MASTER THESIS PROJECT

Towards a brighter DNA

Background

As one of the "molecules of life" DNA has earned its positions as one of the most studied molecules. Despite this, there is still a lot to learn about DNA and how it interacts with other molecules. Understanding DNA is key to understanding many events in the cell, both how they work in the normal case as well as what errs when we get ill.

Fluorescence spectroscopy, with its high precision and possibility to study dynamic events is a tool perfectly suitable to study DNA, except DNA is non-fluorescent. To overcome this, external labels, both covalently linked and intercalated in the DNA, are often used. These, however, have the disadvantage of not reporting on unperturbed DNA. Moreover for some applications, such as FRET, it is important to know exactly where the probe is in relation to the DNA, which is usually not the case with these external probes. Therefore fluorescent base analogues (FBAs)[1] constitute a very important group of DNA-probes that have gained a lot of interest over the last decades. FBAs are molecules that mimic the base-pairing of the natural nucleobases but have additional structural elements making them fluorescent. These molecules are difficult to design since they need to have a structure close to that of the natural DNA bases to not perturb the DNA, but still obviously need to be different to become fluorescent.

Our group has previously synthesized and reported on the excellent cytosine analogue, tC^{o} which together with our tC_{nitro} constitute the first nucleobase FRET-pair[2] – opening up for new detailed studies. We have also reported on a series of triazole adenine analogs[3] and on a quadracyclic adenine analog qA[4].

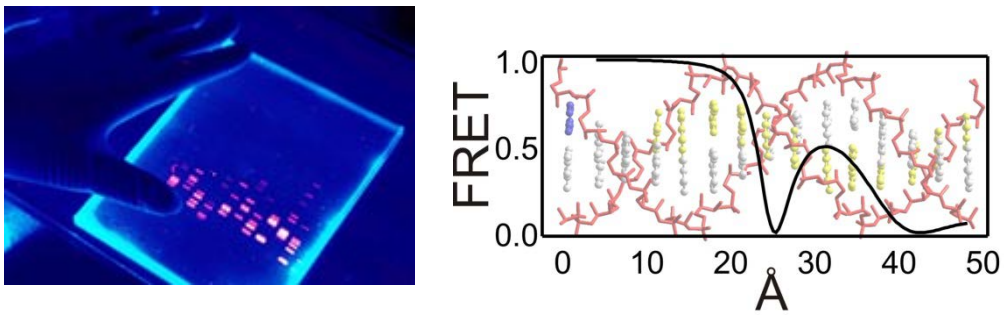

Figure 1. *To the left:* DNA, stained with a fluorescent probe, after gel electrophoresis. *To the right*: Efficiency of the energy transfer between fluorescent base analogue tC^{o} and tC_{nitro} as a function of separation between them in DNA.

Project:

The project is focused on the photophysical characterization of the new FBA candidate, bT, inside DNA. This bicyclic thymine analogue has recently been synthesized within our group and it shows promising properties as a monomer. The study will involve several different techniques as, for example, the stability, the base pairing specificity, the brightness and the fluorescent lifetime needs to be assessed.

Applicant

We are looking for a highly motivated student with interest both in physical chemistry and biology. You should have a bachelor degree in Chemical engineering, Biological engineering, Chemical engineering with physics or equivalent and be fluent in English. The project is most suitable for a 30 hp thesis.

Contacts:

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References: 1) Wilhelmsson, L.M., *Fluorescent nucleic acid base analogues*. Q. Rev. Biophys., 2010. 43: 159 **2)** Börjesson, K., et al., *Nucleic Acid Base Analog FRET-Pair Facilitating Detailed Structural Measurements in Nucleic Acid Containing Systems*. J. Am. Chem. Soc., 2009. 131: 4288 **3)** Dierckx, A., et al., *Characterization of photophysical and base-mimicking properties of a novel fluorescent adenine analogue in DNA*. Nucleic Acids Res., 2011. 39 (10), 4513-4524. **4)** Dierckx, A., et al., *Quadracyclic adenine: a non-perturbing fluorescent adenine analogue.* Chem. Eur. J. 2012, 18, 5987–97