Protein Logic

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The goal of this program is to create a biologically inspired computational engine that is fully integrated with silicon technology [1]. There are numerous examples in nature where biological entities (e.g., cellular structures) work together as a cellular neural network (CNN) to solve complex problems, such as feature extraction in the retina. The goal of this program is to use a protein array as a CNN chemical processor. A schematic of such a "Protein Logic" structure is depicted in figure 1. In this scenario a central protein array processor core communicates chemically with peripheral nanoscale silicon CMOS transistors. Key issues are fabrication of the protein array, interfacing between its chemical environment and the transistor electronics, microfluidic issues associated with chemical transport, and characterization. Progress in these areas will now be discussed.

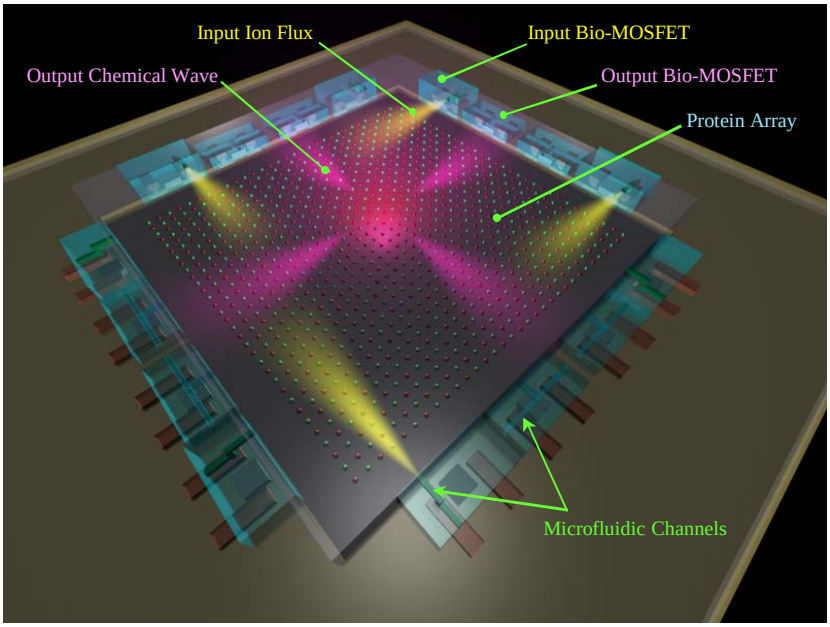

Fig. 1: Depiction of proposed protein logic architecture in which a central protein array interfaces with a Bio-MOSFET I/O periphery. The chemical wave generated in the protein array processing drives the output Bio-MOSFETs via reconstituted ion channels integrated into microfluidic channels. Chemical input into the protein array is controlled by similarly configured Bio-MOSFETs, which electronically gate an ion or molecule flux passing through microfluidic channels.

Protein array fabrication (Lyding, Moore, Sligar) on silicon will be accomplished by templated self-assembly. An ultra-high vacuum scanning tunneling microscope (UHV STM) will be used to pattern a hydrogen passivated silicon (100) surface with atomic precision [2]. Protein linker molecules will then be applied to this template in UHV, followed by protein attachment in an aqueous solution. The robust nature of the UHV H-passivated Si(100) surface is a key enabling factor [3]. A graduate student hired at the beginning of this program has been trained in UHV STM and is now making templates for protein absorption. An undergraduate Senior Thesis student is assisting with this work.

Natural and artificial ion channels are being explored for the interface between the chemical environment of the protein array and the electronic transistor environment. Sligar has developed

10 nm diameter bio-nanodiscs in which a membrane scaffold protein surrounds a phospholipid bilayer into which a biological ion channel can be genetically engineered (see figure 2). Over the past year Sligar's group has perfected the nanodisc self-assembly process to an accuracy of ~2 phospholipid molecules. Timp has developed a fabrication strategy in which a CMOS transistor can be isolated by a thin dielectric layer into which a nanometer scale hole is drilled with an electron beam (see figure 2) to enable ion flow to the transistor control gate. These two efforts will be combined over the next year to splice the nanodiscs to the nanopores.

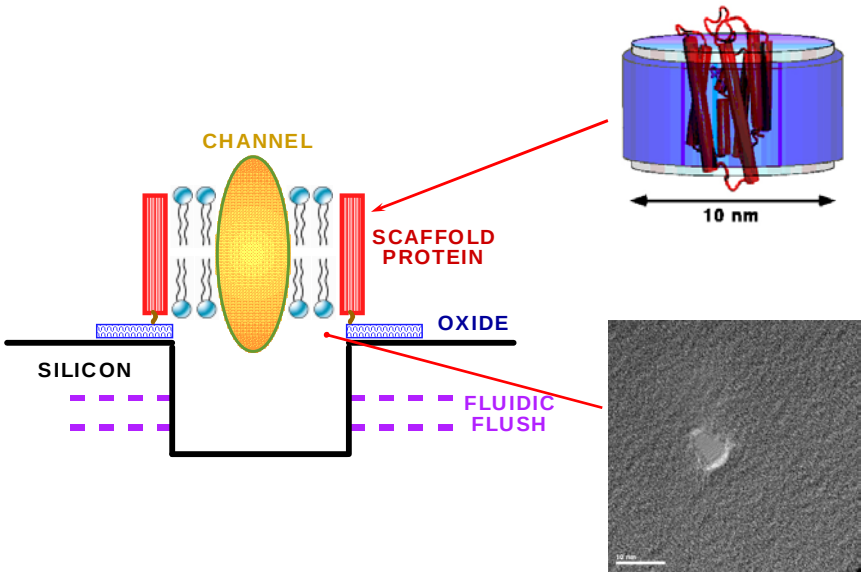

Fig. 2: Depiction of a nanodisc with an integrated ion channel attached to a nanopore. The SEM image shows a ~4 nm diameter nanopore drilled with an electron beam through a thin silicon dioxide layer.

In a new aspect of the program, carbon nanotubes are being evaluated as potential ion channels. Aluru's group has simulated ion flow through single wall carbon nanotubes (SWNTs) asymmetrically functionalized with carboxylate and amino residues at opposite ends (see figure 3) [4]. Aluru will collaborate with Moore over the next year to vary the functionalization to control flow and selectivity through SWNT ion channels. An experimental aspect of this work has been initiated by Lyding's group. Figure 3 also shows a UHV STM image of a SWNT that has been solution deposited onto a H-passivated Si(100) surface [5]. The ability to cut and manipulate SWNTs on silicon has also been demonstrated, setting the stage for molecular functionalization in collaboration with Aluru and Moore.

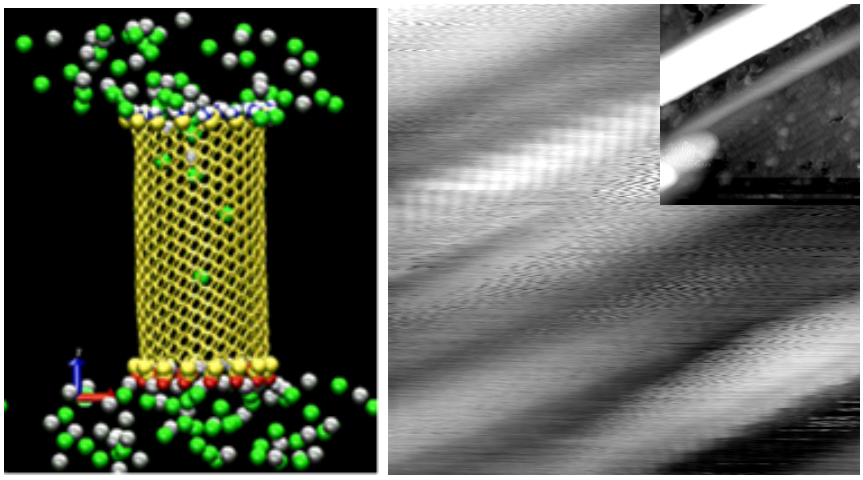

Fig. 3: Simulation result showing that functionalizing the ends of a carbon nanotube effects conduction and selectivity of ion transport through the nanotube. The STM images at the right show atomic level detail of a SWNT rope and an isolated SWNT (inset) on a H-passivated Si(100) surface.

The microfluidics of chemical transport in protein logic chip structures is being studied by Braun's group. Over the past year, they have been developing the underpinnings for the realization of 1-D on-chip diffusive pathways for molecules and ions. The major components of this effort to date have been the synthesis and of appropriate self-assembled monolayers (SAMs) for molecular and ionic transport, routes to patterning these SAMs, and development of techniques to measure and quantify molecular transport. SAMs have been patterned by microcontact printing using the standard PDMS stamping procedure. To date, substrates (bare silica) have been patterned with oligo(ethylene oxide) lines and hydrophobic n-octadecyltrichlorosilane (OTS) lines. Studies of the transport of molecules and ions on these patterned substrates are now in progress and will be a major component of Braun's effort over the next year.

A comprehensive characterization component is also part of this program. Braun's group is using multiphoton fluorescence to study the diffusion and confinement of molecules in their SAM microfluidic structures (see figure 4). Boppart's group has developed an optical coherence tomography (OCT) system combined with multi-photon microscopy for characterizing proteins. Boppart and Braun are also collaborating on the use of multi-photon microscopy to investigate the dynamics of molecular diffusion across planar surfaces. Gruebele and Lyding are in the process of hiring a postdoc to operate a UHV STM that is interfaced to a femtosecond laser spectroscopy system. This system will be used to study the electronic properties and dynamics of individual protein molecules on H-passivated silicon.

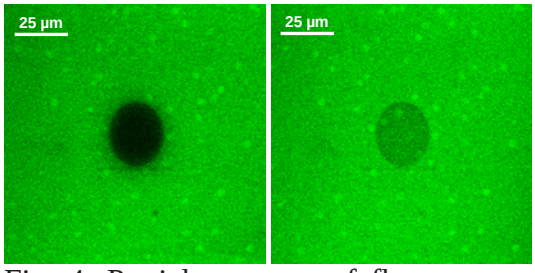

Fig. 4: Partial recovery of fluorescence in a photobleached dot due to dye molecule diffusion on a SAM.

The outreach components of this program have consisted of the development of graduate level courses ("Topics in Nanotechnology" (Lyding) and "Nanoscale CMOS Technology Lab" (Timp)), an undergraduate course on "Biomedical Instrumentation" (Boppart). Aluru is developing a course on "Computational Methods for MEMS" and a short course for the Transducers '03 meeting. An undergraduate course "Introduction to Nanotechnology" is being developed by Lyding for the Fall '03 semester. Approximately fifteen undergraduate students have been involved in this research program to date. We have also made contact with the Worldwide University Network (WUN) and Lyding has attended two of their meetings. The goal of this program is to establish and support exchange programs for students, postdocs and faculty in the United States with their counterpart institutions in Great Britain.

References

[1] For further information about this project email Joe Lyding <j-lyding@uiuc.edu>, Narayan Aluru <aluru@staff.uiuc.edu>, Paul Braun <pbraun@staff.uiuc.edu>, Stephen Boppart <boppart@uiuc.edu>, Leon Chua <chua@fred.eecs.berkeley.edu>, Martin Gruebele <gruebele@aries.scs.uiuc.edu>, Jeffrey Moore <moore@aries.scs.uiuc.edu>, Steve Sligar, Greg Timp <gtimp@staff.uiuc.edu>.

[2] M. C. Hersam, N. P. Guisinger, and J. W. Lyding, "Silicon-based molecular nanotechnology," *Nanotechnology* **11**, 70 (2000).

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