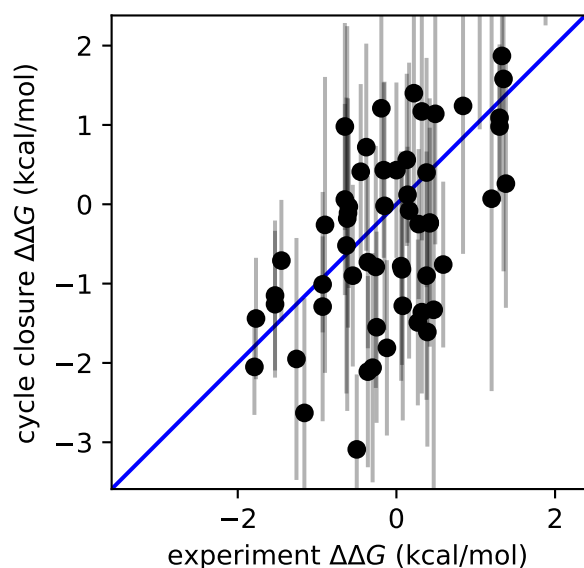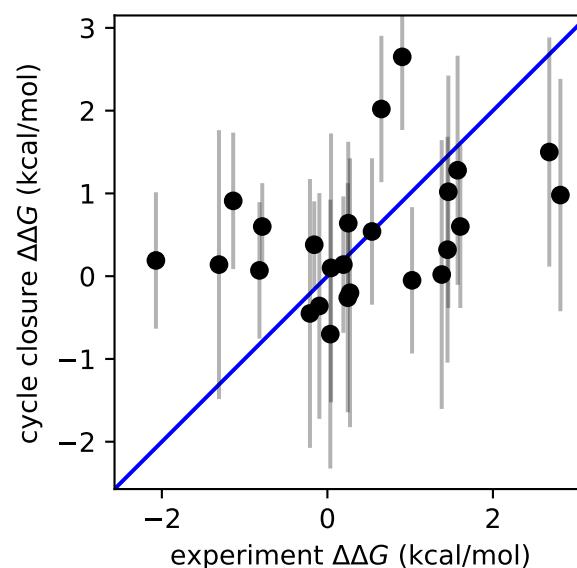**BACE**
RMSE 1.0 [95%: 0.9, 1.2] kcal/mol
MUE 0.8 [95%: 0.7, 1.0] kcal/mol
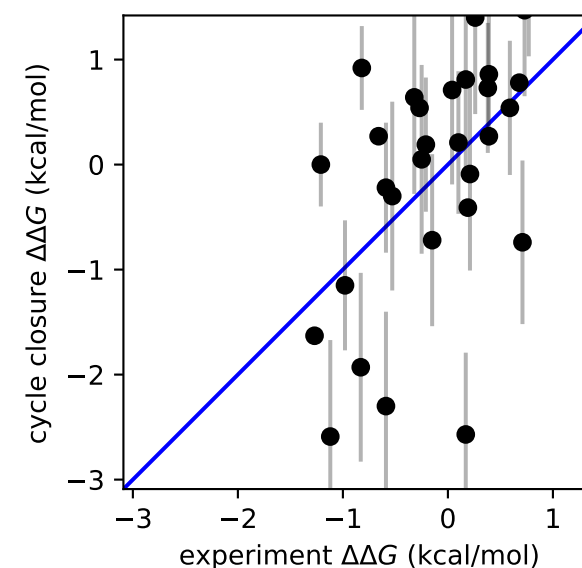
CDK2
RMSE 1.1 [95%: 0.9, 1.4] kcal/mol
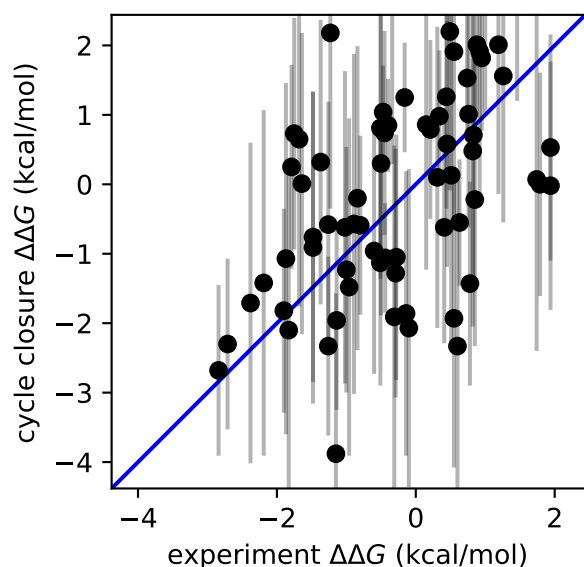MUE 0.9 [95%: 0.7, 1.2] kcal/mol

JNK1
RMSE 1.0 [95%: 0.7, 1.3] kcal/mol
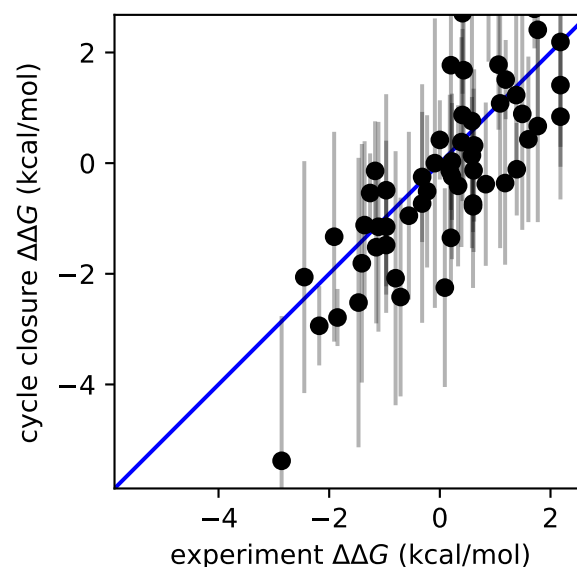MUE 0.8 [95%: 0.6, 1.0] kcal/mol

MCL1
RMSE 1.4 [95%: 1.2, 1.6] kcal/mol
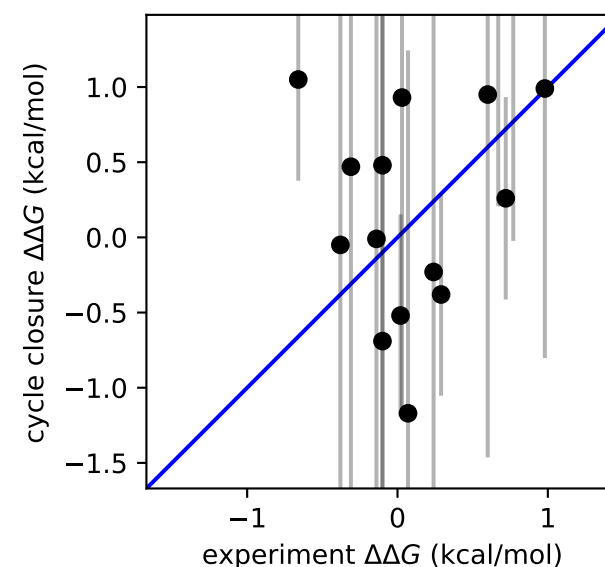MUE 1.2 [95%: 1.0, 1.3] kcal/mol

P38
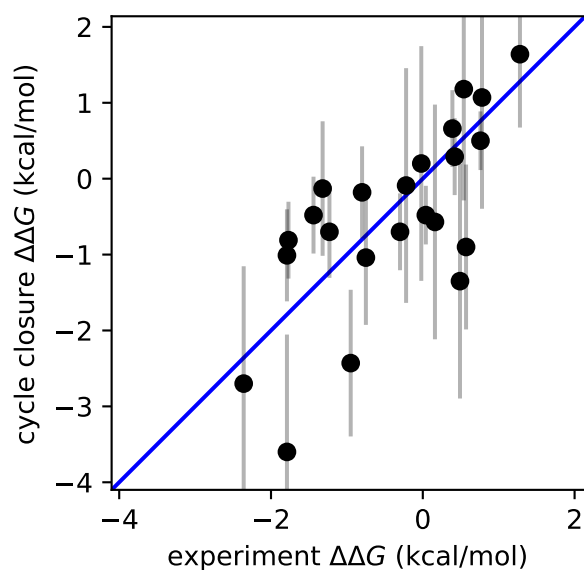RMSE 1.0 [95%: 0.8, 1.2] kcal/mol
MUE 0.8 [95%: 0.6, 1.0] kcal/mol

Thrombin
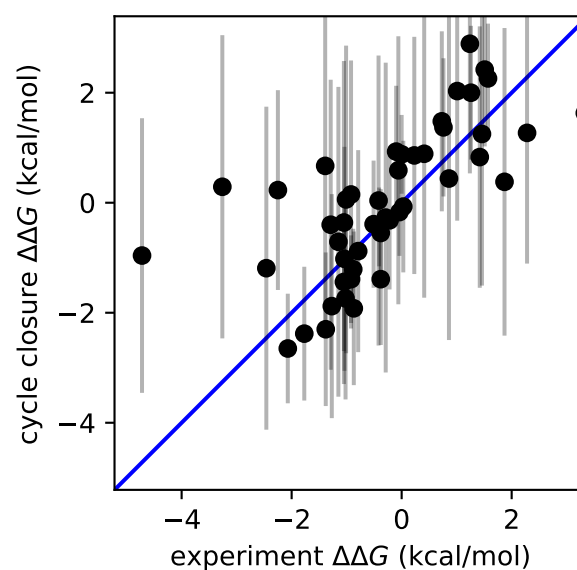RMSE 0.9 [95%: 0.6, 1.2] kcal/mol
MUE 0.8 [95%: 0.5, 1.1] kcal/mol

Tyk2
RMSE 0.9 [95%: 0.7, 1.2] kcal/mol
MUE 0.8 [95%: 0.6, 1.0] kcal/mol

PTP1B
RMSE 1.2 [95%: 0.9, 1.6] kcal/mol
MUE 0.9 [95%: 0.7, 1.1] kcal/mol

all
RMSE 1.1 [95%: 1.1, 1.2] kcal/mol
MUE 0.9 [95%: 0.8, 1.0] kcal/mol

Axis labels (all panels): experiment $\Delta\Delta G$ (kcal/mol); cycle closure $\Delta\Delta G$ (kcal/mol)