Biomedical Data Analysis

Introducing the Problem

Biomedical Data Analysis

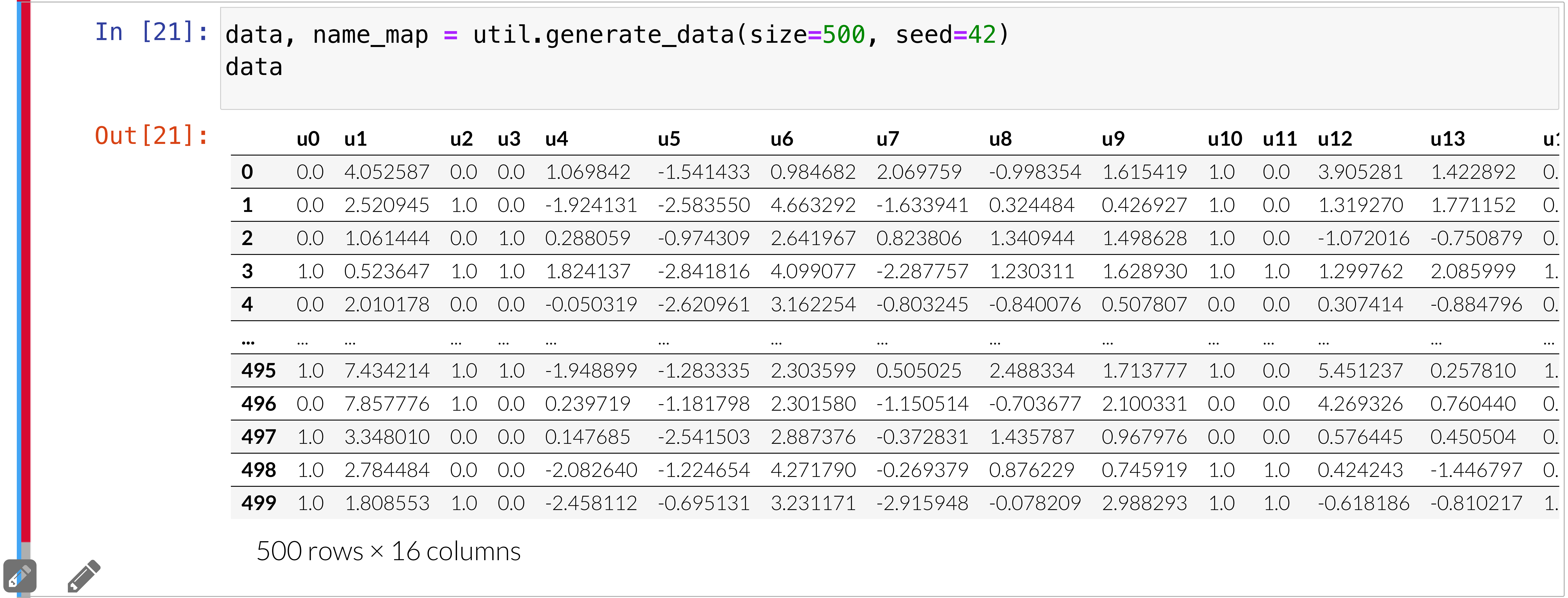
Assume we are concated by a bio-medical lab

- They have collected data about patients with a certain condition
- ...And they want to get a better understanding of the involved process

Our Dataset

This use case is based on a real-world example

...But for privacy and simplicity reasons we are going to use synthetic data



In [21]:

```
data, name_map = util.generate_data(size=500, seed=42)
data
```

Out[21]:

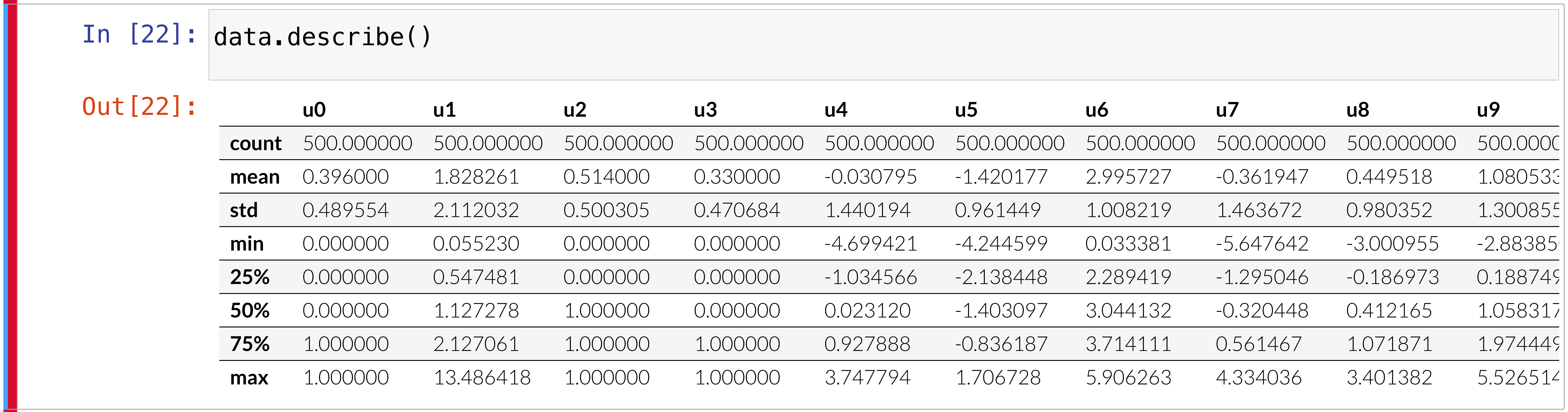
	u0	u1	u2	u3	u4	u5	u6	u7	u8	u9	u10	u11	u12	u13	u1
0	0.0	4.052587	0.0	0.0	1.069842	-1.541433	0.984682	2.069759	-0.998354	1.615419	1.0	0.0	3.905281	1.422892	0.
1	0.0	2.520945	1.0	0.0	-1.924131	-2.583550	4.663292	-1.633941	0.324484	0.426927	1.0	0.0	1.319270	1.771152	0.
2	0.0	1.061444	0.0	1.0	0.288059	-0.974309	2.641967	0.823806	1.340944	1.498628	1.0	0.0	-1.072016	-0.750879	0.
3	1.0	0.523647	1.0	1.0	1.824137	-2.841816	4.099077	-2.287757	1.230311	1.628930	1.0	1.0	1.299762	2.085999	1.
4	0.0	2.010178	0.0	0.0	-0.050319	-2.620961	3.162254	-0.803245	-0.840076	0.507807	0.0	0.0	0.307414	-0.884796	0.
...	...	...	...	...	...	...	...	...	...	...	...	...	...	...	...
495	1.0	7.434214	1.0	1.0	-1.948899	-1.283335	2.303599	0.505025	2.488334	1.713777	1.0	0.0	5.451237	0.257810	1.
496	0.0	7.857776	1.0	0.0	0.239719	-1.181798	2.301580	-1.150514	-0.703677	2.100331	0.0	0.0	4.269326	0.760440	0.
497	1.0	3.348010	0.0	0.0	0.147685	-2.541503	2.887376	-0.372831	1.435787	0.967976	0.0	0.0	0.576445	0.450504	0.
498	1.0	2.784484	0.0	0.0	-2.082640	-1.224654	4.271790	-0.269379	0.876229	0.745919	1.0	1.0	0.424243	-1.446797	0.
499	1.0	1.808553	1.0	0.0	-2.458112	-0.695131	3.231171	-2.915948	-0.078209	2.988293	1.0	1.0	-0.618186	-0.810217	1.

500 rows × 16 columns

How do we start?

Our Dataset

Let's have a first look at the dataset



```
In [22]: data.describe()
```

Out[22]:

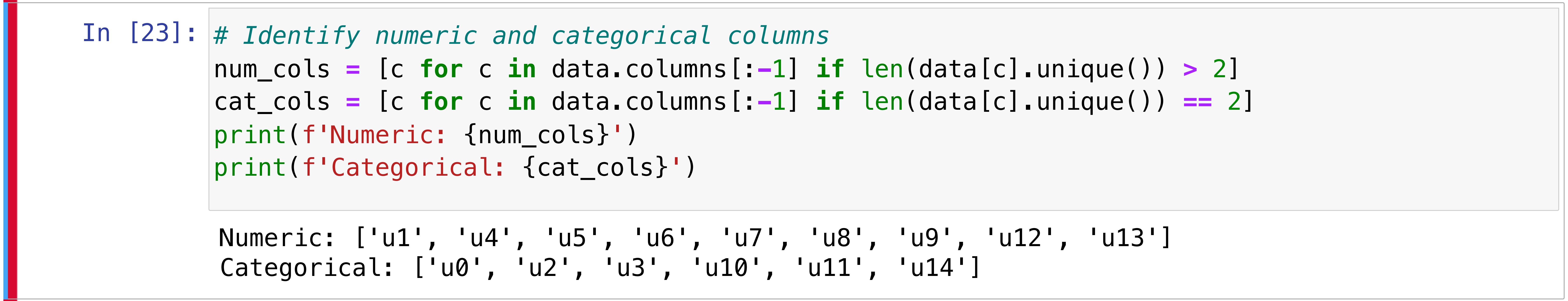
	u0	u1	u2	u3	u4	u5	u6	u7	u8	u9
count	500.000000	500.000000	500.000000	500.000000	500.000000	500.000000	500.000000	500.000000	500.000000	500.0000
mean	0.396000	1.828261	0.514000	0.330000	-0.030795	-1.420177	2.995727	-0.361947	0.449518	1.080533
std	0.489554	2.112032	0.500305	0.470684	1.440194	0.961449	1.008219	1.463672	0.980352	1.300855
min	0.000000	0.055230	0.000000	0.000000	-4.699421	-4.244599	0.033381	-5.647642	-3.000955	-2.88385
25%	0.000000	0.547481	0.000000	0.000000	-1.034566	-2.138448	2.289419	-1.295046	-0.186973	0.188749
50%	0.000000	1.127278	1.000000	0.000000	0.023120	-1.403097	3.044132	-0.320448	0.412165	1.058317
75%	1.000000	2.127061	1.000000	1.000000	0.927888	-0.836187	3.714111	0.561467	1.071871	1.974449
max	1.000000	13.486418	1.000000	1.000000	3.747794	1.706728	5.906263	4.334036	3.401382	5.526514

- There is one target binary variable Y, representing the condition under study
- All other columns represent potentially correlate variables
- We are going to refer to them as "potential correlates"

Typesetting math: 100%

Categorial and Numerical Variables

Some of the potential correlates are numeric, others are categorical



In [23]:
```
# Identify numeric and categorical columns
num_cols = [c for c in data.columns[:-1] if len(data[c].unique()) > 2]
cat_cols = [c for c in data.columns[:-1] if len(data[c].unique()) == 2]
print(f'Numeric: {num_cols}')
print(f'Categorical: {cat_cols}')
```

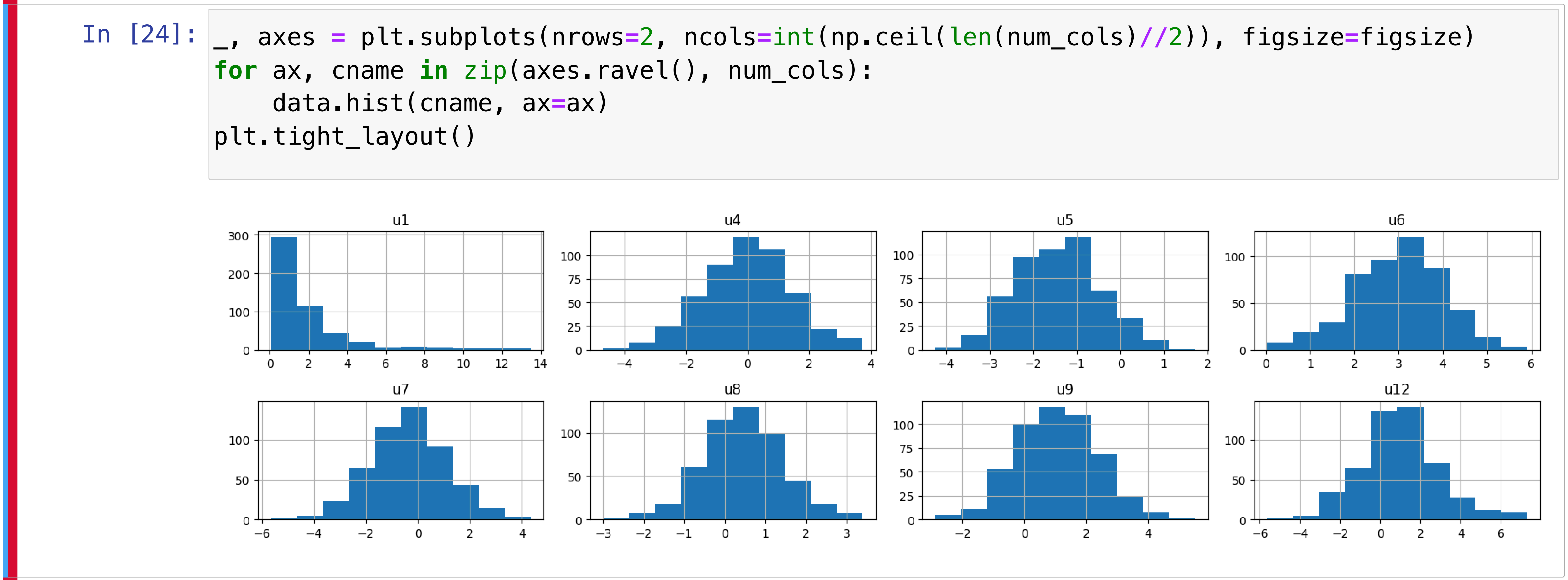
```
Numeric: ['u1', 'u4', 'u5', 'u6', 'u7', 'u8', 'u9', 'u12', 'u13']
Categorical: ['u0', 'u2', 'u3', 'u10', 'u11', 'u14']
```

- In this synthetic dataset, all categorical variables are binary
- ...Which explains the simple filter we used to identify them

In a real world setting, you'd need to talk to a domain expert for this

Checking the Distributions

Let's check the distribution of the numerical candidate correlates



In [24]:

```
_, axes = plt.subplots(nrows=2, ncols=int(np.ceil(len(num_cols)//2)), figsize=figsize)
for ax, cname in zip(axes.ravel(), num_cols):
    data.hist(cname, ax=ax)
plt.tight_layout()
```

Typesetting math: 100%

Checking the Distributions

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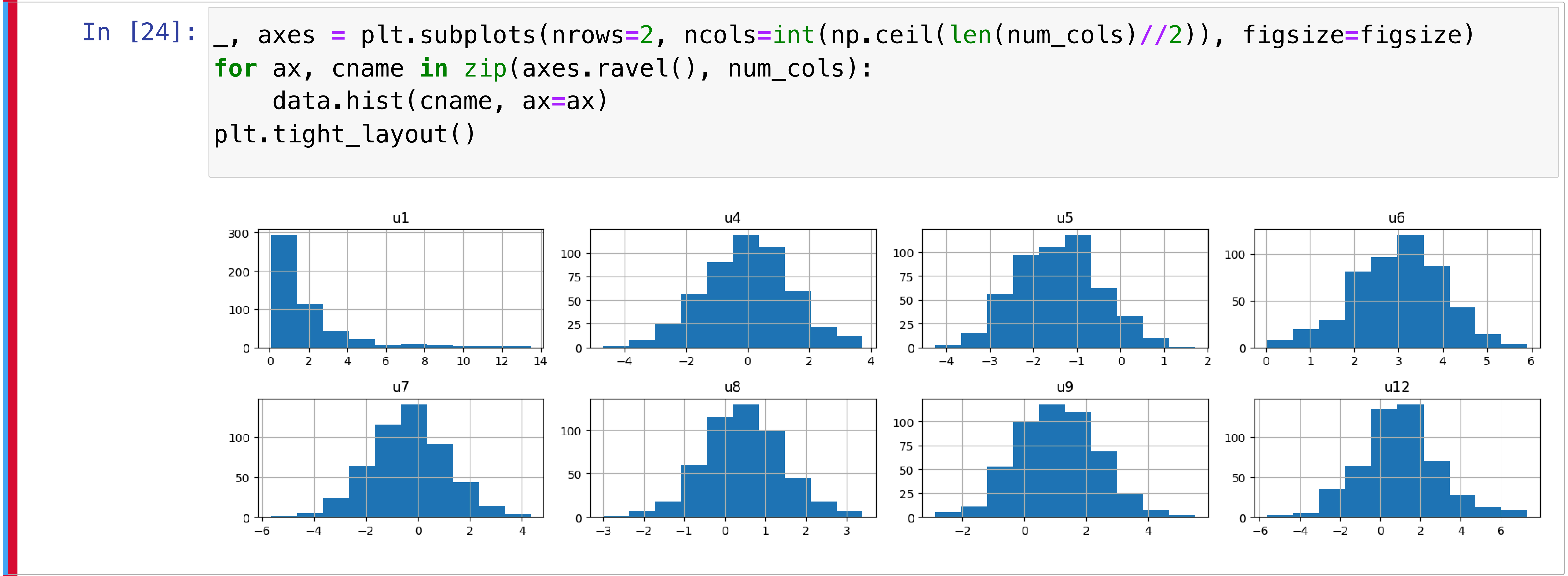

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plt.tight_layout()
```

Most of them seem to follow a Normal distribution

Typesetting math: 100%

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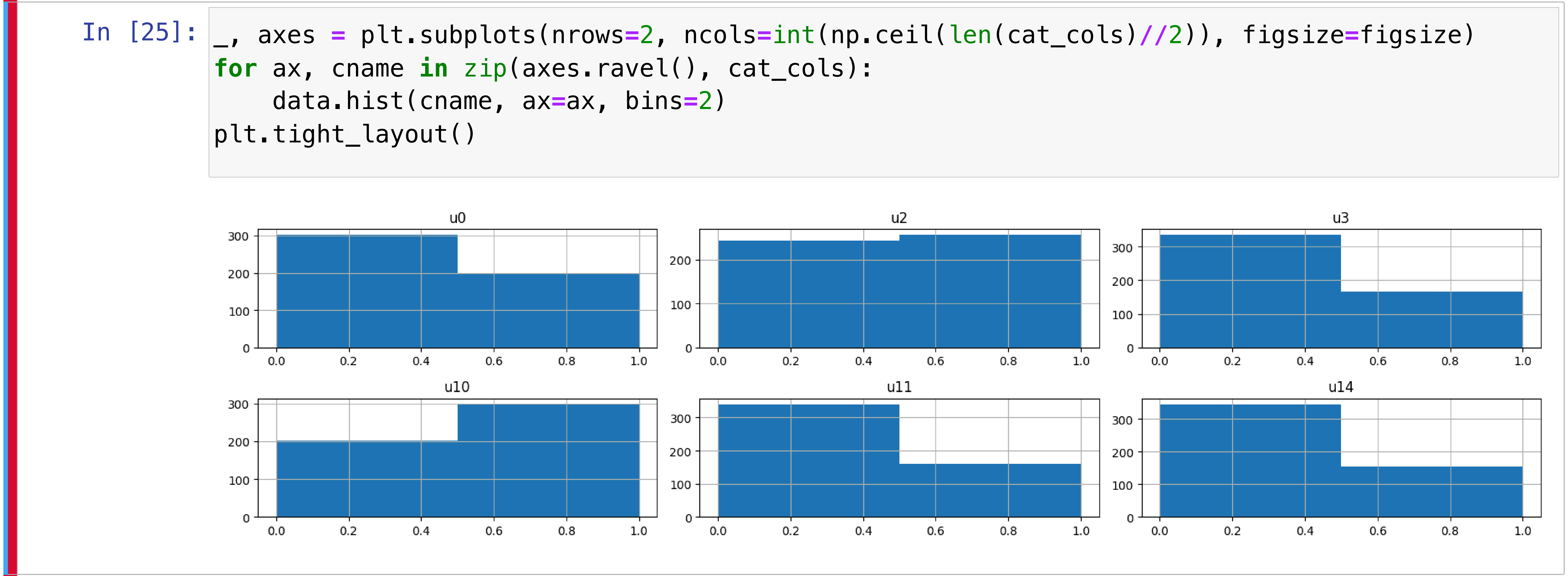

In [25]:

```
_, axes = plt.subplots(nrows=2, ncols=int(np.ceil(len(cat_cols)//2)), figsize=figsize)
for ax, cname in zip(axes.ravel(), cat_cols):
    data.hist(cname, ax=ax, bins=2)
plt.tight_layout()
```

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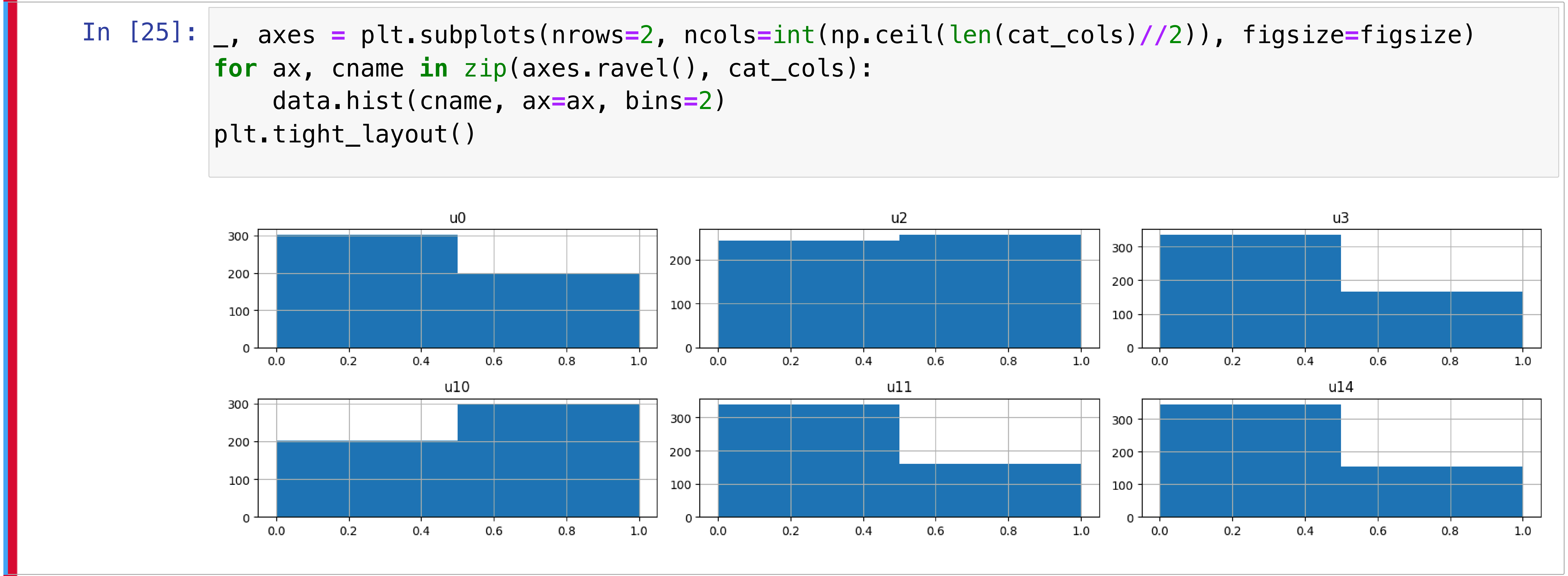

```
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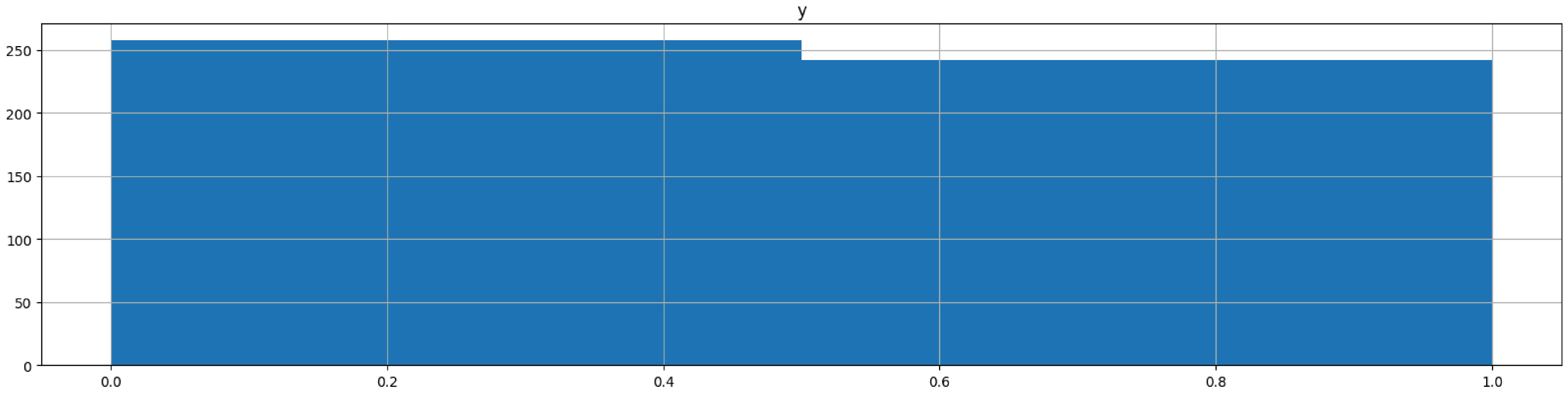
         for ax, cname in zip(axes.ravel(), cat_cols):
             data.hist(cname, ax=ax, bins=2)
         plt.tight_layout()
```

Some are well balanced, othere less so

Checking the Distributions

Let's check the target distribution

In [26]:
```
data.hist('y', bins=2, figsize=figsize)
plt.tight_layout()
```

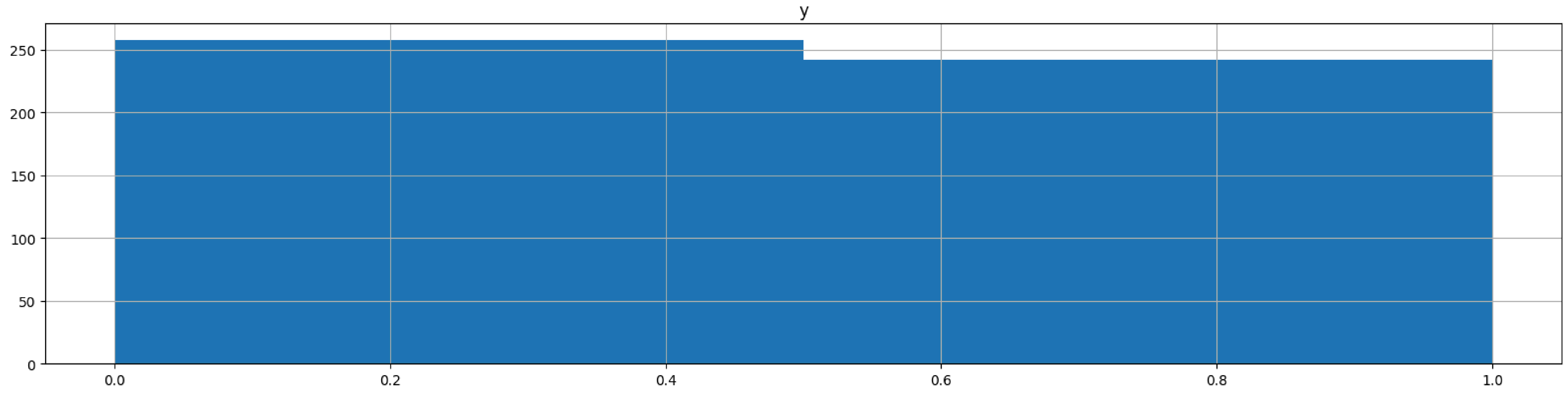


Typesetting math: 100%

Checking the Distributions

Let's check the target distribution

In [26]:
```
data.hist('y', bins=2, figsize=figsize)
plt.tight_layout()
```



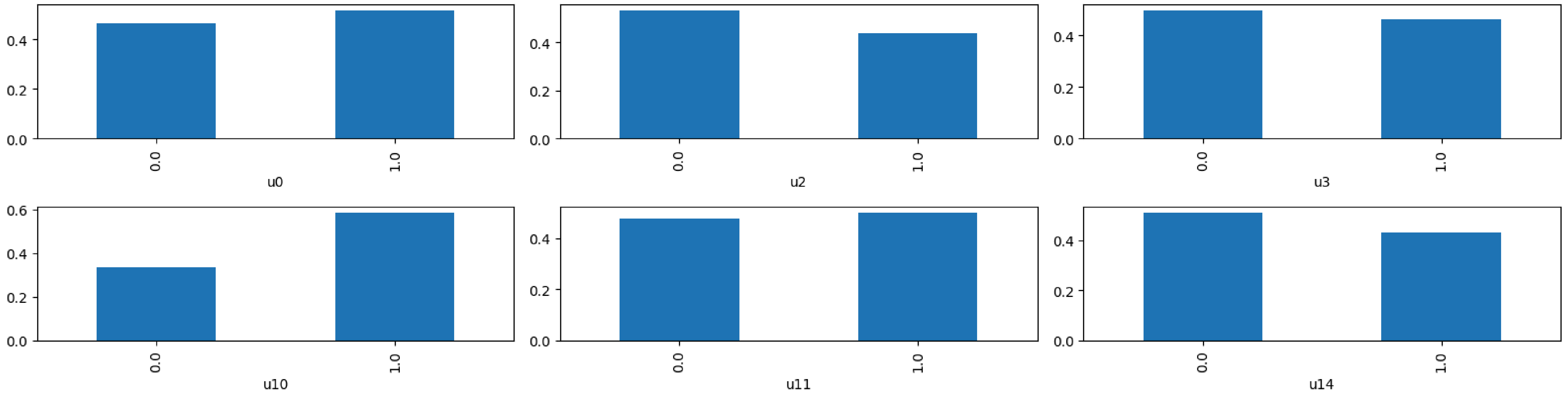
The target distribution quite balanced

Checking Univariate Dependencies

Let's check the fraction of $Y = 1$ for the categorical candidates

In [27]:

```
_, axes = plt.subplots(nrows=2, ncols=int(np.ceil(len(cat_cols)//2)), figsize=figsize)
for ax, cname in zip(axes.ravel(), cat_cols):
    data.groupby(cname)['y'].mean().plot.bar(ax=ax)
plt.tight_layout()
```



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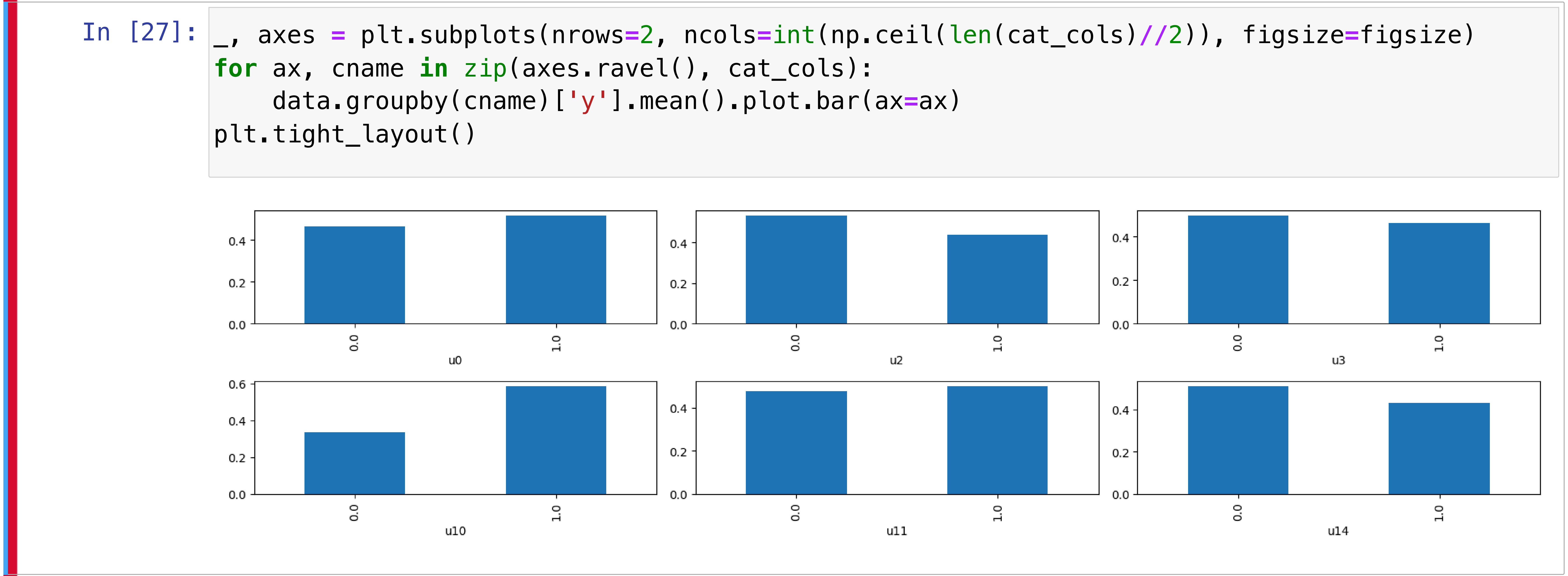


In [27]:

```
_, axes = plt.subplots(nrows=2, ncols=int(np.ceil(len(cat_cols)//2)), figsize=figsize)
for ax, cname in zip(axes.ravel(), cat_cols):
    data.groupby(cname)['y'].mean().plot.bar(ax=ax)
plt.tight_layout()
```

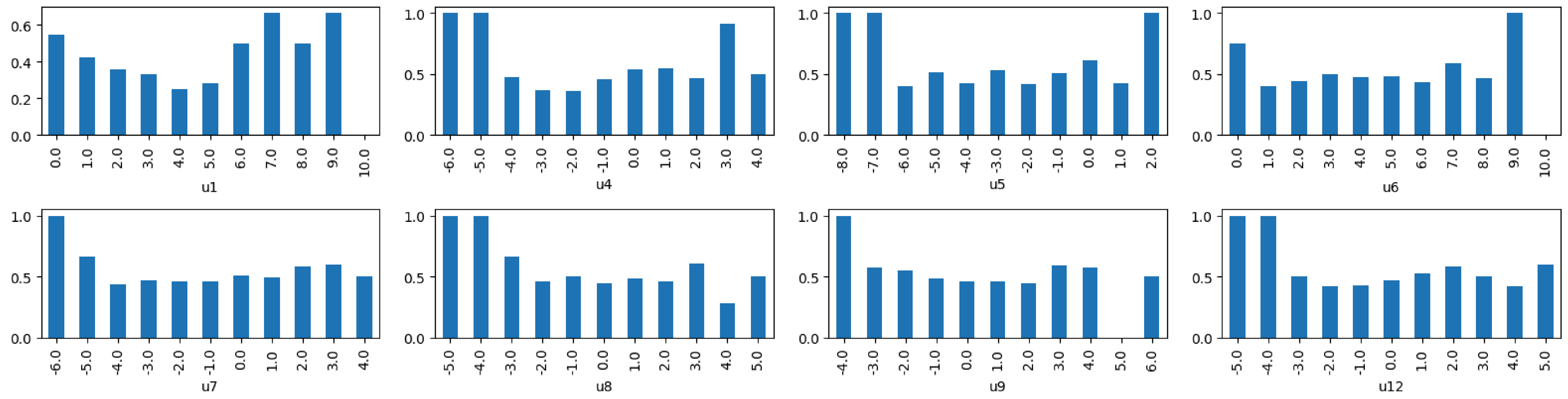
A few of them seems to have a correlation, other cases are less clear

Checking Univariate Dependencies

Let's check the fraction of $y = 1$ for the numerical candidates

In [28]:

```
_, axes = plt.subplots(nrows=2, ncols=int(np.ceil(len(num_cols)//2)), figsize=figsize)
for ax, cname in zip(axes.ravel(), num_cols):
    bin_size = (data[cname].max() - data[cname].min()) / 10
    data['y'].groupby(data[cname] // bin_size).mean().plot.bar(ax=ax)
plt.tight_layout()
```



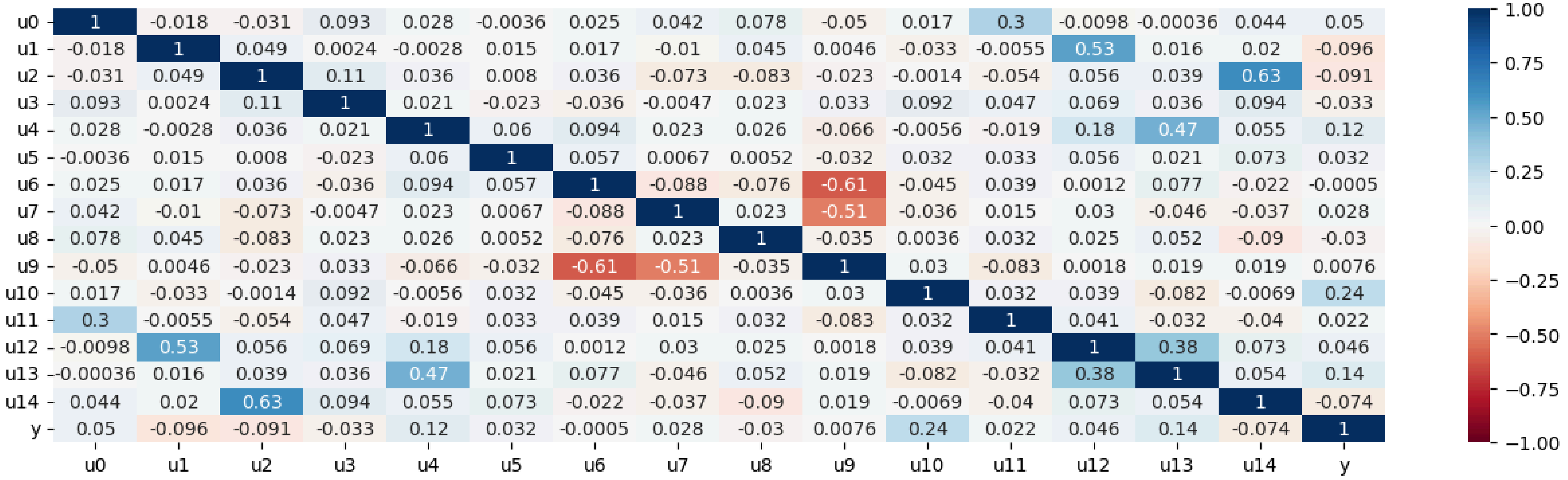
Most of them appear to have some non-linear correlation

Checking Linear Correlations

It's worth checking how all features are correlated

One way to do it is by plotting a correlation matrix (e.g. Pearson)

```
In [29]: plt.figure(figsize=figsize)
         sn.heatmap(data.corr(method='pearson'), annot=True, vmin=-1, vmax=1, cmap='RdBu');
```



	u0	u1	u2	u3	u4	u5	u6	u7	u8	u9	u10	u11	u12	u13	u14	y
u0	1	-0.018	-0.031	0.093	0.028	-0.0036	0.025	0.042	0.078	-0.05	0.017	0.3	-0.0098	-0.00036	0.044	0.05
u1	-0.018	1	0.049	0.0024	-0.0028	0.015	0.017	-0.01	0.045	0.0046	-0.033	-0.0055	0.53	0.016	0.02	-0.096
u2	-0.031	0.049	1	0.11	0.036	0.008	0.036	-0.073	-0.083	-0.023	-0.0014	-0.054	0.056	0.039	0.63	-0.091
u3	0.093	0.0024	0.11	1	0.021	-0.023	-0.036	-0.0047	0.023	0.033	0.092	0.047	0.069	0.036	0.094	-0.033
u4	0.028	-0.0028	0.036	0.021	1	0.06	0.094	0.023	0.026	-0.066	-0.0056	-0.019	0.18	0.47	0.055	0.12
u5	-0.0036	0.015	0.008	-0.023	0.06	1	0.057	0.0067	0.0052	-0.032	0.032	0.033	0.056	0.021	0.073	0.032
u6	0.025	0.017	0.036	-0.036	0.094	0.057	1	-0.088	-0.076	-0.61	-0.045	0.039	0.0012	0.077	-0.022	-0.0005
u7	0.042	-0.01	-0.073	-0.0047	0.023	0.0067	-0.088	1	0.023	-0.51	-0.036	0.015	0.03	-0.046	-0.037	0.028
u8	0.078	0.045	-0.083	0.023	0.026	0.0052	-0.076	0.023	1	-0.035	0.0036	0.032	0.025	0.052	-0.09	-0.03
u9	-0.05	0.0046	-0.023	0.033	-0.066	-0.032	-0.61	-0.51	-0.035	1	0.03	-0.083	0.0018	0.019	0.019	0.0076
u10	0.017	-0.033	-0.0014	0.092	-0.0056	0.032	-0.045	-0.036	0.0036	0.03	1	0.032	0.039	-0.082	-0.0069	0.24
u11	0.3	-0.0055	-0.054	0.047	-0.019	0.033	0.039	0.015	0.032	-0.083	0.032	1	0.041	-0.032	-0.04	0.022
u12	-0.0098	0.53	0.056	0.069	0.18	0.056	0.0012	0.03	0.025	0.0018	0.039	0.041	1	0.38	0.073	0.046
u13	-0.00036	0.016	0.039	0.036	0.47	0.021	0.077	-0.046	0.052	0.019	-0.082	-0.032	0.38	1	0.054	0.14
u14	0.044	0.02	0.63	0.094	0.055	0.073	-0.022	-0.037	-0.09	0.019	-0.0069	-0.04	0.073	0.054	1	-0.074
y	0.05	-0.096	-0.091	-0.033	0.12	0.032	-0.0005	0.028	-0.03	0.0076	0.24	0.022	0.046	0.14	-0.074	1

- Sparse correlations in general, weak (linear) correlations for Y

So far we have just inspected our dataset, but...
what is exactly our goal?

Use Case Objective

Unlike in classical ML tasks, we don't have an estimation problem

Rather, our goal is understanding the process behind the data

- We want to identify the true correlates among our candidates
- We want to see how they are linked to the target y

In an ideal world, we'd like to know about causal relationships

...But in practice, we'll need to be happy with correlations

- Studying causality is indeed possible (a good start is Judea Pearl's book)
- ...But also very challenging, and there's no general and mature tool available

So, we'll count on the domain expert to check the correlations

Use Case Objective

Our setup also explains a quirk in the dataset

All variables except the target are called U_j, for "unknown"

- This is synthetic data, so nothing is really unknown
- In fact, the ground truth process linking Y to U is avaialable

However, for the sake of this exercise, such process will be hidden

- We will analyze the data pretending we have no such knowledge
- At the end of our exercise we'll check the ground truth

...And we'll see how close we got to the truth!

Biomedical Data Analysis

A Baseline Approach

A Baseline Approach

Our goal is understading the process behind the data

Of of many possible ways to do it consist in:

- Training an approximate model via Machine Learning
- Studying the model as a proxy for the real process

Basically, we use a ML model as an analysis tool

For this approach to work, we need the ML model to be explainable

- A few model naturally enjoy this property (e.g. linear models, simple DTs)
- Explaining other models is not obvious (e.g. Neural Networks, large ensembles)

We will start with the simplest option: Logistic Regression

Data Preprocessing

We start with the usual data preprocessing

We will treat all candidate correlates as inputs

```
In [30]: # Input-output separation
         X, y = data[data.columns[:-1]].copy(), data[data.columns[-1]].copy()
         # Train-test split
         X_train, X_test, y_train, y_test = train_test_split(X, y, test_size=0.2, random_state=42)
         # Input standardization
         scaler = StandardScaler()
         X_train[num_cols] = scaler.fit_transform(X_train[num_cols])
         X_test[num_cols] = scaler.transform(X_test[num_cols])
```

Even if we don't care about estimates, we need a test set

- This will allow us to check the model for overfitting

We also need to standardize all numeric features

- This will make the model coefficients more easily interpretable

On the Danger of Overfitting

We plan to use our model as proxy for the true process

...Which makes overfitting is especially bad

- Our results will stricly apply only to the model
- ...And they will be as general as the model

We will use L1 regularization on this purpose

Scikit learn support L1 regularizers for Logistic Regression in the form:

$$\text{argmin}_\theta \ H(y, f(x, \theta)) + \frac{1}{C} \|\theta\|_1$$

- We encourage the weights to be close to 0
- ...And we attempt to sparsify the weights

Training our "Proxy" Model

We can calibrate the C parameter via cross-validation

We'll need the SAGA solver to train our model with L1 regularization

```
In [31]: base_est = LogisticRegression(penalty='l1', solver='saga')
         param_grid={'C': 1. / np.linspace(1e-1, 1e4, 100)}
         gscv = GridSearchCV(base_est, param_grid=param_grid, scoring='roc_auc')
         gscv.fit(X_train, y_train)
         lr, lr_params = gscv.best_estimator_, gscv.best_params_
```

Then we can check the performance of the refitted estimator

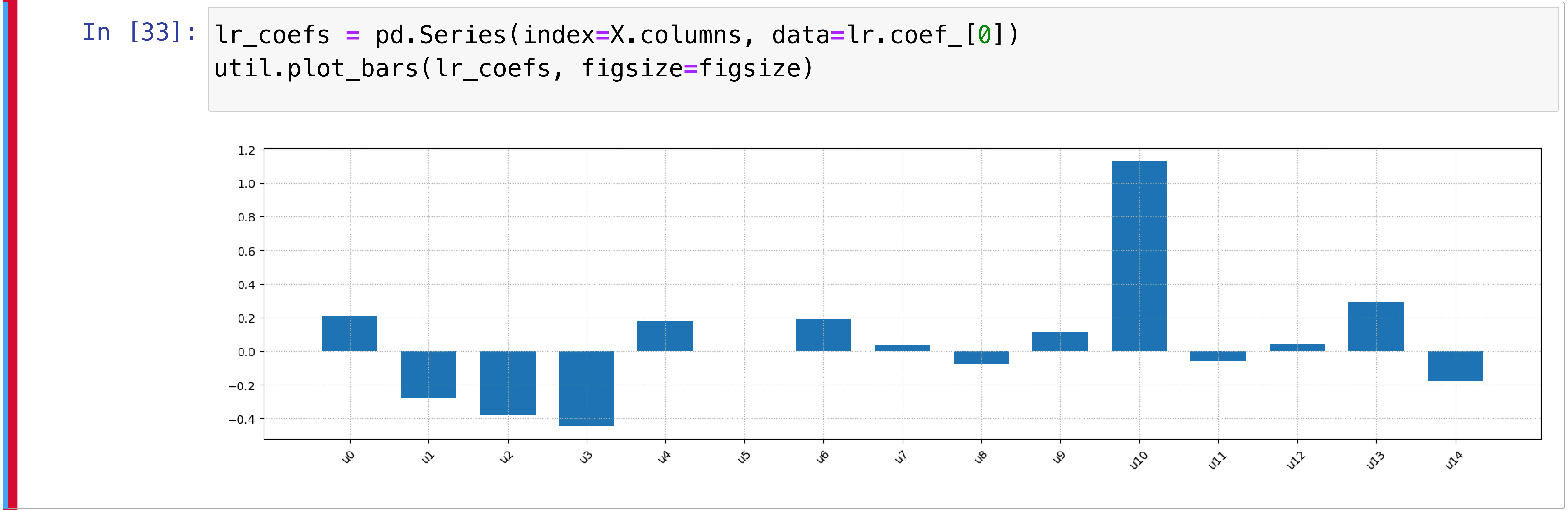
```
In [32]: lr_score_cv, lr_score_test = gscv.best_score_, roc_auc_score(y_test, lr.predict_proba(X_test
         print(f'AUC score for C={lr_params["C"]:.2f}: {lr_score_cv:.2f} (cross-validation), {lr_scor
```

```
AUC score for C=10.00: 0.64 (cross-validation), 0.60 (test)
```

We use the AUC score, since this is not a real classification problem

Coefficient Analysis

Finally, we can analyze the model coefficients



```
In [33]: lr_coefs = pd.Series(index=X.columns, data=lr.coef_[0])
         util.plot_bars(lr_coefs, figsize=figsize)
```

- Some variables seem to be more important than others
- The sign tells us how they are linked to the target

Processing math: 100%

This baseline approach has *many* issues

Can you spot a few ones?

Three Key Issues with our Baseline

Issue 1: our model has poor accuracy

- An AUC score of 0.6 is not much above random
- ...Hence, studying our model will say little about the data

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Issue 2: our model can only capture linear correlations

- We can capture neither non-linear effects
- ...Nor interactions among the variables

Three Key Issues with our Baseline

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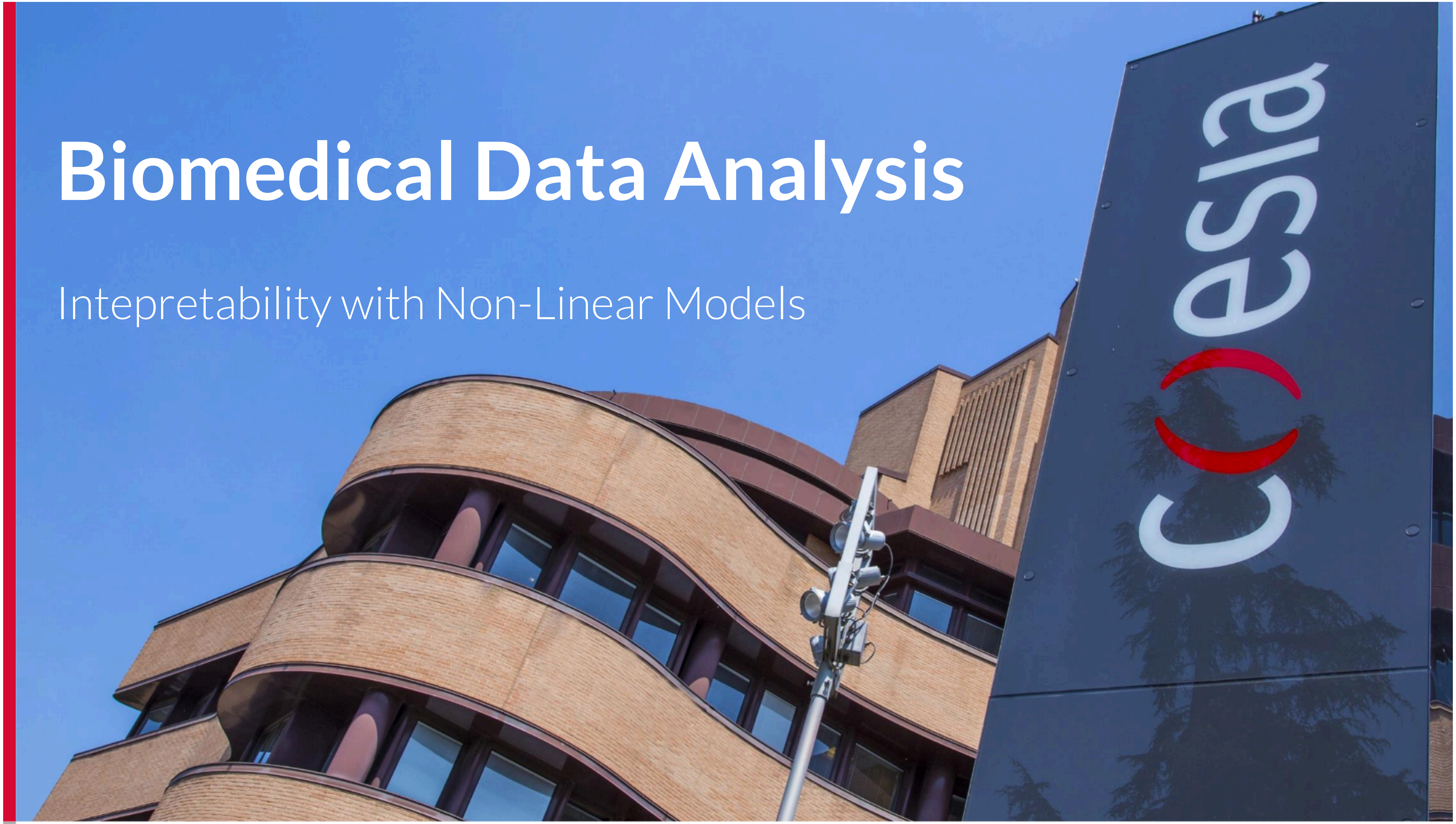
- ...Nor interactions among the variables

Issue 3: the coefficients are not sparse

- The L1 terms needs both to sparsify and to prevent overfitting
- ...And it cannot do both things effectively
- Additionally: it's unclear what a good level of sparsification might be

Biomedical Data Analysis

Intepretability with Non-Linear Models



Dealing with Non-Linearities

We'll start by switching to a non-linear model

By doing so:

- We can still account for non-linear correlations
- We can account for interactions among variables
- We might reach a much better accuracy
- ...And hence have a more representative proxy model

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By doing so:

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- We can account for interactions among variables
- We might reach a much better accuracy
- ...And hence have a more representative proxy model

Of course there is a price to pay

- Non-linear models are less easy to interpret
- ...And they are at a much higher risk of overfitting

Gradient Boosted Trees Model

We'll train a Gradient Bossted Trees model

We'll rely on the Extreme Gradient Boosting package (XGBoost) for this

```
In [34]: base_est = xgboost.XGBRegressor(objective='reg:logistic', tree_method='hist', importance_typ
         param_grid={'max_depth': [2, 3, 4], 'n_estimators': list(range(20, 41, 5)), 'reg_lambda': np
         gscv = GridSearchCV(base_est, param_grid=param_grid, scoring='roc_auc')
         gscv.fit(X, y)
         xbm, xbm_params = gscv.best_estimator_, gscv.best_params_
```

XGBoost is a library for fast, distributed, training of GBT models

It has support for multiple loss functions

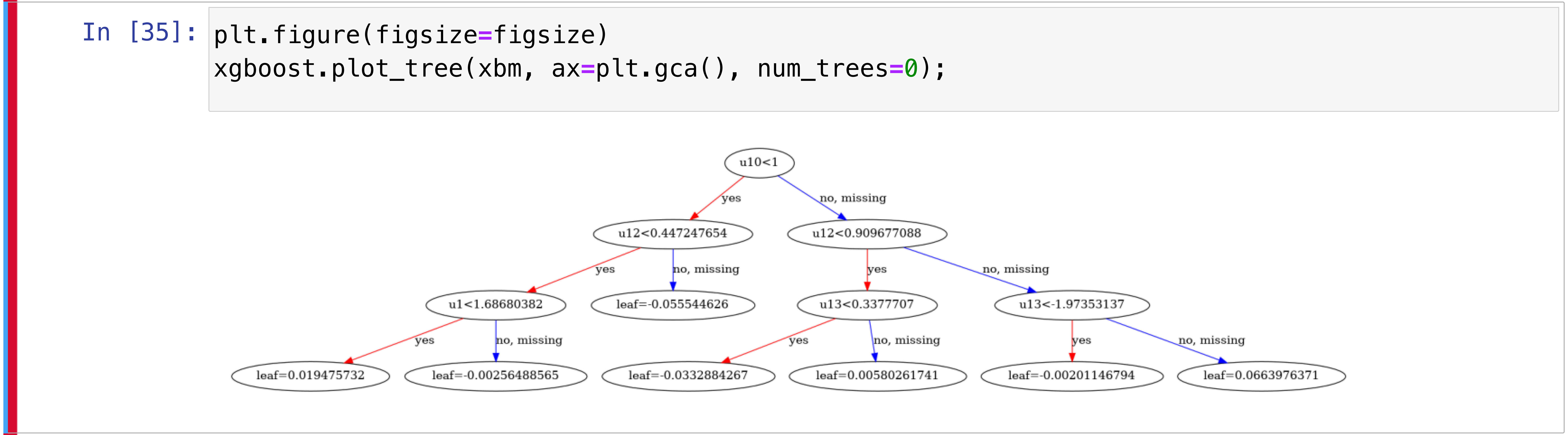
- We are using "reg:logistic", which refers binary cross-entropy

...And for regularization (often missing in tree-based models)

- The "reg_lambda" parameter refers to the weight of an L2 regularization term
  - Which in GBT is applied to the leaf labels

Gradient Boosted Trees Model

It's easier to see how regularization work by checking a tree in the ensemble



```
In [35]: plt.figure(figsize=figsize)
         xgboost.plot_tree(xbm, ax=plt.gca(), num_trees=0);
```

- Assuming T is the number of leaves and w_j is the label assigned to each leaf
- ...Then the regularization term is in the form $\sum_{k=1}^{T} w_j^2$

Typesetting math: 100%

Gradient Boosted Trees Model

On our dataset, a GBT model has substantially better performance

In [36]:
```
xbm_score_cv, xbm_score_test = gscv.best_score_, roc_auc_score(y_test, xbm.predict(X_test))
print(f'AUC score for {xbm_params}: {xbm_score_cv:.2f} (cross-validation), {xbm_score_test:.
```

```
AUC score for {'max_depth': 3, 'n_estimators': 25, 'reg_lambda': 200.0}: 0.81 (cross-valid
ation), 0.79 (test)
```

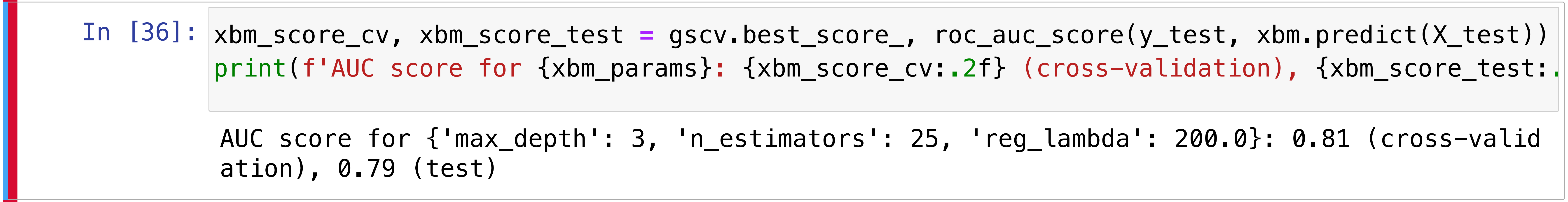
- The AUC score is much higher now
- There is no significant overfitting

It seems we finally have a model that we can trust

Typesetting math: 100%

Gradient Boosted Trees Model

On our dataset, a GBT model has substantially better performance



```
In [36]: xbm_score_cv, xbm_score_test = gscv.best_score_, roc_auc_score(y_test, xbm.predict(X_test))
         print(f'AUC score for {xbm_params}: {xbm_score_cv:.2f} (cross-validation), {xbm_score_test:.
```

```
AUC score for {'max_depth': 3, 'n_estimators': 25, 'reg_lambda': 200.0}: 0.81 (cross-valid
ation), 0.79 (test)
```

- The AUC score is much higher now
- There is no significant overfitting

It seems we finally have a model that we can trust

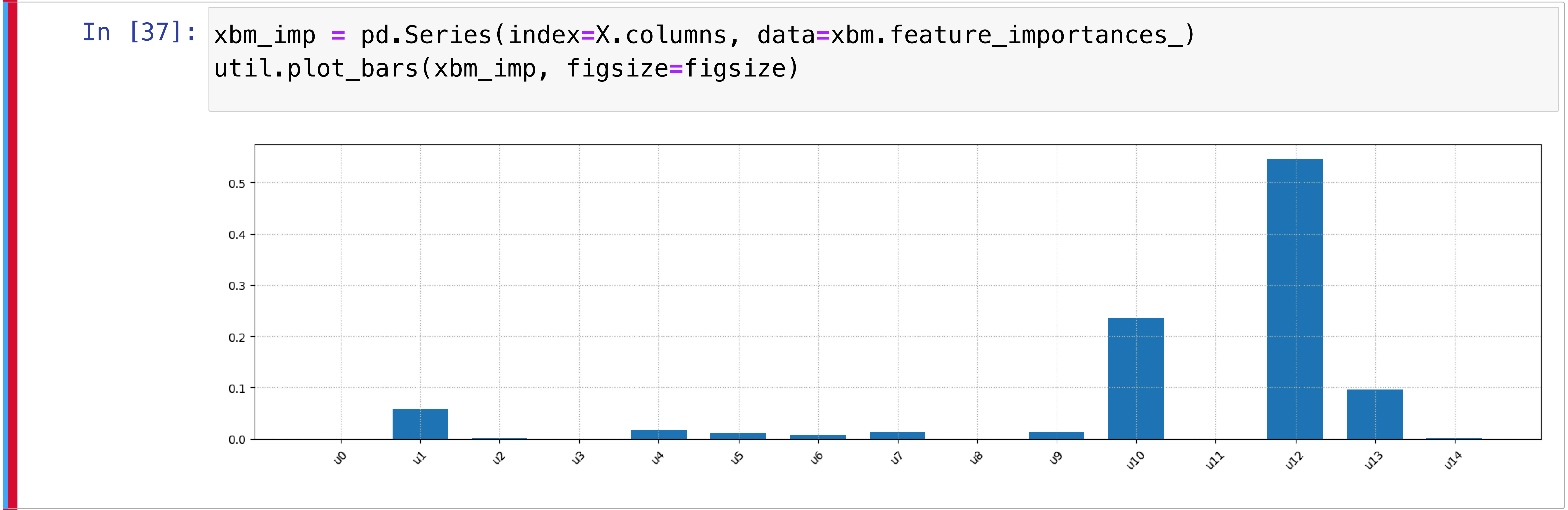
However, we know have an ensemble of many non-linear models

How can we make sense of that?

Typesetting math: 100%

Feature Importances

The first option one can probably think of is using feature importances



```
In [37]: xbm_imp = pd.Series(index=X.columns, data=xbm.feature_importances_)
         util.plot_bars(xbm_imp, figsize=figsize)
```

- The scores differ significanly from those obtained for linear regression (as expected)
- ...But what do they represent?

Which Feature Importances?

Feature importance is typicaly presented as this:

- For each input x_j, we sum the associated gain at training time
- Once training is over, we normalize the scores so that they sum up to 1

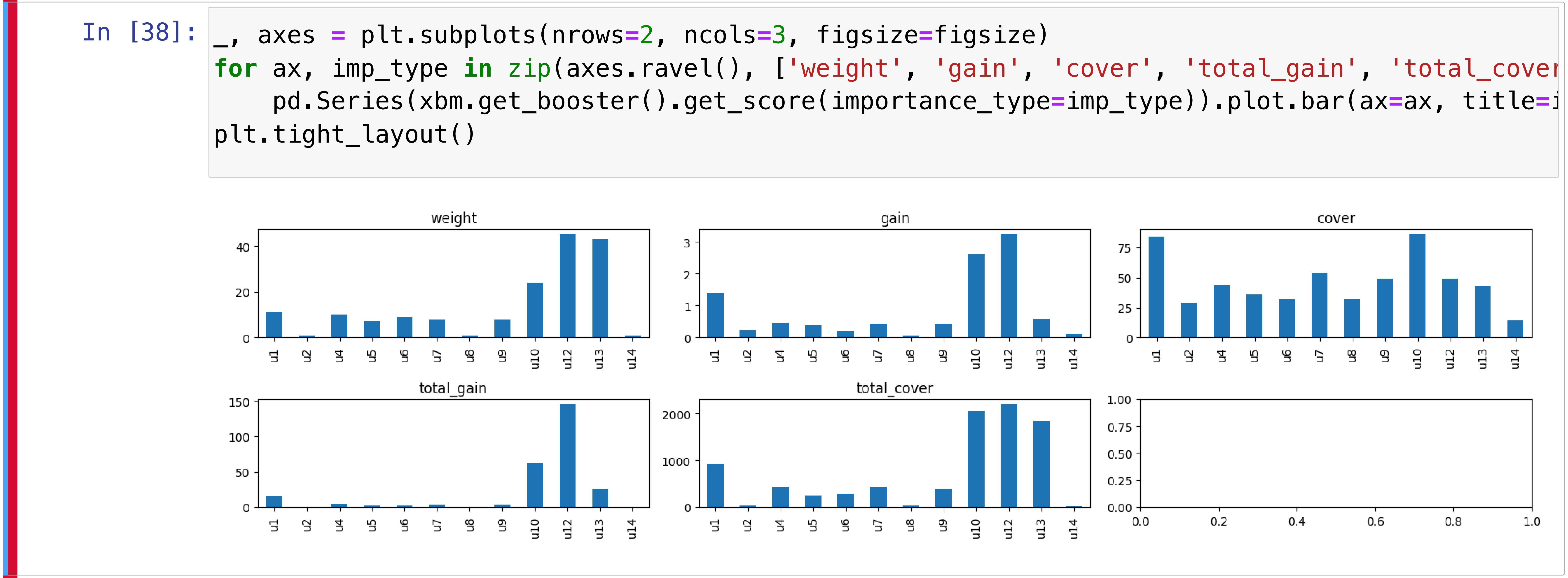
However, there are other ways to define importance

XGBoost supports 5 different approaches:

- "weight": number of times an attribute is used to split
- "gain": average gain associated to splits over an attribute
- "cover": average number of examples for which an attribute is used to decide
- "total_gain": as above, but replacing the average with a sum
- "total_cover": as above, but replacing the average with a sum

Which Feature Importances?

The values of the multiple feature importances can be quite different:



In [38]:

```
_, axes = plt.subplots(nrows=2, ncols=3, figsize=figsize)
for ax, imp_type in zip(axes.ravel(), ['weight', 'gain', 'cover', 'total_gain', 'total_cover
    pd.Series(xbm.get_booster().get_score(importance_type=imp_type)).plot.bar(ax=ax, title=i
plt.tight_layout()
```

Importance and Data

Moreover, most importance scores are computed w.r.t. a dataset:

E.g. in XGBoost "gain", "cover", "total_gain", and "total_cover"

- For this reason, they are not really properties of the model
- ...But rather of the model and a reference sample

This means that the score semantic depends on the reference sample

By default, importances are computed on the training set

...Which means they are susceptible to overfitting

- The model might split on an attribute because it really is importance
- ...But also due to a spurious correlation

Permutation Importance

We can improve things by changing the way we compute importance

Given a reference sample $\{x_i, y_i\}_{i=1}^m$

- We can evaluate the performance of our model on the sample
- ...With that of a modified sample where the j-th input is made unimportant

For example, we can achieve that by permuting the values of the input

- This will preserve the distribution of the input
- ...But it will break all its correlations

Then, we look at the change in the model performance

- If it is small, the attribute is really unimportant
- Otherwise, the attribute is important

These scores are known as permutation importances

Permutation Importance

Permutation importances are robust w.r.t. spurious correlations

- We just need to repeat the process multiple times
- ...And record means and standard deviations

It's unlikely that we get a high score very often by accident

They allow us to choose our reference sample:

On the training set, the model might have overfit over the data

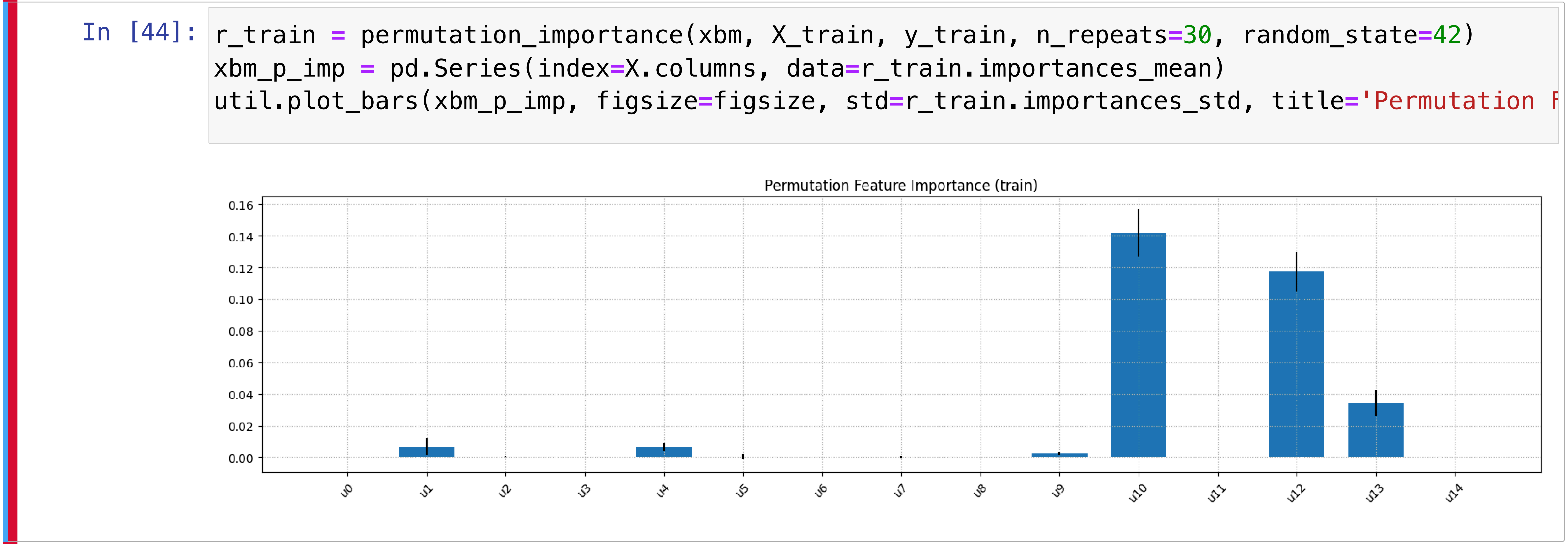
- The performance gap will be wider
- ...And the score will reflect how the model is using the data

On the test set, overfitting will make less of a different

- ...And the score will reflect how correlated the attribute is with the target

Permutation Importances, on our Example

Let's check the training permutation importances in our case study

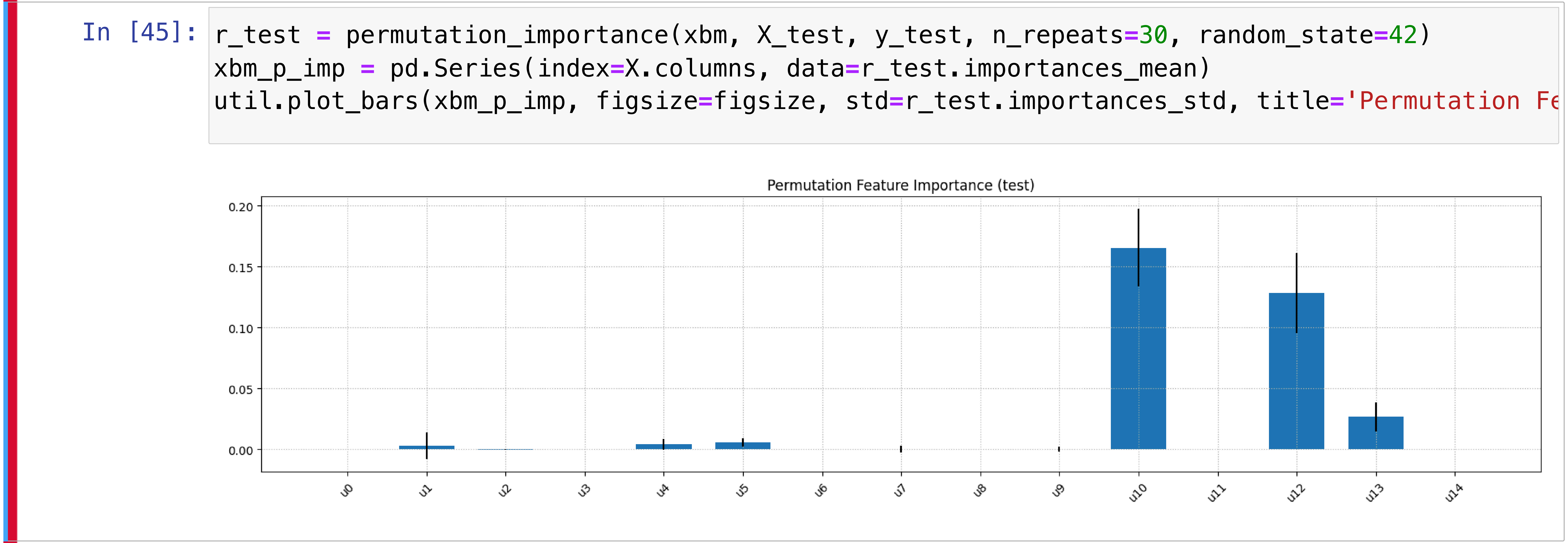


```
In [44]: r_train = permutation_importance(xbm, X_train, y_train, n_repeats=30, random_state=42)
         xbm_p_imp = pd.Series(index=X.columns, data=r_train.importances_mean)
         util.plot_bars(xbm_p_imp, figsize=figsize, std=r_train.importances_std, title='Permutation F
```

- The closely resemble those XGB "total_gain", but they are more sparse

Permutation Importances, on our Example

Let's check the test permutation importances in our case study

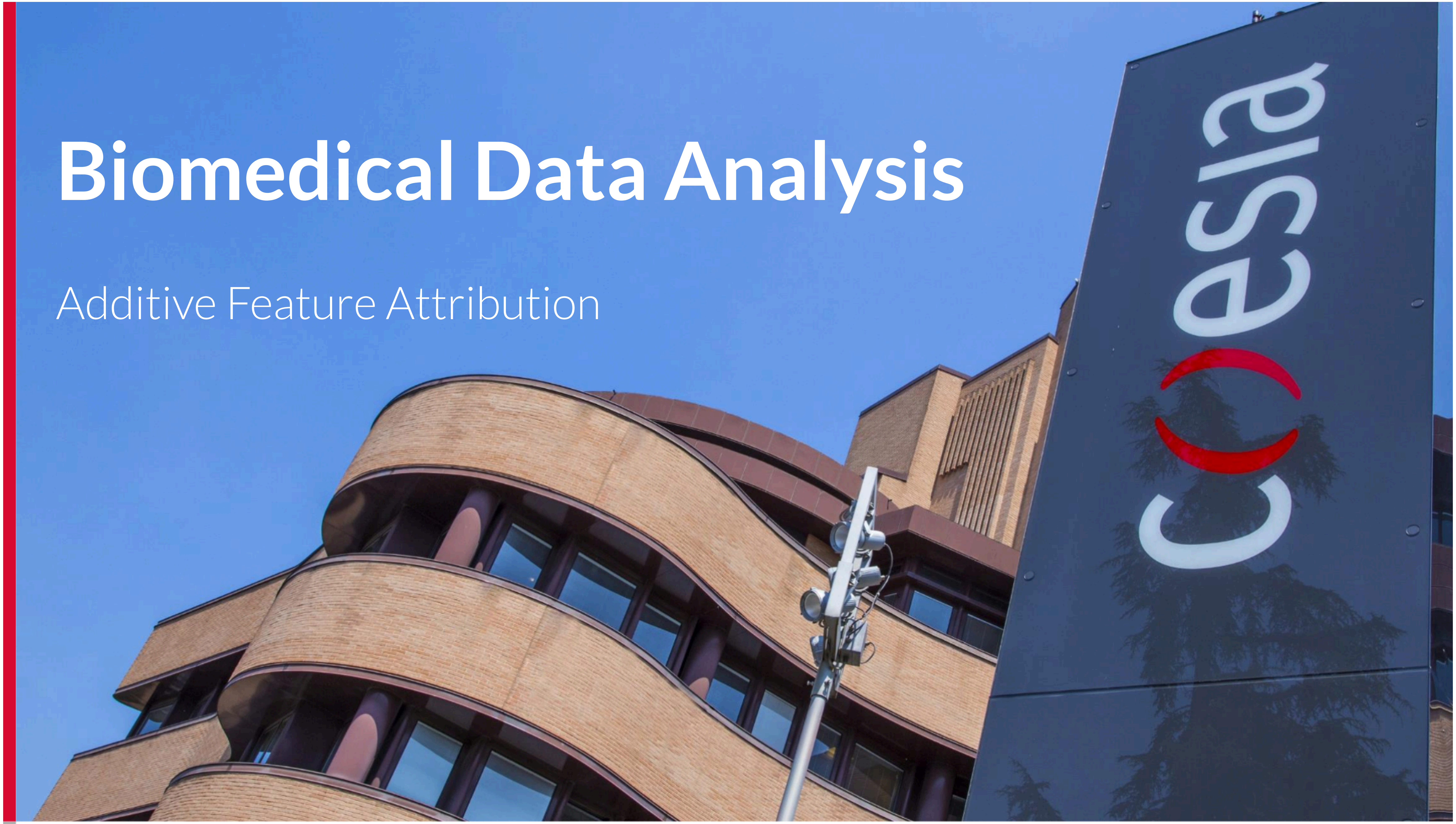


```
In [45]: r_test = permutation_importance(xbm, X_test, y_test, n_repeats=30, random_state=42)
         xbm_p_imp = pd.Series(index=X.columns, data=r_test.importances_mean)
         util.plot_bars(xbm_p_imp, figsize=figsize, std=r_test.importances_std, title='Permutation Fe
```

- A few low-importance features become even less relevant on the test data

Biomedical Data Analysis

Additive Feature Attribution



What we Gained, What we Lost

When we switched from Logistic Regression to GBTs we gained a lot

- A reliable proxy model
- A well defined and transparent feature importance definition
- Sparse and reliable importance scores

What we Gained, What we Lost

When we switched from Logistic Regression to GBTs we gained a lot

- A reliable proxy model
- A well defined and transparent feature importance definition
- Sparse and reliable importance scores

However, we also lost something:

With Linear Regression, we used to be able to:

- Identify the direction of the correlation (through the coefficient sign)
- ...And explain individual examples, by looking at the difference:

$$\theta^T x - \mathbb{E}_{x' \in P(X)} \left[\theta^T x'\right]$$

Explaining Individual Examples

Let's look again at the last equation:

$$\theta^T x - \mathbb{E}_{x' \in P(X)}\left[\theta^T x'\right]$$

- Assuming $P(X)$ is approximated by using a sample...
- ...Then $\mathbb{E}_{x' \in P(X)}\left[\theta^T x'\right]$ is just the average prediction on the data

I.e. it is the prediction we could make without access to any input value

Therefore, the difference above represents the gap between:

- ...What we can predict given all information on one example
- ...And what we can predict with no such information

It's the collective value of all available information

Additive Feature Attribution

Given an example x, we can try to to the same:

$$g(z, x) = \phi_0 + \sum_{j=1}^{n} \phi_j(x) z_j \quad \text{with: } z_j \in \{0, 1\}$$

- Where $z_j = 1$ is the value of attribute j is known
- ...$z_j = 0$ is the value of attribute j is unknown
- ...And $\phi_j(x)$ is the effect of attribute j on the example x

Intuitively, we build a linear explaination for the model local behavior

- There are a few approaches to approximate the effect $\phi_j(x)$
- The one we'll use work by averaging the effect of unknown attributes
- The idea is based on the Game Theory notion of Shapely Value

SHAP

Using Shapely values for explanation became prominent with this paper

The work makes a number of contributions:

- It introduces the general idea of additive feature attribution
- It shows how several previous approaches fall into that category
- It show how Shapely values provide "ideal" attribution scores
- It introduces multiple techniques to approximate the values

Computing Shapely values can be very expensive:

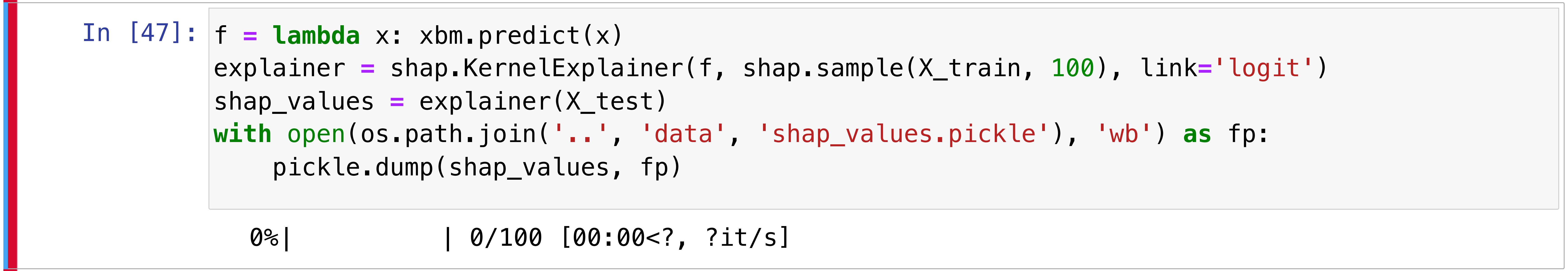
...But the can still be approximated in the general case. We will:

- Consider limited size of example for averaging out unknown attributes
- Obtain a Shapely value approximation by training a local linear model

SHAP in Action

The authors of the SHAP paper maintain a nice Python package

...Which we are going to use to explain our non-linear model



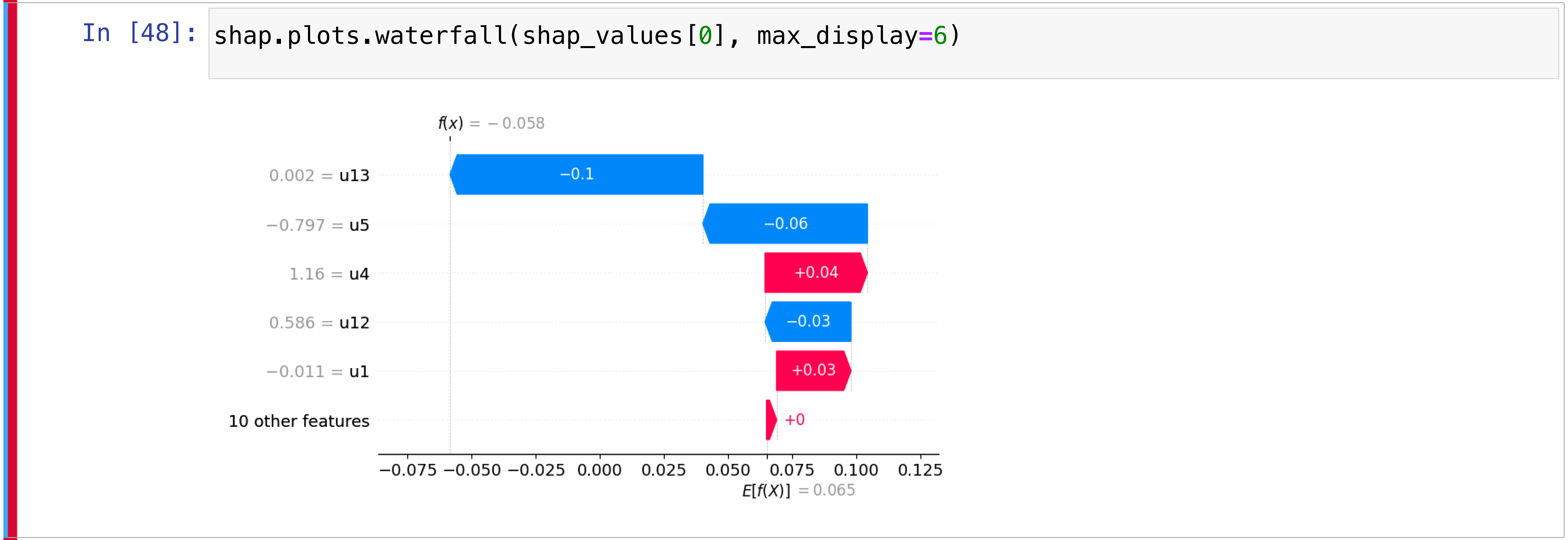
```
In [47]: f = lambda x: xbm.predict(x)
         explainer = shap.KernelExplainer(f, shap.sample(X_train, 100), link='logit')
         shap_values = explainer(X_test)
         with open(os.path.join('..', 'data', 'shap_values.pickle'), 'wb') as fp:
             pickle.dump(shap_values, fp)

           0%|          | 0/100 [00:00<?, ?it/s]
```

- We'll focus on the test data, since we want to find the true correlates
- For classifiers, it easier to explain logits rather than probabilities
- The process can be slow, and using a small backgrond set is recommended
- The result contains the Shapely values, the base values, and the original data

Waterfall Plots

The SHAP library allows us to build waterfall plots



```
In [48]: shap.plots.waterfall(shap_values[0], max_display=6)
```

- The bars represent the Shapely values, the colors their sign

Force Plots

Waterfall plots can be "compacted" into force plots

Here we have again a plot for example 0:

```
In [49]: shap.initjs()
         shap.plots.force(shap_values[0])
```

```
Out[49]:
```

Visualization omitted, Javascript library not loaded!

Have you run `initjs()` in this notebook? If this notebook was from another user you must also trust this notebook (File -> Trust notebook). If you are viewing this notebook on github the Javascript has been stripped for security. If you are using JupyterLab this error is because a JupyterLab extension has not yet been written.

...And have a plot for example 99

```
In [51]: shap.plots.force(shap_values[99])
```

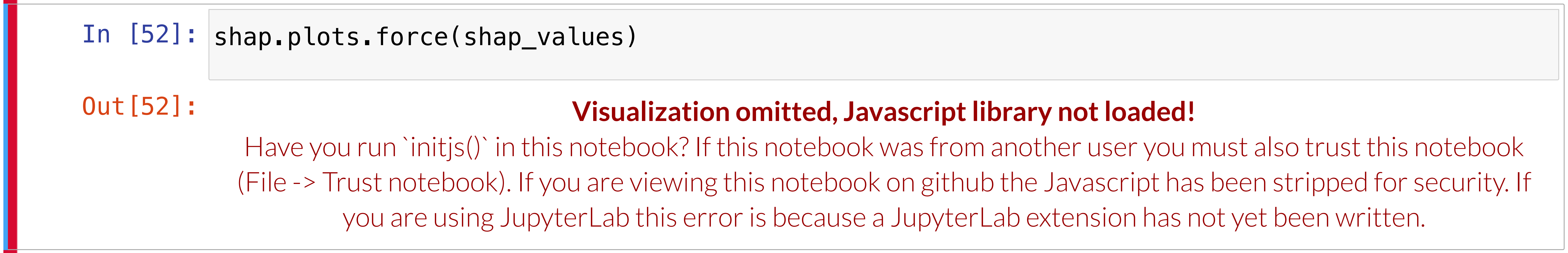
```
Out[51]:
```

Visualization omitted, Javascript library not loaded!

Have you run `initjs()` in this notebook? If this notebook was from another user you must also trust this notebook

Global Force Plots

Force plots can be stacked to inspect many examples at once:



In [52]:

```
shap.plots.force(shap_values)
```

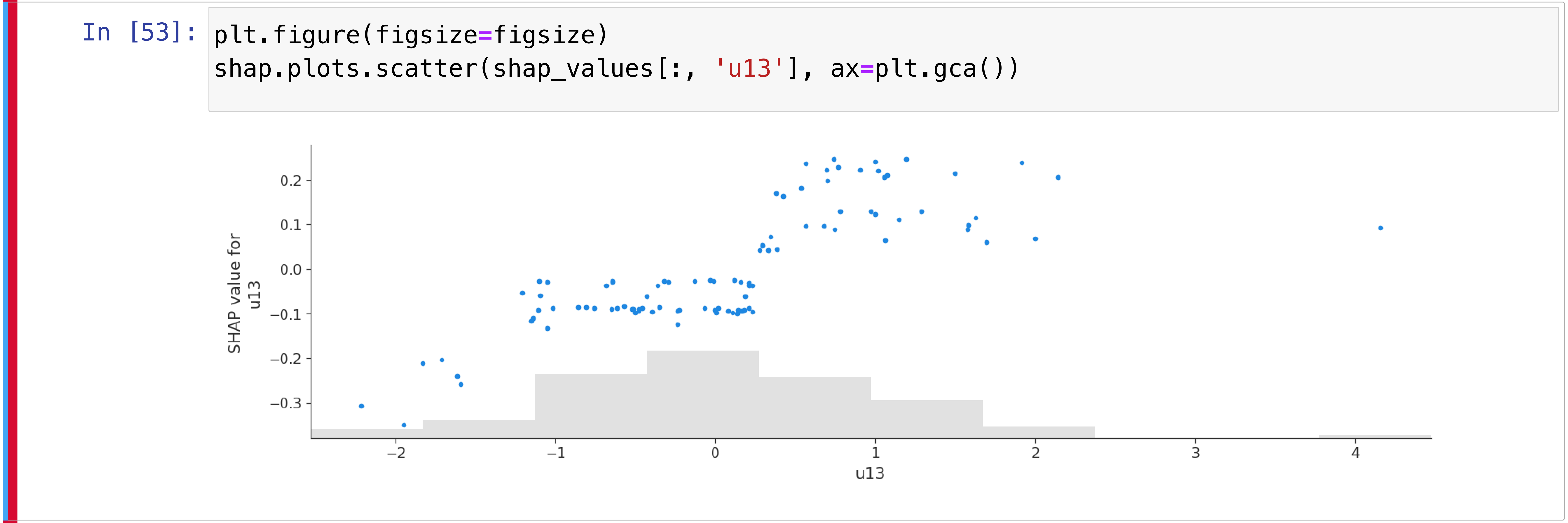
Out[52]:

Visualization omitted, Javascript library not loaded!

Have you run `initjs()` in this notebook? If this notebook was from another user you must also trust this notebook (File -> Trust notebook). If you are viewing this notebook on github the Javascript has been stripped for security. If you are using JupyterLab this error is because a JupyterLab extension has not yet been written.

Scatter Plots

We can use scatter plots to show the effect of a single feature

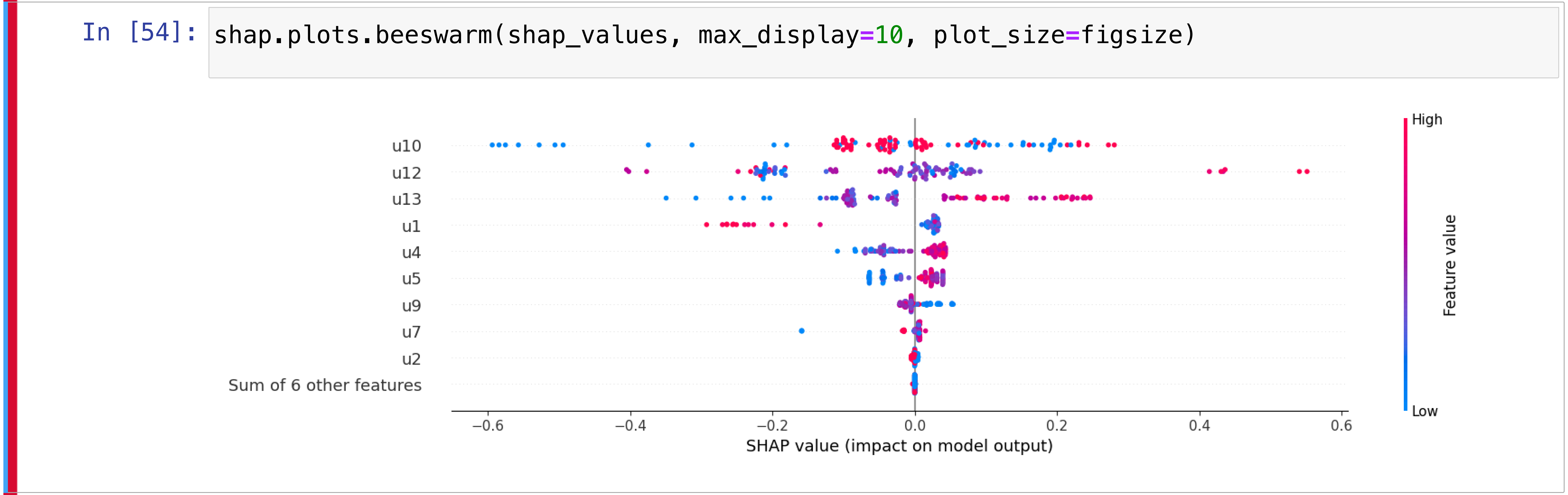


In [53]:
```
plt.figure(figsize=figsize)
shap.plots.scatter(shap_values[:, 'u13'], ax=plt.gca())
```

- The gray area is the histogram of the chosen feature

Beeswarm (Summary) Plot

We can stack (and color) multiple scatter plots to obtain a beeswarm plot:

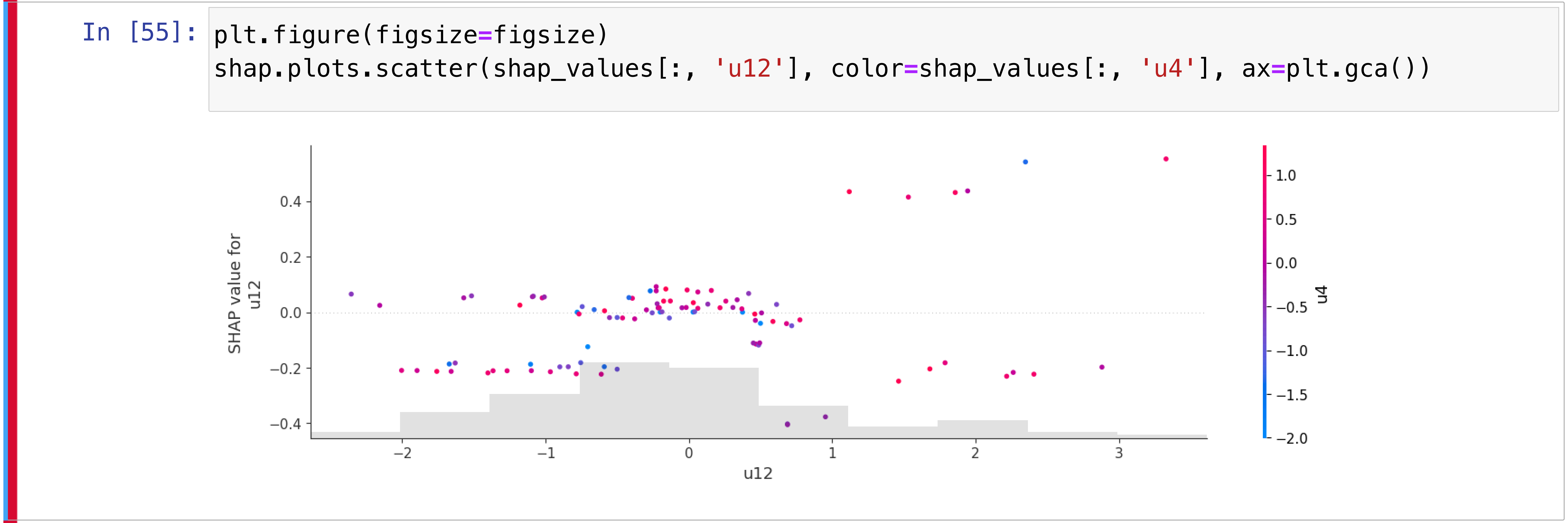


```
In [54]: shap.plots.beeswarm(shap_values, max_display=10, plot_size=figsize)
```

- By checking the color distribution we can indentify linear and non-linear effects

Scatter (Dependency) Plots

We can color scatter plots by using another feature to highlight dependency



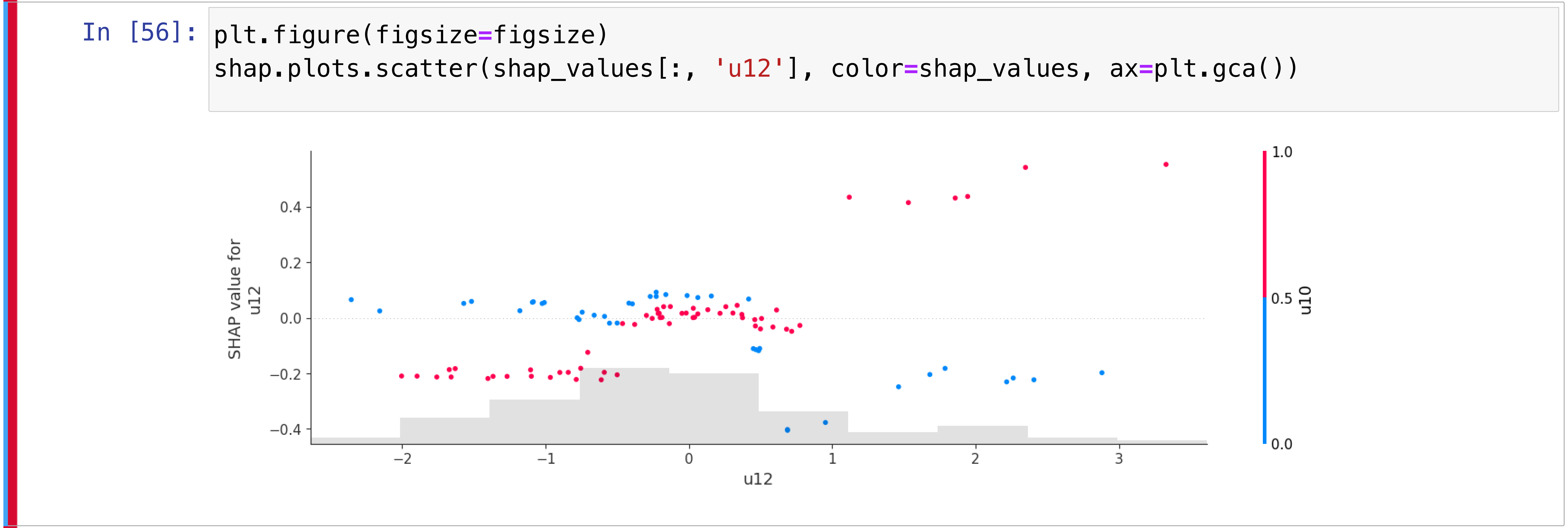
In [55]:

```
plt.figure(figsize=figsize)
shap.plots.scatter(shap_values[:, 'u12'], color=shap_values[:, 'u4'], ax=plt.gca())
```

- In this case we are coloring the "u12" values by using "u4"

Scatter (Dependency) Plots

We can let the library choose the best coloring feature



In [56]:
```
plt.figure(figsize=figsize)
shap.plots.scatter(shap_values[:, 'u12'], color=shap_values, ax=plt.gca())
```

- The chosen coloring feature changes how "u12" impacts the output in a noticeable way

Global Feature Analysis via SHAP

SHAP explanations can be aggregated to get global importance scores

By default, this is done by averaring absolute SHAP values:

$$\bar{\phi}_j(x) = \frac{1}{n} \sum_{i=1}^{m} |\phi_j(x_i)|$$

- Other aggregation functions can also be used (e.g. max)

By using aggregated SHAP scores

...We ensure that our local and global analysis have a similar semantic

- Permutation Importance are a perfectly viable approach
- ...And sometimes may be more appropriate than SHAP

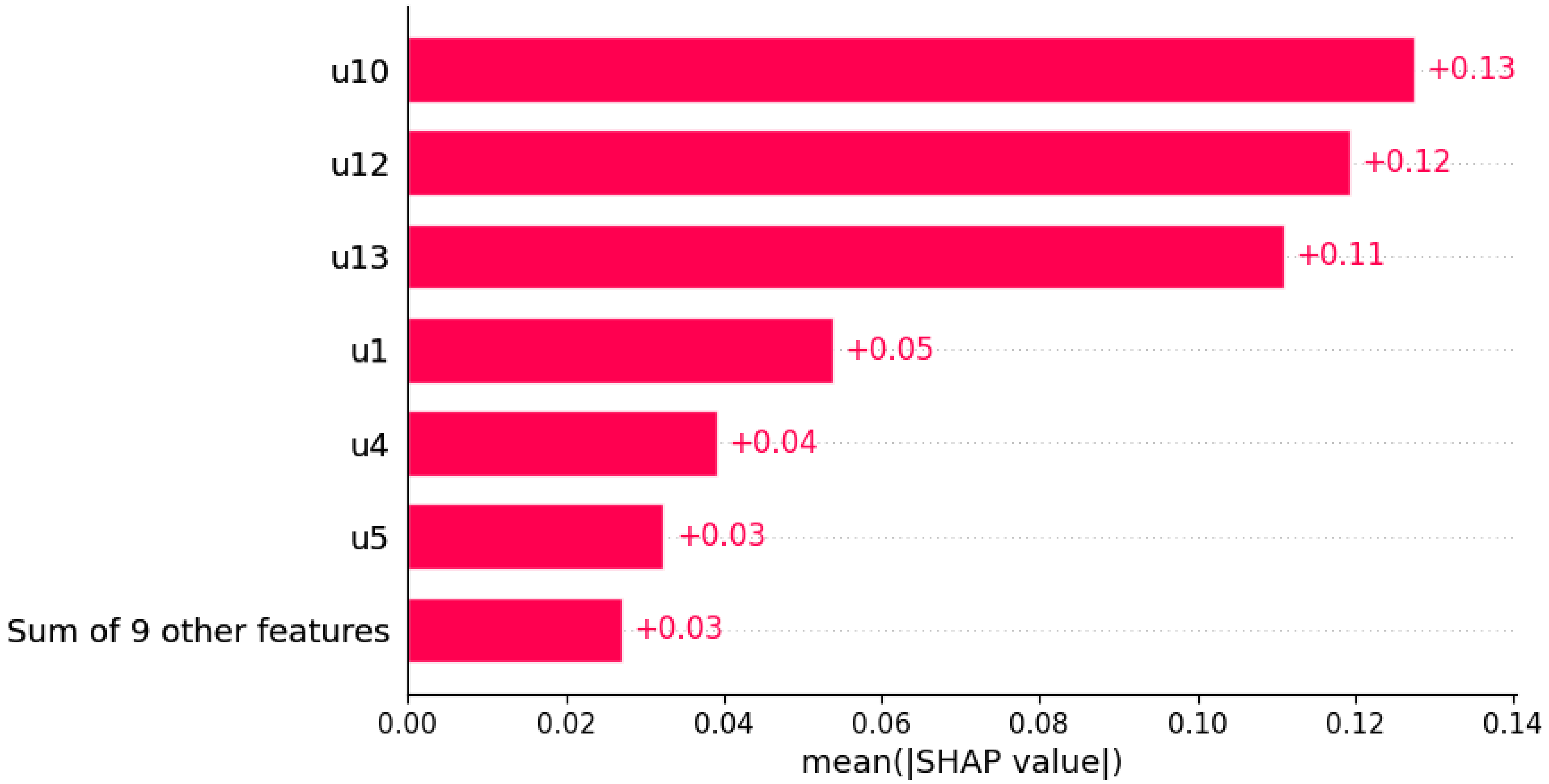
However, when doing a rigorous analysis consistency is important

Global Feature Analysis via SHAP

The SHAP library provide convenience functions to plot aggregated values

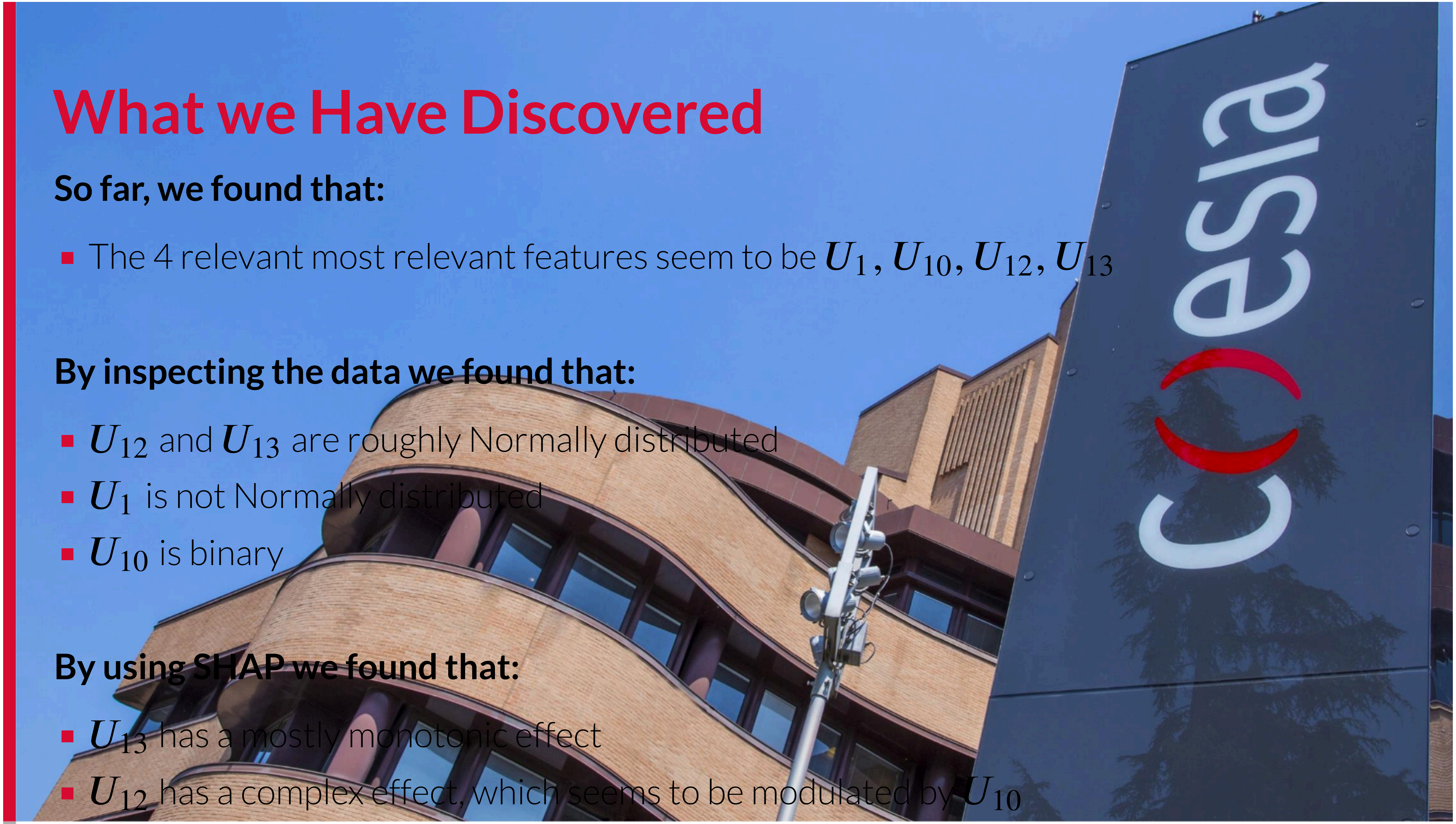
Here's how to plot mean (absolute) SHAP values:

In [58]:
```
shap.plots.bar(shap_values, max_display=7)
```



Biomedical Data Analysis

Wrapping Up



What we Have Discovered

So far, we found that:

- The 4 relevant most relevant features seem to be U_1, U_{10}, U_{12}, U_{13}

By inspecting the data we found that:

- U_{12} and U_{13} are roughly Normally distributed
- U_1 is not Normally distributed
- U_{10} is binary

By using SHAP we found that:

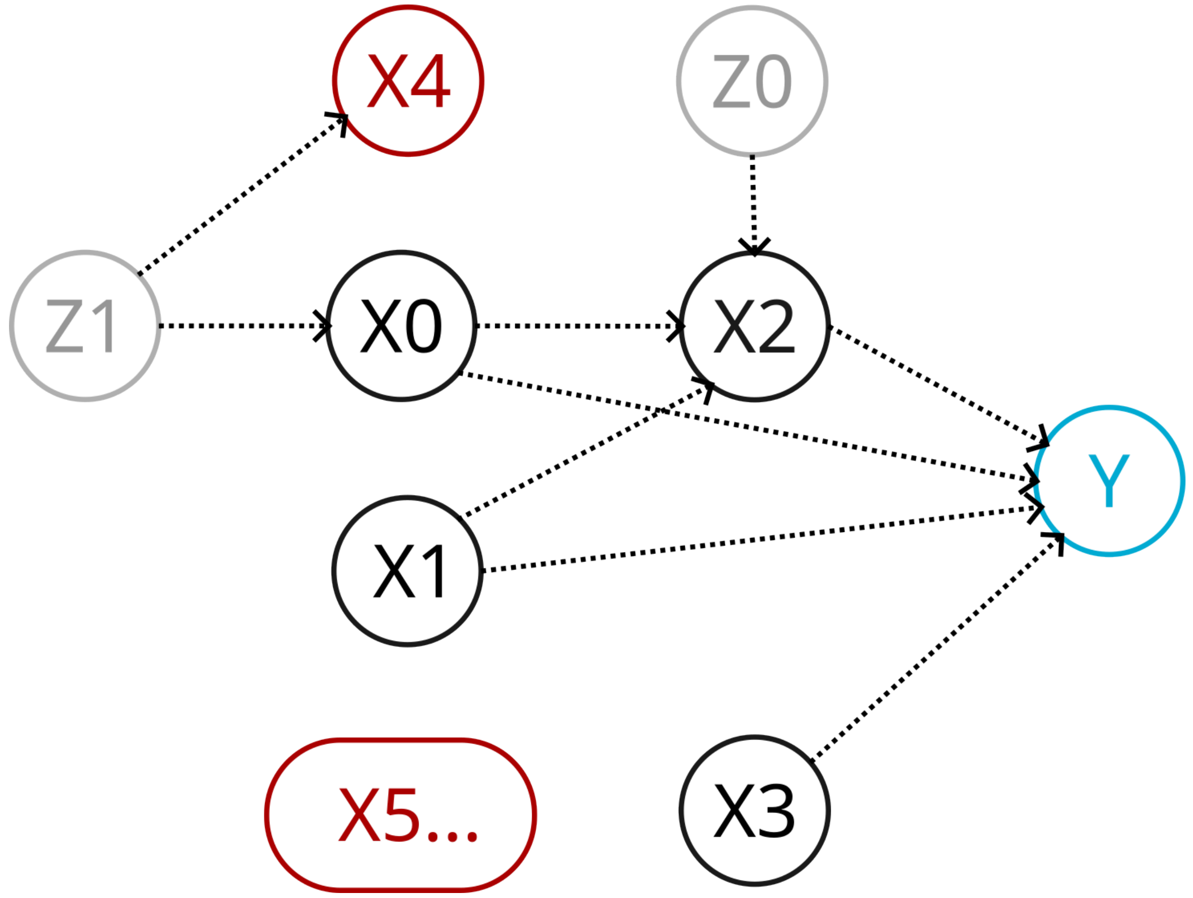
- U_{13} has a mostly monotonic effect
- U_{12} has a complex effect, which seems to be modulated by U_{10}
- U_1 seems to have mostly an anti-monotonic effect

We can now inspect the ground truth process

So we can check whether our results actually hold

Checking the Ground Truth

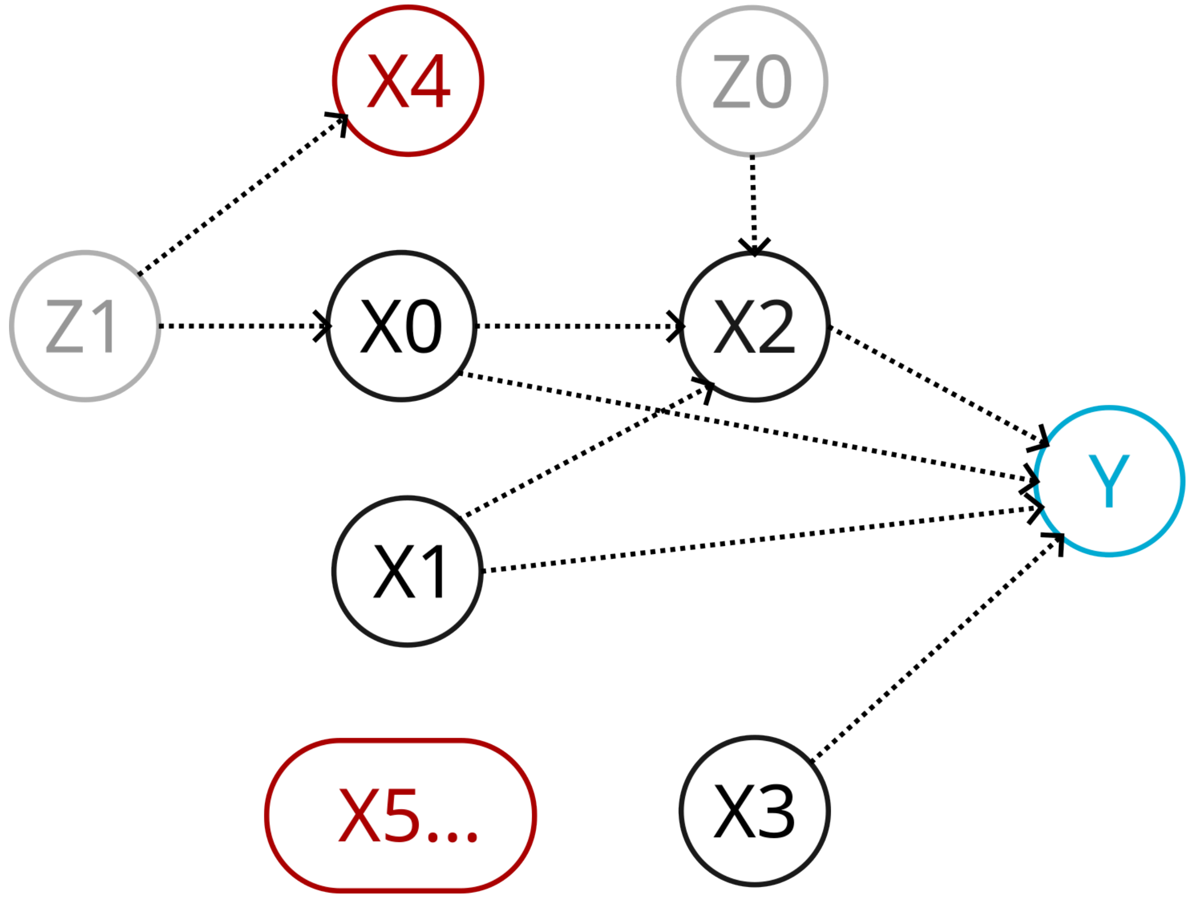
The ground-truth process is described by this causal graph:



- The Y variable (in **blue**) is the target
- The variables in **black** are those that are relevant
- The variables in **gray** are not observable, i.e. latent
- The variables in **red** are irrelevant

Checking the Ground Truth

The process was engineered to contain several classical cases

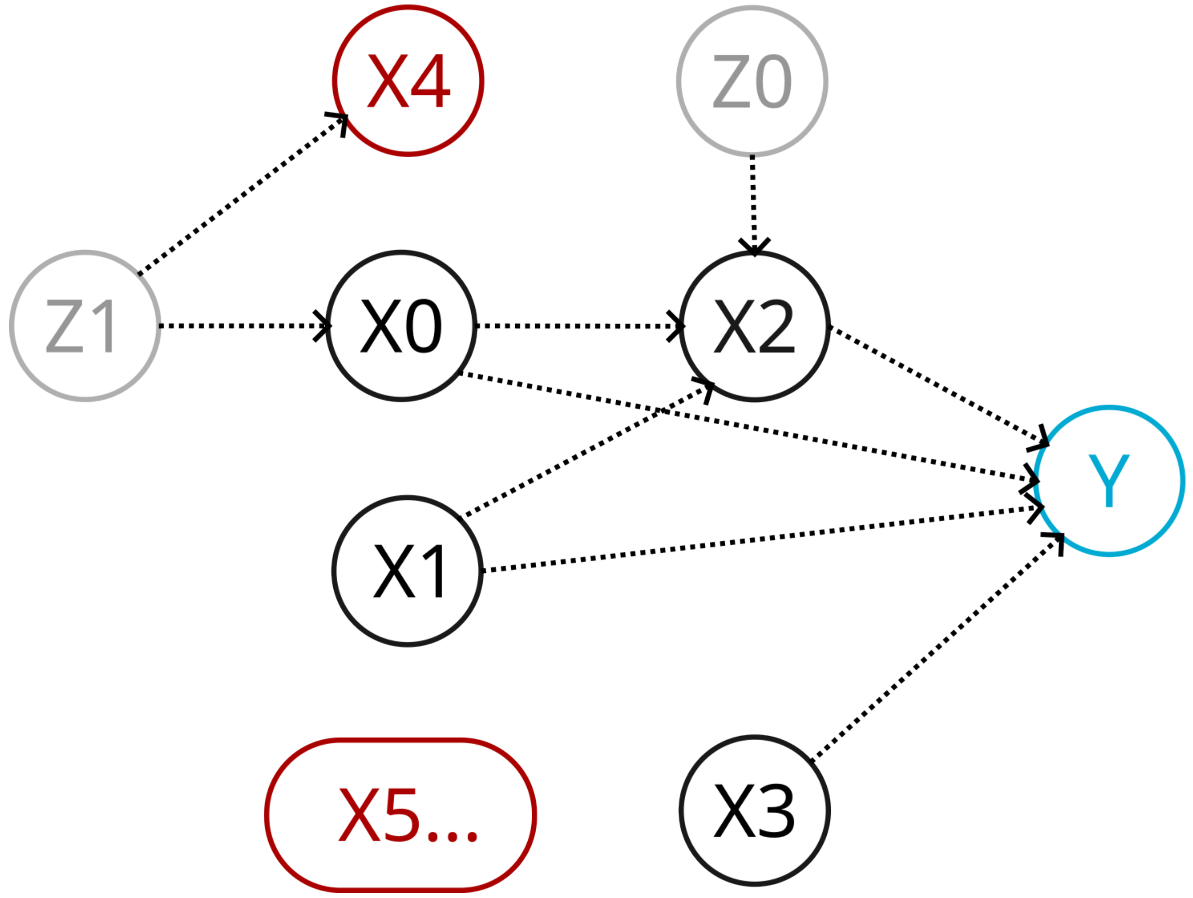


X_2 is a mediator beween X_0, X_1 and Y

- The variable partially hides the effect of X_0 and X_1
- If it does that completely, even Boruta cannot mark X_0 and X_1 as important
- Depending on the use case, this might be an issue

Checking the Ground Truth

The process was engineered to contain several classical cases

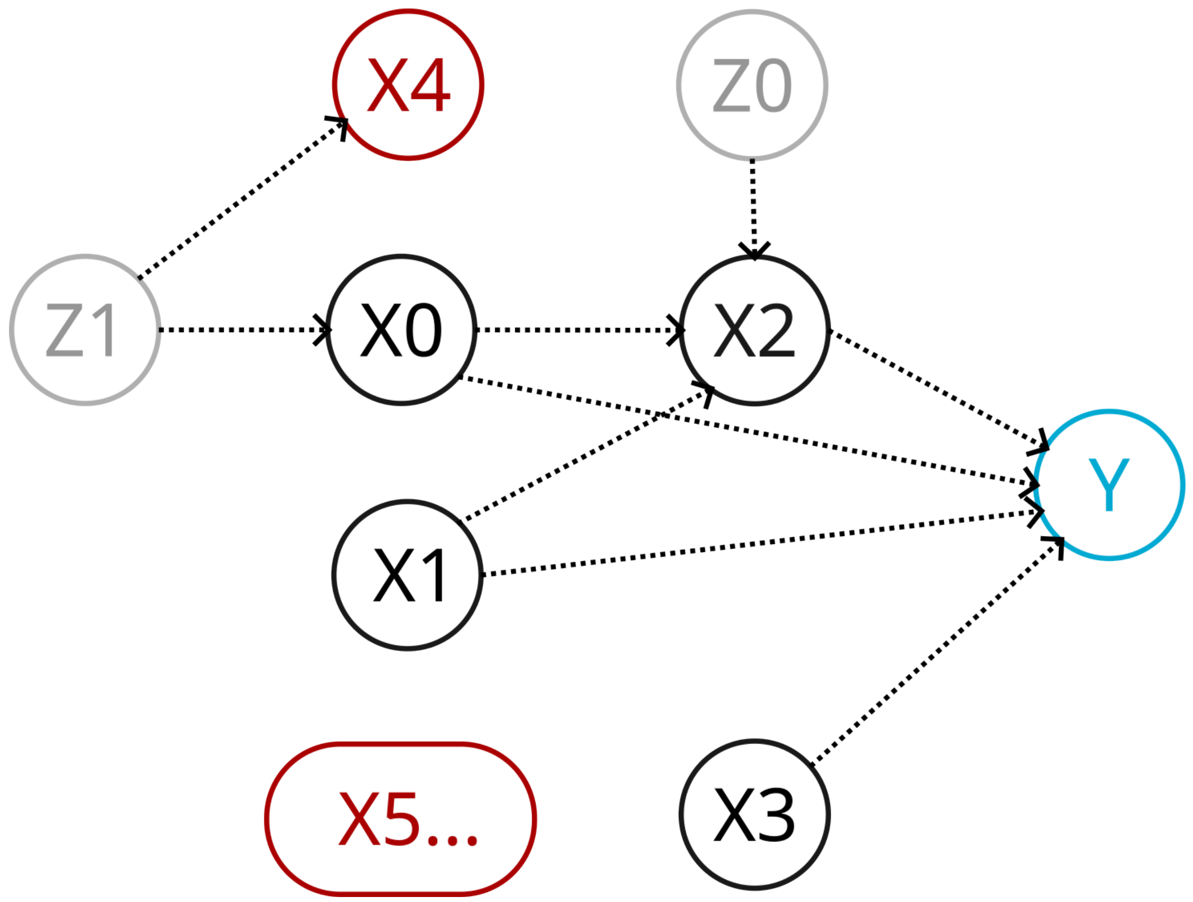


X_2 is also a complete mediator for Z_0

- ...But in this case it is a good thing!
- Z_0 is not observed, but we can account for that at least indirectly

Checking the Ground Truth

The process was engineered to contain several classical cases



Z_1 is a confounder and causes a correlation between X_1 and X_0

- It is totally mediated by X_1, which is a good thing
- ...But it also causes a correlation between X_0 and X_4
- This might trick a model into considering X_4 as important

Checking the Ground Truth

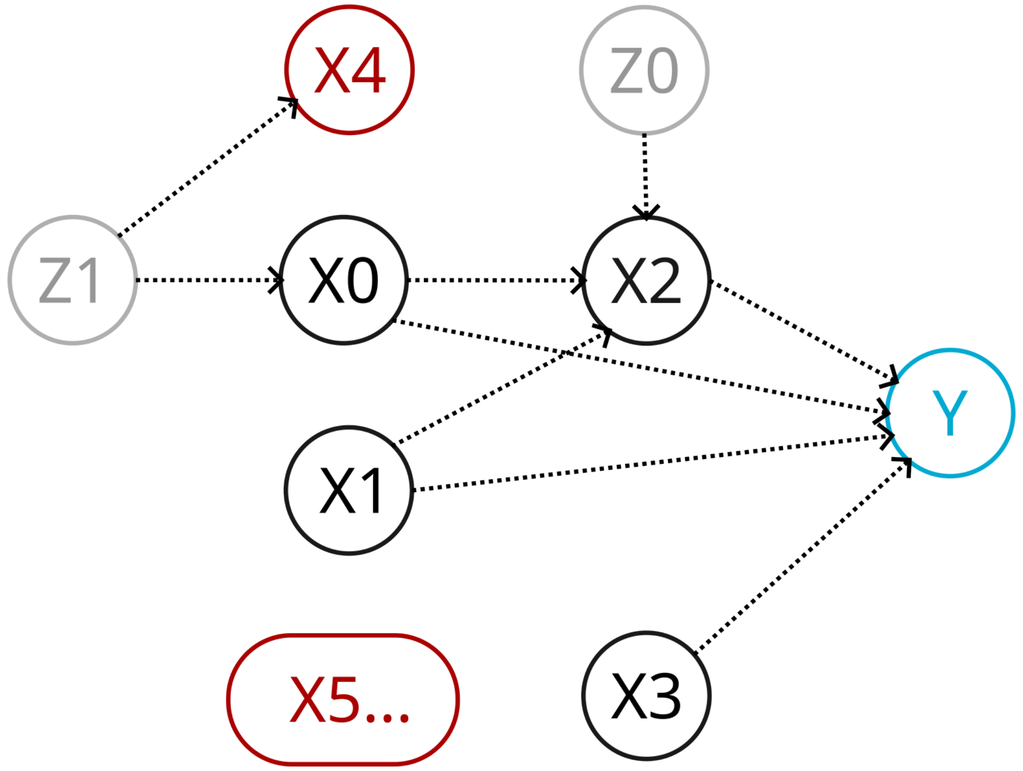
In detail, the data is generated as follows:

$$\begin{aligned}
Z_0 &\sim \mathcal{N}(\mu = 0, \sigma = 1.5)\\
Z_1 &\sim \mathcal{N}(\mu = 0, \sigma = 1)\\
X_0 &\sim \mathcal{N}(\mu = 0, \sigma = 1) + Z_1\\
\log X_1 &\sim \mathcal{N}(\mu = 0, \sigma = 1)\\
X_2 &= {}^1\!/_2(X_0 + X_1) + Z_0\\
X_3 &\sim B(p = 0.6)\\
logitY &\sim (-1 + 2X_3)X_2 + 0.4X_0 - 0.4X_1
\end{aligned}$$

- All other variables are follow either a Normal or Bernoulli distribution
- ...And they have sparse correlations among themselves

Checking the Ground Truth

Now let's check how accurate our importance estimate is:



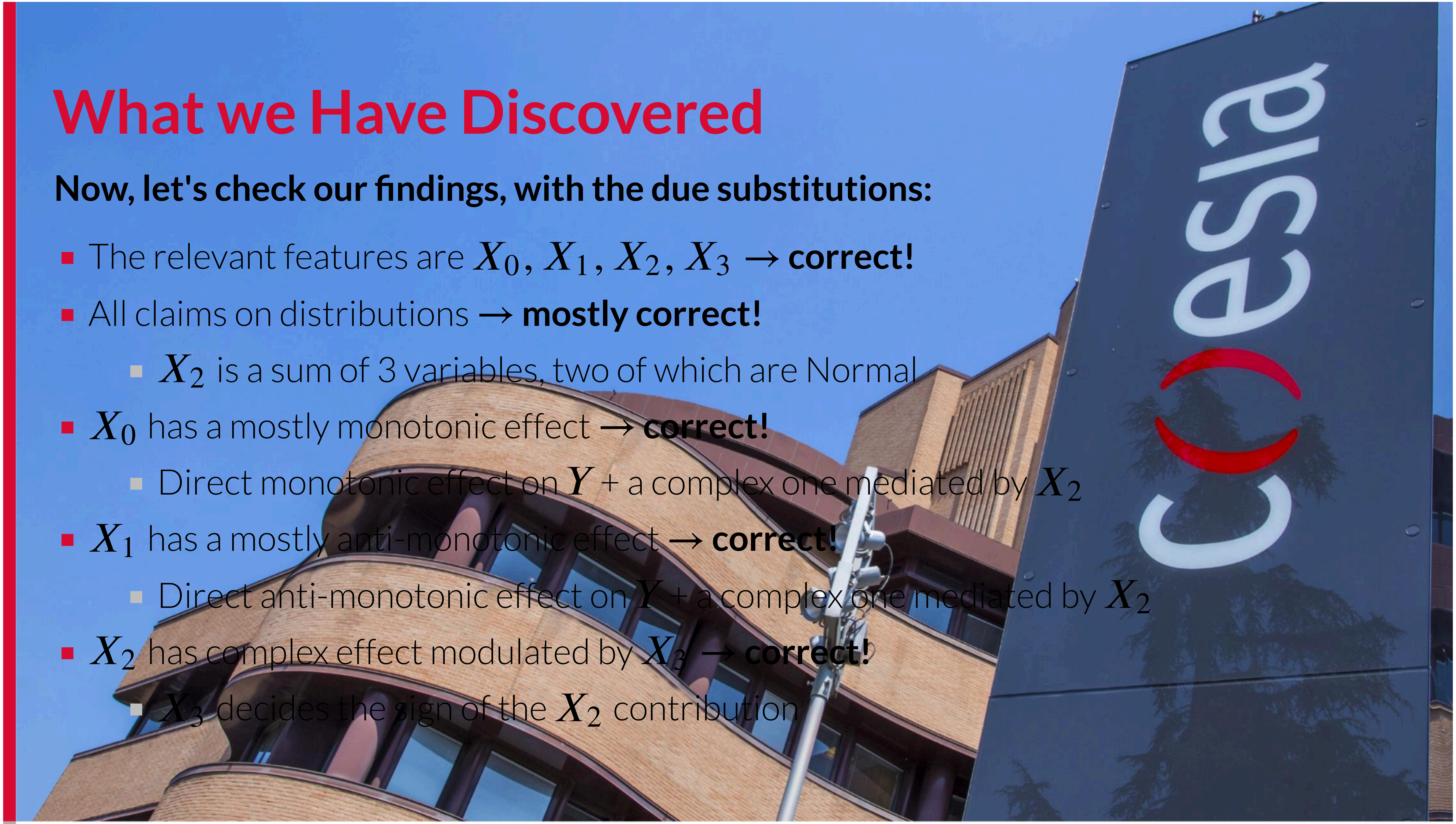
In [63]:
```
accepted = ['u1', 'u10', 'u12', 'u13']
print(f'The most relevant features are {accepted}')
print(f'...And correspond to {[name_map[f] for f in accepted]}')
```

```
The most relevant features are ['u1', 'u10', 'u12', 'u13']
...And correspond to ['X1', 'X3', 'X2', 'X0']
```

What we Have Discovered

Now, let's check our findings, with the due substitutions:

- The relevant features are X_0, X_1, X_2, X_3 → **correct!**
- All claims on distributions → **mostly correct!**
  - X_2 is a sum of 3 variables, two of which are Normal
- X_0 has a mostly monotonic effect → **correct!**
  - Direct monotonic effect on Y + a complex one mediated by X_2
- X_1 has a mostly anti-monotonic effect → **correct!**
  - Direct anti-monotonic effect on Y + a complex one mediated by X_2
- X_2 has complex effect modulated by X_3 → **correct!**
  - X_3 decides the sign of the X_2 contribution



A Few Final Remarks

ML models are not just for prediction!

- They can be used for generation, anomaly detection, decision support
- ...And also as tools for a scientific analysis!

Explainability is an important topic in AI

- It is one of the main approaches to make an AI model transparent
- This critical when AI systems need to interact with human users
- ...And for some domains it is also required by existing regulations

Beware of correlated features

- Strongly correlated features (e.g mediated-mediator) may mislead algorithms
- Dealing with those is still a partially open problem!