AlkahestResultV4b

July 4, 2023

[ ]:

```
import numpy as np
import pandas as pd
import seaborn as sns
import matplotlib.pyplot as plt
from sklearn.impute import SimpleImputer
from sklearn.pipeline import Pipeline
from sklearn.preprocessing import StandardScaler
from sklearn.feature_selection import VarianceThreshold
from stabl.preprocessing import LowInfoFilter
from stabl.stabl import Stabl, save_stabl_results,plot_stabl_path,␣
 ↪plot_fdr_graph
from stabl.visualization import boxplot_features
from sklearn.base import clone
from sklearn.linear_model import LogisticRegression,LogisticRegressionCV,␣
 ↪LinearRegression
from sklearn.model_selection import LeaveOneOut,RepeatedStratifiedKFold
from sklearn.metrics import roc_auc_score
```

This here provides the code that gets us the result of the best model on the V4b (normalized to V3) only unstim data.

The best model found was a ElasticNet model, with hyperparameters C = 0.06 and l1_ratio = 0.55 (i.e. l1 coefficient (lambda_1) is 0.033 and l2 coefficient (lambda_2) is 0.027). Reminder, the ElasticNet solves:

$$\text{argmin}_\beta \frac{1}{2n}\|y - X\beta\|_2^2 + \lambda_1\|\beta\|_1 + \frac{1}{2}\lambda_2\|\beta\|_2^2$$

We also use the usual preprocessing pipeline, with a variance threshold of 0.0005 (i.e. features with lower variance are removed before fitting the model).

0.0.1 Step 1: Setup

We import the data and set up the preprocessing pipeline:

[ ]:

```
dataV4b = pd.read_csv("./Data/Alkahest-V4b.csv",index_col=0)
dataV4b = dataV4b.iloc[:,[x[-6:]  == "Unstim" for x in dataV4b.columns]]
label = pd.read_csv("./Data/AlkahestLabel.csv",index_col=0).iloc[:,0]

preprocessing = Pipeline(
        steps=[
            ("variance", VarianceThreshold(0.0005)),
            ("lif", LowInfoFilter(0)),
            ("impute", SimpleImputer(strategy="median")),
            ("std", StandardScaler())
        ]
    )

X = dataV4b.to_numpy()
y = label.to_numpy()
```

0.0.2 Step 2: Cross-Validation

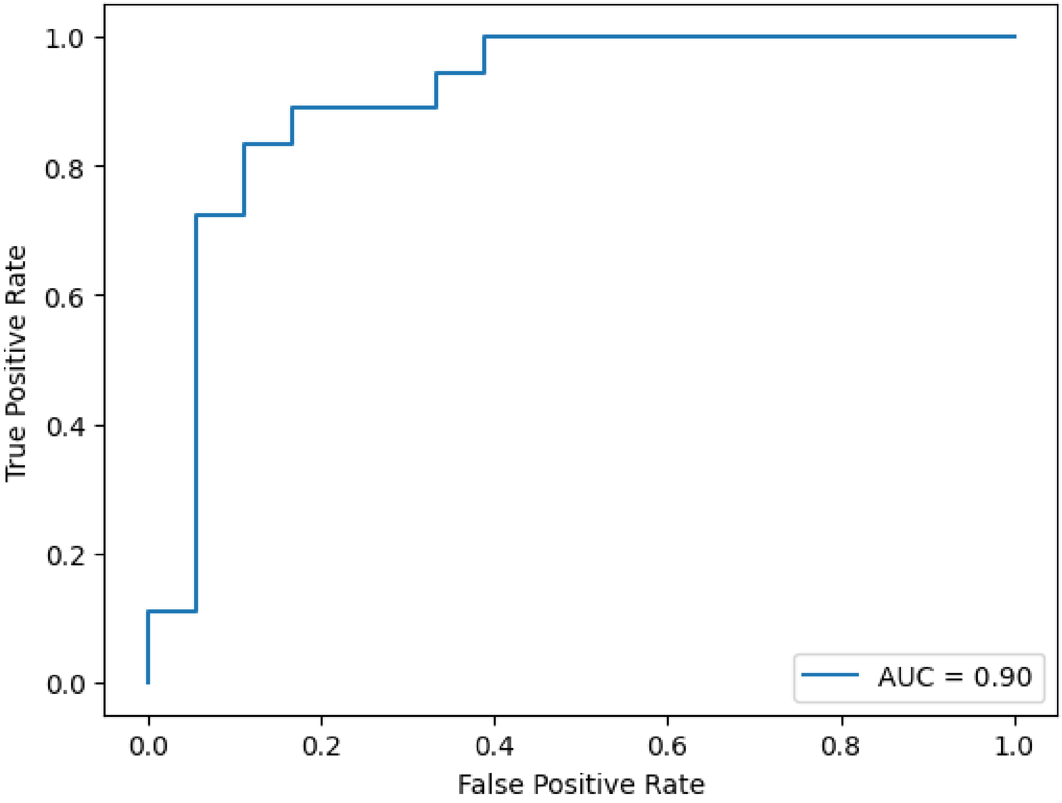
ow we calculate the ROC curve for the cross-validation predictions, using Leave-One-Out cross-validation. We obtain an AUC of 0.9 for the curve.

[ ]:

```
from sklearn.metrics import roc_curve,RocCurveDisplay,auc

c, ratio = 0.060404, 0.55454
model = LogisticRegression(penalty="elasticnet",C=c,l1_ratio=ratio,␣
 ↪max_iter=int(1e5), solver="saga", class_weight="balanced")
kf = LeaveOneOut()
all_probs=[]
for train, test in kf.split(X, y):
    Xtrain = pd.DataFrame(data=preprocessing.fit_transform(dataV4b.iloc[train,:
 ↪]),
                          index=dataV4b.index[train],
                          columns=preprocessing.get_feature_names_out()
                         ).to_numpy()
    Xtest = pd.DataFrame(data=preprocessing.transform(dataV4b.iloc[test,:]),
                          index=dataV4b.index[test],
                          columns=preprocessing.get_feature_names_out()
                         ).to_numpy()
    all_probs.append(model.fit(Xtrain, y[train]).predict_proba(Xtest)[:,1])
all_probs = np.array(all_probs).flatten()
fpr, tpr, thresholds = roc_curve(y, all_probs)
roc_auc = auc(fpr, tpr)
disp = RocCurveDisplay(fpr=fpr, tpr=tpr, roc_auc=roc_auc)
disp.plot()
```

[ ]:

```
<sklearn.metrics._plot.roc_curve.RocCurveDisplay at 0x1597921a550>
```



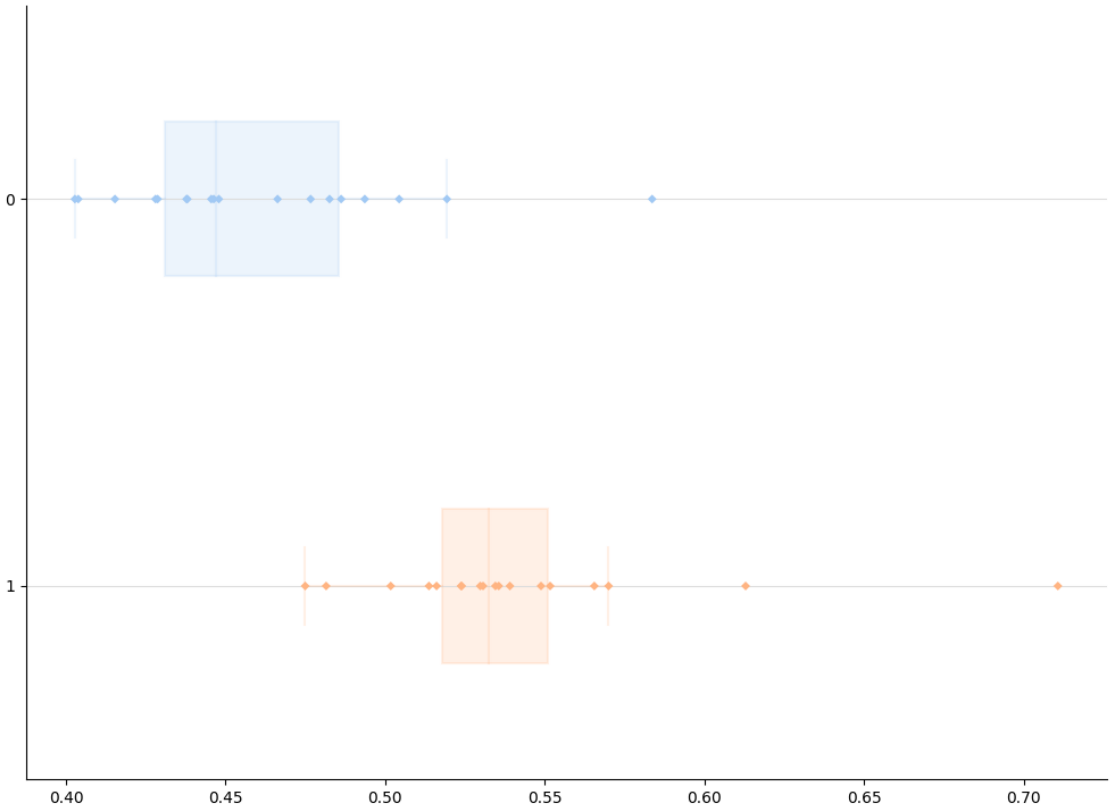
We then calculate the p-value of the same predictions, which is about 0.0006%.

[ ]:
```
from scipy.stats import mannwhitneyu

utest1,upval1 = mannwhitneyu(all_probs[y == 1],all_probs[y == 0],method="exact")
print( "p-value of the U-Test on the CV predictions : ",upval1)
```

```
p-value of the U-Test on the CV predictions :  7.424903075549739e-06
```

The spread of the predictions is in the next figure - 0 is placebo, 1 is Alkahest. The dots are the prediction values. Ideally we want the top line to have all dots at 0, and bottom line all at 1.

[ ]:
```
import matplotlib.patches as pltp
fig, ax = plt.subplots(1, 1, figsize=(10, 8))
palette = ["#4D4F53", "#C41E3A"]
sns.boxplot(data = [all_probs[y == 0],all_probs[y == 1]],
            ax=ax,
            showfliers=False,
            palette="pastel",
            boxprops=dict(alpha=.2),
            whiskerprops=dict(alpha=.2),
            width=.4,
            orient="h",
            saturation=1
        )
sns.stripplot(data=[all_probs[y == 0],all_probs[y == 1]],
            ax=ax,
            palette="pastel",
            jitter = False,
            alpha=1,
            size=4,
            marker="D",orient="h"
        )
box_patches = [patch for patch in ax.patches if type(patch) == pltp.PathPatch]

num_patches = len(box_patches)
lines_per_boxplot = len(ax.lines) // num_patches

for i, patch in enumerate(box_patches):
    col = patch.get_facecolor()
    patch.set_edgecolor(col)
    patch.set_facecolor(col)

    for line in ax.lines[i * lines_per_boxplot: (i + 1) * lines_per_boxplot]:
        line.set_color(col)
        line.set_mfc(col)
        line.set_mec(col)

ax.grid(which='major', color='#DDDDDD', linewidth=0.8, axis="y")

ax.spines['top'].set_visible(False)
ax.spines['right'].set_visible(False)



fig.tight_layout()
fig.subplots_adjust(top=0.9)
ax.set_ylabel('')

plt.show()
```



0.0.3 Step 3: We get the final model

We fit the model on all of the data.

[ ]:
```
Xstd = pd.DataFrame(data=preprocessing.fit_transform(dataV4b),
                          index=dataV4b.index,
                          columns=preprocessing.get_feature_names_out()
                         )
model.fit(Xstd.to_numpy(), y)
```

[ ]:
```
LogisticRegression(C=0.060404, class_weight='balanced', l1_ratio=0.55454,
                   max_iter=100000, penalty='elasticnet', solver='saga')
```

Then we look at which features get a non-zero coefficient, to get a similar understanding of which features were selected by the model.

[ ]:
```
for i in Xstd.columns[np.where(model.coef_[0] != 0)]:
    print(i)
```

```
Treg_ERK_Unstim
Tregmem_ERK_Unstim
```

```
[ ]: pd.DataFrame(data=all_probs,index=dataV4b.index,columns=["LOO CV predictions"]).
      ↪to_csv("./ResultsFinal/V4b/FinalEN_CV_predictions.csv")
```

Boxplots for these features are further down.

0.0.4 Part 2: Stability Selection

With a base estimator an ElasticNet model with l1_ratio of 0.55, we look at what features it selects:

```
[ ]: ss =Stabl(
         base_estimator=clone(model),
         lambda_name="C",
         lambda_grid=np.linspace(0.01, 3, 50),
         artificial_type=None,
         sample_fraction=0.5,
         replace= True,
         hard_threshold=0.7,
         n_bootstraps=2000,
         random_state=42
     )

     ss.fit(Xstd,y)
```

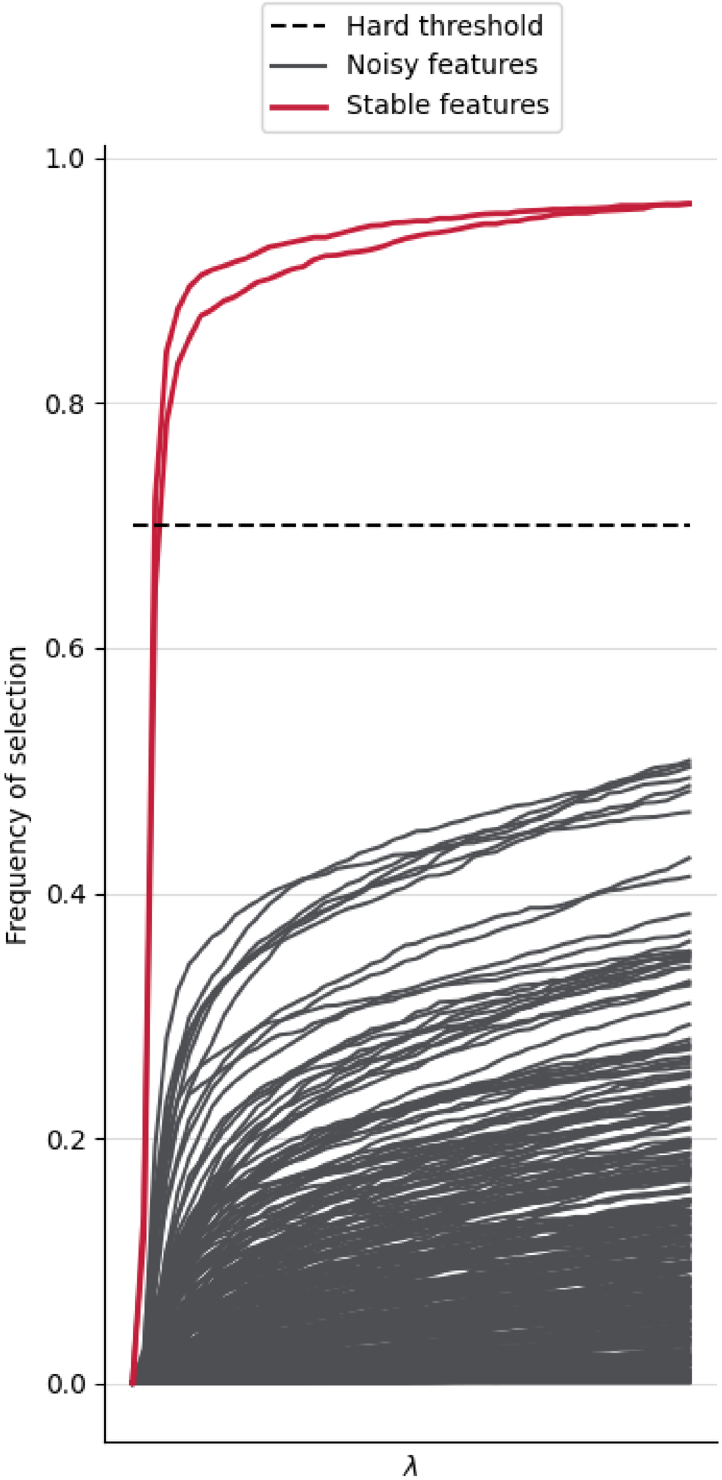
```
                                                                 53<00:00,
38.04s/it]
```

```
[ ]: Stabl(artificial_type=None,
           base_estimator=LogisticRegression(C=0.060404, class_weight='balanced',
                                             l1_ratio=0.55454, max_iter=100000,
                                             penalty='elasticnet', solver='saga'),
           hard_threshold=0.7,
           lambda_grid=array([0.01      , 0.07102041, 0.13204082, 0.19306122,
0.25408163,
            0.31510204, 0.37612245, 0.43714286, 0.49816327, 0.55918367,
            0.62020408, 0.68122449, 0.7422449 , 0.80326531,…
            1.23040816, 1.29142857, 1.35244898, 1.41346939, 1.4744898 ,
            1.5355102 , 1.59653061, 1.65755102, 1.71857143, 1.77959184,
            1.84061224, 1.90163265, 1.96265306, 2.02367347, 2.08469388,
            2.14571429, 2.20673469, 2.2677551 , 2.32877551, 2.38979592,
            2.45081633, 2.51183673, 2.57285714, 2.63387755, 2.69489796,
            2.75591837, 2.81693878, 2.87795918, 2.93897959, 3.        ]),
           n_bootstraps=2000, random_state=42, replace=True)
```

The stability path generated:

```
[ ]: plot_stabl_path(ss)
```

```
[ ]: (<Figure size 400x800 with 1 Axes>,
      <Axes: xlabel='$\\lambda$', ylabel='Frequency of selection'>)
```



The features selected:

```
[ ]: ss.get_feature_names_out()
```

```
[ ]: array(['Treg_ERK_Unstim', 'Tregmem_ERK_Unstim'], dtype=object)
```

```
[ ]: save_stabl_results(ss,"./ResultsFinal/V4b/",dataV4b,y)
```

```
c:\Users\Max\AppData\Local\Programs\Python\Python311\Lib\site-
packages\stabl\visualization.py:260: FutureWarning: Passing `palette` without
assigning `hue` is deprecated.
  sns.stripplot(
c:\Users\Max\AppData\Local\Programs\Python\Python311\Lib\site-
packages\stabl\visualization.py:260: FutureWarning: Passing `palette` without
assigning `hue` is deprecated.
  sns.stripplot(
```

Here are the boxplots for these features.

```
[ ]: boxplot_features(Xstd.columns[np.where(model.coef_[0] != 0)], dataV4b,y)
```

```
c:\Users\Max\AppData\Local\Programs\Python\Python311\Lib\site-
packages\stabl\visualization.py:260: FutureWarning: Passing `palette` without
assigning `hue` is deprecated.
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packages\stabl\visualization.py:260: FutureWarning: Passing `palette` without
assigning `hue` is deprecated.
  sns.stripplot(
```
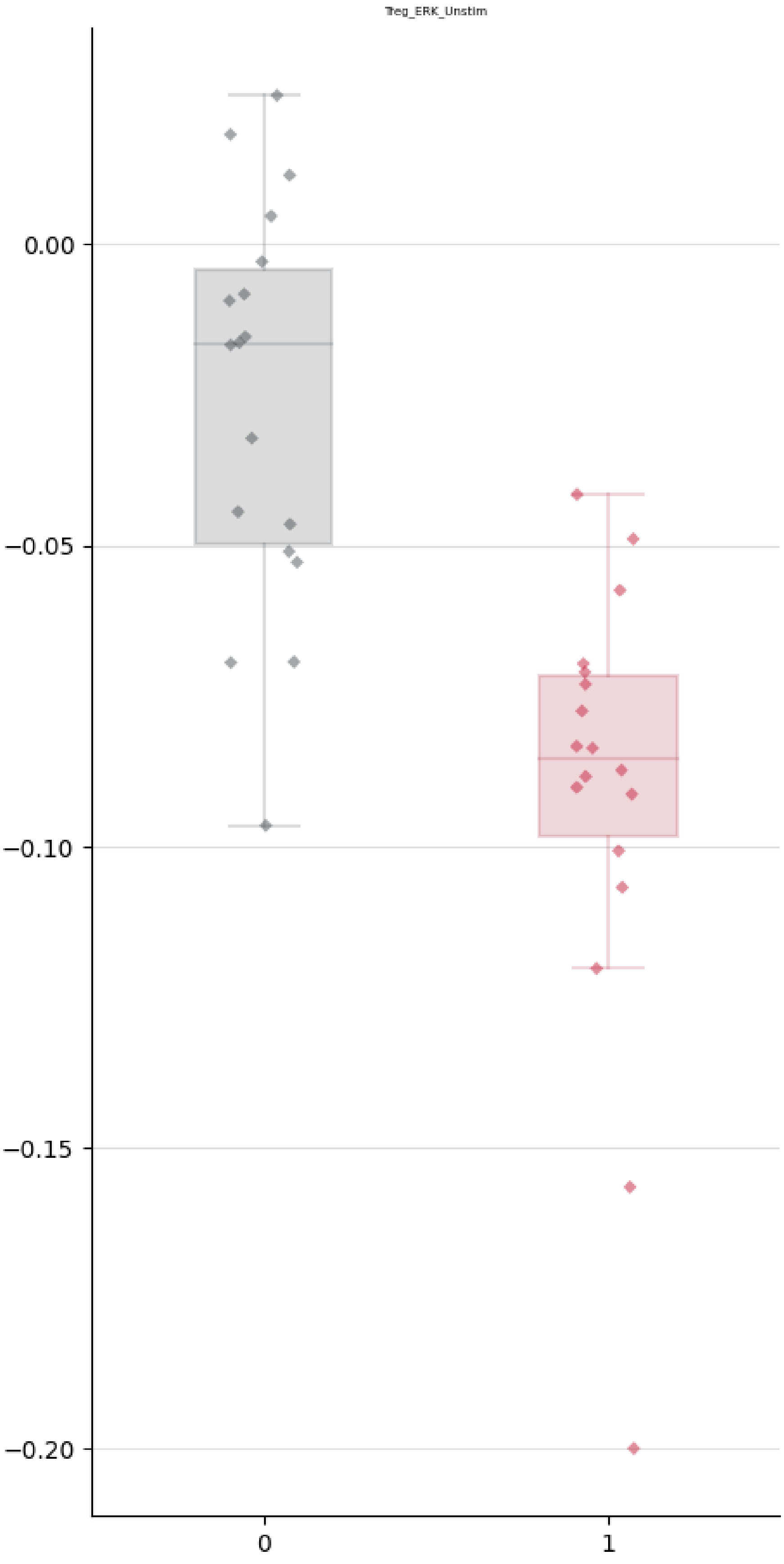
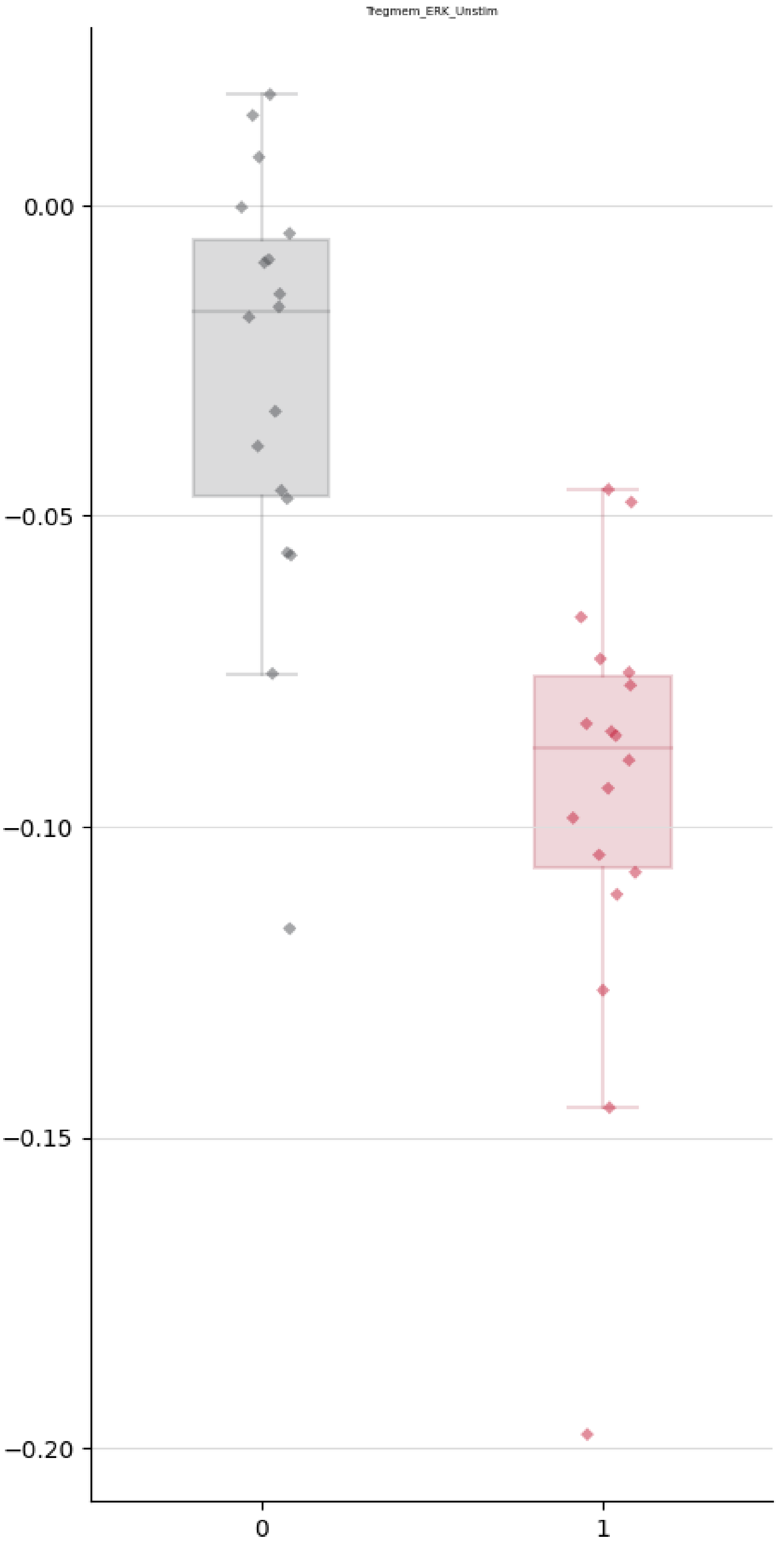


Treg_ERK_Unstim
0.00
−0.05
−0.10
−0.15
−0.20
0
1


Tregmem_ERK_Unstim
0.00
−0.05
−0.10
−0.15
−0.20
0
1

[ ]: