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Buffering protein noise by liquid-liquid phase separation

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The processes that contribute to protein expression are subject to stochastic fluctuations and are affected by the environment in which they operate. As a result, concentration of a given protein can vary greatly between organisms, cells, as well as in time. Since many biological processes demand a tight control over protein concentration, cells have evolved various mechanisms to control the degree of concentration variability often referred to as noise. The best studied mechanisms for buffering protein expression levels rely on feedback through transcriptional regulation. Such regulation systems are slow and can reduce the expression noise only to a certain level. Here, we explore the potential for a phase separated organelle to buffer the noise in protein concentration at the post-translational level. Based on a simple thermodynamic model, we predict that liquid droplets function as dynamic reservoirs which can buffer variations in a highly effective and near-optimal manner. Using an engineered fluorescent protein that forms liquid droplets in the nucleus of Hela cells we show that phase separation attenuates variations in protein concentrations by up to a 100-fold. We propose that phase separation could be a common strategy for achieving stable protein concentrations in cells.

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