Brain-computer interfaces

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Outline

- **Introduction**
- **(1) Learning by neural reassociation**
- **(2) Cortical control of virtual self-motion using task-specific subspaces**
- **(3) High-performance brain-to-text communication via handwriting**
- **Conclusion & Outlook**

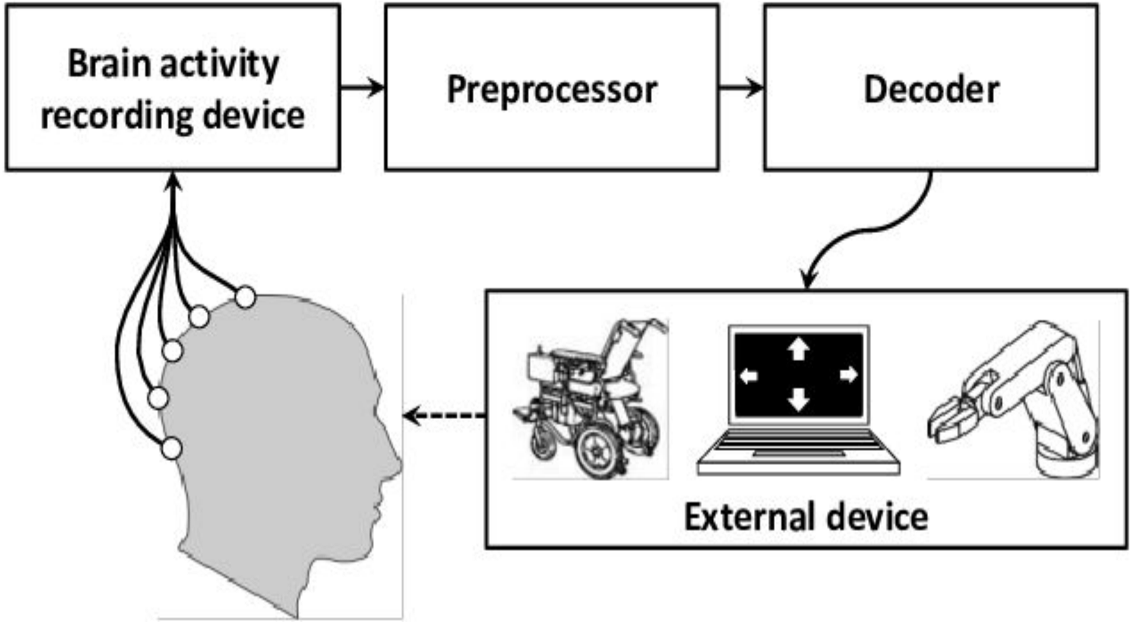
Brain-machine interfaces

Definition, communication channel between biological brain and a computer

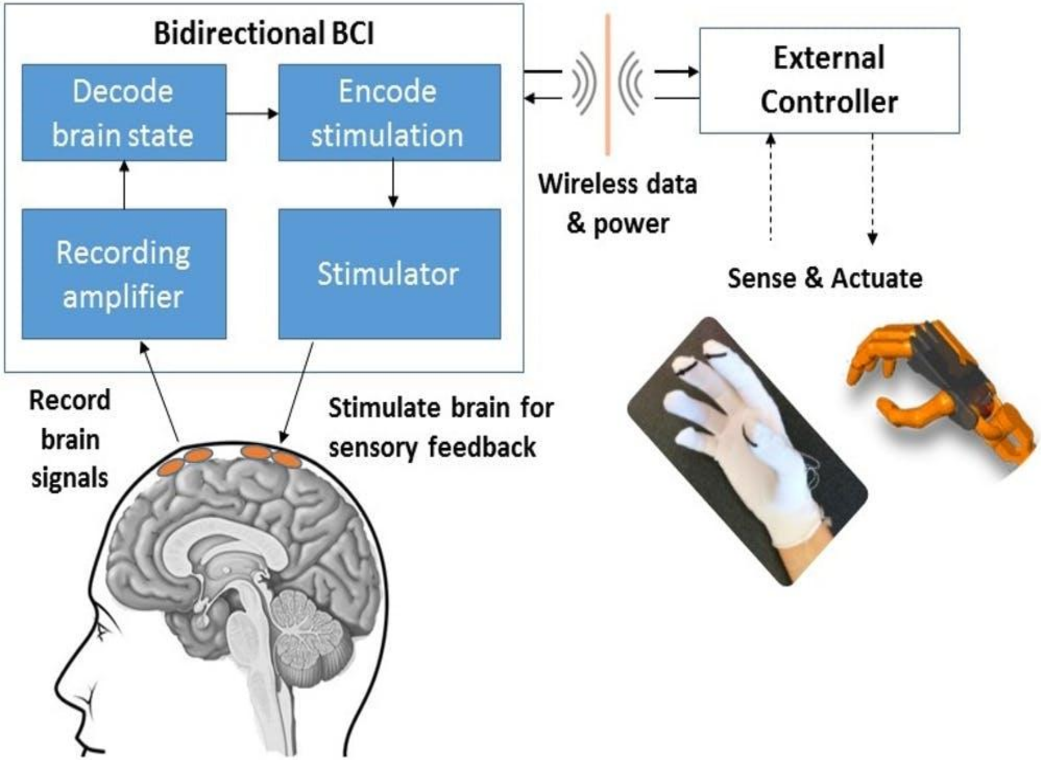
Also called BCI, neuroprosthetics refer to similar work applied to prostheses

Types:

- Invasive (microelectrodes)
  - Highest resolution, but potential scar tissue/electrode rejection
- Partially invasive (ECoG, neurointerventional (Stentrode))
  - Avoids signal distortion by skull, less medical complications
- Non-invasive (EEG, MEG, MRI)
  - Lower signal-to-noise ratio, but no surgery required



- Feedback into sensory organs



- Feedback directly back to neurons

Timeline

1790s: Evidence of electrical activity in nervous system from frog legs (Luigi Galvani)

1924: First recording of human brain activity via EEG (Hans Berger)

1928: Recording electrical discharges in nerve fibers using a Lippman electrometer (Edgar Adrian)

1952: Hodgkin-Huxley model, using recordings from giant squid axon

1959: Mapping of visual cortex with single neuron recordings in cats (Hubel and Wiesel)

1967: First record of multi-electrode arrays (Marg and Adams)

1978: Chronic micro-electrodes in monkey cortex, taught them to control neural firing rates (Schmidt et al.)

1992: Utah Intracortical Electrode Array

1998: Human patient controlled computer cursor through neurotrophic electrode recordings (Kennedy and Bakay)

2016: Neuralink founded to develop ultra-high bandwidth BMIs

2017: Neuropixels electrodes, going from tens to hundreds of neurons per probe

2021: Optical BCI driven by dendritic calcium signals in monkey motor cortex (Trautmann et al)

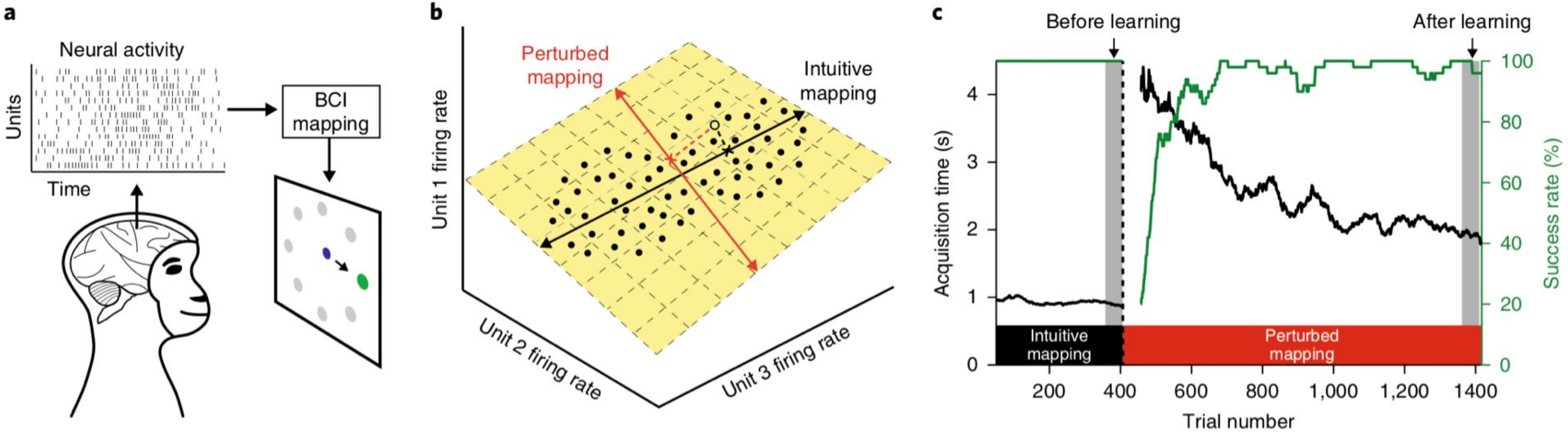
Learning by neural reassociation

Golub, M.D., Sadtler, P.T., Oby, E.R. et al., *Nature Neuroscience* (2018)

Overview

- Monkeys are trained to move a cursor on a screen using neural activity
- They learn to perform the task using a first BCI mapping which is then changed
- This allows to study **how neural activity changes during learning**
- Different hypotheses are compared, and it is found that the neural patterns **reassociate to adapt to the new mapping**

Task

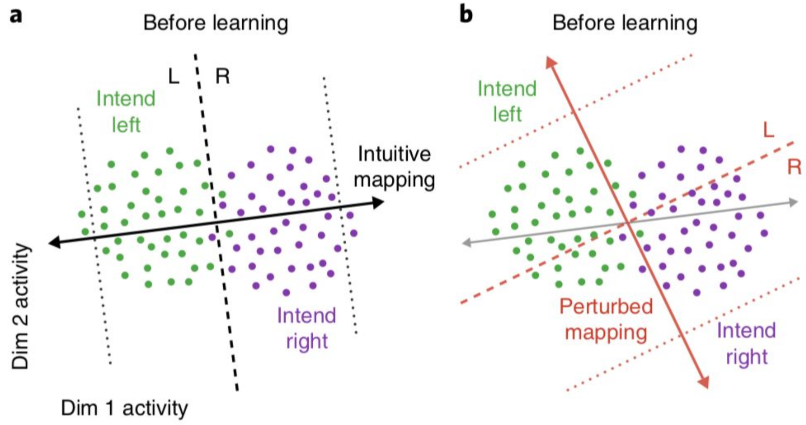


- Decoding activity from M1 as $\mathbf{v}_t = \mathbf{A}\mathbf{v}_{t-1} + \mathbf{B}\mathbf{z}_t + \mathbf{c}$

Cursor velocity

10D factors summarizing neural activity

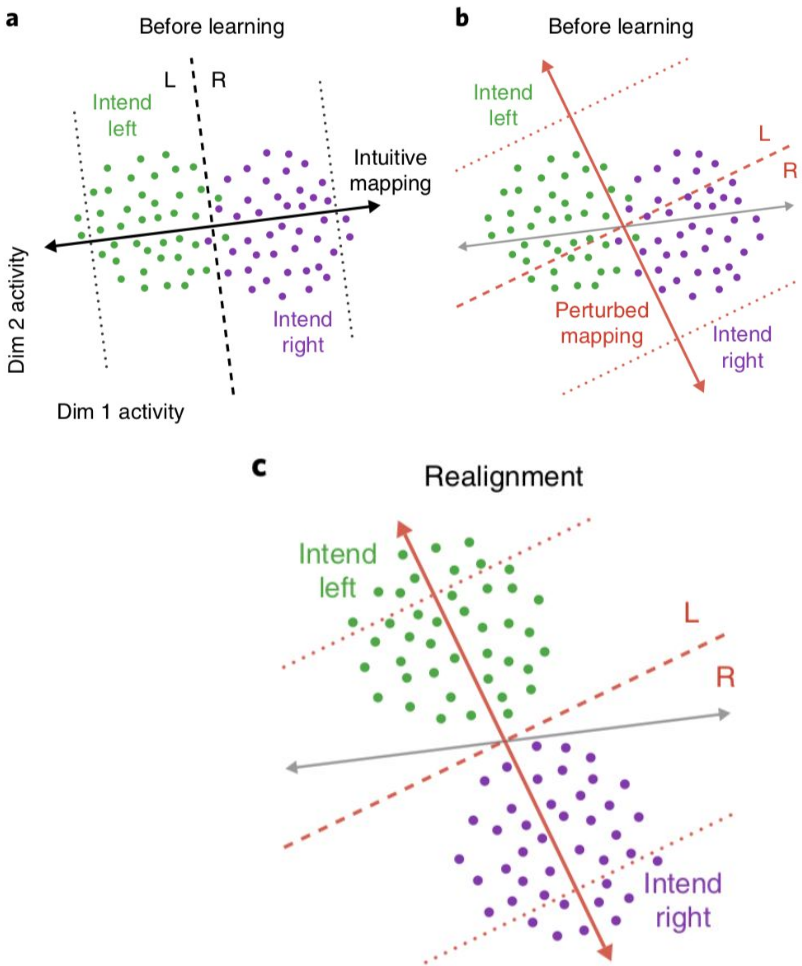
What happens during learning?



What happens during learning?

Three hypotheses :

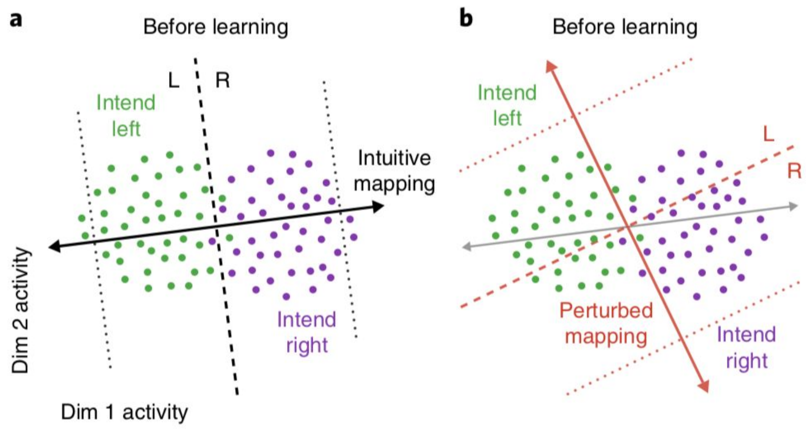
1. Realignement of the activity to the new mapping

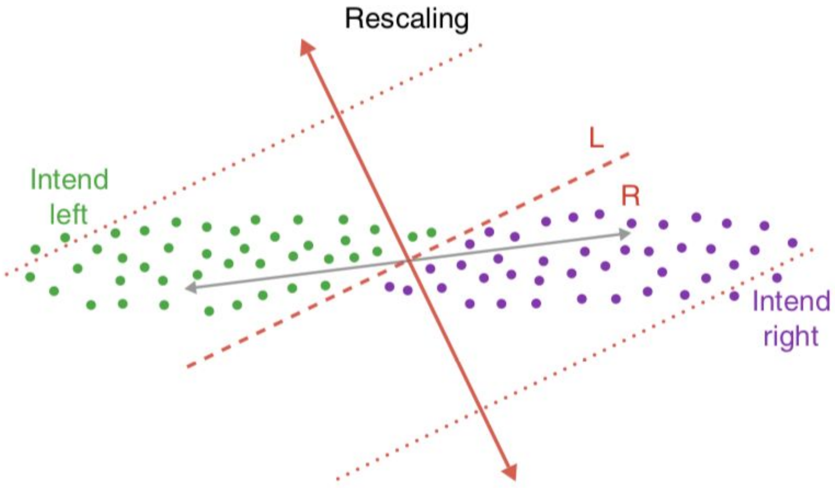


What happens during learning?

Three hypotheses :

1. Realignement of the activity to the new mapping
2. Rescaling of the activity

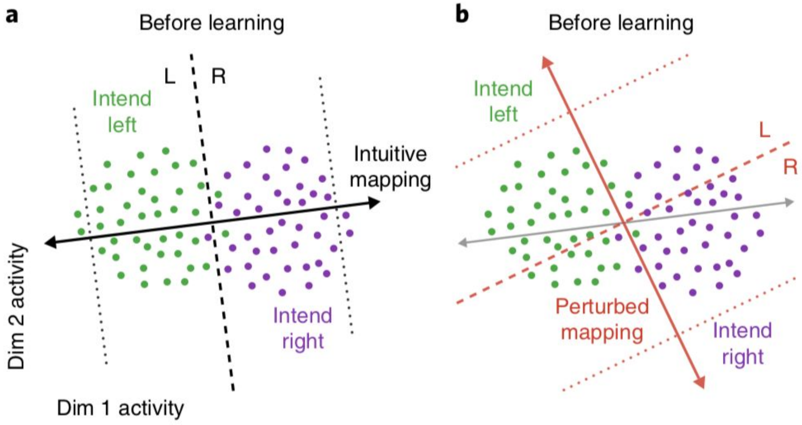


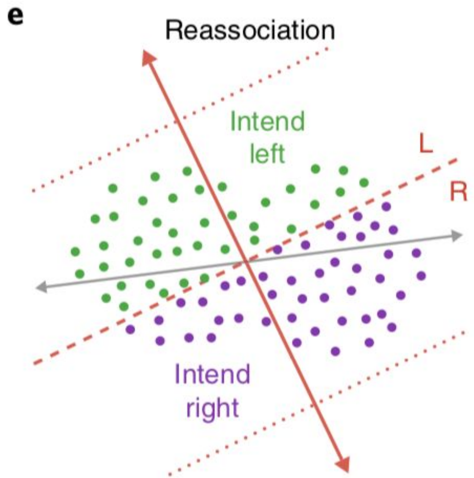


What happens during learning?

Three hypotheses :

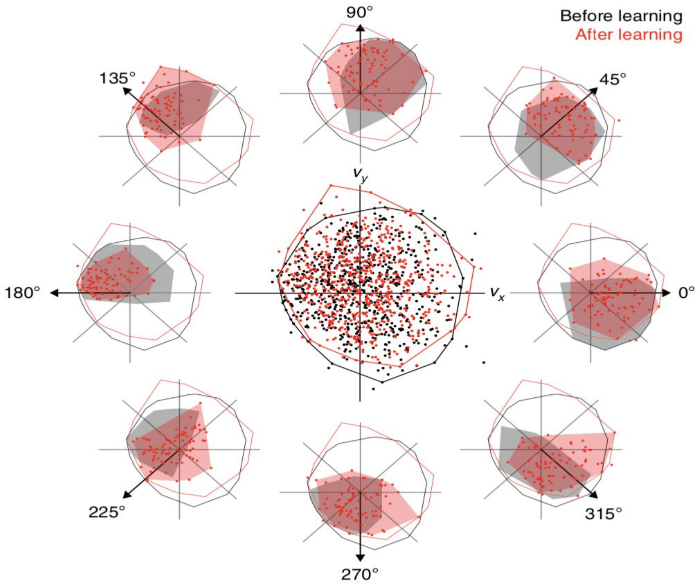
1. Realignement of the activity to the new mapping
2. Rescaling of the activity
3. Reassociation within the initial manifold





What happens in the data?

- The observed activity patterns stay within the same repertoire



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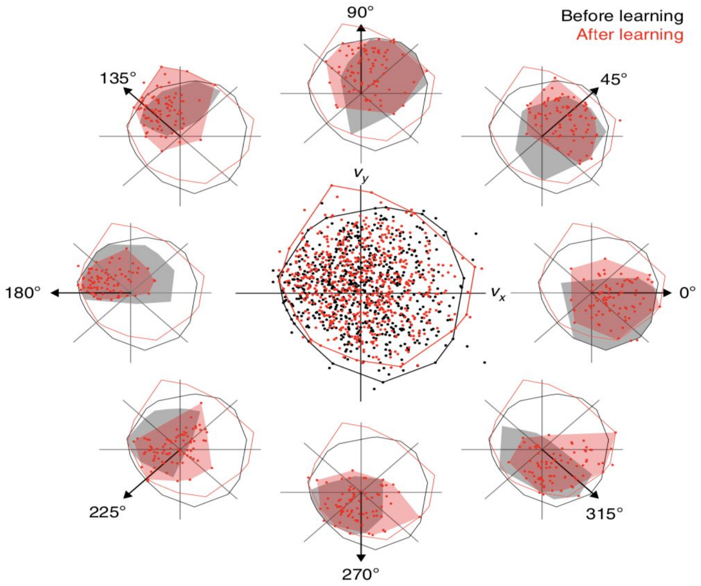
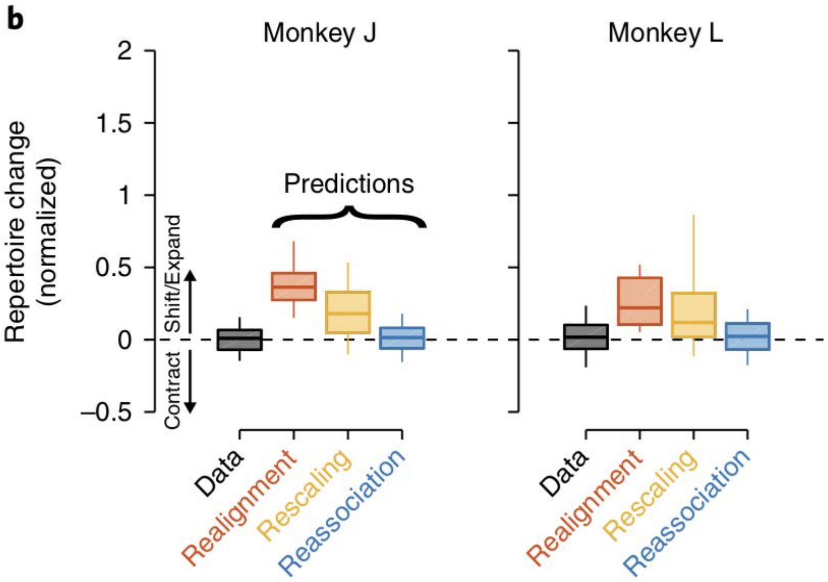
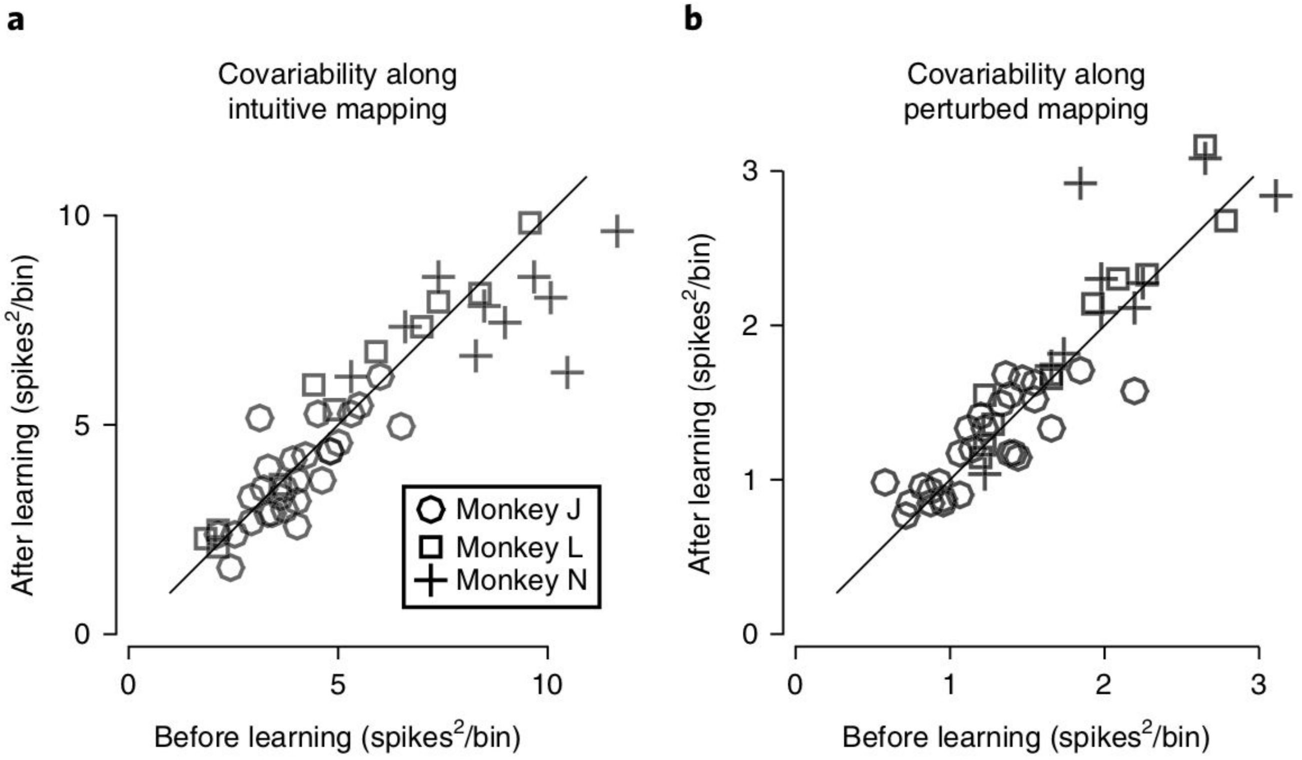


- This is most consistent with reassociation



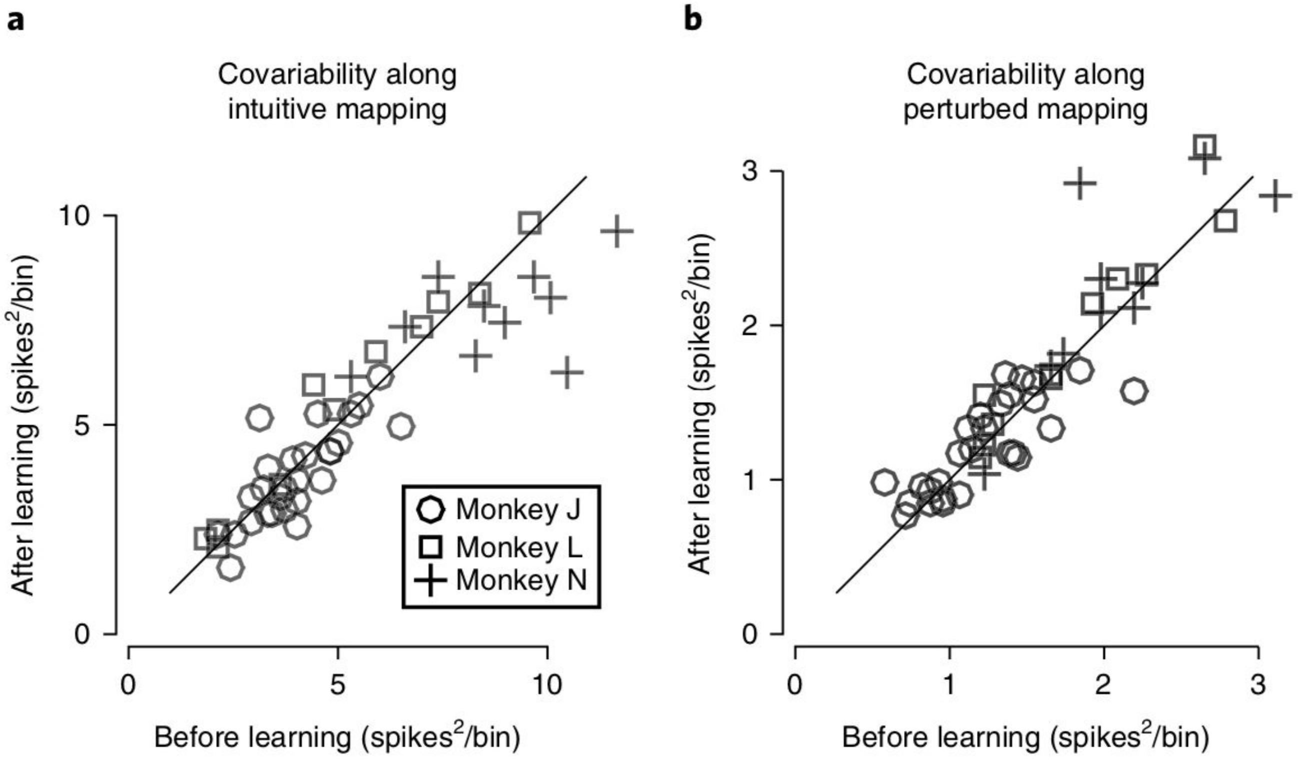
What happens in the data?

- The patterns don't vary much along either axis

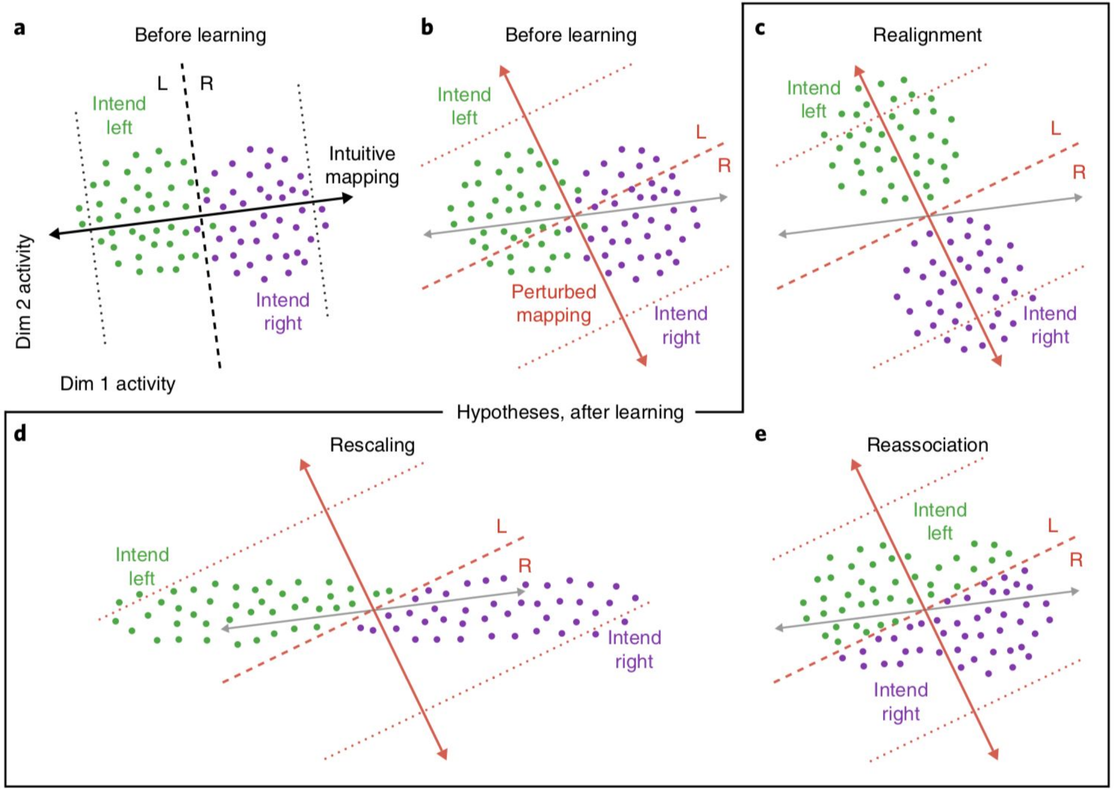


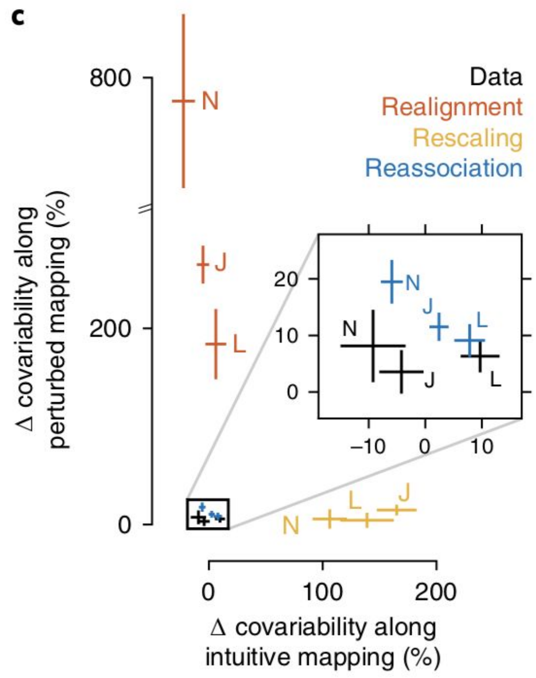
What happens in the data?

- The patterns don't vary much along either mapping
- This is also consistent with reassociation



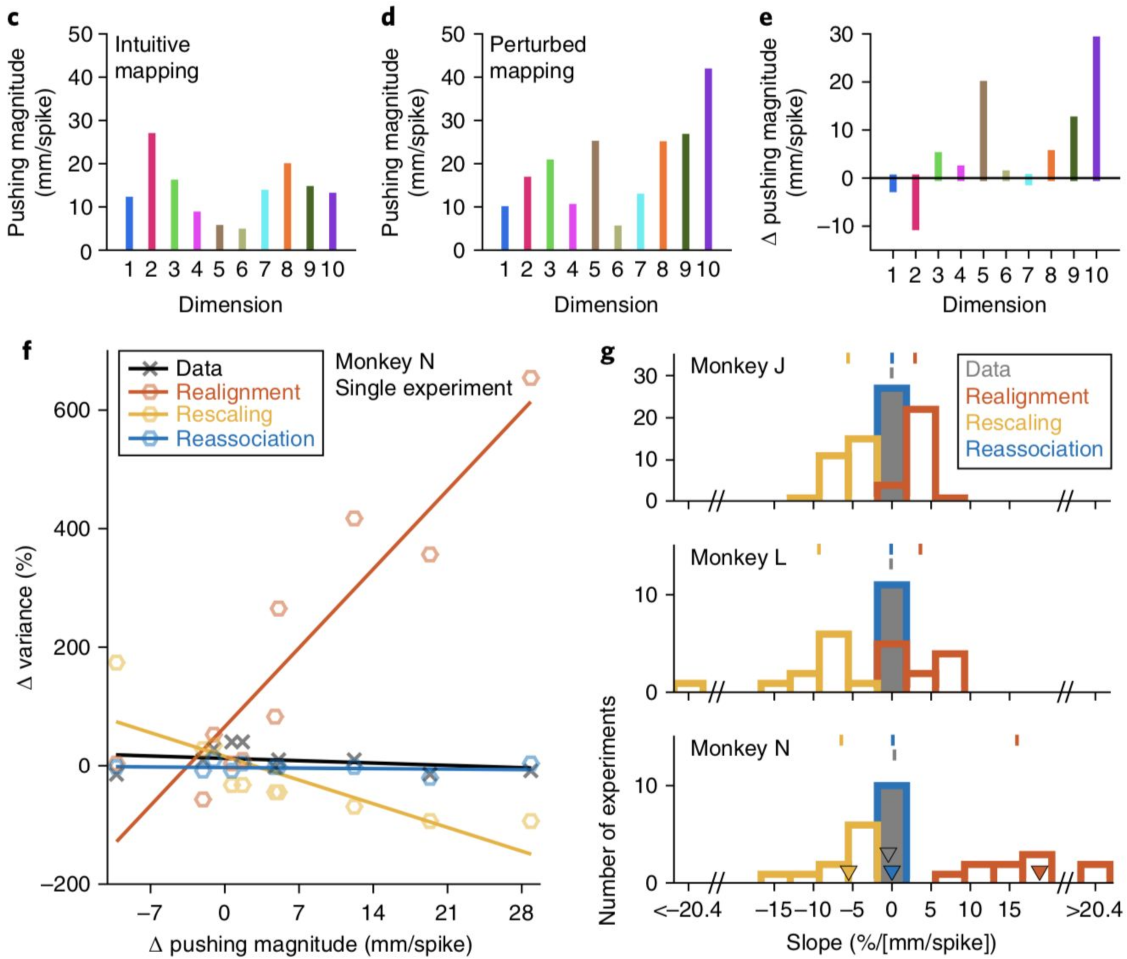
What happens in the data?





What happens in the data?

- Little change in the variance along the different neural dimensions
- Again consistent with reassociation



Summary

- A BCI setup was used to to study **changes in neural activity patterns during learning**
- Appears to be a constraint on learning that **patterns need to stay within a given repertoire**
- Using a BCI allows for tight control of the mapping from neural activity to behaviour, and testing of the changes in neural activity along the axes of the before and after-learning mappings
- Using a BCI allows more information to be gained than purely behavioural perturbation studies

Cortical control of virtual self-motion using task-specific subspaces

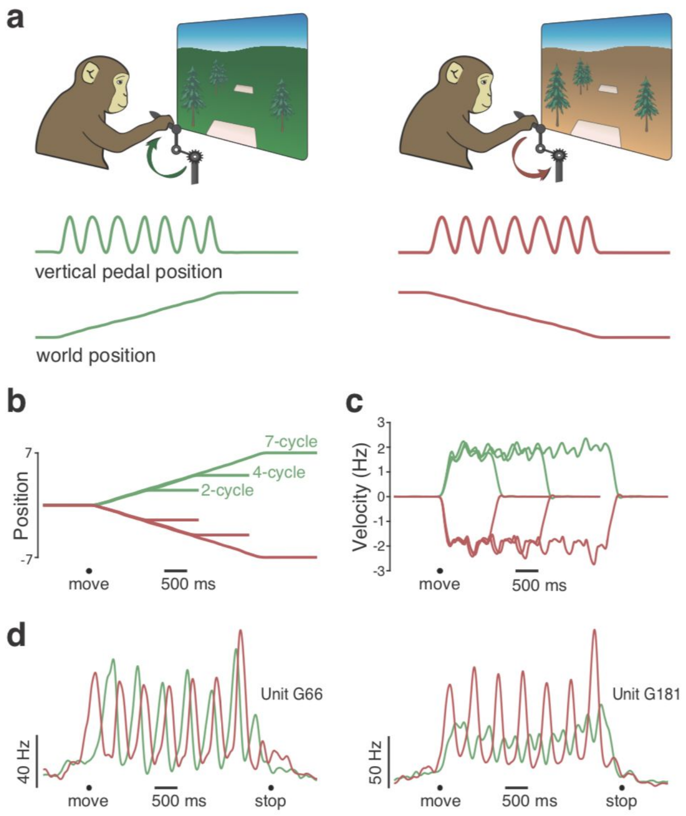
Schroeder, K.E., Perkins, S.M., Wang, Q., Churchland, M.M., *bioRxiv* (2020)

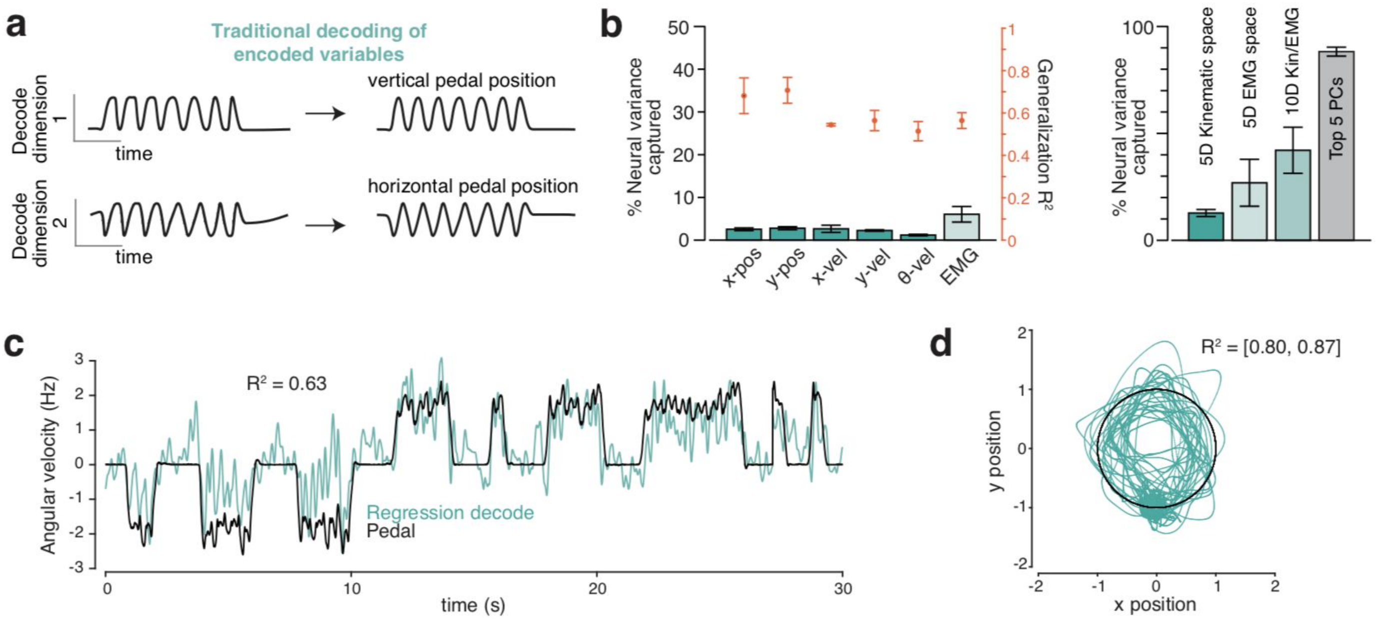
Overview

- Most BCI tasks in non-human primates decode **reaching behaviour** from the motor cortex
- Strong linear correlations between **high variance neural dimensions** and **reaching kinematics** underlies success of linear decoders
- But for **non-reaching behaviour**, are these linear correlations still present?
- Investigate moving along a virtual track in a **hand-held pedal cycling** task for in monkeys
- **Low variance dimensions** correlated with kinematics
- There exist high variance dimensions with reliable **non-linear relationships** to intended self-motion, allowing high accuracy and low latency decoding

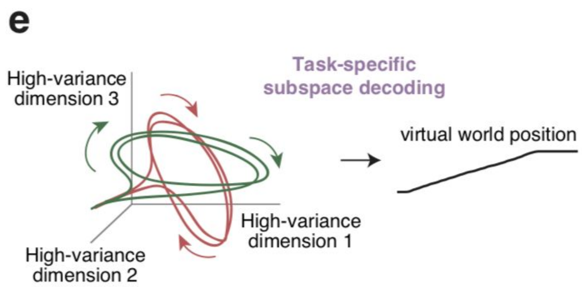
Task

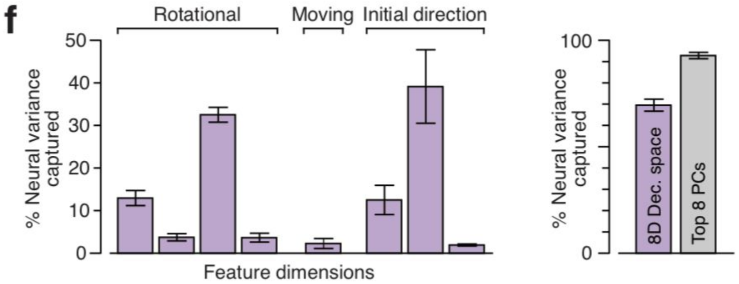
- 2 monkeys cycling with hand-pedals in virtual corridor environment (1D motion)
- Green and desert environments for cycling forward and backward to move
- Task is to reach target and remain on there for some time to receive juice reward
- Manual and BMI control modes
- Right arm free to move in both, left arm fixed
- Additional task of arm cycling speed tracking



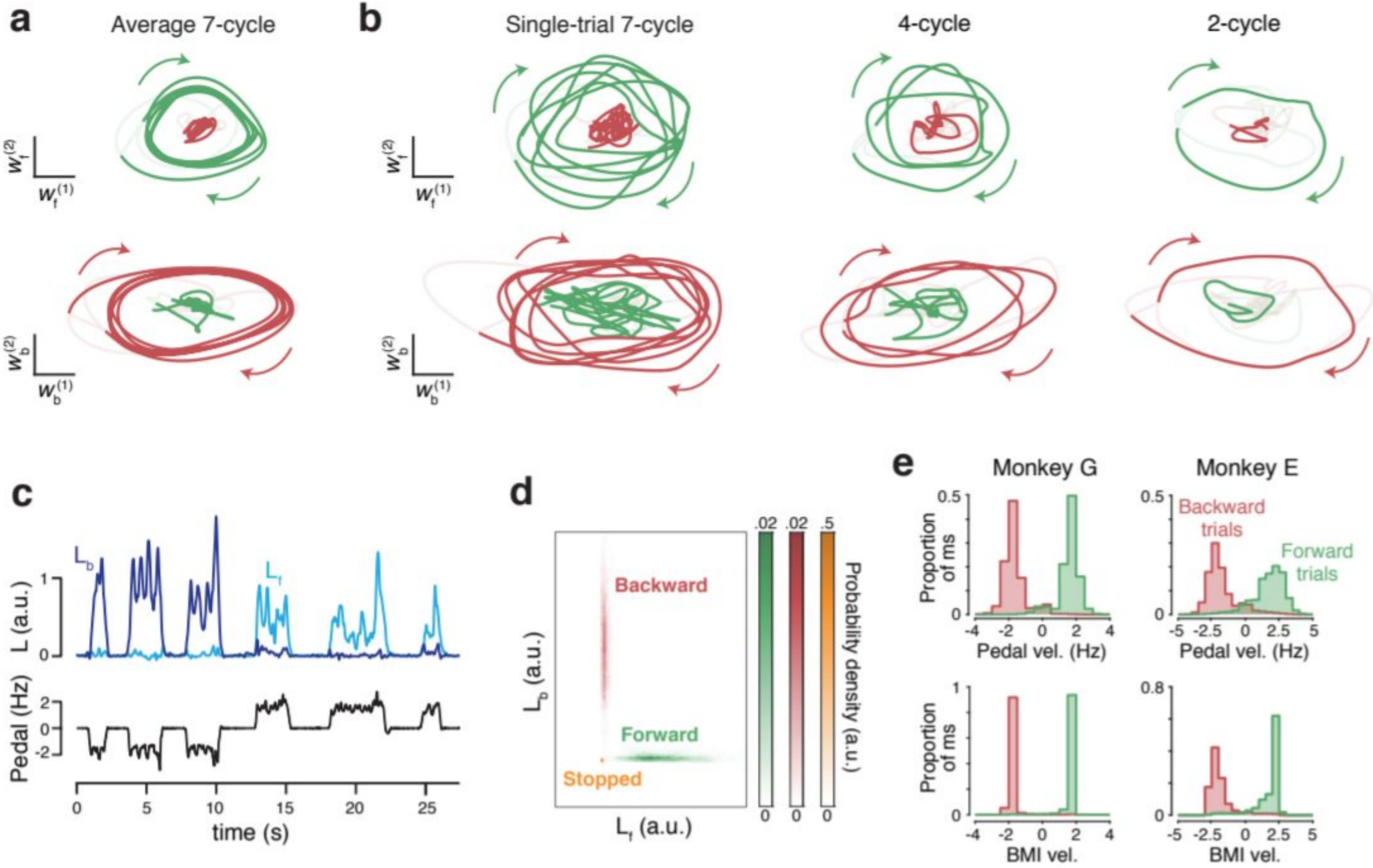


- Dimensions correlated with kinematics capture low percentages of neural variance
- Dimensions correlated with angular velocity (self-motion) exist but are low variance, and suffer from trial-to-trial variability noise

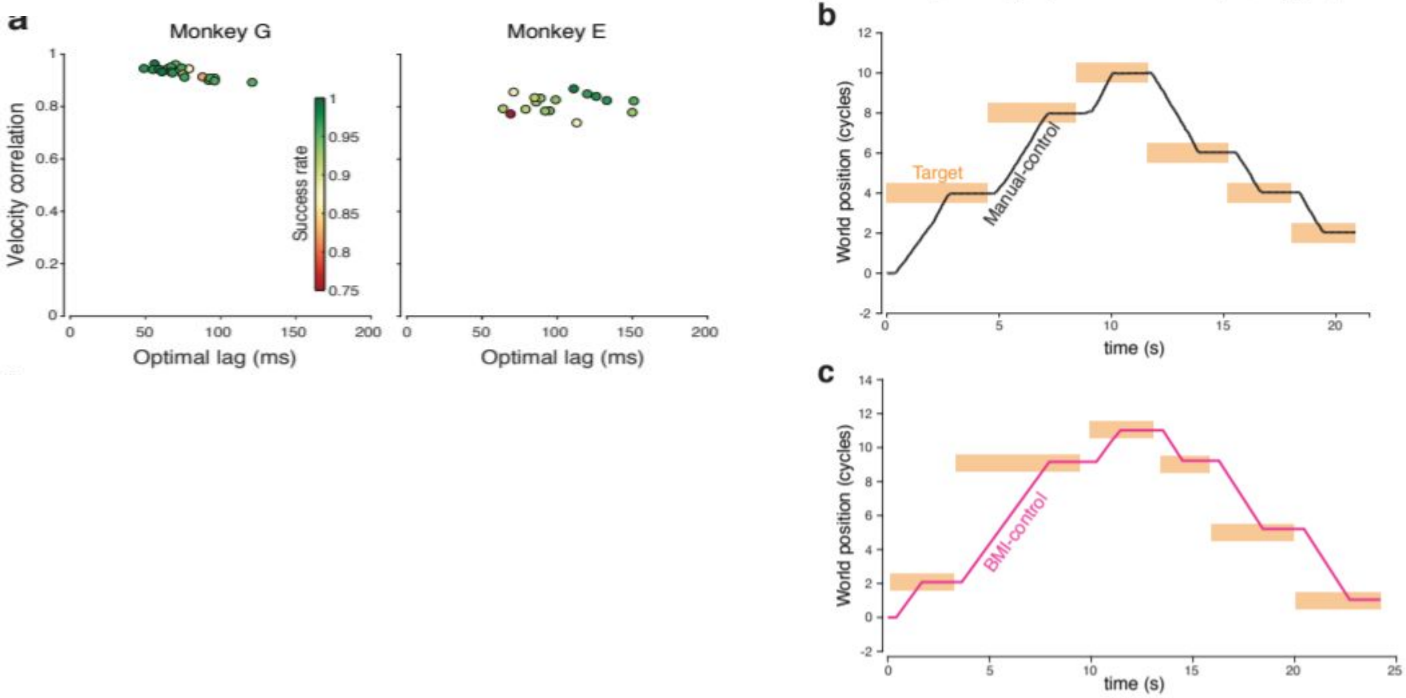


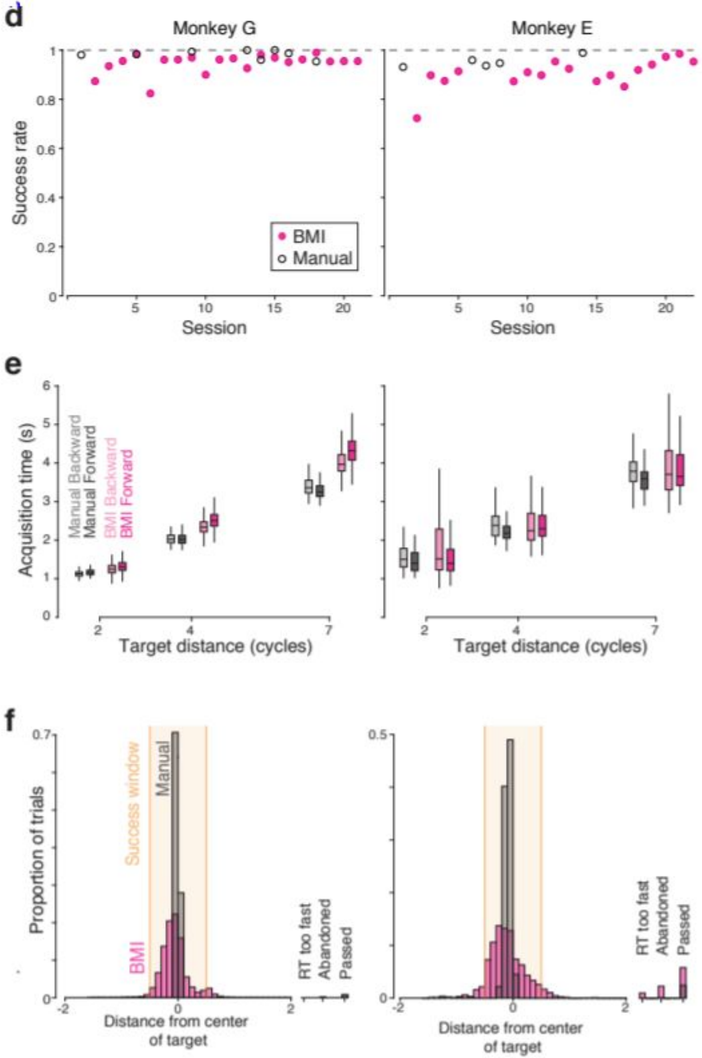


- Task-specific subspaces to obtain isolated features
  - Motion-sensitive direction (linear discriminant analysis, normal vector to separation plane)
  - 4 dimensional rotation space of forward + backward rotation planes (2D subspaces with max difference in variance captured for forward and backward cycling)
  - Maximally different initial neural responses (top 3 PCs of 200 ms segments after movement onset)
  - Note these dimensions (8 in total) are not all orthogonal!
- Kalman filter to obtain smoothed estimate of neural state in rotational planes
- Infer probability of moving using motion-sensitive direction projection and a HMM



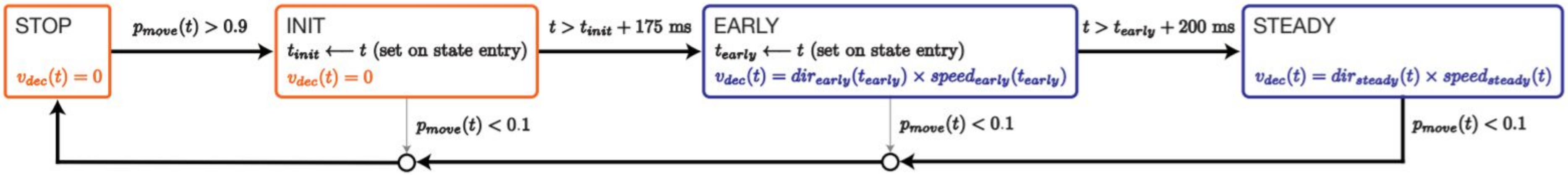
a
Average 7-cycle
b
Single-trial 7-cycle
4-cycle
2-cycle
$w_f^{(2)}$
$w_f^{(1)}$
$w_b^{(2)}$
$w_b^{(1)}$
c
L_b
L_f
L (a.u.)
Pedal (Hz)
time (s)
d
Backward
Forward
Stopped
L_b (a.u.)
L_f (a.u.)
Probability density (a.u.)
e
Monkey G
Monkey E
Proportion of ms
Backward trials
Forward trials
Pedal vel. (Hz)
BMI vel.


a
Monkey G
Monkey E
Velocity correlation
Optimal lag (ms)
Success rate
b
Target
Manual-control
World position (cycles)
time (s)
c
BMI-control
World position (cycles)
time (s)

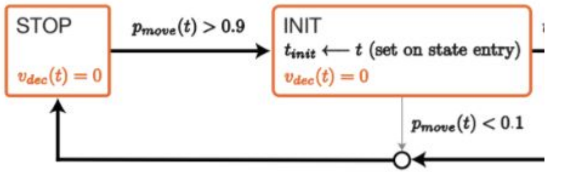

d
Monkey G
Monkey E
Success rate
BMI
Manual
Session
e
Acquisition time (s)
Manual Backward
Manual Forward
BMI Backward
BMI Forward
Target distance (cycles)
f
Proportion of trials
Success window
Manual
BMI
RT too fast
Abandoned
Passed
Distance from center of target

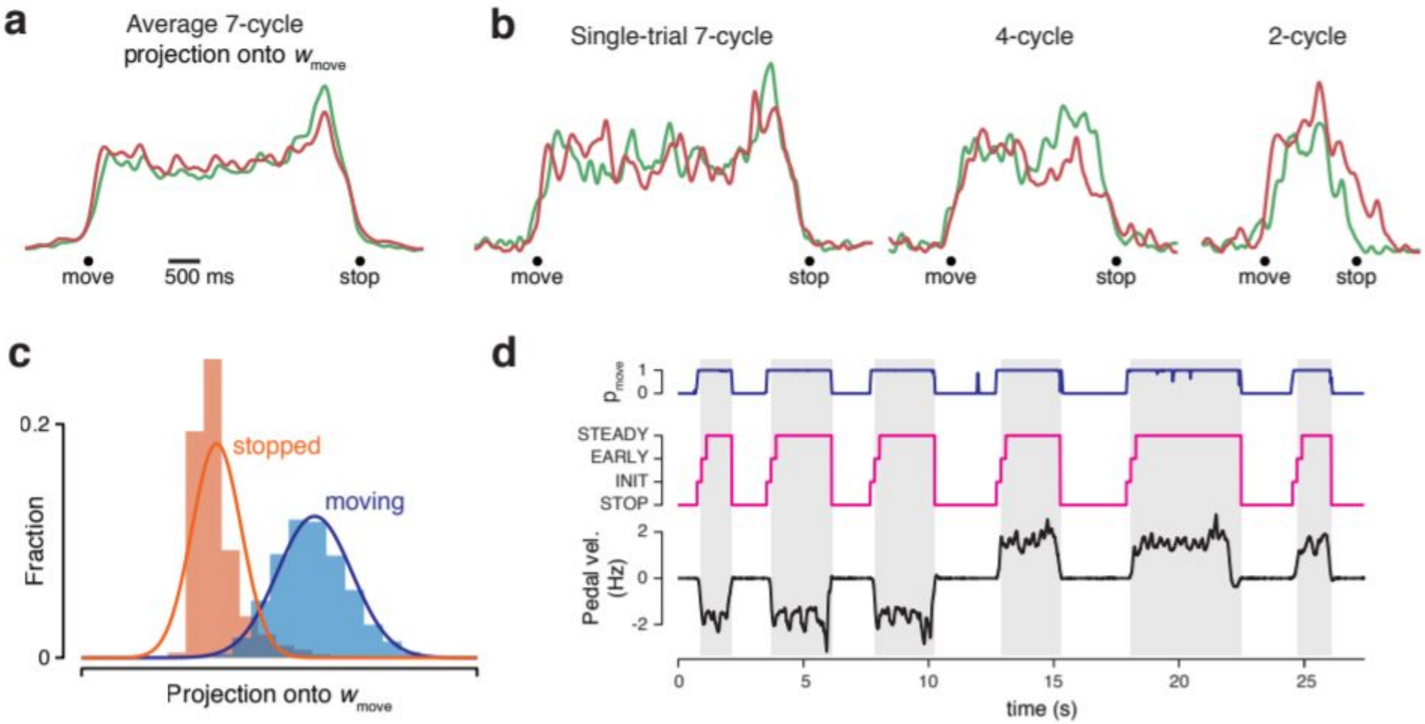
A state-dependent decoder for BCI control

- At each point, the decoder yields an estimate of the decoded velocity
- **Orange states : no motion** | **Blue states : motion**
- The decoding of self-motion occurs in STEADY state : other states help get a more robust performance
- State transitions are governed by the estimated probability of motion, **p**mov
- The use of explicit STOP + INIT states helps avoid false starts

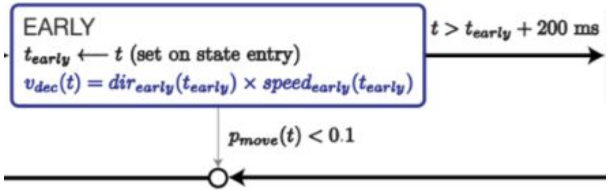


A conservative estimate of motion onset

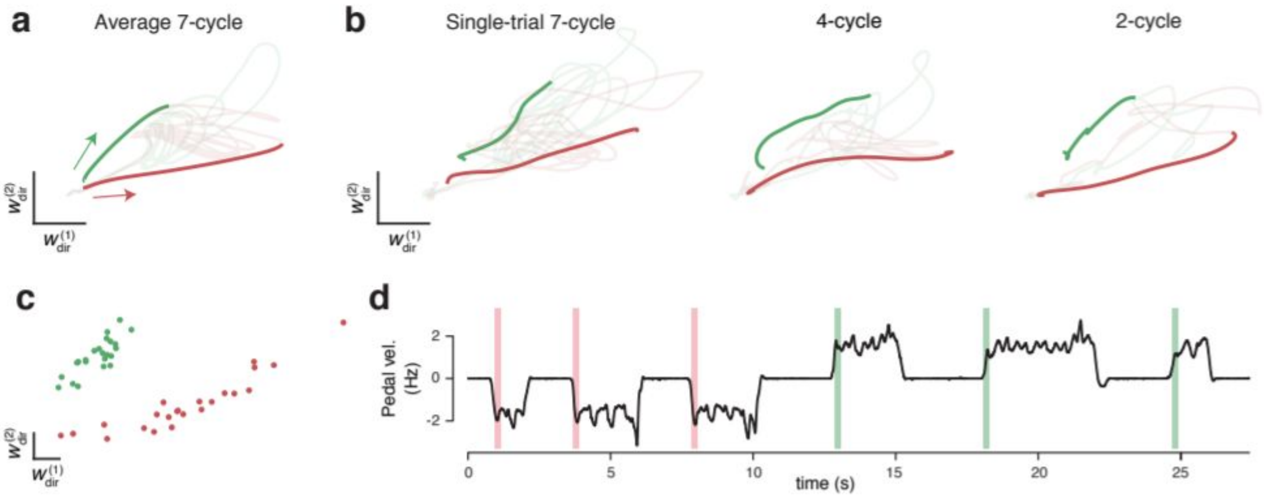




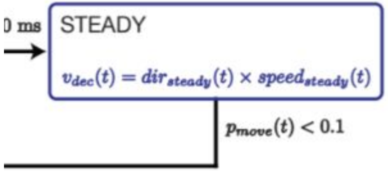
EARLY state : decoding of the initial position



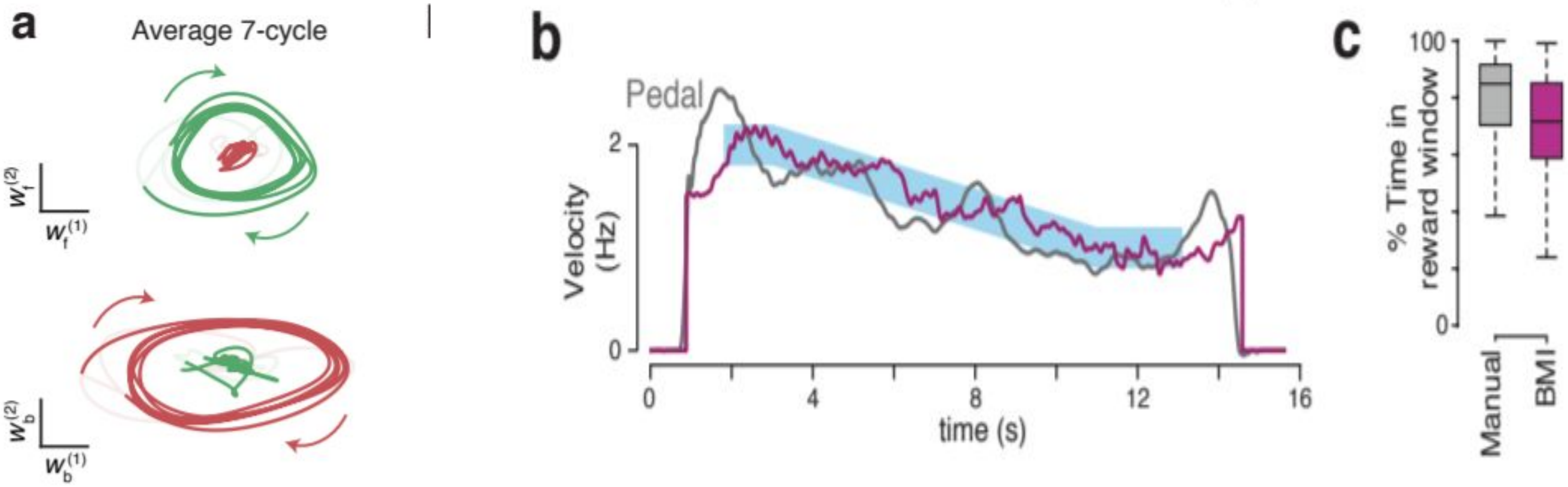
- Right after movement onset, direction cannot yet be decoded from the forward/backward-cycling subspaces



STEADY state : decoding of movement speed

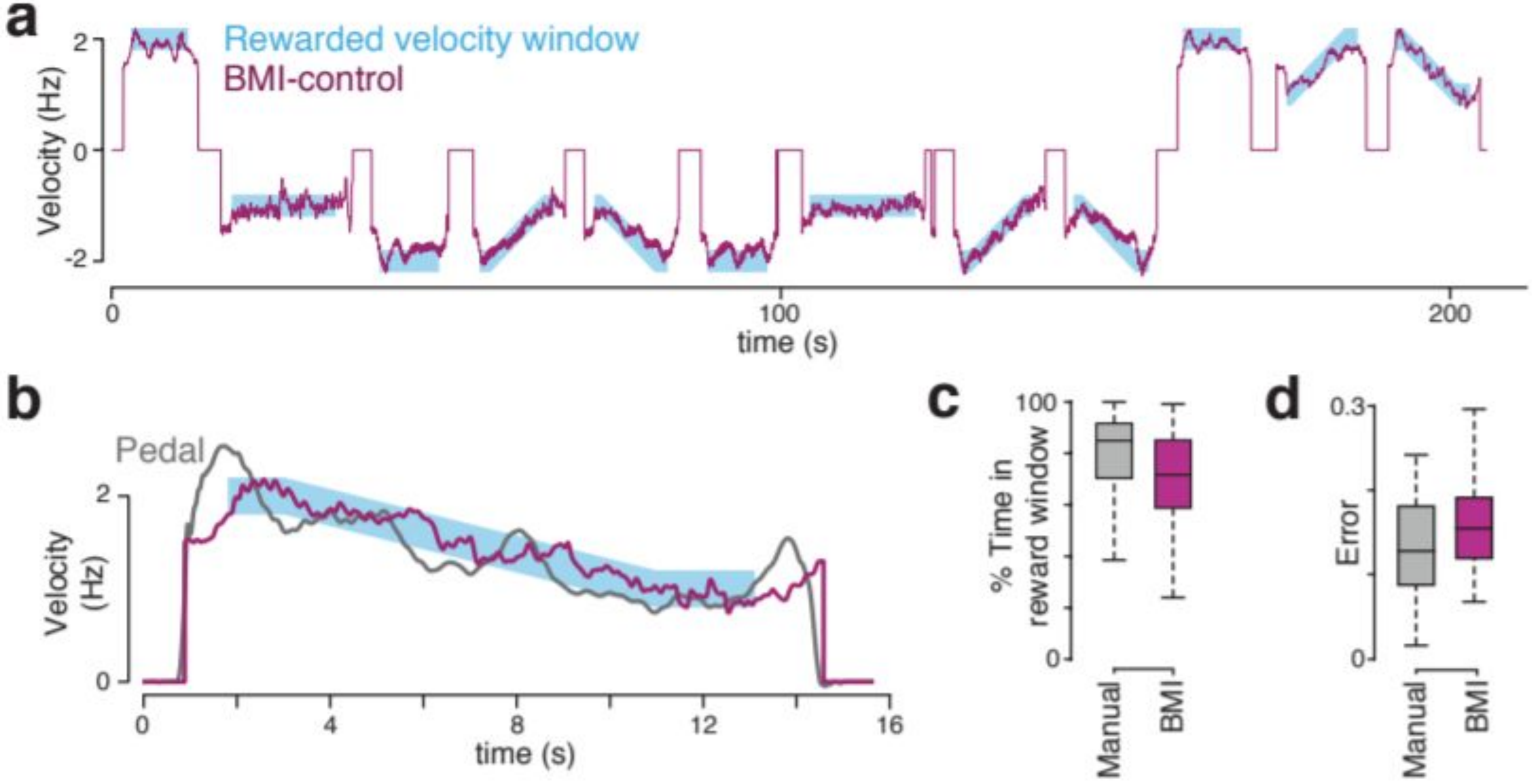


- Use of the 4D rotational subspace
- Made easier by ~constant speed during task
- Extension to a task where monkeys need to adjust the cycling speed



Summary

- New BCI task with monkeys : decoding of angular self-motion rather than reach direction
- This requires more elaborate decoders : suggests that reaching movements are much more correlated to neural activity that most movements
- Neural covariance structure generally changes across tasks, meaning traditional motor cortex decoders only reliably for a restricted set of behaviours
- Despite absence of correlations with kinematics, (non-linear) task-specific relationships exist in motor cortex allowing accurate decoding
- Discussion points :
  - ➢ moving away from the typical reaching paradigm
  - ➢ non-linear decoders yield better performance, but can’t be generalized to other tasks


a
Rewarded velocity window
BMI-control
Velocity (Hz)
2
0
-2
0
100
200
time (s)
b
Pedal
Velocity (Hz)
2
0
0
4
8
12
16
time (s)
c
% Time in reward window
100
0
Manual
BMI
d
Error
0.3
0
Manual
BMI

High-performance brain-to-text communication via handwriting

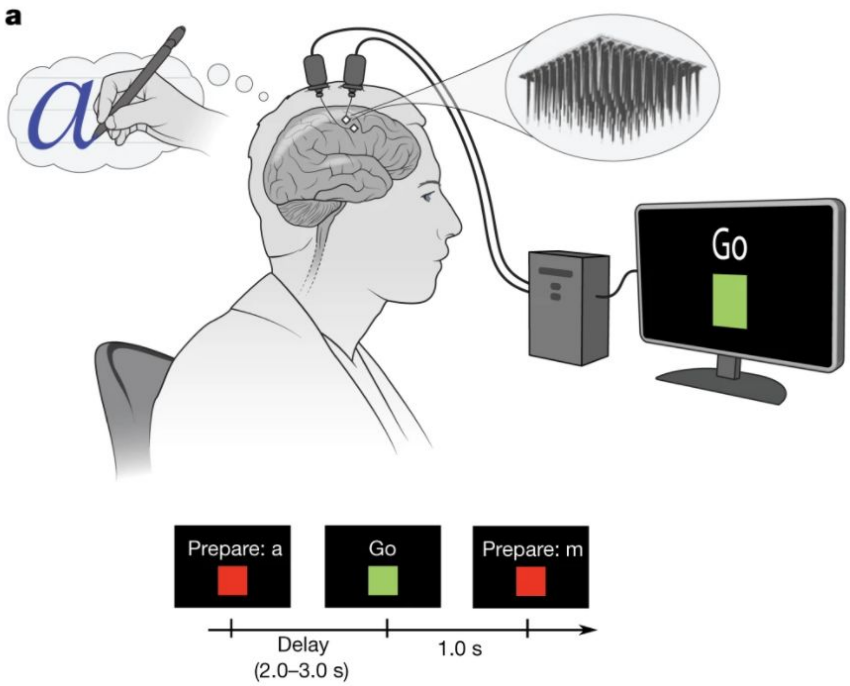
Willett, F.R., Avansino, D.T., Hochberg, L.R. et al., *Nature* (2021)

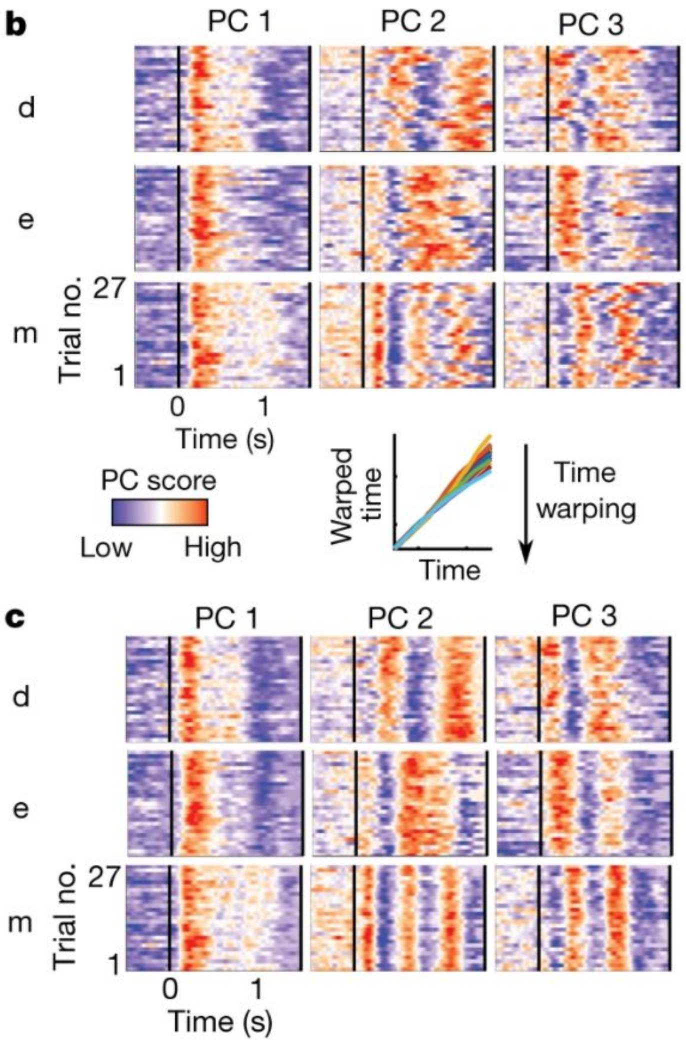
Overview

- Major focus of BCI research on **restoring gross motor skills** (reaching, grasping, point-and-click cursor)
- **Rapid dexterous behaviours** might enable faster rates of communication (handwriting, touch typing)
- Gross skills remain encoded in mortex cortex after paralysis, what about more complex skills?
- This works presents an **intracortical BCI** that **decodes attempted handwriting movements** from neural activity in the motor cortex
- Translates to text in real time using **recurrent neural network decoding**
- Sets new state-of-the-art typing accuracy and speeds (90 characters per minute, 94.1% accuracy online, >99% accuracy offline with autocorrect)
- Neural representations of temporally complex movements may generally be easier to decode and more noise robust than point-to-point movements

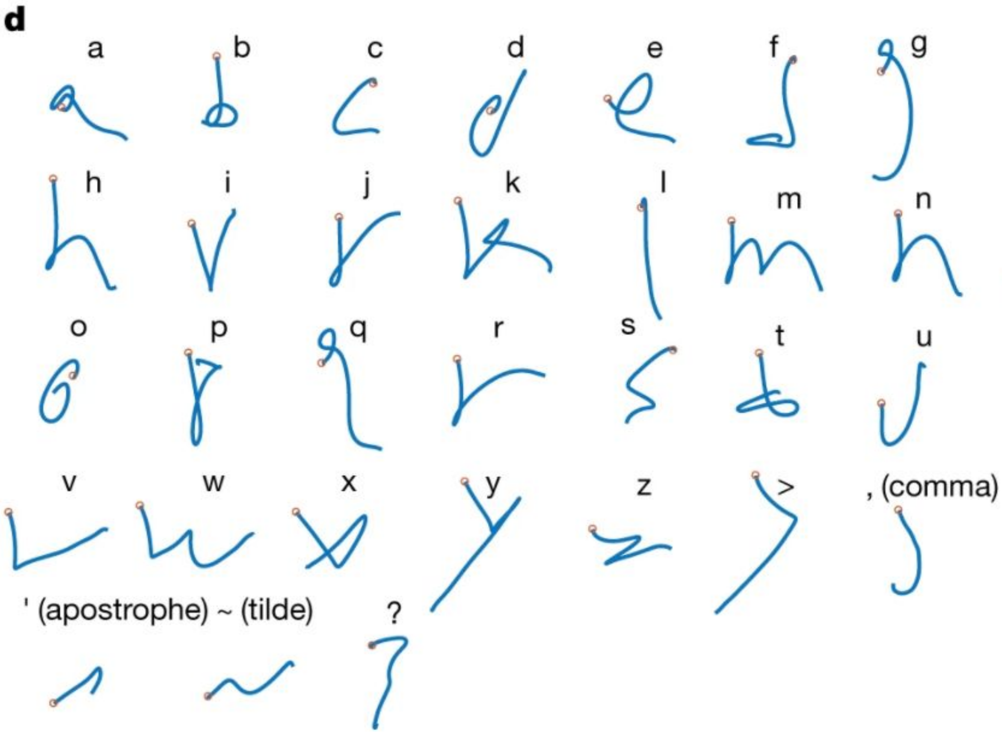
BCI setup

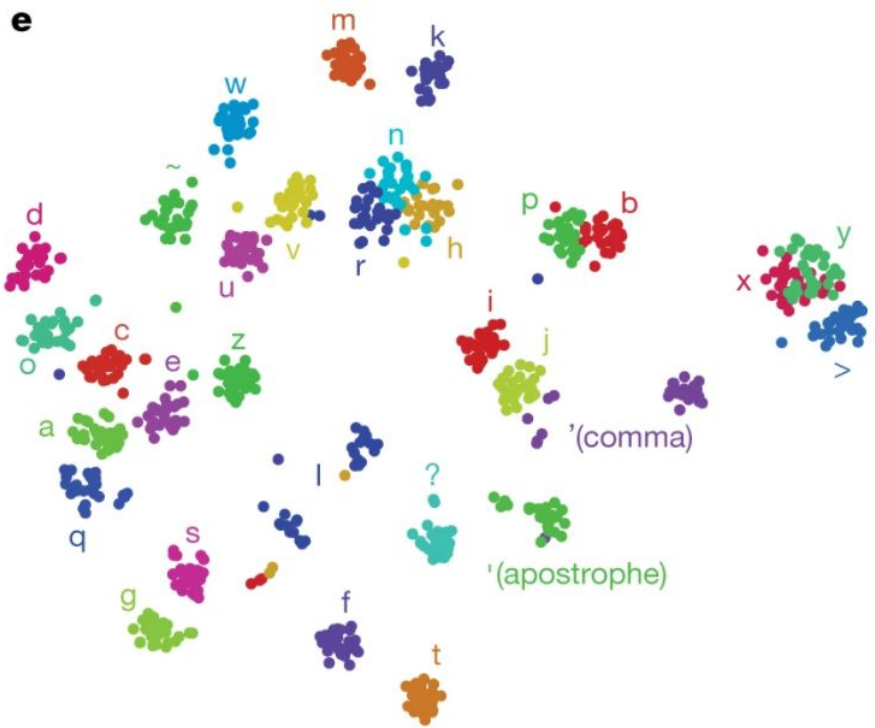
- Two microelectrode arrays in hand knob area of precentral gyrus
- Participant suffered paralysis from neck down
- Analysis of neural representations of handwriting characters
- 1 s output delay for decoder training
- No spike sorting, directly use voltage threshold crossings from waveform signals



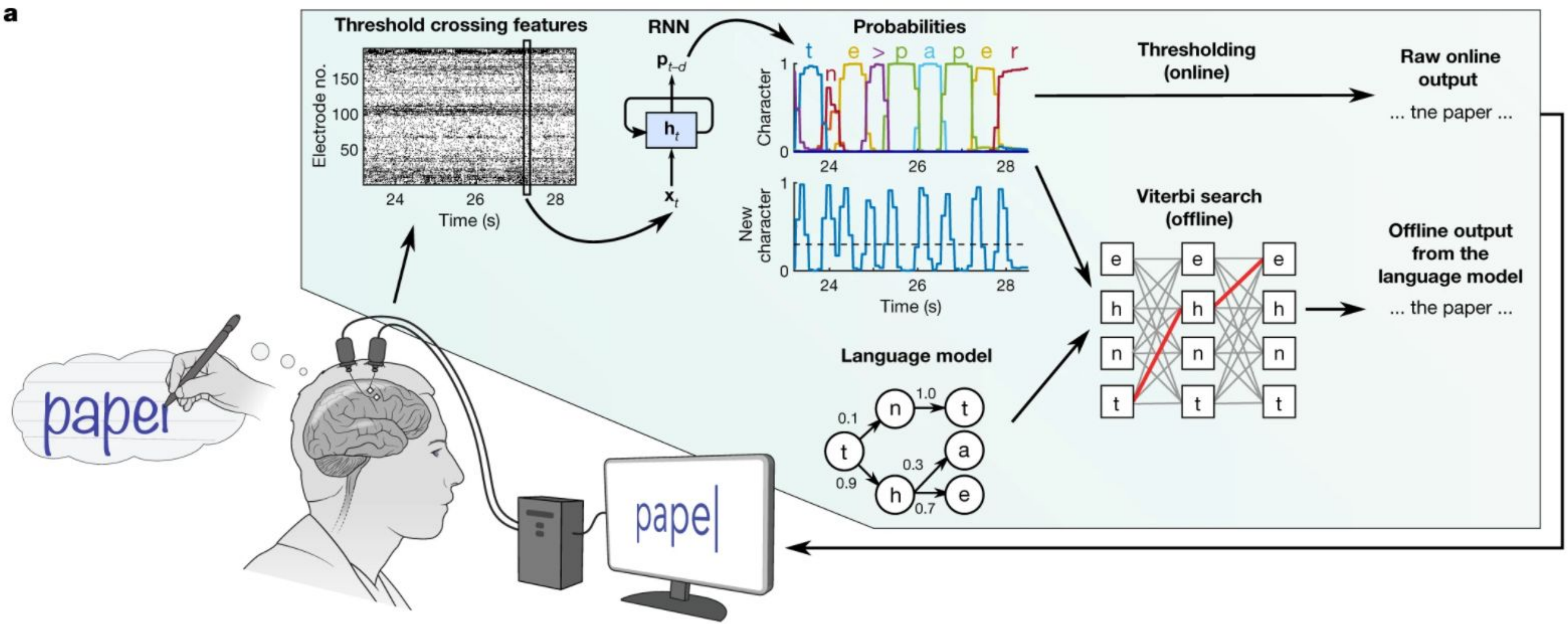


b
PC 1
PC 2
PC 3
d
e
m
Trial no.
27
1
0
1
Time (s)
PC score
Low
High
Warped time
Time
Time warping
c
PC 1
PC 2
PC 3
d
e
m
Trial no.
27
1
0
1
Time (s)



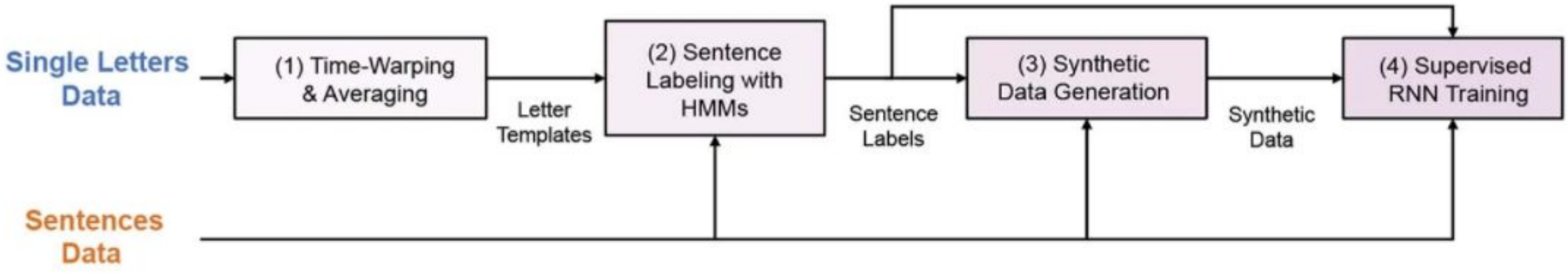


- The characters “>” is used for space, “-” is used for full stop

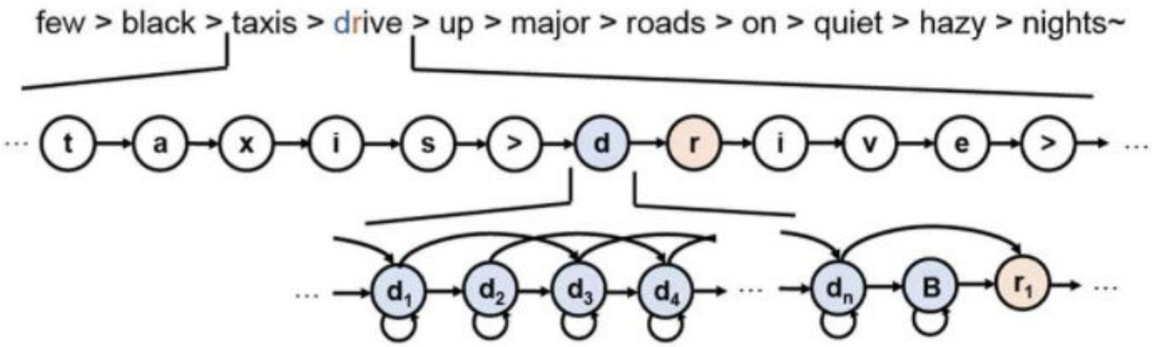


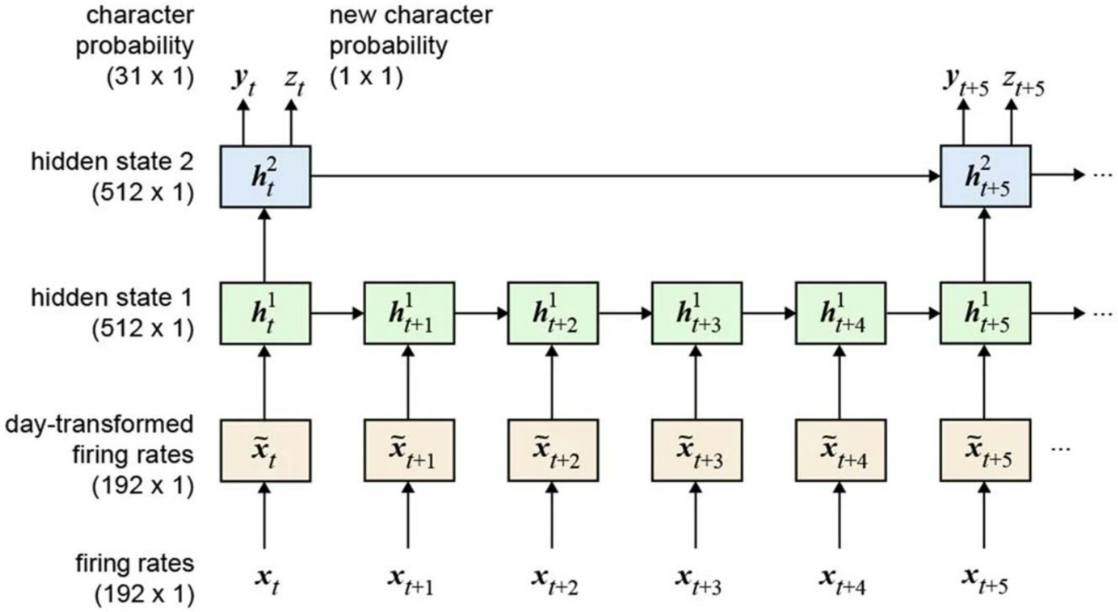
- Training data not available as we do not know when characters were “written”, also small data size
- Forced alignment method to determine starting times of characters for labeling data
  - Uses HMM model with trial-averaged activity of each character in emission distribution

b **Main Training Steps**

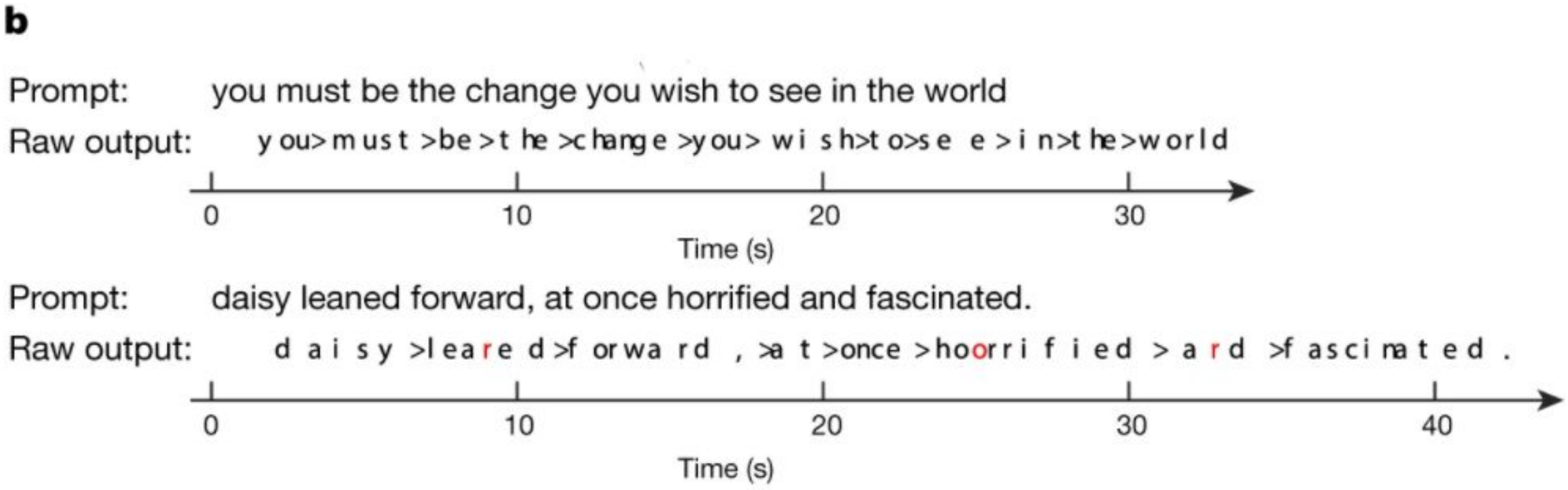


c **Sentence Labeling with HMMs**

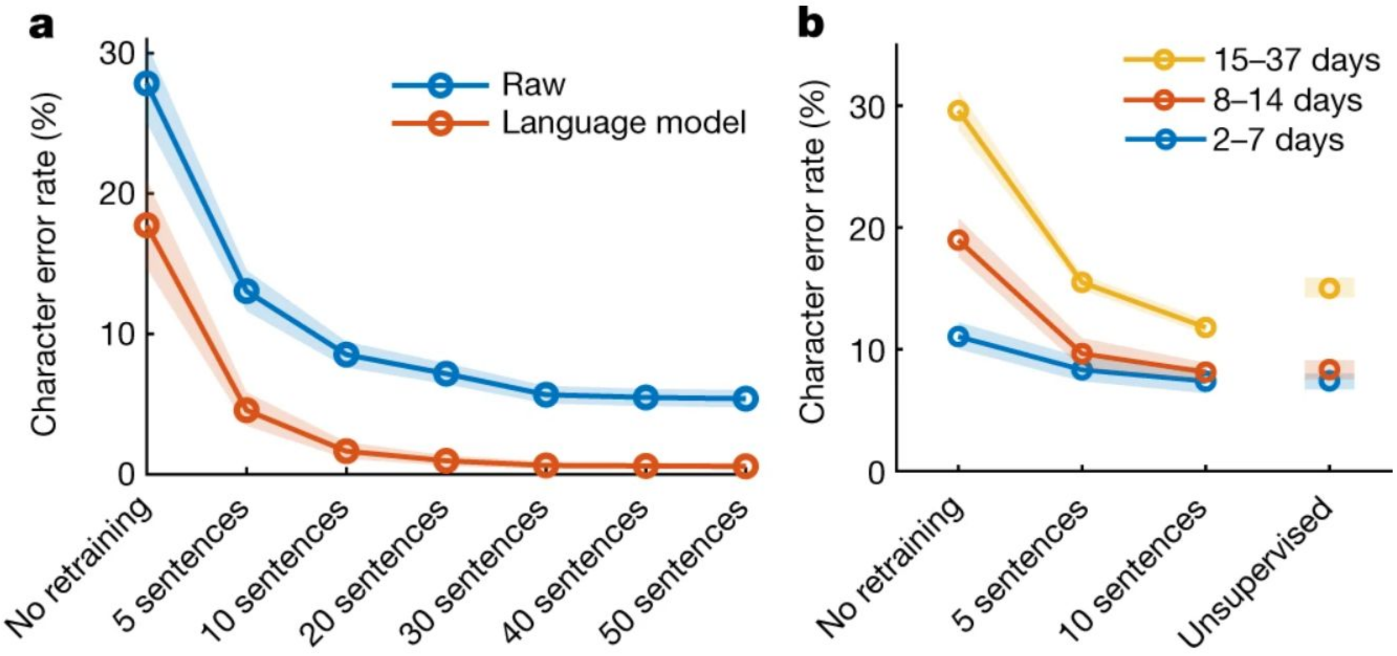




- Neural activity temporally smoothed and binned at 20 ms
- Add white noise and random offset noise to increase robustness to overfitting and nonstationarities
- Two-layer gated recurrent unit (GRU) into character probability vectors y and new character probability z
- Day-specific affine transform to account for day-to-day changes in the neural activity
- Outperforms simple HMM decoder mainly due to nonstationarities

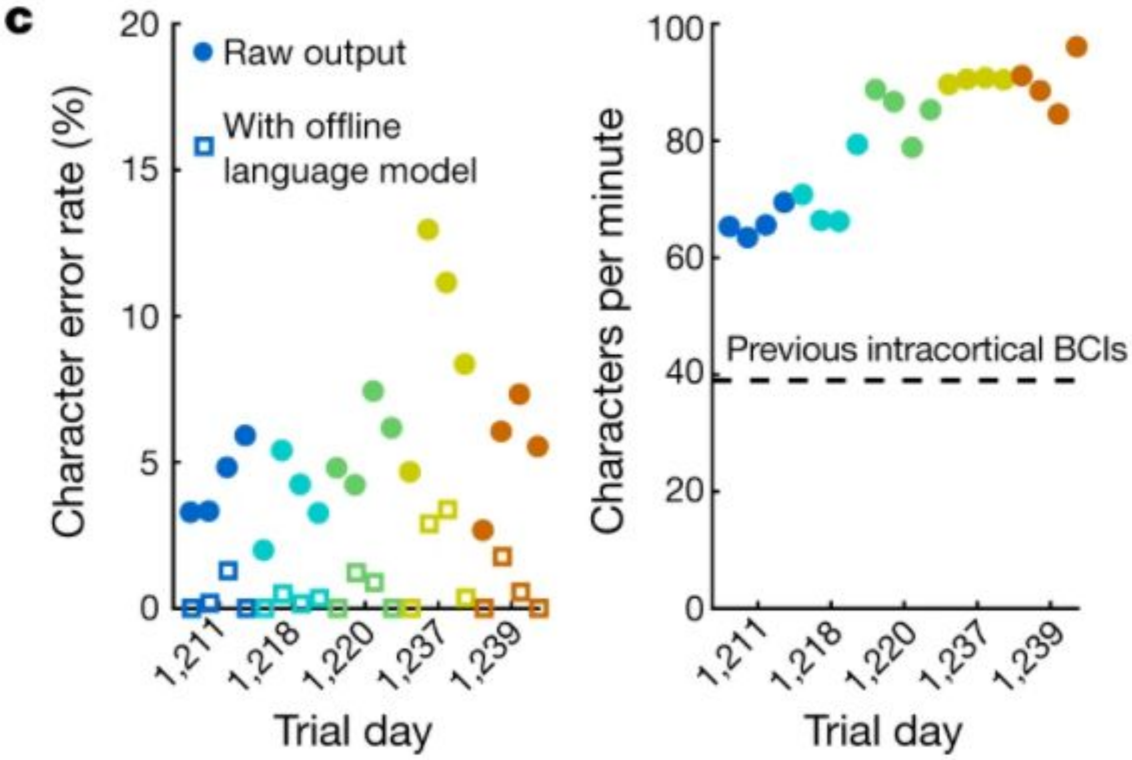


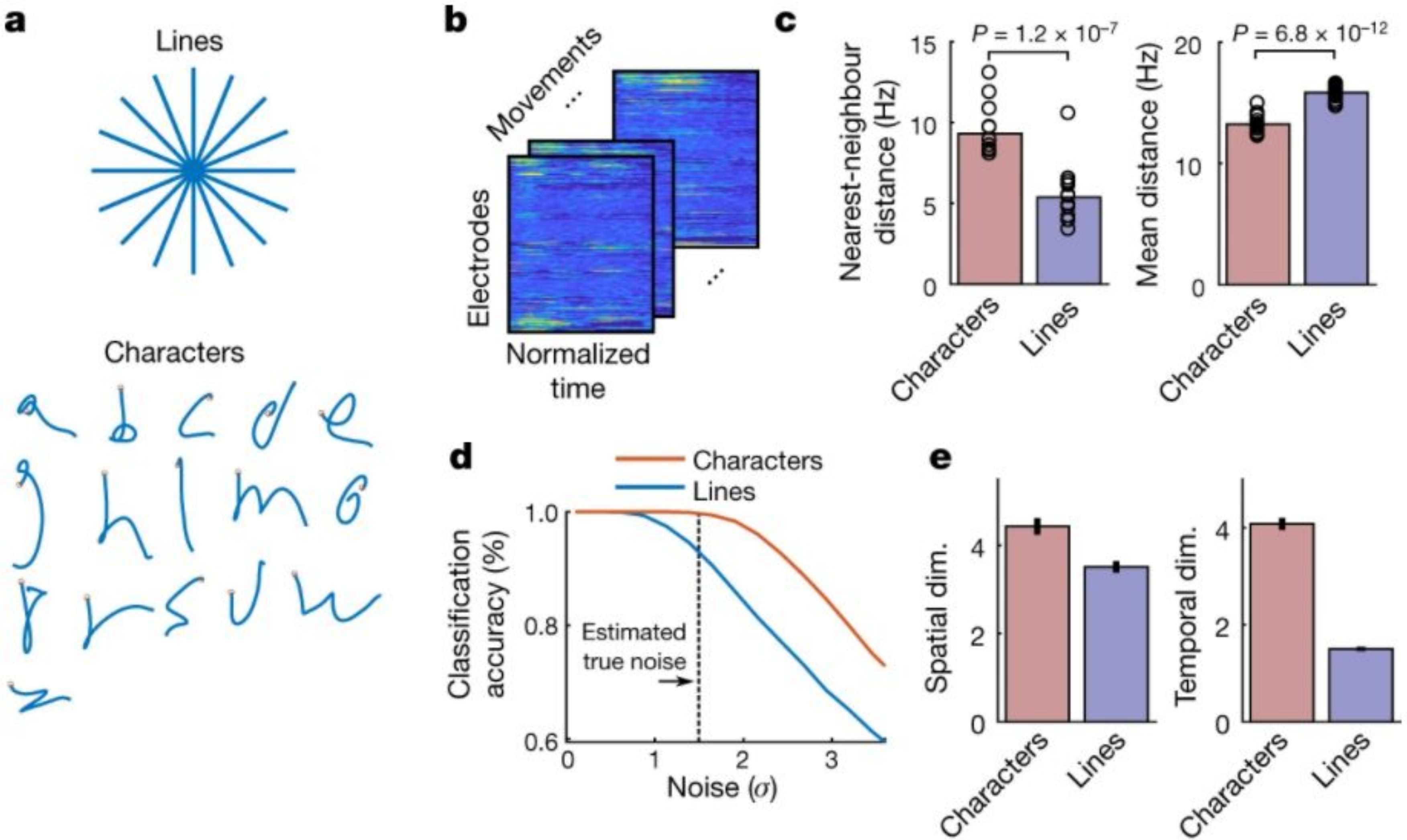
- RNN decoder latency estimated to be 0.4-0.7 s after participant finished “writing”, including 0.3 s delay of emitting most likely character after new character probability threshold crossed

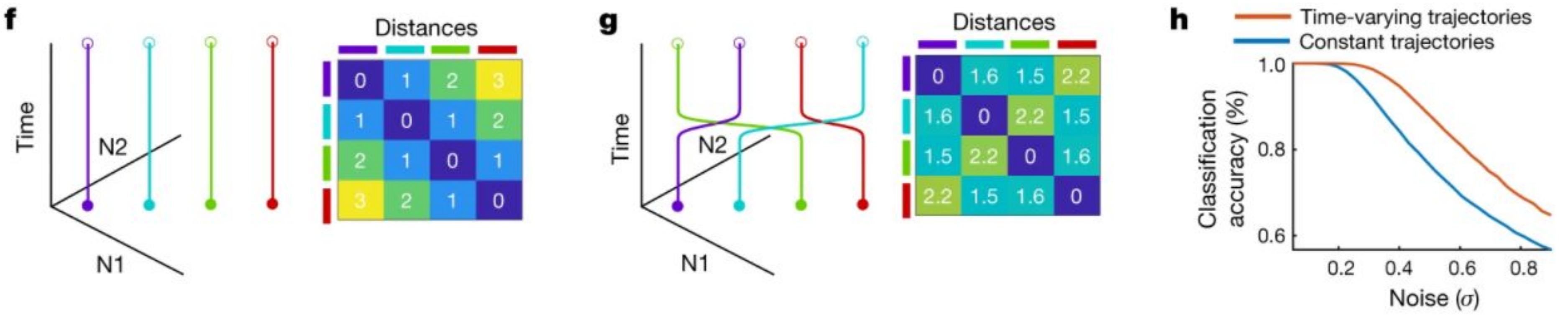


- Unsupervised retraining uses language model to autocorrect and retrain decoder with corrected target

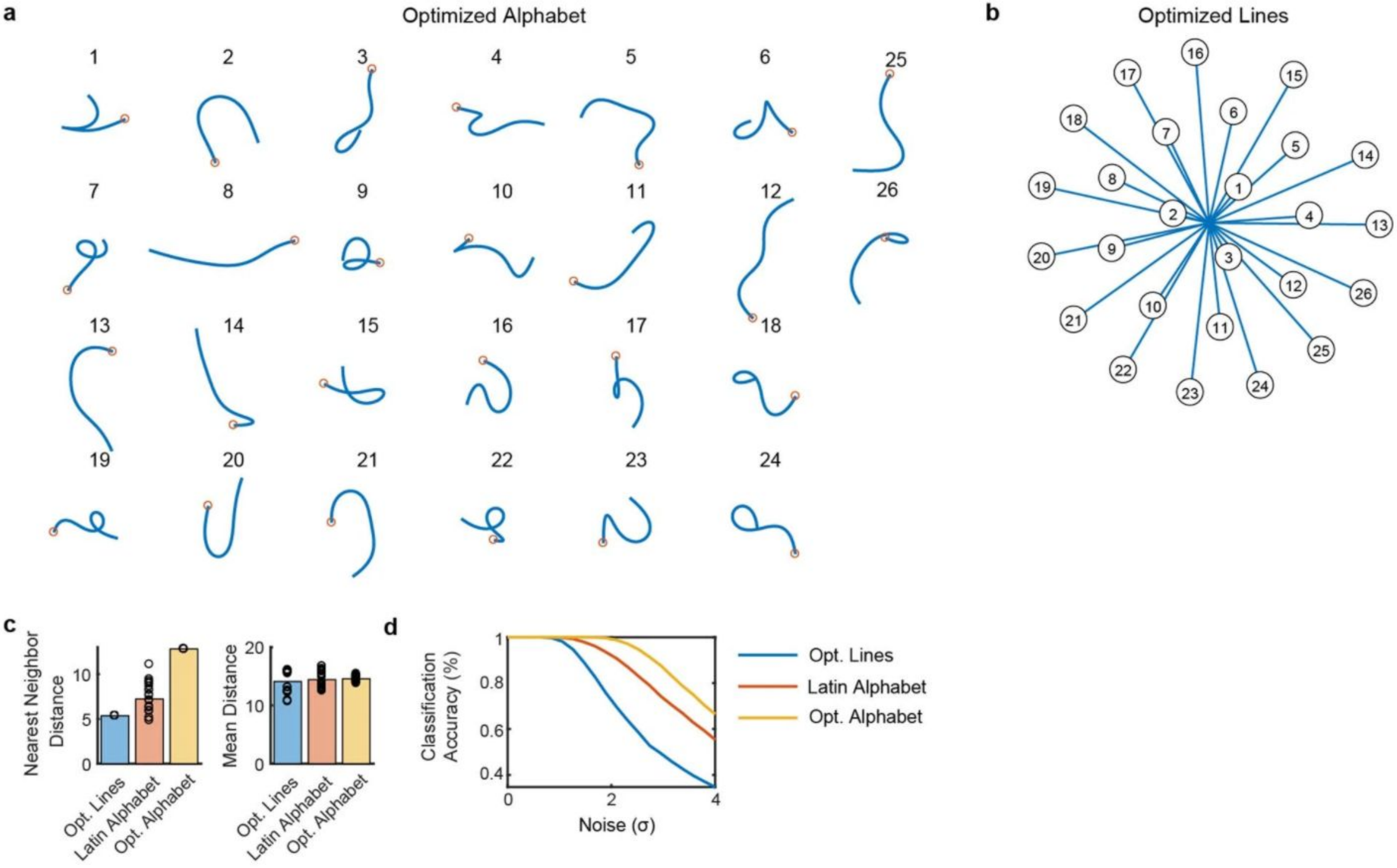
- Point-and-click BCI capped at around 40 cpm
- Limiting factor there is decoding accuracy
- Movements involve mostly straight lines, in contrast to handwriting



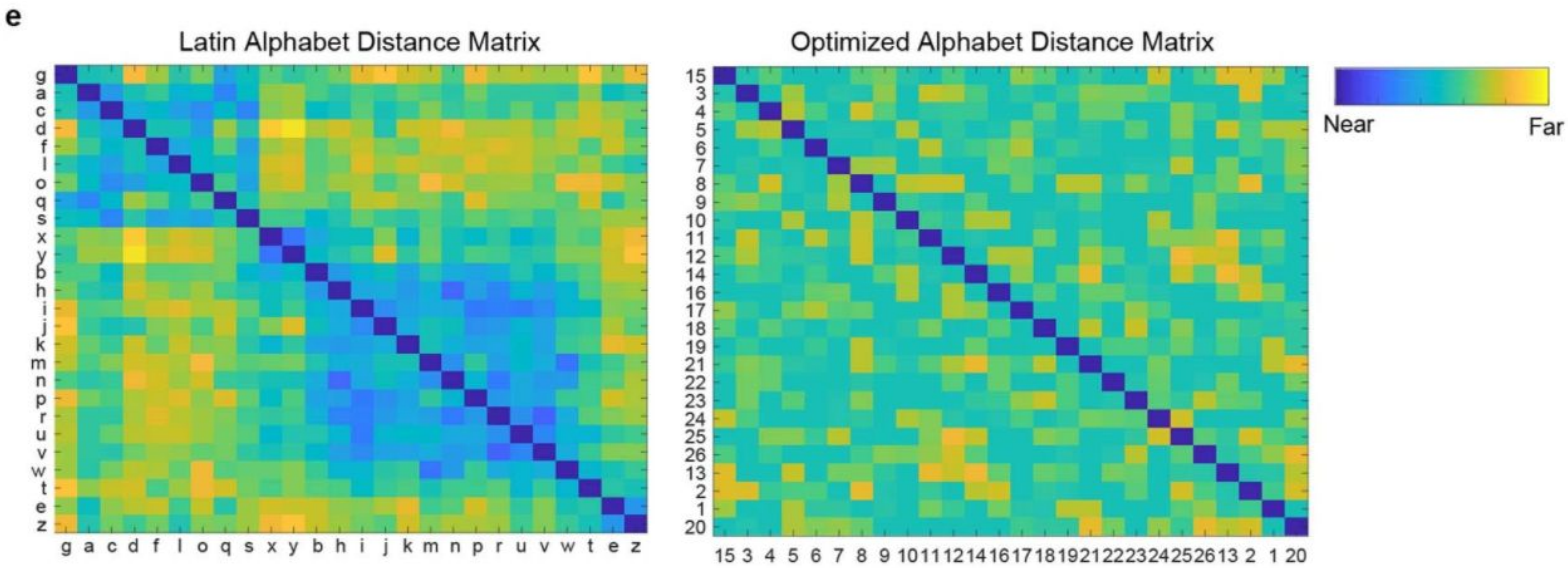

a
Lines
Characters
b
Movements
Electrodes
Normalized time
c
$P = 1.2 \times 10^{-7}$
Nearest-neighbour distance (Hz)
Characters
Lines
$P = 6.8 \times 10^{-12}$
Mean distance (Hz)
Characters
Lines
d
Characters
Lines
Classification accuracy (%)
Estimated true noise
Noise (σ)
e
Spatial dim.
Characters
Lines
Temporal dim.
Characters
Lines



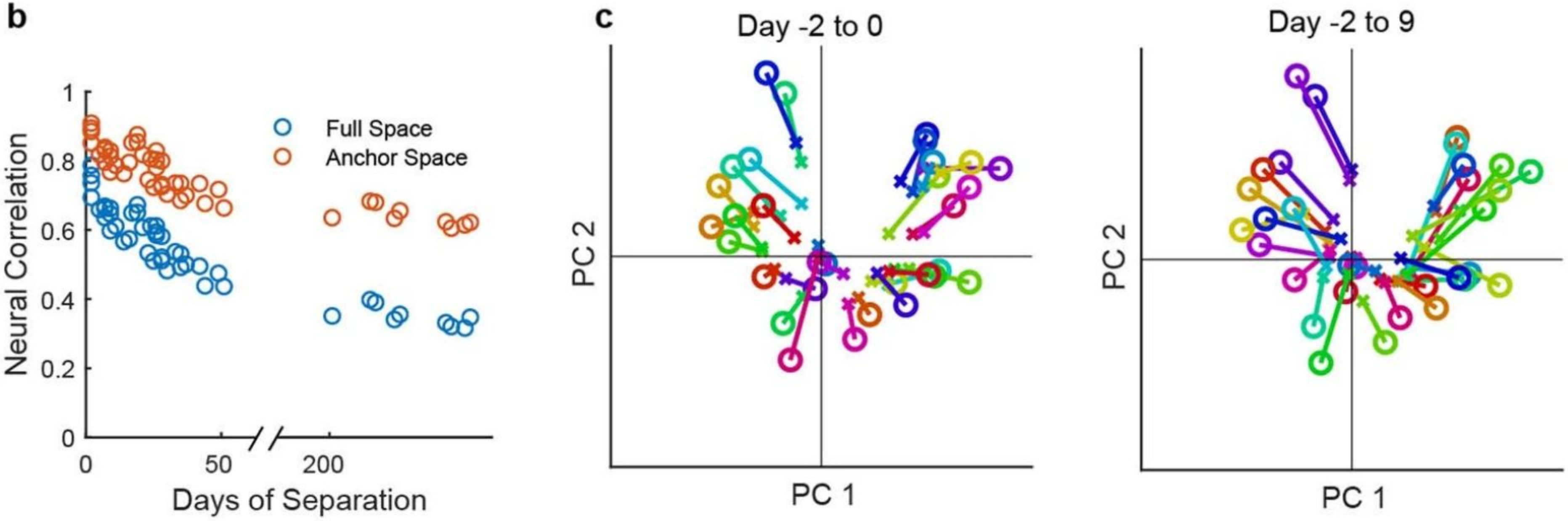
- For optimal classifiability, maximize nearest neighbour distances
- Classification accuracy using nearest neighbour classifier under white noise



a
Optimized Alphabet
1 2 3 4 5 6 25
7 8 9 10 11 12 26
13 14 15 16 17 18
19 20 21 22 23 24
b
Optimized Lines
c
Nearest Neighbor Distance
Mean Distance
Opt. Lines
Latin Alphabet
Opt. Alphabet
d
Classification Accuracy (%)
Noise (σ)
Opt. Lines
Latin Alphabet
Opt. Alphabet



- 2D state space describing pen tip velocity, Euclidean distance between spatio-temporal trajectories
- Same applies for neural representations if uniform linear tuning to velocity
- Latin alphabet neural representations has two big clusters (letters beginning with down stroke or counter-clockwise curl)



- Nonstationarity in neural activity across days, due to neural drift or electrode movement
- Short-term stability of neural features, changes accumulate at steady predictable rate

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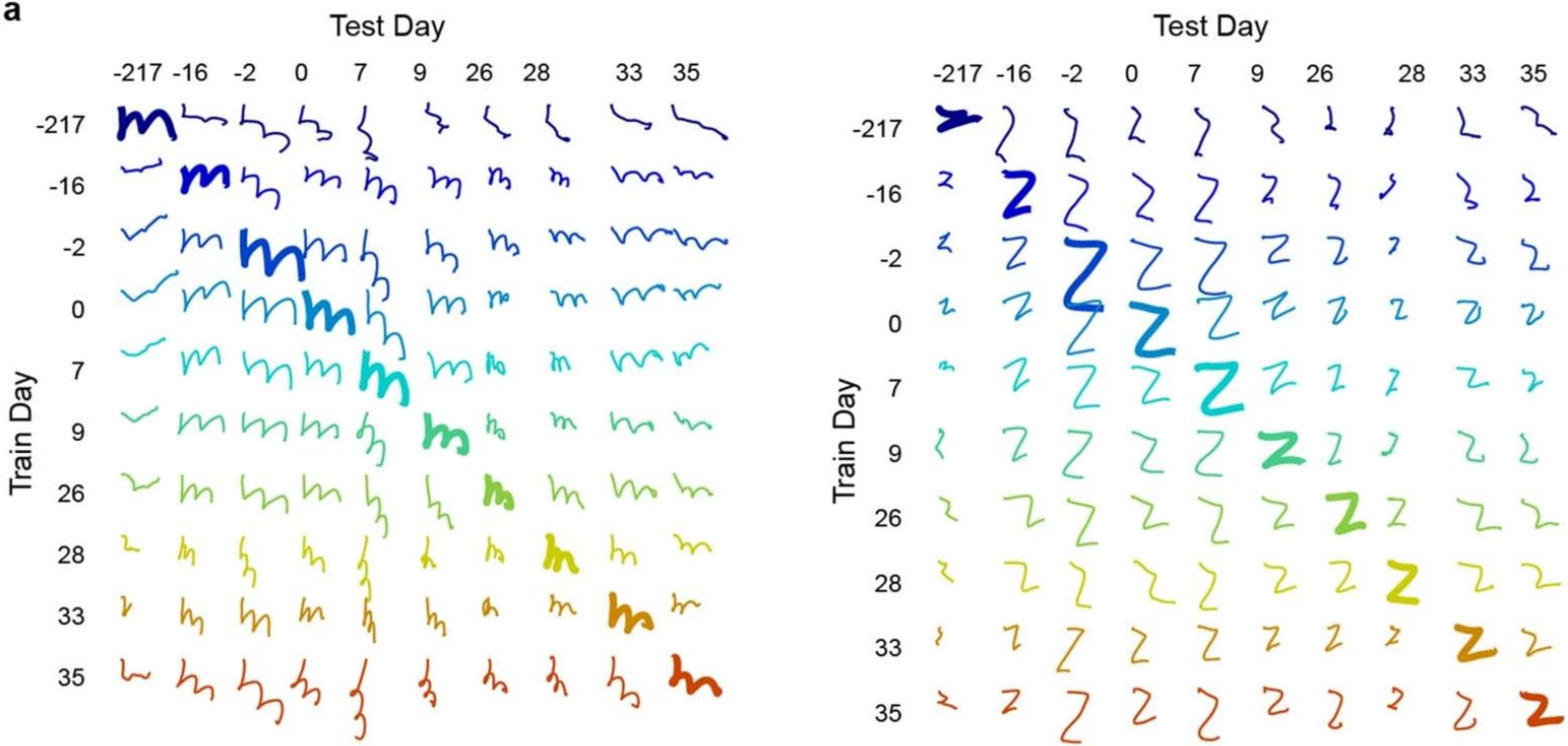
Test Day
-217 -16 -2 0 7 9 26 28 33 35
Train Day
-217 -16 -2 0 7 9 26 28 33 35
Test Day
-217 -16 -2 0 7 9 26 28 33 35
Train Day
-217 -16 -2 0 7 9 26 28 33 35

Summary

- New BCI that decodes handwriting from motor cortex activity in real time
- Communication rate comparable to smartphone typing speed
- Only proof of concept in single participant, not a clinically viable system yet
- Decoder retraining may be reduced with algorithmic innovations
- Intracortical BCIs give highest performance, and new developments are promising for increasing device longevity, physical size and bandwidth

Conclusion & Outlook

- Interesting times: convergence of developments in bioengineering and computational methods
- This raises new ethical questions, especially in cases where BCIs are associated with brain stimulation (e.g DBS treatments, see Yang et al, 2021, Shanechi 2020, Klein et al 2016 for discussions of BCIs for treatment of neuropsychiatric disorders)