31st Annual International Conference of the IEEE EMBS
Minneapolis, Minnesota, USA, September 2-6, 2009

Microfluidic Package Design for Magnetoresistive Biosensors

Mark C. Tondra*, Ron L. Bardell, and Proyag Datta, **Member, IEEE*

***Abstract*—In order for Magnetoresistive Biosensor technology to become a mainstream product for clinical and consumer use, several outstanding technical issues must be solved. This paper will focus on one of those issues, which is the need to adapt standard semiconductor packaging processes to fall within some biosensor fabrication process constraints. A set of materials and interconnection methods that meet these biosensor requirements are presented. The resulting architecture is compatible with laboratory assembly, but can be scaled up to small and medium manufacturing quantities by using larger 2-dimensional areas per production batch.**

I. Introduction

THE predominant mode of magnetoresistive sensor packaging has been plastic encapsulation of a Si chip mounted onto a Cu lead frame. In this familiar chip format, the Cu leads are coated with alloys that are easily soldered to, and the whole package is compatible with wave soldering to a printed circuit board. This process is used for packaging all kinds of magnetic sensors including Hall Effect, Anisotropic Magnetoresistance (AMR), Giant Magnetoresistance (GMR) and Tunneling Magnetoresistance (TMR) sensors. In all cases, the temperatures reached during soldering and plastic encapsulation are too high for typical biological material to survive.

A. Basic requirements of magnetoresistive biosensors relating to:

-- 1) Temperature. For a biosensor carrying biochemically active material, fabrication process temperatures need to be kept within a few K of room temperature.

-- 2) Non-encapsulation. It is essential that the bare surface of the Si chip be kept un-coated and available for sample liquids to interact with the surface.

-- 3) Biocompatible Microfluidic Covering. The process and materials required to complete the microfluidic packaged product must not destroy the applied biomaterial, and must have fluidic connections to other components in the biosensing system such as valves and pumps.

-- 4) Package Clarity. Magnetic sensors packages do not need to be optically clear, or UV transparent as is required for many optical or fluorescence-based detectors.

-- 5) Conductivity and Magnetization; The parts of the package that touch sample fluids and buffers must be insulating. Other parts nearby should be non-magnetic if possible.

These requirements have been satisfied, to some degree, in a number of laboratory prototypes. The transfer to a low cost manufacturing process has been slow due to the complexity of the product and the lack of applicable manufacturing infrastructure. This paper, then, seeks to address some of the manufacturing scale-up problems in biosensors as they relate to, specifically, magnetoresistive sensors. Additional emphasis is placed on finding manufacturable architectures that allow the product to have a very low cost and be consumable or disposable.

B. Previous and ongoing work

One major barrier to entry for Lab-on-a-Chip (LOC) devices is the need to connect the electro-fluidic and microfluidic ports of a product to a larger system. This is sometimes called the macro-to-micro problem. Some of the earliest work in 1998 on solving the macro - to microfluidic interconnection problem in LOC applications was addressed by designing a socket-pin electrical connection in parallel with bonded tube ports [1]. This early work was going in the right direction, but the size of the parts, and consequently the cost, was large. A few years later in 2004, a wider range of options was available; some of them seemed compatible with low cost fabrication [2]. In 2008 the Semiconductor Equipment and Materials (SEMI) organization published a Standard for MEMS-Microfluidics interfaces [3]. This standard has yet to be realized in manufacturing, but it addresses many of the design issues.

None of the forgoing work focused on magnetics, and was, in fact quite broad in application. One of the earliest magnetics-based LOC devices was developed at the Naval Research Lab, and published in 1998 [4]. The same group continued to work on the magnetic LOC technology, and published a macro-micro interface design for Giant Magnetoresistive (GMR) sensors in 2002 [5].

This paper does not claim to present original designs or unique solutions to the magnetic biosensor integration problem. Rather, the purpose is to build upon the prior work, and describe key details of interface design between the best-in-class architectures to enable more rapid and flexible advances in the field of magnetic biosensors.

II. Microfluidics Fabrication Methods

A. Microfluidic Cards

Microfluidic sample processing cards have larger features,

Manuscript submitted on April 7, 2009. This work benefitted from a program supported by the Dept of Homeland Security (NBCHC070080)

Mark C. Tondra is the Chief Manager of Diagnostic Biosensors, LLC, 1712 Brook Ave. SE; Minneapolis, MN 55414 (Corresponding Author: Phone 612 331-3584; e-mail: Mark@DiagnosticBiosensors.com, MarkTondra@ieee.org).

Ron Bardell is with MicroPlumbers® Microsciences LLC, 4150 Alabama Ave S, Minneapolis, MN 55416 (e-mail: ronb@microplumbers.com).

Proyag Datta is with the Center for Advanced Microstructures and Devices (CAMD), Louisiana State Univ., 6980 Jefferson Hwy.; Baton Rouge, LA 70806; USA. (E-mail: pdatta1@lsu.edu)

tolerances of ~100 microns, and easy multi-layering through adhesives and/or lamination [6]. One ideal concept for GMR (use GMR interchangeably with TMR and AMR in this paper) biosensor utilization is integration into a disposable microfluidic device (microfluidic card) that accepts raw sample, performs all sample preprocessing, presents the prepared sample for interrogation by the biosensor, and retains all liquid waste for safe disposal of the biological hazard. This scenario allows the user to simply load the sample, record the result, and dispose of the card. Disposable microfluidic cards that implement these capabilities are typically composed of plastic in a planar format similar to a thicker credit card and are produced by injection molding, soft embossing, or a laminated stack of plastic films patterned by laser, knife plotter, or die cutter [3]. In any of these production methods the GMR biosensor chip can be integrated as part of the card. For example, in the plastic laminates cards, the stack is comprised of alternative layers of plastic film and pressure-sensitive adhesive film. The outer plastic layer can be cut away, exposing the adhesive layer. If the exposed adhesive layer has been patterned with holes that connect to the microfluidic channel network in the card and also match the hole pattern of the acrylic cover of the biosensor chip, then the chip can be simply pressed down on the exposed adhesive to form a good bond that can withstand moderate fluid pressures.

With the GMR biosensor chip in place on the microfluidic card, preparation of the raw sample can be performed "on-card" just prior to presentation to the biosensor chip. Sample preparation often includes sample aliquoting, lysing of blood cells, mixing with dyes or reagents, temporary magnetic or immunological capture of the analyte, washing of captured analyte, and controlled flow of prepared sample solution through the GMR biosensor chip.

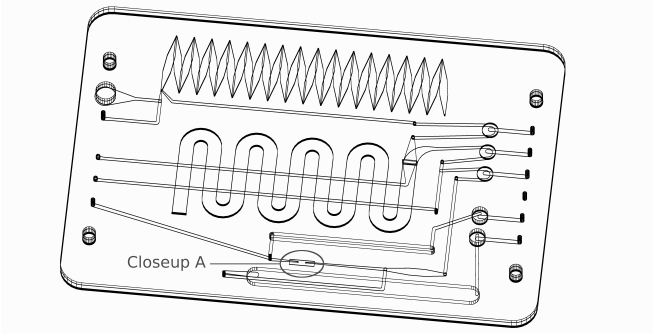

Fig. 1. Schematic drawing of a Microfluidic Card with an integrated magnetoresistive biosensor chip located at Close-up A. The card is 120 by 80 mm in length and width and less than 4 mm thick. It contains microchannels that implement all sample processing, so that a raw sample can be loaded, then automatically processed under control of the reader instrument, which then presents the assay results to the user. The microfluidic sensor chip fits into the rectangular recess highlighted by the Close-up A oval. The card has two ports facing up on the surface that mates to the microfluidic chip (see Fig. 2).

The microfluidic card is typically designed to mate with a reader instrument that contains all expensive components, so that the card itself can be as simple and inexpensive as possible. Thus components like permanent magnets, electromagnets, pumps, valves, optics, and control systems are designed into the reader instrument.

The scale of the magnetoresistive biosensor chip is so small that many can be integrated into a single microfluidic card. The dimensional tolerances of the card is larger by roughly 10X with minimum channel width and hole size of 200 microns (CO_2 laser cut) or 1 mm (steel rule die cut). Channel height can be as small as 25 microns, but is typically 100-150 microns. The overall card size is usually less than 6 in. by 6 in. Since the card is relatively small and two-dimensional, multiple cards can be inserted simultaneously into a high-throughput reader instrument for parallel processing. The reader instrument size ranges from smaller than a benchtop instrument to larger than a cell phone.

B. Micro-scale Microfluidic Structures

The footprint of the actual GMR sensor drives the microfluidic cap (Figure 4) design that mates with the silicon die. Fluid has to flow precisely over the sensor and has to be restricted from undesirable interactions with any reference electrodes or sensors that may exist on the silicon die. In order to ensure that the maximum volume of sample flows over the sensor, the dimensions of the microfluidic channel should be similar to those of the sensor. A typical sensor chip design has a 4 x 5 array of 200 micron diameter GMR sensors with an inter-sensor spacing of 75 microns. It is necessary to have microfluidic channels that are open over the sensor array, but do not hang over the edge of the sensor die. This means the alignment tolerances are about +/- 50 microns. As the tolerance and the dimensional requirements for this part of the device are very different from those of the rest of the lab card, the best solution is achieved by decoupling the design and fabrication methodologies of the two. The microfluidic cap is a component that achieves this objective. It is a separate polymer component that has microchannels compatible with the GMR sensor and also has interfaces that allow it to be connected to the microfluidic card.

Thermoplastic polymers such as Poly methyl methacrylate (PMMA), Polycarbonate, Polystyrene and cyclo olefin copolymer (COC) are the materials of choice for fabricating the microfluidic cap to integrate microfluidics with silicon dice. These polymer components can be mass produced at low cost using processes such as injection molding and hot embossing [7,8]. Using these techniques it is possible to fabricate components with dimension scales ranging from a few millimeters down to nanometers. Micromilled brass tools may be used to hot emboss these polymers, to produce parts with minimum dimensions down to 20 microns and if smaller dimensions are desired, lithography based molding tools can be used. The hot embossing process is an excellent method to fabricate parts for prototyping and small scale production as it is possible to go from the drawing board to fabricated prototypes within a week or two.

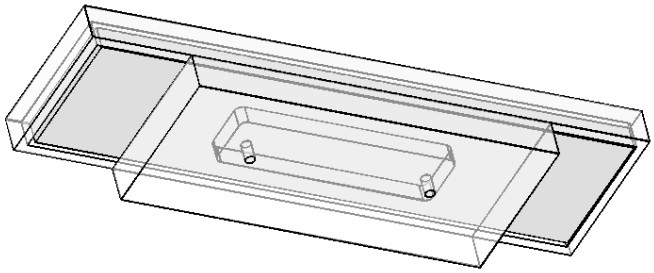

Fig. 2. 3-Dimensional CAD drawing of a Giant Magnetoresistive sensor chip sandwiched between two PMMA micro stamped pieces. The two ports on the downward facing surface of the microfluidic cap have a center-to-center spacing of 2.0 mm. The Si die has outer dimensions of 1.5 mm x 6.0 mm. The total thickness of the sandwiched sensor die is ~0.8 mm. Matching this total thickness to the depth of the well on the lab card is critical for success.

C. *Micro-scale Magnetoresistive Sensor Package*

The GMR sensor chip is mounted onto a printed circuit board (PCB) and electrically connected to the PCB with wire bonds. These wire bonds are visible in the photograph in Fig. 3 below. The PCB has plated "vias" that carry electrical current from the near to far side to the PCB. These vias are, then, the electrical access to the chip from the outside world. The design shown here is such that the external electrical contact is made using spring loaded "pogo" pins that enable an easy and reliable make-break connection. Thus, the card can be contacted to a "reader" instrument, electrically probed, and then removed for disposal or storage.

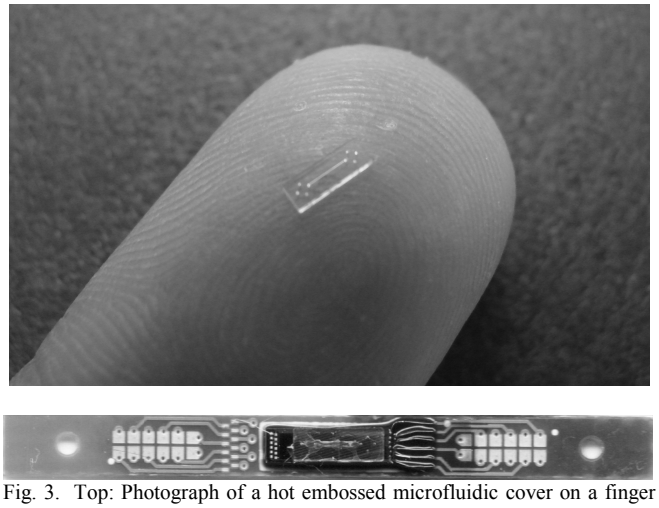

Fig. 3. Top: Photograph of a hot embossed microfluidic cover on a finger to provide a sense of scale. There are four ports visible at each end of this cover. The two ports nearest the center are connected via a microfluidic channel that is 2.0 mm long. Bottom: Photograph of this microfluidic cover on top of GMR sensor die, which is mounted on a Printed Circuit Board (PCB). The sensor dice were manufactured at NVE Corp. Eden Prairie, MN. The PCB was designed by Pyxis Integrated Technologies, Coon Rapids, MN.

III. Microfluidics Interface Architecture

The interface design between the fluidic card and the microfluidic sensor chip is straightforward. The nominal depth of the recess is determined by fabrication factors and is about = 30 mils = 750 microns.

A. *Alignment Methods*

A self-aligning structure in the chip receptacle is indicated in Fig. 4. Passive alignment like this means that the positioning of the chip happens through a mechanical interference fit. This has not yet been demonstrated on these parts; this kind of fitting may be adequate for many applications, and would be easy to implement for small batch work. For higher precision and greater throughput, an optical alignment system can be used.

B. *Bonding*

A layer of acrylic or silicone adhesive is fabricated into the microfluidic card as part of the regular card manufacturing process. This adhesive provides a mechanical gripping and fluidic seal between the card and GMR sensor chip.

C. *Electrical Access and Structural Integrity*

Electrical contact is available through the far side of the PCB, from the card; which is the top of the PCB as drawn in Fig. 4. The thickness of the PCB is not critical. Thinner is better for overall size of the product, however, a thinner PCB provides less structural integrity to the part. Once the permanent interface has been formed, though, the much thicker "lab card" provides ample structural rigidity for the finished part.

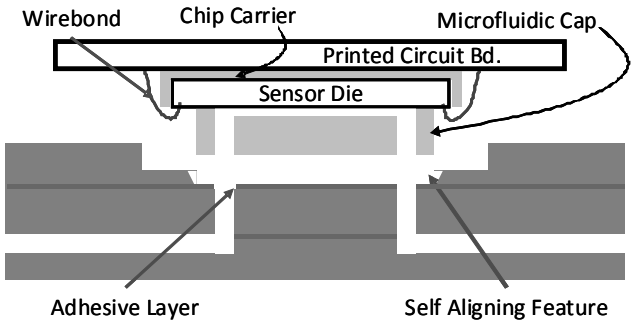

Fig. 4. Schematic drawing of the cross section of the interface between the Lab Card (bottom) and the PCB carrying a GMR sensor die in a microfluidic package. As in other Figs., the closest ports are separated by 2.0 mm. The port diameters are designed to be 200 microns in diameter, which places an upper limit of about 100 microns on allowable mis-alignment between the card and microfluidic chip while still having adequate flow path.

IV. Discussion and Conclusion

A feasible path to high quantity manufacturing of GMR sensors for microfluidic biosensor applications has been described. Interface architectures, and corresponding methods for assembly, have been designed to connect the Si chip micro level, to the larger scale microfluidic card level. If successfully implemented, this architecture will fully address the Macro-micro connection problem for the area of magnetoresistive biosensors. The design requirements for the Si-chip sensors are essentially the same as would be used for a standard injection-molded plastic chip package. The Si chip can be background and sawn to any dimensions that are desired for this microfluidic package style. The package is designed to be compatible with standard wirebonding and chip-on-board (COB) mounting methods.

A. Testing and Performance

This proposed microfluidics interface has not been substantially tested at the time of this writing. It is expected to hold up well to pressures up to 2 Atm., and down to vacuum. Leak-back rates have not been measured. Additional parameters that should be evaluated include: shear stress, tensile stress, leak-back rates under pressure and vacuum, and maximum allowable internal pressure before bursting.

B. Potential Applications

Microfluidic magnetic sensors should find applications in the detection of biospecifically bound magnetic labels; and sorting and actuation of magnetic nanoparticles in flow streams. While the foregoing discussion is focused on microfluidic packaging of magnetic sensors, the same architecture can be used for photonic and electrochemical chips as well. Another possible use in LOC applications would be a miniature solid state pressure gauge. The main benefit of the interface design proposed here is that the biochip sensor component can be made very small, keeping its cost low (estimated under $1 packaging cost).

Acknowledgment

M. Tondra thanks Mark Crockett at Applied Materials for many helpful detailed technical discussions as part of his efforts as the chair of the SEMI MEMS Microfluidics Standards Committee; Kristin Taton and Patrick Guire at ISurTec for their collaborative support and shared laboratory space; Erik Lange at Pyxis who designed the PCBs for the GMR sensors; and several undergraduate students at the Univ. of Minnesota who have contributed to the details of this development work.

References

[1] Galambos, Paul; Benavides, Gil; Electrical and Fluidic Packaging of Surface Micromachined Electro-Micro-Fluidic Devices, in: Harrison J.D., A. van den Berg (Eds.), Micro Total Analysis Systems '98, Banff Canada, October 1998

[2] Fredrickson, Carl K. and Fan, Z. Hugh, "Macro-to-micro interfaces for microfluidic devices," Lab on a Chip, 4, (2004), pp.526-533.

[3] SEMI MS7-0708, "Specification for Microfluidic Interfaces to Electronic Device Packages, (2008).

[4] D.R. Baselt, G.U. Lee, M. Natesan, S.W. Metzger, P.E Sheehan, R.J. Colton, Biosens. Bioelectron, 13 (1998) 731.

[5] Tamanaha, C. R., Whitman, L. J., and Colton, R. J., "Hybrid macro-micro fluidics system for a chip-based biosensor," J. Micromech. Microeng. 12 (2002) N7-N17.

[6] Weigl, B., Bardell, R., and Cabrera, C., "Practical Aspects of Microfluidic Devices: Moving Fluids and Building Devices" in *Handbook of Biosensors and Biochips*. 1st ed. vol. 2, David C. Cullen, Ed. Chichester, England: John Wiley & Sons Ltd, 2007, pp. 711-729.

[7] Becker, H. and W. Dietz. Microfluidic devices for mu-TAS applications fabricated by polymer hot embossing. in Proceedings of the 1998 Conference on Microfluidic Devices and Systems, Sep 21-22 1998. 1998. Santa Clara, CA, USA: SPIE, Bellingham, WA, USA.

[8] Datta, P. and J. Goettert. Polymer Microfluidic Platform. in Smart Systems Integration 2007. Paris, France: VDE Verlag GMBH.