

Supporting Information

LightGBM: An Effective and Scalable Algorithm for Prediction of Chemical Toxicity– Application to the Tox21 and Mutagenicity Data Sets

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Table S1. Hyperparameter settings used for the Bayesian optimization.

ML Algorithm	Parameters
SVM	'gamma':(0.00001,10), 'C':(1,1200), kernel='rbf',
RF	'n_estimators':(100,1000)
LightGBM	'num_leaves':(30,500), 'max_bin':(250,500), 'n_estimators':(50,900), 'min_child_samples':(20,500), 'max_depth':(5,12), 'learning_rate':(1e-6,1e-1,'log-uniform'), bagging_fraction: 0.8
XGBoost hist	'n_estimators':(50,900), 'max_depth':(5,12), 'learning_rate':(1e-6,1e-1,'log-uniform')
DNN	Number of hidden layer: (200,2000), epoch: (20,100), learning rate: (0.0001,0.01,'log-uniform'), batch_size: 128, optimizer: Adam, activation function: relu for three hidden layers, softmax for output layer, Dropout rate: layer 1: 0.25, layer 1: 0.25, layer 1: 0.1

Table S2. Specificity (SP), sensitivity (SE), Matthews correlation coefficient (MCC), Cohen's kappa (Kappa), balanced accuracy (BA) and area under curve (AUC), F1 Score, positive predictive value (PPV) and negative predictive value (NPV) for the five ML algorithms on the validation (V) and test sets (T) of the Tox21 and mutagenicity data sets described with RDKit molecular descriptors (MD) and Morgan fingerprints (FP).

			LightGBM		RF		SVC		XGB		DNN	
Data sets	Features	Metrics	V	T	V	T	V	T	V	T	V	T
mutagenicity	FP	SP	0.814	0.818	0.775	0.773	0.773	0.775	0.799	0.802	0.718	0.717
		SE	0.794	0.794	0.827	0.836	0.744	0.743	0.814	0.813	0.796	0.806
		MCC	0.607	0.610	0.603	0.610	0.516	0.518	0.613	0.615	0.516	0.527
		Kappa	0.606	0.609	0.603	0.610	0.514	0.516	0.612	0.614	0.514	0.525
		BA	0.804	0.806	0.801	0.804	0.758	0.759	0.806	0.808	0.757	0.762
		AUC	0.876	0.806	0.873	0.804	0.820	0.759	0.880	0.808	0.757	0.762
		F1 Score	0.813	0.814	0.819	0.823	0.768	0.767	0.820	0.820	0.781	0.787
		PPV	0.833	0.836	0.811	0.811	0.793	0.793	0.826	0.827	0.767	0.769
		NPV	0.769	0.773	0.798	0.801	0.717	0.722	0.783	0.787	0.757	0.761
	MD	SP	0.808	0.806	0.791	0.798	0.818	0.821	0.803	0.799	0.764	0.772
		SE	0.815	0.816	0.813	0.817	0.803	0.809	0.816	0.815	0.821	0.833
		MCC	0.623	0.621	0.604	0.614	0.620	0.629	0.619	0.614	0.587	0.607
		Kappa	0.622	0.621	0.604	0.614	0.619	0.628	0.619	0.613	0.585	0.606
		BA	0.812	0.811	0.802	0.807	0.811	0.815	0.810	0.807	0.792	0.802
		AUC	0.884	0.811	0.876	0.807	0.875	0.815	0.885	0.807	0.792	0.802
		F1 Score	0.824	0.823	0.816	0.821	0.820	0.825	0.822	0.820	0.812	0.821
		PPV	0.832	0.831	0.819	0.825	0.837	0.841	0.829	0.826	0.802	0.811
		NPV	0.786	0.790	0.786	0.789	0.784	0.787	0.784	0.787	0.795	0.798

nr-ahr	FP	SP	0.859	0.868	0.984	0.986	0.825	0.838	0.876	0.885	0.971	0.967
		SE	0.789	0.792	0.443	0.500	0.763	0.776	0.760	0.774	0.542	0.577
		MCC	0.518	0.523	0.552	0.607	0.456	0.467	0.523	0.540	0.579	0.592
		Kappa	0.484	0.494	0.523	0.584	0.416	0.430	0.497	0.517	0.571	0.587
		BA	0.824	0.830	0.714	0.743	0.794	0.807	0.818	0.829	0.756	0.772
		AUC	0.903	0.830	0.917	0.743	0.871	0.807	0.903	0.829	0.756	0.772
		F1 Score	0.572	0.571	0.568	0.622	0.519	0.519	0.581	0.590	0.617	0.632
		PPV	0.449	0.446	0.790	0.821	0.393	0.390	0.471	0.477	0.715	0.700
		NPV	0.966	0.969	0.931	0.937	0.962	0.966	0.964	0.967	0.940	0.945
nr-ar	MD	SP	0.885	0.897	0.983	0.984	0.855	0.867	0.890	0.901	0.970	0.972
		SE	0.790	0.805	0.478	0.535	0.800	0.812	0.771	0.778	0.476	0.495
		MCC	0.568	0.582	0.574	0.626	0.522	0.536	0.564	0.571	0.522	0.546
		Kappa	0.540	0.561	0.550	0.609	0.486	0.503	0.539	0.554	0.509	0.532
		BA	0.837	0.851	0.730	0.760	0.828	0.839	0.831	0.839	0.723	0.733
		AUC	0.917	0.851	0.918	0.760	0.894	0.839	0.915	0.839	0.723	0.733
		F1 Score	0.626	0.625	0.596	0.646	0.575	0.580	0.624	0.619	0.561	0.583
		PPV	0.518	0.511	0.792	0.816	0.449	0.451	0.524	0.514	0.682	0.710
		NPV	0.969	0.972	0.935	0.941	0.969	0.972	0.965	0.968	0.929	0.935
nr-ar	FP	SP	0.962	0.965	0.992	0.991	0.944	0.949	0.988	0.988	0.994	0.995
		SE	0.623	0.625	0.540	0.564	0.615	0.620	0.572	0.566	0.567	0.580
		MCC	0.505	0.496	0.613	0.624	0.459	0.427	0.610	0.601	0.660	0.684
		Kappa	0.485	0.485	0.601	0.617	0.429	0.405	0.598	0.597	0.648	0.670
		BA	0.792	0.795	0.766	0.777	0.780	0.784	0.780	0.777	0.781	0.787
		AUC	0.812	0.795	0.835	0.777	0.802	0.784	0.798	0.777	0.781	0.787
		F1 Score	0.541	0.515	0.624	0.634	0.503	0.440	0.629	0.615	0.664	0.685
		PPV	0.478	0.438	0.738	0.724	0.425	0.341	0.699	0.674	0.800	0.837
		NPV	0.982	0.984	0.980	0.982	0.981	0.983	0.980	0.982	0.981	0.982
MD	MD	SP	0.959	0.963	0.991	0.991	0.937	0.953	0.988	0.988	0.996	0.996
		SE	0.622	0.620	0.537	0.562	0.617	0.601	0.582	0.596	0.494	0.508

nr-ar-lkd	FP	MCC	0.495	0.484	0.607	0.618	0.428	0.436	0.612	0.616	0.632	0.653
		Kappa	0.473	0.471	0.594	0.611	0.398	0.418	0.601	0.613	0.605	0.626
		BA	0.791	0.792	0.764	0.776	0.777	0.777	0.785	0.792	0.745	0.752
		AUC	0.822	0.792	0.820	0.776	0.800	0.777	0.818	0.792	0.745	0.752
		F1 Score	0.531	0.504	0.618	0.629	0.461	0.456	0.632	0.631	0.624	0.642
		PPV	0.463	0.424	0.728	0.714	0.369	0.367	0.693	0.671	0.849	0.871
		NPV	0.982	0.984	0.980	0.982	0.981	0.982	0.981	0.983	0.977	0.979
nr-ar-lkd	MD	SP	0.975	0.976	0.995	0.995	0.975	0.977	0.993	0.993	0.994	0.995
		SE	0.705	0.711	0.587	0.644	0.687	0.706	0.660	0.692	0.648	0.652
		MCC	0.602	0.596	0.679	0.713	0.608	0.602	0.711	0.729	0.711	0.723
		Kappa	0.588	0.584	0.665	0.706	0.591	0.593	0.703	0.724	0.703	0.714
		BA	0.840	0.843	0.791	0.819	0.831	0.842	0.826	0.842	0.821	0.823
		AUC	0.861	0.843	0.879	0.819	0.865	0.842	0.864	0.842	0.821	0.823
		F1 Score	0.624	0.610	0.684	0.718	0.638	0.617	0.722	0.739	0.720	0.730
		PPV	0.559	0.535	0.818	0.812	0.595	0.548	0.797	0.792	0.809	0.829
		NPV	0.988	0.989	0.986	0.987	0.988	0.989	0.988	0.989	0.986	0.987
		SP	0.976	0.978	0.994	0.994	0.959	0.965	0.991	0.991	0.993	0.995
nr-aromatase	FP	SE	0.688	0.728	0.574	0.630	0.712	0.751	0.648	0.695	0.566	0.541
		MCC	0.604	0.618	0.660	0.692	0.542	0.568	0.676	0.708	0.639	0.651
		Kappa	0.590	0.609	0.646	0.685	0.518	0.546	0.668	0.705	0.624	0.627
		BA	0.832	0.853	0.784	0.812	0.836	0.858	0.819	0.843	0.780	0.768
		AUC	0.869	0.853	0.887	0.812	0.857	0.858	0.874	0.843	0.780	0.768
		F1 Score	0.629	0.630	0.666	0.699	0.563	0.576	0.692	0.720	0.651	0.655
		PPV	0.579	0.555	0.793	0.786	0.466	0.467	0.743	0.747	0.765	0.830
		NPV	0.989	0.990	0.986	0.986	0.990	0.991	0.988	0.989	0.982	0.983
		SP	0.798	0.807	0.994	0.994	0.881	0.892	0.969	0.980	0.982	0.983
		SE	0.733	0.724	0.319	0.385	0.585	0.618	0.465	0.491	0.430	0.435

nr-er	BA	BA	0.766	0.765	0.657	0.690	0.733	0.755	0.717	0.735	0.706	0.709
		AUC	0.853	0.765	0.868	0.690	0.827	0.755	0.858	0.735	0.706	0.709
		F1 Score	0.350	0.263	0.454	0.510	0.385	0.334	0.514	0.522	0.496	0.506
		PPV	0.230	0.161	0.782	0.753	0.286	0.229	0.573	0.558	0.585	0.605
		NPV	0.981	0.983	0.967	0.969	0.977	0.979	0.972	0.974	0.969	0.971
	MD	SP	0.826	0.851	0.994	0.993	0.785	0.796	0.934	0.952	0.992	0.993
		SE	0.728	0.731	0.307	0.373	0.764	0.767	0.518	0.581	0.238	0.273
		MCC	0.365	0.326	0.452	0.499	0.334	0.285	0.411	0.437	0.367	0.418
		Kappa	0.310	0.257	0.400	0.470	0.267	0.200	0.383	0.421	0.307	0.364
		BA	0.777	0.791	0.650	0.683	0.774	0.781	0.726	0.766	0.615	0.633
nr-er	FP	AUC	0.877	0.791	0.884	0.683	0.861	0.781	0.888	0.766	0.615	0.633
		F1 Score	0.401	0.315	0.437	0.490	0.358	0.266	0.478	0.467	0.356	0.397
		PPV	0.276	0.201	0.757	0.716	0.233	0.161	0.443	0.391	0.707	0.726
		NPV	0.983	0.984	0.966	0.969	0.984	0.985	0.976	0.978	0.961	0.964
		SP	0.855	0.871	0.967	0.963	0.811	0.822	0.898	0.904	0.936	0.962
	MD	SE	0.571	0.563	0.350	0.383	0.571	0.590	0.529	0.524	0.424	0.405
		MCC	0.359	0.367	0.390	0.419	0.313	0.321	0.390	0.395	0.390	0.439
		Kappa	0.339	0.357	0.375	0.406	0.287	0.300	0.380	0.391	0.383	0.425
		BA	0.713	0.717	0.659	0.673	0.691	0.706	0.714	0.714	0.680	0.683
		AUC	0.755	0.717	0.757	0.673	0.747	0.706	0.750	0.714	0.680	0.683

		F1 Score	0.464	0.466	0.445	0.485	0.466	0.462	0.468	0.472	0.436	0.474
		PPV	0.380	0.386	0.573	0.599	0.385	0.381	0.398	0.406	0.563	0.651
		NPV	0.934	0.938	0.915	0.921	0.933	0.938	0.931	0.936	0.911	0.917
nr-er-lbd	FP	SP	0.930	0.937	0.991	0.988	0.906	0.906	0.982	0.983	0.988	0.988
		SE	0.614	0.654	0.450	0.502	0.574	0.621	0.519	0.582	0.511	0.512
		MCC	0.421	0.452	0.537	0.564	0.345	0.355	0.539	0.594	0.580	0.579
		Kappa	0.391	0.429	0.514	0.554	0.313	0.318	0.524	0.590	0.569	0.567
		BA	0.772	0.796	0.720	0.745	0.740	0.764	0.750	0.782	0.749	0.750
		AUC	0.826	0.796	0.839	0.745	0.798	0.764	0.813	0.782	0.749	0.750
		F1 Score	0.460	0.471	0.553	0.579	0.379	0.368	0.573	0.615	0.593	0.594
		PPV	0.367	0.367	0.719	0.684	0.283	0.262	0.641	0.653	0.707	0.707
		NPV	0.980	0.981	0.973	0.974	0.977	0.978	0.977	0.978	0.973	0.974
nr-dd-gamma	MD	SP	0.918	0.918	0.991	0.988	0.932	0.933	0.972	0.972	0.987	0.989
		SE	0.619	0.656	0.448	0.532	0.614	0.670	0.545	0.609	0.382	0.390
		MCC	0.405	0.413	0.539	0.592	0.428	0.452	0.509	0.555	0.470	0.485
		Kappa	0.373	0.382	0.513	0.582	0.403	0.425	0.494	0.549	0.445	0.463
		BA	0.769	0.787	0.719	0.760	0.773	0.802	0.758	0.791	0.684	0.689
		AUC	0.826	0.787	0.839	0.760	0.814	0.802	0.826	0.791	0.684	0.689
		F1 Score	0.443	0.432	0.559	0.607	0.464	0.468	0.551	0.584	0.482	0.491
		PPV	0.345	0.322	0.742	0.707	0.373	0.360	0.557	0.561	0.654	0.663
		NPV	0.980	0.980	0.975	0.975	0.981	0.981	0.978	0.979	0.967	0.968
nr-par-gamma	FP	SP	0.931	0.937	0.998	0.998	0.937	0.940	0.994	0.994	0.990	0.989
		SE	0.566	0.585	0.285	0.318	0.478	0.549	0.386	0.422	0.392	0.393
		MCC	0.322	0.323	0.462	0.496	0.273	0.299	0.497	0.522	0.470	0.468
		Kappa	0.284	0.281	0.406	0.442	0.244	0.258	0.471	0.504	0.444	0.446
		BA	0.748	0.761	0.642	0.658	0.708	0.744	0.690	0.708	0.691	0.691
		AUC	0.795	0.761	0.869	0.658	0.768	0.744	0.813	0.708	0.691	0.691
		F1 Score	0.330	0.316	0.418	0.457	0.282	0.296	0.493	0.521	0.483	0.479
		PPV	0.233	0.216	0.782	0.812	0.200	0.202	0.684	0.680	0.628	0.612

		NPV	0.988	0.988	0.982	0.981	0.987	0.987	0.984	0.984	0.984	0.983
MD	MD	SP	0.903	0.901	0.998	0.998	0.843	0.861	0.990	0.990	0.998	0.997
		SE	0.617	0.633	0.272	0.318	0.685	0.667	0.382	0.419	0.146	0.178
		MCC	0.303	0.272	0.448	0.489	0.243	0.237	0.451	0.457	0.265	0.302
		Kappa	0.253	0.208	0.388	0.438	0.168	0.162	0.429	0.447	0.210	0.252
		BA	0.760	0.767	0.635	0.658	0.764	0.764	0.686	0.704	0.572	0.587
		AUC	0.848	0.767	0.876	0.658	0.817	0.764	0.854	0.704	0.572	0.587
		F1 Score	0.299	0.244	0.405	0.454	0.212	0.202	0.465	0.473	0.232	0.273
		PPV	0.197	0.152	0.788	0.790	0.126	0.119	0.592	0.543	0.571	0.585
		NPV	0.989	0.989	0.982	0.981	0.990	0.989	0.984	0.984	0.978	0.978
FP	FP	SP	0.856	0.867	0.979	0.981	0.805	0.810	0.838	0.852	0.950	0.956
		SE	0.620	0.653	0.308	0.375	0.615	0.625	0.637	0.682	0.448	0.452
		MCC	0.421	0.457	0.406	0.490	0.354	0.358	0.408	0.457	0.455	0.479
		Kappa	0.405	0.447	0.363	0.451	0.331	0.339	0.388	0.442	0.445	0.467
		BA	0.738	0.760	0.643	0.678	0.710	0.717	0.737	0.767	0.699	0.704
		AUC	0.815	0.760	0.845	0.678	0.774	0.717	0.808	0.767	0.699	0.704
		F1 Score	0.522	0.546	0.430	0.506	0.470	0.465	0.510	0.546	0.520	0.535
		PPV	0.450	0.469	0.714	0.780	0.380	0.371	0.425	0.455	0.619	0.656
		NPV	0.929	0.933	0.892	0.897	0.919	0.923	0.934	0.937	0.902	0.907
MD	MD	SP	0.849	0.855	0.980	0.978	0.847	0.856	0.840	0.843	0.967	0.962
		SE	0.678	0.735	0.319	0.386	0.650	0.692	0.685	0.746	0.323	0.376
		MCC	0.466	0.501	0.427	0.491	0.437	0.471	0.459	0.491	0.389	0.425
		Kappa	0.440	0.483	0.380	0.456	0.418	0.456	0.432	0.468	0.358	0.403
		BA	0.763	0.795	0.649	0.682	0.749	0.774	0.762	0.794	0.645	0.669
		AUC	0.844	0.795	0.852	0.682	0.830	0.774	0.842	0.794	0.645	0.669
		F1 Score	0.565	0.579	0.448	0.513	0.537	0.557	0.560	0.570	0.431	0.475
		PPV	0.484	0.478	0.753	0.765	0.458	0.466	0.473	0.462	0.646	0.645
		NPV	0.944	0.947	0.893	0.899	0.936	0.939	0.946	0.949	0.890	0.896
at - sr	FP	SP	0.910	0.915	0.997	0.996	0.907	0.912	0.985	0.987	0.992	0.991

sr-hse	FP	SE	0.662	0.690	0.368	0.438	0.632	0.671	0.479	0.483	0.452	0.479
		MCC	0.370	0.372	0.532	0.591	0.349	0.356	0.521	0.528	0.540	0.554
		Kappa	0.324	0.320	0.483	0.560	0.306	0.305	0.503	0.520	0.525	0.544
		BA	0.786	0.802	0.682	0.717	0.769	0.791	0.732	0.735	0.722	0.735
		AUC	0.858	0.802	0.887	0.717	0.829	0.791	0.863	0.735	0.722	0.735
		F1 Score	0.376	0.361	0.510	0.573	0.360	0.345	0.546	0.544	0.545	0.561
		PPV	0.263	0.245	0.833	0.826	0.252	0.232	0.634	0.623	0.688	0.677
		NPV	0.986	0.987	0.977	0.979	0.985	0.986	0.979	0.980	0.979	0.980
		SP	0.922	0.925	0.996	0.996	0.906	0.910	0.981	0.981	0.995	0.994
		SE	0.643	0.683	0.350	0.409	0.666	0.692	0.495	0.538	0.223	0.326
sr-hse	MD	MCC	0.394	0.387	0.509	0.557	0.363	0.363	0.507	0.512	0.355	0.455
		Kappa	0.354	0.341	0.461	0.525	0.314	0.309	0.490	0.511	0.304	0.420
		BA	0.783	0.804	0.673	0.702	0.786	0.801	0.738	0.759	0.609	0.660
		AUC	0.869	0.804	0.898	0.702	0.850	0.801	0.881	0.759	0.609	0.660
		F1 Score	0.416	0.379	0.488	0.540	0.369	0.351	0.540	0.532	0.331	0.442
		PPV	0.308	0.262	0.805	0.793	0.255	0.235	0.594	0.527	0.647	0.688
		NPV	0.986	0.987	0.976	0.978	0.986	0.987	0.981	0.982	0.973	0.974
		SP	0.903	0.912	0.993	0.992	0.871	0.868	0.974	0.976	0.988	0.986
		SE	0.476	0.517	0.186	0.254	0.429	0.480	0.333	0.381	0.295	0.290
		MCC	0.269	0.309	0.299	0.374	0.192	0.214	0.332	0.395	0.388	0.370
sr-hse	MD	Kappa	0.244	0.286	0.251	0.337	0.164	0.181	0.322	0.392	0.363	0.344
		BA	0.690	0.714	0.589	0.623	0.650	0.674	0.653	0.679	0.641	0.638
		AUC	0.741	0.714	0.790	0.623	0.686	0.674	0.737	0.679	0.641	0.638
		F1 Score	0.309	0.340	0.282	0.360	0.234	0.245	0.368	0.421	0.390	0.381
		PPV	0.229	0.253	0.583	0.616	0.160	0.164	0.412	0.470	0.577	0.554
		NPV	0.972	0.972	0.960	0.960	0.968	0.968	0.966	0.966	0.962	0.962
		SP	0.892	0.902	0.993	0.993	0.840	0.849	0.960	0.962	0.992	0.991
		SE	0.511	0.581	0.191	0.267	0.575	0.615	0.380	0.481	0.189	0.173
		MCC	0.275	0.328	0.308	0.399	0.246	0.273	0.328	0.411	0.310	0.280

		Kappa	0.241	0.295	0.258	0.357	0.197	0.221	0.313	0.408	0.253	0.233
		BA	0.702	0.742	0.592	0.630	0.708	0.732	0.670	0.721	0.590	0.582
		AUC	0.793	0.742	0.811	0.630	0.746	0.732	0.791	0.721	0.590	0.582
		F1 Score	0.314	0.347	0.290	0.381	0.268	0.285	0.379	0.443	0.291	0.262
		PPV	0.227	0.248	0.603	0.662	0.175	0.186	0.377	0.412	0.633	0.540
		NPV	0.975	0.975	0.961	0.961	0.976	0.976	0.971	0.971	0.956	0.956
sr-mmp	FP	SP	0.904	0.912	0.979	0.982	0.851	0.862	0.904	0.914	0.958	0.964
		SE	0.747	0.782	0.494	0.560	0.743	0.768	0.749	0.788	0.616	0.608
		MCC	0.606	0.633	0.588	0.648	0.513	0.538	0.607	0.644	0.615	0.627
		Kappa	0.596	0.626	0.561	0.629	0.492	0.520	0.597	0.637	0.611	0.621
		BA	0.826	0.847	0.736	0.771	0.797	0.815	0.827	0.851	0.787	0.786
		AUC	0.908	0.847	0.913	0.771	0.874	0.815	0.906	0.851	0.787	0.786
		F1 Score	0.676	0.693	0.617	0.676	0.598	0.611	0.677	0.702	0.668	0.675
		PPV	0.618	0.622	0.823	0.852	0.500	0.508	0.617	0.632	0.731	0.759
		NPV	0.954	0.958	0.917	0.924	0.949	0.953	0.955	0.959	0.924	0.930
	MD	SP	0.915	0.921	0.976	0.978	0.886	0.892	0.902	0.909	0.966	0.967
		SE	0.794	0.831	0.563	0.628	0.791	0.825	0.803	0.839	0.632	0.643
		MCC	0.663	0.689	0.633	0.685	0.606	0.629	0.648	0.672	0.651	0.664
		Kappa	0.650	0.682	0.615	0.675	0.589	0.616	0.633	0.662	0.644	0.657
		BA	0.854	0.876	0.770	0.803	0.838	0.859	0.852	0.874	0.799	0.805
		AUC	0.932	0.876	0.937	0.803	0.911	0.859	0.932	0.874	0.799	0.805
		F1 Score	0.725	0.738	0.669	0.719	0.676	0.686	0.713	0.724	0.697	0.709
		PPV	0.667	0.664	0.825	0.840	0.590	0.587	0.642	0.637	0.778	0.789
		NPV	0.964	0.967	0.929	0.934	0.962	0.965	0.966	0.968	0.931	0.936
sr-p53	FP	SP	0.901	0.914	0.996	0.996	0.906	0.908	0.970	0.972	0.987	0.986
		SE	0.641	0.641	0.357	0.399	0.603	0.582	0.529	0.540	0.478	0.470
		MCC	0.420	0.415	0.535	0.568	0.402	0.370	0.525	0.522	0.562	0.551
		Kappa	0.390	0.389	0.480	0.522	0.376	0.345	0.512	0.520	0.546	0.532
		BA	0.771	0.778	0.676	0.698	0.755	0.745	0.749	0.756	0.732	0.728

		AUC	0.864	0.778	0.899	0.698	0.805	0.745	0.867	0.756	0.732	0.728
		F1 Score	0.466	0.442	0.506	0.546	0.450	0.408	0.564	0.552	0.574	0.566
		PPV	0.366	0.337	0.865	0.863	0.358	0.314	0.605	0.565	0.719	0.712
		NPV	0.973	0.975	0.959	0.962	0.969	0.970	0.968	0.970	0.964	0.966
MD	SP	0.905	0.919	0.996	0.996	0.883	0.890	0.940	0.950	0.988	0.986	
	SE	0.667	0.699	0.375	0.424	0.692	0.715	0.586	0.608	0.334	0.364	
	MCC	0.462	0.463	0.553	0.587	0.423	0.413	0.480	0.483	0.443	0.460	
	Kappa	0.431	0.434	0.500	0.546	0.383	0.368	0.462	0.474	0.406	0.429	
	BA	0.786	0.809	0.685	0.710	0.788	0.803	0.763	0.779	0.661	0.675	
	AUC	0.876	0.809	0.907	0.710	0.845	0.803	0.876	0.779	0.661	0.675	
	F1 Score	0.515	0.483	0.525	0.570	0.463	0.427	0.535	0.516	0.448	0.472	
	PPV	0.419	0.369	0.878	0.868	0.348	0.304	0.492	0.448	0.681	0.670	
	NPV	0.977	0.979	0.961	0.963	0.978	0.979	0.972	0.973	0.957	0.959	

Table S3. Computation time (mins) for the five ML algorithms on the Bayesian optimization integrated nested cross validation scheme of the Tox21 and mutagenicity data sets described with RDKit molecular descriptors (MD) and Morgan fingerprints (FP).

	Type	LightGBM	RF	SVC	XGB	DNN
nr-ahr	MD	124	162	125	367	5651
	FP	152	315	1052	368	5062
nr-ar	MD	120	229	134	236	5619
	FP	147	615	1114	325	5205
nr-ar-lbd	MD	121	234	102	166	4764
	FP	139	541	914	302	5069
nr-aromatase	MD	98	159	93	258	4226
	FP	107	381	826	300	4702
nr-er	MD	136	212	141	367	4736
	FP	151	485	1157	413	4742
nr-er-lbd	MD	111	223	118	320	5381
	FP	154	601	1186	329	5160
nr-ppar-gamma	MD	107	179	111	233	4418
	FP	138	489	1018	312	5054
sr-are	MD	117	195	123	448	4369
	FP	130	430	991	341	4902
sr-atad5	MD	138	206	112	346	4817
	FP	168	574	1198	373	5724
sr-hse	MD	95	221	125	328	4625
	FP	150	691	1102	338	5338
sr-mmp	MD	124	189	99	441	4479
	FP	141	383	913	377	5156
sr-p53	MD	130	175	118	392	4790
	FP	141	340	1154	461	5339
mutagenicity	MD	149	204	138	505	4400

	FP	151	348	981	366	4796
Mean	MD	121	200	118	339	4790
	FP	144	476	1047	354	5096
Standard deviation	MD	15	25	15	97	474
	FP	14	116	113	44	269
Mean difference between MD and FP		23	276	929	15	306
Average(Time _{MD} -Time _{FP})						

Table S4. The hyperparameter values of LightGBM algorithm suggested by the Bayesian optimization for the Tox21 and mutagenicity data sets described with RDkit descriptors and Morgan fingerprints.

learning_rate	max_bin	max_depth	min_child_samples	n_estimators	num_leaves	Data sets	Feature
0.021	386	9	264	603	232	nr-ahr	MD
0.018	360	8	353	290	145	nr-ar-lbd	MD
0.009	365	7	298	482	246	nr-aromatase	MD
0.005	366	6	136	295	144	nr-ar	MD
0.014	355	7	310	523	286	nr-er-lbd	MD
0.006	403	6	49	675	227	nr-er	MD
0.004	369	8	315	625	159	nr-ppar-gamma	MD
0.014	416	10	24	760	230	mutagenicity	MD
0.020	318	8	176	620	101	sr-are	MD
0.019	373	7	318	448	231	sr-atad5	MD
0.016	362	7	433	438	161	sr-hse	MD
0.023	287	8	153	713	190	sr-mmp	MD
0.034	328	7	431	574	185	sr-p53	MD
0.012	326	11	111	707	140	nr-ahr	FP
0.033	320	7	50	169	236	nr-ar-lbd	FP
0.009	375	7	251	715	155	nr-aromatase	FP
0.013	372	8	69	469	133	nr-ar	FP
0.013	398	10	94	594	328	nr-er-lbd	FP
0.008	433	11	25	434	212	nr-er	FP
0.021	376	9	111	370	248	nr-ppar-gamma	FP
0.025	407	12	22	627	197	mutagenicity	FP
0.014	355	10	36	711	128	sr-are	FP
0.012	363	6	40	421	242	sr-atad5	FP

0.009	401	8	35	371	249	sr-hse	FP
0.017	345	10	55	598	248	sr-mmp	FP
0.042	319	11	230	572	151	sr-p53	FP

Table S5. p-values of statistical comparisons among the balanced accuracies of five algorithms on the Tox21 and mutagenicity data set described with Morgan fingerprints (FP) and RDkit molecular descriptors (MD)

Target Method	Compared Method	Data sets	Features	p-value	Symbol	Bonferroni corrected cut-off value
LightGBM	SVC	nr-ahr	FP	0.00000	<=	0.000192308
LightGBM	SVC	nr-ar-lbd	FP	0.74115	>	0.000192308
LightGBM	SVC	nr-aromatase	FP	0.00000	<=	0.000192308
LightGBM	SVC	nr-ar	FP	0.00000	<=	0.000192308
LightGBM	SVC	nr-er-lbd	FP	0.00000	<=	0.000192308
LightGBM	SVC	nr-er	FP	0.00000	<=	0.000192308
LightGBM	SVC	nr-ppar-gamma	FP	0.73566	>	0.000192308
LightGBM	SVC	mutagenicity	FP	0.00000	<=	0.000192308
LightGBM	SVC	sr-are	FP	0.00000	<=	0.000192308
LightGBM	SVC	sr-atad5	FP	0.33841	>	0.000192308
LightGBM	SVC	sr-hse	FP	0.00000	<=	0.000192308
LightGBM	SVC	sr-mmp	FP	0.00000	<=	0.000192308
LightGBM	SVC	sr-p53	FP	0.05196	>	0.000192308
LightGBM	XGB	nr-ahr	FP	0.02175	>	0.000192308
LightGBM	XGB	nr-ar-lbd	FP	0.00000	<=	0.000192308
LightGBM	XGB	nr-aromatase	FP	0.00000	<=	0.000192308
LightGBM	XGB	nr-ar	FP	0.00000	<=	0.000192308
LightGBM	XGB	nr-er-lbd	FP	0.00000	<=	0.000192308
LightGBM	XGB	nr-er	FP	0.00003	<=	0.000192308
LightGBM	XGB	nr-ppar-gamma	FP	0.00000	<=	0.000192308
LightGBM	XGB	mutagenicity	FP	0.65390	>	0.000192308
LightGBM	XGB	sr-are	FP	0.18319	>	0.000192308
LightGBM	XGB	sr-atad5	FP	0.00000	<=	0.000192308

LightGBM	XGB	sr-hse	FP	0.00000	<=	0.000192308
LightGBM	XGB	sr-mmp	FP	0.53233	>	0.000192308
LightGBM	XGB	sr-p53	FP	0.00000	<=	0.000192308
LightGBM	RF	nr-ahr	FP	0.00000	<=	0.000192308
LightGBM	RF	nr-ar-lbd	FP	0.00000	<=	0.000192308
LightGBM	RF	nr-aromatase	FP	0.00000	<=	0.000192308
LightGBM	RF	nr-ar	FP	0.00000	<=	0.000192308
LightGBM	RF	nr-er-lbd	FP	0.00000	<=	0.000192308
LightGBM	RF	nr-er	FP	0.00000	<=	0.000192308
LightGBM	RF	nr-ppar-gamma	FP	0.00000	<=	0.000192308
LightGBM	RF	mutagenicity	FP	0.80372	>	0.000192308
LightGBM	RF	sr-are	FP	0.00000	<=	0.000192308
LightGBM	RF	sr-atad5	FP	0.00000	<=	0.000192308
LightGBM	RF	sr-hse	FP	0.00000	<=	0.000192308
LightGBM	RF	sr-mmp	FP	0.00000	<=	0.000192308
LightGBM	RF	sr-p53	FP	0.00000	<=	0.000192308
LightGBM	DNN	nr-ahr	FP	0.00000	<=	0.000192308
LightGBM	DNN	nr-ar-lbd	FP	0.00000	<=	0.000192308
LightGBM	DNN	nr-aromatase	FP	0.00000	<=	0.000192308
LightGBM	DNN	nr-ar	FP	0.00000	<=	0.000192308
LightGBM	DNN	nr-er-lbd	FP	0.00000	<=	0.000192308
LightGBM	DNN	nr-er	FP	0.00000	<=	0.000192308
LightGBM	DNN	nr-ppar-gamma	FP	0.00000	<=	0.000192308
LightGBM	DNN	mutagenicity	FP	0.00000	<=	0.000192308
LightGBM	DNN	sr-are	FP	0.00000	<=	0.000192308
LightGBM	DNN	sr-atad5	FP	0.00000	<=	0.000192308
LightGBM	DNN	sr-hse	FP	0.00000	<=	0.000192308
LightGBM	DNN	sr-mmp	FP	0.00067	>	0.000192308
LightGBM	DNN	sr-p53	FP	0.00000	<=	0.000192308

LightGBM	SVC	nr-ahr	MD	0.00000	<=	0.000192308
LightGBM	SVC	nr-ar-lbd	MD	0.00008	<=	0.000192308
LightGBM	SVC	nr-aromatase	MD	0.00000	<=	0.000192308
LightGBM	SVC	nr-ar	MD	0.00160	>	0.000192308
LightGBM	SVC	nr-er-lbd	MD	0.00029	>	0.000192308
LightGBM	SVC	nr-er	MD	0.65632	>	0.000192308
LightGBM	SVC	nr-ppar-gamma	MD	0.00000	<=	0.000192308
LightGBM	SVC	mutagenicity	MD	0.59507	>	0.000192308
LightGBM	SVC	sr-are	MD	0.36371	>	0.000192308
LightGBM	SVC	sr-atad5	MD	0.00096	>	0.000192308
LightGBM	SVC	sr-hse	MD	0.00000	<=	0.000192308
LightGBM	SVC	sr-mmp	MD	0.00000	<=	0.000192308
LightGBM	SVC	sr-p53	MD	0.00000	<=	0.000192308
LightGBM	XGB	nr-ahr	MD	0.97928	>	0.000192308
LightGBM	XGB	nr-ar-lbd	MD	0.00000	<=	0.000192308
LightGBM	XGB	nr-aromatase	MD	0.00000	<=	0.000192308
LightGBM	XGB	nr-ar	MD	0.00000	<=	0.000192308
LightGBM	XGB	nr-er-lbd	MD	0.00000	<=	0.000192308
LightGBM	XGB	nr-er	MD	0.11271	>	0.000192308
LightGBM	XGB	nr-ppar-gamma	MD	0.00000	<=	0.000192308
LightGBM	XGB	mutagenicity	MD	0.59675	>	0.000192308
LightGBM	XGB	sr-are	MD	0.14708	>	0.000192308
LightGBM	XGB	sr-atad5	MD	0.00000	<=	0.000192308
LightGBM	XGB	sr-hse	MD	0.00000	<=	0.000192308
LightGBM	XGB	sr-mmp	MD	0.07275	>	0.000192308
LightGBM	XGB	sr-p53	MD	0.00000	<=	0.000192308
LightGBM	RF	nr-ahr	MD	0.00000	<=	0.000192308
LightGBM	RF	nr-ar-lbd	MD	0.00000	<=	0.000192308
LightGBM	RF	nr-aromatase	MD	0.00000	<=	0.000192308

LightGBM	RF	nr-ar	MD	0.00000	<=	0.000192308
LightGBM	RF	nr-er-lbd	MD	0.00000	<=	0.000192308
LightGBM	RF	nr-er	MD	0.00000	<=	0.000192308
LightGBM	RF	nr-ppar-gamma	MD	0.00000	<=	0.000192308
LightGBM	RF	mutagenicity	MD	0.65877	>	0.000192308
LightGBM	RF	sr-are	MD	0.00000	<=	0.000192308
LightGBM	RF	sr-atad5	MD	0.00000	<=	0.000192308
LightGBM	RF	sr-hse	MD	0.00000	<=	0.000192308
LightGBM	RF	sr-mmp	MD	0.00043	>	0.000192308
LightGBM	RF	sr-p53	MD	0.00000	<=	0.000192308
LightGBM	DNN	nr-ahr	MD	0.00000	<=	0.000192308
LightGBM	DNN	nr-ar-lbd	MD	0.00005	<=	0.000192308
LightGBM	DNN	nr-aromatase	MD	0.00000	<=	0.000192308
LightGBM	DNN	nr-ar	MD	0.00000	<=	0.000192308
LightGBM	DNN	nr-er-lbd	MD	0.00000	<=	0.000192308
LightGBM	DNN	nr-er	MD	0.00000	<=	0.000192308
LightGBM	DNN	nr-ppar-gamma	MD	0.00000	<=	0.000192308
LightGBM	DNN	mutagenicity	MD	0.34536	>	0.000192308
LightGBM	DNN	sr-are	MD	0.00000	<=	0.000192308
LightGBM	DNN	sr-atad5	MD	0.00000	<=	0.000192308
LightGBM	DNN	sr-hse	MD	0.00000	<=	0.000192308
LightGBM	DNN	sr-mmp	MD	0.05168	>	0.000192308
LightGBM	DNN	sr-p53	MD	0.00000	<=	0.000192308
RF	DNN	nr-ahr	FP	0.07118	>	0.000192308
RF	DNN	nr-ar-lbd	FP	0.84659	>	0.000192308
RF	DNN	nr-aromatase	FP	0.02576	>	0.000192308
RF	DNN	nr-ar	FP	0.03500	>	0.000192308
RF	DNN	nr-er-lbd	FP	0.82669	>	0.000192308
RF	DNN	nr-er	FP	0.79281	>	0.000192308

RF	DNN	nr-ppar-gamma	FP	0.01023	>	0.000192308
RF	DNN	mutagenicity	FP	0.00000	<=	0.000192308
RF	DNN	sr-are	FP	0.10091	>	0.000192308
RF	DNN	sr-atad5	FP	0.13085	>	0.000192308
RF	DNN	sr-hse	FP	0.27349	>	0.000192308
RF	DNN	sr-mmp	FP	0.09655	>	0.000192308
RF	DNN	sr-p53	FP	0.13736	>	0.000192308
RF	DNN	nr-ahr	MD	0.00021	>	0.000192308
RF	DNN	nr-ar-lbd	MD	0.33229	>	0.000192308
RF	DNN	nr-aromatase	MD	0.17893	>	0.000192308
RF	DNN	nr-ar	MD	0.13529	>	0.000192308
RF	DNN	nr-er-lbd	MD	0.03330	>	0.000192308
RF	DNN	nr-er	MD	0.97659	>	0.000192308
RF	DNN	nr-ppar-gamma	MD	0.03863	>	0.000192308
RF	DNN	mutagenicity	MD	0.61565	>	0.000192308
RF	DNN	sr-are	MD	0.00541	>	0.000192308
RF	DNN	sr-atad5	MD	0.05451	>	0.000192308
RF	DNN	sr-hse	MD	0.05488	>	0.000192308
RF	DNN	sr-mmp	MD	0.11422	>	0.000192308
RF	DNN	sr-p53	MD	0.00006	<=	0.000192308
SVC	XGB	nr-ahr	FP	0.00000	<=	0.000192308
SVC	XGB	nr-ar-lbd	FP	0.00000	<=	0.000192308
SVC	XGB	nr-aromatase	FP	0.00000	<=	0.000192308
SVC	XGB	nr-ar	FP	0.00000	<=	0.000192308
SVC	XGB	nr-er-lbd	FP	0.00000	<=	0.000192308
SVC	XGB	nr-er	FP	0.00000	<=	0.000192308
SVC	XGB	nr-ppar-gamma	FP	0.00000	<=	0.000192308
SVC	XGB	mutagenicity	FP	0.00000	<=	0.000192308
SVC	XGB	sr-are	FP	0.00000	<=	0.000192308

SVC	XGB	sr-atad5	FP	0.00000	<=	0.000192308
SVC	XGB	sr-hse	FP	0.00000	<=	0.000192308
SVC	XGB	sr-mmp	FP	0.00000	<=	0.000192308
SVC	XGB	sr-p53	FP	0.00000	<=	0.000192308
SVC	RF	nr-ahr	FP	0.00000	<=	0.000192308
SVC	RF	nr-ar-lbd	FP	0.00000	<=	0.000192308
SVC	RF	nr-aromatase	FP	0.00000	<=	0.000192308
SVC	RF	nr-ar	FP	0.00000	<=	0.000192308
SVC	RF	nr-er-lbd	FP	0.00000	<=	0.000192308
SVC	RF	nr-er	FP	0.00000	<=	0.000192308
SVC	RF	nr-ppar-gamma	FP	0.00000	<=	0.000192308
SVC	RF	mutagenicity	FP	0.00000	<=	0.000192308
SVC	RF	sr-are	FP	0.00000	<=	0.000192308
SVC	RF	sr-atad5	FP	0.00000	<=	0.000192308
SVC	RF	sr-hse	FP	0.00000	<=	0.000192308
SVC	RF	sr-mmp	FP	0.00000	<=	0.000192308
SVC	RF	sr-p53	FP	0.00000	<=	0.000192308
SVC	DNN	nr-ahr	FP	0.00000	<=	0.000192308
SVC	DNN	nr-ar-lbd	FP	0.00000	<=	0.000192308
SVC	DNN	nr-aromatase	FP	0.00000	<=	0.000192308
SVC	DNN	nr-ar	FP	0.00000	<=	0.000192308
SVC	DNN	nr-er-lbd	FP	0.00000	<=	0.000192308
SVC	DNN	nr-er	FP	0.00000	<=	0.000192308
SVC	DNN	nr-ppar-gamma	FP	0.00000	<=	0.000192308
SVC	DNN	mutagenicity	FP	0.33900	>	0.000192308
SVC	DNN	sr-are	FP	0.00000	<=	0.000192308
SVC	DNN	sr-atad5	FP	0.00000	<=	0.000192308
SVC	DNN	sr-hse	FP	0.00000	<=	0.000192308
SVC	DNN	sr-mmp	FP	0.00000	<=	0.000192308

SVC	DNN	sr-p53	FP	0.00000	<=	0.000192308
SVC	XGB	nr-ahr	MD	0.00000	<=	0.000192308
SVC	XGB	nr-ar-lbd	MD	0.00000	<=	0.000192308
SVC	XGB	nr-aromatase	MD	0.00000	<=	0.000192308
SVC	XGB	nr-ar	MD	0.00000	<=	0.000192308
SVC	XGB	nr-er-lbd	MD	0.00000	<=	0.000192308
SVC	XGB	nr-er	MD	0.04224	>	0.000192308
SVC	XGB	nr-ppar-gamma	MD	0.00000	<=	0.000192308
SVC	XGB	mutagenicity	MD	0.28888	>	0.000192308
SVC	XGB	sr-are	MD	0.58810	>	0.000192308
SVC	XGB	sr-atad5	MD	0.00000	<=	0.000192308
SVC	XGB	sr-hse	MD	0.00000	<=	0.000192308
SVC	XGB	sr-mmp	MD	0.00173	>	0.000192308
SVC	XGB	sr-p53	MD	0.00000	<=	0.000192308
SVC	RF	nr-ahr	MD	0.00000	<=	0.000192308
SVC	RF	nr-ar-lbd	MD	0.00000	<=	0.000192308
SVC	RF	nr-aromatase	MD	0.00000	<=	0.000192308
SVC	RF	nr-ar	MD	0.00000	<=	0.000192308
SVC	RF	nr-er-lbd	MD	0.00000	<=	0.000192308
SVC	RF	nr-er	MD	0.00000	<=	0.000192308
SVC	RF	nr-ppar-gamma	MD	0.00000	<=	0.000192308
SVC	RF	mutagenicity	MD	0.33050	>	0.000192308
SVC	RF	sr-are	MD	0.00000	<=	0.000192308
SVC	RF	sr-atad5	MD	0.00000	<=	0.000192308
SVC	RF	sr-hse	MD	0.00000	<=	0.000192308
SVC	RF	sr-mmp	MD	0.00000	<=	0.000192308
SVC	RF	sr-p53	MD	0.00000	<=	0.000192308
SVC	DNN	nr-ahr	MD	0.00000	<=	0.000192308
SVC	DNN	nr-ar-lbd	MD	0.00000	<=	0.000192308

SVC	DNN	nr-aromatase	MD	0.00000	<=	0.000192308
SVC	DNN	nr-ar	MD	0.00000	<=	0.000192308
SVC	DNN	nr-er-lbd	MD	0.00000	<=	0.000192308
SVC	DNN	nr-er	MD	0.00000	<=	0.000192308
SVC	DNN	nr-ppar-gamma	MD	0.00000	<=	0.000192308
SVC	DNN	mutagenicity	MD	0.14017	>	0.000192308
SVC	DNN	sr-are	MD	0.00000	<=	0.000192308
SVC	DNN	sr-atad5	MD	0.00000	<=	0.000192308
SVC	DNN	sr-hse	MD	0.00000	<=	0.000192308
SVC	DNN	sr-mmp	MD	0.00000	<=	0.000192308
SVC	DNN	sr-p53	MD	0.00000	<=	0.000192308
XGB	RF	nr-ahr	FP	0.00000	<=	0.000192308
XGB	RF	nr-ar-lbd	FP	0.98131	>	0.000192308
XGB	RF	nr-aromatase	FP	0.01543	>	0.000192308
XGB	RF	nr-ar	FP	0.31532	>	0.000192308
XGB	RF	nr-er-lbd	FP	0.88253	>	0.000192308
XGB	RF	nr-er	FP	0.00000	<=	0.000192308
XGB	RF	nr-ppar-gamma	FP	0.72898	>	0.000192308
XGB	RF	mutagenicity	FP	0.84163	>	0.000192308
XGB	RF	sr-are	FP	0.00000	<=	0.000192308
XGB	RF	sr-atad5	FP	0.00252	>	0.000192308
XGB	RF	sr-hse	FP	0.02153	>	0.000192308
XGB	RF	sr-mmp	FP	0.00001	<=	0.000192308
XGB	RF	sr-p53	FP	0.00003	<=	0.000192308
XGB	DNN	nr-ahr	FP	0.00000	<=	0.000192308
XGB	DNN	nr-ar-lbd	FP	0.86497	>	0.000192308
XGB	DNN	nr-aromatase	FP	0.84715	>	0.000192308
XGB	DNN	nr-ar	FP	0.00188	>	0.000192308
XGB	DNN	nr-er-lbd	FP	0.71383	>	0.000192308

XGB	DNN	nr-er	FP	0.00000	<=	0.000192308
XGB	DNN	nr-ppar-gamma	FP	0.02620	>	0.000192308
XGB	DNN	mutagenicity	FP	0.00000	<=	0.000192308
XGB	DNN	sr-are	FP	0.00000	<=	0.000192308
XGB	DNN	sr-atad5	FP	0.12988	>	0.000192308
XGB	DNN	sr-hse	FP	0.22837	>	0.000192308
XGB	DNN	sr-mmp	FP	0.00546	>	0.000192308
XGB	DNN	sr-p53	FP	0.00756	>	0.000192308
XGB	RF	nr-ahr	MD	0.00000	<=	0.000192308
XGB	RF	nr-ar-lbd	MD	0.81031	>	0.000192308
XGB	RF	nr-aromatase	MD	0.00000	<=	0.000192308
XGB	RF	nr-ar	MD	0.62019	>	0.000192308
XGB	RF	nr-er-lbd	MD	0.00034	>	0.000192308
XGB	RF	nr-er	MD	0.00000	<=	0.000192308
XGB	RF	nr-ppar-gamma	MD	0.02990	>	0.000192308
XGB	RF	mutagenicity	MD	0.93030	>	0.000192308
XGB	RF	sr-are	MD	0.00000	<=	0.000192308
XGB	RF	sr-atad5	MD	0.00021	>	0.000192308
XGB	RF	sr-hse	MD	0.00000	<=	0.000192308
XGB	RF	sr-mmp	MD	0.00000	<=	0.000192308
XGB	RF	sr-p53	MD	0.00000	<=	0.000192308
XGB	DNN	nr-ahr	MD	0.00000	<=	0.000192308
XGB	DNN	nr-ar-lbd	MD	0.46560	>	0.000192308
XGB	DNN	nr-aromatase	MD	0.00000	<=	0.000192308
XGB	DNN	nr-ar	MD	0.04679	>	0.000192308
XGB	DNN	nr-er-lbd	MD	0.14427	>	0.000192308
XGB	DNN	nr-er	MD	0.00000	<=	0.000192308
XGB	DNN	nr-ppar-gamma	MD	0.91744	>	0.000192308
XGB	DNN	mutagenicity	MD	0.67847	>	0.000192308

XGB	DNN	sr-are	MD	0.00000	<=	0.000192308
XGB	DNN	sr-atad5	MD	0.07281	>	0.000192308
XGB	DNN	sr-hse	MD	0.00216	>	0.000192308
XGB	DNN	sr-mmp	MD	0.00019	<=	0.000192308
XGB	DNN	sr-p53	MD	0.00000	<=	0.000192308

Table S6. The percentage of test compounds outside model applicability domain

	Percentage of compounds outside applicability domain	
Data sets	Morgan Fingerprints	RDKit Molecular descriptors
nr-ahr	2.4	2.09
nr-ar	2.49	0.52
nr-ar-lbd	2.34	1.24
nr-aromatase	2.69	1.38
nr-er	2.29	0.58
nr-er-lbd	2.33	0.38
nr-ppar-gamma	2.4	1.14
sr-are	2.09	0.52
sr-atad5	2.21	0.68
sr-hse	2.41	0.61
sr-mmp	2.35	0.06
sr-p53	2.39	0.54
mutagenicity	3.66	0.95

Table S7. Compare average specificity (SP), sensitivity (SE), Matthews correlation coefficient (MCC), Cohen's kappa (Kappa), balanced accuracy (BA) and area under curve (AUC) results on validation (V) and test (T) sets of Bayesian optimization for LightGBM algorithm with either balance accuracy (BA) and Matthews correlation coefficient (MCC) as optimization scoring function (OptScore).

Feature	OptScore	SP		SE		MCC		Kappa		BA		AUC	
		V	T	V	T	V	T	V	T	V	T	V	T
FP	BA	0.892	0.900	0.657	0.672	0.442	0.448	0.415	0.424	0.775	0.786	0.836	0.786
	MCC	0.959	0.958	0.529	0.566	0.536	0.562	0.524	0.555	0.744	0.762	0.815	0.762
MD	BA	0.893	0.900	0.674	0.700	0.461	0.467	0.433	0.440	0.784	0.800	0.855	0.800
	MCC	0.962	0.961	0.530	0.569	0.555	0.578	0.538	0.570	0.746	0.765	0.856	0.765

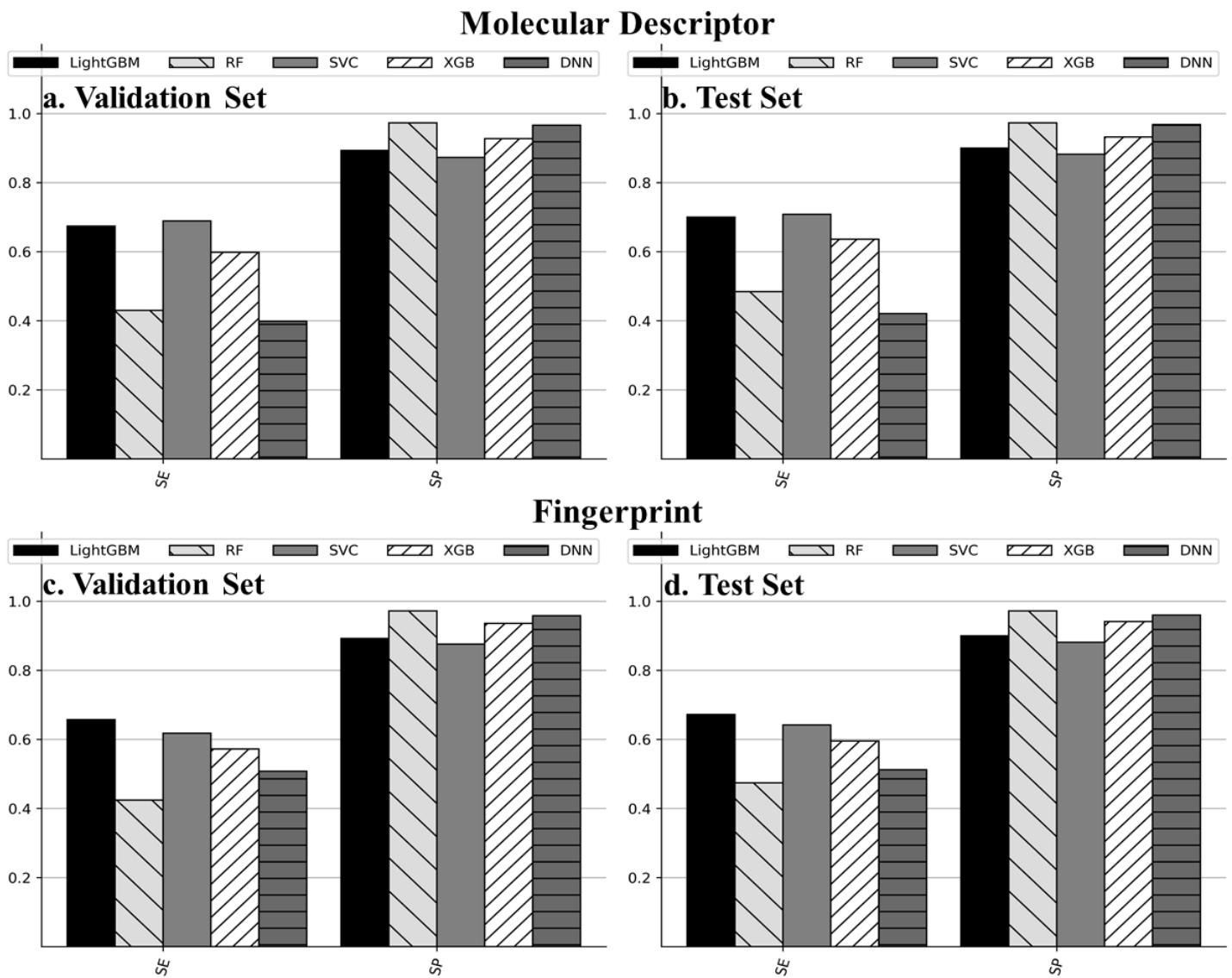


Figure S1. The average sensitivity (SE) and specificity (SP) values of the five algorithms prediction results on both validation (V) and test set (T) of the Tox21 and mutagenicity data sets.

$$Balanced\ Accuracy\ (BA) = \left[\frac{TP}{TP + FN} + \frac{TN}{TN + FP} \right] / 2$$

$$Cohen's\ kappa\ index\ (Kappa) = \frac{P_0 - P_e}{1 - P_e}$$

$$F1\ score\ (F1) = \frac{2 * TP}{2 * TP + FN + FP}$$

$$Matthews\ correlation\ coefficient\ (MCC) = \frac{TP \times TN - FP \times FN}{\sqrt{(TP + FP)(TP + FN)(TN + FP)(TN + FN)}}$$

$$Positive\ predictive\ value\ (PPV) = \frac{TP}{TP + FP}$$

$$Negative\ predictive\ value\ (NPV) = \frac{TN}{TN + FN}$$

$$Specificity\ (SP) = \frac{TN}{TN + FP}$$

$$Sensitivity\ (SE) = \frac{TP}{TP + FN}$$

Where TP is the number of true positives, TN is the number of true negatives, FP is the number of false positives, FN is the number of false negatives, P_0 is the relative observed agreement among raters, and P_e is the hypothetical probability of chance agreement.