Table 1: RMSE on Three Regression Tasks

	Morgan RF	**Morgan XGB**	**Morgan DNN**	**MP graph** NEF^*	**MP graph** GCNN	**MP graph** Weave^*	**N-gram graph RF**	**N-gram graph XGB**	**N-gram graph DNN**
delaney	1.311 ±0.174	1.110 ±0.129	1.231 ±0.109	**0.520** **±0.137**	0.913 ±0.061	**0.460** **±0.157**	0.773 ±0.076	0.700 ±0.091	**0.699** **±0.046**
malaria	**1.028** **±0.029**	**1.008** **±0.031**	1.052 ±0.051	1.160 ±0.059	1.055 ±0.042	1.070 ±0.118	1.030 ±0.023	**1.010** **±0.026**	1.119 ±0.027
cep	1.642 ±0.026	1.410 ±0.040	1.477 ±0.042	1.430 ±0.176	**1.184** **±0.061**	**1.100** **±0.118**	1.379 ±0.013	**1.290** **±0.026**	1.365 ±0.034

- Mean and standard deviation on 5-fold cross validation.
- Top three models on each task are **bolded**.
- Baseline results (marked in *) are from [1, 2].
- For model **Morgan DNN**, we were using the results from [1] in the submitted version. Then we got a hyperparameter set that performs better on all three tasks after submission, so we replace it here. (It was 1.4, 1.13, 2.0 on three tasks.)
- MP graph is short for Message-passing graph.

[1] Duvenaud, D. K.; Maclaurin, D.;Iparraguirre, J.; Bombarell, R.; Hirzel, T.; Aspuru-Guzik,A.; and Adams, R. P. 2015. Convolutional Networks onGraphs for Learning Molecular Fingerprints. 2224–2232.

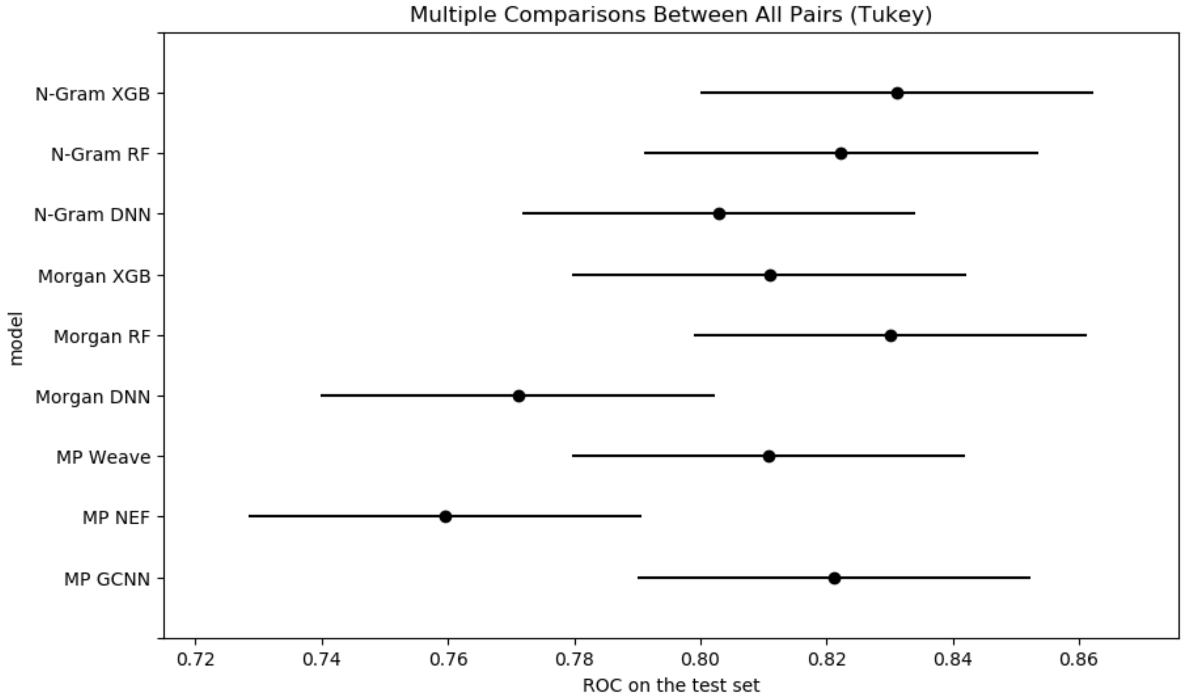
[2] Kusner, M. J.;Paige, B.; and Hernández-Lobato, J. M. 2017. Grammarvariational autoencoder.arXiv preprint arXiv:1703.01925.

Table 4: AUC[ROC] on Tox21

	Morgan RF	**Morgan XGB**	**Morgan DNN**	**MP graph NEF**	**MP graph GCNN**	**MP graph Weave**	**N-gram graph RF**	**N-gram graph XGB**	**N-gram graph DNN**
NR-AR	0.787 ±0.065	0.777 ±0.062	0.756 ±0.057	0.723 ±0.043	0.793 ±0.068	**0.796** **±0.057**	**0.802** **±0.082**	0.790 ±0.073	**0.795** **±0.062**
NR-AR-LBD	**0.864** **±0.056**	0.852 ±0.050	0.817 ±0.057	0.813 ±0.070	**0.858** **±0.037**	0.816 ±0.047	0.844 ±0.039	**0.858** **±0.027**	0.853 ±0.034
NR-AhR	**0.903** **±0.028**	**0.900** **±0.022**	0.854 ±0.036	0.841 ±0.051	0.896 ±0.018	0.869 ±0.036	0.890 ±0.020	**0.898** **±0.020**	0.869 ±0.023
NR-Aromatase	0.827 ±0.070	0.802 ±0.063	0.742 ±0.099	0.738 ±0.061	0.824 ±0.052	**0.830** **±0.050**	**0.845** **±0.066**	**0.852** **±0.053**	0.830 ±0.065
NR-ER	0.724 ±0.019	0.721 ±0.022	0.692 ±0.018	0.673 ±0.039	**0.734** **±0.036**	**0.729** **±0.025**	0.727 ±0.043	**0.733** **±0.035**	0.712 ±0.024
NR-ER-LBD	**0.815** **±0.051**	0.783 ±0.055	0.772 ±0.019	0.725 ±0.078	0.805 ±0.024	0.804 ±0.030	**0.810** **±0.062**	**0.819** **±0.036**	0.787 ±0.038
NR-PPAR-gamma	**0.839** **±0.042**	0.793 ±0.092	0.756 ±0.037	0.758 ±0.084	**0.821** **±0.105**	0.803 ±0.064	0.801 ±0.104	**0.825** **±0.104**	0.783 ±0.106
SR-ARE	**0.818** **±0.039**	**0.809** **±0.039**	0.781 ±0.046	0.740 ±0.031	0.782 ±0.040	0.790 ±0.049	0.808 ±0.028	**0.826** **±0.024**	0.777 ±0.049
SR-ATAD5	**0.857** **±0.051**	0.828 ±0.066	0.738 ±0.079	0.763 ±0.092	**0.839** **±0.037**	0.823 ±0.041	**0.841** **±0.032**	0.837 ±0.041	0.811 ±0.022
SR-HSE	**0.793** **±0.028**	0.764 ±0.043	0.731 ±0.034	0.702 ±0.041	**0.774** **±0.036**	0.771 ±0.036	0.773 ±0.049	**0.786** **±0.065**	0.750 ±0.063
SR-MMP	0.886 ±0.019	0.879 ±0.026	0.856 ±0.027	0.856 ±0.027	**0.888** **±0.018**	0.886 ±0.022	**0.895** **±0.017**	**0.909** **±0.017**	0.865 ±0.024
SR-p53	**0.849** **±0.033**	0.823 ±0.057	0.759 ±0.034	0.782 ±0.094	**0.840** **±0.053**	0.813 ±0.065	0.833 ±0.033	**0.843** **±0.054**	0.805 ±0.036
average	**0.830** **±0.046**	0.811 ±0.048	0.771 ±0.047	0.760 ±0.053	0.821 ±0.045	0.811 ±0.039	**0.822** **±0.045**	**0.831** **±0.046**	0.803 ±0.045

- Mean and standard deviation on 5-fold cross-validation results.
- Top three models on each task are **bolded**.

Figure A.1: Tukey's Test on Tox21



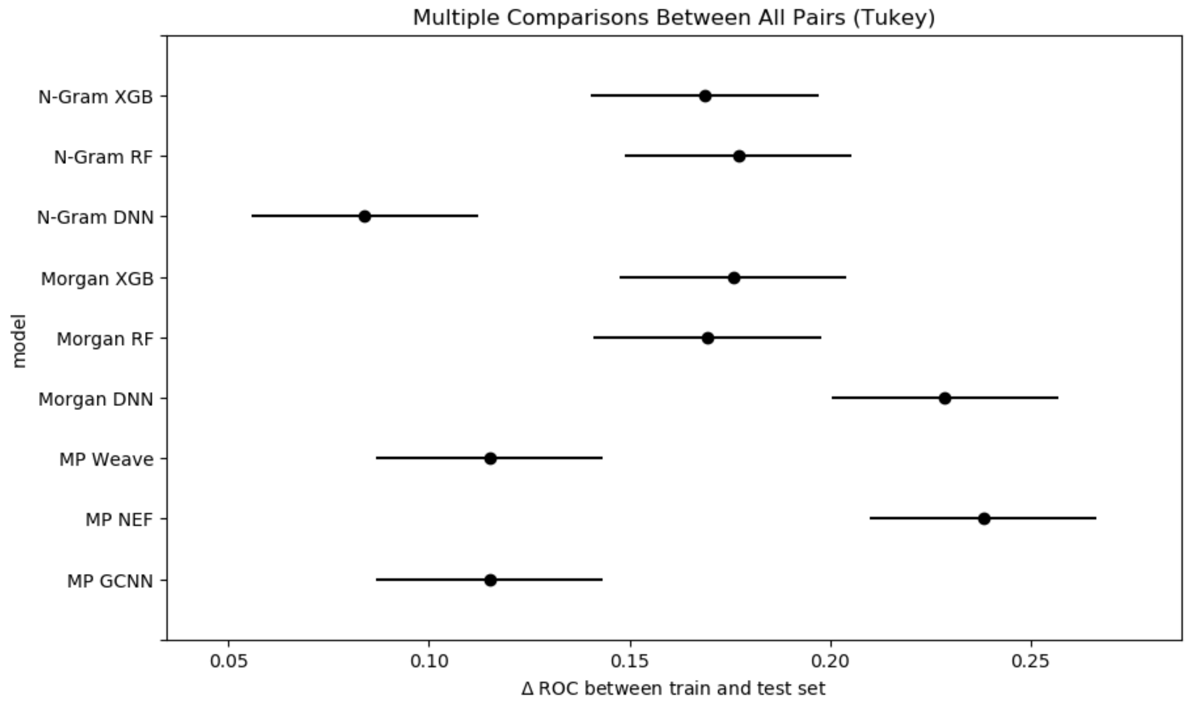
- Tukey's Test on test performance (AUC[ROC]) w.r.t. 8 models.
- XGB on N-gram graph and RF on Morgan Fingerprints are the top two models.

Table 5: Generalization performance: Train and test gap on AUC[ROC]

	Morgan RF	**Morgan XGB**	**Morgan DNN**	**MP graph NEF**	**MP graph GCNN**	**MP graph Weave**	**N-gram graph RF**	**N-gram graph XGB**	**N-gram graph DNN**
NR-AR	0.213 ±0.065	0.209 ±0.063	0.243 ±0.057	0.277 ±0.043	**0.125** **±0.085**	**0.115** **±0.082**	0.198 ±0.082	0.210 ±0.073	**0.093** **±0.072**
NR-AR-LBD	**0.136** **±0.056**	0.144 ±0.051	0.180 ±0.051	0.187 ±0.070	**0.115** **±0.040**	0.156 ±0.036	0.156 ±0.039	0.142 ±0.027	**0.112** **±0.049**
NR-AhR	0.097 ±0.028	0.091 ±0.023	0.146 ±0.036	0.154 ±0.053	**0.054** **±0.020**	**0.059** **±0.045**	0.110 ±0.020	0.102 ±0.020	**0.048** **±0.025**
NR-Aromatase	0.172 ±0.070	0.190 ±0.064	0.258 ±0.099	0.262 ±0.061	**0.112** **±0.057**	**0.099** **±0.064**	0.155 ±0.066	0.148 ±0.053	**0.066** **±0.077**
NR-ER	0.274 ±0.019	0.238 ±0.021	0.307 ±0.018	0.319 ±0.039	**0.129** **±0.033**	**0.129** **±0.036**	0.273 ±0.043	0.267 ±0.035	**0.032** **±0.026**
NR-ER-LBD	0.184 ±0.051	0.205 ±0.056	0.228 ±0.019	0.274 ±0.077	**0.134** **±0.027**	**0.119** **±0.061**	0.189 ±0.062	0.181 ±0.036	**0.105** **±0.069**
NR-PPAR-gamma	0.161 ±0.042	0.199 ±0.094	0.244 ±0.037	0.241 ±0.084	**0.142** **±0.110**	**0.147** **±0.055**	0.197 ±0.105	0.175 ±0.104	**0.147** **±0.129**
SR-ARE	0.181 ±0.039	0.166 ±0.041	0.219 ±0.046	0.255 ±0.033	**0.118** **±0.053**	**0.099** **±0.064**	0.192 ±0.028	0.174 ±0.024	**0.075** **±0.080**
SR-ATAD5	0.143 ±0.051	0.167 ±0.066	0.262 ±0.079	0.234 ±0.090	**0.125** **±0.042**	**0.129** **±0.043**	0.159 ±0.032	0.163 ±0.041	**0.123** **±0.032**
SR-HSE	0.206 ±0.028	0.222 ±0.047	0.269 ±0.034	0.296 ±0.043	**0.155** **±0.052**	**0.155** **±0.037**	0.225 ±0.048	0.214 ±0.065	**0.095** **±0.074**
SR-MMP	0.114 ±0.019	0.109 ±0.026	0.144 ±0.027	0.144 ±0.027	**0.069** **±0.029**	**0.063** **±0.024**	0.105 ±0.017	0.091 ±0.017	**0.047** **±0.037**
SR-p53	0.151 ±0.033	0.170 ±0.058	0.241 ±0.034	0.215 ±0.097	**0.107** **±0.058**	**0.112** **±0.069**	0.167 ±0.033	0.157 ±0.054	**0.064** **±0.050**
average	0.169 ±0.046	0.176 ±0.042	0.229 ±0.047	0.238 ±0.052	**0.115** **±0.027**	**0.115** **±0.030**	0.177 ±0.044	0.169 ±0.046	**0.084** **±0.033**

- Mean and standard deviation on 5-fold cross-validation generalization performance.
- Top three models on each task are **bolded**.

Figure A.2: Tukey's Test on Generalization Gap



- The generalization gap between train ROC and test ROC.
- Morgan DNN and NEF have significantly larger gap.

Table A.1: Performance of Different Vector Embeddings

Original feature presented in baseline papers, and new feature presented in N-gram graph

	NEF original feature	NEF new feature	GCNN original feature	GCNN new feature	Weave original feature	Weave new feature
NR-AR	0.723 ±0.043	0.717 ±0.058	0.793 ±0.068	0.802 ±0.068	0.796 ±0.057	0.792 ±0.076
NR-AR-LBD	0.813 ±0.070	0.817 ±0.070	0.858 ±0.037	0.852 ±0.042	0.816 ±0.047	0.830 ±0.041
NR-AhR	0.841 ±0.051	0.843 ±0.069	0.896 ±0.018	0.898 ±0.018	0.869 ±0.036	0.880 ±0.034
NR-Aromatase	0.738 ±0.061	0.730 ±0.051	0.824 ±0.052	0.819 ±0.047	0.830 ±0.050	0.834 ±0.066
NR-ER	0.673 ±0.039	0.673 ±0.052	0.734 ±0.036	0.735 ±0.023	0.729 ±0.025	0.734 ±0.020
NR-ER-LBD	0.725 ±0.078	0.722 ±0.076	0.805 ±0.024	0.803 ±0.017	0.804 ±0.030	0.809 ±0.013
NR-PPAR-gamma	0.758 ±0.084	0.762 ±0.082	0.821 ±0.105	0.799 ±0.093	0.803 ±0.064	0.801 ±0.083
SR-ARE	0.740 ±0.031	0.747 ±0.032	0.782 ±0.040	0.793 ±0.046	0.790 ±0.049	0.779 ±0.022
SR-ATAD5	0.763 ±0.092	0.764 ±0.088	0.839 ±0.037	0.838 ±0.029	0.823 ±0.041	0.800 ±0.038
SR-HSE	0.702 ±0.041	0.699 ±0.032	0.774 ±0.036	0.786 ±0.030	0.771 ±0.036	0.772 ±0.038
SR-MMP	0.856 ±0.027	0.860 ±0.028	0.888 ±0.018	0.887 ±0.027	0.886 ±0.022	0.885 ±0.015
SR-p53	0.782 ±0.094	0.765 ±0.085	0.840 ±0.053	0.836 ±0.051	0.813 ±0.065	0.813 ±0.052
average	0.760 ±0.053	0.758 ±0.055	0.821 ±0.045	0.821 ±0.043	0.811 ±0.039	0.811 ±0.041

- We compare original NEF, GCNN and Weave features and ones with new feature vector in Eq (1) in the paper.

Table A.2: Tukey's Test on Models with Different Vector Embeddings

Group 1	Group 2	mean diff	reject
NEF new feature	NEF original feature	0.0004	False
GCNN new feature	GCNN original feature	-0.0012	False
Weave new feature	Weave original feature	0.0008	False

- For each model, compare the old and new feature pair.
- Null hypothesis is that both means are same. If `reject=False`, then we accept the null hypothesis: two means are same.
- This result shows that two vector embeddings contain similar information.