SUPPLEMENTARY DATA

BitterSweet: Building machine learning models for predicting the bitter and sweet taste of small molecules.

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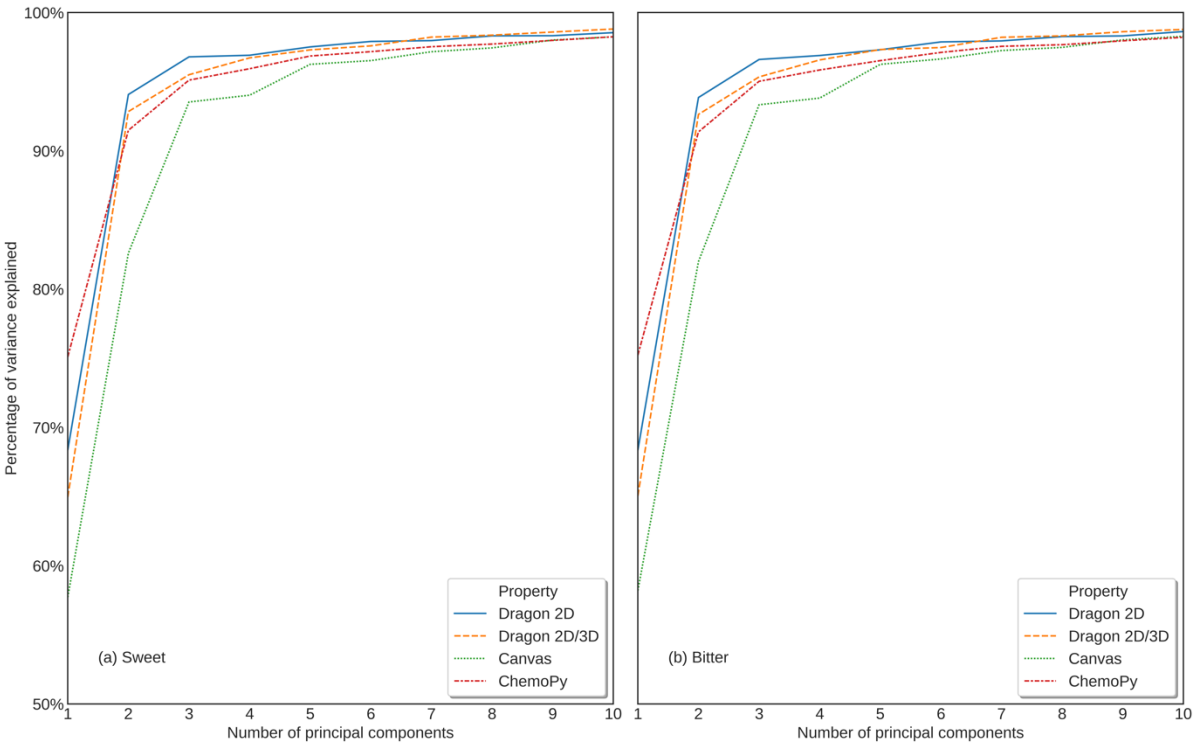
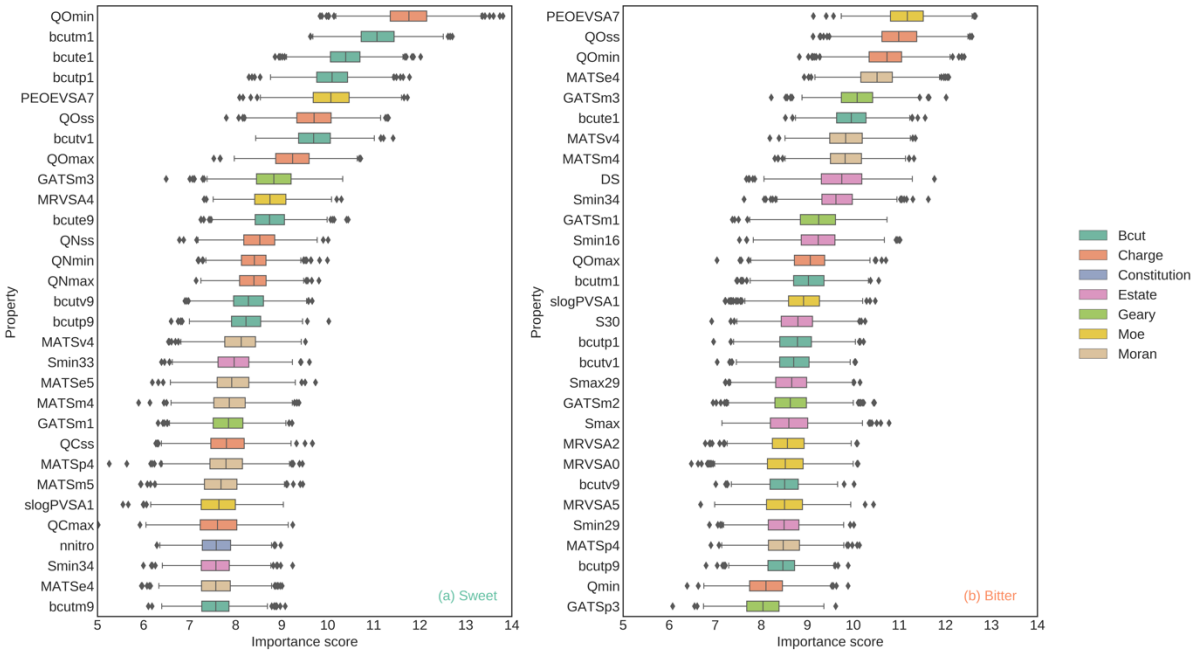
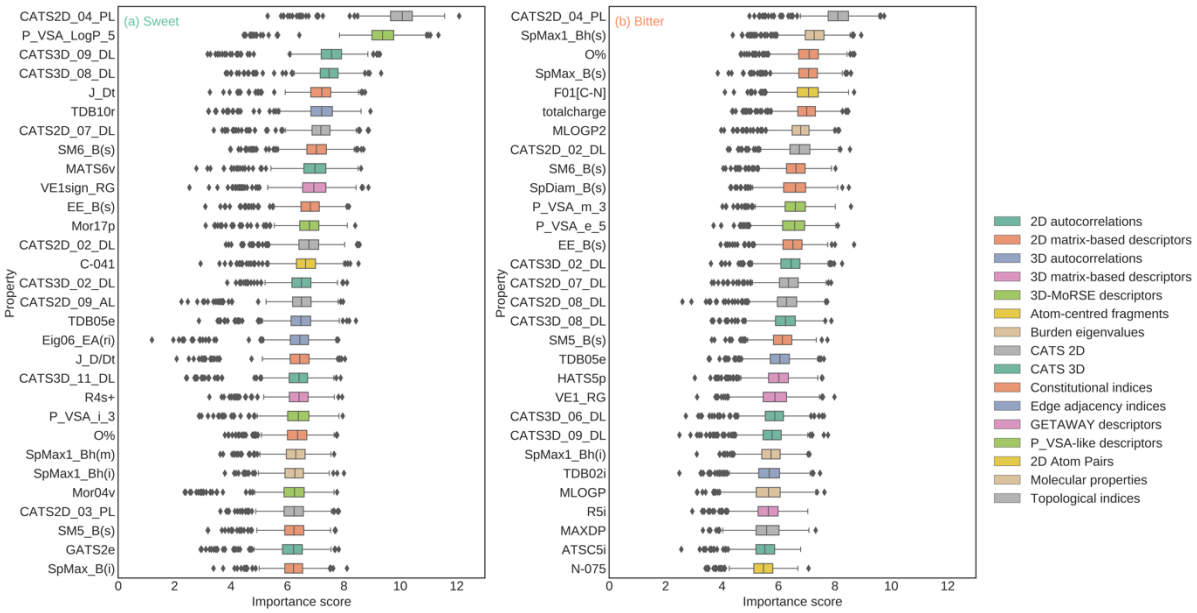
Supplementary Figure S1: Percentage of variation captured by the top 10 principal components in Dragon2D, Dragon2D/3D, Canvas, and ChemoPy molecular descriptor sets, for (a) sweet/non-sweet and (b) bitter/non-bitter prediction datasets.



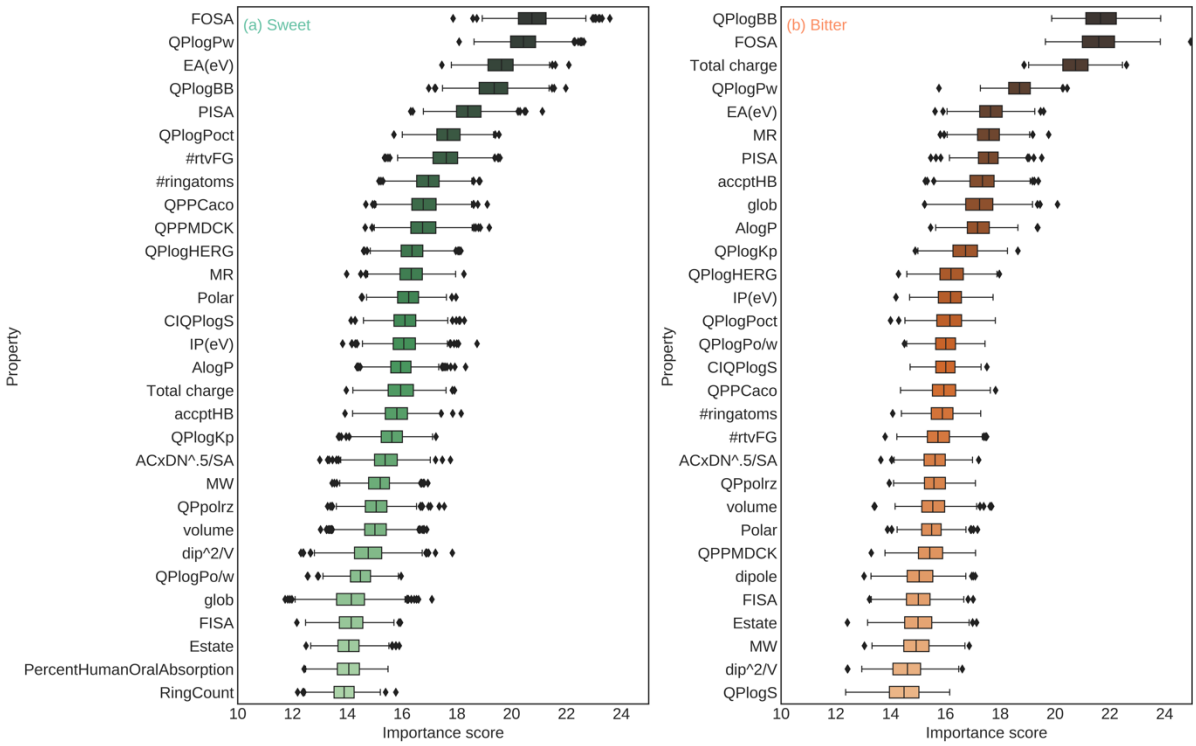
Supplementary Figure S2: Boxplot of importance scores of different ChemoPy descriptors for (a) sweet/non-sweet and (b) bitter/non-bitter prediction.



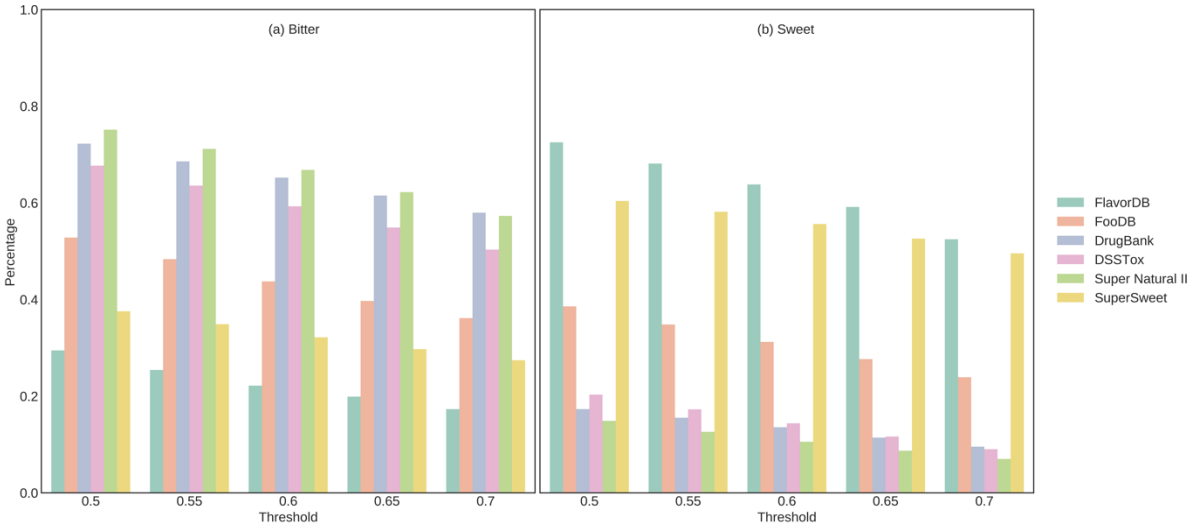
Supplementary Figure S3: Boxplot of importance scores of different Dragon 2D/3D molecular descriptors for (a) sweet/non-sweet and (b) bitter/non-bitter prediction.



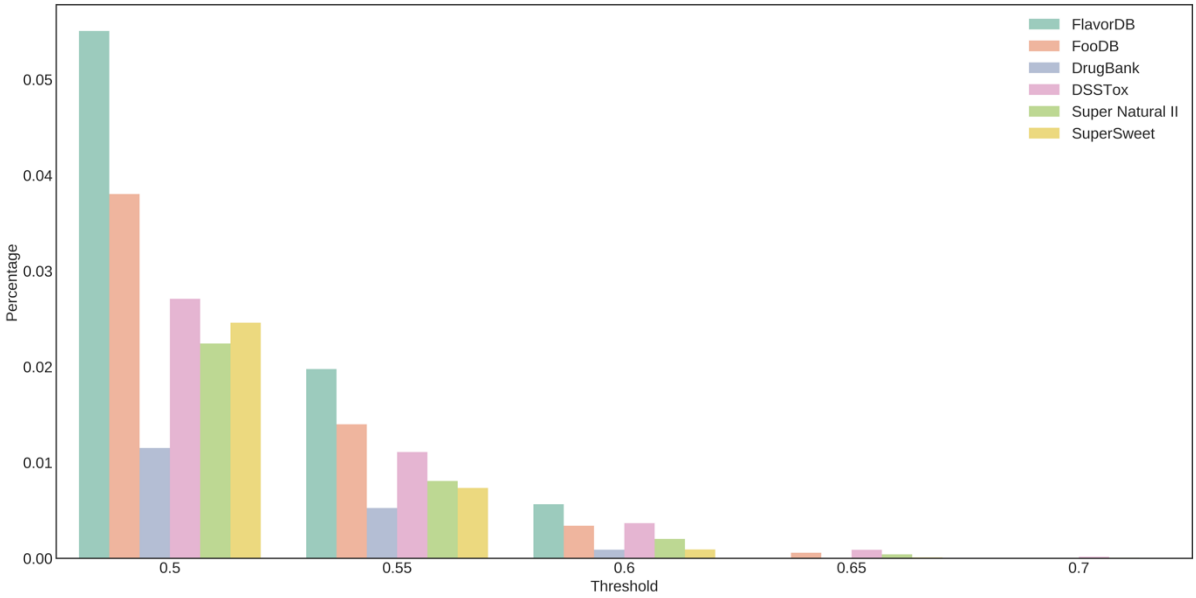
Supplementary Figure S4: Boxplot of importance scores of different Canvas features for (a) sweet/non-sweet and (b) bitter/non-bitter prediction.



Supplementary Figure S5: Proportion of compounds predicted to be (a) bitter and (b) sweet in specialized chemical sets at different thresholds.



Supplementary Figure S6: Proportion of compounds predicted to be both bitter and sweet in specialized chemical sets at different thresholds.



Supplementary Table S1: Number of molecules in training and testing sets for bitter/non-bitter and sweet/non-sweet prediction.

	Type	Taste	Number of molecules
Bitter	Training	Bitter	813
		Non-bitter	1444
	Testing	Bitter	95
		Non-bitter	59
Sweet	Training	Sweet	1139
		Non-sweet	1066
	Testing	Non-sweet	53
		Sweet	108

Supplementary Table S2: Summary of the different feature sets for building bitter-sweet prediction models.

Software	Description
Canvas	Physicochemical and ADMET (absorption, distribution, metabolism, excretion, and toxicity)
Dragon 7	Extended Connectivity Fingerprints
	2D Molecular Descriptors
	2D/3D Molecular Descriptors
ChemoPy	2D Topological and Structural Features

Supplementary Table S3: Performance of BitterSweet models for sweet/non-sweet prediction.

			Cross-Validation						Test					
Performance Metrics			AUPR	AUROC	F1	NER	Sn	Sp	AUPR	AUROC	F1	NER	Sn	Sp
Molecular Descriptors	Model	Pre-processing												
Canvas	RF	Boruta	0.919	0.910	0.832	0.8380	0.823	0.853	0.899	0.816	0.754	0.7735	0.629	0.918
	RLR	Boruta	0.789	0.801	0.758	0.7510	0.759	0.743	0.882	0.789	0.783	0.7505	0.705	0.796
	AB	Boruta	0.895	0.895	0.826	0.8350	0.794	0.876	0.900	0.837	0.791	0.7710	0.705	0.837
Dragon2D	RF	PCA	0.923	0.919	0.841	0.8480	0.827	0.869	0.924	0.839	0.720	0.7740	0.567	0.981
	RLR	PCA	0.881	0.891	0.829	0.8265	0.836	0.817	0.918	0.832	0.747	0.7655	0.625	0.906
	AB	PCA	0.901	0.895	0.820	0.8305	0.802	0.859	0.928	0.851	0.806	0.7755	0.740	0.811
	RF	Boruta	0.924	0.923	0.847	0.8510	0.835	0.867	0.933	0.863	0.798	0.8130	0.683	0.943
	RLR	Boruta	0.872	0.880	0.824	0.8230	0.837	0.809	0.911	0.812	0.761	0.7750	0.644	0.906
	AB	Boruta	0.923	0.918	0.848	0.8515	0.832	0.871	0.944	0.881	0.829	0.7995	0.769	0.830
Dragon2D/3D	RF	PCA	0.925	0.916	0.849	0.8505	0.840	0.861	0.930	0.843	0.809	0.7905	0.724	0.857
	RLR	PCA	0.889	0.896	0.845	0.8365	0.851	0.822	0.918	0.831	0.804	0.8015	0.705	0.898
	AB	PCA	0.906	0.900	0.819	0.8355	0.769	0.902	0.932	0.845	0.770	0.7985	0.638	0.959
	RF	Boruta	0.929	0.921	0.853	0.8505	0.849	0.852	0.945	0.872	0.798	0.8175	0.676	0.959
	RLR	Boruta	0.842	0.842	0.786	0.7805	0.800	0.761	0.892	0.789	0.757	0.7680	0.638	0.898
	AB	Boruta	0.920	0.918	0.858	0.8560	0.853	0.859	0.950	0.883	0.856	0.8340	0.790	0.878
ChemoPy	RF	PCA	0.918	0.914	0.839	0.8460	0.819	0.873	0.925	0.835	0.731	0.7660	0.592	0.940
	RLR	PCA	0.864	0.868	0.796	0.7950	0.802	0.788	0.887	0.802	0.791	0.7590	0.718	0.800
	AB	PCA	0.894	0.892	0.801	0.8230	0.737	0.909	0.910	0.809	0.762	0.7450	0.670	0.820
	RF	Boruta	0.925	0.922	0.842	0.8495	0.829	0.870	0.933	0.852	0.772	0.8005	0.641	0.960
	RLR	Boruta	0.840	0.852	0.788	0.7875	0.792	0.783	0.877	0.786	0.754	0.7605	0.641	0.880
	AB	Boruta	0.907	0.906	0.819	0.8315	0.797	0.866	0.926	0.838	0.753	0.7805	0.621	0.940
ECFP	RF	None	0.930	0.929	0.862	0.8630	0.869	0.857	0.927	0.837	0.763	0.8020	0.623	0.981
	RLR	None	0.895	0.889	0.815	0.8160	0.813	0.819	0.889	0.760	0.699	0.7545	0.547	0.962
	AB	None	0.923	0.926	0.867	0.8675	0.863	0.872	0.929	0.847	0.806	0.7875	0.726	0.849

Supplementary Table S4: Performance of BitterSweet models for bitter/non-bitter prediction aggregated over different test sets.

			Cross-Validation						Test					
Performance Metrics			AUPR	AUROC	F1	NER	Sn	Sp	AUPR	AUROC	F1	NER	Sn	Sp
Molecular Descriptors	Model	Pre-processing												
Canvas	RF	Boruta	0.774	0.840	0.708	0.7635	0.728	0.799	0.908	0.864	0.824	0.7865	0.800	0.773

	RLR	**Boruta**	0.617	0.709	0.595	0.6670	0.694	0.640	0.819	0.740	0.737	0.6620	0.733	0.591
	AB	**Boruta**	0.804	0.849	0.722	0.7830	0.739	0.827	0.907	0.866	0.824	0.7995	0.781	0.818
Dragon2D	**RF**	**PCA**	0.805	0.855	0.715	0.7630	0.727	0.799	0.911	0.857	0.813	0.7535	0.825	0.682
	RLR	**PCA**	0.781	0.847	0.722	0.7735	0.797	0.750	0.915	0.850	0.817	0.8025	0.757	0.848
	AB	**PCA**	0.805	0.863	0.737	0.7915	0.723	0.860	0.912	0.868	0.849	0.7930	0.874	0.712
	RF	**Boruta**	0.814	0.864	0.747	0.7925	0.787	0.798	0.907	0.855	0.830	0.7970	0.806	0.788
	RLR	**Boruta**	0.774	0.825	0.697	0.7505	0.758	0.743	0.909	0.836	0.816	0.7900	0.777	0.803
	AB	**Boruta**	0.812	0.860	0.745	0.7920	0.778	0.806	0.908	0.882	0.837	0.7990	0.825	0.773
Dragon2D/3D	**RF**	**PCA**	0.808	0.857	0.706	0.7670	0.696	0.838	0.919	0.874	0.869	0.8055	0.914	0.697
	RLR	**PCA**	0.797	0.862	0.739	0.8020	0.831	0.773	0.909	0.845	0.833	0.7695	0.857	0.682
	AB	**PCA**	0.738	0.787	0.645	0.7255	0.626	0.825	0.909	0.851	0.842	0.7980	0.838	0.758
	RF	**Boruta**	0.784	0.851	0.726	0.7815	0.753	0.810	0.904	0.853	0.833	0.7855	0.829	0.742
	RLR	**Boruta**	0.770	0.840	0.680	0.7530	0.773	0.733	0.902	0.844	0.829	0.7780	0.829	0.727
	AB	**Boruta**	0.782	0.854	0.714	0.7745	0.696	0.853	0.921	0.873	0.817	0.8110	0.743	0.879
ChemoPy	**RF**	**PCA**	0.797	0.852	0.698	0.7540	0.719	0.789	0.927	0.880	0.838	0.8190	0.790	0.848
	RLR	**PCA**	0.743	0.821	0.685	0.7505	0.756	0.745	0.931	0.884	0.856	0.8180	0.848	0.788
	AB	**PCA**	0.778	0.852	0.713	0.7775	0.705	0.850	0.909	0.869	0.833	0.7855	0.829	0.742
	RF	**Boruta**	0.803	0.852	0.725	0.7705	0.761	0.780	0.917	0.874	0.844	0.7950	0.848	0.742
	RLR	**Boruta**	0.744	0.808	0.669	0.7310	0.751	0.711	0.905	0.846	0.818	0.7390	0.857	0.621
	AB	**Boruta**	0.786	0.850	0.716	0.7665	0.705	0.828	0.897	0.873	0.837	0.8065	0.810	0.803
ECFP	**RF**	**None**	0.791	0.837	0.668	0.7240	0.614	0.834	0.906	0.861	0.850	0.7870	0.892	0.682
	RLR	**None**	0.757	0.815	0.693	0.7430	0.810	0.676	0.846	0.789	0.840	0.7615	0.902	0.621
	AB	**None**	0.823	0.860	0.721	0.7725	0.762	0.783	0.926	0.892	0.846	0.8055	0.838	0.773

Supplementary Table S5: Performance of BitterSweet models for bitter/non-bitter prediction on the Phyto-Dictionary test set.

Molecular Descriptors	Model	Pre-processing	Sn	Sp	F1	AUPR	AUROC
Canvas	**RF**	**Boruta**	0.980	0.76	0.932	0.959	0.931
	RLR	**Boruta**	0.776	0.76	0.817	0.939	0.913
	AB	**Boruta**	0.939	0.76	0.911	0.935	0.968
Dragon2D	**RF**	**PCA**	0.979	0.76	0.931	0.985	0.972
	RLR	**PCA**	0.979	0.64	0.904	0.971	0.884
	AB	**PCA**	0.979	0.84	0.949	0.989	0.979
	RF	**Boruta**	0.958	0.84	0.939	0.971	0.951
	RLR	**Boruta**	0.938	0.68	0.891	0.947	0.898
	AB	**Boruta**	0.979	0.76	0.931	0.978	0.959
Dragon2D/3D	**RF**	**PCA**	0.980	0.68	0.914	0.976	0.946
	RLR	**PCA**	0.959	0.56	0.879	0.950	0.886
	AB	**PCA**	0.939	0.80	0.920	0.982	0.953
	RF	**Boruta**	0.959	0.76	0.922	0.962	0.931
	RLR	**Boruta**	0.980	0.68	0.914	0.952	0.913
	AB	**Boruta**	0.959	0.88	0.949	0.985	0.968
ChemoPy	**RF**	**PCA**	0.959	0.92	0.959	0.988	0.972
	RLR	**PCA**	0.939	0.56	0.868	0.944	0.884
	AB	**PCA**	0.959	0.92	0.959	0.990	0.979
	RF	**Boruta**	0.959	0.84	0.940	0.975	0.951
	RLR	**Boruta**	0.898	0.68	0.871	0.952	0.898
	AB	**Boruta**	0.959	0.88	0.949	0.980	0.959
ECFP	**RF**	**None**	0.979	0.84	0.949	0.972	0.946
	RLR	**None**	0.958	0.64	0.893	0.937	0.886
	AB	**None**	0.959	0.84	0.940	0.970	0.953

Supplementary Table S6: Performance of BitterSweet models for bitter/non-bitter prediction on the UNIMI test set.

Molecular Descriptors	Model	Pre-processing	Sn	Sp	F1	AUPR	AUROC
Canvas	**RF**	**Boruta**	0.826	0.727	0.745	0.810	0.845
	RLR	**Boruta**	0.870	0.364	0.625	0.626	0.664
	AB	**Boruta**	0.739	0.818	0.739	0.844	0.875
Dragon2D	**RF**	**PCA**	0.826	0.576	0.679	0.667	0.794
	RLR	**PCA**	0.609	0.970	0.737	0.848	0.842
	AB	**PCA**	0.783	0.667	0.692	0.557	0.741
	RF	**Boruta**	0.783	0.727	0.720	0.695	0.814
	RLR	**Boruta**	0.696	0.879	0.744	0.854	0.856
	AB	**Boruta**	0.739	0.758	0.708	0.772	0.829
Dragon2D/3D	**RF**	**PCA**	0.913	0.636	0.750	0.687	0.817
	RLR	**PCA**	0.826	0.424	0.623	0.659	0.740
	AB	**PCA**	0.783	0.818	0.766	0.850	0.888
	RF	**Boruta**	0.826	0.697	0.731	0.690	0.802
	RLR	**Boruta**	0.913	0.727	0.792	0.844	0.896
	AB	**Boruta**	0.565	0.879	0.650	0.768	0.830

ChemoPy	**RF**	**PCA**	0.478	0.848	0.564	0.694	0.790
	RLR	**PCA**	0.957	0.515	0.721	0.797	0.840
	AB	**PCA**	0.913	0.545	0.712	0.634	0.727
	RF	**Boruta**	0.957	0.636	0.772	0.716	0.829
	RLR	**Boruta**	1.000	0.515	0.742	0.774	0.831
	AB	**Boruta**	0.739	0.727	0.694	0.741	0.829
ECFP	**RF**	**None**	0.957	0.515	0.721	0.590	0.711
	RLR	**None**	1.000	0.515	0.742	0.547	0.688
	AB	**None**	0.913	0.697	0.778	0.783	0.848

Supplementary Table S7: Performance of BitterSweet models for bitter/non-bitter prediction on the Bitter-New test set.

Molecular Descriptors	Model	Pre-processing	Sn	Sp	F1	AUPR	AUROC
Canvas	**RF**	**Boruta**	0.652	-	0.789	1.0	-
	RLR	**Boruta**	0.565	-	0.722	1.0	-
	AB	**Boruta**	0.783	-	0.878	1.0	-
Dragon2D	**RF**	**PCA**	0.652	-	0.789	1.0	-
	RLR	**PCA**	0.609	-	0.757	1.0	-
	AB	**PCA**	0.739	-	0.850	1.0	-
	RF	**Boruta**	0.652	-	0.789	1.0	-
	RLR	**Boruta**	0.652	-	0.789	1.0	-
	AB	**Boruta**	0.696	-	0.821	1.0	-
Dragon2D/3D	**RF**	**PCA**	0.913	-	0.955	1.0	-
	RLR	**PCA**	0.739	-	0.850	1.0	-
	AB	**PCA**	0.565	-	0.722	1.0	-
	RF	**Boruta**	0.739	-	0.850	1.0	-
	RLR	**Boruta**	0.652	-	0.789	1.0	-
	AB	**Boruta**	0.652	-	0.789	1.0	-
ChemoPy	**RF**	**PCA**	0.565	-	0.722	1.0	-
	RLR	**PCA**	0.826	-	0.905	1.0	-
	AB	**PCA**	0.652	-	0.789	1.0	-
	RF	**Boruta**	0.652	-	0.789	1.0	-
	RLR	**Boruta**	0.696	-	0.821	1.0	-
	AB	**Boruta**	0.696	-	0.821	1.0	-
ECFP	**RF**	**None**	0.739	-	0.850	1.0	-
	RLR	**None**	0.826	-	0.905	1.0	-
	AB	**None**	0.652	-	0.789	1.0	-