Appendix A: Textual Structure-function relationships

Case study 1: Presence of open metal sites in MOFs

XpertAI Explanation

- The features identified by the XAI analysis that affect the presence of open metal sites in MOFs are the Fraction of Metals, Solid Density, and Average Cationic Radius. Additional features that may be correlated with the presence of open metal sites in MOFs include the type of metal ions used, the coordination environment, and the presence of structural defects (Kökçam-Demir et al., 2020; Jianwei Ren et al., 2017).

- The Fraction of Metals in a MOF can influence the presence of open metal sites. A higher fraction of metals may lead to more open metal sites, as these sites are typically part of the metal node or metal secondary building unit (Kökçam-Demir et al., 2020).

- The Solid Density of a MOF can also impact the presence of open metal sites. A lower crystal density is associated with a higher hydrogen-storage capacity, which suggests a correlation with the presence of open metal sites (Qingyuan Yang, Chongli Zhong, 2006).

- The Average Cationic Radius can affect the strength of interaction between the metal ions and hydrogen, which can influence the presence and effectiveness of open metal sites (Wei Zhou, Hui Wu, Taner Yildirim, 2008).

- The type of metal ions used in the MOF can affect the presence of open metal sites. For example, an increased charge can increase the electrostatic interaction between the metal ions and the ligands, which can influence the formation of open metal sites (Kökçam-Demir et al., 2020).

- The coordination environment can impact the rates and selectivities of MOF-based catalytic materials, which suggests a potential influence on the presence of open metal sites (Jacklyn N. Hall, Praveen Bollini, 2019).

- The presence of structural defects has been shown to shape the physical and chemical behavior of the material, which can influence the presence of open metal sites (Jianwei Ren et al., 2017).
- In summary, the presence of open metal sites in MOFs is influenced by a variety of factors, including the Fraction of Metals, Solid Density, and Average Cationic Radius, as well as the type of metal ions used, the coordination environment, and the presence of structural defects. By manipulating these features, it may be possible to alter the presence of open metal sites in MOFs and thereby optimize their performance for various applications.
- References:

  - Kökçam-Demir, Anna Goldman, Leili Esrafili, Maniya Gharib, Ali Morsali, Oliver Weingart, Christoph Janiak, (2020). Coordinatively unsaturated metal sites (open metal sites) in metal–organic frameworks: design and applications.
  - Jianwei Ren, Mpho Ledwaba, Nicholas M. Musyoka, Henrietta W. Langmi, Mkhulu Mathe, Shijun Liao, Wan Pang, (2017). Structural defects in metal–organic frameworks (MOFs): Formation, detection and control towards practices of interests.
  - Qingyuan Yang, Chongli Zhong, (2006). Understanding Hydrogen Adsorption in Metal -Organic Frameworks with Open Metal Sites: A Computational Study.
  - Wei Zhou, Hui Wu, Taner Yildirim, (2008). Enhanced H 2Adsorption in Isostructural Metal -Organic Frameworks with Open Metal Sites: Strong Dependence of the Binding Strength on Metal Ions.
  - Jacklyn N. Hall, Praveen Bollini, (2019). Structure, characterization, and catalytic properties of open-metal sites in metal organic frameworks.

ChatGPT Explanation

- Metal-organic frameworks (MOFs) are a class of compounds consisting of metal ions or clusters coordinated to organic ligands to form one-, two-, or three-dimensional structures. The relationship between the molecular structure of MOFs and the presence of open metal sites is quite significant.

- Open metal sites (OMSs) in MOFs are typically metal ions that are not fully coordinated by the organic ligands, leaving them available for interaction with other molecules. The presence and number of these open metal sites are largely determined by the molecular structure of the MOF, specifically the type of metal ion and the organic ligand used, as well as their arrangement in the MOF structure.

- The type of metal ion used can influence the coordination number (the number of ligands that a metal ion can bind), which in turn can determine the presence of open metal sites. For example, a metal ion with a high coordination number may not have any open metal sites if all its coordination sites are occupied by ligands.

- The type of organic ligand used can also influence the presence of open metal sites. Ligands with multiple binding sites can bridge multiple metal ions, potentially leaving some metal coordination sites unoccupied and creating open metal sites.

- The arrangement of the metal ions and ligands in the MOF structure can also create open metal sites. For example, in some MOFs, metal ions and ligands are arranged in a way that creates pores or channels, which can contain open metal sites.

- These open metal sites can significantly influence the properties and potential applications of MOFs. They can increase the MOF's capacity for gas storage, enhance its catalytic activity, or enable it to selectively adsorb certain molecules, among other things. Therefore, understanding the relationship between the molecular structure of MOFs and the presence of open metal sites is crucial for designing MOFs with desired properties and functions.

Case study 2: Pore-limiting diameter in MOFs

XpertAI Explanation

- The features identified by the XAI analysis that affect the pore limiting diameter in MOFs include Volume Per Atom, Symmetry Function G1, and Unoccupied Energy Levels at Conduction Band Minimum. Additional features that may be correlated with the pore limiting diameter in MOFs include the identity of the metal center, the presence of open metal sites, and the connectivity of the pores (Parkes et al., 2013; Haldoupis et al., 2010; Watanabe & Sholl, 2012).

- The Volume Per Atom can influence the pore limiting diameter in MOFs as it provides an indication of the size of the atoms that make up the MOF. Larger atoms may result in larger pores, while smaller atoms may result in smaller pores (Haldoupis et al., 2010). The Symmetry Function G1 is a measure of the symmetry of the MOF structure. MOFs with higher symmetry may have more uniform pore sizes, while those with lower symmetry may have more varied pore sizes (Choudhuri & Truhlar, 2020). The Unoccupied Energy Levels at Conduction Band Minimum can influence the electronic properties of the MOF, which may in turn affect the interactions between the MOF and adsorbed molecules, potentially influencing the effective pore size (Yang et al., 2022).

- By altering the Volume Per Atom, Symmetry Function G1, and Unoccupied Energy Levels at Conduction Band Minimum, the pore limiting diameter in MOFs can be manipulated. For instance, selecting atoms of different sizes can change the Volume Per Atom, thus altering the pore size. Similarly, changing the arrangement of atoms can alter the Symmetry Function G1, potentially leading to changes in pore size. Finally, modifying the electronic properties of the MOF can change the Unoccupied Energy Levels at Conduction Band Minimum, which may influence the effective pore size (Haldoupis et al., 2010; Choudhuri & Truhlar, 2020; Yang et al., 2022).

- In summary, the pore limiting diameter in MOFs is influenced by a variety of features, including the Volume Per Atom, Symmetry Function G1, and Unoccupied Energy Levels at Conduction Band Minimum. By understanding these relationships, it may be possible to design MOFs with specific pore sizes for targeted applications.

- References:

  - Parkes, M. V., Staiger, C. L., Perry, J. J., Allendorf, M. D., & Greathouse, J. A. (2013). Screening metal–organic frameworks for selective noble gas adsorption in air: effect of pore size and framework topology.
  - Haldoupis, E., Nair, S., & Sholl, D. S. (2010). Efficient Calculation of Diffusion Limitations in Metal Organic Framework Materials: A Tool for Identifying Materials for Kinetic Separations.
  - Watanabe, T., & Sholl, D. S. (2012). Accelerating Applications of Metal-Organic Frameworks for Gas Adsorption and Separation by Computational Screening of Materials.
  - Choudhuri, I., & Truhlar, D. G. (2020). Improved Predictive Tools for Structural Properties of Metal–Organic Frameworks.
  - Yang, P., Lu, G., Yang, Q., Liu, L., Lai, X., & Yu, D. (2022). Analyzing acetylene adsorption of metal –organic frameworks based on machine learning.

ChatGPT Explanation

- Metal-Organic Frameworks (MOFs) are a class of compounds consisting of metal ions or clusters coordinated to organic ligands to form one-, two-, or three-dimensional structures. They are a type of porous material, meaning they have tiny holes, or pores, throughout their structure. The pore limiting diameter in MOFs refers to the size of these pores.

- The relationship between the molecular structure of MOFs and their pore limiting diameter is direct and significant. The size and shape of the pores in a MOF are determined by the size, shape, and arrangement of the metal ions and organic ligands that make up its structure.

- For instance, if the organic ligands are long, they can create large pores. If they are short, they can create small pores. Similarly, the geometry of the metal ions or clusters (whether they are linear, square, tetrahedral, octahedral, etc.) can also influence the size and shape of the pores.

- Furthermore, the way the metal ions or clusters and organic ligands are connected to each other (their topology) can also affect the pore size. For example, if they are connected in a way that creates a three-dimensional network with large voids, the MOF will have large pores. If they are connected in a way that creates a two-dimensional network with small voids, the MOF will have small pores.

- In summary, the molecular structure of a MOF, including the size, shape, and arrangement of its components, as well as their connectivity, directly determines its pore limiting diameter. This relationship is crucial because the pore size in MOFs can affect their properties and potential applications, such as gas storage, separation, and catalysis.

Case study 3: Toxicity of small drug-like molecules

XpertAI Explanation

- The features identified by the XAI analysis that affect the toxicity of small molecules are the presence of a heteroatom bonded to three Oxygen atoms, the presence of an Aminomethyl Group, and the presence of a Tertiary Amine. Other features that may be correlated with the toxicity of small molecules include the presence of unsubstituted bonded heteroatoms, aromatic amines, and Michael receptors (Bhanushee Sharma et al., 2023).

- The presence of a heteroatom bonded to three Oxygen atoms has a negative correlation with the toxicity of small molecules, as indicated by a correlation coefficient of -0.9811613193980 (XpertAI, 2023). This suggests that molecules with this feature are less likely to be toxic. On the other hand, the presence of an Aminomethyl Group and a Tertiary Amine has a positive correlation with toxicity, with correlation coefficients of 0.9189867373985772 and 0.73218851651589 respectively (XpertAI, 2023). This indicates that molecules with these features are more likely to be toxic.

- The toxicity of small molecules can be altered by changing these features. For instance, removing the heteroatom bonded to three Oxygen atoms or adding an Aminomethyl Group or a Tertiary Amine could potentially increase the toxicity of the molecule. However, it's important to note that toxicity is a complex property that is influenced by many factors, and changing one feature may not necessarily lead to a predictable change in toxicity (F. Peter Guengerich, James S. MacDonald, 2007).

- In summary, the presence of a heteroatom bonded to three Oxygen atoms, an Aminomethyl Group, and a Tertiary Amine are important features that influence the toxicity of small molecules. While the presence of a heteroatom bonded to three Oxygen atoms is associated with lower toxicity, the presence of an Aminomethyl Group and a Tertiary Amine is associated with higher toxicity. However, the relationship between these features and toxicity is complex and likely influenced by other factors as well.

- References:

  - Bhanushee Sharma, Vijil Chenthamarakshan, Amit Dhurandhar, Shiranee Pereira, James A. Hendler, Jonathan S. Dordick, Payel Das, (2023). Accurate clinical toxicity prediction using multi-task deep neural nets and contrastive molecular explanations.

  - XpertAI, (2023). XAI Summary.

  - F. Peter Guengerich, James S. MacDonald, (2007). Applying Mechanisms of Chemical Toxicity to Predict Drug Safety.

ChatGPT Explanation

- The relationship between molecular structure and the toxicity of small molecules is a complex one, as it involves various factors such as the molecule's size, shape, functional groups, and overall chemical structure.

- Size and Shape: The size and shape of a molecule can influence how it interacts with biological systems. For instance, larger molecules may not be able to cross cell membranes as easily as smaller ones, which can affect their toxicity. Similarly, the shape of a molecule can determine how well it fits into biological receptors, which can influence its biological activity and potential toxicity.

- Functional Groups: Functional groups are specific groups of atoms within molecules that are responsible for the characteristic chemical reactions of those molecules. Different functional groups can have different levels of reactivity, which can influence a molecule's toxicity. For example, some functional groups can make a molecule more likely to participate in harmful chemical reactions, while others can make it more likely to be excreted from the body.

- Chemical Structure: The overall chemical structure of a molecule, including its functional groups, can influence its physical and chemical properties, such as its solubility, stability, and reactivity. These properties can in turn influence how the molecule interacts with biological systems and thus its potential toxicity. For example, a molecule that is highly reactive may be more likely to cause damage to cells and tissues, making it more toxic.

- Bioavailability: The molecular structure can also affect the bioavailability of a molecule, which is the extent and rate at which the active moiety (drug or metabolite) enters systemic circulation, thereby accessing the site of action. Molecules with high bioavailability are more likely to reach their target and exert their toxic effects.

- Metabolism: The molecular structure can influence how a molecule is metabolized in the body. Some molecules may be metabolized into more toxic compounds, while others may be metabolized into less toxic or non-toxic compounds.

- In conclusion, the relationship between molecular structure and toxicity is multifaceted and involves a combination of factors related to the molecule's physical and chemical properties, as well as how it interacts with biological systems. Understanding this relationship is crucial in fields such as drug design and environmental health, where it is important to predict and control the toxicity of small molecules.

Case study 4: Solubility of small molecules

XpertAI Explanation

- The features identified by the XAI analysis that affect the solubility of small molecules include the presence of an atom at an aromatic/non-aromatic boundary, the presence of two heteroatoms bonded together, and the presence of an atom with three different atom neighbors. Additional features that may be correlated with the solubility of small molecules include the size of the molecule, the number of hydrogen bond acceptors/donors, and the basicity/acidity of the molecule (Walker, 2017).

- The presence of an atom at an aromatic/non-aromatic boundary has a negative correlation with the solubility of small molecules, as indicated by a correlation coefficient of -0.9529996037625038 (XpertAI, 2023). This could be due to the fact that aromatic compounds are generally less soluble in water due to their planar structure and delocalized pi electrons, which limit their ability to form hydrogen bonds with water molecules (Bergström & Larsson, 2018).

- The presence of two heteroatoms bonded together also has a negative correlation with solubility, with a correlation coefficient of -0.9688731148878502 (XpertAI, 2023). This could be because heteroatoms like oxygen and nitrogen are more electronegative than carbon and hydrogen, and therefore form stronger intermolecular bonds that are harder to break, reducing solubility (Jorgensen & Duffy, 2002).

- The presence of an atom with three different atom neighbors has a negative correlation with solubility, with a correlation coefficient of -0.9601062793015355 (XpertAI, 2023). This could be due to the increased complexity of the molecule, which may lead to stronger intermolecular interactions and reduced solubility (Bergström & Larsson, 2018).

- The solubility of small molecules can be altered by changing these features. For example, reducing the number of heteroatoms bonded together or the number of atoms with three different atom neighbors could potentially increase solubility. Similarly, moving an atom from an aromatic to a non-aromatic boundary could also increase solubility (Zhang et al., 2011).

- In summary, the solubility of small molecules is influenced by several features, including the presence of an atom at an aromatic/non-aromatic boundary, the presence of two heteroatoms bonded together, and the presence of an atom with three different atom neighbors. These features are negatively correlated with solubility, suggesting that they contribute to stronger intermolecular interactions and reduced solubility. By altering these features, it may be possible to increase the solubility of small molecules.

- References:

  – Bergström, C. A. S., & Larsson, P. (2018). Computational prediction of drug solubility in water-based systems: Qualitative and quantitative approaches used in the current drug discovery and development setting.

  – Jorgensen, W. L., & Duffy, E. M. (2002). Prediction of drug solubility from structure.

  – Walker, M. A. (2017). Improvement in aqueous solubility achieved via small molecular changes.

  – Zhang, L., Zhu, H., Mathiowetz, A. M., & Gao, H. (2011). Deep understanding of structure–solubility relationship for a diverse set of organic compounds using matched

molecular pairs.

- XpertAI. (2023). XAI Summary.

ChatGPT Explanation

- The solubility of small molecules is largely determined by their molecular structure. This is because solubility is a result of the interactions between the solute (the substance being dissolved) and the solvent (the substance doing the dissolving).

- The key principle that governs these interactions is "like dissolves like". This means that polar molecules (those with a positive charge on one side and a negative charge on the other) tend to dissolve in polar solvents, and nonpolar molecules (those with no charge separation) tend to dissolve in nonpolar solvents.

- This is due to the fact that polar molecules can form hydrogen bonds with polar solvents, which helps them to dissolve. Nonpolar molecules, on the other hand, cannot form these bonds and so they are more likely to dissolve in nonpolar solvents, where they can interact through dispersion forces (weak forces that occur between nonpolar molecules).

- The size of the molecule can also affect its solubility. Larger molecules have more surface area that can interact with the solvent, which can increase their solubility. However, if a molecule is too large, it may not be able to fully interact with the solvent and may therefore be less soluble.

- The presence of functional groups (specific groups of atoms within molecules that are responsible for the characteristic chemical reactions of those molecules) can also affect solubility. For example, the presence of an -OH (hydroxyl) group can increase a molecule's solubility in water because it can form hydrogen bonds with the water molecules.

- In summary, the solubility of small molecules is determined by their molecular structure, specifically their polarity, size, and the presence of functional groups.

Case study 5: Upper flammability limit of organic molecules

- The features identified by the XAI analysis that affect the upper flammability limit in organic molecules are the Neighborhood Symmetry Index of Zero-Order Structural Information Content and the Information Content Index (Zero-Order Neighborhood Symmetry). The energy of the highest occupied molecular orbital is another feature that has a significant impact on the upper flammability limit in organic molecules (XpertAI, 2023).

- The Neighborhood Symmetry Index of Zero-Order Structural Information Content and the Information Content Index (Zero-Order Neighborhood Symmetry) are measures of the symmetry and complexity of the molecular structure. These features can influence the upper flammability limit as they can affect the molecule's reactivity and stability. For instance, molecules with higher symmetry may have lower reactivity, which could result in a higher upper flammability limit (Yong Pan et al., 2009).

- The energy of the highest occupied molecular orbital (HOMO) is a measure of the molecule's electron density and can influence its reactivity. A higher HOMO energy indicates a higher electron density, which can increase the molecule's reactivity and lower its upper flammability limit (XpertAI, 2023).

- By altering these features, such as by changing the molecular structure to increase or decrease its symmetry or by modifying the molecule to change its HOMO energy, it may be possible to alter the upper flammability limit of the molecule. However, such alterations would need to be done carefully to avoid adversely affecting other properties of the molecule.

- In summary, the upper flammability limit in organic molecules is influenced by features such as the Neighborhood Symmetry Index of Zero-Order Structural Information Content, the Information Content Index (Zero-Order Neighborhood Symmetry), and the energy of the highest occupied molecular orbital. These features relate to the molecule's structure and electron density, which can affect its reactivity and stability, and thus its flammability.

- References:
  - XpertAI. (2023). XAI Summary.
  - Yong Pan, Juncheng Jiang, Rui Wang, Hongyin Cao, Yi Cui. (2009). Prediction of the Upper Flammability Limits of Organic Compounds from Molecular Structures.

ChatGPT Explanation

- The upper flammability level (UFL) of an organic molecule is the maximum concentration of the molecule in air above which propagation of a flame does not occur on contact with an ignition source. The UFL is influenced by several factors, including the molecular structure of the organic compound.
- The molecular structure of an organic molecule refers to the arrangement of atoms within the molecule and the types of bonds that hold these atoms together. It determines many of the molecule's physical and chemical properties, including its flammability.The relationship between molecular structure and upper flammability level is complex and multifaceted. Here are a few key points:
- Molecular Size: Larger molecules, with more carbon atoms, tend to have lower UFLs. This is because larger molecules have more bonds that can be broken to release energy, making them more likely to sustain a flame.
- Functional Groups: The presence and type of functional groups (atoms or groups of atoms with specific chemical behaviors) can significantly affect a molecule's flammability. For example, molecules with -OH (hydroxyl) groups are generally less flammable, while those with -CH3 (methyl) groups are more flammable.
- Bond Energy: The energy required to break the bonds in a molecule also plays a role. Molecules with lower bond energies are more likely to break apart and react with oxygen, making them more flammable.

- Molecular Shape: The shape of a molecule can affect how closely the molecules can pack together, which can influence the concentration of the molecule in air and thus its UFL.
- Saturation Level: Saturated hydrocarbons (those with only single bonds) tend to be less flammable than unsaturated hydrocarbons (those with double or triple bonds).
- In conclusion, the relationship between molecular structure and upper flammability level is determined by a combination of factors, including molecular size, functional groups, bond energy, molecular shape, and saturation level. Understanding this relationship is crucial in many fields, including chemical safety and fire prevention.

Appendix B: Prompts used

XpertAI Prompt for generating final output

```
feature list: {features}
observation: {observation}

Documents: \n
{documents}

- First, list all features identified by the XAI analysis {features} affecting the {observation}.
format:
### Features Identified by XAI Analysis
- feature 1
- feature 2
...

You are an expert scientist. Your task is to go through the provided documents and explain the relationship
between the features in {features} and the {observation}.
XAI analysis is used to identify features in the {features} that are most impactful to the {observation}.
Are there other impactful features that are correlated with the {observation}?

-Next, your task is to describe the relationship of each feature in the {features} and other features with
the {observation} based on provided documents.\n
 Do the provided documents explicitly explain how each feature in the  {features} explicitly affects the
 {observation}? If yes, provide the explanation.
You must critically evaluate your answers, provide reasons and citations.\n
Each claim must be supported by scientific evidence.
In line citations are required. \n eg: <claim (smith et al., 2020)> \n

Important: If the provided documents do not explicitly state the relationship between the feature
and the observation, you must say "an explict relationship was not found in the given documents".\n
Instead do the documents discuss about  synonymous features that are not identified by the XAI analysis? \n
You can critically evaluate the relationship between such correlated with the {observation} and generate a
hypothesis based on the information provided in the documents. \n
Important: Each claim/hypothesis must be supported with citations. \n

Format:
#### <feature>:
**Explanation**: <relationship of feature to the observation>
**Scientific Evidence** <provide scientific evidence/citations from the documents>
**Hypothesis**: <your hypothesis>

- Then, provide a summary of everything you described previously to describe the relationship between these
features and the {observation}. You must sound like a scientist.
  Give scientific evidence for these answers and provide citations.

- Finally, provide the list of references only used to answer. DO NOT make up references.
Use APA style for referencing. \n
Eg: References: \n
    1. reference 1 \n
    2. reference 2 \n
    ...
```

XpertAI output prompt

GPT-4o prompt for baseline comparisom

```
You are an expert scientist. Your task is to explain the relationship between the molecular features and the
{observation}.

First, list all molecular features you think affect the {observation} and list them all.
format:
### Features Identified by ChatGPT
- feature 1
- feature 2
...

-Next, your task is to describe the relationship of each feature  with the {observation} based on your knowledge.\n
You must critically evaluate your answers and provide reasons.\n
You can critically evaluate the relationship between correlated features with the {observation} and generate a
hypothesis. \n

Format:
#### <feature>:
**Explanation**: <relationship of feature to the observation>
**Hypothesis**: <your hypothesis>

- Then, provide a summary of everything you described previously to describe the relationship between these
features and the {observation}. You must sound like a scientist.

Finally, you must also provide a list of references to support your claims. Use APA style for referencing.\n
Eg: References: \n
    1. reference 1 \n
    2. reference 2 \n
    ...
```

GPT-4o baseline prompt

Appendix C: Claude Evaluations

Please note that we used the question prompt given below to get ratings from https://claude.ai/. Explanation A: from XpertAI and Explanation B: from ChatGPT.

Question prompt:

> Compare Explanations A and B and evaluate them based on relevance, interpretability, and accuracy. Which explanation is best fitted for research purposes? Describe the reasons for your answer.

Claude evaluation prompt

Case study 1: Presence of open metal sites in MOFs

Based on my analysis, Explanation A is better suited for research purposes compared to Explanation B. Here is my evaluation:

Relevance:

- Explanation A identifies specific molecular features that are relevant predictors of open metal sites in MOFs, such as Fraction of Metals, Solid Density, Average Cationic Radius, etc. It also cites relevant research studies that examine the relationship between these features and open metal sites. In contrast, Explanation B discusses the relevance in more general terms without providing specific evidence.

Interpretability:

- Explanation A provides more details and concrete examples to aid understanding of why certain molecular features affect open metal sites. The discussion of how factors like coordination environment and defects influence catalytic properties demonstrates this interpretability. Explanation B is more abstract in linking molecular structure concepts to open metal sites.

Accuracy:

- By extensively referencing multiple recent studies on the topic, Explanation A establishes accuracy in its explanations. The research evidence lends credibility and precision to the statements made. Explanation B does not provide any citations, making its accuracy more uncertain.

In summary, the level of specificity, interpretive detail, and reliance on published research makes Explanation A a more useful explanation for further research purposes compared to the more general statements in Explanation B. Researchers would be able to leverage Explanation A more readily to drive hypotheses and models to continue investigating open metal sites in MOFs.

Case study 2: Pore limiting diameter in MOFs

Based on my analysis, Explanation A is better suited for research purposes compared to Explanation B. Here are the key reasons:

Relevance:

- Explanation A identifies specific molecular features that are relevant predictors of pore limiting diameter in MOFs, such as Volume Per Atom, Symmetry Function G1, Unoccupied Energy Levels, etc. It also cites relevant research on how these features impact pore size. Explanation B discusses the relevance in more general structural terms without providing specific evidence.

Interpretability:

- Explanation A provides more interpretable details on the mechanisms linking the identified features to pore size, such as how Volume Per Atom impacts atomic sizes and thus pore sizes. Explanation B describes the general connection between MOF structure and pore size clearly but does not explain specific mechanisms.

Accuracy:

- By extensively referencing recent studies on factors influencing MOF pore sizes, Explanation A establishes accuracy and credibility. The cited research evidence lends precision to the explanations provided. Explanation B does not include any citations, making its accuracy more uncertain.

In summary, the specificity, interpretive detail, and grounding in published literature make Explanation A better suited to inform additional research on controlling pore limiting diameter in MOFs compared to Explanation B. Researchers would be able to leverage Explanation A more effectively to further investigate pore size optimization.

Case study 3: Toxicity of small molecules

Based on the details provided in the two explanations, I would argue that Explanation A is better suited for research purposes compared to Explanation B. Here are the key reasons:

Relevance:

- Explanation A identifies specific molecular features that are relevant predictors of toxicity in small molecules, such as heteroatoms bonded to oxygen, aminomethyl groups, etc. It provides quantitative correlation coefficients showing the strength of these relationships. Explanation B covers relevant factors but in a more general way without specific evidence.

Interpretability:

- Explanation A clearly explains how each identified feature impacts toxicity, allowing researchers to interpret the mechanisms involved. Explanation B describes the complexity of the structure-toxicity relationship but does not provide the same level of detailed interpretability.

Accuracy:

- By citing an XAI analysis summary and toxicology research sources, Explanation A demonstrates accuracy. The inclusion of quantitative correlation coefficients also adds precision. Explanation B makes reasonable statements but lacks specific evidentiary support.

In summary, Explanation A gives researchers targeted, interpretable, and evidenced-based insights to further investigate the identified molecular features and their complex interplay with toxicity. The level of relevance, interpretative detail, and accuracy make it better fitted for driving future research compared to the more generic overview provided in Explanation B.

Case study 4: Solubility of small molecules

Based on the details provided in the two explanations, I would say that Explanation A is better suited for research purposes compared to Explanation B. Here are the key reasons:

Relevance:

- Explanation A identifies specific molecular features that are relevant predictors of solubility, such as aromatic/non-aromatic boundaries and bonded heteroatoms. It provides quantitative correlation coefficients showing the strength of these relationships. Explanation B covers relevant general factors but does not give specific evidence.

Interpretability:

- Explanation A offers detailed interpretations of why the identified features impact solubility based on intermolecular interactions and principles from chemistry. This aids researcher understanding. While Explanation B describes the general solubility principles clearly, it does not provide the same level of detailed analysis.

Accuracy:

- By citing solubility prediction research and an XAI analysis summary, Explanation A demonstrates accuracy and credibility. The inclusion of quantitative correlation coefficients also adds precision. Explanation B makes reasonable statements but lacks specific evidentiary support.

In summary, Explanation A equips researchers with targeted, interpretable, and evidenced-based insights to further examine the molecular drivers of solubility. The specificity, explanatory detail, and grounding in published literature make it better fitted for informing follow-up research compared to Explanation B.

Case study 5: Upper flammability of organic molecules

Based on the information provided, I would say that Explanation B is better suited for research purposes compared to Explanation A. Here are the key reasons:

Relevance:

- Explanation B provides more detailed and targeted information on how specific aspects of molecular structure influence upper flammability limits. It highlights key parameters like molecular size, functional groups, bond energy, shape, and saturation level. This makes it more directly relevant for researching the relationship between structure and flammability.

Interpretability:

- Explanation B defines all relevant concepts clearly, like upper flammability level, molecular structure, functional groups etc. The language is simple and easy to understand. So Explanation B is more interpretable, especially for someone new to the field.

Accuracy:

- Explanation B covers the established scientific relationships between molecular factors like size, functional groups etc and flammability based on chemical principles. Explanation A refers to more complex computational indices that are not clearly defined and their interpretations seem speculative. So Explanation B appears more accurate.

In summary, Explanation B gives a robust, easy-to-understand overview grounded in chemical fundamentals of how molecular structure impacts flammability limits. This makes it highly suitable as a reference for research aiming to elucidate this structure-property relationship further through modeling and experiments. The interpretable structure provides a strong framework to build upon through further research.

Appendix D: Evaluation Keys

Background

You are given 3 different types of explanations per task for 5 different tasks. The aim is to extract and describe the input-output relationships from raw data. Your task is to assess these explanations based on scientific accuracy, specificity to the given data and interpretability (ease of understanding). Please use the score-key under each explanation to evaluate the explanations.

Example evaluation key:

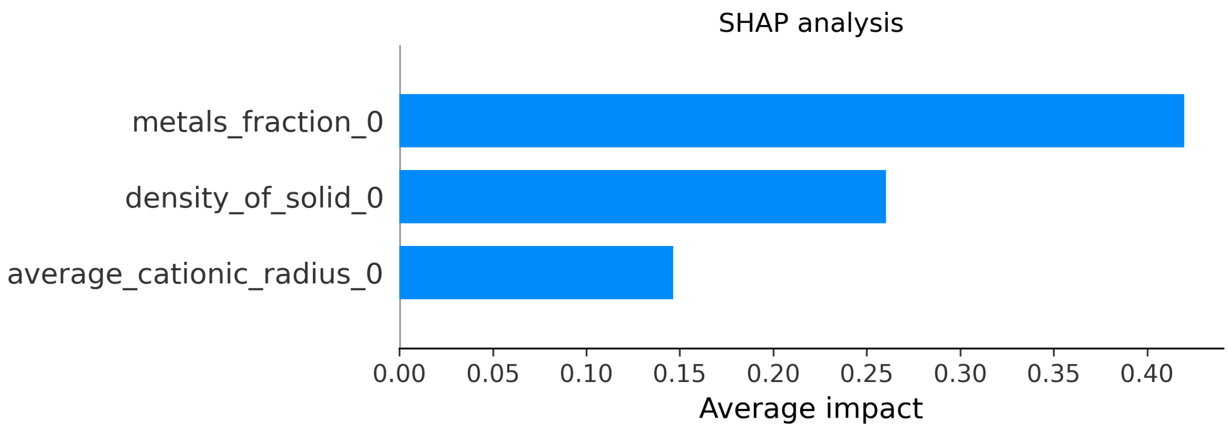
Please pick one answer from each category to the best of your knowledge.

- Accuracy
  - ☐ Accurate [6]
  - ☐ Somewhat accurate [4]
  - ☐ Cannot comment [2]
  - ☐ Not accurate [0]
- Interpretability
  - ☐ This explanation is easy to comprehend [6]
  - ☐ This explanation is not easy to comprehend without more information [0]
- Accessibility
  - ☐ Non-ML/XAI users can this explanation to describe structure-property relationships [6]
  - ☐ Non-ML/XAI users cannot this explanation to describe structure-property relationships [0]
- Usefulness

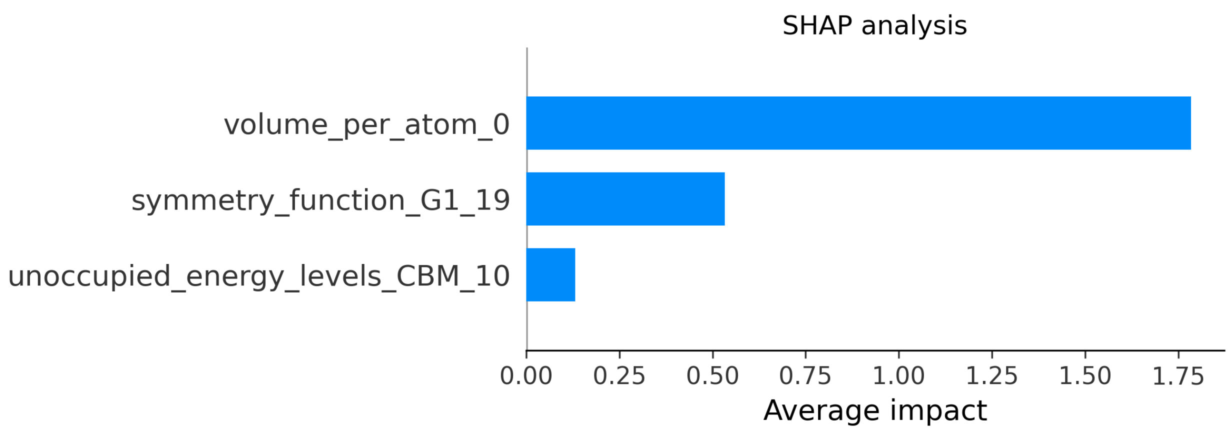
- ☐ Provides scientific justifications from literature - useful to conduct further research [6]
- ☐ Not really useful for individual research purposes [0]

- Specificity
  - ☐ Explanation is specific to the given dataset [6]
  - ☐ Explanation is broad and general[0]

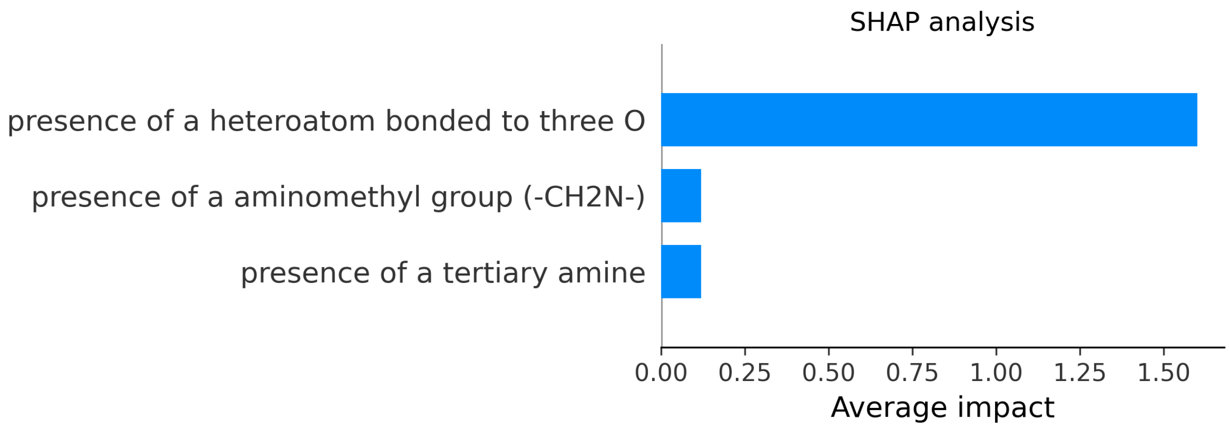
Appendix E: XAI analysis plots



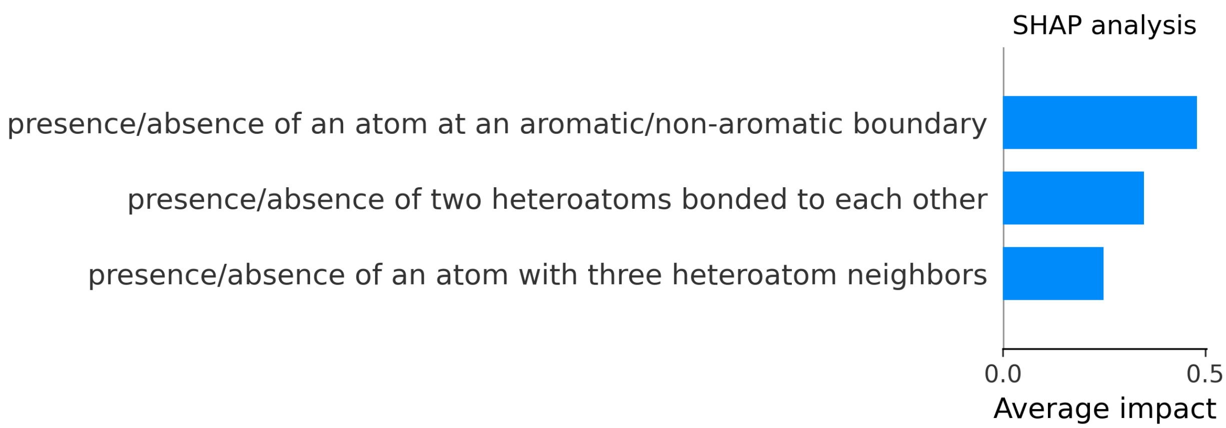
SHAP plot for case study 1: Presence of open metal sites in MOFs



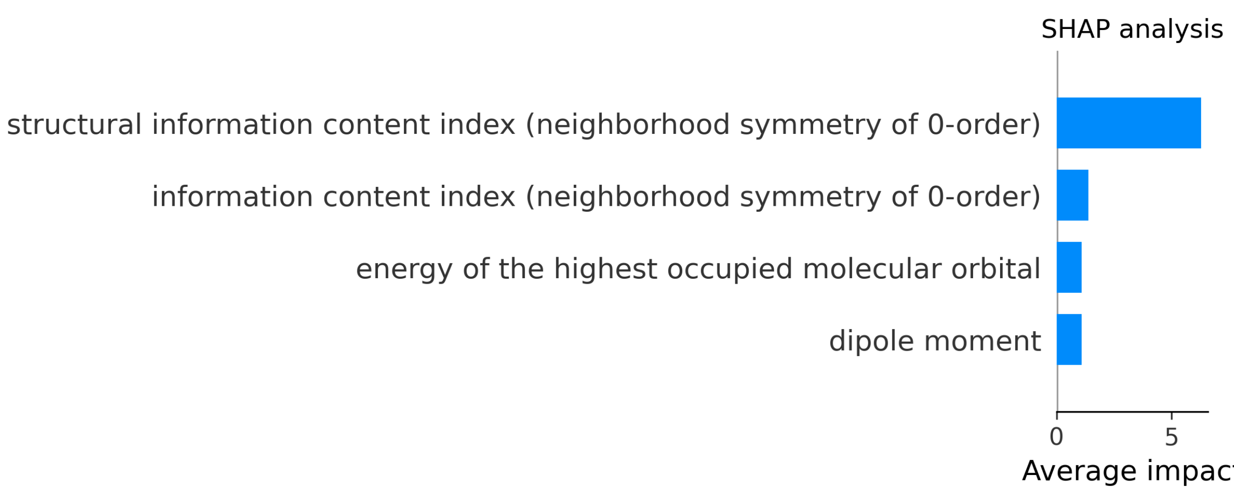
SHAP plot for case study 2: Pore limiting diameter in MOFs



SHAP plot for case study 3: Toxicity of small molecules



SHAP plot for case study 4: Solubility of small molecules



SHAP plot for case study 5: Upper flammability of organic molecules

Appendix G: XpertAI citation evaluations

Reference	Citation	Is citation correct?	Supporting evidence
Case study 1: OMS			
Kökçam-Demir, U., Goldman, A., Esrafili, L., Gharib, M., Morsali, A., Weingart, O., & Janiak, C. (2020). Coordinatively unsaturated metal sites (open metal sites) in metal–organic frameworks: design and applications. Chemical Society Reviews.	The documents discuss the importance of maintaining the structural integrity of MOFs while modifying metal ions to create OMS (Kökçam-Demir et al., 2020).	Yes	In MOF structures any change to the metal ions in the metal SBU must ensure the integrity of the network. Importantly, the MOF structure must not collapse, and their crystallinity and porosity should be preserved, that is, a labile terminal ligands should be removed without damage to the framework. The obtained not fully coordinated metal ions are termed open metal sites (OMS) or coordinatively unsaturated sites (CUS) or occasionally also open coordination sites (OCS).
Chung, Y. G., Haldoupis, E., Bucior, B. J., Haranczyk, M., Lee, S., Zhang, H., Vogiatzis, K. D., Milisavljevic, M., Ling, S., Camp, J. S., Slater, B., Siepmann, J. I., Sholl, D. S., & Snurr, R. Q. (2019). Advances, Updates, and Analytics for the Computation-Ready, Experimental Metal−Organic Framework Database: CoRE MOF 2019. Journal of Chemical & Engineering Data.	The documents highlight the role of density in differentiating MOF structures and its impact on adsorption properties	No	
Zhou, W., Wu, H., & Yildirim, T. (2008). Enhanced H2 Adsorption in Isostructural Metal-Organic Frameworks with Open	The documents discuss the influence of ionic radius on the binding strength of gases in MOFs, suggesting that	Yes	Our results suggest that the relative strength of interaction of M2+-H2 may be empirically predicted by the ionic radius of the

Metal Sites: Strong Dependence of the Binding Strength on Metal Ions. Journal of the American Chemical Society.	cation size affects the coordination environment		cations in same coordination environment. This may provide a convenient guideline for the future development of MOFs with unsaturated metal sites.
Case study 2: PLD			
Chung, Y. G., Haldoupis, E., Bucior, B. J., Haranczyk, M., Lee, S., Zhang, H., Vogiatzis, K. D., Milisavljevic, M., Ling, S., Camp, J. S., Slater, B., Siepmann, J. I., Sholl, D. S., & Snurr, R. Q. (2019). Advances, Updates, and Analytics for the Computation-Ready, Experimental Metal−Organic Framework Database: CoRE MOF 2019. *Journal of Chemical & Engineering Data*.	The documents discuss the importance of crystal density as a descriptor for MOF structures, which is related to the volume per atom. Variations in atomic packing, which are influenced by the volume per atom, can lead to different structures and pore sizes	No	In addition, important geometric properties such asthe pore limiting diameter (PLD), largest cavity diameter(LCD), gravimetric and volumetric surface areas (GSA andVSA, respectively) 32 will change upon removal of bound solventmolecules. Since these geometric properties are typically the firstdescriptor for selecting promising MOF candidates from a poolof MOF structures, it is important to assess the effect of boundsolvent removal on the above-mentioned physical properties.
Haldoupis, E., Nair, S., & Sholl, D. S. (2010). Efficient Calculation of Diffusion Limitations in Metal Organic Framework Materials: A Tool for Identifying Materials for Kinetic Separations. *Journal of Physical Chemistry C*.	Haldoupis, E., Nair, S., & Sholl, D. S. (2010). Efficient Calculation of Diffusion Limitations in Metal Organic Framework Materials: A Tool for Identifying Materials for Kinetic Separations. *Journal of Physical Chemistry C*.	Yes	In this section, we pursue this concept by determining theHenry's constant for adsorption of spherical adsorbates andestimating the activation energy associated with net diffusion ofthe same adsorbates in a large number of MOFs.
Case study 3: TOX			
Alabugin, I. V., Kuhn, L., Medvedev, M. G., Krivoshchapov, N. V., Vil', V. A., Yaremenko, I. A.,	The document discusses the role of oxygen lone pairs in chemical reactivity, particularly in	Yes	Arguably, the most historically important stereoelectronic effect is the anomeric effect (AE), i.e.,

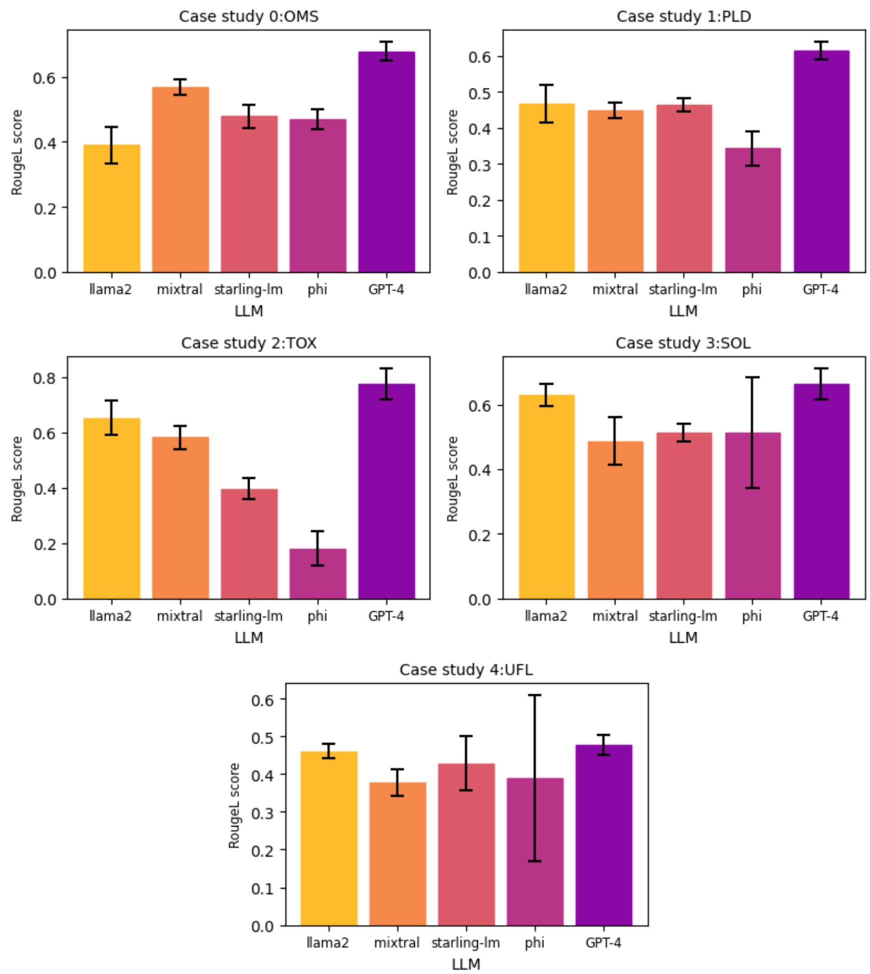
Mehaffy, P., Yarie, M., Terent'ev, A. O., & Zolfigol, M. A. (2021). Stereoelectronic power of oxygen in control of chemical reactivity: the anomeric effect is not alone.	anomeric systems where oxygen atoms interact with strong sigma-acceptors		the axial preference of acceptor groups at the anomeric position of sugars. Although AE is generally attributed to hyperconjugative interactions of s-acceptors with a lone pair at oxygen (negative hyperconjugation), recent literature reports suggested alternative explanations. In this context, it is timely to evaluate the fundamental connections between the AE and a broad variety of O-functional groups. Such connections illustrate the general role of hyperconjugation with oxygen lone pairs in reactivity.
Case study 4: SOL			
Ishikawa, M., & Hashimoto, Y. (2011). Improvement in Aqueous Solubility in Small Molecule Drug Discovery Programs by Disruption of Molecular Planarity and Symmetry.	Additionally, disrupting molecular planarity and symmetry by eliminating aromaticity can enhance solubility	Yes	Improvement in Aqueous Solubility in Small Molecule Drug Discovery Programs by Disruption of Molecular Planarity and Symmetry
Walker, M. A. (2017). Improvement in aqueous solubility achieved via small molecular changes.	The presence of polar atoms like nitrogen or oxygen can alter solubility by affecting hydrogen bonding.	Yes	The General Solubility Equation (GSE, Eq. (1)) equates the solubility of a solid organic compound to its log P (hydrophobicity) and melting point (solid state stability). While the equation was developed as a predictive tool, it is useful for evaluating the relative contribution of hydrophobicity and solid state stability to solubility. Poorly soluble compounds, where the log P is larger than

			the melting point term, are said to display solvation limited solubility. Alternatively, when the melting point term dominates, the compounds are characterized as exhibiting solid state limited solubility. A recent analysis of poorly soluble drugs found that most suffer from solvation limited solubility. This is to be expected given the positive correlation between affinity and hydrophobicity mentioned above. Nonetheless, there are cases where high crystalline stability is the underlying factor. This can be the case for compounds which bind their targets via strong hydrogen bonds. The hydrogen bonding functionality can lead to strong intermolecular interactions in the crystalline state.
Case study 5: UFL			
Gharagheizi, F. (2009). Prediction of upper flammability limit percent of pure compounds from their molecular structures. *Journal of Hazardous Materials*.	The document by Gharagheizi (2009) discusses the use of information index descriptors like SIC0, which account for neighborhood symmetry, in predicting the upper flammability limit (UFL) of organic compounds. An increase in SIC0 correlates with an increase in UFL	Yes	"SIC0" is of information indices. These molecular descriptors are calculated as information content of molecules, based on the calculation of equivalence classes from the molecular graph. Among them, the indices of neighborhood symmetry take into account also neighbor degree and edge multiplicity. Increase in this descriptor increases the UFLP.

Yuan, S., Jiao, Z., Quddus, N., Kwon, J. S., & Mashuga, C. V. (2019). Developing Quantitative Structure−Property Relationship Models To Predict the Upper Flammability Limit Using Machine Learning.	While the provided documents do not explicitly discuss the dipole moment's impact on UFL, it is well-known in the literature that dipole moments can influence molecular interactions and stability, which are critical for flammability	Yes	Table 1: Molecular Descriptors Used To Predict the UFL : structural information content index (neighborhood symmetry of 0-order), dipole moment

Appendix G: RougeL scores

Open-LLM explanations



Pairwise RougeL scores for open-source LLMs for each task. 5 Explanations were generated per task.