

## How the Cellular Environment Influences Hybrid Duplex Conformation

Although biochemical studies often utilize dilute solution environments, actual cellular conditions are very crowded with nearly 40% of the cellular volume occupied by macromolecular crowding agents while smaller osmolytes accumulate in response to environmental stresses. The effects of these cosolutes were observed on the helical conformation of nucleic acids, primarily DNA/RNA hybrid duplexes which play important roles in biological processes such as replication, transcription, reverse transcription, and mRNA degradation. Circular dichroism (CD) analyses revealed that the helical conformation of the hybrid duplexes ranged from A-form like to B-form like, depending on the base composition of each strand. In the presence of macromolecular crowding agents, the conformations shifted to more A-form like while in the presence of osmolytes the conformations shifted to more B-form like. These results suggest that the accessibility of the helical grooves for a given hybrid sequence may be modulated by the cellular environment.