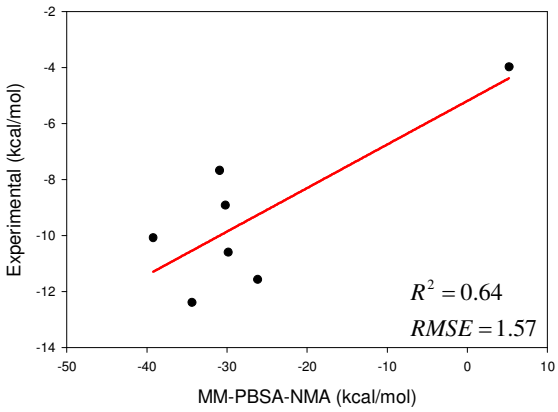
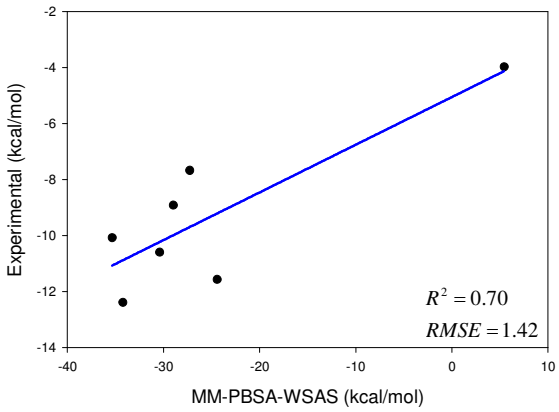
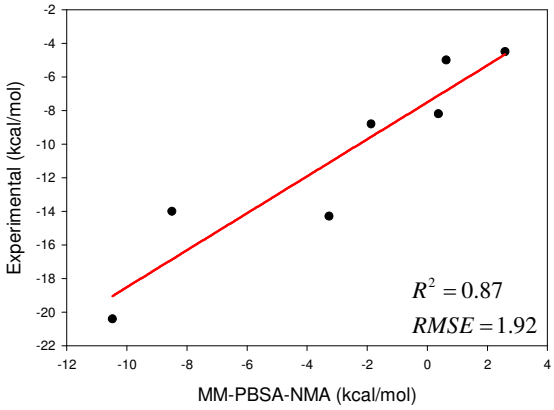
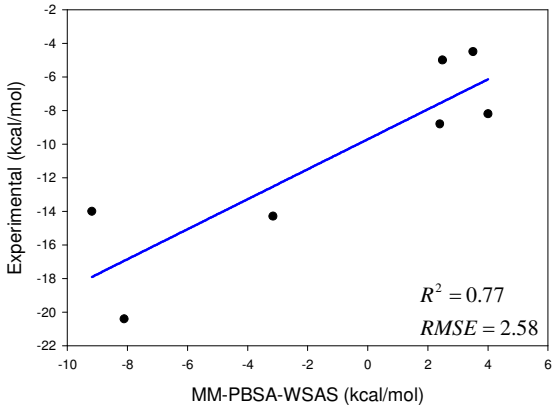

Experimental (kcal/mol)
MM-PBSA-NMA (kcal/mol)
$R^2 = 0.64$
$RMSE = 1.57$

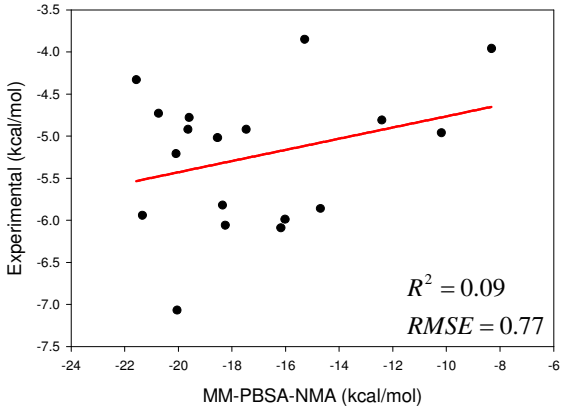

Experimental (kcal/mol)
MM-PBSA-WSAS (kcal/mol)
$R^2 = 0.70$
$RMSE = 1.42$

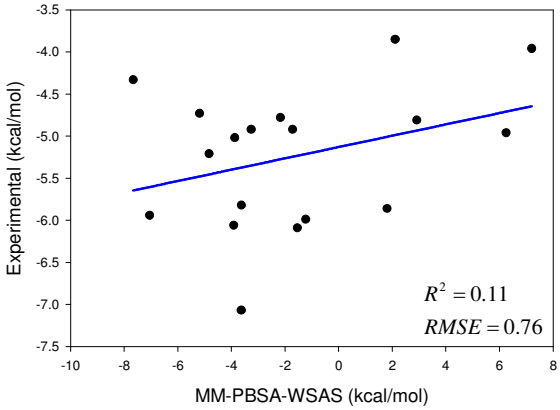
(a)


Experimental (kcal/mol)
MM-PBSA-NMA (kcal/mol)
$R^2 = 0.87$
$RMSE = 1.92$

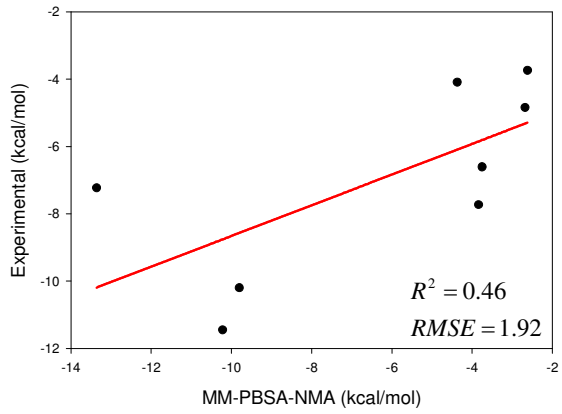

Experimental (kcal/mol)
MM-PBSA-WSAS (kcal/mol)
$R^2 = 0.77$
$RMSE = 2.58$

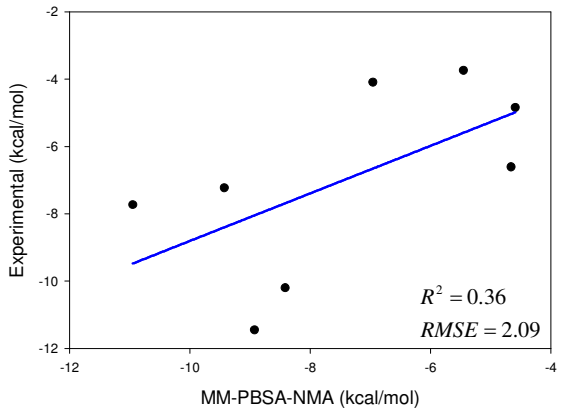
(b)


Experimental (kcal/mol)
MM-PBSA-NMA (kcal/mol)
$R^2 = 0.09$
$RMSE = 0.77$

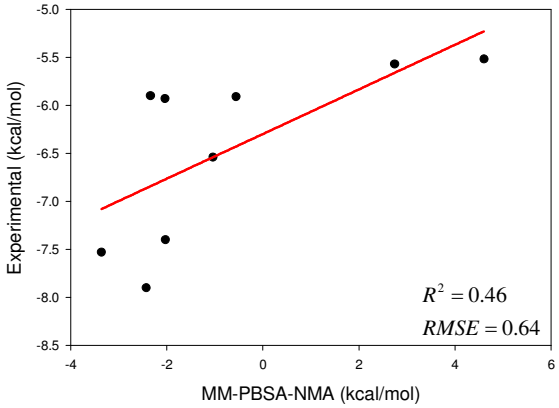

Experimental (kcal/mol)
MM-PBSA-WSAS (kcal/mol)
$R^2 = 0.11$
$RMSE = 0.76$

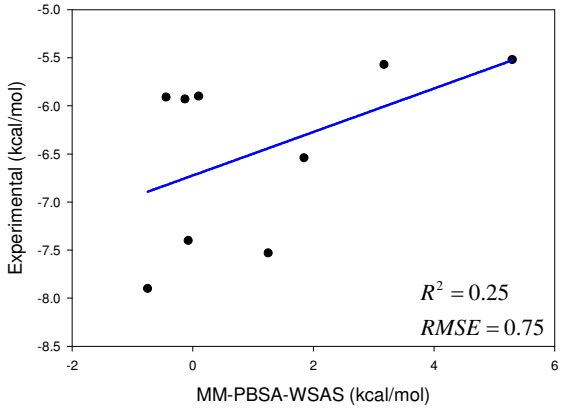
(c)


Experimental (kcal/mol)
MM-PBSA-NMA (kcal/mol)
$R^2 = 0.46$
$RMSE = 1.92$

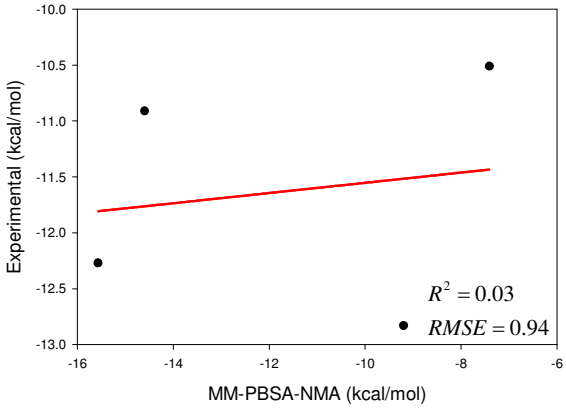

Experimental (kcal/mol)
MM-PBSA-NMA (kcal/mol)
$R^2 = 0.36$
$RMSE = 2.09$

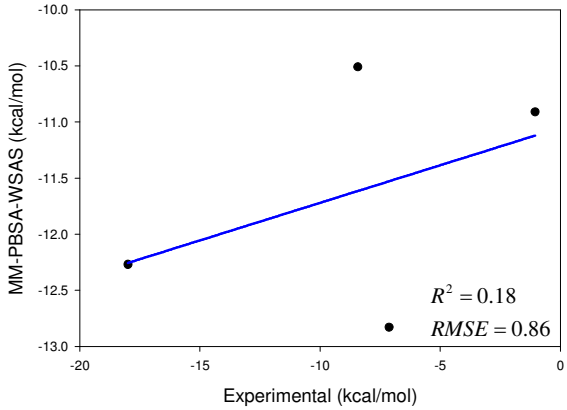
(d)


Experimental (kcal/mol)
MM-PBSA-NMA (kcal/mol)
$R^2 = 0.46$
$RMSE = 0.64$


Experimental (kcal/mol)
MM-PBSA-WSAS (kcal/mol)
$R^2 = 0.25$
$RMSE = 0.75$

(e)


Experimental (kcal/mol)
MM-PBSA-NMA (kcal/mol)
$R^2 = 0.03$
$RMSE = 0.94$


MM-PBSA-WSAS (kcal/mol)
Experimental (kcal/mol)
$R^2 = 0.18$
$RMSE = 0.86$

(f)

Figure S1. Comparison of two MM-PBSA protocols, MM-PBSA-NMA (right) and MM-PBSA-WSAS (left) in binding free energy calculations for six protein-ligand systems: (a) α-thrombin, (b) avidin, (c) cytochrome C peroxidase, (d) neuraminidase, (e) P450cam, (f) penicillopepsin.