Atomic partial charge prediction

with graph neural networks

David Parker
Dr. Cassiano Langini

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Outline

Introduction

Atomic partial charge

Coulomb's law:

$$|F| = k_e \frac{|q_1||q_2|}{r^2} \tag{1}$$

Where

- Coulomb constant: $k_e = 9 \cdot 10^9 \ \frac{\mathrm{N \cdot m^2}}{\mathrm{C^2}}$
- q_1 and q_2 are the charges in Coulombs (C)
- r is the distance between the charges in meters (m)

Atomic partial charge

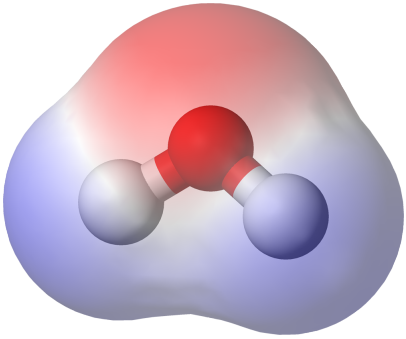

Figure: Representation of the electronic charge distribution of a water molecule. The oxygen atom has a partial negative charge, while the hydrogen atoms have partial positive charges[2].

Partial charge calculation

Experimentally (Spectroscopy):

- X-ray diffraction, Nuclear magnetic resonance, UV-Vis, etc

Computationally: Tradeoffs speed VS accuracy

- Quantum mechanics calculations: Evolution of a system through time

$$i\hbar\frac{\partial}{\partial t}|\psi(t)\rangle = \hat{H}|\psi(t)\rangle \qquad F = \frac{\partial}{\partial t}p$$

Quantum counterpart of Newton's second law of motion

- Force fields: Calculations based on a set of parameters

Goal

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Create a dataset of molecules and use the Charm General Force Field (CGenFF) to calculate partial charges for each atom

Train a graph neural network to predict atomic partial charges

Methods

Graphs

Can also be represented as a graph:

- Nodes with attributes
- Edges with attributes
- Global attributes

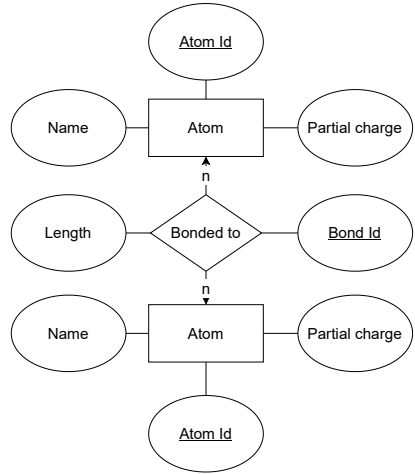


Figure: Data model for the mini-world

Molecular Dataset: mol2 file

```
@<TRIPOS>MOLECULE
0002bf2c5ea40c3014dbcc0182ea4598
50 52
SMALL
USER_CHARGES
CgenFF charge penalty mean/max 2.42094 / 30.403
@<TRIPOS>ATOM
      1 N1          0.1212    0.064    -0.3102 N.pl3     0 0          -0.163
      2 N2          4.9006   -0.7556    0.5231 N.4       0 0          -0.426
      [...]
48 H48           6.451   -0.6653   -0.8628 H         0 0           0.090
     49 H49          5.9904   -2.2808   -0.3819 H         0 0           0.090
     50 H50          6.9083   -1.2723    0.7106 H         0 0           0.090
@<TRIPOS>BOND
1 1 3 1
2 1 10 1
[...]
51 21 49 1
52 21 50 1
@<TRIPOS>MOLECULE
24d10877593ae175c68f8d409e6df5ae
26 25
```

Figure: Example of a mol2 file. Each molecule begins with a $@ < TRIPOS > MOLECULE$ tag, then the different fields are sepearated by their own tags.

Molecular Dataset: Molecules

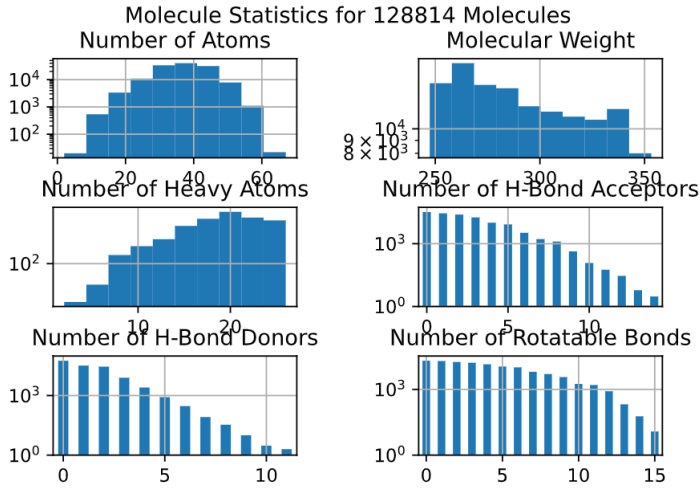


Figure: Distributions of different molecular properties in the dataset.

Molecular Dataset: Atoms

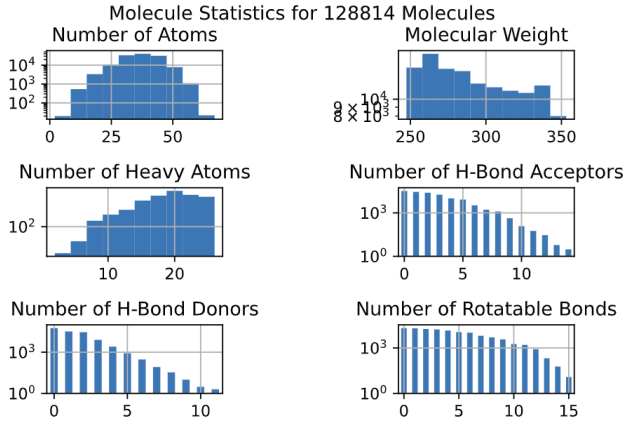


Figure: Distributions of different atomic properties in the dataset.

Message-passing neural network

$$\mathbf{e}'_k = \phi^e\left(\mathbf{e}_k, \mathbf{v}_{r_k}, \mathbf{v}_{s_k}, \mathbf{u}\right) \qquad \overline{\mathbf{e}}'_i = \rho^{e\to v}\left(E'_i\right)$$
$$\mathbf{v}'_i = \phi^v\left(\overline{\mathbf{e}}'_i, \mathbf{v}_i, \mathbf{u}\right) \qquad \overline{\mathbf{e}}' = \rho^{e\to u}\left(E'\right)$$
$$\mathbf{u}' = \phi^u\left(\overline{\mathbf{e}}', \overline{\mathbf{v}}', \mathbf{u}\right) \qquad \overline{\mathbf{v}}' = \rho^{v\to u}\left(V'\right)$$

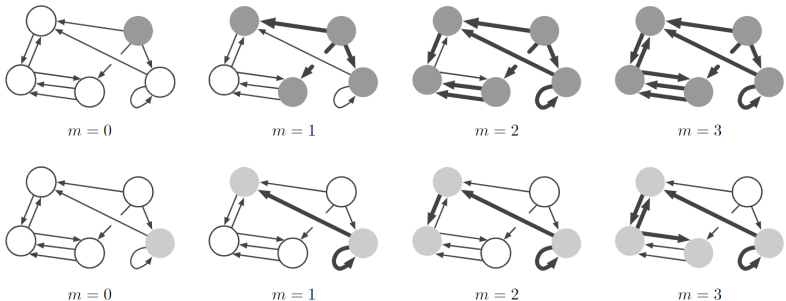


Figure: Message-passing neural network. Three update functions ϕ and three aggregation functions ρ are used to update the edge, node and global attributes[1].

Message-passing neural network

Node features: Element type

- Preprocess layer: 2 linear layers with batch normalization and ReLU activation functions to embed the element type into an internal continuous representation.
- Edge function layer: several linear layers with batch normalization and ReLU activation functions to compute edge features based on the node features of the adjacent nodes.
- GNN layer: applies a convolution operation to update the node features using the edge features as weights.
- GRU layer: applies a gated recurrent unit to update the node features.
- Predict layer: 2 linear layers with batch normalization and ReLU activation functions, followed by a linear layer with a single output.

Results

Benchmarks

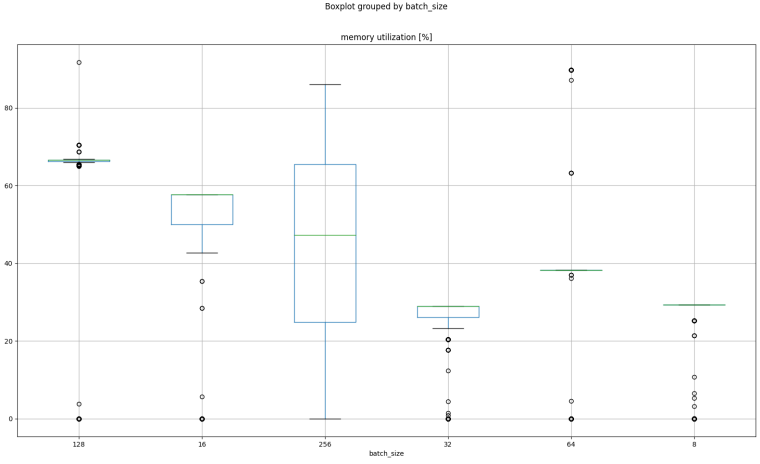


Figure: Benchmarks of GPU utilisation for different batch sizes.

Absolute errors

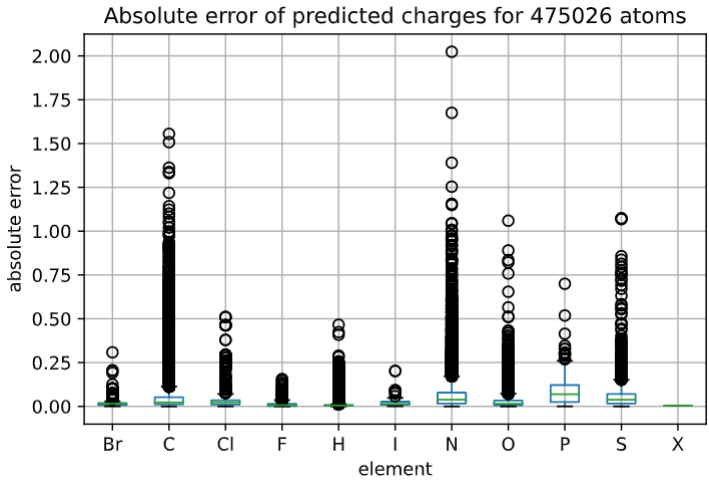


Figure: Distributions of the absolute errors of the predicted partial charges for each type of atom.

Root mean squared error

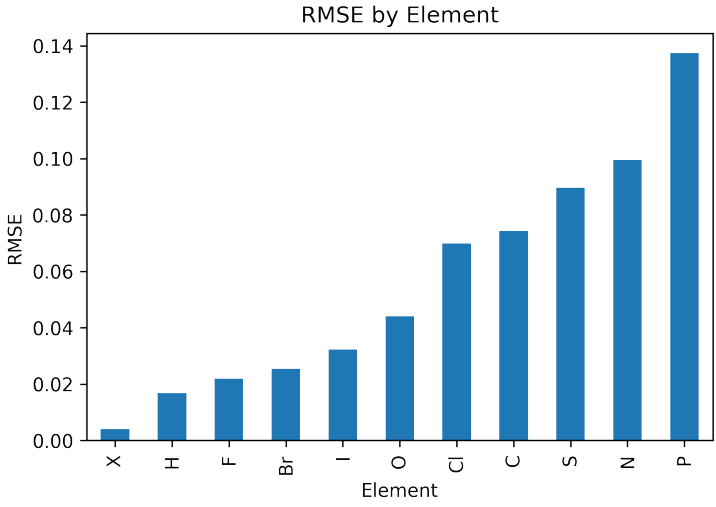


Figure: Root mean squared error for each type of atom.

Mean absolute error

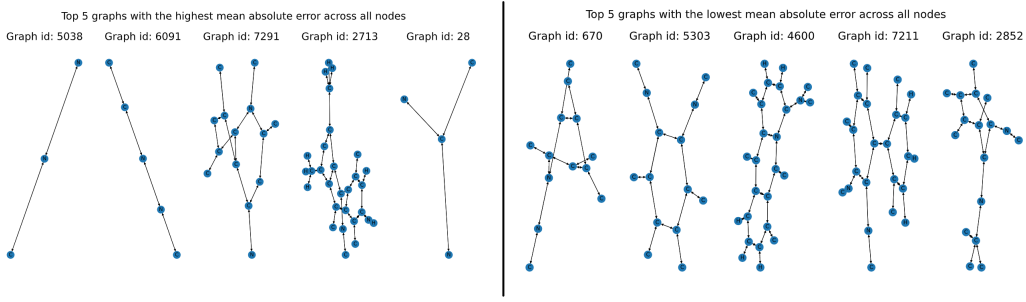
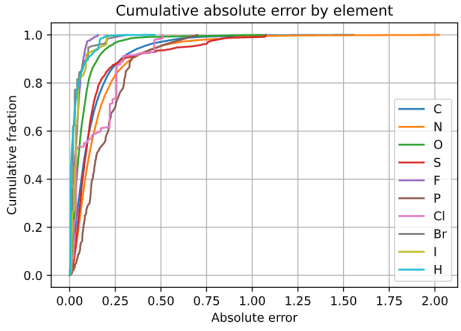


Figure: Visualizations of the graphs with the highest and lowest MAE.

Our results compared to the literature



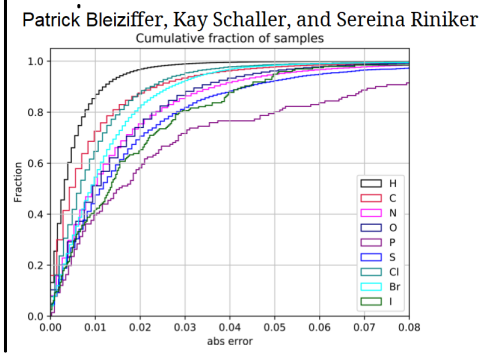


Figure: Cumulative fraction of each type of atom as a function of the absolute error. Our results on the left, the results of the literature on the right[3].

Discussion

Dataset generation

- The dataset is technically easy to generate:
  - SQL queries to extract the data from the database
  - Use a force field to compute the partial charges
- The hard part is to choose relevant molecules:
  - We chose drug-like molecules. Molecular weight around 300 g/mol, specific number of rotatable bonds, etc. (see Figure 4)

Model

- Choice of the model:
  - We went with a MPNN as introduced by Gilmer et al.[4]
- Achitechture of the model:
  - We would like to add physical constraints to the model, so that the predicted partial charges make more sense

Conclusion

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- We used a dataset of 130 000 molecules with partial charges
- We have trained a MPNN to predict the partial charges
- The model has a RMSE of 0.054
  - Elementary charge of a proton: 1.6×10^{-19} C

Acknowledgements

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A big thank you to Kurt and all of you for an exciting lecture!

References

[1] Peter W. Battaglia et al. *Relational inductive biases, deep learning, and graph networks*. 2018. arXiv: 1806.01261 [cs.LG].

[2] Benjah-bmm27. *Water*. URL: https://commons.wikimedia.org/w/index.php?curid=1498405. (accessed: 2023-05-29).

[3] Patrick Bleiziffer, Kay Schaller, and Sereina Riniker. "Machine Learning of Partial Charges Derived from High-Quality Quantum-Mechanical Calculations". In: *Journal of Chemical Information and Modeling* 58.3 (2018). PMID: 29461814, pp. 579–590. DOI: 10.1021/acs.jcim.7b00663. eprint: https://doi.org/10.1021/acs.jcim.7b00663. URL: https://doi.org/10.1021/acs.jcim.7b00663.

[4] Justin Gilmer et al. "Neural Message Passing for Quantum Chemistry". In: *CoRR* abs/1704.01212 (2017). arXiv: 1704.01212. URL: http://arxiv.org/abs/1704.01212.