Electrónica para dispositivos médicos implantables: Necesidades y Perspectivas

Fernando Silveira
Universidad de la República, Uruguay
Agenda

I. Sistema: Dispositivos Médicos Implantables Hoy

II. Circuitos: Algunos ejemplos

III. Conclusiones y Perspectivas
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)
  - Some similar requirements for Wearable / Portable / Swallowable (!) Active Medical Devices
Dispositivos médicos portables, tragables, vestibles ...

http://mobilewellbeing.wordpress.com/

www.givenimaging.com
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 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.
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**: μV 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 10 cms)
  • 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
PSA
Patient 
wand
Battery 
charger
Logger

IPG: Implantable Pulse Generator
Leads: Electrical leads connecting the IPG to the patient's heart
Programmer: Device used to program the IPG
System: The complete medical system
PSA: Patient Specific Analyzer
Patient wand: Device for accessing the patient's body
Battery charger: Device for charging the battery
Logger: Device for logging data

CCC medical devices
Example: Implantable Pacemakers

Programmable Voltage Multiplier
0.1\( V_{DD} \) a 2-3\( V_{DD} \)

Approx. Consumption Distribution

Stimulus

35% / 6\( \mu A \)

Telemetry

Lead Selection (polarity)

Microcontroller

30% / 5\( \mu A \)

Activity Sensing

Sense Channel

17% / 2.8\( \mu A \)

Battery Supervision

Amplification, Filtering and Detection

18% / 3\( \mu A \)
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)
Different variants of Lithium Batteries:

- Lithium Iodine (Li/I₂), Li/SVO, Li/CFx, combinations
- Beguining of life: 2.8V, Operation down to 2.0V
- Capacity: In the order of 1 Ah = 114 μA . Year
- Service Life: 6 to 12 years

=> Average consumption: 19 μA to 9 μA

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

There is room and need for improvement
General Requirements: Power Supply (II)

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**

Courtesy of David Prutchi, Ph.D. © David Prutchi, All Rights Reserved
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.
Agenda

I. Sistema: Dispositivos Médicos Implantables Hoy

II. Circuitos: Algunos ejemplos

III. Conclusiones y Perspectivas
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 μV

Ideal Rectifier

Sensor

Amplifier / filter

3s Averaging
Accelerometer Signal Conditioning (1): Amplifier / Bandpass filter

\[ Vo = A_1 Vs + A_2 Vf \]

- **Input signal**
- **Feedback signal**
- **Double input symmetrical OTA (DDA)**
- **High pass characteristic**

 ISCAS 1998

<table>
<thead>
<tr>
<th>Specification</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gain (V/V)</td>
<td>2900</td>
</tr>
<tr>
<td>Equivalent input noise ((\mu)Vrms)</td>
<td>18</td>
</tr>
<tr>
<td>Consumption ((\mu)A)</td>
<td>2.4</td>
</tr>
</tbody>
</table>
Accelerometer Signal Conditioning (2): Results

The figure illustrates the results of the accelerometer signal conditioning process. The graph shows the digitized output of the circuit over time. The x-axis represents time in seconds, ranging from 0 to 200 seconds. The y-axis on the left represents the cardiac frequency in ppm, ranging from 0 to 200 ppm, while the y-axis on the right represents the digitized output of the circuit, ranging from 0 to 200.

Three lines are plotted on the graph:
- The blue line represents the actual cardiac frequency of a healthy patient.
- The red line represents the simulated pacemaker frequency.
- The green line represents the circuit output.

The graph captures the performance of the signal conditioning circuit as it processes the cardiac frequency signals, demonstrating its ability to accurately simulate the pacemaker frequency and output the digitized data.
Verificación / Validación

Ejercicio en cinta de correr

<table>
<thead>
<tr>
<th>Etapa</th>
<th>Velocidad (mph)</th>
<th>Inclinación (%)</th>
<th>Duración (min)</th>
<th>Trabajo (Mets)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reposo</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>I</td>
<td>1</td>
<td>0</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>II</td>
<td>2</td>
<td>0</td>
<td>2</td>
<td>2.6</td>
</tr>
<tr>
<td>III</td>
<td>2</td>
<td>3.5</td>
<td>2</td>
<td>3.4</td>
</tr>
<tr>
<td>IV</td>
<td>3</td>
<td>5.5</td>
<td>2</td>
<td>5.0</td>
</tr>
<tr>
<td>V</td>
<td>4</td>
<td>5.5</td>
<td>2</td>
<td>8.0</td>
</tr>
<tr>
<td>VI</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Reposo</td>
<td>Sentado</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- Subida y bajada de escaleras a 30, 60 y 90 escalones/minuto
- Registro de:
  - Nivel de actividad calculado por el marcapaso
  - ECG
Aplicado a 22 voluntarios

Treadmill por Etapas

\[ y = 0.4749x^3 - 3.8648x^2 + 20.474x - 2.4054 \]
Las teorías llegan a la práctica …
Example of modules: Neural Recording Amplifier

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

- **Requirements:**
  - $0.5\mu V_{\text{rms}} - 2\mu V_{\text{rms}}$ 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
  - A lot of research in this area ....
Example: Cuff Electrode Recording in Neurostep

Hoffer et al, IFESS 2005

Example: Cortical Recordings

Harrison, Proc. IEEE, July 2008
Ejemplo: Colaboración IIE – IIBCE (Lab. A. Caputi)

- Maestría Julián Oreggioni
- Proyecto Fin de Carrera NESIA ((E. Cilleruelo, A. Nacelle, G. Robert)

Registro intracelular de neuronas de un pez eléctrico realizado en el lab. del Dr. Caputi (IIBCE)
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.

Gain  | 40 dB  
---|---
BW    | 0.13 Hz / 7.5 kHz  
I_{total} | 16 μA  
NEF | 3.8  
v_{noise rms} | 2.1 μV  
CMRR | > 42 dB

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,
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: “Asymmetrical” DDA Based (II)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Architecture</td>
<td>Asym. DDA</td>
<td>Capacitive</td>
<td>Capacitive</td>
<td>DDA</td>
</tr>
<tr>
<td>A (dB)</td>
<td>48</td>
<td>40</td>
<td>41</td>
<td>80</td>
</tr>
<tr>
<td>NEF</td>
<td>4.2</td>
<td>3.8</td>
<td>2.7</td>
<td>53.4</td>
</tr>
<tr>
<td>$I_{\text{total}}$ (μA)</td>
<td>16.5</td>
<td>16.0</td>
<td>2.7</td>
<td>180</td>
</tr>
<tr>
<td>$v_i$ noise ($\mu$Vrms)</td>
<td>2.4</td>
<td>2.1</td>
<td>3.1</td>
<td>7.6</td>
</tr>
<tr>
<td>CMRR</td>
<td>&gt; 107</td>
<td>&gt; 42</td>
<td>&gt; 66</td>
<td>90</td>
</tr>
</tbody>
</table>
Las teorías llegan a la práctica …

- Maestría Julián Oreggioni
- Proyecto Fin de Carrera NESIA (E. Cilleruelo, A. Nacelle, G. Robert)
Agenda

I. Sistema: Dispositivos Médicos Implantes Hoy

II. Circuitos: Algunos ejemplos

III. Conclusiones y Perspectivas
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

Scientists have used the brain signals from a monkey to drive a robotic arm.
Prospects AIMDs: Brain Computer Interface

July 2004: Pilot FDA trial started by spin/off company of Brown Univ., several tetraplegic patients implanted.
Aplicaciones:
Interfaz Cerebro-Computadora

Smart-Cap: gorrito para monitorear fatiga en conductores profesionales

Biobots: controlar insectos desde un PC. NCSU, 2012

Emotiv: vincha para interactuar y jugar en una PC. http://emotiv.com/
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.
Agradecimientos

Franco Simini
Miembros y ex-miembros del Grupo de Microelectrónica del IIE.
CCC S.A., nanoWattics

iie.fing.edu.uy/vlsi
silveira@fing.edu.uy
Gracias a Uds !