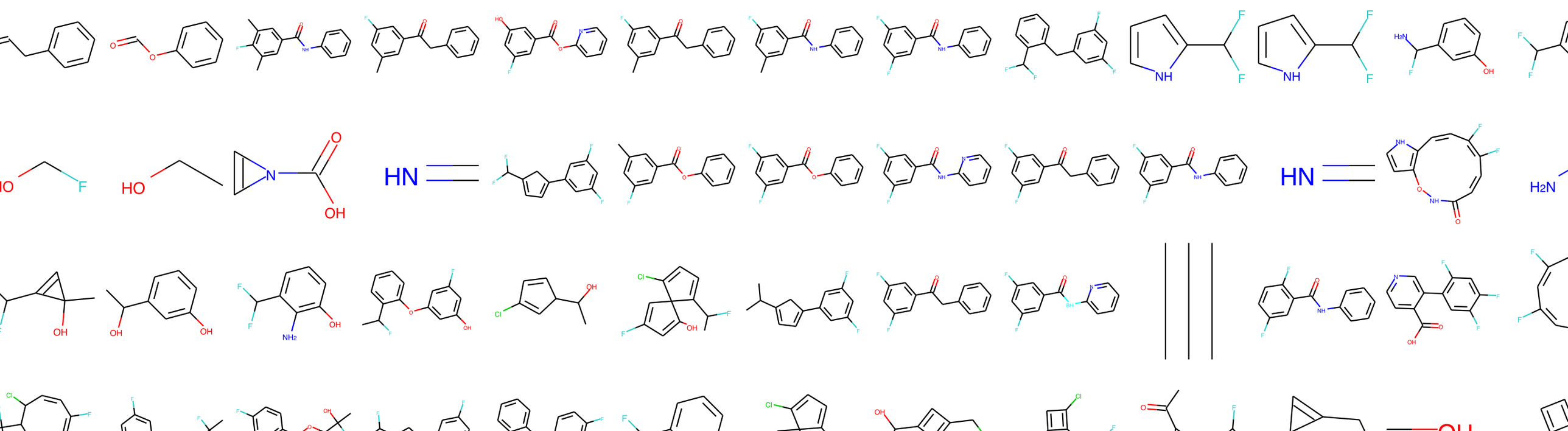
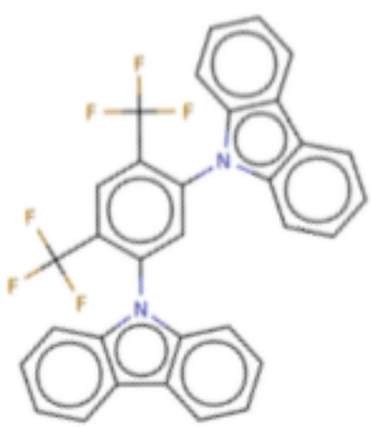
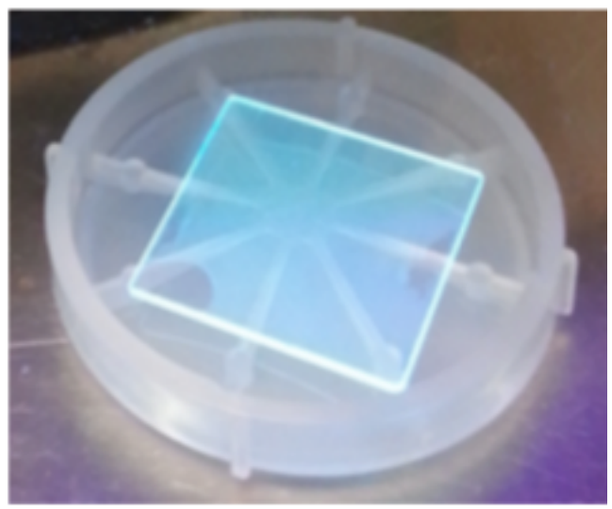
Automatic chemical design using a continuous, data-driven representation of molecules

Rafa Gómez-Bombarelli, David Duvenaud, José Miguel Hernández-Lobato, Jorge Aguilera-Iparraguirre, Timothy Hirzel, Ryan P. Adams, Alán Aspuru-Guzik



How to design molecules?



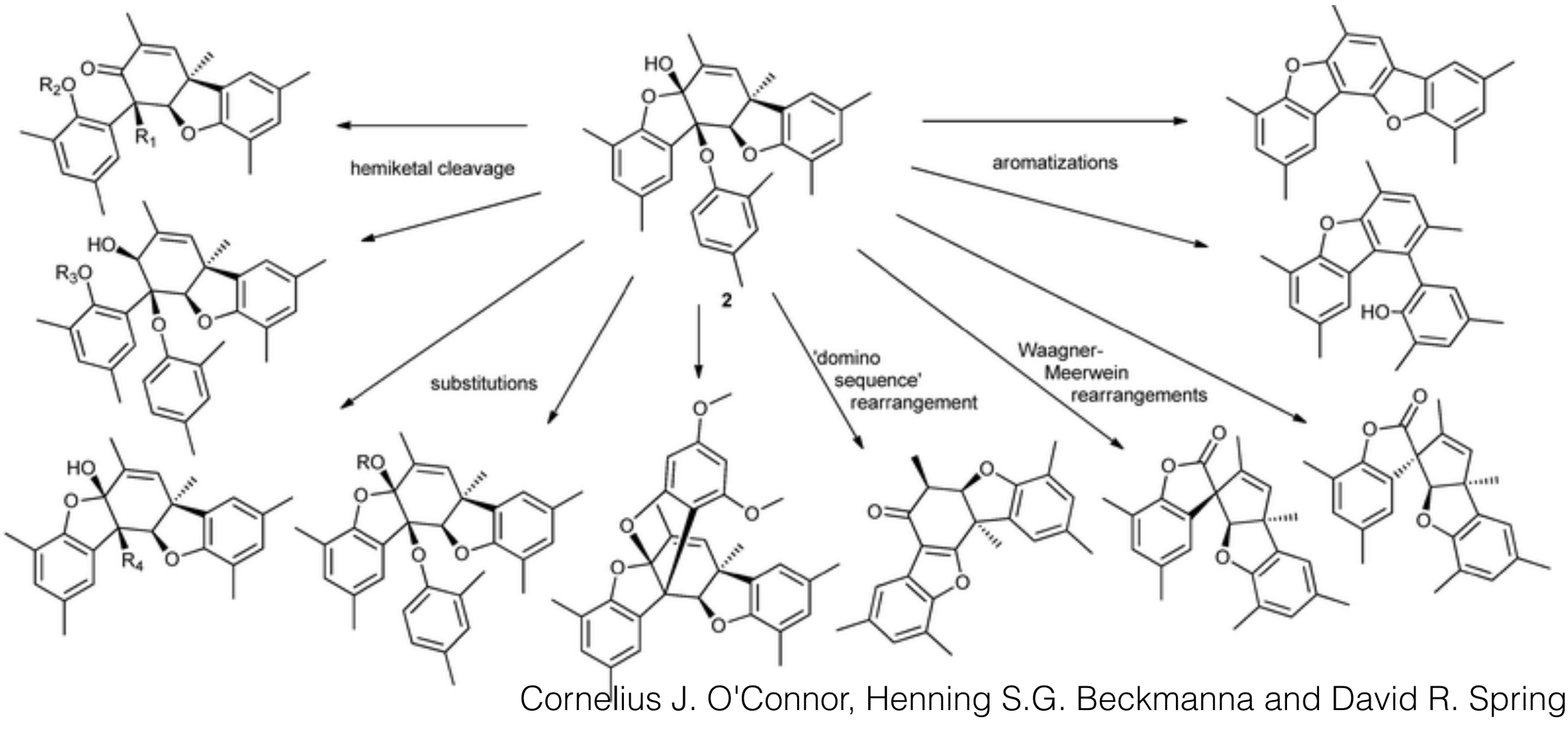


- Can predict properties of molecules (QSAR)

- Want a molecule with a certain property (inverse QSAR)

How to optimize molecules?

- Build a giant library of molecules and try them all
- Or: Local search based on small changes



Cornelius J. O'Connor, Henning S.G. Beckmanna and David R. Spring

Discrete optimization is basically impossible

- In more than 10 or 20 dimensions, search is too slow because no way to know which direction to go

- Gradient gives D hints for your D parameters

- need some version of

$$\frac{\partial \text{molecule}}{\partial \text{property}}$$

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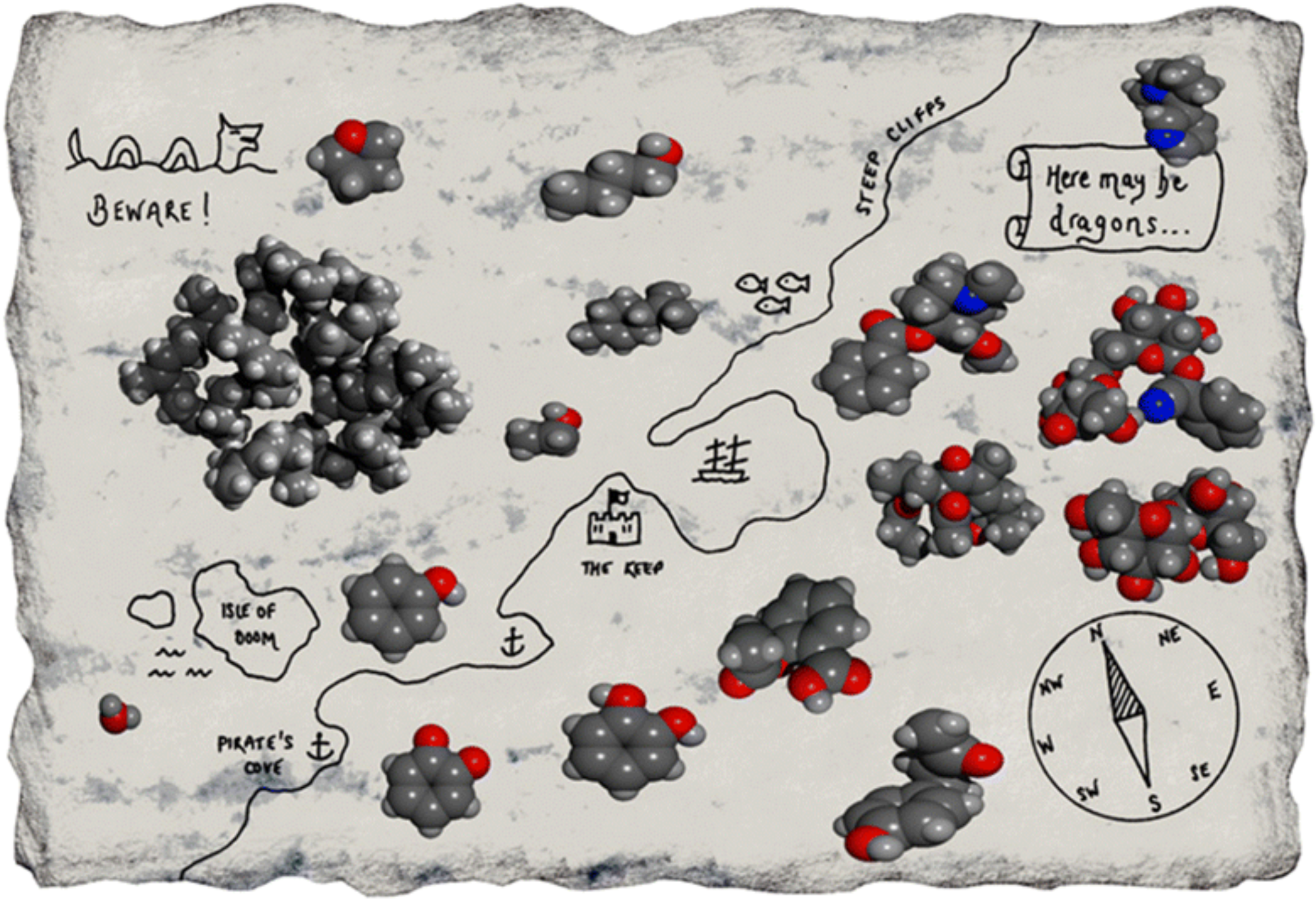
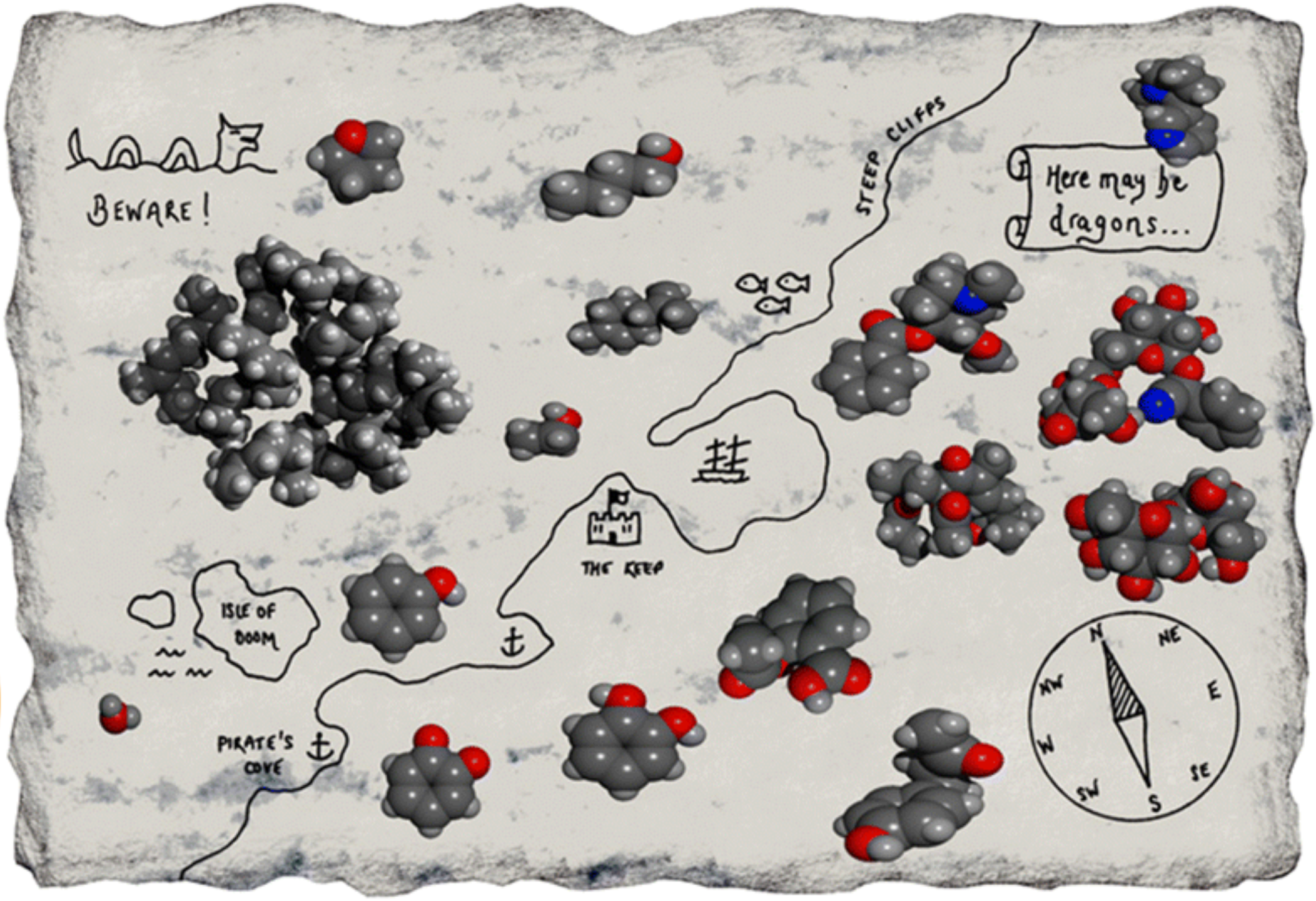
Nguyen, Dosovitskiy, Yosinski, Brox, Clune



Credit: Natalie Fey

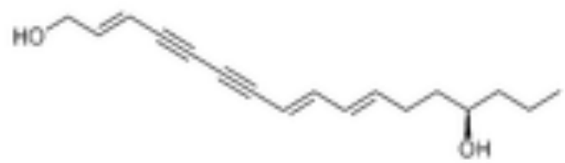
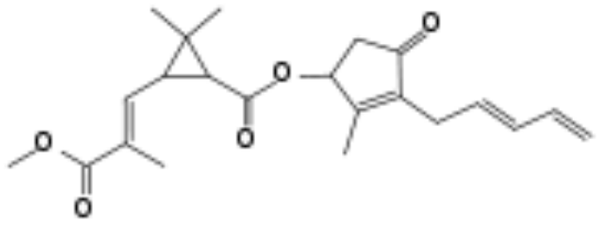
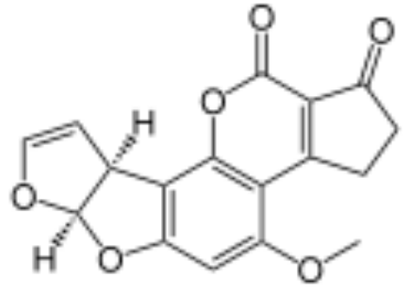
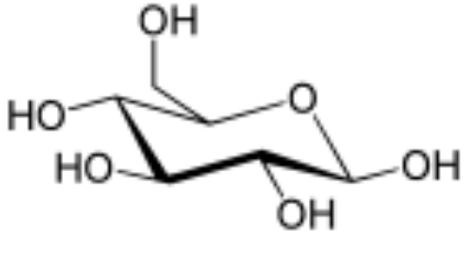
vector

molecule

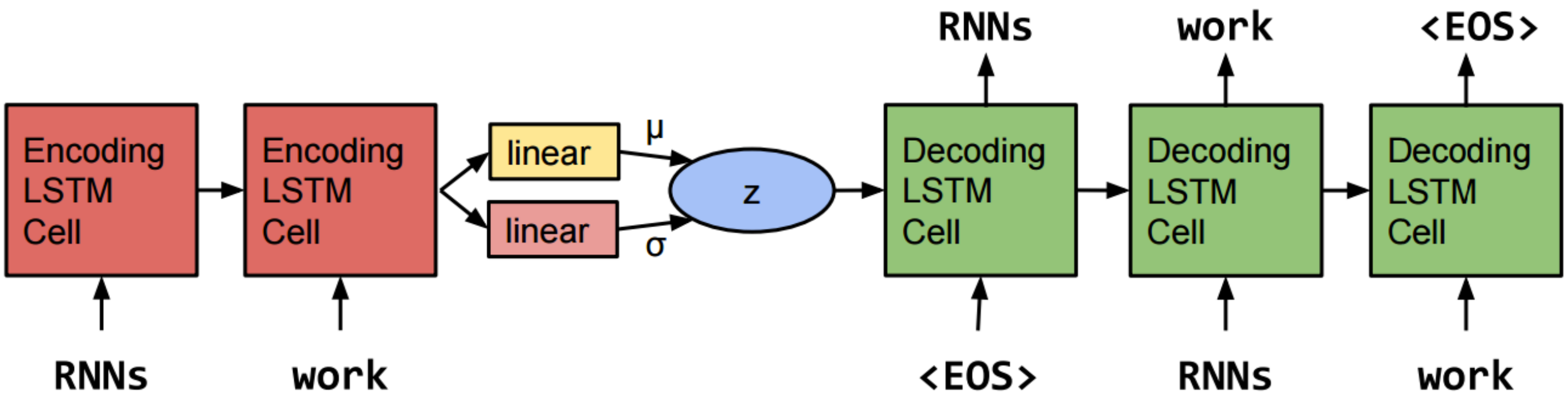


Credit: Natalie Fey

What is a molecule?

Graph	SMILES string
	CCC[C@@H](O)CC\C=C\C=C\C#CC#C\C=C\CO
	COC(=O)C(\C)=C\C1C(C)(C)[C@H]1C(=O)O[C@@H]2C(C)=C(C(=O)C2)CC=CC=C
	O1C=C[C@H]([C@H]1O2)c3c2cc(OC)c4c3OC(=O)C5=C4CCC(=O)5
	OC[C@@H](O1)[C@@H](O)[C@H](O)[C@@H](O)[C@@H](O)1

Text autoencoders

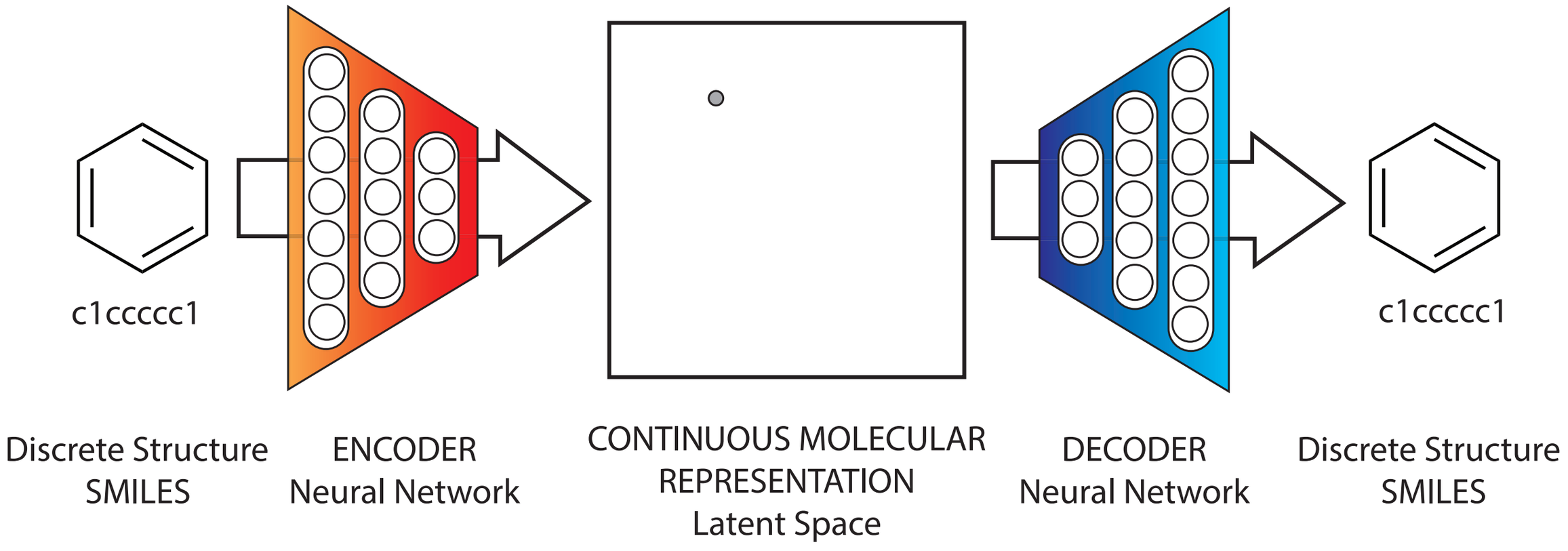


- *Generating Sentences from a Continuous Space.* Samuel R. Bowman, Luke Vilnis, Oriol Vinyals, Andrew M. Dai, Rafal Jozefowicz, Samy Bengio

Text VAE - **Interpolation**

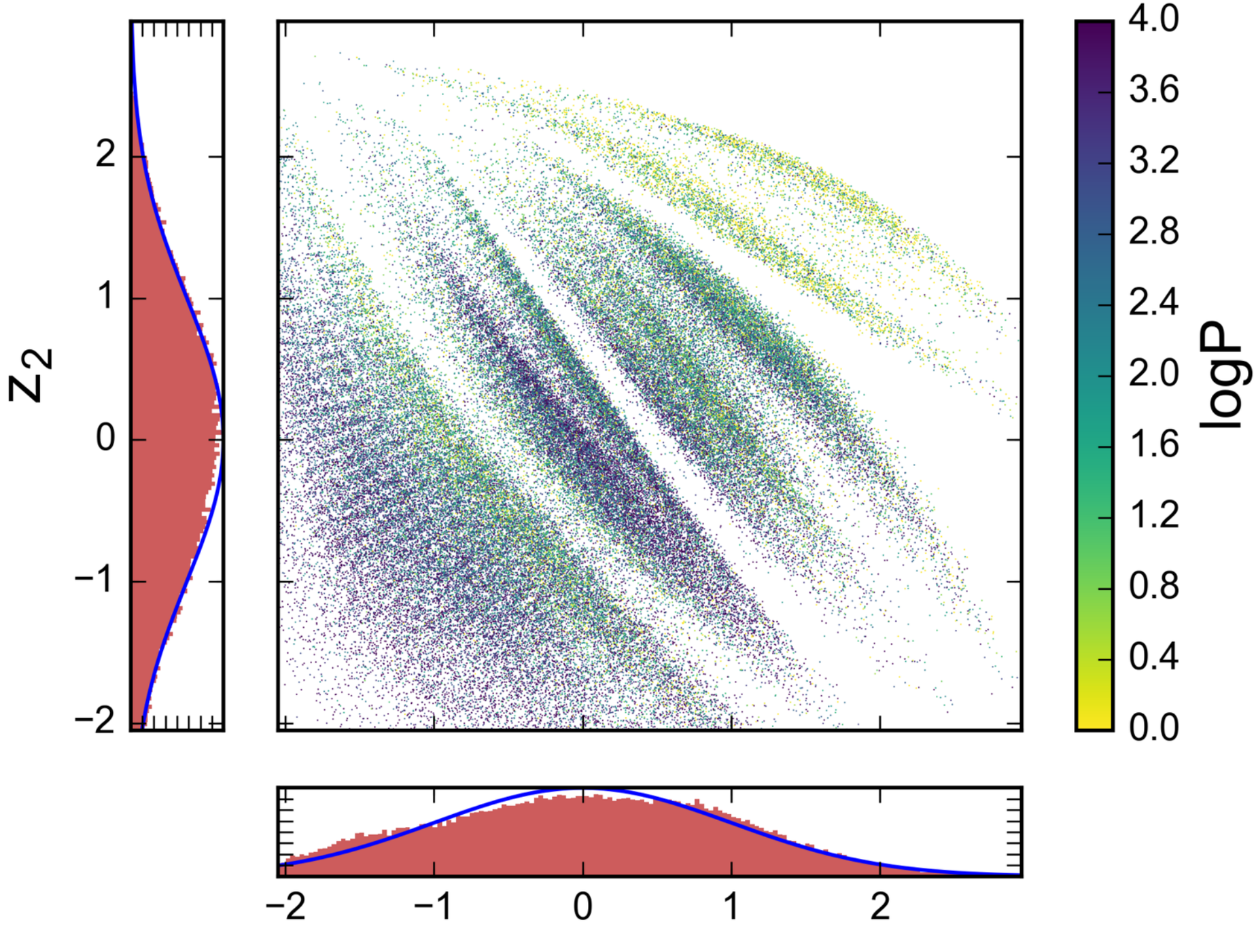
“ i want to talk to you . ”	**it made me want to cry .**	**he was silent for a long moment .**
“i want to be with you . ”	*no one had seen him since .*	*he was silent for a moment .*
“i do n’t want to be with you . ”	*it made me feel uneasy .*	*it was quiet for a moment .*
i do n’t want to be with you .	*no one had seen him .*	*it was dark and cold .*
she did n’t want to be with him .	*the thought made me smile .*	*there was a pause .*
	the pain was unbearable .	**it was my turn .**
	the crowd was silent .	
	the man called out .	
	the old man said .	
	the man asked .	

Repurposing text autoencoders

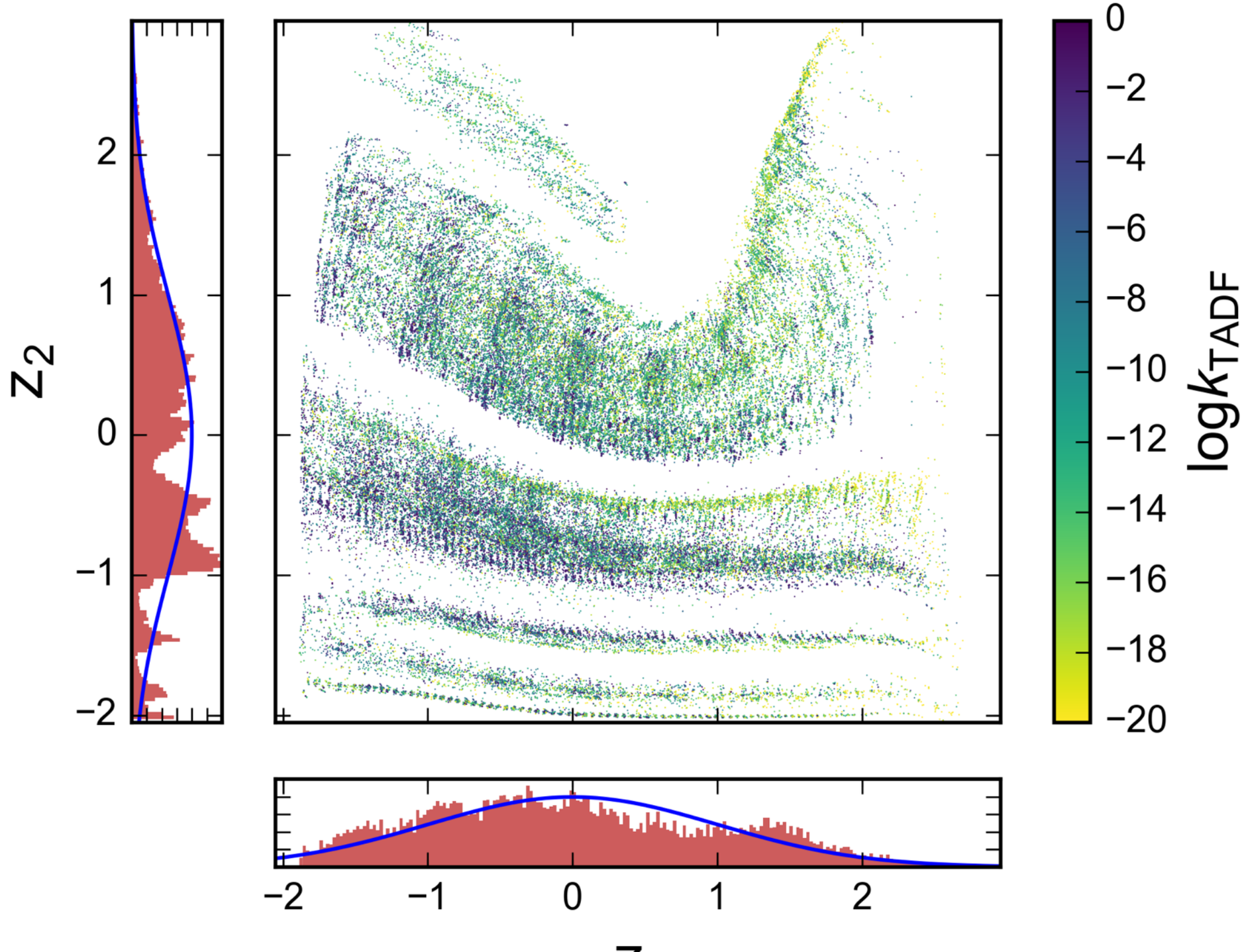


Can be trained on unlabeled data

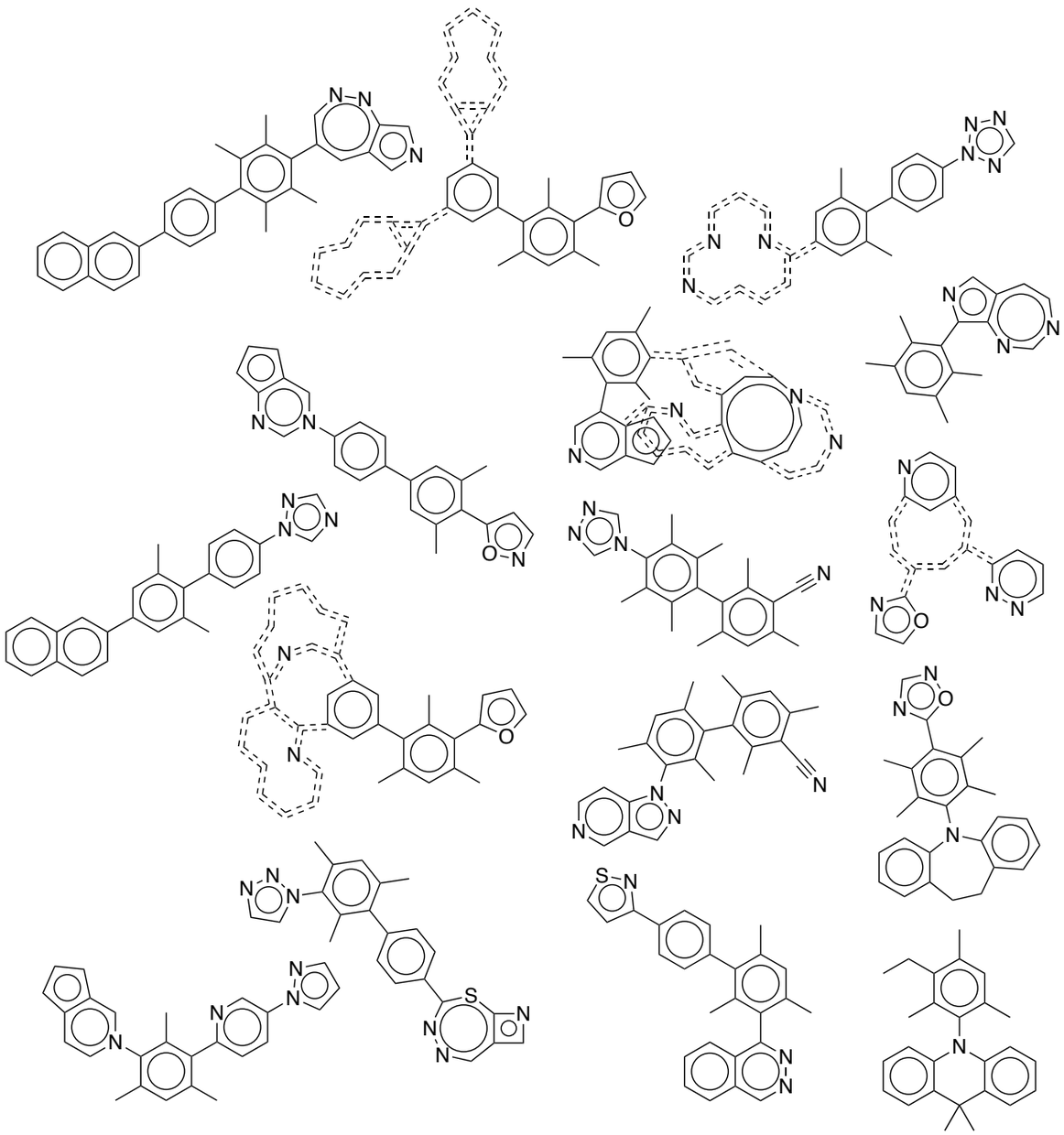
Map of 220,000 Drugs



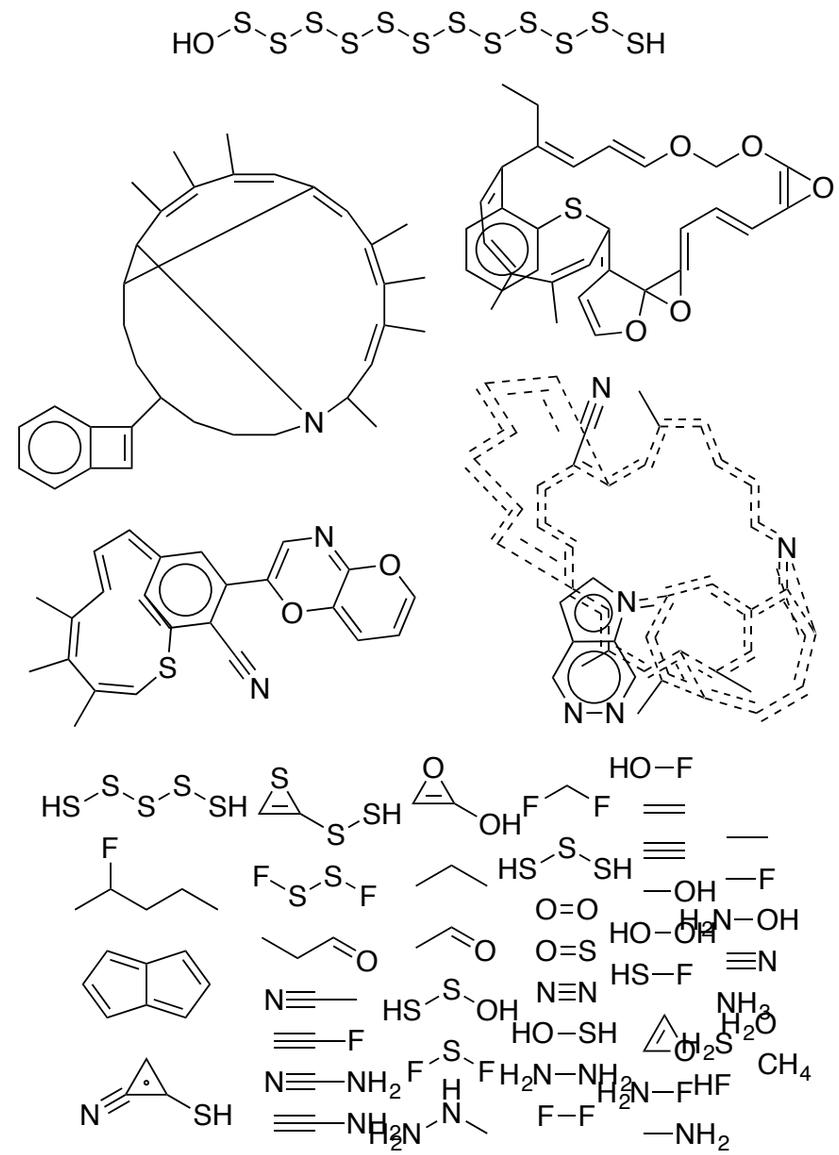
Map of 100,000 OLEDs



Random Organic LEDs

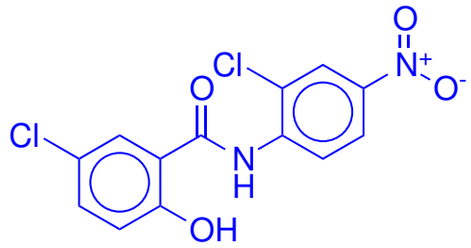


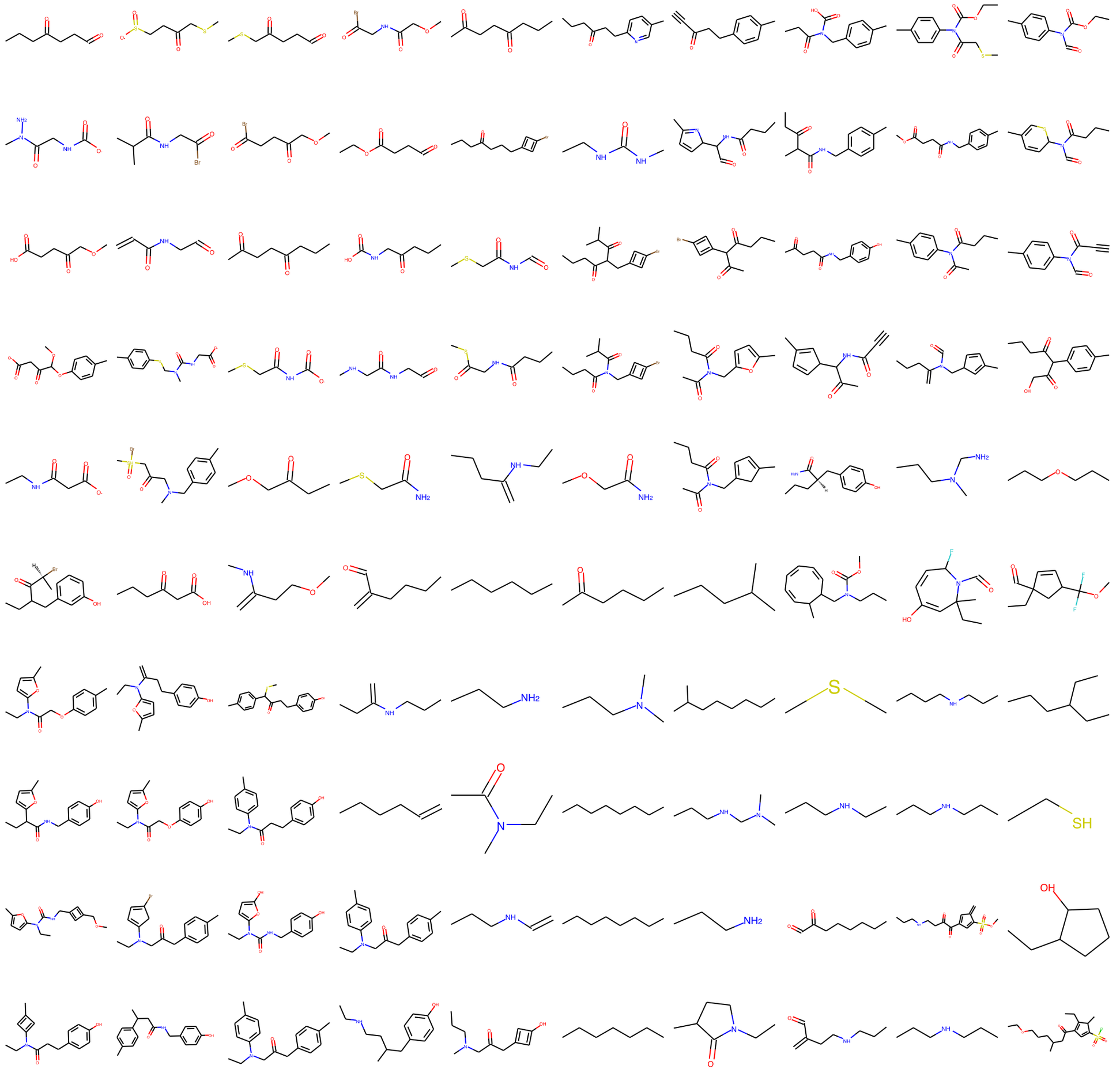
Variational autoencoder

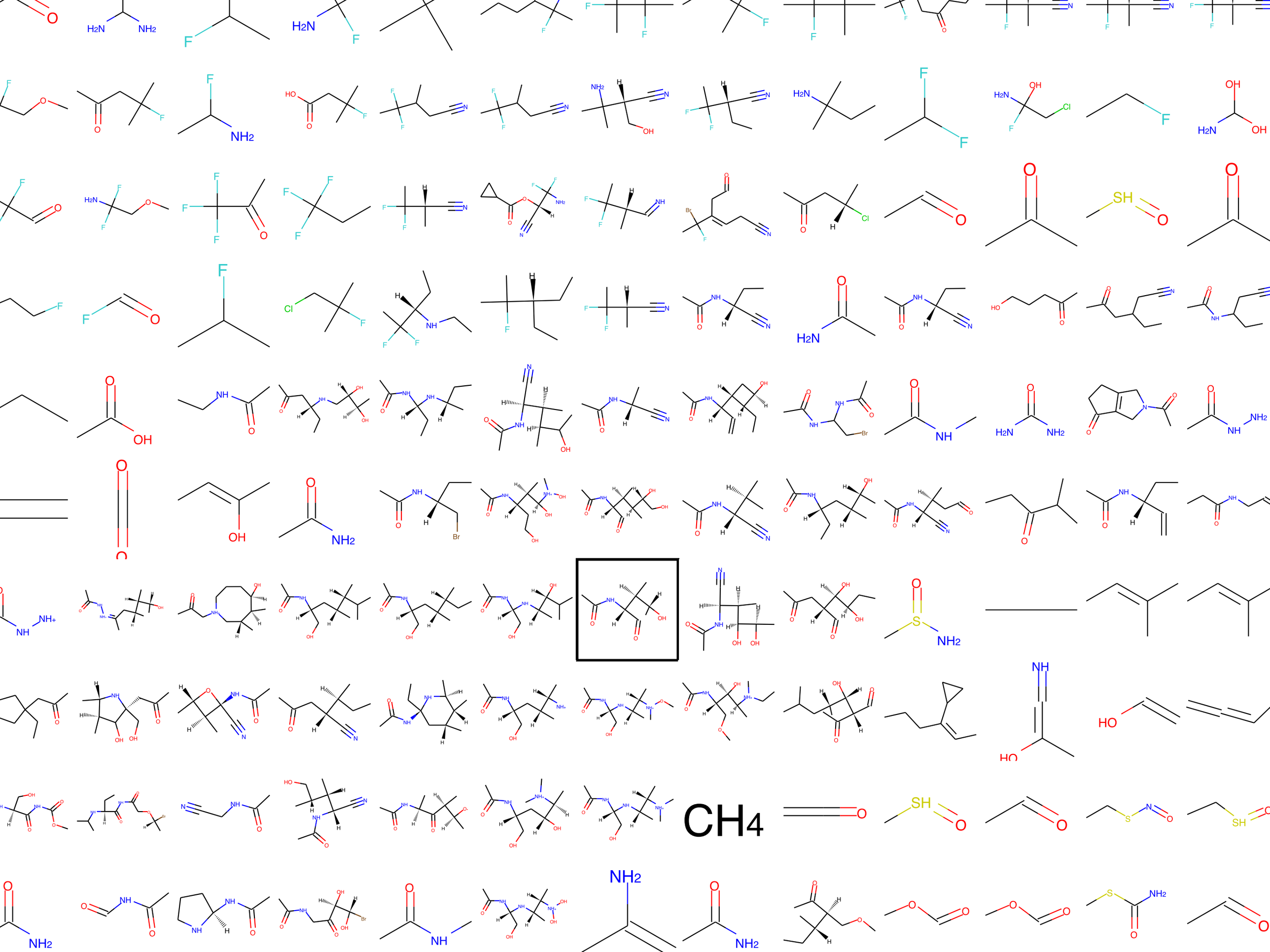


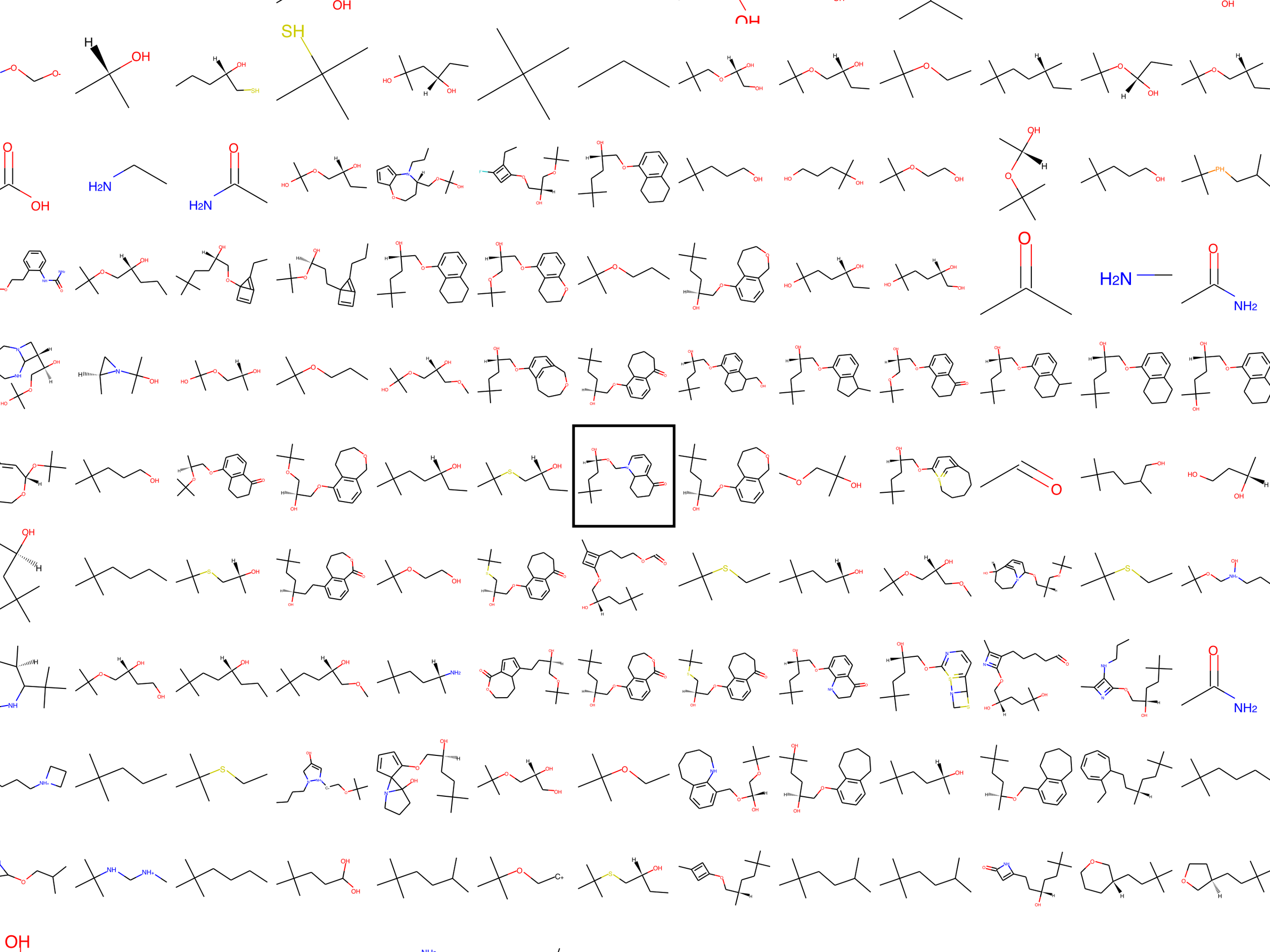
Standard autoencoder

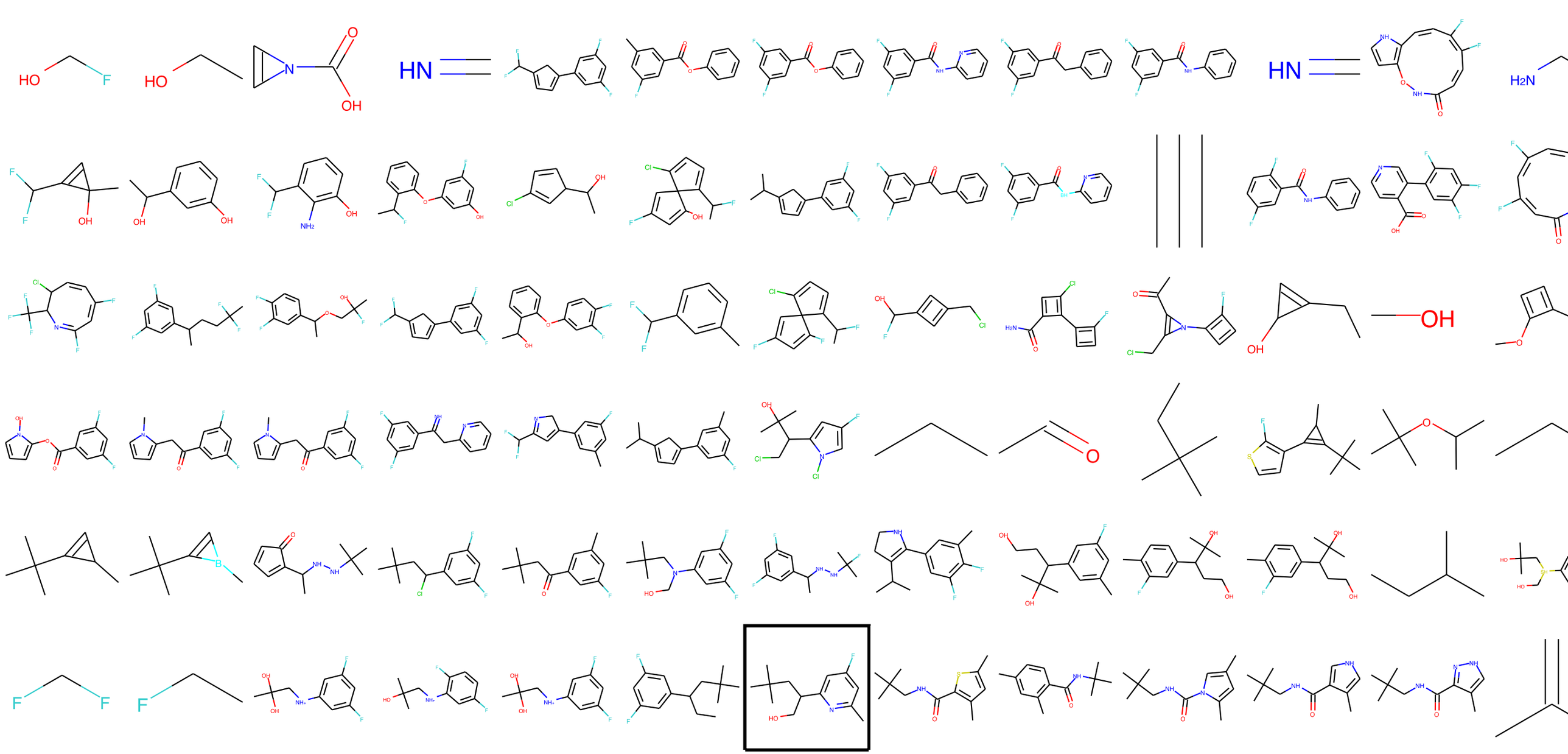
Molecules near aspirin



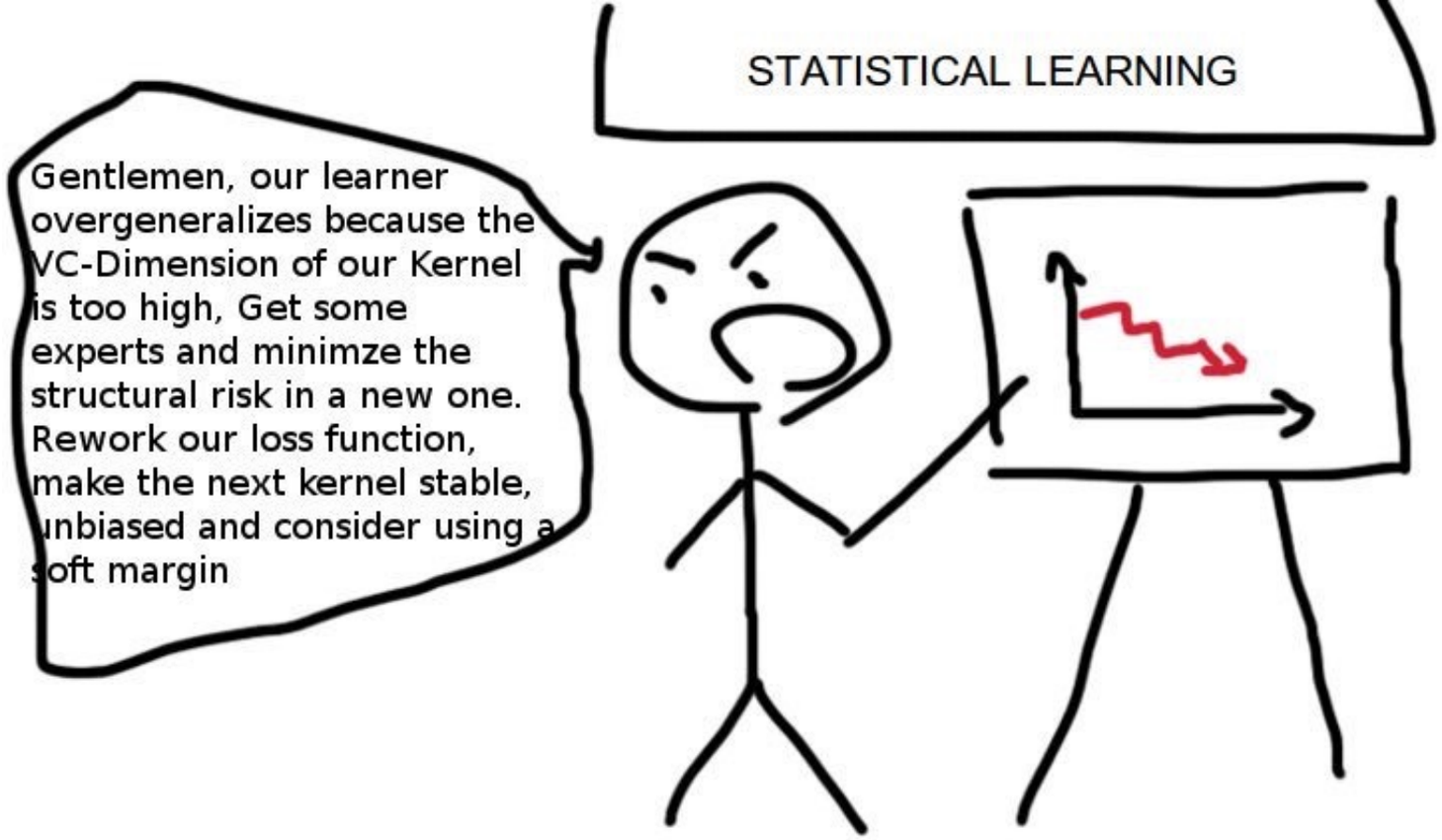


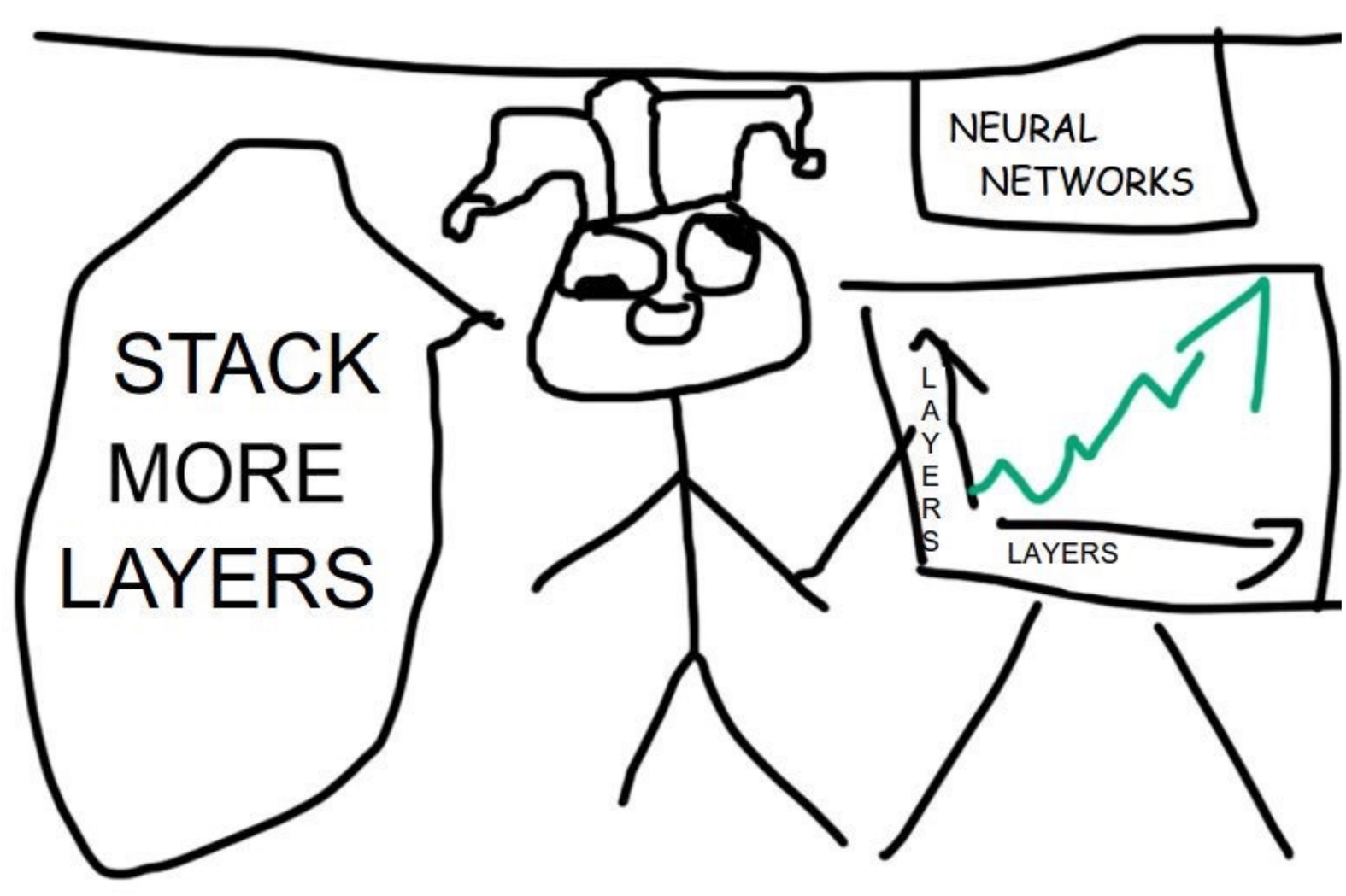




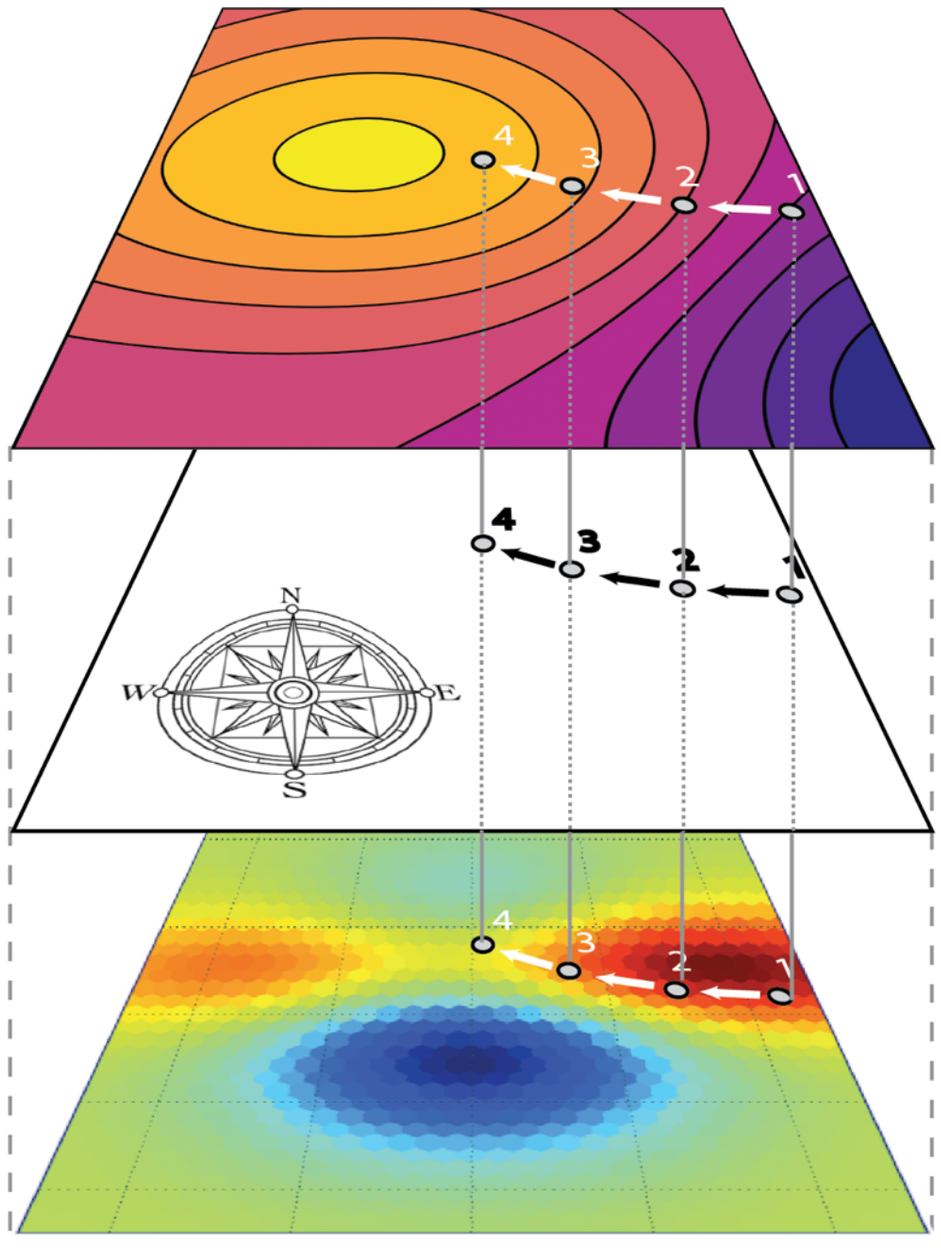


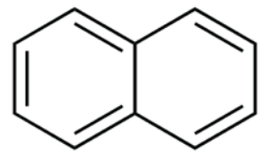
No chemistry-specific design!

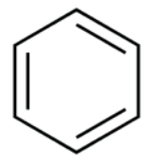


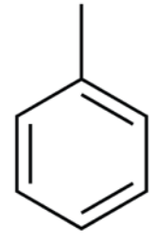


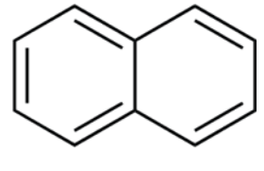
Gradient-based optimization



1. 

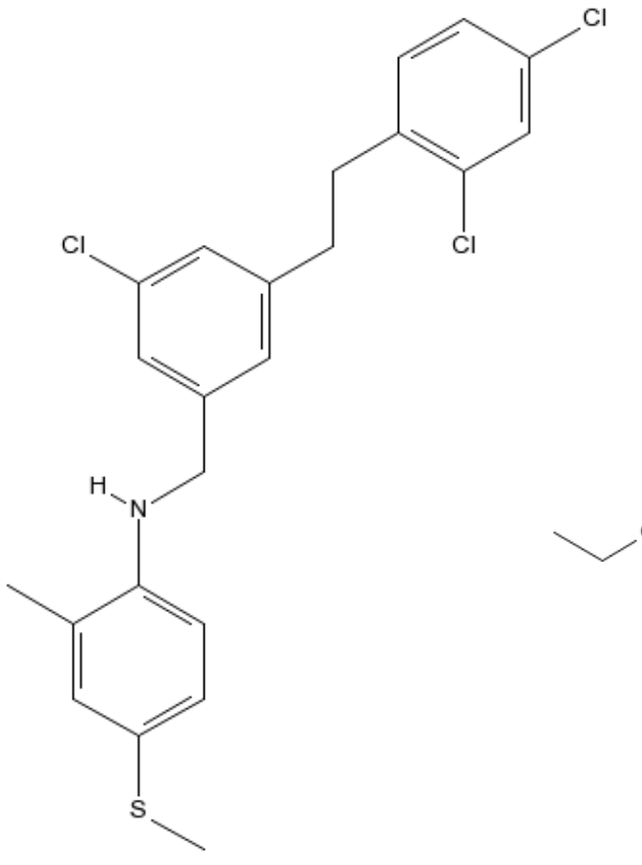
2. 

3. 

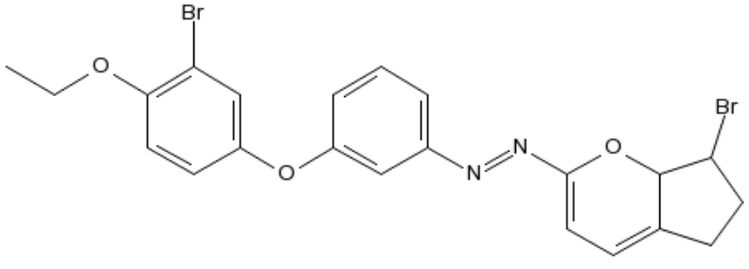
4. 

Proof of concept

But be careful what you wish for

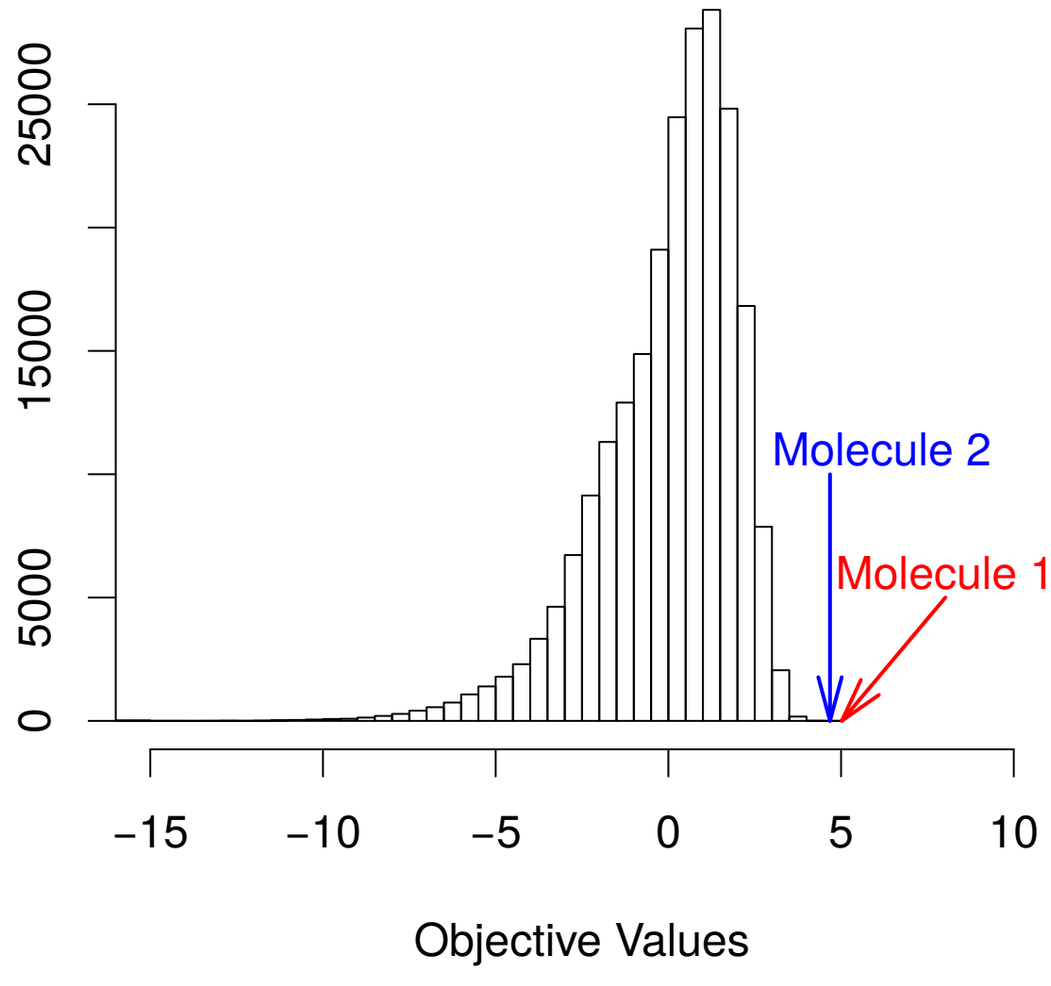


Molecule 1



Molecule 2

Objective Values in Training Data

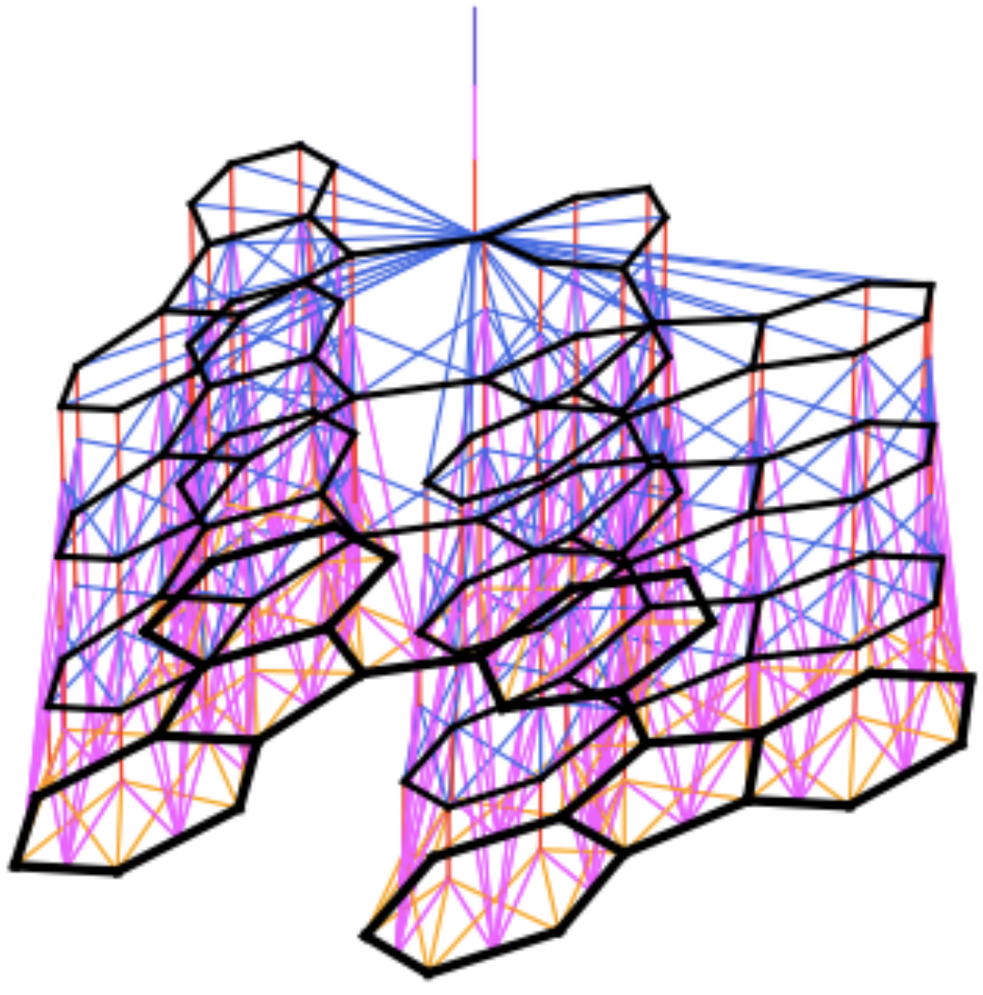


Applications of small-molecule design

Organic LEDs, liquid crystals, organic solar cells, gas dielectrics, supercapacitors, batteries, electronic polymers, homogeneous catalysts, plastic additives, adhesives, sealants, 3D printing, paints and coatings, specialty fibers, biodegradable polymers, medical plastics, pesticides, small molecule drugs

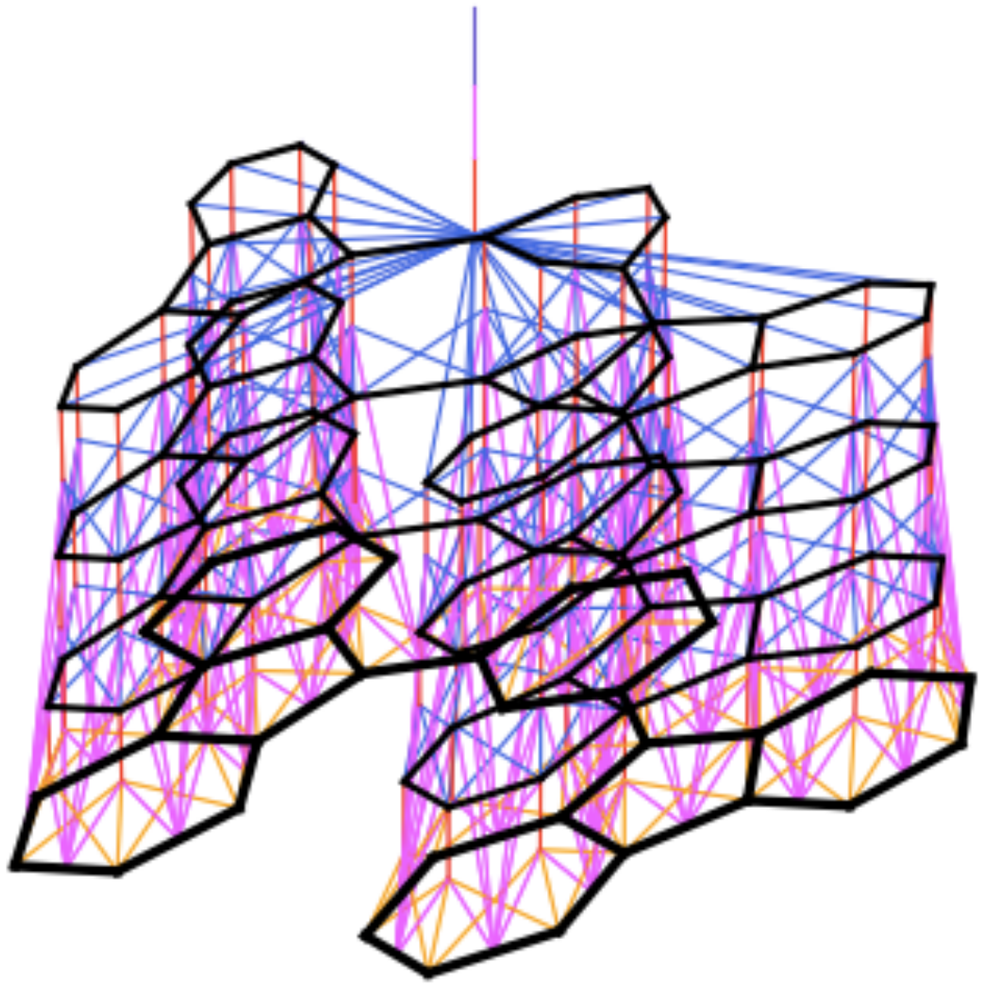
1. ▲ Twitter Plans Hundreds More Job Cuts as Soon as This Week (bloomberg.com)
   198 points by bentlegen 4 hours ago | hide | 147 comments
2. ▲ Microsoft Cognitive Services (projectoxford.ai)
   61 points by igravious 3 hours ago | hide | 13 comments
3. ▲ Apple Introduces What It Calls an Easier to Use Portable Music Player (200
   208 points by daschaefer 7 hours ago | hide | 153 comments
4. ▲ Chrome Requiring Certificate Transparency in 2017 (groups.google.com)
   79 points by edmorley 4 hours ago | hide | 11 comments
5. ▲ Delta functions [pdf] (berkeley.edu)
   7 points by lisper 1 hour ago | hide | 1 comment
6. Keras-based molecular autoencoder (github.com)
   67 points by frisco 5 hours ago | hide | 24 comments
7. ▲ Ask HN: What is your favorite internet rabbit hole?
   763 points by karim 15 hours ago | hide | 382 comments
8. ▲ Web Bloat Score Calculator (webbloatscore.com)
   24 points by zdw 2 hours ago | hide | 2 comments
9. ▲ IHaskell: A Haskell kernel for IPython (github.com)
   19 points by sndean 2 hours ago | hide | discuss
10. ▲ Introducing Initialized Capital (initialized.com)
    489 points by ernestipark 13 hours ago | hide | 130 comments
11. ▲ Social Media's Dial-Up Ancestor: The Bulletin Board System (ieee.org)

Future work



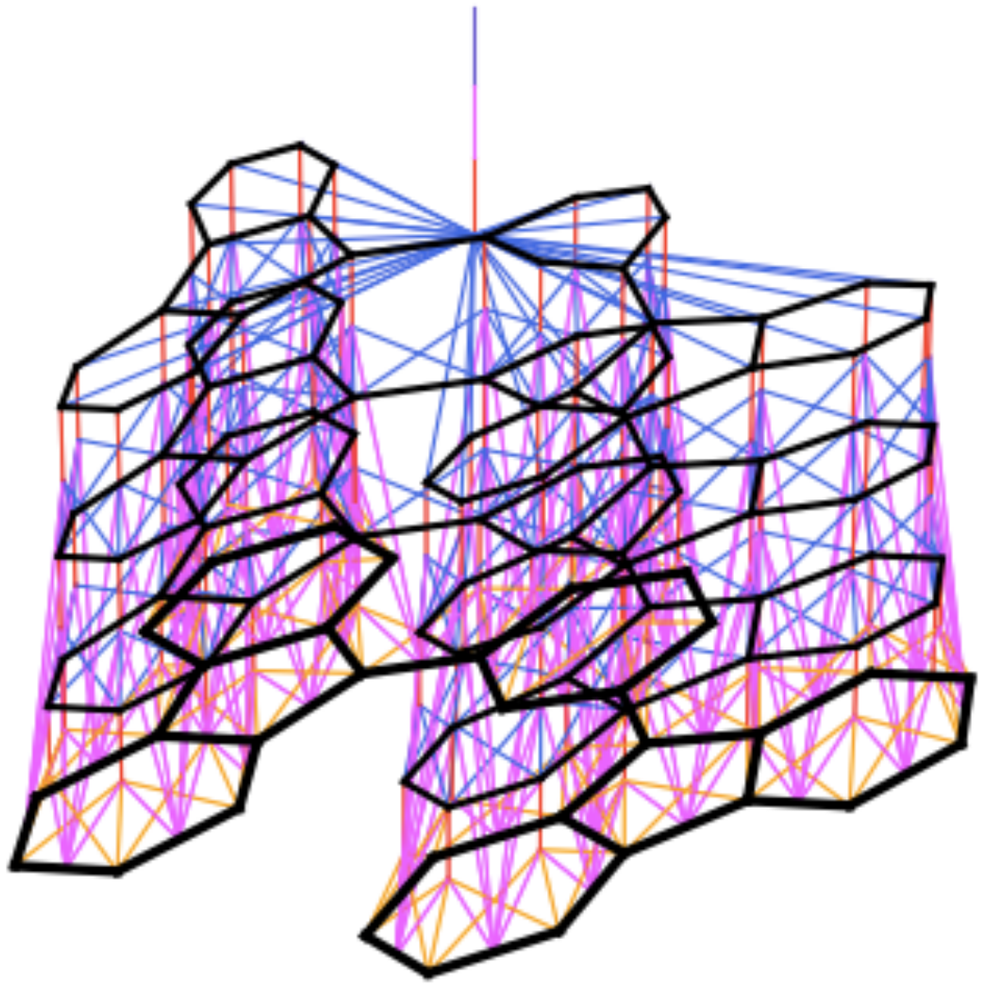
Future work

- Jointly train autoencoder and prediction model



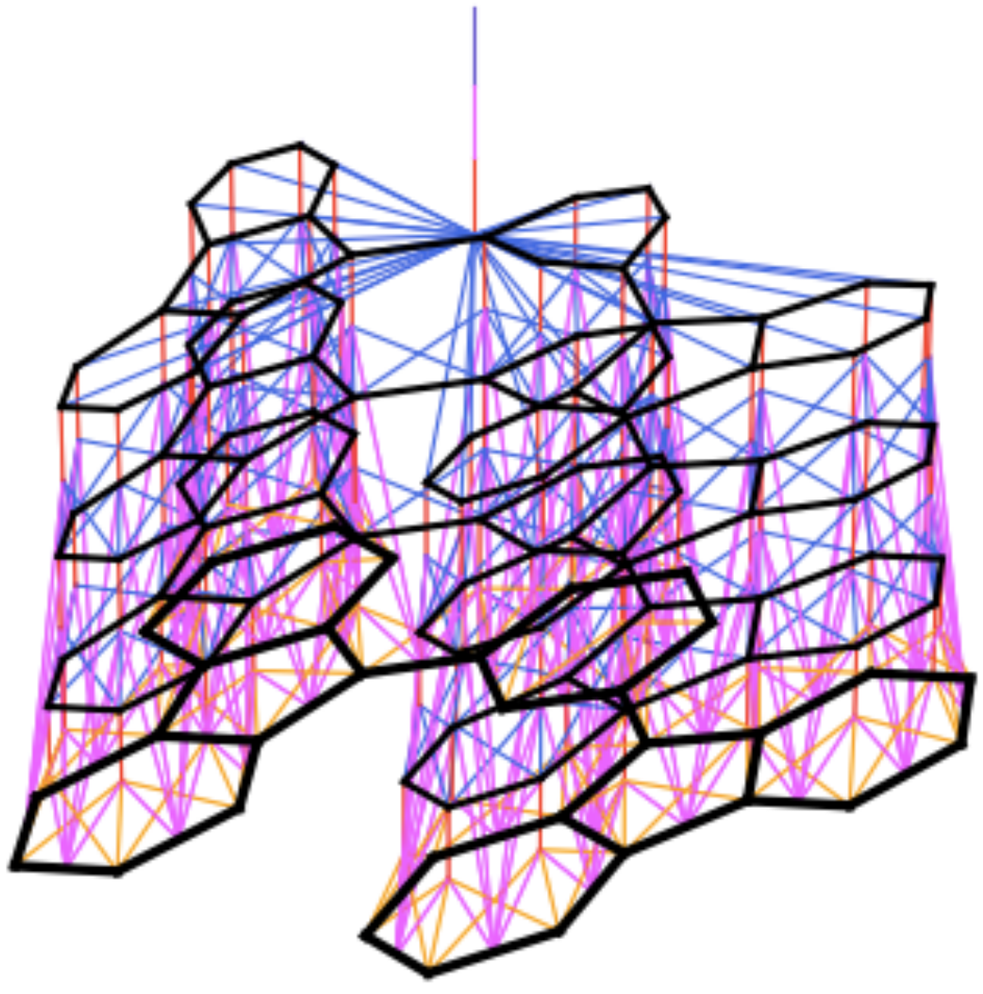
Future work

- Jointly train autoencoder and prediction model
- Decode directly to graphs



Future work

- Jointly train autoencoder and prediction model
- Decode directly to graphs
- Decode directly to recipes for synthesis



Thanks!



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