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Teleonomy: The Feedback Circuit Involving Information and Thermodynamic Processes

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Abstract

Informational and entropic - metabolic aspects are strictly intertwined in organisms. An overview of bacterial chemotaxis is presented as a good and simple model to study these issues. In particular, the paper shall focus on the ability of the organism to restore its homeostasis not only from a metabolic point of view but also from an informational point of view. The organism cannot accomplish this task without a good "model" of the environment and without undertaking appropriate actions that will somehow modify it or at least the relation "organism - environment". Subsequently, the concept of teleonomy is developed as a dynamical trade - off between segregation and openness of the organism both from a thermodynamic and informational point of view.

Keywords: Chemotaxis, *Escherichia Coli*, Methylation, Feedback, Surprisal, Kullback - Leibler Divergence, Bayesian Probability, Anti-Feedback, Teleonomy

1. Introduction

Some general characters of organisms have been so far understood [1,2]:

1) In order to be alive organisms need to display crucial regulations.

2) The regulation machinery involves a massive use of feedback circuits.

3) Such a regulation can happen thanks to a delicate trade-off between openness to the environment and impermeability towards external fluctuations.

4) Openness is required in order to allow the (correct) thermodynamic fluxes between organism and environment.

5) Impermeability is required in order to preserve the informational program, represented in the organism's structures and realized through their performances.

Our problem is how to put all of this into a coherent and single model. In order to advance in this area of research, in the following I shall study the case of bacterial (in particular, *E. Coli*'s) chemotaxis. Some preliminary notions will be useful. Then, the molecular aspects of chemotaxis will be considered and a cybernetic model of the network provided. Subsequently, the specific informational aspects involved here will be examined. Finally, the concept of teleonomy will be developed by showing the evolutionary and adaptive significance of the model.

2 Information and Entropy

All organisms need to feed free energy from the environment and to download entropy in it. Only this exchange can keep the necessary order that enables the display of vital functionalities. This means that the organism cannot be exposed to the random changes of the environment. The probability to remain alive when exposed to random fluctuations is exceedingly low for thermodynamical reasons: the environmental configurations promoting the specific organization needed by the organism are a vanishing subset of all the possible ones. This implies that the organism cannot work as a blind mechanical engine, that is, like a machine that simply maps certain inputs whatsoever into certain corresponding outputs (reactions or actions). The organism must be able on the contrary, to look actively for certain very specific inputs as driving to the appropriate free - energy sources, to select them among many different others (representing noise) and profit from them in an appropriate way by favouring the right metabolic exchange with the environment. In other words, it must split the whole problem into two different parts:

• Dealing with the external inputs;

• Acquiring free energy.

The language needed for dealing with the first problem is that of information: the organism must exercise an informational control on certain environmental parameters that are able to "tell" where the searched sources of free energy are. What do the words "informational control" mean? It is any procedure through which a system 1) ascertains the functional relevance of a certain signal, where a signal can be understood as any modification of a physical or chemical medium, and 2) tends to reestablish a certain steady or default state. The words "functional relevance" denote the vital value of a certain signal from the point of view of certain functions or of a set of functions. In a first, rough approximation this can mean either noxious or life-improving. Ultimately, especially when dealing with bacteria, the survival of the whole organism is the criterion of this evaluation. I have intentionally avoided terms like "meaning", since they would surreptitiously introduce an anthropocentric terminology, whilst we deal here only with biological requirements and therefore biological functions.

The language for dealing with the second problem above is that of thermodynamics. This second step is the metabolic one, which for bacteria was the first to be studied [3,4]. Now, how does this wonderful mechanism come out? How can the organism do all this without having a brain and without having a consciousness?

3. The Molecular Aspects of Chemotaxis

A very relevant example is shown by the chemotaxis of the gram - negative bacterium *Escherichia coli*. The main vital problem of the organism is to find the maximal concentration of sugars. The constraints are the following:

• The bacterium is unable to choose the direction of swimming by itself.

• It is unable to preserve a straight movement for more than a short time of a few seconds, due to the fluctuations of the external fluid.

Consequently, how does it choose and maintain the correct direction? The solution is the following: the bacteria alternate tumble and swim phases (**Figure 1**), so that a random walking comes out that leads to optimal results for the problem at hand [5]: the helical nature of the single flagellar filaments allows for the two types of movement described here. The bacterium will sense the relevant chemical gradient and will base its motion on this parameter: the cell determines its heading in chemical gradients by measuring temporal concentration changes as it moves about (and not by sensing different spatial concentrations, for instance at two opposite sides of the bacterium), and it compares current chemoreceptor

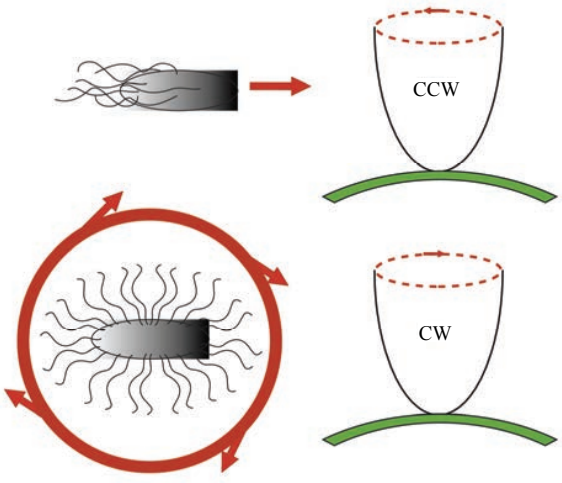

Figure 1. *E. coli's* **movement. Above: Straight swim. In this case, the flagella turn counter-clockwise. Below: Tumbling. In this case, the flagella turn clockwise.**

occupancy with the sensory effects produced during previous few seconds. If the organism senses to swim in the right direction, it will preserve a straight line as long as possible before being forced to tumble because of a random change of direction due to external fluctuations. If it senses that it is swimming into the wrong direction, it will tumble immediately. It is a sort of induced "choice", but ultimately determined by the evaluation that the organism makes of the external environment.

Let us now consider the response mechanism. Chemical gradients are sensed through multiple transmembrane receptors, called methyl accepting chemotaxis proteins (MCPs), which vary in the type of molecules that they detect [6,7]. These receptors may bind attractants or repellents directly or indirectly through interaction with proteins of the periplasmatic space between the exterior and the interior membranes [8] (**Figure 2**). The *E. coli* is attracted by various sugars and amino acids and repelled by fatty acids, alcohols, and other potentially noxious compounds. Attractants lower the activity of the receptors and so determine swimming, whilst repellents increase the activity of receptors determining tumbling [9,10]. The signals from these receptors are transmitted across the plasma membrane into the cytosol, where Che proteins (CheA, CheB, CheR, CheW, CheY, and CheZ) are activated: they are able to alter the tumbling frequency according to the inputs (**Figure 3**). Signals are codified and passed from the transmitter module of one protein to the receiver module of a second protein via phosphotransfer. In the involved pathway, a family of related transmembrane receptors act as the input module by binding either small chemotactic molecules or their

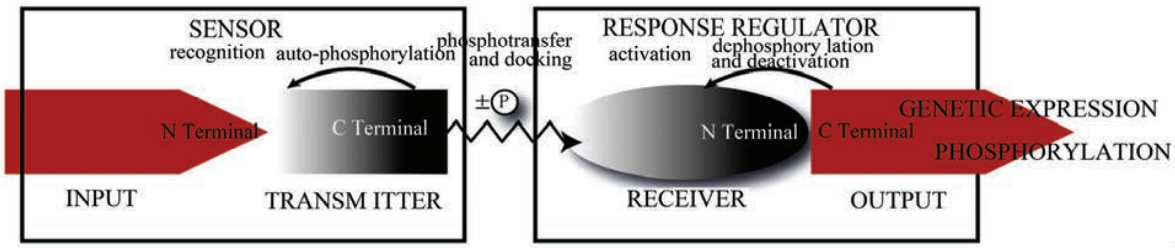

Figure 2. The sensory component processes an environmental signal through its input module to activate the transmitter module, which is auto-phosophorylated: The C terminal of the latter binds to the N Terminal of the former. Phosphoryl transfer from the transmitter module of the sensor component to the receiver module of the response regulator component activates the output module: here, the N terminal of the receiver binds to the C terminal of the output. Adapted from [12].

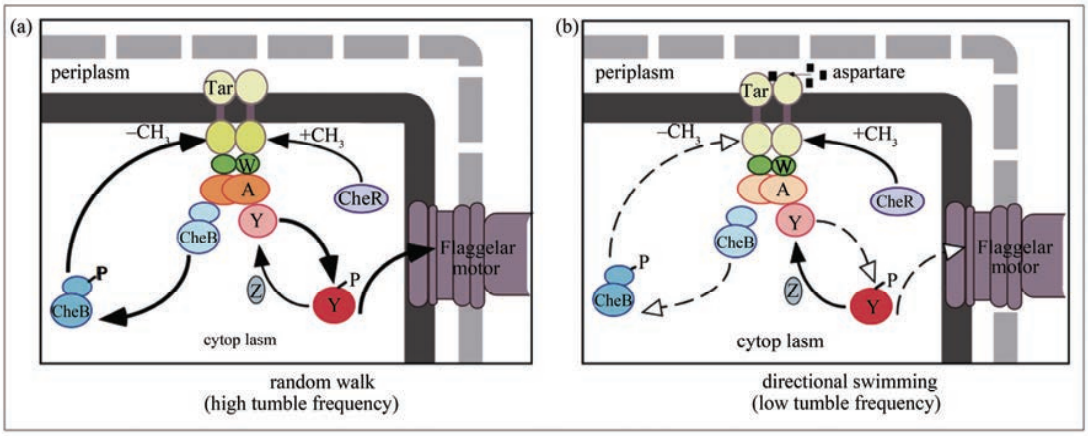

Figure 3. Activated forms of the proteins are shown in a darker colour and solid arrows are used for indicating activation. (a) The high level of phosphorylated CheY increases the frequency of switching to clockwise flagellar rotation and thus determines tumbling. (b) When a receptor binds ligand and/or is unmethylated, CheA is inactive. The levels of phosphorylated CheY are reduced, leading to more counterclockwise flagellar rotation and more running. With CheB inactive, the methyltransferase activity of CheR (purple) serves to decrease receptor sensitivity. Adapted from [6].

periplasmic binding proteins. Once these effectors are bound, the activity of a transmitter histidine kinase (CheA) that is associated with the cytosolic domain of the receptor(s) is rapidly modulated in cooperation with the scaffolding protein CheW. Increase (or decrease) in the activity of this kinase leads to transient increases (or decreases) in intracellular levels of phosphorylated CheY (the targeted *response regulator*) which directly affects flagellar rotation and the frequency of their reversal. The relative level of phosphorylated form of CheY (CheY-P) determines the bacterium's behavior: if high it will tumble. This means that the motors rotate CCW by default and tumbling is induced as a sort of reaction to an external negative feedback. A very important element is reaction timing: because Brownian motion of the fluid medium can randomly reorient the bacterium, this requires very short response latencies. It is here that genetic (instructional) factors play a role by enhancing and damping protein production. In order to account for the extraordinary stimulus sensitivity of the chemoreceptors, one must focus on CheZ, whose function is to accelerate the loss of phosphate from CheY.

Slower habituation (that is, the progressive adaptation to a constant stimulus) of the network response is induced by the reversible methylation and demethylation of a specific group of glutamate residues within predicted coiled - coil regions of the receptor cytosolic domains. These covalent modifications are catalyzed by an S - adenosylmethionine-dependent methyl-transferase (CheR) and a partner methyl-esterase (CheB) that act in order to respectively increase (methylase) or damp (demethylase) the signal by adding or removing the methyl group CH_3, respectively (which also implies the rapid genetic expression or repression of CheR, CheB, and CheZ). When CheR is kept low, the bacterium runs; when CheB's activity is suppressed, the bacterium tumbles [11] (**Figure 4**). The steady-state level is determined by the balance between the production of CheY-P (catalyzed by CheA), and its destruction (catalyzed by CheZ). Now, in the presence of attractants

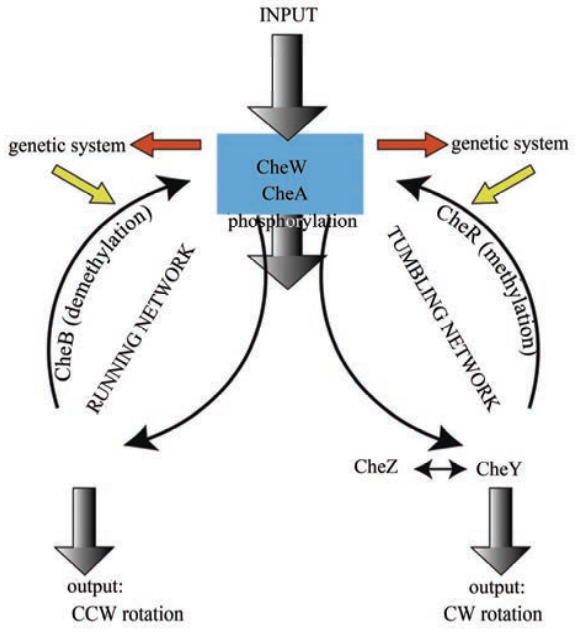

Figure 4. A schematic overview of the chemotaxis network system. Actually, it is a sort of module inside the organism relative to the genetic or metabolic modules. This shows that the organism is built as an organized and concerted cluster of subsystems [1], in such a way that there are much more connections inside a single module than with other modules, although some connections always exist (in the figure schematic connections with the genetic system are shown).

the level of CheA-P, CheY-P and CheB-P remains low, allowing swimming. However, the absence of active Che-B will also raise the level of methylation with the consequence that the bacterium will tumble. On the contrary, in the presence of repellents, the level of CheY-P increases and the bacterium will tumble, but the level of both CheA-P and CheB-P will also rise, with the consequence that there will be less methylation and therefore swimming becomes possible (**Figure 5**).

Summarizing, the whole network combines two completely different molecular-chemical mechanisms: a phosphorylation mechanism (expressed by the path from CheA to CheY) and a methylation-demythilation balance induced by the opposite actions of CheR and CheB. The cybernetic-informational value of this molecular-chemical network is further displayed when considering two aspects:

• Attractant and repellent compounds are sensed by means of the relative specific chemoreceptors and not through their beneficial or harmful physiological effects, as it would be the case for a mechanical engine. It is exactly this that gives to this step the significance of an informational step and not of a metabolic one (a chemoattractant need not be a substance that the bacterium can metabolize in any way). It is important to understand that when the transmitter binds to the input signal, auto-phosphorylation and docking (*i.e.* the binding of the signaling molecule with its partner) are not the sole possible reaction. Alternatively, the transmitter can "choose" undocking [12].

• Temporal comparison is effected between a stimulus experienced during the past second with that experienced during the previous 3 seconds, which implies that the cell recovers from a small step stimulus (a pulse in the concentration of attractants or repellents) within 4 seconds [13,14]. It is very important to understand that any signal is always mixed with noise and there is therefore always the possibility of an error. The length of time over which the signal is averaged is inversely proportional to the filter cut-off frequency (that separates signal from noise) and determines the adaptation time of a differentiating system to step inputs [15-17] (**Figure 6**). This averaging time may also be thought of as a memory length because the cell must remember previous values of the input in order to compute the average. If the averaging or adaptation time is too short, then the noise is not filtered out; alternatively, if the time is too long, then the bacteria cannot detect real changes in the gradient. There is an optimal adaptation time that allows cells to chemotax the farthest and to reach this is the business of the adaptive mechanism.

4. The Cybernetic Aspects of Chemotaxis

Let us now consider an abstract cybernetic model of the previous network [18,19]. To understand following considerations one must recall that by default the bacterium runs straight on (low concentration of CheY-P) and therefore the environmental-signal that induces tumbling is always a sort of negative feedback interrupting the course of the "normal" (expected) operation. The whole network can be thought of in two separated parts (**Figure 7**):

• A sensory system that catches the environmental signals and transmits them downstream in a linear way;

• A feedback circuit that contributes to the new input.

As already mentioned, this machinery also represents a form of rudimentary memory of the system. However, the same mechanism allows to cancel previous chemoreceptors signal outputs or effects in a static environment, no matter what chemoeffectors may be present, whether attractive or repulsive [12]. This enables the bacterium to reset the threshold sensitivity of the signaling system in order to detect any *new* change in the chemical environment. The receptor-kinase activity expressed by the parameter a is known to increase with the receptor methylation level m, that is,

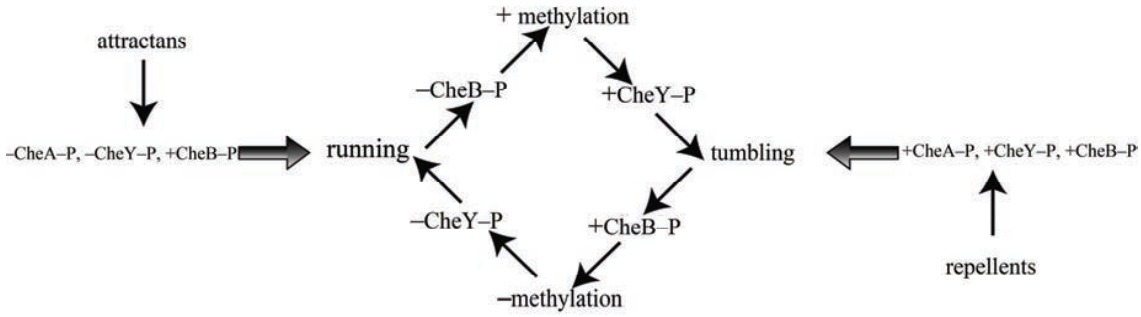

Figure 5. A schematic overview of the chemotaxis--proteins circular network.

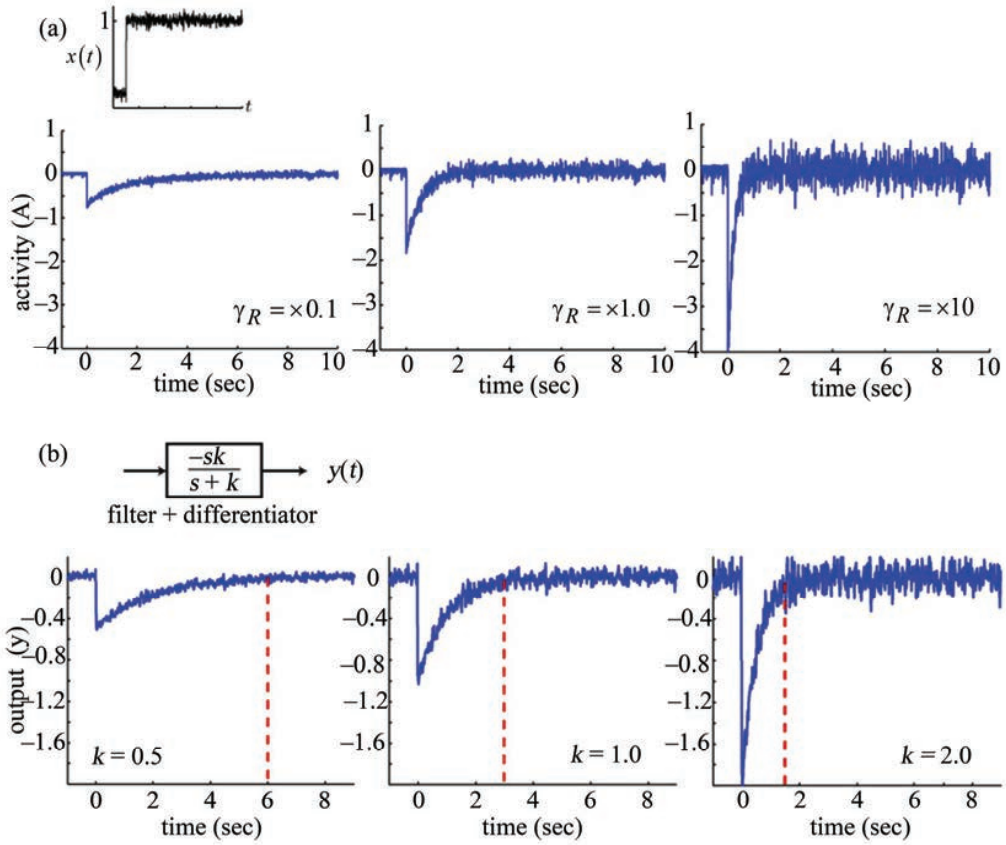

Figure 6. (A) When subjected to an abrupt change in attractant concentration ($x(t)$), the output ($A(t)$) of the model of the *E. coli* signaling pathway responds with an initial transient burst which decays exponentially. The adaptation time depends on the component levels of the signaling pathway such as the methylation rate γ_R. Faster methylation rates yield shorter adaptation times but result in noisier activity levels (panel on the right). Thus, the filtering capabilities of *E. coli* are determined by the time it takes to adapt to step inputs of ligand, where step inputs are described by a (discontinuous) Heaviside function whose value is 0 for a negative argument and 1 for a positive argument (or vice versa); B) The adaptation response of *E. coli* is representative of a system consisting of a low-pass filter ($k/(s+k)$) coupled with a differentiator (S) (inset). A negative gain is used here to mimic the activity response of *E. coli* to positive changes in ligand. Red dashed lines indicate the time it takes the mean output of the filter to reach 95% of its steady state level. The output of the low--pass filter plus differentiator ($y(t)$) is a filtered version of the derivative of the input signal. Smaller filter cut-off frequencies (smaller k), which corresponds to longer averaging times, yield less noisy outputs (panel on the left). Although longer averaging times help to reduce noise, they result in a slower response: the output takes longer to approach zero after the step.

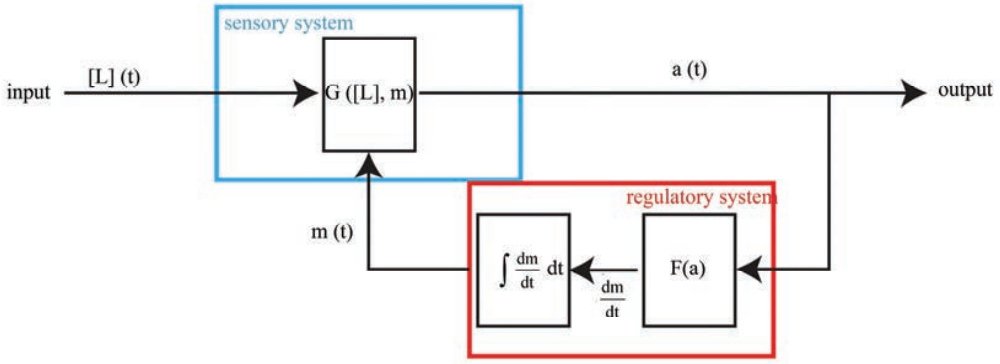

Figure 7. The *E. coli* chemotaxis network is constituted of two main systems: a sensory system for linearly transmitting the input (essentially based on the phosphorylation mechanism) and a feedback-regulatory system (based on methylation--demethylation). $[L](t)$ represents the input ligand concentration as a function of time. The protein CheA shows an auto-phosphorylation activity a. However, the output $a(t)$ is dependent not only on $[L]$ but also a feedback circuit represented by a function $F(a)$ that gives dm/dt and that is further integrated over time to give the contribution $m(t)$ to the new input, where m represents the receptor methylation level.

$$\frac{\partial a}{\partial m} > 0 \tag{1}$$

However, the crucial point is that the increase of a (determined by increasing of m) in turn leads to up-regulation of CheB (which removes methyl groups CH_3), and down-regulation of CheR, which adds methyl groups. The net result is the lowering of the concentration of m. The set of equations ruling this dynamics is then the following

$$\frac{\mathrm{d}m}{\mathrm{d}t} = F(a) \tag{2}$$

$$a = G([L], m) \tag{3}$$

The former equation tells us that the variation of m is due to the transfer function $F(a)$ contributing to the feedback, in particular, lowering the levels of m as a function of the activity-level a. The latter equation tells us that the function G responsible for the final output combines the two different inputs, the ligand concentration input $[L]$ (coming from the sensory system) and m (coming from the regulatory system). Here, the feedback contribution m to the new input is the result of an integration of the results of the feedback function $F(a)$, a mechanism that is called integral feedback control [20]. Therefore, this feedback circuit will restore a towards its steady state value on changes in the input ligand concentration, resulting in a high robustness towards environmental perturbation [21]. In particular, if the input favours low activity of CheA, and therefore low concentration of CheY-P and straight swimming, this is maintained until the next environmental perturbation. If, on the contrary, the environmental input determines a higher activity of CheA and thus a high concentration of CheY-P and m, resulting in tumbling, then the system will spontaneously go back to a state favouring swimming. In such a way, the system tries to efface the environmental perturbation by both:

1) Restoring its steady state,

2) Undertaking an action that has a non-negative probability to overcome the situation that gave rise to the negative feedback, that is, swimming into a direction that does not make tumbling necessary.

Summarizing, chemotaxis appears to be a homeostatic network tending to restore an internal chemical steady-state (low concentration of CheY-P) that is also arranged for responding to (*i.e.* for informationally controlling) a negative stimulus from the environment in a way that increases the probability for the organism to find metabolic resources.

5. The Informational Aspects of Chemotaxis

The cybernetic approach presented above offers the systemic connection between the molecular treatment that has been previously summarized and the informational aspects that are the object of this section. Therefore, the main question I would like to raise is the following: what is the specific informational significance of the process described above? This process can be expressed by employing a variable i which represents a new input as a function of some external (environmental) parameter k and as describing (determining) the state of the receptor of the sensory system [22-25]. It is interesting to remark that this powerful formalism has originally arisen in the context of neurosciences, but I shall show that it can be generalized to apply to *any* organism. The distinction between the input i and the parameter k is

crucial since it has been remarked that the input can present a mix of (correct) signal and noise. Moreover, any signal contradicts to a certain extent the expectation of the organism (even in the case in which the activity of CheA is low, there is indeed always some perturbing noise mixed with the signal). This expectation has been expressed in terms of the default-state of the Che-proteins network. In informational terms this means that any signal always represents a certain *surprisal* relative to such an expectation. If

$$p(i,k \mid A) \tag{4}$$

expresses the conditional probability to have both the parameter-value k and the input i given the action A that the organism undertakes in order to minimize the surprise, its negative logarithm represents the informational value of the new input associated with a particular value k of the parameter given a certain action A:

$$-\lg p(i,k \mid A), \tag{5}$$

where binary logarithms $lg\, x = ln\, x / ln\, 2$ have been used. It is important to recall that the action can be executed on the environment or the organism itself, but to be really efficacious it always implies some effect on the external environment as a way of avoiding further surprising inputs. Now, it can be shown that lowering the surprise (or surprisal) means to lower the following quantity that is an informational analogue of the free energy in thermodynamics [26]

$$g = -<\lg p(i,k \mid A)>_{p'} + <\lg p'(k,s)>_{p'}, \tag{6}$$

where the two mean values are calculated under the probability distribution $p'(k,s)$ and the negative mean value $-<\lg p(i,k \mid A)>$ is related to the entropy of the system. Indeed, the entropy of the set of possible inputs i is given by

$$H(I) = -<\lg p(i)>_I = -\sum_{i \in I} p(i) \lg p(i). \tag{7}$$

The Equation (6) implies that this lowering is in full accord with general statistical laws and can even be considered to be quite natural. The quantity $<\lg p'(k,s)>_{p'}$ represents the mean value of a log probability distribution of both the environmental parameter k and of the internal parameter (state) s of the organism (describing the Che-proteins network). Moreover, this distribution is always positive. The whole expression can also be reformulated as

$$g = -\lg p(i \mid A) + D_{KL}\left(p'(k,s) \,\|\, p(k \mid i,A)\right), \tag{8}$$

where the second term is the so-called Kullback-Leibler divergence (also known as relative entropy) that here measures the distance of the probability distribution $p'(k,s)$ (before the two vertical lines) from the conditional probability of the external parameter k given that there is a certain input and a consequent action (after the two vertical bars). Given two probability distributions $p(j)$ and $p'(k)$, the classical Kullback-Leibler divergence (in the discrete case) is

$$D_{KL}\left(p'(k) \,\|\, p(k)\right) = \sum_k p'(k)\left(\lg p'(k) - \lg p(k)\right) = \sum_k p'(k) \lg \frac{p'(k)}{p(k)}. \tag{9}$$

In our case, we have

$$D_{KL}\left(p'(k,s) \,\|\, p(k \mid i,A)\right) = \sum_k p'(k,s) \lg \frac{p'(k,s)}{p(k \mid i,A)}. \tag{10}$$

Note that the mutual information

$$I(J:K) = H(J) + H(K) - H(J,K), \tag{11}$$

where

$$H(J) = -\sum_j p(j) lg\, p(j), \quad H(K) = -\sum_k p(k) \lg p(k), \quad H(J,K) = -\sum_{j,k} p(j,k) \lg p(j,k), \tag{12}$$

can be expressed as the Kullback-Leibler divergence between the joint probability and the product distribution of two involved parameters:

$$I(J:K) = D_{KL}\left(p(j,k) \,\|\, p(j)\,p(k)\right) = \sum_{j,k} p(j,k) \lg \frac{p(j,k)}{p(j)\,p(k)}. \tag{13}$$

Strictly speaking, surprise is the first term in Equation (8). The surprise is implicitly conditioned upon the organism in question. It can be seen that by minimizing surprise one is effectively maximizing the probability of the selected inputs under a particular action (or state of the organism). In other words, lowering the surprise means to choose a "model of the world" with the smallest g, whilst the latter has the highest marginal likelihood. This follows because g is an upper bound on surprise, given that the Kullback-Leibler divergence is non-negative.

Therefore, minimizing the Equation (6) amounts to minimizing the negative log-probability of the sensory input (reducing the mismatch between the expectation and the input) [27]. This is precisely what we expect any organisms to do and *E. coli* indeed does: it will expose itself selectively to those causes in the environment that it expects (or is programmed) to encounter, that is, those sources of free-energy that are metabolically crucial and therefore relevant for survival. Since these expectations are limited to the repertoire of physical states that the system can occupy by preserving its homeostasis (for

which states it is therefore genetically programmed), the net result is that the expected causes approximate the real ones.

The crucial point to understand here is that, in statistics, the minimization of the surprise is equivalent to a Bayesian probability computation, where the function g above can be used to approximate the likelihood function, *i.e.*, the probability that, given a certain transduction, the parameters that may have caused it are those that the organism expect:

$$p(k\,|\,i) = p(k)\frac{p(i\,|\,k)}{p(i)} \tag{14}$$

where $p(k\,|\,i)$, is the likelihood function that the signal k has indeed given rise to the input i (for the sake of simplicity I do not consider the action A here), $p(i)$ is the a priori probability of the input (here, I do not consider internal parameters for the sake of simplicity), $p(i\,|\,k)$ is the a posteriori probability of having the input i given the parameter k, and $p(k)$ is the probability distribution of the environmental parameter k. Now, maximizing the likelihood of guessing the environmental parameter k, given an input i, is connected with increasing the mutual information between i and k. To show this, let us make use of the expression $p(i\,|\,k) = p(i,k)/p(k)$ so to rewrite the likelihood (14) as

$$p(k\,|\,i) = p(k)\frac{p(i,k)}{p(i)\,p(k)}. \tag{15}$$

By taking the negative mean value of the logarithms of both sides, one obtains

$$\begin{aligned} &-<\lg p(k\,|\,i)>_{I,K} = -<\lg p(k)>_{I,K} - \\ &<\lg\frac{p(i,k)}{p(i)\,p(k)}>_{I,K}, \end{aligned} \tag{16}$$

that according to Equation (7) can be reformulated as

$$\begin{aligned} &H(K\,|\,I) = \\ &H(K) - D_{KL}\left(p(i,k)\,\|\,p(i)\,p(k)\right) = H(K) - I(I:K), \end{aligned} \tag{17}$$

since it is in accordance with an alternative expression for mutual information

$$\begin{aligned} I(I:K) &= H(I) + H(K) - \left[H(K\,|\,I) + H(I)\right] \\ &= H(K) - H(K\,|\,I) \end{aligned} \tag{18}$$

and tells us that a major likelihood to guess the unknown parameters k will increase the mutual information $I(I:K)$ between inputs and environmental parameters and therefore also lower the uncertainty of guessing the parameters, given the inputs as expressed by the conditional entropy $H(K\,|\,I)$. This is the way in which organisms adapt to the environment [28].

The beauty of this simple model is the following: it connects the two pieces of the mosaic that I have mentioned at the beginning: the informational and the entropic-metabolic one. Moreover, it shows that these two aspects essentially deal with the maintenance of a certain homeostasis so that they follow the same general laws.

6. Evolutionary and Adaptive Significance

When the feedback mechanisms displayed in **Figure 7** was introduced, negative feedback has been mentioned. Actually, the environment can be considered as the source of both positive and negative feedback (conditional on a certain action or state of the organism) according to whether the environmental signal amplifies or reinforces the current action or default state of the organism, or perturbs it. However, the kind of *internal* feedback considered in that scheme is totally different. Scholars and engineers working in information theory in general only consider the two previous forms of feedback. The reason is obvious: the kind of engines or networks that they study do not show a crucial character of organisms that was already mentioned in the introduction: organisms are to a certain extent segregated relative to the environment. The significance of the internal feedback is indeed very specific: it is to restoring the default internal state (level of methylation) *independently* of environmental conditions and therefore also of whether the environmental feedback is positive or negative. We do not have a name for this kind of feedback and my proposal is to call it *anti-feedback* since it is directed towards the environmental inputs in order to restore the organism's homeostasis [1]. Since it contributes to the final output together with new environmental inputs, a reasonable guess is that it is the basic scheme of any regulative process in the organism as a combination of different inputs in which balance is crucial. It is indeed very important to understand that the organism cannot cancel the surprisal component of the input or the uncontrolled environmental feedback, since this would make it blind to environmental information and therefore unable to adapt and survive. This is the reason why the organism is not only segregated relative to the environment but also open to it.

J. Monod [29] introduced an interesting terminology, according to which teleonomy is the basic property of living beings, namely to be objects endowed with a project, represented in their structures and realized through their performances. Moreover, he stressed that such a property denotes the ability of organisms to build

themselves through internal forces and mechanisms (in the expression of the genetic program) and not external ones, implying a freedom relative to the exterior. Therefore, teleonomy amounts to the quantity of information that must be transmitted invariantly over the generations in order that the specific organism survives as a biological species. However, this cannot be accomplished independently of a particular environment. Thanks to the segregation of its program, the organism is indeed able to partially *canalize* the action of the environment producing a good fit (appropriate to the current operation). It is a phenomenon of *co-adaptation* [30], a higher manifestation of self-organization. In other words, what is finally selected in the course of evolution is not a single adaptation (although the original selection event is in itself point-like) but the whole co-adaptation of organism-environment. Teleonomy is a mechanism based on the attraction exercised by a "final" or next stable state on a biological system facing uncertain environmental conditions. The crucial point is that the organism is able to regulate its dynamics *from the inside*, and in this sense it is something more than a pure constraint acting only from the outside, as is the case for any pre-biotic physical system. However, the organism is able to do so precisely because its dynamics has been selected in such a way that the organism already possesses, embedded in the cluster of relations characterizing it (in its biological networks), the potential resources to deal with *whole classes* of external and future events in order to eventually reach the next stable state (the attractor of the system). As a consequence, the system can establish a channel with the environment even if it is in full dynamical *independence* from it. This is the reason why, when certain external signals occur (within a certain tolerance window), the organism is able to react properly and even to integrate them. Therefore, this relation with external cues and events makes these cues or events able to concur in determining the final output of the dynamics.

7. Conclusions

I have shown how it is possible to integrate the many aspects listed in the introduction in a way that is quite natural. The new physics that will seriously deal with biological systems needs to take into consideration the way in which organisms deal with information and in particular how they are able to exercise an information control on their environment [31]. In other words, we need to complement the traditional metabolic approach with a model in which the interaction with the environment is mediated by a sensory system that is able to produce models of the external environment. We need therefore a kind of cognitive biology [2] to understand the way in which adaptive processes (playing a crucial role both in phylogenesis and ontogenesis) arise starting from situations that are potentially noxious or dangerous for the organism. As a matter of fact, the organism is able to individuate and to monitor general kinds of stimuli. In other words, it treats different particular stimuli (e.g different levels of concentration of a chemical or their temporal changes) as pertaining to an equivalence class, for instance constituting the sign that the direction of swimming ids good. This is precisely the reason why we have a cognitive component that cannot be reduced to a chemical-mechanical one. Indeed, mechanical processes are only responsive to singular inputs and not to classes of stimuli. On the contrary, precisely the establishment of an equivalence class of stimuli allows the ascertainment of the functional relevance of any particular input. In other words, such any equivalence class of stimuli is a functional one. Moreover, mechanical systems are driven by the inputs whilst it has been remarked that the same concentration of chemicals is maintained during chemotaxis independently of the inputs. These aspects have been considered in Section 2 as crucial evidence for the information control that the organism exerts on the environment which is displayed by its expectancy of the appropriate classes of inputs.

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9. References

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