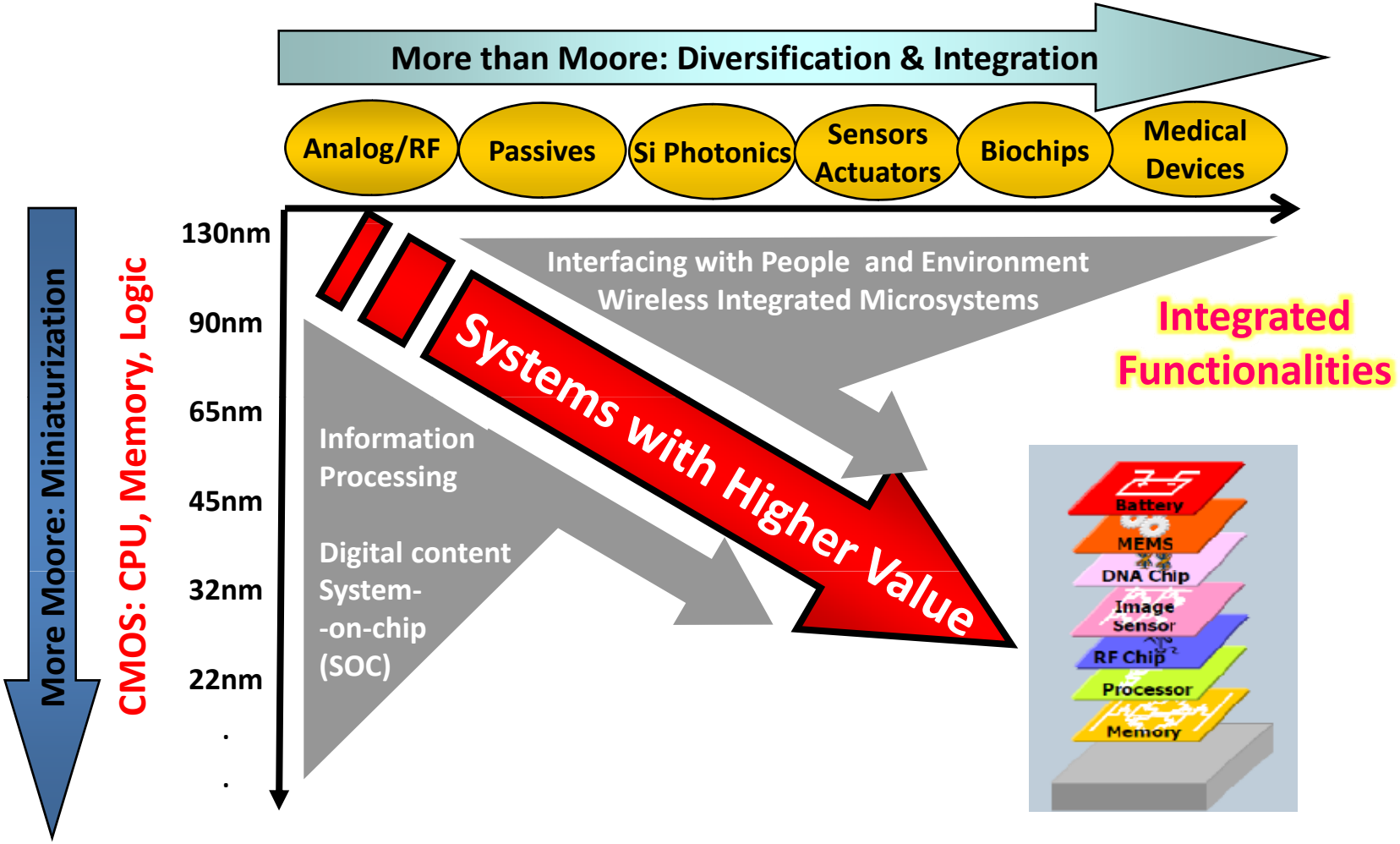
Bringing the Benefits of Moore's Law to Medicine

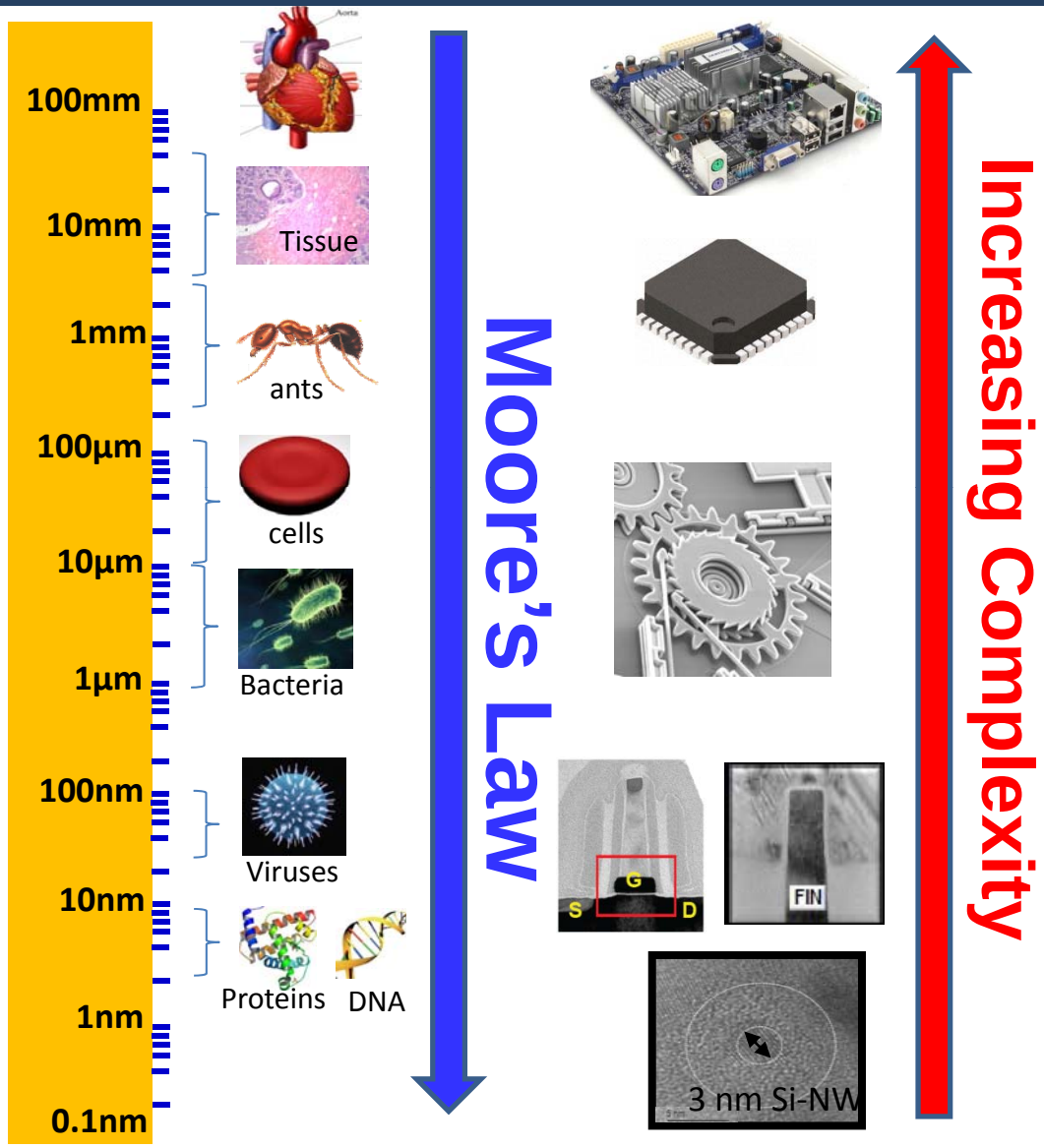
Prof. Dim-Lee Kwong
Institute of Microelectronics
Agency for Science, Technology, and Research
Singapore

More on Moore and More Than Moore



- Using CMOS platform for deploying innovations in material, device, circuit and packaging to improve power and cost as well as to acquire integrated functionalities
- CMOS will continue to supply the world with electronic devices for a long time—and grow to be a much larger industry

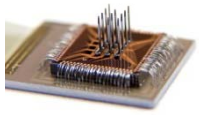
Bringing the Benefits of Moore's Law to Medicine

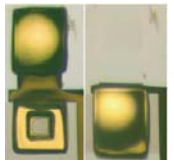


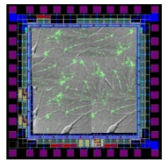

Bionic Eye

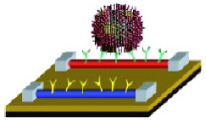

Heart

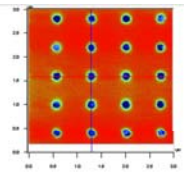

Pace maker

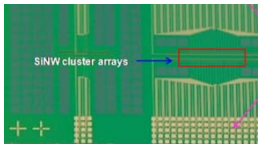

Neuroprobe


Cell Clinics

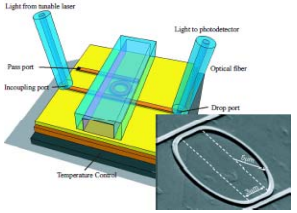

Neural monitoring


SiNW virus detection


Nanosensor array



SiNW array for multiplexed detection

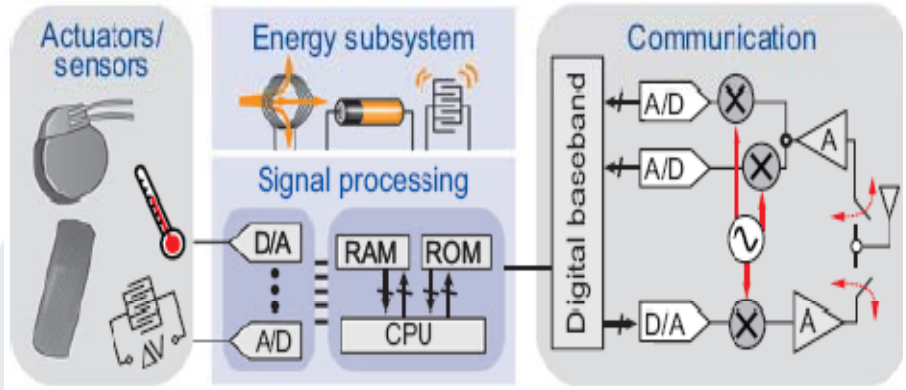


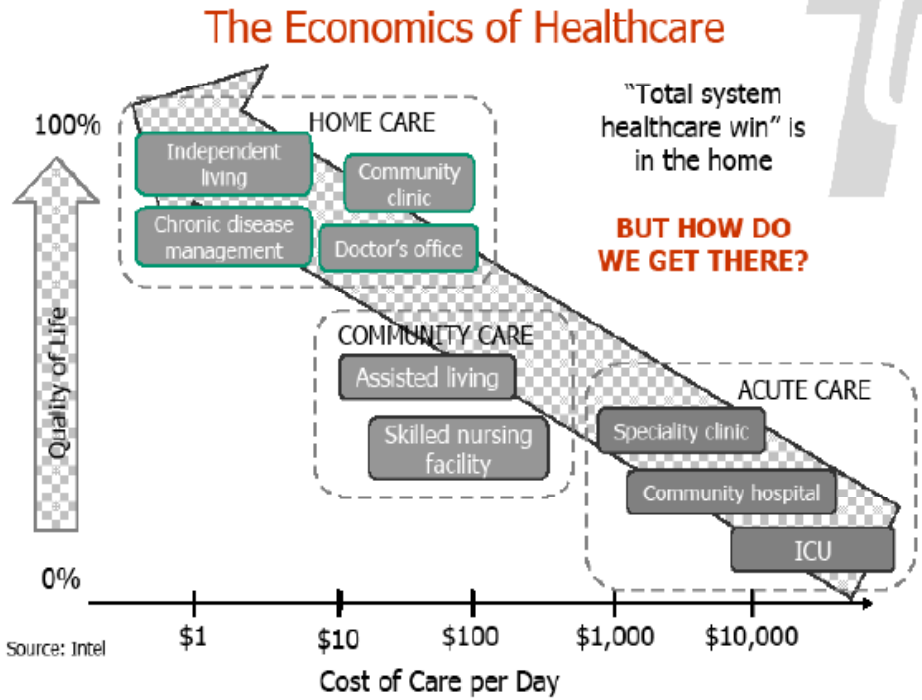
Si micro-ring Resonator array

- **Dimensional matching of electronics device and biomaterials allows manipulation and sensing / monitoring of bio-species or their activity**
- **Advances in MM and MtM increases synergy between electronics and biology**

Medical Device Technology Trend:
Miniturization and Portability

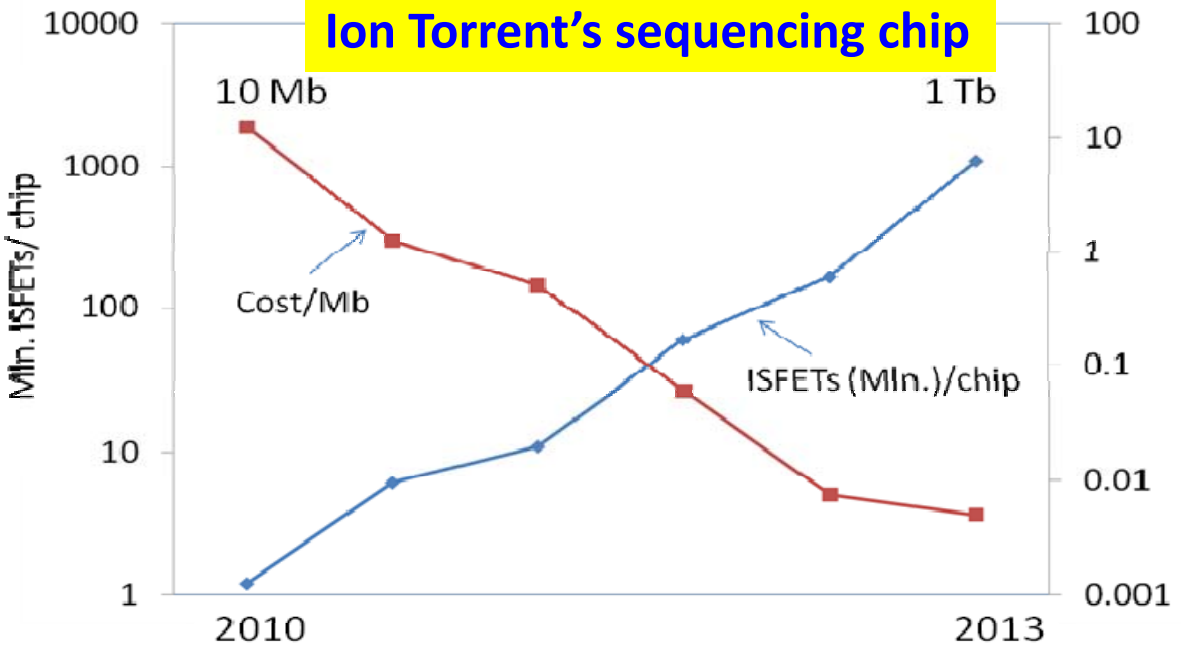
- **Medical manufacturers will move the entire system into a portable unit size of a cell phone or smaller**
  - **For home-based testing, monitoring and diagnostics**
- **Semiconductor technologies enabling the acceleration of medical device technology innovations in**
  - **Sensors with extreme sensitivity and repeatability**
  - **Wireless integrated microsystems**
  - **Ultra low power electronics**
  - **Packaging and assembly (3-D TSV)**

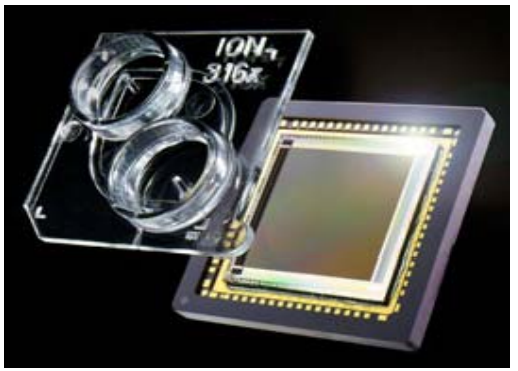




Benefits from Moore's Law: Large-Scale Integration

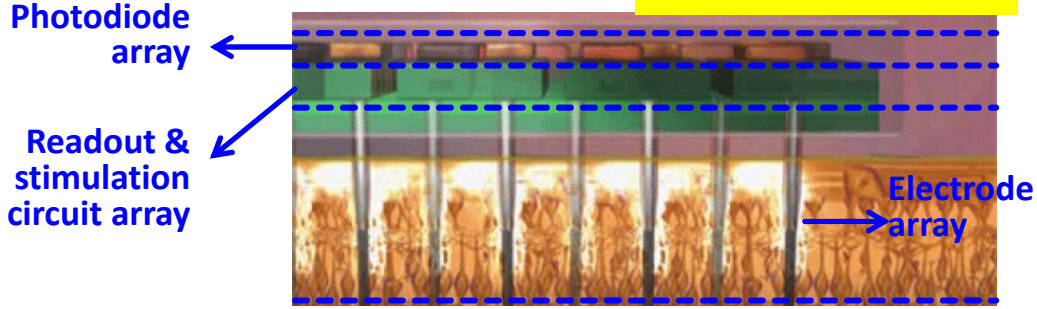
Ion Torrent's sequencing chip

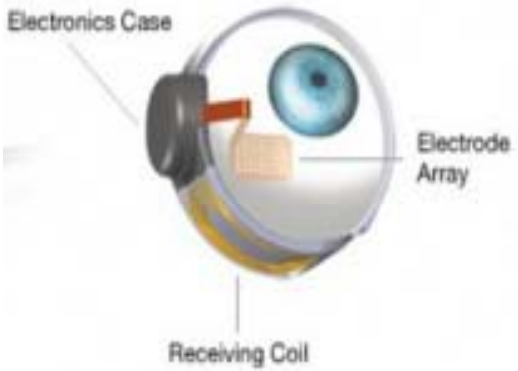




- Large-Scale High-Density Bio Interface Array Multiplexed Detection
- Towards Single-Chip Human Genome Sequencing

Nanoretina





Second Sight

CMOS Silicon Photonics

CMOS IC Platform

DC Electron Supply

Electronic IC
Manipulates electrons using transistors

Electrical I/O

[Copper Lines]

Integrated CMOS Photonics Platform

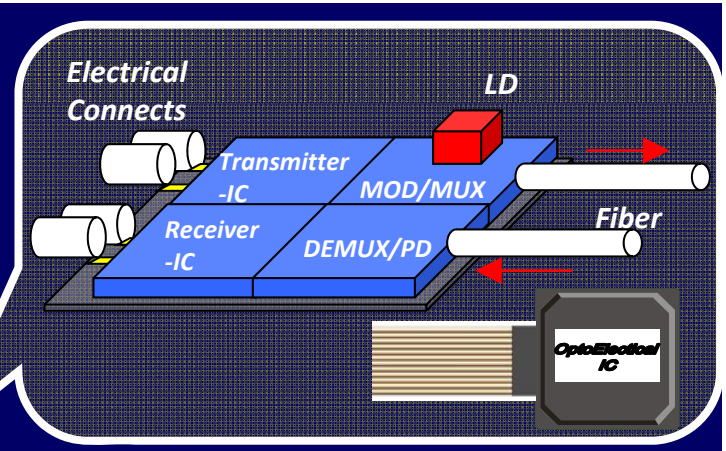
DC Electron Supply

DC Photon Supply

Opto-Electronic IC
Manipulates both photons and electrons using transistors

Optical I/O [Optical Fiber]

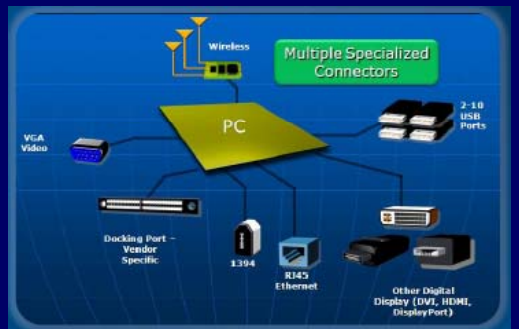
Electrical I/O [Copper Lines]

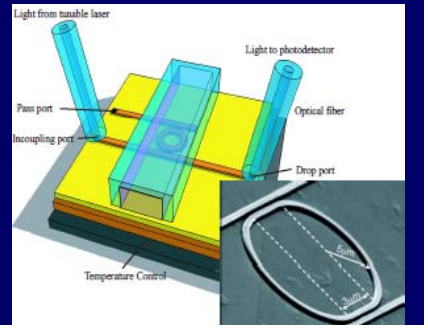


A Low-Cost Platform Technology with Wide Range of High-Volume Applications Leveraging on Existing Semiconductor Infrastructure

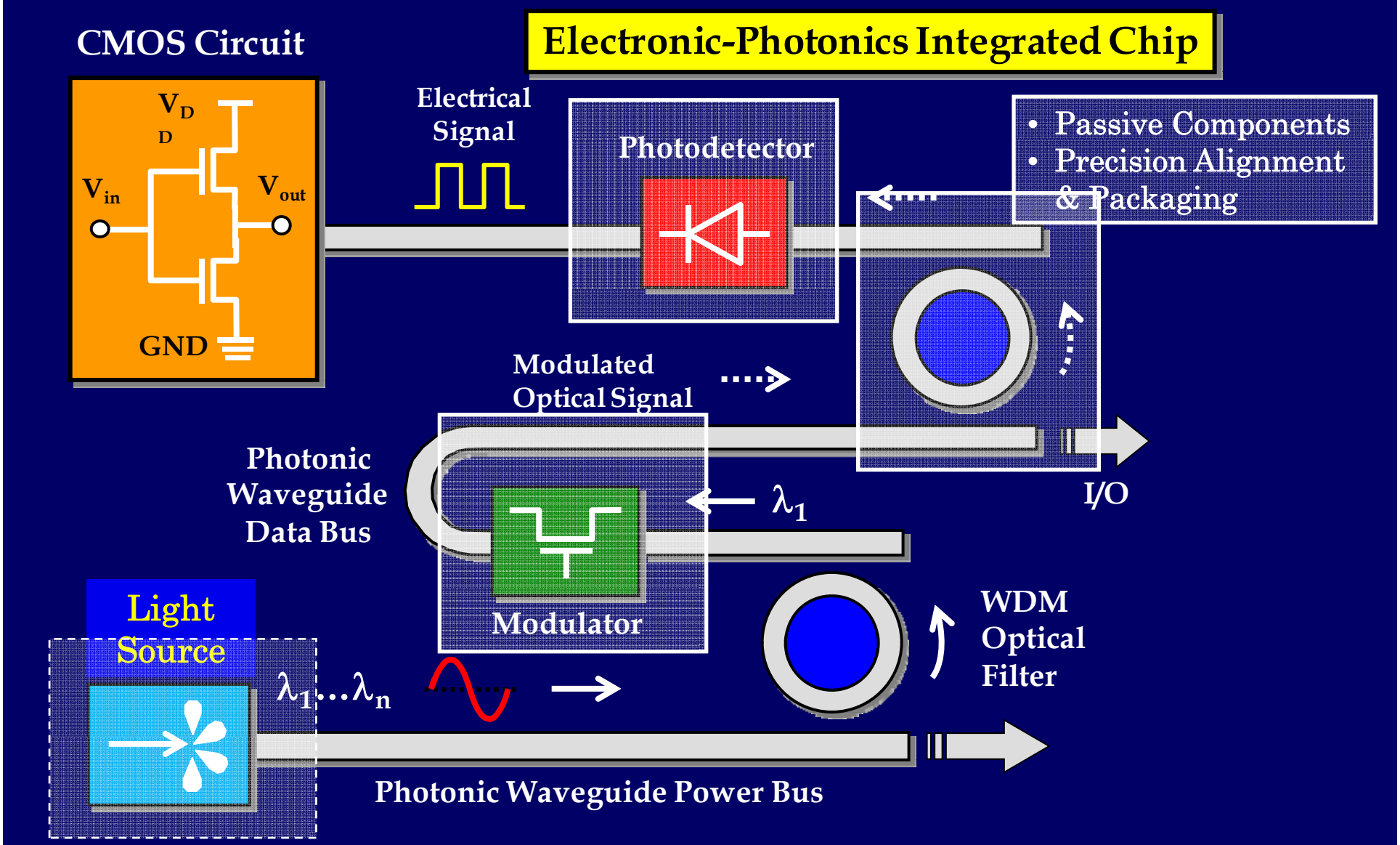
Low-Power, High-Speed, Small-Form Factor & Low-Cost Data-Communication (e.g., Data Center, Home-Entertainment)

Highly Sensitive Mechanical & Biological Sensors



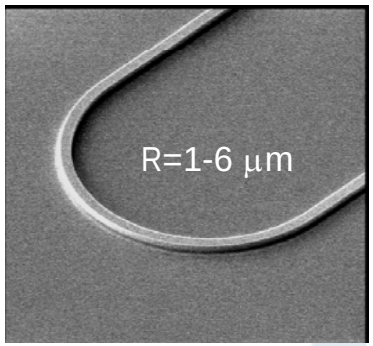


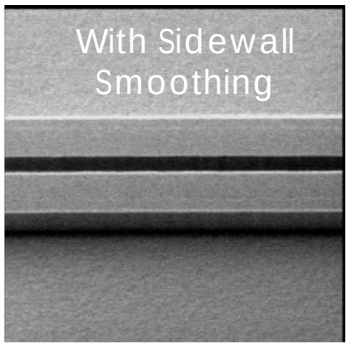
Silicon Photonics Technology Platform

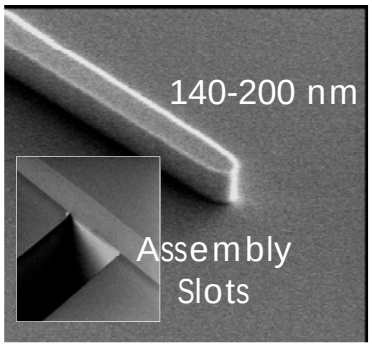


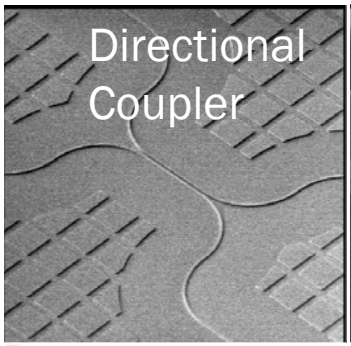
IME's 8" Silicon Photonics: Passive and Active Devices

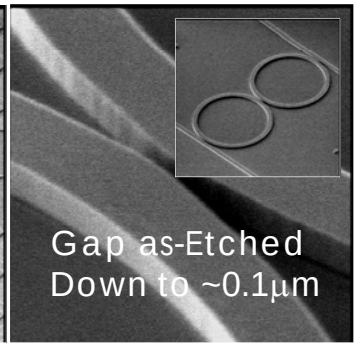
IME's NanoPhotonics

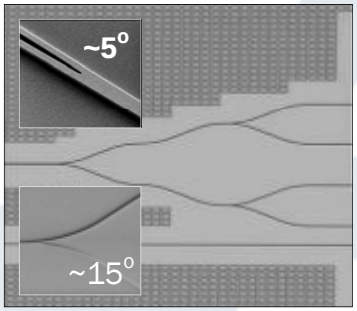


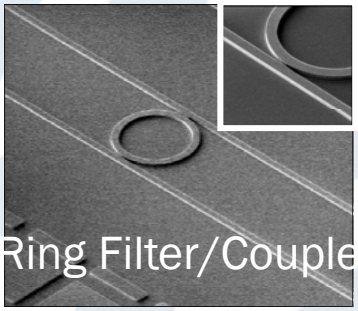


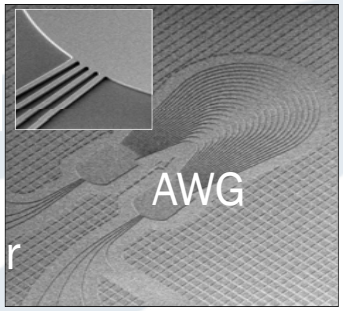


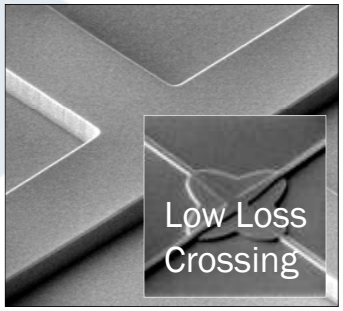


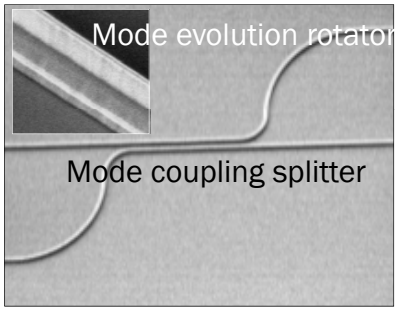






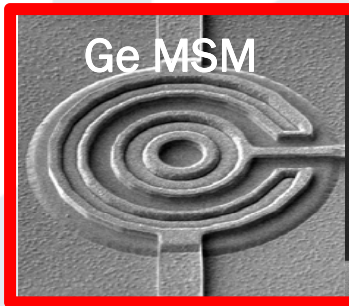


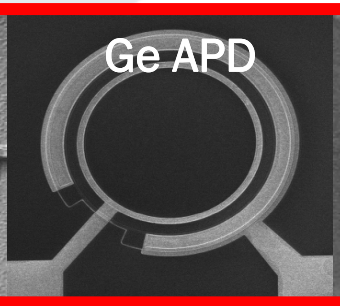


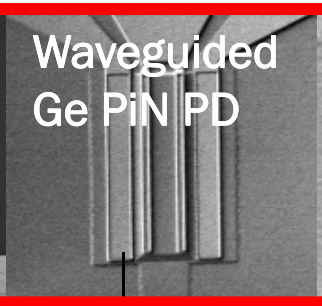


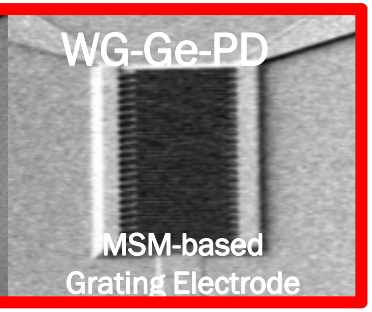
Ge Photo-Detectors

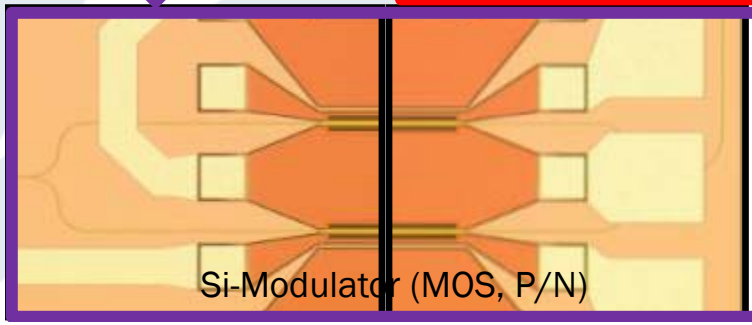
Optical Modulators

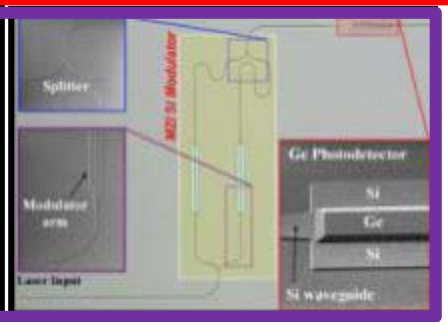












Integrated MOD/PD

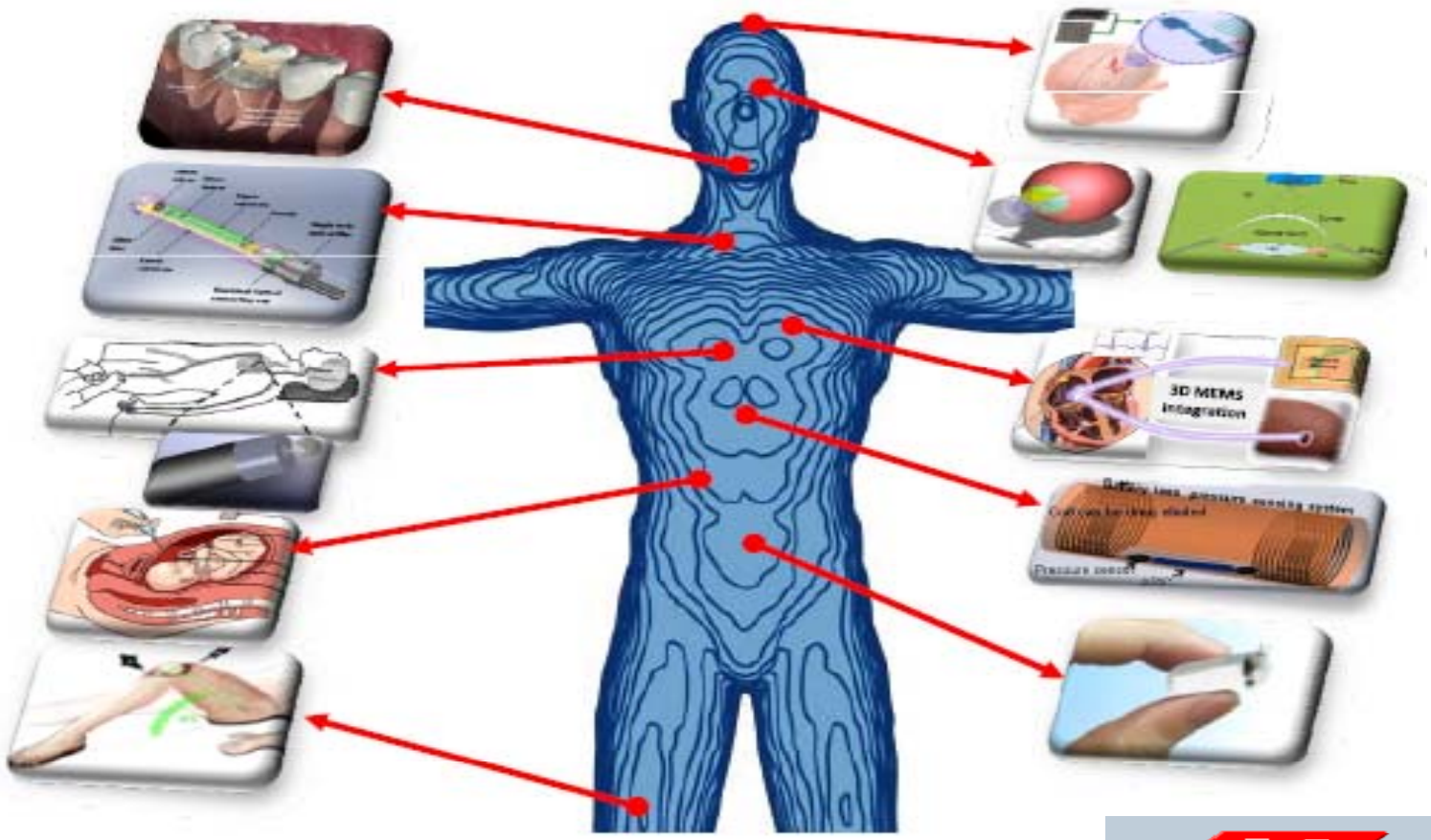
A*STAR IME

IME's Miniaturized Medical Devices Program

Clinical Partnership

NUH, NUHS, NUS-DUKE, SBIC, SERI/SNEC, NNI

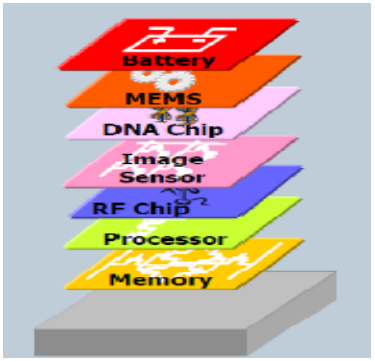
Innovation in microelectronics technology to enable solutions to the most challenging problems in medical and health care



Analog Front End Sensor Interface	ADC	µC	Radio
		DSP	
Power Management, Battery, Harvester			

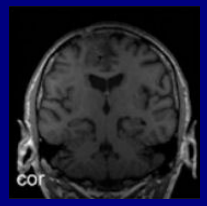
MICS / MEDS ZigBee™ UWB

Ultrasound platform
MEMS sensors and probes
Advanced packaging
Si Photonics



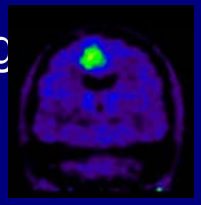
Engineering solutions with impactful clinical and market relevance

Silicon-Photo-Multiplier (SiPM) for Compact Positron Emission Tomography (PET) Imagers



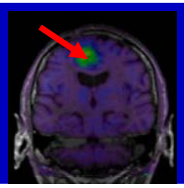
MRI only→ High-quality Imaging

Excellent tissue imaging…
But is there a tumor?



PET only→ Metabolic information

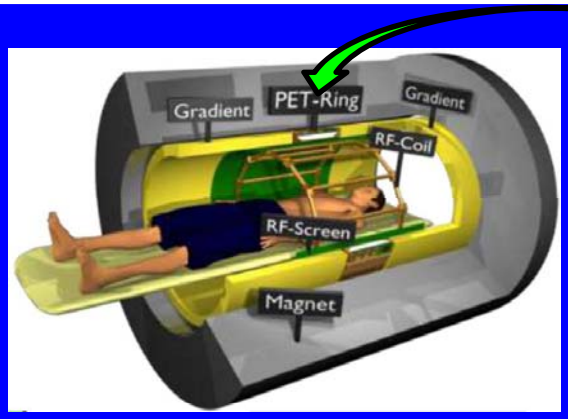
There is a tumor… But where is it exactly?



PET-MRI→ Simultaneous 3-D tomography + Metabolic information

There is a tumor, and we know its exact location!

NUH National University Hospital
Institute of Microelectronics A*STAR
Singapore Bioimaging Consortium A*STAR
FH Hochschule Aachen
Ciemat Centro de Investigaciones Energéticas, Medioambientales y Tecnológicas
WestVirginiaUniversity



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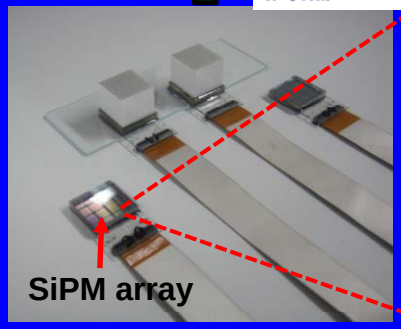
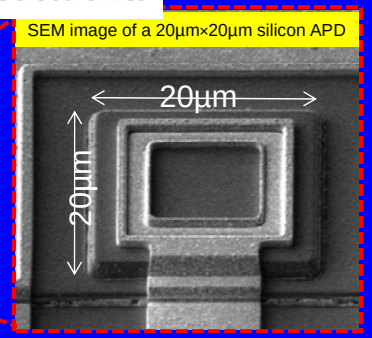
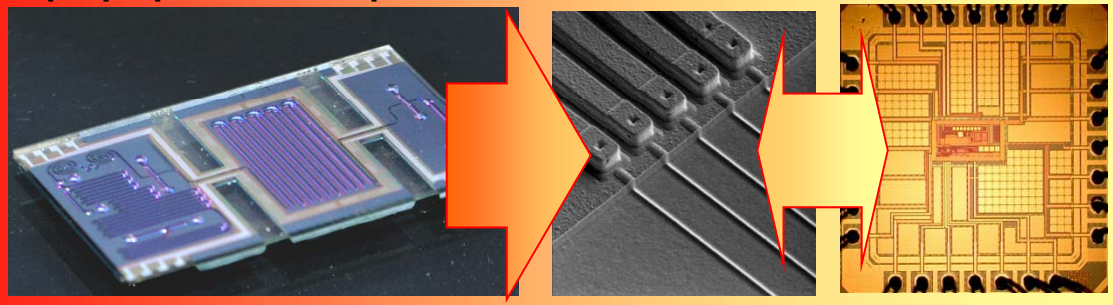




Sample-to-answer integrated microsystems for Point-of-Care (POC) diagnostics

Sample in (blood, saliva, etc…)

Sample preparation | Amplification | Detection | ASIC



Results available for clinical decision

1. Molecular diagnostics

Early diagnosis of diseases

Nucleic acid and protein Biomarker detection

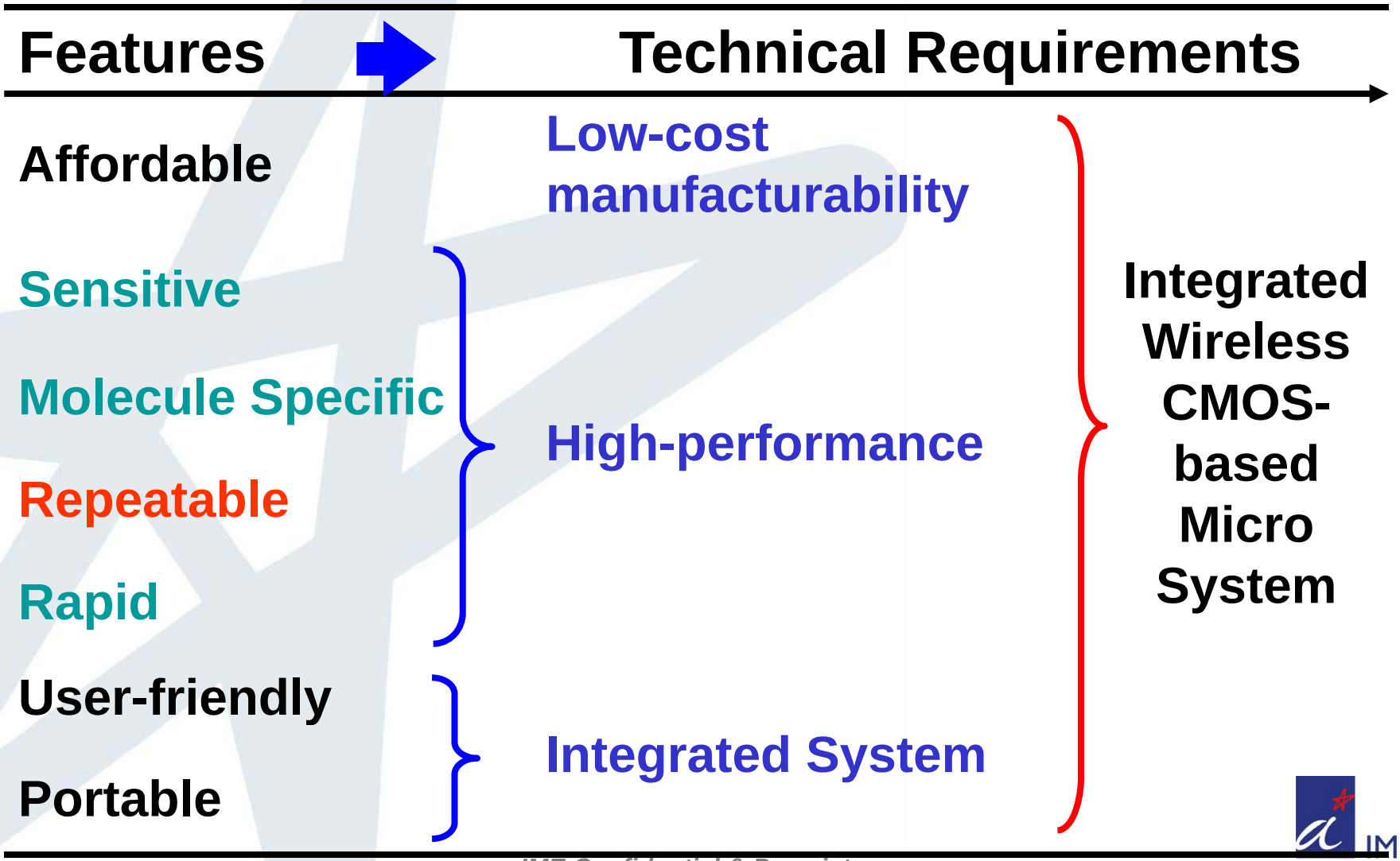
2. Cell-based diagnostics

Therapy monitoring

E.g., Rare circulating cells detection

Holy grails of biomolecular analysis: Single-molecule, label-free, real-time, high bandwidth

Technology for Point-of-Care (POC) Diagnostics for early detection of diseases and disease treatment and management



Si-Based Integrated Microsystems for POC Diagnostic

Complex sample composition, ***low analyte concentration***, and ***fast sample-to-answer response*** have posed the major technical challenges

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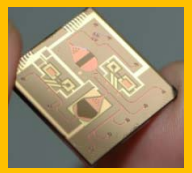
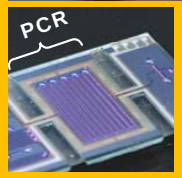
Utilizing microelectronics technologies to overcome these challenges

Microfluidic sampl purification

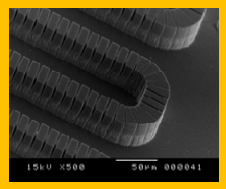
DNA/RNA extraction chip



Micro-PCR for DNA/RNA amplification

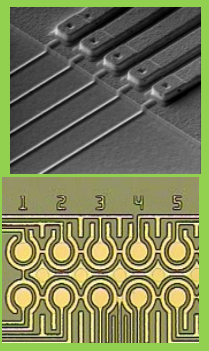


Pillar micro-structure for plasma separation

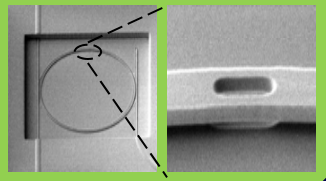


Highly sensitive biosensors

SiNW: nucleic acid and proteins

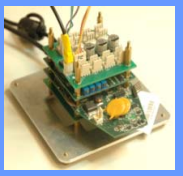


Microelectrode array for cellular biomarkers



Silicon photonic ring resonator

Integrated IC for fast detection

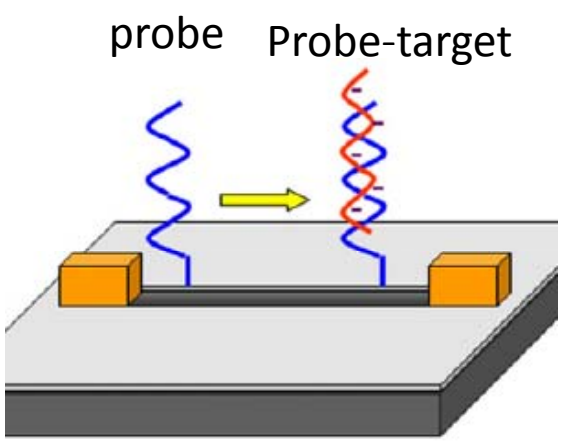


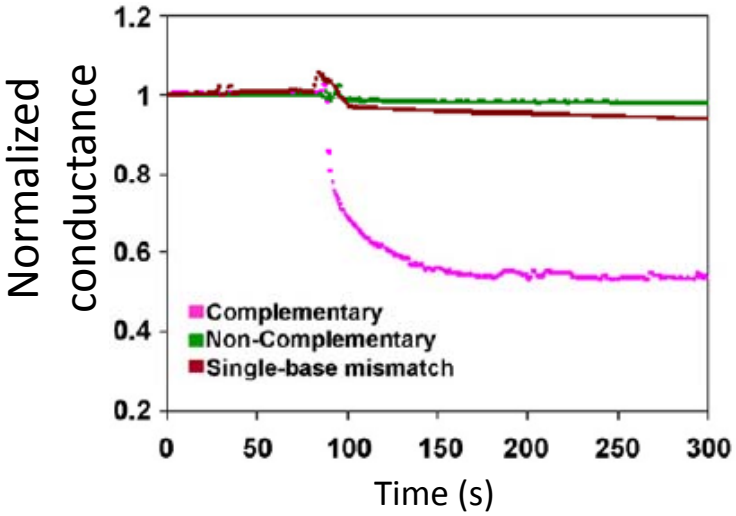
PCR thermal cycling controller

ASIC IC chip for rapid multiplex sensor read-out

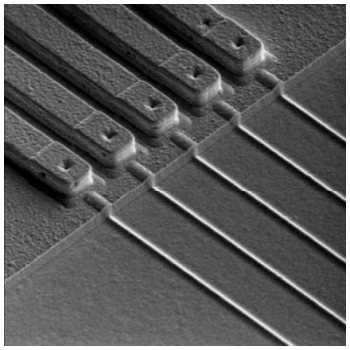
Multi-channel simultaneous EIS system

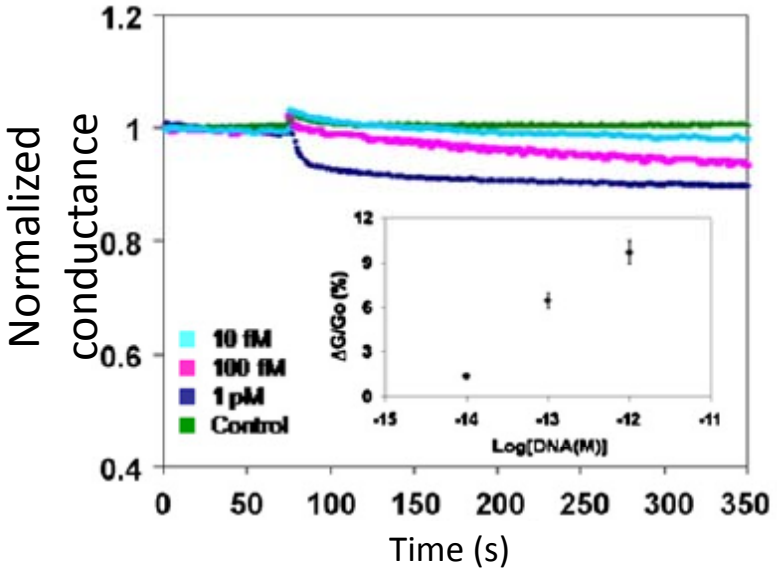
IME's silicon nanowire molecular diagnostic platform





Silicon nanowire array





Application	Detection limit
DNA-DNA hybridization (DNA diagnostics)	10 fM
Protein-DNA (hormone –receptor biology for breast cancer)	10 fM
Troponin-T (cardiac biomarker)	1 fM

Integrated system for multiplexing molecular diagnostics

blood

Sample Preparation
Integrated Microbiofluidic device
Viral RNA Extraction
Amplification by RT-PCR
Denaturation by super-cooling

denaturated PCR product → ssDNA

Detection
Nanowire Biosensor

multiplexed detection → electrical charge

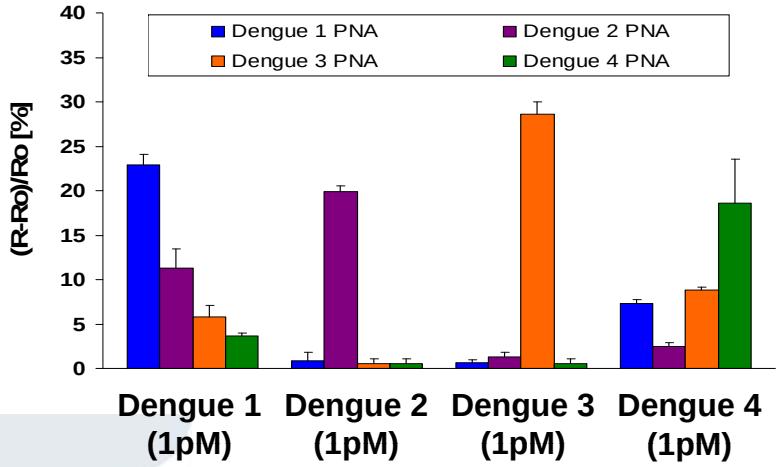
ASIC Readout & Data Processing

Probe station: >1hr /255 wires

results

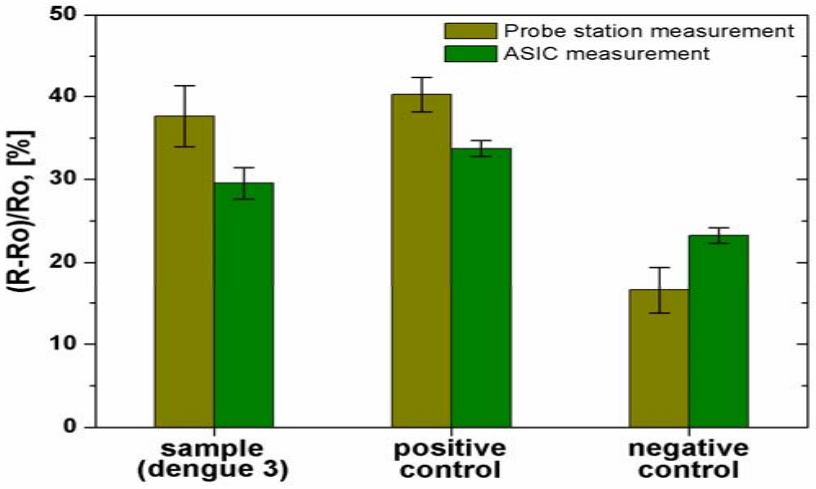
ASIC read out speed: <1min/ 255 NW wires

Multiplexing Specificity



Integrated System Testing

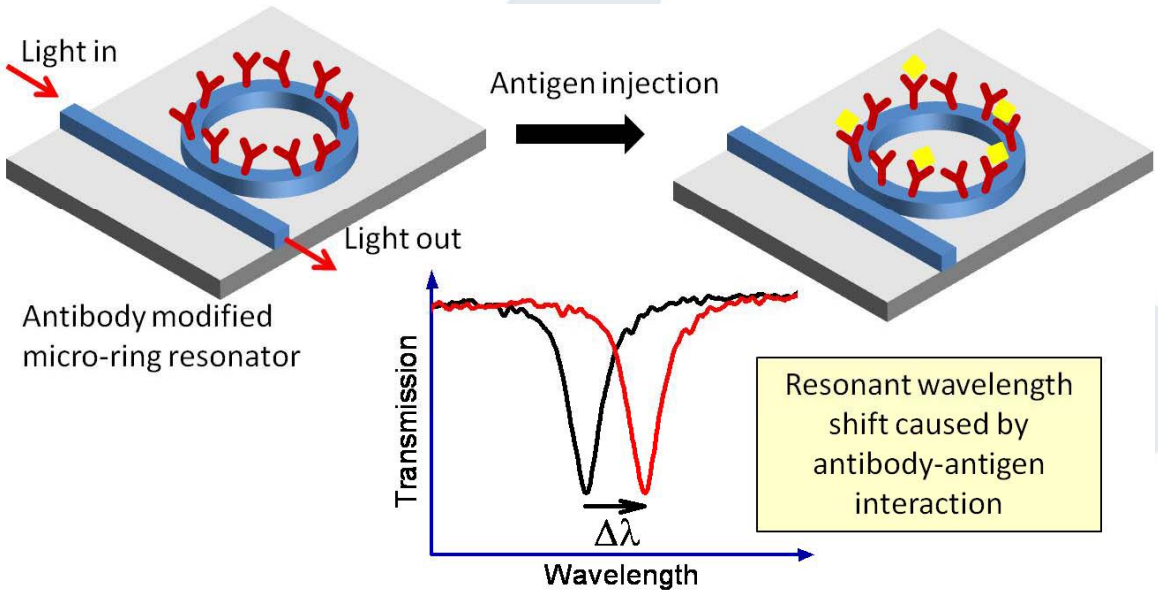
(Probe station *vs* ASIC)



Demonstrated the capability of multiplexing detection of 4 serotypes dengue virus within 4 hrs in few drops of blood. The virus concentration equivalents to at least 2 days before of fever symptoms occur.

A*STAR IME

Micro-ring resonator based biosensor



- SOI micro-ring Resonators
- Refractive index-based (RI) sensor

$$\Delta\lambda = \frac{\Delta n_{eff} \cdot \lambda_{res}}{n_g}$$

Δn_{eff} : the change of the effective index caused by the analyte binding
λ_{res} : the initial resonance wavelength
n_g :the group index

Key Advantages

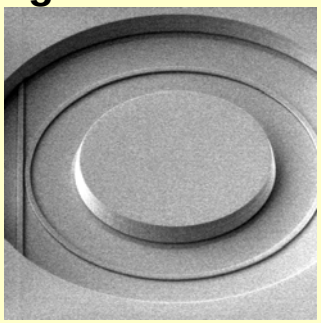
- **Precise quantitative output (linear response to mass change)**
- Low sample volume (due to the small footprint of sensor rings)
- Multiplexed panels
- Label-free detection
- Low-cost (mass manufacturing)

- **Current detection limit of IME's device ~5 pg/mm²**

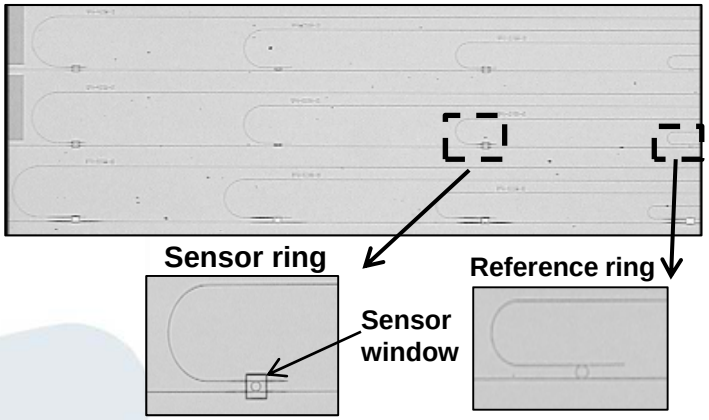
IME's Biophotonics Device

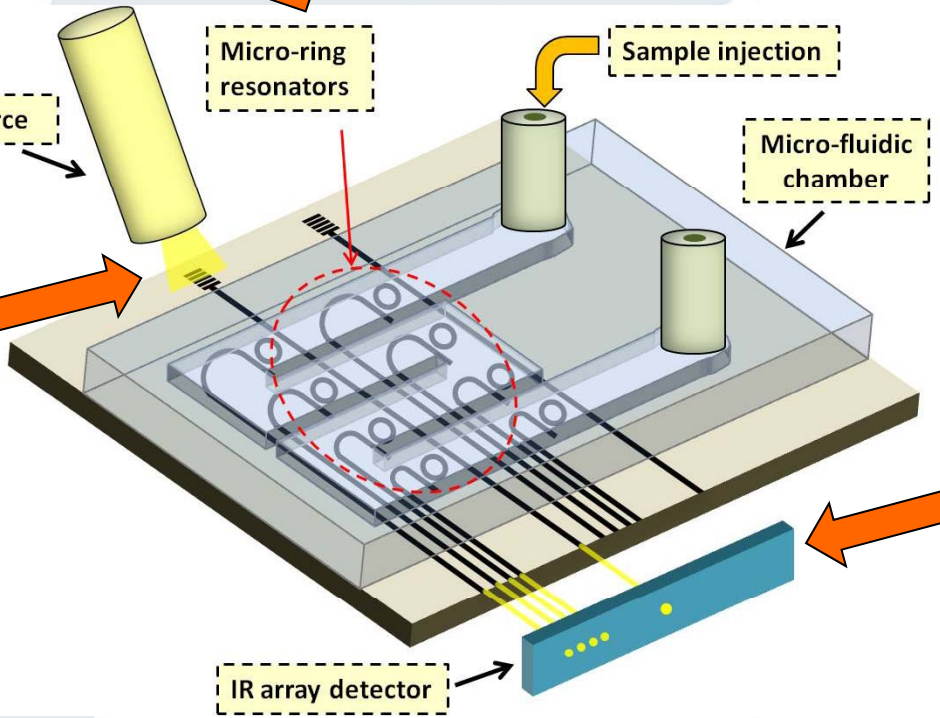
Silicon micro-ring resonators

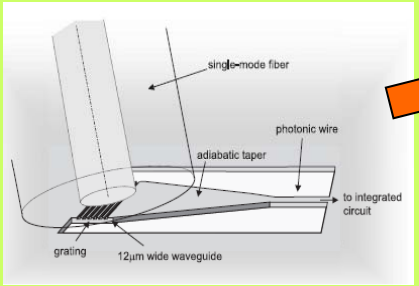
-Biosensor
- small foot-print
-Individually addressable



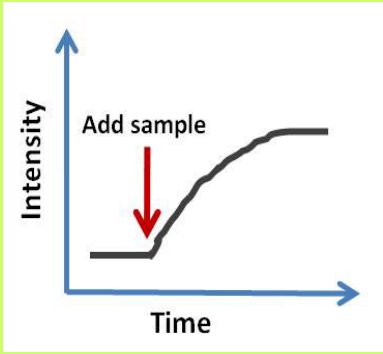
Arrays of micro-ring resonators





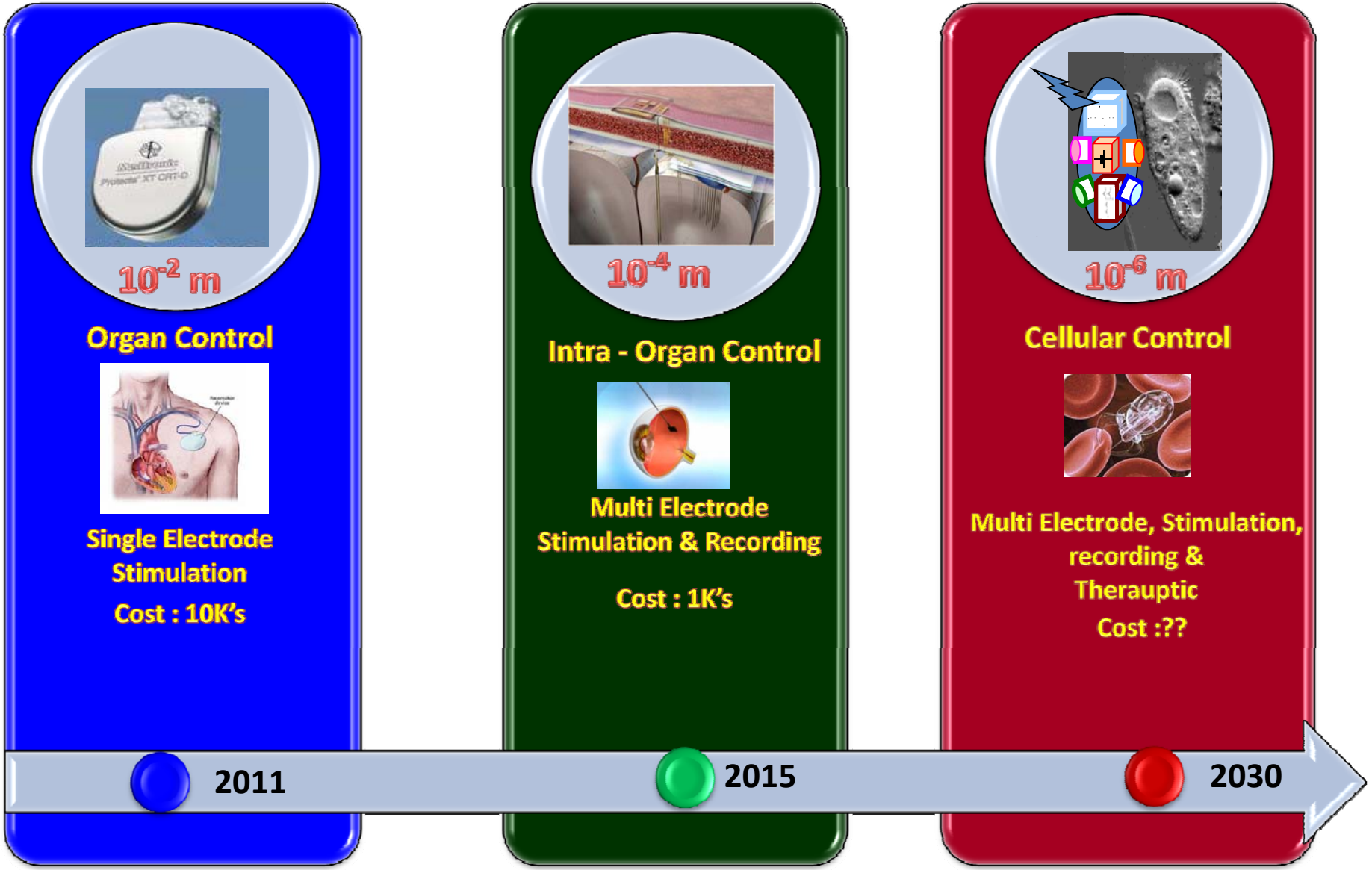


Grating for vertical coupling
-High alignment tolerance (disposable chip)



Detection
-128 pixel IR array
- Real-time
- **Multiplexing**

Moore's Law Benefits to Medical Devices



Tiny implants that can test, diagnose, and alert doctors to problems with their patients will replace costly routine visits.

Conclusions

- **Advances in semiconductor/electronic technology together with bio/medicine will transform healthcare, enabling patient-targeted solutions in preventive, diagnostic, and therapeutic environments.**

- **Significant progress needs to be made in understanding the interactions at the intersection of biology and Silicon or *engineered Silicon*.**

- **The field of bioelectronics and miniaturized medical devices are poised for exponential growth. CMOS, combined with other novel devices, will enable autonomous micro-scale systems with many potential applications, creating huge markets and benefiting to the individuals and society**