

Of Two Minds: A Neuroscientist Balances Science and Faith

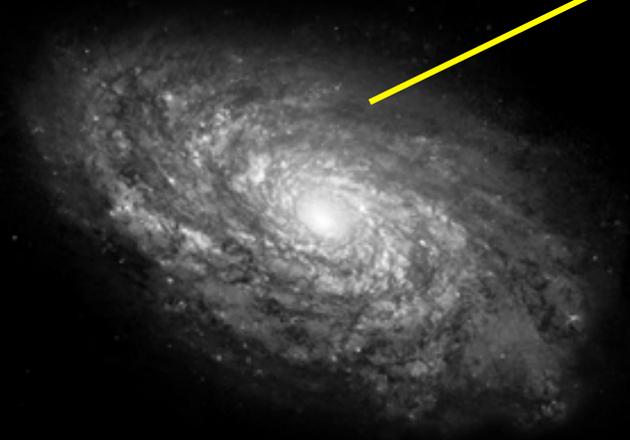
*Bill Newsome
Harman Family Provostial Chair
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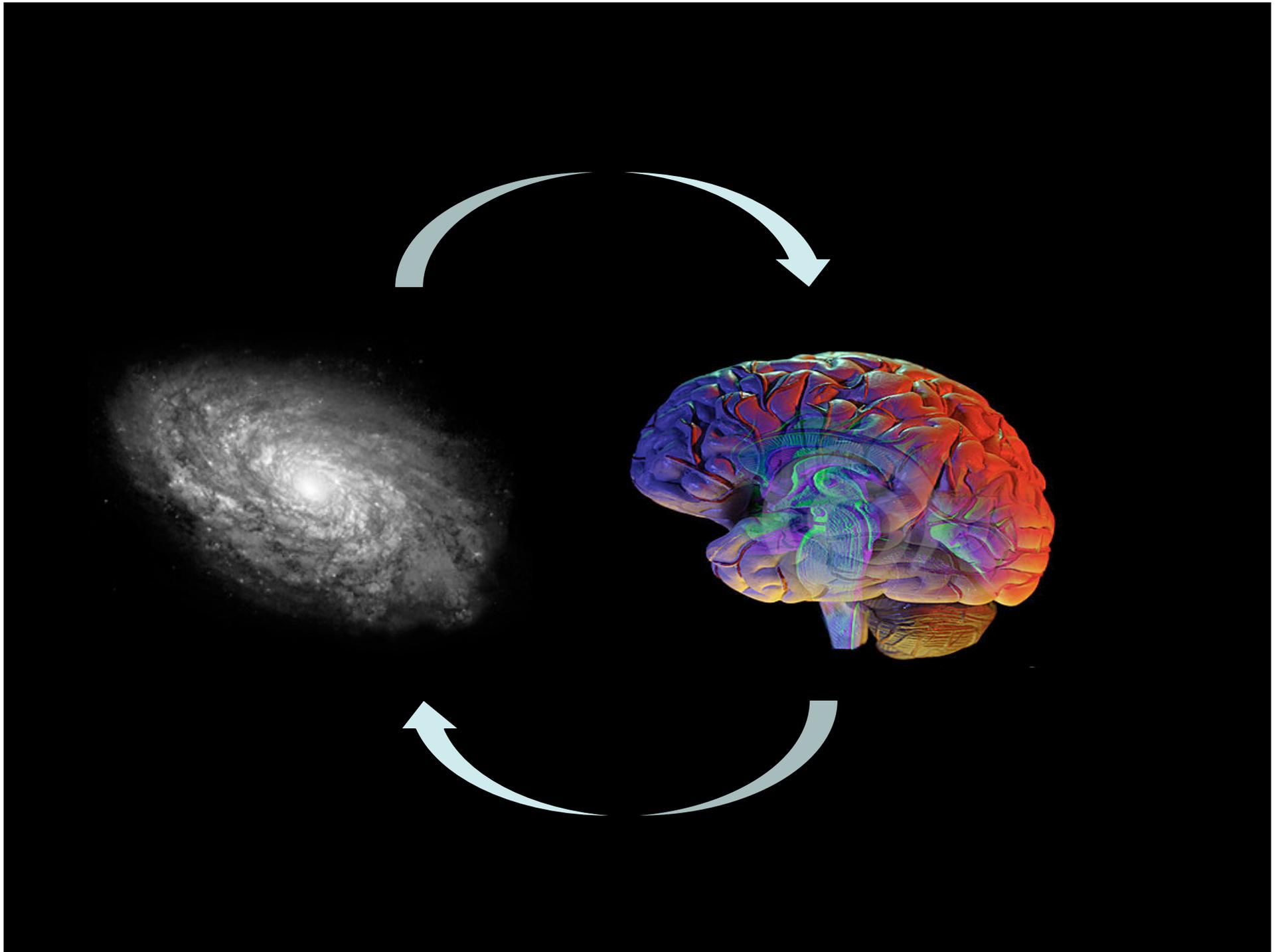
American Scientific Affiliation
Azusa, California
July 22, 2016



THE BIG PICTURE

You are here.





BRAIN 2025: A scientific vision

<http://www.nih.gov/science/brain/2025/index.htm>

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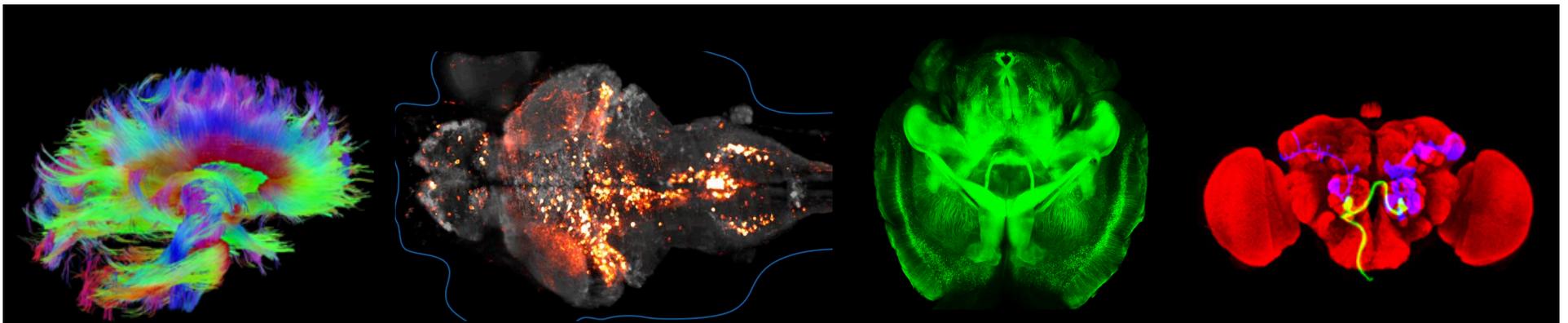
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Co-Chair, ACD BRAIN Working Group



A FOCUS ON CIRCUITS AND NETWORKS

To map the circuits of the brain, measure the fluctuating patterns of electrical and chemical activity flowing within those circuits, and understand how their interplay creates our unique cognitive and behavioral capabilities.



A FOCUS ON CIRCUITS AND NETWORKS

60 years

of single-neuron recordings

40 years

of molecular biology

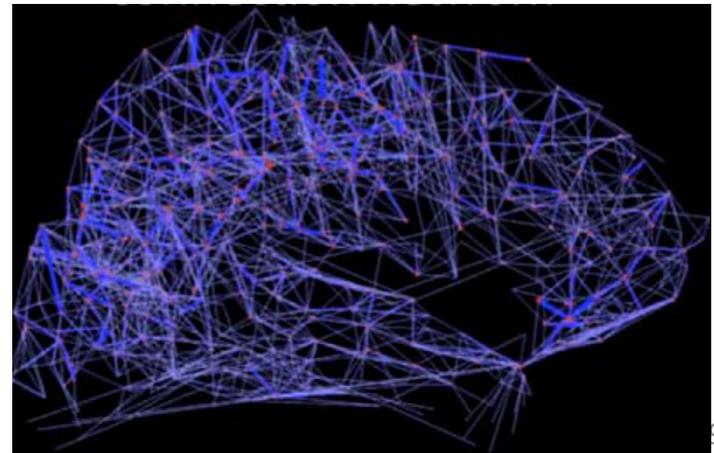
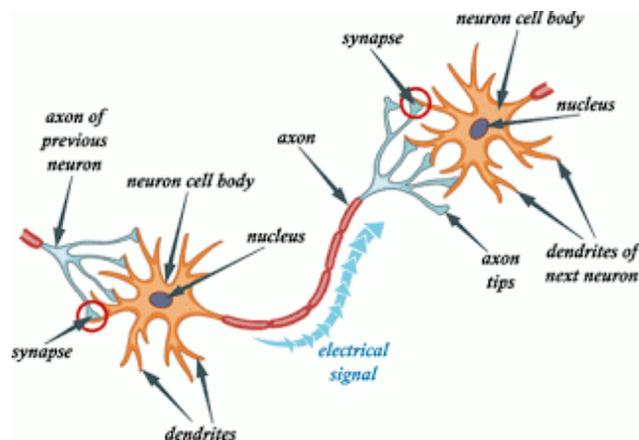
20 years

of brain imaging (fMRI)

What is missing:

Cognition, emotion, memory, action are generated by **circuits and networks** of thousands to millions of interconnected neurons.

How do they work?



REVERSE ENGINEERING THE BRAIN

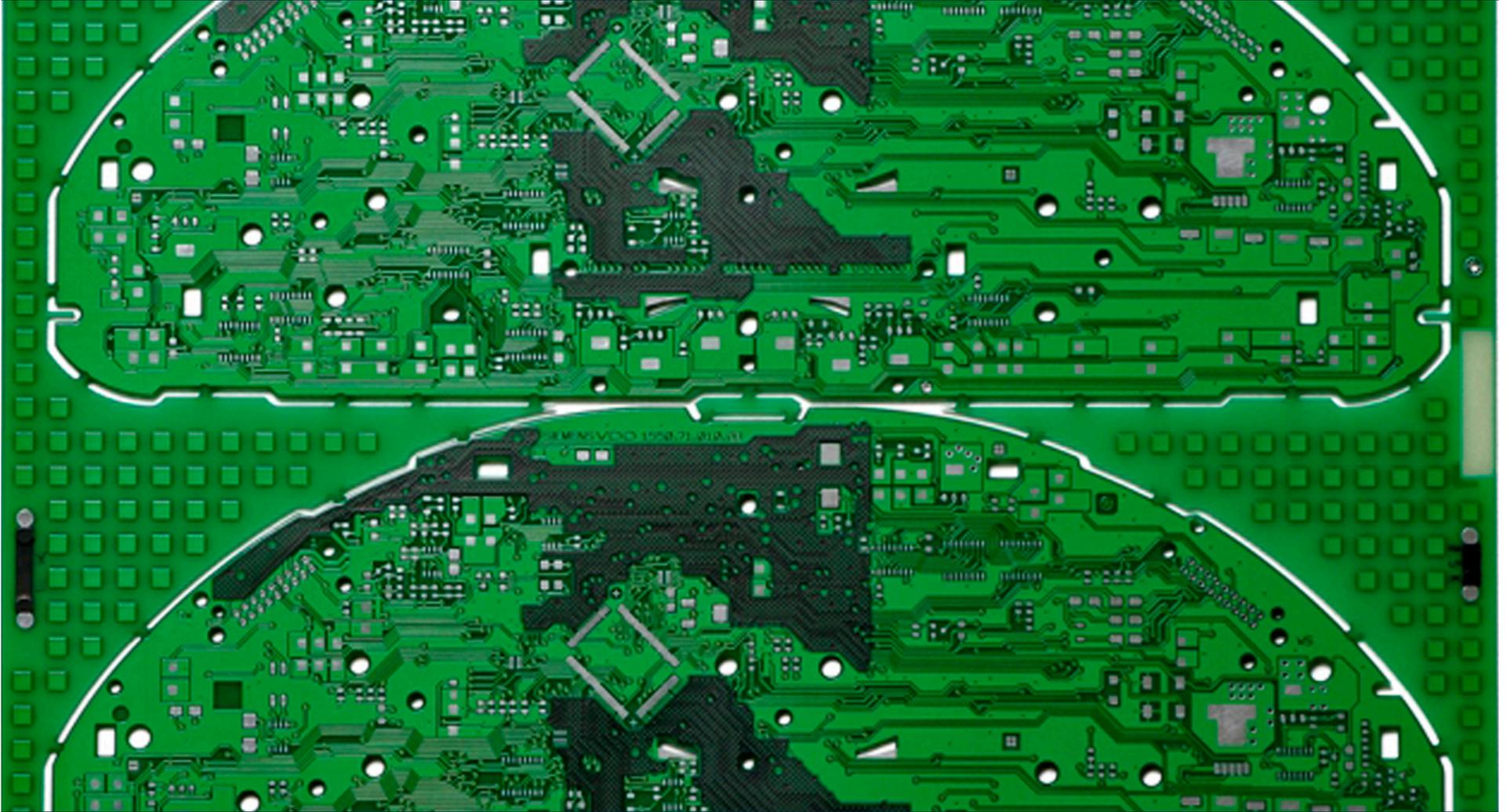


100 BILLION NEURONS, 100 TRILLION SYNAPSES

REVERSE ENGINEERING A DVD PLAYER



CIRCUITS !

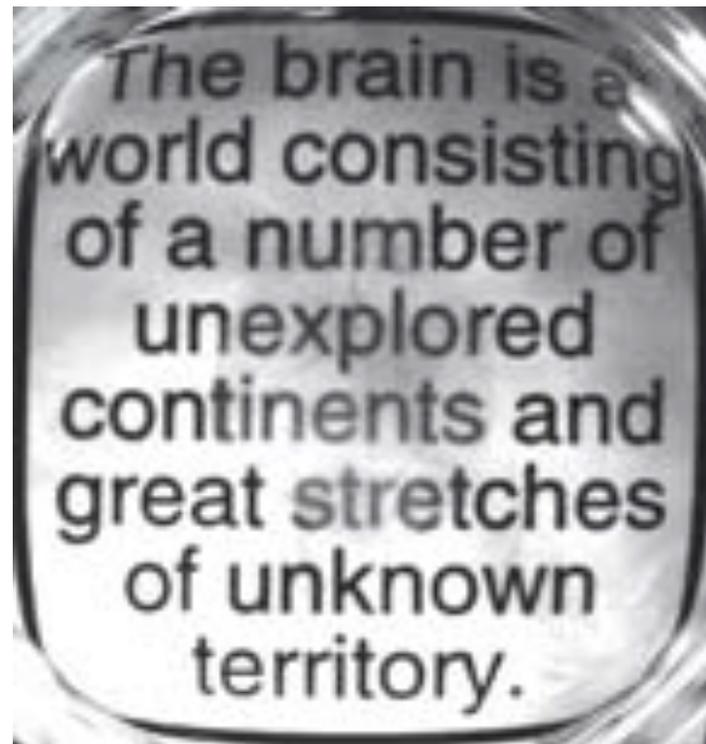
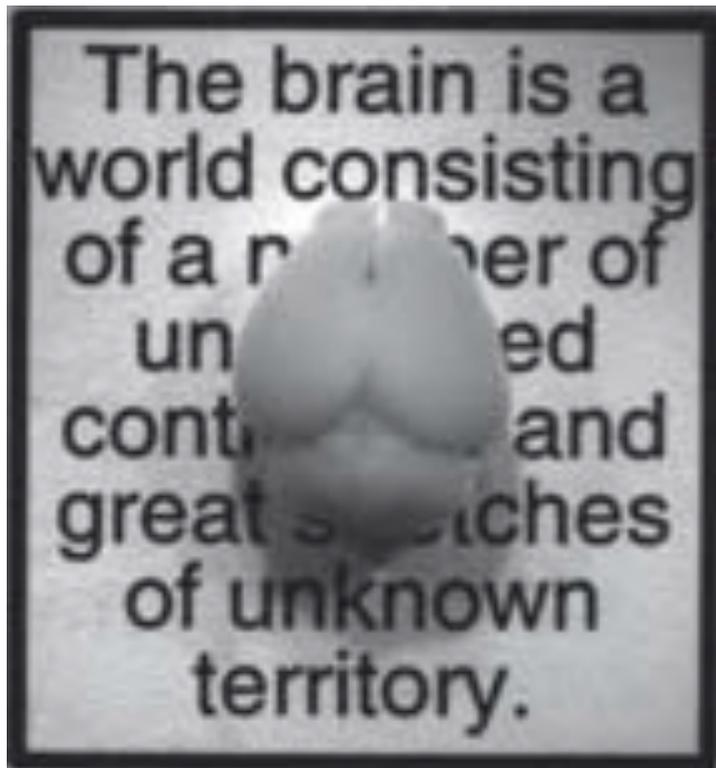


FOUR CRITICAL CHALLENGES

- Map the circuits!
- Measure the signal dynamics!
- Manipulate the signals, test effect on behavior!
- Computation: theory, networks, data analytics!

The barriers are falling on all fronts!

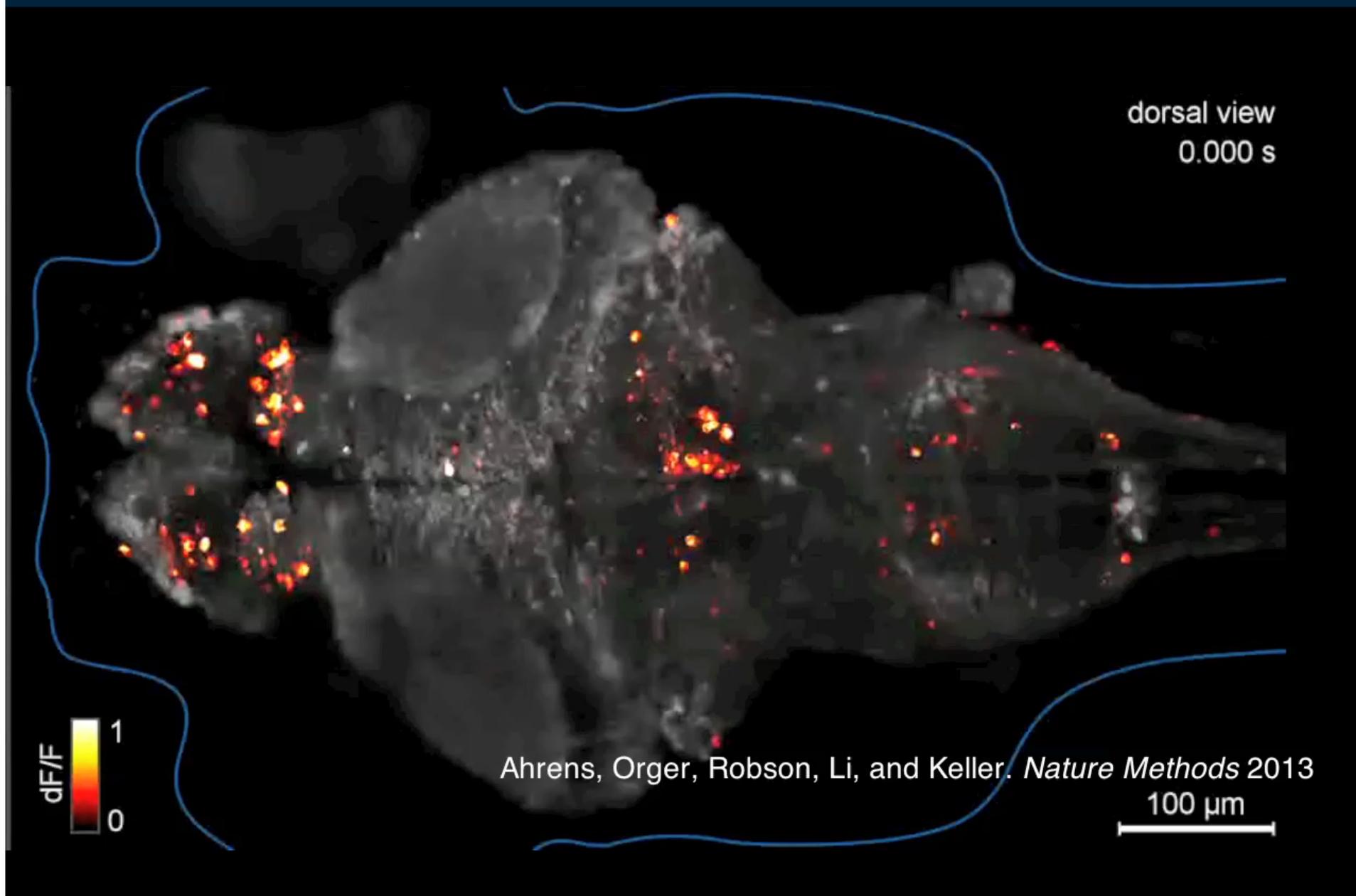
Circuit Diagram – CLARITY
Deisseroth lab – Stanford University
(Nature, 2013)



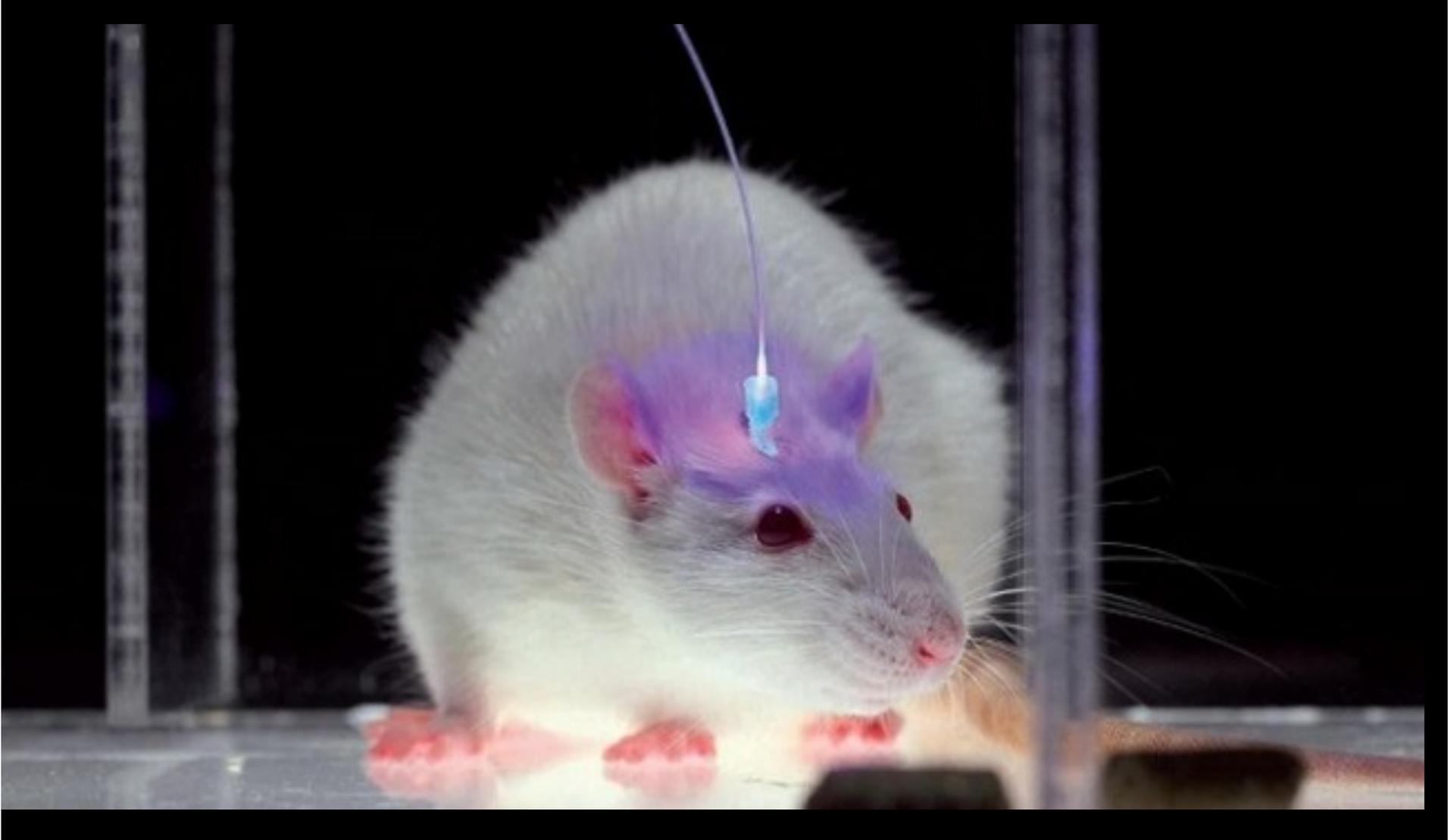
Get rid of lipids – no need to slice & dice physically!

Circuit Diagram – CLARITY
Deisseroth lab – Stanford University
(Nature, 2013)

Activity map



OPTOGENETICS



OPTOGENETICS IN ACTION

Hong, et al, Cell 2015. Anderson lab, Caltech.

FOUR CRITICAL BARRIERS

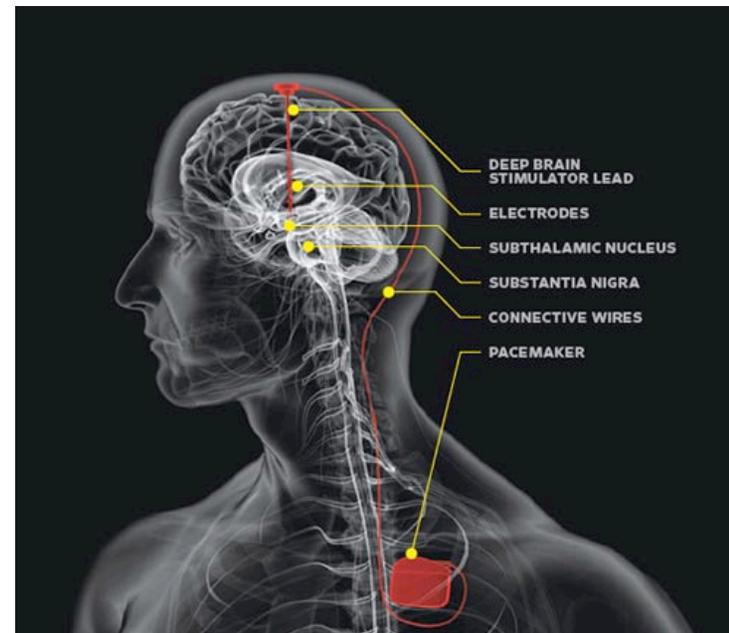
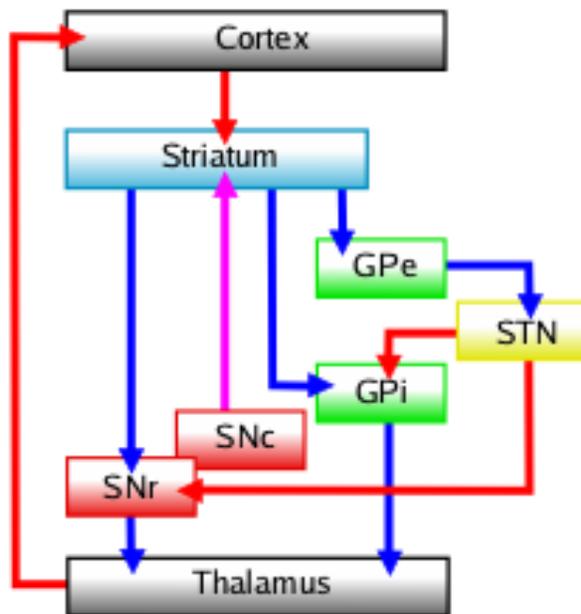
- Map the circuits!
CLARITY, DWI, others?
- Measure the signal dynamics!
New microscopies, calcium imaging hi-field fMRI
- Manipulate the signals!
Optogenetics, DREADDS, TMS, Ultrasound?
- Computation: theory, networks, data analytics!
Dynamical systems, recurrent nets, Bayes, ML

The barriers are falling on all fronts!

THE PROMISE OF CIRCUIT-BASED INTERVENTIONS

Circuit-based interventions have great potential,
but first we must identify the circuits

Deep Brain Stimulation: A circuit-based treatment for Parkinson's Disease



The problem of volition, consciousness

Desmurget, et al,
Science, 2009

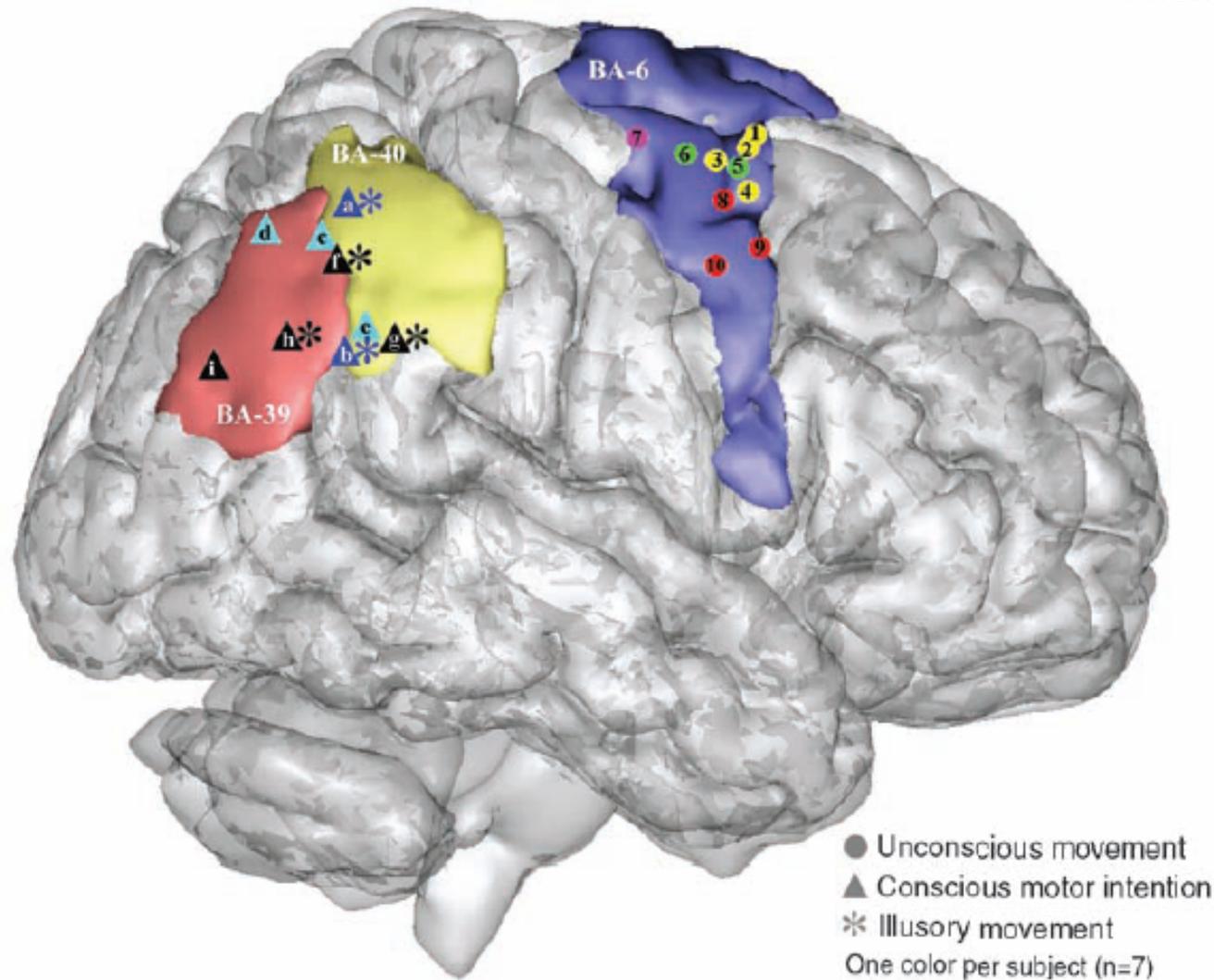


Fig. 1. Premotor and parietal responsive sites shown after registration of the individual MR image to the MNI template. Left stimulations have been reported on the right hemisphere. Colored areas define the anatomical boundaries of BA 40 (yellow), BA 39 (orange), and BA 6 (blue).

The central dogma of neuroscience:

All of our behavior and all of our mental life—including our sense of a conscious, continuing self— is inextricably linked to the biology of the brain.

“What about free will”

“I am not a fatalist...

But even if I were, what could I
do about it?”

Bottom-up determinism

The quantum brain

Freedom = uncaused

Self-determination, or autonomy

Self-determination (autonomy):

My behavior is caused, at least in part, by my beliefs, values, memories, goals and aspirations.

Conscious, rational thought plays a causal role in my behavior.

Key issue: what counts as a “cause”?

Scientific explanation and “reduction”

Quotes from Carl Craver, 2007, [Explaining the Brain](#)

“According to the “classical” model of reduction (Nagel, 1949, 1961) from which [most current] models descend, reduction is a species of covering law (CL) explanation: one theory is reduced to another when it is possible to define the theoretical terms of the first with those of the second and to derive the first theory from the second...”

“The metaphysical fundamentalist argues that nonfundamental things have no causal power over and above fundamental things. They believe, roughly, that everything has cause at the fundamental level (the principle of causal completeness of the physical) and that nothing has more than one complete cause (the principle of non-overdetermination). If so, it follows that no nonfundamental things are causes....”

(Bill's) Problems with fundamentalist reduction

Doesn't work in real life.

Doesn't describe what neuroscientists actually do.

Regression issue: whose "fundamental" level is actually fundamental?

The most fundamental level is arguably acausal.

Poverty of quantum mechanics (QM isn't wrong; just impoverished).

Multilevel, mechanistic explanation in neuroscience

Quotes from Carl Craver, 2007, [Explaining the Brain](#)

“The systems tradition...construes explanation as a matter of decomposing systems into their parts and showing how those parts are organized together in such a way as to exhibit the *explanandum phenomenon*... Systems explanations involve showing how something works rather than showing that its behavior can be derived from more fundamental laws. ”

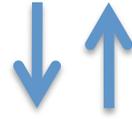
“Mutual manipulability: a part is a component in a mechanism if one can change the behavior of the mechanism as a whole by intervening to change the component, *and* one can change the behavior of the component by intervening to change the behavior of the mechanism as a whole.”

“Making a difference...”

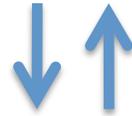
Long-term spatial memory (explanandum)



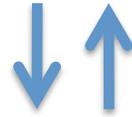
Long-term spatial memory (explanandum)



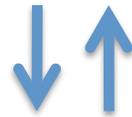
Mouse navigating a water maze



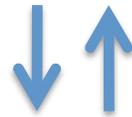
Hippocampus generating a spatial map



Neurons inducing long-term potentiation (LTP)



NMDA receptor activating



Genes producing more receptor molecules

What does all this MEAN?
I lost track of what is at stake here!

Self-determination, autonomy, responsibility
Key issue: what counts as a cause?

If we can find a way to talk meaningfully about nonfundamental causation (and I think we *must*), then we can take mental causation (and responsibility!) seriously.

This is NOT to say that bottom-up causes are unimportant; explanatory relevance runs both upward and downward.

Gene language

[Genes] swarm in huge colonies, safe inside gigantic lumbering robots, sealed off from the outside world, communicating with it by tortuous indirect routes, manipulating it by remote control. They are in you and me; they created us, body and mind; and **their preservation is the ultimate rationale for our existence.**



Richard Dawkins --
The Selfish Gene (1976)

—Courtesy, Dr. Ard Louis, University of Oxford



ALBERT AND MARY
LASKER FOUNDATION

Lasker Award story, New York Times, September 2006

Psychiatrist Is Among Five Chosen for Medical Award

By LAWRENCE K. ALTMAN
Published: September 17, 2006

The psychiatrist who upset Freudian dogma in the 1960's by developing cognitive therapy is one of five winners of this year's Lasker Awards, widely considered the nation's most prestigious medical prizes.



Ryan Donnell for The New York Times

Dr. Aaron T. Beck, a psychiatrist, developed cognitive therapy.

The awards, announced yesterday by the Albert and Mary Lasker

Foundation, are also going to four scientists who made important discoveries about aging and [cancer](#). Mary Lasker created the awards in 1946 as a birthday gift to her husband, Albert, in hopes of curing cancer in 10 years. Each award carries a \$100,000 prize.

The psychiatrist, Dr. Aaron T. Beck, 85, of the [University of Pennsylvania](#), won the Lasker clinical research award. Dr. Beck's technique, cognitive therapy, transformed the treatment of [depression](#) and many other [mental health](#) conditions.

 E-MAIL

 PRINT

 REPRINTS

CYRUS
JULY 9

Bottom-up intervention:
modify neurotransmitters, receptors

Top-down intervention:
change patient's *beliefs*, patterns of *interaction*

“Cognitive restructuring”

Beliefs matter!

Examples?

Is it better to live or to die?

Should I pursue a professional opportunity elsewhere in the country at the cost of uprooting my entire family, all of whom have their own independent lives?

Should I marry this particular person?

Religious quest involves the same sort of reasoning as the marriage example.

Sources of evidence are available: my primary experience in the religious community, the testimony of other seekers throughout the ages, the critical reflections of fellow pilgrims I meet along the way.

In the end, the evidence is not compelling in a scientific sense. Faith, accompanied by commitment is essential. Risks are high.

Simply put, this is the human condition.
It is *life*, and our most consequential
decisions in life have little or nothing
to do with science.

For everyone, the real question is:
Is there an ultimate source of meaning and
value in the universe? If so, what is it?

After this many of his disciples drew back and no longer went about with him. Jesus said to the twelve, “Do you also wish to go away?”

Simon Peter answered him, “Lord, to whom would we go? You have the words of eternal life.”

— John 6:66-68

And we have believed, and have come to know, that you are the Holy One of God.”

— John 6:69

I believe in Christianity as I believe that the Sun has risen – not only because I see it, but because by it, I see everything else.

C.S. Lewis, *The Weight of Glory*, (1942).

What was brought to completion by such a life and such a death only he can know now, wherever he is, if he is anywhere. The Christ of it is beyond our imagining. All we can know is the flesh and blood of it, the *Jesus* of it. In that sense what was completed was at the very least a hope to live by, a mystery to hide our faces before, a shame to haunt us, a dream of holiness to help make bearable our night.

— Frederick Buechner,

Wishful Thinking

Thanks!

Bodies and Souls, or Spirited Bodies?

(Current Issues in Theology) Nancey Murphy