中山醫學大學
Chung Shan Medical University

生醫訊號處理概論

期末報告

中山醫學大學醫學資訊學系

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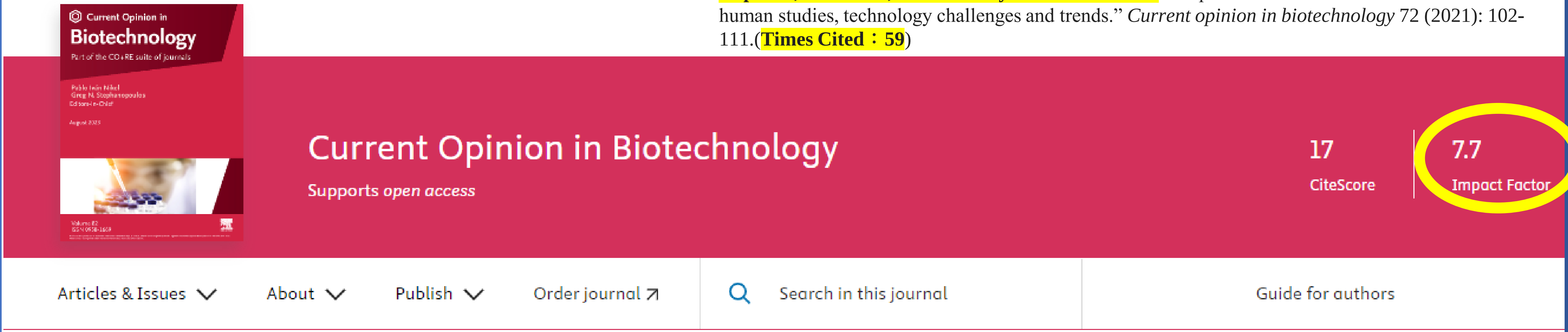
Preliminary Introduction

Name：

<u>Implantable brain machine interfaces: first-in-human studies, technology challenges and trends</u>

Journal：

Rapeaux, Adrien B., and Timothy G. Constandinou. "Implantable brain machine interfaces: first-in-human studies, technology challenges and trends." *Current opinion in biotechnology* 72 (2021): 102-111.(**Times Cited：59**)



Outline

1. Introduction
2. Objective
3. Material and Method
4. Result
5. Discussion
6. Conclusion

Part 1

Introduction

Introduction(1/3)

-BCI&BMI-

- There exists a plethora of methods to **observe neural activity**
- From all these approaches it is widely accepted that：

implantable methods (e.g. ECoG) **outperform** **non-invasive methods** (e.g. EEG, fNIRS) (due to a significantly higher **spatial** and **temporal resolution** and **signal-to-noise ratio**)

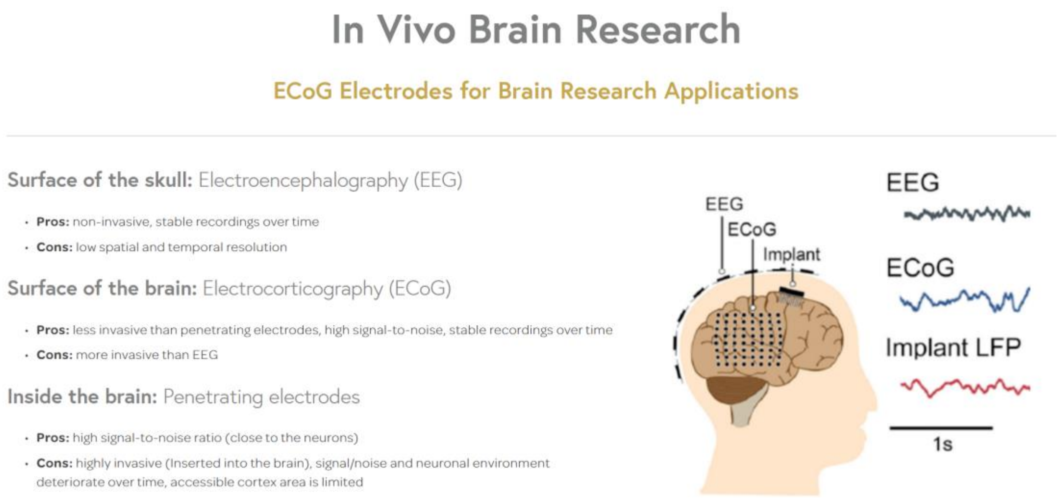


Fig. 1. methods EEG v.s. ECoG by digital

Introduction(2/3)

-BCI&BMI-

- Brain computer interfaces (**BCIs**) and brain machine interfaces (**BMIs**) refer to neurotechnologies that observe activity within the brain and decode or decipher this to extract useful information
- Although the terminology **BCI** and **BMI** are often used interchangeably, there is a tendency within the community to refer to：

➢ **non-invasive interfaces** using **BCI** and **implantable interfaces** using **BMI**

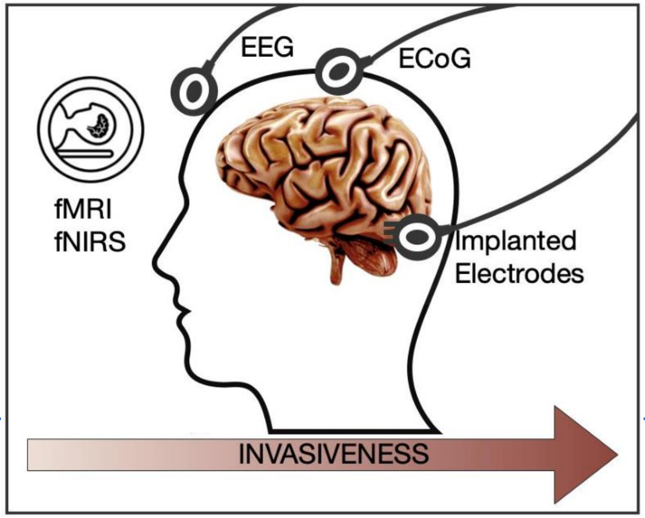


Fig. 2. observation methods invasiveness rate compare

Introduction(3/3)

-BCI&BMI-

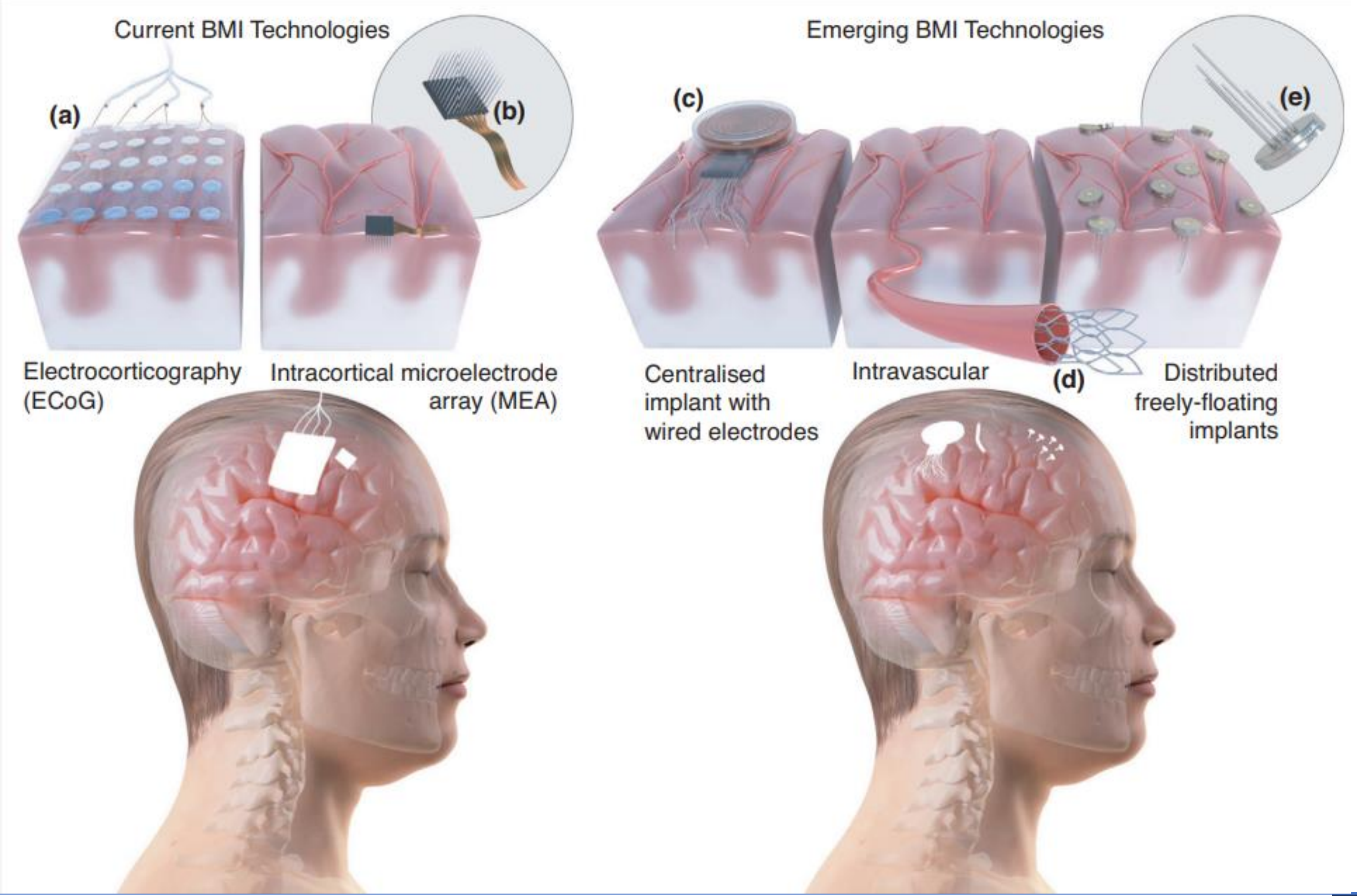


Fig. 3. Neural interface types

Part 2

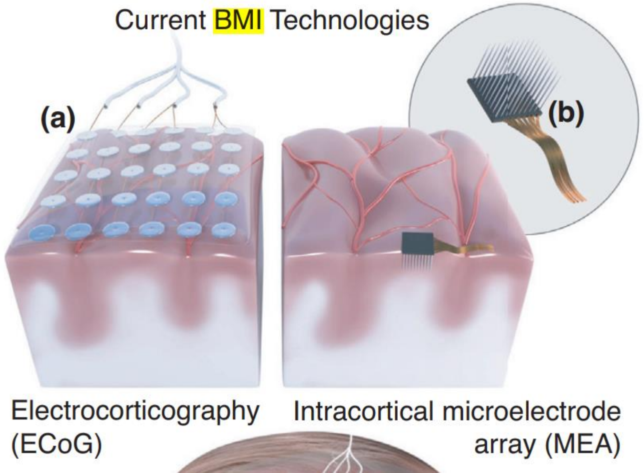
Objective

Objective(1/3)

-Implantable human BMIs today-

- Implantable human BMIs have to date utilised **two main categories** of neural interfaces targeting the motor cortex:
  - **ECoG** grids (placed on the surface of the brain)
  - penetrating microelectrode arrays (**MEA**s) (inserted into cortical tissue)

- The **first** implantable BMI demonstrated in human was in 2004. This used an intracortical **MEA**
- A **second** implantable technology that has been used in human BMIs is **ECoG**



Objective(2/3)

-MEA-

Objective(3/3)

- Technical challenges-

- The challenges can be separated roughly into three categories, namely scalability and portability, electrode stability and yield, and information transfer rate

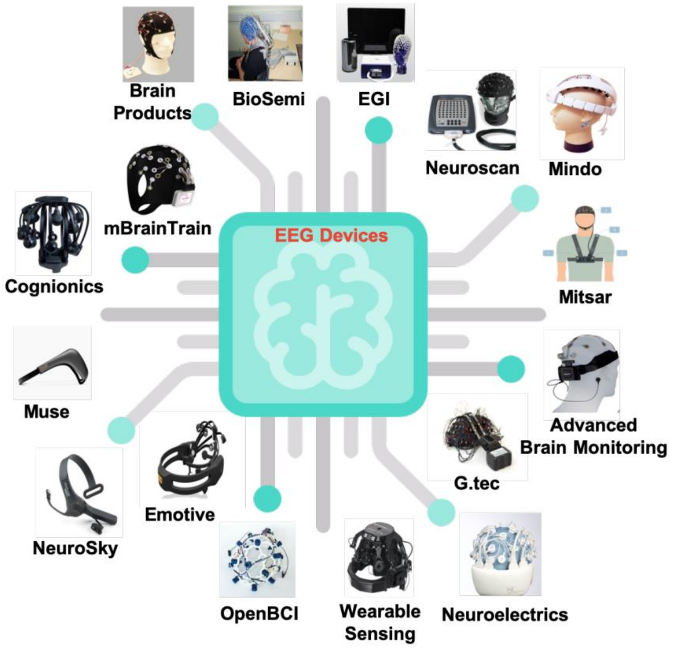


Fig. 4. scalability and portability

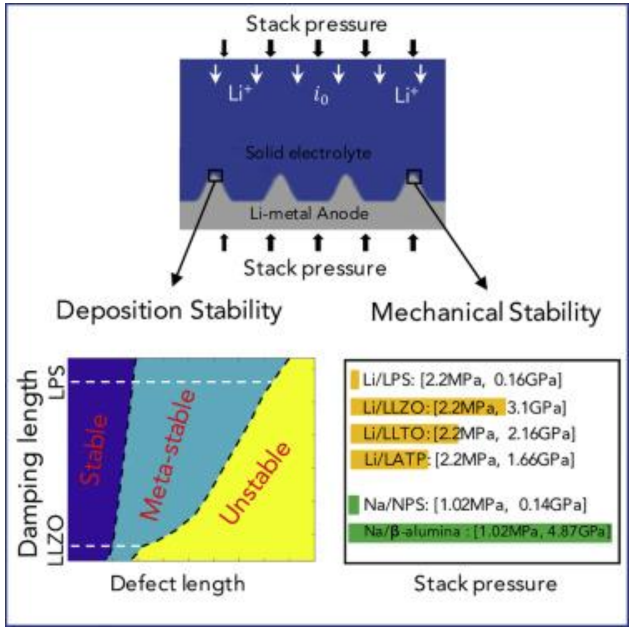


Fig. 5. electrode stability and yield

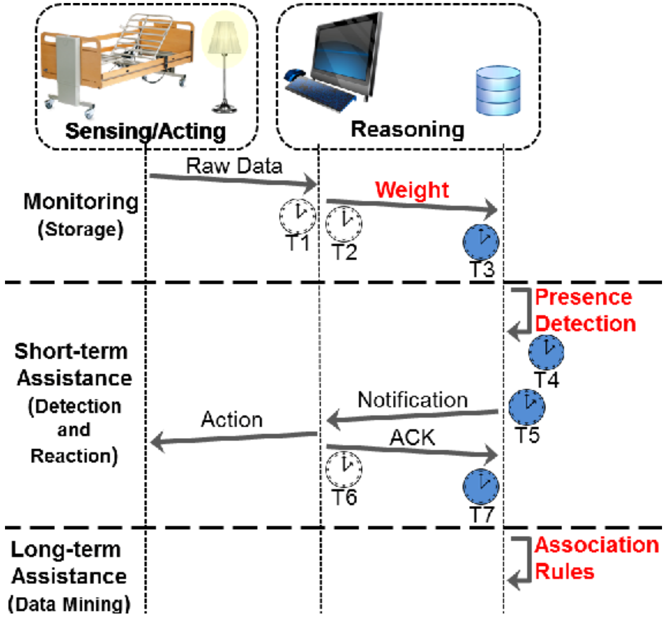


Fig. 6. information transfer rate

Part 3

Material and Method

Material and Method(1/5)

- Main neural interface types -

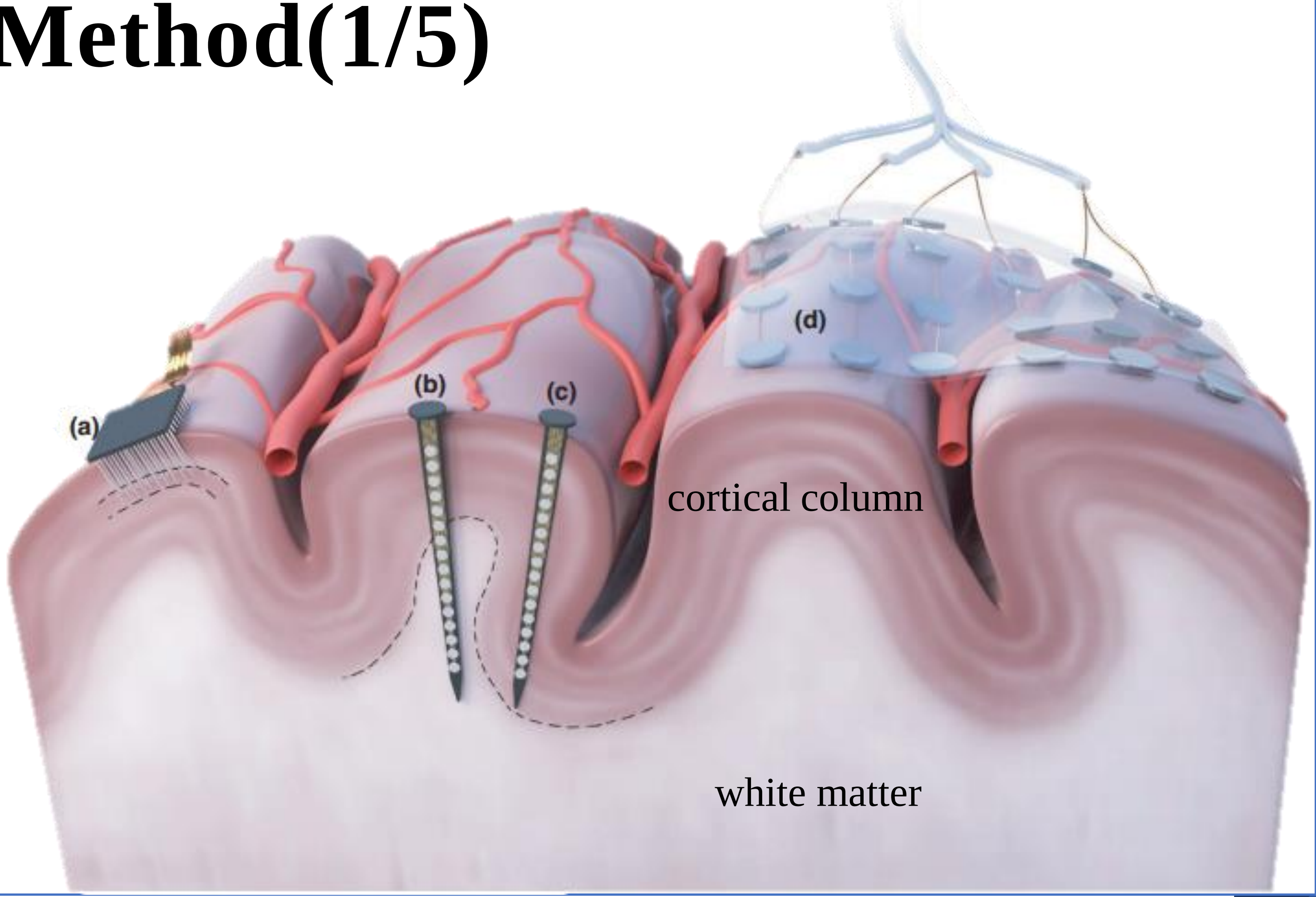


Fig. 4. Main neural types for interfacing with the cortex and associated electrode yield

Material and Method(2/5)

- Main neural interface types -

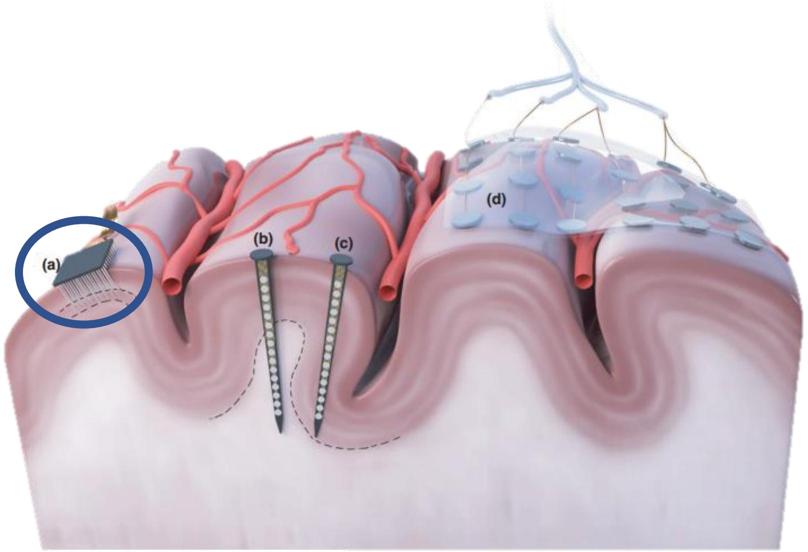
- Penetrating MEAs (a) are **generally positioned** centrally within the gyrus to observe activity at a **fixed depth** (electrodes are on the tips of the shanks) corresponding to a certain layer in the cortical structure

scalability and portability：a rational design and customizable **fit for organoids of different sizes[1]**

electrode stability and yield：US FDA, 510(k) Summary, K110010,

NEUROPORT CORTICAL MICROELECTRODE ARRAY SYSTEM[2]

information transfer rate：**Spectral content** and **bandwidth of vascular electrocorticography** were **comparable** to those of recordings from epidural surface arrays**[3]**



[1] Huang, Q., Tang, B., Romero, J. C., Yang, Y., Elsayed, S. K., Pahapale, G., ... & Gracias, D. H. (2022). Shell microelectrode arrays (MEAs) for brain organoids. *Science advances*, *8*(33), eabq5031.

[2] 510(k) Premarket Notification

[3] Oxley, T. J., Opie, N. L., John, S. E., Rind, G. S., Ronayne, S. M., Wheeler, T. L., ... & O'brien, T. J. (2016). Minimally invasive endovascular stent-electrode array for high-fidelity, chronic recordings of cortical neural activity. *Nature biotechnology*, *34*(3), 320-327.

Material and Method(3/5)

- Main neural interface types -

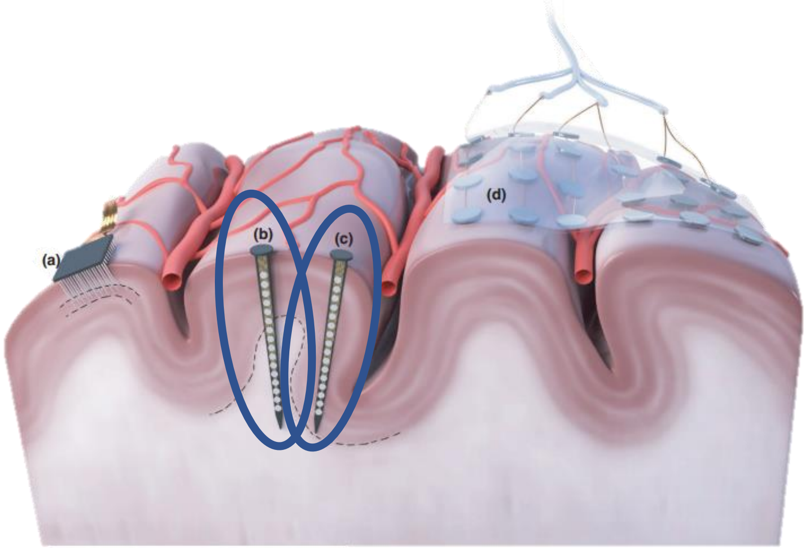
- penetrating neural probes that are **positioned centrally within the gyrus** (b) observe activity parallel to the cortical surface, that is, **along the cortical column**, with possibility of deepest electrode sites situated **in the white matter** (thus reducing yield)

- penetrating neural probes that are **positioned proximal to the sulcus** (c) observe activity **parallel to the cortical** surface so can generally observe similar activity to a penetrating MEA

scalability and portability：
distributed freely-floating implants

information transfer rate：

a penetrating microelectrode can record from a small population of nearby neurons or even a single neuron, **enabling precision recording of neural activity**[4]



[4] Weltman, A., Yoo, J., & Meng, E. (2016). Flexible, penetrating brain probes enabled by advances in polymer microfabrication. *Micromachines*, *7*(10), 180.

Material and Method(4/5)

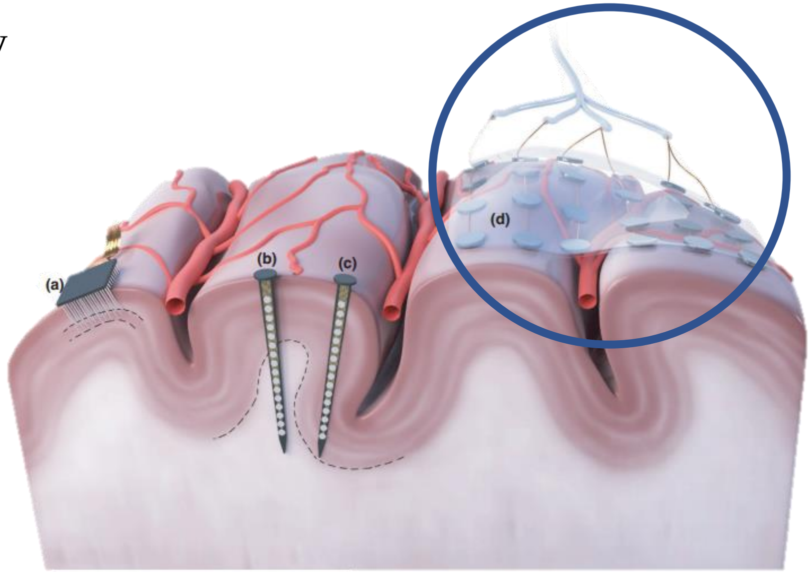
- Main neural interface types -

- surface electrodes (d) require good contact (depending on whether they are placed **epidurally** or **subdurally**)

scalability and portability： Though such modalities have been used successfully for brain-machine interfaces, **the non-portability of these systems** makes them **impractical for clinical BMI use**[5]

electrode stability and yield： A Fully Implantable Wireless ECoG 128-Channel Recording Device for Human Brain–Machine Interfaces: **W-HERBS**[6]

information transfer rate： It is capable of recording 128-ch subdural ECoG signals with **sufficient input-referred noise (3 μV_{rms})** and **with an acceptable time delay (250 ms)**[5]



[5] Degenhart, A. D. (2014). *Evaluation and advancement of electrocorticographic brain-machine interfaces for individuals with upper-limb paralysis* (Doctoral dissertation, University of Pittsburgh).

[6] A Fully Implantable Wireless ECoG 128-Channel Recording Device for Human Brain–Machine Interfaces: W-HERBS

Material and Method(5/5)

- Performance-

Table 1

Estimated end-to-end performance for state-of-the-art BMIs

Reference	Year	Electrode configuration	Decoding strategy	Information transfer rate (bits per second)	Device
[8]	2017	Utah MEA (10 × 10)	Cursor	4.2 BPS	Blackrock Neurotech
[39]	2018	Utah MEA (10 × 10)	Text	0.5 BPS[a]	Blackrock Neurotech
[10]	2019	ECoG strips (4 × 4)	Cursor	1.8 BPS[b]	Medtronic PC+S
[12*]	2019	ECoG grid (8 × 8)	Cursor	6.6 BPS[c]	
[16*]	2019	(≤96) neural threads (2k+ total electrodes)	Cursor	10 BPS[d]	Neuralink N1
[9**]	2019	PMT ECoG grid (16 × 16)	Speech	5 BPS[e]	UCSF
[11**]	2021	Utah MEA (10 × 10)	Handwriting	7.05 BPS[a]	Blackrock Neurotech

[a] Bits per second converted from characters using 4.7-bits per character or as reported in literature.
[b] On the basis of cursor task with 1 Degree of Freedom (DOF), 0.5 s hanning window, 90% average success rate.
[c] Exoskeleton with 8 DOF, assumed to be 1-bit per DOF and measured 82.5% true positive over 1 s ECoG recording epoch.
[d] On the basis of estimated 2-bit directional input with each input frame lasting 200 ms to adequately describe cursor placement performance in Neuralink's published video [40].
[e] Highest bitrate achieved with one-syllable words amongst set of 10, 30% success rate, assuming each syllable is 200 ms long.

Table. 1. Estimated end-to-end performance for state-of-the-art BMIs

Part 4

Result

Result(1/5)

-Trends-

- The hope is that more channels of data will result in an **increased information transfer rate** in addition to improving robustness through increased **redundancy**

- This up-scaling is seeing an emerging trend that is taking a **distributed approach** (**comprising multiple devices, untethered and wireless**) to the system organization, in addition to the current **centralized approach** (**a single device wired to many electrodes**)

- These trends are leading to **increased complexity in the deployment of the neural interfaces** (e.g. more electrodes, flexible, freely-floating)

- The trends we are seeing are all ultimately aimed at improving the overall efficacy of the BMI (**information transfer rate, accuracy**)

Result(2/5)

-Centralized vs Distributed-

Centralized

- This approach builds on the current modular organization of active implantable medical devices that comprise **a single hermetically packaged electronic module**, **multiconductor feedthroughs** and **implanted leads connecting to the electrode array(s)**

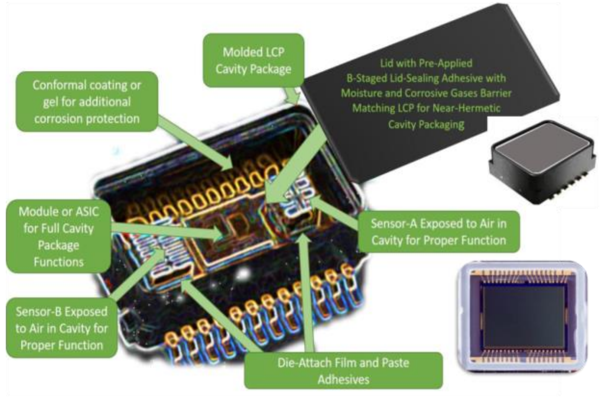


Fig. 5.
a single hermetically packaged electronic module

Fig. 6.
multiconductor feedthroughs

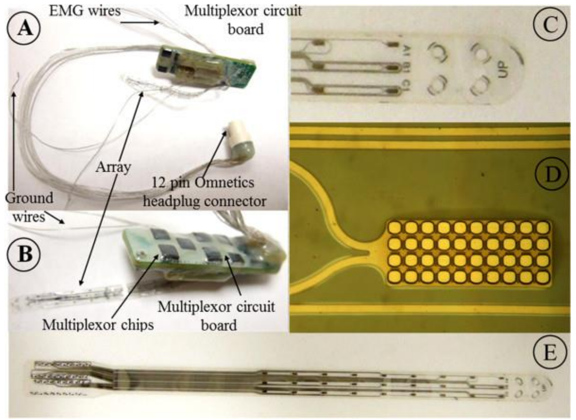


Fig. 7.
implanted leads connecting to the electrode array(s)

Result(3/5)

-Centralized vs Distributed-

Centralized

Weakness : **Power remains fundamentally constrained** by available space for batteries and **maximum thermal output of the implant**

Strength : **well-established inductive links** such as those found in cochlear implants remain the primary powering method for centralized implant architectures, owing to **the space available for larger** and **more efficient coils**

Result(4/5)

-Centralized vs Distributed-

Distributed

- An emerging trend that has gained pace in the last 3 years is that of distributed BMIs. This is achieved by ‘splitting’ the system into several tiny devices that are each freely floating and completely wireless. **neurogranin's (using patterned gold/PEDOT:PSS electrodes)**, **FF-WINeR (using tungsten microelectrodes)**, and **ENGINI (using microwire electrodes)**

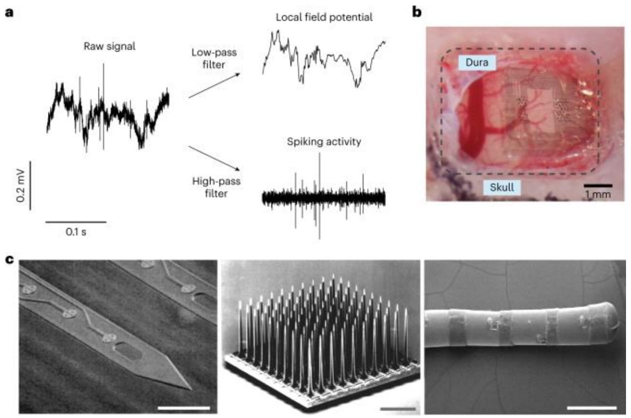


Fig. 8.
neurograins (using patterned gold/PEDOT:PSS electrodes)

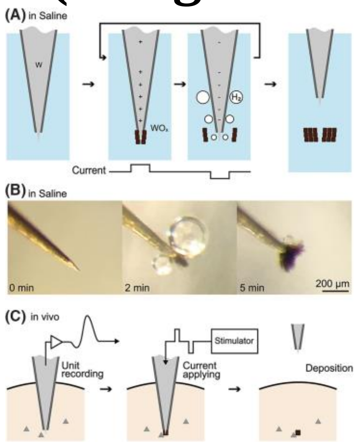


Fig. 9.
FF-WINeR (using tungsten microelectrodes)

Result(5/5)

-Centralized vs Distributed-

Distributed

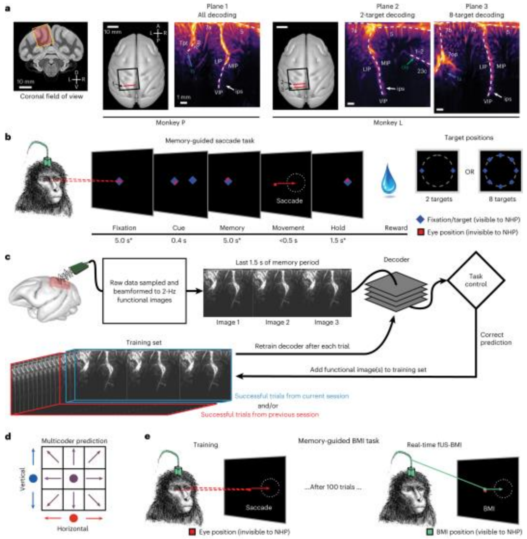


Fig. 10.
ultrasonic transmission

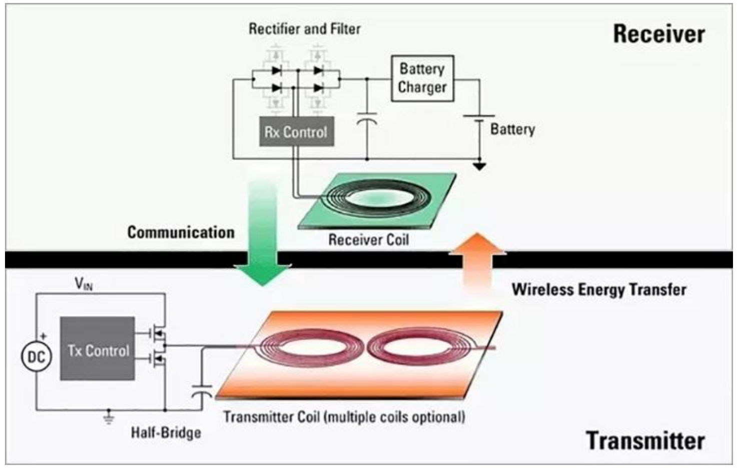


Fig. 11.
multi-coil inductive coupling

Threats : how **to achieve efficient wireless power transmission** to **such small devices**, how to **communicate data robustly**, how the **devices are implanted**, etc.

Opportunities : The two main approaches that have been adopted in recent work to address **the wireless power** challenge are **ultrasonic transmission**, and **multi-coil inductive coupling**

Part 5

Discussion

Discussion(1/2)

- With the increased complexity and miniaturization of implantable devices, there are new challenges for **packaging**. Current work is thus exploring new methods for realizing packaging solutions that are **biocompatible** and **remain reliable for decades**
- The aim of emerging BMI technologies is to **improve the overall performance whilst maintaining safety**
- Performance encompasses :

1) **chronic reliability**
2) **output bandwidth (useful information transfer rate)**
3) **output accuracy/confidence level**

Combining BMI with neuromorphic computing architectures to **implement machine learning models** for neural information decoding while **saving on power** and **area** is also an emerging trend

Discussion(2/2)

- With increased complexity in BMI devices come challenges with the implantation itself.

➢ How can a soft, flexible **probe** or delicate microwire **probe** be implanted **without buckling**?

➢ How can **hundreds** of **tiny implants** **be positioned**?

- This has **motivated** parallel efforts on **surgical workflow**; for each new device, we are also seeing a companion surgical method being developed

➢ **machine-inspired robot inserting neural threads**

➢ **laser ablation surgery or an anti-buckling mechanism for microwire insertion**

➢ **neurovascular surgery for stent rode device insertion**

➢ **a shuttle-based delivery mechanism**

➢ **injectable devices**

Part 6

Conclusion

Conclusion

- The **most recent advances** in **implantable BMIs** have been in **two key directions** :

1) **optimizing performance** for **existing neural interfacing technologies**
2) **developing new neural interface technologies** to allow for **scalability** and/or **new surgical workflows**

- For medical applications in general, **clinical necessity** is **the primary driver**, with validation studies establishing **technology maturity** and **scientific viability**
- It is crucial to assess **the development cost**, **healthcare economics**, and **viability for workflow integration**
- Additionally, BMIs and potential applications pose several **ethical concerns** including **agency/autonomy of the user**, **enhancement limitations**, **perception of normality**, **privacy**, **equality**

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The End

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