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Towards a Metabolic Robot Control System

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Abstract

Bacteria must be able to detect rapid changes in their environment and to adapt their metabolism to external fluctuations. They monitor their surroundings with membrane-bound and intra-cellular sensors. The regulatory mechanisms of bacteria can act as a model for the design of robust control systems based on an artificial chemistry. The capability to process information which is needed to keep autonomous agents surviving in an unknown environments is discussed by means of two examples. (1) is inspired by polymerisation reactions and (2) is inspired by enzyme-substrate kinetics. First experimental results with a real mobile robot are presented.

Keywords: *Molecular Computing, Chemical Computing, Bacteria, Chemotaxis, Information, Adaptation, Autonomous Agents, Artificial Chemistry*

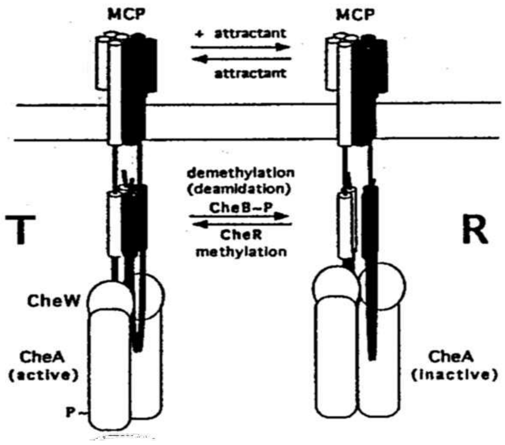

Figure 1: *Ligand binding causes the modulation of the electrostatic properties of the helices and therefore the transition between T and R states. From [22]*

1 Introduction

Biological cells can be seen formally as information processing systems of high complexity [18]. They react to a large number of stimuli which are perceived by sensors. These mostly chemical stimuli are converted by *two-component-systems* into signals that are (1) collected, (2) computed, (3) integrated and (4) transmitted through signal transduction pathways. Biochemical changes of proteins, protein-protein interactions and facilitated diffusion along ordered cell structures play a decisive role.

Cellular signal-transmitting systems are hierarchical and often require communication between hundreds of proteins. Membrane-bound two-component systems (see Fig. 1) provide the connection between the *sensory domain* and an attractant or repellant. This domain is connected via helical transmembrane protein structures with the *regulator domain*.

Conformational changes in the sensory domain at the external surface induce changes in the relative positioning of the helical membrane-cytosol interface. For instance, a binding of ligands cause a change of the electrostatic density and hence a rotation to increase the distance between charged groups [22, 17]. This reaction is transient, i.e. it ends even though the stimulus might continue. Formally, this adaption is achieved through a release of a slow feedback reaction which inhibits the signal. Different pathways interlace and so a hierarchical cellular network emerges with a high capacity to store information [17, 9]. The computational functions in such biochemical reaction networks

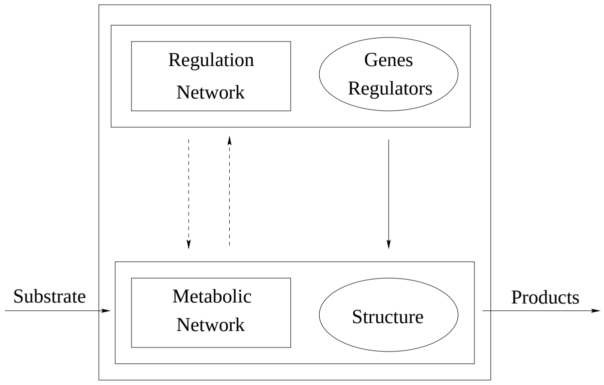

Figure 2: *The metabolic and the regulatory network of a cell. Both are connected through flow of information as well as flow of substances.*

have been analysed by [2, 8, 6] and are supposed to function akin biochemical neuronal networks [14, 13, 20].

Through encapsulation of correlated functions into compartments [19, 10] and the use of superimposed regulating mechanisms (see Fig. 2) the cell reduces the vast flow of information to a communication between a few clearly arranged functional blocks.

The signal processing system of a cell is very robust in its dependence upon the observation of central metabolites and, on the other hand, on the hierarchical division into functional blocks. Therefore it can act as a model for the construction of robust, highly parallel and distributed control systems.

2 Cells as Information Processing Systems

The metabolism of a cell can be divided into two levels: (i) the metabolic network, where all bio-chemical reactions occur and (ii) the regulatory network which controls the velocity of the reactions and supervises the transduction pathways.

All reaction pathways and all regulatory elements together form a kind of highly connected *molecular network*. Each element of this network is a collector of different stimuli (see Fig. 3).

Signals are transmitted depending on the actual state of the adaptor. They are reduced to binary information: by molecules appearing in only two states: *activated* or *inactivated*. Usually these differ only in the absence or presence of a single atom or group at the molecular level. The regulatory network decides

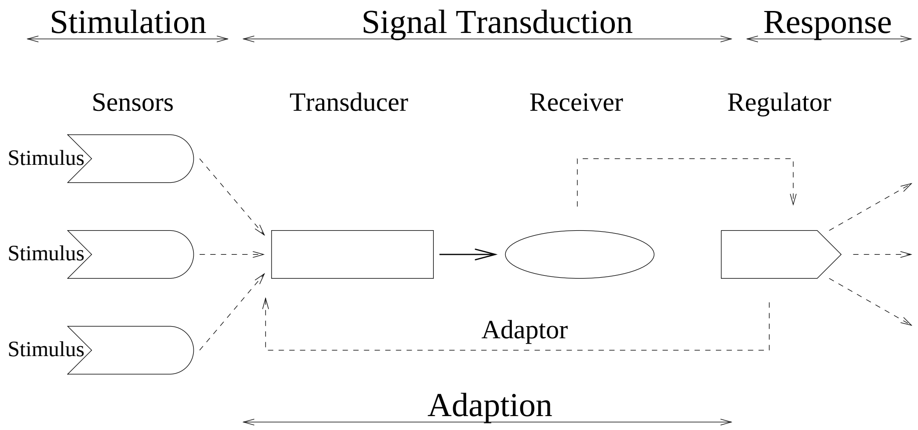

Figure 3: *A node in the molecular network of the cell. Stimuli are collected and transmitted depending on the level of adaption to the specific stimulus. This node can be seen as a more general two-component system. Diagram adapted from [18].*

through slow or fast feedback or forward reactions which of the connections of the molecular network are activated or inhibited [17, 21].

One very interesting information processing system of a bacterium controls its movement. Thus, the rest of this section is devoted to a more detailed discussion of the information flow in the chemotaxis system. *Chemotaxis* is the ability of a bacterium to follow concentration gradients by modulation of tumbling frequency. (Fig. 4).

In *E. coli* there are six cytoplasmic transduction proteins: *CheA, CheB, CheR, CheW, CheY and CheZ* [22]. The increase of CheA, for example, indicates the presence of a carbon source (glucose, fructose, etc.). CheA phosphorylates CheY which binds to the switch complex of the flagellar motor and CheB which closes the feedback loop to reset the receptor. The binding of CheY causes clockwise rotation or, to be more specific, it interrupts counterclockwise rotation. Clockwise rotation of the majority of the flagellar motors causes a re-orientation (*tumble*). In this way, the frequency of tumbling is influenced by the concentration of the carbon source.

The cell thus executes a biased random walk, caused by concentration gradients, towards a more favourable environment. It is assumed [22, 5, 1] that chemotactic responses are mediated by a *temporal*, rather than by a *spatial*, sensing mechanism, for the following reasons: (i) the length of a bacterium is too small and it moves too quickly to allow for spatial sensing. (ii) Bacteria even respond to sudden changes in concentrations when the concentration

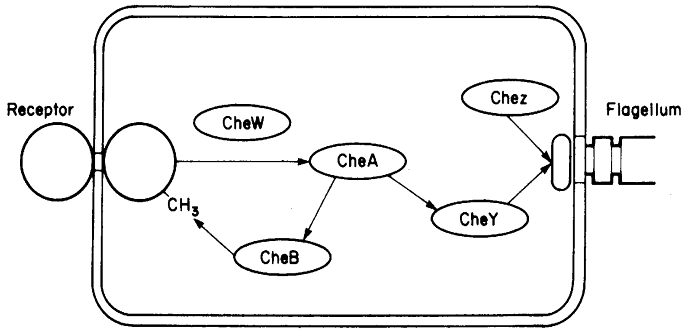

Figure 4: *Information flow in the chemotaxis system of* Escherichia Coli. *Binding of stimulus molecules causes activation of CheA by CheW. CheA activates CheB which resets the receptor thereby closing the feedback loop. CheY binds to the switch complex and causes clockwise rotation. It is antagonised by CheZ. Diagram from [16].*

is spatially homogeneous. The decision to change the movement direction or not depends on the state of some key-metabolites and constitutes an inherent memory of the cell. For a detailed description of bacterial chemotaxis see for example [7, 16, 17, 22].

3 A Spatial Model of the Cell

Information processing in living systems means transduction of substances or molecular interactions. The reception of a stimulus causes the transmission of substances to inner regions of the cell. They arrive either unchanged via diffusion along ordered cell structures or through a cascade of sequential biochemical reactions. Thus, a changing concentration level of X_i can indicate the reception of Y_i. Since chemical reactions take place at very high velocity the delay between encountering a specific substance and a significant change in concentration of the signalling substance is small. Response to an actual stimulus is very fast.

3.1 Compartments

Although a procaryotic bacterium appears to lack a cytoskeletton it must not be seen as a "bag full of enzymes" but as a highly ordered system of interacting molecules which are interconnected and connected to the inner membrane.

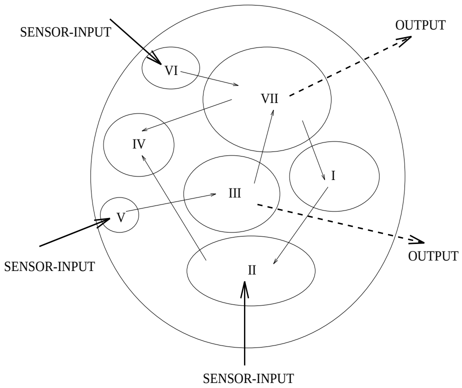

Figure 5: *Spatial model of the cell. Homogeneous subsystems (*compartments*) are connected through diffusion flux. For further details see text.*

A model of spatially continuously distributed substances can be based on non-linear *partial* differential equations. Replacing the spatial derivatives with finite differences divides the system into subsystems (see Fig. 5) which can be treated as homogeneous regions and modelled by a system of coupled *ordinary* differential equations [15]. These subsystems are called *compartments*. The state of a compartment is represented by a concentration vector. A realistic model of a complex bio-chemical system requires 10^2 - 10^5 compartments. In order to keep the simulation of the system tractable the number of compartments should be reduced. The first experiments with a real robot are performed with only one compartment. A model system of this kind can be called a (formal, algorithmic) *reactor*.

3.2 Metadynamics

Describing the dynamics of the reactor leads to a system of coupled differential equations. In order to avoid the number of reactions becoming infinite there must be a focusing on the most relevant ones. A real reactor only contains a finite number of substances and so a possible reaction can only take place when at least one single molecule is inside the reactor. Simulating the dynamics with differential equations, however, assumes a continuous model even with infinitesimal concentrations of substances.

Since a reactor in reality is not continuous but discrete there must be a concentration threshold representing the presence of a single molecule above which the substance is treated as a reactant. If its concentration be lower, it should not participate in the reactor's dynamics. Thus the system has two different time scales: a fast time scale of the concentration changes and a slower time scale for changing the number of participating substances. This change of the ODE system over time is called *metadynamics* [3]. The metadynamics is additionally influenced by diffusion fluxes from other compartments.

4 Artificial Reaction Systems

4.1 Artificial Chemistry

In a real chemistry the kinetic parameters and efficiencies depend on thermodynamics, quantum mechanics and chemical composition of the molecules. For that reason it is impossible to calculate them exactly in practice. To circumvent the troublesome computation of approximations one can formulate an *artificial chemistry* (AC) [3, 11, 12]. An AC is not able to reproduce all properties of real chemistry but it can produce complex behaviour which can be studied instead. By changing the rules different chemistries can be instantiated and, adding layers of more realistic behaviours, it is possible to reproduce properties of the "real" chemistry.

A straightforward way for building a metabolic controller would be, first, to define an arbitrary AC and then use this chemistry to create a controller composed of certain substances. In the following sections we will define two artificial chemistries to show how the abilities of a metabolic controller are depending on its underlying AC.

4.2 Example A: Artificial Polymer Chemistry

We begin our discussion with an artificial *polymer chemistry* which is an AC where only polymerisations reactions exists [3]. A substance is represented by a string $s = (s^1, s^2, \dots s^n) \in A^n$ composed of characters from the alphabet A. The reaction mechanism is simply defined as the concatenation:

$$(s_i^1, s_i^2, \dots s_i^{n_i}) + (s_j^1, s_j^2, \dots s_j^{n_j}) \overset{s_k}{\rightleftharpoons} (s_i^1, s_i^2, \dots s_i^{n_i}, s_j^1, s_j^2, \dots s_j^{n_j}) \qquad (1)$$

The reaction may be catalyzed by a string s_k with catalytic efficiency ν. The dynamic behaviour of the polymer chemistry should be demonstrated by the example shown in figure 6 with the alphabet $A = A, B$. The catalytic constants k_i' are set to $\nu = 10$. Polymerisation is ten times faster than de-polymerisation

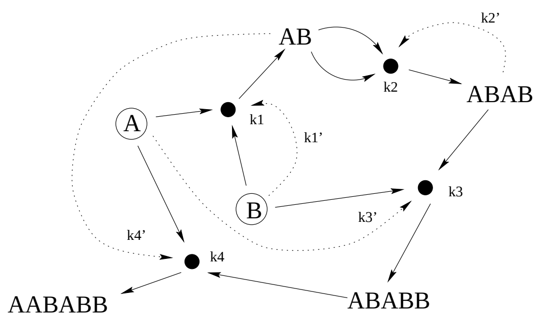

Figure 6: *Example A: Reaction network for the polymer chemistry. The monomers A and B (foot set) will be used as inputs. Dotted arrows indicate catalytic activity.*

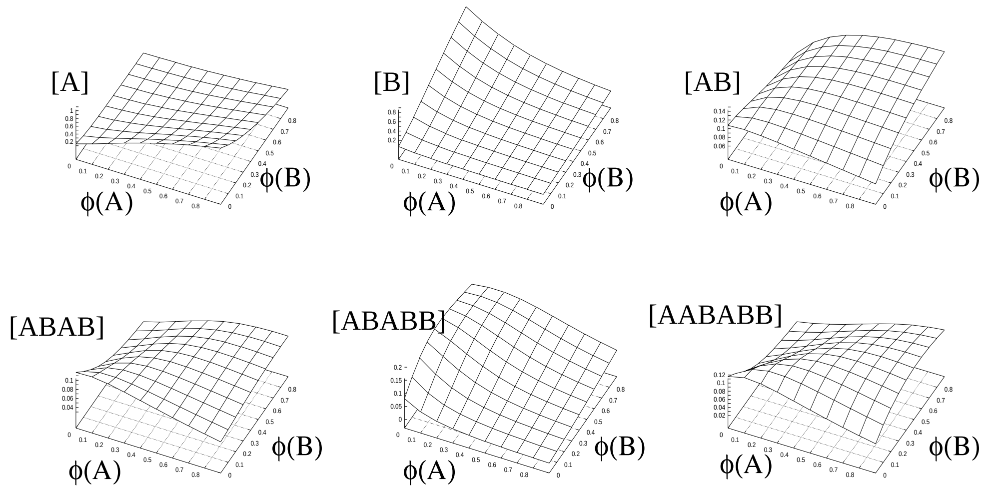

Figure 7: *Example A: Steady-state input-output relation for the polymer chemistry (Fig. 6).*

($k_i = 1.0$, $k_{-i} = 0.1$). Details of the reaction mechanism and its ODE system can be found in the Appendix. Fig. 7 shows the steady-state input-output relation of the example reaction network. The continuous influx flow $\Phi(A)$ and $\Phi(B)$ of the monomers A and B is defined as input.

4.3 Example B: Artificial Enzyme-Substrate Chemistry

The reaction network in Fig. 8 is an example based on enzyme-substrate kinetics. Reaction systems of this kind are refered to as chemical neuronal networks [14, 20]. The input is represented by the substances C and D, the output by T. The substances marked by "*" are held at a constant value. The detailed reaction mechanism and its corresponding ODE model can be found in the

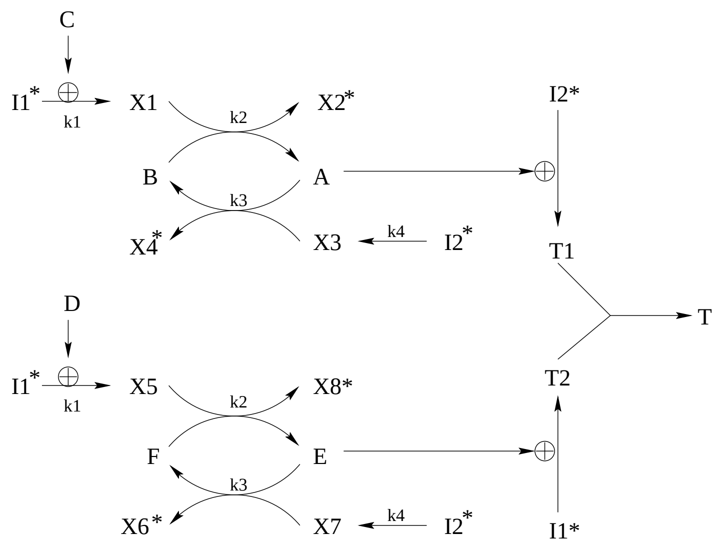

Figure 8: *Example B: Reaction network based on enzyme-substrate kinetics. C and D are input species. T is the output. Substances marked by "*" are held constant.*

Appendix. Fig. 9 shows the steady-state concentrations of the output species T and several internal substances as a function of input C and D.

4.4 Comparison

The polymer chemistry shows a very smooth input-output surface in contrast to the sharp surface of the enzyme-substrate example. The smooth surface insinuates that input information is not processed. The state space which can be reached for different inputs is very large. Given some concentrations of possible output-substances the input-vector can be much more easily reconstructed than in example B. The surface in state space can not be intuitively divided into different regions with different meanings. In the enzyme-substrate example the quasi-continous input information is condensed by mapping it on two regions in state space which can be clearly separated (Fig. 9).

In addition, the total information conservation of the polymer chemistry may lead to information destabilisation when the information should be stored in reaction loops, processed or transmitted. Small fluctuations will be amplified resulting in a quick loss of information. The sigmoidal character of the surface in example B causes a correction of small fluctuations when information is passed from one sub-network to another.

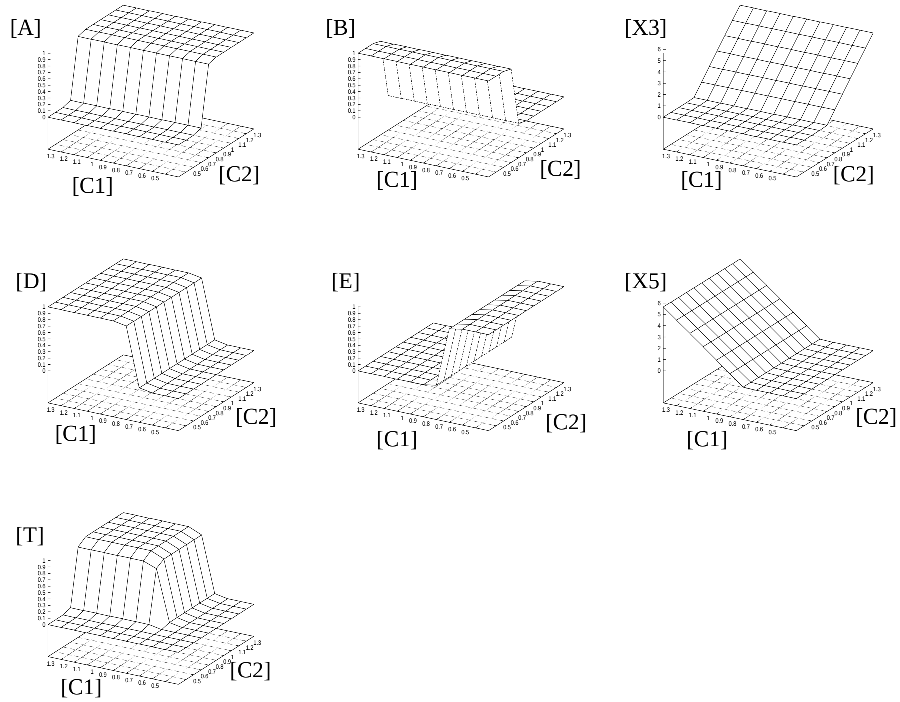

Figure 9: *Example B: Steady-state input-output relation of the enzyme-substrate chemistry example (Fig. 8) which shows the function of an logic AND gate.*

5 The Robot Controller

We shall now discuss the application of the above model to robot control. In order to make use of the computational capabilities of a metabolism it will be necessary to connect it to the environment. If it were simulated without any additional fluxes (e.g. sensor information) the system would run through a transient phase until it finally reached a steady-state.

If we connect the model of our reactor with the infrared sensors of a robot and the motor control with the concentration level of some metabolites we shall be able to use the emerging computational capabilities of the metabolism to control the robot's behaviour. The metabolism is driven away from equilibrium through the sensor information flux, so that all concentrations are influenced by the surroundings of the robot. The sensors are connected with different parts of the metabolism. A change of one sensor value may increase or decrease the concentration of a certain species. The resulting dynamics causes a representation of the environment inside the robot's metabolism.

In Fig. 10 a schematic metabolism is shown based on an enzyme-substrate kinetics which has been used to control a real robot. The robot has 8 prox-

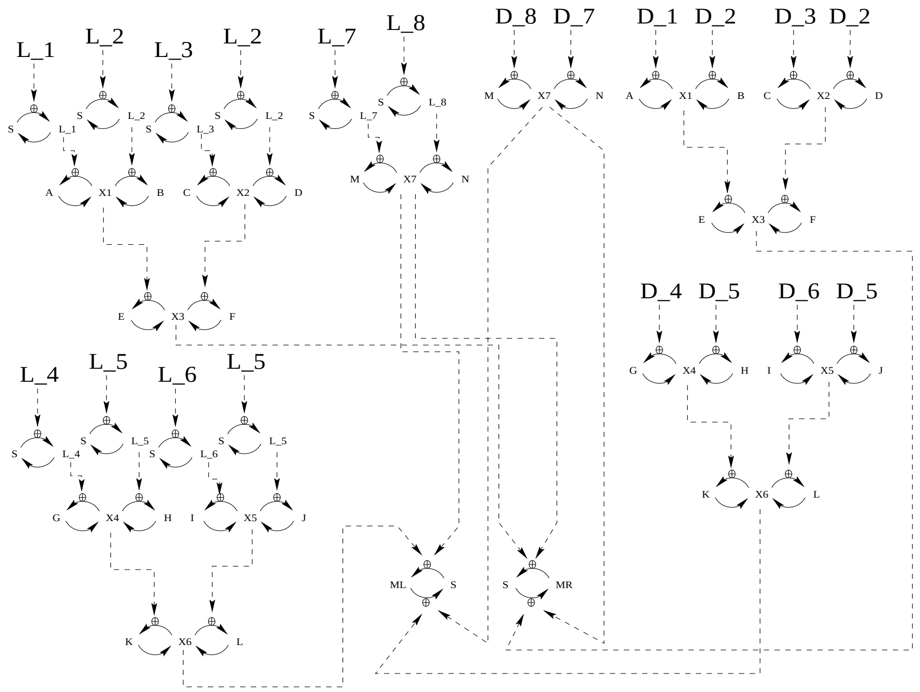

Figure 10: *The robot's metabolism based on enzyme-substrate kinetics. L_i are the sensor substances emitted by the ambient light sensors. D_i are emitted by the distance sensors. Wheel motors are controlled by the substances ML and MR.*

imity and 8 ambient light sensors. Two basic behaviours are integrated into the metabolism: *obstacle avoidance* and *light seeking*. The part of the reaction network mainly concerned with the obstacle avoidance is processing the substances emitted by the proximity sensors. The light seeking behaviour gets its input from the ambient light sensors.

Experiments (Fig. 11) show, that the metabolism is able to control the robot in the desired way. It is also able to perform behaviour selection in critical situations where obstacle avoidance has to suppress light seeking. Further, the controller is shown to be robust against disturbance of the reactor, which has be simulated by inserting small random amounts of substances.

6 Concluding remarks

The behavior of the robot emerges through chemical reactions between metabolites. It is possible for an autonomous robot to get information about its environment by sensors emitting substances into the robots metabolism. The control system is parallel and distributed and the ability of navigation emerges

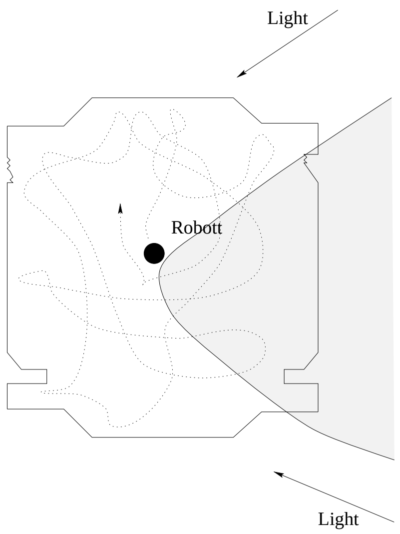

Figure 11: *Example run of the robot. A typical trajectory of the robot's movement is shown in the environment. The robot tries to stay in the lighted area while simultaneously avoiding obstacles.*

only through computation with catalytic reactions [4].

The increase and decrease of key-metabolites allows to achieve primitive goals such as obstacle avoidance or luminance gradient following (*phototaxis*). By adding different sensors it would be possible to solve more complicated tasks by stimulus-specific chemical reactions and alarmones. The current focus in our work lies in developing an algorithm which automatically evolves the metabolism to get a better stimulus-response mechanism, but this work is still in progress.

Appendix: ODE System for Polymer Chemistry

The reaction mechanism for Example A:

$$
\begin{array}{rcll}
A+B & \rightleftharpoons & AB, & \omega_1 = k_1[A][B] - k_{-1}[AB] \\
AB+AB & \rightleftharpoons & ABAB, & \omega_2 = k_2[AB][AB] - k_{-2}[ABAB] \\
ABAB+B & \rightleftharpoons & ABABB, & \omega_3 = k_3[ABAB][B] - k_{-3}[ABABB] \\
A+ABABB & \rightleftharpoons & AABABB, & \omega_4 = k_4[A][ABABB] - k_{-4}[AABABB] \\
A+B & \overset{B}{\rightleftharpoons} & AB, & \omega_5 = k_5\,\nu[A][B][B] - k_{-5}\,\nu[AB][B] \\
AB+AB & \overset{ABAB}{\rightleftharpoons} & ABAB, & \omega_6 = k_6\,\nu\,[AB][AB][ABAB] - k_{-6}\,\nu\,[ABAB][ABAB] \\
ABAB+B & \overset{A}{\rightleftharpoons} & ABABB, & \omega_7 = k_7\,\nu[ABAB][B][A] - k_{-7}\,\nu[ABABB][A] \\
A+ABABB & \overset{AB}{\rightleftharpoons} & AABABB, & \omega_8 = k_8\,\nu\,[A][ABABB][AB] - k_{-8}\,\nu[AABABB][AB]
\end{array}
$$

Kinetic rate constants:

parameter	value
k_i	$1.0 \quad \forall i$
k_{-i}	$0.1 \quad \forall i$
ν	10

Resulting ODE system:

$$\begin{aligned}
\frac{[A]}{dt} &= -\omega_1 - \omega_4 - \omega_5 - \omega_8 + \varphi_A - [A]\,\frac{\varphi}{C} \\
\frac{[B]}{dt} &= -\omega_1 - \omega_3 - \omega_5 - \omega_7 + \varphi_B - [B]\,\frac{\varphi}{C} \\
\frac{[AB]}{dt} &= \omega_1 - \omega_2 + \omega_5 - \omega_6 - [AB]\,\frac{\varphi}{C} \\
\frac{[ABAB]}{dt} &= \omega_2 - \omega_3 + \omega_6 - \omega_7 - [ABAB]\,\frac{\varphi}{C} \\
\frac{[ABABB]}{dt} &= \omega_3 - \omega_4 + \omega_7 - \omega_8 - [ABABB]\,\frac{\varphi}{C} \\
\frac{[AABABB]}{dt} &= \omega_4 + \omega_8 - [AABABB]\,\frac{\varphi}{C},
\end{aligned} \tag{2}$$

where C is the size of the reactor and the influx is defined as $\varphi = \Phi(A) + \Phi(B)$.

ODE System for Enzyme-Substrate Chemistry

The reaction mechanism for Example B:

$$\begin{aligned}
I1^* + C &\rightleftharpoons X1 + C, & \omega_1 &= k_1[C][I1^*] - k_{-1}[C][X] \\
X1 + B &\rightleftharpoons X2^* + A, & \omega_2 &= k_2[X1][B] - k_{-2}[A][X2^+] \\
X3 + A &\rightleftharpoons X4^* + B, & \omega_3 &= k_3[X3][A] - k_{-3}[B][X4^*] \\
X3 &\rightleftharpoons I2^*, & \omega_4 &= k_4[X3] - k_{-4}[I2^*]
\end{aligned}$$

Kinetic rate constants:

parameter	value	parameter	value
k_1, k_5	70	k_{-1}, k_{-5}	1
k_2, k_6	$5 \cdot 10^4$	k_{-2}, k_{-6}	1
k_3, k_7	$5 \cdot 10^4$	k_{-3}, k_{-7}	1
k_4, k_8	1	k_{-4}, k_{-8}	100

Resulting ODE system:

$$\begin{aligned}
\frac{d[X1]}{dt} &= \omega_1 - \omega_2 \\
\frac{d[X3]}{dt} &= \omega_3 - \omega_4 \\
\frac{d[A]}{dt} = -\frac{[B]}{dt} &= \omega_2 - \omega_3,
\end{aligned} \tag{3}$$

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