

Stability of mRNA/DNA and DNA/DNA duplexes modulates mRNA transcription

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The distribution of the four nucleotides along the DNA sequence encodes the genetic information in living systems. However, do nucleic acids possess other attributes that contribute to their biological functions? Recent work of a team led by Stoyno Stoynov, working at the Bulgarian Academy of Sciences, suggests that thermodynamic stability of DNA/DNA and RNA/DNA duplexes influences mRNA transcription. The manuscript appears in the March 14 issue of the international, peer-reviewed, open-access online journal *PLoS ONE*.

"These findings challenge the way we look at DNA," says Stoynov. "Until now we have pretty much simplified our view of DNA helix as a Lego combination of four different pieces, which encodes genetic information and contain patterns, recognized by DNA binding proteins. However, nucleic acids are real molecules with defined physical characteristics, which can influence their biological functions."

In this work the authors present a calculation of the thermodynamic stability of DNA/DNA and mRNA/DNA duplexes across the genomes of four species in the genus *Saccharomyces*. The researchers found that genes of these organisms are more stable than intergenic regions near their 3'-end. In addition, introns (internal non-coding regions in genes) are significantly less stable than exons (coding sequences in genes), suggesting that stable sense duplexes are characteristic of the coding sequences.

Next, the authors showed a relationship between the pattern of

thermodynamic stability and the mRNA level of genes. There is a general trend of increased mRNA level with increasing thermodynamic stability of the respective gene. Positive correlation was observed between the mRNA level and the stability of DNA/DNA and mRNA/DNA duplexes of both exons and introns. In contrast, an inverse relationship exists between mRNA levels and stability of the region near 3'-end of genes. mRNA levels increase with decreasing thermodynamic stability of this region. "The observed correlations are impressive, given that several other factors like promoter effectiveness, promoter regulation, and mRNA half-life directly influence mRNA level, as well," says Stoyanov.

The researchers also observed that, in contrast to intergenic regions, genes have more stable sense RNA/DNA duplexes than potential antisense RNA/DNA duplexes. "The difference between stability of sense and antisense mRNA/DNA is a property that can aid gene discovery," explains Stoyanov.

"Thermodynamic stability of nucleic acid duplexes depends primarily on thermodynamic properties of nearest-neighbor nucleotide interactions. Therefore, the stability of DNA/DNA and RNA/DNA duplexes is determined by the distribution of the ten possible DNA/DNA nucleotide duplets (dAA/dTT, dGC/dCG, etc.) and the sixteen possible RNA/DNA duplets (rAA/dTT, rUA/dAT, etc.). Such duplet code does not carry any genetic information but seems to modulate the level of RNA expression. It is amazing that the same nucleotide sequence can simultaneously encode its respective protein and modulate its level of expression." says Stoyanov.

The mechanism of how DNA/DNA and mRNA/DNA duplex stability influences mRNA level remains unclear. The authors propose two models, but further work is needed to understand how thermodynamic stability modulates mRNA level.

Source: Public Library of Science

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