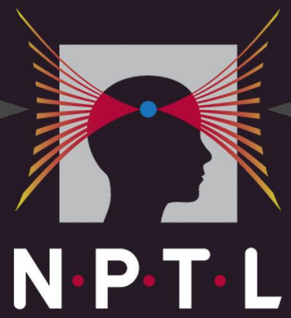
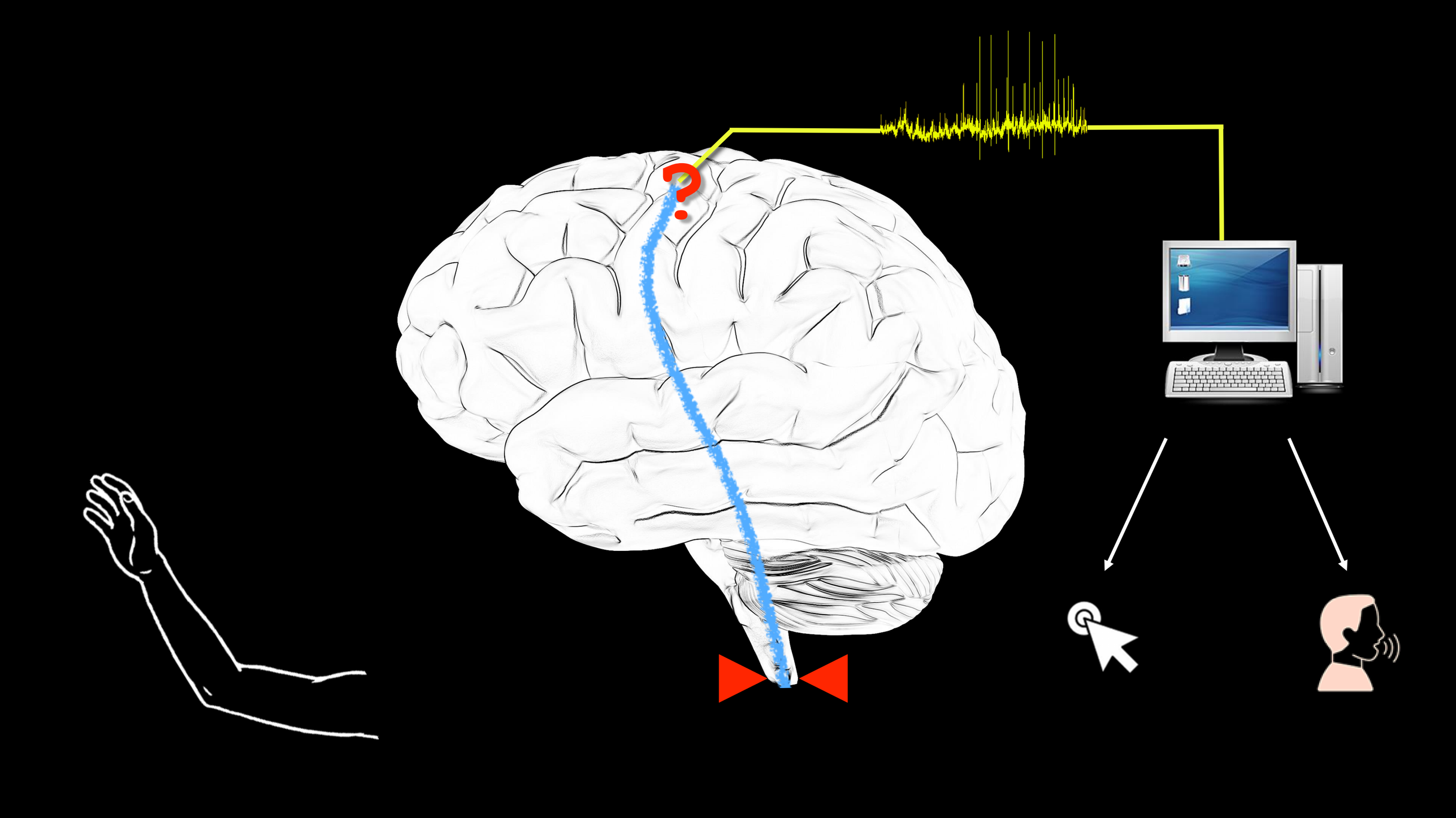


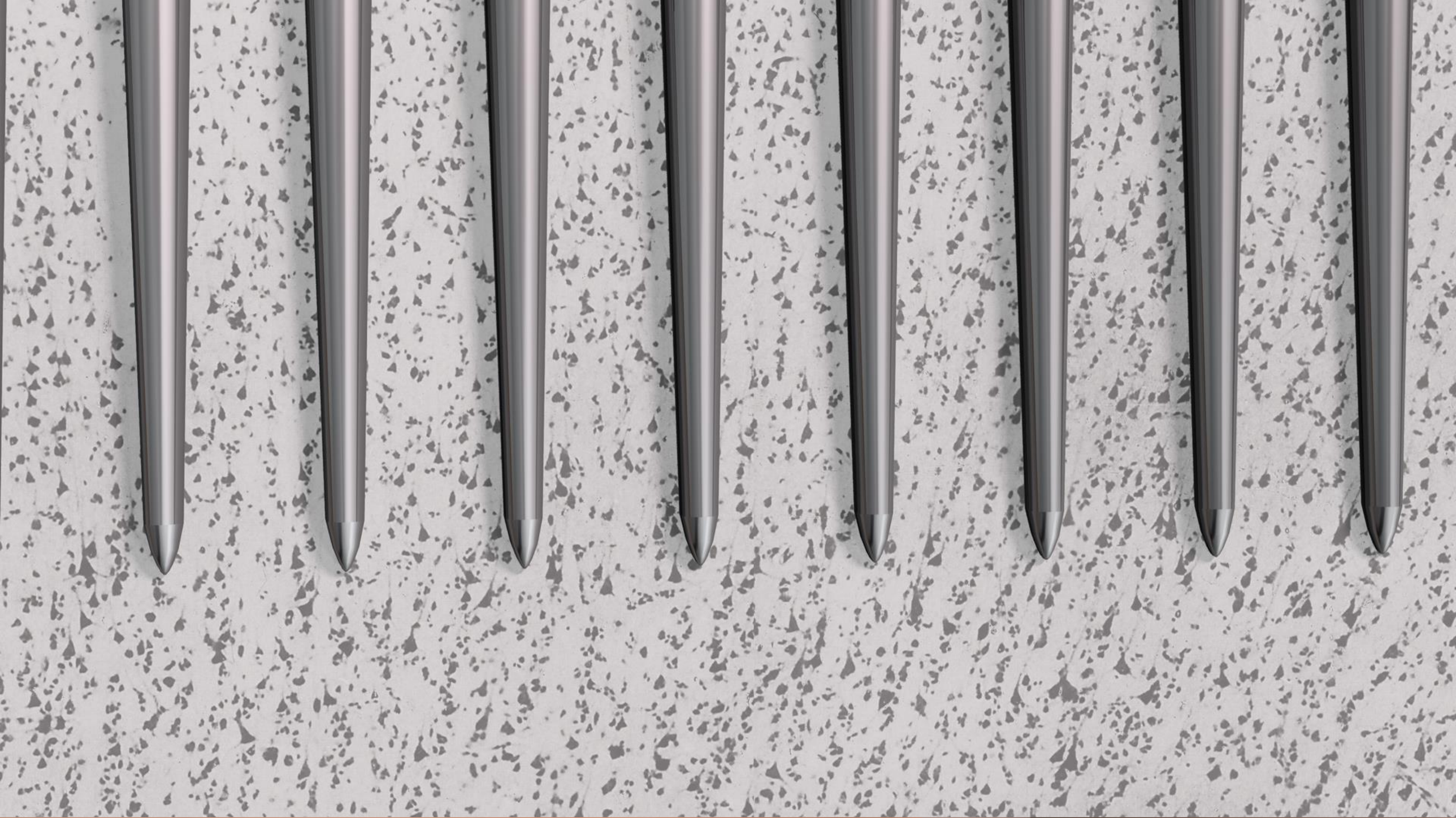
STANFORD UNIVERSITY

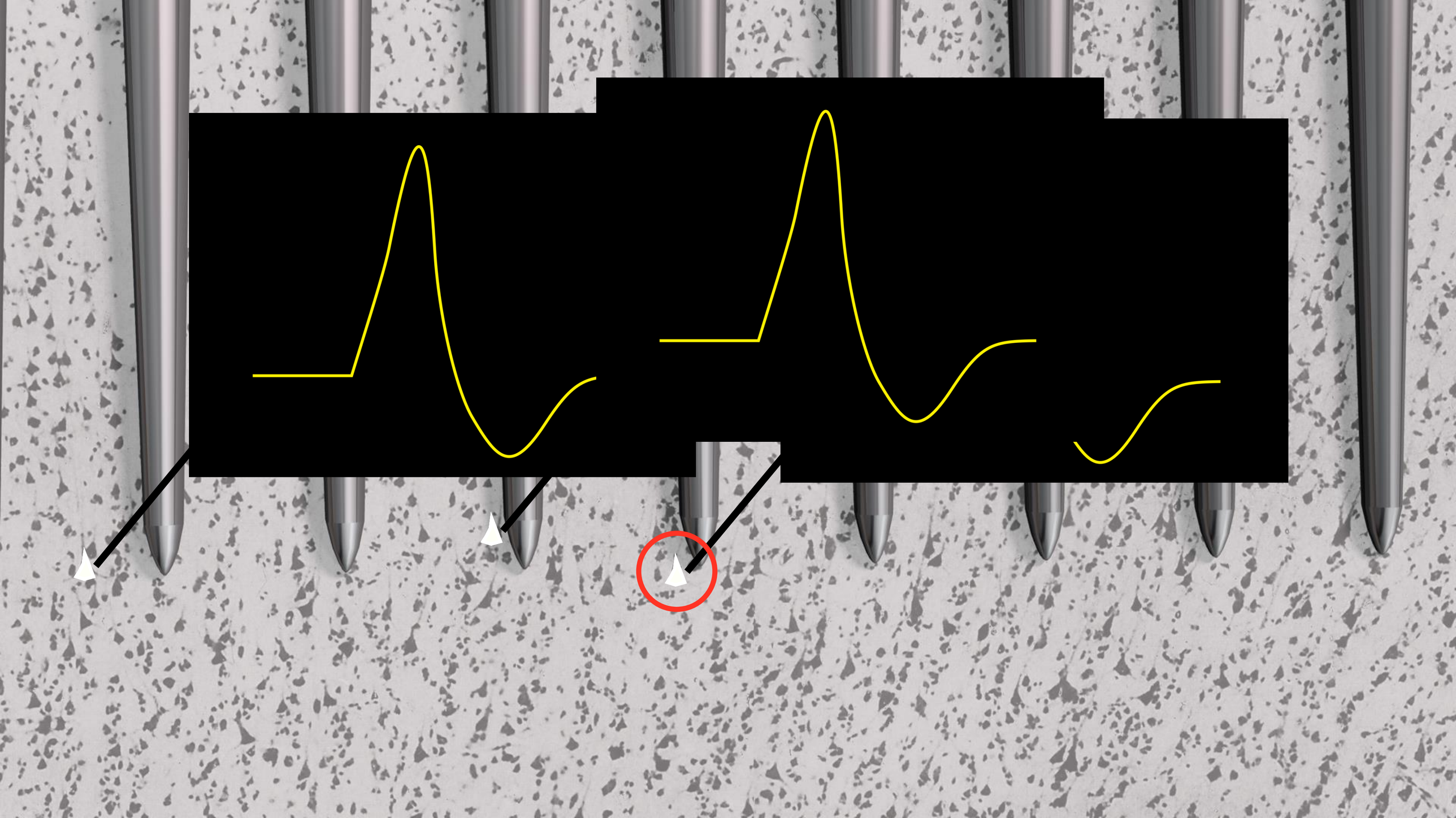
Neural Prosthetics Translational Laboratory

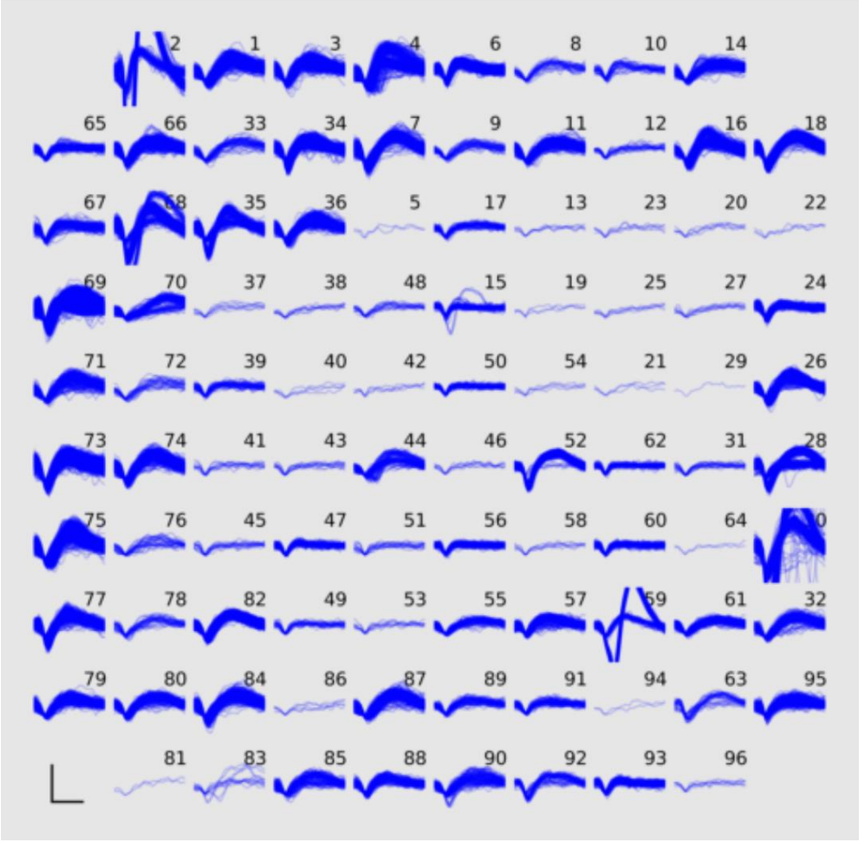
Recent Advances in Intracortical Brain-Computer Interfaces

Francis R. Willett, PhD
Assistant Professor
Department of Neurosurgery
Stanford University

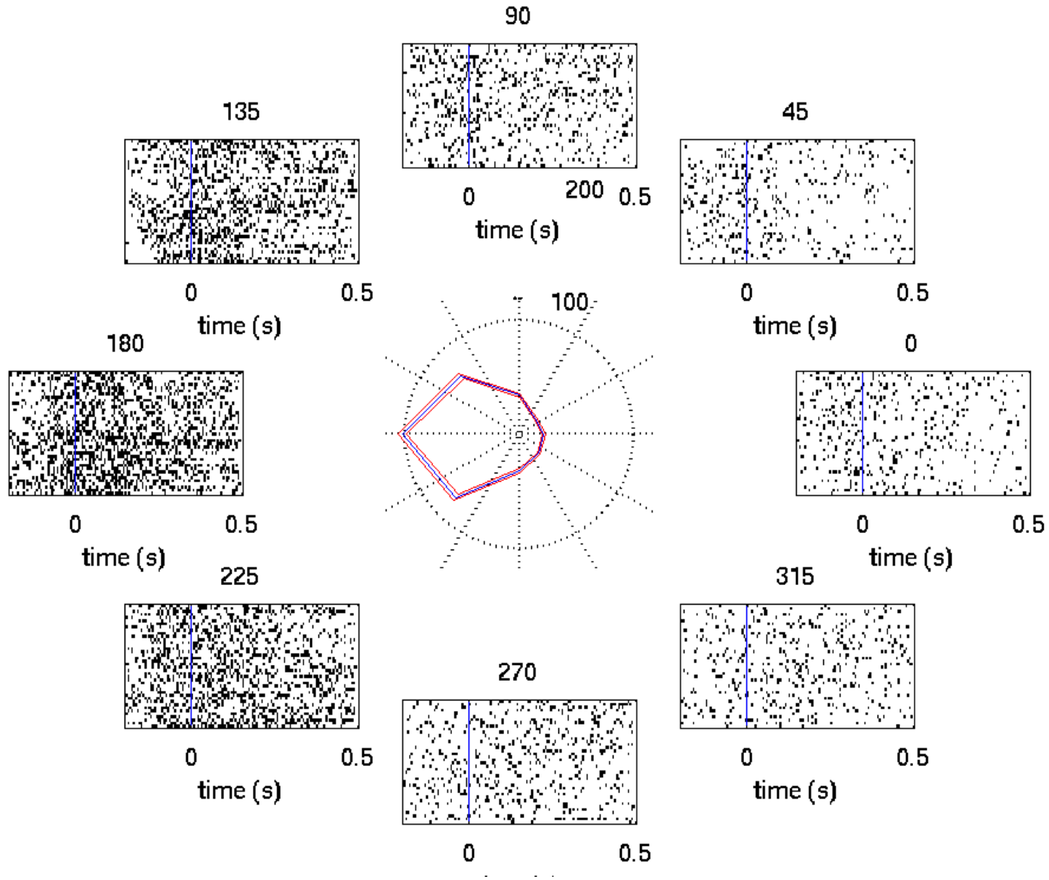


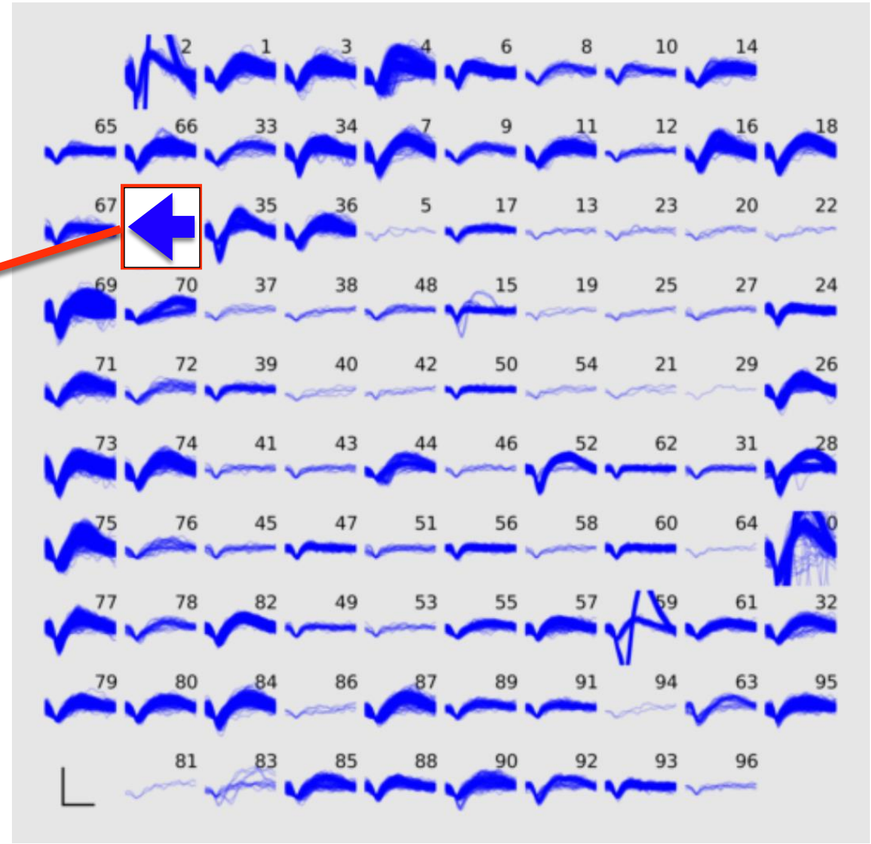


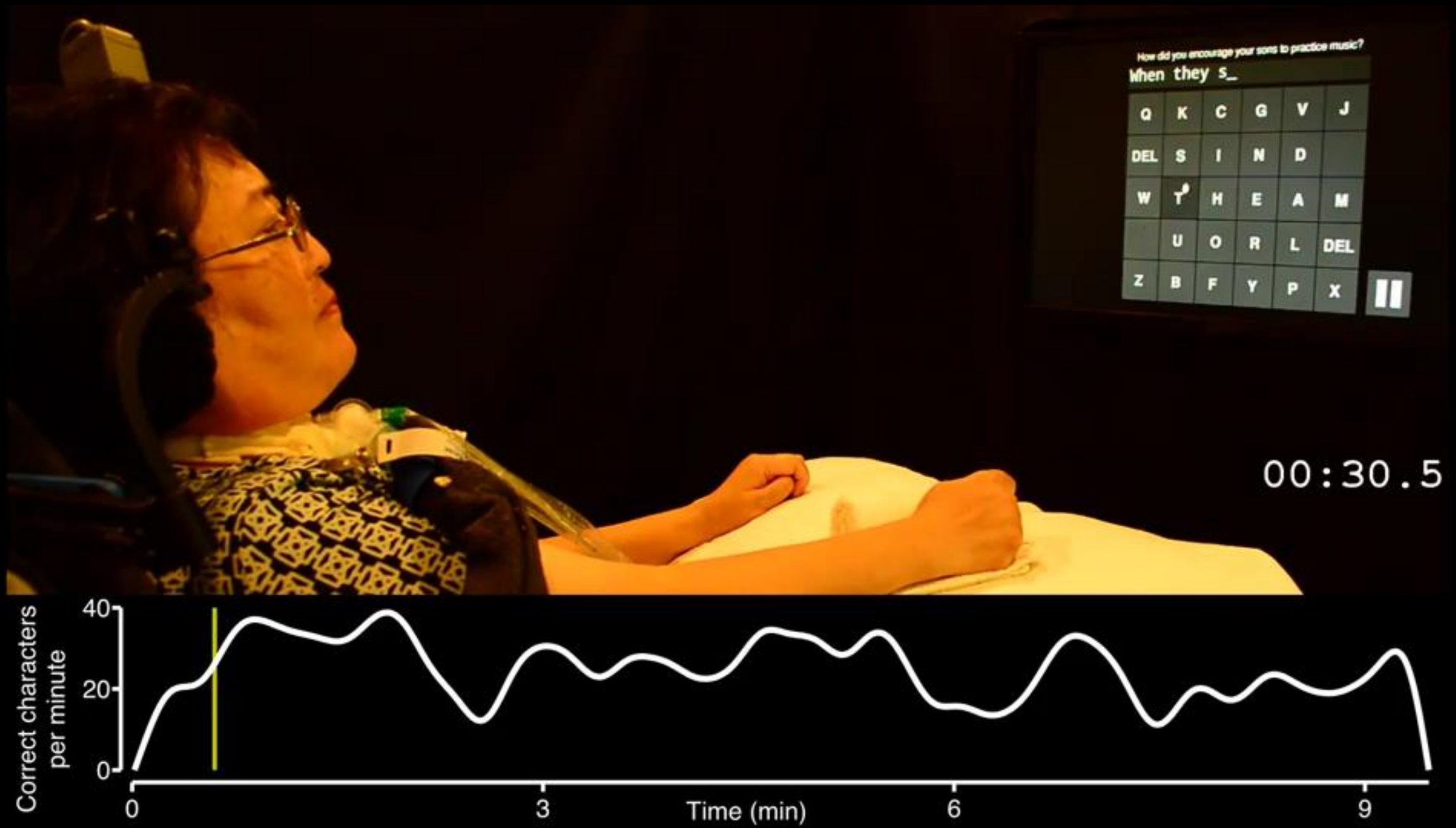



2 1 3 4 6 8 10 14
65 66 33 34 7 9 11 12 16 18
67 68 35 36 5 17 13 23 20 22
69 70 37 38 48 15 19 25 27 24
71 72 39 40 42 50 54 21 29 26
73 74 41 43 44 46 52 62 31 28
75 76 45 47 51 56 58 60 64 30
77 78 82 49 53 55 57 59 61 32
79 80 84 86 87 89 91 94 63 95
81 83 85 88 90 92 93 96

Georgopoulos et al. (1986) *Science*

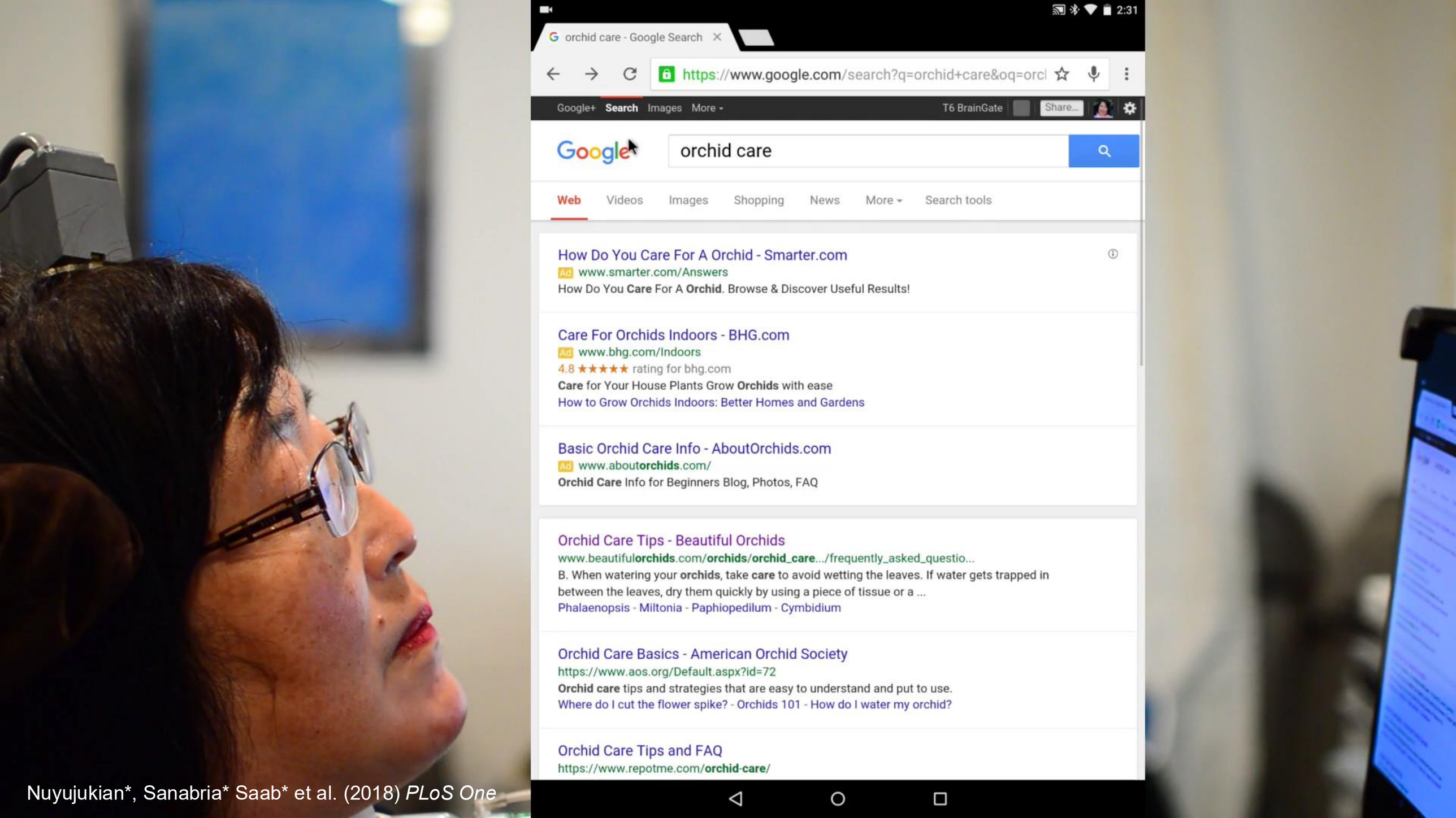






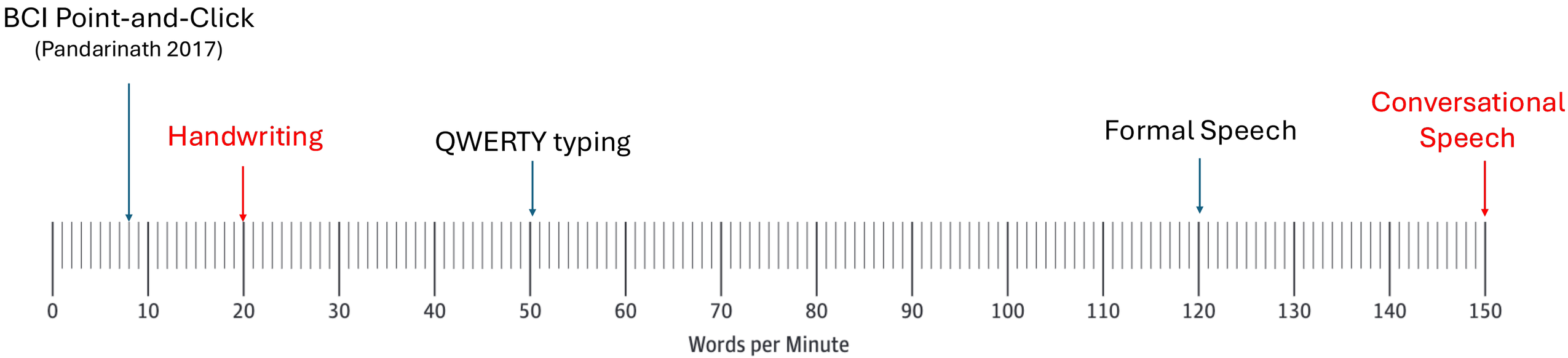
Pandarinath*, Nuyujukian*, …, Shenoy**, Henderson** (2017) *eLife*

BrainGate2 Neural Interface System. CAUTION: Investigational Device. Limited by US Federal Law to Investigational Use



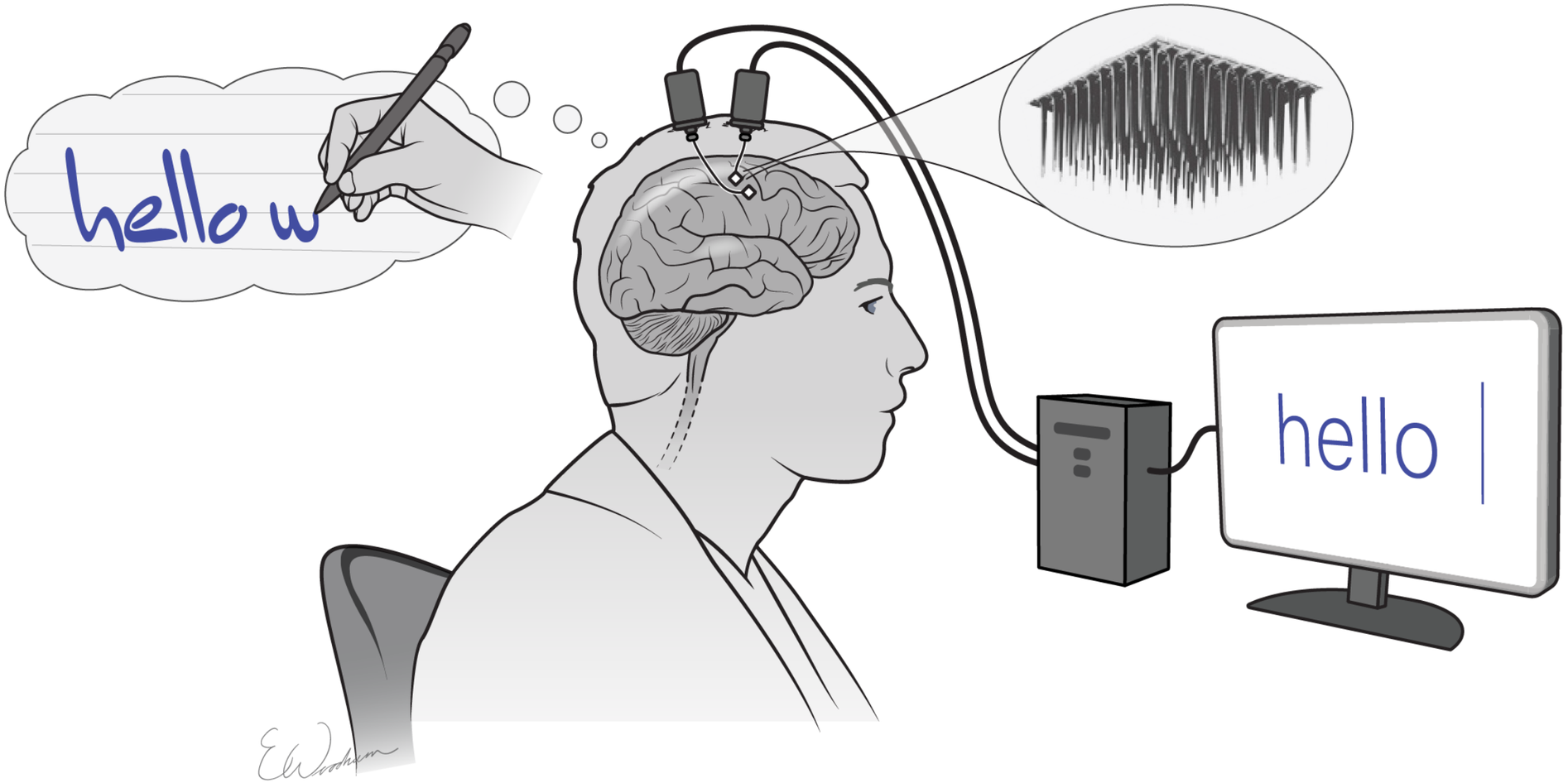
Nuyujukian*, Sanabria* Saab* et al. (2018) *PLoS One*

Words per minute in context



Can BCIs based on faster behaviors like **handwriting** and **speech** improve communication rates?

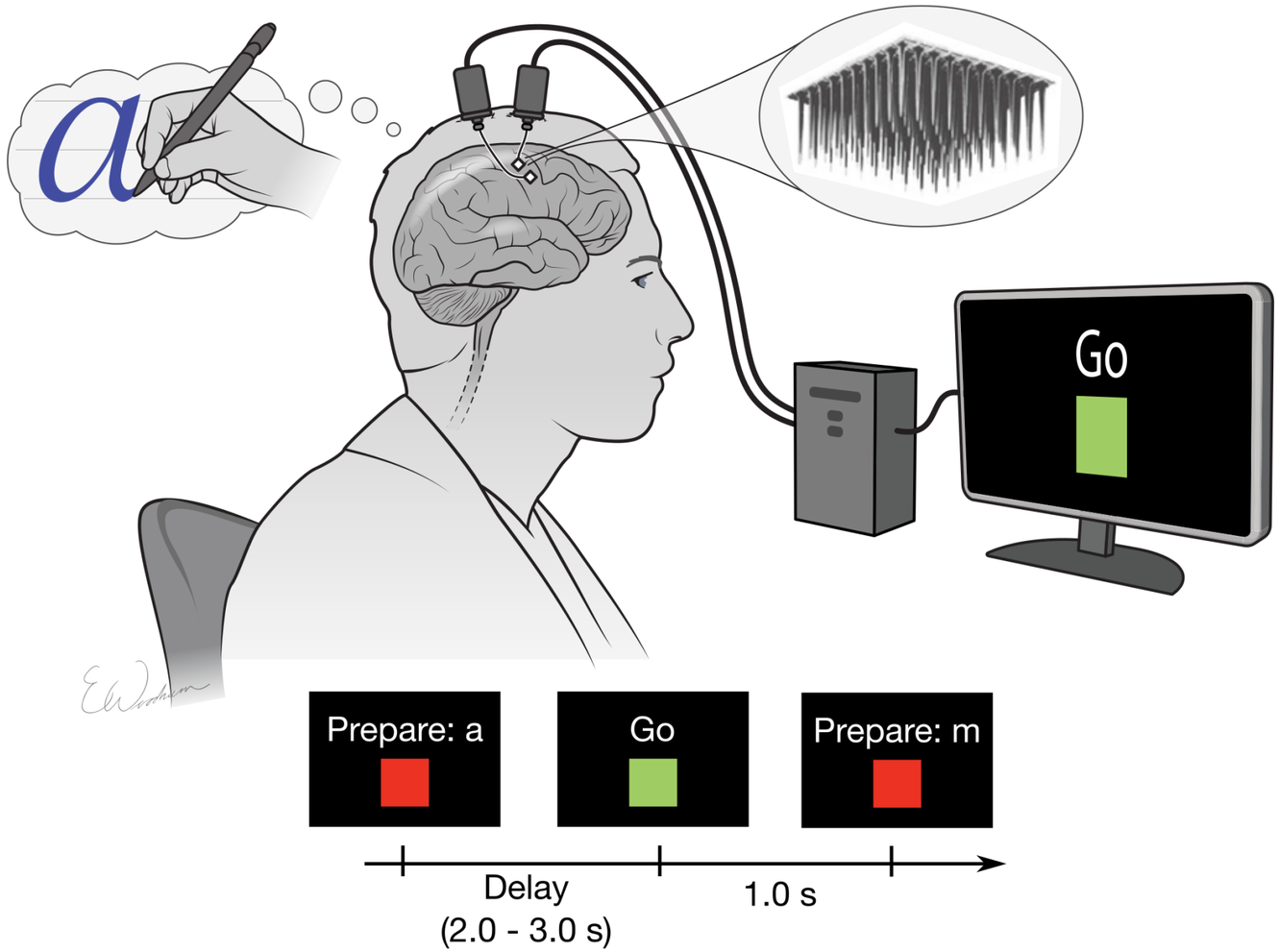
A Handwriting BCI



Willett et al. High-performance brain-to-text communication via handwriting. *Nature* 2021

Neural Representation of Handwriting

Does the neural representation for a highly dexterous skill, like handwriting, remain intact years after paralysis?



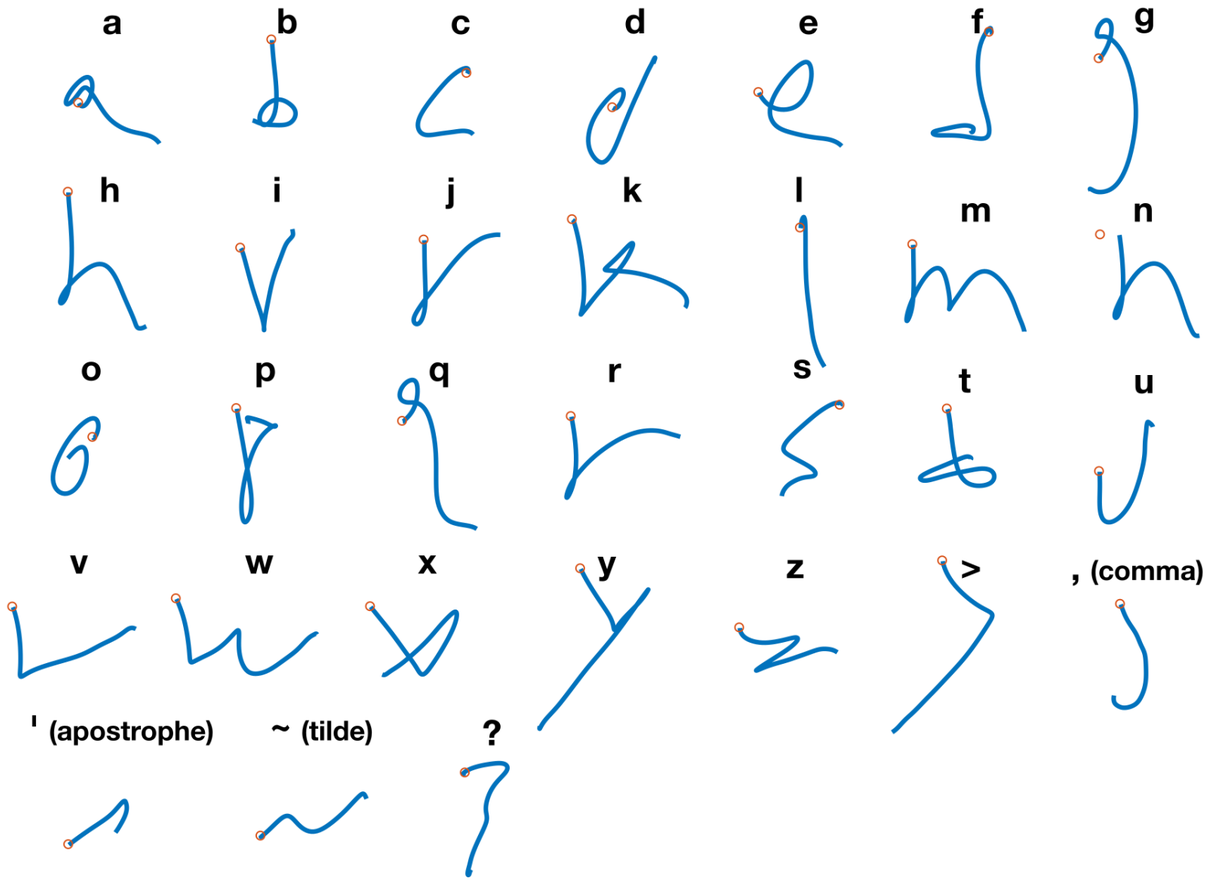
Willett et al. High-performance brain-to-text communication via handwriting. *Nature* 2021

Neural Representation of Handwriting

Can we reconstruct the imagined pen tip trajectory from the neural activity?

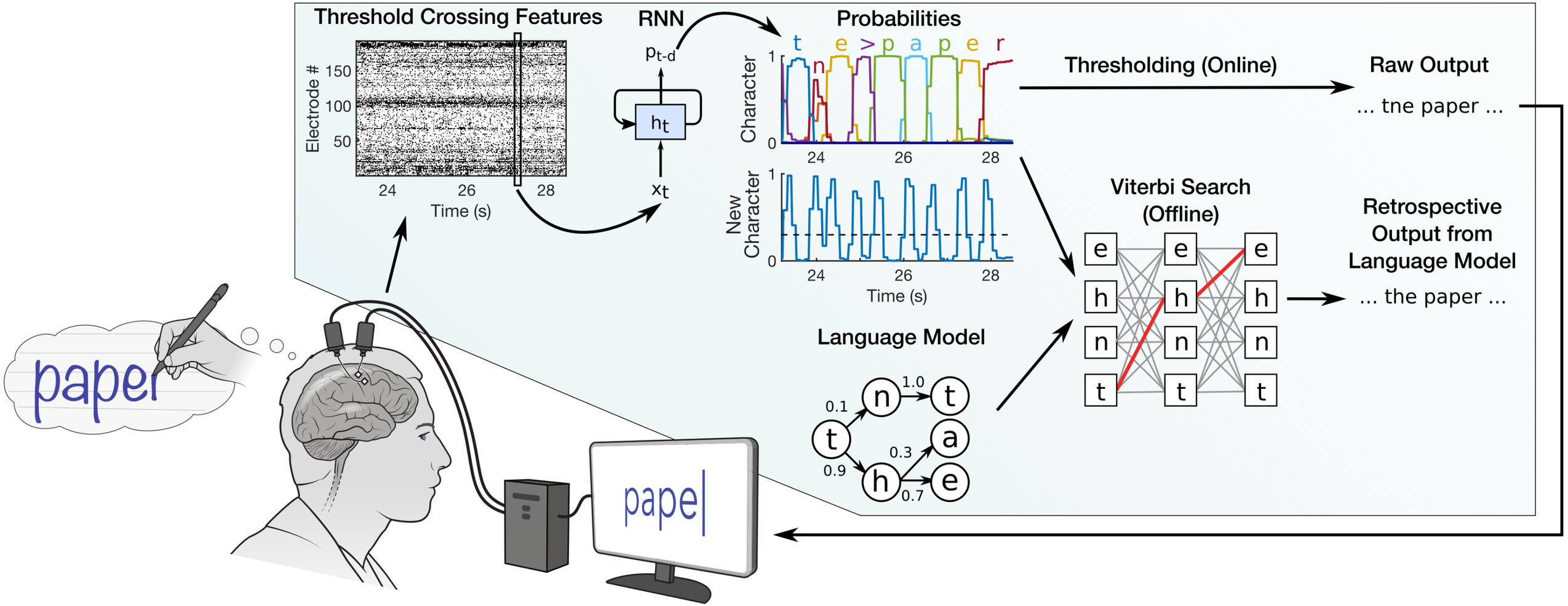
$$v_t = D f_t$$

Pen tip velocity Vector 2 x 1	Linear decoding Matrix 2 x 192	Firing rate vector 192 x 1



Willett et al. High-performance brain-to-text communication via handwriting. *Nature* 2021

System Diagram

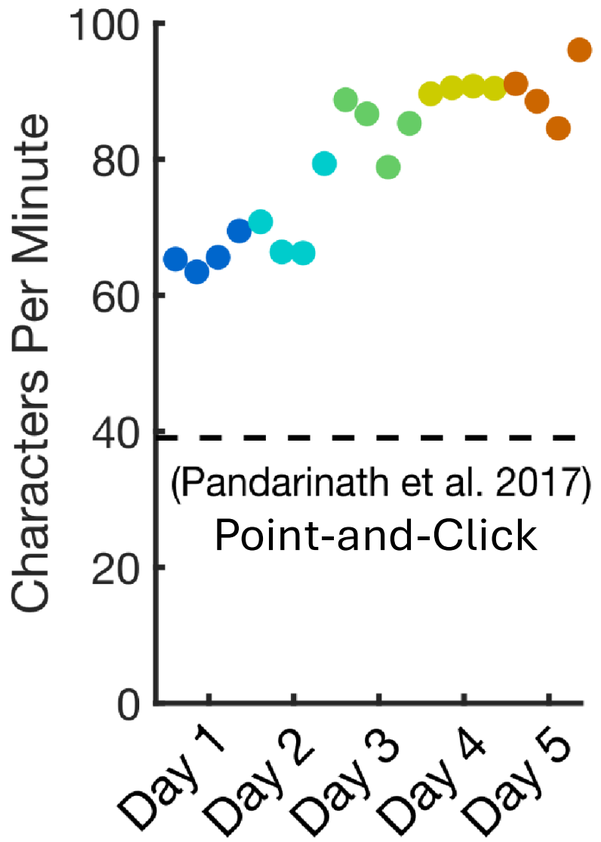


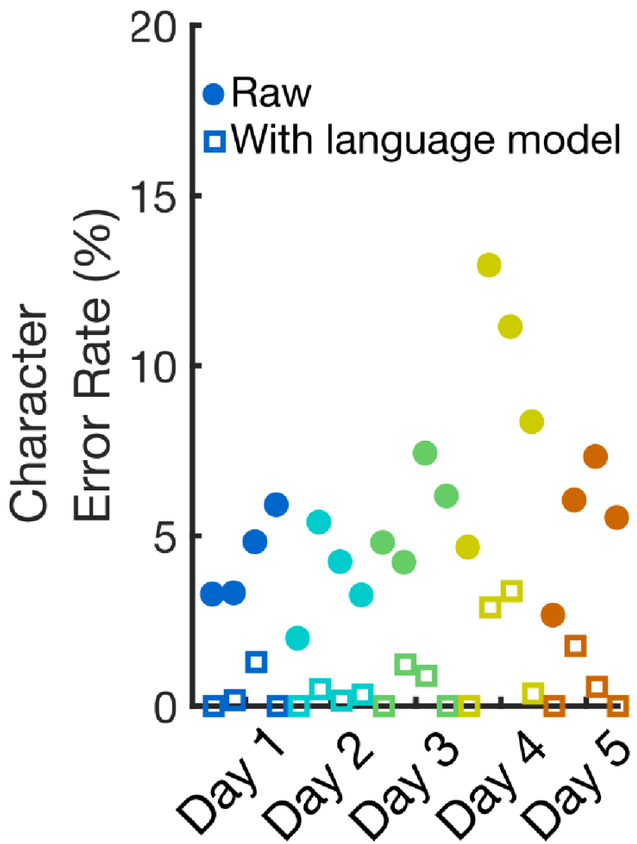
Willett et al. High-performance brain-to-text communication via handwriting. *Nature* 2021

Real-Time Operation

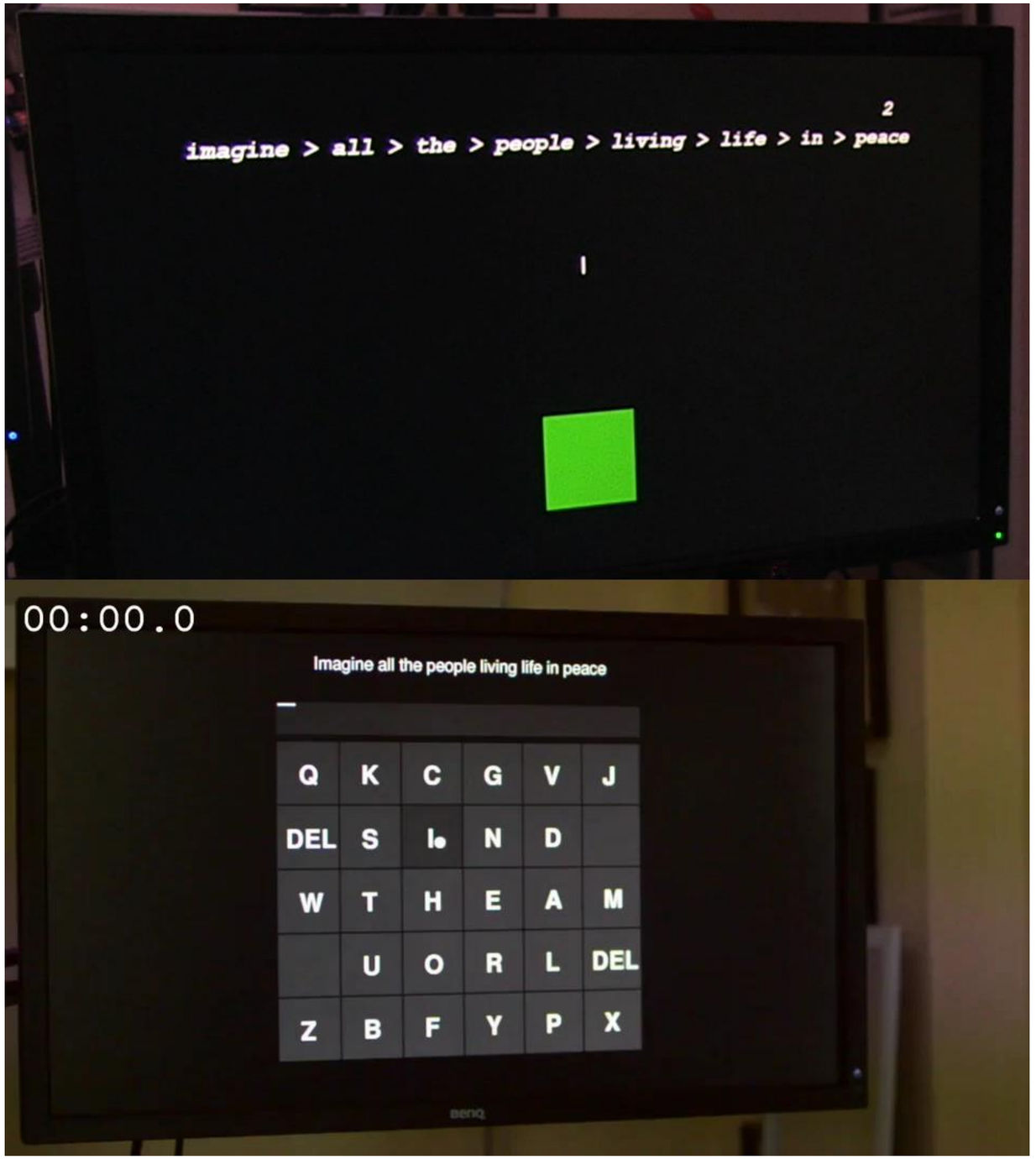
Willett et al. High-performance brain-to-text communication via handwriting. *Nature* 2021

Copy Typing Performance



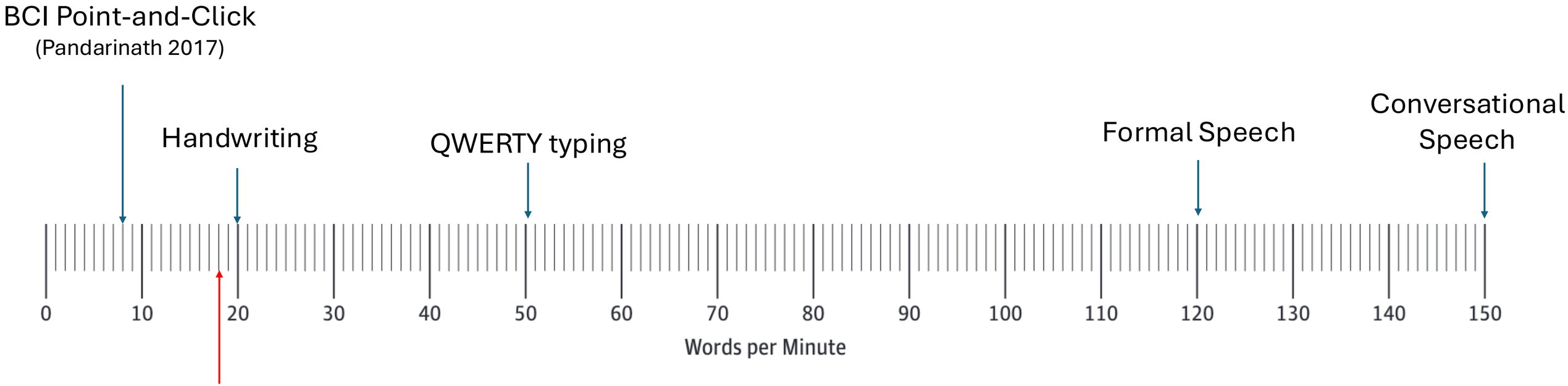


Willett et al. High-performance brain-to-text communication via handwriting. *Nature* 2021



Willett et al. High-performance brain-to-text communication via handwriting. *Nature* 2021

Words per minute in context

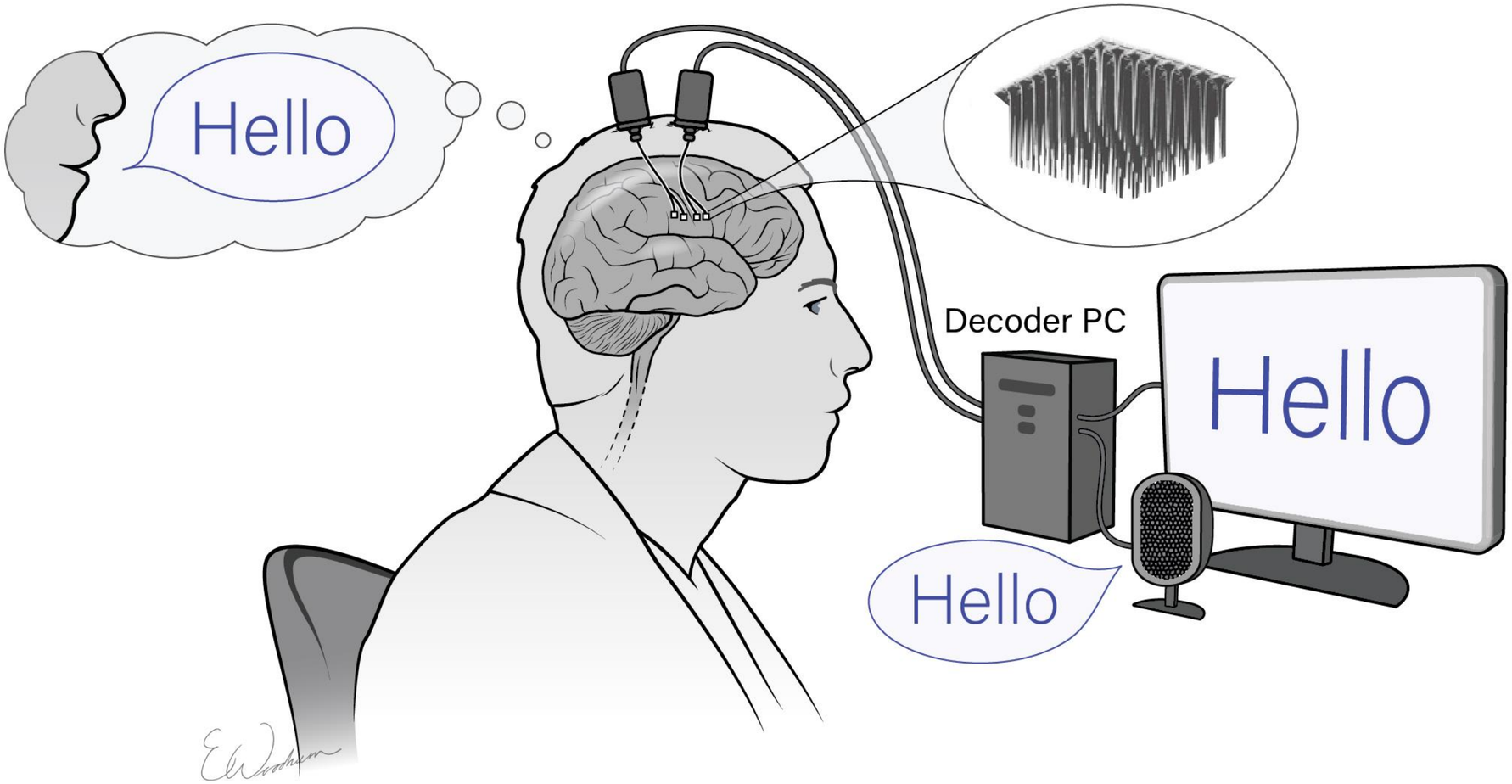


Willett et al. High-performance brain-to-text communication via handwriting. *Nature* 2021

What about speech?

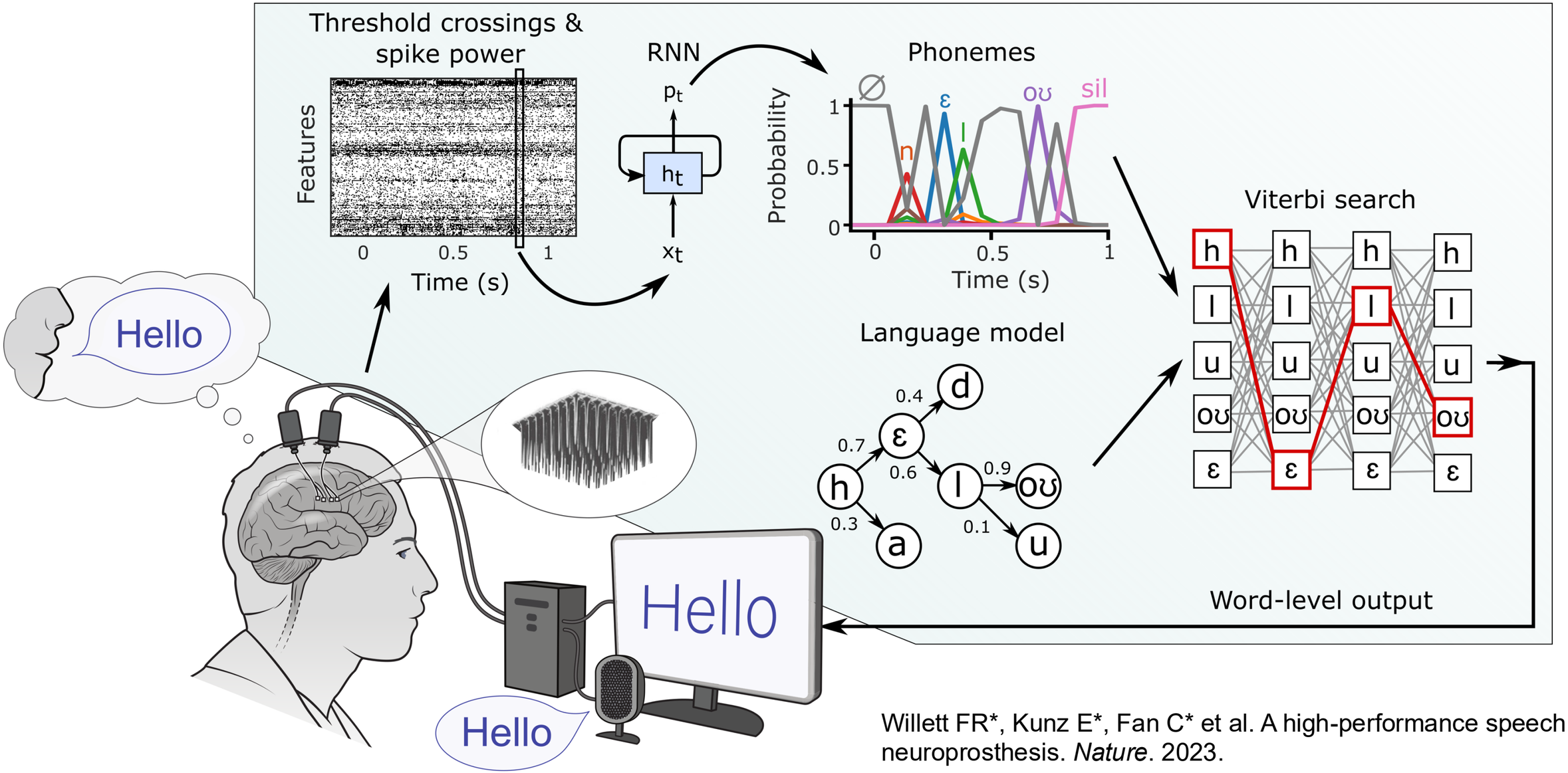
Wilson et al. 2020, Moses et al.2021

A Speech BCI



Willett FR*, Kunz E*, Fan C* et al. A high-performance speech neuroprosthesis. *Nature*. 2023.

Decoding Methods

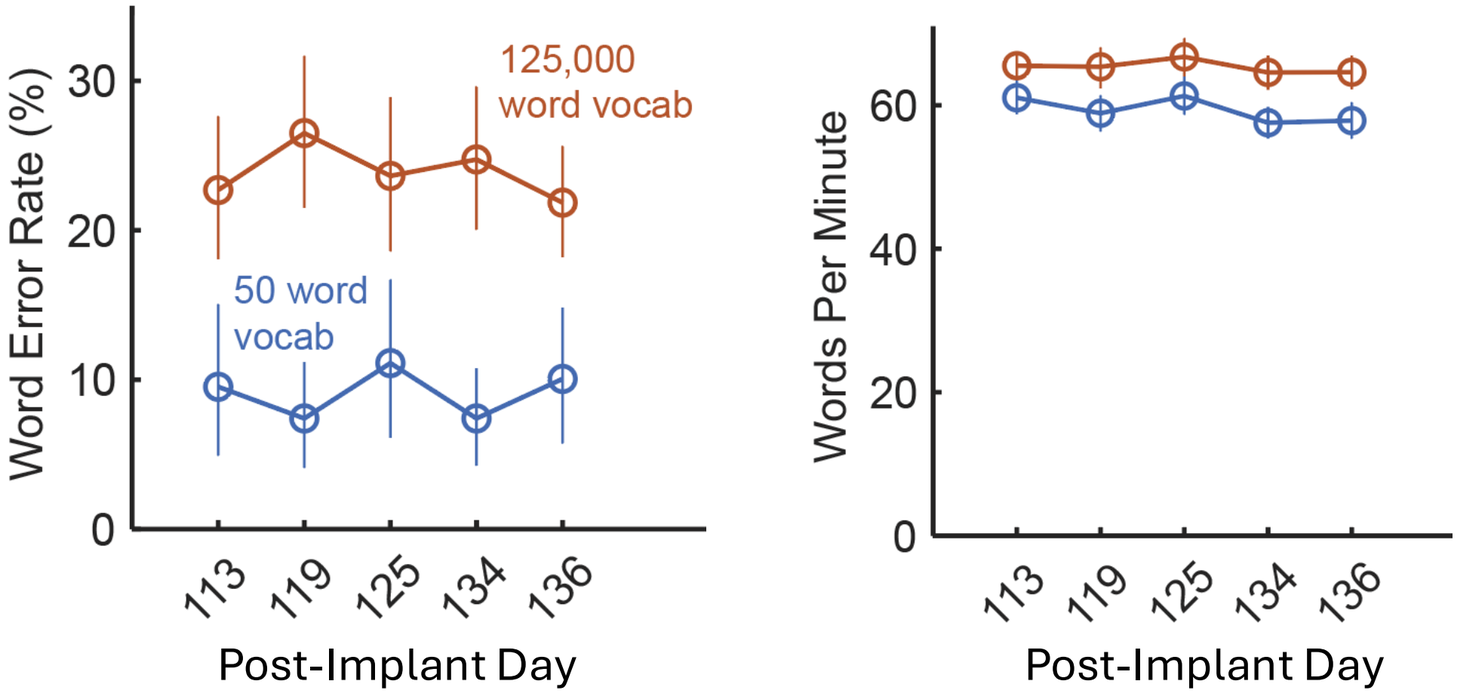


Willett FR*, Kunz E*, Fan C* et al. A high-performance speech neuroprosthesis. *Nature*. 2023.

Willett FR*, Kunz E*, Fan C* et al. A high-performance speech neuroprosthesis. *Nature*. 2023.

Willett FR*, Kunz E*, Fan C* et al. A high-performance speech neuroprosthesis. *Nature*. 2023.

High-Performance Decoding



Willett FR*, Kunz E*, Fan C* et al. A high-performance speech neuroprosthesis. *Nature*. 2023.

Words per minute in context

Willett FR*, Kunz E*, Fan C* et al. A high-performance speech neuroprosthesis. *Nature*. 2023.

BCI Point-and-Click
(Pandarinath 2017)

Handwriting

QWERTY typing

Formal Speech

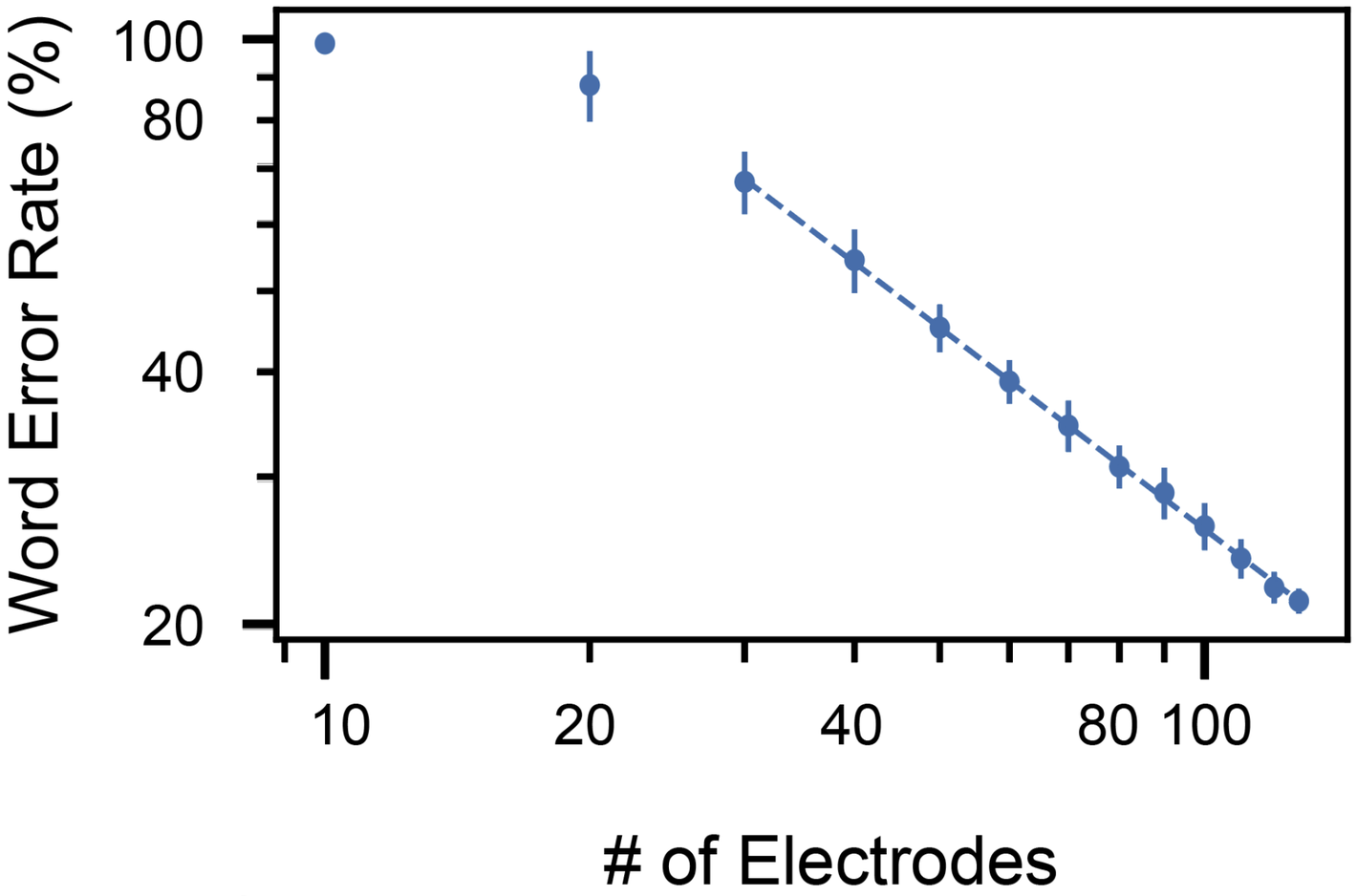
Conversational Speech

0 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150

Words per Minute

Willett et al. High-performance brain-to-text communication via handwriting. *Nature* 2021

Performance Increases with More Electrodes

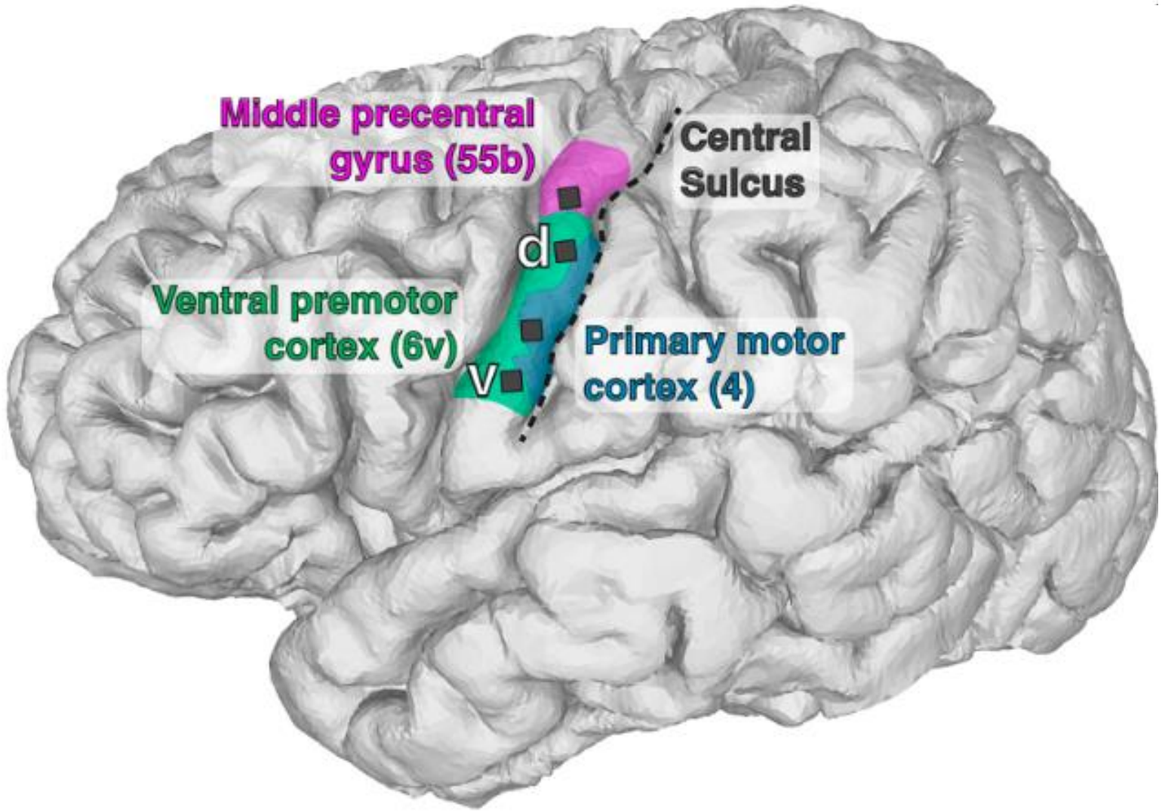


Willett FR*, Kunz E*, Fan C* et al. A high-performance speech neuroprosthesis. *Nature*. 2023.

Latest Results from UC Davis Collaborators

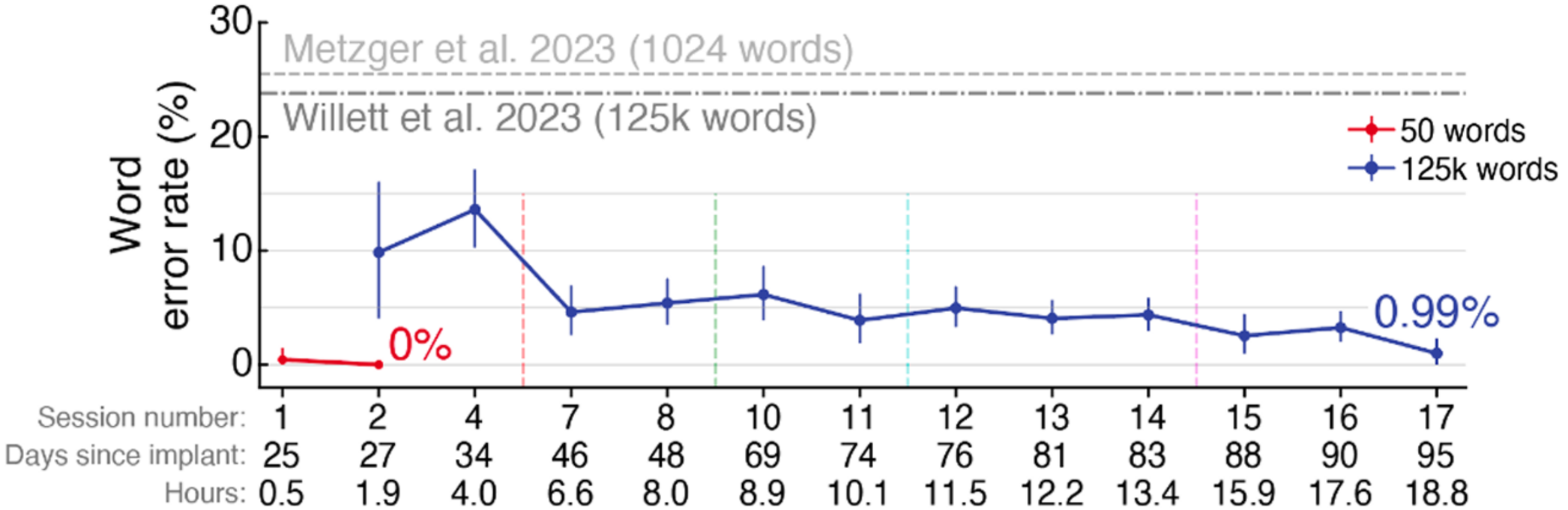
1) Doubled electrode count

2) Improved real-time language model



Card N, …, Brandman D**, Stavisky SD**. An accurate and rapidly calibrating speech neuroprosthesis. *NEJM*. 2024.

New Results from UC Davis Team



Card N, …, Brandman D**, Stavisky SD**. An accurate and rapidly calibrating speech neuroprosthesis. *NEJM*. 2024.

An accurate and rapidly calibrating speech neuroprosthesis

BRAINGATE
TURNING THOUGHT INTO ACTION

UCDAVIS HEALTH

Video 3:
First self-directed use of the speech neuroprosthesis (session 2)

An accurate and rapidly calibrating speech neuroprosthesis

BRAINGATE
TURNING THOUGHT INTO ACTION

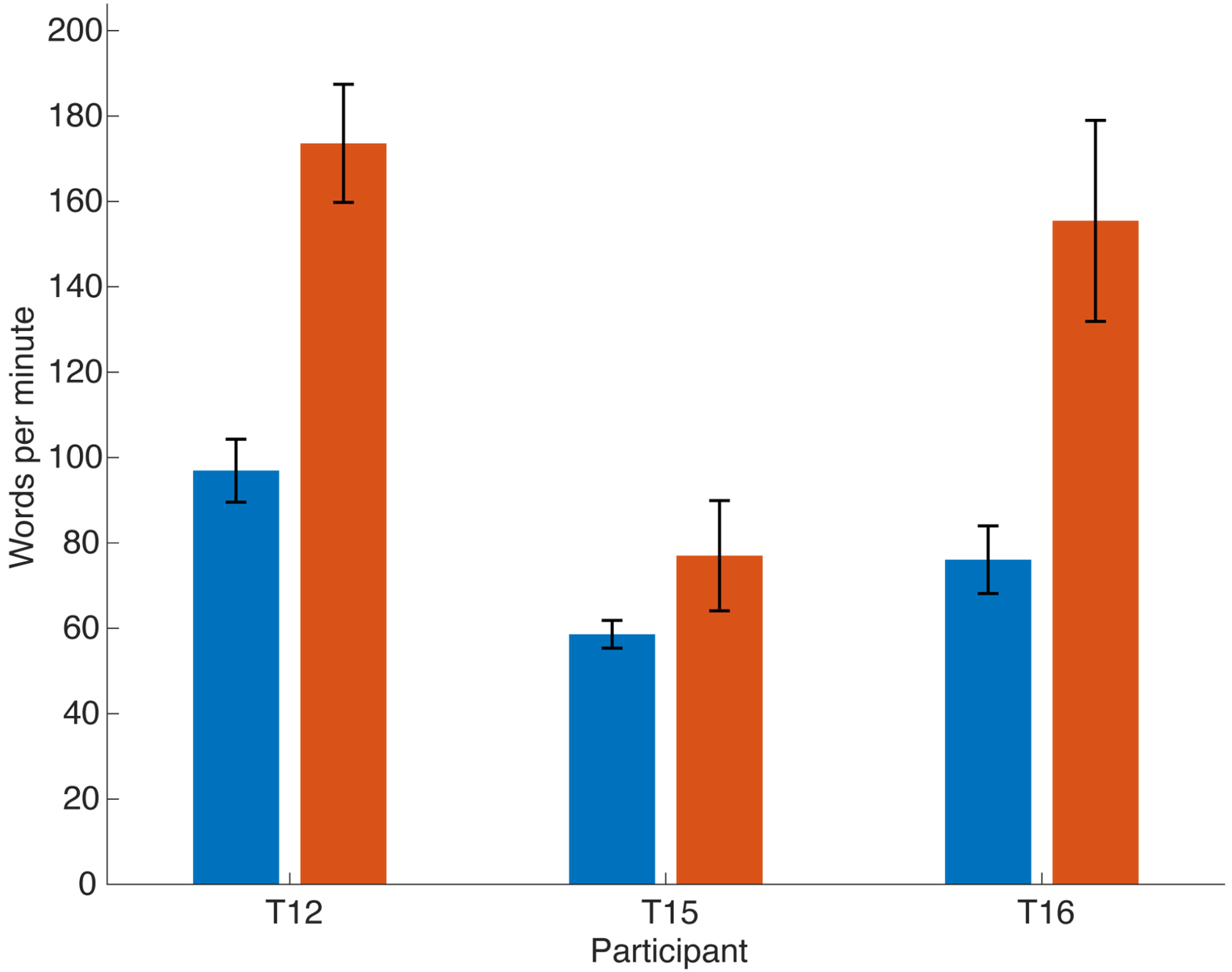
UCDAVIS HEALTH

Video 4:
Conversation Mode speech decoding (session 31)

How can we reach conversational speeds?

Hypothesis: Imagined speech can improve speaking rates in people with paralysis

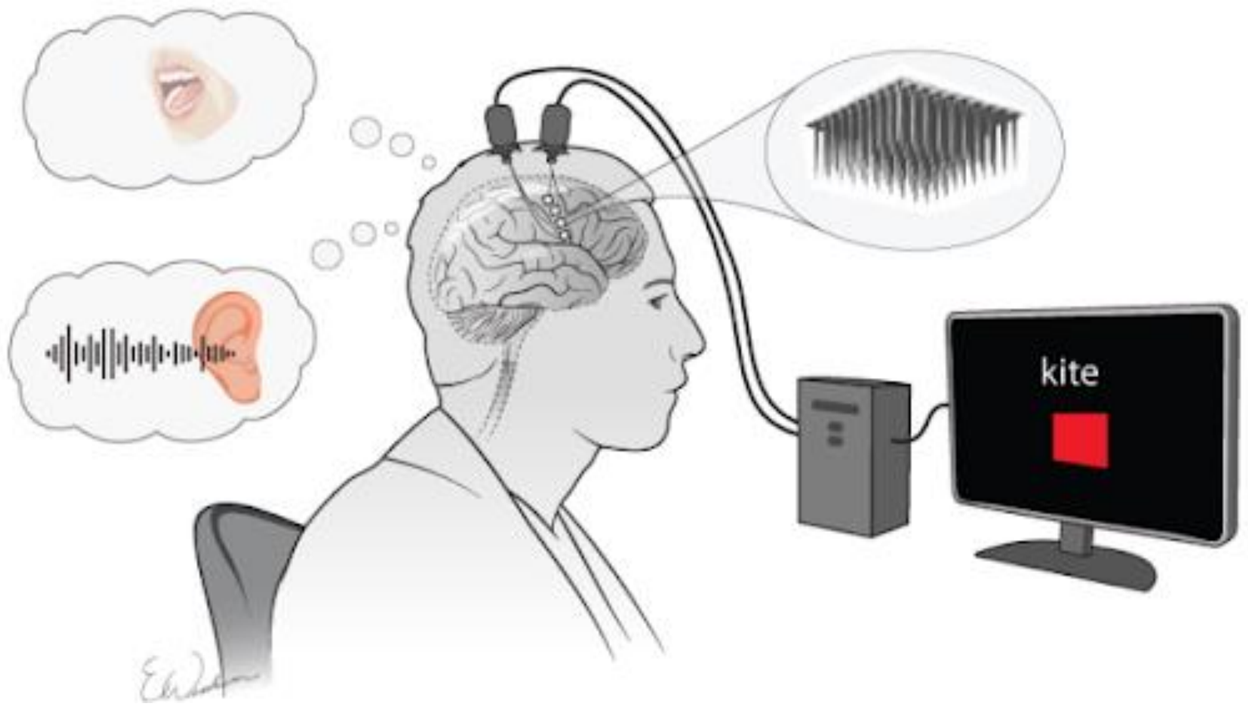
Imagined Speech is Faster than Attempted Speech



"[Attempted speaking] is like you're stuck in quicksand and you have a weighted blanket or two on top of you."

– T15

7 Words Experiment

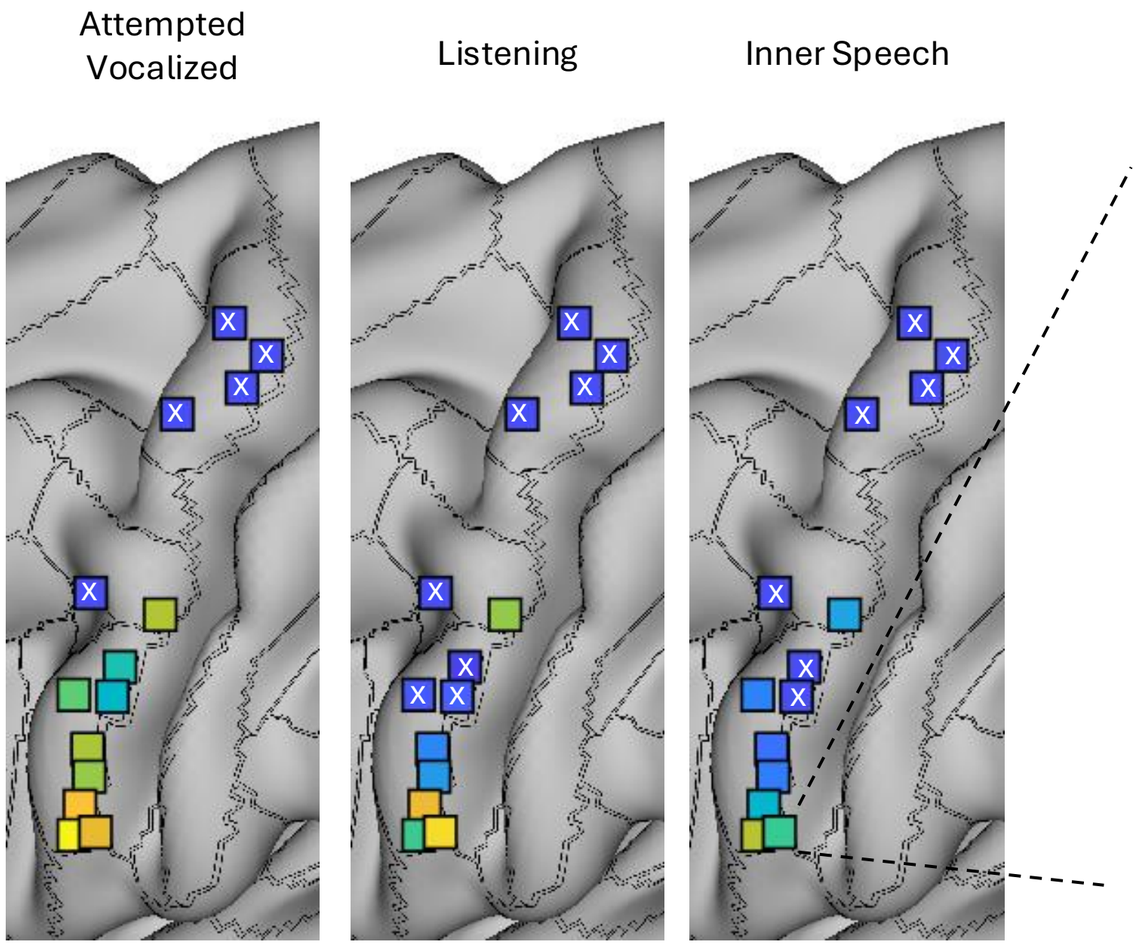


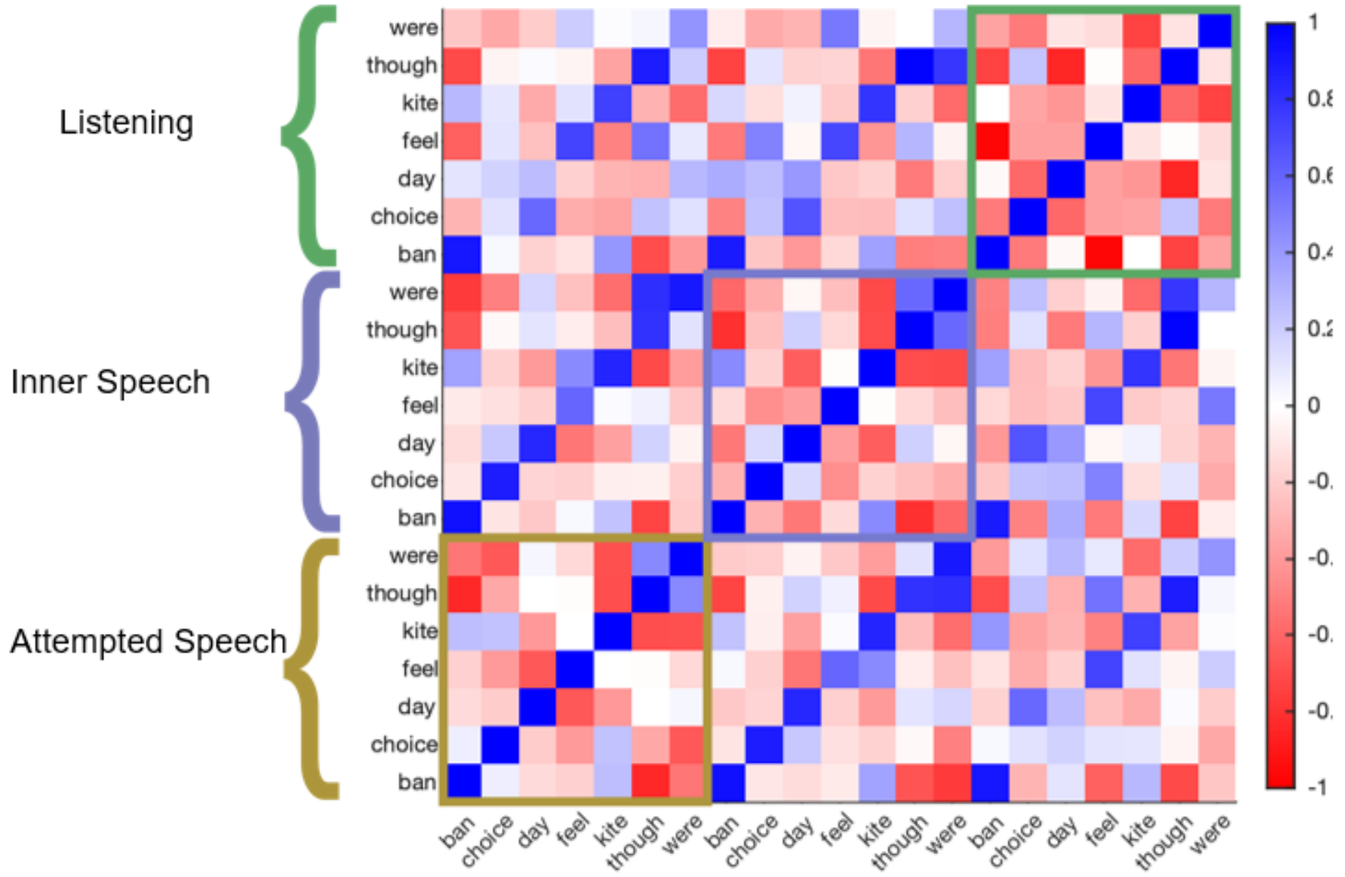
Conditions:
Attempted Vocalized
Inner Speech
Listening

Words:
Ban
Choice
Day
Feel
Kite
Though
Were

Kunz*, Meschede-Krasa*, … Henderson, Willett. Inner speech in motor cortex and implications for speech neuroprostheses. *Cell*. 2025

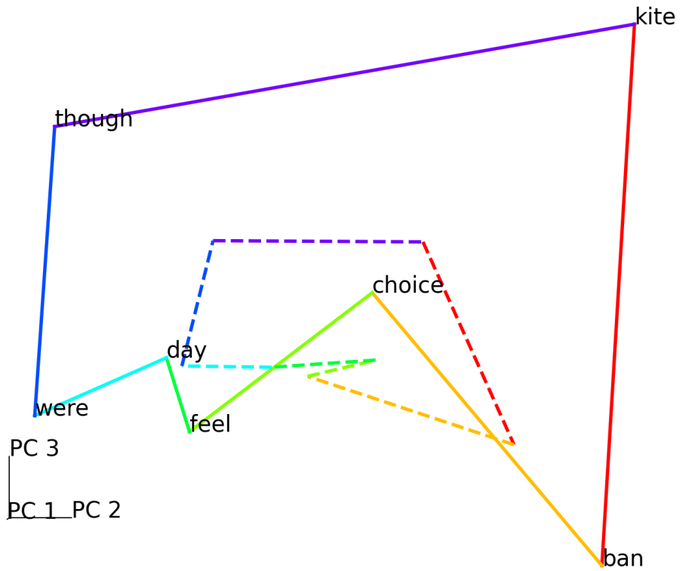
Shared representation across behaviors



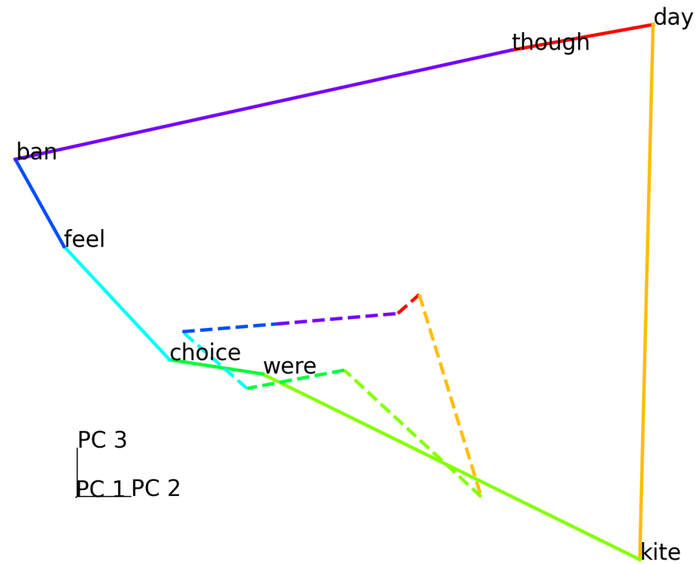


Kunz*, Meschede-Krasa*, … Henderson, Willett. Inner speech in motor cortex and implications for speech neuroprostheses. *Cell*. 2025

Neural Geometry of Attempted vs. Inner Speech



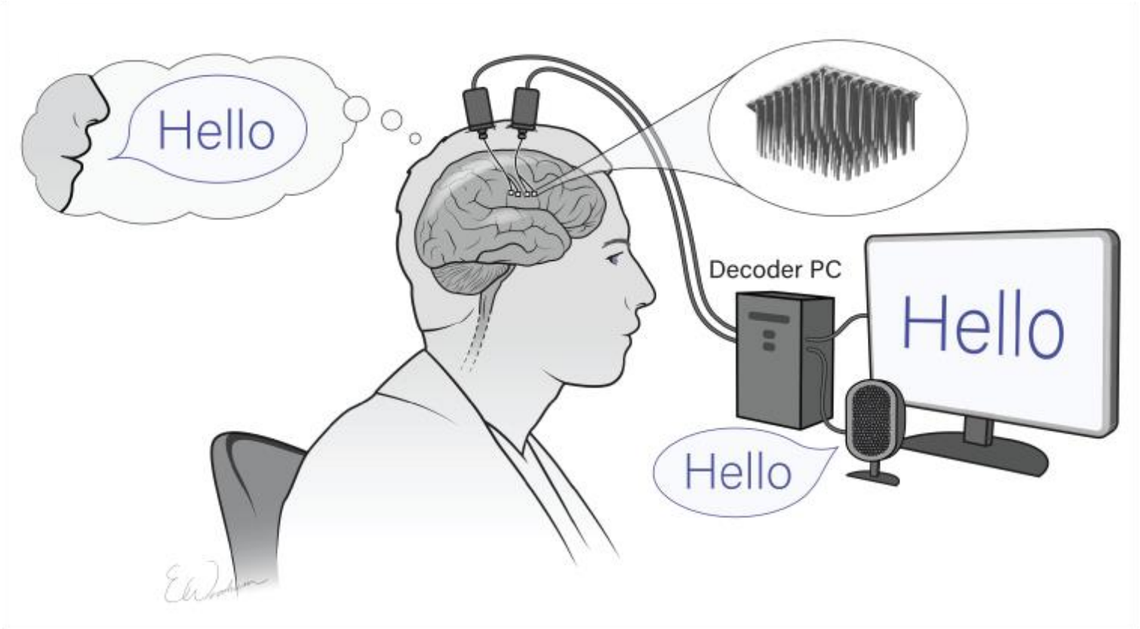
T12



T17

Kunz*, Meschede-Krasa*, … Henderson, Willett. Inner speech in motor cortex and implications for speech neuroprostheses. *Cell*. 2025

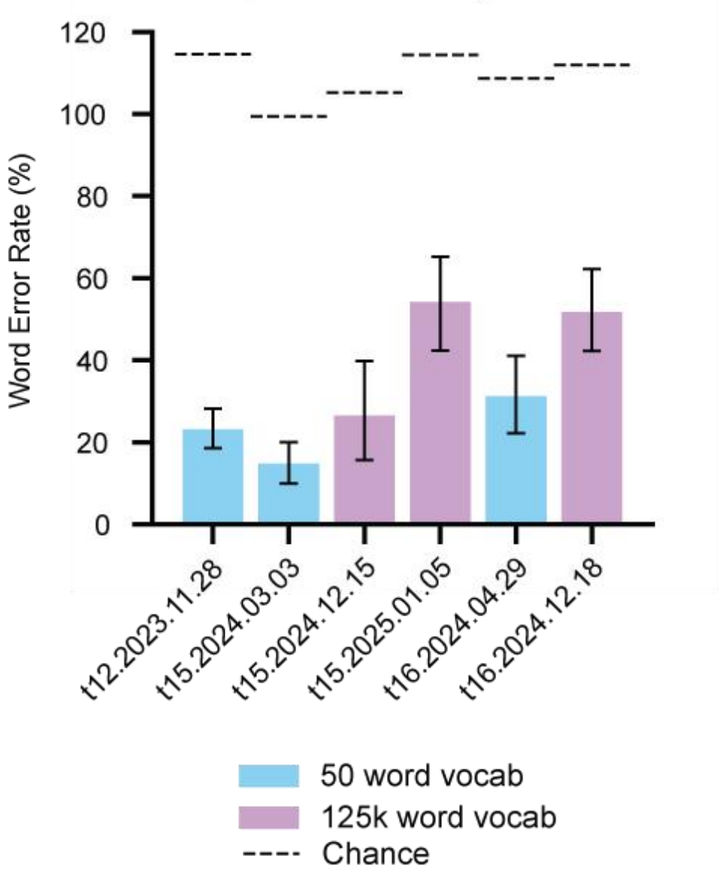
Decoding Inner Speech in Real-Time



Example Online Inner Speech Trials
(125,000-word Vocab)

True Sentence: I don't know how long you've been here.
Decoded Sentence: I don't know how long you've been here.

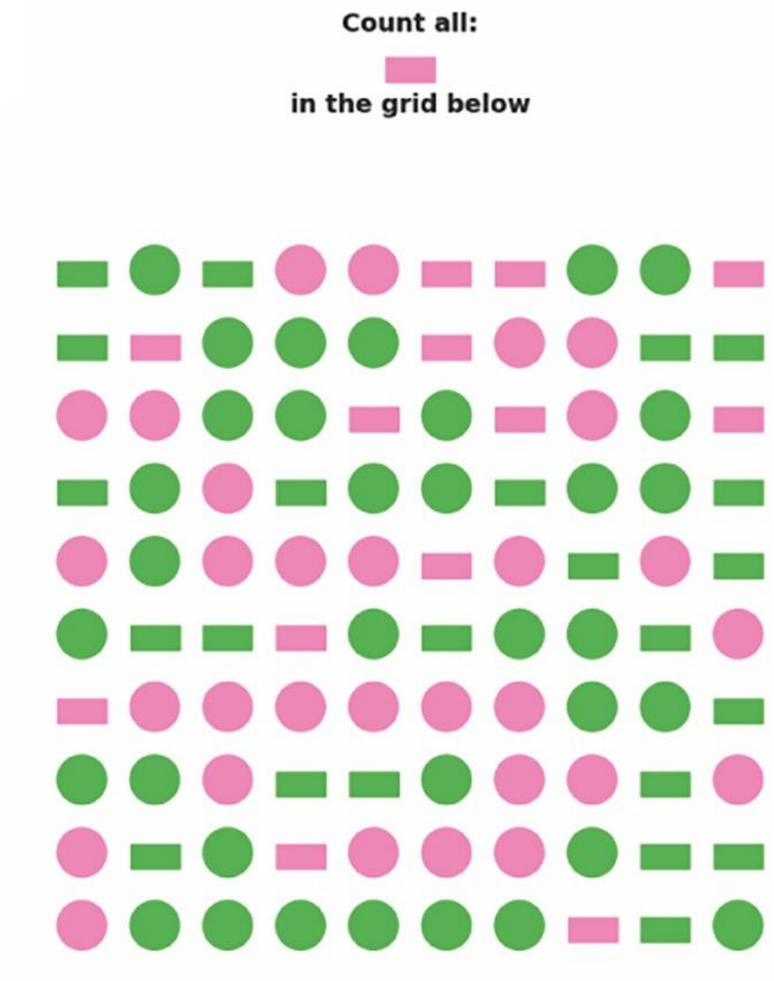
True Sentence: I think it has the best flavor.
Decoded Sentence: I think it has the best player.

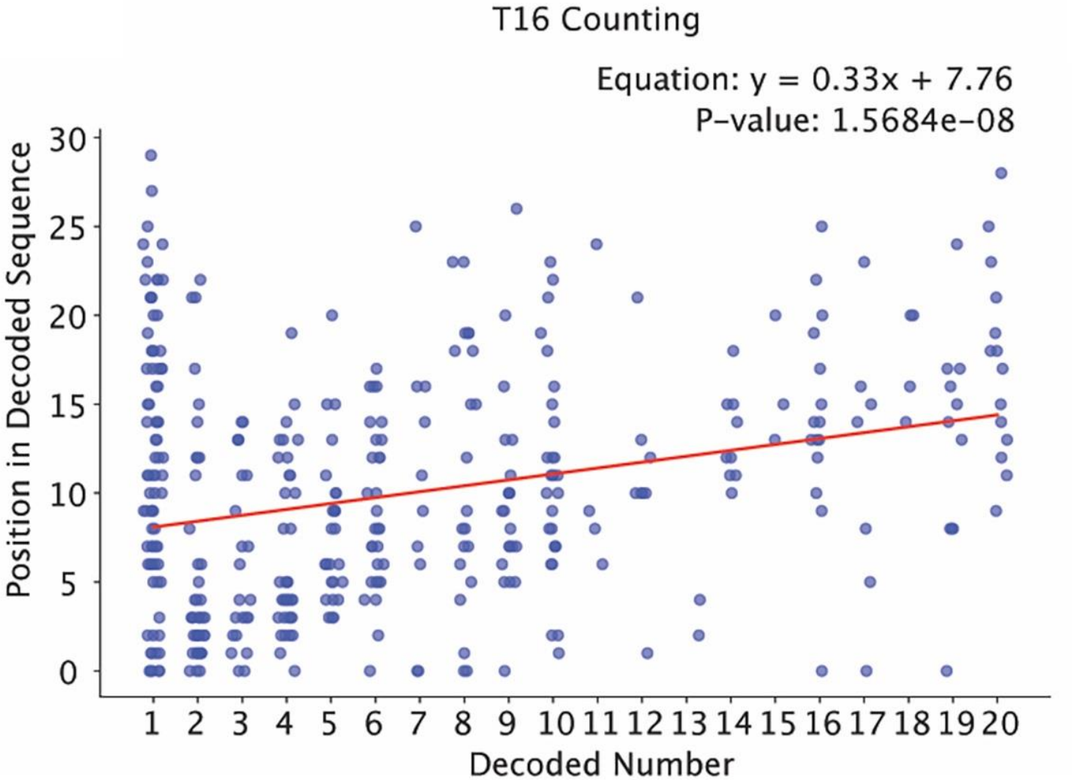


Kunz*, Meschede-Krasa*, … Henderson, Willett. Inner speech in motor cortex and implications for speech neuroprostheses. *Cell*. 2025


29% WER on a 50-word vocabulary
@ 146 WPM (1x speed)

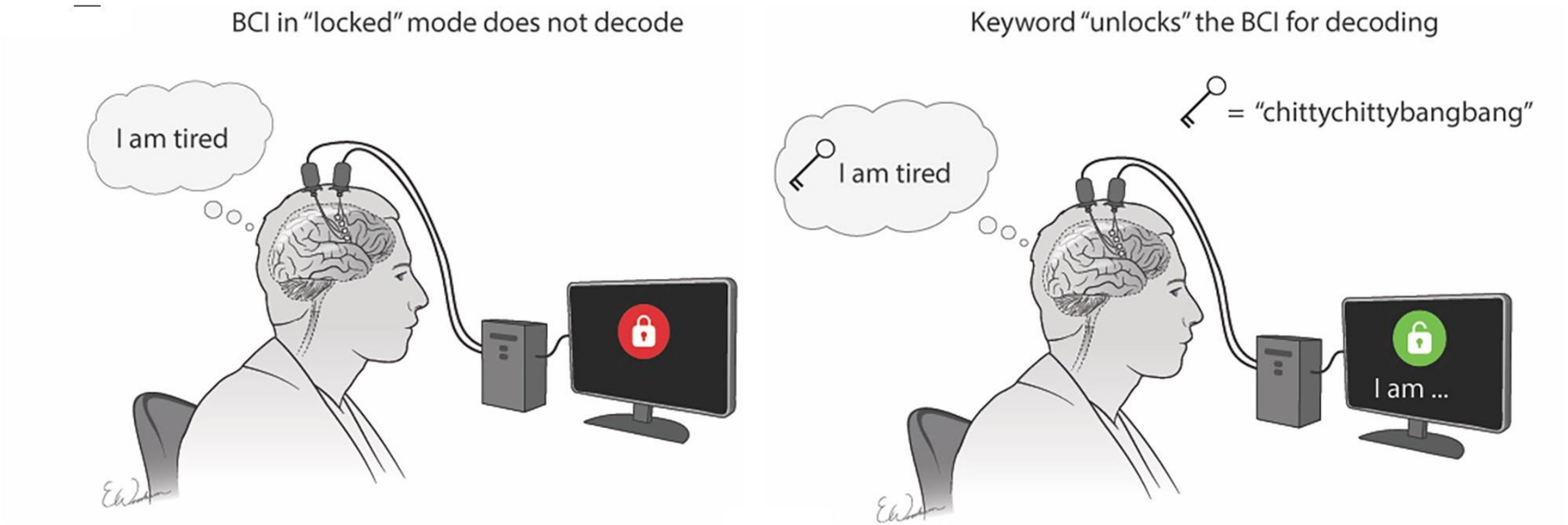
Detection of Spontaneous Inner Speech





Kunz*, Meschede-Krasa*, … Henderson, Willett. Inner speech in motor cortex and implications for speech neuroprostheses. *Cell*. 2025

Password Protection for Inner Speech Decoding



T12 Inner Speech BCI w/ Keyword Performance

Keyword Detection Accuracy (%)	98.75 (93.23, 99.97)
Word Error Rate (%) (50 word Vocab)	42.45 (35.71, 49.41)

Kunz*, Meschede-Krasa*, … Henderson, Willett. Inner speech in motor cortex and implications for speech neuroprostheses. *Cell*. 2025

Where do we go next with BCIs?

Translation is Underway

Goal: Derisk restoring communication in **new** disorders

Marcus Foundation Award to Expand Communication BCIs to Hemispheric Stroke

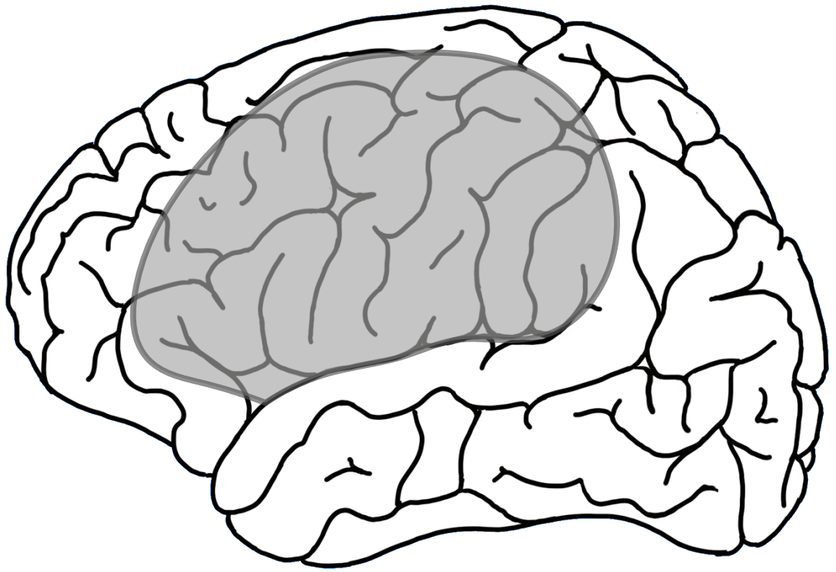
Someone in the US has a stroke every 40 seconds

Every year, more than 795,000 people in the US have a stroke

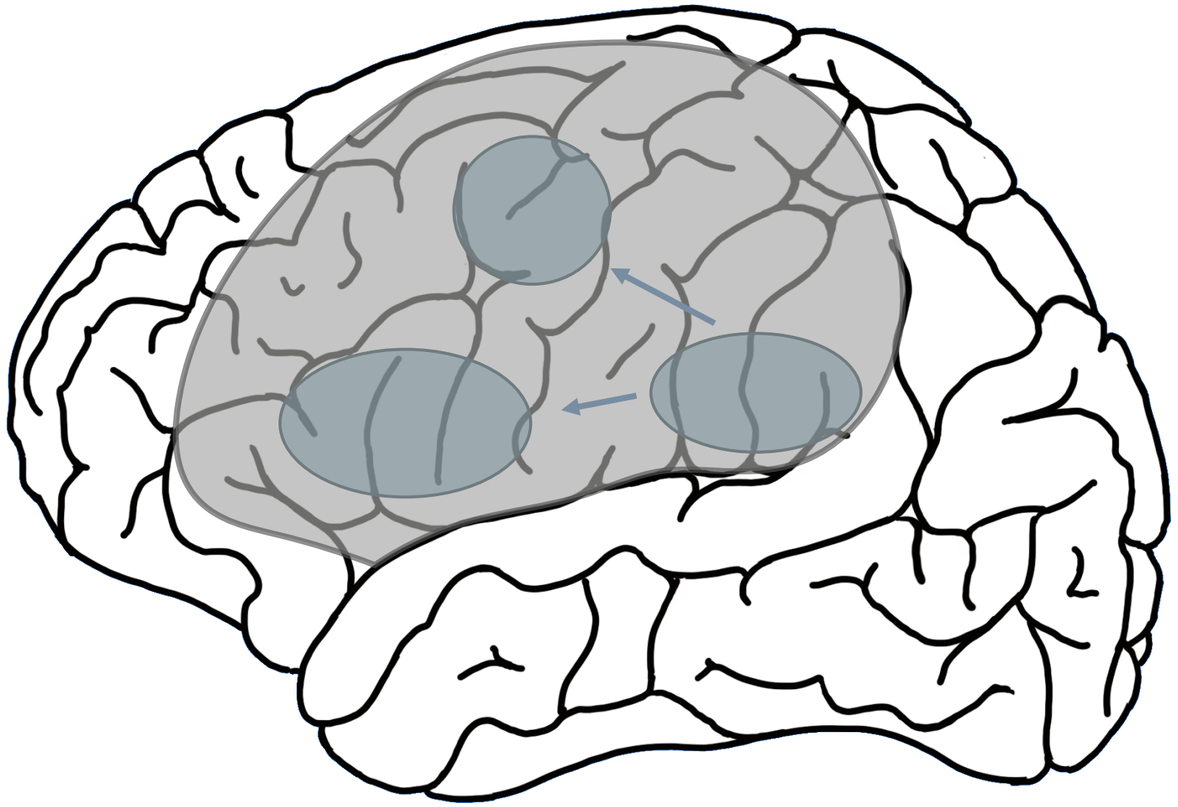
1/3 of stroke survivors have communication problems

- Centers for Disease Control

Broca’s Aphasia

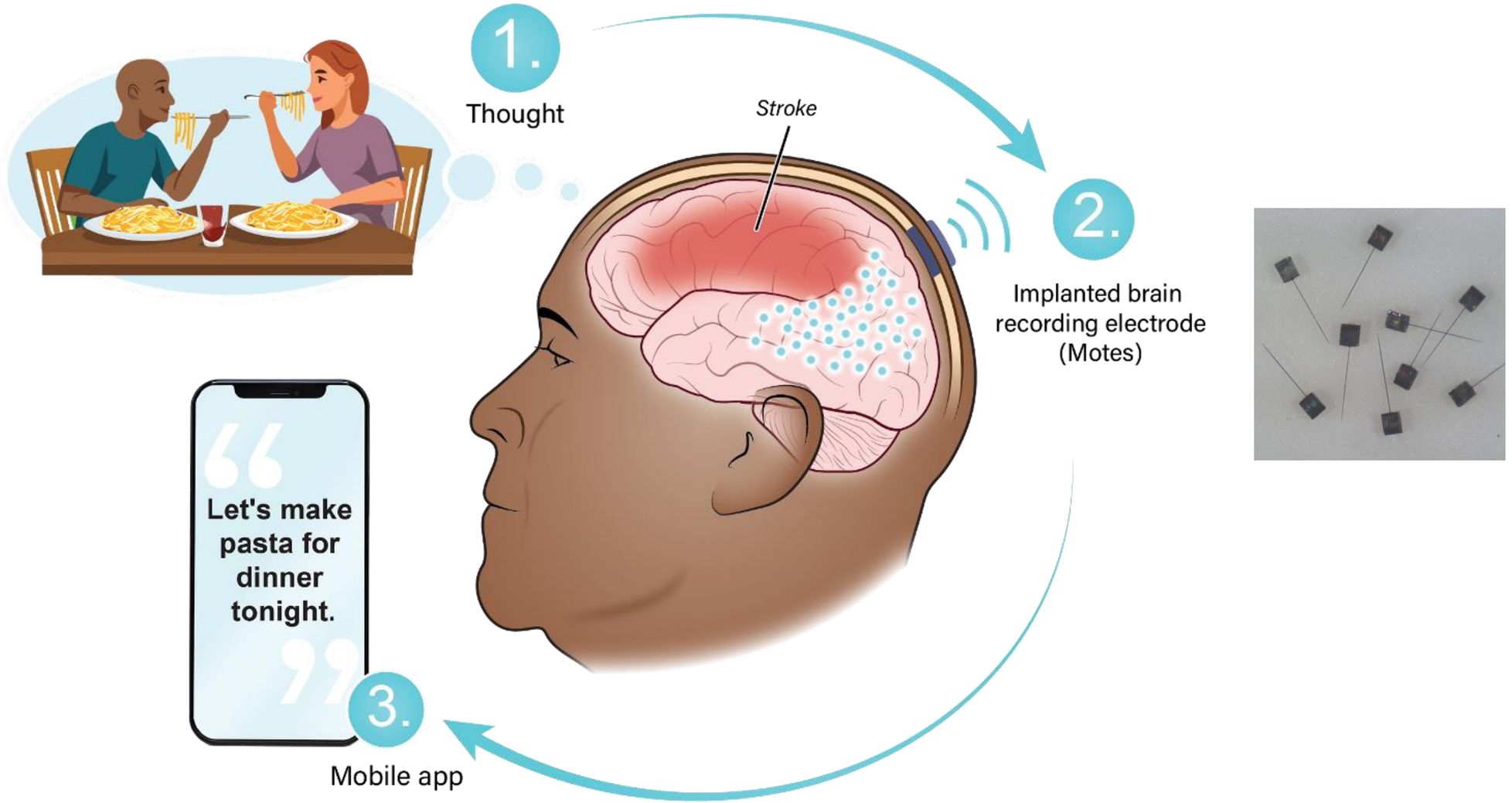


Broca’s Aphasia



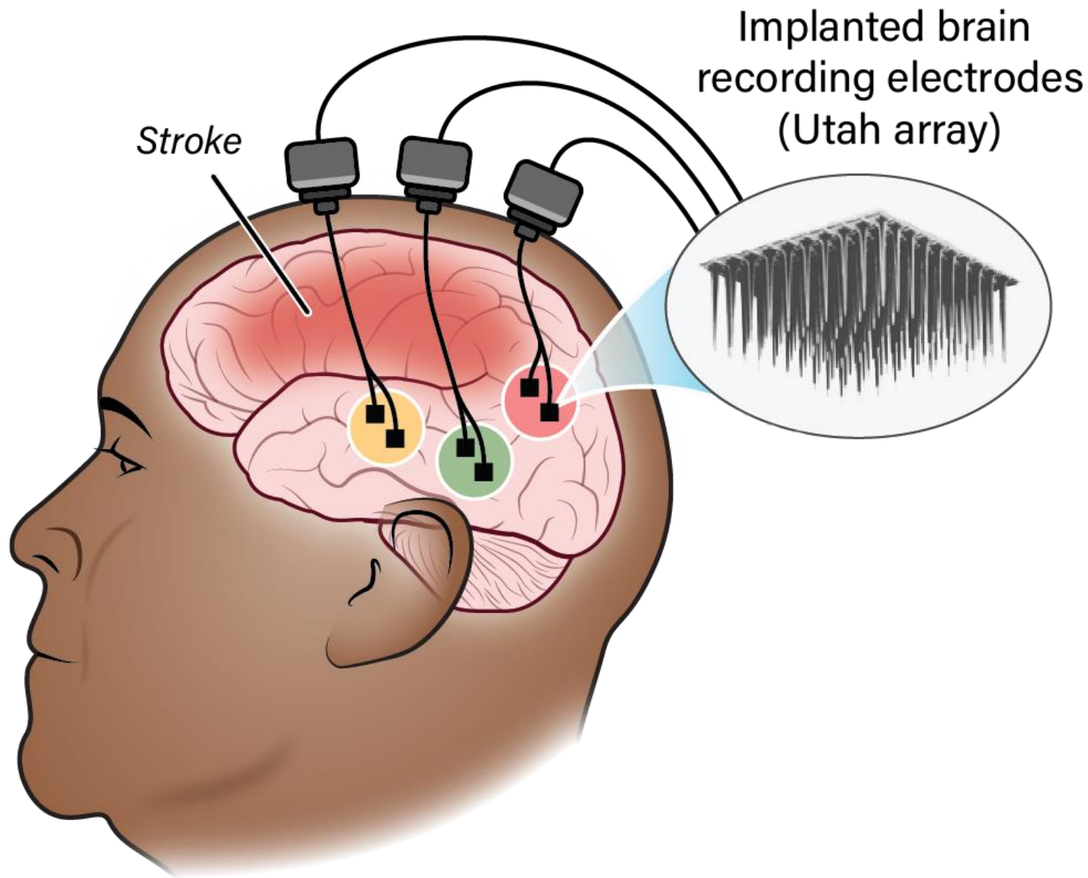
- Brain areas for producing speech destroyed
- Understanding / intent still intact
- Affects ~225,000 people in the US
- Currently no treatment

The Vision -“Marcus Motes”



Stanford Site – Mapping and Decoding Speech in the Post-Stroke Brain

- **Aim 1** – Mapping Speech in Temporal Lobe
- **Aim 2** – Decoding Speech from Temporal Lobe

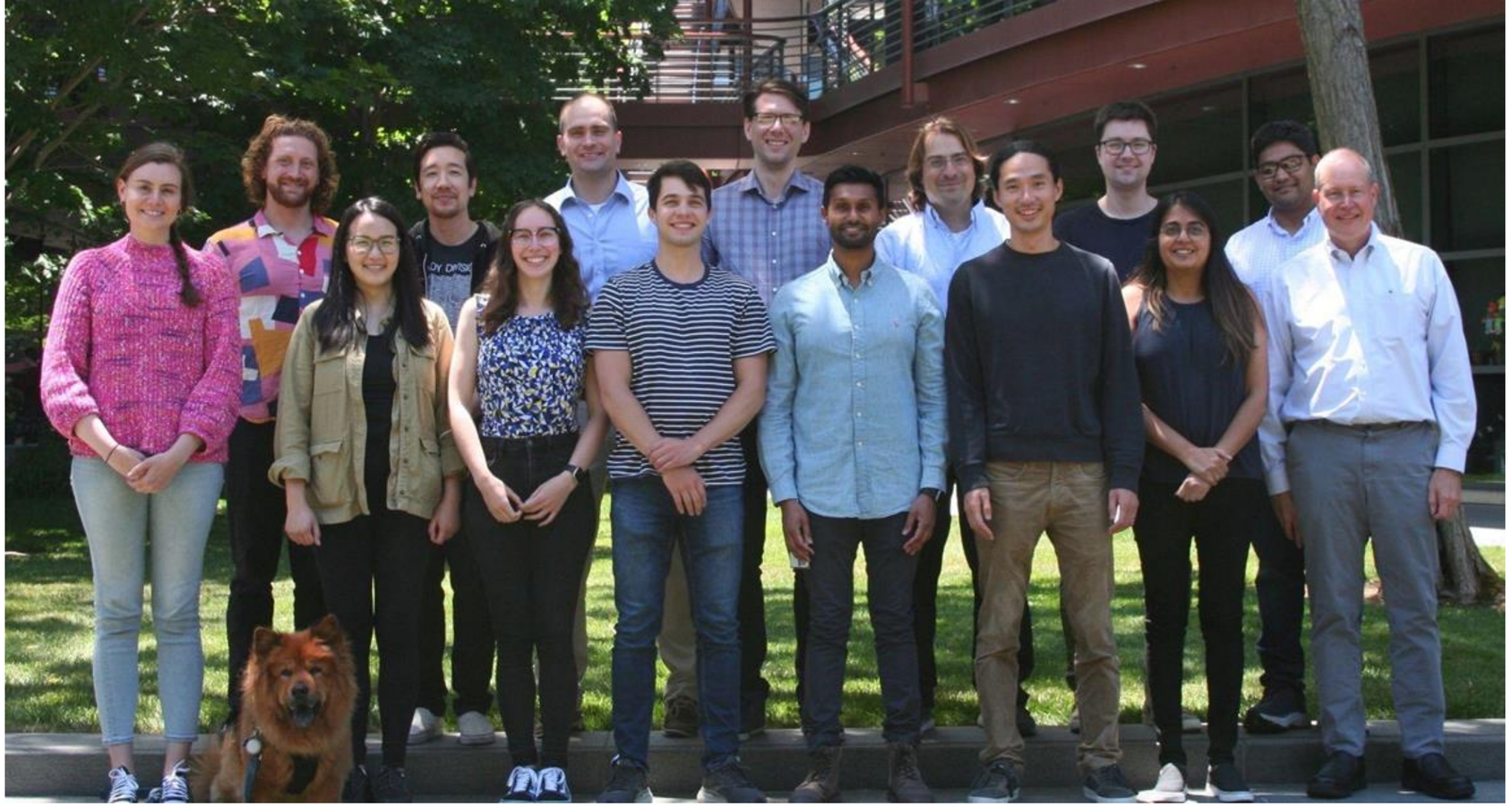


Conclusion

- Highly accurate speech decoding with large vocabularies is possible
- Inner speech is a pathway towards conversational rates
- Decreasing variability in performance is an ongoing challenge (hardware, targeting, disease state)
- New disorders are a big opportunity for communication BCIs (e.g., aphasia)

Conclusion

- Communication BCIs for ALS and brainstem stroke have progressed from point-and-click to speech
- We will soon have systems that can provide real assistance to people with communication disorders and paralysis
- Research vision: expand communication BCIs to new disorders
  - Broca's Aphasia
  - Cerebral Palsy



Stanford Neural Prosthetics Translational Lab (NPTL)

Thank you to our participants: T5, T11, T12, T15, T16, and T17

Providence VA Medical Center

Massachusetts General Hospital

Brown University

Carney Institute for Brain Science

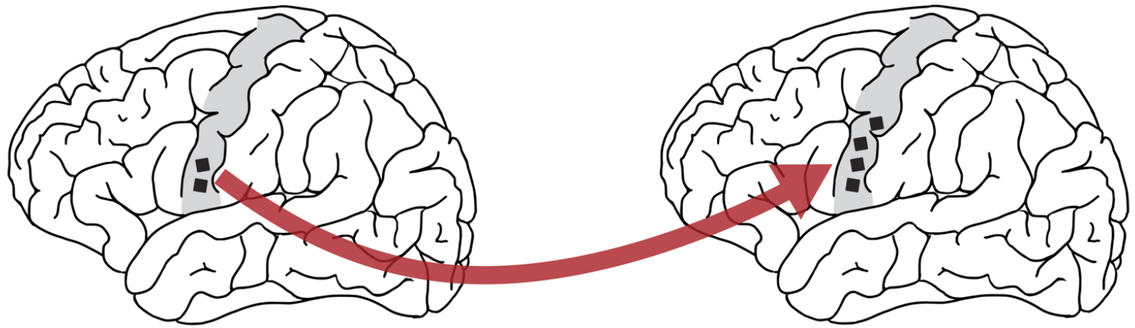
Emory University

Harvard Medical School

Stanford University

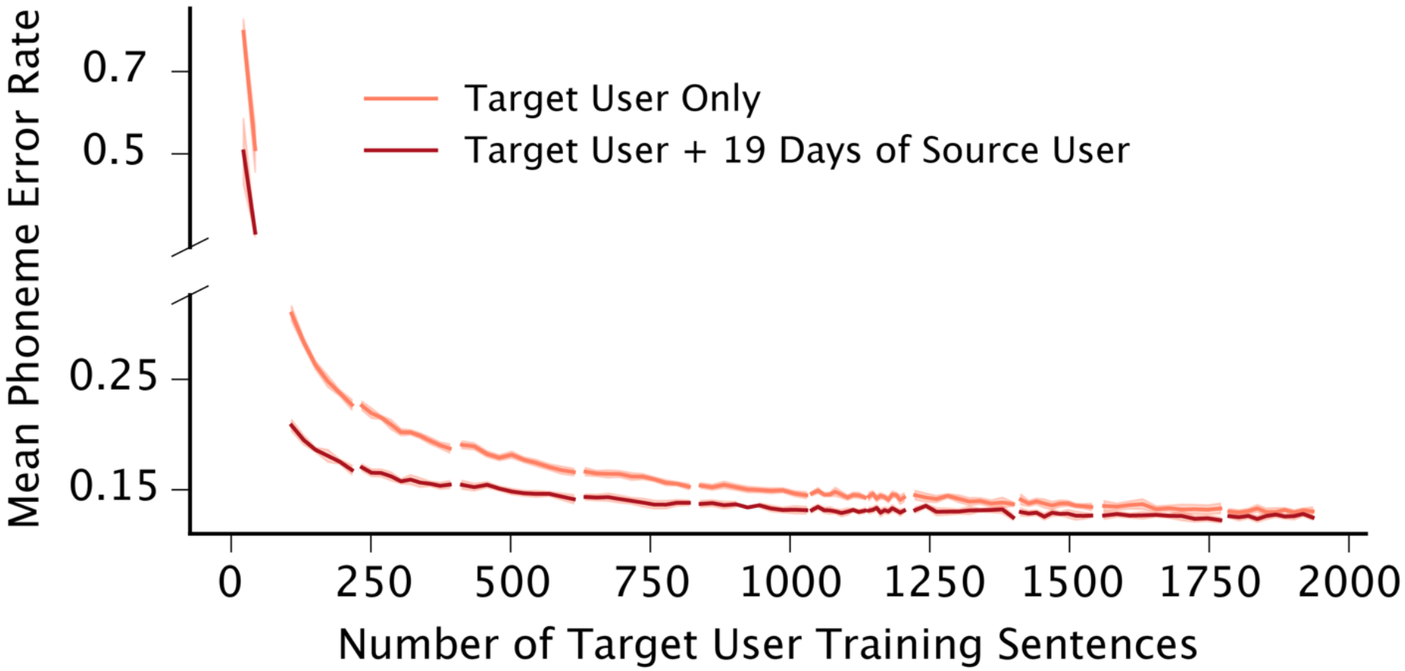
University of California, Davis

Minimizing Calibration Time via Transfer Learning



Source User

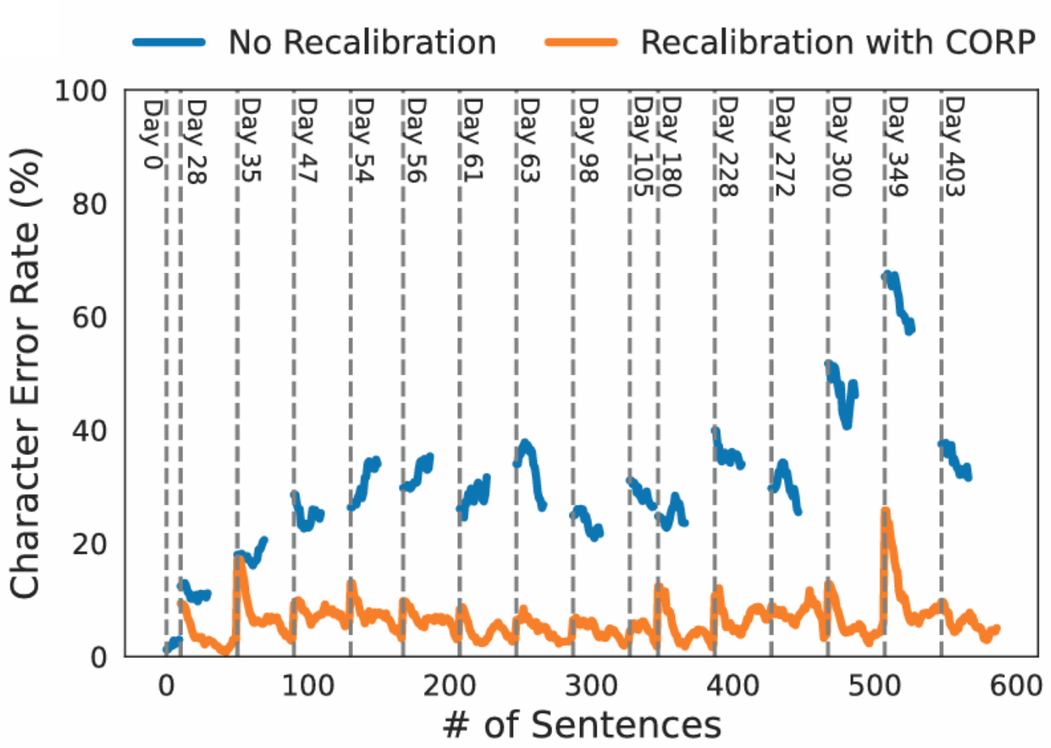
Target User

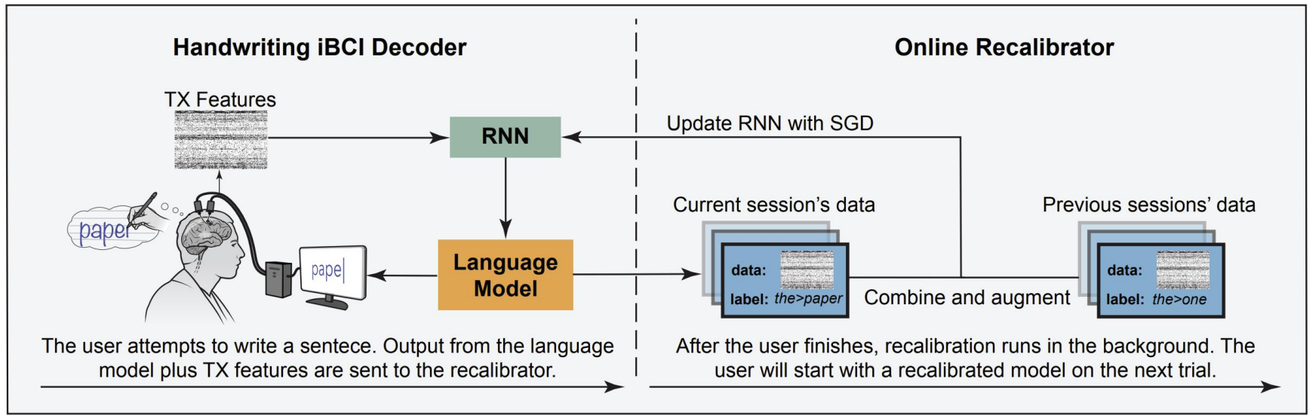


Alisa Levin

Stabilization via Continual Self-Training

Signals change **slowly enough** and decoding is **accurate enough** to enable self-recalibration: retraining on error-corrected outputs.

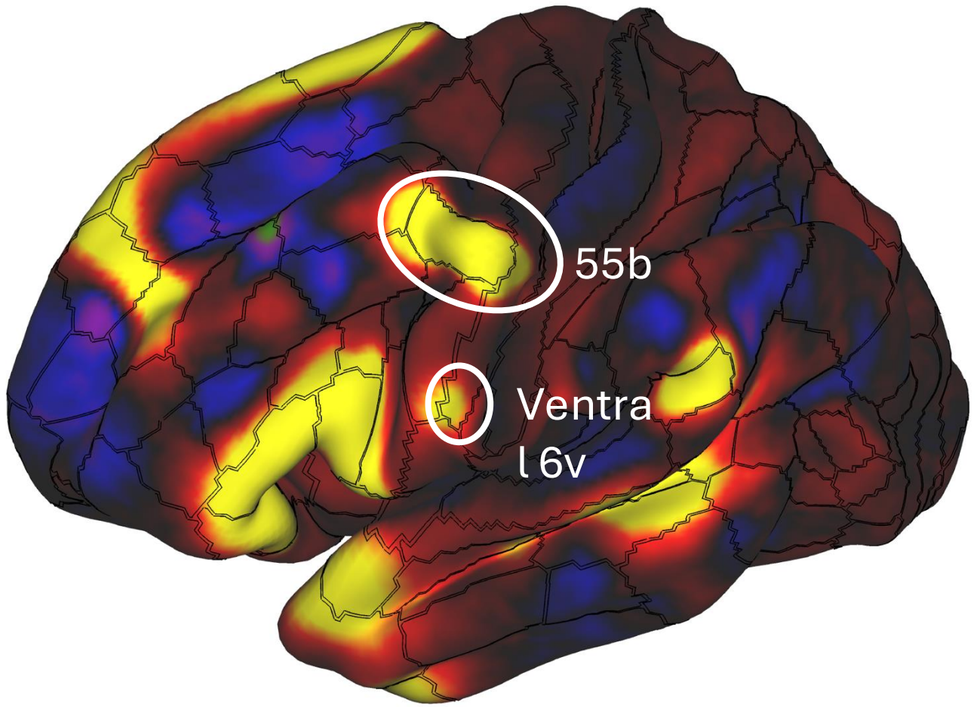




Fan, C. et al. Plug-and-Play Stability for Intracortical Brain-Computer Interfaces: A One-Year Demonstration of Seamless Brain-to-Text Communication. *NeurIPS* 2023.

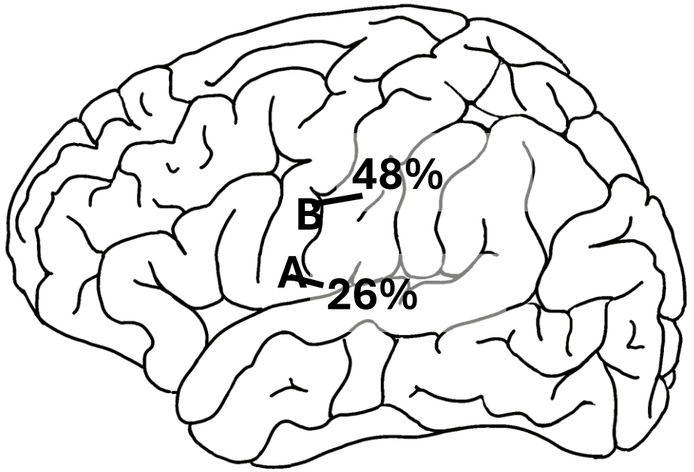
Chaofei Fan

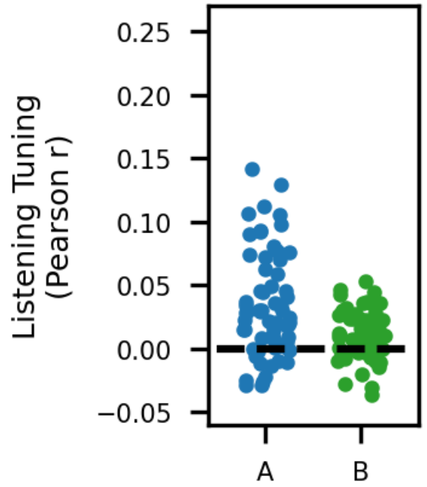
Speech Area Targeting: Two Speech Areas in Motor Cortex?



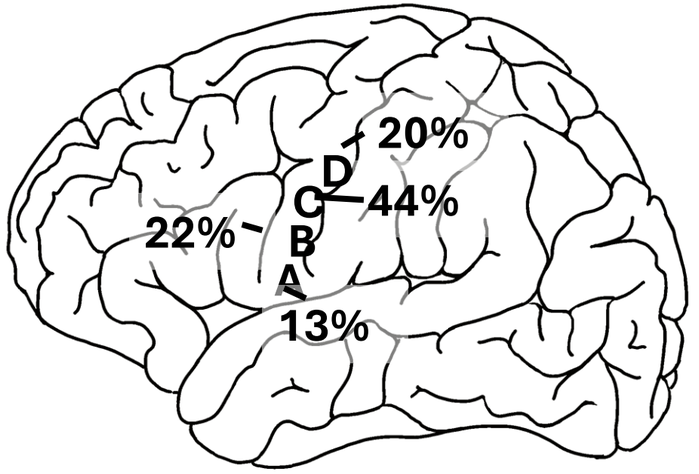
Glasser MF et al. A multi-modal parcellation of human cerebral cortex. *Nature*. 2016.

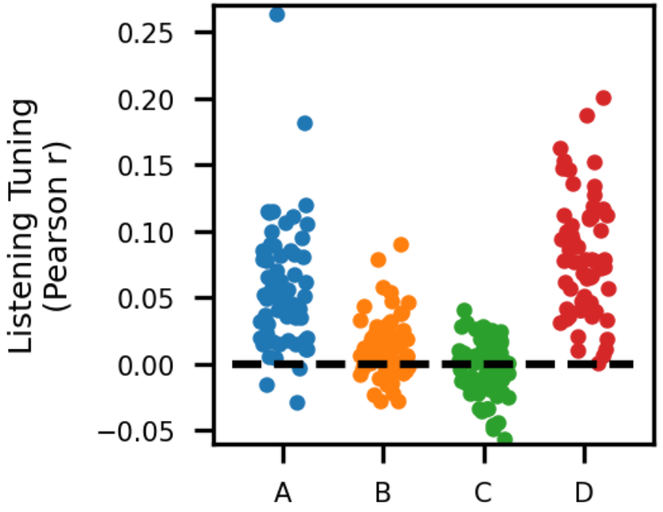
Stanford Participant





Davis Participant





Human Connectome Project Targeting

MRI

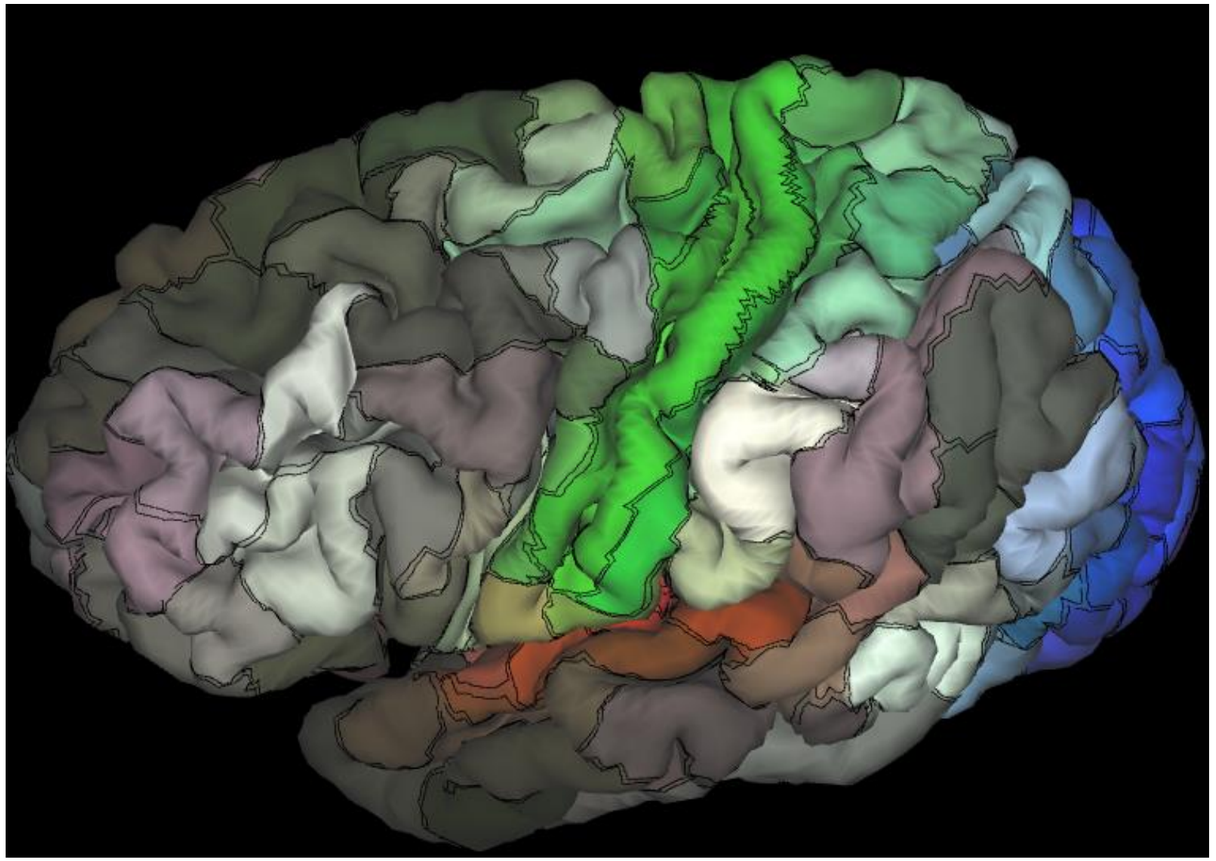
Cortical Thickness

Myelination

Folding

fMRI

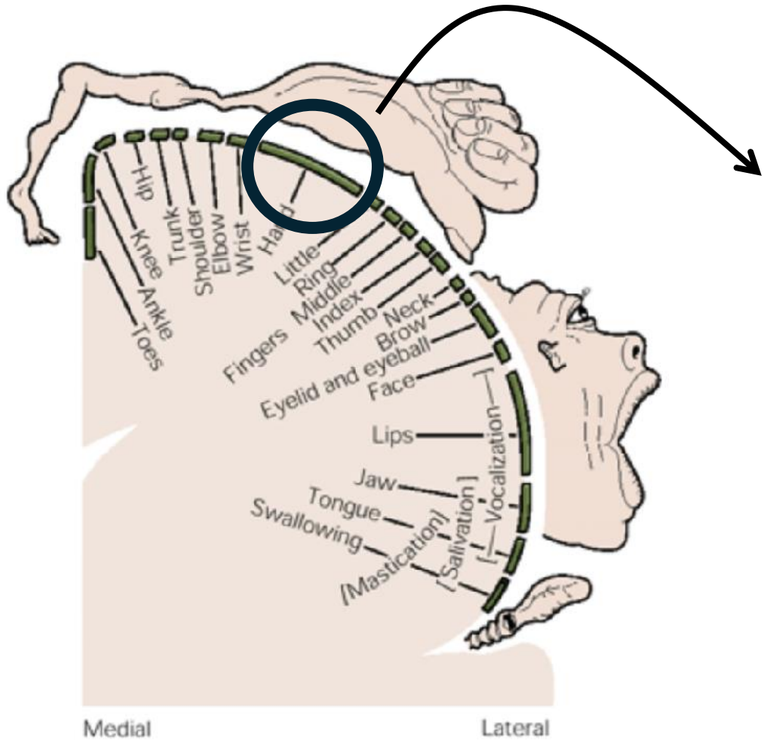
Resting State Networks

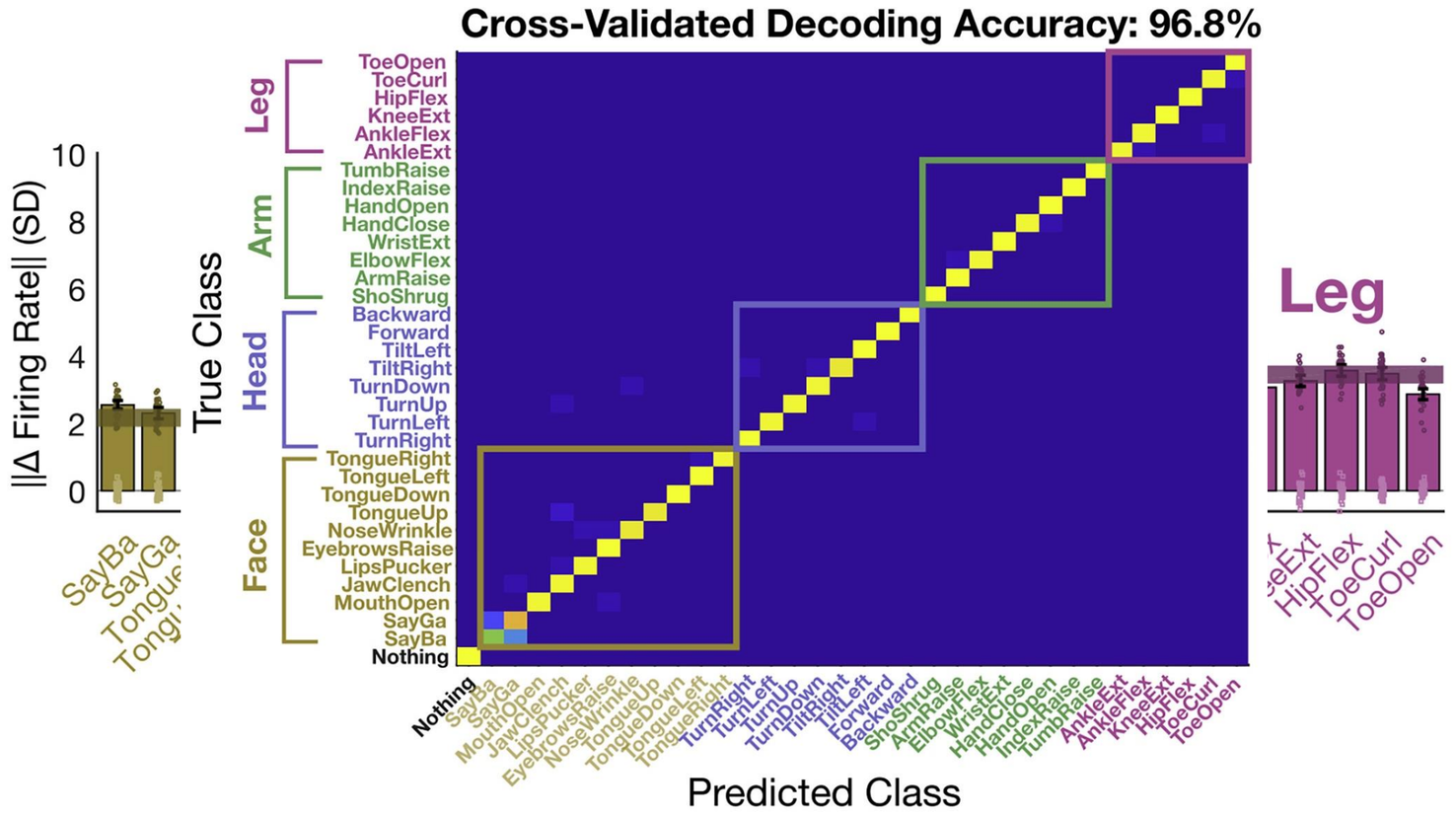


Glasser MF et al. A multi-modal parcellation of human cerebral cortex. *Nature*. 2016.

Enabling Fundamental Neuroscience: Motor Representations in the Human Brain

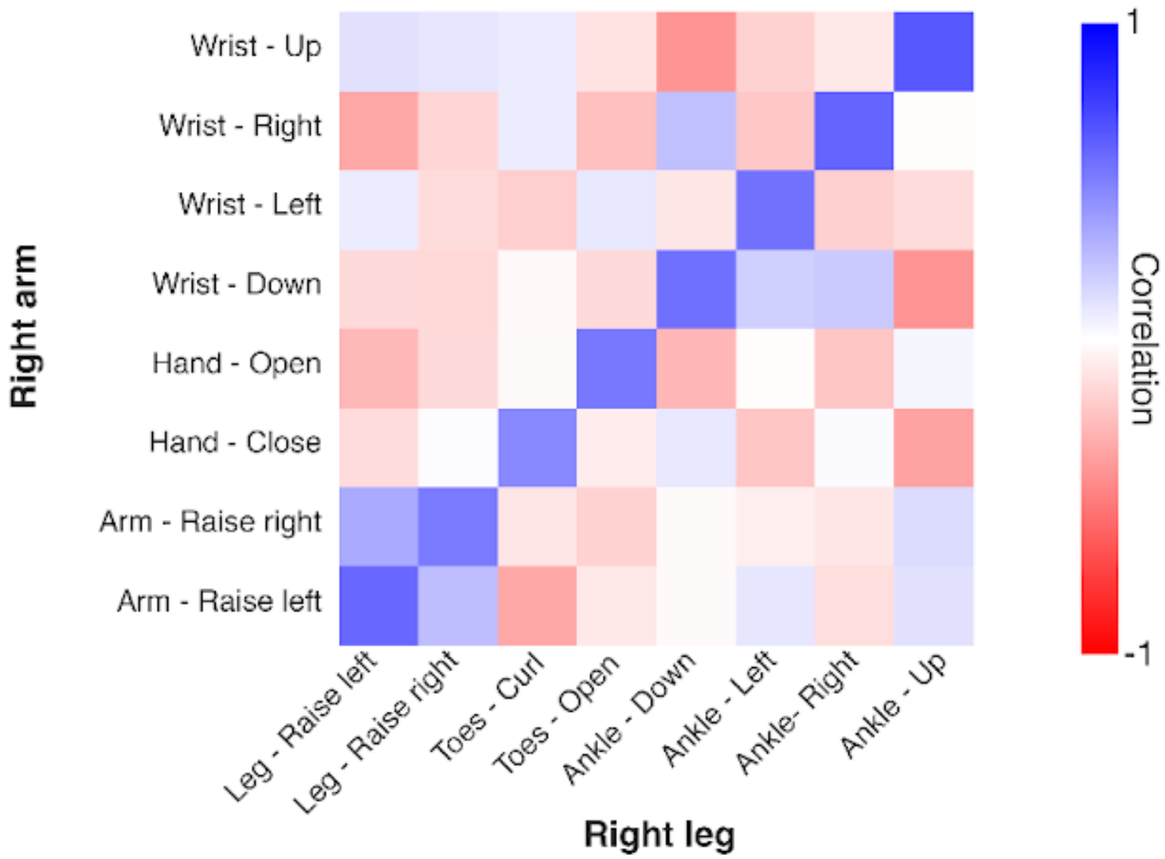
Motor representations in “hand” area



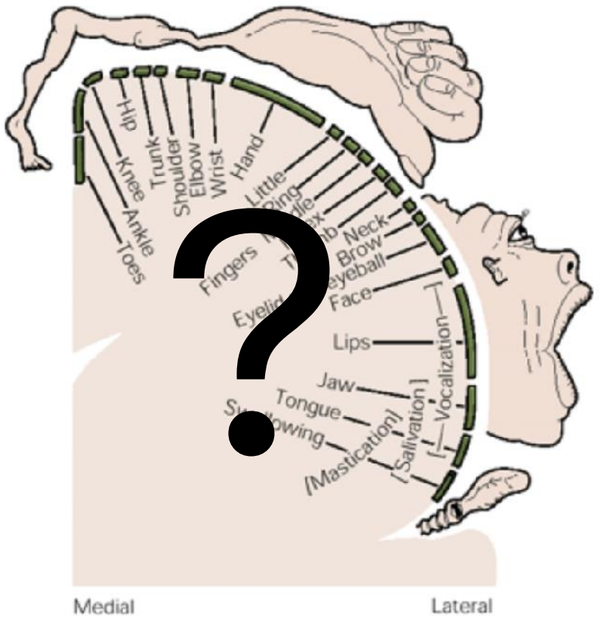


Willett FR*, Deo DR* et al. Hand Knob Area of Premotor Cortex Represents the Whole Body in a Compositional Way. *Cell*. 2020.

Shared Code for Limb Movement

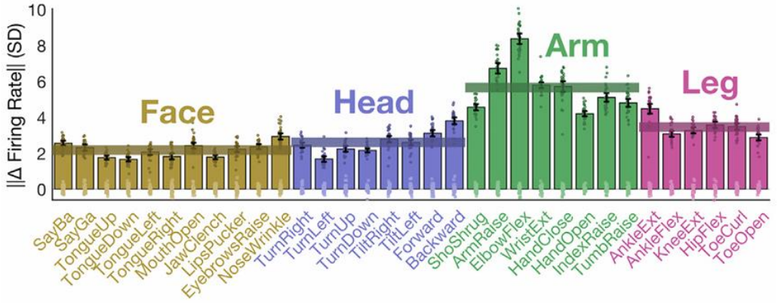


How homuncular is motor cortex?



Hand Knob Area of Premotor Cortex Represents the Whole Body in a Compositional Way

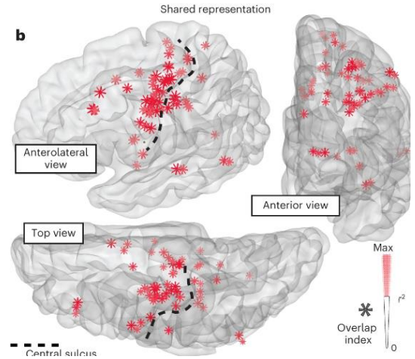
Francis R. Willett,[1,2,10,12,14,*] Darrel R. Deo,[1,2,3,12] Donald T. Avansino,[1] Paymon Rezaii,[1] Leigh R. Hochberg,[4,5] Jaimie M. Henderson,[1,11,13] and Krishna V. Shenoy[2,8,9,10,11,13]



A motor association area in the depths of the central sulcus

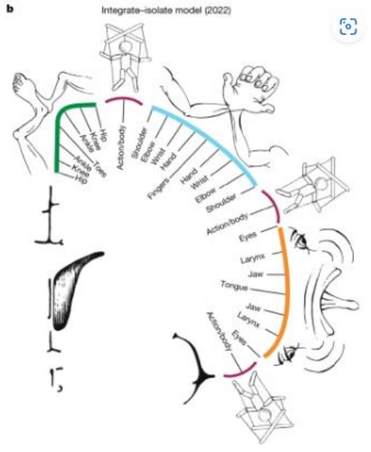
Michael A. Jensen, Harvey Huang, Gabriela Ojeda Valencia, Bryan T. Klassen, Max A. van den Boom, Timothy J. Kaufmann, Gerwin Schalk, Peter Brunner, Gregory A. Worrell, Dora Hermes & Kai J. Miller

Nature Neuroscience **26**, 1165–1169 (2023) | Cite this article

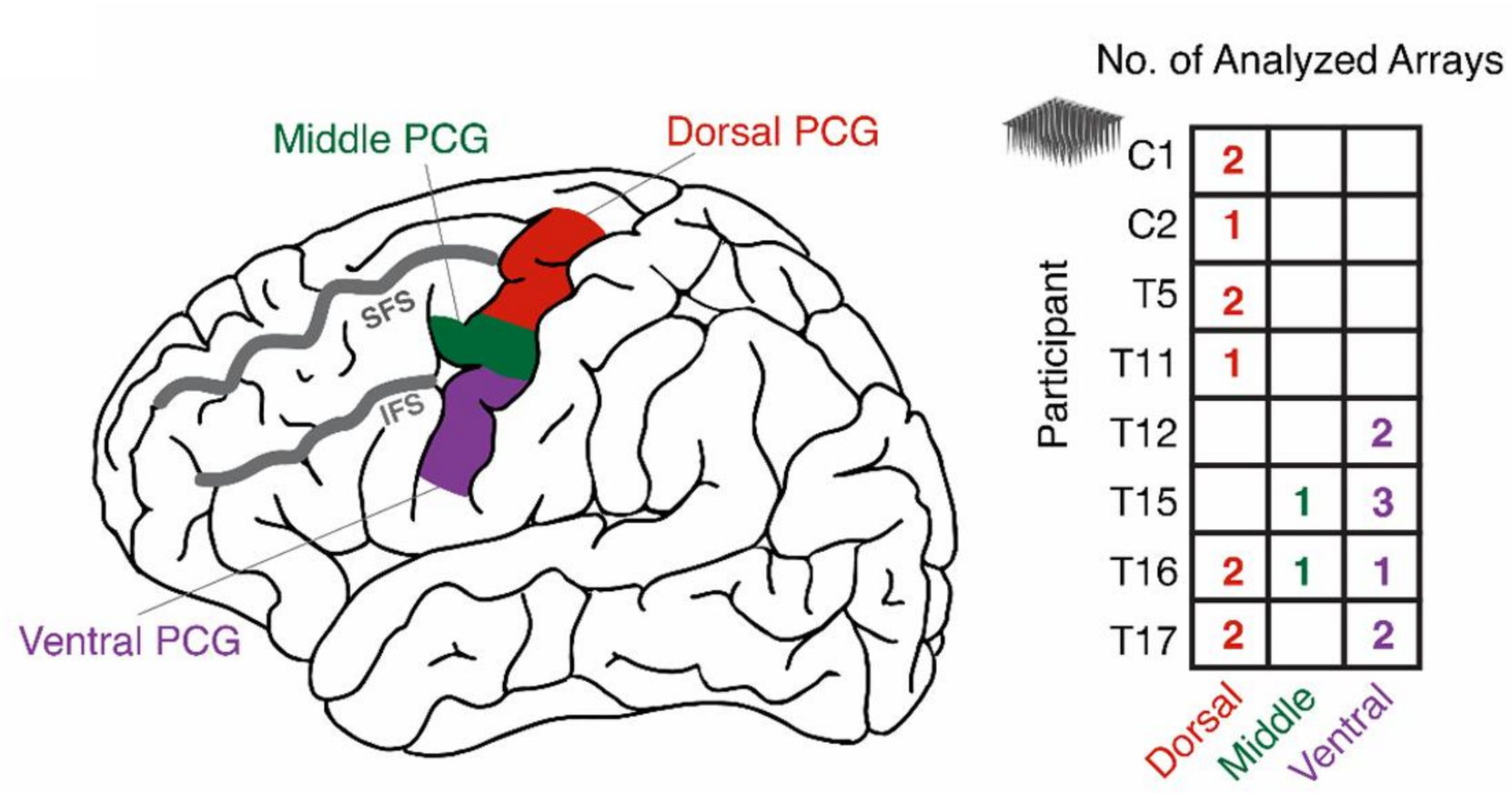


A somato-cognitive action network alternates with effector regions in motor cortex

Evan M. Gordon, Roselyne J. Chauvin, Andrew N. Van, Aishwarya Rajesh, Ashley Nielsen, Dillan J. Newbold, Charles J. Lynch, Nicole A. Seider, Samuel R. Krimmel, Kristen M. Scheidter, Julia Monk, Ryland L. Miller, Athanasia Metoki, David F. Montez, Annie Zheng, Immanuel Elbau, Thomas Madison, Tomoyuki Nishino, Michael J. Myers, Sydney Kaplan, Carolina Badke D'Andrea, Damion V. Demeter, Matthew Feigelis, Julian S. B. Ramirez, ... Nico U. F. Dosenbach + Show authors



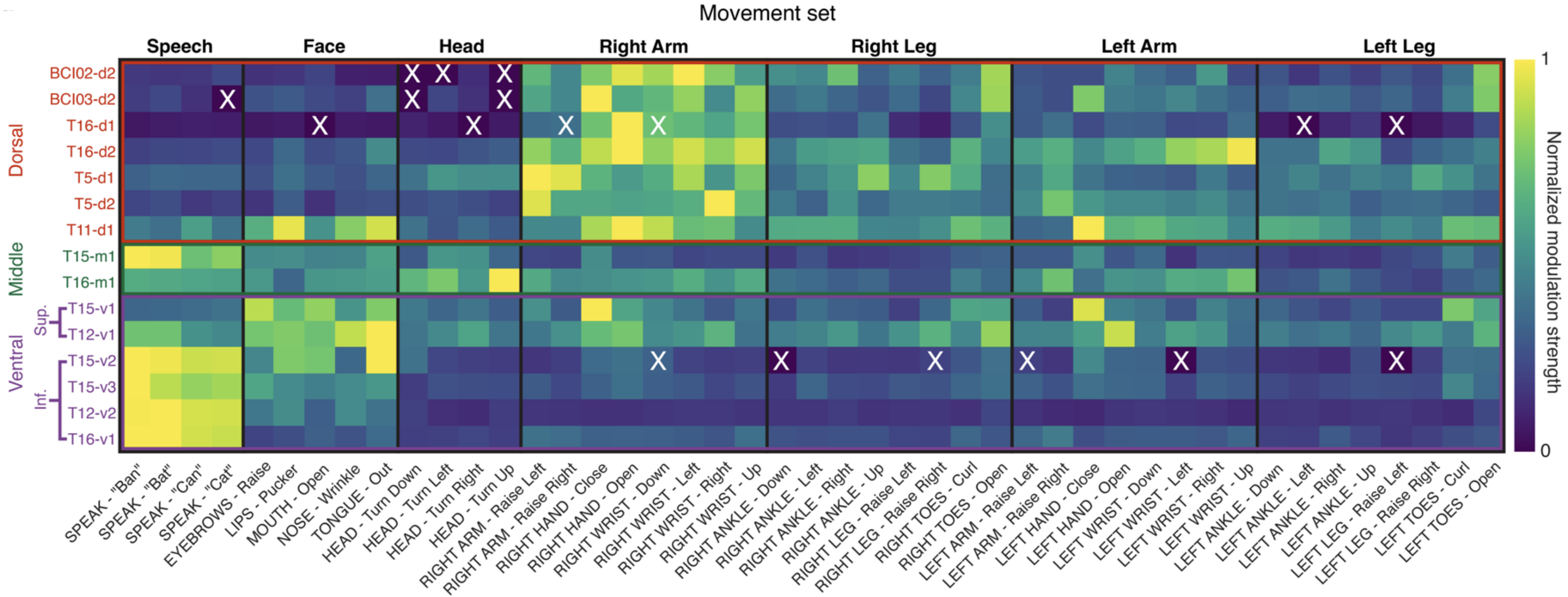
Goal: Build a Comprehensive Map of Motor Cortex at Single Neuron Resolution

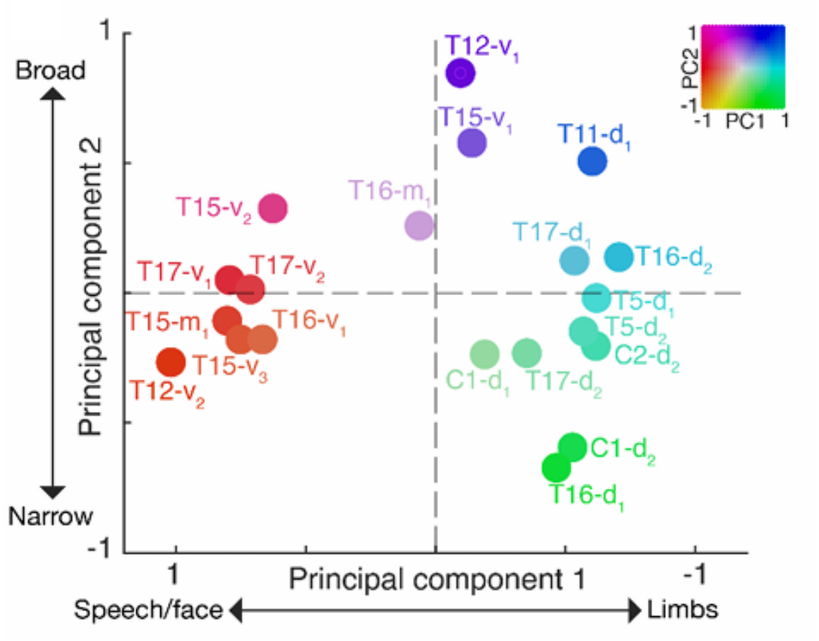


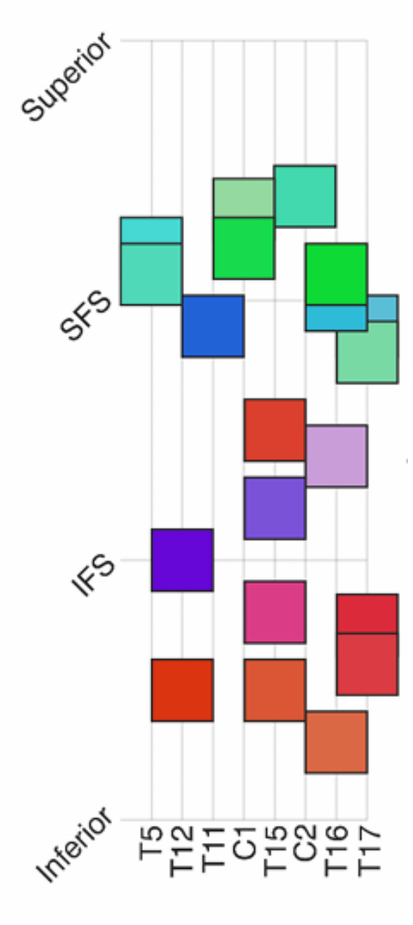
Deo DR, …, Henderson JM**, Willett FR**. A mosaic of whole-body representations in human motor cortex. *bioRxiv*. 2024.

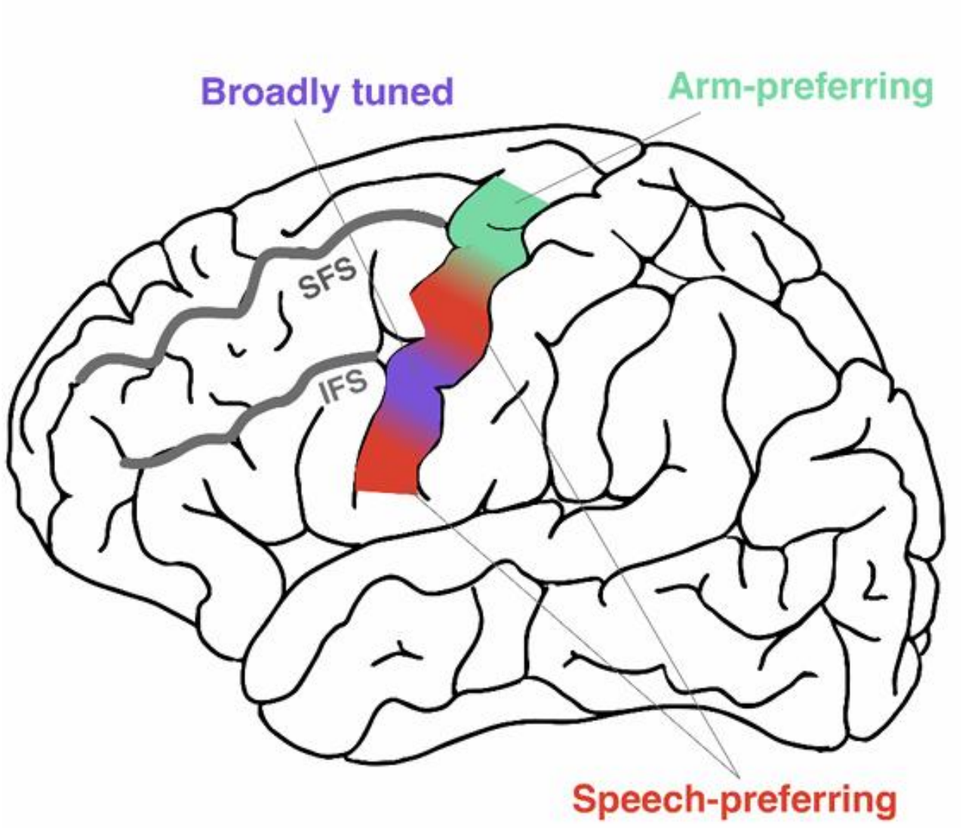
Darrel Deo

A New Map of Human Motor Cortex




Broad
Narrow
Principal component 2
1
-1
Principal component 1
Speech/face
Limbs
PC2
PC1
T12-v1
T15-v1
T11-d1
T16-m1
T15-v2
T17-d1
T16-d2
T17-v1
T17-v2
T5-d1
T15-m1
T16-v1
T5-d2
C2-d2
T15-v3
C1-d1
T17-d2
T12-v2
C1-d2
T16-d1


Superior
SFS
IFS
Inferior
T5
T12
T11
C1
T15
C2
T16
T17


Broadly tuned
Arm-preferring
SFS
IFS
Speech-preferring