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# A stochastic model to study genetic and metabolic effects on N-linked protein glycosylation

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# A STOCHASTIC MODEL TO STUDY GENETIC AND METABOLIC EFFECTS ON N-LINKED PROTEIN GLYCOSYLATION

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Glycosylation is a vital processing step for a large number of cellular proteins as it critically affects protein stability and solubility as well as protein-protein interactions. As a consequence, glycosylation is a major quality attribute of recombinant proteins in biopharmaceutical applications. However, since glycosylation does not follow a template, but instead involves a complex interplay of various influencing factors in the Golgi, tailoring glycosylation towards certain desired attributes is challenging and usually requires trial-and-error experimentation. Computational modeling offers an intriguing option to understand and rationally engineer the complex reaction network underlying glycosylation. Here we present a computational model that describes N-linked protein glycosylation as a stochastic process. The model successfully recapitulates the biological complexity of glycosylation, but does not require the input of kinetic data. We show how the model can be used to predict the effect of glycosyltransferase knock-outs or overexpression on glycosylation in CHO. In addition, we demonstrate how the model can be linked to flux-balance models of CHO metabolism and use it to predict how cell culture conditions, such as extracellular nutrients, affect glycosylation. Thus, our modeling approach offers a promising tool for engineering glycosylation in both academic and industrial contexts.

*Figure 1 – The stochastic model allows to quantitatively predict how a glycoprofile will change upon genetic or metabolic perturbation.*

