

Biosensors and Prostheses for Neuro- recording and Neuro- stimulation

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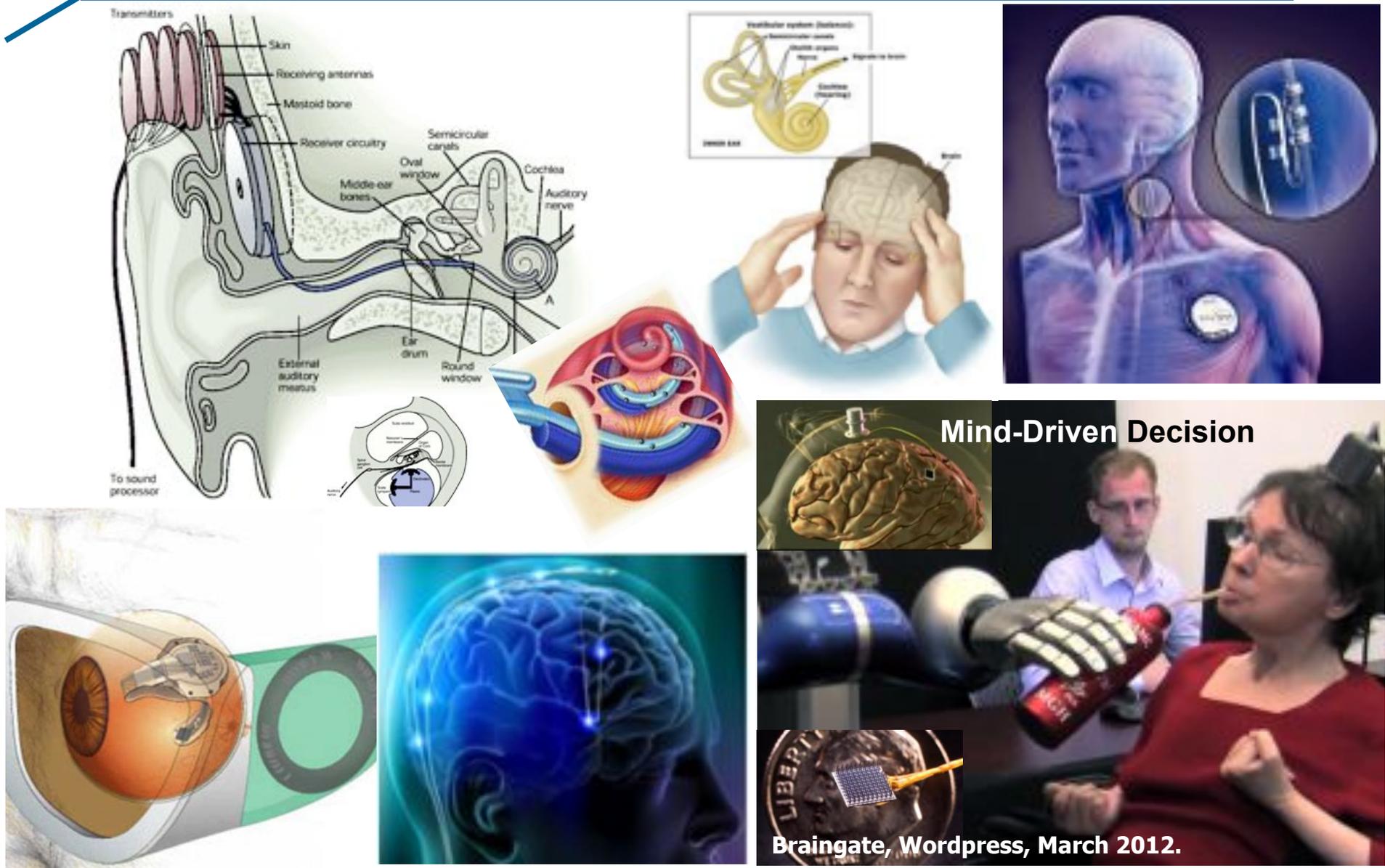
POLYTECHNIQUE
MONTREAL

WORLD-CLASS
ENGINEERING

POLYSTIM
Neurotechnologies



Biomedical Circuits and Systems (Bioelectronics)



Brain and Central Nervous Systems Disorders

- Cochlear (CNS)
- Hearing Loss (CNS)
- Visual (CNS)
- Parkinson (DBS)
- Epilepsy (VNS, CNS)
- Alzheimer (CNS)
- Dystonia (DBS)
- Lesch-Nyhan (DBS)
- Bradykinesia (DBS)
- Depression (VNS)
- Tumors (CNS)
- Spinal-cord injuries
- Paralysis
- Cardiovascular (Stroke)
- Tourette syndrome (DBS)
- etc..

★ Neuroscience

✓ Investigation tools

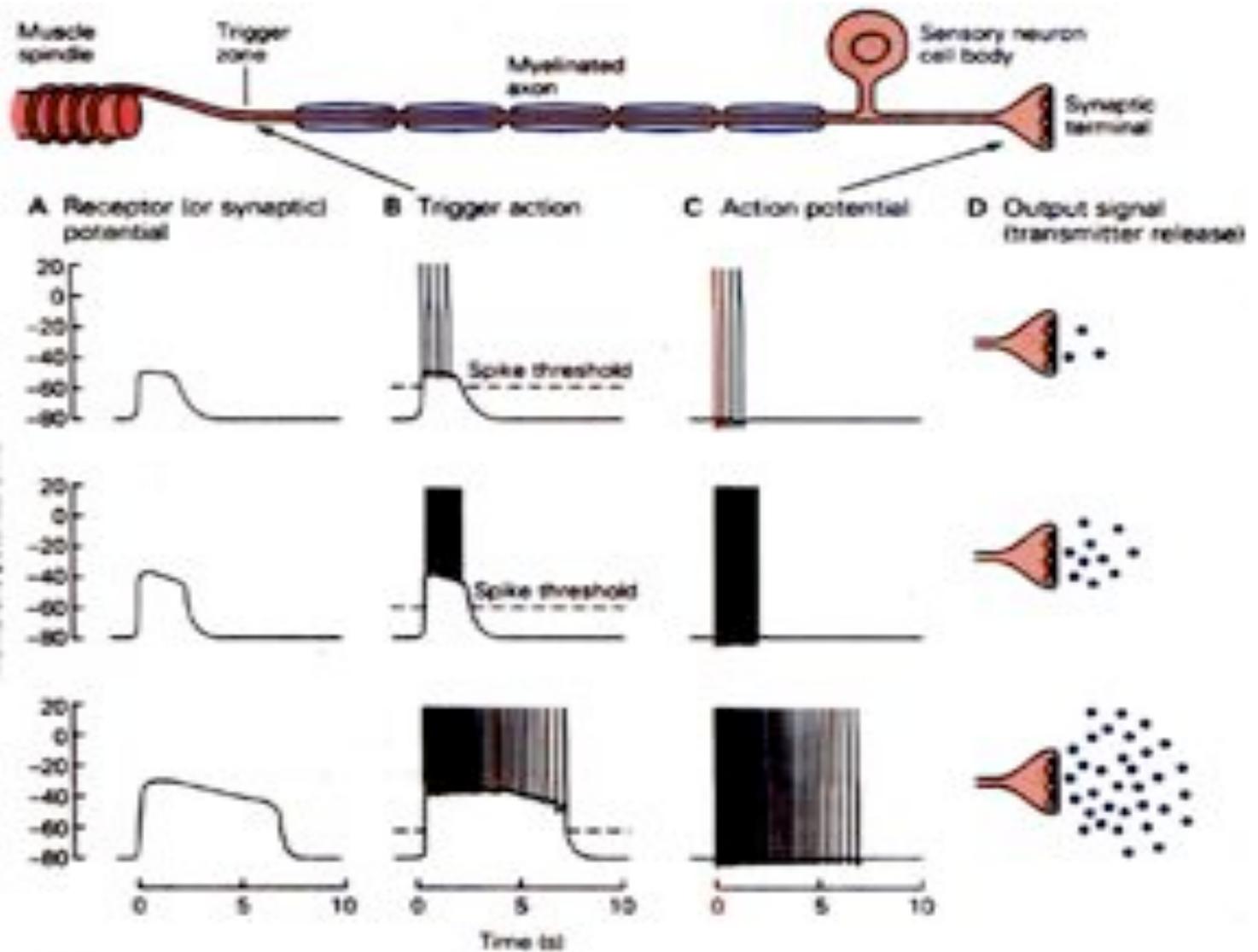
★ Neural prosthetics

✓ Mind-Driven Rehab.

The Toll of Selected Brain/Nervous System Disorders is higher than \$500B/Y.

Neurosignaling Basic Principle

100B Cells
100T Links



Kandel et al, Principles of Neural Science, McGraw-Hill Medical, 2000.

Outline

◆ Motivation

- ✧ Neuroengineering

◆ Wearable Brain-Machine Interfaces

- ✧ NIRS/EEG intended for epileptic seizure localization

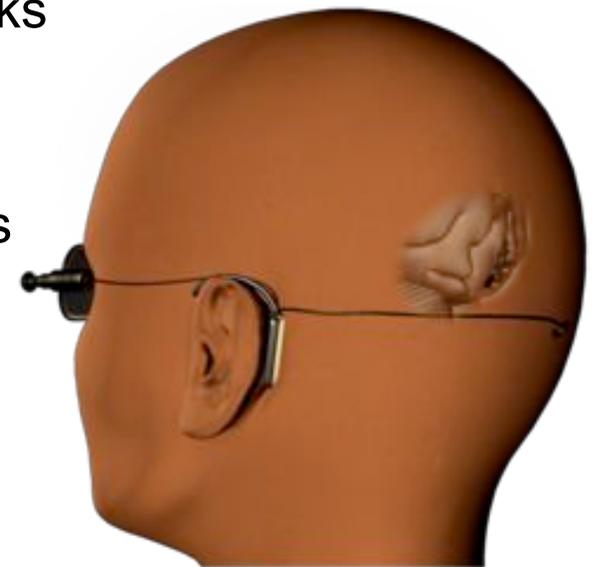
◆ Implantable Brain-Machine Interfaces

- ✧ **Neurorecording:** Massively parallel Networks
- ✧ **Neurostimulation:** Vision, Epilepsy
- ✧ **Wireless Brain Sensor Networks**
- ✧ **Neurotransmitters :** LoC-Based Biosensors

◆ Harvesting Energy & Data Exchange

- ✧ **Electromagnetic Power Transfer**
- ✧ **High-Speed Data Transmission**

◆ Resources/Summary



Brain-Machine
Interface

Functional neuroimaging of brain activities



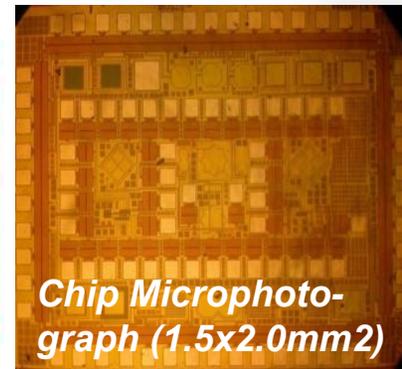
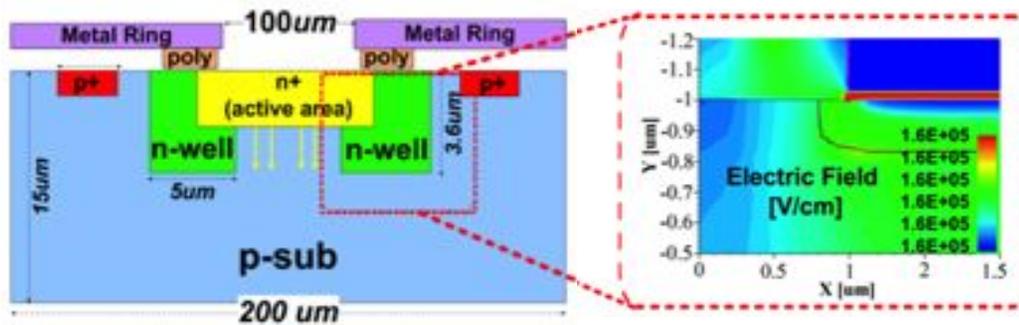
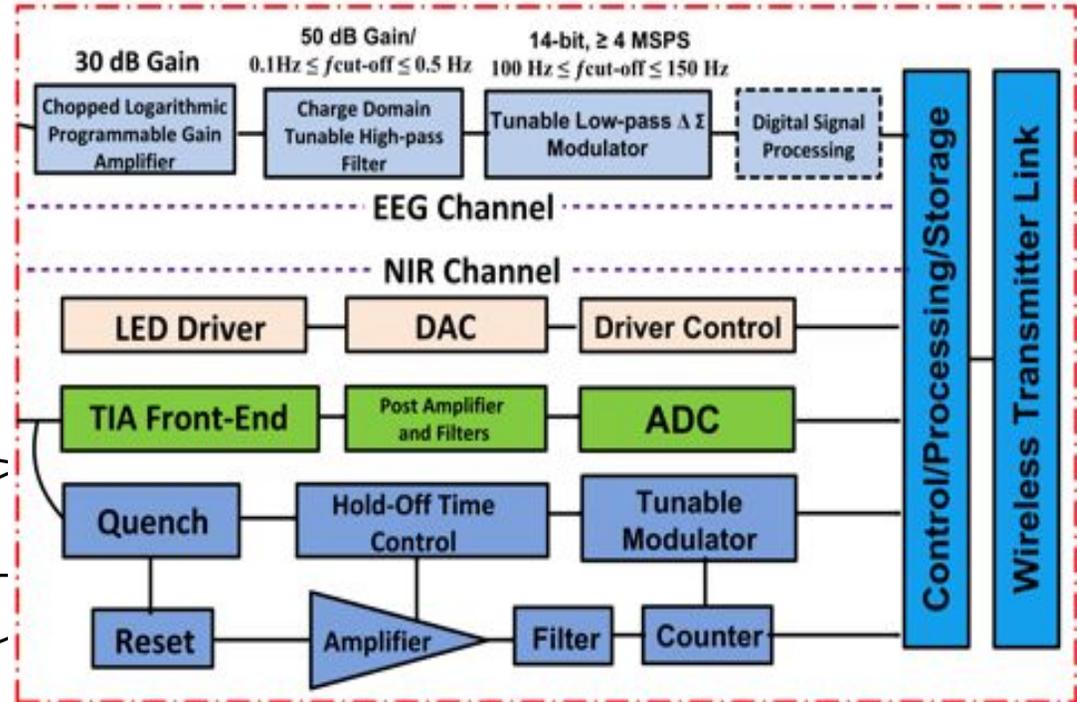
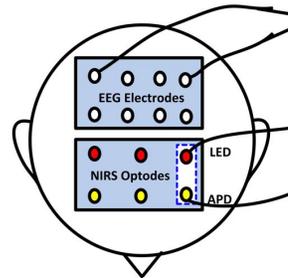
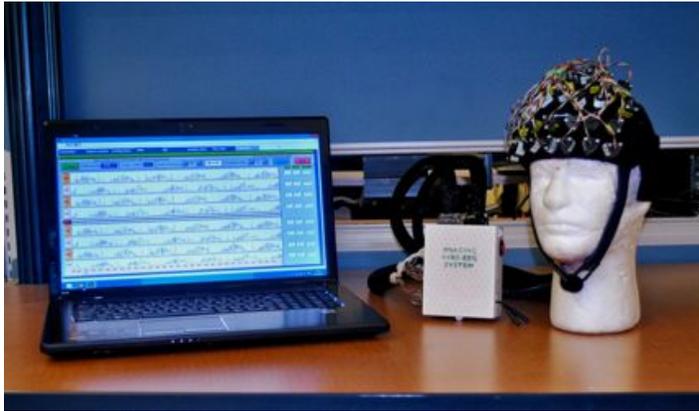
<http://www.imaginc.org>

Light on the brain

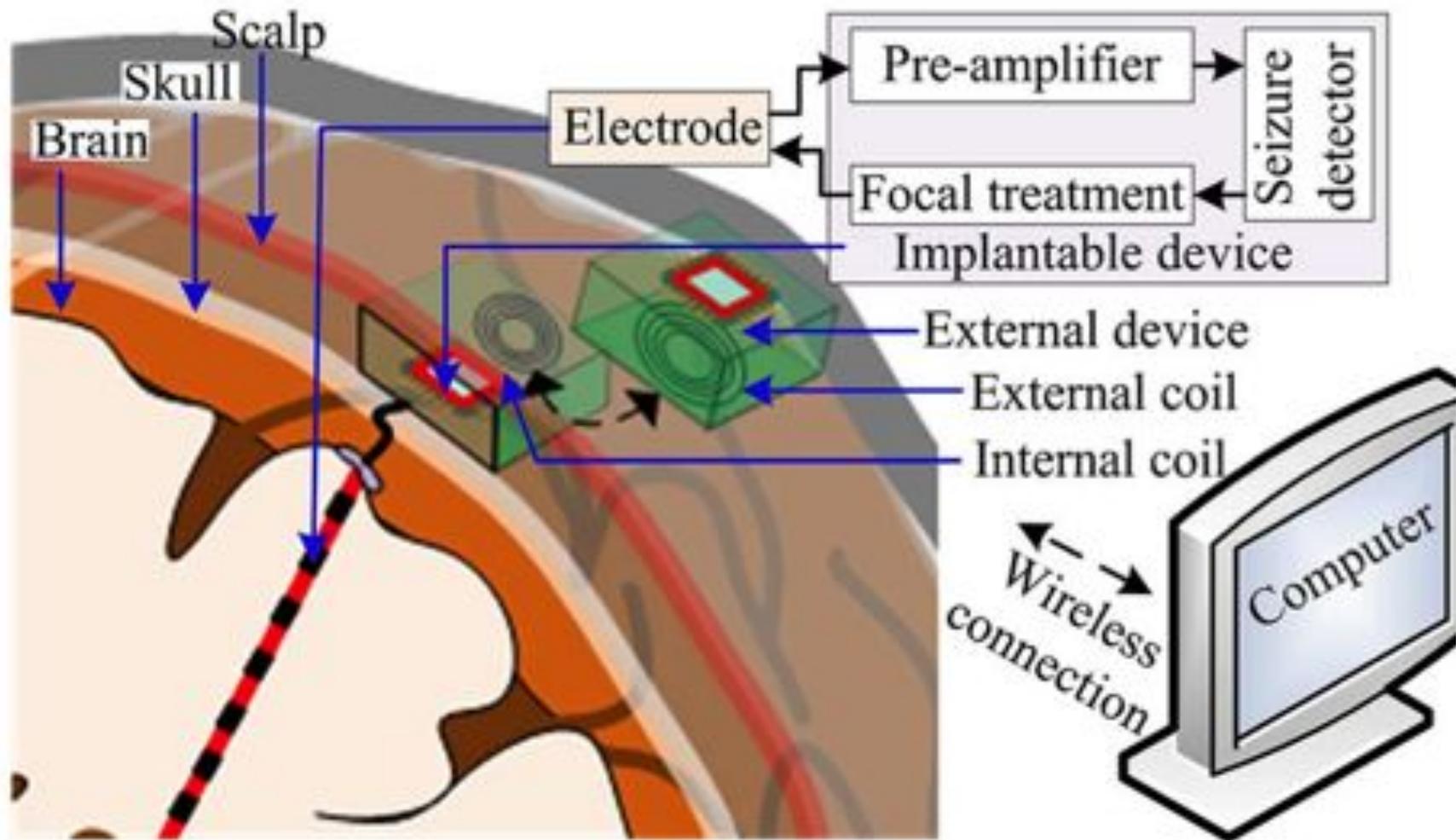
Professor Mohamad Sawan is leading the development of the first portable wireless device capable of non-invasive whole-cortex monitoring with high sensitivity; a prototype is now being tested in clinical settings



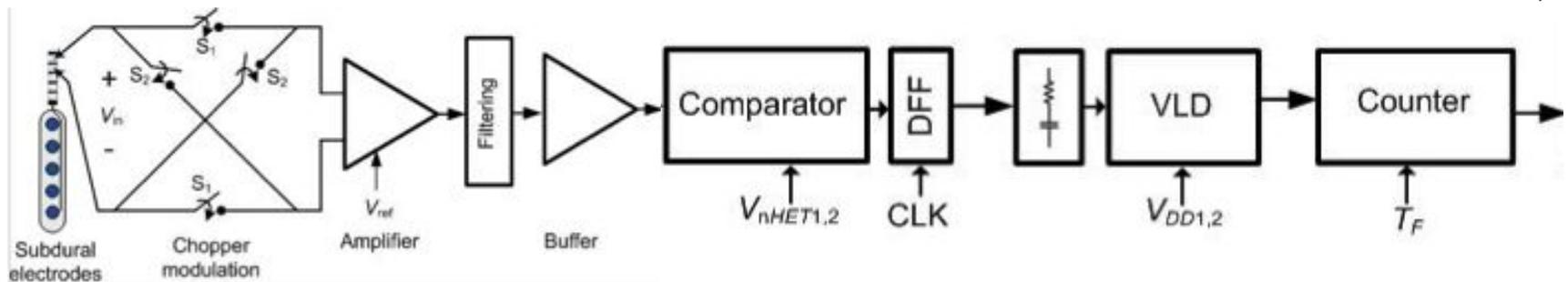
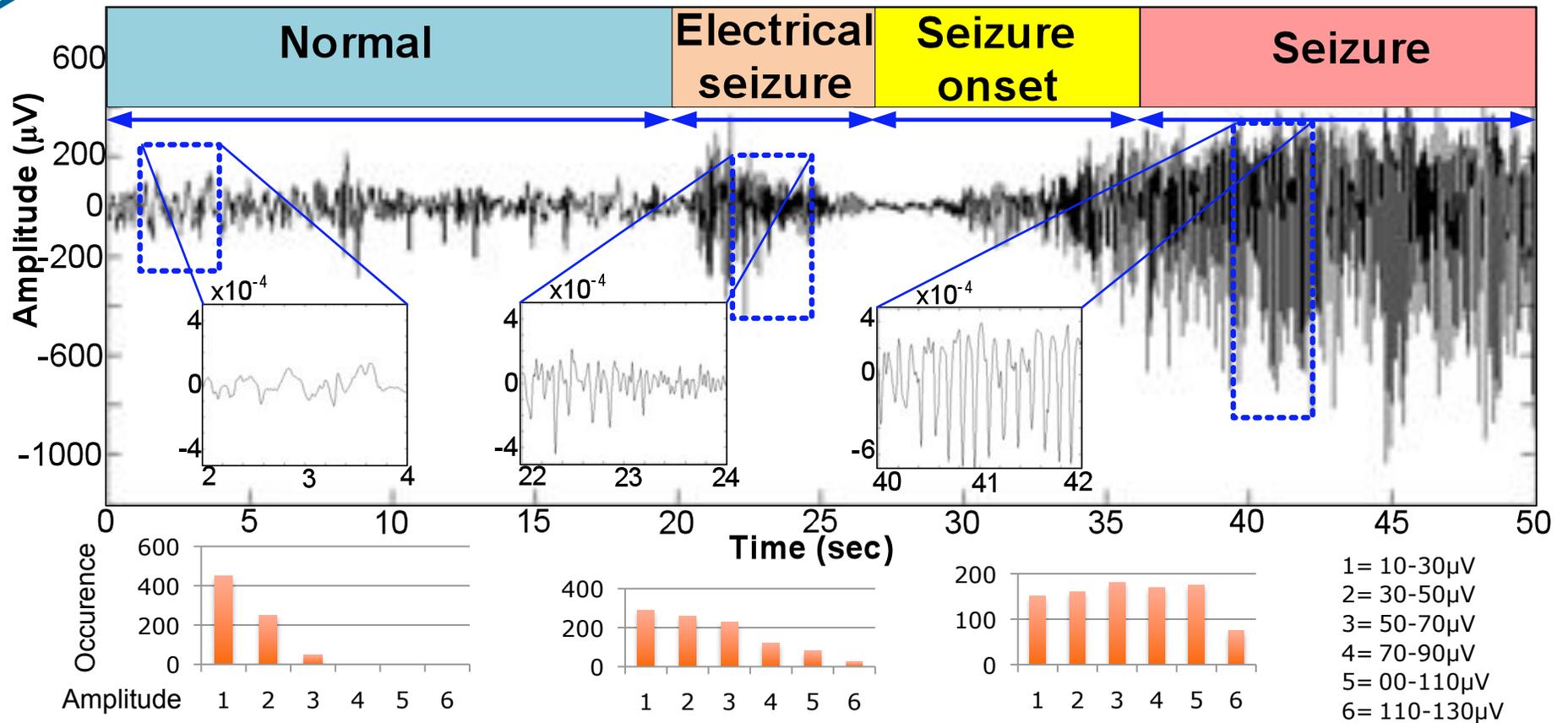
Integrated APD for Real-Time Brain Imaging



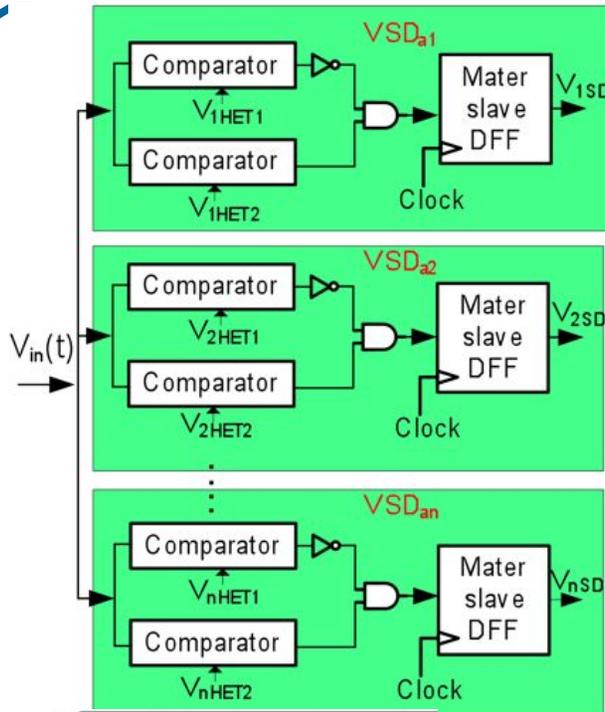
Wireless icEEG recording device



Epileptic Seizure : Analysis



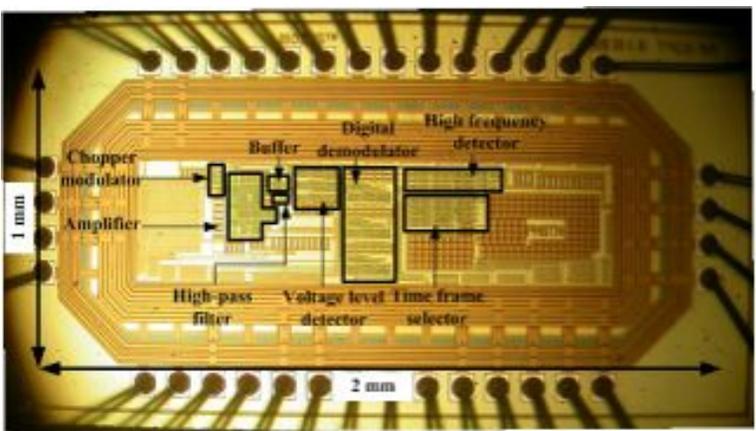
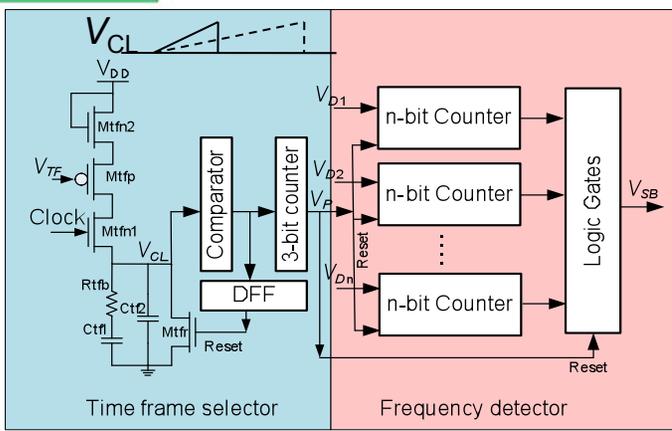
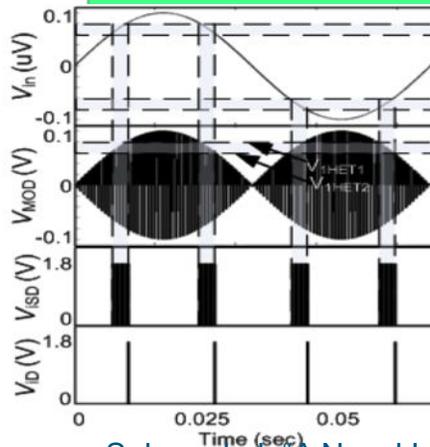
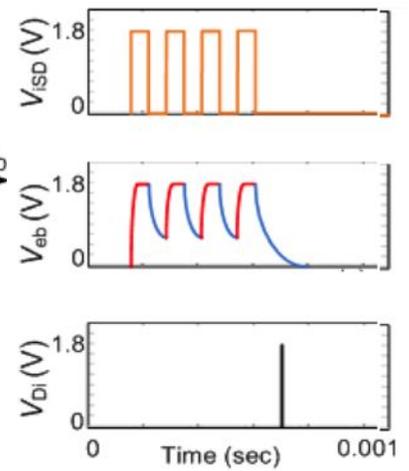
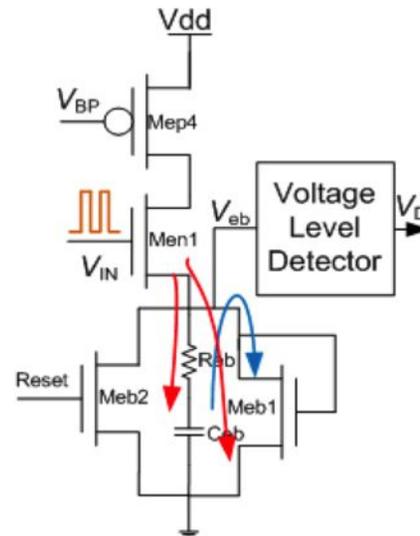
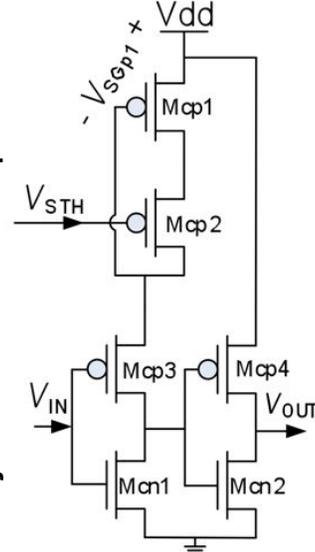
Epilepsy Seizure On Set Detector : Main Building blocks



$$V_{HETi} = \frac{V_{DD} - V_{SGp1} - |V_{tp}| + V_{tn} \sqrt{K_n / K_p}}{1 + \sqrt{K_n / K_p}}$$

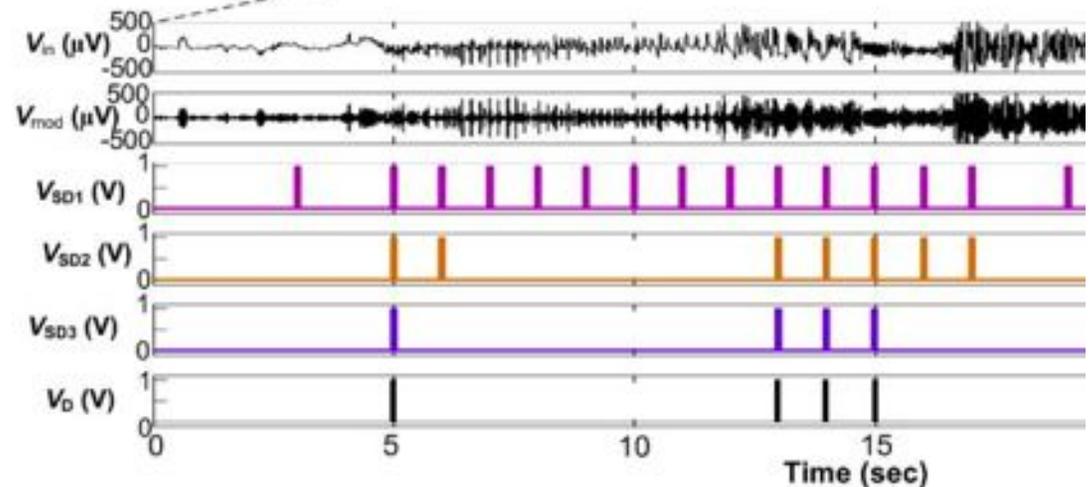
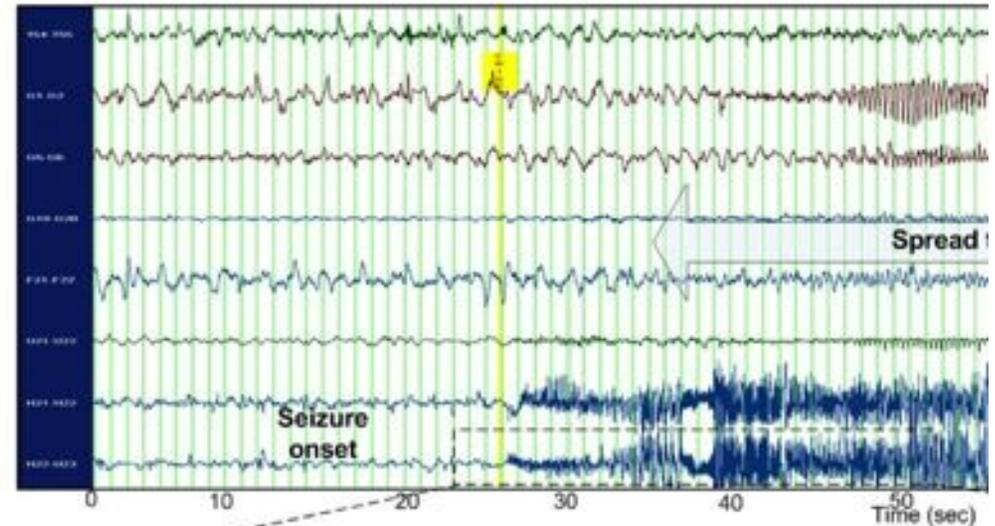
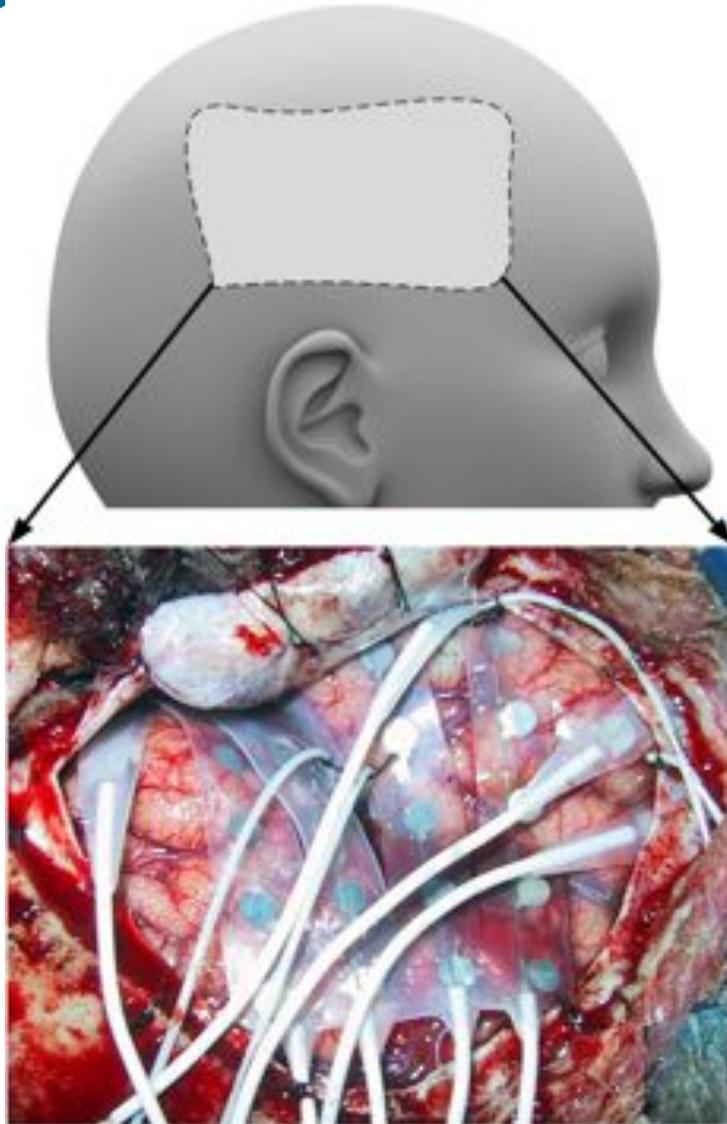
Total power consumption = 6.73μW.

Adjustable Vth comparator



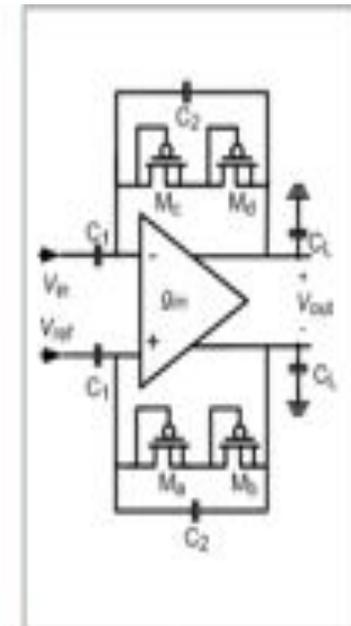
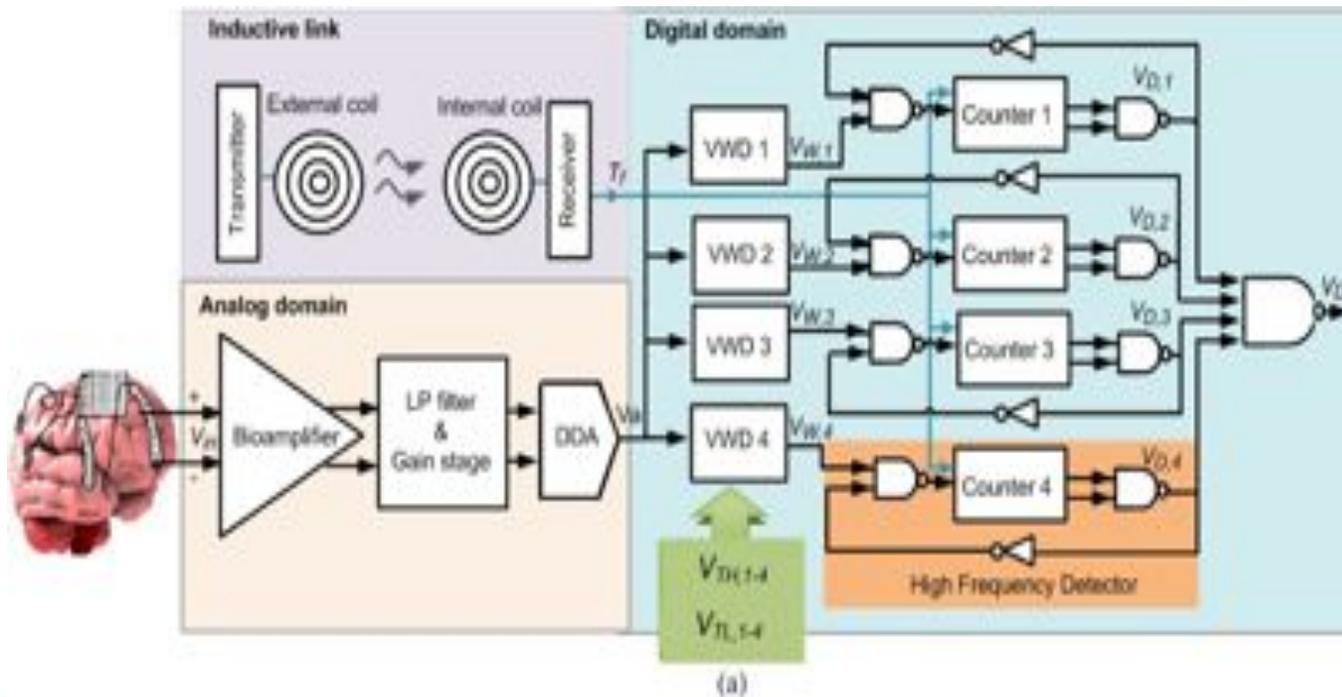
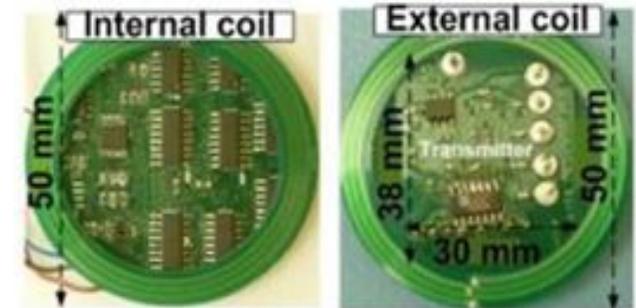
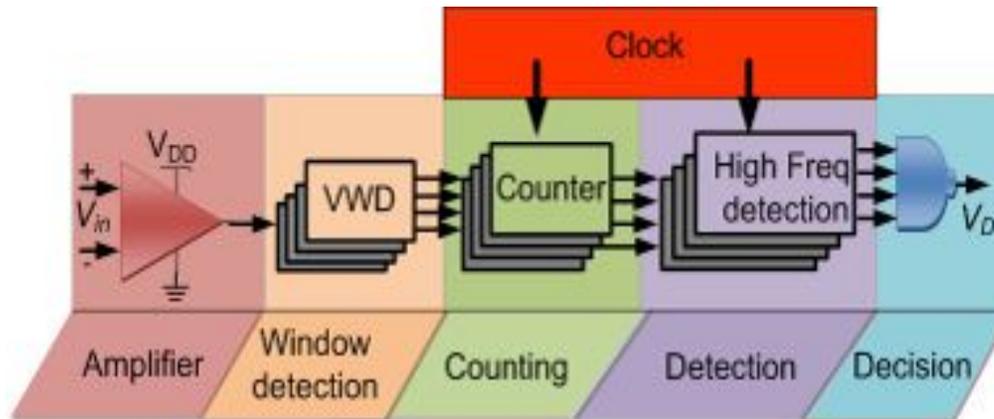
Salam et al, "A Novel Low-Power Implantable Epileptic Seizure-Onset Detector", To appear in *IEEE TbioCAS*, 2011

Algorithm and ASIC Validation

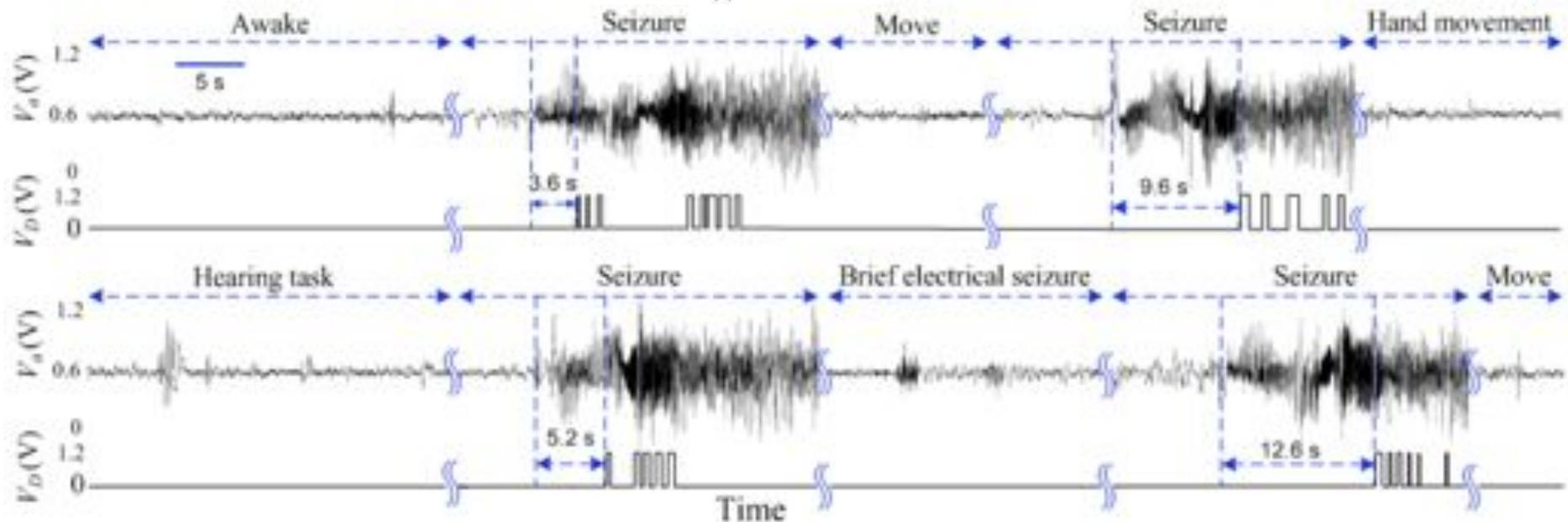
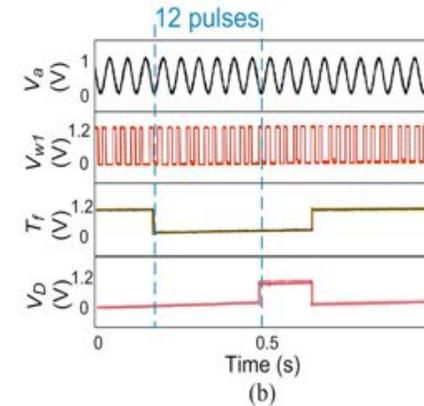
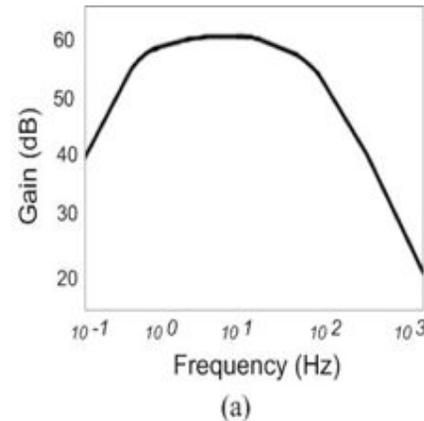
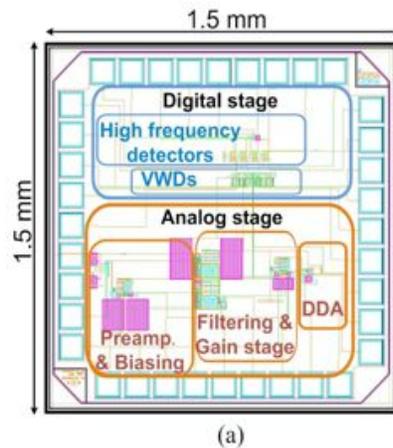


iCEEG recorded by Harmonie and the seizure detection algorithm validated in Matlab.

Asynchronous Detector Topology



Asynchronous Detector Topology (Cont'd)



Typical example from patient: Seizure detection output showing the non-related activities are ignored and the epileptic seizures are detected by the proposed ASD.

Asynchronous Detector Topology (Cont'd)

MEASURED FEATURES OF THE FABRICATED ASYNCHRONOUS SEIZURE DETECTOR

Block	Parameter	Value
Filtering and gain stage	Midband gain	60 dB
	Low-pass cutoff frequency	59 Hz
	High-pass cutoff frequency	< 1 Hz
Seizure detection stage	Highest threshold voltage	1.1 V
	Lowest threshold voltage	100 mV
	Threshold incremental step	15 mV
ASD	Supply voltage	1.2 V
	Power consumption	9 μ W

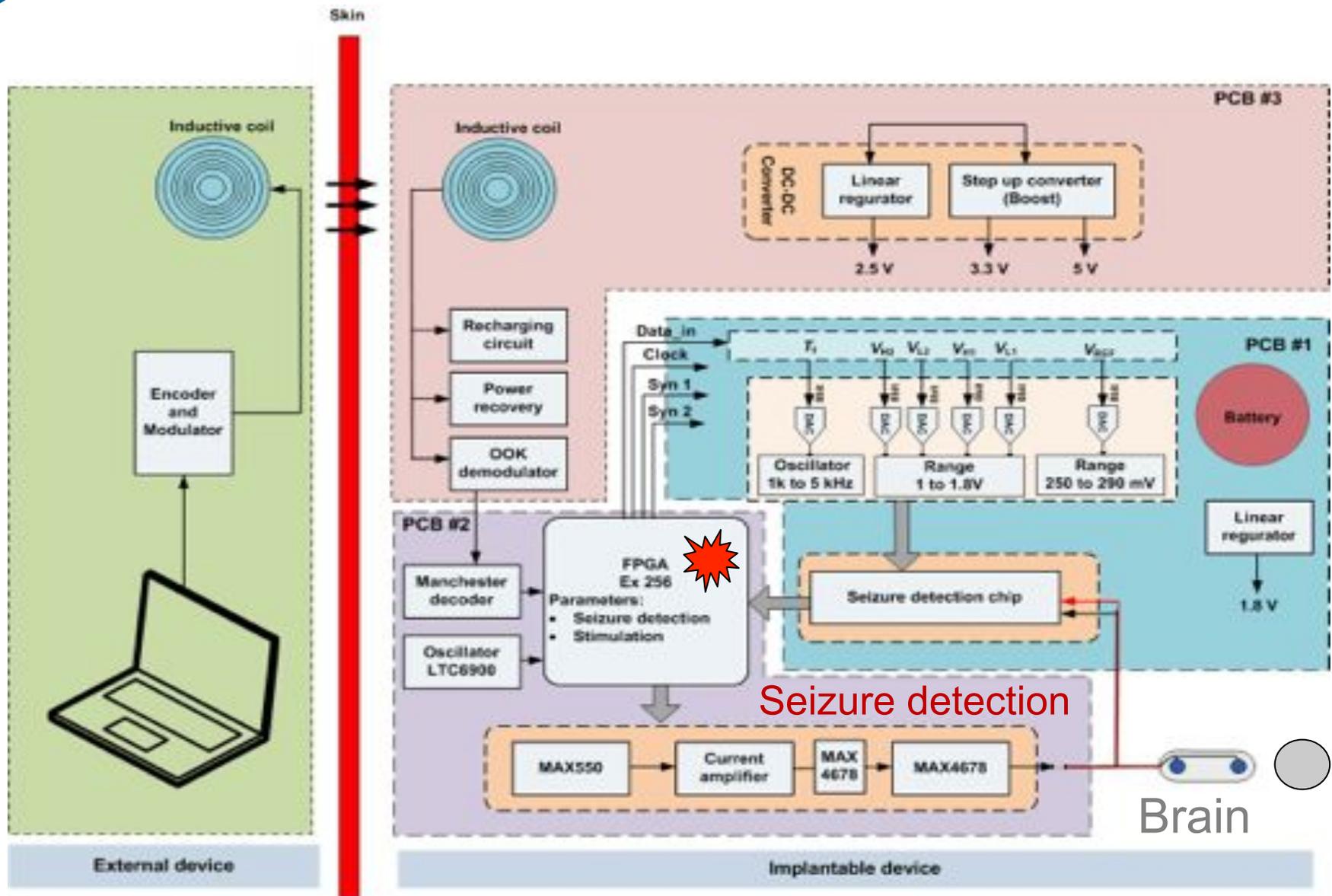
Reference	Total PC ^a	Sensitivity	Detection delay (s)
[2]	50 μ W	100%	13.5
[9]	7.07 μ W (Simulation)	100%	9.7
[10]	N/A	95%	8.5 (Simulation)
[13]	N/A	94%	N/A
[15]	120.1 μ W	93%	8.2
[24]	2.43 mW	N/A	N/A
[25]	N/A	66%	59
This work	9 μ W	100%	13.7

COMPARISON OF LATEST LOW-POWER SEIZURE DETECTORS

Parameter	Synchronous		Asynchronous	
	PCB-based [14]	Micro-chip [2]	PCB-based [11]	This work (ASD)
Power consumption	67.6 mW	50 μ W	47.2 mW	9 μ W
Case1- T _{DET} ^a (s)	21	15	16	17.5
Case2- T _{DET} ^a (s)	7	6	9	10
Size (mm ²)	1256.6	2	1963.5	2.25

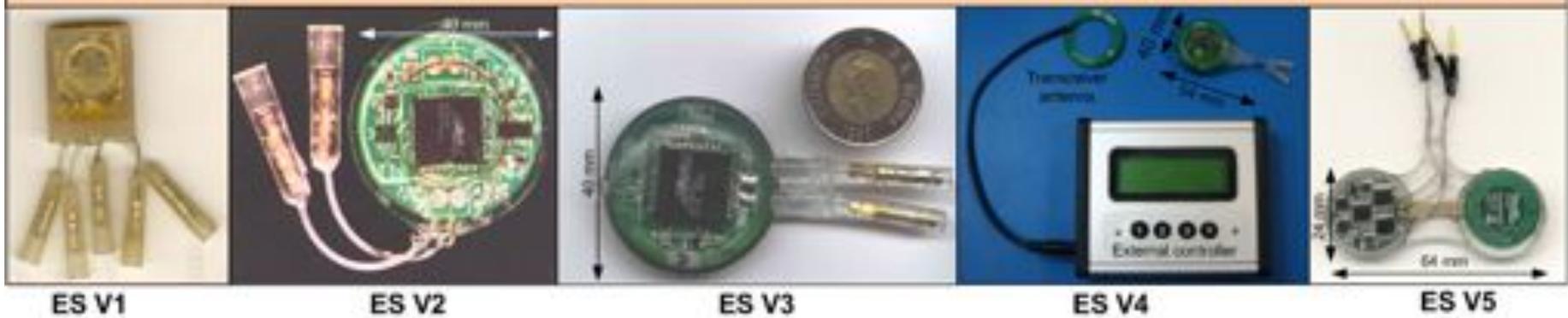
^aT_{DET} is the average detection delay

Feedback Control System : Detection and Treatment

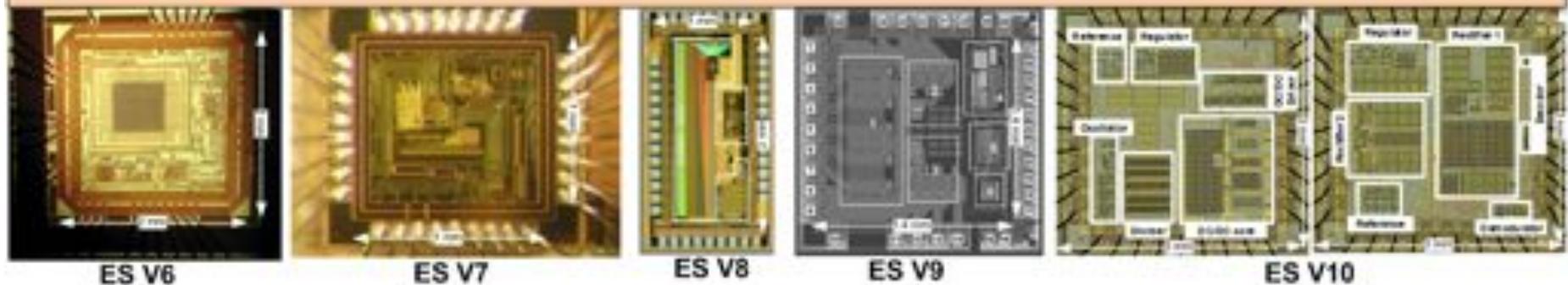


Constant Current Stimulation : Various Devices

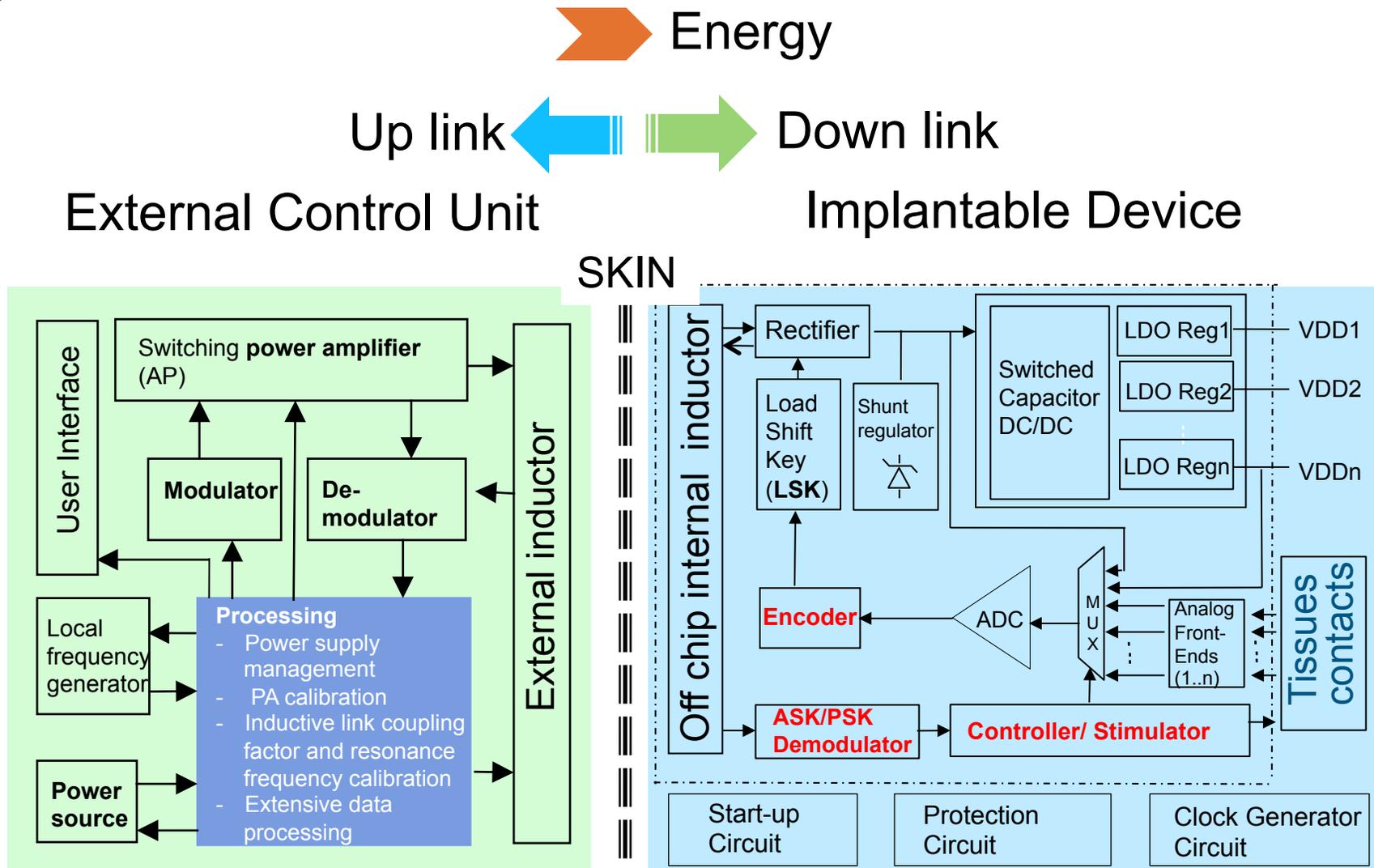
The discrete prototypes of electrical stimulator



The integrated prototypes of electrical stimulator

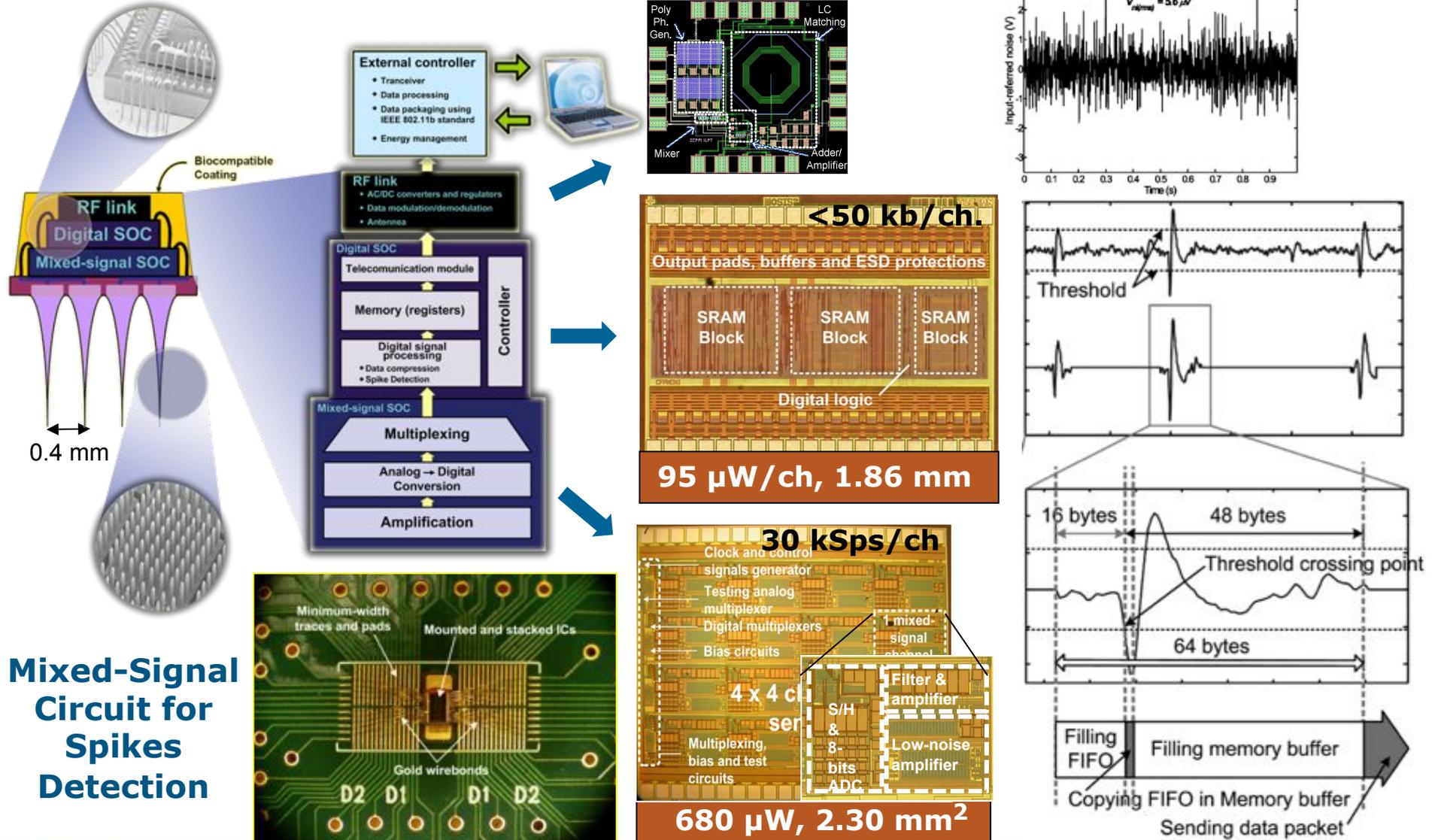


Typical Implantable System Overview

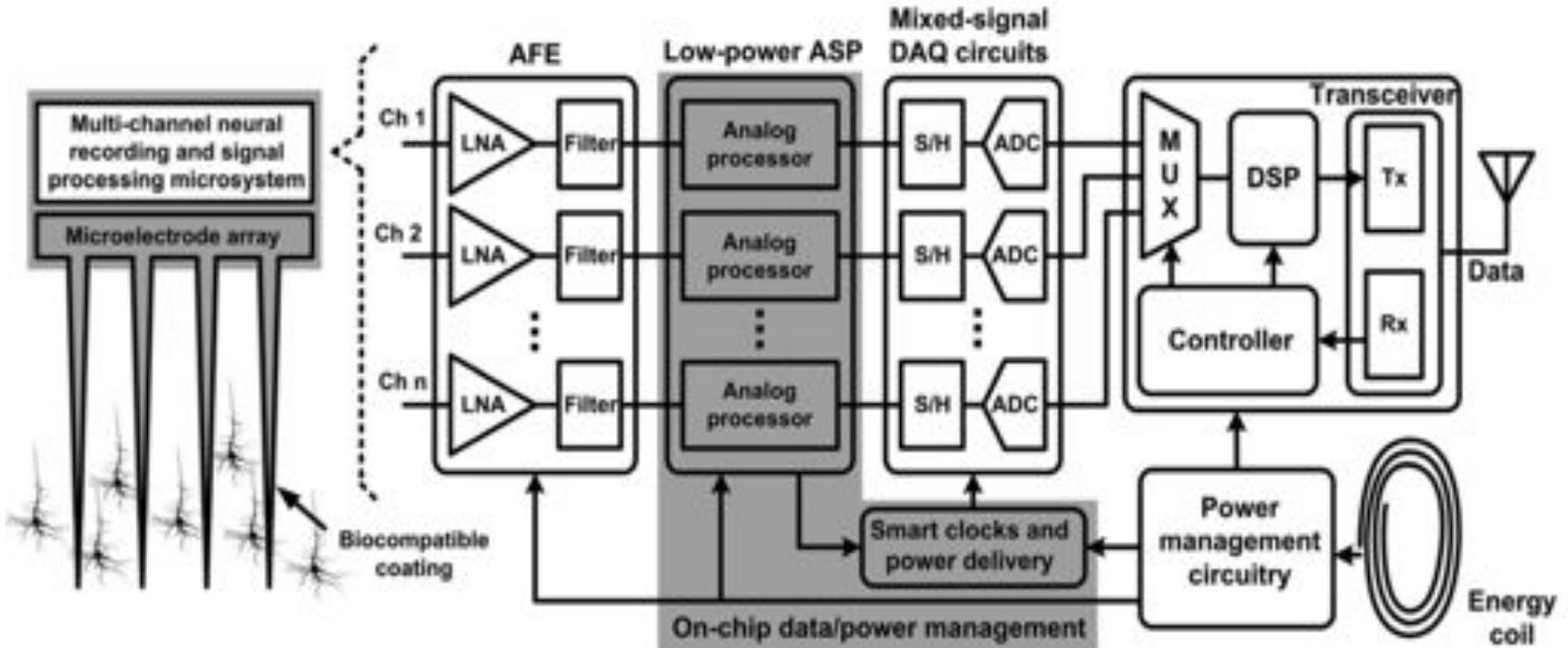


Neurorecording Biopotentials/Spikes

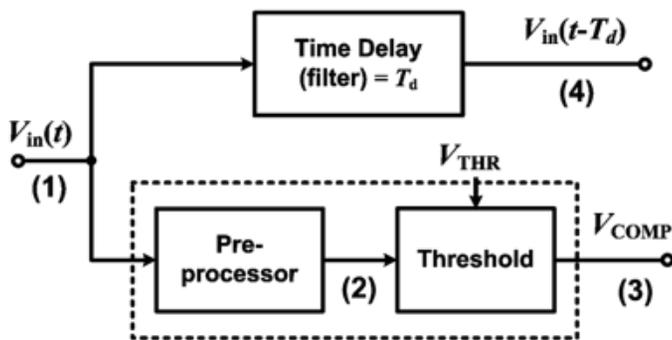
Multi-chip multi-channel neural interface



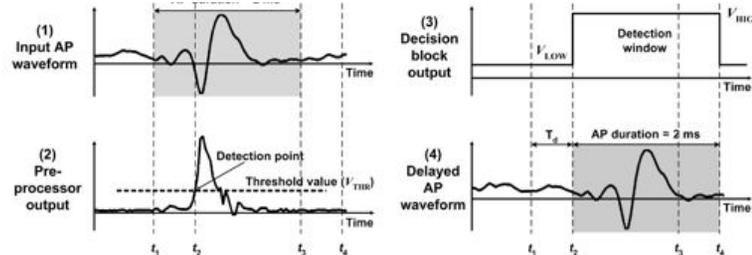
Neurorecording Biopotentials: Power Management



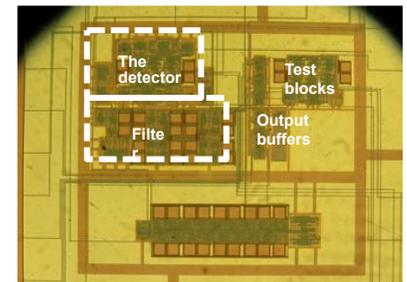
Teager Energy Operator



$$\psi(x(t)) = \left(\frac{dx(t)}{dt} \right)^2 - x(t) \left(\frac{d^2x(t)}{dt^2} \right)$$

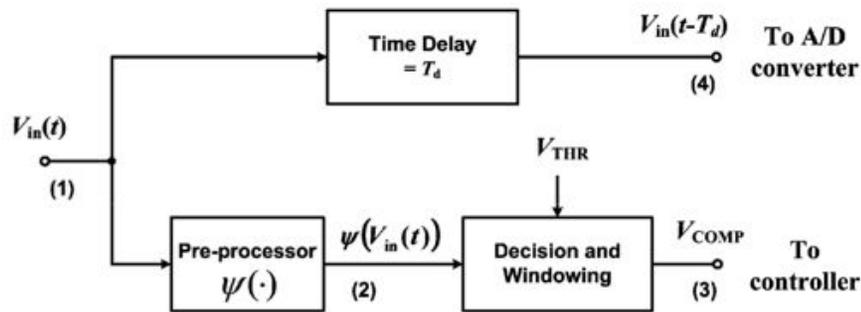


CMOS 0.18 μm
272x257 μm^2 , 780 nW

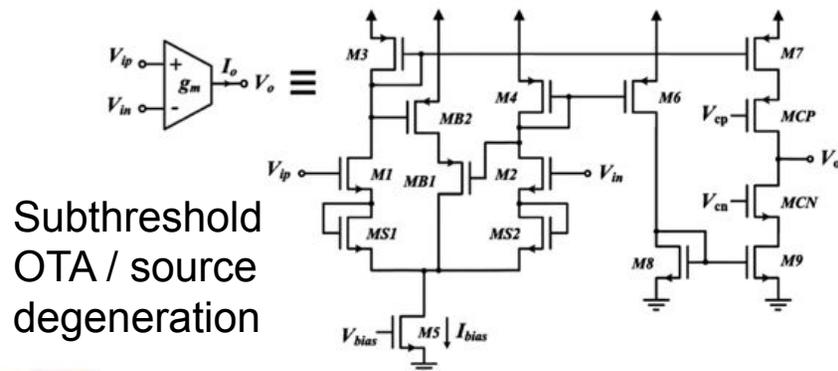
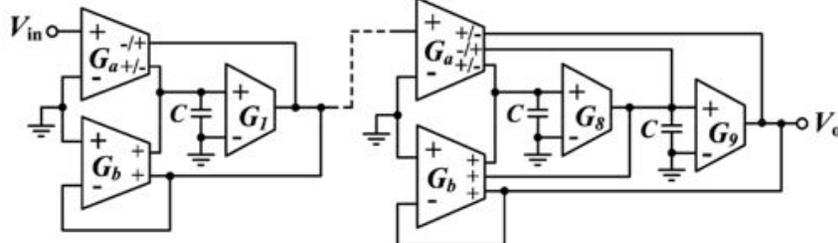


Analog Biopotential Detector: Circuit Implementation

- Sub-microwatt biopotential detector based on a custom analog processor



Delay element: $\psi(V_{in}(t)) > V_{THR} \begin{cases} V_{High}, \\ V_{Low} \text{ otherwise} \end{cases}$
 9th-order AP filter

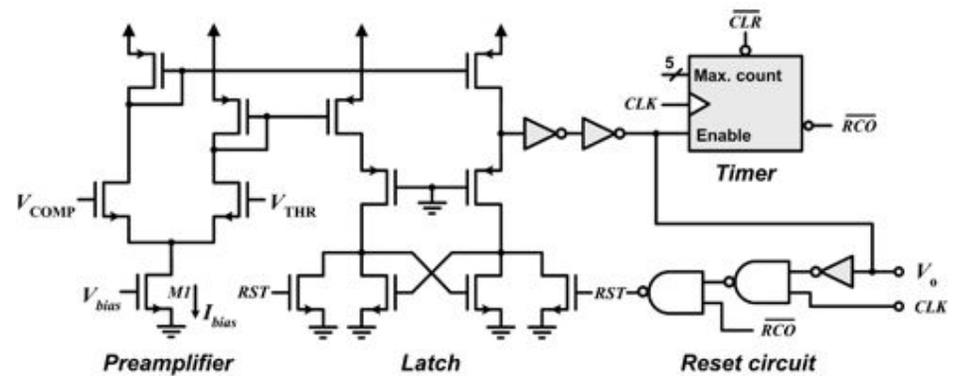
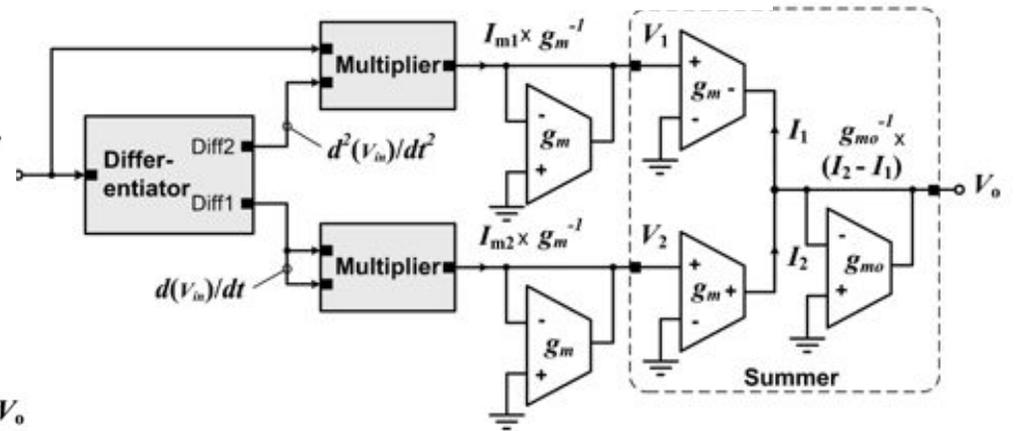


Subthreshold OTA / source degeneration

Gm-C based Analog pre-processor.

$$\psi(x(t)) = \left(\frac{dx(t)}{dt} \right)^2 - x(t) \left(\frac{d^2x(t)}{dt^2} \right).$$

Teager Energy Operator



Decision block : Latched-comparator

Statistical SP : Adaptive Spike Detection

Adaptive Spike Detection Threshold Based on Robust Statistics Theory

- ❖ The definition of the discrete-time TEO is given by:

$$\psi[x(n)] = x^2(n) - x(n+1)x(n-1)$$

- ❖ A spike is present if $\psi_s[x(n)] > T$

$$T = \mu + p\sigma; \mu \text{ \& } \sigma \text{ are statistical moments}$$

- ❖ **Determination** of μ of $\psi_s[x(n)]$

$$\begin{aligned} \mu_{\psi_s} &= E\{\psi_s[x(n)]\} = E\left\{\sum_{k=0}^{L-1} w(k)\psi[x(n-k)]\right\} \\ &= \sum_{k=0}^{L-1} w(k)E\{\psi[x(n-k)]\} \end{aligned}$$

$$\mu_{\psi_s} = 2.24(r_{xx}(0) - r_{xx}(2))$$

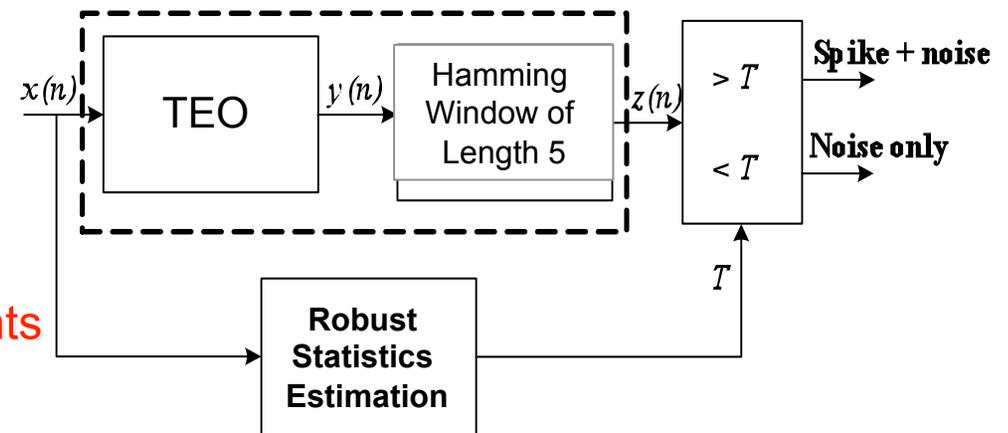
- ❖ **Determination** of σ of $\psi_s[x(n)]$

$$\begin{aligned} \sigma_{\psi_s}^2 &= \text{var}\{\psi_s[x(n)]\} = E\{\psi_s^2[x(n)]\} - E^2\{\psi_s[x(n)]\} \\ &= E\{\psi_s^2[x(n)]\} - \mu_{\psi_s}^2 \end{aligned}$$

$$\begin{aligned} \sigma_{\psi_s}^2 &\approx 4.8r_{xx}^2(0) + 0.7r_{xx}^2(1) + 4.4r_{xx}^2(2) \\ &+ 0.6r_{xx}^2(3) - 9.3r_{xx}(0)r_{xx}(2) \\ &- 1.2r_{xx}(1)r_{xx}(3) \end{aligned}$$

where $r_{xx}(m)$ is the autocorrelation of $x(n)$ at lag m

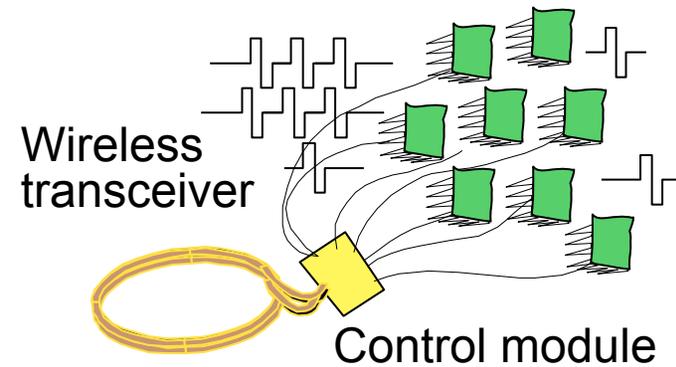
$$r_{xx}(m) = 0.25[\text{var}\{x + x_m\} - \text{var}\{x - x_m\}] \quad Qn\{x\} = \lambda[\text{abs}\{x_i - x_j\}; i < j; i, j = 1, 2, \dots, N]_{(k)}$$



Intracortical Neurostimulation : Recover Vision

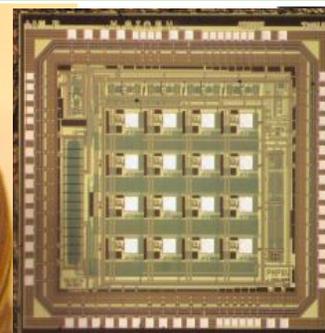
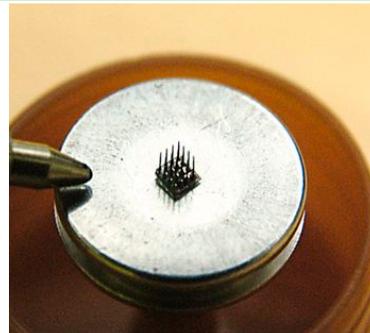
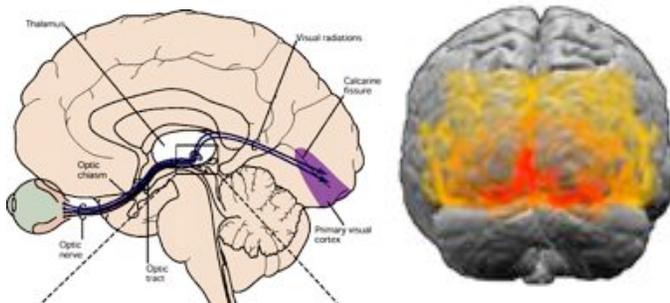
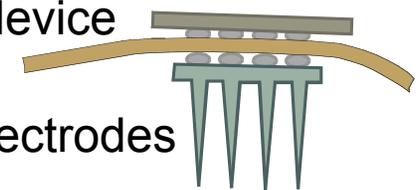
Visual implant

Stimulation & monitoring chips

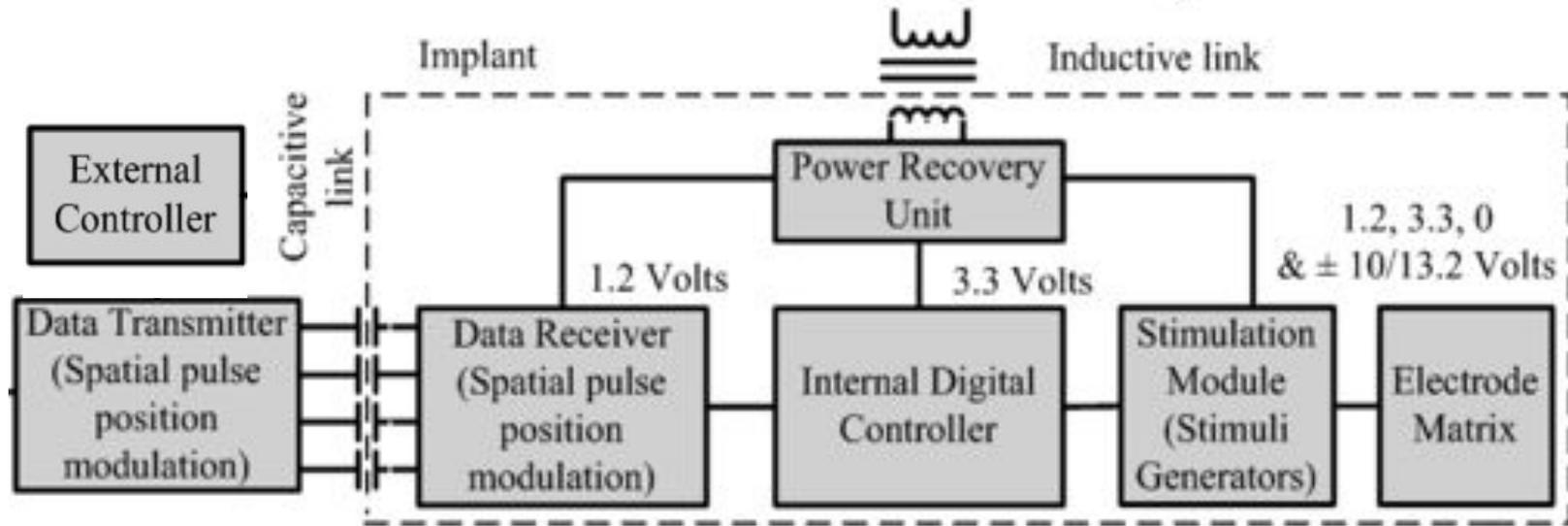


Flip-chip device

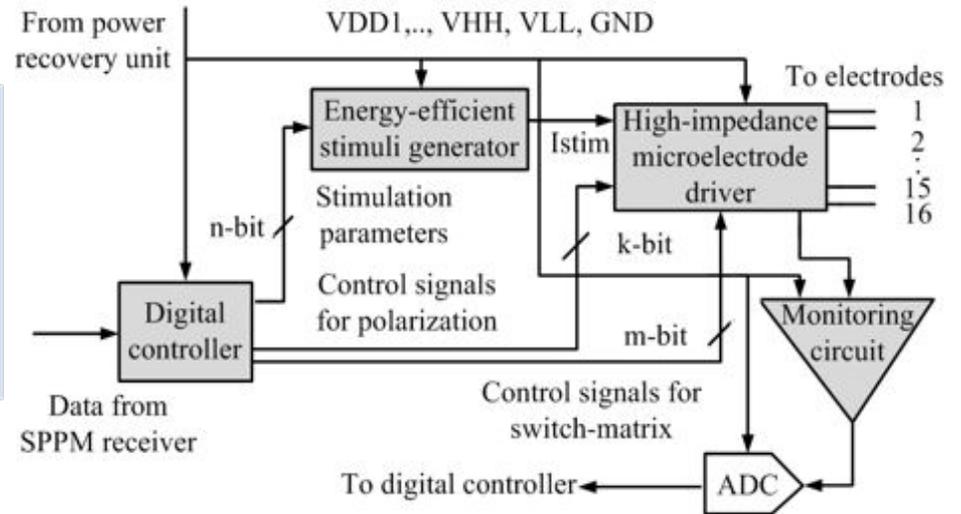
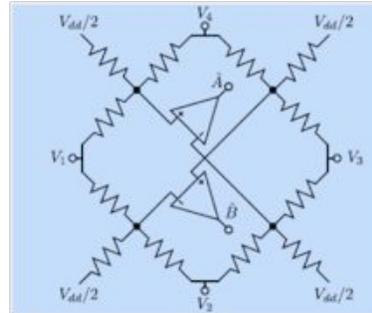
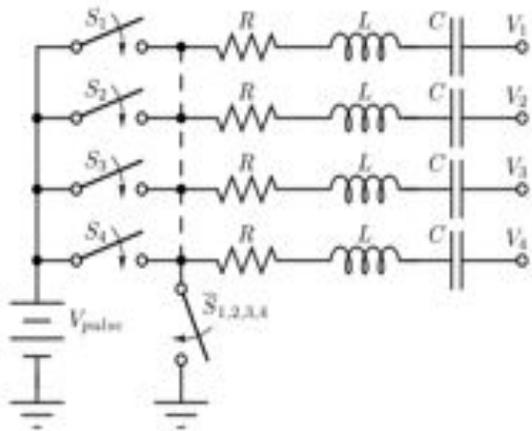
Matrix of electrodes



Visual Microstimulator/Monitor Architecture



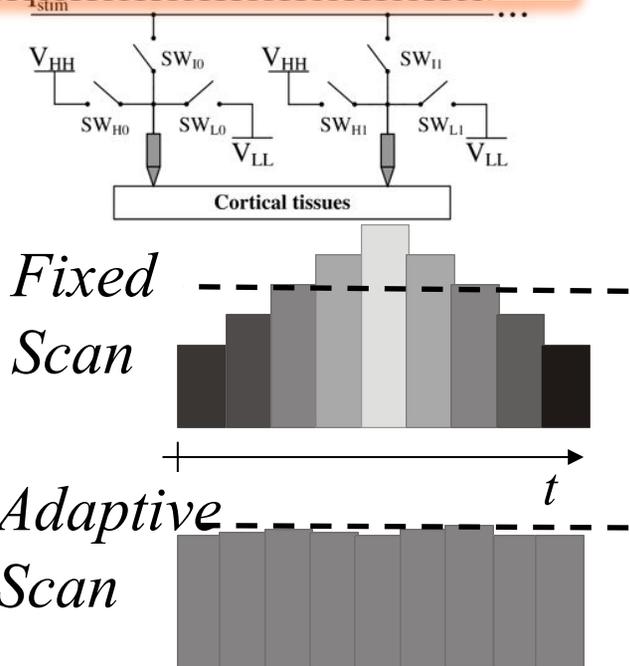
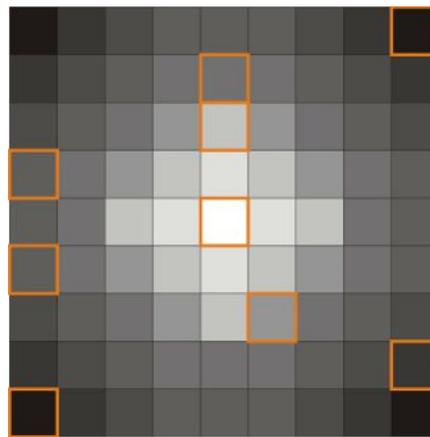
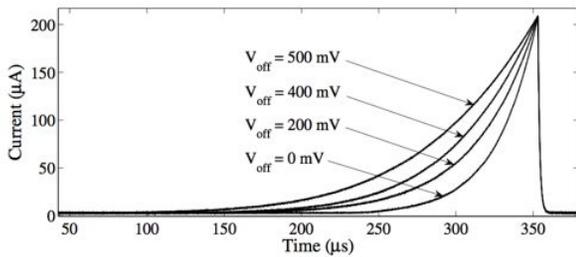
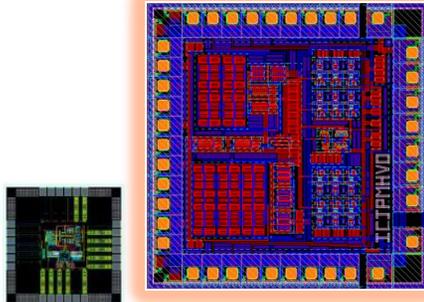
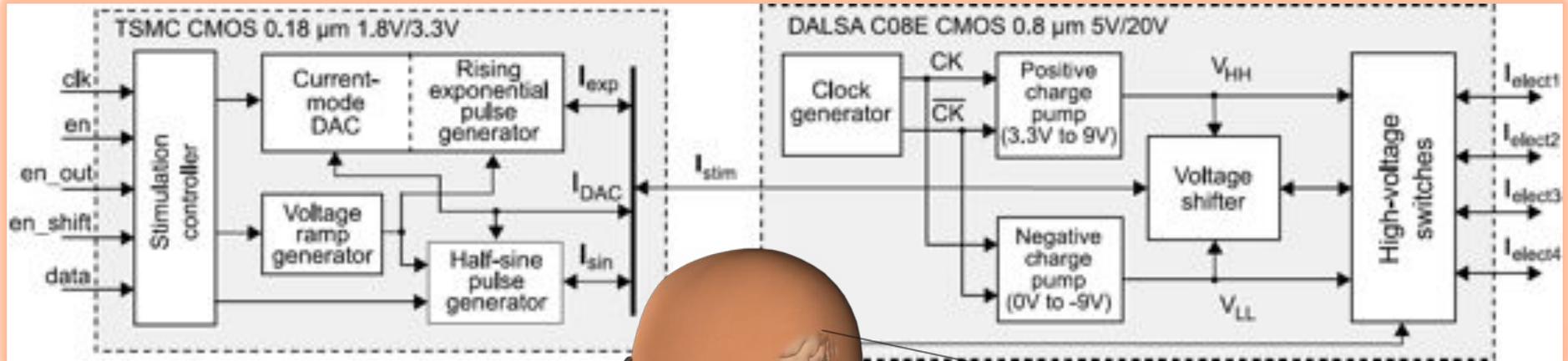
Architecture of the for visual intracortical microstimulation device.



Visual Microstimulator/Monitor Architecture

Area = 1 mm²

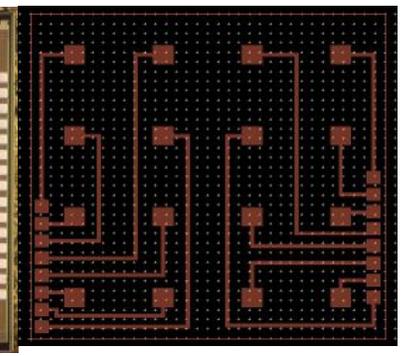
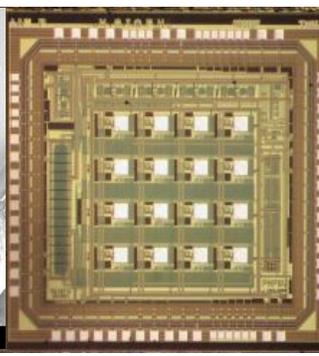
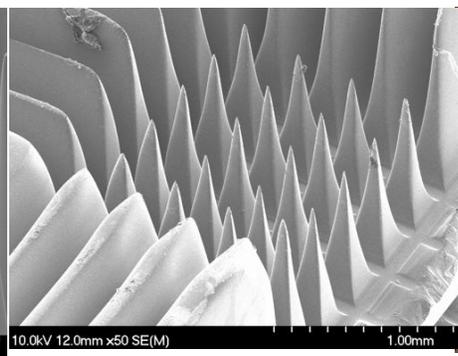
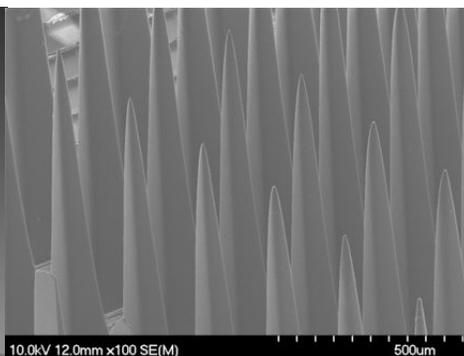
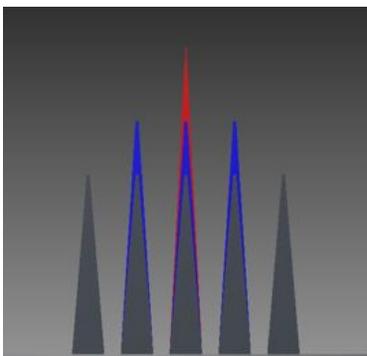
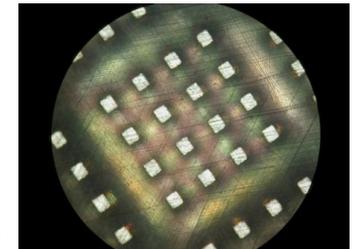
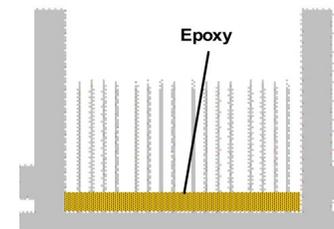
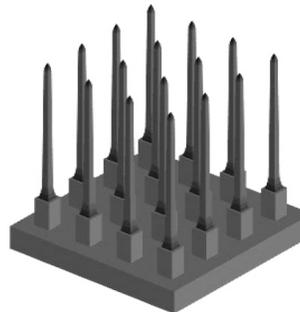
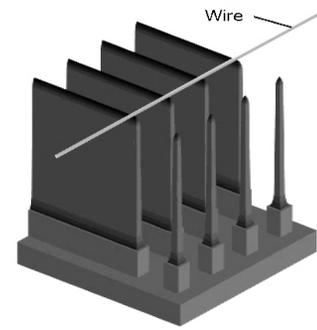
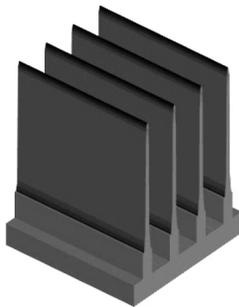
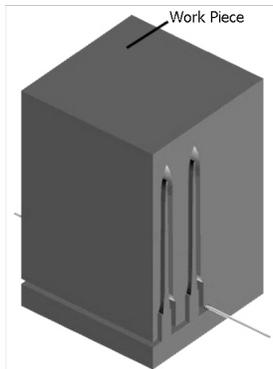
Area = 8 mm²



Ethier & Sawan, Exponential Current Pulse Generation for Efficient Very High-Impedance Multisite Stimulation”, *TBIOCAS*, 2013.

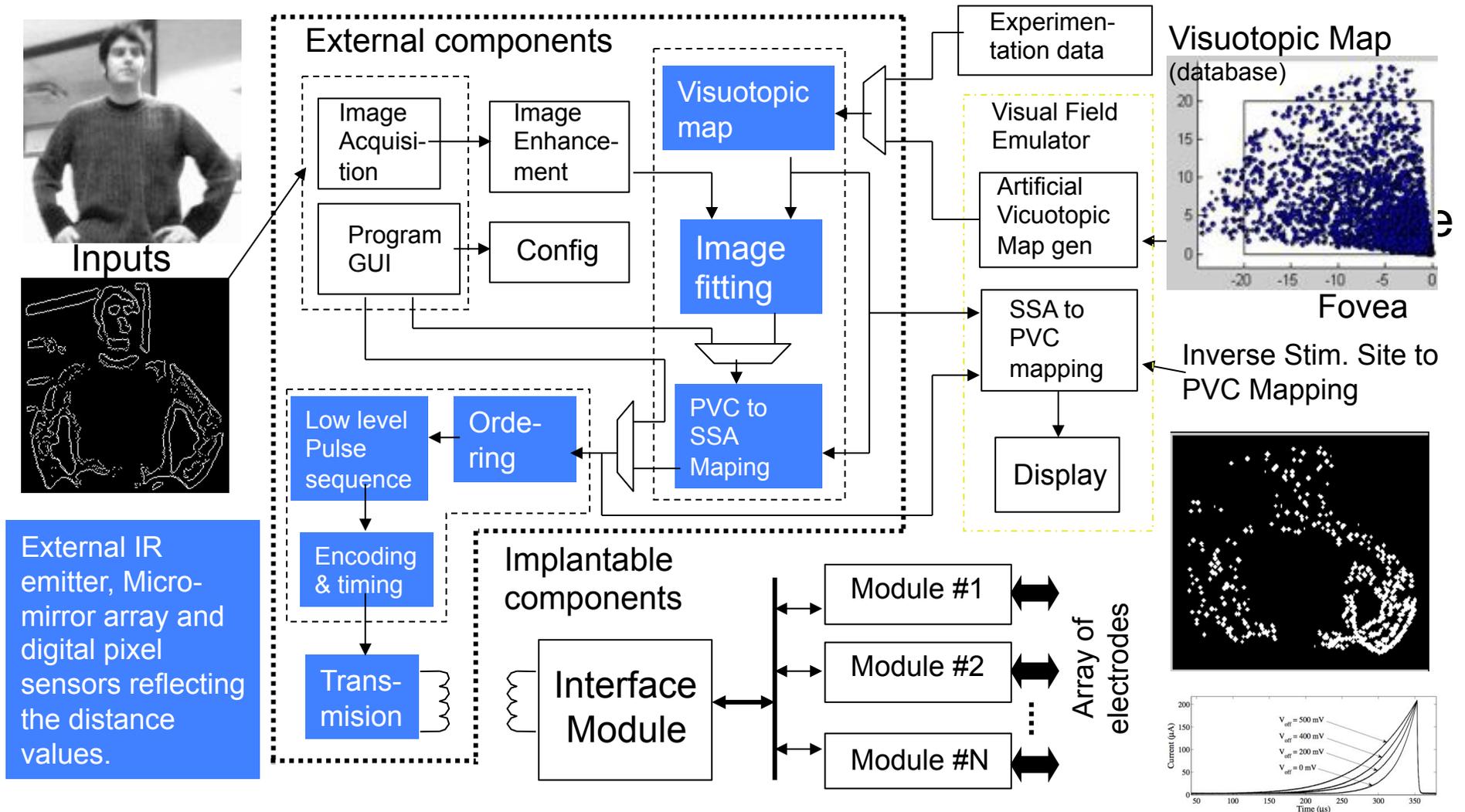
Electrodes-tissues connection : Micromachining

- Wire-EDM cut
- Surface electropolish
- Oxalic acid attack
- Platinum deposition
- Epoxy base
- Support Grinding & assembly.



Visual Microstimulator/Monitor Architecture

The external image processing



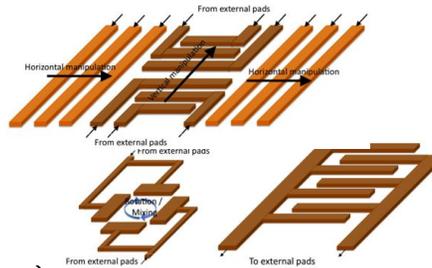
GUI = Graphical user interface ; SSA = Stimulation site address, PVC = Phosphene visual coordinates ; VDB = Visuotopic database

Biosensor for Neurotransmitters Detection

Dielectrophoresis

$$\vec{F}_{sphere} = (\vec{p} \cdot \vec{\nabla}) \vec{E}$$

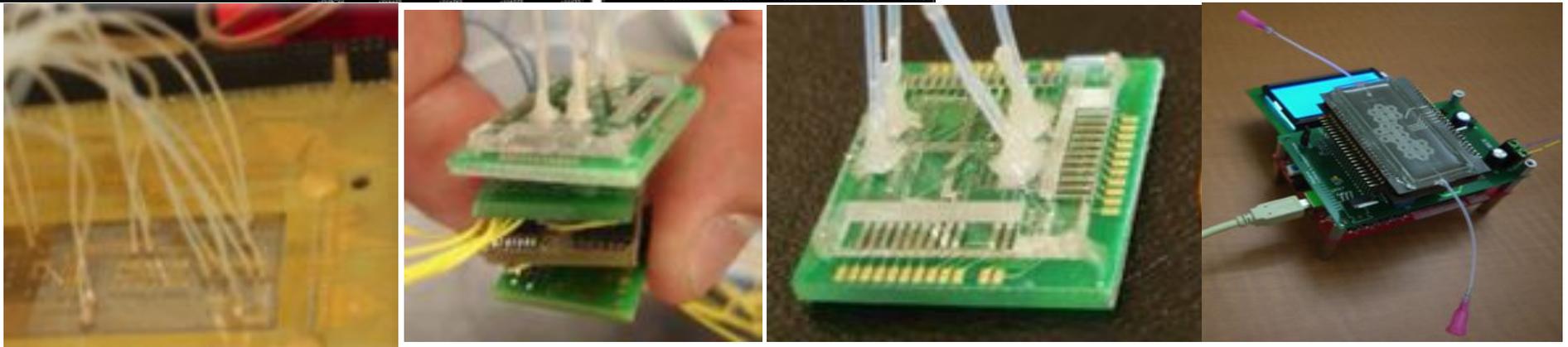
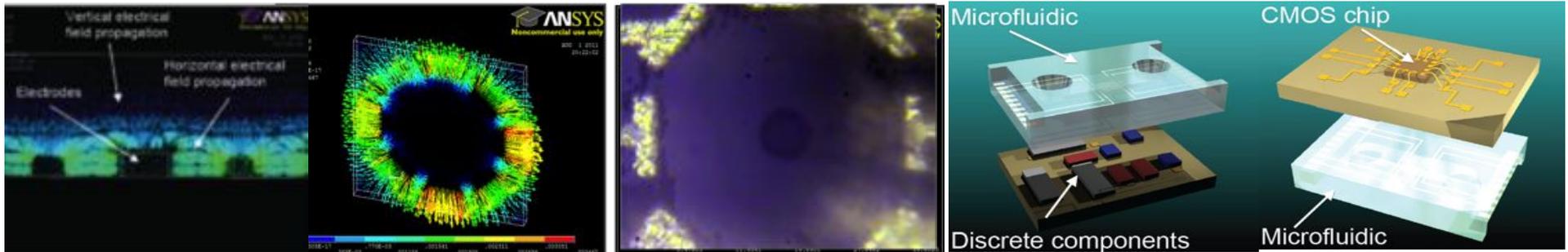
$$\vec{F}_{sphere} = 2\pi a^3 \text{Re} \left(\frac{\epsilon_0 K_1^* (K_2 - K_1)}{2K_1 + K_2} \right) \nabla |E|^2$$



Magnetophoresis

$$\vec{F}_{mag} = V \chi_m (\vec{H} \cdot \nabla) \vec{B}$$

$$F_x = V \frac{\chi_m}{\mu_0} (B_x \frac{\partial B_x}{\partial x} + B_y \frac{\partial B_x}{\partial y} + B_z \frac{\partial B_x}{\partial z})$$



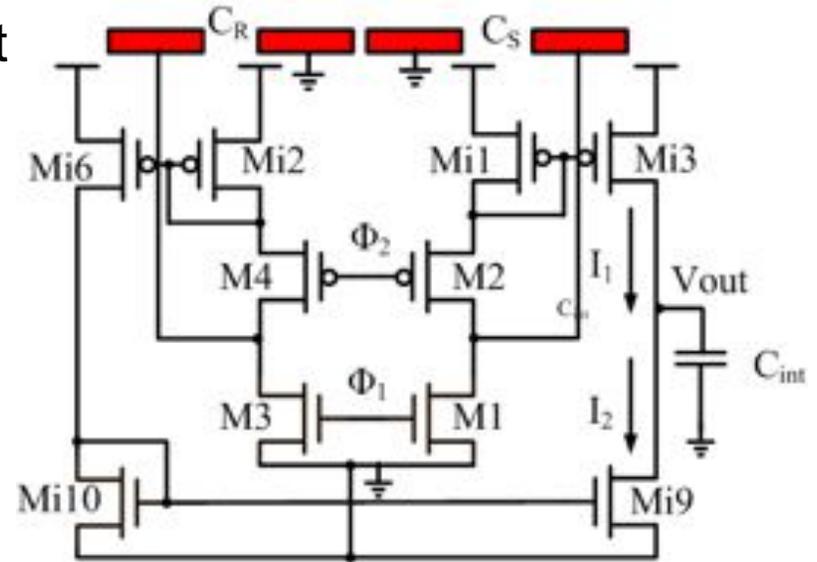
Capacitive Sensor for Lab-on-Chip Applications

Charged Based Capacitive Measurement

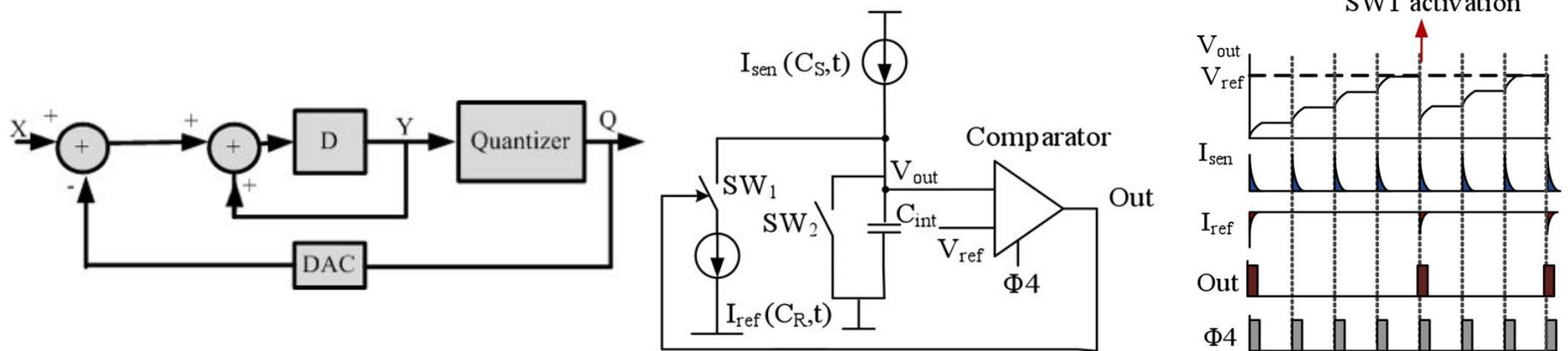
$$I_S - I_R = f \cdot V_{DD} \cdot \Delta C$$

$$V_{out} = \frac{\Delta C}{C_{int}} \cdot K \cdot V_{DD}$$

$$K = \frac{\left(\frac{W}{L}\right)_{M3}}{\left(\frac{W}{L}\right)_{M1}} = \frac{\left(\frac{W}{L}\right)_{M6} \cdot \left(\frac{W}{L}\right)_{M9}}{\left(\frac{W}{L}\right)_{M2} \cdot \left(\frac{W}{L}\right)_{M10}}$$

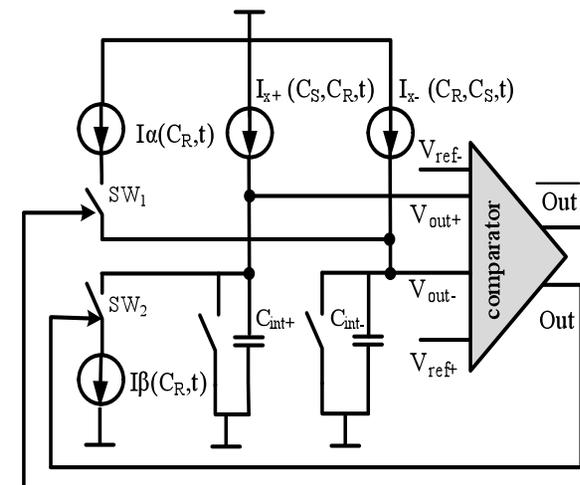
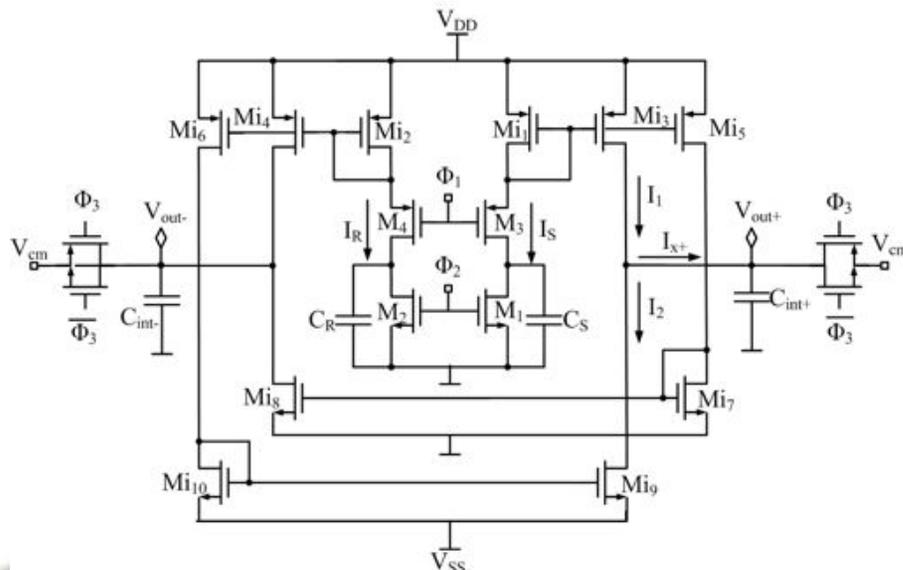
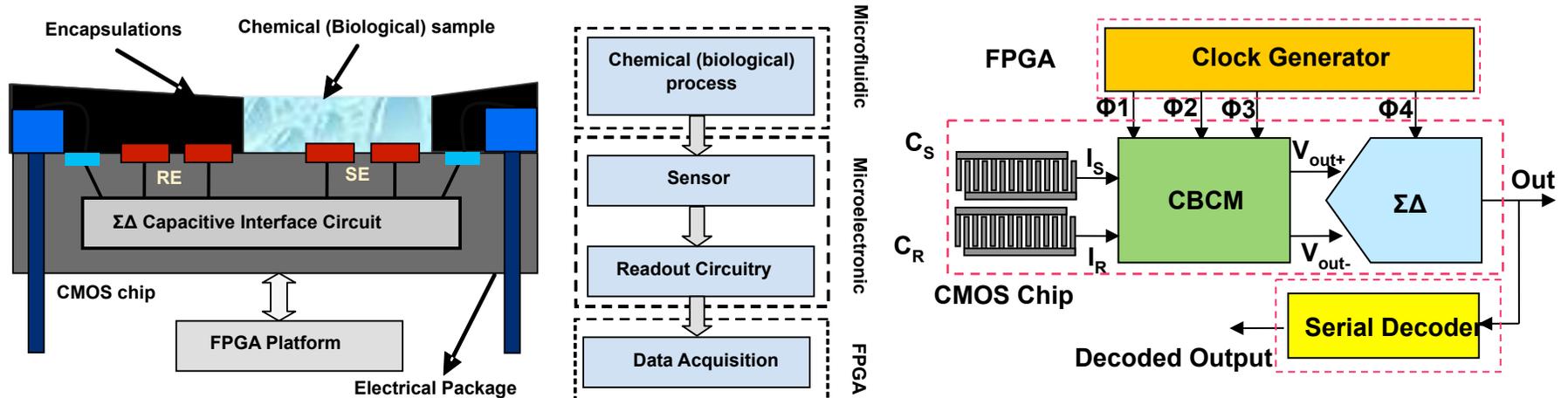


- A DC-input $\Sigma\Delta$ 1st order modulator converts V_c to digital.

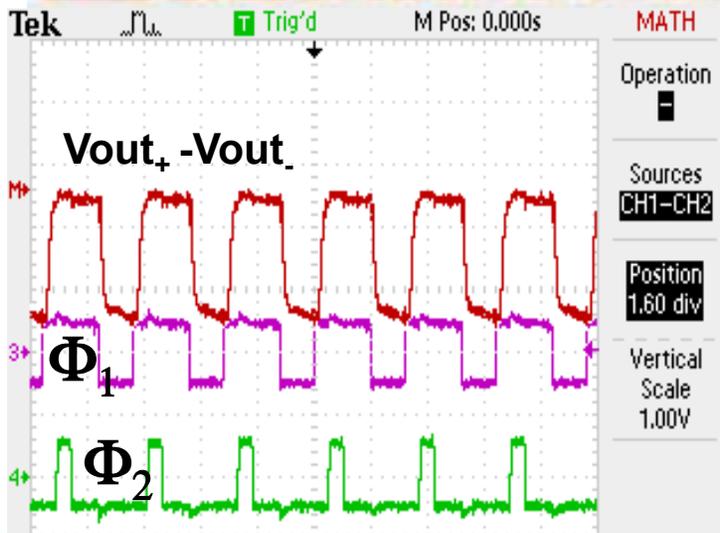
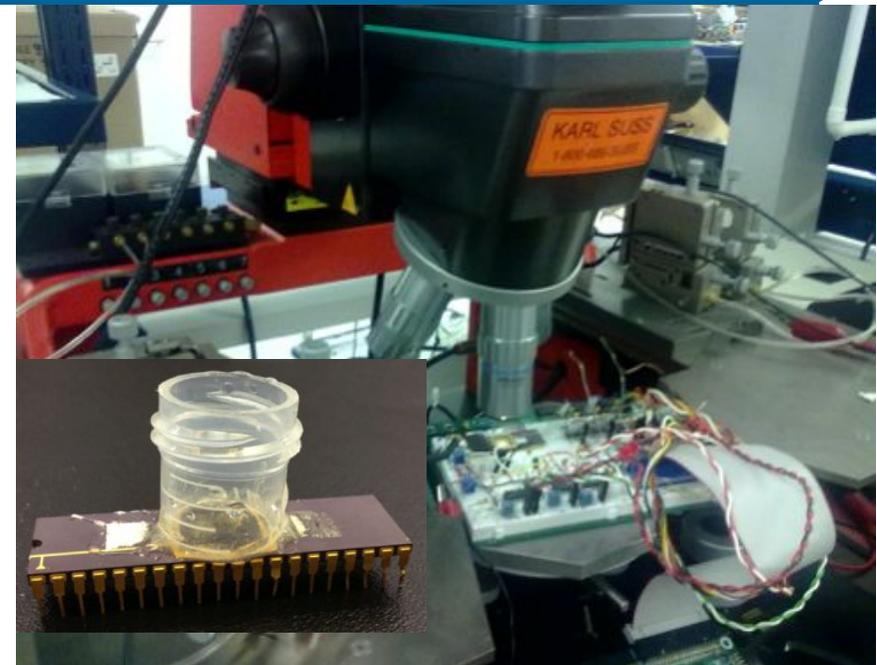
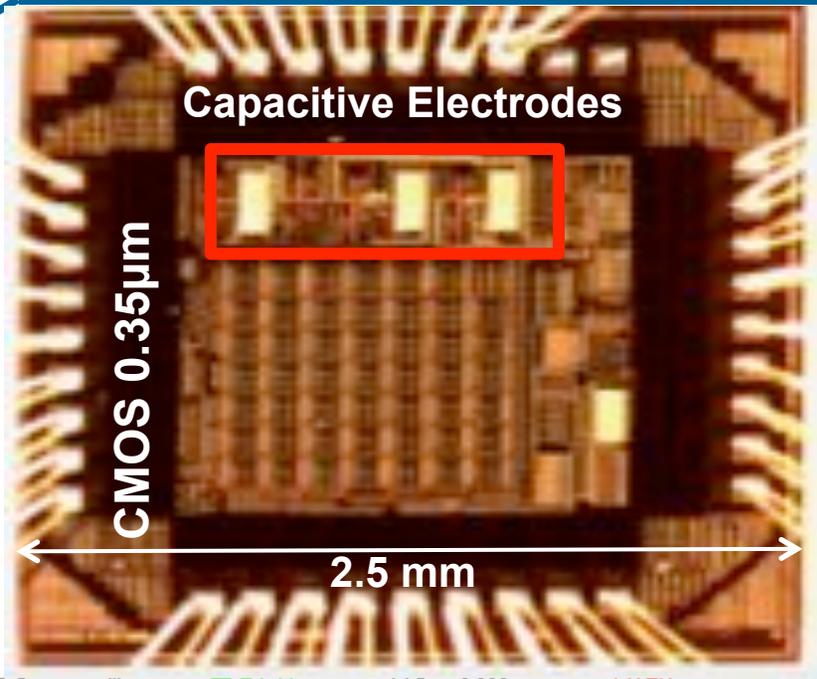


Capacitive Sensor for Lab-on-Chip Applications

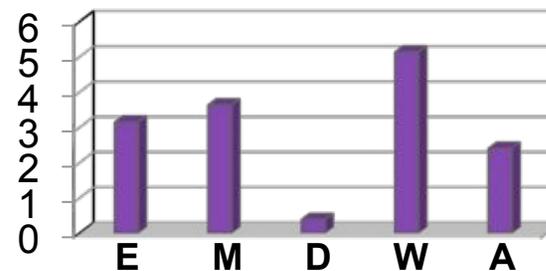
- Differential CBCM circuitry, a dedicated $\Sigma\Delta$ modulator, and an FPGA module used to generate clock pulses and to decode the $\Sigma\Delta$ 1-bit stream



Lab-on-Chip based Devices Measurements

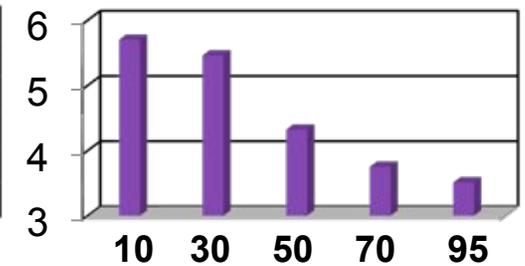


Vout (V)



Organic Solutions

E = Ethanol W = Water
 M = Methanol A = Acetone
 D = Dichlorimethane



Ethanol% in Water

Lab-on-Chip based Devices Measurements (Cont'd)

Comparison

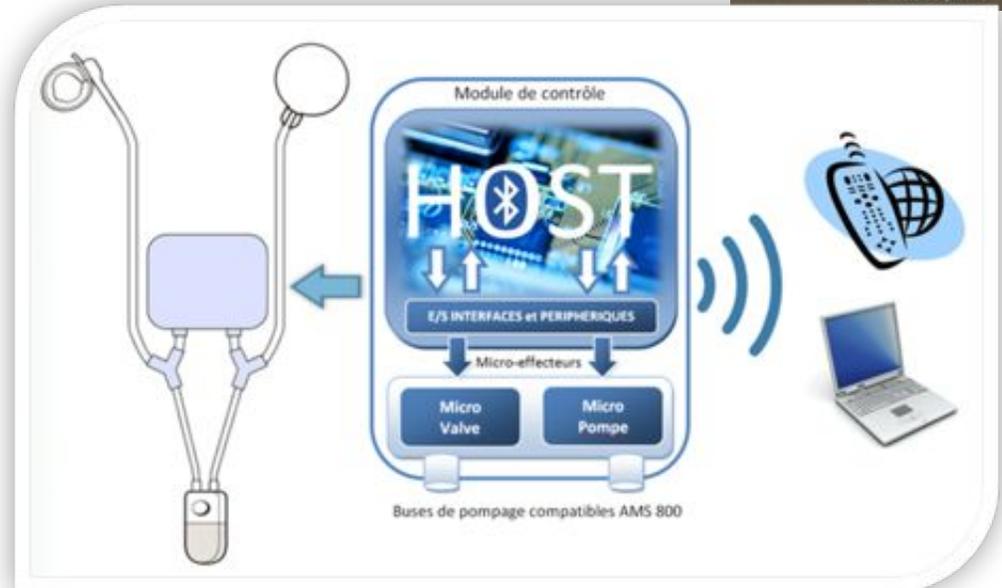
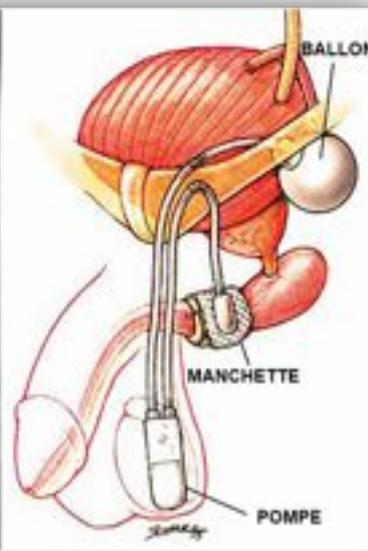
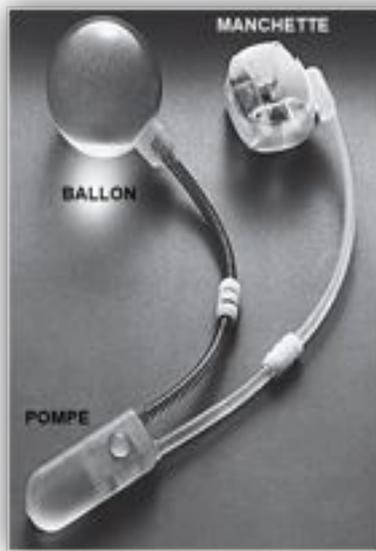
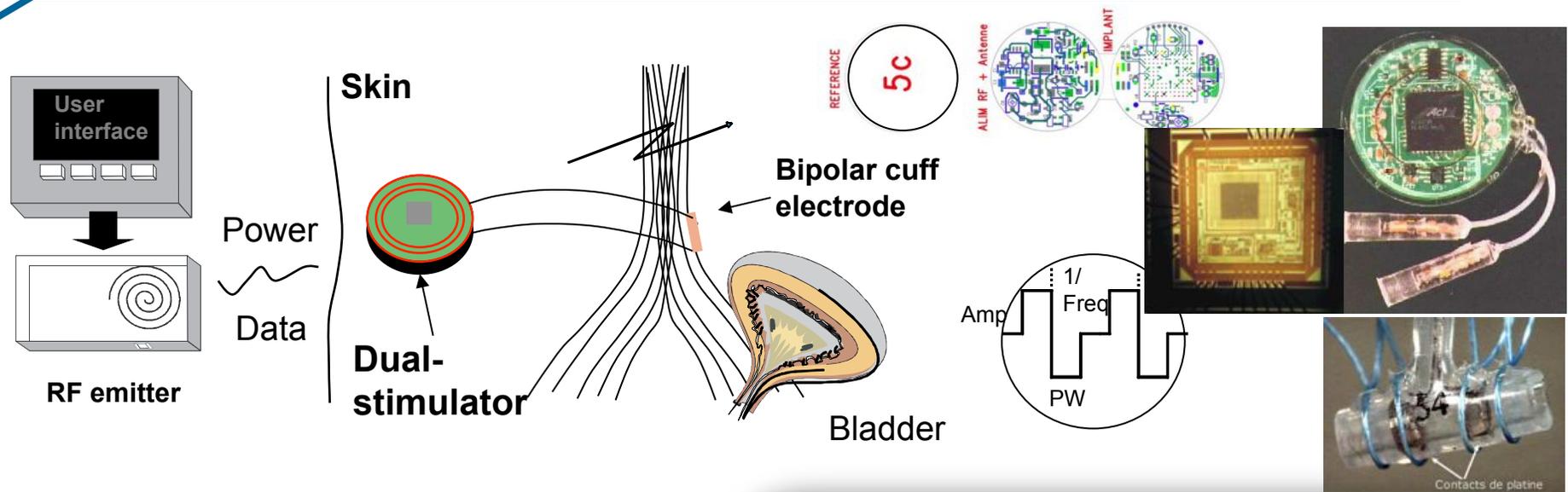
	[1]	[2]	[3]	This work
CMOS Technology	0.18 μ m	0.18 μ m	0.18 μ m	0.35 μ m
Sensitivity (mV/fF)	250	200	42	350
Dynamic range	NA	10fF	NA	10fF
Supply voltage (V)	+1.8	\pm 1.8	+1.8	\pm 3.3
Output voltage	Single	Differential	Single	Differential
Power consumption (μ W)	0.7@10kHz	3×10^{-3} @1kHz	NA	0.3@1kHz

[1] Ghafar-Zadeh and Sawan, "A hybrid microfluidic/CMOS capacitive sensor dedicated to lab-on-chip applications," *IEEE TBioCAS*, 2007.

[2] Prakash and Abshire, "A Fully Differential Rail-to-Rail CMOS Capacitance Sensor With Floating-Gate Trimming for Mismatch Compensation," *IEEE TCAS-I*, 2009

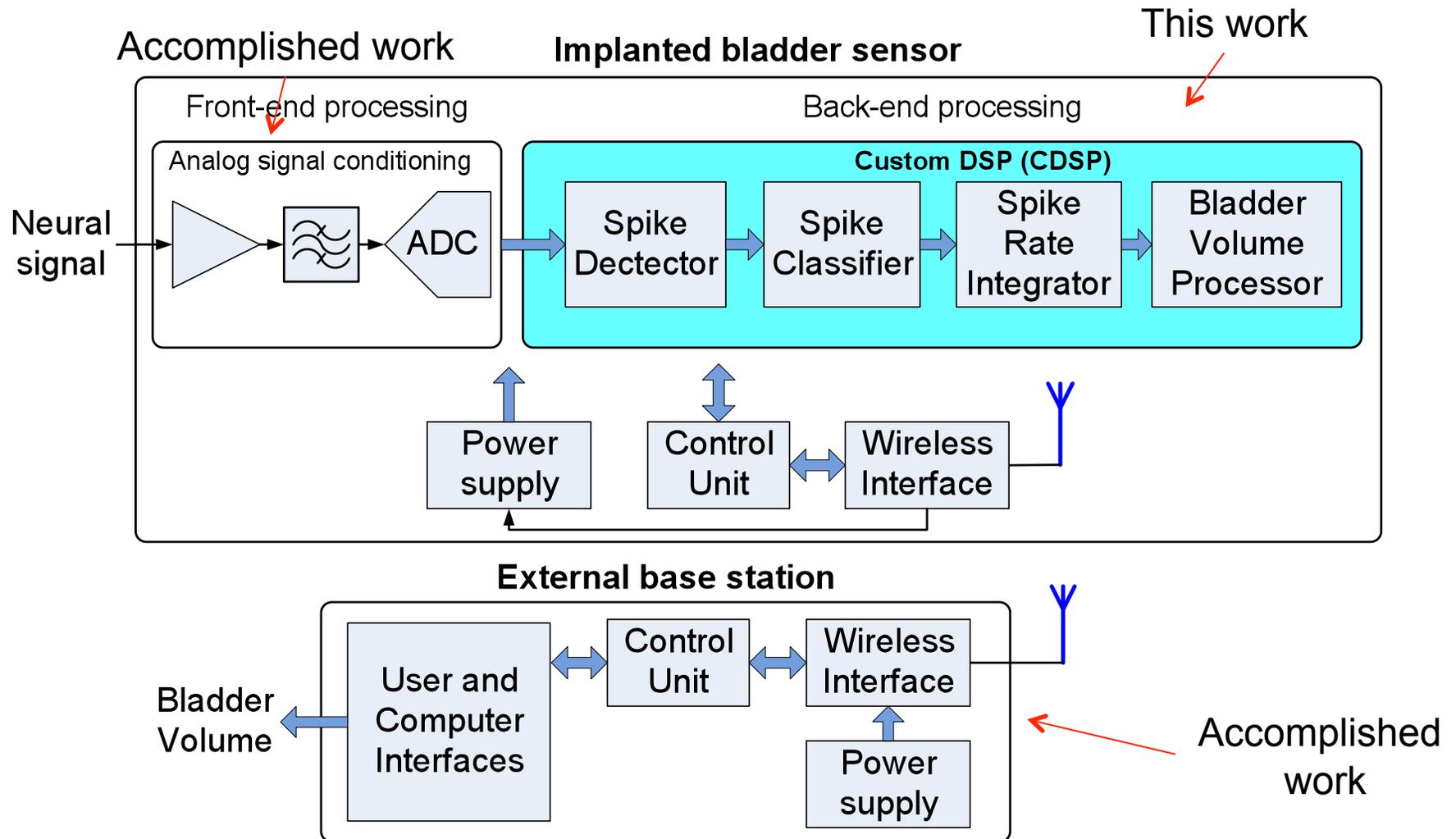
[3] Evans and York, "Microelectronic capacitance transducer for particle detection," *IEEE Sensors* 2004.

Urinary Incontinence and Blockade Control



Sensory feedback for neurostimulation device

Bladder functions restoration

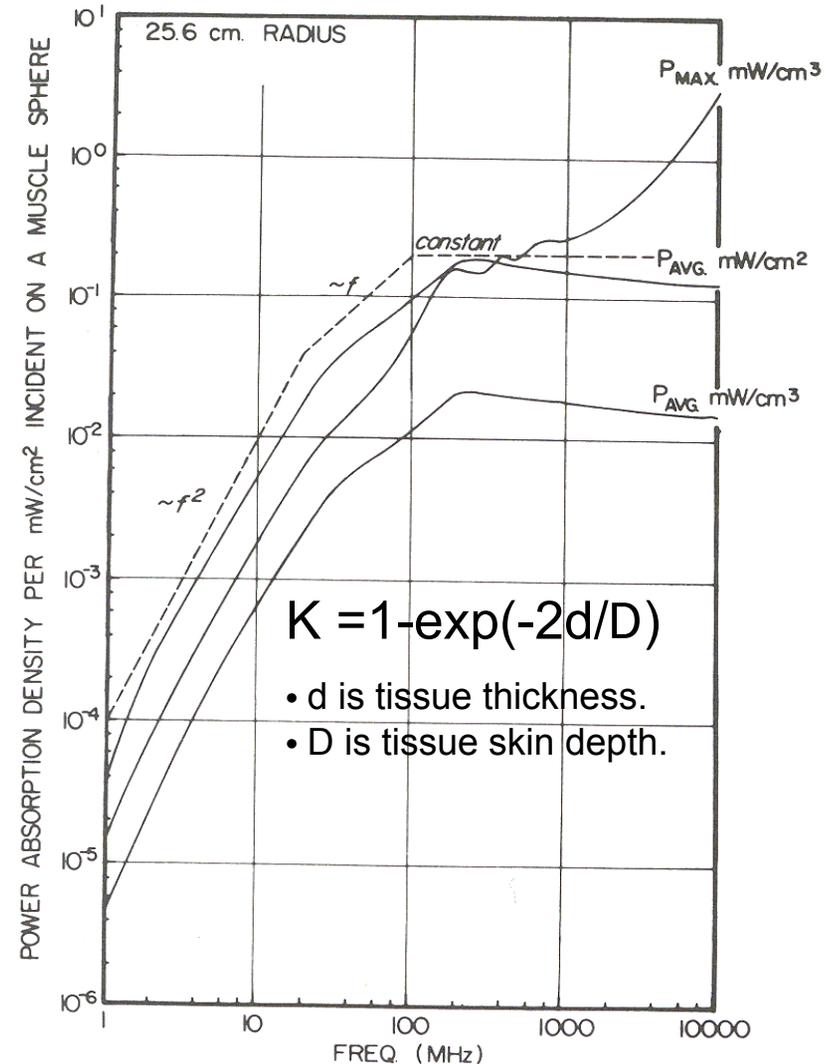
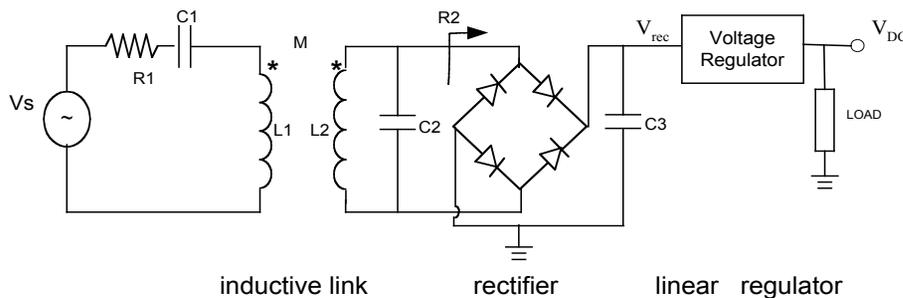


Inductive Powering : Choice of Carrier Frequency

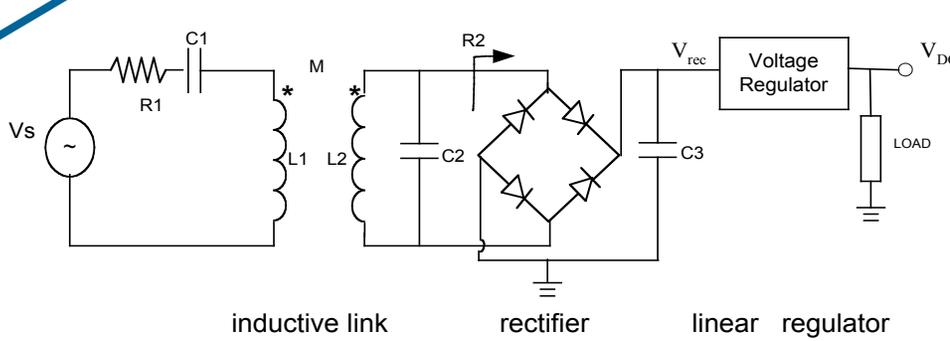
- Limits: Coil self-resonance frequency, and EM energy absorption in tissue (skin, bone, fat, body fluid).
- Power loss increases with frequency
- For $1\text{MHz} < f_c < 20\text{MHz}$, average density of electromagnetic power absorption in tissue increases as f^2
- Carrier Frequency $f_c \sim$ Penetration depth D
- IEEE standard for safety with respect to RF exposure.

Frequency (MHz)	1	4	5.12	10
Maximum Power Density (W/Cm ²)	200	12.5	7.6	2

- The received power depends on the inductive link configuration & distance.



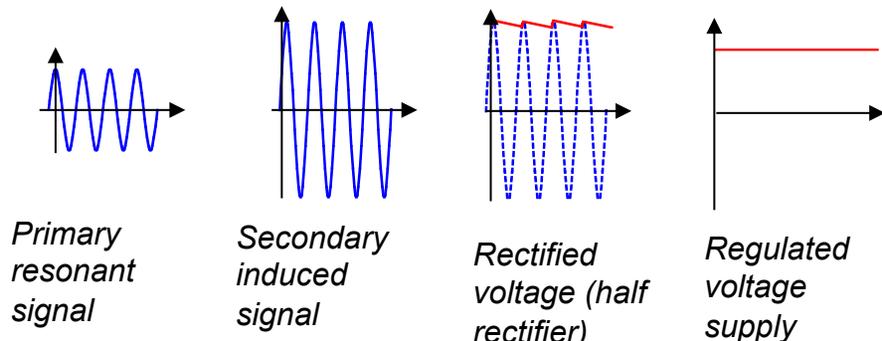
Inductive Powering : Power efficiency



$$\eta_{rfl} = \frac{Z_r}{Z_1} = \frac{k^2 R_2 C_2}{R_1 C_1 + k^2 R_2 C_2}$$

$$\eta_{rectif} = \frac{V_{rect}}{V_{rect} + 2V_{diode}}$$

$$\eta_{reg} \approx \frac{V_{DC}}{V_{rect}}$$



$$\eta_{total} = \frac{\frac{1}{2} k^2 V_{DC}^2 C_2}{R_1 C_1 P_{load} + \frac{1}{2} k^2 C_2 (V_{rect} + 2V_{diode}) \cdot V_{DC}}$$

$$= \frac{\frac{1}{2} k^2 V_{DC}^2}{R_1 P_{load} + \frac{1}{2} k^2 (V_{rect} + 2V_{diode}) \cdot V_{DC}}$$

$$K = \frac{r_{implant}^2 r_{reader}^2}{\sqrt{r_{implant} r_{reader} (\sqrt{x^2 + r_{reader}^2})^3}}$$

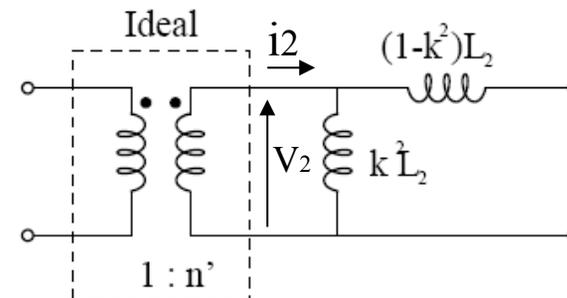
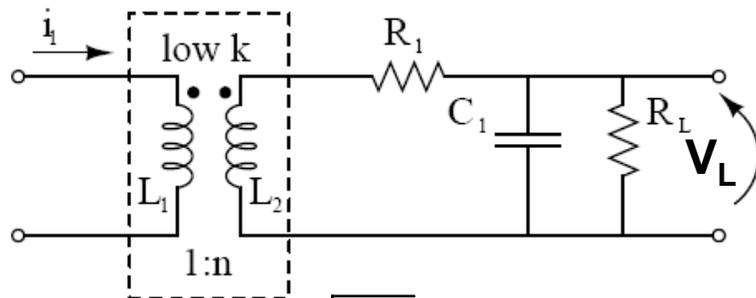
$$V_{rect} = \frac{k \sqrt{C_1 \cdot C_2} R_2}{R_1 C_1 + k^2 R_2 C_2} V_s = \frac{k R_2}{R_1 + k^2 R_2} V_s$$

- $0 < K < 1$; dimensionless; Typical values are 0.01-0.1
- Assume: coils are parallel and center-aligned with only air between them

Inductive Powering : Modeling

Model of the inductive link front-end.

- R_1 = parasitic resistance; C_1 = tuning capacitance; and R_L = system load.
- L_1 and L_2 represent a weakly coupled transformer.



$$n' = k \sqrt{\frac{L_2}{L_1}} \quad i_2 = \frac{i_1}{n'}$$

$$V_2 = j\omega k^2 L_2 \left(\frac{i_1}{n'}\right) = j\omega k \sqrt{L_1 L_2} \cdot i_1$$

$$V_L = \frac{V_2}{1 + (R_1 + j\omega L_2) \cdot \left(\frac{1}{R_L} + j\omega C_1\right)}$$

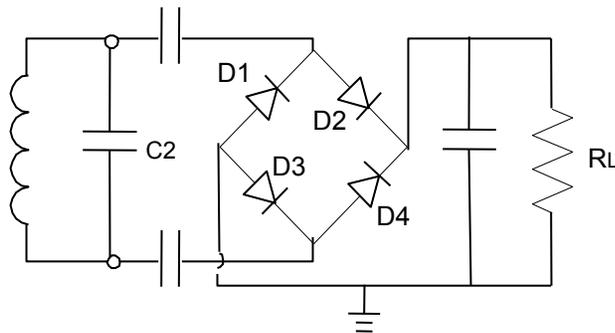
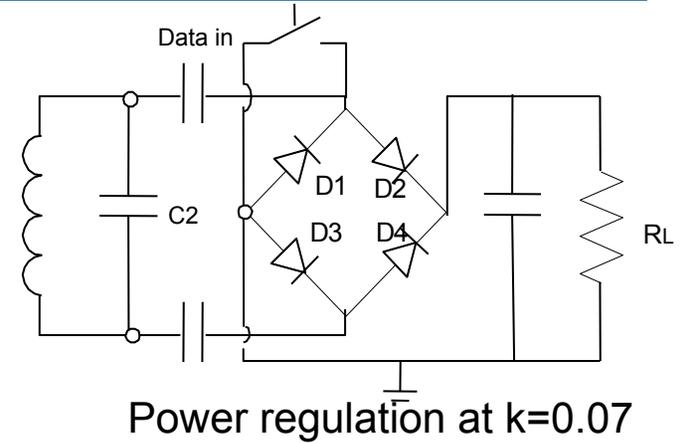
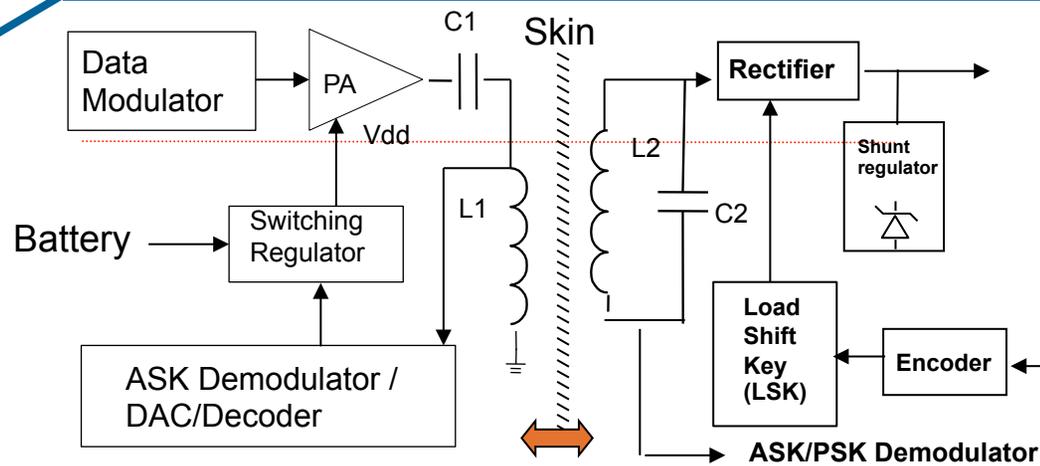
$$V_L = \frac{\omega k \sqrt{L_1 L_2} i_1}{\sqrt{\left(\frac{\omega L_2}{R_L} + \omega R_1 C_1\right)^2 + \left(1 - \omega^2 L_2 C_1 + \frac{R_1}{R_L}\right)^2}} = A k i_1$$

Example

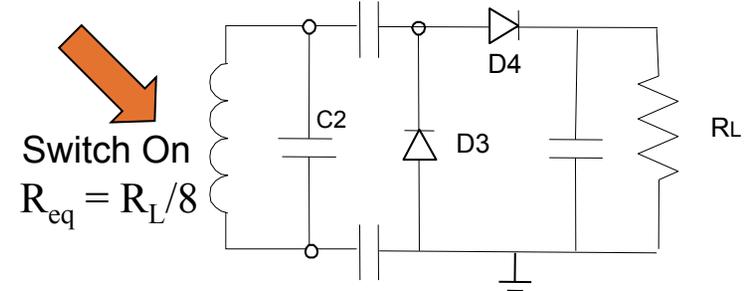
L_1	L_2	C_1	R_1	R_L	f
43.5 μ H	3.7 μ H	330pF	1	1k	4MHz

$$V_L = 1270 \cdot k \cdot i_1$$

Inductive Powering : Calibration, Up link (LSK)

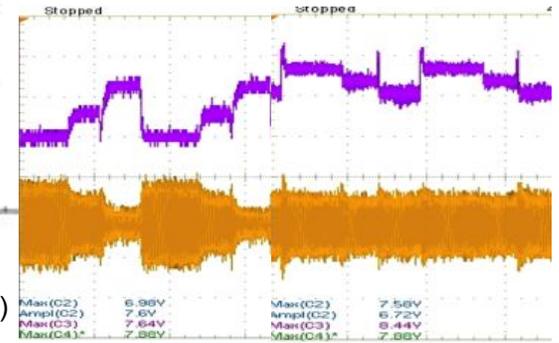
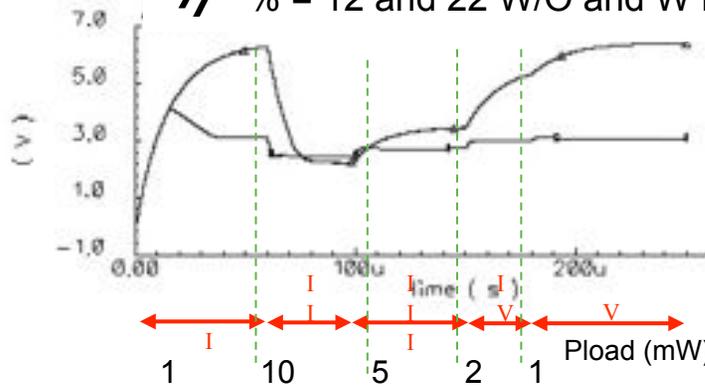
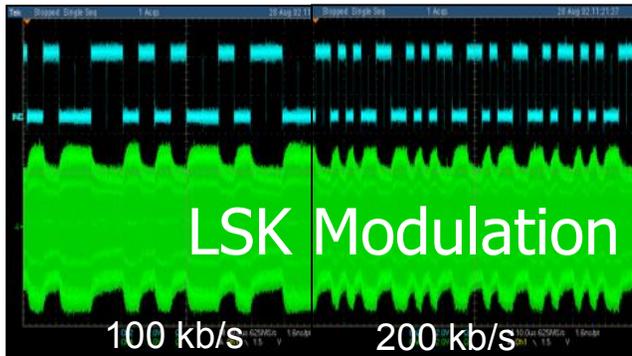


Switch Off
 $R_{eq} = R_L/2$

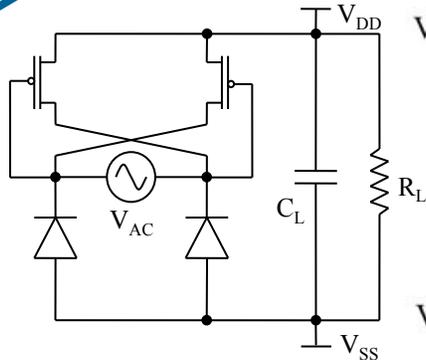


Switch On
 $R_{eq} = R_L/8$

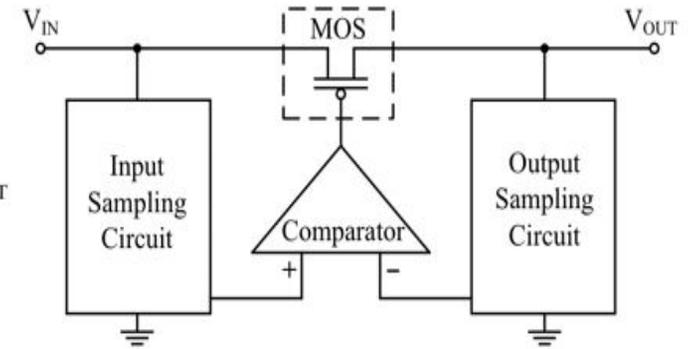
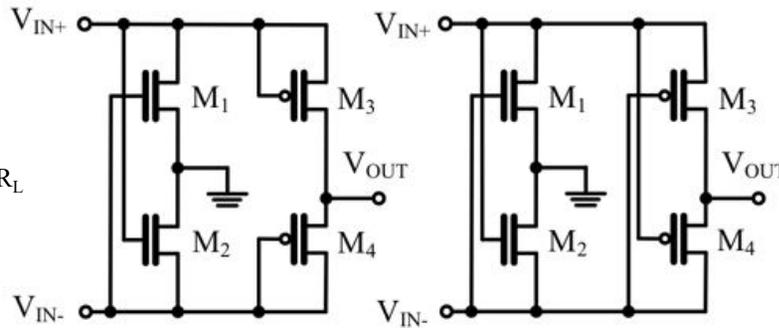
η % = 12 and 22 W/O and W Feedback, respectively



RF Inductive Powering : Conditioning Circuitries

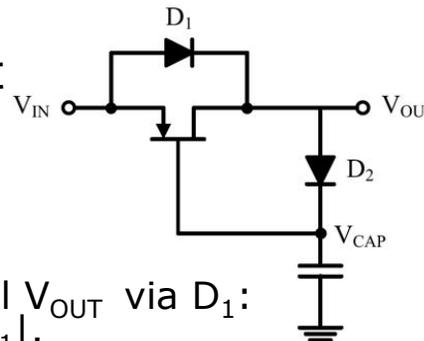


Gates cross & Full-cross coupled



Active Rectifier Typical Topology

Bootstrapping Circuit



Operation:

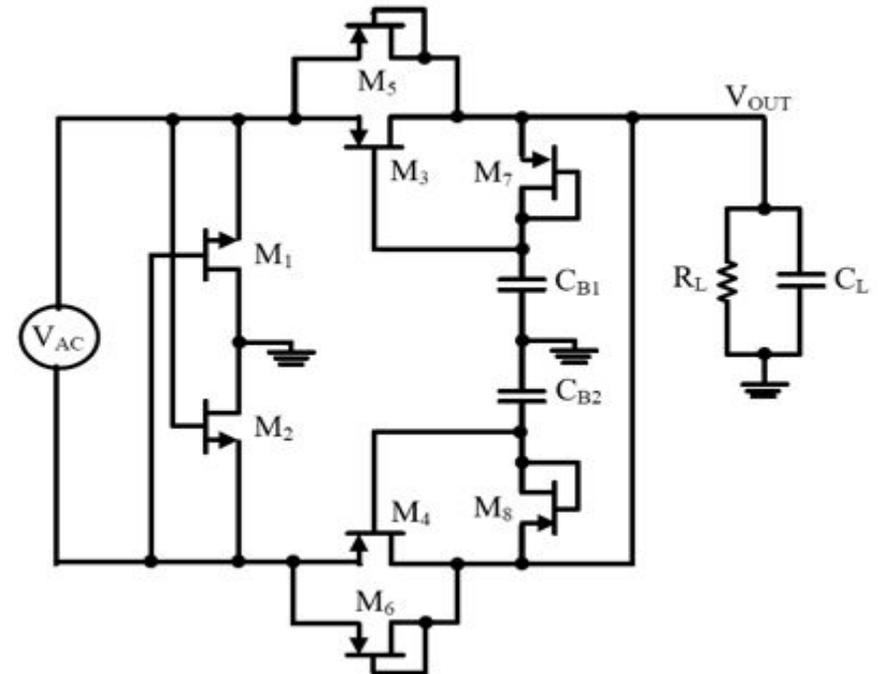
Normal Mode:

- Establish initial V_{OUT} via D_1 :
 $V_{OUT} = V_{IN} - |V_{TH1}|$.
- Charging reservoir via D_2 :
 $V_{CAP} = V_{OUT} - |V_{TH2}|$.

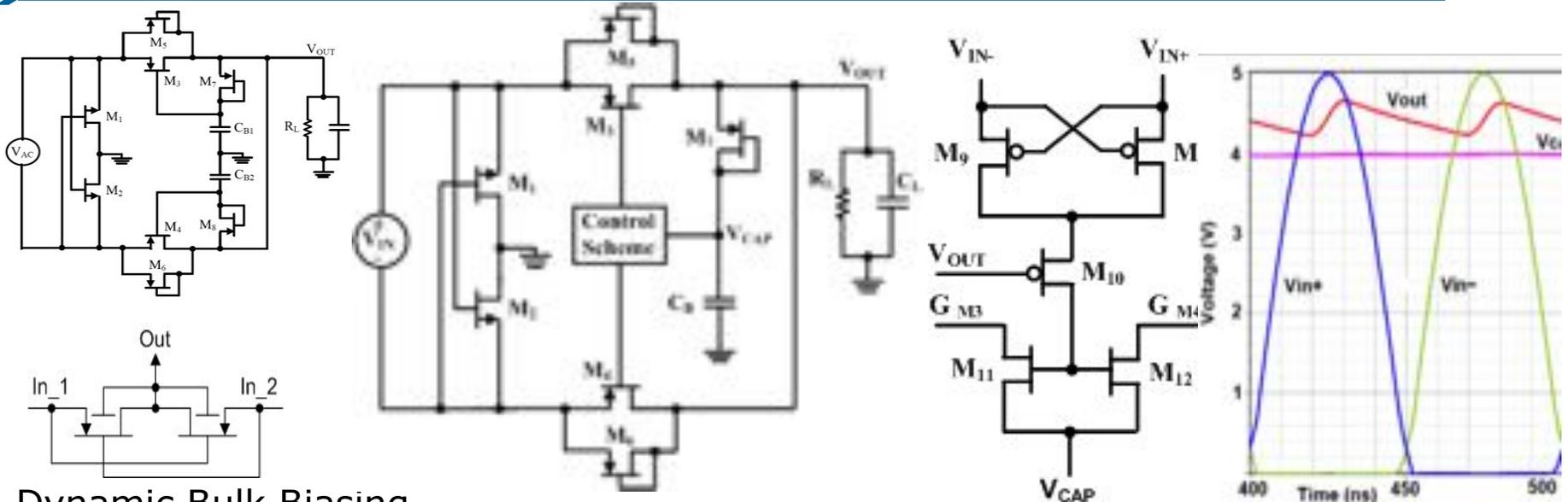
Bootstrap Mode: V_{CAP} to pMOS.

$$V_{OUT} = V_{IN} - (|V_{TH1}| - |V_{TH2}|)$$

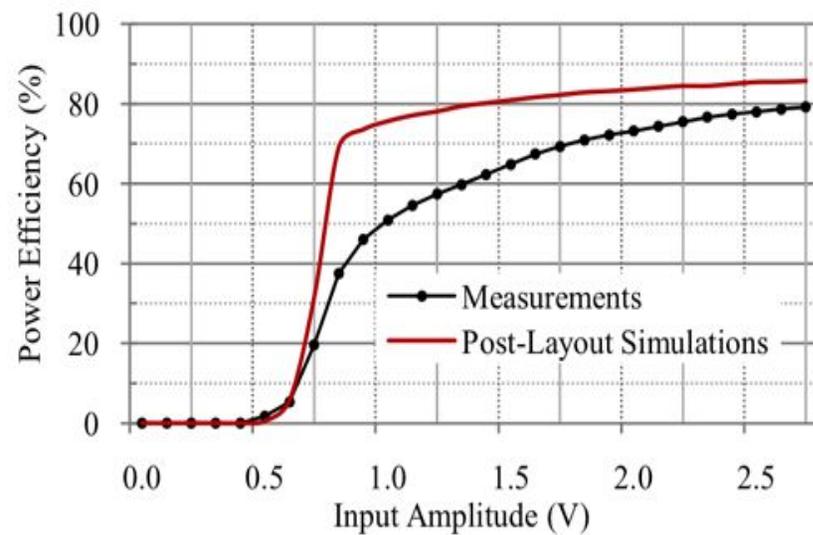
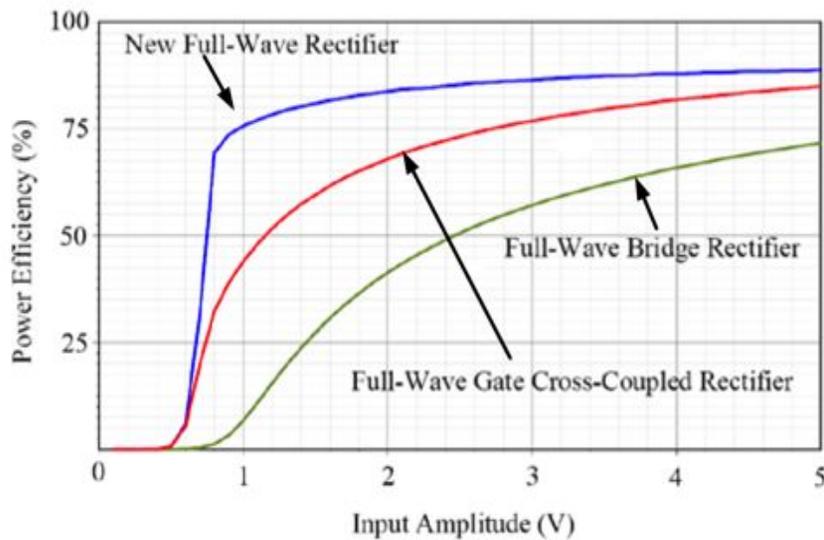
❖ **Effective V_{TH} of circuit is reduced !**



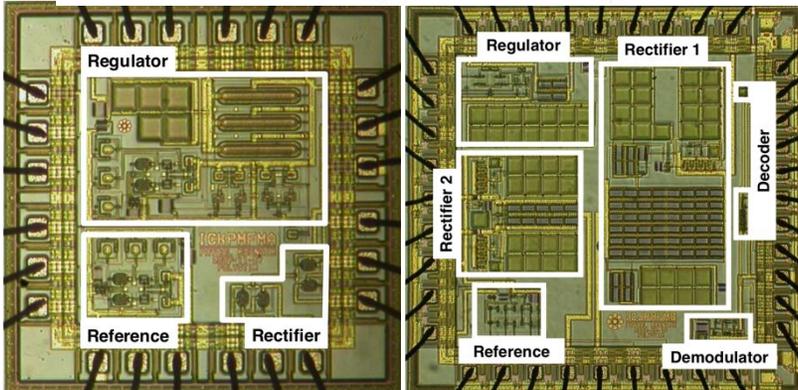
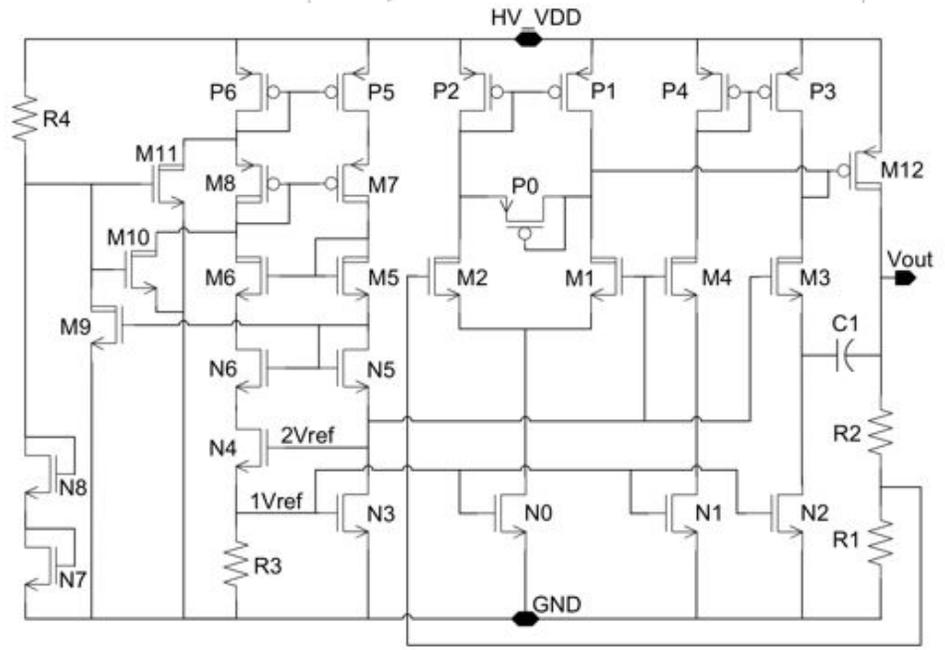
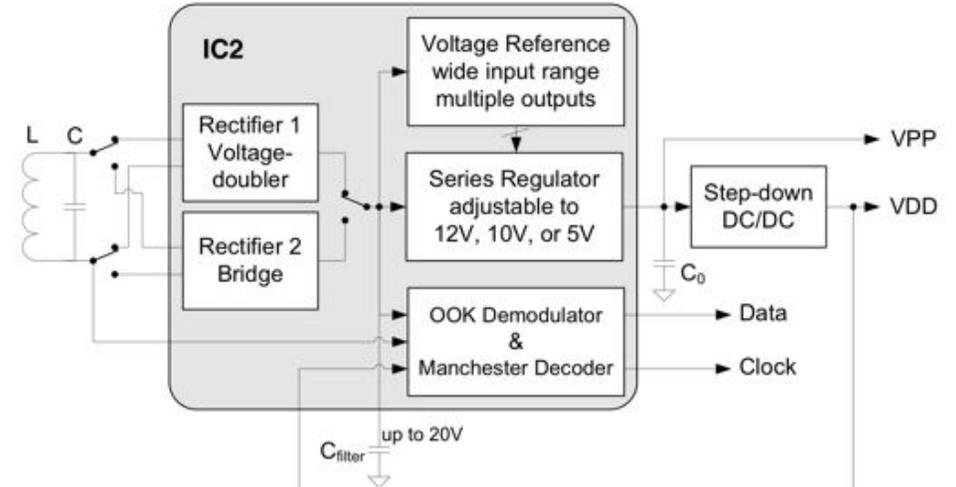
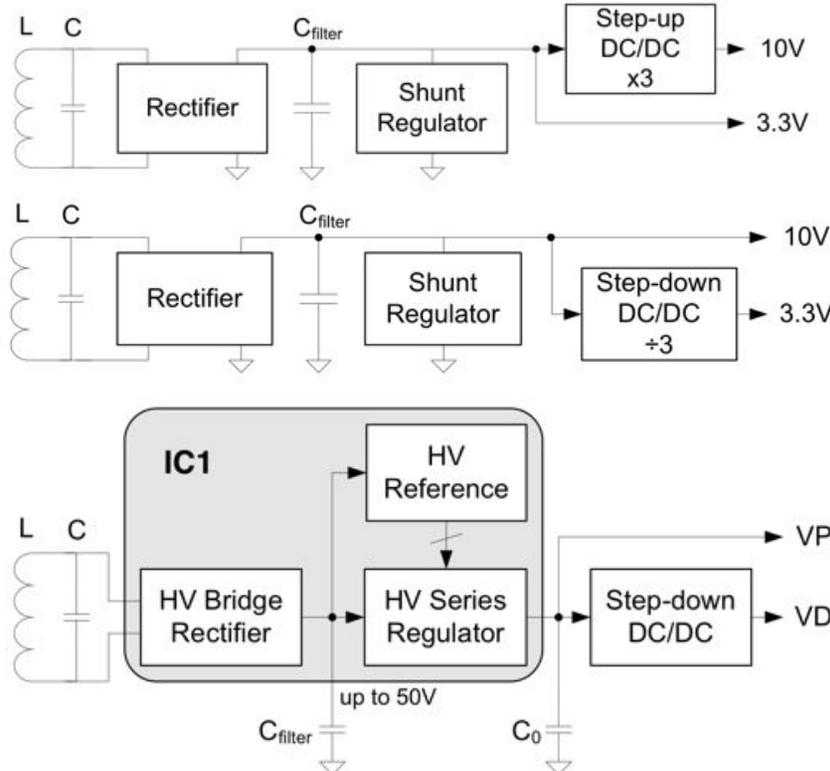
Inductive link : Rectifiers



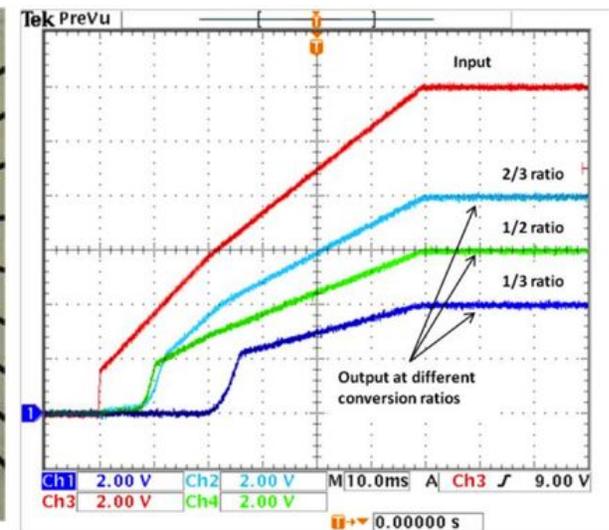
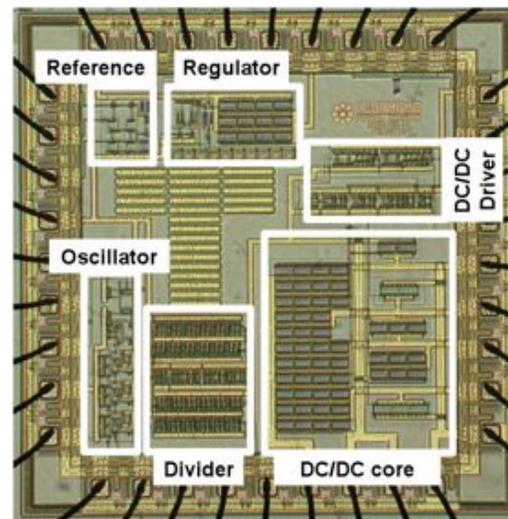
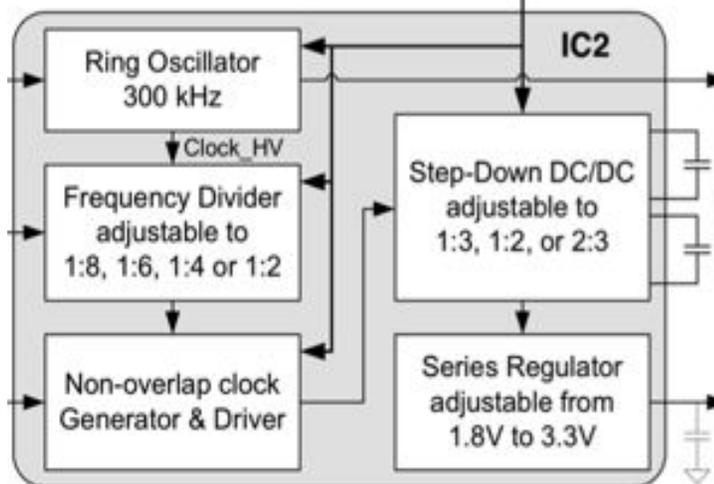
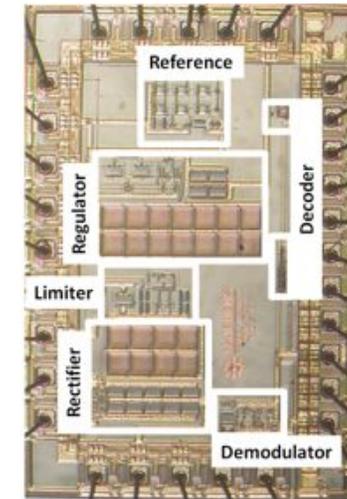
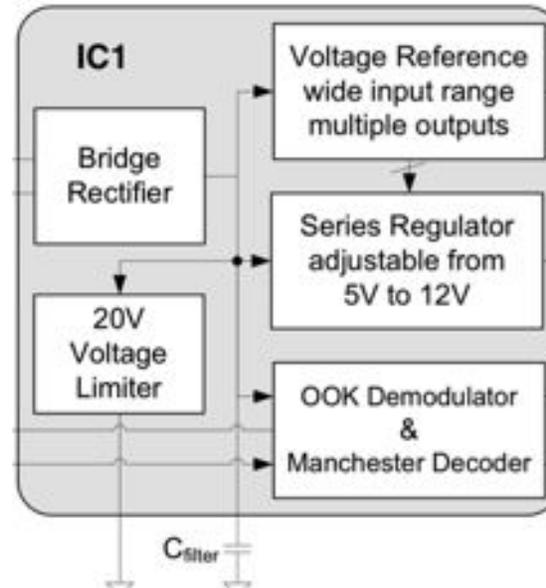
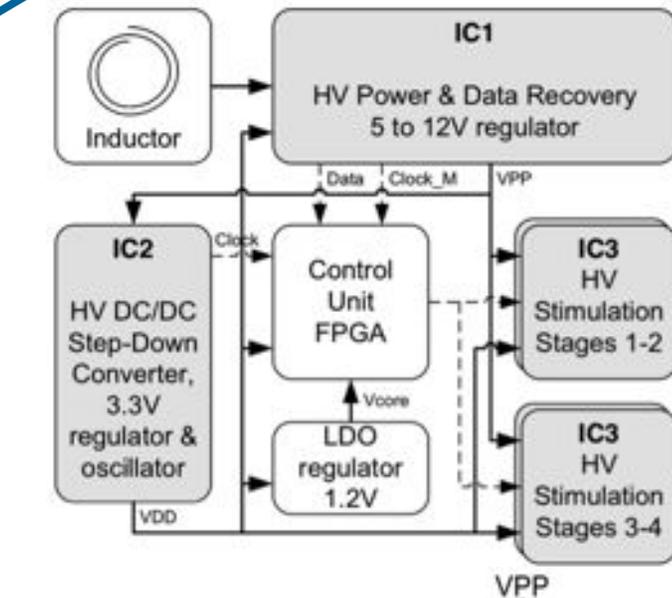
■ Dynamic Bulk Biasing



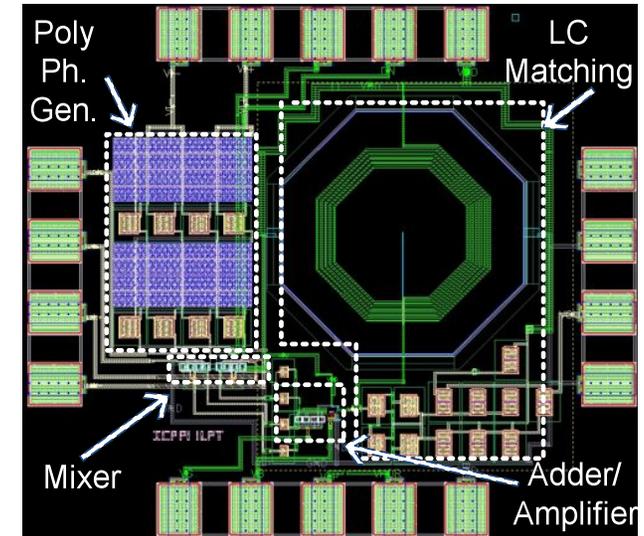
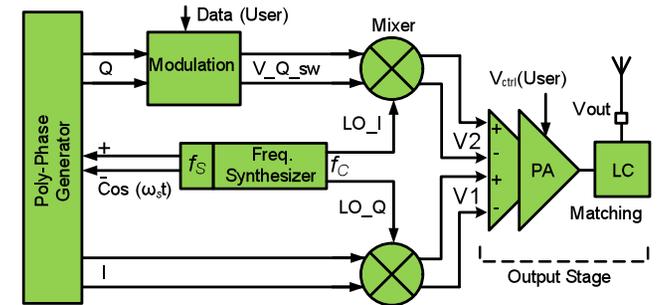
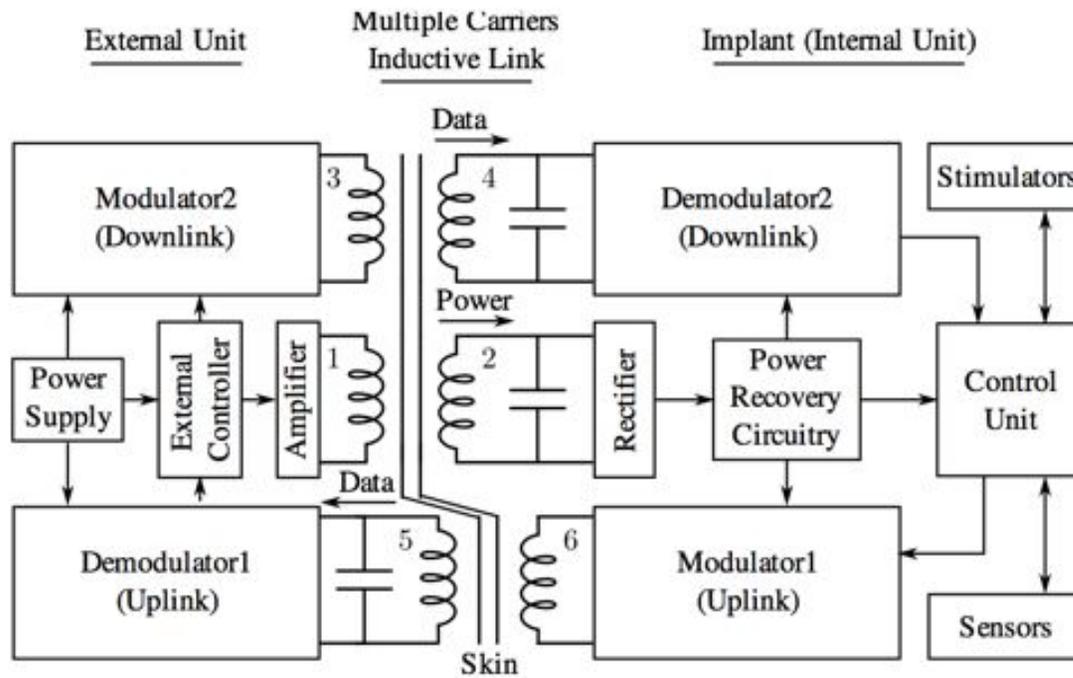
Inductive link : HV Rectifier, DC/DC Converter, Regulator



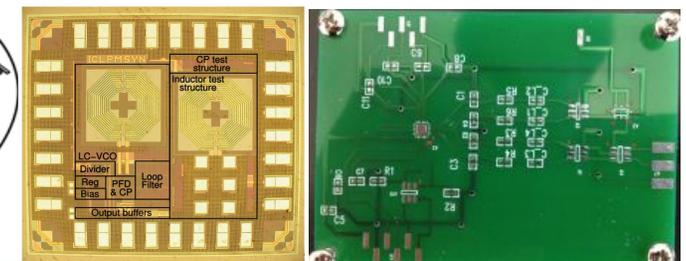
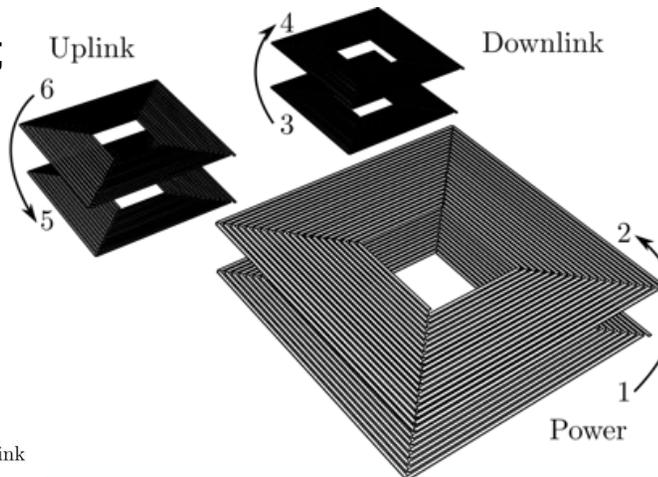
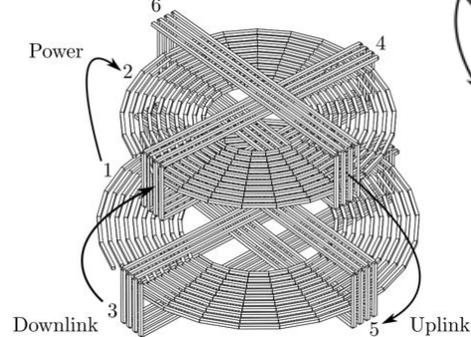
Inductive link : High-voltage series regulator



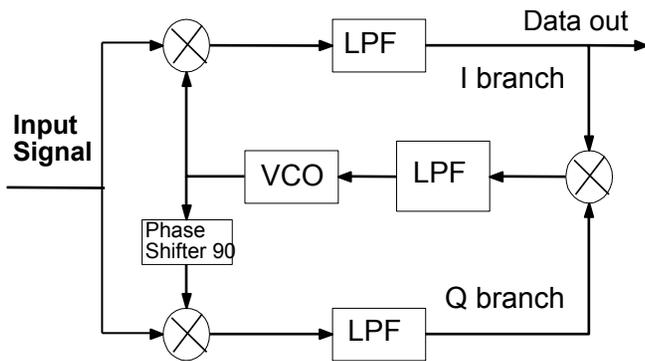
Inductive power and data links : Higher performance



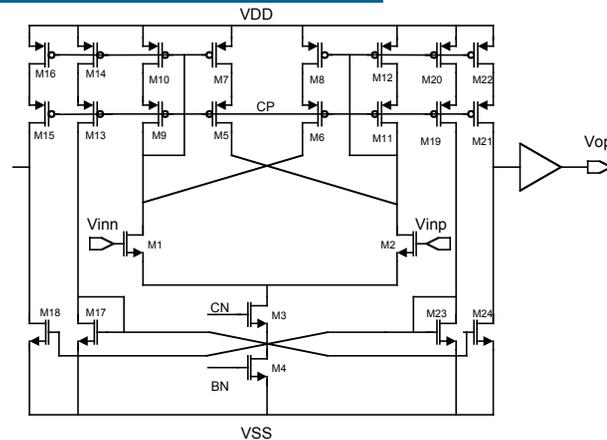
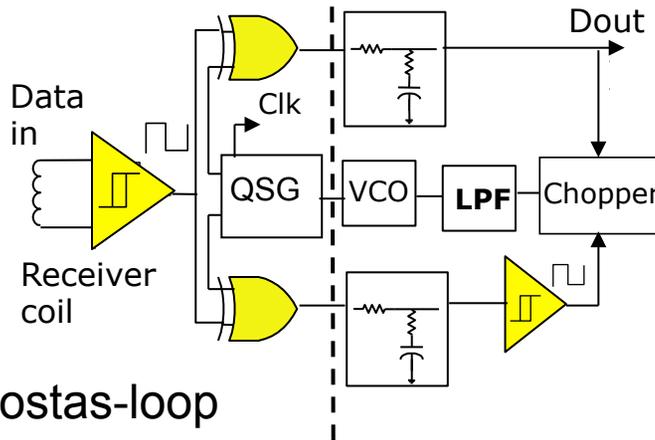
Power link = 1 MHz;
 Downlink = 13.65 MHz;
 Uplink = 6.5 MHz



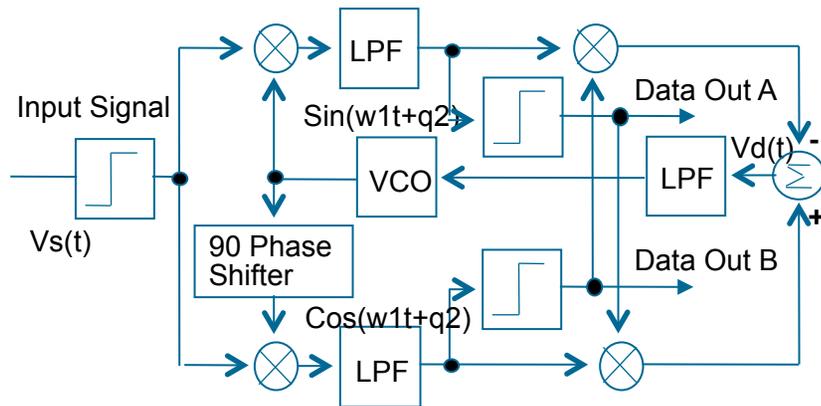
Inductive Data Links : Integrated BPSK/QPSK



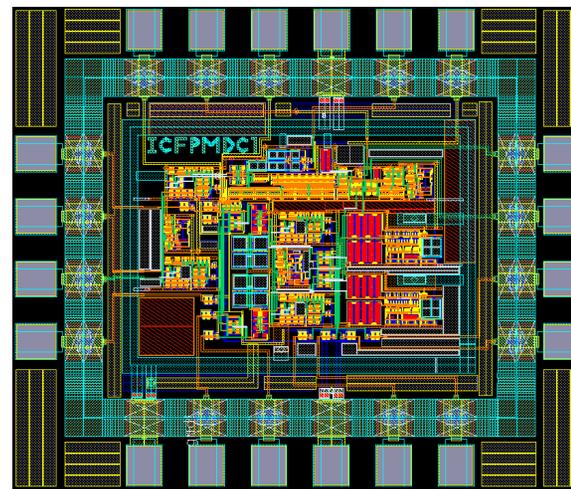
BPSK Costas-loop



Differential comparator



QPSK Demodulator



*Postlayout; **Measured

BPSK	QPSK
CMOS 0.18µm	CMOS 0.18µm
13.56 MHz	13.56 MHz
1.6* Mbps* 1.2* Mbps**	>10* Mbps 8.0** Mbps
0.61 mW**	~1.0 mW**

Neurotechnologies Lab & Research Center

- ◆ Founded in 1994 : ~98 Masters & 27 PhD's completed degrees
- ◆ Currently supervised personal
 - ★ 8 Master and 15 Ph.D. Candidates
 - ★ 1 Postdoc Fellow & 1 Research associate
 - ★ One Technician
- ◆ Collaborators from several Applied Sciences & Medical Institutes
- ◆ Support (\$): NSERC, CIHR, FRQNT, CRC & CFI, and CMC μ systems
- ◆ Partners: Victhom, Clarovita, Telemedic, DALSA, Kyvox, Hardent,



- ◆ ~60 Professors (5 IEEE Fellows)
- ◆ ~400 Grad students
- ◆ 10 Universities are supporting the Center
- ◆ ReSMiQ Innovation Day (RID), Scholarships, etc....



Invitation to ISCAS 2016 in Montreal



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MONTREAL?



 **ISCAS 2016**
MONTREAL **CANADA**

We look forward to seeing you in Montreal for
IEEE ISCAS2016 on May 23-25, 2016 at the Sheraton Hotel.

 **RESMIQ**
Regroupement Stratégique
en Microsystèmes du Québec

Summary

BMBI for Neurosensing and Treatment

- ☑ Wearable Multi-Modal Clinical Imaging
- ☑ Massively-parallel Intracortical Recording
- ☑ Multi-channel Intracortical Neurostimulation
- ☑ LoC-Based Neurotransmitter Detection
- ☑ Inductive-links Calibration to Maximize Efficiency
- ☑ Integration-on-Chip of RF Front-end to Recover Needed Energy.

Design Challenges are Multidimensional

- ☐ System-on-Chip, Data Compression, ..
- ☐ Harvesting & Scavenging Energy : ~ 25 mW
- ☐ Microwatts Wireless : WuRx
- ☐ Fast Data Transmission : ~ 50 Mb/s
- ☐ Tests: Collaborations, Bioprotocoles
- ☐ Systems Must be Safe, not to Generate Undesired Actions.

Acknowledgment

<http://www.polystim.ca>



- ◆ National Sciences and Engineering Research Council of Canada (**NSERC**)
- ◆ Canadian Institutes of Health Research (**CIHR**)
- ◆ Canada Research Chair on Smart Medical Devices (**CRC**)
- ◆ Quebec Research Funds : Nature and technologies (**FRQNT**)
- ◆ **ReSMiQ**, and **CMC** Microsystems
- ◆ **Collaborators** from Engineering and Medical Schools in Montreal.
- ◆ Interns, Master and PhD **Students**
- ◆ Postdoc **Fellows**, **Research Associates** and Invited **Professors**.



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Bem-vindo à
**UNIVERSIDADE FEDERAL
DE SANTA CATARINA**



**Obrigado
por sua
participação**