# Investigating the interconnection between cellular aging and network robustness

# Abstract

Complex gene interactions are often channeled together into phenotypic manifestations of cells as whole systems. Cellular aging, a pleiotropic trait, is likely influenced by many components of gene networks. Here, we aim to dissect the interconnection of network robustness and life-history traits in *Saccharomyces* *cerevisiae*. We evaluated the causal interactions of network connectivity, coefficient of variations of gene expression, evolutionary distance, fitness, morphological plasticity, and replicative life span using partial regressions. Preliminary results show significant correlations between replicative lifespan and several proxies of network robustness.

# Acknowledgements

# Introduction

## Cellular aging, gene network, and robustness

## The connection between robustness and cell aging

# Materials and Methods

## List of data sets

### SCMD saccharomyces cerevisiae morphology database

### RLS

### Fitness

### Protein network

### Genetic network?

### GFP CV, newman

### GEO CV of 3821 (glucose pulse)

## Analysis Methods

# Current results

## RLS-fitness,

Repeat regression analysis and summarize results.

Begin analysis of coefficient of variation using Lipson data.

REGRESSION ANALYSIS

*Fitness vs. lifespan*

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Comparison** | **Medium** | **Multiple R2** | **p-value** | **Std. Dev.** |
| RLS | YPD | 0.02545 | 0.01499 | 10.240 |
| RLS | YPDGE | 0.02824 | 0.01034 | 12.393 |
| RLS | YPG | 0.03613 | 0.003657 | 10.145 |
| RLS | YPE | 0.0632 | 0.0001084 | 12.246 |
| RLS | YPL | 0.03474 | 0.004391 | 11.620 |

YPE gave the largest R2 value and the lowest p-value, thus YPE has the most significant relationship with replicative lifespan.

## *Evolutionary distance vs. lifespan*

|  |  |  |  |
| --- | --- | --- | --- |
| **Species 1** | **Species 2** | **Multiple R2** | **p-value** |
| SCE | SPA | 0.002773 | 0.3758 |
| SCE | SMIK | 0.3482 | 0.386 |
| SCE | SBAY | 0.3646 | 0.8462 |

\*\*Add full names of yeast species

SCE = S. cerevisiae, SPA = S. paradoxus, SMIK = S. mikatae, SBAY = S. bayanus

The large p-values (0.3758, 0.386, and 0.8462) show that there is no significant relationship between evolutionary distance and replicative lifespan in any of the yeast gene species.

## *Genetic Interactions vs. lifespan (??)*

|  |  |
| --- | --- |
| **Multiple R2** | **p-value** |
| 0.08851 | 0.0004161 |

Given small p-value (0.0004161) there is a correlation between the number of interactions and replicative life span. (Negative correlation, insert graph?)

## *Fitness CV ~ RLS*

*summary(lm( sqrt(1/ lifespan$fit.CV) ~ lifespan$RLS\_Del\_alpha))*

*Call:*

*lm(formula = sqrt(1/lifespan$fit.CV) ~ lifespan$RLS\_Del\_alpha)*

*Residuals:*

*Min 1Q Median 3Q Max*

*-8.1666 -1.9302 0.4932 2.4985 8.6263*

*Coefficients:*

*Estimate Std. Error t value Pr(>|t|)*

*(Intercept) 7.30124 1.08133 6.752 1.18e-10 \*\*\**

*lifespan$RLS\_Del\_alpha 0.08393 0.04355 1.927 0.0552 .*

*---*

*Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1*

*Residual standard error: 3.487 on 230 degrees of freedom*

*(352 observations deleted due to missingness)*

*Multiple R-squared: 0.01589, Adjusted R-squared: 0.01161*

*F-statistic: 3.713 on 1 and 230 DF, p-value: 0.05521*

## *summary(lm( lifespan$RLS\_Del\_alpha ~ sqrt(1/ lifespan$fit.CV) + lifespan$pDegree)) #\*\*\*\*\*\* Rickleaf and Scheuerlei 2002*

*summary(lm( lifespan$RLS\_Del\_alpha ~ sqrt(1/ lifespan$fit.CV) + lifespan$pDegree)) #\*\*\*\*\*\* which reference???? Biological Implications of the Weibull and Gompertz Models of Aging*

*Call:*

*lm(formula = lifespan$RLS\_Del\_alpha ~ sqrt(1/lifespan$fit.CV) +*

*lifespan$pDegree)*

*Residuals:*

*Min 1Q Median 3Q Max*

*-18.3589 -3.0924 -0.0744 3.6315 16.3134*

*Coefficients:*

*Estimate Std. Error t value Pr(>|t|)*

*(Intercept) 22.24430 1.16627 19.073 <2e-16 \*\*\**

*sqrt(1/lifespan$fit.CV) 0.26675 0.11293 2.362 0.0193 \**

*lifespan$pDegree -0.04317 0.03091 -1.397 0.1643*

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*Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1*

*Residual standard error: 5.316 on 168 degrees of freedom*

*(413 observations deleted due to missingness)*

*Multiple R-squared: 0.05073, Adjusted R-squared: 0.03942*

*F-statistic: 4.489 on 2 and 168 DF, p-value: 0.01262*

## *RLS ~*

*summary(lm(lifespan$RLS\_Del\_alpha ~ lifespan$scmdstddev))*

*Call:*

*lm(formula = lifespan$RLS\_Del\_alpha ~ lifespan$scmdstddev)*

*Residuals:*

*Min 1Q Median 3Q Max*

*-16.0104 -2.7783 -0.2045 3.1908 14.7606*

*Coefficients:*

*Estimate Std. Error t value Pr(>|t|)*

*(Intercept) 27.4856 0.6872 39.998 < 2e-16 \*\*\**

*lifespan$scmdstddev -3.2701 0.7445 -4.392 1.35e-05 \*\*\**

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*Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1*

*Residual standard error: 5.046 on 543 degrees of freedom*

*(39 observations deleted due to missingness)*

*Multiple R-squared: 0.03431, Adjusted R-squared: 0.03253*

*F-statistic: 19.29 on 1 and 543 DF, p-value: 1.349e-05*

*summary(lm(lifespan$RLS\_Del\_alpha ~ lifespan$scmdMean)) #p=0.0019*

*Call:*

*lm(formula = lifespan$RLS\_Del\_alpha ~ lifespan$scmdMean)*

*Residuals:*

*Min 1Q Median 3Q Max*

*-16.5866 -2.7850 -0.2878 3.1635 14.5010*

*Coefficients:*

*Estimate Std. Error t value Pr(>|t|)*

*(Intercept) 24.610 0.218 112.876 < 2e-16 \*\*\**

*lifespan$scmdMean -2.730 0.874 -3.124 0.00188 \*\**

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*Signif. codes: 0 ‘\*\*\*’ 0.001 ‘\*\*’ 0.01 ‘\*’ 0.05 ‘.’ 0.1 ‘ ’ 1*

*Residual standard error: 5.089 on 543 degrees of freedom*

*(39 observations deleted due to missingness)*

*Multiple R-squared: 0.01766, Adjusted R-squared: 0.01585*

*F-statistic: 9.759 on 1 and 543 DF, p-value: 0.00188*

*Note. SCMD mean and stddev are higly autocorrelated. We probably need a better way to use the morphology dataset.*

# Discussion

# Reference

# Tables & Figures

CV vs. RLS

|  |  |
| --- | --- |
| Multiple R2 | p-value |
| 0.01589 | 0.05521 |

RLS vs. CV + pdegree

|  |  |  |
| --- | --- | --- |
|  | Estimate | Pr(>|t|) |
| CV | 0.26675 | 0.0193 |
| pdegree | -0.04317 | 0.1643 |

|  |  |
| --- | --- |
| Multiple R2 | p-value |
| 0.05073 | 0.01262 |

RLS vs. scmdstddev

|  |  |
| --- | --- |
| Multiple R2 | p-value |
| 0.03431 | 1.349e-05 |

RLS vs. scmdMean

|  |  |
| --- | --- |
| Multiple R2 | p-value |
| 0.01766 | 0.00188 |

SCMD mean and stdev are highly autocorrelated.