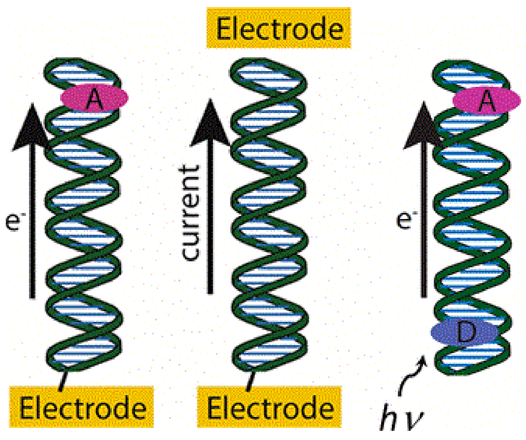
Design and studies of charge transport through G-quadruplex DNA architectures

CHAN JONNY; PASSAY JOHAN; RUBAY CHRISTOPHE; ELIAS BENJAMIN[a]; DEFRANCQ ERIC[b]

[a]*UCLouvain – IMCN - Molecular Chemistry, Materials and Catalysis*
Place Louis Pasteur 1, bte L4.01.02 – 1348 Louvain-la-Neuve – Belgium
[b]*Université Grenoble Alpes - DCM - Ingénierie et Interactions BioMoléculaires*
570 rue de la Chimie Université Grenoble Alpes 38041 GRENOBLE France

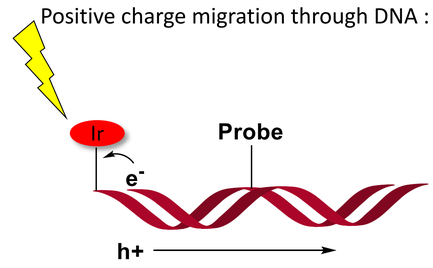
Introduction : Charge Transport through DNA

Charge transport in DNA duplex has been extensively studied during these past dozens of years since its discovery.[1] Due to the π-stack of the bases forming the double helical structure of DNA, positive charge (hole) or negative charge (electron) can migrate along the macromolecule.[2] The detection of oxidative lesion in DNA, potentially leading to cancer formation, through charge transfer has been envisaged.[3]

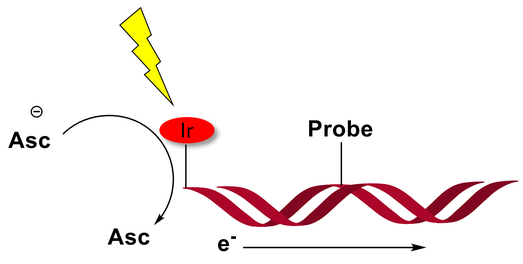


The use of iridium complexes as charge donor allows the migration of positive charge (hole transfer HT) and negative charge (electron transfer ET) through DNA.[4]

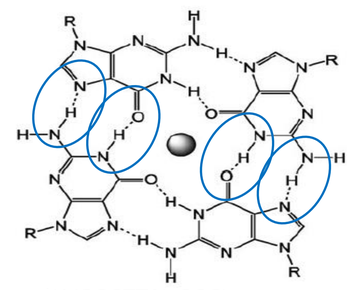
Positive charge migration through DNA :



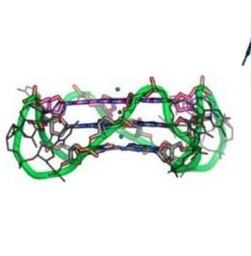
Negative charge migration through DNA :



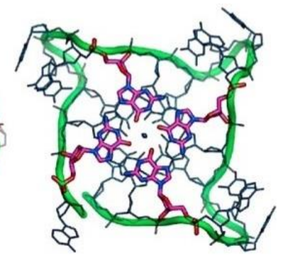
Apart from the canonical form of DNA, the double helical structure, DNA molecule can also be folded into G-quadruplexes (G4). In the 60, it has been demonstrated that four guanines can self-assemble into a G-quartet, stabilized by Hoogsteen like hydrogen bonds.[5] In regions rich in guanine bases, a series of planar G-quartets stack with each other forms the G-quadruplex.[6]



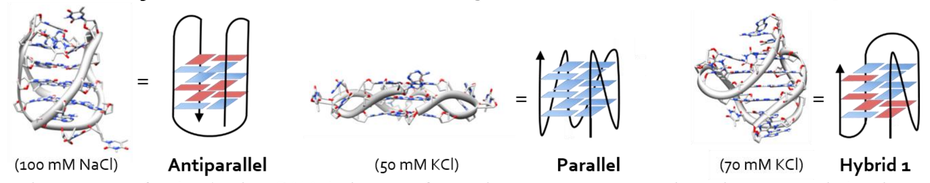
d(A**(GGGTTA)$_3$**GGG)



d(A**(GGGTTA)$_3$**GGG)



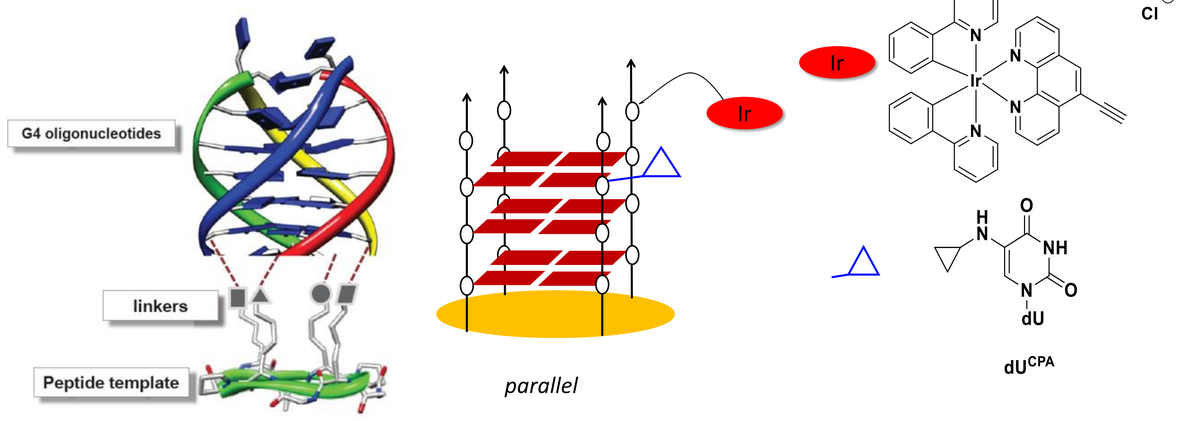
d(AAA**(GGGTTA)$_3$**GGGAA)



The charge transfer in duplex DNA is known for at least twenty years but the research in charge transport through G4 is still in its infancy.

Goal

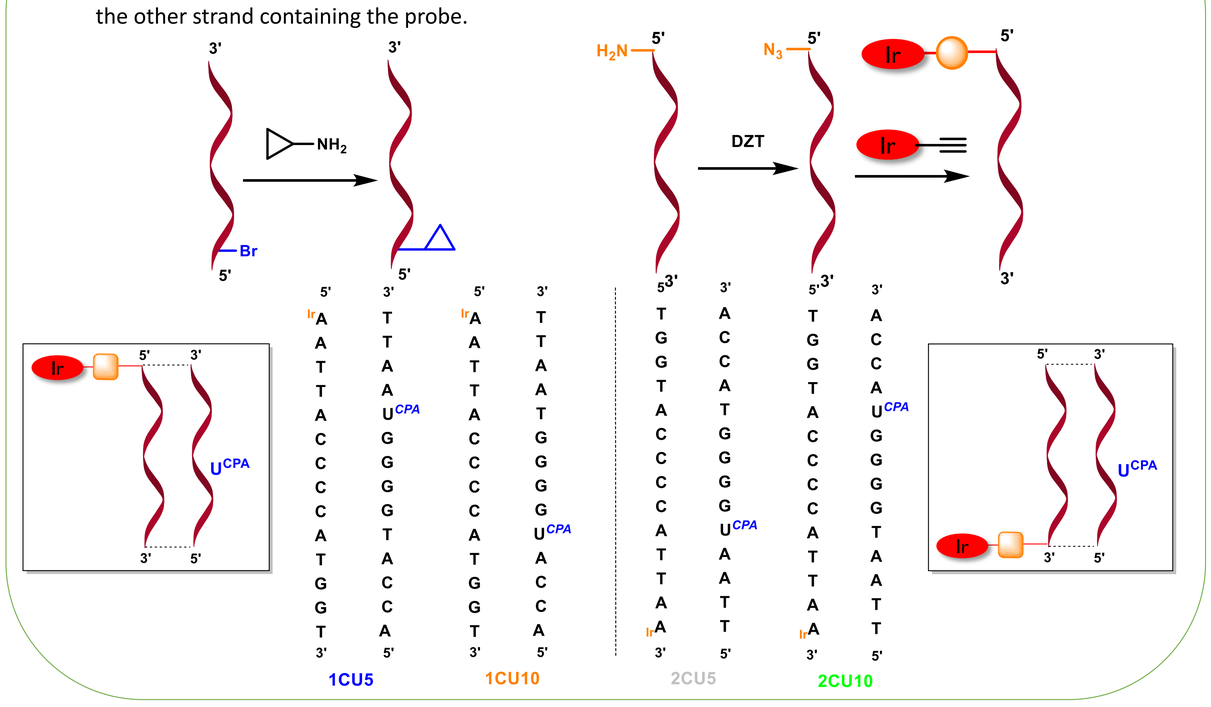
In this project, we will study the charge transfer phenomenon in a G-quadruplex fixed in a particular conformation, thanks to a peptide template. In order to study this phenomenon, we will use a iridium complex as a charge donor and a cyclopropylamine uridine as a probe.



Before we begin the study of charge transport in G4, we will first demonstrate that our charge injector can induce charge transport and our probe can detect the charge, in duplex DNA. This will constitute our proof of concept.

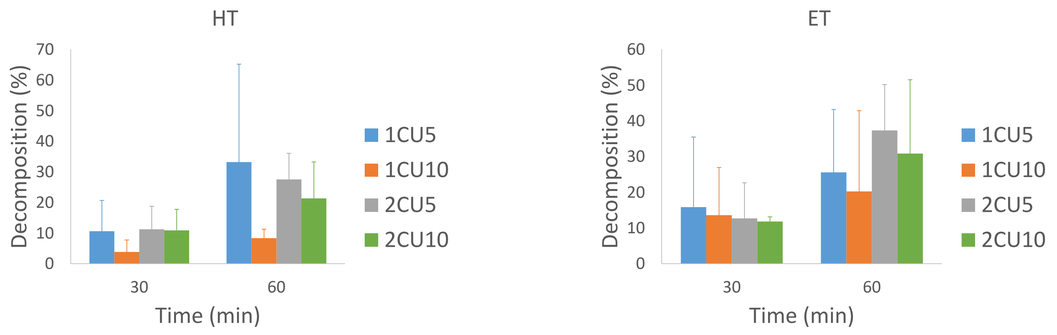
Proof of concept

We first need to prepare two sets of duplex DNA, with one strand containing the charge injector and the other strand containing the probe.



Charges transport experiments in duplex DNA

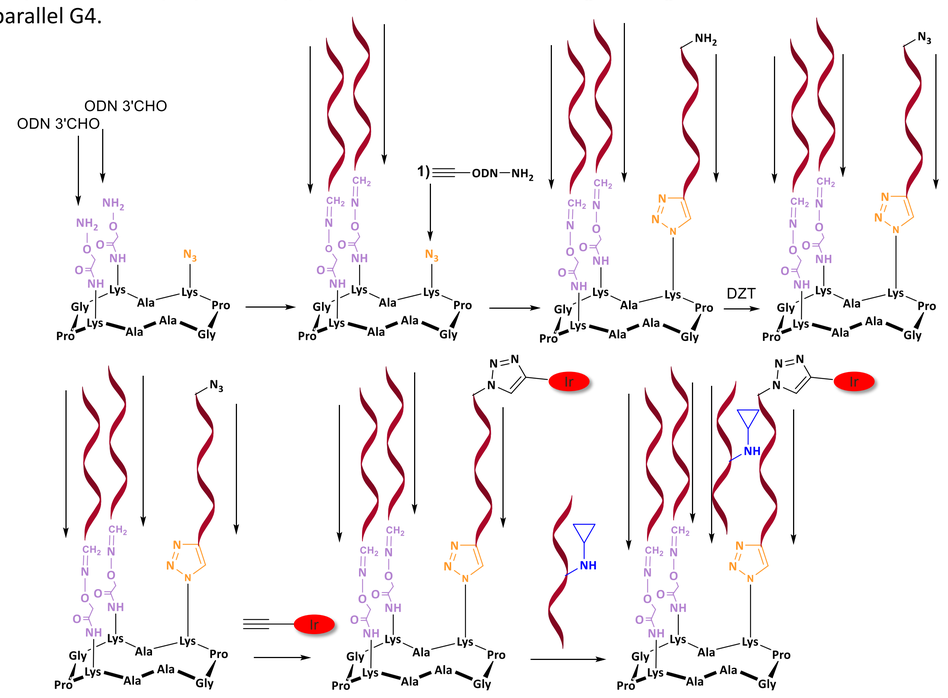
After irradiation, the duplex DNA undergoes an enzymatic digestion, finally an HPLC analysis permits to quantify the decomposition rate of the probe.



The observed results concurred with the observations in the literatture.[7] Now that we have validated our proof of concept, the next step is to study the charge transfer phenomenon in G4.

Future work

Firstly, we need to prepare the peptide template before adding the oligonucleotides in order to form a parallel G4.



Then we will start the charge transfer experiments in G4, using the G4 previously prepared.

References and acknowledgements

[1] P. Valenta and H. W. Nürnberg, Biophys. Struct. Mech., ***1974****, 1, 17–26. [2] J. C. Genereux and J. K. Barton, Chem. Rev.,* ***2010****, 110, 1642–1662. [3] F. Shao, B. Elias, W. Lu and J. K. Barton, Inorg. Chem.,* ***2007****, 46, 10187–10199. [4] Shao, F.; Barton, J. K. J. Am. Chem. Soc.* **2007**, *129* (47), 14733–14738. *[5] M. Gellert, M. N. Lipsett and D. R. Davies, Proc. Natl. Acad. Sci. U. S. A.,* ***1962****, 48, 2013–2018. [6] W. I. Sundquist and A. Klug, Nature,* ***1989****, 342, 825–829.* [7] *Tanaka, M.; Elias, B.; Barton, J. K. J. Org. Chem.* ***2010****, 75 (8), 2423–2428.*

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