0273-2289/01/9601-3/0279/$12.00

Biomolecular Electronics in the Twenty-First Century

Ratna S. Phadke*

TIFR, Mumbai, India 400005, E-mail: ratna@tifr.res.in

Abstract

A relentless decrease in the size of silicon-based microelectronics devices is posing problems. The most important among these are limitations imposed by quantum-size effects and instabilities introduced by the effects of thermal fluctuations. These inherent envisaged problems of present-day systems have prompted scientists to look for alternative options. Advancement in the understanding of natural systems such as photosynthetic apparatuses and genetic engineering has enabled attention to be focused on the use of biomolecules. Biomolecules have the advantages of functionality and specificity. The invention of scanning tunneling microscopy and atomic force microscopy has opened up the possibility of addressing and manipulating individual atoms and molecules. Realization of the power of self-assembly principles has opened a novel approach for designing and assembling molecular structures with desired intricate architecture. The utility of molecules such as DNA as a three-dimensional, high-density memory element and its capability for molecular computing have been fully recognized but not yet realized. More time and effort are necessary before devices that can transcend existing ones will become easily available. An overview of the current trends that are envisaged to give rich dividends in the next millennium are discussed.

Index Entries: Biomolecular electronics; molecular electronics.

Introduction

Feynman *(1)* predicted that ultimately a device will need to be of the dimensions of a functional molecule in order to meet increasing demands for high-density, more-efficient, low-consumption devices. Microelectronics is one of the best scientific developments of the twentieth century. This technology revolves around bulk properties of inorganic materials. In the last decade, the technology has matured quickly and has influenced and enriched every facet of life. The dimensions of active components are becoming half of their previous size every couple of years, and the capabilities

*Author to whom all correspondence and reprint requests should be addressed.

of individual components are improving rapidly. However, this trend toward smaller and faster devices is becoming increasingly difficult and costly *(2,3)*. Moore's law predicts saturation in the reduction in size, which will put an ultimate limit on the advancement in microelectronics. Apart from this, the limitations imposed on the reliability of nanometer-sized components by quantum size effects and thermal fluctuations encountered in microelectronics point toward the need for a new technology: molecular/biomolecular electronics *(4–16)*. Thus, the genesis of biomolecular electronics is microelectronics.

The demand for greater information storage capacity and the preference for three-dimensional design for memory devices, on the one hand, and the inadequacy of meeting requirements for pattern recognition, parallel processing, and acquiring self-learning as well as self-repair capabilities, on the other hand, are prompting developments in new directions other than silicone technology. Recent developments in nanotechnology such as addressing a single molecule/atom using atomic force microscopy, scanning tunneling microscopy, and developments in molecular biology such as genetic engineering, protein engineering, and supramolecular chemistry have been bold leaps for the field of science *(17–20)*. Moreover, the advent of diverse disciplines such as chemistry, biology, physics, and engineering is converging toward a molecular phenomenon. As a consequence, several adventurous attempts are being made and are reported in a variety of journals.

As an obvious choice, one tries to get clues from nature. Biologic analogies are likely to suggest the design and development of novel structures and algorithms to achieve functions that could not be readily accomplished by computing devices of current designs. The bacterial photosynthetic reaction center in *Halobacterium salanerium* has a physical dimension of $3 \times 7 \times 130$ nm *(21)*. It consists of four protein subunits and 14 prosthetic groups forming a supramolecular structure with twofold symmetry. The function of the reaction center is to convert absorbed photon energy to electrical energy in the form of charge separations followed by conversion into the energy-rich compound adenosine triphosphate, the currency of living systems. Noteworthy is that the constituent molecules not only need to be specifically selected, but also need to occupy strategic positions with respect to one another for manifestation of optimum performance. The most advanced machinery of nature—living systems—operate with functional components such as molecules (or molecular assemblies with well-defined architecture) that actually exploit quantum-size effects. It has systems that can exhibit efficient energy and charge transfer. Not all the natural processes are fast, but the complex multiply connected structures of neural networks provide a performance for parallel processes, such as image and speech recognition, far beyond the capabilities of the largest supercomputer. Such examples can provide guidelines for future research. However, success will come only when a multidisciplinary approach is adopted and crossfertilization of ideas is readily spanned. Accomplishing a radical

departure from existing technologies cannot be attempted in a single quantum leap. This has to grow through the innovative though slow path of evolution. Initially, it appears to aim at allowing silicon devices to do whatever they can do best and allowing special functionality of molecules (bio/organic) to be incorporated into existing devices. This warrants techniques for creating and thoroughly understanding the physics and chemistry of interfaces between the organic/bio world and active silicon surfaces.

Historical Background

Biomolecular/molecular electronics is a relatively recent scientific endeavor that was put forward by Dr. Forrest Carter of the US Naval Research Laboratory in 1981. The same year, quickly realizing the importance, Japan established the Research and Development Association for Future Electron Devices. Initially, the subject was being discussed in international symposia consecutively held in Budapest, Moscow, and New York under the name International Conference on Molecular Electronics and Biocomputing. A formal organization, International Society for Molecular Electronics and Biocomputing, was formed in 1990 in Budapest. Subsequently, meetings were held at NIST, Gaithersburg (United States), Goa (India), Okinawa (Japan), and Nanjing (China) that could provide a common forum for scientists from different disciplines. Parallel to this, several conferences organized in the United States and Europe were having biomolecular/molecular electronics as a theme.

Scope

Biomolecular electronics has emerged in order to alleviate bottlenecks encountered during the march of microelectronics toward miniaturization and represents a challenge on all fronts. It is difficult to predict the course of research for a new century. However, in short-term perspectives, molecular materials have great promise for potential applications in electronics; optoelectronics; nonlinear optics; and conductive, piezo-, and pyroelectric materials. Future devices are envisaged to evolve as a result of confluence of different disciplines—basic sciences (e.g., physics, chemistry, biology), engineering sciences, and even medical sciences. Different components originating from biomolecules and microelectronics will operate in concert to have efficiencies and performance that can transcend the existing ones. As a consequence, terms such as *DNA computing*, *neural-network systems*, *single molecular detection*, *molecular rectifiers*, and *intelligent/smart materials* will be a reality.

The research is envisaged to progress in two directions: improvement/tailoring of molecular materials for existing applications, and realization/development of new uses for molecular materials. In either case "molecule" will be the basic building block. However, bio/organic molecules are perceived to be mechanically fragile, physically labile, and chemically unstable. It is therefore essential to devise carefully planned methodolo-

gies to overcome or circumvent these problems. Moreover, one has to take into account the fact that a single molecule lacks exit paths for dissipation of possible excess in energy used for addressing.

Strategies

Organic/bio molecules are an obvious choice because these are imbued with unique combinations of chemical and physical properties that are the result of their built-in conformational and functional diversity. This has been gainfully supplemented by recent developments in supramolecular chemistry and thin film fabrication technology, because often the organic/bio molecular materials are not readily amenable to requirements of device-fabrication capabilities and require tailoring. To optimize macroscopic/mesoscopic properties and address a single molecule or mesoscopic aggregate of molecules, it is necessary to assemble these in films of nanometer thickness. Realizing this importance, researchers have increased studies in the field of thin organic films in the last 5 yr or so. The Langmuir-Blodgett (LB) technique has been utilized for the last several years *(22)*. In addition, several techniques such as self-assembly (a hallmark of living systems), spin coating, vacuum deposition, laser-assisted deposition, dip drying, and vertical descent of monolayers are being utilized and perfected *(23–28)*.

Types of Devices

The envisaged devices can be divided into the following categories:

1. Molecular-Scale Devices (~nm): A single appropriately tailored molecule or a supramolecular complex can act as a device, e.g., a rectifier, diode, switch, or memory element.
2. Molecular Functional Devices: Unique functions of molecules such as recognition, conformation, and self-assembly will be exploited for designing devices such as biosensors and memories.
3. Biodevices: Biological systems such as cells, neurons, and ion channels will form the basis of information-processing systems, systems capable of signal transduction. These may be in the remote future "harvested" with the advent of modern biology and genetic engineering.

Methodology

A molecular device consists of individual molecules of different types interacting in a purposeful manner and devoid of excessive redundancy commonly encountered in "natural" devices. Device fabrication requires several steps:

1. Selection of the molecule, which is dictated by the end function.
2. Tailoring/molecular engineering, which is crucial for assembling selected molecules in well-defined architecture. This can be achieved

following two different routes: synthetic approach or genetic/protein engineering.
3. The molecules need to be assembled with well-defined predesigned architecture. Physical or chemical techniques can be utilized.
4. Networking of different functional regions in correct sequence is mandatory for successful addressing, storing, and retrieving of stored information as well as computational accuracy and efficiency.
5. Interfacing with the macroworld. Input/output paths should be well defined, accurate, and imbued with ease of operation.

It is possible to fine-tune the functionality and incorporate adaptability to the environment. Moreover, the functional molecules can be embedded and not immobilized in the active matrix. In fact, a single molecule can be made self-sufficient by incorporating in it a donor separated with a spacer from an acceptor unit. The spacer prevents spontaneous transfer of electrons and mediates actuated transfer.

Several techniques, such as LB, vertical descent of monolayer, and laser-assisted deposition self-assembly, are being developed. Neuronal networking is being investigated for attaining flexibility of interconnections. Characterization after each step is absolutely essential for efficient functioning of the device. The rich repertoire of organic/bio molecules and their multitude of structures and reactions open up possibilities for designing information storage devices based on conformational change, dimerization/monomerization, *cis-trans* isomerization, charge transfer, intra- or intermolecular hydrogen transfer, and benzoid-quinode transformation. Noteworthy is that these transformations take place at the expense of low energies (a few kilocalories). Addressing need not be done only electrically. However, chemical, optical options will be readily available. The operation of the device is not envisaged to be linked with motion of electrons or holes as in microelectronics, but protons, ions, photons, solitons, and polarons will be equally important. In short, the name *electronics* is merely a generic name, and *electrons* should be looked on as representative of charge carriers in general.

In summary, numerous attempts are being made, some of which are discussed below. However, it is impossible to give an exhaustive review because the field is exploding with innumerable reports of direct and indirect relevance. We discuss only a few with the intention of arousing interest in the minds of researchers. Note that omission of an important issue is not intentional.

Recent Developments

The first successful manifestation of a molecular device is the liquid crystal display. Modest power is needed to reorient the molecules. However, these devices display fatigue after repeated use and are sensitive to the environment. Efforts are under way to make more-efficient and fatigue-free devices. Incorporation of liquid crystal compounds into LB films is also

of considerable interest because the basic optical principle behind the liquid crystal display is the controlled rotation of optical polarization. Attempts made to increase the stability by incorporating liquid crystals in LB film followed by subjecting to ultraviolet irradiation are promising *(29)*.

Thin films form the basis of a nanoscale device. Self-assembly has the advantage of synthetic economy. Unless the molecules do not recognize each other, they will not assemble. Also for the same reasons faults will be minimal. Appropriate positioning of different sets of molecules can be attained by controlling growth conditions while preparing thin films.

It has been demonstrated that organic dye molecules in mono- or multilayers can act as photosensitizers for photoelectric conversion of solar energy or photographic recording *(30,31)*. For integrated optics, LB films provide polar arrangements that can realize the potential of designed molecular units, but they suffer from scattering and time-consuming multiple dipping to produce films of useful thickness. Polymer films are becoming increasingly popular, with active pendent groups for second-order nonlinearity and conjugated backbones for third-order effects. Although nonlinear-optical coefficients achieved are less than those for crystals and LB films, this disadvantage is counterbalanced by greater ease of fabrication. It has been demonstrated that conducting organic polymers can form an active part of electronic devices such as Schottky-type diodes and metal-insulator-semiconductor field-effect transistors. Recently, it has been demonstrated that organic-inorganic hybrid semiconducting channels can be used to form oriented molecular-scale composites to make field-effect transistors. These, with appropriate molecular engineering, are expected to help develop high performance, low cost devices *(32)*. Efforts are being made to use metallated phthalocyanine-based thin film transistors *(33)*.

Self-assembled monolayers have become an essential requirement for molecular devices. Insulating characteristics of self-assembling molecules are being used for generation of well-defined tunnel junctions in quantum dot arrays *(34)* and field-effect transistors *(35)*.

Bacteriorhodopsin has been reported to have been used for making imaging devices, such as Biochrom films, high-speed dynamic RAM, dynamic holograms, and artificial photoreceptors, that are sensitive to the motion of objects. Recently, a protein called amelogenin, which is isolated from rodent's tooth enamel, has been reported to exhibit qualities more suitable for producing more-efficient and reliable protein-based chips than anything developed earlier *(36)*.

Single-wall carbon nanotubes have long been professed to play a key role in molecular electronics *(37)*. Possibly, an important step further in this direction is growing Y-junction carbon nanotubes *(38)*.

Nanomagnetic materials are known to easily reverse their magnetic moments and, hence, are widely used in information storage devices *(39)*. Recently, it was reported that simple molecule-based systems derived from

Prussian blue are capable of switching long-range magnetic properties when light of different wavelengths is shined on it *(40)*. This is likely to facilitate production of three-dimensional molecular memory devices.

The proposition put forth earlier that a single molecule can act as an electrical current rectifier has been recently shown to be a reality *(41,42)*. Similar endeavors will form the basis for future research and fabrication of devices.

Future Directions

With such a wide range of possibilities, we should expect to see something new on the market soon. In years to come, the mainframe of computing devices may not have a static solid-state rigid structure but could be a dynamic fluid one as long as the input/output are deterministic.

Microfabricated devices for biomedical applications have been vehemently proposed for the last 5 yr. Pronouncement of the potential of this technology for analytical purposes to facilitate biodiagnostics is often heard, but actual demonstrations of the capabilities are few. However, it is important to devise a microchip having an integrated sample preparation, reaction, and a detection chip rather than one that can detect nanoliter quantities.

References

1. Feynman, R. (1991), *Science* **254,** 1300.
2. Keyes, R. W. (1975), *Proc. IEEE* **63,** 740–767.
3. Chiabrera, A., Di Zitti, E., Costa, F., and Bisio, G. M. (1989), *J. Phys. D: Appl. Phys.* **22,** 1571–1579.
4. Carter, F. L. (1982), *Molecular Electronic Devices*, Marcel Dekker, NY.
5. Carter, F. L. (1987), *Molecular Electronics Devices II*, Marcel Dekker, NY.
6. Carter, F. L., Saitkowski, R. E., and Wohitjen, H. (1988), *Molecular Electronics Devices*, North-Holland, Amsterdam.
7. Biczo, G. and Rajczy, P. (1989), *J. Mol. Electron.* **4,** 5.
8. Birge, R. R. (1990), *Annu. Rev. Chem.* **41,** 683–733.
9. Hong, F. T. (1989), *Molecular Electronics: Biosensors and Biocomputers*, Plenum, NY.
10. Ashwell, G. J. (1992), *Molecular Electronics*, John Wiley & Sons, NY.
11. Aviram, A. (1992), *Molecular Electronics: Science and Technology*, American Institute of Phys, NY.
12. Hong, F. T. (1994), *IEEE Eng. Med. Biol.*
13. Aluwalia, A. and Phadke, R. S. (1995), *Mater. Sci. Eng. C3* **3,** 4.
14. Phadke, R. S. (1995), *Cond. Matter News* **4,** 18–21.
15. Phadke, R. S. (1995), *Ind. J. Pure Appl. Phys.* **33,** 583–586.
16. Bloor, D. (1991), *Nature* **349,** 738–740.
17. Binning, G. and Rohrer, E. A. (1985), *Sci. Am.* **253,** 50–56.
18. Old, R. W. and Primrose, S. B. (1980), *Principles of Gene Manipulation*, Blackwell Scientific, UK.
19. Ikehara, M., Titani, K., and Oshima, T., eds. (1990), *Protein Engineering, Protein Design in Basic Research, Medicine and Industry*, Springer-Verlag, Tokyo.
20. Lehn, J. M. (1988), *Ang. Chem. Internat. Eddi.* **27,** 89–112.
21. Oesterhelt, D. and Stoeckenius, W. (1971), *Nature (Lond.), New Biol.* **233,** 149.

22. Roberts, G. G. (1990), *Langmuir-Blodgett Films*, Plenum, NY.
23. Ulman, A. (1991), in *An Introduction to Ultra-Thin Organic Films: From Langmuir-Blodgett to Self-Assembly*, Academic, San Diego, CA.
Ulman, A., ed., (1995), *Thin Films, Organic Thin Films and Surfaces: Directions for the Nineties*, vol 20, Academic, San Diego, CA.
24. Patel, A. B. and Phadke, R. S. (1995), *Mater. Sci. Eng. C* **3,** 263–266.
25. Agarwal, G. and Phadke, R. S. (1996), *Supramol. Sci.* **3,** 183–187.
26. Phadke, R. S. and Agarwal, G. (1997), *Mater. Sci. Eng. C* **5,** 237–241.
27. Agarwal, G. and Phadke, R. S. (1998), *Mater. Sci. Eng. C* **6,** 13–17.
28. Agarwal, G. and Phadke, R. S. (1998), *Thin Solid Films* **327,** 9–13.
29. Bardosova, M., Clark, I., Hodge P., Tredgold, R., and Woolley, M. (1996), *Chem. Commun.* 587, 588.
30. Arden, W., Fromherz, P., and Bunsen-Gen, B. (1978), *Phys. Chem.* **82,** 868–874.
31. Fujihira, M., Nishiyama, K., and Yamada, H. (1985), *Thin Solid Films* **132,** 77.
32. Kagan, C. R., Mitzi, D. B., and Dimitrakopoulas, C. D. (1999), *Science* **286,** 945–994.
33. Chaabane, R. B., Guillaud, G., and Gamoudi, M. (1997), *Thin Solid Films* **296,** 145–147.
34. Andre, R. P., et al. (1999), *Science* **273,** 1690.
35. Coller, J. and Vuillaume, D. (1998), *Appl. Phys. Lett.* **73,** 2681.
36. Venkatesh, R. (1999), *Electron. You* May 44–48.
37. Thess, A., et al. (1996), *Science* **273,** 483.
38. Li, C., Papadopoulos, J., and Xu, J. (1999), *Nature* **402,** 253.
39. Kahn, O. (1993), *Molecular Magnetism*, VCH, NY.
40. Sato, O., Iyoda, T., Fujishima, A., and Hashimoto, K. (1996), *Science* **272,** 704.
41. Aviram, A. and Ratner, M. A. (1974), *Chem. Phys. Lett.* **29,** 277, 278.
42. Metzger, R. M., Chen, B., Hopfner, U., et al. (1997), *J. Am. Chem. Soc.* **119,** 10,455.