The self-composing brain: Towards a glial–neuronal brain theory

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Abstract

A brain model is proposed which describes its structural organization and the related functions as compartments organized in time and space. On a molecular level the negative feedback loops of clock-controlled genes are interpreted as compartments. This spatio-temporal operational principle may also work on the cellular level as glial–neuronal interactions, wherein glia have a spatio-temporal boundary setting function. The synchronization of the multi-compartmental operations of the brain is compared to the harmonization in a symphony and appears as an integrated behavior of the whole organism, defined as modes of behavior. For explanation of the principle of harmonization, an example from Schubert’s Symphony No. 8 has been chosen. While harmonization refers to the synchronization of diverse systems, it seems appropriate to select the brain of a composer and the structure of musical composition as a paradigm towards a glial–neuronal brain theory. Finally, some limitations of experimental brain research are discussed and robotics are proposed as a promising alternative.

Keywords: Spatio-temporal compartmentalization; Clock-controlled genes; Glial–neuronal interactions; Modes of behavior; Musical harmonization; Robotics

1. Introduction

In brain research, it is commonly recognized that the complex functions of our brain are based predominantly on the principle of self-organization (Kampis, 1991; von der Malsburg, 1995). Although progressively better definition models of self-organization of biological brains are being developed (Schalow & Zach, 2000), until now two complex problems could not be completely resolved; first, how the brain organizes its intentional genetic program with respect to the perpetually changing and often unpredictable environmental situation, and, second, how the brain synchronizes its many sub-functions or computational domains so that the entire organism can produce integrated behavior. This paper is a modest attempt to describe the structural organization of the brain and to describe the related specific functions as compartments in the sense of operational domains, organized in time and space.

Beginning on a molecular level, the spatio-temporal compartmentalization of clock-controlled genes will be presented. This time–space operational principle will next be considered on the cellular level as compartmentalization which has been previously defined as the “spatio-temporal boundary setting function of glia in their interaction with the neuronal system” (Mitterauer, 1998). Additionally, compartmentalization may be recognized on a behavioral level. In their interaction with environment, humans and animals constantly produce time and space limited “modes of behavior” (Iberall & McCulloch, 1969). These modes of behavior establish an integrated behavior and are qualitatively different from each other.

The subdivision of the neuronal system in compartments has proved fruitful both in brain theory (Van Essen & Deyoe, 1995) as well as in the development of neuronal computers (Arbib, 1995). We hope to further develop this idea by taking into consideration new molecular research results as well as the role of the glial system in its interaction with the neuronal system. Formally defined, a compartment is a biological structure which has a time–space limited operational quality.
With respect to the inner and outer environment, a compartment is an active operational unit for which a certain structure of environment (molecule, object, pattern, etc.) is appropriate or inappropriate; a third possibility does not exist. Parallels in structure may be found in music (Mitterauer, 2001c). Basic concepts of musical composition and instrumentation are transferable to this brain model and will serve as a paradigm. The topic of this study is not how the brain processes musical information but rather how the brain "composes itself" in the sense of self-organization.

(For readers not familiar with the pertinent musical terminology see Appendix A for definitions.)

2. Molecular compartments

Compartment diversity exists already on the molecular level (Alberts et al., 1994) and may be observed, for example, in the vesicular transport within the synapses. Another example of this diversity occurs in zerebrins which are compartmentally distributed in adult rodent cerebellum in the form of parasagittal bands of alternating zerebrins+ and zerebrins− (Seil, Johnson, & Hawkes, 1995). Ghadessy, Ong, and Holliger (2001) have described a compartmentalized self-replication which represents a strategy for the directed evolution of enzymes, especially polymerases. Most important are experimental results that molecular patterns of presumptive visual compartments in both the cortex and thalamus can form independently of one another and suggest a role for EphA family members in both compartment formation and axon guidance within the visual thalamocortical system (Sestan, Rakic, & Donoghue, 2001).

One may also interpret molecular circadian oscillators (Dunlap, 1998; Hardin, 2000) as spatio-temporally limited operation units in the sense of compartments; specifically, as negative feedback loops. These are composed of clock-genes, stimulating proteins, and of proteins which have been produced by clock-genes. In this case, it is possible to regard proteins which stimulate the cycle as corresponding to "environment information," clock-genes as representing an "intentional program," and the production of clock-proteins as equalling the "realization of the intentional program" (Mitterauer, 2000a). Once the clock-gene has produced its protein, this protein stops the cycle by temporarily interrupting the production of further stimulating proteins (Dunlap, 1998). The cycle can again proceed, which in the metaphor of music corresponds to the realization and completion of a rhythmic pattern in time. As in music, these compartments contain a self-repeating meter (rhythm), which is defined as pattern of movement in time.

Negative feedback loops have a spatio-temporal boundary-setting function and can be characterized as "micro-compartments." The function of these circadian oscillators only becomes effective when they control a certain group of genes in their expression, generating a spatio-temporal functional unit. We speak of a "clock-controlled compartment" (Fig. 1). A pianist, for example, "controls" a group of sounds when he presses each key on a keyboard. By organizing the succession of notes in space and giving rhythmic structure in time, the pianist makes audible his own internal impulses at a given moment or makes audible signals he has received from the written page. The search for clock-controlled genes has thus far focused mainly on rhythmically expressed mRNAs. In a few cases, rhythm in protein abundance may even be observed in the absence of underlying mRNA rhythms, indicating that potent clock-dependent posttranscriptional mechanisms are operating. Once a comprehensive collection of clock outputs is available, we will have a better understanding of how the biological clock orchestrates the temporal program that governs the coordinate expression of biological rhythms (Hardin, 2000).

Molecular and cellular processes in the brain, however, are determined by a plethora of various biological clocks. Not only do circadian rhythms exist, but also ultradian rhythms (Iwasaki & Thomas, 1997). These ultradian rhythms include a time scale from pico-seconds and milliseconds to minutes and hours (Lloyd, 1998). The investigation of circadian clocks is making significant progress. Recently, the McKnight group reported that the transcription factor neuronal PAS domain protein 2 (NPAS 2) likely functions as part of a molecular clock operative in the mammalian forebrain (Reick, Garcia, Dudley, & McKnight, 2001). This discovery may provide a molecular link between circadian oscillations and energy homeostasis interlocked through negative feedback.
loops (Schibler, Ripperger, & Brown, 2001). The problem of the synchronization of this rhythmic diversity, however, remains unsolved. The following hypothesis may resolve this issue: a compartment or compartments whose rhythm at a certain moment best corresponds to internal and external environment conditions command and, therefore, determine the rhythm of the molecular processes of the entire system. This is comparable to a melody, which can best be realized by certain instrument groups while other instrument groups assume a secondary function, as accompaniment or rest altogether. However, since theoretically all instruments could be melodic carriers, a “redundancy of potential command” (McCulloch, 1965) rules orchestration. Those instruments best suited through their timbre, tone color or intensity of sound in any given “environmental situation” (the effect the composer attempts to create) will take a predominant role. Concerning the interaction of biological clocks, Lloyd (1998) proposes a safety-net of redundancy and checkpoints, so that if one timing circuit fails another deputizes. However, Lloyd does not penetrate the principle of the redundancy of potential command. The importance of this principle for the synchronization of compartments of diverse operation qualities will be explored on a behavioral level further below.

3. Cellular compartments

The nervous tissue of the brain consists of the neuronal system (neurons, axons, and dendrites) and the glial system (astrocytes, oligodendrocytes with myelin sheaths which enfold the axons and microglia). Glial cells outnumber neurons in the central nervous system (brain) by a factor of 10 to 1 (Kuffler, Nicholls, & Martin, 1984). Virchow (1846) considered them to be merely connective tissue between the neurons (“nerve glue”). Meanwhile, experimental results are inspiring a major re-examination of the role of glia in the regulation of neural integration in the central nervous system. Slow glial calcium oscillations (every 5–6 min) occur spontaneously and can cause excitations in nearby neurons. Although there is experimental evidence that neuronal–glial interactions also occur in the millisecond range (Mennerick, Benz, & Zorumski, 1996; Murphy, Blatter, Wier, & Baraban, 1993), until now rapid glial oscillations within a second are not found. Following the rationale of our brain model, rapid glial oscillations might be observed in the near future. It is notable in this respect that short (about 1 min) song rhythms of Drosophila are controlled by the clock gene per, whose expression is observed only in glia (Hall, 1995).

The hypothesis of this paper concerns the interaction of the glial system with the neuronal system and its spatio-temporal, boundary-setting function. More precisely: the glia divide the brain into spatially limited areas or compartments on the one hand and create functional units in various time scales on the other (Mitterauer, 1998). Rall (1995) developed a compartment model based on the neuronal system which divides a neuron into a number of compartments (soma, dendrites, and axons). Rall was able to show that the complete functions of neurons could only be demonstrated if the different functional parts of neurons were separated (compartmentalization).

The principle of compartmentalization may also be applied to glial–neuronal interaction if one assumes that glia divide or combine neurons in functional units (Varon & Somjen, 1979). Steindler (1993) describes transient glial boundaries that surround functional groups of neurons, their dendrites, and axons during neural development, referred to as “cordons.”

Convincing experimental results indicate that glia have a boundary-setting function and that this function divides the neuronal system into spatio-temporal compartments (Mitterauer, 1998). Recently, it has even been demonstrated that the number of synapses is controlled by glia (Ullian, Sapperstein, Christopherson, & Barras, 2001). But also a glial cell itself may consist of hundreds of independent compartments (“micro-domains”) capable of autonomous interactions with the particular group of synapses that they ensheath (Grosche, Moller, Verkhatsky, Reichenbach, & Kettenmann, 1999). On a molecular level, the negative feedback loops of circadian oscillators have been discussed and a comparable negative feedback system could also exist between glial cells and neurons (Mitterauer, 2001a). The firing of neurons may stimulate glial cells to release certain substances, such as neurotransmitters, ions, etc., which could
subsequently deactivate the neurons. In this case, glia would not only be able to form functional units with neurons, but also could set a time limit for the operational processes (Fig. 2). For example, it is becoming evident that, in response to neuronally released glutamate, astrocytes can themselves release glutamate (Gallo & Chittajallu, 2001). Such a mechanism causes feedback onto both pre- and postsynaptic elements to modify transmission (Haydon, 2001). As music exists in time, the operations of the brain must exist in time. In this sense, one could describe the glial cells (astrocytes, oligodendrocytes) as the “metric pulse” and the neurons as “instruments.”

An astrocyte which can activate or deactivate n-neurons via its processes is displayed in Fig. 3. Here, the neurons are connected among themselves in the sense of a neuronal network (dashed lines). In this very simple diagram, only one negative feedback loop is depicted (see Fig. 2). This interactional structure of an astrocyte with n-neurons can be defined as an elementary compartment of nerve cells. By simultaneously regulating neurotransmission in all of the synapses an astrocyte has enveloped, the astrocyte calcium wave may coordinate synapses into synchronously firing groups (Antanitus, 1998). These elementary compartments can then form larger compartments with typical functions. Not only do neuronal networks exist in the brain, but also glial cells join via gap junctions to form additional networks (syncytium). Gap junctions are essential to astrocytic signalling functions and it is estimated that more than 50,000 gap junction channels interconnect each astrocyte to its neighbors (Cotrina, Gao, Lin, & Nedergaard, 2001). A glial syncytium can structure information provided by a local Ca$^{2+}$ wave into a distinct spatial and temporal pattern of Ca$^{2+}$ oscillations (Strahonja-Packard & Sanderson, 1999).

An elementary glial–neuronal compartment could be compared to the playing of a string instrument. The fingers (processes of the astrocyte) can simultaneously play all strings (neurons) at once, however, to produce a melody, only distinct strings (neurons) are activated. Similarly, as the measures in music determine time and control which notes are played, the operations in the glial–neuronal compartments of the brain could be conceived to function in the same manner. This model of an elementary glial–neuronal compartment on the cellular level could be understood as a “schema” in the sense of Piaget (1952). According to Piaget, the schema is “the way of acting on objects.” If one supposes that the neurons represent objects for the astrocytes on which they will act in different ways via their processes, the glial cells construct an internal pattern of neuronal activity appropriate to the perception of objects or pictures in the environment. Considering the development of the brain, there is experimental evidence that the glia (radial glia) codetermine where the neurons must travel for the construction of the cerebral cortex or in which way the axons must grow (Nadarajah, Brunstrom, Grutzendler, Wong, & Pearlman, 2001; Rakic, 1988, 1995a, 1995b). Hatten (1990) describes this process as “glial scaffolding.” Also of interest is that radial glia, after having finished the brain development, then transform into astrocytes (Levison & Goldman, 1993). One could therefore talk about a “horizontal,” as well as an “orthogonal” glial–neuronal compartmentalization (Mitterauer, 1998).
As evidenced on the molecular level the question also remains on the cellular level of how the numerous glial-neuronal compartments of the brain which possess the same or different operation qualities synchronize in order that the brain can produce integrated behavior. Our hypothesis proposes that all compartments which at a determined moment use the most appropriate environment information for the realization of their intentional programs will command the rhythmic operations of the total system by synchronizing the measures or rhythms. In the language of music we use the term “harmonic structure” which along with meter is the elementary structure or mechanism of synchronization. The way this harmonization mechanism could function will now be considered on the behavior level.

4. The concept of the modes of behavior

According to Iberall and McCulloch (1969), a living system like man is highly dynamic. In order to produce an integrated behavior it must be capable of generating stable system states, the so-called modes of behavior. This concept has been somewhat neglected in Brain and Behavioral Sciences, whereas it adopts a pivotal role in the brain model presented here. We do not normally think of human behavior as modal, though most people would agree that their quality of consciousness is unitary and they can only do one thing well at a time (Kilmer, McCulloch, & Blum, 1969). This may be identified as a dynamic action mode of the system, such as “the system sleeps.” In Table 1, the essential modes of behavior or action modes are listed which will have a time constant of the order of the female menstrual period. Although the list itself could be questioned, we would like to focus on the exploratory power of this scientific approach.

McCulloch (1966) has associated the ability of the brain to integrate its functions with the reticular formation in the brain stem, in the sense of an “integrative matrix” (Hobson & Scheibel, 1980; Scheibel & Scheibel, 1968). Over time, however, the reticular formation seems to have attracted the interest of scientists in its role as an activating or arousal system (Steriade, 1996). In the 1980s, we further elaborated McCulloch’s theory of reticular formation (Mitterauer, 1988). The actual molecular enlightenment of the circadian and ultradian oscillators (rhythms) as well as the undeniable influence with which the glial system acts on the neuronal system is a challenge to reconsider the integrative decision function of the reticular formation using the principles of musical composition as a paradigm.

According to McCulloch (1966), the reticular formation operates by an abductive logic. Abduction is the selection of the appropriate program from a repertoire in accordance with a rule for analyzing program requests. These programs are general in the sense that all are principally adapted for the processing of environment information, however, at the same time, they are highly specialized for the processing of specific environment information. When specific environment information acts on the system, the system can decide or select to which program the information belongs, that means, which program is best suited for information processing. The repertoire of these programs represents a heterarchic system (circular system) which is equipped with a “redundancy of potential command” (McCulloch, 1965), because every program in itself is capable of ruling the whole system for a certain time. When this abductive selection and commanding system is transferred to our brain model, a glial-neuronal compartment corresponds to one respective program structure. These program structures are genetically determined, and the activity of the programs alters with different time scales. Therefore, the brain permanently operates in different system states which correspond not only genetically but also in relation to the environment and to intentions (Mitterauer, 2000b). These program structures or compartments may also be regarded as hypotheses or intentions which are tested in the environment. Since conditions in the environment can quickly change or remain unchanged, the brain must either change its multi-compartmental program structure or “freeze” the biorhythm on a determined

<table>
<thead>
<tr>
<th>Modes of behavior</th>
<th>Percent of time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleeps</td>
<td>30</td>
</tr>
<tr>
<td>Eats</td>
<td>5</td>
</tr>
<tr>
<td>Drinks</td>
<td>1</td>
</tr>
<tr>
<td>Voids</td>
<td>1</td>
</tr>
<tr>
<td>Sexes</td>
<td>3</td>
</tr>
<tr>
<td>Works</td>
<td>25</td>
</tr>
<tr>
<td>Rests (no motor activity, indifferent internal sensory flux)</td>
<td>3</td>
</tr>
<tr>
<td>Talks</td>
<td>5</td>
</tr>
<tr>
<td>Attends (indifferent motor activity, involved sensory activity)</td>
<td>4</td>
</tr>
<tr>
<td>Motor practices (runs, walks, plays, etc.)</td>
<td>4</td>
</tr>
<tr>
<td>Angers</td>
<td>1</td>
</tr>
<tr>
<td>Escapes (negligible motor and sensory input)</td>
<td>1</td>
</tr>
<tr>
<td>“Anxious-es”</td>
<td>2</td>
</tr>
<tr>
<td>“Euphorics”</td>
<td>2</td>
</tr>
<tr>
<td>Laughs</td>
<td>1</td>
</tr>
<tr>
<td>Aggresses</td>
<td>1</td>
</tr>
<tr>
<td>Fears, fights, fights</td>
<td>1</td>
</tr>
<tr>
<td>Interpersonal attends (body, verbal or sensory contact)</td>
<td>8</td>
</tr>
<tr>
<td>Envies</td>
<td>1</td>
</tr>
<tr>
<td>Greeds</td>
<td>1</td>
</tr>
</tbody>
</table>
| **Total**         | **100 ± 20% of**
|                   | **time involvement** |
program structure. In any case, the program structure which best suits the environment information will command. Compartments in which the environment information does not fit will be “switched off” or rejected temporarily. As it seems to be not only a question of the synchronization of the functions of the total system but also of a spatio-temporal structuring in relation to the environment, the term harmonization could be justified. By using the example of a Schubert symphony in conjunction with our musical metaphor, it is possible to more fully examine the concept of harmony vis-à-vis brain function and organization.

5. Harmonization in an orchestra

The comparison of how an astrocyte forms a compartment via its processes with a certain number of

Table 2
An example of musical harmonization in Schubert Symphony No. 8, “unfinished,” D. 759
neurons to the playing of a music instrument has already been proposed. Now we would like to try to demonstrate how a composer organizes the various instruments of an orchestra in order to obtain harmony. Table 2 shows an example from Schubert's Symphony No. 8 (1959). On the left is a list of the diverse instruments. Every instrument corresponds to one compartment, however, every type of instrument can join with others to form a group in the sense of a larger compartment. Such as in the brain, every group of instruments is qualitatively independent in its operation ability and must be regarded individually. We have chosen 12 measures of the symphony (measure 93–104) in order to demonstrate the principle of harmonization. This table or score can be read either horizontally or orthogonally. The whole of music is thought to be divided into three domains: melody, harmony, and rhythm. Melody is opposed to harmony in referring to successive rather than simultaneous sounds, it is also opposed to rhythm in referring to pitch rather than duration. The orthogonal perspective of a score corresponds, therefore, to the harmonic structure, the horizontal development, however, acts in a melodic way.

This example of musical harmonization can be described and interpreted in the following way: the bass (A) gives the fundamental tone. The viola plays an accompanimental figure (B) which always precedes or parallels entrance of the main theme or head motive (C). In the second, vertical row on the left, the viola I then assumes the main theme (orthogonally accompanied by the bass and the viola). In the following measures, various instruments assume alone or in groups the melody. Within the theme emerge frequently rhythmic and/or melodic aspects of the main theme (c1), as well as cadential movements (D) and cadences (E).

Although the whole symphony is based on a harmonic structure which was created in the brain of the composer, there is no given rule as to when an instrument will assume the melody. This decision rests with the composer alone, however, individual properties of instruments (timbre, range, technique, etc.) allow for these instruments to be more commonly used as melodic carriers. In relation to the brain, the theme which dominates a symphonic movement at a particular moment could be seen as the mode of behavior. As various instruments are differently suitable for the intonation of a theme, also the operation quality of the compartments is differently suitable for the single modes of behavior. Every instrument would principally be able to play the main theme, however, to produce a certain aural or emotional effect at a particular moment, the composer selects the best suitable instrument group for the melody (dependent upon environment). Therefore, the principle of potential command is also valid in the symphony. The composer designates rests or he pauses all instruments which are not suitable for the intonation of a theme like trumpet, trombone, and timpani (Table 2). Here, the orchestration of only one theme is dissected. The change of theme or the introduction of a new theme in a musical movement corresponds to a new mode of behavior for which an autonomous structure of compartmental composition is characteristic.

As in a musical movement containing one theme, numerous variations of one theme can exist which may also be observed in the modes of behavior, for example, in human dialogue. The main theme of this mode of behavior is the verbal communication with the discussion partner. The way we communicate and how we listen is very individual. We smile or we look seriously, we gesture with the hand, we jump up or we sit listening curiously, even the voice can change, etc. Compartments which are responsible for sensory-motor integration command the numerous variations of conversation by “turning on” the appropriate operational qualities and “switching off” the inappropriate operational qualities (Mitterauer, 2001c).

Not only in music do harmonies develop from the interplay of orthogonal structures and horizontal melodic movement, but this principle of harmonization may also work in the brain. Harmonization in the sense of an integrative behavior of the entire organism may result from the orthogonal pattern of connectivity of the reticular formation selecting information of the horizontal systems (cerebral cortex) which process environment information. If one supposes that the reticular formation is connected with these “horizontal” compartments, it could then be possible that the reticular formation can structure the elementary network for a distinct mode of behavior by turning off certain axons or dendrites leading to the compartments which is comparable to a hardware structure. Simultaneously, the perception systems compute the intended mode of behavior. If not, either the mode of behavior or the environment must be altered.

How the numerous compartments of the brain harmonize in accordance with behavior and environment can be easily imagined with another musical paradigm: improvisation in a jazz ensemble. Members of a classical orchestra have a strictly defined “environment” as they perform directly from the notes on the page. The jazz ensemble, however, plays within a defined harmonic structure in which every musician can improvise, develop, and vary themes. Also here, there are themes which can be played best by one instrument while other instruments play accompaniment (supporting harmony) or rest until their turn to improvise. Every musician listens to what the others play in that moment and participate in the harmonization or rest. Each musician can in this way synchronize his musical or harmonic intention with the “environment” of the rest of the ensemble by playing with them (accompanimental harmony), by improvising a solo (soloists taking turns
consecutively) or by resting (for example, those members of an instrument group not playing the solo).

This short list of musical building blocks has begun with simple pulses and their organization. With the introduction of the phrase and period, however, and the diversion to motive and what will develop into a larger discussion about theme, we are confronted with the aspect of sound. Meter and its subsequent manifestations is not the sole synchronization factor in music. Sound is a complex tissue which in music divides into two, interdependent systems: melody and harmony. The parallel of this construction in brain theory are the neuronal and glial systems, respectively, and upon closer inspection similarities in musical construction and brain function may become readily apparent.

6. Future prospects

Harmonization is a very complex procedure which depends upon the intentional state of the brain as well as the environmental situation at a given moment in time. Supposing that the variables which constitute all brain functions are not conceivable, one cannot compute the combinatorics of all possible operations of the brain. Therefore, brain sciences are confronted with a metaphysical enigma. This may be valid not only on the cellular level but also for the genome.

As important as the neurobiological results concerning the synchronizations of neurons might be (Eckhorn, Bauer, & Jordan, 1988; Gray & Singer, 1987; Schechter, 1996; Wehr & Laurent, 1996), until now they only indicate that the brain has the ability of neuronal synchronization and that neuronal oscillations in the 30–100 Hz range play a role in perception and might underlie consciousness or visual awareness (Crick & Koch, 1995). Fries, Reynolds, Rosie, and Desimone (2001) demonstrated that selective visual attention has a modulatory effect on oscillatory neuronal synchronization. Galarreta and Hestrin (2001) report results suggesting that networks of fast-spiking inhibitory neurons may play a role in the detection and promotion of synchronous activity within the neocortex. But many unsolved problems remain. For instance, no one yet knows if the rest of the brain is paying attention to the precisely orchestrated performance observed in neocortical areas.

If the brain model suggested here were to be used as a base for experimentation, it would be necessary to know in which mode of behavior the animal is at a given moment within the experiment. Even when we experiment with animals that are awake, we hardly know whether the animal is in a state of fear, for example Munk, Roelfsema, and Koenig (1996) have shown in experiments with lightly anaesthetized cats that the mesencephalic reticular formation can dynamically influence the way in which responses are selected for integration at the higher processing states. However, the interpretation of these experiments is not based on a theory of the reticular formation, such as the concept of the modes of behavior.

In light of the glial-boundary-setting theory (Mitterauer, 1998), the discovery of stimulus related synchronous oscillations over disparate cortical locations can be accounted for by the following mechanisms (Mitterauer et al., 1996):

1. Glial cells, particularly astrocytes, modulate the “efficacy of synaptic transmission” and, therefore, the amplitude and phase of the postsynaptic potentials. Thus, glial cells modulate the phase of the signals received and/or emitted by the neurons.

2. Glia could influence neural signal processing by causing delays via glial-neuronal circuits comprised of neuronal and glial elements.

3. Glia could affect the global threshold modulation in the region of active assemblies, by phase coupling or phase separation of the activity of the individual assemblies.

We should also consider the spatial architecture of the brain (Golledge, Hilgetag, & Tovee, 1996) as well as the topological organization of the perception fields, such as the retinotopy (Arbib, 1972). If one supposes that the brain consists of many compartments with qualitatively different operational domains, synchronization may also be based on a spatial construction process which generates the structure for a specific behavior of the whole organism. This operation is deemed harmonization. As we have already tried to demonstrate, the harmonization in an orchestra is a highly dynamic and complex process. Supposing that a kind of musical harmonization is working in our brains, the identity of a human being is not a constant but probably an ever changing dimension. Even clones become individuals as soon as they interact with the environment. In the language of music, one also could say: subjectivity is a harmonic structure which permanently alters its themes. This harmonic structure is hidden yet determines our behavior. If we speak of the I, the Thou, of cognition or volition, all these terms are only variations of the hidden themes of subjectivity which can never be directly identified (Guenther, 1976).

A real alternative for a better understanding of the functions of biological brains could be robotics. Promising technical mechanisms already exist which attempt to embody biological systems (Arkin, 1999; Nolfi & Floreano, 2000). Unfortunately, until now only the neuronal system of the brain has been the focus of interest. As Haydon (2001) puts it, it is no longer appropriate to consider solely neuron–neuron connections; we also need to develop a view of the intricate web of active connections among glial cells and between glia and neurons. Without such a view, it might be impossible to
decode the language of the brain. As a first technical step in the implementation of glial–neuronal compartments, we have simulated a “clocked perception system” (Mitterauer, 2001b). If we have built a chip then it may be used as a glial–neuronal compartment for the construction of a robotic brain. As in biological brains, one could produce further chips with different operation qualities in order to compose step-by-step complex robotic brains.

Biological brains are capable of composing their own multi-compartmental structure or architecture. Hence, the title of this paper “self-composing brain” may be appropriate. While harmonization refers to the synchronization of diverse systems, it seems duly suitable to select the brain of a composer and the structure of musical works as a paradigm both on a metaphorical level and not least, as an explanatory model towards a glial–neuronal brain theory.

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Appendix A. Definitions of pertinent musical terms

The following abbreviated lexicon has been drawn from more complete entries found in The New Harvard Dictionary of Music (Randel, 1986):

**Meter:** the pattern in which a steady succession of rhythmic pulses is organized.

**Measure:** one complete pattern or its equivalent in length.

**Beat:** a metrical pulse.

**Rhythm:** a pattern of movement in time; used in parallel with the terms melody and harmony and covers all aspects of musical movement as ordered in time and is therefore opposed to aspects of sound conceived as pitch (whether singly or in simultaneous combination) and timbre (tone color); more specifically, a patterned configuration of attacks.

**Melody:** a coherent succession of pitches. The whole of music is thought to be divided into three domains: melody, harmony, and rhythm.

**Harmony:** the relationship of tones considered as they sound simultaneously and the way these relationships are organized in time; also, any particular collection of pitches sounded simultaneously, termed a chord.

**Phrase:** a unit of musical syntax. It is the product, in varying degrees, of melody, harmony, and rhythm and concludes in a moment of tonal stability.

**Motive:** a melodic fragment; usually forms part of a subject, theme or melody and is recognizable in its own right.

**Period:** a complete musical utterance defined in tonal music by arrival at a cadence on some harmony that does not require further resolution.

**Cadence:** a melodic or harmonic configuration that creates a sense of repose or resolution; cadences thus most often mark the end of a phrase, period or complete composition.

**Theme:** a fixed musical idea that forms the basis for a composition or a large section/movement of a composition.

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