



INDIAN INSTITUTE OF TECHNOLOGY GUWAHATI
SHORT ABSTRACT OF THESIS

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Programme of Study : Ph.D.

Thesis Title: *Bacillus subtilis*: a microbial cell factory for human interferon gamma production and process development

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SHORT ABSTRACT

The *B. subtilis* WB800N microbial cell factory was tackled at three levels for enhanced extracellular human interferon gamma production namely: 1) genetic level 2) substrate, medium components and extracellular cultivation environment level and 3) process operation level. The genetic level modulation of the *B. subtilis* WB800N physiology was performed by designing three human interferon gamma genes (*IFN γ*) with different optimum codon usage, RNA free energy and secondary structures. At substrate level complex and completely defined medium were assessed for modulation of the *B. subtilis* physiology along with various carbon and nitrogen sources by applying metabolic modelling and the stoichiometric modelling approaches for higher IFN γ production. Various amino acids were screened for their positive enhancing effects on IFN γ production using stoichiometric modelling and demand. The concentration level of carbon and nitrogen sources along with other medium components were optimized using statistical Design of Experiments (DoE) approach and machine learning based artificial neural network (ANN) based evolutionary programming using genetic (GA) and simulated annealing (SA) algorithms. At process operation level, the batch process was established with physical and environmental condition optimization of the *B. subtilis* WB800N culture for an antifoaming agent, optimum dissolved oxygen mass transfer coefficient and agitation rate. Fed-batch mode of operation was established with organic acid and amino acid feeding for positive stimulatory effect on IFN γ production. The high cell density cultivation of the *B. subtilis* WB800N with glycerol-amino acid-organic acid feeding was established which resulted in further enhancement in IFN γ production.