Machine Learning Predictions of Drug Release from Isocyanate-Derived Aerogels

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Supporting Information

Page No.

Appendix I. Material characterization and drug release amount determination

Table S-1. Release at 2 time points for both 5-Fluorouracil (5-FU) and Paracetamol (PM). (Each data point is an average of three separate results)

***K*-index**	**porosity (% v/v)**	**surface area (m^2/g)**	**macropore/mesopore**	**particle radius (nm)**	**time (h)**	**5-FU release (%)**		**PM release (%)**	
						0.5 h	**24 h**	**0.5 h**	**24 h**
1.2	78.43	232.41	1.448	23	0.5	1.52	4.60	0.41	1.11
1.3	81.78	223.66	1.688	24	0.5	5.80	8.67	0.49	1.03
1.4	74.5	128	4.274	19	0.5	?	?	?	?
1.5	75.65	184.23	4.558	24	0.5	19.73	19.84	2.28	5.15
1.6	82.54	113	1.929	23	0.5	10.61	16.41	1.40	5.58
1.7	80.92	24.2	43.359	102	0.5	5.19	17.98	1.28	4.71
1.8	77.71	9.76	67.14	253	0.5	8.14	13.10	2.36	7.07
1.9	78.03	8.12	102.793	319	0.5	8.47	13.76	3.70	8.03
2	74.92	1.54	1214	2280	0.5	4.05	13.13	3.00	4.85
2.1	73.54	1.34	1129	830	0.5	5.91	16.98	2.24	6.72
2.2	68.42	3.48	353	581	0.5	11.91	18.36	6.76	8.70

Appendix II. Training dataset used for all drug release ML modeling

Table S-2. Release profiles used in all analysis. (Each data point is an average of three separate results)

5-FU release profiles											
Time (h)	release (*K* = 1.2)	release (*K* = 1.3)	release (*K* = 1.4)	release (*K* = 1.5)	release (*K* = 1.6)	release (*K* = 1.7)	release (*K* = 1.8)	release (*K* = 1.9)	release (*K* = 2.0)	release (*K* = 2.1)	release (*K* = 2.2)
0.5	1.83	5.46	?	16.13	11.56	4.87	12.41	12.90	17.80	8.25	1.08
1	7.81	10.58	?	22.85	17.55	9.63	17.02	17.02	20.42	12.21	2.46
3	12.16	14.84	?	25.51	24.52	15.51	27.38	21.72	39.88	49.23	4.58
6	31.46	18.17	?	34.19	47.97	20.46	38.53	34.78	58.32	53.05	7.66
12	32.37	21.65	?	49.07	54.24	45.77	47.62	38.92	61.08	56.83	12.75
24	33.27	38.14	?	59.31	77.01	50.06	51.17	42.72	79.04	62.41	41.97
48	46.14	41.15	?	61.84	88.01	55.08	65.98	55.66	81.72	70.23	70.43
72	46.83	43.96	?	62.63	94.95	58.99	68.35	59.23	84.79	77.86	76.25
PM release profiles											
0.5	1.26	3.30	?	4.32	2.56	2.20	1.55	2.12	3.09	2.94	6.36
1	6.67	5.49	?	8.46	20.05	5.48	2.83	4.02	18.27	17.75	10.69
3	9.45	22.50	?	29.85	23.52	15.81	5.14	9.47	21.61	32.57	21.50
6	16.81	25.73	?	31.47	26.83	25.50	6.97	11.93	24.21	35.79	29.95
12	20.61	34.89	?	31.62	30.57	28.72	9.06	15.10	27.01	39.82	32.91
24	44.72	51.90	?	31.76	34.18	32.57	26.35	18.37	42.19	42.39	41.51
48	50.97	58.44	?	33.43	51.67	49.75	43.64	34.75	44.82	57.20	44.26
72	56.50	62.91	?	54.81	69.16	53.09	47.09	38.41	60.00	60.57	58.69

Appendix III. Drug release modeling parameters and adjustments

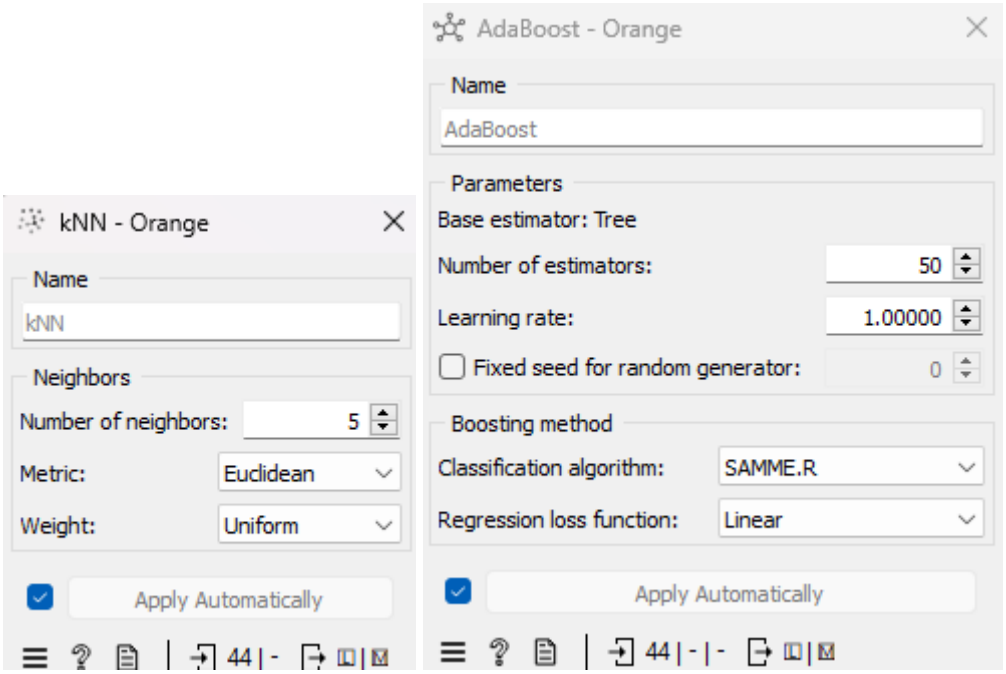

Figure S.1. Parameters used to arrive at each model's prediction for all drug release studies.

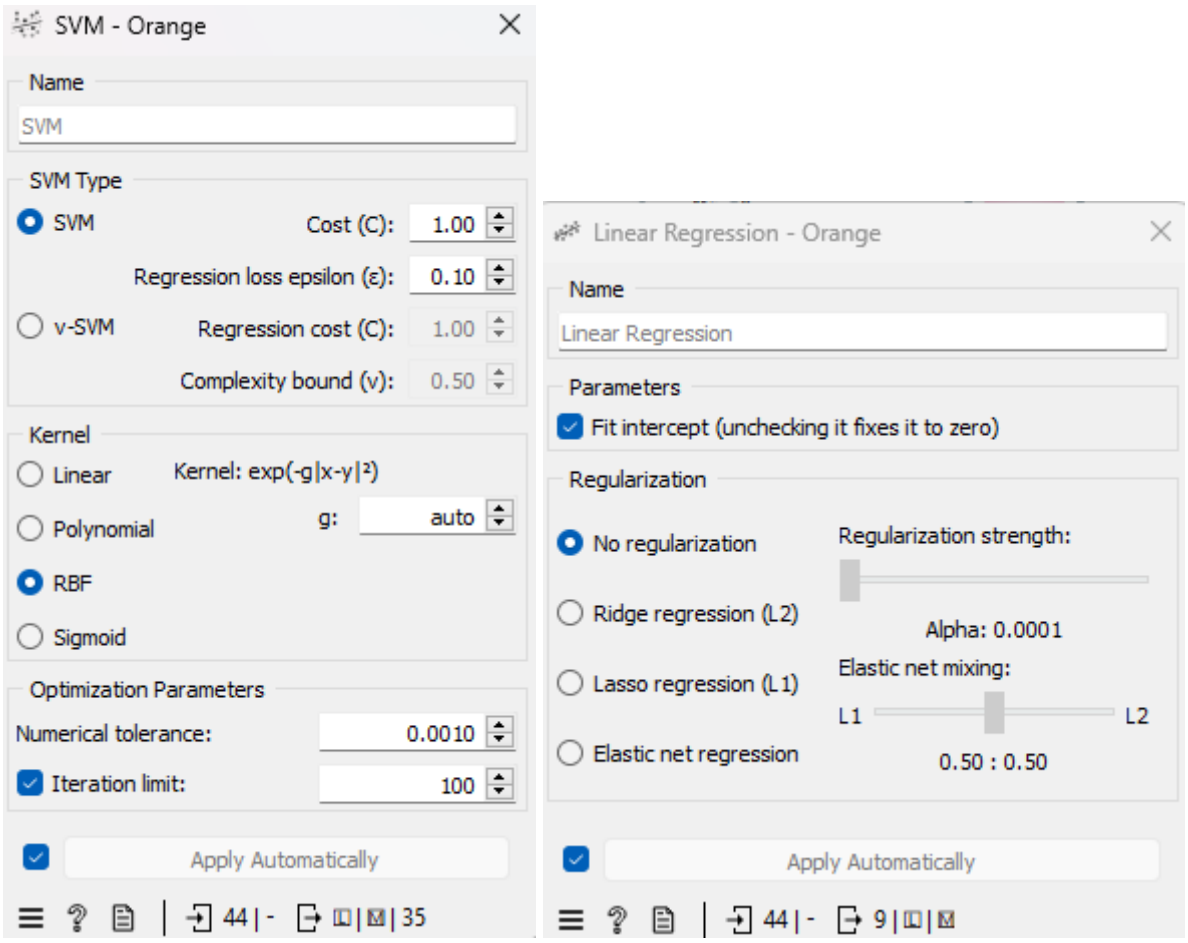

Figure S.1 (continued). Parameters used to arrive at each model's prediction for all drug release studies.

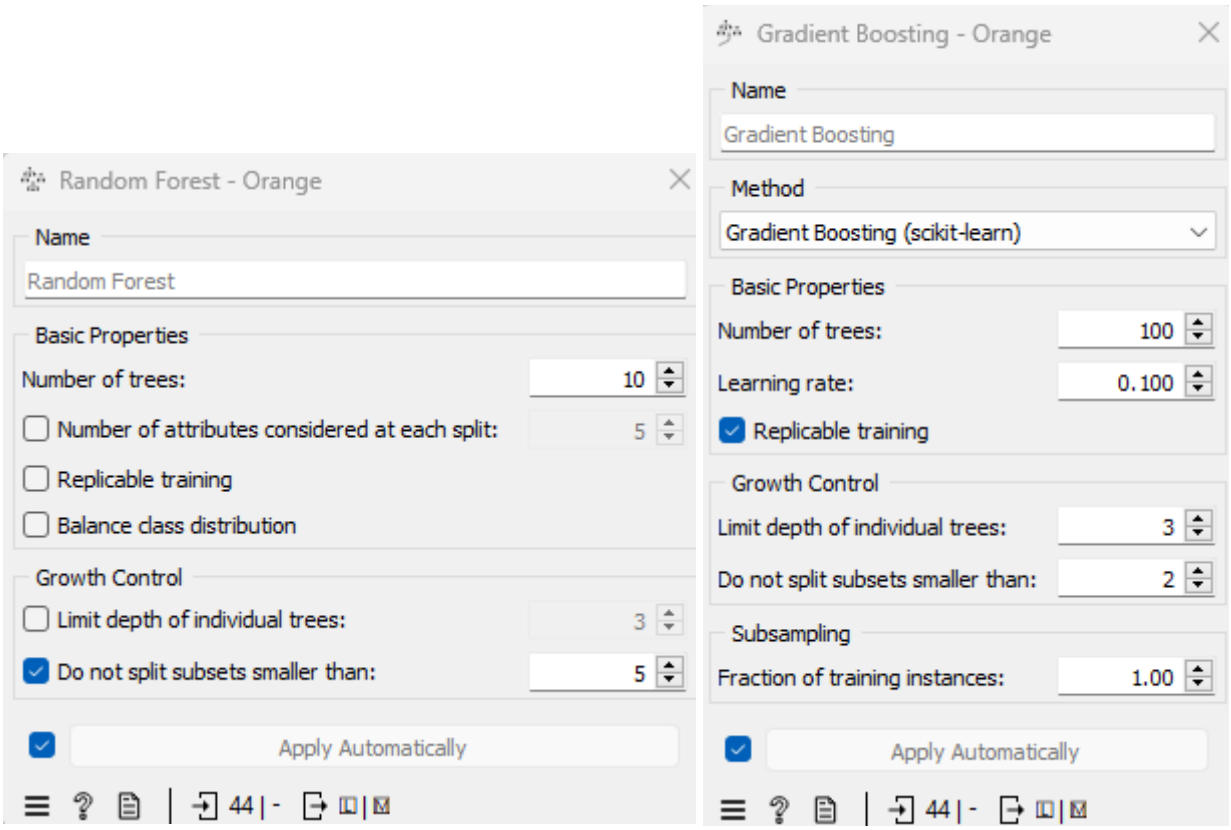

Figure S.1 (continued). Parameters used to arrive at each model's prediction for all drug release studies.

Appendix IV. Predicted drug release profiles for the training data set

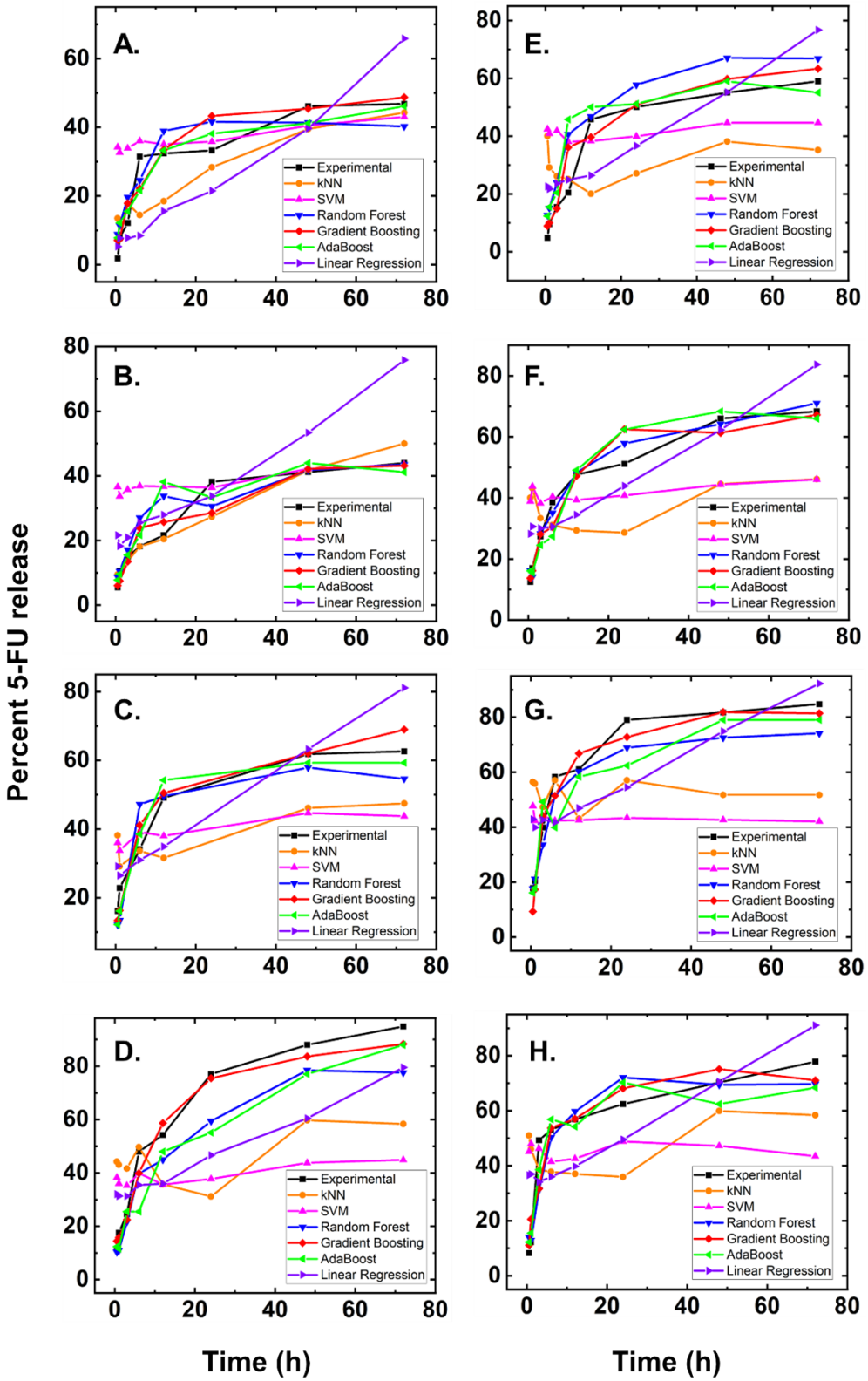

Figure S.2. Prediction of 5-FU release profiles of *K*-indexes whose experimental release profiles are known. *K*-index of training set A is 1.2, B is 1.3, C is 1.5, D is 1.6, E is 1.7, F is 1.8, G is 2.0, and H is 2.1

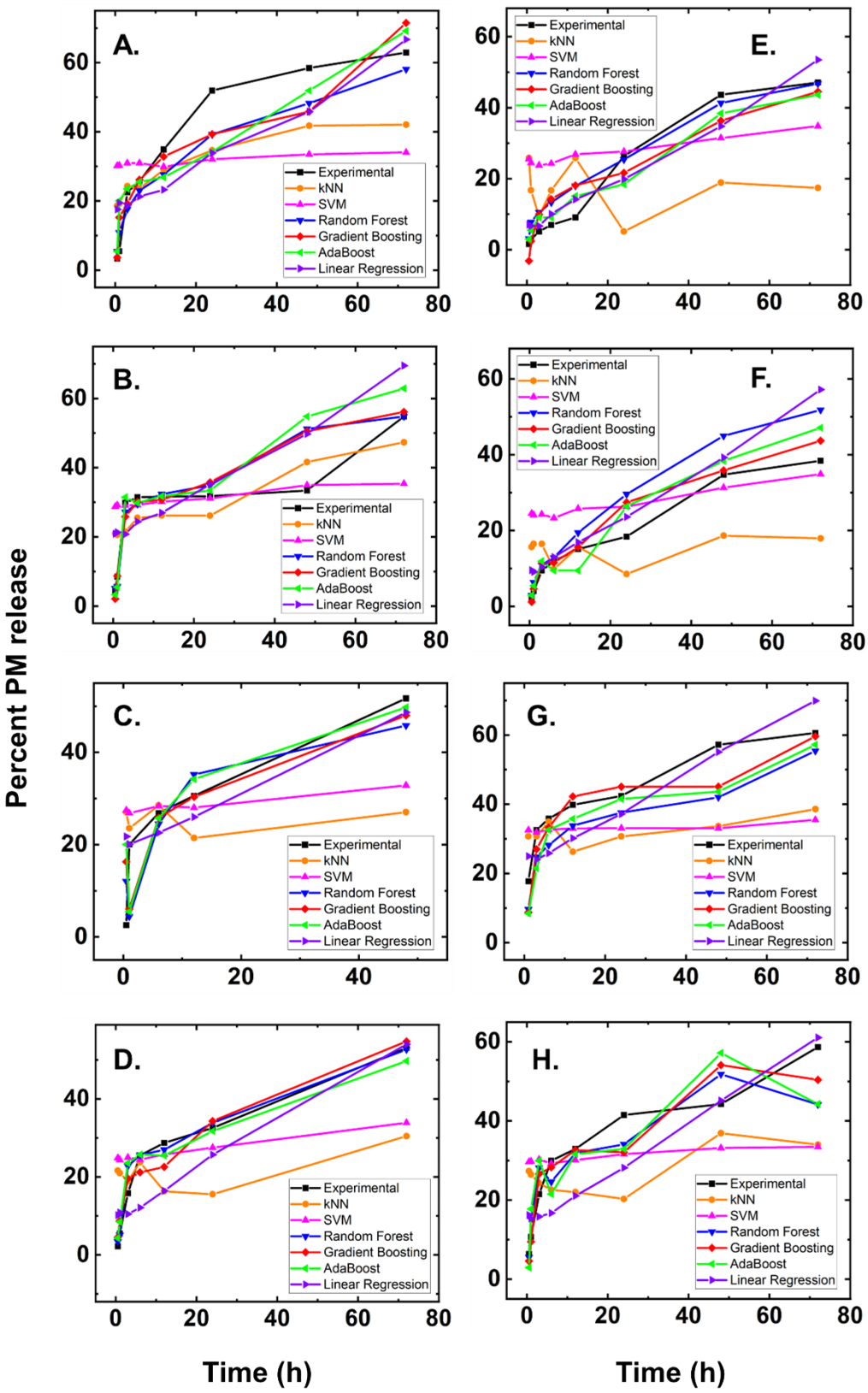

Figure S.3. Prediction of PM release profiles of *K*-indexes whose experimental release profiles are known. *K*-index of training set A is 1.3, B is 1.5, C is 1.6, D is 1.7, E is 1.8, F is 1.9, G is 2.1, and H is 2.2

Appendix V. Validation of the algorithm's predictions

Table S-3. Regression metrics obtained for 5-FU from training the algorithms with isocyanate- and non-isocyanate derived aerogels

Model	MSE	RMSE	MAE	MAPE	R2
kNN	393....	19.837	16.510	0.937	0.379
SVM	483....	21.985	18.929	1.693	0.237
Random Forest	106....	10.308	7.854	0.423	0.832
Gradient Boosting	61.939	7.870	6.024	0.278	0.902
AdaBoost	86.485	9.300	7.153	0.383	0.864
Linear Regression	190....	13.807	11.397	0.668	0.699

Table S-4. Regression metrics obtained for paracetamol from training the algorithms with isocyanate- and non-isocyanate derived aerogels

Model	MSE	RMSE	MAE	MAPE	R2
kNN	396....	19.920	15.028	1.411	0.361
SVM	512....	22.636	17.117	1.841	0.175
Random Forest	149....	12.218	8.153	0.494	0.760
Gradient Boosting	110....	10.509	6.213	0.376	0.822
AdaBoost	156....	12.496	7.299	0.449	0.749
Linear Regression	305....	17.491	14.325	1.322	0.507

Table S-5. Cross-validation results for 5-FU with new training set

Model	MSE	RMSE	MAE	MAPE	R2
kNN	456....	21.370	17.090	0.885	0.354
SVM	527....	22.969	19.723	1.650	0.253
Random Forest	111....	10.571	8.069	0.373	0.842
Gradient Boosting	73.260	8.559	6.355	0.257	0.896
AdaBoost	100....	10.005	7.364	0.387	0.858
Linear Regression	178....	13.376	11.196	0.663	0.747

Table S-6. Cross-validation results for PM with new training set

Model	MSE	RMSE	MAE	MAPE	R2
kNN	428....	20.697	16.299	1.396	0.351
SVM	547....	23.390	18.059	1.902	0.171
Random Forest	135....	11.646	8.491	0.415	0.794
Gradient Boosting	97.194	9.859	5.991	0.344	0.853
AdaBoost	140....	11.862	7.338	0.368	0.787
Linear Regression	304....	17.445	14.222	1.294	0.539