A Stochastic Model of Retinal Development in Zebrafish

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21 April 2009

1 Introduction

1.1 The Zebrafish and the Eye

While there is a large knowledge base in the scientific world of the biological features and physiological processes of the fully-formed eye, many developmental processes remain complete or partial mysteries. For neurological applications, a commonly used model organism is the zebrafish (*danio rerio*), which is related to humans in many ways as a fellow vertebrate. Its eye is similar to the human eye; both use a single lens to project incoming information onto the back of the eye, where cells in a specialized cell layer called the retina convert light information into a chemical signal that the brain can then interpret as an image.

1.2 The Retina

In vertebrates, the retina contains two major types of cells that can detect light, called rod and cone photoreceptors. Individual cone photoreceptors can detect certain colors of light and are largely used for seeing in the daytime, whereas rod photoreceptors detect light in black and white to aid in nighttime conditions. This study will focus on the cone photoreceptors, which are organized in a highly regular pattern in both humans and fishes.

Each cone photoreceptor can perceive certain wavelengths of light, which correspond to different colors. Humans have cones that can perceive red, green, and blue light; zebrafish can perceive ultra-violet light in addition to these three. The pattern of the zebrafish retina, shown in Figure 1, is a mosaic that has both vertical and horizontal patterning of red (R), green (G), blue (B), and ultra-violet (U) photoreceptor cones.[1] The more complex horizontal repeating pattern (BRGUGRB) can be viewed as "mirrored" around the blue and ultra-violet cones, whereas the less-complicated vertical patterns are simply alternations of red and green or blue and ultra-violet cones.

The retina is an epithelium, or a continuous sheet of cells such that all cell borders are flush with one another. This sheet is maintained by attractive adhesive interactions between cell membranes. According to Malcolm Steinberg's

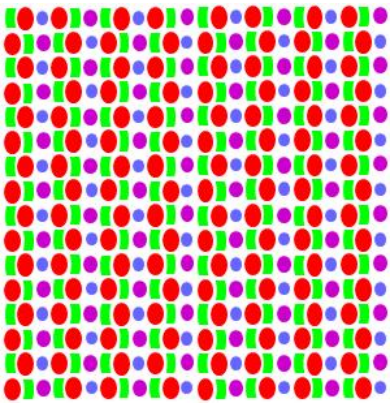

Figure 1: The photoreceptor cone mosaic of the zebrafish retina.

Differential Adhesion Hypothesis, certain cells within organisms can organize themselves based on differing levels of adhesion between different types of cells. Steinberg's studies on cell-cell adhesion show that if cells from two different body tissues are mixed together, with time they will separate into groups, showing that cells can preferentially adhere to one cell over another.[2]

1.3 Retinal Development

While the exact mechanics of the development of new retinal tissue are unknown, biological studies show that new photoreceptors are created in an un-patterned region of the retinal epithelium. As more new cells are created, existing un-patterned photoreceptors are forced to arrange into the correct pattern and add to the mosaic. Biological data suggests that cells undergo only a few rearrangements before becoming a part of the formed retina.

Our hypothesis is that these photoreceptor cones organize themselves in the correct order using preferential adhesion between certain cells. That is to say, as new cells rearrange to form the retina, interactions between certain cells guide them towards the correct pattern rather than letting them fall into pattern by chance. In order to test the hypothesis under a statistical model, the process of cells rearranging was viewed as a stochastic process, where the cells can change positions relative to one another with fixed probabilities in a randomized process.

1.4 Markov Chains

A stochastic model of the cell patterning process would greatly simplify the intricate and largely mysterious process of cell rearrangement. While it obviously leaves out some of the biological nuances involved, a mathematical model can lead us to important general conclusions about how the cells interact with each other. The Markov Chain is a logical choice of model because of the multiple

"states" the developing retina may go through before falling into the correct pattern.

A Markov Chain is stochastic process with the Markov property, which says: *given the current state, future states are independent of the past states.* In other words, if a process is in State X, then moves to State Y, the probability of the system moving from State Y to State Z is dependent only on what State Y is and completely independent of what State X was. In the case of the developing retina, as new, unorganized cells rearrange to form the pattern, they go through transient arrangements, and each subsequent arrangement occurs with a probability based only on the previous one. For a Markov Chain model, these arrangements are the "states" of the system.

1.5 Absorbing Markov Chains and the Drunkard's Walk

Markov Chains can either continue forever, such as a chain that predicts commodity prices, or they can end by "absorbing" into permanent states. An absorbing Markov Chain ends when it enters an absorbing state, or a specific state with the characteristic that once the system reaches that state, it can never leave it. A common example of an absorbing Markov Chain is the Drunkard's Walk problem. [3]

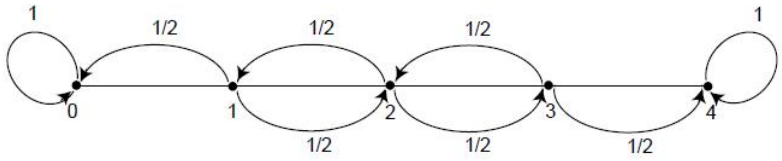

Figure 2: A diagram of the Drunkard's Walk problem. *Source:* [3]

A city block has five buildings on it. At one corner is a drunkard's house (Building 0), and at the other corner is a bar (Building 4), with three closed buildings in between (Buildings 1, 2, and 3). If the man is at one of the closed buildings, he will walk either left or right with equal probability to the building next door. However, if he arrives at his house or at the bar, he will stay there. Thus, Buildings 1, 2, and 3 are transient states since the drunkard can leave them, and Buildings 0 or 4 are absorbing states since once he is there, he will stay. We can construct a transition matrix (below) to represent the probabilities of moving from one state to another, where each entry represents the probability of going from the row's state to the column's state.

$$\mathbf{P} = \begin{array}{c|ccccc} & 0 & 1 & 2 & 3 & 4 \\ 0 & 1.0 & 0.0 & 0.0 & 0.0 & 0.0 \\ 1 & 0.5 & 0.0 & 0.5 & 0.0 & 0.0 \\ 2 & 0.0 & 0.5 & 0.0 & 0.5 & 0.0 \\ 3 & 0.0 & 0.0 & 0.5 & 0.0 & 0.5 \\ 4 & 0.0 & 0.0 & 0.0 & 0.0 & 1.0 \end{array}$$

The third row of the matrix shows that if the drunkard is at Building 2, he can move to either Building 1 or Building 3, each with probability 0.5. However, if the drunkard is at Building 0, his house, he must stay there with probability 1, making Building 0 an absorbing state. Since the drunkard will either move or stay in either the bar or his house, the probabilities across a row must sum to 1. In this case, since he will either go left or right from Buildings 1, 2, or 3, the probability of him staying put at one of these buildings is 0.

While the development of the retina is not exactly analogous to a drunken man walking between buildings, the absorbing nature of the Markov Chain model is. Just as the man will keep going from building to building until he finds a place he wants to be, the photoreceptors will continue to rearrange themselves until they form the correct pattern.

2 Methods

2.1 Markov Chain Model Design, Assumptions, and Limitations

A "state" for the cell rearrangement process was defined as *a uniquely ordered sequence of specifically colored photoreceptor cones*. For example, {Red-Green-Blue}, abbreviated as {RGB}, is a state consisting of three cones, colored red, green, and blue and aligned in that order. The state {RBG} is a different and unique state, as is {GRB}. The states {RGB} and {BGR}, despite being essentially the same sequence but in the reverse order, were considered to be unique states. The reasoning behind this decision will be discussed later.

Since biologically the photoreceptors rearrange themselves in order to align into the correct pattern, a transition from one state to another state represents the cells changing from one sequence to another sequence. For example, a transition can represent the act of cells ordered as {RGB} changing their order to {RBG}; here, the green and blue cones have switched places.

The model assumes that a single transition can only represent the act of two adjacent cells switching places. The example above of {RGB} changing to {RBG} is an allowed transition, since the adjacent green and blue cones switch places. The transition from {RGB} to {BRG}, however, is not allowed, since there is no single place-switch that can accomplish this rearrangement. The only way for the system to achieve a rearrangement like this is through other transient states. The {RGB} to {BRG} rearrangement, for example, can be accomplished through two allowed transitions: {RGB} to {RBG}, and then {RBG} to {BRG}. While it may be biologically possible for non-adjacent cells to switch places, this would happen significantly less often than switches between adjacent cells. Allowing for such transitions would greatly complicate the model without adding much to it, so they were not allowed.

Additionally, just as the drunkard must move to a new building if he is not at home or the bar, this model assumes that when the system is in a transient state, cells must trade places and an allowed transition will occur with probability 1.

Biologically, once the photoreceptors are in the correct pattern, they become part of the retinal mosaic and no longer move relative to one another. Thus, the model's absorbing states represent the photoreceptors having aligned in the correct pattern, where they will switch to a different state with 0 probability.

Our model assumes that all cell colors are represented in the correct proportions. Biological evidence suggests that new photoreceptors are created in the same proportions as are present in the overall mosaic. Thus, if our target pattern (and absorbing state) is {RGB}, all states for the system contain exactly one red, one green, and one blue cone, such that {GRR} or {BGB} are not possible states. We will also assume that as new cells are created, they are created in random sequences, such that the probability of starting in any given state is the same for all possible states.

The number of possible states for the system increases exponentially with the number of cells in the sequence. The system has many more possible states when considering a sequence of twenty cells than when considering a sequence of only four. We therefore considered a sequence of only four cells, which yielded a manageable total of 24 possible states in the full model.

2.2 Simple Red and Green Model

Though the complete retina contains four different types of photoreceptor cones, we started by looking at a simple two-color model of a hypothetical retina. This model contains only red and green cones, and the correct pattern was defined simply as alternating colors.

Modeling a sequence of only four cells, the system has six possible states under our assumptions: {RRGG}, {GGRR}, {RGGR}, and {GRRG} are the transient states, and {GRGR} and {RGRG} are the absorbing states. Each entry in the transition matrix below represents the probability of switching from the state listed for the entry's row to the state listed for the entry's column. In this first model, all allowed transitions occur with equal probability, meaning that adjacent cells are randomly switching places with no preference for one switch over another.

$$\mathbf{P}_{random} = \begin{array}{c|cccccc} & \textit{RRGG} & \textit{GGRR} & \textit{RGGR} & \textit{GRRG} & \textit{GRGR} & \textit{RGRG} \\ \hline \textit{RRGG} & 0.67 & 0.00 & 0.00 & 0.00 & 0.00 & 0.33 \\ \textit{GGRR} & 0.00 & 0.67 & 0.00 & 0.00 & 0.33 & 0.00 \\ \textit{RGGR} & 0.00 & 0.00 & 0.33 & 0.00 & 0.33 & 0.34 \\ \textit{GRRG} & 0.00 & 0.00 & 0.00 & 0.33 & 0.33 & 0.34 \\ \textit{GRGR} & 0.00 & 0.00 & 0.00 & 0.00 & 1.00 & 0.00 \\ \textit{RGRG} & 0.00 & 0.00 & 0.00 & 0.00 & 0.00 & 1.00 \end{array}$$

With a sequence of four cells, there are only three possible allowed switches: cells one and two, cells two and three, or cells three and four can switch places with each other. Since the Markov Chain model assumes that an allowed switch will always occur if the system is in a transient state, the probabilities across a row sum to 1. This matrix is organized in the canonical form of an absorbing Markov Chain transition matrix, where absorbing states are listed at the end

of the row and column lists. The canonical form of the matrix will play an important role later in the numerical analysis of the system.

Unlike the drunken man example, where he *must* leave Buildings 1, 2, or 3 if he is in front of them, this system allows for the system to stay in the same state under our definition of an allowed transition. The first row of the matrix represents transition probabilities from the state {RRGG}. If the first two cells switch places (one of the three aforementioned allowed transitions for a sequence of four cells), the system remains in {RRGG}, since the two red cones switching places yields the same sequence. The same goes for green cells three and four switching; the system remains {RRGG}. Cells two and three switching yields {RGRG}, an absorbing state. Thus, two out of three switches yields {RRGG}, and the other switch yields {RGRG}; these probabilities are reflected in the appropriate column entries of the first row.

The transition matrix above lists probabilities from going from one state to another state in a single transition. Biologically, cells do not simply switch places once and stop – our model assumes that they will continue to switch places until the cells are in the right pattern and the system absorbs. Thus, this matrix can be used to give probabilities not only for one switch into the future, but also the probabilities of being in a certain state after two or ten transitions. This can be achieved by raising the matrix to the second or tenth power, respectively.

$\mathbf{P}^2_{random} =$

	RRGG	*GGRR*	*RGGR*	*GRRG*	*GRGR*	*RGRG*
RRGG	0.44	0.00	0.00	0.00	0.00	0.56
GGRR	0.00	0.44	0.00	0.00	0.56	0.00
RGGR	0.00	0.00	0.11	0.00	0.44	0.45
GRRG	0.00	0.00	0.00	0.11	0.45	0.44
GRGR	0.00	0.00	0.00	0.00	1.00	0.00
RGRG	0.00	0.00	0.00	0.00	0.00	1.00

$\mathbf{P}^{10}_{random} =$

	RRGG	*GGRR*	*RGGR*	*GRRG*	*GRGR*	*RGRG*
RRGG	0.02	0.00	0.00	0.00	0.00	0.98
GGRR	0.00	0.02	0.00	0.00	0.98	0.00
RGGR	0.00	0.00	$< .01$	0.00	0.49	0.50
GRRG	0.00	0.00	0.00	$< .01$	0.50	0.49
GRGR	0.00	0.00	0.00	0.00	1.00	0.00
RGRG	0.00	0.00	0.00	0.00	0.00	1.00

Here, we see that if the system starts in {GGRR}, it will remain {GGRR} after two switches with probability 0.44. Looking at the tenth power of the transition matrix, is becomes clear the probabilities of the system being absorbed after many switches approaches 1. This make sense because if the system absorbs in two out of the six possible states, we would expect that after ten switches, there is a good chance the system would have ended up in an absorbing state.

2.3 Wait Time

What separates an absorbing Markov Chain from other types of chains is that an absorbing chain, given enough time, will end (absorb) with probability 1. The time it takes for the system to end, however, is dependent on where the system starts. The drunken man, for example, will get to his home or the bar faster, on average, if he starts closer to one of them. If he is at Building 3, it is possible for him to end up at the bar after only one transition, but if he starts at Building 2, he must go to one of the other buildings first before he can get to his house or the bar.

While it is not possible to predict exactly which route the drunkard will take to get to either the bar or his house from his starting point, it is possible to predict the average number of transitions it will take. Similarly, while we cannot predict which cell switches will take place, we can predict how many switches, on average, it will take to until the cells align in the correct pattern. The number of transitions it takes for the system to absorb is known as the *wait time*. The wait time for a system which starts in an absorbing state (for example, if the drunkard starts at his house or the bar, or if the photoreceptors are already in the correct pattern), is 0.

When the transition matrix is in canonical form, with the absorbing states' rows at the bottom and their columns at the right, the matrix can be broken down into pieces that have special properties. The diagram below shows the breakdown.

$$\mathbf{P} = \left(\begin{array}{c|c} Q & R \\ \hline 0 & I \end{array}\right)$$

The most important part of the canonical form is the matrix Q, which represents the probabilities of the system switching from one transient state to another transient state. Information in this matrix helps dictate how long the system will stay in transient states until it is absorbed. Q can be used to find average wait times given a certain starting state. The formula $t = (I - Q)^{-1}c$ tells us average wait times based on Q, where t is a vector containing the average wait times given each starting state, c is a column vector with 1 for all entries, and I is an n by n identity matrix, where n equals the total number of transient states (in this case, 4).

In the simple red and green retina example, the matrix Q is comprised of the sixteen entries shared between the top four rows and first four columns of the canonical form transition matrix. Applying the formula above, we can generate a list of the average wait times given a specific starting state. This data is shown in Table 1.

Table 1. R-G Model Average Wait Times

Starting State	*Average Wait Time*
RRGG	3.0
GGRR	3.0
RGGR	1.5
GRRG	1.5
GRGR	0
RGRG	0

Here, we see that if the photoreceptors start out organized as {RRGG} or {GGRR}, the average wait time to absorb is longer than if they start as {RGGR} or {GRRG}. This result can be traced back directly to the transition matrix; two out of three possible switches for {RGGR} or {GRRG} lead to absorption, whereas only one out of three possible switches for {RRGG} or {GGRR} lead to the correct pattern.

2.4 Preferential Switching and State Ranks

The average wait times above are for a model where any of the three possible switches can happen with equal probability. In order to test the hypothesis that the cells are rearranging based on attractive interactions between one another, our model must account for certain switches occurring with higher probability than others.

A *preferential switch* is defined as a transition that would bring the system "closer" to absorbing. Biologically speaking, a preferential switch would make the sequence of cells closer to the correct pattern. In order to define which states are "closer" than others, all of the possible states were ranked based on their average wait times under the no-preference model. States with shorter wait times were ranked higher than those with longer wait times. The absorbing states are already as close as possible to absorbing, so they had the highest possible rank.

Having already calculated wait times under a no-preference switching strategy, we can assign ranks to the simple red and green model. The absorbing states {RGRG} and {GRGR} have rank 1, {GRRG} and {RGGR}, both with average wait times of 1.5 have rank 2, and {RRGG} and {GGRR} with average wait times of 3 have rank 3.

Cells arranged as {GRRG}, for example, can switch to either {GRGR}, {RGRG}, or remain as {GRRG} under the rules of allowed switching. Using preferential switching and these rankings, {GRRG} will switch to {GRGR} or {RGRG}, both absorbing states, with a higher probability than remaining as {GRRG}.

The preferential switching model requires a new transition matrix, since now the probabilities of switching from one state to another are different than in the random, no-preference switching model. In the transition matrix below, preferred switches are given twice as much weight as non-preferred switches. Looking at the third row, we see that {RGGR} absorbs after one transition

with probability .8 (.8 = .4 + .4), whereas before the probability was only .67 (.67 = .34 + .33) under the no-preference model.

$$\mathbf{P}_{pref:2x} = \begin{array}{c|cccccc} & RRGG & GGRR & RGGR & GRRG & GRGR & RGRG \\ \hline RRGG & 0.50 & 0.00 & 0.00 & 0.00 & 0.00 & 0.50 \\ GGRR & 0.00 & 0.50 & 0.00 & 0.00 & 0.50 & 0.00 \\ RGGR & 0.00 & 0.00 & 0.20 & 0.00 & 0.40 & 0.40 \\ GRRG & 0.00 & 0.00 & 0.00 & 0.20 & 0.40 & 0.40 \\ GRGR & 0.00 & 0.00 & 0.00 & 0.00 & 1.00 & 0.00 \\ RGRG & 0.00 & 0.00 & 0.00 & 0.00 & 0.00 & 1.00 \end{array}$$

New wait times can now be generated by finding the new Q matrix and by using the same equation as before. Average wait times for the preferential switching model are shown in Table 2.

Table 2. R-G Model Average Wait Times With Preferential Switching.

Starting State	*Average Wait Time*
RRGG	2
GGRR	2
RGGR	1.25
GRRG	1.25
GRGR	0
RGRG	0

In all cases, the average wait time has decreased, showing that for this hypothetical retina, preferred switching leads to a more efficient process.

Of course, the weight for a preferred switch does not necessarily have to be only two; it could be any weight we choose. Taking the idea of preferential switching to the extreme, we could give complete preference to the higher-ranked switch, meaning the system will always take the preferred switch with probability 1. This "perfect-switching" model, whose transition matrix and wait times are listed below, represents a system which always takes the shortest possible route to the absorbed state.

$$\mathbf{P}_{perfect} = \begin{array}{c|cccccc} & RRGG & GGRR & RGGR & GRRG & GRGR & RGRG \\ \hline RRGG & 0.00 & 0.00 & 0.00 & 0.00 & 0.00 & 1.00 \\ GGRR & 0.00 & 0.00 & 0.00 & 0.00 & 1.00 & 0.00 \\ RGGR & 0.00 & 0.00 & 0.00 & 0.00 & 0.50 & 0.50 \\ GRRG & 0.00 & 0.00 & 0.00 & 0.00 & 0.50 & 0.50 \\ GRGR & 0.00 & 0.00 & 0.00 & 0.00 & 1.00 & 0.00 \\ RGRG & 0.00 & 0.00 & 0.00 & 0.00 & 0.00 & 1.00 \end{array}$$

The average wait times in Table 3 (below) are all 1 for transient states because it is possible to reach an absorbing state from any other state in one and only one transition, assuming the correct switch was always made.

Table 3. R-G Model Average Wait Times With Perfect Switching.

Starting State	*Average Wait Time*
RRGG	1
GGRR	1
RGGR	1
GRRG	1
GRGR	0
RGRG	0

As far as the retina is concerned, the perfect-switching model represents a system in which cells always move into the correct alignment in the fewest number of steps. While it may seem unlikely that insentient objects such as cells somehow "know" what the most efficient route to the correct pattern is, it is possible that cell-cell adhesions could guide cell movements in a near-perfect manner.

If our hypothesis is correct, that cell-cell adhesions play a role in guiding the cells into the correct pattern, we would expect the wait times of the system to be somewhere between those of the randomly-switching model and those of the perfect-switching model. The more significant a role cell-cell adhesions play, the more the system behaves like the perfect-switching model.

2.5 The Four-Color Model

Having tested our methods on the simple, two-color hypothetical retina, we expanded the model to include all four colors to test our hypothesis on the real retina. While in the full mosaic the shortest repeating pattern is seven photoreceptors in length (from one blue cone to the next blue cone), we chose to work with a four cone sequence for reasons previously discussed.

Absorbing states for the four-color model were {BRGU} and {UGRB}, symmetric sequences which are both present in any row of the mosaic. (Starting at any ultra-violet cone in the mosaic, the sequence to the left of it is the first absorbing state, and the sequence to the right is the second). Allowing for both of these absorbing states meant that a sequence of cells could achieve the correct pattern as either half of the full, seven-cell repeat.

Under the assumption that colors are all present in the correct proportions, each of the possible states in the model contained one blue, one green, one red, and one ultra-violet photoreceptor cone, giving a total of 24 possible states: 22 transient states and the 2 aforementioned absorbing states.

As before, an allowed transition represents any two adjacent photoreceptor cells switching places. Also as before, there are three possible transitions that can take place in a sequence of four cells. However, unlike the red and green model, where the system could stay in the same state after a transition, with a four-color model, the system always changes to a different state after a switch, unless, of course, is has already absorbed.

To test the hypothesis that cell-cell interactions are guiding the sequence of cells to the correct pattern by preferential switching, we ranked the states, as before, based on average wait times under a no-preference, randomly switching model. These ranks were then used to determine transition probabilities under preferential-switching models.

Three preferential-switching models were created using the assigned ranks. The first gives a preferred switch twice as much weight as a non-preferred switch, as was done in the simple red and green model above. The second model gives preferred switches three times as much weight, and the final model operates under perfect switching. Average wait times were recorded for each of the models.

All calculations were performed in R version 2.8.1. Transition matrices for the four-color models are displayed in the Appendix.

3 Results

Wait times given by the 24×24 transition matrix for the four-color model yielded state rankings to be used in the preferential switching models. Table 4 shows the average wait times under no-preference switching as well as the rank assigned to each state.

Table 4. Four-Color Model No-Preference Wait Times and Ranks

Starting State	*Average Wait*	*Rank*	*Starting State*	*Average Wait*	*Rank*
BGRU	11.5	3	RBUG	13.5	4
BGUR	15.8	6	RGBU	15.7	5
BRUG	10.7	2	RGUB	16.8	8
BUGR	16.8	8	RUBG	16.0	7
BURG	15.7	5	RUGB	15.8	6
GBRU	15.8	6	UBGR	15.7	5
GBUR	16.0	7	UBRG	16.8	8
GRBU	16.8	8	UGBR	10.7	2
GRUB	15.7	5	URBG	15.8	6
GUBR	13.5	4	URGB	11.5	3
GURB	10.7	2	BRGU	0	1
RBGU	10.7	2	UGRB	0	1

Table 5 shows average wait times under our four total models for each of the possible starting states, which are ordered by their rank. Overall wait times listed at the end of the table are simply the average of the wait times of all possible states in any given model.

These results show that as preferential switches are weighted more heavily, the system gets more efficient. Operating under random, no preference switching, the system takes 13.24 transitions on average to absorb, whereas it takes an average of only 1.83 switches under perfect switching conditions. As weights for preferred switches are increased and the overall wait times for the system decrease, the system behaves more like the perfect-switching model.

Table 5. Average Wait times for various four-color preferential switching models.

		Average Wait Time			
State	*Rank*	*No Preference Model*	*Weighted 2x Model*	*Weighted 3x Model*	*Perfect Model*
UGRB	1	0.0	0.0	0.0	0
BRGU	1	0.0	0.0	0.0	0
BRUG	2	10.7	4.4	3.0	1
GURB	2	10.7	4.4	3.0	1
RBGU	2	10.7	4.4	3.0	1
UGBR	2	10.7	4.4	3.0	1
BGRU	3	11.5	4.8	3.2	1
URGB	3	11.5	4.8	3.2	1
GUBR	4	13.5	6.2	4.4	2
RBUG	4	13.5	6.2	4.4	2
BURG	5	15.7	7.5	5.3	2
GRUB	5	15.7	7.5	5.3	2
RGBU	5	15.7	7.5	5.3	2
UBGR	5	15.7	7.5	5.3	2
BGUR	6	15.8	7.6	5.4	2
GBRU	6	15.8	7.6	5.4	2
RUGB	6	15.8	7.6	5.4	2
URBG	6	15.8	7.6	5.4	2
GBUR	7	16.0	8.4	6.3	3
RUBG	7	16.0	8.4	6.3	3
GRBU	8	16.8	8.6	6.4	3
RGUB	8	16.8	8.6	6.4	3
BUGR	8	16.8	8.6	6.4	3
UBRG	8	16.8	8.6	6.4	3
Overall		**13.24**	**6.31**	**4.51**	**1.83**

4 Conclusions

Results for the overall wait times suggest that our hypothesis is correct. Knowing that *in vivo*, sequences of photoreceptor cones only require several rearrangements to achieve the correct pattern, the overall wait times suggest that the developing retina acts far more like the perfect-switching model than the randomly switching model.

The preferential-switching strategy, which accounted for attractive forces between certain cells by "guiding" the system to absorbing states, helped the models become more similar to the perfect-switching model. This suggests that attractive forces from cell-cell adhesions can help un-patterned cells in the developing retina more efficiently arrange themselves into the correct pattern than if left to chance alone.

This Markov Chain model, of course, does not account for many of the bio-

logical factors that could potentially be at play in the developing zebrafish eye. Within the zebrafish retina, there are many different types of cells (rod photoreceptors, to name one) that could be involved with the process, as could a variety of other physical and chemical interactions within the tissue. Despite the other potential players that may be involved, our results suggest that the adhesive interactions between the photoreceptor cones themselves are likely important and should not be ignored.

As far as a statistical model is concerned, future work could examine more complicated Markov Chains that were outside the limitations of this study. For example, biological evidence could be used to develop a more sophisticated cell rearrangement strategy that also looked at a sequence of more than four cells. Though it is rare for nature to perfectly mimic mathematics, models like these can point biologists in the right direction and help unravel the mysteries behind phenomena such as the development of the photoreceptor cone mosaic in zebrafish.

5 Acknowledgements

I would like to thank Dr. Ed Rothman of the UM Department of Statistics for his invaluable help and guidance in designing the models.

I would also like to thank Dr. Pamela Raymond and Linda Barthel of the UM Department of Molecular, Cellular, and Developmental Biology for their help with biological parts of the study and for four years of teaching and continued support, as well as Dr. David Lubensky and Dr. Guillaume Salbreux of the UM Department of Physics.

Thank you as well to Dr. Ted Allison, currently of the University of Alberta Department of Biological Sciences, for welcoming me into scientific research.

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A Transition Matrices for Four-Color Models

$\mathbf{P}_{random} =$

	BGRU	BGUR	BRUG	BUGR	BURG	GBRU	GBUR	GRBU	GRUB	GUBR	GURB	RBGU	RBUG	RGBU	RGUB	RUBG	RUGB	UBGR	UBRG	UGBR	URBG	URGB	BRGU	UGRB
BGRU	0.00	0.33	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00
BGUR	0.33	0.00	0.00	0.33	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
BRUG	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00
BUGR	0.00	0.33	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00
BURG	0.00	0.00	0.33	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00
GBRU	0.33	0.00	0.00	0.00	0.00	0.00	0.33	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GBUR	0.00	0.33	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GRBU	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GRUB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.33	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GUBR	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00
GURB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33
RBGU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00
RBUG	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RGBU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.33	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RGUB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RUBG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.33	0.00	0.00	0.00
RUGB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.33	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00
UBGR	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.33	0.00	0.00	0.00	0.00
UBRG	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.33	0.00	0.00	0.00
UGBR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.00	0.00	0.33
URBG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.33	0.00	0.00	0.33	0.00	0.00
URGB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.33	0.00	0.00	0.00	0.33	0.00	0.00	0.33
BRGU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00
UGRB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00

$\mathbf{P}_{pref:2x} =$

	BGRU	BGUR	BRUG	BUGR	BURG	GBRU	GBUR	GRBU	GRUB	GUBR	GURB	RBGU	RBUG	RGBU	RGUB	RUBG	RUGB	UBGR	UBRG	UGBR	URBG	URGB	BRGU	UGRB
BGRU	0.00	0.25	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.50	0.00
BGUR	0.50	0.00	0.00	0.25	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
BRUG	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.50	0.00
BUGR	0.00	0.50	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00
BURG	0.00	0.00	0.50	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00
GBRU	0.50	0.00	0.00	0.00	0.00	0.00	0.25	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GBUR	0.00	0.40	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GRBU	0.00	0.00	0.00	0.00	0.00	0.50	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GRUB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.50	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GUBR	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.00
GURB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.50
RBGU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.50	0.00
RBUG	0.00	0.00	0.40	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RGBU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.50	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RGUB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RUBG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.40	0.00	0.00	0.00	0.40	0.00	0.00	0.00
RUGB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.25	0.00	0.00	0.00	0.00	0.00	0.50	0.00	0.00	0.00
UBGR	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.50	0.00	0.00	0.00	0.00
UBRG	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.50	0.00	0.00	0.00
UGBR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.00	0.00	0.50
URBG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.25	0.00	0.00	0.50	0.00	0.00
URGB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.25	0.00	0.00	0.00	0.25	0.00	0.00	0.50
BRGU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00
UGRB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00

$\mathbf{P}_{pref:3x} =$

	BGRU	BGUR	BRUG	BUGR	BURG	GBRU	GBUR	GRBU	GRUB	GUBR	GURB	RBGU	RBUG	RGBU	RGUB	RUBG	RUGB	UBGR	UBRG	UGBR	URBG	URGB	BRGU	UGRB
BGRU	0.00	0.20	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.60	0.00
BGUR	0.60	0.00	0.00	0.20	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
BRUG	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.60	0.00
BUGR	0.00	0.60	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00
BURG	0.00	0.00	0.60	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00
GBRU	0.60	0.00	0.00	0.00	0.00	0.00	0.20	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GBUR	0.00	0.43	0.00	0.00	0.00	0.43	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GRBU	0.00	0.00	0.00	0.00	0.00	0.60	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GRUB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.60	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GUBR	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.43	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.43	0.00	0.00	0.00	0.00
GURB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.60
RBGU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.60	0.00
RBUG	0.00	0.00	0.43	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.43	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RGBU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.60	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RGUB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.60	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RUBG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.14	0.00	0.00	0.00	0.43	0.00	0.00	0.00	0.43	0.00	0.00	0.00
RUGB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.20	0.00	0.00	0.00	0.00	0.00	0.60	0.00	0.00
UBGR	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.60	0.00	0.00	0.00	0.00	0.00
UBRG	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.60	0.00	0.00	0.00
UGBR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.00	0.00	0.60
URBG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.20	0.00	0.00	0.60	0.00	0.00
URGB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.20	0.00	0.00	0.00	0.20	0.00	0.00	0.60
BRGU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00
UGRB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00

$\mathbf{P}_{perfect} =$

	BGRU	BGUR	BRUG	BUGR	BURG	GBRU	GBUR	GRBU	GRUB	GUBR	GURB	RBGU	RBUG	RGBU	RGUB	RUBG	RUGB	UBGR	UBRG	UGBR	URBG	URGB	BRGU	UGRB
BGRU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00
BGUR	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
BRUG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00
BUGR	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
BURG	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GBRU	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GBUR	0.00	0.50	0.00	0.00	0.00	0.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GRBU	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GRUB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
GUBR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.50	0.00	0.00	0.00	0.00
GURB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00
RBGU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00
RBUG	0.00	0.00	0.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.50	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RGBU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RGUB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
RUBG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.50	0.00	0.00	0.00	0.50	0.00	0.00	0.00
RUGB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00
UBGR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00	0.00
UBRG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00	0.00	0.00
UGBR	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00
URBG	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00	0.00
URGB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00
BRGU	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00
UGRB	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	1.00