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AUTOMATISIERUNG VON JURISTISCHEN ENTSCHEIDUNGEN

DIE KÜNSTLICHE INTELLIGENZ AM BEISPIEL DER RÖMISCHRECHTLICHEN KASUISTIK

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Neuroheuristics, a flexible, problem-solving paradigm in Neuroscience

1. Theoretical Framework

Modern scientific thought rests on the assumption of an objective external world, a belief upheld by a rational approach that relies on the mechanical laws of causality and determinism. This approach, which Descartes developed in the 17th century, underpins classical empiricism and has been instrumental in advancing physical and technical sciences, shaping the technoculture we experience today. However, this positivist and reductionist approach has revealed its limitations, even in its areas of greatest success.

For example, in fluid mechanics, understanding turbulence requires the introduction of deterministic chaos theories [1]. In biomedical research, the limitations of classical approaches become even more evident, particularly when confronted with pathological processes and aging. The apparent stability of an individual is, in fact, an illusion, as living organisms constantly renew the majority of their constituent molecules. This continuous interplay of anabolism and catabolism in each cell is the primary consumer of energy in living beings. This process seemingly violates classical thermodynamic theory, which can only be understood by postulating that energy dissipation leads to a new, more stable state. Discontinuity in organizational levels must therefore be accompanied by information flows, which are

[1] U. FRISCH, *Turbulence: The Legacy of A. N. Kolmogorov*, Cambridge, 1995; S.B. POPE, *Turbulent Flows Turbulent Flows*, Cambridge, 2000.

difficult to measure and quantify within the metric dimensions of space where classical scientific approaches have traditionally operated.

In studying brain functions, cognition cannot be considered independently of its neurobiological foundations and its relationship to mental representation, logic, and computational theories of animal and human performance. It is widely acknowledged that biological systems exhibit genetic and epigenetic imprecision, which can fatally damage certain developing cells. Notably, the massive disappearance of 20 to 50% of nerve cell populations at an advanced stage of maturation represents a significant discontinuity, presumably necessary for transitioning to a higher level of organization [2]. However, programmed neuronal death, or *apoptosis*, involves cells that have already expressed their characteristic genes and, in most cases, established connections with their target cells. The purpose of this process, characterized by hyperproduction followed by the loss of many cells, is not easily understood as it differs significantly from the logic of classical ontogenesis. Two points are particularly noteworthy: first, the development of an organism represents a progressive series of constructive stages, including cell accrual, organ growth, and maturation, as well as the differentiation of biochemical and physiological functions. Second, programmed cell death is the only instance in an individual's life where the massive loss of cells does not correspond to a pathological or aging process.

It is challenging to conclude that characteristics defined at the mental level, related to individual experience, are reflected at a lower level, i.e., the constituents of the central nervous system. This perspective cannot explain why the brain of Anatole France, a brilliant writer and Nobel Prize laureate in literature [3], was comparable in weight [4] to that of Java Man (*Pithecanthropus erectus*), or why the brain size of Neanderthal Man was greater than that of *Homo sapiens* [5]. Efforts to understand cerebral functioning encounter the scale problem of the study objects them-

[2] J.K. ANDERSEN, *Oxidative stress in neurodegeneration: cause or consequence?*, in *Nat Med*, 10 Suppl, July 2004, p. 18-25 [doi: 10.1038/nrn1434]; M.P.J. DEKKERS, V. NIKOLETOPOULOU, Y.-A. BARDE, *Cell biology in neuroscience: Death of developing neurons: new insights and implications for connectivity*, in *J Cell Biol*, 203.3, Nov. 2013, p. 385-393 [doi: 10.1083/jcb.201306136]; M. RIVA et al., *Activity-dependent death of transient Cajal-Retzius neurons is required for functional cortical wiring*, in *eLife*, 8, Dec. 2019, e50503 [doi: 10.7554/eLife.50503].

[3] Url: https://www.nobelprize.org/prizes/literature/1921/france/facts/(visited on 08/20/2024).

[4] A. KEITH, *The Brain of Anatole France*, in *Br Med J.*, 2.3491, Dec. 1927, p. 1048-1049.

[5] D. FALK, *3.5 Million years of hominid brain evolution*, in *Seminars in Neuroscience*, 3.5, *Evolving Neural Functions*, 1991, p. 409-416 [issn: 1044-5765; doi: 10.1016/1044-5765(91)90031-I]; I. TATTERSALL, *Endocranial volumes and human evolution*, in *F1000Res*, 12, 2023, p. 565 [doi: 10.12688/f1000research.131636.1].

selves, whether at the molecular, cellular, individual, or social levels [6].

2. A Transdisciplinary Strategy

The research strategy based on 'bottom-up' causality, i.e., moving from lower levels of complexity to higher ones, preferred by neurobiologists, appears potentially necessary and sufficient. However, it remains inaccessible to experimentation due to the impossibility of simultaneously examining all cellular elements of a brain, regardless of how primitive it may be. Conversely, a 'top-down' strategy, which begins with higher levels of complexity and uses 'black boxes' to move toward lower complexity, seems easier to implement but is neither necessary nor sufficient to understand the foundations of brain activity. Attributing functional mechanisms to a specific level of organization results from a reductionist and ambivalent interpretation of the problem. The convergence of 'bottom-up' and 'top-down' causality carries the potential leading to a transformation towards a new and unforeseen approach in neuroscience, characterized by an unexpected combination of pre-existing properties. In the 21st century, such an approach must continually incorporate emerging sciences and technologies, which drive this emergence, with molecular biology and computing being among the most important today. It is through this kind of approach, grounded in a transdisciplinary framework [7] within neuroscience that transcends existing disciplinary boundaries, that the theoretical framework of 'neuroheuristics', or 'neuristics' (derived from the Greek words νεῦρον [*neuron*] meaning 'nerve' and εὑρίσκειν [*heuriskein*] meaning 'to find' or 'to discover'), is developed [8]. This definition refers to the dynamic relationships between the knowledge acquired by neuroscience through an approach that cannot be reduced to expertise alone, as it is constantly renewed at each stage of advancement toward scientific discovery.

Neuroscience offers an ideal field for applying molecular biology techniques, particularly in identifying gene mutations directly responsible for certain pathologies. Approximately 40% of human genes are expressed in the brain [9], and around

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[6] C. Koch, *Does Brain Size Matter?*, in:*Sc. Am. Mind*, 27.1, 2016, p. 22-25; J.M. DeSilva et al., *When and Why Did Human Brains Decrease in Size? A New Change-Point Analysis and Insights From Brain Evolution in Ants*, in *Front Ecol Evol*, 9, Oct. 2021, p. 742639 [issn: 2296-701X; doi: 10.3389/fevo.2021.742639].

[7] R. Kötter, P.W. Balsiger, *Interdisciplinarity and Transdisciplinarity: A Constant Challenge To The Sciences*, in *Issues Integrative Stud*, 17, 1999, p. 87-120.

[8] J.G. Taylor, A.E.P. Villa, *The 'Conscious I': A Neuroheuristic Approach to the Mind*, in *Frontiers of Life* (*ed.* D. Baltimore et al.), 3, 2001, p. 349-368.

[9] D. Wang et al., *Comprehensive functional genomic resource and integrative model for the*

hundreds hereditary diseases producing central nervous system pathology have been identified [10]. It is estimated that there are approximately 20,000 to 25,000 genes expressing proteins, with the average gene being about 1200 base pairs long. Moreover, the completion of the human genome map [11] paves the way for identifying more genes involved in nervous system pathologies. It is important to note that not all genes are expressed as proteins at all times; gene expression can vary by cell type, developmental stage, environmental factors, and other conditions. Additionally, the human genome contains many non-coding regions that play critical roles in regulating gene expression and other genomic functions. The manifestation of several neurological and psychiatric disorders is assumed to be linked to the complex interaction of multiple gene expressions and behavioral factors. This complexity increases as genes that predispose an individual to a particular pathology may remain latent until specific environmental conditions arise.

In an algorithmic approach, the result is certain, but the efficiency of the implemented procedure may require virtually infinite time, making the procedure impractical. A heuristic approach, however, does not guarantee the best possible result but emphasizes the renewal that occurs at each stage of research, leading to a satisfactory outcome that meets clearly established criteria. Exploring the genetic bases of pathologies, such as schizophrenia, manic-depressive syndrome, or Alzheimer's disease, offers an avenue for understanding fundamental biological functions and positions molecular neurobiology as a cornerstone of neuroheuristics. From a research strategy perspective, it is important to note that the discovery of cholesterol's biological functions was achieved by studying only a small fraction of the population with significantly high blood cholesterol levels [12]. The study of a small number of patients with a rare genetic syndrome ultimately contributed to understanding the cellular mechanisms operational in the overall patients affected by hypercholesterolemia.

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human brain, in *Science*, 362.6420, Dec. 2018, aat8464 [doi: 10.1126/science.aat8464]; E. Sjöstedt et al., *An atlas of the protein-coding genes in the human, pig, and mouse brain*, in *Science*, 367.6482, Mar. 2020, eaay5947 [doi: 10.1126/science.aay5947].

[10] E.C. Cooper, L.Y. Jan, *Ion channel genes and human neurological disease: recent progress, prospects, and challenges*, in *Proc Natl Acad Sci USA*, 96.9, Apr. 1999, p. 4759-4766 [doi: 10.1073/pnas.96.9.4759]; A. Shukla et al., *Genetic disorders with central nervous system white matter abnormalities: An update*, in *Clin Genet*, 99.1, Jan. 2021, p. 119-132 [doi: 10.1111/cge.13863].

[11] The Human Genome Project was launched in October 1990 and completed in April 2003, proving a crucial impact in accelerating the study of human biology and improving medical practices. See the site: https://www.genome.gov/human-genome-project.

[12] The work of Brown and Goldstein, who were awarded the Nobel Prize in 1985 for their discoveries concerning the regulation of cholesterol metabolism, was primarily focused on the LDL receptor pathway, which was studied in selected individuals with extremely high cholesterol levels.

3. Neuroscience and New Technologies

The brain processes information through a harmony between heredity and environment, innate and acquired factors. The nature vs. nurture debate has historical roots in philosophy, with early thinkers like John Locke advocating for the 'tabula rasa' or blank slate theory [13], suggesting that individuals are shaped entirely by their experiences. On the other hand, figures like Charles Darwin and the development of evolutionary theory [14] highlighted the importance of innate qualities and biological predispositions. Modern perspective perspective suggests that nature and nurture are intertwined, meaning that genetic predispositions can be influenced, enhanced, or suppressed by environmental factors. For instance, someone may have a genetic predisposition for a certain trait, such as musical ability, but without the right environmental support (such as access to music education), this potential might not be fully realized. Neuroheuristics must maintain this balance in its approach, dealing with dynamic relationships. The existence of laws governing this dynamic equilibrium is a pertinent question. The first biological laws, acknowledged by the scientific community shortly after their discovery, were Mendel's laws [15]. These laws, elucidated by chromosomes and genes in their quantitative aspect at the macroscopic level, still form the basis of many current evaluations in human genetics. Amidst such success, it has been easy to lose sight of the fundamental conditions describing the framework of application of biological laws, especially given the classical mechanistic approach that considers time as a variable that can have negative values. For the past decades, the school of Nobel Prize laureate Ilya R. Prigogine [16] has tackled the paradox of the irreversibility of time by reformulating the laws of physics. As Prigogine himself emphasizes, classical formulations, in terms of trajectories or wave functions, are valid only for stable and stationary systems. *'[...] these physical laws do not constitute the context against which the living must define itself: not because it is alive, but because, physically, it does not fulfill the conditions for the application of these laws, the conditions under which these laws are relevant. The living operates far from equilibrium, in a domain where the consequences of entropy growth can no longer be interpreted according to*

[13] N. Wood, *Tabula Rasa, Social Environmentalism, and the 'English Paradigm'*, in *Journal of the History of Ideas*, 53.4, 1992, p. 647-668 [doi: 10.2307/2709942].

[14] F. Boero, *From Darwin's Origin of Species toward a theory of natural history*, in *F1000Prime Rep*, 7, 2015, p. 49 [doi: 10.12703/P7-49].

[15] M. Keynes, T.M. Cox, *William Bateson, the rediscoverer of Mendel*, in *J R Soc Med*, 101.3, Mar. 2008, p. 104 [doi: 10.1258/jrsm.2008.081011].

[16] Url: https://www.nobelprize.org/prizes/chemistry/1977/prigogine/facts/ (visited on 08/21/2024).

the principle of Boltzmann's order' [17]. This clearly indicates that the laws of nature are constructed in stages.

The paradigm of neuroheuristics aligns with this line of thought. The organization of the nervous system is oriented towards the temporal processing of information, particularly memorization and self-projection into the future, operationally defined as prediction. The prefrontal cortex is particularly involved in mediating temporal contingencies, and this structure has prevailed in the phylogenetic process related to hominization [18]. It is crucial to note that the dynamic relationships between memorization and prediction occur mainly during sleep [19]. In humans, instrumental sleep deprivation can lead to observed memory disturbances that suggest complex neurophysiological disruptions, both frontal and temporo-occipital [20]. In such cases, subjects are no longer able to access 'memories of the future,' the repertoire of constantly updated and optimized action plans based on past experiences and ready to be invoked in the present. The consequences of sleep deprivation include indifference, inactivity, lack of ambition, and an inability to foresee the consequences of an action, defined as self-projection into the future [21]. In the absence of chronological references, the concept of time disappears during sleep. Introspection of dream activity by each of us explicitly indicates how much we mix memories spaced in time with impossible situations, creating virtual memories that can assume a character comparable to virtual reality [22].

[17] This is a translation from the original French text: «[...]ces lois physiques ne constituent pas le contexte par rapport auquel le vivant doit se d´efinir: non pas parce qu'il est vivant mais parce que, physiquement, il ne remplit pas les conditions d'application de ces lois, les conditions sous lesquelles ces lois sont pertinentes. Le vivant fonctionne loin de l'´equilibre, dans un domaine ou` les cons´equences de la croissance de l'entropie ne peuvent plus ˆetre interpr´et´ees selon le principe d'ordre de Boltzmann». I. PRIGOGINE, I. STENGERS, *La Nouvelle Alliance: M´etamorphose de la science*, Paris, 1979, p. 193.

[18] J.M. FUSTER, *The Prefrontal Cortex* [5], London, Aug. 2015 [doi: 10.1016/c2012-0-06164-9].

[19] S. GAIS, J. BORN, *Declarative memory consolidation: mechanisms acting during human sleep*, in *Learn Mem*, 11.6, 2004, p. 679-685 [doi: 10.1101/lm.80504]; J.G. KLINZING, N. NIETHARD, J. BORN, *Mechanisms of systems memory consolidation during sleep*, in *Nat Neurosci*, 22.10, Oct. 2019, p. 1598-1610 [doi: 10.1038/s41593-019-0467-3].

[20] J.A. HORNE, *A review of the biological effects of total sleep deprivation in man*, in *Biol Psychol*, 7.1-2, Sept. 1978, p. 55-102 [doi: 10.1016/0301-0511(78)90042-x]; M. IRISH, O. PIGUET, J.R. HODGES, *Self-projection and the default network in frontotemporal dementia*, in *Nat Rev Neurol*, 8.3, Feb. 2012, p. 152-161 [doi: 10.1038/nrneurol.2012.11].

[21] E. VAN DER HELM, N. GUJAR, M.P. WALKER, *Sleep deprivation impairs the accurate recognition of human emotions*, in *Sleep*, 33.3, Mar. 2010, p. 335-342; M.P. WALKER, *The role of sleep in cognition and emotion*, in *Ann N Y Acad Sci*, 1156, Mar. 2009, p. 168-197 [doi: 10.1111/j.1749-6632.2009.04416.x]; M.E. COLES, J.R. SCHUBERT, J.A. NOTA, *Sleep, Circadian Rhythms, and Anxious Traits*, in *Curr Psychiatry Rep*, 17.9, Sept. 2015, p. 73 [doi: 10.1007/s11920-015-0613-x].

[22] L. BEATTIE et al., *Social interactions, emotion and sleep: A systematic review and research*

The sudden reorganization of information thus seems to correspond to processes characterized by a temporal dimension other than what we know through classical mechanics, suggesting the emergence of brain activities associated with perceptual leaps (the Gestalt switch) that better account for the sudden emergence of certain ideas, intuitions, or mental clicks [23]. This process necessarily involves breaking the temporal constraint [24]. But like axioms in mathematics, the biological laws of neuroscience determined in the 19th and 20th centuries were based on observations made before. These were generally correct, but when observation is strictly limited to description, it becomes reductive. Conversely, when its relevance is no longer dependent solely on quantitative measurement, it can echo what Einstein said about his own experience: 'Words and language, written or spoken, do not seem to play any role in the mechanism of my thought. The psychic entities that serve as elements of thought are certain signs or more or less clear images, which can be reproduced or combined at will' [25].

It should be noted that the seemingly vague or imprecise nature of perceptual leaps accompanying intuition questions the classical notion of space-time [26]. Neuroheuristics cannot escape this questioning either. Indeed, information propagates along the membranes of nerve cells through electrical impulses, action potentials, at speeds ranging from 1 to 300 km/hour [27]. One of the brain's strengths is undoubtedly its ability to process information massively and in parallel [28]. However,

agenda, in *Sleep Med Rev*, 24, Dec. 2015, p. 83-100 [doi: 10.1016/j.smrv.2014.12.005]; C. Picard-Deland, T. Nielsen, M. Carr, *Dreaming of the sleep lab*, in *PLoS One*, 16.10, 2021, e0257738 [doi: 10.1371/journal.pone.0257738].

[23] E. Wright, *Discussion: Gestalt Switching: Hanson, Aronson, and Harré*, in *Philosophy of Science*, 59.3, 1992, p. 480-486 [doi: 10.1086/289685]; K. Brad Wray (*ed.*), *Interpreting Kuhn: Critical Essays*, Cambridge, 2021; T. Metzinger, *The Elephant and the Blind: The Experience of Pure Consciousness: Philosophy, Science, and 500+ Experiential Reports*, Boston, 2024.

[24] E. Fell, *Duration, Temporality, Self. Prospects for the Future of Bergsonism*, Lausanne, 2012.

[25] B.M. Patten, *Visually Mediated Thinking: A Report of the Case of Albert Einstein*, in *J Learn Disabil*, 6.7, 1973, p. 415-420.

[26] Taylor and Villa, *The 'Conscious I'*, cit., see n. 8.

[27] R.B. Stein, E. Roderich Gossen, K.E. Jones, *Neuronal variability: noise or part of the signal?*, in *Nat Rev Neurosci*, 6.5, May 2005, p. 389-397 [doi: 10.1038/nrn1668]; S. Rama, M. Zbili, D. Debanne, *Signal propagation along the axon*, in *Curr Opin Neurobiol*, 51, Aug. 2018, p. 37-44 [doi: 10.1016/j.conb.2018.02.017].

[28] V. Braitenberg, *On the Texture of Brains: An introduction to neuroanatomy for the cybernetically minded*, New York, 1977; G. Palm, *Neural Assemblies: An Alternative Approach to Artificial Intelligence*, 7, *Studies of Brain Function*, Berlin-New York, 1982 [doi: 10.1007/978-3-642-81792-2]; M. Abeles, *Corticonics: Neural Circuits of the Cerebral Cortex* [1], Cambridge, 1991 [doi: 10.1017/CBO9780511574566]; D.J. Amit, *Modeling brain function: The world of attractor neural networks* [2], Cambridge, 1992.

these different transmission speeds cause a temporal distortion of information that is difficult to inscribe into the metric frameworks we usually deal with [29]. In general, we prefer the restrictive framework of the binary causal paradigm discussed earlier. What would happen to communications between Lausanne and Geneva if information about the same event were transmitted via the Internet, by surface mail in a car or with a cycling rider, by naval flag signaling or by the melody of an Alpine horn relayed at regular distances? Yet, all these means of communication are possible, each with its alphabet and code. It is therefore fascinating to question the mechanisms that allow the brain to master several information codes simultaneously.

What distinguishes neuroheuristics from cognitive sciences lies primarily in the renewal that occurs at each stage of research progress, as seen in the understanding of decision-making and volitional processes. By aiming at hypotheses destined to be surpassed, this perspective is very different from most cognitive models. Neuroscience has contributed relatively little to understanding the biological substrates of creativity, despite the many advances made through animal experimentation in understanding the neurobiological foundations of perception, learning, or memory. In contrast, cognitive sciences have tackled the brain-mind problem by separating declarative knowledge (knowing what) from procedural knowledge (knowing how) [30].

It is undeniable that cognitive sciences have benefited in this regard from exchanges with artificial intelligence, which itself leverages breakthroughs in electronics. The discovery of the transistor, followed by the advent of computers, allowed many researchers to confront the theory and technique of computer programming. Analogies between the abstract levels of organization of the computer and the brain go beyond the simple observation that programming represents a deliberate attempt at artificial imitation of human intellectual activity. However, logical-mathematical developments have suggested that cognitive activities are related

[29] A.E.P. VILLA, *Empirical Evidence about Temporal Structure in Multi-unit Recordings*, in *Time and the brain* (*ed.* R. MILLER), 3, *Conceptual Advances in Brain Research*, London, 2000, Chap. 1, p. 1-61 [doi: 10.4324/9780203304570_chapter_1]; M. ABELES, *Neuroscience. Time is precious*, in *Science*, 304.5670, Apr. 2004, p. 523-524 [doi: 10.1126/science.1097725]; R. VARDI et al., *Synchronization by elastic neuronal latencies*, in *Phys Rev E Stat Nonlin Soft Matter Phys*, 87.1, Jan. 2013, p. 012724 [doi: 10.1103/PhysRevE.87.012724]; J. CABESSA, A.E.P. VILLA, *Attractor dynamics of a Boolean model of a brain circuit controlled by multiple parameters*, in *Chaos*, 28.10, Oct. 2018, p. 106318 [doi: 10.1063/1.5042312].

[30] R.C. ATKINSON, R.M. SHIFFRIN, *Human Memory: A Proposed System and its Control Processes*, in *Psychology of Learning and Motivation* (*ed.* K.W. SPENCE and J.T. SPENCE), 2, New York, 1968, p. 89-195 [doi: 10.1016/S0079-7421(08)60422-3]; L.R. SQUIRE, *Memory systems of the brain: a brief history and current perspective*, in *Neurobiol Learn Mem*, 82.3, Nov. 2004, p. 171-177 [doi: 10.1016/j.nlm.2004.06.005]; G. RYLE, *The concept of mind*, 60th anniversary, London, 2009.

to calculations, thus reducing intellectual activity to the computational dimension. This position is not acceptable to neuroheuristics, which subscribes to the synergy of computer science and neuroscience. In the short, yet already rich, history of neuroscience, a similar synergy has occurred. In 1753, the Bernese physiologist Albrecht von Haller (1708-1777) published a groundbreaking essay in G¨ottingen, *A dissertation on the Irritable and Sensitive Parts of Animals* [31]. This work dealt with numerous experiments involving vivisection and stimulation of organs by exploiting the newly offered knowledge to physiology by physics, chemistry, and natural history. With a fairly rudimentary technique of stimulation, von Haller classified parts as irritable, sensitive, or elastic, noting that reactions differed among various parts of the brain. The historical importance of von Haller's work lies not so much in the results obtained but in their systematic methodology within a group of students actively integrating new technologies. It was a turning point in the academic milieu of the 18th century, despite von Haller, with his usual caution, noting that research needed finer techniques for investigating the healthy and diseased brain, as well as broader studies that could allow comparisons across the entire animal kingdom.

By introducing galvanic fluid currents into the brain [32], a powerful new means of investigation emerged in the late 18th and 19th centuries [33]. The use of electricity went beyond its instrumental character, forming the foundation of electrophysiology, and provided the basis for fruitful hypotheses about the propagation and generation of this type of energy. Inspired by von Haller and the works of his compatriot Vincenzo Malacarne (1744-1816), the Piedmontese physician Luigi Rolando (1773-1831) made a fundamental contribution to surpassing the descriptive naturalistic paradigm adopted until then [34]. Drawing from the work of Alessandro Volta (1745-1827), Rolando was influenced by the analogy between the electrical apparatus and certain brain structures. His research was based on a metaphysical postulate, asserting that the brain's conformation must be subject to con-

[31] A. von Haller, *A dissertation on the sensible and irritable parts of animals*, London, 1755. This is an English translation from the Latin by the Bernese Baron Albrecht von Haller with a translation from the French of the Preface by the Genevan physician Samuel Auguste David Tissot. The English text includes the translations of *De partibus corporis humani sensilibus et irritabilibus* and *De motu cordis a stimulo nato*, published in v. 2 (1753) and v. 1 (1752) respectively, in the Transactions of the Royal Society of Sciences at Göttingen.

[32] L. Galvani, *Memorie sulla elettricità animale*, Bologna, 1797.

[33] M. Guarnieri, *Electricity in the Age of Enlightenment [Historical]*, in *IEEE Industrial Elec- tronics Magazine*, 8.3, 2014, p. 60-63 [doi: 10.1109/MIE.2014.2335431].

[34] L. Rolando, *Saggio sopra la vera struttura del cervello dell'uomo e degli animali e sopra le funzioni del sistema nervoso*, Sassari, 1809.

stant and recognizable laws. Rolando criticized the organological concepts [35] suggested by Franz Joseph Gall (1758-1828), which rapidly spread in the Western world, not driven by *a priori* concepts. He acknowledged their anatomical work but repeatedly denounced the lack of evidence for the existence of distinct bodies or organs for the twenty-seven mental functions identified by contemporary phrenologists.

4. A Work Plan for Contemporary Issues

The heuristic paradigm of von Haller-Rolando did not develop among 19th-century neuroscientists, potentially explaining the conceptual lag in biomedical neuroscience compared to mathematics, physics and chemistry. It is rational to say that, about two hundred years ago, the introduction of a new science, electricity, and its associated technology faced a situation similar to today, where neuroscience confronts computing. In neuroheuristics, computing is a pivotal technology with a fundamentally evolutionary nature. It has become commonplace to consider computer equipment over three years old as outdated due to rapidly increasing performance [36]. Using algorithmic analytical methods, many encryption problems would take tens of thousands of years to decipher [37]. However, recently proposed heuristic methods will almost always provide a solution within reasonable timeframes, challenging the notion of unsolvability [38]. The paradoxical questioning of computing, generated by the tension between technological progress and the preservation of structural schemes, such as programming languages, is crucial support for the neuroheuristic approach.

Rationality can be instrumental when behavior is optimized to achieve appropriate goals and can be epistemic when holding beliefs are commensurate with evidence at hand [39]. When the time comes to commit a verdict, the judge is sup-

[35] F.J. GALL, *Anatomie et physiologie du syst`eme nerveux en g´en´eral et du cerveau en particulier, avec des observations sur la possibilit´e de reconnaˆıtre plusieurs dispositions intellectuelles et morales de l'homme et des animaux par la configuration de leurs tˆetes*, Paris, 1819.

[36] G.E. MOORE, *Cramming more components onto integrated circuits*, in *Readings in Computer Architecture* (*ed.* M.D. HILL, N.P. JOUPPI and G.S. SOHI), San Francisco, 2000, p. 56-59 [isbn: 1558605398]; E. BRYNJOLFSSON, A. MCAFEE, *The second machine age: Work, progress, and prosperity in a time of brilliant technologies*, New Yor, 2014.

[37] R.L. RIVEST, A. SHAMIR, L. ADLEMAN, *A method for obtaining digital signatures and public-key cryptosystems*, in *Communications of the ACM*, 21.2, Feb. 1978, p. 110-126 [issn: 1557-7317; doi: 10.1145/359340.359342].

[38] R.E. KORF, *Depth-first iterative-deepening*, in *Artificial Intelligence*, 27.1, Sept. 1985, p. 97-109 [doi: 10.1016/0004-3702(85)90084-0; Kearns1994bk; Papadimitriou1994bk].

[39] K.E. STANOVICH, *What intelligence tests miss: The psychology of rational thought*. New Ha-

posed to make his decision on the basis of a dialectical logic based on the analysis of rational probabilities on the whole of the evidence presented. In the civil law system, the judge is supposed to reach a moral certainty of the rightness of his verdict, given the evidence, as a whole, establishes the requisite intimate conviction of guilt. It is assumed that the absolute truth is out of reach and that a criminal conviction does not require to prove every element of a crime beyond a reasonable doubt [40]. Motivation concepts lie at the core of the model of central coherence with the assumption that neural circuits process on-line cognitive operations and that selection of which action is to be carried out in presence of alternatives or conflicts is the outcome of mutual inhibitory networks [41]. The fact that certain patients were characterized by well-defined impairments in decision making, as they tended to take decisions not advantageous for their personal lives and for their social status, associated with learning impairments and difficulties in processing correctly the perceived information led to define the Somatic Markers Hypothesis [42]. Then, it appears that one possibility to characterize the process of the steps leading a suspect to confess and a judge to decide his verdict may be tested against cognitive and affective models based on previous studies of brain functions [43].

Advancing the understanding of cognitive functions requires provisional hypotheses, whose validity is not universal but functional and limited to the context where these hypotheses operate [44]. The study of sensorimotor integration and decision-making processes, with a focus on the auditory sensory modality, using a loop combining clinical data analysis of patients affected by disorders of the executive functions, animal experimentation, and simulation, has been at the core of re-

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ven, 2009.

[40] W.K. Lietzau, *Checks and Balances and Elements of Proof: Structural Pillars for the International Criminal Court*, in *Cornell International Law Journal*, 32, 3, 2015, p. 610.

[41] U. Frith, F. Happé, *Autism: beyond 'theory of mind'*, in *Cognition*, 50.1-3, Apr. 1994, p. 115-132; K.C. Berridge, *Motivation concepts in behavioral neuroscience*, in *Physiol Behav*, 81.2, Apr. 2004, p. 179-209 [doi: 10.1016/j.physbeh.2004.02.004].

[42] A. Bechara et al., *Insensitivity to future consequences following damage to human prefrontal cortex*, in *Cognition*, 50.1-3, 1994, p. 7-15 [doi: 10.1016/0010- 0277(94)90018-3]; A. Bechara, A.R. Damasio, *The somatic marker hypothesis: A neural theory of economic decision*, in *Games Econ Behav*, 52.2, 2005, p. 336-372 [issn: 0899-8256 - Special Issue on Neuroeconomics; doi: 10.1016/j.geb.2004.06.010].

[43] C.M. Altimus, *Neuroscience Has the Power to Change the Criminal Justice System*, in *eNeuro*, 3.6, 2017, ENEURO.0362-16.2016 [doi: 10.1523/ENEURO.0362-16.2016]; C.J. Kraft, J. Giordano, *Integrating Brain Science and Law: Neuroscientific Evidence and Legal Perspectives on Protecting Individual Liberties*, in *Front Neurosci*, 11, 2017, p. 621 [doi: 10.3389/fnins.2017.00621].

[44] A.E.P. Villa, *Neural Coding in the Neuroheuristic Perspective*, in *The Codes of Life: The Rules of Macroevolution* (*ed.* M. Barbieri), 1, *Biosemiotics*, Berlin, 2008, Chap. 16, p. 357-377.

search leading to the establishment in 1995 of the neuroheuristics laboratory [45]. Laboratory members have diverse backgrounds, including neurobiology, pharmacology, anatomy, physics, computing, and electronics. To overcome disciplinary compartmentalization, the interaction of these branches allows the emergence of neuroheuristics through a transdisciplinary process. Our study theme is currently developed along several overlapping research axes including: (i) the study of functional interactions between higher nervous centers and their relation to clinical pathologies (e.g., attention deficit hyperactive disorder (ADHD), epilepsy, Alzheimer's type senile dementia) [46]; (ii) the 'non-specific' mod- ulation of information in thalamic and cortical circuits [47]; (iii) the behavioral approach to the sen-

[45] The neuroheuristics laboratory was created within the premises of the Institute of Physiology at the Faculty of Medicine of the University of Lausanne, then migrated to the Faculty of Sciences of the same university, then to the Faculty of Medicine at the University of Grenoble, and currently hosted by the Faculty of Business and Economics at the University of Lausanne. Url: https://neuroheuristic.org (visited on 08/26/2024).

[46] G.G. CELESIA et al., *An electrophysiological study of visual processing in Alzheimer's disease*, in *Electroencephalogr Clin Neurophysiol*, 87.3, 1993, p. 97-104 [doi: 10.1016/0013-4694(93)90116-d]; V.N. SYNYTSKY et al., *Neurophysiological and psychophysiological effects of sulpiride in the norm and in patients with opiate addiction*, in *Neurophysiology*, 34.4, 2002, p. 313-320 [doi: 10.1023/A:1021291815652]; T.I. AKSENOVA, V.V. VOLKOVYCH, A.E.P. VILLA, *Detection of spectral instability in EEG recordings during the preictal period*, in *J Neural Eng*, 4.3, Sept. 2007, p. 173-178 [doi: 10.1088/1741-2560/4/3/001]; A.E.P. VILLA, I.V. TETKO, *Cross-frequency coupling in mesiotemporal EEG recordings of epileptic patients*, in *J Physiol Paris*, 104, 2010, p. 197-202 [doi: 10.1016/j.jphysparis.2009.11.024]; A. LINTAS et al., *Event Related Potentials Reveal Fairness in Willingness-to-share*, in *Lect Notes Comput Sci*. *Lecture Notes in Computer Science 10613* (*ed.* A. LINTAS et al.), 2017, p. 191-198 [doi: 10.1007/978- 3- 319- 68600- 4_23]; S.K. MESROBIAN et al., *Event-Related Potentials during a Gambling Task in Young Adults with Attention-Deficit/Hyperactivity Disorder*, in *Front Hum Neurosci*, 12, 2018, p. 79 [doi: 10.3389/fnhum.2018.00079]; M. DOTARE et al., *Attention Networks in ADHD Adults after Working Memory Training with a Dual n-Back Task*, in *Brain Sci*, 10.10, Oct. 2020, p. 715 [doi: 10.3390/brainsci10100715]; M.E. JAQUEROD et al., *A Dual Role for the Dorsolateral Prefrontal Cortex (DLPFC) in Auditory Deviance Detection*, in *Brain Sciences*, 14.10, 2024, p. 994 [doi: 10.3390/brainsci14100994].

[47] A.E.P. VILLA, V.M. BAJO LORENZANA, G. VANTINI, *Nerve growth factor modulates information processing in the auditory thalamus*, in *Brain Res Bull*, 39.3, 1996, p. 139-147 [doi: 10.1016/0361-9230(95)02085-3]; A.E.P. VILLA et al., *Non-linear cortico-cortical interactions modulated by cholinergic afferences from the rat basal forebrain*, in *Biosystems*, 58.1-3, 2000, p. 219-228 [doi: 10.1016/s0303-2647(00)00126-x]; M. HAJÓS et al., *Different tonic regulation of neuronal activity in the rat dorsal raphe and medial prefrontal cortex via 5-HT(1A) receptors*, in *Neurosci Lett*, 304.3, 2001, p. 129-132 [doi: 10.1016/s0304-3940(01)01751-7]; V.M. STOROZHUK et al., *Dopamine modulation of glutamate metabotropic receptors in conditioned reaction of sensory motor cortex neurons of the cat*, in *Neurosci Lett*, 356.2, 2004, p. 127-130 [doi: 10.1016/j.neulet.2003.11.039]; A. LINTAS et al., *Dopamine deficiency increases synchronized activity in the rat subthalamic nucleus*, in *Brain Res*, 1434, Jan. 2012, p. 142-151 [doi: 10.1016/j.brainres.2011.09.005]; CABESSA, VILLA, *Attractor dynamics of a Boolean model*, cit., see n. 29; A. LINTAS et al., *Operant conditioning deficits and modified*

sorimotor process [48]; (iv) neuromimetic models and artificial neural networks progressively integrating experimental research results [49]; (v) the development of new methods for analyzing neuronal activity [50].

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local field potential activities in parvalbumin-deficient mice, in *Sci Rep*, 11.1, Feb. 2021, p. 2979 [doi: 10.1038/s41598-021-82519-3].

[48] A.E.P. VILLA et al., *Chaotic dynamics in the primate motor cortex depend on motor preparation in a reaction-time task*, in *Cah Psychol Cogn*, 17, 1998, p. 763-780; A.E.P. VILLA et al., *Spatiotemporal activity patterns of rat cortical neurons predict responses in a conditioned task*, in *Proc Natl Acad Sci USA*, 96.3, 1999, p. 1106-1111 [doi: 10.1073/pnas.96.3.1106]; A.E.P. VILLA et al., *Stimulus congruence affects perceptual processes in a novel Go/Nogo conflict paradigm in rats*, in *Behav Proc*, 48, 1999, p. 69-88 [doi: 10.1016/S0376-6357(99)00070-4]; D. CARRETTA et al., *c-Fos expression in the auditory pathways related to the significance of acoustic signals in rats performing a sensory-motor task*, in *Brain Res*, 841.1-2, 1999, p. 170-183 [doi: 10.1016/s0006-8993(99)01840-5]; M.A. FARRÉ-CASTANY et al., *Differences in locomotor behavior revealed in mice deficient for the calcium-binding proteins parvalbumin, calbindin D-28k or both*, in *Behav Brain Res*, 178.2, 2007, p. 250-261 [doi: 10.1016/j.bbr.2007.01.002]; M.E. JAQUEROD et al., *Early Attentional Modulation by Working Memory Training in Young Adult ADHD Patients during a Risky Decision-Making Task*, in *Brain Sci*, 10.1, Jan. 2020, p. 38 [doi: 10.3390/brainsci10010038]; LINTAS et al., *Dopamine deficiency increases synchronized activity*, cit., see n. 47.

[49] A.E.P. VILLA, I.V. TETKO, *Efficient Partition of Learning Data Sets for Neural Network Training*, in *Neural Netw*, 10.8, Nov. 1997, p. 1361-1374; S.L. HILL, A.E.P. VILLA, *Dynamic transitions in global network activity influenced by the balance of excitation and inhibtion*, in *Network*, 8, 1997, p. 165-184 [doi: 10.1088/0954-898X_8_2_004]; A.M. TYRRELL et al., *POEtic: An integrated architecture for bio-inspired hardware*, in *Lect Notes Comput Sci. Lecture Notes in Computer Science 2606* (*ed.* A.M. TYRRELL, P.C. HADDOW and J. TORRESEN), 2003, p. 129-140 [doi: 10.1007/3-540-36553-2_12]; J. IGLESIAS et al., *Dynamics of pruning in simulated large-scale spiking neural networks*, in *BioSystems*, 79.1, 2005, p. 11-20 [doi: 10.1016/j.biosystems.2004.09.016]; J. IGLESIAS, A.E.P. VILLA, *Recurrent spatiotemporal firing patterns in large spiking neural networks with ontogenetic and epigenetic processes*, in *J Physiol Paris*, 104, 2010, p. 137-146 [doi: 10.1016/j.jphysparis.2009.11.016]; V. SHAPOSHNYK, A.E.P. VILLA, *Reciprocal projections in hierarchically organized evolvable neural circuits affect EEG-like signals*, in *Brain Res*, 1434, 2012, p. 266-276 [doi: 10.1016/j.brainres.2011.08.018]; Y. ASAI, A.E.P. VILLA, *Integration and transmission of distributed deterministic neural activity in feed-forward networks*, in *Brain Res*, 1434, 2012, p. 17-33 [doi: 10.1016/j.brainres.2011.10.012]; D. MALAGARRIGA, A.J. PONS, A.E.P. VILLA, *Complex temporal patterns processing by a neural mass model of a cortical column*, in *Cogn Neurodyn*, 13.4, Aug. 2019, p. 379-392 [doi: 10.1007/s11571-019-09531-2].

[50] A. CELLETTI, V.M. BAJO LORENZANA, A.E.P. VILLA, *Correlation dimension for paired discrete time series*, in *J Stat Phys*, 89.3, 1997, p. 877-884; I.V. TETKO, A.E.P. VILLA, *A pattern grouping algorithm for analysis of spatiotemporal patterns in neuronal spike trains. 1. Detection of repeated patterns*, in *J Neurosci Methods*, 105.1, 2001, p. 1-14 [doi: 10.1016/s0165-0270(00)00336-8]; V. DEL PRETE, L. MARTIGNON, A.E.P. VILLA, *Detection of syntonies between multiple spike trains using a coarse-grain binarization of spike count distributions*, in *Network*, 15.1, 2004, p. 13-28 [doi: 10.1088/0954-898X/15/002]; Y. ASAI, A. GUHA, A.E.P. VILLA, *Deterministic neural dynamics transmitted through neural networks*, in *Neural Netw*, 21.6, 2008, p. 799-809 [doi: 10.1016/j.neunet.2008.06.014]; VILLA, TETKO, *Cross-frequency coupling in mesiotemporal EEG*, cit.,

Using a metaphor, the neuroheuristic approach observes experimental results beyond the confines of provisional hypotheses, much like a child playing in a garden while observing what happens beyond the fence, be it a hedge, a barrier, or a trellis. This metaphor also underscores the responsibility researchers bear in their approach choices [51]. Among all dangers, persisting in fixed objectives is certainly one of the greatest. Since the Neolithic era, tools have changed shape, but their interactions with the discovery process have essentially remained constant. Unprecedented investigative tools have appeared in neuroscience research thanks to new computing technologies, with medical imaging being a notable example. However, the complexity of problems facing physicians and researchers is of such magnitude that the contribution of computing cannot be reduced solely to its computational performance and disciplinary dimension. By inaugurating a different approach to the problem, neuroheuristics attempts to propose a paradigm emerging from the synergy between computing and neuroscience in relation to discoveries from molecular biology.

see n. 46; J. CABESSA, A.E.P. VILLA, *An Attractor-Based Complexity Measurement for Boolean Recurrent Neural Networks*, in *PLoS One*, 9.4, 2014, e94204 [doi: 10.1371/journal.pone.0094204]; P. MASULLI, A.E.P. VILLA, *Algebro-topological invariants in network theory*, in *Int J Complex Syst Sci*, 5.1, 2015, p. 13-17; T.V. GUY et al., *Theoretical Models of Decision-Making in the Ultimatum Game: Fairness vs. Reason*, in *Advances in Cognitive Neurodynamics (V)* (*ed.* R. WANG and X. PAN), Singapore, 2016, Chap. 26, p. 185-191 [doi: 10.1007/978-981-10-0207-6_26]; D. MALAGARRIGA et al., *Consistency of heterogeneous synchronization patterns in complex weighted networks*, in *Chaos*, 27.3, 2017, p. 031102 [doi: 10.1063/1.4977972]; P. MASULLI et al., *Fuzzy Clustering for Exploratory Analysis of EEG Event-Related Potentials*, in *IEEE Trans. Fuzzy Syst*, 28.1, 2020, p. 28-38 [doi: 10.1109/TFUZZ.2019.2910499]; T. ABE et al., *Detection of quadratic phase coupling by cross-bicoherence and spectral Granger causality in bifrequencies interactions*, in *Sci Rep*, 14.1, Apr. 2024, p. 8521 [doi: 10.1038/s41598-024-59004-8].

[51] TAYLOR, VILLA, *The 'Conscious I'*, cit., see n. 8; A. FARINA, A.E.P. VILLA, *On the semantics of ecoacoustic codes*, in *Biosystems*, 232, Oct. 2023, p. 105002 [doi: 10.1016/j.biosystems.2023.105002].