AN INTRODUCTION TO NEURAL PROSTHESES

UNSW
THE UNIVERSITY OF NEW SOUTH WALES

Never Stand Still | Faculty of Engineering | Graduate School of Biomedical Engineering

Dr Mohit Shivdasani
Graduate School of Biomedical Engineering, UNSW

Little Bit About Me

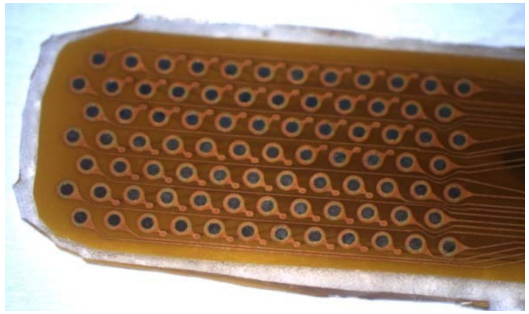
- 2002 - Completed Bachelor of Biomedical Engineering in Mumbai, India
- 27th Feb 2003 - Came to Melbourne as an International Master's Student
- Dec 2003 - Completed Master of Electronic Engineering (Biomedical) from La Trobe University
- 2009 - Completed PhD in Auditory Neuroscience
- 2009-2017 - Worked at the Bionics Institute in Melbourne on developing a bionic eye for vision restoration
- Feb 2018 – Moved to Sydney and joined UNSW!

What I Have Loved About Research in Bionics

- Working in a Multidisciplinary Team: Surgeons, Clinicians (Ophthalmologists), Engineers (All Flavours), Materials Scientists, Mathematicians, Neuroscientists, Biologists, Pathologists

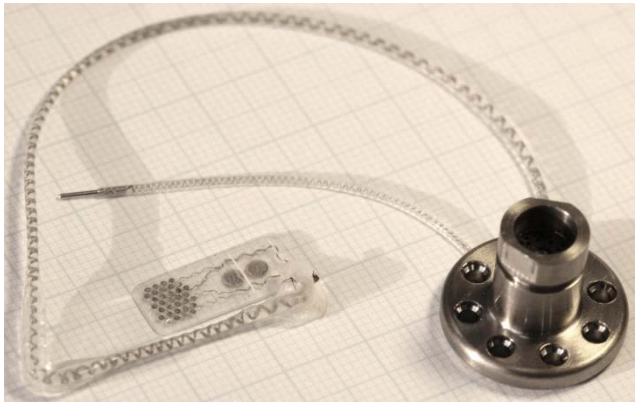
- Even Lawyers, Research Managers, Art Designers & Marketers …

What I Have Loved About Research in Bionics



Concept

Design



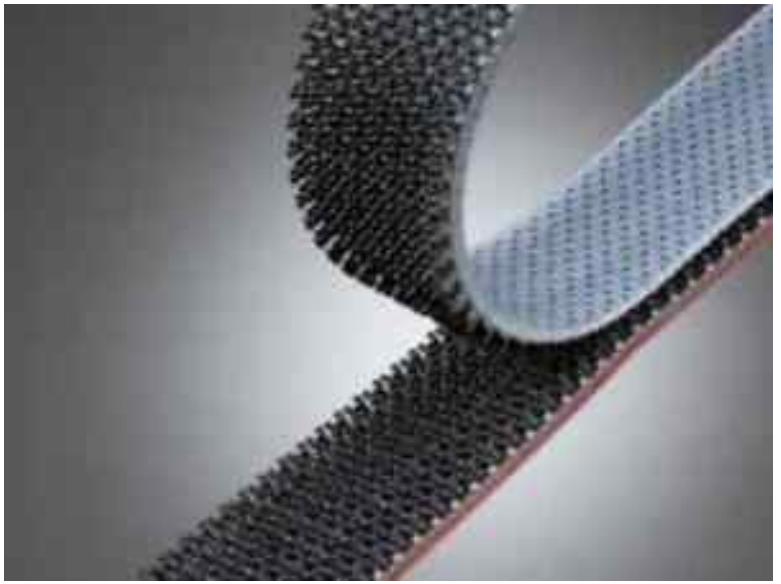
Product

Clinic

Definition of Bionics

Bionics = Inspired by Nature

Burdock Plant Burr Inspired …



Velcro!

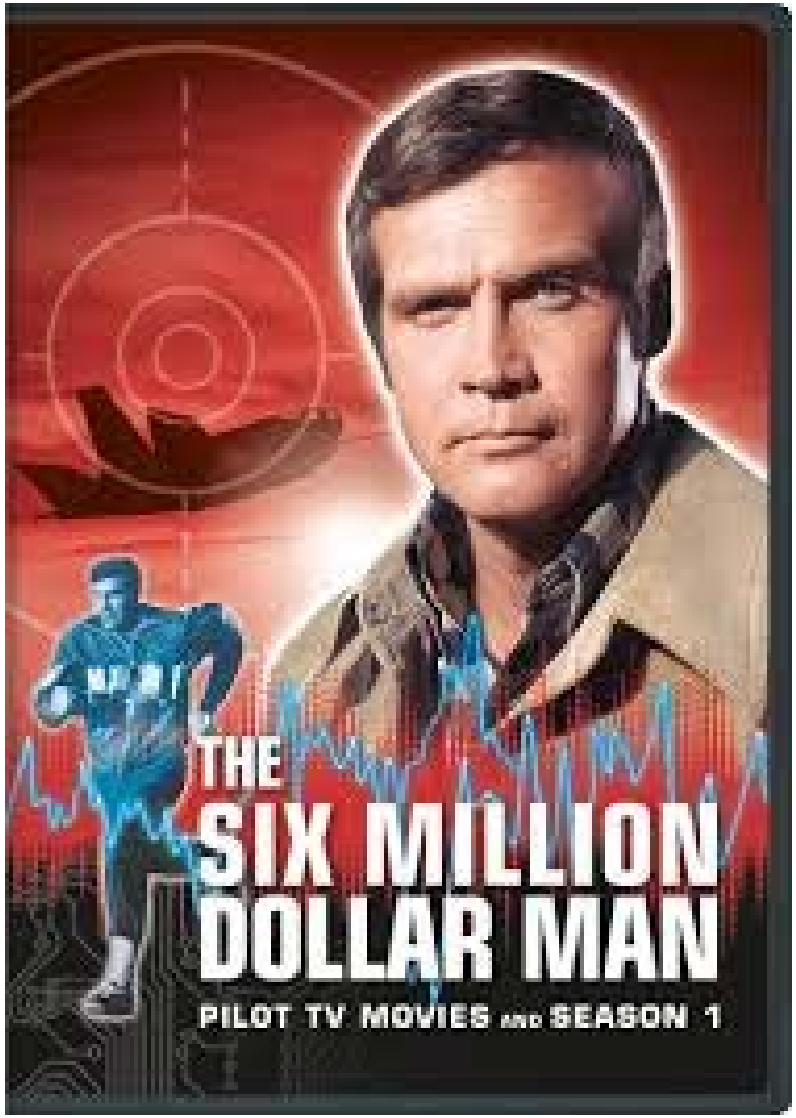
Definition of Bionics

The Bionic Tower

Inspiration Unknown …

Definition of Medical Bionics

Definition of Medical Bionics



Mark Wahlberg's 'Six Billion Dollar Man' Set for 2019 Summer Release

By DAVE MCNARY

CREDIT: TARA MAYS/VARIETY/REX/SHUTTERSTOCK

Warner Bros. has set an early summer release date of May 31, 2019, for Mark Wahlberg's sci-fi action movie "The Six Billion Dollar Man."

Warner Bros. bought the rights to the project late last year from the Weinstein Company, which had been developing the movie with "Wild Tales" director Damian Szifron.

"The Six Billion Dollar Man" is based on the science-fiction television series "The Six Million Dollar Man," about a former astronaut, Colonel Steve Austin, portrayed by Lee Majors. Austin's character had superhuman strength due to bionic implants and was employed as a secret agent. The series ran for five seasons on ABC between 1973 and 1978 and was based on the Martin Caidin novel "Cyborg."

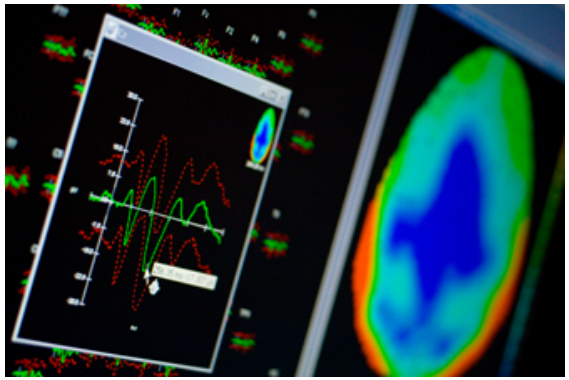
Inflation??

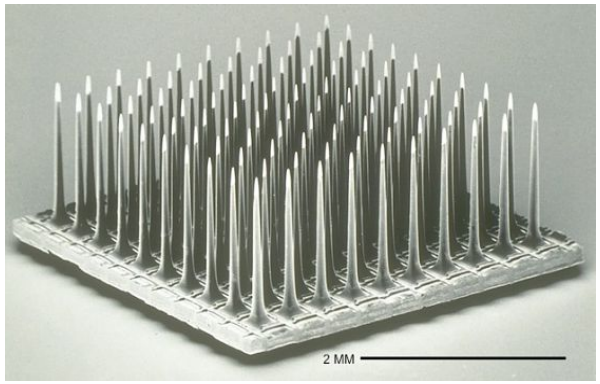
Definition of Medical Bionics

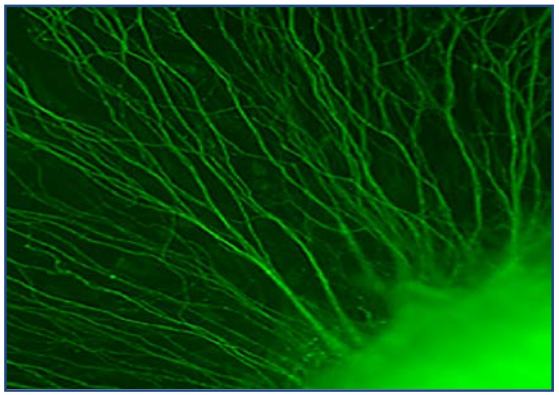
Bionics in Medicine = Biology + Electronics

Functional replacement/support of damaged organs through an artificial **device**:

- Monitor electrical/chemical signals
- Controlled drug release
- Scaffolds for tissue growth
- Electrical stimulation to excite damaged nerve or muscle - Neural prostheses & Heart pacemakers
- Don't want to make people better, stronger, faster … Just want to fix things!!!







Bionic Devices Can be Non-Implantable

FDA Approved Class II Medical Device; Source: Youtube

The "Neural" Problem Being Solved …

Clinical Ophthalmology

Dovepress
open access to scientific and medical research

Open Access Full Text Article

ORIGINAL RESEARCH

A nonrandomized, open-label study to evaluate the effect of nasal stimulation on tear production in subjects with dry eye disease

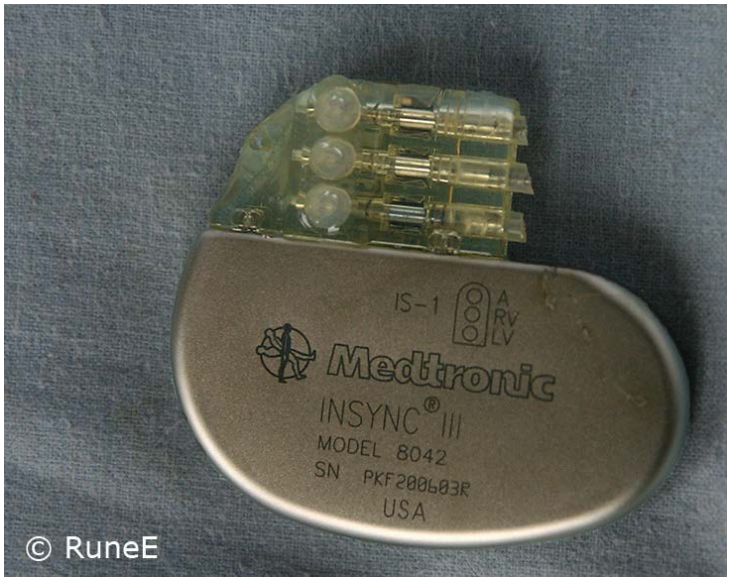
Introduction

Chronic dry eye disease (DED) is a multifactorial disorder of the tears and ocular surface, which results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface as the disease progresses.[1] The condition is accompanied by increased osmolarity of the tear film and ocular surface inflammation.[1] DED is a leading cause of eye discomfort and morbidity globally. Approximately 25 million Americans suffer from DED, and symptoms of the disease are among the leading causes for patient visits to ophthalmologists and optometrists

Implantable Bionics

Heart Pacemakers

- US $13 billion pa industry
- 15% growth pa

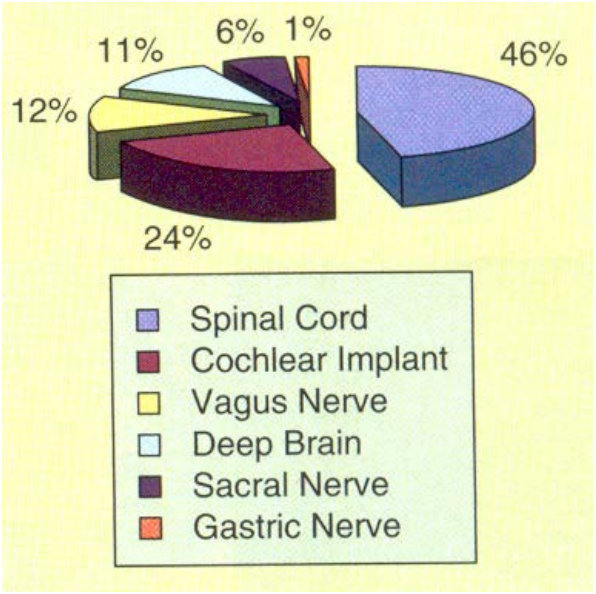


Trimark Publications, 2004

Neural prostheses

- US $1.8 billion pa industry
- 10-15% growth pa

2005 US Sales of neural prostheses



Panescu, 2008

FDA Class III Active Implantable Medical Devices (AIMDs)

Heart Pacemakers (pre-1950s)

Valve Technology

Heart Pacemakers

Balancing the perfect device with the achievable outcomes

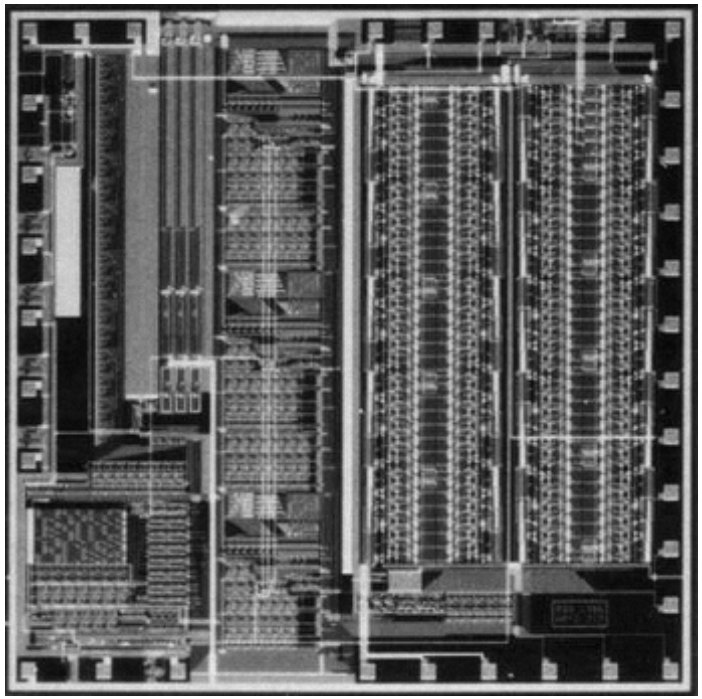
Arne Larsson 1915-2001

- **Received the 1st implantable pacemaker on 8 October, 1958**

Heart Pacemakers (post 1965)

Transistor Technology

Heart Pacemakers (Now)



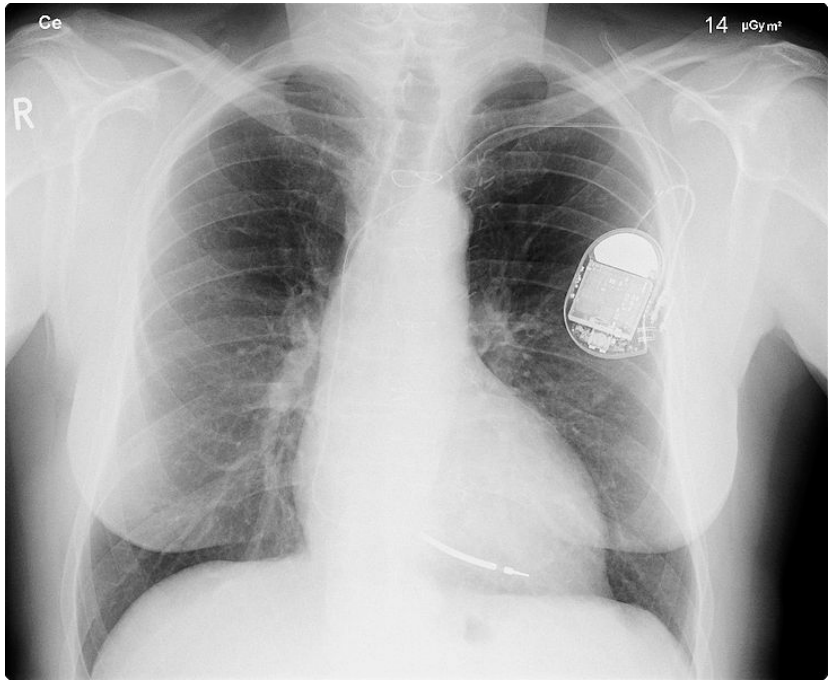
Integrated Circuit Technology (1970s)

Heart Pacemakers

- Just over 1,000,000 units implanted as of 2016
- Unit cost ~ US$30,000

Major FDA approved devices:

- Medtronic
- Boston Scientific
- St Jude Medical



Implantable Bionics

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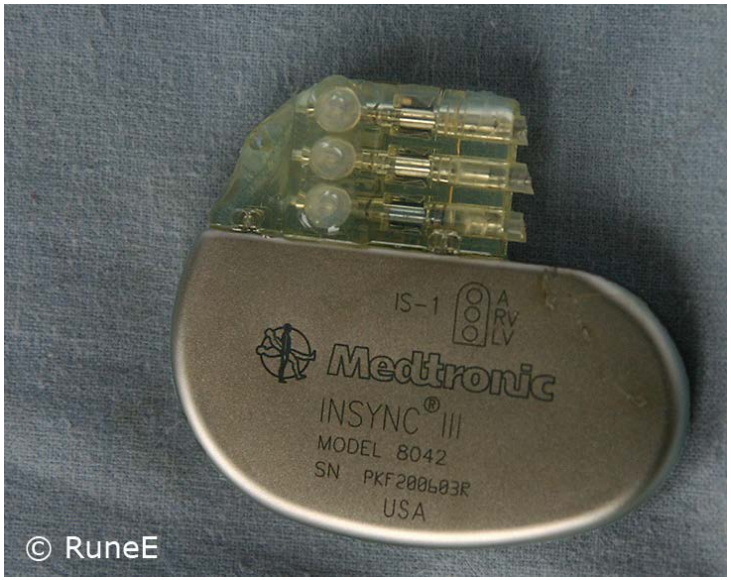

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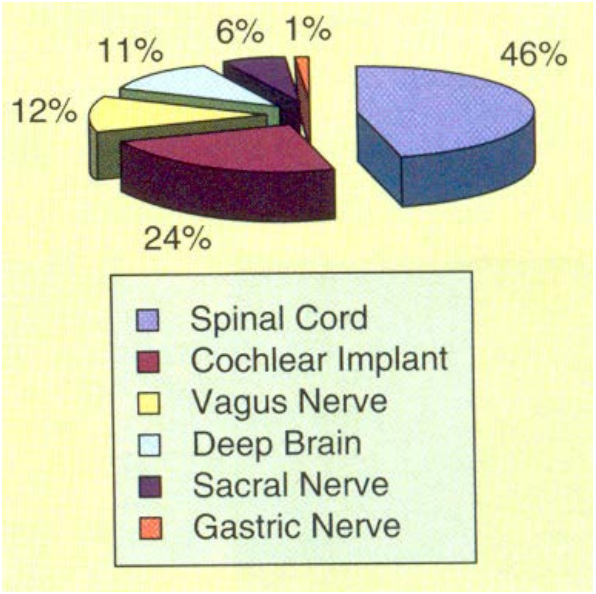
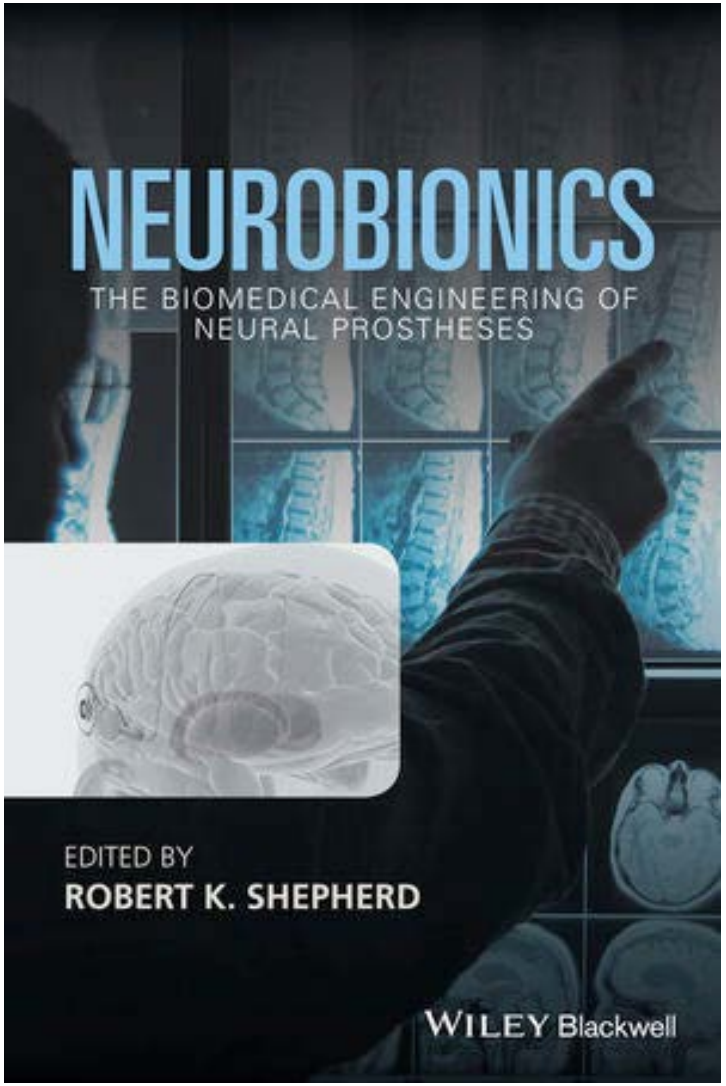
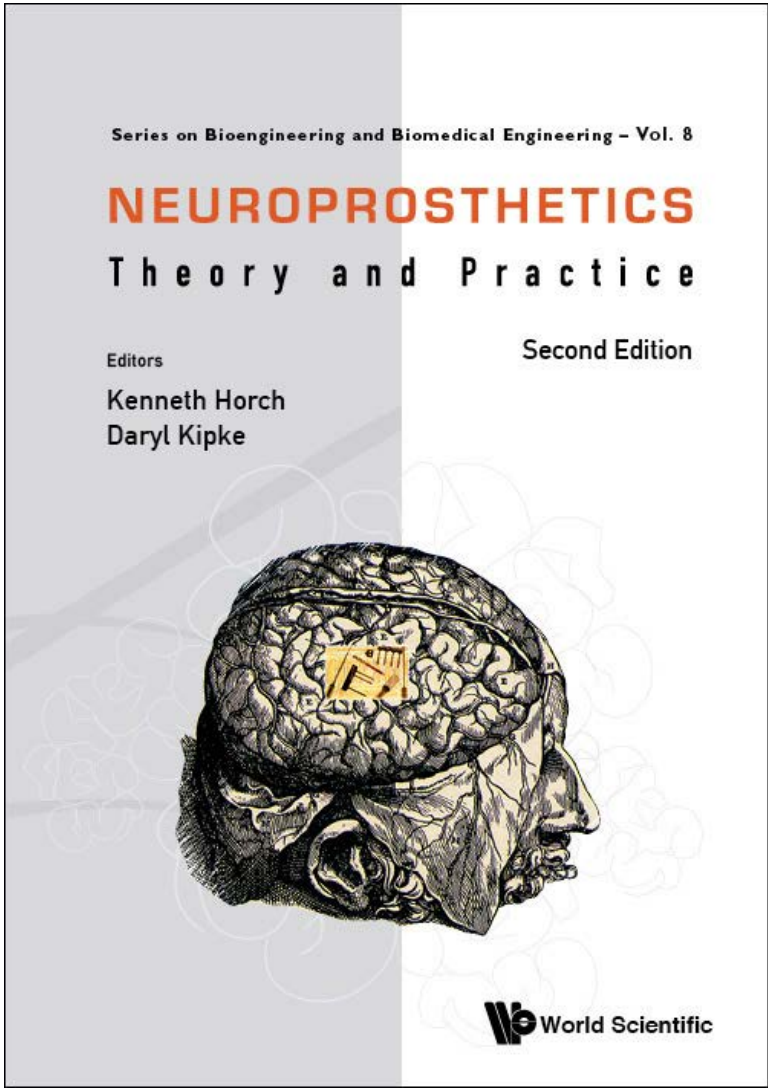


Panescu, 2008

FDA Class III Active Implantable Medical Devices (AIMDs)

Recommended Reading!





Better Than Reading – Join In Your Fourth or Fifth Year!

This course is an introduction to physiological measurement using biosensors and transducers. Its aim is to give the measurement of a biological variable or system by a transducer, which converts the variable into an electrica

By the end of the course you should understand various measurement devices and approaches including the ur measured or controlled. The basic biosensors and transducers used to measure pressure, flow, volume and bio instrumentation.

Course code	Name of course	UoC
BIOM9660	**Implantable Bionics**	**6**

For timetable and contact information see Class Details

You can download the course outline

This course is an introduction to the engineering issues related to implantable bionics for therapeutic electrical s understanding of the requirements (electrical, mechanical, chemical, etc.) of implantable neurostimulators.

During the course, in small groups students will conduct extensive practical tasks to reinforce the material prese

Existing Commercial AIMDs

Spinal cord stimulation for chronic neurological pain

Spinal Cord Stimulation for Chronic Pain

- Largest neurostimulator market in the US (150,000 implants from 1982-2002)
- FDA approved Spinal cord stimulation devices:
  - Medtronics
  - Boston Scientific
  - St Jude Medical
- 53% of SCS sales in the US
- Mechanism of action not known (masking?)
- Device cost ~US$12,000-25,000

Spinal Cord Stimulation for Chronic Pain – Home Grown

Source: Youtube

Vagus Nerve Stimulation for Epilepsy

Courtesy of Cyberonics Inc

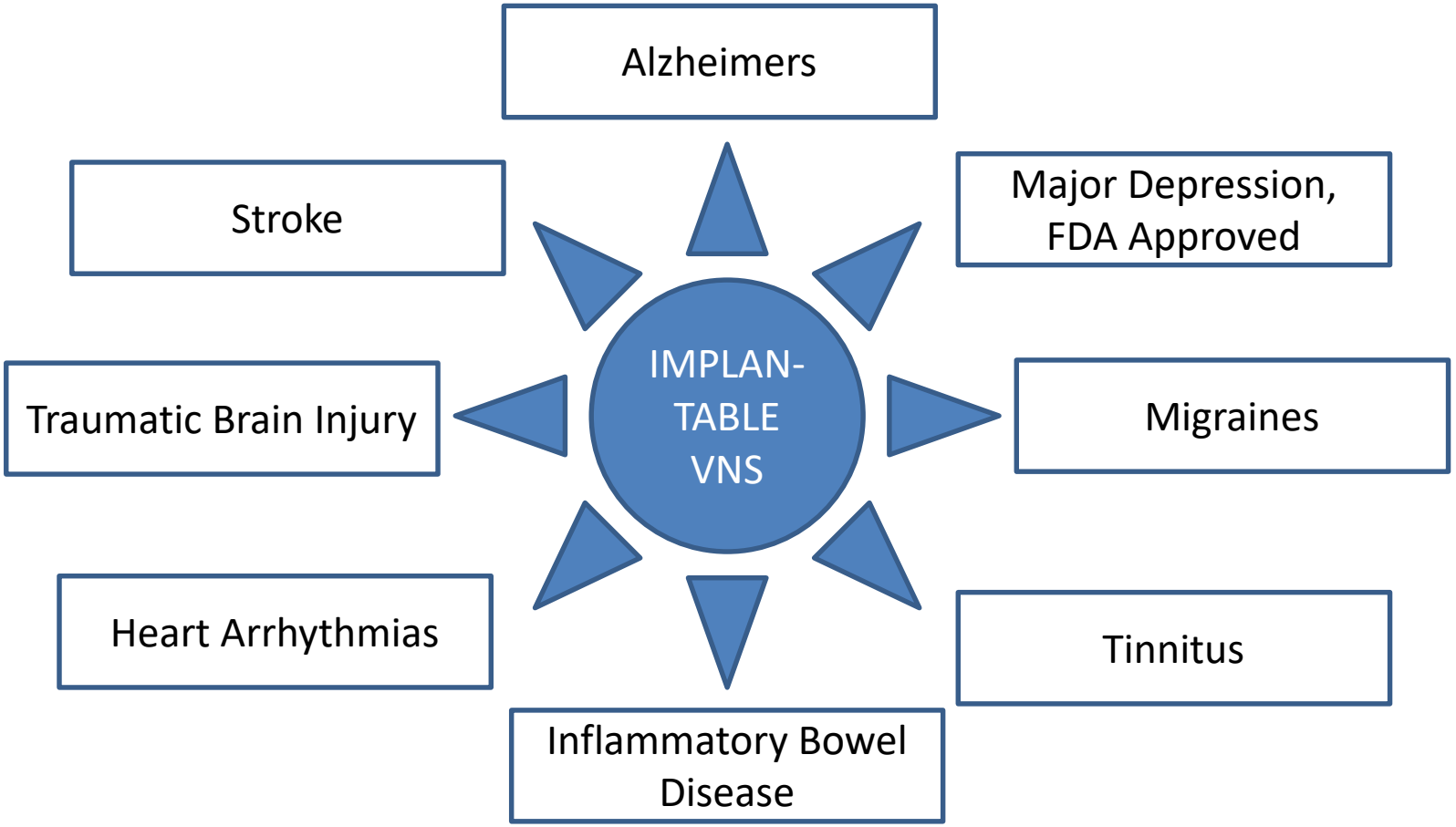
Courtesy of Cyberonics Inc

Vagus Nerve Stimulation for Epilepsy

Courtesy of Cyberonics Inc

- FDA approval for epilepsy in 1997 & chronic depression in 2005
- Effectiveness still questioned
- Mechanism of action unknown
- Device cost ~US$12,000 -15,000
- Major player – Cyberonics Inc, USA now merged with Sorin Group to form LivaNova PLC (Headquarters in London)

The Never Ending Applications of VNS …



NOT ENOUGH SPOKES!!!!

Bernard Dan, Dev Med Child Neurol, 2018

Parkinson's Disease

Source: Youtube

Deep Brain Stimulation for Movement Disorders

From Kringelbach, et al., Nature Reviews Neuroscience 8, 623-635, 2007.

Deep Brain Stimulation for Movement Disorders

Image courtesy of Channel 9

Electrodes implanted in the Sub-thalamic nucleus using stereotaxic surgery

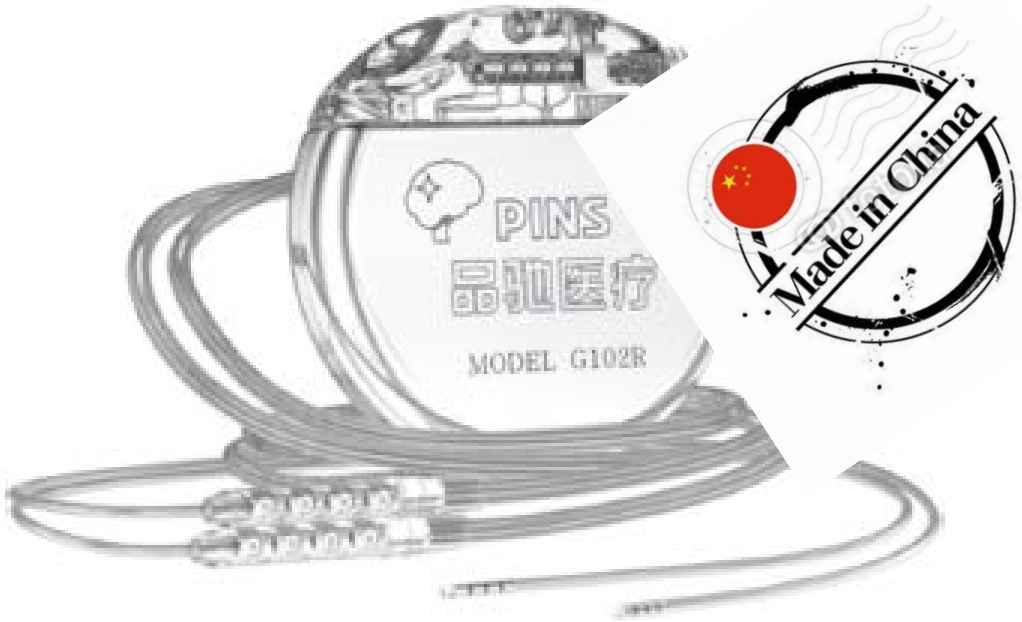
Deep Brain Stimulation for Movement Disorders

- Medtronics Inc. manufactures the only FDA approved DBS system
- FDA approval for Essential tremor in 1997; PD in 2002
- Does not cure PD – assists in the control of any movement disorder
- Physiological mechanism unknown
- Device cost ~ US$12,000-30,000
- 11,000 devices implanted in US in 2008 with a growth rate of >20%

Deep Brain Stimulation for Movement Disorders

Beijing Pins Co Ltd, China

OVERTAKEN MEDTRONIC IN CHINA BUT CANNOT SELL IN THE US



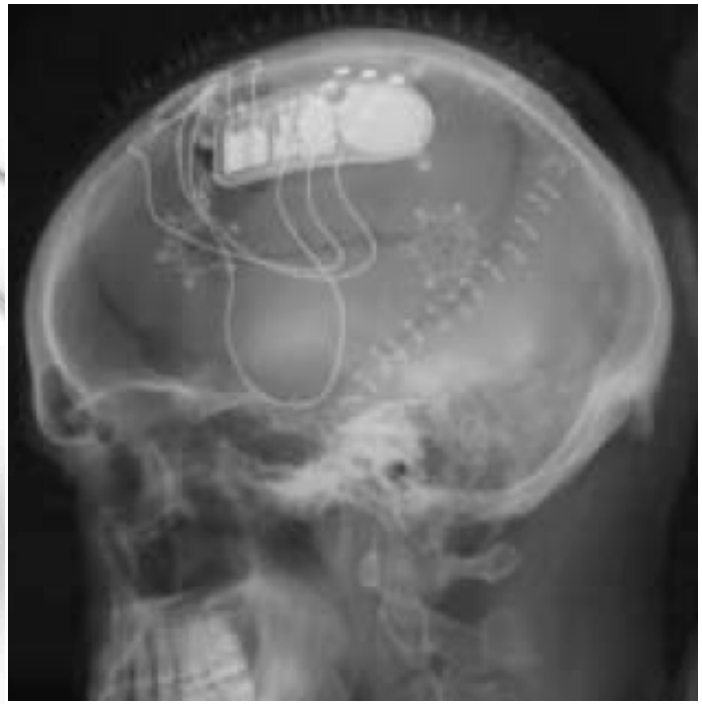
Seems to Control Northern China Market

Sceneray Corporation, Suzhou, China

ALSO USED FOR OTHER CONDITIONS

Seems to Control Southern China Market

Deep Brain Stimulation for Epilepsy Suppression

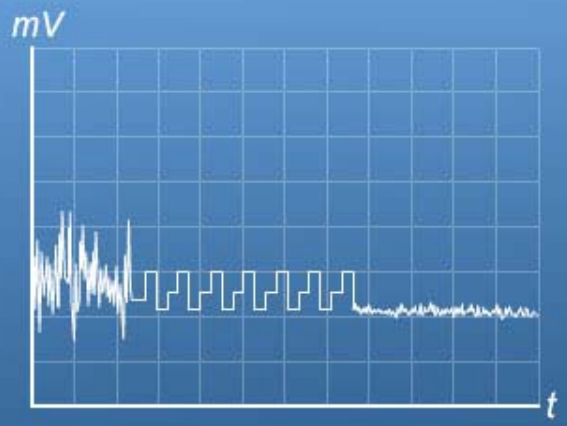


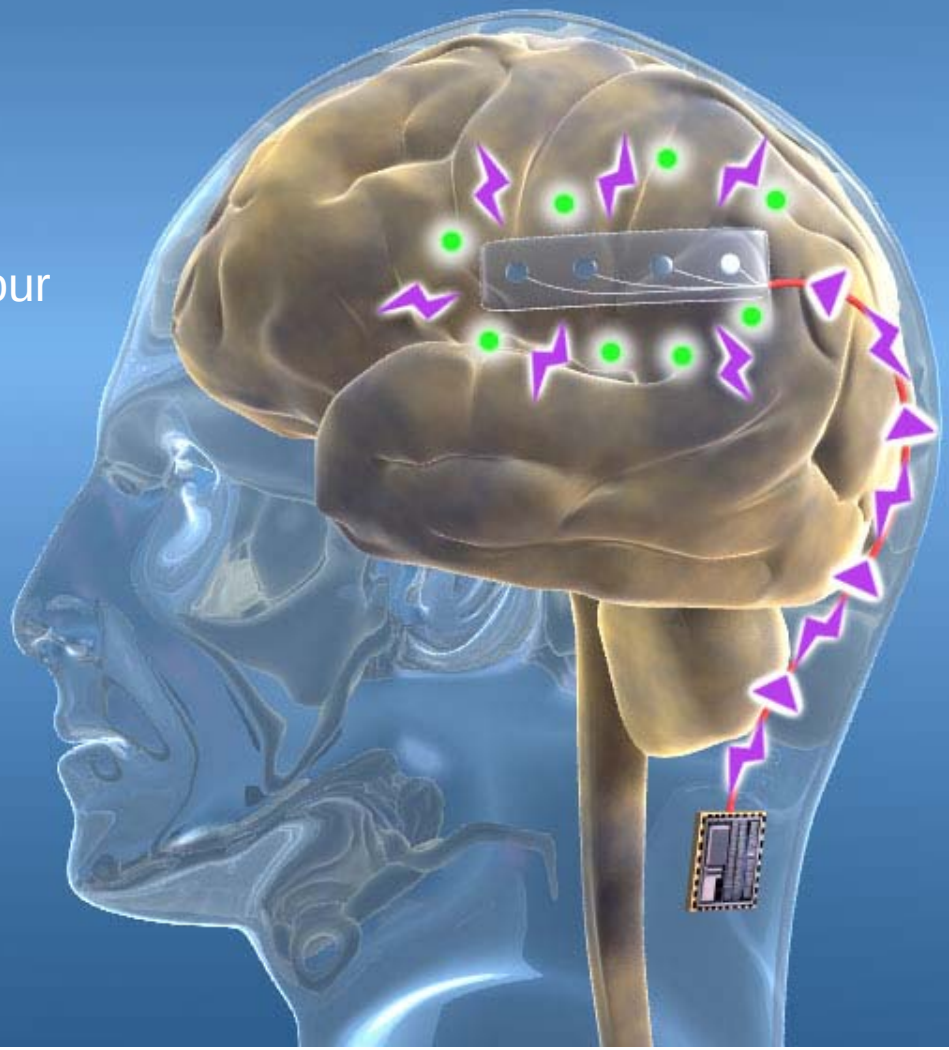
Neuropace Inc. cortical stimulator

Deep Brain Stimulation for Epilepsy Suppression

Performance specification:

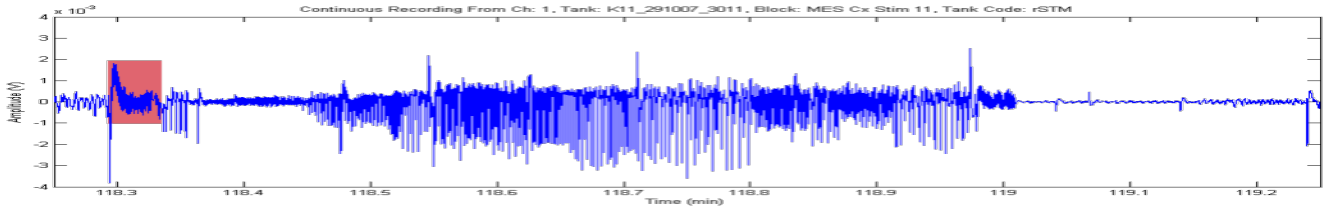
- > 90% sensitivity
- < 1 false detection per hour
- < 5s latency



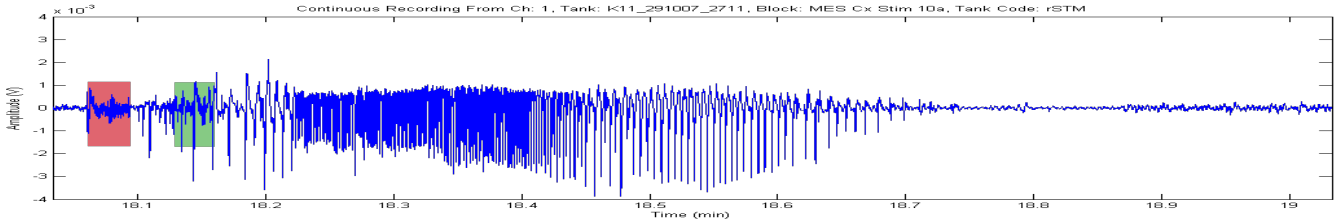


Deep Brain Stimulation for Epilepsy Suppression

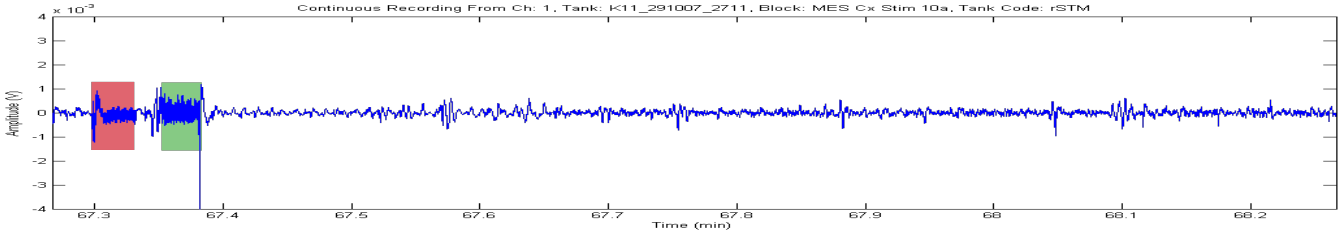
No therapeutic stimulation



Unsuccessful therapeutic stimulation



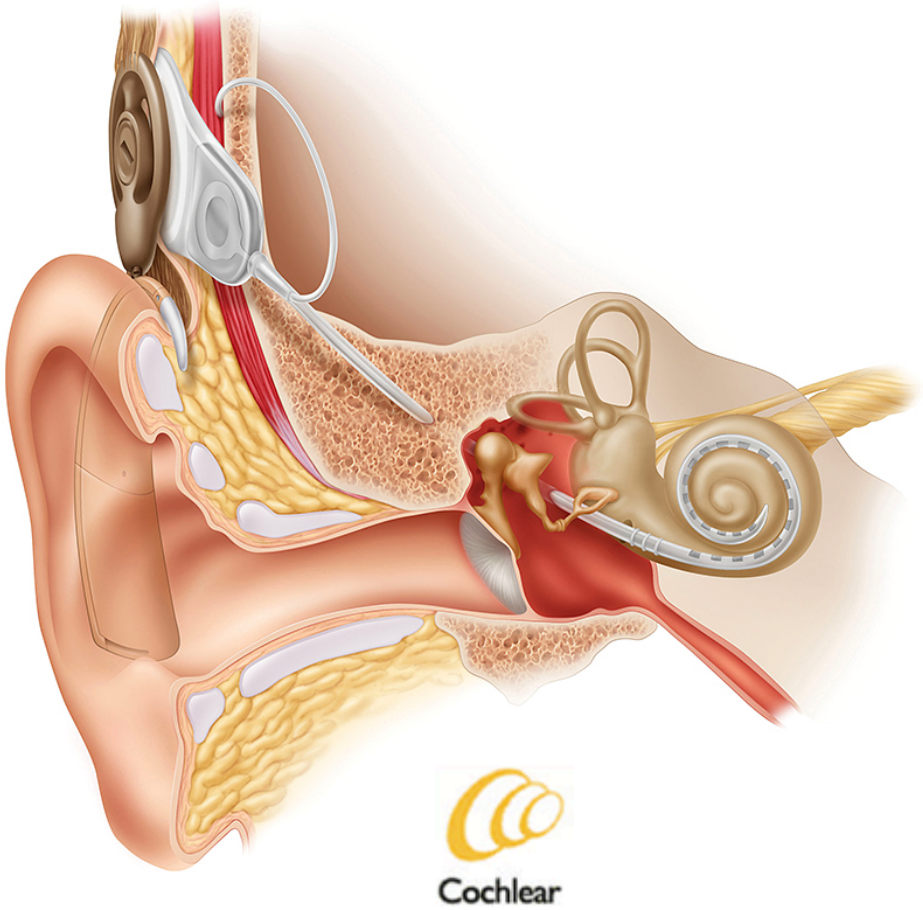
Successful therapeutic stimulation

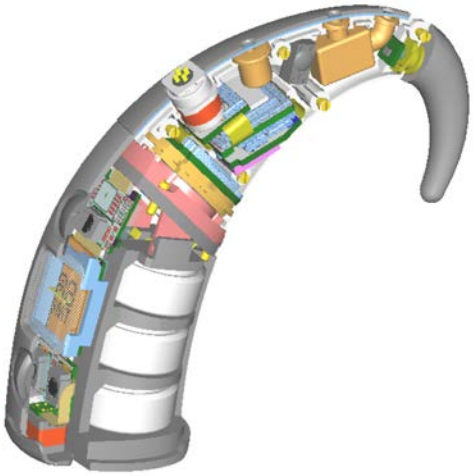


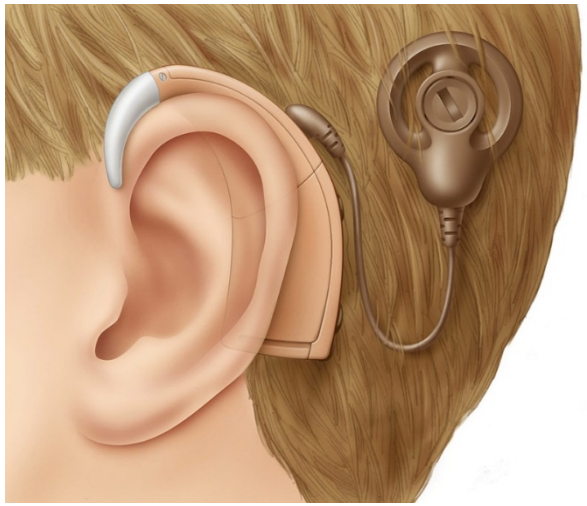
Deep Brain Stimulation for Epilepsy Suppression

Giving Back The Gift of Hearing

The World's Most Successful Implantable Bionic Device







Cochlear Ltd (Over 30 Years Old)

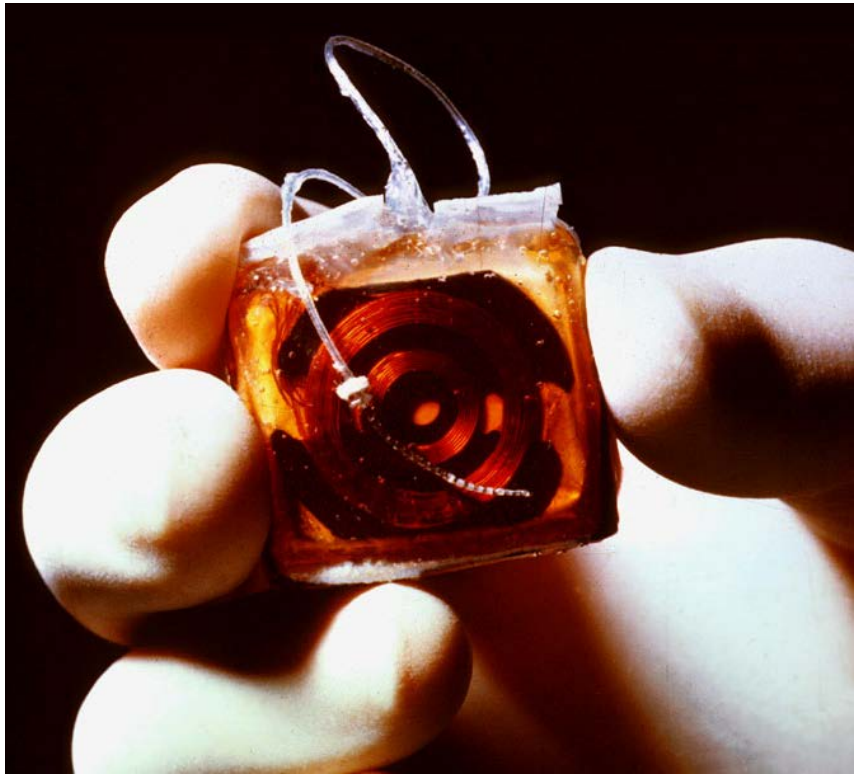
- More than 300,000 cochlear implants
- 2,600 highly skilled employees
- 65-70% of the world market in cochlear implants
- manufacturer of the world's most sophisticated medical bionics device
- 2017 net profit $223,616,000, ASX Share Price on 08/10/18: $202.86

1978 Was The Turning Point …

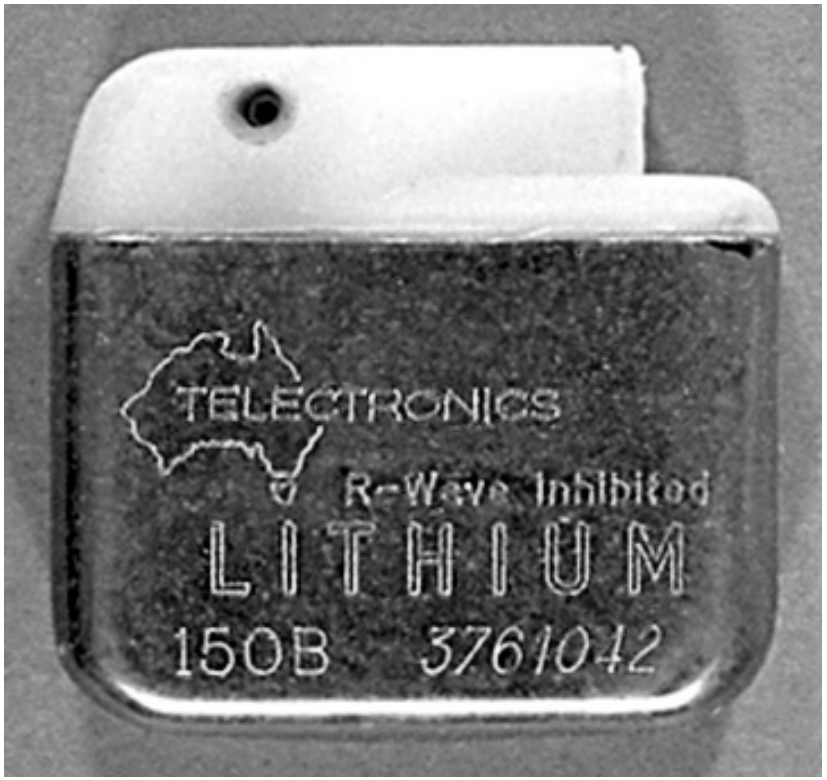
Department of Otolaryngology, University of Melbourne

But It Wasn't All Happy Days From the Start …

The University of Melbourne
Multi-channel Cochlear Implant
1978



Telectronics Australia
Pacemaker
1975



Department of Otolaryngology, University of Melbourne

But It Wasn't All Happy Days From the Start …

Circa 1978

Three Survived …

Source: RNID, 2005

China Has Emerged As A Strong New Player…

Source: RNID, 2005

Aug 17 2016 at 7:38 AM
Updated Aug 17 2016 at 11:40 AM

Cochlear locked in Chinese discounting war

by **Angus Grigg and Lisa Murray**

Hearing implant maker Cochlear has been drawn into a fierce price war in China, its fastest growing market and largest by volume, as a local competitor discounts aggressively.

The battle with the Hangzhou-based Nurotron, which counts Goldman Sachs among its investors, has driven down the average implant price for the central government tender by 25 per cent to about $US6000 ($7800) over the last two years, according to public tender documents. And the price is set to fall even further as Nurotron increases production.

"Without our entry into the market, prices would not have declined this much," said Nurotron founder Li Fangping.

Source: Cochlear Ltd

Cochlear® Hear now. And always

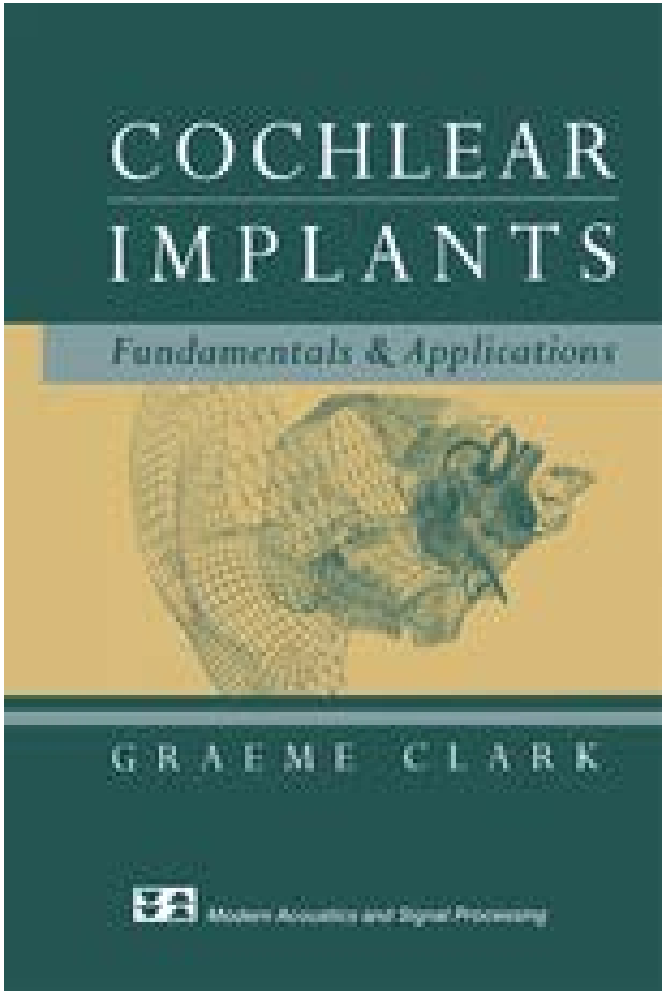
Cochlear to expand global capacity with China manufacturing facility

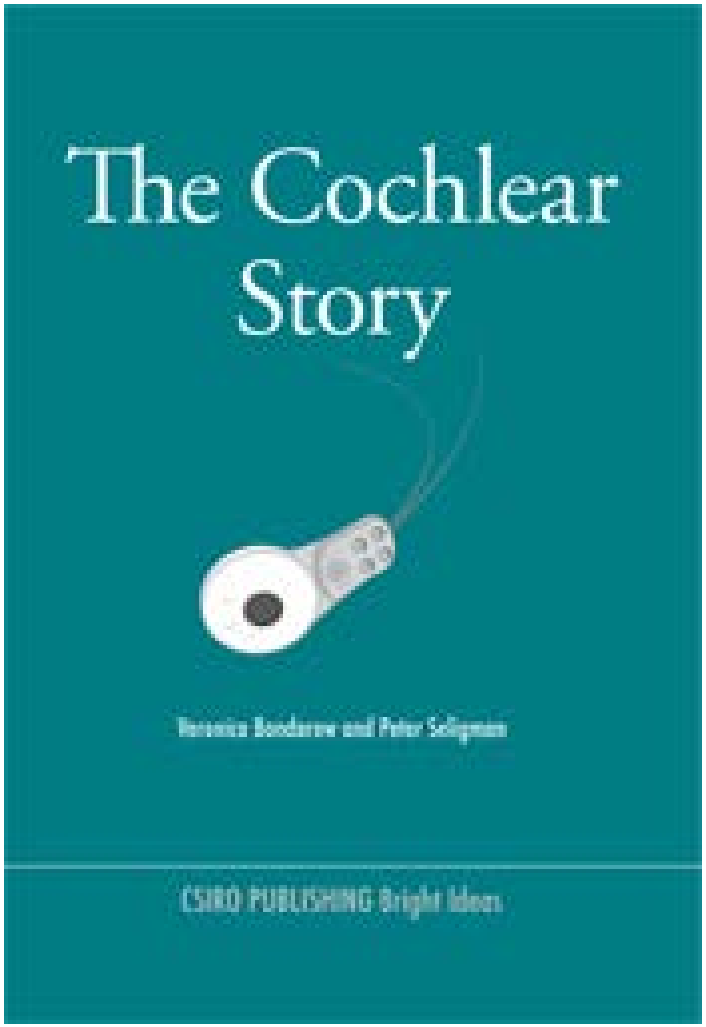
13 July, 2017

- Estimated AUD$50 million investment in state-of-the-art facility in China for the manufacturing of cochlear implants and sound processors for China and emerging markets
- Strengthens presence in a fast growing market for Cochlear and boosts future global manufacturing capacity

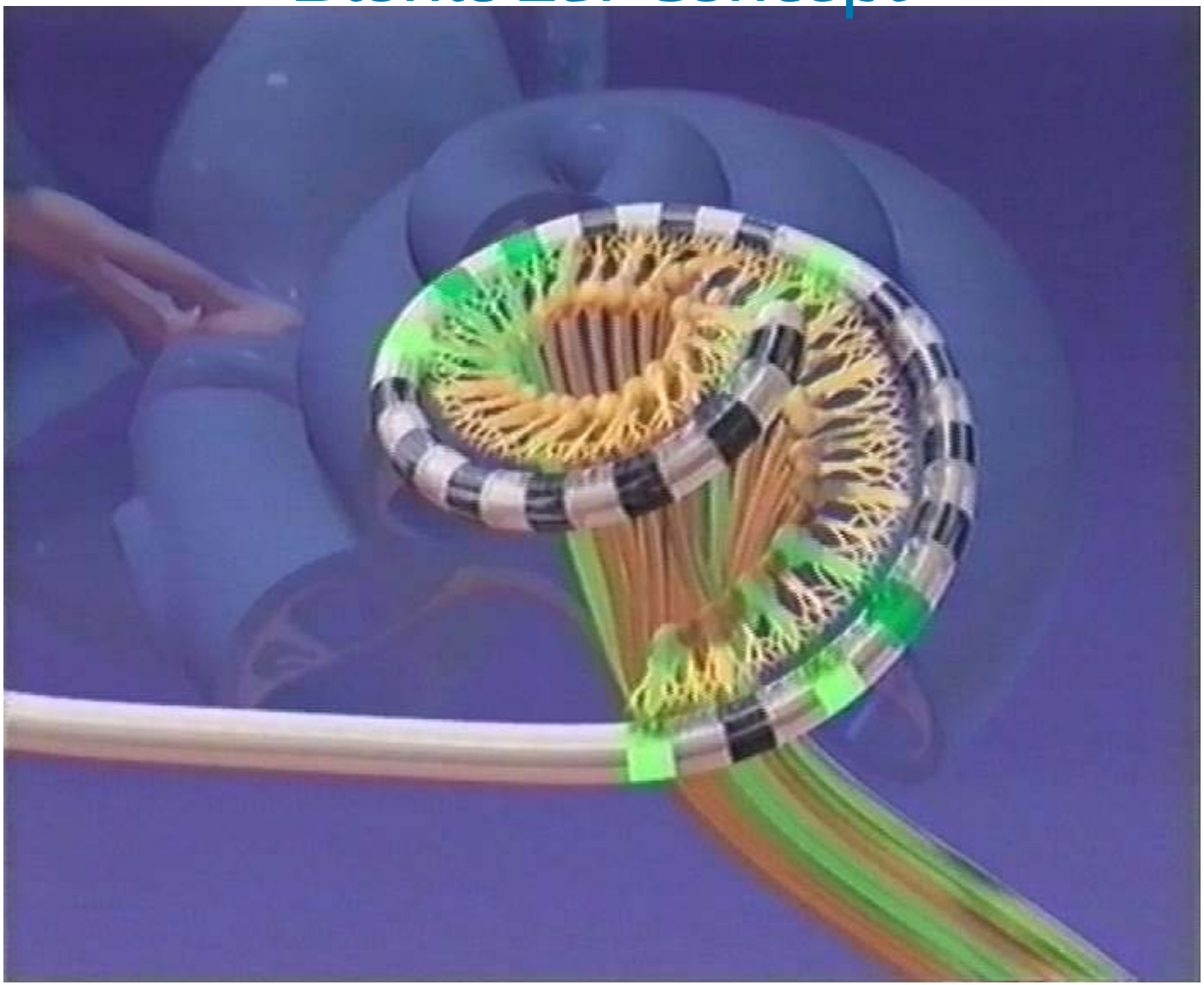
SYDNEY – Cochlear Limited (ASX: COH), the worldwide leader in implantable hearing solutions, today announced plans to expand its global manufacturing capacity with a new facility in China for the manufacture of cochlear implants and sound processors for an estimated AUD$50 million.

Want to Know More???





Bionic Ear Concept



Does it Work?

F0F1 Strategy

F0F1F2 Strategy

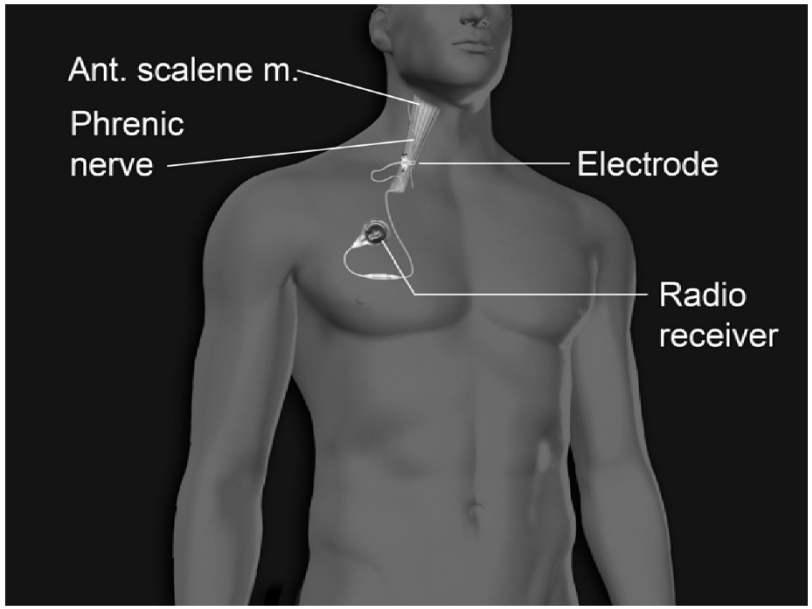
SPEAK Strategy

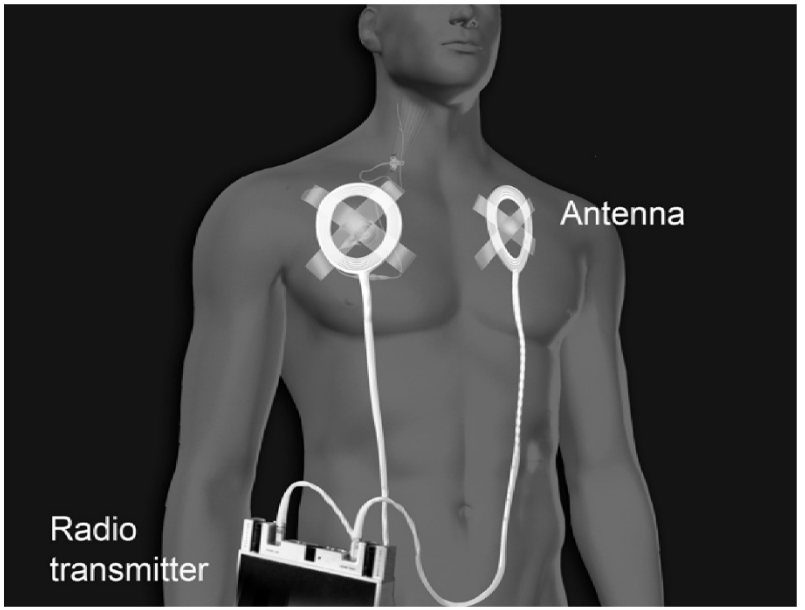
Perhaps Not For Music …

ACE Strategy

Other Peripheral Nerve AIMDs

Phrenic nerve stimulation for diaphragm pacing in SCI – "Breathing Pacemaker" FDA Approved Since 1987





Avery Biomedical Devices Inc.

Other Peripheral Nerve AIMDs

- Avery Biomedical Devices Inc. manufactures the only FDA approved device
- Approved for C1 & C2 Quadriplegia
- Number implanted ?
- Cost ?

Christopher Reeve

The World of Visual Prostheses

First Implantation of Prototype Bionic Eye With 24 Electrodes: 'All of a Sudden I Could See a Little Flash of Light'

ScienceDaily (Aug. 31, 2012) — In a major development, Bionic Vision Australia researchers have successfully performed the first implantation of an early prototype bionic eye with 24 electrodes.

Share This:

Like 431

Tweet 207

+1 35

Share 337

Ms Dianne Ashworth has profound vision loss due to retinitis pigmentosa, an inherited condition. She has now received what she calls a 'pre-bionic eye' implant that enables her to experience some vision. A passionate technology fan, Ms Ashworth was motivated to make a contribution to the bionic eye research program.

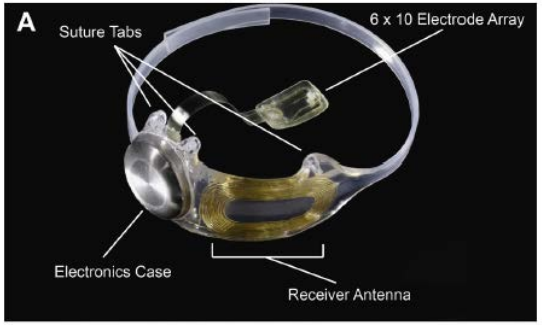
Patients Dianne Ashworth (left) with Dr. Penny Allen, a specialist surgeon at the Centre for Eye Research Australia. (Credit: Image courtesy of Bionic Vision Australia)

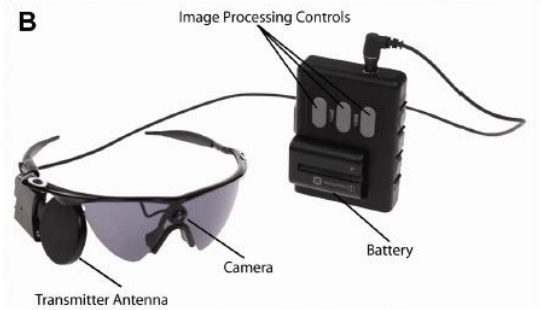
The World of Visual Prostheses

What We Really Want Patients to See

Artificial images are <u>aimed to be represented</u> through multiple phosphenes with varying levels of brightness to closely resemble the original image

Commercial Retinal Prosthesis Systems

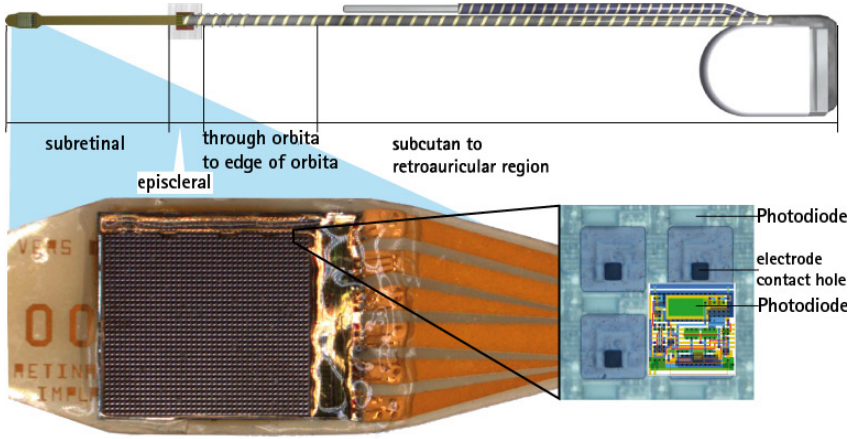




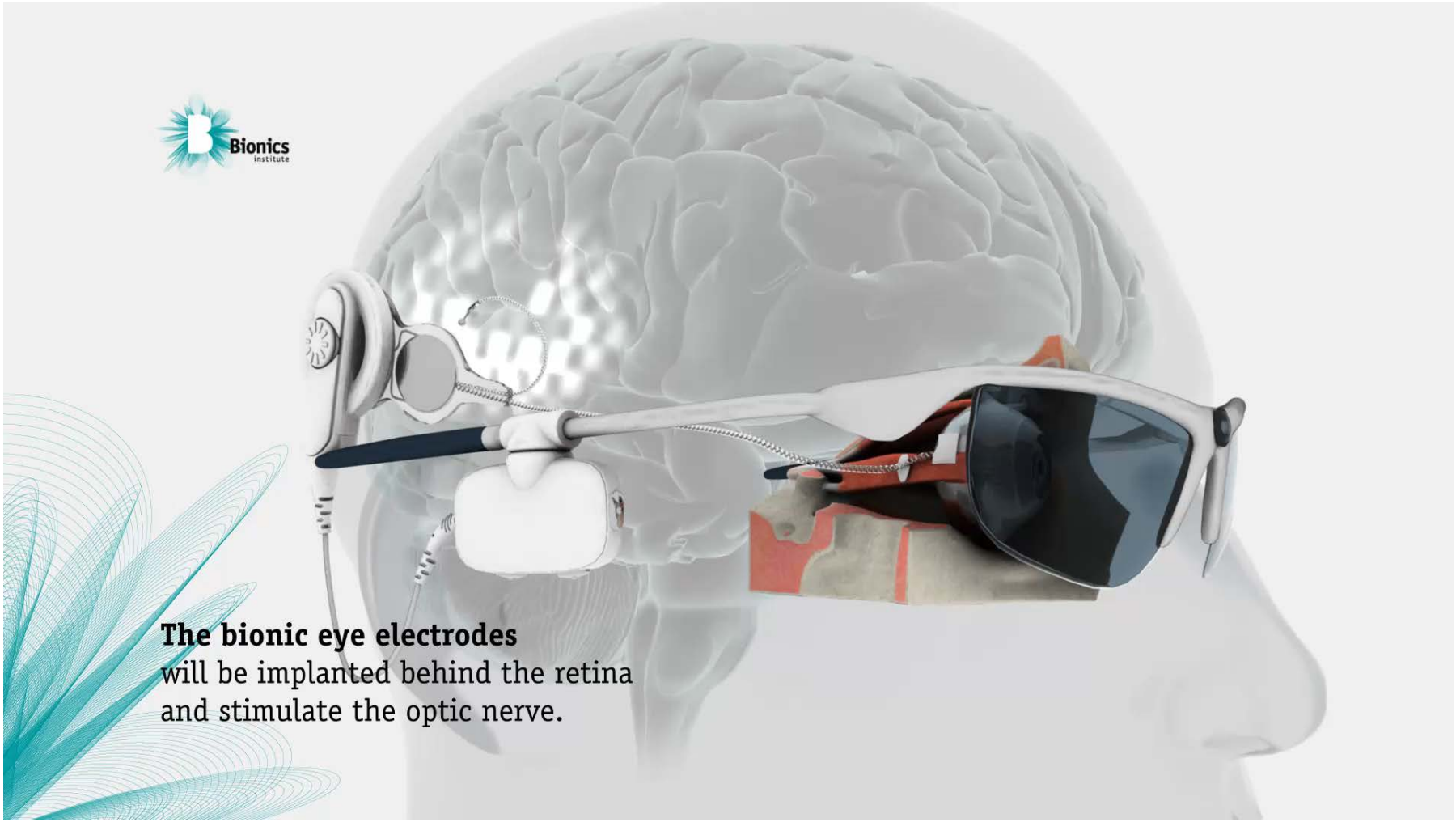
IRIS®II, PIXIUM VISION, FRANCE
(www.pixium-vision.com)

Argus®II, SSMP, USA
(Ho et al 2015)

Alpha IMS/AMS, Retina Implant AG, Germany
(www.retina-implant.de)



General Concept of a Retinal Prosthesis



Don’t Only Believe What I Say …

AIMDs in Active Research But Not Commercially Available

- Brain machine interface (BMI)
- FES for gait & standing in paraplegia
- Non-movement DBS
- Vestibular prostheses for balance restoration

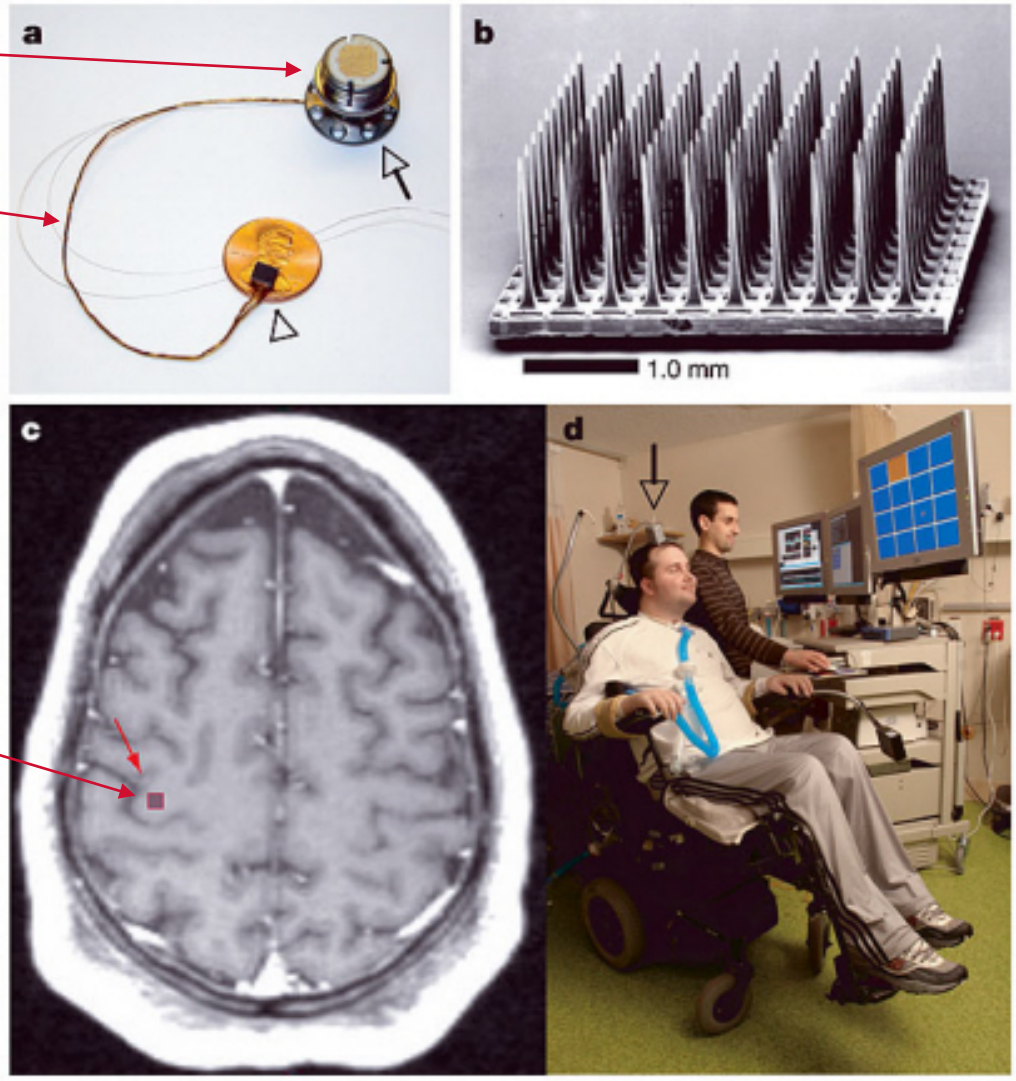
Brain-Machine Interfaces

Video from Disk

Brain-Machine Interfaces

Percutaneous connector

Leadwire



Motor cortex

10 x 10 Silicon Electrode array

Image courtesy of John Donohuge, Brown University/Cyberkinetics

Functional Electrical Stimulation (of Nerves and Muscles) For Standing And Gait

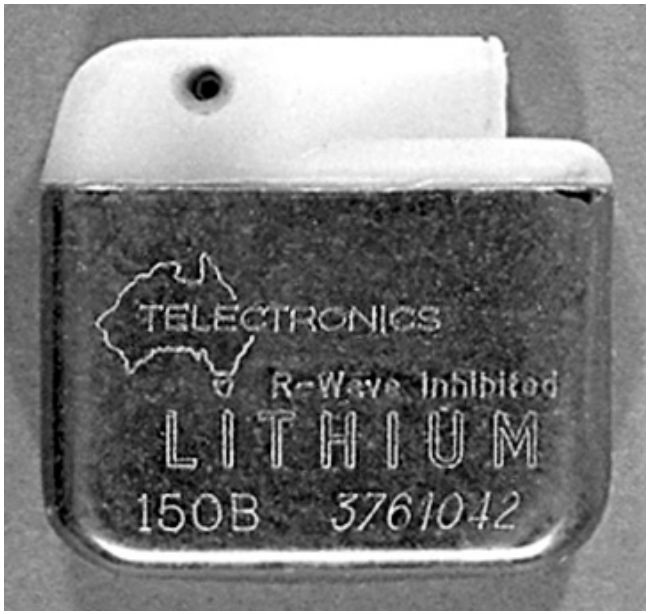
Courtesy Hunter Peckham, FES Lab, Case Western Reserve

(VERY) USEFUL CONCEPTS FOR MEDICAL BIONIC DEVICE DESIGN

Building a successful Medical Bionics device

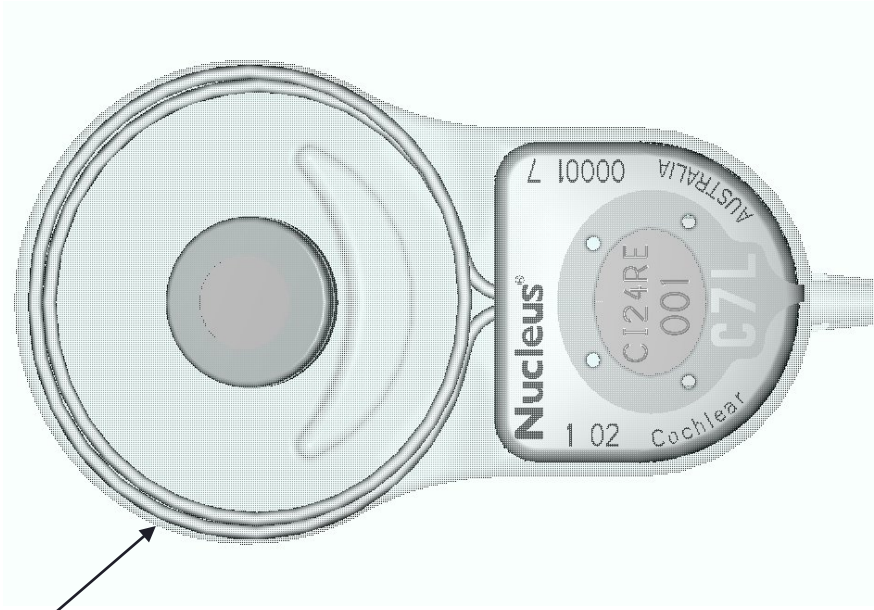
Powering implantable devices:

Telectronics Australia
Pacemaker
1975



Implanted battery (lithium)

Nucleus Australia
Cochlear Implant
2008

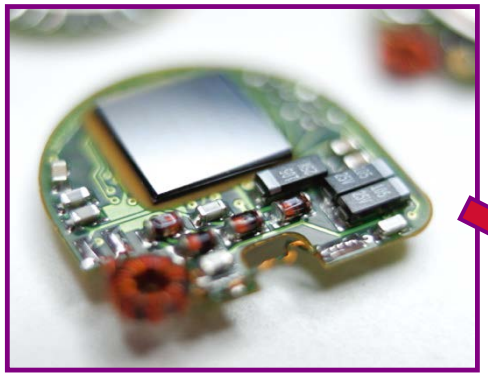


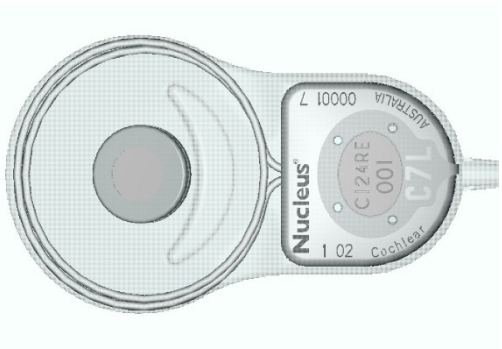
rf coil
for power & data

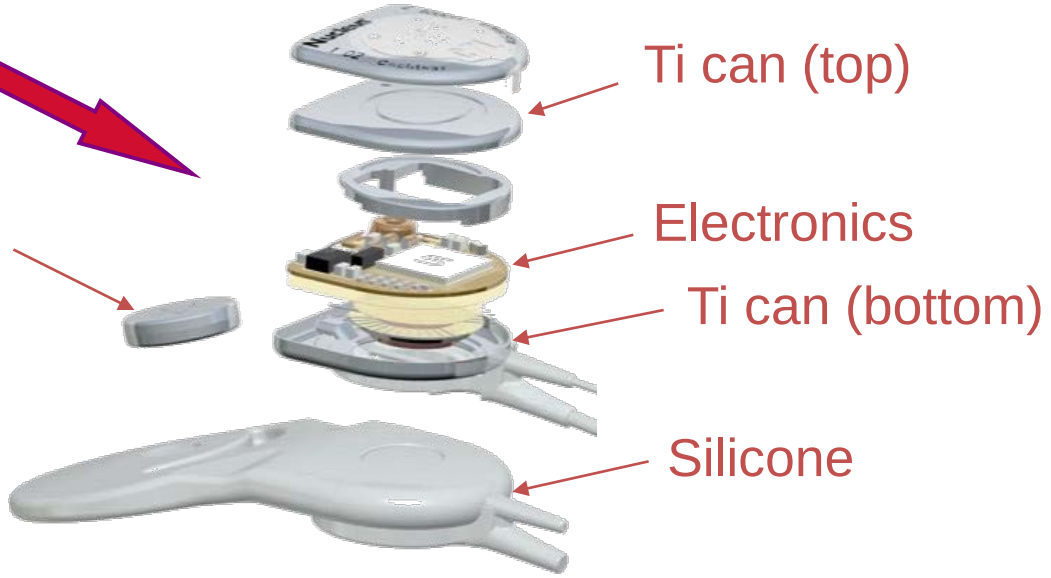
Building a successful Medical Bionics device

Hermetic seals: keeping body fluids away from the electronics

CI chip packaging





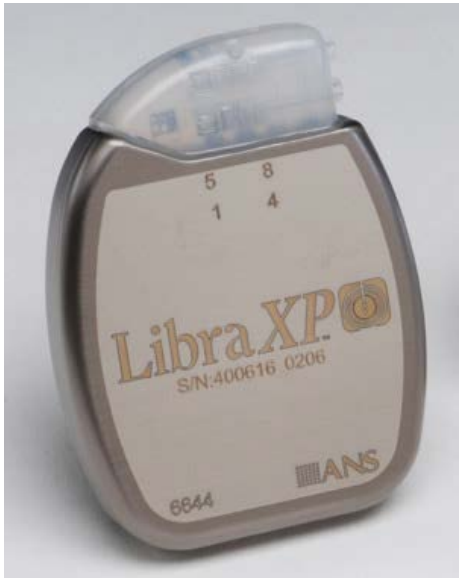


Courtesy of Peter Seligman, Cochlear Ltd.

Building a successful Medical Bionics device

Medical Bionics: Ti hermetically sealed packaging

Common in devices with internal power supply

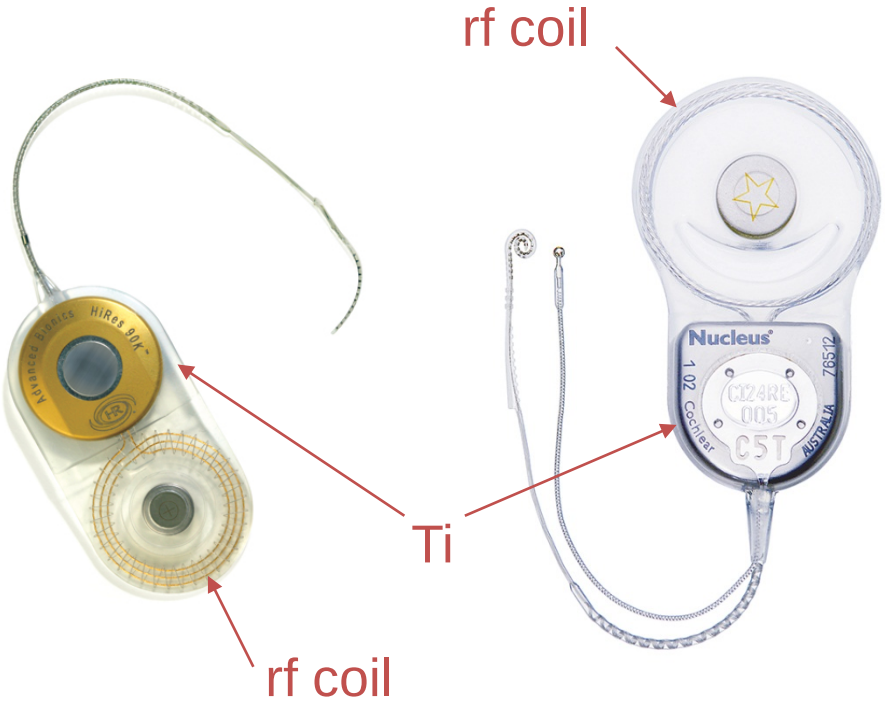


Building a successful Medical Bionics device

Medical Bionics: Ti hermetically sealed packaging

- Ceramic packaging used in some devices that use RF power and data transmission
- ↑ More efficient RF antenna; ↓ brittle/damaged

Ceramic
(rf coil encased)



Building a successful Medical Bionics device

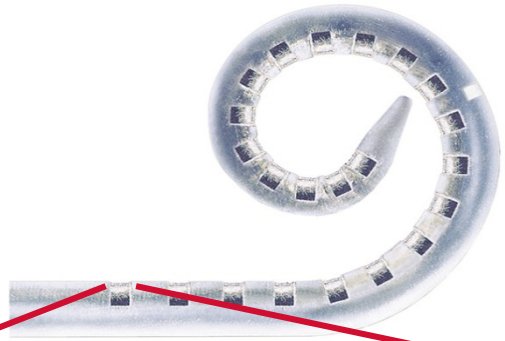
Electrode materials:

http://upload.wikimedia.org/wikipedia/commons/9/97/Corrosion.jpg

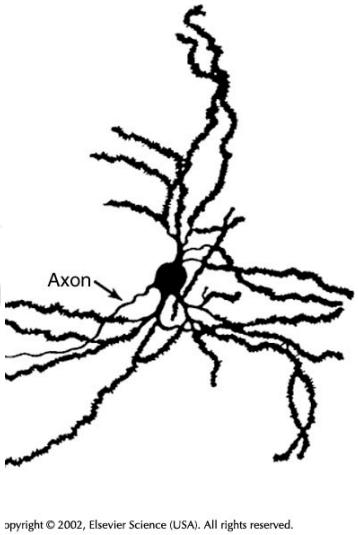
Building a successful Medical Bionics device

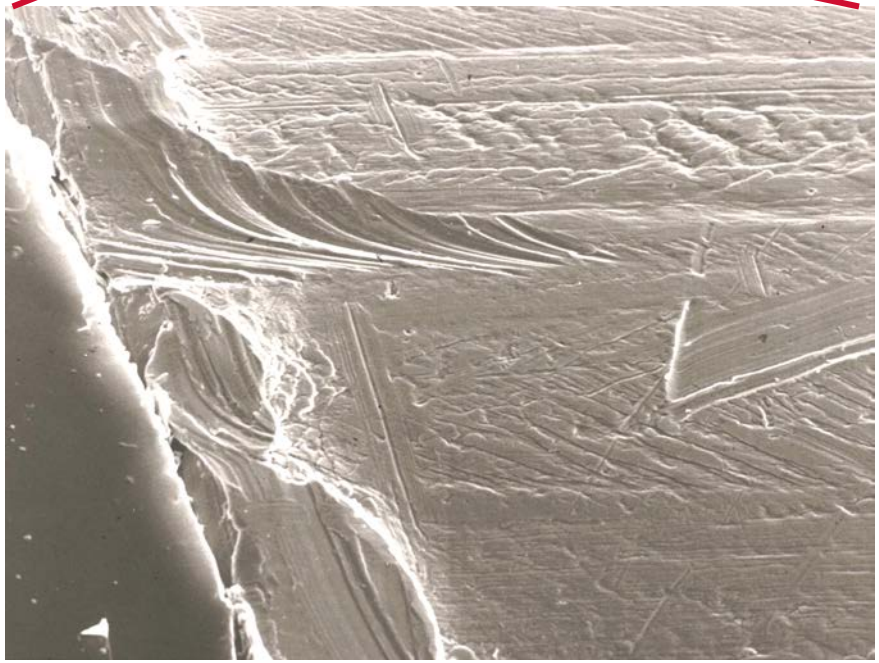
Electrode materials:

- Iridium Oxide or Platinum



Iridium microelectrode



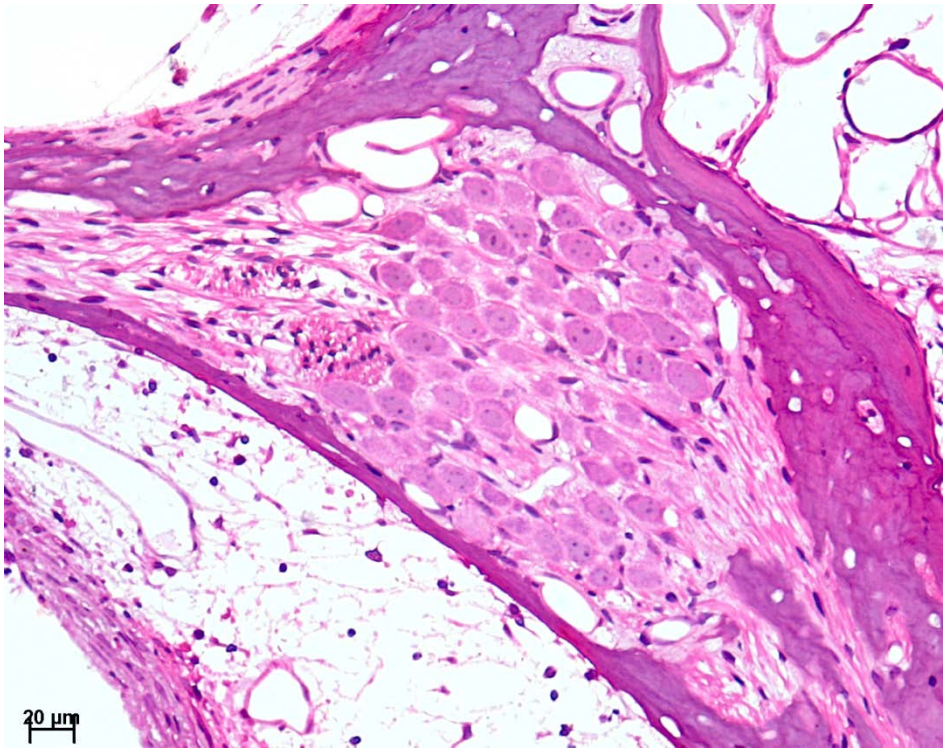


Platinum macroelectrode

Building a successful Medical Bionics device

Biocompatible materials:

- Silicone, Ti, Pt, Ir, Ceramic



Thin tissue capsule

Electrode array

Electrochemical Considerations for Safe Electrical Stimulation of the Nervous System with Platinum Electrodes

S. B. BRUMMER AND M. J. TURNER

1977

Pioneering Work in Late 70s up to Early 90s

CRITERIA FOR SELECTING ELECTRODES FOR ELECTRICAL STIMULATION: THEORETICAL AND PRACTICAL CONSIDERATIONS

S. B. Brummer and L. S. Robblee

EIC Laboratories, Inc.
Newton, Massachusetts 02158

F. T. Hambrecht
National Institute of Neurological and Communicative Disorders and Stroke
National Institutes of Health
Bethesda, Maryland 20014

1983

ELSEVIER

Journal of Neuroscience Methods 141 (2005) 171–198

JOURNAL OF NEUROSCIENCE METHODS

www.elsevier.com/locate/jneumeth

Invited review

Electrical stimulation of excitable tissue: design of efficacious and safe protocols

Daniel R. Merrill[a,*], Marom Bikson[b], John G.R. Jefferys[c]

Merill et al, J Neurosci Methods, 2005

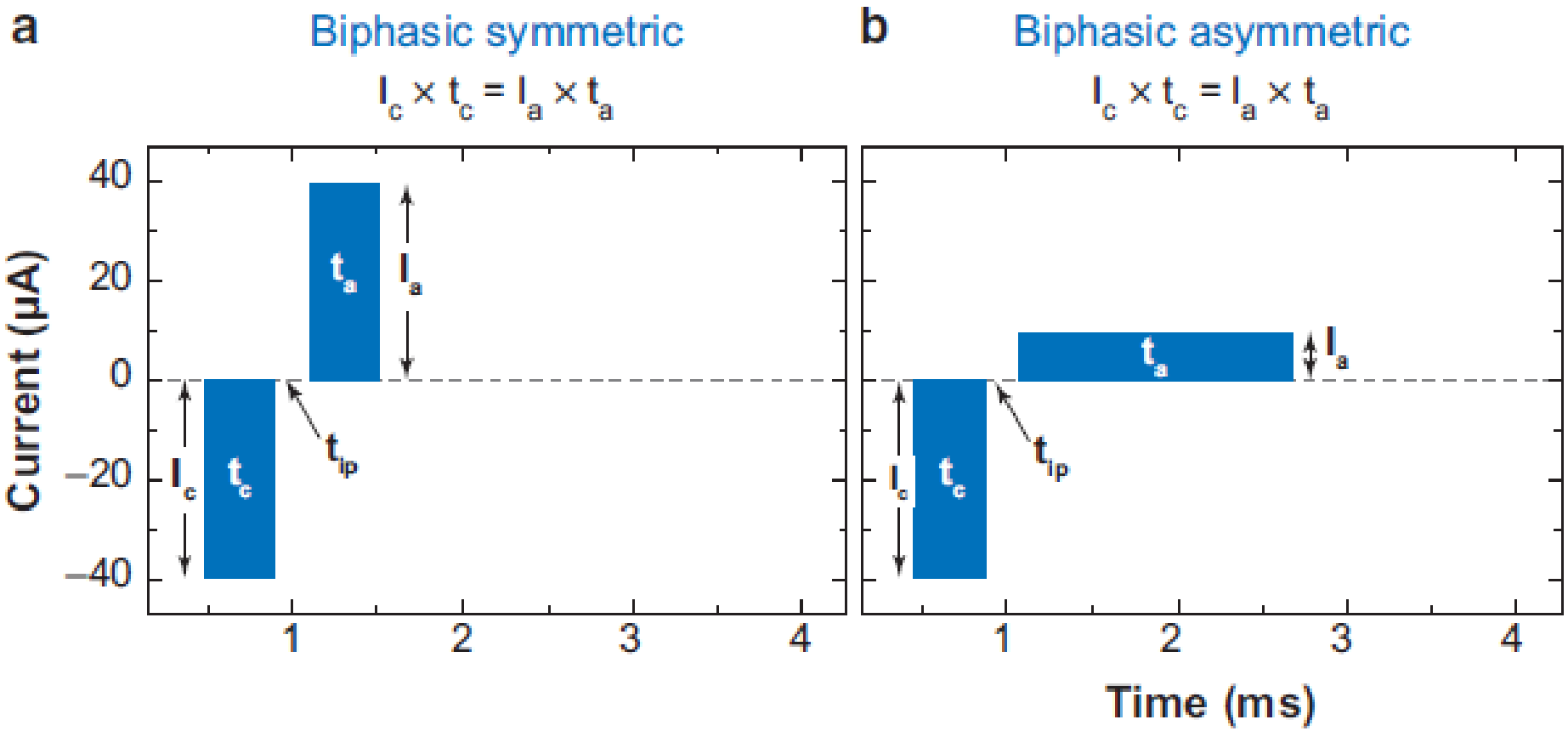
Neural Stimulation and Recording Electrodes

Stuart F. Cogan

EIC Laboratories, Inc., Norwood, Massachusetts 02062; email: scogan@eiclabs.com

Cogan, Annu Rev Biomed Eng, 2008

Basics of Charge Balance



Cogan, Annu Rev Biomed Eng, 2008

Charge Injection Capacity

Material	Mechanism	Maximum Q_{inj} (mC cm^{-2})	Potential Limits V versus Ag|AgCl
Pt and PtIr alloys	Faradaic/capacitive	0.05–0.15	−0.6–0.8
Activated iridium oxide	Faradaic	1–5	−0.6–0.8
Thermal iridium oxide	Faradaic	~1	−0.6–0.8 V
Sputtered iridium oxide	Faradaic	1–5	−0.6–0.8 V
Tantalum/Ta_2O_5	Capacitive	~0.5	
Titanium nitride	Capacitive	~1	−0.9 to 0.9
PEDOT	Faradaic	15	−0.9 to 0.6

Basics of Stimulation Safety – Electrode Damage (Irreversible Reactions)

$$2H_2O + 2e^- \rightarrow H_2\uparrow + 2OH^- \quad \text{(reduction of water)}$$

$$2H_2O \rightarrow O_2\uparrow + 4H^+ + 4e^- \quad \text{(oxidation of water)}$$

- Hydrogen/Oxygen gas evolution (electrode corrosion)
- Release of hydroxyl ions (raises pH)

Basics of Stimulation Safety – Electrode Damage (Irreversible Reactions)

Electrical stimulation with Pt electrodes. VII. Dissolution of Pt electrodes during electrical stimulation of the cat cerebral cortex

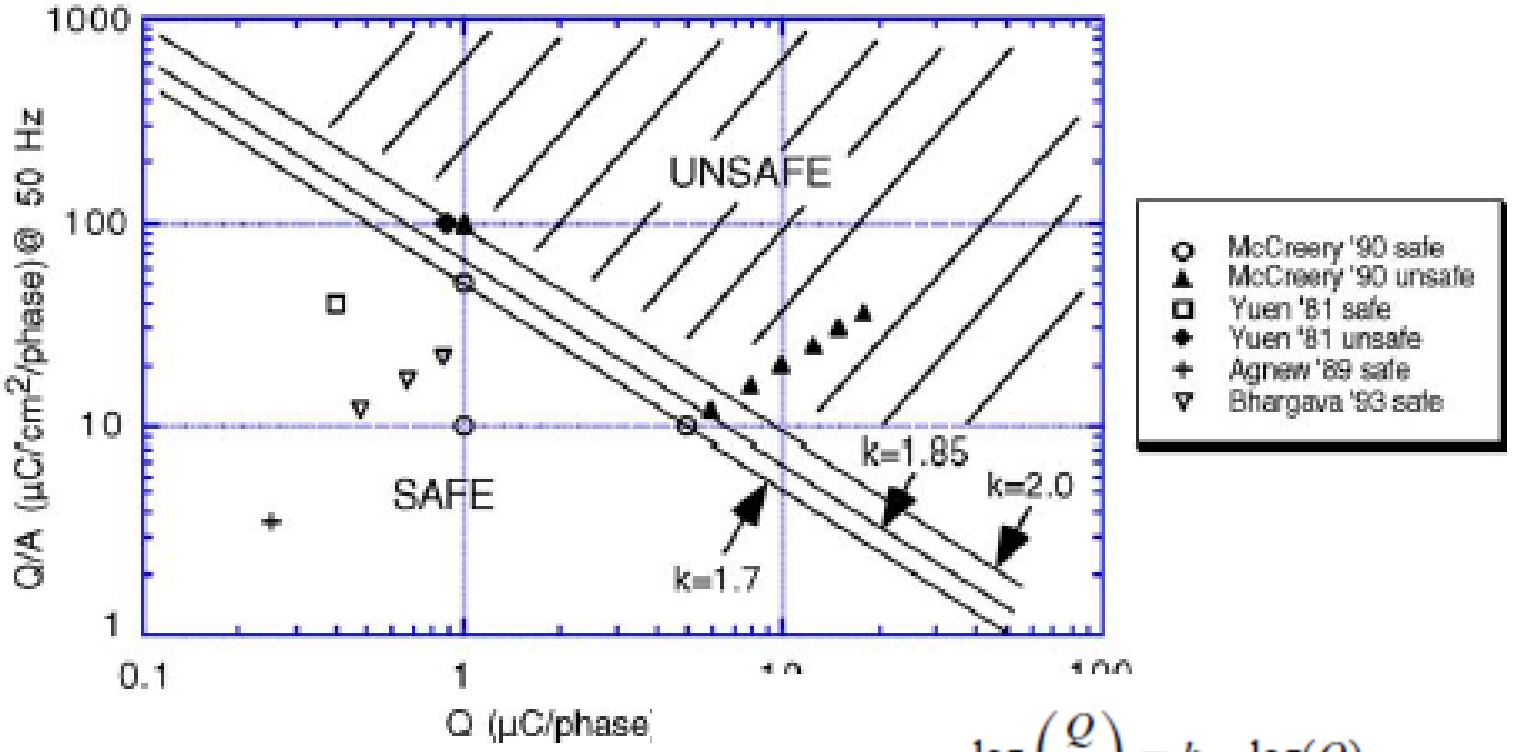
L.S. Robblee [1], J. McHardy [1], W.F. Agnew [2] and L.A. Bullara [2]

Basics of Stimulation Safety – Electrode Damage (Irreversible Reactions)

Procedures are described for determining trace quantities of Pt released into brain tissue directly beneath cortical surface stimulation electrodes.

Implanted electrodes (1.1 mm Pt discs) were stimulated for 4.5 h, 9 h and 36 h (4×9 h/day) with balanced biphasic pulses (20 $\mu C/cm^2$ or 100 $\mu C/cm^2$ per phase, 50 Hz), following which tissue 0–2 mm beneath stimulation electrodes and the encapsulating tissue adherent to electrodes was excised and analyzed for Pt. A time-dependent increase in Pt concentration was observed between 4.5 h (4–20 ng Pt/stimulation site) and 9 h (50–339 ng Pt/site) of stimulation at 100 $\mu C/cm^2$ with nearly all of the Pt located in the encapsulating tissue associated with the electrodes. Somewhat less Pt was observed in the 36 h samples, and it was almost equally distributed between the encapsulating tissue of the electrodes and the first millimeter depth of underlying brain tissue. Little or no Pt was found at electrode sites receiving 20 $\mu C/cm^2$ pulses. Control brain tissue samples as well as samples of blood, CSF and kidney were negative for Pt. The findings indicate that the rate of Pt dissolution gradually decreases during in vivo stimulation, and that dissolved Pt may slowly move away from stimulation sites, possibly by diffusion or fluid exchange.

Basics of Stimulation Safety – Tissue Damage



$$\log\left(\frac{Q}{A}\right) = k - \log(Q) \qquad (5.1)$$

Shannon, IEEE TBME (1992) Formula

where Q is charge per phase (μC per phase), Q/A is charge density per phase (μC/cm² per phase), and $2.0 > k > 1.5$, fit to the empirical data.