

## Neuro-Astro Companionship: Investigate it in the Context of a larger Whole

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### ABSTRACT

Investigation on astrocytes, the largest number of cells in the brain, although ignored for a long period in neuroscience for different scientific mindsets, has been changing slowly for the last twenty five years. Their relationship has transcended from master-servant relation to partnership in metabolic signaling and exchange of useful resources, close friendship with sharing of vital information, and coupling for psychic and emotional relationship. Understanding that neuroscience of consciousness is not the cake-walk of the neurons alone, this paper looks at neuro-astro companionship from the viewpoint of neuroscience of consciousness through the transparency of the yang-yin metaphor. The set perspective leads us to investigate this special companionship in the context of the Buddha-state of the brain.

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### Introduction

Neuro-astrocyte relationship came to the frontier of neuroscience. In the first quarter of this century, when *Cell* published the work on Glia-derived D-serine controlling NMDA receptor activity, and synaptic memory in 2006 with a commentary on the same issue, 'Astrocytes put down the broom and pick up the baton' in the same issue [1,2]. The field was strengthened by a publication in *nature* in 2009, 'Glia more than just brain glue' and an interesting article in the same year in a feminist inter-disciplinary cross-cultural journal, 'Woman in the brain: a history of glial cell metaphor' [3,4]. Inspired by such articles I made an exhaustive review article on the basis of anatomic and physiological facts on the unique neuron-glia relationship with a title, 'Neural fabrics of mind: Systems neuroscience, systems psychology and consciousness' [5]. Till today, different presses of the science industry remain occupied with how astrocyte-neuron metabolic cooperation shapes brain activity [6]. *Science* in a special issue review, pronounces glial cells as architects of the central nervous system and its function [7]. Astrocyte-neuron metabolic crosstalk in neurodegenerative disorders with a mitochondrial perspective has been recently reviewed in *Frontiers of Endocrinology* [8]. Neuro-astrocyte involvement in different physiological and pathological states have been reviewed in 2023 [9]. Based on this beginning this article takes the opportunity to uplift the focus of Neuro-Astro partnership into the perspective of consciousness in neuroscience, which is not the cake-walk of neurons alone!

### Astrocyte Functions in General

Astrocyte has local, focal and global functions. Astrocyte as 'woman' in the brain, may be as mother (lactate shuttle), a sister (common progenitor), or a wife (glial processes wrapping naked axon) of neuron, is not sufficient to describe the neuron-astrocytic

mosaic. Astrocytes manage the 'home', 'finance' and the 'resource' ministry in neuron's governance and also a part of defense by maintaining the blood-brain barrier. In addition to lactate shuttle, there are other metabolic shuttles such as malate-aspartate shuttle and glutamate-glutamine shuttle. Beside adenosine, ATP and glutamate, there are other important gliotransmitters such as prostaglandins, and D-serine (the target of which is NMDA receptors) etc. [10,11]. NMDA is involved in synaptic transmission, excitotoxicity and synaptic plasticity. There are both-way transport between astrocyte and neuron by Extracellular Vesicles (EVs) [12]. Astrocyte-derived thrombospondin, regulates dendritic arborization and synaptogenesis [13,14]. A group of regional astrocytes influences global brain functions. For example, astrocytes being the source of endogenous benzodiazepines-like substance secreted by thalamic reticular nuclei (nRT) [15]. The functions of benzodiazepines-like substances are relevant in inducing sleep, allaying anxiety and controlling seizure, all are considered as global brain functions. Highly pH-sensitive astrocytes in medulla are the source of ATP signaling to neurons of retrotrapezoid nucleus (RTN) during central chemoreception sensing hypercapnia and therefore, astrocytes are actively involved in the control of breathing, considered another global function, through pH-dependant release of ATP [16].

### Warburg Phenomenon

Both cancer cells and neurons remain engaged in synthetic activity in preference to routine metabolic chore. However, cancer cells multiply. Neurons do not! Cancer cells have dysfunctional mitochondria. Neurons haven't! Cancer cells prefer aerobic glycolysis, a kind of glycolysis in the presence of plentiful oxygen designated as Warburg effect. Surprisingly, neurons too! The reason remains the same, shifted emphasis on synthetic activity. For neurons, it is an operation in physiological condition. Cancer is a pathological condition. Neurons are to walk a high wire to maintain this kind of stability [17]. A little imbalance might be

the cause of neurodegeneration [18]. Cancer cells do it alone. Neurons could afford to do so because of cordial cooperation from the astrocytes.

Even regarding mitochondria, there are plenty to compare and contrast between mitochondria of neurons and that of astrocytes; mitochondrial membrane redox potential and mitochondrial DNAs. This kind of cooperation between two different types of cells demands a closer look! Metabolic shuttles in astrocyte-neuron crosstalk, secretions of glial transmitters, thrombospondin, and benzodiazepines by astrocytes are examples of the beginning for a wider frontier for exploration in the context of a global brain.

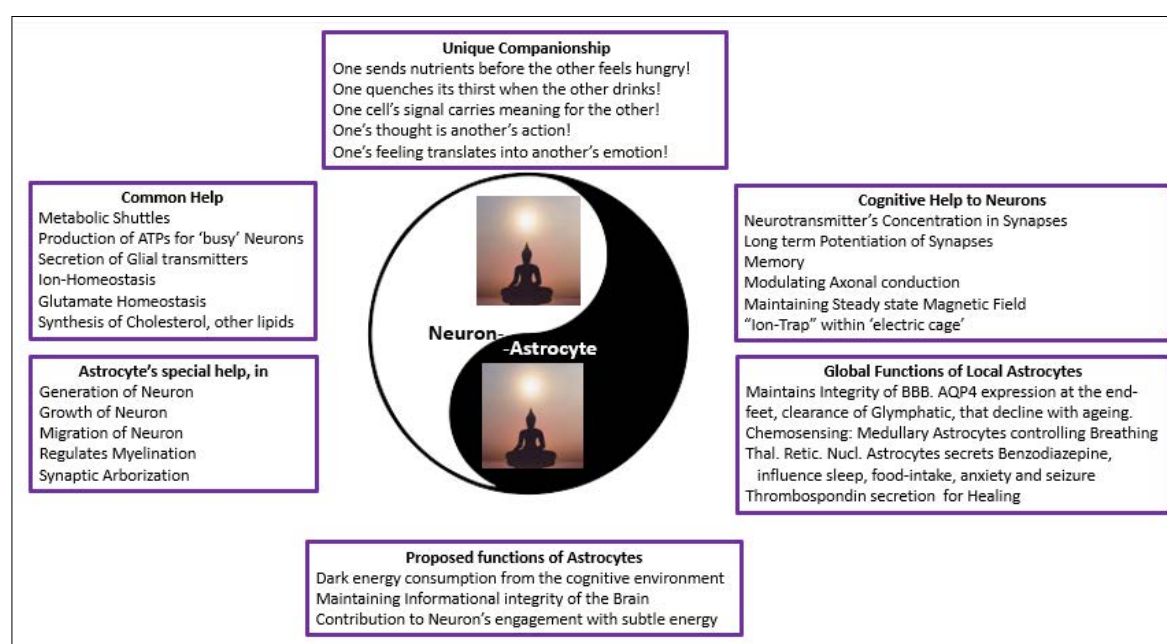
### Exploring the Relationship

In Cell Biology, it is rare to encounter any other example of such intercellular relationship as found between astrocytes and neurons. This never could be a relationship which is observed between the members of a parasitic twin. Nor does this happen to be any competitive. The relation is neither merely symbiotic as observed between commensal bacteria in the gut and intestinal epithelium,

nor merely cooperative on the line of a few common objectives as observed between T-lymphocyte and B-lymphocyte. Also, this is not collaborative merely for achieving respective goals as observed between hepatocyte and Kupffer cells in the liver.

Neurons and astrocytes symbiose, cooperate, and collaborate for a single common goal i.e., to 'biologize' subtle energy and environmental consciousness to implement consciousness's political agenda to synchronize with constantly changing space-time patterns in the surrounding extracerebral environment with the space-time patterns in neuronal firings within the cerebrum.

Astrocyte as 'woman' in the brain has evolved into a yang-yin relationship with neurons (Figure 1), where one quenches its thirst when the other drinks! One sends nutrients before the other feels hungry! One cell's signal carries meaning for the other! One's thought is another's action! One's feeling translates into another's emotion! The evidence has started accumulating. Astrocytes know when to feed neurons [19]. Bregman Glia, a variant of astrocyte, has been influencing the brain to manifest in behavior [20].



**Figure 1:** Roles of Astrocyte in Astro-Neuro Mosaic in the Buddha-State of the Brain

Neuro-astrocyte tango is, in fact, an example of tangled hierarchy in a complex situation of cell biology. At the system-organ level this kind of relationship is observed between the heart and the brain, within the brain between cerebral cortex and thalamus, amongst psychic faculty between 'self' and 'life', and at the level of consciousness between cerebral and extracerebral consciousness.

### Astrocytes in "Mind"-Functions

We do not know where the 'mind' is in the brain! Mind originates with duality. Mind is the organ of communication between two conscious systems. However, the mind is nonlocal, cannot be localized in space and time. Neurons alone, without astrocytes, as in the peripheral ganglion and in the central nucleus, transmit only digitized electrical signals, cannot handle non-digitized information. Mind handles pieces of information as thoughts. No information is an island in the nervous system. Conversion of a signal into a piece of information requires a mind's operation!

From two sets of negative evidence and one set of positive evidence the research question like this could be made, are tripartite synapses within the brain the local infrastructure for nonlocal mind, where astrocytes are intimately involved in different local, regional and global homeostasis of thoughts and emotion? The negative pieces of evidence are (i) Absence of any psychic property in Artificial Neural Network (ANN), and (ii) in several neuropsychiatric disorders e.g., in major depressive disorders (MDD), there is astrocytic atrophy [21]. Primary atrophy and loss of function of astrocytes are observed in toxic brain damage, Wernicke-Korsakoff psychosis/encephalopathy [22,23]. The positive piece of evidence is accumulation of astrocytes in the 'thinking' parts of the brain as we know of the cerebral cortex, and also recently known in the part of the brain that coordinates thinking i.e., cerebellum [24].

What is this mind-operation that collaboration between neuron and astrocyte support, or create jointly, is yet unknown to us. However, its absence explains why all events in the ANN-inspired AI are mindless! Since no astrocytic function has been tried to be incorporated within ANN, mind-operation is absent there! In ANN, there is no trace of information-handling, but only signal transmission! In the real brain, neurons without astrocytes cannot generate 'feeling' and process it as emotion within the complex nervous system. That is why we observe ANN-inspired AI as a feelingless robot. We do not know how neuron-astrocyte collaboration could emerge such an important function of 'life' as feeling! However, emotional disturbance has been noted in disorders with astrocyte loss and atrophy (see Oliveira et al, referred below). Effective collaboration with astrocytes also 'boosts' the 'self'-sense of neurons. In absence of such 'ego-boosting', the self-sense in the ensembles of ANN is absent. A series of events could evolve into a phenomenon inside the nervous system because of this self-sense while all events in an AI robot remain as events only. Astrocyte-neuron cooperation is essential for memory formation by synaptic modulation, and long term synaptic potentiation [25]. Robot AI doesn't have any memory, of any kind whatsoever! It is no wonder that in several neuropsychiatric disorders e.g., in major depressive disorders (MDD) as mentioned earlier, there is predominance of astrocytic atrophy and loss of astrocytic functions with loss of episodic memory. Progression from mild cognitive impairment to dementia stage of Alzheimer disease is hallmarked by a large-scale astrocytic degeneration and atrophy. For such reasons, the doctrine of neuropathology has been shifting to a glial inclusive view [26]. Two models of AI (OpenAI's Chat GPT-4.5, and Meta's LLaMa-3.1 with personal prompt), although, have been reported to pass Turing test [27], it is also reported that American President Donald Trump's Economic Tariff rates (3rd April 2025) are proven to be a product of AI, "Exactly what the dumbest kid in the class would do, without edits." (Tweet of the Editor of Journal of Public Economics).

Astrocyte-neuron collaboration, however, evokes emergence of new properties in the complexity of the system, and supports mind-operation, life-operation for feelings, and emergence of the sense of a self in a complex biological system with stabilization of both semantic and episodic memory. The absence of such collaborations even at the healthy level of human beings might lead the being to operate like a robot! The emergence of supportive infrastructures for the cognitive players of the system psyche (information, mind, self, life and operative consciousness) [28,29] within the brain as an organ cannot happen without a tacit understanding of yang-yin companionship (Figure 1) between the neuron and the astrocytes.

In addition to abundance of neuron-neuron and astrocyte-astrocyte networks and syncytia, the supportive infrastructure for global cognition is built-up by at least four types of astrocyte-neuron networking in the brain; (i) astrocyte modulating neuro-neuronal tripartite synapses (ii) astrocyte modulating nerve conduction at the node of Ranvier, (iii) astrocyte-neuron gap junctions and (iv) neuron-astrocyte synapses. One neuron communicates with about 5000-10,000 other neurons. Therefore the number of synapses in the brain is about 500-1000 trillions. In the human cerebral cortex, one astrocyte is said to modulate approximately two million synapses breaking the man-made boundaries of lobes, hemispheres, connectomes etc.! Because of the ability of "sensing of neuronal activity by astrocyte", there is reuptake of released neurotransmitters at the synaptic gap [30]. There is also release of various glia-transmitters at the synaptic junction like glutamate,  $Ca^{++}$ , ATP and D-serine. Through these wrapping

astrocytic processes in the synapse there is cross talk between presynaptic and postsynaptic neurons. There is also release of neuro-transmitters-binding proteins by astrocyte, which regulates the synaptic-life of transmitters [31].

### **Astrocytes in Brain's Behavior**

When astrocytes maintain the BBB, make neural synapses tripartite, participate in ion-homeostasis, and have metabolic shuttles with neurons, express receptor for neurotransmitters and secrete gliotransmitters, it is likely that evidence will emerge that neuron-astrocyte networks have a formidable role in behavior of the subject. Astrocytes morphologically look like distant "stars". Do the 'stars' govern our fate? A publication by Oliveira et al reviews the role of these star-shaped astrocytes in the rodent model in four domains of behavior, starting from sensory processing to motor response manifesting the behavior at the level of cognition and emotion [32]. The referred review cites a number of papers with molecular evidence of the role of astrocyte during depression in rats, motor coordination, in basic sensory function, and also during perception of pain.

### **Individual Uniqueness of Neurons and Astrocytes**

For conscious activities, neurons themselves are unique because of the polarity of their membrane towards consciousness resulting in consciousness-philial of neurons. Ion channels of the neuronal membrane are spatially disposed in a specific way with a specific temporal pattern of activity that creates a subtle energy-philial in neurons leading environmental consciousness to influence the brain-confined consciousness. On the other way round, there is another kind of a special attraction, neuron-philial of consciousness, probably because of the 'serenity' of neuron's genes. As neurons evolve for their placement in the cerebral cortex, their mitotic activities are down-regulated for maintaining the stability of the microtubules, the conduit of information, so that they are minimally disturbed by the process of mitosis for spindle formation. Besides, the long stretch of noncoding DNA with repetitive sequences of neuronal genes make neurons prone to mutation by subtle energy on the cerebral cortex.

As compared, astrocytes as cells are members of a cool-folk! Both neurons and astrocytes, although, have similar voltage-sensitive ion channels and similar kinds of receptors for neurotransmitters with long range communication systems, astrocytes lack the membrane properties that characterizes specifically the neurons [33]. That is why neurons fire, by means of action potential! Astrocytes do not! Astrocyte is highly permeable to  $K^{+}$ . However, its  $K^{+}$ -equilibrium is extremely stable, and therefore, it is electrically cold! As mentioned, astrocytes are required where a lot of 'thinking' (e.g., in cerebral cortex) and coordination of thinking (e.g., in the cerebellum) are going on!  $Ca^{++}$  waves in an extensive astrocytic network are related to operation of mind. In elephants, 97% of the cell population of the brain is astrocytes! That could be the reason why the elephant is temperamentally so cool, and behaves as a thinking animal with stupendous memory!

### **Higher activities of Neurons-Astrocytes**

It is not possible to investigate brain-consciousness merely with neurons, or neural network, neural oscillations, neural ensembles, neural connectomes, as dictated by the mainstream science of neuro-centric-consciousness. Banaclocha has emphasized that while a steady state (DC) magnetic field is the result of an astrocytic network, a time-varying (AC) magnetic field is the product of neural networks [34]. Astrocytic magnetic field has also been implicated in storage of memory as preservation of

content of consciousness. Both neuron and astrocytes make the brain magneto-sensitive which might help long distant aviation of the migratory birds [35]. Also, it would be interesting to learn how the magnetic field generated by glia can influence techniques like NMR and magnetoencephalography and vice versa. Alfredo Pereira (Jr.), inspired by the architecture of a large scale ion trap quantum computer proposed a mechanism for consciousness where calcium ions trapped within astrocytes are surrounded by electrical fields of neural circuitry creating a quantum protectorate-like situation [36,37]. The proposition of consciousness-protectorate intends to verify consciousness within the verifiable scale of nature. Disturbed calcium waves within astrocytes have been implicated in temporary loss of consciousness in epileptic seizure, in concussion of the brain and even during administration of general anesthesia [38-40].

### Propositions

The author proposes that astrocytes protect neurons from dark energy. The source of dark energy inside the brain is information itself. The author in his paper, A Radical view of Information: On its nature and science, proposed that the fecundity of mind makes it extremely prone to be impregnated by information. Mind conceives information and then splits information to generate 'form' (form is a space-time structure), and energy, which being unobservable, comes under the category of intangible dark energy [41]. This dark energy, if not managed appropriately, may ruin the 'life' of sensitive neurons. On the other hand, dark energy can be managed only by 'life'. Here, comes into focus the role of the orchestra of several live glial cells, astrocytes, around the neurons. The astrocytes 'absorb' this invisible dark energy, and convert it into visible energy. While information-sourced dark energy is managed by astrocytes, the neurons play with consciousness-sourced subtle energy, especially at the top of the cerebral cortex with dendritic mat dynamics and antennae dynamics.

Further, the system brain is informationally integrated. Contrary to a signal-structure transfer between two software devices by the 'blue tooth' technology, transmission of 'Thoughts' from one brain to another adjacent or a distant brain normally does not happen because of healthy astrocytes guarding such transfer. There is no evidence yet in favor of this speculation. Proven true, astrocytes would be held responsible in maintaining informational integrity of the brain. This kind of thought-transfer, at least partially, might happen in some specific conditions where such specific guarding has been altered (in altered state of consciousness), manipulated chemically (in schizophrenia), or willfully overcome (e.g., in higher states of consciousness) or the brains synchronized by practice between the partners.

The ecosystem of energy consists of a) matter-sourced conventional energy, b) information-sourced dark energy, and c) consciousness-sourced subtle energy. It may be grossly said that at the cellular level, conventional energy runs the metabolome, dark energy runs the protein factory and gene machinery, and subtle energy manipulates mainly epigenomic activities but can also influence genomic, proteomic and metabolic activities [42]. In the context of the organ brain, astrocytes, the largest population of cells within the brain handle dark energy while the cortical neurons with apical dendrites remain engaged under the influence of subtle energy! In such a scenario it appears inadequate to investigate such a unique cellular partnership on the basis of only conventional electro-magnetic signal energy!

### Concluding Remarks

With supposition of neuron-astrocyte partnership as that of a companionship of an indissolubly wedded pair, yang-yin, several new frontiers open up! Probably, the best output from such a couple comes when the brain remains at its minimal energy-consumption state, equivalent to zero-point energy state/fluctuation [43], e.g., during dreamless sleep, or awakened in the Buddha-state of the brain. The beginning with a yang-yin metaphoric relationship between neuron and astrocyte, leads us to a real Buddha state of the brain, the real goal of astrocyte-neuron companionship. This is an amazing leap for neuroscience, as well as for humanity. Empirical science, in general, gets the opportunity to advance system neuroscience by cross fertilization between systems physics and system psychology, system cosmology and systems biology, all meeting at the Zero-Point Energy state [44]. The readers may recall the image of Lord Buddha doing meditation. One can only imagine at this phase of science what could be His brain-state that might tentatively be called Buddha-State of the Brain! In a calm and quiet environment, the person in a meditating posture with Buddha-state of the brain has been performing bodily functions par excellence, maintaining a top-grade thoughtless mental hygiene. The 'life' is in the state of complete homeostasis both in terms of body and mind. The mind is still; neither converting any sensory signal into a piece of information, nor splitting information into 'form' and energy, neither 'form'ing nor processing any thought! The decision-making sentient entity, the self, the Chief Executive Officer (CEO) of consciousness within the brain has taken complete control of the mind, and quieted it completely. Consciousness is cool, feels 'at home' with the operations of 'self', 'life', and the mind with little fluctuation from external signals, or internal information. One hundred billion neurons, and several hundred billions of astrocytes, all observable, and 'local'izable within the brain, are fine-tuned with the operations of non-observable and 'non-local'-izable faculty members of the system psyche, namely consciousness, life, self, mind, and information. That is when the brain could be said to be at the Buddha-state of the being, when the billions of neuron-astrocytes are seen to maintain their tangled hierarchical relationship.

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