UniStra activities within the *BigChem* project:

- **data visualization and modeling using GTM approach;**
- **chemical reactions mining with Condensed Graphs of Reactions**

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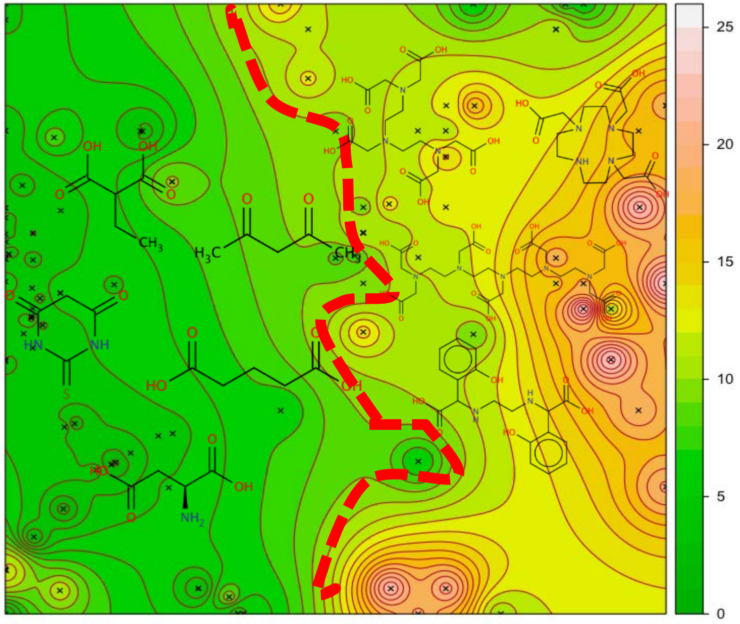
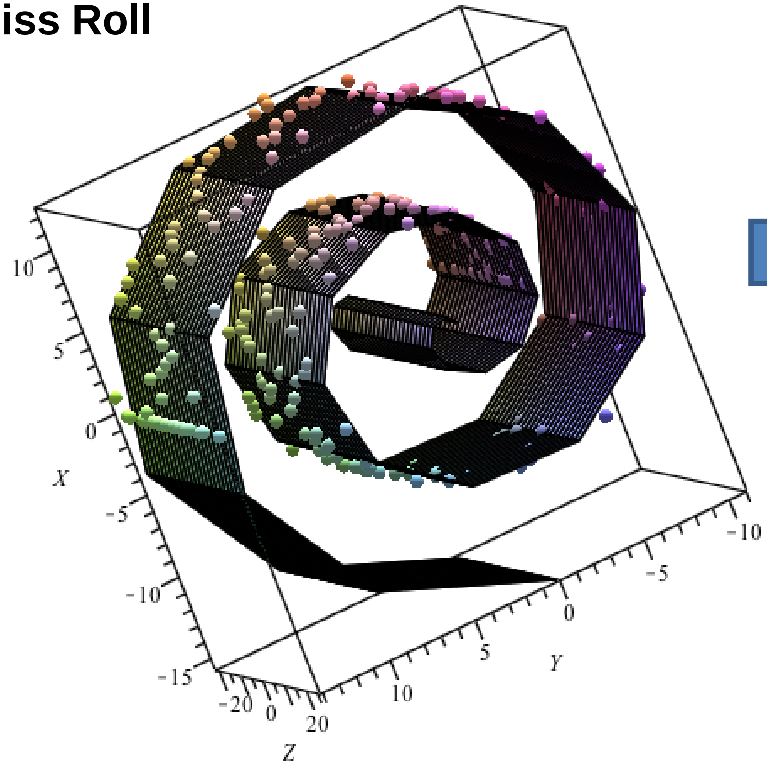
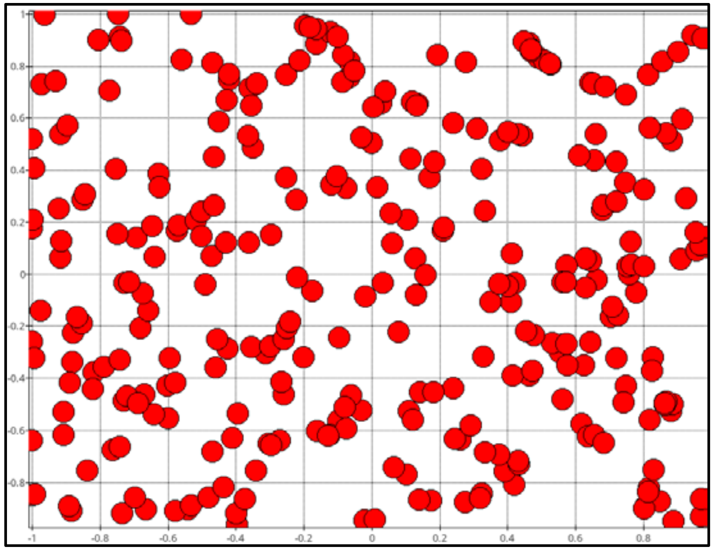
Generative Topographic Mapping (GTM)



Generative Topographic Mapping (GTM)

Swiss Roll





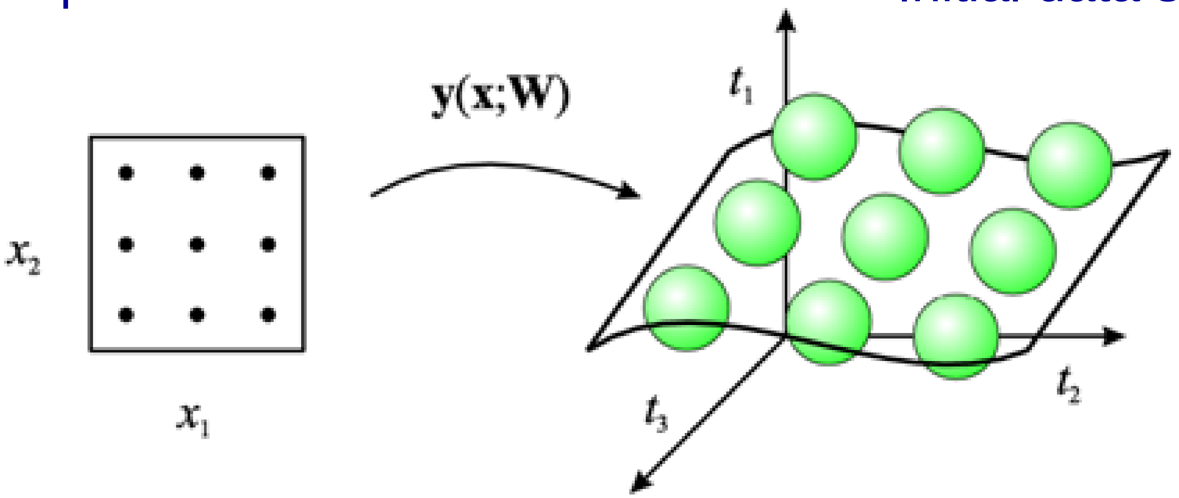
- GTM relates the latent space with a 2D “rubber sheet” (*manifold)* injected into the high-dimensional data space.

- The visualization plot is obtained by projecting the data points onto the manifold and then letting the “rubber sheet” relax to its original form.

Generative Topographic Mapping (GTM)

latent space

Initial data space

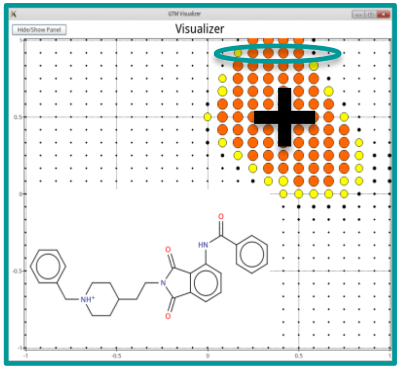


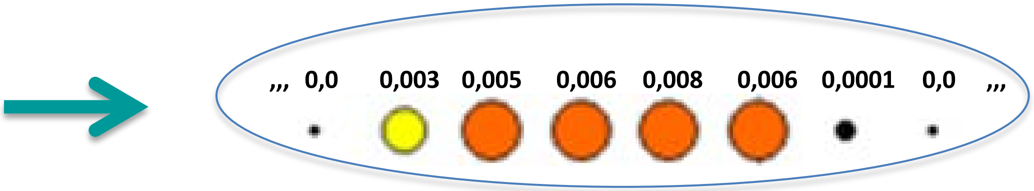
GTM generates a data probability distribution in ***both initial and latent data spaces*.**

This opens an opportunity to use GTM not only to visualize the data but also for structure-property modeling tasks

- C. M. Bishop *Pattern Recognition and Machine Learning*, 2006 Springer
- N. Kireeva, I.I. Baskin, H. A. Gaspar a, D. Horvath, G. Marcou and A. Varnek, *Mol. Informatics, 2012,* **31***,* 201-312

GTM descriptors for molecules and datasets





Map resolution: $\boldsymbol{N_{nodes}} = \boldsymbol{K*K}$

Standard setting: $\boldsymbol{K}$ =25, $\boldsymbol{N_{grid}}$ = 625

Molecule → responsibilities' vector $\{\boldsymbol{R_{tk}}\}$ of $\boldsymbol{N_{nodes}}$ length

Dataset → normalized cumulated responsibilities' vector of $\boldsymbol{N_{nodes}}$ length

1. Chemical Space analysis

1.1 *Big Data* problem: visualization and analysis of large databases

1.2 Concept of « universal » chemical spaces

2. Structure-property modeling

2.1 Individual classification and regression models

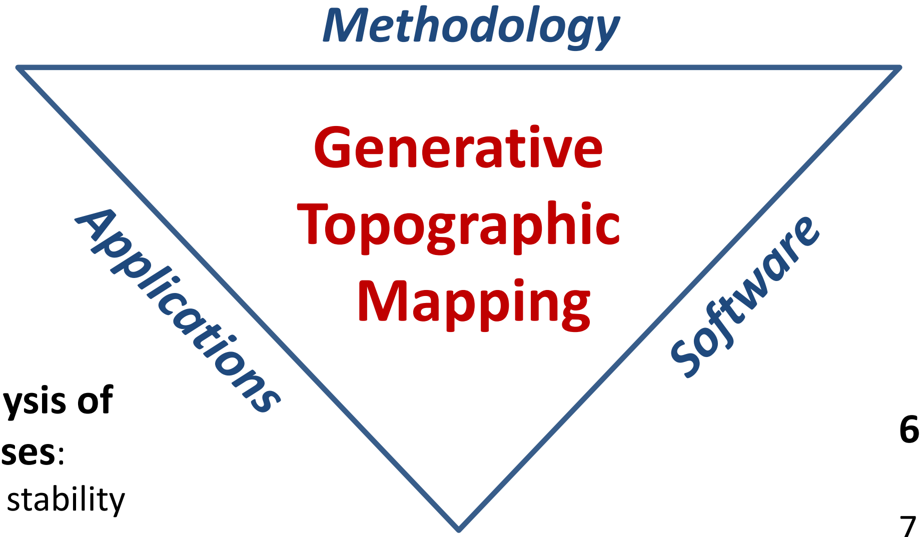
2.2 Profiling models

2.3 Applicability Domain of Models

3. In silico design

3.1 GTM Activity landscapes

3.2 Chemical structures generation (« inverse » QSAR)



Methodology

Generative Topographic Mapping

Applications

Software

4. Visualization and analysis of popular chemical databases: ChEMBL, SuppliersDB, IUPAC stability constants DB …

5. Chemical Reactions Data visualization and analysis using the Condensed Graph of Reaction method

(see Figure 3)

6. New modules in the ISIDA package:

7.1 ISIDA/GTM

7.2 *Stargate* GTM

7.3 On-line GTM tools

References

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- H. Gaspar , I. I. Baskin, G. Marcou, D. Horvath, A. Varnek Stargate GTM: bridging descriptor and activity spaces. *J. Chem. Inf. Model., 2015,* DOI: 10.1021/acs.jcim.5b00398
- H Gaspar, II Baskin, G Marcou, D Horvath, A Varnek, Chemical Data Visualization and Analysis with Incremental GTM: Big Data Challenge, *J. Chem. Inf. Model.*, 2015, 55 (1), 84–94
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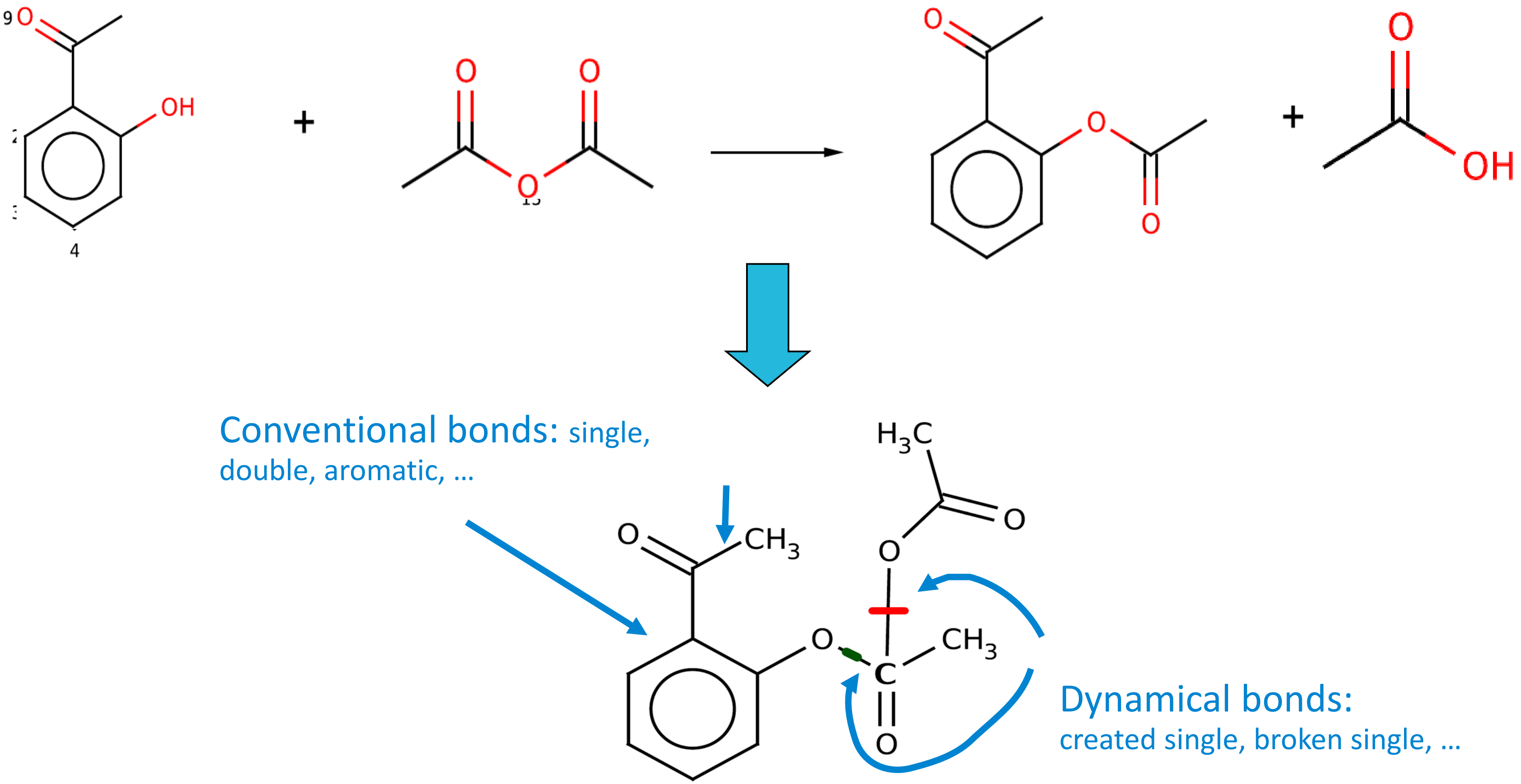
Condensed Graph of Reaction (CGR)

Condensed Graph of Reaction



Conventional bonds: single, double, aromatic, …

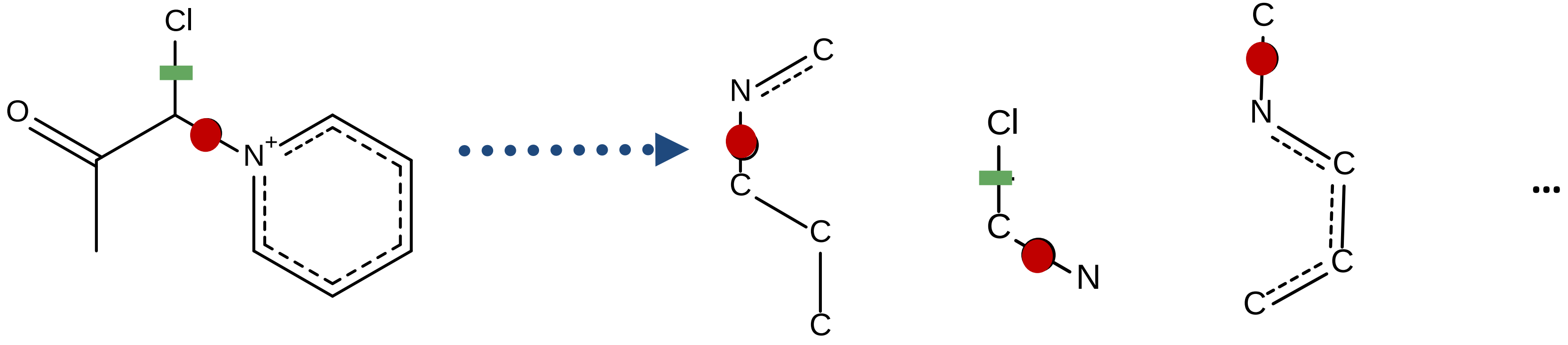
Dynamical bonds: created single, broken single, …

CGR: a pseudo-molecule representing a given reaction

ISIDA/CGR fragment descriptors

Condensed graph of reaction

ISIDA fragment descriptors



2	**1**	**2**	**...**

Reaction can be encoded by a descriptor vector which can be used in structure-reactivity modeling, similarity searching, clustering, etc

A. Varnek In: "*Chemoinformatics and Computational Chemical Biology*", J. Bajorath, Ed., Springer, 2010

1. Automatized processing of raw reaction data

1.1 Reaction data curation

1.2 Atom-to-Atom Mapping

2. Structure-Reactivity modeling

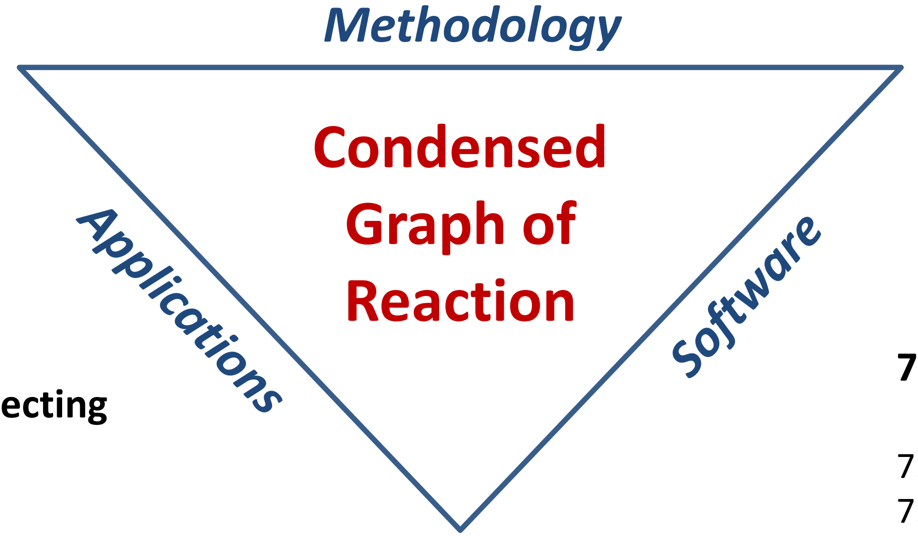
2.1 Classification and regression models

2.2 Similarity-based approach

3. Automatized reactions classification

3.1 Data visualization and clustering

3.2 Extraction of reaction signatures



Methodology

Applications

Software

Condensed Graph of Reaction

4. Expert system for protecting groups reactivity

5. Predictive models for:

5.1 reaction rate (substitution, elimination, cycloaddition and bio-orthogonal reactions)

5.2 tautomeric equilibrium constants

5.3 regioselectivity of enzymatic reactions

5.4 activity cliffs and bioisosters

6. Visualization and analysis of reaction databases using GTM:

Reaxys, FlowReact DB

7. New modules in the ISIDA package:

7.1 ISIDA/GGR designer

7.2 Mapper

7.3 On-line reactivity predictor

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