Implementation of dilution rate-dependent glycolytic enzyme activity

The growth rate dependent change in protein activity was considered in this work. We used the experimental glycolytic enzymes activity quantification between dilution rates of 0.025-0.4 h^{-1} (van Hoek *et al*, 2000). The experimental setup was also chemostats as in the experimental steady sate data used in this work (Canelas *et al*, 2011), making this comparison more reliable. The experimental data from (van Hoek *et al*, 2000) is plotted in Fig 1:

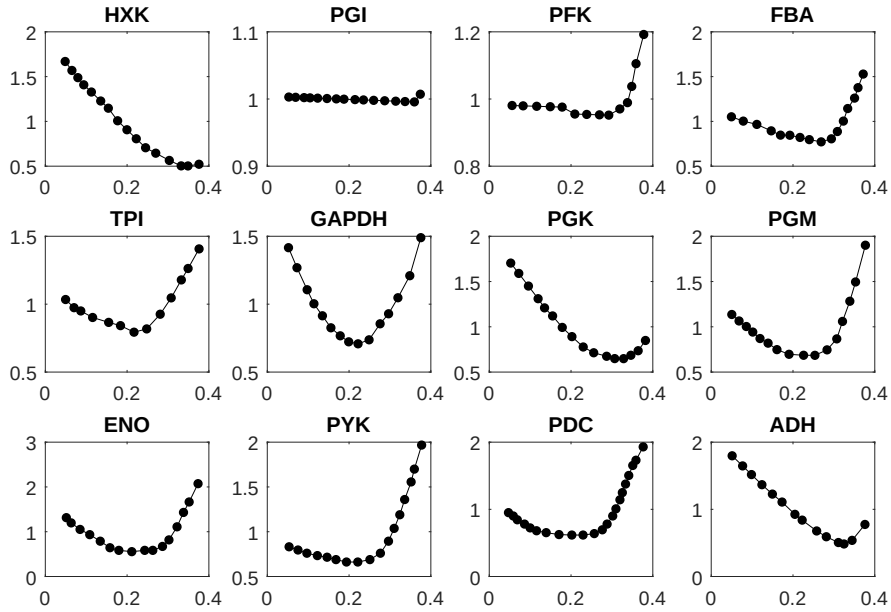

FIGURE 1 Experimental protein activity in the (van Hoek *et al*, 2000) dataset. Activity is plotted in the Y-axis (unitless) and dilution rate in the X-axis (in h^{-1}).

For all the glycolytic enzymes for which the experimental data was available, enzymatic activity was interpolated at a given dilution rate. A ratio was then calculated between this interpolated value and the experimental value at 0.1 h^{-1} accounting for a relative change in activity. The value at 0.1 h^{-1} was taken as a reference, since the kinetic parameters in the model and the single glucose perturbation simulations were performed in this dilution rate. This ratio was then use to alter the V_{max} for each glycolytic enzyme. The example below shows the case for HXK reaction rate:

$$\mathrm{HXK}_{\mathrm{cor,d}} = \frac{\mathrm{activity}_{\mathrm{HXK,d}}}{\mathrm{activity}_{\mathrm{HXK,0.1}}} \tag{1}$$

$$v_{\mathrm{HXK}} = \frac{\mathrm{HXK}_{\mathrm{cor,d}}\, V_m \left(\mathrm{ATP}\,\mathrm{GLCi} - \frac{\mathrm{ADP}\,\mathrm{G6P}}{K_{\mathrm{eq}}}\right)}{K_{m,\mathrm{glc}}\, K_{m,\mathrm{atp}} \left(\frac{\mathrm{ADP}}{K_{m,\mathrm{adp}}} + \frac{\mathrm{ATP}}{K_{m,\mathrm{atp}}} + 1\right) \left(\frac{\mathrm{G6P}}{K_{m,\mathrm{g6p}}} + \frac{\mathrm{GLCi}}{K_{m,\mathrm{glc}}} + \frac{\mathrm{T6P}}{K_{i,\mathrm{t6p}}} + 1\right)} \tag{2}$$

References

Canelas AB, Ras C, ten Pierick A, van Gulik WM, Heijnen JJ (2011) An in vivo data-driven framework for classification and quantification of enzyme kinetics and determination of apparent thermodynamic data. *Metabolic engineering* **13**: 294–306

van Hoek P, van Dijken JP, Pronk JT (2000) Regulation of fermentative capacity and levels of glycolytic enzymes in chemostat cultures of Saccharomyces cerevisiae. *Enzyme and microbial technology* **26**: 724–736