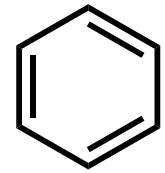
Molecular Property Prediction Based on Scarce Data Using a Novel Machine Learning Framework

Quantitative Structure-Property Relationships (QSPR) is the historical standard machine learning method in cheminformatics

QSPR Paradigm:



Molecule

Constitutional: number of specific atoms, functional group, bonds…

Topological: size, branching degree, ring structure…

Quantum Chemical: Frontier molecular orbitals, partial charge distribution, polarizability, hardness…

…

Hundreds of descriptors have been developed for QSPR models.

Conversion to a set of descriptors (X_i)

$$f(\mathbf{X}) = c_0 + \sum_{i=1}^{N} c_i X_i$$

Calculation of property via linear regression

A particular QSPR model is derived by fitting the c_i parameters to reproduce data from existing databases.

It's interesting to note that this is exactly the now obsolete paradigm that once dominated image recognition.

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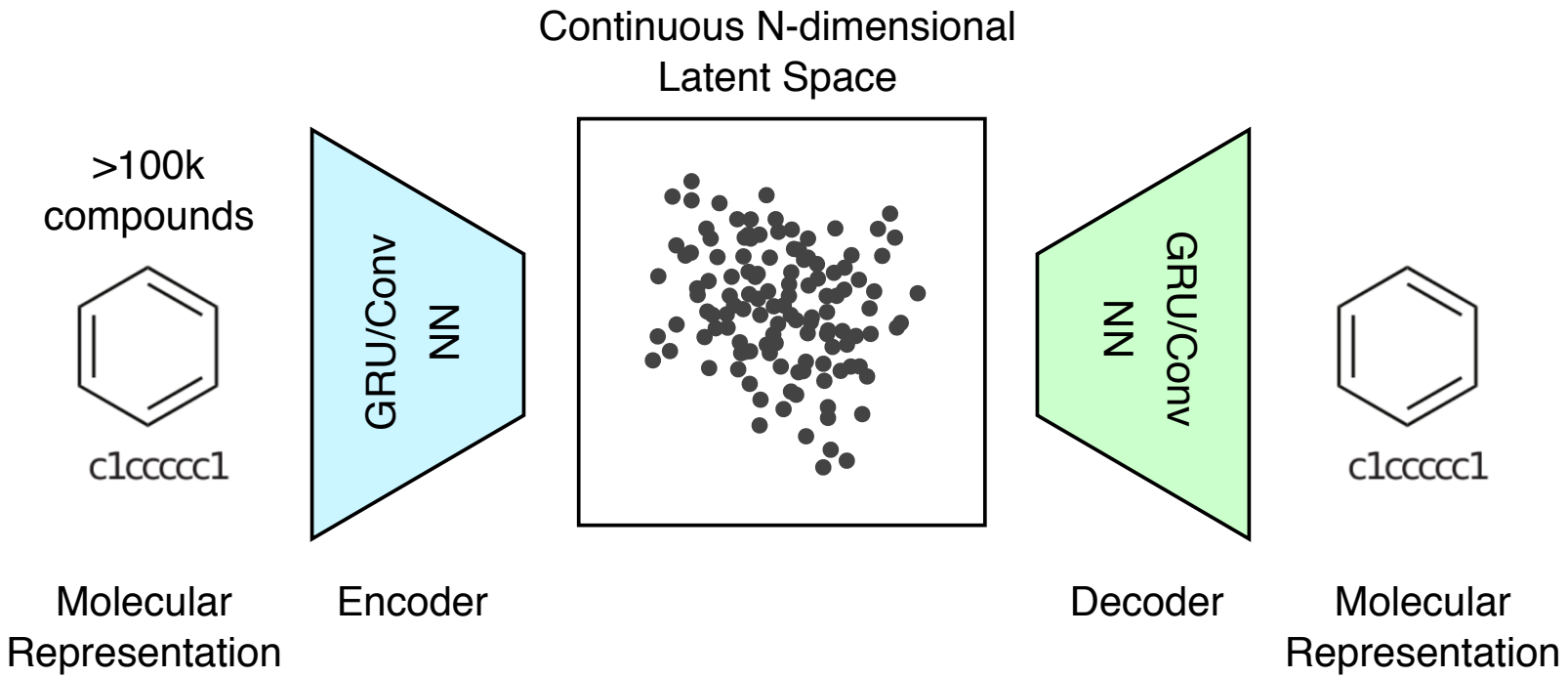
Auto-Encoder Paradigm:



Idea: By forcing the molecular representation through a low-dimensional vector space, the autoencoder “learns” a data-efficient representation of chemical structures.

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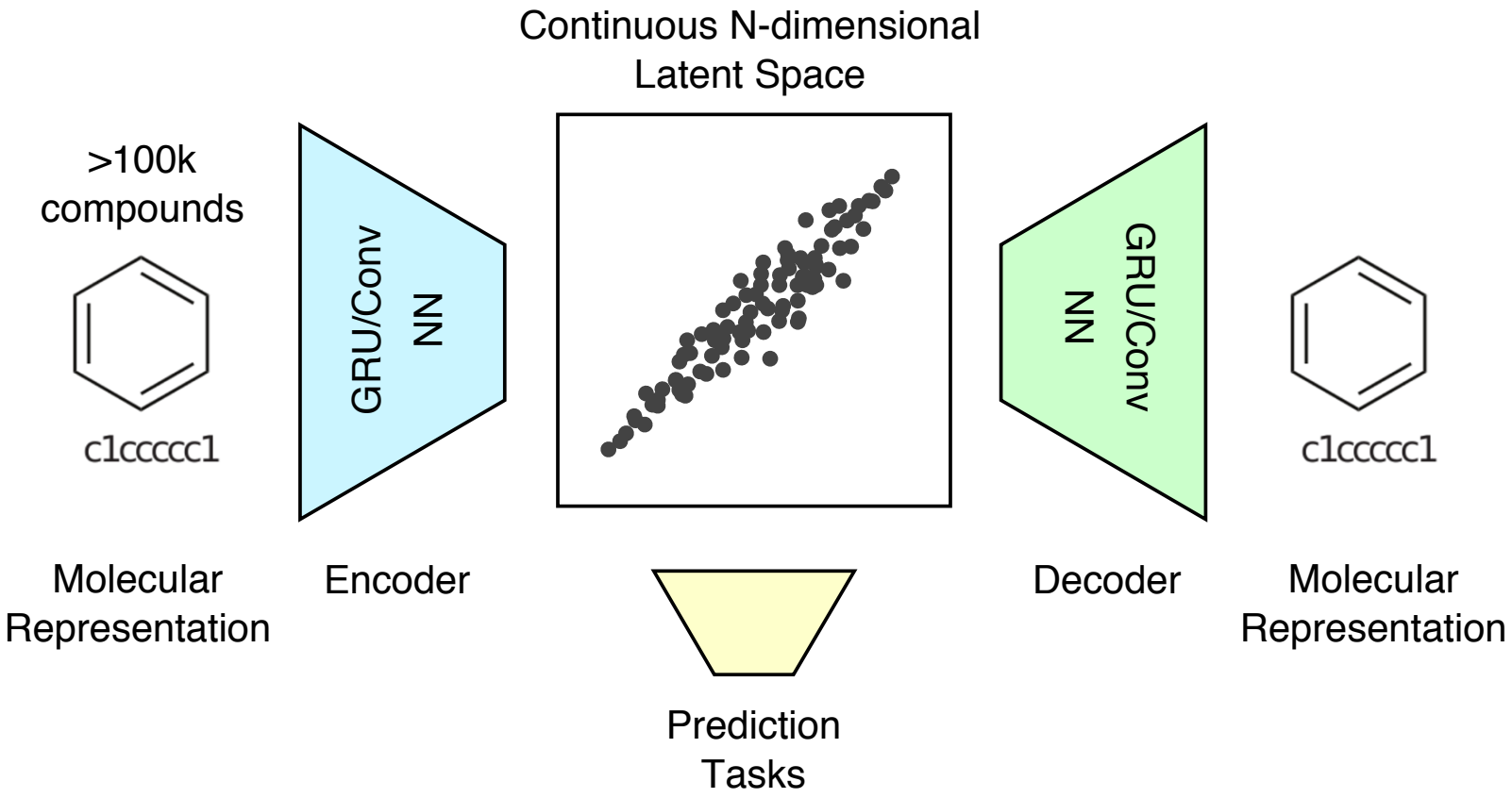
Auto-Encoder Paradigm:



Potential: Joint training of decoding and predictor task reorganizes the latent space to put chemically similar molecules in the same neighborhood. Multi-objective training on correlated properties has the effect of improving the prediction of both.

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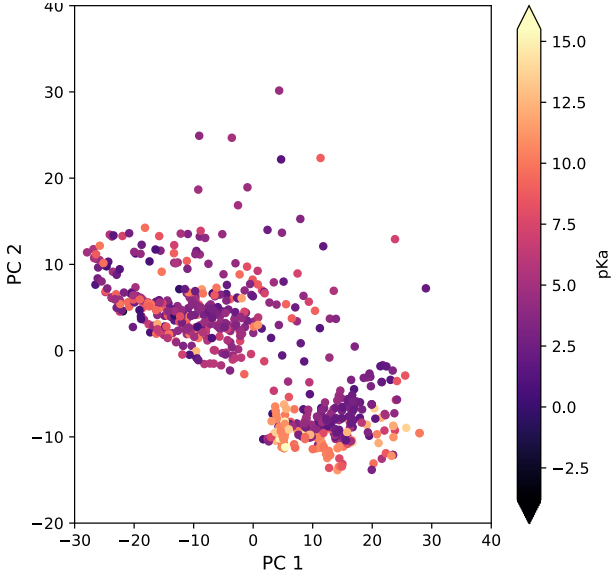
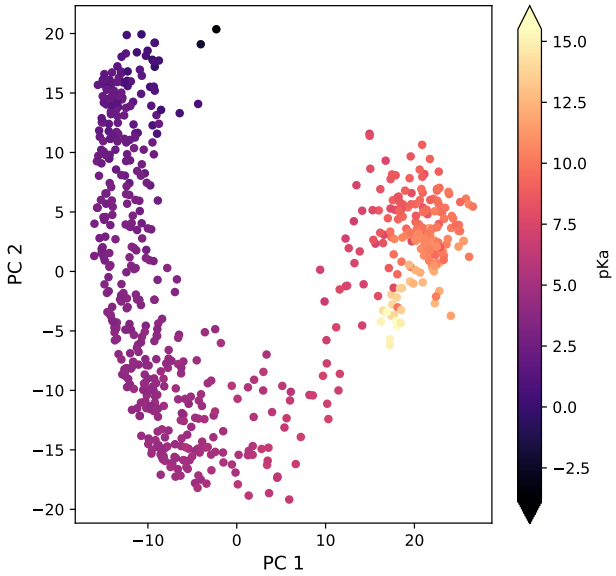
Latent Space Restructuring:
joint-training on pKa (aq) and ΔG_s prediction tasks (N~600) show clear reorganization of latent space.

Errors:
pKa+ΔG_s MUE ~ 0.5
pKa MUE ~1.2

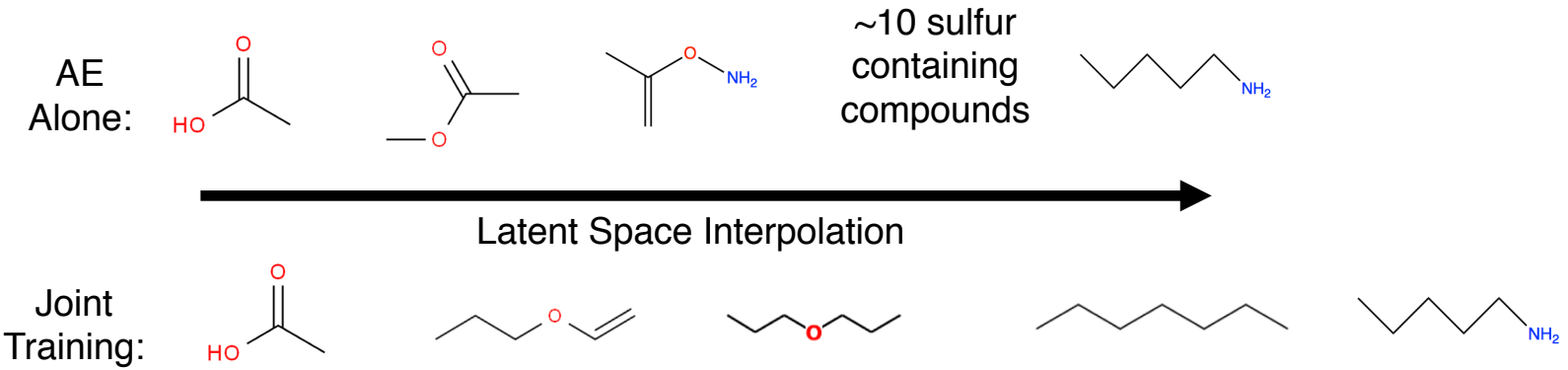
Autoencoder Alone



Joint Training



Inverse Design with Respect to Figure of Merit:



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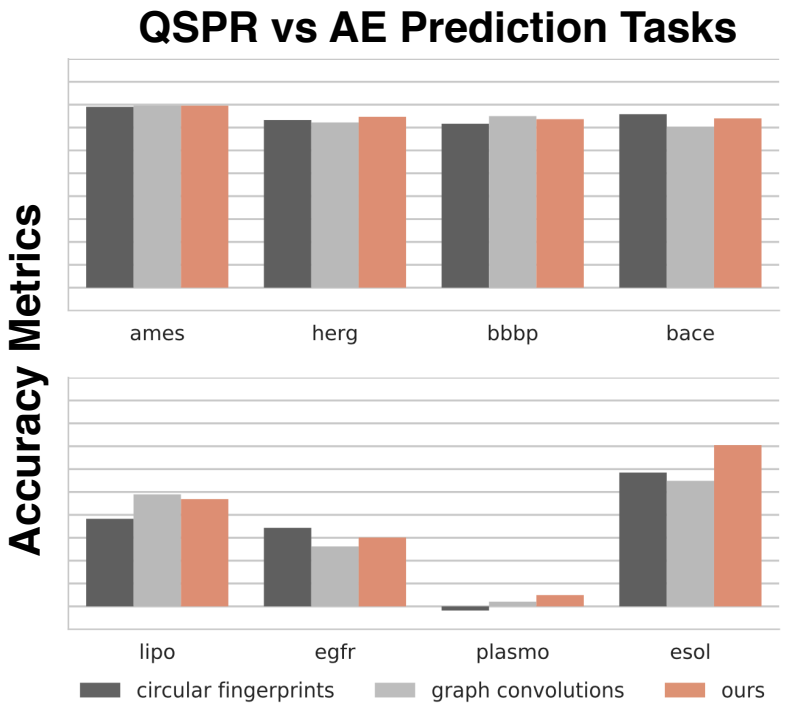
Proposed activities:

- To date, autoencoder based predictions outperform QSPR based models in most head-to-head tasks.
- Autoencoder based models are particularly interesting for scarce data applications, where multiple data sources can be combined.
- Establish a partnership to develop autoencoders that are useful for predicting safety figures of merit. (e.g., SADT, TD_{24})
- Develop training data sets for validation and comparison.
- Deliver novel targets via inverse design to industrial collaborators.



Winter et al. Learning Continuous and Data-Driven Molecular Descriptors by Translating Equivalent Chemical Representations. *Arxiv* **2018**

Gómez-Bombarelli, et al. Automatic Chemical Design Using a Data-Driven Continuous Representation of Molecules. *ACS Cent. Sci.* **2018**, *4* (2), 268–276.