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# What Population Reveals about Individual Cell Identity: Single-cell Parameter Estimation of Models of Gene Expression in Yeast

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## Résumé

Significant cell-to-cell heterogeneity is ubiquitously observed in isogenic cell populations. Consequently, parametric models of intracellular processes, commonly fitted to population-averaged data, should rather be calibrated to individual cells, leading to a population of models of similar but non-identical individuals. In this work, we propose a general modelling framework where intracellular process parameters obey a common population distribution, and statistical methods for inferring both the population distribution and single-cell parameter values from pools of single-cell longitudinal data. Crucially, the joint analysis of all longitudinal data not only made the reconstruction of population distribution robust to datasets of limited size, but also ensured single-cell estimates of unprecedented biological relevance. We demonstrate this on time-lapse fluorescence microscopy data for the osmotic shock response of yeast cells, showing that cell-specific parameters (i) improve the prediction of single-cell behaviors, (ii) are partly inherited from mother to daughter cells, and (iii) exhibit correlations with independently-measured single-cell physiological features. These tools will enable dissecting the influences of cellular or environmental factors on the various components of biological processes.

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