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Synthetic collective intelligence

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Intelligent systems have emerged in our biosphere in different contexts and achieving different levels of complexity. The requirement of communication in a social context have been in all cases a determinant. The human brain, probably co-evolving with language, is an exceedingly successful example. Similarly, social insects complex collective decisions emerge from information exchanges between many agents. The difference is that such processing is obtained out of a limited individual cognitive power. Computational model and embodied versions using non-living systems, particularly involving robot swarms have been used to explore the potentiality of collective intelligence. Here we suggest a novel approach to the problem grounded in the genetic engineering of unicellular systems, which can be modified in order to interact, store memories or adapt to external stimuli in collective ways. What we label as Synthetic Swarm Intelligence defines a parallel approach to the evolution of computation and swarm intelligence and allows to explore potential embodied scenarios for decision making at the microscale. Here, we consider several relevant examples of collective intelligence and their synthetic organism counterparts.

Keywords: Synthetic biology, swarm intelligence, evolution, social insects, cellular machines

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I. INTRODUCTION

Intelligent behaviour has been defined as the ability to successfully operate in uncertain environments by adaptations based on experience (Stenberg 2000). To succeed, intelligent agents have to be able to measure information, sense their inner and environment states, and perform actions, receiving some kind of reward (Legg and Hutter 2006). Additionally, agents have to be able to store these experiences and properly correlate experiences, becoming memory an additional item essential for systems adaptation and the development of an intelligent behavior. Our biosphere is currently populated by a plethora of information-processing entities. They are different instances of life forms. As pointed by John Hopfield, a crucial difference between physical and biological objects is that the second perform computations (Hopfield 1994). Such special feature also distinguishes biological structures as highly non-equilibrium ones, where information plays a role far more relevant from pure energy and matter.

Among the major transitions that have punctuated the history of life on our planet, several great steps involved novel ways of dealing with information and adapting to the external world by means of non-genetic mechanisms. These cellular, physiological, anatomical and behavioral innovations became a key factor in dealing with complex environments. As organisms became capable of processing information in complex ways, they became able of dealing with uncertainty. Intelligent behaviour was largely responsible for the success of costly multicellular systems as a consequence of their potential for being autonomous agents capable of storing and processing epigenetic information. The result was, as Jablonka and Lamb (2006) pointed out, the emergence of the neural individual:

"...with a high level of internal integration and the ability to make rapid adaptive responses. However, the emergence of the neural individual meant more than a change in the nature and speed of adaptation. Neuronal processing led to behaviour based on sensory perception, and this in turn led to a form of communication between individuals that did not require contact or the transmission of physical material from one to the other. This mode of information transmission had interesting consequences, one of which
was the ability of animals to learn from others through perceiving their behaviour or the outcomes of their behaviour, i.e. it led to social learning."

Different kinds of neural structures can be identified within the long road from cellular systems with simple sensors to full-fledged brains (Rose 2005). After cell membranes became complex enough, it became possible to process information in terms of chemical signals and internal metabolic responses. Later on, movement, coupled to these signalling phenomena allowed autonomy to develop beyond simple changes of metabolite concentrations. The rise of multicellularity added a new potential for using specific types of cells facing the external world, whereas the rest could be freed from a direct interaction with the environment. As multicellular life forms further evolved, something close to "behaviour" could be defined. With multicellularity, and with cells already in place having an internal and dynamical skeleton (the so called cytoskeleton) a novel form of cellular structure dominated the scene: neurone and neural nets became the controllers of behavioural patterns and the rudimentary computers. They paved the way to a rapid increase in complexity with the spatial segregation of groups of specialised neurons (distributed over a number of clusters known as ganglia) and eventually to the complex brains.

Along with this neural individual, another major transition of evolution led to the emergence of societies formed by relatively simpler agents (such as ants, termites or bees) capable of performing complex cognitive actions at the collective level. Social insects belong, at the individual level, to the ganglion-based organisation of neural processing. But they reach a higher level of complexity by making these already sophisticated systems to interact within a much more complex, parallel and spatially distributed entity: the super organism (Holldobler and Wilson 2008). By means of their potential for gathering and storing information, systems displaying collective intelligence are capable of making decisions about their internal states, environmental resources, protection against damage or foraging strategies (Deneubourg and Goss, 1989; Camazine et al., 2002). An example of these systems is given by ant colonies (figure 1a) which are blind and communicate mostly by means of pheromones, and yet involve millions of individuals that are capable of coherently exploring vast areas in the rain forests.

In some ways, collective intelligent systems, particularly ant colonies, reminds us the way brains work (Hofstadter, 1980; Gordon et al 1991*?, Solé and Goodwin 2001). However, in such comparison ants must be seen as a fluid neural network (Solé et al 1993) since no stable connections between pairs of ants exist. To a large extent, the cognitive potential associated to social insect behaviour is tied to both individual and collective responses to stimuli. On the one hand, ants and other social insects are capable of responding in sharp, almost digital ways to external inputs. On the other hand, the emergence of nest complexity comes from self-organization (Millonas 1993; Gordon 1999, 2010; Detrain and Deneubourg, 2006; Sumpter 2006), since ants exploit bifurcations and non-linearities as their source of internal structuring and decision making (Deneubourg et al. 1989; Bonabeau 1996).

Collective intelligence has been studied under very different approaches, including controlled experimental systems, simulation and computational models. A great deal of knowledge has been reached though the study of phylogenies and experimental observation or manipulation of social insects. Moreover, computational and mathematical modelling (Bonabeau et al 1999) along with swarm robotics (figure 1b) have contributed to unravel the underlying rules associated to the origins of collective intelligence.

The emergent field of synthetic biology give us an essentially new way of exploring swarm intelligence. This field provides the tools to modify and redesign living systems, instead of building artificial agents or making mathematical models. We could properly claim that we can create living micro-robots by modifying the behavioural repertoire of existing cells.

In this paper we outline this synthetic biology path, pointing a set of minimal circuits theoretically able to implement collective intelligence in bacteria. We label this field as synthetic collective intelligence (SCI). Such type of collective response can be found in many other different contexts, some of which are related to bacterial consortia (figure 1c) known as biofilms, where a collective response leads to the formation of a super-cellular structure. But can also involve tissue-like response phenomena, as it occurs with how pancreatic cells manage glucose regulation (figure 1d). In this case, specific cells in tissues can also react in non-linear ways to the concentration of given molecules and allow the tissue to make decisions on how to react to concentration changes.

As pointed by several authors, microbes are capable of integrating sensory information, store memories and display behaviour control (Lambert and Kussell 2014, Vladimirov and Sourjik 2009). They thus incorporate several relevant components required to build or design complex decision making systems. This starting point allows to consider the engineering of microbes as an achievable goal. Below we show that several essential features exhibited by swarm systems can be mapped into existing or engineered microbial constructs, and how these engineered living swarms map different types of emergent collective behaviour.

II. NATURAL AND SYNTHETIC SWARMS

Why using living systems and genetic engineering? A good reason is to use embodied communicating agents: it has been shown that embodiment is a crucial component of biologically-inspired robotics (Pfeifer et al 2007). Embodiment here needs to be understood as the dynamically linked interactions between ant brains, their body
FIG. 1 Collective decision making in natural and artificial systems. Many different systems are capable of making decisions that are based on detecting and processing information in ways that require population responses. Social insects are the obvious example, Alex as illustrated by army ants (a) where very large swarms emerge out from local interactions (Image by Alex Wild, from wikipedia commons). Swarm robotics (b) has taken some advantage of these collective patterns. In microbial systems collective responses are often associated to the formation of so called biofilms (c) where spatially structured organisations emerge (image by Ronn Friedlander and Michael Bucaro). In physiology too organ-level functions, such as glucose regulation by the pancreas (d), result from sensing and responding to external signals (image by H. E. Fährung, from Wikimedia commons).

and the external world. Since designed microbial agents will live and operate in a given spatial niche, the local nature of interactions and other physical constraints will play a role. On the other hand, we also expect to find universal features that are shared by both insect colonies and their synthetic microbial counterparts. In order to illustrate this point, we consider, in the following text, a selected list of well known cases associated to several relevant forms of collective behaviour. Our approach will describe minimal mathematical models that capture the key aspects of these case studies and finally provide examples of engineered systems that would implement those properties in synthetic biology.

Our aim is to define the minimal set of rules that pervade collective behaviour, where a two-way communication exists between individual and colony-level signals. As an example, if we take ants searching for resources, finding food by a single ant triggers an individual response that involves the release of a chemical signal that other ants can detect. As other ants find the mark and follow it, they reinforce the chemical field and eventually a whole chemical pheromone trail will form. This behaviour can be described as a closed loop connecting two different scales in an unbreakable fashion. Thereby, the trail can be seen as a larger-scale structure that is created by ants while it also affects their individual behaviour. This closed causality is a characteristic pattern in most -if not all- self-organised systems. Such causal loop needs to be considered as a crucial part of our approach to synthetic swarms.

Early experimental and theoretical work on the origins of swarm intelligence, as it occurs with other complex systems, identified the presence of phase transition phenomena similar to those known in physics (Solé 2011). It seems clear that insect colonies are capable of shifting between different global states (phases) when they respond to environmental changes. From a random walking exploration of the environment to a coordinate accomplishment of their tasks. Beyond the accuracy of this comparison, which has also been made in other areas (Solé 2011), examples in insect colonies include the diversity of morphological casts (the abundance of different function-related phenotypes in the colony), nest organisation (Bonabeau et al 1997) or hierarchy (Oster and Wilson, 1978; Valverde et al 2009). But cells are also able to coordinate by diffusible signals. For instance, cells often respond to molecules in their environment via intracellular signalling pathways that eventually result in
altered concentration of extracellular molecular species that triggered the pathway (Wiley et al., 2003, Pribyl et al., 2003; Freeman, 2000).

The analogy with phase transition phenomena is more profound that it might seem at first sight. The emergence of collective behaviour requires from amplification processes that allow the system to shift from less-coherent, noisy behaviour (a disordered phase) to a coherent, more organised (ordered) phase. Existing studies and models of different types of collective intelligence support the idea that the laws governing these transitions are rather universal, as it occurs in physical systems (libres?). But we know from the statistical physics of phase transitions that the way these changes occur obeys rather specific trends. This is a signature of so called universal behaviour (Sole and Goodwin, 2001, Solé 2011). More importantly, it is known from these studies that the global behaviour of the system is rather insensitive of the nature of the individual components. This means that, once the really essential rules and interactions are in place, very different systems sharing this minimal features will behave in the same way. If this can be extrapolated to biological systems, we would be able to engineer the synthetic counterparts of natural swarms.

In this paper we aim to address several important questions. Will synthetic (microbial-based) and natural (insect-based) systems behave in similar ways? Can novel forms of information processing be achieved by engineering living cells? In the next sections we present several examples of proof-of-concept designs that can imitate the ways social insects make decisions, exhibit division of labor, synchronise or simply aggregate as a consequence of threshold-like phenomena. It will be shown that some crucial components of future synthetic swarms are deeply connected to the universality of the rules pervading collective intelligence.

III. QUORUM SENSING AND COLLECTIVE BEHAVIOUR

Living cells both secrete and sense a wide variety of chemical signals (Alberts 2002). Releasing molecules to the external medium can be a consequence of metabolism but also a response to internal and/or external signals. Similarly, cell membranes act as the interface with the external world, with a very large fraction of proteins acting as receptors and information sensors located at this interface (Alberts et al. 2002). Both components (figure 2a,b) are much needed but none in itself is enough to trigger complex adaptive responses. In order to achieve this goal, cells need to do something more: create and sense the same class of molecule, as ants following a pheromone path. This is essential to support many instances of collective intelligence, since releasing a signal that others (including the releaser) can sense provides a feedback between individual and system-level behaviour.

In order to engineer synthetic systems capable of decision making and collective behaviour, one special component can be used: a system capable of sensing the size of the population. In ant colonies, it has been shown that threshold responses are reached once critical numbers of individuals are attained. This is the case of foraging dynamics of the Pharaoh’s ants (Beekman et al 2001) which exhibit a marked transition from disordered to ordered patterns of foraging as the colony size increases beyond a given threshold (cites, afegir Prigogine Ourder Out of Chaos). In this way, exploration can dominate while resources (and the sensing systems associated to them) are low but a shift to active exploitation occurs once enough individuals are engaged in a given task. In many ant species, foragers lay pheromone trails from food sources back to their nest. These trails allow nestmates to locate and exploit the source easily. As more ants collect food they reinforce the trail. Although the pheromone trail is volatile, it can be maintained if sufficient ants use it. This type of dynamics can be modelled, showing how the number of ants walking to a single food source depends on colony size.

In microbial species, a closely related phenomenon occurs. It involves a mechanism known as quorum sensing (QS) and is the key example that illustrates the existence of communication phenomena in microbial populations beyond the single cell (Waters and Bassler 2005). QS allows bacteria to monitor the environment for other bacteria and to alter behavioural responses on a population-wide scale in response to changes in the number and/or species present in a community. As a consequence, microbial colonies can make collective decisions, from host infection (Jones et al. 1993) to the formation of a so called biofilm (Davies et al. 1998). Most QS controlled processes are unproductive when undertaken by an individual bacterium acting alone but become beneficial when carried out simultaneously by a large number of cells. Thus, quorum sensing enables microbes to act effectively as multicellular organisms. That is why QS pervades a large range of phenomena, from biofilm formation to the symbiotic coordination between leguminous plant and rhizobia (González and Marketon 2003). In this section, we will analyse a toy model of QS that enables us to introduce some of the basic methods to analyse other, more complex mechanisms of collective behaviour.

These basic mechanisms underlying QS are illustrated in Figure 2a-c. Three main components are required, namely: i) cell-level system of production of the key signal, ii) a diffusion of this molecule through the cell membrane (in and out) and iii) cellular receptors actually sensing the external (environmental) concentration of the signal. By being both synthesized and detected, a minimal network motif, a feedback control loop is created. QS signaling networks can be more complicated and even perform sophisticated kind of computations (Waters and Bassler 2005). Thereby, QS is postulated here as one of the minimal requirements to implement swarm intelligence in microorganisms.
An essential motif associated to collective intelligence implies the combination of (a) production and (b) sensing of given molecules into a single feedback loop (c) where production and sensing are coupled. Such scenario provides the necessary conditions for sensing—for example—the population density of neighbouring agents (cells, ants etc). Many social insects (as the Pharao’s ants displayed in the right picture) display a characteristic transition from disorganised, low-density groups of individuals to ordered, collective patterns of organisation once the number of individuals crosses given thresholds. QS-related phenomena are responsible for this shifts in microorganism.

We can describe the threshold-like behaviour of a QS system using a simple mathematical model that captures the essential nonlinearities associated to this phenomenon. Instead of looking at individuals and the molecules they send and detect, let us perform a mean field approach. Mean field models are broadly used in physics to reduce the complexity of many-body (or many-agents) problems, by looking at it on a coarse grained level (Solé 2011). Let us here consider that only the average effect of individual (e.g. cellular or molecular) interactions is relevant. In this way, let us take the concentration of the signalling molecule $Q$ as the only state variable of the system. This means that, according to our mean field approach, $Q(t)$ is the only information we need to describe the state of the system at time $t$. Our $Q$ molecule could potentially govern a variety of cellular processes, from the induction of a reporter protein to the secretion of a given pheromone or growth factor.

A simple equation can be written that is able to capture the dynamics of $Q$ over time:

$$\frac{dQ}{dt} = f_\mu(Q) - \delta Q,$$

where $f_\mu(Q)$ is a production term for the signal $Q$, and $\delta$ stands for a degradation rate. We know from the observation of natural systems that the production term display a threshold-like phenomenon, which can be modelled by a so-called Hill-like function, namely

$$f_\mu(Q) = \frac{\mu \rho Q^2}{\theta^2 + Q^2}$$

According to the equation (2), the concentration $Q$ triggers its own production with constant rate $\mu$. Such triggering effect is proportional to the cell population density $\rho$. This dependence on $\rho$ illustrates the role of cells as signal producers: the higher population density, the more production of $Q$. The function $f_\mu(Q)$ displays a special shape, with low values for $Q<\theta$ and large values otherwise. Close to the threshold value $\theta$ it rapidly increases. The full equation of the QS field would thus read:

$$\frac{dQ}{dt} = \frac{\mu \rho Q^2}{\theta^2 + Q^2} - \delta Q$$

and roughly incorporates both the nonlinear, threshold-like production and the linear decay terms, respectively.

Despite its simplicity, the model properly displays the observed threshold-like shift associated to increasing density of individuals. Steady states $Q^*$ are obtained from the condition $dQ/dt = 0$ (i.e. when nothing changes) and it is easy to show that three points exist, namely:

$$Q^* = 0 \quad Q_1^* = \frac{1}{2} \left[ \frac{\mu \rho}{\delta} \pm \sqrt{\left(\frac{\mu \rho}{\delta}\right)^2 - 4\theta^2} \right]$$

The first point is associated to a zero concentration field: production is unable to compensate degradation and no QS response would be observed. The two other points are related to non-zero QS responses, and they only exist provided that the density is larger than a critical value, namely a threshold density:

$$\rho > \rho_c = \frac{2\theta \delta}{\mu}$$
When $\lambda_\mu < 0$ the point is stable, whereas it becomes unstable once $\lambda_\mu > 0$. The case $\lambda_\mu = 0$ corresponds to a so-called marginally stable point.

These results are summarised in figure 3, where the so-called bifurcation diagram of our system is shown. This diagram displays all the fixed points $Q^*$ against a key (bifurcation) parameter. A shift occurs at the critical density: a jump separates the zero state from $Q = \mu \rho / \delta$, where a QS response would be observed for the first time. The existence of this gap implies that something needs to occur if we want to shift from the low (zero) state to the QS state. This can occur, for example, if the underlying cells display stochastic fluctuations. In order to address this component, we would need to include explicitly the role played by noise, which has been shown to be specially relevant in making swarms computationally flexible (Deneubourg et al. **JTB, Bonabeau 1996**). An alternative way of approaching this feature is to use the potential $\Phi(Q)$, defined as an energy-like kind of function. The key idea is that we can write our dynamical system as derived from the potential, namely

$$\frac{dQ}{dt} = -\frac{\partial \Phi(Q)}{\partial Q}. \quad (7)$$

where $\Phi(Q)$ is defined by

$$\Phi(Q) = -\int \Gamma(Q')dQ'. \quad (8)$$

It is not difficult to show that this function is such that its minima and maxima correspond to the stable and unstable fixed points, respectively. This is a desirable property, that makes a strong connection with a physical system where the state of a particle (for example, a point mass under a gravitational field) rolls down on a surface until it reaches the minimum energy.

For our QS model, the potential function is obtained by integrating the right-hand side of the QS dynamical model (3), which gives:

$$\Phi(Q) = \frac{\delta}{2} Q^2 - \mu \rho \int \frac{Q^2}{\theta^2 + Q^2} dQ. \quad (9)$$

Four different examples of this function are displayed in figure 3b-e. Here different values of $\rho$ are used, two below the critical density and two beyond this value. The shape of the potential is very revealing. For $\rho < \rho_c$ we can see that the only stable state is the $Q^* = 0$ point, as expected, but the shape of $\Phi(Q)$ is clearly deforming as we approach $\rho_c$. Once this value is crossed, the deformation grows and two valleys are observed. These correspond to
FIG. 4 Collective communication out of local production and sensing of signals. The top left diagram summarises the genetic logic associated to a QS response. The specific inducible promoter (pQ) controls the expression of the Q molecule, that is in turn responsible for the self-detection feature associated to QS (see text). The sequence of a simulated growing colony has been obtained by plotting the time evolution of a quorum sensing collective response in a stochastic, individual-based model [using the GRO package, (Jang et al. 2010)]. Here five consecutive snapshots of a two-dimensional simulation are shown. Each in silico cell can be described as the basic scheme provided in the upper diagram (a).

the minima associated to the two stable points obtained from the linear analysis (indicated as circles in figures 3d-e). But we can see that the trivial point \(Q^* = 0\) is located at the bottom of a small valley (open circle) from which a small perturbation might push it out (figure 3d). This tendency increases as we keep moving far from the bifurcation (figure 3e). This situation corresponds to a so called metastable state. For this state, we have the two conditions associated to a minimum, i. e.

\[
\frac{\partial \Phi(Q)}{\partial Q} \bigg|_{Q^*} = 0
\]

\[
\frac{\partial^2 \Phi(Q)}{\partial Q^2} \bigg|_{Q^*} > 0
\]

as expected. In this case we can say that

\[
\Phi(Q) > \Phi(Q^*)
\]

when \(|Q - Q^*|\) is small (i.e. when we are really close to the minimum), but we have

\[
\Phi(Q) < \Phi(Q^*)
\]

otherwise (Dill and Bromberg 2011). In these cases, stability is usually a transient phenomenon, provided that the fluctuations associated to the system are strong enough.

A broad, chemically diverse repertoire of QS signal molecules has been described, of which the homoserine lactone (HSL) family have been the most intensively studied (Miller and Bassler 2001; Waters and Bassler 2005; Goryachev 2009). Once the HSL concentration reaches a critical threshold, a sensor molecule or response regulator is activated, triggering the expression of QS-dependent target genes. This knowledge has been used to modulate and modify the behaviour of many different synthetic systems. A minimal synthetic network that describes the basic QS interactions is summarised in figure 4(a). The circuit considers an inducible promoter (pQ) that controls de signalling inducer gene (QI) expression to produce the signalling molecule (Q). This molecule can pass through the cellular membrane and passively diffuse into the surrounding media, potentially reaching other bacteria. Inside cells, Q interacts specifically with a receptor protein (QR) in order to induces gene expression at (pQ), thus controlling bith its own expression and the expression of a green fluorescent protein.

An example of the dynamics of a growing bacterial colony, rising from a unique cell integrating the synthetic circuit described in figure 4(a), is shown by the snapshots series in figures 4(b)-(f). The agent-based (Jang et al 2012) model we use here introduces additional degrees of complexity in comparison to the simple mean field approach described above. A key difference is that we explicitly consider the individual dynamics of cells. This includes cellular growth and reproduction, as well as secretion and sensing processes regarding the AHL concentration Q. Moreover, spatial effects are considered, and diffusion governs the dynamics of Q in the extracellular medium. We also consider that the inducible promoter pQ exhibit a certain leakiness. Although such leakiness is not included in the minimal model described by Eq. (3), it is worth considering it in models for both bacteria (cells typically undergo a minimal HSL production
IV. MAJORITY DETECTION AND SYMMETRY BREAKING

Because ants are capable of creating chemical fields that can amplify existing signals (perhaps an incipient trail) these global responses can be used to sense the environment and its variable clues in order to discriminate, for example, between two nutrient sources selecting the richest (Deneubourg and Goss 1989, Detrain and Deneubourg 2006, Garnier et al 2007). Similarly, ants can use the QS-like mechanisms in order to determine the shortest path to a given source among several existing ones. In this way, colonies (not individuals) become able to decide between two food sources or two paths, finding the optimal solution. Such decision-making process is dramatically illustrated by the two-bridge experiment where the ant nest and a single nutrient source are connected by two alternative paths (figure 5a).

Once ants start crossing the bridges, they will initially do so at random. We should expected at this point equal number of ants on each branch, i.e. \( \rho_1 = \rho_2 \). However, once a successful ant has found the food source and gets back to the nest, it does so while releasing a pheromone trail. Although this trail is faint, it can be detected by others, which will choose it and release further pheromones, thus amplifying the previous mark. The pheromone trail also dissipates as molecules evaporate, but such process will be more effective in the longer trail, where more surface is available. As a result, the shortest path is more likely to be used and is eventually chosen. Ants have computed the shortest path.

The previous experimental setup can be formalized by using a very simple model involving (as it occurs in the QS case) Hill-like functions. If \( \rho_1 \) and \( \rho_2 \) indicate the concentrations of trail pheromone in each branch, their dynamics can be described (Nicolis and Denebourg, 1999) as a pair of coupled equations:

\[
\frac{d\rho_1}{dt} = \mu q_1 P_1(\rho_1, \rho_2) - \nu \rho_1
\]

\[
\frac{d\rho_2}{dt} = \mu q_2 P_2(\rho_1, \rho_2) - \nu \rho_2
\]

where \( \mu \) is the rate of ants entering each branch from the nest, \( q_i \) the rate of pheromone deposition in the \( i \)-th branch and \( \nu \) the rate of pheromone evaporation. The probabilities \( P_i(\rho_1, \rho_2) \) guide the choices made by ants (which bridge is chosen) given the pheromone concentration. It has been shown that experimental observations are well fitted by a threshold response function (Beckers et al., 1992; Deneubourg et al., 1990):

\[
P_i(\rho_1, \rho_2) = \frac{(\rho_i + K)^2}{\Theta(\rho_1, \rho_2)}
\]

where \( \Theta(\rho_1, \rho_2) = \sum_{j=1,2}(\rho_j + K)^2 \) and \( i = 1, 2 \). The parameter \( K \) measures the tendency for ants to explore a path that is free of pheromones (i.e., when \( \rho_i = 0 \)), and the exponent 2 is related to the steepness of the choice function (more abrupt choices could be modelled using higher exponents).

If we use an asymmetric system where branches are different, (i.e. \( q_1 \neq q_2 \)) it can be shown that the amplification process leads to the choice of the shortest path. Let us consider the symmetric case where \( q_1 = q_2 = q \) and thus the set of equations:

\[
\frac{d\rho_1}{dt} = \mu q (\rho_1 + K)^2 \Theta(\rho_1, \rho_2) - \nu \rho_1
\]
The absence of RFP (\( \rho_1 = 0 \)) corresponds to the equilibrium state exhibiting saturation of GFP \( ( \rho_2 = 1) \), and vice versa.

\[
\frac{dp_2}{dt} = \frac{\mu q}{\nu} (p_2 + K)^2 - \nu p_2
\]

This particular scenario might appear not so interesting, since there is no true optimal choice: both branches are equally efficient. We would easily conclude that ants would choose both paths and that individuals will equally spread over both sides. This is not the case: typically, an amplification phenomenon occurs, and nevertheless ants eventually choose one of the two possible branches. Why is that? The phenomenon illustrates a very important class of phase transition phenomena: the so-called symmetry breaking process amplifies initial fluctuations in such a way that even small differences are inevitably expanded by some type of positive feedback loop.

It is not difficult to show using \( dp_i/dt = 0 \) that one possible solution to this system is the symmetric state \( \rho_1^* = \rho_2^* = \rho^* \) when ants equally distribute themselves over both branches. For this special case, we have \( P_i(\rho_1, \rho_2) = P(\rho^*) = \mu q/2 \) and thus a single equation \( d\rho^*/dt = \mu q/2 - \nu \rho^* \) which gives a fixed point \( \rho^* = \mu q/(2\nu) \). This is our symmetric state to be broken. The second state would correspond to the choice of one of the branches \( (\rho_1^* \neq \rho_2^*) \). Since the total pheromone concentration is \( \rho_1 + \rho_2 = 2\rho^* = \mu q/\nu \), we can see that

\[
(\frac{\mu q}{\nu} - \rho_i^*) (\rho_i^* + K)^2 = \rho_i^* (\frac{\mu q}{\nu} - \rho_i^* + K)^2
\]

after some algebra, this gives the new fixed points \( \rho_i^* = (\rho_i^*-\rho_i^+_-) \) and \( \rho_i^* = (\rho_i^- - \rho_i^+_) \) with

\[
\rho_i^+ = \frac{\mu q}{2\nu} + \sqrt{\left(\frac{\mu q}{2\nu}\right)^2 - K^2}, \quad \rho_i^- = \frac{\mu q}{2\nu} - \sqrt{\left(\frac{\mu q}{2\nu}\right)^2 - K^2}.
\]

This pair of fixed points will exist provided that \( \mu q/2\nu > K \) which allows to obtain the critical point at

\[
\mu_c = \frac{2K\nu}{q}
\]

indicating that there is a minimal rate of ants entering the bridges required to observe the symmetry breaking phenomena. Below this value, the only fixed point is the symmetric case with identical flows of ants in each branch. This symmetric model can be generalized to (more interesting) asymmetric scenarios where the two potential choices are different (see Detrain and Deneubourg 2009 and references cited) either because the food sources have different size or because paths have different lengths and the shortest path need to be chosen.

Implementing the previous experiment using a synthetic construct is far from trivial, but a closely related problem can be considered that allows to find an equivalent SCI formulation using synthetic biology. It also implies a decision between two potential solutions resulting from an amplification phenomenon. In computation theory, it is connected to the so called density classification problem (Mitchell et al 1994; Crutchfield and Mitchell 1995). Imagine a system that receives two types of inputs and one must determine which of them is stronger. Specifically, consider two given molecules \( M_1 \) and \( M_2 \) that can be detected by a cell or set of cells. The question to be solved is what was the signal with greater initial concentration \( [M] \), that is deciding between

\[
[M_1]_0 > [M_2]_0
\]

or instead the opposite:

\[
[M_1]_0 < [M_2]_0
\]

where \([M_k]_0\) indicate the initial \((t = 0)\) concentrations of each molecular signal. Since the original concentrations can be small or very similar, the problem is how to amplify the initial condition in such a way that the final state represents a decision between one of the two previous inequalities. This problem has been addressed using deterministic models where a discrete set of elements are set initially in one of two alternative states \((0, 1)\). Each element in the system is connected to a limited number of neighbours and their state is synchronously updated following simple rules. The problem can now be redefined considering a system where two signals can be sensed from the environment by a strain of engineered cells. Let us assume that these cells, as it occurs with the quorum sensing mechanism described above, not only detect...
FIG. 7 Synthetic circuit design for a majority decision problem. The top diagram outlines a possible synthetic implementation, operating under a cross-inhibition design (see text). Six snapshots are shown here, with a constant population of bacteria scattered over a two-dimensional space. Two different reporters (green and red) are used to indicate which potential choice is made by each cell. Using the circuit design outlined in the top diagram, we can see how one or the other solution (top or bottom snapshot series) is amplified and adopted by the bacterial community.

but are also able to produce the two chemical signals. Moreover, each signal induces the production of a specific reporter protein. The perception of both fields is made through a majority detection system, which allows to shift the expression of the linked reporter in some non-linear fashion.

Before we propose an actual implementation of this system, let us consider a mean field description of the basic population dynamics model. Let now \( \rho_1 \) and \( \rho_2 \) be the population densities of cells at state 1 and 2, respectively. For simplicity, we consider a scenario where there is a conservation in the densities, and \( \rho_1 + \rho_2 = 1 \) or, in other words, the total cell population remains stable during the process. Under mean field assumptions, the dynamics of the relative densities would be defined by a set of (symmetric) equations

\[
\frac{d\rho_1}{dt} = \mu \rho_1 \left( \frac{1}{2} - \rho_2 \right) - \rho_1 \varphi(\rho) \quad (25)
\]

\[
\frac{d\rho_2}{dt} = \mu \rho_2 \left( \frac{1}{2} - \rho_1 \right) - \rho_2 \varphi(\rho) \quad (26)
\]

The previous set (25) and (26) essentially tells us that the density of cells having a given internal state (either 1 or 2) will grow at the expense of the other one only if the later has a dominant concentration (i.e. when \( \rho_j < 1/2 \)), while it will decay otherwise. The first term on the right hand side of the two previous equations describes this rule. Here, the term \( \mu \) is a reaction rate determining the speed at which cells can shift from one state to the other. Now, assuming the conservation condition it is
not difficult to see that

\[ \varphi(\rho) = \sum_{i \neq j} \mu \rho_i \left( \frac{1}{2} - \rho_j \right) \]

and thus we have, from \( \rho_i = (1 - \rho_j) \):

\[ \frac{d\rho_i}{dt} = \mu \rho_i \left( \rho_i - \frac{1}{2} \right) - \mu \rho_i \sum_{i \neq j} \rho_i \left( \frac{1}{2} - \rho_j \right) \]  

(27)

Equation (27) can be rewritten as the following cubic equation:

\[ \frac{d\rho_i}{dt} = \Gamma(\mu, \rho_i) = 2\mu(1 - \rho_i) \left( \rho_i - \frac{1}{2} \right) \rho_i \]  

(28)

which has three equilibrium points \( \{ \rho_i^\ast \} : \Gamma(\rho_i^\ast) = 0 \} = \{ 0, 1, 1/2 \} \). The stability analysis of these points reveals that \( \rho_1^\ast = 0, 1 \) are stable whereas the coexistence one, \( \rho_2^\ast = 1/2 \), is unstable.

This is an example of symmetry breaking and can be illustrated by calculating its associated potential function \( \Phi(\rho_i^\ast) \). In this case, we obtain for our problem a function:

\[ \Phi(\rho_i) = -\mu \left( \rho_i^3 - 2\rho_i^2 + \rho_i^2 \right) \]  

(29)

that shows the expected two-well shape (restricted to 0 \( \leq \rho_i \leq 1 \)). As illustrated in figure 6, once an initial fluctuation has favoured a given configuration over the second, the amplification of the original fluctuation forces a collective decision.

How can we map this type of decision making process into a synthetic biological circuit? The fundamental issue here is to have a design that naturally incorporates two alternative states in such a way that initial differences get amplified by the nonlinear interactions. The basic principle is that we need a system involving two stable genetic alternative states, each one acting exclusively and thus forbidding the alternative one. This can only be achieved if there is an interaction between the two actual genes through negative feedback loops. In this scheme, two alternative states are possible because each released signal inhibits the cell sensitivity to the other.

A simple solution is provided by the diagram shown in figure 7 (top diagram). Here, each cell has two different but equivalent signaling circuits able to sense both signaling molecules \( s_1 \) and \( s_2 \) via specific receptors. Signal activated receptor promotes the expression of three different genes, its own signal inducer \( S_n I \), that is the enzyme that synthesizes the signal, its own receptor \( S_n R \) and a fluorescent protein, and the transcription of an antisense RNA that specifically inhibits the opposite receptor by degradation of the mRNA. Considering \( s_1 \), explicit inhibition of the receptor \( S_2 R \) brings the reduction of the sensitivity to \( s_2 \) molecule (Carbonell et al. 2014) and a lower expression of its associated inhibitor. This also leads to a positive feedback on the sensitivity to the signal \( s_1 \), since the fall of \( S_2 R \) will lead to the weakening of the inhibition of \( S_1 R \) in a nonlinear manner.

The resulting dynamical behaviour of this system is illustrated in figure 7 using an agent-based model where a set of previously grown population of bacteria is used to perform the majority detection task. Here two input signals are introduced near the centre of the colony. In the two different in silico experiments, one of the two signals is slightly greater than the other. The genetic circuit is triggered while diffusion propagates the signals through space, and the dominant discloses as a fluorescent circle involving one of the two possible reporters. The two series of snapshots shown in figure 7 illustrate the expected collective pattern. In one case, the initially more abundant signal triggers the expression of the green reporter (top snapshot series in figure 7) which spreads through the dish, whereas in the alternative scenario the balance is just the opposite (bottom series in figure 7) and at the end of the simulation most cells already express only the red reporter.

The amplification phenomenon associated to our synthetic system has all the properties expected from the statistical physics of symmetry breaking found in a broad range of systems (Strocchi 2005; Solé 2011). It provides a clever illustration of the concept of symmetry breaking as a way of creating information (Haken 2010). In this context, choosing between two different options needs a system capable of amplifying fluctuations and exhibiting multiple stable states.

V. SELF-REGULATION OF DIVISION OF LABOR

Among other fundamental features exhibited by systems that display collective intelligence, division of labor is probably one of the most important in terms of allowing efficient and robust decision making. Given a repertoire of tasks to be executed, several relevant factors influence how efficiently are tasks performed. In ant colonies, specific tasks can be performed either by morphologically differentiated organisms (so that a relation exists between the phenotype and the task) or instead by the same type of individuals, as it occurs in monomorphic species. In the second case, some dynamical process might be present in order to redistribute tasks among individuals as a function of the current demand. Moreover, the lack of an external differential trait does not preclude some internal feature, affecting potential behavioural repertoires. An example is the presence of a response threshold that would affect the decision of each individual in relation with some task to be performed.

One example of caste-dependent task allocation is given by the dynamics of the ants of the genus *Pheidole*, which exhibit a characteristic dimorphism into two easily distinguishable types of workers (namely, majors and minors, which are shown in figure 8a, inset). Each type is associated to a preferential task: foraging or nest defense. It has been shown (Detrain and Pasteels 1991, 1992) that the probability that a given ant in any of these groups becomes involved in a given task is a nonlinear,
saturating function of the intensity of the stimulus. This was shown experimentally by artificially altering the frequency of workers in different castes. Once a fraction of workers from one of the castes was removed, it was observed that, after some delay, individuals from the second group became engaged in the task, successfully performing it (Wilson 1984).

By decreasing the fraction of minors in Pheidole colonies, it was possible to observe that the number of majors performing the required task remained low until a critical stimulus intensity is reached, followed by a rapid increase in the fraction of majors involved. In other words, once the balance between castes is altered enough, the caste with higher threshold (which normally does not perform the required function) rapidly restores the adequate levels of task performance. This is a simple and interesting scenario where we can see at work the robust response of a given system to changing conditions. In this section we aim to provide an equivalent engineered design of this response using modified cells.

The probability of switching towards a given task can be described by a Hill-like response function using a fixed threshold model (FTM). If we indicate by $\sigma_k$ the state of a given worker from the caste $k$, it moves from inactive ($\sigma = 0$) to active (indicated as $\sigma = T$) with some probability that depends on the intensity of the stimulus $S$. Once in the active state, it starts performing their possible tasks. Although different tasks $T_k$ could be considered, here we deal with the case of recruiting different castes for a specific task $T$. Here we will use a probability of transition described by a sigmoidal curve, namely:

$$P(0 \to T) = \frac{S^2}{\theta_k^2 + S^2} \quad (30)$$

In figure 8a we show an example of the two transition probability curves. Since two different thresholds are present, the two curves appear displaced along the x-axis.

A simple model of task allocation considers two possible types of workers that interact with $S$ through a simple feedback loop. In figure 8b we summarise the basic assumptions made in (Theraulaz et al 1998, Bonabeau et al 1996). We consider two castes indicated by $C_1$ and $C_2$ that are optimal for different tasks but, if necessary, both can perform the same task $T$. Specifically, individuals of each morphological class have a state $\sigma_k \in \{0, T\}$ indicating no activity and activity, respectively. The stimulus $S$ is constantly raised at a rate $\alpha$ and is also "removed" at a rate $\delta$ that depends on the efficiency at which the task $T$ is performed. The presence of this stimulus triggers the transition from inactivity to activity, following the transition probability given by equation (30). As summarised in this diagram, the whole system operates under a negative feedback control scheme with two regulatory components displaying different activation thresholds. This model and variants of it were shown to account for the nonlinear response of different castes to the intensity of the stimulus.

The caste-dependent task allocation scheme, as defined by the fixed threshold model, can be engineered following the design of the synthetic constructs presented in figure 9a-b. In these synthetic implementations, the two ant castes are substituted by similarly modified cells using manipulated quorum sensing genes. Specifically, the recruiting factor for a single task is replaced by the quorum sensing signalling molecule HSL which is externally introduced in the system. These cells respond under a Hill-like transfer function to the signal, albeit with different thresholds of activation and reaching different levels.
FIG. 9 Implementation of two different "castes" in engineered bacterial cells. In this system (a-b) each cell in the two-cell consortium has been engineered with a genetic circuit with which they can sense an external signal (see text). By using two different promoters and reporter proteins, a minimal synthetic circuit is obtained, formally equivalent to the fixed threshold model applied to insect colonies. In (c) we display the "function" been performed by each caste in terms of protein expression. Specifically, the lines represent the amount of stimulus reduction achieved by the efficient (dotted) or the inefficient (solid) cells, normalized by the maximum stimulus reduction of each type. of protein induction. If the levels of stimulus are externally fixed by the concentration of HSL, then the two synthetic castes are able to relieve task necessity by reducing the levels of the quorum sensing molecule. In order to implement this reduction, the stimulus directly induces the expression of an enzyme able to degrade it (aiiA) in a non-linear fashion. Two fluorescent proteins are also incorporated into the design, one for each cell type, as reporters of the recruitment of each caste. The whole system can be described by the following set of ODEs:

\[
\frac{dQ}{dt} = \alpha - \delta Q - (\eta_1 \rho_1 + \eta_2 \rho_2)Q
\]  

\[
\frac{d\rho_1}{dt} = F_1 \frac{Q^2}{(Q_1^2 + Q^2)} - \delta_1 \rho_1
\]  

\[
\frac{d\rho_2}{dt} = F_2 \frac{Q^2}{(Q_2^2 + Q^2)} - \delta_2 \rho_2
\]

where \(\alpha\) is a constant rate of stimulus production (representing the rate of introduction of the signal \(Q\) into the system), the \(\delta_i\) terms introduce degradation rates for the different species, \(\rho_i\) stands for the population density of active individuals from caste \(i\), and \(F_i\) for its total population density (including both active and inactive cells). Given the conservation equation: \(F_1 + F_2 = 1\), the contribution from each caste to the task can be collapsed into a single equation for \(\rho = \rho_1 + \rho_2\), that reads:

\[
\frac{d\rho}{dt} = \sum_{i=1,2} F_i \frac{Q^2}{(Q_1^2 + Q^2)} - \delta \rho
\]

As in (Denebourg) we use the fraction of cells in the culture pertaining to the second caste, \(F_{N2}\), as the control parameter of the system. Figure 9 shows that the recruitment of type 2 cells displays an abrupt transition owing to the decreasing availability of type 1 cells. These are the first to respond to the stimulus and the efficient in processing the lactone. As their numbers decline the amount of signal rises sharply, forcing the recruitment of the less efficient second caste.

This particular design could, in principle, be expanded into more complicated systems with different tasks and castes by using orthogonal signals and their respective degrading enzymes. Lactones in particular have been shown to display cross-talks at various levels (Wu et al. 2014) and are poor candidates for such expansion. Non-lactone molecules could be used as long as a degrading enzyme can be expressed in the modified cells.

VI. COLLECTIVE OSCILLATIONS

The previous examples deal with systems exhibiting dynamical properties that are characterised by nonlinear responses. These responses lead to new steady states and can be associated to some class of information processing. However, collective computation can also be tied to fluctuating dynamics, as shown by some ant colonies that display pulsatile waves of activity (Holldobler and Wilson 2009). Specifically, in some ant species individuals appear to exhibit synchronised fluctuations of activity: intervals where different individuals display active behavioural patterns are followed by intervals of little or no activity, with a colony essentially inactive.

This phenomenon has been known to take place in social insects and identified as an endogenous process. The first dedicated studies of this phenomenon were conducted by Blaine Cole and Nigel Franks, who measured the synchronised activity in different species of Leptothorax (figure 10a) under experimental conditions (Franks...
In these colonies, it was found that a pulsatile, bursty pattern was involved, as shown in figure 10b from a recorded experiment where the changes of pixels in consecutive moments of time, giving a surrogate of the density of active individuals moving around. These fluctuations have a $\sim 25$ minute period. Using single ants, it has been observed that individuals do not display this regular pattern. Instead, they seem to be chaotic (Cole 1991b) and thus this is not an example of a set of individual oscillators that get entrained due to some class of coupling among individuals (Strogatz 2003).

In these colonies, single individuals are known to become spontaneously active inside an inactive colony. As they move around, they contact other resting individuals and can make them awake. By increasing the density of individuals within a given arena, it is possible to study the influence of the number of ants on the degree of synchronisation and spread of activity. It was found that a disordered burstiness is replaced by a more coherent collective activity pattern as density increases (Cole 1991a), thus indicating that the likelihood of finding active individuals grows as more interactions are allowed to happen. In fact, if the density of individuals is forced beyond the one found in non-manipulated colonies, oscillations also become more coherent, more than observed. This seems to indicate something very interesting, namely that colonies might self-regulate their density in such a way that a special, intermediate density is achieved.

According to Robinson (1992), self-synchronization facilitates the sampling of any information an individual may need from other individuals. Assuming that ants cannot be active all the time, why would self-synchronized behaviour be a better (simpler) strategy than, say, random (in the sense of nonsynchronized) activity patterns? We will need further assumptions to answer this question: the obvious one of locality (an individual is able to get only local information) and second, the quite reasonable (and biologically plausible, see above) assumption that the unique interaction allowed to an inactive individual is to be “awaked” by other(s) individual(s); an inactive individual does not carry any information, namely, it is equivalent to a “sleeping” individual. Now, in this context, it would be clear why we should obtain an increase of efficiency with synchronized patterns of activity: it would maximize the number of simultaneously active neighbours of an active individual. A detailed study of the two alternatives (Delgado and Solé 2000) shows that a fluctuating system actually outperforms the alternative (not observed) constant-activity scenario.

The simplest mean field model that can be formulated is closely related to the propagation of epidemics (Cole 1991c, Solé 2011). Let us now consider our population composed by two groups, namely active and inactive ants, whose numbers will be indicated by $A$ and $I$, respectively. Using the normalized values $x = A/N$ and $y = I/N$, and assuming that the density of occupied space is $\rho \in [0, 1]$, the mean field equation for the fraction of active ants is:

$$\frac{dx}{dt} = \alpha x (\rho - x) - \gamma x$$  \hspace{1cm} (35)

An important difference in relation to epidemic spreading is that the density of ants $\rho$ is now a key control parameter.

The equation displays two equilibrium points. The first corresponds to no-activity at all $x_1^* = 0$ while the second is associated to the presence of a given level of activity, namely

$$x_2^* = \rho - \frac{\gamma}{\alpha}$$  \hspace{1cm} (36)

The colony will display non-zero (i. e. $x_1^*$ will be stable) activity provided that $\lambda_\mu(0) = \alpha \rho - \gamma > 0$ which, in terms of the density of ants corresponds to the condition $\rho > \rho_c = \gamma/\alpha$.

The deterministic model predicts that no activity will be present at subcritical densities, whereas experiments indicate that activity is present, largely due to random individual activations, at small densities. Moreover, it has been found that fluctuations become very large close to the critical point, consistently with real data (Solé et al., 1993; Miramontes, 1995). This is illustrated by the shape of the associated potential, which now reads:

$$\Phi_\mu(x) = \alpha x^3/3 - (\alpha \rho - \gamma) x^2/2$$  \hspace{1cm} (37)

Three examples of this potential are shown in figure 5c for a subcritical, near-critical and supercritical cases. As
expected, the potential becomes flatter as criticality is approached.

The observed variance in colony fluctuations is a consequence of critical slowing down (see chapter 1) and for this model it can be shown that the relaxation time \( \tau(\rho) \), scales as

\[
T(\rho) = \frac{1}{c} \int_{x(0)}^{x(T(\rho))} \frac{dx}{x(\rho - \rho_c - x)} \sim (\rho - \rho_c)^{-1} \tag{38}
\]

As we approach criticality, random activations are likely to propagate for a while before global activation dies out, thus providing the source for higher activity levels and broader fluctuations.

Although some previous studies have shown how to implement a synthetic system capable of displaying periodic dynamics, all of them where based on the presence of oscillators capable of synchronize leading to a collective oscillation (Danino et al. 2010). This is the classical problem of entrainment oscillators through some kind of coupling. Here the lack of an individual-level oscillatory behaviour requires a different approximation.

A possible way to engineer bacteria in such a way that it behaves as an excitable element is by the implementation of a motif able to release a long distance activation signal, like HSL, and a inner cell inhibitory mechanism, like tagged protein degradation by ClpXP [figure 11(a)]. The activator signal is HSL. HSL promote the expression of its own biosynthetic enzyme LuxI and also the expression of a proteolitic protein, ClpX. The inhibitory effect is implemented by means of ClpXP target sequences in LuxR (the HSL receptor), LuxI (the HSL inducer) and the fluorescent protein GFP. Thereby, the equilibrium rate between leakiness of the \( P_{lux} \) promoter upstream of LuxI (activator) and ClpX (inhibitor), keep the systems wondering around a low number of proteins and molecules dynamic equilibrium, where the stochasticity is high (Raser and O’Shea 2005).

When one of those cell overcome the activation threshold, it will start to synthesize actively LuxI enzyme. This will lead to the production and release of HSL, that will diffuse in the media, activating the surrounding cells in a positive loop. However, HSL also promotes the expression of ClpX protein, that will facilitate the degradation of LuxR, LuxI and GFP. This will drive the system to the initial state of relaxation. As ClpXP has not a ClpX target sequence, it will persist more time in the cell giving us a refractory period that each cell has to overcome before to the next activation loop.

An example of emergent collective oscillations in synthetic colonies is shown in figure 11(b). Here, each cell in the colony carries the genetic construct described above. When a single cell is stochastically activated, it can activate its surrounding neighbours by releasing the HSL signal, possibly generating a cascade of activity that propagates in the space. Otherwise, the colony remains at low activity levels. Such dynamics can be traced by plotting average GFP concentration displayed by cells in the colony [figure 11(b)]. Applying standard Fast Fourier Transform techniques reveals a maximum square amplitude peak in figure (c), indicating that the system exhibits a characteristic frequency of oscillation. The shaded area in figure 11(b) shows the corresponding characteristic period of 400 min and the power spectrum in figure 11(c).

A Fast Fourier Transform of this time series is shown in (c), where a peak is observed at 0.25 \( \times \) 10^{-2} min^{-1}, revealing characteristic frequency of collective oscillations.

VII. DISCUSSION AND CONCLUSIONS

The widespread ecological success of insects resulting from the rise of swarm intelligence is undeniable. Such a success required something more than simply get together and evolved into a vast array of social structures. Ants and termites both display outstanding works as architects, but the blueprints for their buildings are not in their small brains. A termite nest has a scale that is several orders of magnitude larger than the size of the individual workers. And these large scale structures possess a rather complex and optimised structure. They result from emergent patterns of construction out of simple rules. Similarly, the behavioural flexibility exhibited by their colonies and their potential for adapting to environmental uncertainty is equally remarkable. As a form of intelligence, swarm intelligence has inspired generations of computer scientists, theoreticians and robot designers alike.

In this paper we considered a novel approach to the problem based on actually constructing living robots by using genetic engineered microorganisms. We propose
FIG. 12 Synthetic microbial emergent oscillations. Synthetic colonies are simulated in a microfluidics context (a) that preserves a constant population number using a trapping chamber where bacteria grow until they are removed by the flow. In (b) we display the engineered implementation using a quorum sensing autoactivated system based on homo-serine lactone (HSL) and a repressive control of a ClpX proteolytic activity, also under the control of HSL (see text). The system is capable of generating collective synchronisation out of non-oscillatory dynamics. An example is shown in the time series in (c) where oscillations in the average activity of the cells is displayed (the black solid line indicates the average GFP concentration within cells in the colony). The power spectrum for this time series is shown in (d). It reveals a characteristic frequency of oscillations at $0.25 \times 10^{-2}$ min$^{-1}$. The corresponding characteristic period (400 min) is highlighted by the shaded area.

This approach as a research field that needs to be fully developed. Many relevant issues and problems are open. Here is our tentative list of open problems:

1. In ant colonies (and social insects in general) there is a very important phenomenon that pervades a large part of their emergent properties. It is known as stigmergy and was first introduced in 1959 by the great French biologists Pierre-Paul Grassé. Because ants use materials to actually create their nests, and since those materials affect their interactions with the nest and to other nestmates, the changing physical organisation and boundaries of their worlds affects their behaviour and eventually the construction rules. An action made on the environment by an agent modifies future actions by other agents.

As defined above, stigmergy includes those effects related to some of the problems we have been considering in the previous section. This includes the collective emergence of a concentration field created by individual bacteria but also affecting back each one. However, many potential scenarios can be considered where stigmergy might actually be engineered. One particularly interesting case study would be related to the emergence of biofilms, where microbes generate an extracellular matrix that eventually surrounds the cell population, protecting them from environmental stresses, toxicity or nutrient shortages. The extracellular matrix is not just a container for the microbial population. It also modifies their behaviour and adaptation potential. One potentially interesting avenue here is engineering interactions among a cell consortium that can perform complex computational tasks.

2. One important target for bioengineering novel tissues and organs involves the interplay between cells and extracellular materials. This is particularly relevant in some contexts, such as the formation of new organs from cell-free matrices. In many cases, the maintenance and morphogenesis of some bio-
materials (such as bones) results from a dynamic process of creation and destruction maintained by interacting populations of cells specialised in each part of the process. In social insects, this feedback between individuals and the structures they build is known as stigmergy (Theraulaz et al).

3. Smart swarms capable of memory and information processing could be useful in making complex decisions related to a number of biomedical issues where there is a need of detecting and targeting specific cells. Cancer is one example of this class. Ongoing work in this area has shown that engineered microbes can be used to target tumor cells thanks to a combination of a special environment associated to most solid tumours (i.e. an acidic environment) that is suitable to microbes and a cytolytic mechanism that is triggered once a given density of microbial cells is reached. Here too a quorum sensing mechanism plays a specially relevant role. Further developments of this scheme could involve exploiting collective intelligence and complex decision-making designs.

4. Insect colonies, as discussed above, have been often compared to a neural network. As it happens with neural systems, individual agents inside an ant colony can exchange bits of information with their nest mates through a range of chemical signals. In our models and examples above we have assumed a single class of signal as the vehicle of exchange but there is a wide variety of QS messenger molecules (figure 13) and thus a potentially wide range of interactions (Williams et al 2014). This is something also in common with ant colonies: multiple chemical signals appear to be associated to exchanges between nest mates. A theoretical framework that can take into account the capacity of a SCI system involving multiple signals is much needed.

5. One potential scenario where SCI can play a relevant role involves the use of synthetic biology for ecosystem repair (Solé 2015; Solé et al 2015). It has been recently suggested that engineered microorganisms and their ecological interactions could be engineered to prevent ecosystem degradation and collapse or even help in reducing the impact of climate change. The proposed engineering motifs were based in a simple set of interactions defined, for example, in terms of mutualistic links. More complex scenarios could be considered here, taking advantage of the views of SCI. Ecosystem bioengineering could be designed under more flexible conditions, allowing decision-making processes to take place in such a way that the engineered consortia could adjust over time to different environmental conditions.

As a final point, we can also ask ourselves to what extent the previous examples are instances of how to map observed classes of swarm behaviour into an equivalent microbial counterpart. This is a correct statement at least in some of the examples presented above, at least under the assumption that we have been searching for rather general, perhaps universal sets of rules that pervade the nonlinearity of collective intelligence. But there is nothing preventing us from moving beyond the boundaries of the observed universe of actual forms of swarm intelligence.

Are there other, different potential ways of engineering intelligent behaviour using synthetic biology? By different this means designs that lead to qualitatively different classes of complex decision-making departing from insect colonies. This is a very important question, since a negative answer could support the view that observed forms of a superorganism are attractors in the landscape of the possible: nothing essentially different exists beyond what evolutionary dynamics has been able to find and strong constraints operate limiting the repertoire of possible behaviours (Alberch 1989). But may be there are other ways of building swarms through genetically engineering living entities in ways that depart (partially or completely) from the observable natural world. If that were the case, we could have evidence for alternative evolutionary scenarios for collective intelligence could have been possible.

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FIG. 13 Structures of some representative quorum sensing signalling molecules. Here we display just seven examples from the large set of QS candidate signalling molecules. Adapted from Williams et al (2014).
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VIII. REFERENCES


