

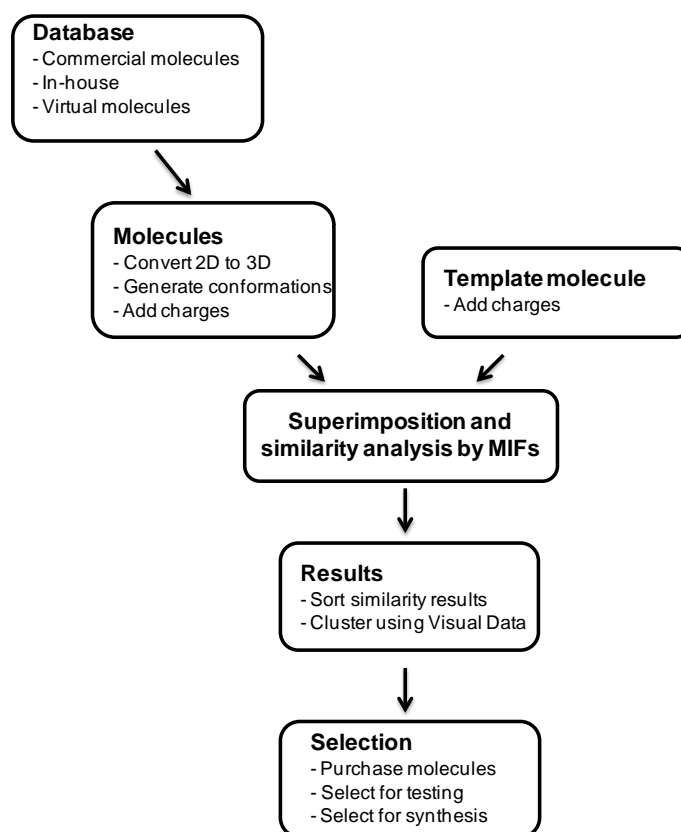
## Research Services/Virtual Screening

Proprietary virtual screening tools of Visipoint can accelerate the discovery process of new molecules in the fields of pharmaceutical, food and nutraceutical, and chemical research.

Virtual screening of compound collections (V-HTS) using methods utilizing molecular interaction fields (MIF) can provide meaningful starting points for Lead Generation and Library Design projects.

Our MIF based method uses ligand information only and thus requires no 3D-structure of a target protein.

The workflow of virtual screening:



**Database:** Molecule databases that would be virtually screened are typically commercial compound collections, in-house molecule collections, or virtual molecule libraries. Molecules are either in 2D or in 3D in these databases.

**Molecules:** Molecules go through a computational process done by using our proprietary tools: 1) If the molecules are in 2D they will be converted to 3D, 2) their conformations are generated and 3) partial atomic charges added. If the molecules are already in 3D only steps 2 and 3 are needed. The software used in steps 1-3 is an internal version of the original Balloon software (Vainio and Johnson, 2007).

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**Template molecule:** 1) An active conformation of the template molecule is taken from a crystal structure of a protein-ligand complex if available or a conformation analysis is performed for the template molecule in order to select a suitable conformation. 2) Partial atomic charges are calculated for the template molecule. The template molecule is prepared for superimposition also by using Balloon software.

**Superimposition and similarity analysis of MIFs:** Molecular interaction field (MIF) of the template molecule is superimposed with the MIFs of database molecules (all generated conformations) (Tervo *et al.*, 2005, Rönkkö *et al.*, 2006, Vainio *et al.*, 2009). We can choose between our two MIF based superimposition/similarity analysis methods (Brutus or ShaEP) or use them both as appropriate in each project.

**Results:** Superimposition results are sorted according to the similarity scoring and clustered by using our SOM technology (Koikkalainen, 1994)

**Selection:** Compounds are selected according to the sorted and/or clustered results and depending on the source molecule database, either 1) purchased for experimental testing, 2) scheduled for experimental testing, or 3) selected for synthesis and then synthesized molecules are tested experimentally.

### References:

Koikkalainen P., Progress with the tree-structured self-organizing map. Proceedings of ECAI'94, 11th European Conference on Artificial Intelligence (Cohn, A. G., Ed.), Wiley and Sons, New York. 1994, pp. 211-215.

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Tervo A.J., Rönkkö T., Nyrönen T. H., Poso A., BRUTUS: Optimization of a grid-based similarity function for rigid-body molecular superposition. 1. Alignment and virtual screening applications. *J. Med. Chem.* **48**, 2005, pp. 4076-4086.

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