

Medical Industry and Chip Industry: Let's Sum Up the Minds!

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In terms of cost and economic productivity, the healthcare sector is facing tremendous challenges. The cost of providing adequate healthcare consumes trillions of dollars and represents an ever-increasing fraction of the GDP in countries across the globe. A major part is spent on hospital and ambulatory care. In addition, despite the enormous spending, many diseases, such as cancer, continue to bereave many productive life years, representing a huge burden on our economic productivity. Another challenge relates to drug development, which has become extremely expensive.

Meanwhile, the semiconductor industry has created ever more powerful chips for computation and communication. This evolution has been enabled by maximal scaling, complex integration, and extreme multiplexing. It has set the trend toward ever more powerful computers and has enabled mobile devices with ever more functionalities.

Imagine what could happen when medical and chip experts team up. Would it be possible for chips to revolutionize healthcare in the same way they have revolutionized the electronics industry? Let's dream: a cheap technology that allows accurate and reliable diagnostics for everyone, at any place and at any time. Or a technology that enables us to hunt for very rare cells inside our body, like circulating tumor cells, giving a very early indication of diseases like cancer. Or tools, like compact bioreactors, to predict drug efficacy, toxicity, and side effects of each individual in an early stage.

Ultimately, semiconductor technology allows tools to be mass-fabricated. It has the

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potential to reduce the cost of healthcare in the same way it reduced the costs of computing and communication. As an example, we take the case of the very quickly advancing field of genomics, where the cost of sequencing a human genome has dropped precipitously over the last decade. While the initial phases of this drop in cost were achieved through conventional technologies (typically fluorescence imaging), the newest generation of genome-sequencing tools employ state-of-the-art CMOS circuits and/or specialty devices.

At imec, we create an environment where the above-mentioned “dreams” can become a reality. We have multidisciplinary teams of cell and molecular biologists, surface chemists, multiphysics modeling and design engineers, process development teams, etc., gathered under one roof. We like to call it “the sum of minds.” They make use of an extensive infrastructure and the knowhow built up in process integration. Next to these researchers, we have residents of industrial partners bringing their knowhow of commercial systems and customer needs.

But let's give a concrete example of a sum-of-minds project: the cell sorter. It is a lab-on-chip (LOC) device with a unique asset—a smart camera without lenses. The LOC will ultimately be able to analyze single cells with a throughput of more than two million cells per second, at the patient's bedside or at the doctor's office. To illustrate its working principle, I want to show you the way a cell travels through the system: First, a sample (e.g., blood sample) is injected into the inlet of the microfluidic channel. With a speed of more than 1.0 m/sec, the cells flow over the imaging area. Above the microfluidic channel, this area consists of a small laser that is used as a light source. The light, which is scattered by the cell, is recorded by the image sensor at the bottom of the microfluidic channel. This principle of using scattered light to reconstruct an object is called holographic lens-free imaging. It uses no lenses and off-the-shelf optical components, making it compact in its realization. The currently achieved optical resolution is 0.7 μm —more than enough to image subcellular features. Next, the images are processed and reconstructed using dedicated algorithms. Within 100 μsec , the cell type is identified and classified based on the images. Depending on the cell type, the cells are pointed toward a specific fluidic channel. This is done by microfluidic switches based on microbubbles. Thermal bubble generators, similar to the generators used in thermal bubble inkjet printers, are integrated at the top surface of the microfluidic channels. The tiny and short-lived steam bubbles that they create are used to gently deflect the cells toward the desired outlet. In this way, cells are sorted based on cell type. The cells are still viable after passing through this sequence of steps. This makes it possible to analyze them further (e.g., the DNA of the circulating tumor cells can be analyzed to collect more information on the type of cells that are causing the metastasis, and on cancer mutations or drug resistances). A blood biopsy based on a cell sorter is more likely to be included as a routine clinical test in follow up cancer patients than the more invasive and labor intensive biopsies that currently are used in cancer diagnostics.

At imec, we believe that this is only one of the many innovations that semiconductor technology can bring to healthcare applications. By bringing together expertise in cell biology, DNA analysis, imaging systems, semiconductor processing, and nanochemistry, real innovations will occur. It will enable smaller,

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cheaper, and smarter diagnostic devices and research instruments.

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