Aluminum Anodization for DNA Integrated Circuits

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Abstract

Published research has indicated that DNA molecules can be adsorbed on the surface of aluminum electrodes in an electrochemical reaction. Exploitation of this phenomenon with aluminum structures in standard integrated circuits may enable fundamentally new microscale and nanoscale systems based on the foundation of current integrated circuit technology. This proposal outlines an effort to demonstrate and characterize this process using a CMOS microsystem, to be fabricated using the MOSIS service, and low-cost DNA printing equipment.

1 Introduction

Molecular self-assembly is increasingly viewed as a critical enabling technology for the development of nanosystems expected to provide dramatic new benefits and radically new capabilities to individuals. The pervasive use of integrated circuit technology in every aspect of modern life provides motivation for the fullest possible exploitation of standard IC processes for the development of molecular self-assembly and molecular nanotechnology in general. Specifically, this preeminence of IC technology, and complementary metal-oxide-semiconductor ICs in particular, justifies a detailed characterization and thorough understanding of molecular adsorption processes on materials present in CMOS integrated circuits, as molecular adsorption on solid surfaces is a fundamental process in the integration of molecules and molecular systems with solid-state technology.

Aluminum alloy is the primary material used to conduct electricity in CMOS integrated circuits. It is well known that aluminum can be coated with an oxide film, in an electrochemical process called anodization, to alter its appearance or mechanical properties, although this coating is usually performed on macroscopic aluminum objects. From the standpoint of micro- and nanofabrication, the anodic aluminum oxide film itself has been the primary focus of contemporary research, as it forms an ordered nanoporous structure under a wide range of processing conditions[1, 2].

When aluminum is anodized in an aqueous solution containing acids such as phosphoric, sulfuric, or carboxylic acid, the molecular acids are incorporated into the film, forming an electrochemical bond with the oxidized aluminum atoms. This incorporation of molecules present in the anodizing bath is key to the modification of the appearance, and other properties, of anodized aluminum. While anodization of aluminum by small-molecule acids is a routine process, the use of macromolecular acids for aluminum anodization is largely unexplored.

Deoxyribonucleic acid is perhaps the most important example of a macromolecular acid. In the course of experiments on the manipulation of DNA molecules by time-varying electric fields generated by aluminum microelectrodes, one group has demonstrated DNA adsorption on aluminum[3]. Their research has provided support for the hypothesis that, by applying a voltage to an aluminum microelectrode, one end of a DNA molecule can be anchored to the aluminum surface, with the other end extending from the surface. Despite the fact that this research has largely been ignored in the years since it was first published, it is best perceived as a tantalizing glimpse of opportunity.

The unique molecular properties of DNA, in addition to its obvious ubiquity, make DNA molecules a natural component of molecular self-assembly processes. The incorporation of DNA molecules into CMOS integrated circuits, using aluminum anodization, potentially presents the opportunity to use standard IC technology as the foundation for complex self-assembled nanosystems.

In the following, we propose an effort to characterize DNA adsorption on aluminum microelectrodes. The proposed research is focused on the design, fabrication, operation, and physical analysis of a CMOS microsystem for performing anodization and controlling hybridization with microelectrode arrays.

After a more detailed description of the evidence for DNA adsorption on aluminum, we provide further motivation for the proposed research by briefly describing some applications of DNA hybridization on standard integrated circuits. This is followed by a description of the CMOS microsystem to be created for the performance of the proposed research, along with a description of the fluidic system necessary for performing electrochemical processing, using DNA solutions, on the surface of the proposed CMOS microsystem.

2 Prior Work and Future Possibilities

2.1 DNA manipulation by Al microelectrodes

One early effort to manipulate cells and molecules using microfabricated electrodes[4], called the fluidic integrated circuit by its creators, used aluminum evaporated onto glass and patterned to form electrodes, which created an electric field when a voltage was applied to the opposing electrodes (see Figure 1). In the presence of a spatially nonuniform electric field, polarizable cells and molecules experience a force in the direction of increasing electric field magnitude, a phenomenon called dielectrophoresis[5]. During experiments to characterize the response of DNA molecules, 48.5kbp (kilo base pairs) in length, to intense (approximately 1MV/m) AC (1MHz) electric fields[6, 7], it was discovered that DNA molecules, which have a random coil conformation in solution, are stretched straight along the field lines. It was also observed that the stretched DNA molecules rapidly migrated to the region of highest field strength by dielectrophoresis, until one end of the stretched molecule contacted the surface of the aluminum electrode. Using fluorescent DNA labels, it was determined that, while one end was anchored at the surface of the electrode, the rest of the molecule extended into the solution. Later investigations used atomic force microscopy to confirm that DNA molecules were adsorbed on the surface of the electrodes[8].

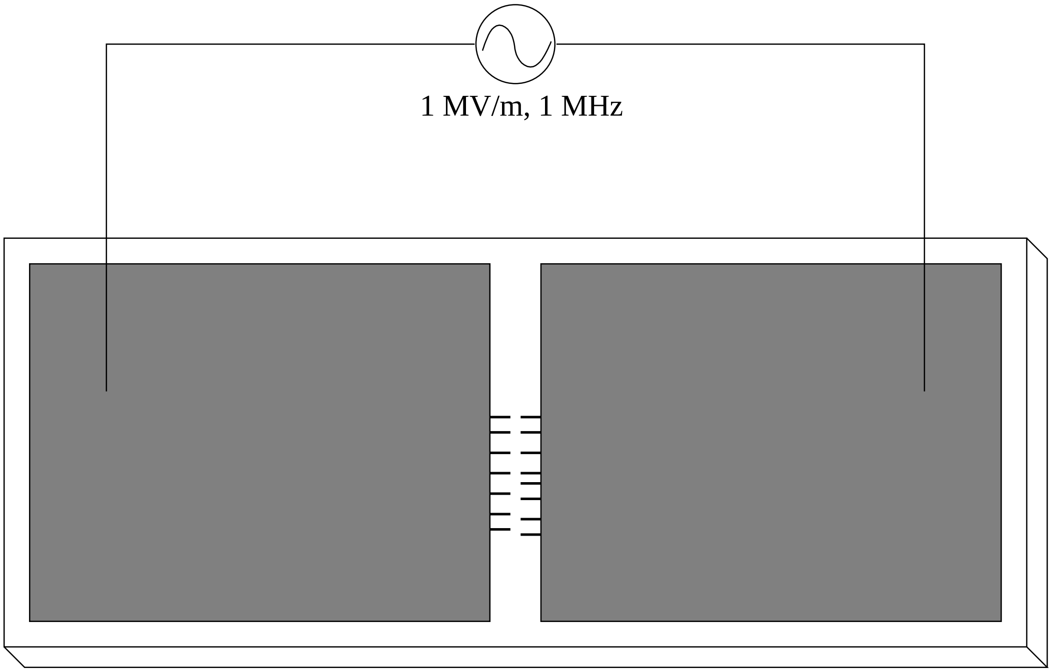

Figure 1: Early demonstration of DNA-aluminum adsorption: Aluminum electrodes evaporated onto a glass cover slip, with an interelectrode spacing of 80 microns. When a 1MHz AC voltage is applied to the electrodes to create an electric field of approximately 1MV/m, DNA molecules (solid lines between electrodes) rapidly migrate to the highest-field region and attach to the electrode surfaces.

While these investigations were important in understanding the interaction of DNA with aluminum, they did not address several questions relevant to the practical application of DNA adsorption on aluminum. Specifically:

- how does the process depend on the applied voltage and frequency? In previous studies, a peak-to-peak voltage of 80V was applied to electrodes spaced 80μm apart, for an electric field of 1MV/m. Not addressed was the effect of smaller electrode separation or smaller applied voltage. Similarly, the applied frequency was 1MHz for all of the experiments performed. The effect on adsorption of varying the electric field frequency was not addressed.

- how does the process depend on the length of DNA molecule used? The only molecule used for these studies was λ-phage DNA, with a length of 48.5 kbp. Many applications use DNA molecules significantly smaller than this, such as cDNA microarrays in which the molecular lengths are on the order of several thousand bp or fewer, and oligonucleotide arrays which are on the order of tens of base pairs. Previous studies of thiolated DNA adsorption on gold[9] have shown that surface coverage is affected by DNA sequence length.

- what is the long-term stability of adsorbed DNA on aluminum? The long-term stability of aluminum interconnect in integrated circuits is an important concern[10], and device applications of DNA adsorption must address this issue.
- what is the microstructure of the interaction between the adsorbed DNA molecules and the aluminum surface?

2.2 Future Possibilities

An obvious application for adsorbed DNA molecules on the surface of an integrated circuit is micropositioning of objects for heterogeneous integration[11]. In this process, a surface used as the platform for integration has single stranded DNA molecules adsorbed at one or more locations, and the objects to be placed on the surface have complementary single stranded DNA molecules attached. By controlling the placement and sequence of DNA molecules on the surface and on the objects to be placed, it is possible to use the hybridization of complementary DNA molecules to self-assemble the components into the desired finished product.

One of the most important applications of heterogeneous integration is the Smart Dust project[12]. Smart Dust motes are projected to be systems, on the order of 1 cubic millimeter in size, with self-contained sensing, computation, and communication capabilities. A key component of Smart Dust systems is CMOS integrated circuits, along with microfabricated optical and mechanical components. The use of DNA-based self-assembly to manufacture Smart Dust motes may contribute to large-scale, low-cost production processes that enable Smart Dust to reach its full potential.

Another important phenomenon that may be demonstrated with DNA adsorbed to aluminum is electronic control of DNA hybridization[13, 14]. This process, illustrated in Figure 2, occurs when a double stranded DNA molecule is exposed to an electric field and a single strand of the molecule is attached to a surface (generally the surface of the electrode generating the electric field). By controlling the applied electric field, the single stranded DNA not adsorbed to the surface can be dissociated from the complementary adsorbed ssDNA. The magnitude of the electric field necessary to cause two ssDNA molecules to dissociate can also indicate whether there are base pair mismatches between the molecules, a fact that is relevant to the diagnosis of genetic disorders.

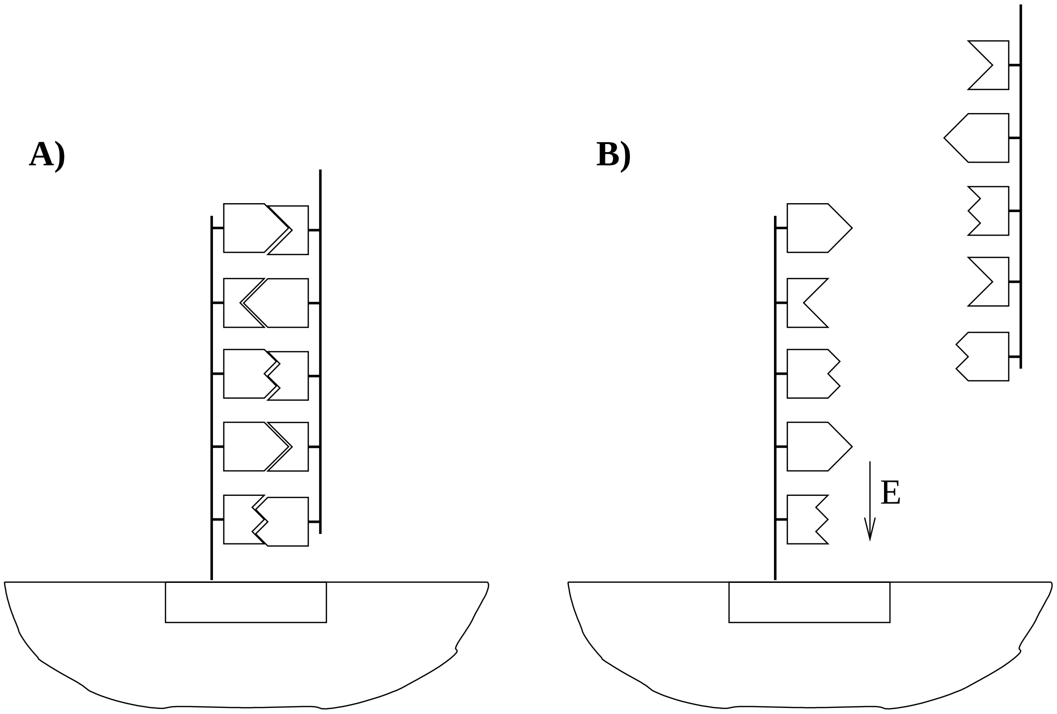

Figure 2: Electronic control of DNA hybridization: (**A**) Complementary single-stranded DNA molecules form a double-stranded DNA molecule, with one of the strands adsorbed on the surface of an electrode. (**B**) By applying a voltage to the electrode, an electric field is created, which forces the negatively charged non-adsorbed ssDNA from the electrode.

3 Research Plan

The goal of the proposed research is the demonstration, characterization, and optimization of DNA adsorption on aluminum, in order to effectively utilize this phenomenon in commercial integrated circuit systems. In order to accomplish this, it may be necessary to conduct a large number of experiments with varying parameters (voltage, frequency, temperature, solution composition, etc.). Because the experiments, if successful, entail surface modifications to the aluminum microelectrodes to be used, it will be necessary to have a large number of the microelectrodes for one-time experiments and subsequent analysis.

The need for large numbers of test structures, and the imperative to apply this research to commercial systems, indicates that the use of CMOS technology to fabricate the microsystem, instead of custom microfabrication processes, is warranted. The feature sizes achievable with CMOS are smaller than those achievable by all but the most specialized and expensive custom microfabrication processes. The availability of active circuitry and transducers in CMOS processes creates the opportunity to integrate a wide variety of capabilities on the finished chip. As well, the use of foundry CMOS increases the relevance of the proposed research to contemporary integrated circuit manufacturing, enhancing the likelihood that this research will be adopted for use in commercial systems.

3.1 CMOS microsystem

For specific discussion of the CMOS process to be used, we refer to the Taiwan Semiconductor Manufacturing Corporation TSMC35_P2 process[15], available from MOSIS. This process has two polysilicon layers and up to four metal layers available, with a minimum transistor length of .35 microns. In this process, chemical-mechanical planarization is used to create flat surfaces for deposition and patterning of thin film layers.

For the creation of the proposed microsystem, the fundamental structure is the aluminum microelectrode. In order to exploit the small feature size possible with CMOS fabrication, the exposed surface of the electrode is 1 micron square. Directly underneath the square electrode is a “via”, connecting the top layer of metal (metal-4) with the lower level of metal (metal-3). Sixteen microelectrodes are arranged on the perimeter of a square 9μm on each side to form an electrode array, with the individual microelectrodes separated by .6μm (Figure 3). While there is generally a thick “overglass” layer present on the surface of a CMOS integrated circuit to protect the circuitry from mechanical damage, the need to have the microelectrodes exposed will require the overglass layer to be removed from the vicinity of the microelectrode array[16].

Conceptually, the simplest scenario for performing anodization on the surface of this microelectrode array is, while the surface is exposed to an aqueous solution containing DNA molecules, to set 15 of the microelectrodes to the ground voltage, and set the microelectrode to be anodized (the so-called “working electrode”) at the positive supply voltage, referred to as V_{DD}. Given the variation of DNA dynamics with frequency in an AC electric field[4], it may be necessary to cycle the working electrode between V_{DD} and ground at an appropriate frequency. Controlling the voltages applied to the microelectrodes in the array can easily be accomplished with CMOS digital circuits incorporated into the microsystem.

Determining the V_{DD} necessary for effecting anodization is a critical goal of the proposed research. The standard reduction potential for the conversion of Al to Al^{3+} is -1.676V[17]. This indicates that, in order to effect the electrochemical reaction of anodization, the applied interelectrode voltage must be greater than 1.676V. The magnitude of the necessary additional voltage is determined by the current flow in the solution, and the associated Ohmic voltage drop.

The most straightforward way to adjust the voltage used for anodization is to adjust V_{DD}. While the maximum voltage that can be used in this TSMC process with standard design techniques is 5.0V, and the preferable maximum voltage is 3.3V, it is possible to design circuits that will operate correctly at lower supply voltages. When electronically controlling DNA hybridization on the surface of the microsystem, it is important to avoid electrochemical reactions at the aluminum surface. Because scaling V_{DD} is expected to be the most economical way to achieve low voltages for hybridization, the circuits used to control the microelectrode array will be engineered to function consistently at supply voltages between 1.0V and 3.3V. Achieving this objective will require low-voltage CMOS circuit design techniques[18] that are critical to the design of portable and power-sensitive systems.

The size of the microelectrode array, including the circuitry necessary to control an individual array, is anticipated to be less than $(250\mu\text{m})^2$. This will make it possible to integrate a sizable number of microelectrode arrays in the CMOS microsystem, in an array-of-arrays system. To effectively utilize the arrayed microelectrodes, it will be necessary to integrate control circuitry into the microsystem to enable input signals to be directed to the appropriate microelectrode array for anodization or hybridization. To simplify this task, a hierarchical approach to system design will be taken. Specifications will be prepared outlining the performance requirements for the array-level circuitry, system control circuitry, and input/output circuitry, as well as the interfaces between each level. Proceeding from this system specification, the system will be designed and thoroughly simulated to ensure correct operation.

3.2 Integrated processing system

The CMOS microsystem is the primary platform for the proposed research, but it is only one component of the system necessary to perform anodization. Development of a system to coordinate microelectrode voltages with fluid deposition and removal will be essential to the success of the proposed research. At the same time, it is important to minimize the complexity of the processing system in order to successfully complete the initial research proposed here.

The deposition system needed for the proposed research has many features in common with systems for DNA microarray fabrication[19]. An important difference, however, is the requirement in this case to remove nonspecifically adsorbed DNA molecules before each deposition step. While it is not necessary to remove nonadsorbed DNA molecules if the goal is to simply demonstrate DNA adsorption on aluminum, for applications of this process it may be necessary to carefully control the DNA molecules present at each microelectrode.

Due to the vulnerability of the exposed microelectrodes to mechanical damage, only noncontact deposition methods are practical in this case. The most cost-effective deposition system in this case is likely to be an inkjet printing system, adapted to use solutions containing DNA molecules instead of conventional inks[20, 21].

A long-term goal for the proposed system is to have a controllable number of DNA molecules of specific sequence on each microelectrode, fabricated in a process that is as rapid as possible. The objective of the current work will be the development of an economical system that balances the short-term need to quickly and inexpensively perform a large number of experiments with the anticipated long-term need for a specialized and powerful system for large-scale manufacturing.

3.3 Microsystem physical analysis

Atomic force microscopy is expected to be the primary tool for determining the effects of the electrochemical processes at the aluminum electrodes. Due to the extremely small size of the microelectrodes, other techniques for surface analysis, such as surface plasmon resonance and

X-ray spectroscopy, are not likely to be applicable to the analysis of individual microelectrodes. Fluorescence microscopy will be used to analyze the hybridization of DNA molecules. Other optical techniques may be applicable to the study of the processed microsystem.

4 Conclusion

The anodization of aluminum by DNA is an almost entirely unexplored process that may have significant applications in future integrated circuit systems. This proposal has outlined a possible first step toward the characterization of this process, but much remains to be done to realize the potential of DNA integrated circuits.

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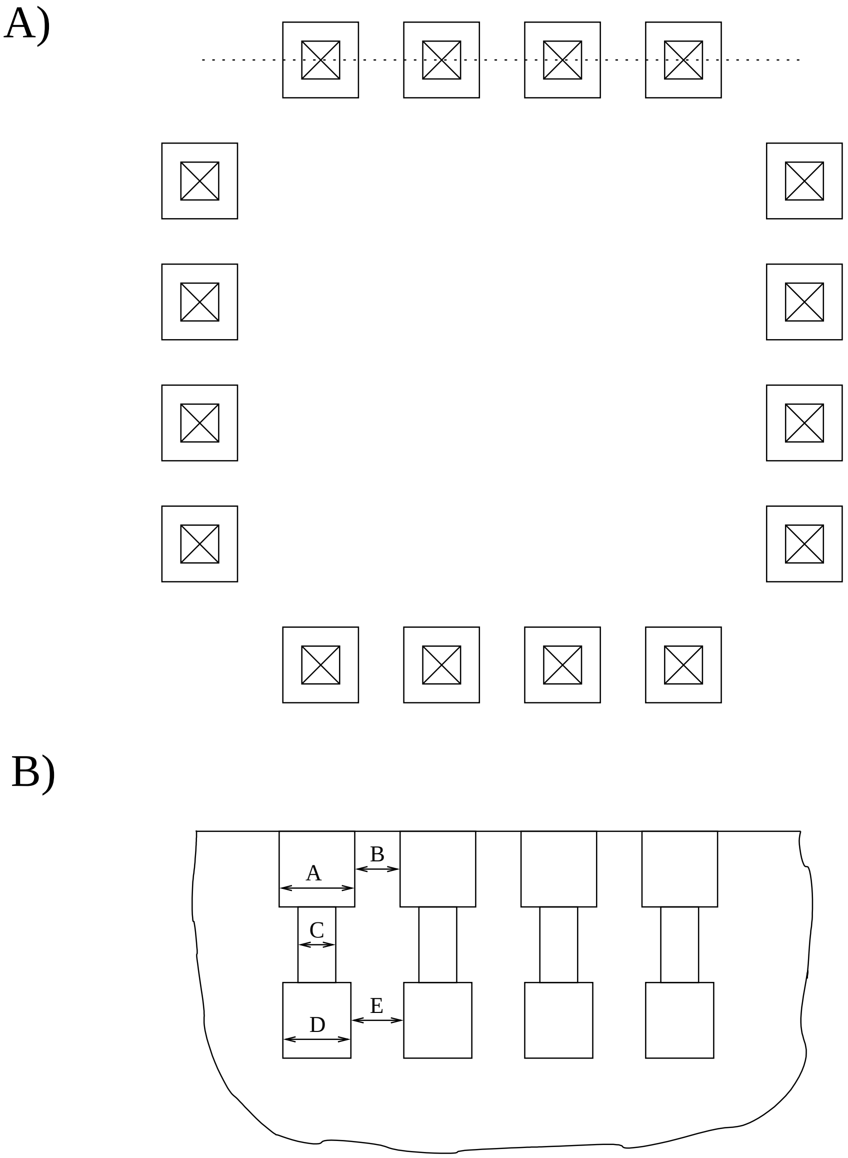

Figure 3: Diagram of the microelectrode array: (**A**) Plan view of microelectrode array, showing 1 μm square microelectrodes, with centered vias, arranged about the perimeter of a 9 micron square. (**B**) A cross-section view from the dotted line in **A** with labeled dimensions. A: 1μm wide metal-4. B: .6μm interelectrode spacing. C: .5μm via width. D: .9μm metal-3 width. E: .7μm separation between metal-3 interconnect.