

Group : Nanochemical Biology
Project : **Protein Modification by Means of a Switchable DNA Devices**
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Keywords: artificial protein modification, DNA nanochemistry, thrombin, lysozyme, antibodies

In this project, we develop DNA-based nanodevices that can site-selectively modify bioactive proteins like thrombin and lysozyme. Using tyramine derivatives in combination with H_2O_2 and a peroxidase mimicking DNAzyme, we generate phenoxyl radicals that cross-react with tyrosine residues in proteins. (see Figure below). **The goal is to develop generally applicable tools for the site-selective modification of native proteins.**

Approach

The DNA device is anchored onto the target protein DNA aptamer. In the presence of an externally applied trigger (which is a piece of DNA), the bound protein is exposed to the modification catalyst that locally produces reactive tyrosine radicals. These will react with tyrosine residues in the protein. The dimensions of the DNA device dictate the location of the modification.

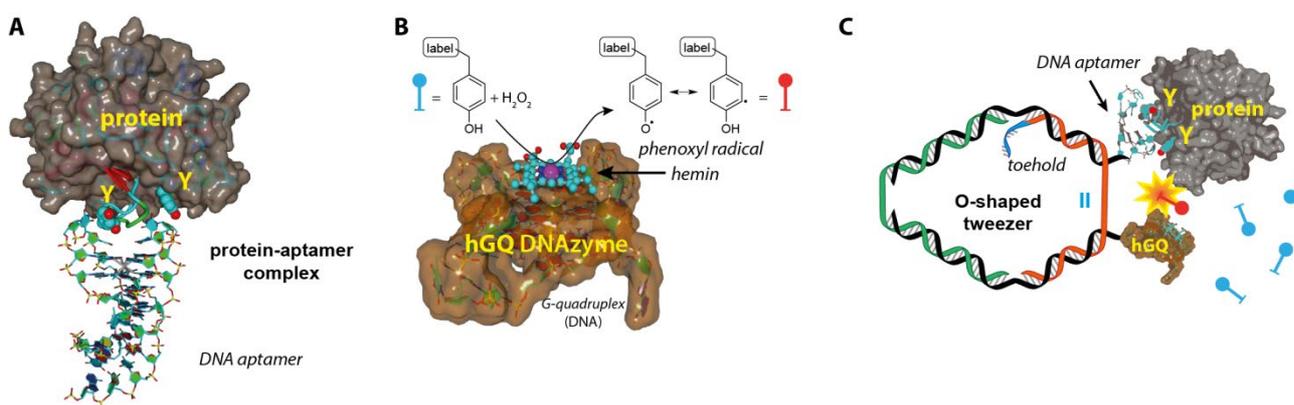


Figure shows how a protein-binding DNA aptamer (A) and a hGQ DNAzyme (B) can locally generate reactive labels in close proximity to the protein (C), resulting in site-selective labelling of the protein.

Topics to be studied (including techniques to be applied and BSc or MSc level)

With respect to the modification of the proteins we will:

- Study under what conditions the protein is labeled most efficiently (HPLC, SDS-PAGE) (BSc/MSc).
- Tailor the reactivity of the horseradish peroxidase (HRP) mimicking hemin/G-quadruplex (hGQ) DNAzyme catalyst that generates the active phenol-radical (UV-vis, fluorescence) (BSc/MSc).
- What DNA-device is needed to achieve site-selective modification of the protein (LC-MS/MS) (BSc/MSc).
- Design a switchable DNA-device that can occupy an ON and an OFF state with respect to the labeling efficiency (HPLC, SDS-PAGE) (MSc).
- Locate the site of modification by means of proteolytic digestion and LC-MS/MS techniques (MSc).
- Determine general applicability of the approach by labeling other native proteins (for example antibodies) (MSc).

Information

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