Visible Light-Activated Self-Assembly of Double-Stranded DNA

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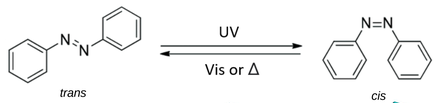
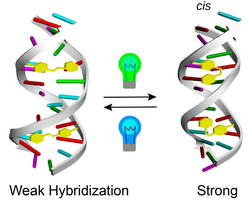
Background

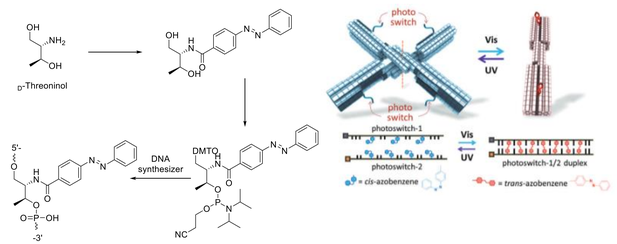
- Azobenzene shows isomerization between the *cis* and *trans* isomers through light irradiation of different wavelengths



- Through this discovery, azobenzene molecules can be incorporated into double-stranded DNA (dsDNA) to control its hybridization and dehybridization



- This research can be applied to DNA nanotechnology such as optical-controlled self-assembly of DNA origami



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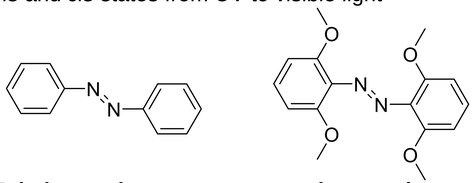
However, UV light has a damaging effect on biological systems such as DNA and human tissue

Purpose

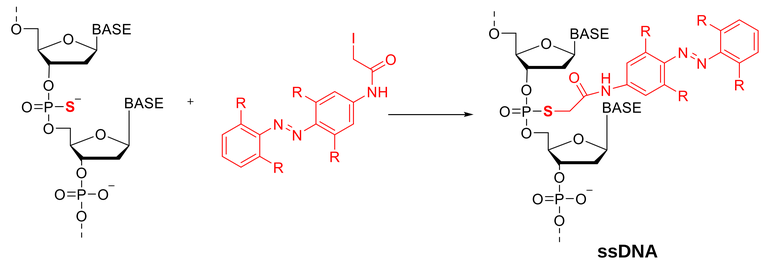
- Recent studies have shown that the *ortho*-functionalization of azobenzene can redshift the isomerization between the *trans* and *cis* states from UV to visible light



Pristine azobenzene **o-methoxyazobenzene**

Goal: Control the hybridization and dehybridization of dsDNA using light by incorporating visible light-activated photo-switches

Methods



2 photo-switches attached

5′-TGCT*CACT*AATG-3′
3′-ACGA GTGA TTAC-5′

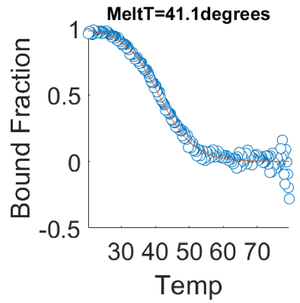
3 photo-switches attached

5′-TGC*TCA*CTA*ATG-3′
3′-ACG AGT GAT TAC-5′

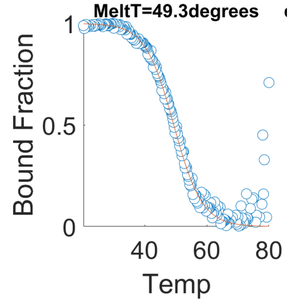
Highlighted Results

Azobenzene Incorporated dsDNA Melting Curve

Trans



Cis



Melting T of DNA duplex	Pristine azobenzene attached		OMe azobenzene attached		No azobenzene attached
	trans	*cis* (340 nm used to isomerize)	*trans*	*cis* (530 nm used to isomerize)	
2 modification sites (°C)	42.7	45.8 ΔT_m=3.1 °C	42.5	45.6 ΔT_m=3.1 °C	47.7
3 modification sites (°C)	41.1	49.3 ΔT_m=8.2 °C	underway	underway	47.7

- The stability of DNA duplex incorporated by the photo-switches can be tuned by light irradiation
- With more photo-switches incorporated into the dsDNA, a much greater stability difference between *trans* and *cis* can be achieved

Conclusion

- Developed a new chemical functionalization method for photo-switchable DNA
- Achieved an entirely visible-light-driven DNA assembly control
- Varied % photoswitch incorporation on DNA strands
- Obtained >8 °C melting point change by irradiation
- No photo-damage to DNA

Future Direction

- A future direction includes incorporating 5 **photo-switches** into the DNA oligos and maximize the stability difference between *trans* and *cis* states

5′-TG*CT*CA*CT*AA*TG-3′
3′-AC GA GT GA TT AC-5′

References

1. Asanuma H.; Liang, X.; Nishioka, H.; Matsunaga, D.; Liu, M.; Komiyama, M. *Nat. Protoc.* **2007**, *2*, 203-212.

2. Shi, Y.; Gerkman, M.A.;Qiu, Q.; Zhang, S.; Han, G.G.D. *J. Mater. Chem.* **2021**, *9*, 9798-9808.

3. Patnaik, S.; Kumar, P.; Garg, B.S.; Gandhi, R.P.; Gupta, K.C. *Bioorg. Med. Chem.* **2007**, *15*, 7840-7849.

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