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Measuring Environmental & Genetic Effects on Cell Differentiation Kinetics in Yeast

Tiara Johnson, and Dr. Daniel Pollard
Biology department at Western University

Abstract
The MAPK pathway is commonly involved in cell differentiation and growth processes. To study the kinetics of this pathway in regards to the effects of several genetic and environmental factors, we have chosen the popular model of pheromone response in yeast, Saccharomyces cerevisiae. Our data showed significant differences based on strain that seem to match previous data. Surprisingly, there were no measurable trends based on concentration, but results indicate that temperature may be positively correlated with response rate and may vary between strains. Future experiments will be aimed towards statistically defining the effects of each variable and creating a mathematical model that can be used to predict the outcomes of untreated temperature and concentration conditions.

Background

Yeast
• Two mating types (a, α) only differentiate into mating-competent shmoo in response to the other's mating pheromone.
• Process controlled my a MAPK pathway (Edman & Snyder 2001)

MAPK Pathway
• Mitogen Activated Protein Kinase
• Pheromone response in yeast is a very popular model for study.
• Errors in this type of pathway are commonly linked to cancer. (Buratto et al. 2014)

Temperature
• Normal growth temp around 25-30 °C
• Some clinical strains have been found to grow at abnormally high temperatures (Steinmetz et al. 2002)

Concentration
• Higher concentrations of pheromone found to increase expression of a mating specific reporter construct in S288c (Falconnet et al. 2012)

Mathematical Models
• Quantitative models have proven to be extremely useful and sometimes essential in describing and predicting how processes or organisms will react in different situations.
• Models in growth and development process have thus far been largely qualitative. (Umulis 2015, Gilbert 2006)

Hypotheses
• We expected S288c to have a higher rate of response because of its known increase in mating efficiency.
• Temperature’s effect on the response rate was expected to be similar to its effect on growth. A less steep rate of response at 30 °C with a strain dependent interaction causing a higher relative rate in YLM145 at 35 °C.
• Based on gene expression results, we expect higher concentration will increase response in both strains.

Methods

• Trials at different temperatures and concentrations randomized into pairs and one pair performed on a single day.
• Proportion of cells transformed using a log odds fit.

Discussion/Conclusions

• Strain specific differences in rate of differentiation fit with our prediction, though our data lacks the power to see how strain differences relate to changes in other conditions.
• Temperature shows trends towards a faster response rate as temperature increases. This partially supports our hypothesis, but is inconsistent with the prediction that response would peak at 30 °C. The effect may become clearer with more data allowing us to separate temperature effects between strains.
• The lack of a trend with concentration is unexpected based on published gene expression results (Falconnet et al. 2011). Is cellular differentiation from a morphological standpoint insensitive to large scale variation in gene expression responses to mating pheromones?
• Our original log odds model was a useful, but poor fit to the data and did not capture the reversal or provide a way to estimate maximum proportion. Adding terms with powers of time seems to correct that problem and more accurately capture the trends shown in the data.
• Maximum proportion magnitude and timing vary across strains and conditions motivating further investigation into more accurate estimation and the biological implications.

Results


Table 1

<table>
<thead>
<tr>
<th>Strain</th>
<th>Description</th>
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<tbody>
<tr>
<td>S288c</td>
<td>Lab</td>
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<tr>
<td>YLM145</td>
<td>Clinical</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Strain</th>
<th>Temperature (°C)</th>
<th>Concentration (mM)</th>
<th>Slope</th>
<th>Intercept</th>
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</thead>
<tbody>
<tr>
<td>S288c</td>
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</tbody>
</table>

* Indicates a significant value, p<0.05

What's Next?

• Expand dataset with more replicates to increase the power.
• Explore the use of additional interaction terms to improve the model.
• Improve estimates of magnitude and timing of maximum response proportion across strains and conditions.
• Test novel conditions to see if the results fit with the model’s predictions.

Works Cited


Acknowledgements

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