Molecular Similarity Search and Clustering using AI

This project performs molecular similarity search and clustering using Morgan fingerprints, Tanimoto similarity, FAISS, KMeans, UMAP, and Butina clustering.

Install Libraries

Step 1: Import Required Libraries

```
import os
import pandas as pd
import numpy as np
!pip install rdkit
!pip install faiss-cpu # Install faiss-cpu
from rdkit import Chem
from rdkit.Chem import AllChem, Descriptors, DataStructs, rdMolDescriptors # Added rdMolDescriptors
from rdkit.ML.Cluster import Butina
import matplotlib.pyplot as plt
import umap
import faiss
```

```
Requirement already satisfied: rdkit in /usr/local/lib/python3.12/dist-packages (2025.9.1)
Requirement already satisfied: numpy in /usr/local/lib/python3.12/dist-packages (from rdkit) (2.0.2)
Requirement already satisfied: Pillow in /usr/local/lib/python3.12/dist-packages (from rdkit) (11.3.0)
Requirement already satisfied: faiss-cpu in /usr/local/lib/python3.12/dist-packages (1.13.0)
Requirement already satisfied: numpy<3.0,>=1.25.0 in /usr/local/lib/python3.12/dist-packages (from faiss-cpu) (2.0.2)
Requirement already satisfied: packaging in /usr/local/lib/python3.12/dist-packages (from faiss-cpu) (25.0)
```

Step 2: Load Dataset

```
CSV_PATH = "molecules.csv"
df = pd.read_csv(CSV_PATH)
df = df.dropna(subset=["SMILES"]).reset_index(drop=True)
```

```
df
```

	ID	SMILES
0	89594	CN1CCC[C@H]1C2=CN=CC=C2
1	2160	CN(C)CCC=C1C2=CC=CC=C2CCC3=CC=CC=C31
2	1615	CC(CC1=CC2=C(C=C1)OCO2)NC
3	135398737	CN1CCN(CC1)C2=NC3=C(C=CC(=C3)Cl)NC4=CC=CC=C42
4	2391	CC(=O)OC1=CC=C(C=C1)C(C2=CC=C(C=C2)OC(=O)C)C3=...
...	...	...
1454	5702260	C[C@@H]1CC(=O)[C@]2([C@@H](O1)OC3[C@H]([C@@H](...
1455	5702292	CN1CC[C@]23[C@@H]4[C@@H](C=CC2[C@H]1CC5=C3C(=C...
1456	5701995	CC[C@@H]1[C@H](COC1=O)CC2=CC=CN2C
1457	5702230	C1[C@@H]([C@H]([C@@H]([C@@H]([C@H]1O)N)O[C@H]2...
1458	5702262	C1[C@H]([C@@H]([C@H]([C@@H]([C@H]1N)OC2[C@@H](...

1459 rows × 2 columns

Step 3: Sanitize SMILES & Compute descriptors

```
# compute descriptors
def sanitize_and_describe(smiles):
    mol = Chem.MolFromSmiles(smiles)
    if mol is None:
        return None, None, None, None, None, None
    can_smiles = Chem.MolToSmiles(mol, isomericSmiles=True)
    mw = Descriptors.MolWt(mol)
    logp = Descriptors.MolLogP(mol)
    tpsa = Descriptors.TPSA(mol)
    hba = Descriptors.NumHAcceptors(mol)
    hbd = Descriptors.NumHDonors(mol)
    return can_smiles, mw, logp, tpsa, hba, hbd

df[['SMILES', 'MW', 'LogP', 'TPSA', 'HBA', 'HBD']] = df['SMILES'].apply(
    lambda x: pd.Series(sanitize_and_describe(x))
)
df = df.dropna(subset=['SMILES']).reset_index(drop=True)
```

```
df.head()
```

	ID	SMILES	MW	LogP	TPSA	HBA	HBD
0	89594	CN1CCC[C@H]1c1cccnc1	162.236	1.8483	16.13	2	0
1	2160	CN(C)CCC=C1c2ccccc2CCc2ccccc21	277.411	4.1686	3.24	1	0
2	1615	CNC(C)Cc1ccc2c(c1)OCO2	193.246	1.5657	30.49	3	1
3	135398737	CN1CCN(C2=Nc3cc(Cl)ccc3Nc3ccccc32)CC1	326.831	3.7227	30.87	4	1
4	2391	CC(=O)Oc1ccc(C(c2ccc(OC(C)=O)cc2)c2ccccn2)cc1	361.397	4.1124	65.49	5	0

```
if 'ID' in df.columns:
    df = df.drop(columns=['ID'])
```

```
df
```

	SMILES	MW	LogP	TPSA	HBA	HBD
0	CN1CCC[C@H]1c1cccnc1	162.236	1.8483	16.13	2	0
1	CN(C)CCC=C1c2ccccc2CCc2ccccc21	277.411	4.1686	3.24	1	0
2	CNC(C)Cc1ccc2c(c1)OCO2	193.246	1.5657	30.49	3	1
3	CN1CCN(C2=Nc3cc(Cl)ccc3Nc3ccccc32)CC1	326.831	3.7227	30.87	4	1
4	CC(=O)Oc1ccc(C(c2ccc(OC(C)=O)cc2)c2ccccn2)cc1	361.397	4.1124	65.49	5	0
...	...	...	...	...	...	...
1454	CN[C@@H]1[C@H](O)[C@H](NC)[C@H]2O[C@@]3(O)C(=O...	332.353	-2.9256	129.51	9	5
1455	CN1CC[C@]23c4c5ccc(O)c4O[C@H]2[C@H](O)C=CC3[C@...	285.343	1.1981	52.93	4	2
1456	CC[C@H]1C(=O)OC[C@@H]1Cc1cccn1C	207.273	1.7668	31.23	3	0
1457	NC[C@@H]1O[C@H](OC2[C@@H](O)[C@H](O[C@@H]3[C@H...	615.634	-8.8617	347.32	19	13
1458	NC[C@@H]1O[C@H](O[C@@H]2[C@@H](CO)OC(O[C@@H]3[...	615.634	-8.8617	347.32	19	13

1459 rows × 6 columns

Step 4: Generate Morgan Fingerprints

```
def morgan_fp(smiles, nBits=1024, radius=2):
    mol = Chem.MolFromSmiles(smiles)
    if mol is None:
        return np.zeros((nBits,), dtype=np.uint8)
    fp = AllChem.GetMorganFingerprintAsBitVect(mol, radius=radius, nBits=nBits)
    arr = np.zeros((nBits,), dtype=np.uint8)
    DataStructs.ConvertToNumpyArray(fp, arr)
    return arr

fps = np.vstack([morgan_fp(s) for s in df.SMILES]).astype("float32")
```

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```

```
# RDKit ExplicitBitVect
bitvects = [DataStructs.ExplicitBitVect(len(f)) for f in fps]
for i, f in enumerate(fps):
    bv = bitvects[i]
    for j, bit in enumerate(f):
        if bit: bv.SetBit(j)
```

```
df
```

	SMILES	MW	LogP	TPSA	HBA	HBD
0	CN1CCC[C@H]1c1cccnc1	162.236	1.8483	16.13	2	0
1	CN(C)CCC=C1c2ccccc2CCc2ccccc21	277.411	4.1686	3.24	1	0
2	CNC(C)Cc1ccc2c(c1)OCO2	193.246	1.5657	30.49	3	1
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4	CC(=O)Oc1ccc(C(c2ccc(OC(C)=O)cc2)c2ccccn2)cc1	361.397	4.1124	65.49	5	0
...	...	...	...	...	...	...
1454	CN[C@@H]1[C@H](O)[C@H](NC)[C@H]2O[C@@]3(O)C(=O...	332.353	-2.9256	129.51	9	5
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1459 rows × 6 columns

```
fp_df = pd.DataFrame(fps)
fp_df.head()
```

	0	1	2	3	4	5	6	7	8	9	...	1014	1015	1016	1017	1018	1019	1020	1021	1022	1023
0	0.0	0.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	...	0.0	0.0	0.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0
1	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	...	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
2	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	...	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
3	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	...	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
4	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	...	0.0	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0

5 rows × 1024 columns

Step 5: Top Tanimoto Similarity Search

```
def topk_tanimoto(idx, k=5):
    q = bitvects[idx]
    sims = DataStructs.BulkTanimotoSimilarity(q, bitvects)
    sims = np.array(sims)
    order = np.argsort(-sims)
    hits = [i for i in order if i != idx][:k]
    return hits, sims[hits]
```

Step 6: Similarity Distance Calculation and Butina Clustering

```
n_fps = len(fps)
dists = []
for i in range(1, n_fps):
    sims = DataStructs.BulkTanimotoSimilarity(bitvects[i], bitvects[:i])
    dists.extend([1 - s for s in sims])

SIM_CUTOFF = 0.7
clusters = Butina.ClusterData(dists, n_fps, 1 - SIM_CUTOFF, isDistData=True)

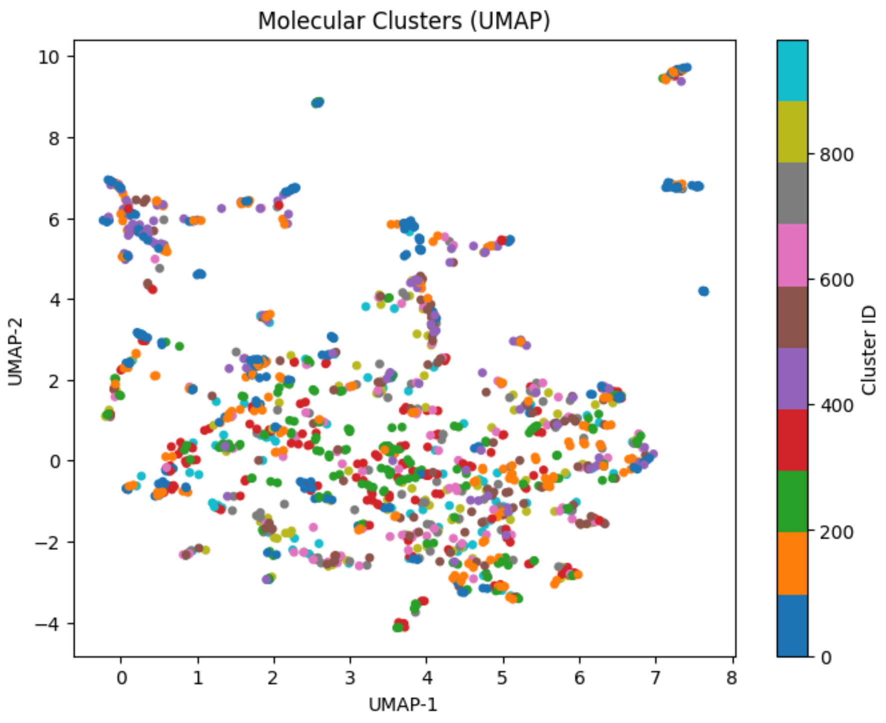
cluster_labels = np.zeros(n_fps, dtype=int)
for cluster_id, cluster in enumerate(clusters):
    for idx in cluster:
        cluster_labels[idx] = cluster_id
df['cluster'] = cluster_labels
```

Step 7: UMAP Visualization of Molecular Space

```
reducer = umap.UMAP(n_neighbors=15, min_dist=0.1, metric='jaccard', random_state=42)
X2D = reducer.fit_transform(fps)
df['x_umap'] = X2D[:,0]
df['y_umap'] = X2D[:,1]

plt.figure(figsize=(8,6))
plt.scatter(df['x_umap'], df['y_umap'], c=df['cluster'], cmap="tab10", s=15)
plt.title("Molecular Clusters (UMAP)")
plt.xlabel("UMAP-1")
plt.ylabel("UMAP-2")
plt.colorbar(label='Cluster ID')
plt.savefig("umap_clusters.png", dpi=300)
plt.show()
```

```
/usr/local/lib/python3.12/dist-packages/umap/umap_.py:1887: UserWarning: gradient function is not yet implemented for j
  warn(
/usr/local/lib/python3.12/dist-packages/umap/umap_.py:1952: UserWarning: n_jobs value 1 overridden to 1 by setting rand
  warn(
```



Step 8: fast Similarity(Optional)

```
index = faiss.IndexFlatL2(fps.shape[1])
index.add(fps)

def faiss_search(idx, k=5):
    q = fps[idx].reshape(1, -1)
    D, I = index.search(q, k+1)
    return I[0][1:], D[0][1:]
```

Step 9: Results

```
df.to_csv("processed_molecules_with_umap.csv", index=False)

topk_list = []
for i in range(len(df)):
    hits, sims = topk_tanimoto(i)
    topk_list.append((i, hits, sims.tolist()))
topk_df = pd.DataFrame(topk_list, columns=['index', 'top5_indices', 'top5_tanimoto'])
topk_df.to_csv("similarity_topk.csv", index=False)
```

```
cluster_ids = [-1] * len(fps)

for cid, cluster in enumerate(clusters):
    for mol_idx in cluster:
        cluster_ids[mol_idx] = cid

df["Cluster_ID"] = cluster_ids
df.to_csv("molecules_butina_clusters.csv", index=False)
```

```
sim = DataStructs.TanimotoSimilarity(bitvects[0], bitvects[1])
print("Tanimoto similarity:", sim)
```

```
Tanimoto similarity: 0.11538461538461539
```

```
from rdkit.ML.Cluster import Butina
from rdkit import DataStructs
import numpy as np
```

```
dists = []
nfps = len(bitvects)

for i in range(1, nfps):
    sims = DataStructs.BulkTanimotoSimilarity(bitvects[i], bitvects[:i])
    dists.extend([1 - x for x in sims])

threshold = 0.4
clusters = Butina.ClusterData(dists, nfps, threshold, isDistData=True)

for i, c in enumerate(clusters):
    print("Cluster", i, ":", list(c))

cluster_id = np.zeros(nfps, dtype=int)

for i, c in enumerate(clusters):
    for mol_idx in c:
        cluster_id[mol_idx] = i

df["Cluster"] = cluster_id
df.to_csv("butina_clusters_output.csv", index=False)
```

```
Cluster 0 : [1400, 286, 792, 1283, 1304, 1366, 1380, 1404, 1441, 1443, 1444, 1449, 1457, 1458]
Cluster 1 : [745, 236, 598, 692, 760, 763, 1071, 1234, 1249, 1314, 1349, 1361, 1408, 1445]
Cluster 2 : [1387, 887, 1143, 1148, 1206, 1208, 1237, 1243, 1299, 1317, 1396]
Cluster 3 : [139, 84, 142, 843, 1233, 1246, 1264, 1286, 1343, 1386, 1406]
Cluster 4 : [288, 511, 567, 751, 848, 1451]
Cluster 5 : [136, 11, 13, 58, 66, 79, 101, 108, 129]
Cluster 6 : [1372, 270, 810, 884, 915, 1047, 1088, 1180]
Cluster 7 : [1298, 247, 345, 643, 691, 694, 773, 1076]
Cluster 8 : [1075, 1203, 1212, 1250, 1251, 1359, 1412, 1447]
Cluster 9 : [837, 493, 545, 725, 800, 835, 855, 878]
Cluster 10 : [765, 429, 629, 690, 821, 856]
Cluster 11 : [1313, 300, 378, 746, 838, 1034, 1273]
Cluster 12 : [1252, 1260]
Cluster 13 : [1140, 1154, 1242, 1245, 1256, 1352, 1371]
Cluster 14 : [351, 127, 424, 474, 744, 770, 1254]
Cluster 15 : [1, 5, 23, 92, 96, 138, 143]
Cluster 16 : [1453, 1355, 1430]
Cluster 17 : [1397]
Cluster 18 : [1265, 1270, 1417]
Cluster 19 : [668, 49, 98, 670, 736, 1053]
Cluster 20 : [513, 557, 721, 1156, 1176, 1213]
Cluster 21 : [490, 386, 518, 558, 801, 962]
Cluster 22 : [93, 51, 132]
Cluster 23 : [85, 34, 43, 78, 83]
Cluster 24 : [1424, 1129]
Cluster 25 : [1320, 1197, 1217, 1267, 1315]
Cluster 26 : [1312, 1168, 1185, 1189, 1257]
Cluster 27 : [1209, 1109, 1282, 1395, 1410]
Cluster 28 : [1158, 1108, 1225, 1365, 1409]
Cluster 29 : [1151, 1169, 1248]
Cluster 30 : [1059, 904, 1399, 1405, 1419]
Cluster 31 : [867, 573, 822, 885, 1095]
Cluster 32 : [784, 133, 134, 665, 1056]
Cluster 33 : [735]
Cluster 34 : [724, 47, 256, 669, 1240]
Cluster 35 : [698, 171, 370, 468, 549]
Cluster 36 : [572, 361, 477, 600, 639]
Cluster 37 : [563, 412, 414, 554, 934]
Cluster 38 : [442, 198, 239, 281, 426]
Cluster 39 : [1454, 358, 1084, 1414]
Cluster 40 : [1420, 1310, 1321, 1381]
Cluster 41 : [1416, 863, 879, 1306]
Cluster 42 : [1403, 761]
Cluster 43 : [1401, 407, 1026, 1325]
Cluster 44 : [1367, 1302, 1307, 1340]
Cluster 45 : [1363, 862, 994, 1308]
Cluster 46 : [1309, 283, 1407]
Cluster 47 : [1305, 930, 1028, 1231]
Cluster 48 : [1292, 153]
Cluster 49 : [1268, 1335]
Cluster 50 : [1261, 1118, 1210, 1390]
Cluster 51 : [1216, 1181, 1278]
Cluster 52 : [1201, 1069, 1135, 1155]
Cluster 53 : [1178, 1150, 1166, 1207]
Cluster 54 : [1165, 857, 1091, 1162]
Cluster 55 : [1153, 2, 7, 88]
Cluster 56 : [1124]
Cluster 57 : [1082, 308, 747, 1080]
```

Results Explanation