

Supplementary Material for

**A regular thymine-tetrad and a peculiar supramolecular assembly in  
the first crystal structure of an all LNA G-quadruplex**

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**Table S1 Packing contacts**

Residue	Atom	Symmetry mate residue (symmetry operation)	Atom	Distance (Å)
Thy1A	N3	Thy1F* (X-Y, X, Z+5/6)	O4'	2.9
Thy1B	O4'	Gua2F* (X-Y, X, Z+5/6)	N9	3.2
Thy1B	O2	Gua2H* (X-Y, X, Z+5/6)	N1	3.1
Thy1C	O4'	Thy1H* (X-Y, X, Z+5/6)	O2	3.3
Thy1C	N3	Thy1E* (X-Y, X, Z+5/6)	O2	2.6
Thy1C	O4	Thy1E* (X-Y, X, Z+5/6)	O2	3.3
Thy1C	O4	Thy1E* (X-Y, X, Z+5/6)	N3	2.8
Thy1D	O3'	Thy1G* (X-Y, X, Z+5/6)	O2	3.2
Thy1F	N3	Gua2E* (X, Y, Z)	O2'	2.8
Thy1G	O4'	Thy1A* (Y, -X+Y, Z+1/6)	O4'	3.1
Thy1H	O2	Thy1C* (Y, -X+Y, Z+1/6)	O4'	3.3

**Table S2 Backbone torsion angle ranges for crystallographic and NMR models of similar LNA, DNA and RNA quadruplexes**

	$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	$\zeta$		$\alpha$	$\beta$	$\gamma$	$\delta$	$\epsilon$	$\zeta$
<b>LNA QUADRUPLEX</b>													
	<b>X-Ray (4L0A)</b>							<b>NMR (1S9L)</b>					
Thy 1 (A)			g+	g+	t	g+				g+	g+	t	g+
Gua 2 (A)	t/g-	t	g+	g+	t	g-		t/g-	t	g+	g+	t	g-
Gua 3 (A)	g-	t	g+	g+	t	g-		g-	t	g+	g+	t	g-
Gua 4 (A)	g-	t	g+	g+	t	g-		g-	t	g+	g+	t	g-
Thy 5 (A)	g-	t	g+	g+				g-	t	g+	g+		
<b>LNA QUADRUPLEX</b>													
Thy 1 (B)			g+	g+	t	g-				g+	g+	t	g-
Gua 2 (B)	g-	t	g+	g+	t	g-		t/g-	t	g+	g+	t	g-
Gua 3 (B)	g-	t	g+	g+	t	g-		g-	t	g+	g+	t	g-
Gua 4 (B)	g-	t	g+	g+	t	g-		g-	t	g+	g+	t	g-
Thy 5 (B)	g-	t	g+	g+				g-	t	g+	g+		
<b>LNA QUADRUPLEX</b>													
Thy 1 (C)			g+	g+	t	g-				g+	g+	t	g-
Gua 2 (C)	g-	t	g+	g+	t	g-		g-	t	g+	g+	t	g-
Gua 3 (C)	g-	t	g+	g+	t	g-		g-	t	g+	g+	t	g-
Gua 4 (C)	g-	t	g+	g+	t	g-		g-	t	g+	g+	t	g-
Thy 5 (C)	g-	t	g+	g+				g-	t	g+	g+		
<b>LNA QUADRUPLEX</b>													
Thy 1 (D)			t/g+	g+	t	g-				t/g+	g+	t	g-
Gua 2 (D)	t	t	t	g+	t	g-		t	t	t	g+	t	g-
Gua 3 (D)	g-	t	g+	g+	t	g-		g-	t	g+	g+	t	g-
Gua 4 (D)	g-	t	g+	g+	t	g-		g-	t	g+	g+	t	g-
Thy 5 (D)	g-	t	g+	g+				g-	t	g+	g+		
<b>DNA QUADRUPLEX</b>													
	<b>X-Ray (1S45)</b>							<b>NMR (139D)</b>					
Thy 1 (A)			g+	g+	g+	t			t	g+	t	t	t
Gua 2 (A)	g+	t	t	g+	t	g-		g-	t	g+	t	t	t
Gua 3 (A)	g-	t	g+	t	t	g-		g-	t	g+	t	t	t
Gua 4 (A)	g-	t	g+	t	t	g-		g-	t	g+	t	t	t
Gua 5 (A)	g-	t	g+	t	t	g-		g-	t	g+	t	t	t
Thy 6 (A)	g-	t	g+	g+/t				g-	t	g+	t		
<b>DNA QUADRUPLEX</b>													
Thy 1 (B)			g+	g+	g+	t			t	g+	t	t	t
Gua 2 (B)	g+	t	t	g+	t	g-		g-	t	g+	t	t	t
Gua 3 (B)	g-	t	g+	t	t	g-		g-	t	g+	t	t	t
Gua 4 (B)	g-	t	g+	t	t	g-		g-	t	g+	t	t	t
Gua 5 (B)	g-	t	g+	t				g-	t	g+	t	t	t
Thy 6 (B)*								g-	t	g+	t		

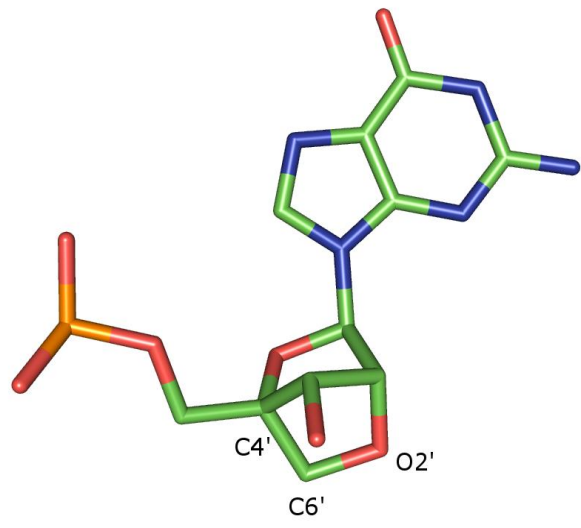
Thy 1 (C)			g+	t	t	g+			t	g+	t	t	t
Gua 2 (C)	g+	t	t	g+	t	g-		g-	t	g+	t	t	t
Gua 3 (C)	g-	t	g+	t	t	g-		g-	t	g+	t	t	t
Gua 4 (C)	g-	t	g+	t	t	g-		g-	t	g+	t	t	t
Gua 5 (C)	g-	t	g+	t	g-	g-		g-	t	g+	t	t	t
Thy 6 (C)	g+	t	g+	g+				g-	t	g+	t		
RNA QUADRUPLEX**													
	<b>X-Ray (1J8G)</b>							<b>NMR (1RAU)</b>					
Thy 1			g+	g+	t	g-				g+	g+	t	g-
Gua 2	g-/t	g+	t	g+	t	g-		g-	t	g+	t	t	g-/t
Gua 3	g-	t	g+	t	t	g-/t		g+/t	t	t	g+	t	g-
Gua 4	g-	t	g+	g+	t	g-		g-	t	g+	g+	t	g-
Gua 5	g-	t	g+	g+	t	g+		g-	t	g+	g+/t	t	g-
Thy 6	t	t	g+	t				g-	t	g+	t		

\*Thy 6 (B) is missing in the crystal structure

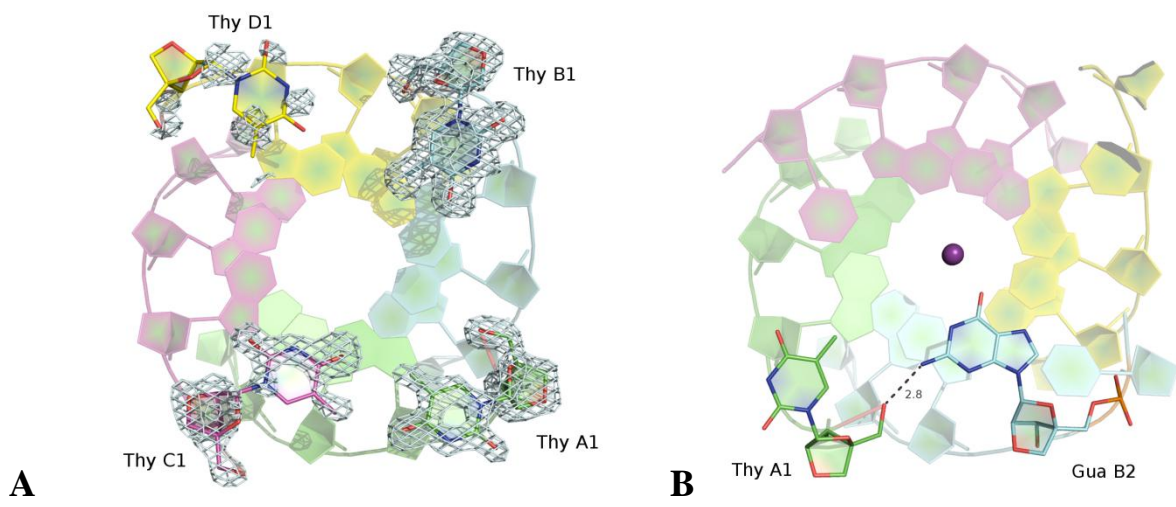
\*\* Since the G-quadruplex is symmetry generated in the crystal structure, the four strands are the same.

**Table S3 Examples of hydrogen bonds in the A-C groove of the LNA quadruplex**

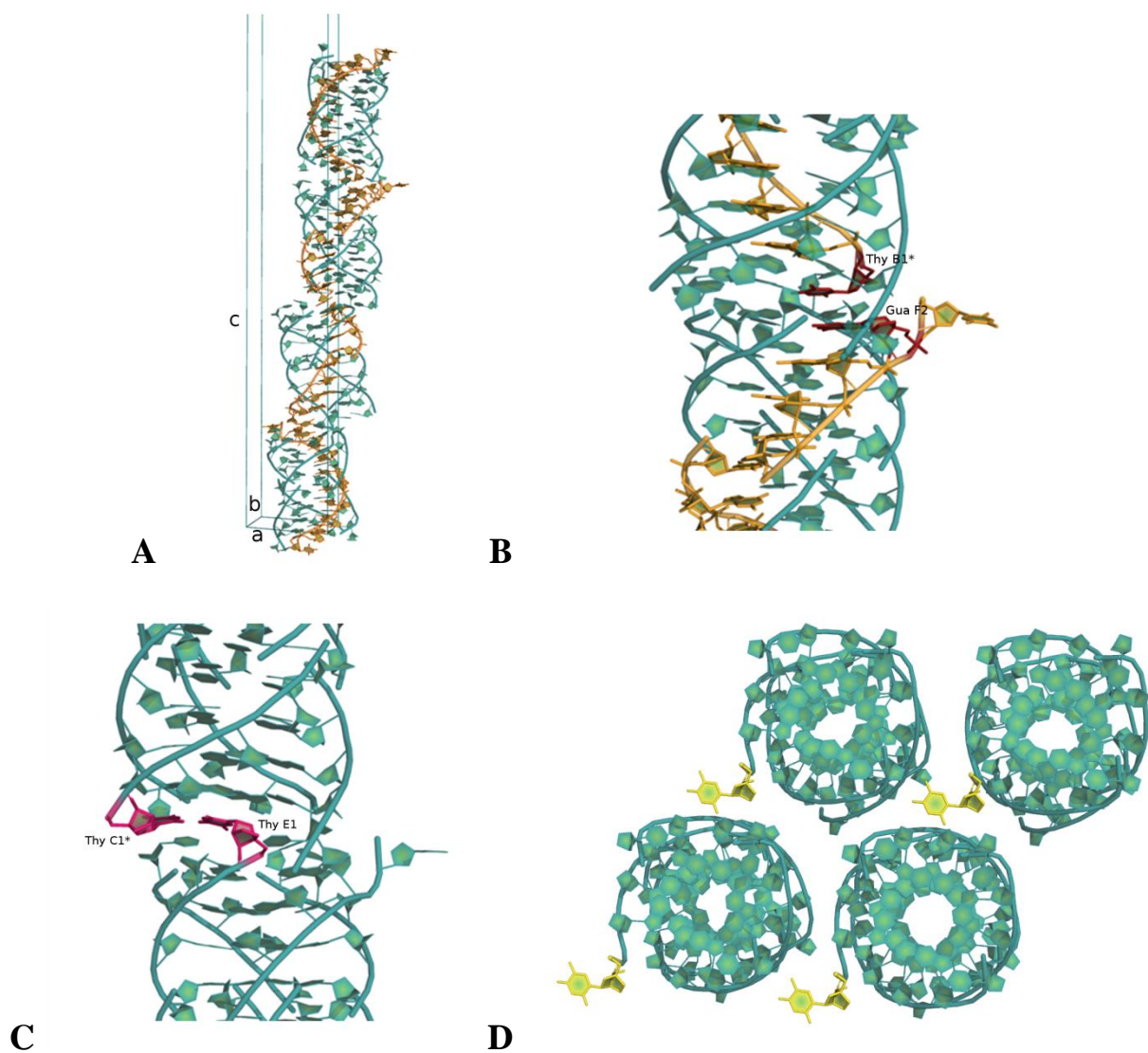
<b>Hydration network</b>	<b>Hydrogen bond distances (Å)</b>
N2 Gua A2 – Water - O2P Gua C2	2.96 – 2.96
N2 Gua A3 – Water - O2P Gua C2	2.78 – 3.06
N2 Gua A4 – Water - O2P Gua C3	2.96 – 2.87
N2 Gua A4 – Water - O2P Gua C4	2.96 – 2.85
N2 Gua A4 – Water - O2P Gua C4	3.34 – 2.87
O2' Gua A3 – Water - O2P Gua C2	3.03 – 2.68
O2' Gua A4 – Water - O2P Gua C3	3.10 – 2.89



**Figure S1 Example of an LNA-modified guanine residue.**

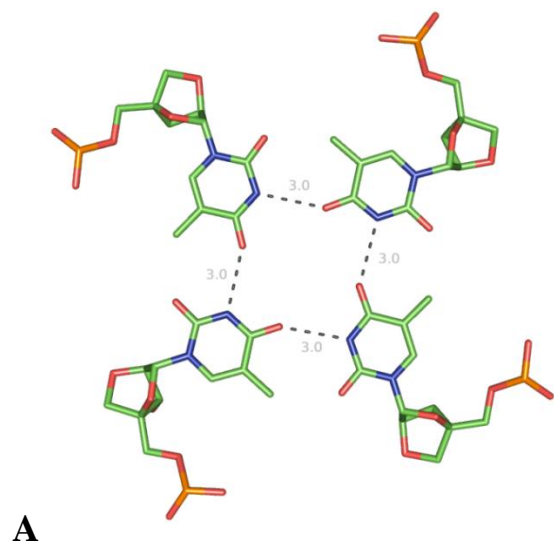


**Figure S2 A) Fo-Fc omit electron density map contoured at 2.5  $\sigma$  level of the 5' thymines of LNA quadruplex. B) Interaction between Thy A1 and Gua B2.**

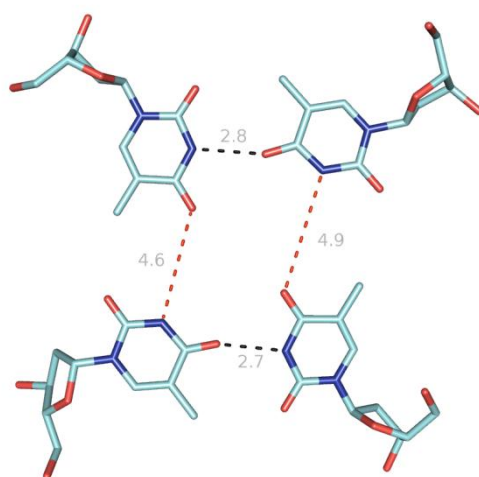


**Figure S3 Packing arrangement of LNA quadruplexes. A) Quadruplexes along the crystallographic *c* axis with strands B and F marked in a different color (orange), B) a zoom on the stacking interaction between Thy B1\* and Gua F2 (red), C) a different view showing the position of the interacting Thy C1\* and E1 (pink). D) Disposition of quadruplexes within a layer. Thy F1 is highlighted in yellow.**

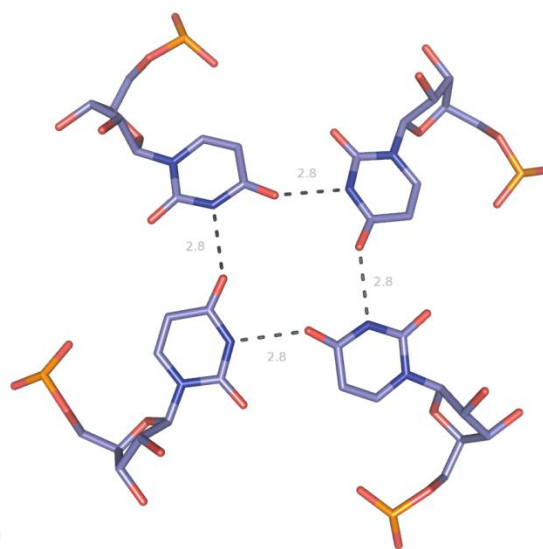




**A**



**B**



**C**

**Figure S4** Examples of T/U tetrads in crystallographic structures. **A)** T-tetrad in the present LNA quadruplex, **B)** T-pairs in A DNA quadruplex (Caceres *et al.*, 2004), **C)** U-tetrad in a RNA quadruplex (Deng *et al.*, 2001). Interactions between bases are explicitly shown as black dotted lines. Distances between non-interacting atoms are shown as red dotted lines.