Benchmarking of Protein Descriptor Sets in Proteochemometric Modeling (Part 2): Modeling Performance of 13 Amino Acid Descriptor Sets

Additional File 1

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Table of Contents:

Supporting Table S1. Model training values ACE inhibitor set.

Descriptor Set	CV RMSE	Q^2	Published R^2	Published Q^2	Published RMSE
BLOSUM	0.52 (±0.06)	0.74 (±0.09)	n/a	n/a	n/a
FASGAI	0.47 (±0.04)	0.80 (±0.05)	0.76	0.73	0.50
MSWHIM	0.49 (±0.04)	0.77 (±0.06)	0.71	0.64	0.54
ProtFP (PCA3)	0.52 (±0.04)	0.76 (±0.05)	n/a	n/a	n/a
ProtFP (PCA5)	0.53 (±0.04)	0.73 (±0.07)	n/a	n/a	n/a
ProtFP (PCA8)	0.53 (±0.05)	0.73 (±0.09)	n/a	n/a	n/a
ProtFP (Feature)	0.69 (±0.06)	0.52 (±0.10)	n/a	n/a	n/a
ST-scales	0.52 (±0.05)	0.74 (±0.08)	0.86	0.77	0.40
T-scales	0.47 (±0.04)	0.78 (±0.06)	0.85	0.79	0.46
VHSE	0.48 (±0.04)	0.78 (±0.06)	0.77	0.75	0.48
Z-Scales (3)	0.47 (±0.04)	0.80 (±0.06)	0.77	0.72	n/a
Z-scales (5)	0.46 (±0.04)	0.80 (±0.05)	n/a	n/a	n/a
Z-scales (Binned)	0.46 (±0.04)	0.80 (±0.05)	n/a	n/a	n/a
Z-Scales (3) and ProtFP (Feature)	0.49 (±0.04)	0.78 (±0.07)	n/a	n/a	n/a
Z-Scales (3) and Z-Scales (Avg)	0.51 (±0.04)	0.76 (±0.06)	n/a	n/a	n/a
Z-Scales (Binned) and ProtFP (PCA3)	0.47 (±0.03)	0.79 (±0.05)	n/a	n/a	n/a

Experiments were performed 10 times and the stddev is given in parentheses. Also shown are the published values obtained from literature if available. CV RMSE is cross validated RMSE

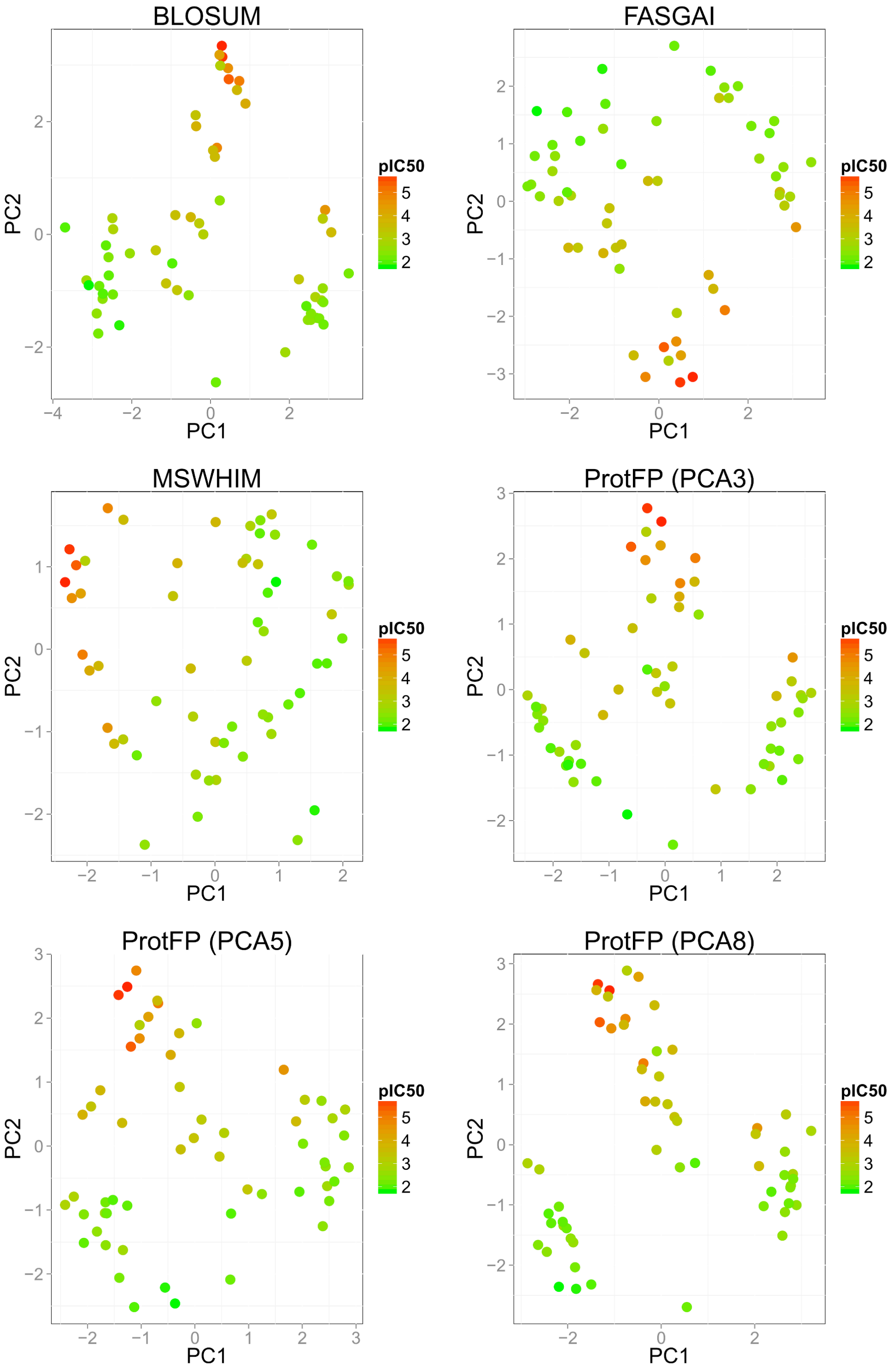
Supporting Table S2. Receptors used in the GPCR set.

Receptor	Family	Actives	Inactives
5HT1A	Serotonin Receptor	100	100
5HT1B		100	99
5HT1D		100	90
5HT2A		100	100
5HT2B		100	100
5HT2C		100	100
5HT4		100	75
5HT5A		35	78
5HT6		100	100
5HT7		100	100
ACM1	Muscarinic Acetylcholine Receptor	100	100
ACM2		100	100
ACM3		100	100
ACM4		79	100
ACM5		46	100
ADA1A	Alpha Adrenergic Receptor	100	100
ADA1B		100	100
ADA1D		100	100
ADA2A		100	100
ADA2B		76	100
ADA2C		100	100
ADRB1	Beta Adrenergic Receptor	71	100
ADRB2		100	100
ADRB3		66	100
DRD1	Dopamine Receptor	100	100
DRD2		100	100
DRD3		100	100
DRD4		100	100
DRD5		53	78
HRH1	Histamine Receptor	100	100
HRH3		100	100
HRH4		100	100

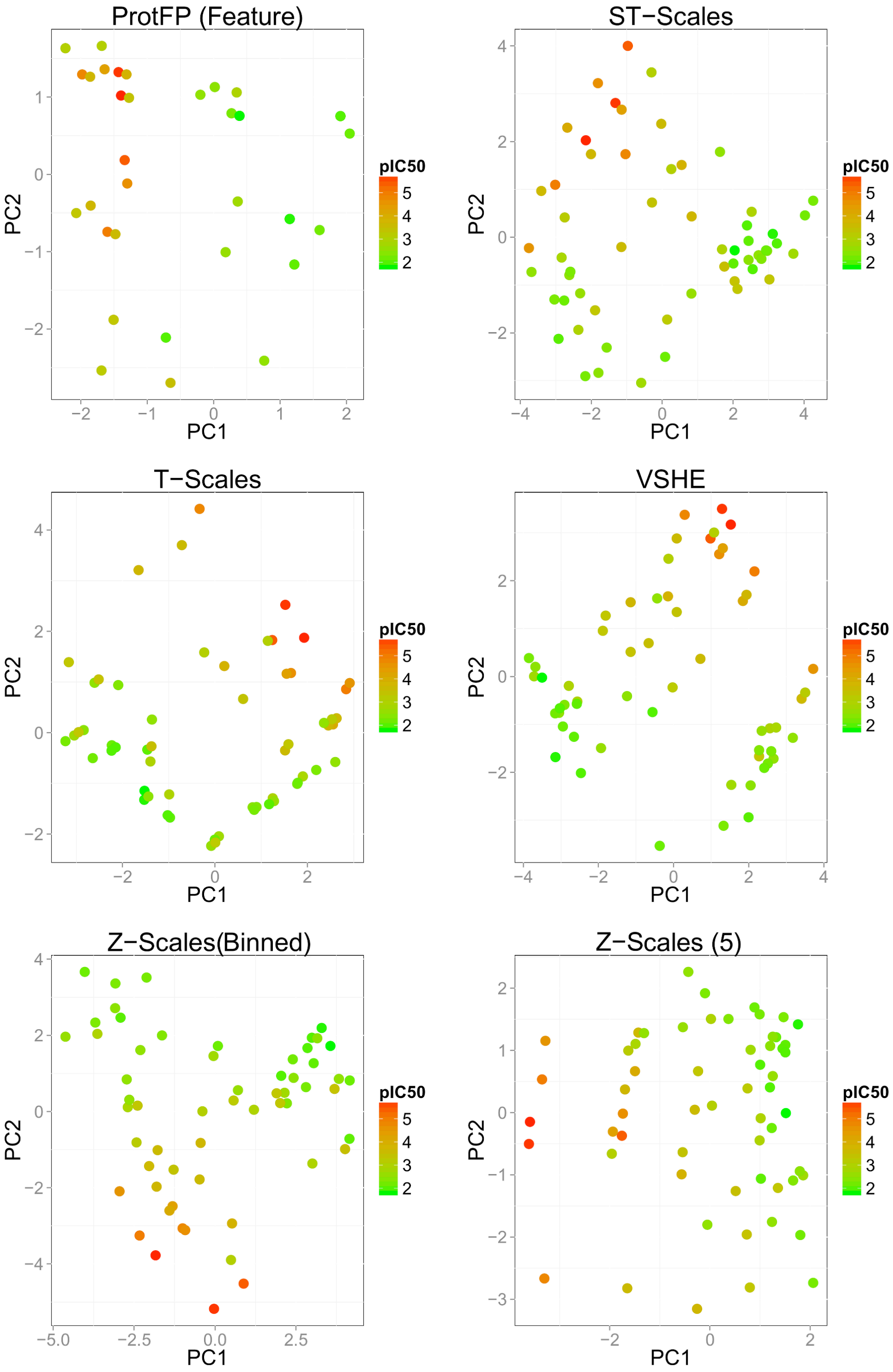
Supporting Table S3. Physicochemical classifiers used as compound descriptors.

Descriptor	Binvalue			
	--	-	+	++
LogD	< - 0.50	>= -0.50 & < 3.40	>= 3.40 & =< 7.50	> 7.50
Molecular Solubility	< -9	>= -9 & < -6.4	>= -6.4 & =< -4	> -4
Number of Atoms	< 20	n/a	>= 20 & =< 40	> 40
Number of Hydrogens	< 16	>= 16 & < 24	>= 24 & =< 40	> 40
Positive Atoms	< 1	n/a	>= 1 & =< 2	> 2
Negative Atoms	< 1	n/a	>= 1 & =< 2	> 2
Hydrogenbond Acceptors	< 3	>= 3 & < 5	>= 5 & =< 8	> 8
Hydrogenbond Donors	< 2	2	>= 3 & =< 4	> 4
Molecular Weight	< 300	>= 300 & < 500	>= 500 & =< 650	> 650
Molecular Surface Area	< 200	>= 200 & < 350	>= 350 & =< 550	> 550
Polar Surface Area	< 100	>= 100 & < 250	>= 250 & =< 500	> 500
Molecular Volume	< 200	>= 200 & <400	>= 400 & =< 700	> 700
Number of Bonds	< 20	>= 20 & < 30	>= 30 & =< 50	> 50
Number of Ringbonds	< 7	>= 7 & < 18	>= 18 & =< 32	> 32
Number of Aromatic Bonds	< 7	>= 7 & < 12	>= 12 & =< 18	> 18
Number of Bridgebonds	< 1	n/a	>= 1 & =< 8	> 8
Number of Rotatable Bonds	< 5	>= 5 & < 7	>= 7 & =< 10	> 10
Number of Rings	< 4	4	>= 4 & =< 6	> 6
Number of Chains	< 5	>= 5 & < 7	>= 7 & =< 11	> 11
Number of Ring Assemblies	< 3	>= 3 & < 4	>= 4 & =< 6	> 6
Number of Chain Assemblies	< 3	>= 3 & < 4	>= 4 & =< 7	> 7
Number of Aromatic Rings	< 3	>= 3 & < 4	>= 4 & =< 6	> 6

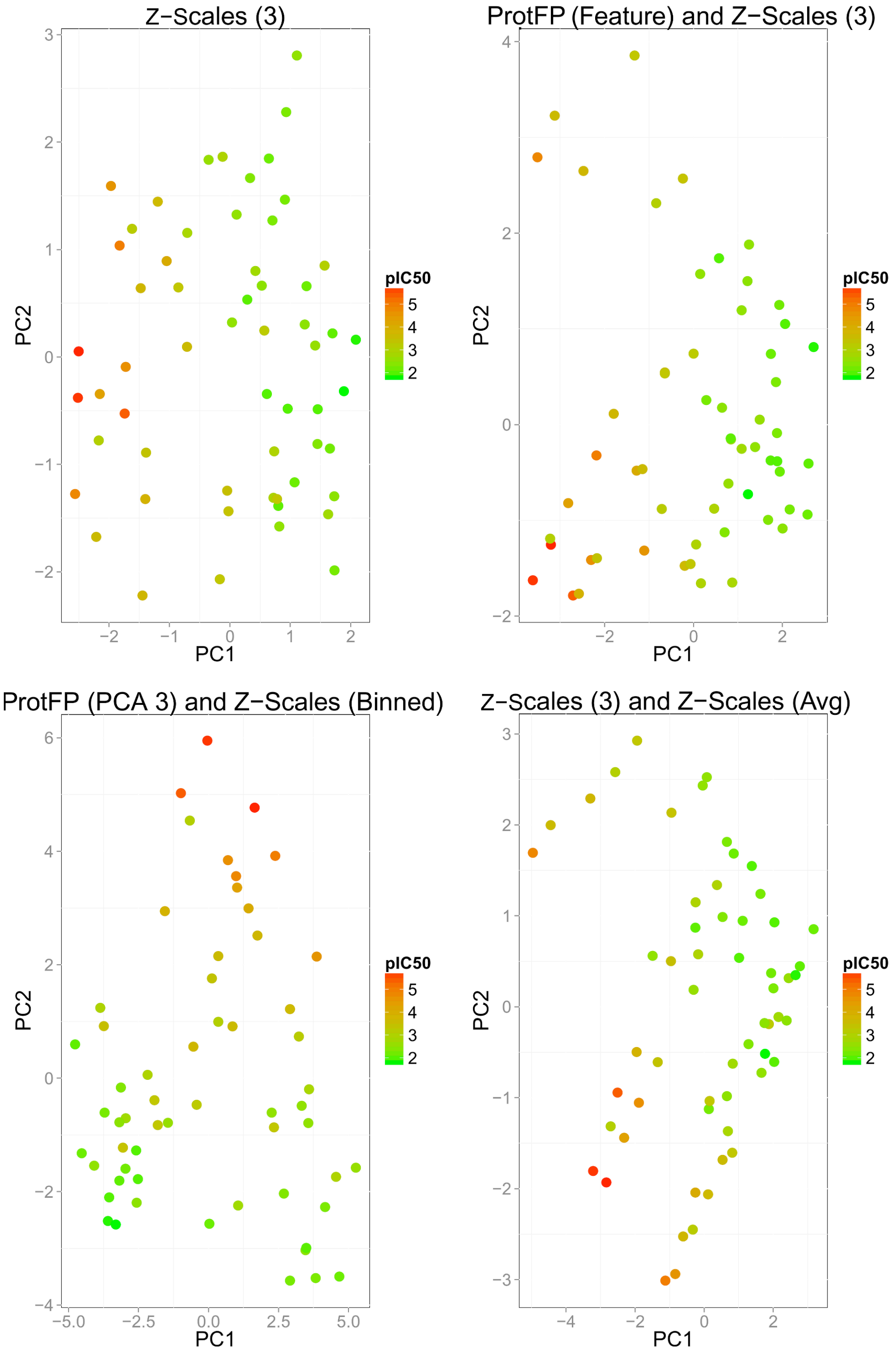
The chemical descriptors were binned after their distribution in the data set was studied. In four cases only three bins were used as the distribution would lead to sparsely filled bins, here - was omitted.



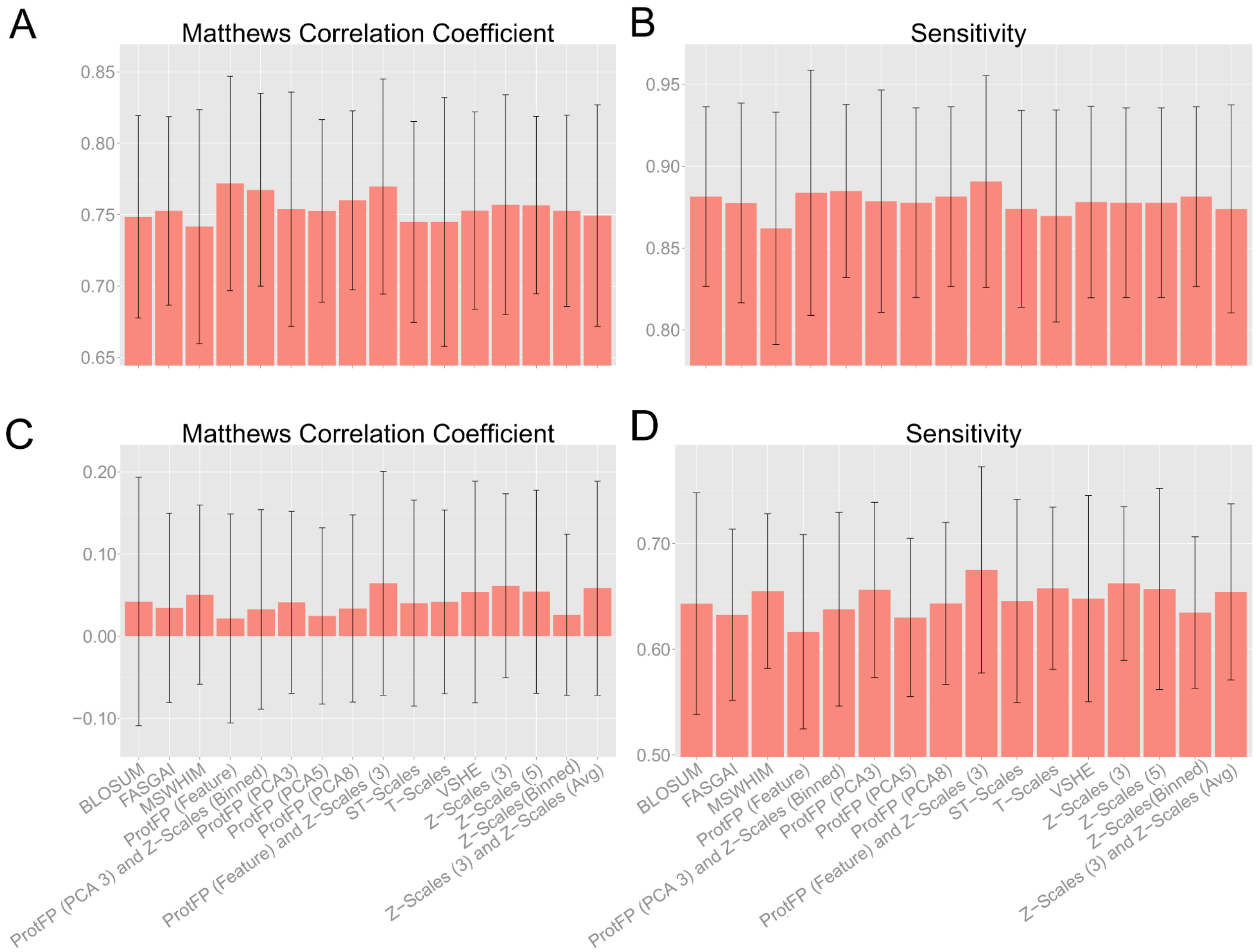
Supporting figure S1. PCA analysis of the 58 ACE inhibiting peptides (I)**.** Data points are colored by activity (green pKi = 2 and red pKi = 6).



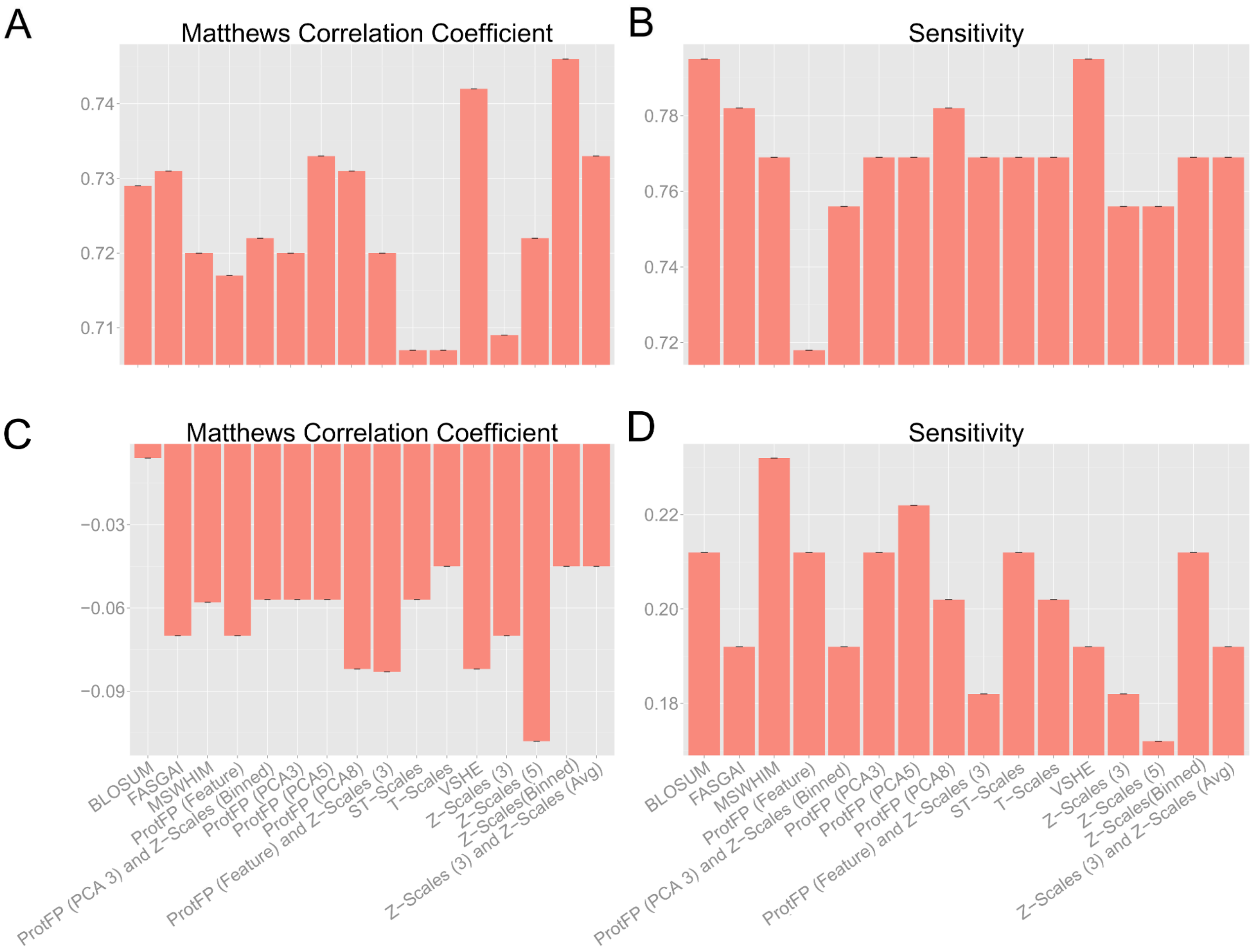
Supporting figure S2. PCA analysis of the 58 ACE inhibiting peptides (II). Data points are colored by activity (green pKi = 2 and red pKi = 6).



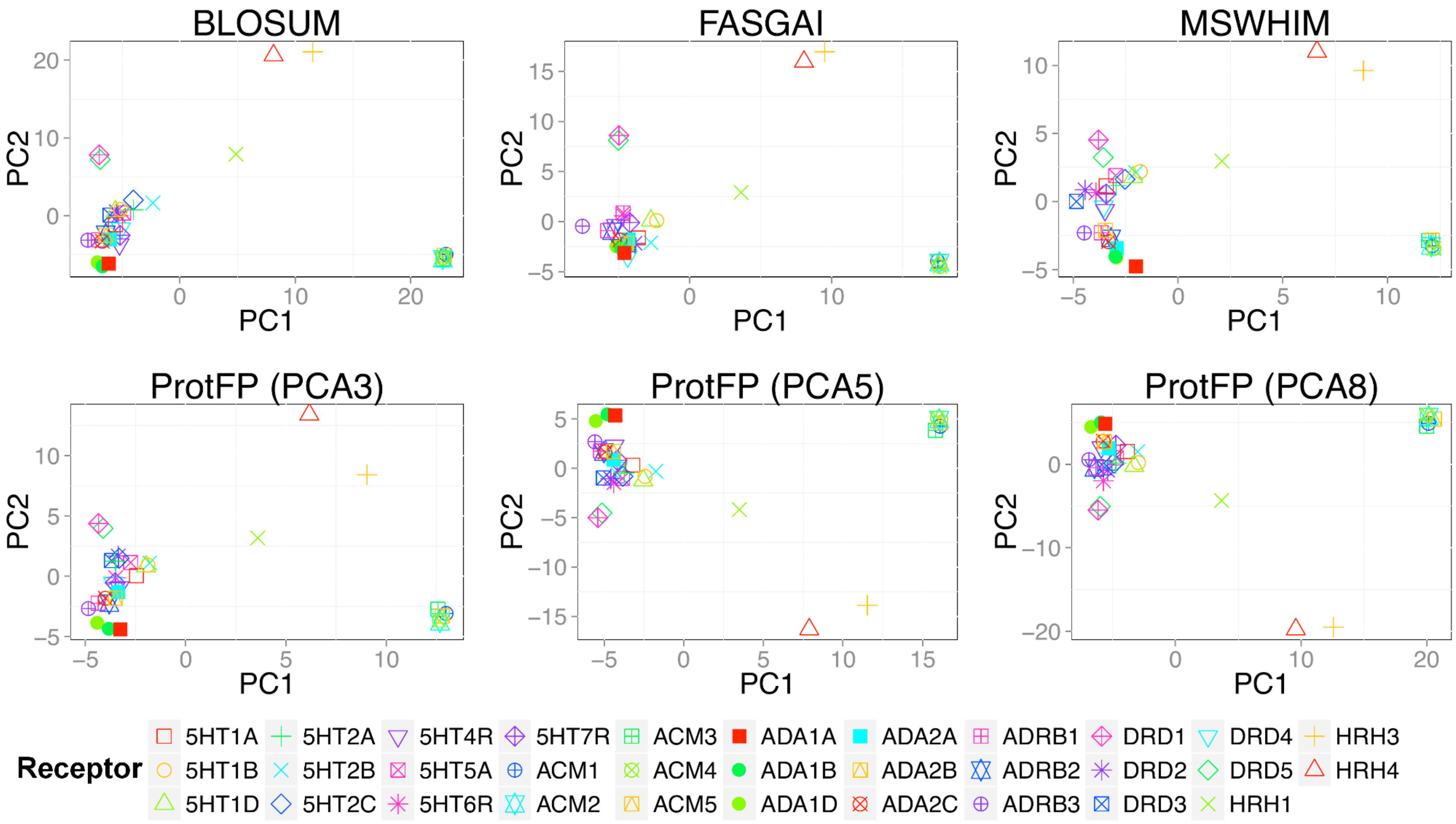
Supporting figure S3. PCA analysis of the 58 ACE inhibiting peptides (III). Data points are colored by activity (green pKi = 2 and red pKi = 6).



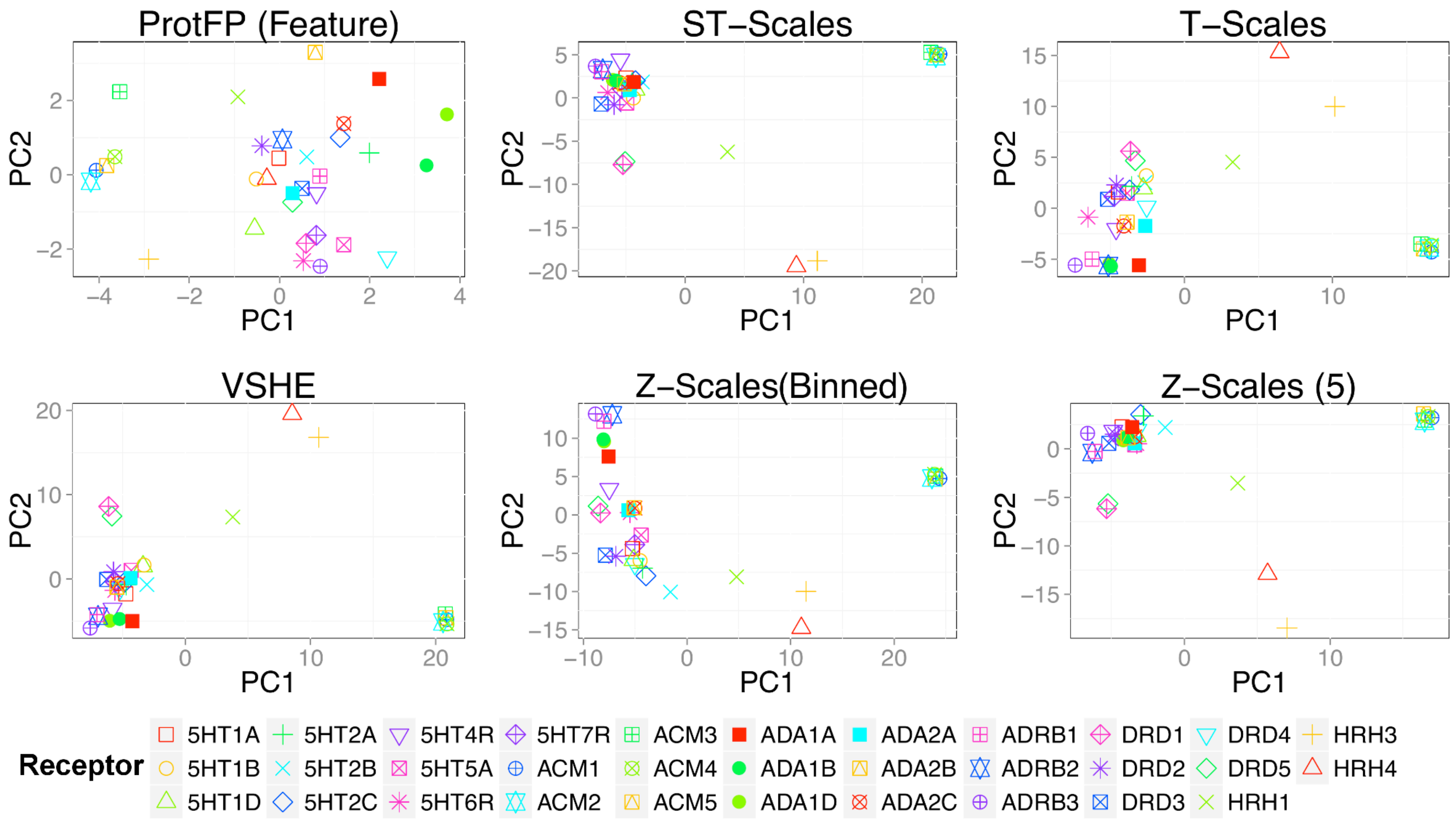
Supporting figure S4. GPCRs in 70-30 validation. Best performing (ACM4; A, B) and worst performing (histamine H3; C, D) GPCRs in the 70-30 validation.



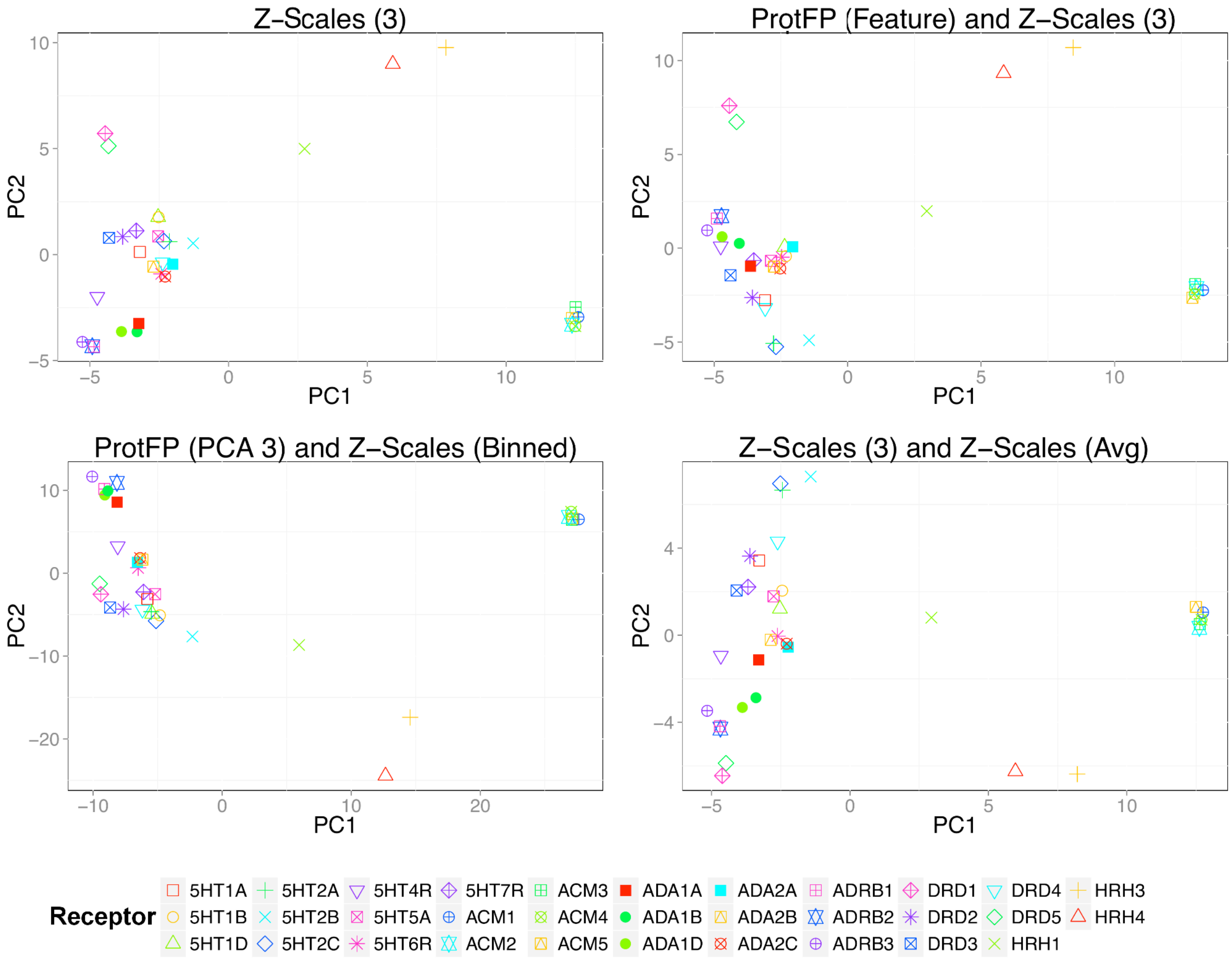
Supporting figure S5. GPCRs in LOSO valiation. Best performing (ACM 4; A, B) and worst performing (histamine H4; C, D) GPCRs in the LOSO validation.



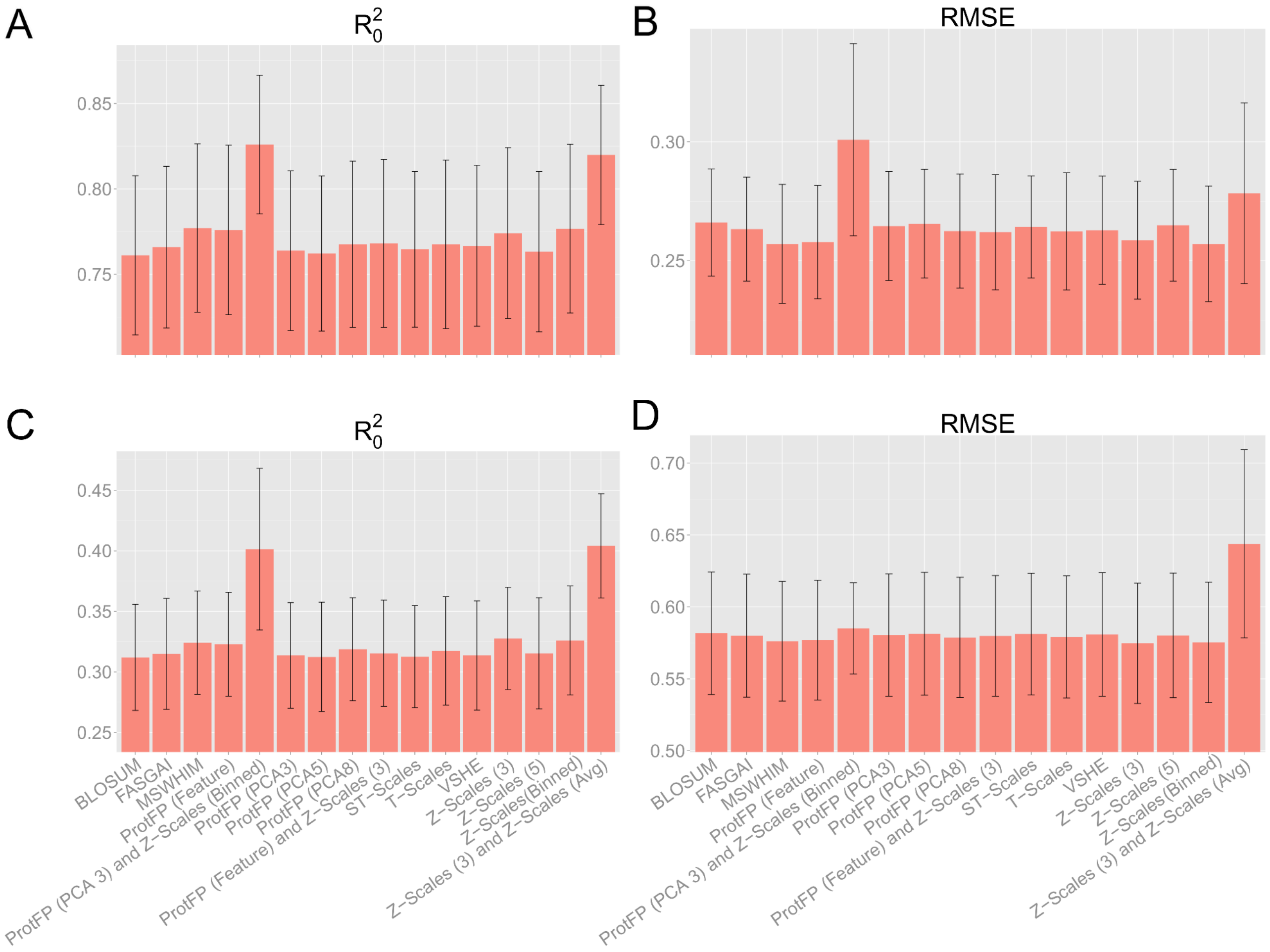
Supporting figure S6. PCA analysis of the GPCR target space (I). Data points are colored by receptor subfamily.



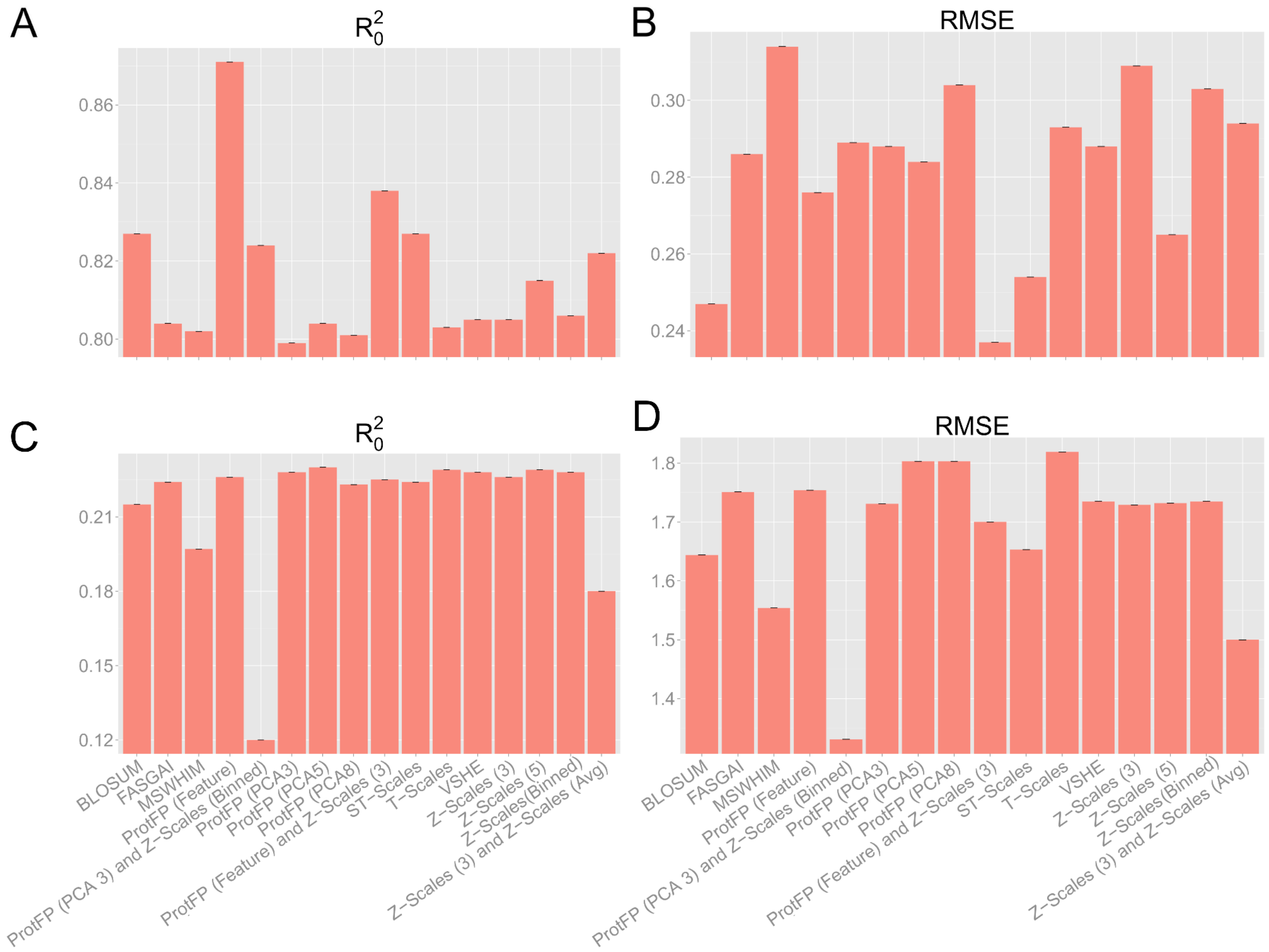
Supporting figure S7. PCA analysis of the GPCR target space (II). Data points are colored by receptor subfamily.



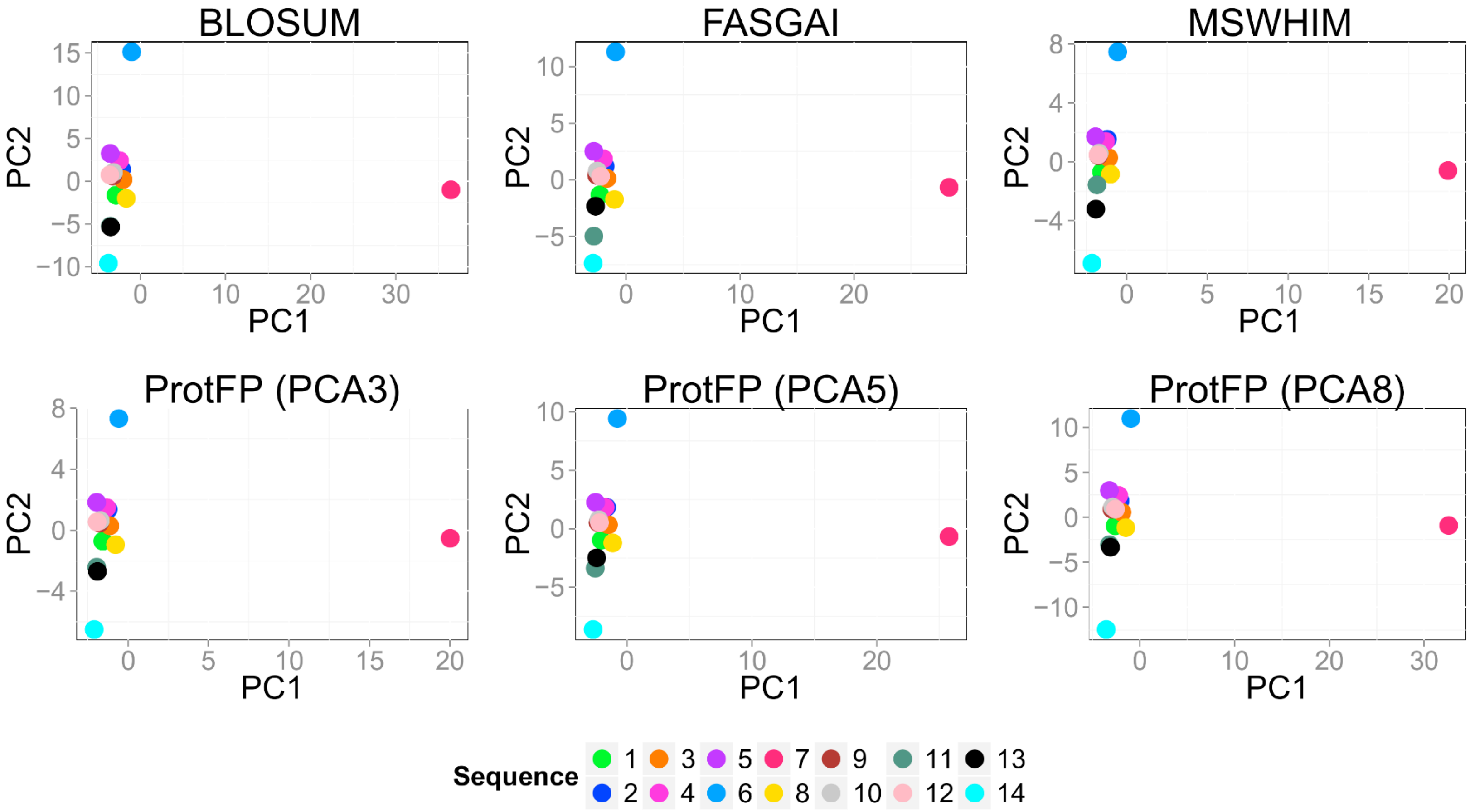
Supporting figure S8. PCA analysis of the GPCR target space (III). Data points are colored by receptor subfamily.



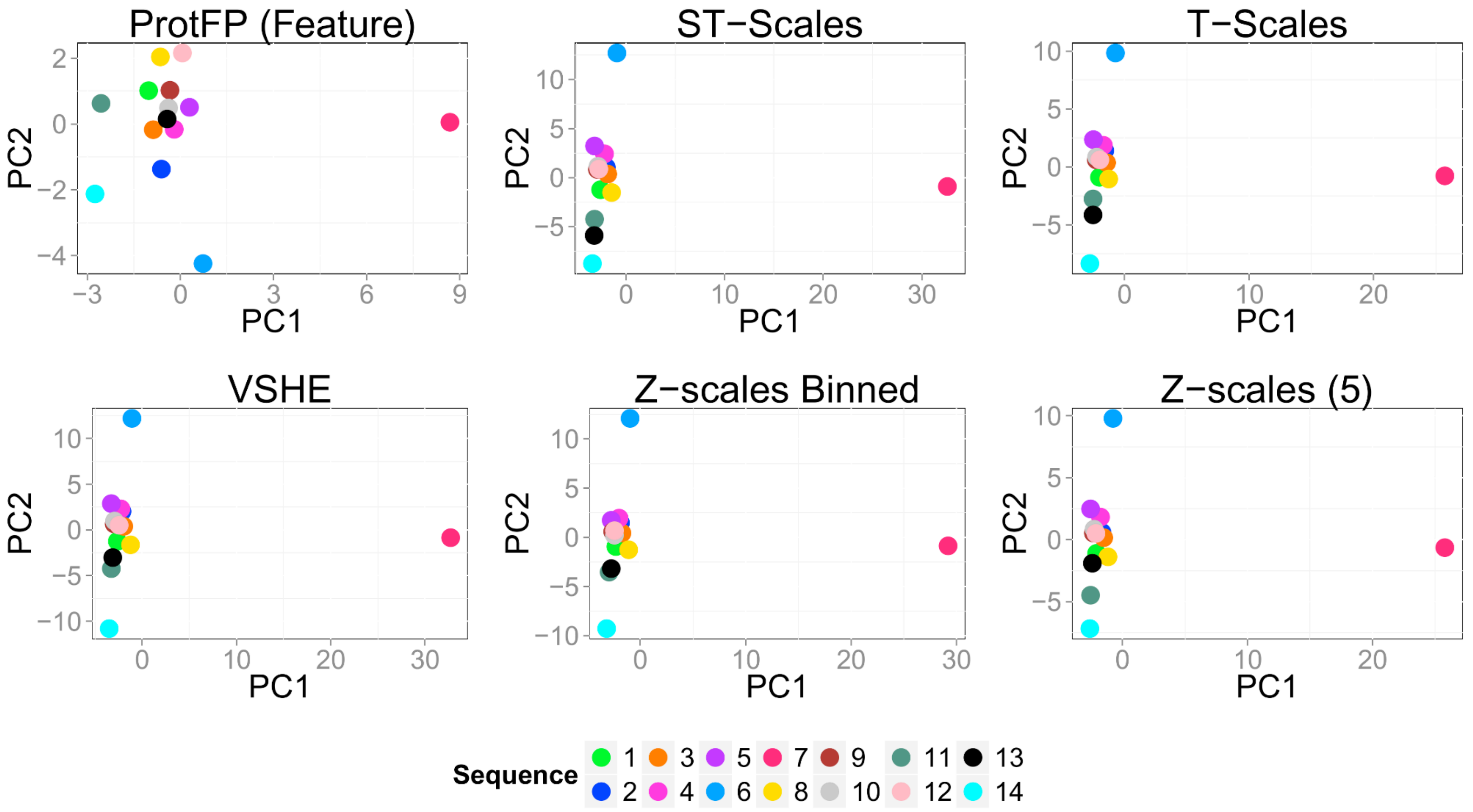
Supporting figure S9. RT mutants in 70-30 validation. Best performing (Sequence 12 and 9; A, B) and worst performing (Sequence 2 and 6; C, D) mutants in the 70-30 validation.



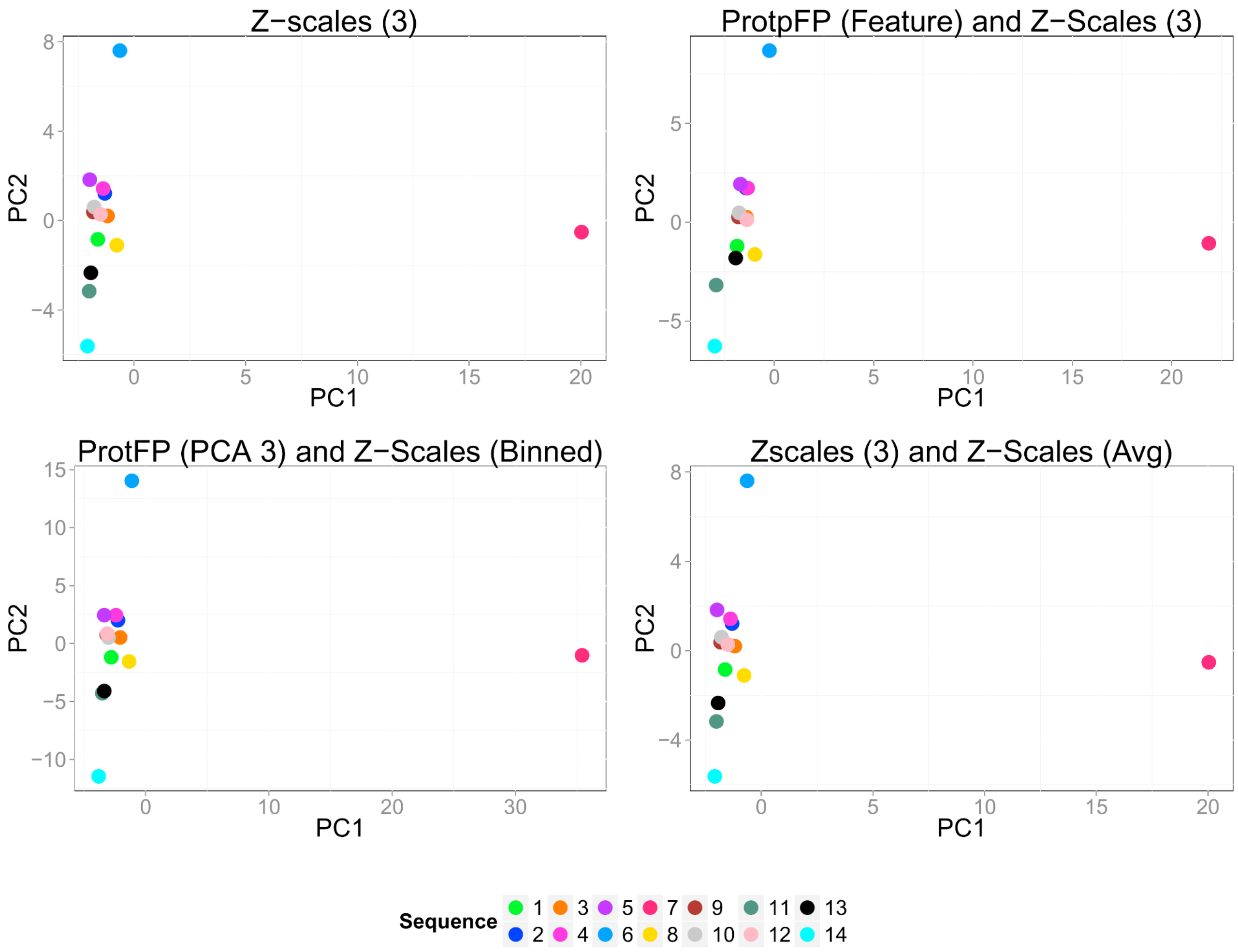
Supporting figure S10 RT mutants in LOSO validation. Best performing (sequence 3/12; A, B) and worst performing (sequence 6; C, D) mutants in the LOSO validation.



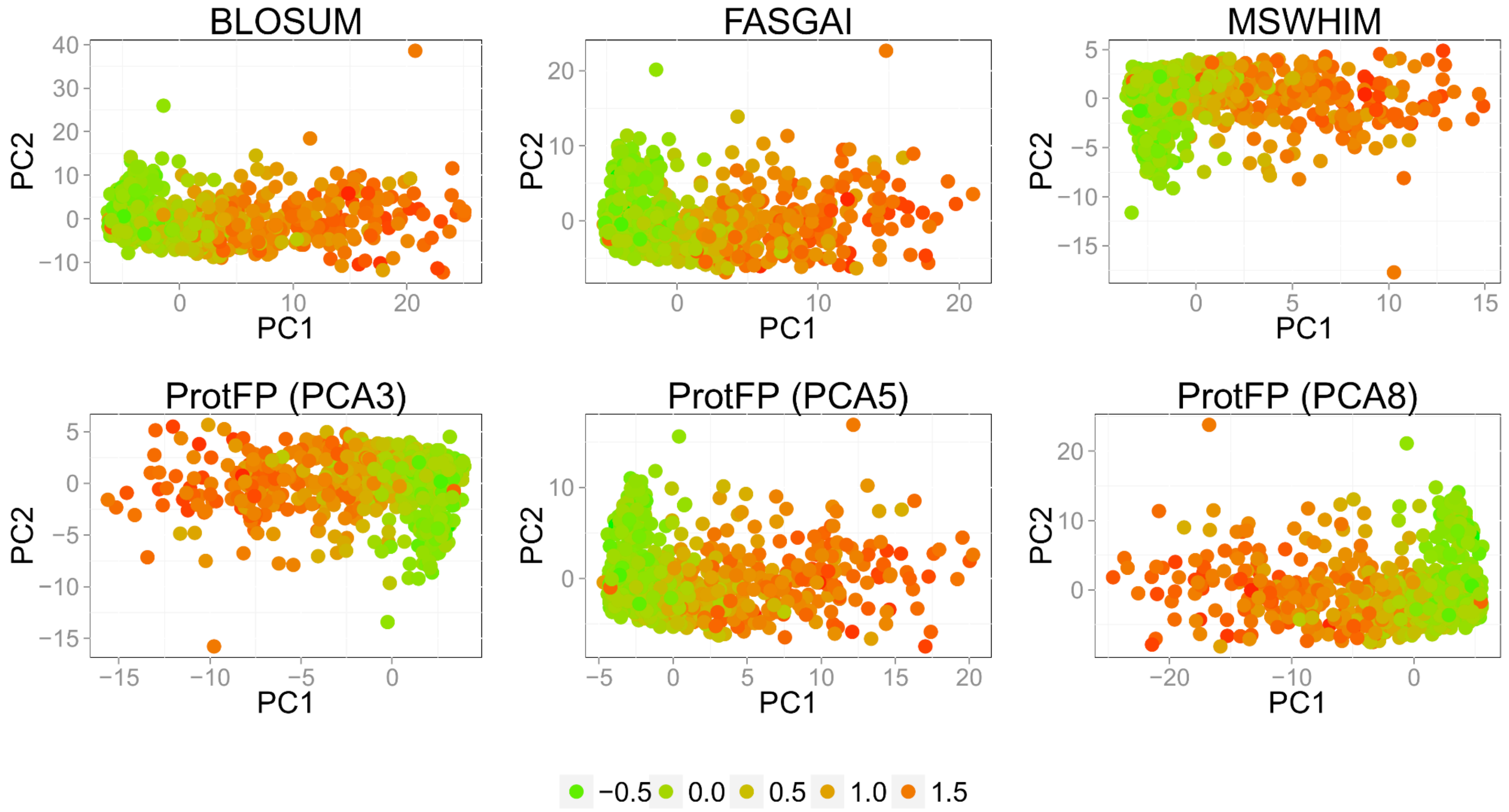
Supporting figure S11. PCA analysis of the NNRTI target space (I). Data points are colored by mutant.



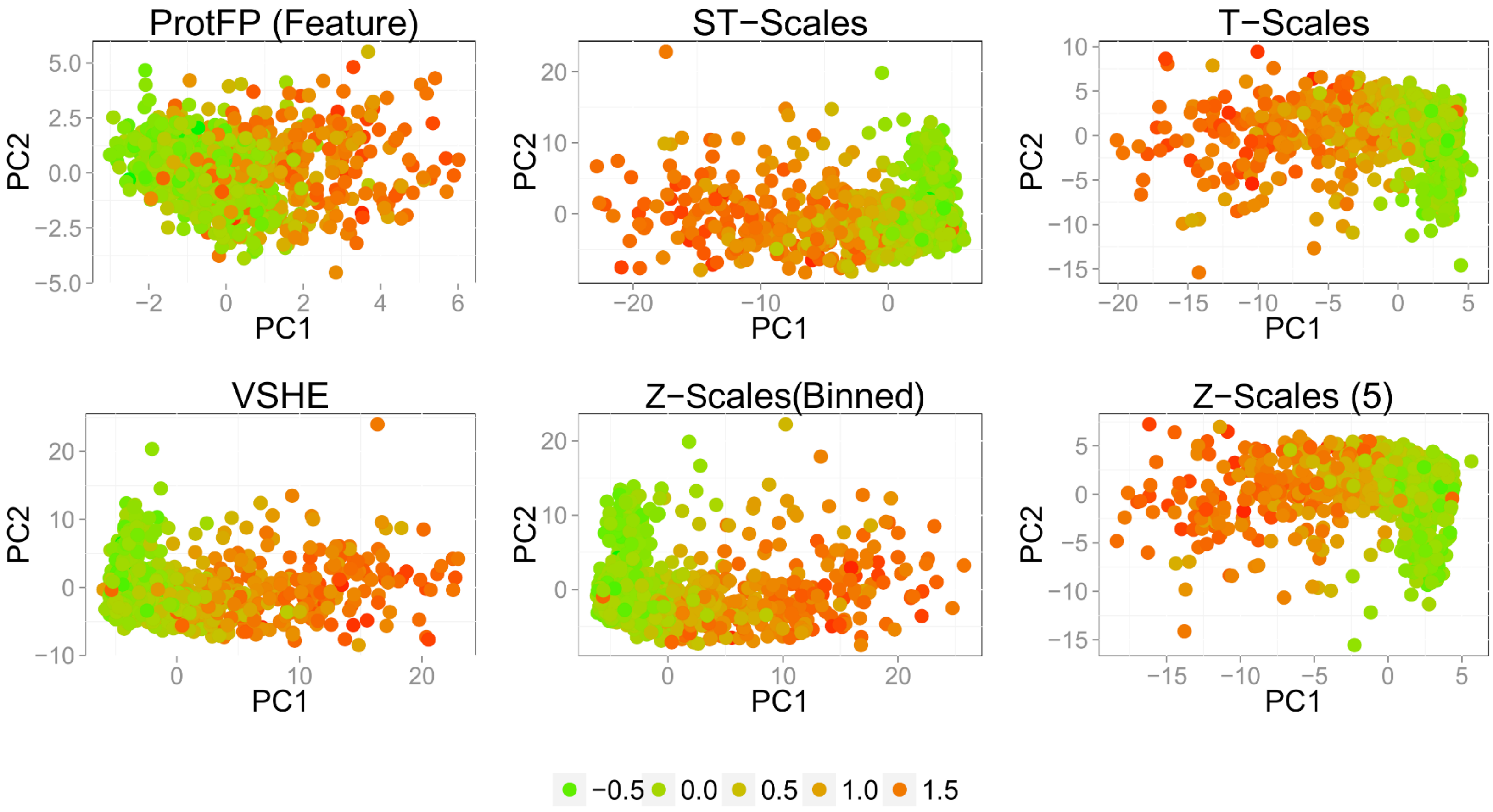
Supporting figure S12. PCA analysis of the NNRTI target space (II). Data points are colored by mutant.



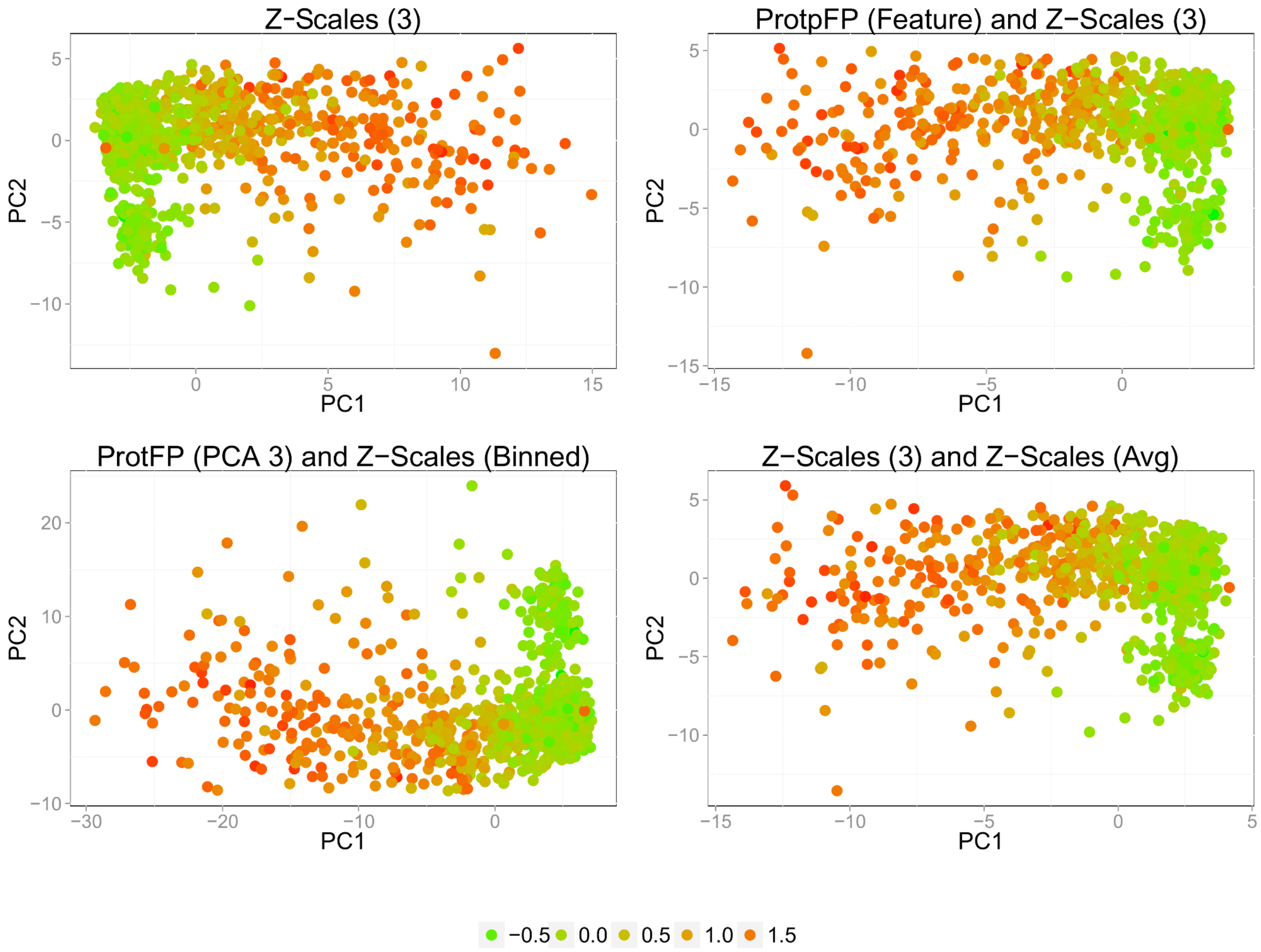
Supporting figure S13. PCA analysis of the NNRTI target space (III). Data points are colored by mutant.



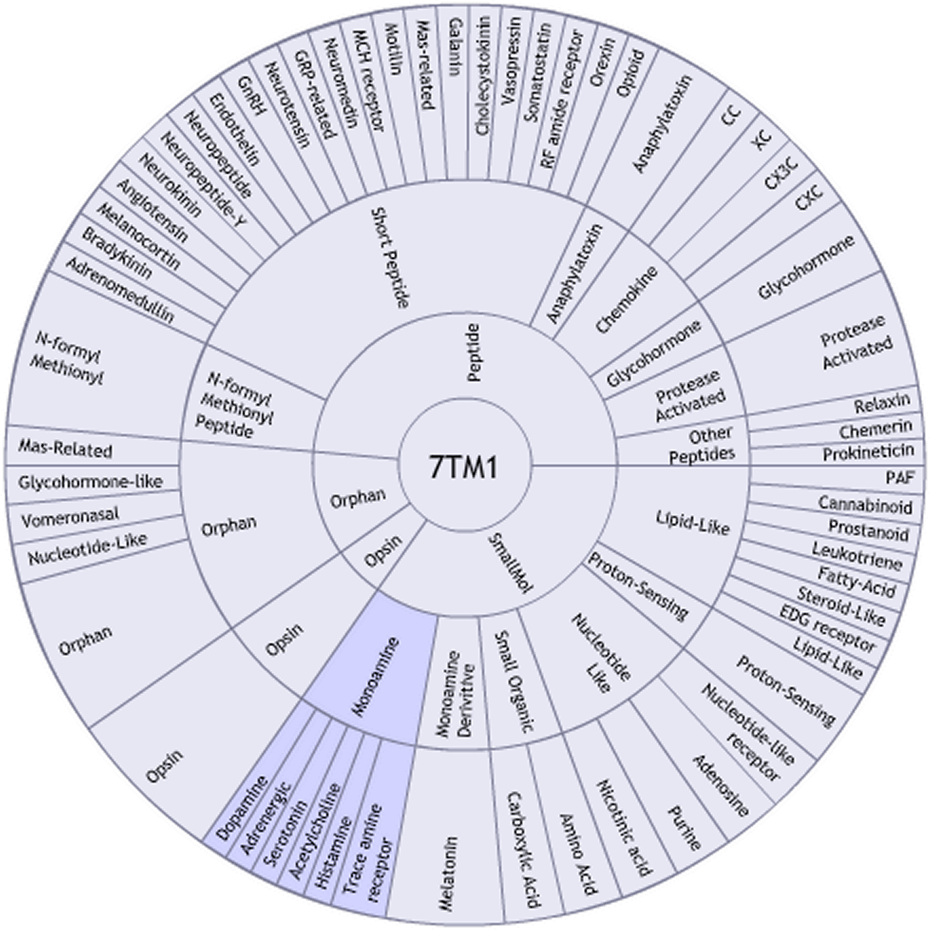
Supporting figure S14. PCA analysis of the PI target space (I). Data points are colored by average resistance for a mutant.



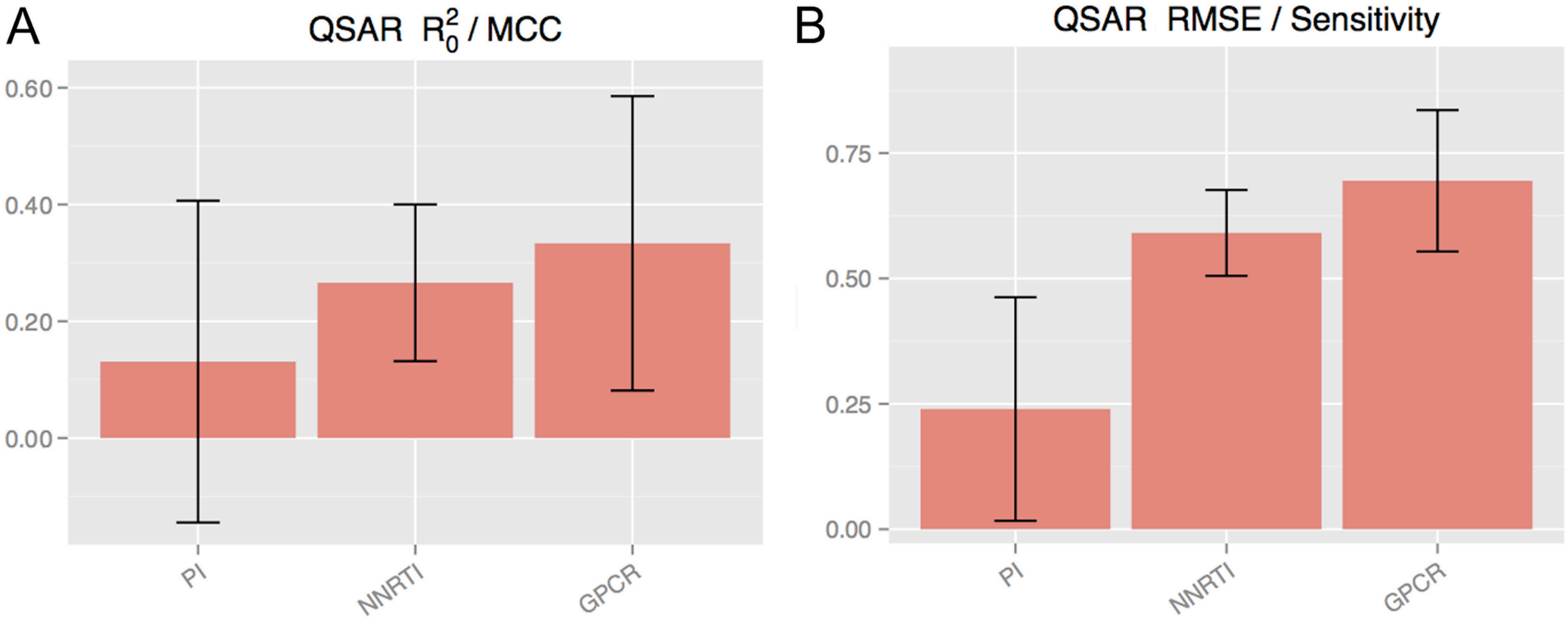
Supporting figure S15. PCA analysis of the PI target space (II). Data points are colored by average resistance for a mutant.



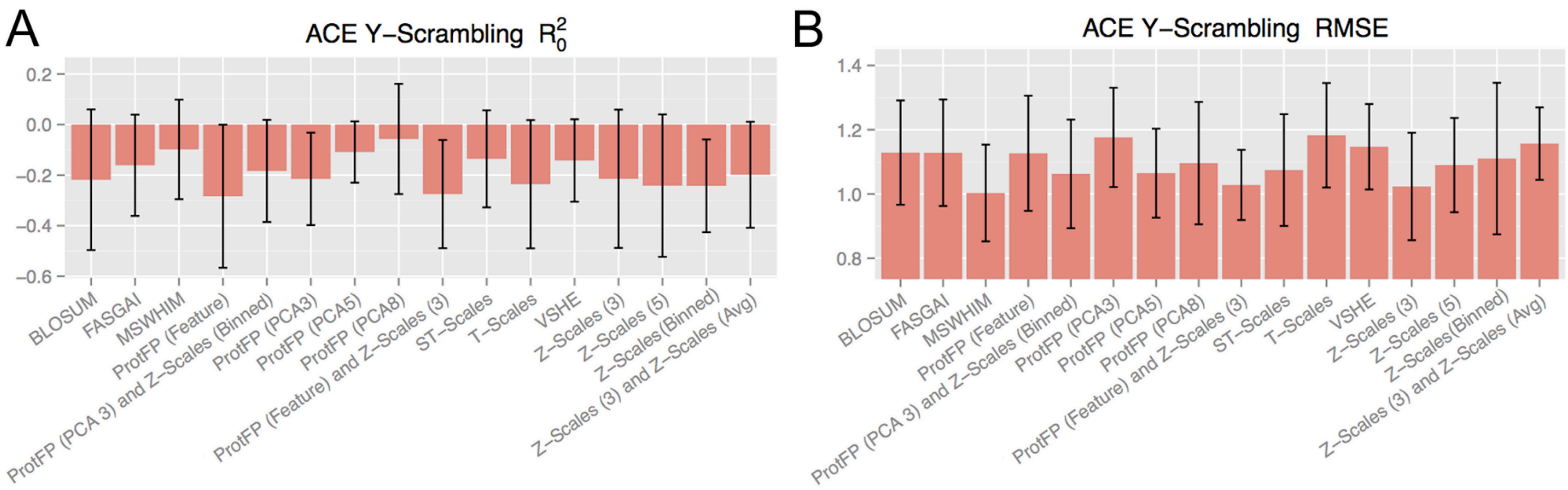
Supporting figure S16. PCA analysis of the PI target space (III). Data points are colored by average resistance for a mutant.



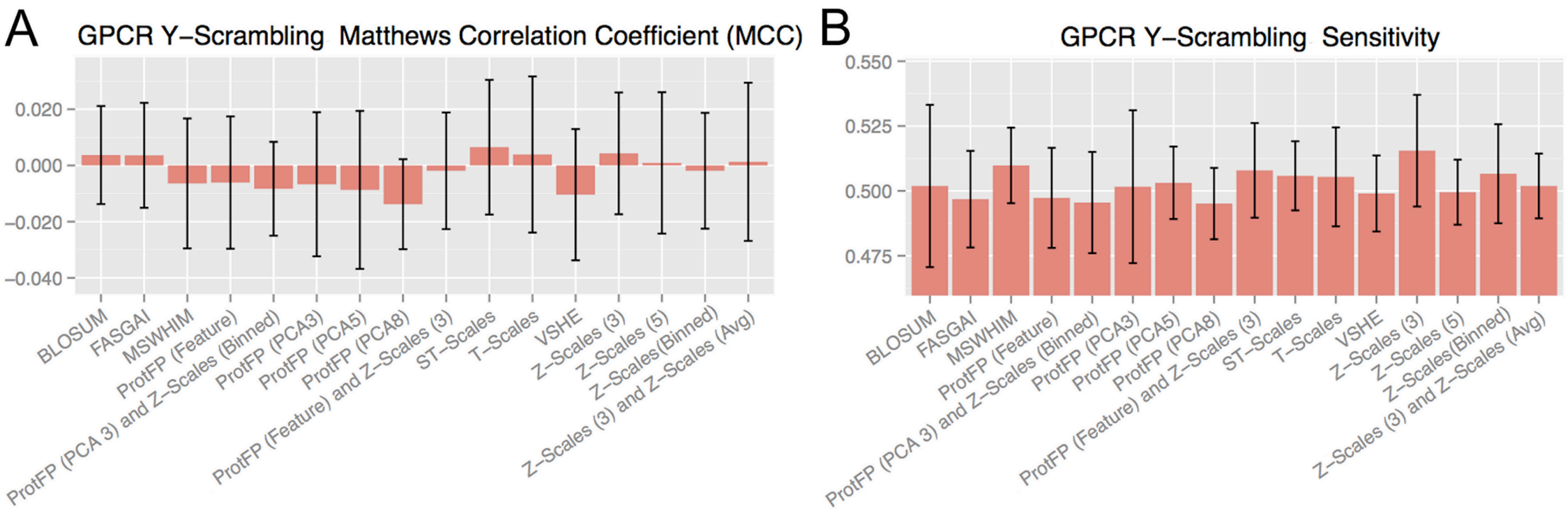
Supporting Figure S17. The GPCR Set was constructed on the monoamine receptor family (highlighted).



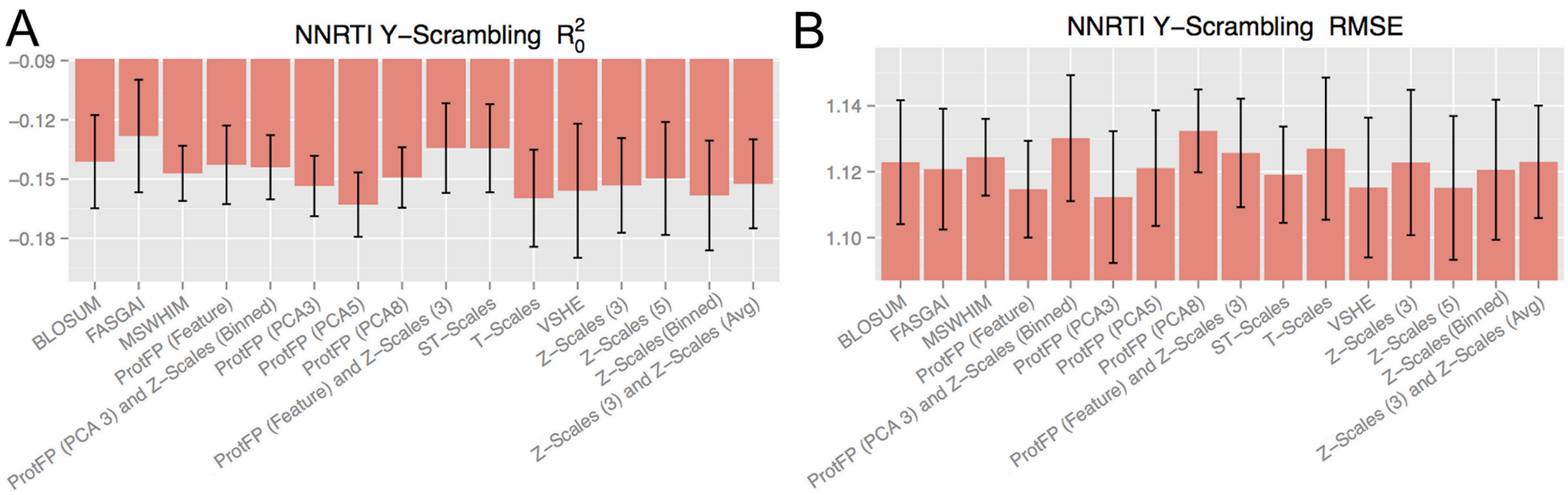
Supporting figure S18. QSAR experiments. Performance of dedicated QSAR models trained on the different descriptor sets.



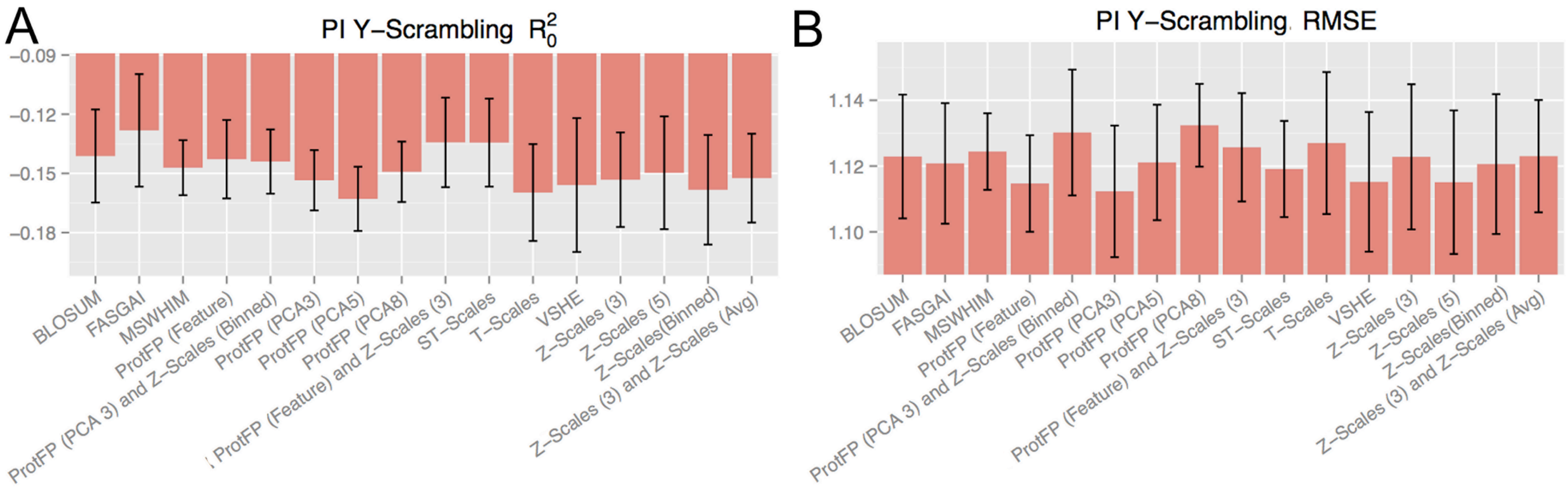
Supporting figure S19. ACE inhibitor 10 fold y-scrambling. Performance of the different descriptor sets on y-scrambled 70-30 ACE inhibitor set.



Supporting figure S20. GPCR 10 fold y-scrambling. Performance of the different descriptor sets on y-scrambled GPCR set.



Supporting figure S21. NNRTI 10-fold y-scrambling. Performance of the different descriptor sets on y-scrambled NNRTI set.



Supporting figure S22. PI 10-fold y-scrambling. Performance of the different descriptor sets on y-scrambled PI set.