Current Biology
Magazine

Book review

If the brain is the answer, what was the question?

Alex Gomez-Marin

The Brain from Inside Out
György Buzsáki
(Oxford University Press, New York, NY; 2019)
ISBN: 978-0-190-90538-5

Stories do not take place in a vacuum, and neither do scientific facts. If the Temple of Apollo were a neuroscience institute, it should probably have this maxim inscribed in its forecourt: “know thy frame”. In other words, experiments entail theoretical commitments. Data do not speak for themselves.

In his recent book, *The Brain from Inside Out*, the neuroscientist György Buzsáki calls into question the conceptual framework that has dominated neuroscience virtually since its inception. Despite neuroscientists’ awe-inspiring technical acumen, the author argues that the current enterprise is theoretically flawed. There is no point in continuing to push forth a sort of neuro-Sisyphean agenda, where the brain is seen as passively processing information fed from the outside world.

The problem can be put in a snarky way by paraphrasing Bob Dylan’s classic: How many electrodes must a neuroscientist implant before one can solve the monkey’s brain? How many neuroscientists does vision require before one can deem it explained? Yes, ‘n’ how many mice must a technician train before learning is really understood?

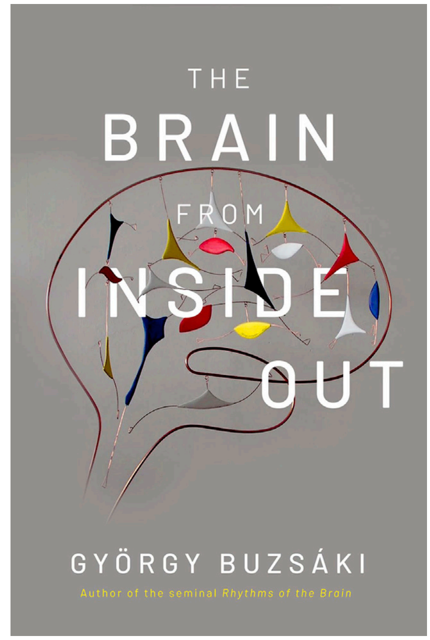
The answer, Buzsáki claims, is oscillations in the brain. As a way forward, he proposes an *inside-out* view: “the brain is a self-organized system with preexisting connectivity and dynamics whose main job is to generate actions and to examine and predict the consequences of those actions”.

Conversely, the *outside-in* neuroscientist seeks to go from less to more: namely, from simple to complex, from parts to whole, from artificial to natural, from anesthetized to behaving, and most crucially from the outside to the inside. Such an approach, Buzsáki argues, is empiricist, associational, and representational. The methodological strategy is powerfully simplistic: present stimuli and measure neural (or behavioral) responses. Perception and action are separated, and cognition is supposed to take place somewhere in the sandwich between them (being precisely what behaviorism denied, cognitivism paradoxically resuscitates some of its fatal vices). In a sort of Cartesian theater, the brain is considered a pliant spectator rather than a creative actor.

Breaking free from stimulus–response chains has unsettling implications for causal logic in neuroscience. Establishing juicy correlations (even causal relations) between neuronal activity and psychological constructs is often more relevant to the scientist studying a brain than to the brain that is being studied. Beyond counterfactual cravings (brain region X is “necessary and sufficient” for behavior Y or cognitive process Z), conceptual sophistication is needed to appreciate the many flavors of causation (co-arising conditions, permissive versus instructive factors), shifting our attention to causal constraints[1]. Reappraising the brain–world relationship, Buzsáki posits that brain activity is fundamentally self-caused.

Presenting a wealth of examples, the author then weaves perception and action together, giving primacy to the latter. Stressing the relevance of the action–perception loop, linear causality gives way to circular causality. We enter into the terrain of closed-loop neuroscience (from where we should have never left). Brains interact with the world rather than detect it. In other words, rather than the world filling in the brain with information, the brain fills out the world with action. “Perception is what we do”, an exploration initiated by the brain. Here Buzsáki is rather Bergsonian[2]: perception is virtual action.

Too often neuroscientists know something that the brains of their experimental subjects do not. As Buzsáki points out, “if something is not noticed by the brain, it is irrelevant from the brain’s point of view”. Therefore, a distinction needs to be made between observer and observed brains. Perspective matters. Neuroscientists enjoy both the blessing and the curse of ideal observers: being in a privileged point of view, they have access to the internal and external *milieu* of the animal, and yet they often miss



its particular *umwelt* (or meaningful environment). Cognition is less in the neuroscientist’s data than in the animal’s brain (body, and world[3]).

Celebrating Buzsáki’s ideas, one must be mindful that brain-centrism can still lead to anthropomorphism. One should not conflate animals with their brains: namely, to ascribe to a part what can only be predicated of the whole. Hands do not play the piano, the pianist does. Neurons do not have points of view, organisms do. And so, the call to understand the brain from within is subtle. Should the word ‘inside’ be construed geometrically (beneath the skull) or also phenomenologically (in the first person)? The challenge of a cognitive science in which situation matters lies ahead[4].

In a deep dive into the brain, Buzsáki explicates the central role of cell assemblies — groups of neurons acting as single functional units — as the fundamental “letter in the brain’s vocabulary”. Brain rhythms are another key player in such a linguistic metaphor. Spanning several orders of magnitude, and organized in nested frequency bands, these fascinating neuronal oscillations support neuronal syntax. Found across species, such a brain-wide coordination of activity integrates distributed (but still rather local) neural processes into global ones. In this view, analog computation is somewhat revitalized; “activity travels in neuronal space, much like waves in a pond”.

Within Buzsáki's neural dynamicism, the brain as a computer processing information gives way to "an orchestra playing polyphonic music". Would a mindless brain make the sound of one hand clapping?

The hard question is this: from where does cognition emerge? According to Buzsáki, one gets cognition from action when the brain disengages from the world (or, more precisely, from the motor action system). In such a case, cognition would be nothing but internalized action. Analogously, emotion would be "a disengagement from the autonomous action system" and speech "a metaphoric form of action". The main thrust of his approach consists in recasting the cognitive into the neural by means of action as a kind of ultimate cognitive source. It is action all the way in, all the way out, and all the way down.

Crucially for the proposal, one still needs to explain how endogenously produced neural syntax gets its meaning, and this leads us to the so-called grounding problem. Buzsáki now finds a solution outside the brain: semantics are selected by the world. When external perturbations modify self-organized neural patterns so that they become useful, meaning is acquired by such internally generated neural trajectories. It is, however, toilsome to imagine how the meaning of ideas such as melancholy or heroism could be acquired in this way. Meaning-making remains a foundational question in life and mind sciences[5].

Along the same lines, Buzsáki conceives learning as a matching process. Existing, spontaneous neural patterns are selected rather than constructed anew. The brain is not a blank slate but one filled with syntactically correct gibberish that progressively acquires meaning via the pruning of the arbitrariness that the world affords. In sum, neural patterns thrown to and influenced by the world provide a 'second opinion' to the brain.

After having "internalized experience", the brain "externalizes thought" to the world. Speech, Post-its, and iPhones enhance its performance, and externalization in turn affects the brain. Our gadgets are not only extensions of the action–perception loop but catalysts of abstraction that hold a key to what makes us human. "Would the teleported child from tens of thousands years ago (…) have the same chance of getting into college as my daughters?" Buzsáki answers with a resounding, "yes".

Central to his pursuit is the neuralization of the mind by means of the elimination of the "human-invented terms" of psychology (as Buzsáki calls them). Abiding by his deflationary project, memory and planning are nothing more than "mental navigation" carried out by neuronal mechanisms that evolved from initially implementing spatial navigation. Episodic memories are then to semantic memories what dead reckoning (egocentric navigation) is to map-based (allocentric) navigation. The neural mechanisms for representing a path through space and through time are interchangeable. And yet, one can come back to one's childhood hometown, but childhood never comes back.

There is a great deal of *élan mental* to expel. In Buzsáki's hands, cognitive neuroscience becomes an oxymoron, or perhaps a pleonasm. Ultimately, all mental faculties (including imagination, reasoning, and decision making) "arise from the brain's ability to break free from external control". Ditto for attention — another "spooky subjective term" — which he recasts as neural gain control. Buzsáki is not willing to renegotiate any term in the table of contents of William James's *The Principles of Psychology*[6]. He argues that they are "constructs of the human mind rather than brain "re-presentations" of real things out there". James's list progressively disintegrates. It is all in our minds, and the rest inside our heads.

Buzsáki's 'psycholoclasm' is not without paradoxes. The very articulation of the inside-out view hardly seems possible when dispensing with the very psychological language that the view seeks to eliminate. It is as if one of Escher's *Drawing Hands* sought to erase the other hand rather than to draw it and be drawn by it. Let us grant a thousand years of successful practice of the inside-out paradigm: how far would we be from a transposition to neural language of Leonard Cohen's genius line "The baffled king composing Hallelujah"? It is challenging to imagine what that neural sentence would even sound like, as John Krakauer has also pointed out[7].

Critiquing the 'man-made' terms of psychology is perfectly fine. That said, should we contrast them with some sort of God-given neural terms? Aren't neural manifolds and feedback loops also "human-invented mental constructs"? In other words, are concepts such as cell assemblies, brain rhythms, and motor commands ontologically privileged with respect to memory, perception, and attention? Buzsáki notes that "most of the terms that form the basis of today's cognitive neuroscience were constructed long before we knew anything about the brain". Leaving presentism aside, the same can be said for many of our cherished neuro-mathematical terms. This leads us to an extremely difficult question, which we can only aspire to enunciate here: is mathematics discovered, invented, or both? As it turns out, the mathematization of nature[8] may be even more pervasive than its mechanization. Academia is full of (secret) Platonists, for whom the world is (described by) mathematics (fatally omitting the parenthesis). For many neuroscientists, cognition *is* (supported by) neural activity.

Whether William James would cherish current 'neuro-phrenology' is anybody's guess. But what is sure is that James wasn't unaware of his own limitations, as the preface of his *magnum opus* explicitly indicates: "Every natural science assumes certain data uncritically, and declines to challenge the elements between which its own 'laws' obtain, and from which its own deductions are carried on. (…) the data assumed by psychology, just like those assumed by physics and the other natural sciences, must some time be overhauled"[6]. This encapsulates the significance of Buzsáki's book. Should the mis-instantiation of certain psychological constructs invalidate psychology as a whole? Moreover, as biology is not just applied physics, how is psychology a mere corollary of neuroscience? The objects of the mind and the objects of the brain belong to different levels. Ongoing attempts seek to go beyond naïve brain-mapping strategies, searching for a functional anatomy of mental processes that would allow the brain to better carve the mind at its joints[9].

Overall, *The Brain from Inside Out* is an impressive display of erudition, rounded off with just the right amount of storytelling and autobiographical notes. Before ending, it is imperative to mention its superb footnotes. From historical detours to compressed journal clubs, they serve as deluxe links to the main text. One cannot overstate how some footnotes are in fact true telegraphic jewels cloaking critical assessments on important topics, such as optogenetics, engrams, and Jennifer Aniston neurons. Such a complex journey through the bewitching mainstream heterodoxy tenders a constellation of crucial neural matters that shall spur apposite discussions within neuroscience writ large[10]. "You may or may not agree with me", Buzsáki says, "but at least you will experience a different perspective". Indeed, one can recognize good thinking without needing to accord with the thoughts.

As always, and in the end, the major (philosophical!) questions remain unanswered. Why the brain[11] and *only* the brain? Psychology might one day be to neuroscience what alchemy was to chemistry. And yet, like Newton, perhaps we should practice them both. Anyhow, it is enlightening to inquire into the psychological significance of neural reductions. There are probably more insights about the human mind in a Dostoevsky novel than in any neuroscience treatise. Proud of what neuroscientists have, can, and will achieve, let us not forget the other two main Delphic maxims, "nothing in excess" and "surety brings ruin".

REFERENCES

1. Ben-Menahem, Y. (2018). Causation in Science (Princeton and Oxford: Princeton University Press).
2. Bergson, H. (2012). Matière et mémoire. Essai sur la relation du corps à l'esprit (Paris: Presses Universitaires de France).
3. Gomez-Marin, A., and Ghazanfar, A.A. (2019). The life of behavior. Neuron *104*, 25–36.
4. Bitbol, M. (2002). Science as if situation mattered. Phenomenol. Cogn. Sci. *1*, 181–224.
5. Fields, C., and Levin, M. (2020). How do living systems create meaning? Philosophies *5*, 36.
6. James, W. (1890). The Principles of Psychology (New York: Dover).
7. Middlebrooks, P. (2020). BI 084 György Buzsáki and David Poeppel. *Brain Inspired*, episode 84.
8. Malet, A. (1997). Isaac Barrow on the mathematization of nature: theological voluntarism and the rise of geometrical optics. J. Hist. Ideas *58*, 265–287.
9. Poldrack, R.A. (2010). Mapping mental function to brain structure: how can cognitive neuroimaging succeed? Perspect. Psychol. Sci. *5*, 753–761.
10. Poeppel, D., and Adolfi, F. (2020). Against the epistemological primacy of the hardware: the brain from inside out, turned upside down. eNeuro *7*, ENEURO.0215-20.2020.
11. Fodor, J. (1999). Why the brain? Lond. Rev. Books *21*, 19.

Instituto de Neurociencias de Alicante, CSIC-UMH, San Juan de Alicante, Spain.
E-mail: agomezmarin@gmail.com
Twitter: @behaviOrganisms

Q & A

Erin Goley

Erin Goley is an Associate Professor of Biological Chemistry at the Johns Hopkins University School of Medicine. She earned her BA at Hood College in Frederick, Maryland, and her PhD in Molecular and Cell Biology at the University of California, Berkeley. After training as a eukaryotic cell biologist with Matt Welch at Berkeley, she pursued postdoctoral research in bacterial cell biology with Lucy Shapiro at Stanford. Her laboratory at Hopkins focuses on understanding the mechanisms of bacterial morphogenesis and the regulation of bacterial growth in changing environments.

What turned you on to biology in the first place? I took a pretty naïve route to biological research, but looking back my biggest early influence was my stepdad, who was a pediatrician. He ran his own small practice out of the old nineteenth-century school building in our town and I spent a lot of time at his office as a kid and early teen doing little odd jobs. I remember being fascinated by how my stepdad would swab kids' throats for suspected strep infection, streak out the samples on blood agar plates, and incubate them on top of the fridge (the warmest spot in the building). A day or two later, he'd look for the halo around bacterial colonies, indicating strep, and prescribe a course of penicillin. This was my first exposure to microbiology and, though it didn't immediately turn me on to research, it certainly piqued my interest in the biological world. I majored in biochemistry and math as an undergrad at Hood College, a small liberal arts college in Maryland, and after a couple of summers in labs I was hooked on being at the bench. It still took me a while to learn that I could get a PhD and do something other than teach — i.e. I could run a lab for a living.

And what drew you to your specific field of research? Some of my earliest research experiences were with microbes: my undergraduate thesis and work as a technician at the USDA post undergrad were focused on fungal and viral plant pathogens. The diversity of the microbial world and the myriad ways that microbes interact with each other and with host organisms were fascinating to me. When I started graduate school in the Molecular and Cell Biology program at UC-Berkeley, thinking that I wanted to be a microbiologist, I did rotations in three labs that each looked at the interactions between pathogens and the actin cytoskeleton of their host (*Listeria monocytogenes* actin-based motility in Dan Portnoy and Matt Welch's labs and nuclear actin assembly induced by baculoviruses in Loy Volkman's lab). At the time, Matt's lab was building on what they'd learned about how *Listeria* activates the host Arp2/3 complex to mediate its motility to understand more about how eukaryotic cells normally activate Arp2/3 for localized actin assembly. Though initially drawn in by the microbes, I joined Matt's lab and got hooked on the cytoskeleton during my time at Berkeley. While there, I was trained broadly as a eukaryotic cell biologist in large part through our joint group meetings with the labs of Rebecca Heald (focused on mitotic spindle assembly) and Karsten Weis (studying nucleocytoplasmic transport).

When the time came to choose a postdoctoral lab, the bacterial homologs of actin, tubulin, and intermediate filament proteins had recently been revealed, and I was excited by the opportunities for discovery in their regulation and function. As an aside, there's been debate in the field about whether bacterial polymers are actually 'cytoskeletal' — they may not be, but if they hadn't been called 'the