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MATHEMATICAL MODELING OF CELL-FREE PROTEIN SYNTHESIS SYSTEMS

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Exploiting microbial cultures through gene manipulation techniques to synthesize the target proteins is popular among pharmaceutical industries. However, the changes in the nutritional and environmental conditions of the culture medium can perturb the protein production rate. Extracting the background machinery of gene expression from cells and assembling them into a reaction vessel to conduct DNA programs in a cell-free format can circumvent many problems associated with cell-dependent norms. In this work, a mathematical model for cell-free protein synthesis (CFPS) was developed. The model encompasses the mechanics of protein synthesis, extract methodology, consumption of biological nutrients, the active duration of protein synthesis, and the DNA template loading capacity, which are lacking in previous CFPS models. In CFPS, the concentrations of molecular components engaged in protein synthesis are within limits to apply continuum hypotheses and mass action-based formalisms. Therefore, by formulating ordinary differential equations for each component, the performance of the system under a particular setting can be evaluated. Further, plugging in the kinetic parameters available in the literature to simulate the model can be justified because it is not biosystem specific and can be treated as independent entities. Simulating the CFPS pipeline using the literature values showed that the maximum concentration of reporter protein yield obtainable is 21.0 pM. Testing for increased resources showed that the maximum concentration of protein obtainable reaches up to 0.4 nM. Testing the DNA template loading capacity indicated that the protein product increases linearly and plateaus after a critical DNA concentration of 2.0 nM. The model developed in this research is not entangled with the fundamental assumptions of Michaelis-Menten kinetics. Therefore, it can be used as a scaffold to formulate more complex and practical CFPS models with nuance parameters appropriate for pharmaceutics and biomanufacturing.

Code availability: The necessary codes to reproduce the key findings of this work are available at GitHub (https://github.com/zachariah-ibrahim/cell-free-protein-expression).

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