Behavioral Metabolution: Metabolism Based Behavior Enables New Forms of Adaptation and Evolution

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Abstract

Both metabolism and behavior play a key role in biological theory and artificial life modelling. Yet, despite their centrality there has been very little exploration of the relationship between these concepts and almost no exploration of how the interaction between the two could impact on evolution or instantiate alternative mechanisms for evolutionary processes. We present a simulation model of bacteria capable of metabolism-based chemotaxis: a minimal metabolic system capable of modulating behavior by influencing the probability of flagellar rotation (like in *E. coli* chemotaxis). We perform two illustrative experiments. In the first, the incorporation of a chemical compound into metabolism qualitatively improves the chemotactic strategy. In the second, an encounter with a specific chemical compound leads to a reaction that opens up a new metabolic pathway while automatically regulating chemotaxis towards that same compound. Both experiments illustrate the adaptive potential of metabolism-based behavior and can be used to explore the idea of "Behavioral Metabolution," a co-evolutionary synergy between behavior and metabolism. We abstract some principles of behavioral metabolution and discuss its application to early prebiotic evolution.

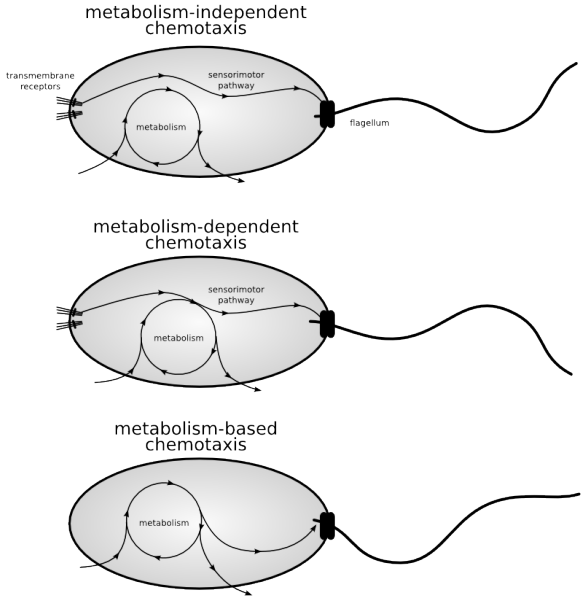

Figure 1: Three different relationships between metabolism and chemotaxis. Arrows indicate only short-term dynamical influence between processes. See text for details.

Introduction: metabolism and behavior

There is a long tradition in artificial life of investigating the origins and essence of life through the study of metabolism. Metabolism is understood as the far from thermodynamic equilibrium organization of chemical networks that produce and sustain their components from available energetic and material resources (Ganti, 1975; Kauffman and Farmer, 1986; Morowitz, 1999). Recent work on protocellular systems (Rasmussen et al., 2008) has re-framed research on metabolism within the framework of minimal forms of (proto)cellular compartments capable of self-maintenance.

Rarely is the environment of such early-life scenarios considered to be controlled or selected by a behaving or moving proto-life-form. However, recent artificial models of self-moving protocellular (autopoietic) systems (Suzuki and Ikegami, 2009; Egbert and Di Paolo, 2009) and real, self-propelled chemical systems (Toyota et al., 2009) suggest that even extremely simple forms of proto-life may have been capable of selectively modulating their environment through behavior.

In parallel to the omission of behavior in the study of the origin of life, studies of minimal adaptive behavior have almost completely ignored the role of metabolism as sustaining or modulating behavioral patterns. In particular, research on bacterial chemotaxis (the paradigmatic case of "minimal adaptive behavior") has long proceeded under the assumption that behavior generating mechanisms operate in an metabolism independent manner (i.e., while behavior subserves metabolic survival, sensorimotor pathways are not influenced by short-term metabolic dynamics). This assump-

tion can be traced back to the pioneering work of Julius Adler (1969) and has since remained almost unquestioned even in the most detailed and systematic simulation models of bacterial chemotaxis (Bray et al., 2007). It is, of course, not the only possible relationship between metabolism and chemotaxis. Figure 1 indicates three different possibilities for this relationship, *independent*, *dependent* (mechanisms in a sensorimotor loop are created by the metabolism) and *based* (metabolism itself modulates behavior). Recently, the growing evidence for metabolism-dependent chemotaxis in many bacteria (Alexandre and Zhulin, 2001), including *E. coli*, has attracted renewed attention to the interplay between metabolism and behavior.

In short, the interaction between behavior and metabolism remains currently under-explored even though empirical and modelling work has begun to address its possible implications. In particular, an aspect that deserves further examination is the effect of this interaction on early (and not so early) evolutionary dynamics. The goal of this paper is to present a model that investigates some potential implications of the interaction between metabolism and behavior in both directions (behavior $\rightarrow$ metabolism and metabolism $\rightarrow$ behavior) as well as the potential impact of these interactions upon evolutionary processes.

We shall first present a model of *metabolism-based chemotaxis* consisting of a minimal metabolism coupled to a simplified motor system inspired by *E. coli*. We use this model to demonstrate, through two experiments, that: 1) metabolism can modulate behavior in an adaptive manner, 2) behavior can change the metabolism by changing the environment in which it exists and, 3) changes in metabolism can produce new types of behavioral patterns. Next, we abstract away some general principles and implications of metabolism-based chemotaxis. Finally, we conclude with some discussion regarding the evolutionary dimension of metabolism-based chemotaxis, what we term "behavioral metabolution", and its potential application to the question of early evolution of life.

Metabolism-based chemotaxis, the model

We consider metabolism as the self-production of a chemical network through the transformation (by the network) of available energetic and material resources into constituents of the network. This process is most simply realized through an auto-catalytic reaction whereby energetic and material resources (E and M respectively) are transformed by network constituent C into more C and a low energy waste V thus: $M + E \xrightarrow{C} C + 2V$. This single reaction may be understood as a higher level abstract representation of a whole network of processes, considering that the essence of metabolism is that of an auto-catalytic network. To capture the requirement of far-from-thermodynamic equilibrium, C and V are considered thermodynamically unstable and degrade rapidly. Their continued presence is therefore only possible through

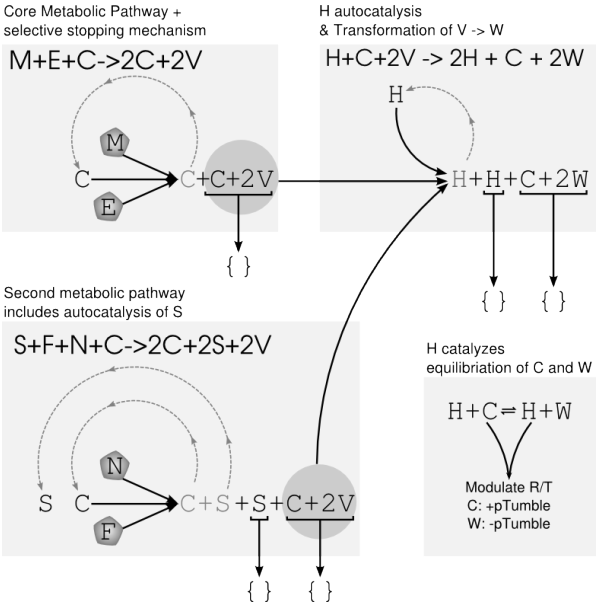

Figure 2: Reactions grouped conceptually by their 'role' in the model. Resources are surrounded by pentagons. Autocatalytic reactions are indicated by circular paths. Degradation of reactants is indicated by an arrow to the empty set.

a *dynamic* equilibrium of degradation countered by production. We label this reaction the "core metabolism" and expose it to various other reactants in different experiments. Table 1 and Figure 2 show all of the chemical reactions that can be active in the bacteria simulated in our model. The upper-left square indicates the core metabolism described in this section. The other pathways are described in the experiments and results section.

The metabolic dynamics are described by the differential equations in Table 2. These equations include some reactants that are only used in some of our experimental scenarios and are explained later in the text. The rate con-

#	reactants		products	k_f	k_b
0:	M + E + C	$\rightleftharpoons$	2C + 2V	0.61	≈ 0
1:	H + C	$\rightleftharpoons$	H + W	0.006	0.006
2:	H + C + 2V	$\rightleftharpoons$	2H + C + 2W	0.37	≈ 0
3:	C + 2V	$\rightarrow$	{}	0.006	n/a
4:	C + 2W	$\rightarrow$	{}	0.006	n/a
5:	H	$\rightarrow$	{}	0.02	n/a
6:	S	$\rightarrow$	{}	0.0001	n/a
7:	S + F + N + C	$\rightleftharpoons$	2C + 2S + 2V	0.99	≈ 0

Table 1: A list of the chemical reactions in each simulated metabolism. Also indicated are the reaction rates (forward and backward). These rates are referred to in Table 2.

$$
\begin{aligned}
dE/dt &= -k_{f0}EMC + k_{b0}C^2V^2/4 + k_d[E](\mathbf{x}) \\
dM/dt &= -k_{f0}EMC + k_{b0}C^2V^2/4 + k_d[M](\mathbf{x}) \\
dC/dt &= -k_{f0}EMC + k_{b0}C^2V^2/4 \\
&\quad -2k_{b0}C^2V^2/4 + 2k_{f0}EMC \\
&\quad -k_{f1}CH + k_{b1}HW \\
&\quad -k_{f3}CV^2/2 - k_{f4}CW^2/2 \\
&\quad -k_{f7}CFNS + k_{b7}C^2V^2S^2/6 \\
&\quad -2k_{b7}C^2V^2S^2/6 + 2k_{f7}CFNS \\
dV/dt &= -2k_{b0}C^2V^2/4 + 2k_{f0}EMC \\
&\quad -2k_{f2}CHV^2/2 + 2k_{b2}CH^2W^2/4 \\
&\quad -2k_{f3}CV^2/2 \\
&\quad -2k_{b7}C^2V^2S^2/6 + 2k_{f7}CFNS \\
dW/dt &= -k_{b1}HW + k_{f1}CH \\
&\quad -2k_{b2}CH^2W^2/4 + 2k_{f2}CHV^2/2 \\
&\quad -2k_{f4}CW^2/2 \\
dH/dt &= -k_{f2}CHV^2/2 + k_{b2}CH^2W^2/4 \\
&\quad -2k_{b2}CH^2W^2/4 + 2k_{f2}CHV^2/2 - k_{f5}H \\
dF/dt &= -k_{f7}CFNS + k_{b7}C^2V^2S^2/6 + k_d[F](\mathbf{x}) \\
dN/dt &= -k_{f7}CFNS + k_{b7}C^2V^2S^2/6 + k_d[N](\mathbf{x}) \\
dS/dt &= -k_{f6}S - k_{f7}CFNS + k_{b7}C^2V^2S^2/6 \\
&\quad -2k_{b7}C^2V^2S^2/6 + 2k_{f7}CFNS + k_d[S](\mathbf{x})
\end{aligned}
$$

Table 2: Differential equations specifying how chemical concentrations change within each simulated bacterium (excluding influence of the environment). k_{fn} and k_{bn} represent the reaction rate constants for the nth reaction in the forward or backward direction. $[\rho](\mathbf{x})$ represents the local environmental concentration of the resource ρ.

stants (k_{fn} and k_{bn}) in the differential equations have been determined by assigning *free-energies* to each reactant and *activation-energies* for each reaction such that the system adhered to the constraints defined in our definition of a minimal metabolism. Given chemical free-energies and reaction activation-energies, reaction rates can be calculated according to $k_f = \exp(A)$ and $k_b = \exp(A + R - P)$ which indicate the reaction rate for a forward (exergonic) reactions and backward (endergonic) reactions respectively. A represents the activation energy of the reaction and R and P represent the combined energy levels of the reactants and the products respectively of the reaction. Figure 3 indicates why the forward and backward equations are different. This method of determining reaction rates allows the exploration of abstract chemistries while remaining congruent with the 2^{nd} law of thermodynamics.

Resources encountered in the environment diffuse into bacteria at a rate proportional to the local concentration of the environmental resource. The rate constant for this diffusion, $k_d = 0.04$, is the same for all resources.

The chemical reactions are simulated as occurring in a compartment surrounded by a membrane that includes a set of flagella. The clockwise and counter-clockwise flagellar rotation is determined by the relation between the concentrations of C and W compounds. In analogy to the working of flagellar rotation in *E. coli* chemotaxis, when the overall movement of flagellar rotation is counter-clockwise the bacterium is propelled in straight direction (what is generally called the "running mode"), whereas when flagella rotate clockwise, the bacterium rotates on its axis changing direction randomly ("tumbling mode"). Bacteria are simulated in a 2D square'petri-dish' of 200 units. By default, bacteria are always running, i.e., moving in a straight line in the direction of their orientation, α, thus: $\frac{dx}{dt} = 0.05 \cdot \cos(\alpha)$, $\frac{dy}{dt} = 0.05 \cdot \sin(\alpha)$. A baseline probability of tumbling allows for the random direction to be changed occasionally. Tumbling bacteria remain at the same location, with α changed to a random value selected from a flat distribution between 0 and 2π. The effect of the influence of C and W concentrations on flagellar rotation is abstracted and summarized in the following equation governing the probability of tumbling of the bacteria (i.e. the probability of the bacteria changing direction randomly): $P_{\text{tumble}} = 0.001 * \max(-0.1 + [C]^2 - 0.9[W]^2, 0.01)$.

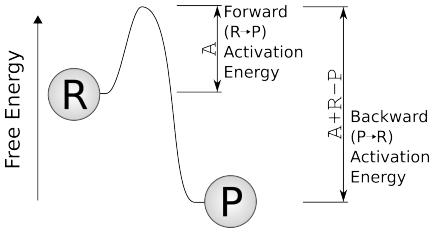

Figure 3: Energy required for a reaction to take place. The line traces the free energy of the reactants as the reaction takes place.

Experiments and results

The goal of these two experiments we now present is to provide a proof of concept of how, in metabolism-based chemotaxis, small changes in metabolism can lead to qualitative changes in behavior (experiment 1) and how behavior can lead to fixation of new metabolic pathways (experiment 2).

E1. Influence of metabolic change in behavior

In this experiment, we demonstrate how a small change in metabolism can lead to a substantial, qualitative difference in behavior. Specifically we demonstrate a scenario whereby one form of chemotaxis (selective-stopping) is transformed into a more sophisticated form (gradient-climbing) through exposure to a new reactant. To do this, we compare two different types of bacteria, placing 100 of each type evenly distributed on a petri dish containing at its center a resource of $M+E$; the concentration of which decays with distance following a Gaussian distribution (indicated in the histograms). The control group starts with only reactant $[C] = 0.5$ which provides a functioning core metabolic pathway. The experimental group is the same as the control except that it starts

with an additional reactant, $[H] = 1.0$. The presence of this chemical produces a self-maintaining gradient-climbing mechanism by enabling reactions 1 and 2 (see Table 1 and Figure 2 top-right and lower-right). These two conditions allow us to examine the differences between bacteria that have not encountered H (control group) and those that have (experimental group).

Figure 4 indicates the behavior of the control group which demonstrates the selective-stopping mechanism accomplishing a simple form of chemotaxis. The histogram at the top indicates the number of bacteria at different distances from the peak resource at the end of the trial, (data taken from 10 trials, each of 100 bacteria). The three plots at the bottom of the figure indicate the spatial distribution of the bacteria in the petri dish at the start, halfway through, and end of a typical trial. The behavior of these bacteria is a simple result of the metabolism and its influence on motion. In the absence of W, the concentration of C will drive the behavior of the bacterium: if the metabolic activity (i.e., the production of C) is high the probability of tumbling will increase and the bacterium will remain in the local area. If C is low the probability of tumbling will decrease and the bacteria will move, still in a random walk, but with increasingly long durations of directional movement until C is produced again (e.g., when the bacterium finds a place where M and E are abundant). The mechanisms resembles the Ashbian principles for adaptation (Ashby, 1952) except that the system is simply altering its relation to the environment, instead of reconfiguring itself internally. In this way, behavior is directly modulated by the rate of metabolic production in a "selective stopping" manner that is beneficial for metabolism: "stay where you are if the metabolism is running sufficiently well, otherwise run". This is the simplest example of what we call *metabolism-based chemotaxis* where the "sensorimotor" pathway is the metabolism itself.

Bacteria with $[H] > 0$ are capable of the the more sophisticated "gradient climbing" strategy (widely found in bacterial chemotaxis) whereby the bacteria are capable of comparing, as they move, the current concentration of a chemical compound with its concentration earlier. To explain how this is accomplished, we must describe the dynamics of the new reactant, H. H is auto-catalytic in the presence of C and V, so once a functioning metabolism encounters H, its concentration will be maintained above 0. In this simulation, H performs two roles. It catalyzes an equilibration between C and W, $(H + C \rightleftharpoons H + W)$ and additionally, in its auto-catalysis, transforms V into W which inhibits tumbling. These equations produce a system that is described conceptually in Figure 6 whereby 1) stoichiometry and reaction rates cause W to change more rapidly than C, 2) W and C tend to equilibriate to equal concentrations, and 3) W inhibits the probability of tumbling and C enhances it. These properties produce an adaptive gradient climbing mechanism (adaptive in the sense used by bacteriologists to describe the ability to adapt to a wide range of base levels of stimulus). It can be seen how in both conditions bacteria approach the resource center but H produces a more efficient result due to its adaptation; as is evident when comparing Figures 4 and 5 where the gradient-climbing bacteria move to the highest concentration of resource, unlike the selective-stoppers that stop when the resources are above a threshold. (In both cases, a secondary peak around a distance of 190 can be observed due to the effect of the petri dish wall).

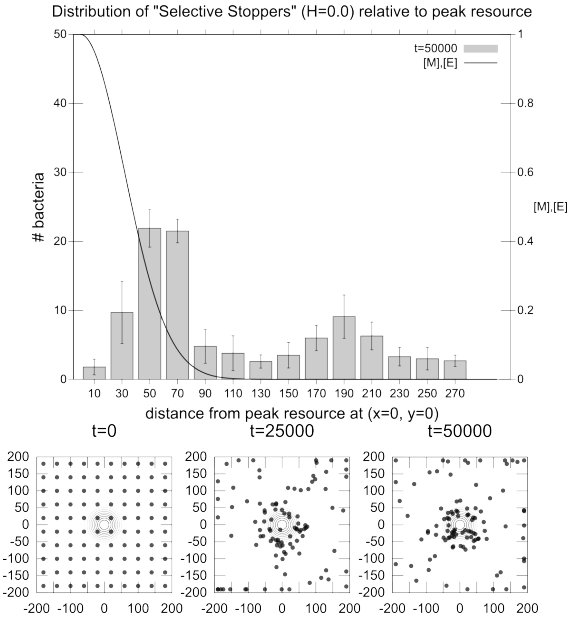

Figure 4: Selective-stopping bacteria distance from peak resource (top) and spatial distribution (bottom).

The experiment shows how changes in the metabolic network of a metabolism-based chemotactic agent can lead to qualitative adaptive changes and improvement on its behavior, through relatively simple means. While moving through its environment, a bacterium can potentially encounter a new component H that is incorporated into the metabolism through its self-catalytic activity and through its capacity to improve the adaptive behavior of the bacterium. The chances of this event happening are enhanced by the self-movement of the bacterium. Note that the specific changes that have occurred here have been designed to make the system as simple to understand as possible, not to suggest that the transformations described have occurred in this way in biology.

E2. Influence of behavioral change on metabolism

In this new experiment we include a second metabolic pathway. In this pathway, energetic and material resources (F

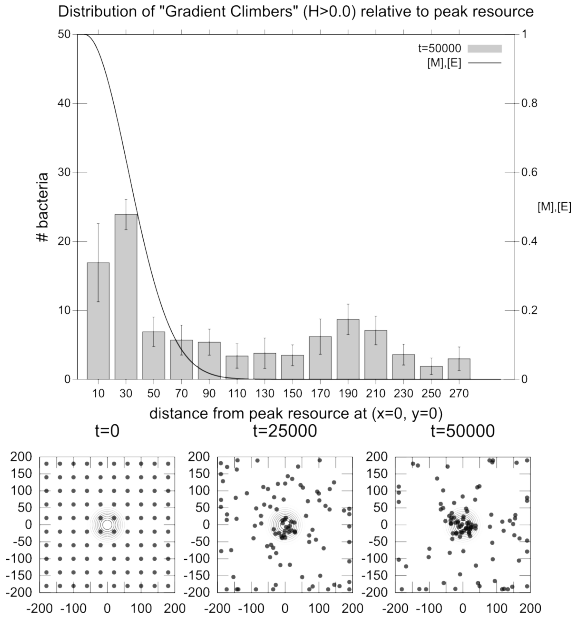

Figure 5: Gradient-climbing bacteria distance from peak resource (top) and spatial distribution (bottom).

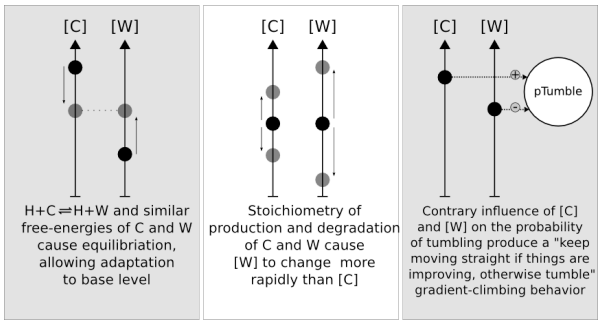

Figure 6: Implementation of gradient climbing mechanism.

and N respectively) are converted into C and V. Like the core metabolic pathway, this is an auto-catalytic production requiring C to be present to occur. However, unlike the core metabolic pathway this reaction is also auto-catalytic with respect to S. This means that S is both produced by the reaction and required for the reaction to occur (see Figure 2 bottom-left).

Bacteria, (initialized with $C = 0.5$, $H = 1.0$ and $S = 0.0$) are placed evenly distributed around a petri dish containing two sources of E and M, located at $(x = -75, y = 0)$ and $(x = 75, y = 0)$. One source of F and N is located at $(x = 0, y = 0)$. There is no S in the environment except within a circle of radius 0.5 around the left peak of resource E and M $(x = -75, y = 0)$, where $[S] = 1.0$.

Figure 7 indicates the distribution of the bacteria over the course of the simulation. The bottom figures are as in Figures 4 and 5, but the histogram now indicates the distribution of bacteria along the x-axis, comparing the distributions of bacteria that have zero and non-zero concentrations of S. Data have been collected at the end of 10 different trials, each of 100 simulated bacteria. As before, at the start of the simulation, the bacteria are evenly distributed around the arena. The gradient climbing mechanism attracts the bacteria to one of the sources of E/M. At this stage, none of the bacteria have any S, so F/N is not metabolizable and has no effect on the behavior of the bacteria as the metabolism based mechanism automatically ignores resources that are irrelevant to the metabolism. As time progresses, bacteria tend to gravitate towards the highest concentrations of E/M, and those that are at the left source have an increasingly high chance of encountering the pocket of S. Those bacteria that come into contact with S become capable of auto-catalyzing S. Their metabolism has been changed and the odds of this change occurring have been significantly influenced by their behavior. Those bacteria with $[S] > 0$ have gained a new metabolic pathway. They are now capable of metabolizing F/N and as time progresses, those bacteria that through their random walk are brought close enough to "taste" F/N, now also climb that gradient. Bacteria that were initially attracted to the right-most source of E/M never encounter S and accordingly never are drawn away from their initial F/N resource source and at the end of the simulation there are in a certain respect two 'species' of bacteria – one that consumes and is attracted to both pairs of resources and one that is only attracted to, and only consumes the original pair.

Discussion: Behavior, metabolism, evolution

The adaptive power of metabolism-based chemotaxis

Adaptive behavior is generally understood and modelled as optimizing some value function or as maintaining essential variables under viability constraints. However, there is generally no reference to the dynamics of the biological organization (e.g., metabolism) that serves as the basis of these viability constraints —see Egbert et al. (2009) for a discussion. When metabolic dynamics are directly coupled to behavior a number of adaptive phenomena come to the surface that generally pass unnoticed due to the typical abstractions made in adaptive-behavior models.

From the previous experiments we can generalize that, despite its simplicity (or perhaps thanks to it), metabolism-based behavior can enable a number of powerful adaptive capacities:

1. The metabolic **consequences of behavior can be eval-**

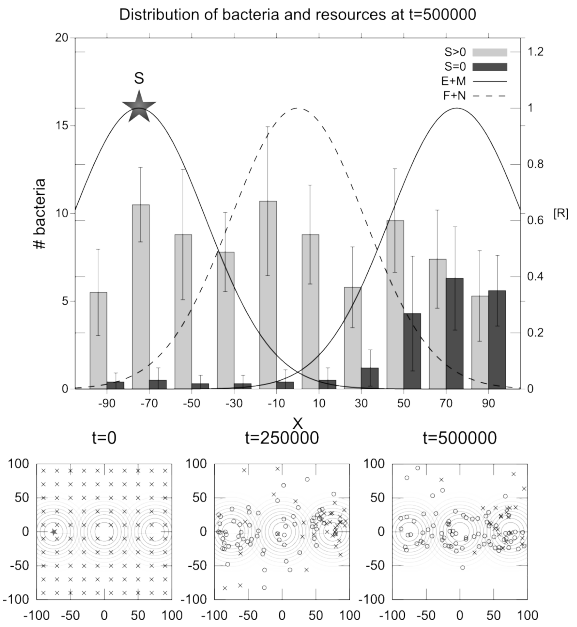

Figure 7: Experiment 2. Bacteria are initially attracted to sources of $M + E$, but those that encounter the metabolic-path-opening reactant S, automatically become also attracted to new resources $N + F$.

uated *online* (i.e., in ontongenetic time and in relatively short timescales) and behavior can be modulated accordingly.

2. Organisms can **adapt not only to the presence of specific chemicals but also to other environmental conditions** (e.g., temperature) that might influence metabolism.

3. Organisms can **adapt not only to changes in the environment, but to changes in their own metabolic organization** by modulating their behavior accordingly.

4. Organisms can **integrate** information from the environment and from within, which means that **behavioral and metabolic processes of adaptation can feed back to each other**.

As a consequence, organisms can adapt (respond appropriately) to various environmental and internal chemical compounds and conditions that were never previously experienced by the individual nor even by any of its ancestors. Note that the system will be attracted to any compound or condition that increases metabolic rate and will be repelled by those that decrease or inhibit metabolism. However, this does not rule out potential cases of maladaptation such as parasitic interactions that override the behavioral mechanism or interactions that increase the short-term rate of production of C but damage metabolism in the long-term by e.g., destroying the membrane.

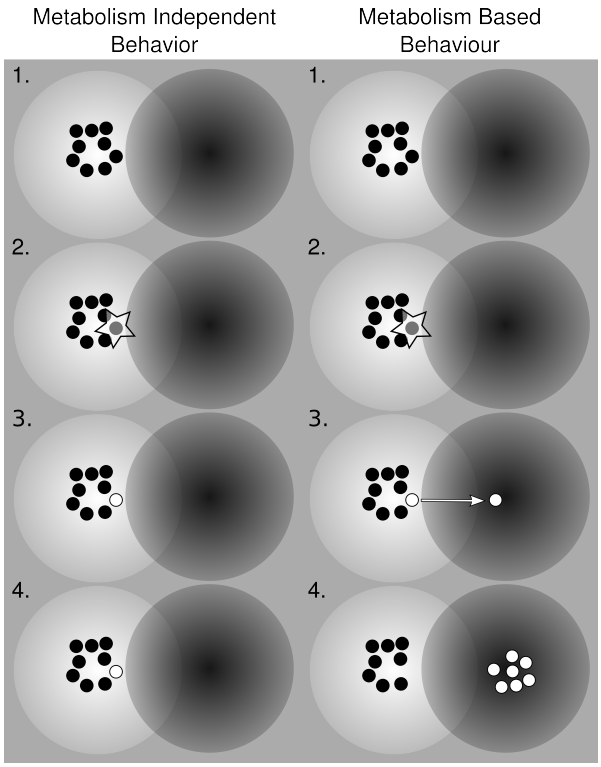

Figure 8: Metabolism-independent and metabolism-dependent responses to a change in organization (represented by a star in frame 2) that allows them to consume a new resource (dark circle).

Behavioral metabolution, the very idea

Not only does metabolism-based behavior unveil a powerful form of adaptation in ontogenetic time, but it also exposes an interesting evolutionary potential. Figure 8 illustrates the case of a mutation (genetic or otherwise inheritable) on metabolic pathways that permits one bacterium to exploit and metabolize a new environmental resource. Metabolism-independent chemotactic agents (left) will remain in place and the benefits of the mutation will pass unnoticed; unless there is an unlikely coincident mutation that makes transmembrane receptors sensitive to the new metabolic source *and* generates attraction to it. Genetic drift dictates that, most probably, such a *potentially* beneficial mutation will be lost since it has no beneficial effect on the bacterium. Metabolism-based chemotactic agents (right), contrarily, will immediately and automatically be attracted to the new resource (for it benefits metabolism) if they are exposed to it. They will benefit from the mutation by in-

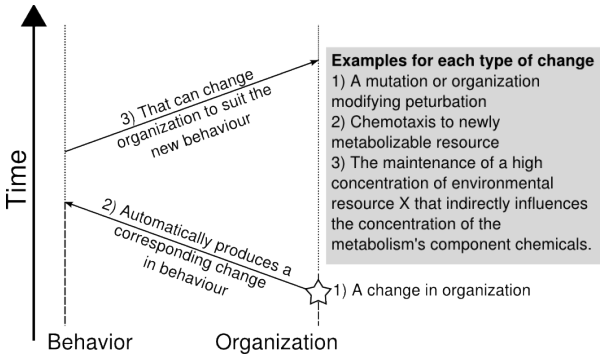

Figure 9: A cycle of mechanisms contributing to adaptation.

corporating a new metabolizable resource into their organization; the mutation will be retained and a new population could emerge in the new resource-rich environment, leading potentially to speciation.

The model presented in this article was inspired on bacterial chemotaxis. But the underlying principles can be easily generalized to a wider context:

1. Behavior modulated by metabolism can produce an online automatic adaptation to change. This change could be *external* (in the sense of an environmental change), or *internal* in that the behaving system has itself changed. Internal change could include genetic mutations or simply perturbations that damage or enhance the behaving system in some way.

2. Automatic, online adaptation to phenomena never experienced before, neither by the individual, nor its ancestors can make otherwise neutral mutations (such as the new ability to consume a resource) more likely to be beneficial mutations (through e.g., moving towards the new resource). It also facilitates speciation events through rapid separation of a newly capable individual from its previous population (discussed above).

3. Behavior can significantly influence metabolism during lifetime. This change can be caused by a persistent behavior (e.g., seeking out of a reactant) or through a random behavioral encounter with a reactant that is incorporated into the auto-catalytic network. In this way, behavior can provide an important source of variation of available chemical compounds, or simply significantly influence the local concentration of reactants.

These type of interactions between behavior, metabolism and evolution we have termed *Behavioral Metabolution*. We can see the cycle of influence in Figure 9, where a change to the organization of an agent causes it to automatically behave differently, in a way appropriate to its change in organization. The new behavior brings the system to a new environment where new mutations (or old mutations) and/or new environmental conditions might be beneficial for metabolism, or as demonstrated in Experiment 1, can produce a new (possibly improved) behavioral mechanism. In this way, a push-me/pull-you dynamic interplay can be established between changes in behavior and changes in metabolism, influencing evolutionary processes in ways that remain mostly unexplored.

The goal of the above experiments is not to provide *evidence* for this phenomenon but to show the very *possibility* and some potential aspects of it. Further extensions of the present work could include an open artificial chemistry with moving protocellular systems that could be used to determine whether the presence of self-movement largely increases the probability of chemical-evolutionary adaptation.

Behavioral metabolution as proto-evolution

It is at the very early stages of life when the coupling between metabolism and behavior could have played a particularly powerful role by instantiating, on its own (and without the presence of a genetic code or even without reproduction!), a form of (proto-)evolution.

Assuming an origins-of-life scenario where membrane compartments or oil-droplets enclose proto-metabolic reaction networks undergoing natural selection (Shenhav et al., 2005; Fernando and Rowe, 2008; Shapiro, 2007) it is evident how any tendency to move (even randomly) would become beneficial to such systems: local metabolic resources would soon be consumed and random movement would lessen competition for local resources. Any bias of random movement towards metabolically more beneficial environments would rapidly be selected. Since the selective-stopping chemotactic strategy has been shown to be easily evolvable (Goldstein and Soyer, 2008) it seems that it would, sooner or later, appear and be metabolism-based (since early metabolic networks would tend to be highly integrated and simple—certainly not with the degree of specialization required for metabolism-independent modes of chemotaxis).

Admittedly, we have implemented an abstract version of a sophisticated flagellar movement, which is highly unlikely to be found at any early stage of evolution. However, at such early stages movement could be implemented on a wide variety of metabolism-controllable ways. For instance, simple reaction-diffusion spots have been shown to be capable of movement (Krischer and Mikhailov, 1994), and more recent work on convection cells (Toyota et al., 2009) also provides an example of potential early prebiotic life-like self-movement. In addition, changes in membrane properties could operate selectively on environmental currents; or, control of protocell buoyancy could lead to upward and downward selective movement. Finally, in its most simplified form, movement could be completely random and provided by environmental factors; to accomplish behavioral metabo-

lution, it would suffice (in this extremely simple form) for the protocell to be capable of influencing the permeability of its membrane.

In any of its possible instantiations, what remains central to the idea of behavioral metabolution (and its relevance to early forms of life) is the potential of the coupling between metabolism and behavior to explore and select the chemical space that is available for metabolic organization (and its behavioral control). In addition, differences between the behavioral trajectories of protocells could lead to differences in their metabolic and behavioral organization, potentially causing speciation and new ecological relationships (e.g., one species consuming another's waste products). An example of a "speciation-like" effect of behavioral metabolution might be to consider irreversible effects on metabolic organization caused by behavioral patterns. Thus, for instance, if the agent continuously moves towards certain types of environments where resources of a certain redundant metabolic pathway are not available it might lose its capacity to metabolize such resources. A variation of experiment 2 could explore this phenomenon by making S act like C (i.e., act as a flagellar rotation modulator), so that agents without C are still viable in environments with $F + N$; without the presence of $E + M$, C could eventually disappear and the agent will lose its capacity to metabolize $E + M$ again.

Conclusion

Despite the central role that both metabolism and adaptive behavior play in artificial life and theoretical biology, very little attention has been paid to the interplay between the two, especially at the ontogenetic and evolutionary scales. When behavior is not controlled by a subsystem that maximizes some function (generally external to the subsystem itself, in the form of selected adaptations or satisfaction of internal "needs") but is, instead, directly modulated by metabolism, then a wide range of adaptive phenomena come to the surface. We have shown, through a model of metabolism-based chemotaxis, how changes to metabolic pathways can qualitatively improve behavioral strategies (e.g., from a selective-stopping to a gradient-climbing strategy; experiment 1) and how behavior might serve to explore and fixate new metabolic pathways (experiment 2). These two examples may be used to reveal the deep role that the behavior-metabolism interplay could have played in evolution: by permitting the behavioral *exploration* of the chemical space available for metabolism, by allowing the behaviorally driven selective and repetitive *exposure* to such chemical compounds and their subsequent incorporation into metabolism and, finally, by the potential behavioral improvements that changes in metabolism could produce. We coined the term "behavioral metabolution" to refer to these phenomena where variations on metabolic dynamics (genetic mutations, creation of new chemical species, etc.) feed back into behavioral changes that, in turn, affect the environmental conditions that feed metabolism.

Different forms of metabolism-behavior coupling could have bootstrapped or driven the evolution of early (pregenetic) life and could be currently instantiating forms of non-genetic inheritance or genetic assimilation of phenotypic plasticity. We hope to have shown that incorporating this type of connection between behavior and metabolism opens up a promising line of artificial life research where the long term (evolutionary) consequences of interactions between behavior, system organisation and environment and can be systematically studied in simulation.

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