Embodied Intentional Dynamics of Bacterial Behaviour

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Abstract

Existing (embodied) chemical models of bacteria are rather complex, due to the thousands of interacting chemical reactions within the cell. To gain a higher level of understanding, more transparent and, thus more abstract, models are needed. Intentional models are sometimes advocated to gain transparent models of complex dynamical systems. However, a main problem with intentional models is the symbol grounding problem: the gap between the symbolic, discrete binary decision processes and the continuous flow of chemical reactions in physical reality. In this paper an intentional modelling approach based on continuous time is introduced and used to simulate the behaviour of *E. Coli*. The model is grounded in physical reality by precisely defined relationships to the chemistry. The intentionalisation approach followed here is relevant in general, not only for biochemistry. In general, our approach enables the incorporation of real continuous time in intentional (BDI) models.

1. Introduction

It is often claimed that the attribution of intentional notions, such as beliefs, desires and intentions, eases the understanding of complex agent behaviour; cf. (Dennett, 1987). However, the relationship of such attributed intentional notions and the real world is not uncontroversial. In principle, to relate them to the real world, two strategies are possible. The first strategy is to relate the intentional notions directly to physical circumstances. This strategy is rejected by (Dennett, 1987); in his view the notions by themselves need not be based on any physical substance, as long as they effectively explain and predict behaviour. The second strategy is to relate the notions to observed behaviour. For example, (Dennett, 1991) suggests that the intentional notions relate to observed behaviour patterns; however, no indication is given about how exactly these relationships are defined. This lack of grounding makes the position of intentional notions to describe behaviour debatable from a foundational perspective. From a pragmatic perspective, however, intentional notions might well have their value in explanation and prediction of complex behaviour at an abstract level.

Using symbolic models for intentional behaviour introduces the well-known symbol grounding problem. For example, in (Sun, 2000) this problem is discussed, and an approach is proposed, where a combination of symbolic and other, e.g., connectionist techniques is used: the symbols get their grounding by relating them to lower level (e.g., sensory) processes within the organism. Also in (Clark, 1997, 1999) a position is put forward to integrate functional and embodied perspectives in explanation of behaviour. The work presented below has a similar perspective: integration of intentional and embodied models to describe bacterial behaviour.

For simple organisms such as the bacterium *E. Coli*, the chemical processes are sufficiently accessible to obtain an explanation of, e.g., their eating (food import) behaviour (Neidhardt, Curtiss III, Ingraham, Lin,

Brooks Low, Magasanik, Reznikoff, Riley, Schaechter & Umbarger, 1996). However, although biologists in principle can describe bacterial behaviour by hundreds to thousands of differential equations for the various chemical reactions, they want more abstract ways of summarising the main paths of processes involved. This motivates for reconsidering the use of intentional notions for this purpose as well, but to avoid the foundational problems this time by using these notions in a grounded, embodied manner. This poses the interesting question how to relate a discrete, binary decision process to the continuous dynamics of (chemical) processes in the real world.

Section 2 briefly describes the bacterial regulation process, introduces the intentional notions used, and relates them. In Section 3 the use of temporal relationships to model both chemical and intentional dynamics is explained. Subsequently, in Section 4, the food import decision process of the common bacterium E.Coli is described using temporal relationships.

2. Relating Chemical and Intentional Notions in E. Coli

Bacteria are small autonomous living systems that interact with their environment; the understanding of the regulation of the behaviour is often complicated by the enormous complexity of the chemistry in the living cell. Using intentional notions to model the regulation of a bacterium, this regulation may be more easily understood. First, the regulation in bacteria is briefly explained in biochemical terms. Second, the behaviour of an agent is explained using intentional notions. Third, the relationships between the intentional notions and the chemicals in the bacterial regulation are presented.

2.1. Bacterial Regulation

In bacteria, as in every living cell, the regulation of its internal processes consists of several steps (Neidhardt, et.al., 1996). In this paper, the regulation of the lactose import is taken as an example; other regulation paths follow similar steps as depicted on the left side of Figure 1. First a substance in the cell relates to the presence of lactose. The transcriptional regulation, translational regulation and metabolic control then interact to modify the behaviour of the cell.

So, the regulation of the processes within a bacterium consists of several steps. First, circumstances in the external environment lead to certain concentrations of specific internal substances. Then, the transcriptional regulation is done, possibly resulting in mRNA. Subsequently, the translational regulation is done, possibly resulting in proteins. The metabolism, comprised of energy production, transport and growth pathways, further regulates the activation and inhibition (inactivation) of certain enzymes. When all this is done, enzymes may be ready to catalyse chemical reactions. When enzymes catalyse reactions, they cause an increased flux, leading to growth of the bacterium.

2.2. Intentional Notions

The intentional notions that are used to describe behaviour are taken from BDI (Beliefs, Desires and Intentions) models; e.g., (Rao & Georgeff, 1991). The *beliefs* represent what the agent deems to be true in its environment. A belief is present due to sensing (in the present or in the past). *Desires* are interpreted as what the agent wants to accomplish or fulfil. Agents can have desires contradictory in their fulfilment, for example desiring lots of ice creams and a slim waist. A desire, together with a sufficient additional reason, leads to an intention to fulfil the desire. An *additional reason* is a set of beliefs that have to hold or not hold, in order for the intention to be generated. *Intentions* are interpreted as that the agent will make something happen (action), as soon as a belief in an opportunity (for the action) occurs. *Opportunities* are states of the environment that give the possibility to perform an action. *Actions* performed by the agent affect its internal or external physical environment. The relations between the intentional notions are depicted on the right side of Figure 1.

2.3. Intentionalisation

The intentional notions used to describe the behaviour can be related to the substances used in the bacterial regulation. The internal substances relating to the situation in the environment are chosen to correspond with the beliefs. DNA parts are chosen to correspond to desires. The conditions needed for the transcriptional regulation correspond with the additional reasons of the intentional model. As can be seen from the left side of Figure 1, DNA is used to create mRNA. Therefore, with DNA as desire, mRNA is chosen to correspond with an intention to prepare for an action. The enzymes created by the translation are used to increase the flux of chemical reactions (which correspond to actions in the intentional model). Thus, the enzymes are chosen to correspond with intentions to perform actions. The (co)factors necessary for the translation of mRNA into enzymes correspond with the additional reasons for the creation of the intentions for performing actions. The opportunity for an action corresponds to the inhibitors of the enzymes. When enzymes cause flux, (i.e., successfully catalyse reactions), this corresponds to the action happening in the world.

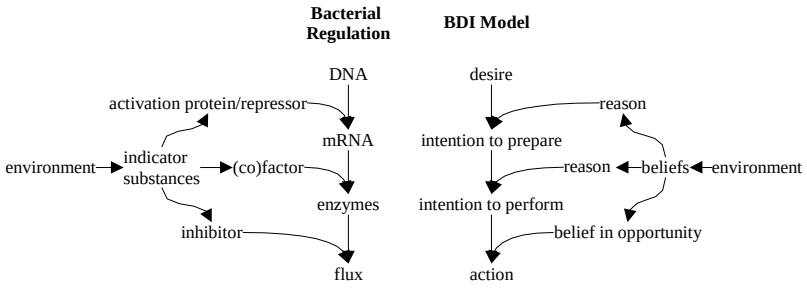

Figure 1: The correspondence between the bacterial regulation and the causation in the BDI model.

3. An Abstract Continuous Time Model of Chemical Processes

The bacterial behaviour results from a multitude of biochemical processes. These operate on each other over time, producing the behavioural regulation. The overall regulation process is not easy to understand; for example, a number of feedback loops between different stages of the regulation process and a high number of chemical reactions are involved.

A more abstract model for the dynamics of biochemical processes can be obtained by introducing categories of concentrations of substances, and relating different categories of the same and of different substances over time. In this section temporal relationships are used to express the timing dynamics. The resulting abstract model captures the timing dynamics of the biochemical reactions in logical temporal relationships using continuous time.

A generally accepted way to describe biochemical reactions is in the form: A + B ↔ C + D. This expresses that substances A and B can be transformed into substances C and D, and that the reverse process is also possible. In the cell the pathways consist of several reactions chained together. For example (1) sketches the pathway for the transcription of the lac operon. The transcription of the lac operon will be the leading example.

transcription lactose: nucleotides + DNA_lactose ↔ …
↔ mRNA_lactose + DNA_lactose (1)

Formulae like (1) do not express inhibitors, activators, speed and equilibrium conditions. For example lactose and CRPcAMP are the activation proteins regulating the transcription of the lac operon. Within the well-known Michaelis-Menten equations the rate of a reaction can be derived on the basis of concentrations of substances, binding constants, stoichiometry values and equilibrium constants. Michaelis-Menten provides formulae for the reactions in continuous time. Equations such as Michaelis-Menten equations can be extended with inhibitors and activators. Using these formulae, a complete description of the processes in the cell could be given if all the reactions and their parameters were known, which is not the case. Example parameter values are given for the transcription of the lac operon reaction, see (2).

Regulators: lactose 0.01, CRP_cAMP 0.01,
kcat = 0.01, keq = 100. (2)

Viewed from a more abstract perspective, what does this reaction do over time? When enough of lactose, CRPcAMP and nucleotides are present, the mRNA_lactose will start to be produced, and after a certain delay a significant amount of mRNA_lactose will be present. The concentrations of lactose and CRPcAMP need to be sufficiently high for a certain period of time in order for the reaction to proceed, a concentration of at least 0.1 mmolair (the threshold) of both is sufficient in the example. The amount of nucleotides needed for the reaction to proceed is at least about 0.1 mmolair again. A ready supply of nucleotides is always synthesised by the cell. In order for the reaction to happen, the amount of mRNA must not be so high as to impede the reaction, a concentration lower than about 10 mmolair in this example. When the reaction proceeds, the amount of nucleotides will slowly decrease. The amount of mRNA will slowly accumulate by this reaction. Other parts of the system will supply new nucleotides and the mRNA will degrade after some time.

The large amount of unknown parameters, and computational complexity of integrating the resulting differential equations make a model using only chemical differential equations unwieldy. Therefore a more abstract description is introduced. The process is modelled in our temporal environment as follows. Temporal relationships are defined between a number of sources and an effect. Parameters are used to specify the minimal duration of the sources, the delay before the effect becomes apparent, and the duration of the effect; for the delay a minimum and maximum value can be set. As an illustration, the temporal relationship between the substances in the transcription of the lactose operon is determined. Since nucleotides are always present, these do not need to be mentioned in the temporal relationship, as it does not influence behaviour. The temporal relationship to determine when the mRNA_lactose is produced is denoted as:

DNA_lactose + lactose + CRP_cAMP

$\bullet\!\!\rightarrow\!\!\!\!\rightarrow_{e,f,g,h}$ mRNA_lactose (3)

On the left-hand side the conditions that have to be met are listed. The DNA_lactose, meaning the presence of the lactose operon in the DNA. Also lactose, meaning the presence of lactose and CRP_cAMP (i.e., concentration above a threshold value), meaning the presence of CRP_cAMP to bind to the activation sites of the operon are listed on the left side. On the right hand side, the change that will happen later is listed, mRNA_lactose meaning the presence of lactose mRNA that is produced. The parameters e, f, g and h are positive real numbers that set the minimum and maximum delay (e and f), the condition duration (g) and the result duration (h). Realistic parameters for the values of e, f, g and h for the example are e = 60, f = 60, g = 1 and h = 40, as the process to create the mRNA takes about 60 seconds, and the mRNA will stay in existence for about 40 seconds on average. When the condition holds for 1 second or more, the transcription process starts.

Previously, a temporal model has been presented of chemical processes using categories of substances and temporal relationships between these. Here the temporal relation $\bullet\!\!\rightarrow\!\!\!\!\rightarrow$ that is called the "*leads to*" relation is more precisely defined. When $\alpha \bullet\!\!\rightarrow\!\!\!\!\rightarrow_{e,f,g,h} \beta$ this means that:

> if property α holds for a while (g), then some time (between e and f) later property β will hold for a while (h).

The definition of the relationships as given above, can be applied to situations where the sources hold for longer than the minimum g. The result for a longer duration of α for $\alpha \bullet\!\!\rightarrow\!\!\!\!\rightarrow \beta$ is depicted in Figure 2. The additional duration that the source holds, is also added to the duration that the result will hold, provided that the condition $e + h \geq f$ holds. This is because the definition can be applied at each subinterval of α, resulting in many overlapping intervals of β. The end result is that the additional duration also extends the duration that the resulting notion β holds. More formally:

$[\alpha \bullet\!\!\rightarrow\!\!\!\!\rightarrow_{e,f,g,h} \beta \;\&\; e+h \geq f] \;\Rightarrow\; \forall a \geq 0: \alpha \bullet\!\!\rightarrow\!\!\!\!\rightarrow_{e,f,g+a,h+a} \beta$

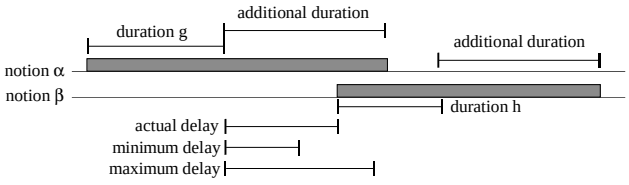

Figure 2: Temporal relationships for longer durations.

Using these temporal relationships, the bacterial regulation can be modelled from the chemical perspective. The temporal relationships capture the timing of the underlying chemical reactions. The durations and delay minimum and maximum can be specified to fit the timing of the chemistry. The formally defined temporal operator "leads to" aids the construction of simulation and derivation software to support the inspection of modelling results.

4. Temporal Modelling of Intentional Dynamics

Formalised models for intentional notions like those of (Rao & Georgeff, 1991) do not take into account their dynamics. To be able to closely relate an intentional model to the bacterial embodiment in chemical processes, such dynamics is crucial. Therefore a temporal modelling approach to intentional dynamics is introduced, based on the temporal "leads to" relation introduced in the previous section. The dynamics of intentional notions is expressed in terms of this "leads to" relation. By applying the correspondences between the intentional notions and the chemical substances from the previous sections a dynamic model based on intentions is obtained. The resulting model is a correct and transparent high level description of the regulation process, understandable for the reader not versed in the technicalities of the chemical pathways in the cell.

The model presented here covers food import behaviour of *E. Coli*. The temporal relationships between desire(lactose_import) and intention(lactose_import), using belief(lactose_externally_present) and belief(not glucose_externally_present) are discussed here as an example. The desire and the beliefs (the reason for the creation of the intention) must hold for at least some duration. After a delay larger than the minimum delay and shorter than the maximum delay, the intention starts to hold for some duration. This temporal relationship is denoted in relation (4).

desire(lactose_import) $\wedge$ belief(lactose_externally_present) $\wedge$ belief(not glucose_externally_present)

$\bullet\!\!\rightarrow\!\!\!\!\rightarrow_{e,f,g,h}$ intention(lactose_import). (4)

The intentional notions are related to the substances, as discussed in the Sections 2.3 and 3.1.

In relation to (4), the lactose and CRPcAMP substances are interpreted as beliefs. The DNA relates to a desire and the mRNA to an intention. The nucleotides and other, intermediate, substances are not labelled with intentional notions. These substances are only the machinery of the embodiment of the bacterial cognition, and play no decisive role in the lactose uptake behaviour. This means that, leaving out these, the intentional model provides a more abstract picture of the processes. If new insights were to prove some substances play a significant role in the decision process, these can easily be added. Assigning the intentional notions to the substances is not enough. It is also necessary to know at which concentration of the substance the intentional notion holds. A threshold is used to determine whether the intention notion holds or not.

The timing parameters e, f, g, and h are the same as those found in the abstract chemical model, thus relation (5) holds.

$$\text{desire(lactose\_import)} \wedge \text{belief(lactose\_externally\_present)} \wedge \text{belief(not glucose\_externally\_present)} \bullet\!\!\rightarrow\!\!\!\!\rightarrow_{60,60,1,40} \text{intention(lactose\_import).} \quad (5)$$

Some more example intentional temporal relationships within the model are:

..... Desires .....

desire(grow).
desire(food_import).
desire(lactose_import) .
desire(glucose_import).

The cell always desires to grow. From this basic desire stem the other desires, which also always hold. The cell desires to import nutrients (in order to grow). The cell also desires to import glucose (in order to import nutrients), and to import lactose (in order to import nutrients).

..... Intentions to prepare import actions .....

$\text{desire(lactose\_import) and additional\_reason}_{1.1} \bullet\!\!\rightarrow\!\!\!\!\rightarrow_{60,60,1,40} \text{intention(prepare\_lactose\_import)}$.
$\text{desire(glucose\_import) and additional\_reason}_{1.2} \bullet\!\!\rightarrow\!\!\!\!\rightarrow_{60,60,1,40} \text{intention(prepare\_glucose\_import)}$.

$\text{additional\_reason}_{1.1} =_{def} \text{belief(lactose\_externally\_present) and belief(not glucose\_externally\_present).}$
$\text{additional\_reason}_{1.2} =_{def} \text{true.}$

The cell will intend to prepare to import a nutrient if sufficient additional reasons are present. The desire to import lactose, combined with the additional reason to import lactose ($\text{additional\_reason}_{1.1}$) results in the intention to prepare to import lactose. The additional reasons to import lactose are the belief that lactose is present outside and the belief that glucose is not present outside. The desire to import glucose, when combined with an additional reason ($\text{additional\_reason}_{1.2}$), results in the intention to prepare to import glucose. There is no additional reason needed to import glucose, it is denoted true.

..... Intentions to perform import actions .....

$\text{intention(prepare\_lactose\_import) and additional\_reason}_{2.1} \bullet\!\!\rightarrow\!\!\!\!\rightarrow_{0,0,60,600} \text{intention(perform\_lactose\_import).}$
$\text{intention(prepare\_glucose\_import) and additional\_reason}_{2.2} \bullet\!\!\rightarrow\!\!\!\!\rightarrow_{0,0,60,600} \text{intention(perform\_glucose\_import).}$

$\text{additional\_reason}_{2.1} =_{def} \text{belief(lactose\_externally\_present).}$
$\text{additional\_reason}_{2.2} =_{def} \text{belief(glucose\_externally\_present).}$

Given some good additional reasons and the intention to prepare an import, the cell will generate the intention to perform the import. When the cell intends to prepare lactose import, and enough additional reason is present ($\text{additional\_reason}_{2.1}$), the belief that lactose is present outside, then the intention to perform the import of lactose is generated. When the cell intends to prepare glucose import, and enough additional reason is present ($\text{additional\_reason}_{2.2}$), the belief that glucose is present outside the cell, then the intention to perform the glucose import is generated.

5. Discussion

The relationship between the chemical regulation substances and the intentional notions for the behaviour description shows that the intentional model presented in Section 4 is grounded by the chemical processes of the regulation. The simulation of the intentional model proves that the intentional model corresponds to the chemical bacterial regulation. In other words, the BDI model apparently matches well with the regulation that happens in living cells.

The value of this work for Biology lies in managing the complexity of living systems. For example, the internal processes within organisms often are so complex that explanations of their behaviour in terms of a large variety of physical and chemical processes are inaccessible. This paper shows how, at least for moderately complex organisms, abstraction and intentionalisation of such continuous processes can be done in a justifiable manner. The resulting models show intentional dynamics embodied in physical and chemical models of real world dynamics.

References

Clark, A. (1997). *Being There: Putting Brain, Body and World Together Agai*n. MIT Press.

Clark, A. (1999). Where brain, body, and world collide. *Journal of Cognitive Systems Research*, 1, pp. 5-17.

Dennett, D.C. (1987). *The Intentional Stance*. MIT Press. Cambridge Mass.

Dennett, D.C. (1991). Real Patterns. *The Journal of Philosophy*, vol. 88, pp. 27-51.

Neidhardt, F.C., Curtiss III, R., Ingraham, J.L., Lin, E.C.C., Brooks Low, K., Magasanik, B., Reznikoff, W.S., Riley, M., Schaechter, M.& Umbarger, H.E., eds. (1996). *Escherichia coli and Salmonella typhimurium*. ASM Press, Washington, D.C.

Rao, A.S. & Georgeff, M.P. (1991). Modelling Rational Agents within a BDI-Architecture. In: J. Allen, R. Fikes & E. Sandewall, eds., *Proceedings of the Second International Conference on Principles of Knowledge Representation and Reasoning*, (KR'91), Morgan Kaufmann, pp. 473-484.

Sun, R. (2000). Symbol grounding: a new look at an old idea. *Philosophical Psychology*, 13, pp. 149-172.