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Review Article

# Chemical Aspects of Emotive Memory

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## Abstract

"Chemistry is the only physical science which offers a pathway to understanding animate biology" Medawar [1] (1967).

Chemistry has been used to clarify most aspects of biology including metabolism, structure and reproduction. However, current neuro-biological descriptions of animate life are incomplete, as they have not "grasped the nettle" of mentality.

The outstanding issue: How do neural nets instigate experiential mental states, such as emotions and memory?

Most chemical approaches to neural memory were skewed to pharmacology, which did not address how neurons and the neural net remember, but focused on physiologic effects of drugs.

We have proposed a biochemical tripartite mechanism of neural memory, whereby neurons interact with their surrounding polysaccharide extracellular matrix (nECM), by deploying dopants (metal cations and neurotransmitters (NTs)) to encode cognitive units of information (cuinfo). Each NT elicits a unique set of physiologic responses entangled with psychic states, which it also signifies in emotive memory. The ~80 NTs can induce a multiplicity of subjective dimensions, far greater than the binary reality of the computer.

As validation of the tripartite mechanism, we review the chemo-electric performance of glass electrodes that were coated with either a NT (oxytocin) or an oligo-saccharide analogue of the nECM (sulfated tetra-saccharide). They could selectively detect various metal cations (Cu+2, Zn+2, etc.) at physiologic levels. Such chemo-electrodes are "neuro-mimetic" analogues of the many NT-sensitive sensors (GPCR, acetylcholine R, integrins) embedded in the neural membrane.

Thus, the discipline of chemistry provides access to the complex totality of physiologic reactions entangled with mental experience.

**Keywords**: Neurotransmitter; Feelings; Emotive Memory; Mentality

## Background

Memory is the crux of mentation (cognition), without which mental processes, such as emotive states, could not be manifest. A most puzzling point, encapsulated by Descarte's Mind/Body conundrum [2], is how bundles of neurons can generate mental states expressed as memory and emotions.

The computer serves as an incomplete metaphor for the brain. It has a function called "memory" and can process binary-coded data very rapidly. But it's memory is "demotive", incapable of achieving an affective dimension. Consequently, it has no innate sense of "meaning" or "value", as do neural creatures striving to survive. "Facial recognition" software cannot love even one face it recognizes.

Similarly, mathematical or quantum mechanical analyses are inadequate to illuminate subjective mentality. Neural synaptic circuits (connectomes) [3] are mum regarding how moods are achieved and remembered.

The electrodynamic mode of neural signaling, as the basis of mental processes, has a long history, which we present as a graphic Timeline in figure 1. It began with Galvani's discovery of bioelectricity (~1780) [4], through to the histologic works by Golgi and Cajal [5] and conceptual development by Hebb [6] and Kandel [7] (Figure 1).

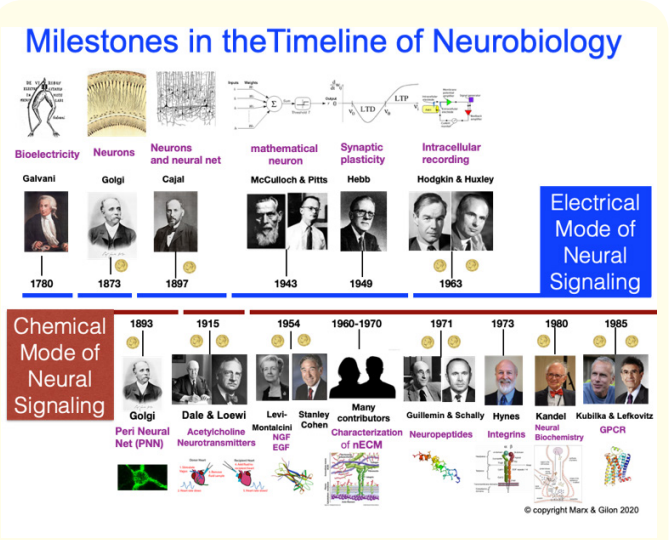


**Figure 1:** Timeline of Neurobiology, acknowledging key contributors to unravelling the electrical and chemical modes of neural signaling. The Timeline (based on reviews [7,18]) emphasizes the parallel discoveries of the two modes of neural signaling: the synaptic electrical mode and the ephaptic chemical mode. Nobel Prizes are indicated.

The chemical neural signaling was instigated by the discovery of acetylcholine (1915), then other neurotransmitters (NTs). To date, more than 80 distinct NTs have been described [8-10]. The selective sensitivity of neural receptors (i.e. NMDA receptors [13,14], integrins [15], GPCRs [16], acetylcholine receptors [17]) to NTs has been noted. These all link a chemodynamic code to electrodynamic signaling.

## Electrical signaling

Living organisms are complex electrochemical systems. Subsequent to Galvani's discovery of bioelectricity [4], Cajal's histologic work identified synaptic contacts between neurons and suggested electrodynamic signaling. A singular contribution to this mode was McCulloch–Pitts' mathematical modeling [11] of a lone neuron (Equ.1).

Equ. 1.

$$N_i(z_1). \equiv. S\{ {}^{q}II \sim N_{jm}(z_1). S\ II\ N_{ie}(z_1)\}$$

$$m=1 \qquad\qquad aeKi\ ae$$

where $N_i$ and $N_{ie}$ are non-afferent neuron, S and II are syntactical symbols for disjunctions and conjunctions, which are finite in each case. But such a formulation says little regarding physiology or the emotive states achieved by neurons, though it inspired John von Neuman to theorize the circuits and processors which underlie modern (electronic) computers [12].

This approach was subsequently conceptualized by the melding of electrical signaling to morphologic of changes neurons who learned, "synaptic plasticity" and "long term potentiation". Consequently, most efforts to analyze brain activity focused on electrodynamic signaling. Recent works summarize the quest to comprehend the brain's electrical activity as it relates to mental states.

Modern techniques employed to monitor mental activity during conscious awareness and during sleep include fMRI (functional magnetic resonance imaging) and EKG (electro-cardiogram) or microendoscopic imaging techniques. Many presume that neural circuits function with design principles similar to those of electronic networks. A diversity of biologists carried out experiments using electromagnetic fields to study the function of neural nets. Such techniques revealed many diverse levels of neural organization and performance. They indicated that fractal processes and properties occurred at many diverse levels of neural organization and performance. But a mathematical analysis of electrodynamic responses does not describe how an emotive dimension is achieved i.e. "subjectivity". The instrumental techniques applied to the brain, focused on electrodynamic signaling, did not illuminate how psychic states were achieved or how emotive memory was rendered operational [13,14].

It has been suggested that "neuromorphic" computing might be able to overcome the efficiency bottlenecks inherent in conventional computers through parallel computing and by employing crossbar memory arrays to execute algorithms of an artificial neural network (ANN) [15]. But like its serial analogue, parallel binary computation cannot address the lack of emotive content. The so-called "neuromorphic" devices of ANN are not really "neuro". They do not mimic the morphology of neurons. Neither do they mimic the synaptic contacts between neurons, as they employ interconnecting cross-bar wiring.

Similarly, quantum computing (QC) crumbles under the weight of physiologic considerations [16]. It has been said that QC would be capable of solving any problem more rapidly than a Turing Universal computer and also to solve non-deterministic (NP) complexity problems. It was hoped that the QC would permit one "to create a true artificial intelligence (AI) that can run independent thoughts". However, the fatal flaw in QC as well as in electrodynamic devices is that they cannot formulate the affective dimensions achieved by neural nets. They are inherently "demotive", "Frankenstein devices" unable to emote or to empathize. Others recognized that long-lasting changes in synaptic chemistry were involved in memory [17,18], but details were lacking.

## Visualizing Neurons

Golgi's development of the silver stain histologic method (Equ. 2) provided a critical tool for Cajal's later explorations of the brain [19,20]. It led to Cajal's recognition of the neuron as a discrete signaling cell in synaptic contact with others.

Equ. 2.

$$Ag^{+} \xrightarrow{\text{cell membrane}} Ag^{o} \xrightarrow{O_2} Ag_2O$$

clear hydrophobic (Golgi stain) → insoluble silver (Tollen' test) → insoluble black

As the silver cation adhered strongly to the hydrophobic membrane of the neuron, it consequently visualized the neuron (Figure 2).

## Visualizing nECM

Later work with periodate PAS stains revealed a web of glycosaminoglycans (GAGs) around the neurons, termed PNN by Golgi

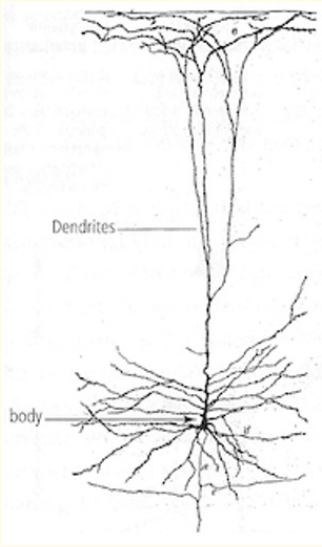


**Figure 2:** Silver stained neuron showing elongated body with many dendrites emanating from both ends.

but now termed neural extracellular matrix (nECM) [21,22]. The PAS staining method of nECM was based on the oxidation of vicinal OH groups in the constituent glucosamino glycans (GAGs), to generate two aldehyde groups (Figure 3). The addition of a clear Schiff base derivatized the aldehydes, colored them and rendered the nECM visually purple or red (Figure 3).

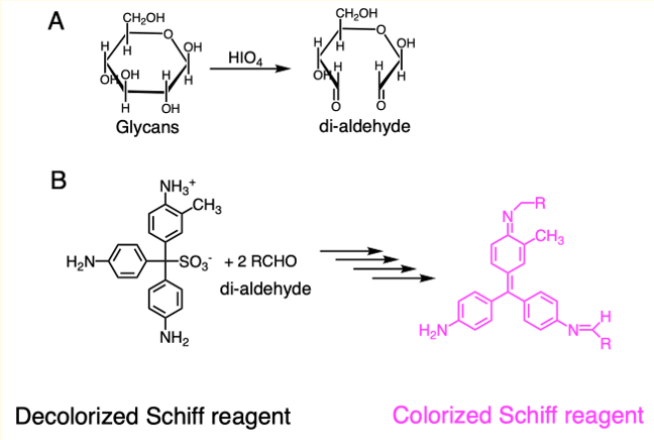


**Figure 3:** The Periodic Acid-PAS stain. Periodic acid oxidizes gem-diols in the glycans into di-aldehydes. B. The di-aldehydes reacts with Schiff reagent (Eosin dye) to yield colorized Schiff reagent that stains the glycans (R) with purple color [23].

The nECM of humans is phylogenetically related to the matrix around the neurons of *Drosophilia*. It is also homologue to the GAGs around (non-neuronal) slime amoeba and bacteria [24-26].

## Neurotransmitters (NTs)

The discovery of peptidic neurotransmitters (NTs) [28,29] was aided by the development of chemical tests and subsequently by instrumental techniques (fluorescence microscopy, HPLC, MS) for detecting and quantifying monoamines in tissues and body fluids [30,31]. Identifying NT receptors (i.e. acetylcholine receptor, GP-CRs, integrins) further encouraged a chemodynamic view of their role in neural signaling. For example, it was shown that inter-neural communication involved the NTs dopamine, noradrenaline and serotonin, by activating tyrosine kinases and other receptors [32-37].

To date, more than 80 NTs have been identified, all which exert both physiologic and psychic effects. While it is accepted that NTs affect mental states (mood, memory loss, dementia), no general theory of memory has been proposed based on chemodynamic NT signaling.

## How can an emotive mental state be encoded in and recalled from memory?

In common parlance, "feelings" and "emotions" are used interchangeably. However, "feelings" are sensations (perceptions) that relate to physiologic events signaled by NTs and their cognate receptors, linked to mental states. "Emotions" are not discrete like numbers or letters, but rather meld into an existential resonance that is hard to describe verbally. They cannot be "captured" by a binary code or a mathematical algorithm. Attempts have been made to present the palette of emotions as a color wheel or Lövheim cube [38-41]. But such graphics are too limited. Literature, poetry and songs attempt to describe the existential states of emotions with words, with varying degrees of success. It is difficult to quantitate feelings and/or emotions. Which are primary? Which secondary, etc.? Does "pain" trump " fear"? Does "anger" trump "love"?

In that "emotions" recall remembered "feelings", they operate through the talent of memory entangled with physiologic reactions (Figure a).

| Chemical Classification | Feelings (Physiologic effects, no memory needed) | | Some Basic Emotions (Psychic effects, memory needed) |
|---|---|---|---|
| **Neurotransmitters** (modulators)<br>Biogenic Amines<br>>10 Amino acids<br>>10 others<br>e.g cAMP, NO, ACh<br>> 75 Neuropeptides<br>endocannabinoids<br><br>**Neurometals**<br>>10 Metal ions [ including Zn, Li, Ca, Co, Cu, Mg, Fe, Ni, Sr] | Breathing<br>Blinking<br>Blood pressure<br>Coughing<br>Crying<br>Dilation of pupil<br>Drooling<br>Erection<br>Evacuation<br>Vasodilation<br>Goose-bumps<br>Heart beat | Laughing<br>Orgasm<br>Pulse<br>Salivation<br>Secretion<br>Spasms<br>Sweating<br>Tremors<br>Urination<br>Fever<br>Vomiting<br>Itching | anger, anticipation, disgust, fear, grief, happiness, joy, love, rage, sadness, surprise, trust |

**Figure a:** Neurotransmitters and neuromata's are involved in encoding feelings and emotions.

Mentality is the new frontier for the chemical description of life processes. Like all other aspects of biology, mental talents of neural nets evolved from the chemical signals employed by more primitive aggregates of cells, bacteria and slime molds. The evolved neurons still employ the identical signaling molecules ("modulaters") now termed "neurotransmitters" (NTs), but expanded with neuropeptides. Thus, the neural net can be considered as an aggregate of signaling cells (i.e. brain) that have evolved a chemical process to encode subjective experience as memory (Equ.3). Our goal is to clarify details of this neural process.

Equ. 3

**Sensation → biochemical code → mental state**

[nECM/metal/NT} memory

The terms "memory" and "emotions" both relate to "cognition" (mentation, mind). Though subjectively experienced, they all remain ultimately mysterious. But clinical experience provides many correlations between NTs and mood. A connection between mentality, memory and the number of neurons in the brain is apparent (Figure).

## Drugs

The development of psycho-active drugs also point to a chemical mode of neural communication that instigate mental capabili-

ties and moods. Clinical experience demonstrated that NT molecules elicited physiologic reactions as well as to induce mental states (Figure a). So too do many synthetic psycho-pharmaceutical drugs (i.e. Prozac, Ritalin, Barbiturates, etc.). Thus, to integrate all these effects into a model of neural mentality, it is reasonable to look for a chemically credible process that accords with the chemical reactivity of the drugs and their psycho-chemical effects on mood and memory.

## Tripartite mechanism of neural memory

A chemical mechanism could clarify our understanding of the transformation of metabolic energy into memory. A biochemical tripartite mechanism (described below) has been proposed which involves neurons that encode units of cognitive information [42-49] as metal- centered complexes within the nECM surrounding the neurons. In this mechanism, NTs ejected from neural vesicles [52], elicit a range of physiologic reactions linked to emotive States (Figure a) and encode these in memory.

## Delete

Complexation with neurotransmittters (NTs) imparts emotive context. Chemographic representations of this coding mechanism are shown in figures 4 and 5.

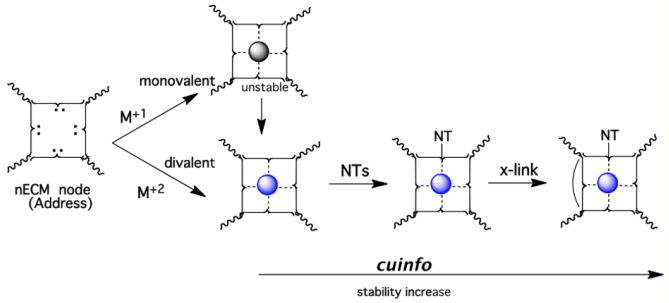


**Figure 4:** Formation of cuinfo complexes with different monovalent and polyvalent metal cations, as well as with different neurotransmitters (NTs), rendered more stable (persistent) by crosslinking.

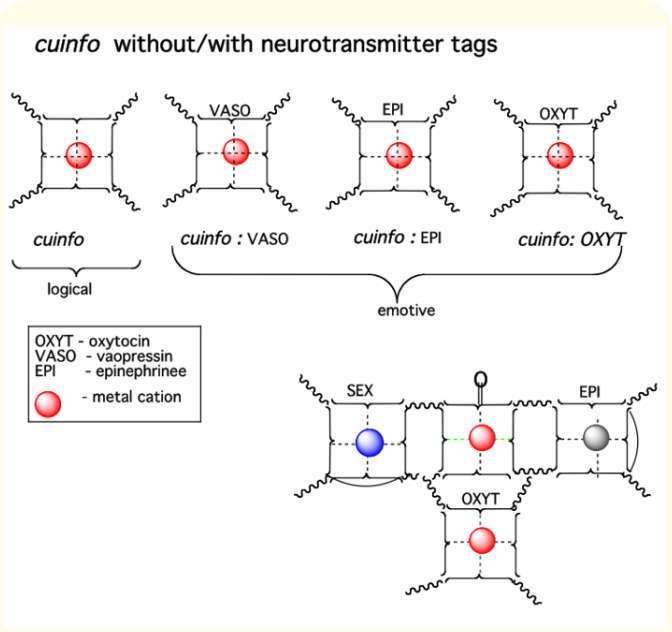


**Figure 5:** A panel of cuinfo complexed with different neurotransmitters (NTs). Stability depends on the binding affinity of the elemental cation and is further increased with covalent crosslinking reactions which can link into supramolecular complexes.

The NTs are the signaling molecules employed by neurons to induce physiologic responses entangled with psychic states (Figure a). Thus, each NT could be considered to present the neural net with a unique code for annotating the many dimensions of emotive experience.

## Calculating cognitive information space

The nECM around each neuron is a 3D volume (Figure 4), with many "addresses". Considering only metal cations as encoders of cognitive information, one is struck by the multiplicity of coding options.

More than 8 mobile elemental cations are found in the brain (Table 1) capable of being bound to the nECM with varying degrees of avidity.

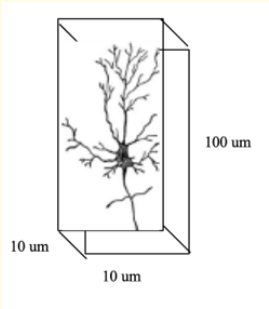


**Figure 6:** Approximation of the nECM volume around the neuron, calculated as $10^{-15}$ L/ neuron.

| Metal cation | Concentration |
|---|---|
| $K^{+}$ | 3.4 M |
| $Na^{+}$ | 2.7 " |
| $Mg^{+2}$ | 0.3 " |
| $Ca^{+2}$ | 60 mM |
| $Fe^{+2}$ | 10 " |
| $Zn^{+2}$ | 6 " |
| $Co^{+2}$ | 6 " |
| $Cu^{+2}$ | 3 " |

**Table 1:** Brain tissue levels*.

*Ignoring lower concentrations of other metal cations (i.e. $Mn^{+2}$, $Ni^{+2}$, $Sr^{+2}$, etc.).

For the purpose of our calculations, we assume that most (~90%) metal is concentrated within the neuron, leaving 10% located within the nECM. A complicating aspect of these is that each metal cation excercises a unique binding geometry (i.e. square planar, octahedral, hexagonal, etc.) with the binding site ("address") of the nECM. Parameters such as metal dissociation constant (KD), solubility of salt constant (Ksp) or critical electrolyte concentrations (CEC) reflect how tightly they might bind to a particular nECM site.

A further complexity is dictated by the number of COO-, SO3- and PO3- groups within the nECM and their isomorphic disposition, which dictate the local geometry of metal and NT binding. The molecular inhomogeneity of nECM in animal brain has only been sporadically explored and awaits more detailed description.

For example, assume that the neuron occupies a volume equivalent to a rectangular box 100 um length x 10x10 $um^2$ area, equivalent to $10^{-11}$ liter. Ignoring for the moment NTs, each metal binding event by itself could be considered to be equivalent to the formation of a single unit of "demotive" cognitive information (cuinfo). For a neural nECM volume ($10^{-11}$ L) doped with 1 mM metal, one can calculate:

Equ 4:

$$[10^{-6}\text{ M metal}] \times [N_A]/[\text{nECM volume}] = [10^{-6}] \times [6\times10^{23}]/10^{-11}$$

$= 6\times10^{17}$ atoms of each element, # cuinfo per neural volume.

Each metal cation could be capable of forming a single cuinfo. Even if only 10% of the total brain level of metal is located outside the cell, in the nECM, the rest within the neuron. One could calculate that the nECM has a capacity of $6\times10^{17}$ cuinfo per neuron. The coding options become much more complex, as each elemental cation has a unique binding strength and geometry. The neural receptors for the NTs are capable of adopting a plethora of signaling conformations that affect metal cation binding and allosteric interactions, further complicating the signaling options.

Consider that >80 NTs impart a large palette of emotive qualities to the cuinfo repertoire. Thus, compared to the puny binary coding options (0 1) available to computers, it is clear that the capacity to encode cognitive information as emotive memory in the nECM around each neuron is exceedingly large.

## "Neuro-mimetic" electrodes

While it is not possible to instrumentally measure a mental state, "neuro-mimetic" electrodes have been coated with some components available to neurons, namely: an NT (i.e. oxytocin) or an oligo-saccharide analogue of the nECM [50,51]. Used as covalent coatings on impedimetric glass electrodes, these components modulated electrodynamic responses to soluble metal cations. The

coated electrodes could be considered as analogues of the mosaic aggregates embedded in the neural membrane (i.e. GPCR, acetylcholine receptors, integrins), which serve as sensors for NTs. Each neuron expresses many thousands of such sensors. Such "neuromimetic" electrodes buttress the concept of the tripartite mechanism of memory.

"Meaning" is inconsequential in any binary or quantal system. Only neural creatures can experience the "meaning" of any event or stimuli, which is invariably tied to an emotive state. Our puzzlement relating to the psychic dimensions achieved by the neural net harkens to Abbott's (1884) parody of 2-dimensional entities attempting to comprehend 3-dimensional reality [52]. But unlike the "Flatlander " (a Circle) who denied the possibility of a 3-dimensional reality (a Sphere), we do not deny the reality of emotive states. We experience them but do not understand how they are achieved.

## Conclusion

Chemistry is the window given to Mankind to glimpse into its material essence Sason Shaik [53]. We agree. Chemistry remains the only analytic discipline capable of piercing the veil of emotive memory. We opine that the brain mentates as a chemo-dynamic system which employs electro-dynamic signals to communicate with distal muscles, glands and organs. Thus, we describe the "neural code" of memory as a "biochemical algorithm" that links recalled physical experience to subjective states. It is rendered operational through chemo-dynamic interactions between neurons and their nECM.

Without memory, there are no emotions; conversely, without an emotive context, memory fades. Like "space and "time" merged into "space-time", "mind" and "body" are conjoined manifestations of conscious life, remembering to survive.

## Acknowledgements

- By GM: In memorium to my late wife, the artist Georgette Batlle (1940-2009), my muse. Thanks to my companion Ahouva Leopold (Jerusalem, Paris) for encouragement and cheers.
- GM CG: We note that Professor Gallistel's (Rutgers University) remarks on our early manuscripts drew our attention to "memory" as the proper focus of our speculations.

## Conflict of Interest

GM is a founder of MX Biotech Ltd., with the commercial goal to develop new "memory materials" and devices.

CG is an emeritus professor at the Institute of Chemistry, The Hebrew University of Jerusalem. He is active in developing technologies for the conversion of peptides and active regions of proteins into orally available drugs.

Notwithstanding, the ideas forwarded here are scientifically genuine and presented in good faith, without commercial clouding of the concepts expressed therein.

## Bibliography

1. Medawar P. "The Art of the Soluble" (1967).
2. Skirry J. "Rene Descartes: The Mind-Body Distinction". *Internet Encyclopedia of Philosophy* (2016).
3. Horn A., *et al*. "The structural-functional connectome and the default mode network of the human brain". *NeuroImage* 102 (2013): 142-151.
4. Piccolino M. "Luigi Galvani and animal electricity: Two centuries after the foundation of electrophysiology".
5. *Trends in Neurosciences* 20 (1997): 443-448.
6. Bentivoglio M., *et al*. "The original histological slides of Camillo Golgi and his discoveries on neuronal structure". *Frontiers in Neuroanatomy* (2019).
7. Hebb DO. "The Organization of Behavior". Wiley, New York (1949).
8. Kandel ER and Squire LR. "Neuroscience: Breaking down scientific barriers to the study of brain and mind".
9. *Science* 290 (2000): 1113-1120.

10. Tansey EM. "Chemical neurotransmission in the autonomic nervous system: Sir Henry Dale and acetylcholine". *Clinical Autonomic Research* 1 (1991): 63-72.

11. van den Pol1 AN. "Neuropeptide transmission in brain circuits". *Neuron* 76 (2012): 98-115.

12. Reith ME. "Neurotransmitter Transporters: Structure, Function, and Regulation/2nd ed.,". Springer-Verlag, New York (2002).

13. McCulloch W S and Pitts W H. "A logical calculus of the ideas immanent in nervous activity". *Bulletin of Mathematical Biophysics* 7 (1943): 115-133.

14. Jeffress LA. "John von Neumann: The Cerebral and Logical Theory of Automata". *The Hixon* 1947 Symposium. Wiley, New York (1951).

15. Fields RD. "Electric Brain". BenBella Books, New York (2020).

16. Kesic S and Spasic SZ. "Application of Higuchi's fractal dimension from basic to clinical neurophysiology: A review". *Computer Methods and Programs in Biomedicine* 133 (2016): 55-70.

17. Pastur-Romay LA., *et al*. "Deep artificial neural networks (ANN) and neuromorphic chips for big data analysis: Pharmaceutical and bioinformatics applications". *International Journal of Molecular Sciences* 17 (2016): 1313-1339.

18. Rosenblum B and Kuttner F. "Quantum Enigma: Physics Encounters Consciousness. 2nd Ed". Oxford University Press, Cambridge, UK (2012).

19. Baudry M., *et al*. "The biochemistry of memory: The 26 year journey of a 'new and specific hypothesis". *Neurobiology of Learning and Memory* 95 (2011): 125-133.

20. Chang C. "Bioinorganic life and neural activity: Toward a chemistry of consciousness?" *Accounts of Chemical Research* 50 (2017): 535-538.

21. de Castro F and Merchán MA. "The major discoveries of Cajal and his disciples: Consolidated milestones for the neuroscience of the XXIst Century". *Frontiers in Neuroanatomy* (2016).

22. Langmoen IA and Apuzzo ML. "The brain on itself: Nobel laureates and the history of fundamental nervous system function". *Neurosurgery* 61 (2007): 891-907.

23. Seidenbecher C. "Compartmentalization from the outside: the extracellular matrix and functional microdomains in the brain". *Trends in Neuroscience* 33.11 (2010): 503-512.

24. Senkov O., *et al*. "Neural ECM molecules in synaptic plasticity, learning and memory". In. In: Dityatev A, Wehrle- Haller B, Pitkänen A. (Eds), Progress in Brain Research 214: Ch 3, Amsterdam (2014).

25. Bancroft JD. "Theory and Practice of Histological Technique". 4th ed. Churchill Livingstone Publications. New York (1996).

26. Broadie K., *et al*. "Extracellular matrix and its receptors in Drosophila neural development". *Developmental Neurobiology* 71 (2011): 1102-1130.

27. Reid C., *et al*. "Slime mold uses an externalized spatial 'memory' to navigate in complex environments". *Proceedings of the National Academy of Sciences of the United States of America* 109 (2012): 17490-17494.

28. Matthews GG. "Evolution of nervous systems. Neurobiology: molecules, cells, and systems". Wiley-Blackwell (2001): 21.

29. Hasselmo ME. "The Role of Acetylcholine in Learning and Memory". *Current Opinion in Neurobiology* 16.6 (2006): 710-715.

30. Matthews GG. "Evolution of nervous systems. Neurobiology: molecules, cells, and systems". Wiley-Blackwell (2001): 21.

31. Poitras D and Parent A. "A fluorescence microscopic study of the distribution of monoamines in the hypothalamus of the cat". *Journal of Morphology* 145 (1975): 387-407.

32. Godse DD., *et al*. "Analysis of acidic monoamine metabolites by gas chromatography-mass spectrometry". *Analytical Chemistry* 49 (1977): 915-918.

33. Grinnell AD., *et al*. "The role of integrins in the modulation of neurotransmitter release from motor nerve terminals by stretch and hypertonicity". *Journal of Neurocytology* 32 (2003): 489-503.

34. McEnery MW and Siegel RE. "Neurotransmitter Receptors". In: Encyclopedia of the Neurological Sciences (2nd Edition) (2014).

35. Newcomer JW., *et al*. "NMDA receptor function, memory, and brain aging". *Dialogues in Clinical Neuroscience* 2 (2000): 219-232.

36. Gilman AG. "G proteins: transducers of receptor-generated signals". *Annual Review of Biochemistry* 56 (1987): 615-649.

37. Trzaskowski B., *et al*. "Action of molecular switches in GPCRs--theoretical and experimental studies". *Current Medicinal Chemistry* 19 (2012): 1090-109.

38. Miyazawa A., *et al*. "Structure and gating mechanism of the acetylcholine receptor pore". *Nature* 423 (2003): 949-955.

39. Lovheim H. "A new three-dimensional model for emotions and monoamine neurotransmitters". *Medical Hypotheses* 78 (2012): 341-348.

40. Plutchik R. "The Nature of Emotions". *American Scientist* (2016).

41. Valdez P and Mehrabian A. "Effects of color on emotions". *Journal of Experimental Psychology* 123 (1994): 394-409.

42. Wang F., *et al*. "Editorial: Neurotransmitters and Emotions". *Frontiers in Psychology* 11 (2020): 21.

43. Marx G and Gilon C. "The molecular basis of memory". *ACS Chemical Neuroscience* 3 (2012): 633-642.

44. Marx G and Gilon C. "The molecular basis of memory. MBM Pt 2: The chemistry of the tripartite mechanism". *ACS Chemical Neuroscience* 4 (2013): 983-993.

45. Marx G and Gilon C. "The tripartite mechanism as the basis for a biochemical memory engram". *Journal of Integrative Neuroscience* 18 (2019): 181-185.

46. Marx G and Gilon C. "Interpreting neural morphology". *Acta Scientific Neurology* 3 (2020): 1-4.

47. Marx G and Gilon C. "Tripartite mechanism of neural memory: Proof-of-concept with neuromimetic impedence electrodes". *Biomedical Research and Clinical Review* 1.3 (2020): 021.

48. Marx G and Gilon C. "The Molecular Basis of Neural Memory. Part 11.Chem-electric Write /Read Processes". *Journal of Neurosurgery Imaging Techniques* 6 (2020): 283-301.

49. Marx G and Gilon C. "Quantum considerations of neural memory". In: Quantum Boundaries of Life, In press. Elsevier, Amsterdam (2020).

50. Tadi KK., *et al*. "Oxytocin-monolayer-based impedimetric biosensor for zinc and copper ions". *ACS Omega* 2 (2017): 8770-8778.

51. Alshanski I., *et al*. "Sulfation patterns of saccharides and heavy metal ion binding". *Chemistry—A European Journal* 25 (2019): 1-9.

52. Abbott EA. "Flatland: A Romance of Many Dimensions". Seely and Co. Ltd, London, Reissued as Dover Publication, 1992, New York (1884).

53. Shaik S. "Chemistry—A central pillar of human culture". *Angewandte Chemie International Edition* 42 (2003): 3208-3215.