‘The brain as a dynamically active organ’ (Brembs, 2021)

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The brain as a dynamically active organ

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A R T I C L E I N F O

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A B S T R A C T

Nervous systems are typically described as static networks passively responding to external stimuli (i.e., the ‘sensorimotor hypothesis’). However, for more than a century now, evidence has been accumulating that this passive-static perspective is wrong. Instead, evidence suggests that nervous systems dynamically change their connectivity and actively generate behavior so their owners can achieve goals in the world, some of which involve controlling their sensory feedback. This review provides a brief overview of the different historical perspectives on general brain function and details some select modern examples falsifying the sensorimotor hypothesis.

1. The most important question in neuroscience

Neuroscience (or neurobiology), as Wikipedia educates us, strives to understand the emergent properties of neurons and neural circuits. The main emergent property of nervous systems is behavior: sedentary animals often have eliminated or strongly reduced their nervous systems, especially compared to ambulatory life stages (e.g. *Tunicata* - sea squirts), or never even evolved any, as in the *Porifera* (sponges). “Nothing in neuroscience makes sense except in the light of behavior. Nervous systems evolved to produce behavior. It is futile to try to understand brains without keeping this in mind” [1]. “One of the foundational aims of neuroscience is to understand behavior, in the broadest sense” [2]. “behavior—the ultimate output of the brain” [3]. “The original and still primary purpose of the brain—to endow organisms with the ability to adaptively interact with their environment” [4]. Thus, arguably, the most important question in neuroscience is whether there is a common organization to all behavior, and if so, what that organization looks like. In other words, the question of whether there is a ‘grand unifying theory’ of neuroscience.

Given the importance of the question, it is hardly surprising that the history of neuroscience is replete with hypotheses aiming to unify all behaviors under a common explanatory framework. However, the diversity of such hypotheses is relatively low. The literature is dominated by essentially two opposing hypotheses, one that sees nervous systems as passive organs (also called the sensorimotor hypothesis) and one that perceives them as active.

Early on, the concept of stimuli triggering reactions in an otherwise passive nervous system proved very attractive. In 1890, Williams James wrote that “The whole neural organism, it will be remembered, is, physiologically considered, but a machine for converting stimuli into reactions” [5]. Around the same time, two developments supported this view. One of them was Golgi's staining that showed that neurons are individual cells. Using this method, Santiago Ramón y Cajal formulated the neuron doctrine, a central tenet of which is the unidirectional conductance of activity [6]. The other discovery was that of reflex arcs. In this time, reflexes as extremely simplified forms of responses attracted the interest of researchers and, e.g., Sherrington proposed that walking was maintained by a series of interacting peripheral reflexes [7]. So popular and successful was the study of reflexes that after the pioneering work of Sherrington, Pavlov and many others, a school of “reflexology” formed [8], which thought to explain all, even human, behavior in terms of chains or webs of reflexes. While reflexology, at least in its radical forms, slowly faded in influence, the same concept of sensory triggered responses as the way in which all behavior is organized can be observed in later works. For instance, in 1949 Donald Hebb published his book entitled “Organization of Behavior” which received the subtitle “Stimulus and response - and what occurs in the brain in the interval between them” [9]. In some fields, this concept has become so dominant

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Experiments with an in-vitro robot brain*

- In-vitro circuits derived from rat cortical tissue, dissociated and then seeded onto micro-electrode arrays to form a monolayer
- This is **probed to determine reliable circuits**: stimulus delivered, responses measured (≤40% false negative, ≤ 20% false positive)
- These circuits are then used for the **wiring of sonar to actuator on a basic wall avoidance task**: sonar fires at ~30cm from the wall
  - They noted **many "spontaneous" firings**
  - These distinguished as "spurious"—as against "meaningful" (sonar response)

*Warwick et al., 2011

Spontaneous activity in neural tissues

- Developmental activity (e.g., retinal cholinergic waves)
  - Interruption **disrupts retinotopic mapping**, etc.
- From seven days, "dense bursts of simultaneous activity across the entire network … subsequently continues through maturity"
  - Unclear whether this is pathological or a part of normal development
  - Speculate it may result from **sensory impoverishment** in a closed loop
- Warwick et al. make some interesting comments—
  - **What is a perfect response?**
    - Tissue culture framed as "asserting its individuality"
  - **What are meaningful responses?**
    - Spurious or "some thought in the culture about which we are unaware"

Some statistical abnormalities …

Results	Simulation	Live Culture
Wall -> Stimulation event	100%	100%
Stimulation -> Response event	100%	67%
Total closed loop time	0.075 s	0.2 - 0.5 s
Run time	240 s	140 s
Meaningful turns	41	22
Spontaneous turns	41	16

"Under the control of the simulation 95 ± 4% (Mean ± SD) meaningful turns were observed whilst the remaining spontaneous turns (5 ± 4%) were easily attributable to aspects of thresholding spike activity. In contrast, the **live culture** displayed a **relatively low number of meaningful turns (46 ± 15%)** and a **large number of spontaneous turns 54 ± 19%** as a result of intrinsic neuronal activity."

“current work aims to quiet the level of ongoing spontaneous activity, reminiscent of epileptiform, present in such cultures”

—Warwick et al., 2011

Is this the right path?

The brain as a dynamically active organ

- **The passive-static view**
  - The nervous system is primarily concerned with turning sensory input into behavioural output
  - Intrinsic activity modulates this
    - If it is not simply seen as noise

- **The active-dynamic view**
  - The nervous system is primarily concerned with intrinsic activity and the generation of behaviour
  - Sensory input modulates this

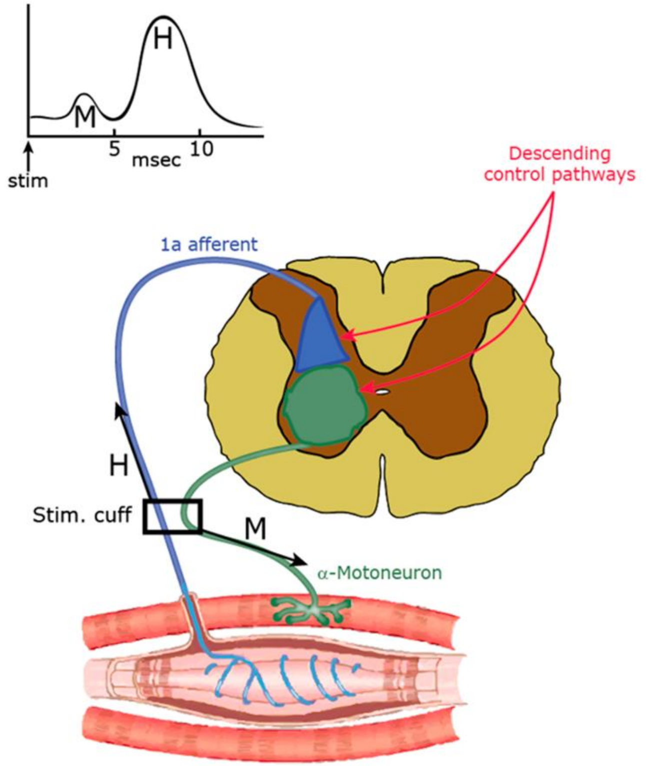
Three arguments in this paper

- There are three intertwined arguments in this paper:
    1. **Intrinsic activity is primary and sensory input modulates this**
    2. **This activity structures reafferent behaviour to probe the world**
    3. **The variability of intrinsic activity is evolutionarily advantageous**
- These are variably supported by a range of examples:
    - Reflex arcs
    - Insect phototaxis
    - Escape responses
    - Feeding behaviours

Note, some elements of this article (e.g., connectomes) have been left aside in my overview

Reflex arcs

- Spinal stretch reflex, simple structure: only two neurons, sensory and downstream motor
  - Taken to be a **classic input–output example**
- Precisely reproducible stimulation via a cuff electrode, record EMG amplitude
  - **Significant and meaningful variability** over time
  - This is susceptible to operant conditioning
    - Contralateral compensatory plasticity maintains gait
- Brembs argues that the H-reflex is best understood as an output-input system
  - Variability conceived of as probing the environment, taking proprioceptive response to make adjustments

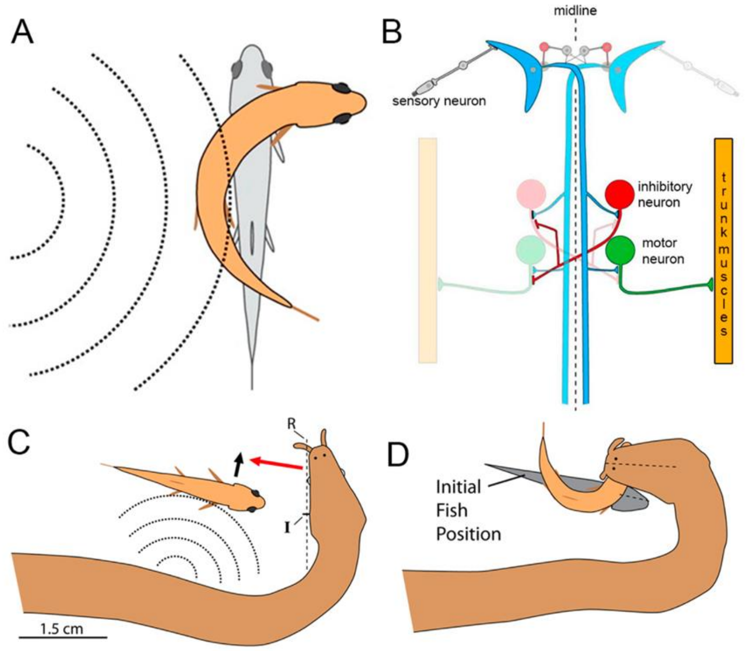


Insect phototaxis

- That insects self-immolate **suggests rigid input-output system**
- Drosophilia placed in a glass tube **walk towards illuminated end**
  - If their wings are shortened, however, then this tendency is reduced
  - Suggested that this is analogous to negative phototaxis during infancy
- Benzer: "… if you put flies at one end of a tube and a light at the other end, the flies will run to the light. But I noticed that not every fly will run every time. If you separate the ones that ran or did not run and test them again, you find, again, the same percentage will run. But **an individual fly will make its own decision**."

Escape responses

- C-start escape response in teleost fish
  - Contraction of contralateral and inhibition of ipsilateral muscles, bends into C shape
  - Head ends up pointed away from stimulus
  - Stereotyped, **little variability between trials and even between animals**
- Hunting behaviour in tentacled snake
  - Sit-and-wait predators, use body to **trigger the teleost 'escape'—into their mouth**
- Brembs argues that such predictability is **not an evolutionarily stable strategy**



Feeding behaviours

- The marine snail, Aplysia, feeds on varieties of seaweed
  - It has poor eyesight, by smell and touch alone cannot readily discern the properties of each piece of seaweed
  - This leads to an approach of 'babbling' for the proper method
    - Starting out each piece of seaweed with a different set of parameters
    - Modifying these chosen parameters during the feeding process itself
- The evidence here suggests that that Aplysia engages in a **random walk biased by feedback**, hence that activity (and variability) is primary and subsequently shaped by a sensory response

Olfactory reversal

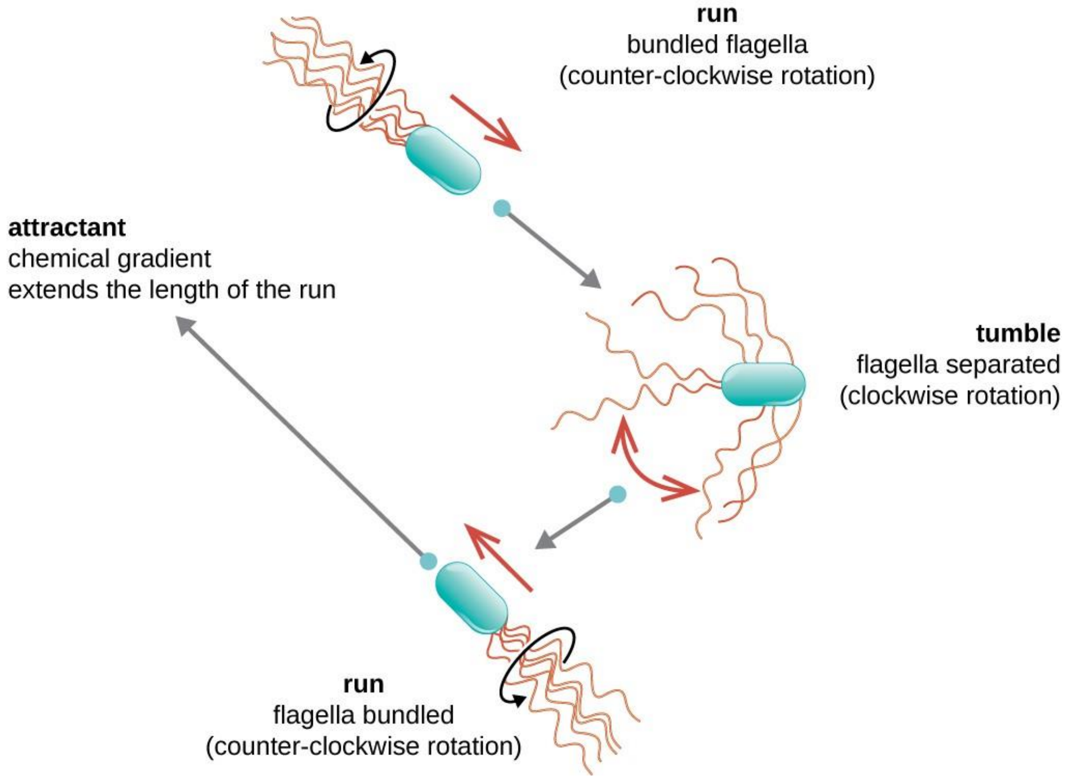
- C. elegans connectome predominantly feedforward input-output
- Taking the **olfactory reversal behaviour**, three roles here:
  - AVA: motor neuron, activation reverses crawling (forwards to backwards)
  - AWC: sensory neuron, provides input via connection to AVA
    - Depolarised by aversive odorants, increases likelihood of AVA activation
    - Hyperpolarised by attractive odorants, decreases likelihood of AVA activation
  - AIB and RIM: interneurons, mediate connection between AWC and AVC
    - **AWC activation corresponds regularly** to odorant concentration
    - **AVA activation varies** in relation odorant concentration
      - **If AIB and RIM are silenced or blocked, this variability is significantly reduced**
- AIB and RIM are thus understood to **inject variability into reversal**
  - Highly parsimonious nervous system, so this phenomenon is not gratuitous
  - Suggests **evolutionary value of variability (e.g., exploration-exploitation)**

What came first?

- Might the passive input–output system have emerged first?
  - We might imagine the **simplest nervous systems**, phylogenetically prior to any extant species, initially serving merely to **translate input into output**
  - This may then have **given rise to more complex cases of variability**, as that injected by the interneurons in the C. elegans olfactory reversal case
- P. dumerilii larvae as a model for last common bilaterian ancestor
  - Sensory neurons in **direct contact with ciliated cells** for propulsion
  - The larvae start out as positively phototactic, later negatively phototactic
  - Motor activity is **ongoing and undirected** in the absence of sensory input
  - Photic response **inhibits ipsilateral cilia; turns toward light**
  - Brembs, p. 6: "If anything, this would be classified as a motor-sensory system."

‘Run and tumble’ chemotaxis in E. coli

- Even the simplest forms of adaptive behaviour follow a principle akin to that of the P. dumerilii larvae
- E. coli, for instance, performs **chemotaxis by ‘run and tumble’**
  - Attractant exposure **decreases the probability of a tumble**
  - Subject to **diminishing returns**
  - Chemotaxis by **biased random walk**
- Intelligent behaviour thus emerges from how **environmental stimuli constrain active dynamics**



Some questions—

How should we define intrinsic activity?

- Some cases define intrinsic activity in terms of internally-generated variability, as with the between-trial variability of spinal reflexes
  - We might readily reply here that such instances are more parsimoniously accounted for by **broadening the notion of inputs to include internal 'senses'**
- Taking Drosophila phototaxis, for instance, where phototactic strength varies with wing-length: that an internal receptor might report the state of its wings, integrating this would determine movement amplitude
  - The simpler method might be reafference: send a signal to the wings and determine the effect of this on movement to assess flight capacity
  - Another way to define intrinsic activity might thus be by integrating the first and second arguments: that it functions via reafference to probe the environment
- **Is it possible to draw a line between intrinsic and 'other' activity?**

Are there any analogues in neural networks?

- Artificial neural networks (ANNs), while loosely based on animal nervous systems, **tend to lack clear analogues of intrinsic activity**
  - Standard ANNs, especially for classification tasks, deterministically transform an input into an output according to the network structure, weights, etc.
  - Some neuron models for spiking neural networks including intrinsic activity (e.g., intrinsically bursting parameters in the Izhikevich model)
- There are, however, other elements of ANNs which could be seen correspond to intrinsic activity or its functions in nervous systems
  - This **partly depends on how we define intrinsic activity (e.g., recurrence)**
  - Some other examples: **dropout, temperature, exploration, random seeds**
- **How can these phenomena be meaningfully integrated into ANNs?**
  - What might be the costs of doing so, what might be the advantages?

What might this mean for biological computing?

- Turning back to the initial paper (Warwick et al., 2011):
  - There were hints even there that this ‘spontaneous activity’ might not be entirely spurious: the culture **“asserting its individuality”** and responding to **“some thought … about which we are unaware”**
  - They explicitly raise the question of **what this means for the notion of a “perfect” response** in a system characterised by such intrinsic activity
- ANNs are already more grown than programmed, with the code primarily setting the parameters for this ‘organic’ development
  - This has costs in terms of interpretability, but it has proved immensely powerful as against “good old fashioned artificial intelligence” (GOFAI)
- **How should biological computing respond to intrinsic activity?**
  - Whether by constraining, harnessing, or otherwise adapting (e.g., metrics)

How does this relate to the notion of free will?

- Brembs (2011), 'Towards a scientific concept of free will as a biological trait: spontaneous actions and decision-making in invertebrates'