Neural circuits for cognition

MIT 9.49/9.490/6.S076

Instructor: Professor Ila Fiete
TA: Gregg Heller
Senior Instruction Assistant: Adnan Rebei

Welcome!

Instructors and assistants

- Instructor:

  Ila Fiete

- Teaching assistant(s):

  Gregg Heller
  +1?
  Adnan Rebei (Technical Instructor/Senior course asst)

Course logistics/communication

- Class times:

  2.30-4 Tu, Th, **in-person** @ MIT: 46-3310 (recordings on request)

- Office hours:

  Ila Fiete: Tu 4-5p ET

  Gregg Heller: TBD

  Adnan Rebei: TBD

- Email: (fiete, greggh, rebeia) @mit.edu

I have questions!?!

- Canvas website: https://canvas.mit.edu/courses/16745

→ Post general questions about class (content, logistics, homework) to Canvas: Discussion tab (not anonymous) or Piazza plugin (anonymous questions possible). All class members will benefit.

- Office hours:

→ Come to office hours!

- Email

→ Reserve email for personal/private questions.

Walk-through of syllabus (on Canvas)

https://canvas.mit.edu/courses/16745

Your input

- Complete math survey on Canvas.
- Give us your input on what you want to learn and see in the class.
- We would like each of you to learn, enjoy, and help improve this class: give feedback (positive and negative constructive criticism).

Overview of the field

Neuroscience and cognitive science

- Cognitive science and psychology go back, in some form, millennia
- Brain surgery also goes back millennia (Africa, India, Peru, Europe,...)
- Modern neuroscience (observation of neural activity, structure) ~ 200 years old
  - Galvani (1780: bioelectricity/can stimulate muscles with electrical current)
  - du Bois-Reymond (1843: co-discovery of nerve action potential)
  - Golgi, Cajal (late 1800's: microscopic structure)
  - Broca, Gall, Wernicke (late 1800's: characterization of functional specialization/gross modularity in brain)
  - Sherrington, Eccles (1920's, 1930: muscle reflexes)
  - Mathematical models of single cells: Hodgkin & Huxley (1952), Rall (1960's)
  - Neuroscience departments founded (1960's); Kuffler, Schmitt, McGaugh, Rioch,
  - Synaptic transmission: Katz (1960's onwards),….
  - Neural and synaptic plasticity: Kandell (1960's onwards), ….
  - Network models: Hopfield (1972), Wilson & Cowan (1973),

https://faculty.washington.edu/chudler/hist.html

Neuroscience and modeling developments

- Galvani (1780: bioelectricity/can stimulate muscles with electrical current)
- du Bois-Reymond (1843: co-discovery of nerve action potential)
- Golgi, Cajal (late 1800's: microscopic structure)
- Broca, Gall, Wernicke (late 1800's: characterization of functional specialization/gross modularity in brain)
- Sherrington, Eccles (1920's, 1930: muscle reflexes)
- Mathematical models of single cells: Hodgkin & Huxley (1952), Rall (1960's)
- Neuroscience departments founded (1960's); Kuffler, Schmitt, McGaugh, Rioch,
- Synaptic transmission: Katz (1960's onwards),….
- Neural and synaptic plasticity: Kandell (1960's onwards), ….

- McCullough and Pitts (1943: first artificial neural model)

https://nautil.us/issue/21/information/the-man-who-tried-to-redeem-the-world-with-logic

$$y_k = \varphi\left(\sum_{j=0}^{m} w_{kj} x_j\right)$$

- Rosenblatt (1958: perceptron algorithm)
- Minsky & Papaert (1969: limits of perceptrons)
- Widrow & Hoff (1960: (M)Adaline – LMS regression with neural networks)
- Network models: Hopfield (1972), Wilson & Cowan (1973)
- Now: RL, Conv nets, memory-augmented models, ….

The brain & cognition & computation & MIT

1941

Francis Schmitt:
Led Biology Dept that combined biology, chemistry, math, physics; studied nerve physiology. Established Neuroscience Research Program (1962)

1948

Norbert Wiener:
Cybernetics (notion of feedback and feedback control); helped recruit cognitive science team that led to AI

1960

Dept. of Psychology/Teuber:
to study mind must study brain
Effectively: first Neuroscience dept.

1961-5

Charlie Gross:
MIT postdoc/asst prof
Subsequent:
hand and face cells, IT

1985

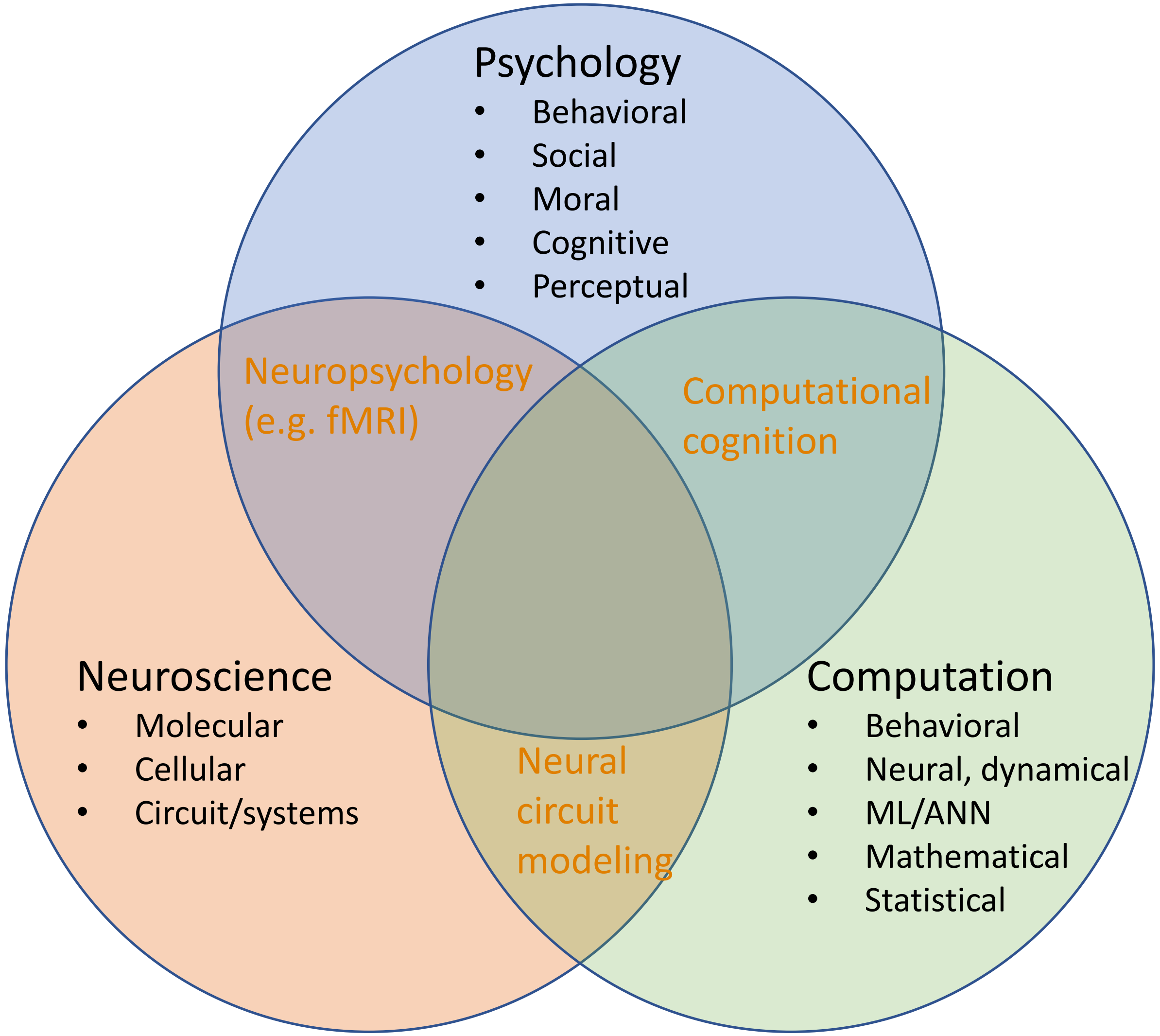
Ann Graybiel:
Modular control of movement;
Subsequent: sequence chunking and hierarchy

1985

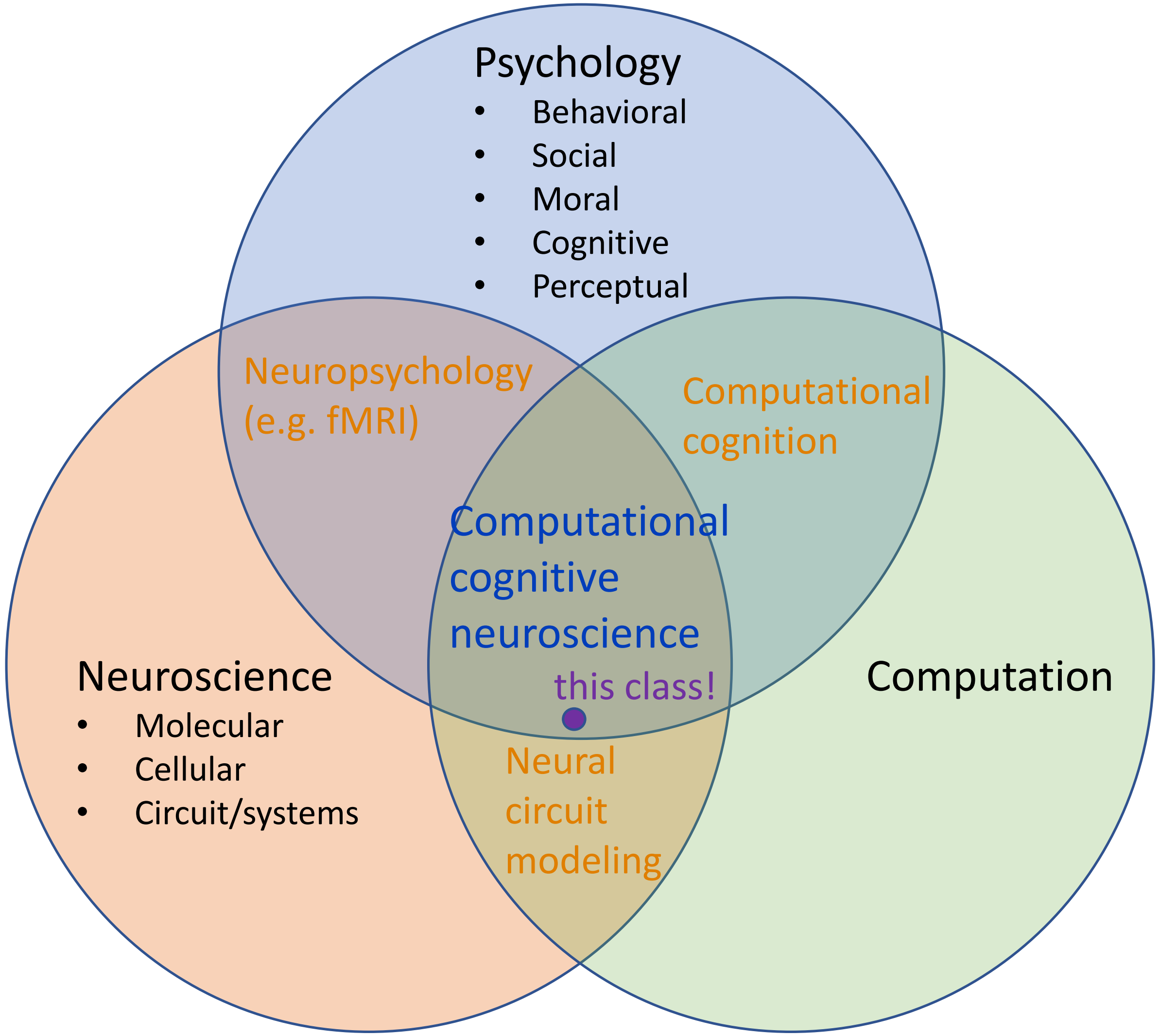
David Marr: Vision
Three seminal treatments:
Cerebellum
Hippocampus
Neocortex

Ted Adelson
Tommy Poggio,
Michael Jordan,
Sebastian Seung,
Josh Tenenbaum,
…

Cognitive neuroscience



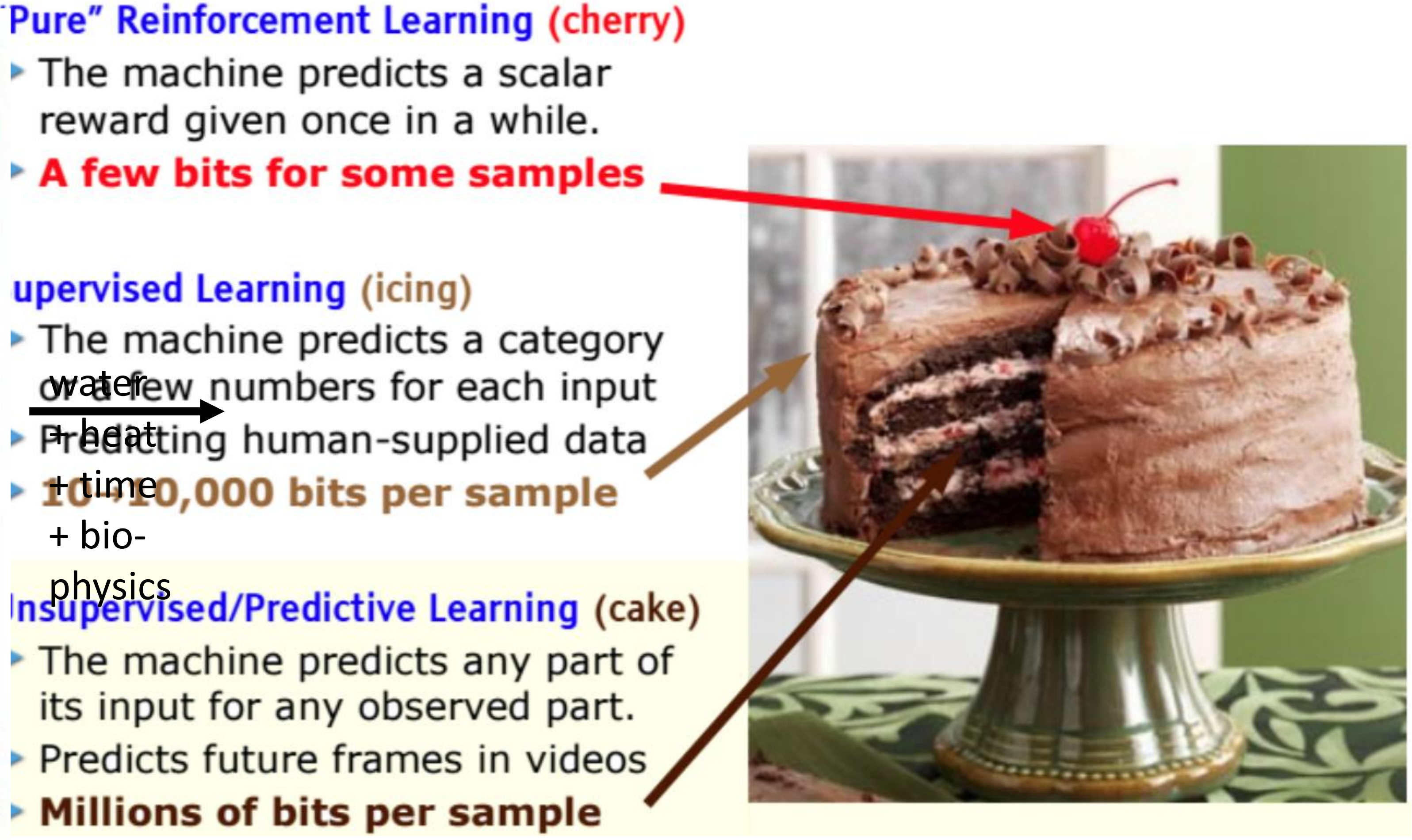
Cognitive neuroscience



Learning in brains, learning in machines

- Non-stationary, streaming data, sequential decisions,…
- Robustness, generalization
- Data-efficiency
- Pre-structured architectures/scaffolds, genes & development
- Internal states, goals

Bottom-up drivers of natural intelligence: large inductive biases from genetic codes and unfolding dynamics

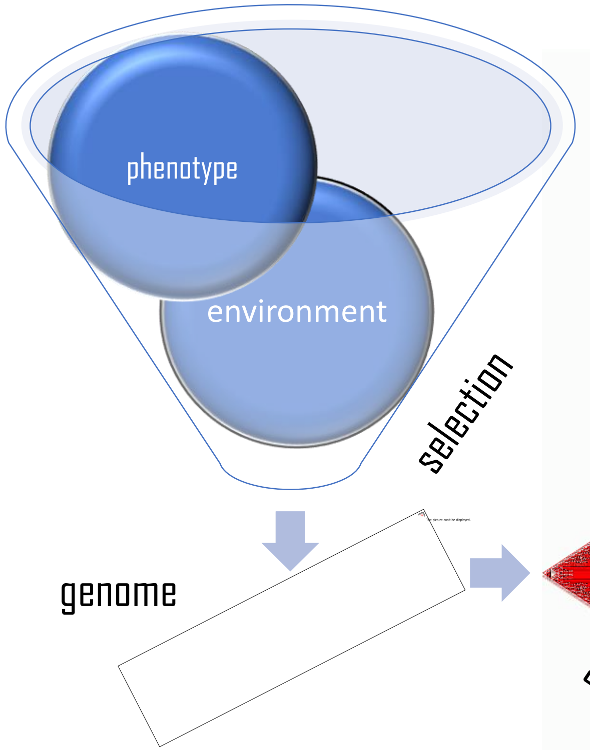


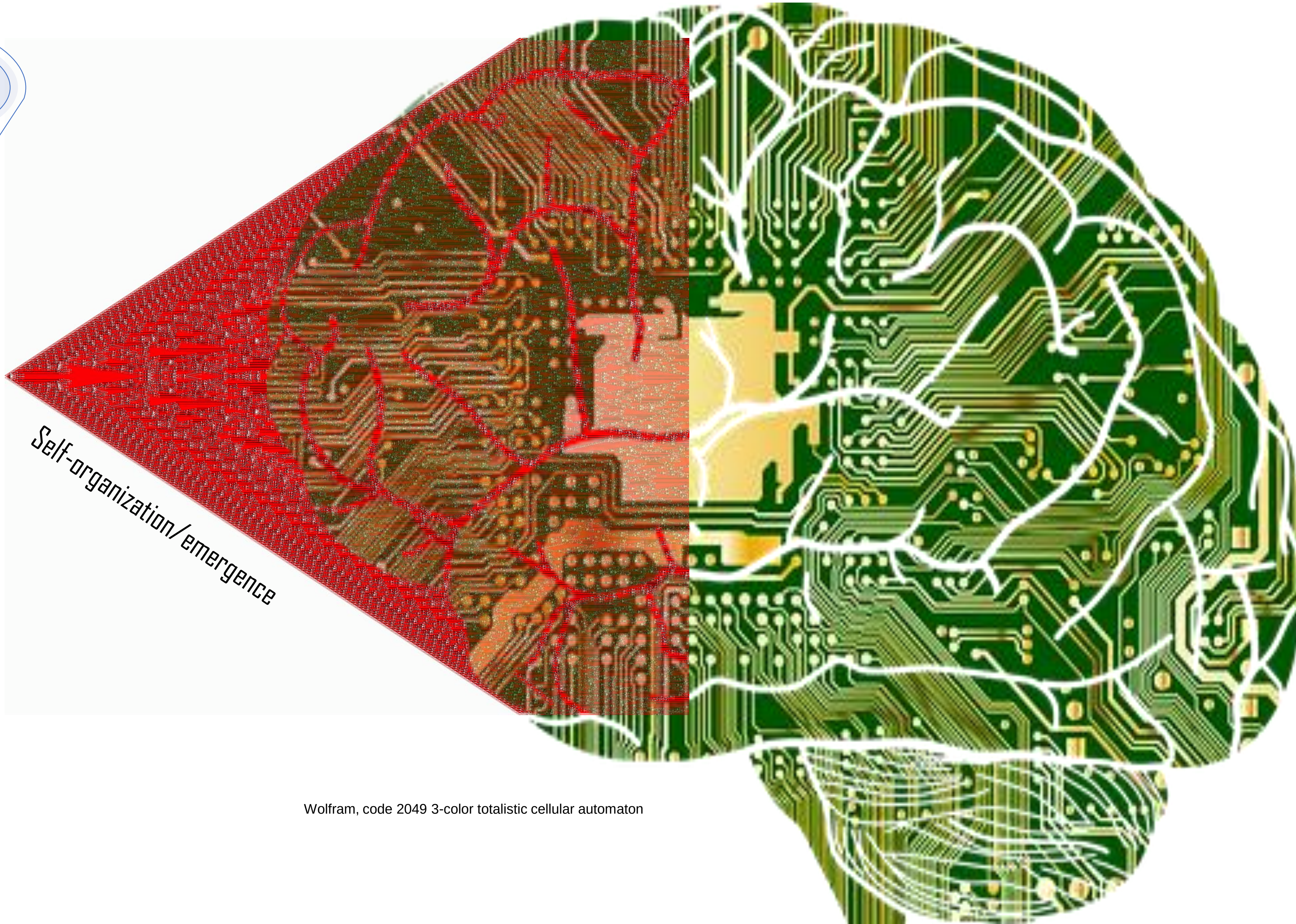
water
+ heat
+ time
+ bio-physics

Y. LeCun

Bottom-up genetically encoded dynamics

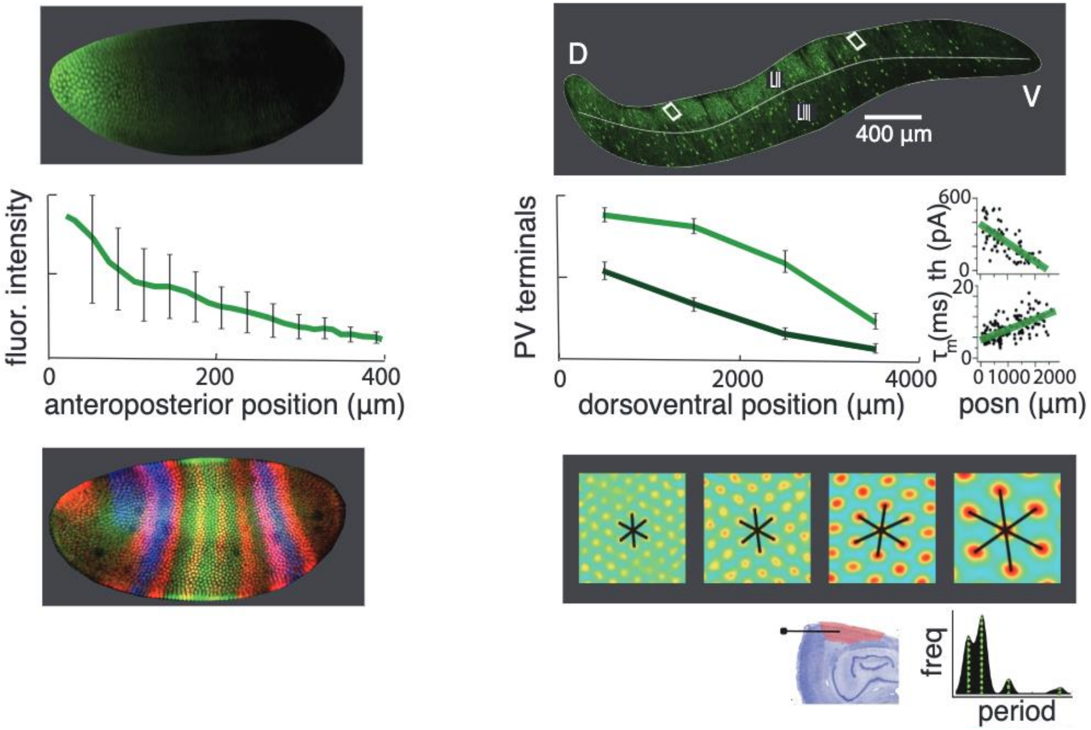
- Very few (highly compressed) bits in, rich self-organized emergent structure out





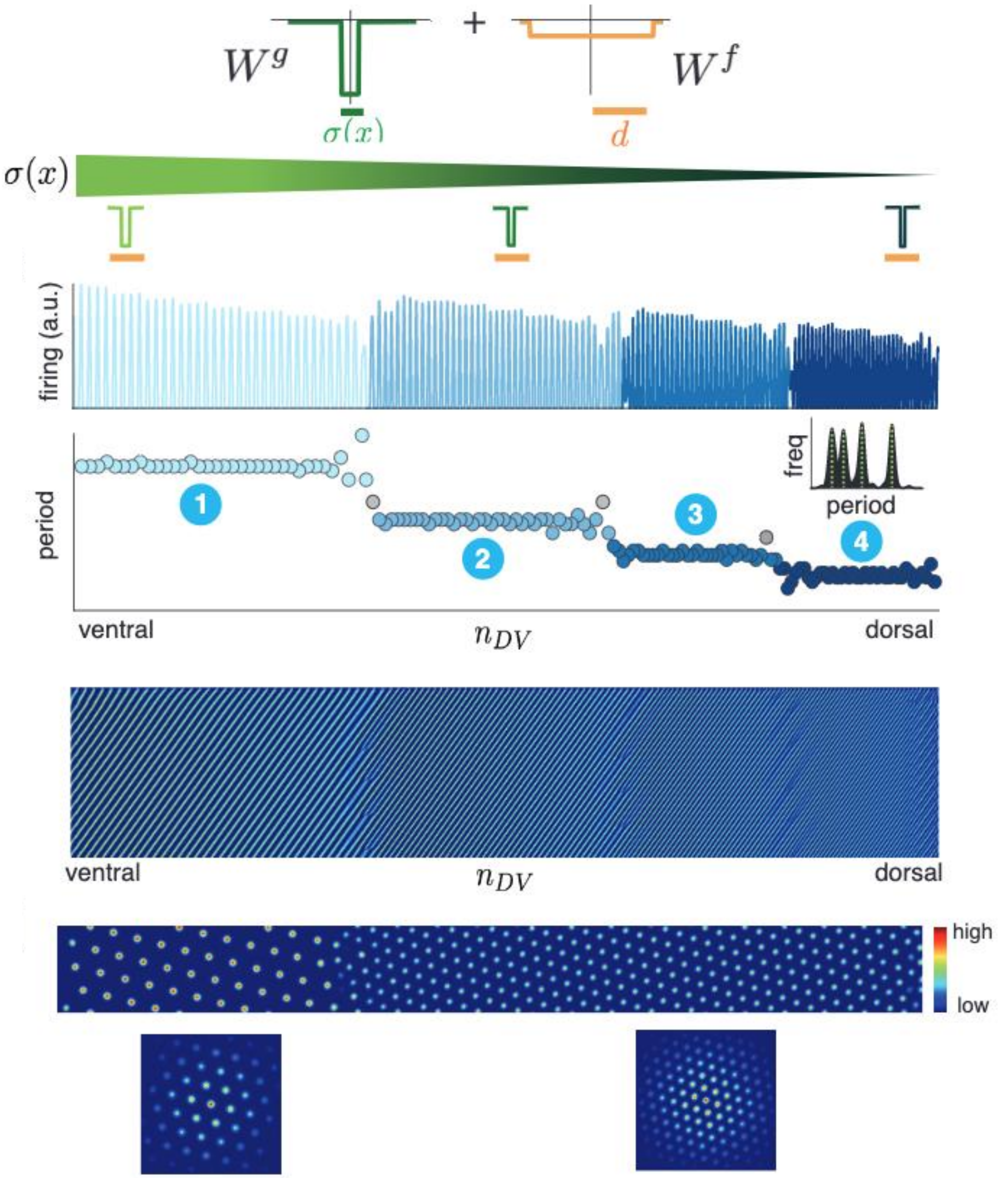
Wolfram, code 2049 3-color totalistic cellular automaton

Bio/genetic gradients as precursors for brain structure emergence



Khona*, Chandra*, et al., 2022 https://doi.org/10.1101/2021.10.28.466284

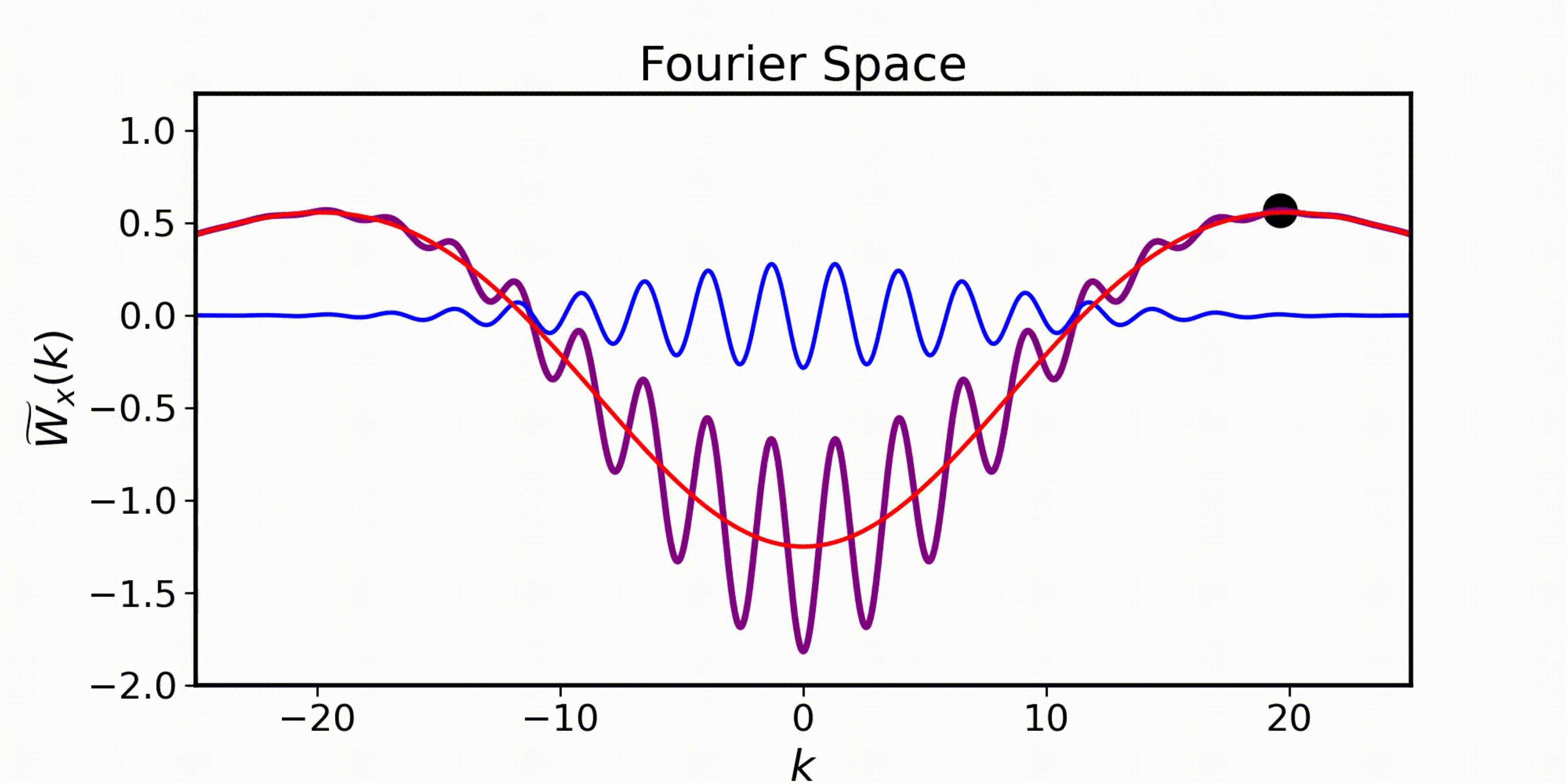
Spontaneous self-organization of modularity in tuning and function



Through interaction of two low-level (local) lateral interactions, one graded and one fixed

Khona*, Chandra*, et al., 2022 https://doi.org/10.1101/2021.10.28.466284

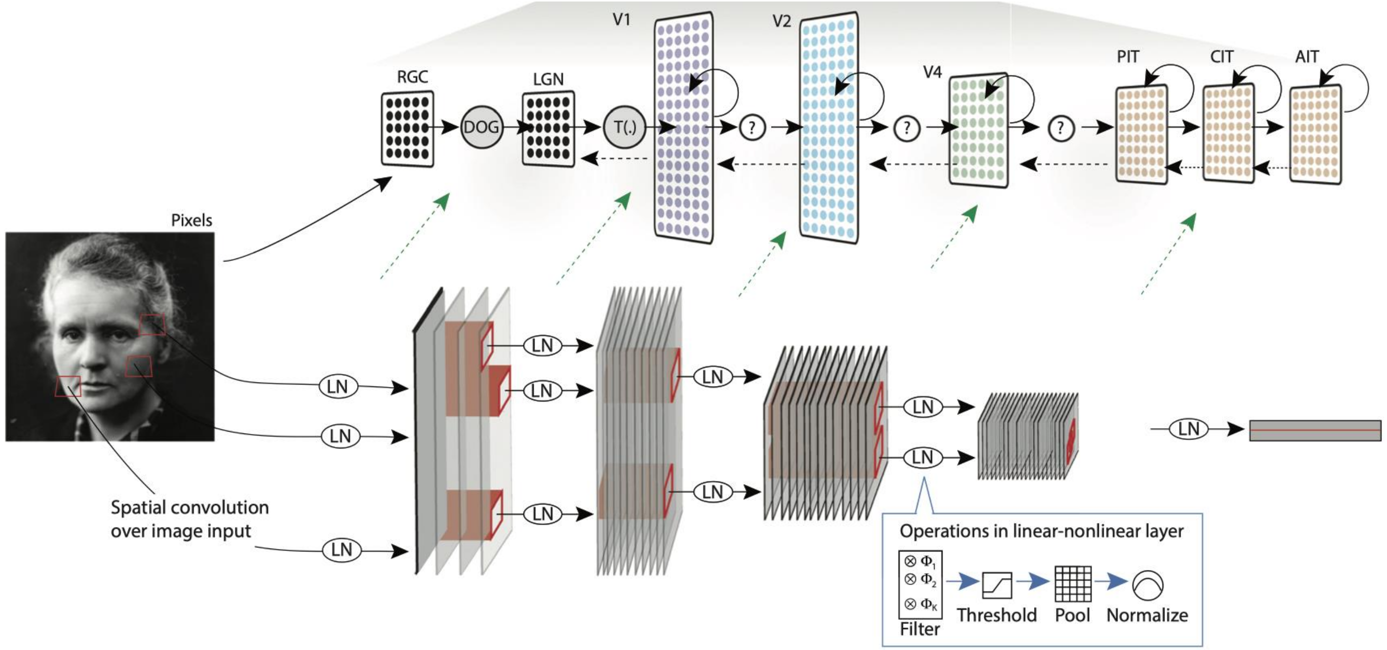
Theory: Multiscale linear instability

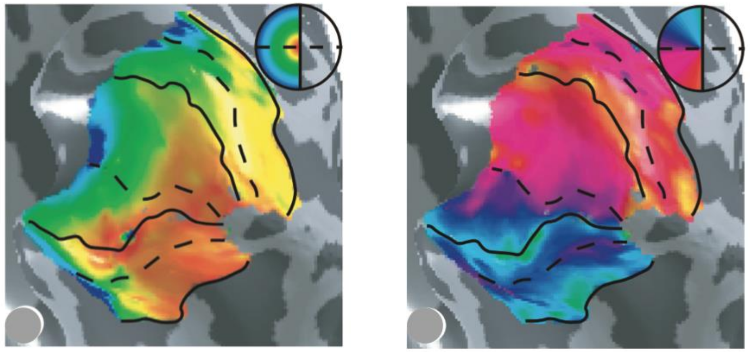


Khona*, Chandra*, et al., 2022 https://doi.org/10.1101/2021.10.28.466284

Grown and self-organized (not built)

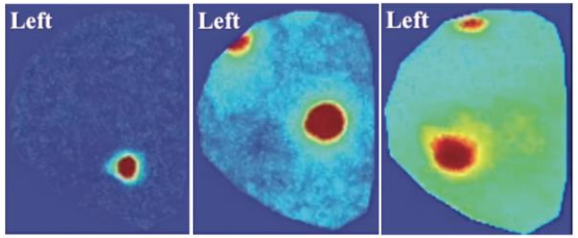
Schrimpf et al.



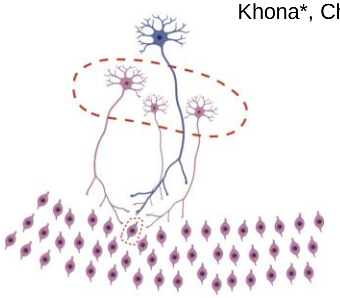


eccentricity   polar angle
(from imaging)

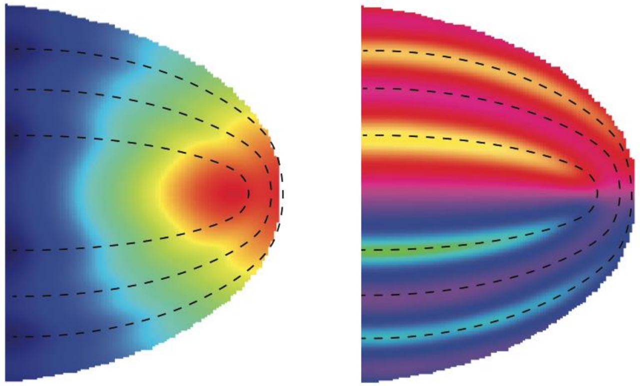
Khona*, Chandra*, et al., 2022, in prep



Spontaneous activity in retina before eye opening



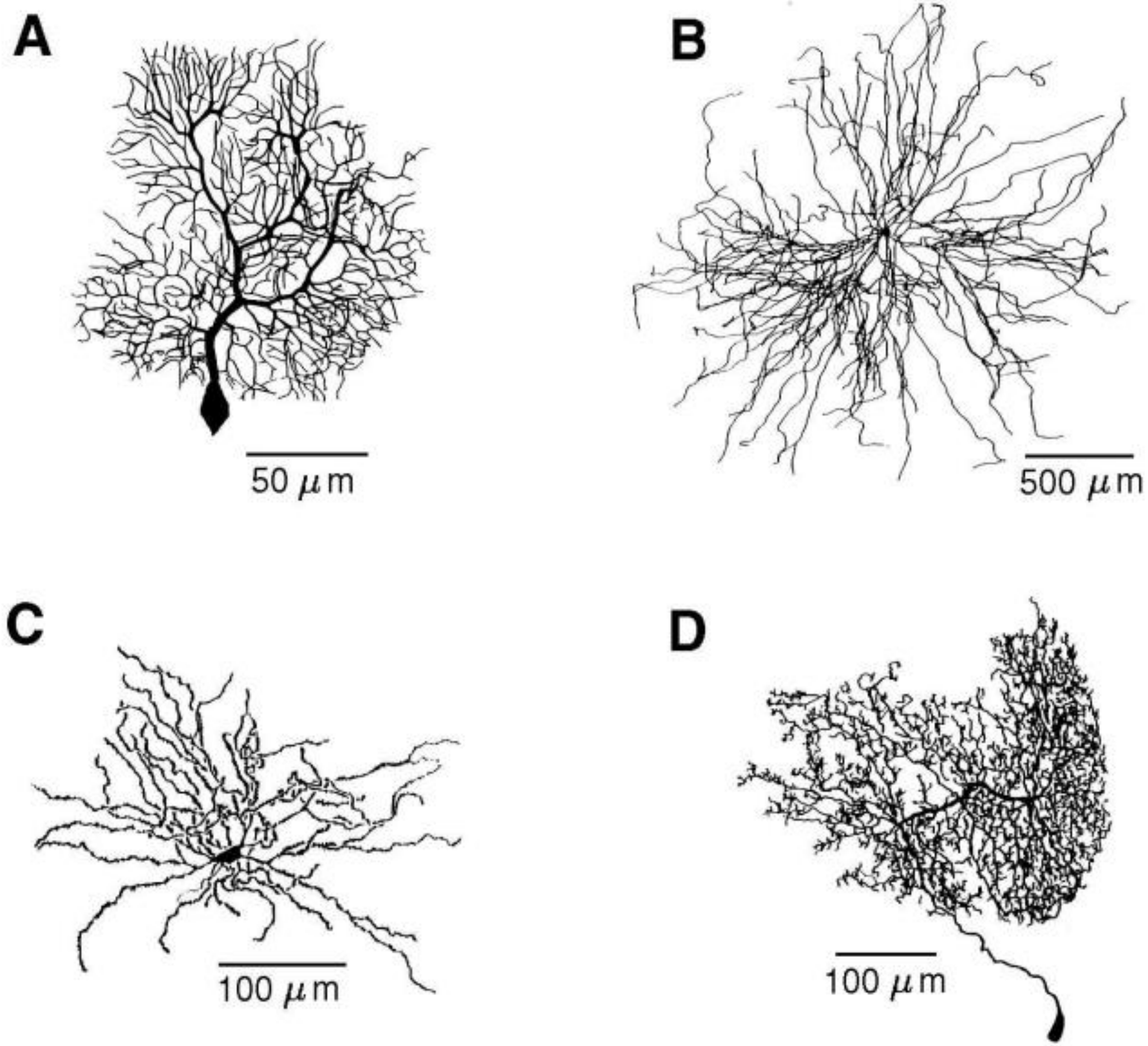
Growth and pruning based on wiring length



eccentricity   polar angle

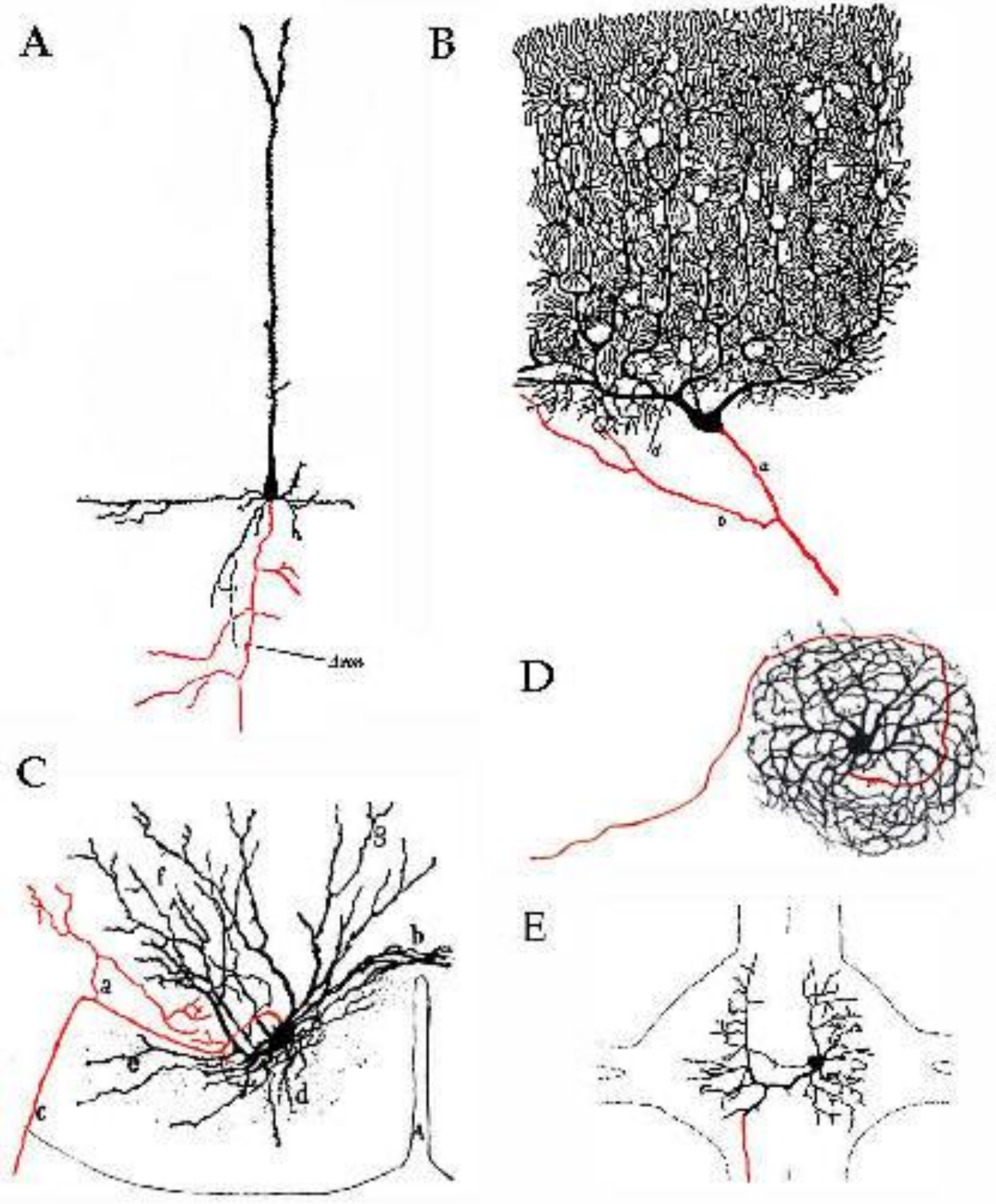
Components

~10000 cell types



Vast complexity in dendritic structure.
Could lead to rich spatial and spatio-temporal input interactions.

Axons (red)



Our (rather modest) goal for this class

Focus on dynamics/mechanism: to examine the basic mechanistic/dynamical underpinnings of the ***brain's*** circuits involved in cognitive computations.

- Memory
- Motor control
- Decision making
- Spatial navigation
- Neural coding
- Pattern formation, learning and development

Bridging neuroscience and cognitive science

Two critical sets of tools to make this possible:

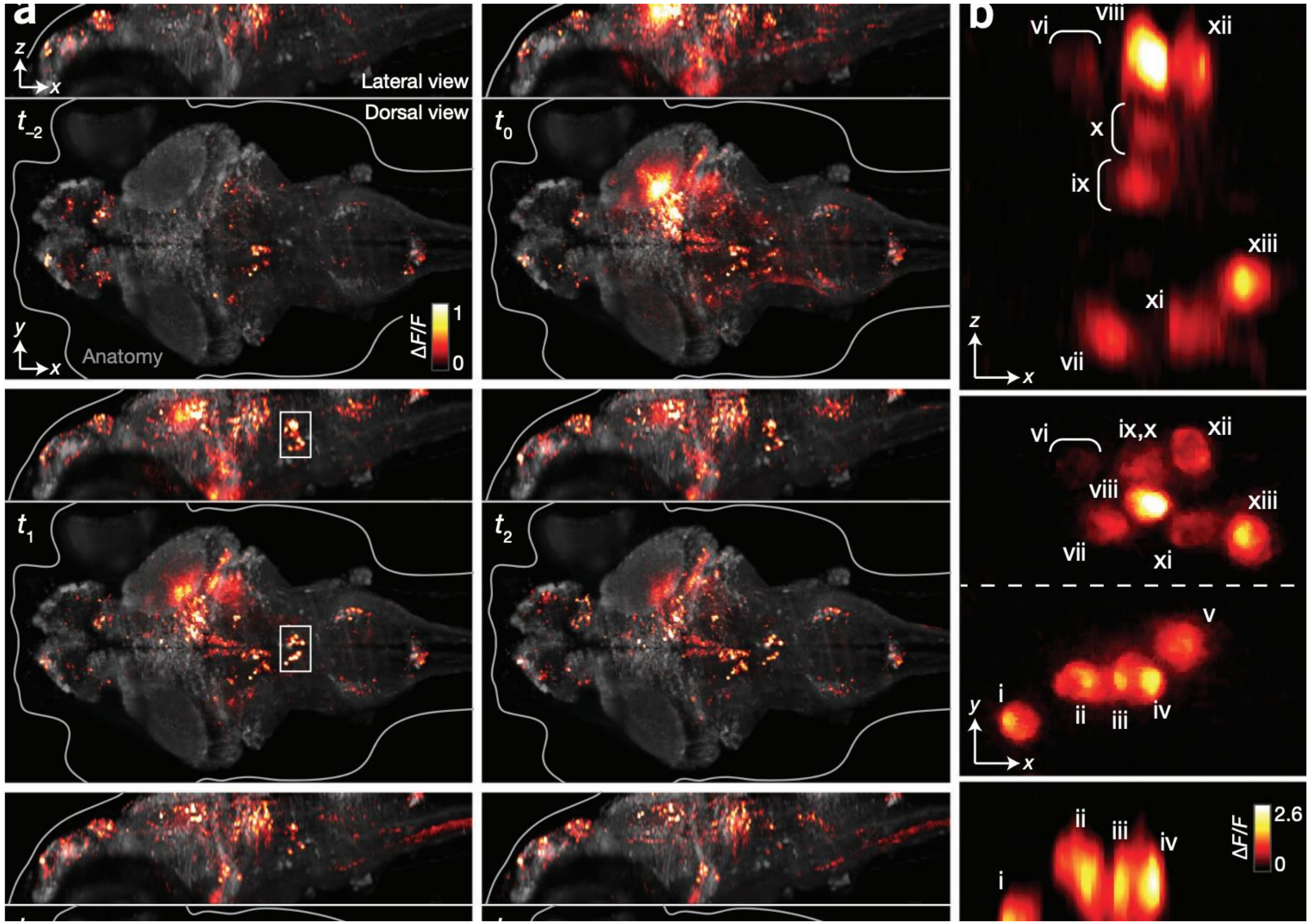
- Empirical tools in neuroscience
- Computational and mathematical tools for modeling and connecting across scales

Powerful new empirical tools in neuroscience

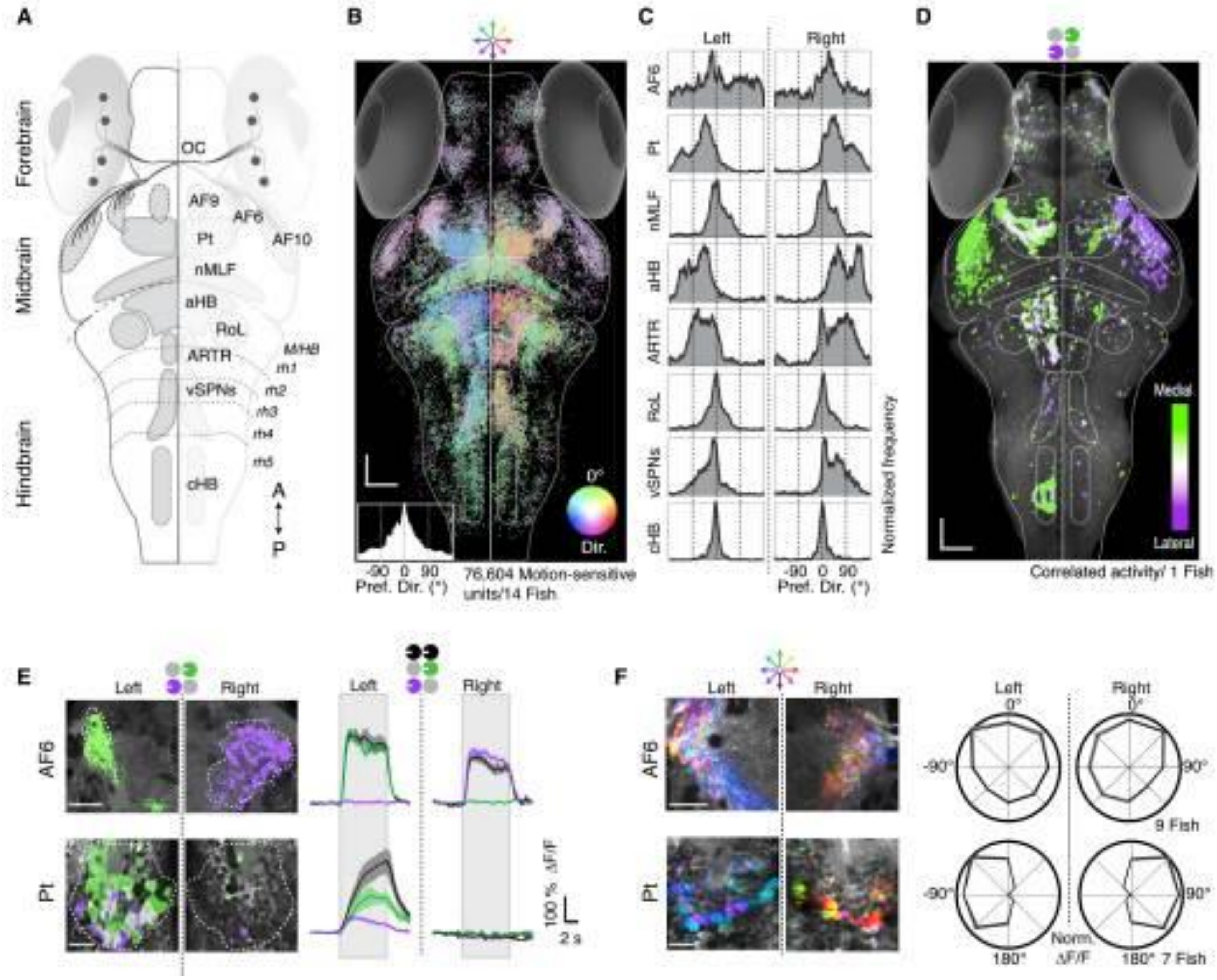
Whole-brain functional imaging at cellular resolution using light-sheet microscopy

Misha B Ahrens[1], Michael B Orger[2], Drew N Robson[3], Jennifer M Li[3] & Philipp J Keller[1]

Nature Methods **volume10**, pages413–420 (2013)



This dataset is publicly available!



Florian Engert lab; whole-brain larval zebrafish

Nguyen,..., Shaevitz, Leifer. PNAS February 23, 2016 113 (8)

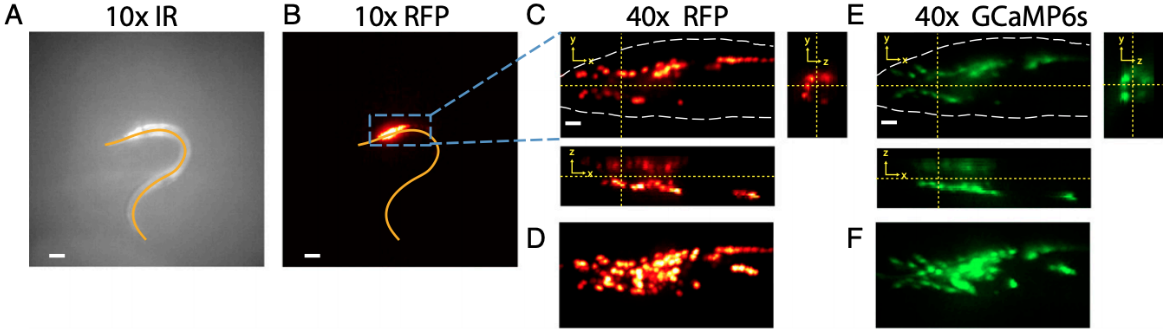
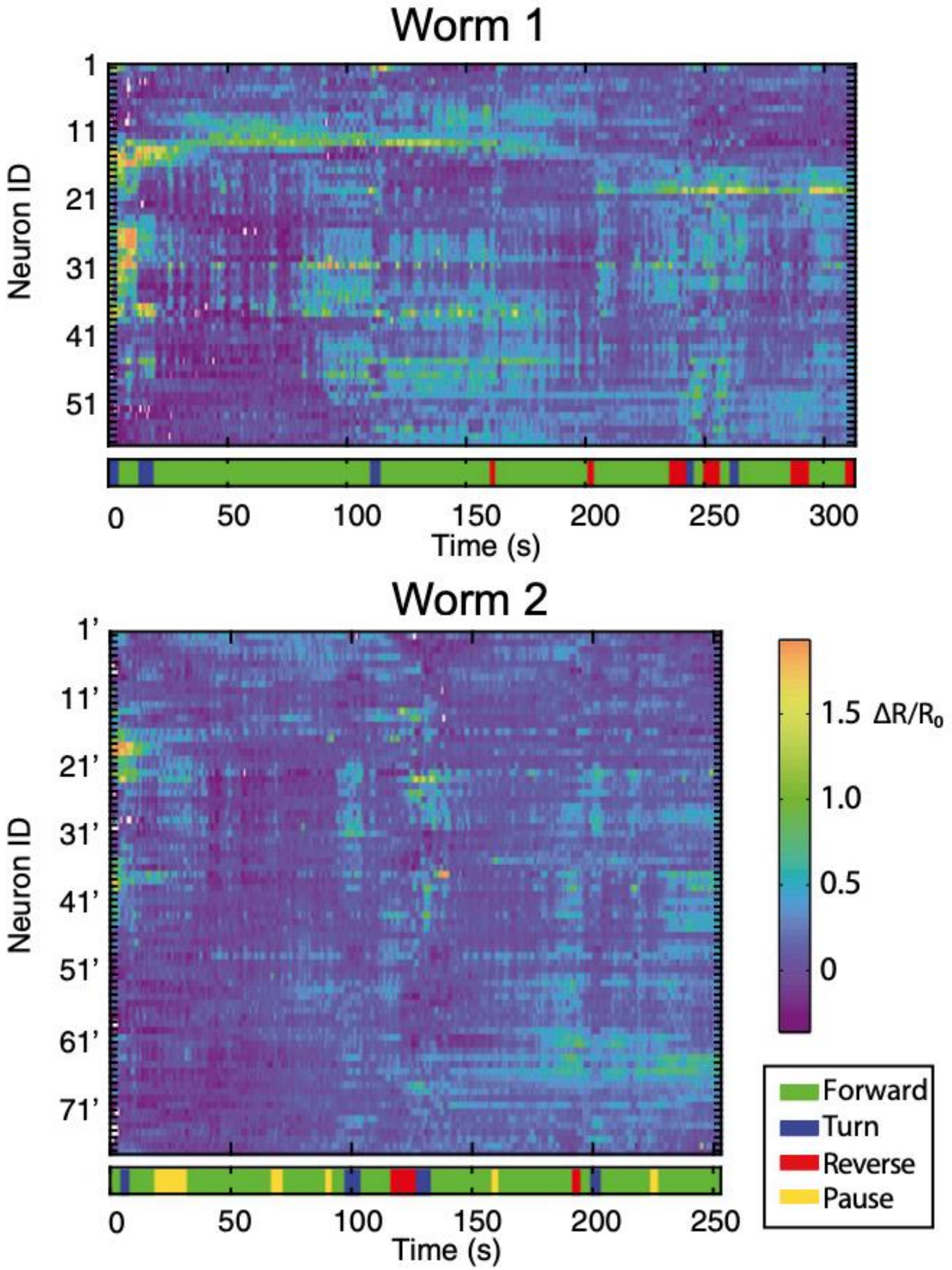


Fig. 2. Simultaneous recording of four video streams showing behavior and neural activity. (*A*) The worm's posture and behavior are recorded via infrared (IR) darkfield imaging through the 10× objective at 42 fps. (*B*) Fluorescence from neurons in the worm's head is tracked in real time to keep the worm centered in the field of view, via the 10× objective at 67 fps. (Scale bar, 100 μm.) Orange line indicates the worm's centerline. (*C–F*) Fluorescence images of neuronal nuclei are simultaneously recorded through the 40× objective at 200 fps as the objective scans through the worm's head along the axial imaging axis, *z*. A 3D volume is reconstructed from a *z*-stack of acquired images. (Scale bars, 10 μm.) (*C* and *E*) Individual *xy*, *xz*, and *zy* slices are shown for (*C*) RFP and (*E*) GCaMP6s. White dashed line indicates approximate outline of the worm's head. (*D* and *F*) Maximum intensity projection of the same volume is shown for (*D*) RFP and (*F*) GCaMP6s.

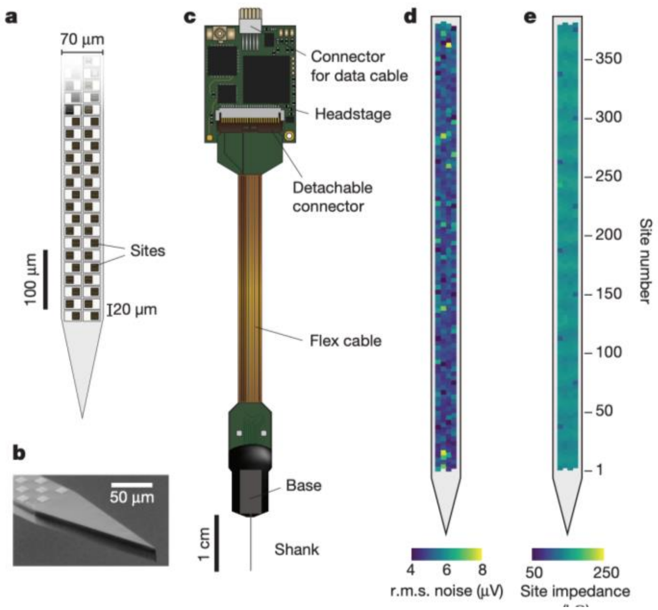


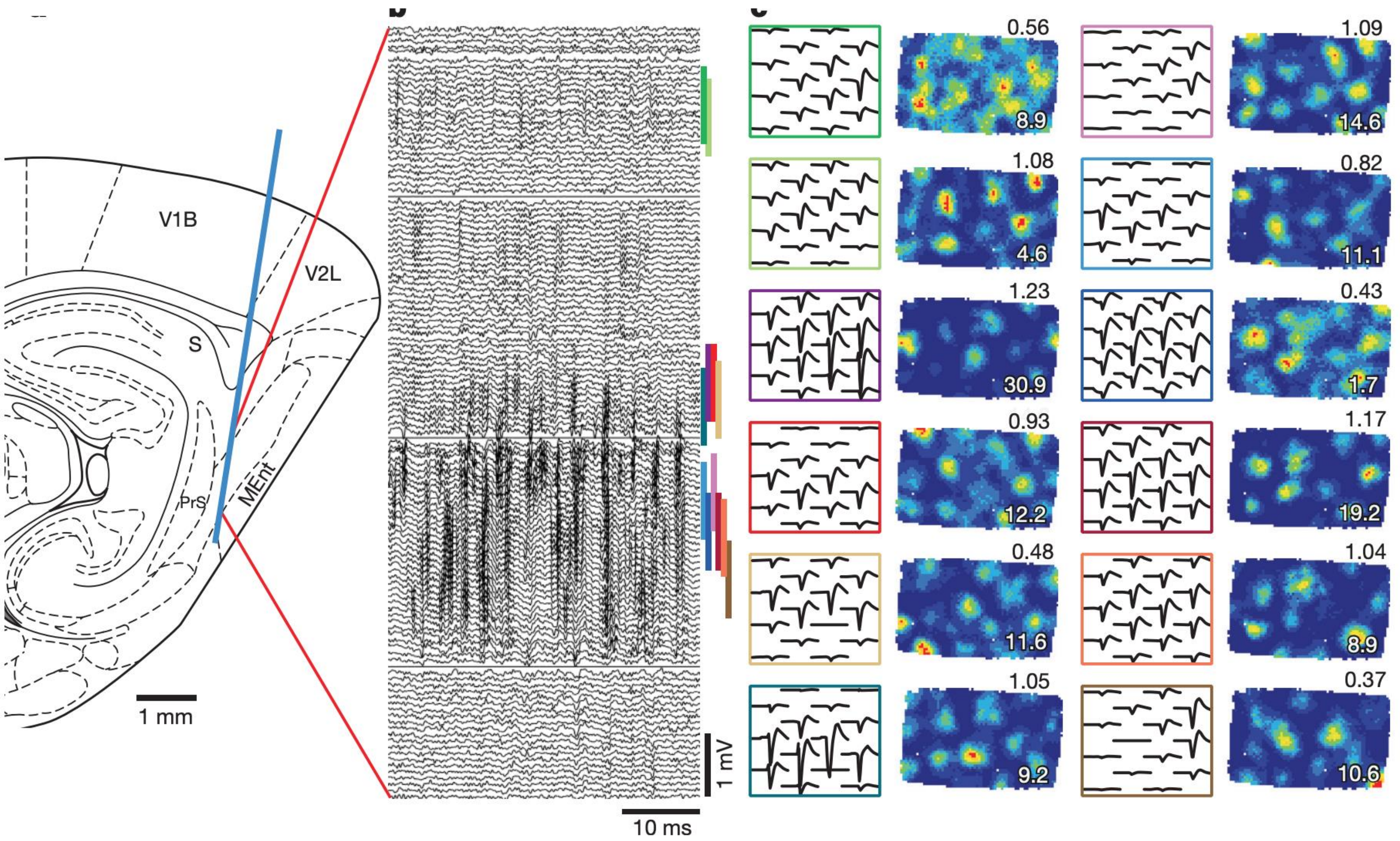
LETTER *Nature* **volume551**, pages232–236 (09 November 2017)

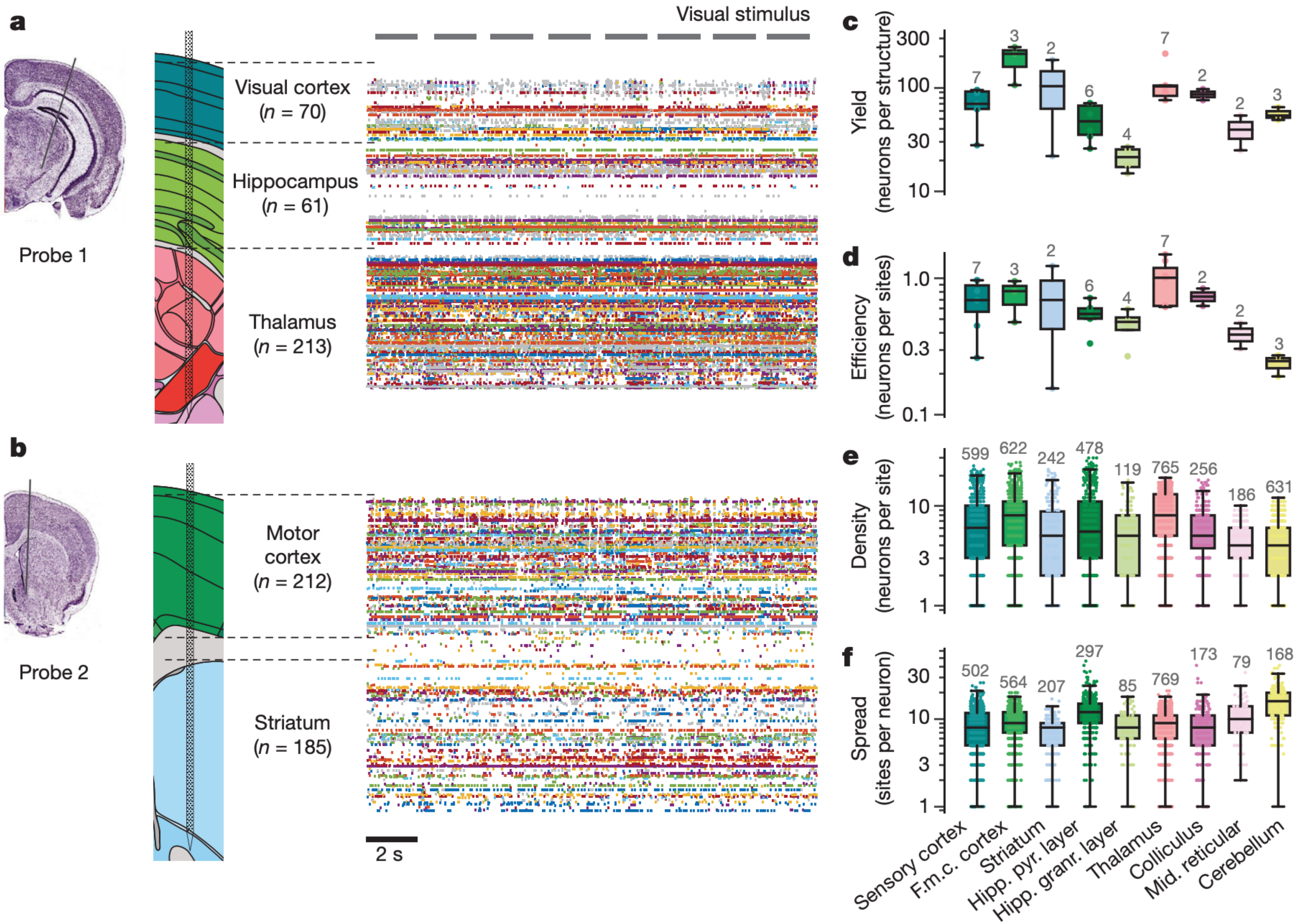
doi:10.1038/nature2463(

Fully integrated silicon probes for high-density recording of neural activity

James J. Jun[1]*, Nicholas A. Steinmetz[2,3,4]*, Joshua H. Siegle[5]*, Daniel J. Denman[5]*, Marius Bauza[6,7]*, Brian Barbarits[1]*, Albert K. Lee[1]*, Costas A. Anastassiou[5,8], Alexandru Andrei[9], Çağatay Aydın[10,11], Mladen Barbic[1], Timothy J. Blanche[5,12], Vincent Bonin[9,10,11,13], João Couto[10,11], Barundeb Dutta[9], Sergey L. Gratiy[5], Diego A. Gutnisky[1], Michael Häusser[3,14], Bill Karsh[1], Peter Ledochowitsch[5], Carolina Mora Lopez[9], Catalin Mitelut[5,8], Silke Musa[9], Michael Okun[2,3,15], Marius Pachitariu[2,3], Jan Putzeys[9], P. Dylan Rich[1], Cyrille Rossant[2,3], Wei-lung Sun[1], Karel Svoboda[1], Matteo Carandini[4], Kenneth D. Harris[2,3], Christof Koch[5], John O'Keefe[6,7] & Timothy D. Harris[1]





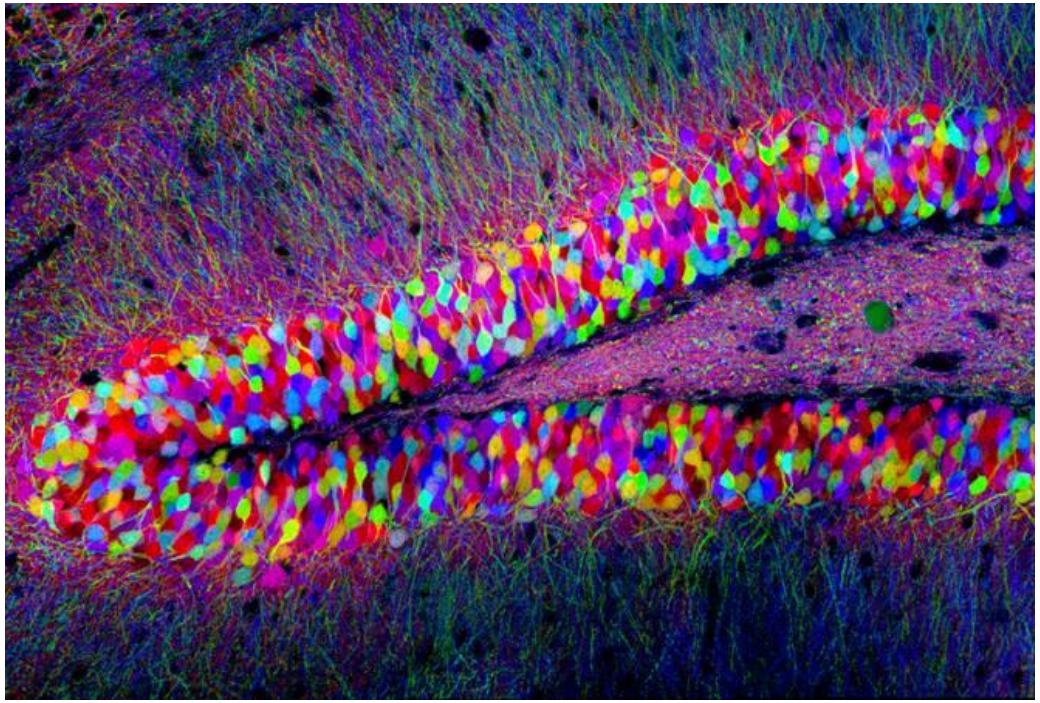


Nature **volume551**, pages232–236 (09 November 2017)

Anatomy

- Brainbow

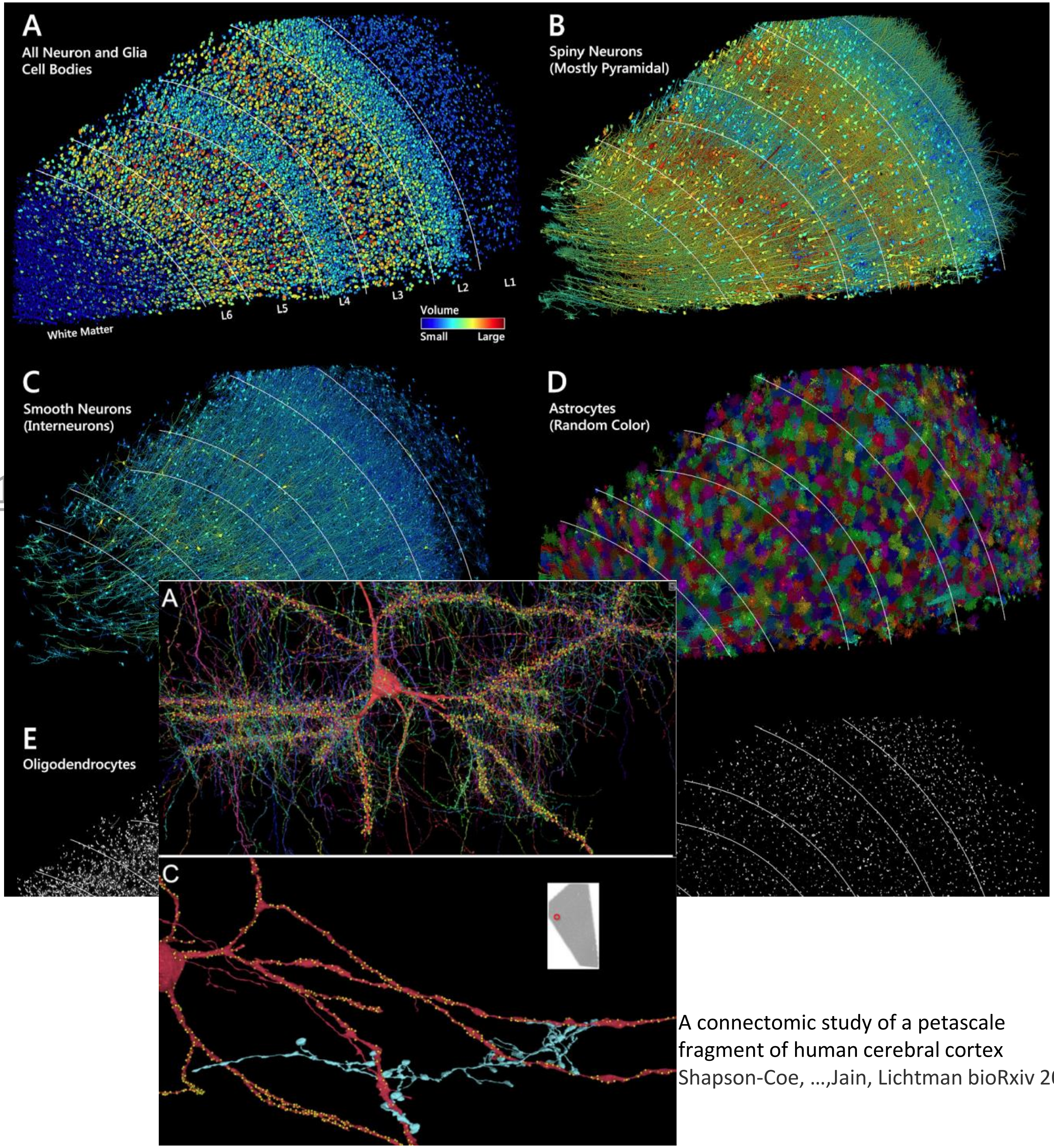
- Clarity with light-sheet microscopy: https://twitter.com/i/status/1338789504992358401



Livet J, Weissman TA, Kang H, Draft RW, Lu J, Bennis RA, Sanes JR, Lichtman, JW. Nature (2007) 450:56–62.

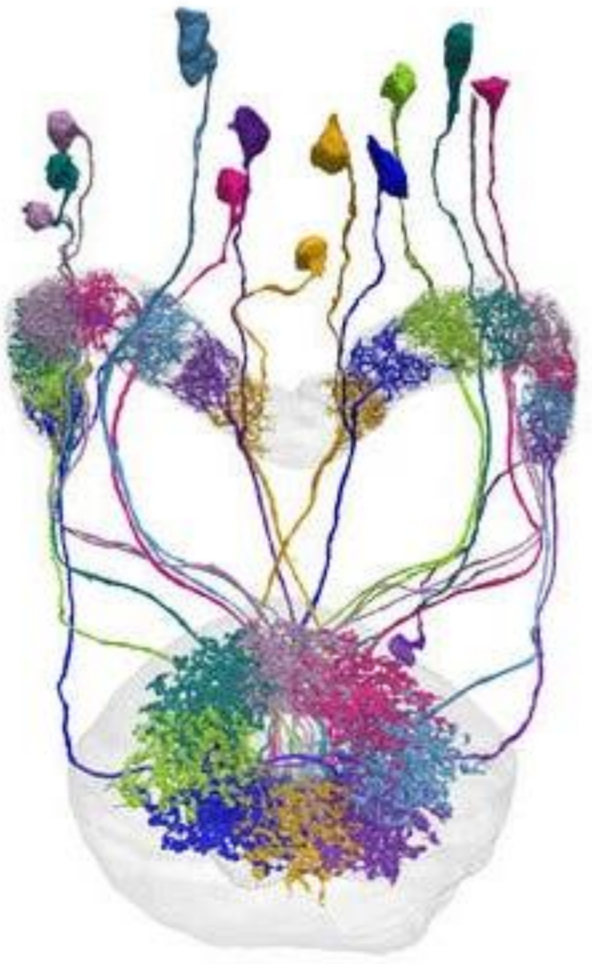
Anatomy

- Brainbow
- Clarity with light-sheet microscopy: https://twitter.com/i/status/1338789504992358401
- Electron microscopy and automated reconstruction
- Barcode-based connectivity analysis
- Dense EM connectivity: connectomics



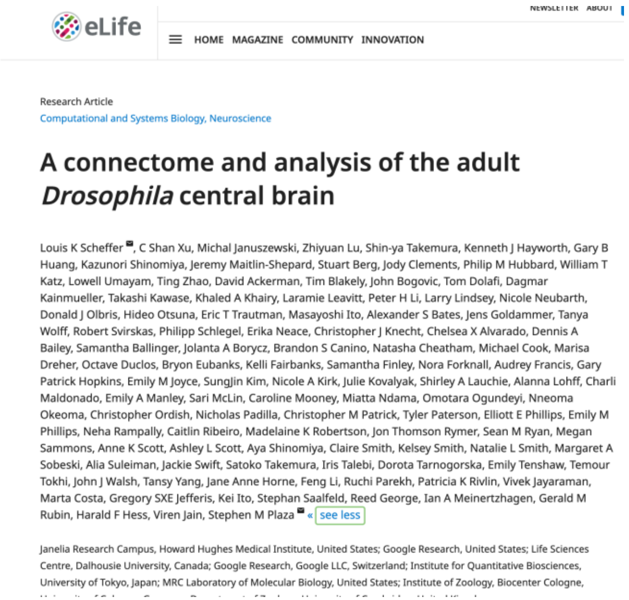
A connectomic study of a petascale fragment of human cerebral cortex
Shapson-Coe, …,Jain, Lichtman bioRxiv 2021

Dense connectivity diagram: ¾ of male fly brain



Head-direction circuit

If you were interested in function/intelligence/disorders, etc., what would you want to know/learn (from this and similar dataset(s))?



eLife

NEWSLETTER ABOUT

HOME MAGAZINE COMMUNITY INNOVATION

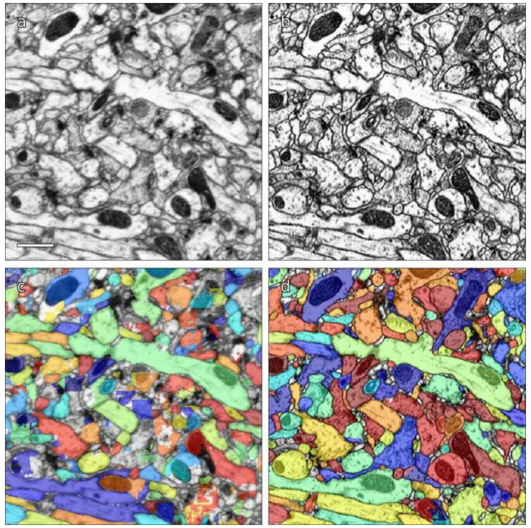
Research Article

Computational and Systems Biology, Neuroscience

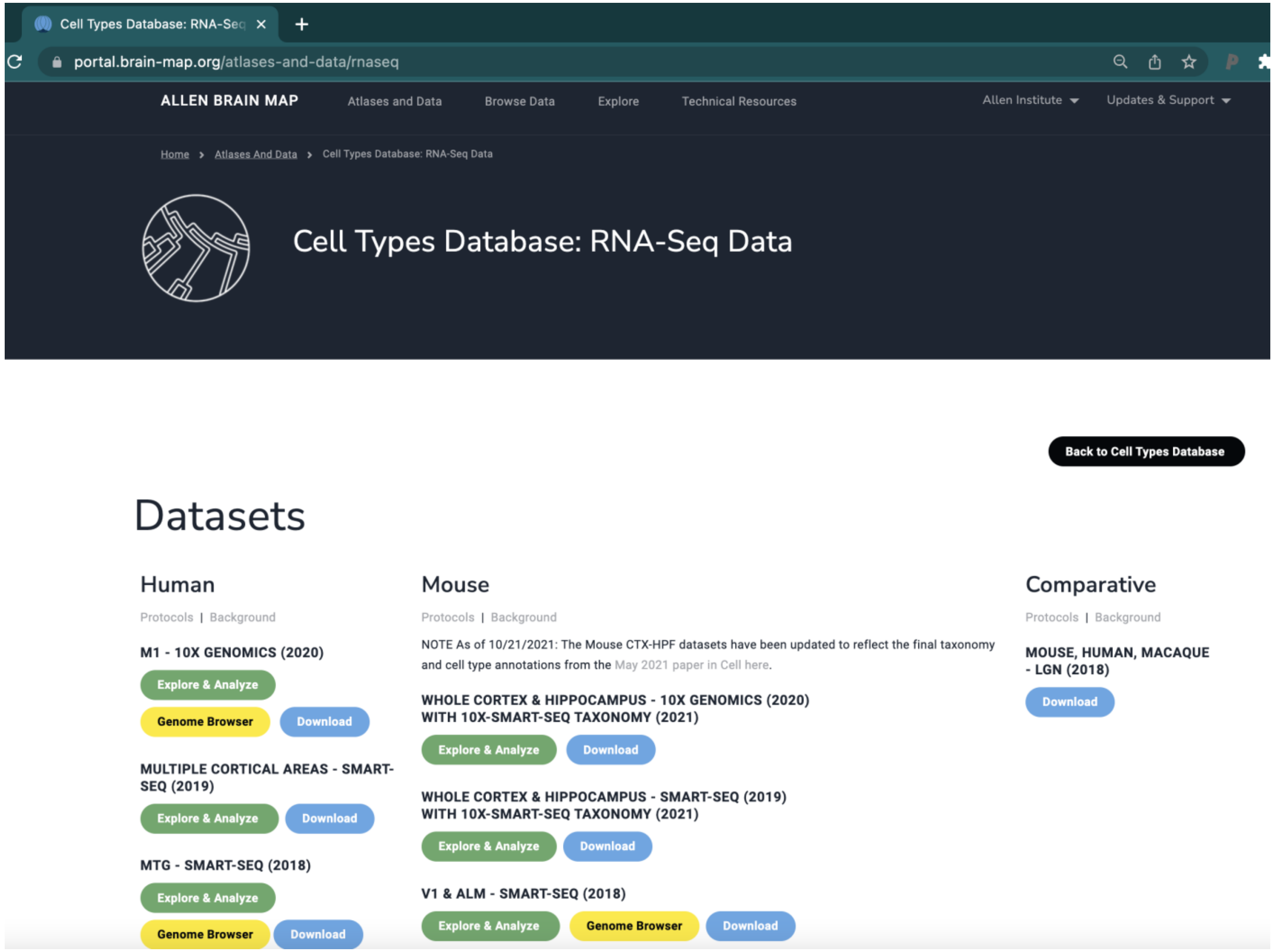
A connectome and analysis of the adult *Drosophila* central brain

Louis K Scheffer, C Shan Xu, Michal Januszewski, Zhiyuan Lu, Shin-ya Takemura, Kenneth J Hayworth, Gary B Huang, Kazunori Shinomiya, Jeremy Maitlin-Shepard, Stuart Berg, Jody Clements, Philip M Hubbard, William T Katz, Lowell Umayam, Ting Zhao, David Ackerman, Tim Blakely, John Bogovic, Tom Dolafi, Dagmar Kainmueller, Takashi Kawase, Khaled A Khairy, Laramie Leavitt, Peter H Li, Larry Lindsey, Nicole Neubarth, Donald J Olbris, Hideo Otsuna, Eric T Trautman, Masayoshi Ito, Alexander S Bates, Jens Goldammer, Tanya Wolff, Robert Svirskas, Philipp Schlegel, Erika Neace, Christopher J Knecht, Chelsea X Alvarado, Dennis A Bailey, Samantha Ballinger, Jolanta A Borycz, Brandon S Canino, Natasha Cheatham, Michael Cook, Marisa Dreher, Octave Duclos, Bryon Eubanks, Kelli Fairbanks, Samantha Finley, Nora Forknall, Audrey Francis, Gary Patrick Hopkins, Emily M Joyce, SungJin Kim, Nicole A Kirk, Julie Kovalyak, Shirley A Lauchie, Alanna Lohff, Charli Maldonado, Emily A Manley, Sari McLin, Caroline Mooney, Miatta Ndama, Omotara Ogundeyi, Nneoma Okeoma, Christopher Ordish, Nicholas Padilla, Christopher M Patrick, Tyler Paterson, Elliott E Phillips, Emily M Phillips, Neha Rampally, Caitlin Ribeiro, Madelaine K Robertson, Jon Thomson Rymer, Sean M Ryan, Megan Sammons, Anne K Scott, Ashley L Scott, Aya Shinomiya, Claire Smith, Kelsey Smith, Natalie L Smith, Margaret A Sobeski, Alia Suleiman, Jackie Swift, Satoko Takemura, Iris Talebi, Dorota Tarnogorska, Emily Tenshaw, Temour Tokhi, John J Walsh, Tansy Yang, Jane Anne Horne, Feng Li, Ruchi Parekh, Patricia K Rivlin, Vivek Jayaraman, Marta Costa, Gregory SXE Jefferis, Kei Ito, Stephan Saalfeld, Reed George, Ian A Meinertzhagen, Gerald M Rubin, Harald F Hess, Viren Jain, Stephen M Plaza « see less

Janelia Research Campus, Howard Hughes Medical Institute, United States; Google Research, United States; Life Sciences Centre, Dalhousie University, Canada; Google Research, Google LLC, Switzerland; Institute for Quantitative Biosciences, University of Tokyo, Japan; MRC Laboratory of Molecular Biology, United States; Institute of Zoology, Biocenter Cologne,



Large-scale single-cell gene expression (scRNAseq)

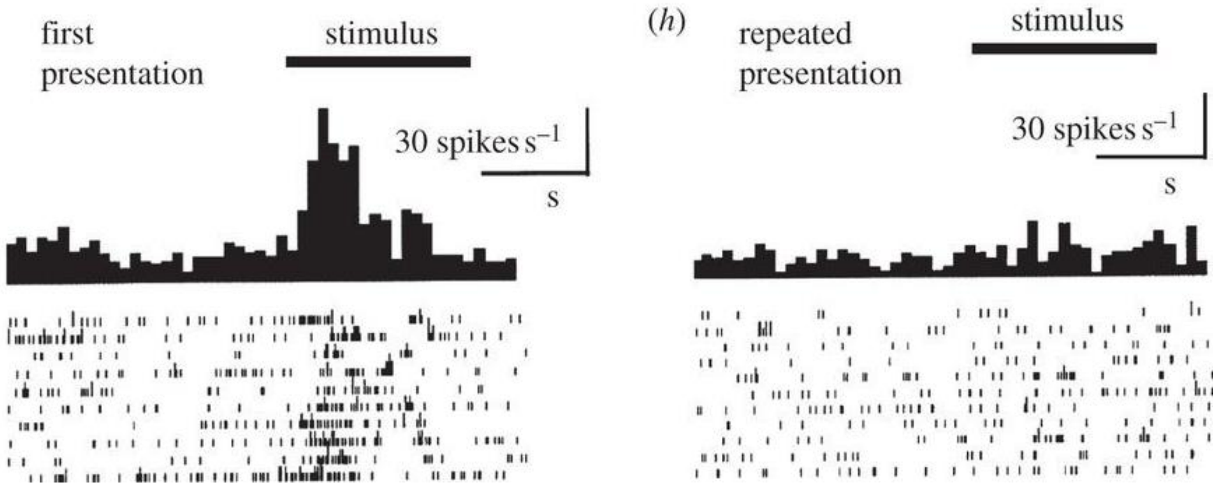


Newest frontiers: Combining activity, connectomics, gene expression data in single brains

Nature vs. nurture?
Function-connectivity relationships?

Functional anatomy and beyond: fMRI (BOLD-contrast) and associated tools

- 1. Repetition suppression

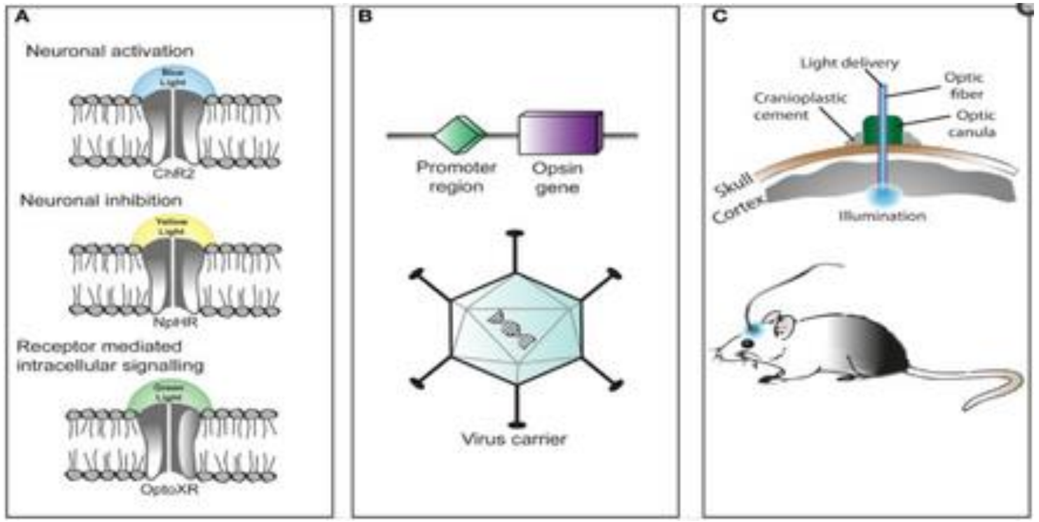


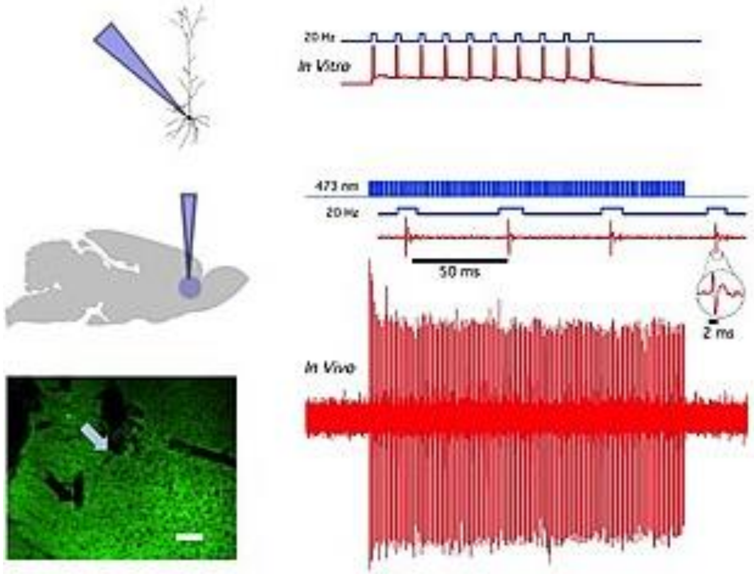
Gross CG, Schiller PH, Wells C, Gerstein GL. 1967Single-unit activity in temporal association cortex of the monkey. *J. Neurophysiol*. **30**, 833–843.

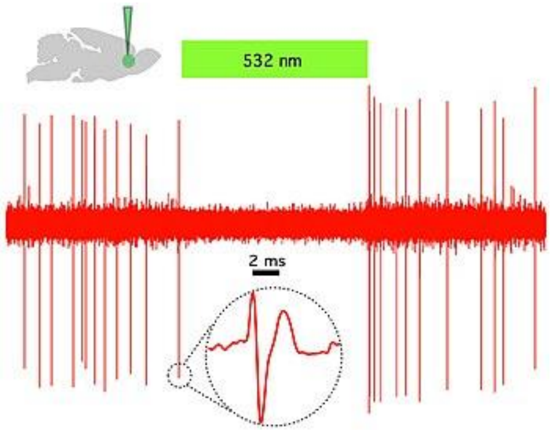
- 2. Multivariate pattern analysis (MVPA)
  - Characterize patterns of voxel intensity
  - Depends on topographic organization of functionally related neurons

Perturbation methods:

Optogenetics: Halo- and channel- rhodopsin







Chemical lesion/agonist/antagonist injection

Chemogenetics: DREADDS
Designer receptors exclusively activated by designer drugs

Cannulae: neuromodulatory measurement and perturbation

See methods review by:
Kim, Adhikari, Deisseroth, Nat Rev Neurosci. 2017

Development of different animal systems to probe cognitive behaviors

Flies can maintain a sense of orientation and make on-the-fly (!) decisions of what to do during courtship.

Mice and rats can navigate mazes and solve other spatial tasks.

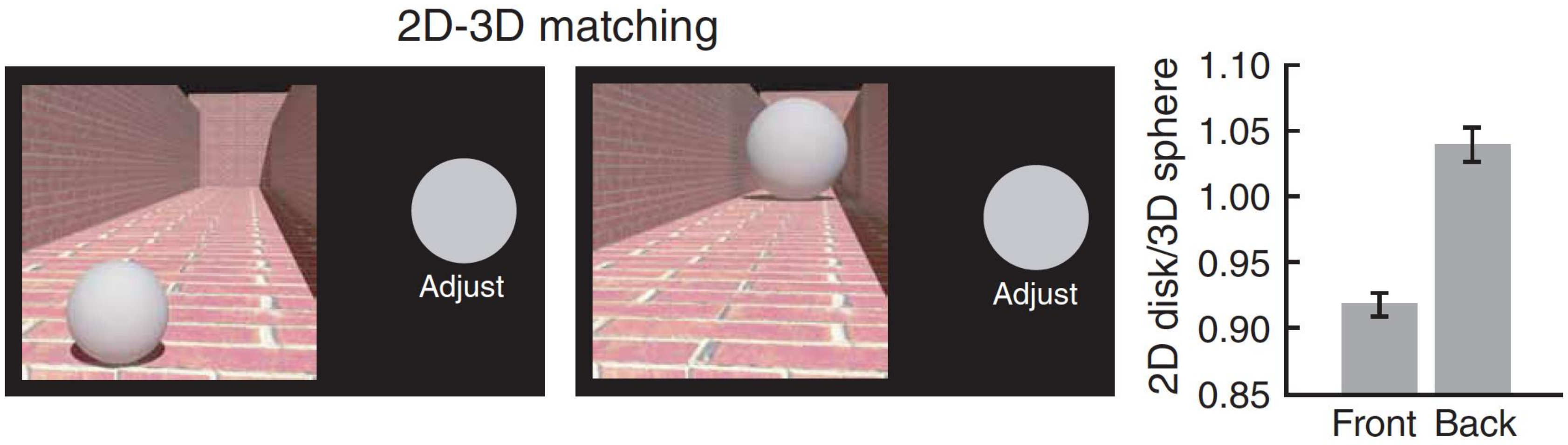
Chimpanzees can play video games: https://www.youtube.com/watch?v=2gnHkOTEsi8

And now neuroscientists can record cellular-resolution activity in neural circuits during such tasks.

Computational tools

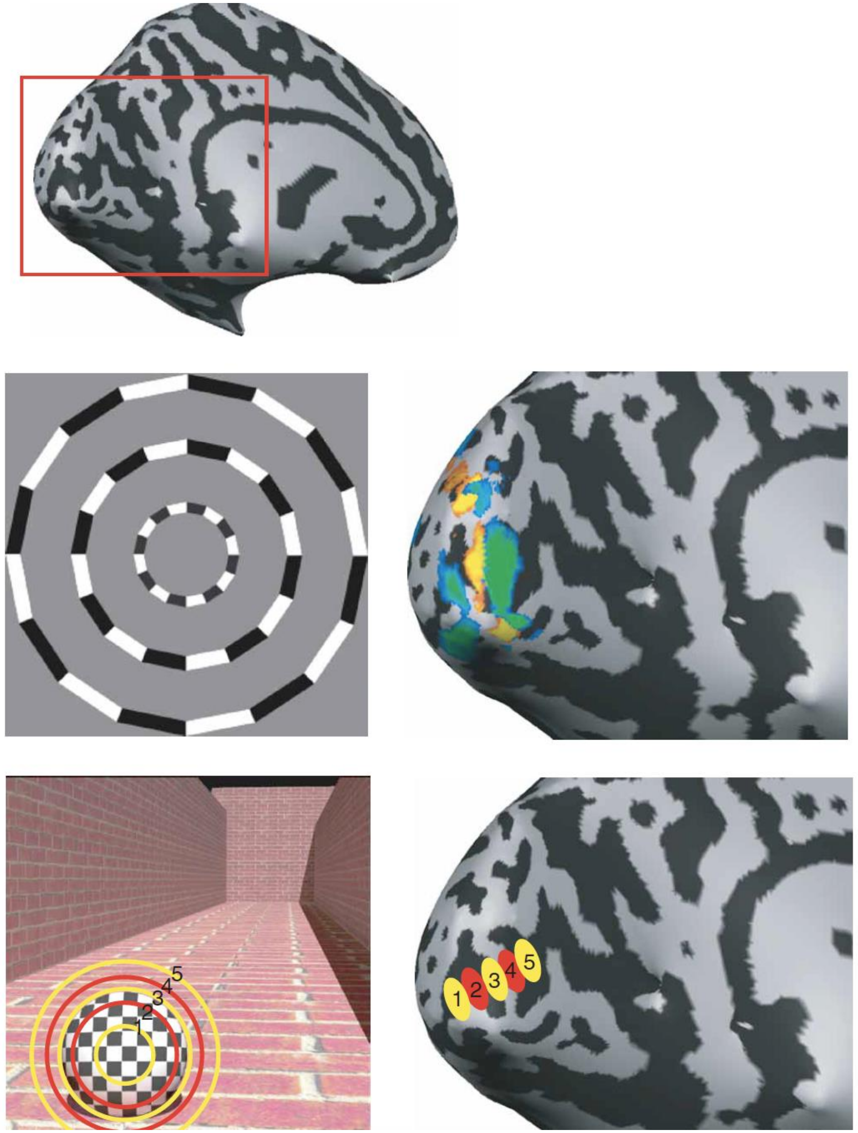
- Trainable hierarchical models: DNNs/ANNs.
- Powerful statistical models for data analysis.
- Mathematical concepts and tools: dynamical systems analysis, topological data analysis and other high-dimensional methods for structure discovery, information theory and error correction, signals detection theory, compressive sensing, control theory, reinforcement learning, simulation, rendering, etc.

Size, shape, and form perception: contribution of brain areas



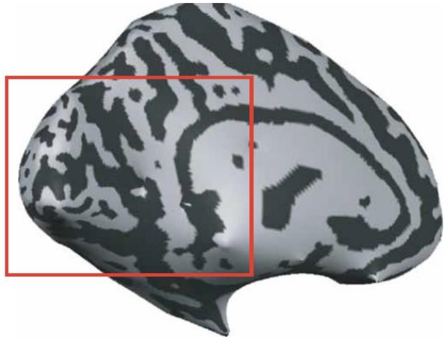
Murray, Boyachi, Kersten, 2006

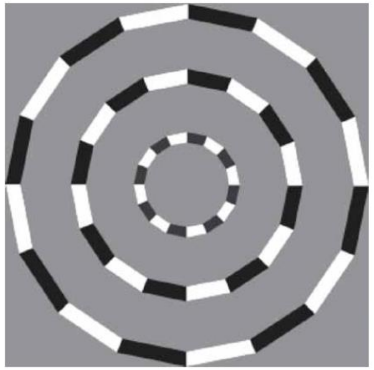
Size, shape, and form perception: contribution of brain areas

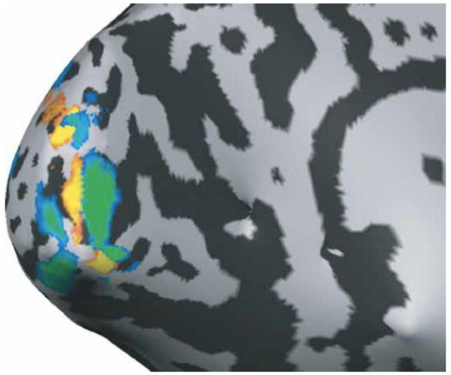


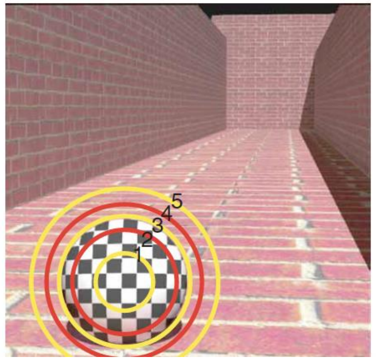
Murray, Boyachi, Kersten, 2006

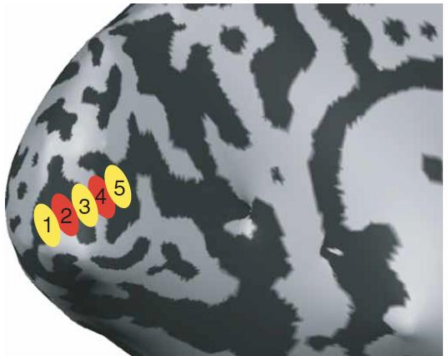
Size, shape, and form perception biases expressed as low in neural hierarchy as V1

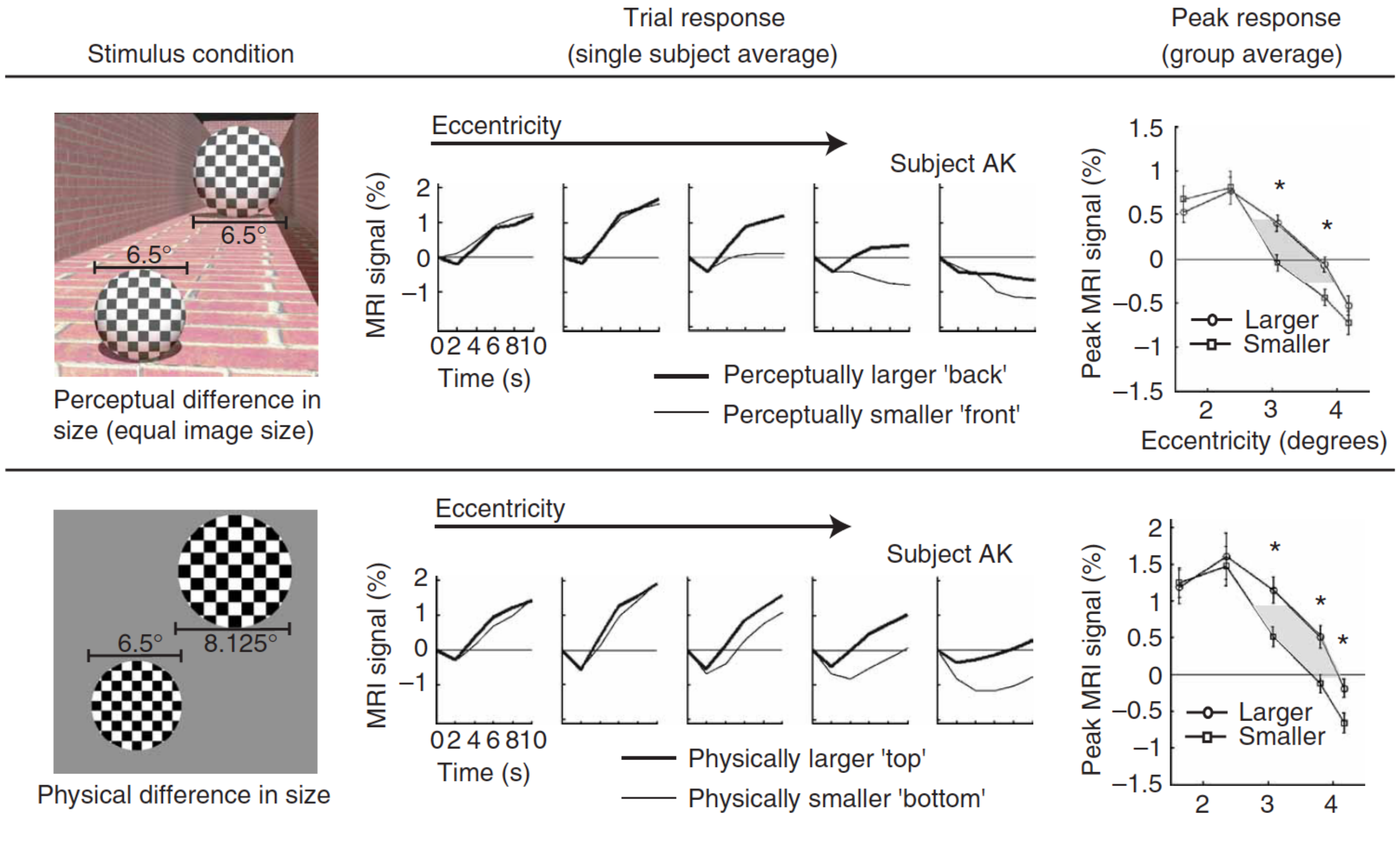






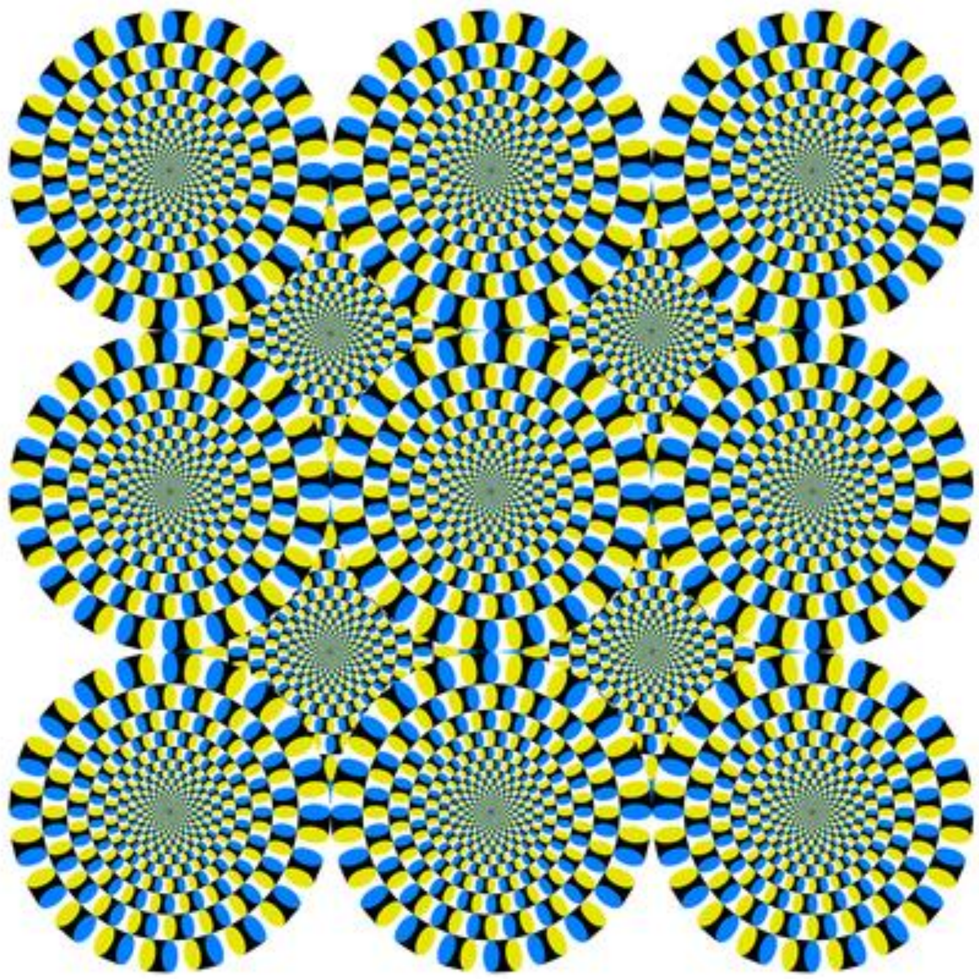


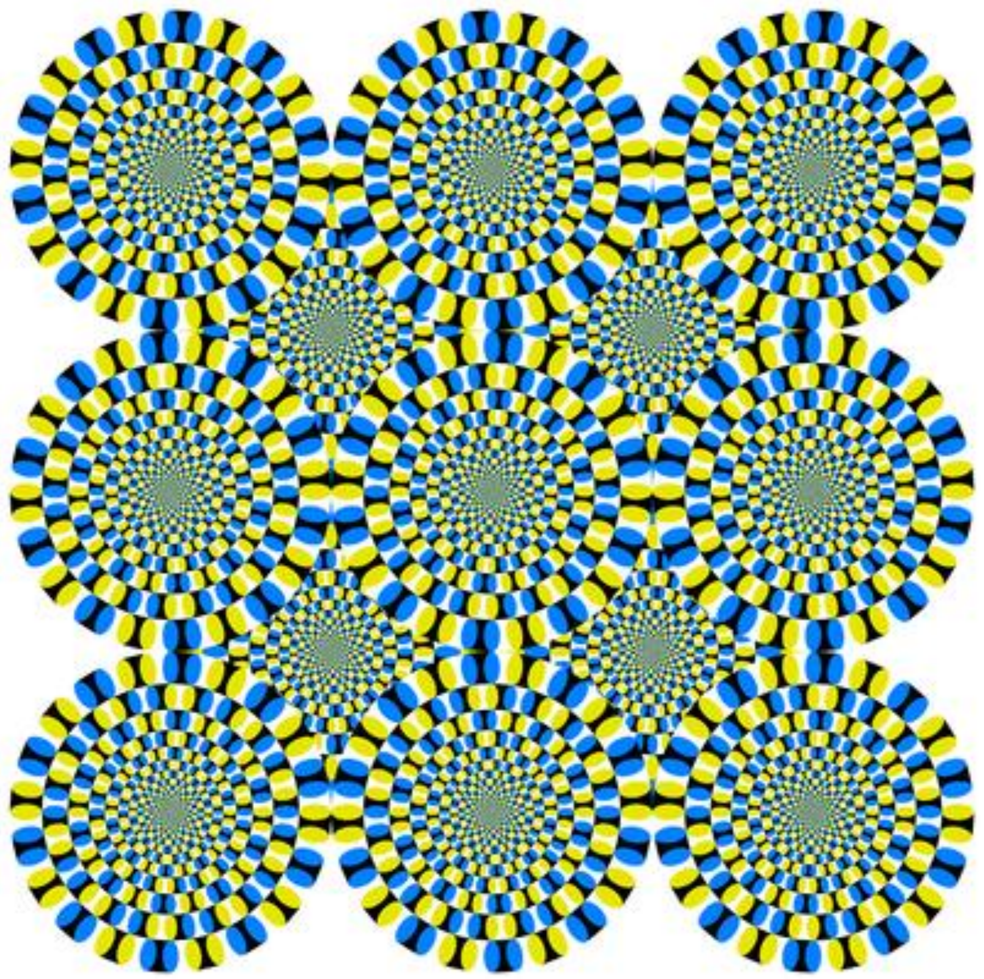




Murray, Boyachi, Kersten, 2006

Motion perception: illusory motion in a static image





Moving snake akiyoshi kitaoka

Motion perception as prediction? The flash-lag effect

Flash-lag effect https://michaelbach.de/ot/mot-flashLag/

Motion perception as prediction: the flash-lag effect

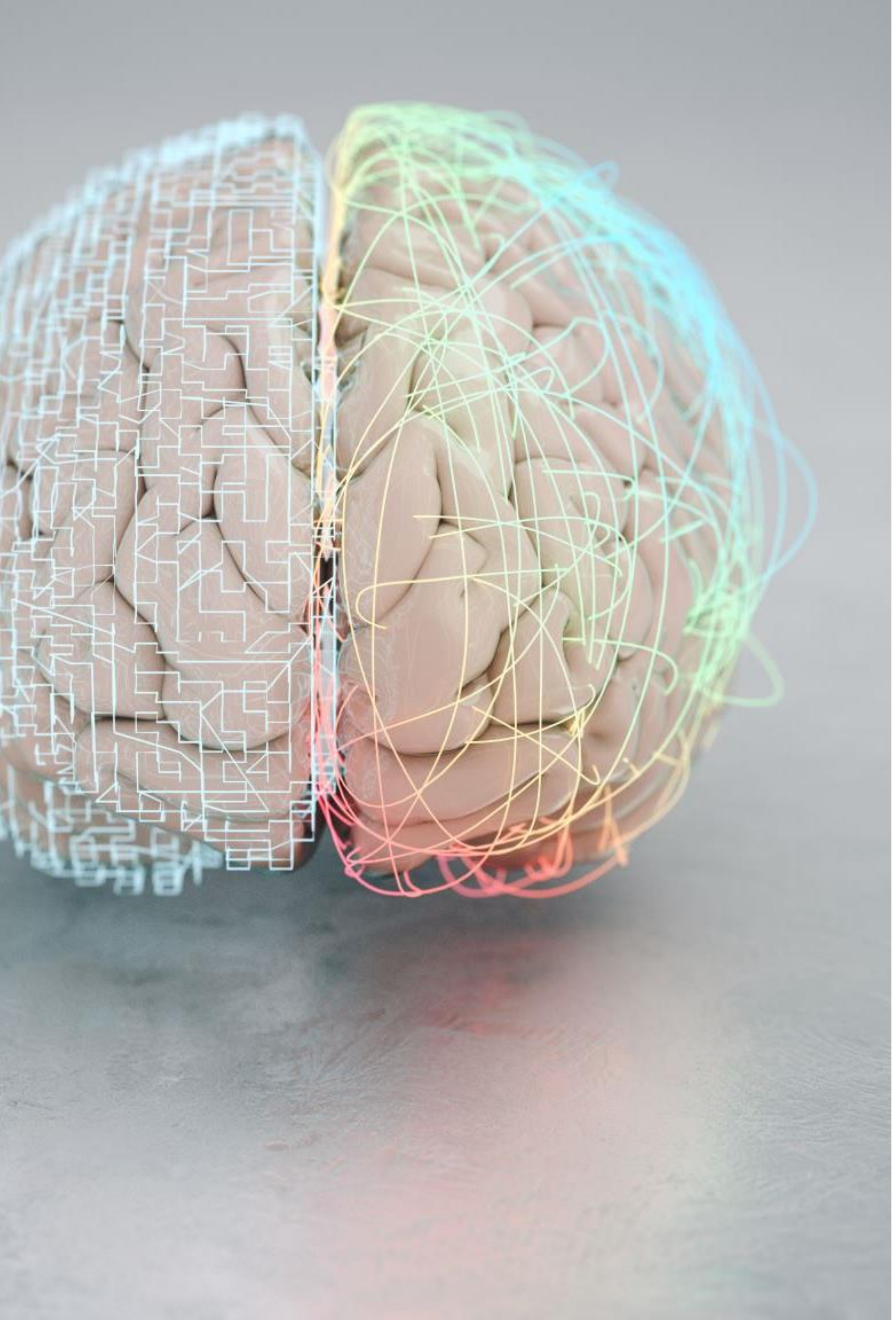
Two explanations:

Prediction: Compensation of slow visual processing by predicting where the continuously moving line will be. Flashed stimulus cannot be similarly compensated, so lags behind.

Filtering: Given that evidence is noisy, it needs to be integrated in time to reach some measure of certainty. Filtering the moving stimulus forward in time causes the overall estimate of its position to be further along than it was at the time of the flash.

If these biases are important for perception, how many of these illusory effects do ML techniques exhibit?

(Not many! Kitaoka moving snake is one example…what about flash-lag in video models?)



Summary

- Reasons to study the brain
- Differences between ML/neuroscience
- Incredible technologies to probe the brain at single-cell and whole-brain level, during rich behavior.
- What is cognition?
- Maybe: Processing that combines sensory experience and internal states to construct abstract representations/interpretations of the world?