Beter worden met elektriciteit

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13-10-2015

Introduction

[Source: De Volkskrant, dd. 15/10/13]

Bianca Saez, suffering from Tourette's syndrome

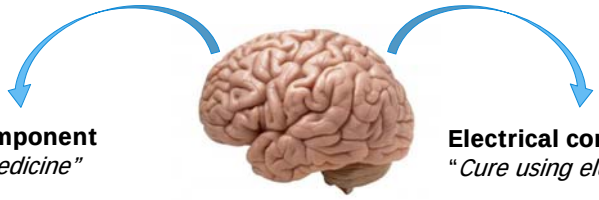
https://www.youtube.com/watch?v=0OPqGx6fSPU

1.

Neurostimulation

The brain: our mainframe

An electro-chemical machine



Chemical component
"*Cure using medicine*"

Global effect (side effects)
19th century approach

Electrical component
"*Cure using electricity*"

Local effect
Instantaneous and reversible
21st century approach

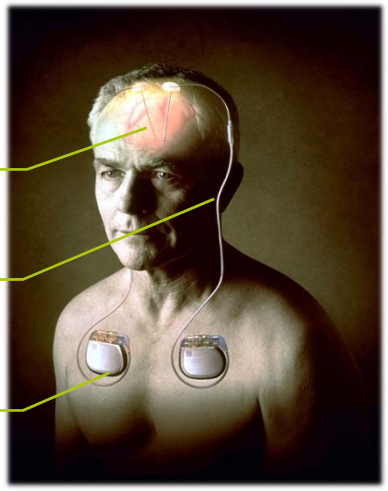
Neurostimulation

Current treatment

Electrodes implanted in the brain
- Suppress undesired activity
- Generate therapeutic activity
- (future) Modulate activity

Wires (leads)
- Connect the electrodes to the pulse generator

Pulse generator in the chest
- Generates electric pulses



Picture courtesy of Medtronic, Inc.

Neurostimulation: example

Stimulator **off** Stimulator **on**

Deep Brain Stimulation of the Subthalamic Nucleus for treatment of Parkinson's disease

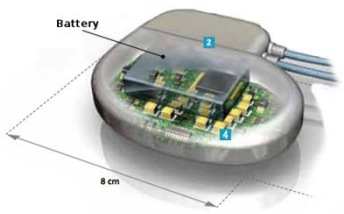
Neurostimulators

The future

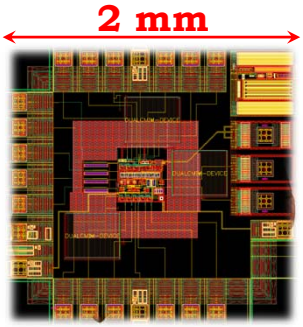
Use new circuit techniques and alternative forms of stimulation to:

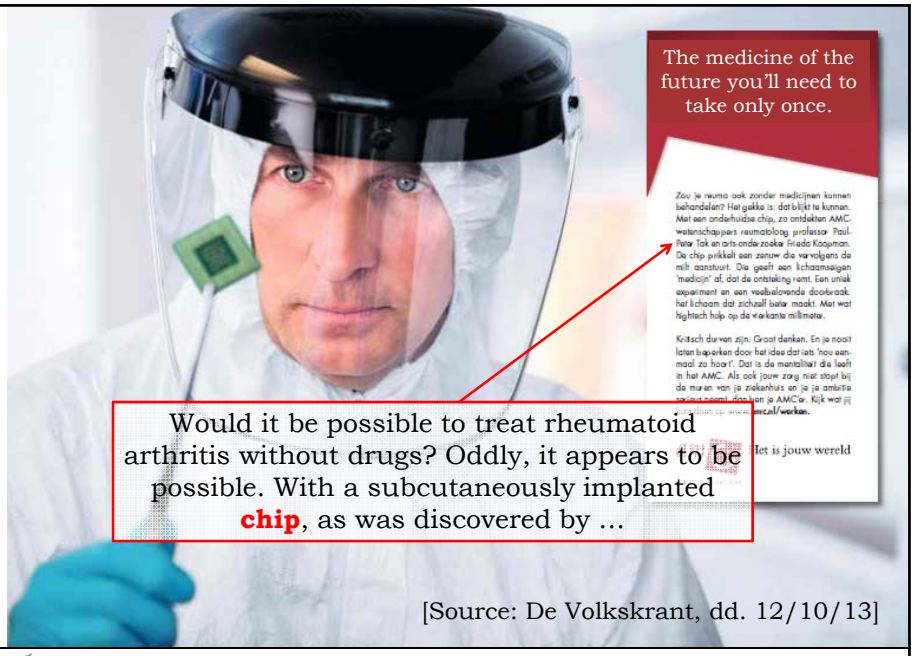
Make implants fully implantable in the head
- Drastically decrease power consumption

Make impants smart
- Close the loop by including feedback



Miniaturization





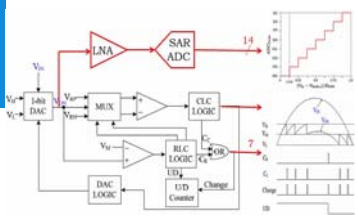
[Source: De Volkskrant, dd. 12/10/13]

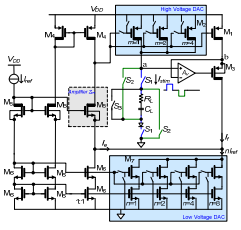
2.

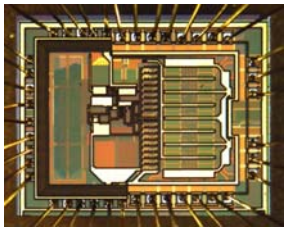
Chips

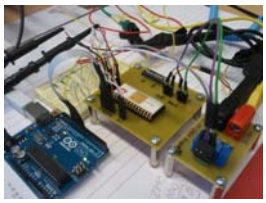
Chips

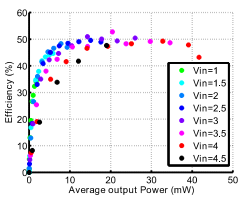
Chips for bioelectronic medicine











A word about electroceuticals (1)

Electroceuticals is a recently coined term that broadly encompasses all **bioelectronic medicine** that employs electrical stimulation to affect and modify functions of the body.

Famm, K.; Litt, B.; Tracey, K.J.; Boyden, E.S.; Slaoui, M. (10 April 2013). "Drug discovery: A jump-start for electroceuticals". *Nature* **496** (7444): 159–161. doi:10.1038/496159a

A word about electroceuticals (2)

Electroceuticals are the **electronic counterparts of pharmaceuticals** and they involve stimulation and/or recording and preferably transcutaneous wireless communication, energy harvesting/scavenging and closed-loop operation

3.

Neurorecording devices

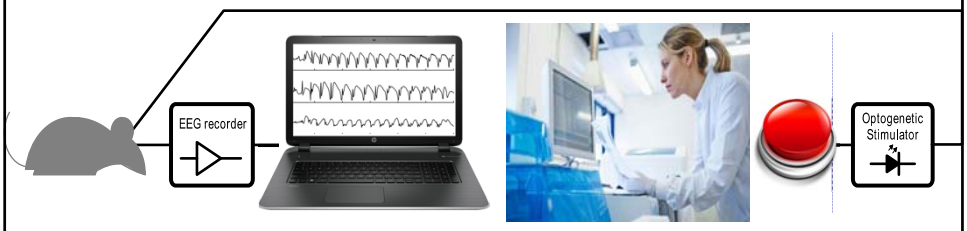
Optogenetic neuromodulation

https://www.youtube.com/watch?v=yhonl9LWWHo

Motivation (1)

Feasibility of closed-loop epilepsy suppression has been shown (a.o. Neuropace)

In early optogenetic stimulation (of mice), the loop was closed via the neuroscientist who would press a button and thereby apply an optical stimulus



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Goal: use in **closed-loop** optogenetic stimulation of the cerebellum of (petit mal) epileptic mice

Realtime seizure detection

Motivation (2)

Performance of these systems depends on detection algorithm:
- Good False Positive / False Negative rate
- Minimum detection delay

Implementation using off-the-shelve hardware:
- Rapid prototyping
- Cheap implementation (< €100,-)

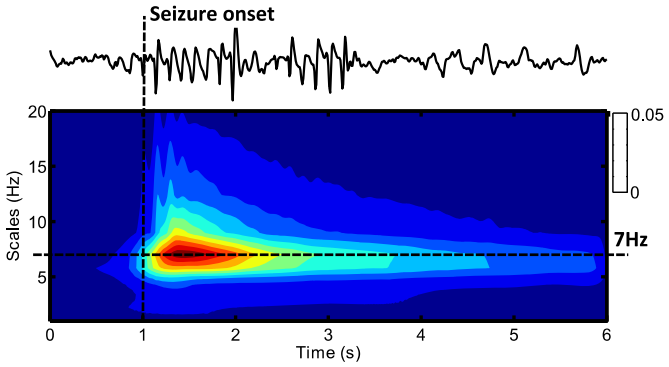
Measurement setup

- ECoG recordings from head-fixed Cacna1a^{P601L} mice with absence seizures
- Teflon coated silver ball tip electrodes (0.2mm) on primary motor and primary sensory cortices
- ECoG is recorded using commerical amplifiers (Cyberamp)
- Seizure is characterized by spike-and-wave discharges (SWD)
  - SWD repetition frequency: 6-8Hz
  - Seizure is defined as continuous SWD for at least 1s

Feature extraction

Complex Morlet

Average Complex Morlet response over all pre-recorded seizures:



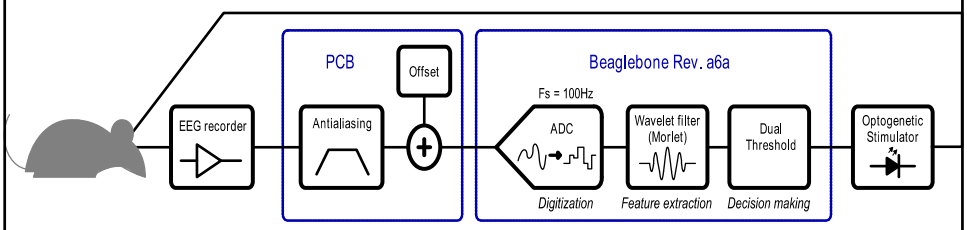
Choose 7Hz wavelet scale to implement as FIR filter

System design

- Analog pre-filter for signal conditioning
  - Anti-aliasing
  - Offset injection to match ADC input range
  - Variable gain
- ADC ($f_s = 100\text{Hz}$)
- Feature extraction: Wavelet filter
- Decision making: Dual adaptive thresholding

Custom PCB

Beaglebone



Results (simulation)

Comparison

Reference	[1]	[2]	[3]	This work
Detection Delay	4.1s	1.5s	0.97s	**0.492s**
FPPS	1.44	0.04	0.091	0.090
FNPS	0.023	0	0.065	0.040
Specificity	Unknown	Unknown	98.2%	93.6%
Sensitivity	Unknown	100%	96.2%	96.03%
ADR	Unknown	Unknown	97.2%	94.81%

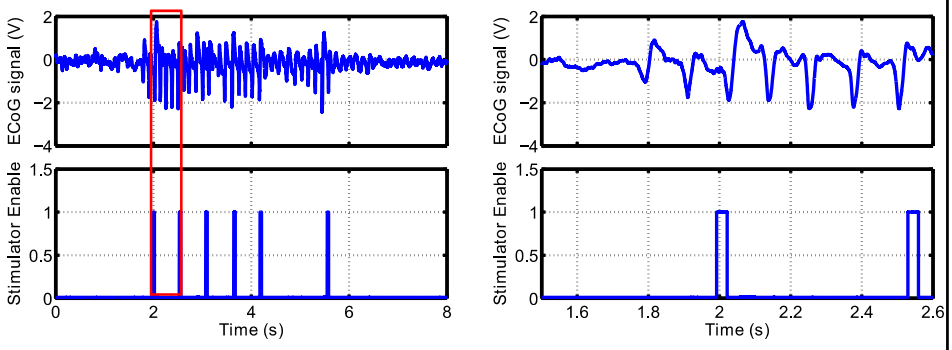
[1] R. Esteller et all. “Line length: An efficient feature for seizure onset detection,” in Proc. of the 23rd Annual EMBS International Conference, October 2001, pp. 1707–1710.

[2] I. Osorio et all, “Real-time automated detection and quantitative analysis of seizures and short-term prediction of clinical onset,” Epilepsia, vol. 39, no. 6, pp. 615–627, June 1998

[3] P. Buteneers et all, “Real-time detection of epileptic seizures in animal models using reservoir computing,” Epilepsy Research, vol. 103, no. 2-3, pp. 124–134, February 2013

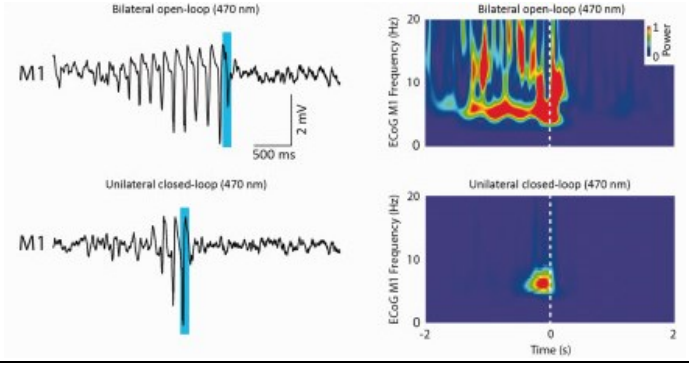
Results (measurements)

- Example of working detection



Results (measurements)

- Example of working detection
- Works well for petit-mal seizures
- More measurements needed to assess performance for grand mal



4.

Closing the loop

Tinnitus (intro)

https://www.youtube.com/watch?v=fIAjJogJ0cs

Tinnitus

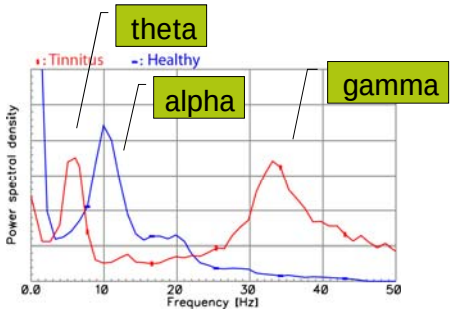
- = the perception of sound without a corresponding external sound
- Due to a restructuring of the auditory cortex
- Approximately a billion people suffer from tinnitus worldwide
- In 2% - 3% of the population, tinnitus can lead to insomnia, anxiety and depression.
- No proven treatments for tinnitus
- Some patients benefit from **electrical brain stimulation**.

http://instagram.com/marleen.serdijn/

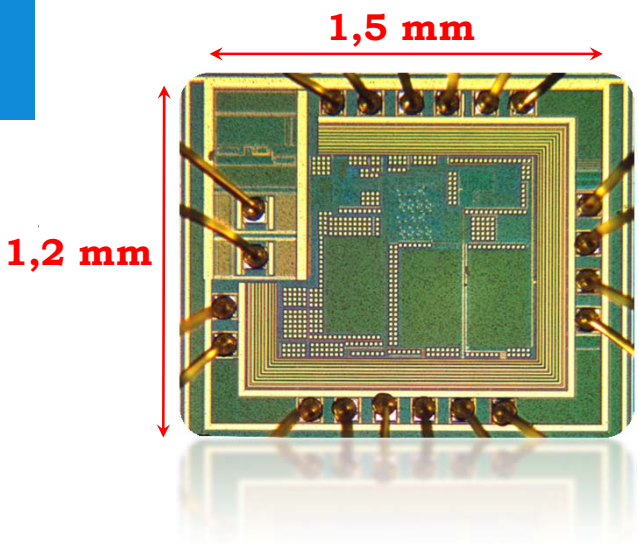
Tinnitus detection and treatment

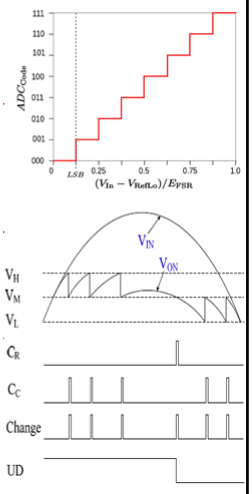
Current stimulation
- requires a patients **subjective** opinion to select an individualized stimulation therapy.

Future stimulation
- Based on an automatic, **objective** tinnitus detector
- to automatically adapt and choose stimulation therapy, in a closed-loop manner.



Neural recording amplifier IC



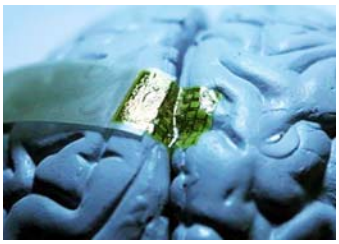


5.

Where it all may lead to…

The plan

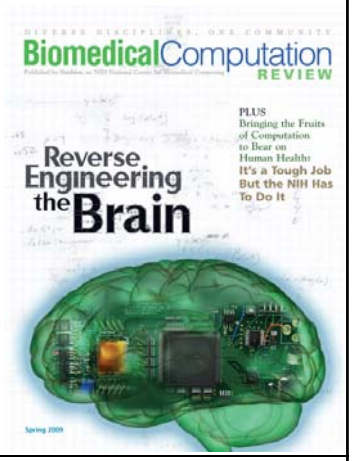
- To design a flexible brain implant for the effective treatment of tinnitus
- To serve as a platform for various types of implantables
- Use a polymer as a substrate
- Use silicon as base material for
  - Electrodes
  - Electronic circuits
    - To measure the brain signals
    - To electrically stimulate brain tissue
    - To power and control the implant
  - Battery foil
  - Antenna
    - For RF energy harvesting
    - And wireless communication



Picture courtesy of University of Pennsylvania

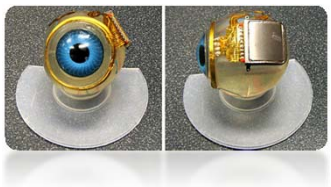
Relevance

- Directly linked to 3 out of 14 Grand Engineering Challenges
  - 4. Reverse-engineer the brain
  - 7. Engineer the tools of scientific discovery
  - 11. Engineer better medicines



Medical impact (1)

- Better treatment of urge incontinence
- **Restore hearing (cochlear implant)**
- Restore sense of balance (vestibular implant)
- Restore sight (ocular implant)
- Better understanding of the peripheral nervous system
- Better treatment of pain (spinal cord implant)
- **Better understanding of the central nervous system**
- **Better understanding of the brain**
- Better brain-machine interfaces



Medical impact (2)

Better treatment of brain disorders

- **Better treat tinnitus and auditory hallucinations,**
- **Better treat addictions (a.o. alcoholism),**
- Better treat essential tremor, Parkinson, dystonia
- Better treat urge incontinence,
- Better treat migraine, cluster headaches and other forms of headache
- Better treat psychoneuroimmunological disorders
- Better treat chronic, phantom and neuropathic pain,
- Better treat depression, mania
- Better treat OCD spectrum disorders
- Better treat PTSD and anxiety
- Better treat schizophrenia
- **Better treat epilepsy**
- Treat autism,
- Treat dementia, including Alzheimer's disease
- Treat Tourette's syndrom, minimally conscious state (MCS) after traumatic brain injury, obesity, anorexia

[Reference: C.O. Oluigbo, A.R. Recai, Addressing Neurological Disorders With Neuromodulation, IEEE Transactions on Biomedical Engineering, Vol. 58, No. 7, July 2011]

2057 The Body

Search for "2057 The Body" on YouTube

Conclusions

- Neurostimulation:
  - Small!
  - Energy efficient
- Chips:
  - Full functionality on a few sq. mm
- Neurorecording:
  - Reliable detection of epileptic seizures
- Closing the loop:
  - Objective detection of tinnitus
- The plan
  - Flexible brain implant
- A glimpse into the future (2057)

Beter worden met elektriciteit en electroceutica

- Dank voor uw aandracht
- Dank2 Han Vrijling en Adriaan de Lange voor de uitnodiging
- Meer info: http://bioelectronics.tudelft.nl