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**Phosphoglycerate kinase in crowded and cellular environments**

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We developed the temperature-jump fluorescence microscope to spatio-temporally resolve fast biomolecular kinetics and stability inside a single mammalian cell. We measured the reversible fast folding kinetics as well as folding thermodynamics of a fluorescent phosphoglycerate kinase construct in a bone marrow cell with subcellular resolution. The same instrument was also used to perform the comparative in vitro measurement in dilute buffer and crowded environments. Investigating an ensemble of cells, each cell has its own unique kinetic signature that can differ substantially from the in vitro result. Variations in the cytoplasmic environment are significant modulators of the protein energy landscape. We quantitate these variations with a statistical analysis of multiple cells and compare folding dynamics on the nm length scale with $\mu$m length scale diffusion processes. Cytoplasmic energy landscape modulation may be a candidate for non-genetic regulation of proteins but also challenges protein homeostasis.