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Mathematical modeling of recombinant DNA expression

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Recombinant DNA (rDNA) technology is used for the commercial synthesis of therapeutic biomolecules in microbial cultures. The rDNA molecules engineered for this purpose are promoter-driven and initialized inside the host by utilizing the biochemical resources allocated for gene expression. In this work, a mathematical model for rDNA expression was developed. The model encompasses the mechanics of protein synthesis, promoter manipulation, internal resource pool engagement, and the effect of plasmid loading that are lacking in current models available in the literature. The concentrations of molecular components engaged in protein synthesis are assumed to be within limits to apply continuum hypothesis and mass action-based formalisms. Therefore, by formulating an ordinary differential equation (ODE) for each component, the overall performance of the system under a particular setting can be evaluated. Plugging in the kinetic parameters available in the literature for simulation can be justified because rate constants are not system-specific and can be treated as independent entities. The calculations of the rDNA expression pipeline showed that the maximum reporter protein synthesized within 60 min is 0.15 nmol L^{-1}. However, unit testing of the internal resource pool engagement showed that the protein yield reaches 0.30 nmol L^{-1}. Analyzing the model for RNA polymerase (RNAP) affinity showed that the batch can theoretically give a protein yield of 60 nmol L^{-1}. The model developed in this research can be used as a scaffold to formulate more complex models with constrained and nuanced biochemical parameters appropriate for industrial-scale pharmaceutics.

Code availability: The R codes used for this work are available at GitHub (https://github.com/zachariah-ibrahim/recombinant-DNA-expression).

Keywords: Recombinant DNA, mathematical modeling, gene expression

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