng, M. A Salt-Driven Mechanism for Precise Chirality Sorting of Carbon Nanotubes. *Sci. Adv.* **2025**, *11* (28), No. eadx3958.
- (30) Kruss, S.; Landry, M. P.; Vander Ende, E.; Lima, B. M. A.; Reuel, N. F.; Zhang, J.; Nelson, J.; Mu, B.; Hilmer, A.; Strano, M. Neurotransmitter Detection Using Corona Phase Molecular Recognition on Fluorescent Single-Walled Carbon Nanotube Sensors. *J. Am. Chem. Soc.* **2014**, *136*, 713–724.
- (31) Williams, R. M.; Lee, C.; Heller, D. A. A Fluorescent Carbon Nanotube Sensor Detects the Metastatic Prostate Cancer Biomarker uPA. *ACS Sens.* **2018**, *3*, 1838–1845.
- (32) Beyene, A. G.; Delevich, K.; Del Bonis-O'donnell, J. T.; Piekarski, D. J.; Lin, W. C.; Thomas, A. W.; Yang, S. J.; Kosillo, P.; Yang, D.; Prounis, G. S.; et al. Imaging Striatal Dopamine Release Using a Nongenetically Encoded near Infrared Fluorescent Catecholamine Nanosensor. *Sci. Adv.* **2019**, *5* (7), No. eaaw3108.
- (33) De Los Santos, Z. A.; Lin, Z.; Zheng, M. Optical Detection of Stereoselective Interactions with DNA-Wrapped Single-Wall Carbon Nanotubes. *J. Am. Chem. Soc.* **2021**, *143*, 20628–20632.
- (34) Kelich, P.; Jeong, S.; Navarro, N.; Adams, J.; Sun, X.; Zhao, H.; Landry, M. P.; Vuković, L. Discovery of DNA–Carbon Nanotube Sensors for Serotonin with Machine Learning and near-Infrared Fluorescence Spectroscopy. *ACS Nano* **2022**, *16*, 736–745.
- (35) Nißler, R.; Kurth, L.; Li, H.; Spreinat, A.; Kuhlemann, L.; Flavel, B. S.; Kruss, S. Sensing with Chirality-Pure near-Infrared Fluorescent Carbon Nanotubes. *Anal. Chem.* **2021**, *93*, 6446–6455.
- (36) Nißler, R.; Ackermann, J.; Ma, C.; Kruss, S. Prospects of Fluorescent Single-Chirality Carbon Nanotube-Based Biosensors. *Anal. Chem.* **2022**, *94*, 9941–9951.
- (37) Nißler, R.; Müller, A. T.; Dohrman, F.; Kurth, L.; Li, H.; Cosio, E. G.; Flavel, B. S.; Giraldo, J. P.; Mithöfer, A.; Kruss, S. Detection and Imaging of the Plant Pathogen Response by Near-infrared Fluorescent Polyphenol Sensors. *Angew. Chem., Int. Ed.* **2022**, *61* (2), No. e202108373.
- (38) Bisker, G.; Dong, J.; Park, H. D.; Iverson, N. M.; Ahn, J.; Nelson, J. T.; Landry, M. P.; Kruss, S.; Strano, M. S. Protein-Targeted Corona Phase Molecular Recognition. *Nat. Commun.* **2016**, *7* (1), 10241.
- (39) Sun, W.; Shen, J.; Zhao, Z.; Arellano, N.; Rettner, C.; Tang, J.; Cao, T.; Zhou, Z.; Ta, T.; Streit, J. K.; Fagan, J. A.; Schaus, T.; Zheng, M.; Han, S.-J.; Shih, W. M.; Maune, H. T.; Yin, P. Precise Pitch-Scaling of Carbon Nanotube Arrays within Three-Dimensional DNA Nanotrenches. *Science* **2020**, *368*, 874–877.
- (40) Zhao, M.; Chen, Y.; Wang, K.; Zhang, Z.; Streit, J. K.; Fagan, J. A.; Tang, J.; Zheng, M.; Yang, C.; Zhu, Z.; Sun, W. DNA-Directed Nanofabrication of High-Performance Carbon Nanotube Field-Effect Transistors. *Science* **2020**, *368*, 878–881.
- (41) Li, Y.; Wen, Y.; Beltrán, L. C.; Zhu, L.; Tian, S.; Liu, J.; Zhou, X.; Chen, P.; Egelman, E. H.; Zheng, M.; Lin, Z. Understanding DNA-Encoded Carbon Nanotube Sorting and Sensing via Sub-Nm-Resolution Structural Determination. *Sci. Adv.* **2025**, *11* (14), No. eadt9844.
- (42) Chi, Q.; Wang, G.; Jiang, J. The Persistence Length and Length per Base of Single-Stranded DNA Obtained from Fluorescence Correlation Spectroscopy Measurements Using Mean Field Theory. *Phys. A* **2013**, *392*, 1072–1079.
- (43) Zheng, X.; Lee, H.; Weisgraber, T. H.; Shusteff, M.; DeOtte, J.; Duoss, E. B.; Kuntz, J. D.; Biener, M. M.; Ge, Q.; Jackson, J. A.; Kucheyev, S. O.; Fang, N. X.; Spadaccini, C. M. Ultralight, Ultrafast Mechanical Metamaterials. *Science* **2014**, *344*, 1373–1377.
- (44) Shankar, A.; Jagota, A.; Mittal, J. DNA Base Dimers Are Stabilized by Hydrogen-Bonding Interactions Including Non-Watson–Crick Pairing near Graphite Surfaces. *J. Phys. Chem. B* **2012**, *116*, 12088–12094.
- (45) Lin, Z.; Yang, Y.; Jagota, A.; Zheng, M. Machine Learning-Guided Systematic Search of DNA Sequences for Sorting Carbon Nanotubes. *ACS Nano* **2022**, *16*, 4705–4713.
- (46) Beyene, A. G.; Alizadehmojarad, A. A.; Dorlhiac, G.; Goh, N.; Streets, A. M.; Král, P.; Vuković, L.; Landry, M. P. Ultralarge Modulation of Fluorescence by Neuromodulators in Carbon Nanotubes Functionalized with Self-Assembled Oligonucleotide Rings. *Nano Lett.* **2018**, *18*, 6995–7003.
- (47) Sonani, R. R.; Alizadehmojarad, A. A.; Hurley, N.; Hihath, J.; Strano, M. S.; Egelman, E. H.; Zheng, M. DNA Assembly Templated by Chiral Nanotube Lattices: From Helix to Rings. *J. Am. Chem. Soc.* **2026**, *148*, 21217–21222.
- (48) Zhu, L.; Lin, Z. DNA-HBN Compiler; https://www.notion.so/36a79e4de5be80248c2ce97668935f40?Source=coppy_link.
- (49) Yang, Y.; Zheng, M.; Jagota, A. Learning to Predict Single-Wall Carbon Nanotube-Recognition DNA Sequences. *Npj Comput. Mater.* **2019**, *5* (1), 3.
- (50) Zhou, X.; Wang, P.; Li, Y.; Han, Y.; Chen, J.; Tang, K.; Shi, L.; Zhang, Y.; Zhang, R.; Lin, Z. Accurate DNA Sequence Prediction for Sorting Target-Chirality Carbon Nanotubes and Manipulating Their Functionalities. *ACS Nano* **2025**, *19*, 2665–2676.
- (51) Dresselhaus, M. S.; Dresselhaus, G.; Jorio, A.; Souza Filho, A. G.; Saito, R. Raman Spectroscopy on Isolated Single Wall Carbon Nanotubes. *Carbon* **2002**, *40*, 2043–2061.
- (52) Fantini, C.; Jorio, A.; Santos, A. P.; Peressinotto, V. S. T.; Pimenta, M. A. Characterization of DNA-Wrapped Carbon Nanotubes by Resonance Raman and Optical Absorption Spectroscopies. *Chem. Phys. Lett.* **2007**, *439*, 138–142.
- (53) Chen, J.; Li, Y.; Wu, J.; Liu, J.; Zhou, X.; Li, Z.; Tang, K.; Shi, L.; Zhang, Z.; Lin, Z. Ordered DNA-Wrapped Single-Chirality Carbon Nanotubes Enable an Unparalleled Sensing Platform for Copper Ion Detection. *ACS Nano* **2025**, *19*, 28743–28754.
- (54) O'connell, M. J.; Bachilo, S. M.; Huffman, C. B.; Moore, V. C.; Strano, M. S.; Haroz, E. H.; Rialon, K. L.; Boul, P. J.; Noon, W. H.; Kittrell, C.; Ma, J.; Hauge, R. H.; Weisman, R. B.; Smalley, R. E. Band Gap Fluorescence from Individual Single-Walled Carbon Nanotubes. *Science* **2002**, *297*, 593–596.
- (55) Zheng, M.; Diner, B. A. Solution Redox Chemistry of Carbon Nanotubes. *J. Am. Chem. Soc.* **2004**, *126*, 15490–15494.
- (56) Roxbury, D.; Jagota, A.; Mittal, J. Sequence-Specific Self-Stitching Motif of Short Single-Stranded DNA on a Single-Walled Carbon Nanotube. *J. Am. Chem. Soc.* **2011**, *133*, 13545–13550.
- (57) Nicholas, J.; Chen, H.; Liu, K.; Venu, I.; Bolser, D.; Saleh, N. B.; Bisesi, J. H.; Castleman, W.; Ferguson, P. L.; Sabo-Attwood, T. Utilization of near Infrared Fluorescence Imaging to Track and Quantify the Pulmonary Retention of Single-Walled Carbon Nanotubes in Mice. *NanoImpact* **2019**, *14*, 100167.
- (58) Zheng, Y.; Bachilo, S. M.; Weisman, R. B. Enantiomers of Single-Wall Carbon Nanotubes Show Distinct Coating Displacement Kinetics. *J. Phys. Chem. Lett.* **2018**, *9*, 3793–3797.
- (59) Xhyliu, F.; Ao, G. Chirality-Pure Carbon Nanotubes Show Distinct Complexation with Recognition DNA Sequences. *Carbon* **2020**, *167*, 601–608.
- (60) O'connell, M. J.; Eibergen, E. E.; Doorn, S. K. Chiral Selectivity in the Charge-Transfer Bleaching of Single-Walled Carbon-Nanotube Spectra. *Nat. Mater.* **2005**, *4*, 412–418.
- (61) Strano, M. S.; Huffman, C. B.; Moore, V. C.; O'connell, M. J.; Haroz, E. H.; Hubbard, J.; Miller, M.; Rialon, K.; Kittrell, C.; Ramesh, S.; Hauge, R. H.; Smalley, R. E. Reversible, Band-Gap-Selective Protonation of Single-Walled Carbon Nanotubes in Solution. *J. Phys. Chem. B* **2003**, *107*, 6979–6985.
- (62) Bergler, F. F.; Schöppler, F.; Brunecker, F. K.; Hailman, M.; Hertel, T. Fluorescence Spectroscopy of Gel-Immobilized Single-Wall Carbon Nanotubes with Microfluidic Control of the Surfactant Environment. *J. Phys. Chem. C* **2013**, *117*, 13318–13323.
- (63) Stuber, A.; Douaki, A.; Hengsteler, J.; Buckingham, D.; Momotenko, D.; Garoli, D.; Nakatsuka, N. Aptamer Conformational Dynamics Modulate Neurotransmitter Sensing in Nanopores. *ACS Nano* **2023**, *17*, 19168–19179.
- (64) Rosenberg, D. J.; Cunningham, F. J.; Hubbard, J. D.; Goh, N. S.; Wang, J. W.-T.; Nishitani, S.; Hayman, E. B.; Hura, G. L.; Landry, M. P.; Pinals, R. L. Mapping the Morphology of DNA on Carbon

Nanotubes in Solution Using X-Ray Scattering Interferometry. *J. Am. Chem. Soc.* **2024**, *146*, 386–398.

(65) Pinals, R. L.; Yang, D.; Rosenberg, D. J.; Chaudhary, T.; Crothers, A. R.; Iavarone, A. T.; Hammel, M.; Landry, M. P. Quantitative Protein Corona Composition and Dynamics on Carbon Nanotubes in Biological Environments. *Angew. Chem., Int. Ed.* **2020**, *59*, 23668–23677.

(66) Satishkumar, B. C.; Brown, L. O.; Gao, Y.; Wang, C.-C.; Wang, H.-L.; Doorn, S. K. Reversible Fluorescence Quenching in Carbon Nanotubes for Biomolecular Sensing. *Nat. Nanotechnol.* **2007**, *2*, 560–564.

(67) Nishitani, S.; Ao, K.; Jalil, A.; Arias-Soto, O. I.; Moudi, A.; Chen, F.; Biyani, A.; Muppirala, P. N.; Landry, M. P. Redox Dye-Mediated Fluorescence Energy Transfer of Carbon Nanotube-Based Nanosensors. *Proc. Natl. Acad. Sci. U. S. A.* **2025**, *122* (12), No. e2419666122.