Brain-Machine-Brain Interfaces for Massively Parallel Neurorecording and Microstimulation

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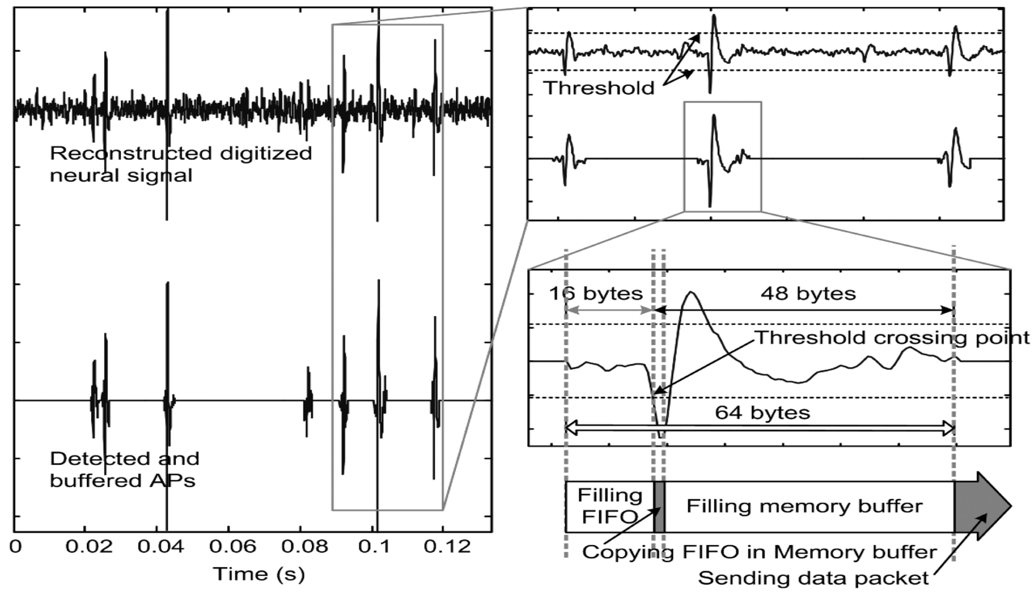
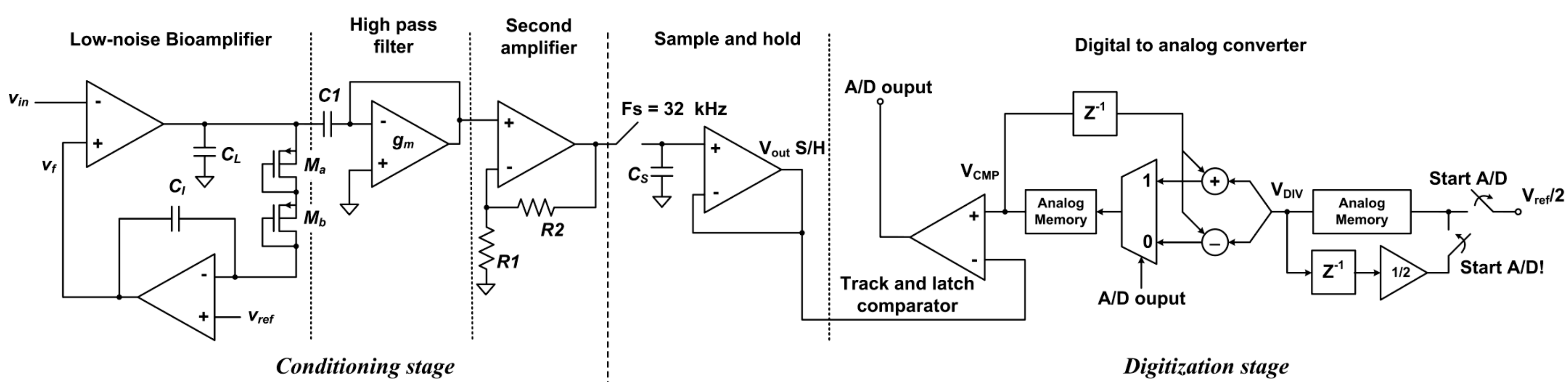
Outline

- **Motivation**
  - Brain-Machine-Brain Interfaces
  - Implantable Neuroprostheses
- **Multichannel Neurorecording**
  - Acquisition, and Compression
  - Spike Detection : Analog/Digital Techniques
  - Thresholding : Conventional, and Adaptive
  - Energy Delivery, and Data Transmission
  - Electrodes, Integration, Assembly and Validation
  - Prototyping and Case Studies
- **Laboratory-on-Chip based Sensors**
  - Neurotransmitters manipulation and characterization
- **Resources/Summary**

Massively Parallel Neurorecording : Mixed-Signal Blocks

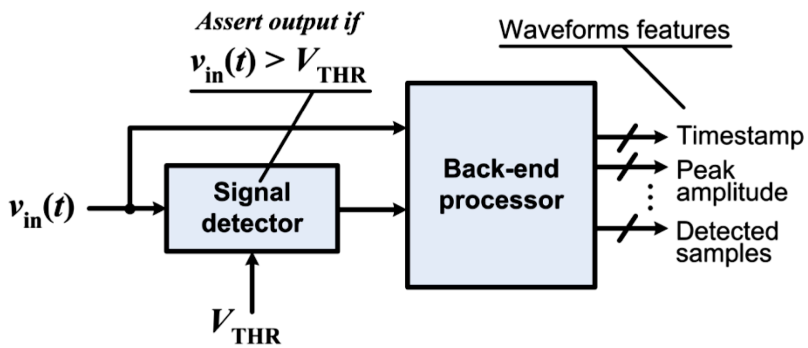


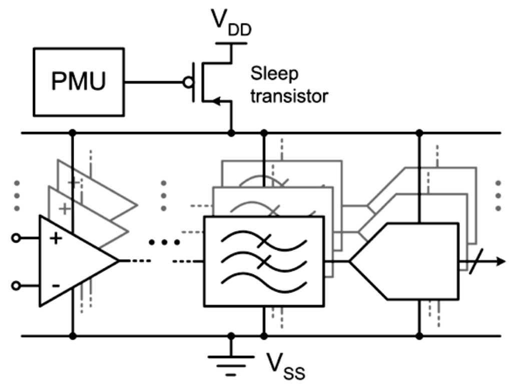


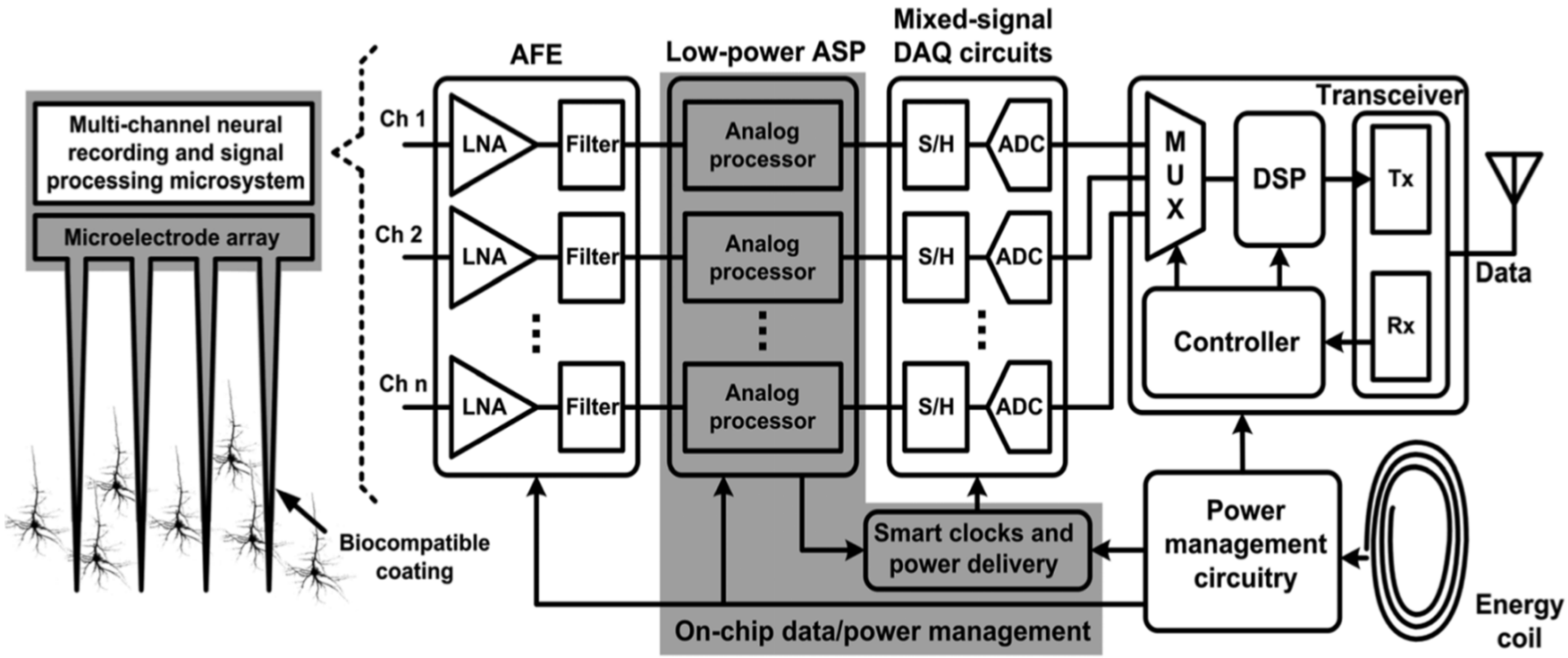
- Input-ref. noise: 5.6 uVrms, Power consumption: 9 uW

Gosselin, Sawan, An Ultra Low-Power CMOS Automatic Action Potential Detector", ***IEEE-TNSRE,*** 2009.

Massively Parallel Neurorecording : Analog Processor



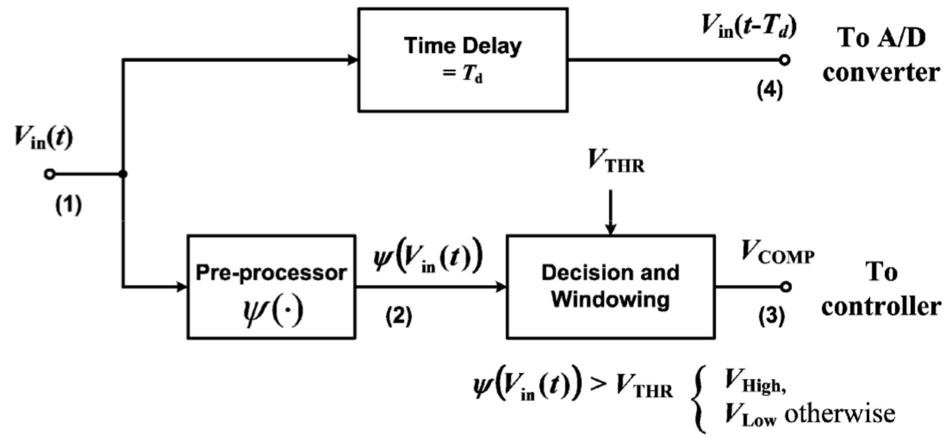


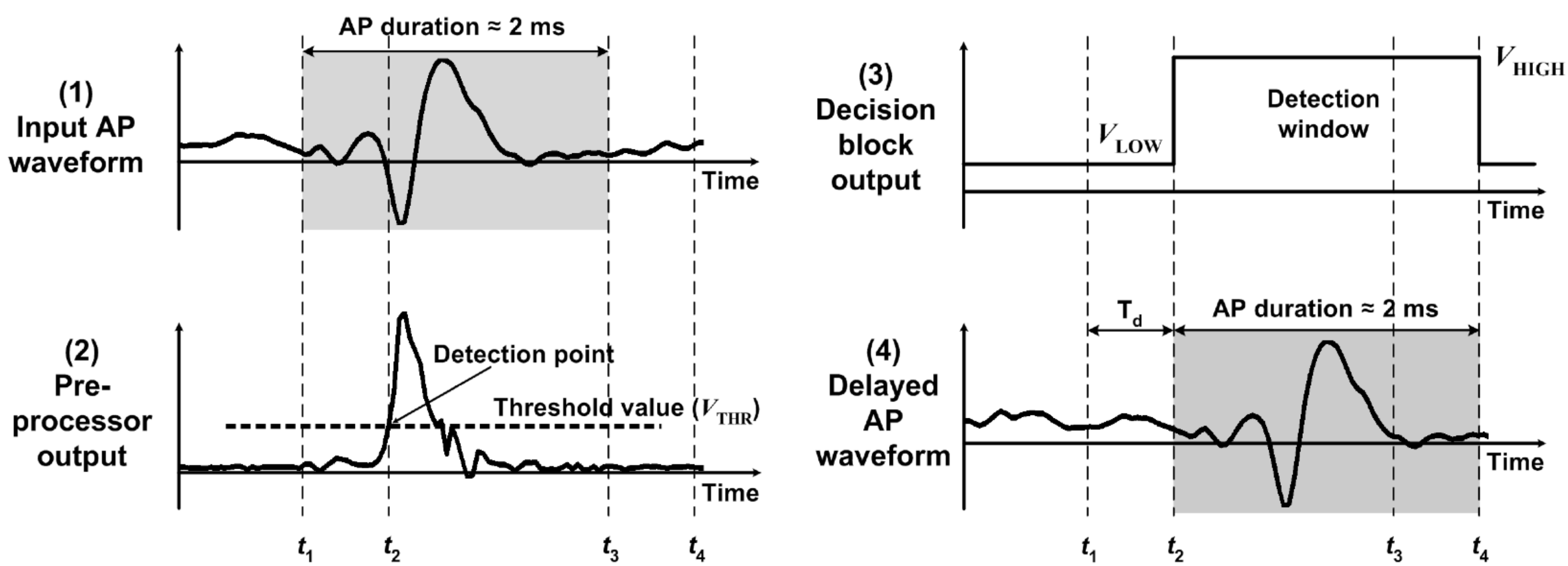


Gosselin, Sawan, An Ultra Low-Power CMOS Automatic Action Potential Detector", ***IEEE-TNSRE,*** 2009.

Analog Biopotential Detector

- Sub-microwatt biopotential detector based on a custom analog processor
- Enhances biopotentials for detectability and captures complete waveforms
- Less overhead than a digital: no A/D conv. & no dig. noise.

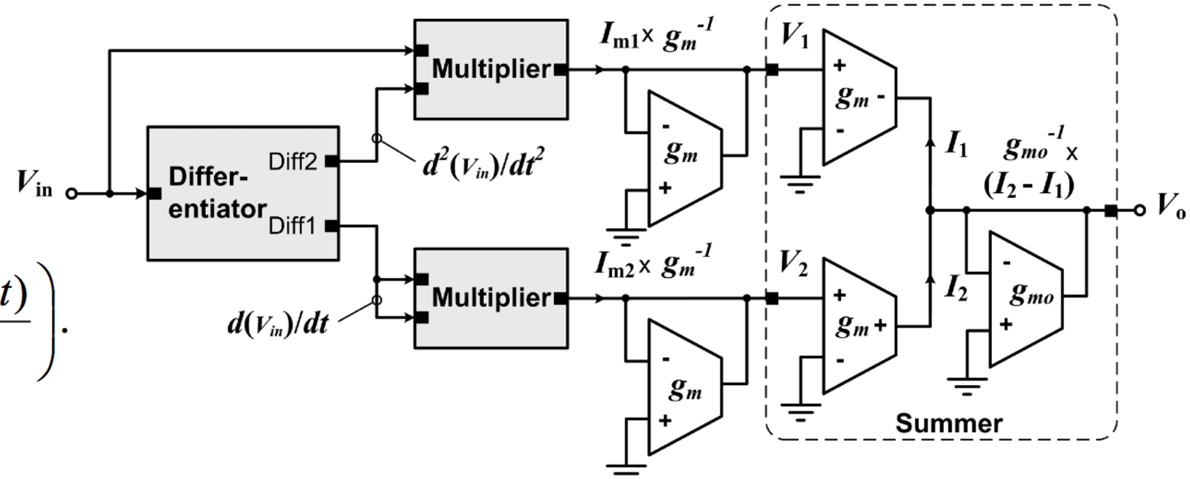


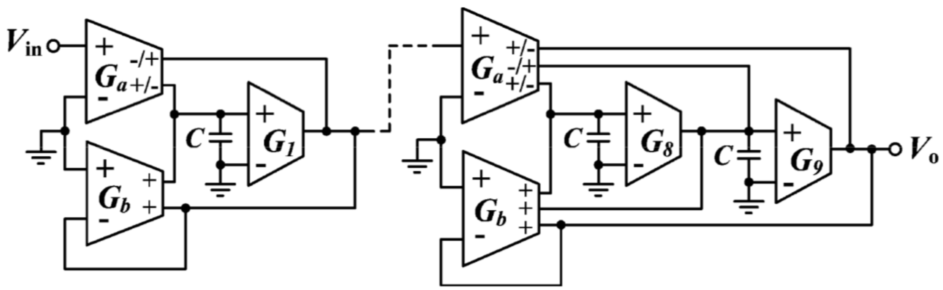


Analog Biopotential Detection: Circuit Implementation

Gm-C based Analog pre-processor. The Teager energy operator (TEO):

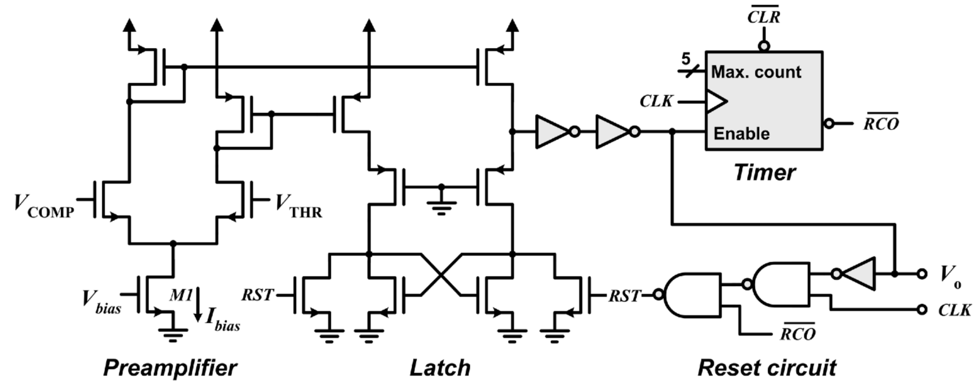
$$\psi\big(x(t)\big)=\left(\frac{dx(t)}{dt}\right)^2 - x(t)\left(\frac{d^2x(t)}{dt^2}\right).$$





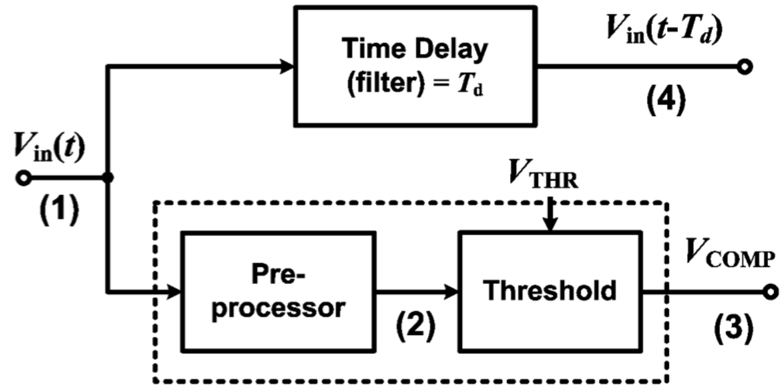
Delay element: 9th-order allpass delay filter

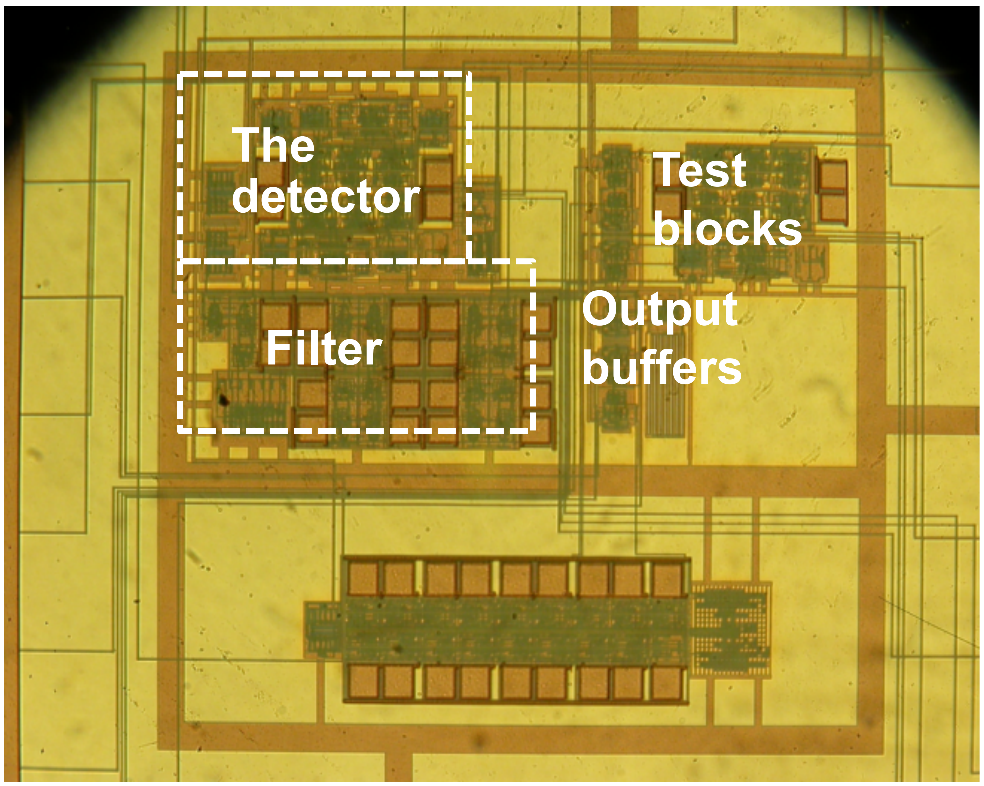
Decision block : Latched-comparator

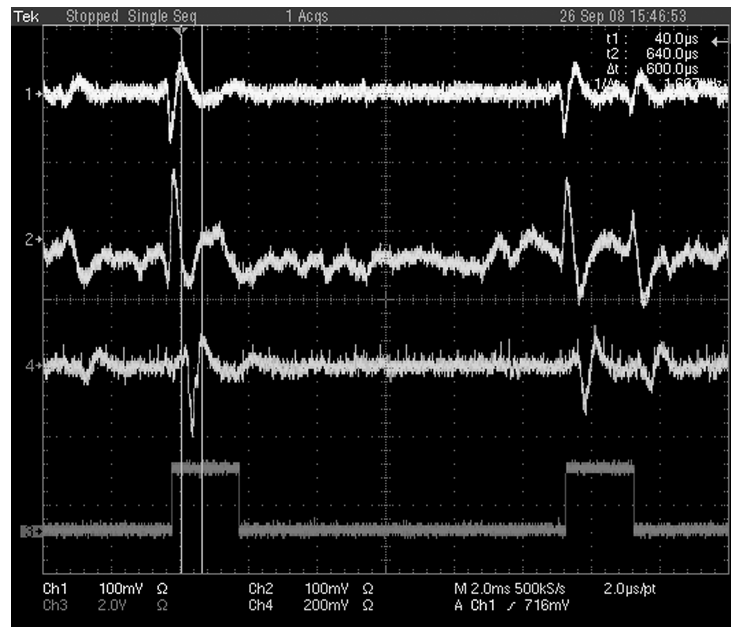


Experimental Results : Analog Biopotential Detection

- Implemented in a CMOS 0.18-μm, it measures **272x257 μm²**.
- Detector + delay filter: ultra-low-power dissipation of **780 nW**: validated with synthetic neural waveforms







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Statistical SP (Cont'd) : Adaptive Spike Detection

- Neural signals are not stationary, and simultaneous recording is required: Setting the detection threshold adaptively and automatically is crucial.
- Various spike detectors have been developed (Matching filter, optimal filter, wavelets, etc.)
- The TEO is a powerful tool : it requires no prior knowledge about spike shapes, and present a good trade-off between the probability of detection (P_D) and the probability of false alarm (P_{FA}).
- The definition of the discrete-time TEO is given by:

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

- $E\{\psi[.]\}$ can serve as an indicator to detect the presence of spikes, where $E\{.\}$ is the expectation operator.
- To estimate $E\{\psi[.]\}$ the smoothed-TEO (STEO) $\psi_s[x(n)]$ is introduced as

$$\psi_s[x(n)] = w(n) * \psi[x(n)] \qquad \psi_s[x(n)] = \sum_{k=0}^{L-1} w(k)\psi[x(n-k)]$$

$\psi_s[x(n)]$ is the test statistic

Statistical SP (Cont'd) : Adaptive Spike Detection

- This detection can be formulated as a binary hypothesis testing:

$$H_0 : x(n) = b(n) \qquad n = 0, 1, 2, \ldots$$
$$H_1 : x(n) = s(n) + b(n) \qquad n = 0, 1, 2, \ldots$$

where H_0 and H_1 are the null and alternative hypotheses.

- A spike is present if $\psi_s[x(n)] > T$; otherwise the signal is only noise.
- To set T of $\psi_s[x(n)]$, the probability density function (pdf) under the null hypothesis H_0 has to be known *a priori*
- As the TEO is a nonlinear operator, the pdf cannot be evaluated in a closed-form. Then a direct parametric approach is introduced, where only noise is present at the input and a multiplier p depends on P_{FA}

$T = \mu + p\sigma$; μ and σ are statistical moments

- Setting T this way assumes that no spike is present, so the estimation of μ and σ can therefore be unbiased by the presence of spikes

Statistical SP (Cont'd) : Adaptive Spike Detection

- In statistics, spikes are considered in this case as outliers. So, robust statistic methods are used to estimate μ and σ
- Determination of μ of $\psi_s[x(n)]$

$$\mu_{\psi_s} = E\{\psi_s[x(n)]\} = E\{\sum_{k=0}^{L-1} w(k)\psi[x(n-k)]\} = \sum_{k=0}^{L-1} w(k)E\{\psi[x(n-k)]\}$$

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

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

$$\sigma^2_{\psi_s} = var\{\psi_s[x(n)]\} = E\{\psi_s^2[x(n)]\} - E^2\{\psi_s[x(n)]\} = E\{\psi_s^2[x(n)]\} - \mu^2_{\psi_s}$$

$$\sigma^2_{\psi_s} \approx 4.8r^2_{xx}(0) + 0.7r^2_{xx}(1) + 4.4r^2_{xx}(2) + 0.6r^2_{xx}(3) - 9.3r_{xx}(0)r_{xx}(2) - 1.2r_{xx}(1)r_{xx}(3)$$

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

- Both $\mu_{\psi s}$ and $\sigma_{\psi s}$ depend on the autocorrelation function of the neural signal $x(n)$
- Autocorrelation function is sensitive to additive outliers (spikes) in the signal
- Noise only cannot be separated from spikes, the use of an autocorrelation estimator, robust to the presence of additive outliers in $x(n)$, is crucial.

Semmaoui et al, Setting Adaptive Spike Detection Threshold for Smoothed-TEO Based on Robust Statistics Theory, *IEEE TBME.*, Vol. 59, No. 2, 2012.

Statistical SP (Cont'd) : Adaptive Spike Detection

- Robust statistics give estimators that are not affected by outliers
- Few approaches to obtain a robust covariance/correlation estimator are available. We choose the highly robust estimation of the autocorrelation based on a scale approach, by means of the following identity

  $$r_{xx}(m) = 0.25[var\{x + x_m\} - var\{x - x_m\}]$$

  for a Wide-Sense Stationary process, the autocorrelation is applied on the random process *x* with a delayed x with a lag *m*
- $r_{xx}(m)$ results from the estimation of the variance. Hence, a robust estimator of the variance is necessary.
- *Qn*-scale estimator is a robust variance estimator especially under the Gaussian distribution. It is defined by:

  $$Qn\{x\} = \lambda[abs\{x_i - x_j\}; i < j; i, j = 1, 2, \ldots N]_{(k)}$$

  where *abs{.}* is the absolute value operator, *N* is the number of samples used to calculate *Qn*, factor λ at the Gaussian distribution case is equal to 2.2191, and *(k)* represents the *k-th* order statistic.

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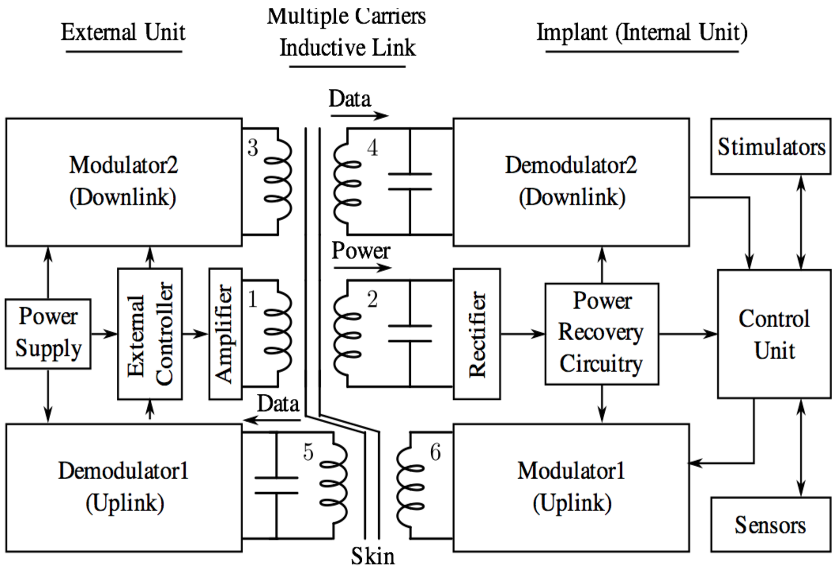
Inductive Power and Data Links

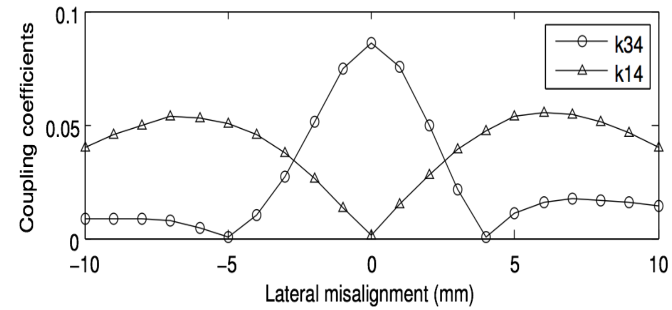


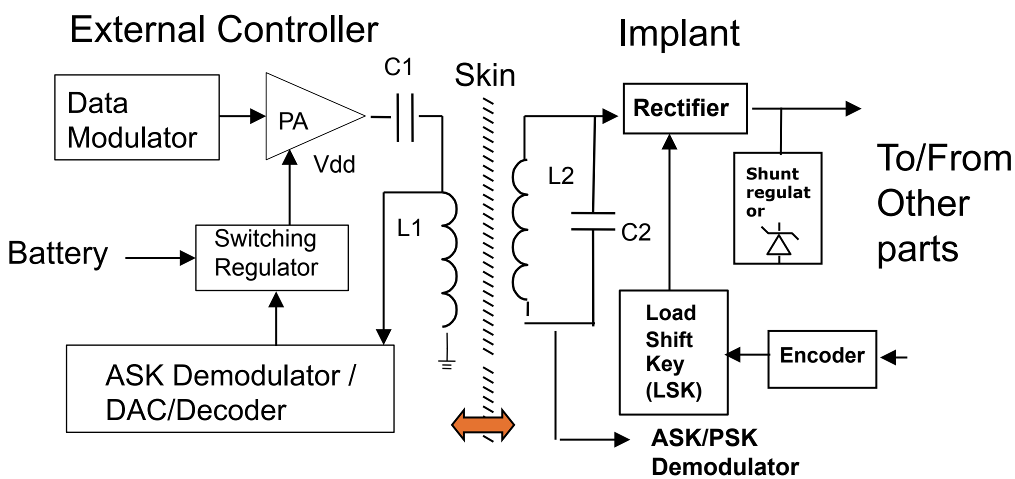
Power link = 1 MHz

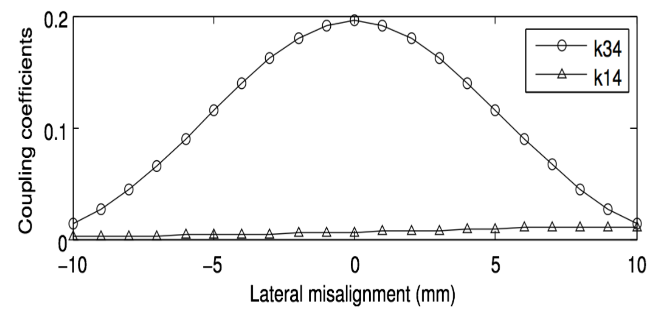
Downlink = 13.65 MHz

&

Uplink = 6.5 MHz

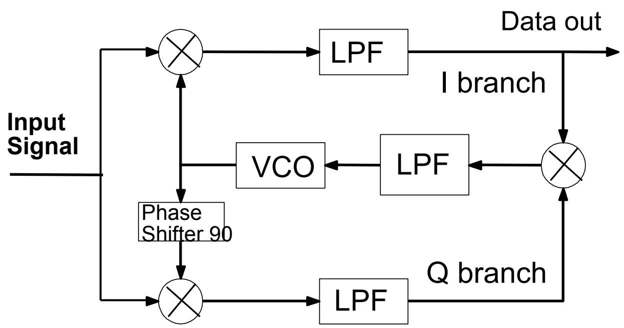




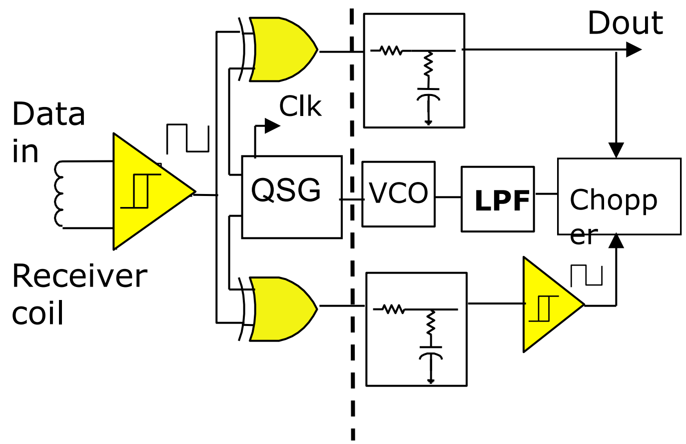


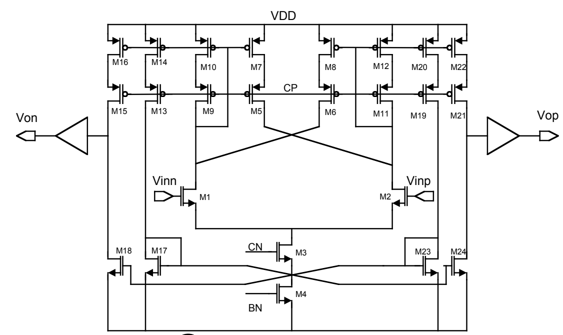
Simard et al, “High Speed OQPSK and Efficient Power Transfer Through Inductive Link for Biomedical Implants”, ***IEEE TBioCAS,*** Vol. 4, No.3, 2010.

Inductive Data Links : Integrated BPSK/QPSK

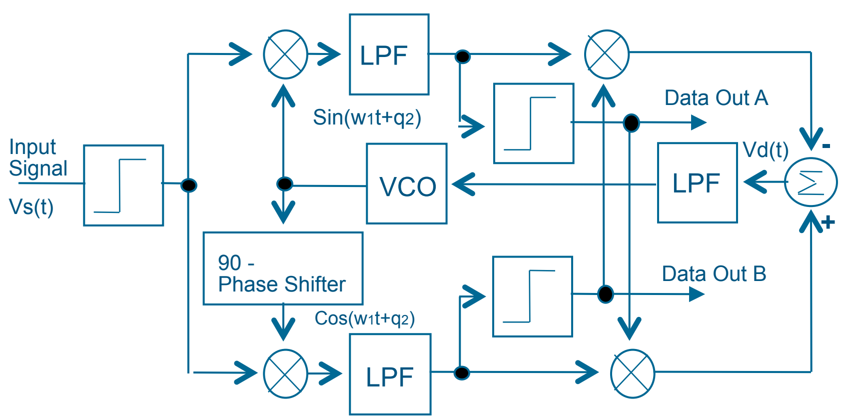


BPSK Costas-loop





Comparator



QPSK Demodulator

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**

*Postlayout; **Measured

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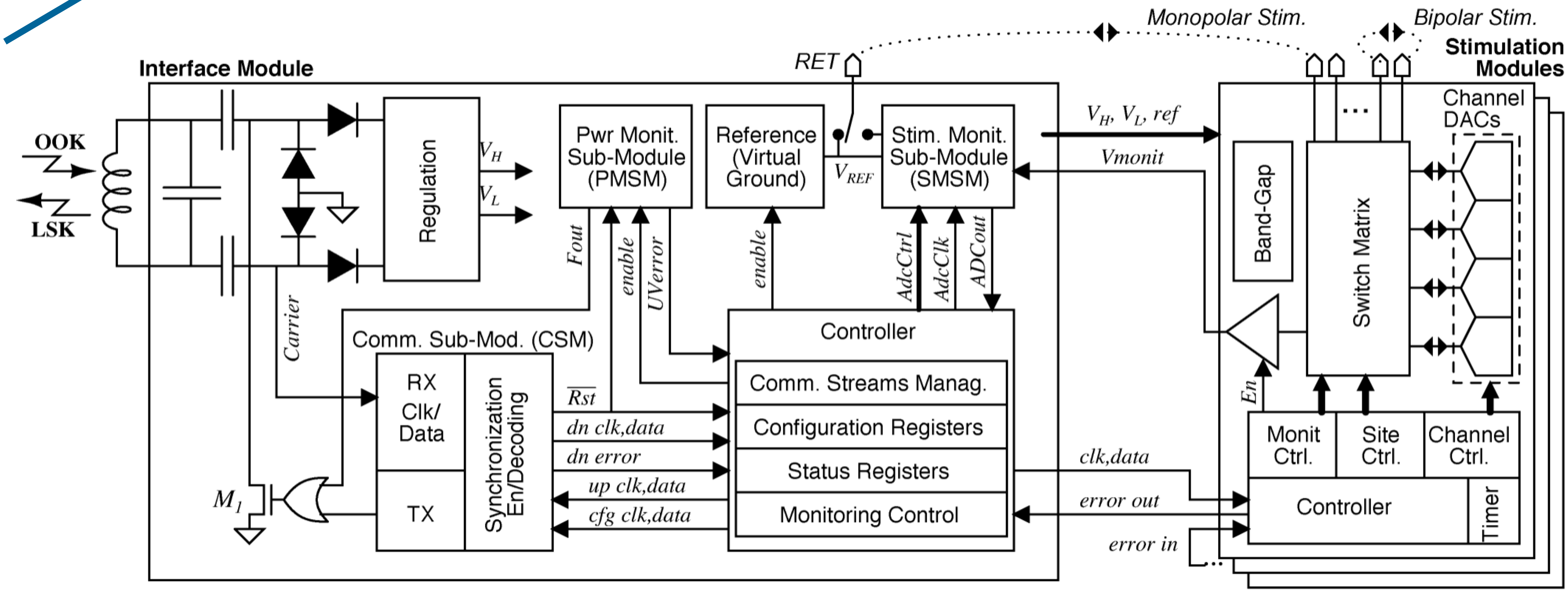
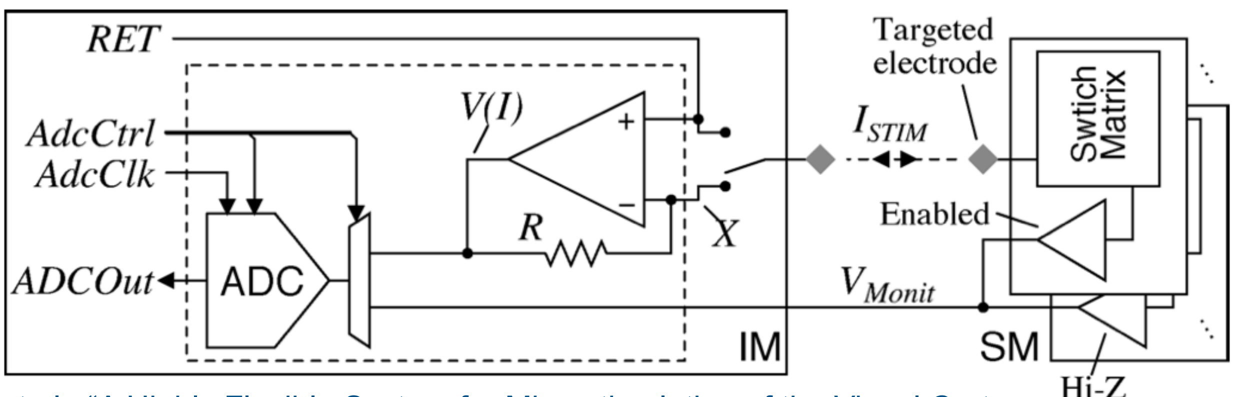
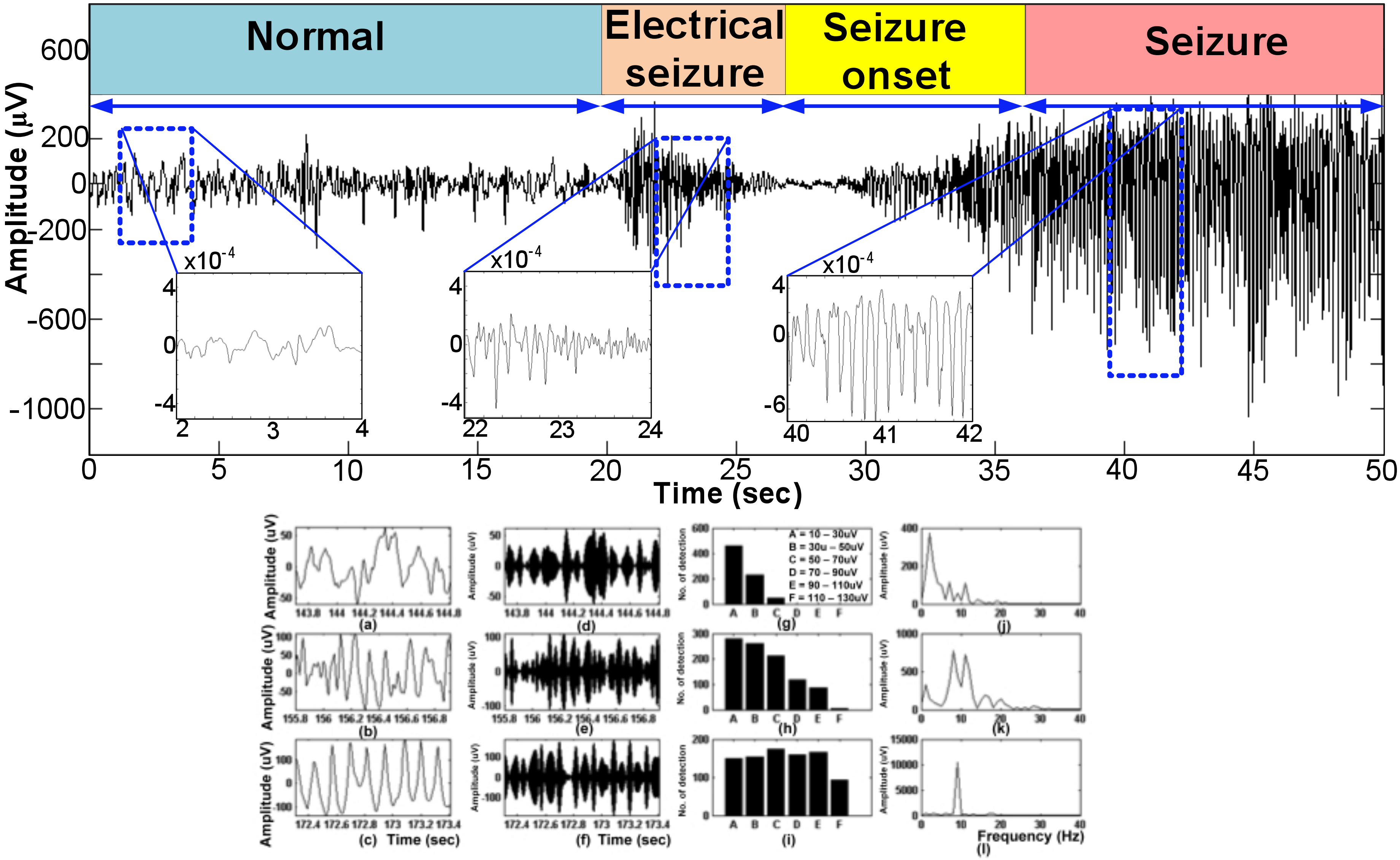
Visual Microstimulator/Monitor Architecture



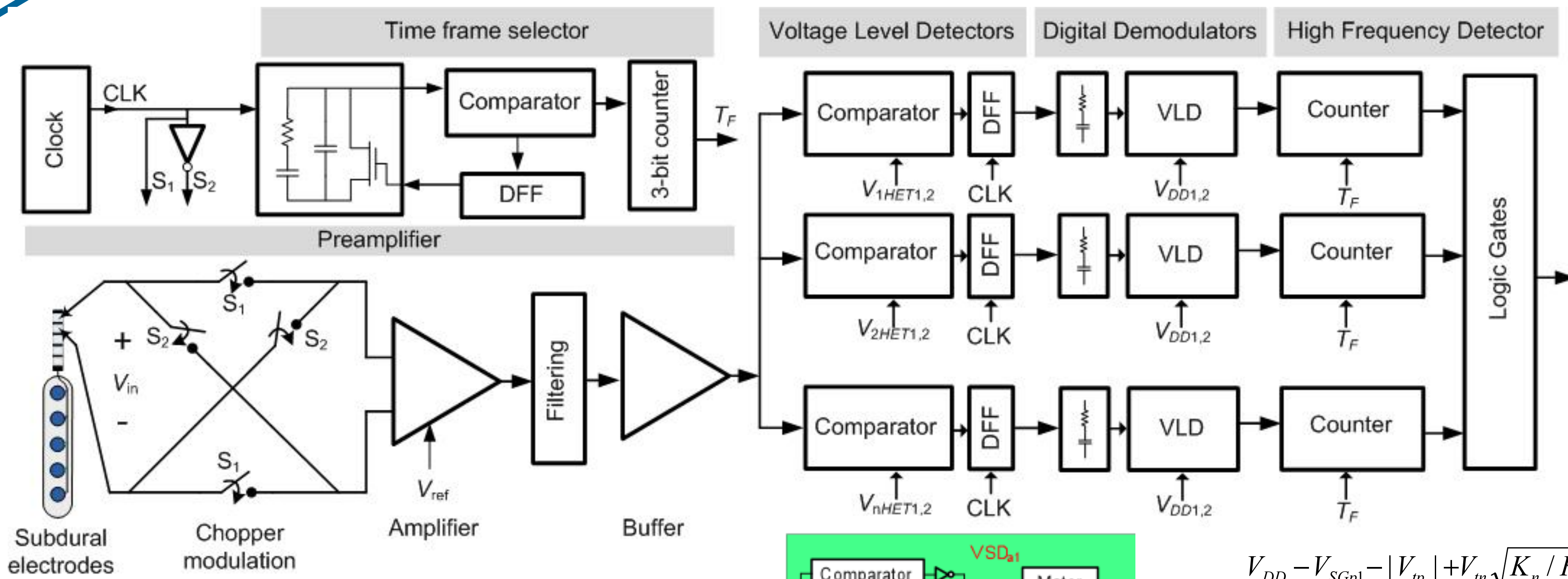


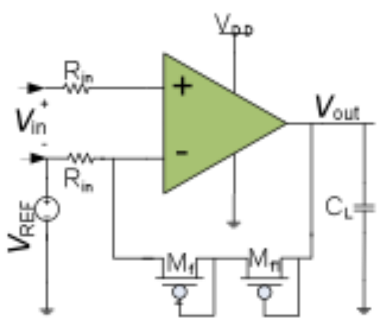
Coulombe et al,, “A Highly Flexible System for Microstimulation of the Visual Cortex: Design and Implementation”, ***IEEE TBioCAS***, Vol. 1, No. 4, 2007, pp. 258-269.

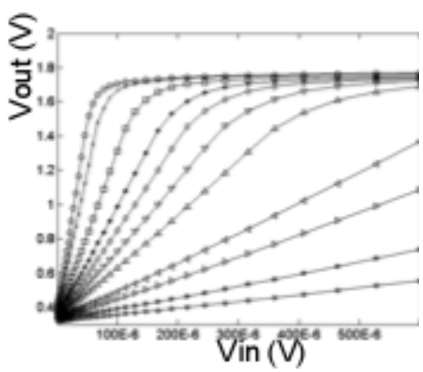
Epileptic Seizure : Analysis

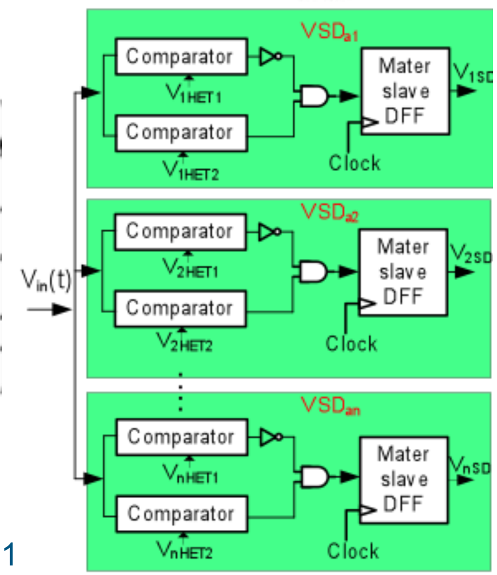


Seizure Onset Detection : Proposed Detector

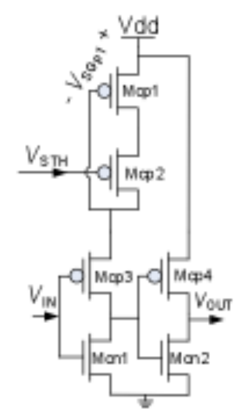








$$V_{HETi} = \frac{V_{DD} - V_{SGp1} - |V_{tp}| + V_{tn}\sqrt{K_n / K_p}}{1 + \sqrt{K_n / K_p}}$$



Adjustable Vth comparator

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

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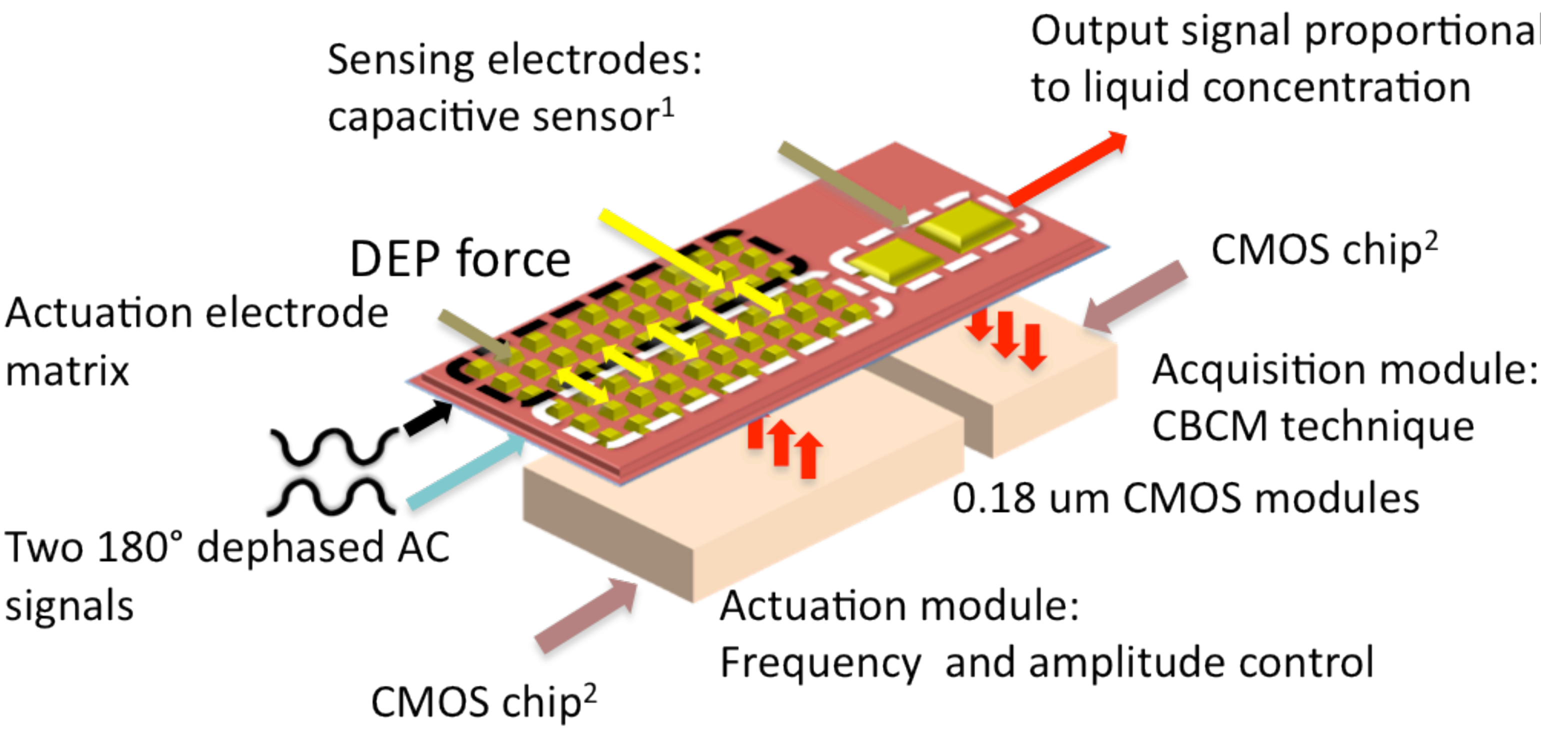
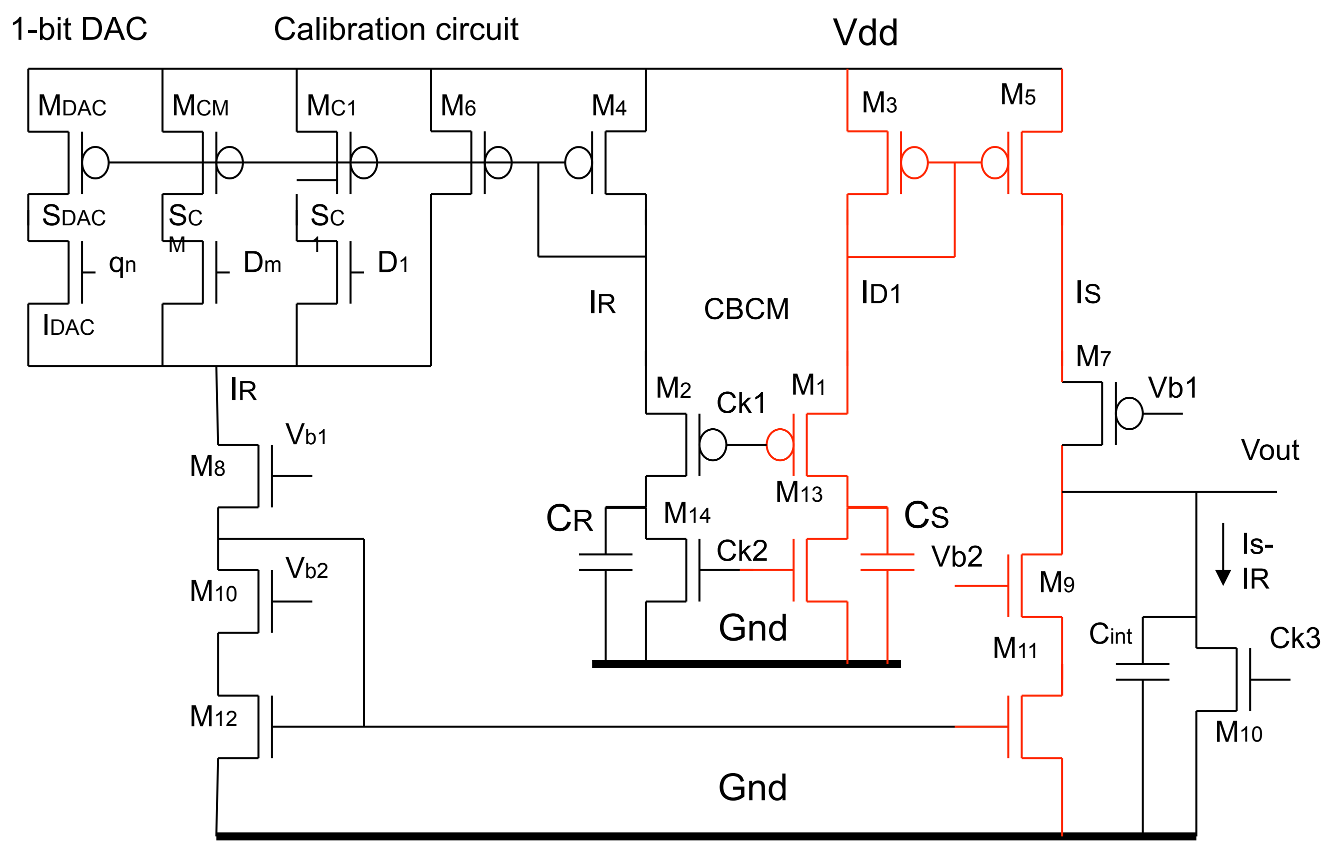
Neurotransmitters Detection and Manipulation



Charge-Based Capacitor Measurement (CBCM)

- Adjustable current mirror gain (D1-Dm)
- Sensing capacitances values for different analytes;
- Different parasitic capacitances of different chip samples.



$I_S - I_R = f\ Vdd\ (C_R - C_0)$

$I_R = I_{R0}\ (1 + 2^{m-1}D_{C1} + \ldots + 2^{m-k}D_{Ck} + \ldots + D_{CM}).$

Invitation to Attend NEWCAS in Montreal

Summary

- ☑ Multi-Channel Intracortical biosensing
- ☑ Adaptive Thresholding and automatique spike detection
- ☑ Epilepsy seizures onset detection
- ☑ LoC-Based neurotransmitter detection

Design challenges are multidimensional

- ☐ Data Compression : CS technique
- ☐ Microwatts Wireless : WuRx
- ☐ Fast data transmission : ~ 50 Mb/s
- ☐ Harvesting & scavenging energy : ~ 25 mW
- ☐ Small size & low weight;
- ☐ Low-power spike detection, sorting & decoding algorithms is needed

Important facts

- ☐ Transition to clinical use must be accomplished with minimal assistance.
- ☐ BMI systems must be safe, not to generate undesired actions.

Acknowledgment

http://www.polystim.ca

- Canada Research Chair on Smart Medical Devices (**CRC**)
- National Sciences and Engineering Research Council of Canada (**NSERC**)
- Canadian Institutes of Health Research (**CIHR**)
- Microsystems Strategic Research Alliance of Quebec (**ReSMiQ**)
- **CMC** Microsystems
- **Collaborators** from Various Medical Institutes and hospitals in Montreal.
- Interns, Master and PhD **Students**
- Postdoc **Fellows, Research Associates** and Invited **Professors.**

Thank You

Polystim neurotechnologies

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CIHR IRSC Canadian Institutes of Health Research / Instituts de recherche en santé du Canada

Institute of Circulatory and Respiratory Health / Institut de la santé circulatoire et respiratoire

Québec FQRNT

POLYTECHNIQUE MONTRÉAL WORLD-CLASS ENGINEERING

CMC MICROSYSTEMS

NSERC CRSNG

RESMIQ Regroupement Stratégique en Microélectronique du Québec