Reversible photoswitch-controlled structure transitions of biomolecules and their real-time visualization by high-speed atomic force microscopy

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Reversible control over DNA and lipid bilayers with light has the potential to allow in vivo regulation of key biological functions like gene expression and transmembrane transport, respectively, with high spatiotemporal precision through the manipulation of interactions with associated proteins.[1] Azobenzene photoswitches, capable of isomerizing between a planar *trans* and a nonplanar *cis* isomer through irradiation with light, have emerged as powerful tools for the non-covalent photocontrol of biomolecules.[2] The evaluation of photoswitch-controlled biomolecular events is, however, so far almost exclusively limited to ensemble techniques and static imaging.

In this study, we present high-speed atomic force microscopy-based visualization[3,4] of reversible dsDNA compaction/unfolding using a water-soluble azobenzene photoswitch (**AzoTAB**; Fig. 1a,b). Irradiation of the non-covalent dsDNA/*trans*-**AzoTAB** complex at 365 nm induces a transition from fully compacted to unfolded DNA on mica surface. This process can be completely reverted via short irradiation at 473 nm. Using the same photoswitch, we furthermore achieved time-resolved observation of the perturbation and relaxation of lipid bilayers (Fig. 1c). The observations provide clear evidence for short-lived membrane protrusions and indentations upon *trans*-to-*cis* isomerization. This insight is potentially useful for the photocontrolled nanomanipulation of membrane-bound proteins.

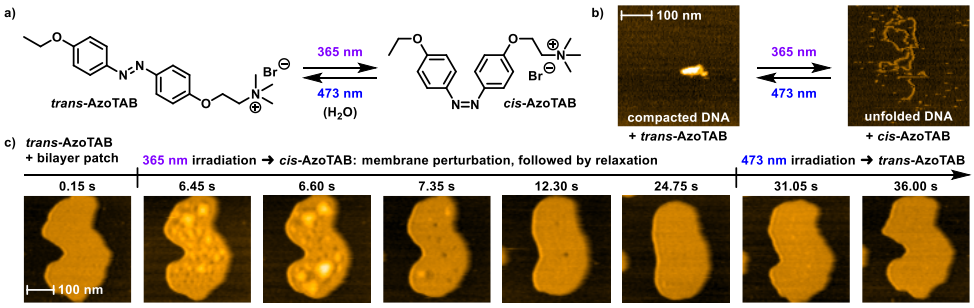

Figure 1. a) Structure of the photoswitch (**AzoTAB**). Photocontrol over b) dsDNA compaction/unfolding and c) lipid bilayers.

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