

A Critical Review of the Scientific Paper

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**Micromachined pipette arrays. Papautsky I, Brazzle J, Swerdlow H, Weiss R, Frazier AB. *IEEE Trans Biomed Eng* 2000 Jun; 47(6):812-9**

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### **A) Introductory Claims and Justifications**

The paper describes the design and characterization of batch fabricated metallic micromachined pipette arrays (MPA). The matter presented in the paper builds on the justification of the fact that current micropipette technologies do not allow for highly parallel microscale sample loading of pL to uL volumes that would allow precise handling of the samples and still be compatible with the size dimensions (center-to-center spacing) of the micromachined biochemical analysis systems. This fundamental claim of the paper is supported by citing short evidences of the drawbacks of current micropipette technologies such as macroscale pipetting, droplet dispensing systems and electromigration amongst the many that are employed in labs today. The citation of these limitations gives the reader a fairly convincing viewpoint of the pressing need for a highly precise micro total analysis system (uTAS). As an adjunct to its main claim of challenging current pipetting technologies, the paper distinctly cites the advantages of employing MPAs which include the ability to transfer precise volumes of samples in the submicroliter range; the ability to manipulate samples, reagents, or buffers in a highly-parallel fashion by operating hundreds of individual pipettes simultaneously; and the compatibility with the submillimeter center-to-center dimensions of the microscale biochemical analysis systems. All these claims are ably supported through the practical results obtained by the application of the MPA to high lane density slab gel electrophoresis. A thorough reading of this paper demonstrates the authors' expertise in the domain of micro-pipette technologies and has actual lab data to justify their claims. The claims appear to be highly significant especially when seen in the light of the

lab results which show a twofold increase in the number of theoretical plates and a six fold increase in lane density.

### **B] Claims in the context of previous literature**

The above mentioned claims are placed in the context of microfabricated chemical analysis systems which include the likes of electrophoresis, free-flow electrophoresis, electrical field-flow fractionation (EFFF), polymerase chain reaction (PCR), gas chromatography and liquid chromatography with the rationale for using them being reduction in instrument size and cost, reduction in sample and reactant volumes, reduction in analysis time, increase in analysis throughput, and possibility of integration of sample preparation and analysis functions. An application of the MPA to slab gel electrophoresis brings the matter presented together in the context of one such currently employed analysis system and thereby gives the reader an ideal platform to grasp the matter in its totality which otherwise is hard to synthesize without a contextual reference. Having said this however, the paper does a fairly basic job of inserting claims in the context of previous literature. The paper would certainly score more points if other contextual application areas were to be explored by the authors or at least referenced to some degree. All in all it only hints the reader as to which previous literature should be referenced and rather encourages him to either be knowledgeable of the authors' domain or have some fairly basic understanding of its allied areas.

### **C] Resolution of Scientific Procedure**

The extent to which the authors have included a description of their scientific construction is indeed extremely detailed. The methods for practically building the MPAs cover approximately 30% of the matter presented in the paper and address every step involved in the process with suitable schematic diagrams and images. The scientific procedure addresses everything from

fabrication procedures of doping and etching to the materials, chemicals, procedures and precise dimensions used. This not only aids the understanding of the user but is quintessential in the paper's ability to morph claims into actual laboratory procedures. Another salient feature of this description is to give a background on electrophoretic gel preparation and the concepts of mini and micro-scale gels which supplements understanding of a contextual real world application of MPAs from a reader's standpoint. The complementing drawback however is that this depth of scientific description can be confounding to the casual reader who is forced to source other scholarly material to aid this understanding.

#### **D] Justification of claims through experimental data**

The experimental data presented in the paper is not profound or illuminating, however in its very sense it contains the required substance to be useful in supporting the mentioned claims. Having said this the experimental data is irrefutable and is obtained from actual scaled experiments performed in the lab. The data is strongly supported by verifiable photographs of slab gel electrophoretic separations of 1kB DNA ladder using standard mini and microscale gels. What is most commendable is the fact that the data are not mere snapshots of some esoteric lab procedure but are extensively supported by in-depth description of the experiment. The embedded graphs also add substance to the discussion and hence this section of the paper commands the most praise from this critical review. The authors have done a very neat job of presenting bottom-line results in an understandable manner. However neither the lab data nor results are novel mainly because of the fact that an application of MPAs to an already existing electrophoresis technique is suggested, and the experiment takes a comparative approach to suggesting superiority of implementation. The paper is also biased in its exploratory application to slab gel electrophoresis and would have strengthened its appeal had other application areas been mentioned with similar

scientifically verifiable data. The results however break new ground in suggesting the useful application of MPAs and the solutions that they bring to the domains of micromachined biochemical and micro total analysis systems.

#### **E] Other experimental data / results that could enhance the paper**

The paper addresses the claim of being able to perform polymerase chain reaction (PCR) within the micropipettes. This claim is one which isn't backed up with solid experimental evidence and it therefore remains as an unverified one. Performing PCR within micropipettes is not a trivial procedure but definitely is an achievable one if performed in a disciplined lab environment. Experiential data from the MPA application to slab gel electrophoresis could be used as a background tool to enhance the procedure for the same. Quantifiable lab results obtained from this experiment would definitely go a long way in enhancing the overall acceptance of the paper and negate any contradictions to its claims.

#### **F] Authenticity of and contradictions to the claims / experimental results**

An extensive scientific search on the critical reviews of this paper yields no contradictory results. In fact the paper seems to be well received within the biomedical engineering community due to the verity and originality of the scientific material presented in the paper. Although the paper builds upon some previously published scholarly articles such as "Parallel sample manipulation using micromachined pipette arrays," in *Proc. SPIE Microfluidic Devices and Systems*, Santa Clara, CA, Sept. 21–22, 1998, pp. 104–114. I. Papautsky, J. D. Brazzle, R. B. Weiss, T. A. Ameal, and A. B. Frazier, it presents previously unpublished experimental evidence which only promotes the acceptability of MPA technology as a formidable solution to the drawbacks of currently employed micropipette technology.

**G] Standing of the paper as regards to its discipline**

The paper presents itself as an extremely well written scholarly article. It addresses a novel solution for the mixing, reaction, and separation steps performed in microfabricated chemical analysis systems which require precise volumes of liquid samples to be accurately positioned in the microchannels. Although at a high level, MPAs can be viewed as nothing but miniaturized versions of their macroscale counterparts, their fabrication and packaging technology is non-trivial and requires a disciplined laboratory construction approach. The paper not only addresses these processes in detail but backs up its claims with solid experimental data. Also the implementation of MPAs as being an interface between the macroscale preparation and microscale analysis systems is truly non-replicated across any other scientific research paper and can be considered to be an industry first. The key highlight of this paper is that the MPA technology is truly scalable and presents solutions to 5 pressing problems in micromachined analytical systems i.e. the ability to transfer precise volumes of samples in the submicroliter range, the ability to handle samples/reagents in a highly parallel fashion by manipulating hundreds of samples/reagents simultaneously, a wide range of pipette center-to-center spacing, the ability to individually address the micromachined pipettes in an array for fluid dispensing and extraction operations, and the possibility of adding functionality to the pipettes, such as performing polymerase chain reaction (PCR) within the micropipettes. Given the strengths of the paper in its originality, integrity, detail, veritable experimental results and practical implementation, this scholarly article can be considered as outstanding in its discipline.

Critical Review written and signed by,

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