Ultra Low Power Analog Integrated Circuits for Implantable Medical Devices

Fernando Silveira
Universidad de la República, Uruguay

CCC Medical Devices
nanoWattICs
Objectives of this talk

- Introduce the needs and characteristics of Active Implantable Medical Devices (AIMDs) from the circuit designer point of view.
- Present the techniques and circuits applied in Analog ULP
  - Device Modeling
  - Design Methodology
  - Circuit techniques
- Show the current research and development topics and prospects of the area
Engineering School
Universidad de la Republica

- Founded 1888, approx. 1k new students / year, 670 teaching staff
Microelectronics Group

• Since 1991
• Under Graduate & Graduate Teaching (MSc, PhD)
• Research
  • Design of Analog / RF and Mixed-Signal Integrated Circuits, particularly Ultra-Low Power (ULP)
  • Also works on ULP Digital / DC-DC and Embedded
  • Strong links with Research groups abroad
• Industrial Experience
  • Implantable Medical Devices
• 2007: spin-off: NanoWattICs
Implantable Devices in Uruguay

**Feb. 3, 1960:** Drs. O. Fiandra and R. Rubio performed the first effective pacemaker implant to a human being in the world.

**1969:** Dr. O. Fiandra founded CCC to develop and manufacture pacemakers.

**1999:** CCC develops a pacemaker line based on an DDDR ASIC designed by the Microelectronics Group of Universidad de la Republica.

**Today:** CCC designs and manufactures active implantable devices and complete medical systems for third parties.
Outline

I. System: Active Implantable Medical Devices Today

II. Transistors and Circuits: Analog Design for ULP.
   Transistor Modeling.
   Design Methodology.

III. Circuit Techniques: Implementation of AIMDs blocks

IV. Conclusions and Prospects
Active Implantable Medical Devices (AIMD)

- **Implantable**: Introduced inside the body by a medical procedure and intended to remain there after the procedure.

- **Active**: Including a Power Source

- Not considered here:
  - Passive implants (e.g. bone prostheses, valves, stents)
  - Wearable / Portable / Swallowable (!) Active Medical Devices
AIMDs: Main Historical Milestones (I)

- Cardiac Pacemaker: first implantable device, 1960

- Cochlear Implants (1960s -)
AIMDs: Main Historical Milestones (II)

- Cardiac Defibrillators (1980)

- Deep Brain Stimulator for Parkinson (1995)
AIMDs: Some of the new developments

- Heart Failure
- Obesity
- Diabetes
- Neurostimulators:
  - Pain control
  - Blood pressure control
  - Foot drop correction
  - Urinary incontinence
  - Sleep Apnea
  - ...
- Patient monitoring
- Brain – computer interface
Some system examples

• Pacemaker:
  • **Goal:** Treat Bradycardia (slow heart rhythm) and conduction disorders between atria and ventricles
  • **How:** Stimulating to contract the heart when it does not contract spontaneously (“watchdog”)
  • **Sensing of:**
    • cardiac muscle signals that indicate ventricles / atria contraction
    • other indicators of physical activity, additionally in some cases
Basic Functions

• **Stimulation (Open Loop)**
  - Early Pacemakers
  - Cochlear Implants
  - Deep Brain Stimulators for Parkinson
  - Neurostimulators (sometimes “Man/Woman in the loop”)

• **Stimulation and Sensing (Closed Loop)**
  - Cardiac area (Pacemakers, Defibrillators, Heart Failure)
  - Obesity
  - Some Neurostimulators

• **Only Sensing**
  - Implanted “long term Holter” (“insertable loop recorder”)

• **Sensing + external actuation: Brain-computer interface**
Stimulation: Voltage mode

- E.g.: Pacemakers
- 0.1V … 7.5V
- 50μs … 1.5ms
- Requires battery voltage multiplier.
- RL: 500 Ohms typ.
Stimulation: Current mode

- Neurostimulators and others
- 0.1mA … 10mA
- 30µs … 300µs
- Load voltages up to 15V => Requires battery voltage multiplier
Sensing: Medical signals in general

- **Low frequency**: from $< 1$ Hz to a few kHz (neural signals)
- **Low amplitude**: $\mu$V to mV
- **Variability**:

  "Most measured quantities vary with time, even when all controllable factors are fixed. Many medical measurements vary widely among normal patients, even when conditions are similar."  
  (Source: J. Webster, *Medical Instrumentation. Application and Design*).

Objective of most analog signal processing: **qualitative** detection for closed loop control.

Traditionally advantage to **analog** implementation in terms of consumption, process scaling is changing this.
Sensing

- Biopotentials:
  - mioelectric signals (mVs, 100s Hz - 1kHz)
  - cardiac signals (mVs, 10s Hz – 300Hz)
  - neural signals (µVs, up to 8kHz)
- Impedance (tens of mOhms => µVs, few Hz)
- Movement (Physical activity, position) => accelerometer (µVs (sensor dependent), up to 10Hz)
Auxiliary Functions

• Telemetry
  • Inductive (up to 10cms)
  • 403 MHz MedRadio Band (a couple of meters)
• Battery Supervision (Voltage / Impedance / Consumed Charge Measurement)
• Lead Impedance Measurement
• Magnet Sensor (Reed Relay / Hall Sensor)
• Battery Recharge (if applicable)
• Control: Microcontroller & Firmware
Non-implantable System Components

Medical System Components

- IPG
- Leads
- Programmer System
- Patient wand
- Battery charger
- Logger
- PSA
Example: Implantable Pacemakers

Programmable Voltage Multiplier
$0.1V_{DD}$ to $2-3V_{DD}$

Approx. Consumption Distribution

Stimulus
- 35% / 6 $\mu A$

Telemetry
- 18% / 3 $\mu A$

Microcontroller
- 30% / 5 $\mu A$

Activity Sensing
- 17% / 2.8 $\mu A$

Sensing Channel

Lead Selection (polarity)

Battery Supervision

Amplification, Filtering and Detection
Example: Closed Loop Stimulator for Drop Foot Correction (I)

- Neurostep System (Simon Fraser Univ, Canada, Neurostream Technologies)
- Closed loop operation based on neural signal sensing and neural stimulation
- On clinical trials
Example: Closed Loop Stimulator for Drop Foot Correction (II)

http://www.youtube.com/watch?v=xH2vNu2BbnU
General Requirements: Size

Currently approximately 12 cc (5cm x 4cm x 0.6cm)

Approx. **30 to 40%** occupied by the **battery**

Less consumption = Smaller size @ Equal Service Life

Biotronik

1968-1998

(Source: M. Wilkinson, course: MST for Medical Devices)
Lithium-Iodine Battery (Li/I₂)

- **THE** pacemaker battery during almost 30 years
- Beguining of life: 2.8V, Operation down to 2.0V.
- High internal impedance, specially near depletion (several kohms)
  - Must be taken into account in complete device (power decoupling) and circuit design (instantaneous consumption, PSRR)
  - Common problem with other non-implantable batteries (e.g. LiMn02)
- Capacity: In the order of 1 Ah = 114 μA . Year
General Requirements: Batteries (II)

• For higher **instantaneous** consumption devices, lower impedance required
  • Lithium-Silver-Vanadium-Oxide (Li/SVO)
  • Lithium-Carbon-Monofluoride (Li/CFx)
  • QMR / QHR: Li + combined SVO / CFx
    • Being applied also in pacemakers recently.

• For higher **average** consumption devices:
  
  Rechargeable lithium batteries (since approx. year 2000, capacity in the order of **0.3Ah**)
  
  Direct powering from RF energy transmitted transcutaneously
General Requirements: Battery and Consumption

- **Capacity:** In the order of $1\text{ Ah} = 114\ \mu\text{A . Year}$
- **Consumption**

  Service Life: **6 to 12 years** $\Rightarrow$ consumption: $19\ \mu\text{A to 9}\ \mu\text{A}$

  Average consumption due to stimulation (pacemakers): $3\ \mu\text{A to 12}\ \mu\text{A}$ $\Rightarrow$ **Unavoidable**

  State of the art: average consumption **internal to the circuit** around **5 to 10\mu A**

  Consumption internal to the circuit: **50% to 75% of total consumption**

  There is room and need for improvement
General Requirements: Safety and Reliability

This is not acceptable !!!
General Requirements: Safety and Reliability

Reliability => Frequency and probability of faults

Safety: Involves many aspects, particularly:

=> A single fault must not provoke a catastrophic event

High Reliability => Probability of single fault is low and double fault is virtually impossible

+ Safety

=> Probability of malfunctioning is low
=> Catastrophic Failure: virtually impossible
General Requirements: Safety and Reliability

Involves all the stages:

- System and Circuit Design
- System and Circuit Verification, Qualification and Medical Validation
- Medical Device Application, Configuration and Use

Strongly conditions design: E.g. Limiting DC leakage towards the heart under single fault conditions => *external capacitors*

Importance of paying attention from the very beginning to applicable standards on AIMD safety, risk analysis and applicable regulations.
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Introduction

• Bipolar (BJT) Analog Design:
  \[ g_m = \frac{I_c}{U_T} \]
  – Basically **1 degree of freedom**: \( I_c \)

• MOS Analog Design:
  \[ g_m = f(I_D, W, L) \]
  – **3 degrees of freedom**
  – Traditionally: only part of the design space: the strong inversion (above threshold) region
MOST Inversion Regimes (1)

Strong Inversion (S.I.)
\[ I_D \propto (V_G - V_T)^2 \]

Moderate inversion

Weak inversion:
\[ I_D \propto e^{V_G/(nUT)} \]

Subthreshold Current
Leakage Current

VG(V)
ID(A)

0 1 2 3

0 10^{-2} 10^{-4} 10^{-6} 10^{-8} 10^{-10}
MOST Inversion Regimes (2)

Weak Inversion (W.I.)
\[ I_D \propto e^{V_G/(n \cdot U_T)} \times 10^{-10} \]
\[ U_T = k \cdot T/q \]

n: slope factor

Moderate Inversion (M.I.)

Strong Inversion (S.I.)
\[ I_D \propto (V_G - V_T)^2 \]

Diffusion Current

Drift Current
All regions, continuous MOST models

- EKV (Enz, Krummenacher, Vittoz, EPFL, AICSP 1995): originally mathematic interpolation between strong and weak inversion equations, now physical
- ... or experimental / simulation curves
“Intrinsic” MOS Amplifier

OTA: Operational Transconductance Amplifier

\[ A_0 = g_m \cdot r_o = \frac{g_m}{g_d} = \frac{g_m}{I_D} \cdot \frac{V_A}{I_D} = \frac{g_m}{I_D} \left/ \frac{g_d}{I_D} \right. \]

\[ f_T = \frac{g_m}{2\pi C_L} , \quad A = \frac{A_0}{1 + \frac{s \cdot A_0}{2\pi f_T}} \]

- Consumption: \( I_D \)
- Speed: \( g_m / C_L \)
- \( C_L \): total: external + parasitics
- Speed - Consumption trade-off: \( g_m / I_D \)
\[ \frac{g_m}{I_D} = \frac{1}{I_D} \frac{\partial I_D}{\partial V_G} = \frac{\partial \log(I_D)}{\partial V_G} \]

- \( g_m/I_D \) is the slope of \( I_D \) vs. \( V_G \) in log scale

Maximum in W1

Equal to \( 1/(n.U_T) \)

n typ: 1.3 a 1.5
As the current increases, the “$g_m$ generation efficiency decreases”

To reach the maximum frequency allowed by the technology:

$\Rightarrow$ high $g_m \Rightarrow$ high current $\Rightarrow$ strong inversion $\Rightarrow$ low efficiency

Bipolar Transistor:

$g_m/I_C$ independent of current in a wide range

W/L = 100 and 0.8 μm technology.
$g_m/I_D$ and transistor size

When short channel effects **are not** significant:

$$I_D = \mu C_{ox} (W/L) \cdot f(V_G, V_S, V_D)$$

$$\left( \frac{g_m}{I_D} \right) = f(I_{norm}) \quad I_{norm} = \frac{I_D}{(W/L)}$$

$$I_{norm} = \frac{I_D}{\mu C_{ox} (W/L)}$$

$$I_{norm} = i_f = \frac{I_D}{I_S}$$

When short channel effects **are** significant:

$$\left( \frac{g_m}{I_D} \right) = f(I_{norm}, L)$$
Design Methodology: \( g_m/I_D \) key variable

\[
A_0 = \frac{g_m}{I_D} V_A \quad f_T = \frac{1}{2\pi} \frac{g_m}{C_L} = \frac{1}{2\pi C_L} \frac{g_m}{I_D} I_D
\]

Circuit Performance

Transistor Operating Mode

Transistor Sizing

\[
I_D = \mu C_{ox} (W/L) f(V_G, V_S, V_D)
\]

Optimum of Power Consumption

Weak inversion: \( I_D \propto e^{V_G/(n \cdot U_T)} \)

Moderate inversion

Strong inversion (\( I_D \propto (V_G - V_T)^2 \))

• Working towards WI

\[ \begin{align*}
g_m/I_D & \quad \rightarrow \quad I_D \\
W/L & \quad \rightarrow \quad C \\
g_m & \quad \rightarrow \quad \end{align*} \]

Usually an optimum exists in moderate inversion
Example
Intrinsic Amplifier: Power Optimum

$ f_T = 10\text{MHz}, C_L = 3\text{pF}, L = 2\mu\text{m}, \text{tech: } 0.8\mu\text{m}$
Example

Intrinsic and extrinsic amplifier, $C_L = 3\text{pF}$
gm/ID in the nanometer and post CMOS era

B. Sensale-Rodriguez et al, accepted for presentation at IEEE SubVt 2012, joint work with U. Notre Dame, Indiana.

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ULP Analog Signal Processing: 1) RC Active Filter

- Limited by values possible to integrate: up to \( k \Omega \) or \( M \Omega \) (special process) and 100s pF
- Large spread in absolute values of integrated components
- \( \Rightarrow \) Drawback: need for external components ..., but ....

\[
\frac{V_o}{V_{in}} = \frac{R_2}{1 + R_2 C s}
\]
ULP Analog Signal Processing: External components should always be avoided?

- A few are required to **avoid single fault risks**.
- Full integration might be paid in terms of consumption in order to accommodate less precise components.

- 0402 SMT components up to 10MΩ and 15μF
- 0402 SMT => 1mm x 0.5mm x 0.35mm = 0.18mm³
- Considering PCB, IC package pin, routing => 2 - 5 mm³
- **Size and Consumption** are linked through **Battery size**

\[
1 \text{ Ah} = 114 \ \mu\text{A}.\text{year} \quad 11.4\ \mu\text{A} \quad 44\text{mm}^3/ 100\text{nA}
\]

10 year service life, 5cc battery
ULP Analog Signal Processing: 2) Switched capacitor filters

- \( \frac{1}{R_2 C} = f_{\text{clk}} \cdot \frac{C_2}{C} \)
- \( \mathbf{+} \) precise, \( \mathbf{+} \) large time constants possible, \( \mathbf{+} \) fully integrated
- \( \mathbf{-} \) op amps consumption, \( \mathbf{-} \) antialiasing
ULP Analog Signal Processing:
3) Gm-C Filters

- $R = 1/g_m \Rightarrow 1/R2.C = g_{m2}/C \Rightarrow \text{spread}
  \Rightarrow \text{on-chip automatic tuning}$

- $+$ large time constants possible

- $-$ input linear range requirements for transconductors
Example of modules: Pacemaker Activity Sense

Objective:

- E.g. Activity indicator: 3s Average of the absolute value of acceleration in the 0.5 - 7 Hz band.

Amplitude: tens to hundreds of $\mu$V
Accelerometer Signal Conditioning (1): Amplifier / Bandpass filter

Double input symmetrical OTA (DDA)

Vo = A1Vs + A2Vf

Input signal
Feedback signal
High pass characteristic

ISCAS 1998
Accelerometer Signal Conditioning (2): Layout and results

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<tr>
<td>Gain</td>
<td>2900</td>
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<tr>
<td>Equivalent input noise ($\mu$Vrms)</td>
<td>18</td>
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<tr>
<td>Consumption ($\mu$A)</td>
<td>3.4</td>
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<tr>
<td>Area ($mm^2$)</td>
<td>1.82</td>
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Accelerometer Signal Conditioning (3): Results

![Graph showing cardiac frequency and pacemaker frequency](image)

- **Actual cardiac frequency of healthy patient**
- **Simulated pacemaker frequency**
- **Circuit output**
Accelerometer Signal Conditioning (4): Gm-C implementation

A. Arnaud (UR), C. Galup (UFSC), ISCAS 2004

**Filtro-Amplificador 0.5-7Hz**

- $G_{m1}$
- $V_{Bias} = 700mV$
- $C_2 = 50p$
- $G_{m2}$
- $V_{Out1}$
- $V_{Bias}$
- $C_1 = 850p$
- $V_{In}$
- Sensor
- $G_{m3}$
- $C_3 = 50p$
- $G_{m4}$
- $V_{Out2}$
- $G_{m5}$
- $G_{m6}$
- $C_4 = 250p$

- $G_{m4} = 21nS$
- $G_{m5} = 2.5nS$
- $G_{m6} = 89pS$

Gain: 390

- Ganancia Preamplificador: $G_1 = 46.4$
- $G = 385$
- $I_{DD} = 290nA$
- Equivalent Input noise: 2.1$\mu$Vrms

- Fully integrated
Example of modules: Neural Recording Amplifier

• **Objective:** Signal detection from e.g. cuff electrodes or cortical electrodes arrays

• **Requirements:**
  • $0.5\mu V_{rms} - 2\mu V_{rms}$ noise
  • BW: 300Hz – 8kHz
  • High CMRR (particularly in Cuff)
  • Block high DC offsets (100mV or more) due to electrode/tissue contact
  • Negligible DC input current
Example: Cuff Electrode Recording in Neurostep

Hoffer et al, IFESS 2005

Example: Cortical Recordings

Harrison, Proc. IEEE, July 2008
Neural Amplifier Front End (1): Capacitive Feedback

- Inversion region for noise / power optimization: e.g. input pair weak inversion, current mirror active load: strong inversion
- CMRR limited by capacitor matching.

\[
\text{NEF} = V_{ni, \text{rms}} \sqrt{\frac{2I_{\text{tot}}}{\pi \cdot U_T \cdot 4kT \cdot \text{BW}}}
\]

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<tr>
<td>Gain</td>
<td>40 dB</td>
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<tr>
<td>BW</td>
<td>0.13 Hz / 7.5 kHz</td>
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<td>I_{\text{tot}}</td>
<td>16 µA</td>
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<tr>
<td>NEF</td>
<td>3.8</td>
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<tr>
<td>v_{noise \text{rms}}</td>
<td>2.1 µV</td>
</tr>
<tr>
<td>CMRR</td>
<td>&gt; 42 dB</td>
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Harrison et al, IEEE JSSC, June 2003

MOS – Bipolar Pseudoresistor (100s Mohms equivalent)
Neural Amplifier Front End (2): DDA Based

- 😊 High CMRR (Given by Input Differential Pair)

- 😞 Both Differential Pairs contribute equally to Input Noise (hence to area and consumption)

J. Sacristán, T. Oses, IFESS 2002,
Another DDA Based Scheme: M. Baru, U.S. Patent 6,996,435, 2006
Neural Amplifier Front End (3): “Asymmetrical” DDA Based (I)

- ☀ Effect of noise (and hence consumption and area) of Gm2 greatly reduced while keeping high CMRR (given by input differential pair)
- Gm2 less effective in compensating input offset and DC components => Output DC and high pass characteristic fixed by local feedback at the output
Neural Amplifier Front End (4): “Asymmetrical” DDA Based (II)

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<td>Architecture</td>
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<td>Capacitive</td>
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<td>DDA</td>
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<td>A (dB)</td>
<td>48</td>
<td>40</td>
<td>41</td>
<td>80</td>
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<td>NEF</td>
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<td>I_total(µA)</td>
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<td>16.0</td>
<td>2.7</td>
<td>180</td>
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<td>vi noise</td>
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<td>2.1</td>
<td>3.1</td>
<td>7.6</td>
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<tr>
<td>(µVrms)</td>
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<td></td>
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<tr>
<td>CMRR</td>
<td>&gt; 107</td>
<td>&gt; 42</td>
<td>&gt; 66</td>
<td>90</td>
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Prospects: Digital vs. Analog

- Theoretical limits of power consumption for Analog and Digital Signal Processing
- Analog better for low S/N, but the border is moving ...
- "Digital" pacemaker already present in marketing

Source: E. Vittoz
Prospects: Analog ULP and AIMD

- Intense growth of applications / therapies on development and reaching the market

- Broad Analog / Circuit research area:
  - Sensing
  - Stimulation, Power Management / Battery Recharge, Communication, …
  - Once very specific area, now wider (wireless sensor networks, body area networks, portable devices, energy scavenging devices, RFID, …).
Prospects: AIMDs
Brain Computer Interface

Set. 2000, Nicolelis, Duke University

You are in: Sci/Tech
Wednesday, 15 November, 2000, 19:37 GMT

Monkey brain operates machine

Monkeys have used the brain signals from a monkey to drive a robotic arm.

As the animal stuck out its hand to pick up...
Prospects: AIMDs
Brain Computer Interface


**Instant neural control of a movement signal**

Hands-free operation of a cursor can be achieved by a few neurons in the motor cortex.

Source: Mijail Serruya
Prospects AIMDs: Brain Computer Interface

July 2004: Pilot FDA trial started by spin/off company of Brown Univ., several tetraplegic patients implanted.
Some Conclusions

• ULP ICs for AIMDs: Each nA counts => **Methodology and Optimization**

• AIMDs: Very broad field in strong expansion
  ✓ Many R & D opportunities
  ✓ Microtechnology is often the enabling factor.

• AIMDs: Price is not the main concern, but application and performance
  ✓ Suitable for developments with lower volume productions than in other areas
  ✗ High investment associated with long development cycles, qualification, clinical testing and regulatory aspects.
More Information

iie.fing.edu.uy/vlsi
silveira@fing.edu.uy

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