This is a brief tutorial regarding the use of Random Forest to develop new scoring function. Needs to install Anaconda (https://www.continuum.io/downloads (https://www.continuum.io/downloads) , python version 3.6)

install package

conda install numpy matplotlib

conda install scipy scikit-learn seaborn

conda install -c conda-forge xgboost=0.6a2

conda install -c conda-forge pydotplus

open the notebook in yourfolder

jupyter notebook

Staring Tutorial

In [1]:
```
%matplotlib inline
%config InlineBackend.figure_format = 'retina'

import numpy as np # linear algebra
import pandas as pd # data processing, CSV file I/O (e.g. pd.read_csv)

import matplotlib.pyplot as plt
import matplotlib.gridspec as gridspec
from mpl_toolkits.mplot3d import Axes3D
import seaborn as sns

color = sns.color_palette()
```

In [2]:
```
# for models

from sklearn.linear_model import LinearRegression
from sklearn.tree import DecisionTreeRegressor, export_graphviz
from sklearn.ensemble import RandomForestRegressor
from sklearn.ensemble import GradientBoostingRegressor
from sklearn.model_selection import GridSearchCV, train_test_split, KFold
from sklearn.preprocessing import StandardScaler

from sklearn.ensemble.partial_dependence import plot_partial_dependence
from sklearn.ensemble.partial_dependence import partial_dependence

from scipy.stats.stats import pearsonr
```

In [3]:
```
from IPython.display import Image
import pydotplus
```

In [4]:
```
# read in data
traindf = pd.read_csv('data/PDBbind_vina6_train.csv')
testdf = pd.read_csv('data/PDBbind_vina6_test.csv')
```

In [5]:
```
traindf.head(3)
```

Out[5]:

	pdb	gauss1	gauss2	repulsion	hydrophobic	hbond	nrot	vina	pkd
0	184l	-33.662306	-528.930696	-0.405366	-53.658468	0.0	2.0	4.893687	4.72
1	185l	-34.230024	-504.172620	-0.712744	-37.732352	0.0	0.0	4.538638	3.54
2	186l	-35.048164	-558.849670	-0.927438	-54.292838	0.0	3.0	4.469118	4.85

In [6]:
```
traindf.describe()
```

Out[6]:

	gauss1	gauss2	repulsion	hydrophobic	hbond	nrot	vina
count	3336.000000	3336.000000	3336.000000	3336.000000	3336.000000	3336.000000	3336.000000
mean	-67.468406	-969.036064	-3.441709	-22.470986	-3.799166	7.404227	5.165168
std	26.703803	410.251945	1.917357	20.377186	2.562255	5.702406	1.764170
min	-218.597332	-3082.383593	-15.844859	-131.225250	-15.993253	0.000000	-4.335666
25%	-85.800302	-1217.174708	-4.517567	-35.601269	-5.395351	3.500000	3.922683
50%	-64.198905	-907.944196	-3.119924	-18.252762	-3.450290	6.000000	5.124965
75%	-47.021020	-664.470041	-2.037401	-4.633696	-1.815735	9.500000	6.349995
max	-5.069520	-96.617791	-0.055892	0.000000	0.000000	42.500000	11.293774

In [7]:
```
testdf.describe()
```

Out[7]:

	gauss1	gauss2	repulsion	hydrophobic	hbond	nrot	vina	
count	195.000000	195.000000	195.000000	195.000000	195.000000	195.000000	195.000000	195
mean	-67.708773	-964.859079	-3.469273	-24.720016	-3.858483	6.720513	5.449859	6.29
std	24.139514	354.752395	1.828057	19.946025	2.732448	5.263186	1.728477	2.25
min	-156.773527	-2102.125535	-10.619956	-102.775730	-15.529963	0.000000	0.502679	2.07
25%	-82.643054	-1226.614619	-4.461743	-37.540748	-5.747944	3.500000	4.184173	4.60
50%	-64.572027	-923.139733	-3.260678	-20.784822	-3.454474	5.000000	5.273505	6.27
75%	-49.590396	-664.408352	-2.150625	-8.959760	-1.714328	8.250000	6.597305	7.98
max	-22.711801	-420.035793	-0.162300	0.000000	0.000000	34.000000	11.819345	11.5

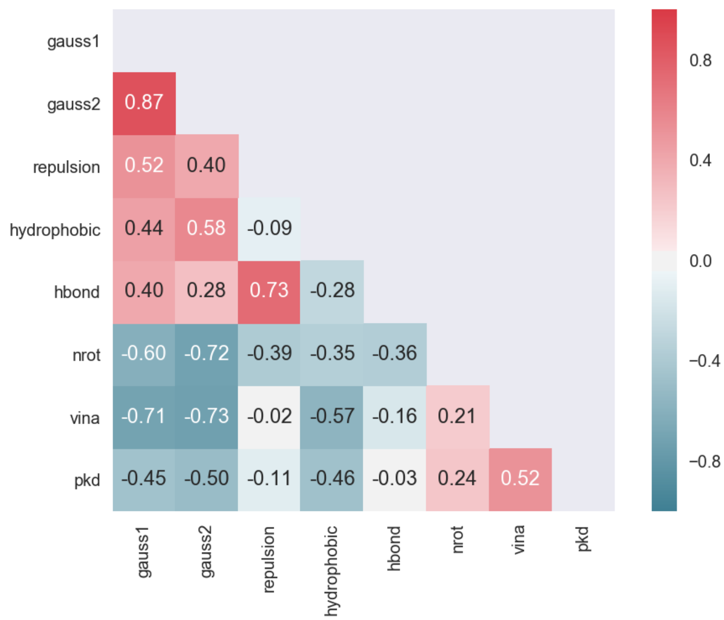
In [8]:
```
testdf.head()
```

Out[8]:

	pdb	gauss1	gauss2	repulsion	hydrophobic	hbond	nrot	vina	pkd
0	10gs	-82.076308	-1008.198967	-3.857677	-25.970168	-5.160107	13.5	4.929232	6.40
1	1a30	-62.847097	-958.542740	-3.455567	-15.031663	-2.636701	12.5	3.666491	4.30
2	1bcu	-45.249317	-635.009529	-0.466092	-8.180374	-0.548346	0.5	4.955308	3.28
3	1e66	-92.762719	-986.928373	-1.611327	-65.450145	0.000000	1.5	8.577114	9.89
4	1f8b	-53.149217	-782.381801	-4.072825	-6.739578	-4.855794	7.0	3.967290	5.40

Pairwise relationship between features and pKd

In [9]:
```
sns.set_style("dark")

def plot_corr(predictors):
    predictors = predictors[:]
    mcorr = traindf[predictors].corr()
    mask = np.zeros_like(mcorr, dtype=np.bool)
    mask[np.triu_indices_from(mask)] = True
    cmap = sns.diverging_palette(220, 10, as_cmap=True)
    g = sns.heatmap(mcorr, mask=mask, cmap=cmap, square=True, annot=True, fmt='0.
2f')
    g.set_xticklabels(predictors, rotation=90)
    g.set_yticklabels(reversed(predictors))
    plt.show()

plot_corr(['gauss1','gauss2','repulsion','hydrophobic','hbond','nrot','vina','pkd
'])
```



In [10]:
```
feats = ['gauss1','gauss2','repulsion','hydrophobic','hbond','nrot']
```

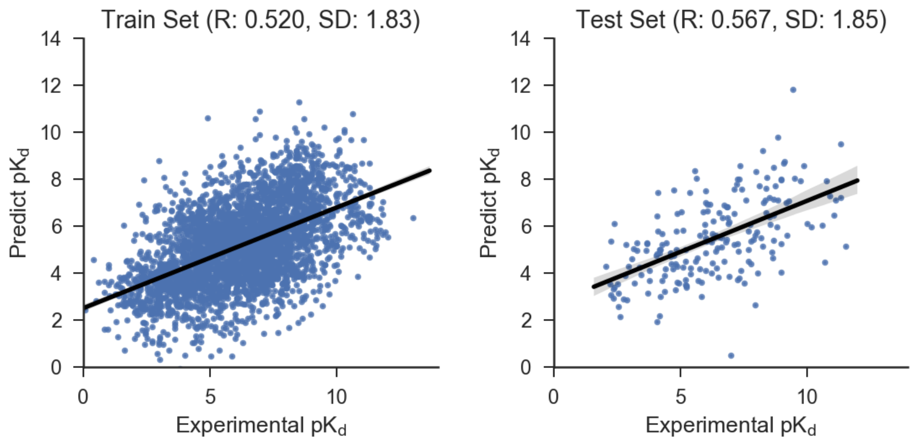
In [11]:
```
trainX = traindf[['gauss1','gauss2','repulsion','hydrophobic','hbond','nrot']]
trainY = traindf[['pkd']]
testX = testdf[['gauss1','gauss2','repulsion','hydrophobic','hbond','nrot']]
testY = testdf[['pkd']]
```

In [12]:
```
def getRSD(trainPredY, trainY, testPredY, testY):
    """
    Calculate the R and SD between predicated values and experimental values
    """

    lm = LinearRegression()
    lm.fit(trainPredY, trainY)
    trainR = lm.score(trainPredY, trainY)**0.5
    trainSD = np.sqrt(np.average((lm.predict(trainPredY) - trainY)**2))

    lm = LinearRegression()
    lm.fit(testPredY, testY)
    testR = lm.score(testPredY, testY)**0.5
    testSD = np.sqrt(np.average((lm.predict(testPredY) - testY)**2))
    print("Train R: %.3f, SD: %.2f; Test  R: %.3f, SD: %.2f"%(trainR, trainSD, te
stR, testSD))

    return trainR, trainSD, testR, testSD
```

In [13]:
```
def plotpKd(trainPredY, trainY, testPredY, testY):
    sns.set_context("notebook", font_scale=1.2)
    sns.set_style("ticks")

    rsd = getRSD(trainPredY, trainY, testPredY, testY)
    plt.figure(figsize = (8,4))

    plt.subplot(121)
    sns.regplot(x = trainY, y = trainPredY.ravel(), color = 'k', scatter_kws = {'
s':3, 'lw':2, 'color':color[0]})
    sns.despine()
    plt.xlabel(r'Experimental pK$_{\mathrm{d}}$')
    plt.ylabel(r'Predict pK$_{\mathrm{d}}$')
    plt.xlim(0,14)
    plt.ylim(0,14)
    plt.title('Train Set (R: %.3f, SD: %.2f)' %(rsd[0],rsd[1]))

    plt.subplot(122)
    sns.regplot(x = testY, y = testPredY.ravel(),color = 'k', scatter_kws = {'s':
3, 'lw':2, 'color':color[0]})
    sns.despine()
    plt.xlabel(r'Experimental pK$_{\mathrm{d}}$')
    plt.ylabel(r'Predict pK$_{\mathrm{d}}$')
    plt.xlim(0,14)
    plt.ylim(0,14)
    plt.title('Test Set (R: %.3f, SD: %.2f)' %(rsd[2],rsd[3]))
    plt.tight_layout()

    plt.show()
```

In [14]:
```
plotpKd(traindf[['vina']].values, trainY, testdf[['vina']].values, testY)
```

```
Train R: 0.520, SD: 1.83; Test  R: 0.567, SD: 1.85
```



Linear Regression

In [15]:
```
rsd = getRSD(traindf[['vina']], trainY, testdf[['vina']], testY)
```

```
Train R: 0.520, SD: 1.83; Test  R: 0.567, SD: 1.85
```

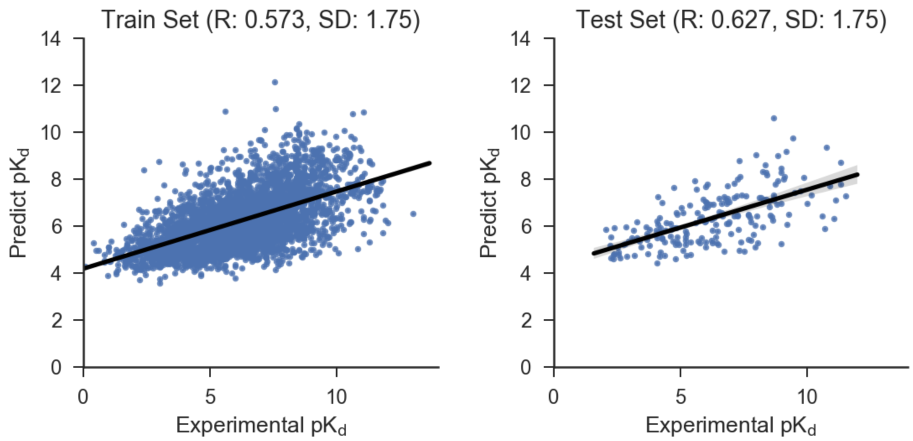
In [16]:
```
# normalize the features for linear regression
scaler = StandardScaler()
scaler = scaler.fit(trainX)

trainXscale = scaler.transform(trainX)
testXscale = scaler.transform(testX)
```

In [17]:
```
# Create linear regression object
lm = LinearRegression()
# Train the model using the training sets
lm.fit(trainXscale, trainY)
# predict on training set
trainPredY = lm.predict(trainXscale)
# predict on test set
testPredY = lm.predict(testXscale)
# get the R and SD
rsd = getRSD(trainPredY, trainY, testPredY, testY)
```

```
Train R: 0.573, SD: 1.75; Test  R: 0.627, SD: 1.75
```

In [18]:
```
plotpKd(trainPredY, trainY, testPredY, testY)
```

```
Train R: 0.573, SD: 1.75; Test  R: 0.627, SD: 1.75
```



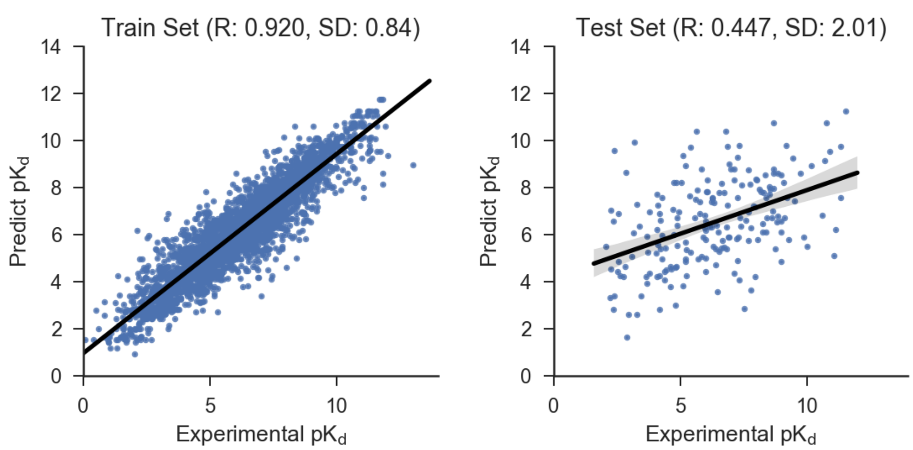
Tree Regression

In [19]:
```
tr = DecisionTreeRegressor( max_depth =20, min_samples_split =10)
tr.fit(trainX, trainY)
trainPredYtr = tr.predict(trainX)
testPredYtr = tr.predict(testX)

rsd = getRSD(trainPredYtr.reshape(-1,1), trainY, testPredYtr.reshape(-1,1), testY
)
```

```
Train R: 0.920, SD: 0.84; Test  R: 0.447, SD: 2.01
```

In [20]:
```
plotpKd(trainPredYtr.reshape(-1,1), trainY, testPredYtr.reshape(-1,1), testY)
```

```
Train R: 0.920, SD: 0.84; Test  R: 0.447, SD: 2.01
```



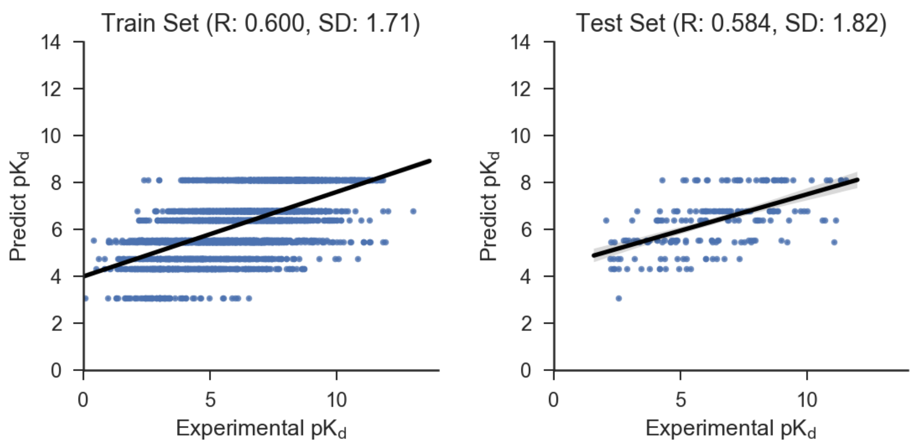
We can see that the above tree regression is significantly overfitted

In [21]:
```
tr = DecisionTreeRegressor( max_depth =3)
tr.fit(trainX, trainY)
trainPredYtr = tr.predict(trainX)
testPredYtr = tr.predict(testX)

rsd = getRSD(trainPredYtr.reshape(-1,1), trainY, testPredYtr.reshape(-1,1), testY
)
```

```
Train R: 0.600, SD: 1.71; Test  R: 0.584, SD: 1.82
```

In [22]:
```
plotpKd(trainPredYtr.reshape(-1,1), trainY, testPredYtr.reshape(-1,1), testY)
```

```
Train R: 0.600, SD: 1.71; Test  R: 0.584, SD: 1.82
```



Random Forest

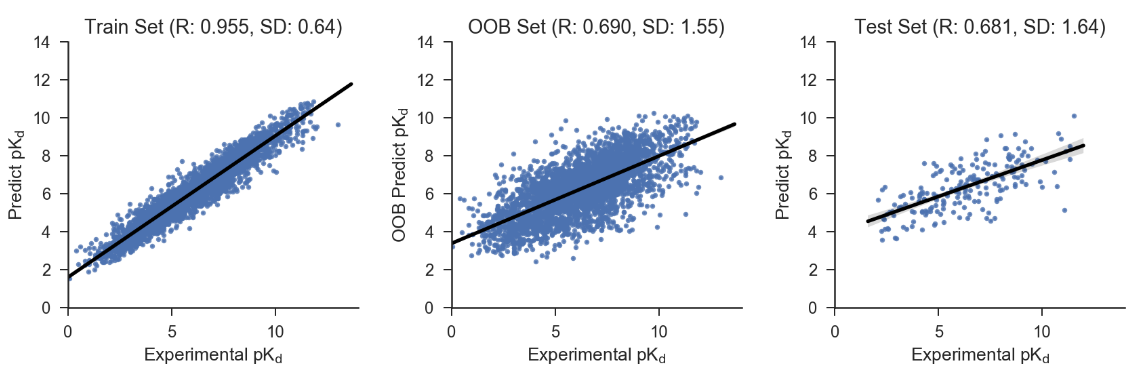
In [26]:
```
# model with 500 trees and mtry = 2, the min_sample to split is 5
rf = RandomForestRegressor( n_estimators = 500, max_features = 2, min_samples_spl
it =5, oob_score = True)
# fit the model
rf.fit(trainX, trainY['pkd'].values)
# predict training set
trainPredYrf = rf.predict(trainX)
# predict test set
testPredYrf = rf.predict(testX)
# get oob prediction
oobPredYrf = rf.oob_prediction_
# get rsd
rsd1 = getRSD(trainPredYrf.reshape(-1,1), trainY, testPredYrf.reshape(-1,1), test
Y)
rsd2 = getRSD(oobPredYrf.reshape(-1,1), trainY, testPredYrf.reshape(-1,1), testY)
```

```
Train R: 0.955, SD: 0.64; Test  R: 0.681, SD: 1.64
Train R: 0.690, SD: 1.55; Test  R: 0.681, SD: 1.64
```

In [28]:
```
def plotpKdoob(trainPredY, trainY, testPredY, testY, oobPredY, oobY):
    sns.set_context("notebook", font_scale=1.2)
    sns.set_style("ticks")

    rsd1 = getRSD(trainPredYrf.reshape(-1,1), trainY, testPredYrf.reshape(-1,1),
testY)
    rsd2 = getRSD(oobPredYrf.reshape(-1,1), trainY, testPredYrf.reshape(-1,1), te
stY)

    plt.figure(figsize = (12,4))

    plt.subplot(131)
    sns.regplot(x = trainY, y = trainPredYrf, color = 'k', scatter_kws = {'s':3,
'lw':2, 'color':color[0]})
    plt.xlabel(r'Experimental pK$_{\mathrm{d}}$')
    plt.ylabel(r'Predict pK$_{\mathrm{d}}$')
    plt.xlim(0,14)
    plt.ylim(0,14)
    plt.title('Train Set (R: %.3f, SD: %.2f)' %(rsd1[0],rsd1[1]))

    plt.subplot(132)
    sns.regplot(x = trainY, y = oobPredYrf,color = 'k', scatter_kws = {'s':3, 'lw
':2, 'color':color[0]})
    plt.xlabel(r'Experimental pK$_{\mathrm{d}}$')
    plt.ylabel(r'OOB Predict pK$_{\mathrm{d}}$')
    plt.xlim(0,14)
    plt.ylim(0,14)
    plt.title('OOB Set (R: %.3f, SD: %.2f)' %(rsd2[0],rsd2[1]))

    plt.subplot(133)
    sns.regplot(x = testY, y = testPredYrf,color = 'k', scatter_kws = {'s':3, 'lw
':2, 'color':color[0]})
    plt.xlabel(r'Experimental pK$_{\mathrm{d}}$')
    plt.ylabel(r'Predict pK$_{\mathrm{d}}$')
    plt.xlim(0,14)
    plt.ylim(0,14)
    plt.title('Test Set (R: %.3f, SD: %.2f)' %(rsd1[2],rsd1[3]))

    sns.despine()
    plt.tight_layout()
    #plt.savefig('images/RF_OOB.pdf')
    plt.show()
```

In [29]:
```
plotpKdoob(trainPredYrf.reshape(-1,1), trainY, testPredYrf.reshape(-1,1), testY,o
obPredYrf.reshape(-1,1), trainY )
```

```
Train R: 0.955, SD: 0.64; Test  R: 0.681, SD: 1.64
Train R: 0.690, SD: 1.55; Test  R: 0.681, SD: 1.64
```

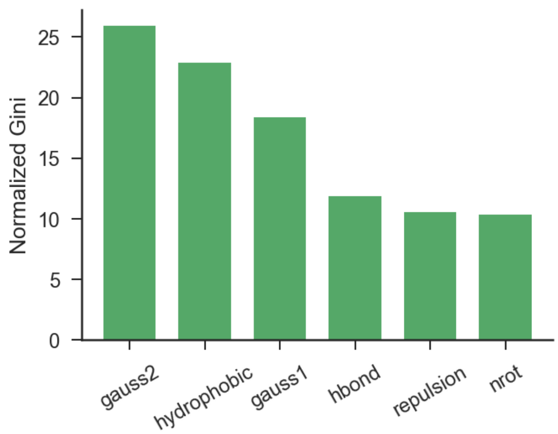


Feature Importance (Gini)

In [30]:
```
imps = rf.feature_importances_
indices = np.argsort(imps)[::-1]
for nm, imp in zip(trainX.columns[indices], imps[indices]):
    print("%16s : %2d %%" %(nm, int(imp*100)))
```

```
          gauss2 : 25 %
     hydrophobic : 22 %
          gauss1 : 18 %
           hbond : 11 %
       repulsion : 10 %
            nrot : 10 %
```

In [31]:
```
fig, ax = plt.subplots(figsize = (5,4))
rects1 = ax.bar(range(6), imps[indices]*100, width = 0.7, align='center', color =
color[1])
plt.xticks(range(6), trainX.columns[indices],  rotation = 30)
plt.ylabel('Normalized Gini')
sns.despine()
plt.tight_layout()
# plt.savefig('images/RF_importance.pdf')
plt.show()
```



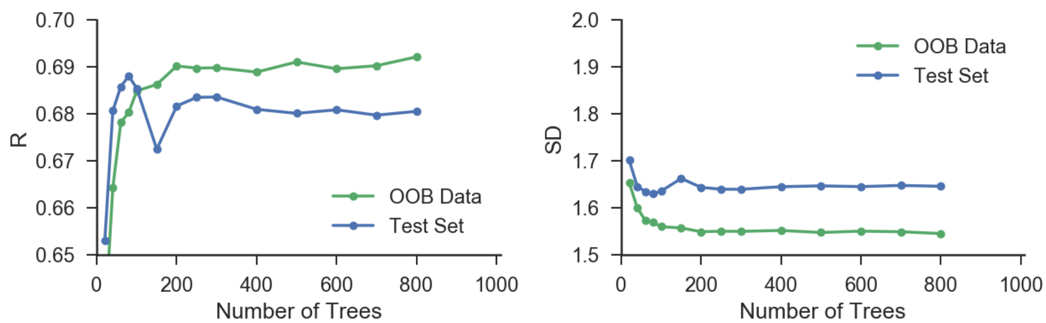
Parameters: number of trees and mtry

In [32]:
```
rfrsd = []
ntree = [20,40,60,80,100,150,200,250,300,400,500,600,700,800]
for i in ntree:
    rf = RandomForestRegressor( n_estimators = i, max_features = 2, min_samples_s
plit =5, oob_score = True)
    rf.fit(trainX, trainY['pkd'].values)
    trainPredYrf = rf.predict(trainX)
    testPredYrf = rf.predict(testX)
    oobPredYrf = rf.oob_prediction_
    print('ntree:',i)
    rsd1 = getRSD(trainPredYrf.reshape(-1,1), trainY, testPredYrf.reshape(-1,1),
testY)
    rsd2 = getRSD(oobPredYrf.reshape(-1,1), trainY, testPredYrf.reshape(-1,1), te
stY)
    rfrsd.append([rsd1[0], rsd1[1], rsd2[0], rsd2[1], rsd1[2], rsd1[3] ])
```

```
/Users/yingkai/anaconda/lib/python3.6/site-packages/sklearn/ensemble/forest.py:7
23: UserWarning: Some inputs do not have OOB scores. This probably means too few
trees were used to compute any reliable oob estimates.
  warn("Some inputs do not have OOB scores. "
```

```
ntree: 20
Train R: 0.943, SD: 0.71; Test  R: 0.653, SD: 1.70
Train R: 0.635, SD: 1.65; Test  R: 0.653, SD: 1.70
ntree: 40
Train R: 0.949, SD: 0.68; Test  R: 0.681, SD: 1.64
Train R: 0.664, SD: 1.60; Test  R: 0.681, SD: 1.64
ntree: 60
Train R: 0.951, SD: 0.66; Test  R: 0.686, SD: 1.63
Train R: 0.678, SD: 1.57; Test  R: 0.686, SD: 1.63
ntree: 80
Train R: 0.952, SD: 0.65; Test  R: 0.688, SD: 1.63
Train R: 0.680, SD: 1.57; Test  R: 0.688, SD: 1.63
ntree: 100
Train R: 0.953, SD: 0.65; Test  R: 0.685, SD: 1.63
Train R: 0.685, SD: 1.56; Test  R: 0.685, SD: 1.63
ntree: 150
Train R: 0.953, SD: 0.65; Test  R: 0.672, SD: 1.66
Train R: 0.686, SD: 1.56; Test  R: 0.672, SD: 1.66
ntree: 200
Train R: 0.954, SD: 0.64; Test  R: 0.682, SD: 1.64
Train R: 0.690, SD: 1.55; Test  R: 0.682, SD: 1.64
ntree: 250
Train R: 0.954, SD: 0.64; Test  R: 0.683, SD: 1.64
Train R: 0.690, SD: 1.55; Test  R: 0.683, SD: 1.64
ntree: 300
Train R: 0.954, SD: 0.64; Test  R: 0.684, SD: 1.64
Train R: 0.690, SD: 1.55; Test  R: 0.684, SD: 1.64
ntree: 400
Train R: 0.954, SD: 0.64; Test  R: 0.681, SD: 1.64
Train R: 0.689, SD: 1.55; Test  R: 0.681, SD: 1.64
ntree: 500
Train R: 0.954, SD: 0.64; Test  R: 0.680, SD: 1.65
Train R: 0.691, SD: 1.55; Test  R: 0.680, SD: 1.65
ntree: 600
Train R: 0.954, SD: 0.64; Test  R: 0.681, SD: 1.64
Train R: 0.690, SD: 1.55; Test  R: 0.681, SD: 1.64
ntree: 700
Train R: 0.955, SD: 0.64; Test  R: 0.680, SD: 1.65
Train R: 0.690, SD: 1.55; Test  R: 0.680, SD: 1.65
ntree: 800
Train R: 0.955, SD: 0.64; Test  R: 0.680, SD: 1.65
Train R: 0.692, SD: 1.54; Test  R: 0.680, SD: 1.65
```

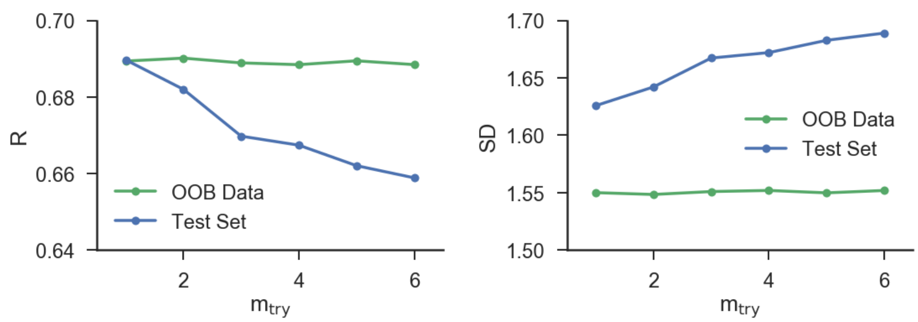
In [33]:
```
rfrsd = np.array(rfrsd)
plt.figure(figsize = (9,3))

plt.subplot(121)
#plt.plot(ntree, rfrsd[:,0], 'o-', color = color[2], ms = 5, label = 'Training Se
t')
plt.plot(ntree, rfrsd[:,2], 'o-',color = color[1], ms = 5, label = 'OOB Data')
plt.plot(ntree, rfrsd[:,4], 'o-',color = color[0], ms = 5, label = 'Test Set')
plt.ylabel('R')
plt.xlabel('Number of Trees')
plt.ylim(0.65,0.7)
plt.xlim(0,1010)
plt.legend(loc = 'best')

plt.subplot(122)
#plt.plot(ntree, rfrsd[:,1], 'ro-', color = color[2], ms = 5, label = 'Training S
et')
plt.plot(ntree, rfrsd[:,3], 'o-',color = color[1], ms = 5, label = 'OOB Data')
plt.plot(ntree, rfrsd[:,5], 'o-',color = color[0], ms = 5, label = 'Test Set')
plt.ylabel('SD')
plt.xlabel('Number of Trees')
plt.ylim(1.5,2)
plt.xlim(0,1010)
plt.legend(loc = 1)

sns.despine()
plt.tight_layout()
#plt.savefig('images/RF_NTrees.pdf')
plt.show()
```



In [35]:
```
rfrsd = []
mtry = [1,2,3,4,5,6]
for i in mtry:
    rf = RandomForestRegressor( n_estimators = 500, max_features = i, min_samples
_split =5, oob_score = True)
    rf.fit(trainX, trainY['pkd'].values)
    trainPredYrf = rf.predict(trainX)
    testPredYrf = rf.predict(testX)
    oobPredYrf = rf.oob_prediction_
    print('mtry:',i)
    rsd1 = getRSD(trainPredYrf.reshape(-1,1), trainY, testPredYrf.reshape(-1,1),
testY)
    rsd2 = getRSD(oobPredYrf.reshape(-1,1), trainY, testPredYrf.reshape(-1,1), te
stY)
    rfrsd.append([rsd1[0], rsd1[1], rsd2[0], rsd2[1], rsd1[2], rsd1[3] ])
```

```
mtry: 1
Train R: 0.946, SD: 0.69; Test  R: 0.690, SD: 1.63
Train R: 0.689, SD: 1.55; Test  R: 0.690, SD: 1.63
mtry: 2
Train R: 0.954, SD: 0.64; Test  R: 0.682, SD: 1.64
Train R: 0.690, SD: 1.55; Test  R: 0.682, SD: 1.64
mtry: 3
Train R: 0.957, SD: 0.62; Test  R: 0.670, SD: 1.67
Train R: 0.689, SD: 1.55; Test  R: 0.670, SD: 1.67
mtry: 4
Train R: 0.959, SD: 0.61; Test  R: 0.667, SD: 1.67
Train R: 0.688, SD: 1.55; Test  R: 0.667, SD: 1.67
mtry: 5
Train R: 0.960, SD: 0.60; Test  R: 0.662, SD: 1.68
Train R: 0.689, SD: 1.55; Test  R: 0.662, SD: 1.68
mtry: 6
Train R: 0.960, SD: 0.60; Test  R: 0.659, SD: 1.69
Train R: 0.688, SD: 1.55; Test  R: 0.659, SD: 1.69
```

In [38]:
```
rfrsd = np.array(rfrsd)

plt.figure(figsize = (8,3))

plt.subplot(121)
#plt.plot(ntree, rfrsd[:,0], 'o-',color = color[2], ms = 5, label = 'Training Set
')
plt.plot(mtry, rfrsd[:,2], 'o-',color = color[1], ms = 5, label = 'OOB Data')
plt.plot(mtry, rfrsd[:,4], 'o-',color = color[0], ms = 5, label = 'Test Set')
plt.ylabel('R')
plt.xlabel('m$_{\mathrm{try}}$')
plt.ylim(0.64,0.7)
plt.xlim(0.5,6.5)
plt.legend(loc = 'best')

plt.subplot(122)

#plt.plot(ntree, rfrsd[:,1], 'o-',color = color[2], ms = 5, label = 'Training Set
')
plt.plot(mtry, rfrsd[:,3], 'o-',color = color[1], ms = 5, label = 'OOB Data')
plt.plot(mtry, rfrsd[:,5], 'o-',color = color[0], ms = 5, label = 'Test Set')
plt.ylabel('SD')
plt.xlabel('m$_{\mathrm{try}}$')
plt.ylim(1.5,1.7)
plt.xlim(0.5,6.5)
plt.xticks()
plt.legend(loc = 'best')

sns.despine()
plt.tight_layout()
#plt.savefig('images/RF_mtry.pdf')

plt.show()
```



In [ ]:

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