Dynamics of immature mAb glycoform secretion during CHO cell culture - DTU Orbit (08/11/2017)

Dynamics of immature mAb glycoform secretion during CHO cell culture: An integrated modelling framework

Ensuring consistent glycosylation-associated quality of therapeutic monoclonal antibodies (mAbs) has become a priority in pharmaceutical bioprocessing given that the distribution and composition of the carbohydrates (glycans) bound to these molecules determines their therapeutic efficacy and immunogenicity. However, the interaction between bioprocess conditions, cellular metabolism and the intracellular process of glycosylation remains to be fully understood. To gain further insight into these interactions, we present a novel integrated modelling platform that links dynamic variations in mAb glycosylation with cellular secretory capacity. Two alternative mechanistic representations of how mAb specific productivity (qp) influences glycosylation are compared. In the first, mAb glycosylation is modulated by the linear velocity with which secretory cargo traverses the Golgi apparatus. In the second, glycosylation is influenced by variations in Golgi volume. Within our modelling framework, both mechanisms accurately reproduce experimentally-observed dynamic changes in mAb glycosylation. In addition, an optimisation-based strategy has been developed to estimate the concentration of glycosylation enzymes required to minimise mAb glycoform variability. Our results suggest that the availability of glycosylation machinery relative to cellular secretory capacity may play a crucial role in mAb glycosylation. In the future, the modelling framework presented here may aid in selecting and engineering cell lines that ensure consistent mAb glycosylatio.

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