Close loop

Guglielmo Foffani

CINAC, Hospital Universitario HM Puerta del Sur, Móstoles, Madrid

Hospital Nacional de Parapléjicos, Toledo

Closed-loop deep brain stimulation

Guglielmo Foffani

CINAC, Hospital Universitario HM Puerta del Sur, Móstoles, Madrid

Hospital Nacional de Parapléjicos, Toledo

Historical perspective

Conflicts of interest

Conflicts of interest

Newronika s.p.a. (Italy)

Conflicts of interest

Newronika s.p.a. (Italy)

Conflicts of interest

Newronika s.p.a. (Italy)

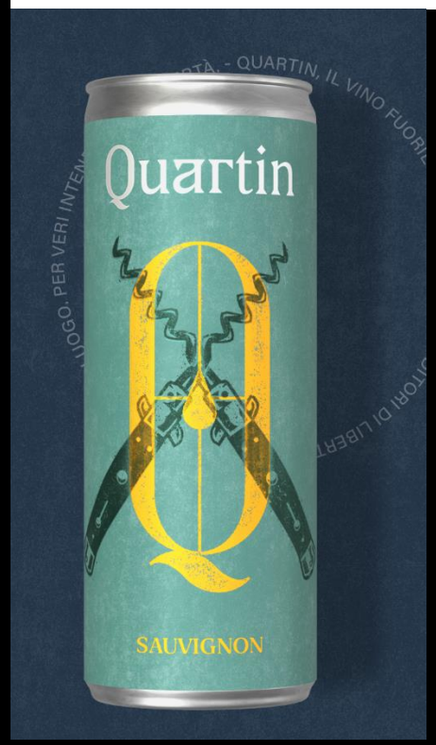
Neurek SL (Spain)

Conflicts of interest

Newronika s.p.a. (Italy)

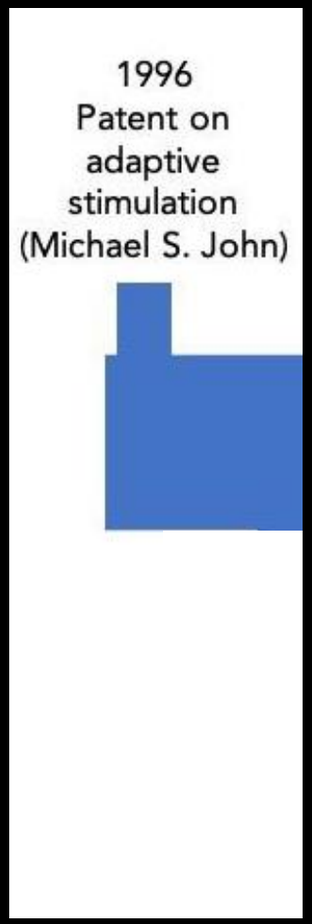
Neurek SL (Spain)

Minuscola s.r.l. (Italy)



Historical perspective

Historical perspective



US006066163A

United States Patent [19]

John

[11] **Patent Number: 6,066,163**

[45] **Date of Patent: May 23, 2000**

[54] **ADAPTIVE BRAIN STIMULATION METHOD AND SYSTEM**

[76] Inventor: **Michael Sasha John**, 1010 Orienta Ave., Mamaroneck, N.Y. 10543

[21] Appl. No.: **08/596,450**

[22] Filed: **Feb. 2, 1996**

[51] **Int. Cl.**[7] **A61N 1/32**; A61N 1/18

[52] **U.S. Cl.** **607/45**; 607/48; 607/62

[58] **Field of Search** 607/45, 48, 62, 607/65, 72

[56] **References Cited**

U.S. PATENT DOCUMENTS

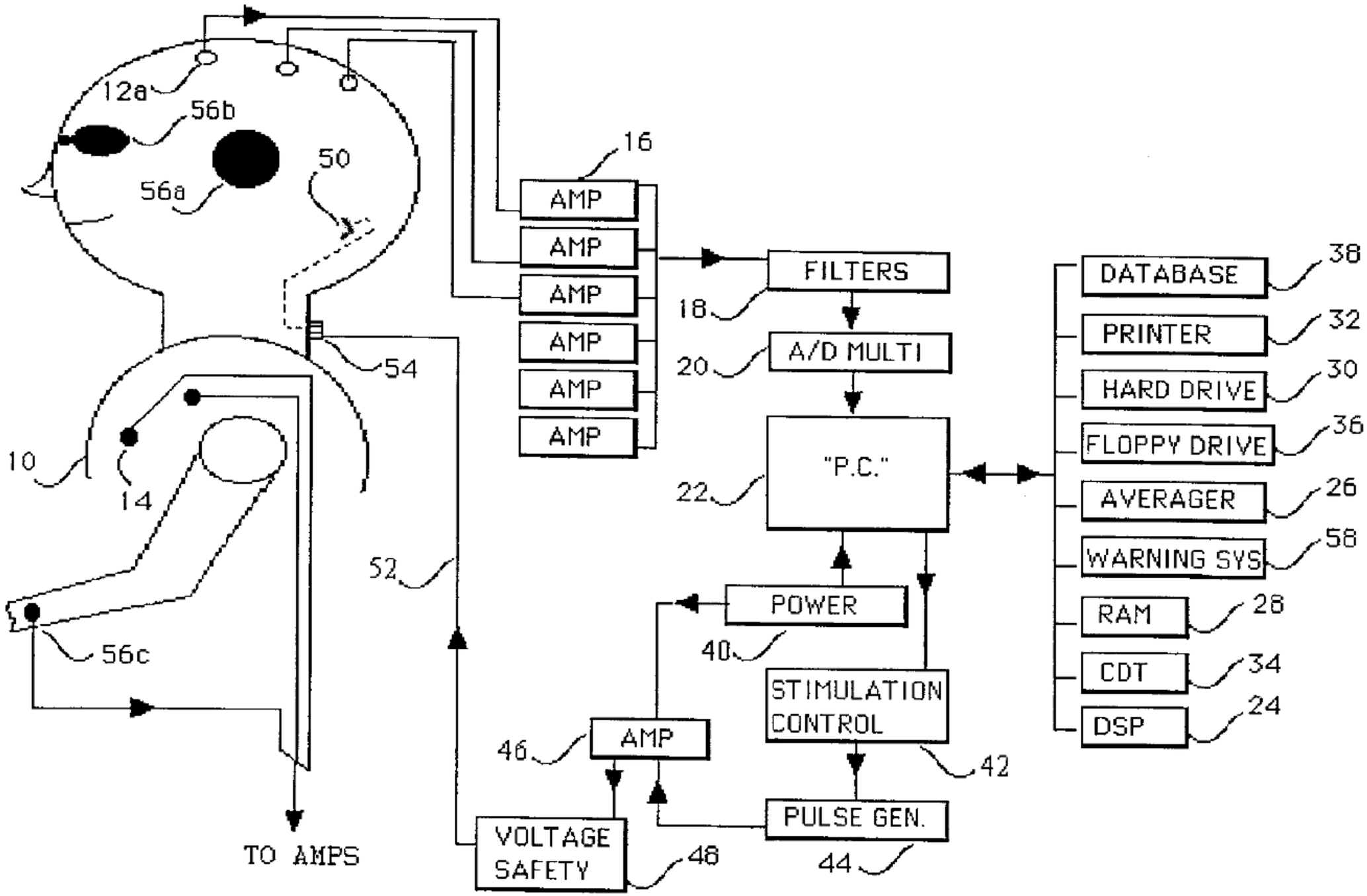
3,850,161	11/1974	Liss	607/45
3,918,461	11/1975	Cooper	607/72
4,305,402	12/1981	Katims	607/62
4,505,275	3/1985	Chen	607/62
5,269,302	12/1993	Swartz et al.	607/45
5,540,734	7/1996	Zabara	607/72
5,571,150	11/1996	Wernicke et al.	607/72
5,611,350	3/1997	John .	
5,683,422	11/1997	Rise .	

Primary Examiner—William E. Kamm
Assistant Examiner—Carl H. Layno
Attorney, Agent, or Firm—Michael S. John

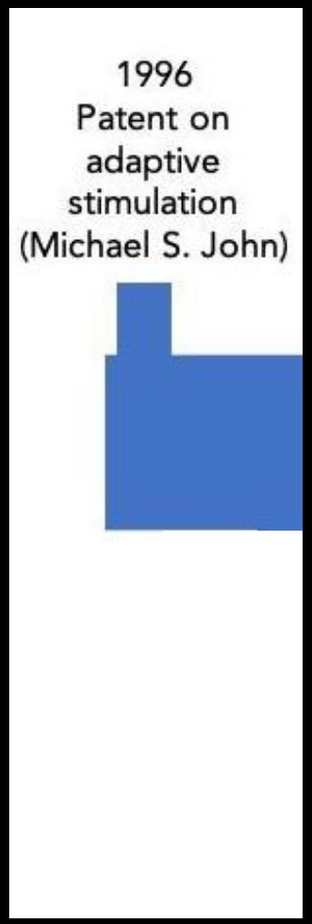
[57] **ABSTRACT**

An adaptive brain stimulation system and method is described which aids in the rehabilitation of patients from traumatic brain injury, coma, or other brain dysfunction. After a direct brain stimulator is implanted in a brain region of a patient, the patient is stimulated according to a set of stimulation parameters. A present state is measured and compared to a reference state by statistical and medically relevant criteria. The subsequent program of stimulation is dependent upon the outcome of the comparison. An adaptive brain stimulation and reinforcement system and method is also described in which a second area of the brain is stimulated when stimulation of the first brain area produces a desired effect, thereby reinforcing the prior response of the brain.

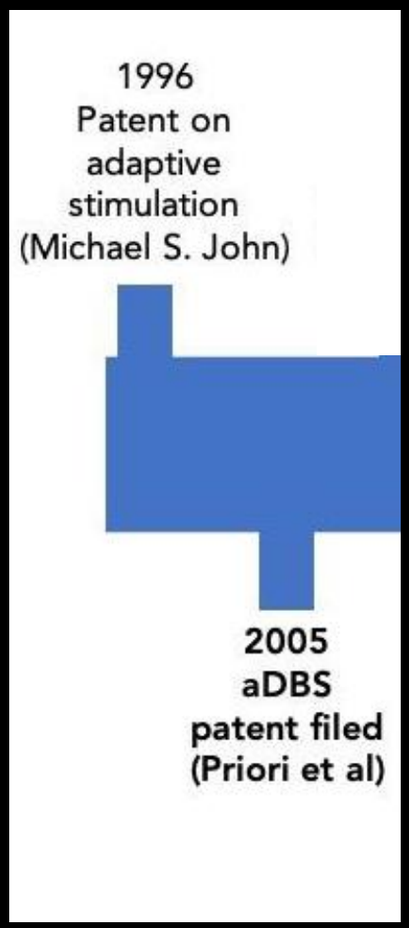
30 Claims, 4 Drawing Sheets


12a
56b
50
56a
16
AMP
AMP
AMP
AMP
AMP
AMP
FILTERS
18
A/D MULTI
20
"P.C."
22
DATABASE
38
PRINTER
32
HARD DRIVE
30
FLOPPY DRIVE
36
AVERAGER
26
WARNING SYS
58
RAM
28
CDT
34
DSP
24
54
10
14
56c
52
TO AMPS
POWER
40
STIMULATION CONTROL
42
AMP
46
VOLTAGE SAFETY
48
PULSE GEN.
44

Historical perspective



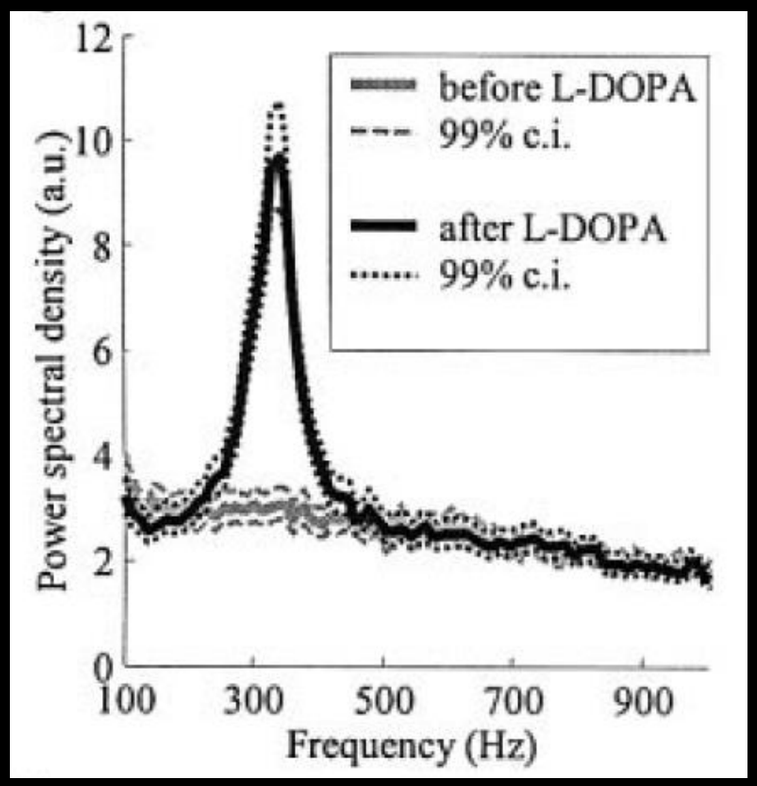
Historical perspective

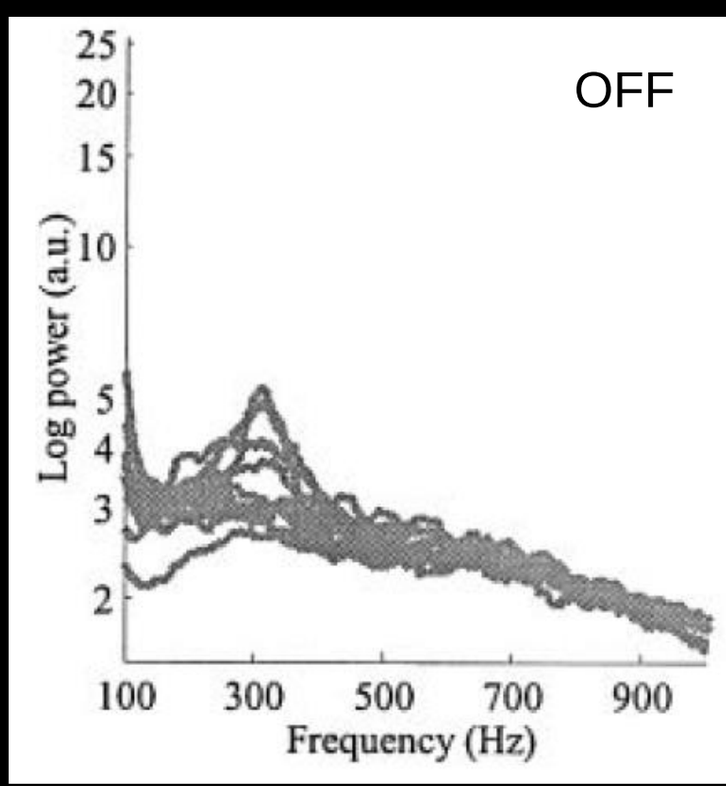


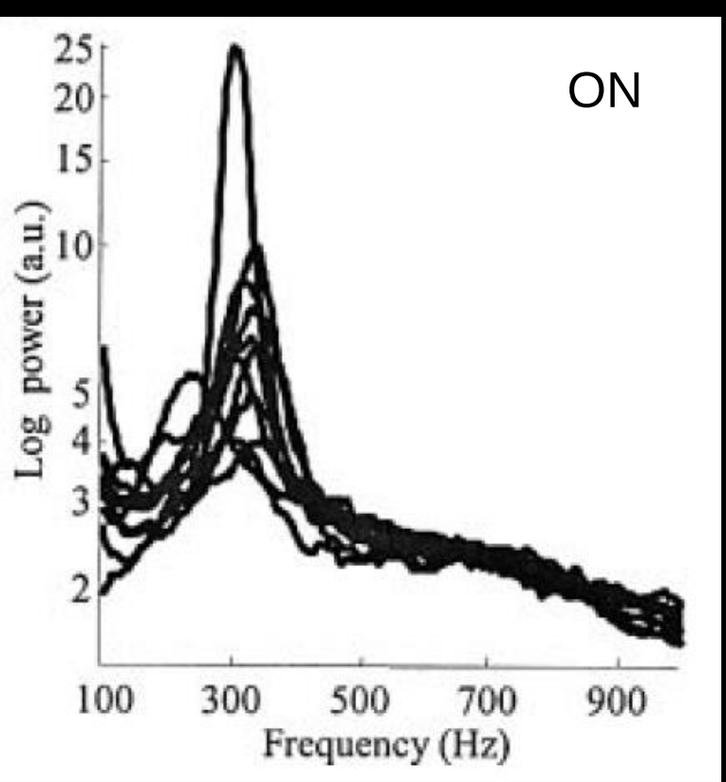
DOI: 10.1093/brain/awg229 Advanced Access publication August 21, 2003 *Brain* (2003), **126,** 2153–2163

300-Hz subthalamic oscillations in Parkinson's disease

G. Foffani,[1,2,4*] A. Priori,[1*] M. Egidi,[1] P. Rampini,[1] F. Tamma,[3] E. Caputo,[3] K. A. Moxon,[4] S. Cerutti[2] and S. Barbieri[1]



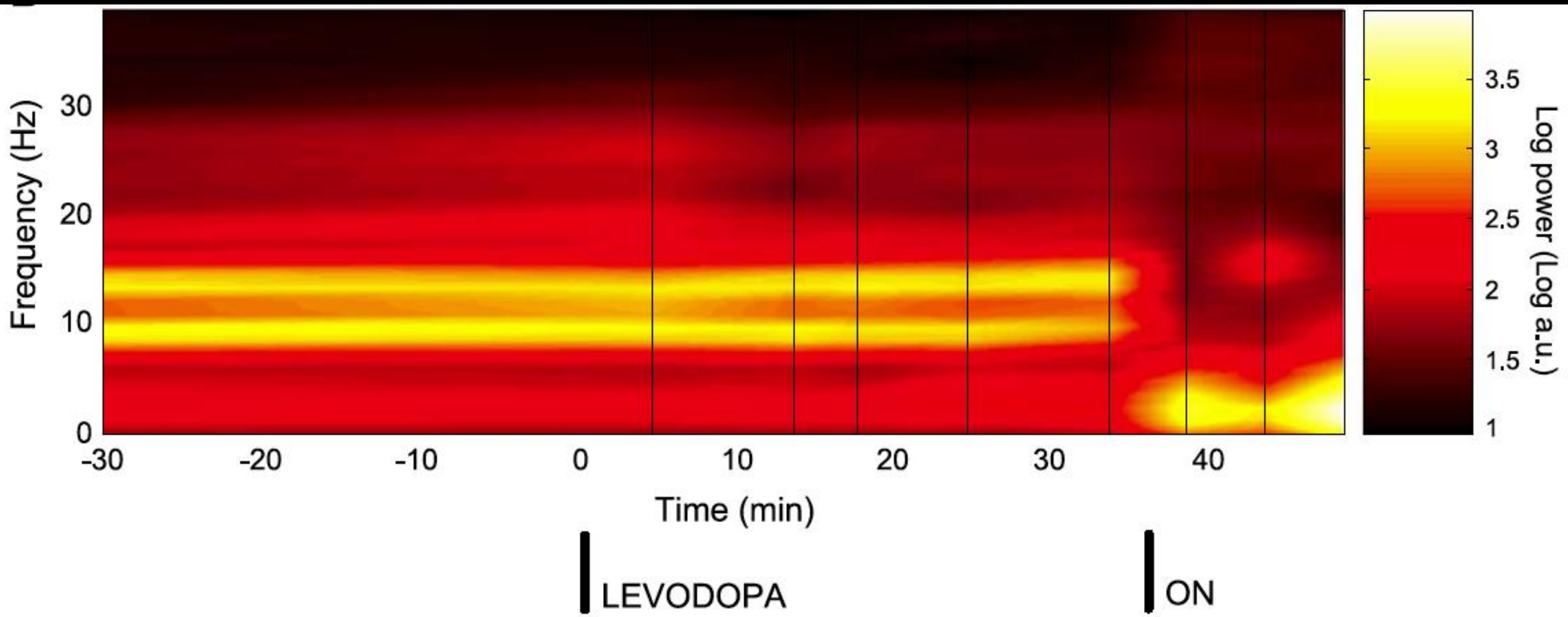




Experimental Neurology 189 (2004) 369–379

Rhythm-specific pharmacological modulation of subthalamic activity in Parkinson's disease

A. Priori[a,*,1], G. Foffani[b,c,1], A. Pesenti[a], F. Tamma[d], A.M. Bianchi[b], M. Pellegrini[b], M. Locatelli[a], K.A. Moxon[c], R.M. Villani[a]



(19) **United States**

(12) **Patent Application Publication**

Foffani et al.

(10) **Pub. No.: US 2008/0269836 A1**

(43) **Pub. Date: Oct. 30, 2008**

(54) **APPARATUS FOR TREATING NEUROLOGICAL DISORDERS BY MEANS OF CHRONIC ADAPTIVE BRAIN STIMULATION AS A FUNCTION OF LOCAL BIOPOTENTIALS**

(75) Inventors: **Guglielmo Foffani**, Milano (IT); **Alberto Priori**, Virgilio (Mantova) (IT); **Lorenzo Rossi**, Trento (IT)

Correspondence Address:
PEARNE & GORDON LLP
1801 EAST 9TH STREET, SUITE 1200
CLEVELAND, OH 44114-3108 (US)

(73) Assignee: **UNIVERSITA' DEGLI STUDI DI MILANO**, I-20122 MILANO (IT)

(21) Appl. No.: **12/091,313**

(22) PCT Filed: **Aug. 3, 2006**

(86) PCT No.: **PCT/IB2006/002184**

§ 371 (c)(1),
(2), (4) Date: **Apr. 24, 2008**

(30) **Foreign Application Priority Data**

Oct. 28, 2005 (IT) MI2005A002061

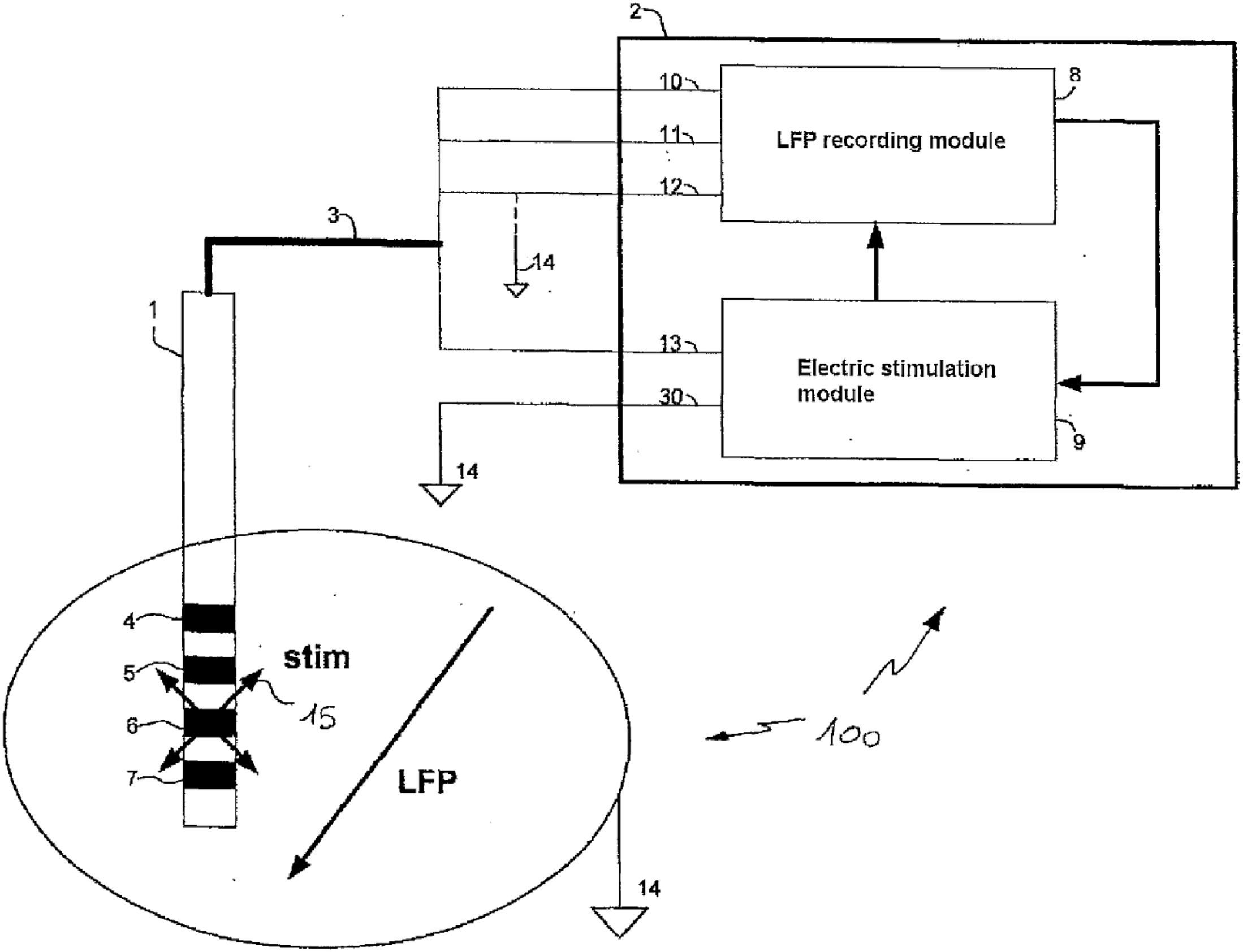
Publication Classification

(51) **Int. Cl.**
A61N 1/05 (2006.01)

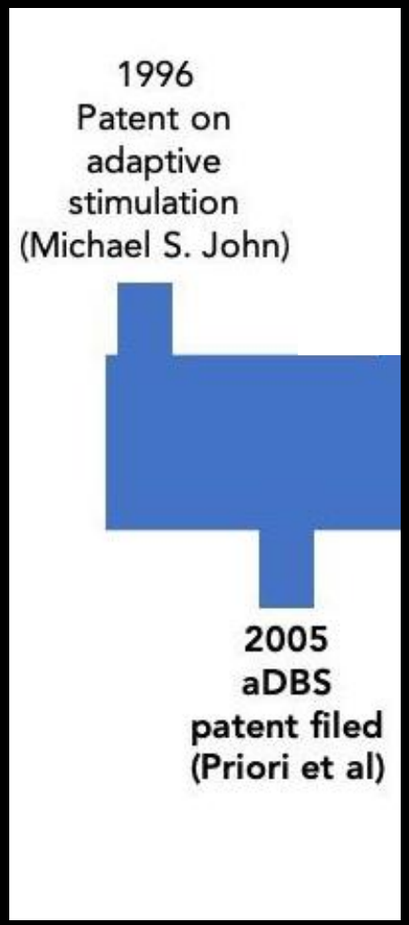
(52) **U.S. Cl.** **607/45**

(57) **ABSTRACT**

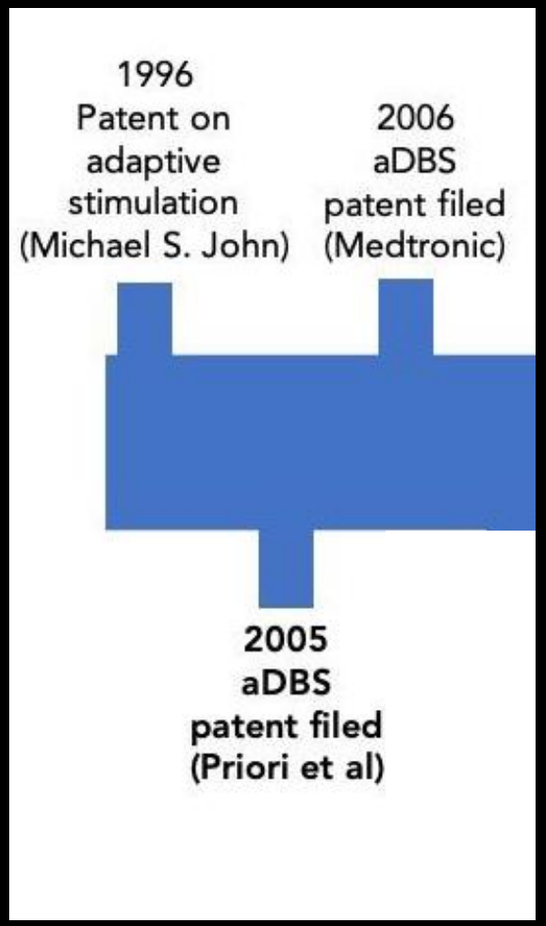
An apparatus and a related method for the deep brain stimulation have been invented wherein the parameters of the stimulation supplied at the human nervous system level are adjusted and optimized continuously by the analysis of the bioelectric signals coming from the tissue adjacent the stimulation electrode itself, adapting the therapy continuously and in line to the patient's clinical state. The apparatus is constituted at least by an electro-catheter (**1**) implantable in a patient's brain and equipped with four contacts (**4**, **5**, **6**, **7**). Then, there is at least a stimulation module (**9**) which generates the stimulating signal (**15**) sent to the electro-catheter (**1**) and in particular to one of the contacts thereof (**6**). The electro-catheter (**1**) contemporarily sends a signal characterizing the brain activity coming from the tissue involved by the stimulating signal (**15**) to an acquisition module (**8**). The characterizing signal is used to determine the feedback of the stimulation parameters (**15**) and, consequently, to adapt the therapy continuously to the patient's clinical state.


2
10
11
12
8
LFP recording module
3
14
1
13
Electric stimulation module
30
9
14
4
5
6
7
stim
15
LFP
14
100

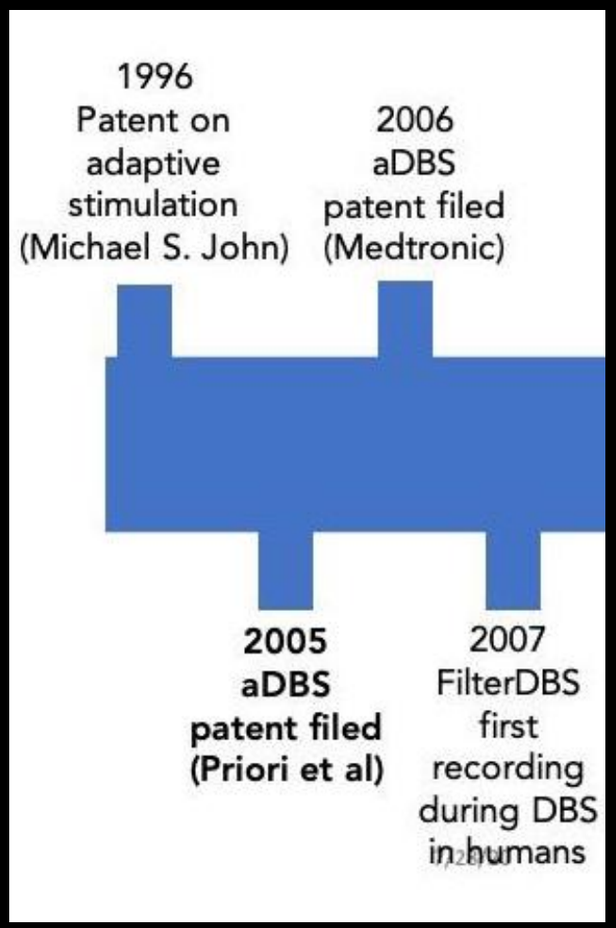
Historical perspective



Historical perspective



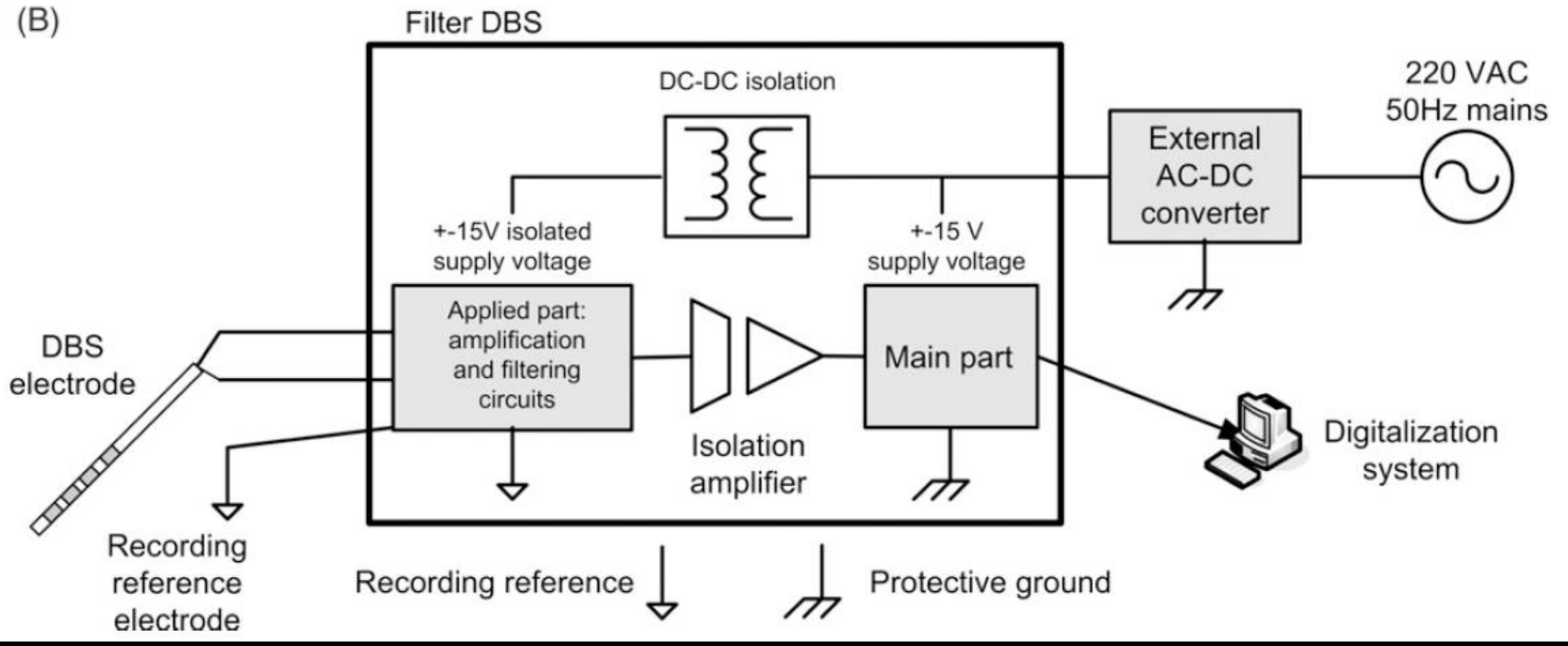
Historical perspective



IOP Publishing
J. Neural Eng. **4** (2007) 96–106
Journal of Neural Engineering
doi:10.1088/1741-2560/4/2/010

An electronic device for artefact suppression in human local field potential recordings during deep brain stimulation

L Rossi[1,5], G Foffani[2,3,5], S Marceglia[1], F Bracchi[4], S Barbieri[1] and A Priori[6]

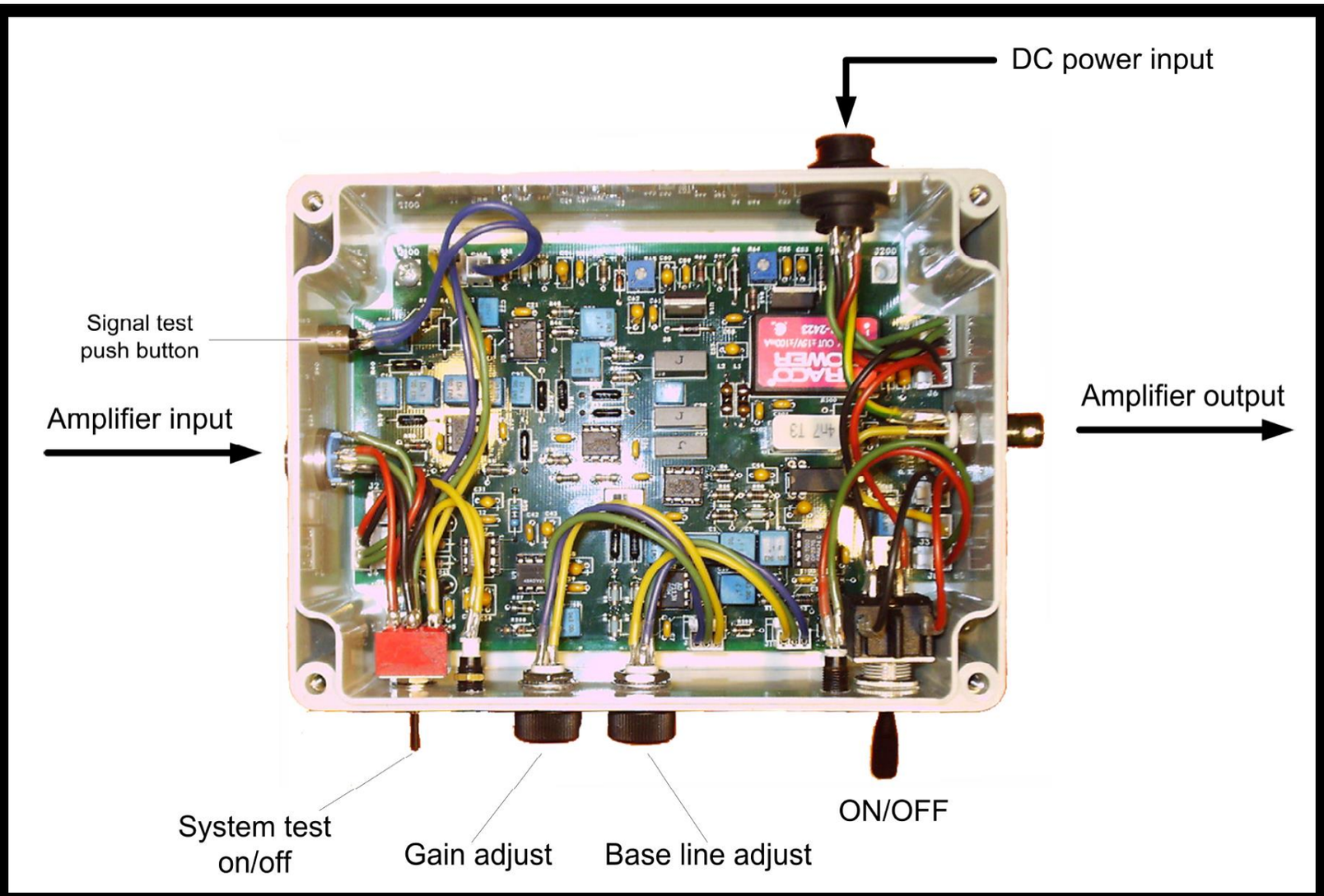


IOP PUBLISHING JOURNAL OF NEURAL ENGINEERING

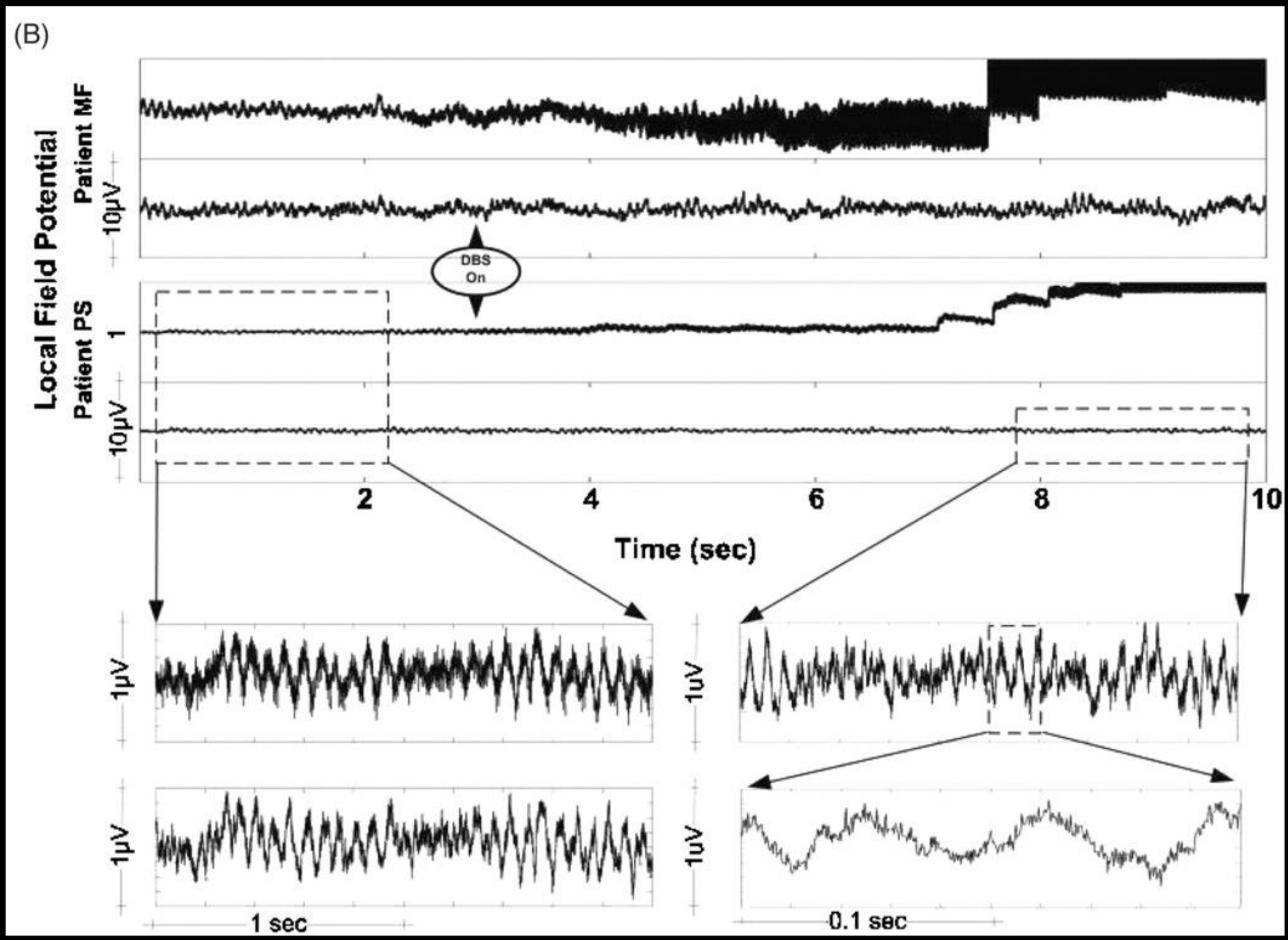
J. Neural Eng. **4** (2007) 96–106 doi:10.1088/1741-2560/4/2/010

An electronic device for artefact suppression in human local field potential recordings during deep brain stimulation

L Rossi[1,5], G Foffani[2,3,5], S Marceglia[1], F Bracchi[4], S Barbieri[1] and A Priori[6]

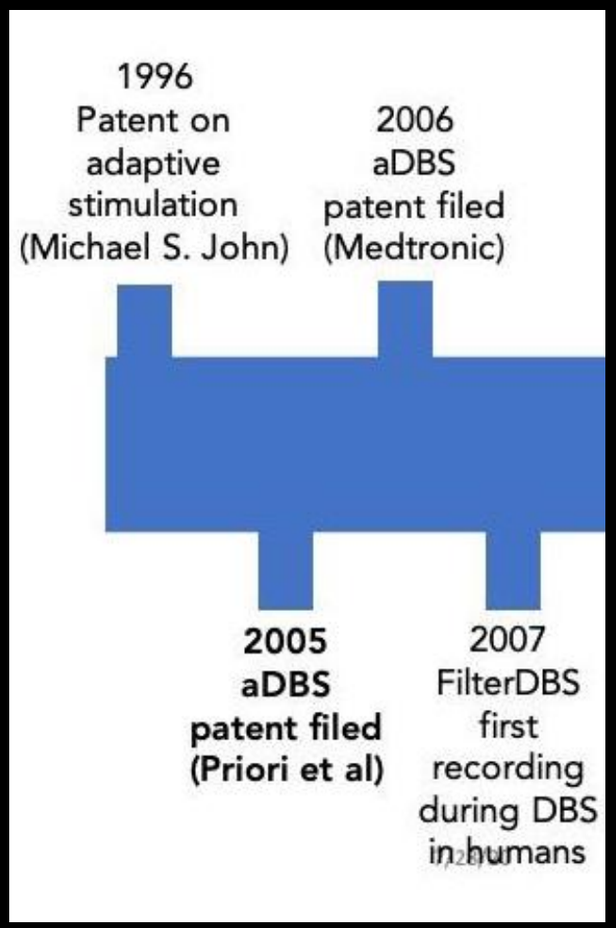


(B)

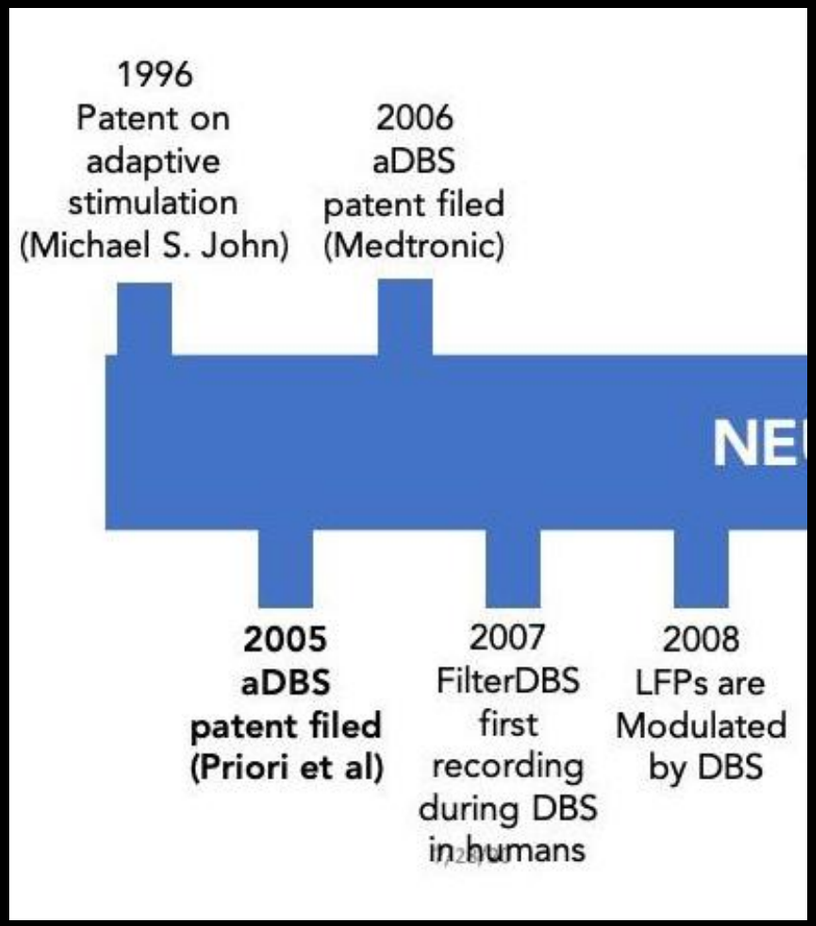


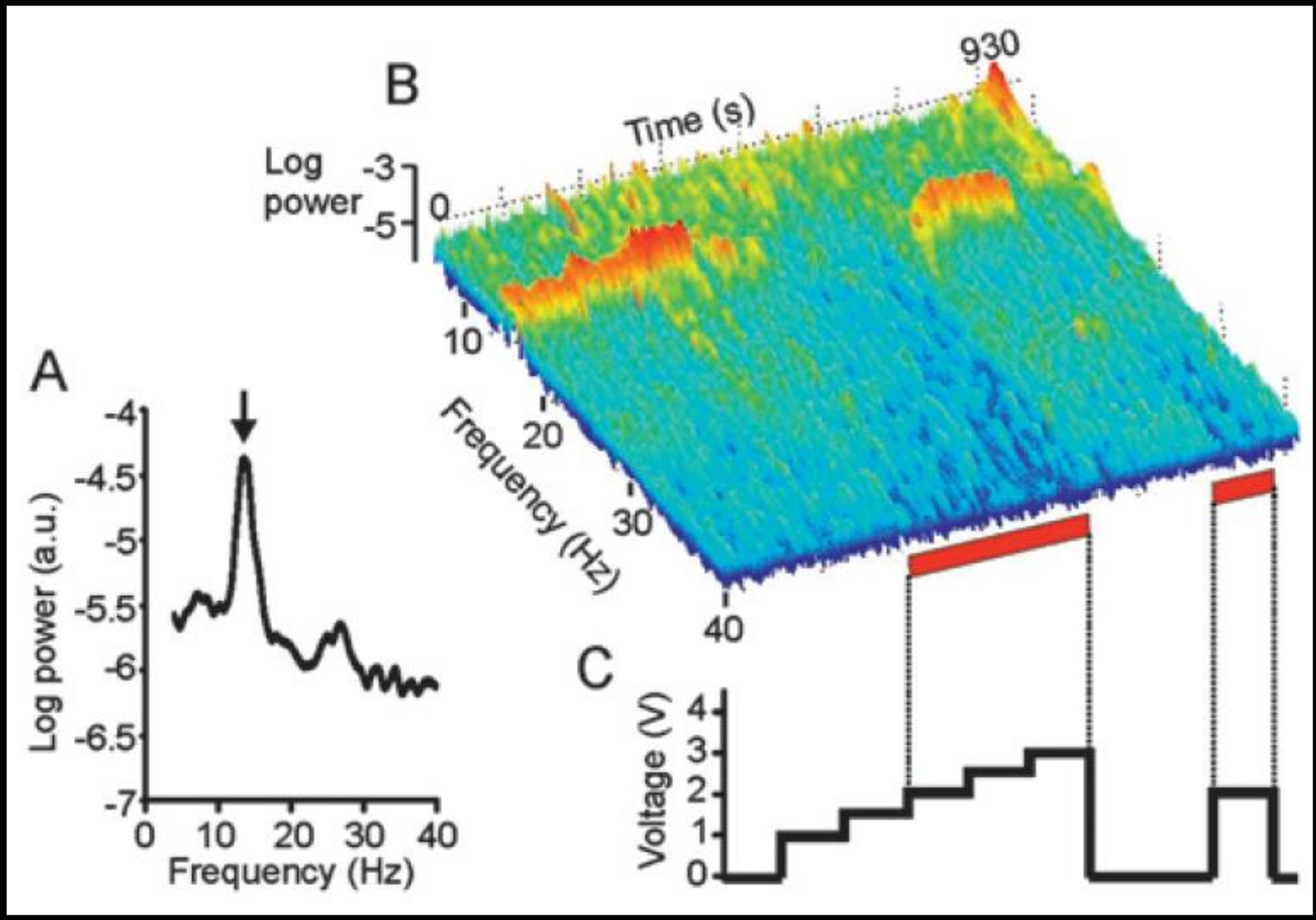
Rossi et al., J Neural Eng 2007

Historical perspective



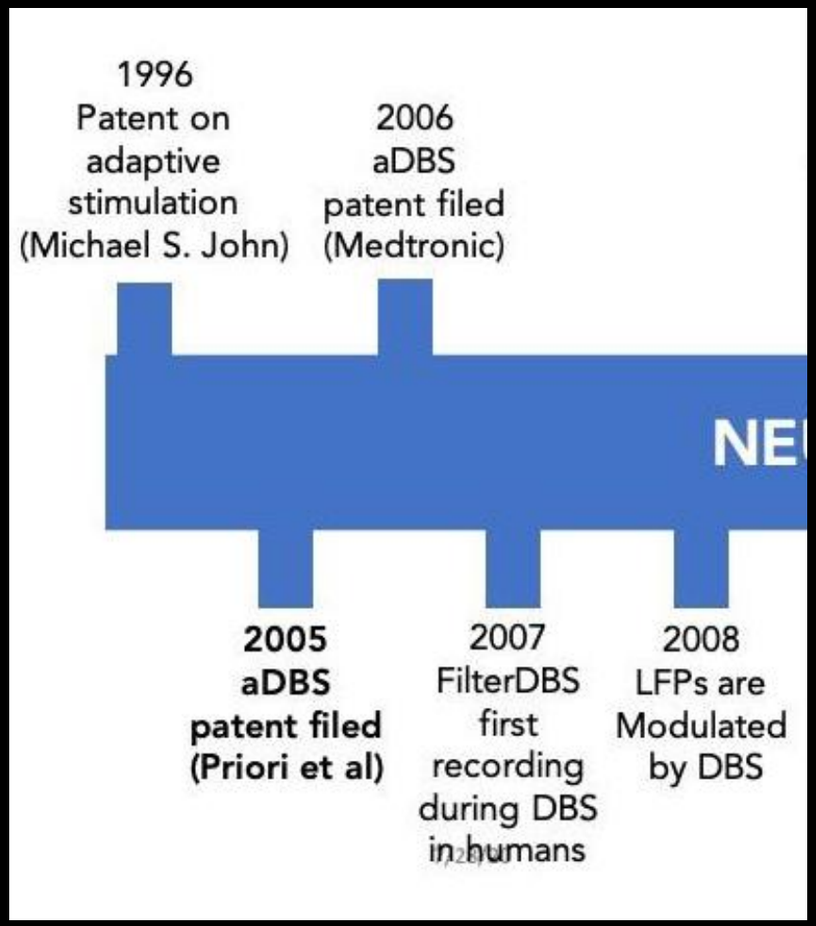
Historical perspective



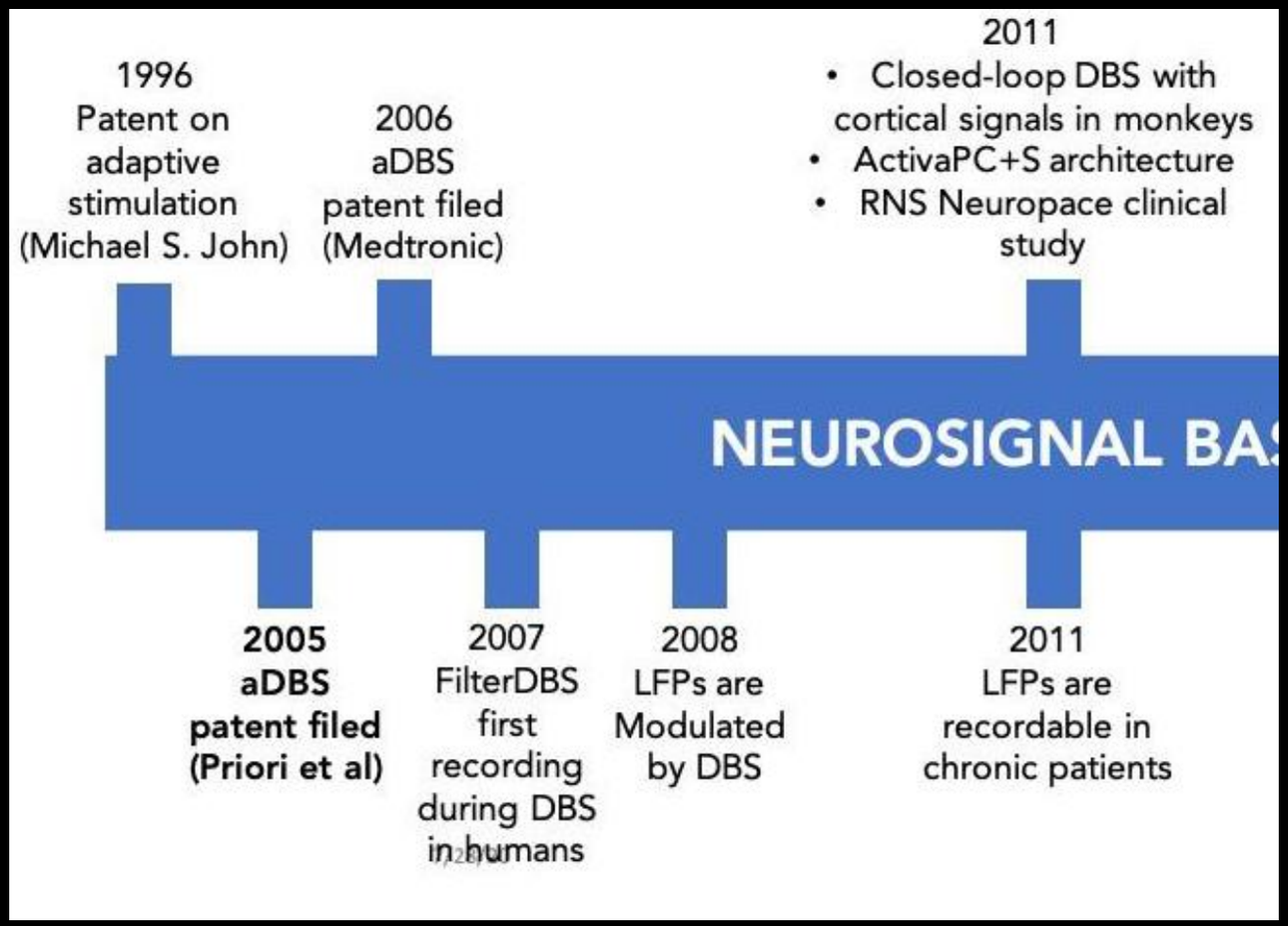


Eusebio et al., JNNP 2011

Historical perspective



Historical perspective



Responsive cortical stimulation for the treatment of medically intractable partial epilepsy

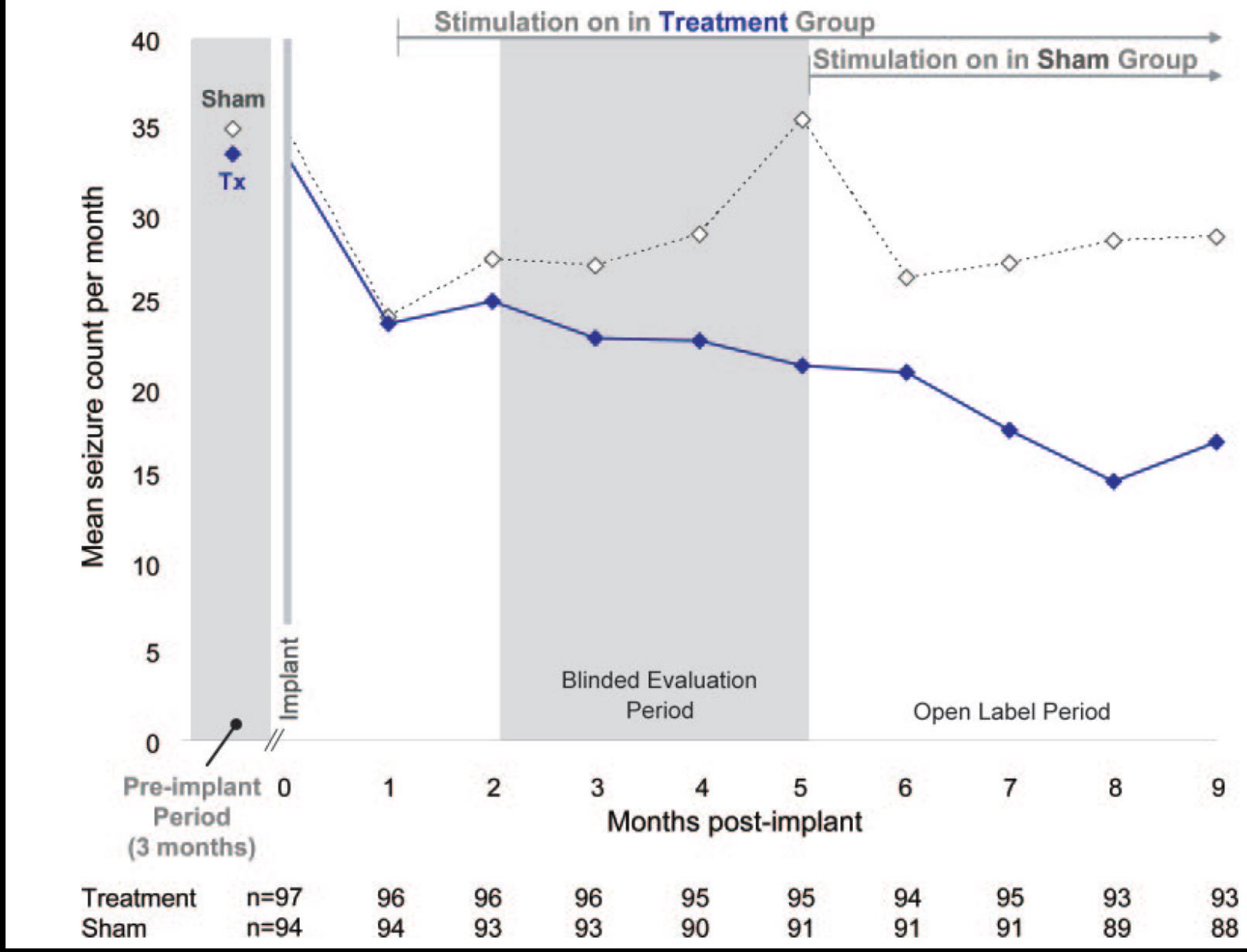
Martha J. Morrell, MD
On behalf of the RNS System in Epilepsy Study Group

ABSTRACT

Objectives: This multicenter, double-blind, randomized controlled trial assessed the safety and effectiveness of responsive cortical stimulation as an adjunctive therapy for partial onset seizures in adults with medically refractory epilepsy.

Morrell et al., Neurology 2011

Figure 2 Mean disabling seizures by month, observed data



Morrell et al., Neurology 2011

Cell PRESS

Neuron
Article

Closed-Loop Deep Brain Stimulation Is Superior in Ameliorating Parkinsonism

Boris Rosin,[1,*] Maya Slovik,[1] Rea Mitelman,[1,2] Michal Rivlin-Etzion,[1,2] Suzanne N. Haber,[3] Zvi Israel,[4] Eilon Vaadia,[1,2,5] and Hagai Bergman[1,2,5]

[1]Department of Medical Neurobiology (Physiology), The Institute for Medical Research Israel-Canada, The Hebrew University-Hadassah Medical Association School of Medicine and Hadassah University Hospital, Jerusalem 91120, Israel

[2]The Interdisciplinary Center for Neural Computation, Givat Ram Campus, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

[3]Department of Pharmacology and Physiology, School of Medicine and Dentistry, University of Rochester, Rochester, NY 14642, USA

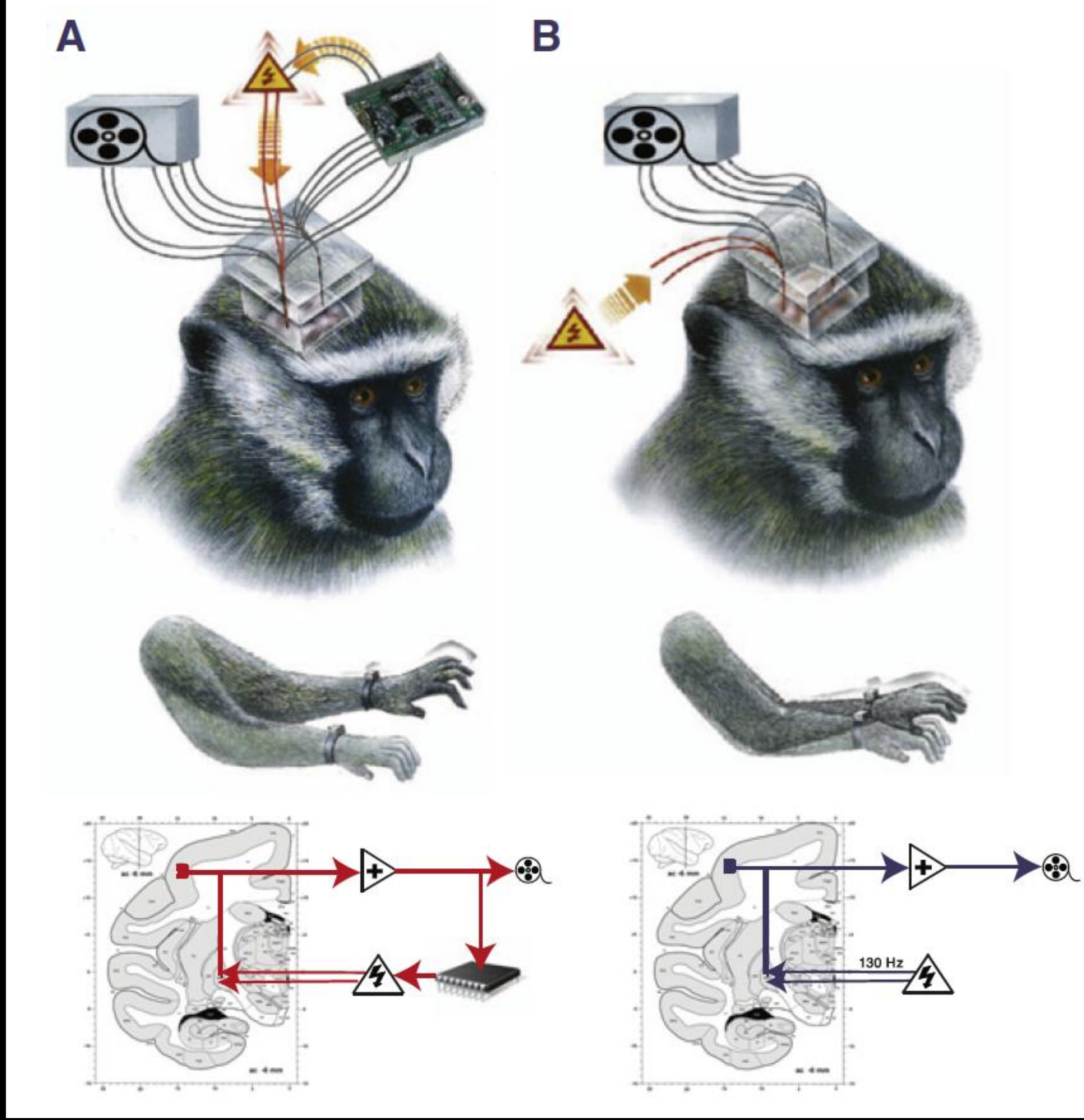
[4]Center for Functional & Restorative Neurosurgery, The Hebrew University-Hadassah Medical Association School of Medicine and Hadassah University Hospital, Jerusalem 91120, Israel

[5]The Edmond & Lily Safra Center for Brain Sciences, Givat Ram Campus, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

*Correspondence: boris.rosin@mail.huji.ac.il

DOI 10.1016/j.neuron.2011.08.023

Rosin et al., Neuron 2011



Rosin et al., Neuron 2011

IOP PUBLISHING JOURNAL OF NEURAL ENGINEERING

J. Neural Eng. **8** (2011) 036018 (19pp) doi:10.1088/1741-2560/8/3/036018

A chronic generalized bi-directional brain–machine interface

A G Rouse[1], S R Stanslaski[2], P Cong[2], R M Jensen[2], P Afshar[2], D Ullestad[2], R Gupta[3], G F Molnar[3], D W Moran[1] and T J Denison[2]

[1] Department of Biomedical Engineering, Washington University, St Louis, MO, USA
[2] Neural Engineering, Medtronic Neuromodulation, Minneapolis, MN, USA
[3] Neurostimulation Research, Medtronic Neuromodulation, Minneapolis, MN, USA

IOP PUBLISHING JOURNAL OF NEURAL ENGINEERING

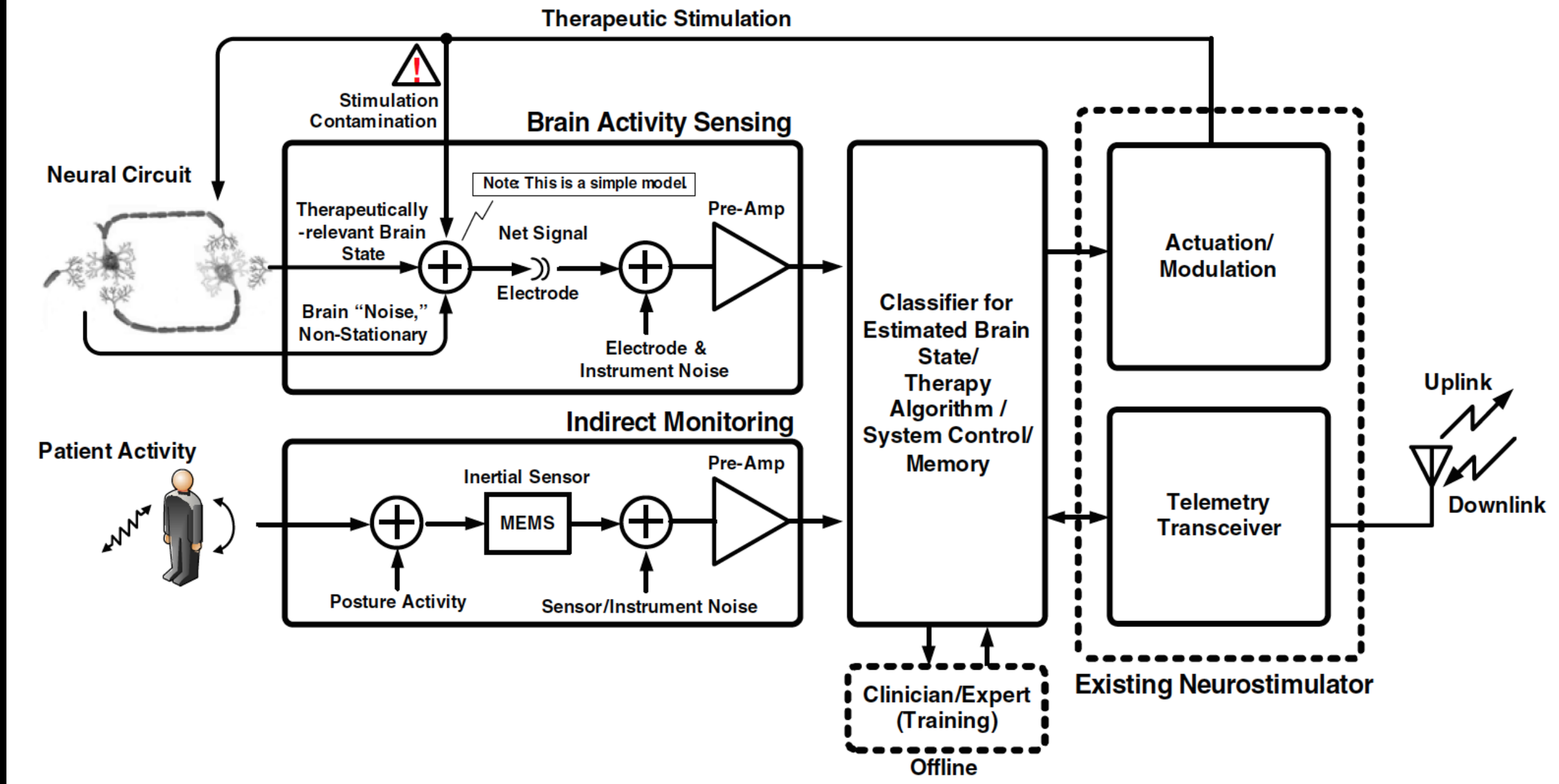
J. Neural Eng. **8** (2011) 036018 (19pp) doi:10.1088/1741-2560/8/3/036018

A chronic generalized bi-directional brain–machine interface

A G Rouse[1], S R Stanslaski[2], P Cong[2], R M Jensen[2], P Afshar[2], D Ullestad[2], R Gupta[3], G F Molnar[3], D W Moran[1] and T J Denison[2]

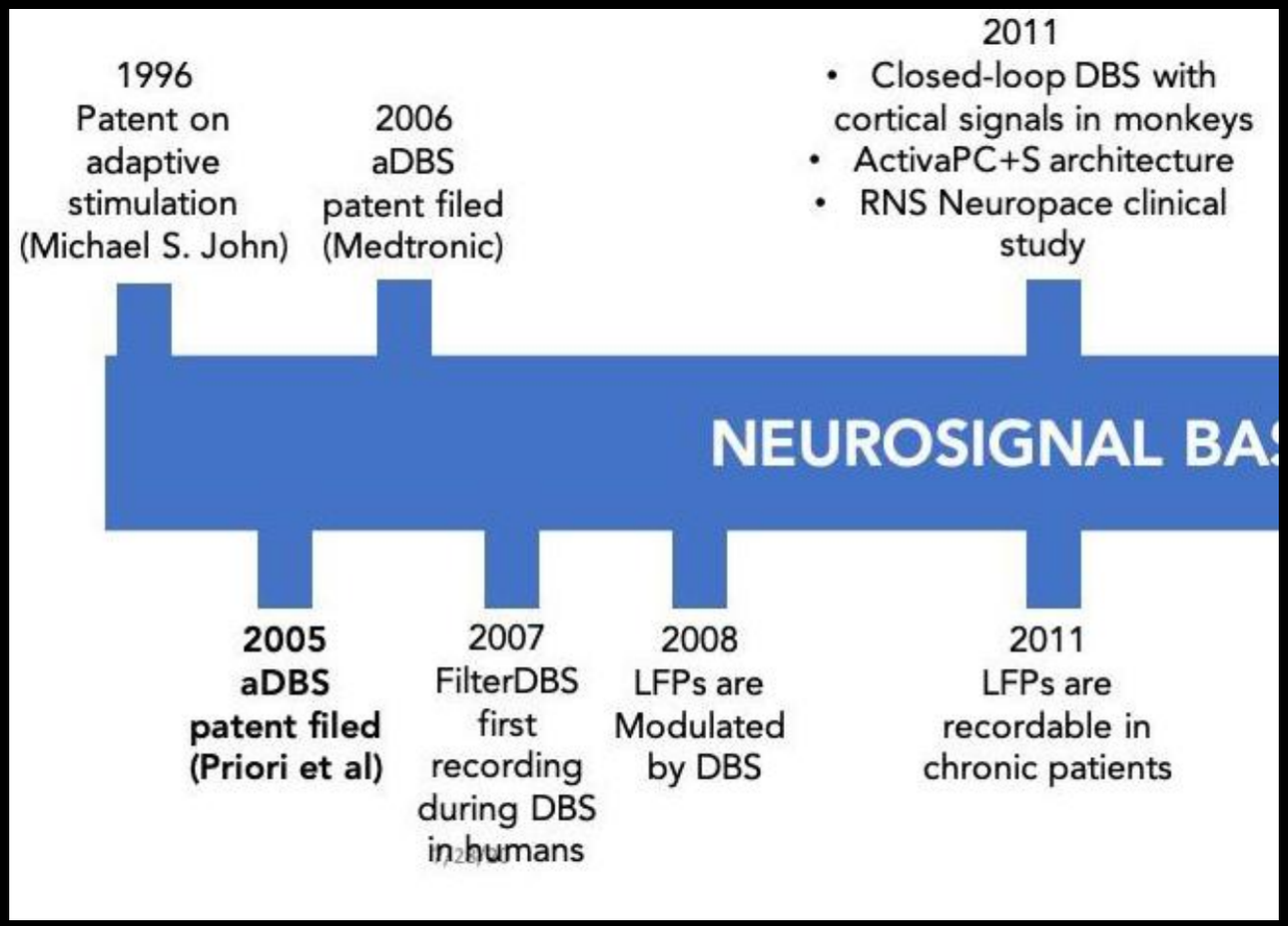
[1] Department of Biomedical Engineering, Washington University, St Louis, MO, USA
[2] Neural Engineering, Medtronic Neuromodulation, Minneapolis, MN, USA
[3] Neurostimulation Research, Medtronic Neuromodulation, Minneapolis, MN, USA

Architecture of the Medtronic ActivaPC+S

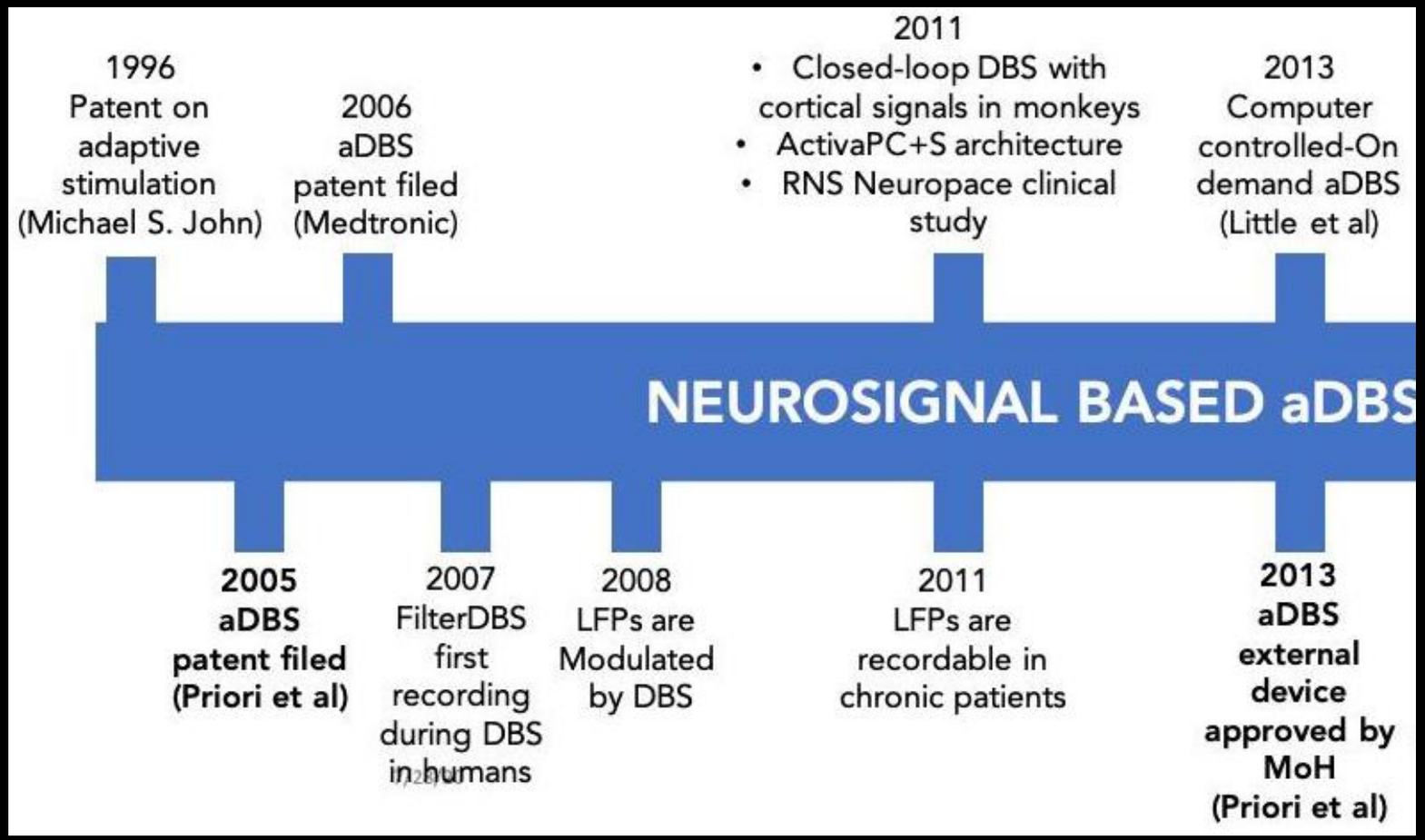


Rouse et al., J Neural Eng 2011

Historical perspective



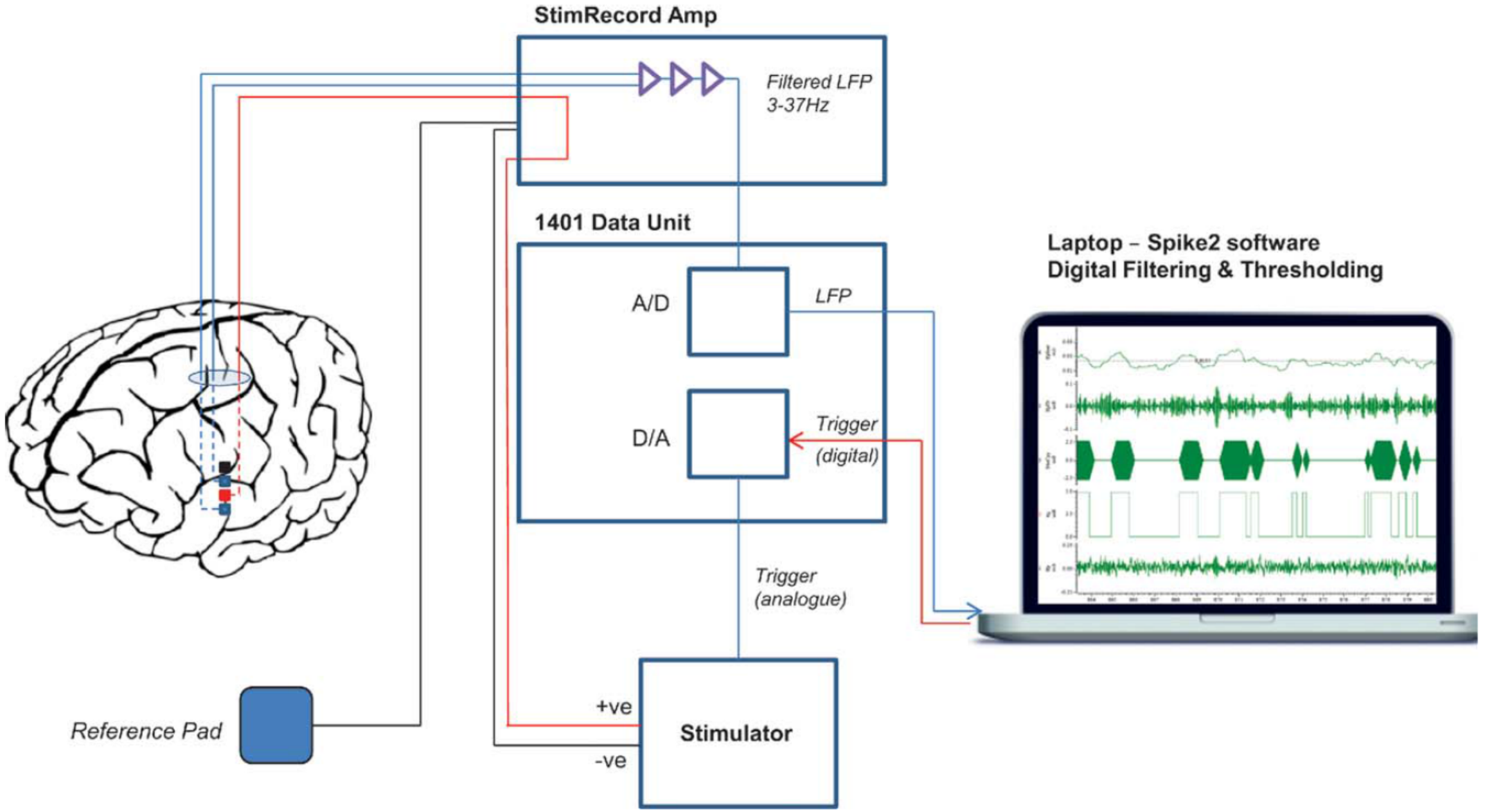
Historical perspective



Adaptive Deep Brain Stimulation in Advanced Parkinson Disease

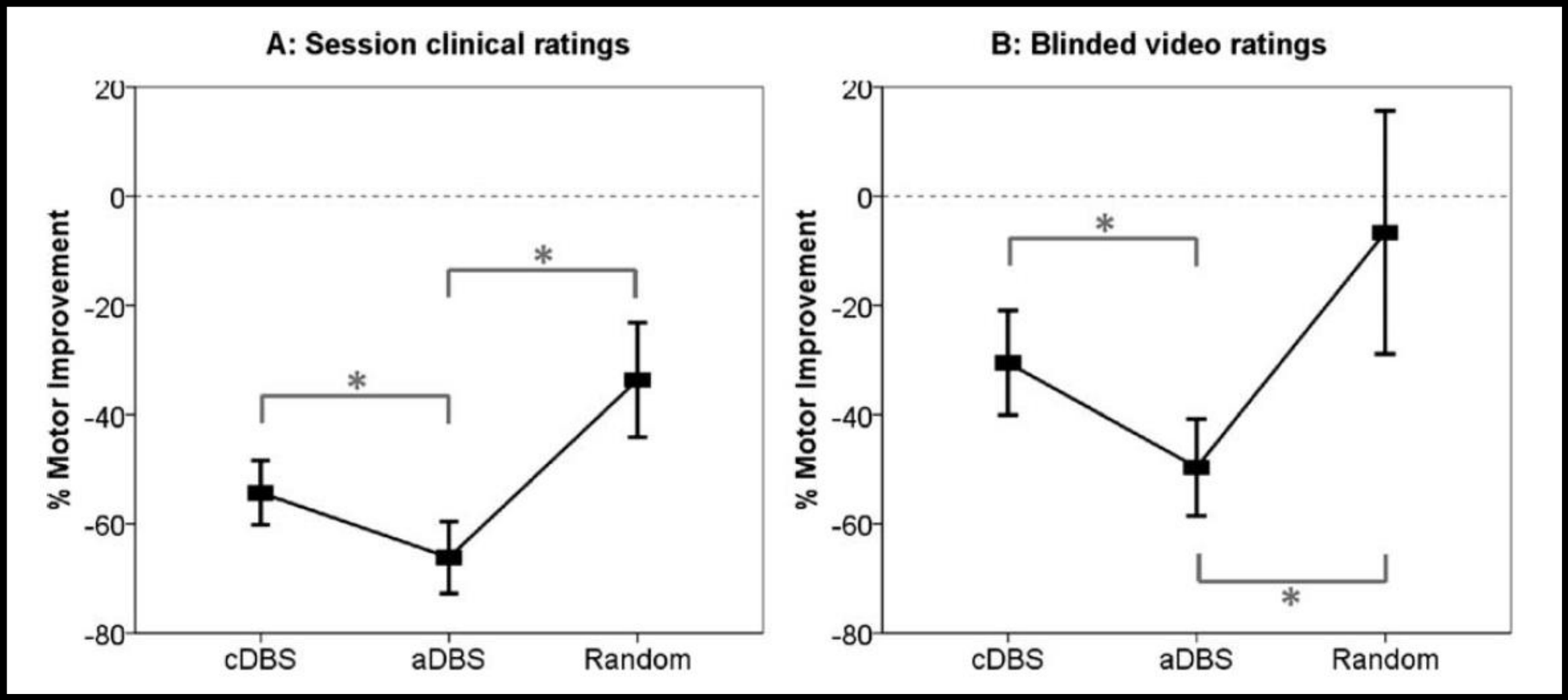
Simon Little, MA, MBBS,[1] Alex Pogosyan, PhD,[1] Spencer Neal, BEng (Hons),[2]
Baltazar Zavala, BA,[1] Ludvic Zrinzo, PhD,[2] Marwan Hariz, PhD,[2]
Thomas Foltynie, PhD,[2] Patricia Limousin, PhD,[2] Keyoumars Ashkan, MD,[3]
James FitzGerald, PhD,[1] Alexander L. Green, PhD,[1] Tipu Z. Aziz, PhD,[1] and
Peter Brown, MA, MBBS, MD[1]

Little et al., Ann Neurol 2013



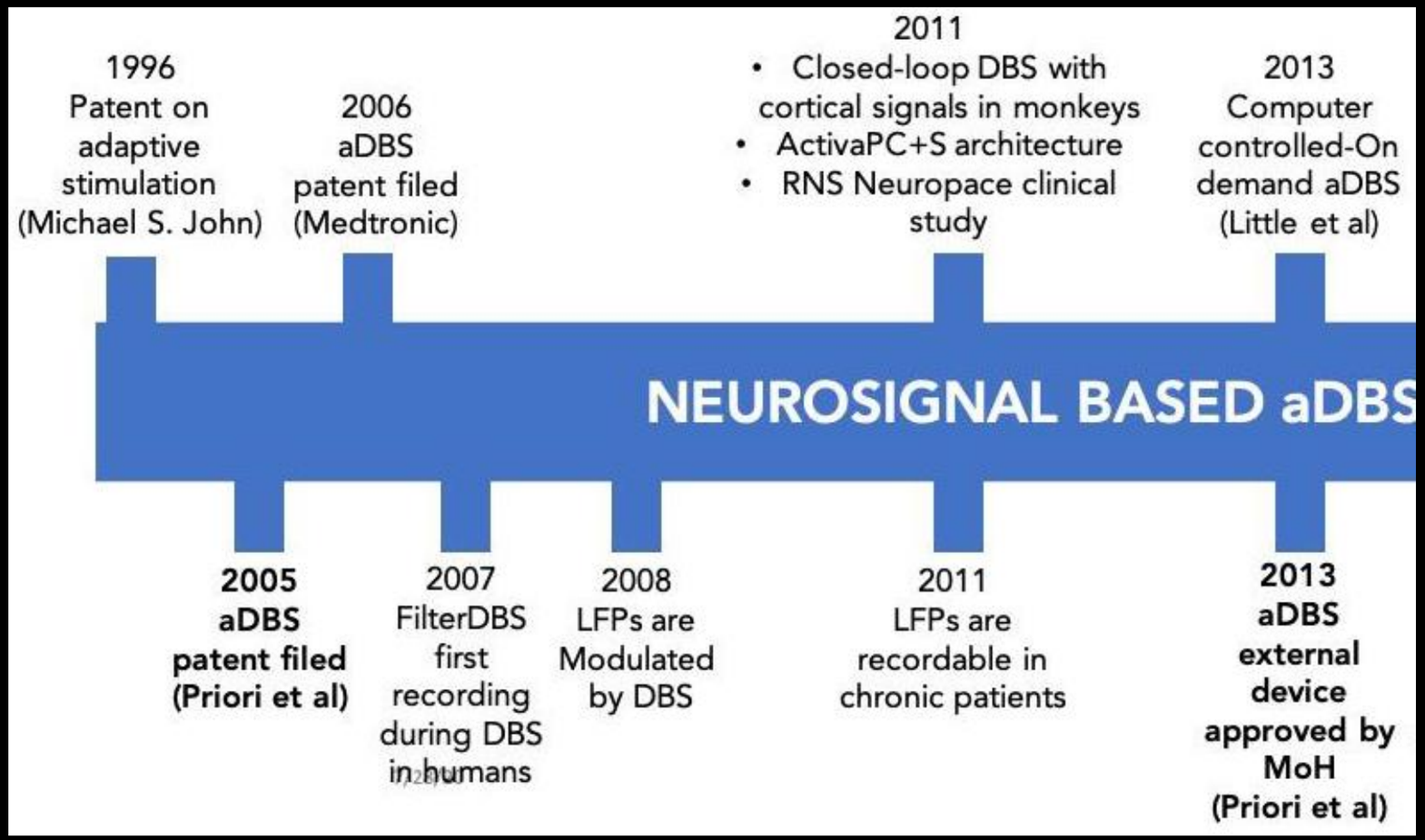
Little et al., Ann Neurol 2013

10 min

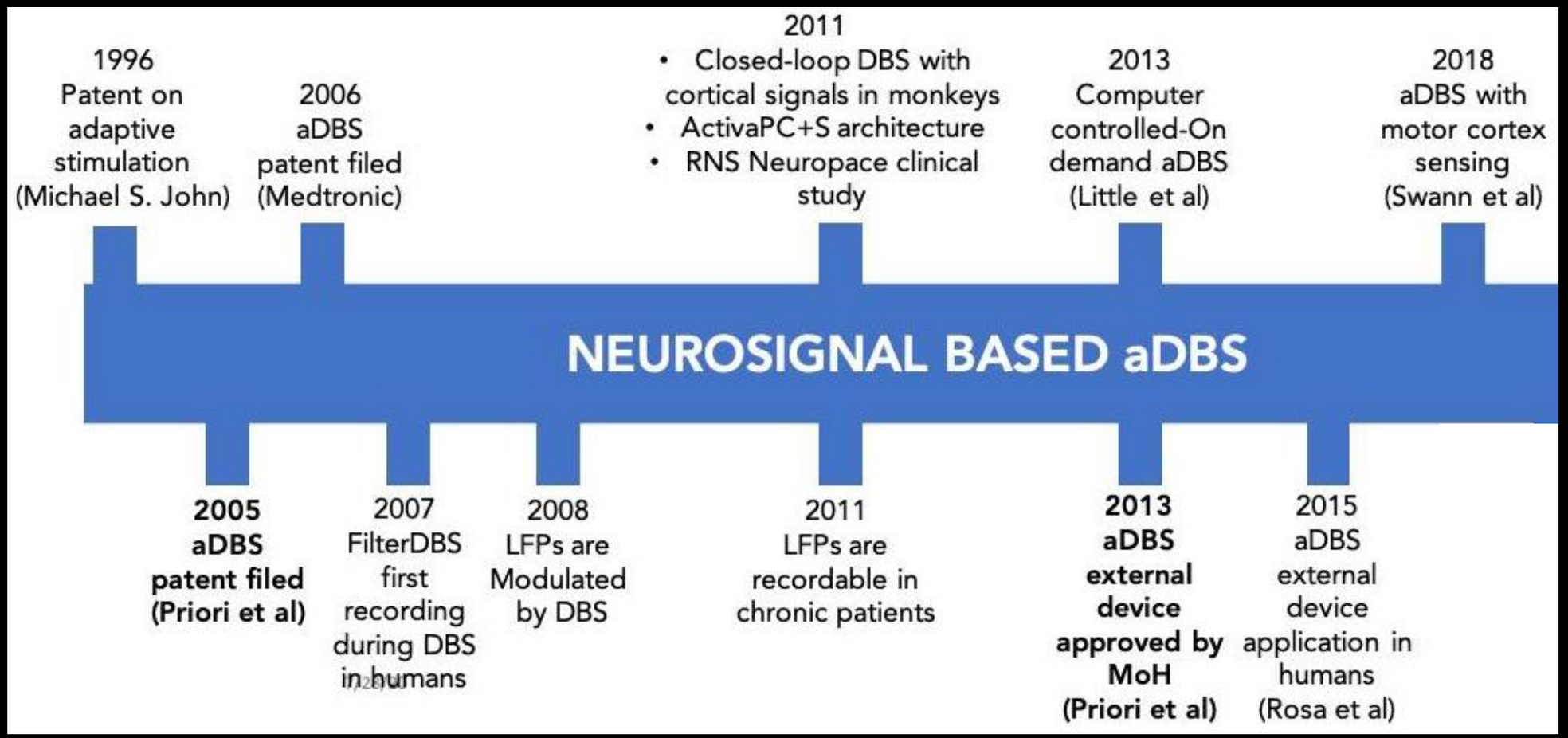


Little et al., Ann Neurol 2013

Historical perspective



Historical perspective



ARTICLE

Eight-hours adaptive deep brain stimulation in patients with Parkinson disease

Mattia Arlotti, PhD,* Sara Marceglia, PhD,* Guglielmo Foffani, PhD, Jens Volkmann, MD, PhD, Andres M. Lozano, MD, PhD, Elena Moro, MD, PhD, Filippo Cogiamanian, MD, Marco Prenassi, Ms, Tommaso Bocci, MD, Francesca Cortese, MD, Paolo Rampini, MD, Sergio Barbieri, MD, PhD, and Alberto Priori, MD, PhD

Correspondence
Prof. Priori
alberto.priori@unimi.it

Neurology® 2018;0:e1-e6. doi:10.1212/WNL.0000000000005121

Abstract

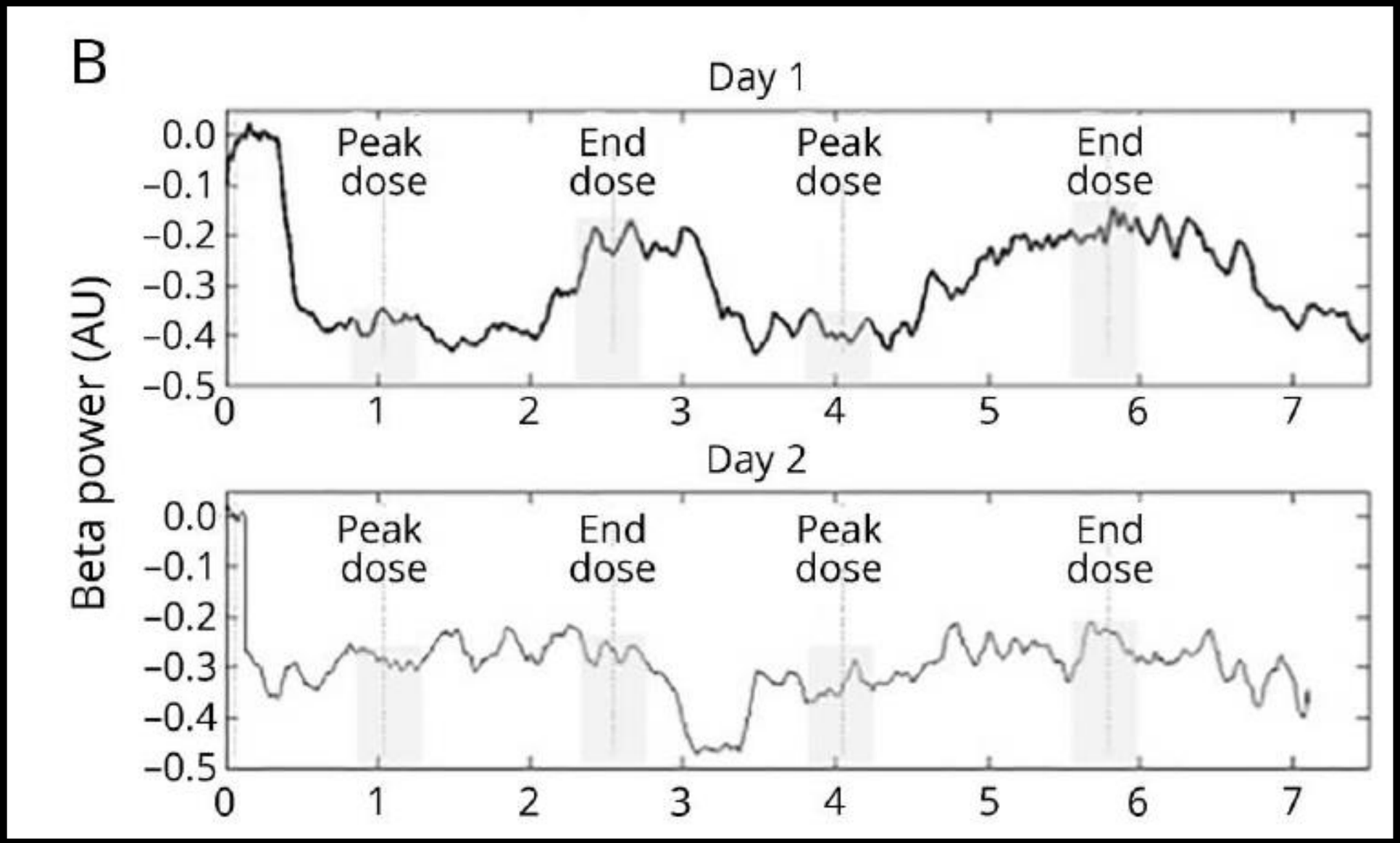
Objectives

To assess the feasibility and clinical efficacy of local field potentials (LFPs)–based adaptive deep brain stimulation (aDBS) in patients with advanced Parkinson disease (PD) during daily activities in an open-label, nonblinded study.

RELATED ARTICLE

Editorial
Approaching adaptive control in neurostimulation for Parkinson disease: Autopilot on

Arlotti et al., Neurology 2018



stim OFF

aDBS

Arlotti et al., Neurology 2018

IOP Publishing

Journal of Neural Engineering

J. Neural Eng. **15** (2018) 046006 (10pp)

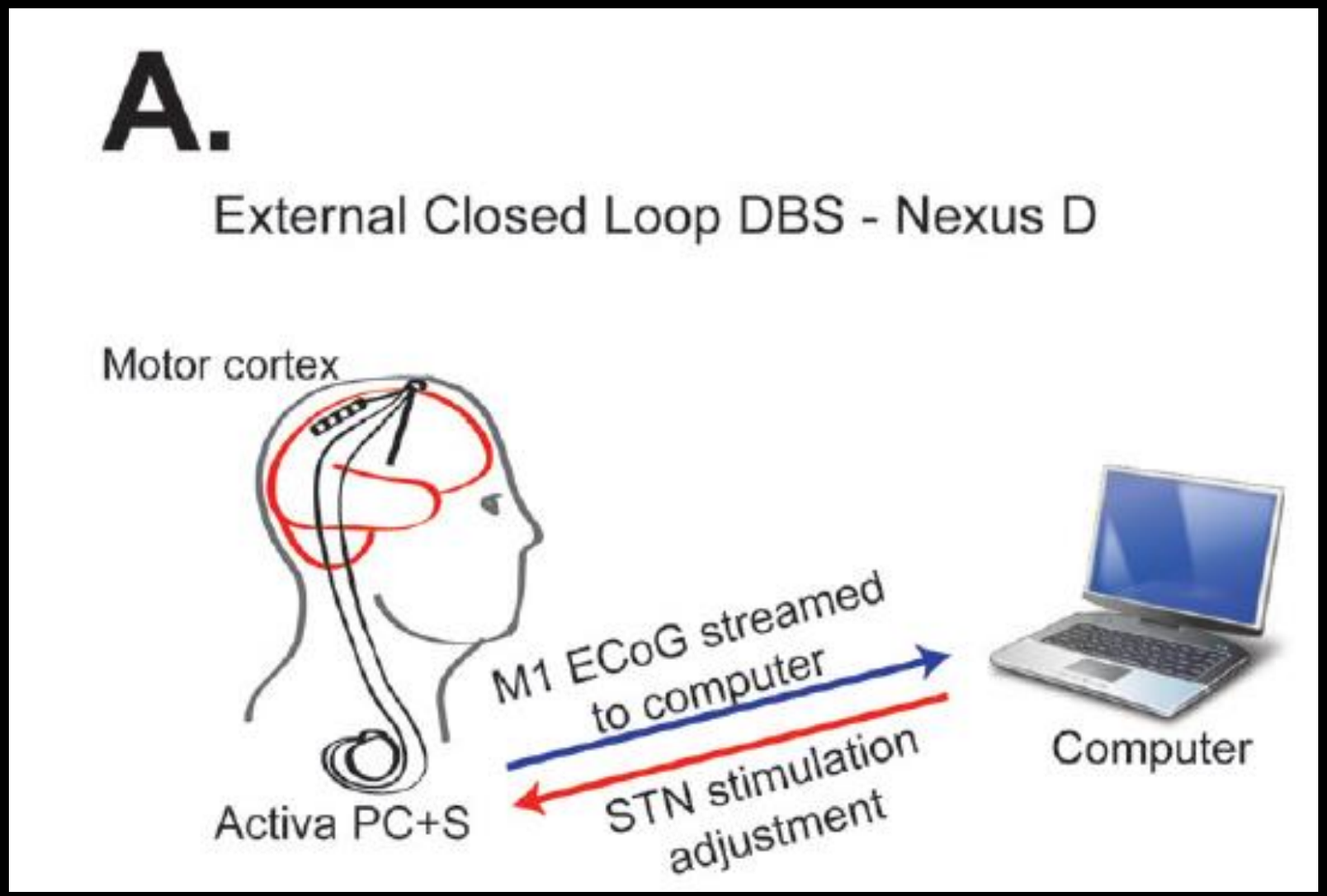
https://doi.org/10.1088/1741-2552/aabc9b

Adaptive deep brain stimulation for Parkinson's disease using motor cortex sensing

Nicole C Swann[1,2,7,8], Coralie de Hemptinne[1], Margaret C Thompson[3], Svjetlana Miocinovic[4], Andrew M Miller[1], Ro'ee Gilron[1] Jill L Ostrem[5], Howard J Chizeck[3,6] and Philip A Starr[1]

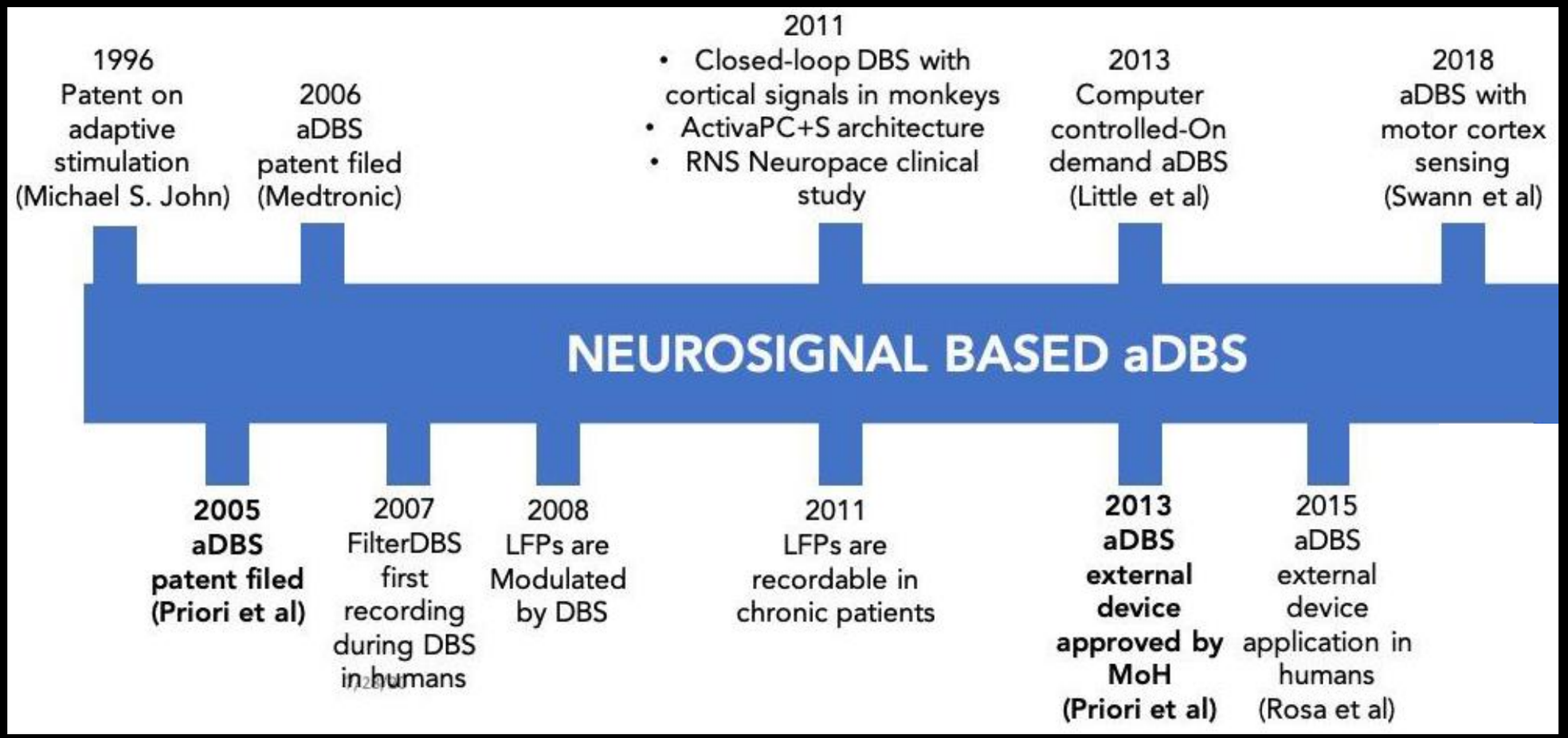
[1] Departments of Neurological Surgery, University of California, San Franciso, CA, United States of America
[2] Department of Human Physiology, University of Oregon, Eugene, OR, United States of America
[3] Department of Electrical Engineering, University of Washington, Seattle, WA, United States of America
[4] Department of Neurology, Emory University, Atlanta, GA, United States of America
[5] Departments of Neurology, University of California, San Franciso, CA, United States of America
[6] Department of Bioengineering, University of Washington, Seattle, WA, United States of America

Swann et al., J Neural Eng 2018

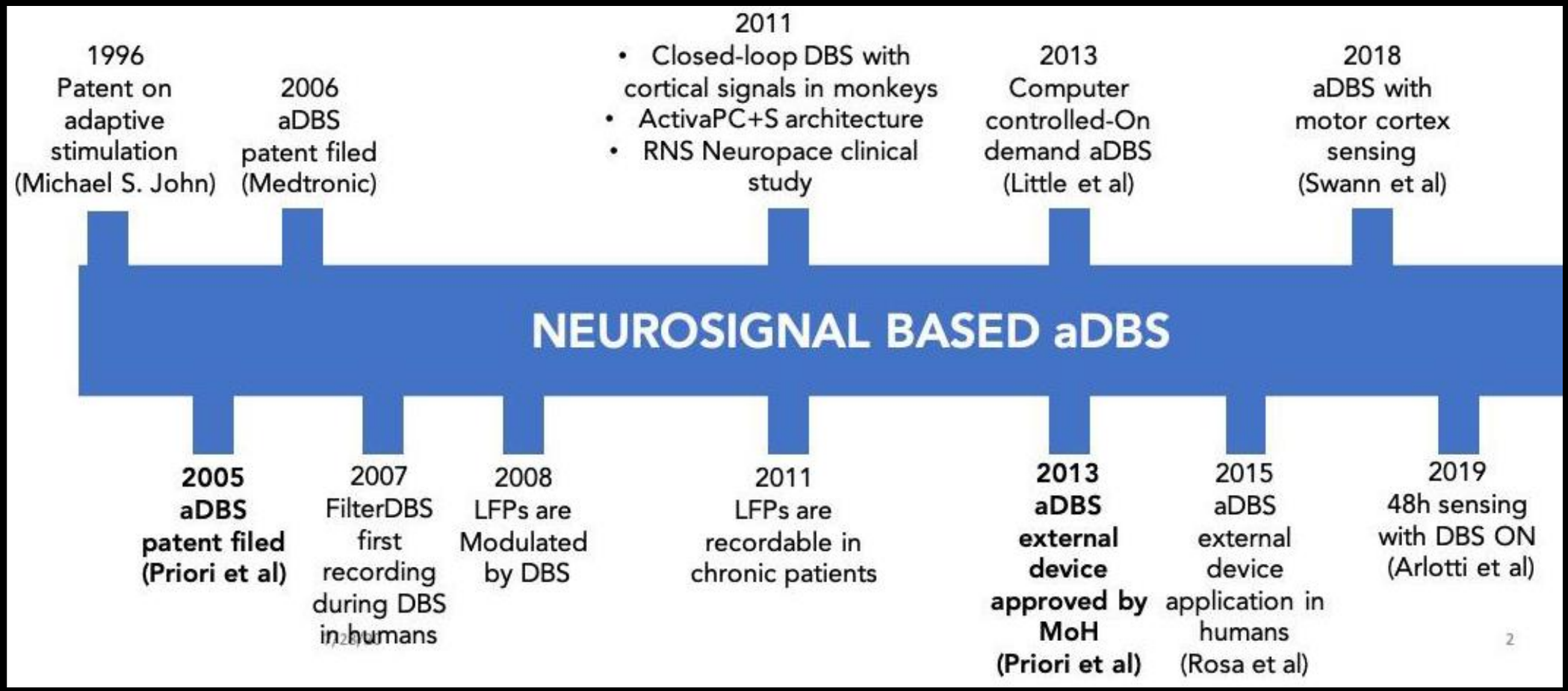


Swann et al., J Neural Eng 2018

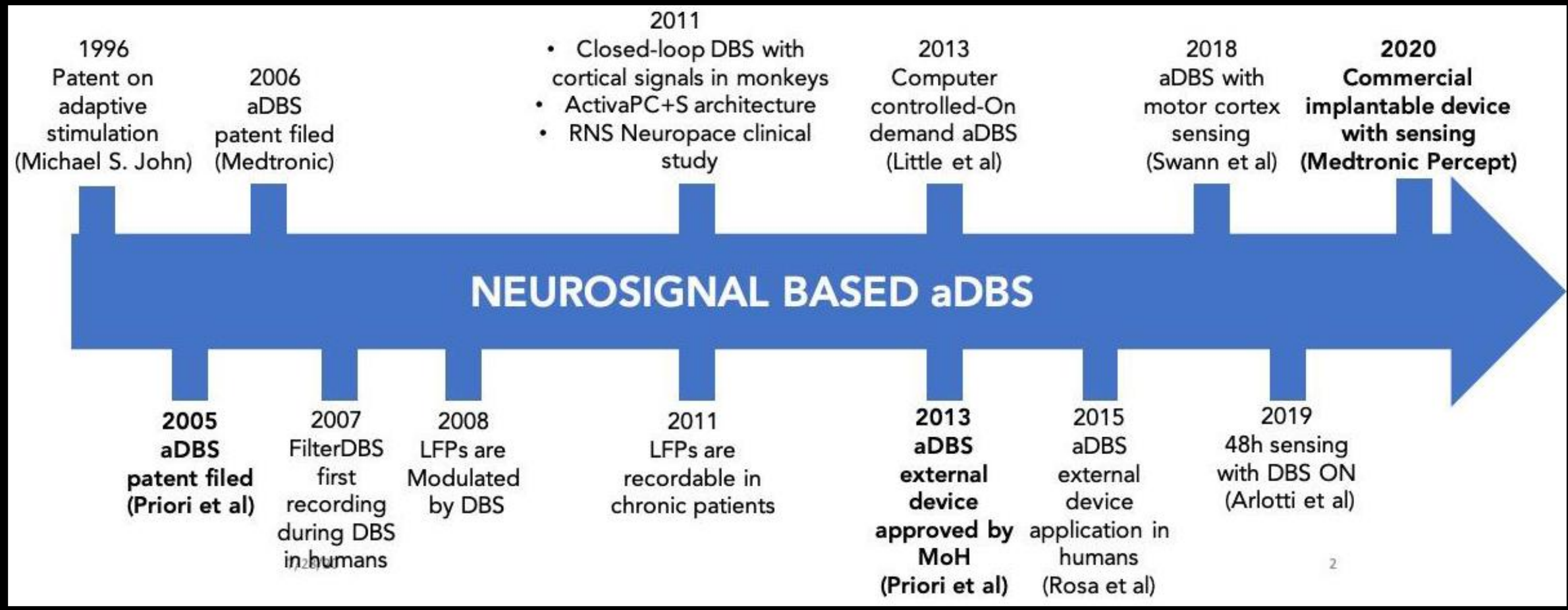
Historical perspective



Historical perspective



Historical perspective



SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

BRAIN STIMULATION

Chronic embedded cortico-thalamic closed-loop deep brain stimulation for the treatment of essential tremor

Enrico Opri[1]*, Stephanie Cernera[1], Rene Molina[2], Robert S. Eisinger[3], Jackson N. Cagle[1], Leonardo Almeida[3], Timothy Denison[4], Michael S. Okun[3], Kelly D. Foote[3†], Aysegul Gunduz[1,2,3†]

Opri et al. Sci Transl Med 2020

RESEARCH ARTICLE

Closed-Loop Deep Brain Stimulation for Essential Tremor Based on Thalamic Local Field Potentials

Shenghong He, PhD,[1,2] Fahd Baig, MB, PhD,[1,2,3] Abteen Mostofi, MA, MBBS, PhD,[3] Alek Pogosyan, PhD,[1,2] Jean Debarros, PhD,[1,2] Alexander L. Green, MD, BSc, MBBS,[2] Tipu Z. Aziz, FMedSci,[2] Erlick Pereira, MA, MBBS, MD,[3] Peter Brown, MA, MBBS, MD, FMedSci,[1,2] and Huiling Tan, PhD[1,2*]

[1]*MRC Brain Network Dynamics Unit, University of Oxford, Oxford, UK*
[2]*Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, UK*
[3]*Neurosciences Research Centre, Molecular and Clinical Sciences Research Institute, St. George's, University of London, Oxford, UK*

He et al. Mov Disord 2021

Brain Stimulation 13 (2020) 1320–1322

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Neural closed-loop deep brain stimulation for freezing of gait

Petrucci et al. Brain Stim 2020

Closed-Loop Deep Brain Stimulation to Treat Medication-Refractory Freezing of Gait in Parkinson's Disease

Rene Molina[1,2†], Chris J. Hass[2,3†], Stephanie Cernera[2,4], Kristen Sowalsky[3], Abigail C. Schmitt[2,3], Jaimie A. Roper[3], Daniel Martinez-Ramirez[5], Enrico Opri[2,4], Christopher W. Hess[2,6], Robert S. Eisinger[2,7], Kelly D. Foote[2,8], Aysegul Gunduz[1,2,4‡] and Michael S. Okun[2,6,8‡]*

Molina et al., Front Hum Neurosci 2021

npj | Parkinson's Disease

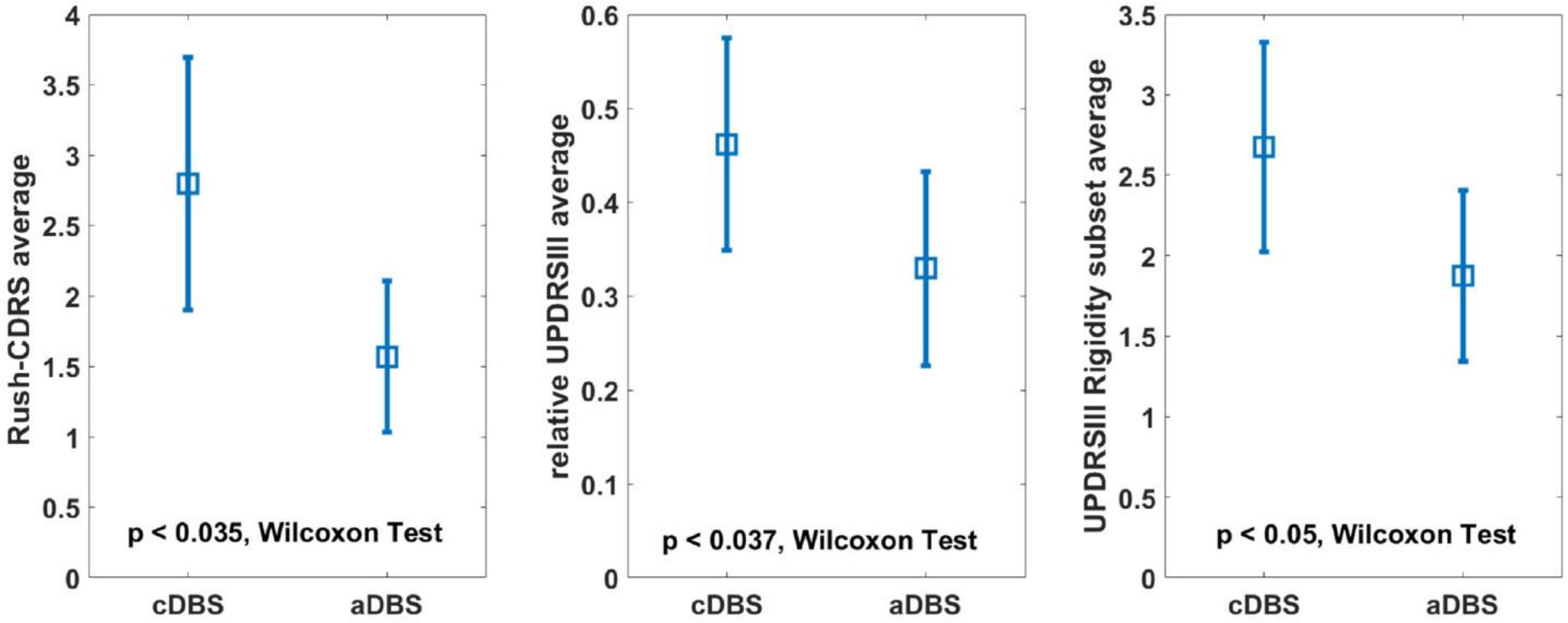
www.nature.com/npjparkd

ARTICLE OPEN

Check for updates

Eight-hours conventional versus adaptive deep brain stimulation of the subthalamic nucleus in Parkinson's disease

Tommaso Bocci[1,2,9], Marco Prenassi[3,9], Mattia Arlotti[4], Filippo Maria Cogiamanian[5], Linda Borrellini[5], Elena Moro[6], Andres M. Lozano[7], Jens Volkmann[8], Sergio Barbieri[5], Alberto Priori[1,2]✉ and Sara Marceglia[3,5]



Bocci et al. NPJ Parkinsons Dis 2021

nature biotechnology

ARTICLES

https://doi.org/10.1038/s41587-021-00897-5

Check for updates

Long-term wireless streaming of neural recordings for circuit discovery and adaptive stimulation in individuals with Parkinson's disease

Ro'ee Gilron[1]✉, Simon Little[2], Randy Perrone[1], Robert Wilt[1], Coralie de Hemptinne[1], Maria S. Yaroshinsky[1], Caroline A. Racine[1], Sarah S. Wang[1], Jill L. Ostrem[2], Paul S. Larson[1], Doris D. Wang[1], Nick B. Galifianakis[2], Ian O. Bledsoe[2], Marta San Luciano[2], Heather E. Dawes[1], Gregory A. Worrell[3], Vaclav Kremen[3], David A. Borton[4], Timothy Denison[5] and Philip A. Starr[1]

Gilron et al. Nat Biotechnol 2021

Brief Communication | Published: 04 October 2021

Closed-loop neuromodulation in an individual with treatment-resistant depression

Katherine W. Scangos ✉, Ankit N. Khambhati, Patrick M. Daly, Ghassan S. Makhoul, Leo P. Sugrue, Hashem Zamanian, Tony X. Liu, Vikram R. Rao, Kristin K. Sellers, Heather E. Dawes, Philip A. Starr, Andrew D. Krystal & Edward F. Chang

Nature Medicine **27**, 1696–1700 (2021) | Cite this article

NIH U.S. National Library of Medicine

ClinicalTrials.gov

MedtronicNeuro

Adaptive DBS Algorithm for Personalized Therapy in Parkinson's Disease (ADAPT-PD)
NCT04547712

Newronika

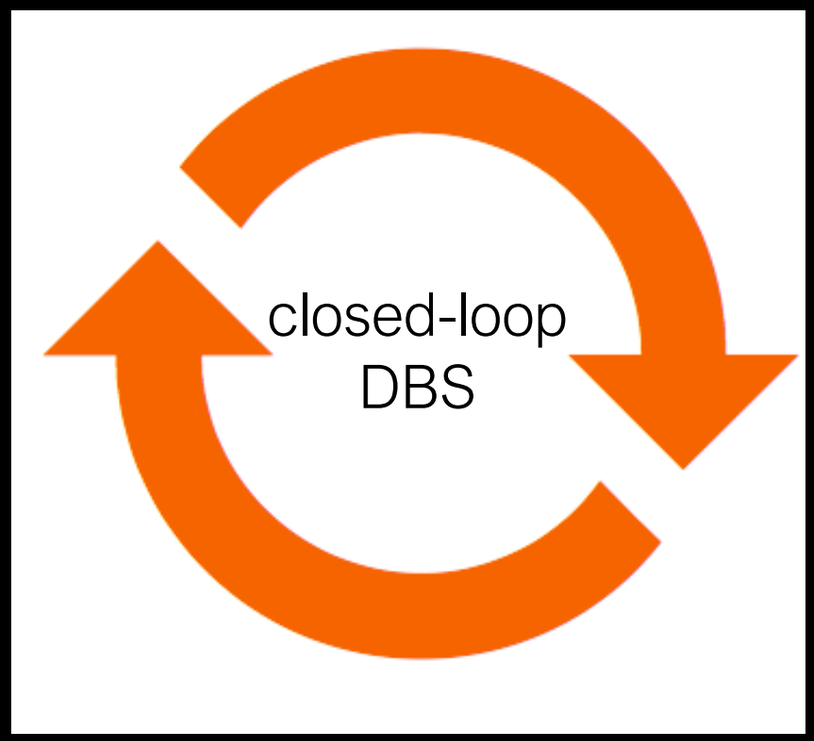
Safety and Efficacy of Adaptive Deep Brain Stimulation
NCT04681534

NeuroPace

Closed-Loop Deep Brain Stimulation for Major Depression (PReSiDio)
NCT04004169

ENERGY

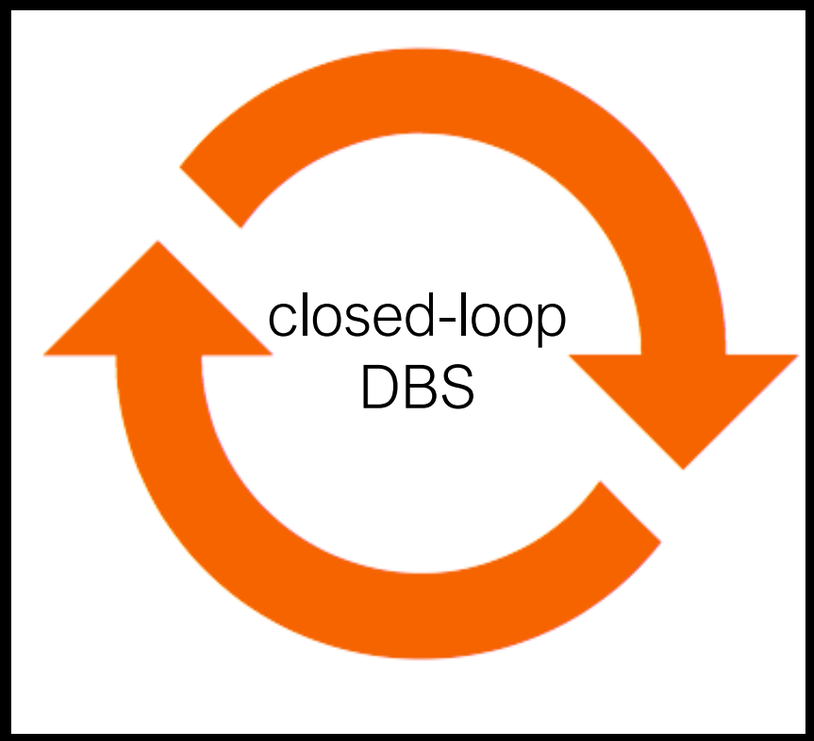
BIOMARKER(S)



TEMPORAL SCALE

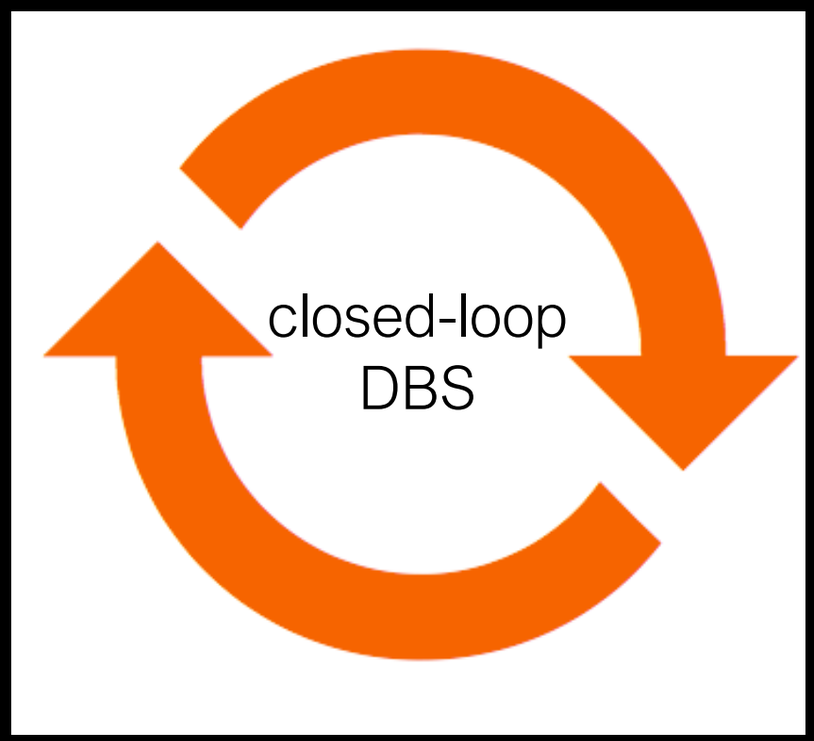
ENERGY

BIOMARKER(S)



TEMPORAL SCALE

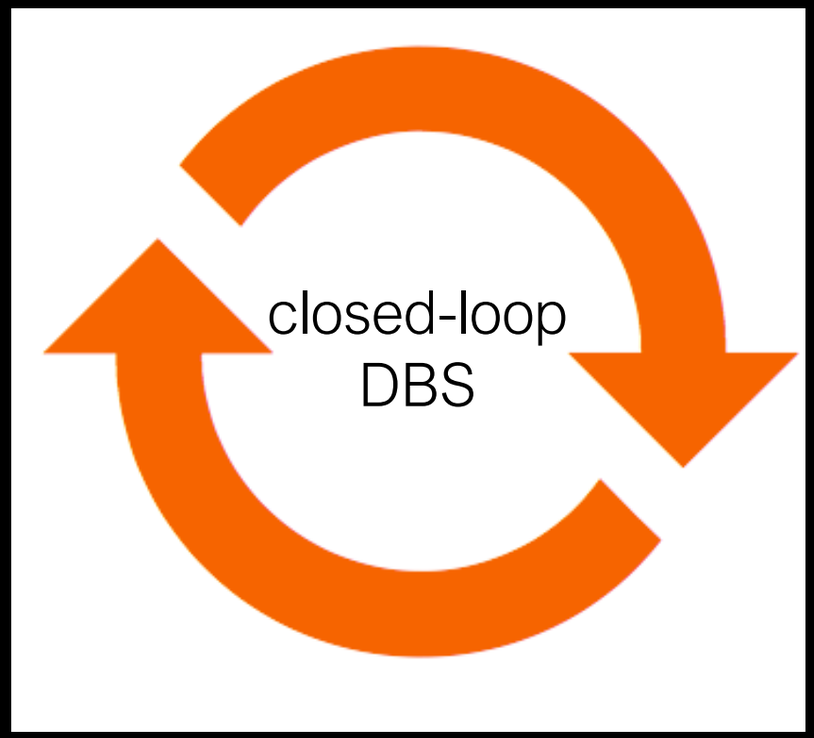
ENERGY



BIOMARKER(S)

TEMPORAL SCALE

ENERGY



BIOMARKER(S)

TEMPORAL SCALE

Clinical objective(s):

- Improve OFF?
- Decrease side effects? (e.g. dyskinesias)
- New indications?