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Using parallel-stranded duplexes to control formation of parallel-stranded G-quadruplexes

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Nucleic acids are gaining quick popularity and utility for creating new nanomaterials [1]. G-quadruplexes (G4) are an attractive alternative to regular B-DNA to assemble nucleic acids, but suffer from a fatal flaw: the rules of recognition, i.e. formation of a G-quartet, in which four *identical* bases are paired, prevent the controlled assembly between different strands. Complex mixtures are obtained instead of well-defined objects.

In this report, we propose a solution to this problem. Three carefully designed parallel-stranded duplexes [2] were used to direct the formation of all parallel G4 DNA from four different strands. The resulting structure consists of a G4 core extended in three directions with parallel duplex DNA. G4 core serves as a 'knot' due to its predicted high stability. The ends of three parallel stranded duplexes present convenient points of attachments for desired DNA sequences prone to formation of specific secondary folds: Watson-Crick duplexes, *i*-motifs, other G-quadruplexes, etc. In addition, fluorescent labels, biotin, and other probes could be easily attached, enhancing the versatility of the structure.

The correct formation of the overall architecture out of four different G-rich strands was assessed using gel electrophoresis. The presence of the G4 core was demonstrated using CD spectroscopy as well as via *UV-vis* and fluorescent titrations with G4-specific ligands. Thermal properties of the target structure and its duplex components were thoroughly analyzed using spectroscopic techniques. The structure obtained displayed unusual but expected stability under denaturing conditions (high temperature, presence of formamide and urea). The design was extended to one dimension using variety of linkers. Resulting nanomaterial was visualized via AFM and EM.

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Références

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