

Spécialité de Master « Optique, Matière, Paris »

Stage de recherche (4 mois minimum, à partir de début mars)

Proposition de stage (ne pas dépasser 1 page)

Date de la proposition : 20/10/2016

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Time-resolved circular dichroism for probing ligand/G-quadruplex interactions

Many guanine-rich regions of the human genome can “*in vitro*” adopt specific four-stranded structures called G-quadruplexes (G4). These structures result from the stacking of a number guanine quartets stabilized by metallic cations such as Na⁺ or K⁺. After intense speculations about their biological pertinence, there is today an increasing amount of experimental evidences showing the “*in vivo*” formation of G4 and their role in various biological functions. Many past experimental studies of G4 have focused on the characterization of their structure, highlighting their high conformational diversity. In parallel, great efforts have been made to develop specific G4-binding ligands in the context of molecular recognition and the development of new cancer treatments. However, very few studies have addressed the dynamical aspects of G4 formation and their interaction with ligands. A detailed characterization of these mechanisms is crucial to gain a better understanding of the biological functions of G4 and possible therapeutic applications. The goal of the present project will therefore be to characterize the nature of the interactions of different ligands (small aromatic compounds) with biologically-relevant G4 structures and to assess their effects on the dynamics of G4 formation. The study of the ligand-DNA interactions will be performed using a combination of steady-state spectroscopic methods (absorption, circular dichroism and fluorescence) and femtosecond transient absorption and circular dichroism. The folding dynamics of G4 will be probed on the nano- to milli-second time range using T-jump measurements combined with circular dichroism detection.

[1] P. Changenet-Barret et al ; Ultrafast electron transfer in complexes of Doxorubicin with Human Telomeric G-quadruplexes and GC duplexes probed by femtosecond fluorescence spectroscopy, *ChemPhysChem* (2016) 17, pp1264-1272

[2] L. Mendonça et al.; Ultrafast carbonyl motion of the photoactive yellow protein chromophore probed by femtosecond circular dichroism, *J. Am. Chem. Soc.* (2013) 135, pp 14637-14643

[3] M.-T. Khuc et al. ; Measurement of circular dichroism dynamics in a nanosecond temperature-jump experiment, *Rev. Sci. Instrum.* (2011) 82, 054302

A good knowledge in photophysics and photochemistry as well as some notions in optics is recommended.

Keywords : DNA, G-quadruplexe, Circular dichroism, Transient absorption, Femtosecond

Ce stage pourra-t-il se prolonger en thèse ? Possibility of a PhD ? : OUI

Si oui, financement de thèse envisagé/ financial support for the PhD: bourse ministérielle

Lumière, Matière, Interactions	x	Lasers, Optique, Matière	x
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