

Guideline for Reproducing the Two-Lineage Dynamic Model Results

This guide describes how to reproduce the results of the two-lineage transmission model used in “**Unraveling the mechanism behind the probable extinction of the B/Yamagata lineage of influenza B viruses**” (Nature Communications, 2025). The workflow consists of four major components:

- 1. Parameter estimation**
- 2. Estimation of uncertainty of fitting curves**
- 3. Simulation of the 2018/19–2019/20 influenza seasons**
- 4. Sensitivity analysis**

For all scripts, please ensure that the input and output paths are correctly specified before running.

1. Parameter Estimation

(1) Directory: ./dynamic_model/parameters_estimation

(2) flu_b_mcmc_parallel_nc.py

- Defines the structure of the two-lineage transmission model via differential equations.
- Implements MCMC-based parameter estimation given a specific set of prior means.
- Before running, modify the paths for saving intermediate and final results.

(3) flu_b_command.py

- Generates **5,000 sets** of prior means using Latin hypercube sampling (LHS) under uniform priors.
- Each sampled set is used to specify normal prior distributions for model parameters.
- For every prior set, the script calls flu_b_mcmc_parallel_nc.py to perform parameter inference.

2. Estimation of Uncertainty of Fitting Curves

(1) Directory: ./dynamic_model/confidence_interval

(2) flu_b_ci.py

- Defines the function that generates epidemic trajectories based on a given parameter set.

(3) flu_b_ci_command.py

- Draws **1,000 samples** from normal prior distributions centered on the optimal MCMC-estimated parameters (via LHS).
- For each sampled parameter set, calls flu_b_ci.py to produce simulated epidemic curves.
- Aggregates results to obtain **95% confidence intervals** for the model-fitted trajectories.

3. Simulations for the 2018/19–2019/20 Seasons

(1) Directory: ./dynamic_model/simulation

(2) flu_b_simulation_data.py

- Simulates the transmission dynamics of **B/Victoria** and **B/Yamagata** during the 2018/19 and 2019/20 seasons under different combinations of Immune escape of B/Victoria, Immune escape of B/Yamagata and Intensity of non-pharmaceutical interventions (NPIs)

(3) flu_b_size_command.py

- Computes the epidemic sizes of both lineages during the **2019/20 season** across all parameter combinations.

4. Sensitivity Analysis

(1) Directory: ./dynamic_model/sensitivity_analysis

(2) The analysis evaluates how key epidemiological assumptions affect the 2019/20 epidemic size of B/Yamagata, including:

- Cross-protection levels
- Amplitude of seasonal forcing
- Peak timing of seasonal drivers

(3) flu_b_simulation_data_change*.py

- Simulates the 2019/20 season under systematically varied parameter settings.

(4) flu_b_distime_change*_command.py

- Computes the corresponding epidemic sizes of B/Yamagata for each scenario.

***Notes**

Path configuration: All scripts may require manual adjustment of import paths and output directories depending on your local environment.