Infusion Micro-Pump Development Using MEMS Technology

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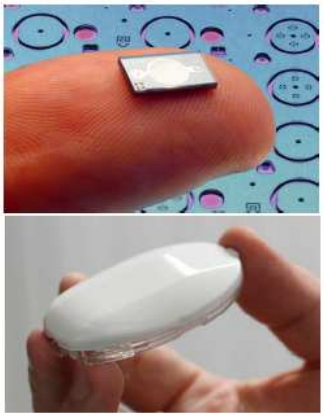
Introduction

Diabetes is a chronic condition that occurs when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces.
People having type 1 diabetes require insulin (10% of all diabetics). People with type 2 diabetes can be treated with oral medication, but may also require insulin; 10% of all type 2 diabetics require insulin. Among the actual different methods to administer insulin (syringes, pens and conventional infusion pumps) a possibility to increase infuser performances is offered by the utilization of silicon based MEMS pumps (Micro-Electro Mechanical Systems). The main two pump families are classified as mechanical and non-mechanical pumps. The former contains check-valve, peristaltic, rectification without valves and rotary ones ("Displacement Pumps") or Ultrasonic and Centrifugal ("Dynamic Pumps"); the latter consists in Pressure, Concentration, Electrical Potential gradients and Magnetic Potential micro-pumps.
The micro-pump described here is an electro-mechanical device actuated with a piezoelectric-element and based on MEMS technology, able to minimize size and costs, offering a high precision pharmacological dispense [1]. Three slices are bonded to reach the final results: top and bottom caps and an intermediate SOI. In case of anodic bonding, top and bottom caps are constituted of micromachined borophosphosilicate wafers, whereas in case of metallic bonding three silicon slices are used. The paper deals with the fabrication evolution of the device according to the different items that had to be faced during development: design, fluidic, mechanical and electrical simulations and characterization, safety requirements and final testing. Built-in reliability is ensured by two inner sensors able to detect any occlusion or malfunctioning and informing so the patient. The result is a compact, core pump chip that can deliver from 0.02 Units of insulin up to 3.6 Units per minute with accuracy better than 5%.

1. Full Device General Characteristics

The insulin dispense device consists of a disposable and a permanent part. The disposable part mainly features a plastic shell containing the MEMS insulin micro-pump, the actuator and the insulin reservoir. The permanent part is basically made of a plastic shell containing the electronics with embedded firmware and the wireless control board (Fig. 1). In fact the basal or the bolus insulin amount can be pre-programmed by a remote control via RF connection. The device is fitted on a patch located on the patient's arms or abdomen. The pump can be attached to or detached from the infusion cannula through-skin inserted.
Schematic cross-sections of the pump in pull (filling) and push (infusion) actuation phases are provided in Fig. 2 and 3 respectively. During pulling the inlet valve opens

and the outlet one remains closed, whereas while the actuator is pushing the pumping membrane the outlet opens, closing the inlet.



Figs.1: Pump chip (top) and insulin dispense device (bottom).

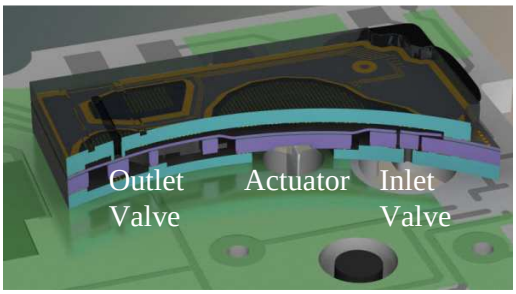


Fig.2: Pump actuation in pull mode.

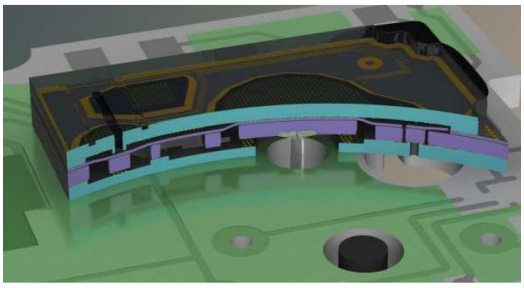


Fig.3: Pump actuation in push mode.

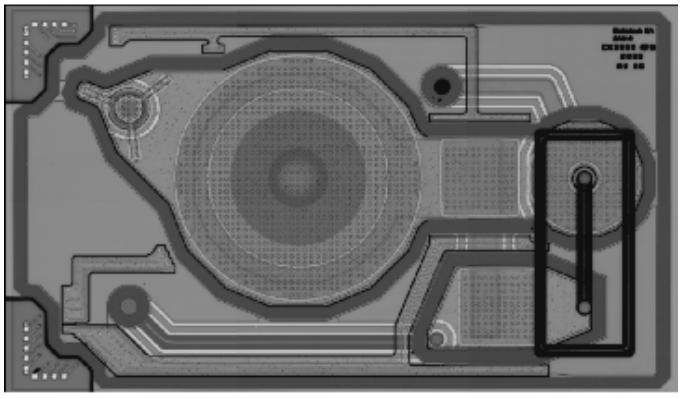


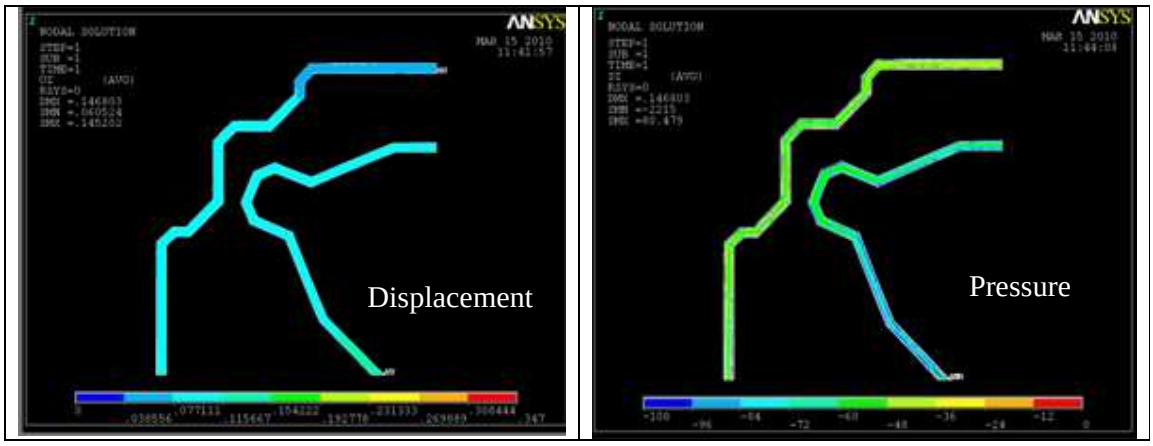
Fig.4: pump chip IR picture; clearly visible the inner and outer metallic bonding rings.

The device is sealed by an inner and an outer metallic ring providing sealing to the pump cavity, fluidic path and dead volumes (Fig. 4).
Built-in detectors monitor each pump beat detecting any occlusion or malfunctions almost instantaneously. Another sensor controls the temperature inside the pump: exposure to external heating will be signaled as warning before possible insulin degradation occurs.

2. Design and Simulations

The design of the MEMS device has been focused on fluidic, mechanical, and electrical requirements. For fluidic dynamics active and dead volumes have been dimensioned and also the insulin fluidic pathway and flow have been calculated on the basis of the desired pharmacological delivery. In particular way solid structures have been placed all along the fluidic path in order to provide continuous, laminar and not turbulent liquid flow. As far as electrical design is concerned, the simulations have been used to reach proper implant doses for p-n junctions, sheet and ohmic contact resistances, diffusion depth, sensor balancing, and parasitic effect account. Finally also mechanical behavior was modeled and performances calculated so that stroke

volume and pumping membrane reliability reached the target specifications. In Fig. 5 it is reported a FEM simulation showing the strain and the stress induced on metal buses and silicon by the bonding operation itself.



Figs. 5: Top cap metallic bonding simulation: strength (in blue) and weakness zones (in orange red) for displacement and pressure parameters, respectively (in A.U.).

Pump inlet valve, normally closed, is maintained under pre-tension by means of arm springs and an apposite counter-bouncing ring. Arm length optimization and relative mechanical stress were also calculated through FEM simulations in order to ensure that the device can be submitted to a shock equivalent to a drop of several meters without damage. The mechanical integrity of the micropump is monitored during the functioning of the device by testing electrically crack-guard rings implanted directly into each moving parts of the MEMS pump.
Several technological aspects have been coped to achieve the final MEMS device:

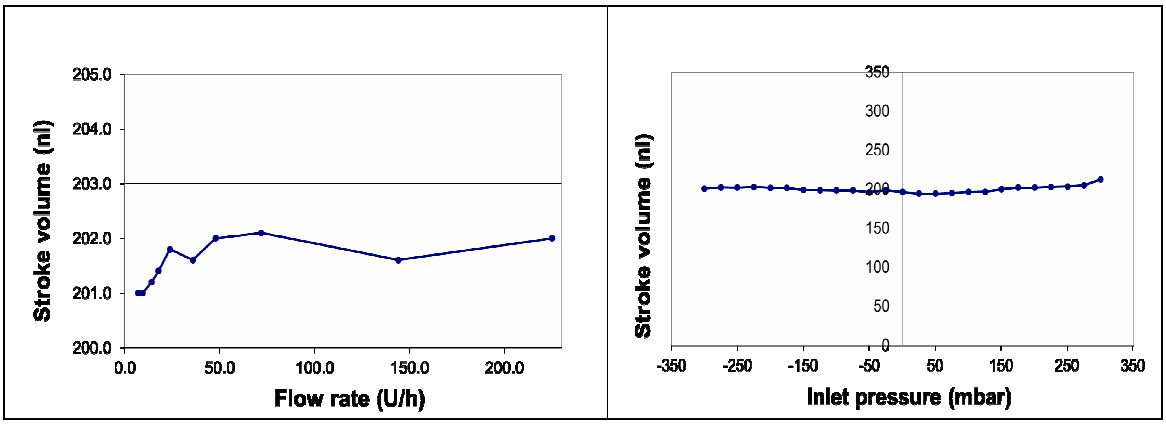
- Cavity etch to get repeatable and precise pumping volume;
- Front to backside alignment for lithographic masking operations;
- Pass through holes into 500 µm thick wafers;
- Ion Implantation simulations of the different atomic species doses to achieve the desired electronic characteristics of the passive elements inside the MEMS device;
- Membrane and valve freed by HF release step;
- Thin wafer handling and processing;
- Stacking of three slices: bonding alignment and tightness;
- Physical and chemical material compatibility and choice.

In particular way original wafer finishing solutions were found in order to obtain clean and bondable surfaces.

3. MEMS Characterization (Fluidic, Mechanical, Electrical)

MEMS pump fluidic characterization has been performed through laboratory equipment in order to study delivery both in dry and wet mode. Liquid delivery repeatability and accuracy were verified by means of gravimetric measurements,

whereas dry tests were carried out using digital precision manometer and pressure regulator, interfaced to a computer.



Figs. 6: Stroke volume versus flow rate (left) and stroke volume versus reservoir pressure (right image).

In Fig. 6 the evolutions of the stroke volume versus the flow rate and the reservoir pressure are shown, indicating that the delivery accuracy does not depend on actuation frequency up to 3 Hz and inlet pressure in the range +/- 300 mbar. Fig 7 illustrates the stroke volume repeatability at low frequency obtained by gravimetry and in Fig. 8 it is shown the so called “trumpet curve”, which gives the maximum positive and negative percentage deviations from the target dose of 1 U/h at different observation intervals.

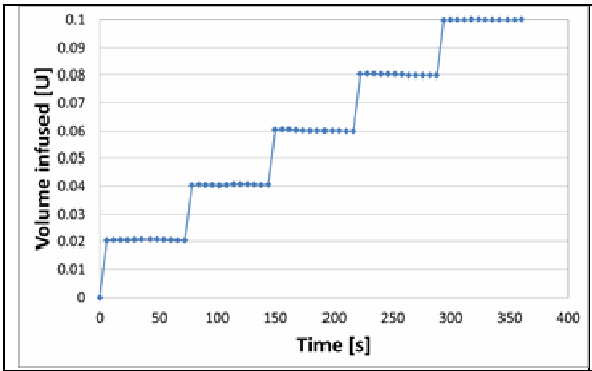


Fig.7: Pneumatic pumping steps of the µ-pump; stroke volume repeatability example.

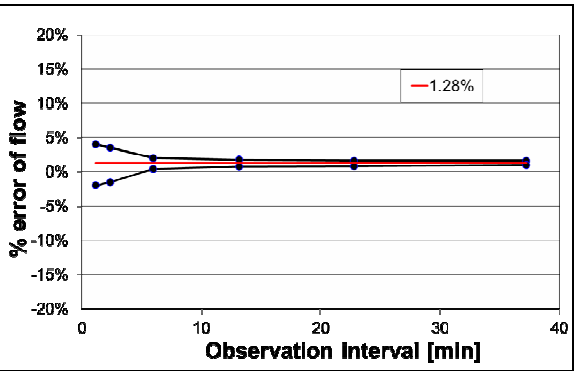


Fig.8: Trumpet curve of a pump actuated at 1U/h (eq. to 0.01 ml/h).

Mechanical characteristics were obtained by studying the piezoelectric element displacement through optical technique and also by means of cycling pumping tests in order to validate valve and pumping membrane reliability. I-V electrical characteristics were obtained instead by classical tester measurements, at the probe bench, for passive components.

5. Safety Features and Reliability

The intrinsic safety features are ensured by built-in device sensors conceived to detect “in real time” eventual occlusion (coming from the catheter for instance) and other anomalies like the presence of air, leaks, incomplete strokes, reservoir under or overpressure. In Fig. 9 the typical signal output shape during a stroke is represented before, during and after a total occlusion, showing the high sensitivity of the detection since only one stroke is necessary to detect this failure. As far as device control is concerned, at least four levels of electrical testing are performed: Parametrical Testing after active circuitry completion on wafer, Electrical Wafer Sorting on stack performed after wafer bonding and before sawing, Functional Testing after pump cell assembly and Final Testing once the full device has been produced. Fatigue and stress tests certify the pumping cycling capability well above the device lifetime.

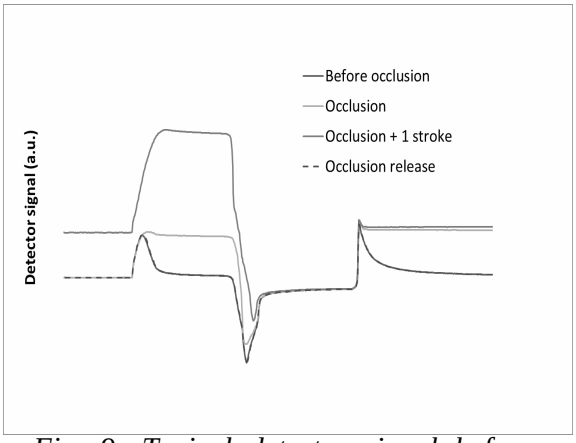


Fig. 9: Typical detector signal before, during and after an occlusion.

6. Comment and Conclusions

A new infusion pump concept, based on MEMS technology, has been presented, able to minimize size and costs, offering a high precision pharmacological dispense. During the design and technological development special effort has been dedicated to mechanical simulations, process integration, self-diagnosis and characterization measurement methods. Process integration was developed in order to stack three slices: two borophosphosilicate glasses as caps onto an intermediate silicon slice for anodic bonding or three silicon wafers for metallic one. The device is finally sawed and mounted on a ceramic substrate where the pumping membrane is actuated with an external piezoelectric element. In field self diagnosis and safety were studied on the pumping volume, electronics and pressures with laboratory characterization and reliability tests. The result is a compact, core pump chip that can deliver from 0.02 Units of insulin up to 3.6 Units per minute with accuracy better than 5%.

Acknowledgements

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References

[1] N. Schneeberger, R. Allendes, F. Bianchi, E. Chappel, C. Conan, S. Gamper, M. Schlund, *Proceedings of the Eurosensors XXIII conference, Procedia Chemistry*, 2009; **1**:1339– 1342.