

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_simmulation_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_simmulation_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.