Molecule2Vec: Vector Space Representation of Organic Molecules for prediction of properties using Deep Neural networks

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Introduction

- Solubility is impacted by various factors
- Dipole - induced dipole interactions, Dipole-dipole attractions, Hydrogen bonding
- Solubility of Hydrocarbons are of special interest in the fields of drug delivery, dyeing, paints, and anywhere that an aqueous solution is desired.

Research Problems

- Aqueous solubility of organic molecules is a problem in research applications where new compounds need to by synthesized and the solubility is paramount.
- It is, therefore, of special research interest to come up with a robust method to be able to predict the solubility of hydrocarbons.
- Generalize this method to be able to predict the physical properties of unsynthesized compounds using Machine learning techniques.

Motivation

- What if there was a way to get the solubility of a compound without even synthesizing them?
- Can we automate the process of discovering features from synthetically designed molecules?

Idea

Structure of Synthetic Molecules

Each molecule's 3D structure can be represented, in a standardized manner, as a text document called the **Structure Data File(SDF).**

Vector Space Models

A **Vector Space Model** is an algebraic model used to represent text documents, and finds wide applications in the field of Natural Language Processing and Information Retrieval, where entire text documents are processed, and represented as a vector.

Automatic feature discovery

Combining these two pieces of information we can **automatically discover features** from SDF files and use them to design a model to predict solubility.

Structure Data Files - SDF

```
12 12  0  0  0  0  0  0  0  0999 V2000
    3.2917    3.3940    0.2349 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.9023    3.5389    0.2241 C   0  0  0  0  0  0  0  0  0  0  0  0
    3.8618    2.1207    0.1613 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.0830    2.4105    0.1396 C   0  0  0  0  0  0  0  0  0  0  0  0
    3.0425    0.9922    0.0768 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.6531    1.1372    0.0660 C   0  0  0  0  0  0  0  0  0  0  0  0
    3.9292    4.2719    0.3006 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.4588    4.5296    0.2813 H   0  0  0  0  0  0  0  0  0  0  0  0
    4.9429    2.0079    0.1699 H   0  0  0  0  0  0  0  0  0  0  0  0
    0.0019    2.5232    0.1310 H   0  0  0  0  0  0  0  0  0  0  0  0
    3.4861    0.0016    0.0196 H   0  0  0  0  0  0  0  0  0  0  0  0
    1.0156    0.2592    0.0002 H   0  0  0  0  0  0  0  0  0  0  0  0
  1  3  1  0  0  0  0
  1  7  1  0  0  0  0
  2  1  2  0  0  0  0
  2  8  1  0  0  0  0
  3  5  2  0  0  0  0
  3  9  1  0  0  0  0
  4  2  1  0  0  0  0
  4 10  1  0  0  0  0
```

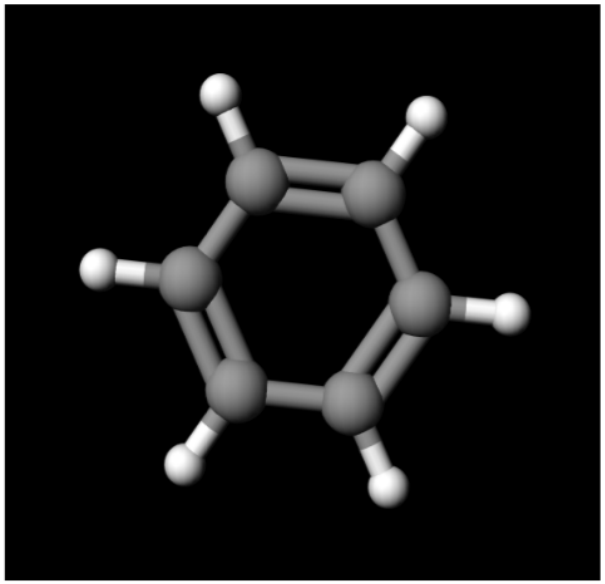


Figure 1: Source: NIST.gov

Word2Vec

- Word2vec is a method of computing vector representations of words introduced by a team of researchers at Google by Mikolov et al. (2013).
- It is a two-layer neural net that processes text. Its input is a text corpus and its output is a set of vectors: feature vectors for words in that corpus.
- While Word2vec is not a deep neural network, it turns text into a numerical form that deep nets can understand.

Word2Vec

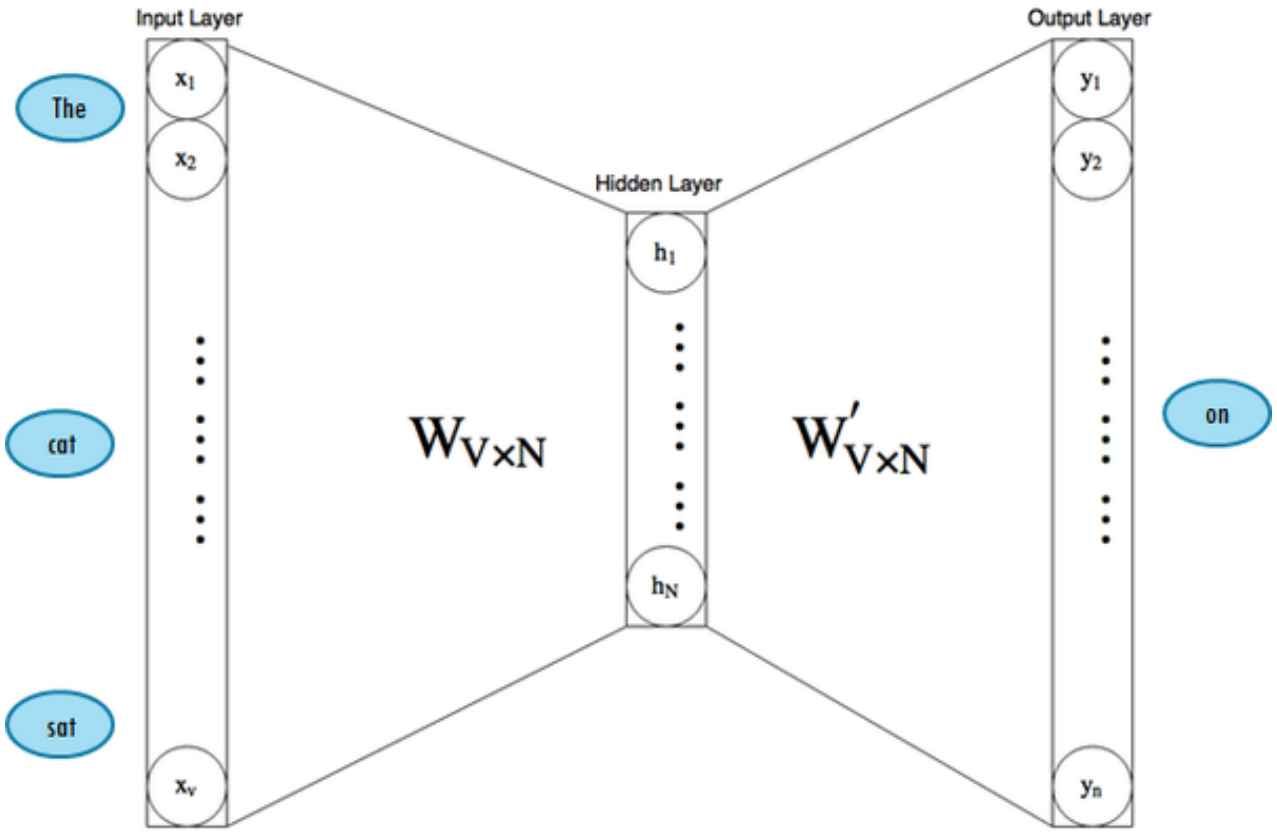


Figure 2: Source: Quora

Doc2Vec

- Doc2Vec, derived from Wor2Vec, was first discussed by Le and Mikolov (2014). It is a method to represent entire complex documents as uniformly sized vectors, regardless of their length.
- To achieve this, the base model of Word2Vec was enhanced by adding a paragraph ID vector for additional context.
- The resulting final vector representation can represent entire documents.

Doc2Vec

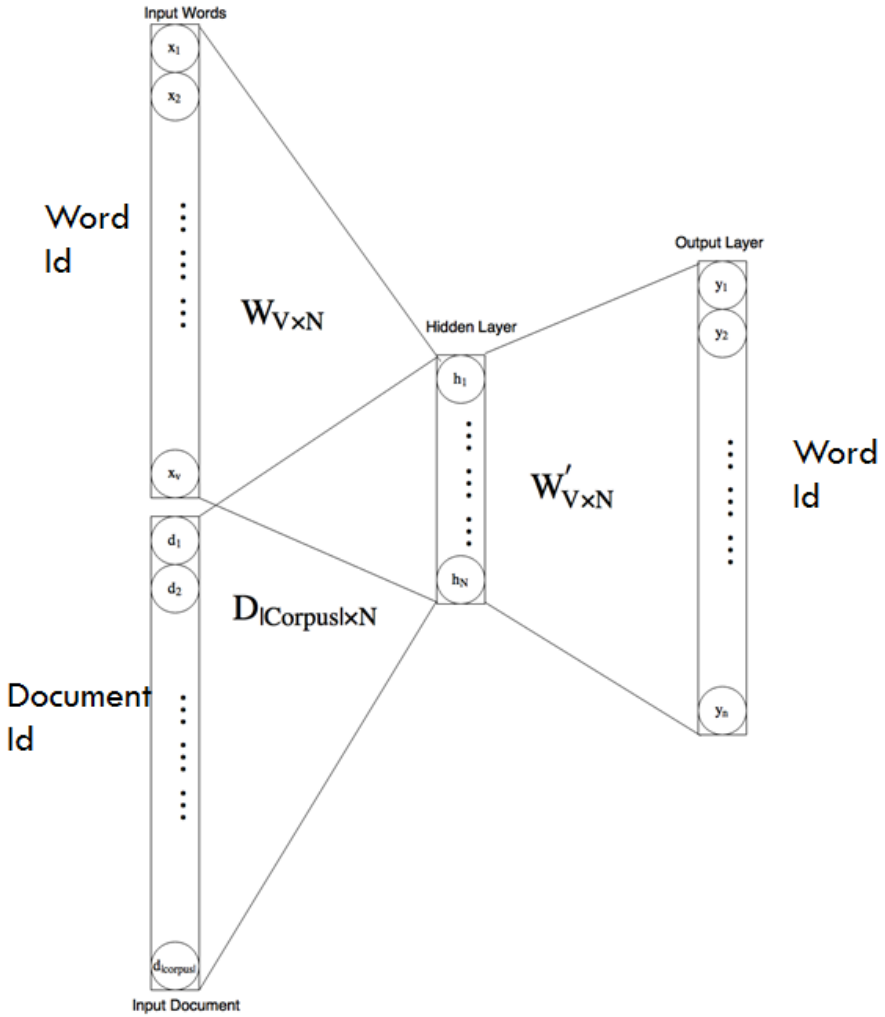


Figure 3: Source: Quora

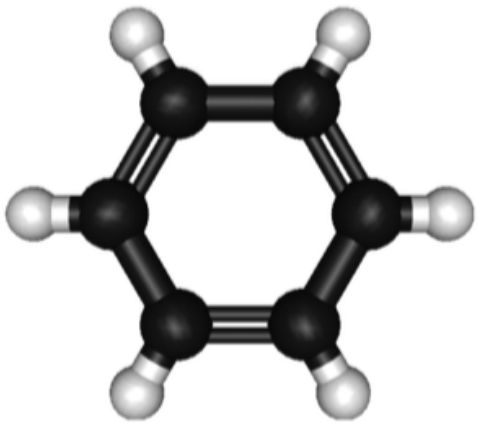
Methodology

I. Data Collection

- Handbook of Aqueous Solubility Data by Yalkowsky et al. (2016).
- The handbook contains the aqueous solubility details of 4661 compounds, which were manually collected and collated in a single database.
- Chemical Structure Data Files (SDF) were collected for each compound from the NIST Chemistry Webbook. Some structures were missing and those compounds were ignored.
- After the complete scraping operation, we had a database consisting of 3263 compounds, with their structures, molecular weight and solubility.

Methodology

II. Converting Structures to Vectors



3D SDF of Molecule

Doc2Vec Training

$$\begin{bmatrix} X_1 \\ X_2 \\ X_3 \\ X_4 \\ \vdots \\ X_{97} \\ X_{98} \\ X_{99} \\ X_{100} \end{bmatrix}$$

Feature Vector

Methodology

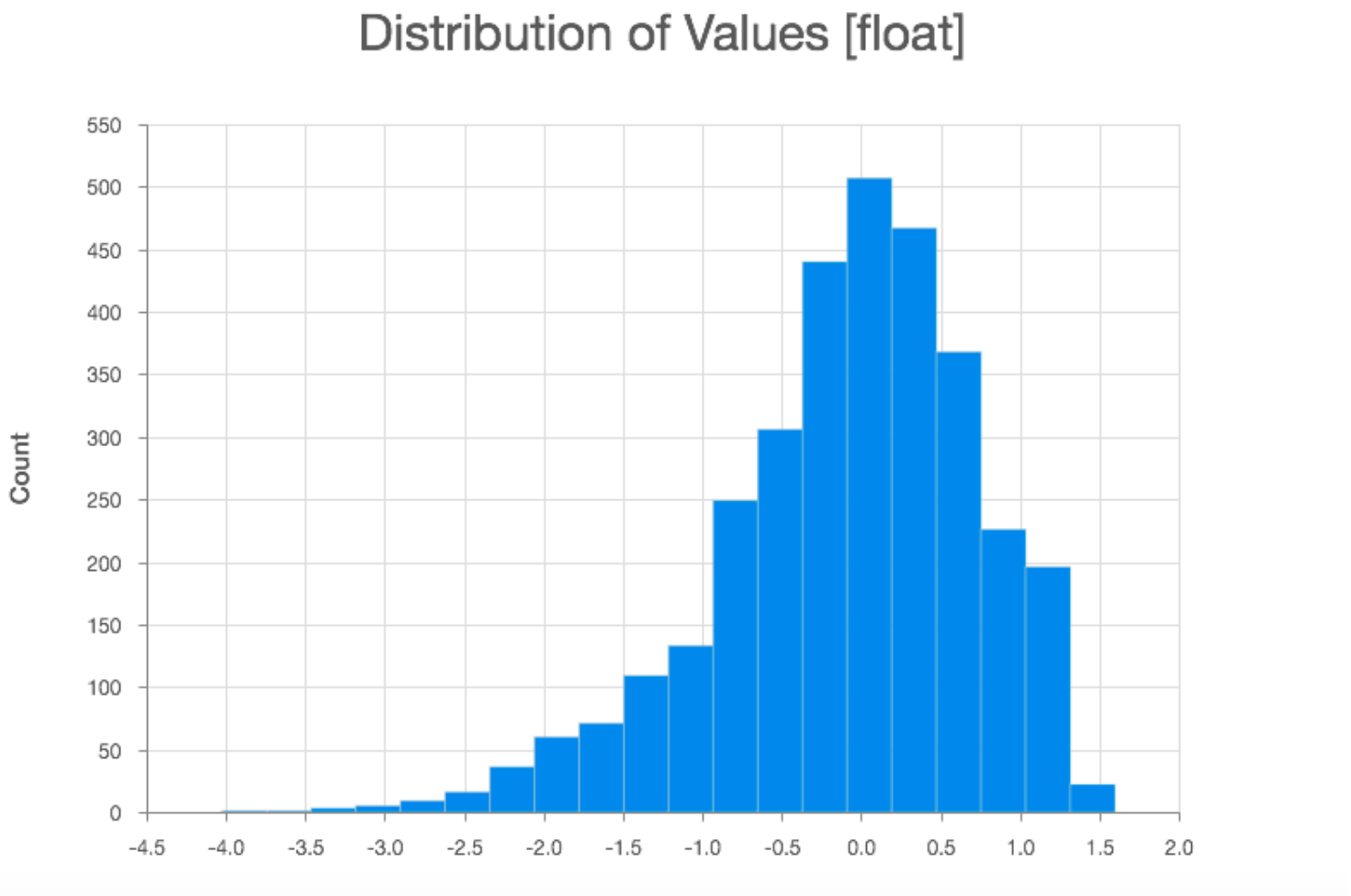
Trained Unsupervised Model

The top five 'similar' compounds to Benzene:

Compound	**Cosine Similarity**
Cyclohexene	0.8457
Tetracene	0.8299
Cumene	0.8229
Chlorobenzene	0.8092
1-Methylphenanthrene	0.8067

Table 1: Benzene Similarity

III. Data Scaling and Normalization



Prediction Algorithms

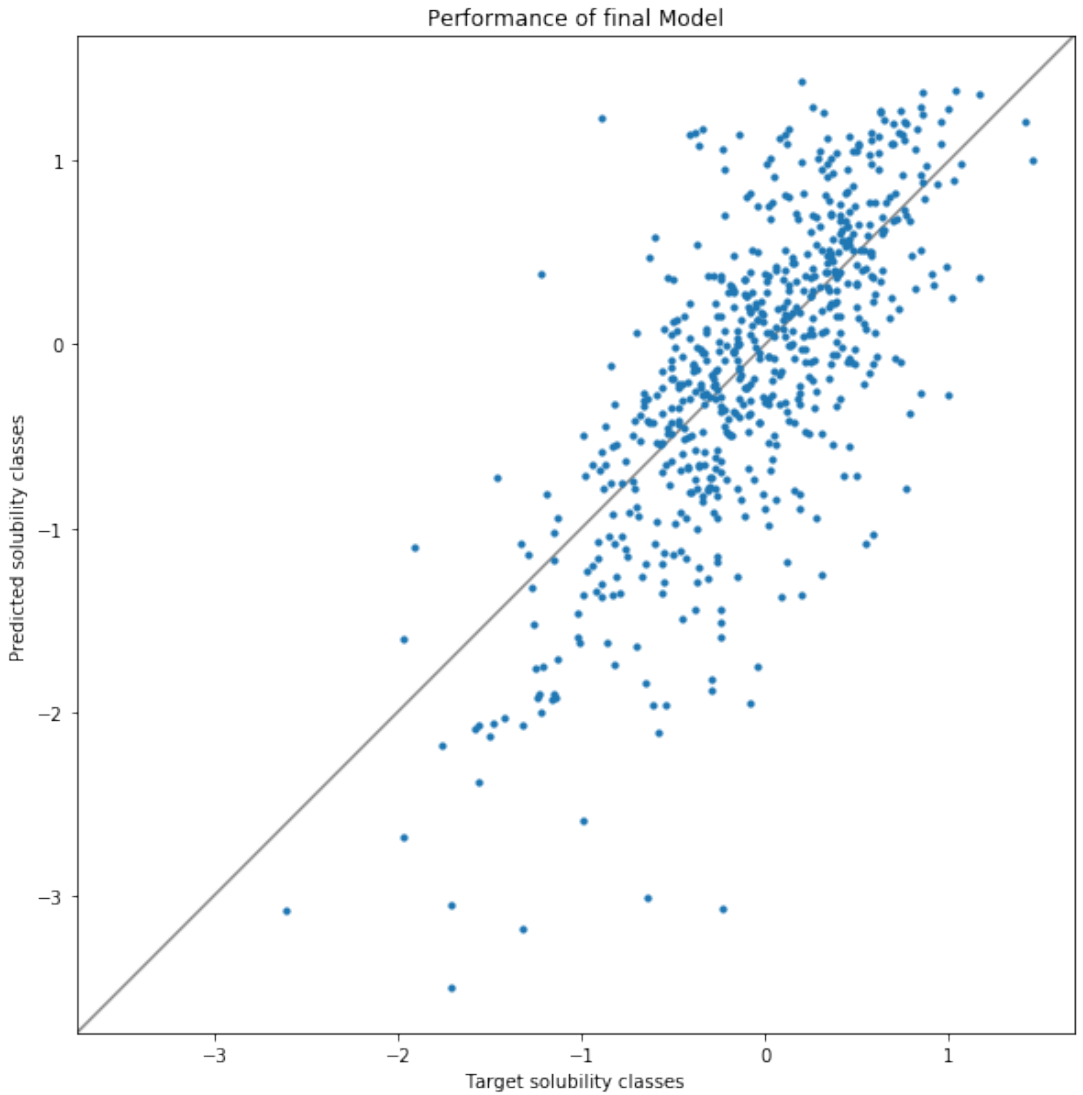
Machine Learning - Simple Regression

- Multiple Linear Regression
- Boosted Trees Regression
- Autosklearn Regression - using combination of various regressors like OLS, XGboost, Random Forest, etc.

Deep Learning - Neural Nets

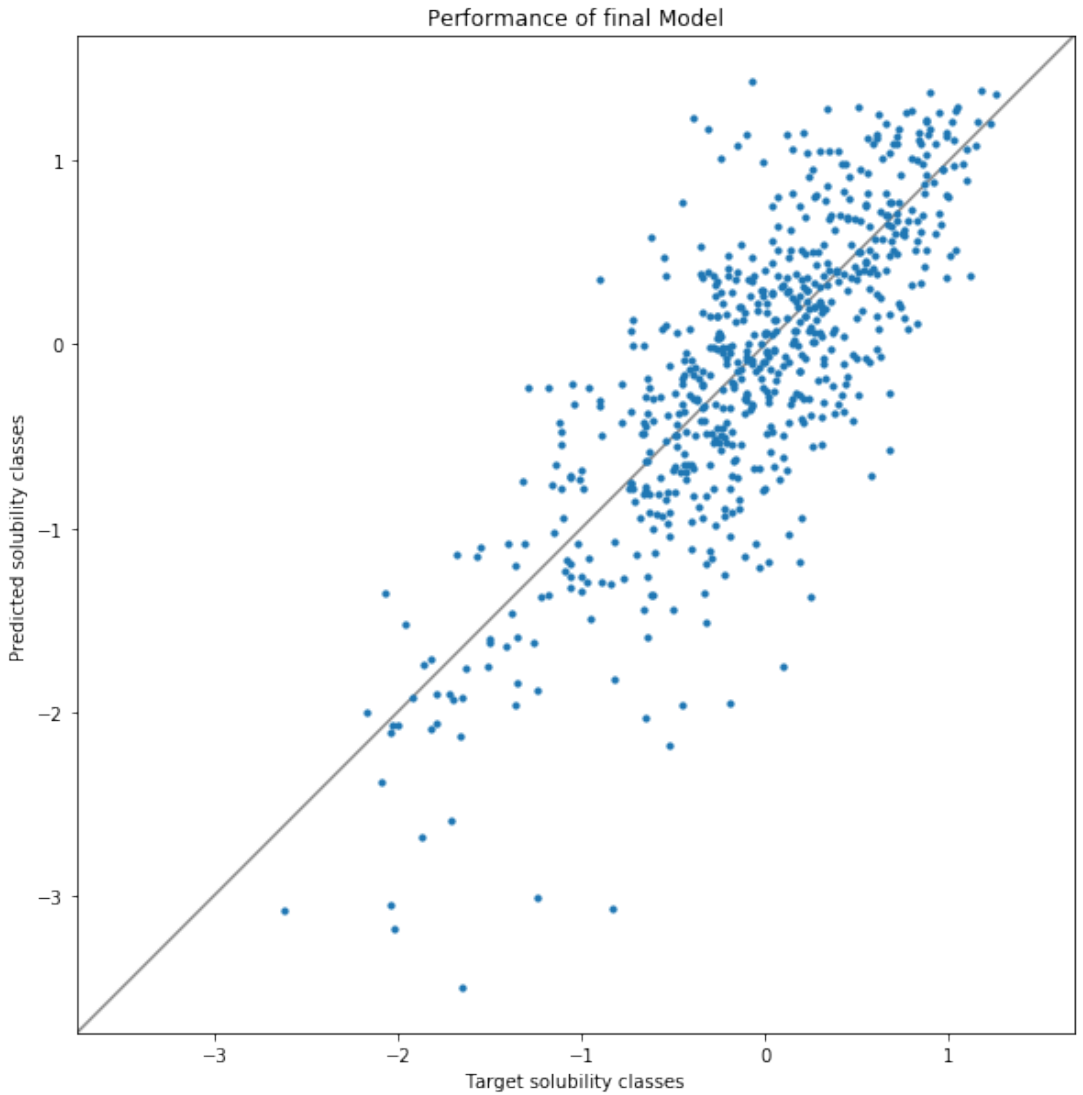
- Dense Neural Network
- Convolutional Neural Network
- SKNN - Automatic Hyperparameter Adjustment

Regression: Linear Regression



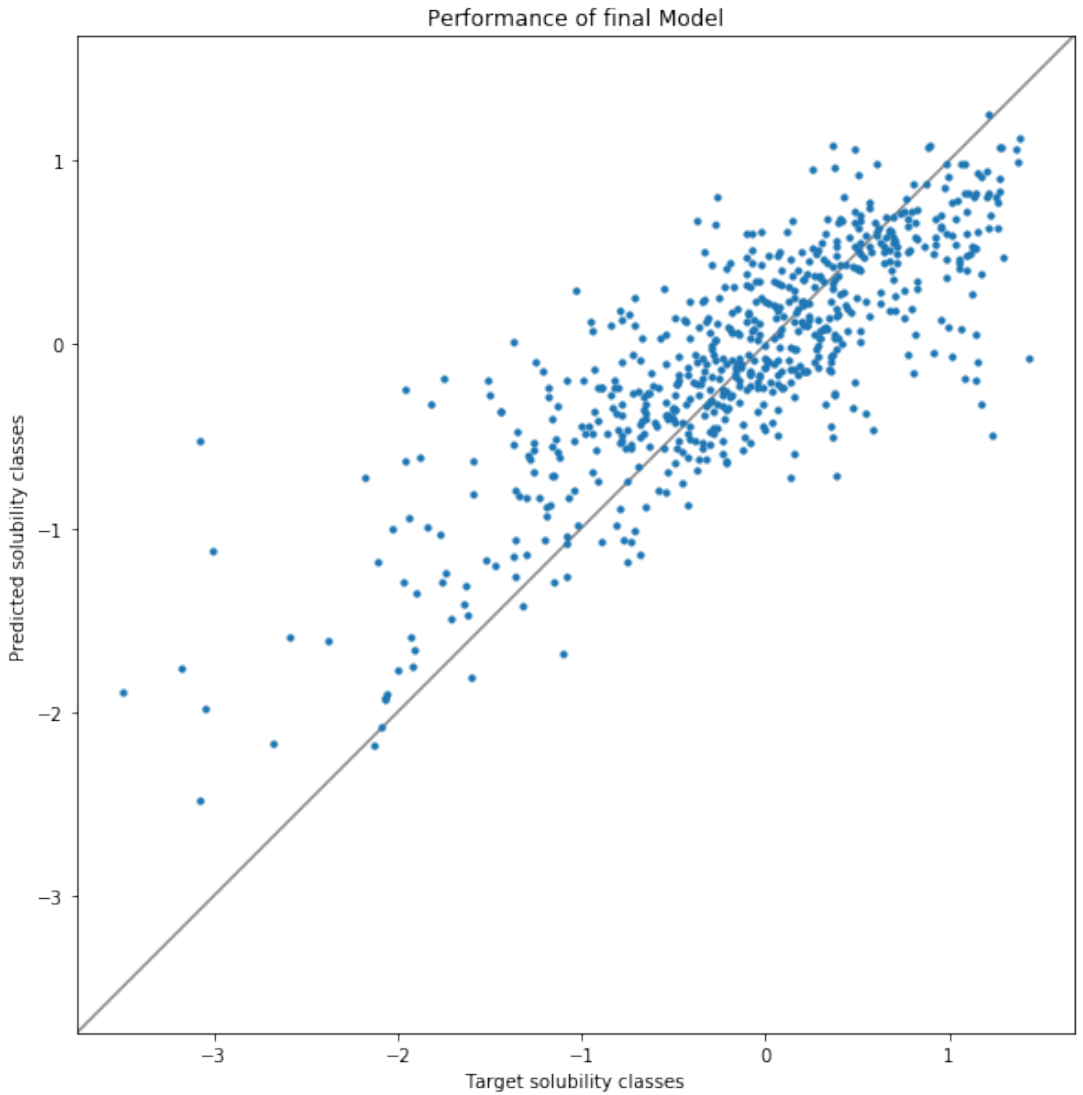
R^2 : 0.5252
MAE: 0.3545 g/litre
RMSE: 1.3486 g/litre

Regression: Boosted Trees Regression



R^2 : 0.6381
MAE: 0.2955 g/litre
RMSE: 1.0847 g/litre

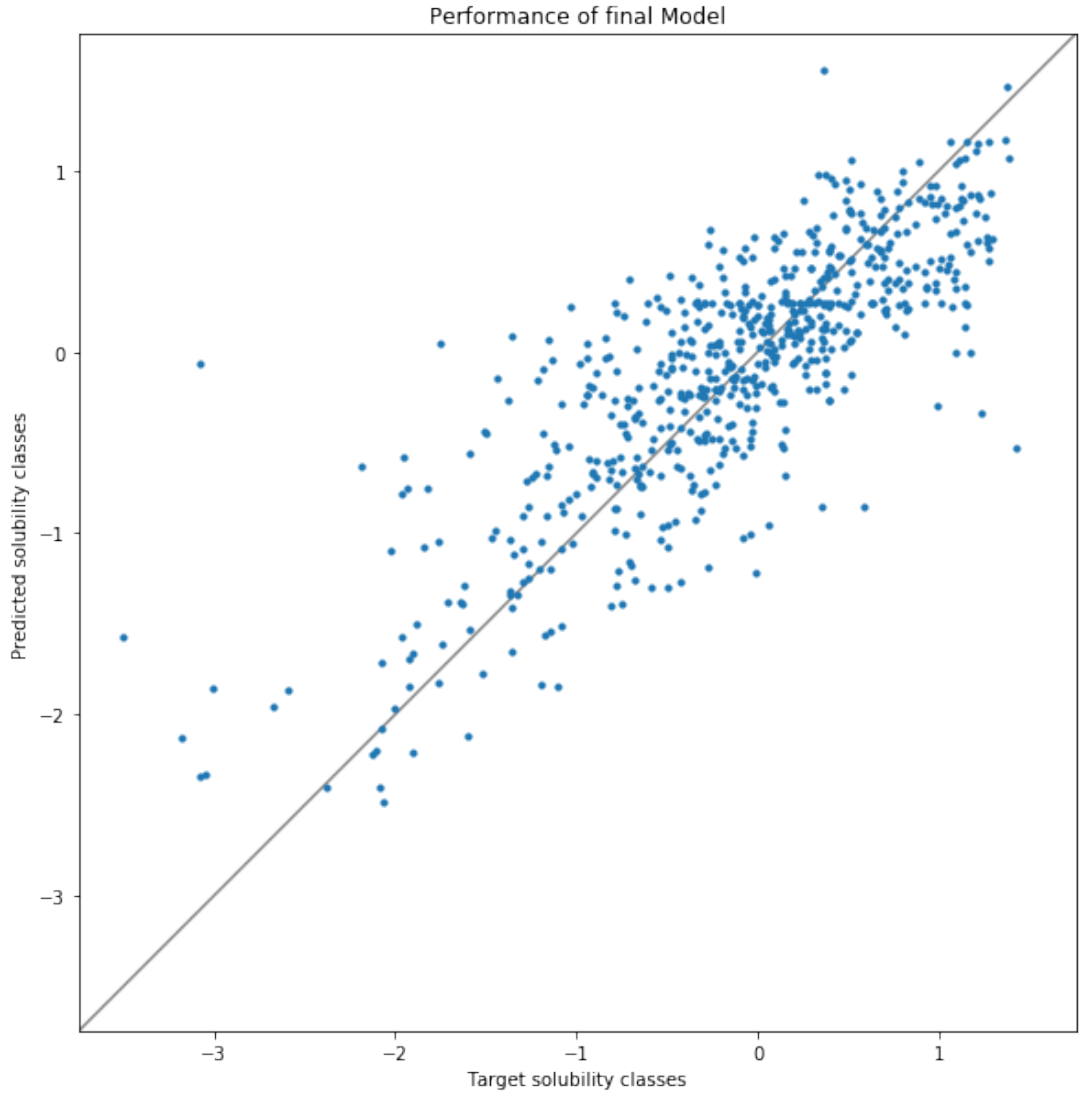
Regression: AutoSklearn Ensemble Regression



R^2 : 0.6540
MAE: 0.3061 g/litre
RMSE: 1.1131 g/litre

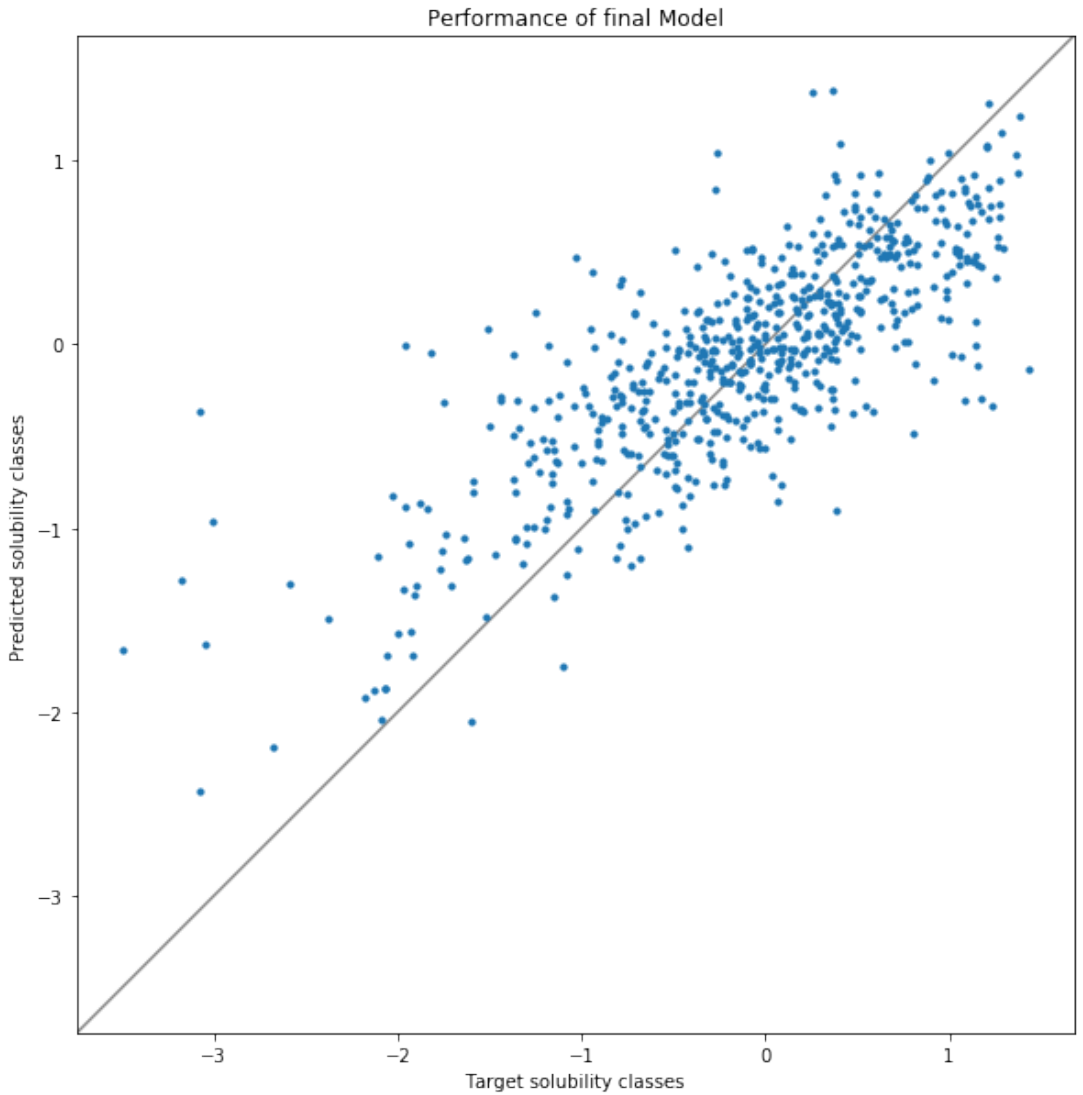
Deep Learning: Dense Neural Network

Layers: $101 \rightarrow 200 \rightarrow 50 \rightarrow 10 \rightarrow 5 \rightarrow 1$



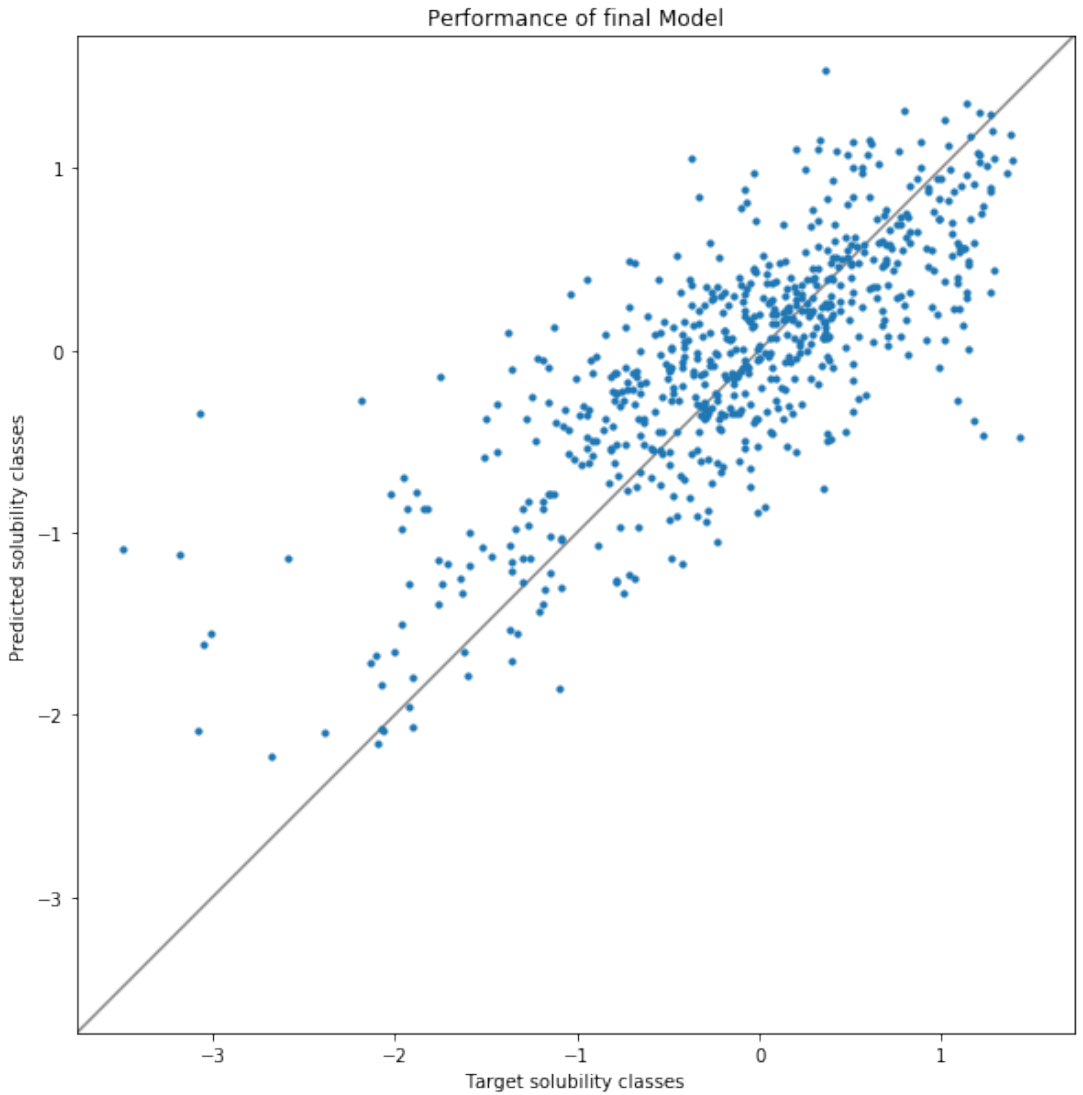
R^2 : 0.6453
MAE: 0.3783 g/litre
RMSE: 1.3804 g/litre

Deep Learning: Convolutional Neural Network



R^2 : 0.6282
MAE: 0.3070 g/litre
RMSE: 1.1441 g/litre

Deep Learning: SkNN - Auto Neural Network



R^2 : 0.5980
MAE: 0.3874 g/litre
RMSE: 1.5594 g/litre

Evaluation results

Method	R^2	MAE	RMSE
Linear Regression	0.525	0.354	1.348
Boosted Trees Regression	0.638	**0.295**	**1.084**
AutoSklearn Ensemble	**0.654**	0.306	1.131
Dense Network	**0.645**	0.378	1.380
Convolutional Network	0.628	**0.307**	**1.144**
SkNN Auto Network	0.598	0.387	1.559

Table 2: Comparison of the Evaluation Performance of the various methods.

Conclusion

- Upto 65% of the solubility patterns can be understood from the structure itself.
- The best model among the regressors is Boosted Trees Regression, which performs slightly better than the deep learning models.
- Probably because different compounds in different solubility zones benefit from the branching of the small zones of binary classifications.
- Deep Learning techniques have room for improvement.

Thanks

Dr. Debasis Sarkar

Volunteering students at the KOSS Winter of Code in the DeepChem project

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