Simulation of Rat Behavior in a Light-Dark Box via Neuroevolution

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Abstract. *The light-dark box is a widely used test for the investigation of animal behavior commonly used to identify and study anxious-like behavioral patterns in rodents. We propose a neuroevolution model for virtual rats in a simulated light-dark box. The virtual rat is controlled by an artificial neural network (ANN) optimized by a genetic algorithm (GA). The fitness function is given by a weighed sum of two terms (punishment and reward). By changing the weight of the punishment term, we are able to simulate the effects of anxiolytic/anxiogenic drugs on rats. We also propose using GAs to optimize the number of the ANN hidden neurons and sensors for the virtual rat. According to the experiments, the best results are obtained by ANNs combining both luminosity and wall sensors.*

1. Introduction

The generalized anxiety disorder is related to the constant abnormal prevalence of feelings connected to anxiety and worry, having a negative impact on the individual's life. Described in the American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders (DSM-V) [Association et al. 2013], this diagnosis is associated with the presence of symptoms such as anticipation of danger, muscle tension, alertness, fatigue, difficulty in concentrating, irritability, and insomnia. Many anxiety disorders also have comorbidities with each other. In 2015, about 3.6% of the world population had some anxiety disorder, with higher prevalence in women (4.6%) than in men (2.6%). In Brazil, this number reached 9.3% of the population with anxiety disorders, making this country the one with the highest rate in the world [Organization 2017].

Given the anatomical and physiological similarities between humans and animals (particularly mammals), biological mechanisms and therapies have been studied in animal models before being applied for humans [Barré-Sinoussi and Montagutelli 2015]. The intention is providing insight and predictions for humans and/or another species than the one studied, or in the same species under different conditions from those under which the research was performed [van der Staay et al. 2009].

In this sense, rodents are often tested in the light-dark box, an apparatus developed in 1980 by Crawley and Goodwin [Crawley and Goodwin 1980]. The apparatus consists of a box with two interconnected compartments: a light one and a dark one. At first, the light-dark box was used for measuring the anxiolytic effects of drugs. The behavior of the rodent in the box is explained by the approach/avoidance conflict model. In this test, the actions of the rodent are explained by the conflict created between the animal's predisposition to explore the environment and its avoidance to the unknown. Rodents have a preference for the dark side, having a repulsion for the light side. It happens because it is harder to be seen in dark side, so the animals feel more protected. However, they still walk occasionally on the bright side for short periods in order to explore the environment.

The use of this apparatus, as well as similar ones, is very frequent in Psychobiology and Pharmacology studies. However, animals are often euthanized after the experiments, as they have their interest in exploring the environment diminished if they are reinserted into the apparatus. In addition, animals are often subjected to drugs or even to invasive procedures to induce neurological disorders. Therefore, in 1959, the Principle of the 3 Rs (replacement, reduction and refinement) in the use of animals in experiments was proposed [Russell and Burch 1959]. Since then, those principles have been incorporated into national and international legislation and regulations on the use of animals in scientific procedures, as well as the policies of organizations that fund or carry out animal research.

Here we propose the use of virtual rats to study the behavior of rodents in the light-dark box. The virtual rats are created by using a neuroevolution [Floreano et al. 2008] approach, consisting a relevant 3R-strategy. The virtual rat for the light-dark box is based on a model originally idealized for another experimental apparatus: the elevated plus-maze (LCE) [Costa et al. 2012, Costa and Tinos 2016]. This approach is different from those presented in other works where real data from rats on the LCE are used to build the behavior models based on ANNs [Salum et al. 2000, Miranda et al. 2009, Shimo et al. 2010] or Markov chains/probability models [Giddings 2002, Tejada et al. 2010]. After the first application to the LCE, the model was adjusted to the arena apparatus [Raineri et al. 2019]. So, with the best of our knowledge, this is the first computational model proposed to study animal behavior the light-dark box.

We compare two neuroevolution approaches. In both, the virtual rats are controlled by artificial neural networks (ANNs) evolved by genetic algorithms (GAs). In the first one, only the weights of the ANNs are evolved, while in the second the network architecture is also optimized. Something similar was done for the LCE [Costa and Tinos 2014], but the analysis performed was different from the one presented here. There, the evolution of the average number of sensors and hidden neurons along the generations of the GA was shown, and it were not presented the specific combinations of sensors and hidden neurons evolved, which are shown in the present paper.

2. Methods

2.1. Virtual light-dark box

The light-dark box is a rectangular apparatus divided in two halves, with 9 positions on each side (Figure 1). The rodent can only switch sides at position 7 (from position 7 in one side to position 7 of the other side).

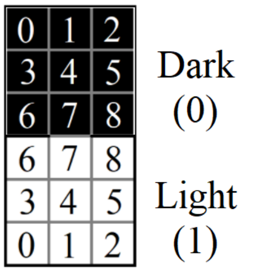

Figure 1. Illustration of the light-dark box used in the simulations. The box has 9 possible positions on both light and dark sides.

2.2. Computational models

We propose two approaches for the virtual rat in the light-dark box.

2.2.1. Model 1:

In the first model, the virtual rat is controlled by an ANN with weights optimized by a GA. The population of the GA is composed of N individuals and the number of generations is G. Each individual of the GA represents an Elman Network [Haykin 1998], i.e., a full-connected ANN with recurrent hidden neurons. The architecture of the ANN in Model 1 is fixed. The chromosome of each individual encodes all the weights of the ANN in a real-valued vector.

The ANN is evaluated by testing the respective virtual rat in the simulated light-dark box. The virtual rat moves in the simulated box and the respective trajectory is recorded. In each step of the simulation, the ANN receives the sensors readings (inputs) and produces an action (output). The inputs of the ANN are given by 6 sensors readings. All sensors readings are binary values. The reading of each one of the 3 luminosity sensors is 1 (light) or dark (0) for the position that is adjacent to the current one on the right (sensor 1), left (sensor 2), or forward (sensor 3). The other 3 sensors are for obstacle detection (1 if there is a wall or 0 otherwise) in the adjacent position, with one sensor on the right side, one on the left, and the last one in the front (see Fig. 2.

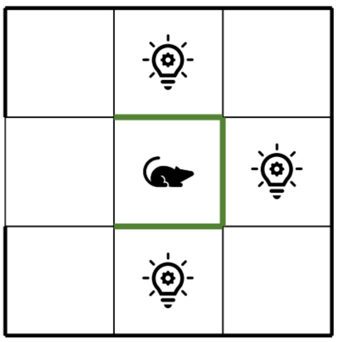

Figure 2. Sensor diagram. The luminosity sensors (lamps in the image) verify whether it is dark or light in front, on the left and on the right of the virtual rat. The obstacle-detection sensors (green bars) check if there are walls in the same directions.

The ANN has 4 neurons in a single hidden layer and 4 output neurons. The output neurons indicates the four possible actions for the virtual rat at every time step, namely: stand still, move forward, rotate 90° to the right without leaving the current position, or rotate 90° to the left keeping the same position. The sigmoid activation function is used in all neurons of the ANN.

In each generation, the virtual rats moves through the virtual apparatus for 300 time steps; experiments with real rats in the light-dark box usually last 5 minutes (i.e., 300 seconds). The fitness function used to evaluate the individuals of the GA are based on the approach/avoidance conflict model [Costa and Tinos 2016]. The fitness for individual $\mathbf{x}$ (vector encoding the weights of the ANN) is:

$$f(\mathbf{x}) = \sum_{t=1}^{300} (r(\mathbf{x}, t) + \beta . s(\mathbf{x}, t)) , \quad (1)$$

where $r(\mathbf{x}, t)$ is the reward and $s(\mathbf{x}, t)$ is the punishment for $\mathbf{x}$ at time step t. The function $r(.)$ adds one point (+1) to the fitness of $\mathbf{x}$ each time the respective virtual rat visits a position that was not recently visited in the last γ time steps (being γ a model parameter). The punishment, $s(.)$, on the other hand, is stochastic: with p_{light} and p_{dark} probabilities, the fitness is reduced by one point (-1) if the virtual rat is on the light side or on he dark side of the box, respectively. These values are model parameters, just like β, which balances the reward/punishment relation.

Elitism is used by the GA, where the 2 best individuals of a population are copied to the next population. The remaining $N - 2$ individuals of the population are selected by tournament selection, in which the best between 2 randomly-chosen individuals is selected with 75% probability; in the other 25% of the cases, the individual with the lowest fitness is selected. These $N - 2$ individuals then are subject, with a 60% probability, to 2-point crossover, and then to Gaussian mutation (with standard deviation $\sigma = 0.05$), with a 5% probability.

2.2.2. Model 2:

In Model 2, the architecture of the ANN is also evolved by the GA. The optimized hyper-parameters are the number of sensors and hidden neurons. In Model 2, the GA individual has two chromosomes: one encoding the ANN weights and another for encoding the ANN architecture. The first chromosome (for encoding the weights) is equal to the chromosome for Model 1. The second chromosome is binary-encoded, where each gene indicates the presence (or not) of an element (sensor or hidden neuron). The ANN can have 1 to 6 inputs (sensors), and 1 to 4 hidden neurons (at least one of each is required). Thus, the second chromosome of each individual has 10 genes. In the second chromosome, bit flip mutation (with 5% mutation rate) is used. All the other hyper-parameters of the ANN and of the GA are equal to those of Model 1.

3. Results

From the simulations we measure: time spent on both sides of the apparatus (light and dark), quantity of movements on each side, and the number of transitions from one side to another. The values presented are for the best virtual rats (according to the fitness) from 30 runs of the GA for each hyper-parameter set. The minimum, average, and maximum fitness of the 30 runs were also calculated. These results are compared for models 1 and 2.

Then we selected a set of hyper-parameters that provided virtual rat behaviors that simulates the expected behavior of real control rats. For this hyper-parameter set, the evolved architectures for Model 2 was analyzed in order to find useful information about sensor combinations and memory required for a good performance in the virtual box[1].

The results were analysed in Python, and the runs of the GA and simulations were performed in C/C++ language.

3.1. Effects of the parameter β and the population size N

In the runs, we have $\gamma = 2$ (the exploration-memory parameter). We then tested different values of β (Eq. 1) and population size N. The β values were ranged from 1 to 8 in increments of 1, and the population sizes were every hundred from 100 to 1000. The punishment probability for the light side was 2.2%, while for the dark side it was 2%. $G = 200$ generations were evolved for each of the 30 runs of the GA.

Fig. 3 shows the variation of the mean time spent for the virtual rats on the light and dark sides of the box as a function of N, for different β values. In all the figures we have results for Model 1 on the left and for Model 2 on the right.

One can observe that, for both static (a) and evolved architectures (b), the mean time spent on the light side gradually increases as the population size increases. On the other hand, in (c) and (d), the time spent on the dark side decreases. This behavior is the same for all β values; however, when increasing β, the virtual rats tend to explore less the light side of the box. Since β is the weight of the punishment (which occurs slightly more on the light side), the higher the β value, the fewer the entries to, time spent, and moves on the light side. It suggests that β can be used to investigate anxiogenic/anxiolytic effects: the more "anxious" the rat, the lesser its exploratory behavior, especially on the light side.

In this way, comparing virtual and real rat behavior [Tarrega 2019, Campos-Cardoso et al. 2021], a low-β value represents a less anxious animal. Different β values can reproduce the effects caused by different types of drugs and drug dosages (as in previous articles studying the LCE [Costa et al. 2012, Costa and Tinos 2016]). This is also evident for the mean of movements on the light and dark sides (not presented here).

In the experiments, because the number of generations is fixed, the population size controls the number of fitness evaluations. The fitness function (Eq. 1) has a term that is stochastic. When the number of evaluations increases, the probability of finding trajectories with smaller number of punishments (that is a random variable) also increases. This explains the results in figures 3, and it also explains the observed for the mean number of entries on both box sides (Fig. 4); although, in this case, the entries increase on both sides as N increases. The behavior on both sides is very similar, since the difference between the entries on one side is always just one unit greater than on the opposite side (that is, every time the rat switches, it leaves one side to the another).

[1] In this context, "good performance" means the expected behavior of real control rats.

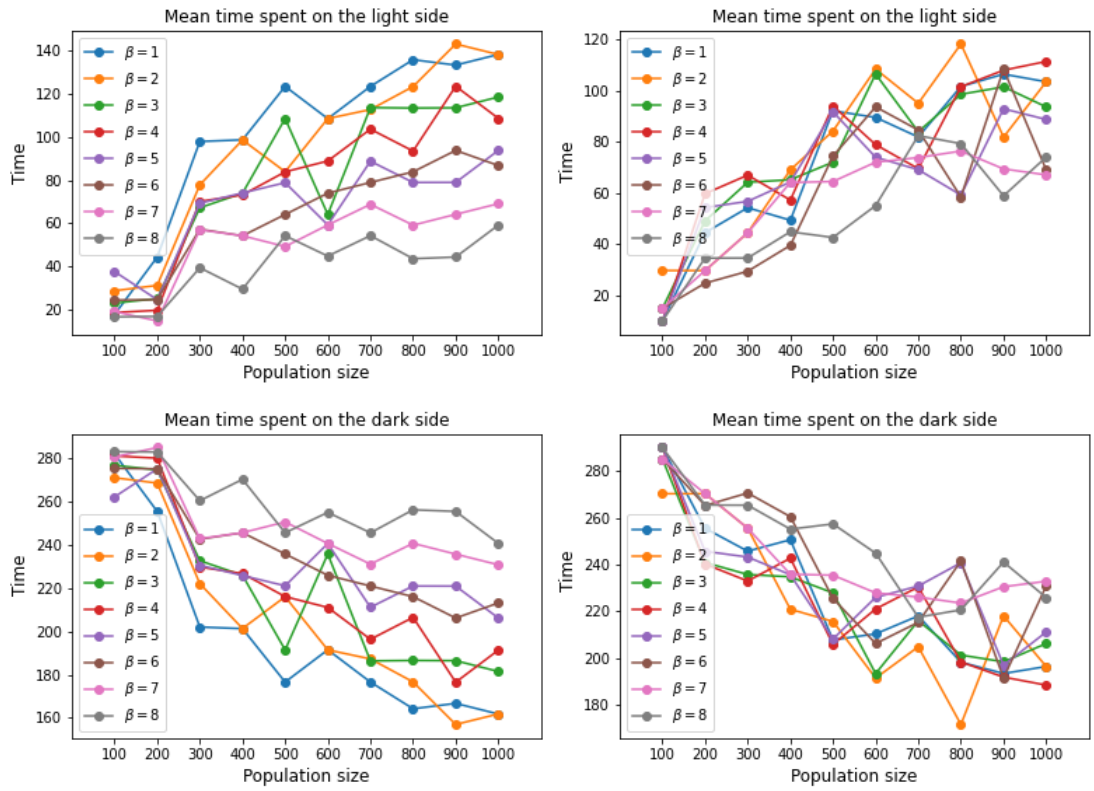

Figure 3. Mean time spent for the virtual rat on each side of the light-dark box as a function of the GA population size (N). Left – (a) and (c) – are results for Model 1, and right – (b) and (d) –, for Model 2. On the top are the comparisons for the light side, whereas on the bottom for the dark one.

In Fig. 5, we have the minimum, mean and maximum fitness found in the 30 runs of the GA. The results are qualitatively similar for both models. The parameter β has considerable influence on the individual's minimum fitness, whereas the population increase does not lead to relevant changes on it. Observing quantitatively, the minimum fitness is lower for Model 1, which suggests the GA evolves better architectures than the predefined static architecture used in Model 1.

As for the mean fitness, the parameter β does not affect it significantly; however, increasing population brings the mean fitness closer to 0.00. In any case, the effects caused by variations on the population size (N) are also small (see the mean fitness range on Fig. 5 for both models).

Similarly to the mean fitness, the variations on the maximum fitness are insignificant in relation to changes on β and N, with the exception of a few cases. These outliers are more prevalent for Model 2. The justification for this is that as the network architecture evolves, so for each of the 30 GA runs we generally have a different best individual (ANN architecture and weights), which causes a greater variability in the results (and therefore on the maximum fitness value) in relation to Model 1, for which the ANN architecture is static (that is, we have the same architecture being used in all GA runs).

These results are interesting because they help to explain biological behaviors without the need of data from real rats for building the models (virtual rats); the results of

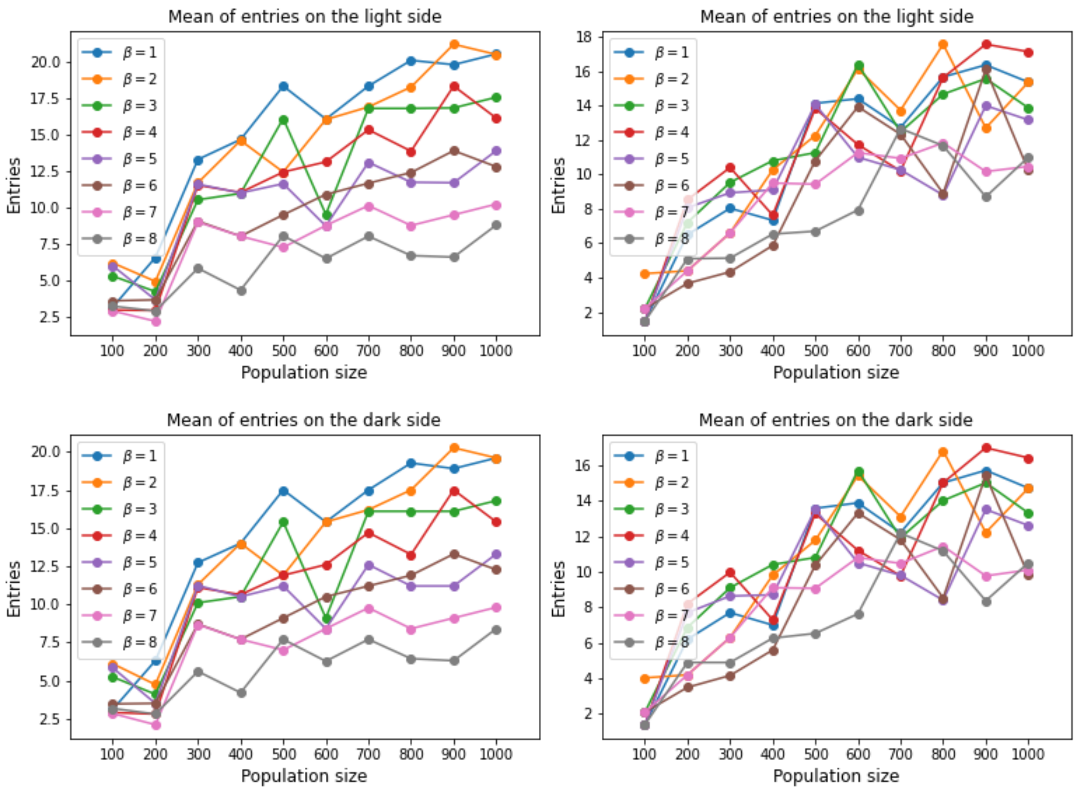

Figure 4. Mean number transitions of one side to another for the virtual rat on the light-dark box as a function of the population size. (a) and (c) are results for Model 1, while(b) and (d) are for Model 2. On the top are the comparisons for the light side and on the bottom for the dark one.)

real rats can be used just for comparison.

3.2. Architectures evolved by the GA for Model 2

To analyze the architectures evolved by the GA, we selected the virtual rats (obtained in the runs of the GA) that presented the behavior expected for average control rats (without drug effects). This virtual rats correspond to the runs of the GA with parameters: $\beta = 5$ and $N = 300$. As explained before, each virtual rat in Model 2 has **a maximum of** 4 neurons in the hidden layer and **a maximum of** 6 sensors.

Table 1 shows the number of sensors used by the 30 virtual rats obtained by each of the 30 runs of the GA. The most incident sensor quantities are 2 and 3 (33.33% each). This incidence was not much higher than that of the 7 virtual agents that used 4 sensors, that is, 23.33% of the total. It shows that an intermediate number of sensors seems to be the most recommendable cost-benefit strategy for the agent (virtual rat) to navigate in the light-dark box. A single sensor is not enough, but 5 or 6 sensors seem to be excessive. Excesses are associated with a high computational cost for chromosome optimization.

Table 2 details the types of sensors used by the virtual rats and the amount of hidden neurons in each of them. We note that 23 of the 30 rats combine at least 1 luminosity sensor with 1 obstacle sensor, which highlights the need to have at least 1 sensor of each type to navigate in the box. The most incident sensor combination was 2 obstacle sensors

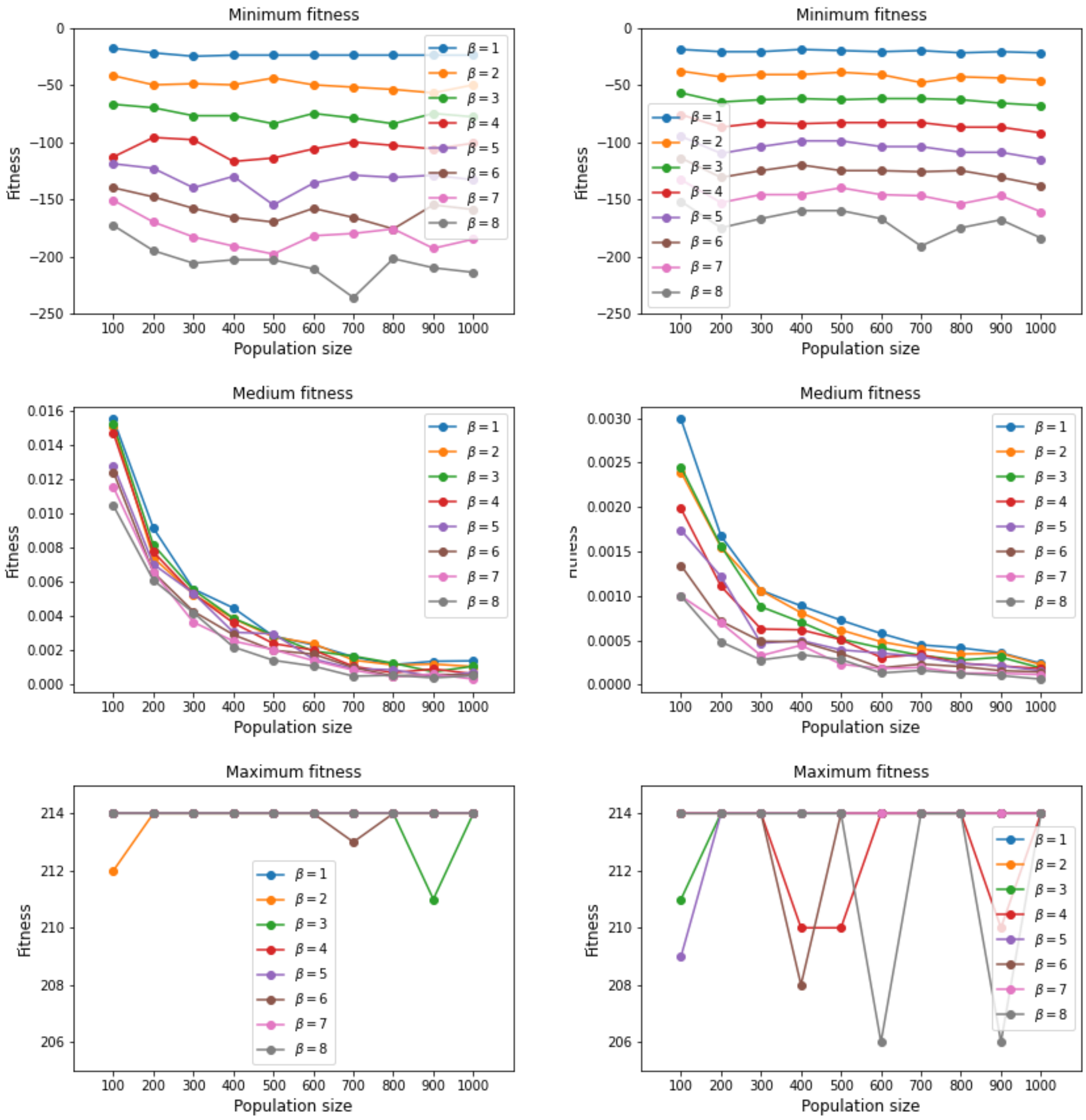

Figure 5. Minimum ((a) and (d)), mean ((b) and (e)) and maximum ((c) and (f)) fitness of virtual rats evolved by 30 executions of the GA for Model 1 (left) and Model 2 (right).

Table 1. Quantity of virtual rats with each possible number of sensors in the input layer (from 1 to 6).

Number of sensors	Quantity (percentage) of virtual rats
1	2 (6.67 %)
2	10 (33.33 %)
3	10 (33.33 %)
4	7 (24.44 %)
5	0 (0%)
6	1 (3.33%)

and 1 luminosity sensor (30% of the virtual rats).

Table 2. Architectures evolved by the GA. In the table, the first letter “W” represents wall (obstacle) sensors, while “L” represents luminosity sensors. The second letters “L”,“R” e “F” indicates the position of the sensors: left, right and front respectively.

Types of sensors	Quantity (percentage) of virtual rats	Sensors
1W e 1L	6 (20%)	LR, WR LR, WR LL, WR LR, WF LF, WR LL, WR
2W	4 (13.33%)	WR, WF WR, WF WR, WF WR, WF
2W e 1L	9 (30%)	LR, WR, WF LF, WR, WF LF, WR, WF LF, WR, WF LF, WR, WF LR, WF, WL LF, WR, WF LR, LL, WF LR, WR, WF
2W e 2L	5 (16.67%)	LR, LR, WR, WF LR, LF, WR, WF LR, LF, WR, WL LR, LR, WR, WL LR, LF, WF, WL
3W e 1L	2 (6.67%)	FL, DW, FW, EW LR, WR, WF, WL
3W e 3L	1 (3.33%)	LR, LF, LL, WR, WF, WL
1L	2 (6.67%)	LR LL
3W	1 (3.33%)	WR, WF, WL

The most prevalent sensor was the “WR”, which indicates the existence of a wall to the right of the virtual rat. This sensor was present in 22 (72.33%) of the 30 rats. The luminosity sensor with the highest incidence was the “LR”, present in 14 (46.67%) of the computational agents. Apparently, side sensors are more useful than frontal ones (also in the LCE [Costa and Tinos 2014]).

Table 3 presents the number of neurons in the ANN hidden layers for the 30 best virtual rats. The number of rats that needed only 1 or 2 hidden neurons were 14 (46.67%)

and 13 (43.33%) respectively, suggesting that the best architectures have 1 to 2 neurons in the hidden layer. These amounts are considerably lower than the 4 hidden neurons on the static network of Model 1, reducing the network complexity and computational costs.

Table 3. Number of hidden neurons and the corresponding amount of virtual rats.

Number of neurons	Quantity (percentage) of virtual rats
1	14 (46.67%)
2	13 (43.33%)
3	3 (10%)
4	0 (0 %)

Comparing these results to the evolved ANNs obtained for the LCE [Costa and Tinos 2014], the light-dark box seems to be a simpler apparatus to navigate on, since it requires less elements in the ANN. The mean number of sensors found for the LCE was 2.4, accompanied by 3 hidden neurons (it is worth mentioning that the mean was calculated over all the rats per generation, not only over the best scored ones). Here, calculating the mean number of hidden neurons of the top 30 virtual rats on the light-dark box, we have only 1.67; however, the mean number of sensors is slightly higher: 2.9.

Many software systems have been developed to accurately track the trajectory of rodents in different experimental apparatus, even aquatic [Krynitsky et al. 2020, Drai and Golani 2001, Nandi et al. 2021]. A recent software was developed for quantifying not only rodent exploration, but also their sensory (whisker) and motor behaviours [Gillespie et al. 2019]. However, the use of sensors, information processing and decision making in animals during the experiments remains largely unknown [Flossmann and Rochefort 2021]. In this way, research involving artificial neural networks can bring inferences about the way the rat navigates the apparatus.

4. Conclusion

Two models were proposed to simulate the behavior of rats in the light-dark box, both based on ANNs optimized by GAs. In the experiments, the virtual rats presented qualitatively similar results to those carried out with real rodents, usually spending more time and moving more on the dark side. The GA fitness function considers the exploration and fear conflict observed in real rats when exposed to the apparatus. Such a function can be used to investigate the behavior of control rats and those under the influence of anxiolytic/anxiogenic drugs through the variation of a parameter (β) that balances the effect of fear (punishment in the function) in relation to the effect of exploration (reward).

From Model 2, it was possible to study the architectures evolved by GA. In the experiments, 2 or 3 sensors were enough for a good performance of the agent in the virtual light-dark box. The apparently best combinations contain 2 wall sensors associated with 1 luminosity sensor. Similarly, just one or two hidden neurons are enough to process information during the test in the virtual apparatus.

In the models studied, the freedom of movement for the virtual rats is limited to: go forward, turn left, turn right or remain stationary. Several increments can be made in the model in the future, for example the inclusion of the ability to move 360^o and have ethological behaviors such as scratching, stretching, etc. In this sense, the model can become more robust, although now, with few adjustments, they can represent the average exploratory behavior (trajectories) of biological rats in different experimental apparatus, as reinforced by previous research.

The probabilistic aspects of the methods and the fitness function can also be explored in future works. A good strategy to deal with the uncertainties can be, for example, explicit averaging fitness [Costa et al. 2013]. However, for quantitative comparisons of virtual and real rats, it will be necessary to obtain data from real rats in the light-dark box.

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