Role of DNA in Nanoarchitectonics and Future Prospects

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Introduction

The ITRS (International Technology Roadmap for Semiconductors) anticipates that the scaling of CMOS (complementary-metal-oxide-semiconductor) technologies may end with 22 nm pitch length (9 nm physical gate length) by 2016. The ability to scale within the last several decades has fueled multiple industries and has led to new industrial and defense products. The ITRS defines several potential research avenues that would lead to new device paradigms and provide alternative technologies, including bio-inspired assembly. The ultimate goal in these efforts is to develop highly controlled and highthroughput fabrication of nanoelectronics as stand-alone devices/systems, or components/devices that could be integrated heterogeneously on existing device platforms. Assembly based on biomolecular recognition provides a promising approach for constructing complex architectures from molecular building blocks, such as single walled carbon nanotubes (SWNT) and nanocrystals (NC). Deoxyribonucleic (DNA) and peptide (PNA) nucleic acids are attractive assembly linkers for bottom-up nanofabrication due to specificity offered by the base sequences. The Ozkan's labs at UCR are following a tiered approach to nanomanufacturing of molecular electronics where understanding charge-carrier transport across bio-inorganic interfaces, error-free repeatability of synthesis of hybrid building blocks and direct integration over Si platforms are among the challenges being addressed. Among the recent publications in the bio-assembly area include ex-vivo assembled discrete devices such as DNA-SWNT and virus-NC nanoarchitectures for electronics components [1,2] and programming of nucleic acid sequences for large scale assembly of nanostructures [3,4]. The use of self-assembly processing and highly-integrated materials will allow novel routes to circumvent current challenges of CMOS such as environmental friendliness, thermal balance, dielectric quality, and capital costs of next generation fabrication facilities. Challenges in developing of future nanoelectronics involve massively parallel integration of SWNTs and semiconducting nanowires in a defect tolerant manner.

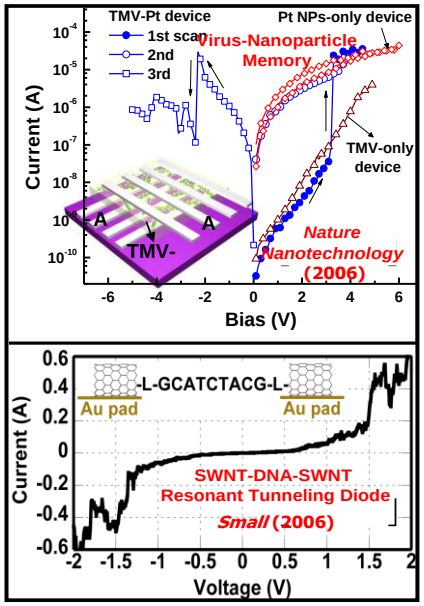

Figure 1. (a) Tobacco Mosaic Virus (TMV) templates for cross bar-memory applications. (b) DNA-CNT nano architectures for resonant tunneling diodes.

Carbon Nanotube Based Functional Nanostructures

Synthesis of hybrid nanoarchitectures based on SWNT-DNA or SWNT-PNA conjugates can provide unique possibilities for nanoelectronics and biotechnology (Figure 2). Such new structures combine the electrical properties of SWNTs with the self assembling properties of the oligonucleotides, or other

biomaterials including proteins, enzymes and viruses. We have recently demonstrated that SWNT-DNA-SWNT conjugates can be employed for fabricating resonant tunneling diodes[2]. We expect that novel devices and applications could be derived from these achievements, including bio-electronic devices, DNA sensors, mechanical actuators, templates for hierarchical assembly, etc. Several studies have reported the utilization of SWNTs for imaging probes in scanning force microscopy [5,6]. Electrochemical studies showed that SWNTs can be utilized as enzyme based sensors, DNA sensors [7-11]. SWNT electrodes have indicated catalytic properties with potential applications as electrodes in fuel cells and electrochemical detectors for medical and warfare applications [12-17]. Functionalized nanotubes have been used in fabricating field effect transistors for applications in nanoelectronics and biosensors [18-20]. Several studies have shown that SWNTs and MWNTs can accommodate the encapsulation of nanoparticles, fullerenes, metallized DNA fragments [21-24] (Figure 3). Other studies have indicated conjugation possibilities of organic and inorganic molecules to sidewalls of carbon nanotubes [25-28].

Bottom-up Fabrication: Hybrid Nanoarchitectures

SWNTs are being utilized as active components in future solid state nanoelectronics [29]. Individual SWNTs have been used to realize molecular-scale electronic devices such as single-electron[30] and field-effect transistors[31]. Several SWNT-based devices have been successfully integrated into logic circuits [32] and transistor arrays [33]. However, the difficulty in precise localization and interconnection of nanotubes so far impeded further progress toward larger-scale integrated circuits. Searching for alternative routes based on the molecular recognition between the complementary strands of DNA has prompted the exploration of its electronic properties for possible use in molecular electronics and templated nanostructures [34-39]. We have synthesized SWNT-DNA and SWNT-PNA (peptide nucleic acid) conjugates at UCR where DNA or PNA sequences are covalently bonded to SWNT ends to achieve a viable bio-inorganic interface. Most research discussing the fabrication of oligonucleotide based nanoarchitectures focused mostly on non-covalent interactions between DNA fragments and SWNTs [40,41]. Intrinsic low conductivity of bare DNA restricts its utilization in electronic circuits. Distributing metal particles on the backbone of DNA has been considered to lower its resistance [42,43].

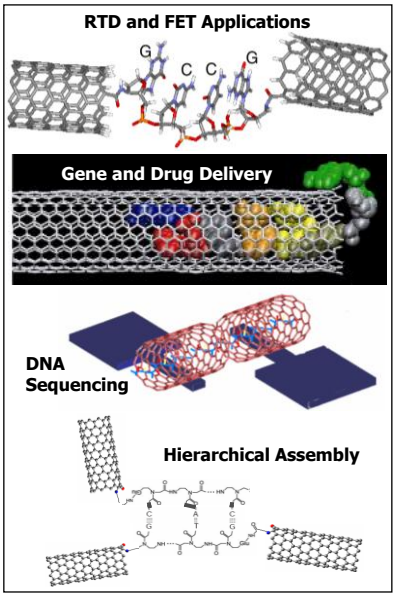

Figure 2. SWNT-DNA systems for hybrid nanoelectronics, biosensors, and bottom-up nanofabrication.

Synthesis of end specific SWNT-DNA and SWNT-PNA complexes (Figure 4) are quite novel and have been studied for the first time at UCR [2]. For the preliminary experiments, ssDNA with a nine base configuration of 5′ (NH_2)GCATCTACG has been used which is diluted to a concentration of 10-4mol/L in ion-free water. ssPNA with a custom sequence of (NH2)-Glu–GTGCTCATGGTG-Glu-(NH_2) has been used for synthesizing SWNT-ssPNA conjugates. SWNTs are oxidized in 2N HNO3 for 24 hours after sonicating mixture for 30 minutes. Sonication makes SWNTs disperse well

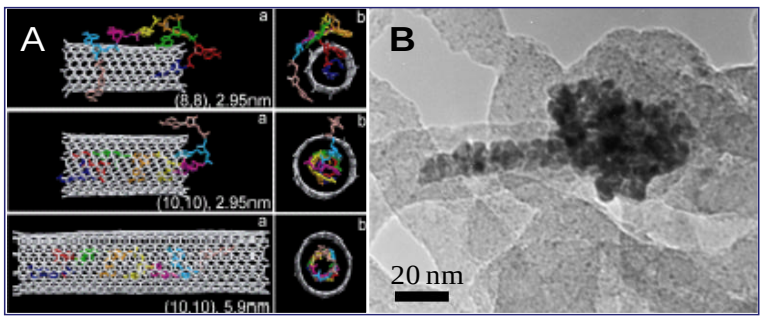

Figure 3. (a) Molecular dynamics simulations of DNA encapsulation in SWNT [23]. (b) Encapsulation of metallized ssDNA in MWNT [24].

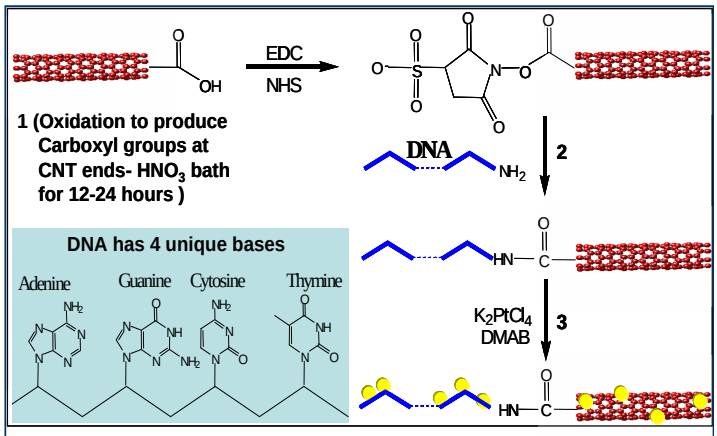

Figure 4. Synthesis of metallized SWCNT-ssDNA hybrids. Step 1 involves selective oxidation of SWCNTs at ends to produce the Carboxyl groups. In step 2, ssDNA fragments are chemically connected with SWCNTs at the ends by the amide groups. Step 3 shows that in the presence of the reductant DMAB, Pt ions are reduced into Pt nanoparticles and localize over the SWCNT-ssDNA hybrids.

so oxidation can proceed properly. Mixture is then filtrated with DI water and dried by heating at 150C for 24 hours. The amine group on DNA is made to react with carboxyl on SWNTs (Figure 4). To achieve SWNT-ssDNA conjugation, we used 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide in the presence of N-hydroxysulfosuccinimide in DI water. SWNT and ssDNA solutions are mixed and incubated for 12 hours. EDC reagent activated the terminal carboxyl groups of the SWNTs forming a highly reactive o-acylisourea intermediate, which undergoes rapid hydrolysis to form acid again. The intermediate undergoes nucleophilic substitution with primary amines on DNA, forming amide linkages [44]. SWNT-ssDNA conjugates were obtained after several cycles of centrifugation to remove salt from the solution (Figure 5(a)). A similar processing scheme was employed in forming the SWNT-ssPNA conjugates (Figure 5(b)). The covalent nature of attachment between SWNTs and the oligonucleotides was established by using FTIR. Interpreting FTIR spectra for various compounds including oxidized SWNTs, PNA, DNA and characterizing the structures of SWNT-ssPNA, SWNT-ssDNA has been a major subject of study in our laboratories. In an FTIR scan, the carbonyl group affects the frequencies of other additional functionalities like (C-O, C-N, and N-H). Infrared spectra were recorded at 2 cm^{-1} resolution on a Bruker Equinox 55 spectrometer at room temperature for mid IR range (400 cm^{-1} to 4000 cm^{-1}). Correction for aqueous nature of different samples was conducted by rationing spectra of all the samples with PBS. Figure 5(c) illustrates infrared spectra for different samples (Oxidized SWNTs, PNA and SWNT-PNA conjugates). We observed a carbonyl peak for oxidized SWNTs at 1641 cm^{-1}. For ssPNA, both Amide (-C= O) peak at 1658 cm^{-1} 26 and Amide (N-H bending) peak at 1641 cm^{-1} were observed. As both of the Amide bands overlap, we do not observe sharp peaks. But the observance of both Amide peaks indicates the peptide structure of PNA backbone and distinguishes it from SWNTs. Formation of covalent bond between SWNTs and PNA is indicated by shifting in position of both Amide peaks, at (1664 cm^{-1}) and (1626 cm^{-1}) with respect to PNA spectra in SWNT-PNA conjugate spectrum. Shifting in the first Amide peak is of particular interest as its band is strongly influenced by carbonyl band of SWNTs. This strongly indicates that there is a covalent interaction between SWNTs and PNA. We also observed change in the position of –NH stretch of SWNT-PNA conjugates, centered around 3088 cm^{-1}, than the corresponding stretch, centered around 3116 cm^{-1} that of PNA. Though for both PNA and SWNT-ssPNA conjugates, –NH stretch will include both primary and secondary amines but left shifting

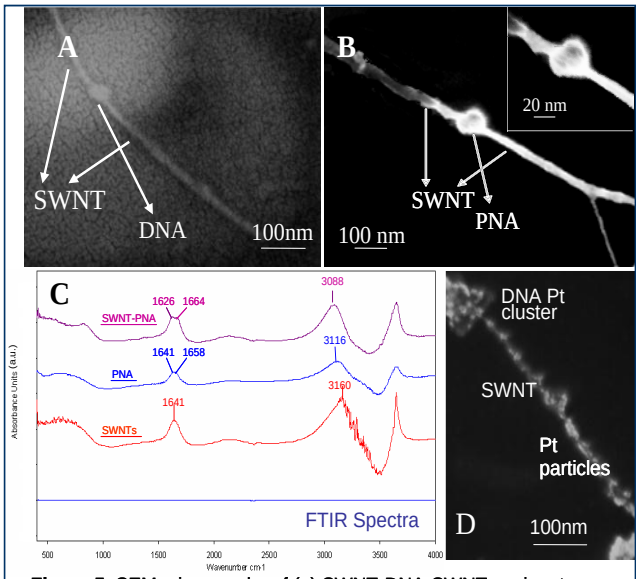

Figure 5. SEM micrographs of (a) SWNT-DNA-SWNT conjugate, (b) SWNT-PNA-SWNT conjugate, (c) FTIR spectra of oxidized SWNT, ssPNA and SWNT-PNA conjugates (d) metallized SWNT-DNA conjugate ("SWNT" labels represent bundles of SWNT).

(decrease in wavenumber) in peak position for SWNT-PNA conjugates indicate increase in secondary amine character of the sample. As quantity of PNA in the SWNT-PNA conjugate is less than that for the only PNA sample, this increase in secondary amine character of –NH stretch could be attributed towards the formation of new amide bonds, which results in conversion of a primary amine to a secondary amine.

Metallized Nanoarchitectures

Synthesis of Pt decorated SWNT-ssDNA complexes is accomplished in a two-step chemical reduction and deposition of metallic colloids [45-48]. First, SWNT-ssDNA conjugates (1μl) are mixed with a salt solution such as K_2PtCl_4 solution (65 μl, 1mM) at room temperature for 8 to 12 hours. During the incubation, the DNA molecules are "activated" and some of the Pt(II) complexes bind covalently to the DNA bases [49]. Using first-principle molecular dynamics (FPMD) simulations, it has been shown that for Guanine and Adenine base of DNA, the preferable binding site is N7 position [50]. To model the Pt(II)-ssDNA adducts, a one-fold hydrolyzed complex [PtCl2(H2O)] is considered as the representative system bound to single base pairs. The monofunctional complexes GP [G-PtCl2(H2O] and AP [A-PtCl2(H2O] are representative for adducts in the early stage[51]. After the activation step, dimethylamine borane (DMAB, 1μl, 10mM) is added and mixed for several seconds. After 4 hours at 27C, Pt (II) is reduced to metallic platinum. In the process of reduction, Pt dimers formed heterogeneously at DNA molecules after a single reduction step present a stronger Pt-Pt bond and are expected to possess higher electron affinity than other Pt dimers formed homogeneously in solution. The initial heterogeneous nuclei quickly develop into bigger particles, consuming the metal complex feedstock present in solution [52]. Figures 5(d) and 6(a)-(c) represent metallized SWNT-ssDNA complexes. Oxidized SWNTs have higher adsorption capacities for heavy metal ions [53], hence Pt ions are absorbed on SWNTs. PNA has the same base pairs as DNA which can be activated by several metal ions in solution similar to DNA metallization. ssPNA fragments (NH2-Glu-TGCTCATGGTG-Glu-NH2), can also be utilized in fabricating the PNA-Pt complexes, following a two-step chemical reduction and deposition of metallic colloids [54]. Pt ion solution was prepared by dissolving K_2PtCl_4 in de-ionized water (1μM) and sonicated for several minutes. K_2PtCl_4 solution was mixed with the ssPNA solution (1.05μM) and incubated at room temperature for 2 hours. ssPNA molecules are first activated by Pt ions, forming initial metallic nanoclusters. Such initial clusters serve as nucleation sites for subsequent chemical reduction and further growth of the Pt nanoparticles and nanoclusters. Reduction bath of 1μl solution of 10m M DMAB was added to the mixture which was kept at 27C for 15 minutes to 6 hours. The reduction process can be terminated by diluting the solution with DI water, followed by a sonication step. During reduction, the Pt ions in the solution are utilized for continuous overgrowth of the Pt clusters on ssPNA molecules.

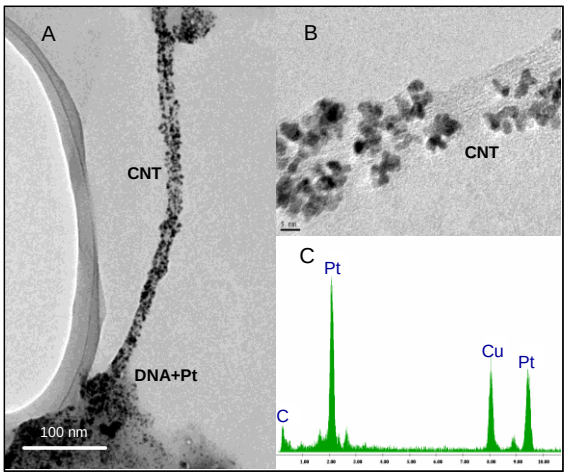

Figure 6. (a),(b) TEM images of a metallized SWNT-ssDNA complex. (c) EDS spectra showing presence of Pt in (b).

Modeling of Band Structures and Carrier Transport Across Bio-inorganic Interfaces

Analysis of the high-lying occupied molecular orbitals (HOMO) and low-lying unoccupied molecular orbitals (LUMO) provides an understanding of the structural and electrical properties of the bio-inorganic interfaces such as CNT/Protein, QD/DNA, QD/Protein, metal/DNA, and metal/protein. In a

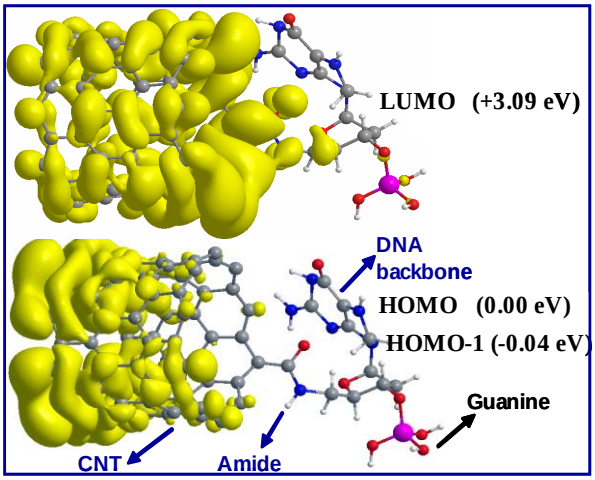

Figure 7 . HOMO -LUMO calculation of SWNT linked by an amide linkage to a deoxyribose nucleoside with the Guanine base (HOMO -LUMO Gap: ~3.1 eV).

CNT, the bandgap is ~0.98 eV. The HOMO orbital is confined on the SWNT while the LUMO orbital extends across the amide linker suggesting a good possibility of electron transfer across the amide bridge for n-type SWNTs. Similar calculations for SWNT-ssPNA revealed that while the HOMO orbital is confined to the glutamate linker, the LUMO orbital extends over the SWNT suggesting that the SWNT-ssPNA conjugates could be useful for building hole conducting devices [2]. An important outcome of such preliminary studies is to realize that bio-inorganic interfaces achieved by conjugating SWNTs with ssDNA (Figure 7) and ssPNA could prvide the opportunity to fabricate n-type and p-type devices, which could be envisioned as a future alternative to the conventional CMOS technology.

Nanopatterning via Dielectrophoresis Using Micro- and Nano-Arrays

Micro- and nano-array platforms can be utilized for precise control of electrophoretic manipulation of (bio)molecules, particles, and micro-LEDs as electronic elements. The platform (Figure 8) for electric-field assisted manipulation and assembly of nano-elements such as metallic and semiconducting nanotubes, carbon nanotubes, quantum dots, dendrimers and/or conjugation molecules such as DNA fragments. The Nanochip platform by Nanogen (Figure 8) enables rapid, parallel transport within seconds to a specific location on the chip array by enabling independent current or voltage control on

recent study, the electrical properties of the interfaces between SWNT-ssDNA and SWNT-ssPNA are deduced via density functional theory (DFT) calculations, where two unit cells of zigzag (10,0) oxidized CNT was linked to a deoxyribose nucleoside with amine on the 5′ position to form an amide linkage. The highest occupied molecular orbital (HOMO) and lowest unoccupied molecular orbital (LUMO) surface plots shown in Figure 8 were generated at the SCF theory level with LANL2DZ basis set [55,56] using Gaussian03 program suite [57]. The HOMO-LUMO gap was found to be about 3.1 eV. For comparison, the HOMO-LUMO gap of bare CNT is ~3.1 eV. The large gap is the result of the short length (2 unit cells) of the modeled SWNT. For an extended (10,0)

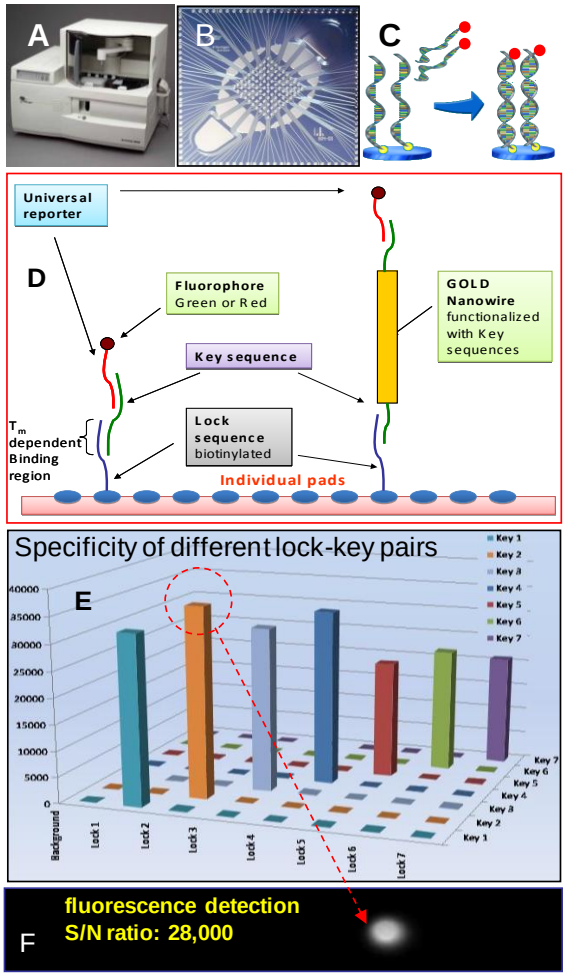

Figure 8. (a)-(c) Nanogen platform and microarray device for dielectrophoresis applications. (d) Assembly of ssDNA sequences and functionalized nanowires onto Si arrays. (e) Specificity of assembly of different lock and key ssDNA sequences. Lock-key sequence-2 resulted in the largest S/N ratio(f).

each electrode. Current commercialized applications of this platform include DNA hybridization and DNA analysis for molecular diagnostics applications where the platform uses fluorescence detection for sensing via fluorophore labeled reporters [58-61]. The commercial DNA detection encompasses highly multiplexed and fully validated assays and panels, including cystic fibrosis, respiratory viral panel, hereditary hemochromatosis, etc. Different types of arrays have been developed so far using silicon micromachining with fully automated and robotized fluidics control including 10,000 sites arrays, 400 and 100 site arrays, for various applications. Figures 8(c) and (d) demonstrate the principle of electric or electrophoretic-field assisted in-situ assembly for manipulation, directing, and assembly of nanoelements. The electrode array, with geometry configurable to the desired application is energized to attract and combine different types of nano-elements (Figure 8(b)). This is significantly different than self-assembly in static solution because it enables site-specific assembly. Controlled parallel assembly of nanowires and nanotubes could be experimented by attaching one end of nanowire to the target DNA immobilized on the nanoarrays, and the other end of the nanowire could be attached to a reporter DNA sequence equipped with a fluorescent tag (Figure 8 (d)). Upon hybridization, fluorescence detection could be used for the assessment and recording of an in-situ assembly event.

Conclusions

While chemical and biological assembly holds promise in many fields, there is still much technology to be developed and science to be learned for the promise to be fully understood and realized. We anticipate that there are rich engineering concepts to be discovered within the near future that will enable massively parallel assembly of nanodevices towards functional systems and applications. Perhaps, the future of assembly engineering depends on gaining the ability to manipulate and control more than one type of molecular force, which is necessary for hierarchical fabrication. We are confident that the first of the applications in this area will be enabled by integration of assembled components onto existing platforms fabricated by top-down approaches.

References

1. R.J. Tseng, C. Tsai, L. Ma, J. Ouyang, Y. Yang, C. Ozkan, “Digital memory device based on Tobacco Mosaic Virus conjugated with nanoparticles”, Nature Nanotechnology, 2006, in press.
2. X. Wang, F. Liu, G.T. Senthil Andavan, X. Jing, N. Bruque, R.R. Pandey, R. Lake, M. Ozkan, Kang L. Wang and C. Ozkan, "*Carbon nanotube-DNA nanoarchitectures and electronic functionality*", *Small*, 2006, in press.
3. J. Ruan, S. Raghunathan, J.Hartley, K. Singh, H. Akin, N.Portney, M.Ozkan, "Fluorescent Tag Based Metrology for Self-Assembled Molecular Devices", NIST, Frontiers of Characterization and Metrology for Nanoelectronics, 2007, 8pp, Gaithersburg, Maryland, March 2007.
4. H. Akin, J. Ruan, S. Raghunathan, X. Wang, J. Hartley, C. Ozkan, M. Ozkan, "Engineered Nucleic Acid Base Pairing for Controlled Assembly of Nanostructures", SRC TECHCON, 3pp, Austin, TX, September 2007.
5. S. S. Wong, E. Joselevich, A. T. Woolley, C. L. Cheung, C. M. Lieber, Nature 1998, 394, 52-55.
6. J. Bernholc, D. Brenner, M. B. Nardelli, V. Meunier, C. Roland, Annu. Rev. Mater. Res. 2002, 32, 347-375.
7. P. J . Britto, K. S. V. Santhanam, P. M. Ajayan, Bioelectrochem. Bioenerg. 1996, 41, 121- 125.
8. M. Melle-Franco, M. Marcaccio, D. Paolucci, F. Paolucci, V. Georgakilas, D. M. Guldi, M. Prato, F. Zerbetto, J. Am. Chem. Soc. 2004, 126, 1646 -1647.
9. Q. Zhao, Z. Gan, Q. Zhuang, Electroanalysis 2002, 14,1609 -1613.
10. J. J. Davis, R. J. Coles, H. A. O. Hill, J. Electroanal. Chem. 1997, 440, 279 -282.
11. J. Wang, M. Li, Z. Shi, N. Li, Z. Gua, Electroanalysis 2004, 16, 140-144.

12. B. S. Sherigara, W. Kutner, F. D'Souza, Electroanalysis 2003, 15, 753-772.
13. J. Qu, Y. Shen, X. Qu, S. Dong, Chem. Commun. 2004, 34-35.
14. M. D. Rubianes, G. A. Rivas, Electrochem. Commun. 2003, 5, 689 -694.
15. J. Wang, G. Chen, M. P. Chatrathi, M. Musameh, Anal. Chem. 2004, 76, 298-302.
16. J. Wang, S. B. Hocevar, B. Ogorevc, Electrochem. Commun. 2004, 6, 176-179.
17. J. N. Wohlstadter, J. L. Wilbur, G. B. Sigal, H. A. Biebuyck, M. A. Billadeau, L. Dong, A. B. Fischer, S. R. Gudibande, S. H. Jameison, J. H. Kenten, J. Leginus, J. K. Leland, R. J. Massey, S. J. Wohlstadter, Adv. Mater. 2003, 15, 1184 -1187.
18. A. Javey, J. Guo, Q. Wang, M. Lundstrom, H. Dai, Nature 2003, 424, 654-657.
19. A. Star, J.-C. P. Gabriel, K. Bradley, G. Gr ，ner, Nano Lett. 2003, 3, 459 - 463.
20. K. Bradley, M. Briman, A. Star, G. Gr ，ner, Nano Lett. 2004, 4, 253 -256.
21. T. J. S. Dennis, G. A. D. Briggs, Angew. Chem. 2004, 116, 1410 -1413.
22. J. J. Davis, M. L. H. Green, H. A. O. Hill, Y. C. Leung, J. Sloan, S. C. Tsang, Inorg. Chim. Acta 1998, 272, 261-266.
23. H. Gao, Y. Kong, D. Cui, C.S. Ozkan, ''Spontaneous Insertion of DNA Oligonucleotides into Carbon Nanotubes,'' *Nano Letters*, 3, 4, 471-473, 2003.
24. D. Cui, C.S. Ozkan, S. Ravindran, Y. Kong, H. Gao, ''Encapsulation of Pt-labelled DNA molecules inside carbon nanotubes,'' *Mechanics and Chemistry of Biosystems*, 1, 2, 113-122, 2004.
25. M. Shim, N. W. S. Kam, R. J. Chen, Y. Li, H. Dai, Nano Lett. 2002, 2,285 -288.
26. T. Lin, V. Bajpai, T. Ji, L. Dai, Aust. J. Chem. 2003, 56, 635-651.
27. A. Hirsch, Angew. Chem. 2002, 114, 1933 ±1939; Angew. Chem. Int. Ed. 2002, 41, 1853-1859.
28. M. Sarikaya, C. Tamerler, A. K. Y. Jen, K. Schulten, F. Baneyx, Nature Mater. 2003, 2, 577 -585.
29.K.Tsukagoshi, N.Yoneya, S.Uryu, Y. Aoyagi, B.W. Alphenaar, Physica B: Condensed Matter 2002, 323 ,107-114.
30. H. W. Ch. Postma, T. Teepen, Z. Yao, M. Grifoni, C. Dekker, *Science* 293, 76 (2001).
31. S. J. Tans, A. R. M. Verschueren, C. Dekker, *Nature* 393, 49 (1998).
32. A. Bachtold, P. Hadley, C. Dekker, *Science* 294, 1317 (2001).
33. A. Javey, Q. Wang, A. Ural, Y. Li, H. Dai, *Nano Letters* 2(9), 929 (2002).
34. J. R. Heath, M. A. Ratner, *Phys. Today* 2003, 43 (May 2003).
35. N. Seeman, *Nature* 421, 427 (2003).
36. Seeman, N., *Trends Biotech.* 17, 437–443 (1999).
37. Arkin, M. R. *et al.* Rates of DNA-mediated electron transfer between metallointercalators. *Science* 273, 475–480 (1996).
38. N. C. Seeman, Annu. Rev. Biophys. Biomol. Struct. 27, 225 -1998.
39. J. L. Coffer, S. R. Bigham, X. Li, Y. Rho, G. Young, R. M. Pirtle, and I. L. Pirtle, Appl. Phys. Lett. 69, 3851 1996.
40. Chris Dwyer, MartinGuthold, MichaelFalvo,SeanWashburn, Richard Superfine and Dorothy Erie, DNA-functionalized single-walled carbon nanotubes. *Nanotechnology* 13 (2002) 601–604.
41. Ming Zhang, Anand Jagota, Ellen D. Semke, Bruce A. Diner, Robert S. Mclean, Steve R. Lustig, Raymond E. Richardson and Nancy G. Tassi *nature materials* | VOL 2 | MAY 2003.
42. *Nucleic Acid - Metal Ion Interaction*s, Spyro T. G., Ed.; Wiley: New York, 1980.
43. Winfree, E.; Liu, F.; Wenzler, L. A.; Seeman, N. C. *Nature* 1998, *394*, 539-544.
44. Sathyajith Ravindran, Sumit Chaudhary, Brook Colburn, Mihrimah Ozkan, Cengiz S. Ozkan, *Nano Letters* 2003 vol. 3, No. 4, 447-453.
45. W. Pompe, M. Mertig, R. Kirsch, R. Wahl, J. Richter, R.Seidel, and H. Vinzelberg, Z. Metallkd. 90, 1085 (1999).

46. J. Richter, R. Seidel, R. Kirsch, M. Mertig, W. Pompe, J. Plaschke, and H. K. Schackert, Adv. Mater. 12, 507-510(2000)
47. M. Mertig, R. Kirsch, W. Pompe, and H. Engelhardt, Eur. Phys. J. D 9, 45 1999.
48.M. Mertig, R. Kirsch, and W. Pompe, Appl. Phys. A: Mater. Sci. Process.196, 723 1998.
49. Lucio Colombi Ciacchi, Ph.D dissertation ”Growth of Platinum Clusters in Solution and on Biopolymers: The Mi croscopic Mechanisms” 2002.
50. Niemeyer, C. M. *et al*. Nanoparticles, proteins, and nucleic acids: Biotechnology meets materials science. *Angew. Chem. Int. Ed*, 40, 4128-4158 (2001).
51. Laxmikant Kalé, Robert Skeel, Milind Bhandarkar, Robert Brunner, Attila Gursoy, Neal Krawetz, James Phillips, Aritomo Shinozaki, Krishnan Varadarajan, and Klaus Schulten. NAMD2: Greater scalability for parallel molecular dynamics. *Journal of Computational Physics*, 151:283-312,1999.
52. Lucio Colombi Ciacchi, Ph.D dissertation ”Growth of Platinum Clusters in Solution and on Biopolymers: The Microscopic Mechanisms” 2002.
53. Braun, E.; Eichen, Y.; Sivan, U.; Ben-Yoseph, G. *Nature* 1998, *391*, 775.
54. Jan Richter, Michael Mertig, and Wolfgang Pompe. Construction of highly conductive nanowires on a DNA template. *Applied Physics Letters,* 78, 536-538 (2001).
55. J.J.P. Stewart, Optimization of Parameters for Semiempirical Methods II. Applications. *J. Comp. Chem.*, 10, 221 (1989).
56. Wadt, W. R.; Hay, P. J., *J. Chem. Phys*. 1985, 82, 284-298.
57. Gaussian 03, Revision B.3, Frisch, M. J. et al., Gaussian, Inc., Pittsburgh PA, 2003.
58. Dubois, L. H.; Nuzzo, R. G. Ann.Phys.Chem.1992, 43, 437.
59. Aliasger K. Salem, Min Chen, Jessica Hayden, Kam W. Leong, Peter C. Searson, Nano Lett., 2004, 4,1163.
60. J. Ruan, S. Raghunathan, J.Hartley, K. Singh, H. Akin, N.Portney, M.Ozkan, "Fluorescent Tag Based Metrology for Self-Assembled Molecular Devices", NIST, Frontiers of Characterization and Metrology for Nanoelectronics, 2007, 8pp, Gaithersburg, Maryland, March 2007.
61. H. Akin, J. Ruan, S. Raghunathan, X. Wang, J. Hartley, C. Ozkan, M. Ozkan, "Engineered Nucleic Acid Base Pairing for Controlled Assembly of Nanostructures", SRC TECHCON, 3pp, Austin, TX, September 2007.