Chapter 4

CELL SOCIAL BEHAVIOR IN PROKARYOTA AND EUKARYOTA

V. V. Isaeva

Institute of Ecology and Evolution, Moscow,
Institute of Marine Biology, Vladivostok, Russia

ABSTRACT

Prokaryota (Archaea and Bacteria) are capable of complex social interactions and dynamic adaptation to environmental changes. Due to coordinated cell movements, many bacteria can produce radial, spiral and fractal patterns of the colonies or "swarming" communities. Filamentous cyanobacteria form biofilms and mats, including strands, multi-arrayed aggregations and polygonal networks.

The capacity of bacterial cells for the communication, collective decisions and adaptive morphogenesis gave rise to write about the bacterial "wisdom" (Ben-Jacob, 1998; Ben-Jacob et al., 2004), "smart" cooperating cells (Ben-Jacob et al., 2012), and "intelligence" of a bacterial "swarm" (Ingham et al., 2012). Bacterial communications include cell-cell chemical signaling that provides a bacterial "quorum" involving coordinated transcription. Sociomicrobiology considers bacteria as social beings capable of "quorum sensing" and "altruism" in bacterial societies.

Eukaryota evolved from Prokaryota. During evolution, Eukaryota improved the ability of adaptive "intelligent" behavior (Albrecht-Buehler, 1985; Lipton, 2001) inherited from Prokaryota. A metazoan organism

strictly controls the self-renewal, differentiation, apoptosis, and behavior of its cells, suppressing cell individuality and promoting their "altruism." Nevertheless, a cell in a multicellular organism retains features of an individual being, as evidenced by experiments with dissociated cells *in vitro* displaying a coordinated behavior and generation of ordered morphological patterns.

It was shown that communities of the filamentous cyanobacteria, *Oscillatoria terebriformis* and *Microcoleus chthonoplastes* as well as some metazoan cells *in vitro* exhibit coordinated social behavior and form similar cell assemblies, for example, polygonal networks (Isaeva, Sumina & Sumin, in print). Thus, communities of both cyanobacterial, prokaryotic, and metazoan, eukaryotic cells, with their essential differences in biological mechanisms of cell motility and cell-cell interactions, are capable of social cell activity resulting in the ordered spatial structures.

INTRODUCTION

The cell is the essence of biology (Woese, 2002). Three major domains of the living world: Archaea, Bacteria and Eukarya (Eukaryota) are distinguished, and the first two domains are prokaryotic cells (Muller et al., 2010; Wassenaar, 2012). Ordered cell patterns are observed in representatives of both Prokaryota and Eukaryota. Certain archaea, in particular, two species of the new genus *Giganthauma*, may form long filaments, which in *G. karukerense* are associated with bacterial cells (Muller et al., 2010).

A new field of research, sociomicrobiology, emerges (Chandler & Greenberg, 2012), considering bacteria as social beings (Chandler & Greenberg, 2012), which manifest "altruism" in some bacterial communities (Refardt et al., 2013). A various spatial patterns of bacterial colonies is observed. Cell-cell communications, developed signaling systems, and coordinated behavior in formation of complex colonial patterns are recognized in bacteria (Brodsky, 2009). Dynamic adaptive patterns in communities of prokaryotic cells are considered as a manifestation of bacterial "wisdom" (Ben-Jacob, 1998; Ben-Jacob et al., 2004), "intelligence" (Ingham et al., 2012). The bacterial colony is a community of smart cooperating cells (Ben-Jacob et al., 2012).

In the evolution of both bacteria and eukaryotes, multicellularity has apparently evolved multiple times (Rainey & Kerr, 2012; Strassmann & Queller, 2012; Olsen et al., 2012). For example, filamentous cyanobacteria *Oscillatoria terebriformis* and *Microcoleus chthonoplastes* are multicellular.

Moreover, most bacterial populations are considered as multicellular organisms (Shapiro, 1988, 1998; Aguilar et al., 2007).

It is usually assumed that organelles of eukaryotic cells have endosymbiotic evolutionary origin. If the mitochondria evolved as a result of the symbiosis of proteobacteria and archaea, it unites prokaryotic domains, Archaea and Eubacteria, with the domain Eukarya (Wassenaar, 2012). Anyway, Eukaryota evolved from Prokaryota (Margulis, 1981; Gould, 2002; Wassenaar, 2012; Strassmann & Queller, 2012).

It was performed a comparative study of morphogenesis in communities of the filamentous cyanobacteria, *O. terebriformis* and *M. chthonoplastes* and in populations of some metazoan cells cultured *in vitro* (Isaeva et al., 2014, in print). For studies of self-organization *in vitro* of metazoan eukaryotic cells, chick embryo myogenic cells (Isaeva, 1980), coelomocytes of the starfish *Asterias amurensis*, hemocytes of the scallop *Mizuhopecten yessoensis* were used (Isaeva et al., 2008). It was shown that cyanobacterial communities as well as chick embryo myogenic cells, molluscan hemocytes and echinoderm coelomocytes *in vitro* exhibit coordinated social behavior and form morphologically similar cell assemblies, for example, polygonal networks. Thus, the communities of both cyanobacterial (Prokaryota) and metazoan (Eukaryota) cells, with their significant differences of biological mechanisms of cell motility and cell-cell interactions, are capable of social cell activity resulting in the ordered morphogenesis.

This review emphasizes mainly the comparison of cultured in laboratory cyanobacterial communities and *in vitro* cultures of the metazoan cells.

SOCIAL BEHAVIOR OF PROKARYOTIC CELLS

For a long time bacteria were regarded as single-cell living organisms that ensure their survival by adaptation to rapidly changing environmental conditions without communication. It is now accepted that bacteria are social creatures that can act together to exhibit a range of group activities. A recent revolution in our collective understanding of bacteria is that the vast majority of these organisms live in communities and lead interactive lives, forming associations with one another and with their living and nonliving environment (Anetzberger & Jung, 2010; Olsen et al., 2012). Prokaryota (Archaea and Bacteria) are capable of complex social interactions and dynamic adaptation to environmental changes. Microbiologists have discovered an unexpectedly high

degree of coordinated multi-cellular behaviors that have led to the perception of bacterial biofilms as "cities" of microorganisms (see Li & Tian, 2012).

The vast majority of microbes form biofilms: complex, differentiated aggregations, typically of multiple species, that thrive on nearly every surface (Li & Tian, 2012; Olsen et al., 2012). Bacteria living in communities display coordinated, synchronized behaviors. Social behaviors – broadly defined as actions with fitness consequences for both actor and recipient – enable microorganisms to build complex, interactive communities that often are associated with multicellular organisms (Olsen et al., 2012).

Coordinated multicellular behavior can be observed in a variety of situations, including development of *Escherichia coli* and *Bacillus subtilis* colonies, swarming by *Proteus* and *Serratia*, and spatially organized interspecific metabolic cooperation (Shapiro, 1998). Bacteria benefits from multicellular cooperation are cellular division of labor, more efficient proliferation, resources that cannot effectively be utilized by single cells, collective defense against antagonists, and optimization of population survival by differentiating into distinct cell types (Shapiro, 1998).

Due to coordinated cell movements, many bacteria can produce multicellular communities with an ordered structure, radial, spiral and fractal patterns of the colonies (Ben-Jacob et al., 1992, 2004, 2012; López et al., 2010) or "swarming" communities (Shapiro, 1998; Ingham et al., 2012; Mastropaolo et al., 2012; Olsen et al., 2012). For example, *E. coli*, *B. subtilis*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* form parallel cell lines, and radial, spiral and fractal patterns of colonies (Ben-Jacob et al., 1992, 2004; Ben-Jacob, 1998; López et al., 2010).

The spiral colony pattern in moving *B. subtilis* is due to the coordinated movement of the cells parallel to each other with a tendency of cell streams to twist. In *Paenibacillus vortex* and some members of the genera *Pseudomonas* and *Proteus*, "swarming" as coordinated movement provided by the flagellar activity is found (Ingham et al., 2012; Mastropaolo et al., 2012). It is shown that three of species newly described genera *Winogradskyella* form a net-like cell aggregates (Nedashkovskaya et al., 2005). Communities of filamentous cyanobacteria form films, bands, multi-array aggregates and polygonal network (Sumina et al., 2008; Sumina & Sumin, 2011, 2013).

There is evidence of cell differentiation in biofilms *B. subtilis* and differentiation of mixospores in myxobacteria; cell differentiation is observed in some filamentous cyanobacteria (Wassenaar, 2012). Myxobacteria are social bacteria capable of complex morphogenesis (Shapiro, 1998; Wassenaar, 2012). Myxobacteria form multicellular structures aggregating into groups of

more than 100,000 cells, which form fruiting bodies for spore dispersal; cell-contact signals have been found, which coordinate developmental gene expression with cellular movement, leading to the construction of fruiting bodies (Kaiser, 2006; Velicer & Vos, 2009; Olsen et al., 2012).

Refardt et al. (2013) demonstrated evidence for altruism in *E. coli* responding to the attack of lytic phage by comitting suicide to prevent parasite transmission to nearby relatives. Many microorganisms as well as some cell types within multicellular organisms secrete small signaling molecules and sense their concentration in the environment (Olsen et al., 2012). The chemical vocabulary used by bacteria for communication is constantly increasing as new molecules are discovered (Anetzberger & Jung, 2010). There are many different types of bacterial cell-to-cell signaling systems considered as quorum-sensing systems. Bacterial communication often, but not always, coordinates transcription as a function of population density, and this type of communication is called quorum sensing (Fuqua et al., 1994). This term was introduced to specifically refer to the cell-density linked, coordinated gene expression in populations that experience threshold signal concentrations to induce a synchronized population response (Fuqua et al., 1994; Bodman et al., 2008). So, bacterial communications include cell-cell chemical signaling that provides a bacterial "quorum" involving coordinated transcription (Waters & Bassler, 2005; Atkinson & Williams, 2009; Chandler & Greenberg, 2012; Olsen et al., 2012). Quorum sensing confuses the distinction between prokaryotes and eukaryotes because it enables bacteria to act as multicellular organisms (Bodman et al., 2008). Quorum-sensing signaling is not restricted to bacterial cell-to-cell communication, but also includes inter-kingdom signaling as communication between microorganisms and their hosts (Hughes & Sperandio, 2012), as prokaryote-eukaryote cross-communication (Bodman et al., 2008; Anetzberger & Jung, 2010). Thus, sociomicrobiology considers bacteria as social beings capable of complex activity (Chandler & Greenberg, 2012; Olsen et al., 2012). This capacity of bacterial cells for the communication and adaptive morphogenesis was named "bacterial wisdom" (Ben-Jacob, 1998) and "intelligence" of a bacterial swarm able to take collective decisions (Ingham et al., 2012).

FILAMENTOUS CYANOBACTERIA

Bacterial communities played a crucial role in the evolution of the biosphere (Little et al., 2012). Filamentous cyanobacterial communities

composed of many multicellular strands can form biofilms, multi-arrayed aggregations and polygonal networks (Castenholz, 1968; Richardson & Castenholtz, 1987, 1989; Sumina et al., 2008; Shepard & Sumner, 2010; Sumina& Sumin, 2011, 2013). Research of modern cyanobacteria and their role in the global sedimentation is important for the understanding of the geological history of the Earth (Petroff et al., 2008; Sumina et al., 2008; Sumina & Sumin, 2011, 2013).

Laboratory cultures of filamentous cyanobacteria with multicellular trichomes, *Oscillatoria terebriformis* and *Microcoleus chthonoplastes* were used (Sumina & Sumin, 2011, 2013; Isaeva et al., 2014, in press). *O. terebriformis* and *M. chthonoplastes* demonstrate exploratory activity, with a fan-shaped divergence of trichomes on the end of the strand. During the attachment strand formation, cyanobacterial filaments are arranged parallel to each other. *O. terebriformis* community often includes multi-array radial aggregates. *O. terebriformis* can form a reticular, polygonal network.

Oscillatoria and other filamentous cyanobacteria have trichome motility by sliding, rotation and flexion. In filamentous cyanobacteria complex movement patterns in bacterial biofilms and mats and changes in trichome motility as an adaptive reaction to light were observed (Castenholz, 1968; Richardson & Castenholtz, 1987, 1989; Sumina et al., 2008; Sumin & Sumin, 2011, 2013). Three-dimensional networks having triangulation and hexagonal tesselation were found in cyanobacterial communities (Petroff et al., 2008; Shepard & Sumner, 2010), in particular, in *O.* terebriformis (Sumina & Sumin, 2011; 2013). It is shown that such cell motility as the trichomes sliding, the parallel alignment of the filaments (Shepard & Sumner, 2010) and the contact inhibition of filament movement (Sumina & Sumin, 2013) are essential for the formation of reticular structures. Reticular geometry revealed in the natural bacterial films and fossil structures can be attributed to the motility of filamentous bacteria (Shepard & Sumner, 2010). The formation of these networks is due to photosynthetic activity and the motility of trichomes.

The physical and chemical effects on the morphology of cyanobacterial associations are revealed (Shepard & Sumner, 2010). Morphological features depend on patterns of cell motility, and laboratory experiments reveal this dependence (Sumina & Sumin, 2013).

A mechanism of bacterial sliding motion m is still a mystery (Adams, 2001; McBride, 2001; Wassenaar, 2012). The displacement of fibrils in cell wall or mucus secretion, probably, can explain sliding motility (Hoiczyk, 2000; Adams 2001; McBride, 2001).

Thus, the studied community of cyanobacteria, as well as other bacteria and archaea, are capable of complex social interactions, and dynamic reversible adaptation to environmental changes. In *O*. terebriformis contact inhibition and contact guidance of trichome movement are found (Sumina, & Sumin, 2013; Isaeva et al., 2014, in press).

EUKARYOTA: SOCIAL BEHAVIOR OF METAZOAN CELLS

Anyway, Eukaryota evolved from Prokaryota (Margulis, 1983; Gould, 2002; Wassenaar, 2012; Strassmann & Queller, 2012; Wassenaar, 2012). In evolution, Eukaryota improved the abilities for adaptive "intelligent" behavior (Albrecht-Buehler, 1985; Lipton, 2001) inherited from Prokaryota. Albrecht-Buehler (1985) in his remarkable article entitled "Is cytoplasm intelligent too?" drew attention to the ability of cells to perceive information from other cells, process it and realize an adaptive answer. Now Lipton (2001) emphasizes cell wisdom and consciousness.

Populations of unicellular eukaryotic organisms, such as *Chlamydomonas*, are capable of self-structuring (Albrecht-Buehler, 1990). Social cell behavior is observed in yeasts, amoebae, and ciliates (see Brodsky, 2009). The aggregation of the myxomycete *Dictyostelium* amoebae became a classic example of biological self-organization. The complex movement and morphogenesis of social *Dictyostelium* amoebae are directed by a simple mechanism of chemotaxis in response to the chemoattractant (cAMP) concentration (Dormann et al., 2011; Li & Purugganan, 2011). Striking social effects such as highly sensitive collective responses and onset of collective behavior in *D. discoideum* mediated by increased levels of cell-secreted signals in higher cell density (Vedel et al., 2013). *D. discoideum* forms a fruiting body in which about a fifth of cells die to form a stalk and may be used as a model to explore the genetic basis of social cell behavior and altruism (Strassmann & Queller, 2012). So, *D. discoideum* is a model system for the study of social evolution and social cooperation. This species exhibits altruism during both asexual and sexual cycles of its life history, and recent studies have uncovered genetic mechanisms associated with kin discrimination and cheating behavior during asexual fruiting-body formation (Li & Purugganan, 2011).

The most important events during the early evolution of multicellular Eukaryota are due to evolutionary innovations at the cellular level, first of all, the symbiotic appearance of a eukaryotic cell, and the emergence of

multicellularity with the system of intercellular communication as well as cell differentiation.

Direct cell-cell communications and social behavior of cells are observed in mammals as well as in protists and bacteria. Cell-cell communications and the resulting self-organization of cells were the earliest control mechanism in multicellular organisms. The emergence of metazoans was mediated by conserved signaling systems, which appeared in bacteria (Brodsky, 2009). A growing number of cell types capable of collective cell decision are described in such different organisms as bacteria, yeast, lower metazoans, and mammals (Balázsi et al., 2011).

Although quorum sensing has been the topic of intense study in prokaryotes, there is also evidence showing that such systems are employed by some eukaryotes (see Atkinson & Williams, 2009). Similar to unicellular organisms, mammalian cells coordinate their responses by detecting changes in concentration of signaling molecules (Conrad, 2012). Sun et al. (2012) studied spatial-temporal dynamics of collective chemosensing in fibroblasts, which synthesize the structural components of the extracellular matrix. When the extracellular matrix is damaged, fibroblasts migrate to the wound and then deposit new collagen and other components to heal it; this process requires coordinated action by multiple cells and collective response to chemical signals. It was shown that the response of fibroblasts was correlated only when the cell density exceeded a critical threshold (Sun et al., 2012). Hickson et al. (2008) compared mammalian tumorigenesis, resulting from the migration of metastatic ovarian cancer cells, with bacterial multicellular biofilm community. It was presented also a modeling and experimental analysis of cell-density-dependent glycolytic oscillations in yeast *Saccharomyces cerevisiae* (De Monte et al., 2007).

A healthy multicellular organism strictly controls the self-renewal, differentiation, behavior and apoptosis of its cells suppressing cell individuality and promoting their "altruism". The "tyranny of the organism" (Gould, 2002) is inevitable. Nevertheless, a cell of a multicellular animal retains features of an individual being, capable of exploratory and collective behavior, and collective self-organization (Vasiliev & Gelfand, 1977, 2006; Kirschner & Gerhart, 2005), as evidenced by experiments with cells cultured outside a metazoan organism, without neural, hormonal and other forms of its control.

Search migrations represent a most important variant of exploratory reactions (Vasiliev & Gelfand, 2006). Cellular movements are inevitable in animal embryogenesis since gastrulation stage. During development, some

cells in metazoan organism reveal competition (Edelman, 1993; Kirschner & Gerhart, 2005).

Experiments with dissociated cells of the organism cultured *in vitro* revealed remarkable capabilities for cell self-organization in the absence of controlling influences from a whole organism. *In vitro*, cells spontaneously form ensembles with coordinated, social behavior of cells and the generation of ordered morphological patterns (Vasiliev & Gelfand, 1977, 2006; Trinkaus, 1984; Lackie, 1986; Deisboeck & Couzin, 2009; Isaeva et al., 2008, 2012). In cell cultures, social behavior of normal cells is displayed *in vitro* as the exploratory cell behavior (Kirschner & Gerhart, 2005), the contact guidance and the contact inhibition of cell reproduction and movement after cell collisions (Abercrombie & Heaysman, 1953, 1954; Weiss, 1958, 1961, 1968; Vasiliev & Gelfand, 1977; Abercrombie, 1980; Heaysman, 1980; Trinkaus, 1984; Lackie, 1986; Isaeva et al., 2008, 2012).

Cell contact guidance and contact orientation (Weiss & Garber, 1952; Weiss & Taylor, 1956; Weiss, 1958, 1961, 1968; Isaeva, 1980; Trinkaus, 1984; Turner, 1986; Lackie, 1986; Clark et al., 1991) determines a preferred direction of cell movement along other cells, fibers of extracellular matrix or oriented elements of an artificial substrate. For example, it was shown cell contact orientation and contact guidance of cell movement along collagen fibers (Elsdale & Bard, 1972; Ebendal, 1974; Dunn & Ebendal, 1978; Warren, 1981; Turner et al., 1983; Klebe et al., 1989).

Thus, isolated *in vitro* cells of multicellular organisms can self-organize into assemblies and generate ordered spatial patterns of cell population displaying coordinated cell behavior and adaptive reactions.

In confluent cell cultures, human epidermal cells form patterns resembling dermatoglyphs (Green & Thomas, 1978). In confluent fibroblast monolayers, diploid human fibroblasts align parallel to one another; a "patchwork" of many local parallel cell association forms, with topological discontinuities between cell arrays (Elsdale, 1972, 1973; Elsdale & Wasoff, 1976). Fibroblasts pack side by due to contact guidance (Weiss, 1961) and contact inhibition (Abercrombie, 1980). In the confluent monolayer culture of chick embryo myogenic cells, myoblasts self-organize into parallel arrays by contact cell-to-cell guidance; later myotubes also align one along another forming cell flows with topological singularities (Isaeva, 1980; Isaeva et al., 2008, 2012).

The influence of physical structure of the substrate on the orientation and morphology of myotubes in the myogenic monolayer culture was studied (Isaeva, 1980; Isaeva et al., 2008). The myoblasts were shown to be oriented on the substrate with parallel grooves along the grooves. The ordered

arrangement of cells determined by physical properties of the substrate is maintained and transmitted by intercellular contact cell orientation. The parallel orientation of myotubes on the substrate with ordered microrelief *in vitro* imitates the parallel arrangement of muscle fibers in the skeletal muscle *in vivo*.

The radial pattern of cell migration from cell aggregates is due to the contact inhibition of cell movement that prevents crossing over of cell migration pathways (Abercrombie, 1980). The radial pattern is the common, typical phenomenon of self-organization in monolayer cell cultures. Radially migrating cells form bridges between aggregates (Isaeva et al., 2008). The following step of self-organization in monolayer culture is the emergence of an integrated reticular pattern by the formation of cell bridges that connect aggregates forming a polygonal reticular system. This integrated pattern is very similar and almost indistinguishable in cell cultures derived from different tissues and animals: chick embryo myoblasts, coelomocytes of the sea urchin *Strongylocentrotus nudus* and the starfish *Asterias amurensis* (Isaeva et al., 2008). Once formed cell bridges direct cell movement along these bridges by contact guidance thus ensuring the maintenance and enhancement of emerging pattern – that is a positive feedback typical of self-organization phenomena (Isaeva et al., 2008). Earlier Stopak and Harris (1982) have shown bands of aligned fibroblasts, which connected explants, so forming a triangular tessellation. Bovine aortic endothelial cells also form polygonal network (Murray, 2000).

Thus, the spatial patterns in monolayer cultures are the result of cell interaction games: the contact cell-to-cell guidance and contact inhibition of cell movement. Cell contact guidance is cellular basis of morphogenesis in these morphogenetic cell fields; so the translation of the local order of cell interactions into the global order of cell fields occurs (Isaeva et al., 2008; Deisboeck & Couzin, 2009).

Blood cells and invertebrate hemocytes are systems of emergent response, characterized by chaotic dynamics and rapid transitions from one state to another. The study of the aggregation of different cells *in vitro* revealed the common scenario of the collective cell behavior as a sudden spontaneous transition from chaos (irregular motility of single cells) to order (correlated cell behavior) similar to a phase transition in physical systems (Isaeva et al., 2008, 2012). Such collective behavior of cells decreases the energy expenses per cell optimizing the energy expenses of the population (Deisboeck & Couzin, 2009). Embryonic cells *in vitro* also exhibit coordinated social behavior and generate ordered morphological patterns displaying

developmental equifinality. It was shown that reaggregates of dissociated embryonic cells developed forming floating "embryoids" and, later, more or less normal larvae (Spiegel & Spiegel, 1975, 1986), which, after metamorphosis, became fertile sea urchins (Hinegardner, 1975). Similar experiments demonstrate the remarkable potential of embryonic cell self-organization *in vitro* (Isaeva et al., 2008; Isaeva, 2010, 2012; Presnov et al., 2010). Reorganization of the cytoskeleton is the basis of morphogenesis (Vasiliev, 2007) in eukaryotic cells. The treatment with cytochalasin (specific inhibitor of the fibrillar actin system) prevents the cell migration and the pattern formation so revealing fibrillar actin-dependence of the pattern formation in monolayer cell culture *in vitro* (Isaeva et al., 2008, 2012). The biological mechanisms of metazoan cell self-organization at molecular level is the fibrillar actin system function and actin–myosin interaction. Cytoskeletal systems transmit and integrate information across cellular dimensions (Li & Bowerman, 2010). Egg cytoskeleton functions as a global morphogenetic determinant in axial patterning of a future animal body, so egg ooplasm possesses long-term epigenetic memory (see Isaeva et al., 2008).

The transition of cytoskeleton into integrated "histoskeleton" (by means intercellular integration through cell–cell contacts) gives the additional coordination of cell behavior. The integration cytomatrix–extracellular matrix through integrins occurs (Yamada & Geiger, 1997). During development, epithelial morphogenetic movements are responsible for much of the reorganization that lays down the overall body plan: the folding, spreading, budding, cavitation, and delamination of epithelia produce the basic structure of most organs (Kolega, 1986). There is increasing evidence on mechanical and geometrical influences in morphogenesis (Nelson et al., 2005; Nelson, 2009). Physical and topological constrains are essential for biological systems as an imperative that restricts and directs biological morphogenesis (Isaeva et al., 2008, 2012; Presnov et al., 2010).

CONCLUSION

Thus, communities of both cyanobacterial (Prokaryota) and metazoan (Eukaryota) cells are able to social cell activity including contact inhibition and contact guidance of cell movement resulting in the ordered morphogenesis. Contact inhibition and contact orientation of cell movement are found in metazoan monolayer cell cultures and also during movement of cyanobacterial trichomes (Sumina & Sumin 2013, Isaeva et al., 2014, in

press), but were not detected in the three-dimensional cell aggregates of eukaryotic cells and, as far as we know, in any community of prokaryotic cells, besides *O. terebriformis* and *M. chthonoplastes*.

Spatial and temporal self-organization in communities of both prokaryotic and eukaryotic cells *in vitro* depends on physical limitations: gravity, attachment to the substrate, the mechanical tension, in cyanobacteria also from light (Sumina & Sumin, 2013). Structures formed by cyanobacteria *O. terebriformis*, in particular, the multi-arrayed aggregates have mechanosensitivity (Sumina & Sumin, 2013).

In bacterial communities of *E. coli* contact-dependent growth inhibition was found (Aoki et al., 2005; Diner et al., 2012), similar to the contact inhibition of metazoan cells reproduction *in vitro*. Contact-dependent inhibition of cell reproduction in both Prokaryota and Eukaryota defines social behavior of cell communities, but the molecular mechanism of this inhibition are distinct in prokaryotic and eukaryotic cells as well as biological mechanisms of cell motility and cell-cell interactions.

The synchronized collective behavior of animals with the appearance of various ordered spatial patterns, which has primarily been investigated for social insects, flocks of birds and fishes, is considered as an example of self-organization (Parrish, Edelstein-Keshet, 1999; Parrish et al., 2002). Biological systems are capable of dynamic self-organization, i.e., spontaneous emergence of a spatial-temporal order with the formation of various spatial patterns. Particularly, bacterial communities are self-organizing complex systems (Shapiro, 1998). During self-organization, the global pattern of a system appears as epiphenomenon by numerous nonlinear interactions between the elements of the lower levels.

The ability of self-organization is directed and fixed genetically by natural selection (Parrish, Edelstein-Keshet, 1999; Camazine et al., 2001; Whitesides & Grzybowski, 2002; Johnson & Lam, 2010 Kirschner, Gerhart, 2005; Isaeva, 2012). The selection of self-organizing systems leads to an increase in robustness, flexibility, and plasticity, i.e., to adaptability and ability to evolve. In evolution the features of organism assemblies or cell associations inevitably become an object of natural selection (Parrish, Edelstein-Keshet, 1999; Camazine et al., 2001; Parrish et al., 2002; Kirschner, Gerhart, 2005). During evolution, Eukaryota inherited from Prokaryota and improved abilities for adaptive, "intelligent" behavior.

Exploratory adaptive cell behavior was selected during evolution. Morphogenetic transformations in cyanobacterial communities are adaptive in nature. Eukaryotic cells have evolved from prokaryotic cells, inheriting and

enhancing their ability to intercellular communication and flexible adaptive behavior.

Natural selection acts on both cooperative and competitive phenotypes, across multiple scales of biological organization, including molecular ones. The growing field of sociogenomics is revealing how complex social behavior can be dissected at the molecular level (Foster, 2011). Multilevel selection theory (including kin selection) provides a theoretical foundation for sociobiology (Hamilton, 1964; Gould, 2002; Wilson & Wilson, 2007). Evolutionary theory interprets social behavior in terms of fitness: the reproductive advantage actions confer on both actor and recipient. Cooperation among relatives can thus extend to altruism, in which an individual sacrifices its chance of reproducing to advance those of a relative (Olsen et al., 2012).

The sociomicrobiology is attractive interdisciplinary field (Velicer & Vos, 2009), and some concepts of cell sociobiology may be exported into other biological sciences. The social phenomena uncovered so far allow the first direct comparisons between microorganisms and macroorganisms, which reveal convergences in behavior that are clearly suggestive of adaptation (Crespi, 2001). Cooperation and division of labor involving microbiology, ecology, and evolutionary theory should lead to accelerating progress in understanding social worlds both large and small (Crespi, 2001).

REFERENCES

Abercrombie, M. (1980). The crawling movement of metazoan cells. Proc. *Royal Soc. Lond*. 207, 129-147.

Abercrombie, M. & Heaysman, J.E.M. (1953). Observations on the social behaviour of cells in tissue culture. I. Speed of movement of chick heart fibroblasts in relation to their mutual contacts. *Exp. Cell Res*. 5, 111-131.

Abercrombie, M & Heaysman, J.E. (1954). Observations on the social behaviour of cells in tissue culture. II. Monolayering of fibroblasts. *Exp. Cell Res.* 6, 293–306.

Adams, D.G. (2001). How do cyanobacteria glide. *Microbiol. Today*. 28, 131-133.

Aguilar, C., Vlamakis, H., Losick, R. & Kolter, R. (2007). Thinking about *Bacillus subtilis* as a multicellular organism. *Curr .Opin. Microbiol*. 10, 638–643.

Albrecht-Buehler, G. (1985). Is cytoplasm intelligent too? In J.W. Shay (Ed.) Cell and Muscle Motility. Vol. 6. New York: Plenum Press, pp. 1-21.

Albrecht-Buehler, G. (1990). In defense of "non-molecular" cell biology. *Internat. Rev. Cytology*. 120, 191-241.

Anetzberger, C. & Jung, K. (2010). Introduction. In R. Krämer & K. Jung (Eds) Bacterial Signaling. Weinheim: WILEY-Verlag GmbH & Co, pp. 3-5.

Aoki, S.K., Pamma, R., Hernday, A.D., Bickham, J., Braaten, B.A. & Low, D.A. (2005). Contact-dependent inhibition of growth in *Escherichia coli*. *Science*. 309, 1245-1248.

Atkinson, S. & Williams, P. (2009). Quorum sensing and social networking in the microbial world. *J. R. Soc. Interface*. 6, 959-9768.

Balázsi, G., van Oudenaarden, A. & Collins, J.J. (2011). Cellular decision making and biological noise: From microbes to mammals. *Cell*. 144, 910-925.

Ben-Jacob, E. (1998). Bacterial wisdom. *Physica A*. 249, 553-577.

Ben-Jacob, E., Aharonov, Y. & Shapira, Y. (2004). Bacteria harnessing complexity. *Biofilms*. 1, 239-263.

Ben-Jacob, E., Schmueli, H., Shochet, O. & Tenenbaum, A. (1992). Adaptive self-organization during growth of bacterial colonies. *Physica A*. 187, 378-424.

Ben-Jacob, E., Coffey, D.S. & Levine, H. (2012). Bacterial survival strategies suggest rethinking cancer cooperativity. *Trends Microbiol*. 20, 403-410.

Bodman von, S.B., Willey, J.M. & Diggle S.P. (2008). Cell-cell communication in bacteria: United we stand. *J. Bacteriol*. 190, 4377-4391.

Brodsky, V.Ya. (2009). Direct cell-cell communications and social behavior of cells in mammals, protists, and bacteria. Possible causes of multicellularity. *Russ. J. Devel. Biol*. 40, 69-82.

Camazine, S., Deneubourg, J.L., Franks, N.R., Sneyd, J., Theraulaz, G. & Bonabeau, E. (2001). Self-Organization in Biological Systems. Princeton: Princet. Univ. Press.

Castenholz, R.W. (1968). The behavior of *Oscilaltoria terebriformis* in hot springs. *J. Phycol*. 4, 132-139.

Chandler, J.R. & Greenberg, E.P. (2012). Sociomicrobiology and quorum sensing − mediated communication. In L.A. Olsen, E.R. Choffnes & A. Mack (Eds.) The Social Biology of Microbial Communities. Washington: The National Academies Press, pp. 213-222.

Clark, P., Connolly, P., Curtis, A.S.G., Dow, J.A.T. & Wilkinson, C.D.W. (1991). Cell guidance by ultrafine topography in vitro. *J. Cell Sci*. 99, 73-77.

Conrad, J.C. (2012). Quantifying collective behavior in mammalian cells. *Proc. Nat. Acad. Sci. USA*. 109, 7591-7592.

Crespi, B.J. (2001). The evolution of social behavior in microorganisms. *Trends Ecol. Evol*. 16, 178-183.

De Monte, S., d'Olivio, F., Danø, S. & Sørensen, P.G. (2007). Dynamical quorum sensing: Population density encoded in cellular dynamics. *Proc. Natl. Acad. Sci. USA*. 104, 18377-18381.

Deisboeck, T.S. & Couzin, I.D. (2009). Collective behavior in cancer cell populations. *BioEssays*. 31, 190-197.

Diner, E.J., Beck, C.M., Webb, J.S., Low, D.A. & Hayes Ch.S. (2012). Identification of a target cell permissive factor required for contact-dependent growth inhibition (CDI). In L.A. Olsen, E.R. Choffnes & A Mack (Eds.) The Social Biology of Microbial Communities. Washington: The National Academies Press, pp.385-408.

Dormann, D., Vasiev, B. & Weijer, C.J. (2011). The control of chemotactic cell movement during *Dictyostelium* morphogenesis. *Philos. Trans. Roy. Soc*. (L.) B. 355, 983–991.

Dunn, G.A. & Ebendal, T. (1978). Contact guidance on oriented collagen gel. *Exp. Cell Res*. 111, 475-478.

Ebendal, T. (1974). Scanning electron microscopy of chick embryo nerve fibres and heart fibroblasts on collagen substrata in vitro. *Zoon*. 2, 99-104.

Edelman, G.M. (1993). Neural Darwinism: Selection and reentrant signaling in higher brain function. *Neuron*. 10, 115-125.

Elsdale, T. (1972). Pattern formation in fibroblast cultures, an inherently precise morphogenetic process. In G.H. Waddington (Ed.). Towards a Theoretical Biology, vol. 4. Edinburgh: Edinburgh University Press, pp. 95-108.

Elsdale, T. (1973). The generation and maintenance of parallel arrays in cultures of diploid fibroblasts. In E. Kulonen & J. Pikkarainen (Eds.). Biology of Fibroblasts. New York: Academic Press, pp. 41-58.

Elsdale, T. & Bard, J. (1972). Collagen substrata for studies on cell behavior. *J. Cell Biol*. 54, 626–637.

Elsdale, T. & Wasoff, F. (1976). Fibroblast cultures and dermatoglyphics: the topology of two planar patterns. *Roux' Arch. Dev. Biol*. 180, 121-147.

Foster, K.R. (2011). The sociology of molecular systems. *Nature Reviews. Genetics*. 12, 193-203.

Fuqua, C., Winans, S.C. & Greenberg, E.P. (1994). Quorum sensing in bacteria: The LuxR-LuxI family of cell density-responsive transcriptional regulators. *J. Bacteriol*. 176, 269-275.

Gould, S.J. (2002). The Structure of Evolutionary Theory. Cambridge, London: The Belknap Press of Harvard University Press.

Green, H. & Thomas, J. (1978). Pattern formation by cultured human epidermal cells: development of curved ridges resembling dermatoglyphs. *Science*. 200, 1385-1388.

Hamilton, W. D. (1964). Genetical evolution of social behaviour, I and II. *J. Theor. Biol*. 7, 1–52.

Heaysman, J. (1980). Processes in cell culture. *Experientia*. 36, 503-504.

Hickson, J., Yamada, S. D., Berger, J., Alverdy, J., O'Keefe, J., Bassler, B. L. & Rinker-Schaeffer, C. (2008). Societal interactions in ovarian cancer metastasis: a quorum-sensing hypothesis. *Clin. Exp. Metastasis*. 26, 67–76.

Hinegardner, R.T. (1975). Morphology and genetics of sea urchin development. *Amer. Zool*. 15, 679–689.

Hoiczyk, E. (2000). Gliding motility in cyanobacteria: observations and possible explanations. *Arch. Microbiol*. 174, 11-17.

Hughes, D.T. & Sperandio, V. (2012). Inter-kingdom signalling: Communication between bacteria and their hosts. In L.A. Olsen, E.R. Choffnes & Mack A. (Eds.) The Social Biology of Microbial Communities*:* Workshop Summary. Washington, DC: The National Academies Press, pp. 484-508.

Ingham, C.J. (2012). Dispersal of cargo microorganisms by swarming bacteria. In L.A.Olsen, E.R. Choffnes & A. Mack (Eds.) The Social Biology of Microbial Communities. Washington: The National Academies Press, pp. 304-322.

Isaeva, V.V. (1980). Contact orientation of myoblasts and myotubes in the differentiating culture of myogenic cells. *Sov. J. Dev. Biol*. 11, 181-187.

Isaeva, V.V. (2010). The diversity of ontogeny in animals with asexual reproduction and plasticity of early development. *Russ. J. Dev. Biol*. 41, 291-301.

Isaeva, V.V. (2012). Self-organization in biological systems. *Biol. Bull*. 39, 1109-1118.

Isaeva, V.V., Kasyanov, N.V. & Presnov, E.V. (2008). *Analysis situs* of spatial-temporal architecture in biological morphogenesis. In J.T. Kelly (Ed.) Progress in Mathematical Biology Research. New York: Nova Science Publishers, pp. 141-189.

Isaeva, V.V., Kasyanov, N.V. & Presnov, E.V. (2012). Topological singularities and symmetry breaking in development. *BioSystems*. 109, 280-298.

Isaeva, V.V., Sumina, E.L. & Sumin, D.L. (2014). Symmetry breaking during morphogenesis in communities of filamentous cyanobacteria (Prokaryota) and *in vitro* cells of some Metazoa (Eukaryota). *Paleontol. J.* (Moscow). 49 (in press).

Johnson, B.R. & Lam, S.K. (2010). Self-organization, natural selection, and evolution: cellular hardware and genetic software. *BioScience*. 60, 879-885.

Kaiser, D. (2006). A microbial genetic journey. *Ann. Rev. Microbiol*. 60, 1-25.

Kirschner, M.W. & Gerhart, J.C. (2005). The Plausibility of Life. New Haven: Yale Univ. Press.

Klebe, R.J., Caldwell, H. & Milam, S. (1989). Cells transmit spatial information by orienting collagen fibers. *Matrix*. 9, 451-458.

Kolega, J. (1986). The cellular basis of epithelial morphogenesis. In W. Browder (Ed.), *Developmental Biology,* vol. 2. New York: Plenum Press, pp. 103-143.

Lackie, J.M. (1986). Cell Movement and Cell Behavior. London e a.: Allen and Unwin.

Li, R. & Bowerman, B. (2010). Symmetry breaking in biology. Cold Spring *Harb. Perspect. Biol.* 2, a003475.

Li, S.I. & Purugganan, M.D. (2011) The cooperative amoeba: *Dictyostelium* as a model for social evolution. *Trends in Genet*. 27, 48-54.

Li, Y.-H. & Tian, X. (2012). Quorum sensing and bacterial social interactions in biofilms. *Sensors.* 12, 2519-2538.

Lipton, B.H. (2001). Insight into cellular consciousness. Bridges (ISSEEEM Org.). 12, 5-9.

Little, A.E.F., Robinson, C.J., Peterson, S.B., Raffa, S.B. & Handelsman, J. (2012). Rules of engagement: Interspecies interactions that regulate microbial communities. In L.A. Olsen, E.R. Choffnes, A. Mack (Eds.) The Social Biology of Microbial Communities. Washington: The National Academies Press, pp. 242-275.

López, D., Vlamakis, H. & Kolter, R. (2010). Biofilms. *Cold Spring Harb Perspect Biol*. 2, a000398.

Margulis, L. (1981). Symbiosis in Cell Evolution. New York: Freeman.

Mastropaolo, M.D., Silby, M.W., Nicoll, J.S. & Levy, S.B. (2012). Novel genes involved in *Pseudomonas fluorescens* Pf0-1 motility and biofilm formation. *Appl. Environ. Microbiol*. 78, 4318-4329.

McBride, M.J. (2001). Bacterial gliding motility: Multiple mechanisms for cell movement over surfaces. *Annu. Rev. Microbiol*. 55, 49–75.

Muller, F., Brissac, T., Le Bris, N., Felbeck, H. & Gros, O. (2010). First description of giant Archaea (Thaumarchaeota) associated with putative bacterial ectosymbionts in a sulfidic marine habitat. *Environ. Microbiol.* 12, 2371-2383.

Murray, J.D. (2000). Pattern formation in integrative biology – a marriage of theory and experiment. C. R. Acad. Sci. Paris, Sci. de la Vie. 323, 5-14.

Nedashkovskaya, O.I., Kim, S.B., Han, S.K., Snauwaert C., Vancanneyt M., Swings J., Kim K.-O. Lysenko A.M., Rohde M., Frolova G.M., Mikhailov V.V. & Bae K.S. (2005). *Winogradskyella thalassocola* gen. nov., sp. nov., *Winogradskyella epiphytica* sp. nov. and *Winogradskyella eximia* sp. nov., marine bacteria of the family Flavobacteriaceae. *Intern. J. Syst. Evol. Microbiol.* 55, 49–55.

Nelson, C.M. (2009). Geometric control of tissue morphogenesis. *Biochim. Biophys. Acta – Mol. Cell Res.* 1793, 903-910.

Nelson, C.M., Jean, R.P., Tan, J.L., Liu, W.F., Sniadecki, N.J., Spector, A.A. & Chen, C.S. (2005). Emergent patterns of growth controlled by multicellular form and mechanics. *Proc. Natl. Acad. Sci. U.S.A.* 102, 11594-11599.

Olsen L.A., Choffnes E.R., & Mack A., Eds. (2012). The Social Biology of Microbial Communities*:* Workshop Summary. Washington, DC: The National Academies Press.

Parrish, J.K. & Edelstein-Keshet, L. (1999). Complexity, pattern, and evolutionary trade-off in animal aggregation. *Science.* 284, 99-101.

Petroff, A., Sim, M.S., Liang, B., Rothman, D. & Rosak, T. (2008). Aggregation phenomena in cyanobacterial analogues of ancient stromatolites. In J. Reitner, N.-V. Quéric & M. Reich (Eds.) Geobiology of Stromatolites. Göttingen: Universitätsverlag Göttingen, pp. 106-107.

Presnov, E., Isaeva, V., & Kasyanov, N. (2010) Topological determination of early morphogenesis in Metazoa. *Theor. Biosci.* 129. 259-270.

Rainey P.B. & Kerr B. (2012). Cheats as first propagules: A new hypothesis for the evolution of individuality during the transition from single cells to multicellularity. In L.A. Olsen, E.R. Choffnes & A. Mack (Eds.) The Social Biology of Microbial Communities. Washington: The National Academies Press, pp. 409-425.

Refardt, D., Bergmiller, T. & Kümmerli, R. (2013). Altruism can evolve when relatedness is low: evidence from bacteria committing suicide upon phage infection. *Proc. R. Soc. B*. 280, 30-35.

Richardson, L.L. & Castenholtz, R.W. (1987). Diel vertical movements of the cyanobacterium *Oscillatoria terebriformis* in a sulfide-rich hot spring microbial matt. *Appl. Environ. Microbiol*. 53, 2142-2150.

Richardson, L.L. & Castenholtz, R.W. (1989). Chemokinetic motility responses of the cyanobacterium *Oscillatoria terebriformis*. *Appl. Environ. Microbiol.* 55, 261-263.

Shapiro, J.A. (1988). Bacteria as multicellular organisms. Sci. Amer. 256, 82-89.

Shapiro, J.A. (1998). Thinking about bacterial populations as multicellular organisms. *Ann. Rev. Microbiol*. 52, 81-104.

Shepard, R.N. & Sumner, D.Y. (2010). Undirected motility of filamentous cyanobacteria produces reticulate mats. *Geobiology*. 8, 179-190.

Spiegel, E. & Spiegel, M. (1986). Cell-cell interactions during sea urchin morphogenesis. In Developmental Biology: A Comprehensive Synthesis. New York, London: Plenum Press. Vol. 2, pp. 195-240.

Spiegel, M. & Spiegel, E. (1975). The reaggregation of dissociated embryonic sea urchin cells. *Amer. Zool.* 15, 583-606.

Stopak, D. & Harris, A.K. (1982). Connective tissue morphogenesis by fibroblast traction. I. Tissue culture observations. *Devel. Biol*. 90, 383-398.

Strassmann, J.E. & Queller, D.C. (2012). Evolution of cooperation and control of cheating in a social microbe. In L.A. Olsen, E.R. Choffnes & A. Mack (Eds.) The Social Biology of Microbial Communities. Washington: The National Academies Press, 509-533.

Sumina, E.L. & Sumin, D.L. (2011). New representations on the nature of stromatolites. In V.C. Tewari & J. Seekbach (Eds.) Stromatolites: Interaction of Microbes with Sediments. Cellular Origin, Life in Extreme Habitats and Astrobiology. Springer, pp. 675-686.

Sumina, E.L. & Sumin, D.L. (2013). Morphogenesis in a community of filamentous cyanobacteria. *Russ. J. Develo. Biol*. 44, 158-172.

Sumina, E., Orleansky, V.K. & Sumin, D. Are the stromatolites the most ancient skeleton organisms? In J. Reitner, N.-V. Quéric & M. Reich (Eds.) Geobiology of Stromatolites. Göttingen: Universitätsverlag Göttingen. 2008, pp. 123-124.

Sun, B, Lembong, J, Normand, V, Rogers, M & Stone, H.A. (2012). Spatial-temporal dynamics of collective chemosensing. *Proc. Natl. Acad. Sci. USA*. 109, 7753–7758.

Trinkaus, J.P. (1984). Cells into Organs. Englewood Cliffs: Prentice Hall.

Turner, D.C. (1986). Cell–cell and cell–matrix interactions in the morphogenesis of skeletal muscle. In: M.S. Steinberg (Ed.). Developmental Biology: A Comprehensive Synthesis. Vol. 3. The Cell Surface in Development and Cancer. New York: Plenum Press, pp. 205–224.

Turner, D.C., Lawton, J., Dollenmeier, P., Ehrisman, R. & Chiquet, M. (1983). Guidance of myogenic cell migration by oriented deposits of fibronectin. *Devel. Biol*. 95, 497-504.

Vasiliev, Ju.M. (2007). Reorganization of cytoskeleton as a basis of morphogenesis. *Russ. J. Devel. Biol*. 38, 90-94.

Vasiliev, J.M. & Gelfand, I.M. (1977). Mechanisms of morphogenesis in cell cultures. *Int. Rev. Cytol*. 50, 159-274.

Vasilev, Yu.M. & Gelfand, I.M. (2006). Cellular search migrations in normal development and in carcinogenesis. *Biochemisty* (Moscow). 71, 821-826.

Velicer, G.J. & Vos, M. Sociobiology of the Myxobacteria. (2009). *Annu. Rev. Microbiol.* 63, 599–623.

Vedel. S., Tay, S., Johnston, D.M., Bruus, H. & Quake, S.R. (2013). Migration of cells in a social context. *Proc. Nat. Acad. Sci. USA*. 110, 129-134.

Warren, R.H. (1981). Myoblasts are aligned with collagen fibrils in regenerating frog tadpole tails. *Tissue Cell*. 13, 773-785.

Wassenaar T.M. (2012). Bacteria: The Benign, the Bad, and the Beautiful. Hoboken, USA: Wiley-Blackwell.

Waters, C.M. & Bassler, B.L. (2005). Quorum sensing: Cell-to-cell communication in bacteria. *Annu. Rev. Cell Dev. Biol*. 21, 319–46.

Weiss, P. (1958). Cell contact. *Int. Rev*. *Cytol*. 7, 391-423.

Weiss, P. (1961). Guidance principles in cell locomotion and cell aggregation. *Exp. Cell Res*. 8 (Suppl.), 260-286.

Weiss, P. (1968). Dynamic of Development: Experiments and Inferences. New York, London: Academic Press.

Weiss, P. & Garber, B. (1952). Shape and movement of mesenchyme cells as functions of the physical structure of the medium. Contribution to a quantitative morphology. *Proc. Natl. Acad. Sci. U.S.A*. 38, 264-280.

Weiss, P. & Taylor, C.A. (1956). Fish scales as substratum for uniform orientation of cells in vitro. *Anat. Rec*. 124, 381.

Whitesides, G.M. & Grzybowski, B. (2002). Self-assembly at all scales. *Science*. 295, 2418-2421.

Wilson, D.S. & Wilson, E.O. (2007). Rethinking the theoretical foundation of sociobiology. *Quart. Rev. Biol*. 82, 327-348.

Woese, C.R. (2002). On the evolution of cells. *Proc. Nat. Acad. Sci. USA*. 99, 8742–8747.

Yamada K.M. & Geiger B. (1997). Molecular interactions in cell adhesion complexes. *Curr. Opin. Cell Biol*. 9, 76-85.