From cell populations to single cells

Quantitative analysis of osmotic regulation in yeast

Elżbieta Petelenz-Kurdziel

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Fakultetsopponent:	Docent Johan Elf Instutionen för Cell- och Molekylärbiologi Uppsala Universitet
Examinator:	Professor Thomas Nyström Institutionen för Cell och Molekylärbiologi Göteborgs Universitet
Huvudhandledare:	Professor Stefan Hohmann Institutionen för Cell och Molekylärbiologi Göteborgs Universitet

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Elżbieta Petelenz-Kurdziel
Department of Cell and Molecular Biology, University of Gothenburg

Abstract

To date, interdisciplinary research is becoming increasingly popular because it combines the achievements of diverse disciplines, having the potential of providing a completely new angle to pertinent research problems. Using increasingly sophisticated tools allowed obtaining large sets of high resolution data but also created the challenge of using this information effectively and interpreting it in a reliable way. Searching for "simplicity in complexity" inspired by engineering and computer sciences, is a new trend in biological sciences, which allows integrating the vast amount of existing knowledge.

Single cell analysis is a good example of interdisciplinary research: dissecting a cell population to specific individuals is at instances necessary in order to obtain information on heterogeneity and cellular dynamics, which might be obscured when investigating, for instance, protein levels in extracts obtained from cell populations. In this thesis I have presented quantitative and time resolved measurements of cellular and nuclear volume, as well as protein shuttling, enabled by the development of a microscope platform dedicated to this type of measurements. I have investigated the response characteristics of the High Osmolarity Glycerol (HOG) pathway in *Saccharomyces cerevisiae* as an example of a MAP kinase network, such as the time scale and amplitude of nuclear Hog1 accumulation, correlated with biophysical changes.

I have also performed experiments on cell populations, aimed at the quantitative characterisation of the downstream effects of the HOG pathway activity, namely glycerol accumulation. In combination of mathematical modelling employing time varying response coefficients, this information allowed us to characterise the importance of each glycerol accumulation mechanism, on different time scales.

In summary, in this thesis I investigated the quantitative aspects of yeast osmotic regulation, providing precise, time resolved information about the biophysical characteristics of osmotic regulation. This work also provides new insight into the network properties of the HOG pathway, indicating the limitations of the response linearity range and the quantitative characterisation of the consequences of HOG activity, namely the interdependence of glycerol accumulation mechanisms. While achieving these goals, I contributed to the development of the single cell analysis platform, dedicated to analysing sub-cellular protein shuttling, correlated with measurements of cellular and nuclear volume.