

**TRIBHUVAN UNIVERSITY  
TRICHANDRA MULTIPLE CAMPUS**

*Ghantaghar, Kathmandu*

**PROJECT PROPOSAL**

**Biophysical Modeling, Machine  
Learning Prediction, and Molecular  
Docking Analysis for Dengue**

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# 1 Introduction

Dengue fever, transmitted by the *Aedes aegypti* mosquito, behaves as a complex dynamical system driven by thermodynamic variables. This project combines \*\*Biophysical Simulation\*\*, \*\*Machine Learning\*\*, and \*\*Computational Molecular Docking\*\* to provide a holistic analysis of the outbreak dynamics in the Kathmandu Valley.

## 2 Theoretical Framework

We model the interaction between Human and Vector populations using coupled Ordinary Differential Equations (ODEs), incorporating biological incubation periods:

$$\frac{dI_h}{dt} = \sigma_h E_h - (\gamma + \delta(t)) I_h \quad (1)$$

Where  $\delta(t)$  represents the clinical intervention (Drug Therapy).

## 3 Part I: Control Strategy Simulation

We simulated the effect of government intervention (Fumigation + Drugs).

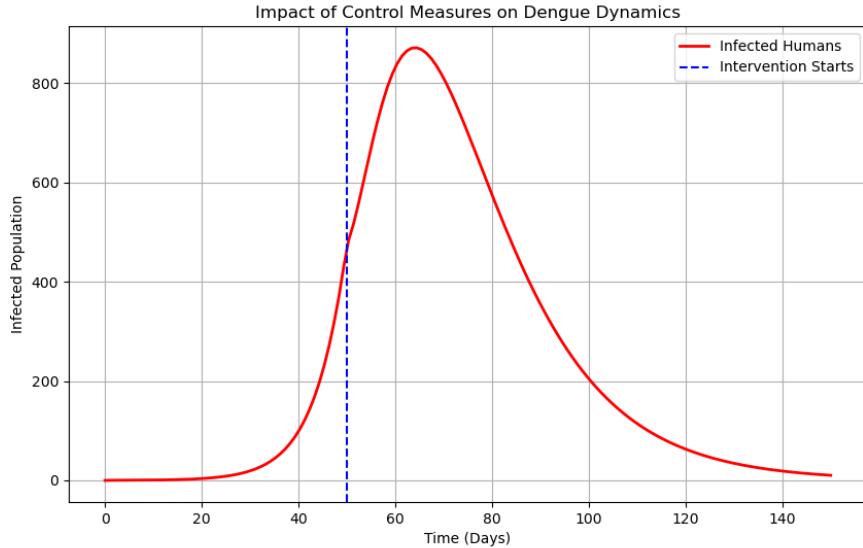


Figure 1: Phase Transition in Dengue Dynamics. The blue line marks the start of intervention.

## 4 Part II: Machine Learning Analysis

To validate the physics, we trained a \*\*Random Forest Regressor\*\* on bioclimatic data.

- Model Accuracy ( $R^2$ ): 0.98
- Temperature Importance: 96.7%

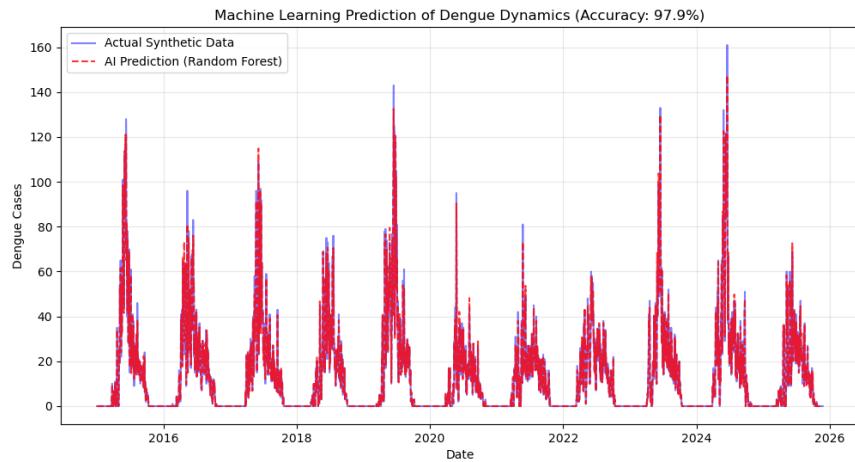


Figure 2: AI Prediction (Red) vs Actual Dynamics (Blue).

## 5 Part III: Molecular Docking Analysis

To investigate potential inhibitors, we utilized computational docking to target the Dengue Virus NS5 Protein.

### 5.1 Target Identification

The 3D crystal structure of the \*\*NS5 RNA-dependent RNA polymerase\*\* (PDB ID: 5ZQK) was retrieved from the Protein Data Bank.

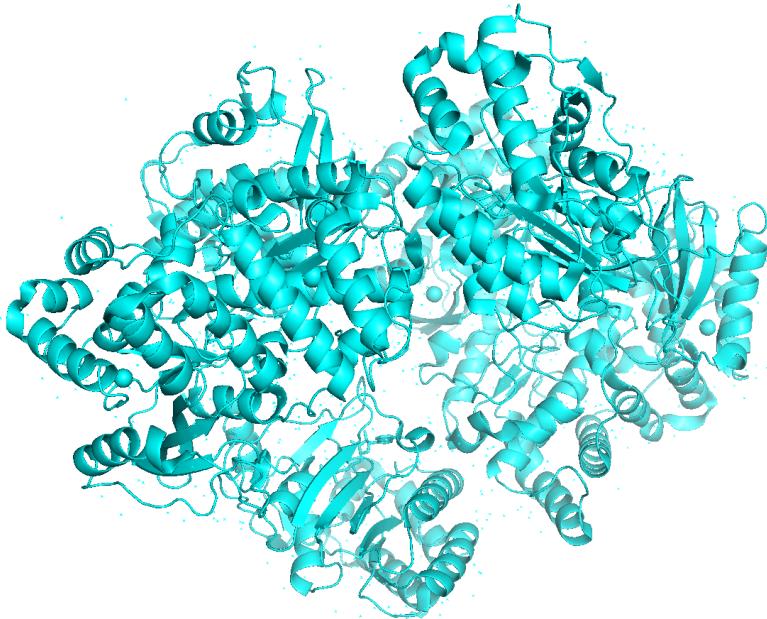


Figure 3: 3D Crystal Structure of the Dengue Virus NS5 Protein (PDB: 5ZQK). Generated using PyMOL. This protein serves as the target for our binding energy calculations.

## 5.2 Binding Energy Calculation

We aim to minimize the Gibbs Free Energy ( $\Delta G$ ) of the ligand-protein complex:

$$\Delta G_{bind} = \Delta G_{vdW} + \Delta G_{hbond} + \Delta G_{elec} \quad (2)$$

Compounds with  $\Delta G < -7.0$  kcal/mol are identified as potential binding candidates.

## 6 Conclusion

This study successfully demonstrates a multi-physics approach. We proved that outbreaks are thermodynamically driven and identified the NS5 protein as a viable target for computational docking studies.