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Review Article

Phase-Aligned Entanglement as a Mechanism for DNA Triple Helix Stabilization in Quantum-Informed Genomic Systems.

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Abstract

Recent advances in quantum biology and DNA nanotechnology suggest that quantum coherence and phase-aligned entanglement may play a fundamental role in stabilizing DNA structures beyond the canonical double helix. This paper proposes that phase-aligned entanglement can facilitate the formation and stabilization of DNA triple helices (triplex DNA), particularly in the presence of Hoogsteen-bonded third strands involved in gene targeting and regulatory modulation. We explore the conditions under which quantum coherence between complementary and third strands allows for a stable triplex state, drawing from empirical data on triplex-forming oligonucleotides (TFOs), synthetic enhancer RNAs, and DNA-graphene hybrid quantum interfaces. Our model integrates entanglement fidelity, spin coherence, and π–π stacking interactions, offering new insights into triplex applications in epigenetic therapy, biosensing, and programmable genome editing.

Key words: triple helix DNA; phase-aligned entanglement; quantum coherence; hoogsteen bonding; enhancer RNA; spin networks; triplex-forming oligonucleotide; π–π stacking; epigenetic therapy; quantum biology

Introduction

1. Background and Molecular Basis of Triple Helix Formation

Triplex DNA involves the interaction of a **third strand**, typically rich in purines or pyrimidines, with a Watson–Crick duplex. It binds via **Hoogsteen base pairing**, forming T·A*T or C*·GC^+ triads under slightly acidic conditions or with synthetic modification [2,4,14]. Applications include gene silencing, site-specific recombination, and chromatin remodeling [5,15,16]. Despite its promise, triplex DNA is often **transient**, with poor in vivo persistence. Enhancing triplex stability has relied on chemical modification of oligonucleotides, incorporation of peptide nucleic acids (PNAs), or tethering via nanoparticles [7,17].

2. Quantum Coherence and Phase-Aligned Entanglement in DNA Systems

Quantum coherence—the preservation of wavefunction phase across spatially or temporally distributed systems—is emerging as a key feature of biomolecular processes [8,18]. **Phase-aligned entanglement** refers to the synchronization of quantum states such that interaction energy and probability distributions remain coherent, even across separate molecular domains [9,19]. Experimental systems involving **DNA-graphene hybrids** have demonstrated **entanglement-preserving π–π stacking**, electron spin transport, and non-classical photonic behavior [11,20,21]. These features have already been used to model DNA as a **spin network** or **Bloch-sphere logic lattice**, offering fault-tolerant logic behavior in quantum computation [22–24].

3. Proposed Model: Triple Helix Stabilization via Entanglement

We propose that a triple helix can be stabilized if:

- The **Watson–Crick duplex** is entangled with a **third strand** through **spin-correlated hydrogen bonds**.
- The **π–π orbital stacking** across all three strands is enhanced via a **graphene-based scaffold**.
- The **phase correlation** between complementary bases (A–T, G–C) and the third strand base is maintained using **synthetic enhancer RNA** or TFO with quantum entanglement potential.

Triplex stability is improved when the third strand aligns in phase with the duplex, minimizing decoherence through **quantum synchronization** across the molecular lattice [19,24].

4. Mechanisms for Engineering Phase-Aligned Entanglement

- **Graphene-DNA interfaces** promote spin preservation and π–π orbital coherence [20,25].

- **DNA polymerases** functioning under spin-coherent conditions can propagate entangled states during strand synthesis [26].
- **Triplex-forming oligonucleotides (TFOs)** engineered with magnetic labels or quantum dots can serve as **spin-encoded qubits**, enabling direct monitoring of entanglement fidelity [27,28].
- **Enhancer RNAs (eRNAs)** may act as biological third strands with embedded regulatory logic and entanglement alignment [13,29].

5. Applications and Implications

Therapeutics: Triplex DNA stabilized by entanglement can be used to **silence genes epigenetically** or **block transcription factors** [4,15,30].

Biosensing: Entangled triplexes integrated into **nano-electronic platforms** allow high-sensitivity detection of genomic states [20,31].

Quantum Genomics: The model offers new directions for **quantum memory encoding** in DNA, enabling hybrid biological-computational architectures [23,32].

Synthetic Biology: Triplex-based control systems could function as **logic gates**, regulated by quantum coherence rather than classical chemical equilibrium [24,33].

Conclusion

Phase-aligned entanglement introduces a new quantum-mechanical pathway for stabilizing DNA triple helices. This model suggests that third-strand binding can be enhanced through spin-aligned π–π interactions, templated coherence, and quantum-assisted polymerase extension. By engineering triplex-forming DNA to participate in entangled quantum networks, a novel class of programmable, biologically relevant, and quantum-stable nucleic architectures can be realized.

Conflict of interest: There is no conflict of interest.

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Supplement Material

Inhibition of Triple Helix Formation by Phase-Aligned Entanglement Using Colloid Gold

Background and Hypothesis

Triple helix DNA structures, formed via Hoogsteen or reverse Hoogsteen hydrogen bonding, involve a third strand binding into the major groove of a canonical DNA double helix. These interactions are particularly favored in homopurine–homopyrimidine sequences and under conditions that stabilize unusual base pairing geometries. Recent theoretical models propose that *phase-aligned entanglement*—coherent synchronization of molecular conformational states or quantum spin–orbital alignment—may facilitate or stabilize the assembly of such triple helices.

We propose that **colloid gold nanoparticles (AuNPs)** may interfere with the formation or stabilization of phase-aligned triple helix structures. Colloid gold is known to interact strongly with nucleic acids due to its high surface area, modifiable surface chemistry, and plasmonic properties. We hypothesize that these interactions may disrupt the quantum or molecular conditions necessary for phase-aligned triple helix assembly.

Potential Mechanisms of Interference

1. **Steric Hindrance:** AuNPs bound to DNA may impose spatial constraints that hinder the third strand from inserting into the major groove of the duplex. This blockage would directly impair triple helix formation irrespective of sequence compatibility.
2. **Surface Charge and Ionic Effects:** Gold nanoparticles, depending on their surface functional groups (e.g., citrate, PEG, thiols), can alter local ionic strength and electrostatic conditions. This alteration can destabilize the Hoogsteen hydrogen bonding network by repelling the third strand or changing DNA hydration and phosphate repulsion dynamics.
3. **Disruption of Quantum Coherence:** If phase-aligned entanglement involves coherent spin or vibrational states across the DNA complex, the introduction of metal nanoparticles—especially those with plasmonic resonance—could act as **sources of decoherence**. This interference may arise from electromagnetic field fluctuations, electron scattering, or vibrational damping, leading to the collapse of entangled conformational states.
4. **Photothermal and Photoelectric Disruption:** Upon light exposure (especially in the visible or near-infrared range), AuNPs can generate localized heating or photoelectrons via surface plasmon resonance. Such perturbations may destabilize the triple helix or preclude the entanglement phase conditions necessary for its formation, particularly in systems where entanglement relies on fine-tuned thermodynamic equilibrium.

Literature Support and Theoretical Basis

Studies have shown that gold nanoparticles can influence DNA conformation, including the denaturation of duplexes and inhibition of G-quadruplexes. Although direct experimental data regarding AuNP effects on triple helix DNA are sparse, the mechanistic parallels with known inhibitory effects on other DNA secondary structures suggest a plausible interference role.

Furthermore, gold's quantum decoherence-inducing capacity is well documented in nanoscale systems. If phase-aligned entanglement is a prerequisite for stable triple helix DNA—as some quantum biological models suggest—then colloid gold could function as an *anti-entanglement agent*, selectively inhibiting the supramolecular ordering required for third-strand binding.

Conclusion

Colloid gold nanoparticles represent a promising candidate for disrupting triple helix formation mediated by phase-aligned entanglement. This inhibition likely results from a combination of steric, electrostatic, and quantum-level effects. Further empirical studies, including spectroscopic and entanglement coherence assays, are required to validate this hypothesis and define the conditions under which AuNPs exert maximal inhibitory effects on DNA tertiary structures.

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