Predicting Reaction Conditions: A Data-Driven Perspective

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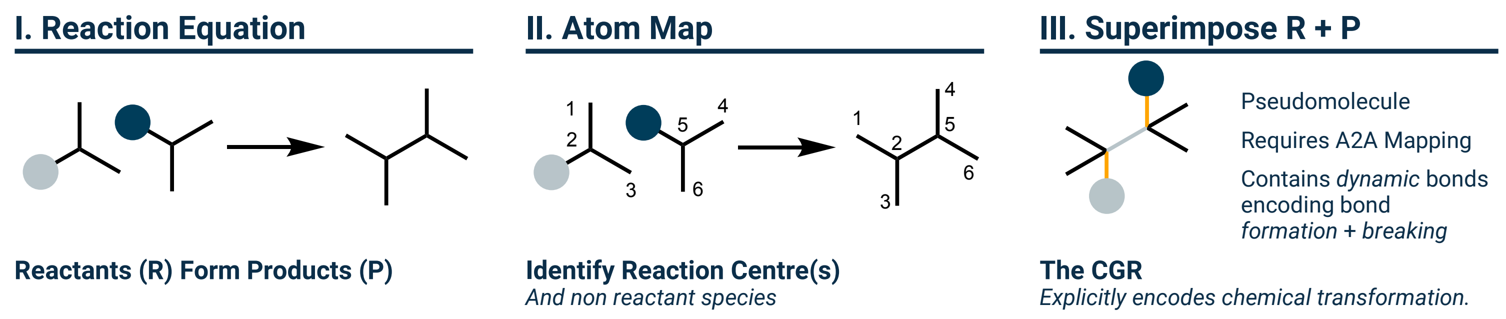
Introduction

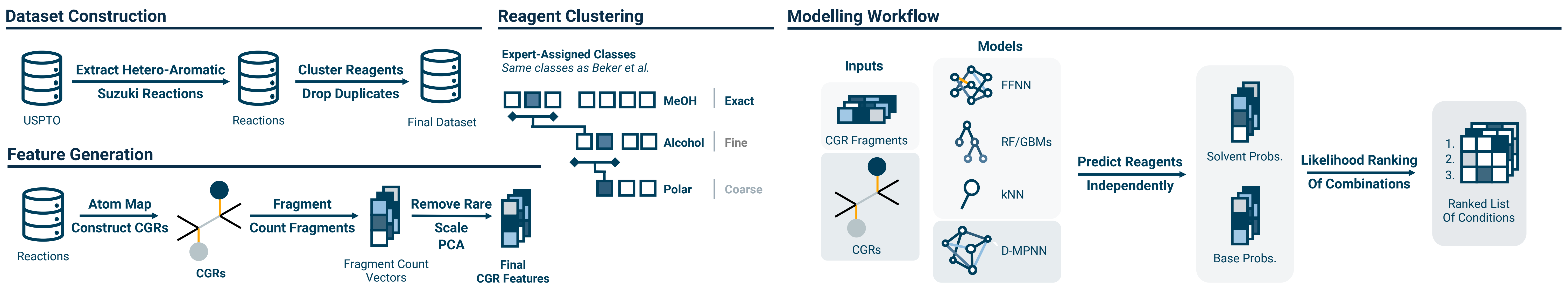
- Reaction conditions play a pivotal role in determining the outcomes of chemical syntheses, but despite this importance, there are still relatively few computational tools to predict optimal reaction conditions directly.
- Underlying problems with reaction data are well documented[1-3] but have underdiscussed implications for the **design** and **evaluation** of condition prediction models.
- These problems manifest themselves in **poor model performance**[4], where state-of-the-art approaches cannot significantly improve upon a literature popularity baseline.
- We suggest alternative approaches for the design and evaluation of condition prediction models and investigate the impact that **reaction representation** can have on existing model performance.


I. Reaction Equation
Reactants (R) Form Products (P)
II. Atom Map
1
2
3
4
5
6
Identify Reaction Centre(s)
And non reactant species
III. Superimpose R + P
Pseudomolecule
Requires A2A Mapping
Contains dynamic bonds encoding bond formation + breaking
The CGR
Explicitly encodes chemical transformation.

Constructing a CGR

The Impact Of Reaction Representation

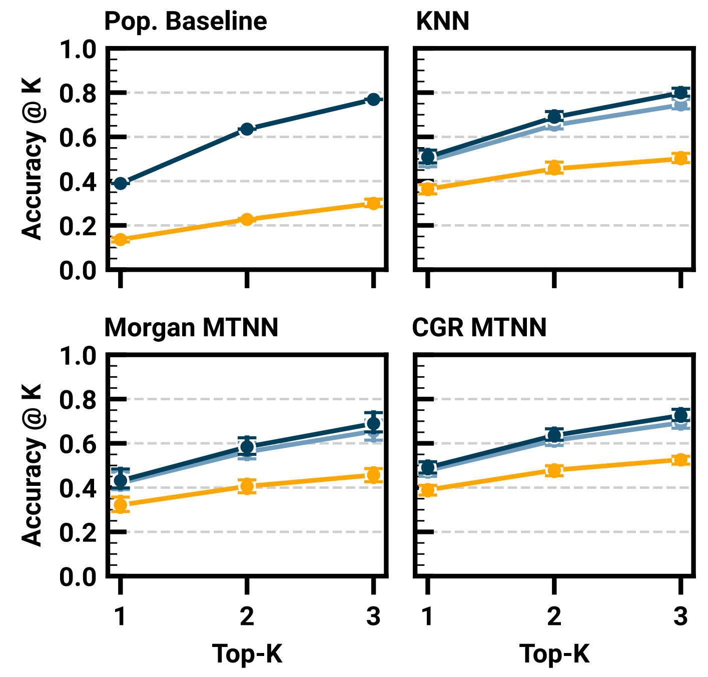
- It has previously been suggested that ML models **cannot significantly improve upon literature popularity baselines**, for a range of models and input representations[4].
- The author's best model, a Multi-Task neural network based on Morgan fingerprints, gave minor improvements compared to popularity when **predicting the expert-assigned class of solvent and base** for heteroaromatic Suzuki-Miyaura reactions.
- To investigate the impact that representation can have on model performance, we build and assess **Condensed Graph of Reaction**-based models on this dataset.



Dataset construction, feature generation and modelling workflow.

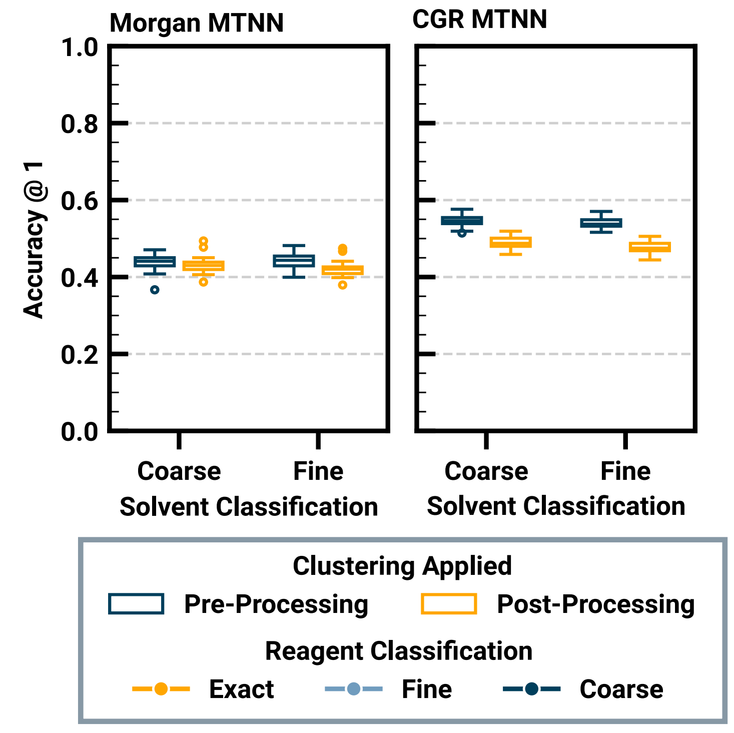
Clustering Impact on Top-K Accuracies

*'Exact' **Solvent** Predicted, Then Clustered.*



Clustering Ordering Matters

Solvent Top-1 Accuracies, Coloured By Clustering Application Time

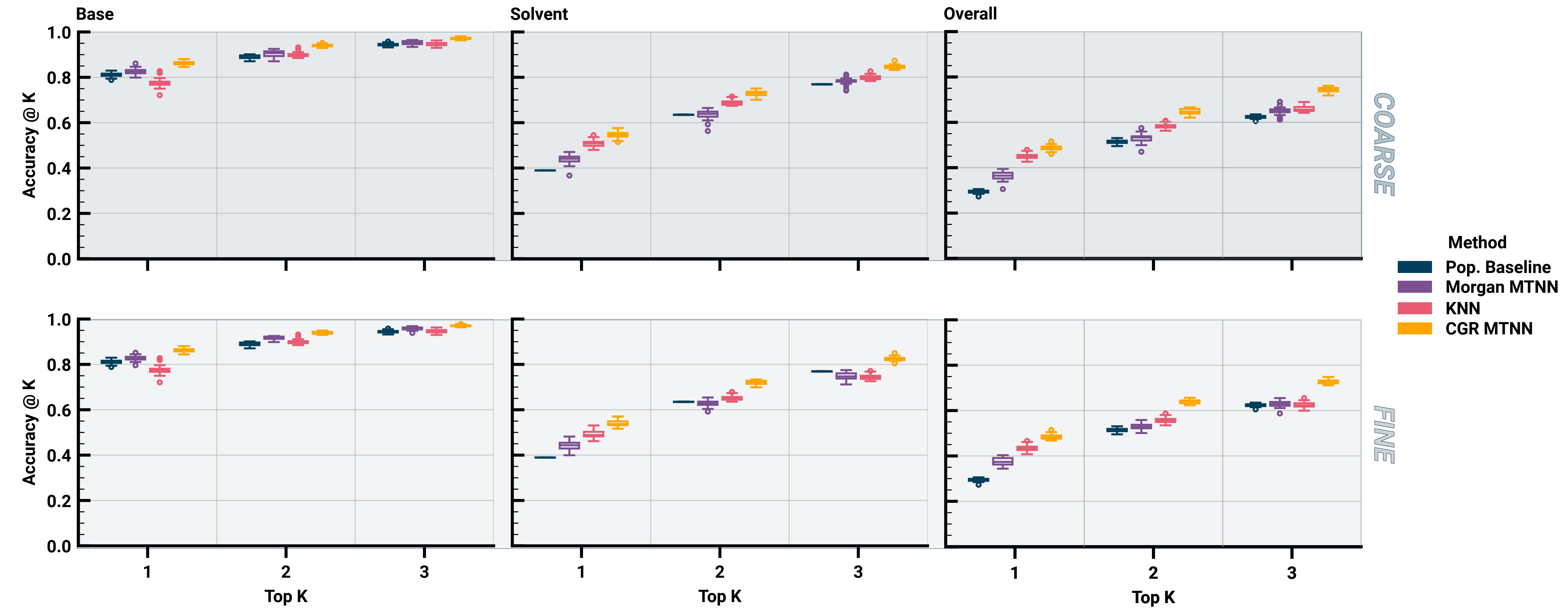


Chemically-Informed Condition Classes Improves Performance

- As expected, **a coarse-grained treatment of reaction conditions improves performance**, and represents a potential approach to **combat data sparsity** in large-scale condition prediction models.
- We see a noticeable difference in performance depending on *when* this categorisation is applied. With models **trained on the 'categorised' conditions performing better** than those trained on the 'exact' conditions and *then* applying categorisation to the outputs.

Top-K Accuracy Comparison For Selected Models

Solvent/Base = Independent Predictions; Overall = Likelihood Ranking of Combinations Applied



CGR-Based Representations Improve Upon A Challenging Literature Baseline

- **CGR-based** representations **improve performance significantly** above Morgan fingerprint and popularity baselines. This is particularly pronounced when considering the '**overall**' accuracy of predicting both solvent and base simultaneously.
- Even a simple similarity search based on these CGR-Fragments performs comparably to a more complex model based on Morgan fingerprints.

Conclusions

- Predictive models using literature data can surpass baseline performance with **appropriate reaction representations**.
- Further gains are possible through **improved input and output encoding** to address data biases and sparsity.
- Evaluation should go beyond **binary accuracy,** incorporating **expert knowledge** or **experimental validation.**
- Expert-defined reagent classes offer a promising strategy to mitigate sparsity, assuming **intra-class reactivity is consistent**.

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