MODELING THE BEHAVIOR OF RATS IN AN ELEVATED PLUS-MAZE

by

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Thesis

submitted in partial fulfillment of

the requirements of the Degree of

Bachelor of Science with Honours in

Mathematics and Statistics.

Acadia University

March 2002

This thesis by Joanna M. Giddings

is accepted in its present form by the

Department of Mathematics and Statistics

as satisfying the thesis requirements for the Degree of

Bachelor of Science with Honours.

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Acknowledgements

Funding from the Natural Sciences and Engineering Research Council of Canada allowed me to devote the summer of 2001 towards my thesis. For this, I am most thankful. During the preparation of this thesis, many individuals have assisted and supported my efforts. The following is a list which includes, but is not limited to, the people whose contributions are greatly appreciated: Dr. Anthony Almudevar, Dr. Tom Archibald, Dr. Paul Cabilio, Latera Carey, Dr. Lisa Kalynchuk, Prof. Vincent Leung, Colin Macdonald, Dr. Franklin Mendivil, Jason Newport, Darlene Preston, Dr. Raymond Spiteri, Dr. Paul Stephenson, and Amanda Wintink. I wish to especially acknowledge the contribution of Dr. Raymond Spiteri, my supervisor, who accepted a position at Dalhousie University during the course of this thesis, but continued to supervise my research to completion. Dr. Spiteri's obvious interest and tireless assistance in offering advice are greatly appreciated. I extend special thanks to Dr. Stephenson, who agreed to be my supervisor at Acadia University, and provided assistance when needed.

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Abstract

The standard elevated plus-maze is commonly used to assess anxiety-like behavior in laboratory rats. This maze, which is elevated 50 centimeters above the floor, consists of two arms enclosed by high walls and two open arms. A mathematical model that could reliably and accurately predict rat behavior in the elevated plus-maze would have many applications in the field of neuroscience. For example, predicting behavior based on a rat's anxiety level would be valuable in assessing new anxiety-reducing drugs.

The first step in building a model to predict behavior on the basis of a rat's anxiety level was to develop a model that predicts the behavior of rats with moderate levels of anxiety. This process resulted in developing 7 probability distributions based on experimental trials that determine a rat's movements. These probability distributions differ depending on the rat's location within the maze and its direction of movement. Together, these distributions serve to determine a rat's next movement in any possible situation in the elevated plus-maze.

Analysis of the model suggests that it has some predictive power when compared to a sample of rats with moderate anxiety levels. Further scoring using more sophisticated equipment could lead to a very powerful model that can be adjusted to predict rat behavior as a function of a rat's anxiety level.

Chapter 1

Introduction

A common objective in many of the sciences is to obtain accurate models of various phenomena. There is a vast collection of phenomena to be modeled, ranging from weather patterns to animal behavior. Because mathematics is the language of science and engineering, it is natural to look for a mathematical description of these models. The objective of this thesis is to develop a mathematical model that predicts the behavior of rats in the elevated plus-maze.

Producing an accurate, reliable mathematical model for various types of animal behavior is very useful to researchers, for practical purposes like drug research, as well as to gain a deeper understanding of the animal behavior being modeled. Research involving animals can provide insight into many aspects of the human experience, including the interaction between physiology and emotion. Within the field of neuroscience, animal research is often undertaken to investigate the effects of physiological changes on anxiety and fear [3]. Animal models of these psychological constructs can involve different types of measurements. Some of these are physiological measurements, while others involve behavioral observation [9]. Laboratory rats are the most common type of animal used in this type of research. Thus, as one might expect, animal research involving anxiety and fear is often conducted by observing the behavior of laboratory rats in mazes.

Over the years, various types of mazes have been used in assessing anxiety in laboratory animals, but perhaps the most widely used maze for this purpose is the elevated plus-maze [9]. Assuming researchers have a firm grasp on the relationship between anxiety levels and behavior in the elevated plus-maze, they can apply that understanding to practical problems. For example, researchers might use the elevated plus-maze as a tool to assess the effect of a new anxiety-reducing drug on behavior. The importance of fully understanding the motivations behind rat behavior on this maze spurs researchers to continue developing their knowledge about the subject. A mathematical model that predicts rat behavior on the elevated plus-maze could provide further insight into its proper use as a tool for measuring anxiety, especially if that model could predict behavior based on a rat's anxiety level.

The following sections give more detailed descriptions of the elevated plus-maze. First, the maze itself is depicted and then the commonly observed behaviors are addressed. Then, some of the possible applications of a mathematical model for rat behavior in the elevated plus-maze are explored.

1.1 The Elevated Plus-Maze

A representation of the standard elevated plus-maze is depicted in Figure 1.1. The elevated plus-maze consists of two open arms and two arms that are enclosed by high walls. The open arms are perpendicular to the closed arms, with the four arms intersecting to form the shape of a plus sign. The elevated plus-maze is usually elevated approximately 50 centimeters above the floor. Security is provided by the closed arms whereas the open arms offer exploratory value. Therefore, one would expect anxious rats to spend less time in the open arms than those that are less fearful [10].

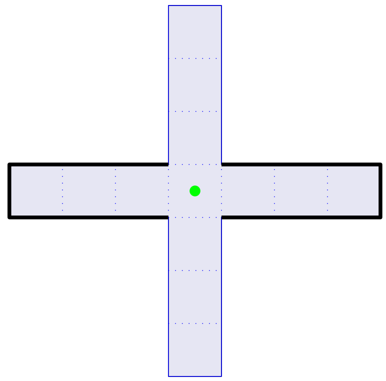


Figure 1.1: Elevated Plus-Maze

1.2 Behavior in the Elevated Plus-Maze

An awareness of the types of behaviors exhibited by rats in the elevated plus-maze is needed before we can discuss the creation and implementation of a model. It is observed that the animals spend a lot of their time staying still or moving from one part of the maze to another. Other common behaviors include rearing up in the closed arms to explore a wall and looking over the edge in the open arms. These activities are similar in that they both involve exploring the sides of the arms rather than the arms themselves. Another common activity is *risk assessment*. The term risk assessment usually refers to specific stretching postures and peering over the sides of open arms [1]. However, we will use this term to refer to a more specific behavior. Sometimes a rat will assess an open arm from a safer place in the maze. It might do this by poking its head out onto that arm while standing at the edge of a closed arm. Rats also engage in this type of risk assessment while standing securely in the center of the maze. Behavioral scientists also tend to refer to looking over the edge in the open arms as risk assessment. However, for the purposes of this model, these will be treated as separate behaviors.

Generally, rats show a strong preference for the closed arms over the open arms. They will spend most of their time in the closed arms and will enter them more often than the open arms [10]. However, this tendency can change depending on factors like the rat's emotional state while it is in the maze [5].

When placed in an elevated plus-maze for the first time, a rat's behavior is largely based on its levels of anxiety and fear. Normal rats that have not received any anti-anxiety drugs will become moderately anxious in this new environment. Thus, they tend to prefer the closed arms over the less secure open arms [10]. Meanwhile, rats treated with anti-anxiety drugs tend to be less fearful, so they spend more time in the open arms compared to normal rats [11], and they are generally less active [4]. On the other hand, anxious rats show more open-arm activity than normal rats (i.e., more entries into the open arms and more time spent in the open arms) and sometimes exhibit extreme behaviors like purposefully jumping to the floor from the open arms [5]. Since rats that jump off the open arms seem to be trying to escape, this is referred to as *escape behavior*.

Because each rat behaves somewhat differently in the elevated plus-maze, it is impossible to accurately predict every individual movement and behavior. Therefore, researchers have isolated several measures that are indicative of a rat's overall behavior while exploring the standard elevated plus-maze. These include the percentage of time spent in the open arms, the percentage of time spent in the closed arms, and the percentage of time spent in the center of the maze. The ratio of open-arm entries to total entries and the ratio of closed-arm entries to total entries are also important indicators of overall behavior. These measures aid in assessing a rat's anxiety level by indicating any preferences for one type of arm over the other when the rat is choosing its next movement from the center of the maze. Other commonly used measurements are the number of closed-arm entries and the total number of entries into any arm. These are thought to give some indication of the amount of locomotion being undertaken by the rat [12].

1.3 Applications of Modeling Behavior in the Elevated Plus-Maze

We have been developing a mathematical model to predict the behaviors displayed by rats in the elevated plus-maze. In particular, our model is designed to predict the behavior of normal rats that have not received any treatments that would affect their anxiety levels. When this model is run, a virtual rat emulates the movements and behaviors exhibited by a real rat during a five-minute trial in the elevated plus-maze.

This type of model could be of great value to researchers in this area, having several applications in future research. For example, if researchers wanted to test a group of normal rats against a group that had received some sort of treatment, they could replace the control group (i.e., the untreated group used for comparison purposes) with a sample of virtual trials that were produced using the model for normal rats. For example, if the experiment was designed to involve an equal number of control subjects and treated subjects, only half as many research animals would be needed. Therefore, this would be a very cost-effective way of conducting research. The assumption behind this application is that the model would be powerful enough to discriminate between different types of rats. A model that produced a range of behavioral measures typical of both groups of rats would be of no use in this situation.

Before researchers could use these models in their laboratories, they would have to ensure that the models did, in fact, accurately predict the behavior of their rats. There are many variables that affect rats' behavior in the elevated plus-maze, including the level of lighting to which they are exposed, the amount of handling they have received, and the sounds and smells that are present during testing [8]. Since there are small variations in the way different researchers treat their animals, a model designed in one laboratory setting might not be appropriate for another. While this issue requires careful consideration, it would not be difficult to adjust the model in order to compensate for the differences in a new testing environment.

The remainder of this thesis is organized as follows. Chapter 2 introduces a previous model designed to predict rat behavior in the elevated plus-maze. A description of the shortcomings of this model leads to Chapter 3, which outlines the development of our model. The next chapter presents statistical analyses of the model, portraying the final stages of its development. Finally, Chapter 5 discusses the successful aspects of this model and their implications, along with a number of improvements that could be made in future work. Before introducing a new model, we first examine a previous computational model for rat behavior in an elevated plus-maze.

Chapter 2

A Previous Model

2.1 Research Basis of the Model

Over the years, many researchers have worked to identify and explain the various behaviors exhibited by rats in the elevated plus-maze. One tendency that has been a subject of much research is rats' preference for the closed arms over the open arms. Recent studies by Treit, Menard, and Royan postulate that *thigmotaxis* (i.e., the tendency of rats to prefer vertical surfaces) is related to this preference [11]. They theorize that the observed preference for the closed arms reflects rats' natural inclination for vertical surfaces.

K. Montgomery, in her 1950's research, investigated the relationship between fear and exploratory behavior in rats. She sought to explain rats' behavioral tendencies in terms of motivation, or drives. One of her major findings was that rats' movements in a maze are related to two primary drives: the fear drive and the exploratory drive. She found that both the fear and exploratory drives are evoked by novel stimuli, creating an approach-avoidance conflict [6]. Exploration through a maze is negatively related to the fear drive. On the other hand, the exploratory drive contributes positively to exploratory behavior. Therefore, the rat experiences a conflict, whereby it is driven to explore while it is also dealing with an aversion to exploration [7]. These findings were used as the theoretical basis for a previous computational model which is described in detail in the following section.

2.2 Implementation

Salum, Morato, and Roque-da-Silva recently published a paper describing a computational model for rat behavior in the elevated plus-maze [10]. Figure 2.1 shows their illustration of the elevated plus-maze.

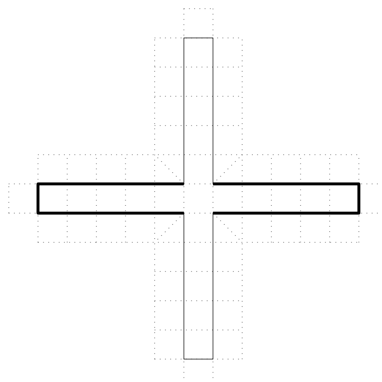


Figure 2.1: Elevated Plus-Maze

The thick solid lines indicate the closed arms and the thin solid lines indicate the open arms. The dotted lines are not physical. They are used in the model to break up the maze into several possible squares that the rat could occupy. The rat never actually occupies the external squares since they are contained outside the maze. These are present so that the model can represent the rat exploring these areas by head-dipping in the open arms and climbing up the walls or rearing in the closed arms. Therefore, if the rat is seen as occupying one of these squares, it is actually exploring it from an adjacent square contained within the maze.

The model consists of a series of time steps. The rat is assumed to be moving at a constant speed of two seconds per movement. In other words, there is an underlying assumption that only one movement can be made during every two-second time step. At the first of each time step, the rat is occupying a particular internal square. If it was exploring an external square during the previous time step, it is placed in the adjacent internal square. This is because the rat was physically occupying the adjacent internal square during this exploration.

From its current position, the rat can stay where it is, move to any connected internal squares, or explore any connected external squares. There are exactly five possible movements from any given square. Curiosity motivates the rat to explore various aspects of the new environment. However, the fear drive is also at work, creating an aversion to exploring the different parts of the maze. If the rat occupies square j, then the model describes its tendency to explore another unit i as:

$$\omega_{ij} = M_{ij} - A_{ij}, \tag{2.1}$$

where M_{ij} is the rat's exploration motivation and A_{ij} is the rat's aversion to exploring i from j. Therefore, we can create a matrix which displays the tendency of the rat to move from any square j to any square i (or remain where it is) in a given time step. Only certain moves are allowed during any given time step, so many of these weights will be multiplied by 0 at the beginning of the time step. Thus, there will only be five nonzero entries in the matrix, corresponding to the five possible movements. Then, the nonzero ω_{ij}'s are compared and the square with the highest weight is activated. As the rat moves to a new square, its fear and exploratory drive relating to that square change. Therefore, the aversion and motivation to explore depend on N_{ij}, which represents the number of times the rat has moved from j to i during the trial. This is reflected in the equations for A_{ij} and M_{ij}, which are described below. Therefore, the weights will continually change from one time step to the next according to Equation 2.1.

According to Montgomery, both the exploratory behavior and the fear drive decay with time spent in the maze [6]. The equation for the motivation to explore square i from square j was postulated as follows:

$$M_{ij} = \frac{M}{(\alpha_i N_{ij} + \mu)^{\beta_i}}. \tag{2.2}$$

M is a constant value assigned for the rats' initial exploratory drive. In creating this model, Salum, Morato, and Roque-da-Silva assumed that the walls offer less exploratory value for the rats. Hence, the tendency to explore decays much more quickly for the external squares representing walls than for the other squares. This was incorporated into the model by giving larger constant values to α_i and β_i for external squares representing walls. Each of these parameters was given one of two values, so they were assigned the smaller values in all other cases. A random variable μ represents the variability between rats. This equation allows the motivation to move from j to i to decay as the number of times the rat executes this movement increases.

The equation for the aversion to movement from j to i was postulated as follows:

$$A_{ij} = C(1 \pm \nu\gamma_i N_{ij}). \tag{2.3}$$

The fear drive motivates the rat to look for safer places in the maze. C is given a constant value that represents the initial fear drive, which is the same for all parts of the maze when the rat enters it. A random variable ν is once again introduced to allow the virtual rats to vary from trial to trial. The model allows for greater aversion to the open arms by using the "+" for open arms and the "$-$" for closed arms. This implies that aversion decays in the closed arms, and this is consistent with Montgomery's finding that the fear drive decays with the time spent in the maze [6]. However, this equation shows an increase in aversion to movement in the open arms as the rat has had more exposure to them. This appears to contradict Montgomery's work. The writers' justification for this increase in aversion is thigmotaxis [10]. You may recall that this is the tendency of rats to prefer to be near a vertical wall. Therefore, as rats become more familiar with the open arms, they will have a higher motivation to avoid them since there are no walls. Although it is not explicitly stated in the report, since there are no walls surrounding the central square, we assumed that in the context of calculating aversion, this should be seen as part of an open arm. That is, in calculating the aversion, a "+" would be used for the central square.

The quantity γ_i is a constant which is assigned a larger value when the square i is an external square on an open arm. This is because they assumed that the rat would be more averse to head-dipping than to staying firmly on an open arm. A smaller value is assigned in all other cases.

The third aspect of the model is spontaneity. Montgomery found that rats make random turns while in the maze [10]. The model incorporates this idea by adding a consideration of random movement at the beginning of each time step. A square is randomly chosen among the squares connected to the square occupied at the beginning of the time step. Then a small value r is added to the weight ω_{ij} associated with this square. The random choice is based on the following probability distribution presented in the paper by Salum, Morato, and Roque-da-Silva [10]:

40% — the rat moves to the square in the forward direction

20% — the rat moves to one of the squares in the perpendicular direction

10% — the rat moves to the square in the backward direction

10% — the rat stays in the same square

Note that the square in the forward direction is the square that corresponds to the same direction as the rat's last movement. Each virtual run through the maze is finished when the rat's motivation to move from j to i, M_{ij}, has decayed to a very small number close to zero for all i relating to a square j. That is, when the rat is at square j and the motivation to explore all adjacent squares has become very small, the trial is finished [10].

The abovementioned parameters were found by trial and error. The random variables, μ and ν, were sampled from a Normal distribution with mean 0.01 and standard deviation 0.003. They chose the following values for the initial exploration drive, the initial fear drive, and the random perturbation in one of the weight elements during each trial:

$$M = 1, \qquad C = 0.03, \qquad r = 0.01.$$

The larger values of α_i and β_i were 1.5 and 5 respectively, and the smaller values were 1 and 3; γ_i was 1.8 when i represented an external square in an open arm and 1 otherwise.

Upon reflecting on this model and attempting to replicate it, several issues arise. They are introduced in the following section.

2.3 Shortcomings of this Model

An unrealistic assumption made in the model was that the rats move at a constant speed of two seconds per movement. In reality, rats move at many different speeds throughout a trial. For example, a rat might stop to look over the edge of an open arm for 20 seconds and then quickly run into a closed arm in less than two seconds. Therefore, it would be more realistic to somehow vary the length of the time steps. The authors of the article also made note of this possible improvement [10]. However, varying the length of the time steps might produce an unnecessarily complicated model.

Another possible improvement would be to shorten the length of each time step. If one could find a time step that was short enough to cover no more than one movement, then there would be no need to vary the length of the time steps. The model that is described in detail in the following sections utilizes a time step representing one second. Systematic observation of experimental trials with rats in the elevated plus-maze reveals that it is rare for a rat to make more than one movement in one second.

As explained above, the virtual trials defined by the computational model ended when M_{ij} decayed to a small number for all i relating to a square j. Considering that the experimental trials were five minutes in length, it seems to make more sense to set the virtual trials to run for five minutes as well. Since the two types of trials were being compared, absolute measurements like the number of entries into the open arms could then be used in the comparison.

Finally, instead of deciding the rats' next movement simply by choosing the adjacent square with the highest weight, it seems more appropriate to add an aspect of randomness to the weight matrix. This could be done by defining a probability distribution based on these weights and randomly choosing the next movement based on the probabilities. Therefore, if the weight representing moving to one square was slightly larger than the weight corresponding to another, the probability distribution would make it possible, though less likely, for the rat to choose the square with the smaller weight.

Although this model's basis in theory is appealing, there are some shortcomings in its design. First, assigning numerical values to such hypothetical constructs as aversion and the motivation to explore is unintuitive. In other words, it is unclear how to assign absolute values to quantify these drives. Furthermore, the equations for A_{ij} and M_{ij} depend on several parameters which were found by trial and error. Since they were merely found using one small sample, the validity of these parameters is questionable. The model may not be applicable to a general population of rats, and may not be replicable.

In fact, we could not replicate their statistical results. The paper outlining this computational model reported the results of several statistical tests, including two t-tests. One set out to show that the percentage of time spent in the open arms was significantly less than the percentage of time spent in the closed arms. Similarly, the experimental hypothesis of the other test was that the number of entries into the open arms was significantly less than the number of entries into the closed arms. Both tests were significant with P-values ≤ 0.001 [10]. However, after we recreated the model, these same tests had entirely different results, both with much larger P-values (entries: 0.031, time: 0.576). Therefore, it appears that the results reported in the paper may not be replicable.

It was decided that an entirely different approach might produce a model with predictive power that avoids all of the problems outlined in this section. The next chapter depicts the development of a new model, from its earliest stages, to the realization of the mechanism behind the final model. There is a visual simulation built into the model that allows one to see a virtual rat in a virtual elevated plus-maze for the equivalent of a 5-minute trial. The representation and implementation of this simulation is established before looking into the development of the underlying mechanism behind the model.

Chapter 3

Development of a New Model

3.1 A Visual Simulation of the Model

The objective behind developing this model is to be able to run virtual trials that consistently generate behavioral measures like those observed in real trials. To aid in conceptualization, the model includes a visual simulation of the virtual trials. This simulation consists of a plus sign drawn on a Cartesian coordinate system with the center of the plus at the origin (as seen in Figure 1.1). Each of the four arms is divided into three squares, for a total of twelve squares, and the center of the maze constitutes the thirteenth square. From the perspective of the model, a rat enters a new square when the front three-quarters of its body enters it. If about half of its body is in two different squares, we assume it is occupying the one containing its back paws. In the virtual trials, the rat is depicted as a green dot. Along with being able to occupy squares representing the surface of the maze, the model accounts for exploration of external squares that are adjacent to the surface of the maze. Exploring one of the external squares corresponds to rearing if the rat is in a closed arm or peering over the edge if the rat is in an open arm. Instead of showing the dot moving outside of the surface of the maze, the dot turns red to symbolize the exploration of an external square. When risk assessment behavior is present, the dot turns blue.

3.2 Implementation of the Simulation

While the underlying mechanism behind the model changed greatly as it developed, the basic structure of the simulation was maintained throughout the development process. Therefore, this structure is described in detail before any further discussion of the model's development.

Each iteration of the simulation, or virtual trial, simulates a five-minute trial in a laboratory setting. A virtual trial completes a predetermined number of time steps, each representing approximately one second. During each time step, the rat's new position in the maze and behavior is determined based on a set of rules. These rules, which are the underlying mechanism behind the model, are discussed further in the following sections.

During each time step, the rat's new position is displayed by the Matlab function, `elevatedplus(a, b, rearing, risk, n, w)`. The code for this function is provided in Appendix A. The parameter, n, represents the number of squares in each arm of the maze and w represents the width of each square. While the program is flexible regarding the number of squares in each arm and the width of each square, a maze with three squares per arm and a width of one for each square is used for the purposes of developing the model. Each rat begins its virtual run through the maze at a coordinate, (aw, bw), where a and b are integers. Since the convention in laboratory settings is to place each rat in the center of the maze, each virtual run through the maze begins at the coordinate, $(0, 0)$, in the central square. Therefore, a and b are initially set to 0.

The other two parameters, *rearing* and *risk*, are dichotomous parameters that indicate the presence or absence of rearing and risk assessment behaviors. Giving *rearing* a value of 1 causes the dot to turn red. As mentioned earlier, this means that the virtual rat is either peering over the edge of an open arm or rearing up in a closed arm. Similarly, setting *risk* to 1 means the rat is engaging in risk assessment behaviors, turning the dot blue, while a value of 0 indicates the absence of such behaviors. At the beginning of every virtual trial, both of these parameters are set to 0.

Of the six parameters used in `elevatedplus(a, b, rearing, risk, n, w)`, only the width of each square and number of squares per arm remains constant throughout the course of each virtual trial. The virtual rat changes position repeatedly, so the values of a and b change from one time step to the next. The model assumes that only one movement can be made per time step, so a and b are never incremented or decremented by more than 1 at one time. Also, because the rat cannot move diagonally, no more than one of these coordinates changes at once. The virtual rat sometimes displays rearing or risk assessment behaviors, so the values of these parameters also varies throughout the trial.

At any given time, there are five possible movements for the virtual rat to make. If it begins to explore an external square (i.e., *rearing* is set to 1), the program automatically sets *rearing* to 0 before the next time step. Also, although the rat is exploring an external square, the model displays the rat in the internal square adjacent to the square being examined. This constraint ensures that the rat does not move from an external square to another square beyond the surface of the maze. That way, the virtual rat is always contained within the maze.

The model also keeps track of the virtual rat's movements, updating measurements that quantify these movements at the end of each time step. Among these measurements are the number of entries into the closed arms and the percentage of time spent in the open arms. Once the virtual trial is complete, these measurements are displayed in the Matlab command window.

Now that the basic structure behind the simulation has been established, a discussion of the underlying mechanism behind the model is possible. The rat's movements are determined by the output of a random number generator and probability distributions that describe the rat's tendencies in certain situations. During each time step, a random number between zero and one is chosen. Probabilities are preassigned to every possible movement in the given situation. Each possible movement is therefore represented by a specific interval of values in a cumulative probability distribution. For example, if there were five possible movements with equal probabilities of occurring, then the third possible movement might be assigned to the interval [0.4, 0.6). If the random number generator produced a value in that interval, then the virtual rat would make the third movement.

3.3 Random Run

Before setting out to build the new model, it seemed appropriate to build a simulation that simulates entirely random movement through an elevated plus-maze. This simulation is set up as described in the previous section. The underlying mechanism involves assigning equal probabilities to each of the five possible movements. Therefore, during each time step, the next movement is determined by a random number's position in the cumulative probability distribution outlined in Table 3.1. If the ran-

Table 3.1: Random Run Probability Distribution

Movement	Cumulative Probability Distribution
East	(0, 0.2)
West	[0.2, 0.4)
North	[0.4, 0.6)
South	[0.6, 0.8)
Still	[0.8, 1)

dom number is less than the probability assigned to moving east, a is incremented by 1, which, in turn, causes the x-coordinate to be incremented by the width of one square. This adjustment results in a movement to the adjacent square in the eastward direction. Similarly, if the random number is between the probability of moving eastward and the cumulative probability of moving east or west, then the x-coordinate is decremented by the width of a square. This approach is used to determine every possible movement throughout the entire trial. The code for the random run, which is written for use in Matlab, is provided in Appendix B.

In testing their model, Salum, Morato, and Roque-da-Silva placed a large focus on two behavioral tendencies in the standard elevated plus-maze [10]. Their model could reliably simulate the tendencies for rats to enter the closed arms more often than the open arms, and to spend a larger percentage of time in the closed arms than the open arms.

In an attempt to replicate these tendencies using the random simulation, the probability distributions were repeatedly adjusted until significant results were obtained. Increasing the probabilities of moving east and west, which correspond to movement in the closed arms, generates results similar to those produced by the computational model and the experimental trials as outlined in the article. However, this is only achieved by substantially changing the probabilities. There is no theoretical or empirical basis for these adjustments. The sole reason behind making the changes is the fact that we want to model the natural tendency to prefer the closed arms. Therefore, the probabilities are simply adjusted to force the simulation to produce the desired results. Significant results are achieved after changing the probabilities of moving east and west from 0.2 to 0.35 (entries: $t(22) = -6.63$, $p = 0.000$; percentage of time: $t(22) = -2.76$, $p = 0.006$). If one considers that increasing these probabilities to 0.5 would guarantee that the entire trial would be spent exploring only the closed arms and the central square, the change that produces significant results (i.e., from 0.2 to

0.35) is very large. Furthermore, the adjusted random simulation is designed only to reflect a preference for the closed arms. No accuracy in the actual values of the measures is likely to be achieved using this approach.

Perhaps adjusting the probabilities in a random simulation would eventually lead to a model that could reproduce behavioral measures in the elevated plus-maze. However, it is clear that this approach would be inefficient and groundless. Although the random simulation is not an appropriate model, this line of research leads to the idea that is the basis of the final model. Before developing a model, a logical foundation in theory and empirical observation is needed. The basic idea leading to the mechanism behind the model is discussed in the following section.

3.4 Simple Inertia Model

This model takes an entirely different approach to predicting behavior in the elevated plus-maze than the first model. Instead of determining a rat's behavior based on the net difference between two opposing drives, this model uses probability distributions to determine each of the rat's movements. The basic idea motivating this model is that inertia governs rats' behavior in the elevated plus-maze. If a rat is moving in a particular direction, it tends to continue in that direction. Therefore, this model assumes that each movement depends on the direction of the last movement. Rather than expressing directions in absolute terms, like east and west, they are now expressed in relative terms. Therefore, the probability distributions define the probabilities of moving forward, backward, staying still, or moving side-to side.

The assumption that the direction of the last movement affects a rat's behavior seems reasonable upon observing rats in the elevated plus-maze. For example, in the open arms, rats tend to spend some time looking over the edges when they are moving away from the center, but they are more likely to move forward when they are moving back to the center.

Another important consideration made in this model relates to the location in the maze. A rat's behavior depends largely on its position within the maze. If it were moving toward the center in a closed arm, it might tend to stay still and rear quite a bit on its way back to the center. However, once a rat started moving toward the center on an open arm, it would likely continue to move toward the center without much delay. Therefore, this model allows the virtual rat to show different tendencies depending on its location and relative movement within the maze. Note that this model implicitly considers the relative difference between fear and curiosity without assigning unintuitive absolute values to these drives. The next movement depends on the rat's fear and curiosity relating to the part of the maze it is exploring.

Taking these considerations into account, the basic mechanism behind the model can now be explored. Within the arms of the elevated plus-maze, a rat can move forward, backward, rear (which corresponds to moving perpendicular to the direction of movement), or it can stay still. A specific probability is assigned to each of the possible movements and behaviors. This distribution changes depending on two factors: the direction of the rat's last movement and its location in the maze. A rat's behavior in the center is determined by probabilities of moving into the open arms and the closed arms, staying still, and rearing. For simplicity, it is assumed that, in the central square, the rat's next movement is independent of its previous movement. All of these possibilities can be summarized using the five probability distributions in Table 3.2. Recall that each probability distribution contains probabilities corresponding to five possible movements. Although there are some obvious trends that

Table 3.2: Simple Inertia Model Probability Distributions

1	Open arm	Moving outward
2		Moving inward
3	Closed arm	Moving outward
4		Moving inward
5	Center	

enable us to guess at the proper probabilities to assign for each distribution, this would be tedious. Therefore, the probabilities were derived empirically based on a sample of 34 experimental trials with rats on the elevated plus-maze. These experiments were conducted in Dr. Lisa Kalynchuk's laboratory at Dalhousie University. The process of estimating these probabilities was fairly rudimentary. It involved observing videotapes of these experiments, breaking each five-minute trial into a series of time steps, each lasting approximately one second. Then, the rat's position and movement in relation to its previous movement was recorded. This was simply done by pausing the VCR every second and making note of the rat's activity. Since this was done using a VCR, each pause took slightly more than one second. Therefore, each trial consisted of approximately 230 time steps rather than the 300 time steps that would be expected in a five-minute trial. Although this process was not very precise, the purpose was merely to find approximate values to use as initial estimates for the probabilities.

As mentioned in the context of the previous model, it has been found that the exploratory behavior and the fear drive decay with time spent in the maze [6]. This model does not account for any changes in behavior over the length of the trial, since all of the probabilities are averaged over the entire trial. It is assumed that the 5-minute trial is short enough that the decay only makes a negligible difference in behavior. This assumption is based on the experience of researchers who were consulted during the development of the model.

When the estimated probabilities are used in the model, it lacks *face validity* in this initial form. In other words, on first glance, it does not appear to be valid. Upon observing the simulation, it is clear that the virtual rats behave somewhat differently from the rats used as a basis for the model. The discrepancy seems to revolve around risk assessment behavior. In the experimental trials, the rats tend to spend a lot of time in the closed arms near the center and in the central square. Much of the time in these locations is spent assessing risk. This involves either staying in the center or in a square adjacent to the center and poking their heads out onto the open arms. The simple inertia model fails to model this activity. Therefore, it is obvious that adjustments need to be made to improve the validity of the model. The next section provides a solution to this problem.

3.5 Final Inertia Model

In order to account for the tendency to stay near the center and engage in risk assessment behavior, the model is adjusted to contain two new probability distributions. Risk assessment is only possible in the central square and those squares that are adjacent to the center in the closed arms. Therefore, risk assessment is added to the possible behaviors in the central square. To account for risk assessment in the closed arms, the arms are divided into two separate areas. The squares adjacent to the central square are treated differently than the rest of the squares, and are assigned their own probability distributions.

The adjusted list of probability distributions used to cover the possible situations is displayed in Table 3.3. The first four involve situations in which it is only possible

Table 3.3: Final Inertia Model Probability Distributions

1	Open arm	Moving outward
2		Moving inward
3	Closed arm, Nonadjacent	Moving outward
4		Moving inward
5	Closed arm, Adjacent	Moving outward
6		Moving inward
7	Center	

to move forward, backwards, rear, and stay still. The next two involve squares that are adjacent to the center of the maze, where it is also possible to engage in risk assessment. Finally, just like in the simple inertia model, the center is treated differently than the rest. There is no consideration of the direction from which the rat has come. A rat's behavior in the center is determined by probabilities of moving into the open arms and the closed arms, staying still, rearing, and engaging in risk assessment.

The seven probability distributions used in the model are outlined in detail in Table 3.4. As can be seen, each of these distributions is quite different from the

Table 3.4: Estimated Probability Distributions

Estimated Based on 34 Experimental Trials								
Distribution	**1**	**2**	**3**	**4**	**5**	**6**	**7**	
P(Forward)	.08	.635	.11	.42	.86	.05	**P(Open)**	.02
P(Backward)	.13	0	.13	.02	.00	.03	**P(Closed)**	.50
P(Still)	.34	.285	.59	.46	.10	.59	**P(Still)**	.14
P(Rear)	.45	.08	.17	.10	.03	.08	**P(Rear)**	.03
P(Risk)	—	—	—	—	.01	.25	**P(Risk)**	.31

others. They reflect intuitive expectations and trends that have been established by researchers. For example, the probability of a rat moving forward when it is moving inward on an open arm is larger than the corresponding probability in a closed arm. Also, the distribution describing tendencies in the central square is in agreement with past research [10]. The probability of moving into a closed arm is much higher than the probability of moving into an open arm, so it makes sense that the number of closed-arm entries is higher than the number of open-arm entries.

These sections have outlined the process of devising a model which applies empirically derived probabilities to many of the possible movements a rat can make during each time step. After randomly selecting a series of movements based on the empirical probability distributions, the end result is a simulation of a rat exploring the elevated plus-maze for the first time. Each virtual trial represents a five-minute experimental trial. The goal in developing this model is for the behavioral measures produced by the model to be the same as those found in experimental trials using normal rats.

The following sections outline the results of statistical analyses that compare the virtual trials to experimental trials. Five different measures are used to test the model: the percentage of open-arm entries, the percentage of time spent in the open arms, the number of closed-arm entries, the number of open-arm entries, and the total number of entries. The percentage of time spent in the open arms is given in terms of the total amount of time spent in the arms of the maze. That is, it is calculated by dividing the amount of time spent in the open arms by the amount of time spent in either the open arms or the closed arms.

Chapter 4

Results

4.1 Preliminary Testing

The first step in testing the model is to determine its ability to produce similar behavioral measures as those observed in the 34 experimental trials upon which the model is based. This is done by comparing the output of 34 virtual trials of the model to the experimental measures as scored by researchers at Dalhousie. These comparisons involve tests on the averages for the real and virtual measurements as well as comparisons of their distributions.

It was decided that using a nonparametric test was not an ideal approach in comparing the averages because zeros are very common among the open-arm data. A large number of the rats never enter an open arm, resulting in open-arm activity measurements of zero. Therefore, nonparametric statistics would not be sensitive to differences in the data sets, since both the virtual and the real data sets are likely to have medians of zero. Furthermore, the large proportion of zeros resulted in highly skewed distributions for the open-arm data, so the assumption of normality required for parametric statistics was not met. Consequently, for the preliminary comparisons, decisions about the model's accuracy are made based on bar graphs displaying the means of the five measures as well as t-tests on the number of closed-arm entries and the total number of entries. First, the results of these t-tests are discussed.

Parametric statistics are frequently used in the literature pertaining to this type of situation. For example, two-way ANOVA tests and t-tests were used to analyze the model proposed by Salum, Morato, and Roque-da-Silva [10]. Therefore, t-tests are now used to compare the means for the model with the experimental data.

Two-sample t-tests on these two measures reveal the results outlined in Table 4.1. Note that, in this situation, the desired hypothesis is that the model means are the same as the real means. These t-tests reveal that the model based on the estimated

Table 4.1: T-tests on the model compared to the original data

H_0: The mean is the same for the virtual rats and the real rats
H_a: The mean is different for the virtual rats and the real rats

	t-value	**t-test p-value**	**Model Mean**	**Real Mean**	**Model SE**	**Real SE**
CA entries	3.39	.001	7.21	5.18	1.81	2.99
Total entries	1.82	.074	7.59	6.21	2.06	3.91

probabilities is not very successful at reproducing the measures from the original 34 trials. The p-values are quite small, suggesting that the model's output may be significantly different from the original data. In general, the results of the t-tests given in Table 4.1 support the undesired hypothesis that the virtual trials are different than the real trials. For example, for α as low as .001, there is sufficient evidence to conclude that the closed entries differ for the two groups. These results make it obvious that the model is not sufficient in its present state. Since these are simply preliminary tests to see if the model can replicate the data upon which it is based, changes can be made to compensate for the observed differences. After finding a model that can produce similar results as the experimental trials used as its basis, further tests can be used against different experimental trials to determine the model's true predictive power.

As can be seen in Figure 4.1, the main problem with the model is that it overestimates the number of closed-arm entries and underestimates the open-arm measurements.

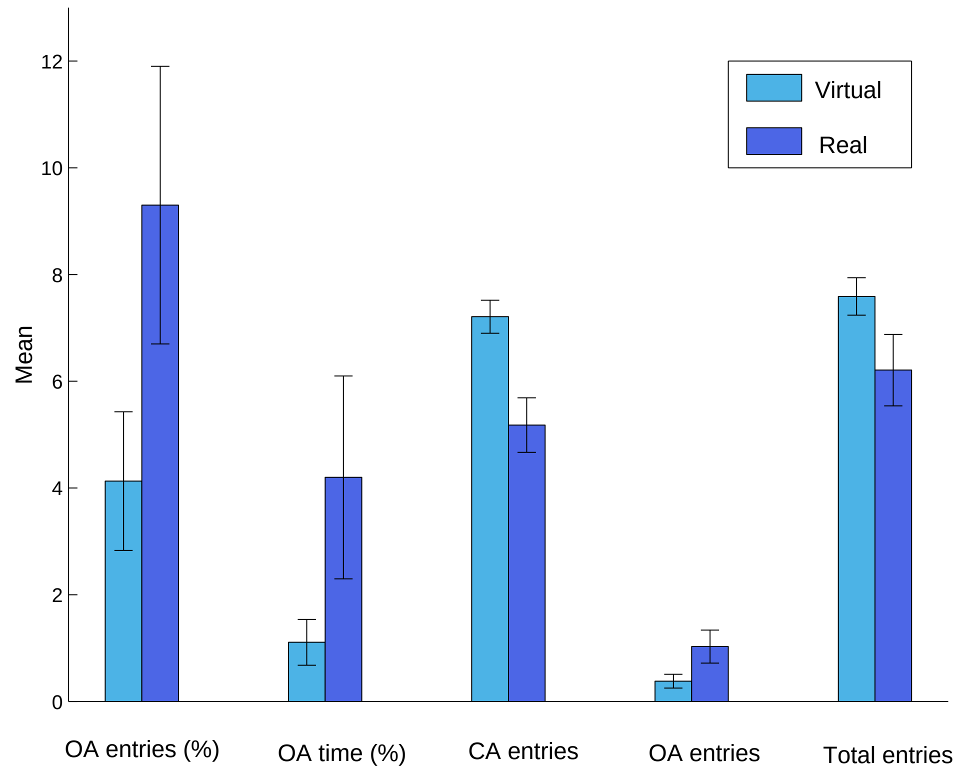


Figure 4.1: Bar graphs of the original model means compared to the means of the original data set, ± one standard error.

Finding an algorithm that optimizes all seven probability distributions used in the model is not tractable. For example, there is no objective function that can be optimized using computer software. Therefore, the most direct way to compensate for the model's overestimates and underestimates is to adjust the central probability distribution according to intuition and expectation. Indeed, it is found that only one of the seven distributions needs to be changed to achieve the desired results. Adjustments can be made to the central probability distribution until the model produces results that are similar to those produced by the real rats. The final probability distributions resulting from these adjustments are displayed in Table 4.2. These dis-

Table 4.2: Final Probability Distributions

Distribution	**1**	**2**	**3**	**4**	**5**	**6**	**7**	
P(Forward)	.08	.635	.11	.42	.86	.05	**P(Open)**	.02
P(Backward)	.13	.00	.13	.02	.00	.03	**P(Closed)**	.13
P(Still)	.34	.285	.59	.46	.10	.59	**P(Still)**	.51
P(Rear)	.45	.08	.17	.10	.03	.08	**P(Rear)**	.03
P(Risk)	—	—	—	—	.01	.25	**P(Risk)**	.31

tributions are used as the final probabilities, describing the rats' tendencies in every possible situation during the trial.

Tests on this model suggest that it is much closer to the original rats used to build the model than the first attempt using the unadjusted probabilities. The results of 2-sample t-tests on the number of closed-arm entries and the total number of entries, comparing the model to the original rats are displayed in Table 4.3. The p-values

Table 4.3: T-tests on the final model compared to the original data

H_0: The mean is the same for the virtual rats and the real rats
H_a: The mean is different for the virtual rats and the real rats

	t-value	**t-test p-value**	**Model Mean**	**Real Mean**	**Model SE**	**Real SE**
CA entries	1.50	.141	6.06	5.18	.29	.51
Total entries	.83	.409	6.82	6.21	.32	.67

indicate the likelihood of observing such differences in means (or larger differences) if the model means are the same as the real means. As the p-values increase, there is stronger evidence for the conclusion that the model means are the same. Therefore, the large p-values obtained using the adjusted model are a strong indication of the strength of this model.

From the visual representation of these data given in Figure 4.2, one can see the means are much closer than they were when the model was relying on the original probabilities.

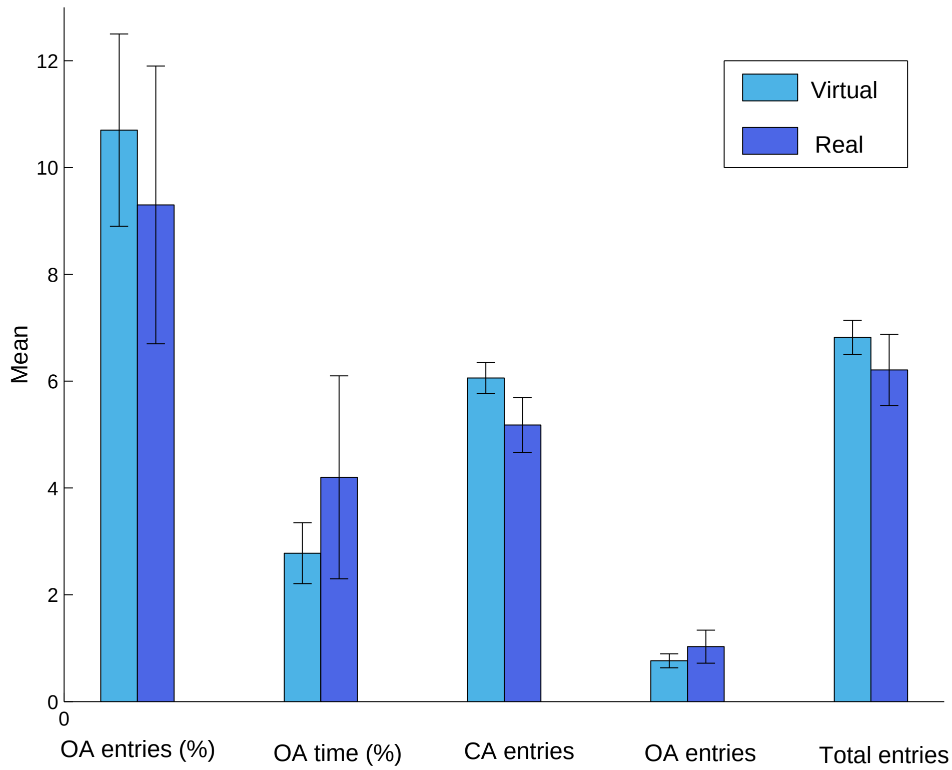


Figure 4.2: Bar graphs of the final model means compared to the means of the original data set, ± one standard error.

Note that the error bars corresponding to each mean do not represent confidence intervals. Instead, they are present to give some idea of the spread of each sample, using the standard error as an indicator of spread.

Upon obtaining a model that is reasonable at predicting some of the mean behavioral measures, the investigation into the model turns to the distributions of the five measures. The question is whether the behavioral measures produced by the model have similar distributions as those observed in experimental trials. This is first addressed by looking at histograms and comparing their shapes. In order to make the comparisons, 100,000 iterations of the model are conducted. For each of the five behavioral measures, a histogram is generated and compared to the corresponding histogram from the 34 rats upon which the model is based. A typical comparison is depicted in Figure 4.3. While the distributions are somewhat different, there is a definite similarity. Both distributions are right-skewed, reflecting the tendency for the rats to have little or no entries into the open arms. Given these histograms, it seems reasonable to accept the idea that the sample of 34 rats might have been sampled from a population with the same distribution as the one depicted in the histogram for the model. In other words, the model appears to produce a distribution similar to that which is observed in the experimental trials.

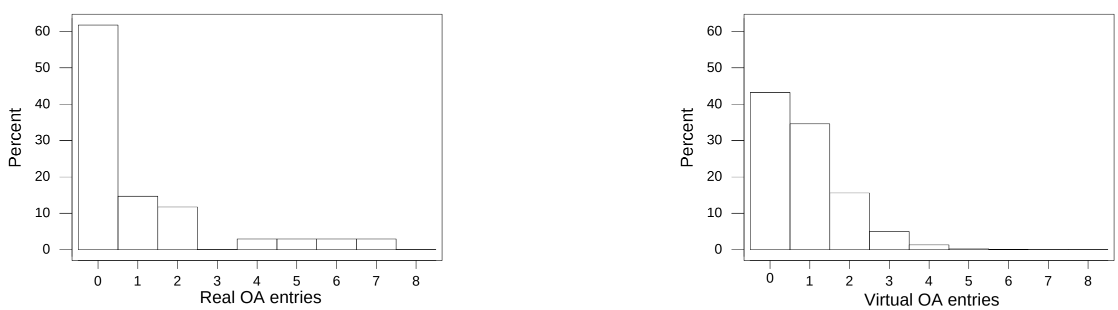


Figure 4.3: The distribution of the number of open-arm entries in the original data set compared to the corresponding distribution produced by the model.

Another test used to compare the model's distribution with the real distribution involves the proportion of zeros in the open-arm measurements. Since the tendency for rats to show no open-arm activity is so strong, a model that can reliably display the same tendency is desirable. Treating the proportion of zeros in 100,000 iterations of the model as a population proportion, a proportion test is used to see if the sample proportion of zeros is similar to that observed in the model.

In 100,000 iterations of the model, 43,199 of the trials resulted in no open arm entries, so all three open-arm measurements were zero. A two-sided test about the population 0.43199 is significant at $\alpha = .05$. The sample proportion of zeros for the experimental trials is 0.61765, resulting in a P-value of .037. Therefore, at the $\alpha = .05$ significance level, there is sufficient evidence to conclude that the model is not successful at generating the proper proportion of zeros for the open-arm measurements.

The results based on the means suggest that the adjusted model is able to reproduce the behavioral measures from the rats used to develop the model. While the model does not accurately capture various other aspects of the distributions, the basic trends in the distributions are still represented. For example, the model does reproduce the skew in the open-arm entries. The following section provides some evidence for the model's ability to generalize beyond this sample.

4.2 Final Testing

After creating a model capable of reproducing various aspects of the data used in creating the model, the next step is to see if the model has any predictive power. In other words, the model's output needs to be tested against a different set of experimental data. These data were obtained through the same researchers at Dalhousie. They provided measures from 69 trials using normal rats on the elevated plus-maze. To test the model, the output from 69 virtual trials was compared to this data set.

Again, the open-arm measurements are considered separately from the other two measures since the large proportion of zeros violates the assumptions of the t-test. Table 4.4 shows the results of 2-sample t-tests comparing the virtual means with the means of the new data set. Considering that the original data set is different from

Table 4.4: T-tests on the final model compared to the new data

H_0: The mean is the same for the virtual rats and the real rats H_a: The mean is different for the virtual rats and the real rats						
	t-value	**t-test p-value**	**Model Mean**	**Real Mean**	**Model SE**	**Real SE**
CA entries	-.30	.761	6	6.12	.21	.32
Total entries	-.66	.512	6.83	7.13	.23	.40

the new data set, it is promising to see that both of these measures appear to be quite similar when comparing the model to the new data. The means are represented graphically in Figure 4.4.

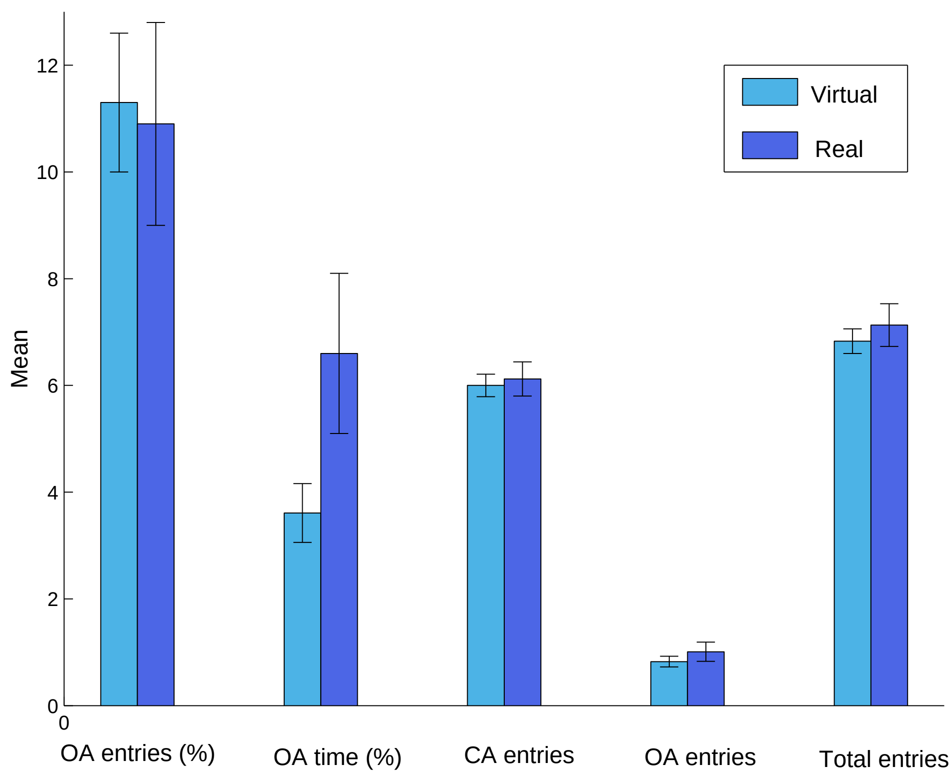


Figure 4.4: Bar graphs of the final model means compared to the means of the new data set, ± one standard error.

The overall distributions of the behavioral measurements can be seen in Figures 4.5 – 4.9. As can be seen in Figure 4.5, Figure 4.6, and Figure 4.7, the model

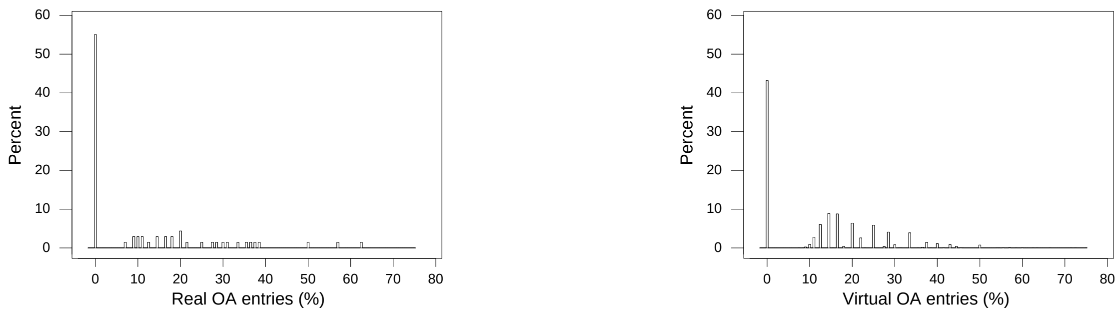
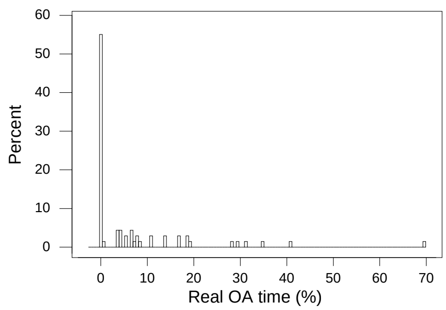


Figure 4.5: The distributions of the percentage of open-arm entries in the new data set compared to the corresponding distributions produced by the model.

is capable of reproducing the right skew observed in the open-arm measurements. It also appears, upon initial inspection, that the model is good at reflecting the proper proportion of zeros for the percentage of open-arm entries and the percentage of open-arm time. For the closed-arm entries and the total entries, both the model output and the experimental data appear to be approximately bell-shaped. However, in both situations, the model shows a much smaller spread.

A test on the proportion of zeros for the open-arm measurements reveals slightly insignificant results. The sample proportion of zeros is 0.55073, with a P-value of .052. This is greater than $\alpha = .05$, failing to reject the hypothesis that the sample proportion is different than the proportion of zeros in the model.



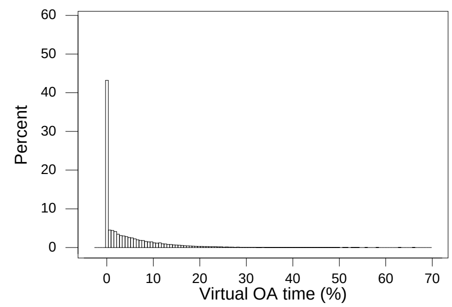


Figure 4.6: The distributions of the percentage of open-arm time in the new data set compared to the corresponding distributions produced by the model.

For the most part, these results suggest that the model has some predictive power. The code for the final model can be found in Appendix C.

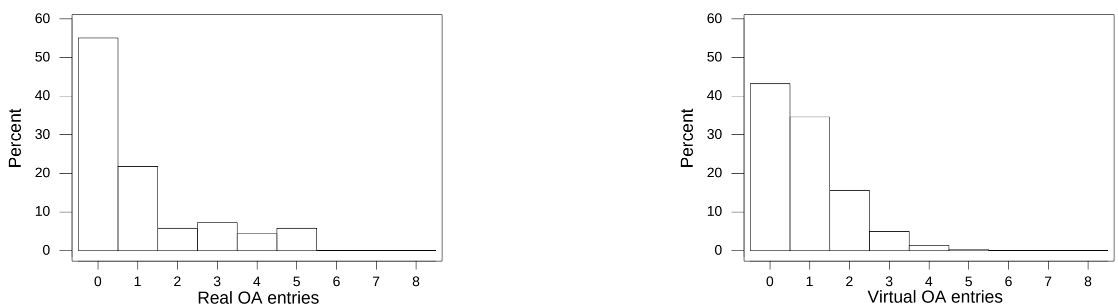


Figure 4.7: The distributions of the number of open-arm entries in the new data set compared to the corresponding distributions produced by the model.

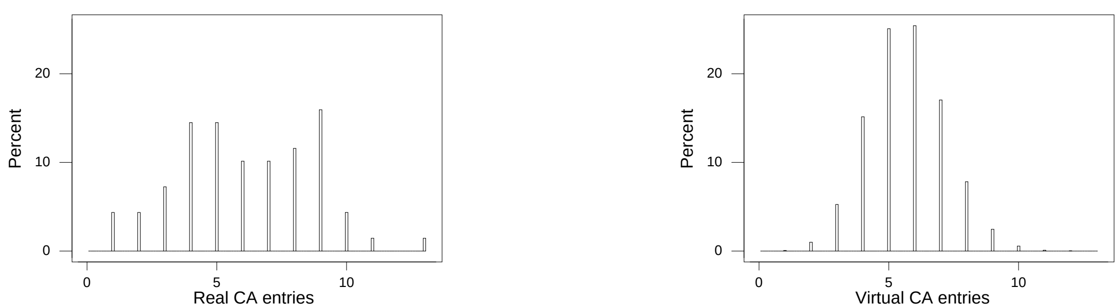


Figure 4.8: The distributions of the number of closed-arm entries in the new data set compared to the corresponding distributions produced by the model.

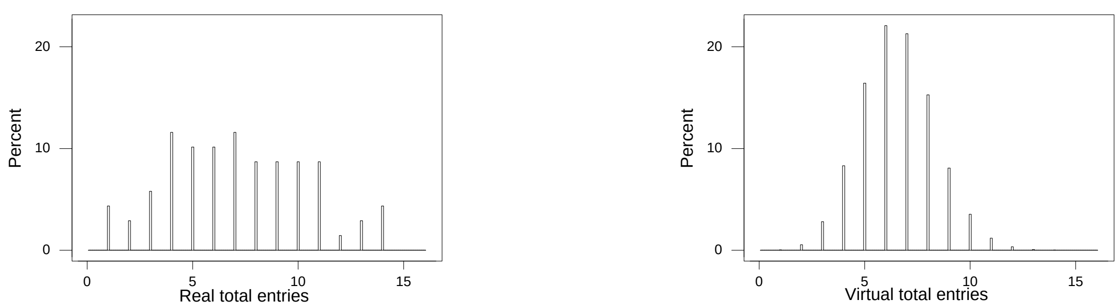


Figure 4.9: The distributions of the total number of entries into the arms in the new data set compared to the corresponding distributions produced by the model.

Chapter 5

Discussion

Tests on the final model suggest that it is very promising. It has some predictive power, suggesting that it could be used to generate control data. There are many advantages to this, including the fact that it would be cost-effective to use fewer laboratory rats when performing experiments comparing treatment groups to control groups.

Furthermore, the model's accuracy and reliability could easily be improved. Lacking more sophisticated technical equipment, the probabilities were estimated using a VCR. Each trial was divided into several time steps that were intended to last one second each. However, this was done by pausing the tape repeatedly, so the intervals were not very precise. Also, each rat's position and behavior was recorded by hand, leaving some room for error in observation. Advanced scoring equipment can be used to obtain more accurate probabilities. Perhaps the new estimates would result in a more accurate model; that is, one that would not need to be adjusted to reproduce the original data set.

The model could also be improved by finding ways to make it more sensitive to subtle differences in behavior across each trial. Some tendencies are hidden by the model's current structure. When placed in the elevated plus-maze for the first time, most rats immediately run into a closed arm. Since the probability of moving into a closed arm from the center is averaged across the whole trial, this tendency is lost in the virtual trials. The average probability distribution over the entire trial gives a relatively small probability of entering a closed arm, so treating the first few seconds in each trial as independent of the rest of the trial might produce a more realistic model. This would involve estimating the probabilities for the first few seconds separately from the rest of the trial.

Similarly, in accordance with Montgomery's finding that fear and motivation to explore decay with time spent in the maze, it might be reasonable to adjust the model to treat different portions of the trial separately [6]. For example, a rat's behavior might be different in the first minute compared to the fifth minute, when the maze is more familiar.

After developing a model that was accurate, reliable, and had discriminant validity (i.e., that could discriminate between rats with different anxiety levels), it could then be applied to different types of rats. By using different probability distributions within the basic structure of the model, it could be used to predict the behavior of rats that had been subjected to manipulations that would effect their anxiety levels. An example of one of these manipulations is kindling. Kindled rats tend to show high levels of anxiety. Kindling is a protocol whereby certain brain regions are stimulated repeatedly. This practice, which is performed by administering electrical stimulations, causes seizures after sufficient repetition [2]. A motivation behind research involving kindling is to learn about the emotional effects of seizures on people who suffer from temporal lobe epilepsy. Therefore, kindled rats' emotionality is gauged using the elevated plus-maze.

Kalynchuk and her colleagues postulated that kindled rats' tendencies can partially be attributed to fear whereas rats treated with anxiolytic drugs behave as they do because of reduced levels of fear [5]. Ironically, although these rats are seen as motivated by entirely different emotional states, they show similar tendencies. For example, unlike rats with moderate levels of fear, both types of rats show increased open-arm activity as indicated by the percentage of open-arm entries and open-arm time. The continuum in Figure 5.1 outlines a possible explanation for this.

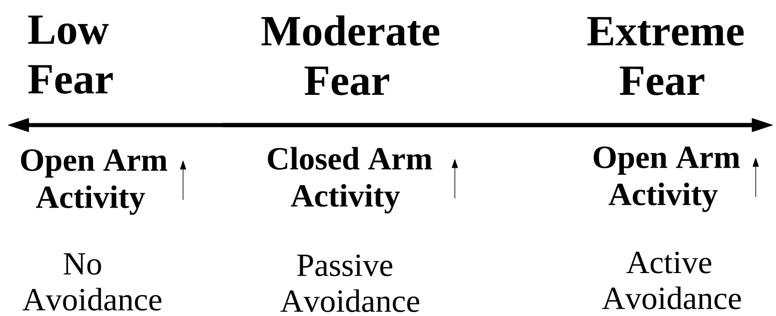


Figure 5.1: The relationship between level of fear and behavior in the elevated plus-maze.

Kalynchuk and her colleagues propose that kindled rats have high levels of fear, so they are motivated to escape the maze. Therefore, they go out onto the open arms in search of escape routes, engaging in active avoidance. On the other hand, rats treated with anxiolytic drugs show no avoidance, as their level of fear is low enough that it does not inhibit open-arm activity [5].

Using probability distributions corresponding to these types of rats within the basic structure of the model, accurate models for rats with varying levels of anxiety could be created. Researchers could then analyze these probability distributions to gain further insight into the subtle effects of treatments. The models themselves would also have many applications to epilepsy and drug research, cutting down on the costs of animal research. Obtaining a model with predictive power and discriminant validity is just the first step in a long and fruitful line of research incorporating mathematical modeling with various aspects of elevated plus-maze behavior.

Appendix A

elevatedplus.m

```
%***************************************************************
%    This is a function which is called from programs designed
% to simulate trials in the elevated-plus maze.  It receives
% the coordinates that determine the square the rat is
% occupying from the program and draws a dot there.  The other
% program also determines whether the rat is firmly within that
% square or exploring the sides (i.e., head-dipping for the
% open arms or rearing for the closed arms).  Also, the other
% program sends the number of squares in each arm -- n, to this
% function.
%    This program draws the maze, representing the walls by
% thick black lines and including dotted lines to show the
% imaginary barriers between squares.
%    The rat sometimes looks over the edges of the open arms
% and explores the walls, so the maze could be represented
% using external squares adjacent to each square in the maze,
% but to simplify the structure of the program, these external
```

```
% squares are not shown.  Instead, these behaviours are
% represented by changing the dot from green to red.
%    This program also represents risk assessment behaviours by
% turning the dot blue.
%***************************************************************

function elevatedplus(a,b, rearing, risk, n, w)

% This gives the  x and y coordinates of the 12 points that
% define the shape of the plus
plus = zeros(2,12);
plus(:,1) = [-0.5*w; (n+0.5)*w];
plus(:,2) = [0.5*w; (n+0.5)*w];
plus(:,3) = [0.5*w; 0.5*w];
plus(:,4) = [(n+0.5)*w; 0.5*w];
plus(:,5) = [(n+0.5)*w; -0.5*w];
plus(:,6) = [0.5*w; -0.5*w];
plus(:,7) = [0.5*w; -(n+0.5)*w];
plus(:,8) = [-0.5*w; -(n+0.5)*w];
plus(:,9) = [-0.5*w; -0.5*w];
plus(:,10) = [-(n+0.5)*w; -0.5*w];
plus(:,11) = [-(n+0.5)*w; 0.5*w];
plus(:,12) = [-0.5*w; 0.5*w];

% Clear figure 1 so we can start fresh every time the function
% is called
figure(1);
clf;
```

```
% Set the axes so our maze is in the centre of the picture
axis([-(n+2)*w,(n+2)*w,-(n+2)*w,(n+2)*w]);
axis square
axis off
hold on;

% This fills in the plus with a blue color
% plus(1,:) is the vector of x values & plus(2,:) gives the y
% values
fill(plus(1,:), plus(2,:),[.9 .9 .95]);

% Create inner dotted lines
for i = 1:(n-1)
plot([-0.5*w 0.5*w], [(i+0.5)*w (i+0.5)*w], 'b:');
plot([-0.5*w 0.5*w], [-(i+0.5)*w -(i+0.5)*w], 'b:');
plot([-(i+0.5)*w -(i+0.5)*w], [-0.5*w 0.5*w], 'b:');
plot([(i+0.5)*w (i+0.5)*w], [-0.5*w 0.5*w], 'b:');
end

% Create middle dotted box
plot([-0.5*w 0.5*w], [(0.5)*w (0.5)*w], 'b:');
plot([-0.5*w 0.5*w], [-(0.5)*w -(0.5)*w], 'b:');
plot([-0.5*w -0.5*w], [-(0.5)*w (0.5)*w], 'b:');
plot([0.5*w 0.5*w], [-(0.5)*w (0.5)*w], 'b:');

% Make the lines in the open arms solid
H1=plot([-.5*w -.5*w .5*w .5*w],[.5*w (n+.5)*w (n+.5)*w .5*w],'b-');
```

```
set(H1,'LineWidth',0.5);
H2=plot([.5*w .5*w -.5*w -.5*w],...
        [-.5*w -(n+.5)*w -(n+.5)*w -.5*w],'b-');
set(H2,'LineWidth',0.5);

% Make the lines in the closed arms thick
H3=plot([.5*w (n+.5)*w (n+.5)*w .5*w],...
        [.5*w (.5)*w -(.5)*w -.5*w],'k-');
set(H3,'LineWidth',2.5);
H4=plot([-.5*w -(n+.5)*w -(n+.5)*w -.5*w],...
        [-.5*w -(.5)*w (.5)*w .5*w],'k-');
set(H4,'LineWidth',2.5);

% Draw the dot representing the mouse
% Make the dot red if the rat is rearing
if rearing
H5 = plot([a*w a*w],[b*w b*w],'r');
set(H5,'Marker','o','MarkerFaceColor','r','MarkerSize',[20/n]);

% Make the dot blue if the rat is engaging in risk assessment
elseif risk
H5 = plot([a*w a*w],[b*w b*w],'b');
set(H5,'Marker','o','MarkerFaceColor','b','MarkerSize',[20/n]);

% Make the dot green if the rat is not rearing
else
H5 = plot([a*w a*w],[b*w b*w],'g');
set(H5,'Marker','o','MarkerFaceColor','g','MarkerSize',[20/n]);
```

```
end
```

Appendix B

randomrun.m

```
%*************************************************************
%    The rat begins its run in the central square (at the
% origin). At the beginning of each time step, a random number
% between 0 and 1 is chosen.  A cumulative probability
% distribution and a series of if statements are used to define
% how this number will determine the rat's next movement.
%    After determining the rat's new position, during each time
% step, this program calls a function, elevatedplus(a,b,
% rearing, n), to display the rat's position in the maze and
% represent its behaviour.
%    The rat sometimes looks over the edges of the open arms
% and explores the walls, so the maze could be represented
% using external squares adjacent to each internal square to
% represent these behaviours.  To simplify the program, the
% external squares are not shown.  Instead, these behaviours
% are represented by changing the colour of the dot to red and
% keeping the dot in the internal square.  At the beginning of
```

```
% each time step, the rat is set to show no rearing behaviours.
% Therefore, if the rat does not explore an 'external square'
% during that time step, the dot will be green.
%    Finally, measures are taken to quantify the rat's movements.
%***************************************************************

% Set the rat to begin its run at the origin
a=0; % multiplied by square width to give x coordinate
b=0; % multiplied by square width to give y coordinate

% Set the number of internal squares in each arm
n = 5;

% In the beginning, the rat is not looking over an open arm
% (head-dipping) or exploring a wall (rearing), so these
% activities are set to 0. (Rearing covers both activities)
rearing = 0;

% Initialize all of the measurements we will be taking to 0.
enclosedentries = 0;
openentries = 0;
numberenclosed = 0;
numberopen = 0;

% This prompts the user to enter the number of time steps
timesteps = input('Enter the number of time steps: ');
% This sets a default if nothing is entered
if isempty(timesteps)
```

```
   timesteps = 10;
end

% Show the rat's intial position in the maze
elevatedplus(a,b,rearing, n)



% This loop is used to determine, execute, and display the
% virtual rat's movements and update each of the measures.
for i = 1:timesteps

% At the beginning of each time step, the program sets the rat
% as not rearing (or head-dipping).  Therefore, unless this is
% changed by the end of the time step, the dot will be green.
rearing = 0;

% This determines the direction of the rat's next movement
% based on a preset probability distribution and executes that
% movement.
a_old=a;
b_old=b;
p=rand;
if p < 0.2
a  = a_old + 1;
b = b_old;
elseif p < 0.4
a  = a_old - 1;
b = b_old;
```

```
elseif p < 0.6
b  = b_old + 1;
a = a_old;
elseif p < 0.8
b  = b_old - 1;
a = a_old;
end

% This changes the colour of the rat to red if it is determined
% to be occupying an external square and replaces the rat in
% the corresponding internal square.
if (a ~= 0)&(b ~= 0) % External square on the side of an arm
rearing = 1;
a = a_old;
b = b_old;
end

% External square at the end of an arm
if (a>n)|(a < -n)|(b>n)|(b < -n)
rearing =1;
a = a_old;
b = b_old;
end

% Display the rat in its new position.
elevatedplus(a,b, rearing, n)
pause(2)
```

```
% Get information on the rat's position
% Count the number of entries into the closed arms
if ((a_old==0)&(b_old==0)&(a==1))|((a_old==0)&(b_old==0)&(a==-1))
enclosedentries = enclosedentries + 1;
end

% Count the number of entries into the open arms
if ((a_old==0)&(b_old==0)&(b==1))|((a_old==0)&(b_old==0)&(b==-1))
openentries = openentries + 1;
end

% Find number of time steps spent in the closed arms
if (b == 0)&(a~=0)
numberenclosed = numberenclosed + 1;
end

% Find number of time steps spent in the open arms
if (a == 0)&(b~=0)
numberopen = numberopen + 1;
end
end
```

Appendix C

finalmodel.m

```
%************************************************************
%    The rat begins its run in the center square (at the
% origin). At the beginning of each time step, a random number
% between 0 and 1 is chosen.  A different cumulative
% probability distribution is set up for the central square, the
% open arms (moving inward and outward), the closed arms (moving
% inward and outward), and the squares adjacent to the center
% in the closed arms(moving inward and outward). There are 7 in
% all.  In the center, there is no consideration of inertia
% (i.e., no dependence on the direction of the last movement).
%    After determining the rat's new position, during each time
% step, this program calls a function, elevatedplus(a,b,
% rearing, N), to display the rat's position in the maze and
% represent its behaviour.
%    The rat sometimes looks over the edges of the open arms
% and explores the walls, so the maze could be represented
% using external squares adjacent to each internal square to
```

```
% represent these behaviours.  To simplify the program, the
% external squares are not shown.  Instead, these behaviours
% are represented by changing the colour of the dot to red and
% keeping the dot in the internal square.  At the beginning of
% each time step, the rat is set to show no rearing behaviours.
% Therefore, if the rat does not explore an 'external square'
% during that time step, the dot will be green. Similarly, if
% it engages in risk assessment, the dot will turn blue.
%   Finally, measures are taken to quantify the rat's movements.
%***************************************************************

% This command ensures that the same sequence of random numbers
% is always generated, so results can be replicated during the
% process of testing the model
rand('state',0);

% This allows the number of time steps to change, thus varying
% the length of the virtual trial. 230 timesteps is meant to
% represent a 5-minute experimental trial.
timesteps = 230;

% This represents the number of trials you would like to run
trials=1;

for f = 1:trials
% Set the rat to begin its run at (a*w, b*w)
a=0; % multiplied by width of squares to give x coordinate
b=0; % multiplied by width of squares to give y coordinate
```

```
% Set the number of internal squares in each arm and their
% widths
n = 3;
w = 1;

% In the beginning, we assume the rat is not looking over an
% open arm (head-dipping) or exploring a wall (rearing), so
% these activities are set to 0. (We use 'rearing' to represent
% both behaviours).  We also assume that the rat is not
% engaging in risk assessment.
rearing = 0;
risk = 0;

% Initialize all of the measurements we will be taking to 0.
closedentries = 0;
openentries = 0;
numberclosed = 0;
numberopen = 0;

% Show the rat's intial position in the maze
elevatedplus(a,b,rearing, risk, n, w)
pause(.9)

% In the experiments, rats were placed in te maze facing a
% closed arm, so this sets its initial head direction (i.e.
% direction of last movement) as facing a closed arm
a_old = (a-1);
```

```
b_old = b;

for z = 2:timesteps
rearing = 0;
risk = 0;

p = rand;

% This distribution determines the rat's next movement if it is
% in the central square
if (a==0)&(b==0)
      if p < .065 % Move into a closed arm
         a_new=a+1;
         b_new=b;
      elseif p < .13 % Move into the other closed arm
         a_new=a-1;
         b_new=b;
      elseif p < .64 % Stay still
         a_new=a;
         b_new=b;
      elseif p < .65 % Move into an open arm
         a_new=a;
         b_new=b+1;
      elseif p < .66 % Move into the other open arm
         a_new=a;
         b_new=b-1;
      elseif p < .69 % Rear up
         rearing=1;
```

```
        a_new=a;
        b_new=b;
     else
        risk=1; % Engage in risk assessment
        a_new=a;
        b_new=b;
     end

% These distributions determine the rat's next movement if it
% is in an open arm
elseif (a==0)&(b~=0)
  % Moving outward on an open arm
  if (abs(b_old)<abs(b))
     if p < .08  % Move forward
        a_new=a;
        b_new=b+(b-b_old);
     elseif p < .21  % Move backward
        a_new=a;
        b_new=b_old;
     elseif p < .55  % Stay still
        a_new=a;
        b_new=b;
     elseif p < .775  % Look over the edge
        a_new=a+1;
        b_new=b;
     else  % Look over the edge
        a_new=a-1;
        b_new=b;
```

```
        end
    % Moving inward on an open arm
    elseif (abs(b_old)>abs(b))
        if p < .635  % Move forward
            a_new=a;
            b_new=b+(b-b_old);
        elseif p < .635  % Move backward
            a_new=a;
            b_new=b_old;
        elseif p < .92  % Stay still
            a_new=a;
            b_new=b;
        elseif p < .96  % Look over the edge
            a_new=a+1;
            b_new=b;
        else  % Look over the edge
            a_new=a-1;
            b_new=b;
        end
    end

% These distributions determine the rat's next movement if it
% is in a closed arm
    % Moving outward on a closed arm
elseif (a~=0)&(b==0)
    if (abs(a_old)<abs(a))
        if a_old==0  % In a square adjacent to the center
            if p < .86  % Move forward
```

```
     a_new=a+(a-a_old);
     b_new=b;
   elseif p < .86  % Move backward
      a_new=a_old;
      b_new=b;
   elseif p < .96  % Stay still
      a_new=a;
      b_new=b;
   elseif p < .975  % Look over the edge
      a_new=a;
      b_new=b+1;
   elseif p < .99  % Look over the edge
      a_new=a;
      b_new=b-1;
   else  % Engage in risk assessment
      risk = 1;
      a_new=a;
      b_new=b;
   end

else  % In a square that is not adjacent to the center
   if p < .11  % Move forward
      a_new=a+(a-a_old);
      b_new=b;
   elseif p < .24  % Move backward
      a_new=a_old;
      b_new=b;
   elseif p < .83  % Stay still
```

```
            a_new=a;
            b_new=b;
         elseif p < .915  % Look over the edge
            a_new=a;
            b_new=b+1;
         else  % Look over the edge
            a_new=a;
            b_new=b-1;
         end
      end

   % Moving inward on a closed arm
   elseif (abs(a_old)>abs(a))
      if abs(a)==w   % In a square adjacent to the center
         if p < .05  % Move forward
            a_new=a+(a-a_old);
            b_new=b;
         elseif p < .08  % Move backward
            a_new=a_old;
            b_new=b;
         elseif p < .67  % Stay still
            a_new=a;
            b_new=b;
         elseif p < .71  % Look over the edge
            a_new=a;
            b_new=b+1;
         elseif p < .75  % Look over the edge
            a_new=a;
```

```
            b_new=b-1;
         else  % Engage in risk assessment
            risk = 1;
            a_new=a;
            b_new=b;
         end
      else % In a square that is not adjacent to the center
        if p < .42  % Move forward
            a_new=a+(a-a_old);
            b_new=b;
         elseif p < .44  % Move Backward
            a_new=a_old;
            b_new=b;
         elseif p < .90  % Stay still
            a_new=a;
            b_new=b;
         elseif p < .95  % Look over the edge
            a_new=a;
            b_new=b+1;
         else  % Look over the edge
            a_new=a;
            b_new=b-1;
         end
      end
   end
end

% This changes the colour of the rat to red if it is determined
```

```
% to be occupying an external square and places the rat in the
% corresponding internal square.
% External square on the side of an arm
if (a_new ~= 0)&(b_new ~= 0)
   rearing = 1;
   a_new = a;
   b_new = b;
end

% External square at the end of an arm
if (a_new>n)|(a_new < -n)|(b_new>n)|(b_new < -n)
   rearing =1;
   a_new = a;
   b_new = b;
end

% Display the rat in its new position.
elevatedplus(a_new,b_new, rearing, risk, n, w)
pause(.9)

% Get information on where the rat goes
% Count the number of entries into the closed arms
if ((a==0)&(b==0)&(a_new==1))|((a==0)&(b==0)&(a_new==-1))
   closedentries = closedentries + 1;
end

% Count the number of entries into the open arms
if ((a==0)&(b==0)&(b_new==1))|((a==0)&(b==0)&(b_new==-1))
```

```
   openentries = openentries + 1;
end

% Find number of time steps spent in the closed arms
if (b_new == 0)&(a_new~=0)
   numberclosed = numberclosed + 1;
end

% Find number of time steps spent in the open arms
if (a_new == 0)&(b_new~=0)
   numberopen = numberopen + 1;
end

% Reset the rat's last position if it has moved.
if (a~=a_new)|(b~=b_new)
   a_old=a;
   b_old=b;
end

% Let the newly occupied (x,y) coordinate become the square
% that is occupied at the beginning of the next time step
a=a_new;
b=b_new;

end

% Display all of the measures that were taken
percentopenentries = openentries/(openentries+closedentries)*100
```

```
percentopen = (numberopen/(numberclosed+numberopen))*100

closedentries

totalentries = openentries+closedentries


end
```

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