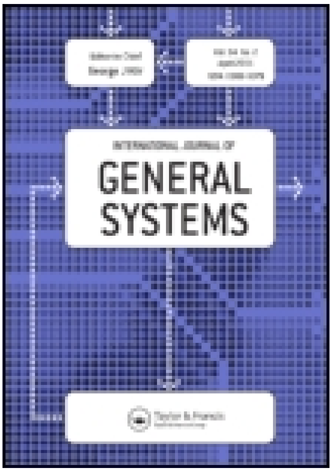

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Synaptic view of eukaryotic cell

František Baluška[a] & Stefano Mancuso[b]
[a] IZMB, University of Bonn, Bonn, Germany
[b] LINV, University of Florence, Sesto Fiorentino, Italy
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Synaptic view of eukaryotic cell

František Baluška[a]* and Stefano Mancuso[b]

[a]*IZMB, University of Bonn, Bonn, Germany;* [b]*LINV, University of Florence, Sesto Fiorentino, Italy*

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Synapses are stable adhesive domains between two neighbouring cells of the multicellular organisms which serve for cell–cell communication as well as for information processing and storing. The synaptic concept was developed over more than 100 years specifically for neuronal cell–cell communication. In the last ten years, this concept was adapted to embrace other cell–cell communication phenomena. Here, we focus on the recently emerged phagocytic synapse and propose new endosymbiotic synapses and "intracellular organellar synapses". All these synapses of eukaryotic cells are in a good position to explain the high capacity of eukaryotic cells for integration of diverse signalling inputs into coherent cellular behaviour.

Keywords: eukraryotic cell; communication; organelles; signallig; symbiosis; synapses

Synaptic concept

In multicellular organisms, cell–cell communication is of central importance for development, homeostasis and growth coordination. Often, cells can achieve this via long-distance transport of diverse soluble signals as well as secreted peptides and proteins. However, some cells are specialized for more effective cell–cell communication requiring specialized adhesion domains known as synapses. To achieve effective cell–cell communication, cells assemble stable adhesive synapses. The word synapse is derived from Greek (*syn* – with, *aptein* – to join). Neural and immunological synaptic relations are well established (Dustin and Colman 2002). Dustin and Colman elaborated requirements which a prototypic synapse needs to meet. First of all, two individual cells establish parallel adhesion contact in which adhesive molecules and molecular clamps guarantee structural stability for this adhesive synaptic contact. Next, membranes of these synaptic domain exchange signalling molecules, preferentially via secretory activities. For instance, the classical neurochemical synapse is characterized by two plasma membranes with a synaptic cleft in between (Dustin and Colman 2002). Recent advances in cell biology illuminated other situations in which synaptic concept is appealing to solve some paradoxes emerging from recent studies on cell–cell communication in plants (Figure 1), as well as studies on phagocytosis, endosymbiosis and organellar interactions in eukaryotic cells (Figure 2). For the overview of synaptic types and their properties, see also Yamada and Nelson (2007) and the Box 1.

Supracellular synapses

Neuronal, epithelial, immunological and virological synapses

The synaptic concept is an extremely useful paradigm for studies on cell–cell communication. In neuronal cell biology, besides chemical there are also electrical synapses. These cell–cell

*Corresponding author. Email: baluska@uni-bonn.de

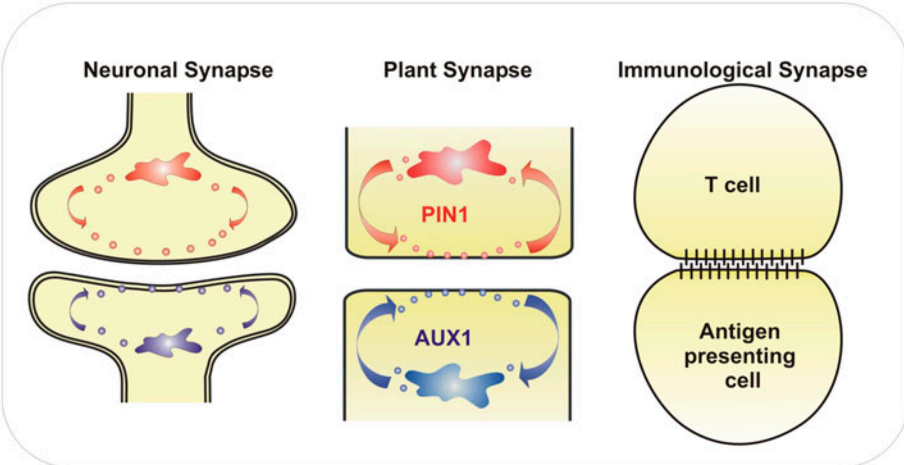

Figure 1. Supracellular synapses between neurons, root stele cells as well as between T cells – antigen presenting cells (APCs) and virus-infected cells (DC or T-cell) and virus non-infected cell (T-cell). All synapses are inherently asymmetric. In neurons and plant cells, this is expressed by different proteins recycling at both synaptic sides. In the case of immunological and virological synapses, this asymmetry is given by two different cells communicating together. Another difference is that while the neural and plant synapses are stable, although dynamic, structures; the immunological and virological synapses are only temporal structures.

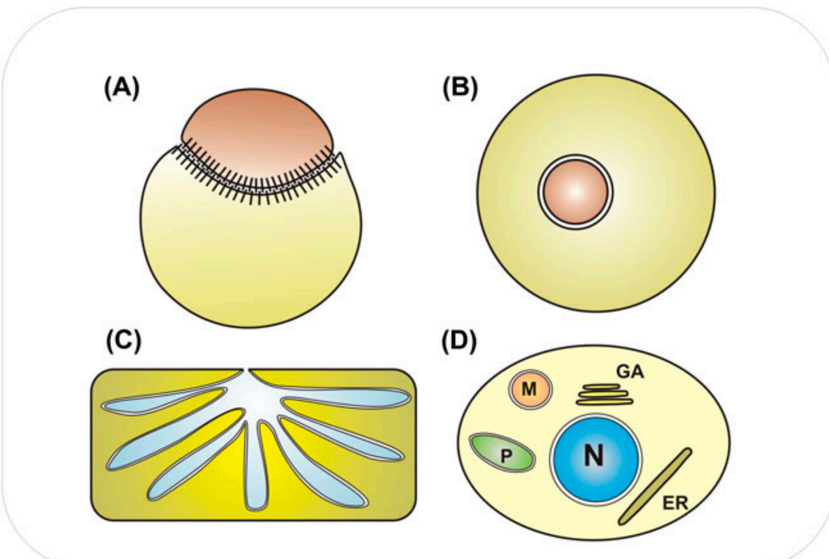

Figure 2. For basic types of intracellular synapses: phagocytic (A) and endosymbiotic (B), symbiotic (C) and organellar (D) synapses. P – plastids, M – mitochondria, N – nucleus, GA – Golgi apparatus, ER – endoplasmic reticulum.

Box 1. Diverse types of synapses: structural organization, adhesive and signalling proteins (for details and references, see the text).

Neuronal synapses:
1. Synaptic cleft: 10–30 nm
2. Structural proteins: cadherins, integrins, neurexin–neuroligin, actin cytoskeleton
3. Signalling proteins: receptors, kinases, phosphatases, Rho GTPases

Immunological synapses:
1. Synaptic cleft: 10–30 nm
2. Structural proteins: integrins, receptors, ICAMs, actin cytoskeleton
3. Signalling proteins: receptors, Rho GTPases

Virological synapses:
1. Synaptic cleft: 10–30 nm
2. Structural proteins: lectins, receptors, ICAMs, actin cytoskeleton
3. Signalling proteins: receptors, adhesive proteins

Plant synapses:
1. Synaptic cleft: 50–200 nm
2. Structural proteins: pectins, actin cytoskeleton, WAK1
3. Signalling proteins: receptors, kinases, phosphatases, Rho GTPases

Phagocytic synapses:
1. Synaptic cleft: 10–30 nm
2. Structural proteins: integrins, receptors
3. Signalling proteins: receptors, kinases, phosphatases, calreticulin

Organellar synapses:
1. Synaptic cleft: 10–100 nm
2. Structural proteins: SUN, KASH, STIM1, Orai, Junctiophilin
3. Signalling proteins: receptors, kinases, phosphatases

Intraorganellar synapses:
1. Synaptic cleft: 10–20 nm
2. Structural proteins: MINOS complex, OPA1, PMI, CURT1, MORN-motif proteins
3. Signalling proteins: ???

channels, based on gap junctions, represent electrical synapses (Connors and Long 2004) which allow direct electrical coupling. Similarly in plants, cell–cell channels known as plasmodesmata allow direct electrical coupling of plant cells (Spanswick 1972). Moreover, epithelial cells also assemble tight cell–cell adhesion domains which show several synaptic features both in animal (Tang 2006; Yamada and Nelson 2007) and plant tissues (Alassimone et al. 2012; Baluška 2012a; Martinka et al. 2012; Geldner 2013).

The synaptic concept was generated and has been used almost exclusively, until the last years, for neuronal communication in brains. However, progress in immunological studies necessitated to introduce this concept for communication between T-cells and antigen-presenting cells (Norcross 1984). The synaptic concept proved to be fruitful in the field of immunological research. Immunological synapses cover not only communicative interactions between T cells and antigen-presenting cells, but were extended to variety of immunological situations including directed secretion of lytic granules, cytokines and other signalling molecules (Dustin 2005, 2012; Čemerski and Shaw 2006; Saito and Yokosuka 2006; Stinchcombe et al. 2006; Krummel and Cahalan 2010; Huse 2012' Angus and Griffiths 2013; Ritter, Angus, and Griffiths 2013; Soares, Lasserre, and Alcover 2013; Martín-Cófreces, Baixauli, and Sánchez-Madrid 2014).

The concept of immunological synapses has been extended to include virological synapses which are induced by some viruses in order to facilitate their own cell–cell transmission (Piguet and Sattentau 2004). Viruses hijack the secretory apparatus of infected cells to assemble new synaptic contacts with the target cells and then use this contact for their cell–cell spread. Interestingly, virological synapses exist in both animal and plant cells (Piguet and Sattentau 2004; Wei et al. 2006). There are even cases known, where a plant virus switches over to an insect by inducing cell–cell contacts to the animal host cells (Wei et al. 2006). Virological synapses also form cell–cell channels, known as tunnelling nanotubes (TNTs) which are known to transmit endosomes from cell-to-cell (Rustom et al. 2004). These TNTs resemble plant-specific electrical synapses known as plasmodesmata (Spanswick 1972).

Quantal release of lysosomal radicals is relevant for another version of immunological synapses, the so-called phagocytic synapse (Tsai and Discher 2008; Goodridge et al. 2011; Bordon 2011; Kerrigan and Brown 2011), which is discussed below. Interestingly, phagosomes can be secreted out of cells to allow quantal release of free radicals (Di et al. 2002). We will discuss all these new aspects of the synaptic concept and try to unify all these diverse systems from signalling and information-integrating point of view. Our speculative proposal is that synaptic concept is important for our better understanding of the eukaryotic cell which is in fact a multicellular assembly due to several endosymbiotic events which paved the way for the evolution of these very complex cells. This synaptic nature of eukaryotic cell explains why the eukaryotic cells have their inherent drive to form multicellular organisms integrated via supracellular synapses.

Plant synapses

In plant roots, cell–cell adhesion domains are assembled which resemble neuronal synapses in generating stable cell–cell adhesive domains for extensive and vesicle recycling secreting neurotransmitter-like auxin (Baluška, Samaj, and Menzel 2003; Baluška, Volkmann, and Menzel 2005; Schlicht et al. 2006; Baluška et al. 2008, 2010; Baluška 2012b). Unique plant-specific feature of these plant synapses is large abundance of direct cell–cell channels, some sort of electrical synapses, which actively exclude free transcellular passage of auxin (Baluška, Samaj, and Menzel 2003; Baluška, Volkmann, and Menzel 2005; Schlicht et al. 2006; Baluška et al. 2008, 2010; Baluška 2012b). These cell–cell channels of plant cells, known as plasmodesmata, are known to support electrical signals (Spanswick 1972) but our knowledge on this aspect of plasmodesmata is very limited. As we are focusing on chemical synapses, we will not go into any details in this respect.

Currently, new information is emerging, which is adding further support to the assumption that synaptic cell–cell communication is a regular phenomenon in plants. Embracing the synaptic concept in plant cell biology might turn out to allow breakthrough advances soon. New data, which had remained unexplained on the basis of the traditional concepts, begin to fall into place. For instance, it is well known that inhibitors of vesicular secretion, such as monensin and brefeldin A, inhibit auxin transport within minutes of application (Wilkinson and Morris 1994; Delbarre, Muller, and Guern 1998; Mancuso et al. 2005). This does not support the classical version of the chemiosmotic concept, which considers that auxin transporters are acting across the plasma membrane (Schlicht et al. 2006; Baluška 2012b). On the other hand, the classical inhibitors of the polar auxin transport in plants, such as NPA and TIBA, emerge to act rather as inhibitors of endocytic vesicle recycling and trafficking.

These data, however, fit well the synaptic concept in which auxin is secreted across a gap between two opposing plasma membranes in a neurotransmitter-like mode (Baluška, Samaj, and Menzel 2003; Baluška, Volkmann, and Menzel 2005; Mancuso et al. 2005; Schlicht et al. 2006; Baluška et al. 2008, 2010; Baluška 2012b; Baluška and Mancuso 2013; Figure 1). Auxin-accumulating and secreting vesicles behave as synaptic vesicles which would perform repeated cycles of auxin exocytosis and refilling. Besides ABP1, PINs at the plasma membrane might act as the long-sought auxin receptors for extracellular auxin inducing electrical responses in plant cells (Baluška 2012b). Such 'transceptors' would allow integration of synaptic transport with signal transduction pathways. Interestingly in this respect, exogenous auxin inhibits endocytosis of PINs (Paciorek et al. 2005), allowing feedback control between the synaptic auxin flux, synaptic activities and auxin signalling. Importantly, auxin flux across plant synapses impinges also on the synapse–nucleus intracellular signalling via protein Brevis Radix (Scacchi et al. 2009), which controls the transition zone (command centre *akin* Darwin's plant brain, Baluška et al. 2009; Baluška and Mancuso 2013) and protophloem development (Scacchi et al. 2010; Depuydt and Hardtke 2011; Depuydt et al. 2013).

Similarities between the neuronal, immunological, virological, epithelial and plant synapses suggest that multicellularity emerged via synaptic cell–cell communication, under pressure of numerous viral, bacterial and fungal infections (Baluška 2009; Baluška and Mancuso 2013), and that this synaptic nature also allow multicellular organisms to act as coordinated units apparently enjoying their agency due to their sense of the *synaptic self*, as proposed for the human brains (LeDoux 2002). Moreover, this synaptic view of multicellular organisms also allow better understanding of neuronal-like nature of plant tissues (Brenner et al. 2006; Felle, and Zimmermann 2007; Schapire et al. 2008; Masi et al. 2009; Szechyńska-Hebda et al. 2010; Karpiński and Szechyńska-Hebda 2010; Michard et al. 2011; Pelagio-Flores et al. 2011; Marder 2012; Ali et al. 2013; Mousavi et al. 2013; Christmann and Grill 2013) as well as of non-brain animal tissues (Skerry and Genever 2001; Julio-Pieper et al. 2011).

Intracellular synapses

Two closely apposed membranes communicating extensively are typical for phagocytosis in eukaryotic cells. This phenomenon fostered the introduction of phagocytic synapse (Tsai and Discher 2008; Goodridge et al. 2011; Bordon 2011; Kerrigan and Brown 2011) as another new member (Figure 2) of the expanding synaptic family which is discussed below. Eukaryotic cells are well known to contain organelles having endosymbiotic origin (Dyall, Brown, and Johnson 2004), which were internalized into ancient host cells via phagocytosis-like process. As these 'cells within cells' retained both the symbiont and host membranes, their double membranes can be proposed to represent the vestige of transformed phagocytic-like synapse, now acting as an organellar synapse.

Phagocytic and endosymbiotic synapses: from battlefield to marketplace

Signalling across the phagocytic synapse is complex (Tsai and Discher 2008; Goodridge et al. 2011; Bordon 2011; Kerrigan and Brown 2011) and resembles signalling across the immunological synapse (Dustin 2005, 2012; Čemerski and Shaw 2006; Saito and Yokosuka 2006; Stinchcombe et al. 2006; Krummel and Cahalan 2010; Huse 2012; Angus and Griffiths 2013; Ritter, Angus, and Griffiths 2013; Soares et al. 2013; Martín-Cófreces, Baixauli, and Sánchez-Madrid 2014; Box 1). In some situations, internalized pathogens affect the signalling across the phagocytic synapses, allowing them to manipulate the composition of the host-derived membrane of the phagosome in such a way that they prevent their digestion.

For instance, *Mycobacterium tuberculosis* manipulates phagosomal maturation via Rab14, maintaining its early endosomal characteristics and avoiding lysosomal degradative processes (Kyei et al. 2006).

If the signalling across the phagocytic synapse is balanced from both partners, this results into endosymbiotic interactions which, in ancient times, allowed eukaryotic cells to generate their organelles. Nice example of this scenario is the algal symbiont of the freshwater polyp *Hydra* which can inhibit the fusion of phagosomes with lysosomes (Hohman, McNeil, and Muscatine 1982). This indicates that communication across phagocytic synapses determines, if the prey will be 'eaten' or if it can survive in the new subcellular niche as endosymbiont. In more recent papers, active retention of the early endosome marker Rab5, and exclusion of the late endosome markers Rab7 and Rab11, was elucidated as part of molecular mechanisms allowing switch from the phagocytic into the symbiotic synaptic communication (Chen et al. 2004, 2005). Besides Rab5, Rab4 was also found to be relevant for transformation of phagocytois synapse into symbiotic synapse in the case of the Symbiodinium symbiosome in the host cells of the sea anemone *Aiptasia pulchella* (Hong et al. 2009).

Similar transformation of pathogenic/phagocytic synapse into symbiotic synapse is useful for plant cells too (Parniske 2000; Oldroyd, Harrison, and Paszkowski 2009; Ivanov, Fedorova, and Bisseling 2010). For example, bacteria of genus *Rhizobia* enter plant roots of genus *Fabaceae* via so-called infection thread which is a transcellular tube generated via inverted tip growth induced by bacteria enclosed via plant plasma membrane and cell wall (Brewin 2004). Root inner cortex cells internalize *Rhizobia* bacteria via a unique process which is resembles phagocytosis (Brewin 2004; Baluška et al. 2006). Bacteria are enclosed by fluidized cell wall (Brewin 2004) and internalized into root-derived nodule cells in the form of symbiosomes enclosed by synaptic double membrane (Cheon et al. 1993; Verma and Hong 1996; Brewin 2004). More dramatic example of the endosymbiotic synapse in plants is the membrane interface between host root cells and mycorrhiza fungal hyphae (for reviews see Genre and Bonfante 2005; Harrison 2005; Hause and Fester 2005; Lima et al. 2009). Similarly as in the animal symbiotic synapses, plant symbiotic synapses are also characterized by balance of interests of symbiotic partners (Ercolin and Reinhardt 2011; Kiers et al. 2011; Selosse and Rousset 2011). In the case of plant root/ arbuscular fungal symbiosis, large areas of plant–fungal synaptic double membranes extend throughout the root inner cortex, resembling tip-growing infection threads of *Rhizobia*. Interestingly, there are similar signalling aspects, using the same signalling molecules, in the bacteria–plant and fungal–plant symbiotic synapses (Box 1). In order to build a composite plant/fungal cell, the partners need to reach compatibility via balanced synaptic communication of both partners (Genre and Bonfante 2005; Harrison 2005; Hause and Fester 2005; Lima et al. 2009), similarly as it was in the case of above described endosymbiotic algae.

Organellar synapses

As discussed in the preceding section, eukaryotic endosymbiotic organelles are enclosed by two closely apposed membranes which extensively communicate together. As eukaryotic cells represent *cells within cells* (Baluška, Volkmann, and Barlow 2004a, 2004b), these organellar double membranes can be considered for symbiotic synapses. In the case of plastids, vesicular trafficking targets the outer membrane of plastid envelope (Villarejo et al. 2005; Millar, Whelan, and Small 2006; Nanjo et al. 2006). Thus, one can further extend the synaptic concept to embrace organellar synapses. Besides the classical endosymbiotic organelles, nuclei are also discussed as vestiges of ancient endosymbiotic events (Baluška, Volkmann, and Barlow 1997; Dolan et al. 2002; Margulis et al. 2006). Interestingly in this respect, nuclei are equipped with specific nucleoskeleton which differs significantly from the cytoskeleton (Pederson 2000; Nickerson 2001). Special proteins have been characterized which span the inter-synaptic space of the nuclear envelope (*nuclear synapse*) and organize nuclear architecture (Tzur, Wilson, and Gruenbaum 2006; Starr and Fridolfsson 2010; Rothballer and Kutay 2013; Tapley and Starr 2013; Zhou and Meier 2013). As the nuclear envelope (synapse) is continuous with ER, it might be that this is a reduced vestige of an ancient endosymbiont too (Figure 3). In fact, the ER evolved together with the nucleus (Soltys, Falah, and Gupta 1996) and was proposed to represent a '*cell within a cell*' (Berridge 1998). In this scenario, both the nuclear envelope and ER represent synaptic vestiges of the primary endosymbiotic events which generated modern nuclei and ER complex. Whereas the nuclear envelope represents host–guest membranes, as with all other endosymbiotic organelles, the ER membranes were formed from two host membranes (Figure 1). The ER membranes are closely apposed by still unknown structural proteins, although first players are already emerging. They serve not only well-known secretory functions but also some key signalling roles with calcium as the most prominent and best studied signal mediator (Berridge 1998). ER networks permeate the whole eukaryotic cell and accomplish important functions in cellular signal computation and integration (for reviews see e.g. Chen et al. 2012; Goyal and Blackstone 2013).

ER networks give rise to Golgi apparatus (GA), which is organized typically in form of stacked cisternae of closely apposed membranes, resembling structurally synaptic contacts. However, simple organisms like *Giardia lamblia* (Stefanic et al. 2006, 2009) or yeast cells (Rida et al. 2006) contain only one GA cisterna suggesting that the putative GA synapse is not essential for secretory functions, as widely believed, but rather for some signalling functions. This attractive scenario is supported by genetic evidence from fungal cells (Rida et al. 2006). For the lack of space and solid data, we will not go deeper here into putative GA synapse. But this type of conspicuous intracellular organellar synapse, when up to seven GA cisternae can be apposed, will be in the focus of future studies.

Besides organellar synapses, outer membranes of organelles often show temporary contacts with other organelles forming interorganellar synapses (Figure 1). These temporary synapses resemble immunological synapses in many aspects. Here, we can mention close connections between the plasma membrane and the cortical ER in plants (Hepler et al. 1990).

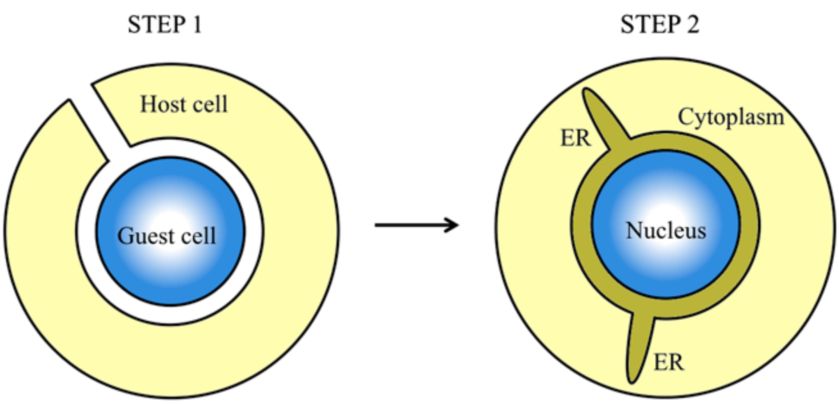

Figure 3. Hypothetical scenario for a symbiotic origin of the ER membranes and nuclear envelope via the primary endosymbiotic event generating the nucleus. Invaginating-limiting membranes of the ancient host cells were first forming a channel linking the ancient guest cells with extracellular space (step 1). Later, this channel transformed into the ER system (step 2).

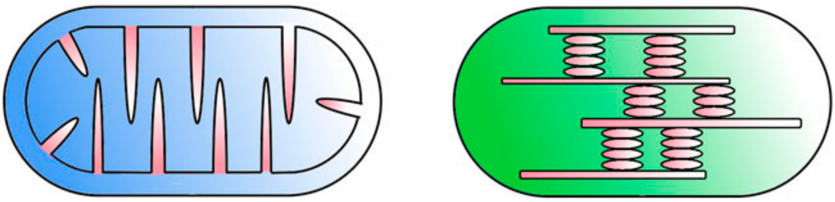

Figure 4. Intraorganellar synapses in mitochondria and chloroplasts. Tubular invaginations of the inner mitochondrial membrane (left) and stacked thylakoid membranes (right) allow synaptic-like close apposition of two membranes allowing effective respiration and photosynthesis.

In animal cells, STIM1-Orai is ER–PM synaptic-like complex regulating store-operated calcium transport at the plasma membrane (Luik et al. 2006; Wu et al. 2000; Fahrner et al. 2009, 2013). Junctophilins were discovered as junctional membrane proteins which keep closely apposed membranes of this synaptic ER–PM complex together (Moriguchi et al. 2006; Takeshima et al. 2000). Importantly, these proteins contain the MORN-motif repeat too and have essential roles for both membrane excitability and for synaptic activities of neurons (Moriguchi et al. 2006; Kakizawa et al. 2007).

Moreover, there are intimate contacts between ER and other organelles such as mitochondria (Csordás et al. 2010; Rowland and Voeltz 2012; Matsuzaki et al. 2013), peroxisomes (Titorenko and Mullen 2006; Titorenko and Rachubinski 2009) and lipid bodies (Robenek et al. 2006; Sturley and Hussain 2012). But other organelles are also known to enter into similar synaptic-like interactions (for review see Levine and Loewen 2006). For example, peroxisomes with membranes of lipid bodies (Binns et al. 2006) in animal cells; and plastids with the plasma membrane (Kwok and Hanson 2004; Huang et al. 2006), ER membranes (Wang and Benning 2012) and the outer membrane of the nuclear envelope (Kwok and Hanson 2004). Although most of these contacts still do not fulfil the synaptic criteria, this is mostly because of our lack of data and understanding. Potential interorganellar synapse is composed of the outer plastid membrane – plasma membrane domain mediated by G-protein GPA localized to the plasma membrane and THYLAKOID FORMATION1 protein localized to the outer membrane of plastids (Huang et al. 2006). Another striking example of the plastid–plasma membrane synapse is the eyespot apparatus of green algae, in which the plasma membrane and two plastid envelope membranes, including thylakoid membranes, are closely apposed (see Figure 1(B) in Schmidt et al. 2006). Proteomic analysis of the eyespot apparatus revealed, besides several signalling molecules like protein kinases, phosphatases, calcium-binding proteins, and photoreceptors, also a synaptic MORN-motif repeat protein and adhesion protein containing fascilin I domains (Schmidt et al. 2006). Interestingly, excitation of this eyespot synaptic-like organelle induces rapid electrical responses leading to changes in flagellar beating and phototaxis (Dieckmann 2003; Schmidt et al. 2006; Kreimer 2009; Trippens et al. 2012).

The next emerging organellar synapse is so-called ‘acrosomal synapse’ characterized in mammalian spermartozoa cells, allowing them to fertilize the receptive oocytes via acrosome reaction (Redecker et al. 2003; Zitranski et al. 2010).

Intraorganellar synapses

The next step in the expanding synaptic concept might be intraorganellar synapses obvious in both endosymbiotic organelles of eukaryotic cells, mitochondria and plastids. In mitochondria, several proteins have been characterized recently, which organize close synapse-like appositions of inner membrane invaginating into organellar lumen and organizing mitochondrial cristae (Frezza et al. 2006; Harner et al. 2011; Bohnert et al. 2012; van der Laan et al. 2012; Zerbes et al. 2012; Cogliati et al. 2013; Jans et al. 2013; Macchi et al. 2013). These synaptic-like mitochondrial membrane-appositions allow the assembly of proteinaceous complexes underlying the high mitochondrial respiratory efficiency. Close proximity of two membranes allows assembling of supercomplexes, leading to effective electron flux in mitochondrial electron transport chains (Zick, Rabl, and Reichert 2009; Lapuente-Brun et al. 2013). Similarly, chloroplasts which are active in photosynthesis are generating prominent stacks of thylakoid membranes organized also in the synaptic-like fashion (Vothknecht and Westhoff 2001; Mustardy and Garab 2003; Kim et al. 2005; Austin and Staehelin 2011; Daum and Kuhlbrandt 2011; Nevo et al. 2012; Armbruster et al. 2013). Importantly, these intraorganellar synapses have been invented already in the prokaryotic ancestors of these photosynthetic organelles of plant cells (Nevo et al. 2007; Liberton et al. 2011, 2013). Intriguingly, MORN-motif synaptic proteins were identified in the thylakoid membrane proteome (Peltier et al. 2004).

Intracellular synapses and the concept of 'conscious cell'

Intracellular synapses support the 'conscious cell' concept proposed by Lynn Margulis in 2001 (Margulis 2001). This concept provides explanation for the complex behaviour of eukaryotic cells in the face of a huge amount of information which they continuously monitor, receive, store and process for making adaptive decisions about their further states and activities (Margulis 2001). Importantly, although the single neuron represents the elementary unit for computation in the brain's integrative information processing; communication, memory storage and computation, all occur at the subcellular levels of neurons (London and Häusser 2005; Sidiropoulou, Pissadaki, and Poirazi 2006; Shemer et al. 2008; Hagenston and Bading 2011; Ashhad and Narayanan 2013; Bading 2013). Intracellular synapses increase the computational capabilities of the eukaryotic cell. One can consider the synaptic membranes for smart scaffolds which keep signalling complexes in the optimal topological distances from each other, in order to optimize information perception, processing and storing. All these increase the efficacy of subcellular and cellular computation. This feature is critical for computational and information processing properties of diverse types of synapses existing within any multicellular organisms, as well as within all eukaryotic cells. Intracellular synapses increase information processing and computational properties of more complex cells that are expected to have conscious experiences which should have profound consequences for the Cell Theory and cellular evolution. Similarly, as this has been proposed for the multicellular organisms above, the eukaryotic cells also seem to enjoy their 'self' agency via their synaptic integration and computation (Margulis 2001; Baluška, Volkmann, and Barlow 2004a, 2004b).

Conclusions

Synaptic contacts and communication appear to be widely used in biological signalling events. Two closely apposed membranes are extremely useful for scaffolding macromolecular signalling complexes which exchange biological information. We have documented several examples from animal as well as plant biology. The synaptic concept may even be applied at the subcellular level. Synaptic communication as widespread as it appears to occur may hold the 'key' for a full appreciation of the cell as an information processing unit and may also help to understand plants as neurobiological organisms (Baluška, Samaj, and Menzel 2003;

Baluška, Volkmann, and Menzel 2005; Brenner et al. 2006; Masi et al. 2009; Trewavas and Baluška 2011). Plant-specific version of neuronal type of synapse is inherently associated with numerous cell–cell channels, known as plasmodesmata, representing plant-specific type of electrical synapses. Interestingly, viruses manipulating host cells can induce synaptic cell–cell contacts, cell–cell channels as well as cell–cell fusions (Baluška 2009), implicating potential importance of viruses in the evolution of both eukaryotic cells and multicellular organisms (Ryan 2004; Villarreal 2005; Bell 2006). Future studies will unveil viral interventions into biological evolution towards higher complexity.

Notes on contributors

František Baluška is plant physiologist and cell biologist at the Rheinische Friedrich-Wilhelms-Universität Bonn, Germany. He does research on plant roots focusing especially on plant signaling and polarity, plant development, and root behavior.

Stefano Mancuso is a plant electrophysiologist and cell biologist at the University of Firenze, Italy. He is an expert in plant electrophysiology, doing research on plant signalling and communication.

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