18th Issue, February 2026

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THE STUDENT JOURNAL IN BORDEAUX

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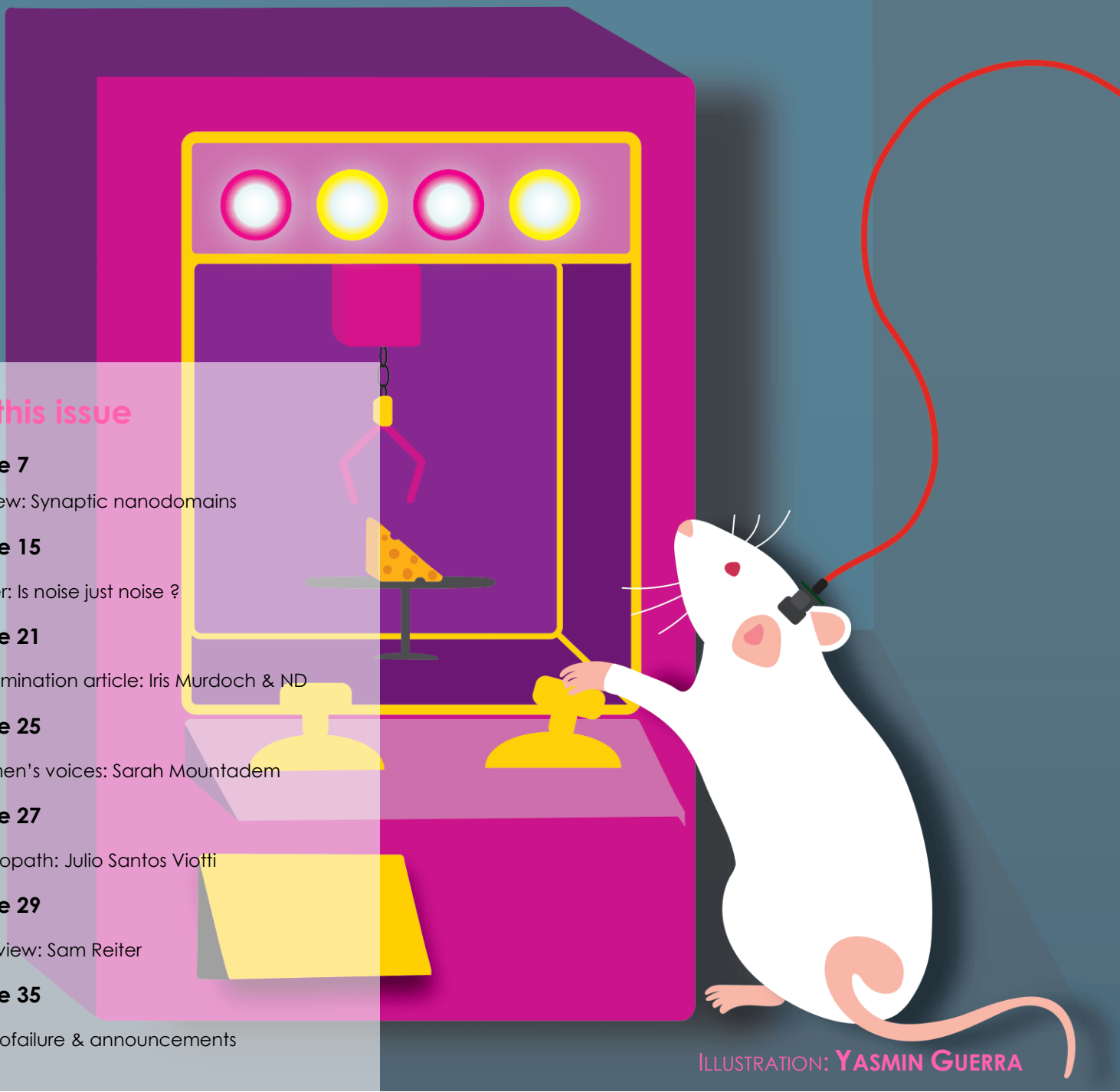

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This journal received funding from the EURE-0028 project

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Good things come in small packages: synaptic nanodomains and their relevance

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Received: 16th January 2026 I Peer Reviewed: 30th January 2026 I Accepted: 6th February 2026

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Abstract

Proper brain function requires efficient synaptic transmission, which relies on the precise organization of pre- and postsynaptic compartments. The presynapse displays active zones, releasing neurotransmitters, and the postsynapse presents a clusterization of receptors to optimally receive the signal. These receptor clusters are further organized into subcompartments, termed nanodomains, which align with their presynaptic partners. Although their formation and modulation remain poorly understood, nanodomains are likely involved in synaptogenesis, synaptic transmission and synaptic plasticity.

Keywords

Nanodomain, Receptor nano-organization, Synapse, Synaptic transmission, Super-resolution,

Abbreviations

AMPAR: α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor

NMDAR: N-methyl-D-aspartate receptor

GluA: Glutamate receptor subunit

AchR: Acetylcholine Receptors

PSD-95: Post Synaptic Density protein 95

CAMKII: Ca2+/calmodulin-dependent protein kinase II

GABAAR: gamma-aminobutyric acid type A receptor subunit

dSTORM: Direct STochastic Optical Reconstruction Microscopy

LRRTM2: Leucine Rich Repeat TransMembrane neuronal 2

LTP: Long-Term Plasticity

LTD: Long-Term Depression

STED: STimulated Emission Depletion

SMLM: Single Molecule Localization Microscopy

VGLUT: Vesicular GLUtamate Transporter

Introduction

Named by Foster and Sherrington in 1897, 'synapses' have been a significant focal point in the field of neuroscience. Constituted by a 'presynapse' containing neurotransmitter vesicles and a 'postsynapse' with neurotransmitter receptors, synapses form specific connections and communication between neurons, and are critical for proper brain function. In the 1950s, with the emergence of electron microscopy, a significant high electron density in the postsynaptic compartment was observed, highlighting for the first time an important protein aggregation at synapses (1).

It is now well known that neuronal circuitry is tuned by two types of synapses: excitatory and inhibitory ones. In the Central Nervous System (CNS), the most abundant excitatory synapses are glutamatergic, which includes ionotropic receptors like NMDA and AMPA receptors. When activated by neurotransmitters, these receptors allow the flux of cations (Na^+, K^+, Ca^{2+}) leading to the depolarization of the postsynaptic element. On the contrary, inhibitory synapses present an aggregation of GABAergic receptors, which, when activated, allow the flux of chloride ions, leading to the hyperpolarization of the postsynaptic membrane (2). The strength of these synaptic connections are modified and optimized over time through plasticity, like Long-Term Potentiation (LTP) and Long-Term Depression (LTD). This regulation has been shown to be vital for brain functions such as learning and memory (3-4).

In the last decades, the development of multiple techniques in the field of molecular biology, imaging, electrophysiology, and computational modelling led to the first evidence of the existence of a postsynaptic receptor organization. The recent advancement in breaking the diffraction limit gave rise to super-resolution imaging techniques, such as STimulated Emission Depletion (STED) (5) and Single Molecule Localization Microscopy (SMLM)(6), that allow us to resolve this receptor organization at the nanoscale. Studies employing these techniques found that synaptic receptors, and their modulators, exhibit a highly specific spatial sub-compartmentalization, termed as 'nanodomains'. Through this review, we will discuss the formation, maintenance, and potential functional relevance of these nanodomains.

Methods

In order to write this review, articles were selected on databases like PubMed, using the following words: nanodomains, development, synaptogenesis, receptors nano-organization, GABAAR, NMDAR, AMPAR, AchR, STORM.

Results and discussion

Initiation of clusterization: still a debate

Currently, two existing schools of thought describe the formation of receptor clustering within the synapse—one that states the requirement of a presynaptic input to induce receptor clustering during synaptogenesis and the other stating receptor cluster formation precedes synaptic transmission, suggesting a starting point for synaptogenesis. Acetylcholine receptor (AChR) clustering in the neuro-muscular junction is the perfect example for these two schools of thought. In live confocal imaging of zebrafish, clustering of AChRs are formed both before and after axon arrival, demonstrating the presence of two different initiation signaling pathways (7). Post-axonal arrival clusterization is dependent on secretion of presynaptic signaling proteins, such as agrin, while the mechanisms dictating the pre-axonal clustering remain largely unclear (8).

In central synapses, the molecular induction mechanism for receptor clusters is still under investigation. Droplet studies of postsynaptic density proteins show Ca^{2+}/calmodulin-induced compartmentalization via liquid–liquid phase separation (9), which persists after Ca^{2+} removal, indicating that calcium triggers nanodomain formation but is not required for their maintenance. In immature rat hippocampal neurons, NMDAR, CamKII, AMPAR, homogeneously distributed, aggregate sequentially at synapses after glutamate induction (10). However, NMDARs clusters were observed very early in development. In this case, glutamate coming from a presynaptic element is unlikely to trigger a signal for clusterization. It was suggested that early NMDAR clusterization initiated by the interaction with dopamine receptor, is a nucleation step for the formation of synapses (11).

Taken together, mechanisms that are capable of initiating receptor clusterization in immature neurons are yet to be further investigated.

A complex regulation of nanodomains:

After initial clusterization, synaptic receptor nano-organization evolves with synapse maturation, and nanodomains change over the course of development and synapse plasticity (12). In the last two decades, super-resolution microscopy has shed light on contributors to this nano-organization. SMLM (dSTORM) analysis demonstrated that CaMKII, recruited before AMPAR at the immature synapse, drives spatial segregation of AMPAR and NMDAR nanodomains during spine maturation (13) (Fig.1A).

Scaffold proteins, such as PSD-95 (14) and Gephyrin (15), were shown to display distinct and synapse-type-dependent clusterization, suggesting a functional role of these proteins in receptor distribution. At excitatory synapses, destabilizing the interaction between the NMDAR GluN2B sub-unit and PSD-95, leads to selective rearrangement of GluN2B nanodomains, disrupting plasticity (12) (Fig.1A). Similarly, in inhibitory synapses, inducing Gephyrin aggregation disperses GABAAR nanodomains, causing them to be displaced from the active zone, leading to a decrease in GABAA currents (16) (Fig.1B).

Furthermore, electron tomography studies show heterogeneous electron density at the synaptic cleft, suggesting that trans-synaptic proteins are also functionally organized (17). Deletion of neuroligin-3, a postsynaptic adhesion molecule, showed a subsequent increase in GluA1 nanodomains. Further computational modeling suggested its role in determining synaptic strength (18). Similarly, LRRTM2, is involved in AMPAR clusterization: deletion of its extracellular domain resulted in a declustering of AMPARs away from the release sites, affecting evoked postsynaptic receptor activation (19) (Fig.1A).

Thus, changes in nanodomains of receptors by these types of modulators clearly impact synaptic activity.

Nanodomain organization underlies multiple functions:

In 2013, a sub-synaptic organization of glutamate receptors was described (20) raising the question of their function. Computational analysis proposed that postsynaptic nano-domains were necessary to optimize neuro-transmission by presynaptic active zone alignment. Indeed, due to AMPAR's low affinity to glutamate, it was suggested that the concentration of glutamate corresponding to the proper activation of AMPAR was only reached within 100 nm of the release site (21). Thus, the pre-post synaptic alignment called a nanocolumn or nanomodule (22) would facilitate efficient synapse transmission (Fig.1A).

NMDAR, on the contrary, has a strong affinity for glutamate. However, its close aggregation induces inhibition of the neighboring receptors. Fluxed Ca2+ ions from active NMDAR lead to receptor inactivation within nanometers distances like a retrocontrol mechanism (23).

Upon activity-dependent structural plasticity, STED microscopy shows VGlut1-PSD95 (24) nanomodules increase in number with the spine volume. The number of GluA1 and GluN1 nanomodules, aligning with the presynaptic active-zone, correlates with spine size. Consistent with the role of GluN2B in synapse development and plasticity, GluN2B-containing NMDAR nanoclusters are enriched in small spines and decrease with increasing spine size. In contrast, GluN2A-containing nanomodule increase in number with spine size highlighting their presence in more mature synapse for stabilization (25). Hence, the nanomodules are modified in both number and composition depending on the state of the synapse: immature or potentiated.

This alignment of receptor nanodomains with presynaptic vesicle release sites plays an important role in optimizing synaptic strength of evoked transmission. However, a synapse has been shown to harbor multiple types of transmission. One such example is spontaneous transmission, which was first considered as a result of random error in the brain, but was then suggested to play a specific role in the development, regulation and maintenance of synapses (26). Upon the addition of the anti-malarial drug artemisinins, known to bind to Gephyrin competing with GABAR interaction site, GABAAR γ2 cluster surface area is reduced (Fig.1B). This reduction results in the suppression of spontaneous GABAergic transmission. This study suggests that the nano-organization of receptors at the synapse helps segregate the different types of neurotransmission evoked and spontaneous (27).

Nanodomains in health and disease:

Given the likely importance of nanodomains in regulating synaptic function, it is not surprising that disruption of receptor cluster organization is associated with diseases. NMDAR autoimmune encephalitis caused by the production of pathogenic autoantibodies against NMDAR alters synaptic retention of NMDAR, resulting in the reduction of synaptic nanodomain area. This alteration in receptor number and nanodomain prevents NMDAR-dependent LTP at the synapse and even promotes LTD (28). This autoantibody-mediated disruption is thought to underlie the psychosis, memory impairment, seizures, and loss of consciousness observed in the patient.

As another example, the epilepsy-related gene products, ADAM22 (transmembrane metalloprotease), identified as major components of PSD95-containing protein complexes, have been shown to be major regulators of brain excitability. In mice, disruption of the interaction between ADAM22 and PSD-95 is associated with less condensed PSD95 nanodomains, decreased excitatory synaptic transmission and lethal epilepsy (29) (Fig.1A).

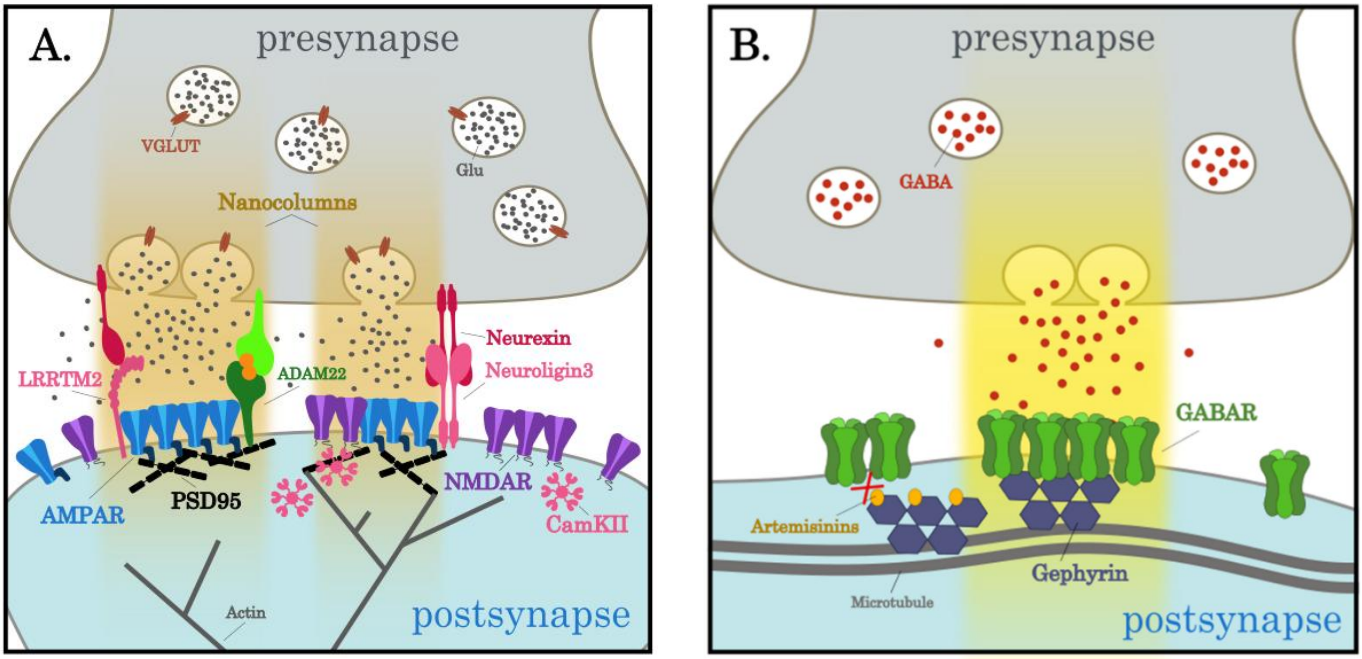

Figure 1: Schematic representation of nanodomains and their modulators in synapses. (A) Excitatory synapse. (B) Inhibitory synapse. *Created on inkscape*.

Conclusions

While the clusterization of AChR at the neuromuscular junction has been extensively studied and mostly characterized, the mechanisms of receptor organization at central synapses are less clear. The multiplicity of regulatory homologous proteins (MAGUK, neuroligins) and the interplay between receptors make it very complex to study. Besides, different types of activity (spontaneous and evoked) can take place at a single central synapse, and due to single-synapse plasticity, their organization is constantly changing. It is likely that receptor organization relies on multiple processes that not only change over development but also between synapses, and understanding the molecular mechanisms dictating this organization is vital to mitigating their pathological consequences.

Although the possibility that synaptic nanodomain is an experimental artefact has not been fully excluded in the field, the past two decades have brought numerous studies supporting their existence. Despite important advances in unraveling the structure and dynamics of these nanodomains, our understanding is still incomplete. Recent studies speculate on a possible contribution of extracellular proteins, which may also play a role in the formation and maintenance of synaptic receptor organization over the synaptic lifetime – a field that remains largely elusive.

Finally, the presence of receptor clusters outside of the synapse begs the question of whether they have their own functions or if they are just a pool to replenish synaptic receptors or create new synapses.

It is safe to say that we have only now begun to chip away at the iceberg, suggesting that we have a lot to look forward to in the coming decades.

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e2022580118.

Is noise just… noise?

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Received: 16th January 2026 I Peer Reviewed: 30th January 2026 I Accepted: 5th February 2026

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'Distinguishing the signal from the noise requires both scientific knowledge and self-knowledge: the serenity to accept the things we cannot predict, the courage to predict the things we can, and the wisdom to know the difference.' Nate Silver (1)

In everyday language, the term noise usually has a negative connotation. For example, noise hinders us from understanding our friends in a crowded bar. In science, noise is also often considered as a problem: it can affect the precise analysis of a microscope image or contaminate experimental measurements. In all these situations, the goal is to increase the 'signal-to-noise ratio' by reducing this unwanted noise.
Research in neuroscience over the past twenty years indicates that the brain probably does not avoid noise, but rather embraces it. In this view, neural noise may contribute to information processing and communication.

The aim of this article is to explore what 'noise' means within the brain, where it comes from, and whether it can play a functional role.

What is noise?

To understand what neural noise is, we can start by examining how brain activity is experimentally measured. When a sensory stimulus (e.g. visual, tactile, auditory) is presented, a change in electrical activity of the brain is typically observed after the stimulus onset (e.g. using EEG, MEG). What is more surprising is the electrical activity recorded before the stimulus appears. This spontaneous activity fluctuates continuously, even in the absence of any external input. As a result, when the same stimulus is presented repeatedly, the brain response is never identical. The amplitude, timing, and shape of the response vary from trial to trial.

These differences suggest that the brain is never in exactly the same state twice. Each stimulus is processed against a different background of ongoing activity. In this sense, neural noise reflects the internal state of the brain at a given moment, and this background noise influences how incoming

information is processed. As Heraclitus said: “no man steps in the same river twice”, we could say: “no stimulus steps in the same brain twice”.

Where does noise come from?

If neural activity is variable at the level of the whole brain, where does this variability originate? A major advance in neuroscience was the ability to record the electrical activity of individual neurons. Neurons are electrically excitable cells: they generate electrical signals called action potentials (i.e. brief, all-or-none changes in membrane potential that actively propagate along the axon) and transmit them to other neurons through synapses, the fundamental units of communication in the brain.

Interestingly, variability is already present at this cellular scale. Even in the absence of external stimulation, individual neurons display spontaneous electrical activity. When a neuron is repeatedly stimulated with the same input, it does not produce identical responses each time. The number and timing of the action potentials it generates fluctuate from trial to trial.

Therefore, the variability observed at the macroscopic-scale is already present at the microscopic level. Background noise and trial-to-trial variability are intrinsic features of neuronal function.

What produces noise?

Even the simplest electrical circuits contain intrinsic fluctuations. At the microscopic level, charge conductors are in constant thermal motion. This thermal agitation generates voltage fluctuations across resistive elements, a phenomenon known as thermal noise. In other words, electrical resistance is inherently associated with random electrical fluctuations.

Neurons are no exception to these physical principles. Their electrical activity arises from the movement of ions across the cell membrane through specialized proteins called ion channels. Because ionic currents pass through resistive elements (the membrane and the channels themselves), neuronal membranes also generate thermal noise.

In addition, ion channels are molecular structures embedded in a fluid membrane, and their opening and closing are governed by stochastic molecular interactions. As a result, even under identical conditions, the exact timing of channel opening and closing varies. This phenomenon, known as channel noise, contributes directly to fluctuations in membrane potential (2).

Variability is further amplified at synapses. In most brain synapses, communication is chemical. When an action potential reaches the presynaptic terminal, neurotransmitter release occurs with a certain probability. On the postsynaptic side, receptors bind neurotransmitters and open ion channels, but these processes are also probabilistic. Vesicle release, receptor binding, and channel opening all introduce additional variability into synaptic transmission (3).

Taken together, these mechanisms indicate that neural noise arises from multiple levels: fundamental physical processes, molecular dynamics of ion channels, and probabilistic synaptic transmission.

Is noise useful for the brain?

Whether neural noise plays a functional role remains an active and evolving area of research. The ideas presented here are not exhaustive but illustrate several influential hypotheses.

The brain must transform noisy, incomplete, and ambiguous sensory signals into meaningful interpretations of the world. To do so, it needs to represent not only estimates of external variables, but also the uncertainty associated with those estimates. Such probabilistic representations would allow the brain to:

1. Combine information from multiple sources (e.g. different sensory modalities or prior experience).

2. Make decisions under uncertainty.

3. Update internal models of the world over time.

In several computational frameworks, variability in neural activity is not interpreted as unwanted noise but as reflecting uncertainty itself (4). In this view, trial-to-trial variability may participate in 'probabilistic inference' (i.e. the process of estimating the likelihood of different possible interpretations of the world based on uncertain or incomplete information) rather than perturb computations (5, 6). However, whether neural variability directly encodes uncertainty remains debated.

A second influential idea is about 'stochastic resonance'. Because neural networks are nonlinear and threshold-based systems, weak electrical inputs that are insufficient to trigger an action potential may become detectable in the presence of an optimal level of noise. In such cases, noise can enhance the detection of subthreshold electrical signals. Experimental and theoretical studies suggest that stochastic resonance may improve sensory processing and, under certain conditions, learning (7, 8). Importantly, this effect occurs only within specific ranges of noise level: too little or too much noise degrades performance.

Finally, from a nonlinear dynamical systems perspective, the impact of noise depends on the operating regime of the network. In strongly stable systems, small fluctuations tend to decay. In contrast, in chaotic regimes near critical points (understood in analogy with phase transitions in physics, where a system shifts between ordered and disordered states), small fluctuations can propagate and influence large-scale activity. Some empirical and theoretical work suggests that neural networks may operate near 'criticality', at the edge of a phase transition between different states (Figure 1), a regime in which variability could enhance the sensitivity of the system to small fluctuations and flexibility (9, 10, 11). However, the extent to which the brain is truly critical or chaotic remains under active investigation (12).

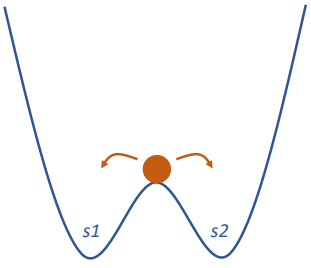

Figure 1. Criticality and phase transition.

This scheme shows a critical point (red) between two possible states (s1 and s2). Noise is hypothesized to drive phase transition to one state or another (arrows) inside the brain.

Taken together, these perspectives suggest that neural noise is not a perturbation. Under certain conditions, it may contribute to inference, sensitivity, and flexibility. Whether it is beneficial or detrimental depends on context, scale, and network state.

Can noise be detrimental to the brain?

Noise is often intuitively viewed as a perturbation, and in some contexts, excessive variability can indeed impair neural function. The relationship between neural noise and brain disorders has therefore become an active area of investigation.

In computational terms, if variability becomes too large, it can reduce the reliability of signal transmission, impair sensory precision, or destabilize network dynamics. Both insufficient and excessive variability may disrupt optimal information processing, as the stochastic resonance hypothesis suggests.

Several neuropsychiatric and neurological conditions have been associated with altered neural variability. For example, some studies report increased trial-to-trial variability or altered signal-to-noise ratios in individuals with autism spectrum conditions compared to control groups (13, 14). However, what is meant by 'noisy brains' varies across studies: it may refer to increased neural response variability, atypical excitation-inhibition balance, altered network synchronization, or changes in 'entropy measures' of brain activity (i.e. quantitative measures of how unpredictable or variable neural signals are). Moreover, findings are not always consistent, and causal interpretations remain cautious.

In general, deviations from an optimal level of variability (too high or too low) may impair the balance between stability and flexibility required for efficient brain computations. Determining when neural noise is adaptive and when it becomes pathological remains an open question.

Conclusion

At first, noise appears as a perturbation, an obstacle to information processing and communication. However, in the brain we find it at every level from ion channels to large-scale neural networks. Yet neural noise needs to be seen as an intrinsic property of the brain, not an unwanted nuisance.

The crucial question is then, how the brain operates with this noise. Hypotheses suggest that variability can, under certain conditions, support probabilistic inference, enhance sensitivity through stochastic resonance, and shape large-scale dynamics near critical points. At the same time, excessive or dysregulated variability may impair reliability and contribute to dysfunctional information processing.

Noise is therefore neither purely detrimental nor inherently beneficial. Its impact depends on context, intensity, scale, and network state. The brain does not eliminate noise: it appears to function with it, and maybe thanks to it.

Neural noise reminds us that the brain is not a deterministic machine performing perfectly reproducible computations like a computer. It is a dynamic biological system subject to physical laws, constantly fluctuating, adapting, and negotiating with uncertainty.

In the end, noise may not be the opposite of signal. It may be one of the conditions that make meaningful signals possible.

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Pages that remain

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This section has been created in collaboration with the Maison du Cerveau, an association that brings together all those involved with diseases from the nervous system. Our goal is to increase visibility and to provide information about these pathologies, treatments, and research advancements for the general public.

"The moral life is something that goes on continually, not something that occurs in rare decisive moments." - Iris Murdoch (1919–1999)

Continuity, the ability to carry thought, memory, and meaning across time, lies at the heart of how we experience life. It allows us to reflect, learn, and carry meaning forward. When this continuity begins to fracture, the effects are not only cognitive, but existential. There is perhaps no clearer illustration of this intricacy and vulnerability than the story of Iris Murdoch herself.

Known for her moral philosophy, her ideas of the self, and her fictional novels, Iris Murdoch's life was both unique and profound. Born in Dublin in 1919 and educated at Oxford, she pursued philosophy and literature side by side, writing twenty-six novels while developing a distinct moral view. Awarded a Damehood in 1987 for her influence on British literature, Iris was a woman of extraordinary mastery of language, paired with a deeply introspective mind.

When Iris referred to moral life, she did not mean isolated moral choices or dramatic ethical decisions. For her, it was not seen to be dictated by sudden epiphanies or "aha" moments. She believed that beneath every apparent decision lies a much longer process already underway, shaped by memory, experience, emotion, and habit. As she wrote, *"At crucial moments of choice, most of the business of choosing is already over"* (1). Decisive moments are not where morality occurs, but where it reveals itself. Moral life, for Iris, was a continuous effort, a slow, ongoing journey requiring attention, intention, and a willingness to reflect on oneself. Attention was central to Iris's thinking. She described it as *"the just and loving gaze directed upon an individual reality."* This kind of attention depends on the mind's ability to remain present and stable over time, to hold thoughts, perceptions, and memories long enough to reflect on them.

Much like the continuous narratives of her novels, the healthy mind ordinarily maintains a coherent sense of self across time. We move through life able to remember, reinterpret, and carry meaning forward. Yet when the brain's white matter, (the brain's long nerve fibers that connect different regions) begins to weaken, when toxic proteins accumulate, and when systems of repair no longer function efficiently, this continuity starts to fracture. The connectivity that allows access to memories, ideas, and a sense of self becomes less reliable (2).

The memories themselves do not vanish immediately. Instead, access to them becomes inconsistent, limited, and sometimes denied. Identity is not reducible to memory alone, but memory helps sustain a continuous sense of self across time by linking experience and meaning. When access falters, this narrative continuity begins to break down. It is as if pages from a novel have been torn out. The pages still exist somewhere, but are lost to the reader. Gaps appear.

A memory is not stored as a single object. For example, Iris recalling *The Sea, The Sea*, her most well-known novel and winner of the Booker Prize in 1978, depends on distributed patterns of connectivity across networks of neurons. These patterns, often referred to as engrams, are not static or permanently fixed, but dynamic and continually modified over time (3). At the synapse, the junction where neurons communicate, repeated activation strengthens connections through processes such as long-term potentiation, altering synaptic efficiency and structure (4). Experience, quite literally, leaves a material trace.

One day, Iris sat at the same desk she had always written at. It was an ordinary day. She put pen to paper to begin a sentence, as she had done thousands of times before. But this time, the sentence refused to come. The thought was there, she could feel it, but it would not take shape. To Iris, this may have seemed like fatigue or writer's block. Not Alzheimer's.

Her final novel, *Jackson's Dilemma*, tells the story of a man's disappearance and the effect his absence had on those around him. Yet the novel also tells another story, one Iris herself could not yet recognize. In retrospect, it marks the beginning of her own disappearance. In this work, the earliest signs of illness begin to surface, leaving behind a pre-symptomatic footprint. Computer-based linguistic analysis comparing *Jackson's Dilemma* with Murdoch's earlier novels later revealed a significant reduction in lexical diversity (how varied one's vocabulary is), with increased use of common words (5). Repetition in vocabulary and sentence structure became more pronounced, a pattern associated with narrowing semantic access. At the early stage Alzheimer's had begun to affect Iris's sustained attention and the temporal stability of thought. The problem is not the loss of knowledge itself, but access to it. The information remains present, but the neural pathways required to retrieve it become impaired. This pattern is typical, early Alzheimer's often involves subtle disturbances in written language, delayed word retrieval, and difficulty maintaining coherence. Neuronal death is not yet the primary issue. The problem is dysfunction (6).

At the synaptic level, communication between neurons becomes less reliable. Amyloid-β, a waste by-product of normal brain activity, interferes with transmission by disrupting NMDA and AMPA receptor signaling, which are key molecular gateways for neuronal communication (7). This results in impaired long-term potentiation, the mechanism that allows memories to be reactivated and held in mind. At the same time, white-matter pathways that integrate distant brain regions weaken, leaving networks structurally intact but poorly synchronized (8). The memory remains, though access to it becomes faulty.

As the illness progressed, Iris's awareness of her condition became quietly visible. In an interview with *The Guardian*, she said, *"I'm just wandering. I think of things and then they go away forever."* She spoke of being in a place she tried to get out of. *"Well, I enjoy it, when I've found a way out, as it were. But otherwise…"* She smiled, almost apologetically. *"Otherwise I'm in a very, very bad, quiet place"* (9). There is no panic in her words. Only awareness. And that, perhaps, is one of the most painful aspects of the disease.

In her later years, Iris depended entirely on the full-time care of her husband, John Bayley, who later wrote about her illness in *Elegy for Iris*. He described a woman who was no longer present in the way she once had been, yet who retained emotional responsiveness, gentleness, and moments of engagement with the immediate world (10).

The tragedy of Alzheimer's has two intertwined dimensions. The first is the loss of the narrative self, the slow erosion of identity, continuity, and the sense of being someone across time. The second is the awareness of that erosion, at least in the earlier stages. The self is not immediately destroyed, but becomes progressively inaccessible. A gradual disconnection from one's own synaptic history.

Murdoch's story does not undermine her philosophy. It reveals its fragility and, with it, the vulnerability of the mind, the brain, and identity itself. The moral life, as she understood it, depends on memory, attention, and continuity. Alzheimer's dismantles these foundations not suddenly, but piece by piece. What remains is not nothing, but something incomplete and fractured. Iris Murdoch passed away in 1999 due to complications from advanced Alzheimer's disease. Though the illness erased her access to the self she once articulated so clearly, it did not erase her from others. Iris Murdoch remains in her language, her stories, and in a philosophy that continues to shape how we think about morality, attention, and what it means to be a self. Her pages were never erased, only made harder to reach.

Iris and her loving husband, John Bayley, in their home in Oxford. Till the very end, Iris was surrounded by the things she loved most. Picture: George Reszeter

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Women's Voices: inspiring the neuroscientist community

Sarah Mountadem

Sara Carracedo[1]
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Women's Voices is an interview section created in partnership with the Neurocampus Parity and Inclusion Committee (NeuroPIC), a local group committed to promoting equality and organizing actions to close the gap between women and men in academia. The goal of this section is to increase the visibility of early career female researchers at the Bordeaux Neurocampus of the University of Bordeaux. We interview researchers about their scientific contributions, insights and opinions about equity, diversity, and gender bias in academia. Through these interviews, we aim not only to highlight their achievements but also to serve as inspiration for our scientific community and other female scientists.

Together, we will bridge the gap!

This month in Women's Voices, we interview **Sarah Mountadem**, a neuroscientist born in Clermont-Ferrand (France) where she completed an Associate's degree in Biological Engineering, followed by a Bachelor's degree in Pharmacology and a Master's degree in Pharmacology and Neurosciences. Her PhD explored the contribution of astrocytic Kir4.1 channels in chronic pain. She is currently a postdoctoral fellow under the supervision of Aude Panatier at Neurocentre Magendie, where her research centers on glial–neuron communication, synaptic transmission, and cognition. In parallel, she is a board member of the French Glial Cell Club. In this interview, she reflects on her scientific journey and discusses with us about female mentorship and leadership in academia.

Sara Carracedo: Could you share your academic path with us?

Sarah Mountadem: I have a fairly traditional academic background. I have always been deeply fascinated by the brain and its mysteries. My initial goal was to become a neurosurgeon. Despite failing my first year of medical school, I never lost my interest in neuroscience and decided to pursue biology instead, aiming to become a neurobiologist.

I began with an Associate's degree in Biological Engineering at Clermont-Ferrand, which included a specialization in Animal Physiology. It was really at that point that I realized I wanted to focus on fundamental research. I then continued with a Bachelor's degree in Pharmacology followed by a Master's in Pharmacology and Neurosciences.

Although I initially doubted my ability to undertake a PhD, the support and encouragement of my internship supervisors motivated me to apply to the doctoral school. As a result, I not only obtained a ministerial scholarship but also secured first place in the entrance exam, demonstrating that it is possible to succeed even when you don't fully believe in yourself at the start.

I subsequently joined the Neuro-Dol team, focused on trigeminal pain and migraine, led by Professor Radhouane Dallel in Clermont-Ferrand. There, I studied the role of astrocytic Kir4.1 channels in chronic pain. This experience was a revelation, as it was then that I developed my interest in glial cells. After completing my thesis, I worked for six months as a research engineer in the same laboratory to finalize my thesis paper.

Finally, since June 2021, I have been pursuing my first postdoctoral position in Dr. Stéphane Oliet's laboratory at the Neurocentre Magendie, Bordeaux Neurocampus under the supervision of Dr Aude Panatier.

Sara Carracedo: Why did you decide to move to Bordeaux for your postdoc? What is your current research focus?

Sarah Mountadem: During the final year of my PhD, I struggled with motivation to look for a postdoctoral position, likely due to accumulated fatigue. What I found most difficult, however, was the prospect of moving away alone while leaving my partner in another city. Fortunately, Aude Panatier was a member of my thesis committee. After my defense, she offered me the opportunity to join her team, a valuable chance that allowed me to balance personal distance with the scientific excellence of the research conducted in Bordeaux, particularly on neuron-glia interactions. I am currently leading a project aimed at studying the role of astrocytic mGluR5 receptors in synaptic transmission, synaptic plasticity, and memory.

Sara Carracedo: Do you perceive that we, as women, have different ways of supervision or leadership styles compared to men? What type of supervision has been most beneficial to you?

Sarah Mountadem: I believe that supervision styles are more influenced by individual personality than by gender, but certain patterns can still be observed. I've noticed that women, perhaps because they often feel additional pressure to prove themselves in environments where inequalities still exist, tend to adopt a very engaged, demanding, yet deeply supportive style of supervision. There's often a strong desire to 'live up to expectations' on every front, which can translate into great attentiveness, rigor, and care for younger researchers. Personally, I've benefited the most from supervision rooted in trust, encouragement, and open communication, regardless of whether it came from women or men. I don't like being overly monitored or closely supervised; instead, I prefer to be trusted and to have my ideas and reflections considered. Above all, this allows me to be recognized and valued as a researcher rather than just a student.

Sara Carracedo: In your view, how does mentorship style affect the professional growth of women? Do you believe there are implicit biases that affect how women are mentored or evaluated in academia?

Sarah Mountadem: Mentorship style plays a crucial role in the professional development of women by fostering confidence and creating opportunities. Although implicit biases persist, I have personally felt somewhat insulated from their impact. Throughout my academic journey, I have been fortunate to encounter male mentors who have consistently provided support and guidance, remaining steadfast in helping me build my future. For instance, my PhD supervisor, continually placed trust in me and contributed significantly to my growth. These people have supported me, and continue to do so, in establishing my academic credentials and shaping my career trajectory. Consequently, I have not personally experienced disparities in recognition based on gender. Nonetheless, it remains imperative to address such biases to ensure equitable mentorship for all.

Sara Carracedo: What advice would you offer to early-career female scientists who are facing systemic challenges while trying to pursue their professional goals?

Sarah Mountadem: My advice to early-career female scientists facing systemic challenges is to build a strong support network, including mentors and peers who believe in you and your potential. Seek out opportunities to develop your skills and voice your ideas confidently, your perspective is valuable. Don't hesitate to advocate for yourself and set boundaries that protect your well-being. Remember that setbacks are often part of the journey, but resilience and persistence are key.

NeuroPath: Exploring careers beyond academia

Julio Santos Viotti, consultant in research and innovation projects

Sara Carracedo[1]
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The world of science offers many exciting paths, and academia is just one of them. Each year, both the public and private sectors actively seek PhD graduates to fill diverse roles. However, many of them may seem unfamiliar to most of us. At Brainstorm, we want to help you explore career options that align with your interests, and aspirations.

That's why we created NeuroPath: a section dedicated to highlight scientific related careers outside academia. We reached out to professionals, who like us, have earned a PhD in neurosciences, most of them from the Neurocampus, but chose to apply their expertise in different fields. Through their stories, they share insights into their career journeys, their current positions as well other practical questions.

Science is a lifelong pursuit, but the path you take is yours to choose.

Follow the one that excited you the most!

This month in Neuropath, we speak with Julio Santos Viotti, working as a consultant in research and innovation projects since 2025. With a bachelor's in Biology from the Federal University of Minas Gerais (UFMG, Brazil), he subsequently pursued an international joint Master's degree in Neurosciences between the University of Bordeaux and the University of Göttingen, which they completed in 2013. From 2013 to 2018, Viotti carried out a PhD in Neuroscience at the University of Göttingen, specializing in synaptic electrophysiology and synaptic transmission. He then continued as a postdoctoral researcher at the IINS from 2019 to 2024, focusing on electrophysiological approaches related to epilepsy.

Are you interested in knowing more about the consultant in research and innovation job as a career path? Then this section is for you!

Consultant in research and innovation projects

Julio Santos Viotti

I help researchers, companies, and NGOs develop and find funding for their research

What is your role about?

My role is to help researchers, companies, and NGOs develop research and innovation projects and secure funding, mainly through the Horizon Europe. I identify and analyze relevant funding calls and build suitable consortia by bringing together the right partners. Then, I work with partners to co-develop the project concept and work plan, coordinating inputs across disciplines. I advise on the scientific, technical, financial, and administrative aspects of proposals. Finally, I support the writing and finalization of the proposal. While I am not an expert in every field, my role is to connect experts and structure their contributions.

What made you choose this professional path?

I chose this path because I am interested in understanding how different pieces fit together rather than going very deep into a single topic, as occurs in academia. This role allows me to bring people and expertise together, without needing to master every detail myself. I also value the strongly collaborative nature of the work, with constant dialogue, rather than working alone on an individual project. Contrary to common misconception, this type of work offers real flexibility and intellectual freedom, as long as the objectives are achieved.

What's a matching profile ?

A PhD is not required, but it is a plus because it helps understand how academia works and how to read scientific literature. Strong communication and organization are essential to manage multiple projects and partners. Finally, being curious, willing to learn, and humble is key in this role.

Do you have some advice for people interested in following this path?

Get familiar with Horizon Europe calls, their structure, and funded projects. Importantly, build a strong network, as many opportunities arise through contacts rather than applying via LinkedIn.

Main responsibilities

- Identify and analyze relevant Horizon Europe calls and select the most suitable one
- Identify, build and coordinate a strong consortium of researchers and partners
- Co-develop the project concept, work plan, and implementation strategy
- Lead and coordinate the writing of the proposal, including scientific, technical, financial, and administrative sections

Requirements

A PhD is a bonus but soft skills such as critical thinking, good communication and organization are the primary requirements for this job.

Working conditions

- **Work environment:** It's great. Highly collaborative and open, with strong communication across all levels of the hierarchy
- **Pressure level:** Can be high close to proposal deadlines, but generally manageable
- **Work-life balance:** This job is project-based. Periods close to deadlines can be intense and require extra hours. However, the company counterbalances extra working hours by allowing to take extra days off
- **Salary:** Comparable to mid-level postdoc but there are bonuses for successful projects and progression with seniority

Do you have further questions?

Contact Julio at julioviotti@yahoo.com.br

Thinking in color

Interview with Sam Reiter

Juan Garcia-Ruiz[1]
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What's neuronhub? It is an outreach website hosting interviews with researchers from all corners of the planet about their work in the field of neuroscience. The idea is that you get something from people who have a long career in science, that you learn something new and cool, and above all that you don't lose track of the latest discoveries in neuroscience that are being made in other parts of the world.

Keep up to date with neuroscience by subscribing to the newsletter. Compensate for the useless spam you receive with high quality material! Scan the QR code here:

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Imagine if people could listen to your thoughts. Just by looking at you, they would know exactly how you feel. Angry? They would see it. Disappointed? No way to hide it. Stressed? It would be obvious. Now imagine that, in response, you could become invisible: simply disappear. This is not science fiction, but reality for some animals, such as octopuses and cuttlefish. They can change colour to communicate with one another and camouflage themselves to avoid predators. It is a remarkable, almost alien ability.

They achieve this thanks to a special type of cell called chromatophores, often described as cells that produce colour. Animals change colour in two main ways: by using pigments that absorb light (pigment-based chromatophores), or through structural changes that scatter or interfere with light (iridophores). Octopuses mainly rely on pigment-based colour change. Their muscle-controlled chromatophores expand and contract rapidly to create complex patterns and camouflage, while deeper reflective cells adjust brightness as a secondary mechanism. Chameleons, by contrast, depend mostly on structural colour change. Layers of iridophores shift the spacing of microscopic crystals to reflect different wavelengths of light, with pigments playing a secondary role by controlling how light or dark the skin appears. Pigment-based systems are especially effective for fast, detailed camouflage, and structural systems allow large shifts in colour, vivid displays, and functions such as signalling and thermal regulation.

As this shows, the living world is full of wonders. One of the most striking is the ability to transform appearance through chromatophores, whether to camouflage with the environment, signal to other animals, or regulate physiological states. I would love to go into more detail, but unlike Sam Reiter, I am not an expert on the subject. Fortunately, I had the opportunity to speak with him, and he was able to share insights from his research.

Sam Reiter is a neuroscientist. He did his undergrad in neuroscience at Brown University and then the PhD at the same university, with a partnership with the US National Institutes of Health. Then he went to Germany to do a postdoc in Max Planck Insitute for Brain Research. Finally he moved to Japan where he's an Associate Professor and head of the Computational Neuroethology Unit at the Okinawa Institute for Science and Technology (OIST).

He's interested in the neural basis of animal behavior, which he studies by combining experimental and computational approaches. His lab is known to study cephalopods such as octopus, cuttlefish, and squid, animal that possess large unexplored brains, and show complex and exciting behaviors such as camouflage.

Juan García Ruiz: When it comes to camouflage, we can think about how octopus change color, but also how some butterflies can go unnoticed because they already possess colors that mimic the environment. From an evolutionary point of view, what could favor the one over the other?

Sam Reiter: Cephalopod camouflage can be described as active camouflage because it is an active, neurally controlled process. It is difficult to compare it, since active camouflage, as far as we know, has evolved only once. Ancient cephalopods had shells, like ammonites, and some modern species, such as nautiluses, still do. Coleoid cephalopods (squids, octopuses, and cuttlefish) shifted into new predatory roles in the ocean and, possibly due to competition with fish, dropped their shells, grew larger brains, and evolved active camouflage along with more mobile lifestyles. These changes likely occurred together and are now seen across all coleoid cephalopods. Active camouflage supports this complex, mobile, predatory way of life. From a biological perspective, active camouflage and more passive forms of camouflage are not closely related, because the former depends on neural control, while the latter does not.

JGR: Camouflage can be used to catch prey, as you mentioned, but I assume it also serves a protective role. Are there other functions of camouflage beyond these?

SR: I think protection and hunting are the main roles of camouflage. That said, the patterns seen in cephalopods do more than just camouflage. They are also used for social signaling and threat displays. It's a fairly rich system that can express many different functions.

JGR: To what extent is camouflage an innate ability in these animals? Do they develop it even in laboratory conditions, even without exposure to predators or the need to hunt?

SR: That is still somewhat an open question. You can distinguish between passive and active camouflage here. Passive camouflage refers to the animal's basic coloration, which they are born with. There is likely some learning involved in choosing the most suitable environments, but it appears to be largely innate. Active camouflage also seems to be present from birth: baby squids, cuttlefish, and octopuses can camouflage immediately. However, certain patterns only appear later in development. Whether this depends on learning, environmental exposure, or maturation is less well understood. It is probably a combination of innate mechanisms and individual experience.

JGR: Do you think these animals would still be able to camouflage if they were unable to see?

SR: Camouflage appears to be largely vision-based. They do not seem to camouflage in complete darkness. There was a study in which animals were blinded, and they showed poor camouflage, although they also fed poorly, which complicates the interpretation. Still, it is clear that cephalopods are highly visual animals, and an impaired vision, either by darkness or eye damage, would strongly affect their camouflage.

JGR: Thinking about it the other way around, if they were able to see but not touch, would they still be able to imitate textures? And are the textures they display purely two-dimensional?

SR: Yes, they can camouflage in response to two-dimensional visual images without any tactile input, which shows that vision alone is sufficient. So you can take an image of a texture, print it in a sheet of paper, place it underneath the animal, and it will adopt the matching pattern. The way I see it, they perceive their environment as a two-dimensional projection onto their eyes, which you could call a visual texture. They then select one of their camouflage patterns, which can include both two-dimensional and three-dimensional components. But from the perspective of the predator, whether it is two dimensional or three dimensional is not making a huge difference because when they look at it, they ultimately see a two-dimensional visual texture.

JGR: Are these animals, to some degree, aware of the camouflage behavior, or is it more like a stimulus–response process?

SR: That's an interesting question. I think there has to be some awareness of their own pattern in order for them to camouflage effectively. If you think about complex motor problems in other animals, there's always some degree of feedback involved. For instance when you are playing tennis, there's proprioceptive feedback when you swing your arms. You know where your arms are in space and you can use that information to refine your swing. In the same way, the animal probably needs to have some sense of how it's doing in order to know whether it should change its pattern. The animal is constantly growing, so if it does the exact same camouflage pattern in the same situation every time, the quality of the camouflage is going to decrease as it gets larger. So there has to be some feedback, I would imagine. And in that sense, I think there has to be some awareness. But at this point, it's unclear how that awareness work.

JGR: Are there specific regions of their brains dedicated to this behavior, or is it more like a general brain activation?

SR: Very little is known about the cephalopod brain. But we do know that there are some areas involved in vision and others involved in the actual motor control of the cells in the skin. We also know there are anatomical connections between those areas, and that already involves a large part of the brain. So it's a visual process to start with, but then they have to decide which camouflage pattern to adopt, and after that there's the actual motor control. So it's definitely not a simple process.

JGR: Have you observed these animals displaying the wrong camouflage output?

SR: Yes. And sometimes they just don't camouflage at all. It's unclear whether they're trying to camouflage and doing it poorly, or whether they don't want to camouflage, or don't feel the need to. Sometimes you can see that they're trying to change their pattern, but they're not doing a very good job. That could be related to the fact that octopuses are apparently colorblind.

Note of the author: Octopuses are essentially color-blind in the human sense. They have only one type of photoreceptor in their retinas, so they can't discriminate wavelengths the way humans do. So how do they camouflage so well? The process doesn't rely on color matching, but on other cues, such as brightness matching (light versus dark, contrast), or pattern matching (stripes, disruptive edges, mottled patterns, and so on).

JGR: What approaches do you use to study camouflage?

SR: Mostly, up to now, it's been quantitative behavioral work. One approach consists of trying to describe these really complicated patterns on the animal's skin. We try to do this at the level of the individual cells that make up the pattern, which is generated by up to tens of thousands individual pigment cells that expand and contract under the control of the brain. Motor neurons projecting from the brain have different levels of activity, which cause different sets of chromatophores to expand and contract, and that's how they generate different patterns. We've done research describing these patterns in terms of the expansion state of all the chromatophores on the animal's back.

That's one way of studying camouflage, but it doesn't tell you how the animal matches the environment. Another approach is to measure visual textures in the environment and compare them to the visual textures generated by the animal. Traditionally, this has been done using a small number of simple visual features. For example, measuring the distribution of spatial frequencies in the environment and in the animal's skin, and then check whether they match. If they do, it's considered good camouflage; if they don't, it isn't. There are many different descriptors of visual texture you could choose.

More recently, we've tried describing the visual textures in the environment and on the animal's skin using deep neural networks, which are cutting-edge methods for analyzing complex visual patterns. These methods allow us to capture many features of the textures at once, providing a detailed way to quantify camouflage.

JGR: Can you develop a bit more on how these chromatophores work?

SR: These cells are arranged radially, like a sunburst, with muscles around them. When a motor neuron projects from the brain to the skin and synapses onto the muscles surrounding a chromatophore, the muscles contract as it fires action potentials, and the chromatophore expands. When it stops firing, the chromatophore contracts

again. So the expansion state, which corresponds to the size of the chromatophore, is basically a proxy for the activity level of the motor neurons driving it.

If you can record the state of all the chromatophores, you get a very rich, indirect description of the brain's output. That gives you a quantitative handle on these complex patterns. The way this translates into color is that different chromatophores contain different pigments, so the expansion and contraction of different ones produces different visible patterns.

Interestingly, they don't have purple chromatophores, so they seem to struggle when they need to appear that color. And there's a pattern they do that looks like they are frustrated. I don't want to anthropomorphize too much, but even when they try to hunt and they miss, they do a specific pattern that could be interpreted as frustration.

They also have other cell types called iridophores that reflect light, so whatever colors are present in the environment, they will get reflected back. Almost like having tiny mirrors in their skin.

JGR: Could you mention some of the findings from your lab that you're most proud of?

SR: The first is that you can describe camouflage quantitatively, which was actually somewhat surprising. The second is that you can infer a lot about motor control from this. By looking at which sets of chromatophores are coordinated, you can infer which ones receive common input from the brain. Those groups are then themselves coordinated into larger blocks, so you can infer an entire hierarchy of motor control just from observing the skin readout.

The thing I'm most interested in right now is that we recently found that when octopuses sleep, they go through two stages of sleep, like we do: a slow sleep stage and an active sleep stage that looks a lot like our REM sleep. During this active sleep, their camouflage rapidly transitions between different patterns. You can also find waking patterns that are identical to the sleeping ones. They seem to have a set of patterns they can produce, a kind of repertoire, and during active sleep they cycle through the different patterns in that repertoire. Whether this reflects previous experience or not, we're not sure yet. But it really looks like they're dreaming.

JGR: What directions is your research taking at the moment?

SR: We're trying to figure out which of these sleep patterns can be manipulated, and on what timescale. We want to understand the function of active sleep and see whether there are any parallels with the REM sleep we see in vertebrates. If there are, that would really point to a case of convergent evolution, potentially underlying some very general functions.

When it comes to waking camouflage, there are a number of questions I'm interested in. One is how the brain does this neutrally: how the motor systems generate these patterns, and how visual input is transformed into a decision about which pattern to adopt. Answering those questions requires going into the brain and doing more neuroscience in cephalopods. So the lab is focused on bringing more modern neuroscience tools to this problem. There have been a lot of recent breakthroughs in neuroscience techniques, and if they can be applied to cephalopods, I think it gives us some hope of cracking the problem a bit further.

JGR: You've studied many different species across very different branches of the evolutionary tree. What makes this neuroevolutionary approach an interesting way to tackle complex questions like intelligence? And what's the added value of studying species that are evolutionarily distant from us?

SR: There are a few benefits to that approach. Cephalopods are very different from us, and our common ancestor was an extremely simple organism. From that ancestor, different evolutionary branches gave rise to cephalopods and to humans, both of which ended up with large brains and complex behaviors that evolved independently. Comparing animals that are this different is a bit like looking at an alien intelligence, and it can help us understand what it really means to be a vertebrate.

Those comparisons are interesting because if you find similarities, they may point to some general features of intelligence, at least in biological organisms. And if you find differences, that tells you there are multiple ways of solving the same kinds of problems. So it's a way of breaking things apart to understand what's general and

what's specific to a particular group. Of course, you can also compare humans to rodents and find differences there, but with cephalopods we're talking about much larger evolutionary distances.

Another benefit is that some animals have unique features that make them especially well-suited for asking certain questions. Humans don't camouflage, for instance, so you might ask why we should care about camouflage at all. But active camouflage gives us a readout of the brain, and that potentially opens a window onto general aspects of brain function that are very difficult to study in vertebrates. Take sleep, for example. We can actually see these patterns evolving during sleep, reflecting something about brain activity. In this case, we have a window into what's going on while they're sleeping, and we don't really have that in vertebrates. If there are general principles to uncover, cephalopods give us access to them. And that's just one example, but there are many systems like this.

And the third reason is simply that it's interesting. If we found aliens, I'd want to know how they worked. I like research that's driven by curiosity and creativity.

JGR: What are the key debates in the field of neuroscience?

SR: I think one of the main issues in neuroscience is that there's a lack of consensus on what the most important questions actually are. There have been rapid advances in techniques, and there are many tools now that would have sounded like science fiction when I was a grad student, which is really exciting. But I don't think there's been the same level of progress on the theory side, in terms of knowing how these techniques should be used.

Everyone agrees that we want to understand things like consciousness, memory, attention, and other big-picture questions. But it's still not clear how to use the techniques we already have, and the ones we're developing, to really start making progress toward those goals. I go back and forth between thinking that this is kind of depressing, and also thinking it's exciting, because the field is so open and there's a lot of room to be creative. Sometimes, though, I'm a bit jealous of other branches of science where things feel more clear-cut. In a way, the debate is really about what the right questions to ask actually are.

JGR: You've worked with turtles, moths, cuttlefish, lizards, and many others. Which one has impressed you the most, and which one did you enjoy working with the most?

SR: I think octopuses are the most impressive. When you work with them, you get the sense that they're quite creative and seem intelligent, even though that's difficult to demonstrate scientifically. Usually, when an animal isn't doing a task, you tend to think it's failing to learn it. But sometimes, when an octopus isn't doing a task, you really feel like it's just bored with the task.

JGR: Do you feel that as you advance in your career, you spend less time actually doing science and more time writing emails and dealing with the bureaucratic side of academia? Or do you feel you've found a good balance?

SR: There are definitely more emails now, and more responsibilities that go beyond being at the bench. But a lot of those emails are still, in some way, related to science. It's a trade-off. There are things you can only do once you reach a certain point in your career and have several people working together on a project. Some of those things just couldn't be done by me alone.

JGR: When it comes to your career as a scientist, do you have a specific goal, or are you more about going with the flow and enjoying the process?

SR: I mostly do this because I want to keep working on interesting topics with interesting people. If you're aiming for one very specific thing, I actually think the best way to get there is by not trying to get to that one thing directly. There's an interesting book about this called Why Greatness Cannot Be Planned: The Myth of the Objective, by Kenneth O. Stanley and Joel Lehman. Many of the things we think of as real breakthroughs weren't planned by someone sitting down and saying: "okay, I'm going to do this". Instead, they followed a kind of meandering path.

I think the point of that book is very deep. The correct stand to take is not about fixing a question in advance, but about exploring. Just moving from one interesting thing to the next. That's what tends to lead to unexpected

and meaningful conclusions. History shows that this is how breakthroughs usually happen, rather than a scientist or a group of people getting together and saying: "this is the goal".

JGR: How do you find doing research in Japan compared to the Western countries you've worked in?

SR: There are definitely cultural differences. Back in Germany, there was a mix of Americans and Europeans, and I had the sense that Americans tended to be overly optimistic, while Europeans were rather pessimistic. Structurally, in Japan there's more of an emphasis on group projects, which has some benefits. In the States, everyone is more focused on getting their own individual grants and papers, whereas Japan encourages large groups of people working together.

JGR: What do you think about the *Publish or Perish* approach in science? Do you think it's here to stay in the long term?

SR: I think that when research is funded with public money, some kind of requirement to produce results isn't going away. But the trend of simply counting the number of papers as a metric for a scientist's quality is something I imagine will change. The problem is that whenever you put a metric like that in place, people will find ways to game the system. And once people start focusing on gaming the metric, it becomes a bad signal for whatever you're actually trying to measure.

Ideally, you'd want a system where everyone reads everyone else's work and takes the time to really think about how it fits into the broader context of scientific progress. But that's not realistic. So there has to be some kind of shortcut for assessing people's work, in order to make decisions about career advancement, grant allocation, publications, and so on. Every metric is going to be flawed in some way. I do think the system will change, but I'm not sure it will actually improve.

JGR: Do you have a message you'd like to share with the readers?

SR: I'd encourage people to really follow their interests. That's always going to lead to the most interesting things.

For more interviews, visit www.neuronhub.org

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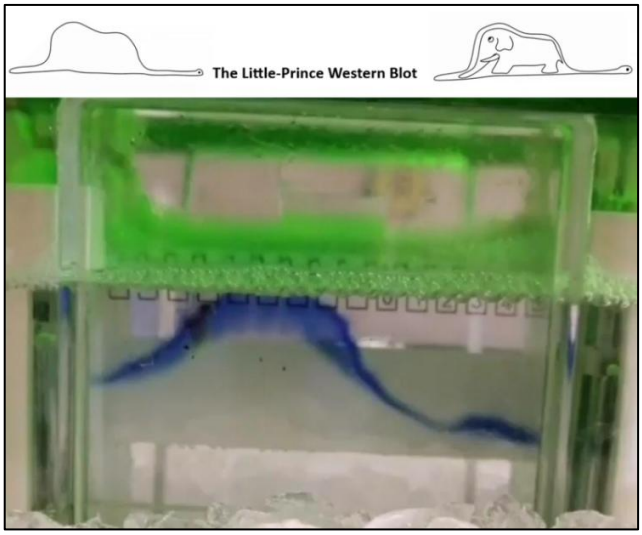
Neurofailure



Some people might call it a failed western blot. I prefer to call it a masterpiece (Ludovica Congiu)

Announcements

PhD seminar series

Remember to register to the PhD seminar series. You have until the end of February to register to the second part on ADUM.

Every first Friday of the month, you can attend the PhD seminar – a presentation by a guest chosen by the PhD community at the Neurocampus.

To keep up to date with the program, take a look at the Neurocampus website.

Call for instructors – Summer school introduction to experimental neuroscience

The workshop will take place from July 20th to August 1st.

The objective is to introduce master or PhD students from various background within or outside the neuroscientific field to the experimental Neuroscience.

As an instructor, you will supervise 2 or 3 students for 6 days to implement a mini project according to your specific technical skills. To develop your project, **you will have the assistance of experienced researchers and university professors** as well as the teams of the Bordeaux School of Neuroscience and the Bordeaux Neurocampus Graduate Program.

You can find more information on the Bordeaux Neurocampus website.

Editorial board

Toshiko Sekijima

Toshiko, originally from New Zealand, is currently PhD student at the Nutrition et Neurobiologie Intégrative (Nutrineuro). She holds a bachelor's in Biology from the University of Hawaii and a master's in agro-biomedical Science from the University of Tsukuba, Japan. She is also passionate by scientific illustration!

Sara Carracedo

Born in Spain, Sara is a Postdoctoral student at the IMN. She holds a Veterinary Medicine Bachelor's degree from the University of Santiago de Compostela, the NeuroBIM Master's degree, and a PhD in neurosciences from the University of Bordeaux. Her Postdoc at the IMN focused on understanding the neuroimmune role of P2X4 receptor in Amyotrophic lateral sclerosis. She is currently project lead in immunotherapies at BiAZ.

Daniele Stajano

Daniele Stajano was born in Naples (Italy). He has a Bachelor's degree in Biology and a Master's degree in Neurobiology. After his Ph.D. in neurosciences at the ZMNH of Hamburg (Germany), he joined as postdoctoral student the IINS. He is currently interested in molecular mechanisms orchestrating brain maturation in neurodevelopmental disorders such as the autistic spectrum disorder.

Ludovica Congiu

Ludovica, originally from Sardinia, Italy, trained in Neuropsychobiology at the University of Cagliari and obtained her Ph.D. in Neuroscience at the Universitätsklinikum Hamburg-Eppendorf (UKE) in Hamburg. She is currently a Postdoctoral Researcher at INCIA, where her research investigates Congenital Central Hypoventilation Syndrome (CCHS), with a particular focus on defining the role of microglia in disease pathophysiology.

Simon Lecomte

Simon is originally from Lyon, France. He did his Bachelor's of Psychology from Strasbourg, after which he did the NeroBIM master's degree from the University of Bordeaux. He was a PhD student at the IINS where he was studying how the Fragile X Syndrome impacts the presynaptic mechanisms at the DG-CA3 synapses.

Aude Verboven

Aude, directly coming from Bordeaux, is a PhD student at the IMN. She previously graduated from the MultiPublic track of Bordeaux Neurosciences Master. She is currently studying the dopaminergic afferences to pain modulating nuclei in the context of Parkinson's disease.

Juan Garcia-Ruiz

With two Bachelor's degree, in Psychology and Biochemistry, and the NeuroBIM Master's degree from the University of Bordeaux, Juan is pursuing a PhD focused on the role of lactate in basal synaptic transmission. Although he speaks near-perfect French, Juan comes from Huelva, Spain. He is also the co-founder of neuronhub (www.neuronhub.org).

BRAINSTORM

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