FOURTH-GENERATION SEQUENCING TECHNOLOGIES

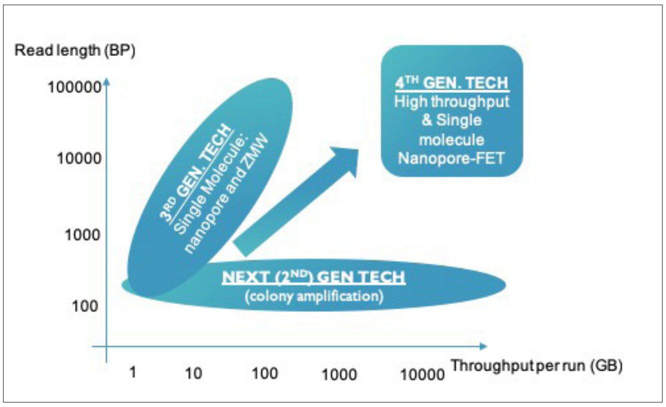
Nanopore-based technologies are the drivers behind fourth generation sequencing, enabling higher throughput, longer reads and lower costs. Silicon nanotechnology can push genomics further forward, making complex workflows cost-efficient, disposable, automated and adapted to the clinical practice. Nanopores can then be integrated on a circuit chip, which opens the way for miniature, portable DNA sequencing devices.

HOW SILICON NANOTECHNOLOGY ENABLES CLINICAL APPLICATIONS

- Automated sample preparation
- Low reagent costs
- Long reads possible
- Fast sequencing
- Low-cost sequencer
- Small, portable devices

SILICON NANOPORES AS THE CORNERSTONE OF SEQUENCING 4.0

Imec's nanopore FET strategy brings the $10 genome closer. Solid-state nanopores as single-molecule sensing technologies have been used to study small molecules such as DNA, RNA, and proteins. An important innovation lies in the large-scale integration of nanoscale transistors to boost the signal and speed up reading time, enabling high-throughput, label-free DNA sequencing. With significant progress in CMOS process technology, we are now able to manufacture nanoscale FETs down to 6nm.



Read length versus throughput for a single sequencing chip

KEY BENEFITS OF NANOPORE FETS

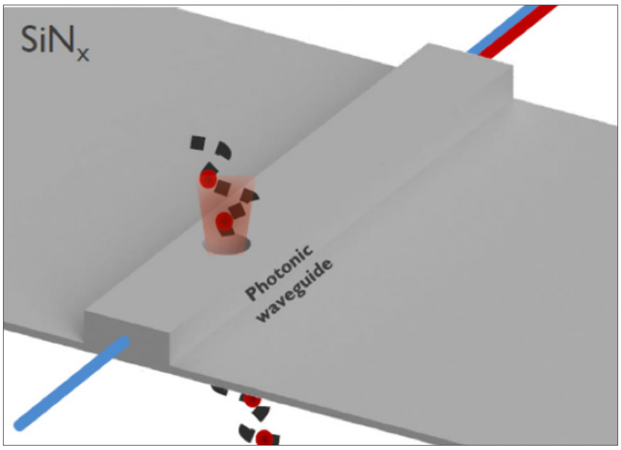
- Molecular biology investigation at the single molecule level
- Higher throughput at a lower cost, towards the $10 genome
- Label-free technique
- Minimal sample preparation
- Highly sensitive: no need for amplification
- Long reads possible
- Parallel architecture through ASIC
- Highly integrated, robust, reliable
- Possibility to build chips in imec's 300mm infrastructure

INTEGRATED PHOTONIC NANOPORE DEVICES OFFER INCREASED SENSITIVITY

The combination of solid-state nanopores and waveguides results in a fast, scalable, optofluidic device for highly-sensitive single-molecule detection. In this device, the molecules travelling through the nanopores are measured optically, taking advantage of the sensitivity and spatial resolution of optical detection methods.

KEY BENEFITS OF PHOTONIC NANOPORE DEVICES

- Optical detection methods offer high sensitivity
- Optofluidic chip: light and fluid flow through the same channel
- Fluorescent labels increase sensitivity, specificity and add the possibility to multiplex with color
- Possibility of particle counting (label-free detection) and ionic current read-out (calcium activated dyes)
- Suitable for sensing applications because of their high compactness, sensitivity, and the inherent ability to transport the light and the analyte in the same physical channel



Nanopore(s) in a photonic waveguide

HOW TO USE NANOPORE SEQUENCING TECHNOLOGIES IN OTHER RESEARCH DOMAINS

- Rapid microbe identification, characterization and analysis in a PCR-free protocol.
- Whole-genome or targeted sequencing and DNA-mapping.
- In-flow immunoassays, for example for concentration measurements.
- Comprehensive analysis of somatic mutations, structural variations, phasing, fusion transcripts and base modifications.
- Rapid insight into infectious disease.
- Full-length characterization of native RNA or cDNA without fragmentation or amplification.
- Flow cytometry.
- Population screening.
- Reproductive health

A BILLION BASE PAIRS A DAY WITH PHOTONIC WAVEGUIDE-BASED SEQUENCING

Light is the most used probe in medical diagnostic testing and can be guided through ultrathin waveguide structures. Outside of the waveguide, it creates an evanescent field. In that tiny volume detection volume DNA can be read out with a 1000-fold improvement in background noise. Because we can repeat this in parallel in 1000s of waveguides on a single chip, a massive amount of data can be processed at the same time.

KEY BENENFITS OF PHOTONIC WAVEGUIDES

- Reduce laser power and instrument cost
- Parallelization possible
- Improve SNR and excitation efficiency
- Reduce laser and photo-damage
- No need for large (fluorescence) microscopes and spectroscopes to measure the characteristics of biological tissues

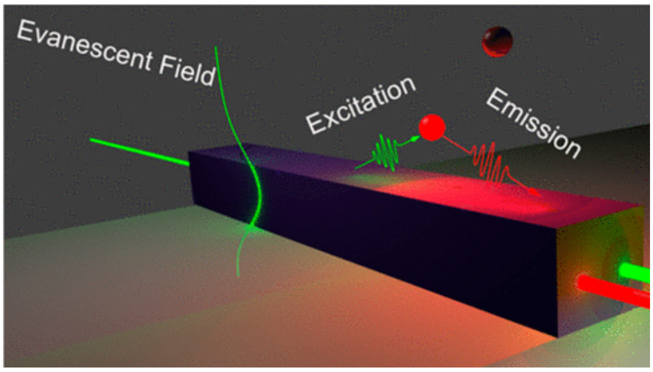
APPLICATIONS

- DNA Sequencing
- Counting and visualizing cells
- All biological applications that use visible light

WHY WORK WITH IMEC?

- We design, prototype and low-volume manufacture solutions for your genomic challenges.
- We have a comprehensive range of know-how in design methodologies and process technology in the field of silicon processing for genomics.
- We have the facilities and expertise to integrate silicon electronics with microfluidic, electrodes, optical and nanophotonic structures. This opens the door to complete lab-on-chip solutions, ideal for handheld and portable genomics devices.
- We help you set-up low-volume production and assist with the transfer to large-volume manufacturing.
- Moreove, we also develop customized ASICs, packaging solutions and analysis software, targeting all the different layers of a sequencing system
- Having all this expertise in house allows for so-called cross-layer optimization, a concept that can truly revolutionize the cost, throughput and the sample-to-answer time.

WANT TO KNOW MORE? DOWNLOAD OUR WHITEPAPER ON: WWW.IMEC-INT.COM/WHITEPAPER-GENOMICS



Waveguide based evanescent excitation and collection

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