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10 Photosensitive polyamines for high-performance
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ABSTRACT

Polyamines are small, ubiquitous positively-charged molecules that play an essential role in numerous biological processes such as DNA packaging, gene regulation, neuron activity, and cell proliferation. Here, we synthesize the first series of photosensitive polyamines (PPAs) and demonstrate their ability to photoreversibly control nanoscale DNA higher-order structure with high efficiency. We show with fluorescence microscopy imaging that the efficiency of the PPAs as DNA compacting agents is directly correlated to their molecular charge. Micromolar concentrations of the most efficient molecule described here, a PPA containing three charges at neutral pH, compacts DNA molecules from a few kilobase pairs to a few hundred kilobase pairs, while subsequent 3 min UV illumination at 365 nm triggers complete DNA unfolding. Atomic force microscopy reveals that the compaction involves a global folding of the whole DNA molecules whereas UV-induced unfolding is an anisotropic modification initiated from the periphery of the compacted DNA.

INTRODUCTION

DNA can undergo a dramatic conformational transition from a wormlike coil to a much smaller globular state.^{1–3} This phenomenon, known as DNA compaction, is a key biological process involved in the packaging⁴ of genetic information as well as in gene regulation.^{5–7} The biomedical applications of compaction, such as transfection in gene therapy,^{8,9} have triggered strong interest as have recent developments in bio- and nanotechnologies.^{10–12} Compaction of DNA is usually achieved by the addition of compacting agents, that include multivalent organic or inorganic cations, proteins, cationic lipids and many other positively charged nano-objects.^{3,13,14} Naturally occurring polyamines, such as spermidine (3+) or spermine (4+), are omnipresent cellular compounds that can induce DNA compaction thanks to multiple protonated amine groups. They play an essential role in numerous biological processes, as they are involved not only in DNA packaging but also in cellular proliferation and neuron signaling.^{15–18} As a result, natural or synthetic polyamines are frequently used as compacting agents for fundamental studies on DNA compaction as well as for transfection applications.^{8,19–22} However, once DNA is compacted with polyamines, its decompaction requires changing the chemical composition of the sample, either through dilution of the solution, modification of the pH or addition of a decompacting agent, usually a lower valence salt.^{3,23,24} To achieve compaction or decompaction prompted by an external stimulus, a different strategy needs to be set up. Although temperature-induced DNA compaction strategies have been successfully implemented, significant achievements were usually obtained for temperatures far from a physiologically relevant range.²⁵ Light is another non-invasive external stimulus especially well-suited for dynamic monitoring of biological systems, due to its high spatial and temporal resolutions as well as satisfactory biocompatibility.²⁶ In the past few years, researchers have attempted to trigger DNA compaction

and decompaction with adequate illumination conditions by developing photoresponsive compacting agents with potential applications for the photocontrol of transfection,²⁷ gene expression^{28,29} and enzymatic activity.³⁰ For most of these molecules, the photosensitivity was due to an azobenzene moiety, able to undergo an isomerization upon appropriate illumination, and the compaction ability was brought about by a single cationic charge or, in very few cases, two charges.^{31–38} The molecules showed different binding affinities to DNA depending on illumination conditions but light-induced DNA decompaction proved to be challenging. In fact, light-gated, dynamic compaction/decompaction sequence was achieved in only a few cases where high amounts of compacting agents and long illumination times were required.^{31,35,38} To achieve efficient and photoreversible DNA compaction at much lower compacting agent concentration and reduced illumination time, we explored the use of polyamines, molecules known for their unique ability to reversibly compact DNA, that we made photosensitive through the incorporation of a photoisomerizable azobenzene motif. In this article, we describe the first series of photosensitive polyamines, demonstrating photoreversible and highly efficient compaction of giant and gene-sized DNA molecules, at concentrations 10- to 100-fold lower than usual photoresponsive compacting agents and much reduced illumination time. The effect of molecular charge and the impact of the illumination conditions on DNA compaction and unfolding processes are studied by fluorescence microscopy and atomic force microscopy.

RESULTS AND DISCUSSION

Photosensitive polyamines. We synthesized three photosensitive polyamines (PPAs), combining an azobenzene unit with side chains containing an increasing number of amine groups (Fig. 1). A short -OCH₂CH₂- chain was used as a linker. To obtain a molecule with 2 amine

groups, we attached ethylenediamine (En) to the azobenzene unit and thus synthesized the shortest PPA studied here, **AzoEn**. Using diethylenetriamine (Deta) increased the number of amine groups to 3 giving rise to an intermediate molecule, **AzoDeta**. Finally tris(2-aminoethyl)amine (Tren) allowed the synthesis of a final PPA with 4 amine groups, **AzoTren**.

Figure 1. Structures of photosensitive polyamines. The azobenzene moiety found in all compounds undergoes a *trans-cis* isomerization under UV illumination (365 nm) and thermally relax back in the dark. The head group is an ethylenediamine entity for **AzoEn**, a diethylenetriamine for **AzoDeta** and tris(2-aminoethyl)amine for **AzoTren**.

Information on the synthesis and standard characterizations of these compounds are given in S.I., Materials and Methods. The amine pK_a values (S.I., Fig. S1) were determined by structure-based calculations with MarvinSketch. From these values, we derived the first important feature of the three molecules, i.e., their charge. In particular, the pH dependency of the charge was calculated for each molecule with the equations given in S.I., Materials and Methods. Figure 2a shows the evolution of the charge as a function of biologically relevant pH values for the three PPAs. All experiments were performed in a buffer at pH = 7.4, fixing the charge of **AzoEn** to 1.2, of **AzoDeta** to 1.9 and of **AzoTren** to 3.0. By changing the number of amine groups in each of the synthesized molecules, we were therefore able to obtain various positively charged polyamines, with overall charges ranging from 1.2 to 3. A second important feature of the polyamines studied here was their photosensitive nature, achieved through the incorporation of an azobenzene motif, for which isomerization from a less polar *trans* state to a more polar *cis* state can be triggered by illumination at the right wavelength.³⁹ Here, the switch from a *trans*-rich state to a photostationary state where the *cis* isomer is predominant was achieved by UV light (365 nm). The distinct UV-Vis spectra of the two isomers enabled a spectrophotometric study of the kinetics of the isomerization process, as seen for example in Fig. 2b for **AzoTren**. The *trans* isomer of all three polyamines displayed a characteristic peak at $\lambda = 365$ nm while the *cis* isomers were characterized by a 2-peak spectrum (320 nm and 430 nm). *Trans*-rich solutions were irradiated for short 5 s periods at 365 nm to give the *cis*-rich solutions, leading to similar results for all three polyamines (S.I., Material and Methods and Figs. S2-S3). For each molecule, the decrease of the optical density at 365 nm was plotted as a function of time, and the resulting curve was fitted with an exponential decay to determine the characteristic time constants (inset Fig. 2b and S.I., Figs. S2-S3).

Figure 2. Properties of photosensitive polyamines. *a)* Calculated charge as a function of pH, for **AzoEn** (orange), **AzoDeta** (green) and **AzoTren** (blue). Arrows indicate the charge of each molecule for the working pH of 7.4. *b)* Absorption spectra of **AzoTren** (0.1 mM in water) in the dark (blue) and after various illumination times (t_{UV}). The arrow indicates increasing t_{UV} by increments of 5 s. The inset shows the optical density at 365 nm (OD_{365}) as a function of t_{UV} where symbols are data points and the solid line is an exponential decay fit with a time constant of 12 s.

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6 The *trans* to *cis* isomerization process was fast, as the three time constants were of the same
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8 order of magnitude of 10 s (12 s for **AzoEn**, 10 s for **AzoDeta** and 12 s for **AzoTren**). The
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10 thermal relaxation of the *cis* isomer to its *trans* counterpart was found to have much longer
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12 timescales, typically of a hundred minutes (S.I., Material and Methods and Figs. S4-S6),
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14 showing that all *cis* isomers displayed high thermal stability. As a result, we have synthesized
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16 three PPAs with two main characteristics: i) an overall charge from 1.2 to 3 at pH = 7.4
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18 depending on the number of protonated amine groups, and ii) a photo-tunable polarity through
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20 azobenzene *trans-cis* isomerization.
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27 **Compaction of genomic DNA by photosensitive polyamines.** The compaction efficiency of the
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29 synthesized PPAs was determined with long, double-stranded T4 DNA molecules (166 kbp)
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31 using fluorescence microscopy imaging. Figure 3a shows representative images of individual
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33 DNA molecules in the presence of the *trans* (-UV) and *cis* (+UV) isomers of the three PPAs at
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35 different concentrations. In these experiments, YOYO-stained T4 DNA molecules were added to
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37 a buffered solution containing a given PPA isomer. Two main types of DNA conformations were
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39 observed in solution. In the absence of compacting agents (Fig. 3a, first column), DNA
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41 molecules appeared as long fluctuating chains, and were referred to as unfolded DNA. The
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43 stretched conformation of DNA was attributed to the electrostatic repulsions caused by the high
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45 negative linear charge density along the phosphate backbone of dsDNA. Note that the elongated
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47 conformation of individual DNA molecules was also observed for low polyamine concentrations.
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49 However, as the polyamine concentrations increased, we observed a transition to a compact state
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51 where DNA molecules appeared as extremely mobile spots with a marked reduction of size. At
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even higher concentrations of polyamine, DNA molecules could no longer be observed in solution, most likely due to a displacement of the YOYO-1 dye by the compaction process.⁴⁰

Figure 3. Polyamines compact giant, genomic DNA in a light-sensitive manner, with marked charge-dependent efficiency. a) Representative fluorescence microscopy images of individual T4 DNA molecules (166 kbp) stained by YOYO-1 for increasing concentrations of photosensitive polyamines before (-UV) and after (+UV) illumination. **b)** Percentage of DNA molecules in the compact state as a function of concentration for the three photosensitive polyamines, before (filled symbols) and after (open symbols) illumination. Symbols are data points and solid (resp. dashed) lines are guidelines for the eyes for -UV (resp. +UV) conditions. [T4 DNA] = 0.1 μM in

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6 10 mM Tris-HCl ($pH = 7.4$); YOYO-1 = 0.01 μM ; -UV: dark; +UV: 365 nm for 10 min prior to
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11 The transition from the unfolded to the compact state was observed for all polyamines but was
12 strongly dependent on polyamine charge and illumination conditions (Fig. 3a). On the one hand,
13 comparing isomers of the same polyamine shows that the concentration required to achieve the
14 compaction of DNA molecules was consistently lower in the case of the *trans* isomer than of the
15 *cis* isomer. Certain concentration ranges therefore compacted DNA in the case of the *trans*
16 isomer, but not for its *cis* counterpart. On the other hand, for a fixed configuration of the
17 azobenzene motif (considering either the *trans* series or the *cis* series), another trend can also be
18 observed, as the concentration needed to achieve DNA compaction strongly decreased as the
19 number of amine groups in the molecule, i.e., the charge of the molecule, increased. For a
20 quantitative analysis of the compaction of genomic DNA molecules by the three polyamines, we
21 established compaction curves giving the percentage of DNA molecules in a compact state as a
22 function of polyamine concentration by analyzing for each set of conditions the conformation of
23 over 150 individual T4 DNA molecules in solution by fluorescence microscopy (Fig. 3b).
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25 Compaction curves show that for intermediate concentrations, compact and elongated DNA
26 molecules coexisted in solution. For dark conditions (-UV), this was for instance the case for
27 concentrations ranging from 40 to 100 μM for *trans*-AzoEn, from 10 to 30 μM for *trans*-
28 AzoDeta and finally from 2 to 5 μM for *trans*-AzoTren. Moreover, considering pairs of isomers
29 (-UV, +UV) for a given polyamine, the curves corresponding to +UV conditions were always
30 shifted to higher concentrations compared to the -UV curves. Table 1 specifies the polyamine
31 concentration required to compact 50% of the DNA molecules (C_{50}), showing a two-fold
32 increase in the concentration required by the *cis* isomer compared to that needed with the *trans*
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isomer. The compaction efficiency of the *trans* isomer was therefore systematically higher than that of the *cis* isomer, in agreement with a higher affinity of the less polar *trans* isomer for DNA molecules. A similar trend was described in the case of monocationic photosensitive surfactants³⁵ but has never been reported for polyamine-based molecules and can be explained as follows. The compaction of DNA by amphiphilic cationic molecules is known to be highly cooperative.⁴¹ As a consequence, for a given polyamine, the less polar *trans* isomer, which is more prone to assembly, is more efficient to cooperatively bind to DNA and induce DNA compaction than the more polar *cis* isomer. Interestingly, the compaction properties were not solely dependent on the isomerization state of the polyamines. Comparing the polyamines for set illumination conditions, we see that their compaction curves were ordered according to the polyamine charge, with *trans*-**AzoTren** as the most efficient compacting agent reaching 100% compaction at 5 μ M. C_{50} values were useful to compare and contrast the compacting efficiencies of the three PPAs according to their charge (Table 1).

	C_{50} (μ M)		Z_{50}^*	
	-UV	+UV	-UV	+UV
AzoEn (1.2+)	75	160	900	1920
AzoDeta (1.9+)	20	40	380	760
AzoTren (3.0+)	3	6	90	180

Table 1. Polyamine concentration (C_{50}) and charge ratio (Z_{50}^*) required to achieve the compaction of 50% of DNA molecules present in solution, under experimental conditions of Fig.3.

While increasing the charge from 1.2 to 1.9 from **AzoEn** to **AzoDeta** decreased the concentration required to achieve 50% compaction by a factor 3.8, increasing the charge to 3 when switching from **AzoDeta** to **AzoTren** led to a further decrease of the C_{50} by a factor 6.7. The C_{50} ratio of 6.7 between **AzoDeta** (1.9+) and **AzoTren** (3+) was of the same order of magnitude as values reported for non-photosensitive polyamines, in particular for 1,3-diaminopropane (2+) and spermidine (3+),²² displaying a concentration ratio for the onset of compaction of about 5. Note that in all cases, for both standard and photosensitive polyamines, the concentrations needed to induce 50% compaction of DNA molecules were higher than the concentration of DNA (0.1 μ M in phosphate bases), corresponding to an accumulation of an excess of positive charges in solution before DNA compaction could occur. We therefore computed the charge ratio at 50% of DNA compaction (Z_{50}^*) defined by:

$$Z_{50}^* = \frac{Z \cdot C_{50}}{[\text{DNA}]}$$

where Z stands for the charge of the polyamine, C_{50} its concentration for 50% of compaction and $[\text{DNA}]$ the concentration of DNA in phosphate groups. Hence, Z_{50}^* represents the ratio of charges brought by the polyamine ($Z \cdot C_{50}$) and the charges of DNA, which has a single negative charge per phosphate group. Therefore, for a given DNA concentration, a high value of Z_{50}^* means a high charge concentration is necessary to achieve compaction. When comparing the charge ratio required to compact 50% of the DNA molecules, we noticed that Z_{50}^* decreased by a factor about 2.5 from **AzoEn** to **AzoDeta** and 4 from **AzoDeta** to **AzoTren** (Table 1). As a result the excess of positive charges necessary to trigger DNA compaction in the case of **AzoTren** is 10 times lower than the excess seen in the case of **AzoEn**. This shows that the increase in efficiency with the number of positive charges is not solely the result of charge concentration, as the required excess charge should then be the same for all compacting agents, but also of inherent polyamine properties

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6 due to the presence of several positive charges within the same molecule. This effect is well-known
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8 for non-photosensitive polyamines and can be rationalized for our photosensitive polyamines by
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10 taking into account the crucial role of DNA counter-ions. The role of the valence of non-
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12 photosensitive polyamines on DNA compaction was analyzed with particular care by Bloomfield¹
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14 who emphasized the role of counter-ions in DNA compaction within the framework of the so-
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16 called Manning-Oosawa counter-ion condensation theory.^{42,43} Despite being a simplified model,
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18 based on a single chain at infinite dilution, this theory gives sound, first-order approximations of
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20 the phenomena that have been confirmed by experimental studies. The Manning-Oosawa counter-
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22 ion condensation theory looks at a DNA molecule as an isolated polyanion with an average
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24 distance b between DNA phosphate charges (0.17 nm) and studies the fraction θ of the DNA
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26 phosphate charges neutralized by the localization of DNA counter-ions in the vicinity of the DNA
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28 backbone. The neutralization parameter θ is especially relevant in the study of DNA compaction,
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30 as it has been experimentally determined that DNA undergoes a coil-globule transition when θ
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32 reaches a value around 0.89 to 0.90.^{21,44} Interestingly, the Manning-Oosawa theory establishes that
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34 the valence Z of the counter-ions plays an important part in setting the value of θ , as $\theta = 1 -$
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36 $b/(Z \cdot l_B)$ where l_B is the Bjerrum length (0.71 nm in pure water at 25 °C) comparing magnitudes of
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38 electrostatic interactions to thermal energy. This shows that θ increases with an increase in the
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40 valence of DNA counter-ions, and underlines the fact that higher valence counter-ions have a
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42 higher compaction efficiency. This corresponds to our experimental observations, as before
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44 addition of photosensitive polyamine, DNA counter-ions are monovalent and upon addition of
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46 compacting agent, there is an ion exchange that results in DNA counter-ions having a higher
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48 valence.¹ As the charge of the polyamine increases, the neutralization of DNA is also enhanced,
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50 giving an insight into why **AzoTren** is a better compacting agent than **AzoDeta** and **AzoEn**. All
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in all, we have shown that the newly described PPAs were able to compact genomic DNA with efficiencies that can be modulated by both their charge and external illumination conditions.

Compaction and decompaction of a linearized plasmid by AzoTren. At micromolar concentrations, **AzoTren** proved to be an efficient compacting agent of genomic DNA. To test the interaction between this PPA and a much shorter, gene-sized DNA molecule, we explored the compaction of a 4.5 kbp linearized plasmid by **AzoTren**. Since fluorescence microscopy was not suitable for the observation of such small DNA molecules, the study was carried out using atomic force microscopy (AFM) (Fig. 4 and S.I., Figs. S7A-H). We first studied the impact of a gradual increase in the concentration of **AzoTren** (Fig. 4A-E). In the absence of compacting agent, the linearized plasmid appear as long, rather stretched out coils with large end-to-end distances (Fig. 4A). The vertical scale indicated typical heights of 0.30 ± 0.04 nm, in agreement with previous measurements on double-stranded DNA adsorbed on mica.^{45,46} We measured a contour length of 1440 ± 44 nm, a value close to the length of a fully stretched 4.5 kbp DNA (1530 nm). Upon addition of $0.5 \mu\text{M}$ **AzoTren** (Fig. 4B), the behavior of DNA molecules changed significantly. The previously long coils started to bend and twist, resulting in shorter end-to-end distances. As the **AzoTren** concentration was further increased to $2 \mu\text{M}$ (Fig. 4C), the morphology of the DNA objects observed by AFM continued to change, with the appearance of dense spots inside each structure. This evolution was even clearer for $[\text{AzoTren}] = 4 \mu\text{M}$ as more than half of the DNA molecules were folded, forming compact DNA objects of an average height of 3.5 ± 0.7 nm. (Fig. 4D). Finally, for $[\text{AzoTren}] = 5 \mu\text{M}$, all DNA molecules were observed as compact objects of an average height of 4.3 ± 1.3 nm, occupying only a fraction of the surface they covered in the absence of compacting agent (Fig. 4E).

Figure 4. AFM shows the compaction process of a gene-sized linear DNA (4.5 kbp) by *AzoTren* and its subsequent unfolding by UV. For images A) to E) the concentration of polyamine increased (respectively 0, 0.5, 2, 4 and 5 mM). For images E) to H), DNA was first compacted by *AzoTren* (5 mM) prior to an increasing exposure to UV at 365 nm (respectively 0, 30, 60 and 180 s). [DNA] = 2 μ M in 10 mM Tris-HCl (pH = 7.4).

This morphology was attributed to a fully compact state of DNA. From the various lateral sizes of these compact objects, we inferred that unimolecular compact states probably coexisted with multimolecular aggregates. The behavior of the linearized plasmids undergoing compaction in the presence of *trans-AzoTren* was therefore determined to be similar to that observed by

fluorescence microscopy for genomic DNA molecules. We then investigated the effect of UV light on compact DNA (Figs. 4E-H). We shone UV light (365 nm) for a fixed time (30, 60 and 180 s) on a sample containing fully compacted DNA molecules by 5 μ M **AzoTren** and then imaged the sample (Figs. 4F-H). The general trend observed was a marked unfolding as the sample was illuminated by UV. Notably, the unfolding steps were distinct from the previously studied compaction process. Indeed, under UV illumination, the unfolding of the short DNA molecules occurred from the periphery, around a small compact core, of the same average height than the compacted DNA observed in Fig. 4E, resulting in flower-like structure of the DNA molecules (Figs. 4F-G). Full decompaction, with elongated molecules of 0.29 ± 0.05 nm height, was achieved after only 3 min illumination by UV. To have a quantitative description of the compaction/unfolding process, we systematically measured the long-axis length of DNA molecules, defined as the longest distance measured on an adsorbed DNA molecule, and plotted the size distribution (Fig. 5). A wide distribution centered on 520 ± 141 nm was obtained in the absence of compacting agent. As the **AzoTren** concentration increased, the long-axis length distributions became much sharper and centered on decreasing values. Full compaction corresponded to an average length of 93 ± 29 nm. Increasing the UV illumination time resulted in the opposite trends, with a sharp distribution getting progressively wider and an increasing average long-axis length. The unfolding of the DNA molecule under UV illumination can be rationalized by considering the isomerization of the *trans*-**AzoTren** to the *cis* isomer induced by UV light (365 nm) described in Fig.2b. As **AzoTren** molecules isomerize due to UV illumination, the concentration of *trans* compacting agent decreases and that of the *cis* isomer increases. Because of the lower affinity of *cis*-**AzoTren** for DNA compared to its *trans* counterpart, the DNA molecules undergo an unfolding process.

Figure 5. Photoreversibility of AzoTren-based DNA compaction. Distribution of the long-axis length of DNA measured by AFM for an increasing **AzoTren** concentration (0 - 5 μM) in the dark, and for an increasing UV illumination time at 365 nm (30 - 180 s) applied on DNA compacted by 5 μM **AzoTren**. The red color intensity indicates the percentage for each size class. $[\text{DNA}] = 2 \mu\text{M}$ in 10 mM Tris-HCl (pH = 7.4).

The systematic analysis of AFM images reinforced the trends seen with a simple qualitative reasoning, clearly establishing the compaction of gene-sized DNA by **AzoTren** for concentrations similar to those observed in the case of genomic DNA, as well as the light-mediated decompaction of DNA, i.e. the reversibility of the compaction by an **AzoTren** compacting agent.

CONCLUSION

The series of photosensitive polyamines (PPAs) described in this paper follow the general trends expected from polyamines. They have high compaction efficiencies that increase with the overall

charge of the molecule, displaying a charge effect that was stronger than a simple neutralization effect. The azobenzene unit of the molecules not only allows the shortest polyamine, **AzoEn**, to act as a compacting agent despite its small positive charge (1.2+), but also gives all three polyamines photosensitive properties. The *trans-cis* isomerization can be seen as a UV-triggered switch for interactions with DNA, due to the higher binding affinity of the *trans* isomer compared to the *cis* isomer, leading to a photoreversibility of the compaction-decompaction process. Although the wide range of experimental conditions makes rigorous comparison with other similar azobenzene-based compacting agents difficult, it is nonetheless possible to establish some major trends in order to compare and contrast the performance of the PPAs seen in this paper with other published photosensitive compacting agents. In general, in the case of compacting agents with a strong affinity for DNA,^{34,35,38} photoreversibility could not be achieved. In fact, for most of these molecules, high DNA affinity was obtained by increasing the hydrophobicity of the compacting agents. It is possible that, in such cases, too strong hydrophobic interactions stabilize the compact state, therefore preventing DNA unfolding by light. In contrast, we exploited here an increase in electrostatic interactions provided by high-valence polyamines resulting in both high affinity and a photoreversible behaviour. In the past, photoreversible compaction was mainly obtained with AzoTAB, a monovalent cationic compound inducing DNA compaction in near millimolar range.^{28,31–33,35} Here, **AzoTren** can induce compaction in the micromolar range, at concentrations about 100-fold smaller than AzoTAB under similar conditions (S.I., Fig. S8). Furthermore, the 3 min illumination time required for a full decompaction was short, as previously reported timescales were typically about 20 min long. The synthesized PPA with 3 positive charges can therefore be described as a high-performance, light-responsive DNA compacting agent. Since DNA compaction/unfolding is a decisive step in fundamental biological processes (e.g., DNA packaging

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and gene regulation) as well as in transfection applications, the developed PPAs constitute a class of promising agents to bring these operations under the control of a light trigger. In this article, we focused on synthetic polyamine moieties but our strategy is also readily applicable to natural polyamines such as spermidine (3+) or spermine (4+). Moreover, as the importance of polyamines in biological processes and diseases is not restricted to DNA packaging and transcription/translation regulation, the range of applications for PPAs can most likely be widen far beyond the demonstrated scope of DNA compaction. For instance, due to the critical role of polyamines in the regulation of ion-channels,^{15,18,47} their photosensitive counterparts could be used for the photoregulation of neuron activity.^{48,49} For their part in cell proliferation, polyamines are now studied in cancer development and therapy,¹⁷ giving their photosensitive derivatives a promising future in novel phototherapeutic strategies.

ASSOCIATED CONTENT

Supporting Information. Experimental Section, Figures S1-S8. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Graphical Table of Contents :

FIGURE 1

R =	Name
 NH ₂ · HCl	AzoEn
 NH ₂ · 2 HCl	AzoDeta
 NH ₂ · 3 HCl	AzoTren

Figure 1
112x146mm (300 x 300 DPI)

FIGURE 2

Figure 2
186x328mm (300 x 300 DPI)

FIGURE 3

Figure 3
187x303mm (300 x 300 DPI)

FIGURE 4

Figure 4
159x149mm (300 x 300 DPI)

FIGURE 5

Figure 5
129x112mm (300 x 300 DPI)