

P036 Flux control analysis of translation initiation and differential control of gene expression
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A simplistic and almost certainly erroneous view of translation rate control is that a small number of steps are rate-limiting and that regulation leads to overall repression or activation. But translational regulation is likely to be much more complex, with multiple steps and initiation factors contributing in varying degrees to rate-control, and with differential modulation of these factors contributing to changes in efficiency with which different mRNAs are translated. To gain insight into translational control in yeast, we are aiming (1) to measure in a semi-quantitative manner the relative contributions of different eIFs to the overall rate of translation, and (2) to determine what effect perturbation of the levels of eIFs causes differential changes in the yeast proteome. Our strategy is systematically to construct a set of yeast strains each with a different eIF gene under control of a conditional promoter, then compare the contribution of each eIF towards the overall flux of translation. Our initial results with eIF4E and eIF4G suggest that overall translation rate is more sensitive to changes in eIF4G than eIF4E, indicating that eIF4G has the greater "flux control coefficient". Changes in the yeast proteome are analysed by labelling with heavy leucine ($^{15}\text{N}^{13}\text{C}$) and comparing labelled and unlabelled samples to obtain quantitative data by LCMSMS.