Uncertainty-aware drug response prediction with chemical foundation models

Team novAIce

Chemical foundation models create informative biological representations

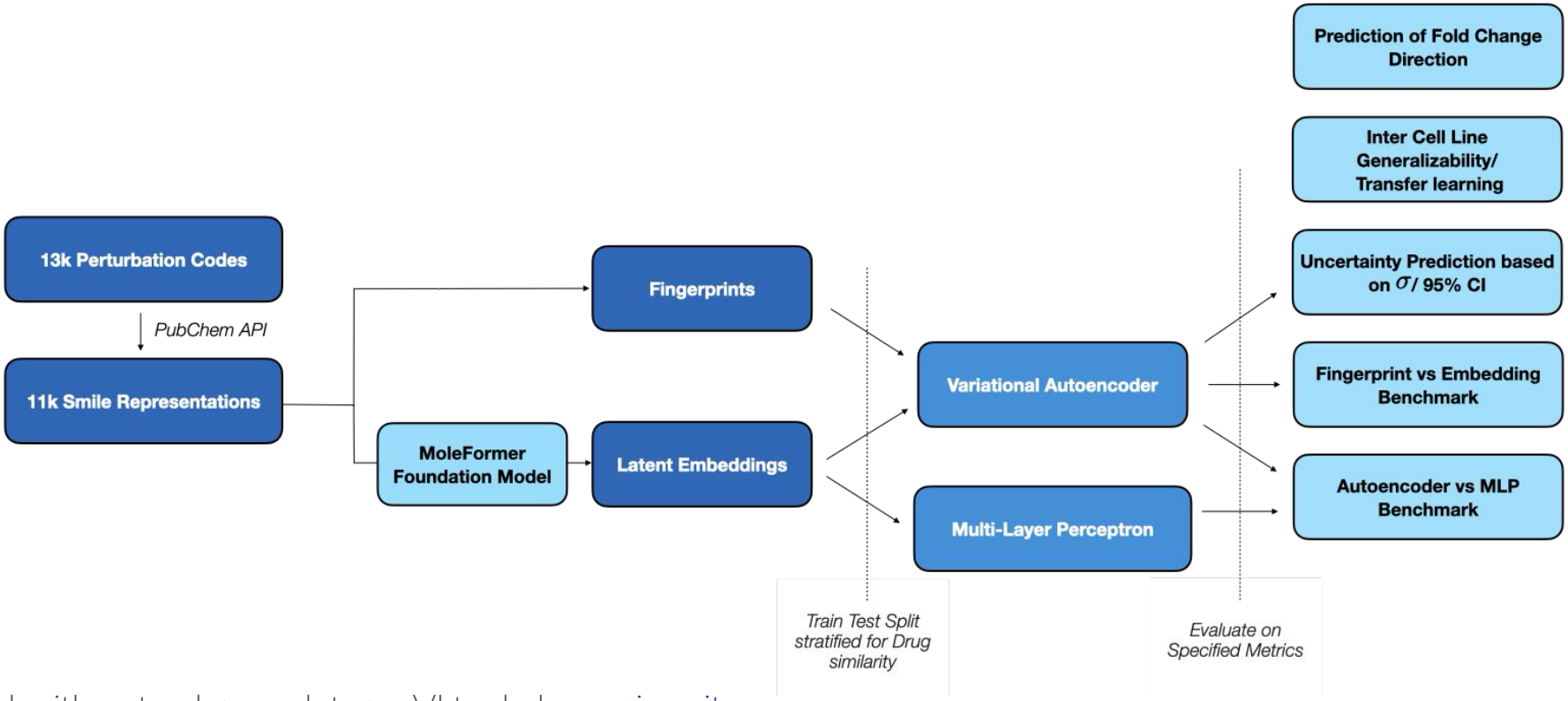
The Problem

- Drug Development is **slow and expensive**

Our approach

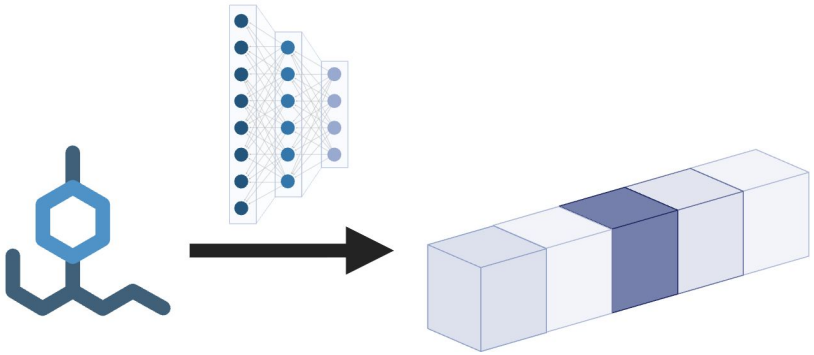
- **Uncertainty aware models** – we predict an effect and quantify how confident we are
- **Foundation models for chemistry** – rich embeddings of compounds to generalize to unseen drugs
- **Fast, robust pipeline** – production style code so Novartis can iterate on new screens quickly

NovAI Genetic Expression Prediction Workflow

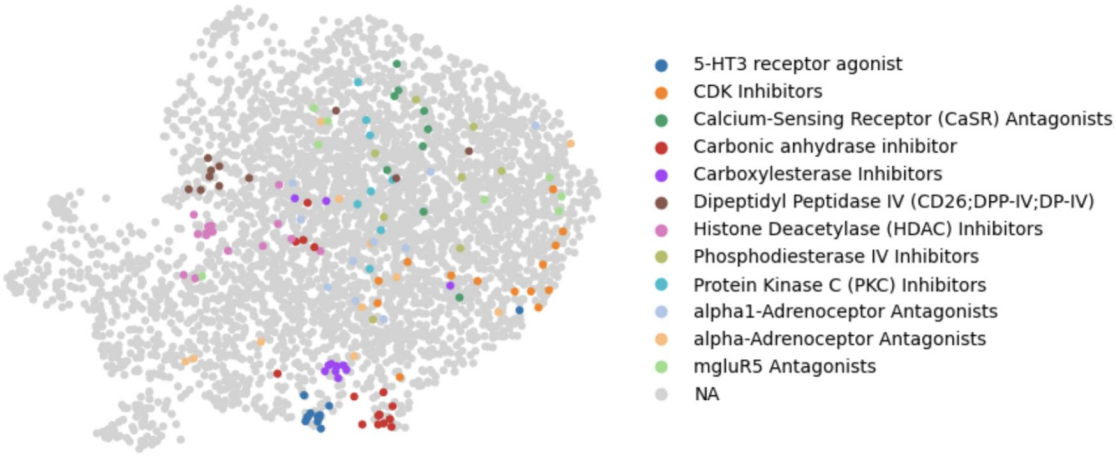


Build with pytorch+anndata+scVI tools | [novaice.git]

Chemical foundation models create informative biological representations

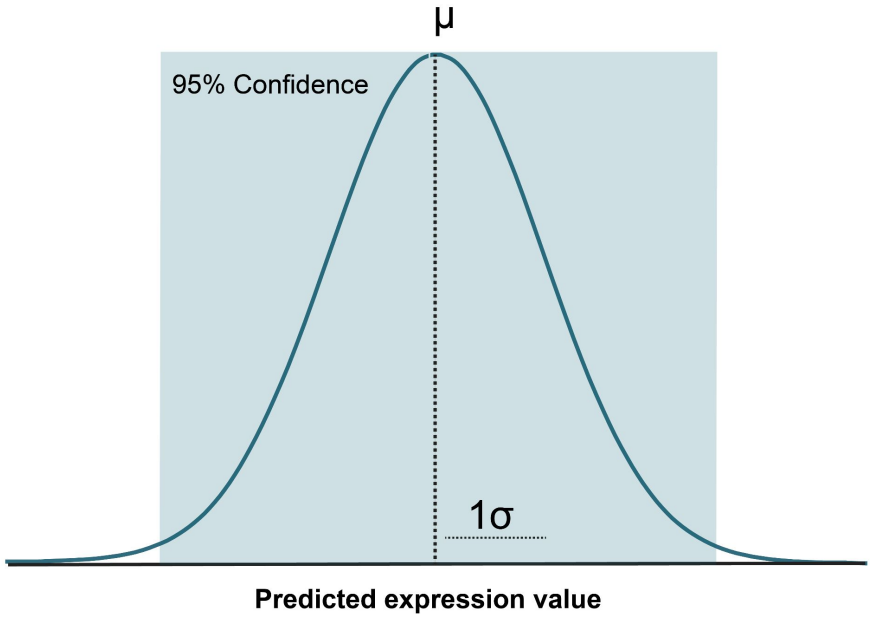


Latent representation

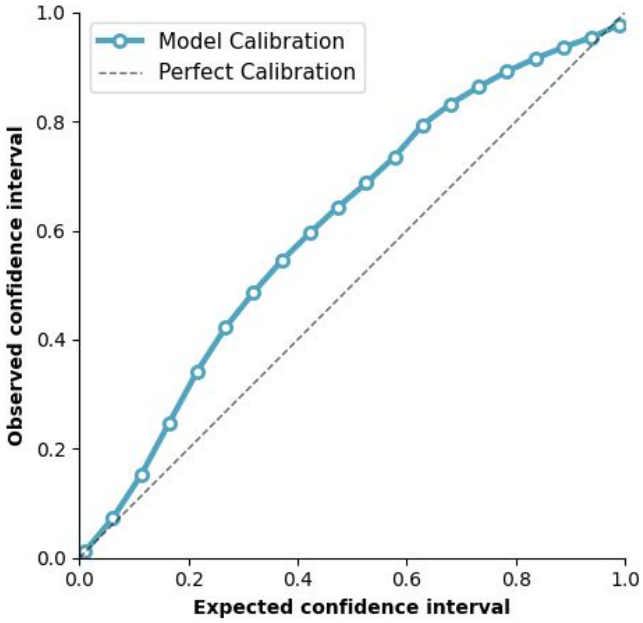


UMAP on Molformer embeddings

Uncertainty prediction with a probabilistic model

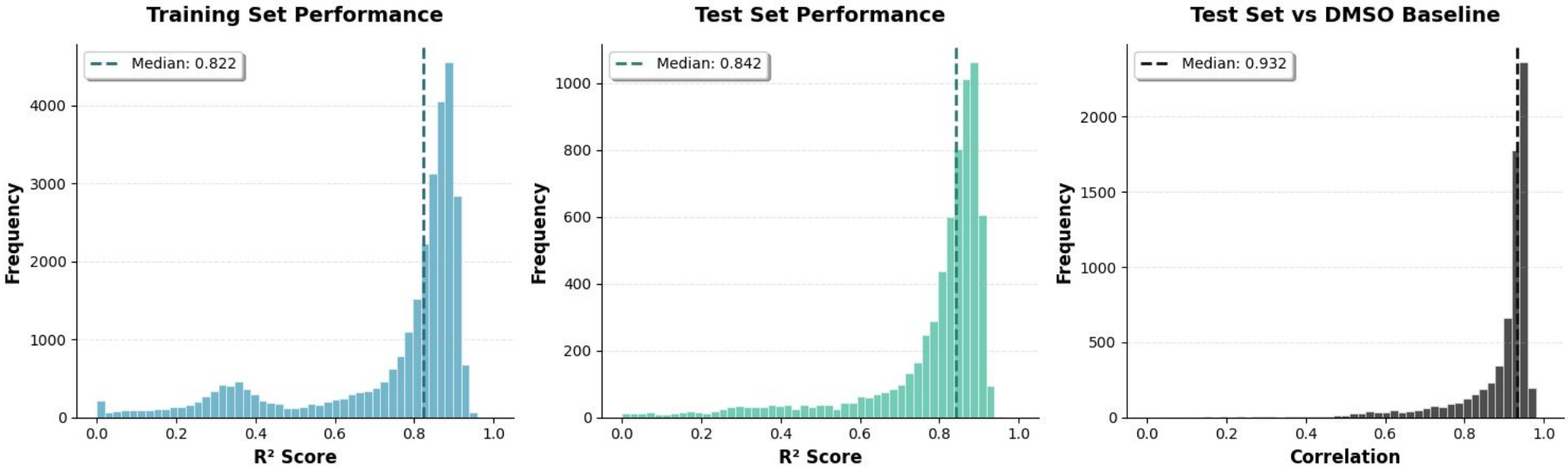


Probabilistic model (scVI generative model)



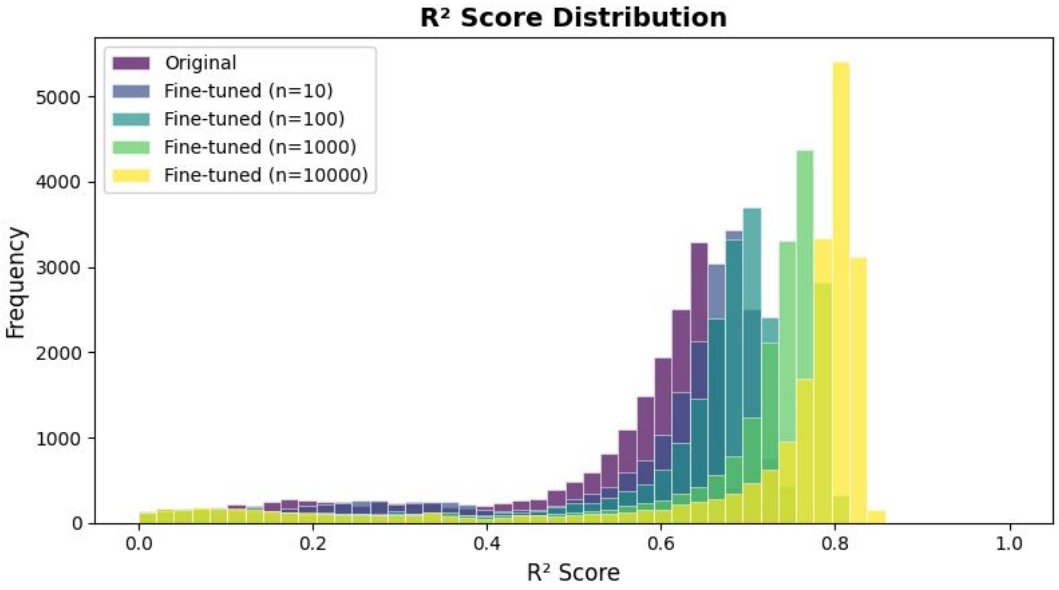
Agreement of expected confidence interval with observed confidence interval (test set)

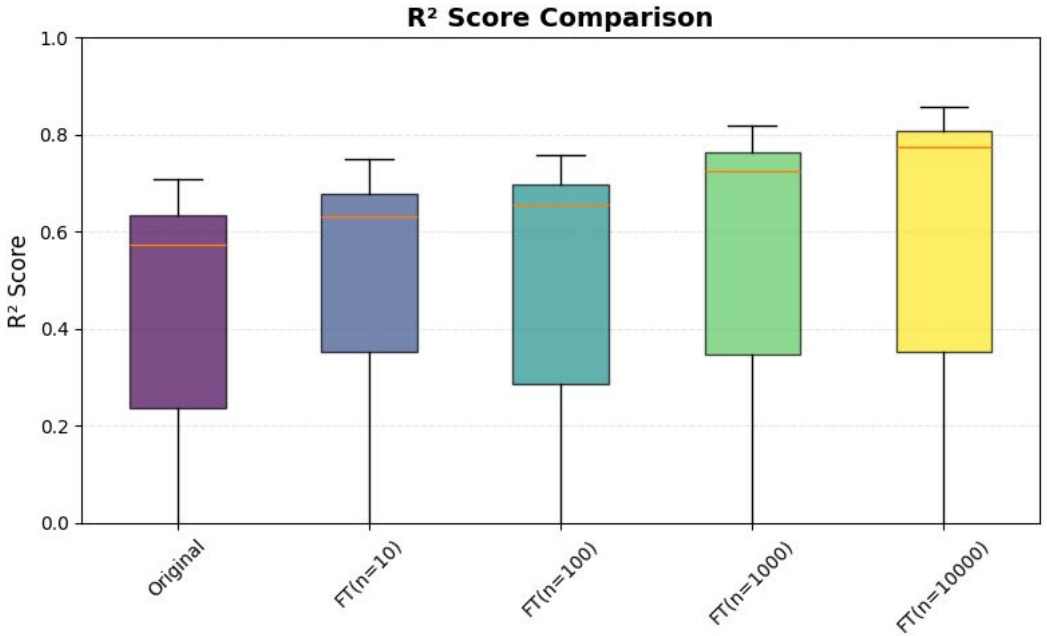
Predicting transcriptional responses to drug perturbations in cell lines



MCE Bioactive Compounds (HEK293T, 10μM) on 2000 highly variable genes. **0.84 median R^2** across test set, **44% accuracy in directional change prediction.** Prediction on 20% test split stratified by compounds

Transfer learning improves generalization between cell lines





24 hours of code. Years of screening time saved.

What we do

- Predict transcriptome responses in silico
- Prioritize compounds that hit disease pathways
- Cut down wet lab compounds, doses and cell lines