TS1 to TS5. Results of the GA(M)E-QSAR algorithm for all the data sets used to validate the algorithm

Each column in the tables stands for: Size of the Ensemble or Meta-Ensemble (Size); Overall accuracy, Sensitivity and Specificity on the training (Train(%)), Selection (Sel.(%)) and external (Ext.(%)) subsets represented as Accuracy (Sensitivity/Specificity); Leave-One-Out cross-validation accuracy (LOO(%)) and Bootstrap cross-validation accuracy (Boot(%)).

In each table we show the statistical parameters of the best model per modeling technique according to the Borda-Kendall consensus ranking approach described in the **Computational Methods** section, as well as the mean value of the parameters of the Ensemble or Meta-Ensemble members. The results displayed in the tables correspond to the Adaboost Ensembles derived from the GA (A.E); Meta-Ensembles built using the Adaboost algorithm and trained with the clustering representative models (ME-AB); Meta-Ensembles built using the Adaboost algorithm and trained with all the Adaboost Ensembles (ME-AB NC); and Voting Meta-Ensembles of the Adaboost models that are the representative models derived from the clustering procedure using weighted (ME-Vot Weighted) and un-weighted (ME-Vot) voting. The last row of the tables shows the results obtained for each data set in the data source reference. For the DILI dataset we show the average values of the five fold modeling approach that they report.

TS1. Results of the GA(M)E-QSAR algorithm for the BZR data set

			BZR			
	Size	**Train(%)**	**Sel.(%)**	**LOO(%)**	**Boot(%)**	**Ext(%)**
			Fold 1			
A.E	18	90 (87/94)	72 (67/78)	88.28	80	70 (62/79)
<A.E Members>		60 (60/62)	60 (57/63)			58 (56/60)
ME-AB	2	88 (86/91)	72 (67/78)	88.28	87.22	69 (62/76)
<ME-AB Members>		87 (84/90)	74 (69/78)	84.83	78.2	70 (63/78)
ME-AB NC	8	90 (87/93)	78 (72/83)	88.28	88.25	74 (67/81)

<ME-AB NC Members>		84 (83/85)	76 (74/78)	82.38	76.87	68 (62/74)
ME-Vot W	11	90 (88/93)	78 (78/78)			74 (67/82)
<ME-Vot W Members>		87 (84/90)	74 (69/78)	80.52	75.76	70 (63/78)
ME-Vot	5	88 (89/86)	78 (67/89)			72 (68/76)
<ME-Vot Members>		81 (83/79)	69 (64/74)	83.31	77.46	68 (67/70)
			Fold 2			
A.E	14	92 (94/91)	78 (71/84)	91.03	83.99	66 (60/71)
<A.E Members>		62 (60/63)	57 (57/58)			59 (56/61)
ME-AB	2	91 (92/90)	75 (71/79)	91.03	90.72	66 (62/69)
<ME-AB Members>		88 (90/87)	78 (79/76)	86.21	82.85	67 (63/72)
ME-AB NC	9	92 (92/93)	81 (76/84)	91.03	90.95	69 (60/77)
<ME-AB NC Members>		88 (89/87)	75 (79/72)	86.32	82.72	69 (66/72)
ME-Vot W	6	93 (94/93)	81 (82/79)			70 (70/71)
<ME-Vot W Members>		88 (90/87)	78 (79/76)	84.37	80.89	67 (63/72)
ME-Vot	23	88 (88/88)	69 (82/58)			72 (68/76)
<ME-Vot Members>		82 (83/82)	66 (82/53)	84.98	81.54	68 (66/70)
			Fold 3			
A.E	9	87 (82/92)	72 (70/77)	85.52	80.89	70 (62/79)
<A.E Members>		64 (63/65)	61 (56/69)			61 (57/64)
ME-AB	15	90 (86/93)	69 (70/69)	89.66	87.72	69 (63/74)
<ME-AB Members>		85 (84/86)	68 (64/75)	82.48	78.08	69 (61/78)
ME-AB NC	2	90 (86/93)	69 (70/69)	89.66	88.53	69 (63/74)
<ME-AB NC Members>		89 (86/93)	69 (67/73)	82.59	78.51	70 (61/80)
ME-Vot W	4	87 (83/91)	69 (61/85)			67 (52/82)
<ME-Vot W Members>		85 (84/86)	68 (64/75)	84.48	78.83	69 (61/78)
ME-Vot	5	87 (86/88)	69 (70/69)			68 (59/77)
<ME-Vot Members>		85 (85/86)	68 (63/75)	82.62	78.44	68 (57/78)
			Fold 4			
A.E	11	84 (80/88)	84 (100/67)	79.86	77.09	65 (67/63)
<A.E Members>		60 (60/60)	61 (63/59)			57 (58/55)
ME-AB	9	85 (83/88)	73 (89/56)	85.42	81.4	66 (68/65)
<ME-AB Members>		82 (79/85)	75 (85/65)	80.48	74.16	68 (63/73)
ME-AB NC	4	87 (87/87)	78 (84/72)	86.81	85.13	71 (67/76)
<ME-AB NC Members>		84 (83/85)	77 (84/69)	78.95	74.04	68 (64/72)
ME-Vot W	26	81 (76/86)	84 (95/72)			71 (59/84)
<ME-Vot W Members>		82 (79/85)	75 (85/65)	78.65	75.36	68 (63/73)
ME-Vot	13	80 (75/86)	76 (89/61)			70 (60/79)
<ME-Vot Members>		76 (72/80)	69 (79/59)	80.56	74.54	67 (61/73)
			Fold 5			
A.E	13	90 (90/90)	75 (82/68)	87.59	81.89	70 (71/69)
<A.E Members>		62 (63/60)	56 (59/54)			58 (59/57)

ME-AB	2	90 (90/90)	75 (82/68)	89.66	89.38	70 (71/69)
<ME-AB Members>		88 (88/87)	75 (71/79)	86.21	81.66	70 (66/75)
ME-AB NC	2	90 (91/88)	72 (76/68)	89.66	88.14	70 (73/68)
<ME-AB NC Members>		88 (91/85)	72 (76/68)	82.94	79.13	67 (63/71)
ME-Vot W	15	92 (91/93)	83 (82/84)			66 (52/81)
<ME-Vot W Members>		88 (88/87)	75 (71/79)	82.76	80.3	70 (66/75)
ME-Vot	25	91 (91/91)	78 (76/79)			68 (52/84)
<ME-Vot Members>		86 (86/86)	72 (70/73)	82.4	78.68	67 (62/73)
Reported						
		79 (81/76)	-	-	-	75 (70/81)

TS2. Results of the GA(M)E-QSAR algorithm for the COX-2 data set

COX2						
	Size	**Train(%)**	**Sel.(%)**	**LOO(%)**	**Boot(%)**	**Ext(%)**
Fold 1						
A.E	10	89 (93/86)	89 (75/96)	87.32	79.73	63 (65/62)
<A.E Members>		61 (62/61)	66 (55/72)			57 (62/54)
ME-AB	1	89 (93/86)	89 (75/96)	88.73	88.56	64 (67/62)
<ME-AB Members>		89 (93/86)	89 (75/96)	85.21	79.28	64 (67/62)
ME-AB NC	2	89 (93/86)	89 (75/96)	88.73	88.24	63 (65/62)
<ME-AB NC Members>		86 (86/86)	88 (71/96)	81.69	76.95	64 (62/64)
ME-Vot W	5	91 (95/88)	92 (83/96)			72 (73/71)
<ME-Vot W Members>		89 (93/86)	89 (75/96)	83.45	78.2	64 (67/62)
ME-Vot	39	91 (93/89)	92 (83/96)			66 (65/67)
<ME-Vot Members>		84 (86/83)	87 (78/92)	81.27	76.56	65 (65/65)
Fold 2						
A.E	11	88 (88/88)	77 (57/90)	88.11	80.69	74 (76/72)
<A.E Members>		61 (59/62)	54 (51/57)			57 (62/54)
ME-AB	11	90 (91/88)	77 (64/86)	89.51	86.25	68 (63/71)
<ME-AB Members>		87 (86/87)	73 (57/84)	85.12	79.45	69 (68/70)
ME-AB NC	2	90 (89/90)	71 (50/86)	83.92	88.39	70 (71/70)
<ME-AB NC Members>		90 (91/88)	71 (54/83)	85.31	79.46	68 (69/66)
ME-Vot W	5	92 (93/91)	77 (64/86)			69 (69/68)
<ME-Vot W Members>		87 (86/87)	73 (57/84)	87.06	81.7	69 (68/70)
ME-Vot	9	92 (91/92)	77 (64/86)			71 (69/72)
<ME-Vot Members>		86 (85/87)	73 (57/83)	85	79.42	68 (67/69)
Fold 3						
A.E	10	90 (90/90)	72 (77/70)	88.73	83.95	72 (76/70)
<A.E Members>		64 (62/66)	58 (59/57)			59 (63/57)
ME-AB	2	91 (93/89)	72 (69/74)	90.85	89.83	74 (76/72)
<ME-AB Members>		90 (94/87)	72 (73/72)	86.62	81.61	73 (80/68)
ME-AB NC	2	92 (91/93)	69 (77/65)	92.25	91.15	74 (76/72)
<ME-AB NC Members>		91 (91/91)	71 (73/70)	86.97	81.55	71 (77/68)
ME-Vot W	6	93 (97/90)	72 (77/70)			74 (82/68)
<ME-Vot W Members>		90 (94/87)	72 (73/72)	86.27	82.57	73 (80/68)
ME-Vot	37	90 (90/90)	78 (85/74)			72 (78/68)
<ME-Vot Members>		88 (91/86)	69 (74/67)	86.09	82	70 (78/64)
Fold 4						
A.E	6	87 (89/86)	77 (81/74)	86.01	80.41	74 (78/71)
<A.E Members>		63 (63/63)	59 (60/57)			58 (67/52)
ME-AB	2	89 (85/91)	71 (56/84)	88.81	87.36	65 (73/59)

<ME-AB Members>		87 (86/88)	73 (69/76)	83.92	79.6	68 (71/66)
ME-AB NC	2	89 (89/89)	69 (69/68)	82.52	87.72	74 (82/68)
<ME-AB NC Members>		89 (88/89)	69 (69/68)	84.7	79.69	72 (80/66)
ME-Vot W	8	90 (87/92)	77 (69/84)			70 (71/68)
<ME-Vot W Members>		87 (86/88)	73 (69/76)	85.31	79.96	68 (71/66)
ME-Vot	9	90 (87/92)	77 (69/84)			68 (76/63)
<ME-Vot Members>		86 (85/86)	71 (72/71)	84.46	79.49	68 (74/64)
			Fold 5			
A.E	10	88 (100/80)	83 (88/80)	87.32	78.53	70 (84/61)
<A.E Members>		62 (61/63)	64 (62/66)			56 (62/51)
ME-AB	46	87 (91/85)	83 (94/75)	87.32	83.16	70 (71/68)
<ME-AB Members>		84 (91/80)	80 (93/71)	81.78	76.64	66 (75/60)
ME-AB NC	2	88 (93/85)	81 (88/75)	88.03	86.64	69 (69/68)
<ME-AB NC Members>		87 (94/83)	79 (88/73)	82.59	76.95	67 (71/64)
ME-Vot W	11	91 (98/86)	81 (94/70)			66 (73/61)
<ME-Vot W Members>		84 (91/80)	80 (93/71)	84.51	77.67	66 (75/60)
ME-Vot	9	90 (98/85)	81 (94/70)			64 (71/59)
<ME-Vot Members>		85 (93/81)	80 (92/71)	82.63	77.14	66 (73/61)
			Reported			
		85 (83/87)	-	-	-	73 (75/72)

TS3. Results of the GA(M)E-QSAR algorithm for the DHFR data set

DHFR						
	Size	**Train(%)**	**Sel.(%)**	**LOO(%)**	**Boot(%)**	**Ext(%)**
Fold 1						
A.E	13	85 (82/87)	83 (88/79)	82.89	78.4	72 (74/71)
<A.E Members>		60 (60/60)	57 (62/55)			56 (58/56)
ME-AB	4	86 (82/88)	76 (82/72)	85.56	84.06	73 (69/75)
<ME-AB Members>		83 (79/85)	77 (85/72)	81.42	76.31	72 (71/73)
ME-AB NC	2	87 (85/88)	78 (82/76)	86.63	86.06	73 (74/73)
<ME-AB NC Members>		84 (81/85)	74 (76/72)	81.55	76.42	69 (64/70)
ME-Vot W	6	88 (84/91)	80 (88/76)			76 (71/78)
<ME-Vot W Members>		83 (79/85)	77 (85/72)	81.28	77.23	72 (71/73)
ME-Vot	11	88 (85/90)	80 (94/72)			74 (74/74)
<ME-Vot Members>		82 (81/83)	74 (86/66)	80.89	75.82	70 (70/70)
Fold 2						
A.E	15	83 (84/83)	85 (81/87)	80.11	76.81	76 (67/79)
<A.E Members>		59 (60/59)	62 (60/63)			58 (59/57)
ME-AB	15	85 (82/86)	85 (81/87)	82.8	80.78	74 (64/77)
<ME-AB Members>		80 (80/80)	81 (75/84)	77.99	72.85	71 (72/70)
ME-AB NC	4	86 (85/86)	83 (81/84)	86.02	84.69	74 (69/75)
<ME-AB NC Members>		82 (82/81)	80 (77/81)	78.12	72.81	70 (68/70)
ME-Vot W	10	86 (85/86)	87 (81/90)			74 (74/74)
<ME-Vot W Members>		80 (80/80)	81 (75/84)	77.28	72.76	71 (72/70)
ME-Vot	13	86 (88/85)	87 (81/90)			74 (79/72)
<ME-Vot Members>		80 (81/80)	81 (75/84)	77.96	72.75	71 (73/70)
Fold 3						
A.E	9	83 (81/85)	78 (71/81)	83.42	77.86	68 (64/69)
<A.E Members>		61 (62/61)	59 (55/61)			58 (59/58)
ME-AB	9	85 (84/85)	80 (71/84)	83.96	81.07	71 (69/71)
<ME-AB Members>		81 (82/81)	77 (65/82)	79.62	75.94	71 (68/71)
ME-AB NC	3	83 (84/83)	85 (79/88)	83.42	82.81	74 (71/75)
<ME-AB NC Members>		83 (83/82)	76 (69/79)	79.34	75.69	71 (68/71)
ME-Vot W	11	84 (86/84)	80 (64/88)			73 (71/73)
<ME-Vot W Members>		81 (82/81)	77 (65/82)	80.39	75.41	71 (68/71)
ME-Vot	9	85 (86/85)	80 (64/88)			71 (62/74)
<ME-Vot Members>		81 (82/81)	77 (65/82)	79.62	75.94	71 (68/71)
Fold 4						
A.E	13	88 (89/87)	72 (61/79)	84.41	79.49	76 (69/78)
<A.E Members>		61 (61/62)	58 (51/63)			57 (54/58)
ME-AB	7	88 (89/87)	68 (61/72)	87.63	85.61	74 (69/76)

<ME-AB Members>		84 (84/84)	68 (49/80)	82.1	78.02	72 (63/76)
ME-AB NC	2	88 (89/87)	70 (61/76)	87.63	87.11	76 (69/78)
<ME-AB NC Members>		85 (83/87)	70 (56/79)	81.91	77.89	74 (64/78)
ME-Vot W	17	88 (89/88)	68 (50/79)			74 (67/76)
<ME-Vot W Members>		84 (84/84)	68 (49/80)	80.38	77.89	72 (63/76)
ME-Vot	25	88 (89/87)	70 (56/79)			73 (67/75)
<ME-Vot Members>		84 (83/84)	69 (53/79)	81.66	77.9	73 (66/75)
Fold 5						
A.E	12	85 (88/83)	70 (58/79)	84.41	79.69	70 (64/72)
<A.E Members>		61 (61/60)	57 (54/59)			55 (55/55)
ME-AB	9	87 (89/86)	64 (53/71)	87.1	84.84	70 (62/73)
<ME-AB Members>		85 (82/86)	65 (58/71)	82.02	78.55	71 (62/74)
ME-AB NC	2	88 (91/86)	64 (53/71)	87.63	86.69	71 (57/75)
<ME-AB NC Members>		87 (86/87)	64 (55/70)	81.72	78.61	71 (57/76)
ME-Vot W	8	88 (85/89)	68 (53/79)			73 (62/77)
<ME-Vot W Members>		85 (82/86)	65 (58/71)	84.95	79.47	71 (62/74)
ME-Vot	29	87 (86/88)	66 (53/75)			73 (64/75)
<ME-Vot Members>		84 (82/85)	65 (56/72)	81.37	77.59	71 (63/74)
Reported						
		82 (85/81)	-	-	-	72 (74/71)

TS4. Results of the GA(M)E-QSAR algorithm for the ER data set

ER						
	Size	**Train(%)**	**Sel.(%)**	**LOO(%)**	**Boot(%)**	**Ext(%)**
Fold 1						
A.E	13	89 (93/85)	80 (91/72)	88.68	82.79	78 (79/78)
<A.E Members>		64 (66/62)	59 (61/58)			60 (61/60)
ME-AB	7	89 (93/85)	80 (86/75)	88.68	86.23	78 (79/78)
<ME-AB Members>		87 (94/81)	73 (81/67)	84.64	82.15	75 (76/74)
ME-AB NC	2	89 (98/82)	76 (82/72)	88.68	87.64	73 (72/73)
<ME-AB NC Members>		88 (93/84)	73 (75/72)	84.96	82	73 (69/75)
ME-Vot W	9	89 (97/84)	72 (82/66)			76 (76/75)
<ME-Vot W Members>		87 (94/81)	73 (81/67)	84.91	80.51	75 (76/74)
ME-Vot	9	90 (98/85)	74 (86/66)			75 (77/73)
<ME-Vot Members>		87 (94/82)	73 (80/69)	84.96	82	74 (75/74)
Fold 2						
A.E	12	86 (90/84)	81 (70/88)	84.98	81.57	77 (70/82)
<A.E Members>		64 (68/61)	66 (64/67)			63 (64/62)
ME-AB	11	87 (91/84)	79 (70/85)	86.85	84.28	77 (73/80)
<ME-AB Members>		85 (89/82)	81 (76/84)	83.74	79.53	76 (71/80)
ME-AB NC	2	87 (92/84)	83 (75/88)	87.32	86.06	77 (72/81)
<ME-AB NC Members>		86 (92/83)	83 (83/83)	83.22	79.27	75 (68/80)
ME-Vot W	15	89 (94/85)	83 (70/91)			79 (75/83)
<ME-Vot W Members>		85 (89/82)	81 (76/84)	84.51	79.36	76 (71/80)
ME-Vot	17	89 (94/85)	83 (70/91)			78 (72/82)
<ME-Vot Members>		85 (89/82)	80 (74/85)	82.96	79.31	76 (70/79)
Fold 3						
A.E	15	86 (89/84)	85 (86/84)	82.16	80.09	76 (69/81)
<A.E Members>		61 (62/61)	64 (66/61)			59 (55/61)
ME-AB	8	86 (88/85)	85 (89/80)	86.38	84.21	77 (75/78)
<ME-AB Members>		84 (89/81)	83 (90/75)	81.98	77.33	74 (71/76)
ME-AB NC	2	87 (90/85)	85 (89/80)	87.32	86.19	77 (75/78)
<ME-AB NC Members>		86 (87/86)	84 (88/80)	81.56	77.3	76 (70/80)
ME-Vot W	11	88 (91/86)	91 (96/84)			76 (72/79)
<ME-Vot W Members>		84 (89/81)	83 (90/75)	84.27	78.31	74 (71/76)
ME-Vot	37	88 (94/85)	89 (96/80)			77 (72/80)
<ME-Vot Members>		84 (88/81)	83 (90/76)	81.02	77.52	74 (71/76)
Fold 4						
A.E	12	86 (90/84)	81 (90/75)	85.45	80.65	76 (70/79)
<A.E Members>		65 (69/62)	64 (70/60)			61 (61/61)
ME-AB	20	87 (92/83)	79 (76/81)	86.85	83.55	78 (76/80)
<ME-AB Members>		85 (91/81)	80 (84/77)	83.57	79.18	76 (72/78)

ME-AB NC	2	87 (91/85)	81 (86/78)	87.32	86.55	74 (75/74)
<ME-AB NC Members>		86 (92/82)	82 (86/80)	82.79	79.09	75 (74/76)
ME-Vot W	9	87 (93/83)	81 (90/75)			79 (79/79)
<ME-Vot W Members>		85 (91/81)	80 (84/77)	82.39	78.97	76 (72/78)
ME-Vot	3	87 (91/85)	81 (86/78)			78 (76/80)
<ME-Vot Members>		85 (90/82)	78 (84/74)	82.47	79.17	76 (77/76)
			Fold 5			
A.E	8	88 (89/88)	75 (68/79)	88.73	84.29	74 (72/76)
<A.E Members>		66 (65/67)	61 (70/57)			63 (61/65)
ME-AB	3	90 (91/89)	72 (79/68)	89.67	88.95	75 (72/77)
<ME-AB Members>		88 (90/86)	72 (79/69)	86.7	82.05	73 (69/76)
ME-AB NC	2	90 (91/89)	72 (79/68)	89.67	88.62	75 (72/77)
<ME-AB NC Members>		89 (91/89)	73 (76/71)	86.15	81.94	76 (70/79)
ME-Vot W	6	90 (93/88)	72 (79/68)			77 (79/76)
<ME-Vot W Members>		88 (90/86)	72 (79/69)	87.79	83.19	73 (69/76)
ME-Vot	5	91 (91/90)	74 (79/71)			77 (75/79)
<ME-Vot Members>		87 (90/85)	73 (78/70)	85.92	81.67	74 (73/76)
			Reported			
		81 (87/76)	-	-	-	79 (77/80)

TS5. Results of the GA(M)E-QSAR algorithm for the DILI data set

DILI						
	Size	**Train(%)**	**Sel.(%)**	**LOO(%)**	**Boot(%)**	**Ext(%)**
Fold 1						
A.E	9	69 (66/72)	63 (60/67)	68.65	62.06	65 (66/64)
<A.E Members>		57 (54/60)	53 (51/56)			57 (55/60)
ME-AB	3	70 (65/74)	62 (58/67)	69.91	69.2	66 (66/66)
<ME-AB Members>		68 (68/69)	63 (61/65)	66.77	61.18	65 (67/64)
ME-AB NC	2	70 (65/74)	60 (58/63)	69.91	68.61	65 (66/64)
<ME-AB NC Members>		69 (68/70)	60 (59/62)	65.89	61.23	64 (65/62)
ME-Vot W	5	70 (69/71)	66 (67/65)			69 (74/64)
<ME-Vot W Members>		68 (68/69)	63 (61/65)	65.83	61.47	65 (67/64)
ME-Vot	39	69 (69/69)	67 (67/67)			65 (68/62)
<ME-Vot Members>		67 (67/68)	63 (62/64)	65.05	60.68	65 (67/63)
Fold 2						
A.E	12	71 (66/76)	64 (54/75)	68.97	64.57	68 (60/75)
<A.E Members>		56 (54/58)	59 (55/63)			57 (53/60)
ME-AB	21	72 (65/78)	61 (54/69)	71.79	69.63	66 (58/73)
<ME-AB Members>		69 (63/74)	62 (53/71)	67	63.65	68 (59/76)
ME-AB NC	2	72 (67/77)	61 (54/69)	72.1	71.14	70 (62/77)
<ME-AB NC Members>		71 (64/77)	62 (53/71)	67.48	63.77	67 (54/78)
ME-Vot W	4	71 (60/79)	62 (50/75)			67 (52/80)
<ME-Vot W Members>		69 (63/74)	62 (53/71)	68.5	64.69	68 (59/76)
ME-Vot	2	71 (65/76)	61 (52/71)			69 (56/80)
<ME-Vot Members>		71 (65/76)	61 (52/71)	70.22	64.75	69 (56/80)
Fold 3						
A.E	9	75 (76/74)	65 (65/66)	73.35	67.91	57 (55/58)
<A.E Members>		59 (58/59)	53 (52/53)			56 (61/52)
ME-AB	11	76 (76/75)	63 (60/66)	75.55	74.45	58 (60/58)
<ME-AB Members>		73 (75/72)	64 (61/66)	71.59	66.79	60 (60/59)
ME-AB NC	2	76 (76/75)	63 (60/66)	75.55	75.18	58 (60/58)
<ME-AB NC Members>		74 (76/71)	62 (60/64)	71.21	66.79	60 (61/59)
ME-Vot W	19	76 (78/73)	67 (63/71)			58 (60/58)
<ME-Vot W Members>		73 (75/72)	64 (61/66)	71.79	67.2	60 (60/59)
ME-Vot	23	76 (78/73)	66 (63/69)			58 (60/58)
<ME-Vot Members>		73 (74/72)	63 (61/65)	71.27	66.77	59 (60/59)
Fold 4						
A.E	9	71 (69/72)	70 (68/72)	69.59	64.2	59 (56/63)
<A.E Members>		57 (58/56)	58 (59/58)			53 (52/53)
ME-AB	2	70 (64/75)	67 (55/80)	70.22	69.43	58 (50/64)
<ME-AB Members>		69 (63/75)	67 (57/78)	67.71	63.96	59 (51/66)

ME-AB NC	2	72 (65/77)	67 (55/80)	71.79	70.94	55 (48/61)
<ME-AB NC Members>		70 (70/71)	67 (64/71)	66.89	62.84	55 (52/57)
ME-Vot W	19	71 (70/72)	69 (64/74)			62 (62/63)
<ME-Vot W Members>		69 (63/75)	67 (57/78)	66.14	62.96	59 (51/66)
ME-Vot	37	71 (70/72)	71 (68/74)			60 (60/61)
<ME-Vot Members>		68 (67/70)	68 (64/72)	66.34	62.78	58 (56/61)
Fold 5						
A.E	9	72 (75/69)	68 (78/61)	72.01	65.48	61 (69/54)
<A.E Members>		57 (59/56)	56 (60/53)			56 (55/57)
ME-AB	9	73 (75/71)	63 (73/56)	72.64	69.92	61 (56/64)
<ME-AB Members>		70 (72/69)	65 (72/59)	69.08	64.15	59 (57/61)
ME-AB NC	2	73 (75/72)	64 (76/56)	73.27	71.94	62 (56/66)
<ME-AB NC Members>		73 (74/72)	64 (69/61)	69.33	64.3	57 (55/58)
ME-Vot W	11	73 (75/71)	68 (76/62)			61 (63/59)
<ME-Vot W Members>		70 (72/69)	65 (72/59)	69.65	64.24	59 (57/61)
ME-Vot	23	73 (75/70)	71 (78/66)			63 (60/64)
<ME-Vot Members>		70 (72/68)	65 (73/60)	68.74	64.24	61 (60/61)
Reported (Dragon descriptors)						
		86	-	-	-	65

TS6. Minimum and Maximum values of the accuracy estimator parameters of the Adaboost Ensembles obtained with the GA(M)E-QSAR algorithm when the overall accuracy is used to filter the LDA models.

	Size	Min (Train)	Max (Train)	Min (Sel)	Max (Sel)	Min (Ext)	Max (Ext)	LOO (Min/Max)	Boot (Min/Max)
					BZR				
A.E	10/15	87 (87/87)	91 (92/90)	72 (74/69)	81 (95/67)	67 (65/69)	74 (63/84)	83/88	80/84
					COX2				
A.E	8/16	86 (82/89)	92 (91/93)	74 (75/74)	92 (92/92)	66 (59/70)	74 (67/78)	86/92	80/86
					DHFR				
A.E	7/11	84 (66/94)	88 (82/91)	70 (68/71)	85 (75/90)	71 (55/77)	79 (60/86)	84/86	79/81
					ER				
A.E	10/17	88 (89/87)	91 (93/89)	77 (79/76)	89 (85/91)	74 (52/88)	80 (65/90)	88/91	83/86
					DILI				
A.E	8/21	71 (51/85)	75 (72/77)	65 (71/60)	69 (54/85)	50 (36/63)	63 (47/79)	70/75	63/69

TS7. Correlation matrices of the four decision makers used to select the optimal Adaboost Ensemble for each target and modeling fold.

BZR

	Fold 1				Fold 2				Fold 3				Fold 4				Fold 5			
	T	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**
T[1]	1.00	0.24	0.65	0.67	1.00	0.01	0.74	0.63	1.00	0.07	0.65	0.49	1.00	0.03	0.59	0.46	1.00	0.04	0.59	0.33
S[2]	0.24	1.00	0.18	0.28	0.01	1.00	0.09	0.03	0.07	1.00	0.00	0.01	0.03	1.00	0.05	0.15	0.04	1.00	0.22	0.16
LOO[3]	0.65	0.18	1.00	0.56	0.74	0.09	1.00	0.72	0.65	0.00	1.00	0.53	0.59	0.05	1.00	0.50	0.59	0.22	1.00	0.58
Boot[4]	0.67	0.28	0.56	1.00	0.63	0.03	0.72	1.00	0.49	0.01	0.53	1.00	0.46	0.15	0.50	1.00	0.33	0.16	0.58	1.00

COX2

	Fold 1				Fold 2				Fold 3				Fold 4				Fold 5			
	T	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**
T	1.00	0.02	0.61	0.57	1.00	0.23	0.66	0.57	1.00	0.08	0.54	0.38	1.00	0.13	0.51	0.32	1.00	0.13	0.51	0.36
S	0.02	1.00	0.07	0.17	0.23	1.00	0.30	0.16	0.08	1.00	0.19	0.25	0.13	1.00	0.08	0.02	0.13	1.00	0.04	0.13
LOO	0.61	0.07	1.00	0.61	0.66	0.30	1.00	0.57	0.54	0.19	1.00	0.51	0.51	0.08	1.00	0.45	0.51	0.04	1.00	0.48
Boot	0.57	0.17	0.61	1.00	0.57	0.16	0.57	1.00	0.38	0.25	0.51	1.00	0.32	0.02	0.45	1.00	0.36	0.13	0.48	1.00

DHFR

	Fold 1				Fold 2				Fold 3				Fold 4				Fold 5			
	T	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**	**T**	**S**	**LOO**	**Boot**
T	1.00	0.24	0.73	0.65	1.00	0.15	0.62	0.69	1.00	0.04	0.49	0.31	1.00	0.05	0.65	0.63	1.00	0.21	0.66	0.72
S	0.24	1.00	0.10	0.23	0.15	1.00	0.15	0.31	0.04	1.00	0.02	0.13	0.05	1.00	0.03	0.06	0.21	1.00	0.22	0.32
LOO	0.73	0.10	1.00	0.61	0.62	0.15	1.00	0.67	0.49	0.02	1.00	0.39	0.65	0.03	1.00	0.63	0.66	0.22	1.00	0.59
Boot	0.65	0.23	0.61	1.00	0.69	0.31	0.67	1.00	0.31	0.13	0.39	1.00	0.63	0.06	0.63	1.00	0.72	0.32	0.59	1.00

ER																				
	Fold 1				Fold 2				Fold 3				Fold 4				Fold 5			
	T	S	LOO	Boot	T	S	LOO	Boot	T	S	LOO	Boot	T	S	LOO	Boot	T	S	LOO	Boot
T	1.00	0.17	0.59	0.44	1.00	0.00	0.53	0.39	1.00	0.04	0.50	0.31	1.00	0.01	0.42	0.43	1.00	0.04	0.77	0.74
S	0.17	1.00	0.37	0.08	0.00	1.00	0.04	0.19	0.04	1.00	0.02	0.13	0.01	1.00	0.14	0.05	0.04	1.00	0.02	0.03
LOO	0.59	0.37	1.00	0.43	0.53	0.04	1.00	0.28	0.50	0.02	1.00	0.24	0.42	0.14	1.00	0.45	0.77	0.02	1.00	0.73
Boot	0.44	0.08	0.43	1.00	0.39	0.19	0.28	1.00	0.31	0.13	0.24	1.00	0.43	0.05	0.45	1.00	0.74	0.03	0.73	1.00

DILI																				
	Fold 1				Fold 2				Fold 3				Fold 4				Fold 5			
	T	S	LOO	Boot	T	S	LOO	Boot	T	S	LOO	Boot	T	S	LOO	Boot	T	S	LOO	Boot
T	1.00	0.09	0.53	0.18	1.00	0.09	0.54	0.30	1.00	0.13	0.68	0.25	1.00	0.37	0.55	0.60	1.00	0.05	0.57	0.35
S	0.09	1.00	0.01	0.02	0.09	1.00	0.08	0.03	0.13	1.00	0.21	0.35	0.37	1.00	0.15	0.41	0.05	1.00	0.24	0.55
LOO	0.53	0.01	1.00	0.27	0.54	0.08	1.00	0.44	0.68	0.21	1.00	0.36	0.55	0.15	1.00	0.53	0.57	0.24	1.00	0.59
Boot	0.18	0.02	0.27	1.00	0.30	0.03	0.44	1.00	0.25	0.35	0.36	1.00	0.60	0.41	0.53	1.00	0.35	0.55	0.59	1.00

[1] Training set accuracy
[2] Selection set accuracy
[3] LOO accuracy
[4] Bootstrap accuracy

TS 8. Overall Sensitivity of the models derived from the GA(M)E-QSAR algorithm and their Sensitivity when only the top 25% most active compounds are considered. The reported values correspond to the external data set

BZR data set			
Fold	**Mod. Method**	**Global Se**	**Top Act. Se**
1	**A.E**	61.90	81.25
1	**ME-AB**	61.90	81.25
1	**ME-AB NC**	66.67	81.25
1	**ME-Vot W**	66.67	81.25
1	**ME-Vot**	68.25	81.25
2	**A.E**	60.32	68.75
2	**ME-AB**	61.90	68.75
2	**ME-AB NC**	60.32	75.00
2	**ME-Vot W**	69.84	75.00
2	**ME-Vot**	68.25	75.00
3	**A.E**	61.90	50.00
3	**ME-AB**	63.49	75.00
3	**ME-AB NC**	63.49	75.00
3	**ME-Vot W**	52.38	75.00
3	**ME-Vot**	58.73	75.00
4	**A.E**	66.67	68.75
4	**ME-AB**	68.25	68.75
4	**ME-AB NC**	66.67	75.00
4	**ME-Vot W**	58.73	75.00
4	**ME-Vot**	60.32	75.00
5	**A.E**	71.43	68.75
5	**ME-AB**	71.43	75.00
5	**ME-AB NC**	73.02	75.00
5	**ME-Vot W**	52.38	68.75
5	**ME-Vot**	52.38	62.50

COX2 data set			
Fold	**Mod. Method**	**Global Se**	**Top Act. Se**
1	**A.E**	65.31	100.00
1	**ME-AB**	67.35	100.00
1	**ME-AB NC**	65.31	100.00
1	**ME-Vot W**	73.47	100.00
1	**ME-Vot**	65.31	100.00
2	**A.E**	75.51	100.00
2	**ME-AB**	63.27	93.33
2	**ME-AB NC**	71.43	93.33
2	**ME-Vot W**	69.39	86.67
2	**ME-Vot**	69.39	93.33
3	**A.E**	75.51	93.33
3	**ME-AB**	75.51	100.00
3	**ME-AB NC**	75.51	100.00
3	**ME-Vot W**	81.63	100.00
3	**ME-Vot**	77.55	100.00
4	**A.E**	77.55	100.00
4	**ME-AB**	73.47	100.00
4	**ME-AB NC**	81.63	100.00
4	**ME-Vot W**	71.43	100.00
4	**ME-Vot**	75.51	100.00
5	**A.E**	83.67	100.00
5	**ME-AB**	71.43	100.00
5	**ME-AB NC**	69.39	93.33
5	**ME-Vot W**	73.47	100.00
5	**ME-Vot**	71.43	100.00

DHFR data set			
Fold	**Mod. Method**	**Global Se**	**Top Act. Se**
1	**A.E**	73.81	81.82
1	**ME-AB**	69.05	72.73
1	**ME-AB NC**	73.81	72.73
1	**ME-Vot W**	71.43	81.82
1	**ME-Vot**	73.81	81.82
2	**A.E**	66.67	63.64
2	**ME-AB**	64.29	54.55
2	**ME-AB NC**	69.05	63.64
2	**ME-Vot W**	73.81	72.73
2	**ME-Vot**	78.57	72.73
3	**A.E**	64.29	54.55
3	**ME-AB**	69.05	63.64
3	**ME-AB NC**	71.43	81.82
3	**ME-Vot W**	71.43	81.82
3	**ME-Vot**	61.90	72.73
4	**A.E**	69.05	72.73
4	**ME-AB**	69.05	81.82
4	**ME-AB NC**	69.05	81.82
4	**ME-Vot W**	66.67	81.82
4	**ME-Vot**	66.67	81.82
5	**A.E**	64.29	63.64
5	**ME-AB**	61.90	72.73
5	**ME-AB NC**	57.14	54.55
5	**ME-Vot W**	61.90	63.64
5	**ME-Vot**	64.29	63.64

Mod. Method: Modeling methodology.
A.E: Adaboost Ensemble,
ME-AB: Clustering derived Adaboost Meta-Ensemble
MA-AB NC: Adaboost Meta-Ensemble trained using the classic greedy search strategy without models clustering
ME-Vot W: Weighted Votes Meta-Ensemble
ME-Vot: Unweighted Votes Meta-Ensemble
Global Se: Global sensitivity of the model.
Top Active Se: Sensitivity of the model when only the 25% most active samples are considered

TS 9 to TS 13. Performance parameters of each optimal classifier per classification experiment. The columns in the tables indicate the used classifier (**Method**), the modeling fold (**Fold**), the number of features in the model (**Size**), the accuracy in predicting the training (**Train**), selection (**Sel.**) and external (**Ext.**) data sets represented as **Accuracy (Sensitivity/Specificity)** as well as the leave one out (**LOO**) and bootstrap (**Boot.**) cross-validation accuracies.

The tables include the accuracy estimators for the classifiers: Adaboost Ensemble (**A.E**), Support Vector Machine (**SVM**), Least Squares Support Vector Machine (**LS-SVM**), classifiers trained with features selected using Bagged Trees (**BT**-*), classifiers trained with features selected using Features Ranking (**R-***) and classifiers trained using Genetic Algorithms (**GA-***).

TS 9. Performance parameters of each optimal classifier. BZR data set

Method	Fold	Size	Train	Sel.	LOO	Boot	Ext.
S.E	1	18	90 (87/94)	72 (67/78)	88	80	70 (62/79)
SVM	1	675	88 (88/88)	72 (67/78)	72	69	75 (70/81)
LS-SVM	1	675	93 (91/96)	72 (67/78)	74	71	72 (62/82)
BT-AB	1	11	72 (74/71)	72 (61/83)	70	68	64 (65/63)
BT-SVM	1	14	81 (74/88)	69 (50/89)	75	69	69 (57/81)
BT-LS-SVM	1	6	100 (100/100)	56 (56/56)	77	69	64 (59/69)
BT-LDA	1	16	80 (76/84)	58 (39/78)	72	68	68 (60/76)
R-AB	1	6	77 (78/75)	78 (67/89)	65	70	67 (63/71)
R-SVM	1	14	88 (84/91)	75 (56/94)	78	75	70 (60/81)
R-LS-SVM	1	23	85 (84/86)	78 (72/83)	77	75	71 (63/79)
R-LDA	1	21	80 (74/87)	72 (67/78)	75	70	64 (52/76)
GA-SVM	1	29	89 (86/93)	75 (78/72)	88	81	70 (67/74)
GA-LS-SVM	1	13	87 (92/81)	78 (83/72)	85	78	67 (68/66)
S.E	2	14	92 (94/91)	78 (71/84)	91	84	66 (60/71)
SVM	2	675	99 (100/99)	67 (71/63)	75	69	75 (73/77)
LS-SVM	2	675	100 (100/100)	69 (71/68)	70	68	72 (71/73)
BT-AB	2	17	79 (86/71)	61 (76/47)	76	75	72 (83/61)
BT-SVM	2	14	86 (88/82)	69 (71/68)	78	73	72 (75/69)
BT-LS-SVM	2	17	84 (87/81)	72 (71/74)	77	74	73 (75/71)
BT-LDA	2	13	81 (83/79)	69 (71/68)	76	72	71 (70/73)
R-AB	2	13	80 (75/85)	75 (88/63)	76	68	65 (57/73)
R-SVM	2	6	74 (73/76)	64 (88/42)	73	72	66 (63/68)
R-LS-SVM	2	6	73 (75/71)	61 (88/37)	72	72	70 (73/66)
R-LDA	2	20	77 (78/76)	69 (88/53)	72	68	66 (63/69)
GA-SVM	2	32	96 (97/94)	67 (76/58)	94	89	70 (68/71)
GA-LS-SVM	2	11	90 (91/88)	67 (71/63)	88	83	66 (67/66)
S.E	3	9	87 (82/92)	72 (70/77)	86	81	70 (62/79)
SVM	3	675	88 (85/92)	72 (70/77)	77	71	74 (60/87)

LS-SVM	3	675	89 (85/93)	75 (74/77)	75	71	75 (62/89)
BT-AB	3	15	74 (76/73)	75 (78/69)	72	68	69 (81/56)
BT-SVM	3	25	97 (96/97)	81 (78/85)	81	75	78 (73/84)
BT-LS-SVM	3	13	100 (100/100)	78 (70/92)	80	75	70 (63/76)
BT-LDA	3	24	80 (77/82)	72 (70/77)	73	67	70 (70/71)
R-AB	3	1	76 (72/80)	61 (52/77)	76	76	65 (54/76)
R-SVM	3	10	90 (85/96)	69 (61/85)	81	72	66 (44/89)
R-LS-SVM	3	11	97 (97/96)	72 (65/85)	76	73	66 (44/87)
R-LDA	3	18	79 (77/81)	72 (70/77)	74	71	69 (56/82)
GA-SVM	3	18	88 (82/95)	72 (65/85)	88	83	74 (62/85)
GA-LS-SVM	3	11	89 (85/93)	75 (70/85)	88	79	74 (67/81)
S.E	4	11	84 (80/88)	84 (100/67)	80	77	65 (67/63)
SVM	4	675	94 (92/96)	70 (84/56)	69	67	74 (71/77)
LS-SVM	4	675	100 (100/100)	59 (74/44)	72	68	74 (70/77)
BT-AB	4	9	72 (68/77)	81 (89/72)	67	66	73 (67/79)
BT-SVM	4	14	83 (85/81)	81 (84/78)	76	73	77 (75/79)
BT-LS-SVM	4	14	82 (84/80)	84 (89/78)	76	73	79 (79/79)
BT-LDA	4	15	76 (76/75)	84 (95/72)	68	66	77 (75/79)
R-AB	4	1	73 (64/83)	73 (79/67)	73	73	65 (54/76)
R-SVM	4	21	87 (79/96)	78 (74/83)	76	72	74 (62/85)
R-LS-SVM	4	20	81 (77/86)	76 (84/67)	76	72	69 (65/73)
R-LDA	4	3	74 (72/77)	68 (79/56)	74	72	69 (70/68)
GA-SVM	4	18	85 (80/90)	78 (89/67)	83	77	71 (65/77)
GA-LS-SVM	4	12	88 (84/91)	89 (95/83)	84	78	73 (68/77)
S.E	5	13	90 (90/90)	75 (82/68)	88	82	70 (71/69)
SVM	5	675	92 (87/99)	67 (65/68)	74	69	77 (68/85)
LS-SVM	5	675	88 (87/88)	72 (71/74)	73	69	75 (68/82)
BT-AB	5	14	79 (74/84)	72 (65/79)	76	72	70 (67/74)
BT-SVM	5	14	89 (86/93)	75 (65/84)	83	73	72 (62/82)
BT-LS-SVM	5	17	87 (86/88)	78 (65/89)	79	73	73 (65/81)
BT-LDA	5	25	83 (81/85)	72 (71/74)	71	69	73 (67/79)
R-AB	5	16	80 (79/81)	69 (71/68)	77	71	66 (62/69)
R-SVM	5	13	83 (82/84)	69 (59/79)	81	78	70 (63/76)
R-LS-SVM	5	11	97 (95/99)	75 (65/84)	81	76	70 (63/76)
R-LDA	5	16	81 (81/82)	64 (59/68)	74	73	70 (65/76)
GA-SVM	5	22	87 (83/91)	72 (65/79)	86	81	70 (62/77)
GA-LS-SVM	5	10	86 (88/84)	72 (71/74)	86	81	63 (57/69)

TS 10. Performance parameters of each optimal classifier. COX2 data set

Method	Fold	Size	Train	Test	LOO	Boot	Ext
S.E	1	10	89 (93/86)	89 (75/96)	87	80	63 (65/62)
SVM	1	745	100 (100/100)	81 (67/88)	78	73	76 (71/79)
LS-SVM	1	745	99 (100/99)	81 (67/88)	73	71	74 (65/80)
BT-AB	1	8	78 (69/84)	86 (75/92)	78	74	66 (65/67)
BT-SVM	1	22	87 (92/84)	89 (75/96)	84	75	71 (78/67)
BT-LS-SVM	1	21	92 (95/89)	89 (83/92)	80	75	74 (78/72)
BT-LDA	1	21	85 (92/81)	89 (83/92)	78	74	70 (84/62)
R-AB	1	9	73 (64/78)	83 (67/92)	61	69	55 (49/59)
R-SVM	1	16	83 (81/84)	94 (83/100)	80	71	70 (65/72)
R-LS-SVM	1	13	85 (85/86)	92 (75/100)	75	71	66 (59/70)
R-LDA	1	12	79 (75/82)	89 (75/96)	73	71	66 (61/70)
GA-SVM	1	40	99 (98/99)	89 (75/96)	97	90	69 (67/70)
GA-LS-SVM	1	14	91 (93/89)	89 (75/96)	89	82	70 (67/72)
S.E	2	11	88 (88/88)	77 (57/90)	88	81	74 (76/72)
SVM	2	745	96 (96/95)	74 (57/86)	83	76	74 (71/75)
LS-SVM	2	745	92 (91/93)	69 (50/81)	78	76	72 (63/78)
BT-AB	2	4	73 (74/73)	60 (57/62)	73	71	62 (73/54)
BT-SVM	2	15	85 (79/88)	71 (50/86)	80	77	78 (78/79)
BT-LS-SVM	2	25	90 (88/92)	71 (50/86)	80	76	73 (63/79)
BT-LDA	2	15	85 (84/85)	71 (50/86)	81	77	78 (82/75)
R-AB	2	2	76 (61/85)	66 (36/86)	76	74	66 (61/68)
R-SVM	2	25	85 (82/87)	71 (64/76)	82	78	65 (63/66)
R-LS-SVM	2	25	96 (93/98)	66 (64/67)	82	77	72 (69/74)
R-LDA	2	16	84 (79/87)	69 (43/86)	80	75	68 (67/68)
GA-SVM	2	24	93 (95/92)	74 (50/90)	91	86	70 (65/74)
GA-LS-SVM	2	12	87 (82/90)	71 (43/90)	86	83	69 (55/78)
S.E	3	10	90 (90/90)	72 (77/70)	89	84	72 (76/70)
SVM	3	745	91 (90/92)	61 (54/65)	82	79	72 (67/75)
LS-SVM	3	745	100 (100/100)	67 (62/70)	82	78	74 (76/72)
BT-AB	3	12	83 (79/86)	69 (77/65)	78	79	70 (76/66)
BT-SVM	3	20	92 (93/92)	72 (85/65)	87	82	75 (73/76)
BT-LS-SVM	3	16	90 (90/90)	75 (85/70)	85	82	72 (71/72)
BT-LDA	3	16	89 (90/88)	78 (92/70)	86	82	74 (80/71)
R-AB	3	15	80 (74/85)	69 (77/65)	78	75	69 (69/68)
R-SVM	3	20	89 (88/89)	72 (100/57)	84	78	72 (76/70)
R-LS-SVM	3	12	87 (81/90)	72 (92/61)	85	79	64 (63/64)

R-LDA	3	23	89 (86/90)	72 (92/61)	82	75	73 (86/64)
GA-SVM	3	39	98 (98/98)	72 (85/65)	96	90	75 (78/74)
GA-LS-SVM	3	14	93 (95/92)	78 (92/70)	91	87	74 (82/68)
S.E	4	6	87 (89/86)	77 (81/74)	86	80	74 (78/71)
SVM	4	745	100 (100/100)	71 (69/74)	80	76	73 (59/82)
LS-SVM	4	745	100 (100/100)	69 (56/79)	78	75	70 (49/84)
BT-AB	4	7	79 (69/85)	60 (56/63)	73	77	64 (61/66)
BT-SVM	4	24	99 (100/99)	74 (81/68)	84	78	70 (71/68)
BT-LS-SVM	4	25	100 (100/100)	71 (75/68)	81	77	73 (71/74)
BT-LDA	4	16	84 (84/84)	71 (81/63)	77	74	74 (82/70)
R-AB	4	2	75 (56/86)	69 (56/79)	75	74	66 (63/67)
R-SVM	4	13	88 (91/86)	71 (75/68)	80	78	68 (69/67)
R-LS-SVM	4	9	99 (100/99)	71 (44/95)	79	76	64 (29/87)
R-LDA	4	10	82 (78/84)	66 (69/63)	78	76	66 (67/66)
GA-SVM	4	37	99 (100/98)	74 (69/79)	98	91	70 (67/72)
GA-LS-SVM	4	15	100 (100/100)	77 (94/63)	95	85	67 (59/72)
S.E	5	10	88 (100/80)	83 (88/80)	87	79	70 (84/61)
SVM	5	745	94 (93/94)	86 (88/85)	76	72	70 (65/74)
LS-SVM	5	745	99 (98/99)	81 (75/85)	77	73	69 (61/74)
BT-AB	5	7	70 (71/70)	81 (94/70)	70	65	68 (88/55)
BT-SVM	5	14	98 (96/99)	81 (75/85)	83	75	71 (59/79)
BT-LS-SVM	5	19	100 (100/100)	75 (69/80)	80	75	69 (59/75)
BT-LDA	5	17	82 (91/77)	83 (81/85)	75	69	74 (78/71)
R-AB	5	17	77 (78/76)	75 (81/70)	74	70	68 (65/70)
R-SVM	5	22	92 (95/90)	86 (81/90)	82	73	71 (65/75)
R-LS-SVM	5	3	94 (100/90)	67 (50/80)	79	76	63 (47/74)
R-LDA	5	10	79 (76/80)	83 (75/90)	76	72	64 (67/62)
GA-SVM	5	44	95 (95/95)	92 (81/100)	92	84	73 (67/76)
GA-LS-SVM	5	18	89 (85/92)	86 (75/95)	85	80	66 (55/72)

TS 11. Performance parameters of each optimal classifier. DHFR data set

Method	Fold	Size	Train	Test	LOO	Boot	Ext
S.E	1	13	85 (82/87)	83 (88/79)	83	78	72 (74/71)
SVM	1	702	83 (66/93)	76 (53/90)	74	70	73 (50/81)
LS-SVM	1	702	97 (91/100)	78 (53/93)	72	70	76 (48/86)
BT-AB	1	6	78 (75/79)	65 (71/62)	76	74	71 (67/72)
BT-SVM	1	11	91 (87/94)	74 (76/72)	80	75	76 (67/80)
BT-LS-SVM	1	20	95 (90/98)	78 (76/79)	81	75	74 (60/79)
BT-LDA	1	22	77 (76/78)	65 (88/52)	72	70	68 (79/64)
R-AB	1	15	72 (76/70)	52 (53/52)	69	63	57 (57/57)
R-SVM	1	24	96 (96/97)	85 (88/83)	75	71	78 (69/81)
R-LS-SVM	1	7	83 (69/92)	78 (76/79)	77	72	74 (67/76)
R-LDA	1	13	78 (78/78)	65 (88/52)	73	70	68 (86/61)
GA-SVM	1	34	87 (66/99)	80 (53/97)	86	81	79 (43/92)
GA-LS-SVM	1	17	88 (82/92)	76 (59/86)	86	80	72 (60/76)
S.E	2	15	83 (84/83)	85 (81/87)	80	77	76 (67/79)
SVM	2	702	99 (100/99)	77 (56/87)	68	67	78 (81/76)
LS-SVM	2	702	100 (100/100)	72 (31/94)	73	71	79 (55/87)
BT-AB	2	9	72 (63/77)	79 (56/90)	68	66	71 (62/74)
BT-SVM	2	18	94 (87/98)	77 (56/87)	80	73	78 (64/82)
BT-LS-SVM	2	22	98 (97/99)	77 (56/87)	80	74	76 (64/81)
BT-LDA	2	23	75 (85/69)	64 (69/61)	67	66	63 (76/58)
R-AB	2	6	67 (71/64)	70 (63/74)	65	61	59 (55/60)
R-SVM	2	21	99 (99/99)	70 (44/84)	80	75	81 (69/85)
R-LS-SVM	2	19	99 (99/99)	70 (44/84)	78	76	81 (71/85)
R-LDA	2	17	74 (81/70)	79 (75/81)	70	69	64 (71/62)
GA-SVM	2	51	96 (93/98)	81 (56/94)	88	81	74 (69/75)
GA-LS-SVM	2	19	95 (93/97)	83 (63/94)	88	79	73 (64/75)
S.E	3	9	83 (81/85)	78 (71/81)	83	78	68 (64/69)
SVM	3	702	87 (69/97)	80 (57/91)	68	69	81 (55/91)
LS-SVM	3	702	98 (97/99)	85 (57/97)	71	69	78 (45/90)
BT-AB	3	13	79 (77/79)	76 (71/78)	76	74	73 (69/74)
BT-SVM	3	23	100 (100/100)	83 (50/97)	76	75	80 (55/89)
BT-LS-SVM	3	22	100 (100/100)	78 (43/94)	78	75	80 (55/89)
BT-LDA	3	16	78 (81/76)	72 (71/72)	72	70	71 (76/69)
R-AB	3	2	68 (61/72)	65 (50/72)	68	66	64 (48/69)
R-SVM	3	18	87 (84/88)	83 (86/81)	77	70	76 (74/76)
R-LS-SVM	3	20	98 (97/98)	87 (64/97)	75	71	82 (69/86)

R-LDA	3	10	73 (77/71)	74 (79/72)	72	69	65 (79/60)
GA-SVM	3	56	93 (89/96)	83 (86/81)	87	81	78 (76/79)
GA-LS-SVM	3	19	97 (97/97)	83 (71/88)	89	79	79 (71/82)
S.E	4	13	88 (89/87)	72 (61/79)	84	79	76 (69/78)
SVM	4	702	100 (100/100)	66 (50/76)	77	75	79 (67/84)
LS-SVM	4	702	100 (100/100)	66 (50/76)	77	75	80 (69/84)
BT-AB	4	11	78 (71/83)	66 (39/83)	76	72	73 (52/81)
BT-SVM	4	25	98 (97/98)	72 (61/79)	83	77	78 (67/82)
BT-LS-SVM	4	13	100 (100/100)	68 (61/72)	82	77	74 (71/75)
BT-LDA	4	23	81 (83/80)	68 (61/72)	74	71	73 (71/74)
R-AB	4	5	75 (76/75)	64 (61/66)	70	70	64 (60/65)
R-SVM	4	18	94 (92/94)	70 (44/86)	81	77	77 (60/83)
R-LS-SVM	4	13	91 (85/94)	74 (50/90)	81	77	78 (62/83)
R-LDA	4	19	78 (85/75)	68 (56/76)	75	71	71 (79/68)
GA-SVM	4	38	94 (92/95)	68 (56/76)	93	87	76 (62/81)
GA-LS-SVM	4	18	96 (92/98)	70 (61/76)	88	84	79 (76/81)
S.E	5	12	85 (88/83)	70 (58/79)	84	80	70 (64/72)
SVM	5	702	82 (58/94)	72 (53/86)	75	71	75 (40/87)
LS-SVM	5	702	95 (89/98)	68 (63/71)	74	72	76 (64/81)
BT-AB	5	18	80 (77/82)	74 (63/82)	78	74	69 (60/72)
BT-SVM	5	15	99 (100/99)	68 (47/82)	82	77	81 (64/86)
BT-LS-SVM	5	19	100 (100/100)	68 (58/75)	81	76	81 (71/85)
BT-LDA	5	12	82 (80/83)	70 (68/71)	77	75	72 (69/73)
R-AB	5	4	68 (62/71)	70 (68/71)	68	65	64 (50/69)
R-SVM	5	24	87 (77/92)	66 (68/64)	80	76	70 (57/75)
R-LS-SVM	5	25	85 (74/91)	70 (68/71)	80	77	71 (57/76)
R-LDA	5	22	82 (86/79)	60 (74/50)	74	73	63 (71/60)
GA-SVM	5	45	89 (75/96)	72 (47/89)	84	78	78 (60/84)
GA-LS-SVM	5	25	89 (74/97)	72 (53/86)	85	81	75 (50/84)

TS 12. Performance parameters of each optimal classifier. ER data set.

Method	Fold	Size	Train	Test	LOO	Boot	Ext
S.E	1	13	89 (93/85)	80 (91/72)	89	83	78 (79/78)
SVM	1	680	96 (99/94)	70 (68/72)	85	81	81 (75/85)
LS-SVM	1	680	100 (100/100)	72 (68/75)	81	79	81 (73/86)
BT-AB	1	13	82 (92/75)	72 (82/66)	80	78	76 (75/76)
BT-SVM	1	10	90 (91/89)	80 (82/78)	89	87	76 (62/85)
BT-LS-SVM	1	8	92 (94/91)	80 (82/78)	87	86	79 (65/89)
BT-LDA	1	7	83 (90/79)	72 (82/66)	83	82	77 (79/75)
R-AB	1	16	76 (90/67)	69 (73/66)	74	71	70 (73/68)
R-SVM	1	24	93 (95/92)	76 (73/78)	84	81	79 (66/87)
R-LS-SVM	1	18	100 (100/100)	76 (64/84)	83	80	78 (62/88)
R-LDA	1	20	81 (90/75)	72 (82/66)	75	75	74 (77/72)
GA-SVM	1	44	96 (98/95)	80 (82/78)	95	90	77 (72/81)
GA-LS-SVM	1	17	93 (98/90)	76 (82/72)	92	88	79 (79/80)
S.E	2	12	86 (90/84)	81 (70/88)	85	82	77 (70/82)
SVM	2	680	96 (99/94)	83 (70/91)	79	76	81 (72/87)
LS-SVM	2	680	99 (100/98)	83 (70/91)	78	75	81 (70/88)
BT-AB	2	10	80 (84/76)	85 (70/94)	77	75	76 (70/80)
BT-SVM	2	22	94 (98/92)	89 (70/100)	85	80	80 (63/91)
BT-LS-SVM	2	21	95 (98/93)	91 (80/97)	84	81	80 (65/90)
BT-LDA	2	11	82 (91/75)	83 (85/82)	80	79	78 (80/77)
R-AB	2	12	71 (81/63)	79 (80/79)	66	68	71 (75/69)
R-SVM	2	18	91 (93/89)	85 (60/100)	79	78	78 (61/89)
R-LS-SVM	2	23	88 (90/87)	87 (75/94)	79	77	79 (70/85)
R-LDA	2	25	79 (89/72)	77 (75/79)	76	72	77 (77/76)
GA-SVM	2	38	93 (97/91)	91 (85/94)	91	86	79 (70/84)
GA-LS-SVM	2	16	90 (94/87)	96 (95/97)	89	85	78 (72/82)
S.E	3	15	86 (89/84)	85 (86/84)	82	80	76 (69/81)
SVM	3	680	95 (98/94)	81 (86/76)	80	76	79 (72/84)
LS-SVM	3	680	96 (98/95)	79 (82/76)	78	77	82 (77/84)
BT-AB	3	3	74 (74/74)	83 (89/76)	74	73	76 (70/80)
BT-SVM	3	6	93 (96/91)	89 (93/84)	82	79	76 (68/81)
BT-LS-SVM	3	6	100 (100/100)	81 (68/96)	85	80	74 (56/85)
BT-LDA	3	23	81 (89/76)	89 (96/80)	77	75	80 (82/79)
R-AB	3	18	76 (84/70)	74 (82/64)	71	67	67 (66/67)
R-SVM	3	18	88 (96/83)	87 (93/80)	80	77	74 (68/79)
R-LS-SVM	3	16	91 (98/87)	89 (93/84)	80	76	76 (65/83)

R-LDA	3	19	78 (89/72)	77 (89/64)	74	72	74 (79/71)
GA-SVM	3	32	93 (98/91)	85 (86/84)	93	88	82 (77/84)
GA-LS-SVM	3	15	90 (93/89)	87 (93/80)	89	85	78 (72/83)
S.E	4	12	86 (90/84)	81 (90/75)	85	81	76 (70/79)
SVM	4	680	93 (98/90)	75 (76/75)	78	78	80 (73/84)
LS-SVM	4	680	98 (100/97)	70 (76/66)	79	76	78 (70/83)
BT-AB	4	1	74 (74/74)	81 (76/84)	74	74	74 (69/78)
BT-SVM	4	15	97 (99/96)	85 (86/84)	87	83	78 (61/90)
BT-LS-SVM	4	16	99 (99/99)	85 (81/88)	87	83	79 (58/93)
BT-LDA	4	22	84 (91/78)	79 (86/75)	81	78	75 (75/75)
R-AB	4	1	71 (89/59)	62 (76/53)	71	71	66 (80/57)
R-SVM	4	23	97 (99/96)	79 (81/78)	85	81	78 (62/88)
R-LS-SVM	4	25	96 (99/94)	79 (76/81)	85	81	78 (62/89)
R-LDA	4	25	79 (90/72)	70 (90/56)	75	73	71 (76/68)
GA-SVM	4	26	94 (98/91)	83 (90/78)	92	87	77 (69/82)
GA-LS-SVM	4	19	91 (94/88)	85 (86/84)	90	85	77 (70/81)
S.E	5	8	88 (89/88)	75 (68/79)	89	84	74 (72/76)
SVM	5	680	97 (99/95)	75 (79/74)	83	79	78 (62/89)
LS-SVM	5	680	100 (100/99)	81 (79/82)	82	78	81 (63/93)
BT-AB	5	9	80 (86/75)	68 (84/59)	79	77	71 (70/71)
BT-SVM	5	23	96 (99/93)	79 (79/79)	88	84	81 (75/84)
BT-LS-SVM	5	25	97 (99/95)	79 (79/79)	88	84	79 (70/85)
BT-LDA	5	24	88 (93/84)	75 (79/74)	84	81	79 (77/80)
R-AB	5	1	71 (85/61)	68 (95/53)	71	71	66 (80/57)
R-SVM	5	23	91 (96/88)	79 (79/79)	84	80	77 (72/81)
R-LS-SVM	5	24	96 (98/94)	75 (74/76)	84	81	79 (65/88)
R-LDA	5	23	83 (91/76)	75 (89/68)	76	75	72 (73/72)
GA-SVM	5	28	93 (98/90)	83 (84/82)	92	88	79 (79/80)
GA-LS-SVM	5	17	95 (98/93)	83 (84/82)	93	88	75 (68/80)

TS 10. Performance parameters of each optimal classifier. DILI data set.

Method	Fold	Size	Train	Test	LOO	Boot	Ext
S.E	1	9	69 (66/72)	63 (60/67)	69	62	65 (66/64)
SVM	1	908	88 (79/96)	58 (35/84)	61	58	59 (32/87)
LS-SVM	1	908	92 (89/95)	59 (44/76)	61	59	58 (40/75)
BT-AB	1	9	59 (59/59)	64 (65/63)	55	56	63 (70/57)
BT-SVM	1	4	100 (99/100)	58 (38/78)	62	60	61 (40/83)
BT-LS-SVM	1	4	100 (99/100)	58 (38/78)	65	61	63 (40/87)
BT-LDA	1	13	63 (72/56)	69 (80/57)	60	58	62 (72/53)
R-AB	1	3	55 (48/61)	53 (49/57)	45	53	55 (58/51)
R-SVM	1	14	92 (91/93)	60 (55/67)	61	59	65 (66/64)
R-LS-SVM	1	17	98 (98/99)	58 (45/71)	62	60	62 (45/79)
R-LDA	1	7	59 (67/52)	60 (75/45)	57	55	68 (87/49)
GA-SVM	1	139	91 (89/93)	66 (60/73)	84	71	68 (66/70)
GA-LS-SVM	1	26	84 (86/82)	74 (75/73)	77	70	67 (72/62)
S.E	2	12	71 (66/76)	64 (54/75)	69	65	68 (60/75)
SVM	2	908	78 (62/91)	67 (44/90)	65	60	67 (56/77)
LS-SVM	2	908	100 (100/100)	67 (56/79)	61	59	54 (50/57)
BT-AB	2	9	65 (50/77)	54 (39/69)	65	63	67 (52/80)
BT-SVM	2	20	88 (88/89)	67 (57/77)	66	60	59 (50/68)
BT-LS-SVM	2	16	81 (76/85)	67 (50/85)	66	60	60 (50/70)
BT-LDA	2	25	65 (63/67)	58 (59/58)	60	58	64 (62/66)
R-AB	2	4	59 (60/58)	57 (56/58)	59	55	51 (60/43)
R-SVM	2	24	86 (76/94)	68 (63/73)	67	63	64 (58/70)
R-LS-SVM	2	23	98 (97/99)	65 (54/77)	66	62	61 (52/70)
R-LDA	2	5	63 (73/55)	66 (74/58)	59	58	62 (82/45)
GA-SVM	2	89	81 (71/89)	73 (57/88)	77	71	66 (62/70)
GA-LS-SVM	2	29	82 (83/81)	66 (65/67)	78	70	62 (62/63)
S.E	3	9	75 (76/74)	65 (65/66)	73	68	57 (55/58)
SVM	3	908	94 (93/95)	61 (56/66)	63	63	63 (55/69)
LS-SVM	3	908	92 (92/92)	58 (44/71)	66	62	61 (51/69)
BT-AB	3	7	65 (76/55)	57 (63/52)	63	63	58 (64/54)
BT-SVM	3	13	71 (80/63)	61 (69/55)	66	63	62 (64/61)
BT-LS-SVM	3	14	72 (73/70)	67 (65/69)	66	64	57 (51/61)
BT-LDA	3	13	66 (74/60)	62 (69/57)	65	64	59 (64/56)
R-AB	3	7	66 (78/56)	59 (69/52)	66	63	59 (68/53)
R-SVM	3	23	75 (84/67)	65 (73/59)	68	65	54 (60/49)
R-LS-SVM	3	16	78 (83/74)	60 (71/52)	70	64	54 (55/53)

R-LDA	3	23	71 (75/66)	62 (65/60)	67	63	59 (62/58)
GA-SVM	3	95	89 (90/88)	63 (67/60)	84	78	56 (51/59)
GA-LS-SVM	3	29	82 (82/81)	64 (69/60)	81	75	62 (64/61)
S.E	4	9	71 (69/72)	70 (68/72)	70	64	59 (56/63)
SVM	4	908	100 (100/100)	59 (54/66)	63	61	59 (54/64)
LS-SVM	4	908	84 (70/94)	69 (59/80)	65	62	58 (44/71)
BT-AB	4	6	65 (53/75)	67 (59/76)	64	62	59 (46/71)
BT-SVM	4	25	88 (90/86)	66 (54/80)	63	63	54 (42/64)
BT-LS-SVM	4	8	100 (100/100)	58 (36/82)	67	64	50 (18/79)
BT-LDA	4	17	68 (79/59)	63 (71/54)	64	61	60 (68/54)
R-AB	4	3	61 (56/64)	63 (59/68)	61	57	55 (52/57)
R-SVM	4	24	76 (60/89)	64 (48/82)	66	63	61 (40/80)
R-LS-SVM	4	25	77 (69/84)	64 (52/78)	65	63	60 (38/80)
R-LDA	4	24	68 (74/63)	58 (64/52)	61	60	49 (52/46)
GA-SVM	4	85	92 (93/92)	67 (64/70)	91	82	56 (52/59)
GA-LS-SVM	4	32	85 (89/81)	65 (68/62)	84	80	63 (64/63)
S.E	5	9	72 (75/69)	68 (78/61)	72	65	61 (69/54)
SVM	5	908	70 (68/72)	64 (71/59)	53	55	63 (58/66)
LS-SVM	5	908	79 (76/82)	63 (67/61)	65	63	60 (60/59)
BT-AB	5	8	65 (56/74)	57 (56/57)	60	60	67 (60/73)
BT-SVM	5	25	100 (100/100)	60 (69/54)	68	63	59 (65/54)
BT-LS-SVM	5	20	100 (100/100)	61 (53/67)	65	64	61 (60/61)
BT-LDA	5	25	69 (72/66)	56 (76/41)	61	59	60 (71/51)
R-AB	5	7	64 (61/67)	56 (58/54)	63	61	60 (56/63)
R-SVM	5	13	77 (81/72)	60 (80/46)	67	63	57 (71/46)
R-LS-SVM	5	21	85 (88/82)	59 (69/52)	66	65	58 (63/54)
R-LDA	5	17	69 (70/68)	63 (78/52)	64	62	60 (65/56)
GA-SVM	5	99	83 (84/82)	66 (73/61)	80	74	62 (63/61)
GA-LS-SVM	5	25	81 (76/85)	69 (76/64)	79	69	57 (46/66)

TS 14. Performance of the top 3 classification approaches per experiment

Method	Fold	Rank	Size	Train	Sel.	LOO	Boot	Ext.
				BZR				
GA-LS-SVM	1	1	13	87 (92/81)	78 (83/72)	85	78	67 (68/66)
GA-SVM	1	2	29	89 (86/93)	75 (78/72)	88	81	70 (67/74)
R-LS-SVM	1	3	23	85 (84/86)	78 (72/83)	77	75	71 (63/79)
S.E	2	1	14	92 (94/91)	78 (71/84)	91	84	66 (60/71)
BT-LS-SVM	2	2	17	84 (87/81)	72 (71/74)	77	74	73 (75/71)
BT-SVM	2	3	14	86 (88/82)	69 (71/68)	78	73	72 (75/69)
BT-SVM	3	1	25	97 (96/97)	81 (78/85)	81	75	78 (73/84)
GA-LS-SVM	3	2	11	89 (85/93)	75 (70/85)	88	79	74 (67/81)
BT-LS-SVM	3	3	13	100 (100/100)	78 (70/92)	80	75	70 (63/76)
GA-LS-SVM	4	1	12	88 (84/91)	89 (95/83)	84	78	73 (68/77)
S.E	4	2	11	84 (80/88)	84 (100/67)	80	77	65 (67/63)
BT-LS-SVM	4	3	14	82 (84/80)	84 (89/78)	76	73	79 (79/79)
S.E	5	1	13	90 (90/90)	75 (82/68)	88	82	70 (71/69)
BT-LS-SVM	5	2	17	87 (86/88)	78 (65/89)	79	73	73 (65/81)
R-LS-SVM	5	3	11	97 (95/99)	75 (65/84)	81	76	70 (63/76)
				COX2				
S.E	1	1	10	89 (93/86)	89 (75/96)	87	80	63 (65/62)
GA-LS-SVM	1	2	14	91 (93/89)	89 (75/96)	89	82	70 (67/72)
BT-LS-SVM	1	3	21	92 (95/89)	89 (83/92)	80	75	74 (78/72)
S.E	2	1	11	88 (88/88)	77 (57/90)	88	81	74 (76/72)
GA-SVM	2	2	24	93 (95/92)	74 (50/90)	91	86	70 (65/74)
R-SVM	2	3	25	85 (82/87)	71 (64/76)	82	78	65 (63/66)
GA-LS-SVM	3	1	14	93 (95/92)	78 (92/70)	91	87	74 (82/68)
BT-LDA	3	2	16	89 (90/88)	78 (92/70)	86	82	74 (80/71)
BT-LS-SVM	3	3	16	90 (90/90)	75 (85/70)	85	82	72 (71/72)
S.E	4	1	6	87 (89/86)	77 (81/74)	86	80	74 (78/71)
GA-LS-SVM	4	2	15	100 (100/100)	77 (94/63)	95	85	67 (59/72)
GA-SVM	4	3	37	99 (100/98)	74 (69/79)	98	91	70 (67/72)
GA-SVM	5	1	44	95 (95/95)	92 (81/100)	92	84	73 (67/76)
GA-LS-SVM	5	2	18	89 (85/92)	86 (75/95)	85	80	66 (55/72)
S.E	5	3	10	88 (100/80)	83 (88/80)	87	79	70 (84/61)
				DHFR				
S.E	1	1	13	85 (82/87)	83 (88/79)	83	78	72 (74/71)
GA-SVM	1	2	34	87 (66/99)	80 (53/97)	86	81	79 (43/92)
GA-LS-SVM	1	3	17	88 (82/92)	76 (59/86)	86	80	72 (60/76)
S.E	2	1	15	83 (84/83)	85 (81/87)	80	77	76 (67/79)
GA-SVM	2	2	51	96 (93/98)	81 (56/94)	88	81	74 (69/75)

GA-LS-SVM	2	3	19	95 (93/97)	83 (63/94)	88	79	73 (64/75)
GA-LS-SVM	3	1	19	97 (97/97)	83 (71/88)	89	79	79 (71/82)
GA-SVM	3	2	56	93 (89/96)	83 (86/81)	87	81	78 (76/79)
R-SVM	3	3	18	87 (84/88)	83 (86/81)	77	70	76 (74/76)
S.E	4	1	13	88 (89/87)	72 (61/79)	84	79	76 (69/78)
GA-LS-SVM	4	2	38	94 (92/95)	68 (56/76)	93	87	76 (62/81)
BT-SVM	4	3	25	98 (97/98)	72 (61/79)	83	77	78 (67/82)
GA-LS-SVM	5	1	25	89 (74/97)	72 (53/86)	85	81	75 (50/84)
S.E	5	2	12	85 (88/83)	70 (58/79)	84	80	70 (64/72)
BT-AB	5	3	18	80 (77/82)	74 (63/82)	78	74	69 (60/72)
				ER				
GA-SVM	1	1	44	96 (98/95)	80 (82/78)	95	90	77 (72/81)
BT-SVM	1	2	10	90 (91/89)	80 (82/78)	89	87	76 (62/85)
BT-LS-SVM	1	3	8	92 (94/91)	80 (82/78)	87	86	79 (65/89)
GA-LS-SVM	2	1	16	90 (94/87)	96 (95/97)	89	85	78 (72/82)
GA-SVM	2	2	38	93 (97/91)	91 (85/94)	91	86	79 (70/84)
BT-LS-SVM	2	3	21	95 (98/93)	91 (80/97)	84	81	80 (65/90)
BT-SVM	3	1	6	93 (96/91)	89 (93/84)	82	79	76 (68/81)
GA-LS-SVM	3	2	15	90 (93/89)	87 (93/80)	89	85	78 (72/83)
GA-SVM	3	3	32	93 (98/91)	85 (86/84)	93	88	82 (77/84)
BT-SVM	4	1	15	97 (99/96)	85 (86/84)	87	83	78 (61/90)
GA-LS-SVM	4	2	19	91 (94/88)	85 (86/84)	90	85	77 (70/81)
GA-SVM	4	3	26	94 (98/91)	83 (90/78)	92	87	77 (69/82)
GA-LS-SVM	5	1	17	95 (98/93)	83 (84/82)	93	88	75 (68/80)
GA-SVM	5	2	28	93 (98/90)	83 (84/82)	92	88	79 (79/80)
BT-SVM	5	3	15	97 (99/96)	85 (86/84)	87	83	78 (61/90)
				DILI				
GA-LS-SVM	1	1	26	84 (86/82)	74 (75/73)	77	70	67 (72/62)
GA-SVM	1	2	139	91 (89/93)	66 (60/73)	84	71	68 (66/70)
S.E	1	3	9	69 (66/72)	63 (60/67)	69	62	65 (66/64)
GA-SVM	2	1	89	81 (71/89)	73 (57/88)	77	71	66 (62/70)
R-SVM	2	2	24	86 (76/94)	68 (63/73)	67	63	64 (58/70)
GA-LS-SVM	2	3	29	82 (83/81)	66 (65/67)	78	70	62 (62/63)
S.E	3	1	9	75 (76/74)	65 (65/66)	73	68	57 (55/58)
GA-SVM	3	2	95	89 (90/88)	63 (67/60)	84	78	56 (51/59)
GA-LS-SVM	3	3	29	82 (82/81)	64 (69/60)	81	75	62 (64/61)
S.E	4	1	9	71 (69/72)	70 (68/72)	70	64	59 (56/63)
GA-SVM	4	2	85	92 (93/92)	67 (64/70)	91	82	56 (52/59)
GA-LS-SVM	4	3	32	85 (89/81)	65 (68/62)	84	80	63 (64/63)
GA-LS-SVM	5	1	25	81 (76/85)	69 (76/64)	79	69	57 (46/66)
GA-SVM	5	2	99	83 (84/82)	66 (73/61)	80	74	62 (63/61)
S.E	5	3	9	72 (75/69)	68 (78/61)	72	65	61 (69/54)

A.E: Adaboost Ensemble derived from the GA(M)E-QSAR approach.
GA-*: Genetic Algorithm feature selection.
BT-*: Bagged Tress feature selection.
R-*: Feature Ranking feature selection
SVM: Support Vector Machine.
LS-SVM: Least Square Support Vector Machine.
LDA: Linear Discriminat Analysis
A.B: Adaboost Ensemble

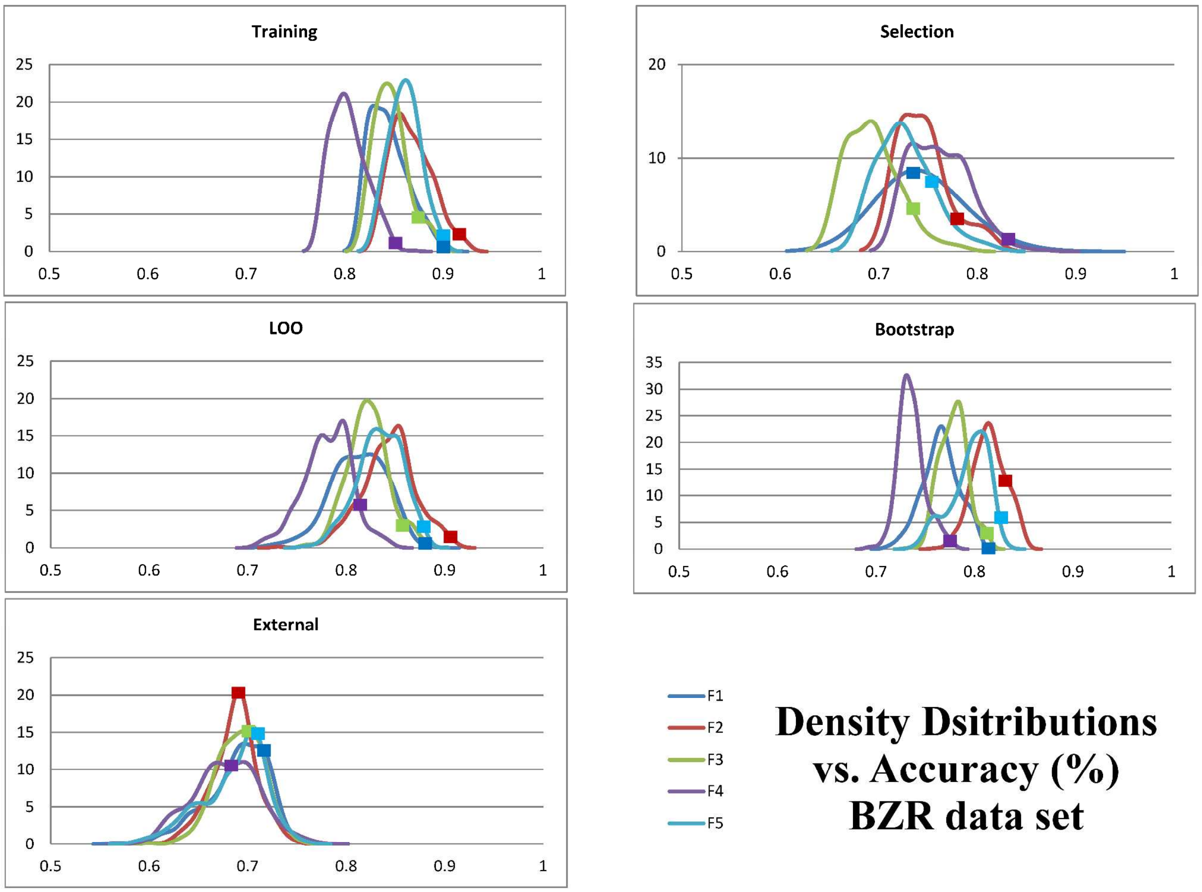
TS 15. Percent of coverage of the external data set by the Applicability Domain defined by the training data set.

Target	Fold	No FS	S.E	BT-AB	BT-SVM	BT-LS-SVM	BT-LDA	R-AB	R-SVM	R-LS-SVM	R-LDA	GA-SVM	GA-LS-SVM
BZR	1	**40.8**	69.6	87.2	87.2	94.4	82.4	88.8	83.2	78.4	80.0	74.4	89.6
BZR	2	**38.4**	81.6	68.0	79.2	76.8	82.4	90.4	95.2	95.2	76.0	61.6	85.6
BZR	3	**46.4**	92.8	81.6	76.8	84.0	78.4	100.0	87.2	84.8	75.2	76.0	90.4
BZR	4	**38.4**	75.2	85.6	87.2	87.2	86.4	100.0	73.6	72.8	90.4	69.6	88.0
BZR	5	**51.2**	81.6	80.8	90.4	86.4	72.0	78.4	82.4	81.6	78.4	80.0	87.2
COX2	1	**43.2**	91.2	88.8	67.2	72.0	72.0	89.6	66.4	76.0	83.2	50.4	84.8
COX2	2	**41.6**	88.0	99.2	79.2	60.0	79.2	96.0	68.0	68.0	86.4	68.0	79.2
COX2	3	**34.4**	81.6	79.2	70.4	68.8	68.8	69.6	71.2	78.4	60.8	55.2	78.4
COX2	4	**36.0**	87.2	91.2	58.4	56.0	70.4	97.6	80.0	87.2	83.2	48.0	87.2
COX2	5	**36.0**	80.8	88.8	78.4	76.0	83.2	72.8	63.2	94.4	84.0	40.0	73.6
DHFR	1	**48.8**	81.9	95.0	90.6	80.6	81.9	90.0	83.8	95.6	89.4	78.1	91.9
DHFR	2	**54.4**	81.3	88.1	85.0	83.1	78.8	95.6	88.8	88.1	88.8	58.8	80.6
DHFR	3	**46.9**	91.9	85.6	84.4	83.1	84.4	99.4	83.8	84.4	94.4	59.4	87.5
DHFR	4	**55.0**	84.4	91.3	80.6	86.3	89.4	96.3	85.6	88.8	85.6	68.1	86.9
DHFR	5	**46.3**	85.0	83.8	87.5	85.0	90.6	96.9	85.0	81.3	85.0	59.4	76.9
ER	1	**52.8**	91.1	96.1	95.0	97.2	97.8	92.8	88.9	84.4	87.2	74.4	86.1
ER	2	**46.1**	91.1	93.3	83.9	85.6	93.3	92.8	93.3	88.3	88.9	71.1	83.9
ER	3	**47.8**	90.0	99.4	94.4	94.4	83.9	89.4	93.3	91.1	91.7	76.1	84.4
ER	4	**51.1**	89.4	100.0	93.9	93.9	88.3	99.4	89.4	86.1	86.1	77.2	83.3
ER	5	**45.6**	92.2	92.2	89.4	88.9	89.4	99.4	89.4	88.9	89.4	79.4	88.3
DILI	1	**48.1**	97.2	92.5	96.2	96.2	93.4	98.1	94.3	93.4	98.1	52.8	94.3
DILI	2	**48.1**	89.6	98.1	93.4	91.5	92.5	96.2	89.6	88.7	96.2	64.2	95.3
DILI	3	**48.1**	97.2	96.2	96.2	94.3	96.2	98.1	98.1	96.2	98.1	61.3	94.3
DILI	4	**47.2**	95.3	96.2	81.1	93.4	87.7	97.2	88.7	84.9	88.7	61.3	87.7
DILI	5	**46.7**	93.5	95.3	90.7	91.6	90.7	94.4	97.2	91.6	90.7	68.2	92.5

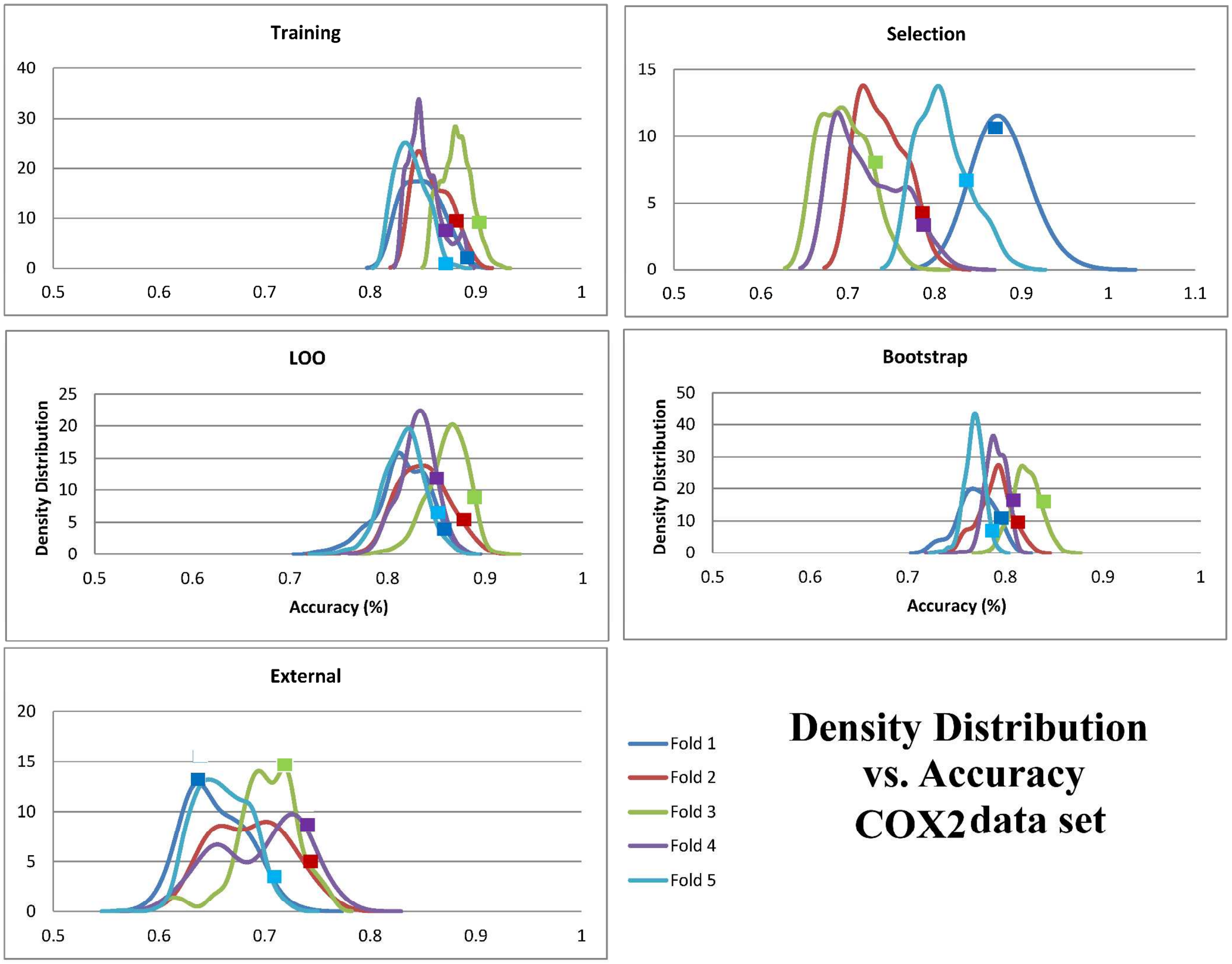
No FS: No feature selection performed.
A.E: Adaboost Ensemble derived from the GA(M)E-QSAR approach.
GA-*: Genetic Algorithm feature selection.
BT-*: Bagged Tress feature selection.
R-*: Ranking feature selection.
SVM: Support Vector Machine.

LSSVM: Least Square Support Vector Machine.
A.B: Adaboost Ensemble.
LDA: Linear Discriminant Analysis.

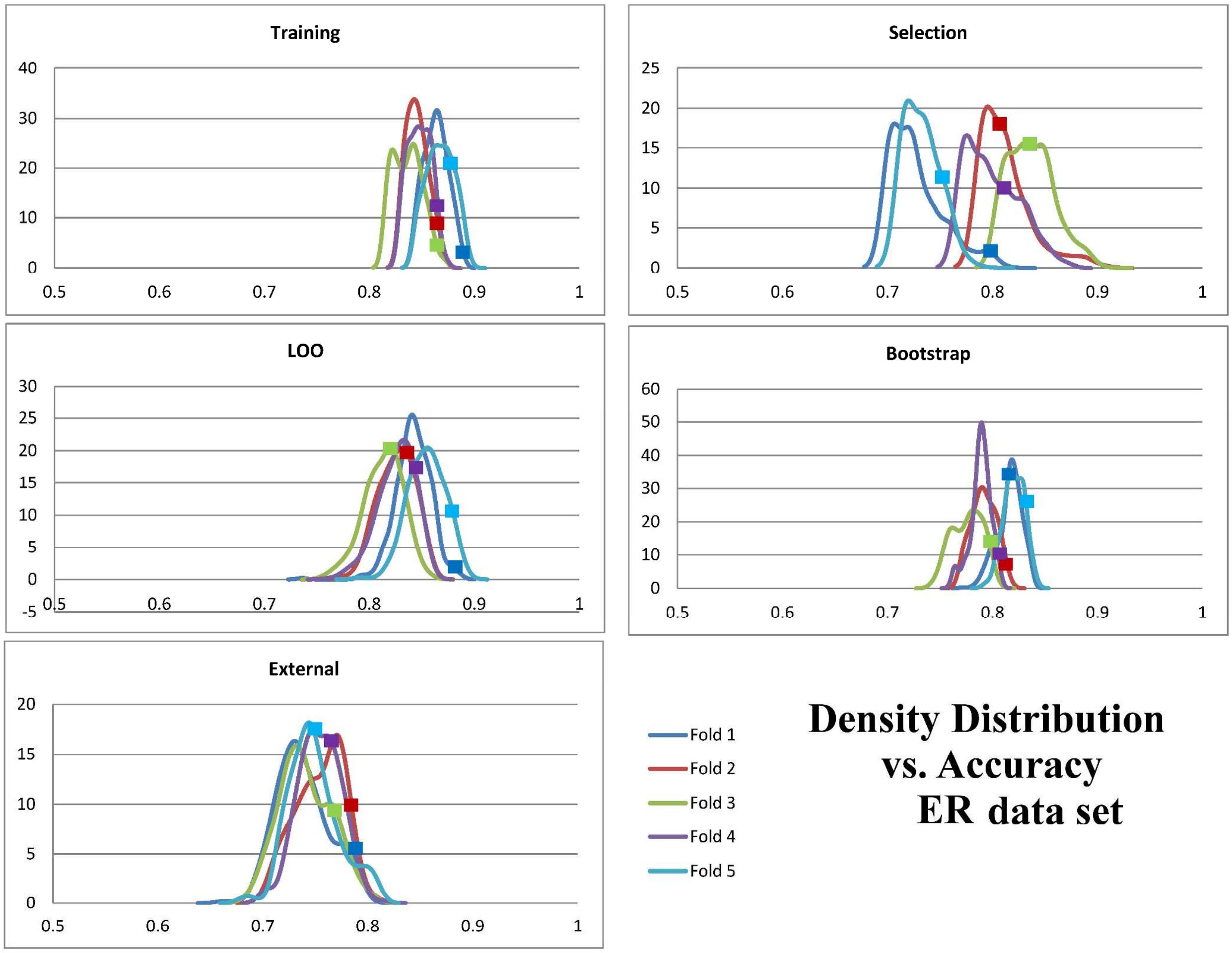
FS. 1 Density Distribution Estimation vs. Accuracy for the four Decision Makers used to rank and select the optimal Adaboost Ensemble. BZR data set.



FS. 2 Density Distribution Estimation vs. Accuracy for the four Decision Makers used to rank and select the optimal Adaboost Ensemble. COX2 data set.



FS. 3 Density Distribution Estimation vs. Accuracy for the four Decision Makers used to rank and select the optimal Adaboost Ensemble. ER data set.



FS. 4 Density Distribution Estimation vs. Accuracy for the four Decision Makers used to rank and select the optimal Adaboost Ensemble. DILI data set.