AI
&
material search

Fraunhofer SCAI

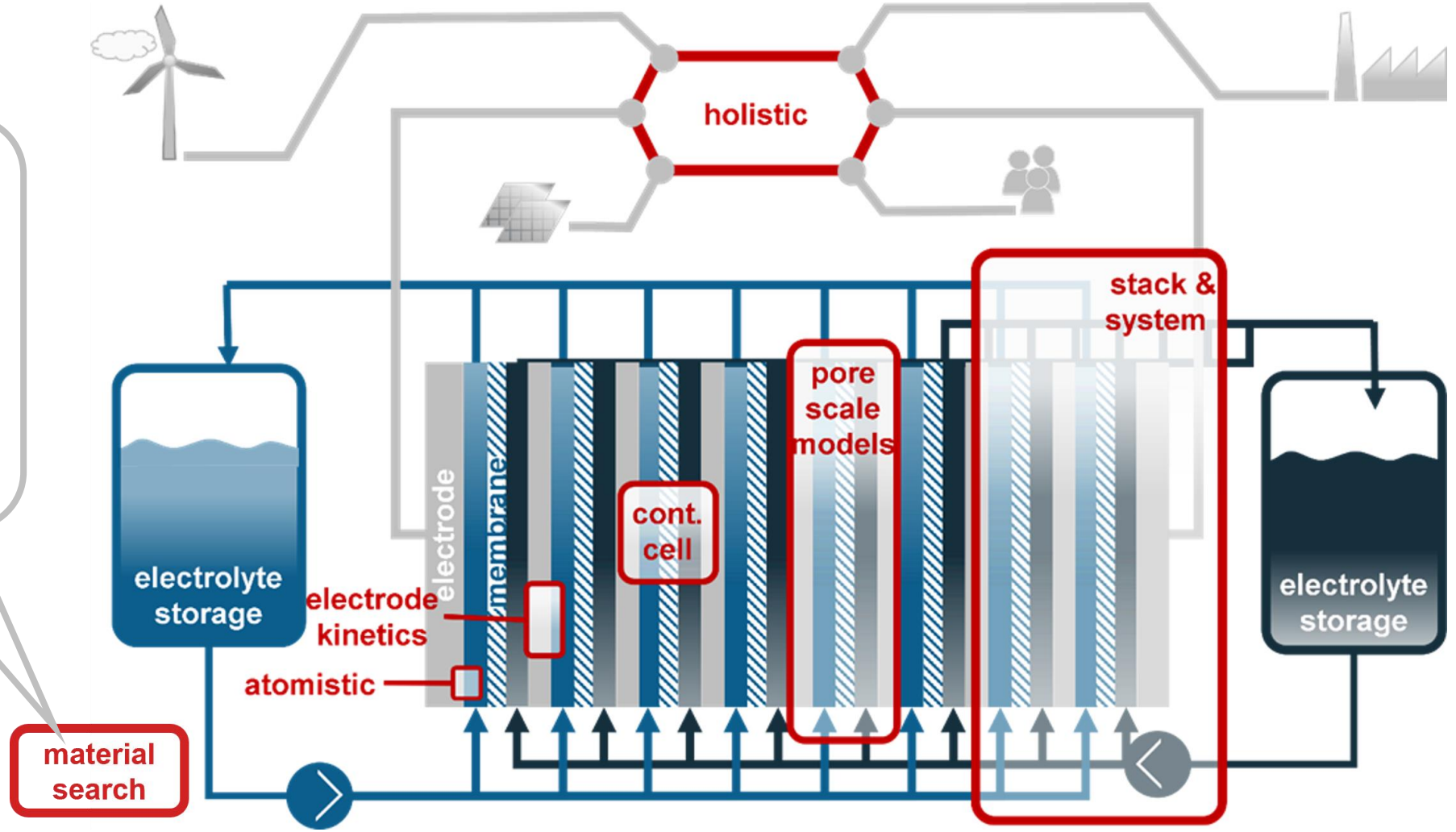
Workshop 2023

St.Augustin, 21.09.2023

SONAR at a glance

task WP1:

tools to identify
organic
affordable
redox-active
materials



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KIT Karlsruher Institut für Technologie
UNSW SYDNEY

Data driven models

search

organic chemical space ~10^{23-60}

for high energy density at low cost

speed & focus

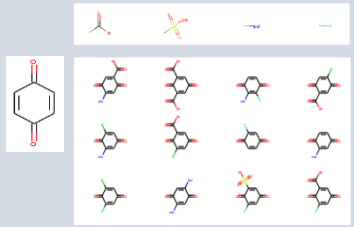
efficient down-selection

cheap filters first

then expensives

all fast

virtual library



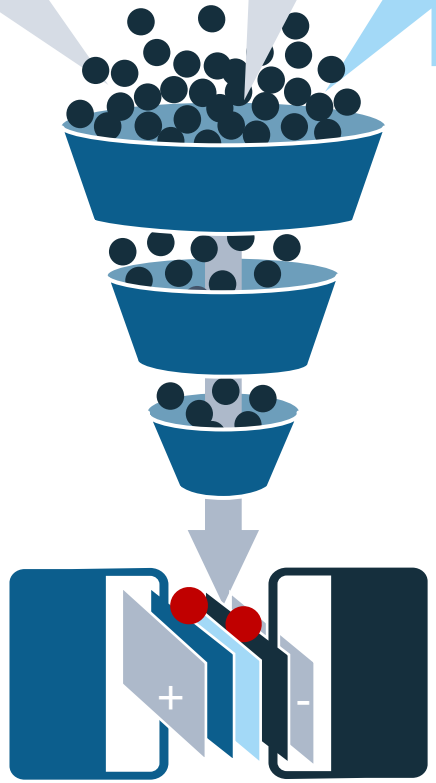
vendor compounds

generative models for new candiates

- VAE
- diffusion models
- transformers

predictive models for screening

1. compounds
   - synthetic accessibility
   - solubility
   - redox potential
2. negolyte/posolyte pairs
   - basic cell performance
   - hand over to ZHAW



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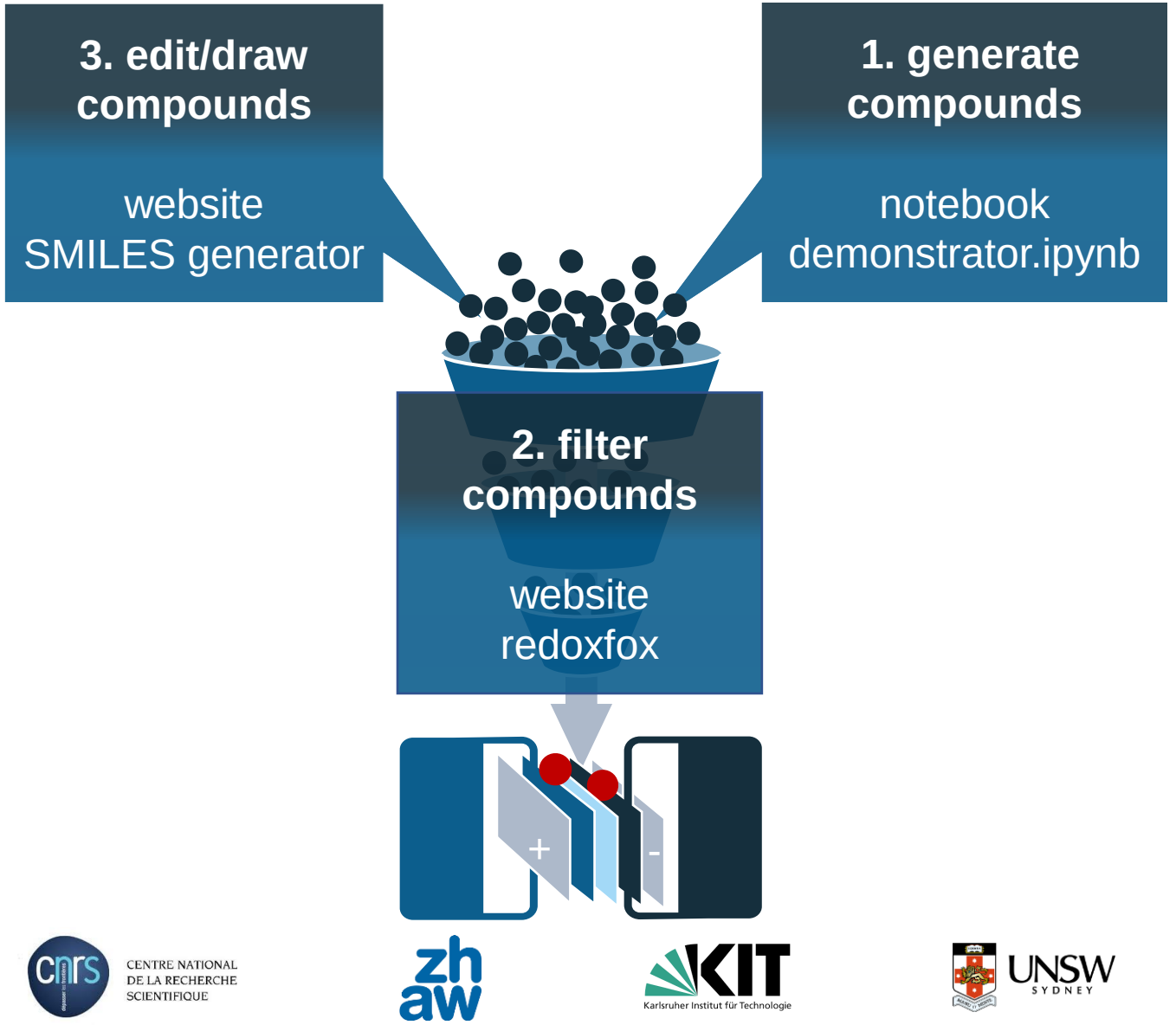
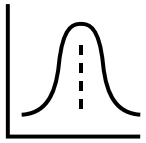
Hands on session

+ page 20 in handout
+ jupyter notebook
+ webinterface
  – chromium-browser &



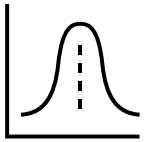
Background



Underlying Distribution

Dataset: (x,y) pairs
x - Molecule
y - Property

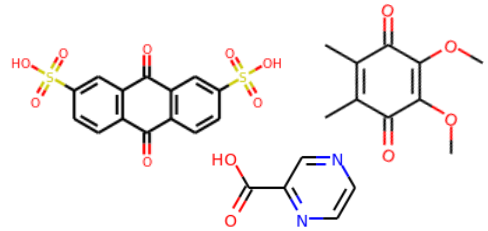
Train



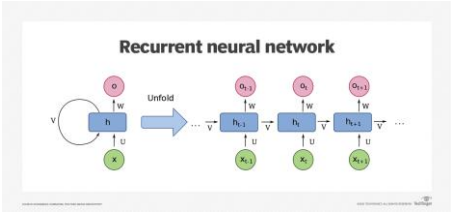
Approximate
Unconditional: x ~ G
Conditional: x ~ G(y)

Generator **G**

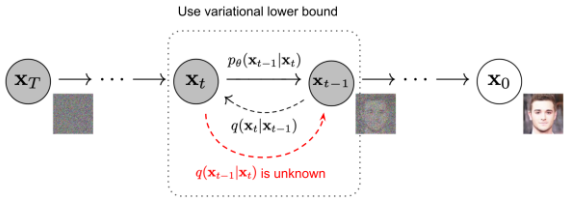
Sample



RNNs



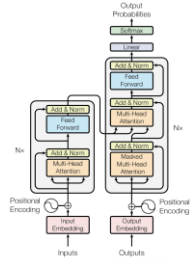
Diffusion



Transformer

BERT

Encoder



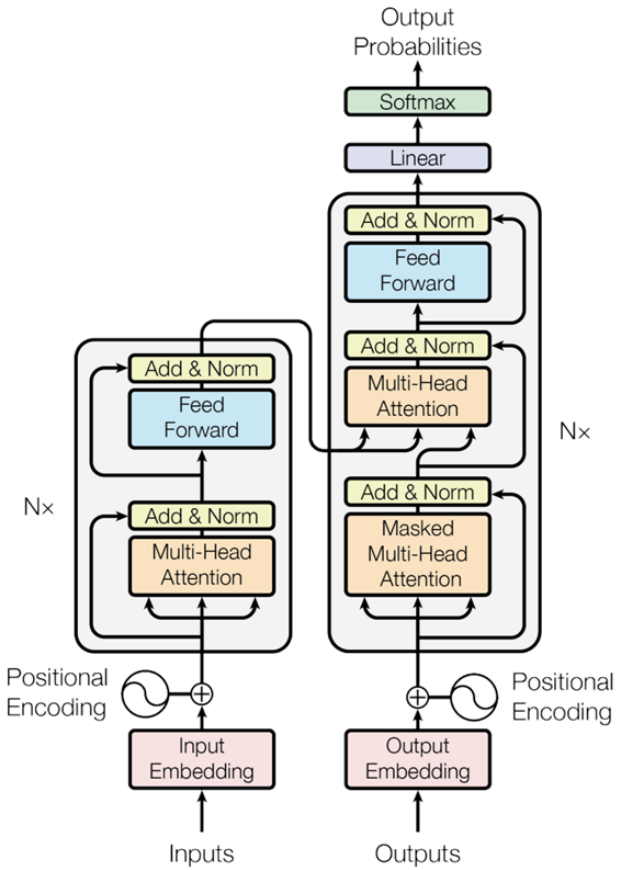
GPT

Decoder

Transformer

BERT

Encoder



GPT

Decoder

Next Token

Softmax

Add & Layer Normalization

Feed Forward

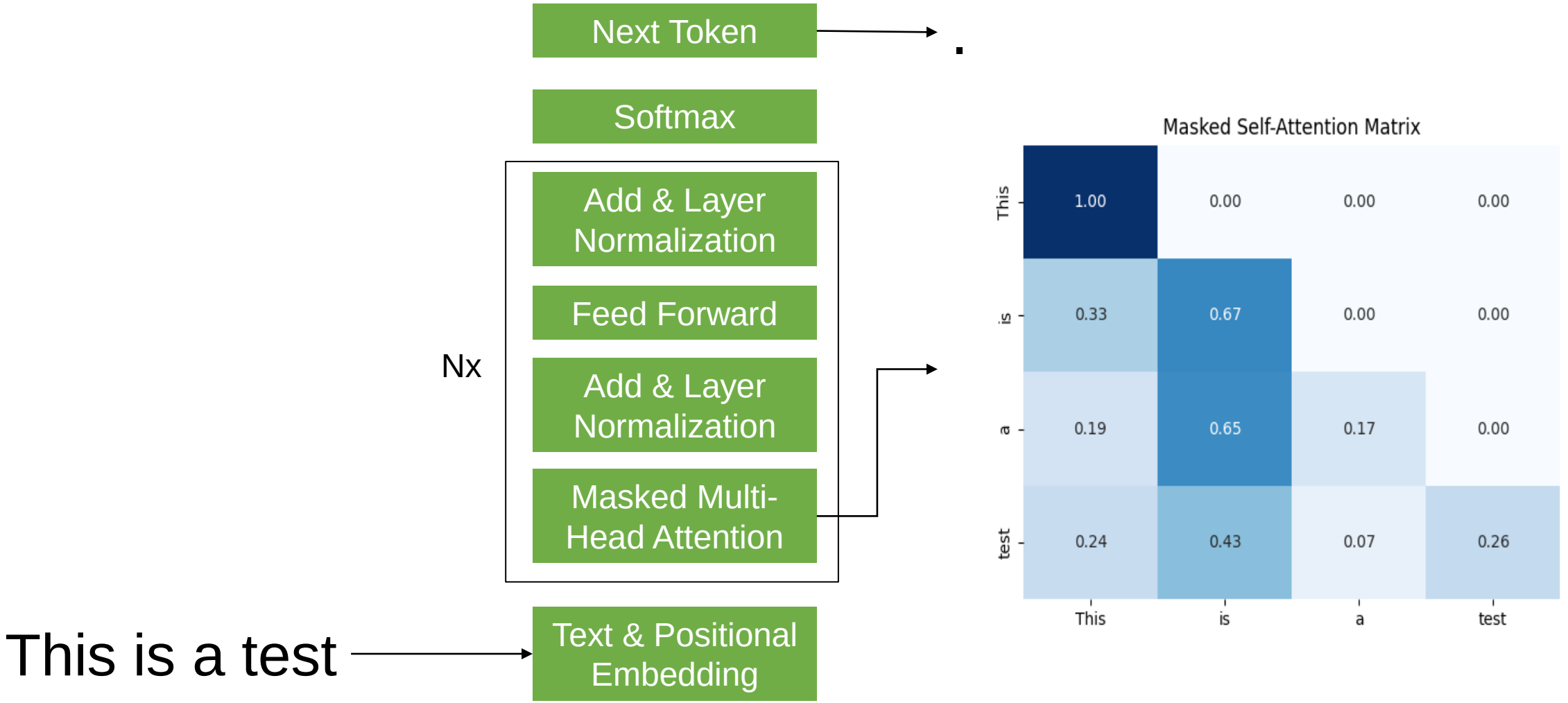
Add & Layer Normalization

Masked Multi-Head Attention

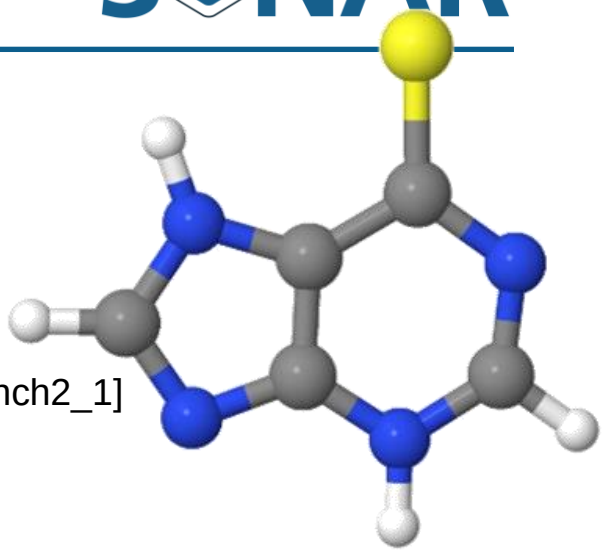
xN

Text & Positional Embedding

Transformer – Basic Generation



Molecule representation



2D

InChi InChI=1S/C5H4N4S/c10-5-3-4(7-1-6-3)8-2-9-5/h1-2H,(H2,6,7,8,9,10)

SMILES C1=NC2=C(N1)C(=S)N=CN2

SELFIES [C][=N][C][=C][Branch1_1][Ring2][N][Ring1][Branch1_1][C][Branch1_2][C][=S][N][=C][N][Ring1][Branch2_1]

3D

Coordinates

C	-2.28752	-0.09279	0.00131
N	-1.52093	-1.16587	0.00160
C	-0.26385	-0.66545	0.00005
C	-0.23058	0.70099	-0.00110
N	-1.55044	1.06537	0.00000
⋮	⋮	⋮	⋮

Descriptors

- matter of choice

→ meaningful

→ Cheap

→ LogP, SAScore and Molecular Weight

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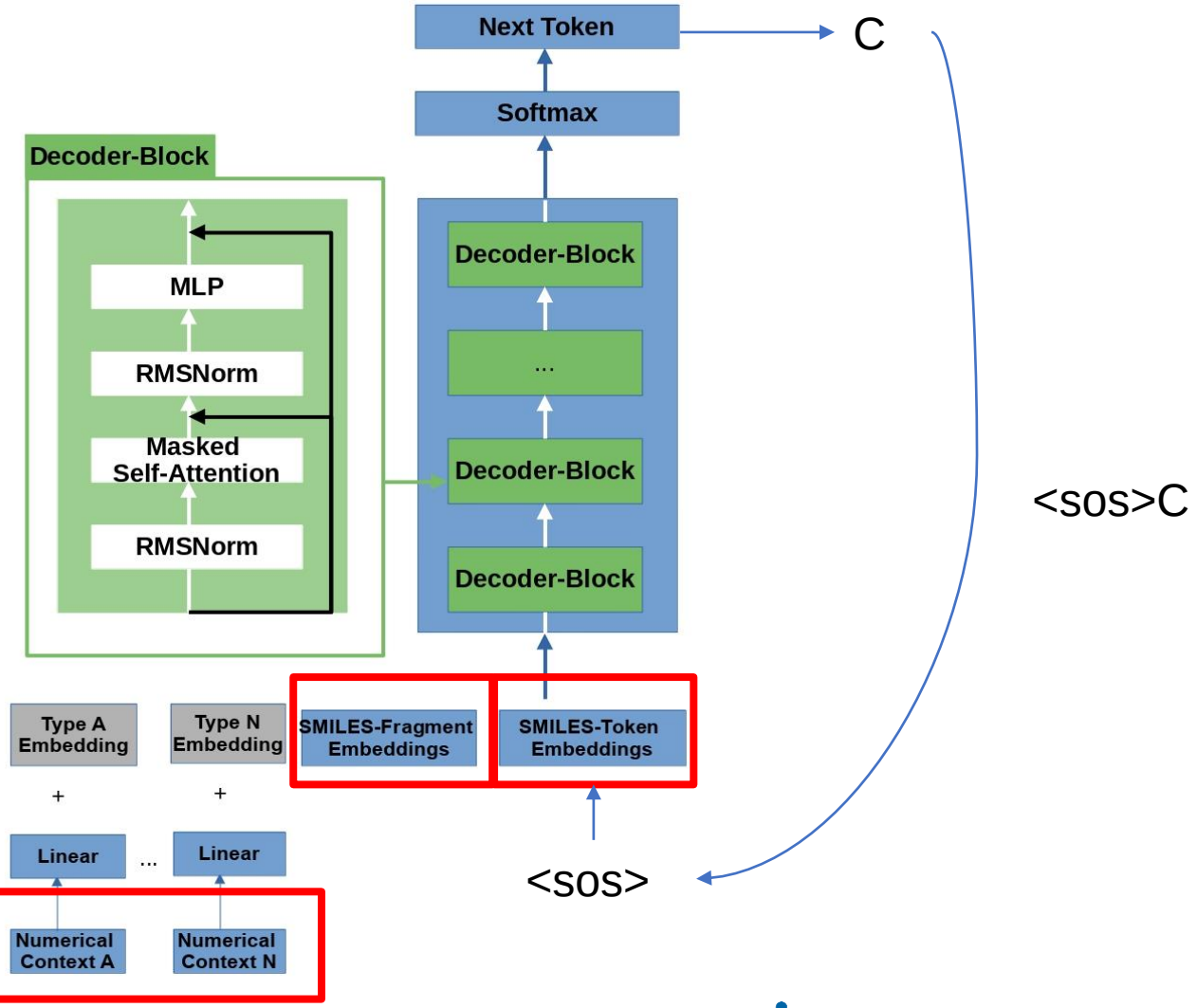
Molecule representation – Conditions

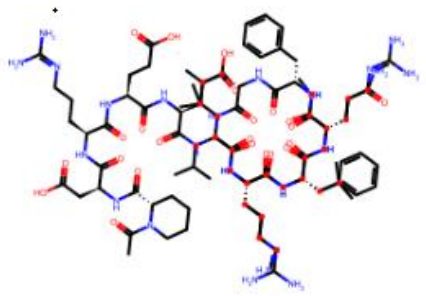
- **LogP** [-4, 8]: How hydrophobic is a molecule?
  - Negative: soluble in water
  - Positive: attracted to non-polar environments
- **SAScore** [0,10]: ease(0) or difficulty(10) to synthesize a molecule
- **Molecular Weight** [0, 10]: proxy for the size of a molecule
  - We divide it by the constant 100 to „normalize“
- **SMILES Fragment**: Can be a full molecule or a part of a SMILES e.g. „c1cccc1“ or „csc“

Transformer – Molecule Generation

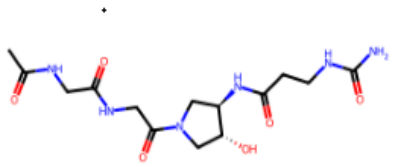


LogP
SAScore
Molecular Weight

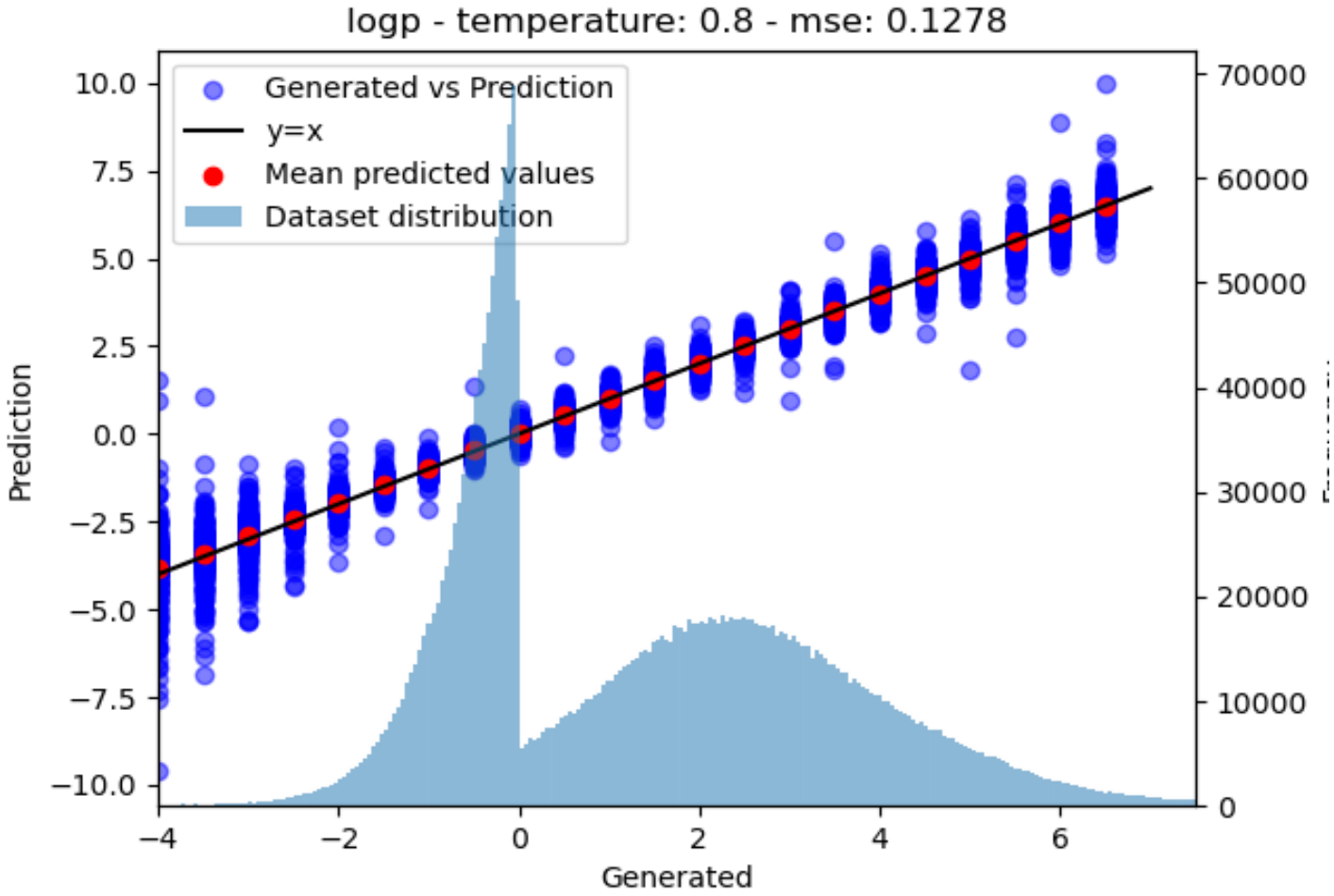
Transformer – Performance LogP

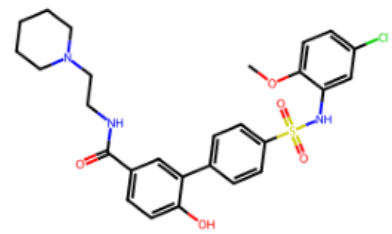


logp: -4.0 vs -4.65

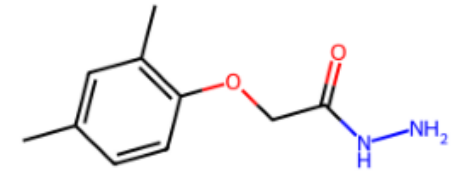


logp: -4.0 vs -4.01



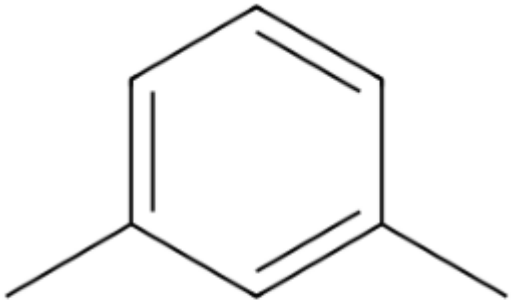


logp: 4.5 vs 4.74

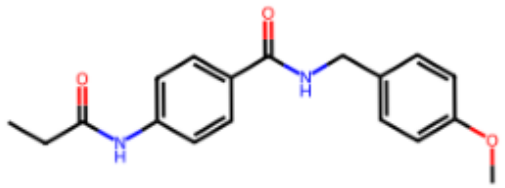


logp: 0.5 vs 0.67

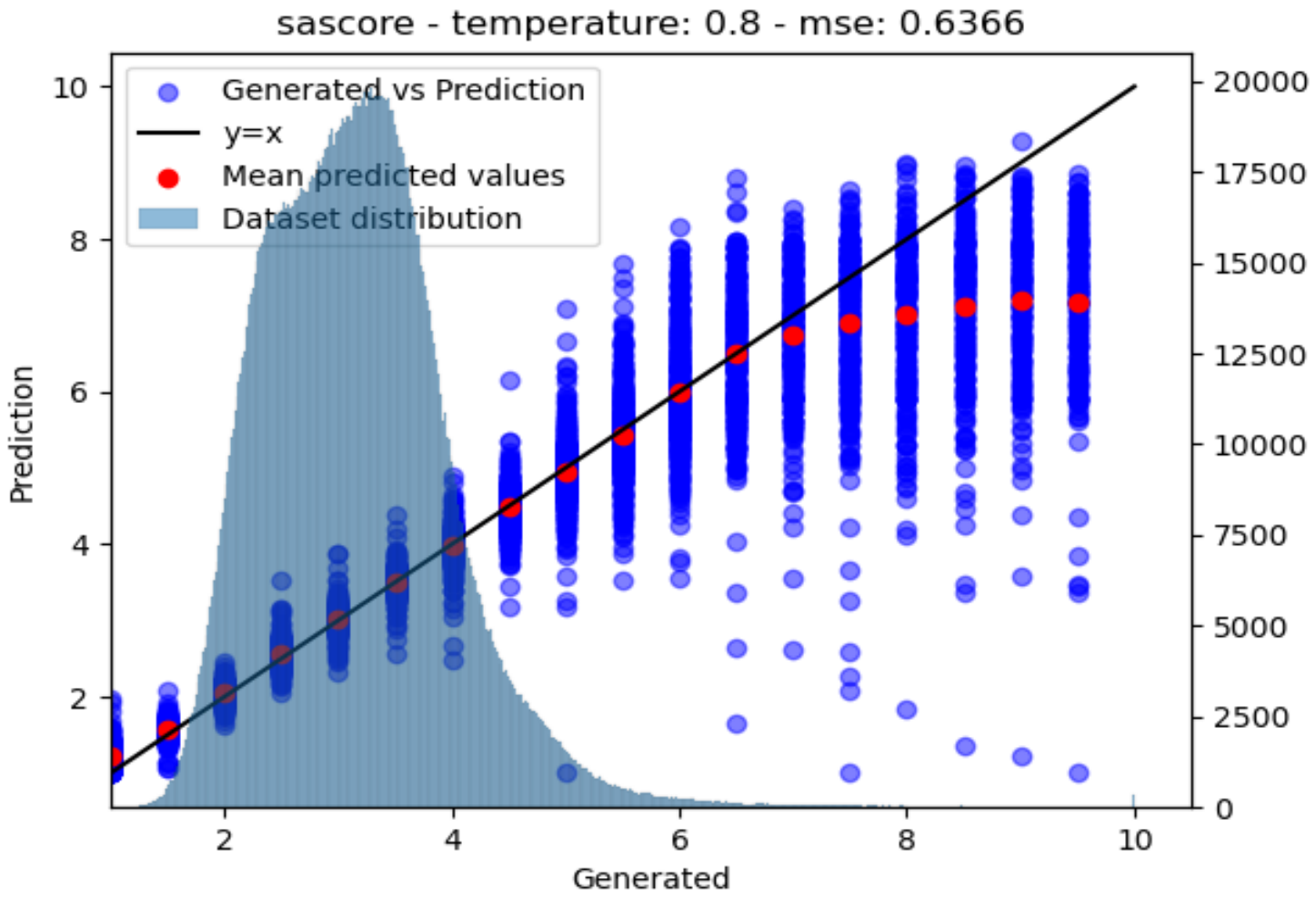
Transformer – Performance SAScore

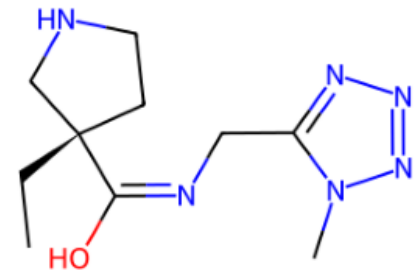


sascore: 0.5 vs 1.14

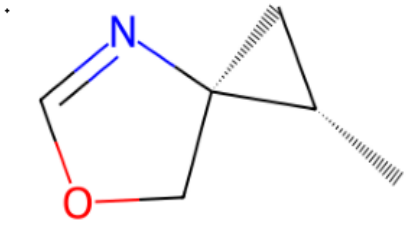


sascore: 1.5 vs 1.54



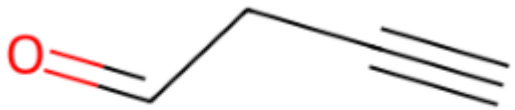


sascore: 4.0 vs 3.93

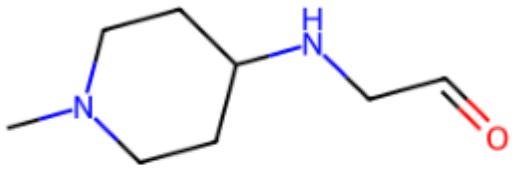


sascore: 5.5 vs 5.53

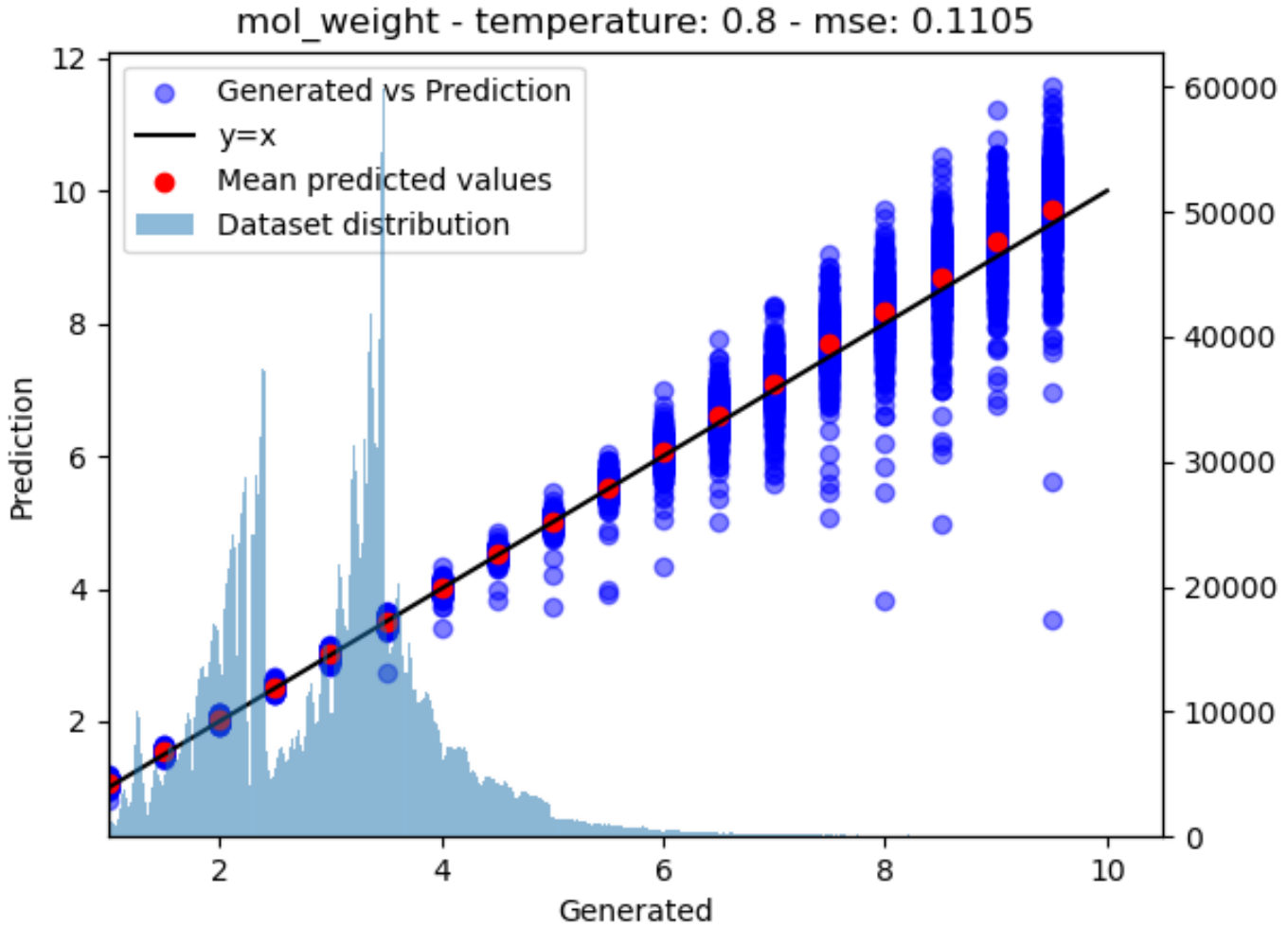
Transformer – Performance Molecular Weight

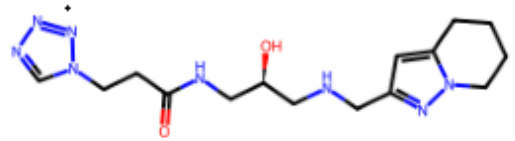


mol_weight: 0.5 vs 0.68

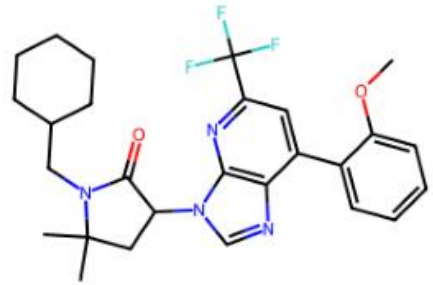


mol_weight: 1.5 vs 1.56



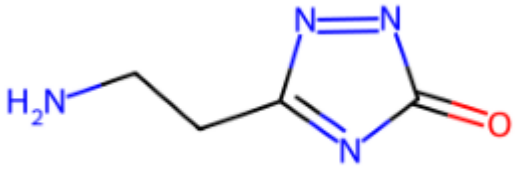


mol_weight: 3.5 vs 3.48



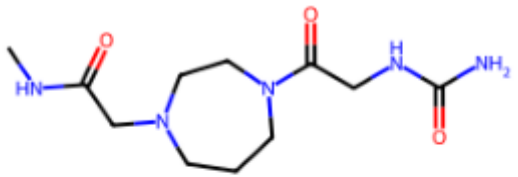
mol_weight: 5.0 vs 5.0

Transformer – Performance Multi Condition



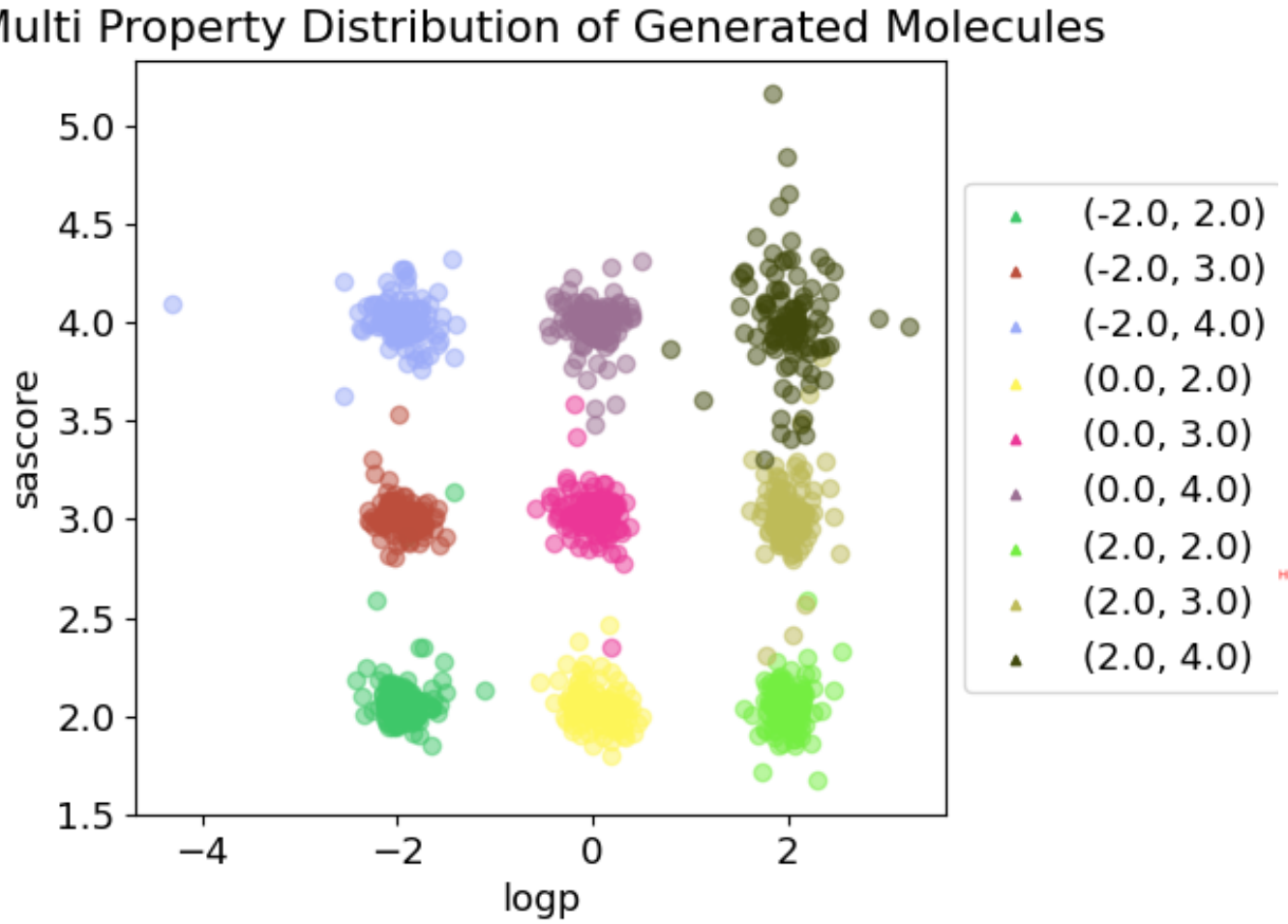
logp: 0.5 vs 0.32

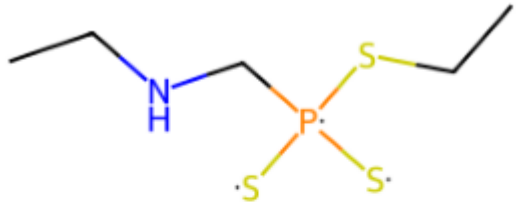
sascore: 4.0 vs 4.12



logp: -2.0 vs -2.06

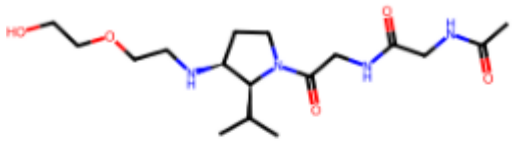
sascore: 2.0 vs 2.13





logp: 3.0 vs 3.46

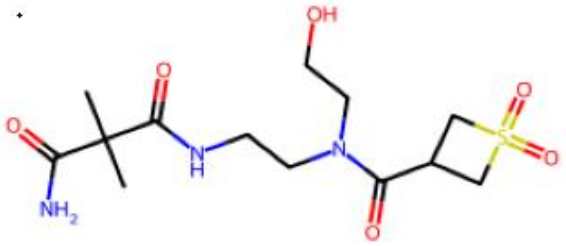
sascore: 5.5 vs 4.45



logp: -1.5 vs -1.54

sascore: 3.5 vs 3.53

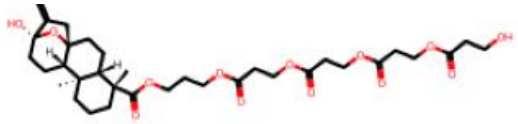
Transformer – Performance Multi Condition



logp: -2.5 vs -2.52

sascore: 3.0 vs 2.95

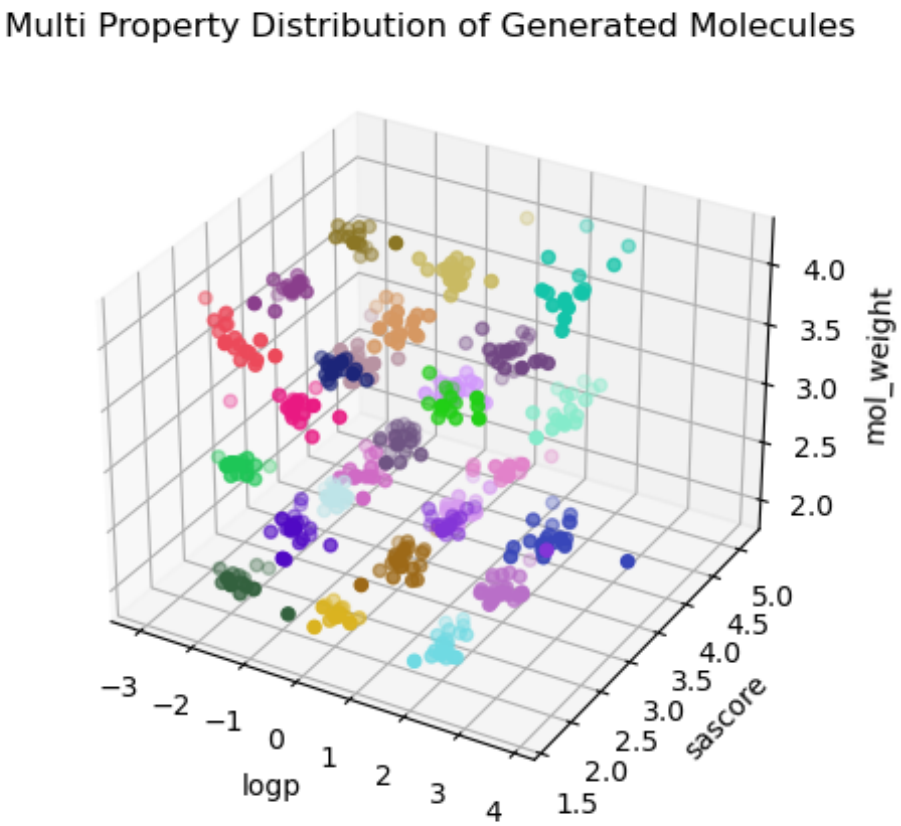
mol_weight: 3.5 vs 3.49

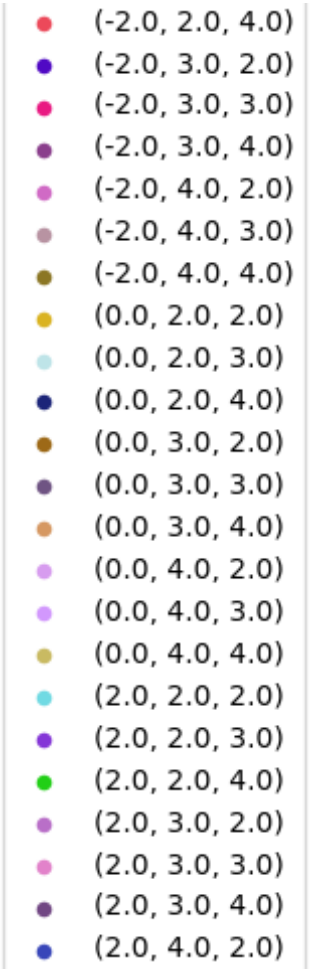


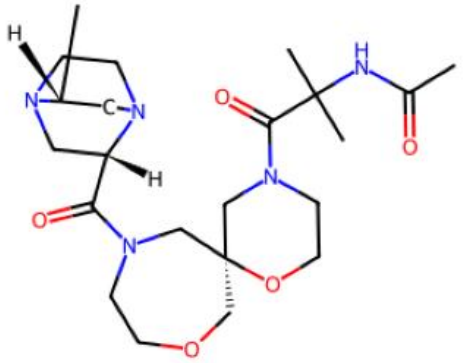
logp: 3.0 vs 3.07

sascore: 6.0 vs 6.07

mol_weight: 6.5 vs 6.66



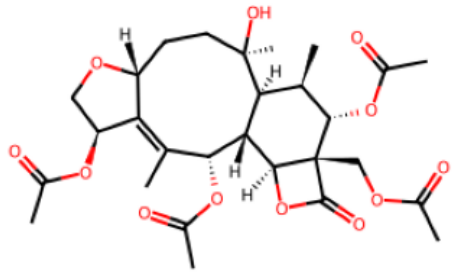




logp: -1.0 vs -1.25

sascore: 5.5 vs 5.61

mol_weight: 4.5 vs 4.51



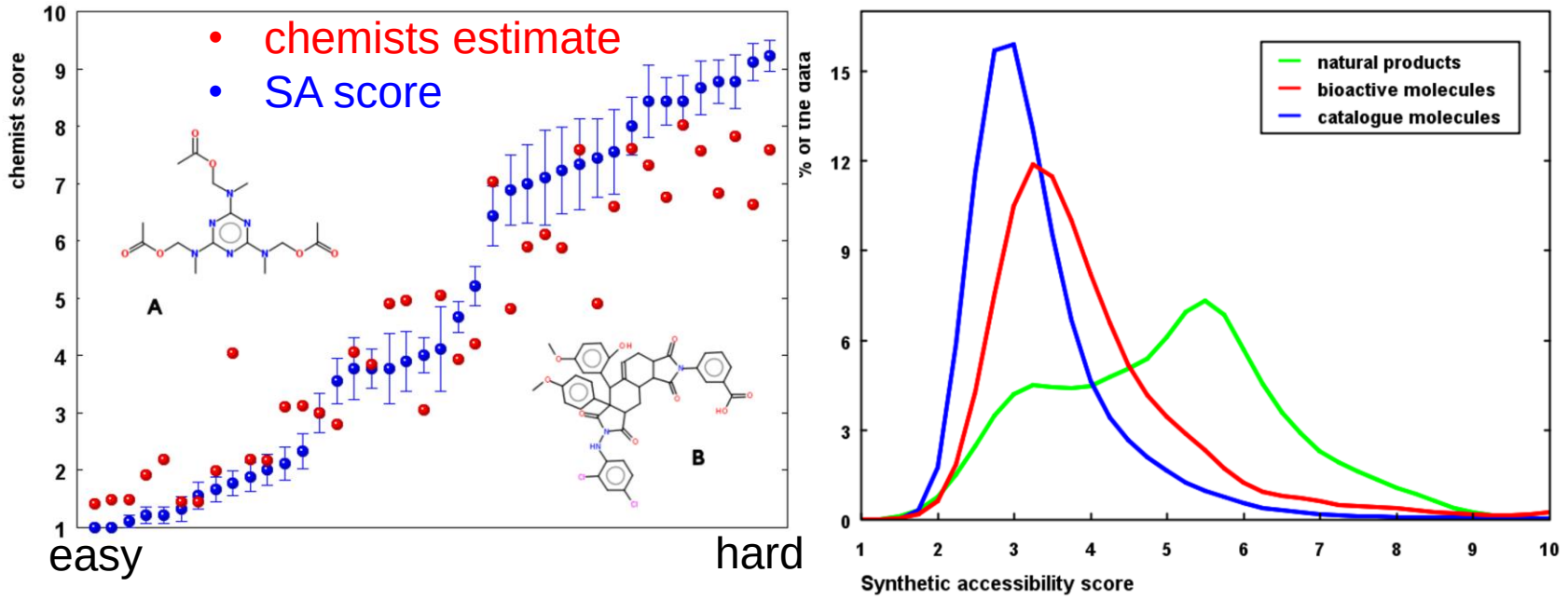
logp: 2.0 vs 1.4

sascore: 6.0 vs 5.92

mol_weight: 5.5 vs 5.66

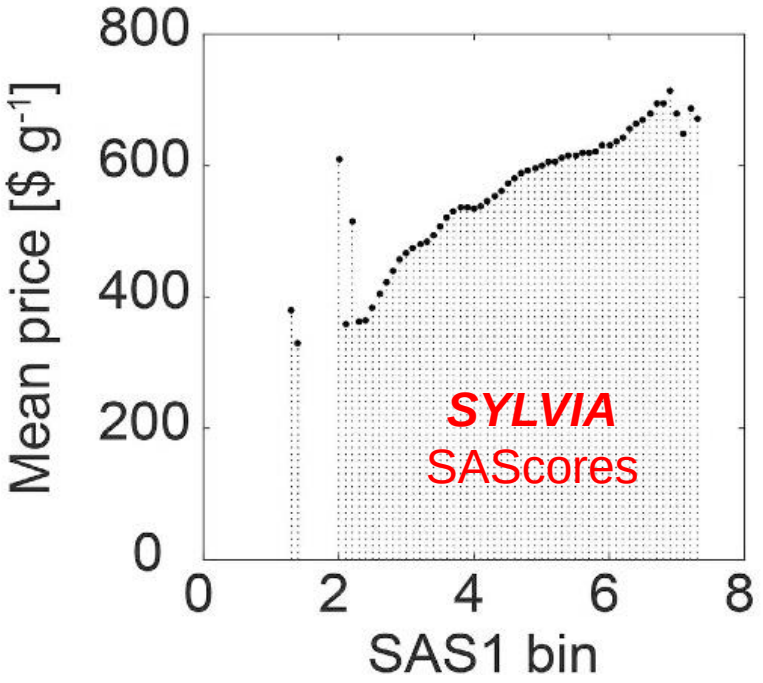
Synthetic accessibility score

Estimate SA score of drug-like molecules based on molecular complexity and fragment contributions



Molecular descriptor data explain market prices of a large commercial chemical compound library

Polanski et al, 2016

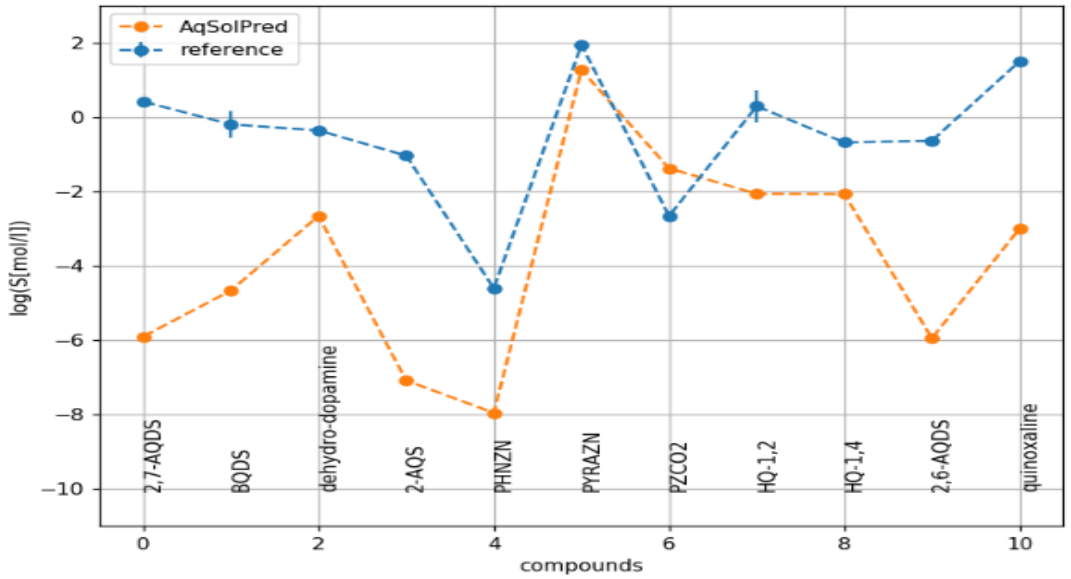


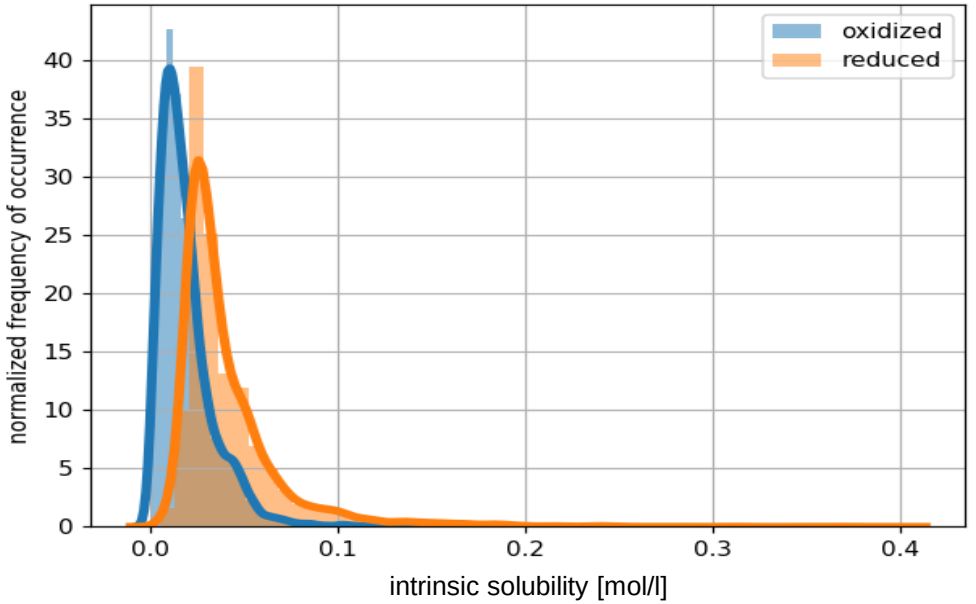
Ertl & Schuffenhauer **2009**. Estimation of synthetic accessibility score of drug-like molecules based on molecular complexity and fragment contributions. *Journal of cheminformatics*, *1*, 1-11.

Solubility by AqSolPred v1.0

consensus model (Sorkun, Vianney, Koelman & Er **2021,** Pushing the limits of solubility prediction via quality-oriented data selection' *science* 24.1 : 101961)

trained on ~10k experimental data (Sorkun, Khetan & Er. **2019,** 'qSolDB, a curated reference set of aqueous solubility and 2D descriptors for a diverse set of compounds, Scientific data 6.1, 1-8)





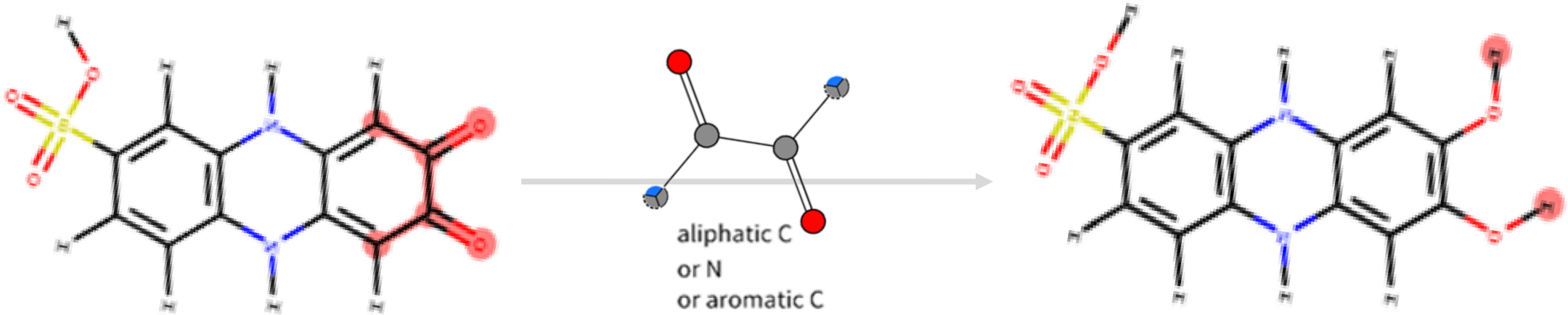
→ *intrinsic* solubility prediction neglects (de)protonation processes

→ oxidized states considered less soluble than reduced ones

Redox potential via ΔH

$$\mathbf{A_{ox}} + \mathbf{H_2} \rightarrow \mathbf{A_{red}} \qquad \Delta G \cong \Delta H_{G4(MP2)} \qquad E^o = -\frac{\Delta G}{zF}$$

neutral, organic, closed shell compounds in gas phase



SMARTS reaction templates

[OX1:1]=[CX3:2](-,:[C,N,n,c:3])-,:[CX3:4](-,:[C,N,n,c:5])=[O:6].[H:7]-[H:8]

>> **[H:7]-[O:1]-[C:2]([C,N,n,c:3])=[C:4]([C,N,n,c:5])-[O:6]-[H:8]**

SMARTSviewer smartsview.zbh.uni-hamburg.de, ZBH Center for Bioinformatics, University of Hamburg

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Predicting ΔH

SONAR

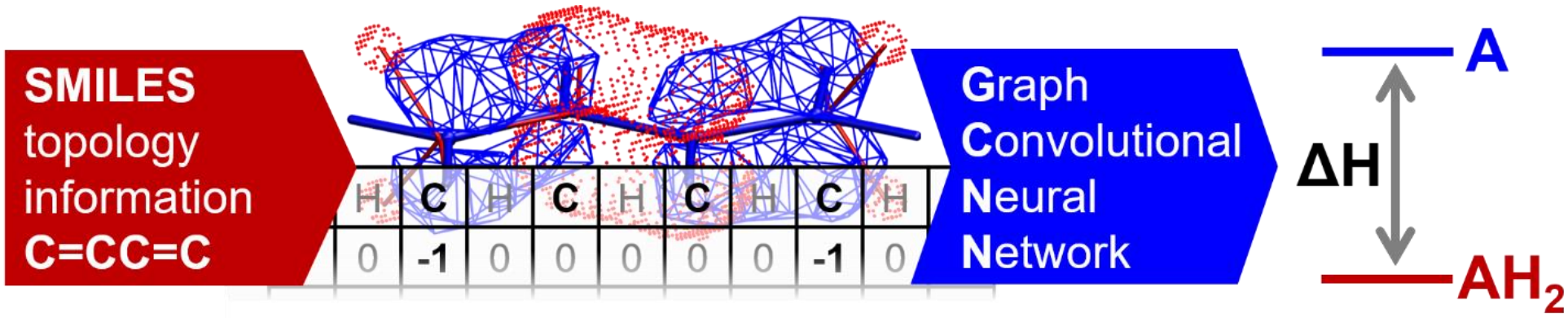
QM9

134 k
molecules +
heat of atomization
(Ramakrishnan (B3LYP), 2014,
Kim: G4(MP2), 2019)

define
reactants & products

qm9

45 k
A/AH_2 pairs +
heat of reaction



working with 2D structures: atomic features + bond graph

- generate differential features from 2D
- train model to heat of reaction

→ predict heat of reaction for new mols

Barker, Berg, Hamaekers & Maass, **2021:** Rapid prescreening of organic compounds for redox flow batteries: a graph convolutional network for predicting reaction enthalpies from SMILES, *Batteries & Supercaps*, 4(9), 1482-1490.

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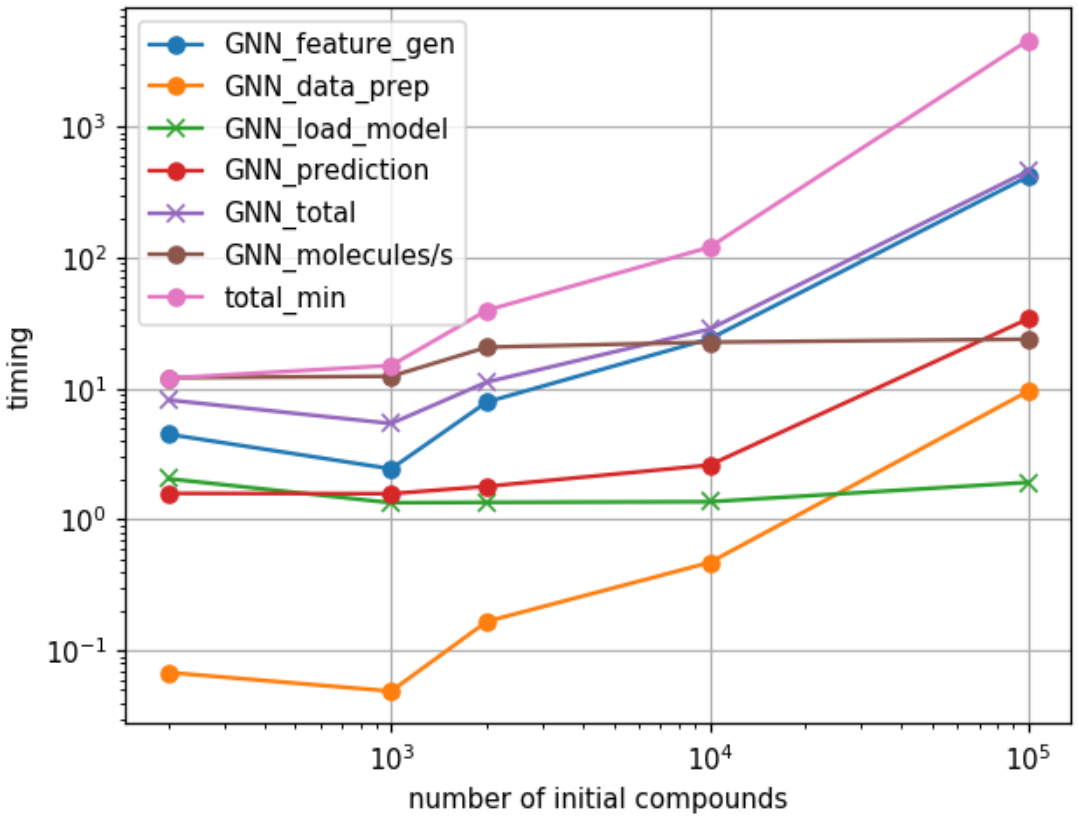
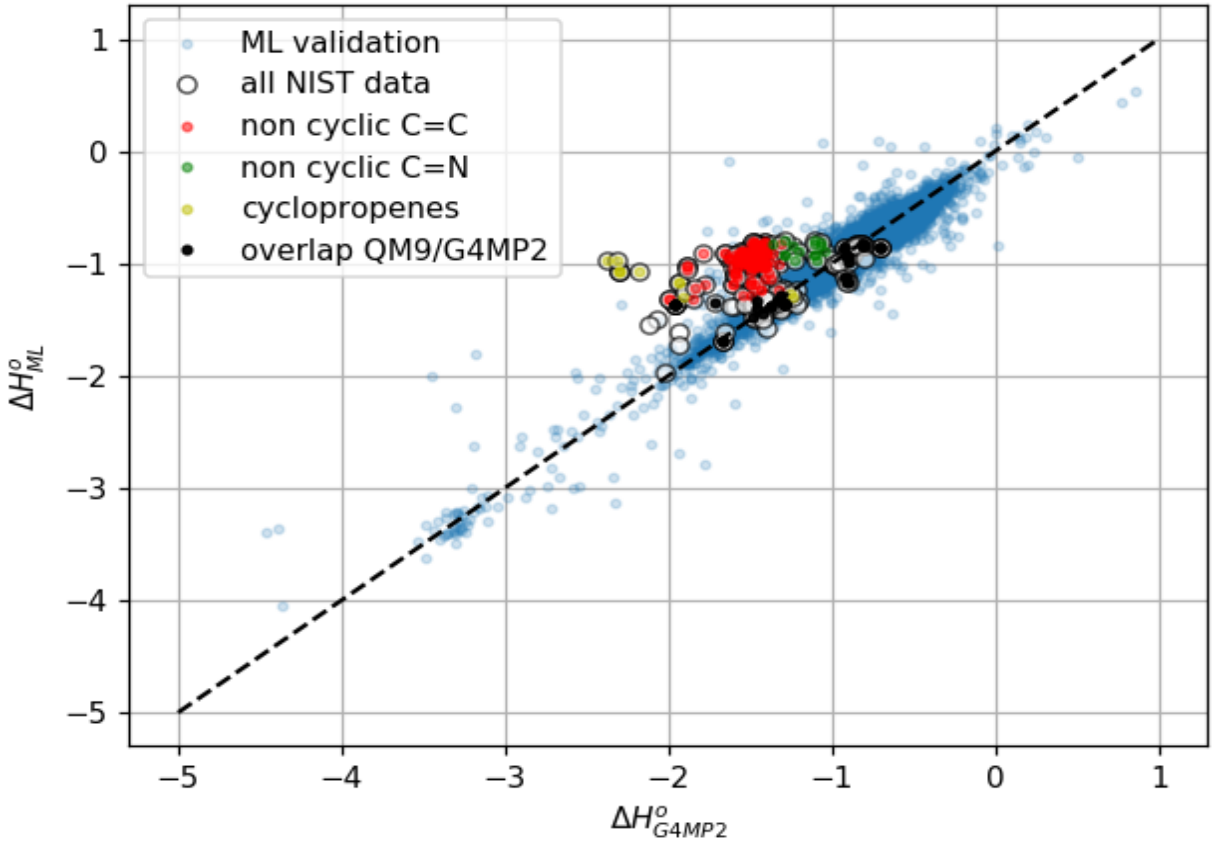
Model performance



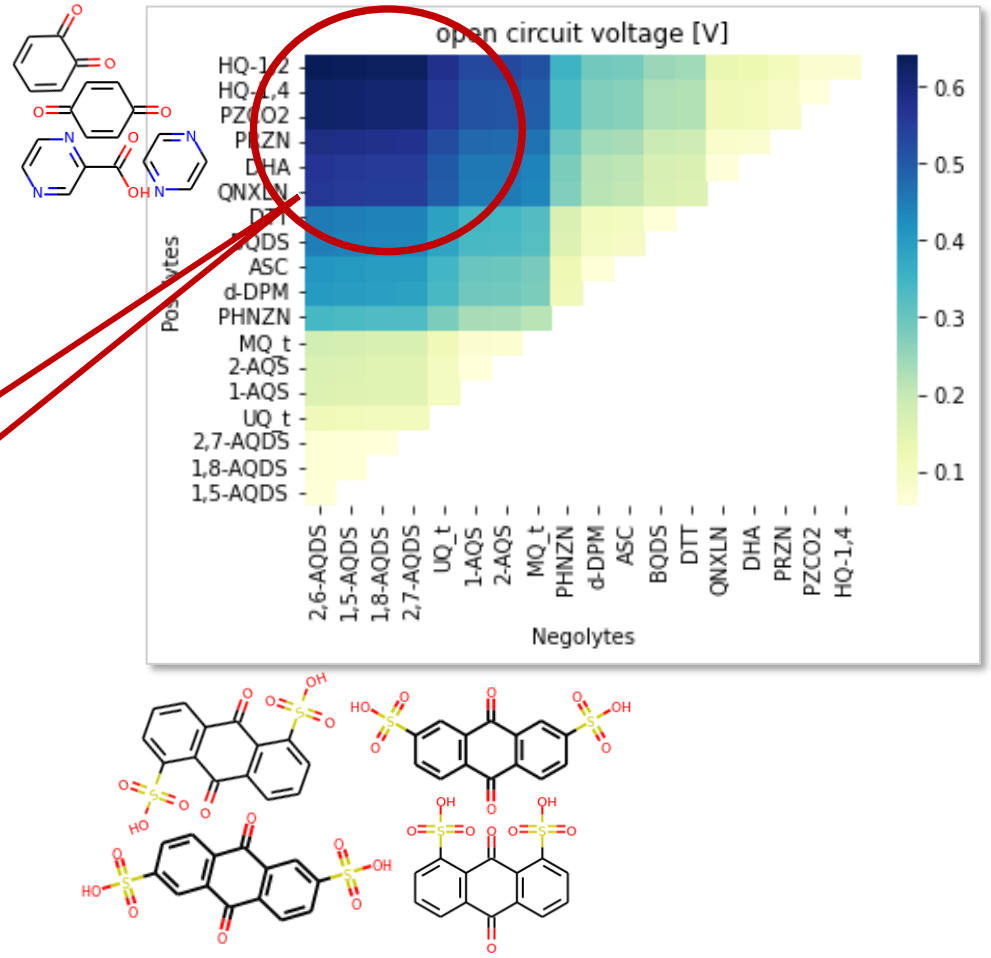
- 50 mols/sec – GNN feature generation most time consuming step
- 10e+5 compounds ≤ 2 hours on std desktop PC (4 cores, 8 GB memory)



- limitation of the chemical space represented within the training set

→ provide larger training set & train again

Full cell performance: OCV



reasonable matches

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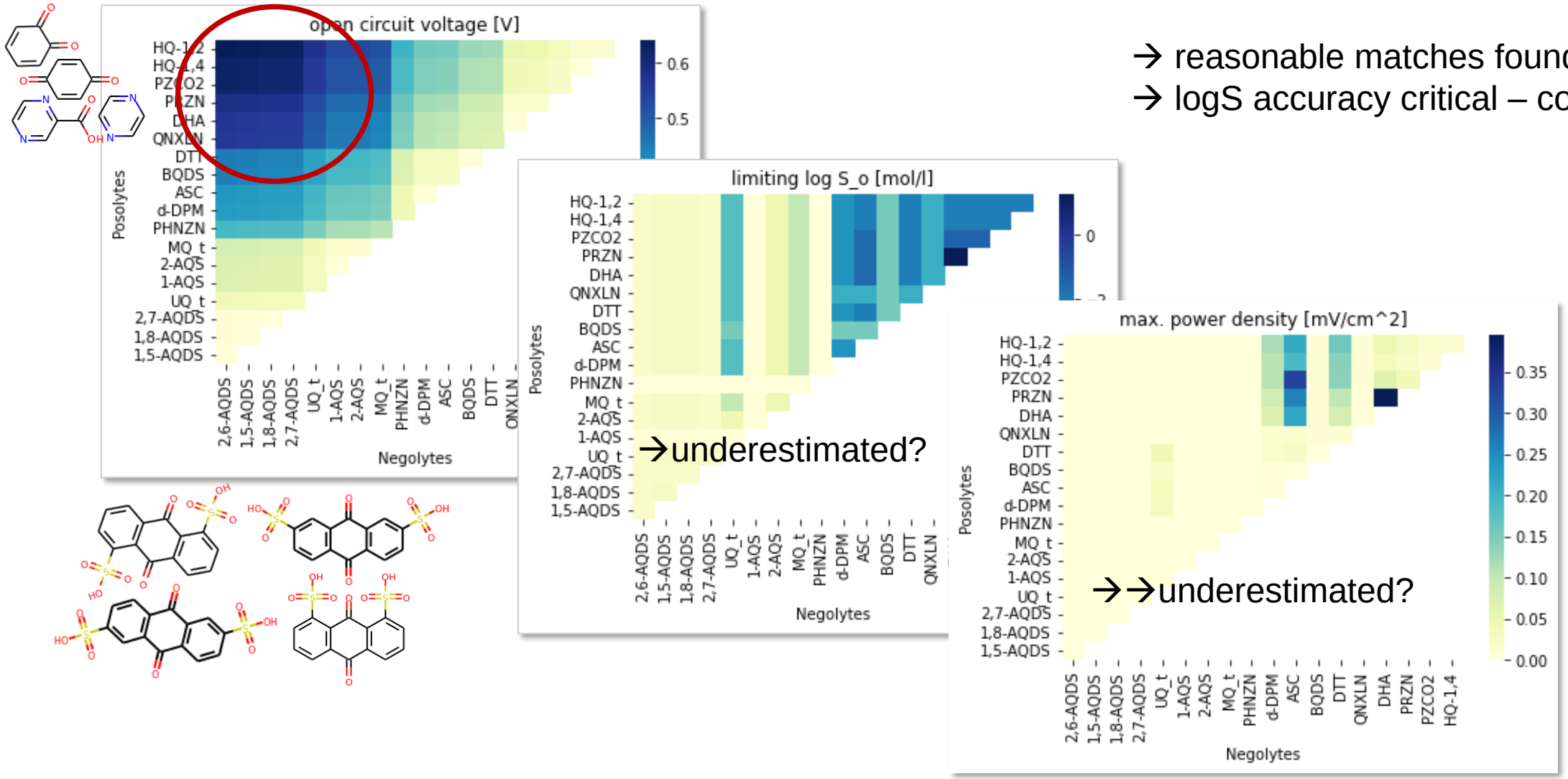
Full cell performance



→ reasonable matches found
→ logS accuracy critical – consider pH

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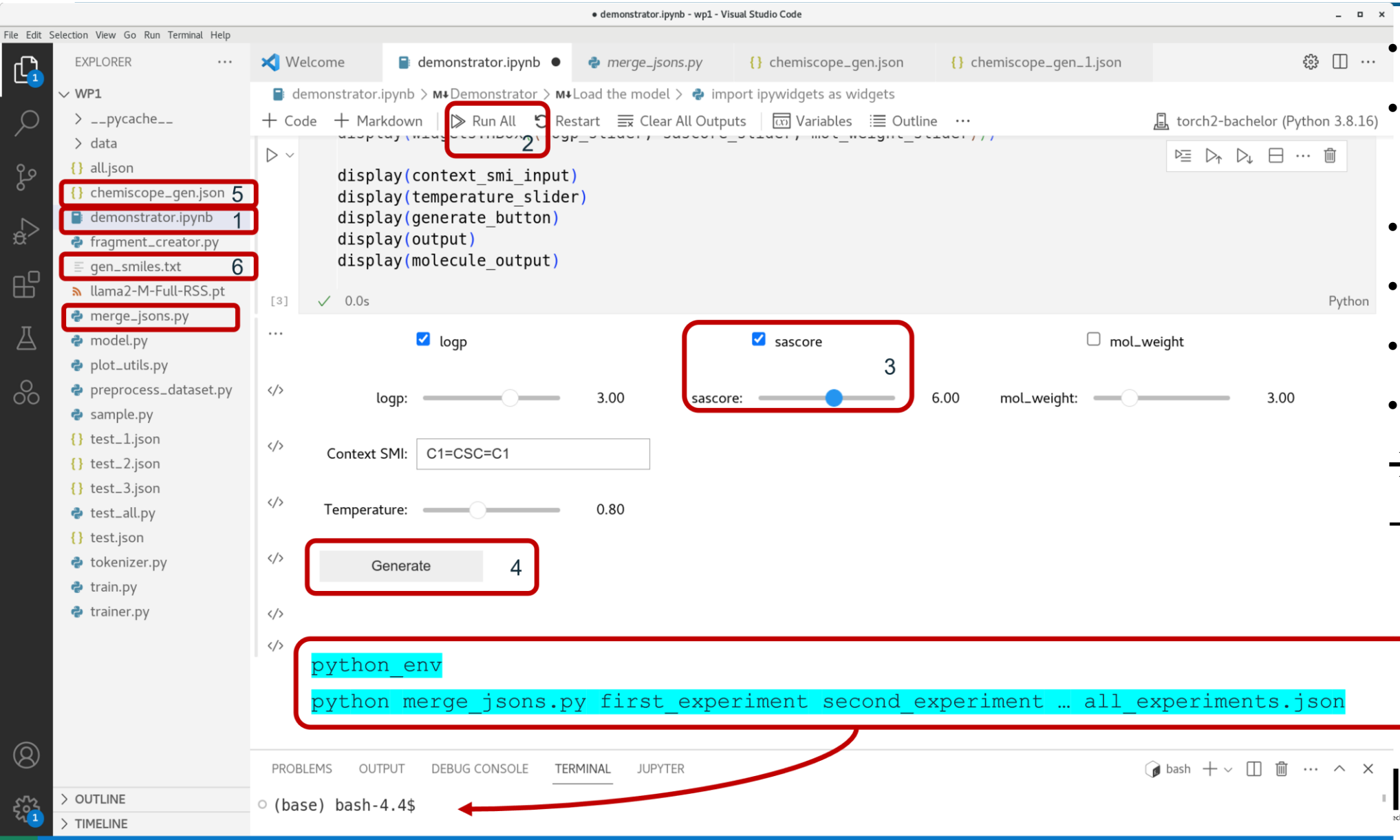
Generate compounds

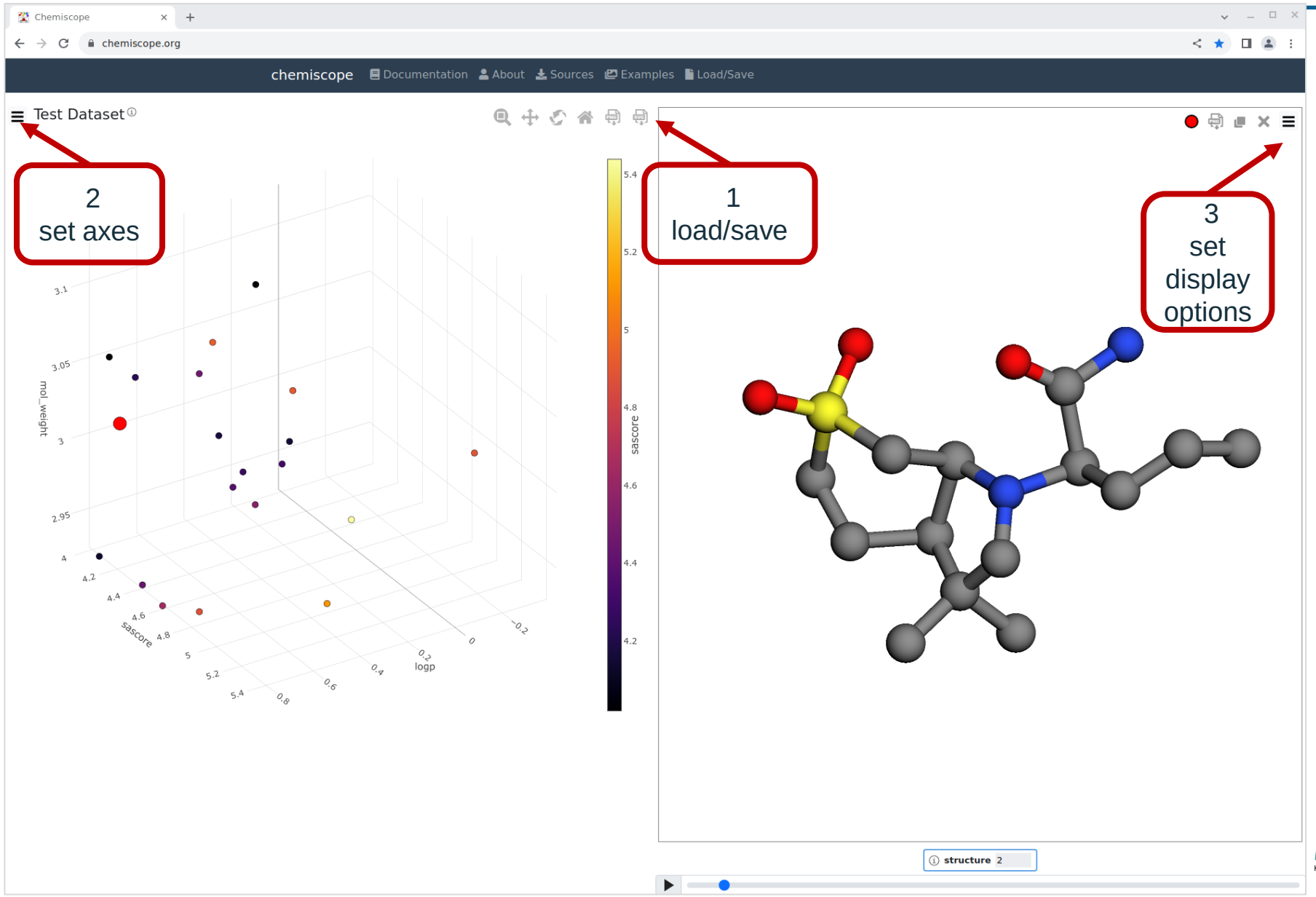


- code .
- open *demonstrator.ipynb*
- **>> Run All**
- scroll down
- [specifiy targets]
- **Generate**

→ scroll down

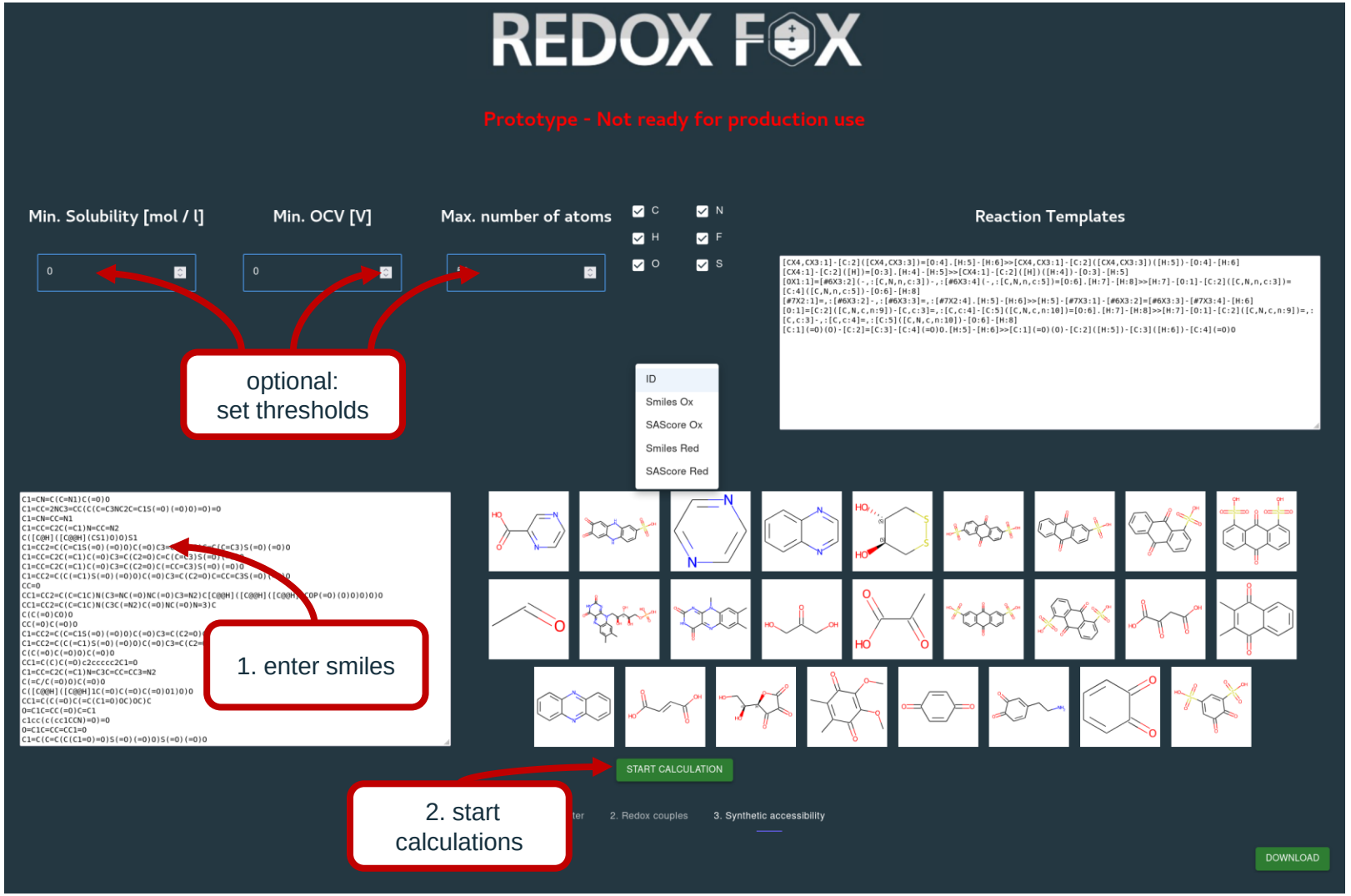
→ continue further analyses with output *chemiscope_gen.json* and/or *gen_smiles.txt*

View results



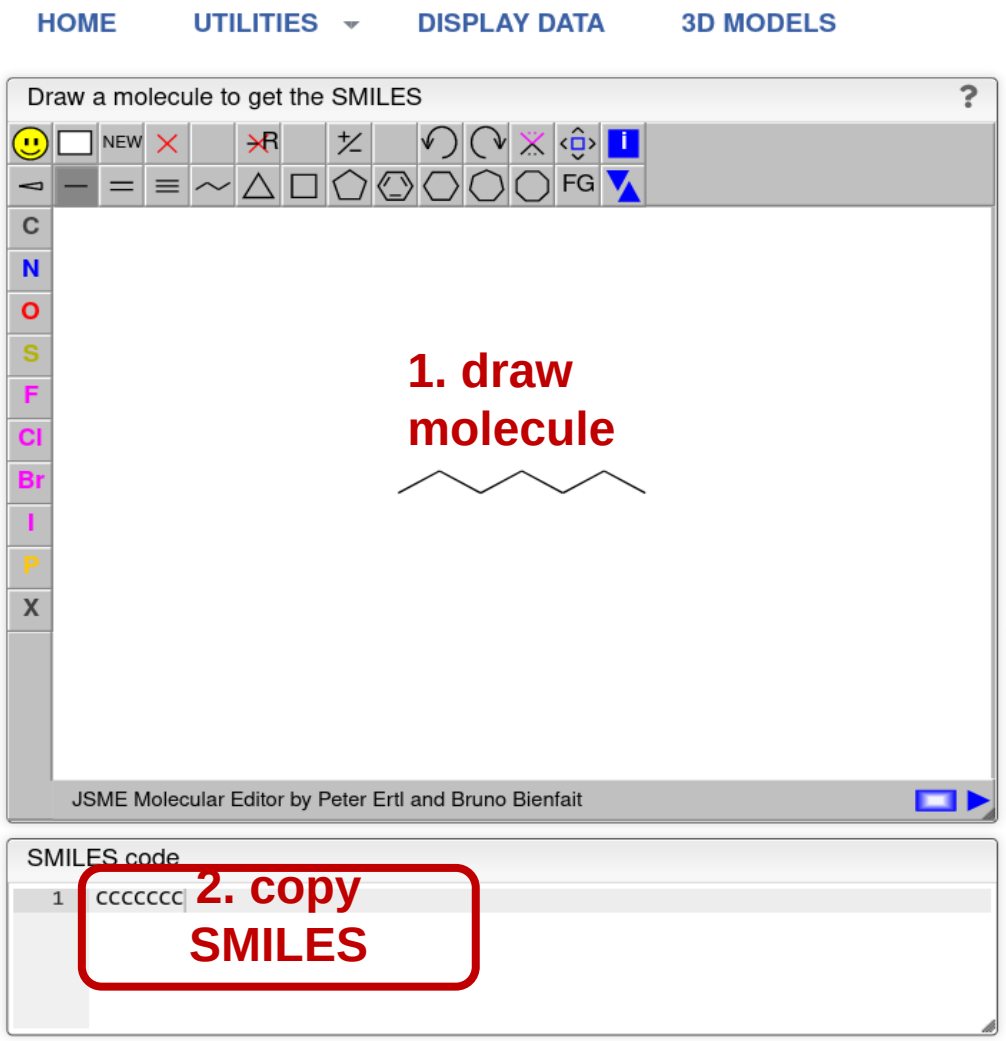
- open Tab Chemiscope in chromium-browser &
- upload *chemiscope_gen.json*

Screening



- open Tab **Redoxfox** in chromium-browser &
- cat gen_smiles.txt
- copy & paste
- [apply filters?]
- start calculation
- scroll down
- choose **OCV** as Y-label
- click on point of interest in diagram → data row

Define target molecule/fragment

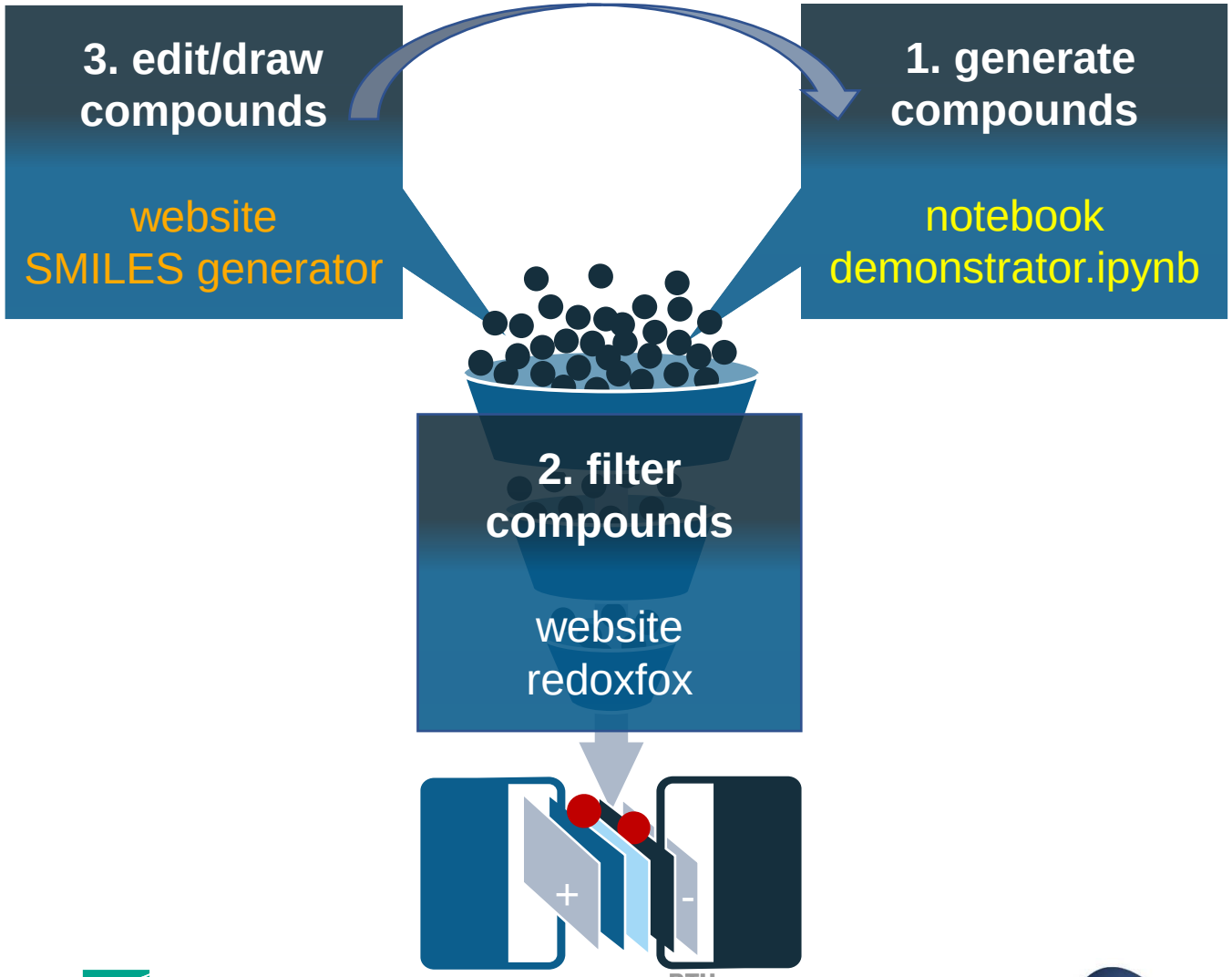


paste into

a) demonstrator

b) redoxfox

Play around…



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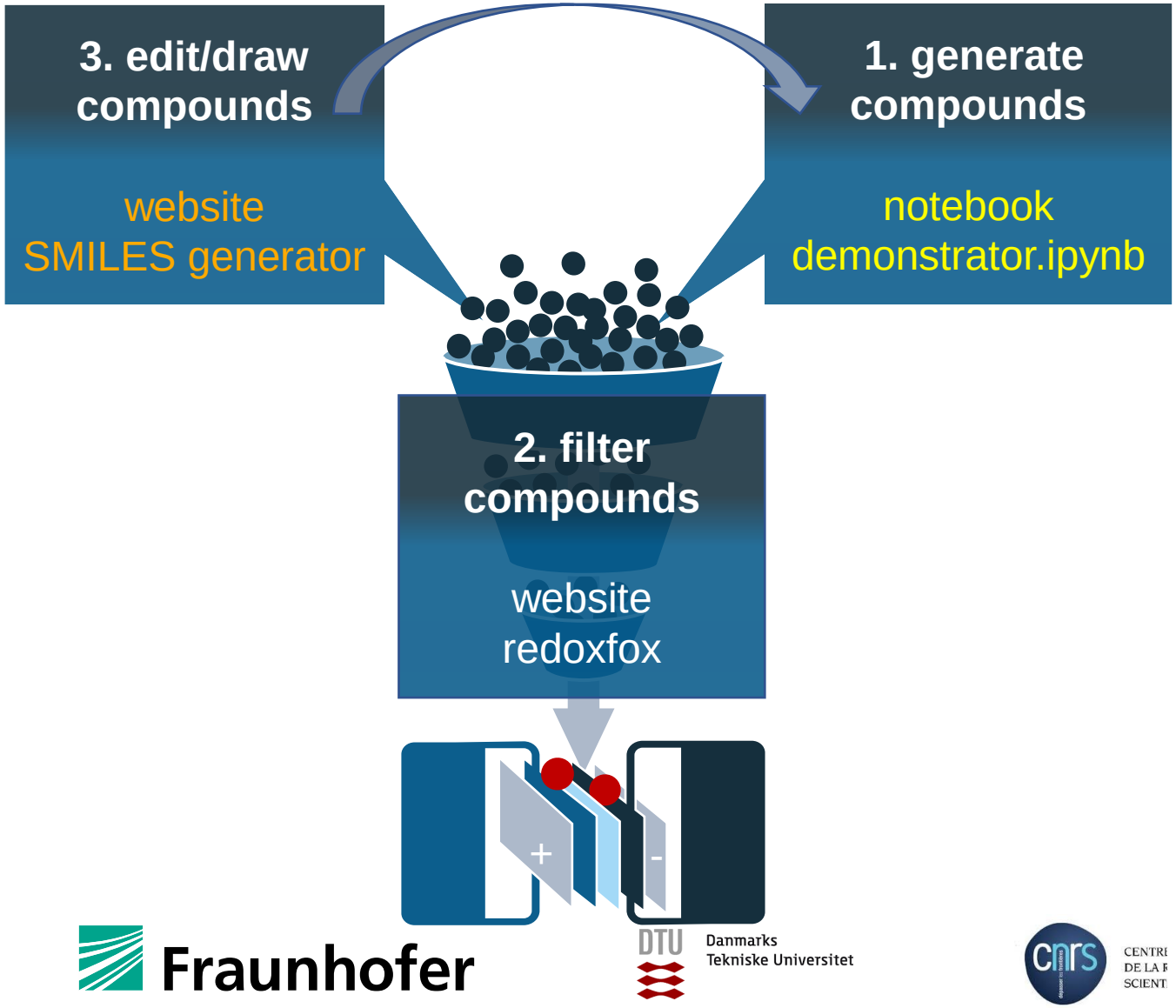
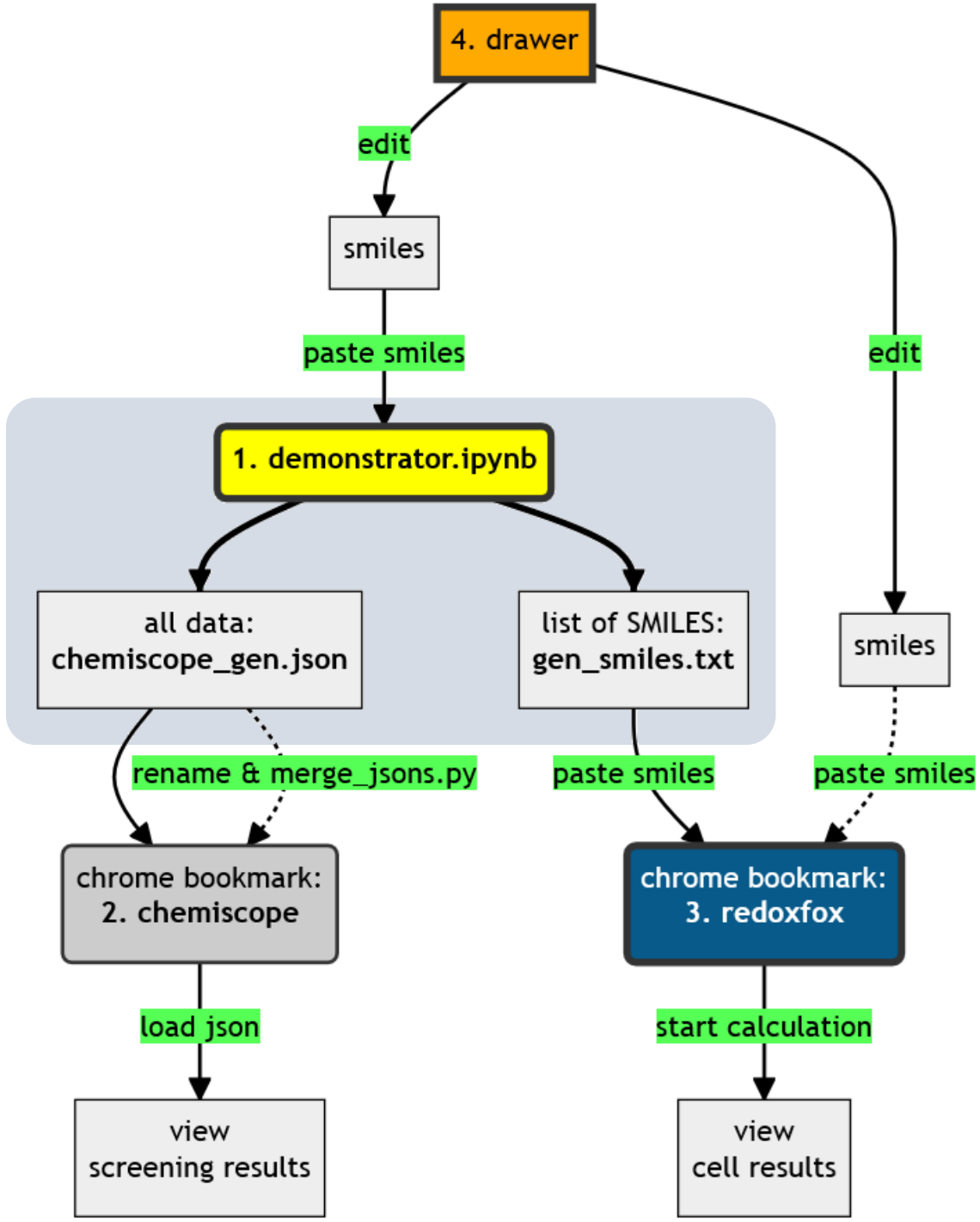
Play around…





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