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Biochemical Inspiration from Chomsky's "Reflections on Language"

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ABSTRACT

The biochemical basis of psychology and memory remain obscure. Psycho- and linguistic- analysis provide few clues regarding the processes that occur in our heads.

Here, I try to give an autobiographical account of the development of a scientific idea of how a mental process such as memory, can be encoded in the brain. My story began (~1980) with an account of how I started as a research biochemist working in blood coagulation, then became inspired by remarks in a book on linguistics (Noam Chomsky), to quote:

- "Since the subject is a physical organism, the system attributed to it must have finite representations."
- "Symbol systems that fit different molds also have different neural representations...different physical representations."
- "An empirical argument must be brought to bear."

I formulated the concept of a "cation array" as the basis for the biochemical coding of information processing in the brain, as required for memory. The core idea was that the neuron employs various elemental cations $(Zn^{+2}, Cu^{+2}, Mn^{+2}, etc)$ to encode experience into the surrounding neural extracellular matrix (nECM). The nECM serves as an chemo-electric lattice, wherein neurons manipulate multiple trace metals (n>10) to encode, store and recall cognitive information. Energy requirements are low, rates are high, and encoding capacity is enormous.

I submitted manuscripts to various journals but was rejected by all. Discouraged, I put aside this work for more than 30 years. In the interim, I continued to experimentally examine the effects of elemental cations on blood coagulation with fair success in terms of publishing the unique modulating effects of physiologic levels of Zn^{+2} , Cu^{+2} on blood coagulation.

After > 30 years of lying fallow, the concept of a "cation array" became revitalised by a collaboration with a fellow biochemist (Chaim Gilon, Hebrew University). Because of weekly meetings (which were videotaped), we developed of a tripartite mechanism for memory which addressed many of the points raised by Chomsky. We articulated and chemographically described a tripartite mechanism for memory, whereby a chemically based code for cognitive information permits the achievement of an emotive state instigated by metals and neurotransmitters (NTs) released by neurons/glial cells. Thus, we link biochemical processes available to neural nets to the achievement of psychic states, including memory, emotions and consciousness.

The evolution of this idea continues and we invite others to join our efforts to dis-entangle psychology with physiological biochemistry.

Keywords

Chomsky's "Reflections, Psychology, Biochemical hypothesis.

Introduction Background

Much as I dislike Chomsky's anti-Israel rhetoric, I admit to the fact that his book "Reflections on Language" inspired me (in 1980) [1,2] to develop a biochemical hypothesis for thought processes (mentation), of which language is a unique human ornament.

Here, I give an autobiographical account of the development of a scientific idea: How a mental process such as memory, can be encoded in the brain.

I had been working in the laboratory of Prof. Yale Nemerson (Mt Sinai Medical Center, NY) and had discovered that coagulation Factor VIII (antihemophilic factor) was sucseptible to trace amounts of Mn⁺² and lost activity when the metal was removed with EDTA (a metal chelator) treatment. On off hours, I discussed this with my wife, the artist Georgette Batlle, and enlisted her graphic skills to visualize the blood coagulation "cascade", a sequence of enzymatic events (factors XI, X, IX, VIII, VII, V etc) which generate thrombin, which in turn instigates the transformation of soluble fibrinogen into an insoluble fibrin clot [3-5]. A schematic cascade of activating Factors that she executed under my direction are presented (Figure 1A), as are other drawings that illustrated the roles of metal cations in forming activating enzyme complexes to form fibrin (Figure 1 B,C,D) or the ability of albumin to bind cations and thereby bind bilirubin to serve as a blood transport vehicle (Figure 1 E).

Essentially, based on my experiments with coagulation factor VIII (anti-hemophilic factor) in the laboratory of Prof. Yale Nemerson (Mt Sinai Medical Center, NY), my experiments indicated that blood coagulation was a subtle physiologic process that could be modulated by trace quantities of metal cations, notably Ca^{+2} and Mn^{+2} Ironically, we never published this work. However, the drawings Georgette executed under my direction drew me to consider other physiologic processes that might be modulated by trace metals.

During this period, I was also heavily involved in a divergent interest; **Conceptual Art**, with some success [see: "Jerusalem River Project", Israel Museum, "Boots Event", Jerusalem Artist House, Concept+ Information show, Israel Museum, Earth, Air, Fire, Water exhibition, Boston Museum, Performance 76, Tel Aviv Artist House, and "Photosculpture" pieces with exhibitions at the Bertha Urdang Gallery (New York)].

Notwithstanding, I spent much time in medical libraries to look up the effects of metal toxicity or metal deficiency. (This was many years before the advent of internet searches). A striking feature in all of the reported results was that the earliest symptoms of metal deficiency or metal toxicity were manifest as skewed mental processes, notably loss of memory, dreaming and mood swings [7-9].

Chomsky's book

It was at this juncture that I read Chomsky's book, *Relections on Language (1)*. A later discussion on his work is cited here for general reference (2). While ostentially about language, Chomsky made a few striking comments that appealed to me, as they could be applied to the biology of mentation, notably the quotations:

- "Imagine a scientist who is unencumbered by the ideological baggage that forms part of our intellectual tradition.... Attribute to the human two cognitive structures:
- 1. A system of beliefs and expectations about the nature and behavior of objects.
- 2. A system of language. (Ch 4).
- "Our very limited progress in developing a scientific theory of any depth to account for the normal use of language or others aspects of behavior. Even relevant concepts seem lacking... These questions will always be shrouded in mystery." (p 25)
- "Our construction of perceptual space is guided by empiriicist maxims." (p 126)
- "...concerned with relations between particular stimuli and particular percepts." (p 143)
- "a schematism innate to the mind, that is refined and further articulated by experience" (146)



Figure 1: Drawings by Georgette Batlle.

A. Coagulation cascade scheme where various coagulation Factors interact with one another via metal cation interactions to generate thrombin, which instigates the fibrinogen to polymerize into a fibrin clot; B. Interaction of prothrombin and factor V with metal cations; C. A drawing of fibrinogen (momomer); D. Drawing of a fibrin clot (polymer); E. Albumin interacting with metal cations to bind bilirubin, to transport it [6].

- "The human mind is a biologically given system with certain powers and traits...Admissable hypotheses(about) this specific biological system (should) account for its ability to construct rich and explanatory theories....Some theories might simply be not among the admissable hypotheses determined by the specific properties of the mind...though these theories might be accessible to a differently organized intelligence." (p 155)
- "Since the subject is a physical organism, the system attributed to it must have finite representations." (p 162)
- "Symbol systems that fit different molds also have different neural representations...different physical representations." (p 175)

• *"An empirical argument must be brought to bear." (p 177)* This last comment resonated and seemed particularly potent.

Epiphany

As a result of my experiences with the modulating effects of metals on blood coagulation and their reported effects on mental processes, a most extraordinary idea occurred to me. Possibly, mental processes like blood coagulation, are also modulated by trace metal cations. ...that **"Thought processes" (mentality) are empowered by metal cation binding from particular sites in the brain.** I formulated the concept of a **"Cation array"** as the basis for the information coding and processing in the brain, as required for memory. Expectedly, his would impact on all aspects of mental processes performed by neurons . An "empirical argument" indeed. In our New York Soho loft, I began to audio tape my ramblings about this idea and wrote a manuscript which I submitted for publication (~ 1982).

After a poetic camel safari with Bedouins through the Sinai desert with a foray to Mt. Sinai, I formulated the concept of a "cation array" as the basis for the information coding in the brain, as required for memory (Figure 2). Expectedly, his would impact on all aspects of mental processes performed by neurons. An "empirical argument" indeed.

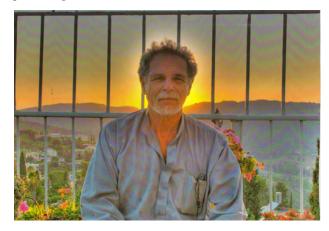


Figure 2: Epiphany: The author thinking about "thinking". (photo: Oferr Callaf).

In our New York Soho loft, I began to audio tape my ramblings about this idea and wrote a manuscript which I submitted for publication (\sim 1982).

Rejections

The mechanism I tried to push was based on the "cation array" model which I wrote up in a number of manuscripts. Finally after numerous rejections over a 5-year period, I gave up. The entire work was buried in the bottom of a file cabinet, not to be revived for more than 30 years.

But I continued experimental research on various aspects of blood coagulation, retaining only an interest in the sensitivity of the system to trace metals. Thus, over the years, I noted and published

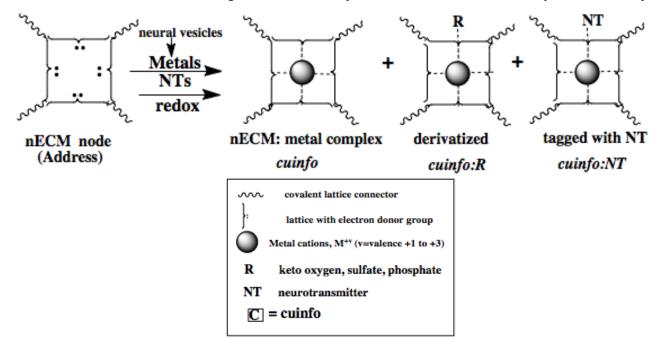


Figure 3: Chemographic representations of the reaction of a nECM electron-rich binding site ("address") for a metal cation complexation of a neurotransmitter (NT) to form a cognitive unit of information (*cuinfo*). The NTs confer emotive context.

on the effects of physiologic levels of Zn^{+2} on thrombin-induced fibrinogen transformation into fibrin and on platelet reactivity. I also found a free radical mode of tranforming fibrinogen into an insoluble clot (neofibe) with physiologic levels of Cu^{+2} and ascorbate. I published a number of articles on coagulation reactions modulated by metal cations [10-18].

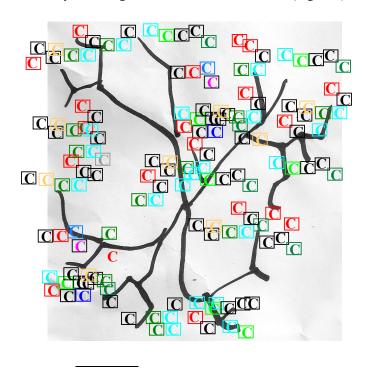
Collaboration

My wife and muse passed away in 2009. During a condolence visit by Prof. Chaim Gilon (Dept. Chemistry, Hebrew University, specializing in peptide synthesis of drugs), I asked him if he wanted to hear a crazy idea. He said yes and I recounted to him my idea about the "cation array" and thought processes. He responded enthusiastically and volunteered to join me in a collaboration on this topic.

Thus, began our weekly meetings which I videotaped. After 2 years and shifting focus to neural memory, we managed to publish our 1st article on the Molecular Basis of Memory (Marx & Gilon, 2012). Over the next 10 years, we succeeded in publishing another 22 peer-reviewed articles on this theme [19-42]. We described metal complexation processes in the neural extracellular matrix (nECM) as central to the storage and processing of cognitive information, a tripartite mechanism.

Tripartite Mechanism Of Encoding Neural Memory

For the neural emotive memory, we proposed that the <u>cognitive</u> <u>unit of information</u> (*cuinfo*) is realized materially (Sic. chemically). Thus, a chemically based code permits the achievement of an emotive state instigated by metals and neurotransmitters (NTs) released by neurons/glial cells and the recall of such (Figure 3).



10 uM

Figure 4: Unlike most representations in textbooks, neurons are not "naked", but enshrouded in a web of glycoaminoglycans which serve

as its "memory material". Neuron morphology reveals multiple intimate contacts with the nECM. Incoming perceptions are encoded with trace metals + neurotransmitters (NTs) to form metal-centered cognitive units of information (*cuinfo*).

Our chemographic notation for the tripartite mechanism captures the essence of this process regarding emotive memory (Figure 2). Operationally, we pictured the neuron as surrounded by the nECM in which coded units (cuinfo) were dispersed, the basis for subsequent consolidation of memory (Figure 4).

Phrased in linguistic terms, the NTs are the coding "alphabet" of emotive states and the physiologic reactions are the "syntax" [43]. Whatever one thinks or remembers must be causally related to a biochemical process in the brain (Figure 5).

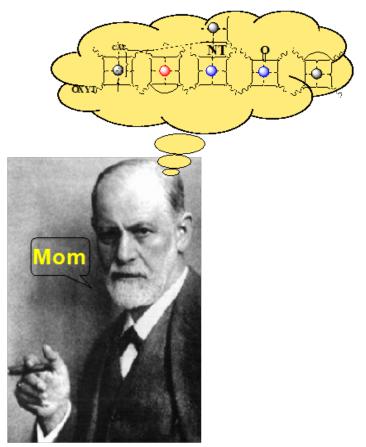


Figure 5: A portrait of Freud, schematically illustrating that his dreams and consciousness are based on the tripartite chemo-dynamic process of memory occurring in his brain.

GNW Hypothesis of Consiousness

Some neuroscientists hypothesized a "Global Neuronal Network" (GNW) as a central feature of consciousness [44-46]. That is, widely distributed *cuinfo* are communicated between various anatomical regions of the brain by way of a "global workspace" (i.e. "brain cloud") (Figure 4). The hypothesis suggests that the GNW performs as a router whereby distributed "cognitive information" is consolidated. The global availability of such is what one subjectively experiences as consciousness. The tripartite

mechanism details the molecular features of the "cognitive information" that is routed between the anatomic compartments of the brain. Thus, we fuse the GNW hypothesis with the tripartite mechanism.

Addressing Chomsky

The neuro-chemical code we developed has many credible features identified by Chomsky, namely:

a. It presents a multi-code (n>100) distinct from the binary code (n=2) of the computer (Figure 1).

b. It suggests a means for encoding emotive states with NTs/GTs (Table 1).

c. It employs NTs to entangle physiologic reactions with psychic states (Table 1).

Table 1. Neurotransmitters (NTs), which elicit both physiologic reactions and psychic states.		
Physiologic ic	Physiologic reactions *	Psychic states !
Neurotransmitter (NT)	(sensations, feelings)	rsychicstates
Biogenic amines (6)	Breathing	Anxiety
Amino acids (>10)	Blinking	Aggression
Neuropeptides(>70)	Blood pressure	Awareness
NO (1)	Blood coagulation	Craving
Endocannabinoids (>10)	Cold (feel)	Curiosity
	Contraction of muscles	Depression
	Coughing	Desire
	Cramps	Dread
	Crying	Dreams
	Defecation	Fantasy
	Dilation of muscles	Fear
	Dilation of pupil	Hate
	Drooling	Joy
	Erection	Love
	Evacuation	Paranoia
	Fever	Sadness
	Goose bumps	Sex drive
	Heart beat	Sociability
	Heat (feel)	
	Hunger (feel)	
	Immune reactions	
	Itching	
	Pain	
	Retching	
	Seeing	
	Shivering	
	Smelling	
	Thirst (feel)	
	Touching	
	Vomiting	
	* Nomemory required.	! Emotions requiring memor

Table 1: Summarizes the entangled physiologic and psychic effects of NTs.

In retrospect, the "tripartite mechanism" of neural memory addressed many of the above quoted issues raised by Chomsky. It was a:

- Realistic physical argument based on materials and processes available to neurons.
- Finite physical representation of a neural code.
- Description of relations between particular stimuli and particular percepts, as for example NTs/GTs which simultaniously elicit physiologic and psychic responses but also encode emotive states in memory (Figure 6).

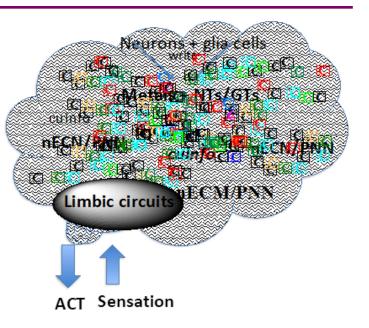


Figure 6: Conceptual schema of the brain whereby memory units (i.e. *cuinfo* ([C]) are encoded and distributed within the nECM throughout the brain (i.e. "nECM cloud"). The limbic circuits integrate and consolidate the many sets of dispersed but entangled *cuinfo*, to enable the experience of memory.

Conclusion

The unique challenge to cognitive scientists is to conceive of a process that explains the emergence of psychic states, like memory and emotions, from the interactions of atoms and molecules comprising neurons in the brain. While inspired in part by the comments of a linguist, we have wandered far from language and entered the realm of the psychic chemistry, the very mysterious process of mentation.

"Iron sharpens iron"

Chaim Gilon and I are well advanced in years but are still mentally agile. We acted as each other's "sounding board". The initial aim of my inchoate idea which I couldn't adequately express or publish on my own, grew into a series of concepts about the neurochemical basis of a mental process, namely memory, on which Chaim and I published many papers (Marx & Gilon, 2012-2022).

Our Collaboration Exemplifies the Sage Proverb

"Iron sharpens iron, and one man sharpens the face of his neighbor" to mean that in a good collaboration, one mind sharpens the abilities of the other (Mishlei, Proverbs 27:17).

Indeed, Chaim's (whose name means "life") revived my long dormant project and infused it and me with energy. We note that today's established neuro-scientists do not readily accept the tripartite mechanism but hope that the next generation of neuroscientists will adopt it, to further clarify the points raised by Chomsky's treatment of language.

The evolution of this exploration continues and I invite others

to join our efforts to dis-entangle psychology with physiological biochemistry.

Acknowledgements

A memorium to my late wife, the artist Georgette Batlle (1940-2009), my muse "more *precious than rubies...she greatly enriched (my) life* "(Proverbs 31.10). Thanks to my daughter Danae (Jerusalem) and son Jonathan (Weehawken, NJ), for warm encouragement and practical support. I thank my brother Rabbi Tzvi Marx (Amsterdam) for critical comments and providing theologic source material. I am indebted to Ahouva Karine Leopold (Paris, Jerusalem) for uplifting my spirits, for providing me with sources of alchemic literature and for bringing me to Tango. Finally, everlasting blessings on Prof. Chaim Gilon (Institute of Chemistry, The Hebrew University of Jerusalem) for reviving my enthusiasm for this project and becoming a collaborator.

Conflict of Interest

GM is a founder of MX Biotech Ltd., with the commercial goals of developing new classes of "memory materials" and "memory technologies".

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