

Supporting Information

A Quantum-Inspired Method for Three-Dimensional Ligand-based Virtual Screening

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S1 Dataset

An overview of the dataset, including the number of actives, decoys, and clusters for each target can be seen in Table S1. We have included the PDB code and the PubChem CID for each search query.

Table S1: Overview of the used data sets. It shows the number of actives, decoys, and clusters for each target class, target RCSB Protein Data Bank (PDB) code, and PubChem Compound ID number (CID) for each search query of target classes.

Target class	Number of actives	Number of decoys	Number of clusters	Target PDB code	Query PubChem CID
ACE ^a	46	1796	18	1o86	5362119
AChE ^a	100	3859	18	1eve	3152
ADA	23	927	8	1ndw	447340
ALR2	26	986	14	1ah3	53359
AMPC	21	786	6	1xgj	657106
AR	68	2848	10	2ao6	261000
CDK2 ^a	47	2070	32	1ckp	448991
COMT	11	468	2	1h1d	4369285
COX-1	23	910	11	1p4g	131704237
COX-2 ^a	212	12606	44	1cx2	1396
DHFR	190	8350	14	3dfr	131704237
EGFr ^a	365	15560	40	1m17	176870
ER agonist	63	2568	10	1l2i	446849
ER antagonist	18	1058	8	3ert	449459
FGFR	71	3462	12	1agw	1633
FXa ^a	63	2092	19	1f0r	445480
GART	8	155	5	1c2t	135460967
GPB	52	2135	10	1a8i	444185
GR	32	2585	9	1m2z	5743
HIVRT ^a	34	1494	17	1rt1	65013
HMGA	25	1423	4	1hw8	446154
HSP90	23	975	4	1uy6	448965
InhA ^a	57	2707	23	1p44	447767
MR	13	636	2	2aa2	5839
NA	49	1713	7	1a4g	60855
P38 MAP ^a	137	6779	20	1kv2	156422
PARP	31	1350	7	1efy	1511
PDE5 ^a	26	1698	22	1xp0	110634
PDGFr ^a	124	5603	22	1t46	5291
PPAR γ	6	40	6	1fm9	170364
PR	22	920	4	1sr7	441336
RXR α	18	575	3	1mvc	3481673
SAHH	33	1346	2	1a7a	5287610
Src ^a	98	5679	21	2src	44462678
Thrombin	23	1148	14	1ba8	137347863
TK	22	891	7	1kim	5789
Trypsin	9	718	7	1bjv	2014
VEGFr-2 ^a	48	2712	31	1fgi	5289418

^a Data sets used in the work of Jahn et al.¹

S2 Criticality and Weighting Schemes

For each feature presented in Table 1, we have set its value to critical (C), non-critical (NC), or off (OFF). Bond order, formal charge, and degree have been set to NC and pharmacophore features have been set to C. For the remaining set of features, we have set various combinations of values as presented in Table S2. Each combination is called a *criticality scheme* (CS). In total, we have generated 12 CSs.

Table S2: Criticality Schemes

Features	CS_1	CS_2	CS_3	CS_4	CS_5	CS_6	CS_7	CS_8	CS_9	CS_{10}	CS_{11}	CS_{12}
Atomic number (single atom)	C	C	C	NC	NC	NC	C	C	C	NC	NC	NC
Atomic number (ring)	C	C	OFF	NC	NC	OFF	C	C	OFF	NC	NC	OFF
Implicit hydrogen	NC	OFF	OFF	NC	OFF	OFF	NC	OFF	OFF	NC	OFF	OFF
Dimensionality	2D	2D	2D	2D	2D	2D	3D	3D	3D	3D	3D	3D

In addition to identifying the features as C or NC, we have assigned them a weighting value to reflect its relevance in the virtual screening (VS) experiments. Each combination of weighting values is called a *weighting scheme* (WS). We set one WS as baseline WS_B , with every feature equally weighted to act as a control. In total we have 10 WSs, shown in Table S3.

Table S3: Weighting Schemes

Features	WS_B	WS_1	WS_2	WS_3	WS_4	WS_{B-5}	WS_{1-5}	WS_{2-5}	WS_{3-5}	WS_{4-5}
Atom	1.0	0.1	0.1	0.1	0.1	1.0	1.0	1.0	1.0	1.0
Ring	1.0	0.1	0.1	0.1	0.1	5.0	5.0	5.0	5.0	5.0
Degree	1.0	0.1	0.1	0.1	0.1	1.0	0.1	0.1	0.1	0.1
Implicit hydrogen	1.0	0.1	0.1	0.1	0.1	1.0	0.1	0.1	0.1	0.1
Bond orders	1.0	0.1	0.1	0.1	0.1	1.0	0.1	0.1	0.1	0.1
Formal charge	1.0	0.1	0.1	0.1	0.1	1.0	0.1	0.1	0.1	0.1
Basic	1.0	1.0	3.0	1.0	2.0	1.0	1.0	3.0	1.0	2.0
Acidic	1.0	1.0	3.0	1.0	2.0	1.0	1.0	3.0	1.0	2.0
H donor	1.0	1.0	2.0	2.0	3.0	1.0	1.0	2.0	2.0	3.0
H acceptor	1.0	1.0	2.0	2.0	3.0	1.0	1.0	2.0	2.0	3.0
Aromatic	1.0	1.0	2.0	1.0	1.0	1.0	1.0	2.0	1.0	1.0
Hydrophobic	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
Zinc binder	1.0	1.0	3.0	1.0	2.0	1.0	1.0	3.0	1.0	2.0

S3 Solver Parameters

The algorithm used to solve the maximum weighted co-1-plex problem is the parallel tempering Monte Carlo with isoenergetic cluster moves (PTICM) heuristic solver, also known as the ‘‘borealis’’ algorithm.² The performance of replica-exchange algorithms, such as the PTICM algorithm, depends on the parameters used, especially the temperature schedule selected. In the main paper, the temperature schedule has been based on the geometric schedule for each replica. The low and high temperature values are determined based on the

values of the coefficients of each quadratic unconstrained binary optimization (QUBO) problem instance. Specifically, we set the high temperature equivalent to the maximum coefficient of the terms in the QUBO problem instance, and we set the low temperature to a tenth of the high temperature. We set the number of replicas to be two and the number of sweeps per run to be 100.

S3.1 Runtimes

A complete overview of the solver runtime for each target class is shown in Table S4

Table S4: Runtimes (in seconds)

Target Class	mean	std	max	75%	50%	25%	min
ACE	0.388	0.182	1.139	0.502	0.363	0.242	0.054
ACHE	0.064	0.030	0.360	0.074	0.057	0.044	0.011
ADA	0.056	0.024	0.194	0.068	0.053	0.040	0.005
ALR2	0.065	0.031	0.216	0.080	0.058	0.043	0.016
AMPC	0.091	0.027	0.219	0.105	0.087	0.071	0.034
AR	0.026	0.007	0.081	0.030	0.025	0.021	0.009
CDK2	0.171	0.073	0.573	0.211	0.163	0.118	0.030
COMT	0.076	0.038	0.317	0.090	0.068	0.051	0.012
COX-1	0.043	0.018	0.134	0.053	0.040	0.031	0.009
COX-2	0.044	0.018	0.269	0.052	0.041	0.033	0.011
DHFR	0.177	0.067	0.767	0.215	0.171	0.130	0.028
EGFr	0.075	0.031	0.351	0.093	0.071	0.053	0.006
ER agonist	0.035	0.012	0.202	0.042	0.034	0.026	0.009
ER antagonist	0.131	0.048	0.310	0.160	0.127	0.096	0.020
FGFR	0.035	0.009	0.107	0.040	0.035	0.029	0.010
FXa	0.061	0.013	0.152	0.068	0.060	0.052	0.016
GART	0.744	0.238	1.404	0.893	0.822	0.583	0.171
GPB	0.046	0.017	0.125	0.056	0.043	0.033	0.011
GR	0.061	0.024	0.235	0.075	0.058	0.044	0.015
HIVRT	0.058	0.021	0.162	0.071	0.057	0.044	0.009
HMGA	0.503	0.191	1.465	0.624	0.478	0.376	0.023
HSP90	0.100	0.043	0.305	0.126	0.098	0.068	0.019
InhA	0.029	0.008	0.101	0.033	0.028	0.024	0.007
MR	0.082	0.026	0.180	0.097	0.078	0.065	0.013
NA	0.206	0.091	0.633	0.255	0.192	0.143	0.042
P38 MAP	0.071	0.025	0.305	0.086	0.068	0.053	0.009
PARP	0.016	0.006	0.051	0.019	0.015	0.012	0.005
PDE5	0.183	0.079	0.672	0.229	0.170	0.126	0.036
PDGFr _b	0.052	0.014	0.231	0.059	0.051	0.043	0.010
PPAR γ	0.242	0.087	0.395	0.305	0.262	0.181	0.038
PR	0.074	0.028	0.181	0.093	0.072	0.053	0.018
RXR α	0.117	0.040	0.266	0.140	0.111	0.091	0.029
SAHH	0.018	0.006	0.054	0.021	0.017	0.014	0.007
Src	0.164	0.075	0.819	0.200	0.152	0.113	0.019
Thrombin	0.301	0.119	1.218	0.370	0.277	0.222	0.035
TK	0.026	0.009	0.086	0.031	0.024	0.019	0.008
Trypsin	0.054	0.017	0.147	0.063	0.052	0.043	0.007
VEGFr-2	0.054	0.018	0.148	0.064	0.053	0.042	0.005

S4 Overall VS Performance for the GMS and Fingerprint Methods

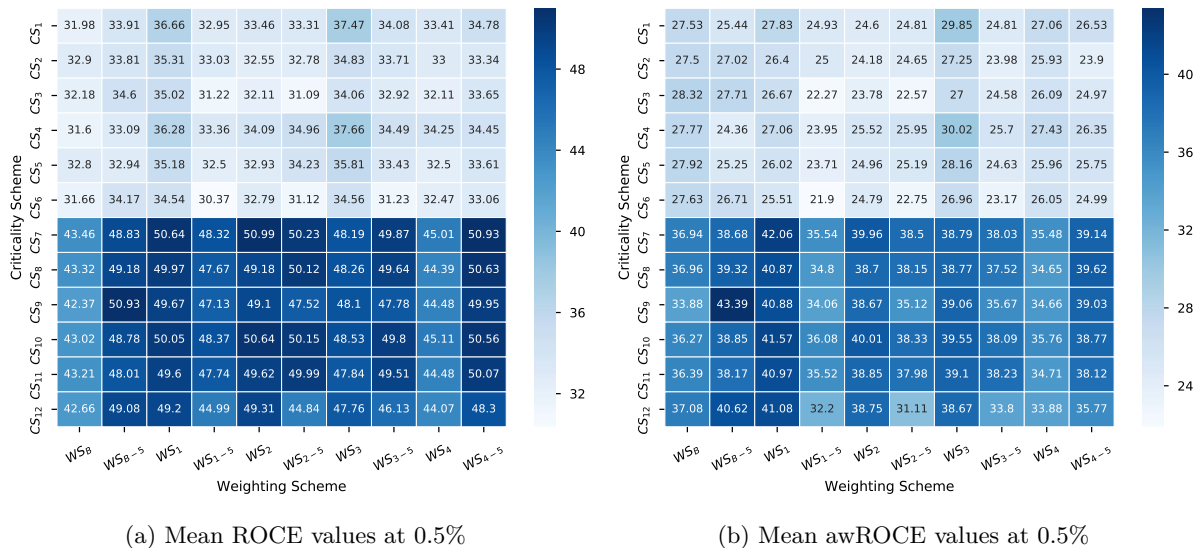


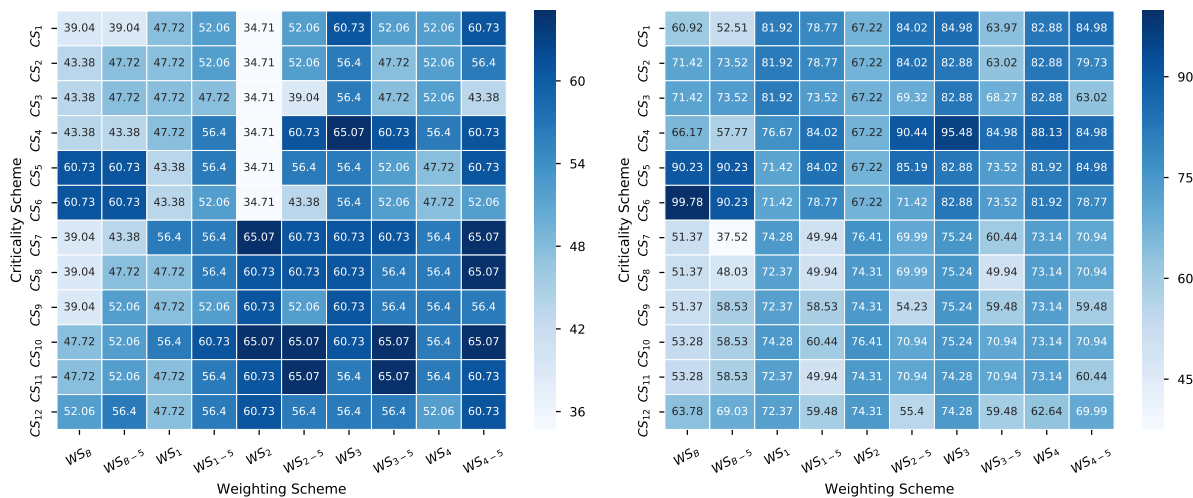
Figure S1: Overall VS performance for each GMS method: a) mean ROCE and b) mean awROCE values at 0.5% over 13 targets in the DUD_LIB_VS_1.0 library

Table S5: Overall VS performance for MACCS and Morgan fingerprints. For Morgan fingerprints, we consider four radii and two bit-vector sizes. We also compare the use of feature-based invariants. We report the mean ROCE and mean awROCE at values at 0.5% over 13 targets in the DUD_LIB_VS_1.0 library

Fingerprint	Bits	Radius	Use Features	Mean ROCE 0.5%	Mean awROCE 0.5%
MACCS	N/A	N/A	N/A	23.79	16.86
Morgan	1024	1	False	41.095	29.160
Morgan	1024	1	True	29.386	25.178
Morgan	1024	2	False	43.981	33.899
Morgan	1024	2	True	40.116	32.147
Morgan	1024	3	False	43.463	32.502
Morgan	1024	3	True	41.205	33.851
Morgan	1024	4	False	41.786	30.422
Morgan	1024	4	True	40.216	29.738
Morgan	2048	1	False	41.910	29.445
Morgan	2048	1	True	29.673	25.426
Morgan	2048	2	False	44.692	32.659
Morgan	2048	2	True	41.291	34.377
Morgan	2048	3	False	44.530	34.868
Morgan	2048	3	True	43.292	34.754
Morgan	2048	4	False	44.455	35.148
Morgan	2048	4	True	42.008	33.794

S5 VS Performance for 13 targets in the DUD_LIB_VS_1.0 Library

S5.1 ACE



(a) ROCE 0.5% values

(b) awROCE 0.5% values

Figure S2: ROCE and awROCE 0.5% values for the ACE class

Table S6: ACE class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	17.35	8.40
Morgan	1024.0	1.0	False	34.71	31.51
Morgan	1024.0	1.0	True	21.69	33.61
Morgan	1024.0	2.0	False	43.38	52.51
Morgan	1024.0	2.0	True	39.04	42.01
Morgan	1024.0	3.0	False	52.06	54.42
Morgan	1024.0	3.0	True	47.72	63.02
Morgan	1024.0	4.0	False	34.71	36.76
Morgan	1024.0	4.0	True	30.37	21.01
Morgan	2048.0	1.0	False	34.71	31.51
Morgan	2048.0	1.0	True	21.69	33.61
Morgan	2048.0	2.0	False	34.71	31.51
Morgan	2048.0	2.0	True	47.72	63.02
Morgan	2048.0	3.0	False	47.72	63.02
Morgan	2048.0	3.0	True	52.06	73.52
Morgan	2048.0	4.0	False	47.72	63.02
Morgan	2048.0	4.0	True	39.04	50.41

S5.2 AChE

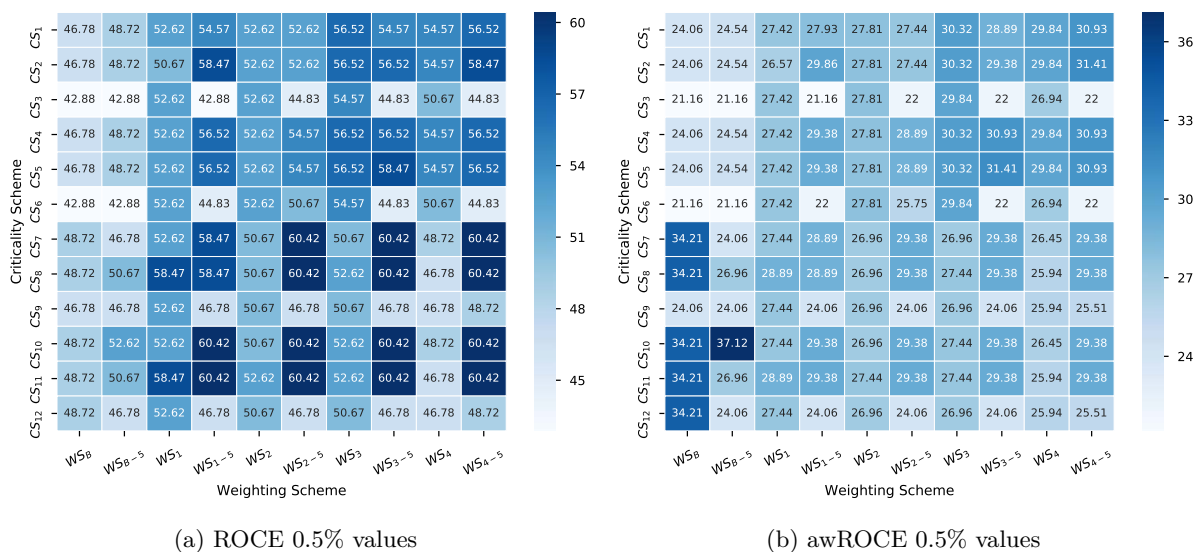


Figure S3: ROCE and awROCE 0.5% values for the AChE class

Table S7: AChE class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	35.08	19.13
Morgan	1024.0	1.0	False	44.83	22.00
Morgan	1024.0	1.0	True	37.03	21.50
Morgan	1024.0	2.0	False	44.83	22.00
Morgan	1024.0	2.0	True	48.72	33.00
Morgan	1024.0	3.0	False	42.88	21.16
Morgan	1024.0	3.0	True	46.78	22.85
Morgan	1024.0	4.0	False	42.88	21.16
Morgan	1024.0	4.0	True	46.78	22.85
Morgan	2048.0	1.0	False	44.83	22.00
Morgan	2048.0	1.0	True	37.03	21.50
Morgan	2048.0	2.0	False	44.83	22.00
Morgan	2048.0	2.0	True	48.72	33.00
Morgan	2048.0	3.0	False	44.83	22.00
Morgan	2048.0	3.0	True	46.78	22.85
Morgan	2048.0	4.0	False	42.88	21.16
Morgan	2048.0	4.0	True	46.78	22.85

S5.3 CDK2

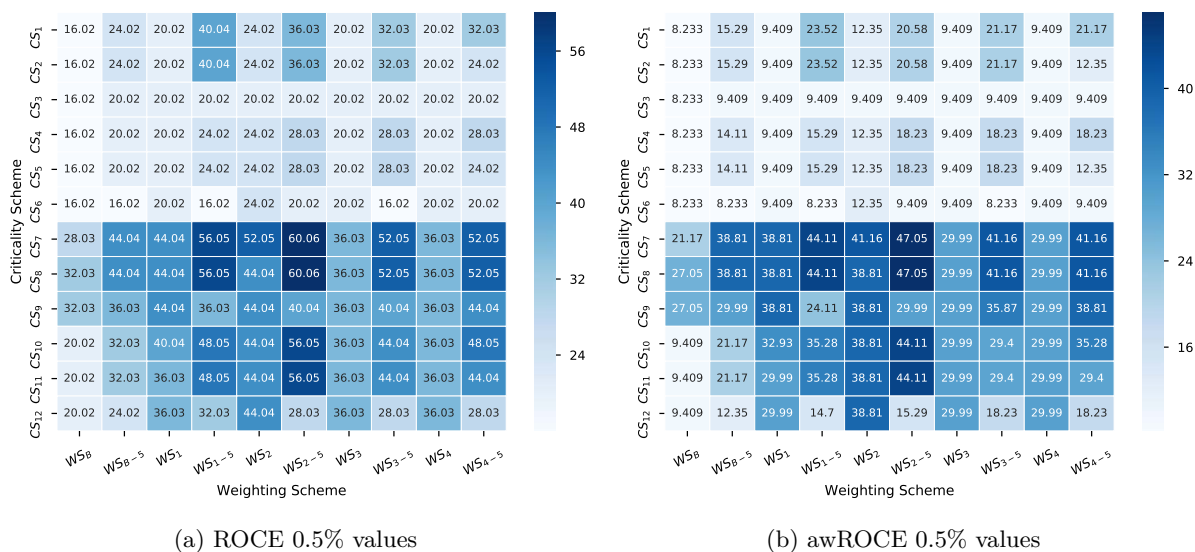


Figure S4: ROCE and awROCE 0.5% values for the CDK2 class

Table S8: CDK2 class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	20.02	9.41
Morgan	1024.0	1.0	False	20.02	9.41
Morgan	1024.0	1.0	True	32.03	27.05
Morgan	1024.0	2.0	False	20.02	9.41
Morgan	1024.0	2.0	True	32.03	27.05
Morgan	1024.0	3.0	False	20.02	9.41
Morgan	1024.0	3.0	True	36.03	32.93
Morgan	1024.0	4.0	False	20.02	9.41
Morgan	1024.0	4.0	True	36.03	32.93
Morgan	2048.0	1.0	False	20.02	9.41
Morgan	2048.0	1.0	True	32.03	27.05
Morgan	2048.0	2.0	False	20.02	9.41
Morgan	2048.0	2.0	True	32.03	27.05
Morgan	2048.0	3.0	False	24.02	15.29
Morgan	2048.0	3.0	True	32.03	27.05
Morgan	2048.0	4.0	False	20.02	9.41
Morgan	2048.0	4.0	True	32.03	27.05

S5.4 COX-2

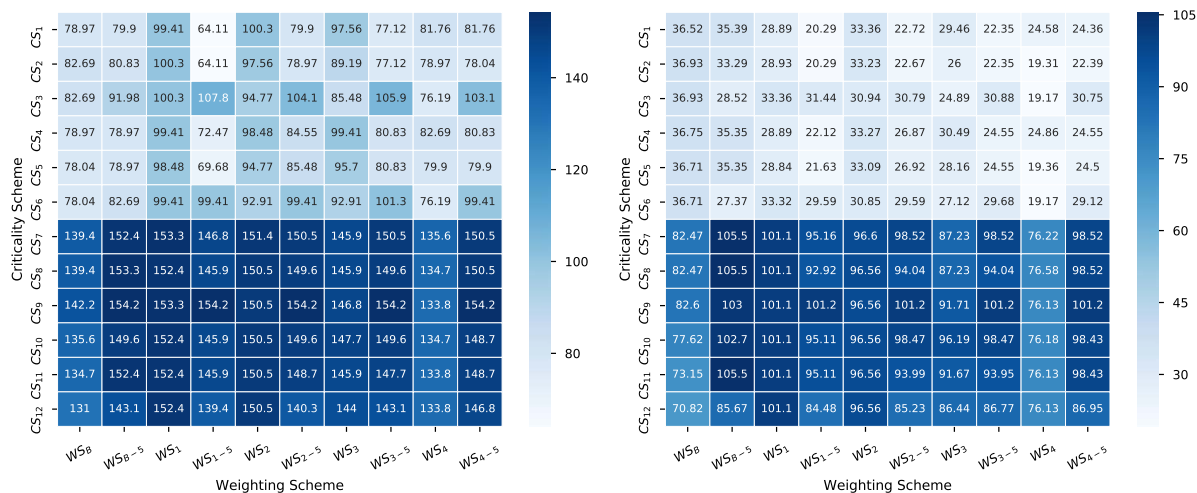
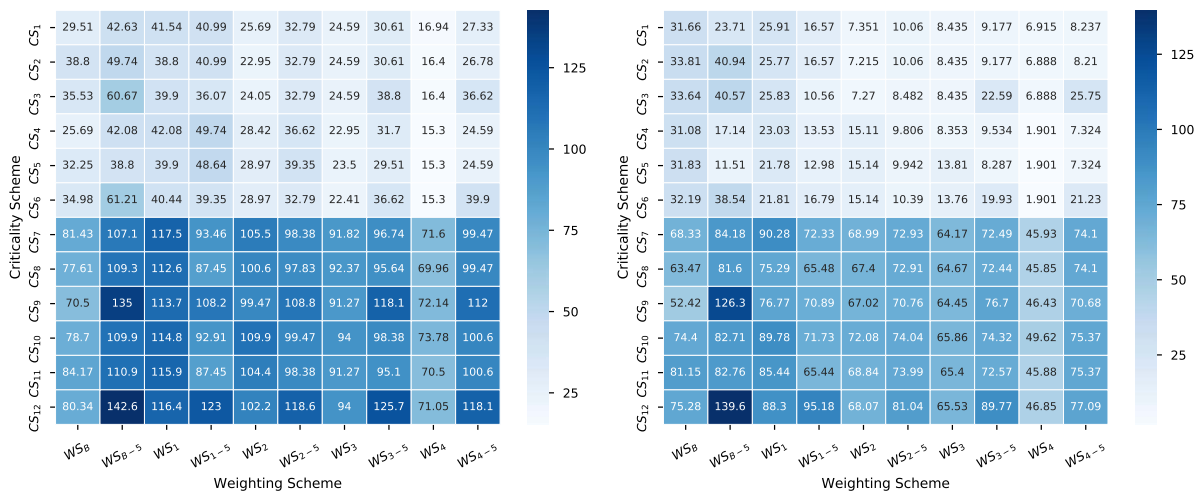


Figure S5: ROCE and awROCE 0.5% values for the COX-2 class

Table S9: COX-2 class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	63.18	17.72
Morgan	1024.0	1.0	False	102.20	41.53
Morgan	1024.0	1.0	True	68.75	19.53
Morgan	1024.0	2.0	False	105.92	43.11
Morgan	1024.0	2.0	True	77.12	22.41
Morgan	1024.0	3.0	False	99.41	36.00
Morgan	1024.0	3.0	True	75.26	23.21
Morgan	1024.0	4.0	False	93.84	31.29
Morgan	1024.0	4.0	True	72.47	22.84
Morgan	2048.0	1.0	False	100.34	41.44
Morgan	2048.0	1.0	True	67.82	19.48
Morgan	2048.0	2.0	False	108.70	43.25
Morgan	2048.0	2.0	True	77.12	21.34
Morgan	2048.0	3.0	False	102.20	38.50
Morgan	2048.0	3.0	True	79.90	23.90
Morgan	2048.0	4.0	False	103.13	38.55
Morgan	2048.0	4.0	True	73.40	23.12

S5.5 EGFr



(a) ROCE 0.5% values

(b) awROCE 0.5% values

Figure S6: ROCE and awROCE 0.5% values for the EGFr class

Table S10: EGFr class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	40.44	39.81
Morgan	1024.0	1.0	False	120.79	97.61
Morgan	1024.0	1.0	True	59.03	52.44
Morgan	1024.0	2.0	False	131.72	120.80
Morgan	1024.0	2.0	True	121.33	110.11
Morgan	1024.0	3.0	False	128.44	112.21
Morgan	1024.0	3.0	True	125.16	114.32
Morgan	1024.0	4.0	False	124.61	100.24
Morgan	1024.0	4.0	True	120.24	104.77
Morgan	2048.0	1.0	False	120.24	96.78
Morgan	2048.0	1.0	True	57.39	51.87
Morgan	2048.0	2.0	False	134.45	123.57
Morgan	2048.0	2.0	True	119.15	101.63
Morgan	2048.0	3.0	False	132.81	123.05
Morgan	2048.0	3.0	True	127.34	114.38
Morgan	2048.0	4.0	False	133.36	123.88
Morgan	2048.0	4.0	True	127.89	116.29

S5.6 FXa

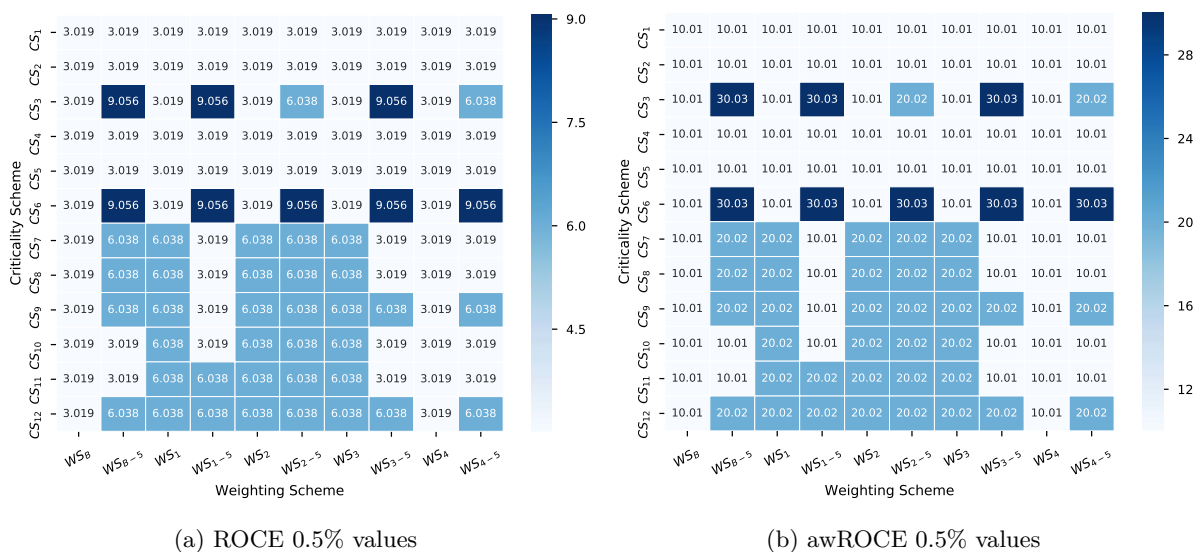


Figure S7: ROCE and awROCE 0.5% values for the FXa class

Table S11: FXa class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	9.06	30.03
Morgan	1024.0	1.0	False	6.04	20.02
Morgan	1024.0	1.0	True	3.02	10.01
Morgan	1024.0	2.0	False	9.06	20.02
Morgan	1024.0	2.0	True	3.02	10.01
Morgan	1024.0	3.0	False	18.11	21.02
Morgan	1024.0	3.0	True	3.02	10.01
Morgan	1024.0	4.0	False	30.19	32.03
Morgan	1024.0	4.0	True	3.02	10.01
Morgan	2048.0	1.0	False	6.04	20.02
Morgan	2048.0	1.0	True	3.02	10.01
Morgan	2048.0	2.0	False	12.08	20.35
Morgan	2048.0	2.0	True	3.02	10.01
Morgan	2048.0	3.0	False	9.06	20.02
Morgan	2048.0	3.0	True	3.02	10.01
Morgan	2048.0	4.0	False	18.11	30.70
Morgan	2048.0	4.0	True	3.02	10.01

S5.7 HIVRT

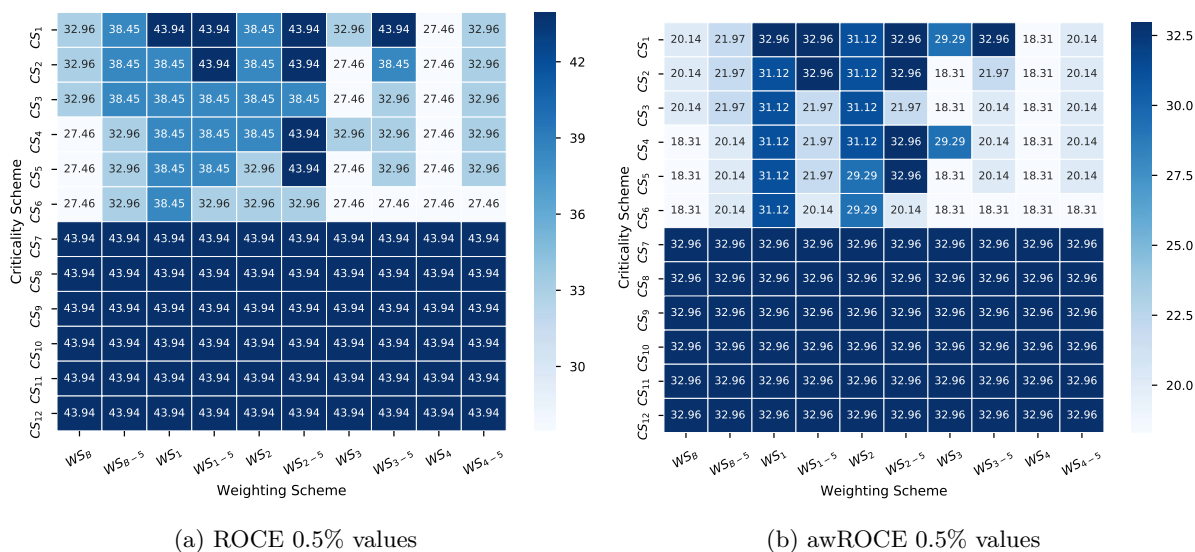


Figure S8: ROCE and awROCE 0.5% values for the HIVRT class

Table S12: HIVRT class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	27.46	18.31
Morgan	1024.0	1.0	False	32.96	20.14
Morgan	1024.0	1.0	True	32.96	29.29
Morgan	1024.0	2.0	False	38.45	31.12
Morgan	1024.0	2.0	True	32.96	29.29
Morgan	1024.0	3.0	False	32.96	29.29
Morgan	1024.0	3.0	True	32.96	29.29
Morgan	1024.0	4.0	False	32.96	29.29
Morgan	1024.0	4.0	True	32.96	29.29
Morgan	2048.0	1.0	False	32.96	20.14
Morgan	2048.0	1.0	True	32.96	29.29
Morgan	2048.0	2.0	False	43.94	32.96
Morgan	2048.0	2.0	True	32.96	29.29
Morgan	2048.0	3.0	False	38.45	31.12
Morgan	2048.0	3.0	True	32.96	29.29
Morgan	2048.0	4.0	False	38.45	31.12
Morgan	2048.0	4.0	True	32.96	29.29

S5.8 InhA

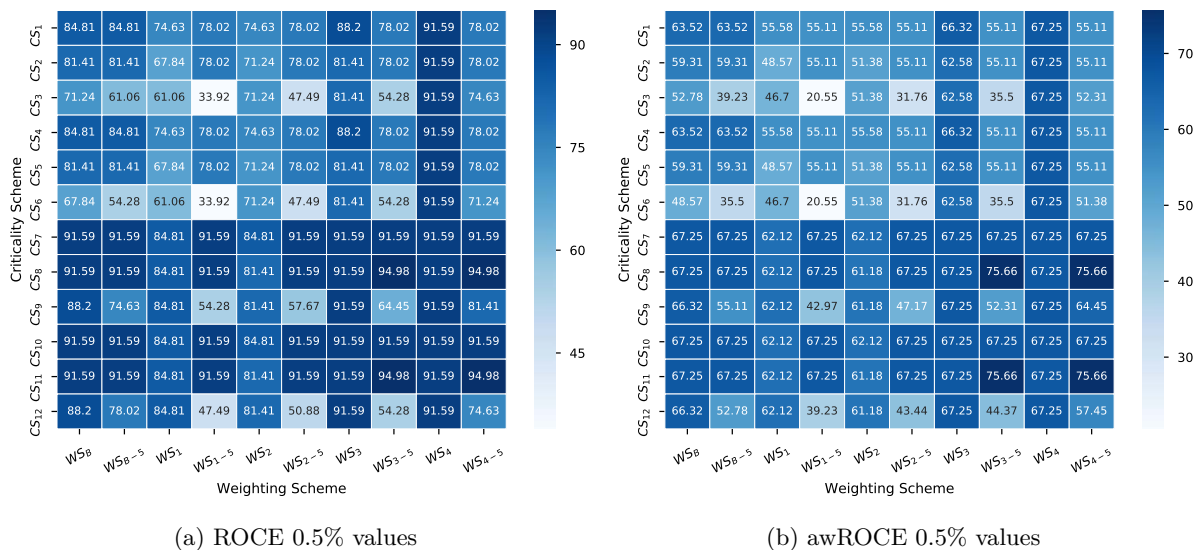
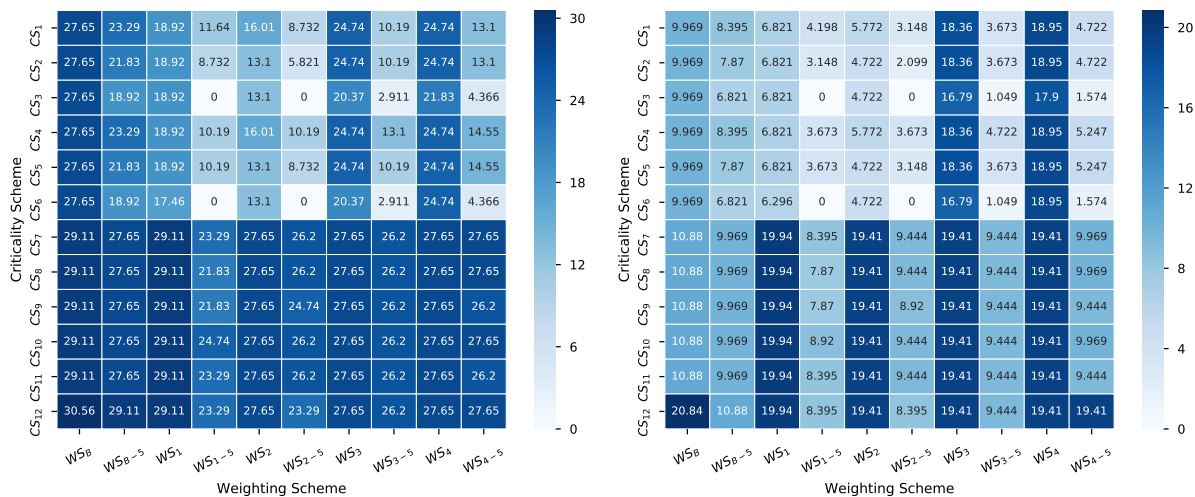


Figure S9: ROCE and awROCE 0.5% values for the InhA class

Table S13: InhA class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	64.45	41.50
Morgan	1024.0	1.0	False	84.81	57.91
Morgan	1024.0	1.0	True	91.59	80.33
Morgan	1024.0	2.0	False	88.20	66.32
Morgan	1024.0	2.0	True	91.59	74.73
Morgan	1024.0	3.0	False	88.20	66.32
Morgan	1024.0	3.0	True	91.59	74.73
Morgan	1024.0	4.0	False	88.20	66.32
Morgan	1024.0	4.0	True	88.20	66.32
Morgan	2048.0	1.0	False	84.81	57.91
Morgan	2048.0	1.0	True	94.98	83.13
Morgan	2048.0	2.0	False	88.20	66.32
Morgan	2048.0	2.0	True	98.37	91.54
Morgan	2048.0	3.0	False	88.20	66.32
Morgan	2048.0	3.0	True	91.59	74.73
Morgan	2048.0	4.0	False	88.20	66.32
Morgan	2048.0	4.0	True	94.98	83.13

S5.9 P38 MAP



(a) ROCE 0.5% values

(b) awROCE 0.5% values

Figure S10: ROCE and awROCE 0.5% values for the P38 MAP class

Table S14: P38 MAP class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	2.91	1.05
Morgan	1024.0	1.0	False	14.55	5.25
Morgan	1024.0	1.0	True	1.46	0.52
Morgan	1024.0	2.0	False	14.55	5.25
Morgan	1024.0	2.0	True	8.73	3.15
Morgan	1024.0	3.0	False	10.19	3.67
Morgan	1024.0	3.0	True	10.19	3.67
Morgan	1024.0	4.0	False	10.19	3.67
Morgan	1024.0	4.0	True	7.28	2.62
Morgan	2048.0	1.0	False	16.01	5.77
Morgan	2048.0	1.0	True	4.37	1.57
Morgan	2048.0	2.0	False	16.01	5.77
Morgan	2048.0	2.0	True	8.73	3.15
Morgan	2048.0	3.0	False	13.10	4.72
Morgan	2048.0	3.0	True	11.64	4.20
Morgan	2048.0	4.0	False	13.10	4.72
Morgan	2048.0	4.0	True	7.28	2.62

S5.10 PDE5

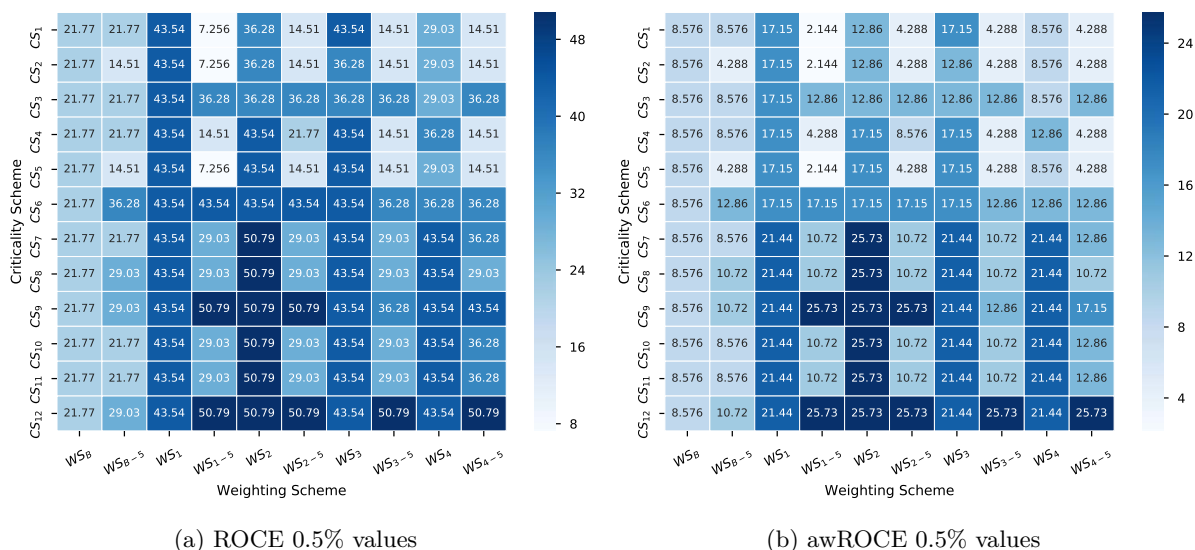


Figure S11: ROCE and awROCE 0.5% values for the PDE5 class

Table S15: PDE5 class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	7.26	4.29
Morgan	1024.0	1.0	False	29.03	17.15
Morgan	1024.0	1.0	True	7.26	2.14
Morgan	1024.0	2.0	False	21.77	8.58
Morgan	1024.0	2.0	True	21.77	8.58
Morgan	1024.0	3.0	False	21.77	8.58
Morgan	1024.0	3.0	True	21.77	8.58
Morgan	1024.0	4.0	False	21.77	8.58
Morgan	1024.0	4.0	True	36.28	15.01
Morgan	2048.0	1.0	False	29.03	17.15
Morgan	2048.0	1.0	True	7.26	2.14
Morgan	2048.0	2.0	False	21.77	8.58
Morgan	2048.0	2.0	True	21.77	8.58
Morgan	2048.0	3.0	False	21.77	8.58
Morgan	2048.0	3.0	True	36.28	12.86
Morgan	2048.0	4.0	False	21.77	8.58
Morgan	2048.0	4.0	True	43.54	17.15

S5.11 PDGFrB

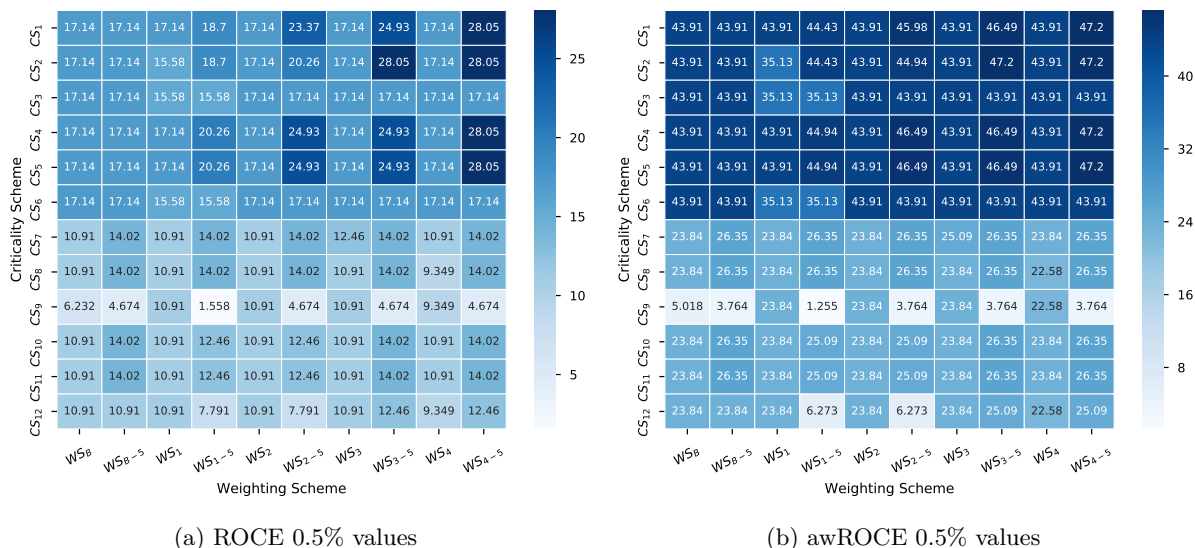


Figure S12: ROCE and awROCE 0.5% values for the PDGFrB class

Table S16: PDGFrB class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	14.02	23.39
Morgan	1024.0	1.0	False	20.26	44.94
Morgan	1024.0	1.0	True	17.14	43.91
Morgan	1024.0	2.0	False	21.81	46.70
Morgan	1024.0	2.0	True	17.14	43.91
Morgan	1024.0	3.0	False	24.93	47.73
Morgan	1024.0	3.0	True	17.14	43.91
Morgan	1024.0	4.0	False	21.81	45.46
Morgan	1024.0	4.0	True	17.14	43.91
Morgan	2048.0	1.0	False	21.81	45.46
Morgan	2048.0	1.0	True	17.14	43.91
Morgan	2048.0	2.0	False	20.26	44.94
Morgan	2048.0	2.0	True	17.14	43.91
Morgan	2048.0	3.0	False	18.70	44.43
Morgan	2048.0	3.0	True	17.14	43.91
Morgan	2048.0	4.0	False	17.14	43.91
Morgan	2048.0	4.0	True	17.14	43.91

S5.12 Src

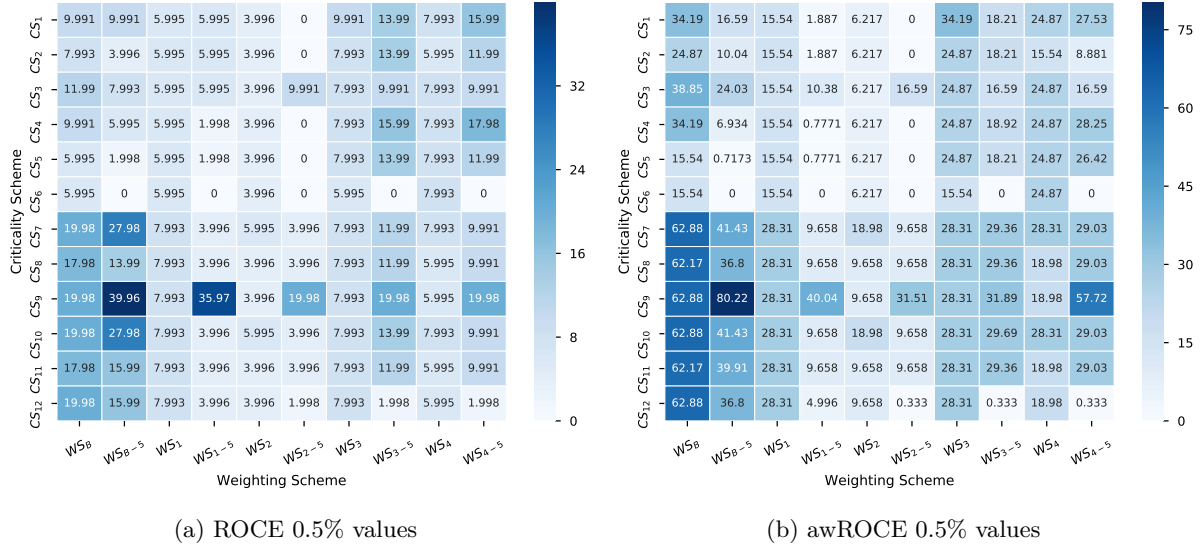
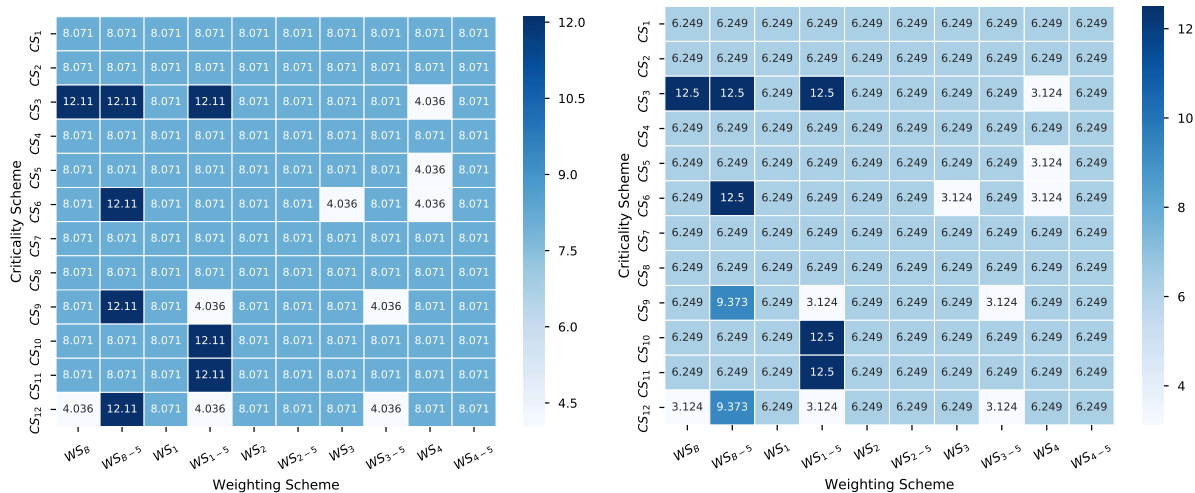


Figure S13: ROCE and awROCE 0.5% values for the Src class

Table S17: Src class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	0.00	0.00
Morgan	1024.0	1.0	False	15.99	5.35
Morgan	1024.0	1.0	True	2.00	0.72
Morgan	1024.0	2.0	False	23.98	8.61
Morgan	1024.0	2.0	True	19.98	7.41
Morgan	1024.0	3.0	False	17.98	6.46
Morgan	1024.0	3.0	True	19.98	7.29
Morgan	1024.0	4.0	False	13.99	5.02
Morgan	1024.0	4.0	True	23.98	8.79
Morgan	2048.0	1.0	False	25.98	8.94
Morgan	2048.0	1.0	True	2.00	0.72
Morgan	2048.0	2.0	False	27.98	9.66
Morgan	2048.0	2.0	True	21.98	8.13
Morgan	2048.0	3.0	False	29.97	9.99
Morgan	2048.0	3.0	True	23.98	8.85
Morgan	2048.0	4.0	False	25.98	9.33
Morgan	2048.0	4.0	True	19.98	7.23

S5.13 VEGFr-2



(a) ROCE 0.5% values

(b) awROCE 0.5% values

Figure S14: ROCE and awROCE 0.5% values for the VEGFr-2 class

Table S18: VEGFr-2 class – Fingerprint results

Fingerprint	Bits	Radius	Use Features	ROCE 0.5%	awROCE 0.5%
MACCS	N/A	N/A	N/A	8.07	6.25
Morgan	1024.0	1.0	False	8.07	6.25
Morgan	1024.0	1.0	True	8.07	6.25
Morgan	1024.0	2.0	False	8.07	6.25
Morgan	1024.0	2.0	True	8.07	6.25
Morgan	1024.0	3.0	False	8.07	6.25
Morgan	1024.0	3.0	True	8.07	6.25
Morgan	1024.0	4.0	False	8.07	6.25
Morgan	1024.0	4.0	True	8.07	6.25
Morgan	2048.0	1.0	False	8.07	6.25
Morgan	2048.0	1.0	True	8.07	6.25
Morgan	2048.0	2.0	False	8.07	6.25
Morgan	2048.0	2.0	True	8.07	6.25
Morgan	2048.0	3.0	False	8.07	6.25
Morgan	2048.0	3.0	True	8.07	6.25
Morgan	2048.0	4.0	False	8.07	6.25
Morgan	2048.0	4.0	True	8.07	6.25

References

- (1) Jahn, A.; Hinselmann, G.; Fechner, N.; Zell, A. Optimal assignment methods for ligand-based virtual screening. *J. Cheminf.* **2009**, *1*, 14.
- (2) Zhu, Z.; Fang, C.; Katzgraber, H. G. borealis – A generalized global update algorithm for Boolean optimization problems. *arXiv:1605.09399*, **2016**.