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

**QSPR Paradigm:**

- **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.

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

Auto-Encoder Paradigm:

![Diagram of 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.
Molecular Property Prediction Based on Scarce Data Using a Novel Machine Learning Framework

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

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

Errors:
pKa+$\Delta G_s$ MUE ~ 0.5
pKa MUE ~1.2

Inverse Design with Respect to Figure of Merit:
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.

Accuracy Metrics

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