The Role of Stochasticity in the Evolution of Animal Pattern and Morphology

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1 INTRODUCTION

This report details an investigation of a gene regulatory network's (GRN's) dynamics to explore trends in the final genotypes for a variety of starting phenotypes. Steven Gould postulated that if one were to rerun the evolutionary process, the outcome and diversity of life would be vastly different;[1] however, much work has been done to understand convergent evolution and how similar phenotypes can evolve through independent pathways.[2] Multiple genotypes can correspond to the same phenotype leading to a many-to-one mapping from the genotype space to the phenotype space. These genotypes may depend on their ancestral genotypes and the path through the phenotype space traversed. By restarting and rerunning the evolutionary process while selecting the same phenotype, a variety of different genotypes can be accessed. Many mechanisms govern the gene interactions in three gene topologies and they can be classified into six distinct mechanisms.[3] We investigate the obtained genotypes for three of the fundamental mechanisms: bistable, classical and the frozen oscillator depicted in figure 1.

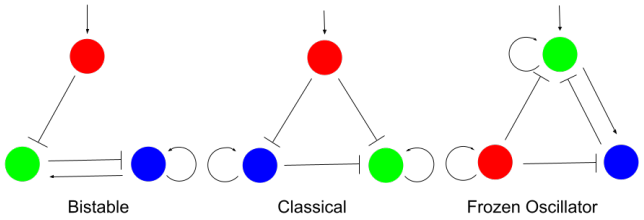


Figure 1: The three gene topology using three distinct mechanisms to generate the stripe pattern with arrows indicating: morphogen inputs, inhibitions and activations.

A series of coupled ordinary differential equations are used to describe the dynamics of GRNs and they are frequently used in evolutionary studies to capture gene expression and protein concentrations. [4] We consider a simple three-gene topology consisting of a red, a blue and a green gene that have activators and inhibitors acting between them. These interactions can be stored as a 3×3 square matrix and each entry can be mutated to obtain a new genotype during evolution.

In this project, the green gene acts as an output and the weights that govern the interactions between the genes are chosen to generate a stripe pattern. These weights were then mutated and a particular phenotype was selected. By analysing how these weights evolve and examining the distributions of the final weights, we investigate how the distance between the initial and selected phenotypes, ΔP affects the final weights and the path that is traversed in the phenotype space for the bistable mechanism. From this, we hope to elucidate the role of stochasticity in evolution and understand common relationships between genotypes when rerunning the evolutionary process. We also aim to understand how a genotype's past constrains its future by determining how the spread of the gene interaction weights varies with ΔP. [5]

2 METHODS

The procedure to carry out the evolutionary process is illustrated in figure 2. Firstly, we solved the GRN for the steady state, this was done numerically by solving the equation

$$\frac{dg_{ij}}{dt} = \phi(\chi(\sum_{l=1}^{3} W^{il} g_{lj} + M)) - \lambda g_{ij} \qquad (1)$$

where χ is a heaviside function and ϕ is a Michaelis-Menten function.[6] This equation encompasses the interaction between the genes in the summation over a column of weights, W, the morphogen input in M and a degradation rate in λ.

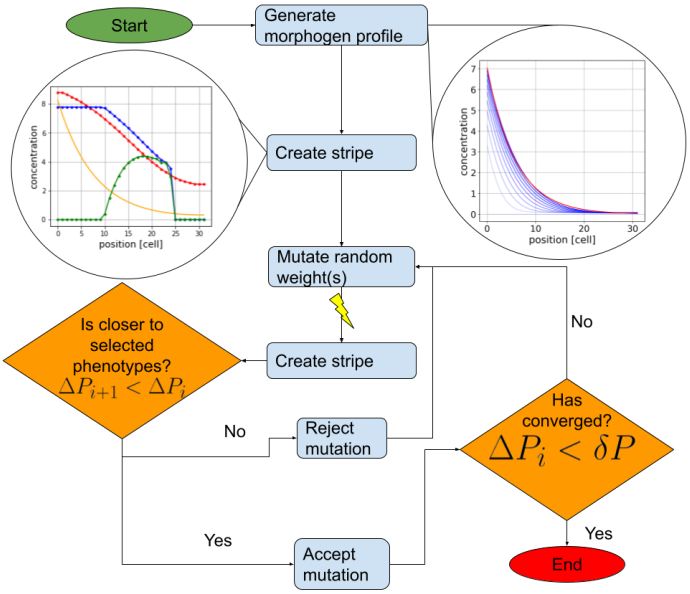


Figure 2: Flowchart illustrating the procedure for generating the stripe, evolving the system and implementing selection.

The morphogen input into the genes was determined by solving the diffusion equation for a single morphogen input in the leftmost cell,[7] this generated an exponentially decaying gradient that was passed into a specified gene (depending on the mechanism). The stripe was then generated and defined by a continuous region consistently above half the maximum concentration with its ends being at least below half of the maximum value. The phenotypes of the system,

being the position and width of the stripe, were then calculated.

We then implemented mutation by varying components of W. After this, the stripe was regenerated and its phenotypes were recalculated. The Euclidean distance between the calculated phenotypes and phenotypes being selected for was calculated (taking into account the usual deviations in each phenotype component) and compared to the previous distance. If this distance was less than the last, the mutation was accepted, otherwise, it was rejected. This process repeats until the phenotype distance falls below a given threshold. This process was repeated for 100 samples for nine different values of ΔP for the bistable mechanism. The final weights were compared against each other for each genotype to determine correlations between them. For ones that did correlate linearly a line of best fit was created and its parameters were recorded.

3 RESULTS

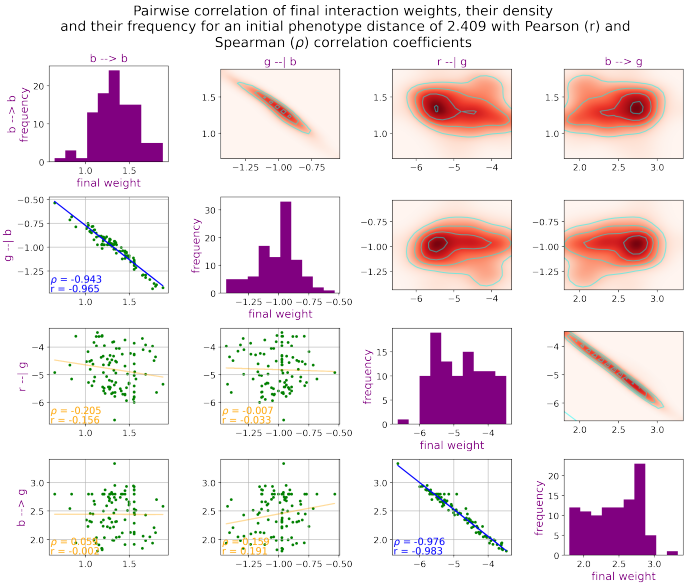
For the bistable mechanism, it was found that it has negative correlations between the final weights of blue-blue activation and the green-blue inhibition, and the red-green inhibition and the blue-green activation. This is shown in the plots between pairs of weights in figure 3a. It can also be seen that the other pairs have no correlation between them indicating that these two pairs of weights change independently throughout the evolution process.

It can be seen from figure 3b that the standard deviations of the final weights increase with an increase in ΔP, but seems to maximise at approximately 2 units. Due to the weight correlations between the blue-blue activation and green-blue inhibition, both plots show similar shapes. The same is true for the red-green inhibition and the blue-green activation. It can also be seen that the graphs in each row are horizontal mirror images of one another.

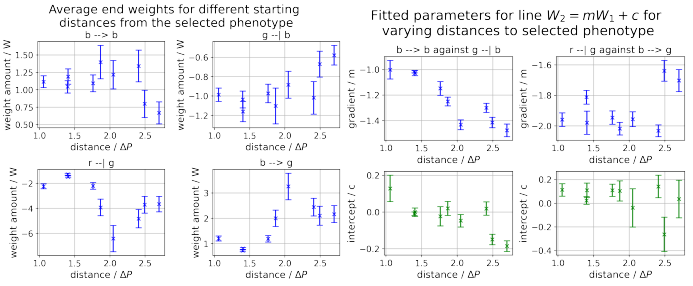
In the weight correlations, the parameters for a line of best fit were calculated and displayed in figure 3c against ΔP. It was found that the gradient and intercept parameters tended to decrease with an increase in distance for the blue-blue against green-blue weight comparison. The gradient parameter range in the blue-blue against green-blue is greater than that of the red-green against blue-green weight comparison, the converse is valid for the intercept.

4 DISCUSSION

By analysing different mechanisms we determined linear correlations between pairs of weights which means that they must change together. The bistable mechanism was primarily analysed due to numerical issues with the other two mechanisms and showed negative correlations between evolutionary runs between the blue-blue activation and green-blue inhibition as well as red-green inhibition and blue-green activation. If the concentration of the green gene decreases the blue gene would increase, in order to prevent too much of it from being produced blue activation of itself would decrease with it. Similarly, if the red inhibition of the green gene decreases the concentration of the green gene would increase, to prevent too much of the green gene the blue activation of green should also decrease. From figure 3c it can be seen that for the blue-blue against green-blue correlation the magnitude of the gradient increases with ΔP. This could be because the spread of the final weights in the blue-blue activation grows at a greater rate than that of the final weights of the green-blue inhibition.



(a)



(b) (c)

Figure 3: a) Pairwise correlation diagram of weights for the bistable mechanism for a distance between the initial phenotype and selected phenotype of 2.409. b) Distribution of weights for the bistable mechanism for varying distances. c) Distribution of parameters for the bistable mechanism when fitting the correlation of weights to a line.

If this project were to be taken further one could explore how using correlations of the weights leads to the same genotypes with reduced degrees of freedom. The genotype space for the bistable mechanism would also be reduced from four dimensions to two so a genotype space could be easily visualised and analysed. One could also incorporate adding additional gene interactions by adding small amounts to zero values in the weight matrix when mutating. This could be useful in understanding the evolvability of the network and how it can transition to another fundamental mechanism. By doing this, correlations between weights corresponding to different mechanisms could be found and investigated to further enhance our understanding of convergence in evolution.

References

[1] Gould SJ. Wonderful life: the Burgess Shale and the nature of history. WW Norton & Company; 1990 Sep 17.

[2] Conway Morris S. The Crucible of Creation. Oxford: Oxford University Press. 1999.

[3] Cotterell J, Sharpe J. An atlas of gene regulatory networks reveals multiple three-gene mechanisms for interpreting morphogen gradients. Molecular systems biology. 2010;6(1):425. Available at: https://www.researchgate.net/publication/47661708_An_atlas_of_gene_regulatory_networks_reveals_multiple_three-gene_mechanisms_for_interpreting_morphogen_gradients

[4] Schaerli Y, Jiménez A, Duarte JM, Mihajlovic L, Renggli J, Isalan M, Sharpe J, Wagner A. Synthetic circuits reveal how mechanisms of gene regulatory networks constrain evolution. Molecular Systems Biology. 2018 Sep;14(9):e8102. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6129954/

[5] François P. Evolving phenotypic networks in silico. InSeminars in cell & developmental biology 2014 Nov 1 (Vol. 35, pp. 90-97). Academic Press. Available at: https://www.sciencedirect.com/science/article/pii/S1084952114001852

[6] Jiménez A, Cotterell J, Munteanu A, Sharpe J. Dynamics of gene circuits shapes evolvability. Proceedings of the National Academy of Sciences. 2015 Feb 17;112(7):2103-8. Available at: https://www.pnas.org/doi/10.1073/pnas.1411065112

[7] Moehlis, J., 2022. Numerical Solution of the Diffusion Equation with No-Flux Boundary Conditions. [online] Sites.me.ucsb.edu. Available at: https://sites.me.ucsb.edu/~moehlis/APC591/tutorials/tutorial5/node6.html