Phenotypic transitions in yeast mating

Alvaro Banderas[1,2] and Victor Sourjik[1]

***Short Abstract* — Haploid *S. cerevisiae* cells mate with complementary mating-type cells using a distance-sensing molecular system based on emission and detection of pheromones. We quantified the phenotypic and gene-expression responses to pheromone of yeast populations at the single cell level. We found ultrasensitive dose-responses in both output types. We analyzed the relation among the EC_{50} values for the different phenotypic transitions and transcription. Multiple phenotypic outputs coexist only in a certain range of pheromone concentration and transition to short-distance phenotypes seems to suppress phenotypic variability. Mating behavior closely resembles sharp developmental cellular decisions in morphogen gradients, but with a different biological significance.**

***Keywords* —** *S. cerevisiae*, mating, pheromone, ultrasensitivity

I. Introduction

During conjugation, haploid *Saccharomyces cerevisiae* cells fuse with opposite mating-type individuals (a-type fuses with alpha-type). The ability to sense the distance that separates mating partners is essential for the development of proximity-coherent phenotypes. [1] For example *membrane protrusion* formation is a short-range interaction where both cells develop a pear-shape morphology and start the fusion process upon contact of the tips. On the other hand, *chemotropic* behavior, where cells approach each other by enlarging their cell bodies towards the partner cell happens when cells are distant to each other. (Fig. 1) Yeast cells achieve this task by a pheromone sensing signal transduction pathway, which is a GPCR/MAPK-type pathway [2]. Specific peptide pheromones are produced by each cell type (a-type produces a-pheromone and alpha-type produces alpha-pheromone) and diffusion of the pheromones from the source cell builds up a gradient that can be functionally coupled to proximity by the receptor cell by a dose-dependent phenotype-selection system.

II. Results

We performed isotropic pheromone stimulations to yeast populations and measured transcriptional and phenotypic outputs at the single-cell level using time-lapse fluorescence microscopy and quantitative image analysis. We observe that the dose-dependency of protrusion formation is sigmoidal with a Hill coefficient of ≈5 and hence ultrasensitive, as reported before [3]. Cell-cycle arrest, a second pheromone-dependent phenotype, also follows a ultrasensitive dose-response with a lower EC_{50} value. Few other dose-dependent phenotypic transitions were also analyzed. The population -level ultrasensitivity we observe is caused by robust response alignment between individual cells.

Depending on the pheromone concentration range used for stimulation, different degrees of phenotypic heterogeneity are observed in the population. The sharp dose-dependent transition to protrusion formation separates the morphologically heterogeneous chemotropic population from the highly homogenous protruding population.

We also observe that the mating pheromone pathway activity at the transcriptional level shows maximal rate at a lower concentration value than the threshold for protrusion formation.

The significance of dose-response misalignments of the different outputs is discussed in the context of pathway architecture, mating behavior and previous studies addressing this issue [4].

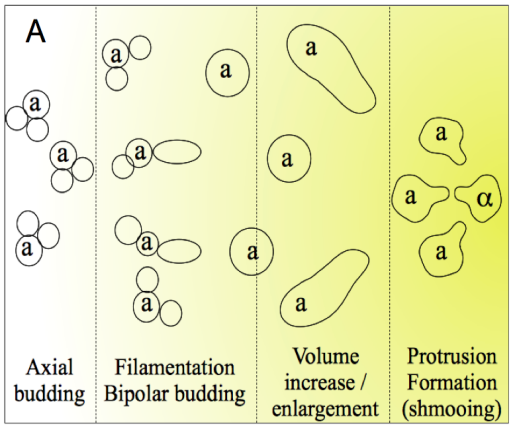

Figure 1. Different phenotypes in the yeast mating response are developed depending on the pheromone concentration (yellow gradient) present at a given position relative to the emitter cell.

III. References

[1] Arkowitz, R. a. (2009). Chemical gradients and chemotropism in yeast. *Cold Spring Harbor perspectives in biology*, *1*(2): a001958.

[2] Schwartz, M. a, & Madhani, H. D. (2004). Principles of MAP kinase signaling specificity in *Saccharomyces cerevisiae*. *Annual review of genetics*, *38*, 725-48.

[3] Malleshaiah, M. K., Shahrezaei, V., Swain, P. S., & Michnick, S. W. (2010). The scaffold protein Ste5 directly controls a switch-like mating decision in yeast. *Nature*, *465*(7294), 101-105.

[4] Yu, R. C., Pesce, C. G., Colman-Lerner, A., Lok, L., Pincus, D., Serra, E., et al. (2008). Negative feedback that improves information transmission in yeast signalling. *Nature*, *456*(7223), 755-61.

[1] Zentrum für Molekulare Biologie der Universität Heidelberg (ZMBH).
[2] HBIGS graduate program. Universität Heidelberg.
E-mail: a.banderas@zmbh.uni-heidelberg.de v.sourjik@zmbh.uni-heidelberg.de