



The Semiotic Approach to Bacterial Chemotaxis

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Received: 21 May 2021 / Accepted: 10 September 2021 / Published online: 25 September 2021
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Abstract

Bacterial chemotaxis is often considered to be a textbook example of the rudimentary semiotic process. As such, it gives an excellent opportunity to better understand both semiosis and biology. Our study reviews this phenomenon in the light of up-to-date scientific knowledge to answer the most basic semiotic questions: what is the sign? What types of signs are there? What is the meaning understood on the molecular level, and by what means can it grow with time? As a case study, the bacterial chemotaxis toward glucose in *E. coli* species is chosen, and the semiotic framework of Charles Sanders Peirce applied. The analyses provide us with the following results: the sign, in its ultimate nature, is a general process. Bacterial chemotaxis can be understood in terms of Peircean type, symbol, and argument. The meaning on the molecular level is entirely pragmatic and, in this case, reduced to a bacterial response to glucose. A sign can grow through sign generalization, the emergence of different sign categories, the integration of these categories in functional cycles, and the introduction of contextuality. The sign of bacterial chemotaxis extends from the cell signaling pathways up to the population level. The presented results advance our knowledge of sign processing in the context of semiotic evolution.

Keywords Ch.S. Peirce · Bacterial chemotaxis · Symbol · Argument · Meaning · Semiotic evolution

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Introduction

Semiotics, the science of sign, has a long and profound history. As a part of logic, it provides the means of expressing the fundamental relations in the world (Bellucci, 2014; Martin, 1992). However, while for a long time the semiotics has been envisioned as restricted to the realm of human culture, the last several decades open a possibility of the presence of the signs in nature. How close is the relation between sign and life itself has to be yet discovered. Recognizing the sign communication among higher animals is straightforward, the problem, however, arises in the context of most primitive organisms apparently deprived of cognition, nervous system, or social structures. Is the basic function of bacteria executed in a semiotic way? This paper aims to address this question.

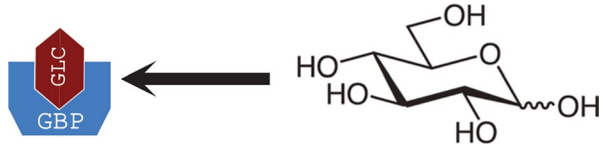
In particular, following specific topics are envisioned. This study intends to (a) provide biosemiotics with the terminology that allows to grasp biological phenomena and to (b) test it on the case of the bacterial chemotaxis. Point (a) and (b) are addressed in Sections *What is a Sign?* and *Sign Taxonomy*. Next, the naturalistic approach to meaning is presented (Section *The Sign Meaning*) and the problem of the meaning growth (Section *The Sign Growth*) in the context of bacteria chemotaxis is considered.

Biosemiotics analyses proposed in this paper are based on the Charles Sanders Peirce theory of sign. This semiosis has unique qualities that make it particularly useful for our purpose. Despite being naturalistic and extremely pragmatic in its approach, Peirce places teleology at the center of his semiosis. This has been achieved by introducing the sign's triadic skeleton, which consists of the sign, the object, and the interpretant. The triad, in turn, with its sequence of the interpretants, transforms semiosis into a process, which broadly corresponds with the very dynamics of life.

For this paper, the case of bacterial chemotaxis in *Escherichia coli* (*E. coli*) has been chosen. Bacterial chemotaxis is a classic example of semiotics in biology, which has been repeatedly referred to (Liszka, 2008; Sharov & Vehkavaara, 2015; Stjernfelt, 2007; Vehkavaara, 2002), however, never discussed thoroughly. This work is a continuation of these studies and similar attempts of semiotic modeling that rely on the Peircean framework. Fine examples of this approach, among others, were applied before to the flow of genetic information (El-Hani et al., 2006; Favareau, 2010a); different aspects of molecular interaction (Queiroz & El-Hani, 2006a; Vehkavaara, 2002); animal communication (El-Hani et al., 2009) and the emergence of semiosis in artificial organisms (Gomes et al., 2007; Loula et al., 2010).

The presented study enriches these efforts by diving deeper into the details of a rapidly developing knowledge of bacterial chemotaxis. Mapping the particular biochemical mechanisms to Peircean terminology should help to understand the abstract semiotic framework better and put it into work in real-life scientific endeavors. Moreover, *E. coli* chemotaxis towards glucose is presented here merely as an example of the broader perspective of the semiotic evolution. Showing potential mechanisms of sign evolution and the gradual accumulation

Fig. 1 The dyadic conception of sign. The sign as something that stands for something else



of semiotic complexity makes probably the most significant contribution of this paper to the general knowledge.

The next chapter begins with the basic explanation of what a sign for Peirce is, and how this sign can be understood in the context of bacterial chemotaxis.

What is a Sign?

Bacterial chemotaxis is the mechanism that allows the organism to react to a stimulus properly in a changing environment. This is a function of very complex phenomena taking place on different levels and it covers a broad spectrum of bacterial behavior. In this paper, we are going to focus on a narrow part of it, i.e., the *E. coli* reaction to glucose. The molecular mechanism of this phenomena is to be presented through the prism of its semiotic function.

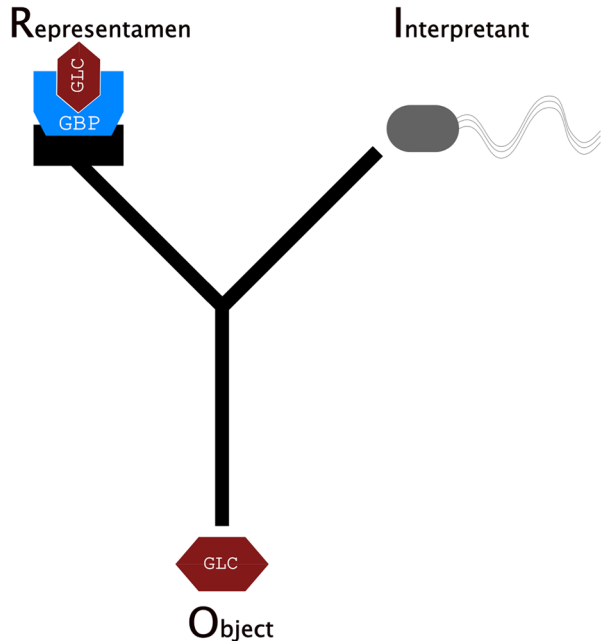
The First Approach

When a bacterium comes across the food source, the glucose molecules cannot be directly detected by the organism. First, they must be bound by the glucose binding protein GBP and then, as a complex GLC-GBP, presented to the chemotaxis receptor (Adler et al., 1973). Therefore, the glucose itself is “invisible” for bacteria, and its detection is possible through something else that indicates the glucose presence. Here, we touch the first and simplest definition of a sign. The sign is something that stands for something else. In our example, the glucose-GBP complex stands for the glucose presence (Fig. 1). In Peirce terminology, this would be called the representamen, which introduced the first and most simplified approach to the sign. However, in this dyadic sign-object semiotic framework, something is missing. The sign presented in this way is static and does not leave much room for interpretation. Therefore, the original sign relation was reinvented by Peirce.

The Second Approach

According to Peirce, the sign is irreducibly triadic. It consists of the “representamen” (this what usually is called a sign). Next, the “object” that the sign stands for. Finally, there is an effect that the sign produces, which Peirce called the “interpretant” (CP 2.228). All these elements constitute the unseparated unity of a sign. Now, translating this into bacterial chemotaxis, one can say that the glucose-BGP complex is the representamen. It stands for the glucose, i.e., the object. Meanwhile

Fig. 2 The sign as a triad. The figure represents the scheme of semiotic approach to bacterial chemotaxis



the bacterial response to that object, precisely “swimming towards glucose gradient” behavior, is the interpretant (see Fig. 2).

In the second approach, the sign reveals itself as a triad. From the perspective of Peirce, the triad is the fundamental and, at the same time, the sufficient relation (Misak, 2004). It constitutes the backbone of all semiotics. However, what is more important, it hides within itself the promise of further development. In the chemotaxis scenario, a lot happens between triggering the chemotaxis receptor and changes in bacterial motor effectors. A complex semiotic process is involved in translating the original sign (representamen) into a reaction of the flagella motor (the Final Interpretant), and diving into details of this process is the only way to understand what the sign really means for bacteria. The triadic conception of sign has become very handy in describing this process, opening for the third and the ultimate approach to the sign.

The Third Approach

The sign ultimately is a semiotic process that starts as follows: the object represented in the form of the first representamen evokes some effect, which we called the interpretant. This interpretant, however, becomes itself the next representamen of the object. It is because the change caused by the sign is telling something about the object (represents it). As it reveals the meaning of the object, it becomes the representamen itself and introduces the second step of semiosis, and so on (CP 2.303).

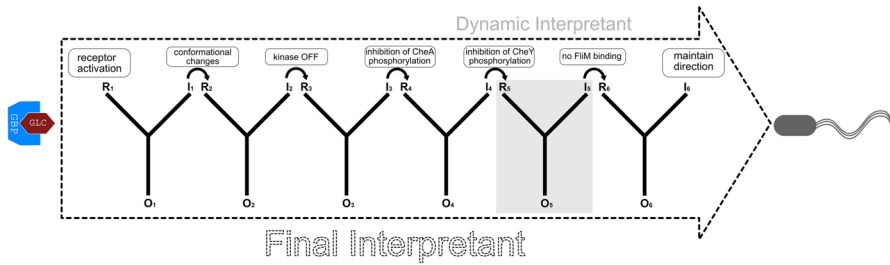


Fig. 3 The sign as a process. The figure shows the semiotic process of bacterial chemotaxis

Figure 3 presents the semiotic process of *E. coli* chemotaxis, where the first sign is translated into the final interpretant, that is, the bacteria movement. It consists of the following steps. First, the object (glucose) is presented as a sign by GBP-glucose dimmer, which is the first representamen (R_1). Only this dimmer-sign can be recognized by the receptor, which, in turn, causes its conformational changes. The reaction of the receptor is recognized as the first interpretant (I_1). Changes of the very same receptor become themselves the new sign (R_2) that gives the signal to switch the receptor kinase to the OFF-position (the second interpretant: I_2). The kinase-OFF position (R_3) inhibits the CheA phosphorylation (I_3), which, in turn, is a sign (R_4) of inhibition of CheY phosphorylation (I_4). The lack of phosphorylated CheY (R_5) ceases the constant changes in the motor rotation due to lack of phosphorylation of FliM molecules (I_5), and this is a sign (R_6) to maintain the current direction (I_6) (Wadhams & Armitage, 2004).

To understand better what happens, let us take a closer look at one exemplary step in this process, the inhibition of CheY phosphorylation (R_5) (Jun et al., 2020). At the fifth step, there is neither a physical connection to the glucose molecule (the molecule that initially triggered the response stayed outside the organism) nor evident relation to the changes in the swimming behavior of the bacterium (which has not yet happened). However, because this particular step is a part of the semiotic response to glucose, we can claim that the lack of phosphorylation of the CheY molecule somehow transfers the information about the glucose. Expressing the same in a more Peircean style, we could say that the representamens R_1, R_2, \dots, R_6 carry the form of the object (MS 793, EP 2:544, n.22). Similarly, interpretants I_1, I_2, \dots, I_6 execute the meaning of the object for that organism, and both of these sequences are connected by means of a “habitual law.” Therefore, the general sign of bacterial chemotaxis shown in Fig. 2, becomes in reality the semiotic process displayed by Fig. 3. The sign is never a static phenomenon but a process of reviling the meaning of the object. To distinguish the effect of the particular step (e.g., I_5) from the final effect of the sign, Peirce introduced two kinds of interpretants. The lack of inhibition of CheY at the step fifth

is (one of many) dynamic interpretant. In contrast, the habit of swimming toward the glucose is here the final interpretant¹ (CP 4.536).

This section was intended to answer the fundamental question of what a sign is. The adequate answer would be, a sign is a process that, by the sequence of representamens aims to exhibit the object, or, to be more precise, expresses the meaning that object has for the sign user. This basic definition of the sign will be further explored in the next part of this paper, providing different faces of a sign in the light of sign taxonomy.

Sign Taxonomy

During his lifelong solitary intellectual endeavor, Peirce came out with intricate and original sign's taxonomy.² One who aspires to use his semiotic framework as a conceptual matrix to understand the world around must address the sign's classification problem. This section is intended to familiarize the reader with different classes of sign and explained them in the context of bacterial chemotaxis. It will help to clarify and conceptualize the process of bacterial chemotaxis and allow us to understand better the sign itself.

In the previous section the triad was shown to be at the center of Peircean semiosis. Therefore, it should not be a surprise that it is also the source of three-fold division in sign categories (Liszka, 1989, 2008). The logic behind this sign taxonomy is that the sign can be considered from the perspective of the representamen, of the object, and from the interpretant point of view (see Fig. 4).

The First Trichotomy

The sign from the perspective of representamen could be a type, a token, or a tone (CP 4.537; Hilpinen, 2012) (or in canonical Peirce terminology a legisign, a sinsign, and a qualisign, respectively). The type (the legisign) is a general sign. As such, it cannot be actualized by itself. Something general in nature needs to be embodied in the actual, that is, the existing things or events (CP 2.246). These things are called tokens (or sinsigns). Therefore, the general kind of the sign is a type, and every instance of that type is a token (called by Peirce a replica or a sinsign). At the same time, the replica may be a sign only because of some quality, that is, the tone (or the qualisign). To sum up, being a sign from the representamen's point of view could mean three different things, the general law, the individual existing object or event, and the property or quality (CP 2.244). However, this distinction of three different sign categories should not be confused with the sign separation. On the contrary, the type, token, and tone are complementary. Here, the general type consists of

¹ For the sake of clarity, the narrowed conception of interpretant was presented. For full account on Peircean interpretant's type see (Atkin, 2013; Liszka, 2008).

² Description of the full sign's taxonomy may be found in (Farias & Queiroz, 2000).

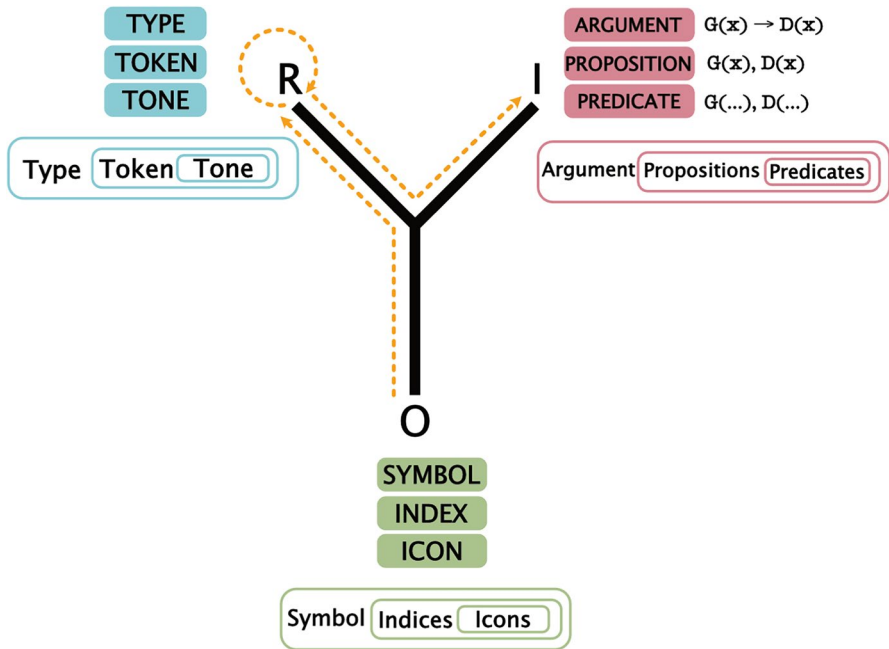


Fig. 4 The Peirce’s classification of sign

the individual tokens, which existence involve some properties, the qualitative tones. The nested nature of signs is a common feature that applies to all classes of sign.

In the present case, the general idea of chemotaxis in *E. coli* is the type. We can think of it as the evolutionary trait preserved by the species; a fixed response of the bacterium to the particular environmental factor. The certain implementation of this general sign, that is, the individual *E. coli* bacterium swimming towards glucose gradient, is the token. Whereas, the mobility, the ability to move could be recognized as a tone. Note that the abstract, general idea of bacterial chemotaxis needs an actual organism to perform this evolutionary imprinted behavior, and this would not happen without specific qualities.

The Second Trichotomy

The sign considered in relation to the object introduces the second trichotomy. A sign may be a symbol, an index, and an icon. When a sign refers to an object by virtue of the law, it is called a symbol. When the relation to the object is established directly via connection in space and time, it is an index. Finally, when the sign quality (i.e., a broad idea of similarity to the object) is the case, the sign is classified as an icon (EP 2:291–2; CP 2.247–9).

To explain the second sign’s trichotomy, the familiar example of the inhibition of CheY phosphorylation (Fig. 3) will be used. This particular step of the chemotaxis

Table 1 The third class of sign with its implementation to the bacterial chemotaxis

Argument	$G(x) \rightarrow D(x)$	$GLUCOSE(x) \rightarrow KEEP_DIRECTION(x)$	<i>“There is glucose detected, therefore, keep swimming in this direction”</i>
Propositions	$G(x);$ $D(x)$	$GLUCOSE(x);$ $KEEP_DIRECTION(x)$	<i>“There is a glucose in the environment”;</i> <i>“Keep current swimming direction”</i>
Predicates	$G(...);$ $D(...)$	$GLUCOSE(...);$ $KEEP_DIRECTION(...)$	<i>“glucose”;</i> <i>“swimming direction”</i>

pathway seems not to be directly connected to glucose. Looking for its similarity to the glucose would also be in vain. Unphosphorylated CheY does not imitate the size of the glucose molecule nor its structure. It does not have the glucose property or its energetic potential. Therefore, the CheY relation to the object (glucose) is not simply indexical or iconical, but more abstract and executed by virtue of law (evolutionary crafted). This law-like connection to the object falls under the Peirce category of symbol. Strictly speaking, the symbol shapes the sequence of representamens and its interpretants. One can think of it as some kind of blueprint designed here for passing the information about the glucose presence from the receptor to the organs of motion. The symbol (the general idea, the blueprint) combines in proper order the “molecular machines” (indices) like CheA, CheY, FliM etc. (Fig. 3) to form signaling pathway and execute desire action. Finally, every molecule in this process to correctly perform its task needs some qualitative-iconic properties (proper shape, phosphorylation, charge and van der Waals potential, etc.). As before, the sign here has the matryoshka-like structure: symbol (indices (icons)) and largely overlaps with signaling pathway (molecules (properties)). The symbol consists of indices, and indices engage the icons.

The Third Trichotomy

Taking into consideration the interpretant, the sign can be divided into an argument, a proposition, and a predicate (CP 2.250–3). The argument is a general meaningful semiotic response to the object. The argument consists of at least two propositions, namely the premises and the conclusion, and it will take form $G(x) \rightarrow D(x)$. Propositions, in turn, are the separated parts of this argument like $G(x)$, $D(x)$, whereas predicates are the unsaturated qualitative possibility of it, i.e., $G(...)$, $D(...)$ (Stjernfelt, 2014). Following the original Peirce terminology, the third trichotomy would be called an argument, a dicent, a rHEME.

The simplest form of an argument in bacterial chemotaxis can take a form: *“There is glucose detected, therefore, keep swimming in this direction.”* The same expressed in the language of predicates is $GLUCOSE(x) \rightarrow KEEP_DIRECTION(x)$. This argument consists of two propositions: *“There is a glucose in the environment”* and *“keep current swimming direction,”* which is identical with $GLUCOSE(x)$ and $KEEP_DIRECTION(x)$ notation. The unsaturated predicates that form the basis of the preceding propositions are $GLUCOSE(...)$, $KEEP_DIRECTION(...)$. See Table 1.

The argument with its persistent imperative to follow the truth is one of the driving forces of semiosis. The natural tendency of signs to grow, interact with other signs, and form more complex semiotic processes is the consequence of this urge. Therefore, it should not come as a surprise that the argument presented in Table 1 is only a part of a more complex semiotic system. The *Functional Cycle and the Integration of Different Signs Category* and *Further Growth of a Complex Argument and Born of Sign Contextuality* sections of this paper, in more realistic terms, are going to express the convoluted argument that stands behind bacterial chemotaxis.

The compositional structure of the argument is even more evident than in previous cases. The hierarchy of the argument (propositions (predicates)) exposes the intrinsic interdependency of one sign upon another. Overall, the more complex (general) sign consists of the specific (simpler) one. However, the integration of the signs is holistic in nature (Stjernfelt, 2014). One should not perceive primitive signs as isolated building blocks that, when put together, create general ones. This relation—as the entire Peirce's philosophy—is penetrated by the notion of continuity (the doctrine of synechism, see Hausman, 1993). In Peircean semiosis, the basic, full-fledged, and therefore the most real signs are the most general ones. Those existing in the form of the law, namely a type, a symbol, and an argument. The other types of signs are perceived as the degenerative forms of the basic ones and, in the long term, cannot exist independently.³ Therefore, the semiosis, instead of being the bottom-up process of accumulation of small changes, resembles more the top-down growth, where the general sign directed by the final cause is discovering different ways of self-realization (CP 1.22, 1.26; Braga, 1999; Queiroz & El-Hani, 2006b)⁴. Along the way, it organizes and accommodates the available elements according to the general law that the sign express. The natural consequence of this sign's generality and indeterminacy is, of course, the possibility of different realization of a general sign, which is addressed in Section *Signs Generality and Many Faces of Bacterial Chemotaxis* of this paper.

The last important note concerning sign taxonomy is that this distinction made with regard to the representamen, the object, and the interpretant is only a formal one. Therefore, the type of bacterial chemotaxis, its symbol and the argument are not three different signs, but the same semiotic process described from various perspectives.

³ The existence of the lower sign outside the more general one is possible, but always it is unusual. The single token or tone is a degenerative form of sign that seeks its placement in more general sign (Stjernfelt, 2007).

⁴ Fernández claims that those two modes of causation (the top-down and the bottom-up) are rather joined in the semiotic process (Fernández, 2017).

The Sign Meaning

The first section of this paper has shown the sign of glucose. The second distinguishes the different types of chemotaxis response to the glucose. Still, the basic question concerning the meaning of the glucose for bacteria need to be explicitly addressed.

The Pragmatic Theory of Meaning

The Peirce theory of meaning is entirely pragmatic (Nesher, 1983). Therefore, the whole meaning of the sign is expressed by the effect that the sign evokes (MS 290: 33). These changes, from the point of view of the agent, manifest themselves in the sequence of interpretants. However, the interpretant here has to be taken in the broadest possible sense as a physical, biological, social, conceptual, or emotional effect and so on. Note that the meaning defined in this way is not tied to the realm of the conscious mind.

According to Peircean pragmatism, there is no other way to get know the object than via the mediation of signs. As the direct access to the object is impossible, whole knowledge about the object is to be learned by experience, that is, by observing its sign's effect. Peirce illustrates it by the well-known example of a diamond. We define the diamond as a hard object, not otherwise, but by scraping it with other objects. While other objects come out of this trial scratched, the diamond remains intact (EP 1:132; CP 5.403). From this experience, we learn something about the object. Naturally, the sign only partially approximates the object, introduces it from some perspective, emphasizes one feature and ignores others. Scraping a diamond can tell us about the hardness of the diamond, but not about its transparency or the social status it introduced when worn as jewelry, etc. Knowing the full meaning of the object would require consideration of every possible interaction with that object (EP 2:354; CP 5.453).

The Meaning of the Glucose

In the context of bacterial chemotaxis, the meaning of the glucose is revealed in the habit of swimming towards the glucose source. From the Peircean theory of meaning, the sign of glucose launches the process of interpretation that ends up with the appropriate response of bacterial flagellum. Ultimately, it is the bacterial reaction that defines the meaning of this object and consequently the category it falls under (see Section *Different Classes of Category and the Changes of the Sign Meaning*). At the level of the simple organism, as Uexküll rightly points out, this meaning is hard-wired in the functional cycle that connects the perceptual organs with the effector ones (Favareau, 2010b; Uexküll, 1973). In *E. coli*, the chemotaxis receptors serve as proto-perception, the flagellum motors are the effector organs, and the glucose means the object worth pursuing.

However, the reality of bacterial chemotaxis is much more complicated. It is not true that the bacteria would always follow the growing gradient of glucose.

Swimming towards glucose source is one of many outcomes of bacterial behavior. Section *The Sign Growth* will show a more accurate approach to bacterial chemotaxis than presented so far. At this point, it is enough to keep in mind that the pragmatic theory of meaning is contextual. The process of interpretation depends on other signs, environmental conditions, and various stimuli. All that may cause the deviation from the default program.

Moreover, the bacterial chemotaxis does not exhaust the full meaning of the glucose. Like any sign, it only partially approximates the object. For now, the glucose for bacteria means head towards, digest, oxidize, inform other bacteria, prefer it to galactose, etc. However, the whole meaning of glucose would require examining every present and possible interaction *E. coli* with a glucose molecule (Vehkavaara, 2018). The bacterial chemotaxis implements only a small part of that meaning and hard-wires it in bacterial metabolism and signaling pathways. The rest is still waiting to be discovered. The possibility of further exploration of sign meaning makes the sign growth viable.

The Sign Growth

The sign can grow in several ways (Nöth, 2014; Short, 2007) and some of these possibilities in this section are to be visualized by the growth of bacterial chemotaxis. The simplest form of sign growth is the semiotic process itself. With each interpretant emerging in the process of semiosis, the meaning of this sign is growing. An example of such growth is presented in Fig. 3. However, besides this explicit case, the growth of meaning can occur with the process of categorization.

Categorization and the Growth of Sign Generality

The fundamental law that governs semiosis is for Peirce the process of acquiring habits, which is nothing more than “the objective generalization taking place in time” (NEM 4, 139- 140). Imposing the general rule (law, habit) on the initially unregulated events is the first face of generalization (EP 1:243). Yet, the law of habits does not stop there but forces existing habits to collide with others, joins and contradicts them and finally collapses into more complex ones. As a result, more general semiotic traits emerge, and sign may grow into broader categories (Fernández & Campbell, 2019).

Up to now, for the sake of clarity, our considerations were restricted to the simple case of bacterial chemotaxis, that is, the response to the glucose. However, the identical habit of swimming upward the substance gradient is observed for maltose, similar for ribose, galactose, mannitol, serine, and dipeptides, etc. (Adler et al., 1973; Webre et al., 2003). Since in presented pragmatic theory of meaning the object is directly linked to the behavioral pattern, therefore, the same bacterial response to different objects allows to join them into one general semiotic category. In this way, the meaning of the glucose can be generalized. Thus, all objects that invoke similar attraction and are used as a building material for an organism may

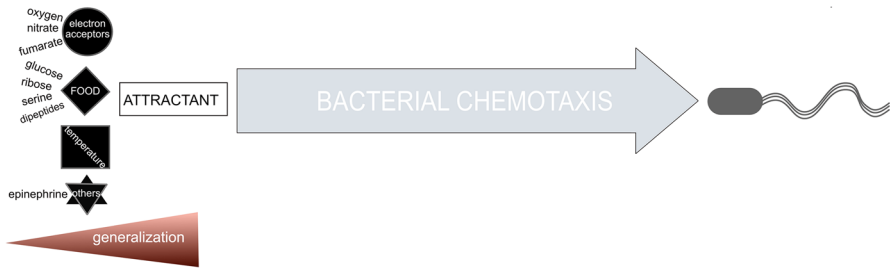


Fig. 5 The sign grows through categorization

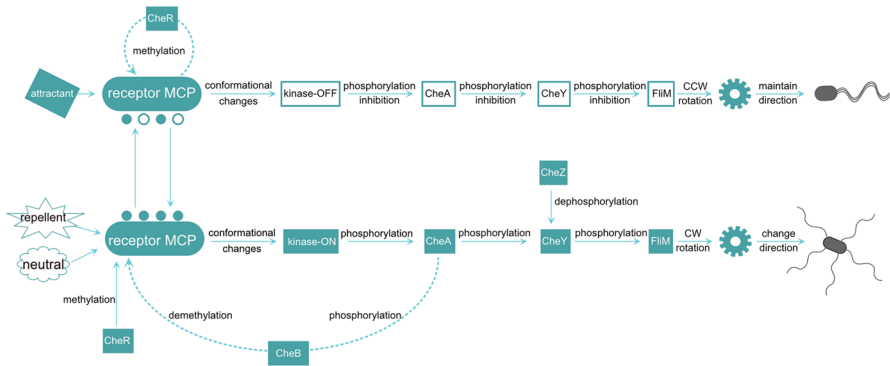


Fig. 6 The diagram shows the functional cycle of bacterial chemotaxis described on the molecular level. The negative feedbacks are shown with a dotted line

be classified as “food.” Going further, not only the food attracts bacteria. Another category causing similar behavior is “electron acceptors.” This category consists of oxygen, nitrate, fumarate, and others (Taylor et al., 1979). Besides that, *E. coli* is heading towards preferred temperature, pH, (Bi & Sourjik, 2018), epinephrine (Bansal et al., 2007) etc. Therefore, the broader category of “x-es” that evokes the “KEEP_DIRECTION(x)” effect is called the “attractant.” Based on the chemotaxis response to the objects, the more general categories of sign are created and so the meaning of the sign is growing (Fig. 5).

Different Classes of Category and the Changes of the Sign Meaning

With time, the sign not only generalizes but also evolves and changes its meaning. At some point, it is unavoidable in the process of growth. In Peirce’s own words “[t]he body of the symbol changes slowly, but its meaning inevitably grows, incorporates new elements and throws off old ones”. (EP 2:264; CP 2.222). Similarly, the chemotaxis pathway used to approach the attractant could

be adapted for a different task. At the end three main sign categories, namely the "attractant," the "repellent," and the "neutral" objects operate in bacterial chemotaxis. The first of aforementioned categories consists of all substances which cause bacteria to swim towards the substance gradient (see *Categorization and the Growth of Sign Generality*). The second class evokes the opposite behavior and prompts the retreat from a potentially dangerous environment. The representatives of this second category are ethanol, leucine, tryptophan, cobalt, glycerol, indole, etc. (Berg, 2004). Meanwhile, the whole range of objects that do not fall under the attractant nor the repellent category is simply ignored by bacterial perception. The default response in this case is a random walk. All three behavioral modes are written into the functional cycle.

Functional Cycle and the Integration of Different Signs Category

The default performance of the bacterium in the absence of both attractant and repellent is a random movement (the lower level of Fig. 6). After some time of swimming in one direction, the stochastic process causes the flagella to tumble, and a new course is set. Attachment of the repellent to the chemotaxis receptors fixes this reaction, ensuring that a random walk is continued until the bacterium leaves the hostile environment. The upper level of Fig. 6 shows the opposite mode of action and describes the chemotaxis pathway in the presence of the attractant. This part of the scheme corresponds with the previously discussed Fig. 3. The presence of attractant in the surroundings in an active way counteracts the random walk by inhibiting of the flagella motors phosphorylation. This active blockage of random spikes in effector organs allows bacteria to keep a stable swimming direction for a longer time⁵. All three patterns, the random walk, the retreat action, and the following substance gradient to be useful for bacteria must be combined into one functional cycle. The ability of changing between these different modes of behavior is the hard part. In bacteria, it is done by switching the receptors between the ON/OFF position. The kinase is the switching button here. Finally, proper work of this cycle requires a periodic reset of receptors. Without that, the system, once activated would keep the same program as long as the ligand is attached to the receptor. In this way, the chemotaxis would react only to the first signal neglecting a further update of the information. To detect the constant changes in the environment, the pathways must be equipped with automatic negative feedback (the Weber-Fechner law). This mechanism has to work regardless of the presence or the absence of the attractant, gradually restoring receptors to the default level. In bacterial chemotaxis, this process is called the adaptation and is controlled by the receptor methylation (Colin & Sourjik, 2017). Precisely the methylation of the receptor causes its activation and demethylation of the MCP complex deactivates it, no matter whether there is any attractant attached or not.

⁵ For a more detailed description of this process, see for example (Wadhams & Armitage, 2004)

In the upper part of Fig. 6, attachment of attractant induces conformational changes of receptors following inhibition of phosphorylation of signaling pathway. However, at the same moment, a reverse process is initiated. The methyltransferase CheR slowly restores the methylation level of receptors (the first negative feedback). Once the MCP complex reaches its default level of methylation, the kinase switches ON, and the process of phosphorylation starts anew, even if the attractant is still attached to the receptor. The system switches to mode presented at the lower level of Fig. 6. Here, as the wave of phosphorylation advances along the chemotaxis pathway, the CheA molecule is activated. This molecule serves a double purpose. For once, it phosphorylates the CheY molecule and further transduces the sign, but, at the same time, it activates the CheB molecule. The demethylase CheB counteracts the CheR molecule and, with time, strips of the MCP receptors from the methyl groups. This is the second negative feedback. As demethylation of the receptor complex reaches its critical level, the receptor is switching to the OFF position, and the system completes a full cycle. The vertical arrows between the upper and lower levels in Fig. 6 symbolize these transitions. Because of this adaptation, the bacterium can follow the ligand gradient and learn about the changes in the environment. Naturally, the process of adaptation is about 100 times slower than the response to the ligand and serves bacteria as a kind of short-time memory (Vladimirov & Sourjik, 2009). The Uexküll's idea of the functional cycle can be useful for describing this mechanism. Figure 6 schematically explains how the receptors are connected with the organ motors and how they integrate different modes of action.

From the semiotic perspective, the described mechanism is an example of a complex semiotic process whose role is to recognize signs and interpret them correctly. In respect to the object, the interacting molecules match the description of the indices, whereas the over-all blueprint of chemotaxis functional cycle is a complex symbol. The same semiotic system from the perspective of interpretant can be described as a complex argument, created as a composition of a few simpler ones. The sketch of these arguments could be presented as follows:

- (1) ATTRACTANT(x) \rightarrow KEEP_DIRECTION(x)
- (2) REPELLENT(x) \rightarrow not KEEP_DIRECTION(x)
- (3) not (ATTRACTANT(x) and REPELLENT(x)) \rightarrow KEEP_DIRECTION(x) or not KEEP_DIRECTION(x)

This argument of bacterial chemotaxis presents ways of interpretations of three general classes of signs, that is, the class of (1) the attractant, (2) the repellent, and (3) the neutral object. The final interpretant of the argument integrates those three modes of action in one ultimate response, which is a function of time. The functional cycle combining different habits into one general symbol and different final interpretants into one complex argument is just another example of sign growth.

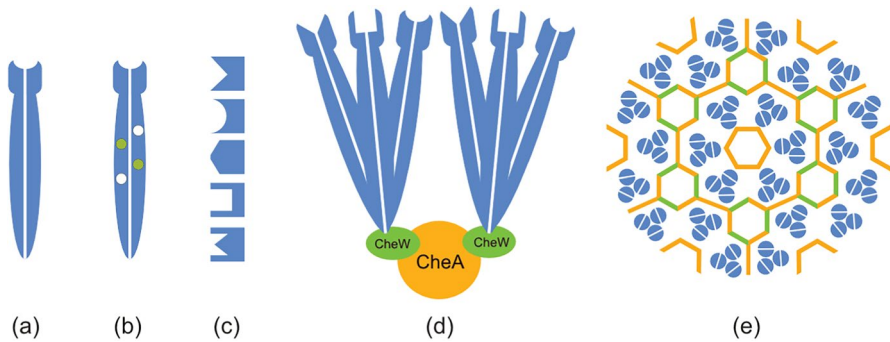


Fig. 7 Elements of bacterial chemotaxis receptors clusters. (a) the receptor dimers (the native form of the receptors), (b) the methylation pattern of receptor dimers, (c) receptor types in *E. coli*, (d) trimer of dimers, TDs, (e) the cluster of receptors. See (Piñas et al., 2016)

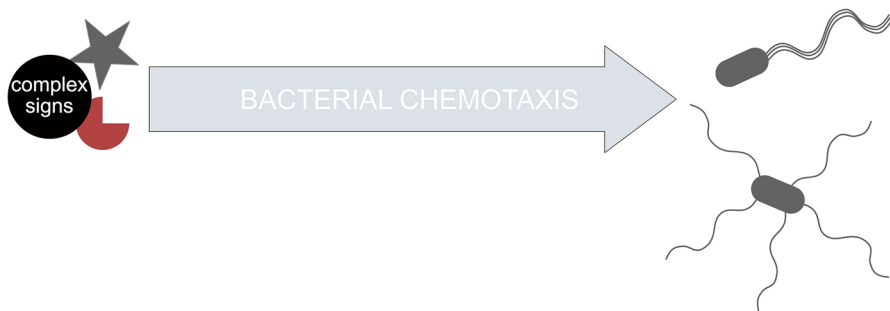


Fig. 8 The sign contextually. The clusterdependent integration of different signs can alter the bacterial response

Further Growth of a Complex Argument and Born of Sign Contextuality

The functional cycle integrates three independent sign categories and defines the rules of switching between them. However, its ability stops there. Creating even more advanced arguments and pushing forward the semiotic process would require a further interaction between signs. After all, it is through the integration of different processes of interpretations, through colliding signs and opposing them new ideas are born. It is a common experience that the context plays a significant role in arguments. The additional facts can change the meaning, the weight of arguments and make them look different. Signs are never alone but always presented in the company of others.

The introduction of contextuality in bacterial chemotaxis is achieved by joining receptors into a bigger structure. These receptors in nature are mostly found in their primary forms of dimers. Usually, an assembled dimer is required to form ligand attachment and to initiate the chemotaxis response. The dimers are next combined into trimers of dimers (TDs). These structures can integrate the signal from up to six

different ligands. TDs, in turn, with the help of scaffolding molecules (like CheW and CheA), construct the clusters of receptors that elevate the sign integration to an entirely different level (see Fig. 7) (Frank et al., 2016).

To put it into perspective, the total number of receptor monomers in one bacteria is about 10,000 (Webre et al., 2003) (Fig. 7a). Each receptor has 16 possible methylation patterns (Fig. 7b) responsible for receptor activation, and there are five different receptor types in *E. coli* (Fig. 7c). The receptor of different types can be mixed in the trimers of dimers (see Fig. 7d), and 10–20 homodimers contribute to regulating one of many CheA molecule in the clustering units (Fig. 7e). Finally, there are 1 to 6 working independently receptor clusters per individual *E. coli* (Koler et al., 2018). All this, multiplied by each other, results in a staggering number of possible states that a bacterium can take (Fig. 8). In fact, this number is so high that there is no fixed connection between stimulus and bacterial response. Two *E. coli* bacteria with identical genetic make-up will behave slightly differently in the face of the same object (Webre et al., 2003).

With clustering, the new mode of receptor operation is created. The integration of receptors by CheA and CheW causes the cooperative interaction between chemoreceptors in arrays. The presence of clusters has several important consequences. First, there is signal integration. Stimuli that came from different receptors are integrated in such way as to execute a single response at a time. The integration in the case of *E. coli* is simply achieved by adjusting the adaptation time to the strength of stimulation but not to its nature (Krembel et al., 2015; Neumann et al., 2010). Next, scientists confirmed the enormous signal amplification. Less than one percent of relative changes in chemotaxis concentration of the signal may be detected, creating an incredibly sensitive mechanism (Bi & Sourjik, 2018). Finally, one of the unexpected features connected to receptor clustering is noise harvesting. The sensory array seems to amplify the noise created during chemotaxis processes, increasing the already outstanding repertoire of bacterial behavior. Both thermal fluctuations and stochastic actions of enzymes are magnified by clusters causing surprisingly large variation at the pathways of chemotaxis activity (Colin et al., 2017; Keestra et al., 2017; Waite et al., 2018). From biological perspectives, these phenomena explain the non-genetic variability in bacterial population and could have some evolutionary advantages (Frankel et al., 2014; Vladimirov et al., 2008). From the semiotic point of view, the noise harvesting corresponds well with Peircean theory of tychism (Coscolluela, 1992), which assumes that pure change is an integral part of every semiotic process, no matter by how conservative law (habit) it is governed (CP 6.201).

As a result of clustering, the meaning of the sign becomes context-dependent. The accompanying signs can alter the interpretation process, strengthen the response, weaken it, or wholly attenuate. The primitive net of interrelation between signs is formed, and some preferences appear. Therefore, *E. coli* will follow the glucose gradient, in most cases, but not in the presence of serine. The amino-acids win in competition to most of the other attractants, yet, even the influence of so high value target is canceled in the presence of high temperature or harmful pH (Paulick et al., 2017). Reaching such level of semiotic complexity, bacteria can perform very

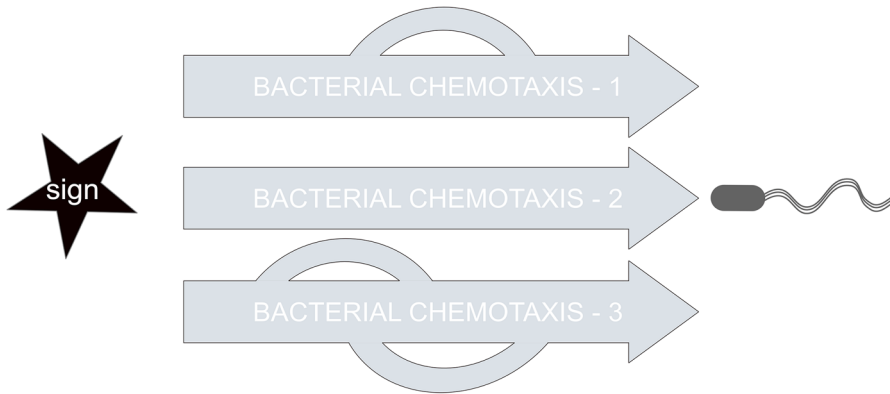


Fig. 9 Various realization of the general sign of bacterial chemotaxis in different species

complex arguments and form the basis of proto-reasoning by assigning different values to objects.

Signs Generality and Many Faces of Bacterial Chemotaxis

One of the primary metaphysical assumptions of the Peirce system is that general rather than particular signs create the very fabric of reality (MS 681: 35–36, 1913; Lane, 2018). The complex symbol of bacterial chemotaxis presented so far is such a general sign that evolution preserved in *E. coli* species. However, the very idea of chemotaxis could be realized in different ways. This section is going to show the evidence supporting these claims.

The generality of sign plays an important role in the Peirce system. Along with the sign's vagueness it is the hallmark of semiotics process (Lane, 2014). The mechanical processes are always executed in the same predictable and repetitive manner. There is no place for freedom or interpretation. In contrast, the semiotic processes (due to the sign's generality and vagueness) are only partially determined, in the way that they follow the logic of an argument, yet, the specific steps of its realization are not predetermined. This is also precisely the difference between the efficient and the final cause (CP 1.211–212; Hulswit & Romanini, 2014). The efficient cause works in a deterministic way. The final cause is pushing towards a specific direction while not determining particular steps. The first one applies to mechanical processes, the second to semiosis. The different realizations of sign are the consequences of this sign generality and its teleological nature.

Let us take the example of the general sign in question, which is the symbol of bacterial chemotaxis. One implementation of this symbol is the chemotaxis mechanism in *E. coli*. Here, the chemotaxis blueprint is well defined. All molecules on this pathway are known and the physico-chemical mechanism of its interaction in the overwhelming part is well understood. Therefore, it is tempting to say that the efficient cause connects each step of chemotaxis pathway and mechanically executes the

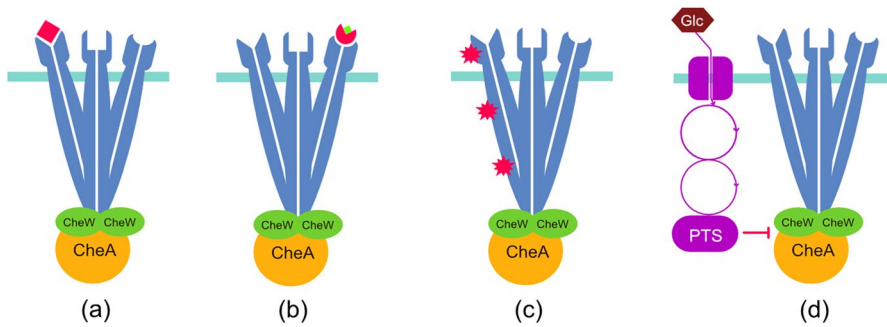


Fig. 10 Different sensing mechanisms of bacteria chemotaxis. The receptor dependent sensing: (a) direct binding, (b) indirect binding, (c) unconventional sensing, without involvement of the receptor binding site. The receptor independent sensing: (d) chemotaxis respond to PTS-mediated influx of sugars

molecular program. This statement could be correct, but only while examining this individual bacterium and only at the t_0 point of time, because the same bacterium at time t_1 will proceed in a slightly different way. Different ligands will be attached; some of the mediated molecules will be degraded, while others new will occur. A different number of molecules can be phosphorylated at time t_1 , and the methylation of MCP certainly will be changed. In addition, amplified stochastic noise may cause further disruption. Therefore, when biologists are describing the so-called mechanism underlying the living phenomena, they are not speaking about the actual mechanistic process but a general blueprint or the symbol in semiotic terminology. Similarly, the molecule that is a part of that pathway is not the particular molecule but the general, idealized type of molecule that is able to perform certain (general) action. Because of its generality and indeterminacy, the bacterial chemotaxis of *E. coli* should be regarded as a semiotic phenomenon, precisely as a complex symbol.

However, even the bacterial chemotaxis symbol in *E. coli* is only a sub-type of the more general type of symbol. One can easily imagine that the very idea of chemotaxis can be realized in different ways in bacteria (Bi et al., 2018); and, actually, it is, as we can find out by scrutinizing chemotaxis pathways of different species (see Fig. 9). Each of the critical parts of this process can be somehow changed and substituted, whether it is the sensing part, signaling pathway, and even the sign effector. Here are some examples.

The signal in bacterial chemotaxis is typically recognized through the mediation of the receptors. In the glucose case, it is an indirect binding (Fig. 10b) to the receptors because the ligand to be recognized must be attached first to the other molecule (here, the GBP). However, other ligands (like aspartate, serine) can directly target receptors (the so-called direct signaling, Fig. 10a) (Neumann et al., 2010). The third type of receptor-mediated sensing is a little unconventional because the ligand does not use the binding site at all. Instead, it can affect the receptor along its entire length (the unconventional sensing, Fig. 10c). Changes of pH (Yang & Sourjik, 2012), osmolarity (Vaknin & Berg, 2006) and the presence of phenol (Pham & Parkinson, 2011) are detected in this way. Curiously enough, bacteria can sense glucose even without receptors (Fig. 10d). The

PTS-mediated influx of sugars into a cell decreases phosphorylation of PTS proteins which in turn affects the CheA activity, and by doing so, interferes with the whole chemotaxis pathway (Neumann et al., 2012; Somavanshi et al., 2016).

The sensing mechanism is not the only part that can be modified. The transduction of the signals from the receptor to the effector organs also allows for alternative scenarios. The additional molecules, than the ones presented in Fig. 6, may be introduced besides, or instead, of the canonical ones. In different bacterial species substitutive molecules, like CheC, CheV, CheD, CheX are common (Bardy et al., 2017; Ortega et al., 2017; Tindall et al., 2012).

Finally, even the chemotaxis effector can vary. The flagellum motor is not the only organ that can cause changes in bacteria movement. A similar effect may be achieved, for instance, through the rearrangements of the filaments (so-called IV pili-base motility) (He & Bauer, 2014; Shi & Sun, 2002).

As the above examples show, the general sign of bacterial chemotaxis may be realized by means of different symbols yet still conduct the same argument. Evolution will always find various ways to realize the same general traits. Alternatively, putting it in more Peircean way, the argument will find its own way to reach the true conclusion. At the very end, chemotaxis of glucose can shed light on yet another level of sign generality that stretches beyond an individual organism.

The Sign Growth Beyond the Organism

One of the very controversial Peirce claims was that it is not us that uses signs, it is more that signs use us as their replica, and we live inside these signs (CP 2.302). These words, which initially referred to a human agent, can be perfectly well addressed to bacteria. There is no place here to discuss the accuracy of such a strong claim, let alone its metaphysical implications. Nevertheless, the very topic of this paper, revolved around glucose chemotaxis, obliges us to raise this last issue.

The narration of this paper has accustomed the reader to look at chemotaxis as a semiotic process that takes place inside the organism. However, the notion of bacterial “quorum sensing” can change that entirely. Through the production and sensing of the AI-2 molecule, bacteria can communicate with one another and simultaneously read and interpret signs like some kind of super-organism. What is particularly interesting, for this purpose the mechanism of bacterial chemotaxis is used. The AI-2 molecule, after binding to the LsrB adaptor, is recognized by the chemotaxis receptor (Trs) in a similar way like glucose is. The AI-2/LsrB complex, while reaching the receptor, causes the conformational changes and lunches subsequent steps of chemotaxis pathways similar to the process described in Section *The Third Approach*. Depending on the bacteria species, the chemotaxis at the population level leads to different behaviors. It can cause the bacteria to swim together in large groups (Laganenka et al., 2016), to aggregate and form biofilm (González Barrios et al., 2006; Jani et al., 2017), prompt the virulence response (Bansal et al., 2008) or even gleam via bioluminescence (Surette et al., 1999). Bacteria quorum sensing,

with chemotaxis at its core, make one think that the bacteria are actually living inside the sign.

Discussion

The following objectives were posted in this paper. The first goal was to find the conceptual framework for biosemiotics congruent with both the scientific and the philosophical language. Second, to test it on the example of bacterial chemotaxis. Next, to use this exemplification for the naturalistic theory of meaning explanation, and finally, to illustrate the evolution of sign.

The semiotics of Ch. S. Peirce proved its usefulness in describing biological phenomena. The language of molecular biology can be translated into this terminology. Both the semiotic and the biochemical description work side by side in a complementary way. The application of the Peircean semiosis to bacterial chemotaxis seems to add, however, some extra value. Without neglecting the molecular interaction, it focuses on more general knowledge of the biological process, on some blueprint that exceeds the here and now of the biochemical realm. It also introduces the teleological approach, the missing link in understanding the biological agency. Finally, the semiotic terminology emphasizes the function and evolutionary role of biological processes, explaining how the things work and why they are arranged in this way and not the other. Additionally, some contribution to the naturalistic theory of meaning was made. Peircean pragmatic theory of meaning applied to bacterial chemotaxis confirmed that, without running into contradiction, one could discuss the meaning of the sign on the level of a simple organism deprived of cognitive ability. Showing how the meaning of the sign can grow along with the increasing complexity of the biological systems can be another contribution of the presented paper. However, all these behavioral patterns are only one of many ways of realization the general idea of bacterial chemotaxis that can grow even beyond the individual organism.

Themes addressed in this study may open new interesting perspectives. The functional cycle, along with the teleological approach seem to be the prerequisites for the notion of the biological agency and the starting point for exploration of the birth of subjectivity. Equally exiting one can find the scalability property of semiotics systems. The same definition of a sign may be applied to one part of the signaling pathway (like Fig. 3), the complete complex signaling mechanism (Fig. 6), as well as to the whole organism, or even the cluster of bacteria connected through quorum sensing. Because of that, one can look at life as a complex semiosis, where different signs intermingling with one another are joining together, producing more general signs and splitting apart, differentiating into new signs, or dying in the dead-end of evolution. Applying the same conceptual framework from biochemical pathways up to the ecological or even cultural interactions opens the unique opportunity for cross-disciplinary studies. It may allow biosemiotics to join its forces with the systems biology and the study of complexity. The view of life as semiosis may shed new light on the process of evolution. A large part of this paper has already

been devoted to the description of the examples of such growth and evolution of chemotaxis sign; however, a more systematic and in-depth research is needed on this topic. Finally, the potential contribution of biosemiotics to synthetic biology should be taken into consideration. The synthetic biology is a relatively new discipline but it can boast numerous successes. Its final desire is to rewrite the coincidental and complicated solution that evolution comes out into the more designed, planned, and engineered fashion. The specialists working in this field are not so much interested in deciphering how nature actually works but are trying to find how it could work differently. With its general conception of sign and its teleological approach, biosemiotics may be a valuable tool in this project.

Conclusion

The aim of this paper was to approach bacterial chemotaxis from the perspective of the Charles Sanders Peirce's theory of sign. The sign considered as a triad and processed with the naturalistic theory of meaning makes this approach particularly useful for modeling biological phenomena. The biochemical and semiotic approaches look like different languages describing the same reality. On the one hand, they seem to be complementary, but also irreducible to one another. The dialog of these two disciplines may be beneficial to everyone, and the authors hope that this paper is a small step towards bringing these two areas closer and make this discourse possible.

Abbreviations of Ch. S. Peirce works: CP: Peirce Ch.S. (1931–1960) *Collected Papers of Charles Sanders Peirce*, C. Hartshorne, P. Weiss, A. Bruks (Eds.), Harvard University Press, vols. 1–8.; EP 1, EP 2: Peirce Ch.S. (1992) *The Essential Peirce. Selected Philosophical Writings*, N. Houser, C. Kloesel (Eds.), vol. 1; (1995), The Peirce Edition Project (Ed.), vol. 2; Indiana University Press; MS: Peirce Ch.S. (1996) *The Charles S. Peirce Papers, microfilm edition*, Harvard University Photographic Service, Cambridge 1996; cited after Peirce Ch.S. (1967) *Annotated Catalogue of the Papers of Charles S. Peirce*, R.S. Robin, (Ed.), University of Massachusetts Press.; NEM: Peirce Ch.S. (1976) *The New Elements of Mathematics by Charles S. Peirce*, C. Eisele (Ed.), Mouton.

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References

- Adler, J., Hazelbauer, G. L., & Dahl, M. M. (1973). Chemotaxis toward sugars in *Escherichia coli*. *Journal of Bacteriology*, 115(3), 824–847. <https://doi.org/10.1128/JB.115.3.824-847.1973>
- Atkin, A. (2013). Peirce's Theory of Signs. In E. N. Zalta (Ed.), *The Stanford Encyclopedia of Philosophy*. Metaphysics Research Lab, Stanford University. <https://plato.stanford.edu/archives/sum2013/entries/peirce-semiotics/>.
- Bansal, T., Englert, D., Lee, J., Hegde, M., Wood, T. K., & Jayaraman, A. (2007). Differential effects of epinephrine, norepinephrine, and indole on *Escherichia coli* O157:H7 chemotaxis, colonization, and gene expression. *Infection and Immunity*, 75(9), 4597–4607. <https://doi.org/10.1128/IAI.00630-07>
- Bansal, T., Jesudhasan, P., Pillai, S., Wood, T. K., & Jayaraman, A. (2008). Temporal regulation of enterohemorrhagic *Escherichia coli* virulence mediated by autoinducer-2. *Applied Microbiology and Biotechnology*, 78(5), 811–819. <https://doi.org/10.1007/s00253-008-1359-8>
- Bardy, S. L., Briegel, A., Rainville, S., & Krell, T. (2017). Recent advances and future prospects in bacterial and archaeal locomotion and signal transduction. *Journal of Bacteriology*, 199(18), e00203–e217. <https://doi.org/10.1128/JB.00203-17>
- Bellucci, F. (2014). “Logic, considered as Semeiotic”: On Peirce's Philosophy of Logic. *Transactions of the Charles S. Peirce Society*, 50(4), 523–547. <https://doi.org/10.2979/trancharpeirsoc.50.4.523>
- Berg, H. C. (2004). *E. coli in motion*. Springer.
- Bi, S., & Sourjik, V. (2018). Stimulus sensing and signal processing in bacterial chemotaxis. *Current Opinion in Microbiology*, 45, 22–29. <https://doi.org/10.1016/j.mib.2018.02.002>
- Bi, S., Jin, F., & Sourjik, V. (2018). Inverted signaling by bacterial chemotaxis receptors. *Nature Communications*, 9(1), 2927. <https://doi.org/10.1038/s41467-018-05335-w>
- Braga, L. S. (1999). A new causality for the understanding of the living. *Semiotica*, 127(1–4), 497–520.
- Colin, R., & Sourjik, V. (2017). Emergent properties of bacterial chemotaxis pathway. *Current Opinion in Microbiology*, 39, 24–33. <https://doi.org/10.1016/j.mib.2017.07.004>
- Colin, R., Rosazza, C., Vaknin, A., & Sourjik, V. (2017). Multiple sources of slow activity fluctuations in a bacterial chemosensory network. *Elife*, 6. <https://doi.org/10.7554/eLife.26796>.
- Cosculluela, V. (1992). Peirce on tychism and determinism. *Transactions of the Charles S. Peirce Society*, 28(4), 741–755.
- El-Hani, C. N., Queiroz, J., & Emmeche, C. (2006). A semiotic analysis of the genetic information system. *Semiotica*, 2006(160), 1–68. <https://doi.org/10.1515/sem.2006.039>
- El-Hani, C., Queiroz, J., & Stjernfelt, F. (2009). Firefly Femmes Fatales: A Case Study in the Semiotics of Deception. *Biosemiotics*, 3, 33–55. <https://doi.org/10.1007/s12304-009-9048-2>
- Farias, P., & Queiroz, J. (2000). Notes for a dynamic diagram of Charles Peirce's classification of signs. *Semiotica*, 131, 19–44. <https://doi.org/10.1515/semi.2000.131.1-2.19>
- Favareau, D. (2010a). Information and Semiosis in Living Systems: A Semiotic Approach. In D. Favareau (Eds.), *Essential Readings in Biosemiotics: Anthology and Commentary* (pp. 629–656). Springer Netherlands. https://doi.org/10.1007/978-1-4020-9650-1_20.
- Favareau, D. (2010b). *Essential readings in biosemiotics : Anthology and commentary*. Springer.
- Fernández, E. (2017). Semiosis and Emergence. *Chinese Semiotic Studies*, 13(4), 399–409. <https://doi.org/10.1515/css-2017-0023>
- Fernández, E., & Campbell, C. (2019). Habit and Generalization. *Chinese Semiotic Studies*, 15(1), 153–163. <https://doi.org/10.1515/css-2019-0010>
- Frank, V., Piñas, G. E., Cohen, H., Parkinson, J. S., & Vaknin, A. (2016). Networked Chemoreceptors Benefit Bacterial Chemotaxis Performance. *mBio*, 7(6). <https://doi.org/10.1128/mBio.01824-16>.
- Frankel, N. W., Pontius, W., Dufour, Y. S., Long, J., Hernandez-Nunez, L., & Emonet, T. (2014). Adaptability of non-genetic diversity in bacterial chemotaxis. *Elife*, 3. <https://doi.org/10.7554/eLife.03526>.
- Gomes, A. N., Gudwin, R., El-Hani, C. N., & Queiroz, J. O. (2007). Towards the emergence of meaning processes in computers from Peircean semiotics. *Mind & Society*, 6(2), 173–187.
- González Barrios, A. F., Zuo, R., Hashimoto, Y., Yang, L., Bentley, W. E., & Wood, T. K. (2006). Auto-inducer 2 controls biofilm formation in *Escherichia coli* through a novel motility quorum-sensing regulator (MqsR, B3022). *Journal of Bacteriology*, 188(1), 305–316. <https://doi.org/10.1128/JB.188.1.305-316.2006>
- Hausman, C. R. (1993). *Charles S. Peirce's Evolutionary Philosophy*. Cambridge University Press. <https://doi.org/10.1017/CBO9780511570773>.

- He, K., & Bauer, C. E. (2014). Chemosensory signaling systems that control bacterial survival. *Trends in Microbiology*, 22(7), 389–398. <https://doi.org/10.1016/j.tim.2014.04.004>
- Hilpinen, R. (2012). 2012 Presidential Address: Types and Tokens: On the Identity and Meaning of Names and Other Words. *Transactions of the Charles S. Peirce Society*, 2, 188–217. <https://doi.org/10.2979/trancharpeirsoc.48.3.259>
- Hulswit, M., & Romanini, V. (2014). Semeiotic Causation and the Breath of Life. In V. Romanini & E. Fernandez (Eds.), *Peirce and Biosemiotics. A Guess at the Riddle of Life* (pp. 95–126). https://doi.org/10.1007/978-94-007-7732-3_6.
- Jani, S., Seely, A. L., Peabody, V. G. L., Jayaraman, A., & Manson, M. D. (2017). Chemotaxis to self-generated AI-2 promotes biofilm formation in *Escherichia coli*. *Microbiology*, 163(12), 1778–1790. <https://doi.org/10.1099/mic.0.000567>
- Jun, S. Y., Pan, W., & Hazelbauer, G. L. (2020). ATP Binding as a Key Target for Control of the Chemotaxis Kinase. *Journal of Bacteriology*, 202(13), e00095–e120. <https://doi.org/10.1128/JB.00095-20>
- Keegstra, J. M., Kamino, K., Anquez, F., Lazova, M. D., Emonet, T., & Shimizu, T. S. (2017). Phenotypic diversity and temporal variability in a bacterial signaling network revealed by single-cell FRET. *Elife*, 6. <https://doi.org/10.7554/eLife.27455>.
- Koler, M., Peretz, E., Aditya, C., Shimizu, T. S., & Vaknin, A. (2018). Long-term positioning and polar preference of chemoreceptor clusters in *E. coli*. *Nature Communications*, 9(1), 4444. <https://doi.org/10.1038/s41467-018-06835-5>
- Krembel, A. K., Neumann, S., & Sourjik, V. (2015). Universal response-adaptation relation in bacterial chemotaxis. *Journal of Bacteriology*, 197(2), 307–313. <https://doi.org/10.1128/JB.02171-14>
- Laganenka, L., Colin, R., & Sourjik, V. (2016). Chemotaxis towards autoinducer 2 mediates autoaggregation in *Escherichia coli*. *Nature Communications*, 7(1), 12984. <https://doi.org/10.1038/ncomms12984>
- Lane, R. (2014). Peircean Semiotic Indeterminacy and Its Relevance for Biosemiotics. In R. Vinicius & F. Eliseo (Eds.), *Peirce and Biosemiotics : A Guess at the Riddle of Life* (pp. 51–78).
- Lane, R. (2018). *Peirce on realism and idealism*. Cambridge University Press.
- Liszka, J. J. (1989). *Semiotic of Myth: A Critical Study of the Symbol (Advances in semiotics)*. Indiana University Press.
- Liszka, J. (2008). Information, Meaning and the role of Semiosis in the Development of Living Systems. *Signs - International Journal of Semiotics*, 2(0). <https://tidsskrift.dk/signs/article/view/26842>.
- Loula, A., Gudwin, R., El-Hani, C. N., & Queiroz, J. (2010). Emergence of self-organized symbol-based communication in artificial creatures. *Cognitive Systems Research*, 11(2), 131–147. <https://doi.org/10.1016/j.cogsys.2008.10.002>
- Martin, R. M. (1992). *Logical semiotics and mereology*. <http://site.ebrary.com/id/10515899>.
- Misak, C. J. (2004). *The Cambridge companion to Peirce*. Cambridge University Press.
- Nesher, D. (1983). Pragmatic theory of meaning: A note on Peirce's 'last' formulation of the pragmatic maxim and its Interpretation. *Semiotica*, 44(3–4), 203–258. <https://doi.org/10.1515/semi.1983.44.3-4.203>
- Neumann, S., Hansen, C. H., Wingreen, N. S., & Sourjik, V. (2010). Differences in signalling by directly and indirectly binding ligands in bacterial chemotaxis. *The EMBO Journal*, 29(20), 3484–3495. <https://doi.org/10.1038/emboj.2010.224>
- Neumann, S., Grosse, K., & Sourjik, V. (2012). Chemotactic signaling via carbohydrate phosphotransferase systems in *Escherichia coli*. *Proceedings of the National Academy of Sciences*, 109(30), 12159. <https://doi.org/10.1073/pnas.1205307109>
- Nöth, W. (2014). The Life of Symbols and Other Legisigns: More than a Mere Metaphor. In V. Romanini & E. Fernández (Eds.), *Peirce and Biosemiotics: A Guess at the Riddle of Life* (pp. 171–181). Springer Netherlands. https://doi.org/10.1007/978-94-007-7732-3_9.
- Ortega, Á., Zhulin, I. B., & Krell, T. (2017). Sensory Repertoire of Bacterial Chemoreceptors. *Microbiology and Molecular Biology Reviews*, 81(4), e00033–e117. <https://doi.org/10.1128/MMBR.00033-17>
- Paulick, A., Jakovljevic, V., Zhang, S., Erickstad, M., Groisman, A., Meir, Y., Ryu, W. S., Wingreen, N. S., & Sourjik, V. (2017). Mechanism of bidirectional thermotaxis in *Escherichia coli*. *eLife*, 6, 26607. <https://doi.org/10.7554/eLife.26607>
- Pham, H. T., & Parkinson, J. S. (2011). Phenol sensing by *Escherichia coli* chemoreceptors: A non-classical mechanism. *Journal of Bacteriology*, 193(23), 6597–6604. <https://doi.org/10.1128/JB.05987-11>

- Piñas, G. E., Frank, V., Vaknin, A., & Parkinson, J. S. (2016). The source of high signal cooperativity in bacterial chemosensory arrays. *Proceedings of the National Academy of Sciences of the United States of America*, 113(12), 3335–3340. <https://doi.org/10.1073/pnas.1600216113>
- Queiroz, J., & El-Hani, C. N. (2006a). Towards a Multi-Level Approach to the Emergence of Meaning Processes in Living Systems. *Acta Biotheoretica*, 54(3), 179. <https://doi.org/10.1007/s10441-006-8177-0>
- Queiroz, J., & El-Hani, C. N. (2006b). Semiosis as an emergent process. *Transactions of the Charles S. Peirce Society*, 42(1), 78–116.
- Sharov, A. A., & Vehkavaara, T. (2015). Protosemiosis: Agency with reduced representation capacity. *Biosemiotics*, 8(1), 103–123. <https://doi.org/10.1007/s12304-014-9219-7>
- Shi, W., & Sun, H. (2002). Type IV pilus-dependent motility and its possible role in bacterial pathogenesis. *Infection and Immunity*, 70(1), 1–4. <https://doi.org/10.1128/iai.70.1.1-4.2002>
- Short, T. L. (2007). *Peirce's Theory of Signs*. Cambridge University Press.
- Somavanshi, R., Ghosh, B., & Sourjik, V. (2016). Sugar Influx Sensing by the Phosphotransferase System of Escherichia coli. *PLOS Biology*, 14(8), e2000074. <https://doi.org/10.1371/journal.pbio.2000074>
- Stjernfelt, F. (2007). *Diagrammatology an investigation on the borderlines of phenomenology, ontology, and semiotics*. Springer.
- Stjernfelt, F. (2014). *Natural propositions : the actuality of Peirce's doctrine of discisigns*. Docent Press.
- Surette, M. G., Miller, M. B., & Bassler, B. L. (1999). Quorum sensing in Escherichia coli, Salmonella typhimurium, and Vibrio harveyi: A new family of genes responsible for autoinducer production. *Proceedings of the National Academy of Sciences*, 96(4), 1639–1644. <https://doi.org/10.1073/pnas.96.4.1639>
- Taylor, B. L., Miller, J. B., Warrick, H. M., & Koshland, D. E., Jr. (1979). Electron acceptor taxis and blue light effect on bacterial chemotaxis. *Journal of Bacteriology*, 140(2), 567–573. <https://doi.org/10.1128/JB.140.2.567-573.1979>
- Tindall, M. J., Gaffney, E. A., Maimi, P. K., & Armitage, J. P. (2012). Theoretical insights into bacterial chemotaxis. *Wiley Interdisciplinary Reviews: Systems Biology and Medicine*, 4(3), 247–259. <https://doi.org/10.1002/wsbm.1168>
- Uexküll, J. V. (1973). *Theoretische Biologie*. Suhrkamp.
- Vaknin, A., & Berg, H. C. (2006). Osmotic stress mechanically perturbs chemoreceptors in Escherichia coli. *Proceedings of the National Academy of Sciences*, 103(3), 592–596. <https://doi.org/10.1073/pnas.0510047103>
- Vehkavaara, T. (2002). Why and how to naturalize semiotic concepts for biosemiotics. *Sign Systems Studies*, 30, 293–313.
- Vehkavaara, T. (2018). From the Logic of Science to the Logic of the Living. In B. M. (Ed.), *Introduction to Biosemiotics* (pp. 257–282). Springer. https://doi.org/10.1007/1-4020-4814-9_11.
- Vladimirov, N., & Sourjik, V. (2009). Chemotaxis: How bacteria use memory. *Biological Chemistry*, 390(11), 1097–1104. <https://doi.org/10.1515/BC.2009.130>
- Vladimirov, N., Løvdok, L., Lebedez, D., & Sourjik, V. (2008). Dependence of bacterial chemotaxis on gradient shape and adaptation rate. *PLOS Computational Biology*, 4(12), e1000242. <https://doi.org/10.1371/journal.pcbi.1000242>
- Wadhams, G. H., & Armitage, J. P. (2004). Making sense of it all: Bacterial chemotaxis. *Nature Reviews Molecular Cell Biology*, 5(12), 1024–1037. <https://doi.org/10.1038/nrm1524>
- Waite, A. J., Frankel, N. W., & Emonet, T. (2018). Behavioral Variability and Phenotypic Diversity in Bacterial Chemotaxis. *Annual Review of Biophysics*, 47, 595–616. <https://doi.org/10.1146/annurev-biophys-062215-010954>
- Webre, D. J., Wolanin, P. M., & Stock, J. B. (2003). Bacterial chemotaxis. *Current Biology*, 13(2), R47–R49. [https://doi.org/10.1016/s0960-9822\(02\)01424-0](https://doi.org/10.1016/s0960-9822(02)01424-0)
- Yang, Y., & Sourjik, V. (2012). Opposite responses by different chemoreceptors set a tunable preference point in Escherichia coli pH taxis. *Molecular Microbiology*, 86(6), 1482–1489. <https://doi.org/10.1111/mmi.12070>

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