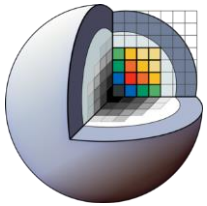
Applications of SSA: Growth Modeling

Ezgi Mercan
Murat Maga
Richard Hopper

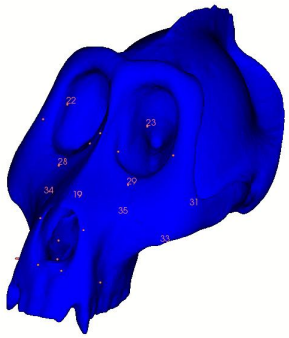
Life After SlicerMorph



Images

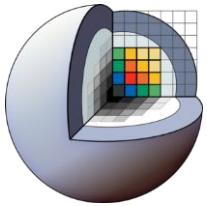
Landmarks (or semi-landmarks)

Mean shape, PCs, eigen values…



Now what?

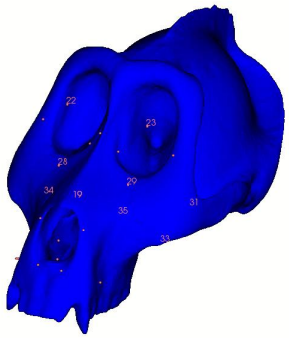
Life After SlicerMorph



Images **+ Variables**

Landmarks (or semi-landmarks)

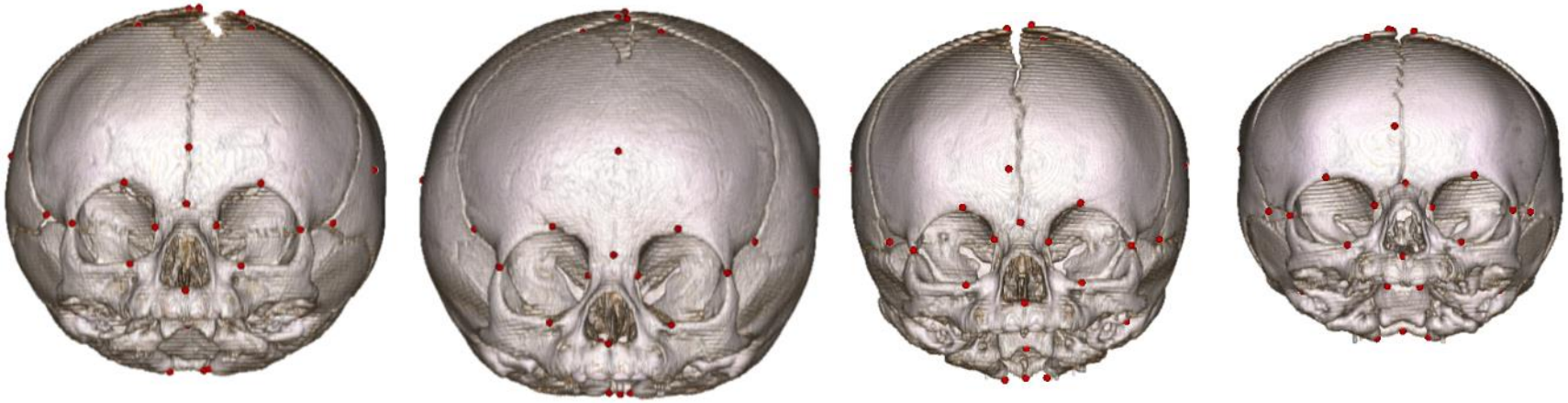
Mean shape, PCs, eigen values…



Now what? **Statistical Models**

Growth Modeling

- CT scans of pediatric human skull
- Variables: Age, Sex, Diagnosis
- Anatomical Landmarks
- Linear model: $landmark.position \sim age$



Growth Modeling

- Linear regression on age to predict coordinates of each landmark

$$LM1_x \sim a_{1x} \times age + b_{1x}$$
$$LM1_y \sim a_{1y} \times age + b_{1y}$$
$$LM1_z \sim a_{1z} \times age + b_{1z}$$
$$LM2_x \sim a_{2x} \times age + b_{2x}$$
$$LM2_y \sim a_{2y} \times age + b_{2y}$$
$$LM2_z \sim a_{2z} \times age + b_{2z}$$
$$\dots$$

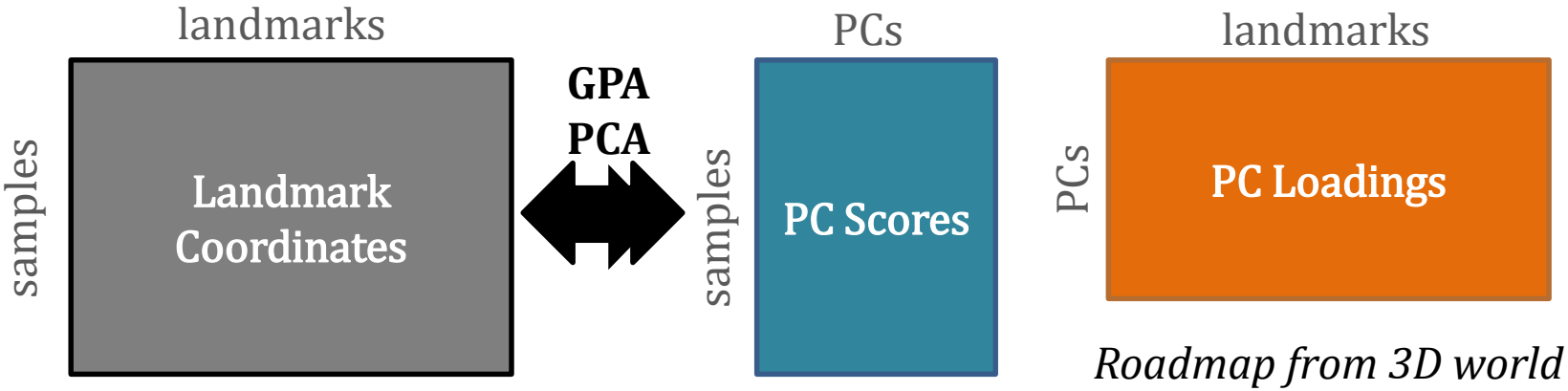
- **Problems:**
  - **Landmark positions are <u>not independent</u>**
  - **Number of landmarks x 3 models**

GPA + PCA

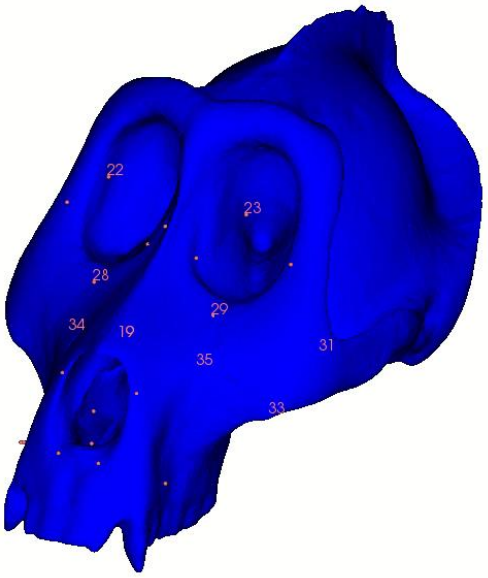
$$PC.scores \sim age$$

- In our data, first 20 PCs explains 90% of the variation, i.e. just 20 models
  - Dimensionality reduction
  - Noise removal
- PCs are orthogonal
- Each PC is a linear combination of all landmarks.

Growth Modeling

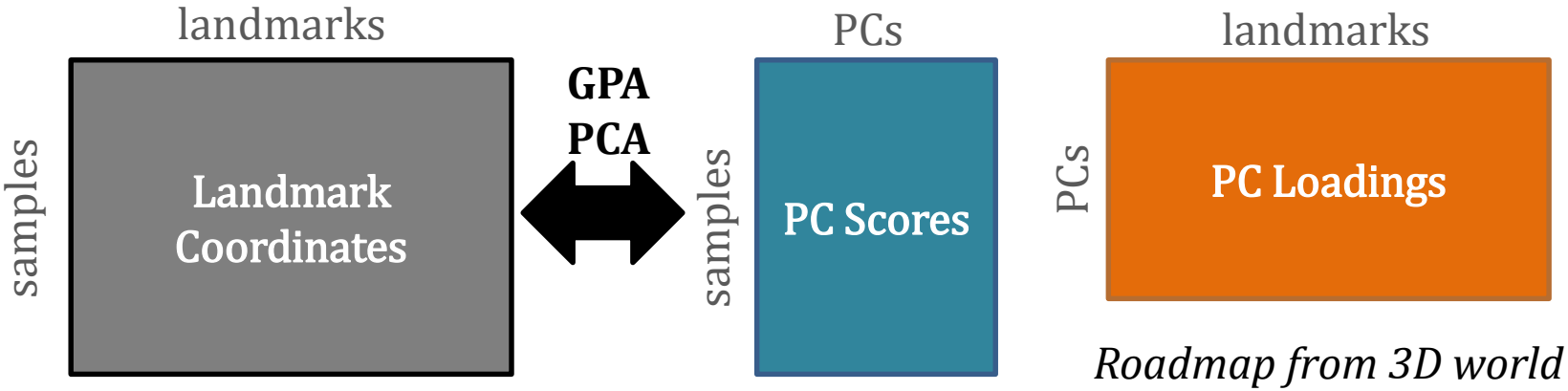


Roadmap from 3D world to PCA-space and back



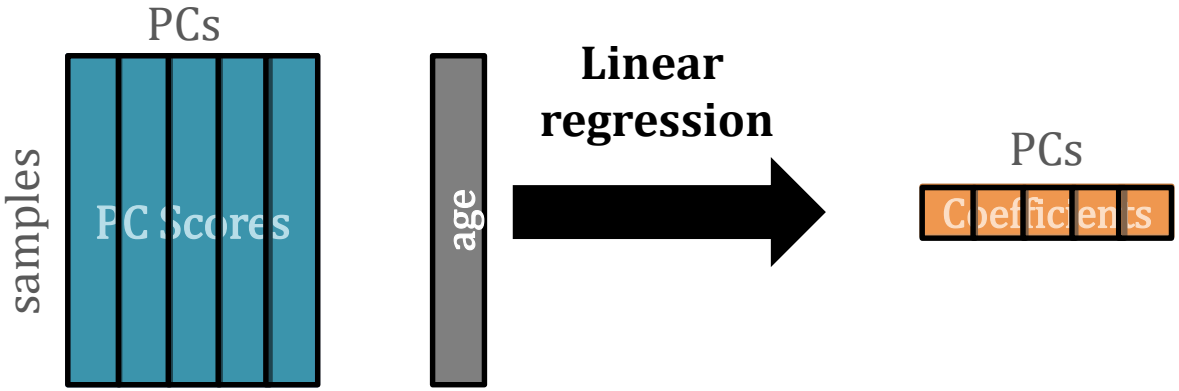
- Using the PC loadings and new PC scores, you can create new landmark coordinates.
  - Then morph a mesh to these new landmark positions.
- Morphs are realistic as long as your new PC scores are within the population parameters.

Growth Modeling

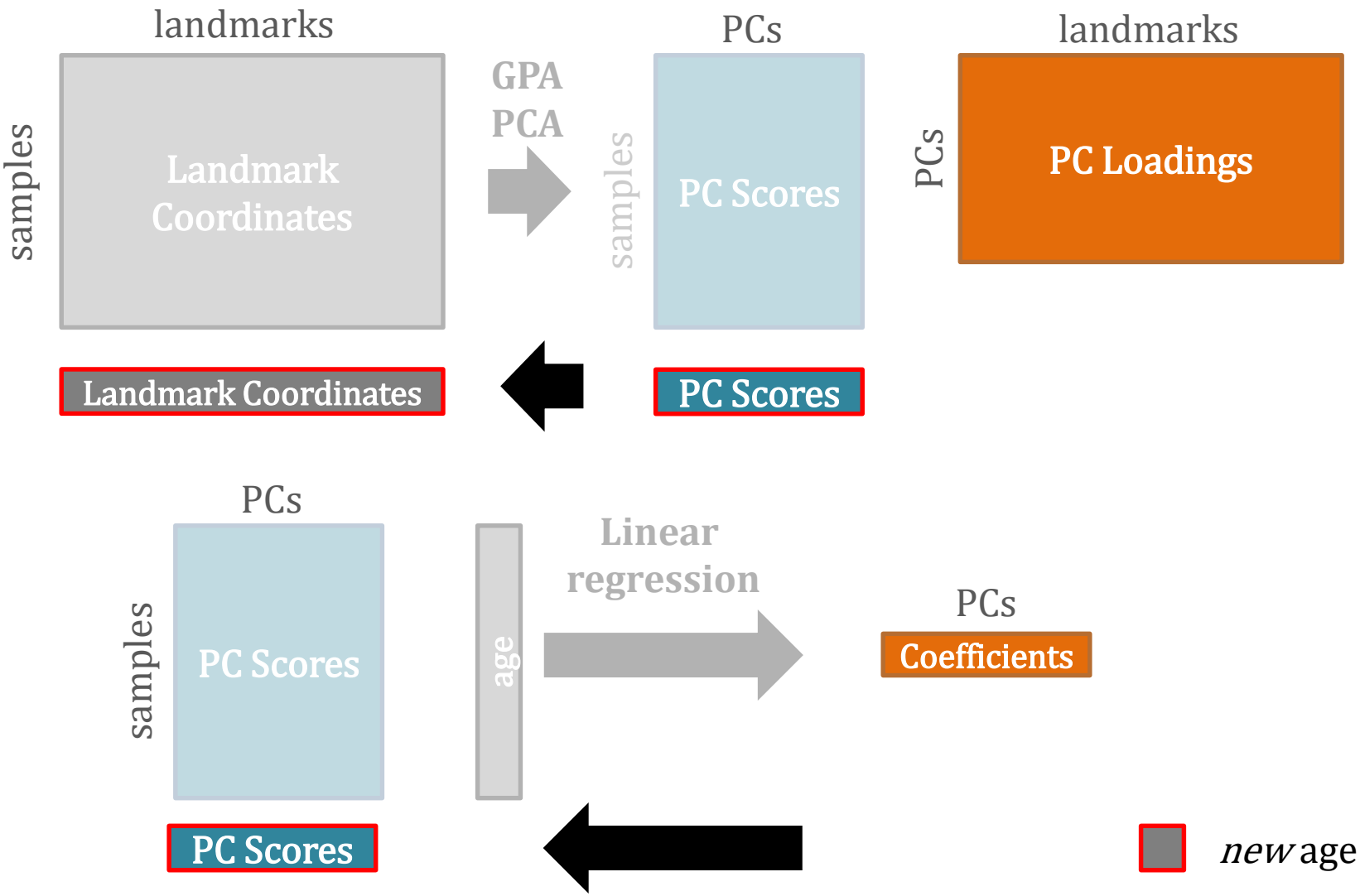


Roadmap from 3D world to PCA-space and back

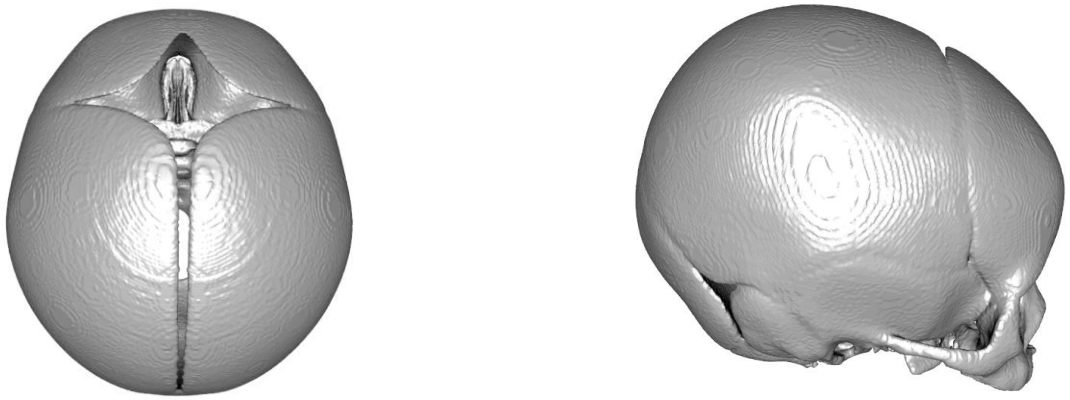
Model each PC as a function of age



Inference


landmarks
samples
Landmark Coordinates
GPA
PCA
PCs
samples
PC Scores
landmarks
PCs
PC Loadings
Landmark Coordinates
PC Scores
PCs
samples
PC Scores
age
Linear regression
PCs
Coefficients
PC Scores
new age

0-6m Normal Growth Model

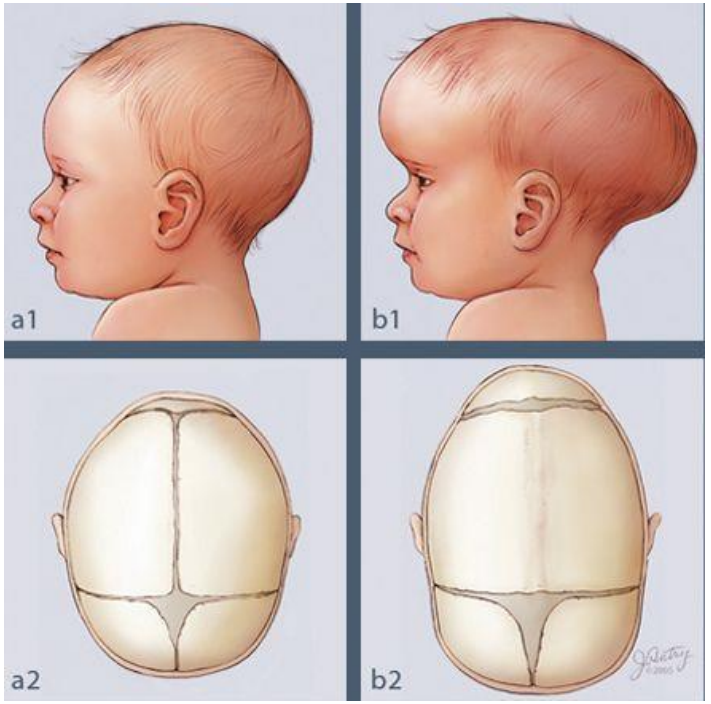


- Thin Plate Splines to warp a reference mesh to *inferred* landmark positions

!! TPS is accurate at and around the landmark locations but *interpolates* other surfaces.

Population-level Growth Models

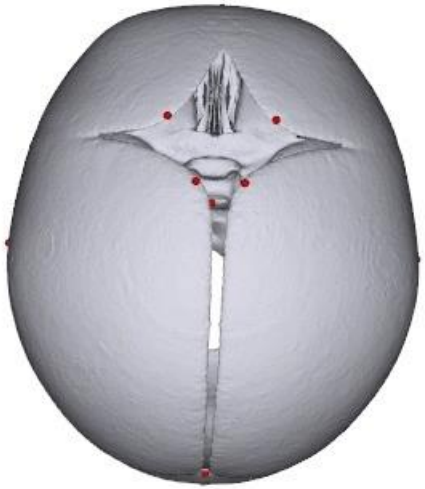
- Sagittal craniosynostosis (premature fusion of sagittal suture) occurs in approximately 1 in every 5000 births.
- If not surgically corrected, it can cause increased intracranial pressure which can lead to developmental problems.



Population-level Growth Models

- Apply the same methodology to unoperated 0-6mo patients with sagittal craniosynostosis.

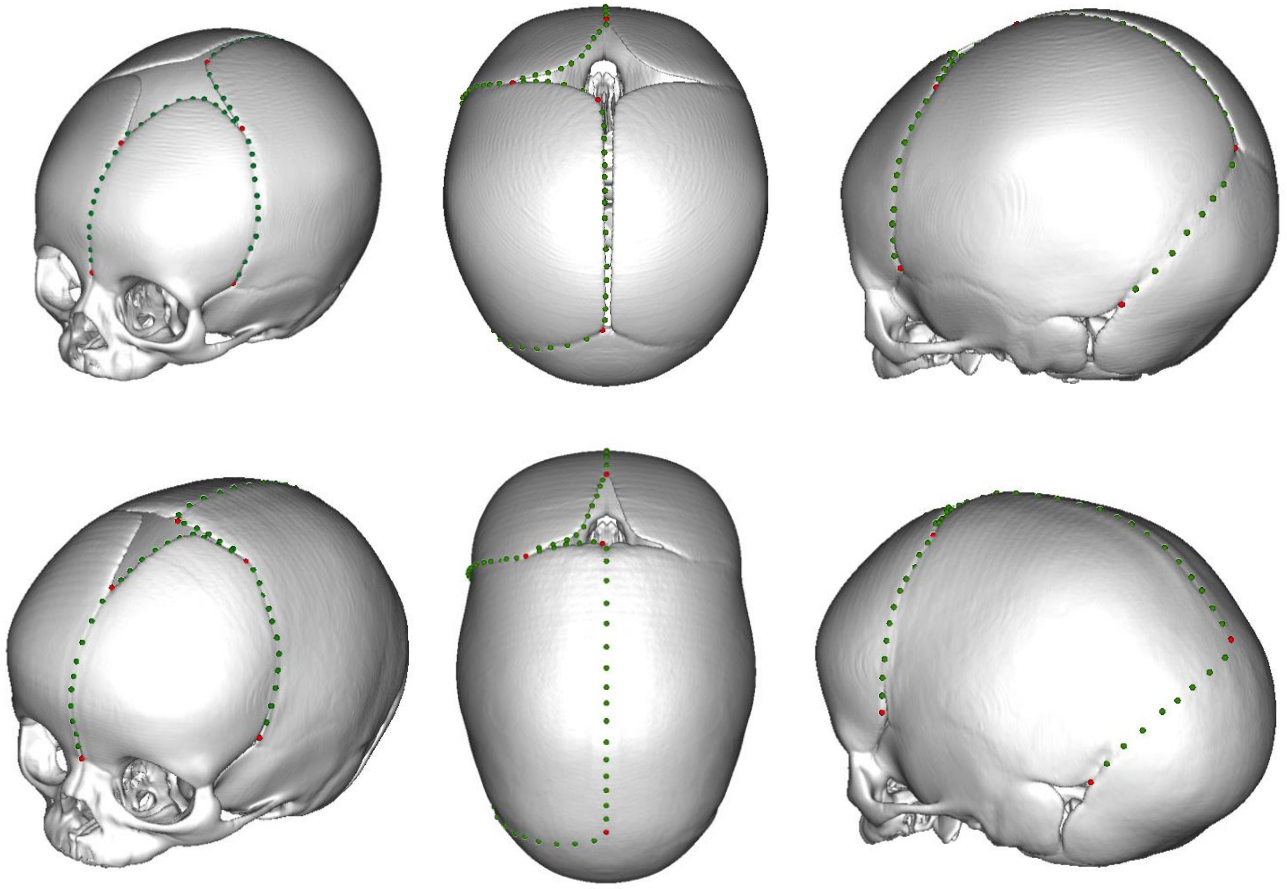
Normal Infant Model



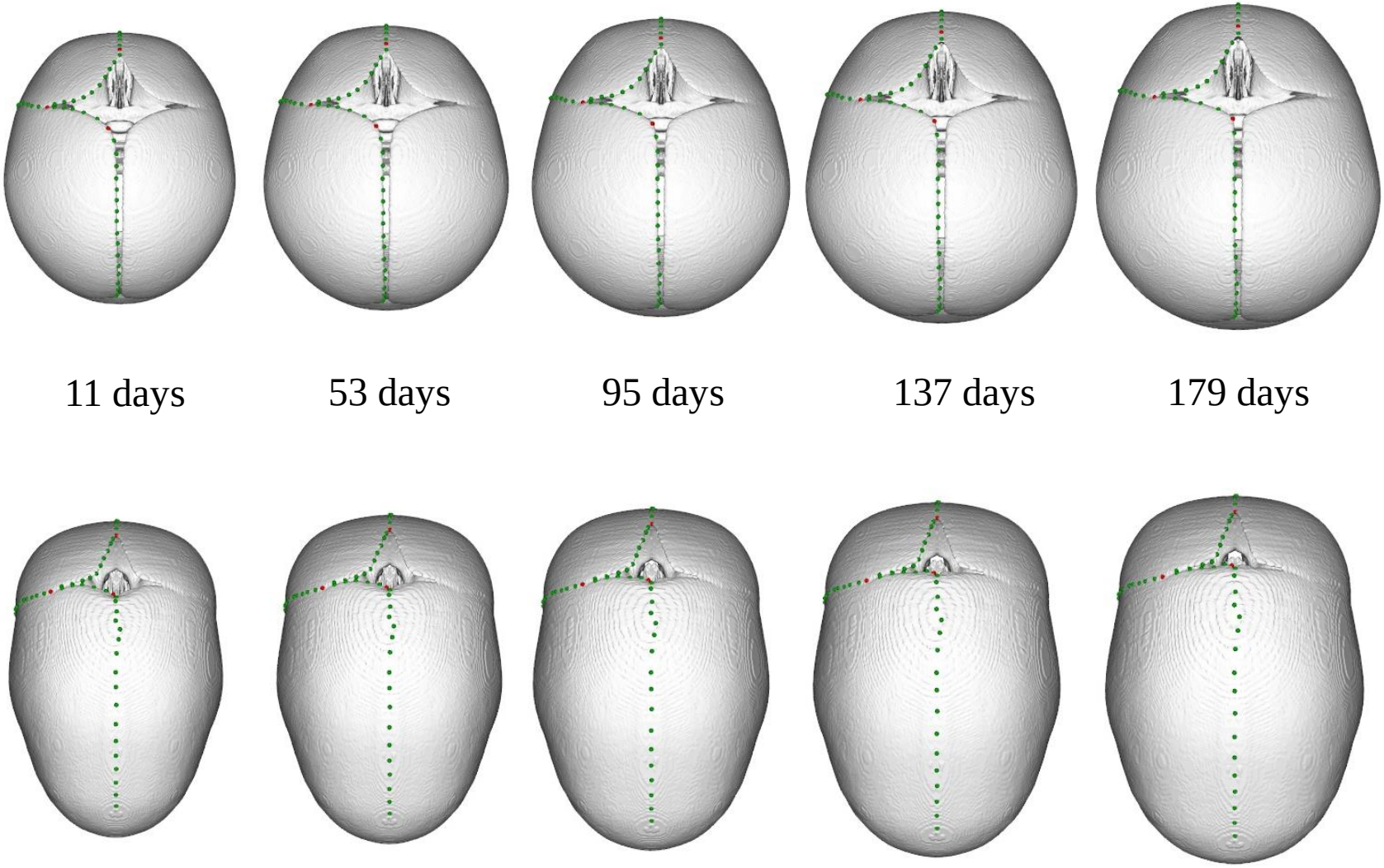
Sagittal Craniosynostosis Model

Population-level Growth Models

- Semi-landmark the reference image and transfer them to all instances in the model

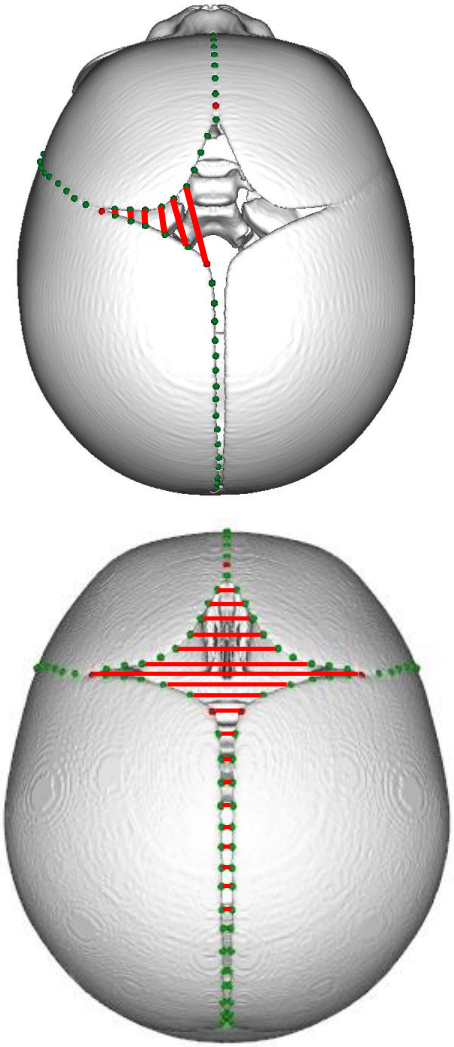


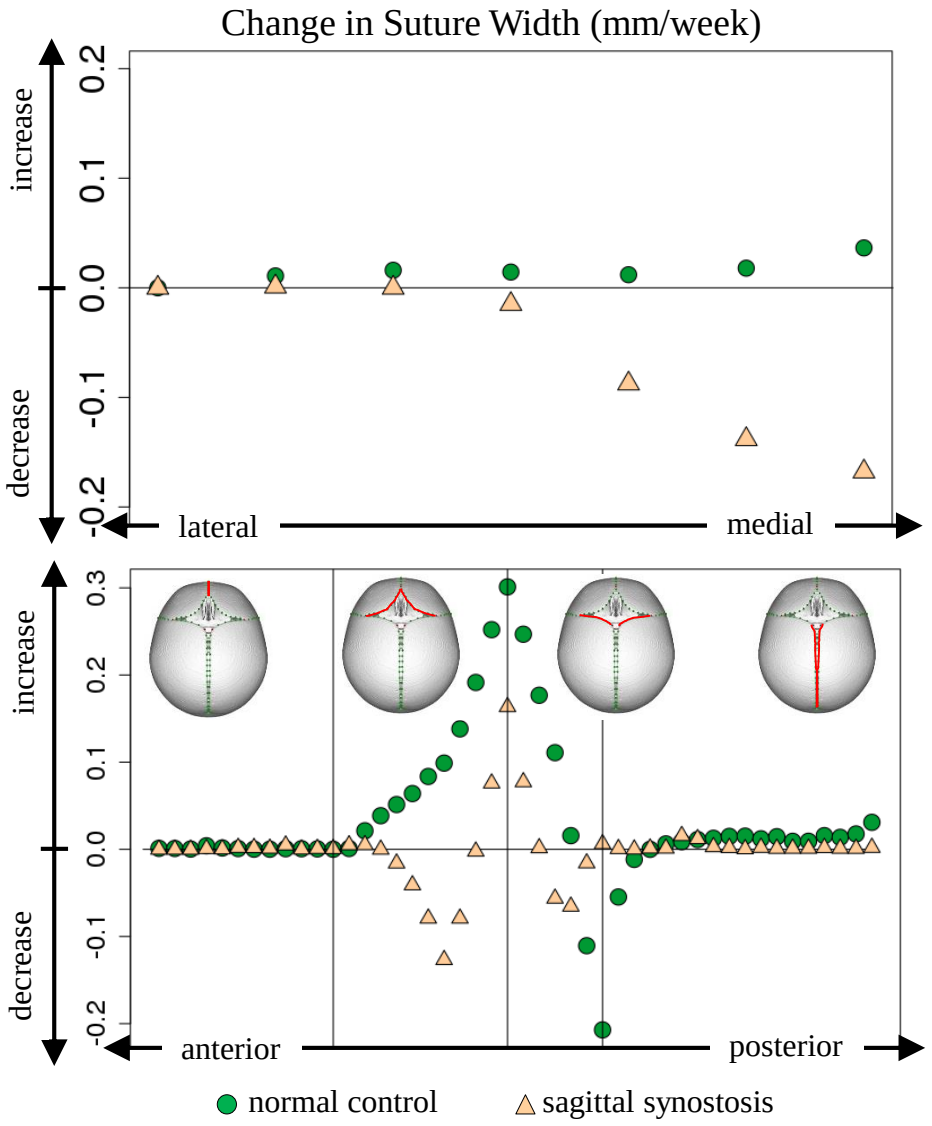
Growth at the Sutures



11 days 53 days 95 days 137 days 179 days

Suture Closure



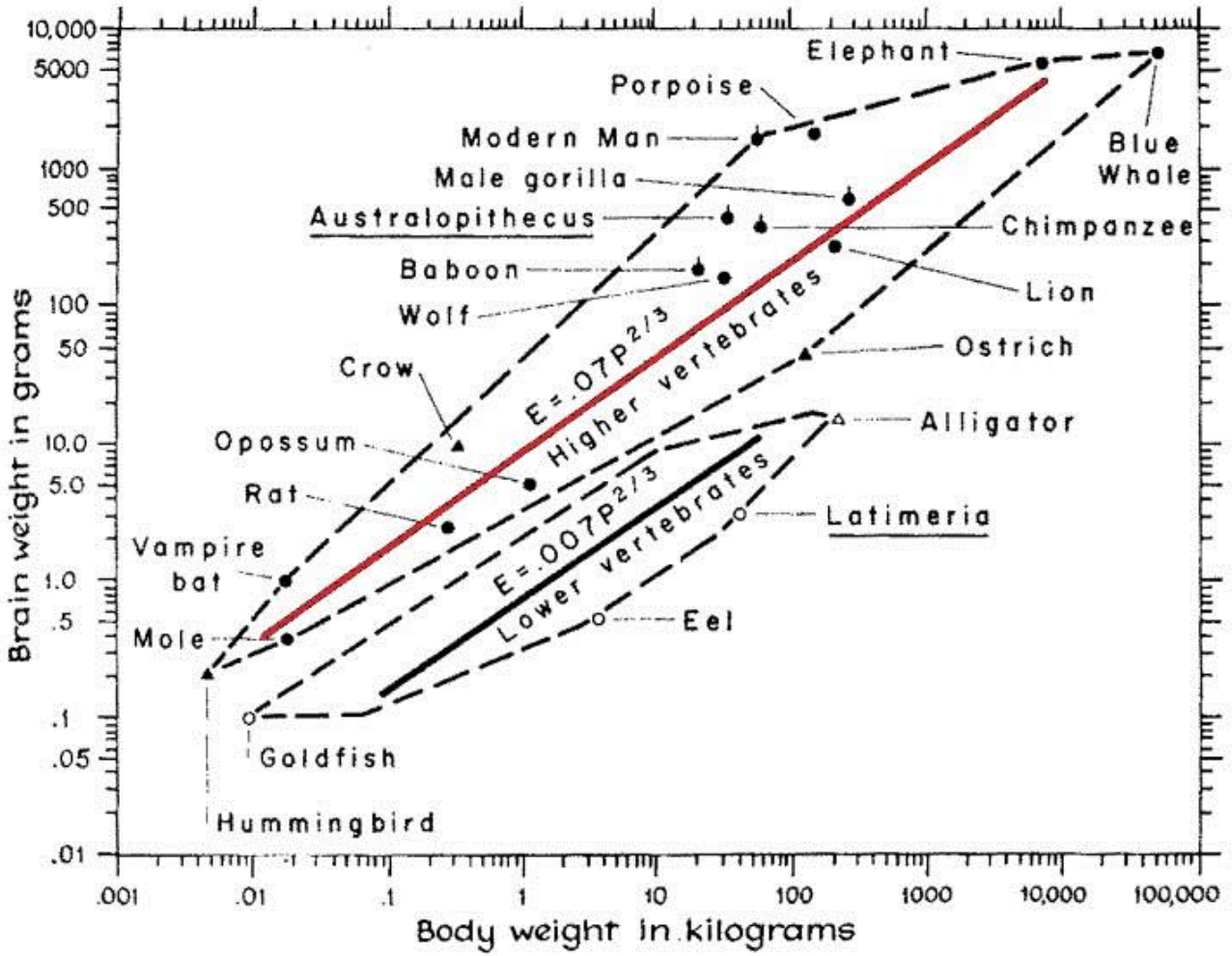


Cranial Growth in Isolated Sagittal Craniosynostosis Compared with Normal Growth in the First 6 Months Of Age, **E. Mercan**, R.A. Hopper, A.M. Maga, Journal of Anatomy, 2019.

Design Decisions

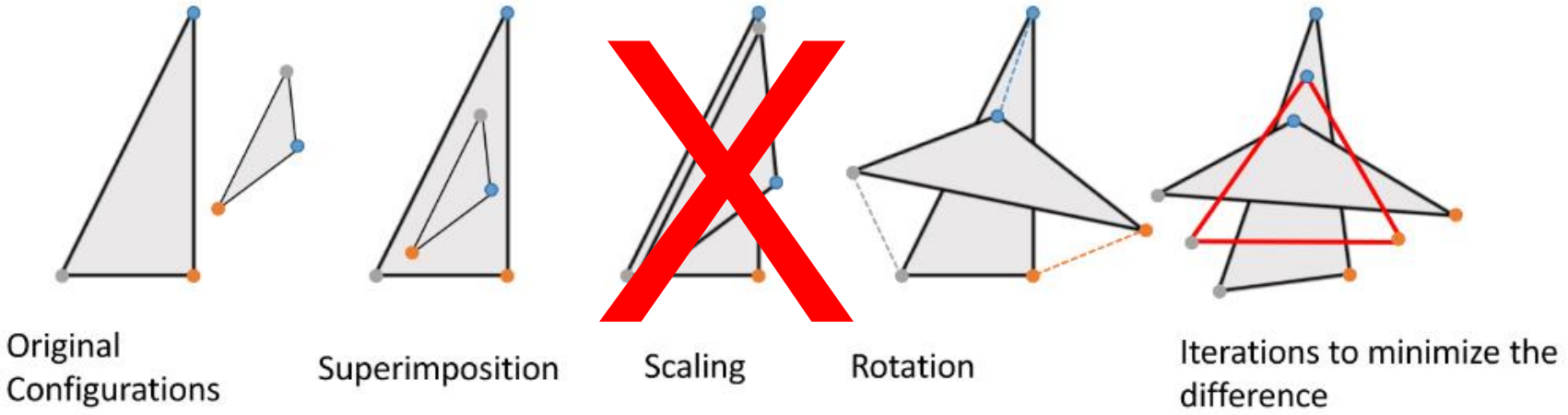
- Size
- Symmetry
- Landmark positions
- Statistical model

Allometry: Size + Shape



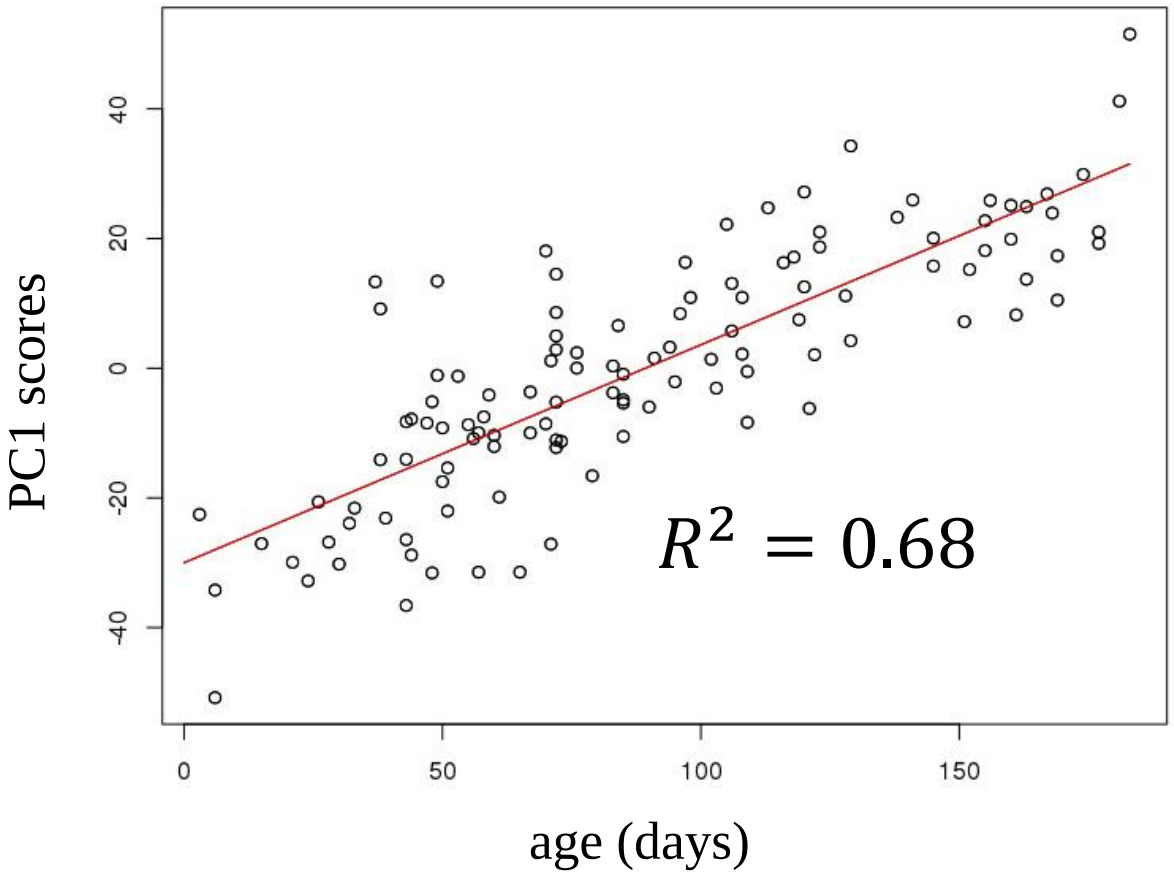
Scale in GPA

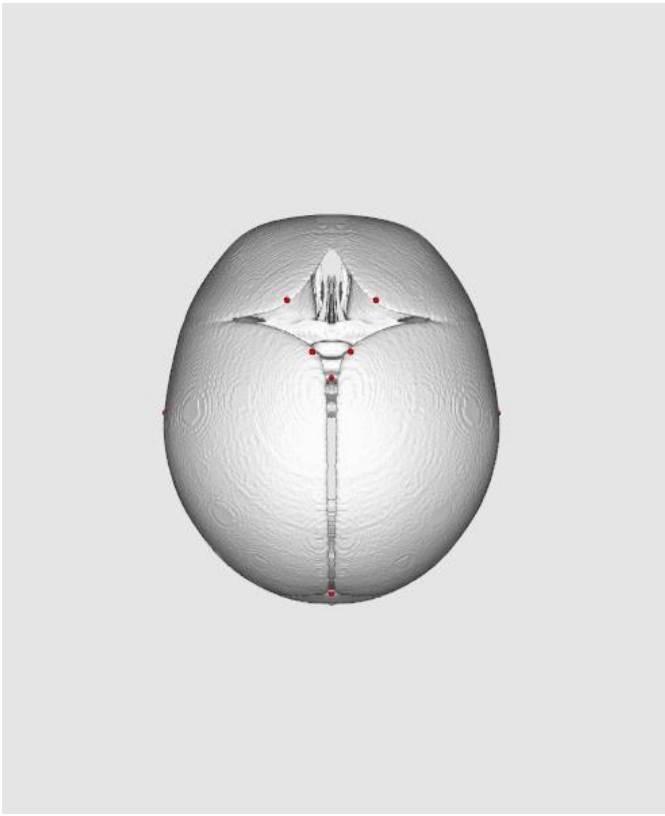
- Since we were interested in growth, we did not scale samples during Procrustes' alignment – which preserved size.



Generalized Procrustes Analysis (or GPA)

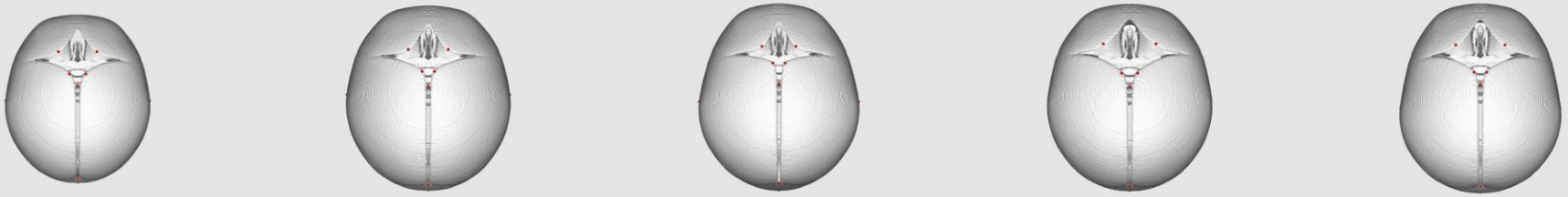
Dominant Shape Changes: PC1





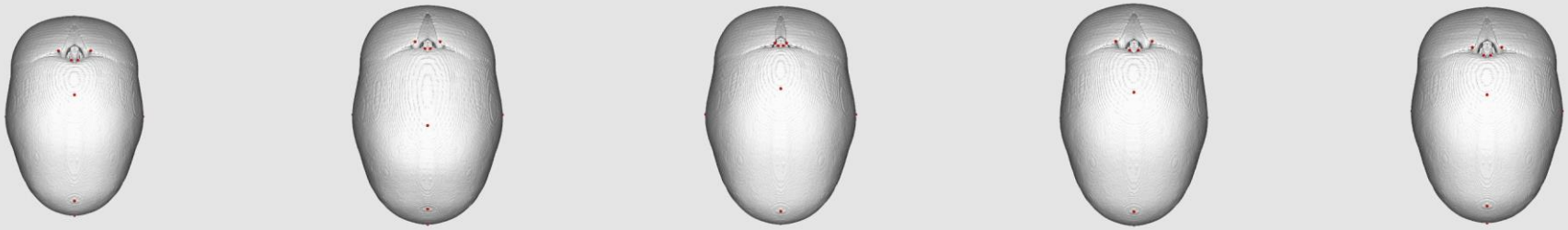
First 5 PCs

Normal Infant Template



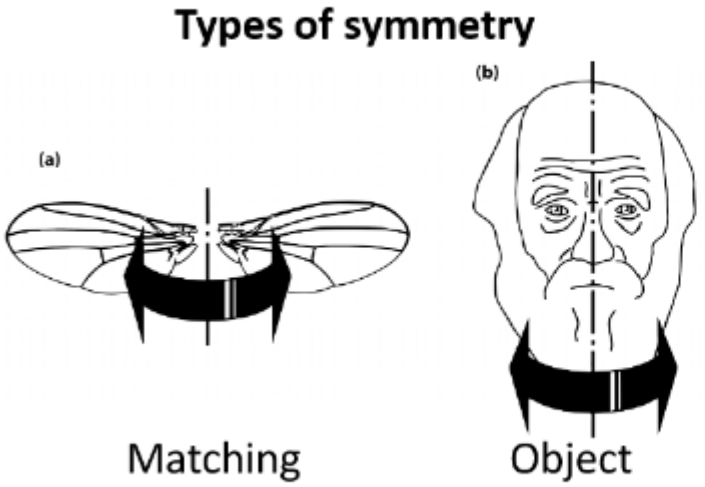
PC1 PC2 PC3 PC4 PC5

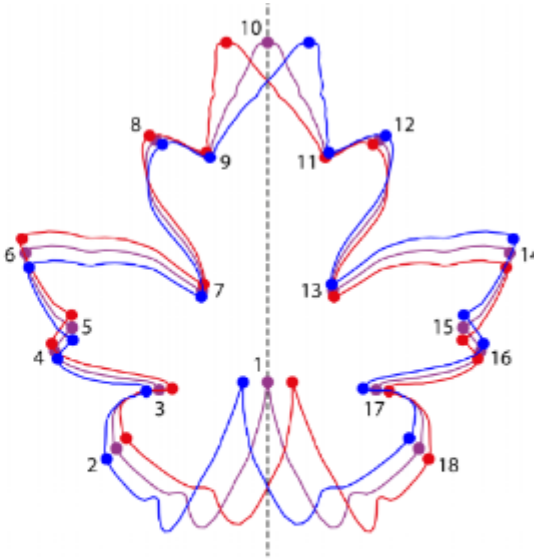
Sagittal CS Template



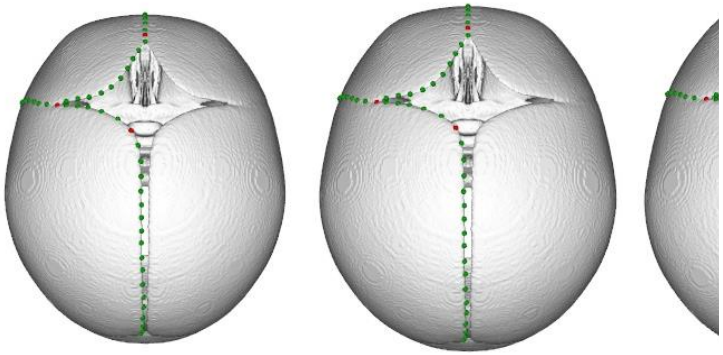
Symmetry

- We symmetrized landmarks by flipping around mid-sagittal plane
  - We lose normal asymmetry
  - A design decision to simplify the analysis

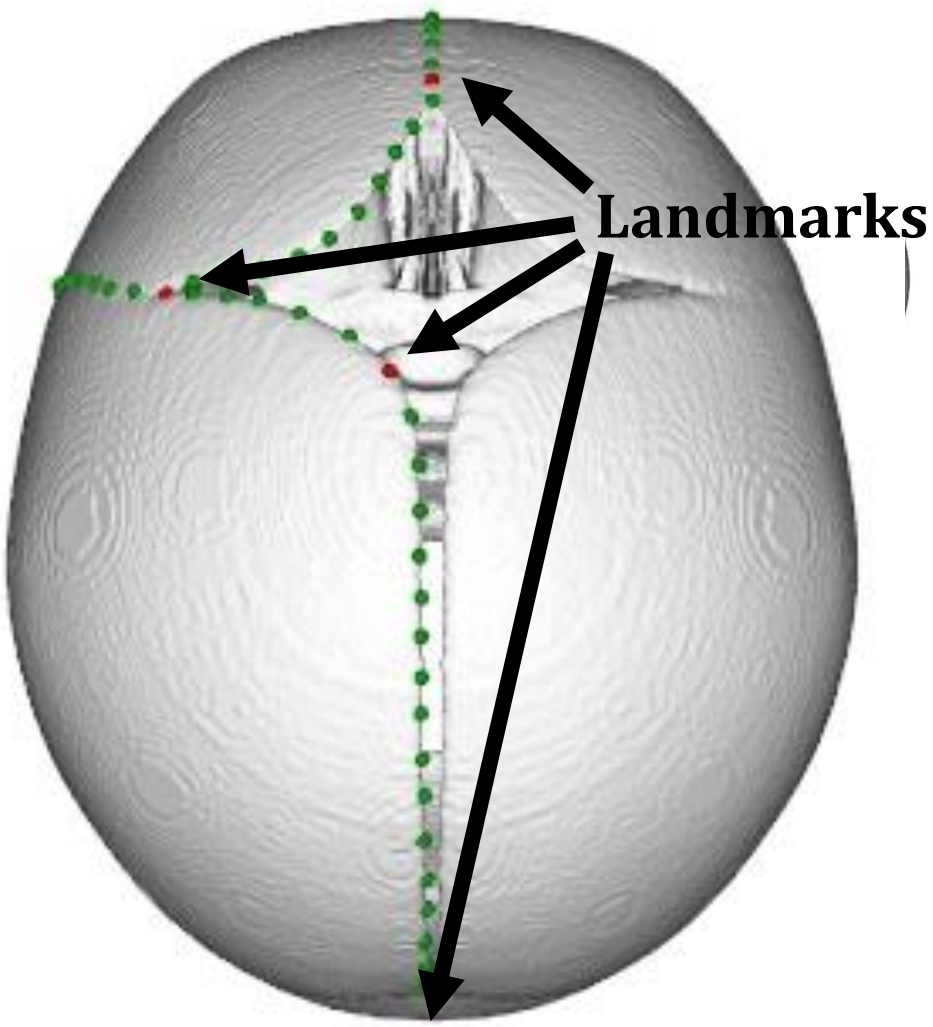




Growth at the Sutures



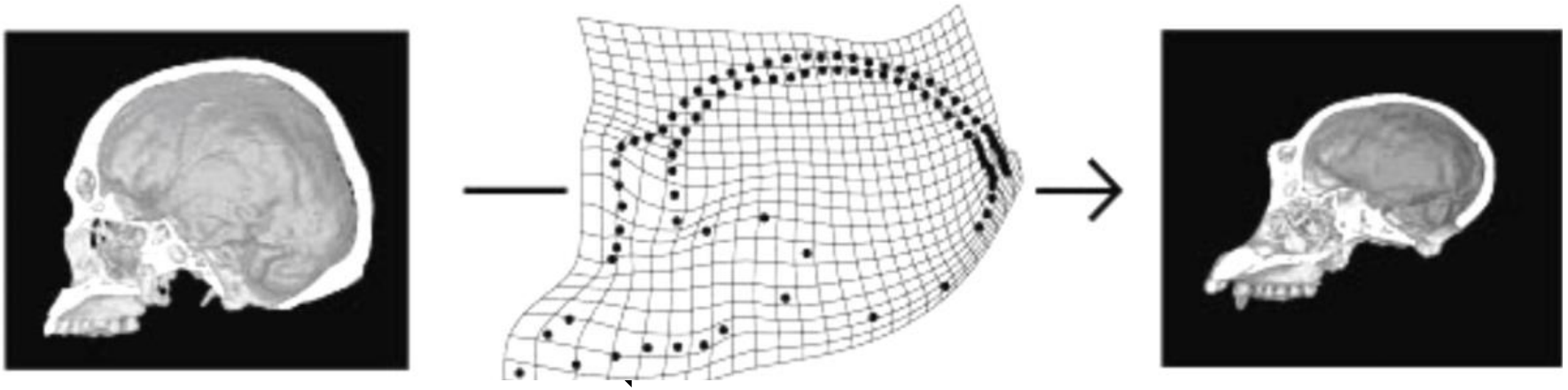
11 days 53 days



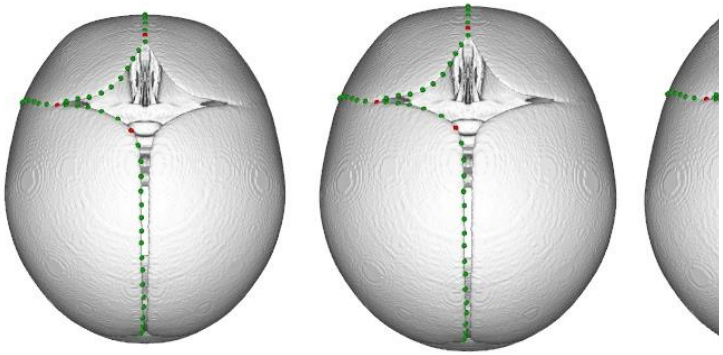
What are we measuring exactly?

Inference

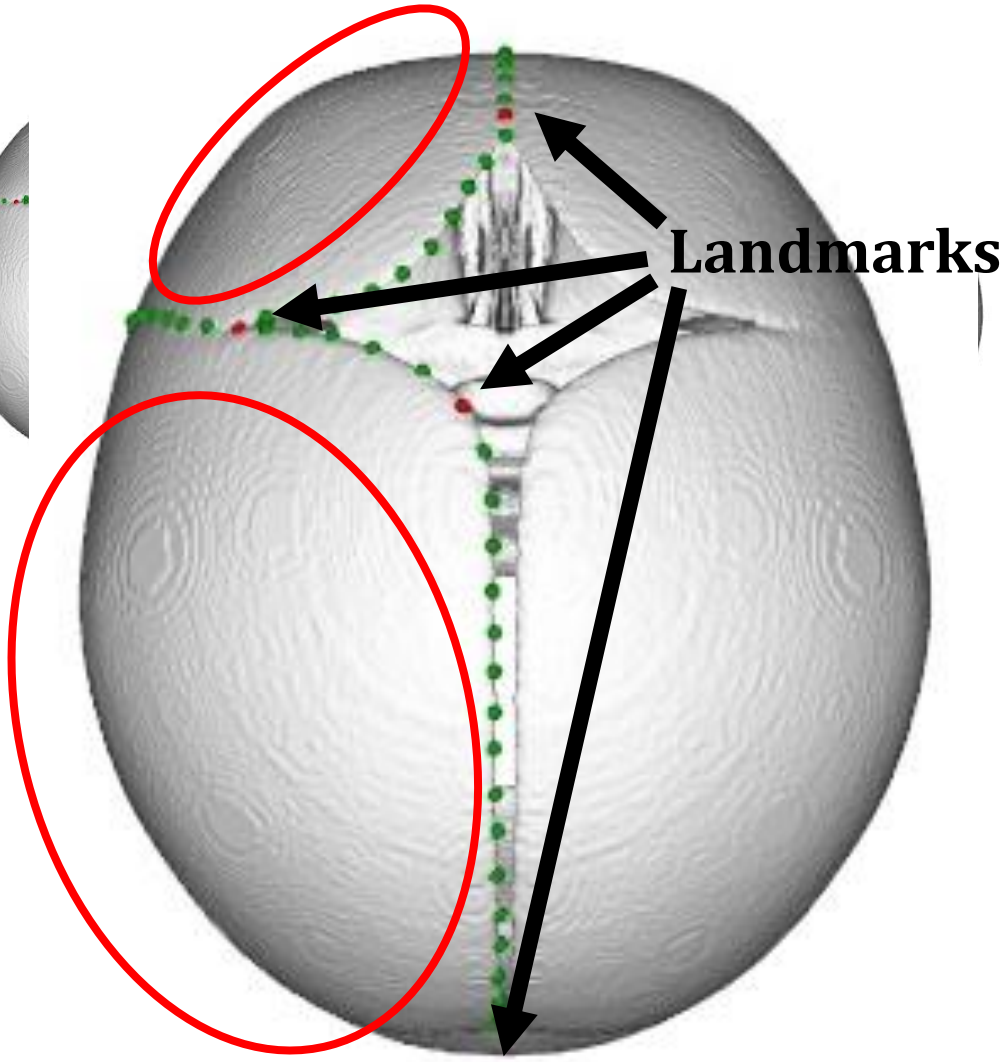
- Landmark coordinates are predicted for ages from 0 to 6mo using the linear model + PCA.
- Population template (with semi-landmarks at the sutures) is warped to predicted landmark coordinates using Thin Plate Splines.



Growth at the Sutures

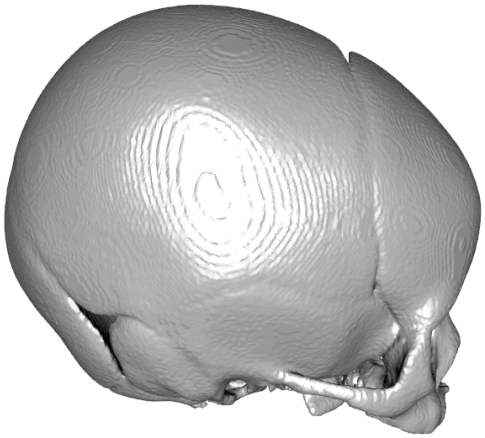


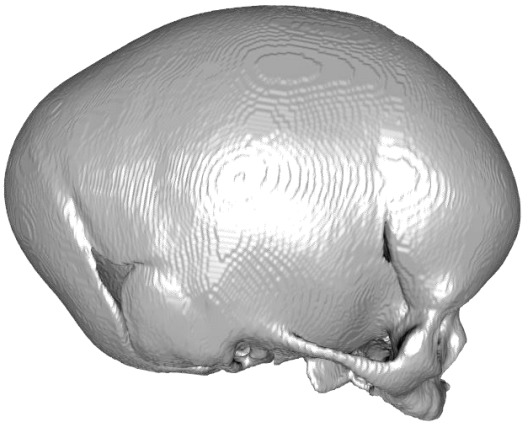
11 days 53 days

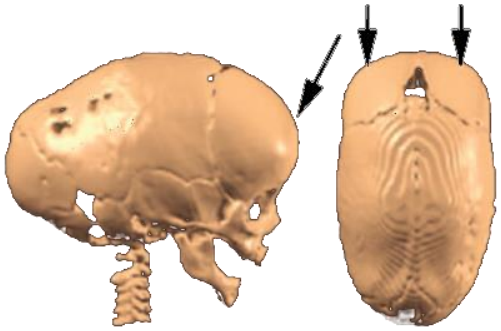


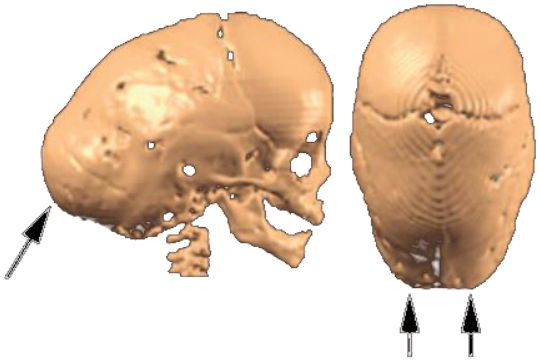
The areas without landmarks are "interpolated" by Thin Plate Splines.

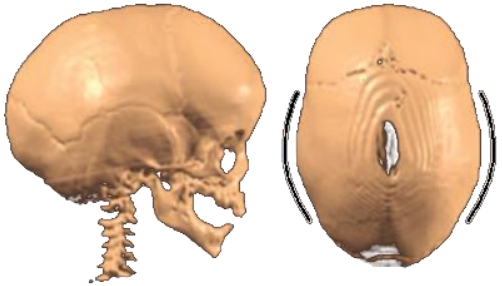
Growth at "Landmark-less" Areas











We need a better model based on semi-landmarks or landmark-free deformations to capture characteristic sagittal craniosynostosis phenotypes like

- frontal bossing,
- occipital protuberance and
- bitemporal protrusion.

Linear Regression

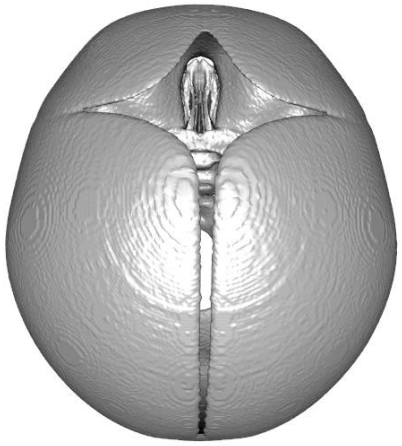
Leave-One-Out-Cross-Validation errors

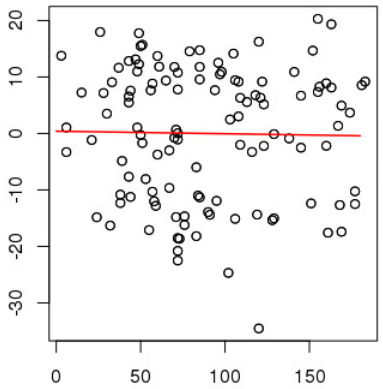
	Control						Sagittal Craniosynostosis					
	LOESS	**L1**	**L2**	**LOESS PC20**	**L1 PC20**	**L2 PC20**	**LOESS**	**L1**	**L2**	**LOESS PC20**	**L1 PC20**	**L2 PC20**
euR	9.22	9.11	9.17	9.26	9.14	9.21	6.25	6.11	6.17	6.16	6.06	6.10
euL	8.96	8.94	8.99	8.97	8.94	9.00	5.74	5.70	5.72	5.74	5.70	5.72
g	4.42	4.45	4.48	4.38	4.41	4.45	4.70	4.79	4.81	4.71	4.80	4.81
v	NA	NA	NA	NA	NA	NA	10.92	10.81	10.94	10.94	10.83	10.95
op	8.94	8.86	8.88	8.97	8.88	8.89	7.31	7.40	7.45	7.28	7.39	7.43
poR	3.10	3.08	3.11	3.09	3.09	3.10	2.86	2.88	2.91	2.85	2.89	2.91
⋮												
Avg	**4.00**	**3.99**	**4.01**	**4.00**	**4.00**	**4.01**	**3.77**	**3.80**	**3.82**	**3.77**	**3.80**	**3.82**

- You want the model with the least complexity (number of parameters) and least error.

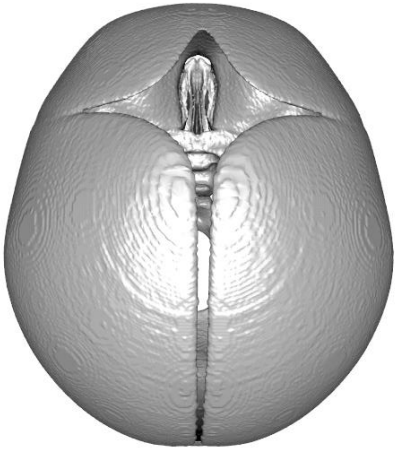
Linear Regression

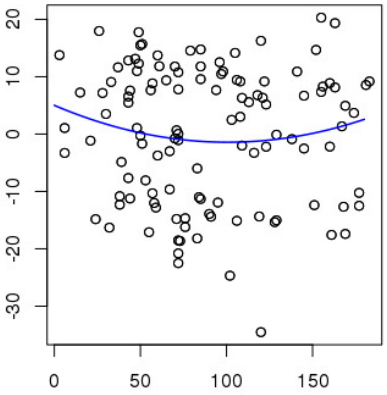
L1



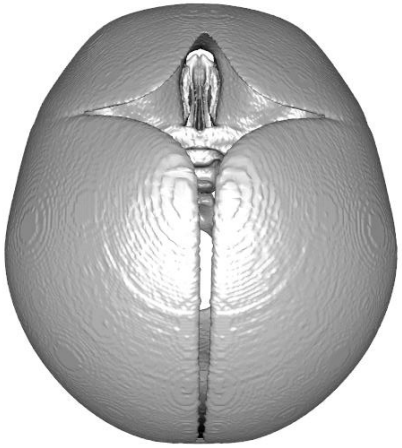


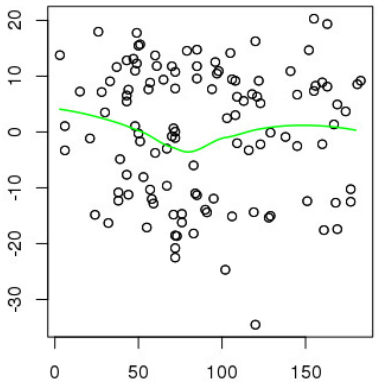
L2



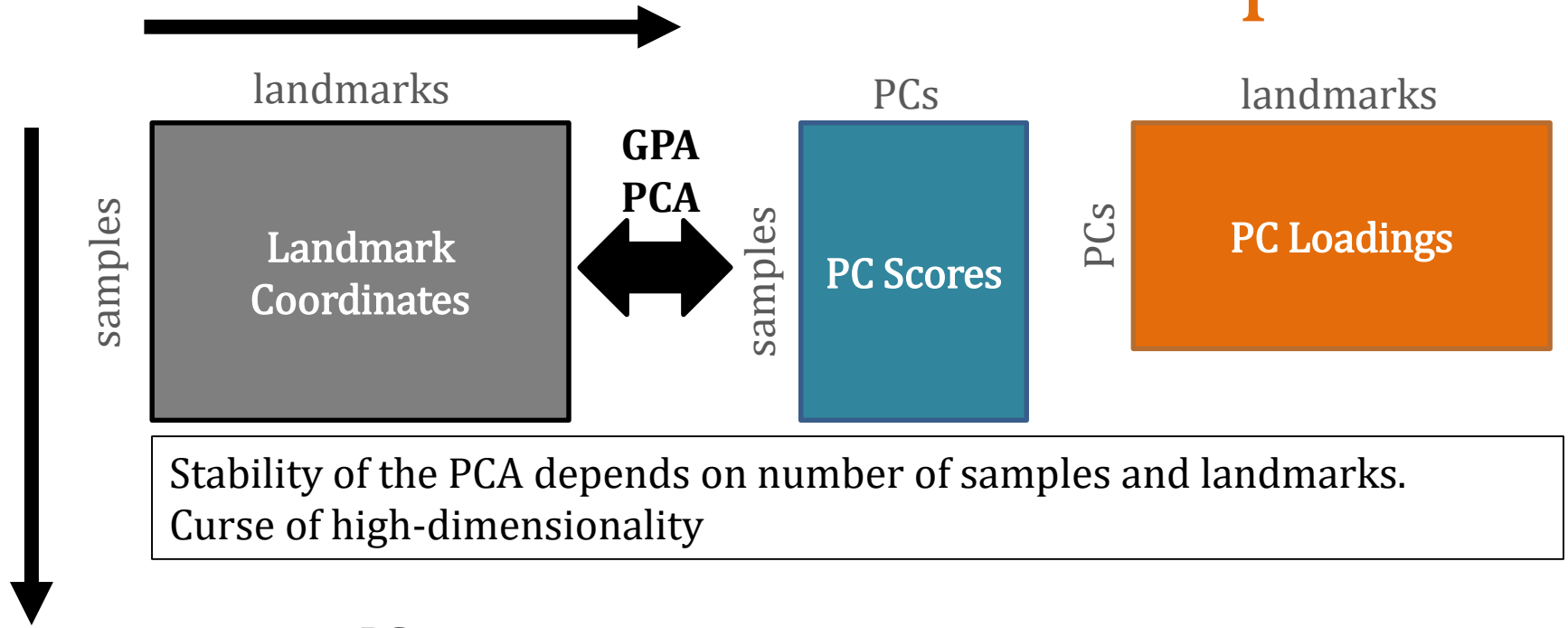


LOESS

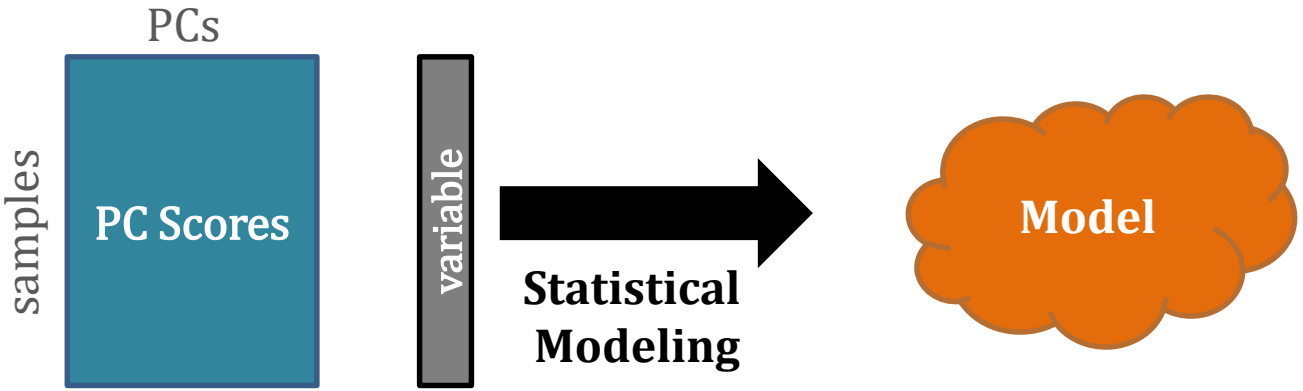




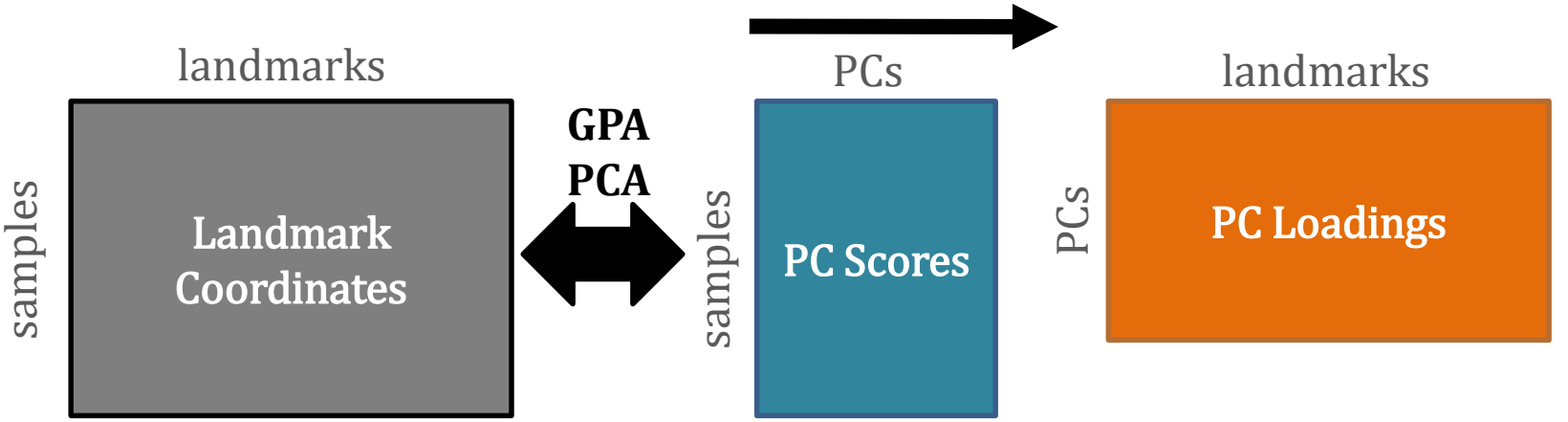
Life After SlicerMorph



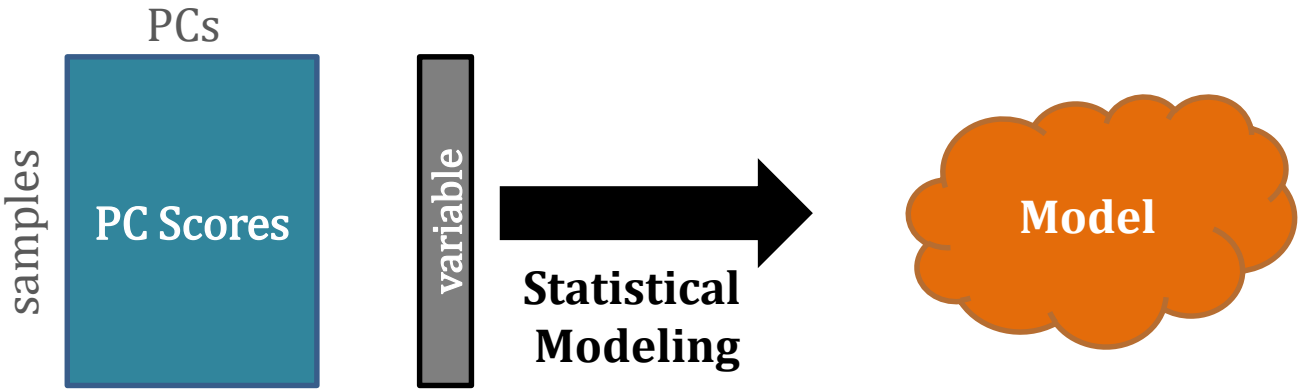
Stability of the PCA depends on number of samples and landmarks.
Curse of high-dimensionality



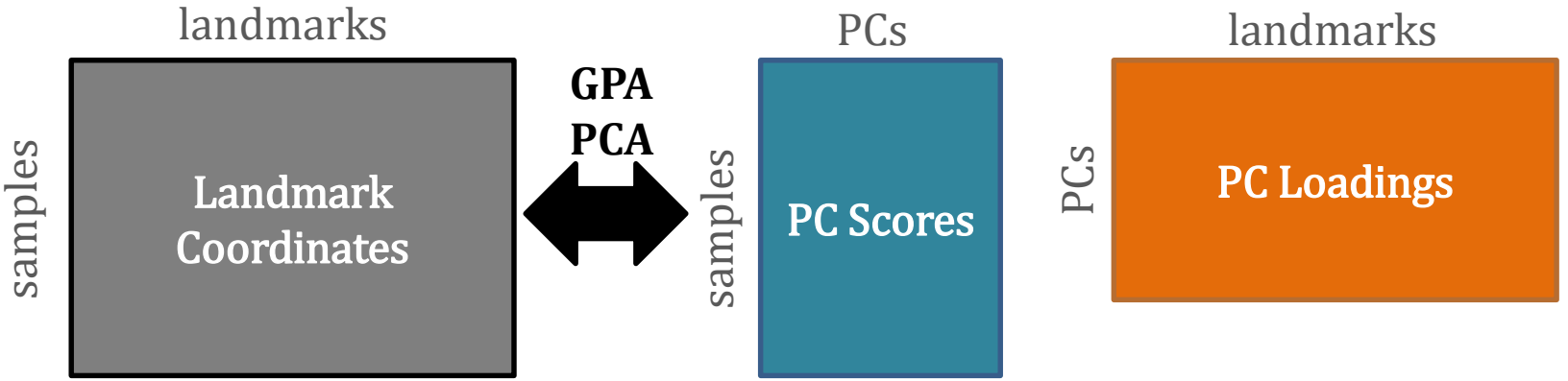
Life After SlicerMorph



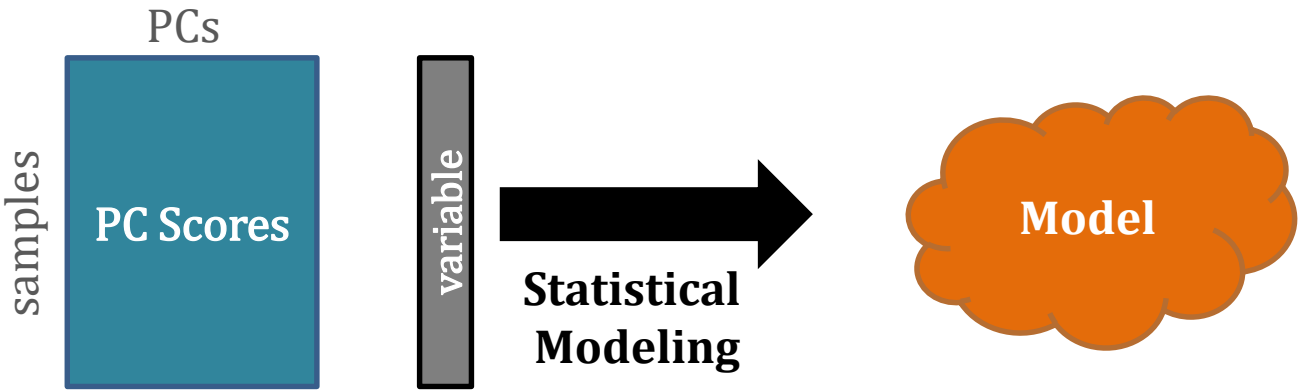
The variance explained by your PCs:
- Quality check
- Dimensionality reduction



Life After SlicerMorph

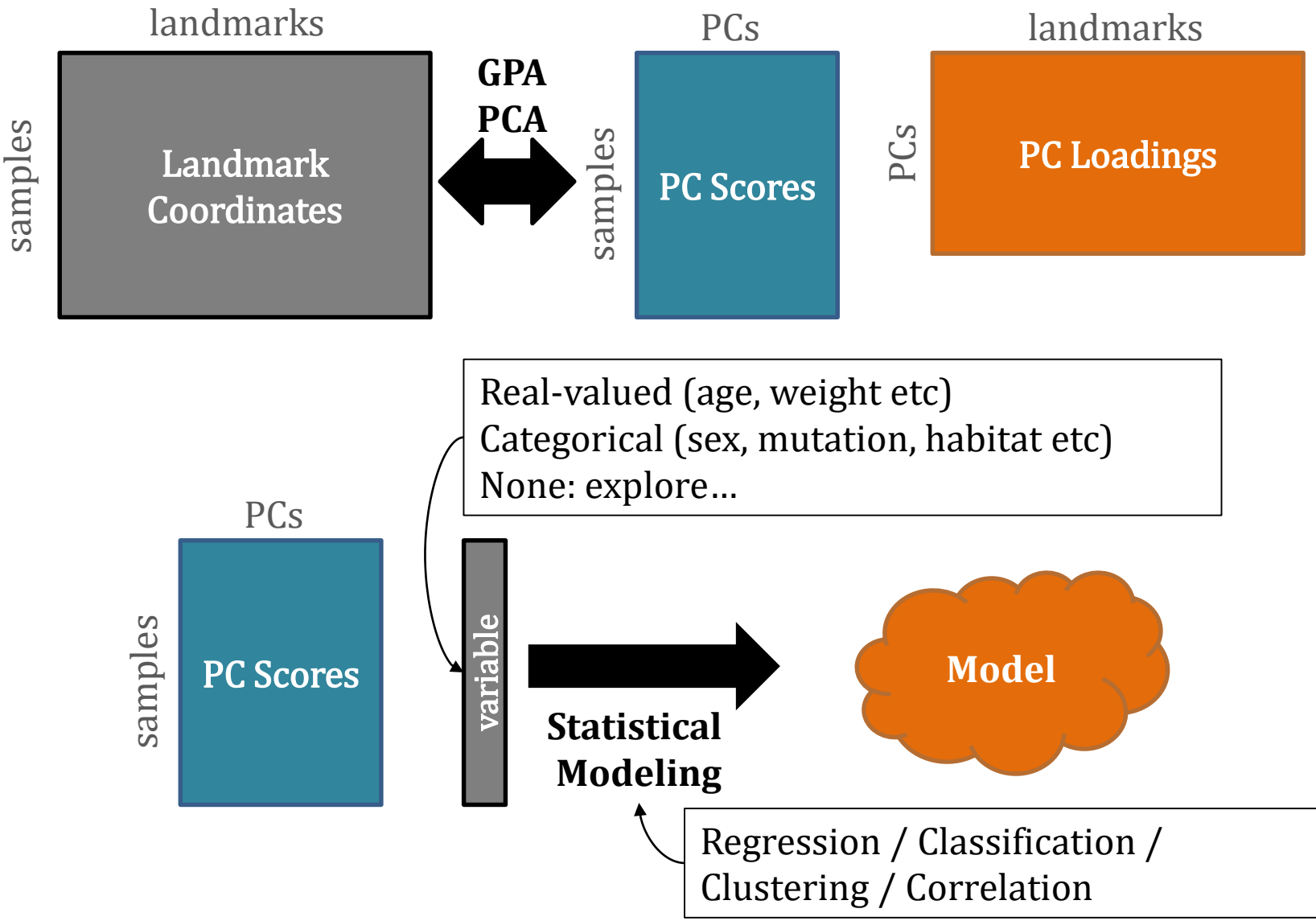


Both PC scores and loadings are specific to your data.



So is the *Model.*

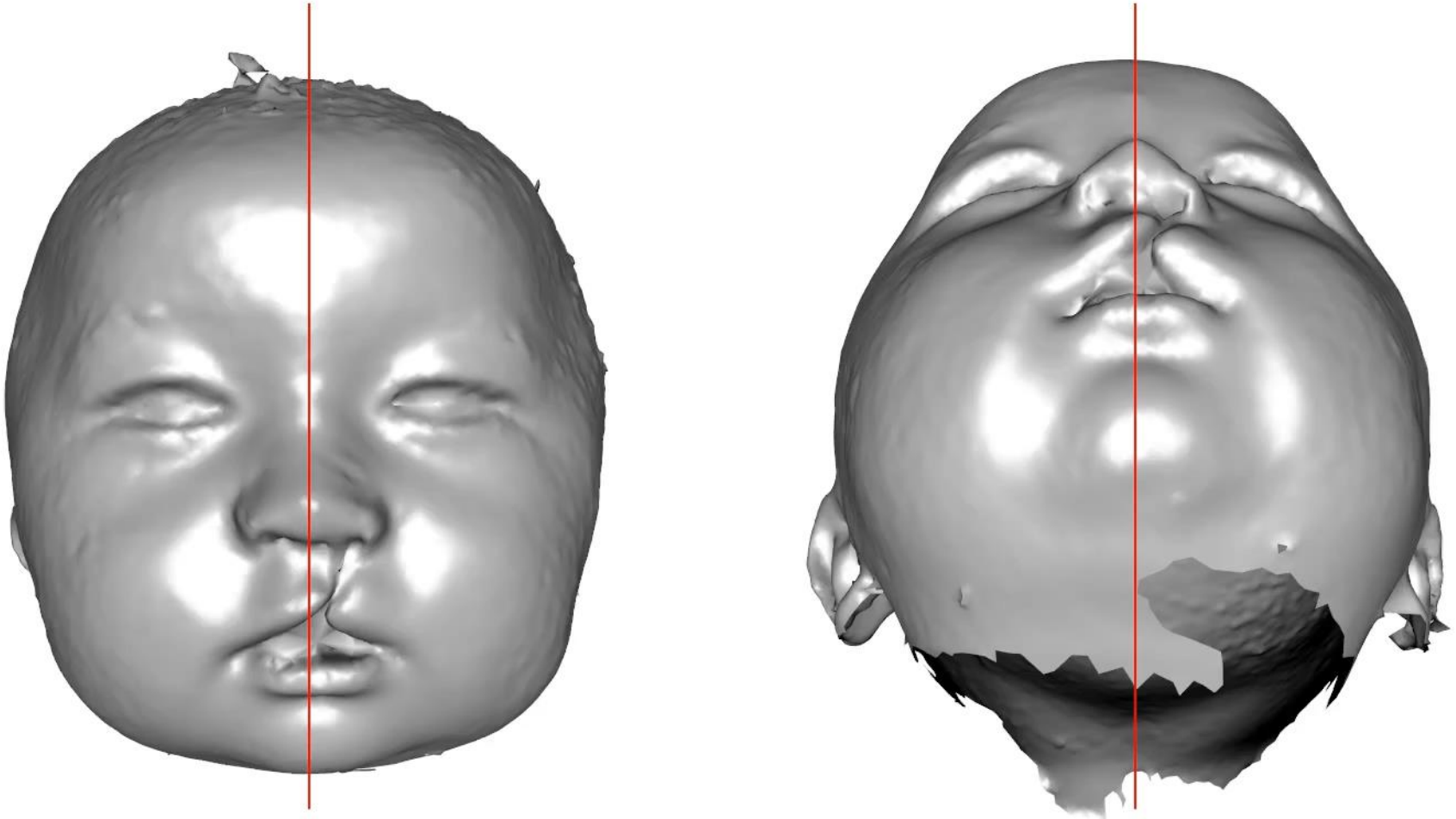
Life After SlicerMorph



OTHER EXAMPLES

Cleft Lip Severity

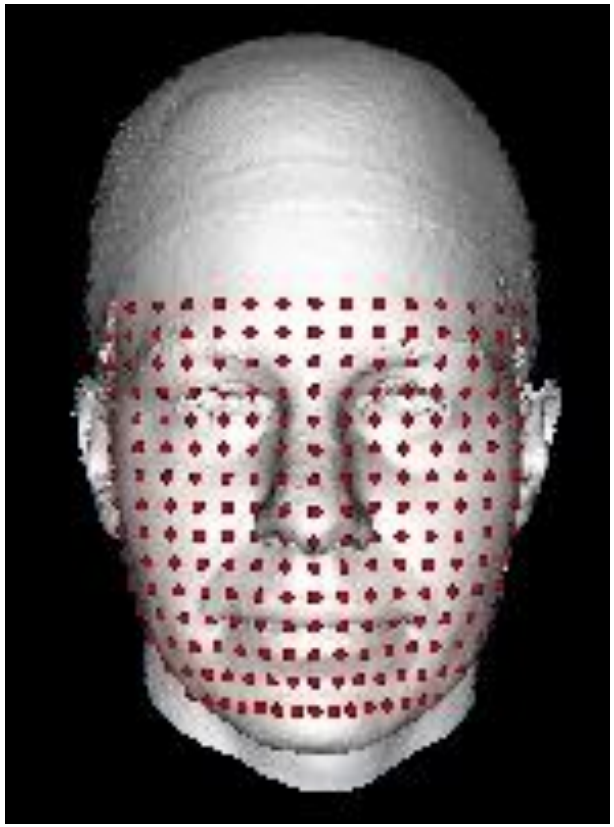
$$landmark.positions \sim \boldsymbol{severity} + age$$

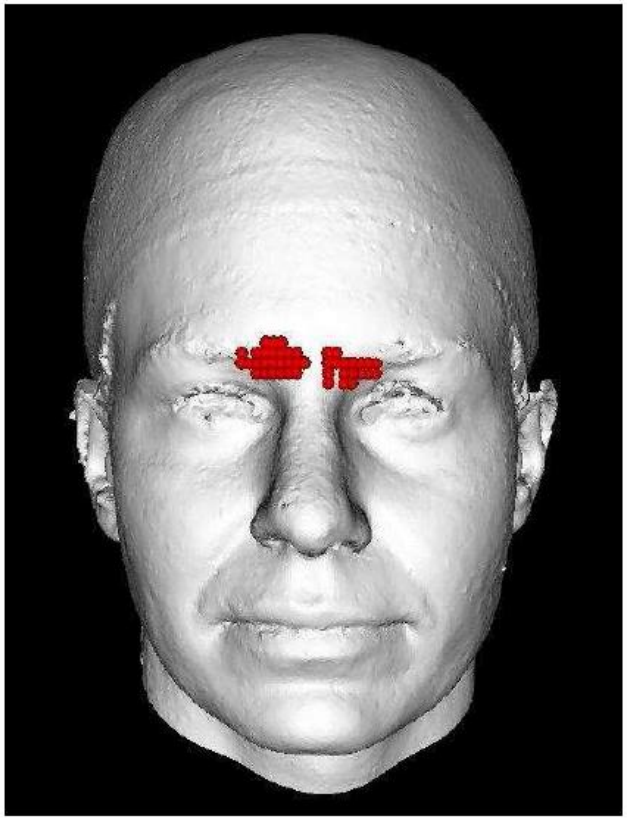


Revisiting the unrepaired unilateral cleft lip and nose deformity using 3D surface image analysis: a model and its implications, R.W. Tse, E. Mercan, Journal of Plastic Reconstructive and Aesthetic Surgery, in submission.

Feature Selection

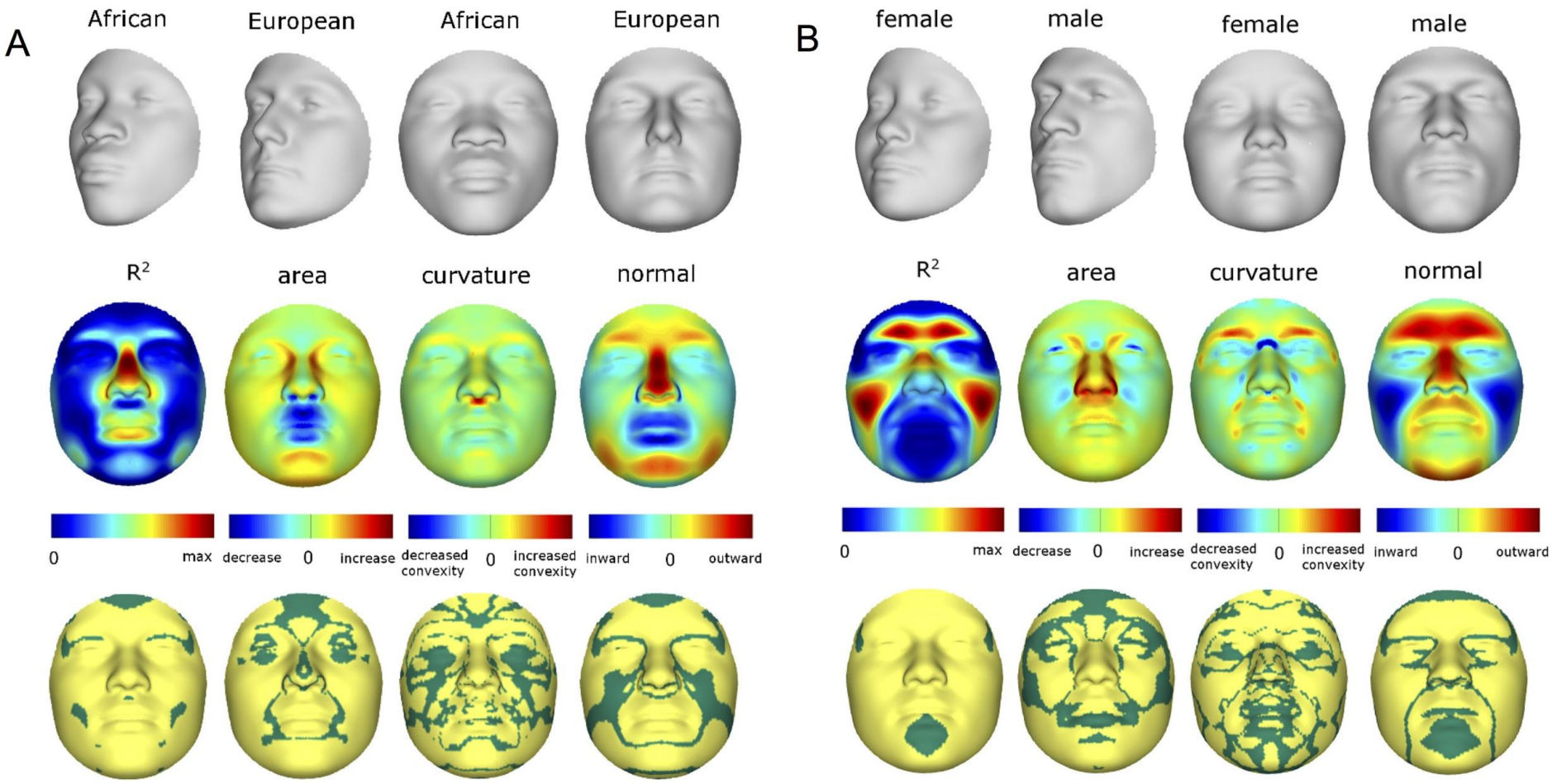
$$semilandmark.positions \sim sex$$





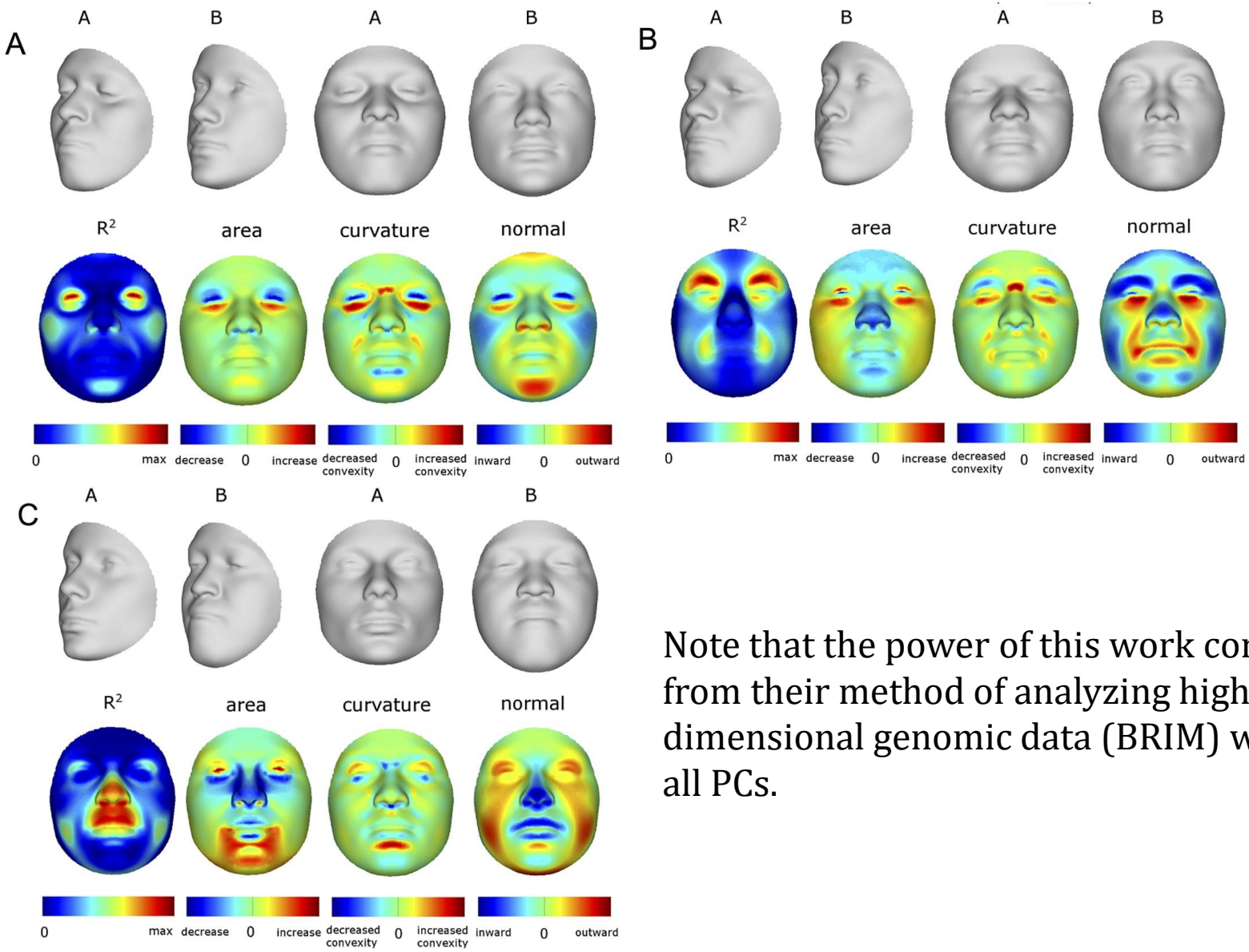
The Use of Pseudo-landmarks for Craniofacial Analysis: A Comparative Study with L1-Regularized Logistic Regression, **E. Mercan**, L.G. Shapiro, S.M. Weinberg, S. Lee, *International Conference of the IEEE Engineering in Medicine and Biology Society (EMBC)*, 2013.

Sex and Genomic Ancestry



Claes P, Liberton DK, Daniels K, Rosana KM, Quillen EE, Pearson LN, McEvoy B, Bauchet M, Zaidi AA, Yao W, Tang H. Modeling 3D facial shape from DNA. PLoS genetics. 2014 Mar 20;10(3):e1004224.

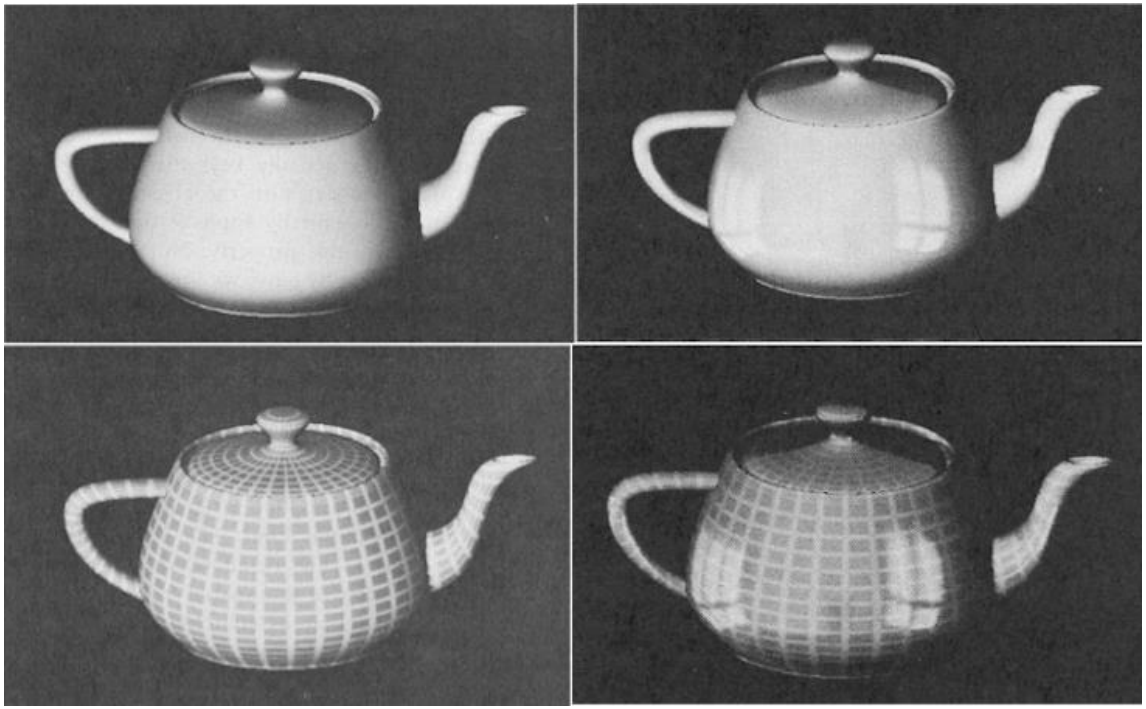
Genomics: Candidate SNPs



Note that the power of this work comes from their method of analyzing high dimensional genomic data (BRIM) with all PCs.

Life After SlicerMorph

"Integrating SlicerMorph with R" lab after break.



With Great Power, Comes Great Responsibility

- Both PCA and most statistical models are sensitive to data size / dimensionality.
  - **Cross-validation** to check stability and reproducibility.
- Your model is as good as your data and your assumptions
  - Garbage in > Garbage out
  - SlicerMorph and other simple quality checks
- Understand what your model does
  - All models are wrong… but some are useful