

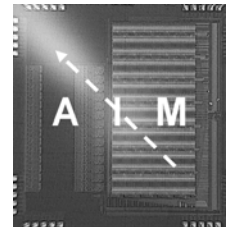


A Time-Based Forward Error Correcting Biosensor Based on Silver-Enhanced Gold Nanoparticles



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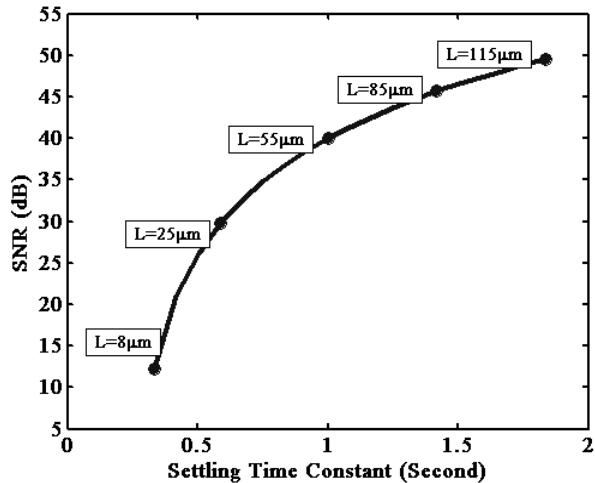




Motivation

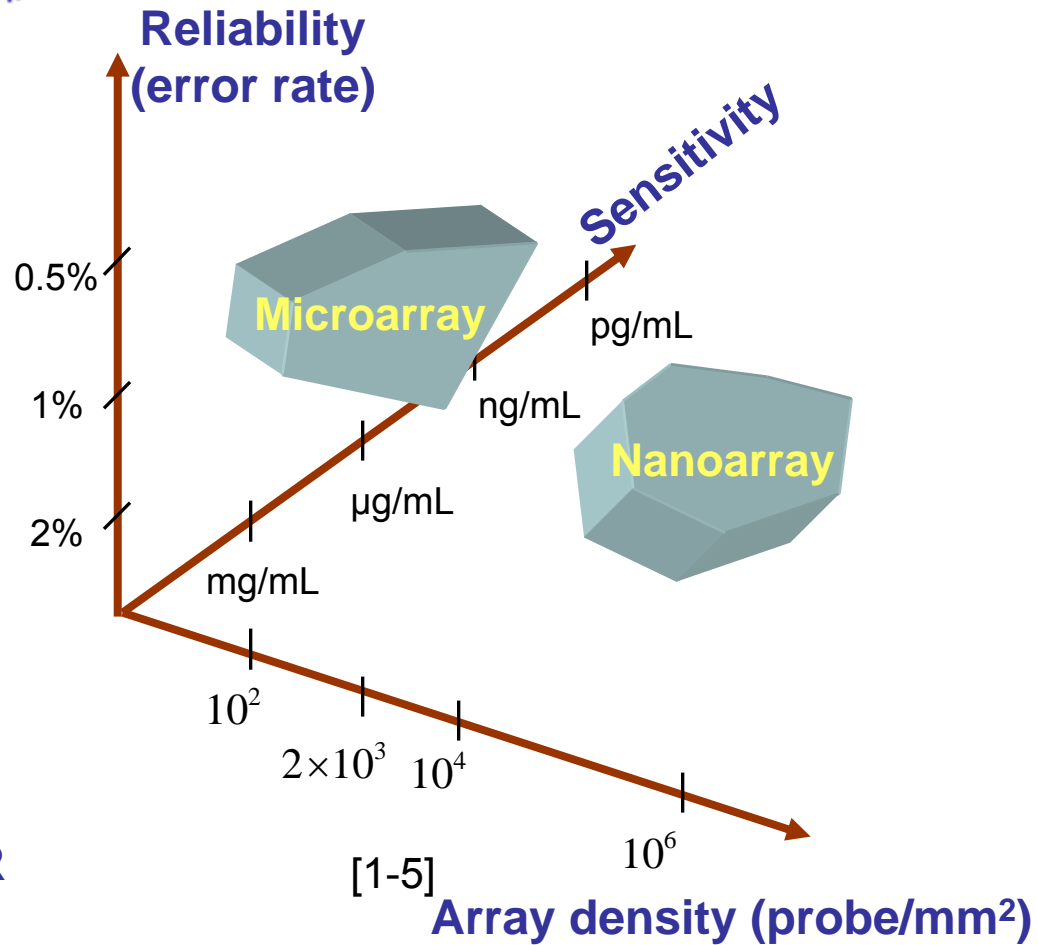


SNR and the scaling factor In ISFET biosensors



[6]

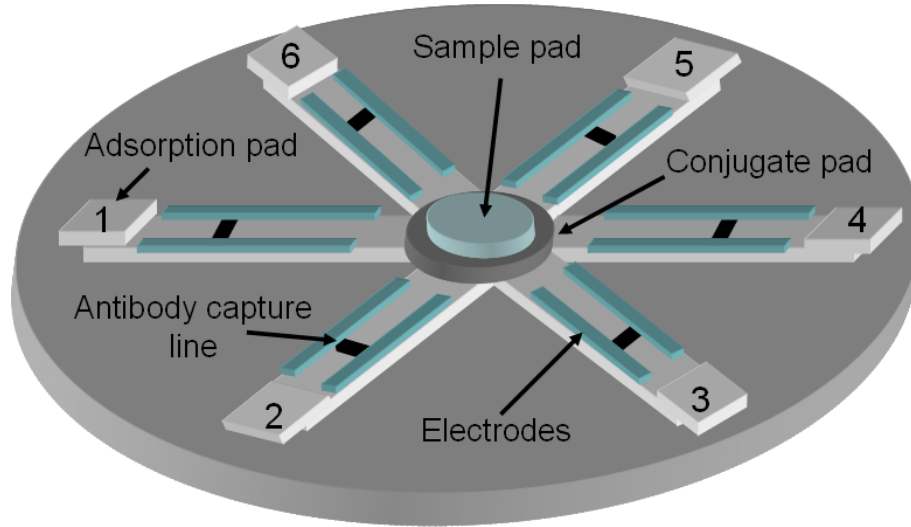
Many micro-fluidic analytical systems are limited by this SNR degradation [7]



- Reliability issue in biosensor systems has been largely overlooked in the literatures.



Past Work: Forward Error Correction (FEC) Biosensor Based on Lateral Flow Immunoassay

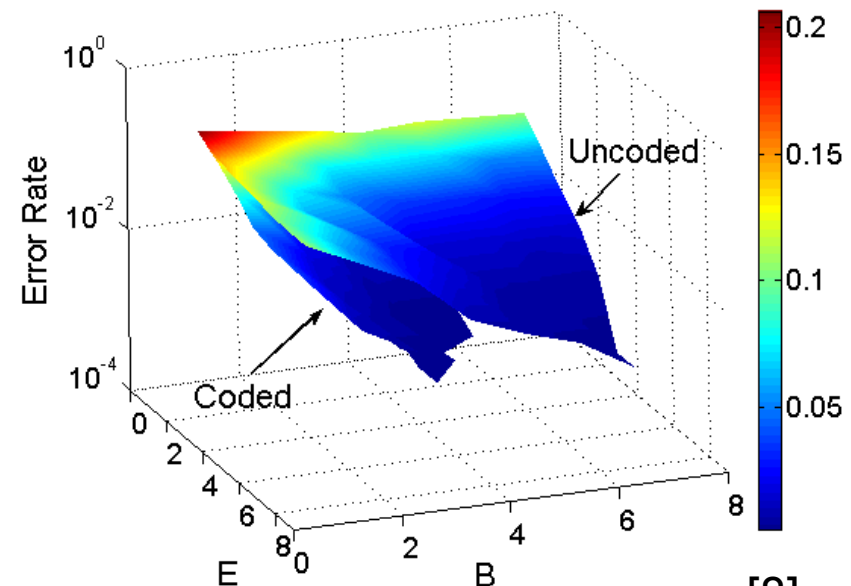


□ Biosensor encoder CD

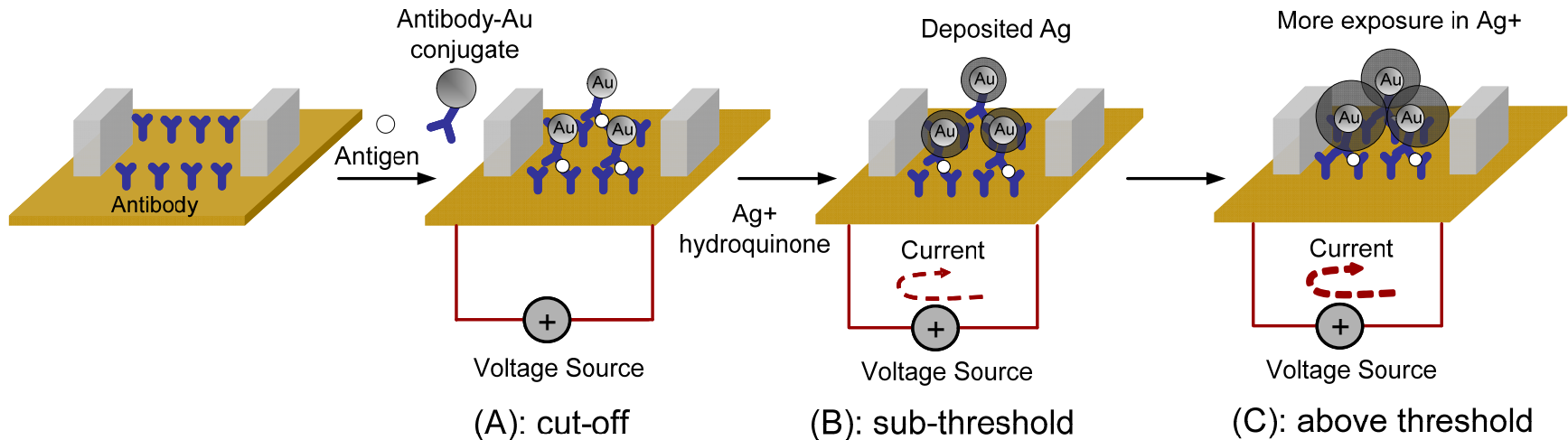
- Lateral flow immunoassay
- Low signal-to-noise ratio, repeatability and reproducibility
- Patterning biomolecular logic gates is hard

□ Improving the reliability

- Adding redundancy
- Hardware: biomolecular encoder; basic building blocks: logic gates

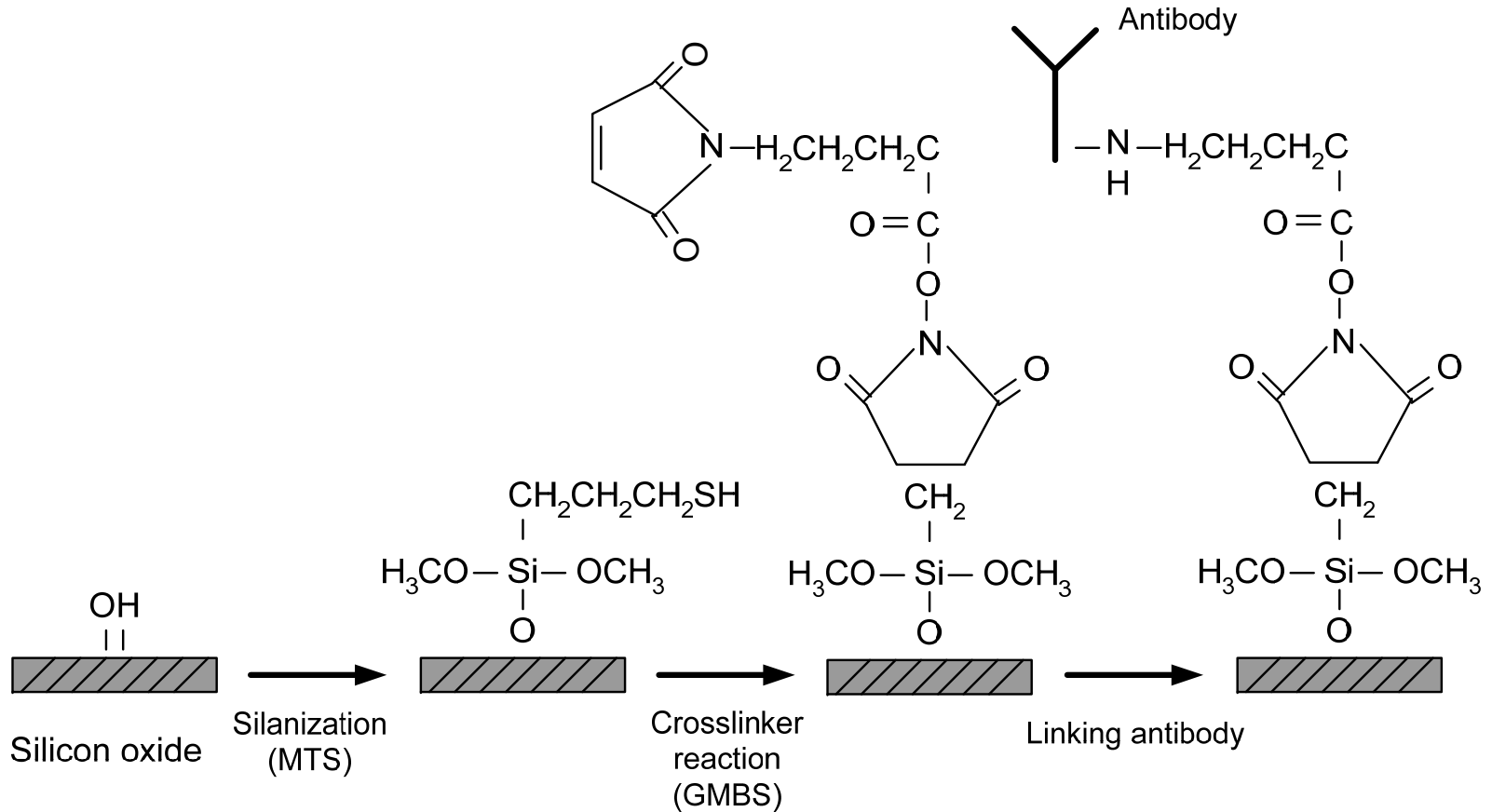


New Platform: The Operating Principle

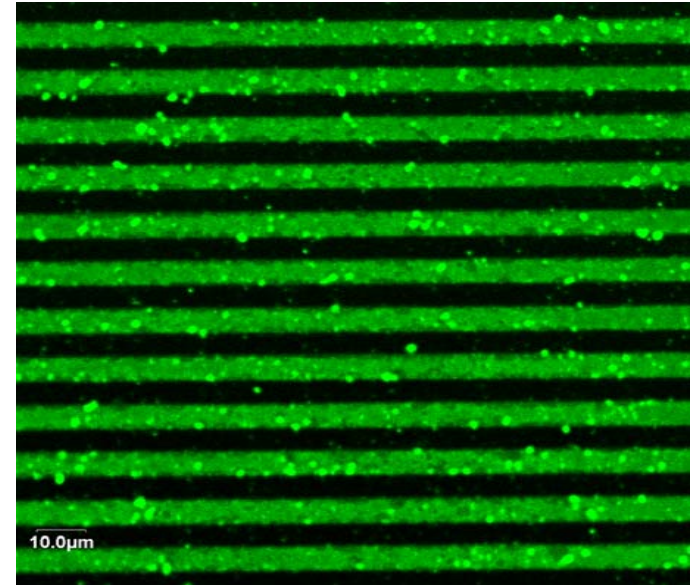
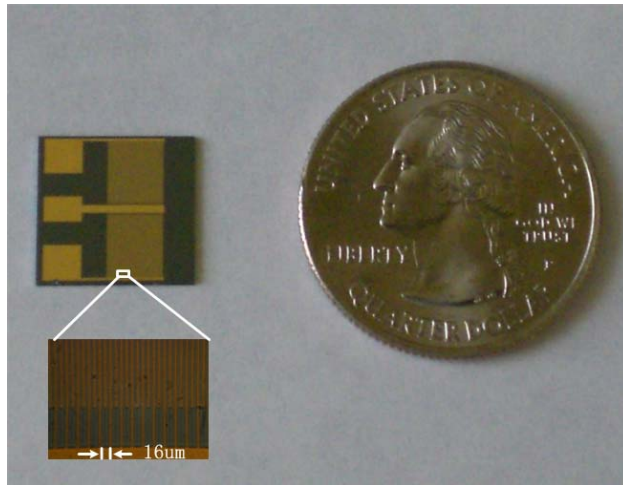


- The gold nanoparticles act as a catalyst and reduce silver ions into metallic silver in the presence of a reducing agent (hydroquinone).
- The reduced silver deposits on the gold surface, thus enlarging the size of the gold nanoparticles.

Surface Functionalization



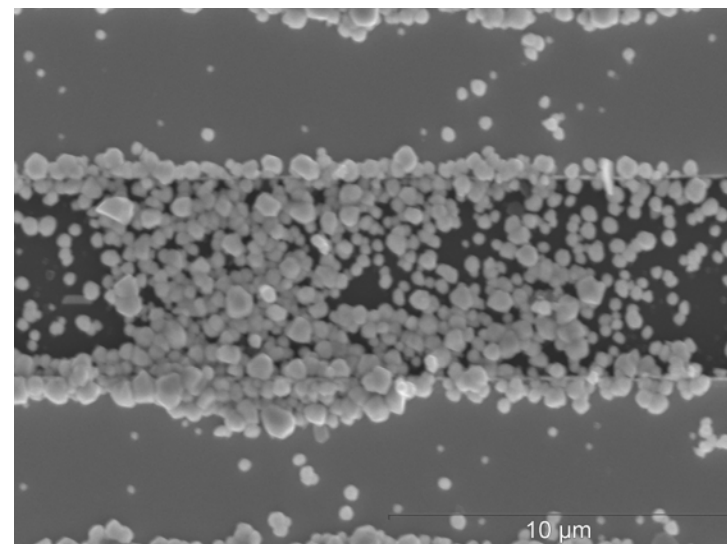
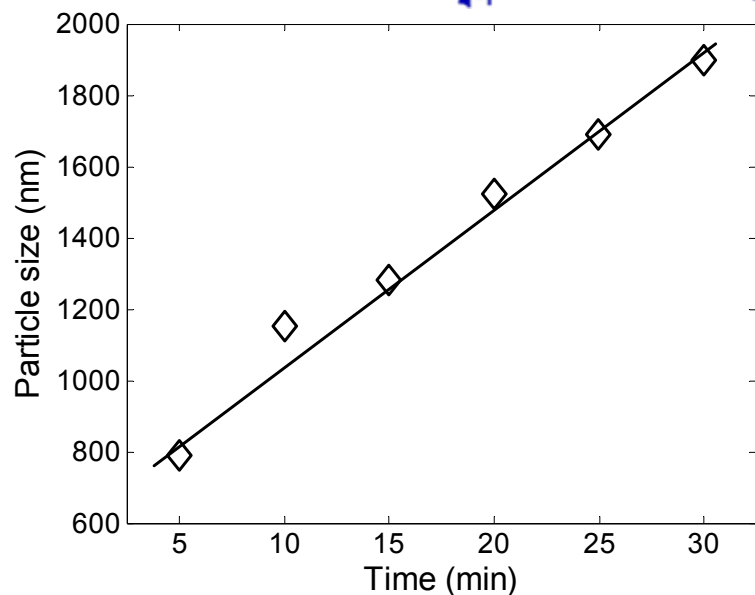
Biochip and Protocol Verification



- Photolithograph: 10 nm chrome and 100 nm gold layer
- Each electrode finger has a length of 5000 μm , a width of 5 μm and inter-electrode spacing of 6 μm .

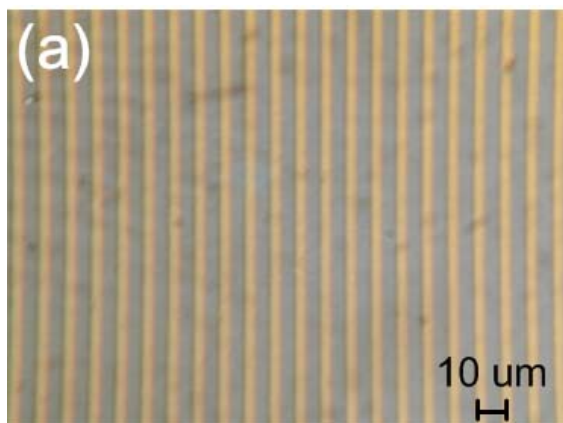
FITC labeled bovine IgG only immobilized to the silicon dioxide surfaces

The Verification of the Principle



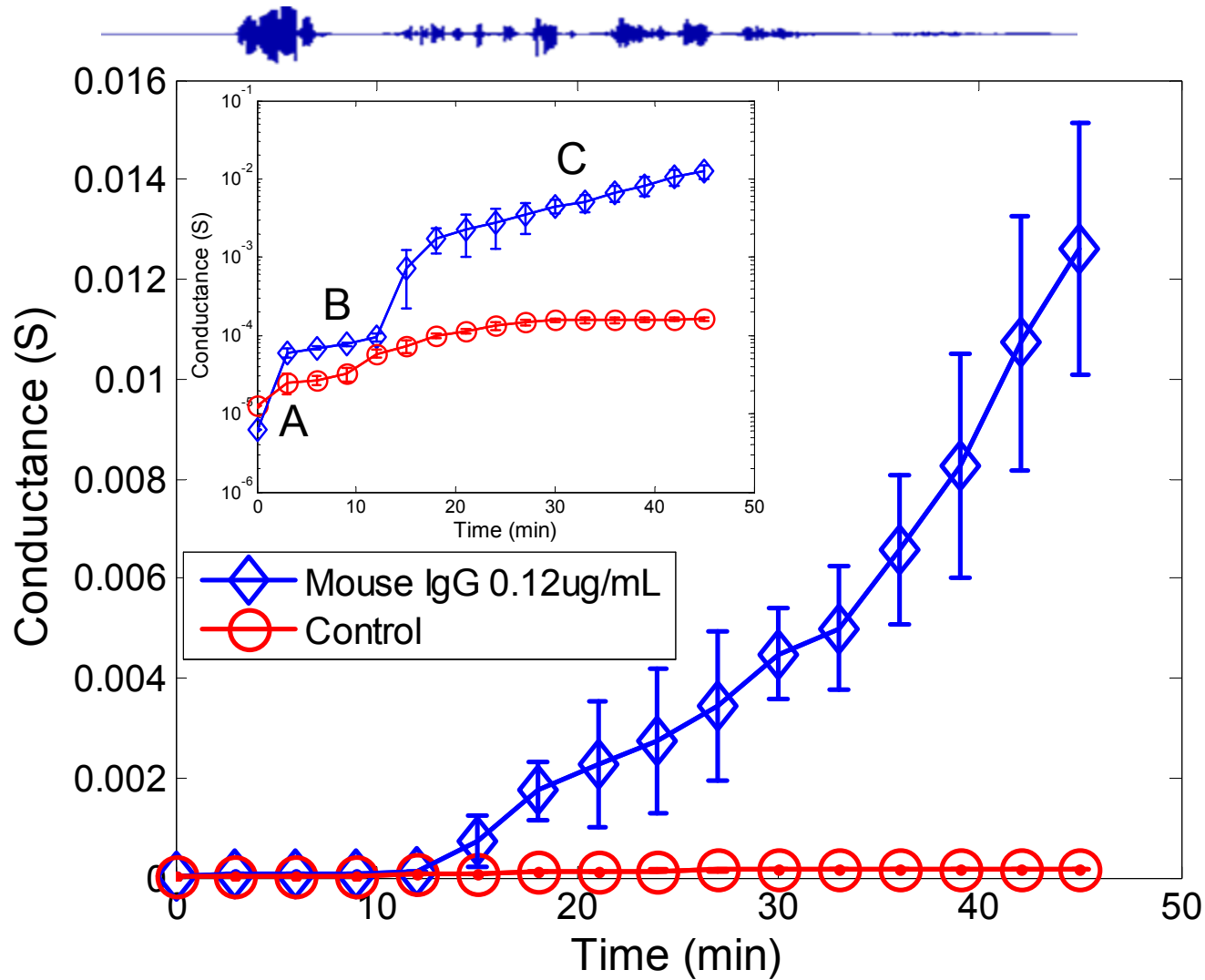
SEM image of the bridge formed by enlarged gold particles.

The relationship between the gold particle size and the silver enhancing time.



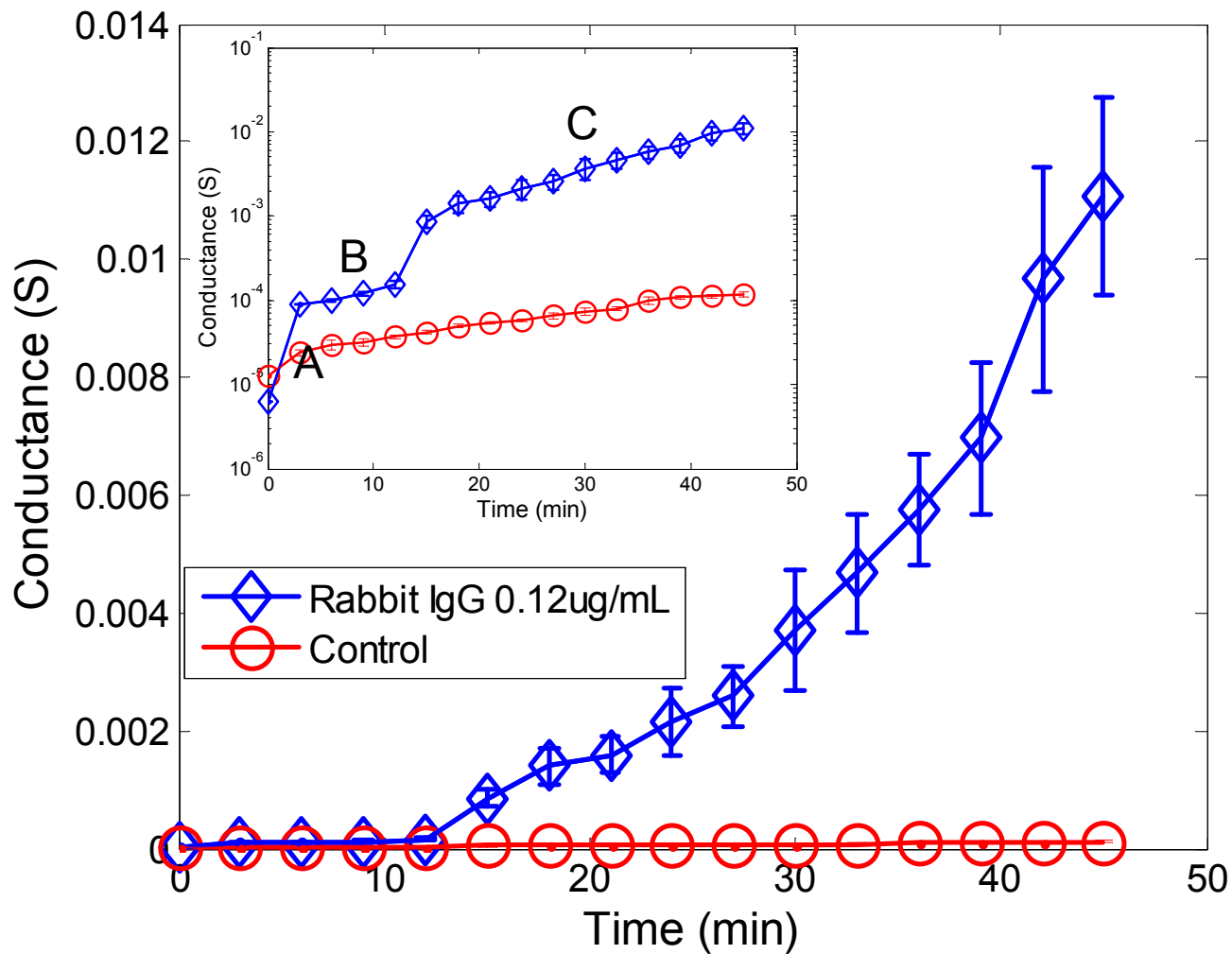
Microphotographs for the biochip active surface. (a) before silver enhancement (b) 35 min after silver enhancement.

Experimental Results



A: cut-off region; B: sub-threshold C: above-threshold region

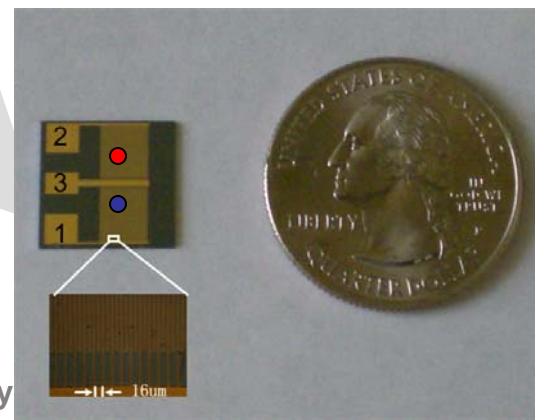
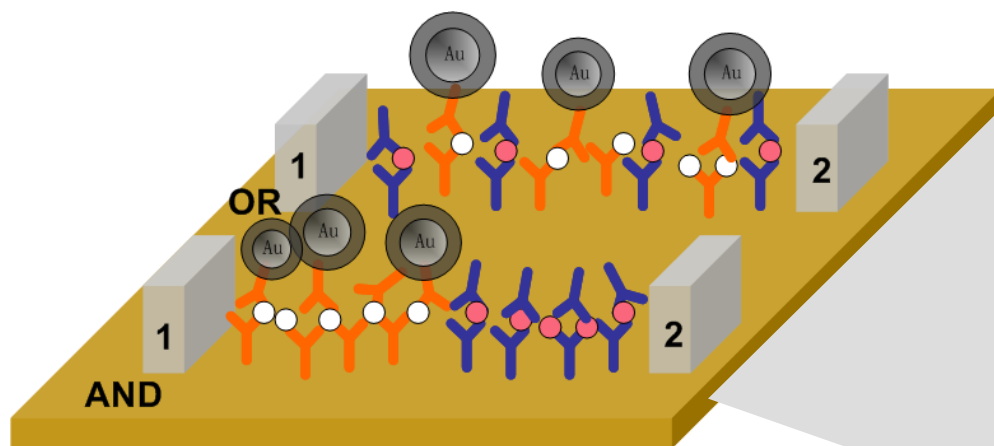
Experimental Results



Building Blocks for Biomolecular Encoder: Logic Gates



- Possible high level of false positive errors due to the sensitivity of the presence of gold nanoparticles when exposing to silver
- Analog Logic Gates (biomolecular circuits) vs. Digital Logic Gates (digital circuits)

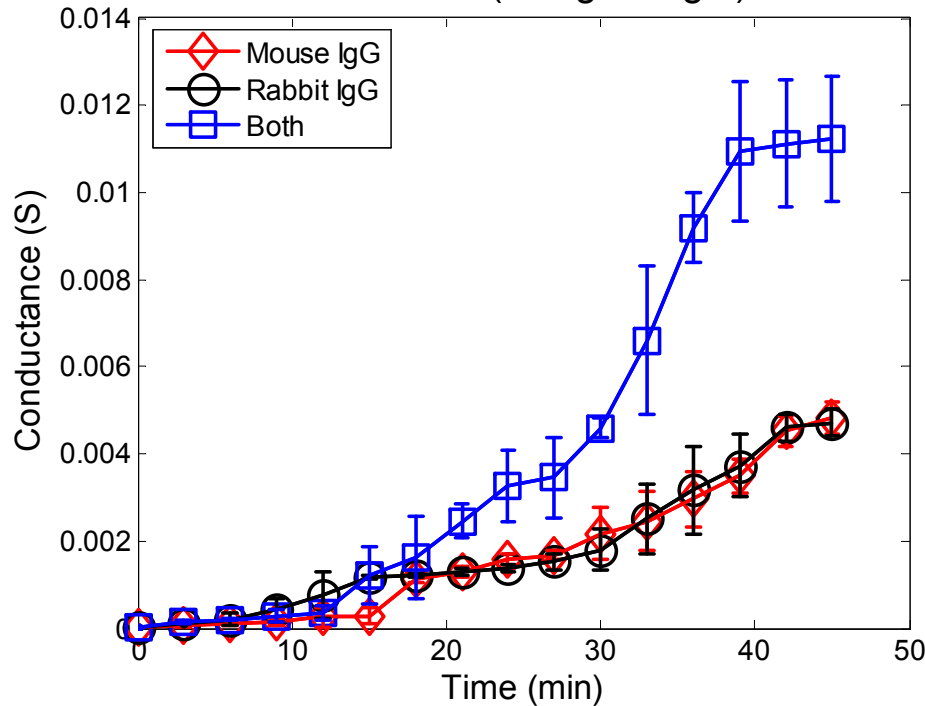


- Logic gates for biosensor encoder

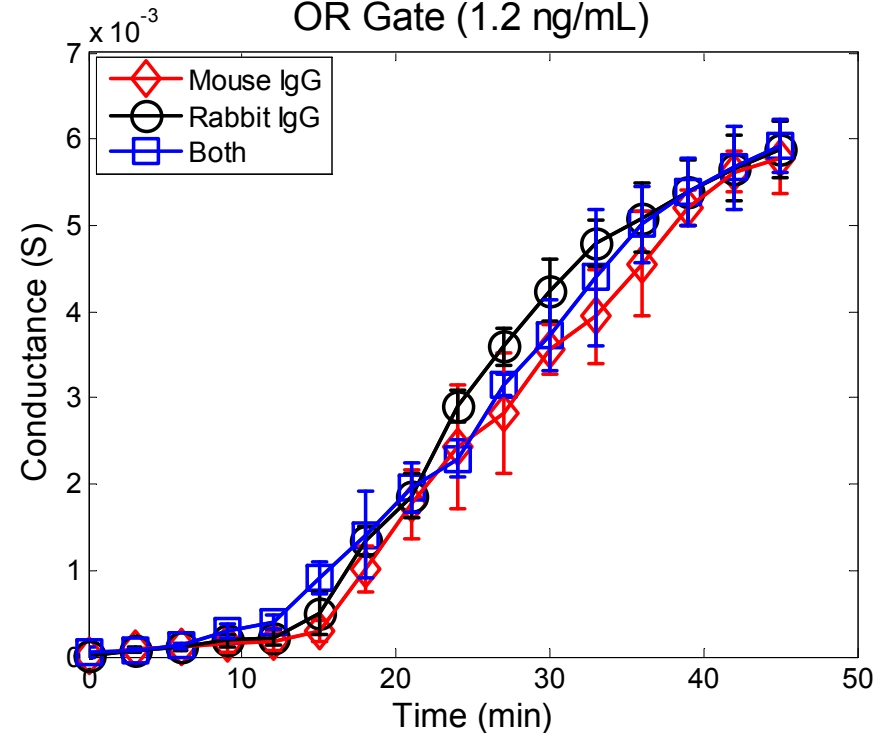
Logic Gates Verification



AND Gate (1.2ng/mL IgG)

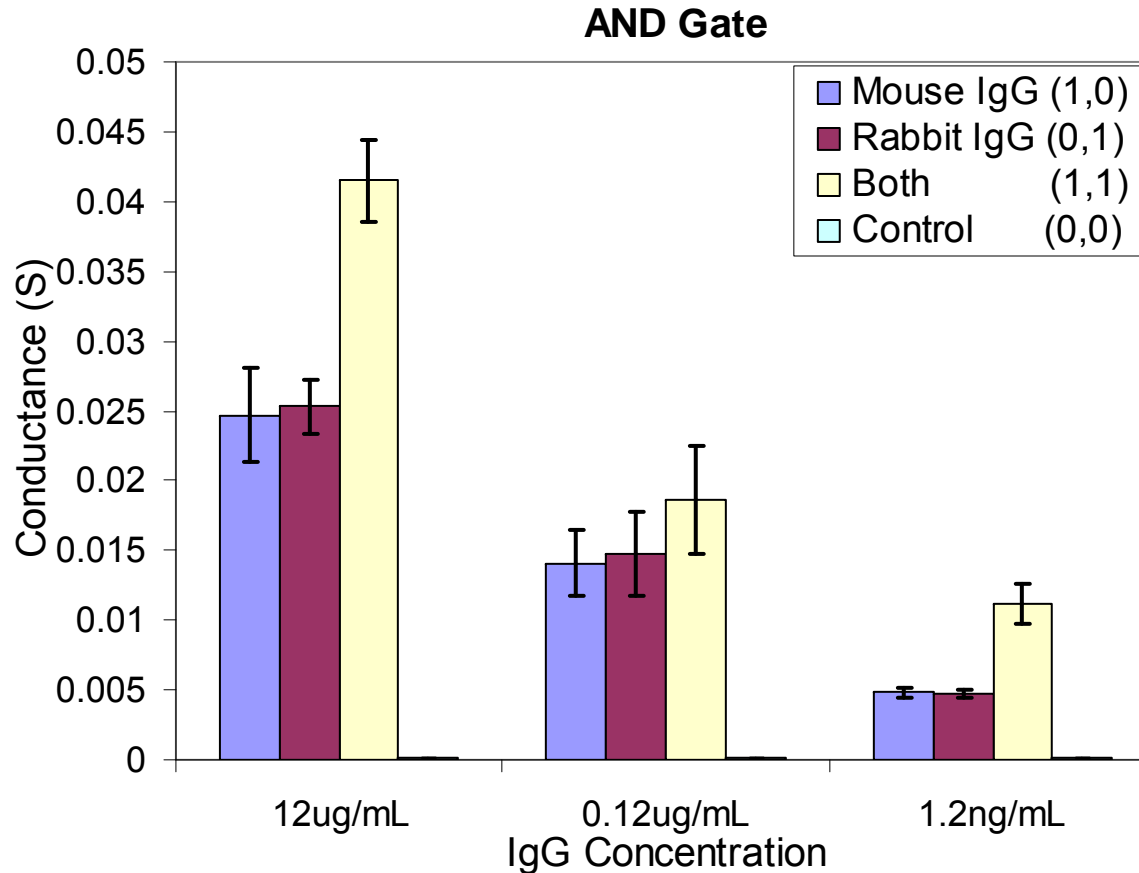


OR Gate (1.2 ng/mL)



Different solutions applied to simulate different logic states:
Only mouse IgG: (1,0); only rabbit IgG: (0,1); both mouse and rabbit IgG (1,1).

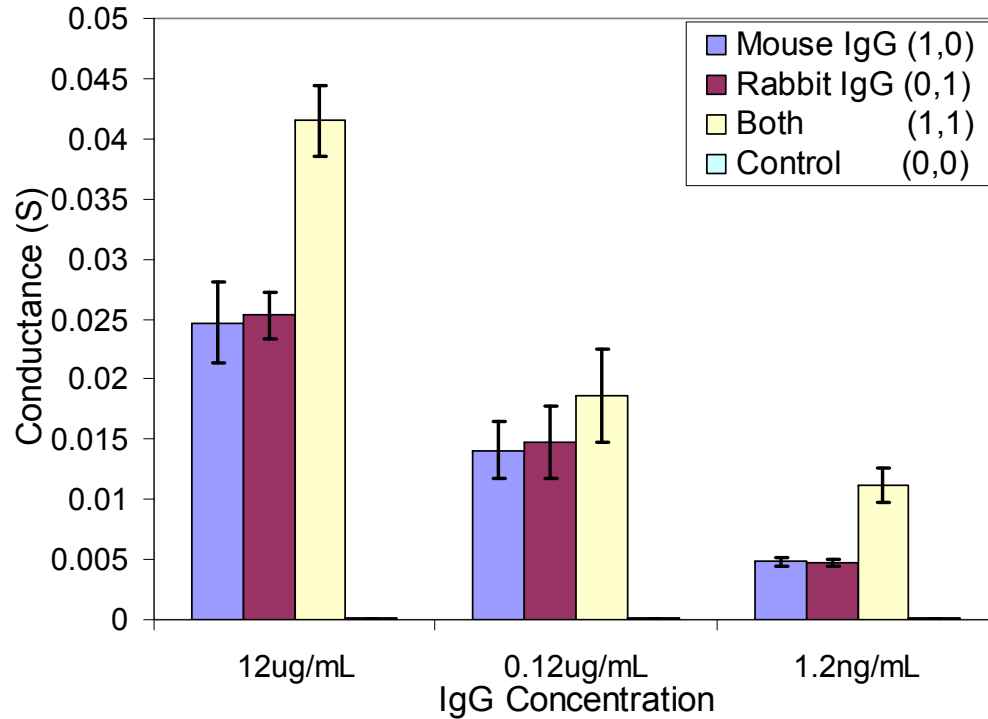
Logic Gates Verification Continued



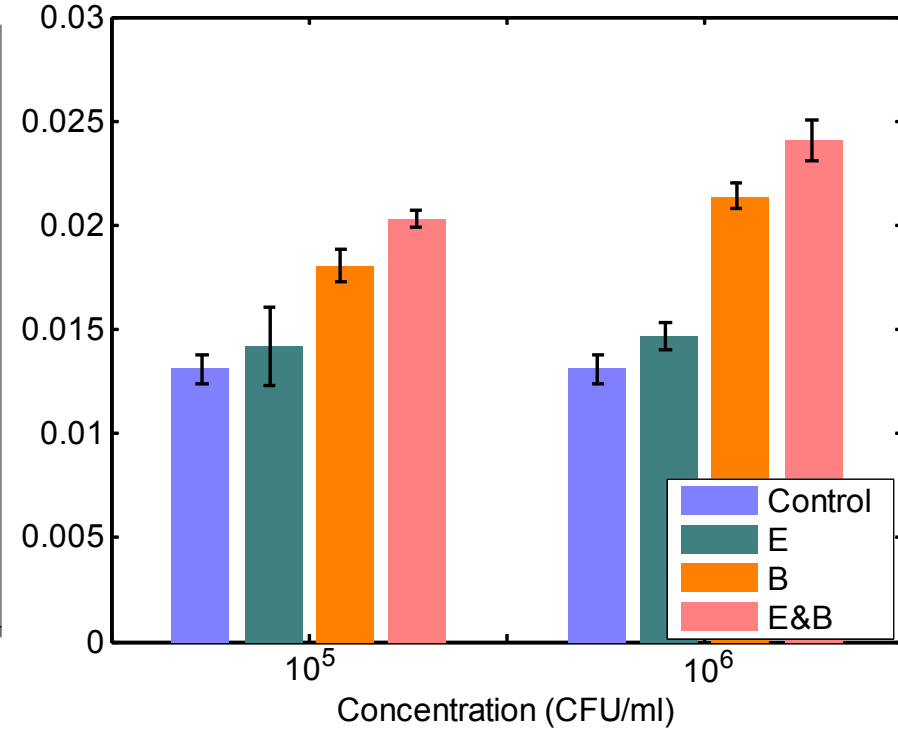
Improvement of AND Gate



AND Gate



New AND gate using gold NP biochip

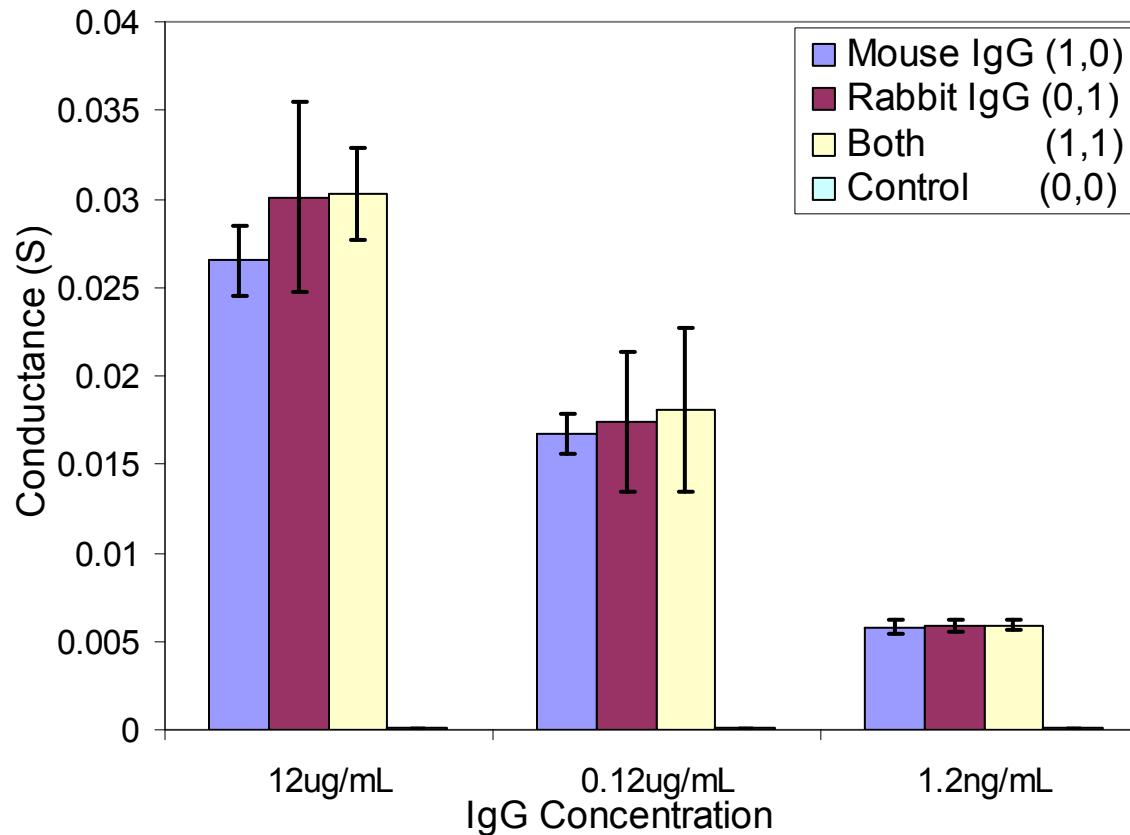


Old AND gate using lateral flow immunoassay

Logic Gates Verification Continued



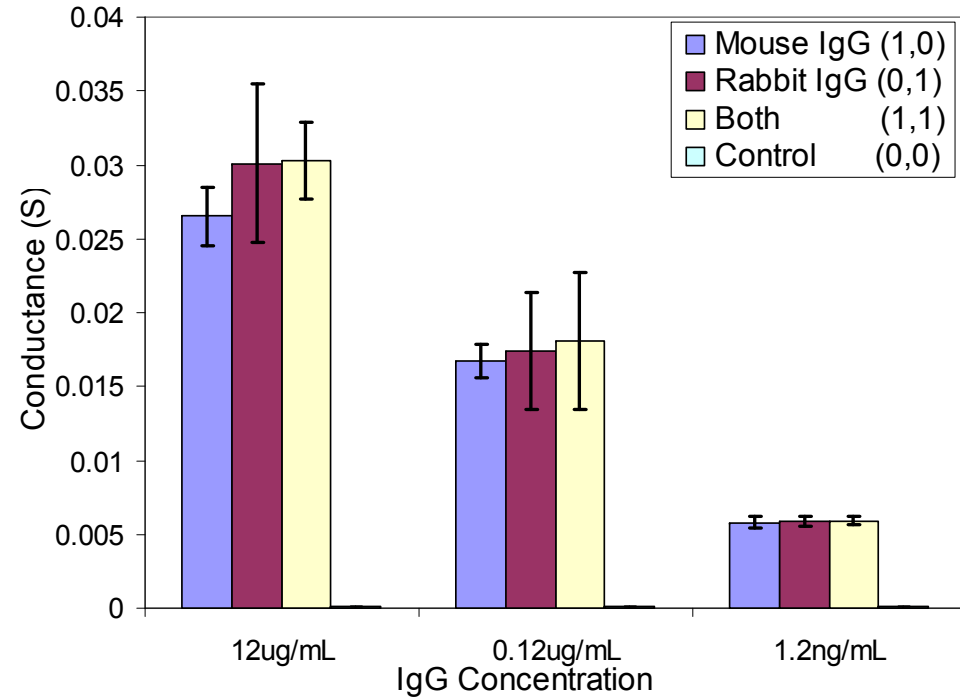
OR Gate



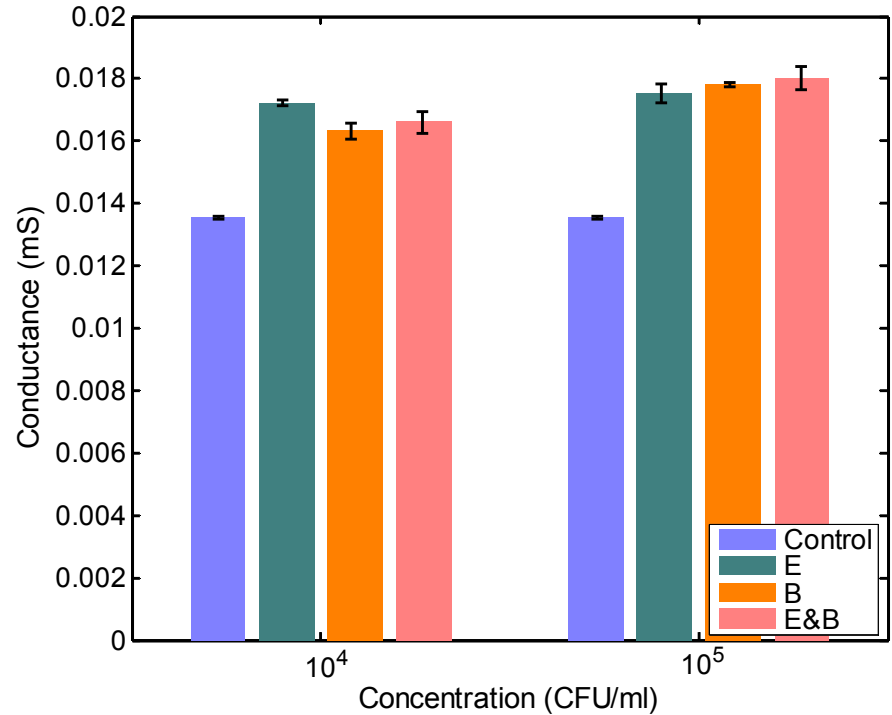
Improvement of OR Gate



OR Gate



New OR gate using gold NP biochip



Old OR gate using lateral flow immunoassay

Summary



- A simple and robust electrical detection method using a combination of gold NP labels and silver amplification
- We have demonstrated that fundamental building blocks (AND and OR logic gates) for biomolecular encoder using fabricated gold NP biochip with the silver enhancement
- The idea of biomolecular logic gates is general regardless biosensor platforms

This work is supported in part by a research grant from the National Science Foundation (NSF- ECCS:0622056)



Reference



- [1] Christer Wingren and Carl A.K. Borrebaeck, "Progress in miniaturization of protein arrays—a step closer to high-density nanoarrays", *Drug Discovery Today* Volume 12, Numbers 19/20 October 2007
- [2] Dirk Janasek, Joachim Franzke, and Andreas Manz, "Scaling and the design of miniaturized chemical-analysis systems," *Nature*, Vol. 442, pp. 19-27, July 2006.
- [3] Lin-Li Lv¹ *et.al* , "Construction of an antibody microarray based on agarose-coated slides" *Electrophoresis*, Vol. 28, pp. 406-413, 2007.
- [4] F. Vinet, P. Chaton, Y. Fouillet, "Microarrays and microfluidic devices: miniaturized systems for biological analysis," *Microelectronic Engineering*, Vol. 61-62, pp. 41-47, July 2002.
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- [6]. A.Hassibi, H.Vikalo, A.Hajimiri, "On Noise Processes and Limits of Performance in Biosensors," *Journal of Applied Physics*, Vol. 102, Issue 1, pp. 014909(12pp), 2007
- [7]. J. Madou and R. Cubicciotti, "Scaling issues on chemical and. Biological sensors," *Proc. IEEE* 91-830, 2003
- [8]. Yang Liu, Shantanu Chakrabarty, and Evangelyn C.Alocilja, "Fundamental Building Blocks for Molecular Bio-wire based Forward-error Correcting Biosensors," *Nanotechnology*, Vol. 18, No. 42, pp. 424017(6pp), 2007.

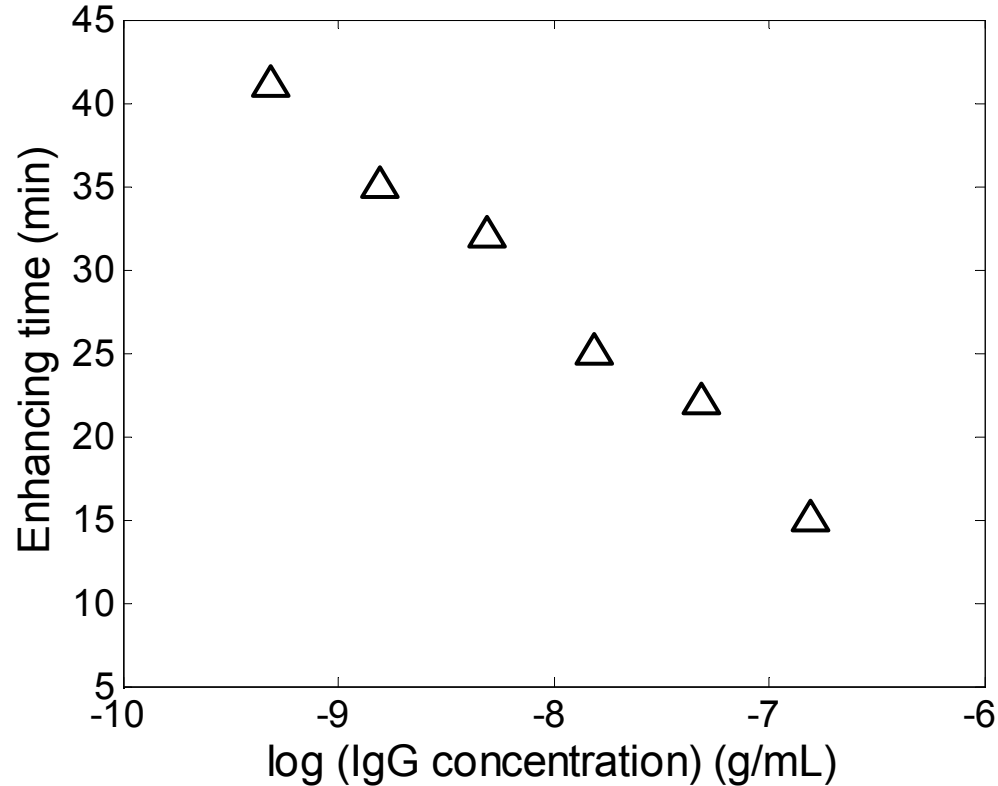




Thank You for Your Attention!



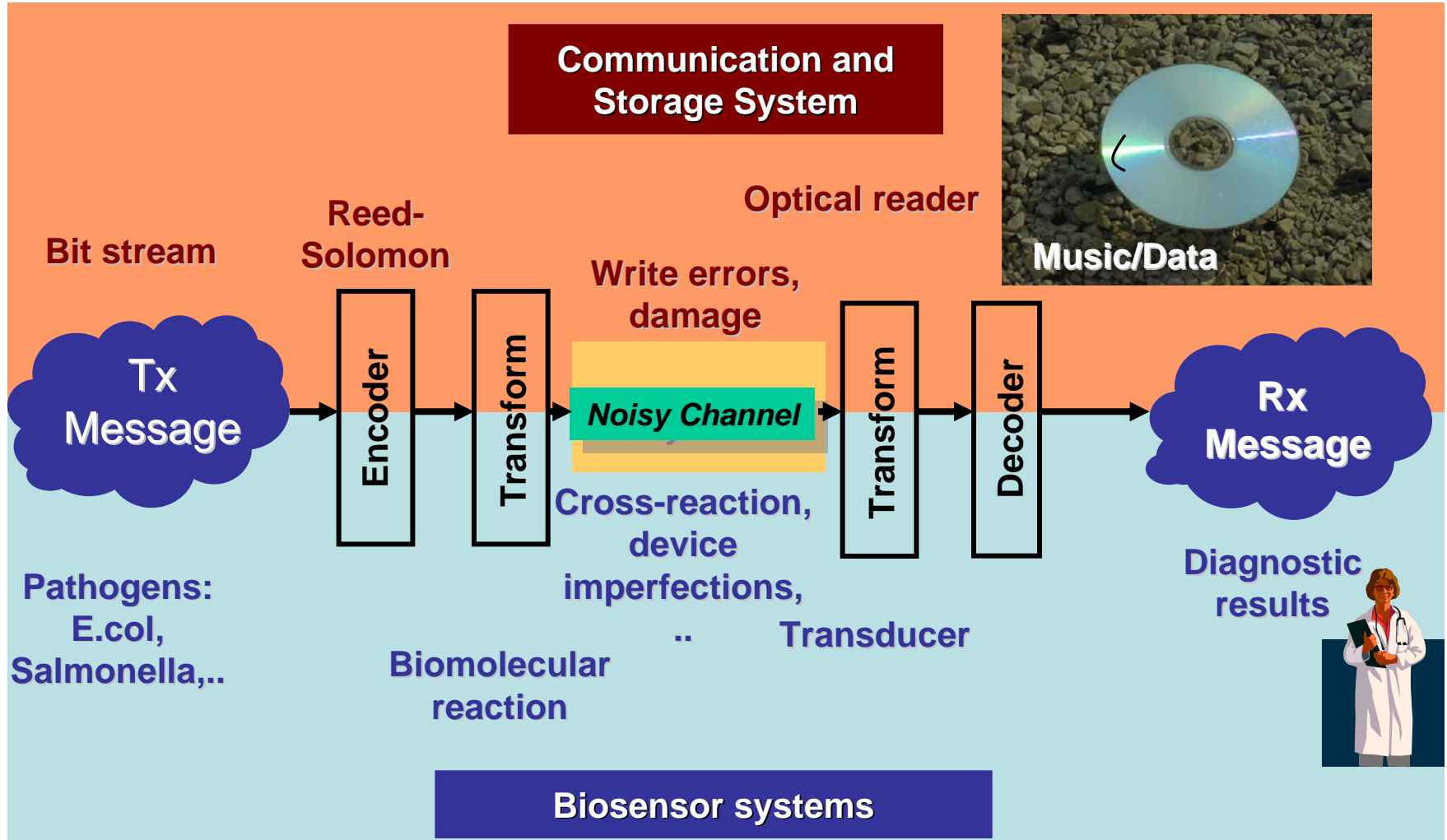
Enhancing Time as an Concentration Indicator



Quantitative analysis: the silver enhancing time required to reach a conductance range of 3.8-5 mS as a function of gold particle concentrations.

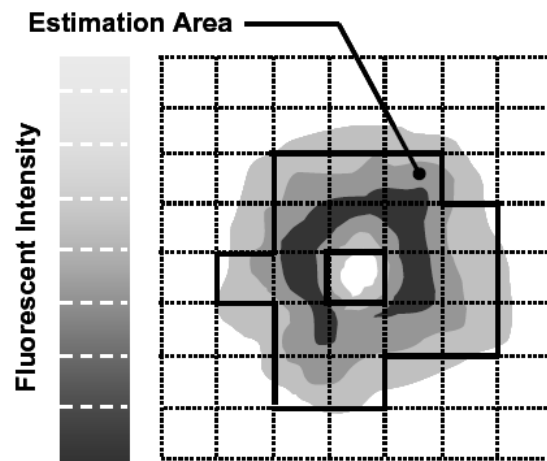


Similarity Between Communication, Storage Systems and Biosensor Systems



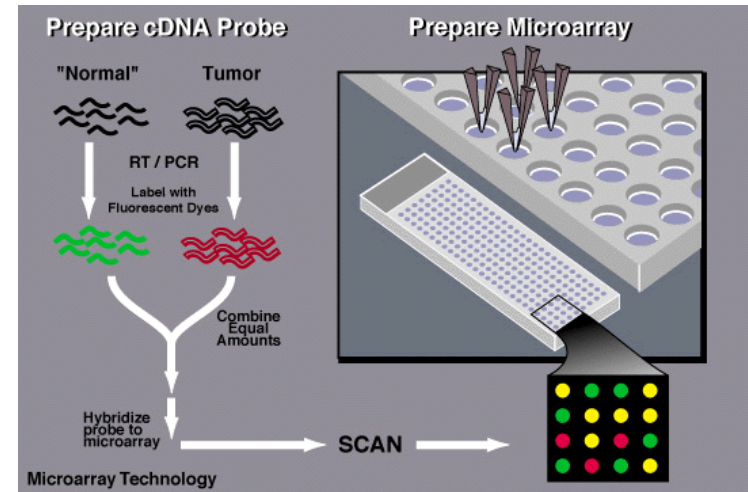
Current Techniques for Reducing Biosensor Errors

- Normalization [10]
- Repetition and averaging [11-12]
- Define a confidence threshold [13]
 - reduced detection limit
 - not always valid



The fluorescent intensity profile of a single spot in microarrays

[14]



Source & courtesy:
www.genome.gov

- Optimal estimation (Hassinbi07[14])
 - Incorporate non-specific binding statistics
 - Challenging for high density binding sites in microarray
- Real-time detection [9]