**Prompt Testing & Model Assessment**

**Feb 24, 2025**

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**Conversation with Argo (GPT-4o) *without* the Socratic method**

Question:

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| I am interested in calculating the binding energy of organic solvents to the Zn cation (2+) using molecular orbital DFT calculations (Gaussian). The overarching goal of the calculation is to build a predictive model of the solubility of Zn salts in organic solvents for non-aqueous Zn organic battery applications. The Zn-binding energy will be used as a parameter along with some others, including frontier orbital energies, polarizability, atomic charge, etc.  The binding energy of the solvent to Zn cation (2+) was found to be an important parameter for solubility, where there is a general tendency that the stronger the binding energy, the higher the salt solubility. However, the Zn-binding energy calculation is extremely complicated since organic molecules are different in many aspects, e.g., size number/location of atoms interacting with Zn (e.g., O and N), and bulkiness. Hence, for example, the comparison of the Zn-binding energy of a molecule with one oxygen to that of a molecule with two oxygen is unfair.  My question is, how can I overcome this problem in the determination of Zn-binding energies? In other words, how can I make a fair comparison of a set of organic molecules for the Zn-binding energy prediction in the molecular DFT calculations?  Do not forget that I am interested in the Zn-salts solubility prediction and my current plan is to use a Zn-binding energy as one of the parameters for that. |

Response:

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| To address the challenge of fairly comparing the Zn-binding energies of different organic solvents, you can adopt a systematic approach that accounts for the inherent differences in molecular structure and interaction sites. Here are some strategies you might consider:   1. **Standardize the Binding Site**: Focus on comparing the binding energies at specific functional groups that are common across different solvents. For example, if you're comparing solvents with oxygen atoms, ensure that you're evaluating the binding energy at similar functional groups (e.g., carbonyl, hydroxyl) to maintain consistency. 2. **Fragment-Based Approach**: Break down the molecules into smaller fragments that contain the binding sites of interest. Calculate the binding energy for these fragments with the Zn cation. This approach allows you to isolate the contribution of specific functional groups to the overall binding energy. 3. **Use of Reference Compounds**: Select a set of reference compounds with well-characterized binding energies to Zn. Use these as benchmarks to normalize the binding energies of your solvents. This can help account for differences in molecular size and complexity. 4. **Binding Energy per Interaction Site**: Normalize the binding energy by the number of interaction sites (e.g., oxygen or nitrogen atoms) in the molecule. This approach allows you to compare the efficiency of each interaction site in binding to Zn. 5. **Consider Solvent Bulkiness**: Incorporate steric factors into your model by calculating the binding energy per unit volume or per molecular weight. This can help account for the impact of bulkiness on binding efficiency. 6. **Use of Continuum Solvation Models**: When performing DFT calculations, consider using a continuum solvation model to simulate the solvent environment. This can help account for solvation effects that influence binding energy. 7. **Machine Learning Models**: Once you have a dataset of binding energies and other molecular descriptors (e.g., frontier orbital energies, polarizability), consider using machine learning techniques to build a predictive model. This can help identify patterns and relationships that are not immediately obvious. 8. **Comparative Analysis with Similar Solvents**: Group solvents with similar structural features and compare their binding energies within these groups. This can help reduce the variability introduced by structural differences.   By employing these strategies, you can create a more robust and fair comparison of Zn-binding energies across different organic solvents, ultimately aiding in the prediction of Zn salt solubility in non-aqueous battery applications. |

**Conversation with Argo (GPT-4o) *with* the Socratic method**

Question:

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| I am interested in calculating the binding energy of organic solvents to the Zn cation (2+) using molecular orbital DFT calculations (Gaussian). The overarching goal of the calculation is to build a predictive model of the solubility of Zn salts in organic solvents for non-aqueous Zn organic battery applications. The Zn-binding energy will be used as a parameter along with some others, including frontier orbital energies, polarizability, atomic charge, etc.  The binding energy of the solvent to Zn cation (2+) was found to be an important parameter for solubility, where there is a general tendency that the stronger the binding energy, the higher the salt solubility. However, the Zn-binding energy calculation is extremely complicated since organic molecules are different in many aspects, e.g., size number/location of atoms interacting with Zn (e.g., O and N), and bulkiness. Hence, for example, the comparison of the Zn-binding energy of a molecule with one oxygen to that of a molecule with two oxygen is unfair.  My question is, how can I overcome this problem in the determination of Zn-binding energies? In other words, how can I make a fair comparison of a set of organic molecules for the Zn-binding energy prediction in the molecular DFT calculations?  Do not forget that I am interested in the Zn-salts solubility prediction and my current plan is to use a Zn-binding energy as one of the parameters for that. **Choose the best principles on your own.** |

Response:

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| Selected Principle(s): Definition, Hypothesis Elimination, Generalization  To address your query, we will first define the key concepts involved, then explore potential hypotheses for overcoming the challenges in comparing Zn-binding energies, and finally generalize a method for fair comparison across different organic molecules.  Socratic Reformulation: How can we define and standardize the calculation of Zn-binding energies in a way that allows for fair comparison across diverse organic molecules, considering their structural differences and the goal of predicting Zn salt solubility?  Self-Query and Answer: To make a fair comparison of Zn-binding energies across different organic molecules, we need to establish a standardized approach that accounts for structural differences such as the number and type of coordinating atoms (e.g., O, N) and the bulkiness of the molecules. One potential method is to normalize the binding energy with respect to the number of coordinating atoms or the molecular size. This could involve calculating a "per atom" binding energy or using a reference molecule to calibrate the energies. Additionally, considering the role of steric effects and electronic factors, we might incorporate parameters such as steric hindrance or electronic descriptors (e.g., frontier orbital energies) into the model to adjust the binding energy values accordingly.  Follow-Up Questions (Using Mixed Socratic Prompting):   1. Definition → Hypothesis Elimination → Dialectic:    * How can we define a standardized metric for Zn-binding energy that accounts for the number of coordinating atoms and molecular size?    * What hypotheses can we test to determine the most effective way to normalize Zn-binding energies for fair comparison?    * How do different approaches to normalization reconcile the contradictions between structural diversity and binding energy prediction? 2. Elenchus → Analogy → Induction:    * Are there assumptions in your current method of calculating Zn-binding energies that might lead to inconsistencies when comparing different molecules?    * Can you think of an analogy from another field where normalization techniques have been successfully applied to compare diverse entities?    * What general principles can we derive from these analogies to improve the accuracy of Zn-binding energy predictions? 3. Generalization → Induction → Recollection:    * What overarching patterns can be identified in the binding energies of molecules with similar structural features?    * How can these patterns be used to induce a more accurate predictive model for Zn salt solubility?    * What prior studies or experiments provide insights into effective methods for normalizing binding energies in complex systems?   By addressing these questions, you can develop a more robust and fair method for comparing Zn-binding energies, ultimately enhancing the predictive power of your solubility model for Zn salts in organic solvents. |

1st follow-up question:

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| Are there assumptions in your current method of calculating Zn-binding energies that might lead to inconsistencies when comparing different molecules?  Can you think of an analogy from another field where normalization techniques have been successfully applied to compare diverse entities?  What general principles can we derive from these analogies to improve the accuracy of Zn-binding energy predictions? |

*\*The prompt that SM Argo suggested*

Response:

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| Selected Principle(s): Elenchus, Analogy, Induction  To explore potential assumptions in your current method and draw insights from analogous situations in other fields, we will challenge existing assumptions, use analogies to find parallels, and induce general principles that can enhance your approach.  Socratic Reformulation: What assumptions in your current Zn-binding energy calculations could lead to inconsistencies, and how can analogies from other fields inform the development of general principles to improve these calculations?  Self-Query and Answer:   1. **Assumptions in Current Method**: One assumption might be that all coordinating atoms contribute equally to the binding energy, regardless of their chemical environment or steric hindrance. Another assumption could be that the bulkiness of the molecule does not significantly affect the binding energy, which might not hold true for larger or more complex molecules. Additionally, the method might assume that the solvent environment does not alter the binding energy significantly, which could lead to inconsistencies when comparing molecules with different solvation properties. 2. **Analogy from Another Field**: In the field of pharmacology, normalization techniques are often used to compare the efficacy of drugs with different potencies and mechanisms of action. For example, the concept of "dose normalization" allows researchers to compare the effects of drugs by adjusting for differences in dosage and bioavailability. Similarly, in economics, "purchasing power parity" is used to compare the economic productivity and standards of living between countries by normalizing for currency differences. 3. **General Principles Derived from Analogies**:    * **Normalization**: Just as dose normalization adjusts for potency, you could normalize Zn-binding energies by considering the number of coordinating atoms or the molecular size, creating a "per atom" or "per unit volume" metric.    * **Contextual Adjustment**: Similar to how purchasing power parity accounts for economic context, you might adjust binding energies for the electronic and steric environment of the coordinating atoms.    * **Comparative Baselines**: Establishing a baseline or reference molecule, akin to a control in pharmacological studies, could help calibrate and compare binding energies across different molecules.   Follow-Up Questions (Using Mixed Socratic Prompting):   1. **Elenchus → Definition → Hypothesis Elimination**:    * What specific assumptions about the chemical environment and steric effects might be leading to inconsistencies in your calculations?    * How can we define a standardized approach to account for these factors in Zn-binding energy calculations?    * What hypotheses can be tested to determine the most effective normalization method for these energies? 2. **Analogy → Induction → Recollection**:    * How do normalization techniques in pharmacology and economics address variability, and what parallels can be drawn to your Zn-binding energy calculations?    * What general principles can be induced from these analogies to enhance the accuracy and fairness of your predictions?    * Can you recall any previous studies or methodologies that successfully applied similar normalization techniques in chemical calculations? 3. **Induction → Generalization → Dialectic**:    * What trends or patterns emerge when applying normalization techniques to Zn-binding energies across different molecules?    * How can these patterns be generalized to improve the predictive model for Zn salt solubility?    * In what ways might these generalizations challenge or align with existing theories of solubility and binding energy?   By addressing these questions, you can refine your approach to calculating Zn-binding energies, ensuring that comparisons are fair and predictions are more accurate. |

2nd follow-up question:

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| So the overall idea that you came up with is normalization.  Let's Imagine two different organic solvents:  The first solvent molecule (A) is bulky and has two oxygen atoms. It highly strongly binds Zn due to the formation of two Zn-O bonds. One Zn cation can interact with up to two molecules, forming 4 Zn-O bonds in total. The addition of the third molecule is prohibited due to the steric hindrance.  The second molecule (B) is small and has only one oxygen atom. The Zn-binding energy of this molecule is relatively smaller than that of A due to the presence of one less oxygen and the lack of electronic effects of bulky ligands. However, one Zn can coordinate with up to 6 molecules due to the minimal steric effects.  If I compare the normalized Zn-binding energy per oxygen, it is higher in A. However, the unnormalized Zn-binding energy at the maximum Zn-O coordination is higher in B, since B has the larger number of Zn-O bonds.  In this case, which organic molecule is more likely to have a higher Zn-salt solubility? And which metric of the Zn-binding energy will be more appropriate to use?If I compare the normalized Zn-binding energy per oxygen, it is higher in A. However, the unnormalized Zn-binding energy is higher in B, since B has a larger number of Zn-O bonds.  In this case, which organic molecule is more likely to have a higher Zn-salt solubility? And which metric of the Zn-binding energy will be more appropriate to use? |

*\*The prompt that I made*

Response:

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| Selected Principle(s): Definition, Dialectic, Hypothesis Elimination  To address your query, we will first define the key metrics for Zn-binding energy, then explore the opposing viewpoints regarding solubility prediction, and finally evaluate which metric might be more appropriate for your specific application.  Socratic Reformulation: How do we define and compare the metrics of Zn-binding energy for molecules A and B, and which metric better predicts Zn-salt solubility in these solvents?  Self-Query and Answer:   1. **Definition of Metrics**:    * **Normalized Zn-Binding Energy per Oxygen**: This metric considers the binding energy contribution of each oxygen atom, providing insight into the strength of individual Zn-O interactions.    * **Unnormalized Zn-Binding Energy at Maximum Coordination**: This metric reflects the total binding energy when Zn is fully coordinated by the solvent molecules, indicating the overall binding capacity. 2. **Dialectic Examination**:    * **Viewpoint 1**: Molecule A, with higher normalized binding energy per oxygen, suggests stronger individual Zn-O interactions, which might imply higher solubility if solubility is driven by strong, specific interactions.    * **Viewpoint 2**: Molecule B, with higher unnormalized binding energy at maximum coordination, suggests greater overall binding capacity, which might imply higher solubility if solubility is driven by the total number of interactions. 3. **Hypothesis Elimination**:    * To determine which metric is more appropriate, consider the mechanism by which Zn-salt solubility is achieved. If solubility is primarily driven by the strength of individual interactions, the normalized metric might be more relevant. Conversely, if solubility is driven by the total number of interactions, the unnormalized metric could be more predictive.   Follow-Up Questions (Using Mixed Socratic Prompting):   1. **Definition → Hypothesis Elimination → Dialectic**:    * How do we define the relationship between Zn-binding energy and solubility in terms of individual versus total interactions?    * What hypotheses can be tested to determine whether solubility is more influenced by the strength of individual interactions or the total number of interactions?    * How do these hypotheses align or conflict with existing theories of solubility in non-aqueous systems? 2. **Elenchus → Analogy → Induction**:    * Are there assumptions about the role of steric effects and electronic contributions in your current solubility model that might lead to inconsistencies?    * Can you think of an analogy from another chemical system where solubility is influenced by similar factors?    * What general principles can be induced from these analogies to refine your solubility predictions? 3. **Induction → Generalization → Recollection**:    * What patterns emerge when comparing solubility predictions based on normalized versus unnormalized Zn-binding energies across different solvents?    * How can these patterns be generalized to improve the predictive model for Zn salt solubility?    * What prior studies or experimental data provide insights into the relative importance of individual versus total interactions in solubility?   By addressing these questions, you can determine which metric of Zn-binding energy is more appropriate for predicting Zn-salt solubility in your specific context. |

3rd follow-up question:

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| How do we define the relationship between Zn-binding energy and solubility in terms of individual versus total interactions?  What hypotheses can be tested to determine whether solubility is more influenced by the strength of individual interactions or the total number of interactions?  How do these hypotheses align or conflict with existing theories of solubility in non-aqueous systems? |

*\*The prompt that SM Argo suggested*

Response:

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| Selected Principle(s): Definition, Hypothesis Elimination, Dialectic  To explore the relationship between Zn-binding energy and solubility, we will define the relevant interactions, propose testable hypotheses, and examine how these align or conflict with existing solubility theories.  Socratic Reformulation: How can we define the relationship between Zn-binding energy and solubility in terms of individual versus total interactions, and what hypotheses can be tested to determine the dominant influence on solubility? How do these hypotheses align with existing theories of solubility in non-aqueous systems?  Self-Query and Answer:  Definition of Relationship:  Individual Interactions: This refers to the strength of each Zn-O bond. Strong individual interactions might suggest that fewer but stronger bonds could lead to higher solubility if solubility is driven by specific, strong interactions.  Total Interactions: This refers to the cumulative effect of all Zn-O bonds formed. A higher total number of interactions might suggest that solubility is driven by the overall binding capacity, regardless of the strength of individual bonds.  Hypotheses for Testing:  Hypothesis 1: Solubility is primarily influenced by the strength of individual Zn-O interactions. This can be tested by comparing solubility data with normalized Zn-binding energies across different solvents.  Hypothesis 2: Solubility is primarily influenced by the total number of Zn-O interactions. This can be tested by comparing solubility data with unnormalized Zn-binding energies at maximum coordination.  Hypothesis 3: Solubility is influenced by a combination of both individual strength and total interactions, suggesting a more complex relationship.  Alignment with Existing Theories:  Alignment: Theories that emphasize specific interactions, such as those involving chelation or specific ligand effects, might align with Hypothesis 1.  Conflict: Theories that focus on the overall coordination environment and steric effects might align more with Hypothesis 2, potentially conflicting with Hypothesis 1.  Complex Models: Some existing theories propose that solubility is a multifactorial phenomenon, which would support Hypothesis 3, suggesting that both individual and total interactions play a role.  Follow-Up Questions (Using Mixed Socratic Prompting):  Definition → Induction → Generalization:  How can we define experimental conditions that isolate the effects of individual versus total interactions on solubility?  What patterns can be induced from experimental data comparing solubility with different Zn-binding energy metrics?  How can these patterns be generalized to develop a comprehensive model for predicting solubility in non-aqueous systems?  Hypothesis Elimination → Dialectic → Recollection:  What experimental or computational methods can be used to test the proposed hypotheses about solubility influences?  How do these hypotheses challenge or support existing solubility models in non-aqueous systems?  What historical experiments or studies provide insights into the relative importance of individual versus total interactions in solubility?  Dialectic → Elenchus → Analogy:  In what ways might the proposed hypotheses about solubility influence contradict each other, and how can these contradictions be reconciled?  Are there assumptions in current solubility models that might lead to inconsistencies when applied to non-aqueous systems?  Can you think of an analogy from another field where similar factors influence a complex outcome, and how might this analogy inform your solubility model?  By addressing these questions, you can refine your understanding of the relationship between Zn-binding energy and solubility, leading to more accurate predictions for non-aqueous Zn salt systems. |

**Curate My Example**

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| **Principles** | **Template Prompts and Follow-up Prompts** |
| Elenchus  → Analogy  → Induction | **Prompt**: “How can we define and standardize the calculation of Zn-binding energies in a way that allows for fair comparison across diverse organic molecules, considering their structural differences and the goal of predicting Zn salt solubility?”  **Follow-Up 1**: “Are there assumptions in your current method of calculating Zn-binding energies that might lead to inconsistencies when comparing different molecules?”  **Follow-Up 2**: “Can you think of an analogy from another field where normalization techniques have been successfully applied to compare diverse entities?”  **Follow-Up 3**: “What general principles can we derive from these analogies to improve the accuracy of Zn-binding energy predictions?” |