Evolving cellular automata for diversity generation and pattern recognition: deterministic versus random strategy

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Abstract. Microbiological systems evolve to fulfil their tasks with maximal efficiency. The immune system is a remarkable example, where the distinction between self and non-self is made by means of molecular interaction between self-proteins and antigens, triggering affinity-dependent systemic actions. Specificity of this binding and the infinitude of potential antigenic patterns call for novel mechanisms to generate antibody diversity. Inspired by this problem, we develop a genetic algorithm where agents evolve their strings in the presence of random antigenic strings and reproduce with affinity-dependent rates. We ask what is the best strategy to generate diversity if agents can rearrange their strings a finite number of times. We find that endowing each agent with an inheritable cellular automaton rule for performing rearrangements makes the system more efficient in pattern-matching than if transformations are totally random. In the former implementation, the population evolves to a stationary state where agents with different automata rules coexist.

Keywords: cellular automata, mutational and evolutionary processes (theory), systems biology
1. Introduction

Biologically motivated models serve a twofold purpose: to give insight into the possibilities of real processes and systems [1]–[3] or to inspire the development of new artificial devices, such as neural networks [4, 5] and DNA computers [6, 7], touching upon issues such as the definition of life, computation and self-awareness [8]–[12]. We address the latter and seek inspiration in the problem of diversity generation by the adaptive immune system of vertebrates, where protein receptors expressed by B cells (called antibodies) ‘recognize’ complementary antigenic patterns by means of very specific molecular interactions that initiate an immune response whenever a threshold affinity is reached [13]–[15]. Each B cell expresses its own unique receptor and a human being can make about $10^{12}$ different receptors [14]–[16], an astonishing number if compared to the number of genes in its whole genome (about 50 000) making it impossible to have antibody genes encoded in the DNA. Instead, a relatively small number of disjoint gene segments is inherited and the antibody region relevant for binding is assembled during B cell development by rearrangement of some gene segments [15, 17, 18]. After stimulation by antigen, B cells reproduce and introduce further mutations in the antibody-binding region greatly increasing diversity [14, 19, 20].

One might ask whether these genomic modifications are completely random or if they are guided by some organizing principles [21, 22]. Inspired by this question, we study how one could improve the probability that an immune system with its antibodies can recognize a random antigen. In particular, we encode each molecular pattern relevant to binding by $L$ binary features on Hamming shape space [23] and allow for a finite number of modifications of each string characterizing an antibody. We ask if cellular automata (CA) rules of Wolfram type can outperform the rule of random search when strings are randomly shuffled. We develop a genetic algorithm where agents from a population are faced with an antigen’s string, perform the specific computational task of string matching [24] and reproduce if overlap exceeds an arbitrary threshold $T$. Minimum overlap for reproduction can be achieved by evolving the agent’s string a finite number of times according to its specific grammar rules. Algorithms inspired by human immune system are abundant in the literature and, even if it is not possible to identify one archetypal model [25], they are usually named Artificial Immune Systems [26]. In this context, our approach is built...
on the fundamental difference of evolving not simple bit strings but rules, in the form of Cellular Automata [24].

This study has been clearly motivated by the determinism versus randomness debate with respect to diversity generation in the immune systems. However, our goal is not the definition of a toy model for simulating the biological immune system. In contrast, we focus on answering the general and abstract question whether it is possible to obtain better efficiency in the pattern recognition task using a random or a deterministic computation. This question is strongly connected with the exploration of how collective computation can emerge throughout an evolutionary stochastic process [9, 24, 27]. A better understanding of this approach could generate methods for information processing and engineering of new forms of computing systems.

The paper is organized as follows. In section 2 we study, both analytically and numerically, the case where the only rule is random shuffling. Like Perelson and Oster, [23], we find a step-like behavior for the probability that an antibody will bind a random antigen as a function of the minimum overlap for reproduction. In section 3, we analyze the case where agent rules are those defining elementary cellular automata and find that efficiency in the pattern recognition task is enhanced. Moreover, maximal efficiency is achieved when agents with different automata rules coexist, showing that in this system unsupervised collective computation emerges from evolution.

2. The random model

We develop a genetic algorithm where agents coexist in a population that, at each time step \( t \), faces a recognition challenge originating from a randomly chosen bit-string \( Y \) of size \( L \) (agents’ strings are of same size) that persists for \( P \) time steps before being replaced by another random string. One time step is accounted for when all agents have undergone the following selection rules:

1. death with population-dependent rate \( N(t)/K \) where \( K \) is the carrying capacity of the medium and \( N(t) \) is the number of agents at time \( t \). This process is responsible for limiting the size of the total population.

2. Overlap-dependent replication: after assembling a random string \( X \), the agent determines its affinity with \( Y \) as the Hamming distance \( H(X, Y) \) from antigen \( Y \). Replication occurs if \( H(X, Y) \leq T \) where \( L \) is the size of the string. Step (2) is repeated \( S \) times by each agent and reproduction adds a new agent to the population.

The last step of rule (2) mimics the mechanisms of diversity generation. This model is implemented on a computer in which an initial population of \( P_0 = 10^3 \) agents with strings of size \( L = 32 \) evolves in a medium with carrying capacity \( K = 10^5 \), eventually reaching a steady state. In this state an average population is estimated over \( 10^5 \) time steps (simulation parameters are summarized in table 1).

We repeat this procedure for different values of \( T \) and \( S \) and investigate the effect of binding specificity and sequence recombination on the average repertoire size, \( N_{S,T} \). This quantity can be obtained in the mean-field level from the solution of

\[
N(t + 1) - N(t) = G_S \left[ N(t) - \frac{N(t)^2}{K} \right] - \frac{N(t)^2}{K}
\]  

(1)
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Figure 1. The random model and its analytical description match perfectly and exhibit a sharp transition in the size of the mean population as a particular value of the dissimilarity threshold $T$ is reached. Results for different values of $S$ are presented where circles depict simulations and solid lines represent the mean-field description. Mean populations were averaged over the last 100,000 time steps after a stationary-like state was reached in the simulations (other parameters: $K = 10^5$, $P = 100$).

Table 1. Parameters of the model.

| Parameter | Meaning                        |
|-----------|--------------------------------|
| $K$       | Carrying capacity (controls population size) |
| $T$       | Threshold for Hamming distance   |
| $P$       | Time steps each stimulus remains in the system |
| $S$       | Number of tests                 |
| $M$       | Mutation rate of CA             |

when $N(t + 1) = N(t) = N_{S,T}$. Here, $G_{S,T} = \sum_{j=0}^{S} F_T(1 - F_T)^j$ is the probability that matching with antigen has occurred in at most $S$ attempts and $F_T = 2^{-32} \sum_{i=0}^{T} \binom{32}{i}$ is the probability of occurrence of two random strings with Hamming distance less or equal to $T$.

For $T \leq 10$, $G_0 \approx 1$ and so the population at equilibrium is equal to $K/2$. For higher $T$ values the population decreases until it becomes extinct. Increasing the $S$ values leads to a higher reproduction rate (larger $G_S$ values) which maintains the equilibrium population nearer to the classical equilibrium solution of $K/2$. In figure 1 we can see how well the mean-field description captures the results generated by the simulations. The important global quantity which we need to quantify is the success in the recognition task, obtained by evaluating the efficiency of the system. One simple measure of efficiency can be the ratio between the total number of successful recognitions ($H \leq T$) and the total number of tests performed.

Figure 2 depicts efficiency in the recognition task as a function of the threshold $T$ when a stationary regime is reached. For the random model, efficiency is equal to the

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Figure 2. The CA model outperforms the random model both in terms of population size and efficiency. Top: efficiency as a function of the threshold $T$. The squares represent the data obtained by the model of random somatic mutations. The solid line shows the perfect match with the function $F_{T-32}$. The circles represent the data obtained by the CA model for structured somatic mutations with $S = 1$, $M = 0.01$. As can be appreciated, cellular automata can be more efficient in bringing antibodies closer to antigens ($K = 10^5$, $P = 1000$). Bottom: mean population versus dissimilarity threshold $T$ for different $S$ ($P = 100$). For comparison, the solid line represents results for the random model when $S = 1$. Inset: mean population versus $T$ for different values of $P$ ($S = 10$). Averages were taken over the last 100,000 time steps after a stationary state was reached and divided by the carrying capacity $K$ (other parameters: $M = 0.01$, $K = 10^5$).

The probability of two 32-bit strings to have a Hamming distance less or equal to $32 - T$: $F_{32-T}$. The efficiency of the model does not depend on the other parameters $S$ and $P$. As expected, the requirement of larger overlaps between stimulus and agents leads to a sudden decrease of the efficiency.

Our dynamics can be illustrated with an abstract description. Given a metric space $\mathcal{V}$, a stimulus is represented by a feature vector $\vec{x} = (x_0, \ldots, x_N)$ and an agent is represented
by a vector $\vec{y} = (y_0, \ldots, y_N)$. The distance $|\vec{x} - \vec{y}|$ decides whether a test is successful and the agent reproduces. Working with binary features, as in our case, the distance between stimulus $\vec{x}$ and detector $\vec{y}$ can be given by the Hamming distance $H$ (the number of distinct binary features). The agent carries out random jumps of $\vec{x}$ which might move it closer to $\vec{y}$. From the analysis developed by Perelson and Oster [23], in the continuum limit, a step-like behavior is found for the probability of binding a random antigen (stimulus). These results are analogous to the ones we have presented for our model and, effectively, our simulations, for $S = 0$, correspond to a discrete version of the model studied in [23].

3. The CA model

In the following we introduce the CA model which is motivated by the analogy between antibody generation and grammatical structures. Each agent is now characterized by one rule to deterministically change its bit-string. This rule is taken from one of the possible 256 elementary Wolfram cellular automata [28]. These automata are composed of a one-dimensional array of two-state cells and by rules operating on the nearest neighbors.

The model is based on the following steps:

(1) each agent dies with a rate $N(t)/K$ where $K$ is a carrying capacity.

(2) Surviving agents get a random bit-string. They reproduce if a positive presentation is reached within $S$ tests. After each unsuccessful test ($H > T$), the agent’s CA rule is applied on the bit-string and the mutated string is compared again with the stimulus. Successful detection generates one new agent with the same CA as the ancestor or, with probability $M$, a different random CA rule. The stimulus bit-string is randomly generated every $P$ time steps.

In figure 2, we show the mean population as a function of the threshold $T$ for different values of $S$. For all $S$ values, we notice that the mean population is larger than it is for the random model for $T$ values where strong selective processes are forcing adaptation of the CA system. In the inset, we present the mean population as a function of the threshold $T$ for different values of $P$. It is possible to see how for higher $P$ values the population grows, indicating that it reaches an adapted phase with a structure in the CA rule distribution, which allows more efficient recognition of stimuli.

The performance improvement of the CA model can be quantified by examining the efficiency measure. As shown in figure 2, CA rules perform better than random changes. These results can be clarified by looking at the time evolution of the efficiency for a given simulation (figure 3). The efficiency of the CA model is higher than in the random model if the same stimulus is presented for a sufficiently long time. In fact, if $P = 1$, the CA model exhibits the same mean efficiency but higher fluctuations than the random model. The system is not capable of adapting to the new stimulus within one iteration. In contrast, a selective dynamics operates for $P = 1000$. After a change of the stimulus, the efficiency drops down, followed by a rapid transient where the efficiency grows towards a new plateau higher than the corresponding value for the random model. This is because the most efficient CA rules are selected and thus an initially random agent can be successfully mutated closer to the stimulus. Specific CA rules map specific sub-spaces which contain strings close to the stimulus. These rules are able to take different random strings and to take them closer to the antigen following deterministic paths.
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Figure 3. Fast adaption of the system in the CA model leads to better performance. The data show the temporal behavior of efficiency. For large enough $P$, the CA model outperforms the random model. The green curve is obtained for $P = 1000$, the red for $P = 1$, and the black one is the result generated by the random model. parameters: $T = 20$, $M = 0.01$, $K = 10^5$, $S = 10$.

Figure 4. The CA model outperforms the random model for small $S$-values. The figure shows the difference between the efficiency of the CA model and the random model as a function of the threshold $T$ for different values of $S$. Each point is the time average over the last 500 000 steps (parameters: $K = 10^5$, $M = 0.01$, $P = 100$).

In figure 4, we analyzed the efficiency in the recognition task for different values of $S$. We can see an improvement of more than 40% ($S = 1$, $T = 18$). For high $S$ values, this advantage reduces and for $S > 20$ the random model begins to outperform the CA model. In general, efficiency increases for higher $P$ values, when the selection can effectively operate in defining the ensemble of the best CA rules.

Furthermore, we studied the distribution of the population in terms of the CA rules. Figure 5 depicts the Zipf plot of the rules. If reproduction success is not affected by the recognition operation ($T \leq 10$), all possible CA rules are maintained in the population.
thereby generating a flat distribution with equal probability for each rule. In contrast, for higher selection pressures, some rules are selected over the ensemble of all the CA rules and a structured distribution appears. The rules coexist in the population and they correspond to the ones which allow better performance in the recognition task. For very high $T$ values, only a minimal fraction of the rules survives. This happens in correspondence to a very small population where random drift effects become dominant.

Figure 6 represents the frequency of the CA rules for different values of $P$ and $T$. From these figures it is clear how when selection is operating well (high $P$ and small $S$), a subset of the rules is suppressed and a structured population develops with a larger number of lively and coexisting CA rules switched on. We tried to quantify if this subpopulation of CA rules can be related to some particular class following the heuristic Wolfram’s classification scheme, but unfortunately we were not able to distinguish any specific class of CA rules among the ones that better perform in our simulations. In contrast, an assortment
of CA rules from different classes persists in the population. In table 2 we present some of the most successful rules in a specific simulation where $T = 19$ and $P = 1000$.

The frequencies of the CA rules exhibit a peculiar temporal behavior in simulations where the selection pressure is high (e.g. $T = 27$). Figure 7 shows that the introduction of new stimuli leads to a sudden switching on of single rules that begin to dominate the population. They however remain in the system over several cycles of new stimuli, leading to long-term correlations between different stimuli due to memory effects. This also explains why prevailing CA become selected without following the general trends observed in figure 6 for intermediate $T$ values. Rules are selected depending on the context of their co-efficiency with the other rules already in the system.

As a consequence, the CA model relies on the possibility of disposing of a large number of different rules that might be switched on as soon as their specific properties are required. A reduction to the mostly best performing rules therefore results in a decrease of its performance in recognizing random patterns for high selection pressures (large $T$), or, in other words, for demanding recognition tasks.

Figure 6. Suppression of a subgroup of CA rules for intermediate $T$ values. The frequency of the CA rules ($\log_{10}$-values) is shown as a function of the threshold $T$ (on the ordinate) for different values of $P$ and $S$ (other parameters: $M = 0.01$ and $K = 10^5$).
Figure 7. Fast switching on but slow switching off of new rules when selective pressure is high. The temporal behavior of the log_{10}-frequencies of the CA rules is shown for different $T$ values. For higher $T$, the system relies on a small number of highly abundant CA rules (parameters: $S = 10$, $P = 1000$ and $K = 10^5$).

4. Conclusions

We have presented the study of a collective model for pattern recognition inspired by the basic biomolecular mechanisms that enable an immune system to detect new antigens. We explore how different mechanisms of antibodies diversity generation can improve the performance in antigen recognition. As usual, we represent antigens and antibodies by using bit strings and we test two possible strategies for generating antibodies diversity: to randomly shuffle or to apply deterministic rules to the strings which represent them. In the last case we have been influenced by Jerne’s analogy between some properties of the immunologic system and the concept of generative grammars [16]. We have implemented these ideas by introducing a genetic algorithm which evolves an ensemble of Wolfram’s cellular automata which performs the computational task of string identification. Thanks to the employment of evolutionary simulations based on a genetic algorithm, we find that not one, but a group of rules, performs the recognition task better than dull random shuffling.

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Table 2. Best performing CA, identified by their number, and the corresponding frequency in the population. Data are averaged over the last 500,000 time steps of one simulation ($M = 0.01$, $K = 10^3$, $S = 1$, $T = 19$, $P = 1000$).

| Cellular automaton | Frequency |
|--------------------|-----------|
| 1                  | 0.1935    |
| 256                | 0.1256    |
| 248                | 0.0842    |
| 128                | 0.0839    |
| 192                | 0.0535    |
| 252                | 0.043     |
| 58                 | 0.0272    |
| 51                 | 0.0228    |
| 52                 | 0.0181    |
| 56                 | 0.0169    |
| 20                 | 0.0166    |
| 19                 | 0.0165    |
| 64                 | 0.016     |
| 168                | 0.0156    |
| 49                 | 0.0153    |
| 232                | 0.0146    |
| 244                | 0.0118    |

Our study outlines interesting results which can be useful for general information processing. Because of the biomolecular nature of the biological problem which we have theoretically explored, we speculate that our abstract result could be transposed into practical applications for designing computational devices for pattern recognition implemented by the means of a biomolecular computer.

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