NIRT: Molecular Sensing and Actuation by CMOS Nonvolatile Charges with Independently Addressed Nanoscale Resolution

NSF NIRT Grant ECS-0304483
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GRAND VISION

The biological system achieves high molecular selectivity in sensing and actuation through specific redox receptors on a relatively rigid carbon-based backbone, notably between antigens and antibodies. The level of sophistication in such molecular systems is still beyond the reach of any programmable inorganic systems today. On the other end, the electronic revolution based on silicon technology in the last 50 years has not only provided the necessary computing power for understanding the biomolecular interactions, but also rapidly approaches the dimensions of several nanometers that are critical to the molecular attributes. Can this degree of molecular selectivity and adaptivity in the biological system be provided through an electronic silicon device? If yes, through what interface? What is the operational principle? How can we use it in biomedical applications? What is the main limitation? What kind of social and consumer market implication will this technology bring? Although we may not be able to answer all these challenging, intriguing questions in the short period of this NIRT effort, we will attempt laying down the essential ground work and baseline operating principles in search of a programmable "drug", which may become a "magic panacea" since the backend silicon device can dynamically program the redox receptors through information in the immunology data base.

PROJECT OBJECTIVES AND MAJOR RESULTS

The primary objective of this NIRT effort is to *investigate how to build electronic devices extended from the present silicon technology that can achieve individually controllable chemical receptors with nanoscale resolution*. The key interface between the distinctive molecular and silicon systems lies in the control of charge density to the nanometer precision. Due to the power and invasiveness concerns, instead of using electrodes, the charge density will be implemented by static charges as in the floating gates of Flash memory or the Coulomb islands of single electron transistors (SET). The floating gate approach can have both electrostatic attractive and repulsive forces, and also eliminate the need of a reference electrode. Five major tasks are conducted in interdisciplinary collaboration to establish the working principles:

1. *Build nanometer-size metal nanocrystal [2] and fullerene [3] floating gates whose charge density is exactly measurable and controllable from the underlying CMOS devices*. The electrical measurements for metal nanocrystals on silicon Flash memory are shown in Figs. 1 (a)-(c), while the charge injection in nanotube is shown in Figs. 1 (d)-(e). The positive and negative nonvolatile charge will serve as attractive or repulsive receptors like remote cation and anionic ends to the molecules in fluids as illustrated by the Poisson equation solution in Fig. 1(f).
2. *Establish the charge interaction between the floating gates and the molecules through the coarse grain lattice models in kinetic Monte Carlo (MC) simulation.* As illustrated in Fig. 2, we have achieved proof-of-concept simulations demonstrating interaction between

proteins and *designer* charge surfaces, which suggests that closely similar protein mutants can still be preferentially adsorbed based on their difference on charge distribution. Figure 3 shows another example of the electronic counter part to the ribosome channel [4] in nature, where the channel with different configurations of charges can retard folding in small easily foldable proteins.

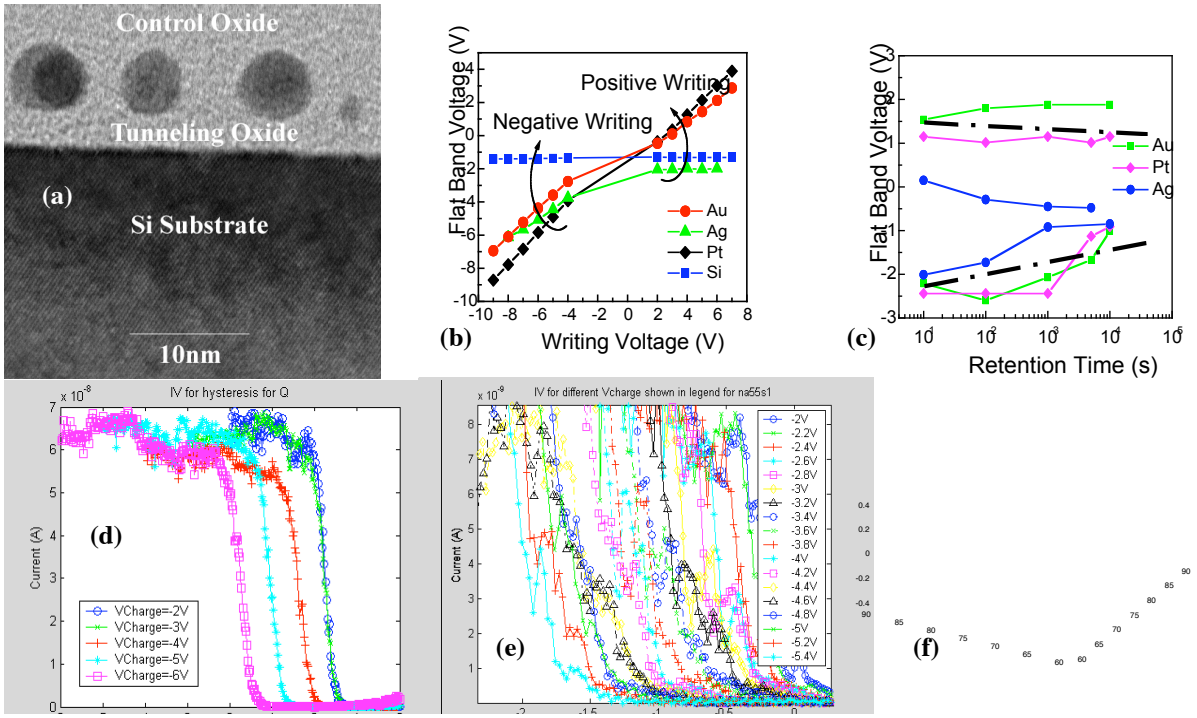

Fig. 1. Conceptual illustration of charge injection into nanoscale entites in CMOS Flash memory structures. (a): STEM pictures of embedded metal nanocrystals; (b) charge windows of metal nanocrystals; (c) retention time of charges in metal nanocrystals; (d) and (e): charge injection into carbon nanotubes entities; (f) charge density maps by simulation as seen from the device top surface.

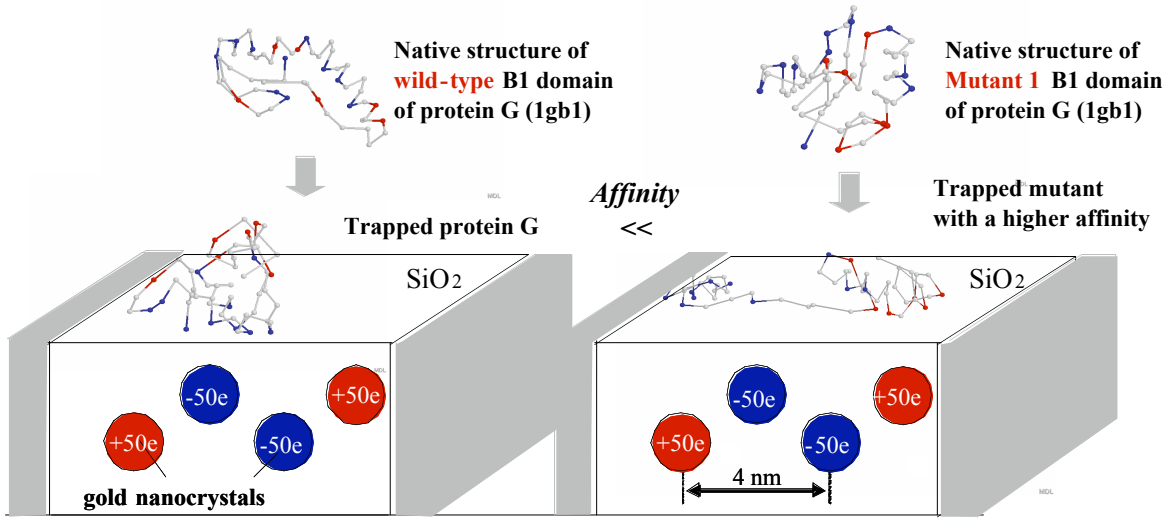

Fig. 2. Kinetic MC simulation of adsorption of protein G (lgb l) on surfaces with specific charge density controlled by the metal nanocrystals. Mutant 1 has much larger affinity than the wild type.

Fig. 3. Simulation of an electronic ribosome channel shows that the charge density distribution on channel walls can retard folding for easily foldable proteins. (a) Rough lattice representation of the ribosomal tunnel; (b) Model lattice representation of simulated tunnel (25 lattice sites) and a sample protein model.

3. *Build MEMS beams with flexible arms controlled by injected static charge location.* To illustrate the initial working principle, we have fabricated conventional nitride cantilever beams and used STM probes to inject local charges at the joint locations to observe the morphology change. For nanoscale manipulation, we plan to build carbon nanotubes of semiconductor type and observe the morphology change through surface charges.
4. *Build microfluidic channels and associated material characterization for in-situ biomolecular testing*. We will design and conduct realistic test cases including single molecule trapping/actuation of fluorescence labeled DNA fragments, and corroborate the simulation prediction of protein recognition based on surface charge distribution.
5. *Study the consumer liability implications* through a test case when a "programmable drug" is available on the market. We have designed a panel discussion session (three lecture sessions) in the "Consumer Liability" course at Cornell Law School in Fall 2004. The major discussions include the interaction between technology developers and regulation legislators, consumer liability on new material introduction, and the role of legal system on new biomolecular tools.

Conclusion and Future Work

By both experimental and simulation studies, we have successfully demonstrated the feasibility of artificial chemical receptors for biomelecular interface from the silicon platform. For the remaining period of the NIRT effort, we will focus on the demonstration of larger realistic systems and integration with microfluidic devices. The consumer liability case study will be further revised based on the results from the implementation this semester. Student feedbacks will be collected and assessed to make the case study more usable and complete.

References

[1] For further information about this project link to http://people.ece.cornell.edu/kan or email kan@ece.cornell.edu
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