



# FluNexus: a versatile web platform for antigenic prediction and visualization of influenza A viruses

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<https://doi.org/10.1002/imt2.70127>





# Background

## Antigenic map

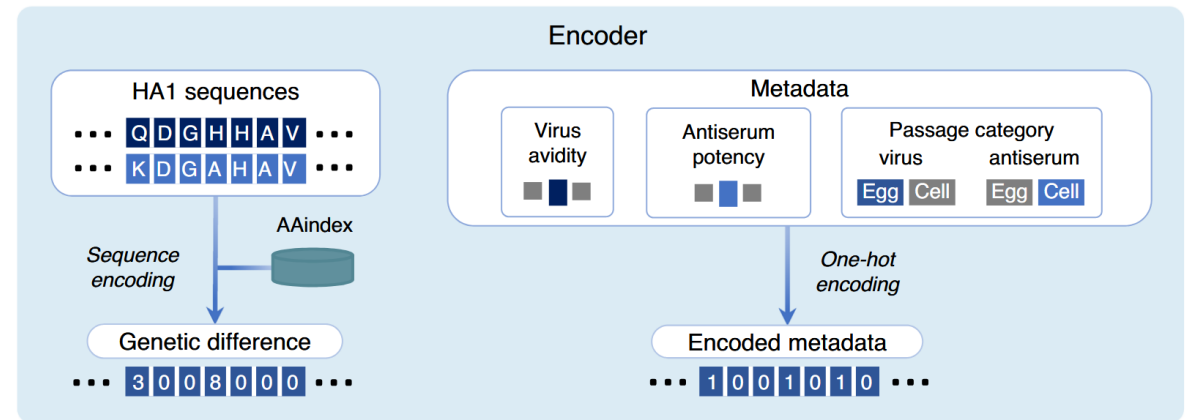
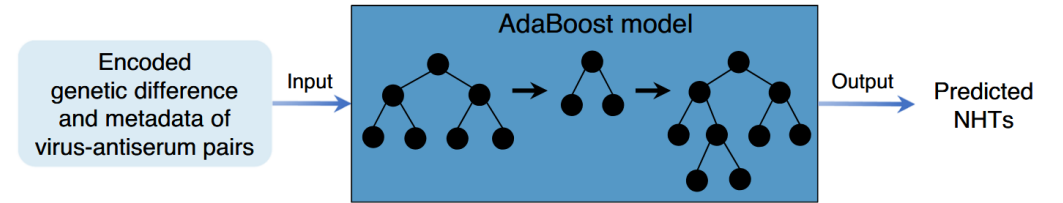
- Racmacs
- AntigenMap 3D
- MC-MDS

## Machine learning

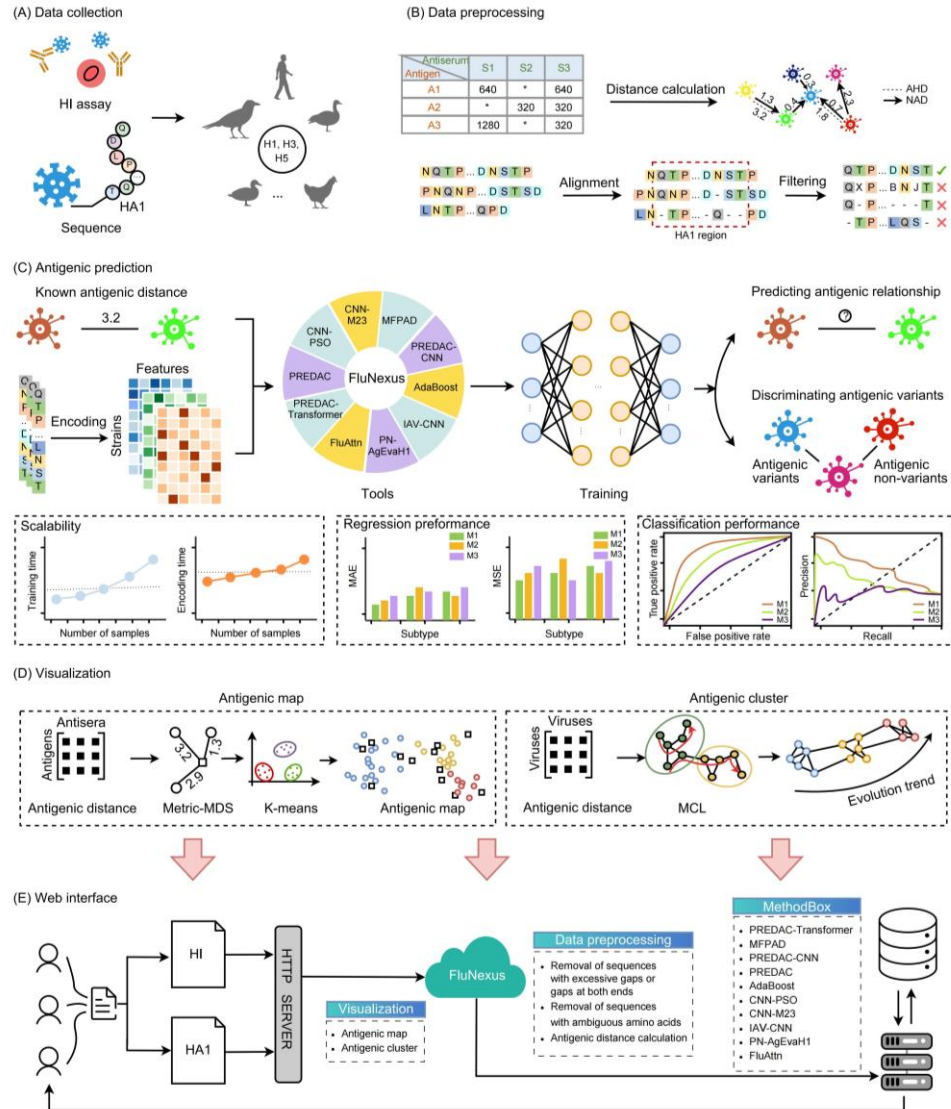
- PREDAC
- MFPAD
- AdaBoost
- PN-AgEvaH1

## Deep learning

- CNN-M23
- CNN-PSO
- PREDAC-CNN
- IAV-CNN
- FluAttn
- PREDAC-Transformer



# FluNexus: antigenic prediction and visualization platform



**FluNexus** Home Data Preprocess Antigenic Prediction Visualization Support

**Data Preprocessing**  
Data preprocessing for HI and HA1.

**Tutorial**  
Guidelines for data input, tool usage, and result interpretation.

**Antigenic Prediction**  
Sequence-based tools for online antigenic prediction with practical guidance.

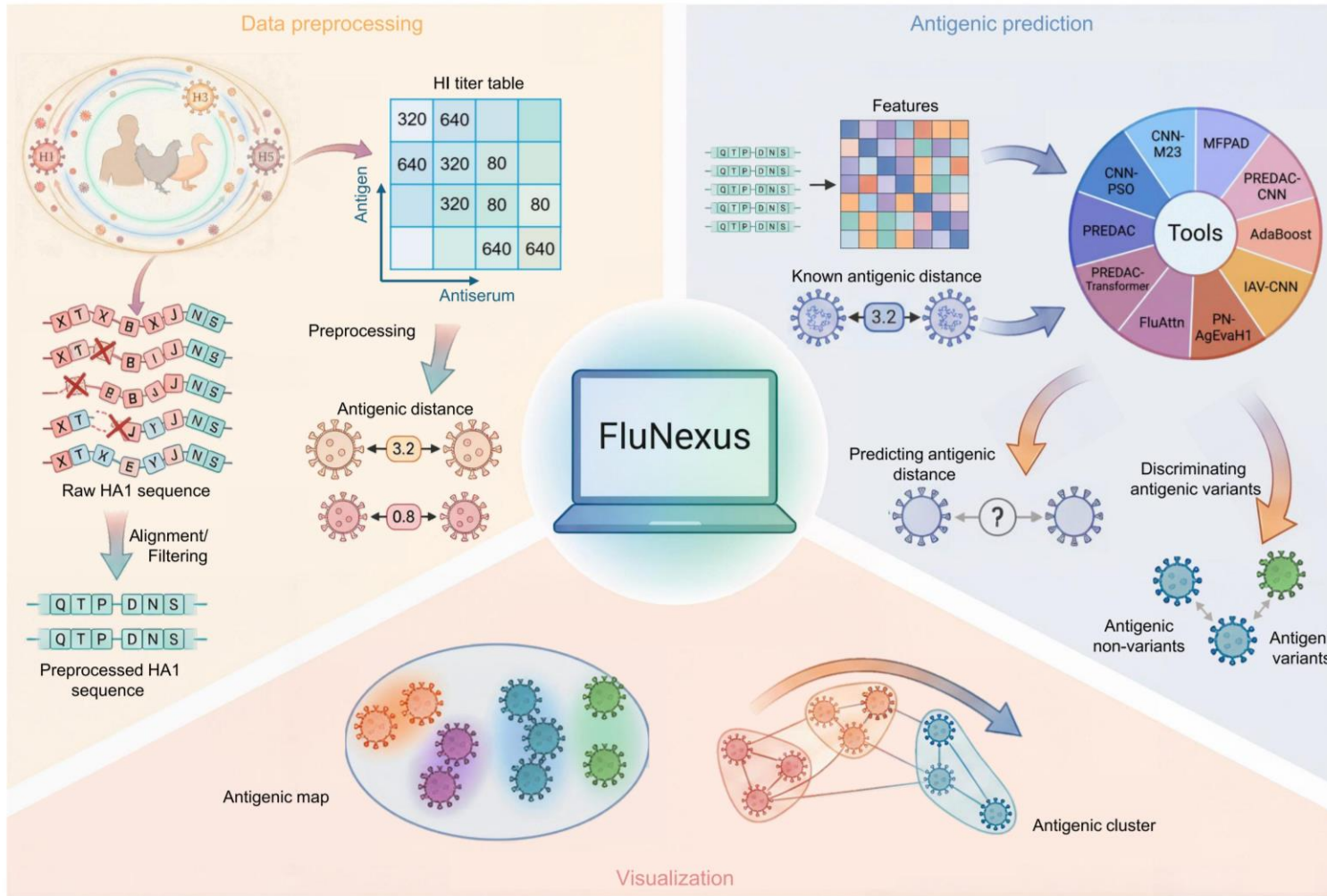
**Antigenic Cluster**  
Mapping the antigenic relationship of influenza A virus.

**Antigenic Map**  
Mapping the antigenic evolution of influenza A virus.

<https://flunexus.com/>

Overview of FluNexus.

# Highlights



- FluNexus features a data preprocessing module for HA1 and HI data of influenza A viruses;
- FluNexus facilitates online antigenic prediction, utilizing ten state-of-the-art antigenic prediction tools, and offers practical guidance based on a comparative evaluation of their performance;
- FluNexus provides a visualization module for mapping antigenic evolution of influenza A viruses, incorporating a novel manifold-based method for antigenic cartography.

# Data preprocessing

The screenshot displays the FluNexus Data Preprocess interface. At the top, there is a navigation bar with links for Home, Data Preprocess, Antigenic Prediction, Visualization, and Support. The main content area is divided into several sections:

- Data Input:** Shows two upload areas. The first, 'Upload HA1 sequence data (.fasta)', contains a file named 'HA1\_preprocess\_H3.fasta' (33.59KB). The second, 'Upload HI data (.csv/.xlsx)', contains a file named 'HI\_preprocess\_H3.csv' (54.26KB).
- Options:** Contains two toggle switches for 'Preprocess HA1' and 'Preprocess HI', both of which are turned on. Below these is a 'Subtype' selection with radio buttons for H1, H3 (selected), and H5.
- HA1 Preprocessing Options:** Includes three toggle switches: 'Remove ambiguous amino acids', 'Remove sequences with gaps at both ends', and 'Remove sequences with high gap ratio', all of which are turned on.
- HI Preprocessing Options:** Includes a 'Distance type' selection with radio buttons for NAD (selected) and AHD.
- Preprocessed Data:** A table showing the results of the preprocessing. The table has two columns: 'virus' and 'sequence'. It lists three entries:

virus	sequence
A/BI/16190/1968	QDLPGNDNSTATLCLGHAVPNGTLVKITITDDQIEVTNATELVQSSSTGKICNNPHRILDGINCTLIDALLGDPHCDVFQDETNDLFFVERSKAFSNICYPPYDPAASLRSLVASSGTLFEITEGFTWTGVTQNGGSNACKRGP SGFFSRLNMLTKSGSTYPVNLVTPMNDNFDKLYIIGVHHPTNQEQTSLVYQASGRVTVSTRSQTIIPNIGSRPWVRLSSRISLYWTIVKPGDVLVINSIGNLIAPRGYFKMRTGKSSIMRSDAPIDTCISECITPNGSI PNDKPFQIVNIKITYGACPKYVKQNTLKLATGMRNVPEKQT
A/BI/16398/1968	QDLPGNDNSTATLCLGHAVPNGTLVKITITDDQIEVTNATELVQSSSTGKICNNPHRILDGINCTLIDALLGDPHCDVFQDETNDLFFVERSKAFSNICYPPYDPAASLRSLVASSGTLFEITEGFTWTGVTQNGGSNACKRGP SGFFSRLNMLTKSGSTYPVNLVTPMNDNFDKLYIIGVHHPTNQEQTSLVYQASGRVTVSTRSQTIIPNIGSRPWVRLSSRISLYWTIVKPGDVLVINSIGNLIAPRGYFKMRTGKSSIMRSDAPIDTCISECITPNGSI PNDKPFQIVNIKITYGACPKYVKQNTLKLATGMRNVPEKQT
A/HK/1/1968	QDLPGNDNSTATLCLGHAVPNGTLVKITITDDQIEVTNATELVQSSSTGRICNSPHRILDGKDCITLIDALLGDPHCDVFNKDETNDLFFVERSKAFSNICYPPYDPAASLRSLVASSGTLFEITEGFTWTGVTQDGGSNAFKRGPG

<https://flunexus.com/DataPreprocessing.html/>

FluNexus features a data preprocessing pipeline for users to process their own uploaded data on the “Data Preprocess” page.



# Antigenic prediction tools

The screenshot shows the FluNexus Antigenic Prediction web interface. The navigation bar at the top includes 'FluNexus', 'Home', 'Data Preprocess', 'Antigenic Prediction', 'Visualization', and 'Support'. The main content area is titled 'Antigenic Prediction' and is divided into three main sections:

- Data Input:** Features a 'LOAD EXAMPLE' button and a text input field for 'Upload HA1 sequence data (.csv/.xlsx/.fasta)'. Below this is a dashed box with a file icon and the text 'Drop file here or click to upload data'.
- Options:** Contains three rows of controls:
  - Tools:** A dropdown menu currently set to 'MFPAD'.
  - Distance type:** Radio buttons for 'NAD' (selected) and 'AHD'.
  - Subtype:** Radio buttons for 'H1', 'H3' (selected), and 'H5'.
- Predictive Result:** A table with three columns: 'virus1', 'virus2', and 'antigenic\_distance'. Below the table are two buttons: 'Upload to Visualization' and 'Download result'.

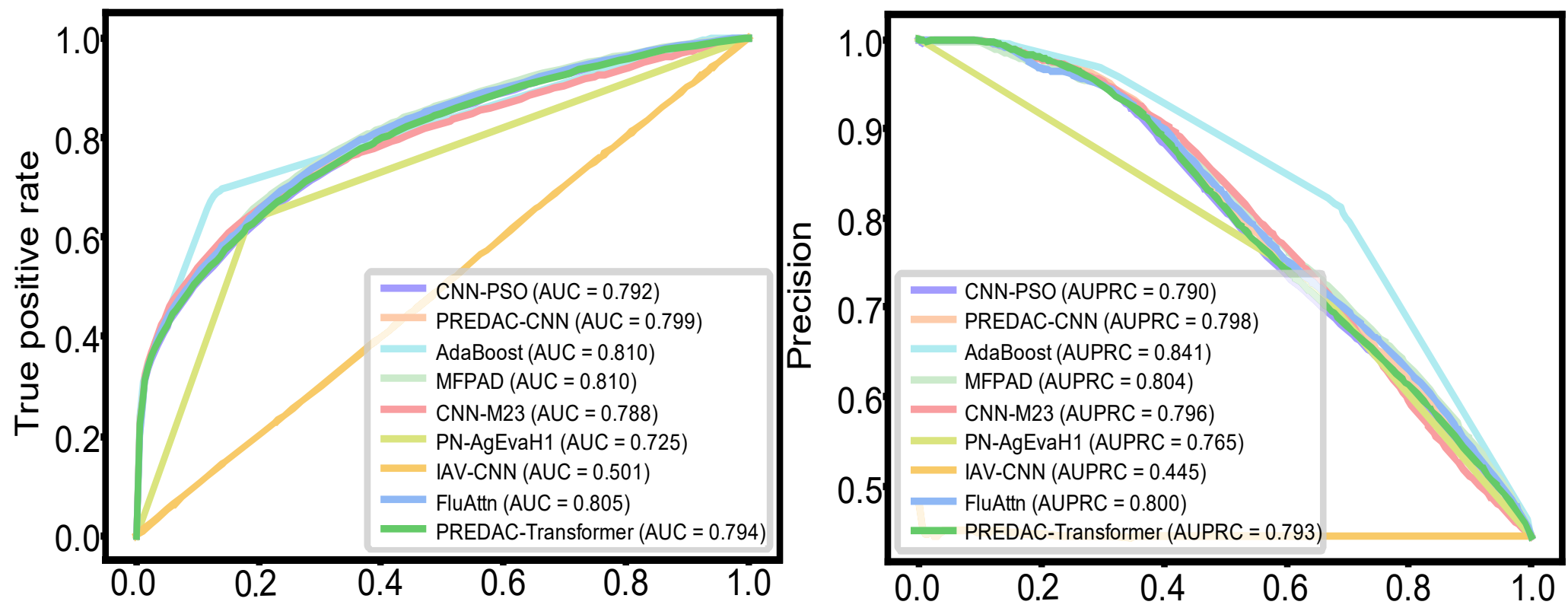
At the bottom of the interface are two large buttons: 'EXECUTE' (red) and 'RESET' (grey). The URL bar at the bottom left shows 'https://flunexus.com/AntigenicPrediction.html#'. The background of the interface features a faint, stylized image of a virus particle.

<https://flunexus.com/AntigenicPrediction.html/>

FluNexus provides both online and open-source implementations of ten sequence-based tools for antigenic prediction. The integrated tools comprise PREDAC, CNN-M23, CNN-PSO, MFPAD, PREDAC-CNN, AdaBoost, IAV-CNN, PN-AgEvaH1, PREDAC-Transformer, and FluAttn.

# Benchmarking of antigenic prediction methods

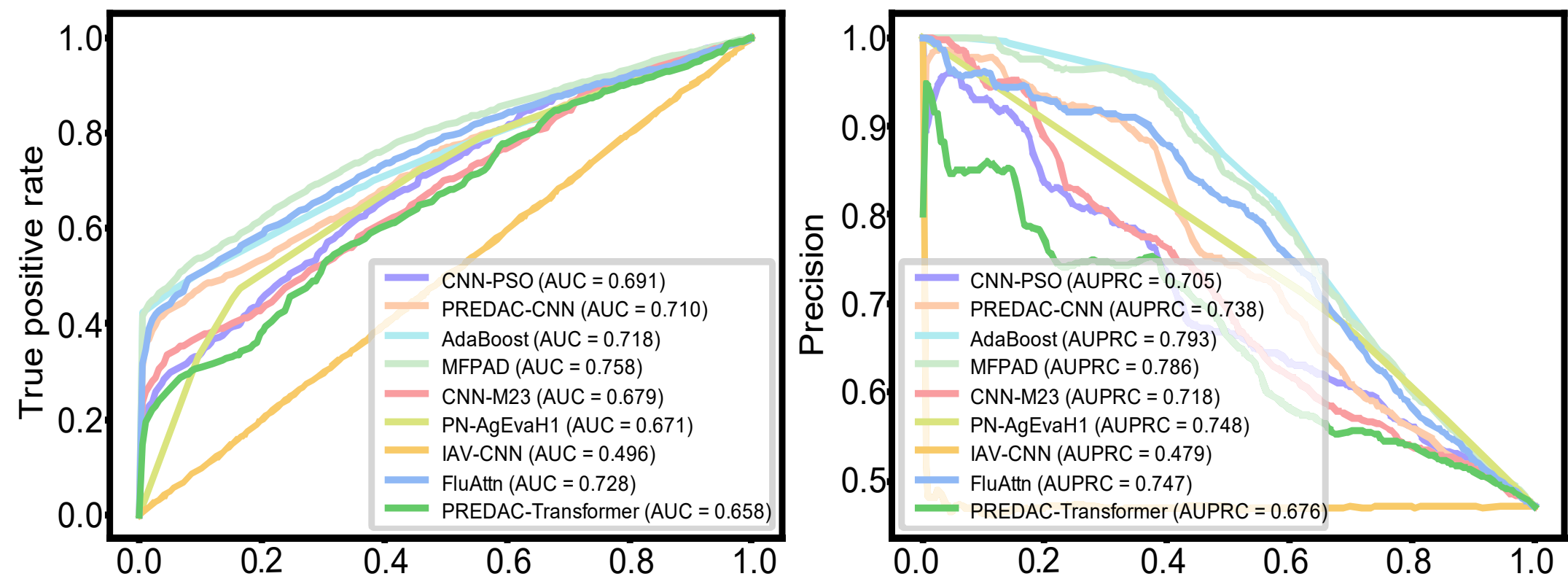
## Cross-validation



Comparison of the ability to discriminate antigenic variants from non-variants across methods.

# Benchmarking of antigenic prediction methods

## Retrospective test

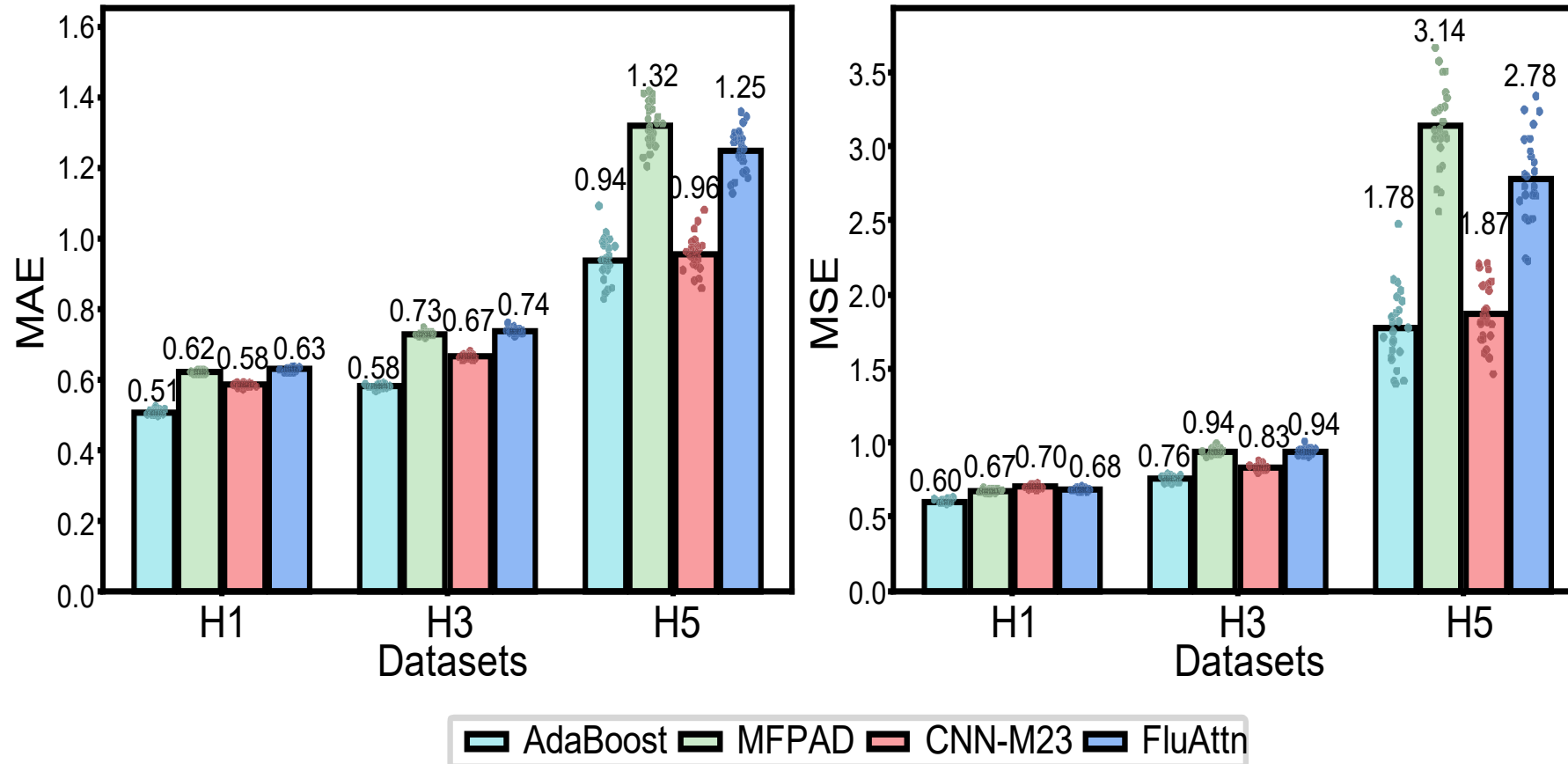


Comparison of the ability to discriminate antigenic variants from non-variants across methods.



# Benchmarking of antigenic prediction methods

## Cross-validation

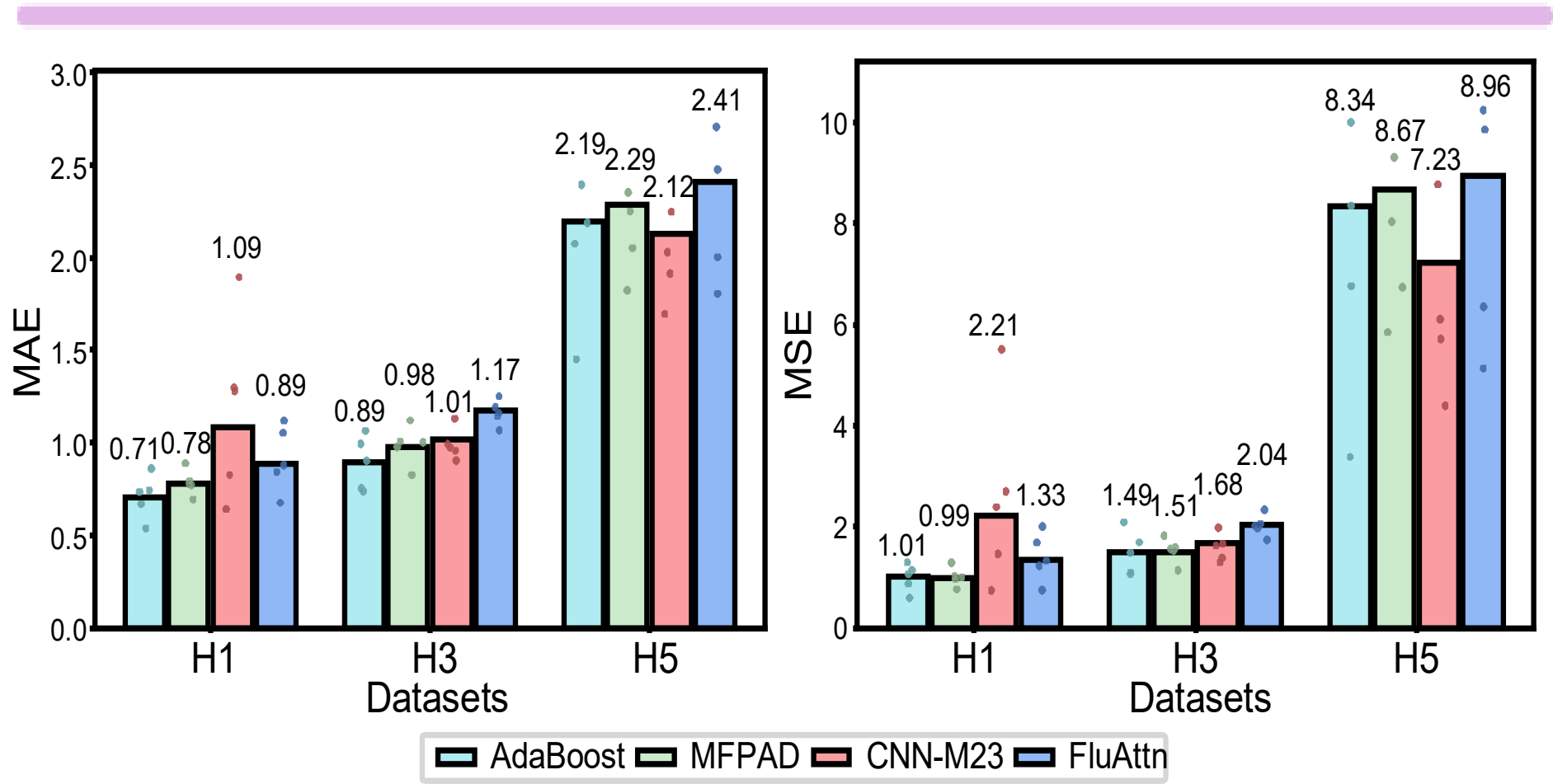


Comparison of the accuracy in inferring antigenic distances across methods.



# Benchmarking of antigenic prediction methods

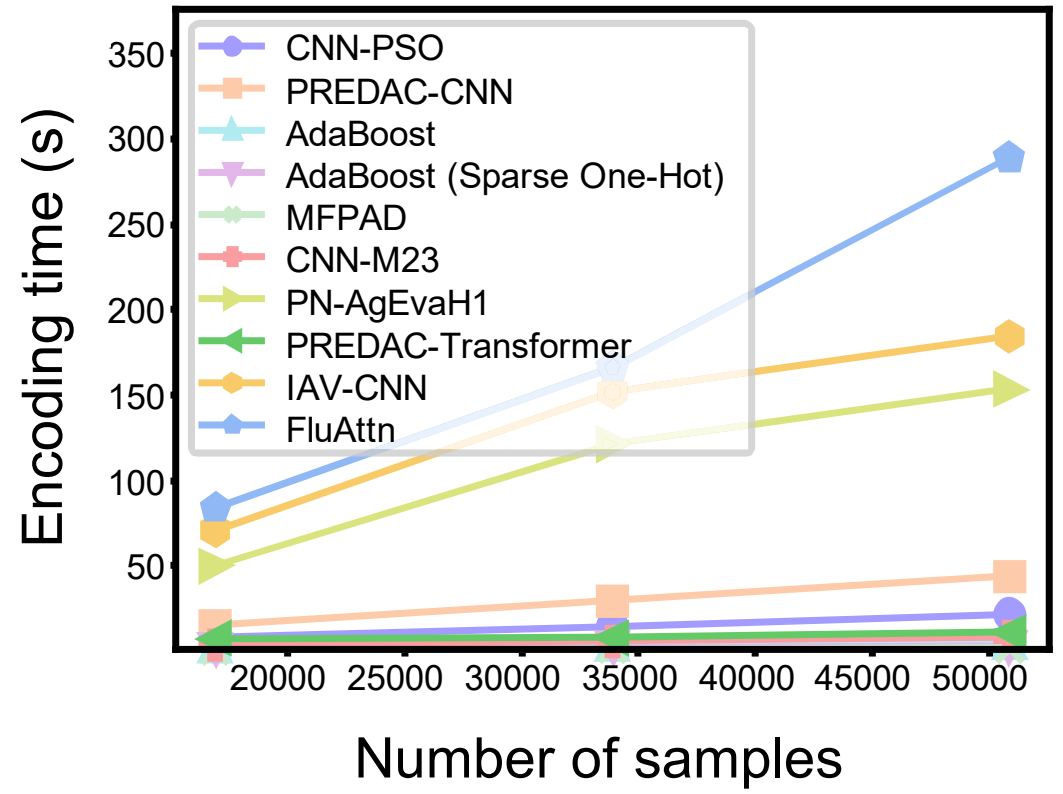
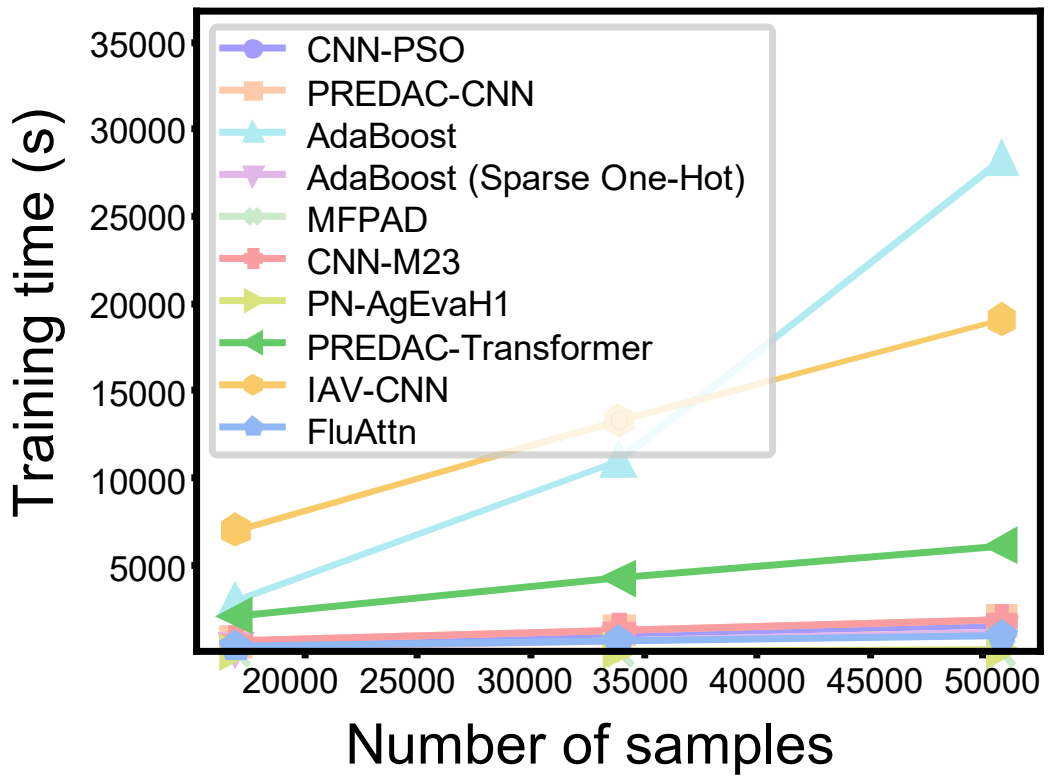
## Retrospective test



Comparison of the accuracy in inferring antigenic distances across methods.



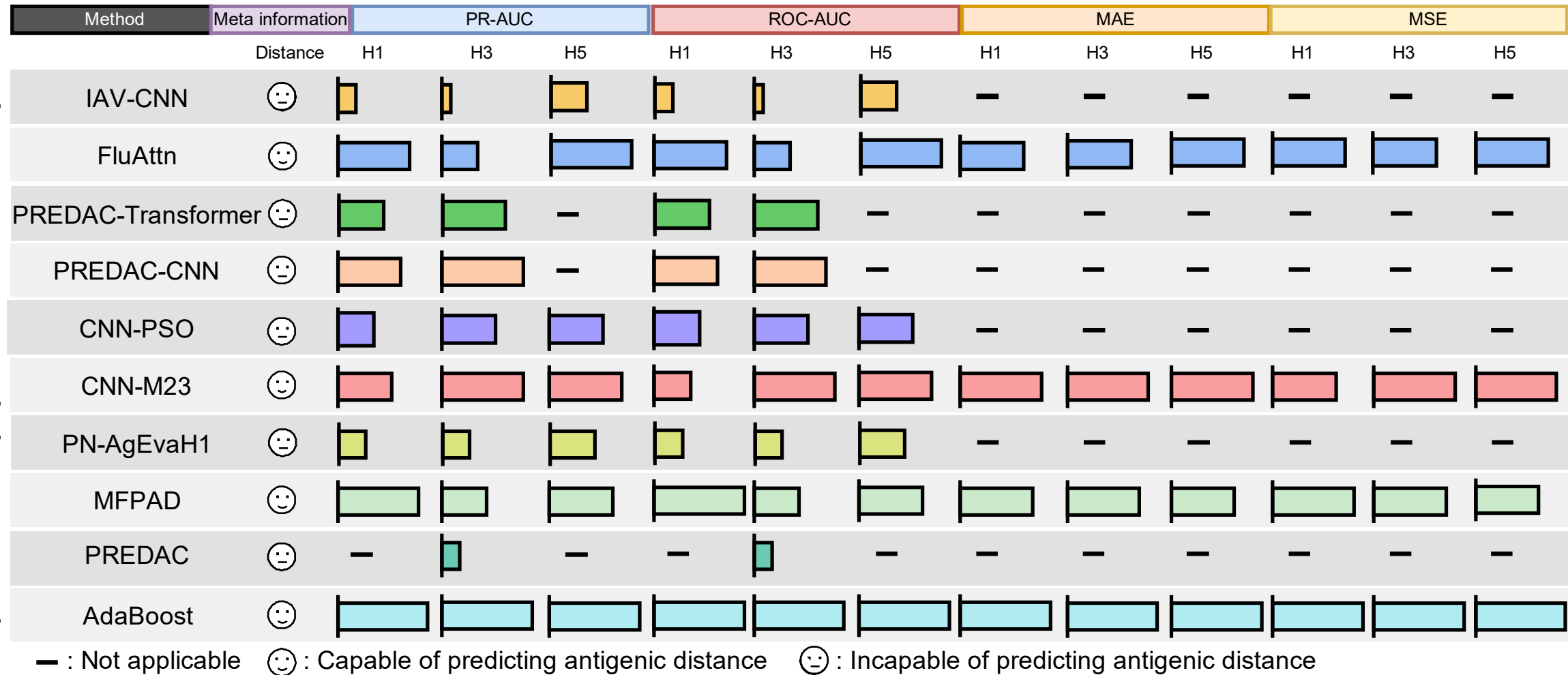
# Benchmarking of antigenic prediction methods



Comparison of feature encoding and training time across methods.

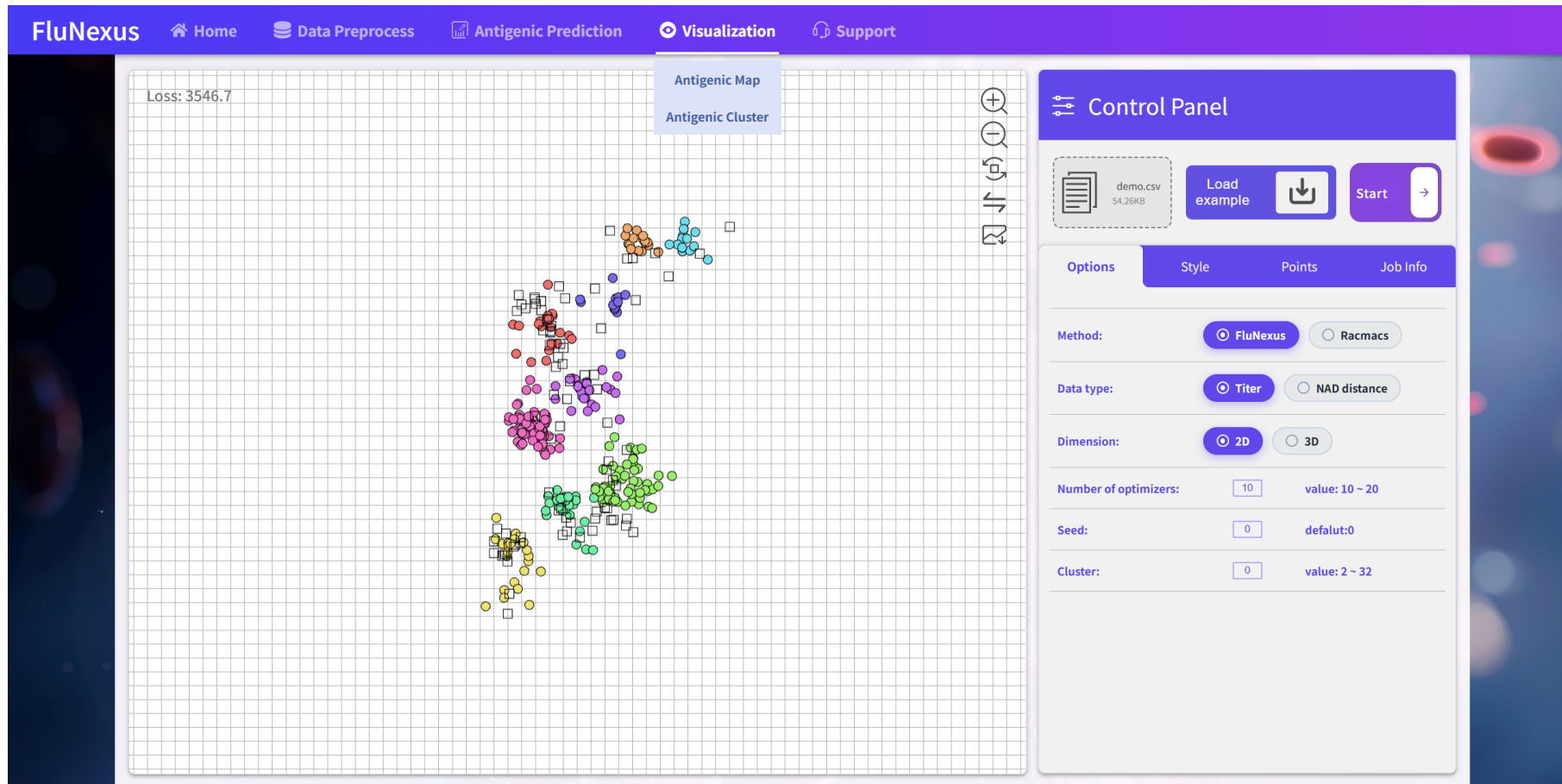


# Benchmarking of antigenic prediction methods



Overview of method performance.

# Improved mapping of antigenic evolution and visualization



Antigenic map:

<https://https://flunexus.com/atmap.html/>

Antigenic cluster:

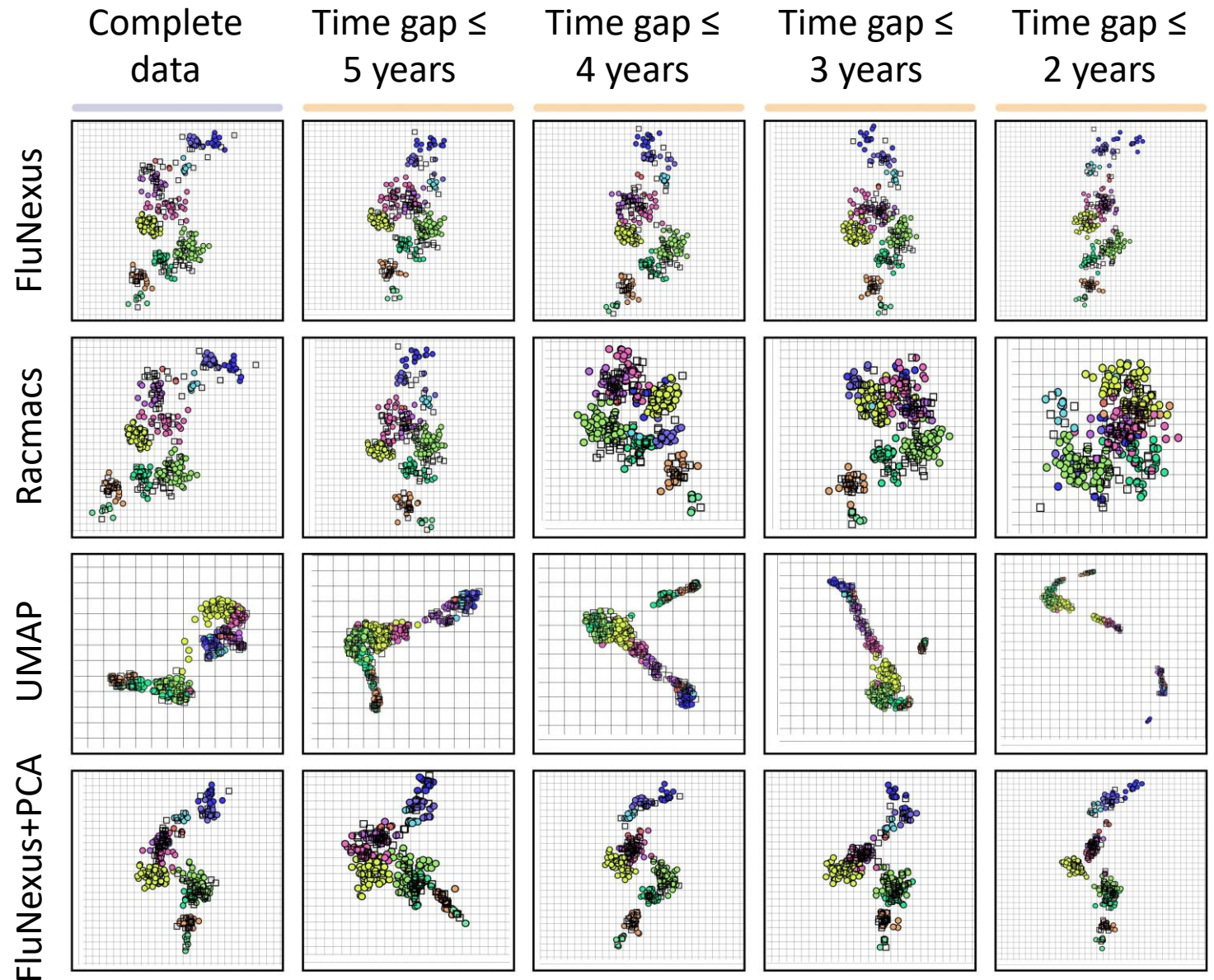
<https://https://flunexus.com/mcl.html/>

The FluNexus web platform incorporates two interactive visualization modules:

- ❑ Antigenic map
- ❑ Antigenic cluster

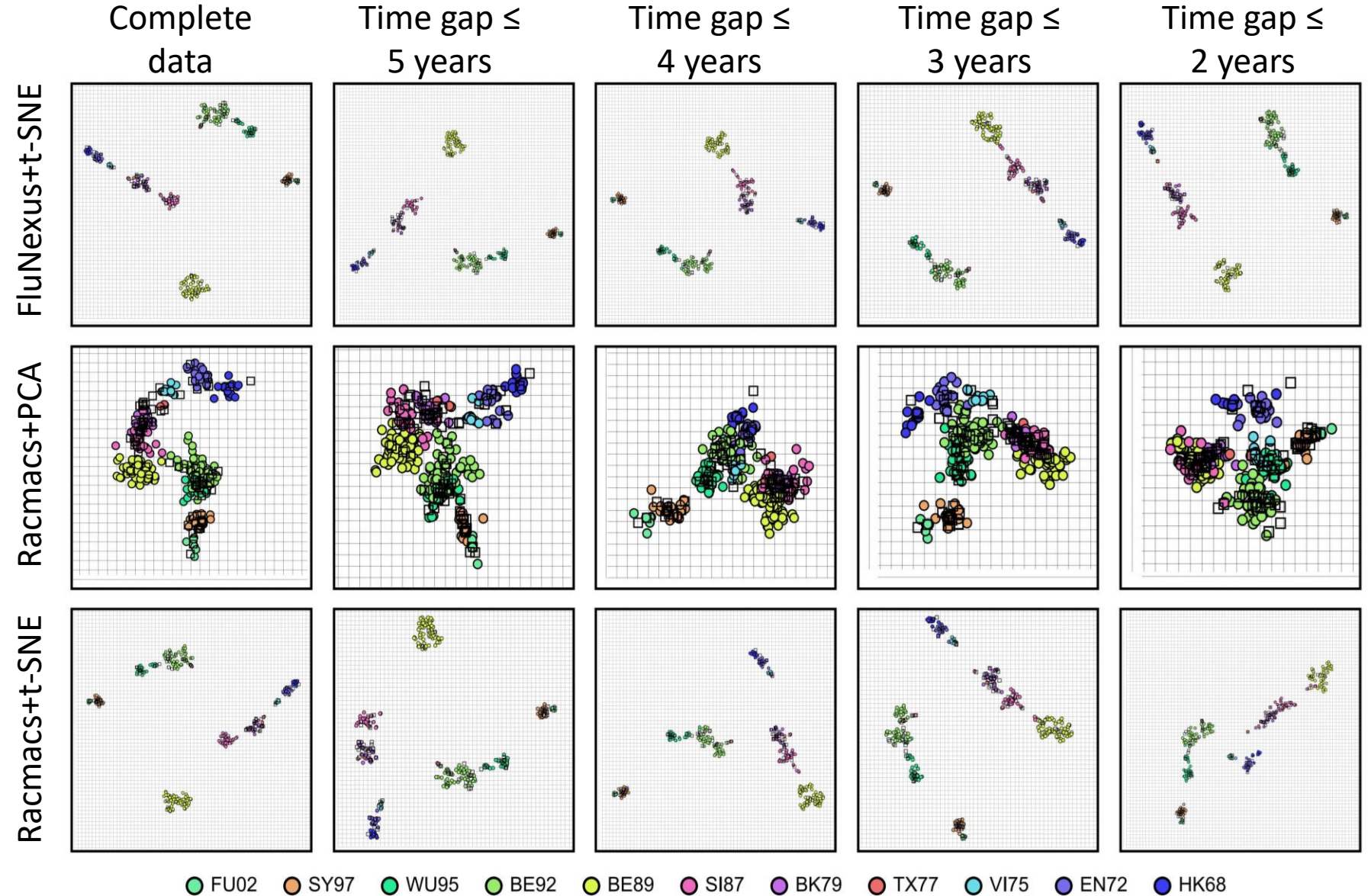
# Improved mapping of antigenic evolution and visualization

Antigenic maps generated by FluNexus, Racmacs, UMAP, PCA, and t-SNE using the HI data under temporal sampling.



# Improved mapping of antigenic evolution and visualization

Antigenic maps generated by FluNexus, Racmacs, UMAP, PCA, and t-SNE using the HI data under temporal sampling





# Summary

- ❑ In this study, we present FluNexus, a one-stop-shop web platform that streamlines antigenic prediction and visualization for influenza A viruses.
- ❑ FluNexus is a versatile platform that integrates interactive modules for data preprocessing, online antigenic prediction with practical guidance for researchers, and visualization of influenza A virus antigenic evolution.
- ❑ The core workflow and visualization framework of FluNexus can also be applied to other pathogens when assay-derived antigenic measurements and corresponding genomic sequences are available.
- ❑ Website: <https://www.flunexus.com/>

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