During cellular processes, modifications of the geometry and topology of DNA and RNA can yield multi-stranded structures such as R-loops. An R-loop is a 3-stranded structure composed of an RNA-DNA complex and another single strand of DNA. Experimental studies indicate that R-loops can play either destructive or regulatory roles in cellular processes [6, 7, 8].

Project Overview

Markov chains are used to explore models of 3-stranded RNA-DNA complexes known as R-loops. Two first-step models are explored: one for R-loop formation and the other for R-loop geometry. R-loop formation: Soteros and coworkers are developing a DNA-sequence-dependent method for predicting the formation of R-loops. Their approach is based on a formal grammar model and is informed by experimental data [1, 2]. Here, we use a simpler Markov chain model derived from a formal grammar model [3] to explore whether this simpler random model can capture any of the DNA-sequence-dependent features of R-loop formation.

R-loop geometry: Soteros and coworkers have developed lattice models to study the geometry and topology of 2-stranded (polymers) under tubular confinement [4, 5]. Here, the simplest such 2-stranded model is used to model R-loop geometry. Markov chain theory and simulations are used to explore the effect of strand flexibility on R-loop geometry.

What is an R-loop?

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A Formal Grammar Model for R-loops

• Symbols correspond to about 4 or 5 nucleotides in the DNA sequence; symbol set = {σ, δ, α, τ, ω, σ, δ}
• DNA-DNA; α (stable), σ (unstable)
• RNA-DNA & R-loop: ω (start), δ (stable), τ (unstable), ω (end)
• Symbol stability depends on the CG-content of the corresponding DNA sequence [3]

A Lattice Model for R-loop Geometry/Topology

• DNA and RNA can be thought as polymers.
• In the standard lattice model, a polymer is represented by a set of vertices in Z^2 joined by unit edges.
• (L,M)-tubes: the vertex coordinates are such that x > 0, 0 < y ≤ L, 0 < z ≤ M.

Conclusions

• Exact and Monte Carlo analyses of the two Markov models for R-loops provide consistent results.
• R-loop formation: a purely random model is not sufficient to capture features of the experimental data.
• R-loop geometry: a simplified model can take into account differing flexibility for the R-loop components.
• Future directions: visible lattice tube configurations in the 3-dimensional space.

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