

Python packages only · the interpretable protein-feature & workflow layer between bioinformatics I/O and ML / XAI / causal / design

UPSTREAM COMPLEMENTS · data in

1 · Biological data, I/O & fetch

- Biopython
- bs bioservices
- UP UniProt
- FASTA / PDB I/O · UniProt · NCBI · PDB · gget / bioservices
- Biotite
- gget
- scikit-bio

2 · Protein representations

- fair-esm
- bio-embeddings
- Bio.PDB
- transformers
- AlphaFold DB
- ProtT5
- embeddings · structure · PTM / site → pseudo-scales

3 · Feature engineering

input + benchmark

- iF iFeature
- p3 propy3
- PB PyBioMed



single-residue · contrastive · explained

4 · CORE LAYER — interpretable protein-feature layer v1.1



sequence → physicochemical scales → interpretable features → explainable ML
 CPP · Part × Split × Scale · CPP.run_num (numeric) · AAontology
 SequenceFeature · AAclust · NumericalFeature · dPULearn · AAWindowSampler
 TreeModel · ShapModel · CPPPlot · AAlogoPlot · AAMut · SeqMut · SeqOpt
 where on the sequence × how to read it × which physicochemical property

10 · Omics inputs

optional

- MS · proteomics
- pt pyteomics
- pyopenms
- AlphaPept
- single-cell · spatial
- scverse
- ad AnnData

DOWNSTREAM COMPLEMENTS · consume the interpretable feature matrix, explanations & objectives

5 · ML / DL models

- scikit-learn
- XGBoost
- LightGBM
- PyTorch
- compatible · trained on matrix X

6 · Optimization

- Optuna
- pymoo
- DE DEAP
- BoTorch / Ax
- candidate · ΔCPP objectives

7 · Protein design

- PyRosetta
- ProteinMPNN
- RFdiffusion
- ESM-IF
- candidate · score / steer ΔCPP

9 · XAI evaluation

- Quantus
- OpenXAI
- faithfulness · robustness · localization · complexity
- candidate · benchmark explanations

8 · Explainability (XAI) · method taxonomy

■ implemented in AAanalysis

○ candidate to adopt from other packages

METHOD CATEGORY	AIM	METHOD EXAMPLES	STATUS
Feature attribution	local & global importance	SHAP · PFI · PDP · ICE · ALE · LIME · LRP · IntGrad · Grad-CAM	ShapModel
Example-based	representative & counterfactual	MMD-CRITIC · Wachter · DiCE · CEM	to adopt
Rule-extraction	logical IF-THEN rules	ANCHOR · RULE-FIT · LORE · TREPAN	to adopt
Neural methods	explain DL internals	LRP · IntGrad · Grad-CAM · TCAV · GNNExplainer · XGNN	Captum
Non-post-hoc / complementary trust layers			
Surrogate models	distill black-box	train white-box on black-box predictions	to adopt
Uncertainty estimation	prediction confidence	conformal prediction · MAPIE	MAPIE
Causal modelling	cause → effect	DoWhy · EconML (PyWhy)	DoWhy / EconML

Already in AAanalysis: ShapModel (SHAP) & TreeModel importance — the rest are candidates to adopt; CPP makes them biologically readable.

CROSS-CUTTING · Model validation (protein-specific protocols)

homology-aware splits · same/different-protein splits · shuffled-label controls · feature stability · per-protein AP · PU-label sanity checks | tracking: MLflow

Relationship to AAanalysis

- Upstream complement (data in)
- Downstream complement (models · XAI · causal · design)
- Direct comparison / benchmark
- Optional side branch

Maturity ■ implemented □ candidate / future □ optional bridge

Core message: AAanalysis is the interpretable middle band — it complements the stack around it, and competes only with classical descriptor libraries, on interpretability and task-awareness rather than breadth.