DATE: 09/10/2022

WEBLEM 4

Introduction to Molecular Descriptors and PaDELPy software

Molecular descriptors can be defined as mathematical representations of molecules' properties that are generated by algorithms. The numerical values of molecular descriptors are used to quantitatively describe the physical and chemical information of the molecules. An example of molecular descriptors is the LogP which is a quantitative representation of the lipophilicity of the molecules, it is obtained by measuring the partitioning of the molecule between an aqueous phase and a lipophilic phase which consists usually of water/n-octanol. Molecular descriptors can be useful in performing similarity searches in molecular libraries, as they can find molecules with similar physical or chemical properties based on their similarity in the descriptors' values. The molecular descriptors are used in ADMET prediction models to correlate the structure–property relationship to help in predicting the ADMET properties of molecules based on their descriptors values (Khan and sylte, 2007).

The molecular descriptors that are used in ADMET models can be classified as being one-dimensional (1D), two-dimensional (2D), or three-dimensional (3D) descriptors based on the level of molecular representation required for calculating the descriptor. The 1D descriptors are the simplest type of molecular descriptors, these represent information that are calculated from the molecular formula of the molecule, which includes the count and type of atoms in the molecule and the molecular weight.

The 2D descriptors are more complex than the 1D descriptors, usually, they represent molecular information regarding the size, shape, and electronic distribution in the molecule. Calculating the 2D descriptors depends mainly on the database size, and the calculation of parts of a molecule in which the data is missing could largely result in a false result.

The 3D descriptors describe mainly properties that are related to the 3D conformation of the molecule, such as the intramolecular hydrogen bonding. Examples of descriptors obtained from calculations involving the 3D structure of the molecules are the polar and nonpolar surface area (PSA and NPSA, respectively). More advanced calculation like quantum mechanics calculations can be used to obtain 3D descriptors that describe the valence electron distribution in the molecules (Bergström, 2005).

Common Molecular Descriptors:

Constitutional

- Functional groups
- Molecular weight
- Simple counts e.g., number of atoms, bonds, rings

Topological

- Atom-pairs5
- Balaban index6
- BCUT7
- Information content indices8
- Kappa shape indices9
- Kier and Hall connectivity indices10
- Kier flexibility index11
- Kier shape indices11
- Molecular walk counts12
- Randic indices13
- Wiener index14

Geometric

- Gravitation index[20]
- Molecular surface area
- Molecular volume[21]
- Shadow indices[22]
- Solvent accessible molecular surface area

Electrostatic

- Charged polar surface area[33]
- Galvez topological charge indices[34]
- Hydrogen bonding capacities
- Maximum and minimum partial charges[35]
- Molecular polarizabilities[36]

Fingerprints

- Daylight[37]
- MDL keys[38]
- UNITY[39]

Hydrophobic

- Aromaticity indices[3]
- Hansch substituent constant[4]
- Log D
- Log P

Steric

- Charton steric parameter[15]
- Molar refractivity[16]
- Parachor[17]
- Taft steric parameter[18]

Quantum chemical[19]

- Charges
- HOMO and LUMO energies
- Orbital electron densities
- Superdelocalizabilities
- Atom-atom polarizabilities
- Molecular polarizabilites
- Dipole moments and polarity indices
- Energies

Combination

- 3D-MoRSE[23]
- Electrotopological state indices[24]
- GETAWAY
- LSER[26]
- MolSurf[27]
- Moreau-Broto topological autocorrelation[28]

- Randic molecular profiles29
- RDF30
- VolSurf31
- WHIM32

PaDELPy: A Python wrapper for PaDEL-Descriptor software

PaDELPy provides a Python wrapper for the PaDEL-Descriptor molecular descriptor calculation software. It was created to allow direct access to the PaDEL-Descriptor command-line interface via Python.

Installation

Installation via pip:

$ pip install padelpy

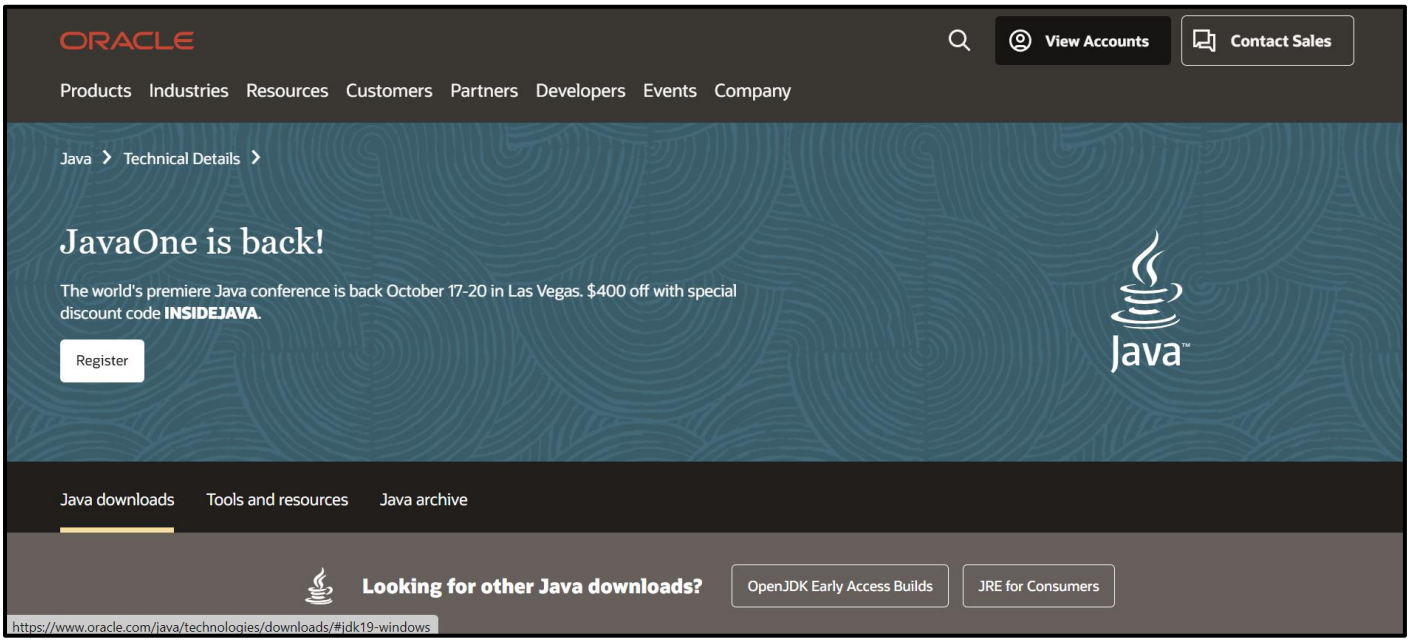
PaDEL-Descriptor is bundled into PaDELPy, therefore an external installation/download of PaDEL-Descriptor is not necessary. There are currently no additional Python dependencies for PaDELPy, however it requires an installation of the Java JRE version 6+.

Basic Usage

In addition to providing a complete interface between Python and PaDEL-Descriptor's command line tool, PaDELPy offers two functions to acquire descriptors/fingerprints within Python - obtaining descriptors/fingerprints from a SMILES string, and obtaining descriptors/fingerprints from an MDL MolFile

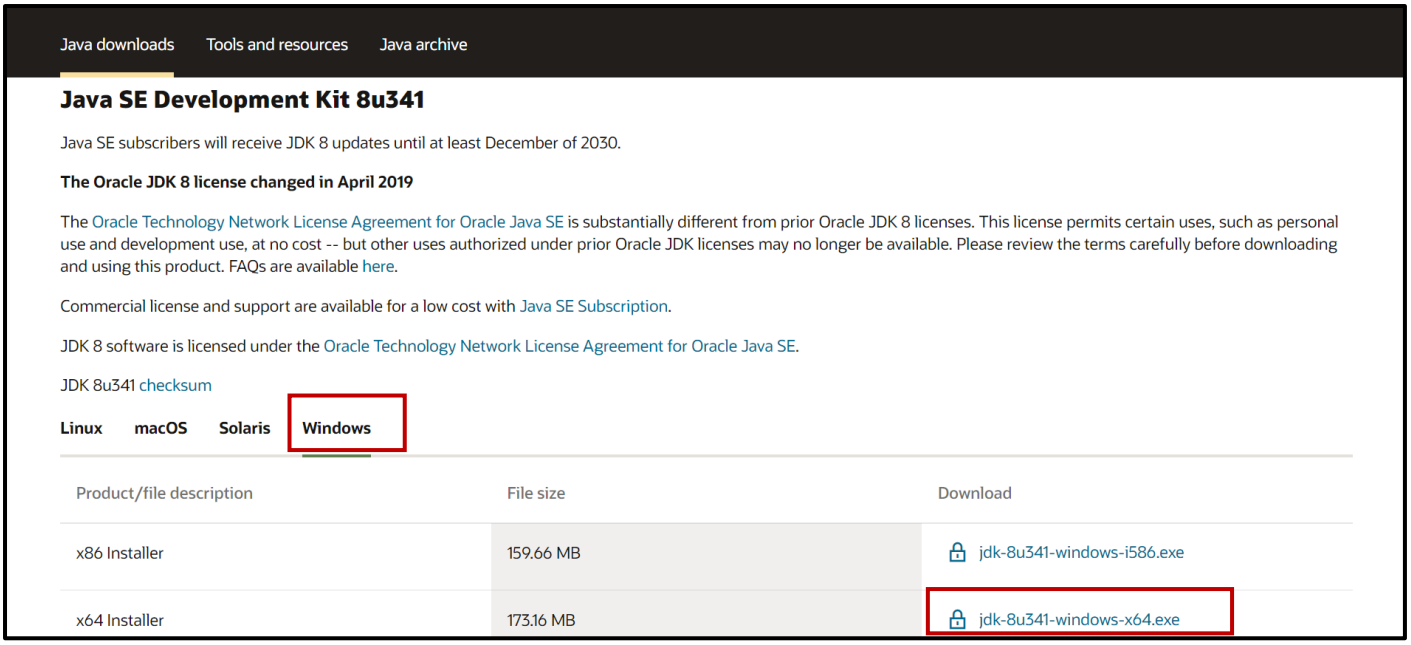
STEPS FOR INSTALLATION OF PADELPY:

Installation of Java JDK and JRE:

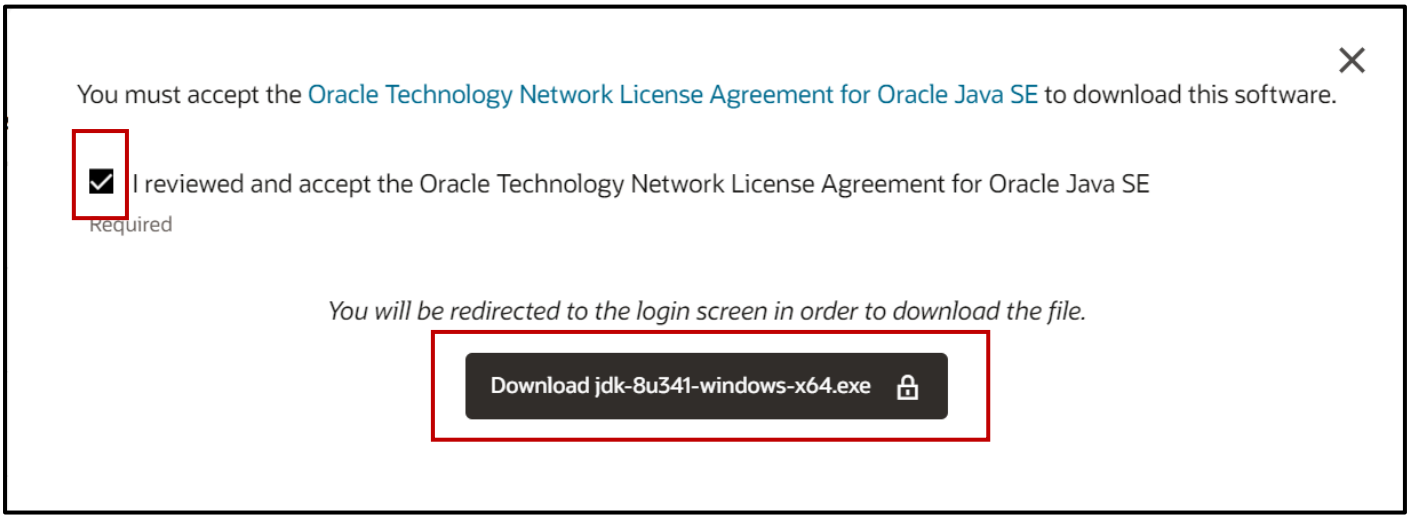


STEP 1: Go to homepage of Oracle

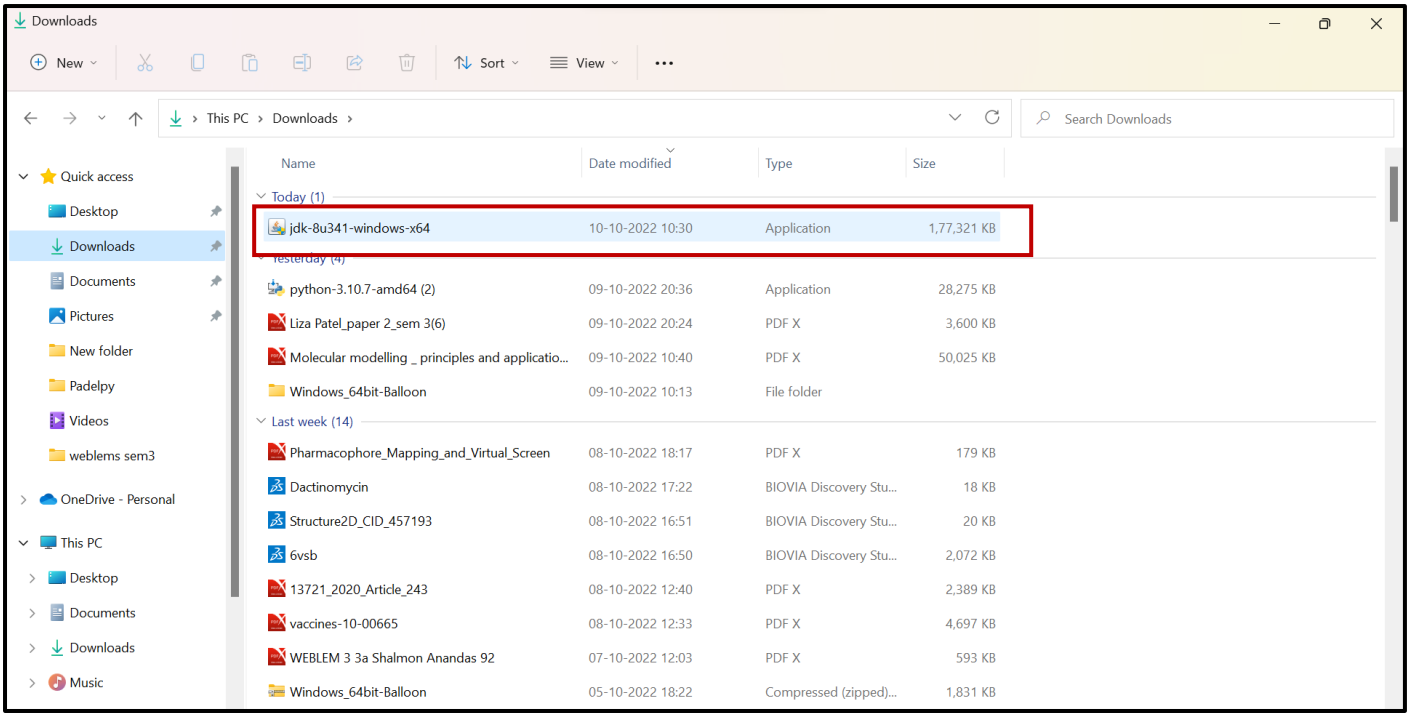
(URL: https://www.oracle.com/java/technologies/downloads/)



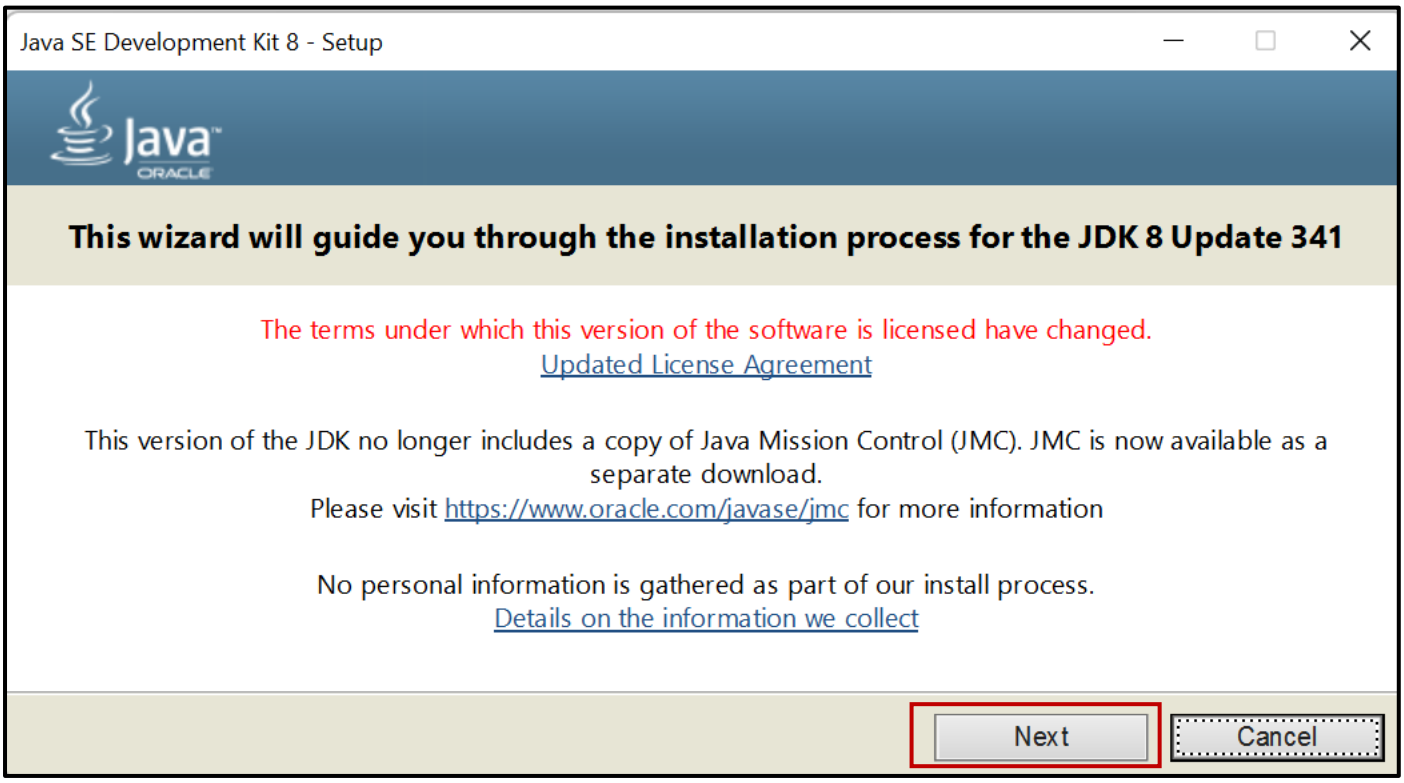
STEP 2: Scroll down to Java 8 for windows and download .exe file



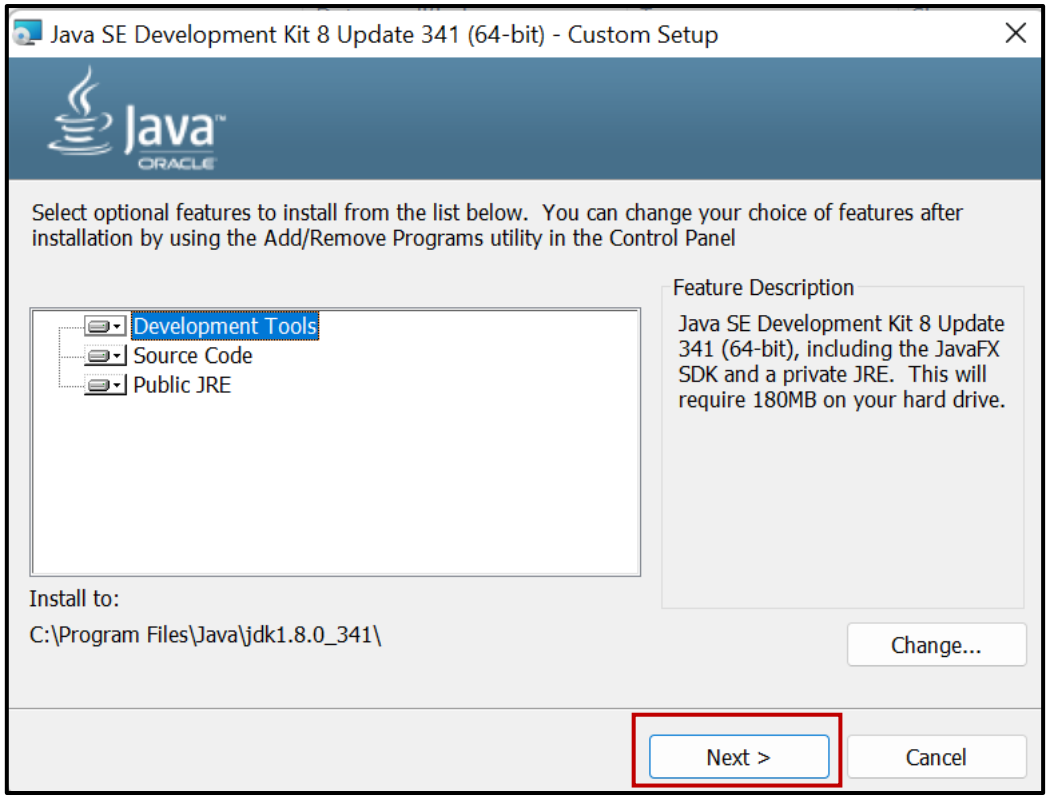
STEP 3: Accept the license agreement and click on download



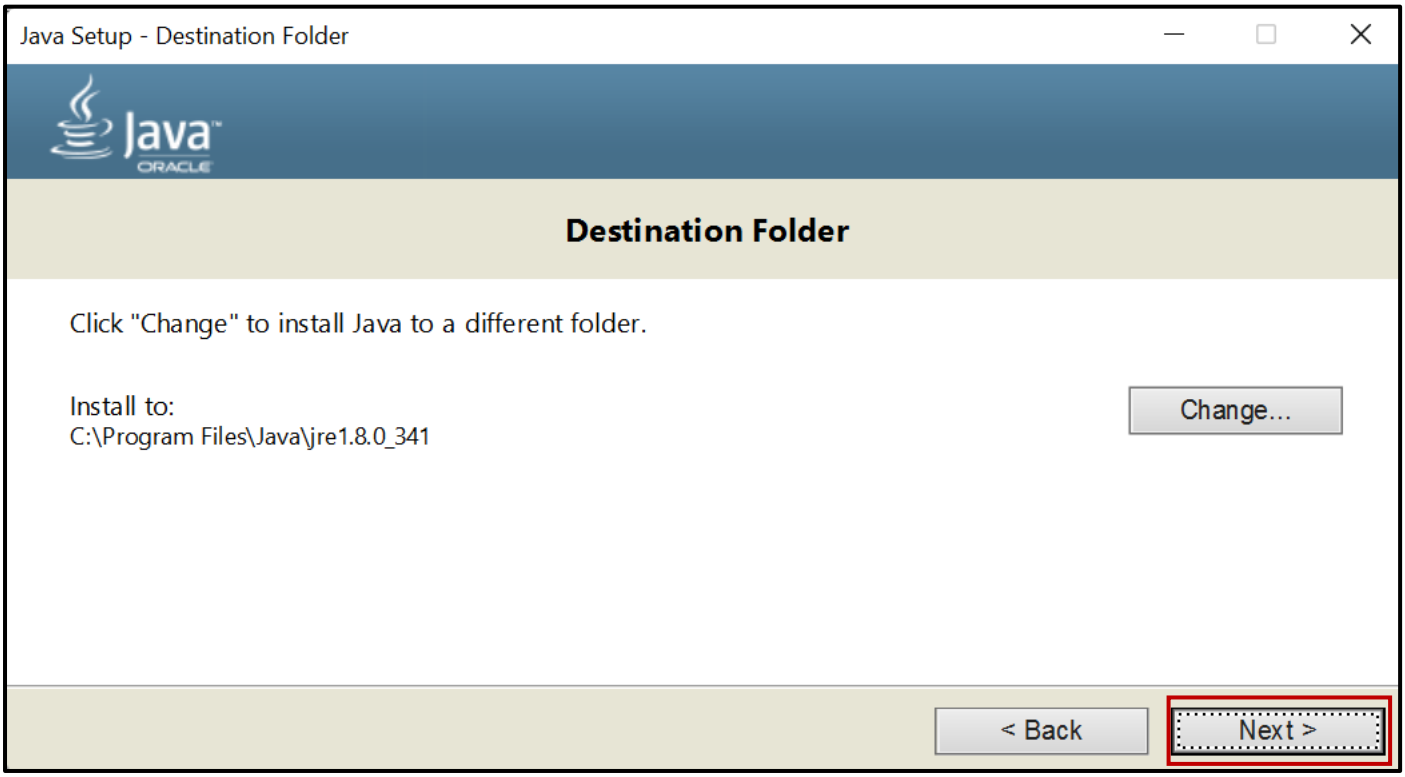
STEP 4: Click on the downloaded .exe file from downloads



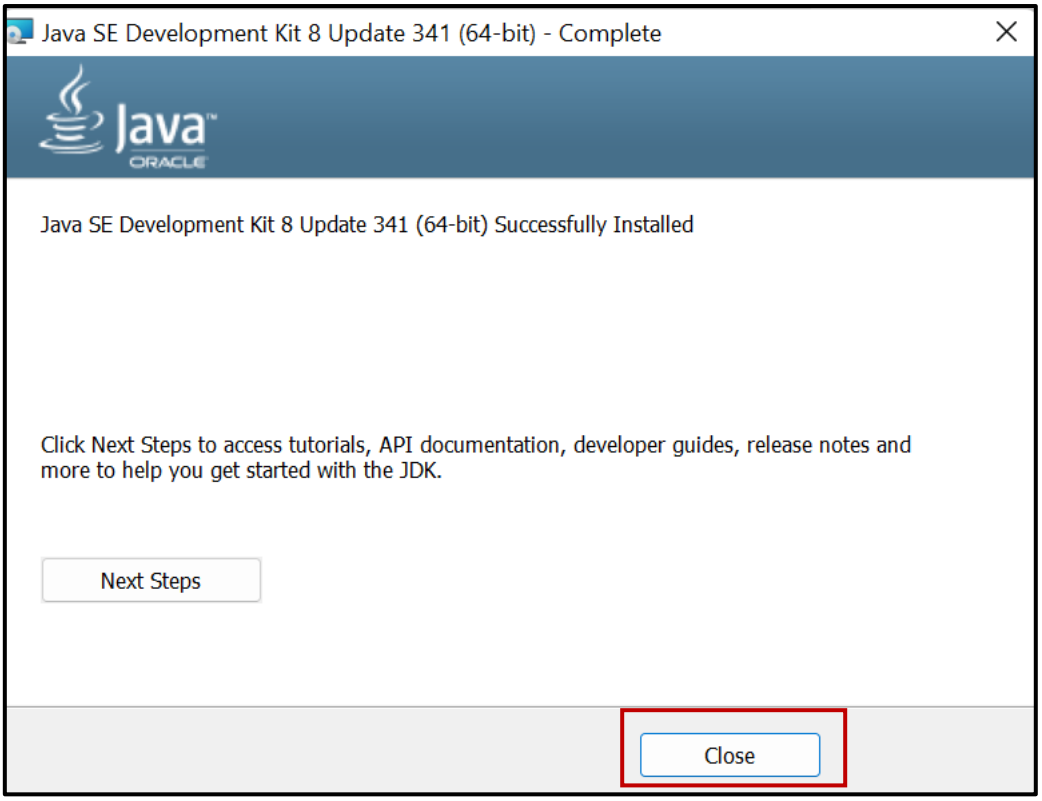
STEP 5: Click on next option for setup



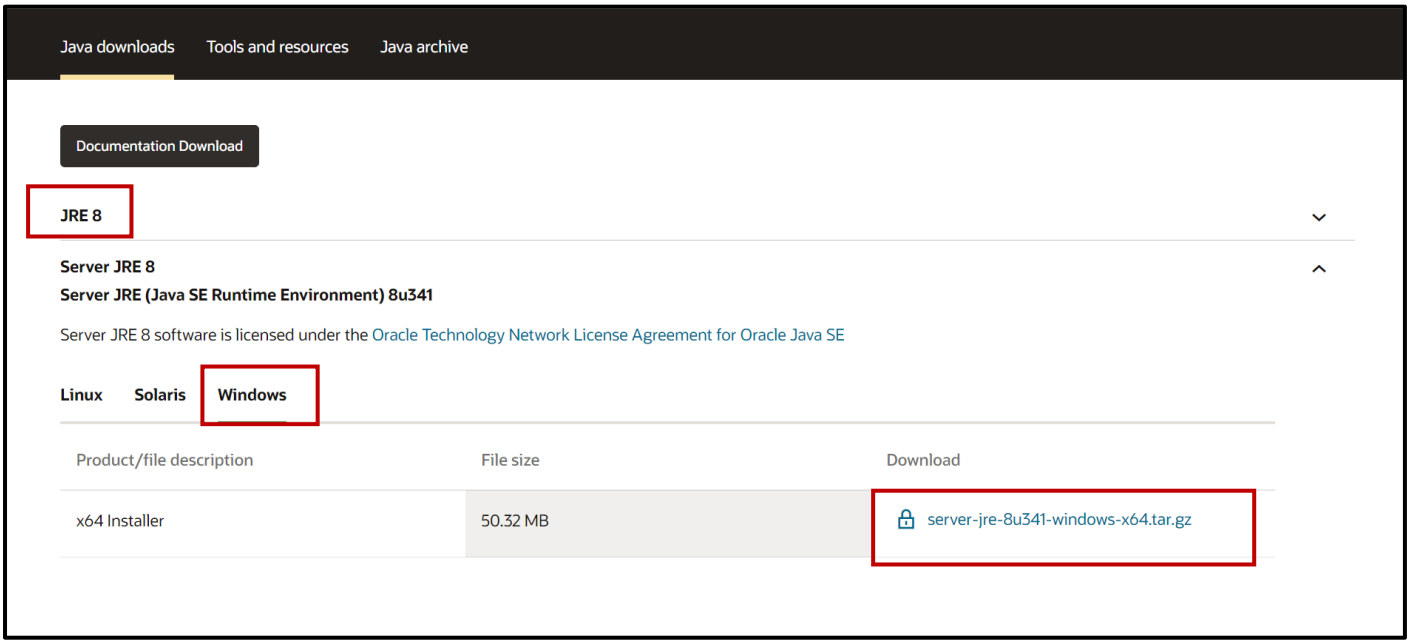
STEP 6: Click on next for custom setup



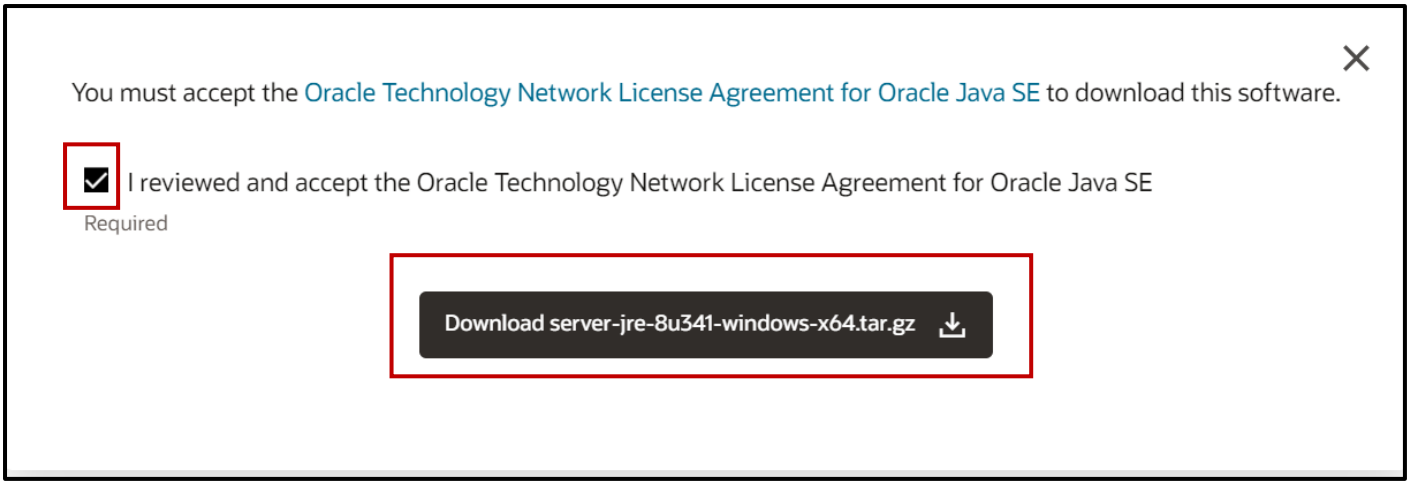
STEP 7: Click on next for selection of destination folder



STEP 8: After installation is complete click on close option



STEP 9: Scroll down to JRE 8 on oracle page and download .gz file for windows

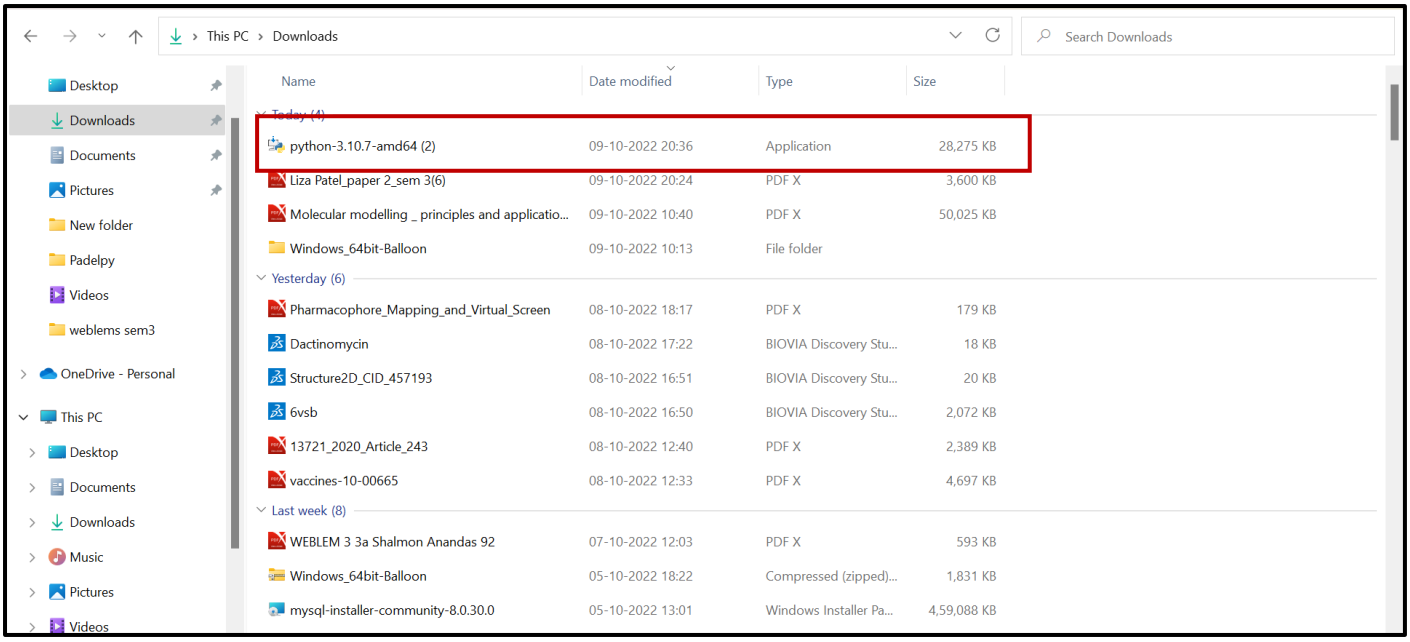


STEP 10: Accept license agreement and click on download

Installation of Python:

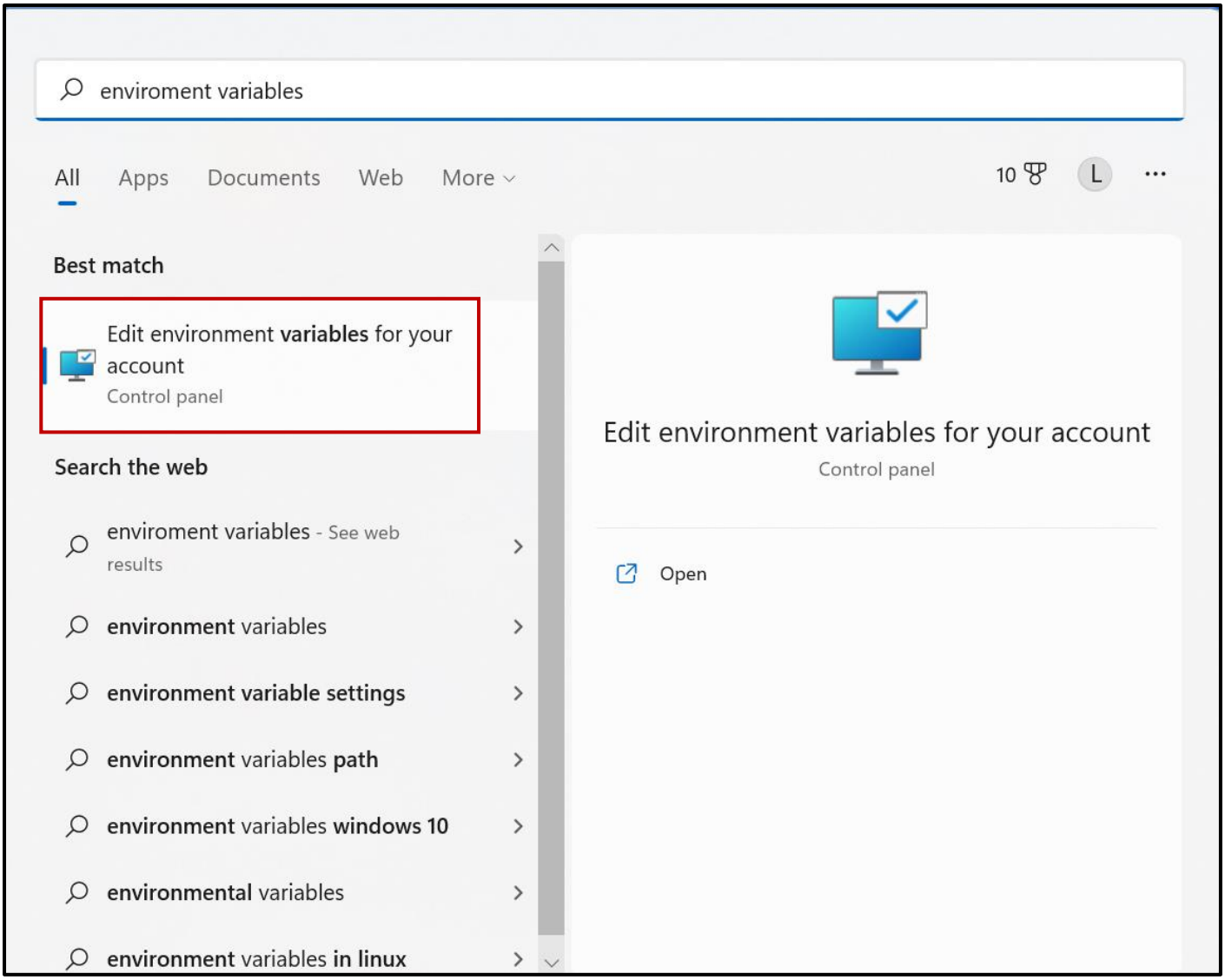
STEP 11: Go to homepage of python and click on download python 3.10.7

(URL: https://www.python.org/downloads/)

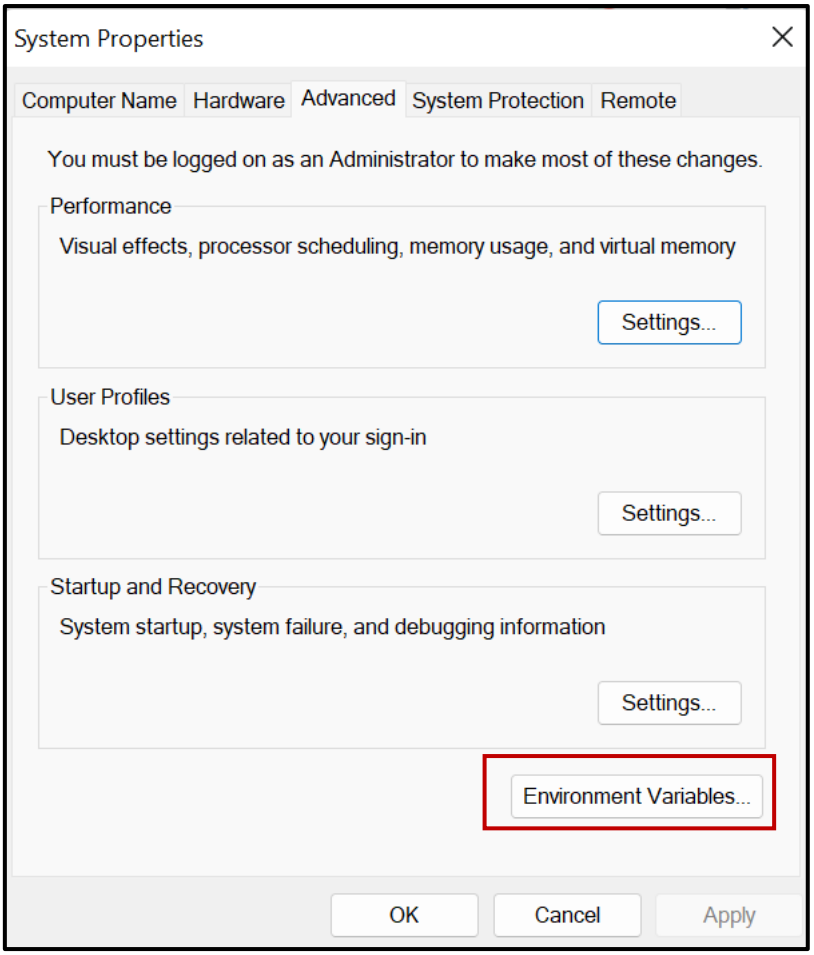


STEP 12: Go to downloads and open the .exe file

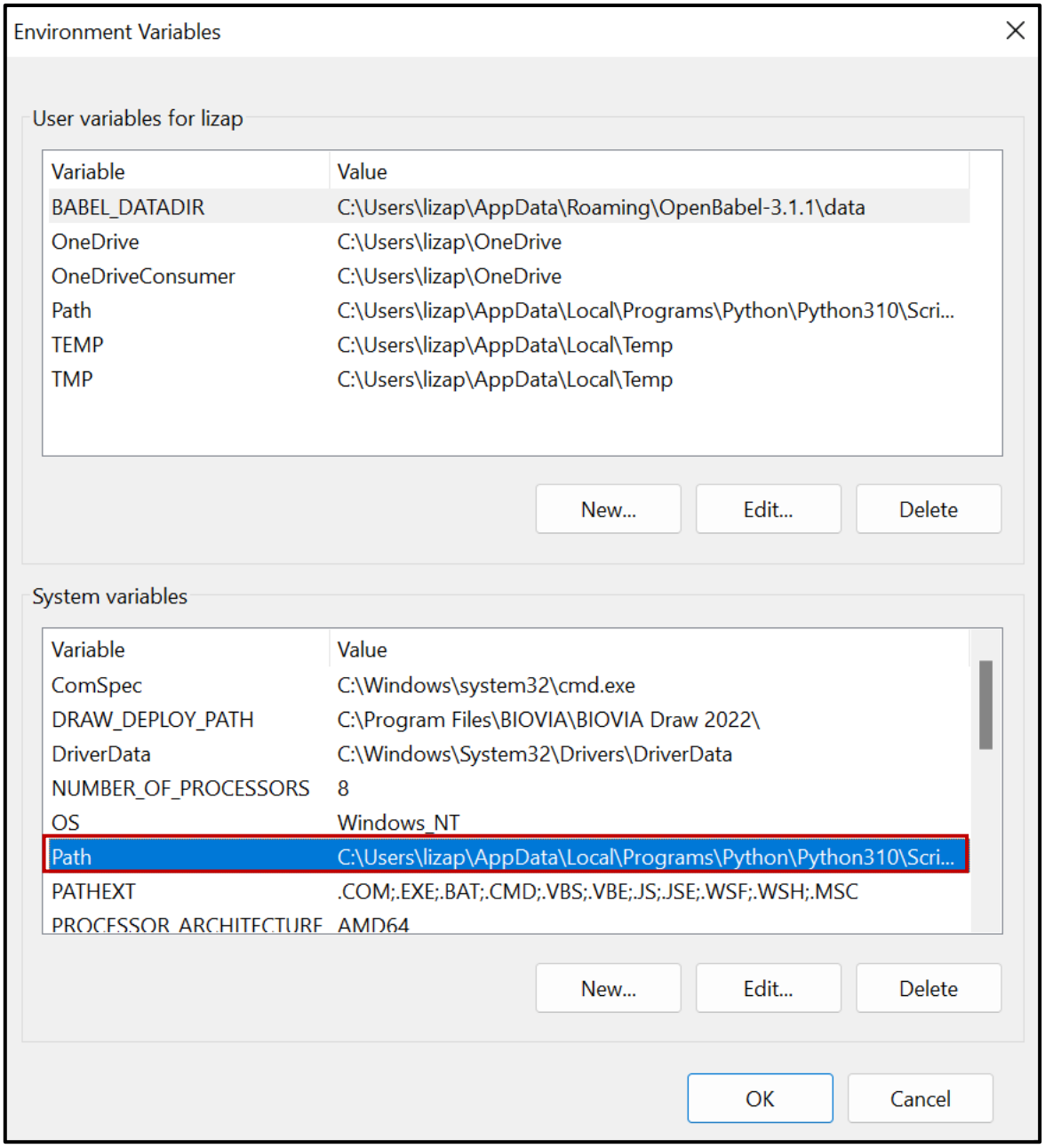
STEP 13: Select Add Python 3.10 to PATH and click on Install Now



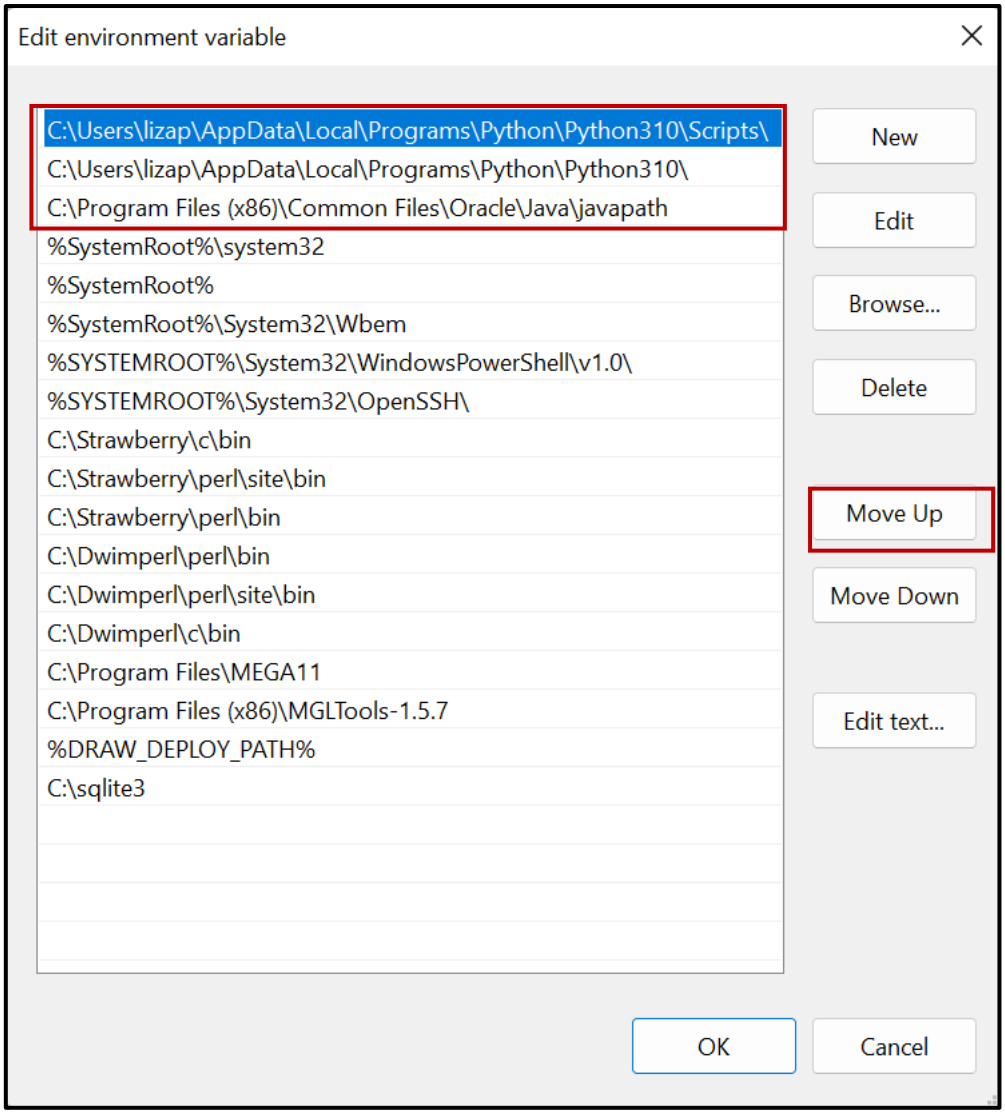
STEP 14: Search for environment variables option on your system and open it



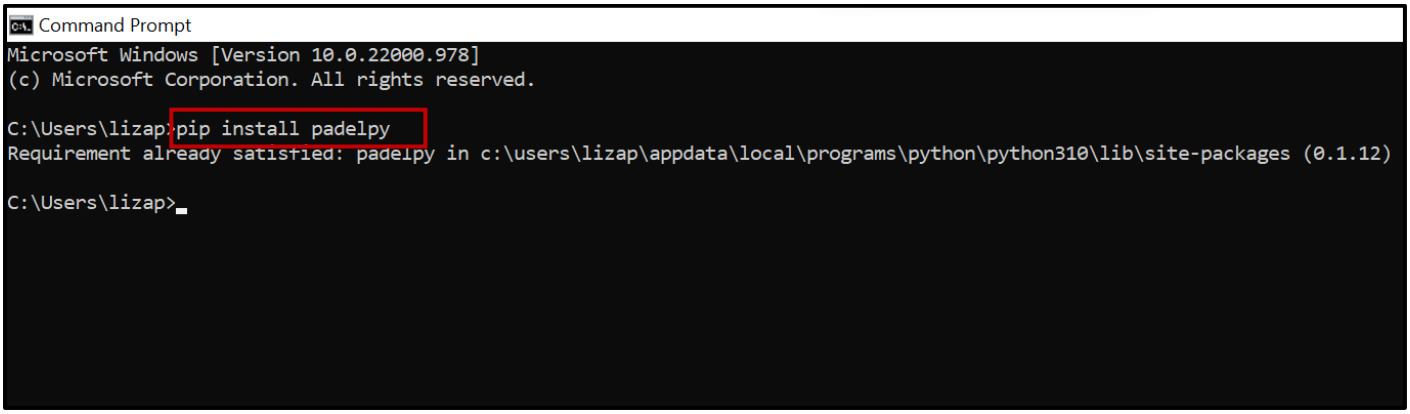
STEP 15: Click on environment variables option



STEP 16: Double click on path



STEP 17: Pull path for python and java to the top using move up key and click on ok



STEP 18: Open command prompt and type “pip install padelpy” and press enter

Application:

Molecular descriptors play important roles in the fields of quantitative structure–activity relationship studies (QSAR) as well as quantitative structure– property relationship studies (QSPRs). The path breaking progress in the field of chemoinformatics has showed us new paths for identifying key links between the molecular structure and their biological properties. Molecular descriptors can be useful in performing similarity searches in molecular libraries, as they can find molecules with similar physical or chemical properties based on their similarity in the descriptors’ values.

REFERENCES:

1. *Molecular Descriptor - an overview | ScienceDirect Topics*. (n.d.). Www.sciencedirect.com. Retrieved October 9, 2022, from https://www.sciencedirect.com/topics/medicine-and-dentistry/molecular-descriptor#:~:text=A%20molecular%20descriptor%20is%20a
2. Kamath, V., & Pai, A. (2017). Application of Molecular Descriptors in Modern Computational Drug Design-An Overview. *Research Journal of Pharmacy and Technology*, *10*(9), 3237. https://doi.org/10.5958/0974-360x.2017.00574.1
3. *PaDELPy: A Python wrapper for PaDEL-Descriptor software*. (2022, September 28). GitHub. Retrieved October 9, 2022, from https://github.com/ecrl/padelpy#readme
4. *Download Python*. (2019). Python.org; Python.org. Retrieved October 9, 2022, from https://www.python.org/downloads/
5. *Download the Latest Java LTS Free*. (2021). Oracle.com. Retrieved October 9, 2022, from https://www.oracle.com/java/technologies/downloads/

DATE: 09/10/22

WEBLEM 4a

PaDELPy

(URL: https://github.com/ecrl/padelpy#readme)

AIM:

To study molecular descriptors for Ibuprofen (Pubchem Id- 3672) using PaDELPy software and analyze the results.

INTRODUCTION:

Ibuprofen is (2RS)-1[4-(2-methyl propyl) phenyl] propionic acid (BP. 2004). Ibuprofen was the first member of propionic acid derivatives to be introduced in 1969 as a better alternative to Aspirin. Gastric discomfort, nausea and vomiting, though less than aspirin or indomethacin, are still the most common side effects.

Ibuprofen is the most commonly used and most frequently prescribed NSAID.2,3 It is a non-selective inhibitor of cyclo-oxygenase-1 (COX-1) and Cyclooxygenase-2 (COX-2). Although, its anti-inflammatory properties may be weaker than those of some other NSAIDs, it has a prominent analgesic and antipyretic role. Its effects are due to the inhibitory actions on cyclo-oxygenases, which are involved in the synthesis of prostaglandins. Prostaglandins have an important role in the production of pain, inflammation and fever.

PaDELPy provides a Python wrapper for the PaDEL-Descriptor molecular descriptor calculation software. It was created to allow direct access to the PaDEL-Descriptor command-line interface via Python.

PaDEL-Descriptor is bundled into PaDELPy, therefore an external installation/download of PaDEL-Descriptor is not necessary. There are currently no additional Python dependencies for PaDELPy, however it requires an installation of the Java JRE version 6+.

In addition to providing a complete interface between Python and PaDEL-Descriptor's command line tool, PaDELPy offers two functions to acquire descriptors/fingerprints within Python - obtaining descriptors/fingerprints from a SMILES string, and obtaining descriptors/fingerprints from an MDL MolFile

METHODOLOGY:

- Retrieve canonical SMILES for Ibuprofen from Pubchem database (URL: https://pubchem.ncbi.nlm.nih.gov/)
- Open github page for PaDELPy: A Python wrapper for PaDEL-Descriptor software (URL: https://github.com/ecrl/padelpy#readme)
- Copy script for SMILES to Descriptors/Fingerprints to notepad
- In the script for function “from_smiles” pass canonical SMILES of Ibuprofen as parameter.
- Save it as script1.py to a folder named Padelpy
- Open command prompt
- Give path for Padelpy folder
- Run script1
- Observe and interpret the results

OBSERVATIONS:

FIG 1. Python script for SMILES to Descriptor/Fingerprints

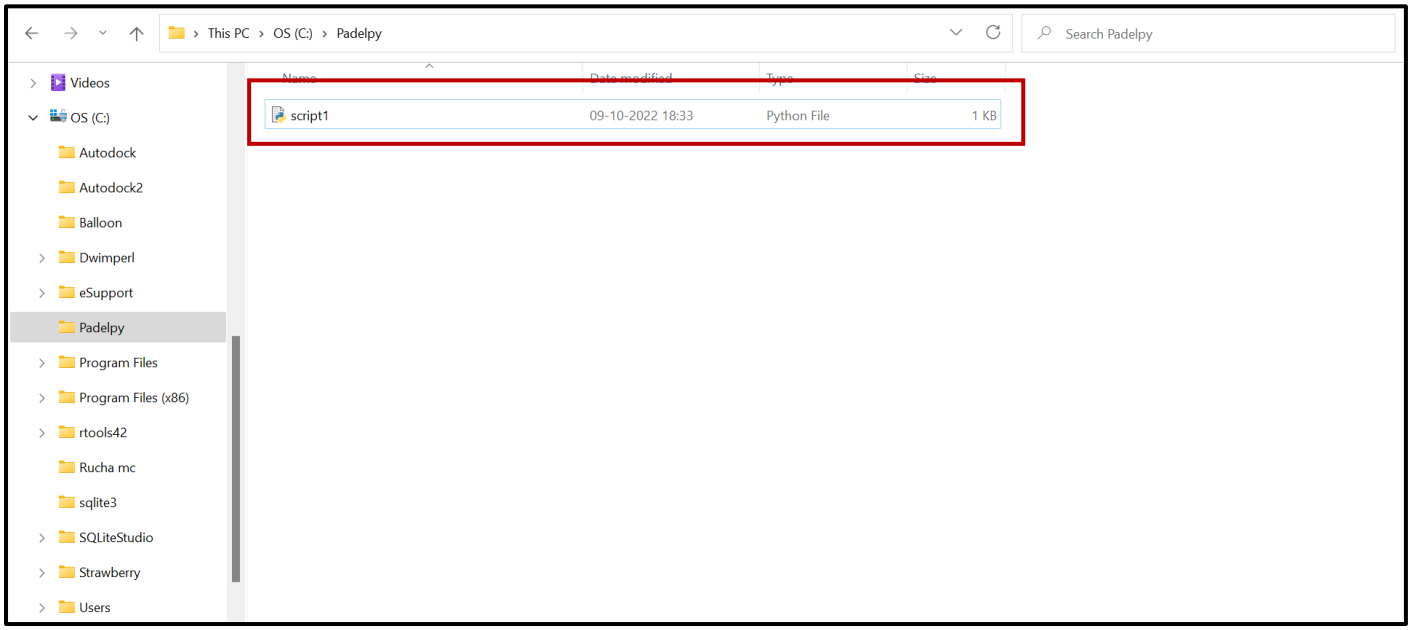


FIG 2. Script saved as script1.py in Padelpy folder

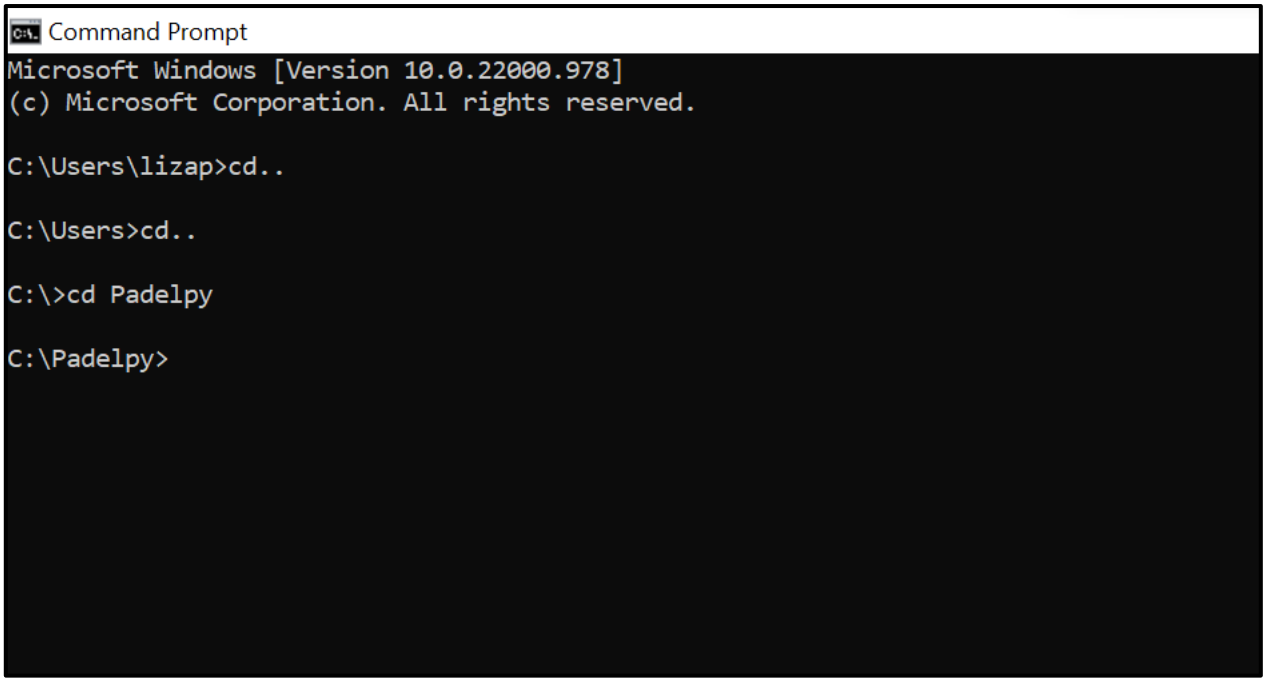


FIG 3. Path to Padelpy folder in command prompt

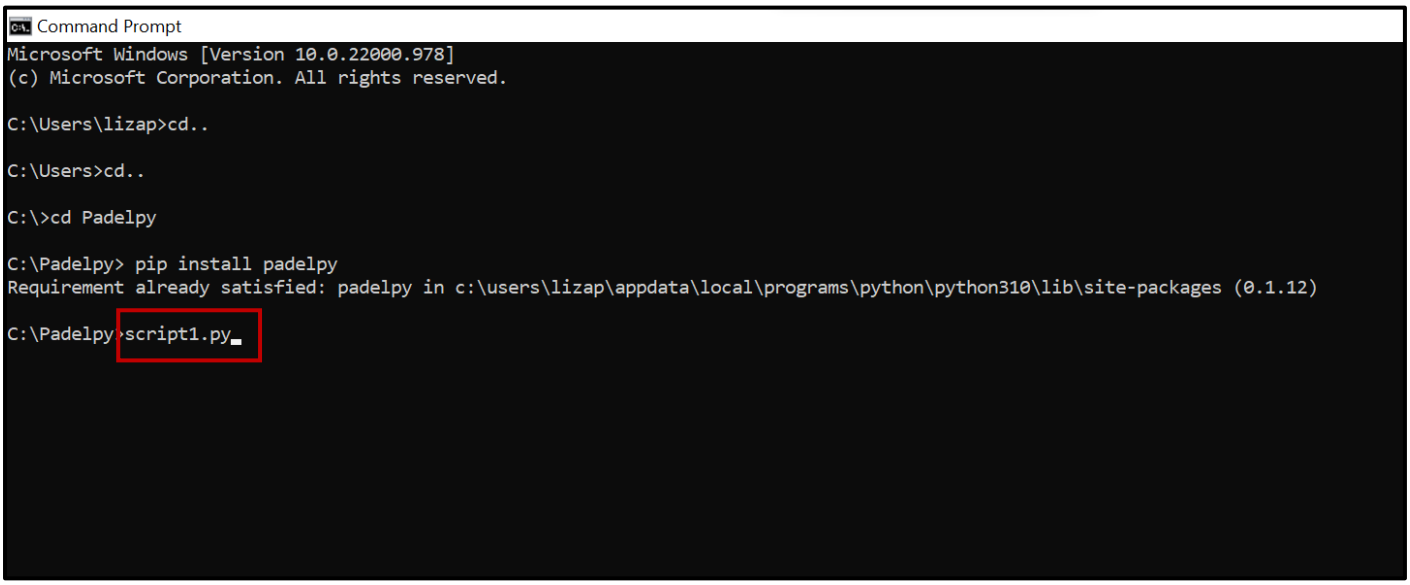


FIG 4. Running script1.py

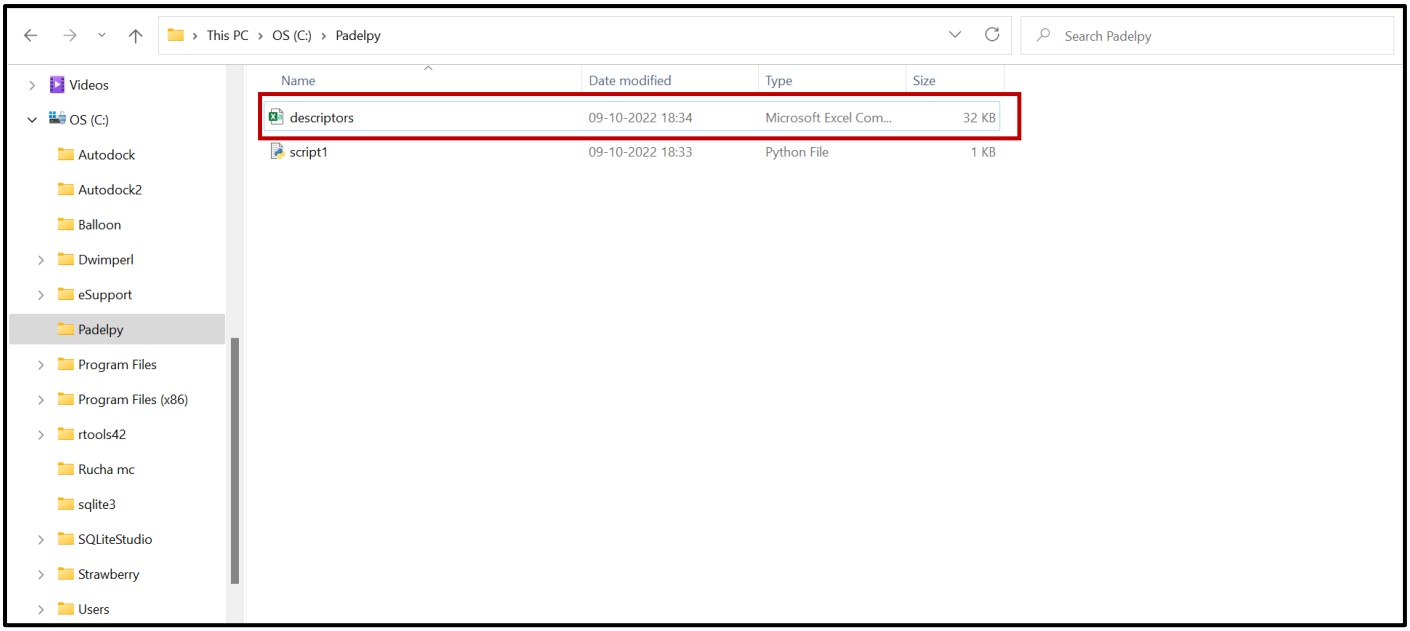
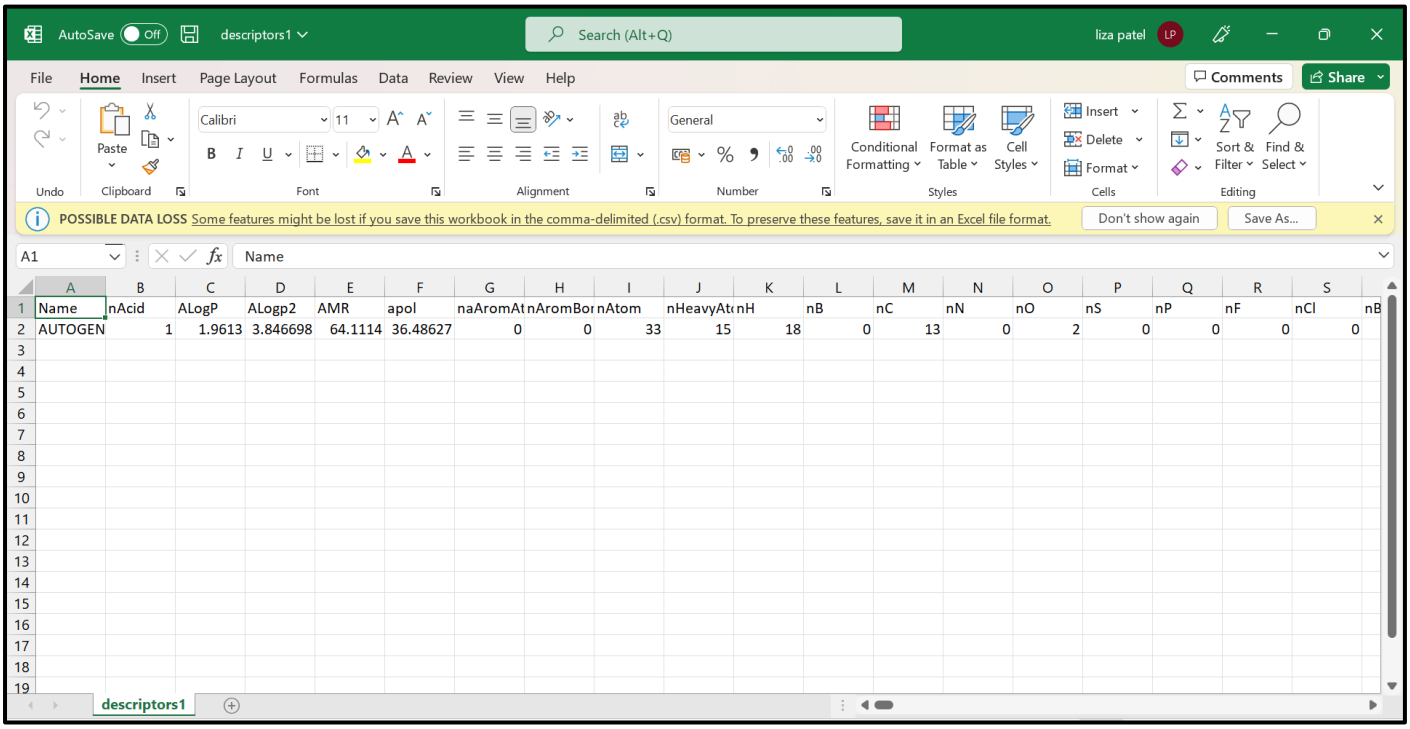


FIG 5. Descriptors excel file as .csv generated in Padelpy folder



Name	nAcid	ALogP	ALogp2	AMR	apol	naAromAt	nAromBor	nAtom	nHeavyAt	nH	nB	nC	nN	nO	nS	nP	nF	nCl	nB
AUTOGEN	1	1.9613	3.846698	64.1114	36.48627	0	0	33	15	18	0	13	0	2	0	0	0	0	

FIG 6. Descriptors calculation for Ibuprofen molecule

RESULTS:

PaDELPy which is a Python wrapper for the PaDEL-Descriptor molecular descriptor calculation software was used to calculate molecular descriptors of Ibuprofen.

CONCLUSION:

PaDELPy provides a Python wrapper for the PaDEL-Descriptor molecular descriptor calculation software. It allows direct access to the PaDEL-Descriptor command-line interface via Python. Thus, PaDELPy can be used for quantitative structure–activity relationship studies (QSAR) as well as quantitative structure– property relationship studies (QSPRs) as molecular descriptors play an important role here. Molecular descriptors can be useful in performing similarity searches in molecular libraries, as they can find molecules with similar physical or chemical properties based on their similarity in the descriptors' values.

REFERENCES:

1. *Molecular Descriptor - an overview | ScienceDirect Topics*. (n.d.). Www.sciencedirect.com. Retrieved October 9, 2022, from https://www.sciencedirect.com/topics/medicine-and-dentistry/molecular-descriptor#:~:text=A%20molecular%20descriptor%20is%20a
2. Kamath, V., & Pai, A. (2017). Application of Molecular Descriptors in Modern Computational Drug Design-An Overview. *Research Journal of Pharmacy and Technology*, *10*(9), 3237. https://doi.org/10.5958/0974-360x.2017.00574.1
3. *PaDELPy: A Python wrapper for PaDEL-Descriptor software*. (2022, September 28). GitHub. Retrieved October 9, 2022, from https://github.com/ecrl/padelpy#readme
4. Bushra, R., & Aslam, N. (2010). An overview of clinical pharmacology of Ibuprofen. *Oman Medical Journal*, *25*(3), 155–1661. https://doi.org/10.5001/omj.2010.49