

Life Science Solutions at Silex Microsystems

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ABSTRACT

What if there were a technology so smart that it could detect biohazards in the air, so small that it could make cameras that fit inside of pills to swallow, so effective that it could revolutionize the production of everything from hearing aids to automobiles, and so efficient that you could make thousands of uniform components at a time, each for mere pennies. What would you do with it?

Imagine the possibilities!

Keywords: life science, biomems, MEMS, microfluidics, production, silicon, glass, lab-on-chips

1. INTRODUCTION

At Silex we do more than imagine—we make it happen. With miniaturization, the possibilities are endless—not just for designing revolutionary applications, but also for reducing production costs, increasing product effectiveness and manufacturing accuracy, and saving time. Our mission is to help telecommunications and life science companies pioneer new applications using MEMS technology and stay a step ahead.

Our customers don't just come to us to buy components; they come to us for problem solving. We understand how to reformulate a customer's product concept in MEMS terms and turn it into a reality, and we've got specialists who understand each of our customers' industries and needs. So when we're presented with challenges, we don't just design and manufacture customized MEMS components—we revolutionize the way our customers do business.

Solving a problem is only the first step—actually working from start to finish can take hundreds. And we do them all ourselves. We design and produce every component in our own fab and we guarantee that everything we create is of the highest quality. We have a state-of-the-art cleanroom production facility in Järfälla, so we can produce large volumes of high quality components in-house. And we do it faster. The process from concept to prototype can take just weeks.

Even though we're an industry leader in Sweden, we don't take our position for granted. We understand that incorporating a new technology is a big investment and we think of every project as the beginning of a partnership. We work closely with each of our customers around the world, and we

keep the lines of communication open every step of the way, from concept to finished product. And even though we're growing fast, we limit the number of projects we take on every year to make sure that we can devote ourselves fully to each customer. Because if we can't do something well, we won't do it.

We're problem solvers who like to make the impossible possible. We're also scientists with Ph.D.'s in MEMS technology. We recognized the potential of MEMS and we wanted to find a way to use it to help companies remain at the forefront of development. Because many of us have worked in the optics and microelectronics industry, it was a natural step for us to begin designing MEMS applications for the life science and telecommunications industries. But we didn't stop there. Today we help a variety of companies produce new applications more effectively, more efficiently, and more affordably.

We use MEMS technology to design and manufacture components for the telecommunications and life science industries. We make specialized components on demand to be integrated with customers' end products. MEMS technology offers many of the same advantages as integrated-circuit technologies—high yields, repetition and mass production capabilities, and lower integration and packaging costs. A few examples of MEMS-based life science applications that are developed and/or produced at Silex will be presented below.

2. LIFE SCIENCE APPLICATIONS

Miniaturization makes it possible to create life-saving applications that were impossible before. Lab-on-a-chip devices that conduct standard techniques such as electrophoresis, PCR and DNA sequencing have advanced significantly in the past few years. We've designed and manufactured a number of standard applications that can be used separately or together as a lab-on-a-chip. We have also created a number of devices for medical applications. In figure 1, for example, there is a picture of spiked electrodes beside a human hair that is used for measuring bio-signals by Datex-Ohmeda. The individual spikes are designed to penetrate the human skin and are typically 40 μm wide and 150 μm high. The spike array is fabricated using deep reactive ion etching and is a promising alternative to standard electrodes in biomedical applications.

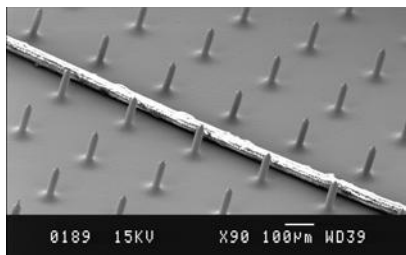


Figure 1. SEM picture of spiked electrodes.

For drug delivery applications we develop and manufacture a micropump (shown in figure 2) for the company Debiotech in Switzerland. It is a high performance micropump with a low flow rate range of typically 1 ml/min and the pump demonstrates linear and accurate ($\pm 5\%$) pumping characteristics for flows up to 2 ml/h. The working principle is a volumetric pump with pumping membrane, which compresses a chamber in a reciprocating movement and which is associated to a pair of check valves in order to direct the pumping flow. The chip is a stack of 3 layers bonded together: one silicon plate with micromachined pump-structures and two glass plates with through-holes. Added to the stack is a piezoelectric actuator. The fluidic path is designed to minimize dead volume. Thanks to the resulting high compression ratio, the pump is self priming and tolerant to small air bubbles. In order to protect the sensitive elements and to ensure a long-term leak-free functioning of the pump, a fine filter is integrated on-chip. In addition, the pump chip is equipped with a detector allowing the detection of occlusion or the presence of air. The micropump can be used in various drug delivery devices for accurate delivery of various therapeutical compounds with dedicated delivery profiles.



Figure 2. Micropump for drug delivery applications.

We also develop chip-based solutions for high-throughput ion-channel characterizations for Sophion Bioscience in Denmark. Ion channels govern the electrical properties of all living cells. In particular, the coordinated activity of several ion channels is the mechanism underlying action potentials in excitable cells. A multitude of human and animal diseases are caused by dysfunction of ion channels for example cystic fibrosis and epilepsy. The search for new, potent and selective drugs that interact with specific ion channels is strongly technology driven and focused on high-throughput screening. The only direct way of validating the effect of a chemical entity on an ion channel is to measure the ionic current through the channel and determine the change in current caused by the compound. The patch clamp technique has proven extremely useful in revealing many aspects of ion channel function. However, traditional patch clamp has serious shortcomings in pharmaceutical discovery and screening, as the throughput is low, and it requires highly specialized personnel. One possible key to high-throughput screening is the combination of patch clamp and microtechnology. A large number of silicon chip designs, see example in figure 3, have been produced by Silex and tested for their ability to be used for patch clamp measurements by Sophion. Numerous patch clamp

measurements on whole-cell configuration have been conducted by Sophion on a multitude of ion channels expressed in various cell lines. Sophion's silicon chip constitutes a complete measuring unit, and comprises pipetting wells, integrated flow channels, and the measuring site.

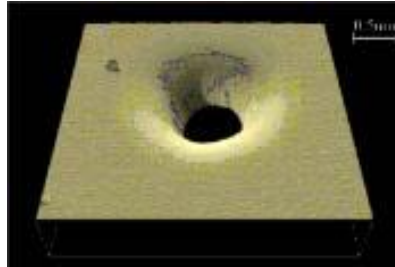


Figure 3. Sophion's silicon chip for patch clamping.

A pressure sensor that is used for measuring the blood pressure inside coronary arteries is shown in figure 4. The chip size is 0.1x0.1x1.3 mm and is developed for a Swedish company called Radi Medical. The state-of-the-art pressure sensor offers superior handling characteristics and reliable and stable signal performance, providing the physician with more ease-of-use and decision-making opportunities in coronary assessment



Figure 4. Pressure sensor chips beside a cannula needle.

We fabricate a microneedle device for transdermal drug delivery and diagnostics for Nanopass Technologies, see figure 5. The microneedles are sharp, robust and minute enough to penetrate the outer layers of the skin in a completely painless manner. Microneedles are designed in various heights, lengths, channel positions and sizes. This low-cost, disposable, self-employed, biocompatible product may be used for the controlled release of large molecules, including therapeutic proteins, antibodies, vaccines and peptides.

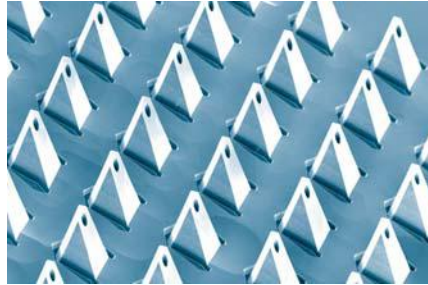


Figure 5. Microneedle array fabricated for Nanopass Ltd.

In addition, we design and manufacture a variety of microfluidic devices for biotech applications. For example, we design lab-on-a-chips to make standard techniques like DNA-, protein- and cell analysis faster and more accurate, see figure 6. The lab-on-a-chip functions like a miniature lab and conducts standard techniques like electrophoresis, PCR, and DNA sequencing. Because the dimensions are much smaller, the required amount of reagents and sample substances can be kept to a minimum. That makes it easier to obtain information, harder to contaminate the samples, and faster to perform the analysis.

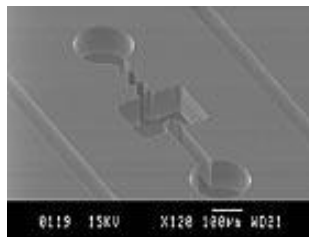


Figure 6. Part of a lab-on-a-chip

3. MANUFACTURING FACILITY

Silex has a fully operational state of the art 6" fab from October 2003 with end capacity to produce 100'000 wafers per year, see figure 7. It is a lease contract with Zarlink Semiconductor Järfälla of 450m² clean room area and 500 m² of office space. It is a cost effective operation – renting existing clean room facilities and favorable timing for purchasing new machineries. This will hopefully open up for new type of customers.



Figure 7. Silex new manufacturing facility