Title: **Rethinking Microbial Biomanufacturing: Lessons from Biological Interactions**

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Abstract:

Despite remarkable advances in microbial biomanufacturing, progress continues to be driven predominantly by the optimization of individual process variables. Yet microbial production systems operate as integrated biological networks, in which interactions among cultivation factors often influence system behavior more profoundly than the individual variables themselves. Consequently, optimization alone may improve production performance without necessarily advancing our understanding of the biological relationships that govern system-level responses.

This presentation proposes a complementary perspective in which biological interactions are viewed not only as components of optimization models, but also as sources of transferable biological insight. Rather than simply identifying optimal cultivation conditions, interpreting interaction effects can reveal how microbial production systems behave as integrated biological networks whose responses cannot be fully explained by isolated cultivation variables.

To explore this perspective, interaction effects among $FeSO_4$, NaCl, and $NaNO_3$ on phycobiliprotein production in *Arthrospira platensis* were systematically investigated using a multivariable response surface framework. Rather than serving solely as an optimization tool, the experimental design was interpreted as a framework for revealing biologically informative interaction patterns. In this way, interaction effects were considered not merely as statistical descriptors, but as biological clues to system behavior under combined cultivation conditions.

The interaction-driven experimental framework revealed robust interaction patterns, with statistically significant interaction effects demonstrating that microbial production behavior could not be adequately explained by the independent effects of individual cultivation variables alone. Instead, interaction patterns exposed biological dependencies that emerged only when environmental factors were considered collectively, highlighting the inherently context-dependent nature of production optimization. Collectively, these findings suggest that interaction effects should be interpreted not merely as statistical descriptors within optimization models, but as biologically informative clues capable of generating transferable insight into system behavior beyond the identification of optimal cultivation conditions.

Although illustrated through phycobiliprotein production, the perspective presented here extends well beyond a single product or cultivation system. The broader value of biological interactions lies not merely in identifying optimal cultivation conditions, but in deepening our understanding of how microbial production systems behave under combined process

conditions. By reframing interaction effects as sources of transferable biological insight rather than solely as optimization outcomes, this perspective invites us to rethink microbial biomanufacturing—not simply as a process of finding better conditions, but as a process of learning how biological systems behave.