

## Review Article

# Bacterial collective behavior: role of mitochondria.

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Submitted on: 20 April, 2015. Accepted on: 10 June, 2015

**Key words:** Behavior, Mitochondria, Symbiosis

### Introduction

The pioneering biologist Konstantin S. Merezkhovsky first argued in 1909 that the little green dots (chloroplasts) in plant cells, which synthesize sugars in the presence of sunlight, evolved from symbionts of foreign origin. He proposed that "symbiogenesis" - a term he coined for the merger of different kinds of life-forms into new species - was a major creative force in the production of new kinds of organisms. A Russian anatomist, Andrey S. Famintsyn, and an American biologist, Ivan E. Wallin, worked independently during the early decades of the twentieth century on similar hypotheses. Wallin further developed his unconventional view that all kinds of symbioses played a crucial role in evolution, and Famintsyn, believing that chloroplasts were symbionts, succeeded in maintaining them outside the cell. Both men experimented with the physiology of chloroplasts and bacteria and found striking similarities in their structure and function. Chloroplasts, they proposed, originally entered cells as live food-microbes that fought to survive - and were then exploited by their ingestors. They remained within the larger cells down through the ages, protected and always ready to reproduce. Recent studies have demonstrated, however, that the cell's most important organelles - chloroplasts in plants and mitochondria in plants and animals - are highly integrated and well-organized former bacteria<sup>1</sup>.

### Symbiosis between bacteria and human

By playing this reverse game with bacteria, - Nature's fundamental organisms from which all life emerged - we should be able to learn about the very essence of our self. This is especially so when keeping in mind that the life, death and well being of each of our cells depend on the cooperation of

its own intelligent bacterial colony - the mitochondria<sup>2</sup>. Specifically, the understanding of bacterial natural intelligence as manifested in mitochondria might be crucial for understanding the meaning-based natural intelligence of the immune system and the central nervous system, the two intelligent systems we use for interacting with other organisms in the game of life. Indeed, it has recently been demonstrated that mice with identical nuclear genomes can have very different cognitive functioning if they do not have the same mitochondria in their cytoplasm. The mitochondria are not transferred with the nucleus during cloning procedures<sup>3</sup>. Namely, the assumption is that any organelle, our brain included, as well as any whole organism, is in principle equivalent to, and thus may in principle be mapped onto a universal Turing Machine - the basis of all man-made digital information processing machines. We argue otherwise. Before doing so we will place Turing's notions about "Intelligent Machinery"<sup>4</sup> and "Imitation Game"<sup>5</sup> within a new perspective<sup>6</sup> in which any organism including bacteria, is in principle beyond machinery<sup>7</sup>. This realization will, in turn, enable us to better understand ourselves and the organisms our existence depends on - the bacteria.

### The mitochondria

The idea is that the hardware can be self-altered according to the needs and outcome of the information processing, and part of the software is stored in the structure of the hardware itself, which can be self-altered, so the software can have self-reference and change itself. Such mechanisms may take a variety of different forms. The simplest possibility is by ordinary genome regulation - the state of gene expression and communication-based collective gene expression of many organisms. For eukaryotes, the mitochondria acting like a bacterial colony can allow such collective gene expression of their own independent genes. In this regard, it is interesting to note that about 2/3 of the mitochondria's genetic material is not coding for proteins. Genome cybernetics has been proposed to explain the reconstruction of the coding

DNA nucleus in ciliates<sup>8</sup>. The specific strains studied have

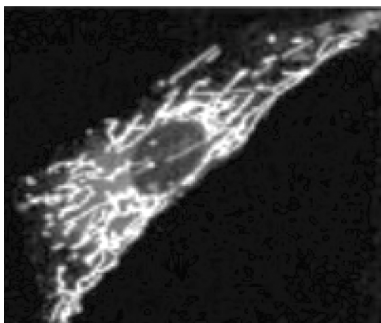
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two nuclei, one that contains only DNA coded for proteins and one only non-coding DNA. Upon replication, the coding nucleus disintegrates and the non-coding is replicated. After replication, the non-coding nucleus builds a new coding nucleus. It has been shown that it is done using the transposable elements in a computational process. More recent work shows that transposable elements can effectively re-program the genome between replications<sup>9</sup>. In yeast, these elements can insert themselves into messenger RNA and give rise to new proteins without eliminating old ones. These findings illustrate that rather than wait for mutations to occur randomly, cells can apparently keep some genetic variation on tap and move them to 'hard disk' storage in the coding part of the DNA if they turn out to be beneficial over several life cycles. Some observations hint that the collective intelligence of the intracellular mitochondrial colonies play a crucial role in these processes of self-improvement<sup>10,11,12</sup>.

In the prologue we quoted Margulis' and Sagan's criticisms of the incompleteness of the Neo-Darwinian paradigm and the crucial role of symbiogenesis in the transition from prokaryotes to eukaryotes and the evolution of the latter. With regard to eukaryotic organisms, an additional major difficulty arises from the notion that all the required information to sustain the life of the organism is embedded in the structure of its genetic code: this information seems useless without the surrounding cellular machinery<sup>13</sup>. While the structural coding contains basic instructions on how to prepare many components of the machinery - namely, proteins - it is unlikely to contain full instructions on how to assemble them into multi-molecular structures to create a functional cell. We all know that mitochondria carry their own genetic code. In addition, membranes, for example, contain lipids, which are not internally coded but are absorbed from food intake according to the functional state of the organism<sup>14</sup>.



**Fig 1. Confocal image of mitochondria**

within a single cultured rat cortical astrocyte stained with the calcium-sensitive dye rhod-2 which partitions into mitochondria, permitting direct measurements of intramitochondrial calcium concentration (courtesy of Michael Duchon).<sup>1</sup>

### Natural intelligence of bacteria

Bacteria have natural intelligence beyond machinery: unlike a machine, a bacterial colony can improve itself by alteration of gene expression, cell differentiation and even generation of new inheritable genetic 'tools'. During colonial development, bacteria collectively use inherited knowledge together with causal information it gathers from the environment, including other organisms. For that, semantic chemical messages are used by the bacteria to conduct dialogue, to cooperatively assess their situation and make contextual decisions accordingly for better colonial adaptability. Should these notions be understood as useful metaphors or as disregarded reality? Another example of natural intelligence game could be a Bridge game between a machine and human team playing the game against a team of two human players. This version of the game is similar to the real life survival 'game' between cooperators and cheaters (cooperative behavior of organisms goes hand in hand with cheating, i.e., selfish individuals who take advantage of the cooperative effort)<sup>15,16</sup>. An efficient way cooperators can single out the defectors is by using their natural intelligence - semantic and pragmatic communication for collective alteration of their own identity, to outsmart the cheaters who use their own natural intelligence for imitating the identity of the cooperators<sup>17,18</sup>. Today we understand that bacteria utilize cooperatively the principles of self-organization in open systems. Yet bacteria must thrive on imbalances in the environment; in an ideal thermodynamic bath with no local and global spatio-temporal structure, they can only survive a limited time<sup>19</sup>.

Even stronger clues can be deduced when social features of bacteria are considered: Eons before we came into existence, bacteria already invented most of the features that we immediately think of when asked to distinguish life from artificial systems: extracting information from data, assigning existential meaning to information from the environment, internal storage and generation of information and knowledge, and inherent plasticity and self-alteration capabilities<sup>20</sup>. Let's keep in mind that about 10% of our genes in the nucleus came, almost unchanged, from bacteria. In addition, each of our cells (like the cells of any eukaryotes and plants) carries its own internal colony of mitochondria - the intracellular multiple organelles that carry their own genetic code (assumed to have originated from symbiotic bacteria), inherited only through the maternal line. One of the known and well studied functions of mitochondria is to produce energy via respiration (oxidative phosphorylation), where oxygen is used to turn extracellular food into internally usable energy in the form of ATP. The present fluorescence methods allow video recording of the mitochondria dynamical

behavior within living cells reveal that they play additional crucial roles for example in the generation of intracellular calcium waves in glia cells<sup>21</sup>. Looking at the spatio-temporal behavior of mitochondria, it appears very much like that of bacterial colonies. It looks as if they all move around in a coordinated manner replicate and even conjugate like bacteria in a colony. From Schrödinger's perspective, it seems that not only do they provide the rest of the cell with internal digestible energy and negative entropy but they also make available relevant information embedded in the spatio-temporal correlations of localized energy transfer. In other words, each of our cells carries hundreds to thousands of former bacteria as colonial Maxwell Demons with their own genetic codes, self-identity, associated identity with the mitochondria in other cells (even if belong to different tissues), and their own collective self-interest (e.g., to initiate programmed death of their host cell). Could it be, then, that the fundamental, causality-driven schemata of organisms collective intelligence, as well as our natural intelligence, has been invented by bacteria - our natural intelligence is an 'evolution-improved version', which is still based on the same fundamental principles and shares the same fundamental features? If so, perhaps we should also learn something from bacteria about the fundamental distinction between our own Natural Intelligence and the Artificial Intelligence of our created machinery<sup>21</sup>.

### Bacteria as a turing machine

Accordingly it is now largely assumed that all aspects of life can in principle be explained solely on the basis of information storage in the structure of the genetic material. Hence, an individual bacterium, bacterial colony or any eukaryotic organism is in principle analogous to a pre-designed Turing machine. In this analogy, the environment provides energy (electric power of the computer) and absorbs the metabolic waste products (the dissipated heat), and the DNA is the program that runs on the machine. Unlike in an ordinary Turing machine, the program also has instructions for the machine to duplicate and disassemble itself and assemble many machines into an advanced machine - the dominant Top- Level Emergence view in the studies of complex systems and system-biology based on the Neo-Darwinian paradigm. The idea is that biotic self-organization involves self-organization and contextual alteration of the constituents of the biotic system on all levels (down to the genome)<sup>22</sup>. The alterations are based on stored information, external information, information processing and collective decision-making following semantic and pragmatic communication on all levels. For example, in the colony, communication allows collective alterations of the

intracellular state of the individual bacteria, including the genome, the intracellular gel and the membrane. For bacterial colony as an organism, all-level generativism requires collective 'natural genetic engineering' together with 'creative genomic webs'<sup>23</sup>.

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