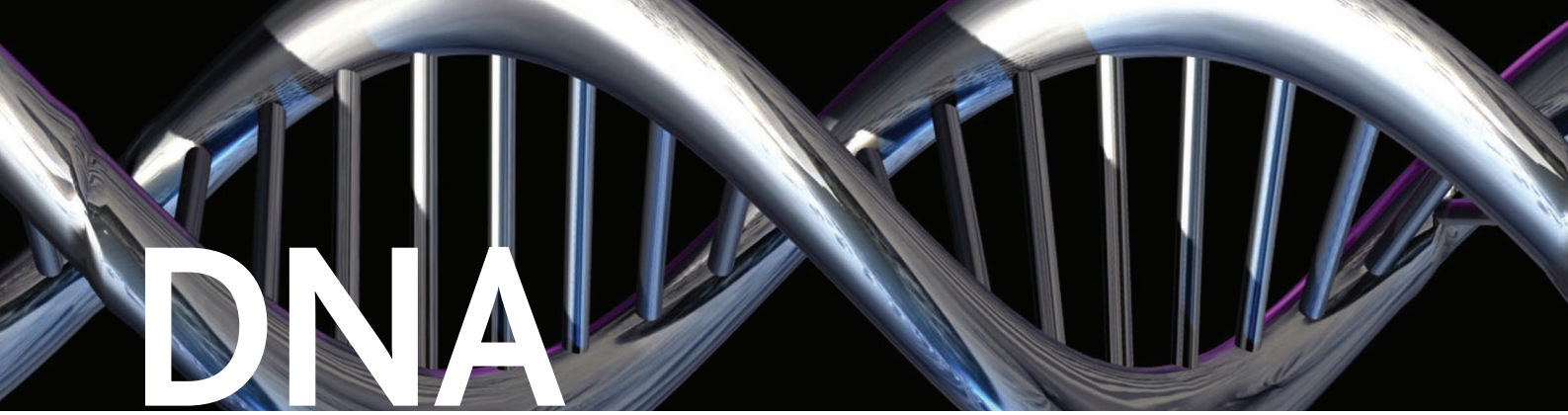

DNA nanobiostructures

by Rashid Bashir

DNA (deoxyribonucleic acid)-mediated assembly of nano- and micrometer scale structures can have a profound impact in the fields of nanoelectronics and nanotechnology. Such structures can also find applications in microelectromechanical systems, hybrid biosensors, and potential to continue the scaling of Moore's law beyond the 50 nm node. While engineers and scientists have been long aspiring to manipulate structures controllably and specifically at the micro- and nanometer scale, nature has been performing these tasks and assembling structures with great accuracy and high efficiency using highly specific biological molecules such as DNA and proteins.

School of Electrical and Computer Engineering,
Department of Biomedical Engineering,
Purdue University, West Lafayette,
IN 47907, USA
E-mail: bashir@ecn.purdue.edu

Much of this paper was previously published in:
Bashir, R. (2001) *Superlattices and Microstructures* **29** (1), 1-16 and is reproduced with kind permission.

The image above shows the DNA double helix. (Credit: Oliver Burston Wellcome Trust Medical Photographic Library.)

Recent advances in the field of nanotechnology and nanobiotechnology have been fuelled by the advancement in fabrication technologies that allow construction of artificial structures that are the same size or smaller than many biological entities.

Since the invention of the junction transistor in 1947 and the subsequent invention of the integrated circuit, the complexity of microelectronic integrated circuits and devices has increased exponentially. Fig. 1 shows the trends in miniaturization and complexity using silicon CMOS (complementary metal-oxide-semiconductor) technology. The minimum feature size has decreased from 2 μm in 1980 to 0.13 μm in 2001 in volume production[1]. In research labs, minimum feature sizes, which are a factor of 5-10 smaller, have been demonstrated. The SIA (Semiconductor Industry Association) roadmap projects that these trends will continue for another 15-20 years but it is becoming increasingly difficult to continue to down-scale because of real physical limitations including size of atoms, wavelengths of radiation used for lithography, interconnect schemes, etc.. No known solutions currently exist for many of these problems[2,3].

Bio-self-assembly and motivation

As the construction of artificial computational systems, i.e. integrated circuits, continues to become insurmountably difficult, more and more engineers and scientists are turning towards nature for answers and solutions. 'Bottom-up' fabrication and organic biological synthesis techniques can provide new opportunities and directions. A variety of extremely sophisticated and complicated molecular systems occur in nature that vary in density, sense and relay

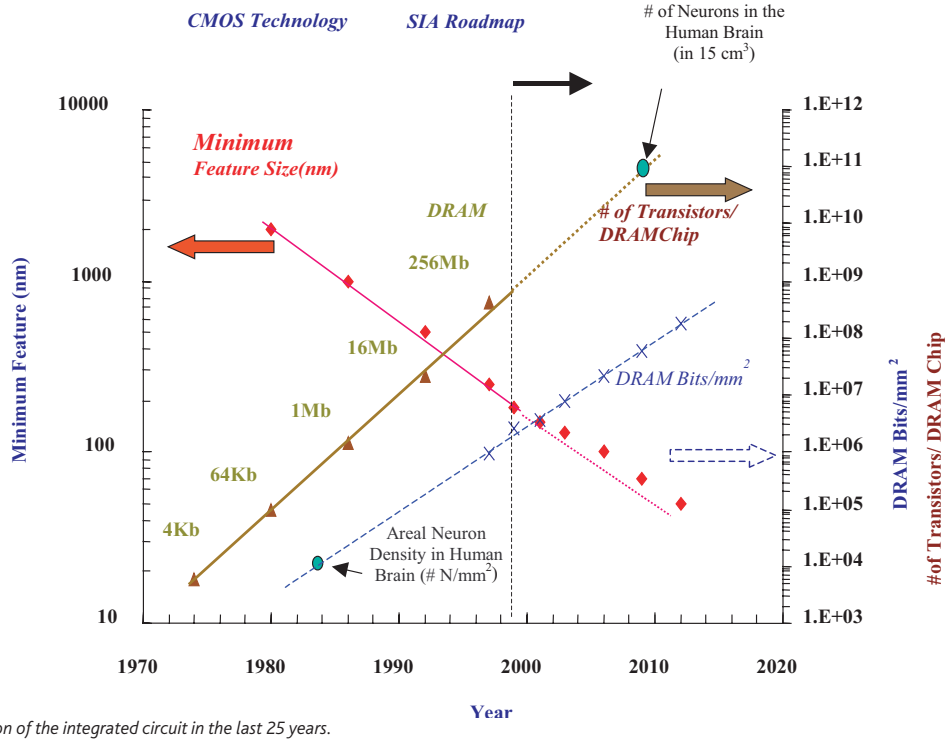

Fig. 1. Trends in miniaturization of the integrated circuit in the last 25 years.

information, perform complex computational tasks, and self-assemble into complex shapes and structures. Two examples can be considered, that of human brain and genomic DNA in the nucleus of the cell. There are about 10^{11} neurons in the human brain[4] in a volume of about 15 cm^3. The total number of transistors on a two-dimensional chip will actually reach the number of neurons in the human brain by about 2010. The area density of the neurons was actually surpassed in mid 1980s, but it is the three-dimensional nature and parallel interconnectivity of the neurons that makes the exquisite functions of the brain possible. So even though computers have or will soon achieve a similar density of basic computational elements to that of brain, the replication of brain functions is far from reality. Similarly, the case of DNA is also far-reaching and intriguing. Human DNA[4] is about 6 mm long, has about 2 x 10^8 nucleotides, and is tightly packed in a volume of 500 μm^3. If a set of three nucleotides is assumed to be analogous to a byte (since a 3 codon set from mRNA is used to produce an amino acid), then this represents 1 Kb/μm (linear density) or 1.2 Mb/μm^3 (volume density). These numbers are not truly quantitative but give an appreciation of how densely stored information is in DNA molecules. Certainly, a memory chip based on DNA as the active elements could have extremely high density!

Self-assembly can be defined as *'the process of self-organization of one or more entities as the total energy of the system is minimized to result in a more stable state'*. This process of self-assembly inherently implies: (i) some mechanism where movement of entities takes place using diffusion, electric fields, etc.; (ii) the concept of 'recognition' between different elements, or 'bio-linkers', that result in self-assembly; (iii) where the 'recognition' results in binding of the elements dictated by forces (electrical, covalent, ionic, hydrogen bonding, van der Waals, etc.), such that the resulting physical placement of the entities results in the state of lowest energy.

Self-assembly processes are not only interesting from a scientific point of view, but could have a variety of applications. These could include any case where micro- or nanoscale objects of one type need to be placed or assembled at specific sites on another substrate. Applications could include (i) detection and diagnostics, (ii) fabrication of novel electronic/optoelectronic systems, and (iii) new material synthesis. For example, in the case of detection of DNA oligonucleotides, avidin-coated gold or polystyrene beads are assembled onto a biotinylated target DNA to indicate complementary binding. Proteins and DNA attached to carbon nanotubes or silicon nanowires can be used to

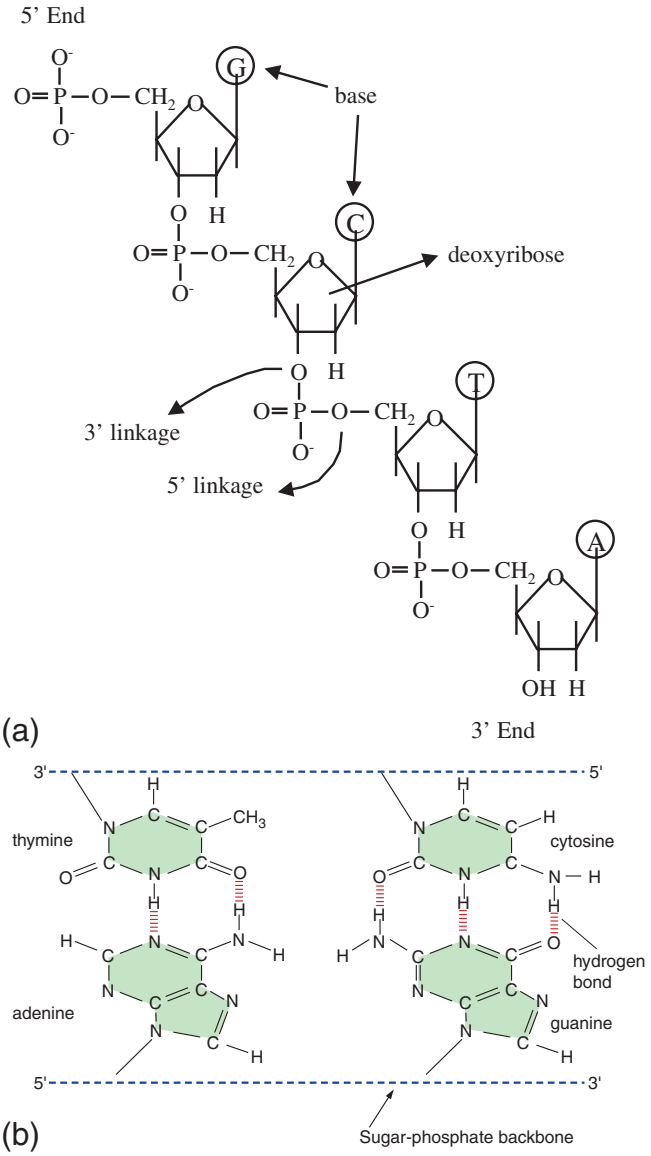

Fig. 2. (a) Sugar-phosphate back-bone of DNA, (b) the four bases of DNA showing their complementary binding properties[4].

assemble these devices on substrates for ultra-dense electronics or flexible displays. Heterogeneous integration of materials can be achieved using such biologically-mediated assembly of components. Since these techniques provide micro- and nanoscale placement of objects, assembly can be repeated for novel three-dimensional material synthesis.

DNA fundamentals

Biologically mediated self-assembly uses complementary molecules, termed 'bio-linkers'. These molecules (actually macro-molecules) act like a 'lock and key' and bind to each other under appropriate conditions, as a result of a variety of non-covalent interactions.

One possible bio-linker is DNA, the basic building block of life. The double-stranded helical structure of DNA is key to its use in self-assembly applications. Each strand of DNA is about 2 nm wide and composed of a linear chain of four possible bases (Adenine, Cytosine, Guanine, Thymine) on a backbone of alternating sugar molecules and phosphate ions (Fig. 2). Each unit of phosphate, sugar molecule, and base is called a nucleotide and is about 0.34 nm long. The specific binding through hydrogen bonds between Adenine (A) and Thymine (T), and Cytosine (C) and Guanine (G), as shown in Fig. 2(b), can result in the joining of two complementary single stranded (ss) DNA to form double stranded (ds) DNA.

The phosphate ion carries negative charge in the DNA molecule – the resulting drift of the molecule under an electric field is used in electrophoresis applications. The negative charge produces electrostatic repulsion of the two strands and to keep the two strands together positive ions need to be present in the ambient to neutralize the negative charges. The joining of two ssDNA through hydrogen bonding to form dsDNA is called hybridization. Two single strands of DNA can be designed to have complementary sequences and made to join under appropriate conditions. If dsDNA is heated above a certain temperature, called the melting temperature T_m, the two strands will separate into single strands. T_m is a function of temperature, ion concentration of the ambient, and the G-C content in the sequence. When the temperature is reduced, the two strands will eventually come together by diffusion and rehybridize or renature to form the double stranded structure. These properties of the DNA can be used in the ordering and assembly of artificial structures if these can be attached to ssDNA. It should be pointed out that the sequence of DNA can be chosen and the molecules obtained from a variety of commercial sources[5].

Attachment of DNA to gold surfaces

The most widely used attachment scheme between DNA and surfaces uses the covalent bond between sulfur and gold[6-19]. The formation of long chain ω-substituted dialkyldisulfide molecules on a gold substrate was first reported in 1983[6]. Films of better quality were formed and reported by the adsorption of alkyl thiols[7-13]. Bain and Whitesides presented a model system consisting of long-chain thiols, $HS(CH_2)_nX$ (where X is the end group) that adsorb from a solution onto

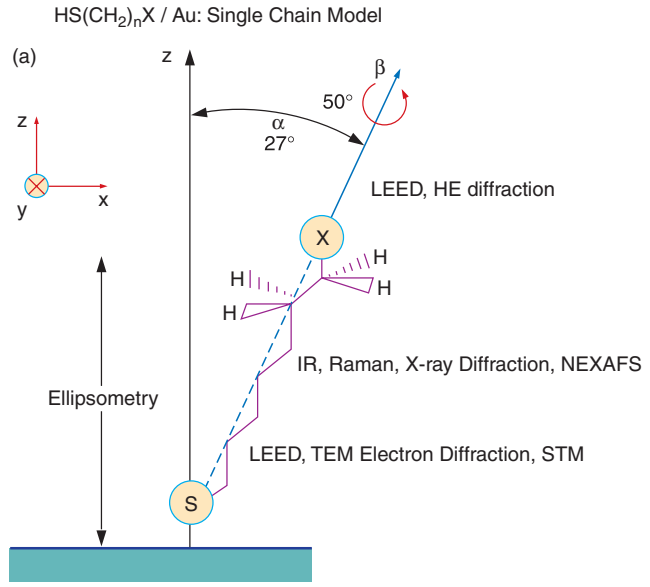

Fig. 3. Schematic of a long chain thiol molecule on a gold surface[9]. (Reprinted, with permission, from the Annual Review of Physical Chemistry, Vol 43, © 1992 by Annual Reviews, www.AnnualReviews.org.)

gold and form densely packed, oriented monolayers[7-8]. Fig. 3 shows a schematic of the gold-sulfur bond[9].

The bonding of the sulfur head group to the gold substrate is in the form of a metal thiolate, which is a very strong bond (~44 kcal/mol), resulting in stable films suitable for surface attachment of functional groups. For example, DNA can be functionalized with a thiol (S-H) group at the 3' or 5' end. Upon immersion of clean gold surfaces in solutions of thiol-derivatized oligonucleotides, the sulfur adsorbs onto the gold surfaces forming a single layer of molecules, where the hydrocarbon is now replaced with ssDNA or dsDNA[16-19]. Chemisorption of thiolated ssDNA[18] leads to surface coverage of about 10^{13} molecules/cm^2, corresponding to about 1 strand per 10 nm^2. Hickman *et al.* demonstrated the selective and orthogonal self-assembly of disulfide with gold and isocyanide with platinum[10]. This can be important in the orientation dependent self-assembly of structures that have both platinum and gold surface exposed for functionalization. Thiol-based chemistry serves as the fundamental attachment scheme for DNA and oligonucleotides for the self-assembly of artificial nanostructures.

DNA-inspired self-assembly

There has been tremendous interest in recent years to develop concepts and approaches for self-assembled systems for electronic and optical applications. Material self-assembly has been demonstrated in a variety of semiconductors (GaAs, InSb, SiGe, etc.) using Stranksi-Krastanov strain-dependent growth of lattice mismatch epitaxial films[20-23].

While significant work continues, it has been recognized by engineers, chemists, and life scientists that the exquisite molecular recognition of various natural biological materials could be used to form complex networks of potentially useful particles for a variety of optical, electronic, and sensing applications. This can be considered a 'bottom-up' rather than 'top-down' approach of conventional scaling and much work has been reported towards this front.

Nano-structures by DNA itself

Pioneering research extending over a period of more than 15 years by Seeman has laid a foundation for the construction of structures using DNA as scaffolds, which may ultimately serve as frameworks for the construction of nanoelectronic devices[24-28]. Branched DNA is used to form stick figures by choosing the sequence of the complementary strands. Macrocycles, DNA quadrilateral, DNA knots, Holliday junctions, and other structures can be designed. Fig. 4(a) shows a stable branched DNA junction with the hydrogen bonding indicated by dots between the nucleotides. It is possible to take this structure and devise a two-dimensional lattice as shown in Fig. 4(b) if hybridization regions ('sticky ends') are provided in region B. It is easier to synthesize these structures but more difficult to validate the synthesis. The design and observation, via atomic force microscopy (AFM), of two-dimensional crystalline forms of DNA double cross-over molecules that are programmed to self-assemble by the complementary binding of their 'sticky ends'[28] is also possible. Single domain crystal sizes, as large as 2 μm x 8 μm, were shown by AFM. The lattices can also serve as scaffolding for other biological materials. The 2 nm wide stiff DNA molecules are themselves used to form these two and three-dimensional structures.

Nanostructure assembly by DNA

Among roles envisioned for nucleic acids in nanoelectronic devices, the self-assembly of DNA conjugated nanoparticles has received the most attention. Mirkin *et al.*[29] and Alivisatos *et al.*[30] were the first to describe self-assembly of gold nanoclusters into periodic structures using DNA.

Mirkin's method of assembling colloidal gold nanoparticles into macroscopic aggregates using DNA as linking elements[29] involves attaching non-complementary DNA oligonucleotides

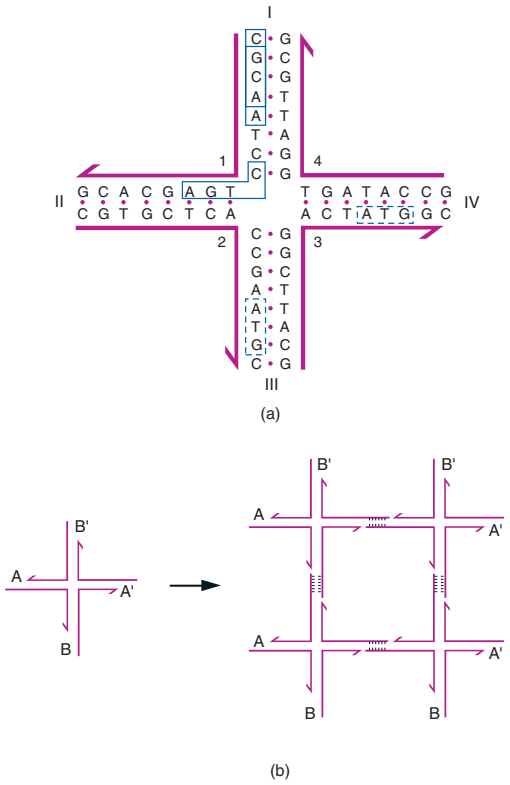

Fig. 4. (a) A four-armed stable branched junction made from DNA molecules, (b) use of the branched junction to form periodic crystals[25]. (Reprinted, with permission, from Nanotechnology, © 1991, p. 149. IOP Publishing Limited, and with kind permission from N. C. Seeman.)

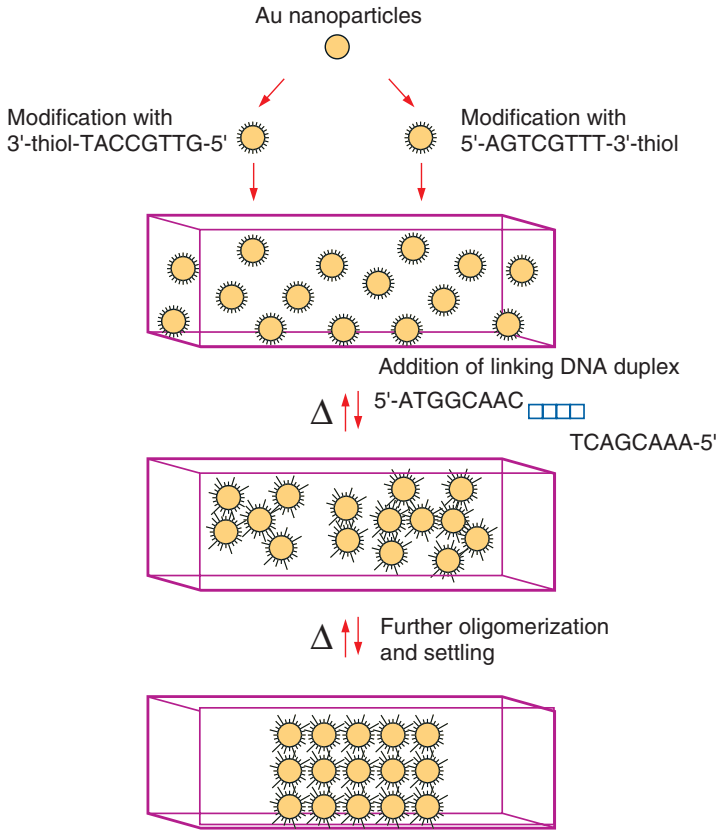

Fig. 5. Fabrication process for the aggregated assembly of DNA conjugated gold nanoparticles[29]. (Reprinted, with permission, from Nature ***382*** *p. 607. Macmillan Magazines Limited, and with kind permission from C. Mirkin.)*

to the surfaces of two batches of 13 nm gold particles capped with thiol groups, which bind to gold. When another oligonucleotide duplex with ends complementary to the grafted sequence is introduced, the nanoparticles self-assemble into aggregates. The process flow is shown in Fig. 5 and can be reversed, because of the denaturation of DNA oligonucleotides, when the temperature is increased. Close-packed assemblies of aggregates with uniform particle separations of about 60 Å were demonstrated.

Simultaneously, techniques were reported where discrete numbers of gold nano-crystals are organized into spatially defined structures based on DNA base pair matching[30]. Gold particles, 1.4 nm in size, are attached to either the 3' or 5' of 19 nucleotide long ssDNA codon molecules through the well-known thiol attachment scheme. Then, 37 nucleotide long ssDNA template molecules are added to the solution containing the gold nanoparticles functionalized with ssDNA. The nano-crystals can assemble into dimers (parallel and antiparallel) and trimers upon hybridization of the codon molecules with the template molecule. The ability to choose the number of nucleotides means the gold particles can be placed at defined positions as shown schematically in Fig. 6. transmission electron microscopy (TEM) shows the distance between the parallel and antiparallel dimers is 2.9-10 nm and 2.0-6.3 nm, respectively. These structures could potentially be used for applications such as chemical sensors, spectroscopic enhancers, and nanostructure fabrication. These techniques have been used to devise sensitive colorimetric schemes for the detection of polynucleotides based on distance dependent optical properties of aggregated gold particles in solutions[31].

Mucic *et al.* also describe the construction of binary nanoparticle networks composed of 9 nm and 31 nm citrate-stabilized colloidal gold particles[32]. These particles were coated with different 12-mer oligonucleotides via a thiol bond. When a third DNA sequence (24-mer) complementary to the oligonucleotides on both particles is added, hybridization leads to the association of particles. A large ratio of 9 nm to 31 nm particles results in the formation of

an assembly[32]. Loweth *et al.* present further details of the formation of hetero-dimeric and hetero-trimeric non-periodic nano-cluster molecules based on earlier work of Alivisatos[33]. Showing exquisite control of the placement of 5 nm and 10 nm gold nano-clusters derivatized with ssDNA, various schemes of hetero-dimeric and hetero-trimers were designed and demonstrated using TEM. Nanoparticle DNA-mediated hybridization also forms the basis of genomic detection using colorometric analysis[34]. Hybridization of the target with the probes results in the formation of a nanoparticle/DNA aggregate, which produces a red to purple color change in solution caused by the red-shift in the surface plasmon resonance of the gold nanoparticles. The networks show a sharp melting transition curve allowing single base mismatches, deletions or insertions to be detected. The same approach can be taken on a surface combined with reduction of silver at the site of nanoparticle capture using a conventional flatbed scanner as a reader. Sensitivities 100 times greater than conventional fluorescence based assays have been described[35-38].

Csaki *et al.* used gold nanoparticles (with mean diameters 15, 30 and 60 nm) as a means of labelling DNA and characterizing hybridization on a surface[39,40]. Single strands of DNA are attached to unpatterned gold substrates. Colloidal gold particles labelled with thiolated complementary DNA strands are captured by the strands on the surface. Niemeyer *et al.*[41] also show site-specific immobilization of 40 nm gold nanoparticles which are citrate-passivated and modified with a 5'thiol derivatized 24-mer DNA oligomers. The capture DNA is placed at specific sites using nano-liter dispensing of the solution.

Mirkin and co-workers also demonstrate the formation of supra-molecular nanoparticle structures where up to four layers of gold nanoparticles are produced. The scheme is shown in Fig. 7 where a linking strand can bind the DNA strand, which is immobilized on the surface and a DNA-derivatized nanoparticle[42]. The linking strand can then be used to bind another layer of nanoparticle and a multi-layered network structures can be produced.

Interconnects, wires and other devices

The concepts of DNA-mediated self-assembly of gold nanostructures have been extended to metallic nanowires and rods[43-45]. Though feasible, this has not yet been completely demonstrated. The basic idea is to fabricate gold

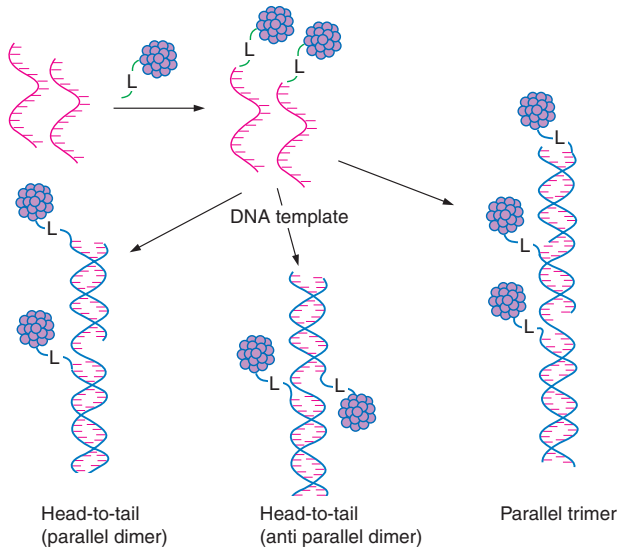

Fig. 6 Assembly of nano-crystals to form dimers and trimers based on DNA hybridization[30,33]. (Reprinted, with permission, from Nature **382** *p. 60 ©1996, Macmillan Magazine Limited, and with kind permission from A. P. Alivisatos.)*

and/or platinum metal wires, functionalize with ssDNA and assemble onto substrates, which have complementary ssDNA molecules attached at specific sites. Self-assembly of interconnects and wires is thus possible. The metallic wires are formed by electroplating in porous alumina membranes (pores sizes of 200 nm)[45]. Processes for the formation of alumina films with nano-hole arrays have been developed and demonstrated[46,47]. Metallic rods, ranging from 1-6 μm in length can be produced, depending on the conditions. The goal is to form platinum rods with gold at the ends or vice versa. More recently, attachment and quantification of ssDNA on the gold ends of the Au/Pt/Au rods has been shown[48]. The rods attach to the substrates only when the DNA strands are complementary. The attachment of the DNA strands is not patterned and the complementary binding of the rods is not site specific. This is, however, the next logical step.

The use of DNA as a template for the fabrication of nanowires has been demonstrated through a very interesting process by Braun *et al.*[49-51]. A DNA bridge is formed, again using thiol attachment, between the 12-16 μm spacing of two gold electrodes. A chemical deposition process vectorially deposits silver ions along the DNA through Ag^+/Na^+ ion exchange and formation of complexes between the gold and the DNA bases (Fig. 8). The result is a silver nanowire formed using the DNA as a template or skeleton. Current-voltage characteristics demonstrate the possible use

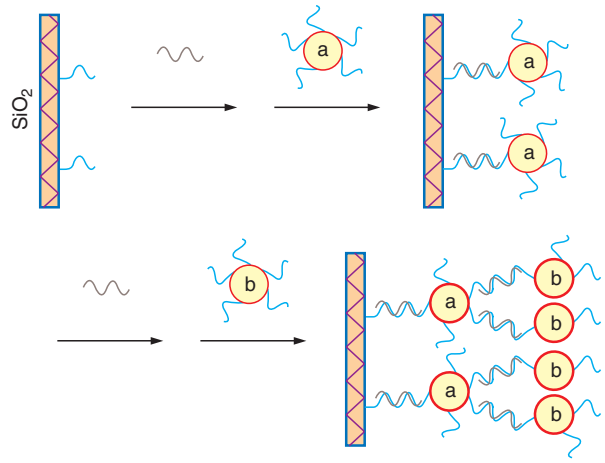

*Fig.7. Synthesis of three-dimensional assembly using DNA and nanoparticles[42]. (Reprinted, with permission, from J. Am. Chem. Soc. **122**, p.6305 © 2000 American Chemical Society, and with kind permission from C. Mirkin.)*

of these nanowires. The formation of luminescent self-assembled poly(*p*-phenylene vinylene) wires for possible optical applications is also possible[51]. The work has potential, but room exists for further research to control the wire width, contact resistances between the gold electrode and the silver wires, and use of other metals and materials. DNA inspired self-assembly of active devices (complementary strands of DNA on a device and a substrate) has been proposed by Heller and co-workers[52] for assembling optical and optoelectronic components on a host substrate, but the basic concept has not been demonstrated yet.

Semiconductor nanoscale quantum dots (QDs) have gained attention in recent years because of the improvement in synthesis techniques, for example CdSe or ZnSe quantum dots of predetermined sizes. The optical properties of these structures have been studied in great detail and have many advantages over conventional fluorophores such as narrow, tunable emission spectrum and photochemical stability. The programmed assembly of such quantum dots using DNA is also possible[66]. Typically these quantum dots are soluble only in non-polar solvents, which makes them difficult to functionalize with DNA by a direct reaction. However, 3-mercaptopropionic acid can be used to passivate the QD surface and act as a pH trigger to control water solubility. DNA-functionalized QDs allow the synthesis of hybrid assemblies with different optical nanoscale building blocks.

The assembly of micro-beads using DNA and the avidin/biotin complex has also been demonstrated. A single strand of capture DNA is first attached to a substrate; a second biotinylated target strand is brought in and if complementary, will hybridize to the first strand exposing the biotin. Next, beads coated with avidin (or related receptors) are exposed to the surface and if the target strand did hybridize then the beads will be captured due to the avidin-biotin interaction. The presence of beads signals the presence of the complementary strands. Fig. 9 shows a schematic of a chip surface where avidin coated polystyrene beads were captured when the DNA strands were indeed complementary[54]. The same scheme can be used to develop detectors for biological warfare agents by attaching the DNA on thin films exhibiting a giant magnetoresistive (GMR) effect. Capture of target DNA and the presence of 1 μm magnetic beads can be detected electrically using GMR sensors[55]. The intensity and location of the signal indicates the concentration and identity of pathogens in the sample.

The charge on the devices can be provided by molecules and that on the substrate by applying a voltage potential, all within a fluid medium. This well-known principle of electrophoresis is used to separate charged molecules and macromolecules according to size. The fixed charges on the devices and objects are generally neutralized by the presence

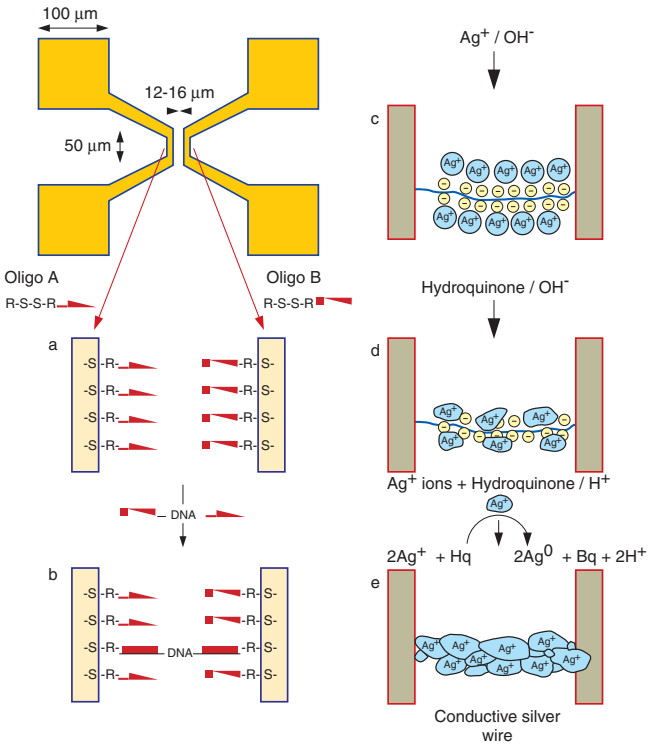

Fig. 8. The process flow for the formation of DNA-directed silver nano-wires[49]. (Reprinted, with permission, from Nature ***391*** *p. 775 © 1998 Macmillan Magazine Limited and with kind permission from E. Braun.)*

of counter-ions in the fluid, but on application of a voltage the molecule is polarized and the charged object moves to one electrode, whereas the counter ions move to the other. Perhaps the most well known example is that of Heller and co-workers[56-59] who showed the electrophoretic placement of DNA capture strands at specific sites on biochips to realize DNA arrays. Subsequent hybridization of fluorescently-labelled target probes at specific sites provides an insight into the sequence of the target probes. These active microelectronic arrays allow electrophoretic fields to perform accelerated DNA hybridization reactions and improve selectivity for single nucleotide polymorphism (SNP), short tandem repeat (STR), and point mutation analysis[60]. Generating electric fields at the micro-scale allows charged molecules (DNA, RNA, proteins, enzymes, antibodies, nanobeads and even micron-scale semiconductor devices) to be transported electrophoretically to or from any micro-scale location on the planar surface of the device[61]. Recently, silicon-on-insulator (SOI) wafers have been used to fabricate trapezoidal shaped silicon islands, 4 μm x 4 μm at the top and 8 μm x 8 μm at the base with a thin gold layer on one side[62,63]. The gold surface is functionalized with 4-mer DNA or a charged molecule (2-mercaptoethane sulfonic acid sodium salt) to provide negative charges on the islands[64]. Releasing the islands from the substrate into a fluid medium over an electrode array allows manipulation at the micro-scale using voltages applied at the electrodes (Fig. 10). The molecules provide negative charges on the devices, allowing the electrophoretic transport to specific sites.

Bio-inspired 'active' device assembly

Much has been accomplished in the last ten years towards the biologically-mediated assembly of artificial nano- and microstructures. Nevertheless, a great deal remains to be done to bridge the gap between electronic devices that will be constructed on a 20-50 nm scale within the next ten years and molecules of a few nanometers or less in size.

A large amount of work has been done on assembly of passive electronic components and devices (gold clusters, metal rods, etc.) and on optical devices (QDs). Lately, there are more reports of assembly of carbon nanotubes and quantum wires, which can be used as active devices. The processes for self-assembly of active devices such as semiconductor transistors[2,3], carbon nanotubes [65,66], silicon quantum wires[67,68], needs to be pursued more actively.

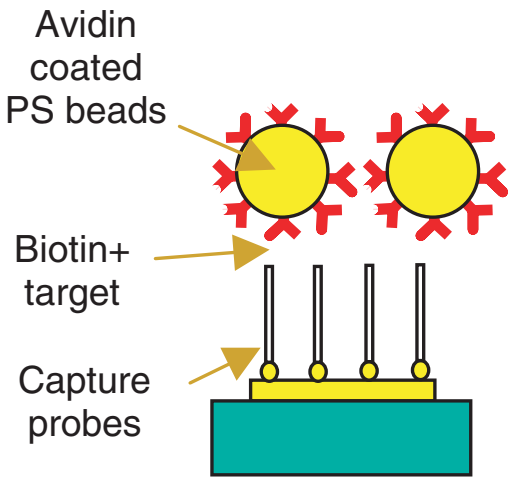

Fig. 9. Schematic representation of avidin coated polystyrene beads collected on biotinylated DNA on a gold pattern on oxide surface[54].

As an example, the entire foot-print of a current silicon CMOS transistors in production, with W/L = 0.8 μm/0.15 μm, is less than 1.1 μm on a side. Can such active devices of such sizes be assembled in two- and three-dimensions using bio-inspired assembly using DNA? The active devices should include scaled-down silicon transistors and nanowires, as well as related materials and carbon nanotubes. Can silicon nanowires and/or carbon nanotubes be assembled into regular arrays for memory and logic applications? Currently, these one-dimensional devices are either placed one at a time at desired sites by AFM tip manipulation or grown at specific sites. If hundreds of thousands of these devices are to be used in a circuit, self-assembly using linker molecules is attractive. It is also important to note that for use in future scaled nanoelectronic systems, interconnects as well as devices will be needed. This direction of research will result in heterogenous integration of material at the micro- and nanoscale.

New devices and switches

In the recent years, possible candidates for molecular-scale electronics have been developed such as rotaxane[69] and nitroaromatic[70]. As the search for molecular devices continues, DNA could also provide possible solutions.

There are no active device concepts using DNA itself, but the electronic properties are being studied. Even though there are contradictory measurements of DNA conductivity[71], recent reports show that DNA measured between two electrodes behaves like a large band-gap semiconductor[72]. Resistance in the conductive regime is of the order of

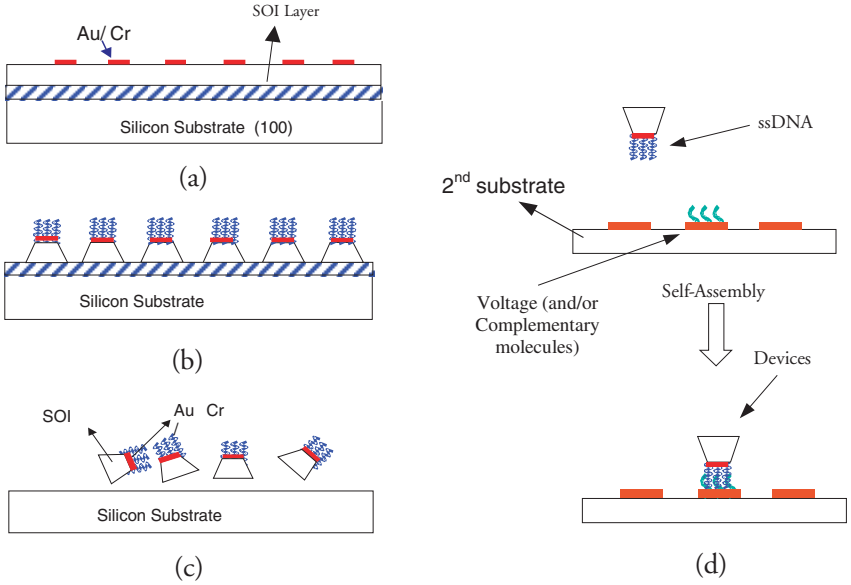

Fig. 10. Process flow for active device fabrication, release, and self-assembly: (a) define patterns of Au/Cr contacts on an SOI wafer; (b) etch the silicon down to the buried oxide and attach molecules (DNA, etc.) to the top layer; (c) release the islands (devices) from the substrate and collect/concentrate; (d) assembly of the devices on another surface with voltage (or the complementary ssDNA). (Adapted from[64].)

40 x 10^9/100 Å long molecule. The ideas assume that DNA behaves as a conductor in specific voltage/current regimes. The specificity of the Watson-Crick base pairing is an interesting and useful property that can be exploited to propose novel DNA-based interconnect functionalities and devices. Denaturing two complementary strands of DNA can be used to make a DNA-based switch (Fig. 11). Two gold electrodes are defined and thiol-derivatized ssDNA attached to each electrode such that parts of these strands have a complementary sequence. Once the two molecules have hybridized, current can be passed between the two electrodes. If joule heating from the current increases the temperature of the molecule above T_m, the strands denature and current flow stops. An external heater lithographically defined under the two electrodes (as shown) can also be used to increase the temperature. The hybridization can be direct (as shown), or indirect where a third DNA strand is used to connect the first two strands.

The denaturing phenomenon could also provide a basis to realize DNA-based devices with characteristics suitable for functional elements. If heating is produced by current flow through the DNA strands, a negative differential resistance device may be possible. Such a device could also be used to form an oscillator. Two strands that have denatured upon internal or external heating, could rejoin as a result of diffusion in a certain time, given some thermal energy. Thus strands denature on heating, cool when there is no current flow, and then hybridize again once in close proximity to

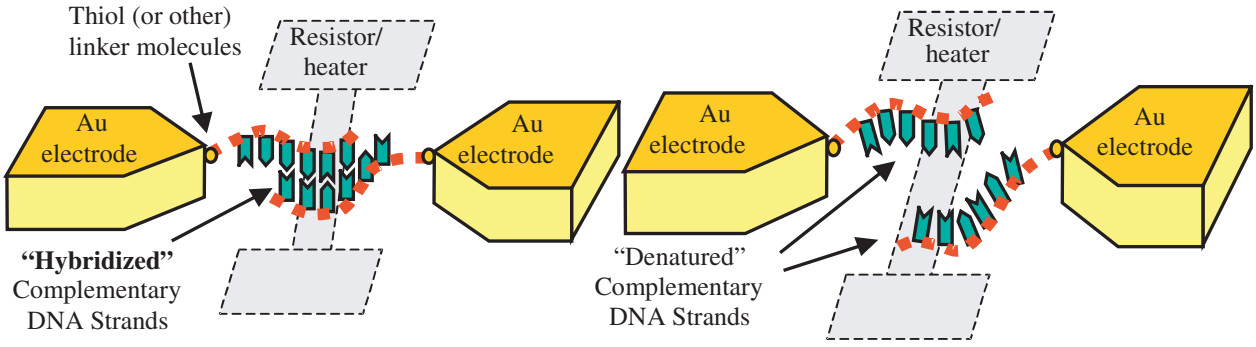

Fig. 11. (a) Single stranded DNA attached to each electrode using a linker molecule, (b) if $I > I_{critical}$, Joule heating will result in $T > T_m$(DNA), which will denature the DNA and the current flow will stop flowing. Alternatively, the temperature around the DNA strand can also be increased above T_m by a metal heater/resistor.

each other. The rehybridization might be slow at first examination since it is controlled by diffusion. However, since the molecules are in such close proximity, the time for rehybridization might not be as slow as expected.

Conclusion

The field of nanotechnology has emerged as one of the most important areas of research and DNA-mediated self-assembly has the potential to profoundly impact this field. The ability to choose the sequence of nucleotides and hence provide addressability during the self-assembly processes makes DNA an ideal molecule for these applications. MT

Acknowledgments

The author would like to acknowledge many valuable discussions with Prof. D. Janes, Prof. D. Bergstrom (Co-PI with the author on NSF funded active device self-assembly project), Prof. M. Lundstrom, and Prof. S. Datta. The author would like to thank Mr. S. Lee, Dr. H. Mcnally, Mr. D. Guo, and Dr. M. Pingle for results, assistance with references, and manuscript review. The author would also like to acknowledge funding from the National Science Foundation, State of Indiana, and Center of Nanoscale Electronic Devices at Purdue University.

REFERENCES

1. Geppert, L. (2000) *IEEE Spectrum* **37** (1) p.63
2. *The National Technology Roadmap for Semiconductors (NTRS)* (1997) SIA
3. *The International Technology Roadmap for Semiconductors (ITRS)* (1999) SIA
4. Alberts, B. *et al. Molecular Biology of the Cell, 3rd Edition*, Garland Publishing, N.Y.
5. http://alphadna.com/, http://www.biosyn.com/, http://www.genemedsyn.com/
6. Nuzzo, R. G. and Allara, D. L. (1983) *J. Am. Chem. Soc.* **105**, p.4481
7. Bain, C. D. and Whitesides, G. M. (1989) *Agnew. Chem. Int. Ed. Engl.* **28** (4) 506
8. Bain, C. D. *et al.* (1989) *J. Am. Chem. Soc.* **111**, p.321
9. Dubois, L. and Nuzzo, R. G. (1992) *Ann. Rev. Phys. Chem.* **43** p.437
10. Hickman, J. J. *et al.* (1992) *Langmuir* **8** p.357
11. Tour, J. M., *et al.(1999) J. Am. Chem. Soc.* **117**, p.9529
12. Weisbecker, C. S. *et al.* (1996) *Langmuir* **12** p.3763
13. Nelles, G., H. *et al.*(1998) *Langmuir* **14** (4) p.808
14. Jung, C. *et al.* (1998) *Langmuir* **14** (5) p.1103
15. Tarlov, J. M. and Newman, J. G. (1992) *Langmuir* **8** p.1398
16. Peterlintz, K.A. *et al.*(1997) *J. Am. Chem. Soc.* **119** p.3401
17. Herne, T. M., and Tarlov, M. J.(1997) *J. Am. Chem. Soc.* **119** (38) p.8916
18. Steel, A. B. *et al.* (1998) *Analytical Chemistry* **70** p.4670
19. Yang, M., *et al.* (1998) *Langmuir* **14** p.6121
20. Madhukar, A. *et al.* (1994) *Appl. Phys. Lett.* **64** (20) p.2727
21. Moison, J. M. *et al.* (1994) *Appl. Phys. Lett.* **64** (2) p.197
22. Kamins, T. I. *et al.* (1997) *J. Appl. Phys.* **81** (1) p.211
23. Bashir, R. *et al.* (1999) *Applied Surface Science* **152** p.99
24. Seeman, N. C. (1982) *J. Theor. Biology* **99** p.237
25. Seeman, N. C. (1991) *Nanotechnology* **149**
26. Seeman, N. C. *et al.* (1993) *J. Vac. Sci. Technol. A* **12** p.1895
27. Winfree, E. *et al.* (1998) *Nature* **394** p.539
28. Seeman, N. C. (1998) *Annual Rev. Biophys. Biomol. Struc.* **27** p.225
29. Mirkin, C. A. (1996) *Nature* **382** p.607
30. Alivisatos, A. P. *et al.* (1996) *Nature* **382** p.609
31. Elghanian, R. *et al.* (1997) *Science* **277** p.1078
32. Mucic, R. C. *et al.* (1998) *J. Am. Chem. Soc.* **120** p.12674
33. Loweth, C. J. *et al.* (1999) *Agnew. Chem. Int. Ed.* **38** (12) p.1808
34. Storhoff, J. J. *et al.* (1998) *J. Am. Chem. Soc.* **120** p.1959
35. Taton, T. A. *et al.* (2000) *Science* **289** p.1757
36. Andres, R. P. *et al.* In: (1998) *The Handbook of Nanostructured Materials and Nanotechnology*, Academic Press
37. Niemeyer, C. M. (1999) *Appl. Phys. A.* **69** p.119
38. Storhoff, J. J. and Mirkin, C. A. (1999) *Chem. Rev.* **99** p.1849
39. Csaki, A. *et al.* (2001) *Nucleic Acid Research* **29** (16) p.81
40. Reichert, J. *et al.* (2000) *Analytical Chemistry* **72** p.6025
41. Niemeyer, C. M. *et al.* (2001) *Colloid Polymer Science* **279** p.68
42. Taton, T. A., *et al.* (2000) *J. Am. Chem. Soc.* **122** p.6305
43. Huang, S. *et al.* (1999) *41st Electronic Materials Conference Digest* p.41
44. Martin, B. R. *et al.* (1999) *Adv. Mater.* **11** (12) p.1021
45. Mayer, T. S. *et al.* (1999) Materials Research Society Fall Meeting Digest p.157
46. Masuda, H. and Fukuda, K. (1995) *Science* **268** p.1466
47. Li, A. P. *et al.* (1998) *J. Appl. Phys.* **84** (11) p.6023
48. Mbindyo, J. K. N. *et al.* (2001) *Advanced Materials* **13**(4) p.249
49. Braun, E. *et al.* (1998) *Nature* **391** (19) p.775
50. Eichen, Y. *et al.* (1998) *Acta Polym.* **49** p.663
51. Braun, E. *et al.* (1998) *24th International Conf. on the Physics of Semiconductors* p.269
52. Ackley, D. E. et al. (1998) *Proc. - Lasers and Electro-Optics Society, Annual Meeting-LEOS* **1** p.85
53. Mitchell, G. P. *et al.* (1999) *J. Am. Chem. Soc.* **121** p.8122
54. Mcnally, H, and Bashir, R., unpublished results
55. Edelstein, R. L. *et al.* (2000) *Biosensors & Bioelectronics* **14** (10)
56. Heller, M. J. (1996) *IEEE Engineering in Medicine & Biology Magazine* **15** (2) p.100
57. Sosnowski, R. G. *et al.* (1997) *PNAS* **94** (4) p.1119
58. Huang, Y. *et al.* (2001) *Analytical Chemistry* **73** (7) p.1549
59. http://www.nanogen.com
60. Heller, M. J. *et al.* (2000) *Electrophoresis* **21** (1) p.157
61. Fan, C. (1997) *SPIE-Int. Soc. Opt. Eng. Proceedings of SPIE* **2** p.3290
62. Bashir, R. et al. (2000) *Proc. of the MRS Fall Meeting, Boston, MA., 2000*
63. Bashir, R. (2001) *Superlattice and Microstructures* **29** p.1
64. Lee, S. *et al.* Submitted to *APL*
65. Derycke, V. *et al.* (2001) *NanoLetters* **1** (9) p.453
66. Liu, J. *et al.* (1999) *Chemical Physics Letters* **303** p.125
67. Huang, Y. *et al.* (2001) *Science* **291** p.630
68. Cui, Y. and Lieber, C. M. (2001) *Science* **291**, p.851
69. Collier, C. P. (1999) *Science* **285** p.391
70. Chen, J. *et al.* (1999) *Science* **286** p.1550
71. Fink, H-W. and Schonenberger, C. (1999) *Nature* **398** p.407
72. Porath, D. *et al.* (2000) *Nature* **403** p.635