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Evolvable Biological Interfaces: An Outline of the New Computing System

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Abstract: In this paper, we represent architecture of a new individual-based model of evolvable biological interfaces. The model is based on three parts: mutable coding sequence, individual agents produced by the coding sequence and external environment represented by various virtual substances. Agents are able to recognize external substances and to perform transformations on them. However, unlike general computational scheme currently used in evolutionary computation which is based on predefined list of actions, where each action have predefined fitness value defined strictly within current problem, the recognition and corresponding transformation in this model are organized in completely different way. Here we merged input-action-output system into one unified interdependent whole where each element's role is relative to its surrounding, and instead of unambiguous symbols we introduced alphabet where each symbol is characterized by a set of characteristics. As a result, we obtained system which is able to eventually, through evolution, recognize and assimilate unlimited number of new substances and to perform on them non-fixed set of transformations.

Keywords: Biological interface; Evolvability; Individual-based model.

1. INTRODUCTION

In most general terms interface can be defined as a surface that forms a common boundary between two media (objects, phases or systems). We can see that environment is abundant with various interfaces and that any kind of functioning or processing that can be described with input/output schema, by definition deals with interfaces. Such interfaces have been defined as interfaces between the two either abiotic or biotic environments which are in a relative motion exchanging energy through biophysical and chemical processes and fluctuating temporally and spatially regardless of its space and time scale [Mihailovic and Balaž, 2007]. This broad definition allows us to apply a numerous different approaches when dealing with environmental interfaces, depending on problems that are in focus of our attention. For example, great number of particular problems can be solved using formalisms taken from nonlinear dynamics [see: Doelman and Van Harten, 1995] or environmental fluid mechanics [see for example contributions from Gualtieri and Mihailovic, 2008]. However, dealing with biological interfaces, we are entering a peculiar field, which, in order to be fully grasped, demands development of new conceptual and formal tools.

As it is already implied, one of the pillars of establishing and maintaining functionality in living systems is successful formation of operative interface with external environment. It should provide robust and prompt translation of vast diversity of external physical and/or chemical changes into a set of signals that are "understandable" for an organism [Amils et al., 2007; May and McLean, 2007]. Through organism's physiological processes, such signals are then processed resulting in activation of adaptive reactions to observed changes. However, process of creation of understandable signals from raw environmental material is far from simple and unambiguous. There have been several attempts to analyse it, either from the most wider perspective by developing general theory of signs by C.S.Peirce [for

an overview see: Atkin, 2006], or from more particular perspectives, taking human language [de Saussure, 1965] or animal communication [Hoffmeyer, 1997] as focal points. Although they provide us with some very useful concepts and make a solid path for further investigations, they are primarily developed as philosophical considerations and as such have to be further operationalised for our present purpose. Therefore, in this paper we will take most general concepts developed in aforementioned literature:

- each individual is considered as an observer which resides within some environment;
- observation is an act of assimilating a segment of external changes with appropriate set of internal operations in order to produce reaction;

and extend them further with more specific postulates, derived from general patterns of functioning of living systems:

- operational environment is defined from the perspective of that individual so that external changes are functionally existent for individual only if they can be observed;
- by observing, the environment is divided (schematized) into operative segments, spatial and temporal;
- schematisation models are the same endogenous factors that determine internal functioning of the individual;

The whole process, described in these five postulates will be called "operative assimilation".

Since all organisms are result of slow and long process of evolution, their interfaces (realized through operative assimilation) are well suited to recognize environmental changes, which can occur in their niches. However, environment is not a fixed system with fully predictable outcomes, especially on a long-term scale. Accordingly, interfaces, as well as complete organization of living systems, is organized in such a way to eventually enable later incorporation of external changes not existent or not accessible at a current moment. Such property is called evolvability. More precisely, it has been defined as the capacity to generate heritable, selectable phenotypic variation [Kirschner and Gerhart, 1998]. Since that definition is formulated having real living organisms in mind, it presuppose a great number of conditions which, in the field of modelling, should be one by one explicitly stated and generated. However, full analysis will lead us to far more famous question of how living systems are organized and how their organization can be grasped by formal language, which is out of scope of this paper. Therefore, we will concentrate only on a subset of posed problem, i.e. what kind of computational architecture can be able to eventually incorporate occurrence of arbitrary complex objects in time t_{n+1}, which are not existent or not accessible at time t_n, behaving in accordance with outlined approach termed as operative assimilation. In achieving this goal, we employed individual-based modelling strategy.

Individual-based modeling is somewhat imprecise umbrella term for a loosely connected group of computational models that relies on population-based techniques. Foundations for them lies in machine learning technique called Learning Classifier Systems [Holland, 1992], which is a rule-based system where rules are in form of IF/THEN conditions. Such systems are composed of (i) input interface, which receive allowable information from the environment, (ii) base of rules consisting of N condition-action rules (called classifiers), (iii) internal mechanism for evolution usually based on application of Genetic Algorithm and Reinforcement learning techniques, and (iv) of output interface which define corresponding action of an individual, after receiving input information. Like in natural systems, not all external changes are observable by an individual, but only those for which it have appropriate receptors. These receptors are able to recognize strings composed from defined ternary alphabet $T = \{0,1,\#\}$, where # is a wildcard, which can take a role of either 0 or 1. After recognizing external information, list of classifiers is scanned and all rules that match the external information are selected to form the current "match set". Each rule has assigned fitness value to indicate its usefulness in receiving external reward. From the formed match set, appropriate rule is selected, according to its highest fitness value, and transferred to the output interface to become the individual's external action. Such

architecture is very general and applicable to a variety of disciplines like artificial intelligence, ecological modeling, robotics, adaptive control [Bull, 2004].

In this paper we represent architecture of a new individual-based model of evolvable biological interfaces based on the notion of operative assimilation, which is evolutionary able for autonomous recognition of potentially unlimited number of new substances and changeability of performed transformations on them. The model has been written using Python language, Firebird database and kinterbasdb API.

2. DESCRIPTION OF THE MODEL

2.1 Introduction

It is clear that, in order to obtain non-trivial, real-life reflecting evolvability of the formal system, it should be placed in environment with which it have some kind of functional interaction, defined in this paper through process of "operative assimilation". Otherwise, system can produce variations, and they can be selected according to some rule(s) but within a framework of modeling ecological process of evolution, it is a dead-end procedure which can be useful for solving some specific problem, but will lack general flexibility. Another necessary condition is existence of common pattern of creating building blocks of both: elements of the system itself and elements of external environment. Here, external environment is composed of other systems, as well as of extra-systemic influences. It should be emphasized that, no matter how variable are extra-systemic influences, they all share a common property of being a milieu in which particular building blocks of systems are created. In other words, all of them greatly affect formation of outcomes of systemic processes and, even more important, these processes evolved to have particular organization and dynamics exactly because existence of typical set of external influences. It means that there cannot exist rule that is valid for external environment, and non-valid for the system itself (valid does not means the same).

2.2. Mathematical background

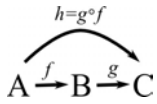
Stated more precisely, and following Mesarovic's mathematical Theory of General Systems [Mesarovic, 1972], if we observe interactions of agents with surrounding environment, such system can be defined as a set of interacting objects $S \subseteq O_1 \times O_2 \times O_3 \times ... \times O_n$. If we denote population of agents under consideration by $P = \{p_1, p_2, p_3, ..., p_n\}$ and a set of external influences by $E = \{e_1, e_2, e_3, ..., e_n\}$ (to recall: these influences can be either other agents, or extra-systemic influences), then state of such formed system at any particular moment in time can be defined as a Cartesian product $S \subseteq P \times E$. Since our system is not a static graph, but a dynamical network of interactions where at each moment hierarchical status of network elements can be significantly changed, we have to define state of the population P as a mapping $\omega : e \to p | e \in E, p \in P$, where both e and p are defined as temporal sequences of events, such that $E = \{e : T \to I\}$ and $P = \{p : T \to R\}$, where T is a set of time points t, I is a set of external stimuli on a particular agent such that at each time point system receive stimulus $i(t)$ and R is a set of appropriate responses, $r(t)$. Further, both P and E are formal systems that stands for themselves. Therefore, occurrence of p and occurrence of e at some particular time point t are governed not only by mapping ω but also by internal rules of these systems, which are partially (see further text) independent. Structure of these systems applied here in creating computing architecture will be explained later.

From above stated, it is obvious that changes in environment induce appropriate responses in agents through the model of coupled input/output pairs. In real systems, reverse situation is also possible, such that some external changes can be influenced by the activity of organisms but for the sake of simplicity, and since it is not directly connected with the main topic of this paper, here we will not consider that problem. It is clear that critical point in

building an evolvable model as described above, is in choosing appropriate structure of the mapping $I \to R$. When dealing with usual models developed as a prediction tools, it is enough to take an attitude of analyzing a "black box". In that case we can propose a function which should sum up available experimental data, and obtain a set of more or less accurate predictions for various initial conditions. However, in that case we will neglect a real meaning of the nature of mappings within E and P. Taking a slightly closer look at these relations, and having in mind a notion of "operative assimilations", we can see that somewhat hidden problem is how I is generated from the wholeness of external changes, and what is a connection between generating I, with constitution of corresponding R. Although this connection can be efficiently represented using a segment of applied lattice theory called Formal Concept Analysis [Crvenkovic et al., 2007], its evolvability demands more advanced formal treatment in order to be fully comprehended.

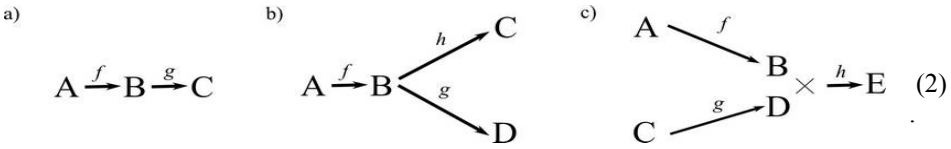
Firstly, we should more strictly define what could be considered as external environment. Let us define set $A = \{a_1, a_2, a_3, ..., a_n\}$ as a set of all external changes. In order to functionally treat them, agent needs to associate each observable external change with some attribute. Hence, we define set of attributes $M = \{m_1, m_2, m_3 ... m_n\}$. From the Formal Concept Analysis [Wille, 1982] we could apply the rule which states that objects and attributes are mutually defined, so we automatically obtain set of external influences $E \subseteq A : \{\forall g \in E \,|\, (g,m) \in \mathrm{O}\}$, where O is a binary relation between M and E. In other words, every object (attribute) which does not form a binary relation with corresponding attribute (object), simply does not exist from the perspective of particular agent. In that way, the concept of "whole" environment changes its epistemological status and is reduced to an observable environment, i.e. to a set of treatable objects. Also, since E is a derivate of p, mapping $I \to R$ can now be realized only as an indirect derivate of each p.

Secondly, if we put additional attention on mapping ω, we can see that from the perspective of both formal systems E and P, it is unentailed. It does not belong to neither formalism, and accordingly cannot be derived from anything within these formalisms. We have in hand two possible solutions to that problems. On the one side, we can leave it as it is. In that case, appropriate function for the focal problem can be applied and the model will be valid until field conditions change out of defined boundaries. If that happens, we have to create a new formal system by choosing another function or/and by modifying organization of the whole system. However, on the other side, we can incorporate ω into another formalization that deals with comparison of formalisms [Rosen, 1991]. This discipline is called category theory and is developed by McLane [1971]. Within such formalism, if domain of one mapping intersects the range of another, they can be composed into:



(1)

where by capital letters are denoted objects within formal systems, while by small letters are denoted corresponding mappings between objects. For aforementioned case of two systems E and P, following cases are valid:



(2)

Accordingly, if we properly transfer them into domain of the category theory, situations denoted by b and c in (2) can be collapsed into $\varphi : A \to C \times D$, where $\varphi(a) = \big(f \circ g(a), f \circ h(a)\big)$, and $\psi : A \times C \to E$, where $\psi(a,c) = \big(h(f \times g)(a,c)\big)$

respectively [Rosen, 1991]. In other words, regardless of complicity of interacting pathways, they can be reduced into corresponding simpler mappings. In a similar manner, we can perform mappings from one category to another that preserves the categorical structure (being an object, being a morphism, the composition, and the identities). Such mapping is performed by functors. Therefore, if we have categories ✌ and ✍, then the functor F from ✌ to ✍ is a mapping that sends objects from ✌ to objects of ✍, and mappings from ✌ to mappings of ✍ preserving identities and composition. Going back to the context of evolvable biological interfaces, it means that within proposed formal framework we finally came to the stated precondition in order to construct open evolvability; namely: there cannot exist rule that is valid for external environment, and non-valid for the system itself. In other words, structure of mapping ω is construed so that no matter how I is changed as a result of dynamics within the E, there can be constructed response R given only a set of rules within the P.

Since further development of rigorous mathematical treatment of stated problem, and more generally, development of mathematical theory of evolvable biological systems is out of scope of this paper, here we are leaving strict mathematical derivations, and continue with presenting a new computing system, based on outlined approach, and using individual-based modeling strategy, which should demonstrate practical possibilities of outlined conceptualization.

2.3 Structure of individuals

Following above described strategy, we introduce two major differences to usual Learning Classifier System (LCS) architecture. Firstly, instead separating input, action-rules, output parts of an individual, we merged them into one unified interface which structure is organized so that recognition of external signal automatically means performing an action defined by the structure of the individual itself. In that way, mimicking most elementary level of functioning of living systems (molecular level of proteins), we fully applied notion of operative assimilation. By taking this strategy, we didn't imply pre-existence of any developed regulatory or operative mechanisms, as it is a case in LCS architecture. Also, in our model it is not possible to arbitrarily include, change or exclude operative rules, without any consequences for (and any inherent connection with) input/output interfaces. Instead, our model is organized so that in order to be functional on a higher level (not only on a level of local actions) it should self-organize after a period of adaptive evolution. It could look like a disadvantage, but again, such opinion is a matter of perspective and chosen framework of consideration.

Secondly, in order to incorporate such strategy, instead of unambiguous symbols in above-mentioned ternary alphabet including one wildcard, we introduced alphabet where each symbol is characterized by a set of characteristics.

As it is already mentioned, this model is based on reflecting level of proteins and pattern of their structure and mode of functioning. Since each protein is characterized by primary, secondary and tertiary structure, we also introduced a gap between primary structure of an agent and its final, operative structure. Primary structure is determined as a string composed of elements from the basic alphabet Ω (Table 1). We construed Ω following empirical data of properties of proteins' basic building blocks. These data can be further abstracted, but we left them in original form in order to make simulation results more obvious for possible applications in a domain of environmental modeling. Each element of alphabet is represented as ordered tuple characterized by its identification (ID) symbol and six properties:

$$\Lambda = (\lambda[+,-,/], \lambda[+,-,/], \aleph[0,1,2,3], \aleph[0,1,...,5], \aleph[0,1,...,14], \lambda[Am, Ca, Al, Ke, Th, /]) \qquad (3)$$

where Λ denotes any ID symbol, $\aleph$ denotes any real number in a given range indicated by square brackets, while λ denotes any symbol from the corresponding sub-alphabet indicated within square brackets. Properties of all elements of Ω are stored in a database. During all processes, desired property of Λ has been called by indicating appropriate place in the tuple, such that $\Lambda[0]$ indicate first place $\Lambda[1]$ second, and so on.

Table 1. Composition of the basic alphabet Ω. One letter ID symbols, charge, polarity, influence radius and existence of functional group are taken in accordance to Whitford [2005] so that for indicating charge and polarity we preserve original nomenclature, while for influence radius we applied Van der Waal index and normalized it for a real number scale in a range [0-3]. For functional groups we take first two letters of their names. Hydrophobicity index and pKa values are taken from Copeland [2000]. Hydrophobicity index is normalized for interval [0-5], while for pKa we preserved original values, rounded to nearest real number.

ID	Charge	Polarity	Hydrophobicity index	Influence radius	pKa	Functional group
R	+	/	**0**	**3**	**12**	***Am***
H	+	/	**0**	**2**	**6**	***Am***
K	+	/	**0**	**3**	**11**	***Am***
D	-	/	**0**	**2**	**4**	***Ca***
E	-	/	**0**	**2**	**4**	***Ca***
S	/	**δ-**	**0**	**2**	/	***Al***
T	/	**δ-**	**0**	**2**	/	***Al***
N	/	**δ+**	**0**	**2**	/	***Ke***
Q	/	**δ+**	**0**	**2**	/	***Ke***
Y	/	**δ-**	**0**	**3**	**10**	***Al***
G	/	/	**0**	**1**	/	/
C	/	/	**3**	**2**	**8**	***Th***
P	/	/	**0**	**2**	/	/
A	/	/	**2**	**1**	/	/
I	/	/	**5**	**3**	/	/
L	/	/	**4**	**3**	/	/
M	/	/	**2**	**3**	/	/
F	/	/	**3**	**3**	/	/
W	/	/	**0**	**3**	/	/
V	/	/	**4**	**2**	/	/

Initially, each individual is obtained as a randomly generated string Ψ, with variable length between 10-20 ID symbols from Ω. Such primary structure is then evaluated by decentralized rule-based algorithm with nested levels of evaluation, in order to determine its functional, secondary structure. Outline is given by following pseudocode:

FOR Λ IN Ψ :

IF $\Lambda_n[x] == \Lambda_{n+1}[x]$ THEN $(\Lambda_n = \Lambda_n^{t_x}) \wedge (\Lambda_{n+1} = \Lambda_{n+1}^{t_x})$

FOR Λ^{t_x} IN Ψ :

IF $(\Lambda_{n+1}^{t_x} == \Lambda) \wedge (\Lambda_{n+2}^{t_x} == \Lambda^{t_x})$ THEN $(\Lambda^{t_x} == \Lambda_x^{t_x^2}) \wedge (\Lambda == \Lambda_x^{t_x^2})$

FOR $\Lambda^{t_x^2}$:

IF $x == 2 \wedge (\Lambda^{t_x^2}[0] \vee \Lambda^{t_x^2}[1] == \neg/)$ THEN $\Lambda^{t_x^2} = \Lambda^{t_x^3}$

Here, n denotes sequence number of Λ in Ψ, x denotes place in the tuple for Λ in a range [0-2], t_x is a first-level grouping tag, t_x^2 and t_x^3 are second- and third-level grouping tags, respectively. As it can be seen, here we applied stepwise top-down approach in evaluating primary structure. First step is formation of "groups" in accordance to selected properties of Λ. For a given property, group is formed if two or more Λ with that property are in a sequence. In a second step, "groups" are evaluated and if they are separated only by

a single Λ, they are grouped together into the second-level groups. Finally, third-level of groups are formed if some "charge/polar" Λ occurred within "hydrophobic" group. All remaining second-level groups where number of $\Lambda \geq 3$ are marked as "active places".

After establishing secondary structure for an individual, it obtains a new ID tag Θ and its new properties are stored into a database. Finally, it has been released in artificial environment characterized by following structure:

$$\Theta = (\aleph[0-x], \aleph[0-y], \aleph[0-z], \aleph[0-5], \aleph[0,1]) \quad (4)$$

where $\aleph$ denotes any real number in a given range indicated by square brackets. First three places in the tuple indicate spatial dimensions, and *x,y,z* are determined by the size of the environment, fourth place indicate scale of instability (see section 2.3.1), while current state (active/inactive) is determined by the last place in the tuple. At each time step, one of three spatial dimensions have been randomly changed by 1, while active/inactive fluctuations are performed in accordance to the level instability indicated by $\Theta[3]$. If value is 5, probability of being active is up to 1/10, while for the value of 0 in the scale, probability of being active is defined in the range above 9/10 of total time spent in the environment.

2.3.1 Stability of individuals

Since in empirical world, proteins can become unstable if their primary structure is altered, resulting in partial or full loss of functionality, we introduced that property by making third level groups. During simulation running, total number of third-level groups for a given Θ has been calculated and normalized for a real number "instability" scale in a range [0-5]. Larger the value in the scale, Θ will spend more time as inactive. In that way, on a long run and in competitive environment, some regions of primary structure will become conserved, thus alleviating preserving of evolutionary achieved level of functionality.

2.3.2 Operative assimilation performed by individuals

All steps considered under the term operative assimilation, are defined to be performable only by an individual's active place(s). Within active place each Λ is characterized by "index of substrate affinity" which is determined in accordance to $\Lambda[3]$ property. Two Λ in boundary regions (up to three places from start/end of active place) with greatest affinity values have been marked as potential sites for binding. When encountering virtual substance, its structure (see section 2.4) is compared with properties of binding sites ($\Lambda[0,1,2]$) and if achieved complementarity, appropriate operation on that substance is launched. Such operation is not defined as a separate list of available actions, but is determined by the composition of a region between active sites. For each Λ in that region values for $\Lambda[4]$ and $\Lambda[5]$ are compared with structurally corresponding indexes in the substance and if complementary matching is achieved, properties of substance's elements are evaluated calling rules from separate database (see section 2.4).

2.3.3 Evolution of individuals

For presented simulation we introduced only single point mutations, deletions and insertions. More advanced possibilities for changing primary structures, like crossing-over are not included for the sake of simplicity, but overall architecture is such that they can be easily incorporated. Given relatively short strings Ψ, and in order to alleviate evolutionary process, we set mutation frequency at $1/10\,\Lambda$/generation. At each generation time, Ψ have been duplicated so that type of mutation is randomly chosen and in accordance to defined frequency an element of Ω have been replaced, inserted to or deleted from Ψ. It should be strongly emphasized that in a given architecture, single point mutation can have no consequences at all or can lead to complete loss/change of functionality of an individual, depending on a relative position in the primary structure. This is a completely new property in the domain of individual-based models.

2.4 Artificial environment

Each virtual substance is described in accordance to real chemical species and similarly as Λ, they possess various characteristics: charge, polarity, hydrophobicity, pKa and functional groups. Same as with constructing individuals their structure is determined as a string composed of elements from the basic alphabet $\mathrm{H} = \{H, C, N, O, Na, Mg, P, S, Cl, Ca, K\}$. As it is obvious, for elements of H we utilized most common chemical elements observable in living systems. Each element here have its set of properties (charge, number of bonds which it can make and electronegativity) which are stored in separate database. Based on that we also construed small generator (not described here) of substances which have been introduced into the virtual environment, based on given atomic properties. Resulting substance is characterized by:

$$\Phi = (\lambda[+,-], \aleph[0-5], \aleph[1-4], \lambda[Am, Ca, /]) \tag{5}$$

where Φ denotes assigned ID symbol, $\aleph$ denotes any real number in a given range indicated by square brackets, while λ denotes any symbol from the corresponding sub-alphabet indicated within square brackets. Substances do not have secondary structure, but they can be decomposed or merged together under appropriate conditions. For presented simulated model, on the side of virtual substances we introduced only two functional groups, but overall architecture is organized so that arbitrary number of functional groups can be included, each with its own reaction patterns, as long as they satisfy condition for mapping ω. Of course it will demand more computational power but having in mind that in nature exists only around 10 life-significant chemical functional groups, great complexity can be achieved even utilizing relatively small number of functional groups. What is major difference from elements of Ω is the lack of individual properties when composed in unaltered substance. If some operation by individual have been performed on them (decomposition, transfer of functional groups…) only then individual properties will be visible on Φ by changing corresponding values in the tuple.

Common space for individuals and substances is composed as a 3D grid denoted by U, containing a number of grid units $u_{x,y,z} \in U$ where x, y, z are space coordinates. Each individual Θ and each substance Φ can occupy only one grid unit at some particular time point. Their movement is defined by random-walk algorithm. If encounter each other, and if individual is in active state, recognition/action process is started following procedure described in 2.3.2.

3. SIMULATION RESULTS

In order to demonstrate general pattern of behavior of the model, we run two kind of simulation. First, in a common space with dimensions 100x100x100 we injected 20 randomly generated individuals and 10 different, randomly generated substances, each in 5 copies, and run a model for 1000 time steps. Results can be seen in the Table 2.

Table 2. Overall results for 1000 steps run in the common space including 20 individuals and 50 substances.

Number of individuals	Number of substances	Number of individual-substance encounters	Number of tried assimilations	Number of successful operative assimilations
20	50	3842	136	0

As it can be seen, very small number of individuals have been in active state during encounters (indicated by the number of tried assimilations) which reveal their very unstable secondary structure. As it was expected, none of external substances was recognized. After that, we take these 20 individuals and run them through evolutionary process for 100 generations. After each generation, we repeated first experiment. Results for five of these individuals, regarding number of successful operative assimilations can be seen in Figure 1.

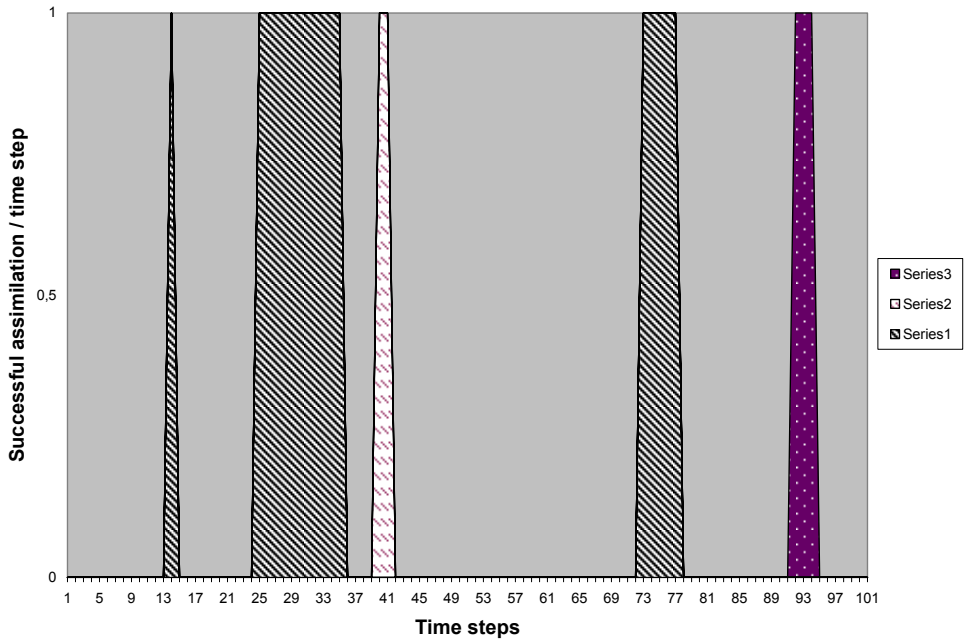


Figure 1. Number of successful operative assimilations of three chosen individuals during 100 time steps

In showed case three of 20 individuals, during evolutionary process successfully assimilate some of external substances. Since competitions are not included at this stage, there were no favouritism of successful individuals, and hence, due to further mutations, successful assimilations were only observed transiently. Nevertheless, it is a clear example of possibilities of proposed computational architecture.

4. CONCLUSIONS

We have presented a novel approach to modeling of evolvable biological interfaces. It is based on the notion of operative assimilations inspired by mechanisms which living systems use in interaction with their environment. Practical implementation relied on paradigm of learning classifier systems but with two key modifications: merging of input-action-output system into one unified interdependent whole where each element's role is relative to its surrounding, and instead of unambiguous symbols we introduced alphabet where each symbol is characterized by a set of characteristics. As a result, we obtained system which is able to eventually, through evolution, recognize and assimilate unlimited number of new substances and to perform on them non-fixed set of transformations.

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