

BIOCOMMUNICATION

Sign-Mediated Interactions between Cells and Organisms

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Dedication to the Memory of Eshel Ben-Jacob (1952–2015)



Eshel Ben-Jacob was a theoretical and experimental physicist at Tel Aviv University, holder of the Maguy-Glass Chair in Physics of Complex Systems, and Fellow of the Center for Theoretical Biological Physics (CTBP) at Rice University. During the 1980s he became an international leader in the theory of self-organization and pattern formation in open systems, and later extended this work to adaptive complex systems and biocomplexity. His specialization in self-organization of complex systems yielded the breakthrough of solving the long-standing (since Kepler) snowflake problem. In the late 1980s, he turned to the study of bacterial self-organization, believing that bacteria hold the key to understanding the larger biological systems. He studied pattern forming bacteria species, and became a pioneer in the study of bacterial intelligence and social behaviors of bacteria, thus being an important contributor to this book. He was an influential figure in establishing the now rapidly evolving Physics of Living Systems (Biological Physics and Physical Biology) disciplines. Eshel was an exceptionally creative interdisciplinary scientist. He was one

of the world's leading experts in biocomplexity, with a scientific profile that integrated a remarkable mix of physics and biology, immunology and mathematical modeling, engineering and econophysics. Not many scientists contributed to so many different fields with innovative and influential research as he did.

Eshel Ben-Jacob was a superb teacher and lecturer, his teachings and presentations inspired a wide range of audiences, from expert physicists at numerous international conferences and students at his courses, to high school students and hi-tech workers. Eshel Ben-Jacob generously shared his knowledge and love of science. As a mentor, he advised and collaborated with many students and junior associates who later had a successful career of their own. He was a devoted advisor, his deep and extreme passion for science was magnetizing, and he was intense and genuine both as a person and as a scientist.

His many honors for contributions to science included his election in 2014 to the American Philosophical Society, the United States' oldest learned society, the 1986 Landau Research Prize, the 1996 Siegle Research Prize of the Israel Academy of Sciences and Humanities and the 2013 Weizmann Prize in Exact Sciences. Ben-Jacob was former president of the Israel Physical Society and a former chair of the Israel Ministry of Education's Advisory Council of High School Physics Education.

Eshel's sudden death on Friday June 5, 2015 came as a shock to all of us. He was a bright star who gave for free, so much to so many. We were lucky to get to know him and learn from him. His death was a devastating event for all of us. We will miss him.

Alin Finkelshtein, June 11, 2015

Dedication to the Memory of Fernando Palop (1954–2015)



In Memoriam of Fernando Palop, born in Barbastro 1954, died in Valencia 2015, Associate Professor, Polytechnic University of Valencia and co-founder of TRIZ XXI (<http://www.triz.es>).

Editors and friends would like to thank Professor Fernando Palop for his valuable contribution to this book. Palop dedicated a big part of his life to teaching the business of tech mining and its importance in increasing corporate intelligence of organizations. He worked with both students and professionals, either through his university career or his own company, TRIZ XXI.

His work focused on designing and creating competitive intelligence methods to reduce risk in innovation processes and knowledge management. Through this he worked closely with universities and institutions, and later became a member of the 166th Committee of The Spanish Association for Standardization and Certification. As a distributor of knowledge, Palop gave numerous speeches and seminars on competitive intelligence and TechMining throughout Latin America, including Brazil, Colombia and Chile.

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Preface

Who is Who in Biocommunication

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*“Three things are beyond me: The way of an eagle in the sky ... how a
snake makes its way over a rock ... how a man has his way over a maiden”*

Proverbs 30: 18–19

1. Introduction

The concept of biocommunication is very broad and has several meanings: it involves linguistics, cognition, and even outer space, including astrobiology. Biocommunication can also cover molecular genetics, plant physiology (chemotropism), and plant perception. Moreover, the term includes inter-personal exchange of information in various modes.

Biocommunication exists in almost all organisms from bacteria to man. Every organism uses signs of communication to exchange information for purposes of coordination and cooperation. This communication also serves for organization between members of the same, related, or unrelated species. All coordination between cells, organs, and organisms depends on successful biocommunication processes. For example, between single cells we find the chemical attraction between sperm migrating toward an egg within the body or outside in the wet environment. In this respect, diseases in organisms are often the results of disturbed or damaged communication between cells.

In the Bible are a few cases of communication between man and other creatures: such as the conversation of the snake with Eve about eating from the fruit of the Tree of Knowledge in the Garden of Eden (Genesis 3: 1–6), the case of Balaam’s ass who spoke to him and complained about his beating her three times (Num. 22: 28–30). It is said that King Solomon was gifted to talk to plants, animals, fowl, creeping things, and fish. Given recent successful attempts to “speak” with primates, and our increasing interest in communicating in some way with animals, these ancient stories show that interest in interspecific biocommunication is thousands of years old.

In our study of biocommunication, we are aiming at more specific types of communication, intraspecific or interspecific, between species of bacteria, fungi, plants, animals, and humans. Communication also incorporates linguistics, sign-mediated interactions following syntactic, pragmatic, and semantic rules. Biocommunication of animals includes vocalizations (as between bird species, canines and others), the use of pheromone production, (between insects or mammals and chemical signals between plants and animals. Animal communication is related to zoosemiotics. Some biocommunication has tentatively been connected to the concept of instincts in insects and animals (Tautz, 2008).

2. Human Communication — the King of Communication

In human beings, we have direct speaking and the senses of vision, hearing, odor, and touching the body as means of communication.

Human's senses are related to links from person to person, such as male–female — including the courtship period — and mankind to their surroundings. The five senses of humankind enable the mastery of humans over other animals. Man is able to communicate with some domestic animals and birds and receive responses from them. For example, the wagoner orders his horses or mules to go forward or to halt. People can command dogs, cats, goats, sheep, or pet birds to perform various actions and they often obey.

In India, street performers with flutes entice cobras to respond to their music (though this is mostly a reaction to movement). On the other hand, we know about communication between man and dolphins, which amazes large crowds of spectators.

3. Biocommunication in Plants

There are plants, such as the orchids, whose flowers mimic others so as to appear as females to their pollinators, so that male insects are happy to land on these flowers, being certain that they are his female; this way pollination and fertilization take place. Other plants can “communicate” with their pollinators through bright colors or pleasant or repulsive odor.

There are chemical signals between plants and animals (such as tannin production by plants to warn away insects). We have heard about chemically mediated communication between plants. Plant physiology covers some processes such as geo- or heliotropism. Some consider plants intelligent (Buhner, 2014). Plants may have perception and are sentient; perhaps they experience pain or pleasure of emotions (Tompkins and Bird, 1973). According to the last two references (popular works), plants have the ability to communicate with humans and other forms of life. Others plants display trembling, moving, and shaking of the whole plant over an insect visit. This is the case of *Mimosa* plants which defend themselves against animals through stimuli responses that rapidly fold its leaves. Still others repulse their plant eating grazers by producing offensive odors or poisonous chemicals to repulse neighboring plants or other predator enemies. The relation between plants and other organisms has been recently published (Seckbach and Dubinsky, 2010).

4. Insects and Animals

Social insects (such as bees, ants, termites, and wasps) use pheromones for communication. We know about the bees' dance (which communicates how to get to flowers). The pollination period is vital for nature and for development of fruit; at this stage plants signal (through their odor, shape and colors) pollinating insects (mainly flying ones) and humming birds to land on their flowers.

Dogs have abilities to smell; this feature has been used by police and armies for their activities. A male dog may appear from several kilometers away during a female's rutting period, a sample of odor communication. On some butterflies their wings mimic the patterns of toxic butterflies to ward off predators.

5. Fowls' Communication

Among the birds are strongly social species; communication among them is seen in a variety of ceremonies, gestures, and specific calls. We recognize vocalization (bird species) and know about pairs of birds (e.g., pigeon couples) — how they divide their functions in the nest, sitting on the eggs and bringing food for the youngsters. There are singing birds learning to sing complicated songs from their parents and even to mimic human voices. Another point is the behavior of the male birds, such as, turkeys or peacocks, to impress the female during the courting period with full-blown colored feathers and special sounds. All their displays are aimed at attracting mates. Among penguins, we find close relations of couples using their voices in communication. They operate with division of duty, in order to protect the huge crowd against the cold polar winds or to warm their eggs. There are the young penguins who find their parents among millions of other members in the surrounding flock by their sounds. Some birds may alert their neighbors against an enemy in the vicinity by making warning sounds.

We'll add a personal story about bird communication. Many years ago, when JS was a tractor driver he was plowing the fields near the Kishon River (northern Israel). The plow exposed and

raised up from the ground a large black snake, which started to wiggle between the freshly lifted soil sections. Suddenly, a carnivorous bird, perhaps a vulture or eagle, landed and started to “deal” with the snake. A few minutes later, the bird lifted up the snake but let it drop from high above, leaving the snake on the ground. Perhaps it proved too heavy. Then the bird flew away and returned with another one [its mate?]. Both of them landed near the prey and together lifted the snake from the ground and flew away with it to have their full meal.

6. General Concepts

In this volume, we describe more specific types of communication. Such exchange of information, and sign-mediated interaction within (intraspecific) or between (interspecific) takes place among species of bacteria, plants, fungi, and animals. Biocommunication means strong interaction via a special “language” used within a species, including that between primates, birds or insects. In most cases, there are chemical molecules (semiochemicals) involved. Biocommunication also occurs between the cells of a developing embryo, as it forms itself.

Biocommunication is expressed in different ways. One may associate it with the concept of symbiosis and organismal language and interaction between species. For example, such communication exists within the soil between roots of higher trees and symbioses with arbuscular mycorrhizal fungi.

The purpose of this book to demonstrate the panoply of biocommunication, interaction, and “language” in the biological world. Such interrelations range from molecules and cells, bacteria, fungi, cyanobacteria, and other organisms as well as from micro-animals to mammals.

Topics covered within this book include: molecular biocommunication, superfast evolution via interspecies, bacterial communication, communication languages and agents in biological systems, carnivorous plants and insects, the crosstalk between plants and their symbionts, global communication within the embryo, how

neurons find their target, animal communication under noisy conditions above and below water, chemical communication, sexual communication by pheromones, and artificial communication.

Acknowledgment

We thank Fern Seckbach for her comments.

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Introduction to Biocommunication

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Biocommunication (BC) as a field is concerned with describing the exchange of information between various organisms. Tembrock outlined a first draft of the BC theory in 1975. There are abundant cases of communication within intra- and interspecies in the biological world. It exists in almost all organisms from bacteria to man. Every organism uses signs of coordination, cooperation, and organization between members of the same, related, or non-related organisms. All coordination between cells, organs, and organisms depends on successful biocommunicative processes. In this respect, diseases in organisms are the result of damaged communication between cells. Such interaction is revealed among single and multiple microorganisms (Prokaryotes) and higher forms (Eukaryotes).

We know of communication between humans, but humankind talks to domestic animals such as dogs, cats, or birds, flocks, cattle, and donkeys, or horses (and get responses from them). Some claim that music in the cattle barn increases the production of milk by cows. Here, JS wishes to share with you a little episode: a few years ago, we watched a TV program on a big screen; adjacent to us sat two Chihuahuas. When dogs in the show appeared on the TV monitor, the little domestic dogs started to bark at the foreign penetrators of their territory and warn them to go away.

In the Bible are cases of communication between man and other creatures (such as the archaic snake and Eve; Balaam and the donkey, the wisdom of King Solomon, etc.) or the Almighty talking to man (for details, see the preface in this volume).

Our aim in this volume is to present information about and examples of the BC concept to a broad audience. This is accomplished through several different chapters of separate examples of BC from molecules to the level of monkeys and dolphins. We describe specific types of communications within molecules, species of Bacteria, plants, fungi, and animals. Although there are many more cases of this field, the contents offered in this book will give the audience a good overview of the BC phenomena. The interaction of birds or animals may include vocalization (such as between competing bird species, a pair of pigeons, or higher animals), pheromone production (in insects and in animals), chemical or color signals, between insects, plants, and animals inter-relationships (Seckbach and Dubinsky, 2011; Tautz, 2008) and altruistic behavior.

In the volume we describe more specific types of communication, exchange of information, bioinformatics, and sign-mediated interaction within (intraspecific) or between (interspecific) species of plants, animals, fungi and bacteria. BC means strong interaction via a “language” between the species (even between real language of primates, between birds, or insects). In most cases, chemical molecules involved. BC is expressed in different ways. One way associate it with the concept of symbiosis (Seckbach, 2002; Seckbach and Grube, 2010), organismal language, and interaction between species.

For example, such communication exists within the soil between roots of higher plants and symbioses with arbuscular mycorrhizal

fungi. We may also include BC between single cells, e.g., the chemical attraction between the sperm migrating toward the egg within the body or outside in a wet environment. Some organisms may use pheromone production, as between various species of insects and animals such as vertebrates. There are also chemical signals between plants and animals, as in tannin and phyto-poison production used by vascular plants to warn away insects or inhibit germination of other plants. Such chemically mediated communication is between plants and within plants.

We offer this book to graduate students, researchers in biology, ecology, zoology, to related applied areas of environment and to adventurously curious readers.

Ille Gebeshuber has done a splendid job in outlining our book in her Foreword.

This book came about through a colleague at Louisiana State University (LSU), Professor Maud Walsh, who was interested in environmental communication and that concept led us to BC.

Acknowledgments

We thank all our contributors for their chapters and for their long patience. This book could not be published without the effort and persistence of our contributors and reviewers. We apologize to any person who assisted us in this volume who may have been overlooked.

The following are the names of are our reviewers and advisors. We also wish to express our gratitude to colleagues who pointed out new reviewers who agreed to evaluate chapters. Among the reviewers are Bashir Ahmad, Bradly Alicea, Luciano Avio, Frantisek Baluska, Kara Loeb Belinsky, Francisca Bronfman, Michael Y. Galperin, Ille Gebeshuber, Vera Kolb, Laurent Legendre, Michael Levin, Howard H. Pattee, Bartosa J. Plachno, Vladimir Seleznev, James A. Shapiro, Alexei A Sharov, John S. Torday, Jack A. Tuszyński, Clément Vidal, Luis P. Villarreal, Günther Witzany. Additional appreciation is due to Lubomir Adamec, David J. Chapman, Julian Chela-Flores, Natan Gadoth, Rob Hengeveld, Arie S. Issar, Shmuel Nussinov, Florence Raulin, Luis P. Villarreal.

To our readers: In addition to our volume, there is also a set of books on BC edited by Günther, and we thank him for his initial cooperation in this book.

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Foreword

Biocommunication in the Web of Life: Theoretical and Experimental Approaches

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The question “What is life?” has puzzled mankind since the early beginnings. Biocommunication provides a distinct marker between life and non-life: only living entities communicate via signs and codes. Dead matter follows physics and chemistry, without the additional magic sparkle of communication.

This book is a compilation of chapters by key authors from important fields in biocommunication. The book has two major parts, with Part 1 being more concerned with theoretical aspects, and Part 2 presenting important experimental approaches.

Biocommunication denotes communication on all levels in the web of life: communication takes place inside cells, across cells, within an organism and from one to another, within one species, across species, and even across time. Table 1 denotes which chapter

deals with which biocommunication actors, Table 2 denotes the respective signal types the authors are dealing with and Table 3 establishes further synergies besides biocommunication actors and signal types. From these tables, synergies in all three categories across the chapters in the book can easily be identified, and the reader can direct his or her attention to the respective works.

Below, the individual chapters are described in more detail.¹

PART I Theoretical Approaches

Chapter 1 Alexei A. Sharov: Molecular biocommunication

If life started out with pure chemistry, at some point in time, signs entered the game: chemical molecules that stand for something else than their chemistry alone. As Charles Peirce (Peirce, 1955) wrote: “A sign is something which stands for something in some respect or capacity”. Codes came up. The genetic code for example. How? Why? When?

Since this is the first chapter in the book, we will explain Tables 1, 2, and 3 regarding this work. The main category of Chapter 1 is theoretical; in Tables 1 and 2 this is indicated by the capital T in the first line, respectively. Harari & Sharon’s chapter 9 is the first experimental one, it has a capital E in these tables. Chapter 1 (Sharov, 2016) deals with the biocommunication in all of life, indicated in the last line in Table 1, and the signal types he especially focuses on are chemical signals, codes, epigenetics, eusemiotics, genetic signals, informational communication protosemiotics and signs. All these are marked in grey for this chapter in Table 2. Synergies of his work with the work of others in this book can easily be identified by checking who else deals with “all life” in terms of actors in biocommunication (and the result is: Witzany, Chapter 2; Harari & Sharon, Chapter 9). From Table 2 one can see the other authors who deal with the same signal types, in a similar way. Table 3 identifies further synergies within the book, regarding

¹In some cases we have copied some sentences from an author’s chapter.

Table 1. Biocommunication actors as treated in the book.

Biocommunication	Author(s)																
	Sharov	Witzany	Martinelli	Negrotti	Gordon & Stone	Gebeshuber and Macqueen	Tamir & Priel	Kak	Harari	Finkelshtein <i>et al.</i>	Sbrana	Darnowski	Slabbekoorn	Rocha <i>et al.</i>	Gershony-Emek <i>et al.</i>	Rumbaugh <i>et al.</i>	Frohoff and Oriol
Theoretical/Experimental	T	T	T	T	T	T	T	T	E	E	E	E	E	E	E	E	E
Animals																	
Bacteria interspecific																	
Bacteria intraspecific																	
Bacteria — fungi																	
Birds																	
Carnivores																	
Cells — neurons																	
Dolphins — humans																	
Dolphins non-human animals																	
Fish																	
Herbivores																	
Human cells																	
Humans																	
Interneuronal																	
Interspecific																	
Intraneuronal																	
Intraspecific																	
Multicellular organisms																	
Neuro-muscular																	
Organisms with brains																	
Organisms with DNA																	
Pan/Homo bonobos — humans																	
Pan/Homo chimpanzees — humans																	
Plants — fungi																	
Plants — pollinators																	
Plants — prey																	
Plants animals																	
Quantum biology																	
With the past																	
All life																	

Table 2. Biocommunication signal types as treated in the book.

Signal Type	Author(s)																
	Sharov	Witzany	Martinelli	Negrotti	Gordon & Stone	Gebeshuber and Macqueen	Tamir & Priel	Kak	Harari & Sharon	Finkelshtein <i>et al.</i>	Sbrana	Darnowski	Slabbekoorn	Rocha <i>et al.</i>	Gershony-Emek <i>et al.</i>	Rumbaugh <i>et al.</i>	Frohoff and Oriel
Theoretical/Experimental	T	T	T	T	T	T	T	T	E	E	E	E	E	E	E	E	E
Acoustic																	
Chemical																	
Codes																	
Differentiation waves																	
Electrical																	
Epigenetic																	
Eusemiotics																	
Gene expression																	
Genetic																	
Infochemicals																	
Informational communication																	
Knowledge-based communication																	
Language																	
Language (printed signs)																	
Language (vocal)																	
Material properties																	
Mechanical																	
Names																	
Noise induced protein mutations via DNA mutation																	
Nucleotide flips																	
Olfactory																	
Physical																	
Proteins																	
Protosemiotics																	
Quantum biology																	
RNA																	
Signals that induce cell differentiation																	
Signs																	

(Continued)

Table 3. Synergies of authors and articles with regard to the topic as treated in the book

Synergies of Authors and Articles with regard to the topic	Sharov	Witzany	Martinelli	Negrotti	Gordon & Stone	Gebeshuber and Macqueseen	Tamir & Priel	Kak	Harari	Finkelshtein <i>et al.</i>	Sbrana	Darnowski	Slabbekoorn	Rocha <i>et al.</i>	Gershony-Eimek <i>et al.</i>	Rumbaugh <i>et al.</i>	Frohoff & Oriel
Co-cultural evolution																	
Co-cultural processes																	
Co-experiencing																	
Cognitive ethology																	
Cohabitation																	
Collaboration																	
Communication with the past																	
Computers																	
Embryo development																	
Horizontal gene transfer																	
Informational communication																	
Interspecies cooperation																	
Knowledge-based communication																	
Legal rights (non-human animals)																	
Male–female																	
Molecular signaling																	
Mutations																	
Mutual respect																	
Neuromuscular junction																	
Neurons																	
Noise																	
Non-coding parts of the genome																	
Personhood (non-human animals)																	
Protosymbols																	
Quantum biology																	
Shared interests across life forms																	
Signals to another sensory universe																	
Signs																	
Stem cell differentiation																	
Synergies																	
Transferable genetic units																	
Wave propagation																	

(Continued)

Table 3 (Continued)

Synergies		
<i>theme</i>	<i>chapter</i>	<i>chapter</i>
Co-cultural processes	Negrotti	Rocha <i>et al.</i>
Co-experiencing	Gorman	Rumbaugh <i>et al.</i>
Co-feeling	Gorman	Rumbaugh <i>et al.</i>
Co-sensing	Gorman	Rumbaugh <i>et al.</i>
Communication with the past	Gebeshuber & Macqueen	Finkelshtein
Communication with the past	Gebeshuber & Macqueen	Rumbaugh
Computers	Sharov	Negrotti
Embryo development	Gordon & Stone	Harari
Horizontal gene transfer	Gebeshuber & Macqueen	Gershony-Emek <i>et al.</i>
Knowledge-based communication	Negrotti	Rumbaugh <i>et al.</i>
Male–female	Gebeshuber & Macqueen	Harari
Molecular signaling	Gershony-Emek <i>et al.</i>	Sharov
Mutations	Witzany	Tamir & Priel
Mutations	Gebeshuber & Macqueen	Tamir & Priel
Mutations	Tamir & Priel	Witzany
Mutual respect	Gorman	Sbrana
Neuromuscular junction	Gershony-Emek <i>et al.</i>	Sharov
Neurons	Gershony-Emek <i>et al.</i>	Sharov
Noise	Gordon & Stone	Tamir and Priel
Noise	Tamir & Priel	Kak
Noise	Tamir & Priel	Slabbekoorn
Non-coding parts of the genome	Witzany	Gebeshuber & Macqueen
Non-coding parts of the genome	Gebeshuber & Macqueen	Witzany
Protosymbols	Sharov	Gebeshuber & Macqueen
Quantum biology	Kak	Rumbaugh <i>et al.</i>
Shared interests across life forms	Gorman	Sbrana
Signals to another sensory universe	Darnowski	Slabbekoorn
Signs	Sharov	Martinelli
Stem cell differentiation	Gordon & Stone	Rocha <i>et al.</i>
Synergies	Gorman	Sbrana
Transferable genetic units	Sharov	Gebeshuber & Macqueen
Wave propagation	Gershony-Emek <i>et al.</i>	Sharov

molecular signaling associated with biological processes yields substantially more information than a simple chemical approach. Cells use molecular signs to encode and control their activities. Molecular signals directly guide actions of specific cell components without reference to an object. Molecular signaling can be described in a “code-semiosis” signification model (Barbieri, 2003). A semiosis code is defined as a mapping between a set of signs and a set of meanings. Examples are the genetic code with ribosomes as code-makers (specific agents).

In protosemiosis, signs are associated with actions of agents rather than with objects. Responses of the biological system are not determined by the physical nature of the signs. Instead, they are shaped by the agent’s semiotic architecture, which is a product of long-term adaptive evolution.

Automatic processing of signs is common in living systems. It does not imply determinism, because responses are often checked for errors and adjusted to the environment and internal context within the agent. Automatic processing of signs does not include learning. Learning emerged historically via adaptive evolution, which is a learning-like process at the population level (Sharov, 1992). Evolution is a learning process at the population level. A sign can initiate, inhibit, or modify agent activities, but it never fully determines the outcome. “*A computer contains codes but it is not a semiotic system*” (Barbieri, 2008: 594).

Molecular proto-signs can be classified into three major categories: proto-icons, proto-indices and proto-symbols. They are nested in each other: one includes the previous one as a component. Proto-icons interact via one particular feature, for example the complementary binding of proto-icons to surfaces of molecules in a key and lock manner. The “shape” of the key and lock is a shape in an abstract space that includes geometry, charges and hydrophobic/-philic aspects. An example for a proto-icon is single stranded deoxyribonucleic acid (DNA) without any particular shape, which, upon meeting its complementary segment, spontaneously assembles into a double-stranded rigid DNA helix. Proto-symbols are members of a family of similarly structured molecular signs that

are processed uniformly by the same subagents and the same set of adapters. An example is the genetic code.

However, the processing of proto-symbols is based on a “heritable convention” rather than the socially-mediated conventions of eusemiotic symbols.

Contemporary organisms use all three kinds of proto-signs for their molecular communication. At the origin of life, no protosymbols may have been present. Proto-semiosis, to interconnect otherwise separate processes, is necessary for life to develop. However, proto-icons alone cannot make a functional living system because they have no capacity to organize a semiotic scaffold. The molecular signaling process is of paramount importance in fabrication, sensing, memory, movement and wave propagation in organisms. According to Rosen (Rosen, 1991) each component of a cell should be fabricated by other components, thus enabling the full capacity for self-repair, growth and self-reproduction. Sensing is needed to monitor external and internal conditions. All living organisms need memory to store information that encodes and controls their functions. Memory is preserved across generations in memory carriers such as DNA. Operational memory of smaller units such as proteins or ribosomes is often based on reversible or irreversible protein modifications. Larger units, such as gene cascades involved in cell differentiation or other functions, suggest a hierarchical structure to DNA memory. DNA and mRNA store large amounts of functional information that is needed to produce and regulate other molecular agents. Because it cannot be edited much, DNA is rather a passive information resource than an agent. An additional layer of rewritable memory that is preserved after cell division emerged in eukaryotic cells in the form of chromatin (DNA + histones) and DNA methylation: epigenetic memory.

Faster signaling does not take place via the generally slow process of the transport of large molecules, but by a signal traveling through an array of linked transmission agents without movement of the agents themselves. Action potentials in neurons, the electrical spikes that travel along the axon, are an example for this (Gershoni-Emek *et al.*, 2016), as are muscle cells that receive a

neural impulse respond by opening the voltage-gated channels, which allow extracellular Ca^{++} to enter the cell and initiate muscle contraction, and differentiation waves (Gordon and Stone, 2016).

Each component of a cell should be fabricated by other components, thus enabling error-control, robustness, and modularity in molecular communication. In any organism, at any point in time, the whole signaling network should be prepared for various kinds of disruptions of both internal and external origin. Life can only persist via error correction, compensation, robustness and protection from foreign signals. Template-based synthesized products are proofread, and tagged for degradation when erroneous, misfolded proteins are repaired by chaperones, and the threshold for initiating cell actions can be adjusted. Related to pluri- and omnipotency, differentiated cells are protected from transforming into pluripotent cells which may cause cancer. Accidental activation of any single transcription factor associated with pluripotency has no consequences, because it cannot function alone without its partners.

Molecular signaling networks often have modular organization, such as is the case in the cell cycle of eukaryotic cells where the transition between the major modules (five in the case of the cell cycle) are checkpoints with specific inputs and outputs. One of the checkpoints in cell division (the one at transition to mitosis, cell division) has elements of the advanced level of semiosis, or eusemiosis. Sharov says that this checkpoint in cell division shows signs of eusemiosis, since *"The output of the checkpoint is a sign of a specific state of the cell, and this state is an object."*

Categorization mechanisms in molecular signaling networks are context-dependent and adaptable even in organisms without neural systems (Ginsburg and Jablonka, 2009; Sharov, 2013). The epigenetic system offers enormous capacity of dynamic memory storage.

Chapter 2 Guenther Witzany: Key levels of biocommunication

Chapter 2 of the book is the theory chapter "Key levels of biocommunication" by Günther Witzany (Witzany, 2016) from Austria.

Language is life. Günther Witzany, seasoned biocommunication expert, identifies in his contribution the key levels of biocommunication. Antagonistically to Tamir and Priel's approach to noise as an enabler of genome mutations in their Chapter 7 "Channel capacity and rate distortion in amino acid networks" in this book (Tamir and Priel, 2016), Witzany thinks that natural genome editing is not the result of replication errors but of a group interaction of competent ribonucleic acid (RNA) agents.

Witzany opposes assumptions such as that communication is limited to humans or that non-human organisms function mechanically as machine-like stimulus reaction automatons determined by genetic programs. He also opposes behaviorism. Biocommunication is primarily a social interaction between living agents that share a real life world's traditions and environmental circumstances (Tomasello, 2008). In everyday life we do things with words that have serious consequences. A coherent model of language and communication must be the basis of all reasoning, as a good basis for knowledge about the world. Indeed, Witzany states that the only sure knowledge is how language and communication function. Witzany argues that in natural languages there cannot be such a thing as context free grammar.

The four key levels of biocommunication as identified by Witzany are found in all species and domains of life. They are (1) Sensing of abiotic circumstances (organisms of all domains store information about these indices in memory, to adapt better to repeated life situations), (2) Transorganismic communication processes (such as in the human mouth with its 500+ bacterial communities), (3) Interorganismic communication with a species specific vocabulary, between members of the same or related species), and (4) Intraorganismic communication (this also includes genetic parasites and mobile genetic elements, both important in Witzany's approach).

Key features of natural languages/codes in biocommunication processes comprise the fact that languages/codes inherently depend on social groups. The language tool serves to do things with signs combined with context-dependent markings such as conscious and unconscious body expressions.

Language is important. It is a new way of matter to interact, distinct from chemistry and physics. It is typical for life, and its use distinguishes between life and non-life. Communication provides appropriate tools for differentiation at specific levels, which is otherwise difficult to describe in reductive terms by means of pure physics and chemistry (molecular biology). Language-like structures and communication processes occur at the simplest level of living nature. All coordination and organization needs signs. Communication is highly complex; it cannot be reduced to mechanistic input/output or cause/reaction descriptions.

Communication is a sign mediated interaction between at least two living agents that share a repertoire of signs that are combined in varying contexts which transport content. Communication is interactions that depend on a shared repertoire of signs and rules. Such features are lacking in abiotic interactions.

In Witzany's view DNA provides stable habitats for unstable RNA colonizers. Viruses (who are older than cellular life) and viral-derived elements are the agents that edit the genome in host organisms. Viral colonizers play major roles in evolution and diversity of organisms. Mobile genetic elements such as non-coding RNAs are actively engaged in nearly all cell processes to meet both evolutionary and developmental needs. DNA is the storage medium, and there are species-specific active RNAs. Non-coding RNAs interact with DNA, RNA, and proteins and play important roles in nuclear organization, transcription, post-transcriptional and epigenetic processes. Non-coding RNA can undergo nuclear-cytoplasmic, nuclear-mitochondrial and axodendritic trafficking.

Very interesting and highly unusual are Witzany's thoughts about RNA agents that form consortial biotic structures. With language came life, and material left the purely physical chemical interaction patterns. Mixtures of RNA fragments form cooperative networks. RNA populations evolve to greater complexity through cooperation (Vaidya, 2012) — cooperation outcompetes selfishness. RNA stem loop consortia have selective (biological) group-building competence, and higher order structures such as pseudoknots show strictly context sensitive base-pairing. Witzany argues that

nucleic acid language has a language/code nature which represents the possibility of coherent *de novo* generation and context dependent alterations for a diversity of different meanings (functions) relating to the same syntax structures.

Biocommunication can be defined as the sign-mediated interactions of groups of living agents that share syntactic, pragmatic and semantic rules for sign use. Biocommunication cannot be sufficiently explained by materialistic and reductionist concepts. The biocommunication approach allows for a clear distinction between life and non-life, and could serve as an appropriate complementary tool for interpreting empirical data of biological disciplines coherent with current knowledge about communication and language.

For synergies of Chapter 2 with other chapters see Tables 1, 2, and 3.

Chapter 3 Dario Martinelli: Zoosemiotics, typologies of signs and continuity between humans and other animals

In his work on zoosemiotics, Dario Martinelli (Martinelli, 2016) deals with typologies of signs and continuity between humans and other animals. A sign is something that stands for something else. In the field of semiotics, a signal, i.e., any form of behavior aimed to transmit information from one animal to another, is the simplest unit of a sign. A sign is a more complex display involving more than one signal. Animal communication must also be thought in terms of channels, i.e., sensory modes employed to transmit a message. Signals can either be digital (two possible states, on/off, color/no color) or analogue, where signal variability is important, and the message's content depends on the different degrees of emission. Analogue signals give a higher communicative potential. The meaning of a signal often depends on the context. Many signals evolved from basic patterns that initially had no communicative intention. Growling in dogs for example, might initially have been a part of being angry, and later became ritualized, detached from fight, as a more complex form of signification. Growling can lead to a fight, or prevent it. Semiotic (i.e., sign process related) phenomena that occur among

animals are signification, representation and communication — they are constructed, organized, assembled, distinguished, interpreted and codified. Sign production and exchange among animals can be proprioceptive, intra- or interspecific. In organisms, language adds a series of communicative and cognitive elements on top of the existing ones. The use of symbols (and a consequent mental/interactive capacity) has for many years been a concept of which only humans were claimed to be capable. Insects supposedly have a very low and rigid degree of reasoning, and yet — from their world comes a beautiful example on the use of symbols in animals: Dipterans (flies) of the family Empididae practice cannibalism. In order not to risk being eaten, the male, before the copulation, offers the female an empty balloon. Another example is the highly symbolic dance of bees, in which they indicate where and how far away food can be found. Bees sign the distance to the food source with the time employed to cover the middle axis of the waggle dance, which looks like the Fig. 8. Honeybee communities in different countries use the very same articulation of this distance sign in their dance to represent completely different distances: the same amount of time signifies 5 m for an Egyptian bee, 25 m for an Italian one, and 75 m for a German bee.

Also alarm cries in monkeys are examples of symbolicness. Such cries inform conspecifics of the arrival of a predator. The response of the other monkeys is appropriate for escaping the corresponding predator: leopard — run to the trees, eagle — look up and seek shelter, snake — stand up on two legs and look in the grass). The cries do not just differ for different animals, but also with the distance of the animal to the caller. The syntax of the monkey callers is phonological and lexical. *Phonological syntax* is a combination of signs that, taken alone, do not necessarily have a specific meaning, or at least not a quantitatively different one from the combination. There are many examples of phonological syntax in animals. However, lexical syntax was for a long time only attributed to humans. It denotes a combination of signs that are meaningful as single units, and that also mean “something else”. Vervet monkeys

for example use the call “pyow” to designate a leopard, and the call “hack” for an eagle. Pyow pyow hack hack does not mean two leopards and two eagles, but “Let’s move to another place”. Language leads to change in behavior. If the monkeys did not possess a “language” their reaction would have been of another type (namely, most probably, escaping from the danger). The richer and more complex the “semigram” (i.e., the complete sign catalog of an individual), the more sophisticated the mental life. The active participation to semiosis opens up for further — and increasingly articulated — cognitive abilities.

Also names seem not to be unique to humans. Dolphins have individual specific names, which they choose in the first year of their life.

The six main functions within a communication system are expressive, conative, phatic, referential, metalinguistic and poetic. These functions are mutually inclusive.

When reading Martinelli’s chapter the author of this foreword was especially intrigued by the fact that some dancing flies give empty nuptial gifts (Fig. 1) to the females. It caused her to write the public outreach text given below:

*“***Marry me, marry me. I have the best empty balloon.****

The use of symbols has been for many years a concept (and a consequent mental/interactive capacity) of which only humans were claimed to be capable.

When we go on a date, we bring a little present for our sweetheart. Highly nutritious chocolate, a beautiful rose as a symbol of love or a piece of precious jewellery. Dancing flies are no different. Some male dancing flies bring highly nutritious packages as nuptial gifts, and some bring more ritualized presents — such as empty balloons (Sadowski et al., 1999). The girls love them, and off they fly into the sunset.”

Martinelli’s chapter has synergies with Sharov’s Chapter 1 “Molecular biocommunication” (Sharov, 2016) and Negrotti’s Chapter 4 “Communication as an artificial process” (Negrotti, 2016) in this book regarding their treatment of signs. For synergies of Chapter 3 with further chapters see Tables 1, 2, and 3.



Figure 1. Balloon flies at their nuptial dance. In some species, the balloons are filled with a present for the female (such as an insect); in some they are empty. Left: © 2013 Mark Shields. Right: *Empis aerobatica* Melander, © E.M. Fisher.

Chapter 4 Massimo Negrotti: Communication as an artificial process

Negrotti (Negrotti, 2016) deals in his chapter with communication as an artificial process. Language is in his view the sole technology intrinsically oriented towards giving birth to something artificial, while the materials adopted in all fields of naturoids, i.e., technological reproductions of natural subjects at a certain level of observation, historically come from a wide range of uses. He categorizes communication in two main areas: informational communication, that humans and animals share, and knowledge-based communication, which only humans are capable of.

Informational communication mainly transmits messages about facts in the outside world that might be verified by anyone, and takes place amongst people, animals, plants, and microorganisms; it can be denoted as biosemiotic management of standardized signals. Animals and plants such as trees communicate through physical or chemical signs supporting information that allows, or even forces, the living system to adopt some stereotyped behavior. Informational communication is a flow of effects, i.e., ordered physical events, as for example also takes place in a computer.

Human communication acts at two levels: the one we share with animals, and that which we have constructed culturally through language. Negrotti argues that the informational process

consists of a sort of mechanism, more or less plastic, of codified translation of signals. Knowledge, on the other hand, is the creation of individual meaning through particular processes of association constituting one's semantic history.

Knowledge-based communication, Negrotti argues, only takes place between humans. It is an open process with a dynamic code and complex processes of relationships between mental states and related meanings. Human communication of personal knowledge is difficult — Negrotti describes it as an attempt to reproduce one's mental state in the mind of someone else, by exploiting the seeming representational power of the words — knowledge-based messages are therefore artificial objects, results of a design process that is trying to reproduce a mental state by means of words. We can put our feelings, desires, thoughts and wishes into words, express our inner state, and communicate it to somebody else. However, the receiver does not perceive the same message as the sender sends, since both intertwine words they speak or hear with personal history, memories and experiences. Knowledge-based messages require decoding and interpretation. And interpretation strongly depends on the personal knowledge of the interpreter, who cannot prevent linguistic signs from triggering memories of past experience relating to that sign. Humans have deep differences in their individual disposition and experience. An important concept related to knowledge-based messages in Negrotti's chapter is the "observation level" of the speaker and the listener, respectively. Normally, the observation level selected by the speaker poses no problem. However, if the listener changes the observation level at which he wants to understand the message, he will be unable to see and feel what the speaker tried to reproduce in his or her mind. Even if speaker and listener share the same observation level, reproduction of the mind of the speaker is uncertain and not assessable. Words are signs that fire imagination. The listener sees and feels dependent on his own mind, and not the speaker's. Their two maps have a very low probability of overlapping substantially. Reality does not know any observation level. Unpredictability in the communication process is a rule.

When scientists analyze natural objects, they isolate them from the rest of the world, although reality does not have such separations or boundaries. A truly holistic view, whilst at the core of human ambition, does not allow us to generate any taxonomy and to induce any general law — something that is possible through isolating, under some profile, homogeneous classes of objects in empirical reality. We will often gain knowledge of the object in isolation, but lose several possible relationships between it and other phenomena that may be significant when trying to predict the behavior of the investigated phenomenon.

Also in human communication we isolate single statements from the discourse, and seemingly gain an increase in clarity. However, possible relationships may be lost. Even “context analysis” guarantees nothing, owing to the huge dimensional difference between the context analysis, however rich, and the whole structure of personal mental states. Selecting and reproducing “the essential” is important. Biomedical engineers “reproducing” a muscle need to concentrate on other factors than producers of lab-made burgers (*in vitro* meat). For the biomedical engineers, the main ambition is to make the material invisible to the body. Widely, in every field of automation, the final performance to be achieved is evaluated as more important than the reproduction of the natural structures of processes that generate the performance. This has, in some cases, catastrophic effects. Mining of resources, manufacturing, transportation, use and disposal of technological devices is optimized along a selected small range of parameters, and currently the effects of our ways of doing things are visible in dangerous changes in biogeochemical cycles and in a decline in the Earth ecosystem, including a humankind-induced mass extinction of species (Rockström *et al.*, 2009; Barnosky *et al.*, 2011; Steffen *et al.*, 2015). Even fields originally proposing to address such problems, such as biomimetics, i.e., learning from living nature for new, potentially disruptive ways in engineering and science, make the mistake to reduce the parameters they take into consideration to a much too small set (Gebeshuber *et al.*, 2009).

Negrotti also includes reflections on art in his chapter. Art is often regarded the human activity that best maximizes the efficacy of communication. For Negrotti, in the arts, the meaning of the message resides in its formal beauty rather than its content. The artist expresses himself in a way that is most suitable for him, rather than for others. Exemplified by travel journals, he describes the typical transfiguration that characterizes every artistic production.

In human communication we have no possibility of reproducing the essential performance of our mental state in an automatic way, i.e., attempting to reproduce it directly, avoiding the adoption of some observation level. The word can be simultaneously beneficial and dangerous.

The distance between words as signs and corresponding mental states is far greater than between the materials adopted by bio-engineers and the corresponding materials adopted by nature when building natural phenomena.

For many reasons due to the personal history of each of us, many words or styles may be stored in our mind along with bad memories, and, as a consequence, listening to them or reading them may trigger a repulsion or, at least, a strong deviation from their intended meaning. Only in a dictionary words are pure signs, i.e., informational structures. Their meaning strays very far from their informational content.

Humans express their mental states in knowledge-based communication, and the result is an artificial object whose destiny is largely independent of the intentions of the speaker.

Knowledge-based communication is the most ambitious and least assessable technique invented by humans for enhancing their relationships.

Negrotti's chapter has synergies with various chapters in this book: In their tissue engineering and regenerative medicine tech mining study "The contribution of the bio-communication (BICO) to biomedical and tissue engineering: A tech mining study" presented in Chapter 14 (Rocha *et al.*, 2016) Rocha and co-workers also treat co-cultural processes (i.e., simultaneous culture of different

cell types) and informational languages in tissue engineering. Sharov (2016) and Negrotti both deal with computers, however, from different viewpoints: Sharov quotes Barbieri, who says “*A computer contains codes but is not a semiotic system*” (Barbieri, 2008. 594); for Negrotti, computers deal with informational communication. Rumbaugh and co-workers present in chapter 16, “Ethical Methods of Investigation with Pan/Homo Bonobos and Chimpanzees”, the communication of Pan/Homo beings with each other and with humans (Rumbaugh *et al.*, 2016). Synergies with Negrotti’s Chapter 4 are in the area of informational language and knowledge-based communication. Negrotti and Rumbaugh *et al.* mention communication on inner mental states. Negrotti says that only humans are able to communicate in a knowledge-based way. Rumbaugh and co-workers say otherwise in Chapter 16. For synergies of Chapter 4 with further chapters see Tables 1, 2, and 3.

Chapter 5 Richard Gordon and Robert Stone: Cybernetic embryo

Growth is one of the fascinating aspects of life. How does a little fertilized cell develop to a fully-fledged organism? How do cells differentiate into new cell types? We have so many different types of cells in our bodies, so many organs, connections between all of them, and continuous communication going on, during embryogenesis, during growth from child to adult and in the adult form. Simply amazing.

Organisms grow in genuine, highly complex feedback conditions. Machines are assembled. This provides food for thought, touching biology, engineering, philosophy, materials science, control and communication aspects. Which shall result in a new, sustainable, disruptive approach to engineering.

Machines and organisms have paramount differences in various aspects. Organisms grow from a single cell whereas machines are assembled from manufactured parts. Embryogenesis is the field that investigates how an embryo forms and develops. Gordon and Stone present in Chapter 5 “Cybernetic embryo” (Gordon and Stone, 2016) their views on embryo development from a cybernetics perspective, concentrating on feedback systems that provide

control and communication. Cybernetics as an engineering discipline is a quite mature field known as ‘control theory’ (Gebeshuber, 2014); using control theory’s deterministic vocabulary and set of concepts on ‘reverse engineering’ of the embryo shall provide valuable inspiration for major steps forward in the field. The cybernetic embryo is a system in which communication and control via signals affect its process as it develops from one state to the next. The communication is provided via differentiation waves, i.e., waves of change of cell type, providing regional and global communication within the embryo. Their differentiation tree concept provides an experimentally and computationally testable hypothesis on self-construction of complex embryos, explaining pattern formation of complex systems of a nested character, with ‘meta-complexity’ of self-organization and adaptation on multiple levels. Each stage is viewed not as an end in itself, but rather as a preparation for the next stage. Important themes such as purpose and goals, teleonomy (purposive behavior controlled by processing of coded information) and teleology (purposive behavior controlled by feedback), are addressed from various angles, including citations of paramount work in various fields of specialization, and going back in time all the way to Aristotle, who described embryo development as an epigenesis, a chain of one genesis after another, where new structures and functions appear at various steps, with an increase of complexity during embryo development. Gordon and Stone treat differentiation waves as cybernetic feedback systems, and establish a binary code in the memory of each cell, giving history and memory of differentiation steps from the single cell state to the current stage. Each bit of this code corresponds to the triggering of a cascade of gene products and gene expression. Differentiation in embryos might be a lot less complex than we have imagined.

Synergies exist with Chapter 14 (Rocha *et al.*, 2016) regarding treatment of the differentiation of stem cells, and with Chapter 9 (Harari and Sharon, 2016), since both deal with embryo development. Harari and Sharon describe in the worm *C. elegans* dauer larvae that — upon receipt of chemical signals — are produced in

harsh conditions. They do not feed, survive on fat stores, and can survive for several months before they proceed maturation to adults. And both Chapter 7 (Tamir and Priel, 2016) and Gordon and Stone (2016) deal with noise. For synergies of Chapter 5 with further chapters see Tables 1, 2, and 3.

Chapter 6 Ille C. Gebeshuber and Mark O. Macqueen: Superfast evolution via trans- and interspecies biocommunication

Gebeshuber and Macqueen propose in Chapter 6, “Superfast evolution via trans- and interspecies biocommunication” that the real speed of evolution can be explained by a combination of natural selection with permutative and constructive elements (Gebeshuber and Macqueen, 2016). Selective elements are genetic units that are transferable across species and biological kingdoms, which is why the uniformity of the genetic code is of such great importance. Permutative elements include permutation by recession (biocommunication with the past via a genome that can repair itself and even reverse mutations) and innovation (communication with other organisms). Constructive elements comprise quantitative environmental (partner selection, competitor elimination) and qualitative genetic factors (selecting the probability for the sex of the offspring, on the male side by adapting prostate liquid, on the female side by variable egg hull permeability for X and Y carrying sperm) — which accounts for biocommunication with the environment and the partner. Exemplified by horizontal gene transfer and the most conserved protein present in all organisms, the chaperone protein HSP70, that is present in most organisms but not in the common ancestor, the authors argue that mutualism, a collaborative association of life forms, often from different species, that benefits all partners, might be the rule, and not the exception.

For synergies of Chapter 6 with other chapters see Tables 1, 2, and 3.

Chapter 7 Boaz Tamir and Avner Priel: Channel capacity and rate distortion in amino acid networks

The first intriguing fact about Chapter 7 “Channel capacity and rate distortion in amino acid networks” by Tamir and Priel (2016) on noise and information in protein channels is the perfect combination of highly exact mathematical concepts and beautiful translation of related mathematics into words. This is a precious kind of communication ability in itself.

Chapter 7 deals with the application of information theory to the analysis of amino acid sequences. The approach uses the analogy between the process of translating DNA sequences (source) to proteins (target) and the process of communicating information via a noisy channel (channel). The messages are words (codons) based on a four-letter alphabet (bases). Important concepts are channel capacity and signal distortion rate. Noise is important in biological systems, and in many cases beneficial, for example, via the process of stochastic resonance (Petracchi *et al.*, 2000). Tamir and Priel argue that biological systems must maintain a certain level of noise, since it facilitates evolutionary processes. Mutation rates for RNA viruses could be 10^{-3} to 10^{-5} per base per generation (Drake and Holland, 1999).

The competition between capacity and distortion is calculated as a function of a single parameter, the point mutation rate, which is the probability for a single nucleotide flip to occur. The amino acid channel is modelled as a transition matrix, statistically mapping each pair of amino acids from the source to the target. The authors establish a metric space of amino acids, where each amino acid is represented as a vector in a high dimensional space where the coordinates correspond to the amino acid’s physico-chemical properties such as volume, bulkiness, polarity, hydrophobicity, etc.

For synergies of Chapter 7 with other chapters see Tables 1, 2, and 3.

Chapter 8 Subhash Kak: Communication languages and agents in biological systems

Chapter 8 is on quantum biology (Kak, 2016). The author proposes that communication languages and agents in biological systems

are based on entities for which quantum mechanical objects are the primitives.

The hierarchy of languages and metalanguages that must be associated with biological systems are explained via communication and cognitive agents that are viewed as collections of quantum particles. Autonomous cognitive agents as they exist in the brain are viewed as self-organized systems with strong dynamical nonlinearities. Biological systems are considered from the perspectives of communication and complementarity.

Kak asks questions about the hierarchy of languages and metalanguages in biological systems. Quantum effects have been proposed for certain biological processes, including photosynthesis, olfaction, vision, long-range electron transfer and bird navigation. Kak views the brain as a classical/quantum hybrid system. He says that the cognitive system is quantum at a deeper level but coupled to the conscious system, which is classical. He talks about the Copenhagen Interpretation and that its early pioneers viewed the unconscious mind as quantum mechanical and different from the classical mind of the internal dialog within the individual. There is a field of research called quantum cognition.

Kak asks questions such as "*If subsystems within biological systems are quantum mechanical what is the nature of communication between these subsystems?*". Biocommunication includes associative (classical) and reorganizational (adaptive) elements in addition to those that are quantum. For the associative language, the medium is chemical and electrical; the quantum language is the one that is characterized by quantum processes. Biocommunication language is adaptive. In the brain the expectation affects the way the incoming sensory information is processed.

The way in which information is exchanged across areas is more important than the contents of any specific area. Neuroscience only provides clues about the lowest levels of the neuronal hierarchy; about the higher levels we do not possess knowledge that is independent of language. More complex concepts in children emerge under the influence of language. In his chapter, Kak combines quantum mechanics and biology, by

proposing a Bose–Einstein quantum probability distribution for certain molecular structures and shapes as a model of human memory. His assumption is that bosonic quasiparticles or fermions are assembled in different arrangements to become cognitive agents. Agents and memories should in his view be set apart by number, structure and informational content. Agents, unlike memories, are linked to sensors and actuators. An agent must be invariant to certain types of transformation and it should be resistant to noise within a certain limited range. From this resistance to noise follows a necessary minimum separation between patterns, not in 3D geometry but in an abstract space.

There are two kinds of quantum particles, bosons and fermions. Bosons are governed by the Bose–Einstein statistics, whereas fermions are governed by the Fermi–Dirac statistics. The number of permissible arrangements of particles decreases from classical to bosonic to fermionic states. A memory or cognitive agent as a collective of quantum particles must have a unique structure.

Kak proposes an algorithmic approach to information content in which the length of the program required to generate the pattern is a measure of the information — in this way, such a structure can mimic the object of information in form. The number of items in short-term memory is four to six in humans, and much higher in chimpanzees. Kak speculates whether processing in the workspace corresponding to short time memory has a quantum basis and whether the number of items can help determine its physical structure correlates. In his view it is plausible that agents are fermion collectives and memories are boson collectives.

For synergies of Chapter 8 with other chapters see Tables 1, 2, and 3.

PART II Experimental Approaches

Chapter 9 Ally R. Harari and Rakefet Sharon: Chemical communication

Chapter 9 of the book is Ally Harari and Rakefet Sharon’s work on chemical communication (Harari and Sharon, 2016), which is the

most ancient mode of information transfer in organisms. This is a basic chapter, very wide and interesting. Harari and Sharon deal extensively with infochemicals in the whole phylogenetic tree and give detailed examples for the usage of infochemicals as pheromones in insects.

When reading Harari and Sharon's chapter the author of this chapter was especially intrigued by the fact that plants can call other plants to call for help against herbivores (Fig. 2). It caused her to write the public outreach text given below:

"Most of us see plants as quite defenceless organisms. But if threatened, some of them can call enemies of their enemies! And not just this: the damaged plants ask their plant friends to join their chemical call, to make it better audible!

One example for this type of chemical biocommunication are Lima bean leaves that are damaged by a certain plant-eating spider mite. The leaves emit chemicals that induce in other Lima bean plants the emission of similar chemicals that attract predatory mites who attack the spider mites (Choh et al., 2004)."

This is one of the examples that Harari and Sharon describe in their overview chapter on chemical communication. Chemical communication is the most ancient method of information transfer between individuals. Communication via infochemicals is the oldest sense. Intentionally transferred information is termed signals, unintentionally transferred information is known as cues. Infochemicals can be beneficial or harmful for sender and/or receiver.

Ponderosa pines, bark beetles and wasps are for example all part of a complex chemical communication network: bark beetles are attracted to the pine trees by volatile compounds that are emitted by weakened trees, and start excavating a nuptial chamber. In this process, they release further infochemicals known as aggregation pheromones. The resulting high number of beetles weakens the tree's defence and subjugates it to beetle colonialization. In certain species, the aggregation pheromone is only attractive until a certain number of animals is reached, and becomes repellent in



Figure 2. Left: Lima bean *Phaseolus lunatus*. Public domain image. Middle: Lima-bean-eating Two-spotted Spider Mite (*Tetranychus urticae*). © J. Holopainen, image reproduced with permission. Right: Spider-mite-eating predatory mite (*Phytoseiulus persimilis*), called by the beans. © Mick E. Talbot, image reproduced with permission.

character when too many individuals aggregate — preventing starvation of the beetles who are already here. The aggregation pheromone of the bark beetles also attracts parasitic wasps who parasitize the adult beetles.

Infochemicals seem to be as complex as necessary and as simple and less diverse as possible: infochemicals released by plants recruiting predators of their herbivores share a common molecular structure, whereas sex pheromones are highly species specific to avoid mating mistakes resulting in potentially hybrid offspring.

Further important infochemicals are trail-marking pheromones, e.g., in army ant colonies that consist of up to 20 million blind individuals who communicate via chemical and tactile stimuli, and territory-marking pheromones that are for example used by desert ants when they mark insect carcasses “as their own”. These ants do not use trail-marking pheromones, but orient themselves with the help of the polarization of the skylight and further cues (Karman *et al.*, 2012).

One story that might be interesting to follow up regarding communication between plants and animals is what colleague Alfonso Donnarumma told the author of this chapter about goats: “A friend of mine told me long ago something like that; goats, eating some plants, use a guerrilla-type strategy, that means hit and run,

because they were aware of the reaction of the plant. For this reason, he told me, the goats were immune to neoplastic diseases (cancers)."

Harari and Sharon's chapter has synergies with Chapter 5 "Cybernetic embryo" by Gordon and Stone (Gordon and Stone, 2016) regarding embryo development and Chapter 6 "Superfast evolution via trans- and interspecies biocommunication" by Gebeshuber and Macqueen (Gebeshuber and Macqueen, 2016) regarding the competition of males with other males for mating with females. For synergies of Chapter 9 with further chapters see Tables 1, 2, and 3.

Chapter 10 Alin Finkelshtein, Alexandra Sirota-Madi, Dalit Roth, Colin J. Ingham and Eshel Ben-Jacob: *Paenibacillus vortex* — A bacterial guide to the wisdom of the crowd

The chapter by Finkelshtein and co-workers (Finkelshtein *et al.*, 2016) deals with the social bacterium *P. vortex* and its communication strategies. This bacterium has two subpopulations, termed builders and explorers. Builders have less flagellae, reproduce fast, and mainly live in the center of the colony. Explorers have multiple flagellae, and explore new grounds for a colony to potentially live on. *P. vortex* is a social, motile, pattern forming bacterium. It has an exceptionally high number of communication related genes. Its two subpopulations allow an adjustment to other microorganisms, namely fungi. Fungi bridge air gaps with their mycelia, and allow bacteria to traverse these and colonize new niches. *P. vortex* cooperatively forms complex colonies with elevated adaptability — the colonial patterns are collectively engineered according to the environmental conditions. *P. vortex* uses quorum sensing. It contextually interprets chemical messages and formulates appropriate complex responses. This allows exchange of information across colonies and species (quorum sensing of competitions is inhibited).

Bacterial linguistics refers to structural aspects of communication, corresponding to the structural (lexical and syntactic) linguistic motifs, and not semantic (pragmatic) aspects. Cognition is communication based; colonial self-organization forms multicellular super-organisms. Bacteria glean information from

both the environment and neighboring bacteria. They use transduction networks and genomic plasticity, collectively creating the colony and maintain its integrity by sharing interpretations of chemical cues and exchanging chemical messages. The colony can thereby alter its structure and make decisions. These bacteria show social intelligence and fundamental (primitive) forms of cognition.

Paenibacillus shows advanced defensive and offensive strategies and has various genes that are important for agricultural, medical and industrial applications, such as its capability to fix nitrogen and degrade various polysaccharides. *P. vortex* and *P. dendritiformis* can develop colonies that behave much like a multicellular organism, with cell differentiation and task distribution.

P. vortex is a social microorganism with remarkable complex and dynamic architectures. It shows collective motility and foraging swarms that have an aversion to crossing each other's trail and that collectively change direction when food is sensed. Swarms can split and reunite again.

Flagellae are entwined with those of the near neighbors, and their velocity can be more than 1 cm in an hour. When grown in liquid, they lose both flagellae and motility.

The social intelligence of the species shows in an individual's capacity to perceive and understand the environment and to respond to that understanding in a personally and socially effective manner. They develop knowledge based on their experiences, influencing the development of their progeny. Bacterial social intelligence can be estimated by their ability to communicate, sense their environment and adapt accordingly. Measured in bacterial IQ, *P. vortex* has the highest IQ score.

Ancestor bacteria can influence progeny in ways other than by stable mutations. Subpopulations of builders and explorers occupy different locations in the colony: the builders are in the central parts, whereas the explorers are localized to the vortices.

Each morphotype is capable to convert to the other and has a different stability. While builders are stable (without explorers) only for eight hours, explorers remain stable for days to weeks as

long as they are kept in liquid culture. Both subpopulations eventually convert to the mixed culture composition.

Explorers have resistance to antibiotics and a decreased reproduction rate. They have hyperflagellation and are highly motile, actively communicating with their environment. The colony sends explorers to seek for new and favorable niches for colonization.

The swarm shows intelligence: they transport non-motile asexual fungal spores and benefit from the fungal ability to bridge air gaps. About two to nine bacteria capture the spores with 6 to 30 flagellae. This capturing shows specificity — only a certain type of fungal species is transported. The benefit for the spores is large motility at high velocity; the benefit for the bacteria is the crossing of air gaps that generally represent a significant barrier to bacteria.

When reading Finkelshtein *et al.*'s chapter the author of this foreword was especially intrigued by the fact that bacteria carry the spores of fungi with them, which then, when growing, allow them to cross air bridges (Fig. 3). It caused her to write the public outreach text given below:

“****Living bridges, built by men — and friends of social bacteria****

Paenibacillus vortex is a social, motile, pattern forming bacterium that establishes colonies that respond cooperatively to challenges

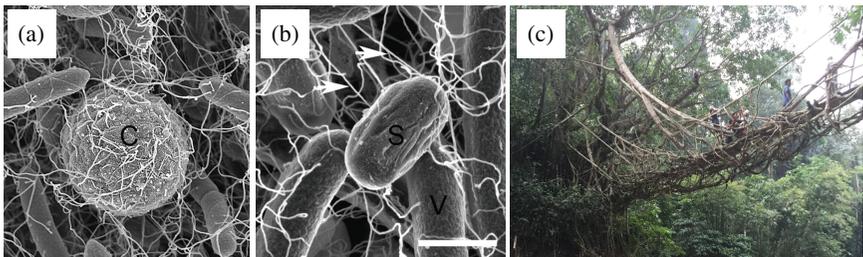


Figure 3. Left: *P. vortex* bacteria transporting fungi spores (Ingham *et al.*, 2011). Their flagellae selectively bind to one certain spore type. Scale bar: A, 3 μm ; B, 1 μm . Right: Living bridge in Indonesia. © 2015 Ille C. Gebeshuber, image reproduced with permission.

in complex environments. It exists in two subpopulations, the builders and the explorers. The builders reproduce and mainly live in the center of the colony, whereas the explorers reach out, and look for new places to live in.

The explorers have various whip-like structures that allow them to move, and on their journeys, they take cargo: spores of fungi (Fig. 3). Two to nine bacteria jointly carry one of these spores on the journey. They need them when air gaps block their way: the bacteria alone could not cross the gap, but when the fungi grow there, the bacteria can simply cross the gap on the fungi. So they carry the “seeds” of living bridges with them (reminds me of the living bridges (Fig. 3) that the people in Indonesia and India build across rivers, from ficus trees, which are, when small, bent across the gap, and woven back and forth, until some decades later people can cross the gaps over the living bridges, see photo). The advantage of the fungi is a dispersal that is about 40 times faster than without being carried around by bacteria friends.

Researchers have established bacterial linguistics of this species, referring to their structural aspects of communication, corresponding to the structural (lexical and syntactic) motives. They form multicellular super-organisms, who obtain information both from the environment and neighbouring bacteria. They collectively share interpretations of these signals, and exchange chemical messages. Based on joint decisions they alter their structures. They have social intelligence, and fundamental (primitive) elements of cognition.

The middle image shows bacteria transporting a fungus spore (only the spore of one certain fungus is easily transported by these specific bacteria, there is a glue between these two that glues only one certain type of bacterium to one certain type of spore — wow!! Imagine such a glue for the separation of materials in waste — one for each metal, one for each type of plastic, one for wood, one for paper, one for organic compostable materials, etc.).

The middle image of Fig. 3 shows bacteria transporting a fungus spore.

The right image of Fig. 3 shows a living bridge in Indonesia.

For synergies of Chapter 10 with other chapters see Tables 1, 2, and 3.

Chapter 11 Cristiana Sbrana, Alessandra Turrini and Manuela Giovannetti: The crosstalk between plants and their arbuscular mycorrhizal symbionts: A mycocentric view

There were various fascinating aspects that the author of this foreword experienced when moving from the little central European country Austria to tropical South East Asian Malaysia. One that still startles her is the difference in the concept of a tree in these two regions of the world. In Austria, a tree is seen as one tree. Sometimes, there are bird nests on the tree, and sometimes, ants and squirrels run up and down. But that is essentially it. In Malaysia a tree is an organism that is host to many other organisms. There are ferns living on trees, lichens, orchids, bromeliads. There are ants on the tree, and squirrels, and flying foxes and bats, and lantern bugs, and the occasional sun bear. Each of the giant rainforest trees is a multilevel entity, home to hundreds of different species — untamed and unmanicured. Similarly unidirectional was her view of roots. *“A root is something that branches finer and finer, and that takes up nutrients from the soil, nutrients that are dissolved in water. There is no place for fungi on roots. If I see fungi on roots, the tree rots, and the fungi are a sign of death.”* This her view was flipped over in 2013 on her visit to Peter Goldsbury in New Zealand. He told her about the intimate relationships of plants with root fungi. Symbiotic relationships seem to occur more often in plants than previously assumed.

When reading Sbrana *et al.*'s Chapter 11 “The crosstalk between plants and their arbuscular mycorrhizal symbionts: a mycocentric view” (Sbrana, Turrini and Giovannetti, 2016) the author of this foreword was especially intrigued by the fact that symbioses of plants and fungi seem to be much more common than previously assumed (Fig. 4). It caused her to write the public outreach text given below:

*“***Plant friendship****

My dad has a great hand for plants (as opposed to Mark and myself). What you can see here is a two-year-old pine tree baby, bred from the seed from our Italy holiday, and a young silver leaf



Figure 4. Friendship between silver leaf and pine tree. © 2015 Ille C. Gebeshuber, image reproduced with permission.

(a favourite plant from my childhood, also known as Jew's shilling). The silver leaf plant was sick and small, and not happy at all, until its leaves started to touch the pine needles. They became friends, and need and support each other, and ever since they touch each other, the silver leaf is strong and beautiful, and grows well. My father sees such relationships in plants."

Many plants live in symbiosis with root fungi that provide them with valuable Phosphorus and further chemical elements while the plants provide the fungi with complex carbon compounds products that the fungi cannot produce by themselves. This symbiotic relationship is initiated by complex chemical communication between the host plant and the fungi. 80% of land plants live in such symbiotic relationships with arbuscular mycorrhizal fungi (which are organisms that can be viewed as living fossils).

Plants that live in symbiosis with such fungi need less fertilizer and less pesticides, and have enhanced nutrient uptake. The arbuscular mycorrhizal fungi need the contact with a host plant to complete their life cycle. In the absence of a host plant the growth of fungal germlings is arrested after three weeks and — following a signaling cascade — the protoplasm is retracted close to the mother spore.

Multifold signals of different nature act at different steps of the interaction between fungal symbionts and host plants. There are various interdependencies between host plants and arbuscular mycorrhizal fungi, such as some stimulatory signals and/or inhibitory factors in the fungus that are regulated by the host plant. Already before physical contact pre-contact recognition events from both sides enable switching of the fungi from the asymbiotic to the pre-symbiotic stage. Physical contact is established with the formation of an appressorium, a minute cell that presses onto the plant root, injecting a peg into the root, thereby establishing physical contact. The establishment of appressoria is the key sign of fungal recognition of host plants. Host plants react “friendly” to appressoria formation, whereas plants that are either no host plants of the arbuscular mycorrhizal fungi or that have certain genetic mutations would start defence responses, trying to forcefully stop the physical contact between the arbuscular mycorrhizal fungi and the root.

The symbiont and the host cross-talk during cell-to-cell interactions. After the differentiation of appressoria, the arbuscular mycorrhizal fungi colonize host roots forming intracellular and intercellular hyphae, vesicles and arbuscules. Arbuscules are structures inside the host cells, allowing for nutrient exchange, membrane biogenesis and metabolism, cell wall reorganization and hormone balance. Despite the importance of nutrient exchanges in the symbiosis, where partners offering the best rate of exchange are rewarded, little is known on the mechanisms that regulate such processes. The exchange of Carbon for phosphate is tightly linked and requires both fungal and plant control.

In the presence of non-host plants, fungi behave different. Why some plant species cannot establish symbiotic relationships with

arbuscular mycorrhizal fungi is poorly understood. Many such plants have inhibitory compounds reducing fungal growth. Interestingly, non-host plants that are grown in the presence of a mycorrhizal companion plant (or nurse plants) often show variable extent of root colonization.

The establishment of a functional arbuscular mycorrhizal symbiosis is the outcome of multifold signals of different nature, acting at different steps of the interaction between fungal symbionts and host plants. Various plant and fungal genes are activated during symbiosis establishment.

For synergies of Chapter 11 with other chapters see Tables 1, 2, and 3.

Chapter 12 Douglas William Darnowski. Attraction of preferred prey by carnivorous plants

Chapter 12 “Attraction of preferred prey by carnivorous plants” by Douglas William Darnowski presents a nice overview of carnivorous plants and some of their ways to communicate with their prey (Darnowski, 2016).

Darnowski describes how carnivorous plants attract preferred prey. Carnivorous plants thrive in nutrient-poor habitats, such as heavily weathered soils with low abundance of Nitrogen and Phosphorus. Placed in a habitat with more abundant nutrients, most carnivorous plants are quickly outcompeted by non-carnivores and perish. They lure their prey via odors, rewards and bright markings to their site, and then trap and digest them, with significant ecological benefit derived from this (Adamec, 2011). Many plants readily absorb material placed on their surfaces, especially leaves. The author proposes a new index, the prey preference index (PPI), to describe such behavior. Carnivorous plants use deceptive communication via visual, olfactory and taste signals with their prey — they are liars! With their pollinators they communicate non-deceptively. Traps from carnivorous plants can be active or passive. Digestion happens via enzymes; some plants wait to produce these enzymes until they are sure that prey has been caught well enough and escape is prevented.

The wild tomato is a plant species that might be on the way towards becoming a carnivorous plant. Carnivorous plants use signals according to the abilities of their intended prey. Some use UV markings, similar to the nectar guides in flowers (Fig. 5). Some pitcher plants use a nectar reward to draw prey to themselves. Some plants do not directly digest the insects they catch, but use another species to prepare their food: *Roridula* plants have sticky epidermal hairs that are resinous and therefore hydrophobic. The water-based enzymes cannot readily digest any caught insects. Inside the *Roridula* plant live bugs that are not caught by the sticky resin, eat the trapped insects and provide the plant with especially rich nutrient mixtures in their faeces.

In a similar way, the bird toilet pitcher plant serves as ideal perch for tree shrews and birds, whose faeces is rich in N and P. The new mathematical index proposed by the author is termed PPI; it helps in identifying deceptive communication in plants.

When reading Darnowski's Chapter 12 "Attraction of preferred prey by carnivorous plants" the author of this foreword was especially intrigued by the fact that carnivorous plants signal to their prey in fluorescent signals (Fig. 5). It caused her to write the public outreach text given below:

"Plants communicate with insects in a language that insects understand. Many insects see ultraviolet light (UV), and various plants show the insects by patterns that are only visible in the UV range where the nectar (and pollen) can be found (Figure 5). In this way, the plants stay inconspicuous for grazing mammals who might eat them, but are very attractive to pollinators.

And now comes the interesting twist: carnivorous plants use similar signals (Fig. 5), tricking insects who are up for a nice sweet nutritious meal into their traps, where they will be digested and incorporated into the plant (Kurup et al., 2013)."

For synergies of Chapter 12 with other chapters see Tables 1, 2, and 3.



Figure 5. Top: Flowers that appear uniformly yellow to humans have markings and nectar guides for insects, who can see in the UV range. The *Mimulus* flower photographed in visible light (left) and ultraviolet light (right) shows a nectar guide visible to bees but not to humans. © 1999 by Plantsurfer, image reproduced with permission. Middle and bottom: some pitcher plants trick insects with similar markings to their traps. Middle: *Nepenthes khasiana* pitcher peristomes with lids in white light. Bottom: Blue fluorescence emissions from *Nepenthes khasiana* pitcher peristomes and lids at UV 366 nm. © Rajani Kurup, Anil J. Johnson and Sabulal Baby, image reproduced with permission.

Chapter 13 Hans Slabbekoorn: Animal communication: Competition for acoustic space in birds and fish

We all know that birds communicate by sounds. Their singing attracts partners, or deters other birds, they make warning calls, etc.

What might be new to many is that also fish make sounds. For communication, e.g., in spawning choruses. Birds and fish face acoustic noise, from the living and non-living environment, and from anthropogenic sources.

Sound is an excellent medium to convey information in natural habitats in air and in water. Noise pollution influences communication by acoustic signals. In Chapter 13 (Slabbekoorn, 2016), “Animal communication: competition for acoustic space in birds and fish”, Hans Slabbekoorn treats bird and fish side by side in terms of signaling problems and solutions and thereby provides insight into general concepts and current gaps in our knowledge.

Birds hear in a similar frequency range as humans do (20 Hz to 20 kHz), with their best range in the 1–5 kHz range. Some pigeons are sensitive to infrasound, some birds use echolocation (on calls that are audible to people) and the male blue-throated hummingbird generates ultrasonic song components that are not audible to himself. We currently do not know why he is doing this (the ultrasonic parts of his song are not just harmonics of song parts in the audible range). It might be that he sends signals into a sensory universe that is remote from his own perceptions. Here, synergy can be established with the chapter on UV signals in lying pitcher plants (Darnowski, 2016), carnivorous plants that mimic signals of nectar plants to pollinators. Such facets are highly interesting aspects of biocommunication.

Songbirds sing different dialects in different neighborhoods, and each bird has its own vocal signature. Female birds can discriminate amongst almost identical song types sung by either their mate or his neighbor — such fine sensitivity to detail also means that ambient noise may prevent auditory detection or adequate recognition of relevant details.

The song learning process involves copying sound elements and ways of singing from conspecifics that modify the ontogenetic trajectory of individuals but also determine the dialectal pattern formation at the population level. Such phenomena yield cultural transmission and cultural evolution and allows parallels to cultures in general such as e.g., in non-human primates and human dialects and languages (synergy with Chapter 3 and co-cultural processes in Table 3).

Most fish hear in a much more restricted frequency range than humans do. They detect both underwater sound components, sound pressure and particle motion, and with their lateral line system can sense nearby sources of very low frequencies. Some eels hear infrasound, some shads hear ultrasound (up to 180 kHz). Fish use sound for orientation and predator-prey interactions, but many species also listen for the communicative sounds generated by conspecifics. 800 species of fish are known to generate sounds. Many fish have small repertoires and context-associated within-species variation, just like birds. Variety in fish sounds stands for many potential messages for individuals of the same species that are within earshot, just like in birds. Fish are able to locate sound sources. They may also be bothered by interference of auditory detection and recognition of conspecific signals or environmental cues.

There is a competition for acoustic space in air and in water, as background noise changes the signal-to-noise ratio: rain-induced noise can decline the signal range in air from 600 m to 100 m. At the seaside many shorebirds have piercing calls. There are noise-related modifications, and the evolution of better hearing is not primarily driven by acoustic communication but instead by relative noise levels in the environment.

Anthropogenic noise (sounds generated by human activities) is detrimental: there is a close link between ambient noise conditions and avian signal efficiency. Traffic noise has most energy in the low frequency range. Birds start to sing louder in noisy conditions, they sing louder on weekdays than on weekends, and in places where human activity starts very early, dawn choruses shift into the more quiet nocturnal conditions. In Leipzig, Germany, it was found that birds at the noisy ring road woke up more than five hours earlier than birds in the quieter urban forest. Birds also start to sing higher in frequency.

Human activities in, on or close to water also cause considerable elevation of natural ambient sound levels underwater. Anthropogenic noise may not only deter but also interrupt important activities such as courting, spawning and foraging, or disturb fish during migration. The fish sounds are mainly at low

frequencies, as is anthropogenic noise. Only a single case is known where fish adjust their sounds to anthropogenic noise, by increased pulse rate when exposed to noisy boat passages. Fish may also be able to generate louder sounds in response to elevated noise levels, but their moderate flexibility in terms of sound production and their limited range of hearing sensitivity may make spectral adjustments that would yield at least some masking avoidance less likely.

Acoustic signals are an excellent way to communicate in air and in water. Noise interference can be a challenge for fish and birds, since it has serious impacts on acoustic signal efficiency. Ambient noise influences the evolution of acoustic signals. More insight into the impact of anthropogenic noise will not only provide insight to animal vulnerability but also has the potential to raise awareness about the intrinsic beauty and ecological value of natural soundscapes in air and in water.

For synergies of Chapter 13 with other chapters see Tables 1, 2, and 3.

Chapter 14 Angela Machado Rocha, Fernando M. Palop, Maria Clara Melro and Marcelo Santana Silva: The contribution of biocommunication (BICO) to biomedical and tissue engineering: A tech mining study

Replacing damaged or dysfunctional body parts has a long history. 1954 the first kidney was transplanted, and in the 1990s, Dolly the sheep was cloned and first human embryonic stem cells were isolated.

The chapter of Rocha and co-workers (Rocha *et al.*, 2016) is a tech-mining study on more than 8,000 scientific papers published in the years 2003 and 2013 in an interdisciplinary field between engineering and the life sciences covering tissue engineering and regenerative medicine (TERM) as well as biomaterials.

In TERM, communication processes are of utmost importance: Human organs and cells communicate (crosstalk) with each other directly without the interference of the central nervous system. Cells can only multiply when growth factor commands are given by way of protein molecules and peptides emitted by the nucleus.

Biomaterials are materials that are intended to be in contact and interact with a biological system, evaluating, treating, augmenting or replacing existing functions. Biomaterials must be biocompatible. “Cell Biology and Biochemistry” and “Molecular Biology” are the top categories represented in 27% of the publications evaluated in the study. How cells naturally interact with each other is increasingly investigated in co-cultural processes, which are a simultaneous culture of different cell types. Stem cells are cells that can differentiate in various potential directions. Their crosstalk with other cells in the human body influences their proliferation, migration, differentiation, apoptosis, etc.

Understanding communications of the cells and tissues in bodies is important for the development of tissue architecture and tissue regeneration.

Three categories of biomaterials are inert materials, bioactive materials and biodegradable materials. All of them communicate with the body in different ways. Factors such as nerve growth factors cross-talk with cells, and can activate different answers by the cell nucleus related with its cell fate (differentiation, apoptosis, multiplication, etc.). The interaction of biomaterials with extracellular matrices influences this communication, and can influence the decision on cell fate. The extracellular matrix provides structural and biochemical support to the surrounding cells. It serves an important role in tissue and organ morphogenesis and in the maintenance of cell and tissue structure and function.

The relation between biomaterials and the nanoscale is intrinsic — small patterns and structures on the biomaterials can have a “loud voice” in cross-talk with cells and tissues.

Further important materials are bioceramics. Its three categories are inert, active and degradable or reabsorbable. Bioceramics can be found in the form of microsphere layers or thin coatings on metallic implants with a porous network and compound polymer components (composites). The most successful classes of bioceramics are Calcium phosphate biodegradables and alumina, which is highly inert and resistant. The body tries to isolate foreign bodies by forming a layer of non-adherent fibrous tissue around the implant where possible.

Biopolymers are suitable as biomedical material due to their structural similarity with tissue components. This structural similarity is important in biocommunication. The three categories of biopolymers are proteins, polysaccharides and polynucleotides. They perform certain functions due to their molecular configuration, composition and organization. The most widely used biopolymer is collagen — it is a key material for fibers, sponges and scaffold matrices.

Biomaterials implanted into the body induce a response called foreign body reaction. Macrophages fuse to form multinucleated giant cells, which often persist for the life of the implant. In its final stage, the foreign body reaction involves walling off the device by fibrous collagen. Novel smart materials shall in the short term minimize this foreign body reaction and promote normal wound healing. In the long term they should actively participate in the regeneration of damaged tissue and respond to stimuli from their environment. Interactive smart biomaterials such as electrospun fibers or hydrogels from peptides, collagen and further materials imitate extracellular matrices in order to stimulate cellular invasion, adhesion and proliferation. Biological approaches that focus on the repair and restoration of the structure and function of tissues are necessary.

Regenerative medicine aims at creating or regenerating new biological tissues, based on pre-existing tissues. The three pillars for Tissue Engineering are scaffolds, cells and growth factors. TERM is concerned with the regeneration of organs and living tissues through tissues of the patient. The cells grow in a scaffold, in the presence of growth and differentiation factors (see also Gordon and Stone, 2016).

Today, it is impossible to build a large organ three dimensionally where all cells are in direct contact with the nutrient solutions.

Important characteristics of the materials for the construction of the scaffold are biocompatibility, having a surface that allows cells to adhere, proliferate and migrate to the scaffold, biodegradability, sufficient mechanical properties to maintain the structure and function immediately after transplantation and structural and functional properties that allow extracellular-matrix biomolecular transfer signals between cells.

The implant material must not inhibit the biological functions of the host tissue. This is sometimes achieved by changes in the nanotopography of the scaffold surface with the aim of controlling and directing physical and molecular signals that govern cell behavior.

Bones and cartilages are the mainstream applications of TERM research. Better understanding of the extra- and intracellular communication mechanisms open important advances and new approaches in cancer treatment and tissue regeneration. There is an increasing interest for biocommunication in TERM, including investigations of proteins and their role in cell growth.

3D printing and patterning of scaffolds, and bioprinting, are new trends in TERM. A big challenge is still how to emulate blood vessels in the bioprinted tissue.

For synergies of Chapter 14 with other chapters see Tables 1, 2, and 3.

Chapter 15 Noga Gershoni-Emek, Eitan Erez Zahavi, Shani Gluska, Yulia Slobodskoy and Eran Perlson: Communication languages and agents in biological systems

When reading Gershoni-Emek *et al.*'s Chapter 15 "Communication languages and agents in biological systems" (Gershoni-Emek *et al.*, 2016) the author of this foreword was especially intrigued by the fact that neurons can of course be viewed under different aspects than just conducting action potentials (Fig. 6). It caused her to write the public outreach text given below:

"I have a beautiful blowpipe (Fig. 6) I once bought from Ms. Reita Rahim, from Gerai OA, a volunteer-run, nomadic stall selling crafts by the Orang Asal (indigenous minorities) of Malaysia; 100% of sales is paid to the named artisan. One of her friends from the indigenous communities in Malaysia made it. The poison that is used with blowpipes in Malaysia is not from frogs, as it is used in South America, but from poisonous latex from the Ipo tree. I once was shown such a tree by the Orang Asli here in Malaysia, impressive.

The poisonous latex contains chemicals that lead to arrest of the heart, and cause death. The poison of poison dart frogs attacks the



Figure 6. Left: Artists impression of firing neurons. Permission pending. Right: Orang Asal from Malaysia with blowpipe. Image © Sarawak Tourism Board, Malaysian Borneo. Image used with permission.

central nervous system, arrests muscles and finally breathing, leading to death. Have you ever thought how such poisons work? They are chemicals talking to our bodies. Which brings us again to the field of biocommunication, this time at a neural level — the level of the single nerve fibres.

Electrical signals travel along nerve fibres, but this is not all: there are also various chemical signals, that give the fiber information about its surrounding, about its status (Is there a damage somewhere? An injury? Is the nerve fiber very young and still needs to grow? In which direction? And connect with whom? Where?) Chemical signals are sent back and fro along and inside nerve fibres, and in many cases, chemical signals that are important during growth are not produced anymore when the person is grown up. Unless they have neurodegenerative diseases.

Sometimes the neural language needs to be translated, into a language that for example the muscle can understand. At the neuromuscular junction, the electrical signal that has travelled along one of your motor neurons from your brain to your little toe is translated into a chemical signal.

Neurons are masters in biocommunication, they travel through the whole body, meeting so many different environments, and talking so many languages. Understanding and speaking this language in typical and atypical situations (pathophysiology of neurological and psychiatric disorders) is important for basic knowledge, but also to be able to help people with neurodegenerative diseases.”

Neurons communicate with their environment as well as with the cell's different compartments: soma, axon and synapses. They are highly polarized cells with axons that are many orders of magnitude longer than the diameters of their bodies. Neuron communication comprises action potentials, as well as protein and RNA trafficking mechanisms in order to regulate the specific task of spatial communication. Axonal transport mechanisms to and from the neuron body takes place on kinesin and dynein "highways" in the cell. Altered actions in neurocommunication and spatial changes in the cellular balance of survival versus stress/death signals contribute significantly to the rapid onset of neurodegeneration, and suggest a non-cell autonomous mechanism in neurodegenerative diseases.

Signaling in neurons includes trafficking of neurotrophic factors, which are growth factors that act specifically on neurons, such as glial cell-derived neurotrophic factors (GDNF) signaling that supports the survival of motor, dopaminergic, sensory and sympathetic neurons. Neuronal death signaling such as tumor necrosis factor (TNF) and guidance factors are means for neural communication.

A neuron's diverse microenvironment contains secreted negative signals that can lead to synapse disruption, axon pruning and neuronal death: physiological processes in the developing embryo, but pathological in adults.

Neuronal receptors are localized in a spatiotemporal way at the plasma membrane. Rafts, some tens of nanometers long, comprised of lipids and proteins, are microdomains that contribute to spatiotemporal signaling in neurons. Microtubules can regulate spatial localization and function of receptor domains.

The organization of neurotrophic factors in neurons is sophisticated, with lipids, proteins, actin and microtubules as well as endocytic and transport machinery working together to ensure signaling takes place at the right place, time and intensity.

Also local protein synthesis is of paramount importance in neuron communication. mRNA allows to respond locally to stimuli that affect general cell function. Both axons and dendrites respond to extrinsic cues in order to regulate growth, navigation and

synapse formation — as well as for maintenance and repair. mRNA is in a translationally repressed state until the arrival of a triggering signal — such as a guidance cue, or injury.

The growth cone is a specialized structure at the tip of a growing axon. During growth and path finding, it responds to various stimuli from the environment providing guidance information. Locally synthesized proteins help with this.

Another interesting aspect of communication in a neuron is how the neuronal cell body receives information about an injury from distant lesion sites in the axon. Injury signaling activates the nerve regeneration process.

There are thousands of different mRNAs in neurons. Also microRNAs are important — they hold key roles in gene regulatory networks, and their dysregulation plays a role in the pathophysiology of neuronal and psychiatric disorders. Exosomes transfer miRNAs between cells, ensuring horizontal transfer of genetic information.

At the neuromuscular junction, motor neurons converse with the skeletal muscle. This happens quickly and reliably, ensuring precise control of skeletal muscle contraction.

For synergies of Chapter 15 with other chapters see Tables 1, 2, and 3.

Chapter 16 E. Sue Rumbaugh, Itai Roffman, Elizabeth Pugh and Duane M. Rumbaugh: Ethical methods of investigation with *Pan/Homo* bonobos and chimpanzees

For the author of this foreword the most amazing aspect of Rumbaugh's Chapter 16 "Ethical Methods of Investigation with Pan/Homo Bonobos and Chimpanzees" (Rumbaugh *et al.*, 2016) is when they describe the arousal of a joint language that is understandable for all species joining the game in the joint society of humans and apes, living together in a forest, in semi wild conditions. ICG heard that apes have language, and that they communicate with each other not just on present, but also on past and future events, as well as feelings, hopes and expectations. We know the same for people. But that, when the groups live together, in a

non-laboratory setting, a new language arises, is stunningly touching and beautiful.

Bonobos, humans and chimpanzees share 99% of our genome. Apes are generally greatly underestimated. Chimpanzees and bonobos are sentient beings that are self-aware, capable of symbolic thought, and can construct mental worlds, social rules and cultures. Rumbaugh and co-workers address aspects of communication with these beings, and ethical methods of learning from such highly cultural species. Most of the time apes used in such studies are in captive environments that are devoid of choice, freedom of expression, the execution of free will, and the right to self-determination.

Studies of how apes react in such an environment might also give important input regarding how to curb human aggression when people are kept in such tight and supervised conditions.

Behavioral and genetic data tell that apes belong to the human side of the man/animal dichotomy that still is very prominent in our mind. Apes, when reared in different ways, display radically different cognitive competencies. They show two types of using language: the first one is used for ritualistic communicative purposes (Hello, how are you) and can serve true social functions and promote social cohesion, regardless of whether the state of knowledge of the recipient is known or not. In the other type of language, however, the state of knowledge of the recipient is of paramount importance. This type of language can convey truly new information. Chimpanzees can communicate novel and appropriate information to each other, they can do so with intent and they can display sensitivity to the knowledge state of the recipient. Chimpanzees and bonobos who are reared in the right cultural environment, in loving and stable family settings, have a theory of mind, i.e., they understand that others can have knowledge that is different from one's own knowledge. Most other animals do not think about the state of mind of the others, but co-feel, co-sense and co-experience with them, e.g., through mirror neurons. Chimpanzees recognize themselves on television and distinguish between taped and real-time videos of themselves. An entity that cannot see itself

as others see it lives in a distinctly different world. Non-sentient beings are time locked to the desires of the moment. Chimpanzees not only recognize themselves in a mirror, they also check with the help of a mirror how lipstick looks on them — they are not only interested how it feels or tastes. Apes are conscious about being conscious.

The emergence of the sentience of selfhood, a concept of moral action and an understanding of the theory of mind require a socio-cultural world. Without such a world, humans and apes fall back into an animal like existence. Culture plus biology are important to seed reason, reflective thought, purposeful action and planning. This emergence is on the verge of vanishing if not passed on successfully to the next generation.

Very few researchers have the privilege to work with linguistically competent apes. Bonobo Kanzi is one of them. The chapter contains the highly interesting and unique report of researcher Itai Roffman (IR) who grew up with his brother Orr who only started to talk at the age of 14, when he watched videos of communicating apes. Orr only then started to share his inner thoughts. Due to his childhood experience with five-year younger brother Orr, IR had a different, very open way to communicating with chimpanzees and bonobos. Their conversations were bilateral, and contextually appropriate. They only took place when they felt comfortable with each other. Only if people really live in their world, these apes communicate in a true way. Arrogant students who do not appreciate them as beings and who bribe them to collaborate in laboratory setting experiments obtain wrong data. Kanzi was very careful in what he shared, with whom he shared and when he shared. Kanzi and Orr talked in three word sentences, sharing inner feelings, stories, ideas, wishes and interests. When IR was accepted into the bonobo community, he had to go through some kind of initiation ceremony. Orr found his own language with the help of the bonobos. Before watching the videos, miming language capacities and the complex statements made through the use of gestures, glances and joint contextual reference and knowledge were absent. Orr now could initiate — not by just doing, but by expressing his desires to

do so. A second breakthrough occurred when Orr watched a video of bonobos painting. His scribbles started to transform to geometric shapes to figurative forms, and he could very well interpret bonobo paintings — at times better than the researchers. Art is a spatial, not a linear medium. IRs early life with Orr prepared him to be more sensitive to the communication of apes than others. They are creative, thinking, reasoning feeling beings capable of foresight, planning and moral action.

Humanness as we experience it does not exist outside of human language. This also holds for science. To study deep into the essence of language is to reach deeply into what it is to be human. Language seems to have appeared 40,000 years ago, whereas we achieved our physical forms 200,000 years ago. Perhaps our human language is the limit of our cognitive world. Only by jumping across cultural and linguistic boundaries can one's eyes be opened to the cultural blinders imposed by one's own rearing. We have almost no means of understanding any human who does not develop language in a normal manner unless we spend time with them while co-constructing dialogues co-filled with meaning. Any being capable of becoming conscious of being conscious has the potential for some form of truly symbolic language. Language is a symbolic/grammatical system of representational communication that functions to convey intention and meaning to its users.

Socio-cultural interactions initiate, force and perpetuate the acquisition of grammars in species with executive function control over their own conscious processes. Grammar arises with the desire and effort to make meaning of acts that remain incoherent and disconnected until they become linked by grammar and symbols. Grammar folds back upon itself and becomes reflexive. Grammar does not need to be taught — and so parents do not bother.

Both humans and bonobos focus on whom, what and where, but humans also focus on why, how and when. Bonobos less likely attribute personal causality to complex events than humans do. The human socio-cultural world does not map precisely onto the

socio-cultural world of a closely related species. In symbolic self-conscious beings, speciation is about co-constructing a conscious reality that all share via the operating system of a particular language. It is the lifting process — the extension of meaning beyond the here and now — that truly defines language. Creativity and imaginations seem to be uniquely hominid. Given stable and rich environments, apes and humans will turn their attention to an endless range of objects and activities. Humans and apes are clearly something apart from the rest of the world. Why this is so and what does this mean?

Gebeshuber and Macqueen write “*Members of the same species were found to differ dramatically in gene content: In a study by Welch et al. (2002) three E. coli genomes were sequenced. Less than 40% of the genome was common to all three bacteria!*”. On the other hand, the genome of bonobos, chimpanzees and humans is 99% similar. Perhaps various important aspects of a species are not stored in the genome, but in another space. Humans, bonobos and chimpanzees construct symbolic world and moral systems.

The two chimpanzees Sherman and Austin developed a gestural symbolic language similar to the twin languages sometimes reported for co-reared twins.

Wild chimpanzees are sentient self-reflexive moral beings with complex non-material cultures and symbolic systems. Language builds new interpretations and creative combinations through shared exchanges across time and during development. Matata, Kanzi’s mother, was caught in the wild, and came to the laboratory already with knowledge of the culture of wild bonobos. She clearly had some form of language. Culture is very important for the development of the mind. Human culture and bicultural rearing of young bonobos in groups comprising older bonobos and humans over-rides the supposed absence of language. Even though our species is known for its vocal emulation skills, it is impossible to emulate bonobo speech with the precision pitch control they employ. (Potential way to address this: Ask a Thai student to help — the Thai language very much focuses on pitch.) Matata did not communicate with the humans, but she would ask Kanzi or some other

language apt ape to convey requests to people. She realized that people could not understand her, but that Kanzi could, and that he could act as translator. Kanzi and friends translated various information for Matata, most often about danger, food, travel, visitors, or unusual events.

In a group of people and bonobos that used to live in the forest together, the human companions were not caretakers, they were companions. Bonobos develop vocal utterances, different from Matata's language, when together with such a group in the forest. This language was one that was beginning to be comprehensible by human members. Language appeared to drive all other changes, and the apes who spoke it became increasingly diverse, and sentient beings were suddenly emerging.

Human groups have always separated themselves across time and they continue to do so on the basis of epi-cultural markers such as speech, dress, food, etc. Any group of symbolic self-sentient beings will naturally become uncomfortable when the behaviors they extend to others fail to meet with their anticipated results. Humans have historically found it difficult to look across cultural borders and to see humanity as one entity, even less so all that is alive.

In *Pan/Homo* beings, the bonobos who were reared with people and older bonobos in the forest, symbolic meanings literally jumped into existence everywhere.

Formal tests — which do not involve real world communications — will cause bonobo meanings to be withdrawn instantly. Language fundamentally alters the hardware of the modern chimpanzees and bonobos. In the course of the experiments, their bodily form changed, and became more human-like. Culture is the ratchet that made man from ape. If we define culture as the glue which allows self-conscious beings to make meaning of each other's actions and communications by binding together acts that co-mean, ape cultures may well be found more similar to ours than we have previously acknowledged. The sudden (in evolutionary terms) onset of language, speech, music, art, architecture, writing, metallurgy, centralized government, etc., cannot be explained by

standard scientific models of evolution. All the seemingly vast differences between living groups of humans are a result of culture. Kanzi could understand fire, kinship and cooking. Could he perpetuate this knowledge in the wild? (Potential issues that can arise: what if he finds out that there is a way to get rid of mean people by setting their house on fire? What if animals suddenly developed an idea of their strength? And started self-defence against people?).

Humans have increased susceptibility to cancer. Apes normally do not get cancer that metastasizes. Modern genetics finds that the gradualist argument is being undermined by genetic data on species other than apes and human beings. The discontinuity between ape and man is more on the psyche level. The symbolic mind is generating the world around it through an infinite myriad of cultural lenses. The human genome displays far less variability than that of any living apes. *Homo sapiens* went through an evolutionary hourglass approximately 70,000 years ago (Petraglia K *et al.*, 2012), when our numbers were reduced to between 2,000 and 15,000 individuals. Inbreeding seems to be a particular problem in the human species.

In humans, behavior can be completely freed from the environment and possibly even from genetic control by the power of symbolic thought. Changes in behavior affect gene expression directly. Scientists are only now beginning to think about the true behavior/biology relationship. We long for a more precise model to explain the integrated behavior of life forms across time on the planet (synergy with Chapter 9, Harari and Sharon, 2016). Epigenetic factors have no finite number. Genes can travel for millions of years doing nothing and reappear as active again, when conditions change. Populations change when they are in contact with different environments, and when they undergo behavioral change. Science has still not found the answer in selectionism and mutation. The Darwinian model provides scientists with a mechanistic description of what would otherwise be a totally mysterious process. In natural settings, all genes and all species are constantly co-evolving within a system that is itself self-evolving. Epigenetics challenges

the established theories on selection processes. The genome is a tool-kit that has evolved in order to allow the organisms to differently manifest across geological eras of time. The genome represents its history (synergy with Chapter 6, Gebeshuber and Macqueen, 2016, regarding communication with the past and permutation by recession).

Bacteria come with a set of genes designed to do many different things in different environments. Genes can be activated by internal gut biota — diet is a critical factor (synergy with Chapter 6, Gebeshuber and Macqueen, 2016). Chimpanzees seem to be changing rapidly at the genetic level, while we are not.

Chapter 17 Toni Frohoff and Elizabeth Oriel: Conversing with dolphins: The holy grail of interspecies communication?

Chapter 17 deals with the communication of dolphins with other animals and with humans. One extremely anthropocentric misconception is the “smile” of the dolphin — it has nothing to do with an emotional expression, but is a static feature of the dolphin’s jaw. Dolphins are viewed as very positive by a major fraction of the population, and in many cases scientific paradigms merge with policy, politics, emotion and ethics. These sentient marine mammals have fascinated people since before Aristotle.

Toothed whales, including dolphins and orcas, demonstrate amongst the most sophisticated biocommunicative abilities of any animal. When studying their communication, various reductionist and mechanistic approaches need to be overcome, in a more expansive, multidisciplinary approach to biocommunication. The authors of Chapter 17 (Frohoff and Oriel, 2016) pledge for respectful research, on wild animals, to fully explore the collaborative relationship between humans and dolphins. “Respectful” refers to the fact that the wellbeing of the dolphins or other non-human animals takes priority over the success of the research. Furthermore, they stress the importance of positive co-habitation with dolphins from a multispecies, co-cultural context (fishing cooperatives, between

humans and dolphins, seabirds and dolphins, humans and seabirds and dolphins).

Dolphins communicate with acoustic signals, via visual posturing and movements, chemoreception, tactile exchange and the use of water for making bubbles and splashes (visual and acoustic signals). Free-ranging cetaceans show vocal learning and referential signaling. They have varied and rich social cultures, and use tools. Only female humans and whales live long past menopause, being “repositories of ecological knowledge and cultural wisdom”.

Similar to Rumbaugh *et al.* in the previous Chapter 16 (Rumbaugh *et al.*, 2016), Frohoff and Oriel stress personhood as an important concept when dealing with non-humans. Anthropocentrism and the resulting cultural assumptions are inherent in Western thought and activity, whereas in certain non-Western and indigenous cultures, the concept “person” may apply to animals, plants, humans, life systems, climatic events, landscapes and spirits (Ingold, 2000: 90).

For further synergies of Chapter 17 with chapters of this book see Tables 1, 2, and 3.

The next to last sentence of Chapter 17 shall also conclude the red thread through the single chapters of this book on biocommunication: “*Communicative connection points between species can all serve to build on a more thriving relationship between, and for, the benefit of humans and all animals*” (and, in principle, the whole biosphere).

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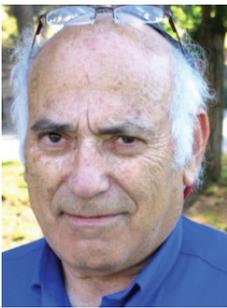
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