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# ChemVA: Interactive Visual Analysis of Chemical Compound Similarity in Virtual Screening


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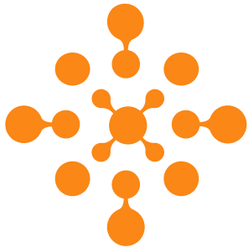
Masaryk University, Czech Republic



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# Motivation

- Virtual screening → accelerate drug discovery
- Large sets of potential drug candidates
- Visualization tools:
  - Explore compounds and their features
  - Select the best candidates for testing *in-vitro*

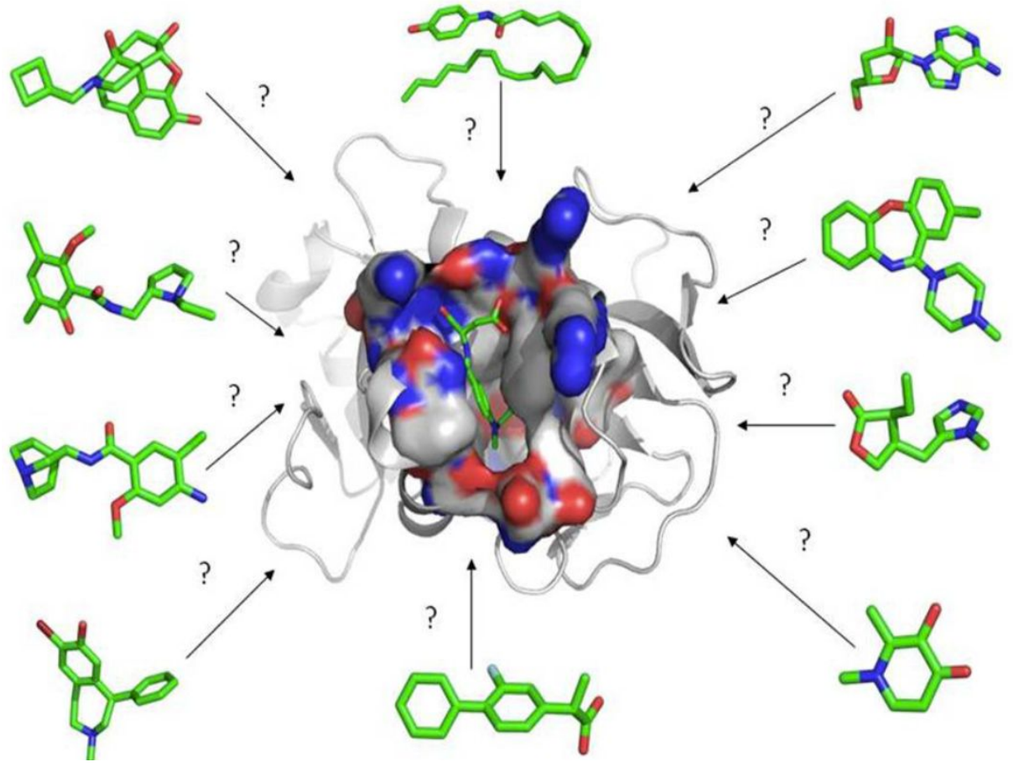

Image source:
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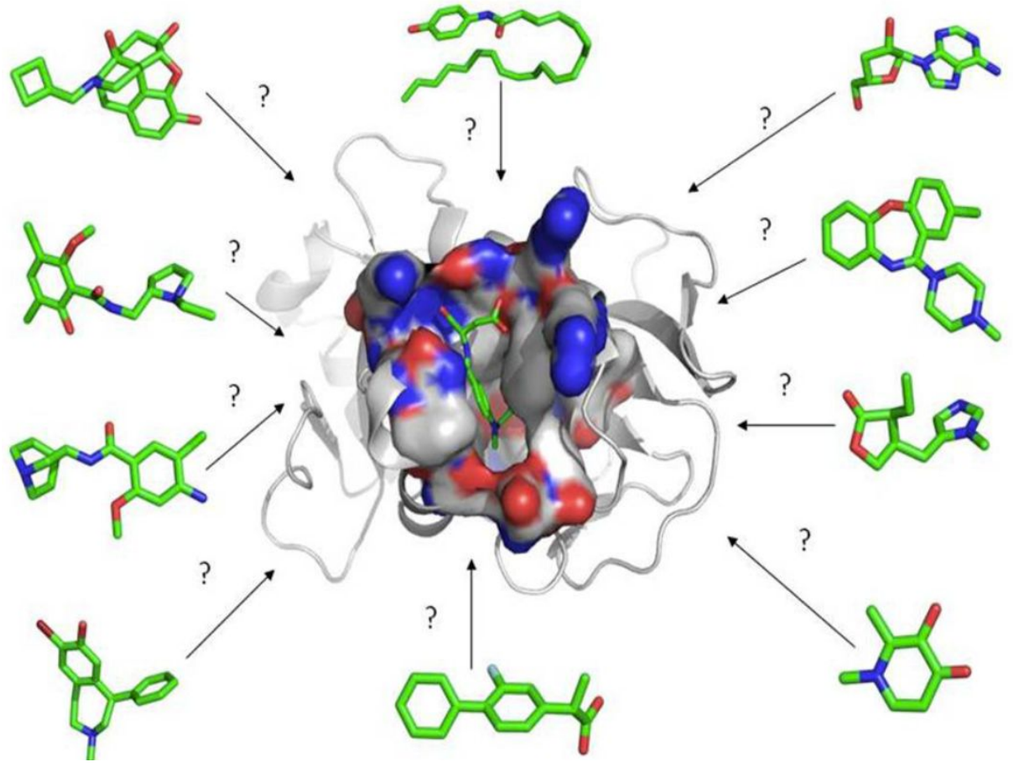

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# Challenge 1: Multidimensional Nature of Molecules

- Similarity of compounds depends on many factors

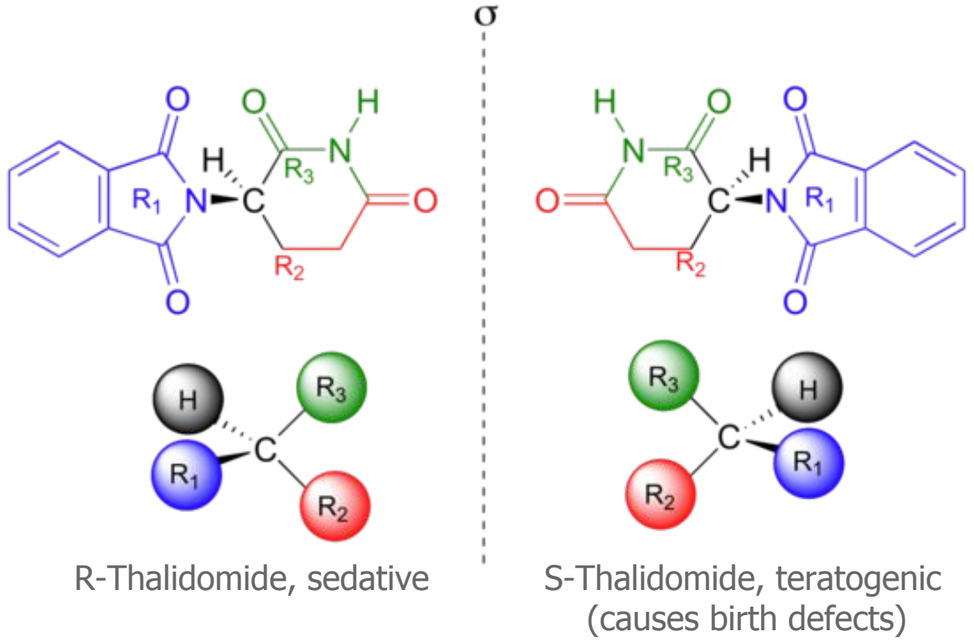


Image source: https://courses.lumenlearning.com/suny-mcc-organicchemistry/chapter/introduction-to-cycloalkanes/

! Structural similarity does not guarantee similar bioactivity!

- Multiple high-dimensional vector-based abstractions of a compound
- Visual support for the exploration of similarity

# Challenge 2: Dimensionality Reduction and its Trustworthiness

- Dimensionality reduction to visualize the molecular space

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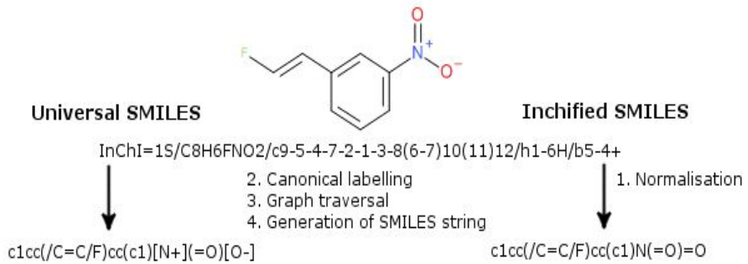


Image source: Towards a Universal SMILES representation - A standard method to generate canonical SMILES based on the InChI, Journal of Cheminformatics, 2012

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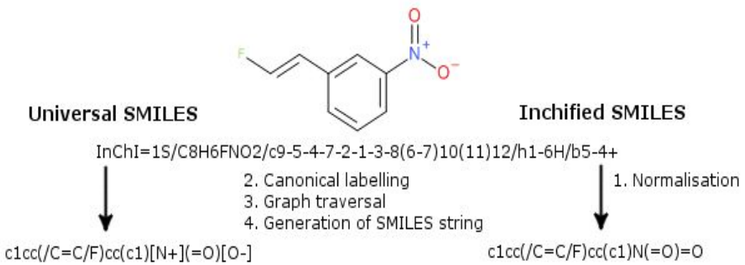


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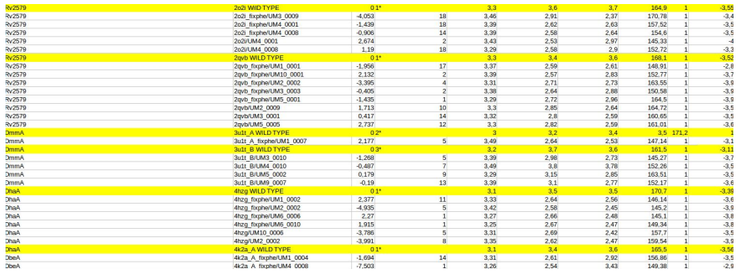

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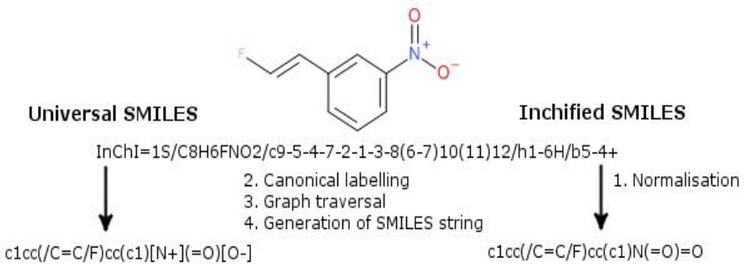


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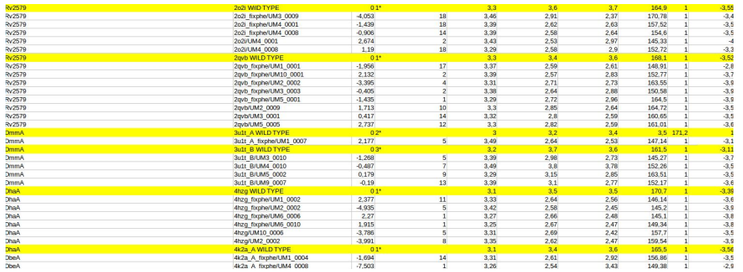

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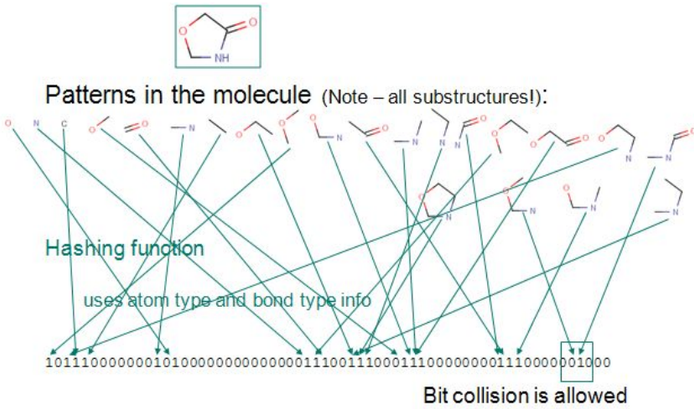


Image source: https://docs.chemaxon.com/Chemical_Hashed_Fingerprint.html

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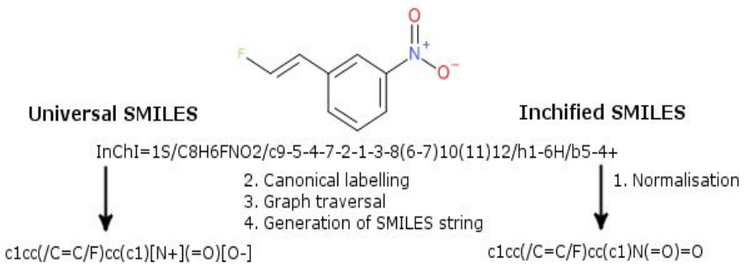


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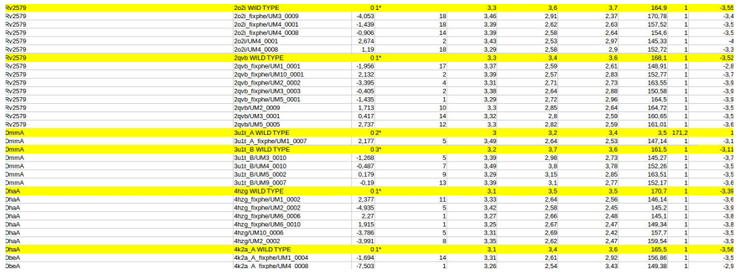

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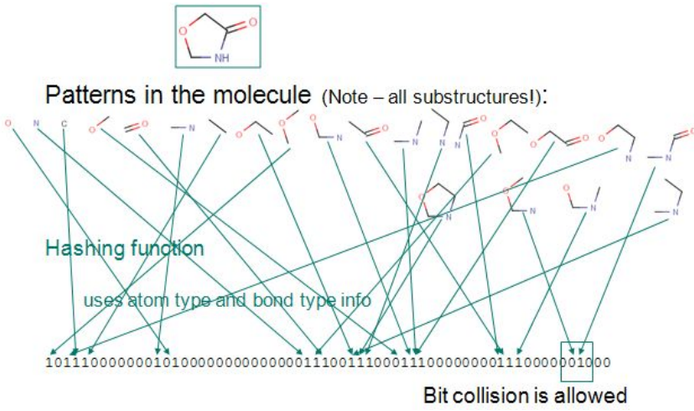


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Dimensionality Reduction

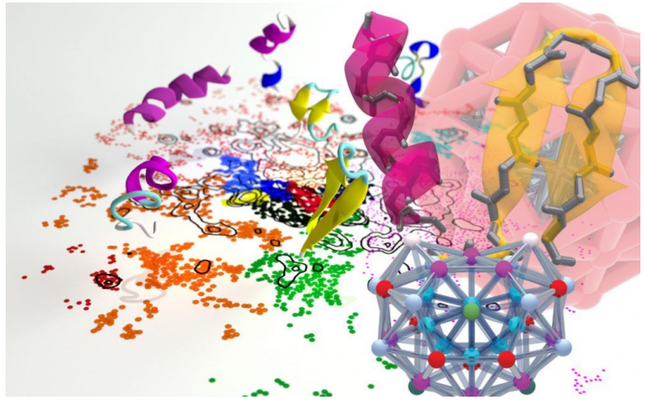

Image source: https://www.epfl.ch/labs/cosmo/research/page-148964-en-html/

# Challenge 2: Dimensionality Reduction and its Trustworthiness

- …but how to tell if a DR projection is trustworthy?

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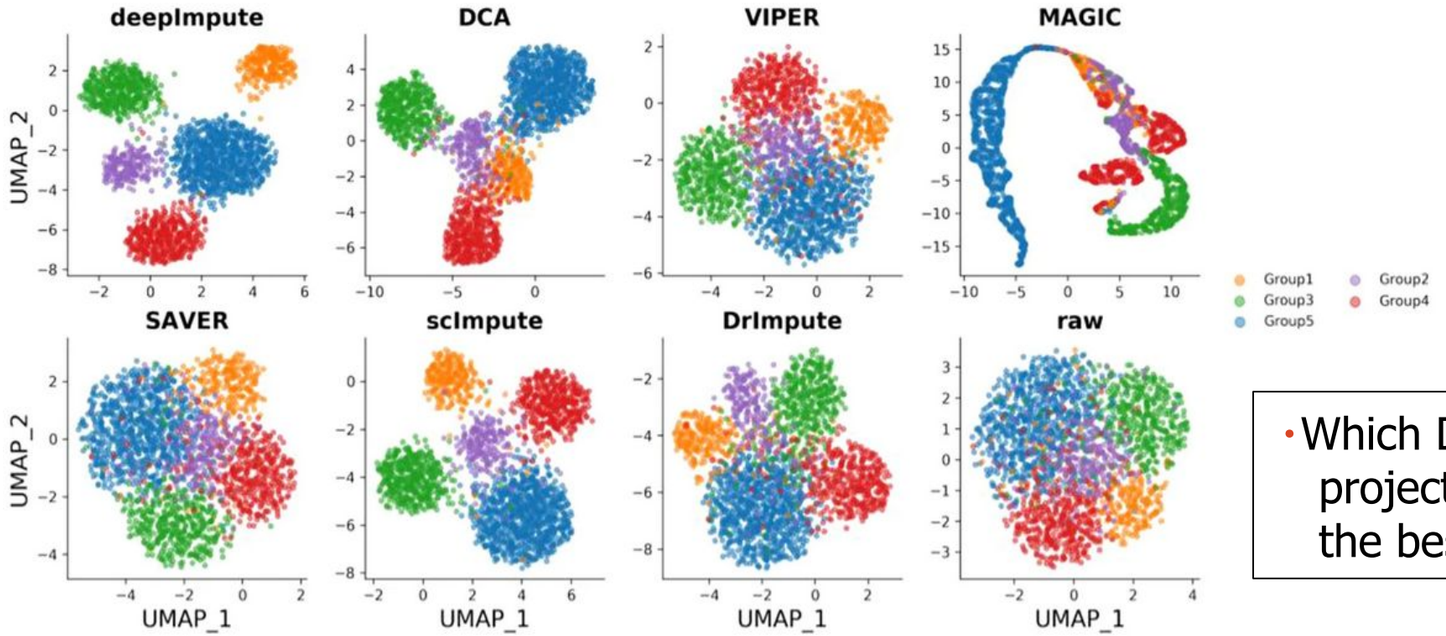


- Which DR projection is the best one?

Image source: DeepImpute: an accurate, fast, and scalable deep neural network method to impute single-cell RNA-seq data, Genome Biology, 2019

- Comparative visualization for assessing trustworthiness

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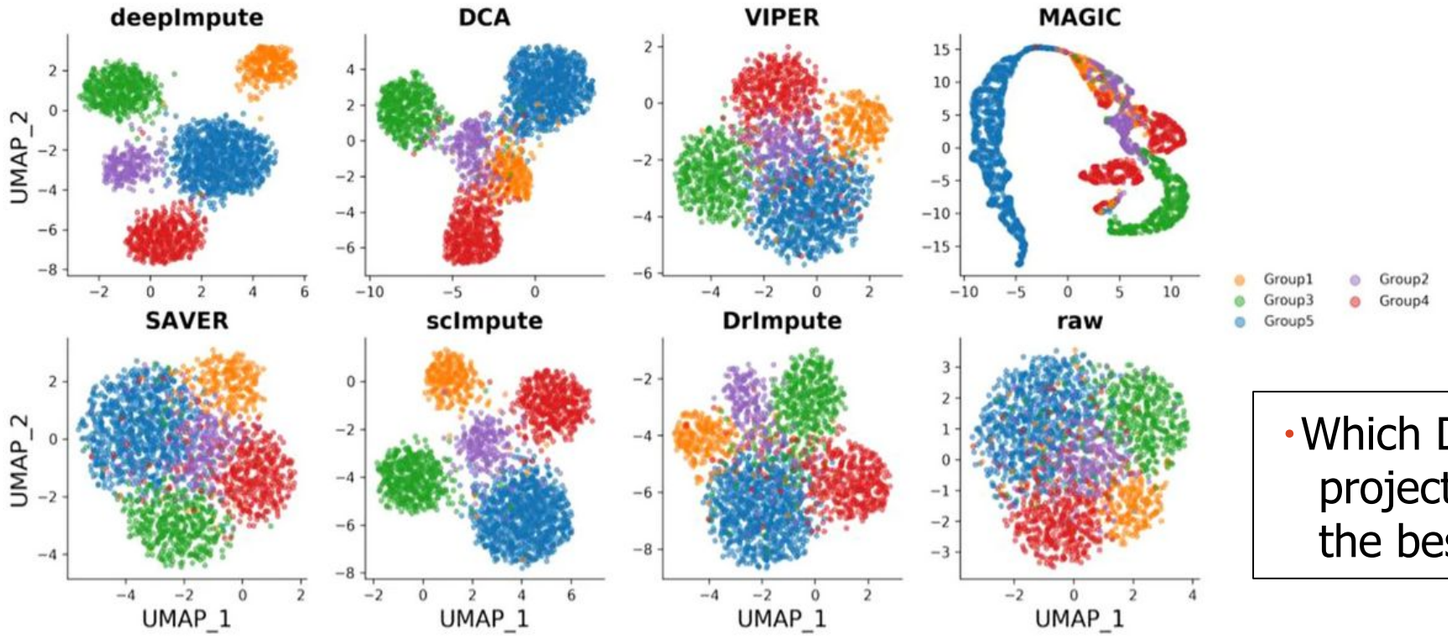


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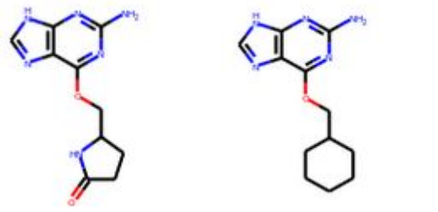
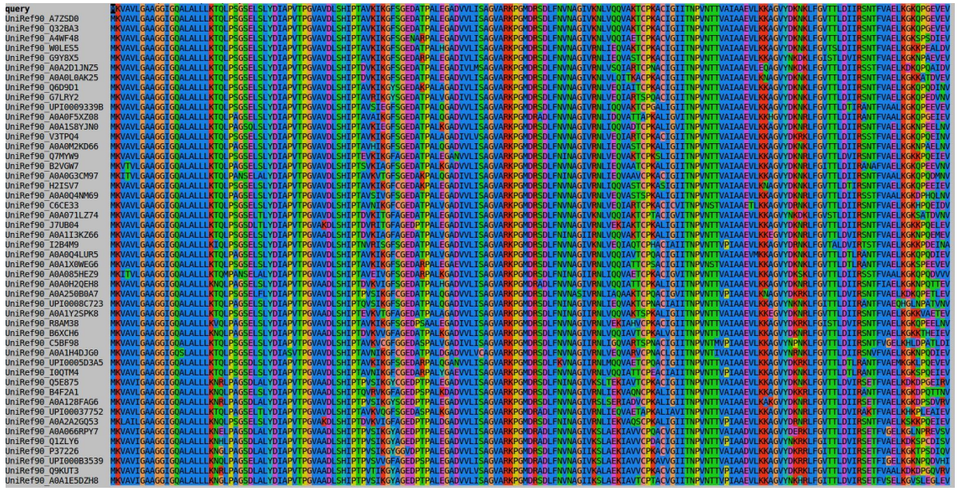



- Are similar molecules projected near each other in the latent space?

- Comparative visualization for assessing trustworthiness

# Challenge 3: Efficient Exploration of Large Molecular Ensembles

- Molecular ensembles → hundreds to thousands of compounds



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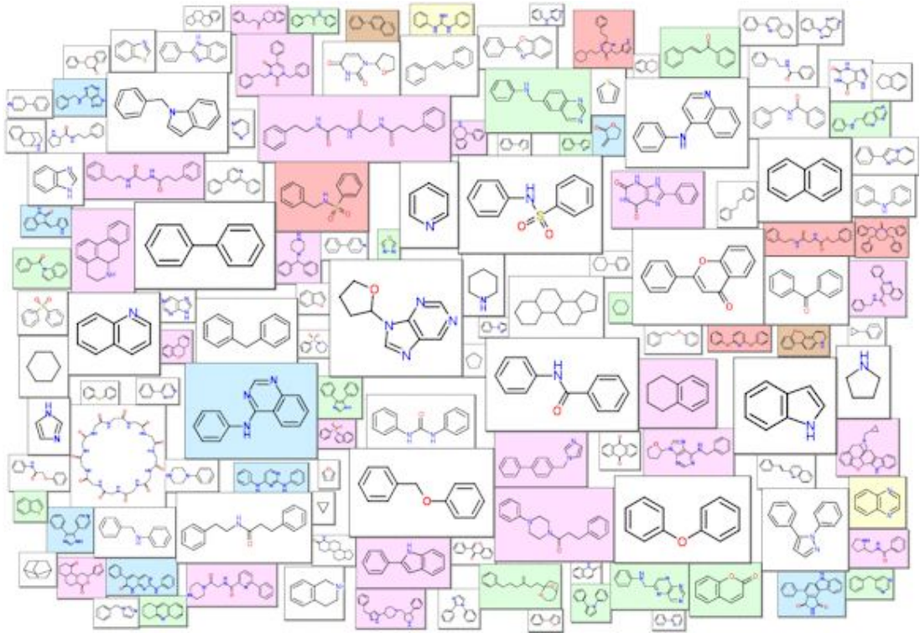
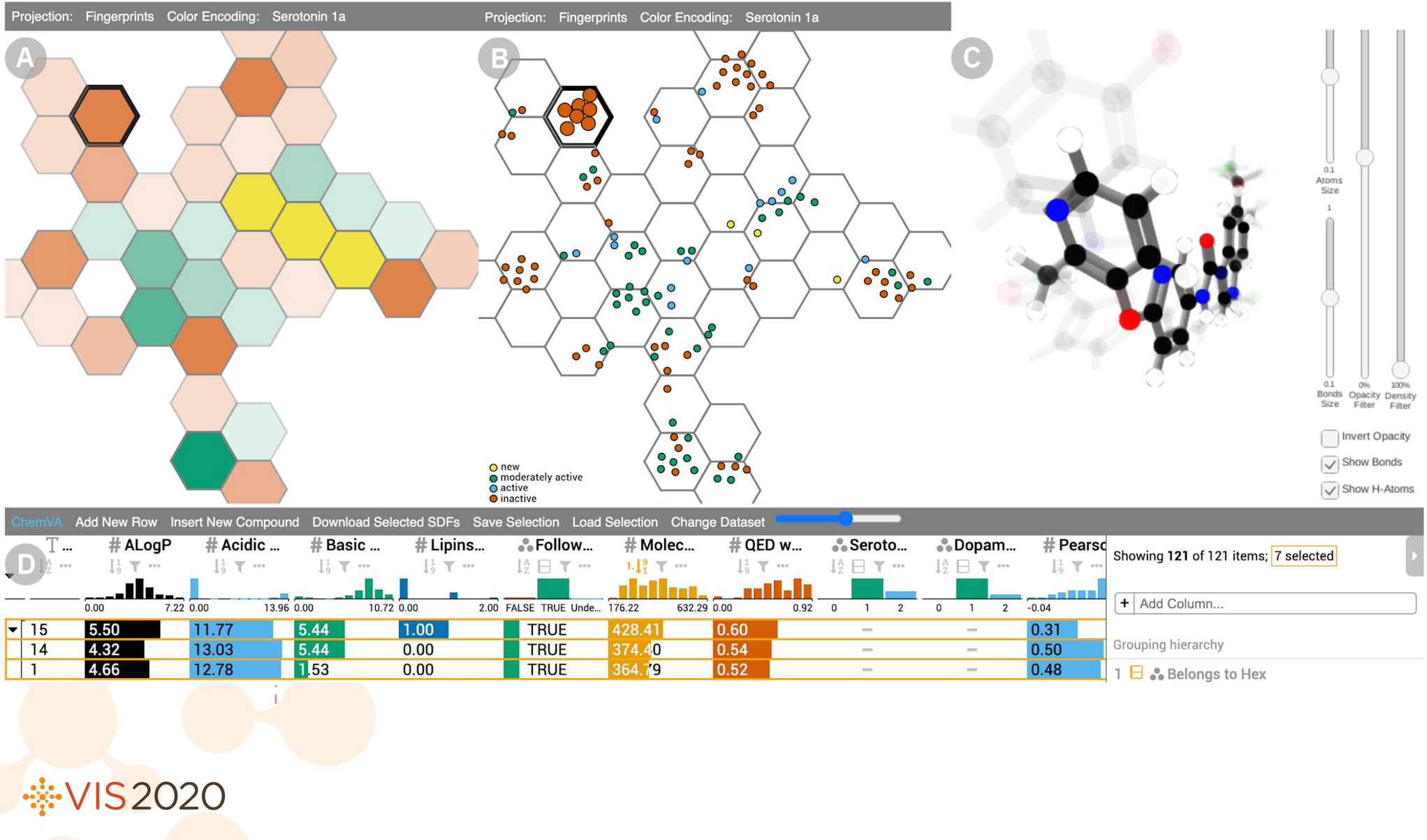


Image source: Ertl and Rohde, The Molecule Cloud - compact visualization of large collections of molecules, Journal of Cheminformatics, 2012

- Views and interactions for efficiently exploring molecular features


Projection: Fingerprints Color Encoding: Serotonin 1a
A
Projection: Fingerprints Color Encoding: Serotonin 1a
B
new
moderately active
active
inactive
C
0.1
Atoms Size
1
0.1
Bonds Size
0%
Opacity Filter
100%
Density Filter
Invert Opacity
Show Bonds
Show H-Atoms
ChemVA
Add New Row
Insert New Compound
Download Selected SDFs
Save Selection
Load Selection
Change Dataset
D
# ALogP
# Acidic ...
# Basic ...
# Lipins...
Follow...
# Molec...
# QED w...
Seroto...
Dopam...
# Pearsc
0.00 7.22
0.00 13.96
0.00 10.72
0.00 2.00
FALSE TRUE Unde...
176.22 632.29
0.00 0.92
0 1 2
0 1 2
-0.04
15 5.50 11.77 5.44 1.00 TRUE 428.41 0.60 0.31
14 4.32 13.03 5.44 0.00 TRUE 374.40 0.54 0.50
1 4.66 12.78 1.53 0.00 TRUE 364.79 0.52 0.48
Showing 121 of 121 items; 7 selected
Add Column...
Grouping hierarchy
1 Belongs to Hex

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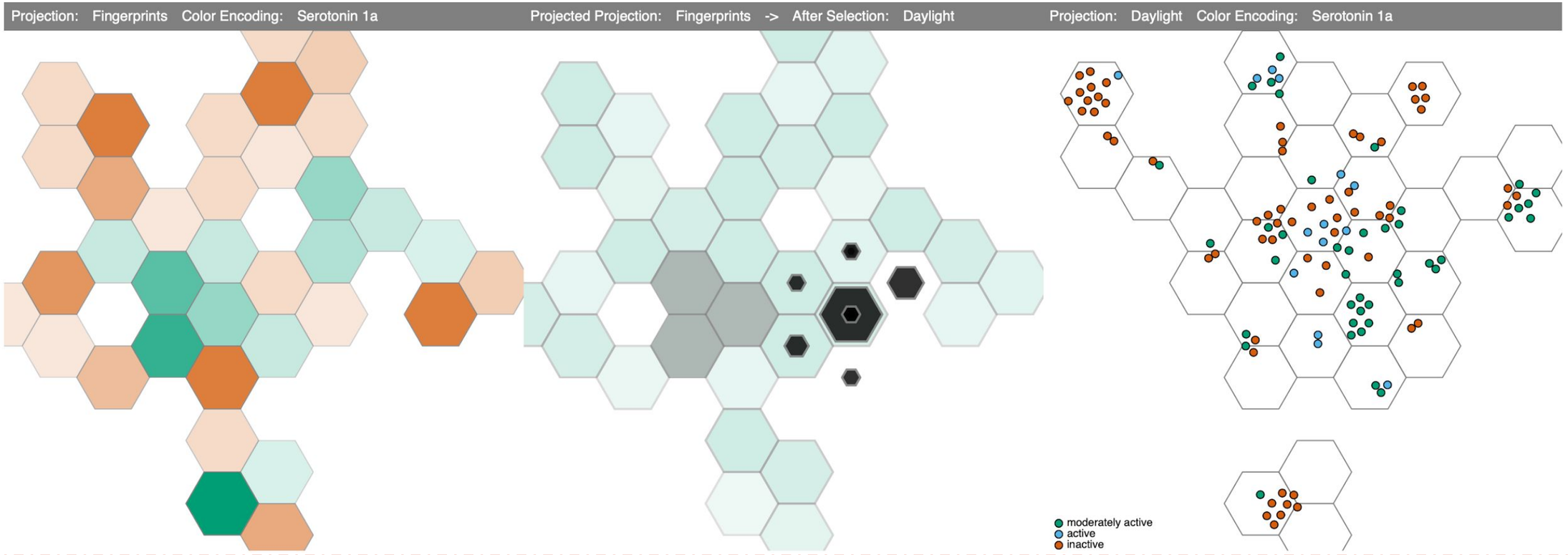
# Hexagonal View & Detail View

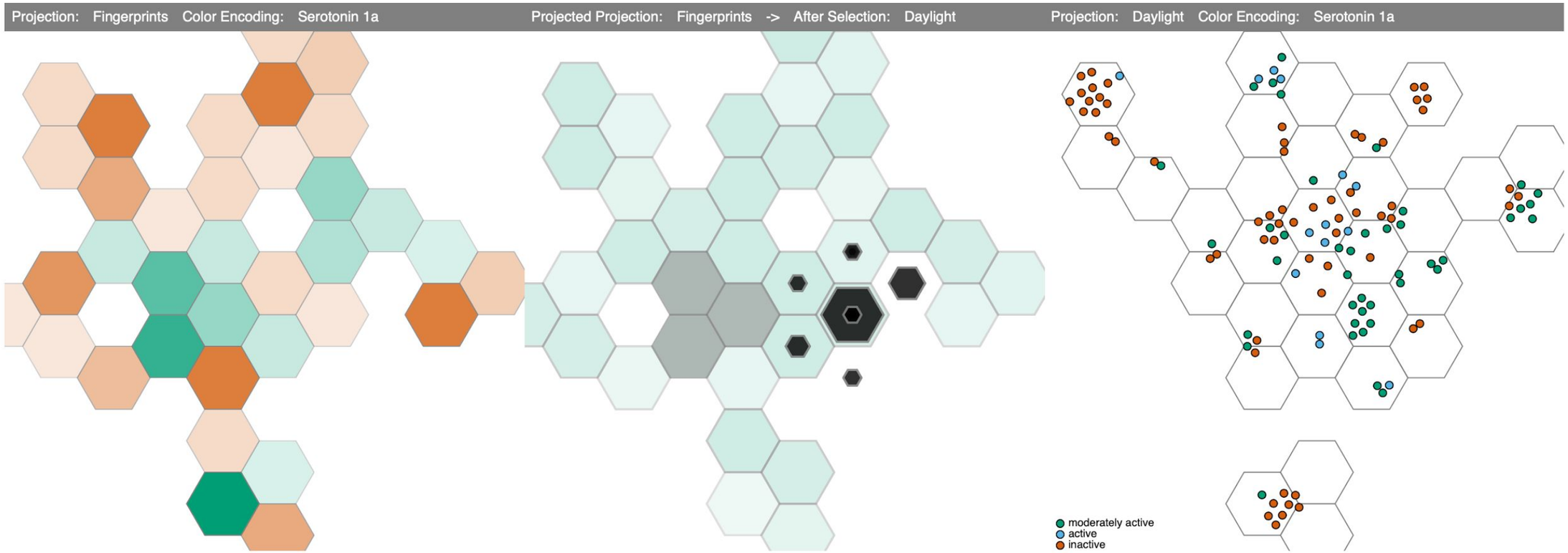
- Data from multiple input sources viewed from different perspectives
  - Variable color and opacity encoding



# Hexagonal View & Detail View

# Difference View for Evaluation of Projections

- Trustworthiness of DR projections

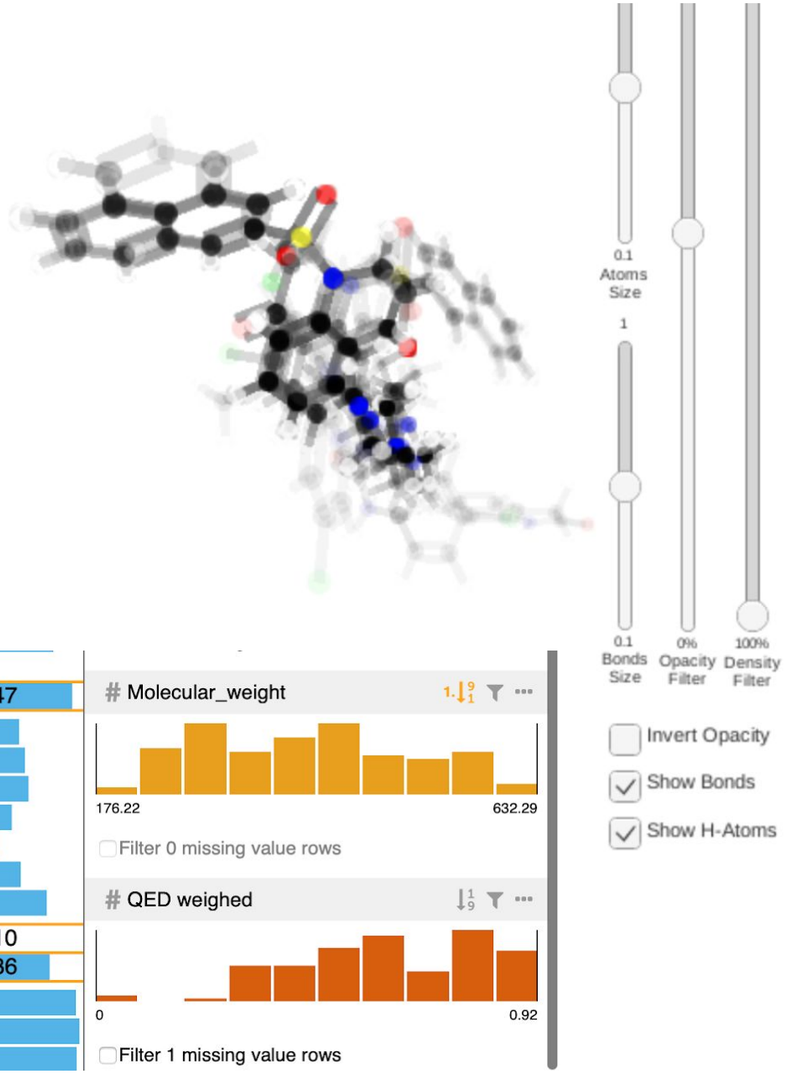


# Difference View for Evaluation of Projections

# Correlation Encoding

# Table View & 3D View

- Provides additional insight into the data
  - Spatial alignment with opacity modulation
  - Sorting, filtering, advanced selection

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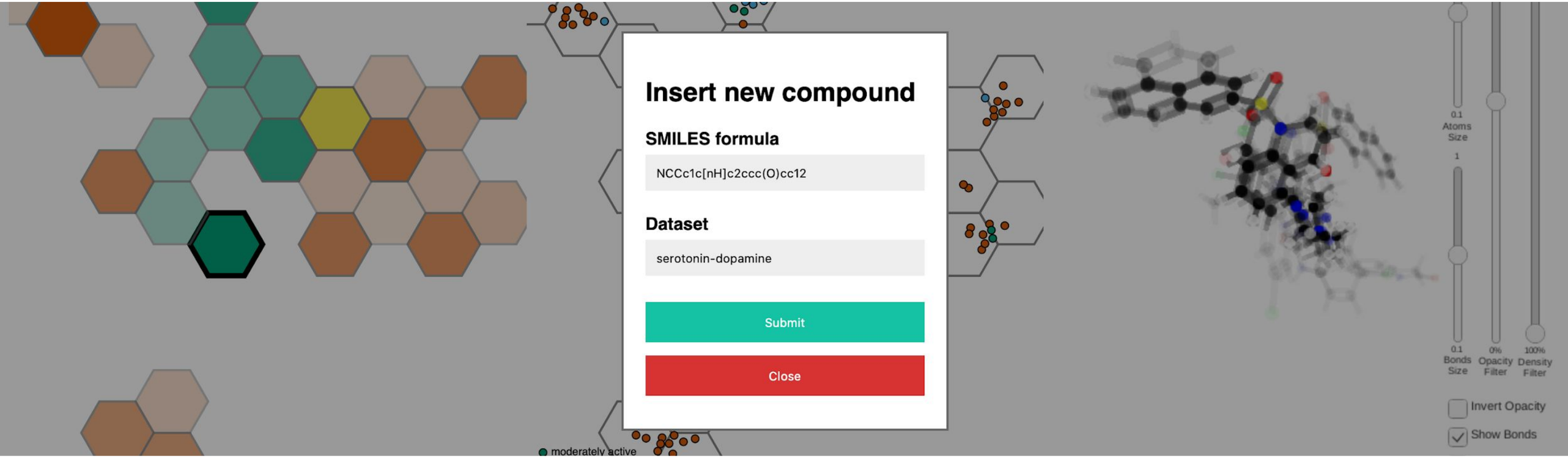
K. Furmanová, S. Gratzl, H. Stitz, T. Zichner, M. Jarešová, A. Lex, and M. Streit. Taggle: Combining overview and details in tabular data visualizations. Information Visualization, 19(2):114–136, 2020. doi: 10.1177/1473871619878085

# Table View & 3D View

# Application Scenario: Adding New Compounds

- Highlighted with yellow color in the dataset



# Case Study:

## Activity towards Serotonin and Dopamine receptors

# Results from Evaluation

- ChemVA was evaluated by three domain experts and one DR visualization expert
  - Five new compounds designed using ChemVA
  - Intuitive and easy to use
  - Saves time and effort in drug design tasks
  - Difference view is effective for comparing DR projections in terms of their trustworthiness

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# Conclusions and Future Work

- Techniques behind ChemVA would apply to other domains and types of data

- Future extensions of the tool:
  - Load and customize your own datasets
  - Provide options for advanced search: substructures, molecular descriptors.

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# Thank you!

arXiv.org

Please refer to our paper:
ChemVA: Interactive Visual Analysis of Chemical Compound Similarity in Virtual Screening
(preprint available on arXiv)

All resources are publicly available on GitHub.
Check out our repository!

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# Agenda

- Challenges
  - Multiple sources of molecular data
  - Efficient exploration of large molecular ensembles
  - DR trustworthiness
- ChemVA overview
  - 2D views
  - 3D view and Table view
  - Adding new compounds
- Case study
- Results from evaluation
- Conclusions and future work

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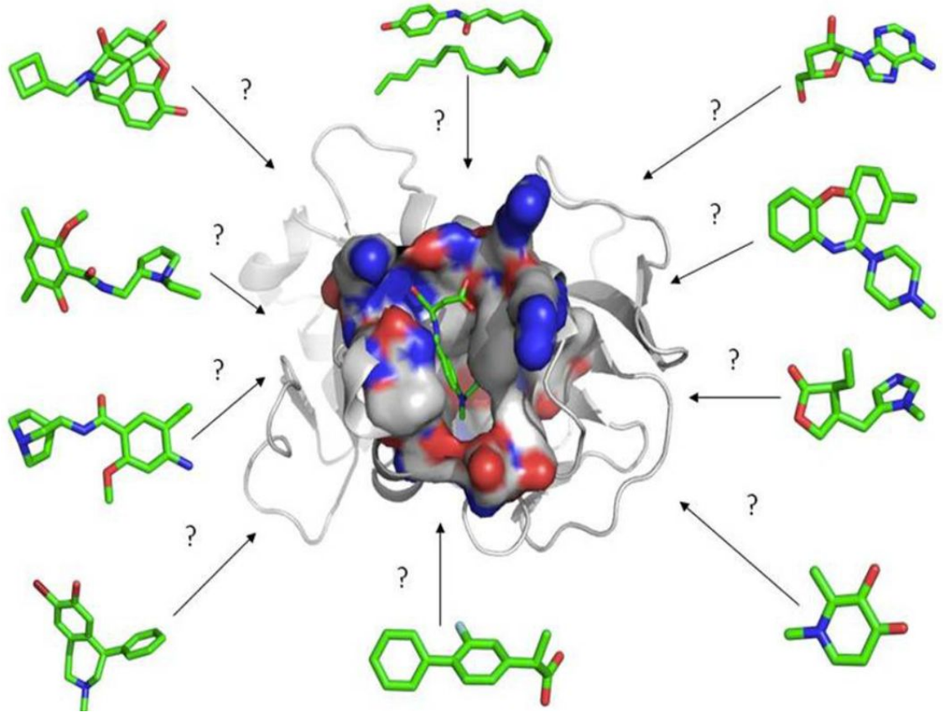

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