Probing DNA radiation damage by DNA nanotechnology

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High-energy radiation is routinely used to treat cancer in combination with radiosensitizing therapeutics such as halogenated nucleosides. The treatment relies on an accurate modeling of DNA radiation damage, which is to a large extent ascribed to the indirect damage by low-energy electrons [1]. To accurately quantify DNA strand breakage induced by low-energy radiation we have developed an approach using AFM analysis of target DNA arranged on DNA origami platforms [2-5]. In this way we can effectively study the dependence of DNA strand breakage on the sequence and higher-order structure and assess the effect of radiosensitizers. The main advantages of the technique are (i) the analysis and comparison of multiple sequences at the same time, (ii) the analysis of more complex higher-order structures [6], and (iii) a rather simple determination of absolute cross sections for strand breakage at specific irradiation conditions.

We have applied the DNA origami technique to DNA strand breaks induced by low-energy electrons (0.5 - 18 eV) [2-4], and vacuum UV photons (5 – 9 eV) [7]. In this presentation the following aspects in electron-induced DNA strand breakage will be discussed: (i) The dependence on the DNA sequence and the electron energy, (iii) the effect of radiosensitizers such as halogenated Adenines incorporated into the DNA sequences, and (iii) the role of the secondary structure by comparing linear telomeric DNA with folded G quadruplex structures. Furthermore, the effect of gold nanoparticles on DNA damage will be demonstrated [8].
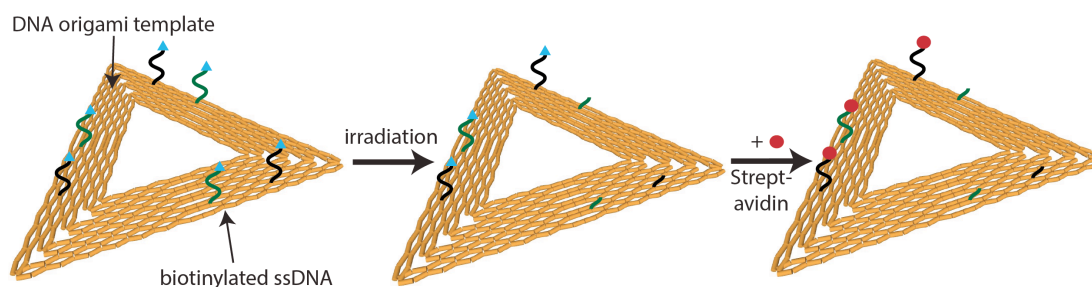
Fig. 1: Scheme of the procedure to quantify DNA strand breakage using triangular DNA origami substrates. The streptavidin labeled target sequences can be identified by AFM.

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