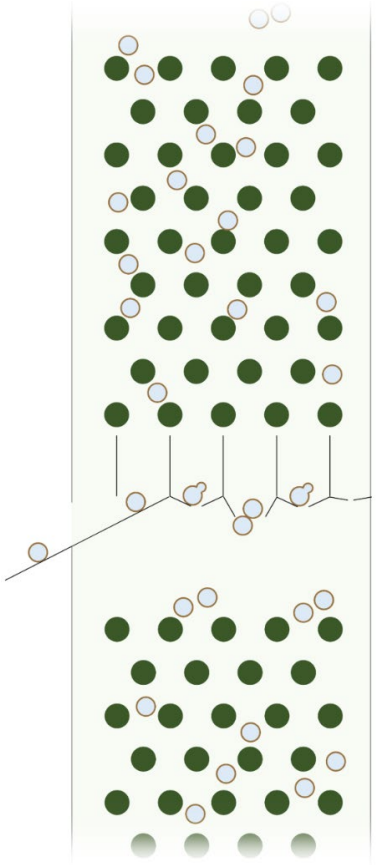
Master Project “Epigenetic dosage adaptation”



Evolution requires traits to emerge robustly from genes, but also flexibly when adaptation is needed. Ideally, nature exploits adaptive mechanisms that do not involve a trade-off between both situations. To elucidate such a potential mechanism, we turn to a model system where trait emergence is so well determined that we can predict and interpret the results of evolutionary forces. For this purpose, we study in our lab how the unicellular organism budding yeast establishes the direction of future daughter cell growth, an essential process called ‘polarization’.

Conveniently, we can identify evolutionary targets for optimizing polarization, even though the process involves many interacting proteins. Key to the identification is time-dependent consideration of the protein Cdc42p, which must exceed a minimal concentration to allow polarization [1,2]. As expression of this protein is very noisy, the fates of individual cells in an isogenic population can be diverse. Small cells with fortuitous Cdc42p overexpression proliferate better, pass down their favorable state to their progeny and subsequently bias the population traits we observe. The inheritance of luck implies an epigenetic, transgenerational feedback (akin to [3]), which theoretically always steers the population distribution of Cdc42p into the beneficial direction. As this feedback only emerges in response to a selective pressure on Cdc42p dosage, it would constitute an adaptive mechanism that provides robustness and flexibility without trade-off.

Our goal is hence to observe how large the influence is of the proposed epigenetic adaptation on Cdc42p. For this purpose, you will work with budding yeast mutants that have fluorescently labelled proteins to trace the heterogeneity in Cdc42p dosage across the population. Experimentally, this would involve flow cytometry, and/or fluorescence microscopy, possibly in combination with image analysis. You will also perform growth assays, as a reference for the selection pressures perceived by the genetic mutant background. The fluorescence and fitness data can be compared to simulation outputs of a polarization model, to assist you in choosing statistical metrics that show if and how much Cdc42p distributions change in selective genetic environments. Ideally, you would be able to quantitatively answer what the magnitude of the epigenetic dosage effect and the importance of its inheritance is.

Are you a master student with affinity for lab work and likes to connect your observations to theory? Knowledge of statistics is helpful, as is basic knowledge of Matlab or Python.

Please contact Liedewij if you are interested in this project (l.laan@tudelft.nl).

Bibliography

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2. Daalman WK-G, Laan L. Predicting an epistasis-rich genotype-phenotype map with a coarse-grained bottom-up model of budding yeast polarity. bioRxiv. 2020 Jan 1;2020.11.09.374363.

3. Xue B, Leibler S. Evolutionary learning of adaptation to varying environments through a transgenerational feedback. Proc Natl Acad Sci. 2016 Oct 4;113(40):11266–71.