

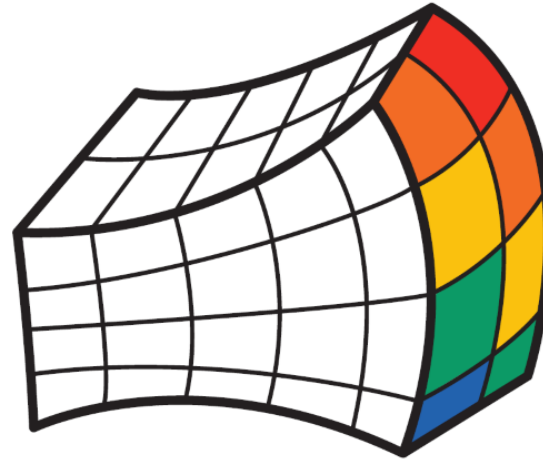
# Multi-template ALPACA (MALPACA) & K-means template selection

Chi Zhang

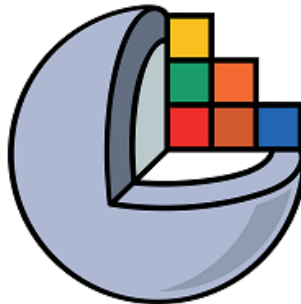
Maga Lab

Center for Developmental Biology &  
Regenerative Medicine

Seattle Children's Research Institute



**SLICERMORPH**

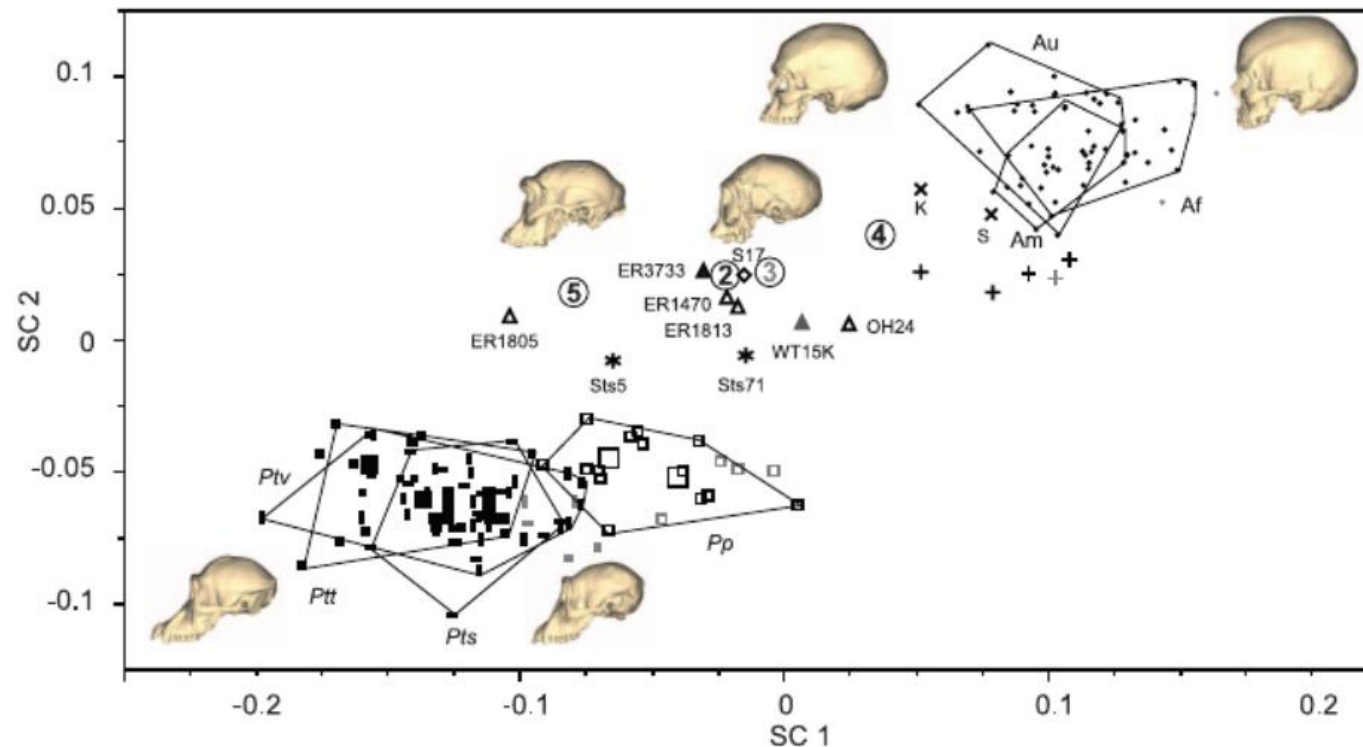


3D Slicer



# A limitation of ALPACA (& most previous automated landmaking methods as well)

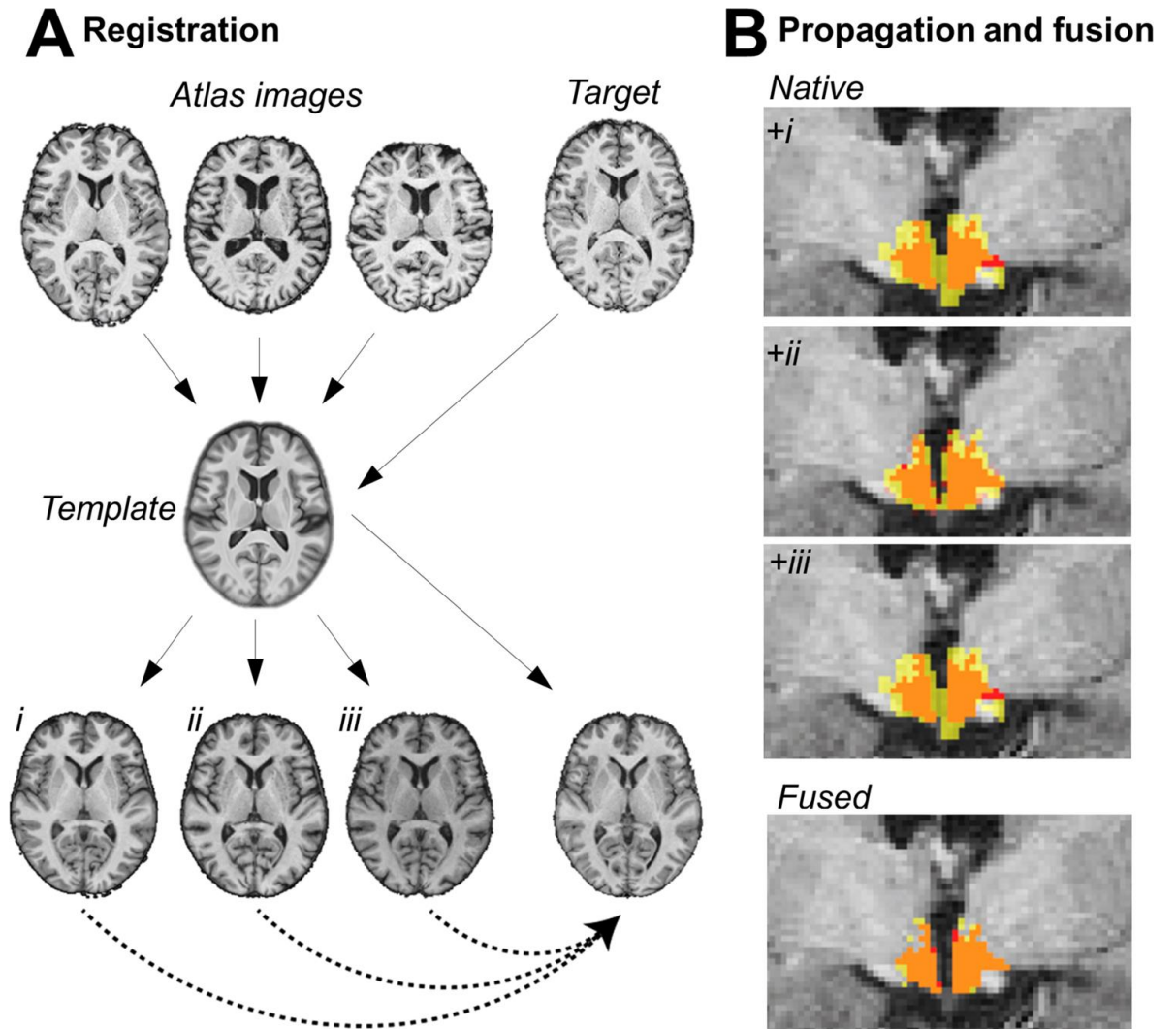
- Using a single template
  - Variations & taxonomic diversity
  - One specimen cannot represent all: inconsistent accuracy



Lordkipanidze, D., Ponce de León, M. S., Margvelashvili, A., Rak, Y., Rightmire, G. P., Vekua, A., & Zollikofer, C. P. (2013). A complete skull from Dmanisi, Georgia, and the evolutionary biology of early Homo. *Science*, 342(6156), 326-331.

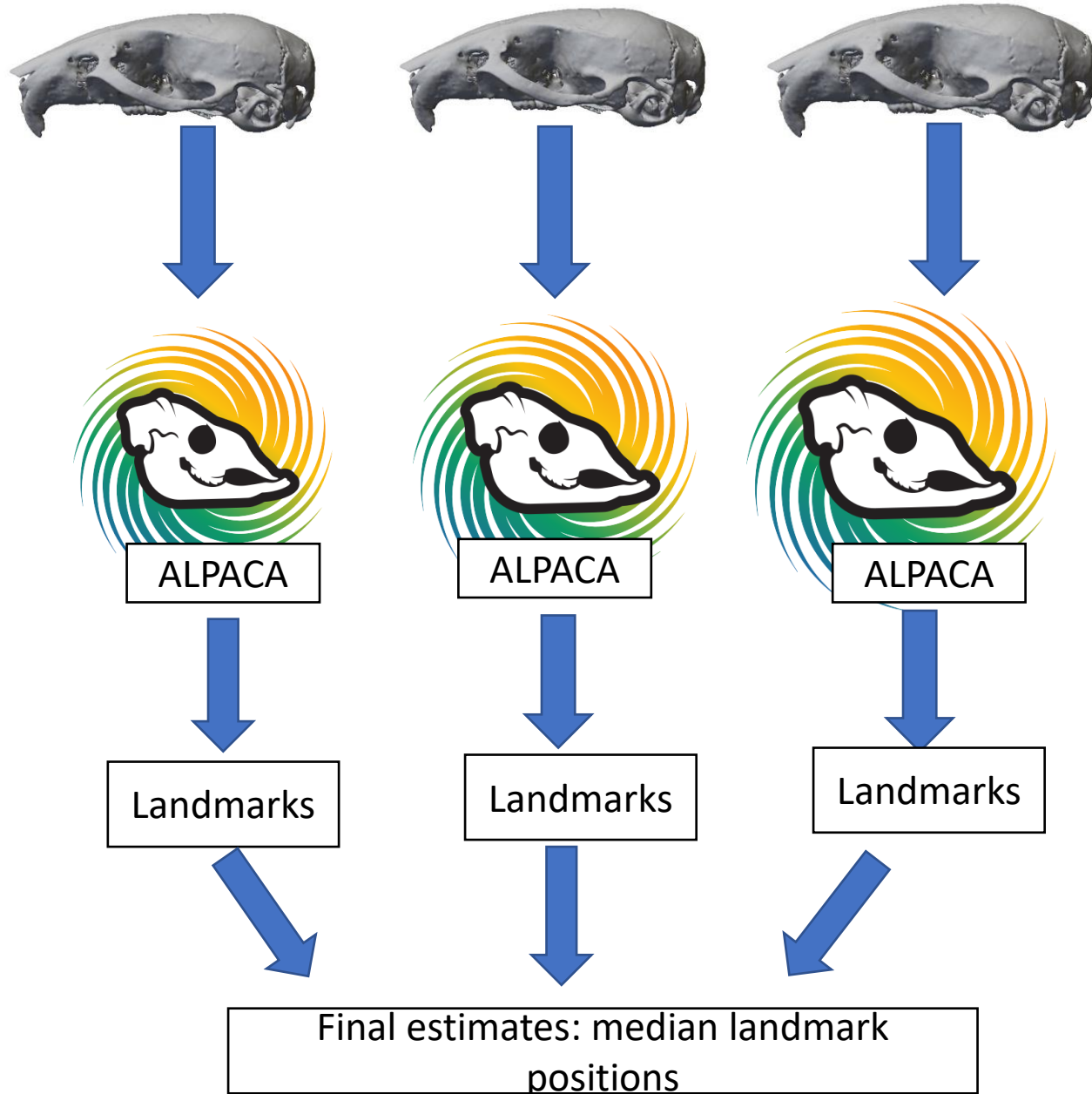
# Solution: use multiple templates

- A more holistic representation of the whole sample
- Multi-templates methods: commonly used in automated segmentation



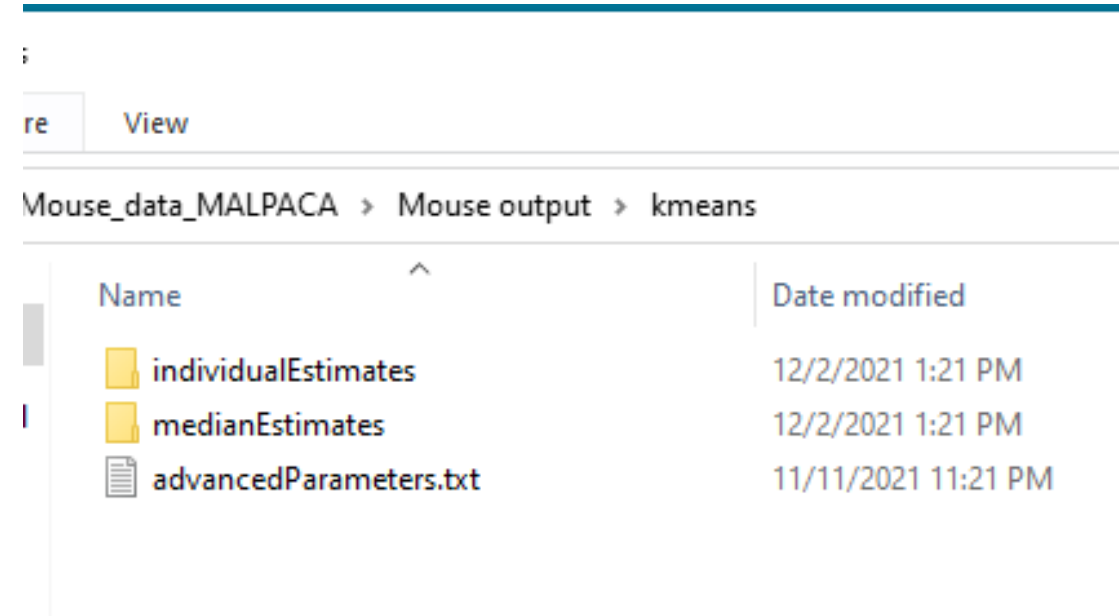
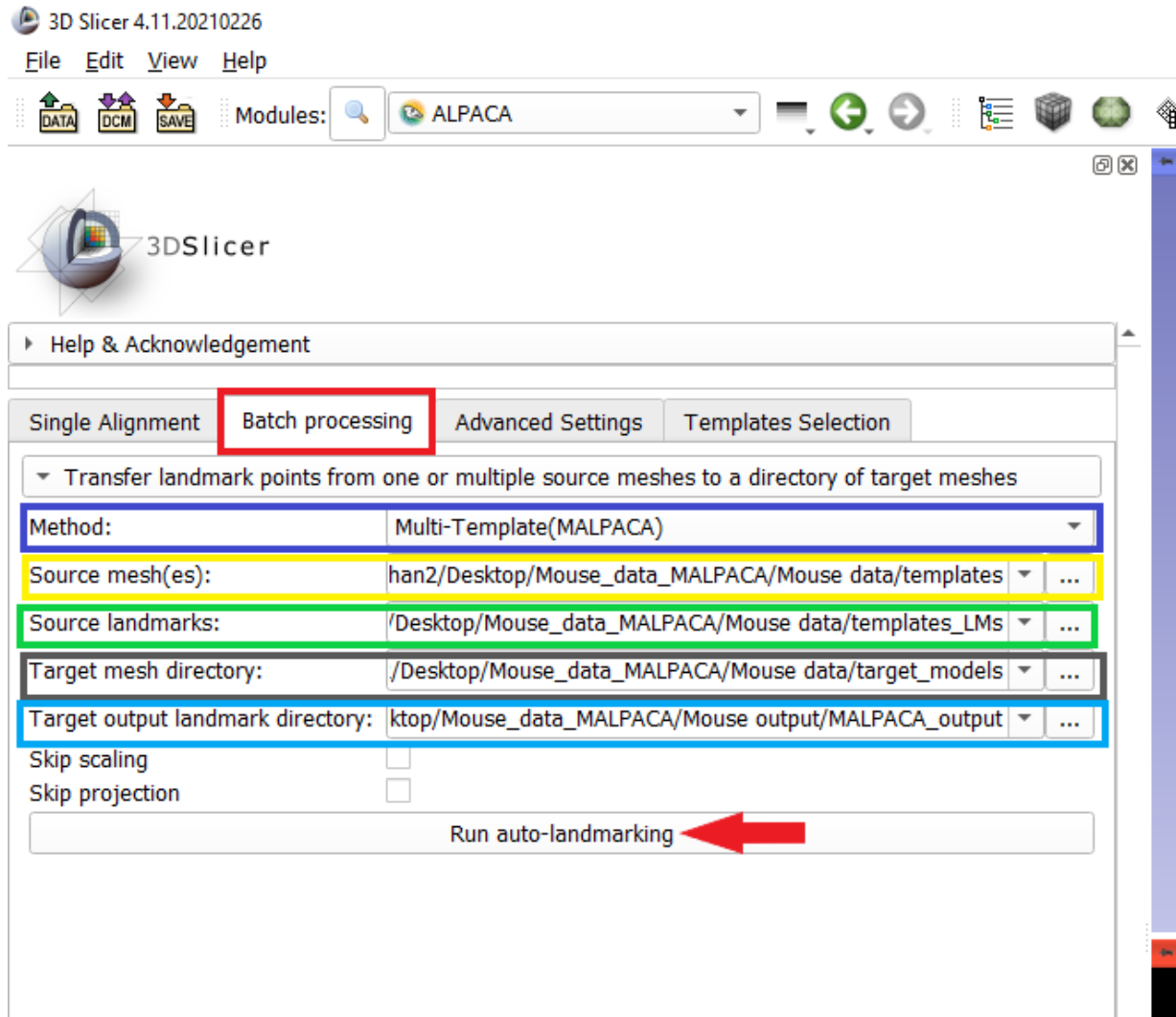
# MALPACA pipeline

- MALPACA = running separate ALPACAs
- Median of ALPACA estimates for each landmark = final output



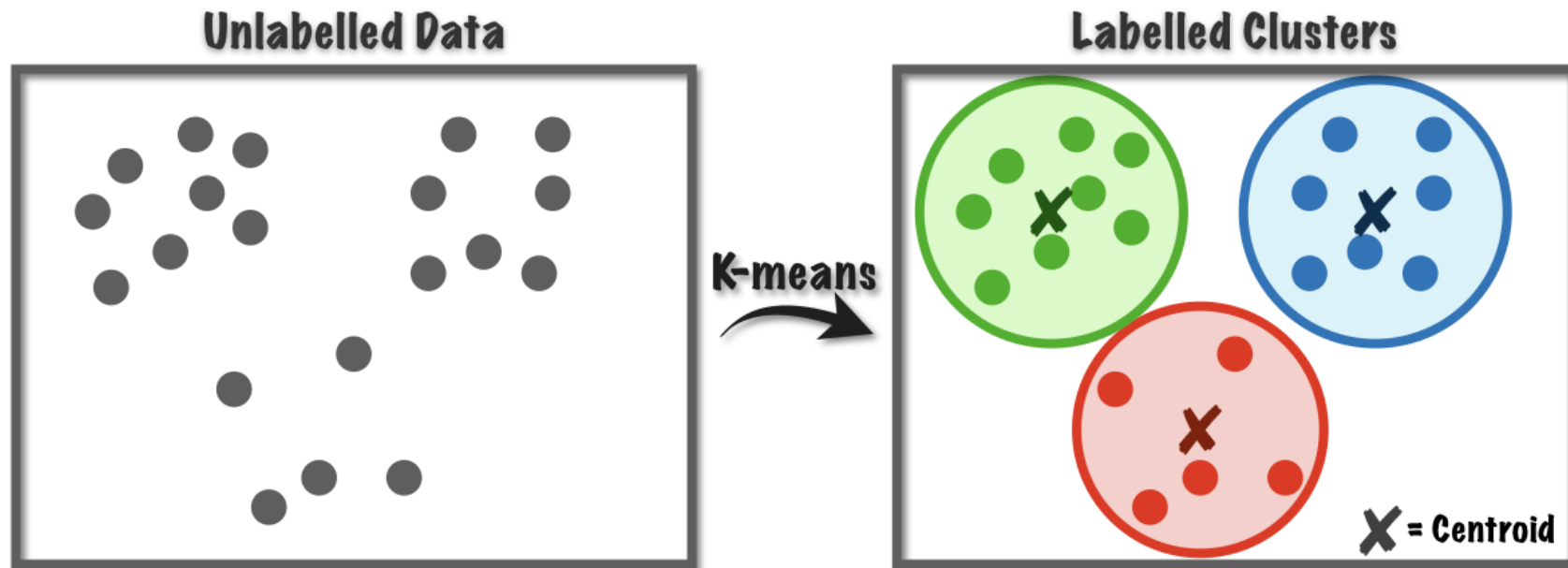
# SlicerMorph implementation

- MALPACA in batch mode in the ALPACA module



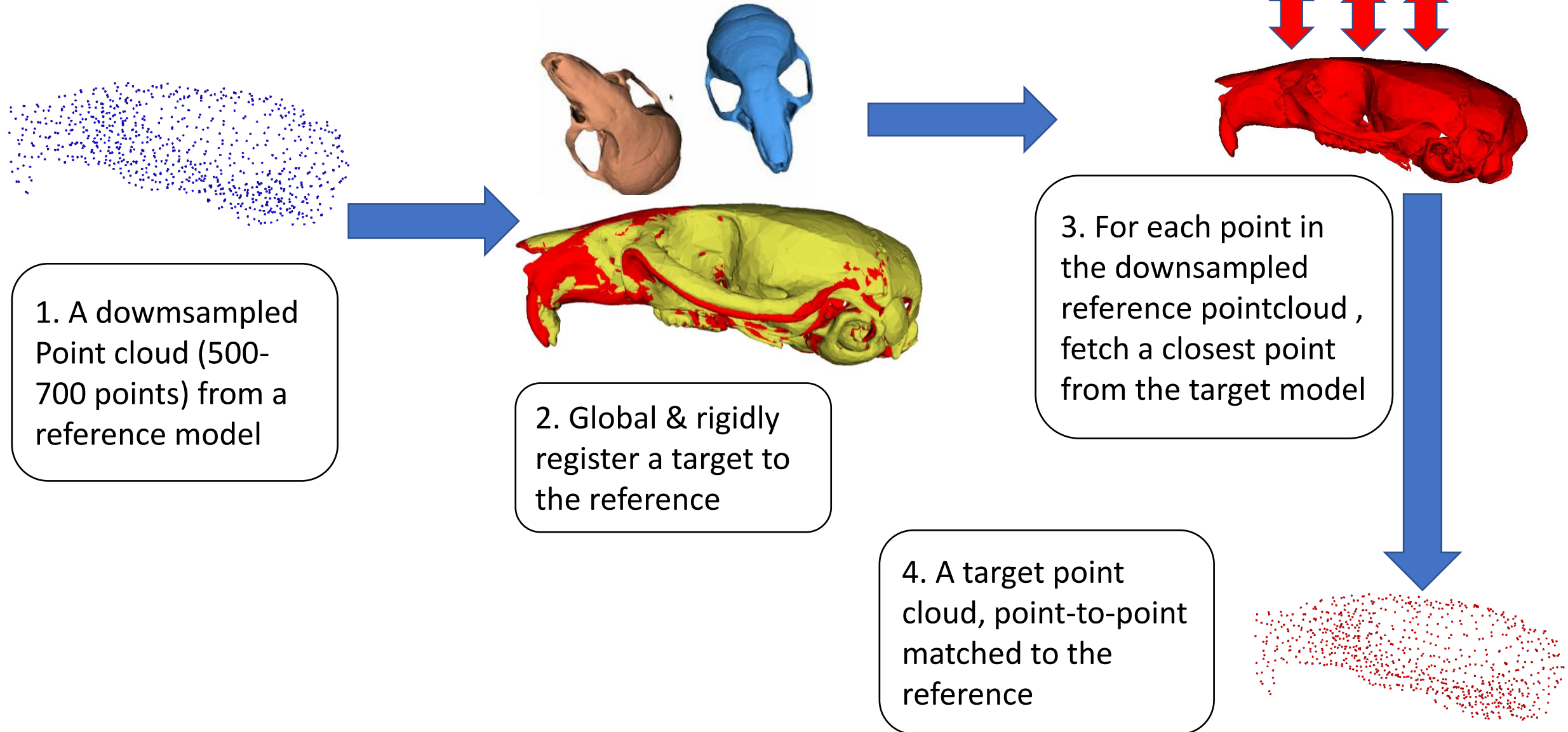
# Templates selection

- K-means clustering for estimating group structures
  - Start: randomly selecting k specimens as cluster centroids
  - Then allocating specimens to clusters according to Euclidean distances to the centroids
  - Re-calculating centroids (means), re-allocating according to distances
  - Iterate this process
  - Stop when centroids become stable/convergent → optimal clustering



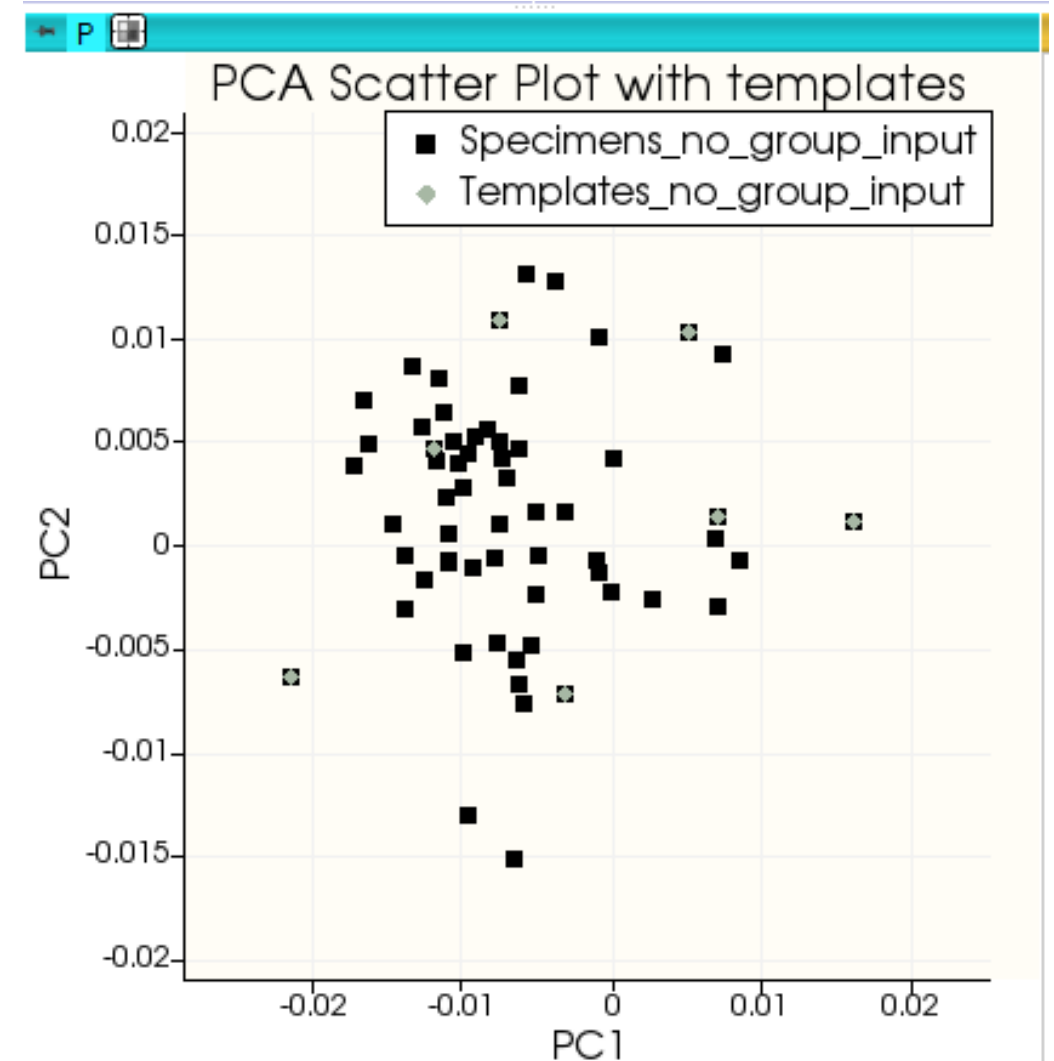


# K-means templates selection based on downsampled point clouds



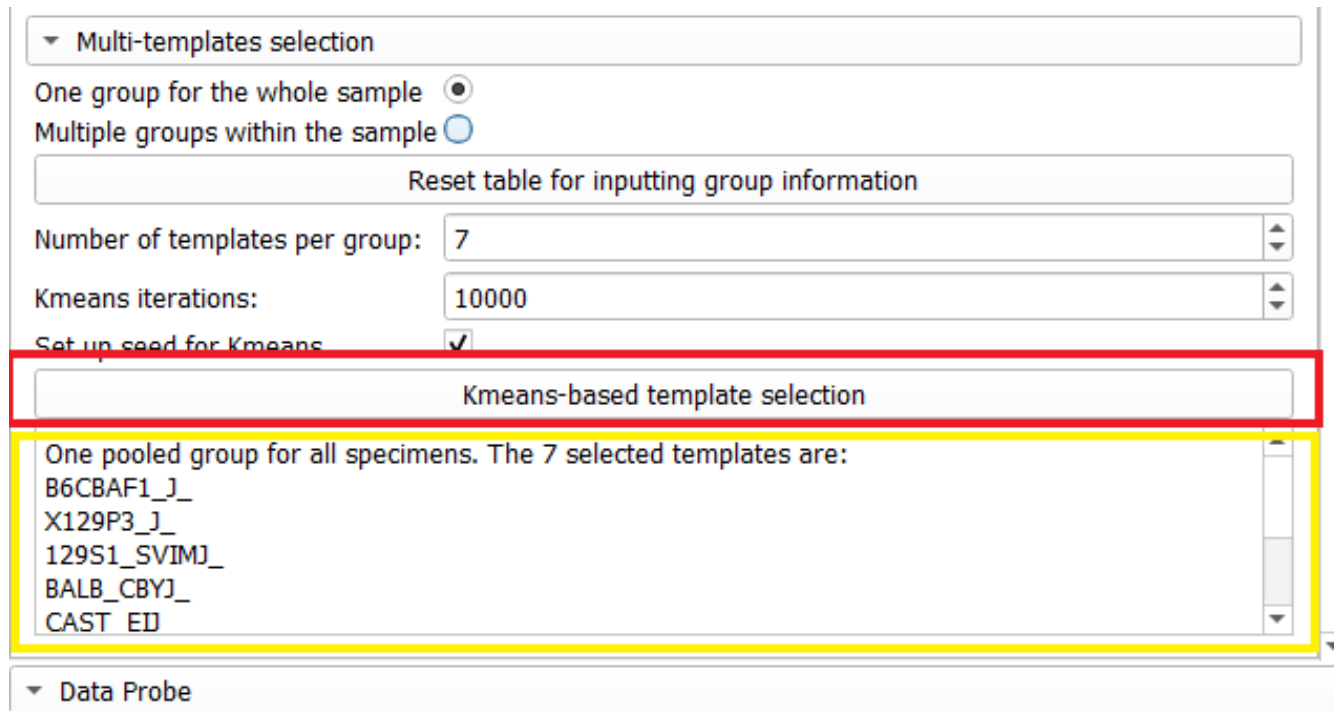
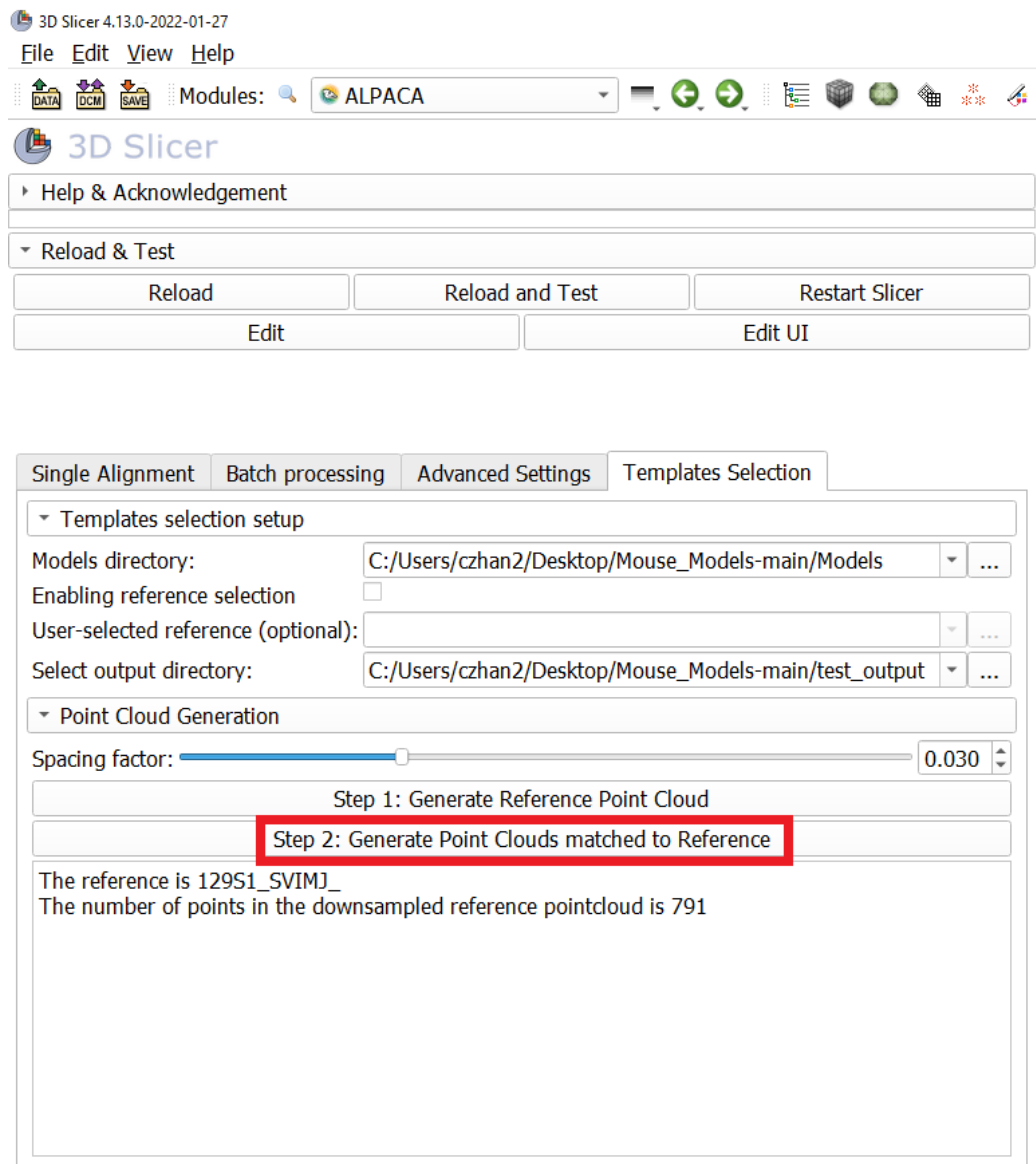
# K-means templates selection based on downsampled point clouds

- All point clouds as landmark sets with point-to-point correspondence
- Run GPA, export the full set of PC scores
- K-means based on PC scores
  - To roughly capture patterns of overall variability
- A template = the specimen closest to a centroid





# SlicerMorph implementation



# Samples with known groups (e.g., a multi-species example): select templates for each group

## Multi-templates selection

One group for the whole sample ☐

Multiple groups within the sample ☒

Reset table for inputting group information

Number of templates per group: 2

Kmeans iterations: 10000

Set up seed for Kmeans ☒

Kmeans-based template selection

The sample is divided into 3 groups. The templates for each group are:

Group G

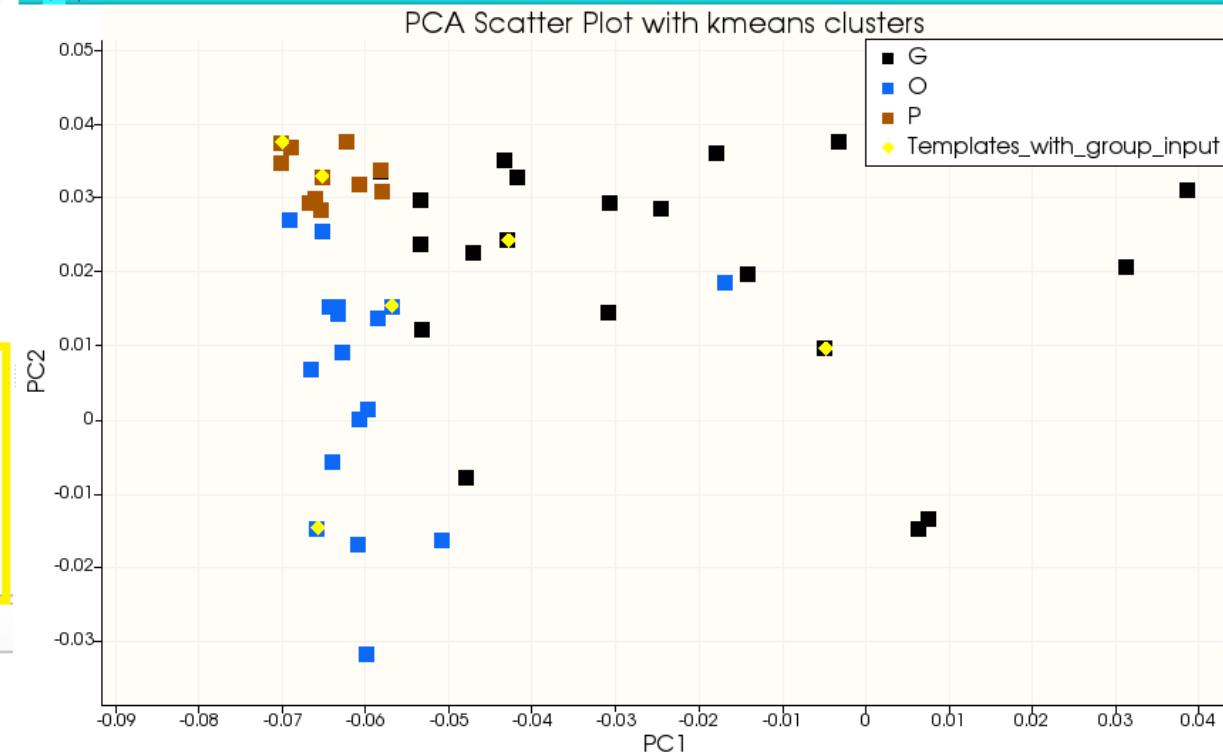
USNM590953\_CRANIUM

USNM599167\_CRANIUM

Group O

USNM153830-Cranium

## Data Probe




bioRxiv posts many COVID19-related papers. A reminder: they have not been formally peer-reviewed and should not guide health-related behavior or be reported in the press as conclusive.

New Results

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## Automated Landmarking via Multiple Templates

Chi Zhang, Arthur Porto, Sara Rolfe, Altan Kocatulum,  A. Murat Maga

**doi:** <https://doi.org/10.1101/2022.01.04.474967>

This article is a preprint and has not been certified by peer review [what does this mean?].



**Abstract**

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### Abstract

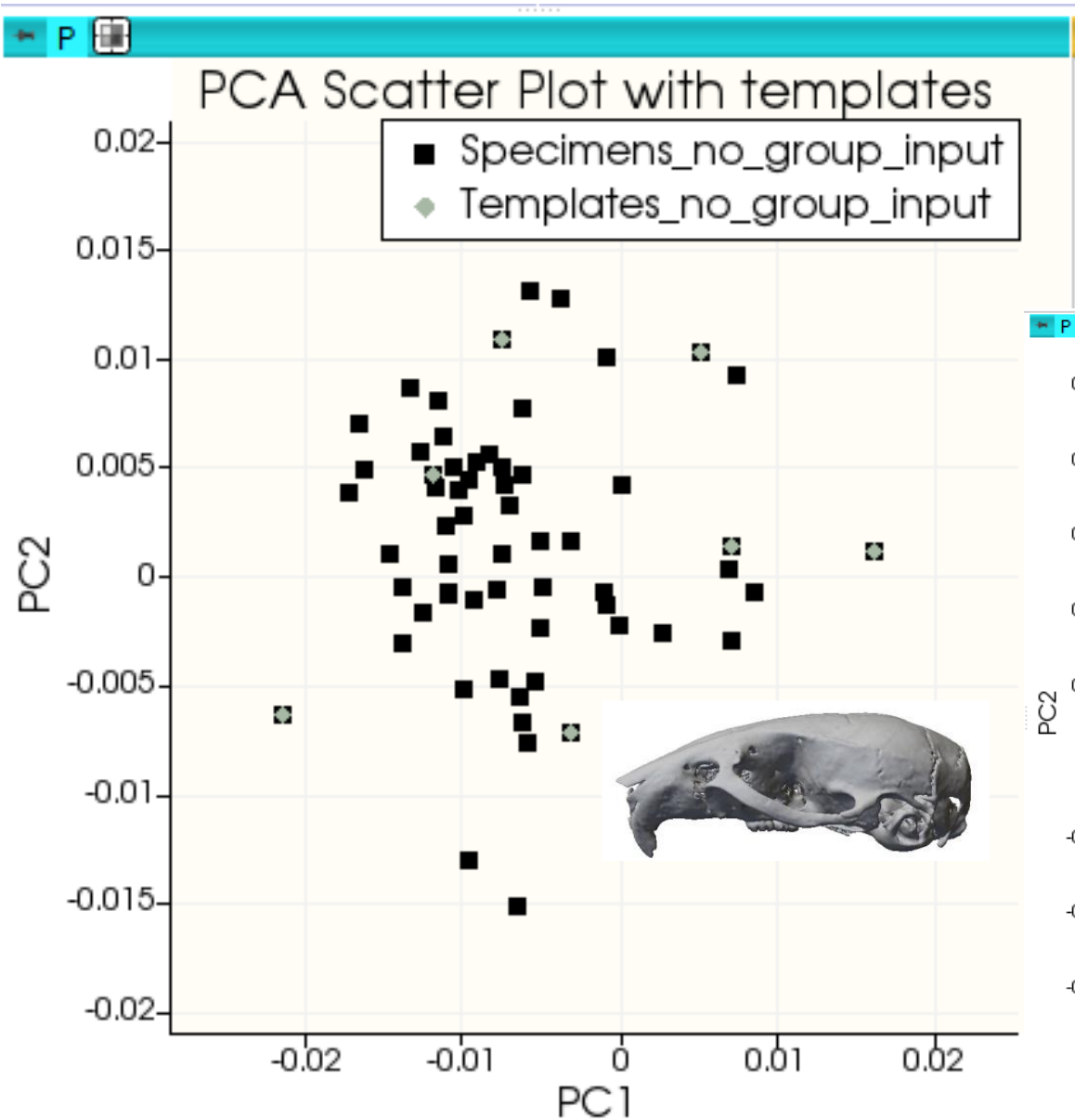
Geometric morphometrics based on landmark data has been increasingly used in biomedical and biological research for quantifying complex phenotypes. However, manual landmarking can be laborious and subject to intra and interobserver errors. This has motivated the development of automated landmarking methods. We have

# Two samples

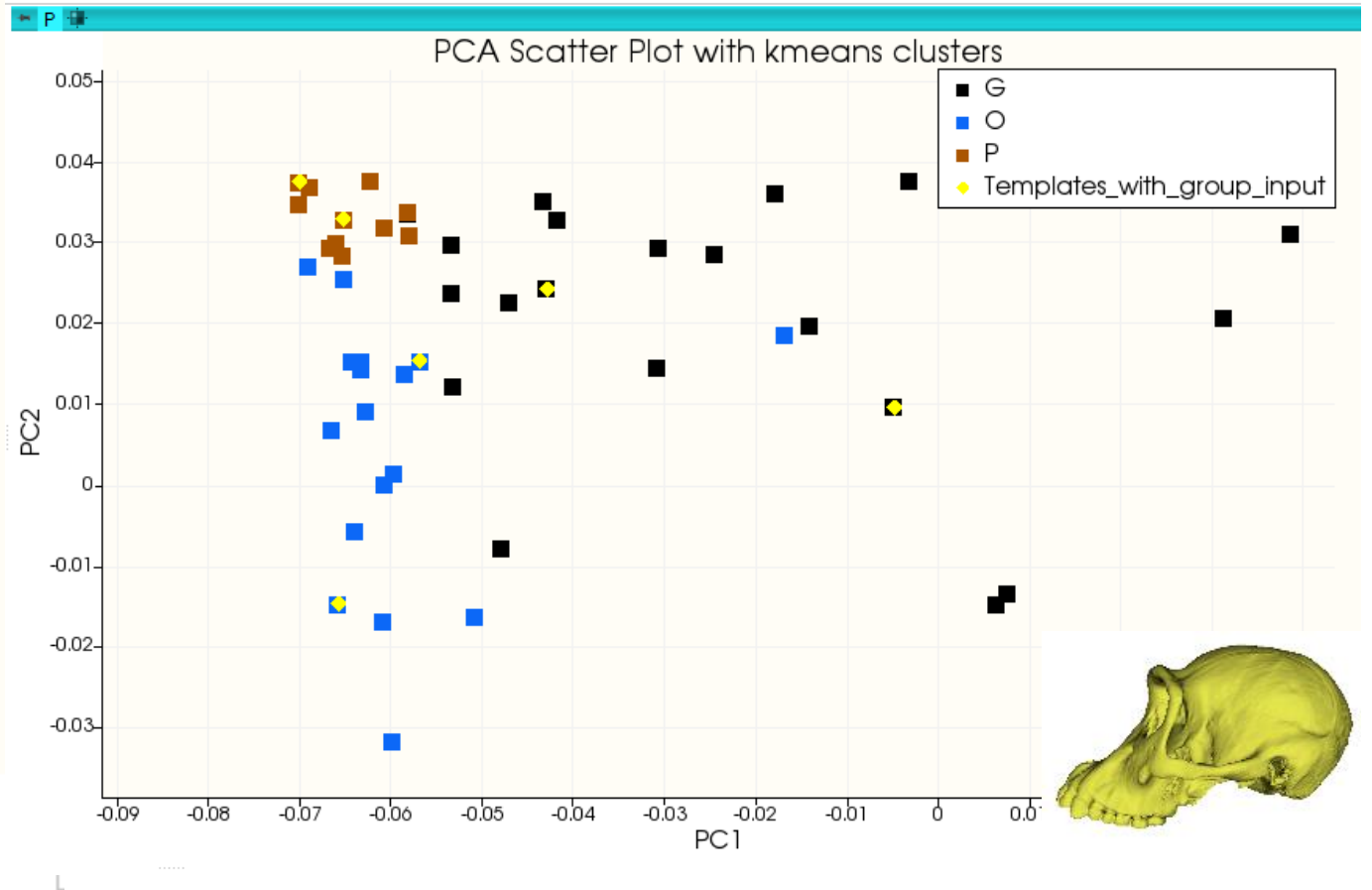
- 61 laboratory mice
  - Simulating single-population sample
  - A synthetic template (average mouse model)
  - 51 manual landmarks/specimen = “Gold Standard”
- 52 great apes (11 *Pan*; 23 *Gorilla*; 18 *Pongo*)
  - Simulating multi-species sample
  - Two manual landmark sets;
    - 41 landmarks/specimen
    - use the mean as the “Gold standard”
  - Intraobserver error



## Mouse sample: 7 templates

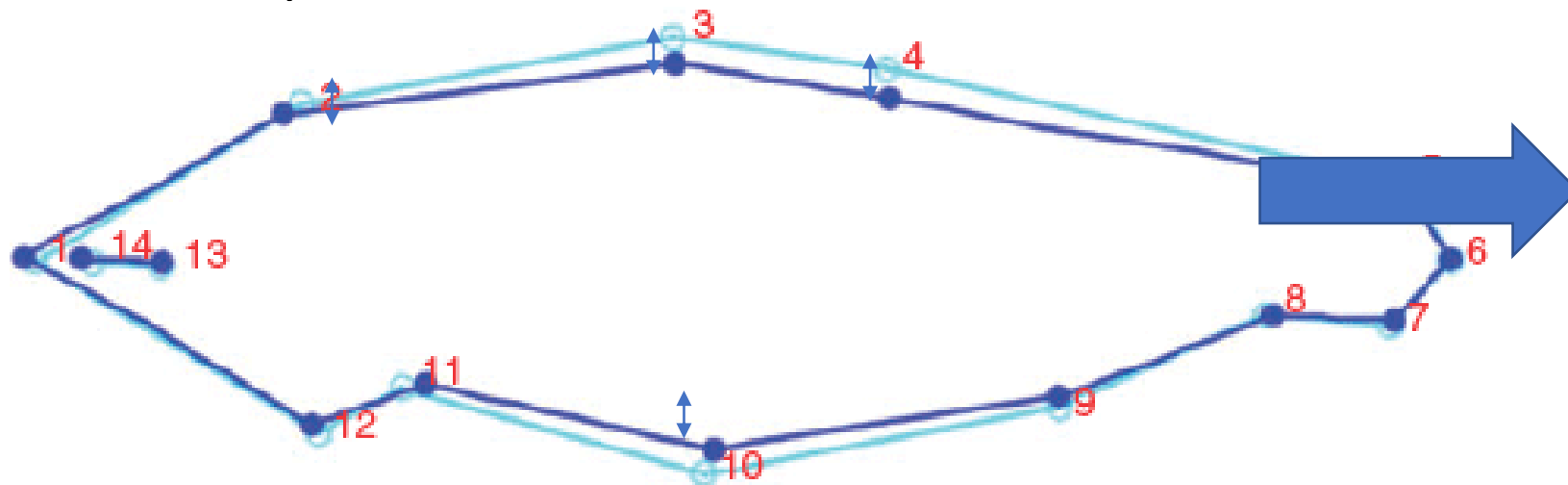


Ape sample: 2 templates each species; 6 templates in total



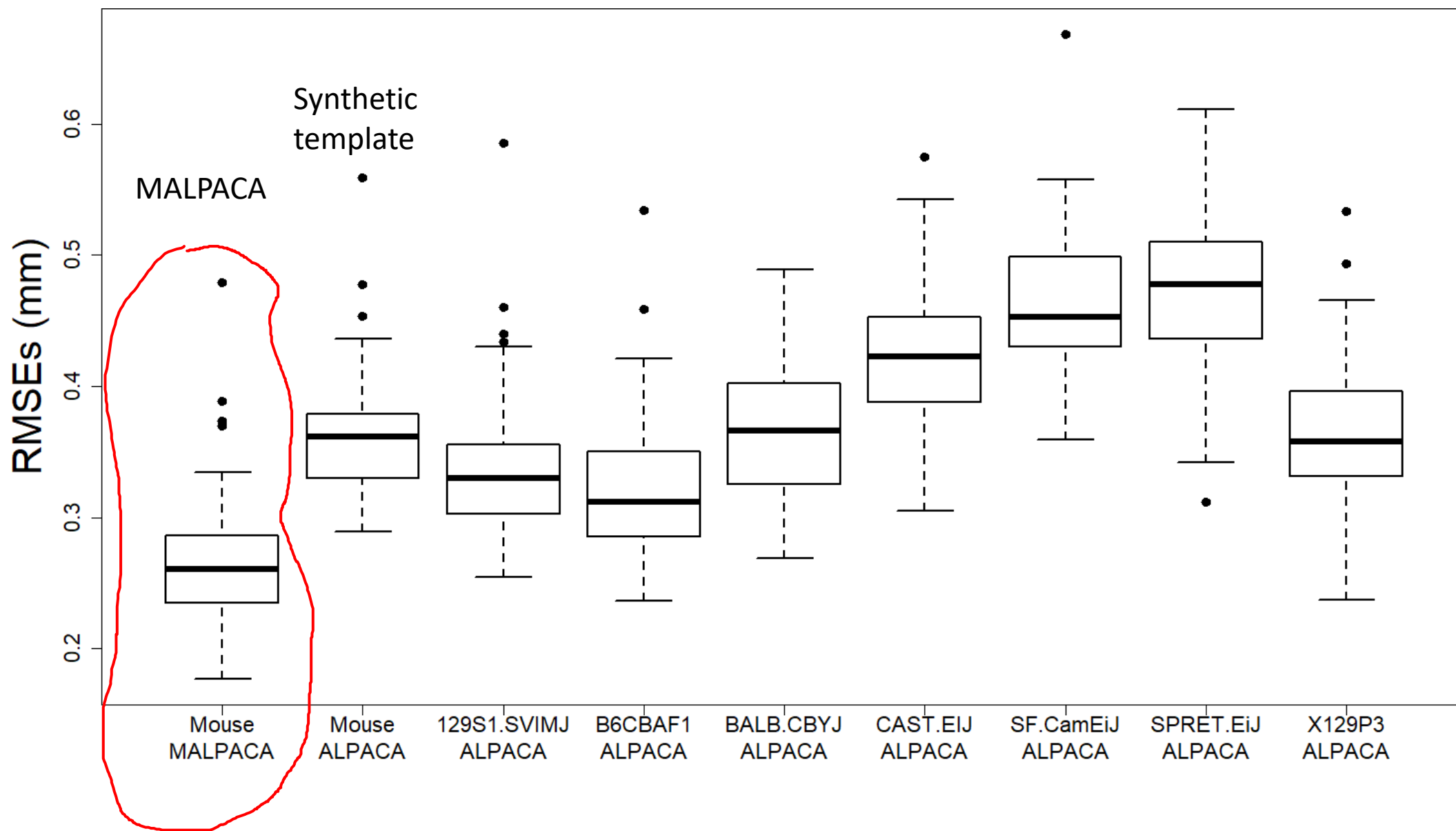
# Evaluating MALPACA & ALPACA performance

- Deviations (errors) between estimates & “Gold Standard (GS)” (manual LMs)
  - LM errors/specimen summarized by root mean square error (RMSE)
  - Smaller RMSE = better performance
- Correlations in morphometric shape variables (Procrustes distances & PC scores)



**RMSE:** root of mean sum of squared errors between each pair of corresponding estimated & GS landmarks

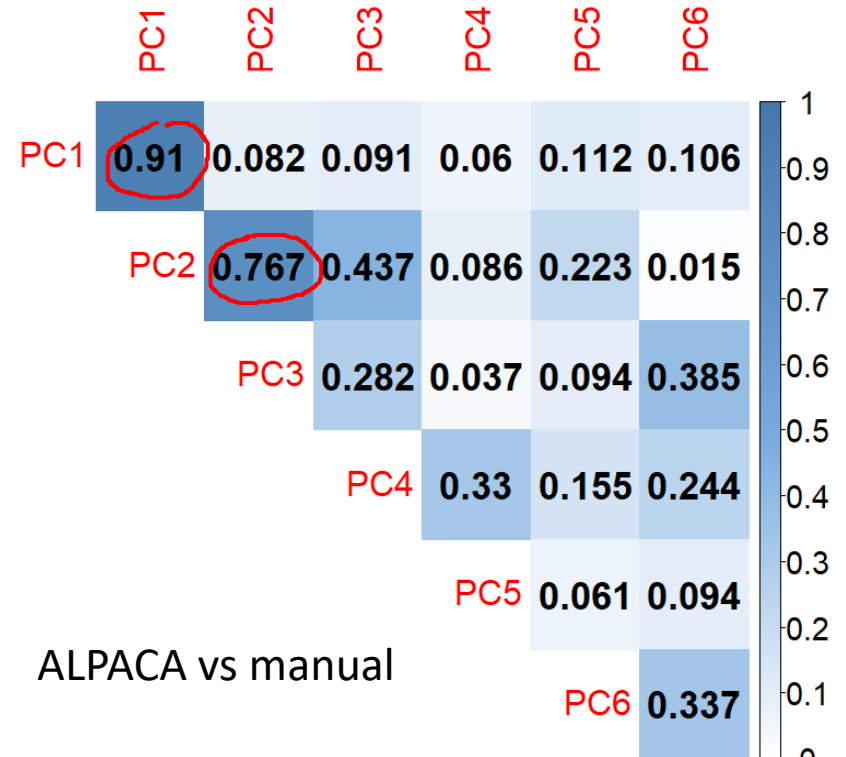
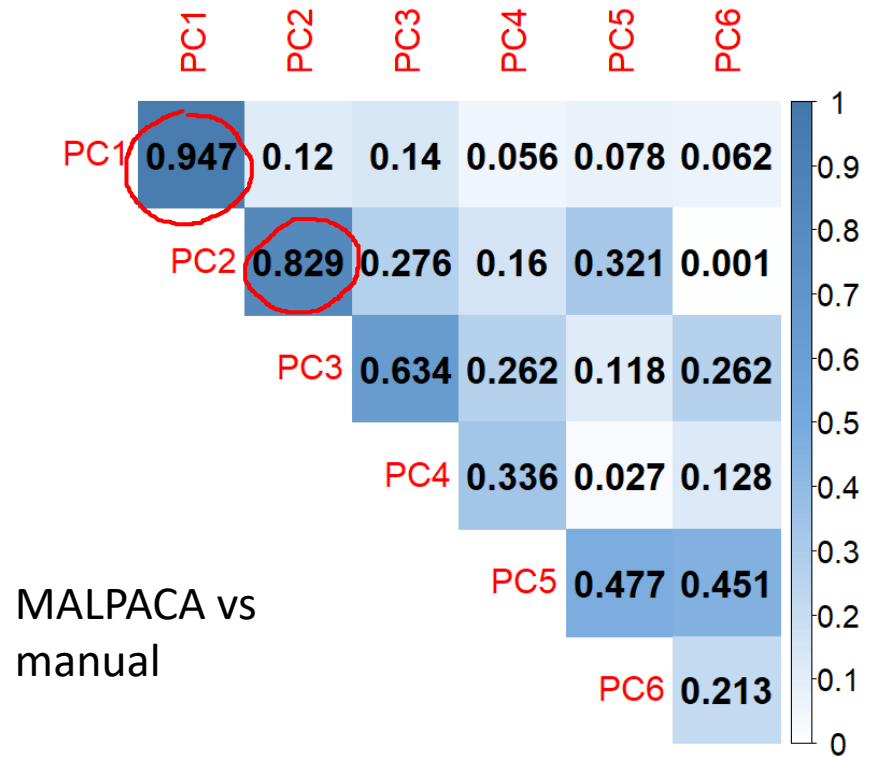
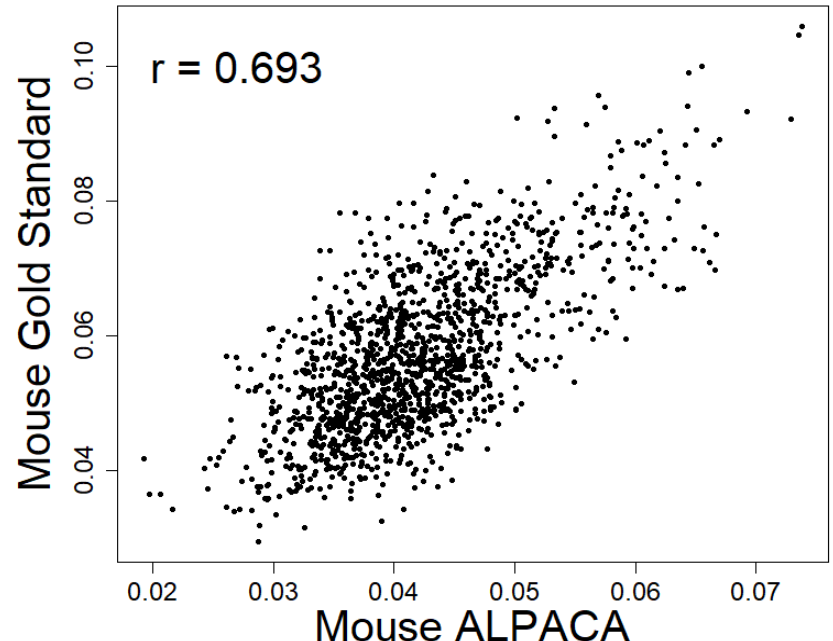
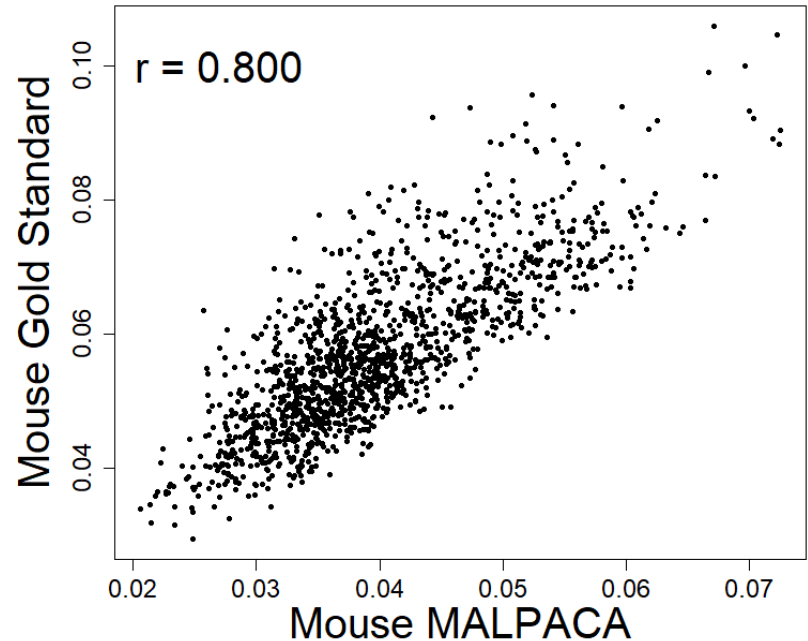
# RMSEs of the mouse samples



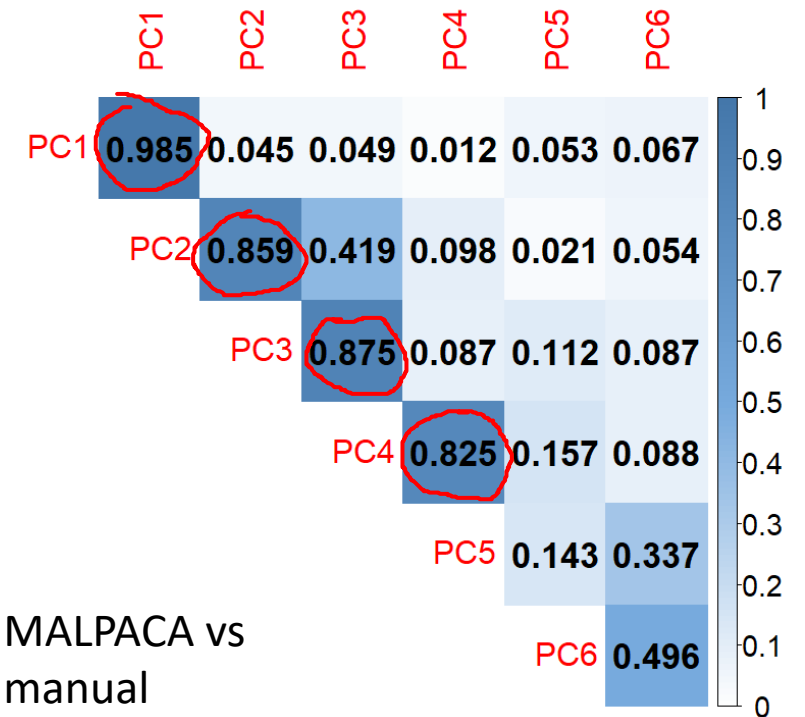
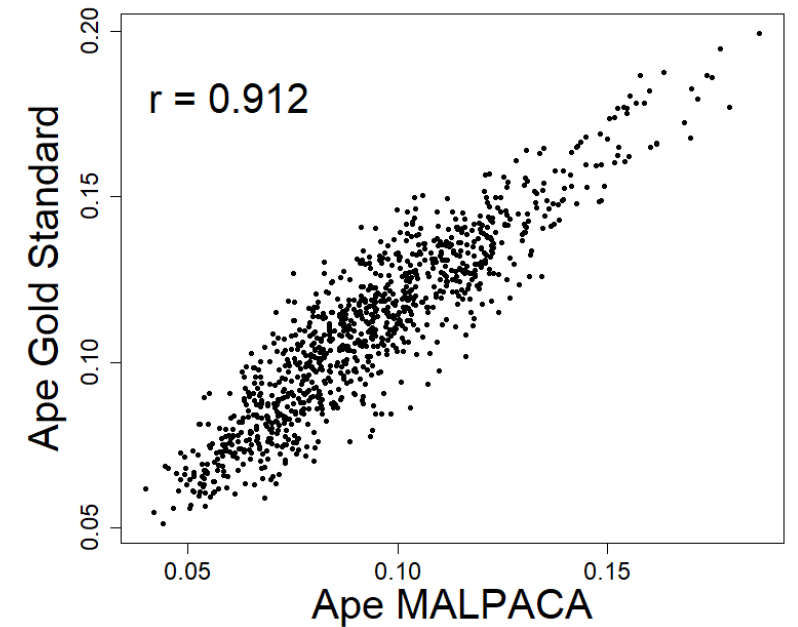
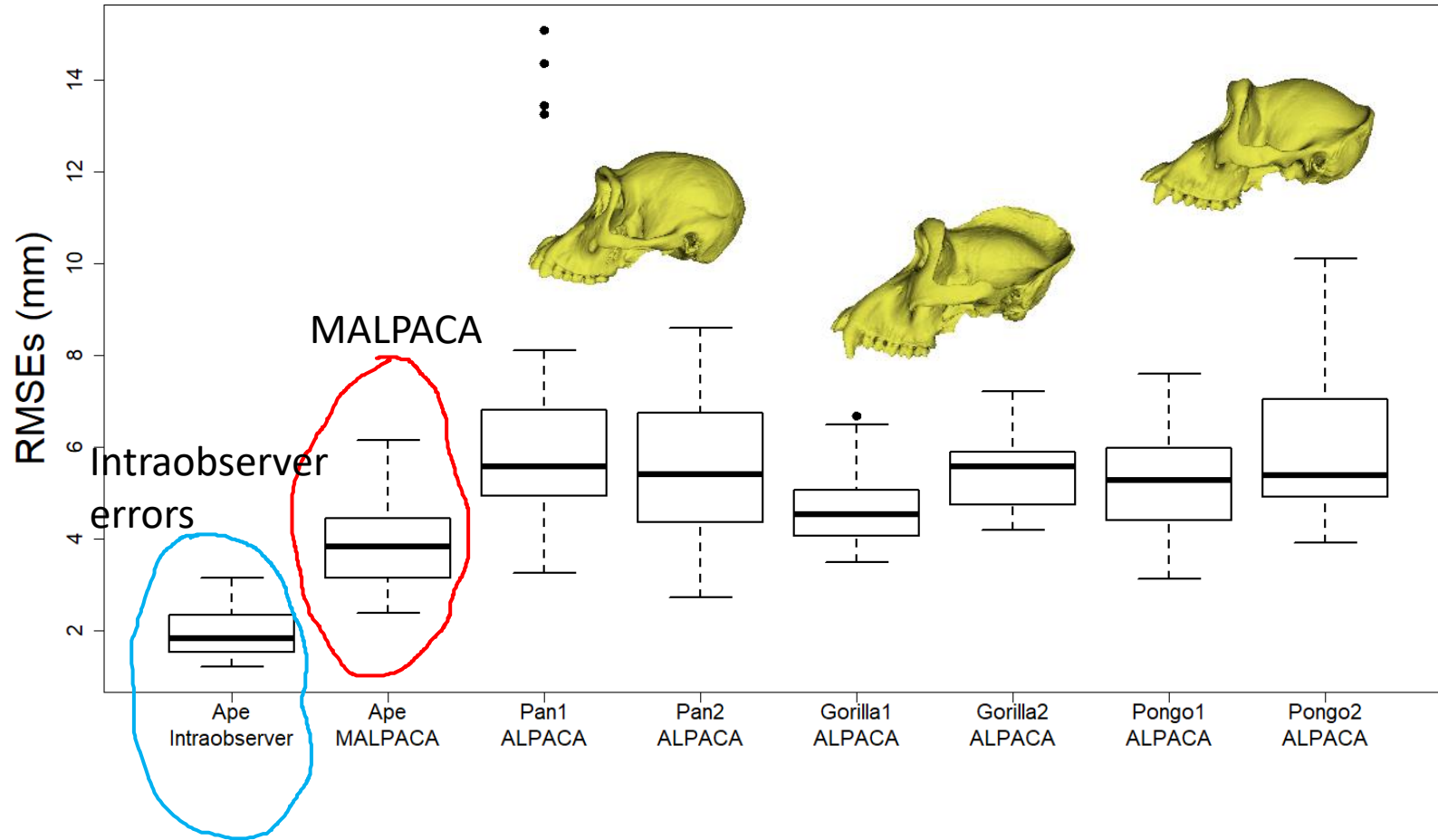


Separate GPA of MALPACA estimates & manual LMs:

- MALPACA with higher correlations



# RMSEs of the ape sample



# The efficacy of K-means templates selection

- Permutation analysis: randomly selected templates each round, do MALPACA, compute RMSEs
  - Mouse: 100 rounds; Ape: 50 rounds
- Compare K-means RMSEs to the 50<sup>th</sup> percentile of all permuted RMSEs.
  - **Mouse:** 25 of 54 (**46.2%**) K-means MALPACA RMSEs are smaller
  - **Apes:** 20 of 46 (**43.5%**) K-means MALPACA RMSEs are smaller
- **K-means not significantly better**
  - K-means can avoid choosing the worst template set
  - If having no prior information, k-means can be a safe choice

