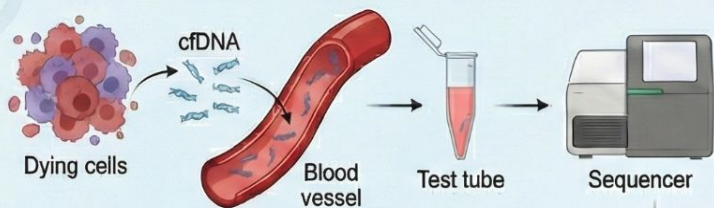


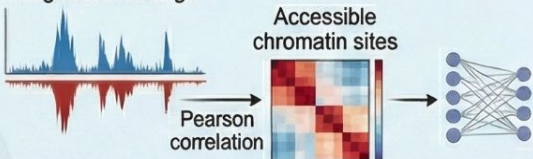
Reproducing LIONHEART: A Novel cfDNA-Based Cancer Detection Method

Method

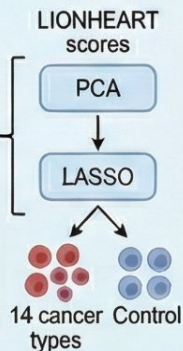


Dying cells release cell-free DNA fragments into the bloodstream. The fragments are extracted from the plasma and whole genome sequenced. The fragment coverage is counted in 10bp bins and correlated to the accessible chromatin locations of 896 cell types.

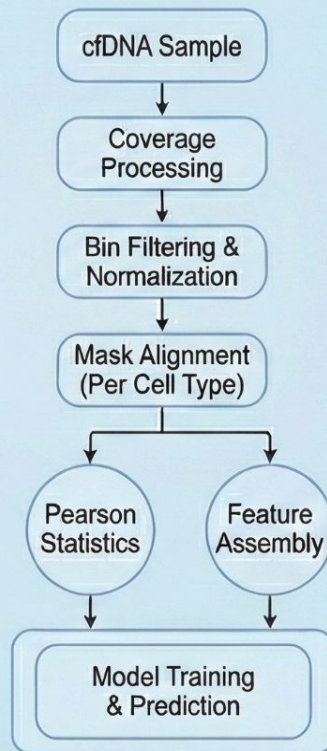
Fragment coverage



The correlation coefficients are PCA-transformed and fed to a LASSO logistic regression model that classifies samples as either 10 cancer or control.

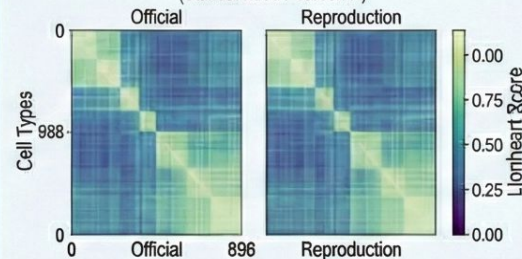


Reproduction Pipeline



Results Comparison

LIONHEART Scores Heatmap Comparison (Standardized Pearson R)



Validation AUC



● Reproduce Model

P(Cancer) on Test



● Reproduce Model

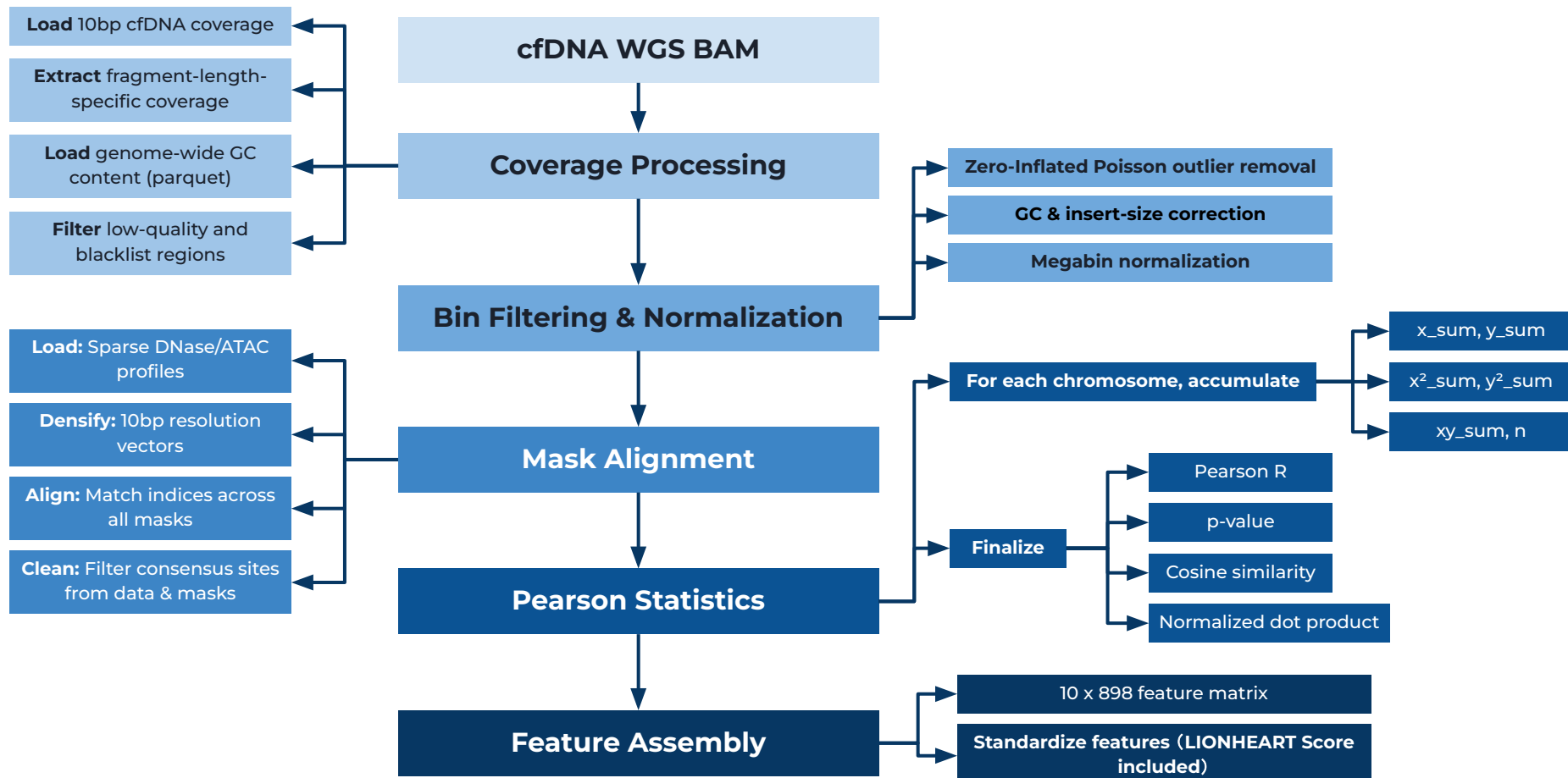


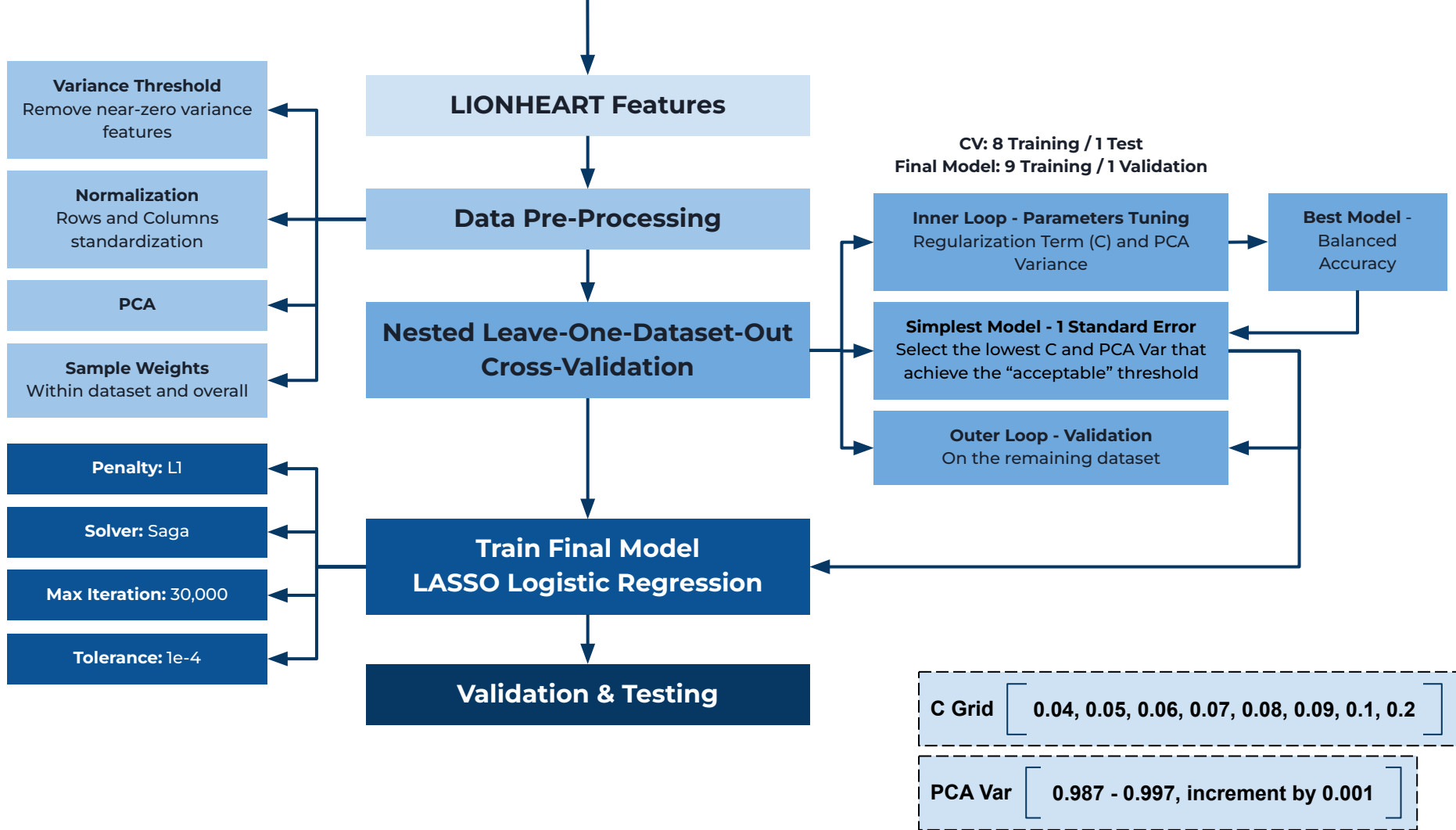
● Reference Model



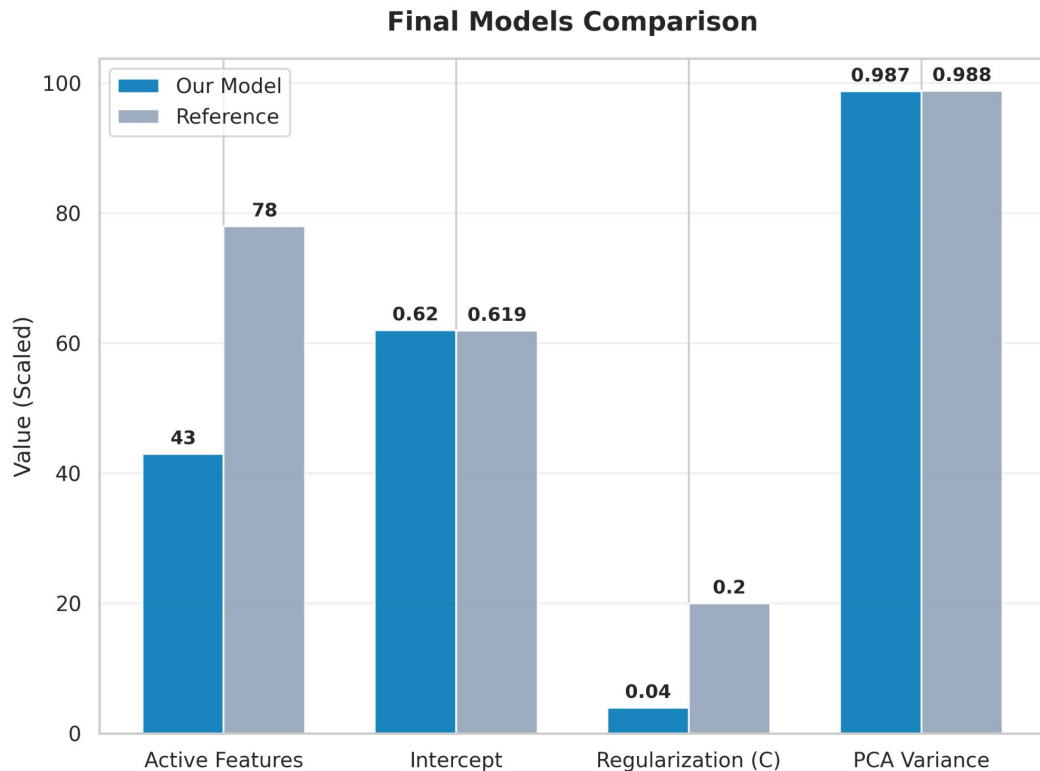
● Reference Model

REPRODUCTION PIPELINE





MODELING RESULTS



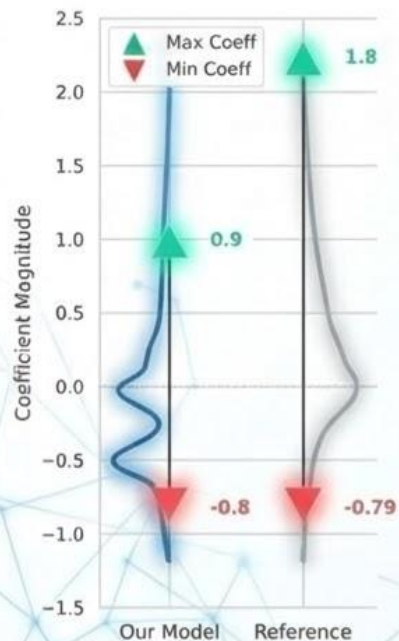
Stronger penalty → Much more conservative model

45% fewer features to achieve a comparable AUC

Identified the “**core**” biological signals

MODELING RESULTS

Final Model Coefficients



Validation AUC



✓ Our Model



✓ Reference

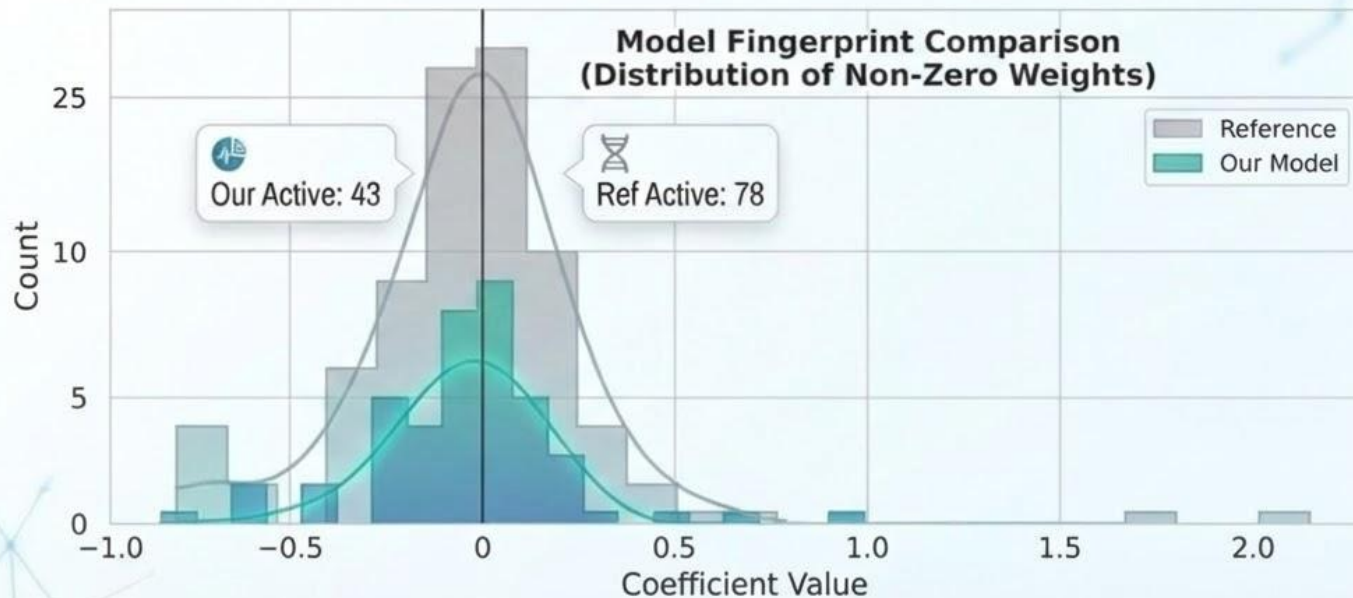
P(Cancer) on Test



✓ Our Model

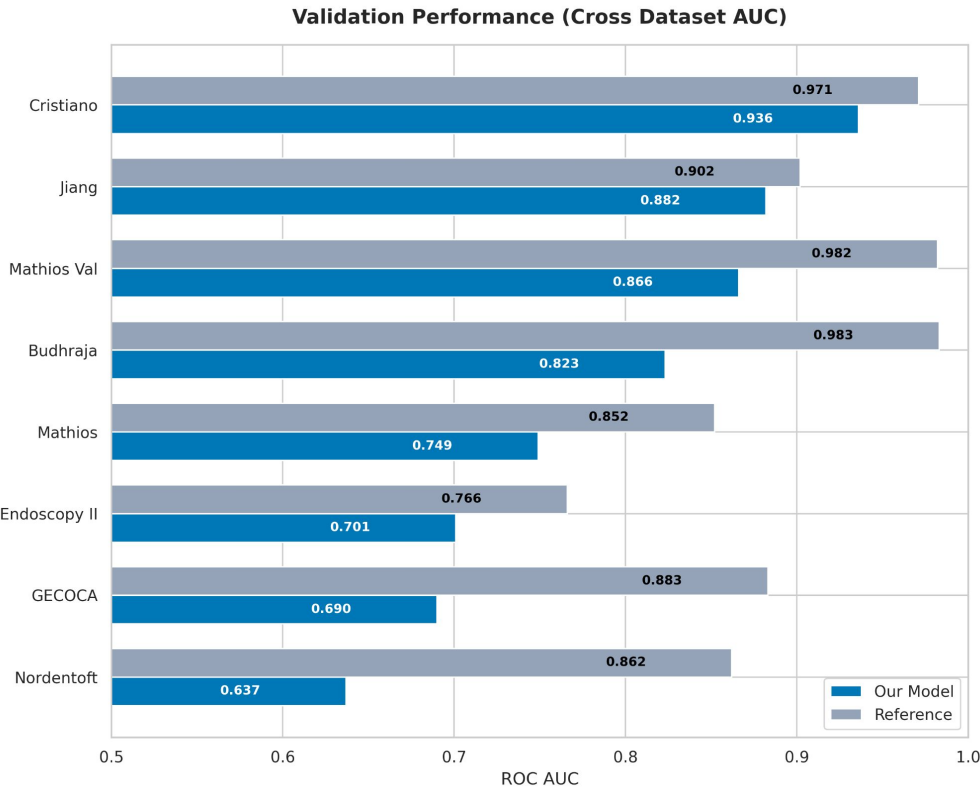


✓ Reference



MODELING RESULTS

Cross Validation Performance



Reference Stats

0.90	0.983	0.766
Weighted Mean	Max (Budhraj)	Min (Endoscopy)

Reproduced Stats

0.802	0.936	0.637
Weighted Mean	Max (Cristiano)	Min (Nordentoft)