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DISCRETE PHOTOSWITCHABLE NUCLEIC-ACID NANOAGGREGATES FOR REMOTE SENSING

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"Discrete Photoswitchable Nucleic-Acid Nanoaggregates for Remote Sensing"

Final Technical Report for 9/15/2010 - 9/14/2013
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Abstract

The goal of this project was to study the properties of clusters of metal nanoparticles assembled with photoswitchable synthetic oligonucleotides. Major accomplishments of the program include: (1) synthesis of photoswitchable gold nanoparticle/DNA conjugates containing azobenzene-modified oligonucleotides and their reversible assembly into both extended (100-1000+ particles) and discrete (2-20 particles) nanoaggregates; (2) the demonstration that the assembly of these nanoaggregates can be controlled by remote optical illumination and that this behavior enables an all-optical "photostringency" wash that has the ability to discriminate single-base mismatches in DNA hybridization assays without the need for a temperature, salt, or pH gradient; (3) the discovery that the quantum yield for azobenzene photoswitching depends on the local sequence including type and position of single-base mismatches; and, (4) measurement of the force-induced melting of photoswitch modified oligonucleotides using dynamic force spectroscopy, showing that the photo-induced melting behavior is consistent with local (~few bases) disruption of the dsDNA. These results will help underpin the design of optical sensing schemes for biological and chemical sensors based on control of DNA hybridization and structure.

Project Objectives

The original objectives of the project are described below. The periods over which the objectives were pursued are listed in parenthesis.

1) Produce photoswitchable oligonucleotide nanoparticles to assemble discrete nanoparticle cluster aggregates. Assemble the resulting particles into photoswitchable nanoaggregates. (9/2010-9/2013)

2) Characterize the fundamental biophysical properties of the aggregates by conducting meaurements such as AFM pulling (Dynamic Force Spectroscopy, DFS) both in the dark and under phototriggered conformational changes. (9/2010-9/2013)

3) Characterize the assembled structures and measure the rates and intensity dependence of photoswitchabel DNA-melting using plasmon-ruler methods, and use the results to demonstrate the feasibility of using photomodulatable DNA aggregates as reporter agents in remote sensing. (9/2010-9/2012)

Findings:

Year 1 (9/2010-9/2011):

Objective 1: The production of robust, photoswitchable oligonucleotide-functionalized gold nanoparticle conjugates was spectacularly successful. The project successfully prepared multiple-mL quantities of gold nanoparticles in a range of sizes (15-90 nm diameter) conjugated with a high-density of azobenzene-modified oligonucleotides. The project showed that shining UV light on the samples causes a trans-cis photoisomerization of the azobenzene, which leads to a drop in the DNA melting temperature and subsequent photo-induced DNA melting or "photomelting" of DNA-linked nanoparticle aggregates. The project showed that in bulk solution, the photomelting process can be quantified by UV-Vis spectroscopy, and cycled repeatedly many times (Fig. 1).[1]

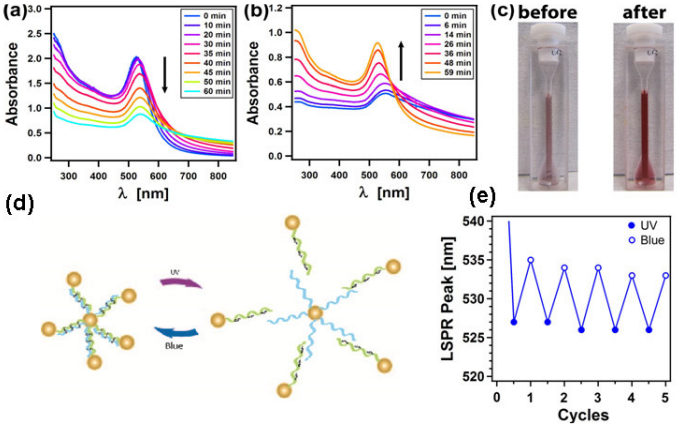

Fig. 1. Photoswitching of azobenzene-modified-DNA-functionalized gold nanoparticles. (A) UV-Vis vs. time upon initial addition of complement. (B) UV-Vis vs. time following illumination with UV LED.
(C) Photos of the solution before and after photomelting. (D) Photomelting schematic. (E) UV-Vis peak of the nanoparticles in solution after exposure to illumination from UV and Blue LEDs for showing robust cycling

Furthermore, the project demonstrated that the photon dose required for photomelting is very sensitive to single-base mismatches. This sensitivity means that it is possible to discriminate a perfectly matched target from a target with a single-base mismatch on the basis of the *optical response* only. In other words, the photoswitching process can be used to replace conventional temperature- and buffer-based stringency washes and complementary and mismatch strands can be distinguished isothermally using only illumination from an LED (Fig. 2). In year 1 the project filed a Record of Invention (ROI) with the University for this method, (in subsequent years this led to provision and full patent filings).

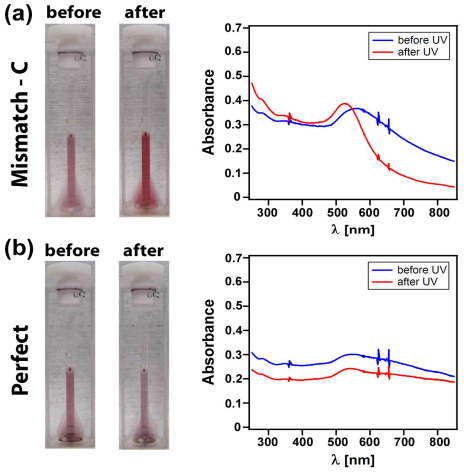

Fig. 2 "Photostringency" discriminates a single-base mismatch. (A) Shining a UV LED onto aggregates formed with a mismatched strand results in photomelting and deeper red color of the solution, whereas shining UV on the perfect complement has no effect (B) on the spectra.

Objective (2) during year 1 was to begin studies of the biomechanical properties of

photoswitchable DNA oligomers during hybridization and melting by single molecule force measurements with Atomic Force Miroscope. This proved to be the most

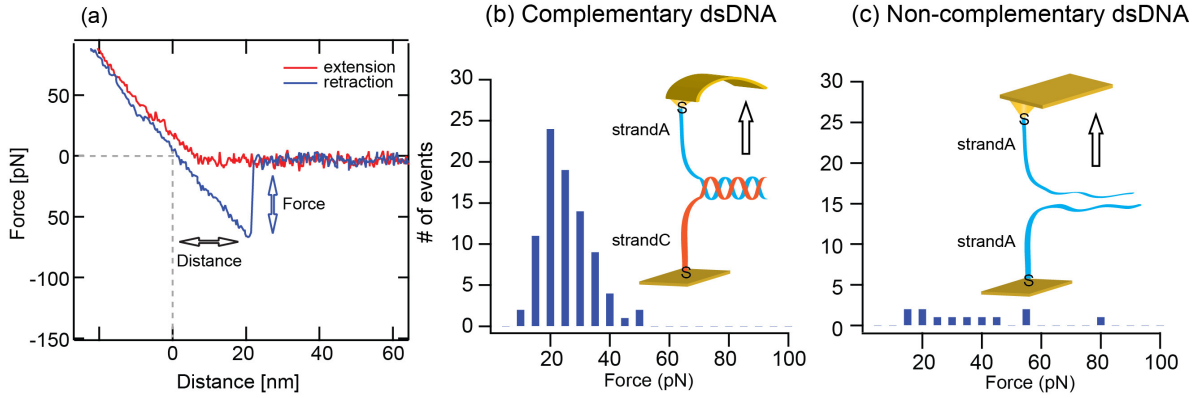

Figure 3:
(a) a typical force-distance curve from a melting event of complementary sequences. Histogram of forces recorded at 500 nm/sec with complementary pairs of DNA (b) and non-complementary pairs of DNA (c) modified between the AFM tip and the Au film surface.

challenging aspect of the project, and was only completed at the end of year 3. Year 1 was spent validating our experimental protocols and measuring multiple force vs. distance (F-D) curves as the DNA functionalized AFM tips are brought into and out of contact with a DNA-functinalized gold surface using only ordinary oligonucleotides. When the tip is brought close to the surface, DNA duplexes will form between the AFM tip-bound DNA and the surface-bound DNA. When the distance between the surface increases as the tip is pulled upward, the formed duplexes will dehybridize. Fig. 3 shows a typical force vs. distance (F-D) curve obtained from a single approach and retrace event. Each curve was analyzed and the force and the distance (piezo displacement) values were recorded. As a control experiment, F-D curves of melting events were measured between AFM tips and the surface modified with complementary and non-complementary DNA (Figure 3 b-c scheme). Figure 1 b-c show histograms of melting forces recorded for complementary and noncomplementary 15-mer duplex sequences. The results seem to be different between the two samples with complementary duplex melting events resulting in larger melting more frequently. These results are in qualitative agreement with previous DNA F-D curve measurements, and confirm we have successfully established the experimental protocols necessary to perform these measurements.

Objective 3 during year one was to study the kinetics and thermodynamics of melting using plasmon ruler methods and was largely completed in year 1 with the main conclusions analyzed and published in year 2. Via scanning electron microscopy (SEM) the project was able to confirm that for small planar aggregates on flat surfaces the total scattering intensity was proportional to the number of metal nanoparticles in an aggregate (Fig. 5A). Using this observation, the project team was able to use light-scattering intensity as a proxy for aggregate size to monitor the disaggregation kinetics at different temperatures and photon doses for many individual aggregates at the same time via darkfield microscopy (Fig. 5B shows a series of frames from a movie of nanoparticle melting). The data indicated that the photomelting kinetics follow simple Arrhenius-like activation as a function of temperature, while the light-intensity dependence is consistent with that of an optically non-cooperative multi-photon method: in other words, the single controlling variable in the disaggregation progress is the total delivered photon dose (a long-time low-intensity dose is equivalent to a short-time high-intensity dose with the same delivered energy). This observation suggests that thermal back-reactions are negligible over the time-scale of these measurements (seconds to hours), and indicates that photostringency methods discussed in the Objective 1 findings section could be used in quantitative biosensors and diagnostic applications, perhaps simplfying many sensor designs by replacing heaters and mixers with a compact solid state light source.

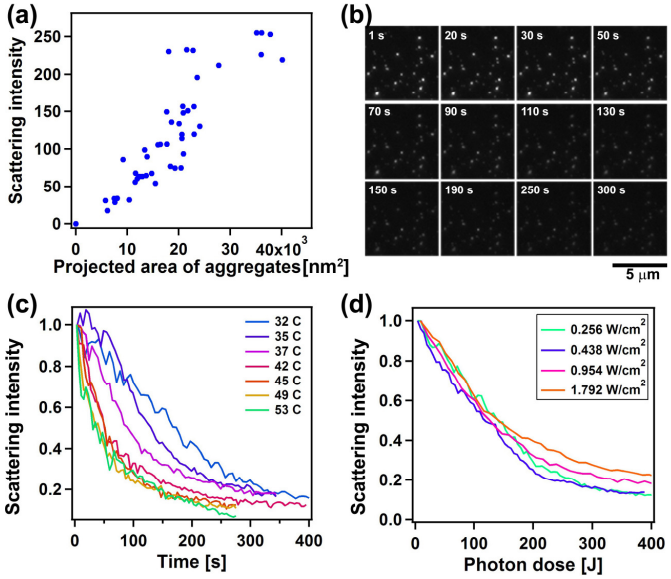

Figure 5. (a) Linear dependence of scattering intensity on size of aggregates obtained from SEM-darkfield correlation. (b) Movie frames of darkfield images of aggregates on a substrate at different duration of UV irradiation. (c) Average scattering intensity of aggregates as a function of UV irradiation time – the rate of photodisaggregation increases with increasing temperature. (d) Kinetics of photodisaggregation under different UV intensities show no dependence on photon dose, suggesting negligible thermal back reaction.

Year 2 (9/2011-9/2012):

Objective (1)

In year 2 the project continued to build upon the initial success using azo-benzene photoswitches to control hybridization states of DNA and the assembly of DNA-functionalized nanoparticles.

In 2012, complete versions of many of the preliminary results described in year 1 were published.[1] For instance, the project demonstrated that UV and blue illumination

could be used to control the assembly state of the DNA-functionalized particles, and showed that we could use the unique sequence-depending photo-disaggregation properties of these particles to perform all optical "hybridization stringency" washes with the ability to discriminate single-base mismatches using an optical readout and only "optical" reagents (replacing temperature, pH, or salt gradients with a controlled photon dose) (Fig. 2). The university of Washington completed filing of a provisional patent application for this technology in Nov. 2011.

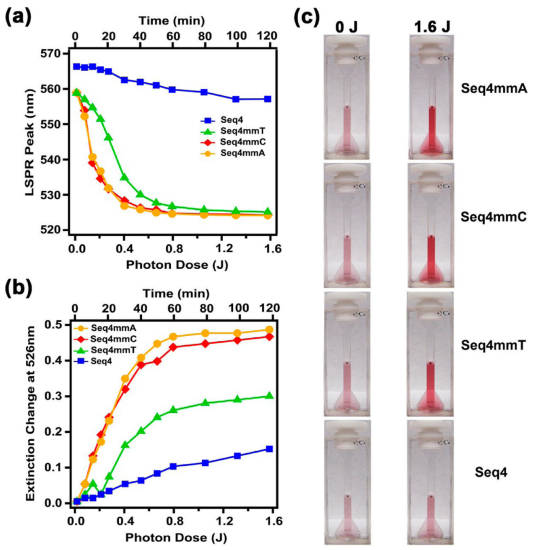

Fig. 6. Photostringency experiments demonstrating the discrimination of complementary from single-base-mismatched sequences linking Seq1Azo-AuNP and Seq3-AuNP assemblies. (a) LSPR peak wavelengths and (b) changes in the extinction at 526 nm of the four solutions as a function of UV photon dose. The complementary sequence (blue squares) is clearly distinguished from the single-base mismatches. (c) Photographs of the solutions before and after 1.6 J (2 h) of UV irradiation.

This unexpected, but potentially technologically important result motivated a great deal of experimentation. In particular, the origin of the mechanism that gives rise to the sequence dependent photo-induced disaggregation rates for photoswitch modified DNA-nanoparticle conjugates was initially unclear.

We proposed that the stability of the dsDNA (it's melting temperature) in turn affects the quantum yield (QY) for photoisomerization of the intercalated azobenzene. To test this hypothesis, we began measuring the QY for photoisomerization of azobenzenes linked to different DNA sequences both as ss and dsDNA. These experiments were completed and published in Year 3,[2] and are described more fully in that section.

Objective (2) of the proposal during was to study the biomechanical properties of photoswitchable DNA oligomers during hybridization and melting by single molecule

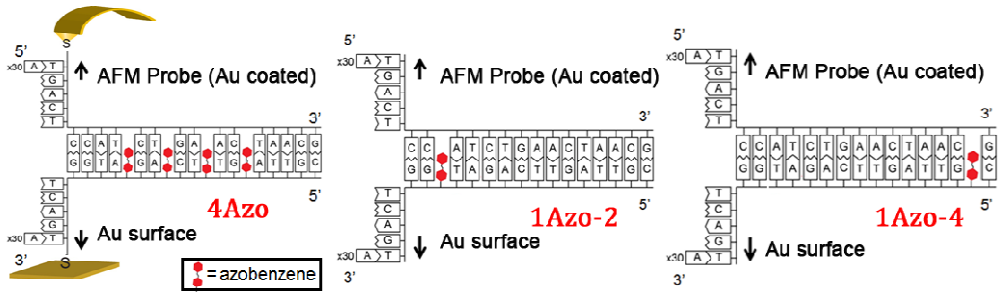

Figure 7: Geometry and sequences used for the AFM pulling experiments. By changing the azobenzene position relative to the unzipping front it is possible explore the effect of photoisomeriztion on the overall structure, and get a better understanding of the spatial extent of the unzipping front (what factors control the activation energy and off rate in this experiment).

force measurements with an Atomic Force Miroscope via Dynamic Force Spectroscopy (DFS). In year 2 the project began focusing on 3 different sequence variations in DFS experiments as shown in Fig 7. These sequences were designed to test specifically how the position of the azobenzene relative to the force-loading point affected force-induced unzipping/melting.

The pulling experiments using sequence 4Azo (shown in Fig. 7) showed clear reversibility in both the number of dsDNA binding events and the rupture forces required to pull the tip off the surface during UV exposure. More importantly, the project performed a large number of force-loading rate curves aimed at measuring the thermal off rate (k_{off}) for rupturing DNA with various photoswitch modifications. In particular the project compared the forces required to unzip the 4Azo, 1Azo-2, and 1Azo-4 sequences shown in Figure 4. The 4Azo sequence has 4 azobenzenes throughout the molecule. The 1Azo-2 sequence has only one azobenzene, situated very near the "front" of the dsDNA zipper, while the 1Azo-4 sequence has only one azobenzene at the "back" of the dsDNA zipper. During year 2, the project attempted to analyze much of the acquired force data using the classic Bell-Evans model, but encountered poor fits to the data. In year 3, this problem was finally resolved as discussed below.

Objective 3 to study the kinetics and thermodynamics of melting using plasmon ruler methods was largely complete by the end of this period. Although the year 1 and 2 results were sufficient to answer the initial program objectives we still sought a deeper level of quantitative understanding of interparticle distances as a spin-off project. Absolute calibrations performed using cryoEM were promising, however, the availability of cryoEM time of quality sufficient for tomography of a statistically meaningful sample set was not consistent with needs or resources available to this program. Following suggestions received at the Dec 2011 program review, we began a new spin-off collaboration with Dr. Nigel Browning at UC Davis/Pacific Northwest National Lab (PNNL) to leverage external expertise and use D-TEM both to measure the DNA-linked nanoparticle distances in liquid, in real time. We acquired preliminary data in the first quarter of 2012, prior to moving of the D-TEM facility to PNNL, after which the instrument was unavailable for an extended period. We believe these experiments would prove fertile ground for a future research project.

Year 3 (9/2012-9/2013):

Objective (1)

In year 3 the project completed its studies of the origin of the novel result that DNA mismatches affected the photon does required to achieve reversible photoswitching of the DNA-linked nanoparticle aggregates.[3] Specifically, the project studied the sequence and hybridization dependence of the photoisomerization quantum yield of azobenzene attached to DNA. Fig. 8 shows representative photokinetic curves that were used to extract the photoisomerization quantum yields from variation sequences, while Table 1 tabulates the measured data. Compared to free azobenzene it was found that the quantum yield for photoisomerization from trans to cis form was decreased 3-fold (from 0.094±0.004 to 0.036±0.002) when the azobenzene wasincorporated into ssDNA, and was further reduced 15-fold (to 0.0056±0.0008) for azobenzene incorporated into

dsDNA. In addition, the project found that the quantum yield is sensitive to the local sequence including both specific mismatches and the overall sequence-dependent melting temperature (Tm).

By demonstrating that the trans-to-cis photoisomerization quantum yield for azobenzene decreases upon incorporation into DNA, and is sensitive to both the local DNA sequence and DNA hybridization state the project has provided design rules for creating efficient photoswitchable DNA sequences tailored for sensing, drug delivery, and energy harvesting applications, while also providing a foundation for understanding phenomena such as photonically controlled hybridization stringency.

In general, the photoisomerization quantum yield tends to increase as the Tm of the attached dsDNA decreases. However, the biggest variations in quantum yield are associated with dsDNAs bearing a single-base mismatch immediately next to the azobenzene site. It is likely that these variations arise due to the structural fluctuations caused by the adjacent mismatched base inducing an increase in the local free volume.

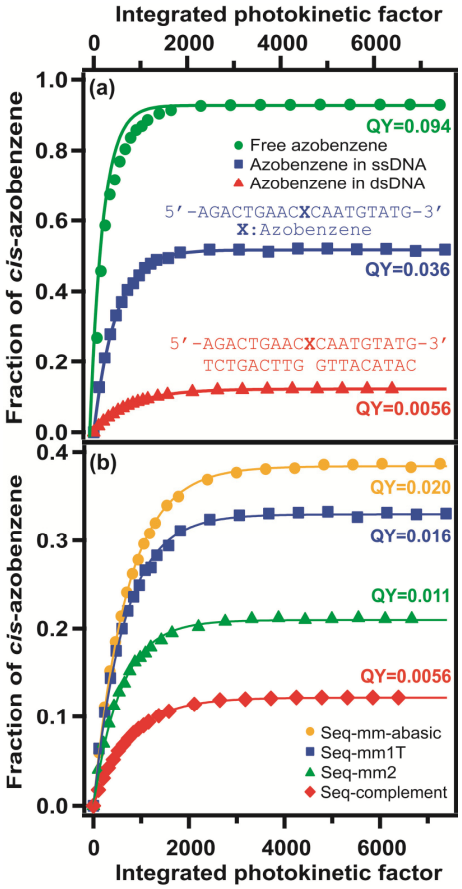

Fig. 8. (a) Representative plots of the measured fraction of cis-azobenzene vs. the integrated photokinetic factor (Equation 2) used to obtain quantum yield. Solid lines are fits of Equation 1 to the data shown, and are labeled with the average quantum yield values measured from at least three separate experiments. Traces are for azobenzene in isooctane (green circles), azobenzene incorporated in ssDNA (blue squares) and dsDNA (red triangles). (b) Similar plots for azobenzene incorporated in different dsDNA sequences including Seq-mm-abasic (yellow circles), Seq-mm1T (blue squares), Seq-mm2 (green triangles) and Seq-complement (red diamonds) (see Table 1 for sequences).

Table 1. Quantum yields and melting temperatures (T_m) of the azobenzene-modified DNA

Names	Sequences	Quantum Yield	T_m (°C)
ssDNA	5′-AGACTGAACXCAATGTATG-3′ X: azobenzene	0.036±0.002	
Seq-mm-abasic (mm: mismatch)	5′-AGACTGAACXCAATGTATG-3′ TCTGACTTG OTTACATAC O:abasic site	0.020±0.001	46.7
Seq-mm1T	5′-AGACTGAACXCAATGTATG-3′	0.016±0.001	48.0

	TCTGACTTG **T**TTACATAC		
Seq-mm1C	5′-AGACTGAAC**X****C**AATGTATG-3′	0.015±0.001	48.0
	TCTGACTTG **C**TTACATAC		
Seq-mm1A	5′-AGACTGAAC**X****C**AATGTATG-3′	0.0078±0.0007	48.0
	TCTGACTTG **A**TTACATAC		
Seq-mm2	5′-AGACTGAAC**X**C**A**ATGTATG-3′	0.011±0.001	52.0
	TCTGACTTG G**C**TACATAC		
Seq-mm3	5′-AGACTGAAC**X**CA**A**TGTATG-3′	0.0070±0.0002	54.0
	TCTGACTTG GT**G**ACATAC		
Seq-mm4	5′-AGACTGAAC**X**CAA**T**GTATG-3′	0.0069±0.0006	54.0
	TCTGACTTG GTT**G**CATAC		
Seq-complement	5′-AGACTGAAC**X**CAATGTATG-3′	0.0056±0.0008	60.0
	TCTGACTTG GTTACATAC		

Objective (2) In year 3 a major breakthrough in analyzing the DFS data was achieved by discarding the Bell-Evans analysis in favor of a more complicated model. A number of authors have pointed out circumstances in which a simple fitting to the Bell-Evans model might fail [4,5] In particular, the Bell-Evans model ignores the asymmetric behavior of the rupture forces at high loading rates as suggested by Dudko *et al.*[5] as well as the possibility of more than a single binding of interacting molecules.[6] Thus, the project began analyzing its DFS data using a generalized model proposed by Friddle, Noy, and DeYoreo.[7,8] This model explains the non-linearity in the force spectra as a consequence of reforming of a single bond at slow loading rates as well as asynchronous fluctuations of several independent interactions that comprise a multivalent attachment. Thus, this model takes into account the harmonic potential of the cantilever and the number of bonds formed between the probe and the substrate (N). The force spectrum from this model is given by equations 1-3:[7]

$$< f >_N = f_{eq} + N\frac{k_B T}{x_t}\exp\left(\frac{N}{R\left(\frac{f_{eq}}{N}\right)}\right)E_1\left(\frac{N}{R\left(\frac{f_{eq}}{N}\right)}\right) \quad (1)$$

$$R\left(\frac{f_{eq}}{N}\right) = \frac{r x_t}{k_{off}\left(\frac{f_{eq}}{N}\right)k_B T} \quad (2)$$

where,

$$k_{off}(f) = k_{off}^0 exp\left[\beta\left(f x_t - \frac{1}{2}k_c x_t^2\right)\right] \quad (3)$$

k_{off}^0 is the intrinsic unbinding rate at zero force, k_c is the spring constant of the cantilever, f_{eq} is a force given by $f_{eq} = \sqrt{2k_c \Delta G_{bu}}$, $E_1(z) = \int_z^\infty \frac{e^{-s}}{s} ds$, r is the loading rate and x_t is position of the energy barrier, and ΔG_{bu} is the free energy of the bond

relative to the free cantilever. Using this model, the project verified that the rupture force vs. loading rate data was dependent upon the cantilever spring constant as predicted in the above equations, and then was able to fit the DFS data to obtain physically meaningful k_{off} values (Fig. 9)

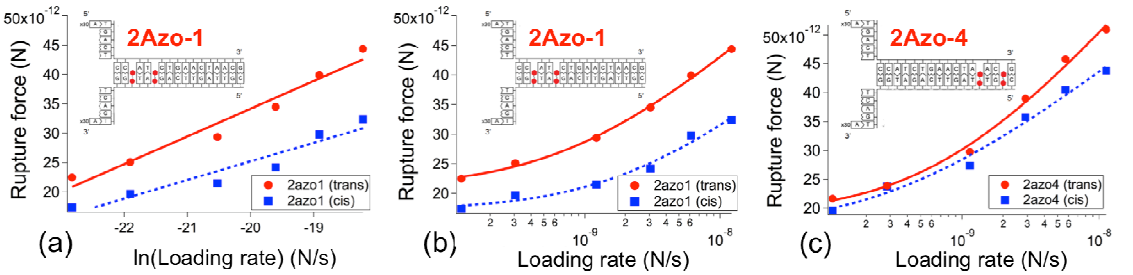

Figure3. (a) The rupture force is plotted as a function of natural log of force loading rate for DNA strands modified with two azobenzenes (red dots: *trans*-form and blue squares: *cis*-form) proximal to the unzipping end (2Azo-1). The data are fitted with Bell Evan's model (straight and dashed lines); (b) same data from (a) are fitted with Friddle model. (c) The data of DNA strands modified with two azobenzenes distal to the unzipping end (2Azo-4) are fitted with Friddle model.

As a consequence, the project has been able to show that, in qualitative agreement with computational predictions, the obtained experimental data suggest that the position of the azobenzene within the unzipping sequence controls the magnitude of change in k_{off} rate upon azobenzene photoisomerization. The project measured a significant (4X) increase in k_{off} when the azobenzene is in close proximity to the unzipping end of the DNA, and a smaller difference (within experimental uncertainty) when the azobenzene is at the opposite end of the DNA. These results provide important insights into the melting kinetics of photoswitch-modified oligonucleotides that should be useful for designing photoswitch-modified sequences for specific applications. They also show that photoswitches may provide a new tool for studying classic mechanisms in DNA hybridization and melting.

Objective 3 goals were largely completed in years 1 and 2. These results seeded a new collaboration with the group of Nigel Browning at PNNL.

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(6) Bizzarri, A. R.; Cannistraro, S. *Chem Soc Rev* **2010**, *39*, 734.
(7) Friddle, R. W.; Noy, A.; De Yoreo, J. J. *P Natl Acad Sci USA* **2012**, *109*, 13573.
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Publications --

1) “Dynamic Force Spectroscopy of Photoswitch-Modified DNA” Esha Sengupta, Yunqi Yan, Xin Wang, Keiko Munechika, and David Ginger, (Submitted) (2013)

2) "Photoisomerization Quantum Yield of Azobenzene-Modified DNA Depends on Local Sequence" Yunqi Yan, Jennifer I. L. Chen, David, S. Ginger J. Am. Chem. Soc. 135 (22) pp8382-8387 (2013).

3) "Photoswitchable Oligonucleotide-Modified Gold Nanoparticles: Controlling Hybridization Stringency with Photon Dose," Yunqi Yan, Xin, Wang, Jennifer I.L. Chen, and David. S. Ginger, Nano Letters 12 (5) pp2530-2536 (2012).

4) "Electron Accumulation on Metal Nanoparticles in Plasmon-Enhanced Organic Solar Cells," Michael Salvador, Bradley A. MacLeod, Angela Hess, Abhishek P. Kulkarni, Keiko Munechika, Jennifer I. L. Chen, and David S. Ginger, ACS Nano 6 (11) pp10024-10032 (2012)

5) "Quantum Dot/Plasmonic Nanoparticle Metachromophores with Quantum Yields That Vary with Excitation Wavelength", Keiko Munechika, Yeechi Chen, Andreas F. Tillack, Abhishek P. Kulkarni, Ilan Jen-La Plante, Andrea M. Munro, and David. S. Ginger Nano Letters 11 (7) pp2725-2730 (2011)

6) "Optical Detection of Protein in Complex Media with Plasmonic Nanoparticle Dimers", Jennifer I. L. Chen, Heather Durkee, Beth Traxler, and David. S. Ginger Small 7 (14) pp1993-1997 (2011)

Additional information requested by program manager:

Supported Personnel (Where listed, affiliated personnel includes graduate students, undergrads, postdocs, and visiting scientists who were materially supported by the project and contributed to project goals and findings but received salary from independent fellowships or teaching assistanceships). The award supported approx. 1 PhD student and 1 postdoc FTE, when more than one is listed each were supported in part with TA funds and/or external fellowship (or each were supported for part of the year due to staff turnover).

9/2010-9/2011
David S. Ginger, Professor
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Heather M. Durkee, PhD student
Raj Giridharagopal, postdoc
Angela Hess, undergrad
Keiko Munechika, postdoc
Glennis E. Rayermann, Ph.D. Student (received NSF Fellowship)

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Xin Wang, postdoc
Yunqi Yan, PhD Student

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Esha Sen Gupta, postdoc
Yunqi Yan, PhD Student

Affiliated Personnel not receiving direct salary support:
Kristi Bischoff, undergrad
Hannah Zeitler, undergrad

Invited Seminars during program period–

33. *ECME: European Conference on Molecular Electronics, London, U.K. Sep. 3-7, 2013
32. *16th Int. Conf. on Non-Contact AFM, Maryland, Aug 5-9, 2013
31. *Air Force Research Lab, Wright-Patterson AFB, July 22, 2013
30. *Advances in Structural and Chemical Imaging (ASCI 2013), Eugene, OR, May 29-30, 2013
29. *Seeing at the Nanoscale, Northwestern University, April 17, 2013
28. *Ajou University, Molecular Science and Technology, Suwon, Korea, Nov. 3-7, 2012
27. *Optoelectronics Group, Cavendish Lab, University of Cambridge, Sept 27, 2012
26. *SPMonSPM Scanning Probes Meeting, Mons, Belgium, Sept 23-26, 2012
25. *Fall ACS Meeting, Philadelphia, PA, Aug. 19-23, 2012
24. *Microscopy & Microanalysis Society Meeting, July 30-Aug 2, 2012
23. *International Conference on Synthetic Metals, Atlanta, GA July 7-13, 2012
22. *Gordon Conference, Electronic Processes in Organic Materials, Italy, June 3-8, 2012
21. *Rochester Physical Chemistry Seminar, Rochester, NY Apr. 30, 2012
20. *MIT Physical Chemistry Seminar, Boston, MA Apr. 24, 2012
19. *Spring MRS Meeting, San Francisco, CA, Apr. 9-12, 2012
18. *Spring ACS Meeting, San Diego, CA, Mar. 25-28, 2012
17. *Fall MRS Meeting, Boston, MA, Nov-Dec, 2011
16. *Nanoscale Systems for Renewable Energy Workshop, National Renewable Energy Lab, Nov. 11, 2011
15. *ALS Users Meeting, Lawrence Berkeley National Lab, Oct. 4, 2011
14. *UC Berkeley, Physical Chemistry Seminar, Sept. 27, 2011
13. *Mirkunite 2011, Northwestern University, Aug. 26, 2011
12. *ICMR Thin Film Solar Workshop, UC Santa Barbara, Aug. 8-10, 2011
11. *ICMAT2011 Singapore, June 26-July 1, 2011
10. *Emerging Opportunities in Nanostructured Semiconductors, Northwestern, Evanston, IL, June 2-3, 2011
9. *DOE EFRC Summmit and Forum, May 25-27, 2011
8. *European-MRS Spring Meeting, Nice, France, May 13-19, 2011
7. *MRS Spring Meeting, San Francisco, CA, April 25-29, 2011
6. *ACS Spring Meeting, Anaheim, CA, March 27-32, 2011
5. *APS March Meeting, Dallas, TX, March 20-24, 2011

4. *Materials Research Society, Boston, MA, Nov. 29-Dec. 3, 2010
3. *UC Irvine Chemistry Seminar, Irvine, CA, Nov. 9, 2010
2. *IEEE Photonics Society, Denver, CO Nov. 7-11, 2010
1. *Scanning Probe Microscopy for Energy Applications, Keynote Speaker, ORNL, Oak Ridge TN, Sept. 15-17, 2010

Collaborations and Interactions with Other Groups

Dr. Nancy Kelley and Jorge Chavez, beginning exploratory project to look at reversible photoswitching of aptamer binding

Dr. Kelly Lee, UW, CryoEM

Dr. James Evans and Nigel Browning, PNNL – begin liquid cell experiments to measure photocontrol of DNA-linked nanoparticle distances.

Transitions –

1) University of Washington Commercialization Gap Fund has invested ~$45K to obtain pre-clinical data based on photoswitch modified DNA for use in isothermal, isotonic DNA hybridization assays

2) AFRL scientists Dr. Jorge Chavez and Dr. Nancy Kelley-Loughnane are exploring photoswitch modified DNA as a means to control and recycle aptamer binding

3) Patent Application; entitled “Compositions and Methods for Photocontrolled Hybridization and Dehybridization of a Nucleic Acid” provisional Serial Number 13/681,209 Filed Nov. 19, 2012.

Awards –

Fellow, American Association for the Advancement of Science, 2013
Burton Medal, Microscopy Society of America, 2012
Defense Sciences Study Group, 2012-2013 class