

The Capillary Electrode Array: A CMOS DNA Separation System

J. Patrick Bedell
jpb@infoeng.org

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1 Introduction

This proposal is motivated by a key problem in molecular biology and biochemistry: starting from a heterogeneous ensemble of biopolymers in an aqueous solution with a homogeneous concentration profile, create an aqueous solution with a highly heterogeneous concentration profile of localized concentrations of certain biopolymer species. Although this procedure is important for all of the biological macromolecules in an organism, DNA molecules are the exclusive focus of this report.

Currently, the most widely used technique for DNA analysis is electrophoresis (see, for example,[1]) in which an electric field is applied to a gel or cross-linked polymer solution. Negatively charged DNA molecules migrate through the solution, with the molecules of the separation medium slowing the DNA molecules through mechanical interactions. Longer DNA molecules experience more obstructions than smaller DNA molecules, and move more slowly through the medium.

In a seminal 1991 paper[2], Ajdari and Prost proposed the use of an inhomogeneous electric field, transverse to the direction of flow, for free-flow (i.e. without a gel-based medium) separation of molecules. Their theoretical analysis indicated separation efficiency significantly greater than that of conventional electrophoresis systems.

Here, we propose the use of CMOS microfabrication and maskless postprocessing to create a molecular separation system that operates on the principle described in [2]. This device contains a microchannel, an array of electrode pairs surrounding the microchannel, and a microheater element to actuate, by bubble creation, bulk flow through the microchannel. While the bubble actuator creates the hydrodynamic force to drive DNA molecules through the microchannel, the electrode pairs create electric fields perpendicular to the direction of the microchannel flow. In the following, we describe the basic architecture of the proposed system, and outline areas requiring further development for realization of a practical system for preparative DNA separation.

2 Fabrication

In the following, our focus will be directed towards the 1.5 micron “ABN” process offered by AMI Semiconductor. This process provides two levels of polysilicon for MOS transistor gates and capacitors formed between the polysilicon layers, and two layers of aluminum metallization for electrical interconnection between circuit elements. The minimum width of a polysilicon line in this process is $1.5\ \mu\text{m}$, thus the description above. This process is significantly behind the cutting edge of CMOS processes, having been introduced in 1987; currently (2004) MOSIS offers a process with a $.13\mu\text{m}$ polysilicon line width.

A process flow for fabrication of the proposed device is shown in Figure 1.

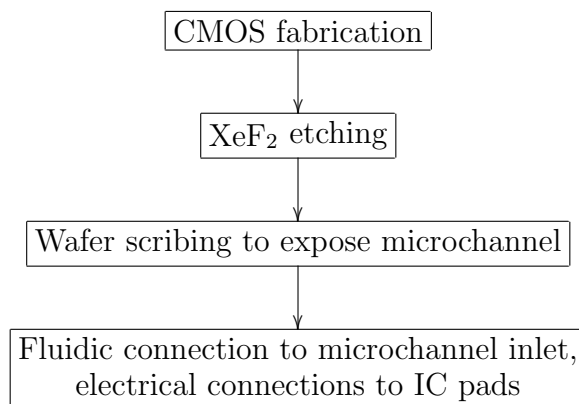


Figure 1: Process sequence for capillary electrode array fabrication.

A cross-section view of the microchannel before and after processing is shown in Figure 2. Prior to etching with XeF₂, a polysilicon-2 minimum-width line has polysilicon-1 and metal-1 electrodes below and above, respectively.

Figure 3 shows 10 electrode pairs. Each poly-1 electrode is $1.6\mu\text{m}$ wide, and each metal-1 electrode is $2.4\mu\text{m}$ wide. The spacing between the metal-1 electrodes is $1.6\mu\text{m}$, for a center-to-center electrode spacing of $4\mu\text{m}$.

The fabrication of the microchannel opening is shown in Figure 4.

A crucial difference between the system analyzed in [2] and the device proposed here is the use of bubble-actuated bulk flow instead of an electrophoretic potential to drive molecules through the microchannel. This mechanism is conceptually very similar to that of a bubble-driven inkjet print head, and has been demonstrated in a CMOS-fabricated microsystem [3]. DNA microarray formation using a standard bubble-jet print head has been demonstrated [4], and it is expected that the mechanism in the proposed system will not damage DNA molecules. One concern is the effect of heating on separation efficiency. An increase in temperature will have the effect of broadening the concentration profile, countering the effect of the separation process.

References

- [1] Jean-Louis Viovy. Electrophoresis of DNA and other polyelectrolytes: Physical mechanisms. *Reviews of Modern Physics*, 72:872, 2000.
- [2] Armand Ajdari and Jacques Prost. Free-flow electrophoresis with trapping by a transverse inhomogeneous field. *Proceedings of the National Academy of Sciences*, 88:4468–4471, 1991.
- [3] David Westberg and Gert I. Andersson. A novel CMOS-compatible inkjet head. 1997 International Conference on Solid-State Sensors and Actuators, pages 813–816. IEEE, 1997.
- [4] T. Okamoto, T. Suzuki, and N. Yamamoto. Microarray fabrication with covalent attachment of DNA using bubble jet technology. *Nature Biotechnology*, 18:438–441, 2000.

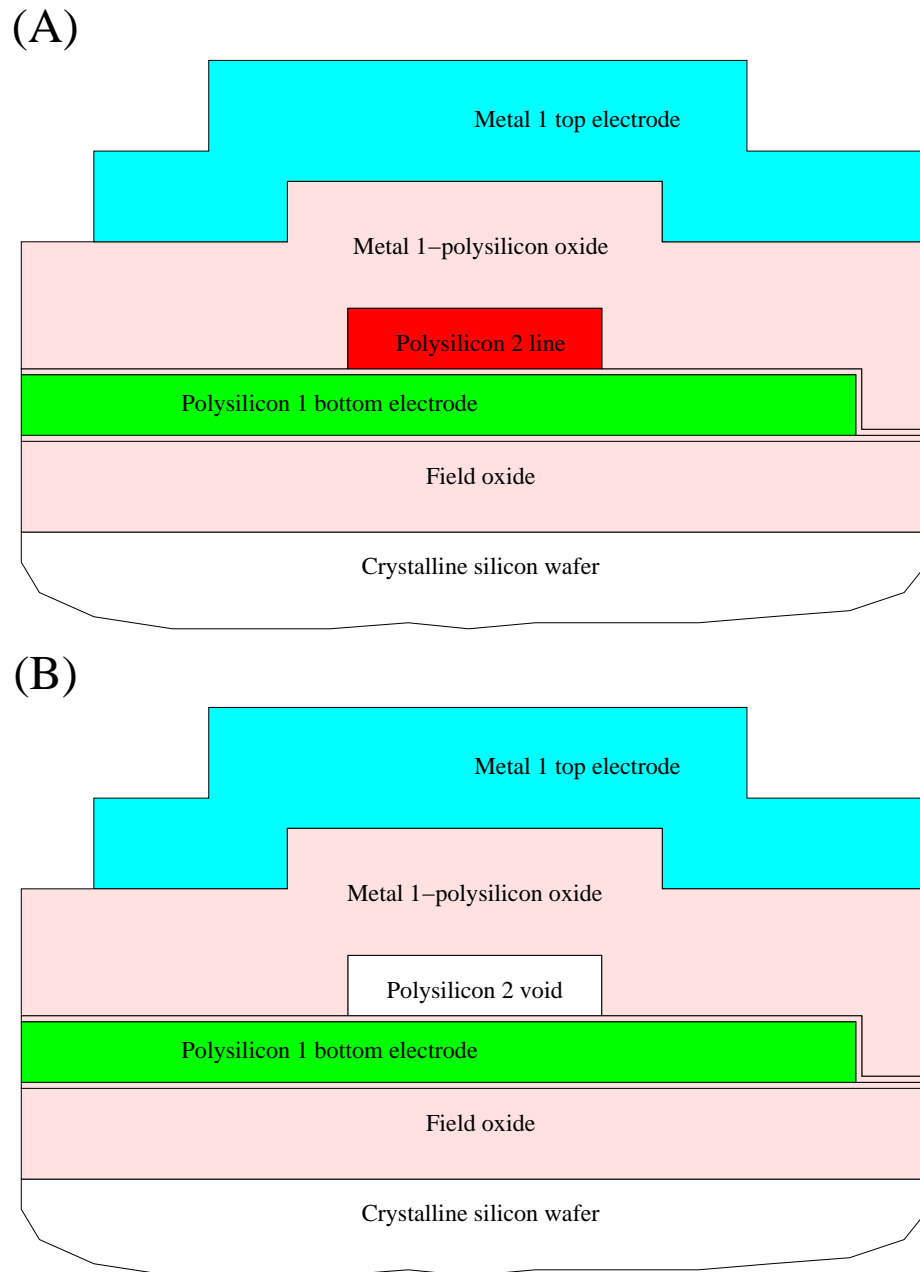


Figure 2: Microchannel cross section: (A) A polysilicon-2 line has electrodes below (polysilicon-1) and above (metal-1). (B) After etching with XeF_2 , the polysilicon-2 line is removed to form a microchannel.

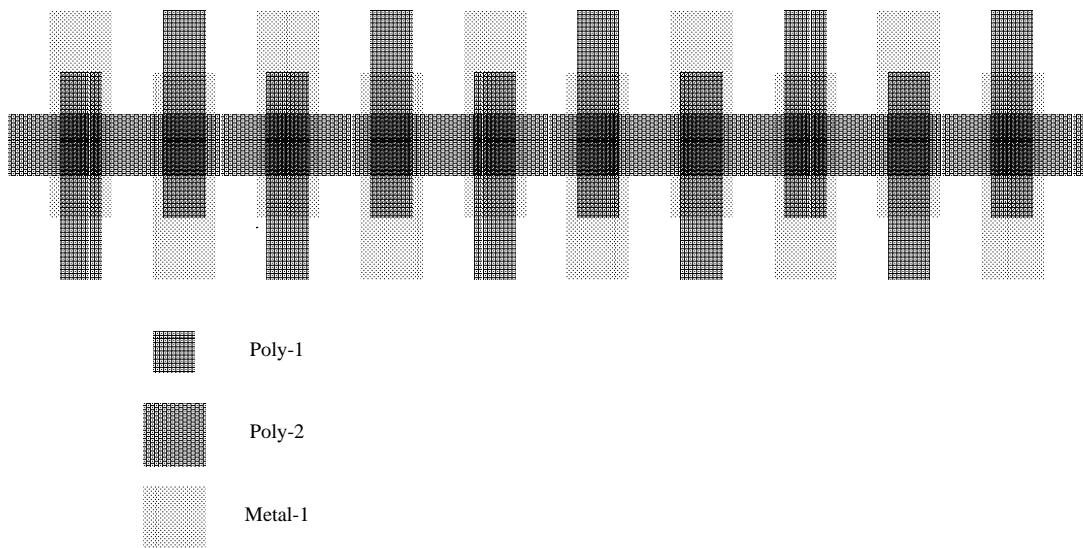
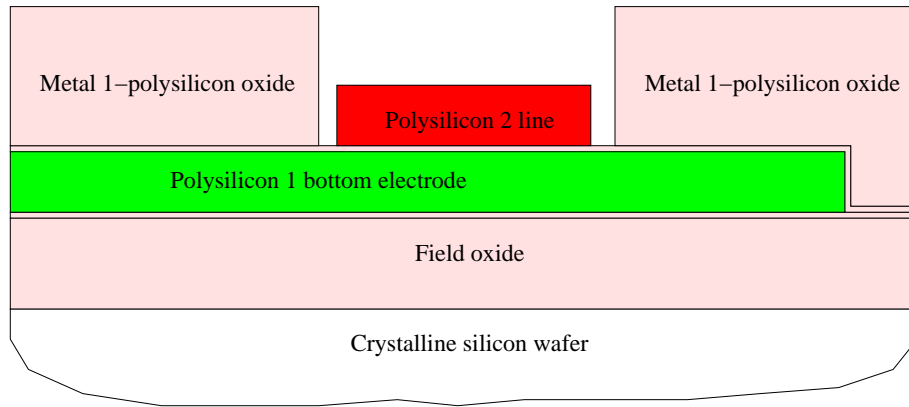


Figure 3: Plan view of 10 electrode pairs.

(A)



(B)

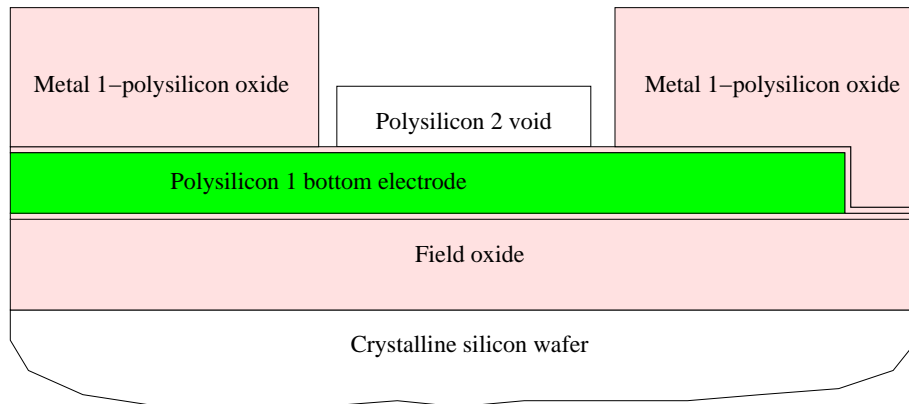


Figure 4: Microchannel opening cross section (not to scale): (A) Polysilicon-2 is exposed to the atmosphere, with a polysilicon-1 electrode beneath. (B) After etching with XeF₂, the polysilicon-2 line is etched to form the opening to the microchannel.