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Social behavior of bacteria: from physics to complex organization

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Abstract. I describe how bacteria develop complex colonial patterns by utilizing intricate communication capabilities, such as quorum sensing, chemotactic signaling and exchange of genetic information (plasmids) Bacteria do not store genetically all the information required for generating the patterns for all possible environments. Instead, additional information is cooperatively generated as required for the colonial organization to proceed. Each bacterium is, by itself, a biotic autonomous system with its own internal cellular informatics capabilities (storage, processing and assessments of information). These afford the cell certain plasticity to select its response to biochemical messages it receives, including self-alteration and broadcasting messages to initiate alterations in other bacteria. Hence, new features can collectively emerge during self-organization from the intra-cellular level to the whole colony. Collectively bacteria store information, perform decision make decisions (e.g. to sporulate) and even learn from past experience (e.g. exposure to antibiotics) – features we begin to associate with bacterial social behavior and even rudimentary intelligence. I also take Schrdinger's' "feeding on negative entropy" criteria further and propose that, in addition organisms have to extract latent information embedded in the environment. By latent information we refer to the non-arbitrary spatio-temporal patterns of regularities and variations that characterize the environmental dynamics. In other words, bacteria must be able to sense the environment and perform internal information processing for thriving on latent information embedded in the complexity of their environment. I then propose that by acting together, bacteria can perform this most elementary cognitive function more efficiently as can be illustrated by their cooperative behavior.

PACS. 87.10.-e General theory and mathematical aspects – 87.18.-h Multicellular phenomena – 87.18.Fx Multicellular phenomena, biofilms – 87.18.Gh Cell-cell communication; collective behavior of motile cells

1 Introduction

The idea that bacteria are simple solitary creatures stems from years of laboratory experiments in which they were grown under artificial conditions. Under the demands of the wild, these versatile life forms work in teams, in association and dynamic communications [1–10]. They jointly, can live on many sources of energy and thermodynamic environmental gradients, from inside the Earth's crust and sulfuric Cityplacehot springs to icebergs. Bacteria are "smart" in their use of cooperative behaviors that enable them to collectively sense the environment. They use advanced communication, and lead complex social lives in colonies whose populations exceed the number of people on Earth.

Eons before humans, bacteria inhabited a very different Earth. As the earliest life form they devised ways to counter the spontaneous course of increasing entropy and convert high-entropy, inorganic substances into low-entropy, organic molecules [11–14]. They paved the way for other forms of life by changing harsh physical and chemical conditions on the Earth's surface and its atmosphere into the modern life-sustaining environment.

To face changing environmental hazards, bacteria resort to a wide range of cooperative strategies. They alter the spatial organization of the colony in the presence of antibiotics for example. Bacteria form complex patterns as needed to function efficiently. Bacteria modify their colonial organization in ways that optimize bacterial survival. Bacteria, we argue, have collective memory by which they track previous encounters with antibiotics [8,9,12–16]. They collectively glean information from the environment, communicate, distribute tasks, perform distributed information processing and learn from past experience [8,9].

The motivation of this article is to present the observations and the conceptual challenges posed by self-engineering of bacteria during colonial development. We review some of the exciting discoveries about the cooperative behavior of bacteria in colonies, guided by the

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assumption that they might shed new light on the foundations and evolution of Biocomplexity in general. The review is aimed at researchers from different disciplines – microbiology, biology, chemistry, physics, mathematics, and computer science. To make the presentation comprehensible to such a wide audience, we avoid the use of the specialized terminology of these different disciplines and limit the experimental and computational details.

When bacteria encounter environmental stresses, they employ a wide range of tactical behaviors to enable a proper adaptive response. One aspect of these behaviors has to do with the formation of complex spatial organization of the colony, with the bacteria forming different patterns as needed to better cope with the environment. For example, there is evidence that colony structure can enhance antibiotic survival rate, allowing enough time for genetic experimentation in search of resistance; exactly how this works in detail is only now being elucidated. Some recent findings show that colony structures are modified in the presence of antibiotics [8,9,12–16] in ways which might optimize bacterial survival and that the bacteria might be using a sort of short-term epigenetic memory which enables them to keep track of the previous exposures to antibiotic.

The bacteria utilize pattern-formation mechanisms that we have begun to understand only in last few decades [17–21]. In this article, I guide the reader through some of the remarkable patterns that have been discovered in one class of bacteria, Paenibacillus. These patterns have been created by mimicking hostile conditions in a laboratory setting by growing the colony in a Petri dish containing a very low level of nutrients and/or a hard surface (high concentration of agar gel) preventing normal bacterial motion and exposure to non-lethal levels of antibiotics.

Compared to pattern formation in non-living systems, bacterial self-organization involves an additional inherent degree of plasticity: the building blocks of the colony are themselves living organisms, each with internal degrees of freedom, internally stored information and internal assessment of external chemical messages [8,9]. These afford each bacterium to respond flexibly and even alter itself, by means of modifying its genetic expression patterns. One well studied example is the increase of competence (the ability of a cell to import snippets of DNA) under colonial stress [22,23]. It would therefore be interesting to learn whether competence and genetic transformation are related to colony structure. At the same time, efficient adaptation of the colony to adverse growth conditions requires self-organization which is enabled by bacteria communication that makes use of a broad repertoire of biochemical agents and intricate intracellular communication mechanisms involving, for example, signal transduction networks [24].

As we are discovering, bacterial communication-based cooperation encompasses colony morphogenesis, which includes coordinated gene expression, regulated cell differentiation and division of tasks. Collectively, bacteria can glean latent information from the environment and from other organisms, process the information, develop common knowledge, and thus learn from past experience [5]. The colony behaves much like a multicellular organism, or even a social community with elevated complexity and plasticity that afford better adaptability to whatever growth conditions might be encountered.

With the rapid development in genome sequencing, system level measurements of genome wide response based on DNA chips and new modeling investigations of gene-networks we are close to be able to relate the social behavior of bacteria with the gene level dynamics. As a step toward this challenge I start with extension of Schrdinger's thermodynamics considerations regarding "feeding on negative entropy". I present physics to cybernetic perspective of each bacterium as a hybridization of a *thermodynamic engine* that uses imbalances in the environment to do work, and a *machine* that uses this energy to act against the natural course of entropy increase, for the synthesis of organic substances. And third information-processing system is assumed for the coordination and synchronization of the engine and the machine [13]. In this picture a living bacteria cell is analogous to a complex man-made cybernetic system composed of information-processing systems and at least two thermodynamic machines. Their outer membranes enable them to sense the environment and to exchange energy, matter, and information with it. The internal state and stored information of the cell and the surrounding conditions regulate the membranes.

While an individual bacterium can sense only a limited volume before it replicates, a colony composed of thousands of millions of bacteria sense large volumes and over long time periods. For that, bacteria evolved communication abilities to exchange information about myriad detections that are stored then as newly acquired information. As members of complex organizations – colonies, each bacterium possesses the ability to sense and communicate with the others comprising the collective and perform tasks in coordination with others.

2 From thermodynamic machines to cybernetic systems

Bacteria developed unique ways to use energy sources of and chemical gradients (entropy imbalances) encountered in their different environments, to convert high entropy inorganic substances into low entropy life sustaining organic molecules. In spite of our scientific and technological advances, this unique living know-how is still mysterious. We propose that a first step towards deciphering the mystery requires a new perspective: The realization that every organism and individual cell in a multi-cellular organism is an information-based cybernetic cognitive system that operates to execute efficiently meaningful functions.

Returning to bacteria, from the perspective of a thermodynamic machine, each is a hybridization of two kinds of machines. The first type use imbalances in the environment to extract energy. The second type of machines use

this energy to act against the natural course of entropy increase, e.g. for the synthesis of organic substances. Note that the first type of machines is equivalent to an engine, while the second one functions as a pump that reduces its own entropy. In this fashion, each of the machines performs an open cycle in contrast to the ideal thermodynamic engine that operates on closed cycles, i.e. the system returns to its initial state. In other words, on each individual cycle the machines can return to a state that is close but not equal to the initial state. As a result the internal state of the cell being itself an open system continuously changes in time.

At present we are missing a physical theory to describe such situation and can only use equilibrium and close to equilibrium thermodynamics for approximate description over finite interval of times. And even so we need additional assumption about the use of internal supply of "negative entropy" that is provided by ATP as we explain further below.

The coordination of the two machines is regulated by utilizing the contextual information stored in the system and relevant information extracted from the environment during the execution of the cycles. It means that a third – information processing machine is coupled to the other two machines. Namely a biotic machine is analogous to hybridization of three man-made machines – thermodynamic engine, a pump and an information processing system. Note that the pump represents the internal cellular metabolism of synthesis of the organic materials that is similar to a reduction of entropy.

3 ATP nano-machines

Photosynthetic bacteria invented an additional operating principle. Low-entropy energy is first stored in transferable packets of quickly usable "currency" as ATP molecules [13]. Namely, the photon energy, from visible light in the solar spectrum between 350 to 650 nm, is stored in nano-size negative entropy quanta. These "coins" are usable energies available to efficient operation as needed. They are "injected" directly into molecular assemblies (engines) for movement and into enzymes for meaningful, timed catalyses. ATP molecules are not randomly consumed but are employed in a regulated manner according to stored information.

From physics perspective, ATP molecules are negative-entropy nano-quanta that feed low-entropy quanta of energy directly into the system micro-level degrees of freedom. They do this with state dependent spatio-temporal distribution. The process of energy consumption in living cells differs from man-made machines in which ordered energy (say, mechanical work) is dissipated homogenously into the microscopic degrees of freedom, which lead to spontaneous entropy production.

An individual bacterium should not be compared to a single man-made machine, but rather to an entire factory composed of many interacting man-made machines and information processing systems that regulate their operation, exchange of energy and materials, and generate new information. The "factory" is regulated according to a common "currency" for assessment of the "value" of the raw materials, the "cost" of the manufacturing processes, and the value of the manufactured products. The operation is also regulated according to an assessment of the state of resources and of the "market."

4 The maxwell demons of nature and self-sensing

The receptors and gates on the bacterial membranes act as Maxwell demons. By use of ATP coins energy and matter are exchanged with the environment so that they lower their internal entropy. The gene-network performs information processing. For example, *E. coli* have different sets of genes for digesting different sugars [24]. The question is how they to activate (express) the appropriate set of genes to digest only the preferred sugar, glucose (a better source of carbon), when it is present. When the cell needs not digest other sugars, say lactose, a specific gene continuously produces a repressor of the *lac* gene (whose product is required for lactose digestion). Under normal conditions, the *lac* gene is OFF. The presence of lactose turns off the repressor gene. This is not sufficient to turn on the *lac* gene on. Other specific genes produce, catabolic activator protein (CAP) activator of the *lac* genes. The enzymes of the energy-yielded glucose degeneration pathway repress these genes. Therefore, in the presence of glucose the expression of the CAP genes is disabled. Hence, the *lac* genes express only in the presence of lactose and absence of glucose.

We hypothesize that ATP provides a "sensory system" for the genome, or in another parlance, the "contextual information" required for function.

5 Sensing for extraction of latent information

All organisms, including bacteria, we infer, sense their environment, perform internal information processing, which translates latent environmental data into "active" information that initiates organic change. The *lac* case illustrates what we mean by "internal information processing" and justifies the notion of intracellular cybernetics. Other sensing systems are used during bacterial taxis. Photosynthetic bacteria sense light and assess its level to move or grow phototactically towards higher light intensity.

Feeding and sensing faculties co-evolved. In chemotaxis [25–28], bacteria assess the local energy source level and then swim or glide towards higher food supplies. Too small to detect chemical gradients, they sense temporal ones and bias their movement accordingly. To move towards elevated food concentration, they frequently assess local environments as they swim. If food concentration increases their tumbling is delayed and their directed course of swimming sustained. For that, bacteria 'taste' their food before they eat it. A biased random walk (or drift) towards higher concentrations ensues.

6 Bacteria communication for social behavior

Communication capabilities that create of cooperative behaviors among individuals to afford social behavior evolved from individual sensory-motor behaviors. Under natural growth conditions, adapted bacterial species self-organize into complex structured colonies that contain 109–1012 organisms. The colonies behave like multicellular organisms [4]. They show differentiation, "division of labor", and in some cases, even "reproductive organs" where differentiated groups of cells reproduced. These observations imply that the colony performs collective sensing, distributed information processing, and gene-regulation of individual bacteria by the group. Colonial internal sensing is crucial since the complex patterns of certain colony-forming bacterial depend on the communication between individual cells (the microlevel), as well as sensing characteristics of the collective (the macro-level).

Collective sensing is illuminated by bacterial behaviors. In *Myxococcus Cityplacexanthus*, foraging parties of cells priced the advancing edge of the colony. Upon chemical sensing of a food source, the scouts return environmental information to the colony. It then collectively expands by both gliding movements and cell division growth towards the newly detected food source [4].

Quorum sensing [29,30] that is employed in communication-based cooperation, use bacterial sensing faculty. Many Gram-negative bacteria use quorum-sensing molecules to induce expression light luminescence, antibiotics, bacteriocines, nitrogen fixing enzymes etc, once the population density exceeds a threshold. A typical case arises in Vibrio fischeri, where production of a membrane-permeable homoserine lactone by LUXI is sensed by the LUXR protein and turns on luminescence.

For coordination of cooperative ventures, various methods of biochemical communication have evolved. Molecular classes include proteins or peptides, polymers, genes and even "cassettes of genetic information" such as plasmids and viruses. The recently identified, autoinducer AI-2 in V. harveyi seems to be responsible for interspecies message-passing of the type that probably occurs quite regularly in multi-species biofilms. For instance, some pheromone-based negotiation for the trade of genetic information seems likely. Frequently, such contextual information (semantic aspect of communication), is directly transferred by conjugation following chemical courtship played by the potential partners: bacteria resistant to antibiotics emit chemical signals to announce this fact. Bacteria in need of that information, upon receiving the signal, emit pheromone-like peptides to declare their willingness to mate. Sometimes, the decision to mate is followed by exchange of competence factors (peptides). This pre-conjugation communication modifies the membrane of the partner cell into a penetrable state needed for conjugation [31].

Bacterial discourse can be illustrated in the starvation response of sporulation. When growth is stressed by desiccation or starvation members of the colony transform into inert, enduring spores. Sporulation begins only after "consultation". A collective assessment of colonial stress as a whole is determined by cooperative perception. Starved cells emit chemical messages that convey stress. The other colony members use the information for contextual interpretation of the state of the colony relative to its own individual situation. Accordingly, each bacterium "votes" – it sends a message for or against sporulation. Once each member has sent it preferences and read the other messages, sporulation is initiated if the "majority vote" is in favor [9].

7 Complex organization I: branching patterns of lubricating bacteria

Social lives of bacteria are revealed by exposure to adverse growth conditions that mimic those usually encountered in nature [6–10,12–16]. The patterns (Fig. 1) are generated during self-organization in response to growth on nutrient-poor and hard surfaces [32]. To cope, the colony produces a lubricating layer of fluid that permits swimming on hard surfaces. The individual bacteria at the front of the colony push the layer forward. Then pave the way for colony expansion. By careful adjustment of lubricant viscosity, the bacteria stay together and keep the population density high enough for protection and for efficient use of food.

The exact mechanisms and the chemical agents employed by the P. dendritiformis bacteria are yet to be discovered. However, based on accumulated knowledge from other bacterial species, it is reasonable to expect that two classes of chemical agents are used to perform two distinct functions: 1. extraction of fluid from the substrate (probably by polysaccharides) 2. regulation of the surface tension and viscosity of the lubricating layer probably by surfactants. Microscope observations reveal that as they swim, they push the layer forward, paving their own way.

The lubricant requires collective action of dense bacterial population, which the food-depleted substrate can not sustain. The solution comes in the form of a branching structure of the colony – within each branch the bacterial density is sufficiently high, yet the average population density of the colony is sufficiently low to match the availability of food. Based on model simulations (in which the effects of different parameters are tested) we realize that the lubricant properties and its production rate have to be carefully adjusted to generate specific branch structures with specific widths according to fit the substrate hardness and food level [33,34]. In summary, then, this adaptable organization can be viewed as the solution to a challenging self-consistency mathematical problem between two contradictory constraints – the need for high bacterial density for movement and the lack of sufficient level of food to support high bacterial densities.

8 Complex organization II: utilizing chemotaxis

Chemotaxis is cell movement in response to gradients in the concentration of a chemical agent [25–28,32]. The

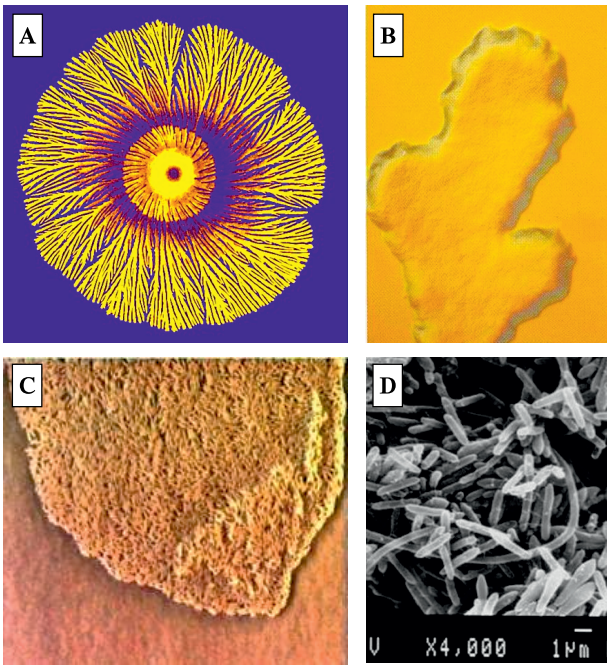

Fig. 1. Example of branching colonial patterning: (a) Typical branched colonial pattern formed by the *Paenibacillus dendritiformis* bacteria when grown on hard and food depleted substrate. The substrate is prepared from an LB solution with about 2% agar and less than 2 g/l peptone. 22 cc of the substrate solution (in a liquid state) is poured into a standard Petri-dish 8.8 cm in diameter. The solution is let cool and dry at 25 °C and 50% humidity for about 60 h until its weight is reduced by 1 g. The colony starts from a droplet (5 μl) inoculation at the center of the Petri-dish. The droplet is taken after 24 h bacterial growth in a shaker to guarantee that the stationary phase has been reached. The dark dot at the center of the colony is the area of the inoculated droplet that usually contains about 104 bacteria. After inoculation, the bacteria go through an 'embryonic' colonial stage for several hours and only then does the colony start to expand outward on the surface [6–10]. It takes the colony about two days to reach the observed size of about 5 cm in diameter shown here. The observed pattern can be associated with quantified measures, as explained in Appendix A. (b) A closer look at the branches through a polarized optical microscope to show the layer of lubricant collectively produced by the bacteria. (c) A snapshot from a video clip taken through an optical microscope with ×500 magnification [47]. The video clip observations reveal bacteria swimming – segments of straight motion for about 1–3 s at a speed of about 1 μ/s interrupted by bacterial tumbling terminating in a random new direction. That is why the bacterial movement is usually modeled as random walk. (d) A scanning electron microscope picture. Note the variability in the individual bacteria.

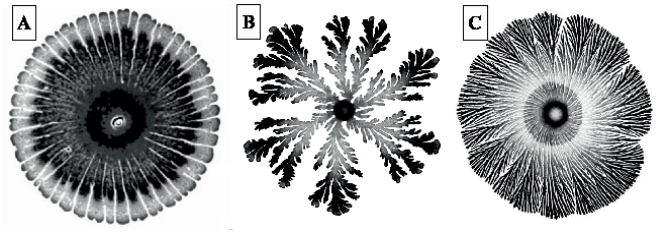

Fig. 2. Branching patterns exhibited by *Paenibacillus dendritiformis bacteria*. To organize their colonial structure these bacteria regulate the balance between attractive and repulsive chemotactic signaling as well as their food chemotaxis. Panel (a) shows the pattern at higher food levels when attractive chemotactic signaling is activated. Panel (b) shows the typical pattern when food chemotaxis dominates the growth at intermediate levels of food depletion. Panel (c) shows the growth for a very low level of food when repulsive chemotactic signaling is intensified. Note that the pattern is organized into narrow straight branches. The above examples of bacterial engineered self-organization provide the colony the ability to make a more efficient use of the available resources while being able to overcome the challenge posed by the hardness of the substrate. For more detailed discussion we refer the reader to refes [6–10,12–16].

movement can be biased either towards higher concentrations (attractive) or away from high concentrations (repulsive). Bacteria are too short to detect chemical gradients, yet swimming bacteria found a smart solution to detect gradients and bias their movement accordingly. For attractive (repulsive) bias, they simply detect the concentration as they swim, and if the concentration increases (decreases) they delay their tumbling. The net result is biased random walk towards the higher (lower) concentration, which can be directly incorporated into a mathematical model as a drift term. The most familiar example of chemotaxis is attraction to an external chemical such as a nutrient. There is evidence that such chemotaxis occurs in these colonies and is responsible for an increased expansion rate and colony "bushiness" at intermediate values of the nutrient concentration.

Very different patterns form at low nutrient levels (Fig. 2). To explain the mechanism, we recall that part of the branch-making dynamics relies on the cells going into a non-motile state further back from the colony front, where the nutrient levels is extremely low. In a variety of systems, there has emerged the idea that cells emit a repellent chemical as they are entering this state. For the repellent to accomplish its task, namely to persuade other cells to move away from such locations, the range of this signal must be fairly large. This can be tested by generic modeling, as illustrated in Figure 2.

So, the picture that emerges is that the basic branching pattern is sculpted into a variety of forms by the combined action of a variety of chemotactic strategies. These strategies serve to coordinate the actions of otherwise independent cells so as to make maximal use of the resources at their disposal. As these different influences sort themselves out, changing conditions and changing bacterial strains always lead to new structures. Exactly how information from the outside is utilized to help decide which if any of these processes need to be turned on is still an open question. Yet there are increasing hints that these decisions are made cooperatively, much like what is known to be true regarding the collective decision-making of bacteria to sporulate or the decision to share genetic information [9].

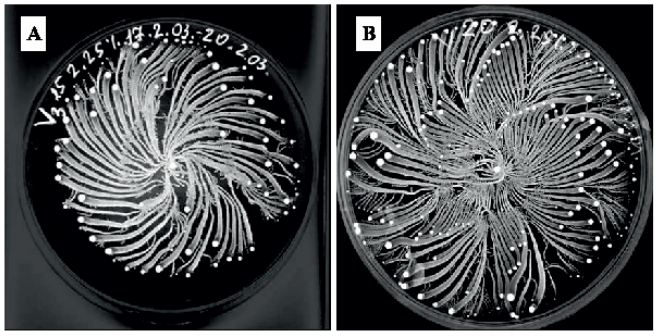

Fig. 3. Hierarchical colonial organization. Colonial patterns generated by the *Paenibacillus vortex* bacteria when exposed to different growth conditions. The pictures (a) and (b) show a whole colony view. The petri-dishes are 8.8 cm in diameter. The bacterial population of these colonies is larger than that of people on earth, yet they coordinate their behavior. The agar concentration is 2.25% and the peptone (food) level is 15 g/l (a) and 20 g/l (b). Each vortex (the condensed group of bacteria) is composed of many cells that swarm collectively around their common center at about 10 μ/s. The vortices vary in size from tens to millions of bacteria, according to their location in the colony. Both clockwise and anticlockwise rotating vortices are observed, although the majority has the same handedness. The cells in the vortex replicate, and the vortex expands in size and moves outward as a unit, leaving behind a trail of motile but usually non-replicating cells – the vortex branch. The twist of the vortex branch is determined by the handedness of the vortex rotation. The dynamics of the vortices is quite complicated and includes attraction, repulsion, merging and splitting of vortices. Yet, from this complex, seemingly chaotic movement, a colony with complex but non-arbitrary organization develops.

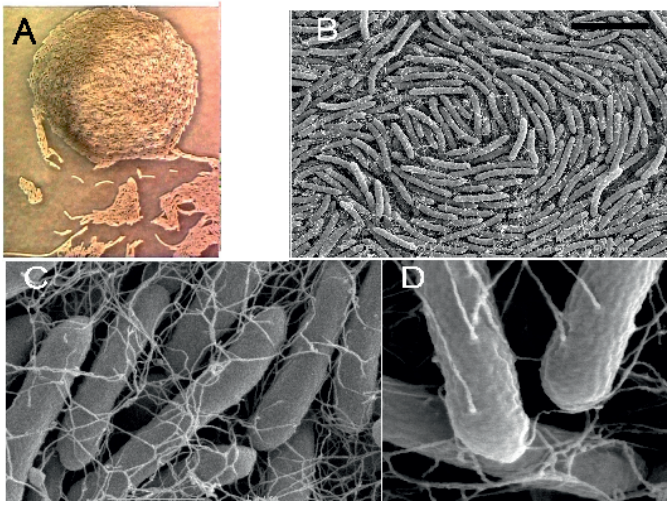

Fig. 4. Closer look at the *Paenibacillus vortex* growth on very hard surface. In (a) we show optical microscope picture of a vortex with magnification ×500. SEM observations of increasing magnifications are shown in (b),(c) and (d). These pictures were taken by Colin Ingham [39].

9 Complex organization III: hierarchical organization

Some bacterial strains organize their colonies by generating modules, each consisting of many bacteria, which are used as building blocks for the colony as a whole. This behavior is observed, for example, in the lubricating bacteria *Paenibacillus vortex* [7,8] that produce the bacterial vortices shown in Figure 5, and in other strains like *Bacillus circulans* [35] and *Paenibacillus alvi* [36]. Model simulations suggest [37,46] that a combination of short-range attractive and long-rage repulsive chemotactic signaling mechanisms can lead to the formation of the observed patterns, as is illustrated in Figures 3 and 4.

This idea of hierarchical organization brings us to a key conceptual question regarding the role of mathematical models in describing these patterns. For some aspects of what we have been studying, models that treat the bacteria as relatively simple interacting particles suffice. As we ask more complex questions, however, more and more detailed levels of possibly relevant degrees of freedom can reveal themselves. For example, genetic degrees of freedom (i.e. the dynamics which determine which genes are expressed) are irrelevant if one merely wishes to explain branching but appear to be crucial if we want to understand observed transitions between different colony patterns. The vortex itself can be studied using simple notions, but the way in which the complex exchange of information takes place between the colony as a whole and the vortex substructures requires much more. If we take into account the incredible complexity present at all scales (from molecular up to ecological community) in the bacterial system, it is fair to say that there will always be phenomena at the macroscopic scale that are not captured by any sort of tractable model. An example of such phenomenon is presented in the following section.

To illustrate the above notions, I show in Figure 5, the patterns exhibited by bacteria inoculated from the center of the colony vs. those created by bacteria taken from the leading vortices [14]. Interestingly even after several generations of growth the colonies started from inoculums from the center and the leading vortices are different. These observations suggest that the cells at different location go through some unknown process of epigenetic and inheritable differentiation that can be viewed as a precursor of cell differentiation in multicellular organisms. This epigenetic phenomenology goes well-beyond what can be discussed using current modeling ideas.

10 Bacterial collective memory and learning from experience

It has been proposed that bacteria seem to be able to store information about 'past experience'. In Figure 6 I show that bacteria exposed to the same antibiotic stress a second time can cope better with the stress. This effect can be erased (depending on the growth conditions and duration of exposure) by exposure to neutral conditions (i.e. growth on plates in the absence of antibiotic or in LB media) between the two encounters. Therefore it seems that the bacteria can generate erasable, collective

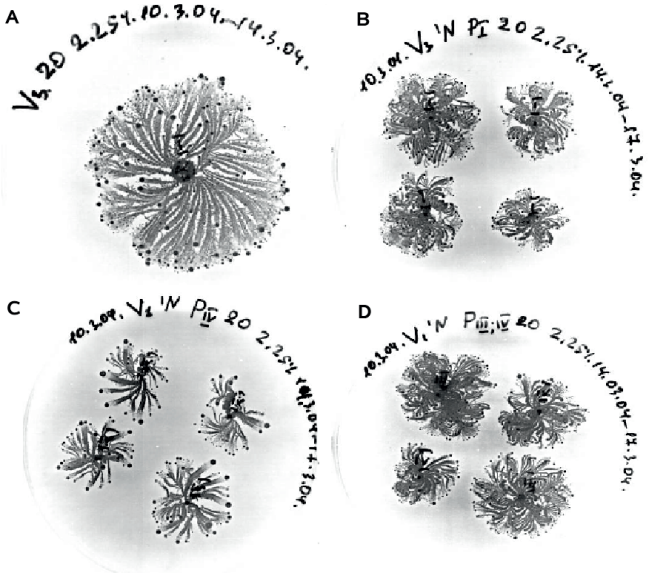

Fig. 5. Vortices inheritable self-identity. (a) A picture of the 'mother' colony used as a source of bacteria for the consequent growth experiments. The pictures on the right (b) and (d), show two plates with 4 colonies each that started from bacteria taken (by picking) from the center of the mother colony (a). These colonies have distinctively different patterns in comparison with those shown in (c). In this case the colonies started from bacteria taken (by picking) from large vortices at the front of the mother colony.

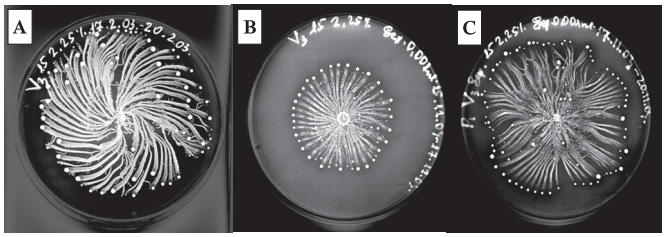

Fig. 6. Bacterial colonies learn. The observations show the response of the *P. vortex* bacteria to non-lethal levels of Septrin. In (a) we show the normal growth pattern in the absence of antibiotic. The effect of first exposure of the bacteria to the antibiotic is shown in (b) and the response in a second encounter is shown in (c). In response to the antibiotic stress, the bacteria intensify chemotactic attraction to form larger vortices. This clever strategy protects the bacteria, since in larger vortices the antibiotic is diluted by the lubricating fluid excreted by the bacteria. At the same time, the bacteria also enhance their repellent chemotactic signaling to push the vortices faster away from the encountered antibiotic. The "higher complexity for better adaptability" behavior is manifested in the fact that the growth pattern in (b) has lower complexity in comparison to that in (a). Learning from experience (c) is manifested by the fact that upon second encounter with the antibiotic the colony expands faster and the pattern is more complex. Taken from [9]

epigenetic memory, as if to learn from their past experience. One possibility is that this effect is caused by a genotypic shift in the population, namely that the antibiotics select for some pre-existing (otherwise neutral) genetic variation. Another possibility involves heritable epigenetic states in the gene-network of the cells. Irrespective of the exact mechanism, it is clear that the bacteria can retain memory of the conditions and that this acquired memory is expressed in the colonial pattern in consequent colonial developments.

We should mention in this context the evolvment that is taking place in our overall understanding of the power of genomic degrees of freedom. "Natural genetic engineering" [40], or "genome cybernetics", refers to the ability of the genome to perform information processing and alter itself accordingly [13,46]. Genome cybernetics upon replication has been illustrated in ciliates [40], and more recent work shows that transposable elements can effectively reprogram the genome between replications [43]. Small RNA molecules [44,45] have been shown to playa role in bacterial quorum sensing and might provide new intracellular and gene-network mechanisms needed to support some of these exotic processes. As our study of bacterial social behavior continues, we expect to find cases where these extraordinary capabilities of the genome become dynamically coupled to the social behavior; perhaps we have already seen some hints of this in the dialogues bet een cells that appear to underlie the more complex patterns found to date.

11 Conclusions

I have shown that as the individual cells in a growing colony begin to respond to the colony itself (i.e. information flow from the colony to the individual), these individuals response by regulating their movements, growth rates, various tasks they perform, the chemical signals they send to other bacteria and even their gene-network state (phenotypic state) according to the received signals. By doing so, the individual cells collectively alter the colony so as to increase its adaptability.

The essential new lesson learned from bacteria is that colonial high complexity provides the degree of plasticity and flexibility required for better adaptability of the whole colony to a dynamic environment. According to this picture, new features collectively emerge during bacteria complex organization on every level, from the membranes and cytoplasm to the whole colony. The cells thus assume newly co-generated traits and abilities that are not explicitly stored in the genetic information of the individuals. For example, bacteria can not genetically store all the information required for creating the colonial patterns for all possible environmental conditions. In the new picture, they do not need to, since the required information is cooperatively generated as self-organization proceeds by bacterial communication, informatics and self-plasticity capabilities. Thus, the bacteria need only have genetically stored the guidelines for producing these capabilities and using them to generate new information as required.

I have illustrated these remarkable capabilities by exposing the bacteria to non-lethal levels of antibiotics. Recent findings indicate that the bacteria purposefully

modify their colonial organization in the presence of antibiotics in ways which optimize bacterial survival, and that the bacteria have a special collective epigenetic memory which enables them to keep track of how they handled their previous encounters with antibiotic – learning from experience [9,13].

To conclude, we now begin to realize the power of bacterial social behavior, which allow them to store past information when solving newly encountered problems. The new findings bear the promise to provide satisfactory explanations to bacterial threat for our health: the world wide phenomenon that an increasing number of bacterial strains of disease-causing bacteria can today resist multiple antibiotic drugs. Bacteria are clearly capable of developing antibiotics resistance at a higher rate than scientists develop new drugs, and we seem to be losing a crucial battle for our health. To reverse this course of events, we must outsmart the bacteria by taking new avenues of study which will lead to the development of novel fighting strategies. One such promising direction is to perform gene-expression studies during colonial development, when bacteria are exposed to antibiotic stress and most challenging during bacterial learning from experience.

We expect that such and other future experiments will soon lead us to reverse the current notion of bacteria as mere solitary and simple creatures with limited capabilities, and recognize that bacteria are cooperative beasts that lead complex communal lives with rapidly evolving self-engineering skills [14]. We might even discover that the last five decade's evolution in bacterial resistance to antibiotic is largely a result of their encounter with our socially irrational massive use of antibiotic materials in agriculture and human intakes.

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