Imports

In [182]:
```
import copy
import random
import numpy as np
import pandas as pd
import matplotlib.pyplot as plt

from modAL.models import BayesianOptimizer
from modAL.acquisition import max_EI, max_PI
from sklearn.preprocessing import StandardScaler
from sklearn.gaussian_process import GaussianProcessRegressor
from sklearn.gaussian_process.kernels import Matern, RBF, max_UCB



### Suppresses Warning
import warnings
warnings.filterwarnings('ignore')

seed = 42
random.seed(seed)
np.random.seed(seed)
```

Ideas

- perform feature selection before running model
- set the initial training set to be informative by choosing same 22 + 80 random as the authors

Data Prep

Load Data

In [106]:
```
data = pd.read_csv('data/DataPool.csv')
print(data.shape)
data.head(5)
cols = data.columns
```

```
(1017, 12)
```

Split into features and target

In [202]:
```
X = data.drop(['Yield'],axis=1)
print(X.shape)
y_pool = data['Yield'].to_numpy()
print(y_pool.shape)
```

```
(1017, 11)
(1017,)
```

Scale data

So all variables have the same mean and std dev

In [70]:
```
scaler = StandardScaler()
X_pool = scaler.fit_transform(X)
```

Define initial dataset

- 11 data points in which each compound is minimized except one is maximized
- 11 data pionts in which each compound is maximized except one is minimized
- 80 random data points

In [215]:
```
def get_min_max_combinations(ranges_dict, feature):

    # min of all other features, max of this feature
    min_combo = []
    for key in ranges_dict.keys():

        if key == feature:
            min_combo.append(min(ranges_dict[key]))
        else:
            min_combo.append(max(ranges_dict[key]))


    # max of all other features, min of this feature
    max_combo = []
    for key in ranges_dict.keys():

        if key == feature:
            max_combo.append(max(ranges_dict[key]))
        else:
            max_combo.append(min(ranges_dict[key]))

    return tuple(min_combo), tuple(max_combo)
```

In [211]:
```
ranges_dict = {
    'Mg-glutamate (mM)':[0.4,1.2,2,4],
    'K-glutamate (mM)':[8,24,40,80],
    'Amino Acid (mM)': [0.15,0.45,0.75,1.5],
    'tRNA (mg/ml)':[0.02,0.06,0.1,0.2],
    'coA (mM)':[0.026,0.078,0.13,0.26],
    'NAD (mM)':[0.033,0.099,0.165,0.33],
    'cAMP (mM)':[0.075,0.225,0.375,0.75],
    'Folinic Acid (mM)':[0.0068,0.0204,0.034,0.068],
    'Spermidine (mM)':[0.1,0.3,0.5,1],
    '3-PGA (mM)':[3,9,15,30],
    'NTP (mM)':[0.15,0.45,0.75,1.5]
}
```

In [221]:
```
min_combo, max_combo = get_min_max_combinations(ranges_dict,'Mg-glutamate (mM)')
min_combo
```

Out[221]:
```
(0.4, 80, 1.5, 0.2, 0.26, 0.33, 0.75, 0.068, 1, 30, 1.5)
```

In [276]:
```
def get_index(df, combo):

    # split into components
    Mg_glutamate, K_glutamate, Amino_Acid, tRNA, coA, NAD, cAMP, Folinic_Acid, Spermidine, Three_PGA, NTP = combo

    # get index of matching row in data
    a = df.index[(df['Mg-glutamate (mM)'] == Mg_glutamate) \
            & (df['K-glutamate (mM)'] == K_glutamate) \
            & (df['Amino Acid (mM)'] ==Amino_Acid) \
            & (df['tRNA (mg/ml)'] == tRNA) \
            & (df['coA (mM)'] == coA) \
            & (df['NAD (mM)'] == NAD) \
            & (df['cAMP (mM)'] == cAMP) \
            & (df['Folinic Acid (mM)'] == Folinic_Acid) \
            & (df['Spermidine (mM)'] == Spermidine) \
            & (df['3-PGA (mM)'] == Three_PGA) \
            & (df['NTP (mM)'] == NTP)]
    print(len(a))
    return a.tolist()
```

In [252]:
```
get_index(data, min_combo)
```

Out[252]:
```
[245]
```

In [255]:
```
data.loc[245,:]
```

Out[255]:
```
Mg-glutamate (mM)      0.40000
K-glutamate (mM)      80.00000
Amino Acid (mM)        1.50000
tRNA (mg/ml)           0.20000
coA (mM)               0.26000
NAD (mM)               0.33000
cAMP (mM)              0.75000
Folinic Acid (mM)      0.06800
Spermidine (mM)        1.00000
3-PGA (mM)            30.00000
NTP (mM)               1.50000
Yield                  0.00001
Name: 245, dtype: float64
```

In [274]:
```
def get_initial_22_idx(df, ranges_dict):

    initial_idx = []

    # for each feature
    for key in ranges_dict.keys():
        min_combo, max_combo = get_min_max_combinations(ranges_dict,key)
        print(max_combo)
#         idx = get_index(df, min_combo)
#         initial_idx.append(idx)
        idx = get_index(df, max_combo)
        initial_idx.append(idx)

    return initial_idx
```

In [277]:

```
get_initial_22_idx(data, ranges_dict)
```

```
(4, 8, 0.15, 0.02, 0.026, 0.033, 0.075, 0.0068, 0.1, 3, 0.15)
0
(0.4, 80, 0.15, 0.02, 0.026, 0.033, 0.075, 0.0068, 0.1, 3, 0.15)
0
(0.4, 8, 1.5, 0.02, 0.026, 0.033, 0.075, 0.0068, 0.1, 3, 0.15)
0
(0.4, 8, 0.15, 0.2, 0.026, 0.033, 0.075, 0.0068, 0.1, 3, 0.15)
0
(0.4, 8, 0.15, 0.02, 0.26, 0.033, 0.075, 0.0068, 0.1, 3, 0.15)
1
(0.4, 8, 0.15, 0.02, 0.026, 0.33, 0.075, 0.0068, 0.1, 3, 0.15)
0
(0.4, 8, 0.15, 0.02, 0.026, 0.033, 0.75, 0.0068, 0.1, 3, 0.15)
0
(0.4, 8, 0.15, 0.02, 0.026, 0.033, 0.075, 0.068, 0.1, 3, 0.15)
0
(0.4, 8, 0.15, 0.02, 0.026, 0.033, 0.075, 0.0068, 1, 3, 0.15)
0
(0.4, 8, 0.15, 0.02, 0.026, 0.033, 0.075, 0.0068, 0.1, 30, 0.15)
0
(0.4, 8, 0.15, 0.02, 0.026, 0.033, 0.075, 0.0068, 0.1, 3, 1.5)
0
```

Out[277]:

```
[[], [], [], [], [861], [], [], [], [], [], []]
```

Build Bayesian Optimizer

- with Gaussian process
- define the sample space as the data pool. this is an ad-hoc version of membership query synthesis, because we can't draw from any possible point, only the points we have values for.

In [22]:

```
def get_next_sample(optimizer, X_pool, y_pool):

    # call the query strategy defined in the learner to obtain a new sample
    query_idx, query_sample = optimizer.query(X_pool)

    # modify indexing to interpret as collection of one element with d features
    query_sample_reshaped = query_sample.reshape(1, -1)

    # obtain the query label
    query_label = y_pool[query_idx]

    # modify indexing to interpret as 1D array of one element
    query_label_reshaped = query_label.reshape(1, )

    return query_sample_reshaped, query_label_reshaped, query_idx
```

In [80]:

```
def get_next_batch(optimizer, X_pool, y_pool, batch_size):

    n_col = X_pool.shape[1]
    X_batch = np.zeros((batch_size, n_col))
    y_batch = np.zeros((batch_size,))


    for i in range(batch_size):

        X_sample, y_sample, query_idx = get_next_sample(optimizer, X_pool, y_pool)

        # add to batch
        X_batch[i] = X_sample
        y_batch[i] = y_sample

        # remove queried point from pool
        X_pool = np.delete(X_pool, query_idx, axis=0)
        y_pool = np.delete(y_pool, query_idx)

    return X_batch, y_batch, X_pool, y_pool
```

In [174]:

```
def run_bayesian_optimization(optimizer, X_pool, y_pool, n_batch, batch_size, initial):

    selected = [initial]
    for b in range(n_batch):

        # get next set of points to learn
        X_batch, y_batch, X_pool, y_pool = get_next_batch(optimizer, X_pool, y_pool, batch_size)
#         print(X_batch.shape)
#         print(y_batch.shape)
#         print('X_pool size, y_pool size', X_pool.shape, y_pool.shape)

        # save data
        batch_col = np.array([b]*len(X_batch)).reshape(-1,1)
        y_col = y_batch.reshape(-1,1)
        result = np.append(X_batch,y_col, axis=1)
        selected.append(result)

        # use new sample to update the model
        optimizer.teach(X_batch, y_batch)

        # score results
#         print('score results for batch ', b)

    return selected
```

Run model

?? Does initial training set count among total query number of 510?

- random initial training set

In [203]:

```
%%time
# 15 min

# copy data for this section
X_cp = copy.deepcopy(X_pool)
y_cp = copy.deepcopy(y_pool)
# print(X_cp.shape)
# print(y_cp.shape)

# define initial training set
n_initial = 102
initial_idx = np.random.choice(range(len(X_cp)), size=n_initial, replace=False)
X_training, y_training = X_cp[initial_idx], y_cp[initial_idx]
initial = np.append(X_training, y_training.reshape(-1,1),axis=1)
# print(X_training.shape)
# print(y_training.shape)

# remove initial training set from data
X_cp = np.delete(X_cp, initial_idx, axis=0)
y_cp = np.delete(y_cp, initial_idx)
# print(X_cp.shape)
# print(y_cp.shape)


# define optimizer
kernel = Matern(1.0)
optimizer = BayesianOptimizer(
    estimator=GaussianProcessRegressor(kernel=kernel),
    X_training=X_training,
    y_training=y_training,
    query_strategy=max_EI
)

# Bayesian optimization
n_batch = 50
batch_size = 5
selected = run_bayesian_optimization(optimizer, X_cp, y_cp, n_batch, batch_size, initial)
```

```
CPU times: user 13.9 s, sys: 407 ms, total: 14.3 s
Wall time: 3.73 s
```

Results

- Selected points ?? how do they define how much yield has improved? what is the starting yield?

In [149]:
```
def build_results_dataframe(selected, cols):

    # empty dataframe with correct column number
    df = pd.DataFrame(columns=cols)

    for i,each in enumerate(selected):

        # create rows
        df_i = pd.DataFrame(each, columns=cols)

        # add col for batch
        df_i['Batch'] = i

        # append to final dataframe
        df = df.append(df_i)

    return df
```

In [163]:
```
def yield_stats(df, batch):
    """
    Average yield and min and max yield.
    """

    df_yield = df[df['Batch']==batch]['Yield']

    # mean
    mean_yield = df_yield.mean()

    # std dev
    std_yield = df_yield.std()

    # min
    min_yield = df_yield.min()

    # max
    max_yield = df_yield.max()

    return mean_yield, std_yield, min_yield, max_yield
```

In [205]:
```
df_results = build_results_dataframe(selected, cols.tolist())
df_results
```

Out[205]:

	Mg-glutamate (mM)	K-glutamate (mM)	Amino Acid (mM)	tRNA (mg/ml)	coA (mM)	NAD (mM)	cAMP (mM)	Folinic Acid (mM)	Spermidine (mM)	3-PGA (mM)	NTP (mM)	Yield	Batch
0	-0.638449	-1.414753	0.322945	-0.981173	-0.792611	-0.900332	1.781938	-1.104683	0.164205	1.057689	-0.777751	8.326	0.0
1	0.946763	0.923136	-0.280242	2.177701	1.036283	-0.175362	-0.533273	0.386309	-0.696601	-0.251708	0.933571	20.632	0.0
2	0.946763	0.923136	-0.883429	0.422771	0.121836	-0.900332	-0.533273	2.250049	1.025011	-0.251708	0.933571	11.405	0.0
3	0.946763	0.923136	-0.883429	-0.981173	-0.792611	0.549609	0.624333	2.250049	1.025011	-0.251708	0.933571	14.025	0.0
4	-1.272534	-0.746785	-0.280242	-0.981173	-0.792611	-0.900332	-0.533273	0.386309	1.025011	-0.251708	-0.777751	11.328	0.0
...	...	...	...	...	...	...	...	...	...	...	...	...	...
0	0.946763	0.923136	-0.883429	-0.981173	0.121836	0.549609	-0.533273	0.386309	0.164205	-0.251708	0.933571	19.521	50.0
1	0.946763	0.923136	-0.883429	-0.981173	-0.792611	0.549609	-0.533273	-1.104683	0.164205	-0.251708	0.933571	16.957	50.0
2	0.946763	0.923136	-0.280242	-0.279201	-0.792611	0.549609	-0.533273	0.386309	1.025011	-0.251708	0.933571	13.485	50.0
3	0.946763	0.923136	-0.280242	-0.279201	-0.792611	-0.900332	0.624333	0.386309	0.164205	-0.251708	0.933571	19.658	50.0
4	0.946763	0.923136	-0.883429	0.422771	1.036283	-0.900332	0.624333	2.250049	-0.696601	-0.251708	0.933571	13.212	50.0

352 rows × 13 columns

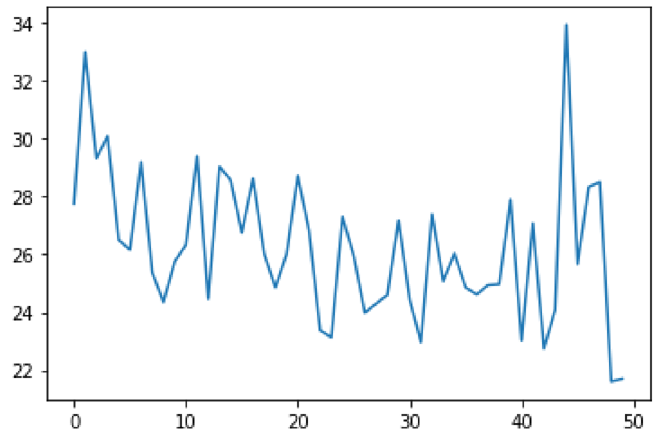
In [206]:
```
mean_yields = []
std_yields = []
min_yields = []
max_yields = []

for b in range(n_batch):
    mean_yield, std_yield, min_yield, max_yield = yield_stats(df_results, b)

    mean_yields.append(mean_yield)
    std_yields.append(std_yield)
    min_yields.append(min_yield)
    max_yields.append(max_yield)
```

```
In [207]: plt.plot(max_yields)
```

```
Out[207]: [<matplotlib.lines.Line2D at 0x7fa832088748>]
```



```
In [ ]:
```