Effect of hydrostatic pressure on the stability of mono- and multi-molecular G-Quadruplexes

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Using spectroscopy, we have studied the effect of hydrostatic pressure on the conformational stability of monomolecular and multimolecular 4-stranded DNA molecules (G4). In earlier work, we showed that pressure destabilizes the G4 structure formed by the monomolecular, single stranded oligonucleotide, HTel[1]. The folded structure of HTel has three G-tetrads and three loops, that remain single stranded. The molar volume change of unfolding HTel, ΔV, is approx. -50 – -60 cm^3 mol^{-1} at Tm ~ 60 °C. Thus, it is de-stabilized by pressure. Mechanistic-ally, the large, negative volume change was assumed to arise predominately from the release of the cations coordinated by the G-tetrads. In an effort to better understand the behaviour of G4 molecules at elevated pressure, we have studied several oligonucleotides with sequences similar to that of HTel and the tetramolecular G4, $d(TG_4T)_4$, a four-stranded molecule without loops. The molar volume changes observed for the modified HTel oligo-nucleotides are all negative, they are all destabilized by pressure. By looking at the effect of pressure on $d(TG_4T)_4$, we hoped to obtain information on the volume change that arises from the destabilization of the G-tetrad. However, the pressure does not appear to influence the stability of $d(TG_4T)_4$; thus, ΔV ~0 cm^3 mol^{-1} under the conditions of our study. This unexpected result implies that the factors that contribute to the volume change arising from the formation of tetra-molecular GQ structures balance each other with the result that the net ΔV is zero.

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[1] J. Am. Chem. Soc. 2011, 133, 4518–4526