

Hands-On Tutorial: Data-Mining the QM9 Dataset

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This tutorial introduces the application of the QM9 dataset using Python. We explore basic aspects of data retrieval, statistics, and analysis using the `qm9pack` Python module.

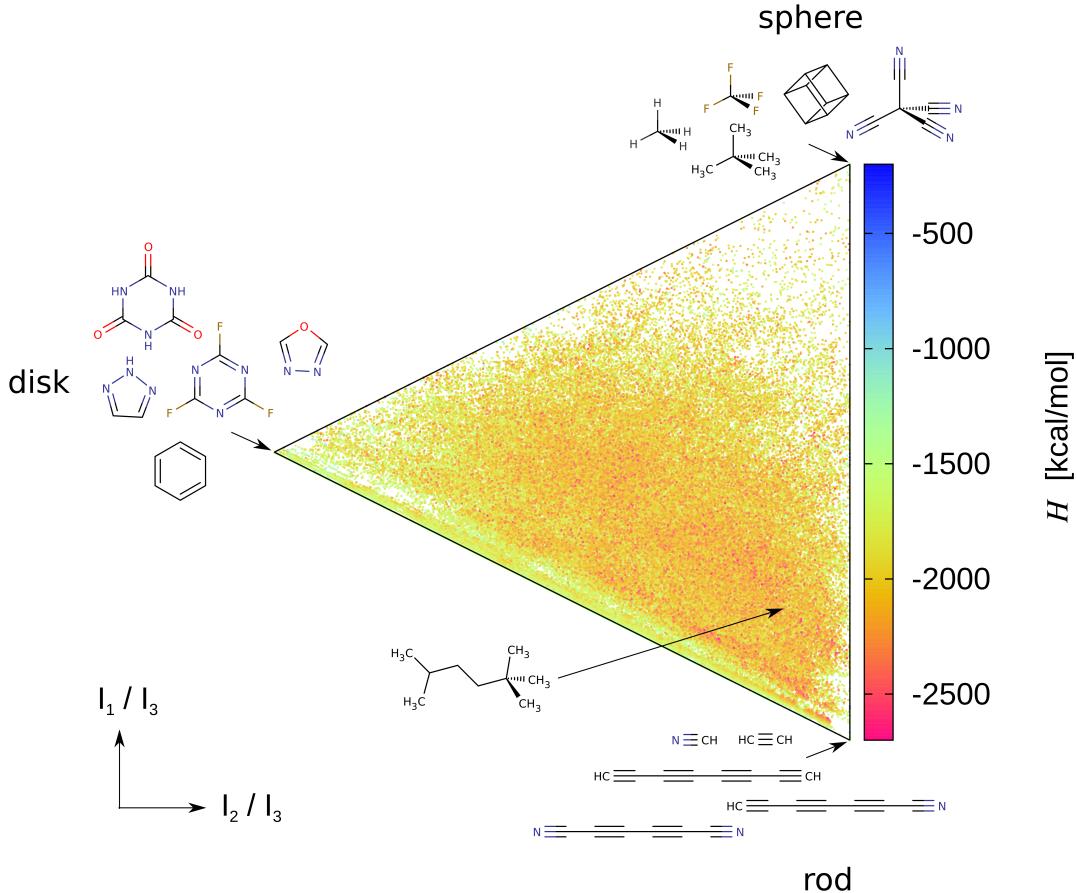


FIG. 1. Distribution of QM9 molecules as a function of their shape and stability. The x and y axes are normalized moments of inertia (I_1/I_3 and I_2/I_3), and the atomization enthalpy (H in kcal/mol) from density functional theory calculations is color-coded. Also shown are the representative 1D (rod-shaped), 2D (disc-shaped), and 3D (near-spherical) molecules at the corners. Each single dot corresponds to one or many QM9 molecules.

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CONTENTS

I. Introduction	3
1. Energies in the QM9 dataset	3
II. Basic Exercises	4
A. Loading the QM9 Dataset	4
Exercise A.1: Load the dataset	4
B. Exploring the Content of QM9 Dataset	4
Exercise B.1: Overview of <code>columns</code>	4
Exercise B.2: <code>helper</code>	5
Exercise B.3: <code>helper</code> for all <code>columns</code>	5
Exercise B.4: <code>Cartesian coordinates</code> using <code>makexyz</code>	6
Exercise B.5: Collect <code>coordinates</code> of all molecules	7
Exercise B.6: Filter molecules using <code>Stoichiometry</code>	8
III. Advanced Exercises	8
Exercise C.1: All stoichiometries in QM9	8
Exercise C.2: Atomization energy	9
Exercise C.3: Multiproperty query	10
IV. Acknowledgments	11
V. Data Availability	11
References	11

I. INTRODUCTION

The QM9 dataset [1] contains minimum energy geometries and various properties of 133,885 molecules, calculated using the density functional theory method B3LYP and the 6-31G(2df,*p*) basis set. Among these, 3,054 molecules faced convergence issues during structure optimization and were excluded, resulting in a final dataset of 130,831 molecules. The 3,054 ‘uncharacterized’ molecules have been analyzed separately, highlighting the critical role of quantum chemistry approximations in establishing the correspondence between a molecular graph and its three-dimensional structure [2]. For each of the 130,831 molecules, the dataset contains the SMILES representation[3] collected from the GDB17 database[4] containing 166.4 billion molecular graphs. In this tutorial, we will use the Python modules Pandas[5, 6], Matplotlib[7], NumPy[8], and SciPy[9]. The QM9 dataset is shared through the module `qmlpack`, which uses Pandas and Numpy.

1. Energies in the QM9 dataset

The QM9 dataset reports four thermochemistry energies defined according to Ref. 10: internal energy at zero kelvin (0 K), denoted customarily as U_0 ; internal energy at 298.15 K (room temperature), denoted customarily as U_T ; enthalpy at 298.15 K, denoted customarily as H_T ; Gibbs free energy at 298.15 K, denoted customarily as G_T . These four energies can be queried using the keys (or column names): `InternalEnergy_0K_au`, `InternalEnergy_298K_au`, `Enthalpy_298K_au`, and `GibbsFreeEnergy_298K_au`. Here are the formal definitions of these energies:

1. U_0 is the energy of the molecule at 0 K, which is the sum of its electronic energy (including the classical electron-electron repulsion term), $E_{\text{electronic}}$, and the zero-point vibrational energy (ZPVE)

$$U_0 = E_{\text{electronic}} + \text{ZPVE}. \quad (1)$$

2. U_T is the room temperature internal energy, which is the sum of the $E_{\text{electronic}}$ and the total thermal corrections to energy along all degrees of freedom (translational, rotational, vibrational, and electronic), E_{tot}

$$U_T = E_{\text{electronic}} + E_{\text{tot}}. \quad (2)$$

Note that E_{tot} includes ZPVE.

3. H_T is the room temperature enthalpy, which is the sum of $E_{\text{electronic}}$, E_{tot} , and the energy due to the volume of the system, which under the ideal gas assumption is $k_B T$.

$$H_T = E_{\text{electronic}} + E_{\text{tot}} + k_B T. \quad (3)$$

The enthalpy correction $E_{\text{tot}} + k_B T$ is often denoted as H_{corr} .

4. G_T is the room temperature Gibbs free energy, which is the sum of $E_{\text{electronic}}$, free energy correction defined as $G_{\text{corr}} = H_{\text{corr}} - TS_{\text{tot}}$, where S_{tot} is the total entropy along all degrees of freedom (translational, rotational, vibrational, and electronic).

$$G_T = E_{\text{electronic}} + G_{\text{corr}}. \quad (4)$$

The absolute values of U_0 , U_T , H_T , and G_T of molecules can be used to calculate the change in the corresponding property during a reaction. For example, for a reaction $A \rightarrow B$, one can calculate the change in the free energy as $\Delta G = G_B - G_A$.

For most applications, one might prefer energies that quantify the stability of the molecule. Hence, one has to consider the relative values of the energies compared to a reference, such as free atoms. The molecular atomization energy is the sum of all bond energies, defined as

$$E_{\text{atomization}} = U_0^{\text{molecule}} - \sum_{A \in \text{atoms}} U_0^A \quad (5)$$

According to this definition, $E_{\text{atomization}}$ is a negative number, implying all QM9 molecules are thermodynamically more stable than the free atoms. As stated above, U_0^{molecule} includes the ZPVE. For the free atoms, there are no

vibrational degrees of freedom; hence, U_0^A is the same $E_{\text{electronic}}$. TABLE I contains the energies of the CHONF atoms calculated using the DFT method, B3LYP, using the basis set, 6-31G(2df, p), as reported in [1] and can be accessed from the original data repository[11].

TABLE I. Reference thermochemical energies of H, C, N, O, F atoms in hartree, collected from Ref. 11.

Element	U_0	U_T	H_T	G_T
H	-0.500273	-0.498857	-0.497912	-0.510927
C	-37.846772	-37.845355	-37.844411	-37.861317
N	-54.583861	-54.582445	-54.581501	-54.598897
O	-75.064579	-75.063163	-75.062219	-75.079532
F	-99.718730	-99.717314	-99.716370	-99.733544

II. BASIC EXERCISES

A. Loading the QM9 Dataset

Exercise A.1: Load the dataset

In the first exercise, we will load the `qm9pack` module, fetch the QM9 dataset (`qm9`), and perform initial exploratory analysis.

```
import qm9pack # Import the qm9pack module

# Fetch the QM9 dataset and store it in a DataFrame
df = qm9pack.get_data('qm9')

# Print the summary statistics of the dataset
print(df.describe())

# Print the first 5 rows of the dataset
print(df.head())

# Print the last 5 rows of the dataset
print(df.tail())
```

<OUTPUT>
Long output, not shown.

B. Exploring the Content of QM9 Dataset

Exercise B.1: Overview of columns

Let us find the names of all columns (properties) in `qm9`.

```
import qm9pack # Import the qm9pack module

# Fetch the QM9 dataset and store it in a DataFrame
df = qm9pack.get_data('qm9')

# Iterate over each column in the DataFrame and print the column name
for key in df.columns:
    print(key)
```

```
<OUTPUT>
XYZ_file
Index
SMILES
InChi
N_atoms
Stoichiometry
Elements
XYZ_Ang
Mulliken_pop
Harmonic_Freq_cmi
RotA_GHz
RotB_GHz
RotC_GHz
Dipole_debye
Polarizability_bohr3
HOMO_au
LUMO_au
HOMO_LUMO_gap_au
R2_bohr2
ZPVE_au
InternalEnergy_0K_au
InternalEnergy_298K_au
Enthalphy_298K_au
GibbsFreeEnergy_298K_au
Heatcapacity_Cv_cal_mol_K
```

Exercise B.2: helper

Get more details about one of the columns in `qm9`.

```
import qm9pack # Import the qm9pack module

# Fetch the QM9 dataset and store it in a DataFrame
df = qm9pack.get_data('qm9')

# Define a specific column name for which to print more details
key = 'RotC_GHz'

# Use the helper function from qm9pack to print more details for the
# specified column
qm9pack.helper(key)
```

```
<OUTPUT>
'RotC_GHz': Rotational constant C in GHz.
```

Exercise B.3: helper for all columns

Get more details about all the columns in `qm9`.

```

import qm9pack # Import the qm9pack module

# Fetch the QM9 dataset and store it in a DataFrame
df = qm9pack.get_data('qm9')

# Iterate over each column in the DataFrame and print more details for
# each column
for key in df.columns:
    qm9pack.helper(key)

```

<OUTPUT>

'XYZ_file': The file containing the XYZ coordinates of the molecule as submitted in the original QM9 article (<https://doi.org/10.1038/sdata.2014.22>). The name 'dsgdb9nsd_000001.xyz' contain data for molecule-1 and so on. Overall, qm9 contains 130831 molecules

'Index': A unique identifier for each molecule in the dataset which ranges from 1 to 133885 of which 3054 will be missing as the corresponding molecular structures failed to converge with the DFT method, B3LYP, and the basis set, 6-31G(2df,p)

'SMILES': Simplified Molecular Input Line Entry System representation of the molecule.

'InChi': IUPAC International Chemical Identifier for the molecule.

'N_atoms': The number of atoms in the molecule.

'Stoichiometry': The stoichiometric formula of the molecule encoded as the array containing numbers of H, C, N, O, and F atoms. For CH4, the list corresponds to [4,1,0,0,0]

'Elements': List of elements present in the molecule. For CH4, the list is ['C','H','H','H','H']

'XYZ_Ang': The XYZ coordinates of the molecule in Angstroms calculated using the DFT method, B3LYP, and the basis set, 6-31G(2df,p).

'Mulliken_pop': Mulliken population analysis data for the molecule in units of charge of an electron, e.

'Harmonic_Freq_cmi': Harmonic vibrational frequencies of the molecule in cm⁻¹.

'RotA_GHz': Rotational constant A in GHz.

'RotB_GHz': Rotational constant B in GHz.

'RotC_GHz': Rotational constant C in GHz.

'Dipole_debye': Dipole moment of the molecule in debye.

'Polarizability_bohr3': Polarizability of the molecule in bohr³.

'HOMO_au': Highest Occupied Molecular Orbital energy in atomic units, hartree.

'LUMO_au': Lowest Unoccupied Molecular Orbital energy in atomic units, hartree.

'HOMO_LUMO_gap_au': Energy gap between HOMO and LUMO in atomic units, hartree.

'R2_bohr2': Spread of the electron density calculated as the expectation value of the operator, R², in bohr²

'ZPVE_au': No help content available for this key.

'InternalEnergy_0K_au': Internal energy of the molecule at 0 kelvin.

'InternalEnergy_298K_au': Internal energy of the molecule at 298.15 kelvin.

'Enthalphy_298K_au': Enthalpy of the molecule at 298.15 kelvin.

'GibbsFreeEnergy_298K_au': Gibbs free energy of the molecule at 298.15 kelvin.

'Heatcapacity_Cv_cal_mol_K': Heat capacity at constant volume in cal/(mol K).

Exercise B.4: Cartesian coordinates using makexyz

Store the Cartesian coordinates of a molecule in qm9 corresponding to an index.

```

import qm9pack # Import the qm9pack module

# Fetch the QM9 dataset and store it in a DataFrame
df = qm9pack.get_data('qm9')

# Save XYZ for a molecule using its index
index = 0
filename = 'Mol_0.xyz'
qm9pack.makexyz(index, df, filename)

index = 1
filename = 'Mol_1.xyz'
qm9pack.makexyz(index, df, filename)

```

```

<OUTPUT>
5
Mol_0.xyz
C   -0.01269814    1.08580416    0.00800100
H    0.00215042   -0.00603132    0.00197612
H    1.01173084    1.46375116    0.00027657
H    -0.54081507    1.44752661   -0.87664372
H    -0.52381363    1.43793264    0.90639729
4
Mol_1.xyz
N   -0.04042605    1.02410775    0.06256380
H    0.01725746    0.01254521   -0.02737716
H    0.91578937    1.35874519   -0.02875776
H    -0.52027774    1.34353213   -0.77554261

```

Exercise B.5: Collect coordinates of all molecules

Store the Cartesian coordinates of all molecules in qm9 in the file qm9_130831_molecules.xyz. WARNING: The code will run for a while and will create an approximately 108 MB file.

```

import qm9pack                      # Import the qm9pack module
import os                           # Import the os module

df = qm9pack.get_data('qm9')         # Fetch the QM9 dataset

filename = 'qm9_130831_molecules.xyz' # Output filename

# Create the output file
with open(filename, 'w') as f:
    pass

# Loop through each molecule in the dataset
for index in range(len(df)):
    tmpfile = 'mol_' + str(index) + '.xyz' # Temporary filename

    qm9pack.makexyz(index, df, tmpfile)     # Create the XYZ file

    # Append contents to the main output file
    with open(tmpfile, 'r') as temp_file:
        contents = temp_file.read()

```

```

with open(filename, 'a') as final_file:
    final_file.write(contents)

os.remove(tmpfile)                                # Remove temporary file

```

<OUTPUT>
Long output, not shown.

Exercise B.6: Filter molecules using Stoichiometry

Let us find all molecules in `qm9` matching a stoichiometry. Let us use C2H6O corresponding to two constitutional isomers, ethanol (CH3CH2OH) and dimethylether (CH3OCH3). We will filter the dataset to make a filtered DataFrame. Then, we will go over each molecule in this subset and print SMILES and InChi strings. Note that `_` (underscore) is a placeholder for the index of the DataFrame (which is not used).

NOTE: You can modify this exercise and retrieve any other properties for a set of constitutional isomers. You can use the names of the columns from II B Exercise B.1. For example, if you want to print SMILES and dipole moment, you can modify the last line of the code as

```
print(mol['SMILES'], mol['Dipole_debye'])
```

```

import qm9pack

df = qm9pack.get_data('qm9')

# stoichiometry is a string of list with number of H, C, N, O, and F atoms
stoi = "[6,2,0,1,0]" # Six H, two C, zero N, one O, and zero F

# Filter the DataFrame to match the stoichiometry
filtered_df = df[df['Stoichiometry'].apply(lambda x: x == stoi)]

# Iterate over each row in the filtered DataFrame
for _, mol in filtered_df.iterrows():
    # Print SMILES and InChi for each molecule
    print(mol['SMILES'], mol['InChi'])

```

<OUTPUT>
CCO InChI=1S/C2H6O/c1-2-3/h3H,2H2,1H3
COC InChI=1S/C2H6O/c1-3-2/h1-2H3

III. ADVANCED EXERCISES

Exercise C.1: All stoichiometries in QM9

Let us find all the unique stoichiometries in `qm9` and find their counts. We will find that the most populated stoichiometry corresponds to C7H10O2, containing 6095 molecules, which has been extensively studied in Ref. 12. NOTE: Remember, Python counts from zero.

```

import qm9pack

df = qm9pack.get_data('qm9')

# Get counts of unique values in the 'Stoichiometry' column, in descending order
value_counts = df['Stoichiometry'].value_counts(ascending=False)

```

```
# Iterating over each unique value and its count
for index, count in value_counts.items():
    print(f"{index}: {count}") # Printing each unique value and its count
```

<OUTPUT>

```
[10,7,0,2,0]: 6094
[11,7,1,1,0]: 5858
[9,6,1,2,0]: 5630
[9,7,1,1,0]: 5215
[12,8,0,1,0]: 4918
[12,7,0,2,0]: 4612
[7,6,1,2,0]: 3872
[8,6,2,1,0]: 3556
[10,8,0,1,0]: 3171
[14,8,0,1,0]: 3154
[8,7,0,2,0]: 3009
...
...
```

Exercise C.2: Atomization energy

Let us calculate the atomization energy of a molecule using its index. As an example we will set `index=0` corresponding to methane. We will use U_0 of free atoms collected in TABLE. I.

NOTE: You can also consider atomization energy as a positive number by defining it as the energy of the reaction Molecule→atoms. In that case, you can change the line

```
U0_atomization = U0_mol - np.dot(stoi, U0_atoms)
to
U0_atomization = np.dot(stoi, U0_atoms) - U0_mol
```

```
import numpy as np
import qm9pack

df = qm9pack.get_data('qm9')

# Conversion constants from Hartree to other units
hartree2ev = 27.211386245
hartree2kcm = 627.5094740631
hartree2kJm = 2625.4996394799

# U0 for H, C, N, O, and F atoms from the manual (in atomic units)
U0_atoms = np.array([-0.500273, -37.846772, -54.583861, -75.064579, -99.718730])

# Selecting the molecule at index 0
index = 0
mol = df.loc[index]

# Extracting the internal energy of the molecule at 0 K in atomic units (au)
U0_mol = mol['InternalEnergy_0K_au']

# Extracting the stoichiometry of the molecule
stoi = mol['Stoichiometry']

# Convert the stoichiometry string to an array of float
str_list = stoi.strip('[]').split(',')
```

```

stoi = [float(num) for num in str_list]

# Calculating the atomization energy
U0_atomization = U0_mol - np.dot(stoi, U0_atoms)

print(f'Atomization energy is {U0_atomization:.8f} hartree')
print(f'Atomization energy is {U0_atomization * hartree2ev:.6f} eV')
print(f'Atomization energy is {U0_atomization * hartree2kcm:.5f} kcal/mol')
print(f'Atomization energy is {U0_atomization * hartree2kJm:.4f} kJ/mol')

<OUTPUT>
Atomization energy is -0.63106600 hartree
Atomization energy is -17.172181 eV
Atomization energy is -395.99989 kcal/mol
Atomization energy is -1656.8636 kJ/mol

```

Exercise C.3: Multiproperty query

Let us do a multiproperty query and get the SMILES of all molecules in qm9 with dipole moment in the range 5–8 debye and HOMO-LUMO gap in the range 2–5 eV. Let's print the output in a file `multiquery.txt` with molecules arranged in ascending order of dipole moment.

```

import qm9pack

df = qm9pack.get_data('qm9')

# Conversion factor from hartree to eV
hartree2ev = 27.211386245

# Define minimum and maximum values for Dipole moment and HOMO-LUMO gap (in eV)
min_dipole = 5.0
max_dipole = 8.0

min_gap = 2.0 / hartree2ev # Minimum HOMO-LUMO gap converted to eV
max_gap = 5.0 / hartree2ev # Maximum HOMO-LUMO gap converted to eV

# Combined condition to filter rows based on two criteria
combined_condition = (
    (df['Dipole_debye'] >= min_dipole) & (df['Dipole_debye'] <= max_dipole) &
    (df['HOMO_LUMO_gap_au'] >= min_gap) & (df['HOMO_LUMO_gap_au'] <= max_gap)
)

# Apply the combined condition to filter the DataFrame
filtered_df = df[combined_condition]

# Sort filtered DataFrame by 'Dipole_debye' column in ascending order
sorted_df = filtered_df.sort_values(by='Dipole_debye', ascending=True)

# Write SMILES, HOMO-LUMO gap (in eV), and Dipole moment to file
with open('multiquery.txt', 'w') as f:
    for _, mol in sorted_df.iterrows():
        f.write(f'{mol["SMILES"]} {mol["HOMO_LUMO_gap_au"]} * hartree2ev {mol["Dipole_debye"]}\n')

```

```

<OUTPUT>
printed in the file 'multiquery.txt'

```

IV. ACKNOWLEDGMENTS

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V. DATA AVAILABILITY

The qm9pack is maintained here: <https://github.com/raghurama123/qm9pack>

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