

# Statistical evidence for structural strand asymmetry in non-coding RNAs

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## Abstract

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Many RNA functions are determined by their specific secondary and tertiary structures. These structures are folded by the canonical G::C and A::U base pairings as well as by the non-canonical G::U complementary bases. G::U base pairings in RNA secondary structures may induce structural strand asymmetries in the corresponding transcribed DNA sequences. This is likely so as the corresponding C::A nucleotides of the complementary strand do not pair. As a consequence, the secondary structures that form from a genomic sequence depend on the strand transcribed. We explore this idea to investigate the size and significance of structural strand differentials in microRNA, non-coding RNA, and mRNA sequences. We show that RNA structure strand asymmetry is statistically larger than randomized versions preserving the same mono-nucleotide and di-nucleotide base composition and length, which is especially pronounced in microRNA precursors. This finding implies that sequences that have evolved functional RNA structures show an asymmetry in stable structural features preferentially conserved on the transcribed strand, and this signal is likely due to conservation of RNA secondary structures rather than a secondary effect of base compositional biases.

Keywords: microRNA; miRNA; non-coding RNA; ncRNA; mRNA; RNA structure strand asymmetry; RNA secondary structures; base composition; minimum free energy; MFE

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