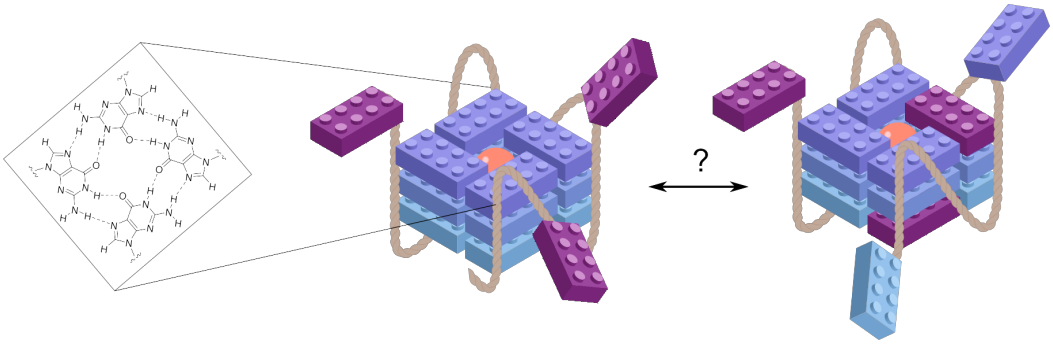
Characterising RNA G-quadruplex structure

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In guanine-rich DNA and RNA sequences, non-canonical nucleic acid structures called G-quadruplexes can form. While DNA G-quadruplexes have been extensively studied since their discovery, RNA G-quadruplexes have gained attention due to their involvement in gene regulation, such as the G-quadruplex in the 5'-untranslated region of the B-cell lymphoma gene 2 (*BCL2*). Abnormal expression of Bcl-2 has been associated with various diseases [1]. However, the mechanism of regulation remains unknown.

G-quadruplexes are composed of a cyclic arrangement of four guanines through Hoogsteen hydrogen bonds, resulting in a single plane [2]. Typically, a G-quadruplex consists of three stacking planes connected through the backbone by flexible loops.



RNA G-quadruplexes adopt a parallel orientation of the backbone strands due to the ribose sugar's C3'-endo preference [3]. The exchange of guanines between the planes and loops contributes to the high structural dynamics. By strategically mutating the G-quadruplex sequence, the dynamics can be minimized, enabling the elucidation of individual conformers. Using NMR is an ideal method for analysing their structure, characterising their dynamics, and providing insights into their mechanism of regulation.

Through detailed analysis of the various mutant structures by our newly developed NMR-based approach, valuable insights into essential structural features were obtained. Understanding these characteristic elements is crucial for elucidating the regulatory mechanisms and designing future drug treatments.

[1] Ramala Shahid, Anthony Bugaut, Shankar Balasubramanian, *Biochemistry*, **2010**, 49, 8300-8306
[2] Michael Adrian, Brahi Heddi, Anh Tuân Phan, *Methods*, **2012,** 57, 11-24
[3] Prachi Agarwala, Satyaprakash Pandey, Souvik Maiti, *Organic & Biomolecular Chemistry*, **2015**, 13, 5570-5585