Emerging neurotechnology: Implanted brain interfaces

Ochsner Regional Neuroscience Symposium

Andrew S. Whitford

May 2023

Disclosures

- No conflicts
- No affiliation with any commercial entities covered in this presentation
- Staff researcher at Carnegie Mellon University
- Research contract with Ochsner Health

Objectives

1. Compare current and emerging neurotechnology devices.
2. Describe several products planned for the next decade.
3. Discuss the role of clinicians in neurotechnology development.

Outline

- Current technology
- Context and motivation
- Emerging technology
- Expected products
- Clinical research

Current technology

Medtronics DBS

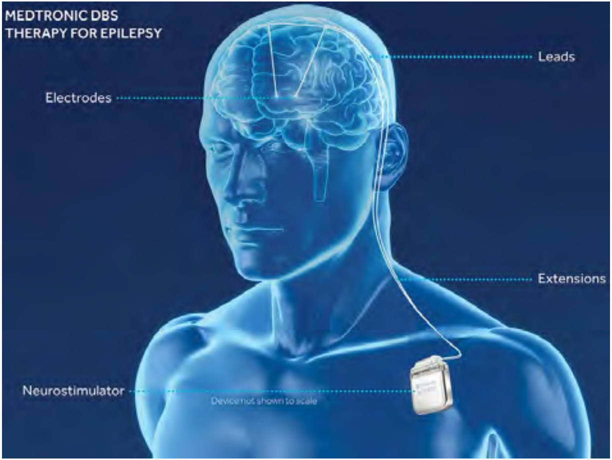


Figure 1: Waltz 2020 [1]

[1] How Do Neural Implants Work?

Neuropace RNS

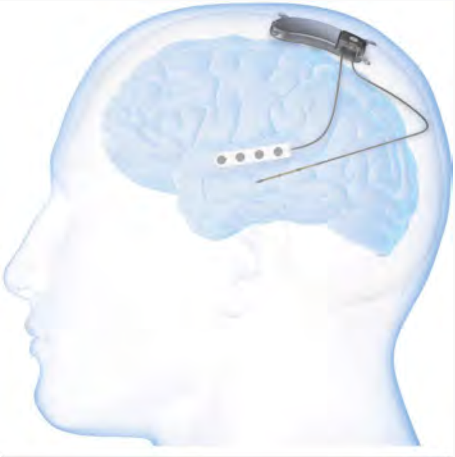


Figure 2: Nair et al. 2020 [2]

[2] Nine-year prospective efficacy and safety of brain-responsive neurostimulation for focal epilepsy

Medtronic Summit RC+S

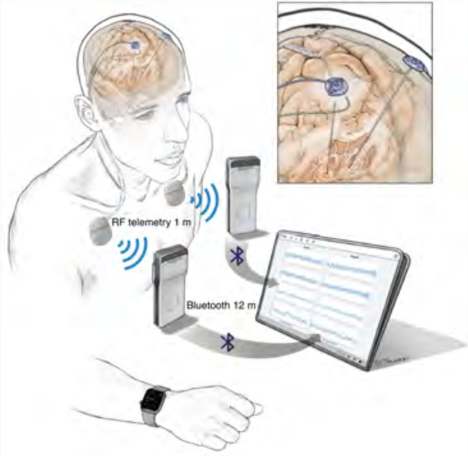


Figure 3: Gilron et al. 2021 [3]

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

Context and motivation

Emerging neurotechnology

Figure 4: Brain Initiative event 2016

Surge in attention, funding, (and hype)

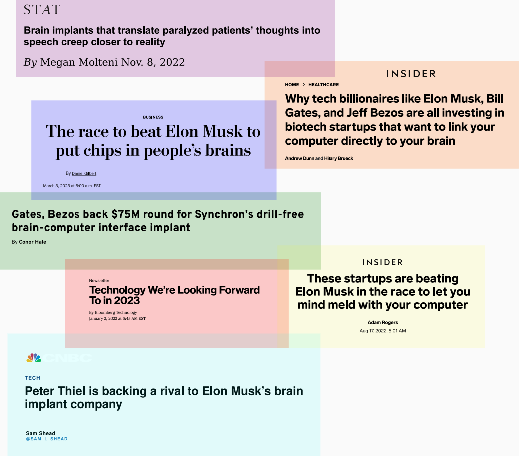
In the last year there has been increasing interest and investment into developing devices to interact with the central nervous system, in particular developing a robust brain-computer interface (BCI).

[T]here has been an explosion of interest by entrepreneurs looking to become actively involved... spurred on in part by the BRAIN Initiative.

– Mitrasinovic et al. 2018 [4]

[4] Silicon Valley new focus on brain computer interface: hype or hope for new applications?

Media coverage (2021-2023)


STAT

Brain implants that translate paralyzed patients' thoughts into speech creep closer to reality

By Megan Molteni Nov. 8, 2022

INSIDER

HOME > HEALTHCARE

Why tech billionaires like Elon Musk, Bill Gates, and Jeff Bezos are all investing in biotech startups that want to link your computer directly to your brain

Andrew Dunn and Hilary Brueck

BUSINESS

The race to beat Elon Musk to put chips in people's brains

By Daniel Gilbert

March 3, 2023 at 6:00 a.m. EST

Gates, Bezos back $75M round for Synchron's drill-free brain-computer interface implant

By Conor Hale

INSIDER

These startups are beating Elon Musk in the race to let you mind meld with your computer

Adam Rogers

Aug 17, 2022, 5:01 AM

Newsletter

Technology We're Looking Forward To in 2023

By Bloomberg Technology

January 3, 2023 at 6:45 AM EST

CNBC

TECH

Peter Thiel is backing a rival to Elon Musk's brain implant company

Sam Shead

@SAM_L_SHEAD

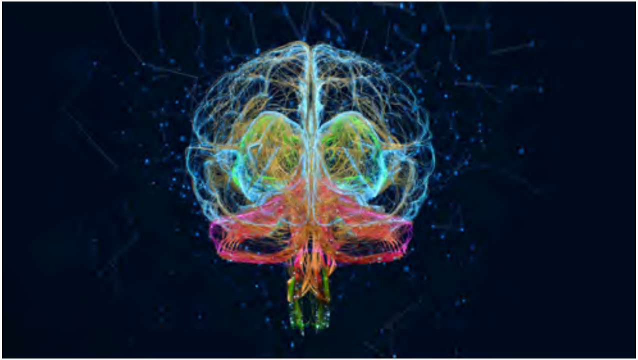
Figure 5: Washington Post, CNBC, Bloomberg, Insider, etc.

Next step: Healthcare market

02-14-23 | FUTURE OF HEALTH

How VCs are vying for a piece of your brain—literally

To pay for futuristic brain implants, companies are eyeing a surprising business model: Medicare reimbursements.



Digital image of artificial intelligence human brain.

BY REBECCA HEILWEIL
6 MINUTE READ

Figure 6: Fast Company 2023

Emerging technology

FDA

Implanted Brain-Computer Interface (BCI) Devices for Patients with Paralysis or Amputation - Non-clinical Testing and Clinical Considerations

Guidance for Industry and Food and Drug Administration Staff

Document issued on May 20, 2021.

The draft of this document was issued on February 22, 2019.

For questions about this document, contact the OHT5: Office of Neurological and Physical Medicine Devices/DHT5B: Division of Neuromodulation and Physical Medicine Devices/Acute Injury Devices Team at (301) 796-6610.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health

Figure 7: 2021 Guidance

Example: Utah array

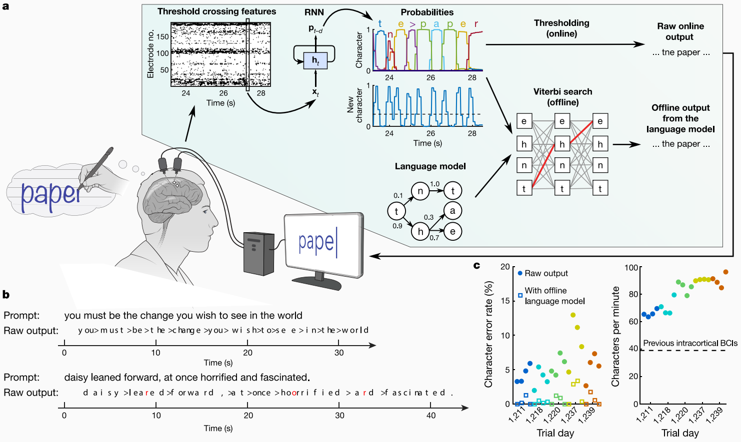


Figure 8: Willett et al. 2021[5]

[5] High-performance brain-to-text communication via handwriting.

Example: HD-ECoG

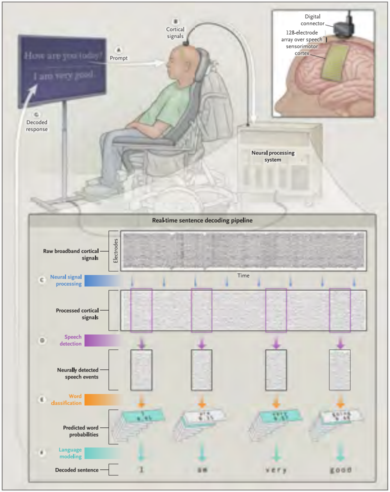


Figure 9: Moses et al. 2021 [6]

[6] Neuroprosthesis for Decoding Speech in a Paralyzed Person with Anarthria

Expected products

Neuralink

- Launched in 2016
- Existing IP from UCSF
- Elon Musk
- Funding: $363M
- Planned human trials:
    - ~~2020~~
    - ~~2021~~
    - ~~2022~~
    - 2023

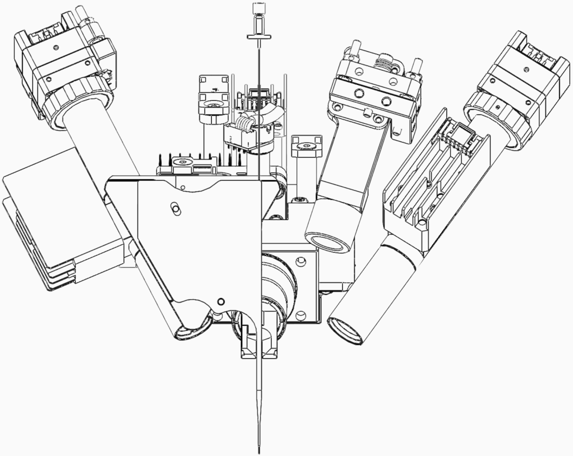


Figure 10: Surgical robot [7]

[7] neuralink.com/robotics

Results (recruiting)

- 2019: Musk et al.: [8]

  "simultaneous broadband recording from over 3000 inserted electrodes in a freely moving rat"

- 2020: Live demonstration of recording in pigs
- 2021: Pager / Pong demonstration

[8] An Integrated Brain-Machine Interface Platform With Thousands of Channels

Synchron [9]

synchron

- Bootstrapped by DARPA
- Funding: $130M
- Endovascular approach
- SWITCH trial (Australia)
- COMMAND trial
  - UPMC / Pittsburgh
  - Mount Sinai / Buffalo

Goals

- 15 implants before 2024
- Product by 2026
- 1M implants by 2037

[9] synchron.com

Figure 11: brain.io [10]

[10] https://synchron.com/technology/brain-io

Synchron (3/3)

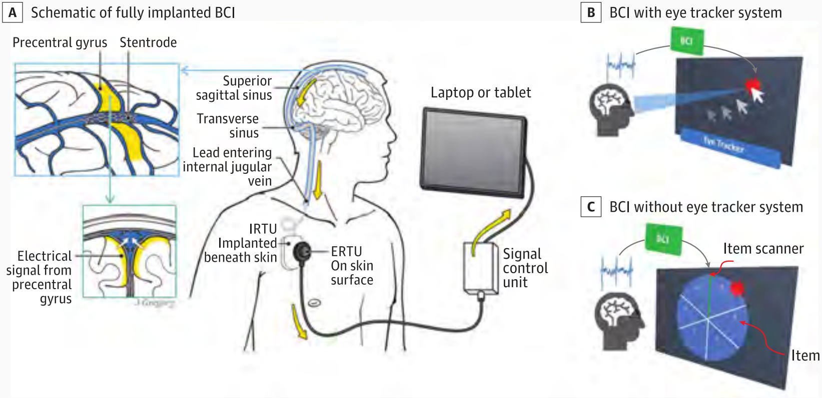


Figure 12: Mitchell et al. 2023 [11]

[11] Assessment of Safety of a Fully Implanted Endovascular Brain-Computer Interface for Severe Paralysis in 4 Patients: The Stentrode With Thought-Controlled Digital Switch (SWITCH) Study

Precision

- Cofounder of Neuralink
- Funding: $53M
- High-density ECoG
- Layer-7: 1,000-fold higher electrode density than standard cortical grid (Ho et al. 2022 [12])
- "Advancing toward clinical trials in 2023" [13]

[12] The Layer 7 Cortical Interface: A Scalable and Minimally Invasive Brain–Computer Interface Platform

[13] Precision Neuroscience Raises $41 Million to Build and Scale the Next Generation of Treatments for Neurological Illnesses

Non-damaging, upgradeable interfaces

Our electrode arrays will be implanted using a novel, minimally invasive, cranial micro-slit technique. Unlike other approaches, Precision's surgery is designed to be fully reversible. The arrays are configured to conform to the surface of the brain, maximizing bandwidth without doing damage to brain tissue. [14]

[14] precisionneuro.io

Minimally invasive, cranial micro-slit surgery:

Figure 13: Precision Neuroscience: Layer-7 [15]

[15] precisionneuro.io/product

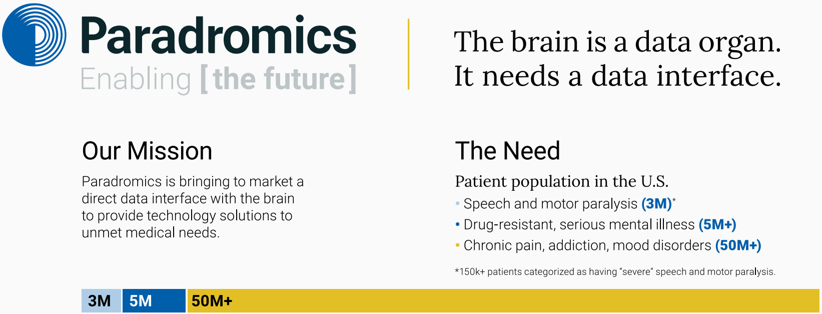


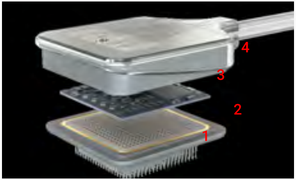
Figure 14: Paradromics fact sheet [16]

[16] https://www.paradromics.com

Enabling [technology]

Connexus® Direct Data Interface

- Revolutionary leap beyond today's lab-confined brain-computer interfaces (BCI)
- Collects an unprecedented number of individual neural signals
- Fully-implantable device designed for long-term daily service



The Connexus Direct Data Interface cortical module: (1) Fine (<40 μm) microelectrodes minimize tissue impact (2) Hermetic electrode feedthrough protects electronics during long-term implantation (3) Patented on-chip Quartet™ Neural Signal Transform provides low-power conversion of neural signal to usable data (4) Signals leave the module on a small, flexible lead.

Enabling [people]

First clinical application

Our first use will be as an assistive communication device for patients who've lost the physical ability to speak or type–essentially transforming their neural data into text or synthesized speech.

Enabling [the future]

New medical paradigm

By making the brain accessible to direct communication with digital interfaces, we can leverage technology to solve some of our most difficult neurological and brain-related medical challenges. With their first clinical use on the horizon, we've only begun to realize the vast impact that direct data interfaces with the brain will have on the future of medicine.

Figure 15: Paradromics fact sheet

Paradromics

- Founded in 2015
- Funding:
  - $47M (venture)
  - $18M (DARPA and NIH)
- Sahasrabuddhe et al. 2021 [a]
  - 65,536 channels
  - 32 kHz, 12-bits
- Products
  - Quartet NST
  - Connexus DDI

- Goal: Clinical trials by 2024

[a] The Argo: a high channel count recording system for neural recording in vivo

Blackrock Neurotech

- Formerly:
  - Blackrock Microtech
  - Cyberkinetics
- Funding: $10M
- 30+ patients since 2009

Planned products [a]

- *MoveAgain*: ~~2022~~, 2024
- *TalkAgain*: Similar timeline
- *HearAgain*: 40-50 patients by 2026
- *SeeAgain*: First-in-human by 2028

[a] Partnered with Clearpoint Neuro.

Blackrock Neurotech

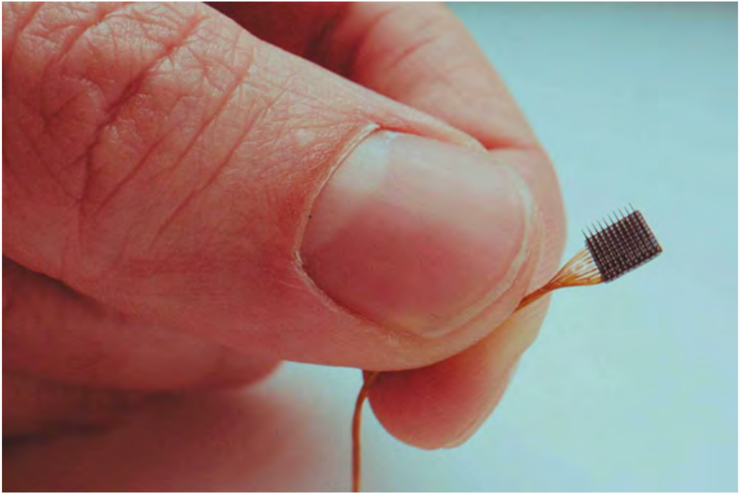


Figure 16: Utah Array

Blackrock Neurotech

Utah arrays remain the sole penetrating electrode architecture approved for human use under the Investigational Device Exemption of the FDA and Institutional Review Board approvals.

– *Shen et al. 2023* [17]

[17] Translational opportunities and challenges of invasive electrodes for neural interfaces

Blackrock Neurotech

e1182 Neurology | Volume 100, Number 11 | March 14, 2023

Table 3 Summary of Demographic and Safety Data

Participant	Sex	Etiology	SCI motor level–ASIA impairment scale	Age at implant	Time from injury/ diagnosis to implant (y)	No. of arrays	Duration of implant (d)	Array-implant d	Status	Total AEs	Total SAEs	Possibly, probably, or definitely device-related or procedure- related AEs	Possibly, probably, or definitely device-related or procedure- related SAEs	Skin-related device AEs[a]	Surgery-related AEs[a]
S1	M	SCI	C4-A	24	3	1	484	484	Explanted	0	0	0	0	0	0
S2	M	SCI	C4-A	55	6	1	790	790	Explanted	2	1	0	0	0	0
A1	M	ALS		36	7	1	298	298	Deceased	3	2	1	0	1	0
S3	F	Stroke[b]		51	10	1	1,994	1994	Explanted	21	1	5	0	3	2
T1	F	ALS		48	7	1	307	307	Deceased	13	3	2	0	2	0
T2	M	Stroke[b]		66	5	1	950	950	Explanted	35	10	2	1	0	0
T3	M	ALS		52	2	1	440	440	Deceased	21	6	1	0	0	1
T5	M	SCI	C4-C	63	9	2	1,962	3,924	Enrolled	27	14	3	0	3	0
T6	F	ALS		50	7	1	1,216	1,216	Explanted	62	9	11	0	6	1
T7	M	ALS		57	3	2	552	1,104	Deceased	48	5	10	1	6	3
T8	M	SCI	C4-A	53	8	2	1,104	2,208	Deceased	12	8	3	0	2	0
T9	M	ALS		51	4	2	759	1,518	Deceased	54	13	17	1	6	3
T10	M	SCI	C4-A	34	9	2	518	1,036	Explanted	14	10	5	2	2	1
T11	M	SCI	C4-B	35	11	2	829	1,658	Enrolled	30	5	8	1	4	1

Abbreviations: AEs = adverse events; ASIA = American Spinal Injury Association; SAEs = serious adverse events; SCI = spinal cord injury.
[a] Possibly, probably, or definitely device-related or procedure-related AEs are inclusive of skin-related device AEs and surgery-related device AEs.
[b] Participants S2 and T2 enrolled after tetraplegia caused by ischemic brainstem stroke.

Figure 17: Rubin et al. 2023 [18]

[18] Interim Safety Profile From the Feasibility Study of the BrainGate Neural Interface System

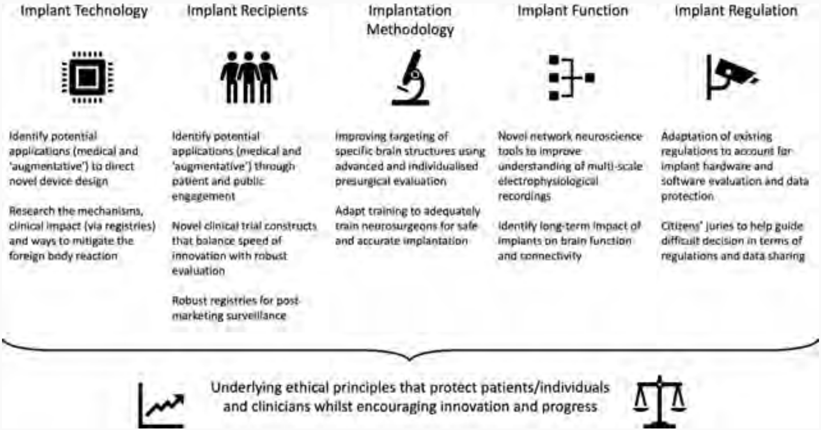
Clinical research

Chari et al. 2021 [19]

Our key message is to encourage the neurosurgical community to proactively engage in collaborating... By doing so, we will equip ourselves with the skills and expertise to drive the field forward and avoid being mere technicians in an industry driven by those around us.

[19] Brain–Machine Interfaces: The Role of the Neurosurgeon

Chari et al. 2021 [20] (cont.)



[20] Brain–Machine Interfaces: The Role of the Neurosurgeon

Collaborations: Aademic/industry partnerships

Synchron

- Royal Melbourne Hospital
- University of Melbourne
- University of Pittsburgh
- UPMC
- Carnegie Mellon
- Mount Sinai
- Buffalo General
- Team Gleason

Blackrock Neurotech

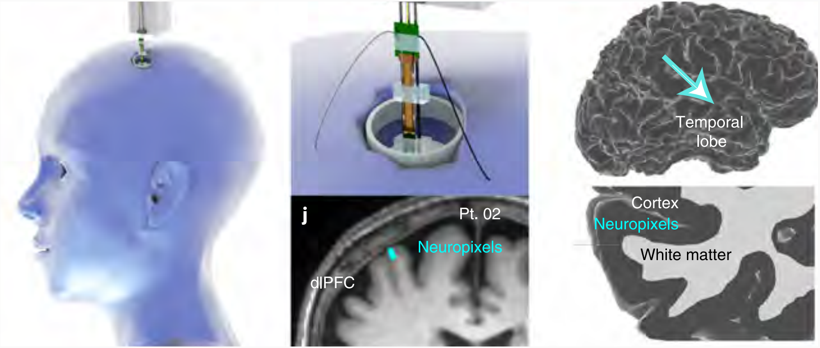
- Clearpoint Neuro
- AE Studios
- Phantom Neuro
- Columbia University
- Stanford University
- University of Pittsburgh
- Mass General
- Caltech
- Brown University
- ...

Paulk et al. 2022 [21]

Recording single-unit neural activity in humans is increasingly common in both research and clinical care... In this study, we... record brain activity acutely during clinically indicated neurosurgery.

[21] Large-scale neural recordings with single neuron resolution using Neuropixels probes in human cortex

Paulk et al. 2022 [22]



[22]Large-scale neural recordings with single neuron resolution using Neuropixels probes in human cortex

Chung et al. 2022 [23]

Table 1. Participant information

ID	Spikes	Isolable units	Sex	Age	State	Hemisphere	Region and procedure	Pathology	Failure reason
NP01	no	no	M	31	awake	left	anterior temporal resection	tumor	shank broke upon insertion
NP02	no	no	F	25	anesthetized	right	resection, frontal lobe	epileptic foci (focal cortical dysplasia)	noise issues
NP03	yes	yes	M	49	asleep	right	resection, frontal lobe	tumor	–
NP04	yes	yes	F	33	awake	left	anterior temporal lobectomy (ATL)	temporal epilepsy	noise issues
NP05	no	no	F	22	awake	left	ATL	temporal epilepsy	probe broke soon after insertion
NP06	yes	no	F	32	awake	left	resection, motor cortex	epileptic foci (focal cortical dysplasia)	probe broke soon after insertion
NP07	no	no	F	54	awake	left	ATL	temporal epilepsy	noise issues
NP08	no	no	M	38	awake	left	resection, post-central gyrus	epileptic foci (focal cortical dysplasia)	no spikes
NP09	no	no	F	57	awake	left	anterior temporal resection	tumor	–
NP10	yes	yes	F	36	anesthetized	right	ATL	temporal epilepsy	–
NP11	yes	yes	M	49	awake	right	resection, motor cortex	cavernoma	–
NP12	yes	yes	F	46	anesthetized	right	ATL	temporal epilepsy	–
NP13	yes	yes	M	25	awake	left	ATL	temporal epilepsy	–
NP14	yes	yes	M	35	awake	left	ATL	temporal epilepsy	–
NP15	yes	yes	M	27	awake	left	resection, angular gyrus	cavernoma	–

Participants are listed in chronological order. The majority had surgery for medically refractory epilepsy. Note that participant NP03 was asleep but not anesthetized during recording.

[23] High-density single-unit human cortical recordings using the Neuropixels probe

Sun et al. 2022 [24]

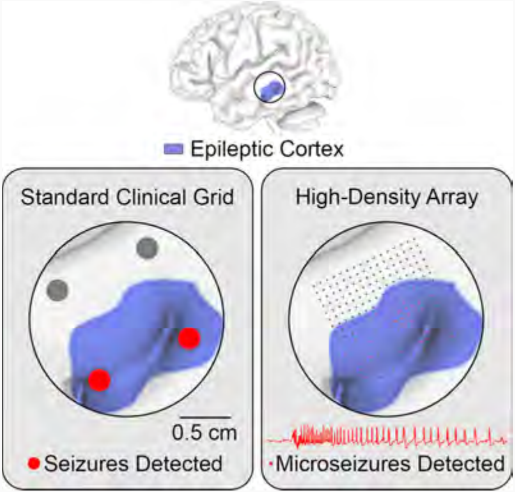


Figure 18: Standard vs. HD ECoG

[24] Intraoperative microseizure detection using a high-density micro-electrocorticography electrode array

End

Questions?

Appendix

What distinguishes “next-generation” technology?

	Current	Emerging
Channels	< 20	$100+$ $(1000+)$
Sensors	depth, ECoG	diverse
Algorithms	low-complexity	AI/ML
Conditions	Parkinson’s, epilepsy	SCI, ALS, stroke, etc.
Objectives	Treat symptoms	Restore function

Non-invasive approach: HDEMG

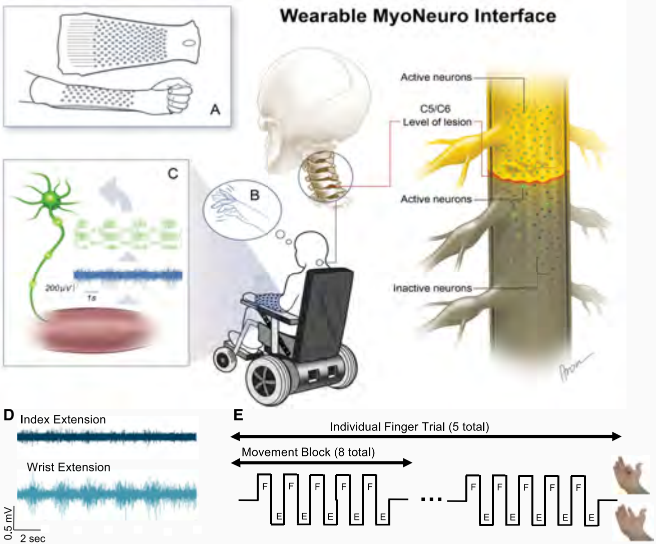


Figure 19: Ting et al. 2021

Rapeaux and Constandinou 2021 [25]

The neural interface itself (Utah electrode array, marketed under BlackRock Microsystem 'NeuroPort') to this day remains the only intracortical electrode array that has been approved for human use (FDA 510(k) cleared) for temporary (<30 day) monitoring of neural activity. All chronic implants are occurring under investigational device exemptions from the FDA led by each University.

[25] Implantable brain machine interfaces: first-in-human studies, technology challenges and trends

Paulk et al. 2022 [26]

Performed since the mid-1950s, at least four high-resolution, single-neuron recording technologies can currently be used in human participants in acute, subacute and even chronic settings.

These include microwire bundles, laminar microelectrode arrays, microelectrode contacts arranged on a grid for use above the pia or on the shaft of a depth electrode and the 'Utah' planar array of penetrating microelectrodes.

[26] Large-scale neural recordings with single neuron resolution using Neuropixels probes in human cortex

Interface: diverse candidates

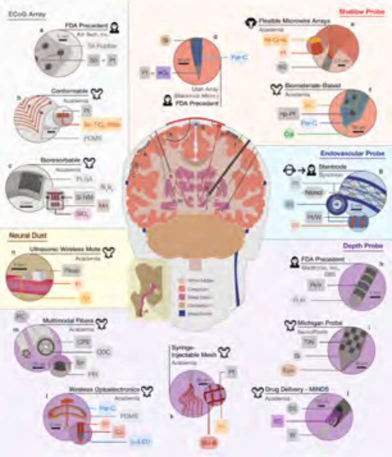


Figure 20: Obidin et al. 2019[27]

[27] The Future of Neuroimplantable Devices: A Materials Science and Regulatory Perspective

Obidin et al. 2019

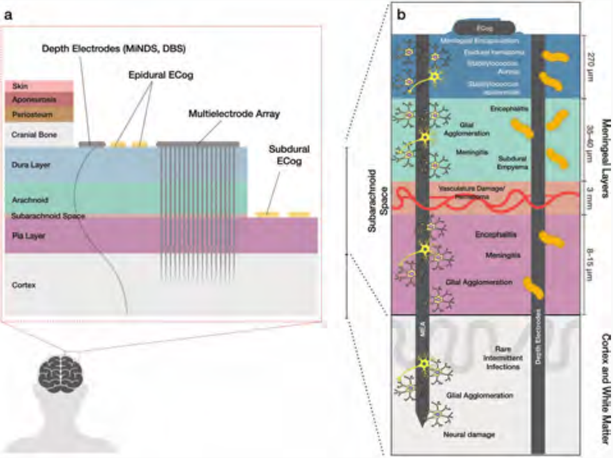


Figure 21: Obidin et al. 2019[28]

[28] The Future of Neuroimplantable Devices: A Materials Science and Regulatory Perspective

FDA guidance

Table of Contents

Figure 22: FDA BCI guidance 2021[29]

[29] Implanted Brain-Computer Interface (BCI) Devices for Patients with Paralysis or Amputation – Non-clinical Testing and Clinical Considerations

Inner Cosmos “Digital Pill”

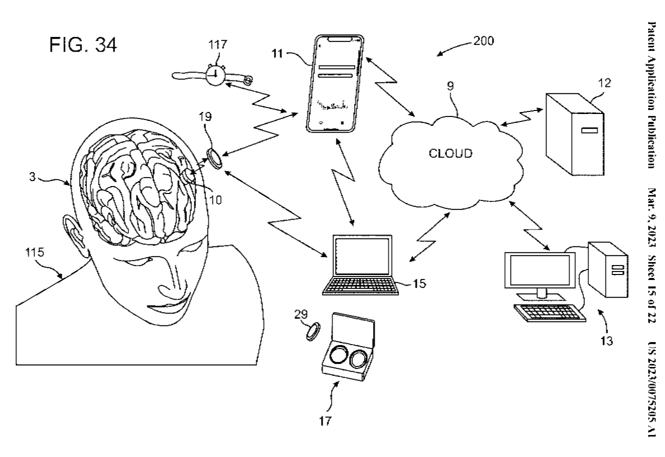


Figure 23: Moran et al. 2023[30]

[30] Devices, systems and methods for cortical stimulation (US patent application US20230075205A1)

RNS technical specifications

RNS® System ECoG Sensing Specifications

Feature	Specifications
Electrodes	4 electrodes per lead (depth or strip) Depth: 1.27 mm Ø x 2.00 mm, 0.08 cm^2 surface area Strip: 3.175 mm Ø, 0.08 cm^2 surface area
ECoG Channels	4 differential channels, 2 electrodes per amplifier user-selectable sensing montage
Dynamic Range	10-bit A/D conversion (digital values 0-1023, 512 = 0 volts)
Gain Levels	4 gain levels (low, med-low, med-high, high)
Resolution	0.8, 1.2, 2.0, 3.8 μV per bit
Dynamic range	0.8, 1.2, 2.1, 3.9 mV range
Sampling Rate	250 samples/second
Low-Pass Filter	-3dB at 30, 60, 90, 120 Hz (default = 90 Hz)
High-Pass Filter	-3dB at 4, 8, 12 Hz (default = 4 Hz)
ECoG Storage	30.5 channel*minutes total storage 1 to 4 channels selectable 30, 60, 90, 180, 240 seconds duration 2/3 of ECoG pre-trigger, 1/3 post-trigger 1-61 maximum ECoGs stored (e.g. 30 4-channel 30-sec ECoGs) older ECoGs are overwritten unless reserved
ECoG Triggers	Magnet, Responsive Therapy, Pattern A or B Detection, Long-Episode, Saturation, Noise, Scheduled
Real-Time ECoG	The most recent 4 minutes are stored in the Programmer

Figure 24: Neuropace RNS[31]

[31] The NeuroPace® RNS® System for Responsive Neurostimulation – Company Materials

Willet et al.

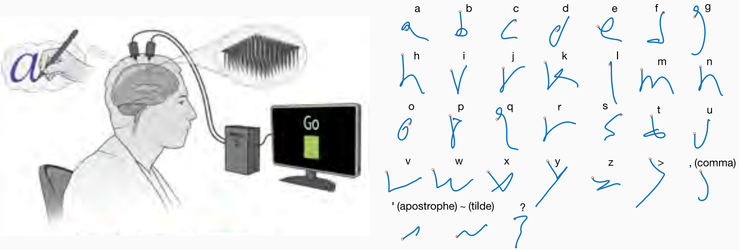


Figure 25: Willet et al. 2021

What is “next-generation” neurotechnology?

Distinguishing dimensions:

- **Interface**: electrodes and placement
- **Compute**: hardware and algorithms
- **Application**: indications and generalization

Interface:

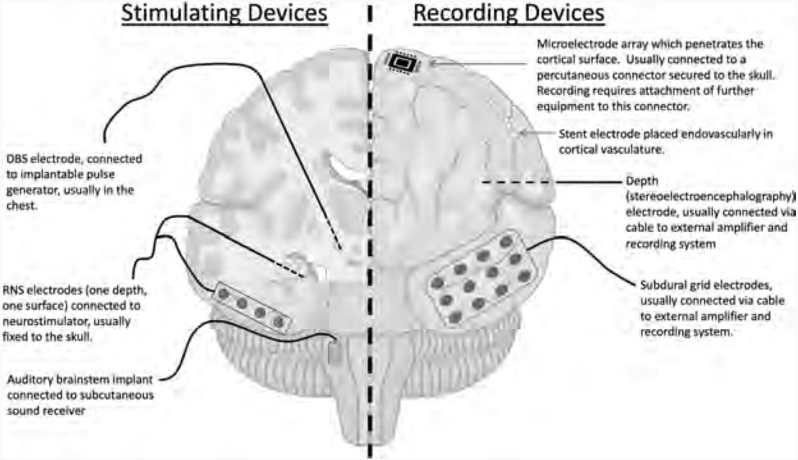


Figure 26: Chari et al. 2021[32]

[32] Brain–Machine Interfaces: The Role of the Neurosurgeon

Interface:

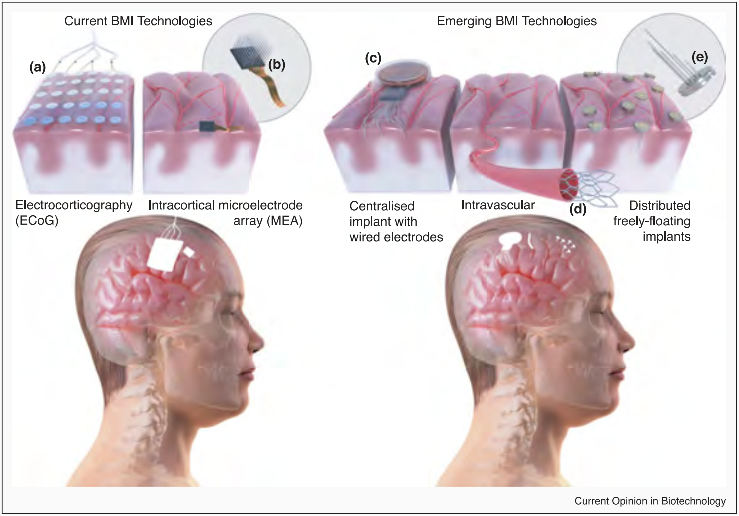


Figure 27: Rapeux et al. 2021 [33]

[33] https://www.frontiersin.org/articles/10.3389/fnsys.2021.578875/full

Interface:

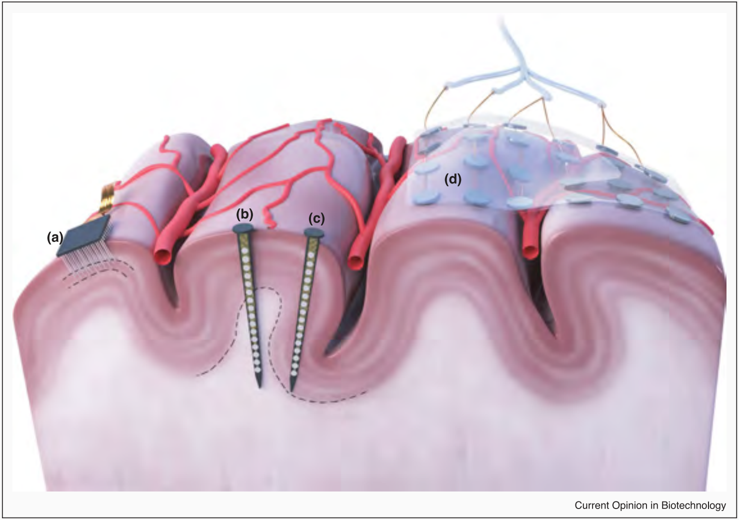


Figure 28: Rapeux et al. 2021 [34]

[34] https://www.frontiersin.org/articles/10.3389/fnsys.2021.578875/full

On-device compute

On-chip computation is currently limited to simple signal processing and feature extraction.

– Yoo and Shoaran 2021 [35]

[35] Neural interface systems with on-device computing: machine learning and neuromorphic architectures

On-device compute

This recent trend on combining artificial intelligence and machine learning with modern neural interfaces will lead to a new generation of low-power, smart, and miniaturized therapeutic devices for a wide range of neurological and psychiatric disorders... 'On-chip' machine learning... is one of the key puzzles in devising next-generation clinically viable neural interface systems.

– *Yoo and Shoaran 2021* [36]

[36] Neural interface systems with on-device computing: machine learning and neuromorphic architectures