Proposal for a book project by
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Gliocentric brain models of consciousness, psychiatric disorders, robotics, and philosophy

Selected papers
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Chapter 1: Brain models

- Tripartite synapses and the glial network.. Quantum Biosystems 6, (2015). 1 – 9.
- Qualitative information processing in tripartite synapses: a hypothetical model. Cognitive Computation 4, (2012). 181 – 194.
- Where and how could intentional programs be generated in the brain? A hypothetical model based on glial-neuronal interactions. Bio Systems 88, (2007). 101 – 112.
- Model of the reticular formation of the brain stem based on glial-neuronal interaction. Cognitive Computation 7, (2015). 64 – 73.
- The self-composing brain: towards a glial-neuronal brain theory. Brain and Cognition 51, (2003). 357 – 367. (Co-author: K. Kopp).
- Neuromodulatory systems. Frontiers in Neural Circuits 7, (2013). doi: 103389/fncir.2013.00036 (co-author: G. Werner).

Chapter 2: On consciousness

- An interdisciplinary approach towards a theory of consciousness. Bio Systems 45, (1998). 99-121.
- The proemial synapse: consciousness-generating glial-neuronal units. In: Pereira J. A. And Lehmann, D. (eds.). The unity of Mind, Brain, and World, pp. 233 – 264, Cambridge University Press, Cambridge, UK.
- Disorders of human consciousness in the tripartite synapses. Medical Hypotheses 136, (2020). 109523 (co-author W. Baer).

Chapter 3: Pathophysiological hypotheses of psychiatric disorders

- Clock genes, feedback loops, and their possible role in the etiology of bipolar disorders: an integrative model. Medical Hypotheses 55, (2000), 155 – 159.
- The loss of ego boundaries in schizophrenia: a neuromolecular hypothesis. Medical Hypotheses 56, (2001), 614 – 621.
- Gene silencing: a possible molecular mechanism in remission of affective disorder. Medical Hypotheses 62, (2004), 907 – 910.
- The incoherence hypothesis of schizophrenia based on decomposed oligodendrocyte-axonic relations. Medical Hypotheses 69, (2007), 1299 – 1304.
- Loss of function of gap junctions may cause severe cognitive impairments in schizophrenia. Medical Hypotheses 73, (2009), 393 – 397.
- The syncytiopathy hypothesis of depression: downregulation of glial connexins may protract synaptic information processing and cause memory impairment. Medical Hypotheses 74, (2010), 497 – 502.
- The gliocentric hypothesis of the pathophysiology of the sudden infant death syndrome (SIDS). Medical Hypotheses 76, (2011), 482 – 485.
- Ketamine may block NMDA receptors in astrocytes causing a rapid antidepressant effect. Frontiers in Synaptic Neuroscience 4, (2012), doi: 10.3389/fmsyn.2012.00008
- Astrocyte mega-domain hypothesis of the autistic savantism. Medical Hypotheses 80, (2013), 17– 22.
- Balancing and imbalancing effects of astrocytic receptors in tripartite synapses. Commonpathophysiological model of mental disorders and epilepsy. Medical Hypotheses 84, (2015), 315

Chapter 4: Psychobiological models of mental disorders

- Imbalance of glial-neuronal interaction in synapses: a possible mechanism of the pathophysiology of bipolar disorder. Neuroscientist 10, (2004), 199 – 206.
- Nonfunctional glial proteins in tripartite synapses: a pathophysiological model of schizophrenia. Neuroscientist 11, (2005). 192 – 198.
- Synaptic imbalances in endogenous psychoses. Bio Systems 100, (2010), 113 – 121.
- Pathophysiology of schizophrenia based on impaired glial-neuronal interactions. Open Journal of Medical Psychology. 3, (2014), 126 – 140.
- Towards a comprehensive psychobiological model of major depressive disorder. Open Journal of Depression 7 (2018), 31 – 49.
- Mitterauer, B. J. (2018). Psychobiological model of bipolar disorder: based on imbalances of glial-neuronal information processing. Open Journal of Medical Psychology 7, 91 – 110.
- Disintegration of the astroglial domain organization may underlie the loss of realitycomprehension in schizophrenia: a hypothetical model. Open Journal of Medical Psychology 8, (2019), 15 – 35.
- Psychobiological model of volition-implications for mental disorders. Open Journal of Medical Psychology 9, (2020), 50 – 69.

Chapter 5: On robotics

- Some principles for conscious robots. Journal of Intelligent Systems 10, (200), 27 – 56.
- Clocked perception system. Journal of Intelligent Systems 4, (2001), 269 – 297.
- Robots with consciousness: creating a third nature. International Journal of Machine Consciousness 5, (2013), 179 – 193.
- Outline of a brain model for self-observing agents. Journal of Artificial Intelligence and Consciousness 8, (2021), 171 – 182.

Chapter 6: Brain philosophy

- Many realities: outline of a brain philosophy based on glial-neuronal interactions. Journal of Intelligent Systems 19, (2010), 337 – 362.
- The principle of self-embodiment. Architectonic philosophy of technique. Journal of the BWW Society. www.bwwsociety.org/bwwsociety.org/journal/current/2018/mar–apr/the principle-of-self-embodiment (2018), 1 - 9.

Introduction

On the microscopic level the brain shows a cellular structure composed of neurons and glial cells with their pertinent networks. This allows the brainphilosophical interpretation that the brain embodies at least two distinct ontological realms. Therefore, a pure neurophilosophical approach to brain theory is based on an ontological fault in exclusively considering the neuronal system.
The novelty of the brain models I propose lies in the distinction between a structure of objective information processing and a structure of subjective information processing. Guenthers (1976) theory of subjectivity introduce these brain models: „Subjectivity is a phenomenon that is distributed over the dialectic antithesis of the 'Ego' as the subjective subject and the 'Thou' as the objective subject, both of them having a common mediating environment." My core thesis is that glial-neuronal synaptic units, called tripartite synapses, may embody a candidate system of subjectivity consisting of the astrocyte (glial cell) as the subjective component and the pre-postsynapse (neuron) as the objective component that interact bidirectionally. In parallel, glial-neuronal interactions run in the glial network via gap junctions generating dynamic memory structures that may also function as intentional programs.

The book is organized into six chapters.

The brain models presented in Chapter 1 concern tripartite synapses and the glial network (syncytium). Here I propose a new form of synaptic information processing. It is hypothesized that in the astroglial network intentional programs may be generated that determine the expression of astrocytic receptors. Based on a formalism of qualitative computing (tritogrammatics) astrocytic receptors may be capable of qualitatively modifying synaptic information processing. Similarly, information processing in the glial network of the reticular formation of the brainstem is formally described. In the study „the self-composing brain" the principle of harmonization, shown on Schubert's symphony Nr. 8, is introduced. Furthermore, in collaboration with Gerhard Werner (University of Texas) we examined the interactions and interdependencies between Neuroglia, Brain-cell Microenvironment, and the processes commonly subsumed under Neuromodulation.

Chapter 2 starts with the study „an interdisciplinary approach towards a theory of consciousness" that focuses on the concept of reflection. It is suggested that glia has a boundary-setting function in the spatio-temporal interactions with the neuronal system. This function, compartmentalize the brain in different self-systems each with the ability to self-organize. A tree of reflection consisting of a number of places (ontological loci) on which reflection processing of varying complexity take place, is proposed as a formal model.
The study „the proemial synapse: consciousness-generating glial-neuronal units" concentrates in synapses, the astroglial domain organization, and the glial network. Significantly, a novel relationship, called proemial relationship (Guenther, 1976) is introduced for the description and interpretation of the feedforward-feedback mechanism operating in glial-neuronal synaptic units (tripartite synapses). The brain may be composed of many ontological realms consisting of myriads of glial-neuronal synaptic units with their volitive-intentional and cognitive-perceptive networks embodying many subjective realities operating on Ego-You reflections. In this fashion, these structures and functions of our brain enable it to prelude or reflect all possible interactions with the environment. Here we may deal with reflection mechanisms that determine consciousness, but do not reach awareness.

The paper „disorders of human consciousness in tripartite synapses" (co-author W. Baer) addresses three topics supporting the Conscious Action Theory of quantum theory (Baer, 2020) for normal consciousness functioning and its medical deviations. First, we present the architecture of a pan-psychic theory, which supports the hypothesis that tripartite synapses are locations of human conscious experience. Second, the inner working of the glial network to underpin long-term memory and central functions corresponding to the inner feeling of the self is discussed. Third, we consider the relation between psychiatric conditions and the balance states between the number of neuronal transmitters and astocytic receptors.

Chapter 3 comprises pathophysiological hypotheses of affective disorders, schizophrenia, the sudden infant death syndrome (SIDS), and autistic savantism. Essentially, a common psychopathological model of mental disorders and epilepsy is proposed. Receptors in astrocytes in tripartite synapses determine the balance or imbalance of synaptic information processing. Applying a logic of balance it can be shown that synaptic information processing is underbalanced (by overexpression of astrocytic receptors) in depression, overbalanced (by underexpression of astrocytic receptors) in mania, and completely unbalanced (dysfunctional astrocytic receptors) in schizophrenia. Comparable imbalances may be responsible for epilepsy.
Regarding affective disorders it is hypothesized that mutations in clock genes cause disturbances in molecular feedback loops that are responsible for the symptomatology of bipolar disorder on the behavioral level. Interestingly, a case observation inspired the hypothesis that a virus infection could be responsible for the remission of a bipolar disorder by causing gene silencing. Next, the syncytiopathy hypothesis of depression suggests that the downregulation of glial connexins may protract synaptic information processing and cause memory impairment. In a short opinion article it is hypothesized that the rapid antidepressant effect of Ketamine may be caused by its blocking of NMDA receptors in astrocytes. Given that patients with schizophrenia cannot distinguish between the self and others, a neuromolecular hypothesis proposes that the loss of the rejection function on the molecular level exerted by intron splicing leads to a loss of the glial boundary-setting function in their interactions with the neuronal system and the loss of ego boundaries on the behavioral level. A further hypothesis suggests that severe cognitive impairment in schizophrenia may be caused by a loss of function of glial gap junctions.
In addition, the decomposition of the oligodendrocyte-axonic system may be responsible for symptoms of incoherence in schizophrenia. It can be formally shown how processes of oligodendrocytes tie the various properties of axonic information conductance together into categories. Notably, Lakhan and Vieira (2009) characterize this model as „oligodendrocytic computation capacity theory." In the case of a decrease or loss of oligodendrocytes (and myelin) in schizophrenia, the brain is incapable of categorizing information processing leading to symptoms of incoherence (e. g. Thought disorder) on the behavioral level.
Two further hypotheses concern sudden infant death syndrome (SIDS) and autistic savantism. Based on a model of glial-neuronal-vascular interactions in the networks of the cardio-respiratory center in the brainstem, possible impairments of glial function that may be responsible for SIDS are discussed. In the end, the Astrocyte mega-domain hypothesis of the autistic savantism assumes that the number of the astrocytic processes which build a domain with the neuronal system, is genetically increased enabling a higher complexity of computation. From this model of a mega-domain savant capabilities can be deduced.

Chapter 4 presents my basic psychobiological models of mental disorders focusing on abnormalities of glial-neuronal interactions in the brain. In 2004 I published the first model of imbalances of information processing in tripartite synapses responsible for the pathophysiology of bipolar disorder (Verkhratsky and Bult, 2007). The hypothesis is that an imbalance between neurotransmitters and glial binding proteins in the synaptic cleft is determined by glia. If glia binding proteins are overexpressed, synaptic transmission is suppressed due to reduced levels of bioavailable neurotransmitters. This state may cause depression on the behavioral level. In contrast, if glial binding proteins are underexpressed, the excess of neurotransmitters in the cleft leads to an overbalanced state of synaptic information processing. This state may cause manic behavior. Moreover, the first pathophysiological model of schizophrenia centered on non functional glial binding proteins causing total imbalance of synaptic information processing was published in 2005. It is hypothesized the glia lose their negative feedback function due to the loss of function mutations in the genes encoding the binding proteins and glial receptors. These mutations generate proteins that cannot be occupied by their cognate substances of the neuronal system, primarily neurotransmitters. In this fashion glial-neuronal interactions become totally unbalanced, since glia lose their inhibitory or boundary-setting function. As a result, neural flux is unconstrained, also the flux of thought on the phenomenological level.
Since glial binding proteins have only been identified in the snake, I modified the model of synaptic imbalances in mental disorders focusing on receptors in astrocytes disregarding the binding proteins.

Introducing the formalism of logic of balance (modified after Guenther 1963), typical imbalances of information processing in tripartite synapses may be responsible for the pathophysiology of depression, mania, and schizophrenia. According to the logic of balance in living systems, the number of values (neuronal components) and the number of variables (glial components) must be equal. Three types of synaptic imbalances can be deduced. First, tripartite synapses are underbalanced, if the variables outnumber the values. This system state may cause depression. Second, if the values outnumber the variables, the tripartite synapses are overbalanced responsible for mania. Third, if no functional variables are available at all, information processing is totally unbalanced which may cause schizophrenia. The basic symptoms of depression, mania, and schizophrenia can be deduced from these pathophysiological models. Importantly, Mahdavi and colleagues developed an extended mathematical model of an imbalanced tripartite synapse based on our model of pathophysiology of schizophrenia. Two comprehensive psychobiological models of major depression and bipolar disorder have been elaborated over the years. Based on genetic-epigenetic and chronobioloical factors a hyperintentional personality structure, if faced with non feasible intentional programs in the environment, suffers from inner and outer stress. This stress situation leads to imbalances of information processing in glial-neuronal synaptic units (tripartite synapses). In depression the overexpression of astrocytic receptors and of gap junctions in the glial network causes prolonged information transmission that affects the behavior generating systems in the brainstem reticular formation. Since the activation of the behavior generated systems is protracted they are incapable of selecting an appropriate mode of behavior (e. g. eating, working, communicating etc) from sensory information in real time.

Inversely, in mania astrocytic receptors and gap junctions are underexpressed causing shortened synaptic information processing with rapid changes in behavior. Switching of mood states may represent a coping-attempt with depression by mania and vice versa. Towards a comprehensive pathophysiological model of bipolar disorder it is not only focused on imbalances in tripartite synapses, but also on dysfunctions and impairment of the oligodendrocyte-axonic system and microglia. Furthermore, a pathophysiological model of schizophrenia attempts to describe gliopathologic events as a cause – and effect – relationship. Bernstein and colleagues (2015) conceive my model as follows: It describes „that dysfunctional astrocytic transmitter receptors and disruption of gliotransmitter release from astrocytes are primary causes for impaired glial function in schizophrenia. Reduced gliotransmitter release from astrocytes seriously affects synapses that consequently liberate an excess of neurotransmitters. This may cause axonal hyperexcitation leading to disconnection of neural networks and toxic effects on oligodendrocytes. According to this paradigm the activation of microglia is a secondary event.“ Basically, unconstrained synaptic information flux may lead to a generalization of information processing in the neuronal networks responsible for delusions and hallucinations on the behavioral level. In addition, it is suggested that the ontological confusion of astroglial domain boundaries progressively disorganize reality comprehension and may represent the core pathology of schizophrenia underlying the main symptoms of the disorder. Note, normally astroglial domains exert a categorization of information that becomes progressively lost in the schizophrenic process.

In the end of this chapter a new psychobiological model of volitive processes and its implications for the etiopathology of mental disorders is presented. The model is established upon five elementary volitive processes. These are the volition to act; the volition to self-instrumentalize; the volition to program intentions; the volition to generate realities, and the volition to permanent existence. Imbalances of information processing in tripartite synapses and their network may be responsible for dysfunctions of self-instrumentalization. It is suggested that the volition to permanent existence unconsciously works in mental disorders, but the volition to intentional programming of realities and the volition to generate realities by communication with subjects and objects in their environment are impaired. In depression, the volition to act is constrained by hyperintentional programs that are non feasible in the environment. In mania volitive processes are totally oriented on events in the environment without any goal-directed programming. Dysfunctions of volitive processes in schizophrenia are fundamentally caused by severe impairments of self-instrumentalization. A gap between sensory information processing in the neuronal network and the glial network shown in tripartite synapses causes the inability of schizophrenics to distinguish between the self and the other.

In delusions, the destiny for communication becomes staged as pseudo-communication. Together, the study outlines a new model of volitive processes and deduces dysfunctions that may play a key role in communication pathology and abnormal reality experiences of patients with mental disorders.

Chapter 5 presents basic brain-inspired models for conscious robots. I propose some principles upon which the construction of robots capable of consciousness could be based. Beginning with a simple concept of reflection in the sense of feedback mechanisms, further principles are added since feedback mechanisms alone cannot produce consciousness. The robot brain should have a material composition enabling specific functions to be executed (the architectonic principle). From this diversity of material structures, compounds are formed according to the lock-key principle of complementarity. The robot should also be equipped with intentional programs that it attempts to realize in the environment by movement (the principle of intentional movement). In this fashion, the robot accepts objects or stimuli that correspond to its specific intentional program, whereas non-appropriate objects or stimuli are rejected (the principle of acceptance and rejection). In addition, a robot brain should have the capability to coordinate a large number of parameters which set spatio-temporal limits and the ability to self-organize (the principle of spatio-temporal boundary-setting and the principle of self- organization). My core hypothesis is that the glial networks exert a spatio-temporal boundary-setting function in their interaction with the neuronal networks. If the robot were aware of the creeping decay of its material parts then it could sense its intention in the environment under deadline pressure. This principle of spatio-temporal limitation of material properties could trigger emotions that may indicate a conscious state of the robot.
The paper „Clocked perception system“ is one of a series investigating the time-coding principle from a biological and formal technical perspective. Here, I introduce a clocked perception system that is based upon an extended biological brain model focusing on receptors within the perception sheet. As an elementary framework, I apply a combinatorial structural theory explaining how to construct phase programs that decide which receptors are to be activated in a specific perceptual phase, thus, suitable to specific stimuli. Moreover, the system is capable of integrating sensory-motor information, and the problem coordinating different perception systems is elucidated in the paradigm of „harmonization in a jazz ensemble“.
Next, the paper „robots with consciousness: creating a third nature“ is brain-theoretically based on the study „the proemial synapse: consciousness-generating glial-neuronal units“ (see chapter 2). Fundamentally, a distinction is made between auto-reflection and hetero-reflection of the robot and self-reflection of the constructor. Whereas conscious robots are able to auto-reflect their mechanical behavior and hetero-reflect the behavior regarding to the environment, the ability of self-reflection must remain within the constructor of the robot. Although robots with self-consciousness are ruled out in this model, the self-objectivation of man by technology is even further extended by robotics as compared to spacecraft or computer technology. In cases of conscious robots, the objective mind is objectified by creating new creatures – man would have created a third nature. Finally the paper „Outline of a brain model for self-observing agents“ is offered in this chapter. This model also focuses on glial-neuronal synaptic units (tripartite synapses). While the neuronal component of the synapse embodies objective subjectivity processing sensory information, the glial component (astrocyte) embodies subjective subjectivity producing subjective behavior (intentions, consciousness) in its interactions with the neuronal part of the synapse. The fundamental principle of the implementation of self-observing agents is the following: a brain is capable of self-observation, if the concept of the intention to observe something and the concept of the observed are located in different places. With a formalism of qualitative information processing the architecture of self-observation is described in increasing complexity, building networks. It is suggested that if a robot brain is endowed with a network of modules for self-observation, the robot may generate subjective perspectives of self- observation indicating self-consciousness.
Man cannot perceive himself by introspection, since what he finds inside himself is really a picture of the universe that is not he himself. Self-cognition is only possible by repeating our behavior in an attempt to technically copy existential functions. In this fashion, we learn more from our technical product who we really are. Similarly, given the methodical and ethical limits of experimental brain research, robotics represent a true alternative.

In chapter 6 two studies of architectonic philosophy are selected. The paper „many realities“ outlines a new brain philosophy based on my model of glial-neuronal interactions. The organization of glial- neuronal interactions in domains is interpreted as a polyontolgical structure in the sense of many ontological loci or subjective realities. Significantly, ontological loci can cooperate (polycontexturality) or gaps exist between them (discontexurality). For the formal description of a polyontolgical structure of the brain the combinatorics of morphogrammatics (Guenther, 1962) is applied. Furthermore, it is suggested that the holistic and integrative function of selfreference guarantees the maintenance of the circular organization of the brain implying the time conception of permanence. Tripartite synapses may operate as consciousness-generating units, called proemial synapses. It is suggested that the intentional programming of these synapses may occur in the glial network (syncytium). According to this brain model we have the ability to „prelude“ the interactions with subjects and objects in the environment already within the brain. Since the brain operates both polycontextually and discontexturally, we can at a given time only communicate with a finite number of subjects in the environment, and most people must be rejected, as has been experimentally verified in visual perception. Note, discontexturality also means that we cannot understand all subjective realities of the others including the partner. Though my work on architectonic philosophy is mostly written in German, the study „The principle of self-embodiment. Architectonic philosophy of technique“ outlines the essence of my philosophic-metaphysical world view. First, the brain model developed over the years is described focusing on subjectivity and qualitative mechanisms of brain function. Then, the elementary brain operations in ontogenetic and evolutive time scales are discussed. Basically, the theory of Transphysics of self-embodiment of human subjectivity in humanoid robots and the self- embodiment of the human soul in „timeless“ permanence represents the core-theses of the architectonic philosophy of technique.
Gotthard Guenther, the great German-American philosopher of cybernetics and technique established awareness in 1956 that “we do not lose our soul in humanoid robots. On the contrary, the human subject implements its reflection process in the mechanism and increasingly acquires a new reflection power from the mechanism of the robot.”

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