

Molecular-level engineering of THz/IR-sensitive materials for future biological sensing application

Dwight Woolard^{*a,c}, Greg Recine^{b,c}, Alexei Bykhovski^c & Weidong Zhang^c

^aU.S. Army Research Office, Durham, NC, USA 27709

^bFordham University, Bronx, NY, USA 10458

^cNorth Carolina State University, Raleigh, NC, USA 27695

ABSTRACT

While the unique spectral information associated with chemical and biological molecules within the terahertz frequency regime (~ 3.0-3.0 millimeters) motivates its use for practical sensing applications, limiting factors at the macroscale (weak spectral absorption, broad line widths and masking geometrical effects introduced by the samples) provides motivation for man-engineered sensing materials that allow for the transduction of the spectral information about target molecules from the nanoscale. This brief letter will overview work being performed by our research group to define molecular-level functionality that will be useful for realizing “THz/IR-sensitive” materials. Here the goal is to define switchable molecular components that when incorporated into larger DNA-based nanoscaffolds lead to THz and/or IR regime electronic and/or photonic material properties that are dictated in a predictable manner by novel functionality paradigms. In particular, theoretical modeling and design studies are being performed to engineer organic and biological switches that can be incorporated into DNA-based architectures that enable the precise extraction of nanoscale information (e.g., composition, dynamics, conformation) through electronic/photonic transformations to the macroscale. Hence, these studies seek to define new spectral-based sensing modalities useful for characterizing bio-molecules

Keywords: molecular, terahertz, infrared, sensing, engineered materials, biological sensing

1. INTRODUCTION

Very long-wavelength spectroscopic science and technology has long been a research area of emphasis due to the fact that many biological and chemical molecules possess unique spectral fingerprints in the very far-infrared (far-IR) and terahertz (THz) frequency (~ 3.0-0.3 millimeters) regimes. Furthermore, since long-wavelength spectral absorption is known to be representative of the structural detail of molecules, electronic/phonics interactions in this regime are very important for many fundamental research areas (e.g., chemistry, biological, material science, etc.) and for many important application areas (e.g., threat agent detection, medical diagnostics, etc.). While these facts suggest that long-wavelength spectroscopy should be an effective sensing and characterization tool, practical problems (e.g., weak signatures, limited number of discernable features, and sensitivity to environmental factors) often reduce their effectiveness in practice. These general issues motivate one to consider the concept of engineering specialized nanoscale architectures that would allow for the enhanced extraction and controllable multiplication of the THz/IR regime spectral signatures associated with specific target and/or transduction molecules that have been strategically included into these architectures.

Research efforts will be overviewed here that are defining strategically designed nano-assemblies (i.e., either materials or structural devices) that incorporate the functionality of the organic and/or biological molecules such that they effect highly predictable and controllable changes into the electro-optical properties of the resulting superstructures. Two basic schemes will be considered here, each in the context of transduction-based sensing of target molecules. In the case where the functionality is defined by organic molecules, the goal is to define compound organic-biological architectures that will respond to the polarization of other small molecules, whereas in the case where the functionality arises from the

*dwight.woolard@us.army.mil; phone 1 919 549-4297; fax 1 919 549-4310

biological molecule (e.g., DNA) then the goal is to define fully-biological architectures that reveal information related to the functionalized biological component. The first example to be reported on here is the use of long-chain organic molecular switches (OMSs) that utilize multiple molecular-ring structures to achieve conductivity properties that are dependent on exposures to the 3-D polarizations of other molecules. As will be discussed, with these types of OMS components it is possible to envision artificially engineered materials that exhibit a dielectric tensor response upon exposure to polar gases, which is useful for defining THz/IR based sensors. A second example to be reported on here is the use of biological molecular switches (BMSs) such as DNA-derivatives that can be shown to possess multiple metastable states and light-induced multiple-coordinate transition paths. As will be discussed, these types of properties can be used to define THz/IR-sensitive material systems and associated devices with measurable macroscopic THz/IR electro-optical properties that reveal the underlying states and vibration dynamics of the constituent BMSs. The results from recent modeling and simulation studies will be used to illustrate the basic physical properties of these OMS and BMS as well as their use in realizing functional electronic materials and devices in the context of THz/IR spectral sensing and characterization.

2. ORGANIC MOLECULAR SWITCH PARADIGM

The first strategy being considered to realize THz/IR sensitive material systems is to define long-chain organic molecular switches (OMSs) for inclusion into larger DNA superstructures. All the OMSs under consideration in these research studies are based upon derivatives of very long-chain, single-bonded carbon atoms that are made semi-periodic through the introduction of groups of aromatic (carbon-based) ring structures. A good representative OMS design which appears to possess the desired properties for realizing the sought after sensing materials is illustrated in Fig. 1 (A). Here, a long zig-zag chain of carbon atoms (i.e., 101 Carbons: n-Thiohenihectane (C₁₀₁H₂₀₄S₂)), where each carbon atom has been made neutral by the binding of two hydrogen atoms, is terminated on each end by a single sulfur (thiol) atom. In addition, the periodicity of the long-chain has been interrupted in the center by a substructure molecule consisting of one Benzoyl Chloride (Q) ring that is two-carbon bonded to a pair of surrounding benzene (O) rings. The goal of this particular design is to achieve a compound molecule with an electron conductivity that can be made very sensitive to exposure to other polar molecules. Indeed, the conductivity of this OMS may be significantly modulated due to the fact that the center O-Q-O structure will introduce a defect state into the center of the potential barrier of the molecule that is dependent on the deflection-angle of the Q ring in relation to the outer O rings (i.e., that have a tendency to remain aligned to each other) and this dependence is given in Fig. 1 (B). If large changes to the conductivity result when the long-chain OMS is subjected to the electric-field profile of polar molecules, then it is possible to envision unit cells of the type illustrated in Fig. 2 (A). This hypothetical unit cell consists of a single OMS bound across an aperture defined inside the structure of a DNA nanoscaffold where it has been assumed that the DNA is highly resistive.

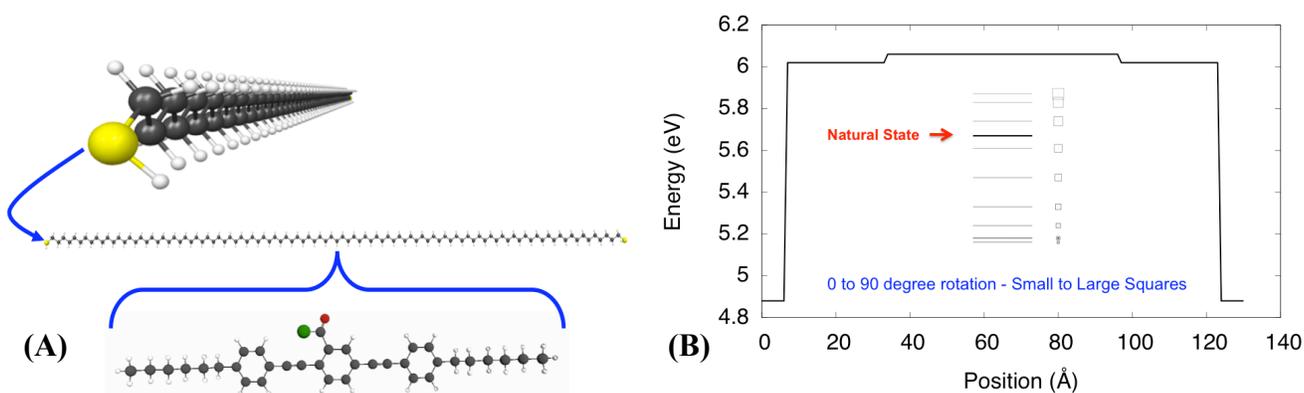


Fig. 1. (A) Long-chain OMS design, where the basic zig-zag carbon structure is illustrated in the upper inset and the substructure providing the switching function is illustrated in the lower inset. (B) LUMO potential energy barrier structure of the OMS design from (A) and the relative energy position of the defect energy state introduced by the O-Q-O structure as a functional of the angle of Q relative to the outside O's (i.e., that can be shown to remain aligned upon exposure to polar molecules.)

Since this OMS-DNA unit cell spans 3-D coordinate space, it is possible to further envision complete structural material architectures of the type shown in Fig. 2(B) where the tensor dielectric constant would depend on the state of the OMSs. If a target molecule was then introduced into some predefined void in the material as indicated by the dashed line, the resulting perturbation to the various conductive elements could lead to large changes in the tensor dielectric constant (i.e., and the indices of refraction) sufficient to modify the amplitude and/or direction of a propagating wave (i.e., perhaps at THz or IR frequencies). Hence, this type of hypothetical design could define an electro-optical transduction method for inferring information about the 3-D polarity of the target molecule.

In order to realize the type of sensing material paradigm described in Fig. 2, it will be necessary to: successfully execute the nanoscale fabrication of complex DNA unit cells and compound DNA structures, and define and implement OMSs that produce large changes in the complex component of the dielectric constant (e.g., electron conductivity) when exposed to dipole moments. Therefore, the OMS design studies described here are being coordinated with an independent research group [1] that has made significant progress towards fabricating DNA origami panels (i.e., with predefined linkers that are compatible with the OMS discussed here) and compound structures as would be needed to realize a concept as shown in Fig. 2. Furthermore, first-principles molecular modeling and Marcus electron-hopping transport theory has been applied [2] to estimate the conductivity characteristics of the OMS described in Fig. 1(A). Assuming that the proper electron donor/acceptor molecules can be defined for the terminus ends of the OMSs used in the unit cell of Fig. 2(A), one can expect to realize the conductivity characteristics for O-Q-O type OMS of Fig. 1(A) as is given in Fig. 3. Here, each of the three major conductivity components - i.e. the dc σ_{DC} , the low-frequency $A\omega^{1-s}$ & the high-frequency and photon-assisted $\sigma_{PA}(\omega)$ - are given and these results serve to illustrate the point that the low-frequency conductivity (i.e., which is the major contributor to the complex dielectric constant) can be expected to reach measurable levels even for a unit cell with single OMS chains. Furthermore, if one applies these results to the Drude model for electrical conduction it can be shown that unit cells based upon this basic OMS design (i.e., either of 100 nm size with 10 OMSs per window, or 10 nm size with one OMS per window) can produce “relative” dielectric constants with imaginary components that can be switched between “0” and “1”. These are promising results that will be detailed later in [2].

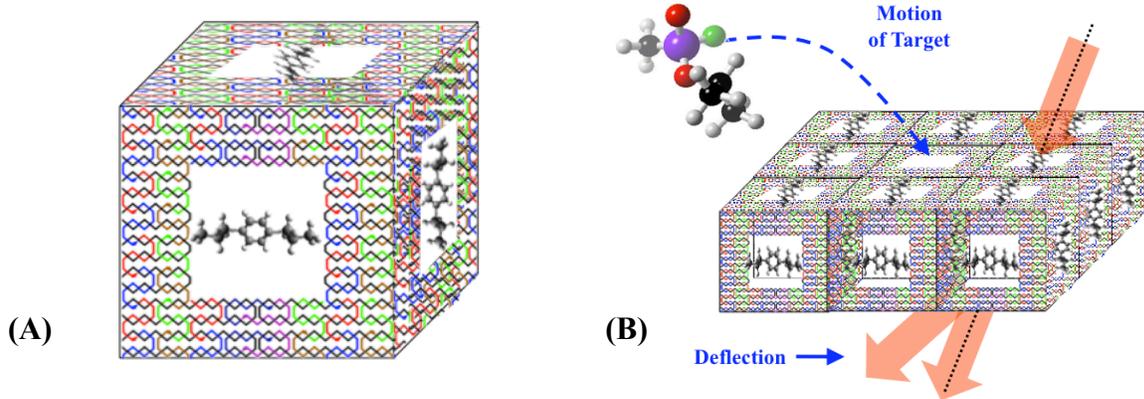


Fig. 2. (A) Hypothetical OMS-DNA unit cell that spans 3-D coordinate space. (B) Hypothetical sensing material using the unit cell from (A) where the dashed line indicates a possible approach of a target polar molecule that induces an assumed change in the tensor dielectric constant large enough to cause a measurable diffraction of a wave transmitting through the material.

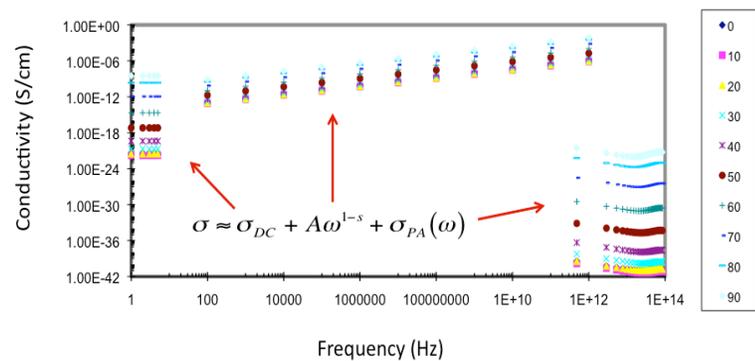


Fig. 3. Simulated conductivity results for the O-Q-O type OMS defined in Fig. 1(A) at various angles of the Q rotation. Here, the dc conductivity result (which is only defined at zero frequency) has been extended over a finite frequency range to allow for comparison.

3. BIOLOGICAL MOLECULAR SWITCH PARADIGM

The second strategy being considered to realize THz/IR sensitive material systems is to define DNA derivative-based biological molecular switches (BMSs) for inclusion into larger DNA superstructures. This BMS paradigm differs from that in the earlier section in that the molecular target that is to be sensed (or characterized) is actually a component part of the BMS itself, and the switching action (which is conformational based) is to be induced by light-based (THz, IR, Visible) excitations that produces changes in the THz/IR absorption. Hence, one can then either use these prescribed changes in the imaginary part of the dielectric constant to define a transduction strategy as discussed earlier in Fig. 2, or to execute traditional spectroscopic measurements but with the added advantage of being able to access multiple sets of spectral absorption signatures for each biological target. To date, this work has focused on the problem of deriving information regarding sequence structure of short DNA chains, with one avenue of interest being the use of BMS designs that utilize stilbene derivatives (e.g., trimethoxystilbene carboxamide (TMS)) as end capping to the DNA chains. While a significant amount the work by our group in this area is available for review (see [3]), it is somewhat useful and instructive to briefly overview here some of the major technical issues and explain how they relate to the remaining research challenges.

While the complete scope of the studies on stilbene-derivative based BMSs encompasses a significant number of structural variations (e.g., single and double stranded DNA, single and double TMS capping, etc.) and related dynamical phenomenology, the main goal of the work is well represented by the results illustrated in Fig. 4. Here, Fig. 4(A) depicts the basic structure of a potential BMS that consists of a double-stranded DNA chain (ds-TGCGCA) with single TMS capping, and symbolic sequence structure TMS-ds-TGCGCA. Figure 4(A) also indicates an important molecular coordinate (see arrow) in the TMS molecule (represented by colored spheres) that is amenable to torsion rotation and as will be shown leads to a definable switching functionality in the compound TMS-DNA molecule. Hybrid Ab-Initio/Empirical modeling that employed both Hartree-Fock combined (HF) with Molecular Mechanical (MM) and Density Functional Theory (DFT) combined with MM were utilized to successfully discover two new stable conformations of TMS-ds-TGCGCA. Figures 4(B) and 4(C) illustrate these two conformations, which differ in the fact that the former has the TMS molecule aligned with the end T-A base-pair and the later has the TMS aligned mostly along the backbone of the ds-DNA chain. Figure 4(D) provide the results from a modeling analysis of ground- and excited-states energy profile dependence as a function of the torsion coordinate defined in Fig. 4(A). These single-coordinate energy profiles do not reveal any obvious opportunities for using light excitation to induce transitions between the stable states for the purposes of accessing the very different

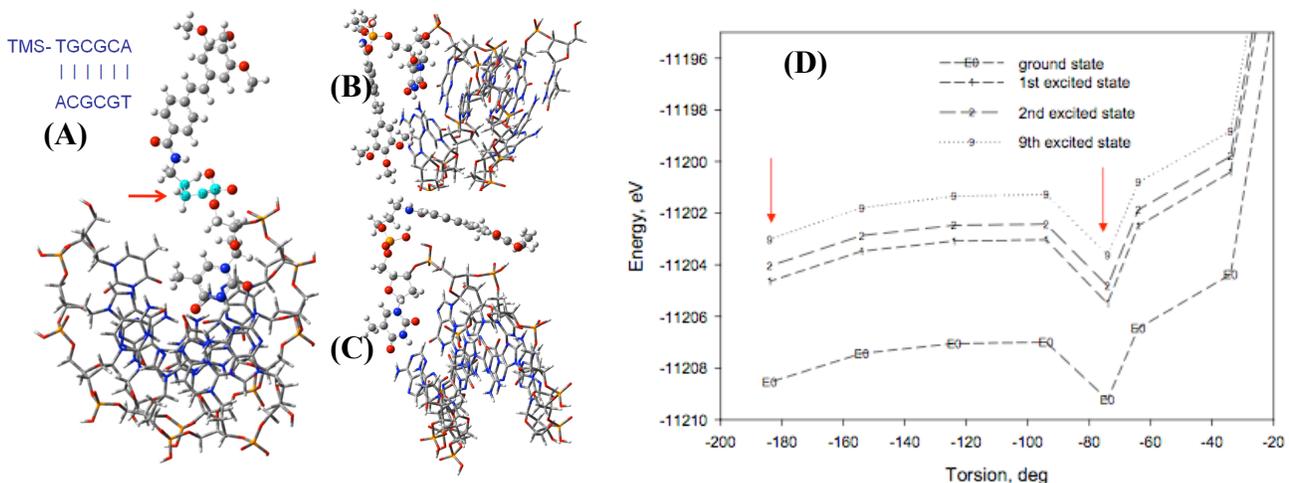


Fig. 4. (A) Illustration of TMS-ds-TGCGCA molecule with designation (see arrow) of energy scan coordinate. (B) Conformation with TMS chain aligned approximately along the end base pair. (C) Conformation with TMS along DNA backbone. (D) Energy-scan profiles for the 0th, 1st, 2nd and 9th states, where the arrows indicate stable conformations with the left energy minimum corresponding to case shown in (B) and the right energy minimum corresponding to the case shown in (C).

spectral absorption characteristics (see Ref. [3]). Indeed, in treating such a complex molecule one would not necessarily expect that it would be possible to utilize a single-coordinate based transformation as is true for example in the case of 2-Butene. To clarify this point, Fig. 5(A) illustrates the trans- and cis- conformations of 2-butene and Fig. 5(B) shows a physical model that can be used to explain the light induced transition in terms of only a single rotation about the D5 coordinate (i.e., as defined in Fig. 5(A)). However, a more careful analysis [4] can be used to more accurately characterize this same transition in terms of two (i.e., D5 and D8) dynamical coordinates as illustrated in Fig. 5(C). While the D8 coordinate can be argued as irrelevant in this transformation of 2-Butene, it illustrates the point that in larger molecules (e.g., TMS-ds-TGCGCA) one might be able to utilize the richness of the coordinate transformation space in combination with multiple frequency- and/or time-domain light-pumping to access complicated switching-trajectory pathways between known stable states. As this is a very challenging problem, our group is cooperating with the authors of [4] to develop new simulation tools that combine molecular modeling with efficient optimization algorithms and proper interfaces for human-guided analysis of light-induced transitions in complex molecules. Here the goal is to define novel BMSs useful in bio-sensing applications.

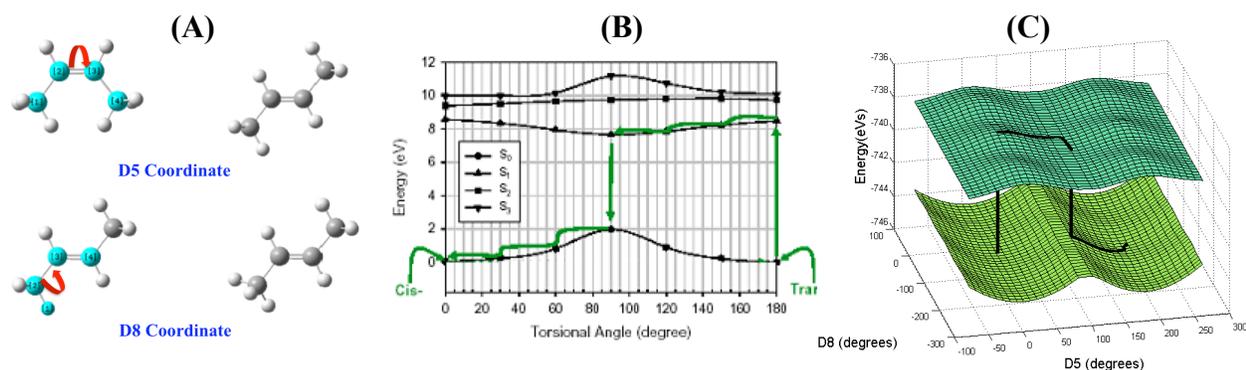


Fig. 5. (A) 2-Butene molecule with coordinate rotations for D5 (upper) and D8 (lower) labeled. (B) One-dimensional analysis (i.e. D5 coordinate only) that successfully predicts the trans- to cis- transition of 2-Butene. (C) Actual two-dimensional transition path associated with conformational transformation defined by (B) that shows transversals (back and forth) in D8 space.

4. CONCLUSIONS & FUTURE DIRECTIONS

This letter has overviewed research work on the development of novel long-chain organic molecular switches (OMSs) and DNA-based biological molecular switches (BMSs), both for use in realizing “THz/IR-sensitive” materials for future bio-sensing applications. The long range goal of these investigations is to define switchable molecular components that when incorporated into larger DNA-based nanoscaffolds lead to THz and/or IR regime electronic and/or photonic material properties that are dictated in a predictable manner by novel functionality paradigms, and that therefore define new methods for the electro-optical based transduction of molecular information at the nanoscale (e.g., composition, dynamics, conformation) to the macroscale. The preliminary results demonstrate promise both for OMSs and BMSs.

REFERENCES

- [1] Michael Norton, et. al., “The Generation and Characterization of Origami Constructs containing Biosynthetic vs. Synthetic Fluorophores,” presented to the 2010 ISSSR, 21-24 June (2010).
- [2] Dwight Woolard, et. al., “The THz-IR Functionalization of long Molecular Chains by Aromatic Derivatives,” to be submitted to IEEE Trans. on Nanotechnology (2010).
- [3] Alexei Bykhovski and Dwight Woolard, “Hybrid Ab-Initio/Empirical Modeling of the Conformations and Light-Induced Transitions in Stilbene-Derivatives Bonded to DNA,” accepted to IEEE Trans. on Nanotechnology (2010).
- [4] Dave Mokrauer, C. T. Kelley and Alexei Bykhovski, “Efficient Parallel Computation of Molecular Potential Energy Surfaces for the Study of Light-Induced Transition Dynamics in Multiple Coordinates,” accepted to IEEE Trans. on Nanotechnology (2010).