G-quadruplexes (G4s) are a common type of higher-order nucleic acid structures formed from G-rich sequences, typically with the pattern \(G_4N_1G_4N_1G_4N_1G_4\). For example, the human telomere DNA has a repetitive sequence of \((GGGTTA)_n\). G-quadruplexes (G4s) are a common type of higher-order nucleic acid structures formed from G-rich sequences, typically with the pattern \(G_4N_1G_4N_1G_4N_1G_4\). For example, the human telomere DNA has a repetitive sequence of \((GGGTTA)_n\).

Experimentally solved 3D structures of G4s, deposited in the Protein Data Bank (PDB), provide important insights into their functions at the atomic level. However, limited annotations of G4s in the PDB unavoidably lead to false positive and false negative search results based on keywords. The lack of a widely accepted annotation tool also makes results reported in the literature difficult, if not impossible, to compare. Schematic representations that capture the essential features of G4s in a simple yet revealing manner are missing: it is easy to get lost in detailed descriptions and complicated graphics while reading publications on G4s. Clearly, the increasing number of G4s detected and annotated G4s, starting from atomic coordinates in PDB or PDBx/mmCIF format. It identifies G-tetrads and arranges representations that capture the essential features of G4s in a simple yet revealing manner are missing: it is easy to get lost in detailed descriptions and complicated graphics while reading publications on G4s. Clearly, the increasing number of G4s detected and annotated G4s, starting from atomic coordinates in PDB or PDBx/mmCIF format. It identifies G-tetrads and arranges visualizations of G-quadruplexes.

The DSSR (Dissecting the Spatial Structure of RNA) program detects and annotates G4s, starting from atomic coordinates in PDB or PDBx/mmCIF format. It identifies G-tetrads and arranges visualizations of G-quadruplexes. G4 stems are characterized by the stacking of G-tetrads stabilized by cations. They are hydrogen-bonded via four consecutive G+G pairs. G4s are formed arranged in a cyclic planar manner, held together by eight stacking interactions. G4 stems are categorized in terms of loops connecting the four strands, by common names [e.g., chair, stack, transition, and the three guanines in a \(3\text{-P-Lw-Ln}\) conformation with a \((1+3)\) hybrid conformation, emphasizing the duplex-quadruplex transition, and the three guanines in syn conformation.

Innovative block representations introduced in DSSR to simplify the visualization of G-quadruplexes. (A) The \textit{anti} guanine (lower-left) leads to a counter-clockwise orientation of H-bonding interactions (dashed lines in magenta) from the WC edge to the major-groove (Hoogsteen) edge. (B) The syn guanine (colored teal) reverses the direction of the H-bonds to clockwise, and it also creates a wide groove and a narrow groove. (C) A parallel G-quadruplex illustrated with square blocks for G-tetrads, highlighting a six-layered G4-helix composed of two three-layered G4-stems via coaxial stacking interactions. The two bulged cytosines are marked. (D) Another G4 with a \((1+3)\) hybrid conformation, emphasizing the duplex-quadruplex transition, and the three guanines in syn conformation.

The DSSR-PyMOL integration supersedes that approach; it is easier to use, and generates better schematic images. In DSSR, a G4-stem is defined as a G4 helix with backbone connectivity. Bulges are also allowed along each of the four strands.

### Schematic Blocks

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| Definition of various types of DSSR blocks, illustrated using idealized, planar Watson-Crick (WC) base-pair and G-tetract geometries. (A) Purine (A, G) and pyrimidine (C, T, U) base blocks and the WC-pair block in default dimensions. (B) The slim purine block and the square G-tetrad block for simplified visualizations of G-quadruplexes. |}

### Simplified Representations

#### DSSR-Enabled Automatic Identification and Annotation of G-quadruplexes in the PDB

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### Abstract

G-quadruplexes (G4s) are a common type of higher-order nucleic acid structures formed from G-rich sequences, typically with the pattern \(G_4N_1G_4N_1G_4N_1G_4\). For example, the human telomere DNA has a repetitive sequence of \((GGGTTA)_n\). The building block of G4s is a tetrad of guanines (G-tetrad) arranged in a cyclic planar manner, held together by eight hydrogen-bonds via four consecutive G+G pairs. G4s are formed by the stacking of G-tetrads and stabilized by cations. They are known to play important roles in the regulation of gene expression, the maintenance of genome stability, and serve as potential therapeutic targets.

Experimentally solved 3D structures of G4s, deposited in the Protein Data Bank (PDB), provide important insights into their functions at the atomic level. However, limited annotations of G4s in the PDB unavoidably lead to false positive and false negative search results based on keywords. The lack of a widely accepted annotation tool also makes results reported in the literature difficult, if not impossible, to compare. Schematic representations that capture the essential features of G4s in a simple yet revealing manner are missing: it is easy to get lost in detailed descriptions and complicated graphics while reading publications on G4s. Clearly, the increasing number of G4s available in the PDB calls for a pragmatic software tool that can identify this important class of structures automatically, characterize them consistently, and visualize them intelligibly.

The DSSR (Dissecting the Spatial Structure of RNA) program detects and annotates G4s, starting from atomic coordinates in PDB or PDBx/mmCIF format. It identifies G-tetrads and arranges visualizations of G-quadruplexes. (A) The \textit{anti} guanine (lower-left) leads to a counter-clockwise orientation of H-bonding interactions (dashed lines in magenta) from the WC edge to the major-groove (Hoogsteen) edge. (B) The syn guanine (colored teal) reverses the direction of the H-bonds to clockwise, and it also creates a wide groove and a narrow groove. (C) A parallel G-quadruplex illustrated with square blocks for G-tetrads, highlighting a six-layered G4-helix composed of two three-layered G4-stems via coaxial stacking interactions. The two bulged cytosines are marked. (D) Another G4 with a \((1+3)\) hybrid conformation, emphasizing the duplex-quadruplex transition, and the three guanines in syn conformation.

### Cover Images of the RNA Journal

Nine out of 12 in 2019 and Jan-Jun in 2020 cover images of the RNA Journal, contributed by the NDB, have been generated via 3DNA-blocview and PyMOL. The DSSR-PyMOL integration supersedes that approach; it is easier to use, and generates better schematic images.

### Comprehensive Annotations

- **PDB entry 2gku**
  - 3(-Lw-Ln) hybrid (3+1) UDU
- **PDB entry 2cjd**
  - 3(-P-Lw-Ln) hybrid (3+1) UDU
- **PDB entry 4mc6**
  - Intermolecular parallel (4+0) UED
- **PDB entry 6hk9**
  - 2(P+PK) UD (3+1) UDGD

### PDB Survey

[http://G4.x3dna.org](http://G4.x3dna.org)

### References


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