Supplementary Material

Overview of the SAMPL5 Host-Guest Challenge: Are We Doing Better?

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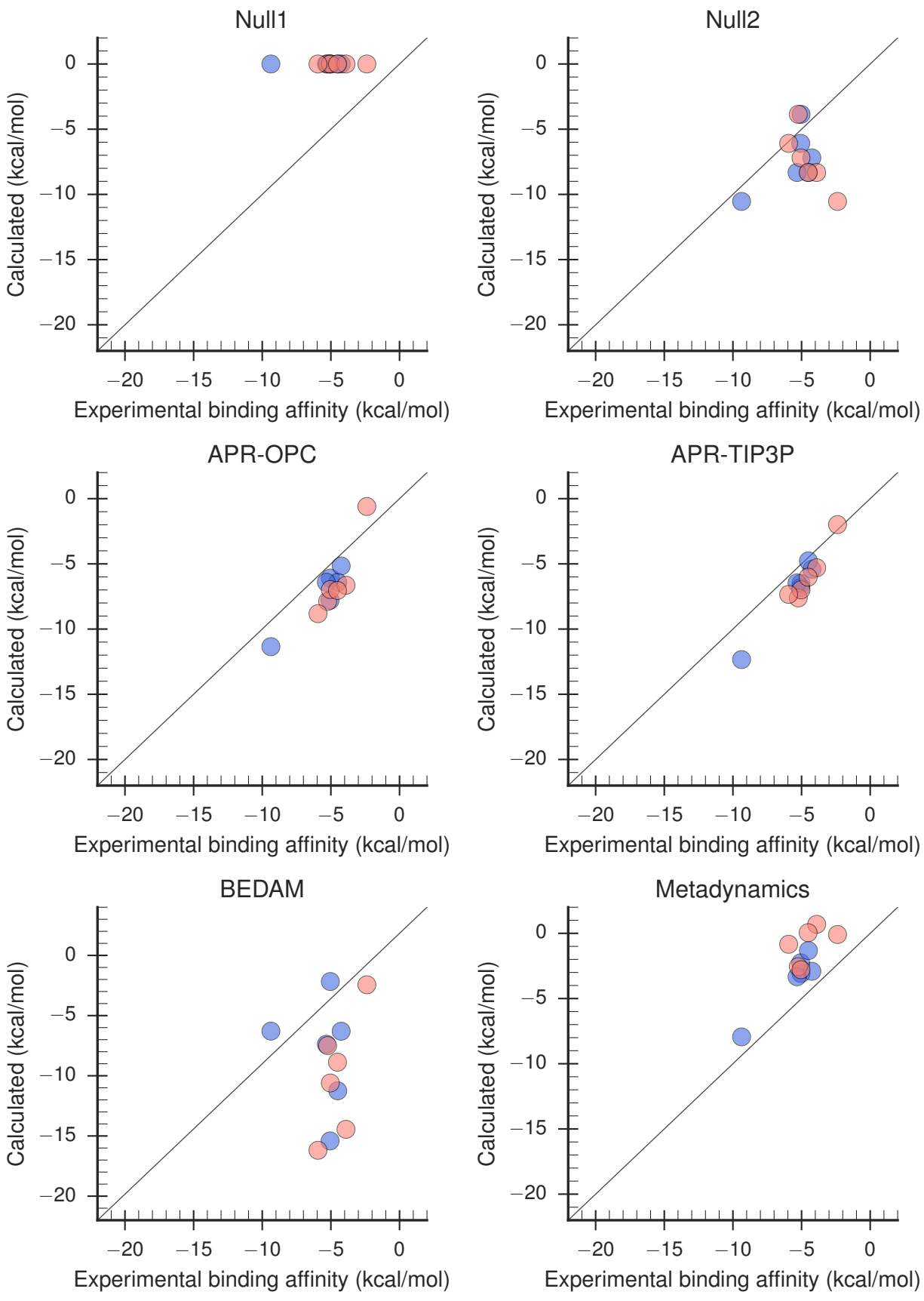
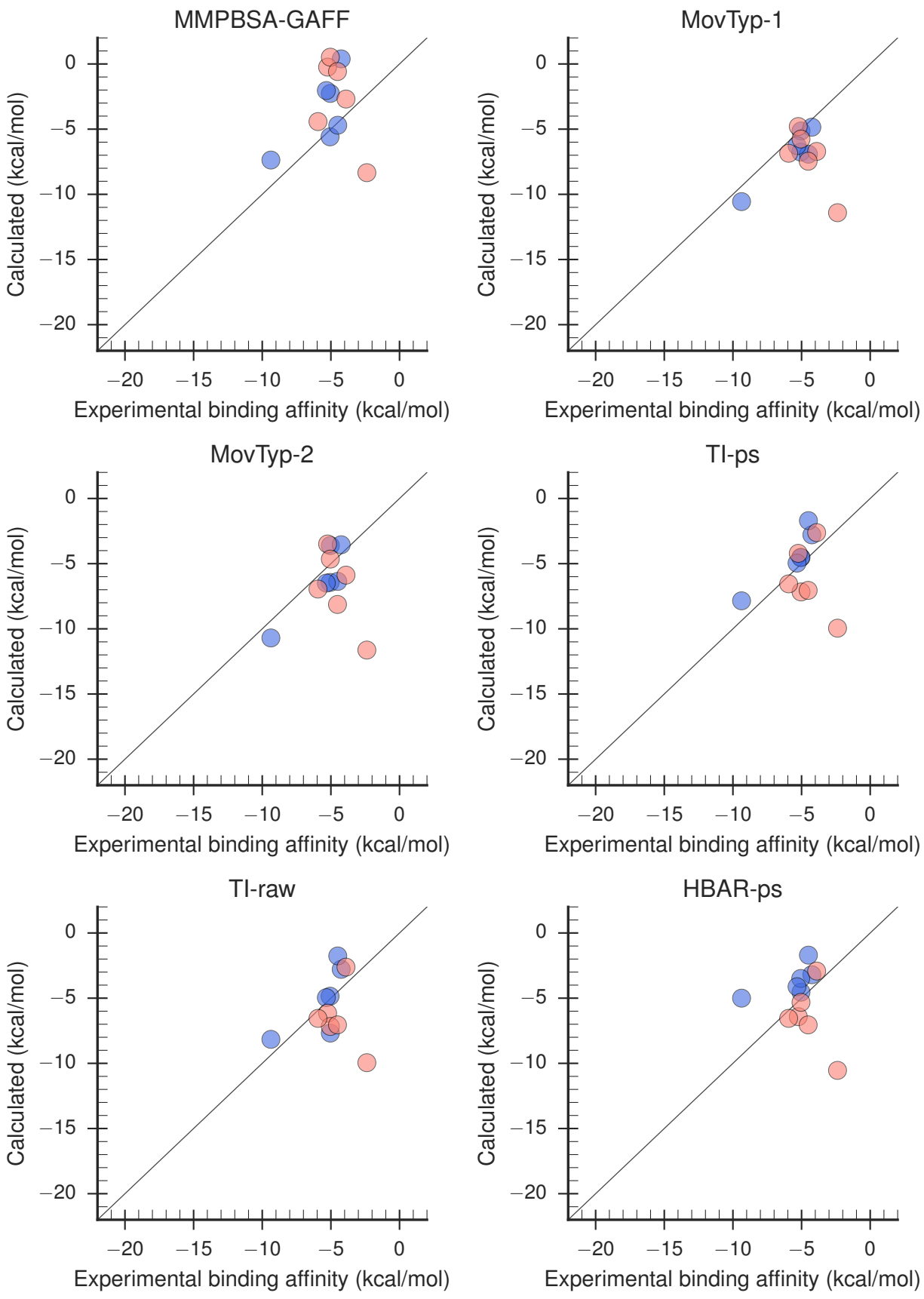
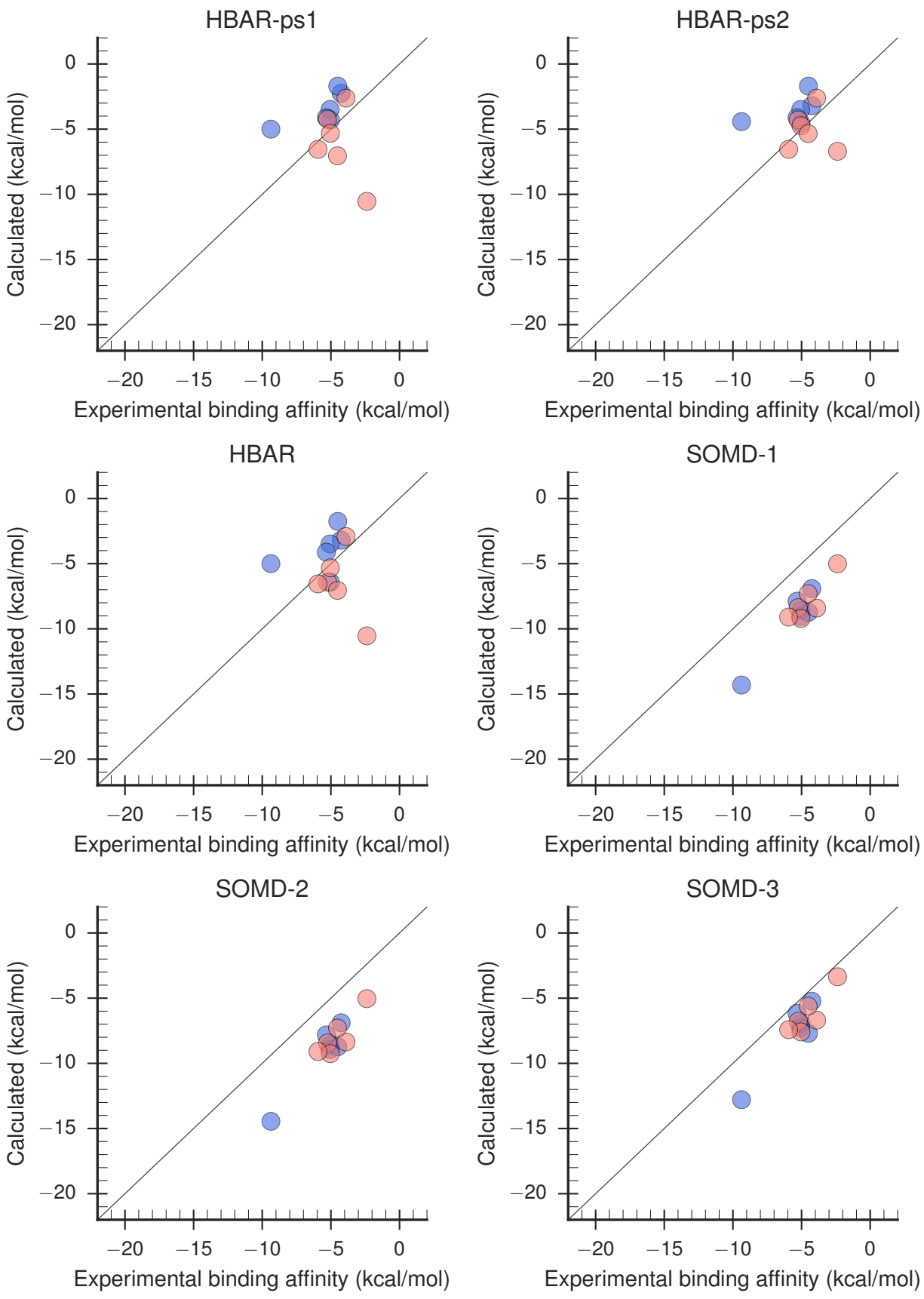
Table S1. Binding constants of OAH and OAMe systems, measured by NMR and ITC.

Guest	OAH (octa acid, OA)		OAMe (TEMOA)	
	K_a (M^{-1}), ITC	K_a (M^{-1}), NMR	K_a (M^{-1}), ITC	K_a (M^{-1}), NMR
G1	9040 9000 **9080**	5055 4949	1.02×10^4 1.01×10^4	7475 6407
G2	2900 2870 **2900**	1279 1335	7240 6930	4691 5221
G3	1980 1940 **1960**	5099 5229	1.75×10^4 1.45×10^4	18360 27761
G4	7.47×10^6 7.41×10^6 **7.41×10^6**	-	-	58 54
G5	528 539	2000 1993	-	706 753
G6	8200 8100 **8120**	3809 4061	1980 2120	1525 2110

At the time of this analysis, Dr. Bruce Gibb had kindly provided us with duplicate measurements for each system, each based on preparation of fresh solutions of the host and guest. At some point the Gibb lab added a third ITC replicate for the OAH subset, as stated in the experimental paper (ref 37 in the main text), with results similar to those reported here. The third set of results, listed in bold, is not included in our analysis. ITC experimental conditions: 298 K, 50 mM sodium phosphate buffer, pH = 11.5; NMR experimental conditions: 298 K (278 K for OAMe-G4), 10 mM sodium phosphate buffer, pH = 11.3.


Null1
Null2
APR-OPC
APR-TIP3P
BEDAM
Metadynamics
Calculated (kcal/mol)
Experimental binding affinity (kcal/mol)
0
−5
−10
−15
−20


MMPBSA-GAFF
MovTyp-1
MovTyp-2
TI-ps
TI-raw
HBAR-ps
Calculated (kcal/mol)
Experimental binding affinity (kcal/mol)
0
−5
−10
−15
−20


HBAR-ps1
HBAR-ps2
HBAR
SOMD-1
SOMD-2
SOMD-3
Calculated (kcal/mol)
Experimental binding affinity (kcal/mol)
0
−5
−10
−15
−20

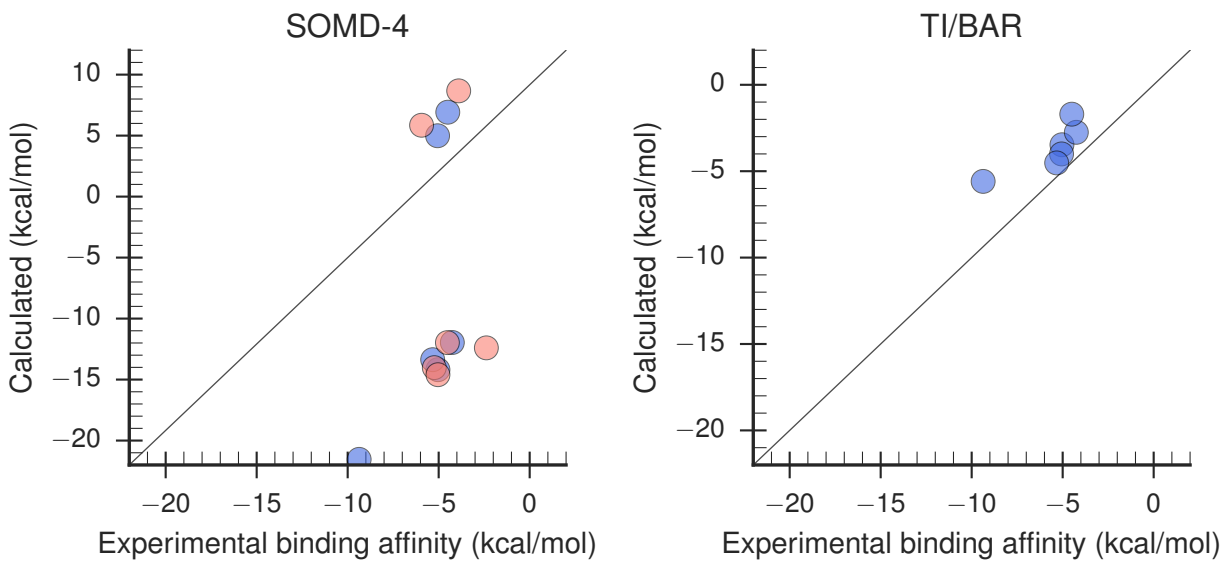
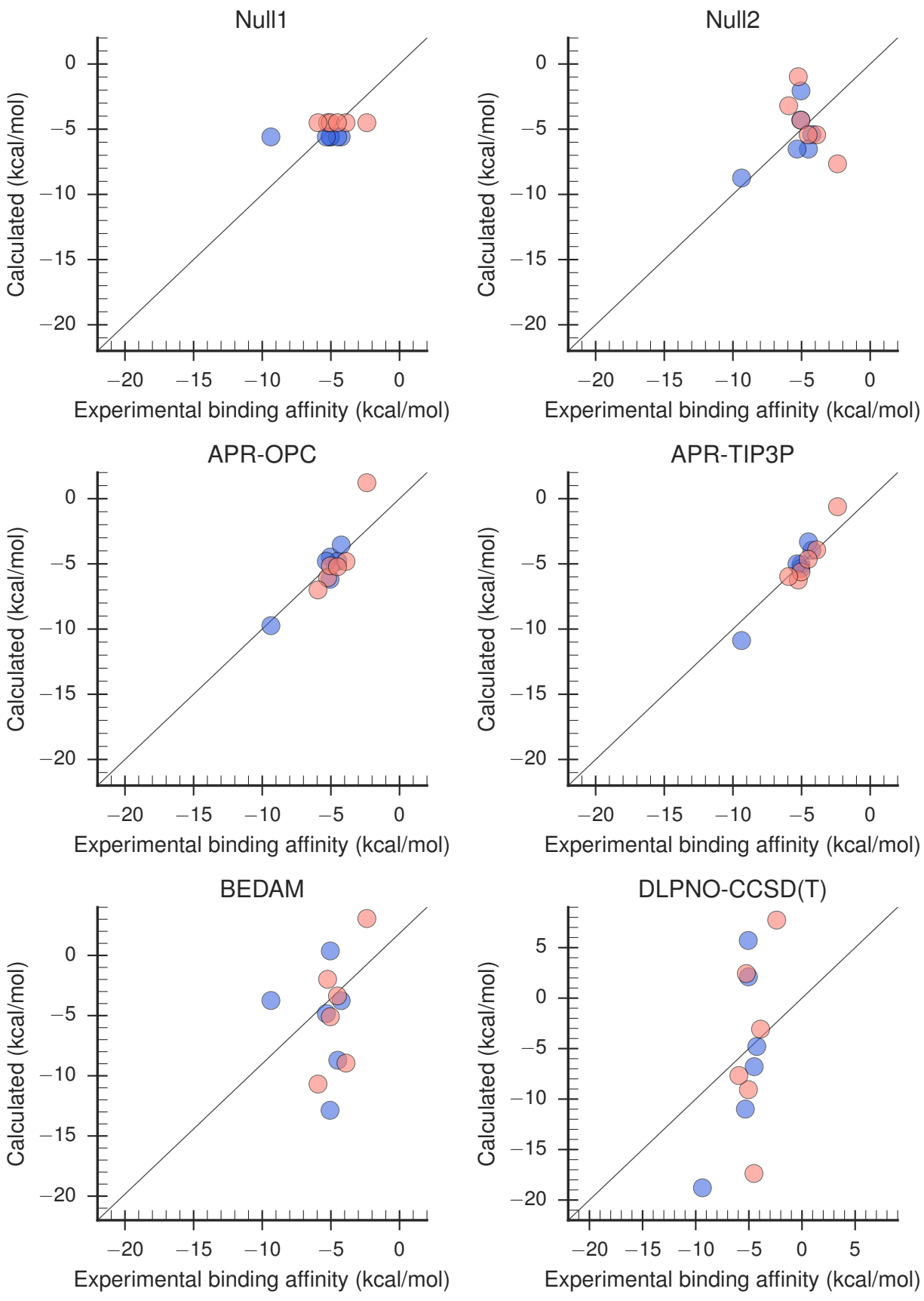
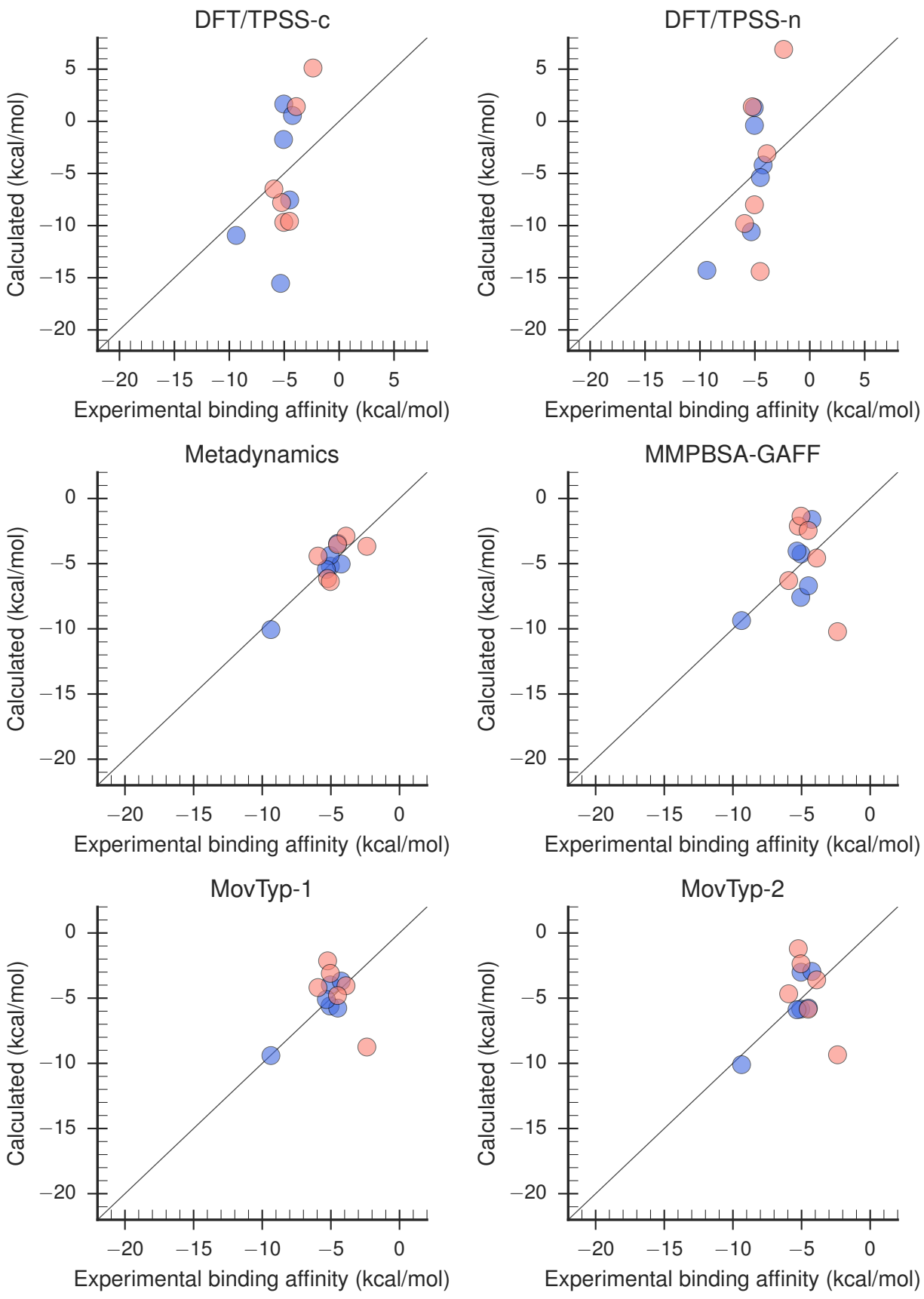
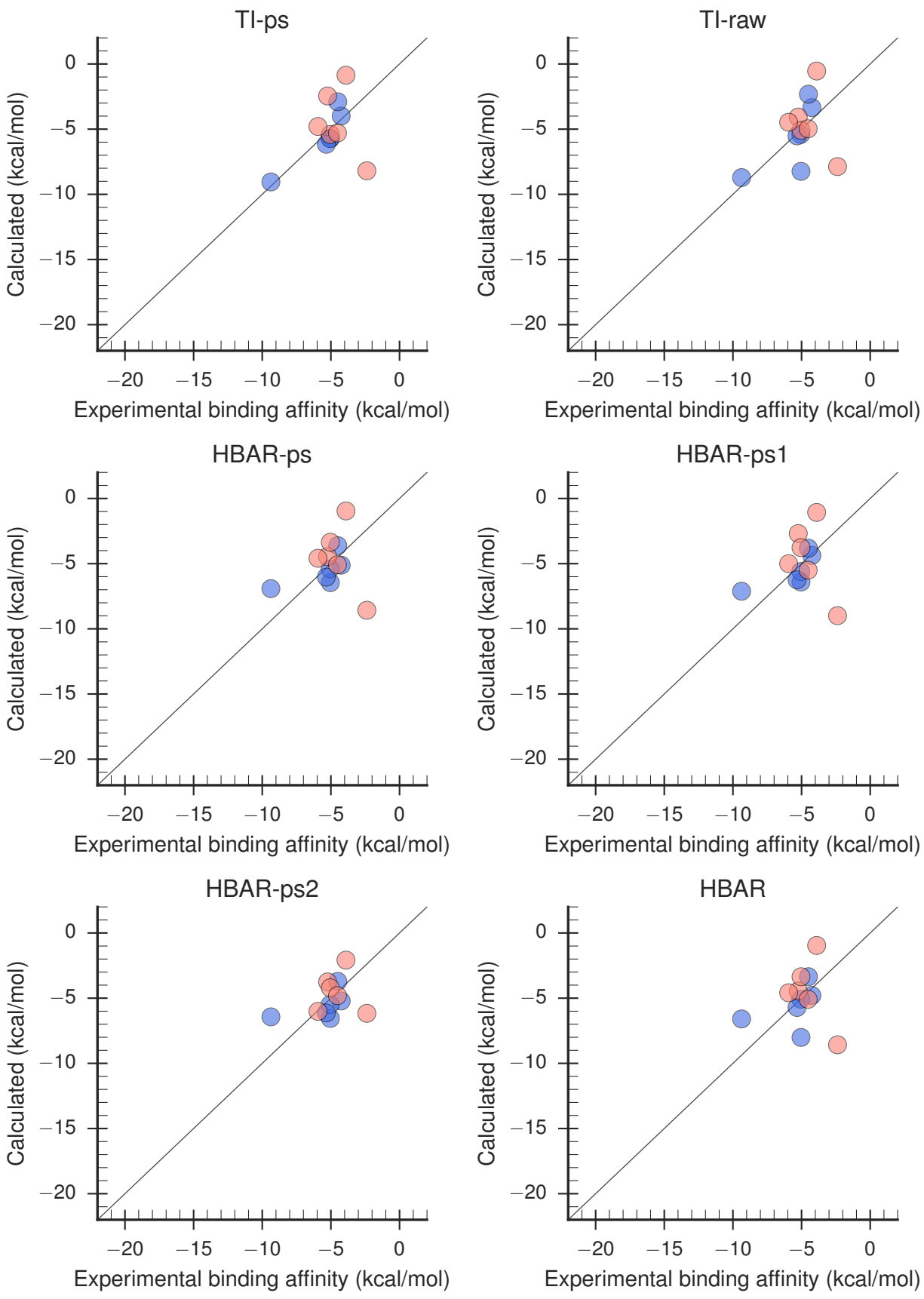


Fig S1. Combined OAH/OAMe predictions, one set of predictions for the OAH subset and two null models. Original data from the submission files were compared to the selected NMR/ITC binding affinities. A constant value of 0.0 was assigned to all guests in the Null1 model, and the estimates in Null2 were generated based on the linear regression between the number of heavy atoms and experimental binding affinities of host OA in SAMPL4 challenge (see main text). Purple dots: OAH; red dots: OAMe; solid black: line of identity.


Null1
Null2
APR-OPC
APR-TIP3P
BEDAM
DLPNO-CCSD(T)
Calculated (kcal/mol)
Experimental binding affinity (kcal/mol)


DFT/TPSS-c
DFT/TPSS-n
Metadynamics
MMPBSA-GAFF
MovTyp-1
MovTyp-2
Calculated (kcal/mol)
Experimental binding affinity (kcal/mol)
5
0
−5
−10
−15
−20


TI-ps
TI-raw
HBAR-ps
HBAR-ps1
HBAR-ps2
HBAR
Calculated (kcal/mol)
Experimental binding affinity (kcal/mol)
0
−5
−10
−15
−20

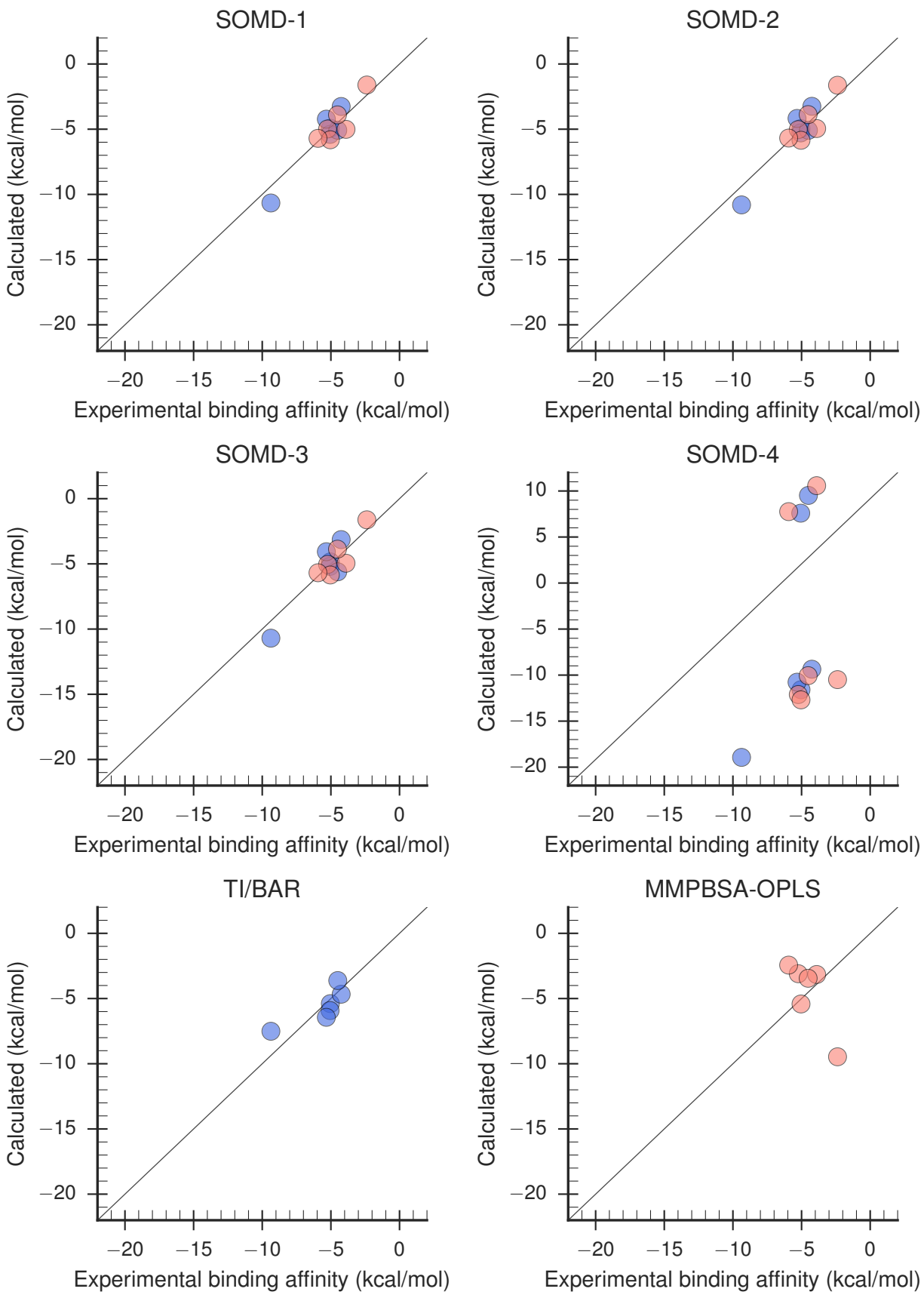
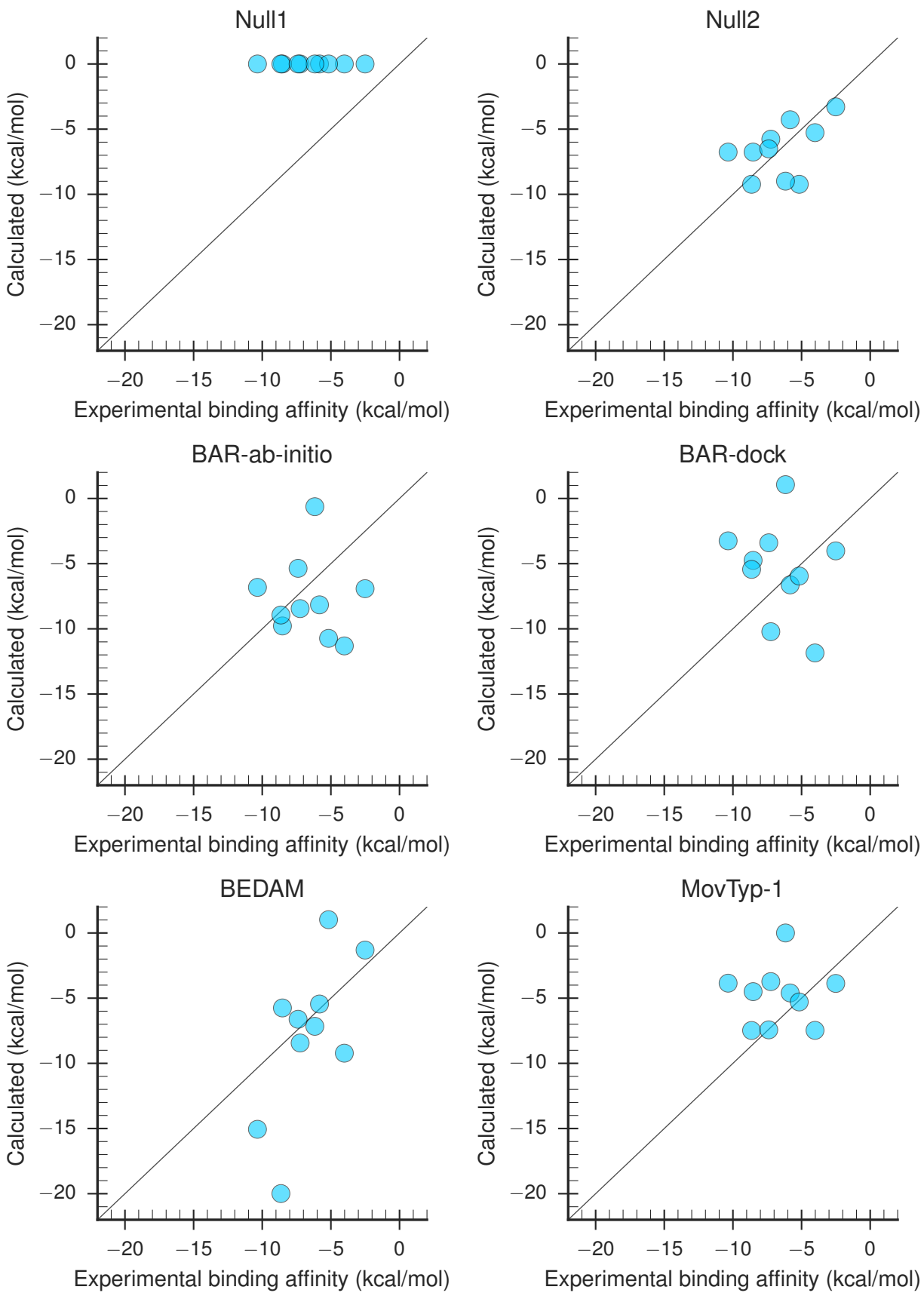
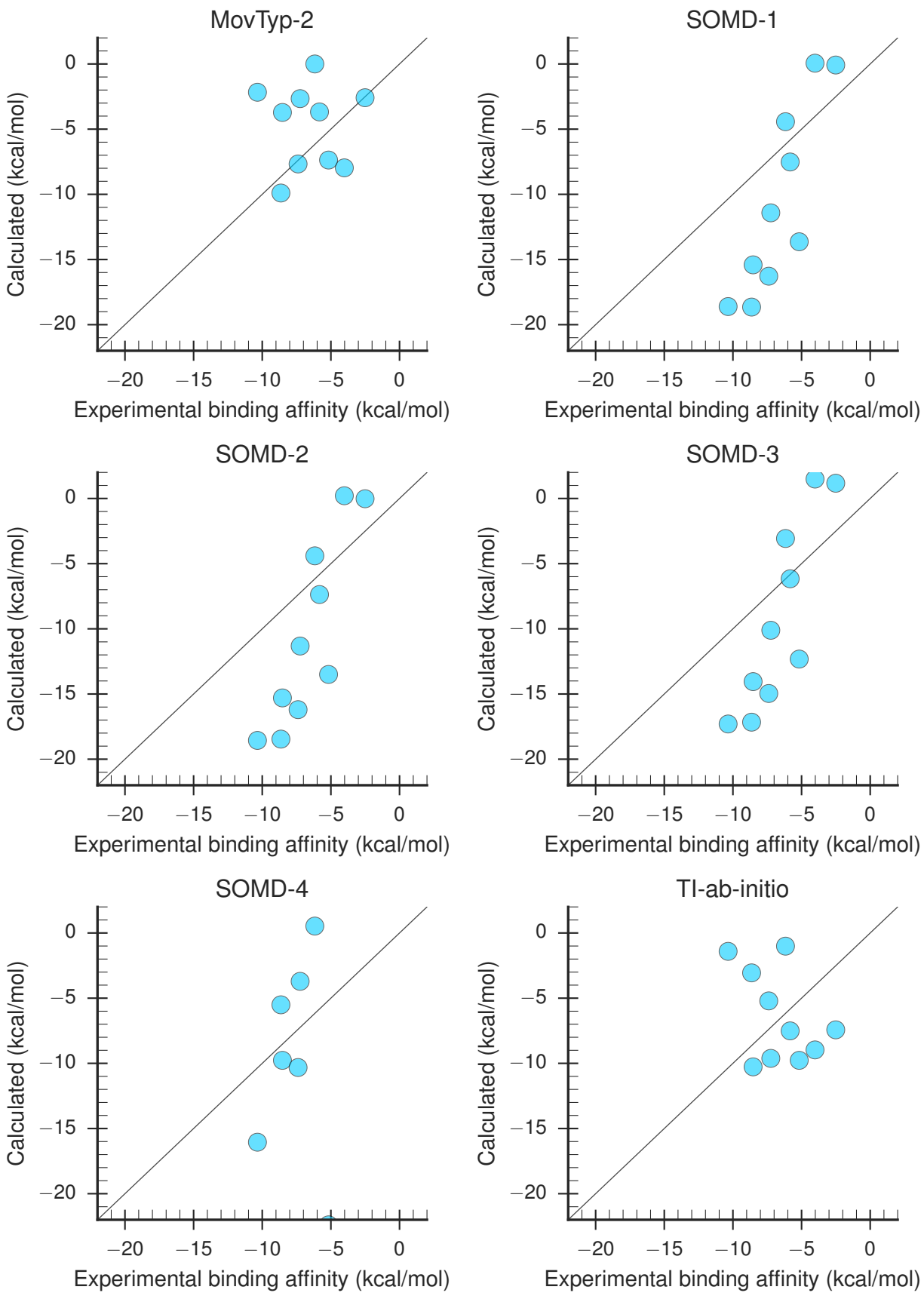

SOMD-1
SOMD-2
SOMD-3
SOMD-4
TI/BAR
MMPBSA-OPLS
Calculated (kcal/mol)
Experimental binding affinity (kcal/mol)
0
−5
−10
−15
−20
10
5
−20
−15
−10
−5
0

Fig S2. Combined OAH/OAMe predictions, two sets of predictions for the OAH or OAMe subset and two null models. Offsets equal to the mean signed error (MSE) of predicted binding affinities relative to the selected NMR/ITC binding affinities were applied. A constant value 0.0 were assigned to all guests in Null1 model, and the estimates in Null2 were generated based on the linear regression between the number of heavy atoms and experimental binding affinities of host OA in SAMPL4 challenge. Purple dots: OAH; red dots: OAMe; Solid black: line of identity.


Null1
Null2
BAR-ab-initio
BAR-dock
BEDAM
MovTyp-1
Calculated (kcal/mol)
Experimental binding affinity (kcal/mol)
0
−5
−10
−15
−20


MovTyp-2
SOMD-1
SOMD-2
SOMD-3
SOMD-4
TI-ab-initio
Calculated (kcal/mol)
Experimental binding affinity (kcal/mol)
0
−5
−10
−15
−20

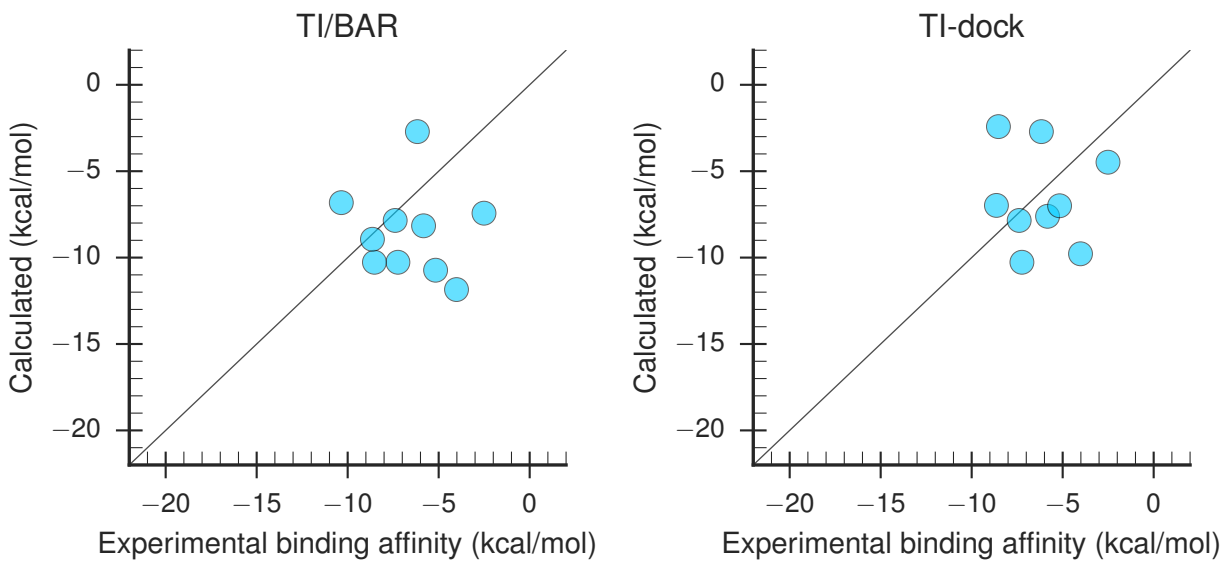


Fig S3. Submissions for CBClip systems and two null models. Original data from the submission files were compared to the experimental binding affinities. A constant value 0.0 was assigned to all guests for the Null1 model, and the estimates for the Null2 model were generated based on the linear regression between the number of heavy atoms and experimental binding affinities of host H1 in SAMPL3 challenge (see main text). The solid black line indicates perfect agreement.

Python code for generating the error metrics with resampling and replacement

The python 3 code used to generate Figure 2-4 in the main text is shown below, which can also be found online at https://github.com/GilsonLabUCSD/SAMPL5-bootstrapping-error-analysis/blob/master/SAMPL5-error-metrics.ipynb and up to date versions, including the data files necessary to recreate the graphs, can be found online at https://github.com/GilsonLabUCSD/SAMPL5-bootstrapping-error-analysis.

```
# # Boostrapping error metrics for SAMPL5

# This notebook reads in SAMPL5 submission data, performs bootstrapping on the uncertainties, and
plots the results.
# This file needs the following directory structure and will write pickles of the results if
`run_calculation = True` or
# read pickles of the results if `run_calculation = False`.
# ```
# .
# ├── Calc-CB
# │   ├── BAR-ab-initio.txt
# │   ├── BAR-dock.txt
# │   ├── BEDAM.txt
# │   ├── CBClip-absolute.pickle (will be created if missing)
# │   ├── MovTyp-1.txt
# │   ├── MovTyp-2.txt
# │   ├── Null1.txt
# │   ├── Null2.txt
# │   ├── SOMD-1.txt
# │   ├── SOMD-2.txt
# │   ├── SOMD-3.txt
# │   ├── SOMD-4.txt
# │   ├── TI-ab-initio.txt
# │   ├── TI-dock.txt
# │   └── TIxBar.txt
# ├── Calc-OA
# │   ├── APR-OPC.txt
# │   ├── APR-TIP3P.txt
# │   ├── BEDAM.txt
# │   ├── CCSD(T)-neutral.txt
# │   ├── DFT-charged.txt
# │   ├── DFT-neutral.txt
# │   ├── Metadynamics.txt
# │   ├── MMPBSA-GAFF.txt
# │   ├── MMPBSA-OPLS.txt
# │   ├── MovTyp-1.txt
# │   ├── MovTyp-2.txt
# │   ├── Null1.txt
# │   ├── Null2.txt
# │   ├── OAH-OAMe-absolute.pickle (will be created if missing)
# │   ├── OAH-OAMe-offset.pickle (will be created if missing)
# │   ├── OAH-OAMe-offset-allavg.pickle (will be created if missing)
# │   ├── OAHOnly-offset.pickle (will be created if missing)
# │   ├── OAMeOnly-offset.pickle (will be created if missing)
# │   ├── PERT-bound-c.txt
# │   ├── PERT-bound.txt
# │   ├── PERT-combo.txt
# │   ├── PERT-hrex-c1.txt
# │   ├── PERT-hrex-c2.txt
# │   ├── PERT-hrex-c.txt
# │   ├── PERT-hrex.txt
# │   ├── SOMD-1.txt
# │   ├── SOMD-2.txt
# │   ├── SOMD-3.txt
# │   └── SOMD-4.txt
# ├── SAMPL5-error-metrics.ipynb (this file)
# └── Exp
#     ├── CBClip.txt
#     ├── OAAllAvg.txt
#     ├── OAEnth10.txt
#     └── OASaltDep.txt
# ```


get_ipython().system('date')

import sys, re
import numpy as np
from scipy import stats
import matplotlib as mpl
import matplotlib.pyplot as plt
```

```
# Wrangle the data
import pandas as pd
# Nice figures
import seaborn as sns
# Access data
import os
# Save the results of bootstrapping
import pickle

get_ipython().magic('matplotlib inline')
# LaTeX
mpl.rc('text', usetex=True)
# amsmath for \text{}
# helvetic to for Helvetica font
# sansmath to make math in Helvetica
mpl.rcParams['text.latex.preamble'] = [
    r'\usepackage{amsmath}',
    r'\usepackage{helvet}',
    r'\usepackage{sansmath}',
    r'\sansmath',
    r'\renewcommand{\familydefault}{\sfdefault}',
    r'\usepackage[T1]{fontenc}',
    r'\usepackage{graphicx}'
]


# ## Function definitions for setting the error metrics, reading the data, performing bootstrap
analysis,
# and plotting the results.


def geterrormetrics(x, y, Nm):
    """
    Returns an array MTmp that stores the output of the error metrics on data given in (x, y).
    Written by Niel.
    """
    MTmp = np.zeros([Nm], np.float64)
    # Slope, Intercept, R
    MTmp[0], MTmp[1], MTmp[2], pval, stderr = stats.linregress(x, y)
    # R^2
    MTmp[3] = MTmp[2] ** 2
    # RMSE
    MTmp[4] = np.sqrt(np.mean(((y - x) ** 2)))
    # MSE
    MTmp[5] = np.mean((y - x))
    # MUE
    MTmp[6] = np.mean(np.absolute(y - x))
    # Tau
    MTmp[7], prob = stats.kendalltau(x, y)
    if np.isnan(MTmp[7]):
        MTmp[7] = 0.0
    return (MTmp)


### BootStrapping Definition
def bootstrap(x, xsem, y, ysem, Nm, BootCyc, OAHOnly, OAMeOnly, CalcPairDiffs, CorrectOA,
CorrectCB, WithUncert,
              WithRep):
    """
    Performs bootstrap error anaysis on data (x, y) and errors (xsem, ysem) for a number
    of bootstrapping cycles given by BootCyc. The remaining parameters specify subsets of
calculations
    that can be performed which are determined in the function `compute_bootstrap`.
    Returns an array of values, uncertainties, and MBoot which holds an array of all values for
    the error metrics for all bootstrapping cycles.
    Written by Niel.
    """

    MBoot = np.zeros([Nm, BootCyc], np.float64)
    MVals = np.zeros([Nm], np.float64)
    MSEMs = np.zeros([Nm], np.float64)
```

```
    xtmp = np.zeros([len(x)], np.float64)
    ytmp = np.zeros([len(x)], np.float64)
    yfit = np.zeros([len(x)], np.float64)

    for b in range(BootCyc):
        for i in range(len(x)):

            # Sample with/without replacement?
            if WithRep:
                j = np.random.randint(len(x))
            else:
                j = i

            # Sampling Statistical Uncertainty
            if not WithUncert or xsem[j] == 0.0:
                xtmp[i] = x[j]
            else:
                xtmp[i] = np.random.normal(x[j], xsem[j])
            if not WithUncert or ysem[j] == 0.0:
                ytmp[i] = y[j]
            else:
                ytmp[i] = np.random.normal(y[j], ysem[j])

            MBoot[0:Nm, b] = geterrormetrics(xtmp, ytmp, Nm)

    for m in range(Nm):
        MVals[m] = np.mean(MBoot[m])
        MSEMs[m] = np.std(MBoot[m])

    return (MVals, MSEMs, MBoot)


def compute_bootstrap(args):
    """
    Read in data from disk given by `args`, convert to common units if necessary,
    set calculation subsets, and call `bootstrap`.
    Returns the number of calculations (i.e., the number of data files), the name of those files,
    the raw (i.e., reported by submission) value of the error metrics, all bootstrapped values of
the
    error metrics, and all bootstrapped mean values.
    Written by Niel.
    """

    OAHOnly = False
    OAMeOnly = False
    CalcPairDiffs = False
    CorrectOA = False
    CorrectCB = False
    WithUncert = True
    WithRep = True

    ### Arguments: <Flags> <ExpType> <ExperimentFile> <CalculationFile1> [<CalculationFile2> ...]
    ### Note, files should have the same number of data points
    calcfiles = []
    for arg in args:
        if arg == 'OAHOnly':
            OAHOnly = True
        if arg == 'OAMeOnly':
            OAMeOnly = True
        if arg == 'CalcPairDiffs':
            CalcPairDiffs = True
        if arg == 'CorrectOA':
            CorrectOA = True
        if arg == 'CorrectCB':
            CorrectCB = True
        if re.search(r'^(ka|dg|dh)$', arg):
            exptype = arg
        if re.search(r'\.txt$', arg):
            if re.search(r'Exp', arg):
                expfile = arg
            else:
```

```
            calcfiles.append(arg)

### Settings
R = 0.0019872036
T = 298.0
BootCyc = 100000
MNames = ('Slope', 'Interc', 'R', 'R^2', 'RMSE', 'MSE', 'MUE', 'TAU')
Nm = len(MNames)

### Load experimental file and place data in array
# print(expfile)
with open(expfile, 'r') as expraw:
    explines = expraw.readlines()
exp = []
for line in explines:
    if not re.match(r'^\s*$', line):
        exp.append(line.rstrip().replace('\t', ' '))

### If "Only" flag, just do first six, or last six
if OAHOnly:
    exp = exp[0:6]
if OAMeOnly:
    exp = exp[6:12]
if OAHOnly and OAMeOnly:
    print("OAHOnly=True and OAMeOnly=True! Not compatible")
    exit()
N = len(exp)  # Number of data points
Np = (N - 1) * N / 2  # Number of data pairs

### Are these binding constants or free energy (or enthalpy)? Convert.
emean = np.zeros([N], np.float64)
esem = np.zeros([N], np.float64)
for i in range(len(exp)):
    cols = np.asarray(exp[i].split(), dtype=np.float64)
    if exptype == 'ka':
        dG = -R * T * np.log(cols)
        emean[i] = np.mean(dG)
        esem[i] = np.std(dG, ddof=1) / np.sqrt(len(dG))
    elif exptype == 'dg':
        emean[i] = cols[0]
        esem[i] = cols[1]
    elif exptype == 'dh':
        emean[i] = np.mean(cols) / 1000
        esem[i] = np.std(cols, ddof=1) / np.sqrt(len(cols)) / 1000
    else:
        print(exptype, "... is not a valid experimental type")

### Calculate Experimental Pairwise Differences
if CalcPairDiffs:
    h = 0
    epmean = np.zeros([Np], np.float64)
    epsem = np.zeros([Np], np.float64)
    for i in range(len(exp)):
        for j in range(i + 1, len(exp)):
            epmean[h] = emean[i] - emean[j]
            epsem[h] = np.sqrt(esem[i] ** 2 + esem[j] ** 2)
            h += 1

### Read in Calculated data.
### I should add a check to make sure number of data points is the same as experiment
Nc = len(calcfiles)
cmean = np.zeros([Nc, N], np.float64)
csem = np.zeros([Nc, N], np.float64)
if CalcPairDiffs:
    cdmean = np.zeros([Nc, Nd], np.float64)
    cdsem = np.zeros([Nc, Nd], np.float64)

RawMs = np.zeros([Nc, Nm], np.float64)
AllMBoot = np.zeros([Nc, Nm, BootCyc], np.float64)
AllMVals = np.zeros([Nc, Nm], np.float64)
AllMSEMs = np.zeros([Nc, Nm], np.float64)
```

```
    nc = 0
    for calcfile in calcfiles:
        calc = np.loadtxt(calcfile, np.float64)
        if OAHOnly:
            calc = calc[0:6]
        if OAMeOnly:
            calc = calc[6:12]
        for i in range(len(calc)):
            if np.isscalar(calc[i]) == True:  ### If scalar instead of array; ie, no SEM given.
                cmean[nc, i] = np.mean(calc[i])
                csem[nc, i] = 0.0
            else:  ### Assume Mean and SEM given
                cmean[nc, i] = calc[i, 0]
                csem[nc, i] = calc[i, 1]

        ### Correct data set with MSE
        if CorrectOA:
            cmean[nc, 0:6] = cmean[nc, 0:6] - (np.mean(cmean[nc, 0:6]) - np.mean(emean[0:6]))
            if len(calc) == 12:
                cmean[nc, 6:12] = cmean[nc, 6:12] - (np.mean(cmean[nc, 6:12]) -
np.mean(emean[6:12]))
        if CorrectCB:
            cmean[nc, 0:10] = cmean[nc, 0:10] - (np.mean(cmean[nc, 0:10]) - np.mean(emean[0:10]))

        if CalcPairDiffs:
            h = 0
            for i in range(len(calc)):
                for j in range(i + 1, len(calc)):
                    cpmean[nc, h] = cmean[nc, i] - cmean[nc, j]
                    cpsem[nc, h] = np.sqrt(csem[nc, i] ** 2 + csem[nc, j] ** 2)
                    h += 1

        RawMs[nc] = geterrormetrics(emean, cmean[nc], Nm)
        AllMVals[nc], AllMSEMs[nc], AllMBoot[nc] = bootstrap(emean, esem, cmean[nc], csem[nc],
                                                             Nm, BootCyc, OAHOnly, OAMeOnly,
                                                             CalcPairDiffs, CorrectOA, CorrectCB,
                                                             WithUncert, WithRep)
        nc += 1

    CalcNames = []
    for name in calcfiles:
        cols = name.split('.')
        CalcNames.append(cols[0])

    return (RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc)


def plot_summary_horizontal_narrow(Nc, RawMs, AllMBoot, AllMVals, CalcNames, absolute, offset,
prefix, filename=None):
    """
    Make a horizontal violin plot (methods on the y-axis) of the bootstrapped error metrics and
save to disk.
    Points are overlaid to represent the mean of each submission and lines are drawn
    to shown the bootstrapped mean. For each error metric, a single graph is drawn:
    RMSE, slope, R squared, and Kendall tau. There is manual tweaking of names, labels,
    and colors.
    v2: The aspect ratio is changed to make the plots a bit more narrow and long.
    v3: Order first by reported mean, then bootstrapped mean for rounded values.
    v3: 'Slope' goes to 'm' and 'Tau' goes to '\tau'
    v3: Increase grid thickness
    v3: KDE bandwidth of 0.2 to reduce some jitteriness in the discrete tau values.
    Also, bigger font size.
    The figures are saved given by the parameter `filename`.
    """

    # Set the graph labels to different for absolute and offset calculations.
    if absolute:
        calculation_name = ["RMSE (kcal/mol)", "Abs(1-m)", "$R^{2}$", "$\tau$"]
    if offset:
        calculation_name = ["RMSE_o (kcal/mol)", "Abs(1-m_o)", "$R^{2}$_o", "$\tau$_o"]
```

```
    calculation_index = [4, 0, 3, 7]  # From Niel's MTmp

    # Convert slope into abs(1-slope)
    for n in range(Nc):
        tmp = RawMs[n, 0]
        RawMs[n, 0] = np.abs(1.0 - tmp)
        tmp = AllMBoot[n, 0]
        AllMBoot[n, 0] = np.abs(1.0 - tmp)
        AllMVals[n, 0] = np.mean(AllMBoot[n, 0])

    for i in calculation_index:
        tmp = np.argsort(RawMs[0:Nc, i])
        Order = [j for j in tmp]
        # print('Calculation = {}, best method index = {}, best method name = {}'.format(i,
        #
np.argsort(RawMs[0:Nc,i])[0],
        #
CalcNames[np.argsort(RawMs[0:Nc,i])[0]]))
SS
        # Order first by reported mean, then by bootstrapped distribution mean.
        round_RawMs = np.around(RawMs[:, i], 2)
        round_AllMVals = np.around(AllMVals[:, i], 2)
        rounds = pd.DataFrame()
        rounds['b'] = AllMVals[:, i]
        rounds['r'] = round_RawMs
        rounds['o'] = range(len(round_AllMVals))
        rounds['m'] = [CalcNames[i] for i in range(len(AllMVals))]
        # Reorder array based on raw value first, then mean of the boostrapped distribution.
        ordered = rounds.sort_values(['r', 'b'], inplace=False)
        # Grab the values of the third column, which was original order, based on
        # values of first two columns.
        Order = ordered['o'].as_matrix()
        # For R squared and Tau reverse the ordering so the graphs always present best to worst
case
        # (left to right or top to bottom).
        if calculation_name[calculation_index.index(i)] == '$R^{2}$' or calculation_name[
            calculation_index.index(i)] == '$\tau$' or
calculation_name[calculation_index.index(i)] == '$R^{2}$_o' or \
                        calculation_name[calculation_index.index(i)] == '$\tau$_o':
            Order = ordered['o'].as_matrix()[::-1]

        # Cleanup submission names grabbed from the filenames.
        CalcNames = ['TI/BAR' if i == 'TIxBar' else i for i in CalcNames]
        CalcNames = ['MovTyp-1*' if i == 'MovTyp-1' else i for i in CalcNames]
        CalcNames = ['MovTyp-2*' if i == 'MovTyp-2' else i for i in CalcNames]
        CalcNames = ['Null1*' if i == 'Null1' else i for i in CalcNames]
        CalcNames = ['DFT-neutral*' if i == 'DFT-neutral' else i for i in CalcNames]
        CalcNames = ['DFT-charged*' if i == 'DFT-charged' else i for i in CalcNames]
        CalcNames = ['CCSD(T)-neutral*' if i == 'CCSD(T)-neutral' else i for i in CalcNames]

        # Updated suggested names from reviewers...
        CalcNames = ['DLPNO-CCSD(T)*' if i == 'CCSD(T)-neutral*' else i for i in CalcNames]
        CalcNames = ['DFT/TPSS-c*' if i == 'DFT-charged*' else i for i in CalcNames]
        CalcNames = ['DFT/TPSS-n*' if i == 'DFT-neutral*' else i for i in CalcNames]
        CalcNames = ['TI-raw' if i == 'PERT-bound' else i for i in CalcNames]
        CalcNames = ['TI-ps' if i == 'PERT-bound-c' else i for i in CalcNames]
        CalcNames = ['TI/BAR' if i == 'PERT-combo' else i for i in CalcNames]
        CalcNames = ['HBAR' if i == 'PERT-hrex' else i for i in CalcNames]
        CalcNames = ['HBAR-ps' if i == 'PERT-hrex-c' else i for i in CalcNames]
        CalcNames = ['HBAR-ps1' if i == 'PERT-hrex-c1' else i for i in CalcNames]
        CalcNames = ['HBAR-ps2' if i == 'PERT-hrex-c2' else i for i in CalcNames]

        # Exclude Null1 model from Tau calculation and plotting.
        if i == 7 and absolute == True:
            # Exclude Null1 model from Tau calculation and plotting.
            element_to_remove = np.where([CalcNames[i] == 'Null1*' for i in Order])[0][0]
            Order_without_null1 = np.delete(Order, element_to_remove)
            Order = np.copy(Order_without_null1)

        # Wrangle the data into a `DataFrame` so we can do categorical plotting with seaborn.
        # The bootstrapped error distributions.
```

```
        df = pd.DataFrame()
        df['AllMBoot'] = np.hstack(([AllMBoot[n, i] for n in Order]))
        df['Method'] = np.hstack(([np.repeat(CalcNames[n], len(AllMBoot[n, i])) for n in Order]))
        # The 'raw' (i.e., submitted) values for the error metrics.
        df2 = pd.DataFrame()
        df2['RawMs'] = [RawMs[n, i] for n in Order]
        df2['Method'] = [CalcNames[n] for n in Order]
        # The bootstrapped error means.
        df3 = pd.DataFrame()
        df3['AllMVals'] = [AllMVals[n, i] for n in Order]
        df3['Method'] = [CalcNames[n] for n in Order]
        # Set axes labels for the submissions.
        labels = [CalcNames[n] for n in Order]
        # Blue for everything except red for null models.
        palette = ['#4169e1' if i != 'Null1*' and i != 'Null2' else '#fa8072' for i in labels]

        # Set up plot aesthetics.
        sns.set_style("whitegrid", rc={'legend.frameon': False})
        sns.set_context("paper", font_scale=3.0, rc={"lines.linewidth": 5, 'legend.frameon':
False})
        sns.despine(left=True, bottom=True, right=True, top=True)
        fig, ax = plt.subplots(1, figsize=(8, 19), dpi=300)
        ax.grid(linewidth=2)
        g = sns.violinplot(y='Method', x='AllMBoot', data=df, inner=None, linewidth=0,
palette=palette, cut=0,
                           orientation='h', split=True, scale='width', gridsize=400, bw=0.2)

        for n in Order:
            # Plot the 'raw' (submitted) values for the error metrics as white circles with a
black border
            ax.scatter(y=np.where(Order == n)[0], x=df2[df2['Method'] == CalcNames[n]]['RawMs'],
s=150, marker='o',
                       color='w', edgecolor='k', linewidth=2.5, zorder=21)
            # Plot the bootstrapped mean values as a line.
            # This gets the column position because we are plotting using `Order` and the width
of the line is 1/len(CalcNames).
            # We could shorten the line a little bit for better readability.
            ax.axvline(x=AllMVals[n, i], ymin=1 - (np.where(Order == n)[0] / len(Order) + 0.01),
                       ymax=1 - (np.where(Order == n)[0] / len(Order) + 1 / len(Order) - 0.01),
                       linewidth=2, c='k', lw=4, zorder=20, alpha=0.5)
            # This adds a bit of a white background around the lines by plotting underneath a
slightly larger line.
            ax.axvline(x=AllMVals[n, i], ymin=1 - (np.where(Order == n)[0] / len(Order) + 0.01),
                       ymax=1 - (np.where(Order == n)[0] / len(Order) + 1 / len(Order) - 0.01),
                       linewidth=2, c='w', lw=6, zorder=19, alpha=1.0)

        plt.xlabel(calculation_name[calculation_index.index(i)], labelpad=10)
        plt.ylabel('')
        # Let's limit slope and R^2 for better aesthetics.
        if calculation_name[calculation_index.index(i)] == '$R^{2}$' or calculation_name[
            calculation_index.index(i)] == '$R^{2}$_o':
            ax.set_xlim([0, 1])
        # Let's limit for Tau, too:
        if calculation_name[calculation_index.index(i)] == '$\tau$' or calculation_name[
            calculation_index.index(i)] == '$\tau$_o':
            ax.set_xlim([-1.0, 1.0])
        # Fix the lower limit only for the Abs(1-slope) aesthetic.
        if calculation_name[calculation_index.index(i)] == 'Abs(1-m)' or calculation_name[
            calculation_index.index(i)] == 'Abs(1-m_o)':
            ax.set_xlim([0, 6])
        if prefix != 'CBClip':
            if calculation_name[calculation_index.index(i)] == 'RMSE (kcal/mol)' or
calculation_name[
                calculation_index.index(i)] == 'RMSE_o (kcal/mol)':
                ax.set_xlim([0, 14])
        else:
            if calculation_name[calculation_index.index(i)] == 'RMSE (kcal/mol)' or
calculation_name[
                calculation_index.index(i)] == 'RMSE_o (kcal/mol)':
                ax.set_xlim([0, np.max(df2['RawMs']) + 0.5 * np.max(df2['RawMs'])])
        ax.tick_params(axis='both', which='major', pad=5)
```

```
        # Because LaTeX rendering, we have to escape these underscores...
        if i == 0:
            if offset:
                latex_label = 'Abs(1-$\\text{m}_{\\text{o}}$)'
            if absolute:
                latex_label = 'Abs(1-m)'
        if i == 4:
            if offset:
                latex_label = '$\\text{RMSE}_{\\text{o}}$ (kcal/mol)'
            if absolute:
                latex_label = 'RMSE (kcal/mol)'
        if i == 3:
            if offset:
                latex_label = '$\\text{R}^{\\text{2}}_{\\text{o}}$'
            if absolute:
                latex_label = '$\\text{R}^{\\text{2}}$'
        if i == 7:
            if offset:
                latex_label = '$\\tau_{\\text{o}}$'
            if absolute:
                latex_label = '$\\tau$'

        plt.xlabel(latex_label)
        plt.title(prefix, y=1.01)

        if filename:
            if i == 0:
                label = 'slope'
            if i == 4:
                label = 'rmse'
            if i == 3:
                label = 'r-squared'
            if i == 7:
                label = 'tau'
            plt.tight_layout()
            plt.savefig(filename + '-' + str(label) + '-narrow.pdf', dpi=300, bbox_inches='tight',
pad_inches=0.3)
    return


def PrintTable(CalcNames, RawMs, AllMVals, AllMSEMs, AddDFT=False, Offset=False, OAHOnly=False,
OAMeOnly=False):
    """
    Print the method names and error metrics (RMSE, R^2, m, τ) in a format ready
    for the SAMPL5 Overview manuscript.
    Using the same naming tweaks that Dave used above.  (Should we put this in a
    function?)
    Print '-' for missing data.
    The format isn't aligned well because I'm using tabs so it will go directly into Excel/Word
    Written by Niel
    """
    # Cleanup submission names grabbed from the filenames.
    CalcNames = ['TI/BAR' if i == 'TIxBar' else i for i in CalcNames]
    CalcNames = ['MovTyp-1*' if i == 'MovTyp-1' else i for i in CalcNames]
    CalcNames = ['MovTyp-2*' if i == 'MovTyp-2' else i for i in CalcNames]
    CalcNames = ['Null1*' if i == 'Null1' else i for i in CalcNames]
    CalcNames = ['DFT-neutral*' if i == 'DFT-neutral' else i for i in CalcNames]
    CalcNames = ['DFT-charged*' if i == 'DFT-charged' else i for i in CalcNames]
    CalcNames = ['CCSD(T)-neutral*' if i == 'CCSD(T)-neutral' else i for i in CalcNames]

    # Updated suggested names from reviewers...
    CalcNames = ['DLPNO-CCSD(T)*' if i == 'CCSD(T)-neutral*' else i for i in CalcNames]
    CalcNames = ['DFT/TPSS-c*' if i == 'DFT-charged*' else i for i in CalcNames]
    CalcNames = ['DFT/TPSS-n*' if i == 'DFT-neutral*' else i for i in CalcNames]
    CalcNames = ['TI-raw' if i == 'PERT-bound' else i for i in CalcNames]
    CalcNames = ['TI-ps' if i == 'PERT-bound-c' else i for i in CalcNames]
    CalcNames = ['TI/BAR' if i == 'PERT-combo' else i for i in CalcNames]
    CalcNames = ['HBAR' if i == 'PERT-hrex' else i for i in CalcNames]
    CalcNames = ['HBAR-ps' if i == 'PERT-hrex-c' else i for i in CalcNames]
    CalcNames = ['HBAR-ps1' if i == 'PERT-hrex-c1' else i for i in CalcNames]
```

```
    CalcNames = ['HBAR-ps2' if i == 'PERT-hrex-c2' else i for i in CalcNames]

    MetricNames = ['m', 'b', 'R', 'R^2', 'RMSE', 'MSE', 'MUE', 'tau']
    calculation_index = [4, 3, 0, 7]
    # calculation_index = [4, 6, 5, 3, 2, 0, 1, 7]  ### All Metrics

    # Print Header
    if Offset:
        offchar = '_o'
    else:
        offchar = ''
    print("{0:12s}\t".format('Method'), end='')
    for i in calculation_index:
        print("{0:14s}\t".format(MetricNames[i] + offchar), end='')
    print('')

    # Print Data
    for n, name in enumerate(CalcNames):
        print("{0:12s}\t".format(name), end=''),
        for i in calculation_index:
            if AllMSEMs[n, i] == 0.0 or (i == 7 and name == "Null1*"):
                print("    -    \t", end='')
            else:
                print("{0:.1f}({1:.1f} ± {2:.1f})\t".format(RawMs[n, i], AllMVals[n, i],
AllMSEMs[n, i]), end='')
        if AddDFT and name == 'BEDAM':
            for missname in "DFT/TPSS-c DFT/TPSS-n DLPNO-CCSD(T)".split():
                print('')
                print("{0:12s}\t".format(missname), end='')
                for j in range(len(calculation_index)):
                    print("    -    \t", end='')
        if OAHOnly and name == 'TI/BAR':
            print('')
            print("{0:12s}\t".format('MMPBSA-OPLS'), end='')
            for j in range(len(calculation_index)):
                print("    -    \t", end='')
        if OAMeOnly and name == 'SOMD-4':
            print('')
            print("{0:12s}\t".format('TI/BAR'), end='')
            for j in range(len(calculation_index)):
                print("    -    \t", end='')
        print('')


# ## Calculations and plotting!


# Path to data files (set absolute path if you execute cells out of order)
run_location = '.'

# If false, there needs to be .pickle files available from a previous run
run_calculation = False

# ConsistentSalt-Abs (Table 3)
os.chdir(run_location + '/Calc-OA')
string = 'ka ../Exp/OASaltDep.txt Null1.txt Null2.txt APR-OPC.txt APR-TIP3P.txt ' \
         'BEDAM.txt Metadynamics.txt MMPBSA-GAFF.txt MovTyp-1.txt MovTyp-2.txt ' \
         'PERT-bound-c.txt PERT-bound.txt PERT-hrex.txt PERT-hrex-c.txt PERT-hrex-c1.txt ' \
         'PERT-hrex-c2.txt SOMD-1.txt SOMD-2.txt SOMD-3.txt SOMD-4.txt'
args = string.split()
if run_calculation:
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = compute_bootstrap(args)
    results = [RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc]
    pickle.dump(results, open('OAH-OAMe-absolute.pickle', 'wb'))
else:
    results = pickle.load(open('OAH-OAMe-absolute.pickle', 'rb'))
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = results
PrintTable(CalcNames, RawMs, AllMVals, AllMSEMs, AddDFT=True)
# Why is RawMs being treated as global scope when it goes into plot_summary_horizontal_narrow?
plot_summary_horizontal_narrow(Nc, RawMs, AllMBoot, AllMVals, CalcNames, absolute=True,
offset=False, prefix='OAH/OAMe',
```

```
                                filename='OAH-OAMe-absolute')

# ConsistentSalt-Offset (Table 3)
os.chdir('../')
os.chdir(run_location + '/Calc-OA')
string = 'CorrectOA ka ../Exp/OASaltDep.txt Null1.txt Null2.txt APR-OPC.txt ' \
         'APR-TIP3P.txt BEDAM.txt DFT-charged.txt DFT-neutral.txt CCSD(T)-neutral.txt ' \
         'Metadynamics.txt MMPBSA-GAFF.txt MovTyp-1.txt MovTyp-2.txt PERT-bound-c.txt ' \
         'PERT-bound.txt PERT-hrex.txt PERT-hrex-c.txt PERT-hrex-c1.txt PERT-hrex-c2.txt ' \
         'SOMD-1.txt SOMD-2.txt SOMD-3.txt SOMD-4.txt'
args = string.split()
if run_calculation:
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = compute_bootstrap(args)
    results = [RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc]
    pickle.dump(results, open('OAH-OAMe-offset.pickle', 'wb'))
else:
    results = pickle.load(open('OAH-OAMe-offset.pickle', 'rb'))
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = results
PrintTable(CalcNames, RawMs, AllMVals, AllMSEMs, Offset=True)
plot_summary_horizontal_narrow(Nc, RawMs, AllMBoot, AllMVals, CalcNames, absolute=False,
offset=True, prefix='OAH/OAMe',
                                filename='OAH-OAMe-offset')

# ConsistentSalt-Offset-OAHOnly (Table 4)
os.chdir('../')
os.chdir(run_location + '/Calc-OA')
string = 'CorrectOA OAHOnly ka ../Exp/OASaltDep.txt Null1.txt Null2.txt APR-OPC.txt  ' \
         'APR-TIP3P.txt BEDAM.txt DFT-charged.txt DFT-neutral.txt CCSD(T)-neutral.txt ' \
         'Metadynamics.txt MMPBSA-GAFF.txt MovTyp-1.txt MovTyp-2.txt PERT-bound-c.txt ' \
         'PERT-bound.txt PERT-hrex.txt PERT-hrex-c.txt PERT-hrex-c1.txt PERT-hrex-c2.txt ' \
         'SOMD-1.txt SOMD-2.txt SOMD-3.txt SOMD-4.txt PERT-combo.txt'
args = string.split()
if run_calculation:
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = compute_bootstrap(args)
    results = [RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc]
    pickle.dump(results, open('OAHOnly-offset.pickle', 'wb'))
else:
    results = pickle.load(open('OAHOnly-offset.pickle', 'rb'))
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = results
PrintTable(CalcNames, RawMs, AllMVals, AllMSEMs, Offset=True, OAHOnly=True)

# ConsistentSalt-Offset-OAMeOnly (Table 4)
os.chdir('../')
os.chdir(run_location + '/Calc-OA')
string = 'CorrectOA OAMeOnly ka ../Exp/OASaltDep.txt Null1.txt Null2.txt APR-OPC.txt ' \
         'APR-TIP3P.txt BEDAM.txt DFT-charged.txt DFT-neutral.txt CCSD(T)-neutral.txt ' \
         'Metadynamics.txt MMPBSA-GAFF.txt MovTyp-1.txt MovTyp-2.txt PERT-bound-c.txt ' \
         'PERT-bound.txt PERT-hrex.txt PERT-hrex-c.txt PERT-hrex-c1.txt PERT-hrex-c2.txt ' \
         'SOMD-1.txt SOMD-2.txt SOMD-3.txt SOMD-4.txt MMPBSA-OPLS.txt'
args = string.split()
if run_calculation:
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = compute_bootstrap(args)
    results = [RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc]
    pickle.dump(results, open('OAMeOnly-offset.pickle', 'wb'))
else:
    results = pickle.load(open('OAMeOnly-offset.pickle', 'rb'))
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = results
PrintTable(CalcNames, RawMs, AllMVals, AllMSEMs, Offset=True, OAMeOnly=True)

# CBClip-Abs (Table 5)
os.chdir('../')
os.chdir(run_location + '/Calc-CB')
string = 'ka ../Exp/CBClip.txt Null1.txt Null2.txt BAR-ab-initio.txt BAR-dock.txt ' \
         'TI-ab-initio.txt TI-dock.txt TIxBar.txt BEDAM.txt MovTyp-1.txt MovTyp-2.txt ' \
         'SOMD-1.txt SOMD-2.txt SOMD-3.txt SOMD-4.txt'
args = string.split()
if run_calculation:
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = compute_bootstrap(args)
    results = [RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc]
    pickle.dump(results, open('CBClip-absolute.pickle', 'wb'))
else:
```

```
    results = pickle.load(open('CBClip-absolute.pickle', 'rb'))
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = results
PrintTable(CalcNames, RawMs, AllMVals, AllMSEMs)
plot_summary_horizontal_narrow(Nc, RawMs, AllMBoot, AllMVals, CalcNames, absolute=True,
offset=False, prefix='CBClip',
                               filename='CBClip-absolute')

# AllAvg-Abs
os.chdir('../')
os.chdir(run_location + '/Calc-OA')
string = 'ka ../Exp/OAAllAvg.txt Null1.txt Null2.txt APR-OPC.txt APR-TIP3P.txt ' \
         'BEDAM.txt Metadynamics.txt MMPBSA-GAFF.txt MovTyp-1.txt MovTyp-2.txt ' \
         'PERT-bound-c.txt PERT-bound.txt PERT-hrex.txt PERT-hrex-c.txt PERT-hrex-c1.txt  ' \
         'PERT-hrex-c2.txt SOMD-1.txt SOMD-2.txt SOMD-3.txt SOMD-4.txt'
args = string.split()
if run_calculation:
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = compute_bootstrap(args)
    results = [RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc]
    pickle.dump(results, open('OAH-OAMe-absolute-allavg.pickle', 'wb'))
else:
    results = pickle.load(open('OAH-OAMe-absolute-allavg.pickle', 'rb'))
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = results
PrintTable(CalcNames, RawMs, AllMVals, AllMSEMs, AddDFT=True)

# AllAvg-Offset
os.chdir('../')
os.chdir(run_location + '/Calc-OA')
string = 'CorrectOA ka ../Exp/OAAllAvg.txt Null1.txt Null2.txt APR-OPC.txt ' \
         'APR-TIP3P.txt BEDAM.txt DFT-charged.txt DFT-neutral.txt CCSD(T)-neutral.txt  ' \
         'Metadynamics.txt MMPBSA-GAFF.txt MovTyp-1.txt MovTyp-2.txt PERT-bound-c.txt ' \
         'PERT-bound.txt PERT-hrex.txt PERT-hrex-c.txt PERT-hrex-c1.txt PERT-hrex-c2.txt ' \
         'SOMD-1.txt SOMD-2.txt SOMD-3.txt SOMD-4.txt'
args = string.split()
if run_calculation:
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = compute_bootstrap(args)
    results = [RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc]
    pickle.dump(results, open('OAH-OAMe-offset-allavg.pickle', 'wb'))
else:
    results = pickle.load(open('OAH-OAMe-offset-allavg.pickle', 'rb'))
    RawMs, AllMBoot, AllMVals, AllMSEMs, CalcNames, Nc = results
PrintTable(CalcNames, RawMs, AllMVals, AllMSEMs, Offset=True)
```

Starting structures of free hosts provided to the SAMPL5 participants (in PDB format)

OAH

```
ATOM      1  C1  OCT X   1       1.978  -2.913   2.556  0.00  0.00
ATOM      2  C2  OCT X   1       3.789  -0.891   1.798  0.00  0.00
ATOM      3  C3  OCT X   1       2.095  -1.737   3.319  0.00  0.00
ATOM      4  C4  OCT X   1       2.809  -3.113   1.440  0.00  0.00
ATOM      5  C5  OCT X   1       3.750  -2.126   1.094  0.00  0.00
ATOM      6  C6  OCT X   1       2.873  -0.651   2.862  0.00  0.00
ATOM      7  O1  OCT X   1       4.548   0.204   1.313  0.00  0.00
ATOM      8  C7  OCT X   1       2.984   0.584   3.717  0.00  0.00
ATOM      9  C8  OCT X   1       3.932   1.363   0.655  0.00  0.00
ATOM     10  O2  OCT X   1       3.658   2.395   1.672  0.00  0.00
ATOM     11  C9  OCT X   1       2.364   2.527   2.188  0.00  0.00
ATOM     12  C10 OCT X   1       2.015   1.664   3.219  0.00  0.00
ATOM     13  C11 OCT X   1       0.711   1.822   3.759  0.00  0.00
ATOM     14  C12 OCT X   1       1.508   3.442   1.630  0.00  0.00
ATOM     15  C13 OCT X   1      -0.186   2.733   3.185  0.00  0.00
ATOM     16  C14 OCT X   1       0.221   3.530   2.110  0.00  0.00
ATOM     17  O3  OCT X   1      -0.647   4.303   1.401  0.00  0.00
ATOM     18  C15 OCT X   1      -1.653   2.755   3.681  0.00  0.00
ATOM     19  C16 OCT X   1      -2.574   1.870   2.877  0.00  0.00
ATOM     20  C17 OCT X   1      -3.132   2.412   1.652  0.00  0.00
ATOM     21  C18 OCT X   1      -1.538   3.660   0.425  0.00  0.00
ATOM     22  O4  OCT X   1      -2.783   3.646   1.111  0.00  0.00
ATOM     23  O5  OCT X   1       2.544  -4.128   0.497  0.00  0.00
ATOM     24  C19 OCT X   1       0.819  -3.840   2.830  0.00  0.00
ATOM     25  C20 OCT X   1      -0.432  -3.444   2.049  0.00  0.00
ATOM     26  O6  OCT X   1       0.282  -4.753  -0.020  0.00  0.00
ATOM     27  C21 OCT X   1      -0.654  -3.991   0.770  0.00  0.00
ATOM     28  C22 OCT X   1      -3.975   1.673   0.870  0.00  0.00
ATOM     29  C23 OCT X   1      -4.264   0.367   1.137  0.00  0.00
ATOM     30  C24 OCT X   1      -1.802  -3.727   0.033  0.00  0.00
ATOM     31  C25 OCT X   1      -2.775  -2.918   0.554  0.00  0.00
ATOM     32  O7  OCT X   1      -4.839  -0.410   0.131  0.00  0.00
ATOM     33  O8  OCT X   1      -3.844  -2.574  -0.224  0.00  0.00
ATOM     34  C26 OCT X   1      -3.930  -1.164  -0.733  0.00  0.00
ATOM     35  C27 OCT X   1      -1.468  -2.726   2.607  0.00  0.00
ATOM     36  C28 OCT X   1      -2.672  -2.464   1.903  0.00  0.00
ATOM     37  C29 OCT X   1      -2.927   0.510   3.198  0.00  0.00
ATOM     38  C30 OCT X   1      -3.920  -1.740   2.617  0.00  0.00
ATOM     39  C31 OCT X   1      -3.767  -0.267   2.328  0.00  0.00
ATOM     40  C32 OCT X   1       1.448  -3.948  -0.413  0.00  0.00
ATOM     41  C33 OCT X   1      -1.723   2.568   5.183  0.00  0.00
ATOM     42  C34 OCT X   1      -3.116   2.732   5.795  0.00  0.00
ATOM     43  C35 OCT X   1      -3.094   2.468   7.322  0.00  0.00
ATOM     44  O9  OCT X   1      -2.147   1.947   7.819  0.00  0.00
ATOM     45  C36 OCT X   1       2.971   0.333   5.244  0.00  0.00
ATOM     46  C37 OCT X   1       3.474   1.504   6.068  0.00  0.00
ATOM     47  C38 OCT X   1       4.965   1.511   5.971  0.00  0.00
ATOM     48  O10 OCT X   1       5.655   0.841   6.749  0.00  0.00
ATOM     49  C39 OCT X   1       0.619  -4.262   4.357  0.00  0.00
ATOM     50  C40 OCT X   1      -0.442  -5.344   4.488  0.00  0.00
ATOM     51  C41 OCT X   1       0.254  -6.613   4.033  0.00  0.00
ATOM     52  O11 OCT X   1       1.048  -7.176   4.790  0.00  0.00
ATOM     53  C42 OCT X   1      -3.973  -2.277   4.180  0.00  0.00
ATOM     54  C43 OCT X   1      -5.178  -1.580   4.856  0.00  0.00
ATOM     55  C44 OCT X   1      -5.150  -1.922   6.342  0.00  0.00
ATOM     56  O12 OCT X   1      -4.272  -1.622   7.098  0.00  0.00
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ATOM     57  C45 OCT X   1       4.853   1.891  -0.409  0.00  0.00
ATOM     58  C46 OCT X   1       6.419   2.722  -2.526  0.00  0.00
ATOM     59  C47 OCT X   1       4.806   3.188  -0.838  0.00  0.00
ATOM     60  C48 OCT X   1       5.701   1.021  -1.069  0.00  0.00
ATOM     61  C49 OCT X   1       6.516   1.418  -2.128  0.00  0.00
ATOM     62  C50 OCT X   1       5.539   3.576  -1.883  0.00  0.00
ATOM     63  C51 OCT X   1       1.924  -4.169  -1.843  0.00  0.00
ATOM     64  C52 OCT X   1       2.574  -4.172  -4.542  0.00  0.00
ATOM     65  C53 OCT X   1       1.045  -4.683  -2.706  0.00  0.00
ATOM     66  C54 OCT X   1       3.164  -3.671  -2.347  0.00  0.00
ATOM     67  C55 OCT X   1       3.512  -3.700  -3.673  0.00  0.00
ATOM     68  C56 OCT X   1       1.359  -4.680  -4.087  0.00  0.00
ATOM     69  C57 OCT X   1      -4.364  -1.263  -2.171  0.00  0.00
ATOM     70  C58 OCT X   1      -5.103  -1.290  -4.808  0.00  0.00
ATOM     71  C59 OCT X   1      -5.192  -0.247  -2.658  0.00  0.00
ATOM     72  C60 OCT X   1      -3.934  -2.346  -3.026  0.00  0.00
ATOM     73  C61 OCT X   1      -4.279  -2.305  -4.398  0.00  0.00
ATOM     74  C62 OCT X   1      -5.509  -0.217  -4.001  0.00  0.00
ATOM     75  C63 OCT X   1      -1.585   4.405  -0.927  0.00  0.00
ATOM     76  C64 OCT X   1      -1.514   5.285  -3.524  0.00  0.00
ATOM     77  C65 OCT X   1      -2.738   4.357  -1.719  0.00  0.00
ATOM     78  C66 OCT X   1      -0.357   4.883  -1.423  0.00  0.00
ATOM     79  C67 OCT X   1      -0.365   5.285  -2.742  0.00  0.00
ATOM     80  C68 OCT X   1      -2.680   4.755  -2.998  0.00  0.00
ATOM     81  O13 OCT X   1       4.656  -3.132  -4.231  0.00  0.00
ATOM     82  O14 OCT X   1      -3.921  -3.316  -5.269  0.00  0.00
ATOM     83  O15 OCT X   1      -6.153   0.774  -4.597  0.00  0.00
ATOM     84  O16 OCT X   1       7.371   0.558  -2.749  0.00  0.00
ATOM     85  O17 OCT X   1       5.564   4.887  -2.369  0.00  0.00
ATOM     86  O18 OCT X   1      -3.800   4.813  -3.884  0.00  0.00
ATOM     87  O19 OCT X   1       0.847   5.553  -3.374  0.00  0.00
ATOM     88  C69 OCT X   1      -3.125  -4.382  -4.843  0.00  0.00
ATOM     89  C70 OCT X   1      -1.388  -6.331  -3.996  0.00  0.00
ATOM     90  C71 OCT X   1      -1.766  -4.242  -5.099  0.00  0.00
ATOM     91  C72 OCT X   1      -3.620  -5.488  -4.090  0.00  0.00
ATOM     92  C73 OCT X   1      -2.747  -6.471  -3.632  0.00  0.00
ATOM     93  C74 OCT X   1      -0.884  -5.201  -4.698  0.00  0.00
ATOM     94  O20 OCT X   1       0.436  -5.077  -4.966  0.00  0.00
ATOM     95  C75 OCT X   1       7.014  -0.794  -2.812  0.00  0.00
ATOM     96  C76 OCT X   1       6.603  -3.480  -2.776  0.00  0.00
ATOM     97  C77 OCT X   1       7.868  -1.619  -2.056  0.00  0.00
ATOM     98  C78 OCT X   1       5.857  -1.299  -3.437  0.00  0.00
ATOM     99  C79 OCT X   1       5.691  -2.675  -3.448  0.00  0.00
ATOM    100  C80 OCT X   1       7.644  -2.951  -2.013  0.00  0.00
ATOM    101  C81 OCT X   1      -6.108   2.039  -4.170  0.00  0.00
ATOM    102  C82 OCT X   1      -6.042   4.566  -3.046  0.00  0.00
ATOM    103  C83 OCT X   1      -7.256   2.507  -3.505  0.00  0.00
ATOM    104  C84 OCT X   1      -4.968   2.764  -4.247  0.00  0.00
ATOM    105  C85 OCT X   1      -4.902   4.035  -3.665  0.00  0.00
ATOM    106  C86 OCT X   1      -7.216   3.792  -2.924  0.00  0.00
ATOM    107  C87 OCT X   1      -8.342   4.264  -2.014  0.00  0.00
ATOM    108  O21 OCT X   1      -9.273   3.577  -1.677  0.00  0.00
ATOM    109  C88 OCT X   1       3.543   9.301  -1.437  0.00  0.00
ATOM    110  O22 OCT X   1       4.604   9.675  -1.044  0.00  0.00
ATOM    111  C89 OCT X   1       8.522  -3.870  -1.065  0.00  0.00
ATOM    112  O23 OCT X   1       8.505  -5.024  -1.277  0.00  0.00
ATOM    113  O24 OCT X   1      -4.010   2.747   7.993  0.00  0.00
ATOM    114  O25 OCT X   1      -6.186  -2.444   6.728  0.00  0.00
ATOM    115  O26 OCT X   1       0.095  -6.983   2.900  0.00  0.00
ATOM    116  C90 OCT X   1      -3.155  -7.597  -2.769  0.00  0.00
ATOM    117  O27 OCT X   1      -2.341  -8.300  -2.191  0.00  0.00
ATOM    118  O28 OCT X   1       2.509   9.998  -1.355  0.00  0.00
ATOM    119  O29 OCT X   1      -8.324   5.429  -1.640  0.00  0.00
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ATOM    120  O30 OCT X   1      -4.375  -7.763  -2.582  0.00  0.00
ATOM    121  O31 OCT X   1       9.054  -3.461  -0.061  0.00  0.00
ATOM    122  O32 OCT X   1       5.522   2.279   5.195  0.00  0.00
ATOM    123  C91 OCT X   1       4.411   5.670  -2.419  0.00  0.00
ATOM    124  C92 OCT X   1       2.175   7.280  -2.247  0.00  0.00
ATOM    125  C93 OCT X   1       3.154   5.130  -2.838  0.00  0.00
ATOM    126  C94 OCT X   1       4.539   7.013  -1.988  0.00  0.00
ATOM    127  C95 OCT X   1       3.389   7.886  -1.858  0.00  0.00
ATOM    128  C96 OCT X   1       2.037   5.990  -2.767  0.00  0.00
ATOM    129  H1  OCT X   1       1.314  -1.538   4.047  0.00  0.00
ATOM    130  H2  OCT X   1       4.395  -2.261   0.229  0.00  0.00
ATOM    131  H3  OCT X   1       3.941   1.091   3.577  0.00  0.00
ATOM    132  H4  OCT X   1       2.952   1.069   0.250  0.00  0.00
ATOM    133  H5  OCT X   1       0.467   1.098   4.533  0.00  0.00
ATOM    134  H6  OCT X   1       1.843   4.022   0.774  0.00  0.00
ATOM    135  H7  OCT X   1      -1.997   3.784   3.552  0.00  0.00
ATOM    136  H8  OCT X   1      -1.286   2.608   0.223  0.00  0.00
ATOM    137  H9  OCT X   1       1.122  -4.790   2.385  0.00  0.00
ATOM    138  H10 OCT X   1      -4.370   2.125  -0.036  0.00  0.00
ATOM    139  H11 OCT X   1      -1.891  -4.197  -0.944  0.00  0.00
ATOM    140  H12 OCT X   1      -2.873  -0.867  -0.683  0.00  0.00
ATOM    141  H13 OCT X   1      -1.500  -2.400   3.644  0.00  0.00
ATOM    142  H14 OCT X   1      -2.532   0.040   4.095  0.00  0.00
ATOM    143  H15 OCT X   1      -4.883  -1.929   2.138  0.00  0.00
ATOM    144  H16 OCT X   1       1.041  -2.929  -0.343  0.00  0.00
ATOM    145  H17 OCT X   1      -1.264   1.614   5.448  0.00  0.00
ATOM    146  H18 OCT X   1      -1.085   3.347   5.606  0.00  0.00
ATOM    147  H19 OCT X   1      -3.414   3.770   5.630  0.00  0.00
ATOM    148  H20 OCT X   1      -3.774   1.984   5.347  0.00  0.00
ATOM    149  H21 OCT X   1       3.406  -0.656   5.402  0.00  0.00
ATOM    150  H22 OCT X   1       1.996   0.097   5.676  0.00  0.00
ATOM    151  H23 OCT X   1       3.011   2.450   5.779  0.00  0.00
ATOM    152  H24 OCT X   1       3.270   1.145   7.080  0.00  0.00
ATOM    153  H25 OCT X   1       1.554  -4.578   4.823  0.00  0.00
ATOM    154  H26 OCT X   1       0.270  -3.368   4.877  0.00  0.00
ATOM    155  H27 OCT X   1      -0.679  -5.340   5.554  0.00  0.00
ATOM    156  H28 OCT X   1      -1.368  -5.264   3.915  0.00  0.00
ATOM    157  H29 OCT X   1      -4.199  -3.340   4.277  0.00  0.00
ATOM    158  H30 OCT X   1      -3.135  -2.014   4.830  0.00  0.00
ATOM    159  H31 OCT X   1      -5.092  -0.496   4.762  0.00  0.00
ATOM    160  H32 OCT X   1      -6.105  -1.869   4.357  0.00  0.00
ATOM    161  H33 OCT X   1       6.926   3.160  -3.381  0.00  0.00
ATOM    162  H34 OCT X   1       4.022   3.841  -0.465  0.00  0.00
ATOM    163  H35 OCT X   1       5.818   0.034  -0.628  0.00  0.00
ATOM    164  H36 OCT X   1       2.747  -4.136  -5.614  0.00  0.00
ATOM    165  H37 OCT X   1       0.027  -4.951  -2.431  0.00  0.00
ATOM    166  H38 OCT X   1       3.824  -3.227  -1.606  0.00  0.00
ATOM    167  H39 OCT X   1      -5.329  -1.262  -5.872  0.00  0.00
ATOM    168  H40 OCT X   1      -5.436   0.603  -2.026  0.00  0.00
ATOM    169  H41 OCT X   1      -3.285  -3.112  -2.607  0.00  0.00
ATOM    170  H42 OCT X   1      -1.580   5.825  -4.465  0.00  0.00
ATOM    171  H43 OCT X   1      -3.625   3.890  -1.298  0.00  0.00
ATOM    172  H44 OCT X   1       0.549   4.837  -0.824  0.00  0.00
ATOM    173  H45 OCT X   1      -0.683  -7.078  -3.639  0.00  0.00
ATOM    174  H46 OCT X   1      -1.448  -3.328  -5.595  0.00  0.00
ATOM    175  H47 OCT X   1      -4.698  -5.582  -3.982  0.00  0.00
ATOM    176  H48 OCT X   1       6.286  -4.519  -2.731  0.00  0.00
ATOM    177  H49 OCT X   1       8.671  -1.164  -1.482  0.00  0.00
ATOM    178  H50 OCT X   1       5.075  -0.643  -3.812  0.00  0.00
ATOM    179  H51 OCT X   1      -6.130   5.577  -2.656  0.00  0.00
ATOM    180  H52 OCT X   1      -8.178   1.933  -3.529  0.00  0.00
ATOM    181  H53 OCT X   1      -4.108   2.291  -4.715  0.00  0.00
ATOM    182  H54 OCT X   1       1.273   7.875  -2.370  0.00  0.00
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ATOM    183  H55 OCT X   1       3.063   4.090  -3.141  0.00  0.00
ATOM    184  H56 OCT X   1       5.499   7.465  -1.750  0.00  0.00
END
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ATOM      1  C1  OCB X   1       2.059  -2.526   2.919  0.00  0.00
ATOM      2  C2  OCB X   1       3.765  -0.415   2.140  0.00  0.00
ATOM      3  C3  OCB X   1       2.121  -1.325   3.660  0.00  0.00
ATOM      4  C4  OCB X   1       2.869  -2.623   1.775  0.00  0.00
ATOM      5  C5  OCB X   1       3.753  -1.604   1.419  0.00  0.00
ATOM      6  C6  OCB X   1       2.978  -0.262   3.289  0.00  0.00
ATOM      7  O1  OCB X   1       4.589   0.587   1.695  0.00  0.00
ATOM      8  C7  OCB X   1       3.010   1.075   4.038  0.00  0.00
ATOM      9  C8  OCB X   1       3.854   1.602   0.976  0.00  0.00
ATOM     10  O2  OCB X   1       3.612   2.767   1.787  0.00  0.00
ATOM     11  C9  OCB X   1       2.333   2.775   2.281  0.00  0.00
ATOM     12  C10 OCB X   1       1.975   2.006   3.396  0.00  0.00
ATOM     13  C11 OCB X   1       0.630   2.053   3.816  0.00  0.00
ATOM     14  C12 OCB X   1       1.407   3.597   1.637  0.00  0.00
ATOM     15  C13 OCB X   1      -0.336   2.866   3.172  0.00  0.00
ATOM     16  C14 OCB X   1       0.073   3.601   2.045  0.00  0.00
ATOM     17  O3  OCB X   1      -0.785   4.371   1.295  0.00  0.00
ATOM     18  C15 OCB X   1      -1.789   2.927   3.675  0.00  0.00
ATOM     19  C16 OCB X   1      -2.651   1.928   2.902  0.00  0.00
ATOM     20  C17 OCB X   1      -3.197   2.278   1.655  0.00  0.00
ATOM     21  C18 OCB X   1      -1.656   3.550   0.490  0.00  0.00
ATOM     22  O4  OCB X   1      -2.973   3.506   1.080  0.00  0.00
ATOM     23  O5  OCB X   1       2.817  -3.711   0.939  0.00  0.00
ATOM     24  C19 OCB X   1       1.089  -3.668   3.273  0.00  0.00
ATOM     25  C20 OCB X   1      -0.228  -3.456   2.521  0.00  0.00
ATOM     26  O6  OCB X   1       0.639  -4.578   0.548  0.00  0.00
ATOM     27  C21 OCB X   1      -0.378  -3.938   1.213  0.00  0.00
ATOM     28  C22 OCB X   1      -3.972   1.381   0.921  0.00  0.00
ATOM     29  C23 OCB X   1      -4.117   0.071   1.371  0.00  0.00
ATOM     30  C24 OCB X   1      -1.588  -3.806   0.533  0.00  0.00
ATOM     31  C25 OCB X   1      -2.639  -3.096   1.114  0.00  0.00
ATOM     32  O7  OCB X   1      -4.781  -0.799   0.539  0.00  0.00
ATOM     33  O8  OCB X   1      -3.778  -2.940   0.362  0.00  0.00
ATOM     34  C26 OCB X   1      -3.846  -1.614  -0.199  0.00  0.00
ATOM     35  C27 OCB X   1      -1.311  -2.754   3.093  0.00  0.00
ATOM     36  C28 OCB X   1      -2.535  -2.581   2.415  0.00  0.00
ATOM     37  C29 OCB X   1      -2.855   0.609   3.356  0.00  0.00
ATOM     38  C30 OCB X   1      -3.698  -1.799   3.041  0.00  0.00
ATOM     39  C31 OCB X   1      -3.588  -0.337   2.606  0.00  0.00
ATOM     40  C32 OCB X   1       1.644  -3.646   0.102  0.00  0.00
ATOM     41  C33 OCB X   1      -1.892   2.880   5.233  0.00  0.00
ATOM     42  C34 OCB X   1      -3.277   3.244   5.784  0.00  0.00
ATOM     43  C35 OCB X   1      -3.320   3.681   7.259  0.00  0.00
ATOM     44  O9  OCB X   1      -2.280   3.497   7.949  0.00  0.00
ATOM     45  C36 OCB X   1       2.963   0.933   5.580  0.00  0.00
ATOM     46  C37 OCB X   1       3.421   2.199   6.318  0.00  0.00
ATOM     47  C38 OCB X   1       4.943   2.357   6.418  0.00  0.00
ATOM     48  O10 OCB X   1       5.527   1.568   7.218  0.00  0.00
ATOM     49  C39 OCB X   1       0.947  -3.926   4.802  0.00  0.00
ATOM     50  C40 OCB X   1       0.127  -5.172   5.167  0.00  0.00
ATOM     51  C41 OCB X   1       0.921  -6.479   5.126  0.00  0.00
ATOM     52  O11 OCB X   1       1.685  -6.687   6.115  0.00  0.00
ATOM     53  C42 OCB X   1      -3.882  -2.063   4.565  0.00  0.00
ATOM     54  C43 OCB X   1      -5.222  -1.552   5.113  0.00  0.00
ATOM     55  C44 OCB X   1      -5.610  -2.138   6.479  0.00  0.00
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ATOM     56  O12 OCB X   1      -4.670  -2.373   7.287  0.00  0.00
ATOM     57  C45 OCB X   1       4.693   2.039  -0.235  0.00  0.00
ATOM     58  C46 OCB X   1       6.129   2.770  -2.537  0.00  0.00
ATOM     59  C47 OCB X   1       4.545   3.324  -0.799  0.00  0.00
ATOM     60  C48 OCB X   1       5.564   1.129  -0.861  0.00  0.00
ATOM     61  C49 OCB X   1       6.270   1.487  -2.010  0.00  0.00
ATOM     62  C50 OCB X   1       5.242   3.678  -1.955  0.00  0.00
ATOM     63  C51 OCB X   1       2.049  -3.987  -1.343  0.00  0.00
ATOM     64  C52 OCB X   1       2.712  -4.470  -4.028  0.00  0.00
ATOM     65  C53 OCB X   1       1.145  -4.644  -2.204  0.00  0.00
ATOM     66  C54 OCB X   1       3.292  -3.566  -1.869  0.00  0.00
ATOM     67  C55 OCB X   1       3.627  -3.809  -3.202  0.00  0.00
ATOM     68  C56 OCB X   1       1.470  -4.884  -3.539  0.00  0.00
ATOM     69  C57 OCB X   1      -4.312  -1.729  -1.663  0.00  0.00
ATOM     70  C58 OCB X   1      -5.031  -1.898  -4.378  0.00  0.00
ATOM     71  C59 OCB X   1      -5.100  -0.726  -2.263  0.00  0.00
ATOM     72  C60 OCB X   1      -3.876  -2.805  -2.468  0.00  0.00
ATOM     73  C61 OCB X   1      -4.235  -2.896  -3.814  0.00  0.00
ATOM     74  C62 OCB X   1      -5.443  -0.803  -3.615  0.00  0.00
ATOM     75  C63 OCB X   1      -1.741   4.125  -0.944  0.00  0.00
ATOM     76  C64 OCB X   1      -1.822   4.957  -3.625  0.00  0.00
ATOM     77  C65 OCB X   1      -2.943   4.057  -1.690  0.00  0.00
ATOM     78  C66 OCB X   1      -0.579   4.620  -1.586  0.00  0.00
ATOM     79  C67 OCB X   1      -0.621   5.036  -2.919  0.00  0.00
ATOM     80  C68 OCB X   1      -2.980   4.465  -3.025  0.00  0.00
ATOM     81  O13 OCB X   1       4.801  -3.441  -3.826  0.00  0.00
ATOM     82  O14 OCB X   1      -3.878  -3.907  -4.682  0.00  0.00
ATOM     83  O15 OCB X   1      -6.213   0.127  -4.283  0.00  0.00
ATOM     84  O16 OCB X   1       7.136   0.651  -2.684  0.00  0.00
ATOM     85  O17 OCB X   1       5.145   4.900  -2.580  0.00  0.00
ATOM     86  O18 OCB X   1      -4.092   4.480  -3.839  0.00  0.00
ATOM     87  O19 OCB X   1       0.440   5.464  -3.685  0.00  0.00
ATOM     88  C69 OCB X   1      -2.943  -4.831  -4.270  0.00  0.00
ATOM     89  C70 OCB X   1      -1.141  -6.841  -3.591  0.00  0.00
ATOM     90  C71 OCB X   1      -1.584  -4.650  -4.576  0.00  0.00
ATOM     91  C72 OCB X   1      -3.402  -6.021  -3.692  0.00  0.00
ATOM     92  C73 OCB X   1      -2.512  -7.060  -3.376  0.00  0.00
ATOM     93  C74 OCB X   1      -0.683  -5.646  -4.165  0.00  0.00
ATOM     94  O20 OCB X   1       0.661  -5.537  -4.450  0.00  0.00
ATOM     95  C75 OCB X   1       6.928  -0.712  -2.589  0.00  0.00
ATOM     96  C76 OCB X   1       6.768  -3.490  -2.477  0.00  0.00
ATOM     97  C77 OCB X   1       7.930  -1.450  -1.946  0.00  0.00
ATOM     98  C78 OCB X   1       5.854  -1.353  -3.233  0.00  0.00
ATOM     99  C79 OCB X   1       5.765  -2.752  -3.121  0.00  0.00
ATOM    100  C80 OCB X   1       7.882  -2.853  -1.903  0.00  0.00
ATOM    101  C81 OCB X   1      -6.167   1.437  -3.853  0.00  0.00
ATOM    102  C82 OCB X   1      -6.309   4.113  -3.105  0.00  0.00
ATOM    103  C83 OCB X   1      -7.365   1.969  -3.356  0.00  0.00
ATOM    104  C84 OCB X   1      -5.038   2.253  -4.054  0.00  0.00
ATOM    105  C85 OCB X   1      -5.110   3.583  -3.605  0.00  0.00
ATOM    106  C86 OCB X   1      -7.466   3.324  -3.006  0.00  0.00
ATOM    107  C87 OCB X   1      -8.799   3.932  -2.614  0.00  0.00
ATOM    108  O21 OCB X   1      -9.812   3.162  -2.595  0.00  0.00
ATOM    109  C88 OCB X   1       3.092   9.309  -2.201  0.00  0.00
ATOM    110  O22 OCB X   1       4.259   9.752  -1.948  0.00  0.00
ATOM    111  C89 OCB X   1       9.040  -3.653  -1.335  0.00  0.00
ATOM    112  O23 OCB X   1       9.015  -4.916  -1.494  0.00  0.00
ATOM    113  O24 OCB X   1      -4.406   4.235   7.616  0.00  0.00
ATOM    114  O25 OCB X   1      -6.853  -2.332   6.644  0.00  0.00
ATOM    115  O26 OCB X   1       0.679  -7.242   4.149  0.00  0.00
ATOM    116  C90 OCB X   1      -3.031  -8.405  -2.902  0.00  0.00
ATOM    117  O27 OCB X   1      -2.180  -9.347  -2.775  0.00  0.00
ATOM    118  O28 OCB X   1       2.064  10.036  -2.385  0.00  0.00
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ATOM    119  O29 OCB X   1      -8.833   5.189  -2.407  0.00  0.00
ATOM    120  O30 OCB X   1      -4.287  -8.532  -2.762  0.00  0.00
ATOM    121  O31 OCB X   1      10.005  -3.002  -0.816  0.00  0.00
ATOM    122  O32 OCB X   1       5.441   3.311   5.753  0.00  0.00
ATOM    123  C91 OCB X   1       3.941   5.579  -2.586  0.00  0.00
ATOM    124  C92 OCB X   1       1.703   7.249  -2.754  0.00  0.00
ATOM    125  C93 OCB X   1       2.730   5.047  -3.067  0.00  0.00
ATOM    126  C94 OCB X   1       4.036   6.944  -2.266  0.00  0.00
ATOM    127  C95 OCB X   1       2.933   7.809  -2.379  0.00  0.00
ATOM    128  C96 OCB X   1       1.602   5.890  -3.083  0.00  0.00
ATOM    129  C97 OCB X   1       2.616   3.636  -3.578  0.00  0.00
ATOM    130  C98 OCB X   1       4.823  -0.575  -4.000  0.00  0.00
ATOM    131  C99 OCB X   1      -1.115  -3.424  -5.303  0.00  0.00
ATOM    132  C   OCB X   1      -3.811   1.729  -4.742  0.00  0.00
ATOM    133  H1  OCB X   1       1.473  -1.198   4.524  0.00  0.00
ATOM    134  H2  OCB X   1       4.406  -1.722   0.563  0.00  0.00
ATOM    135  H3  OCB X   1       4.002   1.514   3.863  0.00  0.00
ATOM    136  H4  OCB X   1       2.920   1.199   0.549  0.00  0.00
ATOM    137  H5  OCB X   1       0.323   1.436   4.656  0.00  0.00
ATOM    138  H6  OCB X   1       1.722   4.213   0.804  0.00  0.00
ATOM    139  H7  OCB X   1      -2.157   3.934   3.430  0.00  0.00
ATOM    140  H8  OCB X   1      -1.239   2.537   0.349  0.00  0.00
ATOM    141  H9  OCB X   1       1.537  -4.601   2.901  0.00  0.00
ATOM    142  H10 OCB X   1      -4.414   1.683  -0.021  0.00  0.00
ATOM    143  H11 OCB X   1      -1.701  -4.242  -0.452  0.00  0.00
ATOM    144  H12 OCB X   1      -2.852  -1.141  -0.259  0.00  0.00
ATOM    145  H13 OCB X   1      -1.202  -2.337   4.090  0.00  0.00
ATOM    146  H14 OCB X   1      -2.405   0.300   4.295  0.00  0.00
ATOM    147  H15 OCB X   1      -4.621  -2.205   2.603  0.00  0.00
ATOM    148  H16 OCB X   1       1.240  -2.620   0.038  0.00  0.00
ATOM    149  H17 OCB X   1      -1.608   1.897   5.628  0.00  0.00
ATOM    150  H18 OCB X   1      -1.158   3.589   5.639  0.00  0.00
ATOM    151  H19 OCB X   1      -3.695   4.072   5.199  0.00  0.00
ATOM    152  H20 OCB X   1      -3.955   2.390   5.668  0.00  0.00
ATOM    153  H21 OCB X   1       3.610   0.098   5.881  0.00  0.00
ATOM    154  H22 OCB X   1       1.955   0.673   5.919  0.00  0.00
ATOM    155  H23 OCB X   1       2.976   3.095   5.873  0.00  0.00
ATOM    156  H24 OCB X   1       3.049   2.150   7.350  0.00  0.00
ATOM    157  H25 OCB X   1       1.951  -4.017   5.237  0.00  0.00
ATOM    158  H26 OCB X   1       0.484  -3.064   5.295  0.00  0.00
ATOM    159  H27 OCB X   1      -0.230  -5.056   6.199  0.00  0.00
ATOM    160  H28 OCB X   1      -0.774  -5.259   4.549  0.00  0.00
ATOM    161  H29 OCB X   1      -3.831  -3.147   4.735  0.00  0.00
ATOM    162  H30 OCB X   1      -3.065  -1.630   5.153  0.00  0.00
ATOM    163  H31 OCB X   1      -5.196  -0.461   5.208  0.00  0.00
ATOM    164  H32 OCB X   1      -6.024  -1.798   4.406  0.00  0.00
ATOM    165  H33 OCB X   1       6.688   3.056  -3.422  0.00  0.00
ATOM    166  H34 OCB X   1       3.885   4.049  -0.327  0.00  0.00
ATOM    167  H35 OCB X   1       5.699   0.137  -0.434  0.00  0.00
ATOM    168  H36 OCB X   1       2.971  -4.665  -5.064  0.00  0.00
ATOM    169  H37 OCB X   1       0.191  -4.981  -1.807  0.00  0.00
ATOM    170  H38 OCB X   1       3.997  -3.061  -1.217  0.00  0.00
ATOM    171  H39 OCB X   1      -5.320  -1.964  -5.422  0.00  0.00
ATOM    172  H40 OCB X   1      -5.451   0.110  -1.665  0.00  0.00
ATOM    173  H41 OCB X   1      -3.264  -3.581  -2.018  0.00  0.00
ATOM    174  H42 OCB X   1      -1.853   5.275  -4.664  0.00  0.00
ATOM    175  H43 OCB X   1      -3.851   3.692  -1.218  0.00  0.00
ATOM    176  H44 OCB X   1       0.358   4.658  -1.039  0.00  0.00
ATOM    177  H45 OCB X   1      -0.430  -7.623  -3.326  0.00  0.00
ATOM    178  H46 OCB X   1      -4.467  -6.162  -3.513  0.00  0.00
ATOM    179  H47 OCB X   1       6.709  -4.578  -2.452  0.00  0.00
ATOM    180  H48 OCB X   1       8.776  -0.935  -1.494  0.00  0.00
ATOM    181  H49 OCB X   1      -6.360   5.166  -2.833  0.00  0.00
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ATOM    182  H50 OCB X   1      -8.244   1.332  -3.271  0.00  0.00
ATOM    183  H51 OCB X   1       0.834   7.897  -2.858  0.00  0.00
ATOM    184  H52 OCB X   1       4.999   7.359  -1.969  0.00  0.00
ATOM    185  H53 OCB X   1       3.537   3.317  -4.073  0.00  0.00
ATOM    186  H54 OCB X   1       2.381   2.952  -2.758  0.00  0.00
ATOM    187  H55 OCB X   1       1.832   3.543  -4.337  0.00  0.00
ATOM    188  H56 OCB X   1       4.010  -0.268  -3.335  0.00  0.00
ATOM    189  H57 OCB X   1       5.260   0.313  -4.467  0.00  0.00
ATOM    190  H58 OCB X   1       4.401  -1.166  -4.820  0.00  0.00
ATOM    191  H59 OCB X   1      -1.859  -3.093  -6.035  0.00  0.00
ATOM    192  H60 OCB X   1      -0.923  -2.612  -4.596  0.00  0.00
ATOM    193  H61 OCB X   1      -0.201  -3.621  -5.874  0.00  0.00
ATOM    194  H62 OCB X   1      -3.124   1.286  -4.015  0.00  0.00
ATOM    195  H63 OCB X   1      -4.070   0.977  -5.495  0.00  0.00
ATOM    196  H64 OCB X   1      -3.289   2.521  -5.289  0.00  0.00
END
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CBClip

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ATOM      1  C1  CLP X   1       3.196  -0.441   3.284  0.00  0.00
ATOM      2  C2  CLP X   1       1.800  -0.805   3.965  0.00  0.00
ATOM      3  N1  CLP X   1       3.400  -1.513   2.343  0.00  0.00
ATOM      4  N2  CLP X   1       1.314  -1.888   3.115  0.00  0.00
ATOM      5  N3  CLP X   1       2.923   0.805   2.600  0.00  0.00
ATOM      6  N4  CLP X   1       1.037   0.422   3.786  0.00  0.00
ATOM      7  C3  CLP X   1       2.271  -2.295   2.196  0.00  0.00
ATOM      8  C4  CLP X   1       1.688   1.318   2.948  0.00  0.00
ATOM      9  O1  CLP X   1       2.149  -3.208   1.391  0.00  0.00
ATOM     10  O2  CLP X   1       1.241   2.391   2.567  0.00  0.00
ATOM     11  C5  CLP X   1       0.135  -2.673   3.360  0.00  0.00
ATOM     12  C6  CLP X   1       4.447  -1.485   1.354  0.00  0.00
ATOM     13  C7  CLP X   1       3.857   1.433   1.674  0.00  0.00
ATOM     14  C8  CLP X   1       3.905   0.775   0.307  0.00  0.00
ATOM     15  C9  CLP X   1       3.792   1.555  -0.865  0.00  0.00
ATOM     16  C10 CLP X   1       4.053  -1.189  -1.130  0.00  0.00
ATOM     17  C11 CLP X   1       3.703   0.981  -2.159  0.00  0.00
ATOM     18  C12 CLP X   1       4.108  -0.616   0.161  0.00  0.00
ATOM     19  C13 CLP X   1       3.812  -0.420  -2.292  0.00  0.00
ATOM     20  C14 CLP X   1       3.505   1.755  -3.323  0.00  0.00
ATOM     21  C15 CLP X   1       3.426   1.174  -4.589  0.00  0.00
ATOM     22  C16 CLP X   1       3.509  -0.203  -4.718  0.00  0.00
ATOM     23  C17 CLP X   1       3.685  -0.990  -3.582  0.00  0.00
ATOM     24  O3  CLP X   1       3.769   2.935  -0.766  0.00  0.00
ATOM     25  O4  CLP X   1       4.133  -2.561  -1.226  0.00  0.00
ATOM     26  C18 CLP X   1       5.105   3.455  -0.676  0.00  0.00
ATOM     27  C19 CLP X   1       5.281   4.666  -1.588  0.00  0.00
ATOM     28  C20 CLP X   1       4.479   5.897  -1.176  0.00  0.00
ATOM     29  C21 CLP X   1       5.434  -3.008  -1.607  0.00  0.00
ATOM     30  C22 CLP X   1       5.595  -4.472  -1.200  0.00  0.00
ATOM     31  C23 CLP X   1       6.850  -4.775  -0.384  0.00  0.00
ATOM     32  S1  CLP X   1       5.469   7.371  -0.965  0.00  0.00
ATOM     33  O5  CLP X   1       6.575   7.124  -0.072  0.00  0.00
ATOM     34  O6  CLP X   1       5.644   8.063  -2.229  0.00  0.00
ATOM     35  S2  CLP X   1       8.392  -4.957  -1.290  0.00  0.00
ATOM     36  O7  CLP X   1       8.942  -3.667  -1.664  0.00  0.00
ATOM     37  O8  CLP X   1       9.224  -5.926  -0.617  0.00  0.00
ATOM     38  O9  CLP X   1       4.405   8.230  -0.112  0.00  0.00
ATOM     39  O10 CLP X   1       7.841  -5.638  -2.642  0.00  0.00
ATOM     40  C24 CLP X   1      -3.249  -1.045   2.896  0.00  0.00
ATOM     41  C25 CLP X   1      -1.898  -1.147   3.742  0.00  0.00
ATOM     42  N5  CLP X   1      -3.219   0.300   2.369  0.00  0.00
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ATOM     43  N6  CLP X   1      -1.389   0.218   3.690  0.00  0.00
ATOM     44  N7  CLP X   1      -3.053  -1.992   1.828  0.00  0.00
ATOM     45  N8  CLP X   1      -1.091  -2.053   2.933  0.00  0.00
ATOM     46  C26 CLP X   1      -2.157   1.032   2.867  0.00  0.00
ATOM     47  C27 CLP X   1      -1.758  -2.468   1.789  0.00  0.00
ATOM     48  O11 CLP X   1      -1.920   2.204   2.613  0.00  0.00
ATOM     49  O12 CLP X   1      -1.285  -3.145   0.884  0.00  0.00
ATOM     50  C28 CLP X   1      -0.236   0.707   4.407  0.00  0.00
ATOM     51  C29 CLP X   1      -4.184   0.793   1.406  0.00  0.00
ATOM     52  C30 CLP X   1      -3.997  -2.167   0.750  0.00  0.00
ATOM     53  C31 CLP X   1      -3.923  -1.102  -0.322  0.00  0.00
ATOM     54  C32 CLP X   1      -3.853  -1.499  -1.682  0.00  0.00
ATOM     55  C33 CLP X   1      -4.028   1.199  -1.091  0.00  0.00
ATOM     56  C34 CLP X   1      -3.808  -0.570  -2.749  0.00  0.00
ATOM     57  C35 CLP X   1      -4.007   0.278  -0.016  0.00  0.00
ATOM     58  C36 CLP X   1      -3.897   0.805  -2.449  0.00  0.00
ATOM     59  C37 CLP X   1      -3.657  -0.032  -5.139  0.00  0.00
ATOM     60  C38 CLP X   1      -3.743   1.319  -4.845  0.00  0.00
ATOM     61  C39 CLP X   1      -3.847   1.731  -3.516  0.00  0.00
ATOM     62  O13 CLP X   1      -3.750  -2.845  -1.982  0.00  0.00
ATOM     63  O14 CLP X   1      -4.090   2.545  -0.796  0.00  0.00
ATOM     64  C40 CLP X   1      -5.045  -3.420  -2.198  0.00  0.00
ATOM     65  C41 CLP X   1      -4.907  -4.935  -2.364  0.00  0.00
ATOM     66  C42 CLP X   1      -5.396  -5.723  -1.152  0.00  0.00
ATOM     67  C43 CLP X   1      -5.437   3.042  -0.880  0.00  0.00
ATOM     68  C44 CLP X   1      -5.369   4.524  -0.540  0.00  0.00
ATOM     69  C45 CLP X   1      -6.710   5.219  -0.711  0.00  0.00
ATOM     70  S3  CLP X   1      -7.033  -6.430  -1.325  0.00  0.00
ATOM     71  O15 CLP X   1      -7.290  -7.311  -0.212  0.00  0.00
ATOM     72  O16 CLP X   1      -8.003  -5.427  -1.720  0.00  0.00
ATOM     73  S4  CLP X   1      -6.611   6.954  -0.282  0.00  0.00
ATOM     74  O17 CLP X   1      -5.395   7.518  -0.821  0.00  0.00
ATOM     75  O18 CLP X   1      -7.906   7.565  -0.462  0.00  0.00
ATOM     76  O19 CLP X   1      -6.759  -7.383  -2.595  0.00  0.00
ATOM     77  O20 CLP X   1      -6.422   6.785   1.311  0.00  0.00
ATOM     78  C46 CLP X   1      -3.678  -0.963  -4.103  0.00  0.00
ATOM     79  C47 CLP X   1      -4.531  -1.313   3.697  0.00  0.00
ATOM     80  C48 CLP X   1      -2.113  -1.649   5.176  0.00  0.00
ATOM     81  C49 CLP X   1       1.938  -1.236   5.432  0.00  0.00
ATOM     82  C50 CLP X   1       4.369  -0.289   4.262  0.00  0.00
ATOM     83  H1  CLP X   1       0.072  -2.903   4.403  0.00  0.00
ATOM     84  H2  CLP X   1       0.241  -3.559   2.769  0.00  0.00
ATOM     85  H3  CLP X   1       4.659  -2.481   1.025  0.00  0.00
ATOM     86  H4  CLP X   1       5.309  -1.054   1.820  0.00  0.00
ATOM     87  H5  CLP X   1       4.836   1.437   2.103  0.00  0.00
ATOM     88  H6  CLP X   1       3.501   2.430   1.517  0.00  0.00
ATOM     89  H7  CLP X   1       3.414   2.779  -3.235  0.00  0.00
ATOM     90  H8  CLP X   1       3.307   1.766  -5.425  0.00  0.00
ATOM     91  H9  CLP X   1       3.441  -0.643  -5.649  0.00  0.00
ATOM     92  H10 CLP X   1       3.723  -2.016  -3.683  0.00  0.00
ATOM     93  H11 CLP X   1       5.812   2.695  -0.936  0.00  0.00
ATOM     94  H12 CLP X   1       5.277   3.765   0.334  0.00  0.00
ATOM     95  H13 CLP X   1       5.024   4.395  -2.591  0.00  0.00
ATOM     96  H14 CLP X   1       6.310   4.947  -1.506  0.00  0.00
ATOM     97  H15 CLP X   1       3.949   5.690  -0.269  0.00  0.00
ATOM     98  H16 CLP X   1       3.803   6.100  -1.980  0.00  0.00
ATOM     99  H17 CLP X   1       6.186  -2.408  -1.139  0.00  0.00
ATOM    100  H18 CLP X   1       5.548  -2.917  -2.667  0.00  0.00
ATOM    101  H19 CLP X   1       5.585  -5.086  -2.076  0.00  0.00
ATOM    102  H20 CLP X   1       4.768  -4.689  -0.556  0.00  0.00
ATOM    103  H21 CLP X   1       6.683  -5.659   0.196  0.00  0.00
ATOM    104  H22 CLP X   1       6.996  -3.900   0.214  0.00  0.00
ATOM    105  H23 CLP X   1      -0.331   1.764   4.550  0.00  0.00
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ATOM    106  H24 CLP X   1      -0.229   0.178   5.337  0.00  0.00
ATOM    107  H25 CLP X   1      -4.159   1.863   1.399  0.00  0.00
ATOM    108  H26 CLP X   1      -5.130   0.416   1.731  0.00  0.00
ATOM    109  H27 CLP X   1      -4.989  -2.202   1.148  0.00  0.00
ATOM    110  H28 CLP X   1      -3.736  -3.088   0.272  0.00  0.00
ATOM    111  H29 CLP X   1      -3.579  -0.347  -6.118  0.00  0.00
ATOM    112  H30 CLP X   1      -3.729   2.017  -5.606  0.00  0.00
ATOM    113  H31 CLP X   1      -3.890   2.740  -3.306  0.00  0.00
ATOM    114  H32 CLP X   1      -5.501  -2.992  -3.067  0.00  0.00
ATOM    115  H33 CLP X   1      -5.669  -3.213  -1.354  0.00  0.00
ATOM    116  H34 CLP X   1      -3.885  -5.181  -2.564  0.00  0.00
ATOM    117  H35 CLP X   1      -5.532  -5.214  -3.186  0.00  0.00
ATOM    118  H36 CLP X   1      -5.372  -5.094  -0.286  0.00  0.00
ATOM    119  H37 CLP X   1      -4.729  -6.554  -1.055  0.00  0.00
ATOM    120  H38 CLP X   1      -6.077   2.524  -0.196  0.00  0.00
ATOM    121  H39 CLP X   1      -5.844   2.889  -1.858  0.00  0.00
ATOM    122  H40 CLP X   1      -4.633   5.002  -1.154  0.00  0.00
ATOM    123  H41 CLP X   1      -5.097   4.604   0.491  0.00  0.00
ATOM    124  H42 CLP X   1      -7.450   4.736  -0.106  0.00  0.00
ATOM    125  H43 CLP X   1      -6.988   5.149  -1.742  0.00  0.00
ATOM    126  H44 CLP X   1      -3.596  -1.967  -4.328  0.00  0.00
ATOM    127  H45 CLP X   1      -4.626  -0.584   4.473  0.00  0.00
ATOM    128  H46 CLP X   1      -4.508  -2.298   4.115  0.00  0.00
ATOM    129  H47 CLP X   1      -5.375  -1.242   3.043  0.00  0.00
ATOM    130  H48 CLP X   1      -2.710  -0.944   5.716  0.00  0.00
ATOM    131  H49 CLP X   1      -1.172  -1.789   5.665  0.00  0.00
ATOM    132  H50 CLP X   1      -2.622  -2.591   5.146  0.00  0.00
ATOM    133  H51 CLP X   1       2.507  -2.140   5.487  0.00  0.00
ATOM    134  H52 CLP X   1       0.971  -1.380   5.868  0.00  0.00
ATOM    135  H53 CLP X   1       2.443  -0.467   5.978  0.00  0.00
ATOM    136  H54 CLP X   1       4.549  -1.222   4.753  0.00  0.00
ATOM    137  H55 CLP X   1       4.154   0.472   4.983  0.00  0.00
ATOM    138  H56 CLP X   1       5.246  -0.003   3.719  0.00  0.00
END
```

SAMPL5 instruction file

SAMPL5 Host-Guest Systems, Measurements and Starting Files

Updated October 6, 2015

This challenge is based on three different hosts, which we are calling OctaAcidH (OAH), OctaAcidMe (OAMe) and CBClip, in aqueous solution. The measurements for these systems were generously carried out specifically for SAMPL5 by Professors Bruce Gibb (Tulane University; OctaAcids) and Lyle Isaacs (U. Maryland; CBClip). Data will be provided for one set of 6 guests with both OctaAcids, for a total of 12 measurements; and for a different set of 10 guests for CBClip.

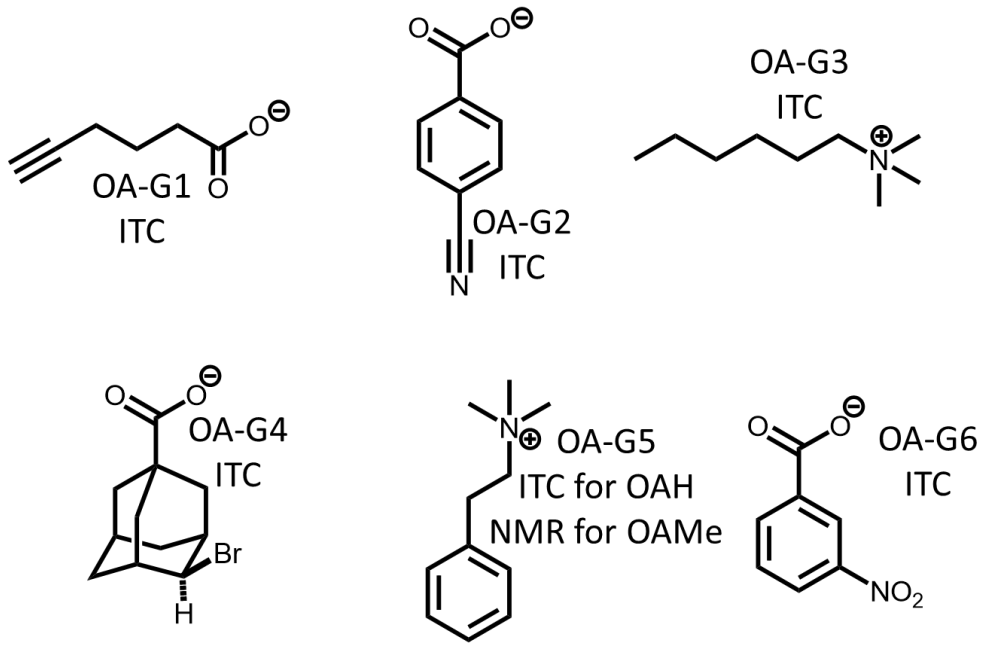
The following subsections describe these systems, the experimental conditions and measurements, the quantities to be predicted, and how the molecule and simulation files provided in the download were set up.

OctaAcids

Two of the host molecules, OctaAcidH and OctaAcidMe, are closely related to each other, as the Me version simply has four methyl groups in place of four hydrogens. This change modifies the shape of the

binding cavity. Host OctaAcidMe is described here: doi:10.1021/ja200633d and host OctaAcidH is described here doi:10.1007/s10822-013-9690-2. There are also a number of papers from SAMPL4 which discuss calculations for this system, as summarized here: doi:10.1007/s10822-014-9735-1. OctaAcidH was used in the previous SAMPL4 challenge, but with a different set of guest molecules.

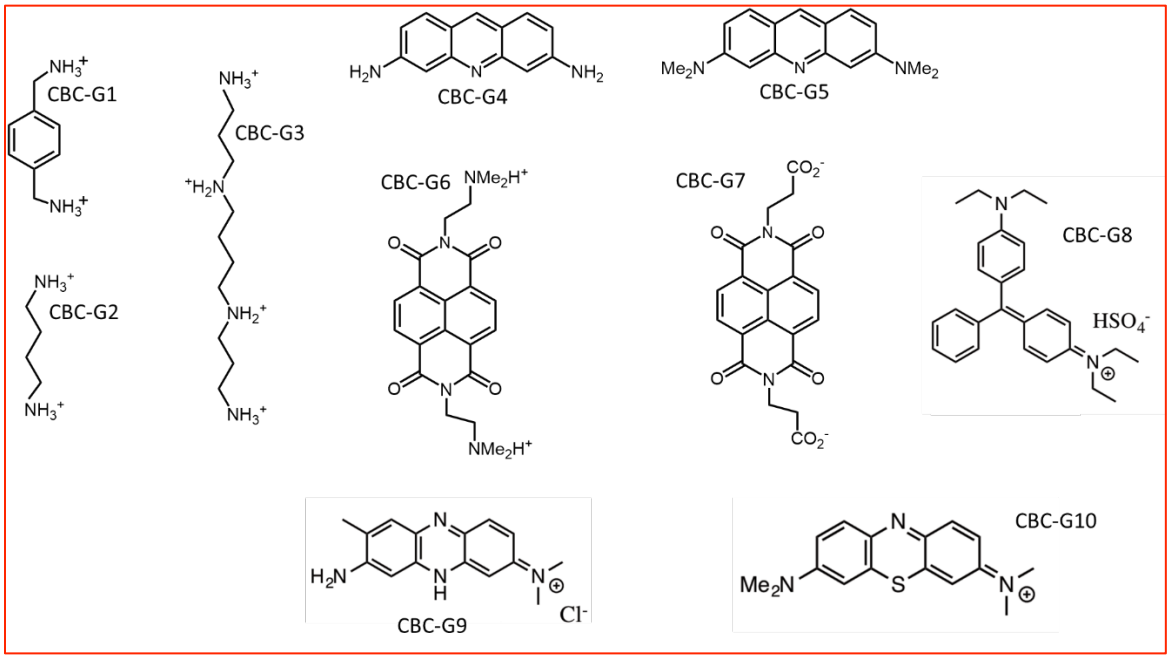
For the present SAMPL5 challenge, experimental binding data were obtained for the association of the following set of six guest molecules, OA-G1 to OA-G6, to both OctaAcidH and OctaAcidMe:



Binding affinities (Ka) values will be available for all of these, measured by either isothermal titration calorimetry (ITC) or NMR, as indicated, and binding enthalpies also will be available for the studied by ITC, but not the ones studied by NMR, as noted in the graphic. The main challenge is to compute 12 binding free energies (or association constants), and participants are also invited to compute the binding enthalpies. All measurements were done in aqueous 10mM sodium phosphate buffer at pH 11.5, at 298K, except for OA-G6 (nitrobenzoic acid), for which the buffer was 50mM sodium phosphate at pH 11.5.

CBClip

The CBClip host is a new “molecular clip” that is chemically related to the cucurbituril class of synthetic hosts. A paper describing this family of clips may be found here: doi:10.1039/c5ob00184f doi:10.1021/jm501276u, and the clip used in SAMPL5 is 2b (R = $(CH_2)_3SO3_Na$) in this paper. The SAMPL5 challenge is to compute the binding free energies (association constants) of ten guest molecules to this host. The initial download on 9/15 had seven of the ten guests as a starting point, and the remaining three were identified by Dr. Isaacs during the first week of October, and are provided in this updated document. Here is the full set of ten:



All CBClip measurements were done by NMR in 20 mM sodium phosphate buffer at pH 7.4, at a temperature of 298K.

Molecule and simulation setups

An idealized model of the 3D structure of host CBClip was provided by Prof. Lyle Isaacs. The starting 3D structures of hosts OAH and OAMe were built manually with MOE and mildly energy minimized. The initial structures of free guest molecules were found via the conformational search feature in MOE. For CBClip, the experimental studies were done at pH 7.4, so the host's four sulfonic acid acids were treated as fully ionized, for a net host charge of -4. For the octa-acids, OAH and OAMe, the experimental studies were done at pH 11.5, so all eight carboxylic acids were treated as fully ionized, for a net charge of -8. The protonation states of all guest molecules were also assigned based on their expected pKas and the experimental pH values, as shown in the figures above, and were assumed to remain the same on binding their respective hosts. The resulting structures are provided in the download as PDB, mol2 and SDfiles. Please note that all of the structures provided here are meant only as reasonable starting points. There is no guarantee that they are optimal. Please take full advantage of your chemical knowledge and intuition in considering this and all other aspects of the challenge, and feel free to use computational tools beyond those used for the actual binding calculations.

As noted in the instructions, the organizers plan to carry out a complete set of binding free energy and enthalpy calculations with GAFF/RESP force field parameters and the TIP3P (non-modified) water model, and our starting files for the solvated bound complexes are being provided as part of the downloads for this challenge. The starting files were set up as follows. Partial charges were generated with the restrained electrostatic potential (RESP) fitting procedure, with electrostatic potentials at the HF/6-31G* level. Bonded and van der Waals parameters were assigned by GAFF in Antechamber. For the octa-acids, which have a well-defined hydrophobic cavity, the bound conformations were set up with the guests'

ionized groups at the opening and their hydrophobic parts in the cavity. For the CBClip, the positions of the guests in the binding site were constructed by manual docking in MOE.

Each bound complex was placed in a cubic simulation box with edge length of about 40 Å, and containing 2100 TIP3P (non-modified) water molecules. Sodium ions were added to neutralize all systems. Given the low concentration of the buffer used in experiments, no extra ions were added to mimic the buffer. The sodium ions were modeled with the TIP3P-specific sodium parameters of Joung and Cheatham (*J Phys Chem B.* **2008**, *112*: 9020–9041). Each system was then subjected to a short equilibration phase (first NVT, then NPT) to heat the system and change the volume so the pressure would be about 1 atm. The solutes were restrained during the entire process, so further equilibration will be needed to relax them. Note that the AMBER.rst7 files contain velocities appropriate to 298.15 K.

The AMBER format files generated by these procedures were then converted to GROMACS, Desmond and LAMPPs formats with custom scripts and the energies of the starting conformations were compared. The results are summarized in the Instructions and detailed in the file SAMPL5Energies.xls.