

# COMPUTATIONAL APPROACH TO THE MOLECULAR CATALYSIS BY 3D TRANSITION METALS BY DFT SPECTROSCOPIC WITH MOLECULAR DOCKING

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## ABSTRACT

Metal structures play an important role in agriculture, pharmacy and industry. Ligand, a metal surrounded by a set of ions or molecules, is used to prepare complex substances called Schiff bases. Two approaches are particularly popular within the molecular docking community. One approach uses matching technique that describes the protein and the ligand as complementary surfaces. The second approach simulates the docking process in which the ligand-protein pairwise interaction energies are calculated. Both approaches are outlined below. Shape / shape complementarity methods describe the protein and ligand as a set of features that make them dockable. Two approaches are particularly popular within the molecular docking community. One approach uses matching technique that describes the protein and the ligand as complementary surfaces. The second approach simulates the docking process in which the ligand-protein pairwise interaction energies are calculated. Both approaches are outlined below. Shape complementarity Geometric matching/ shape complementarity methods describe the protein and ligand as a set of features that make them dockable

**KEY WORDS-** Metal structures, Ligand, ligand-protein, complementarity, dockable, molecular docking, Geometric matching.

## INTRODUCTION

Metal structures play an important role in agriculture, pharmacy and industry. Ligand, a metal surrounded by a set of ions or molecules, is used to prepare complex substances called Schiff bases which are products of the dissolution of essential amines and aldehydes or ketones ( $RCH = NRC$ , also representing alkyl and / or aryl substituent's. Augmentation of biological activity

was reported by implementation of transition metals into Schiff bases [19]. Schiff bases played an influencing role in development of coordination chemistry and were involved as key point in the development of inorganic biochemistry and optical materials [20]. Schiff bases have been utilized as synthons in the preparation of a number of industrial and biologically active compounds.

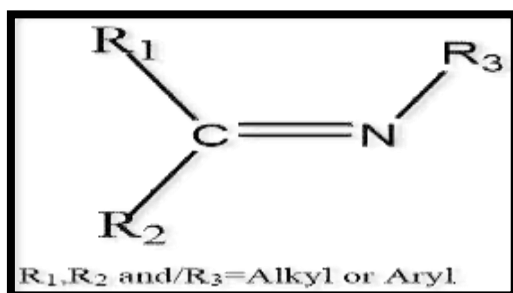


Fig.1 General Structure of Schiff base



Fig.2 3D Structure of Schiff base

## Metal complex with Sulphadiazine drug moiety

The sulfonamides and their structurally related derivatives, such as the sulfamates and sulfamides, possess the general formula  $A-SO_2NHR$ , in which the functional group is either directly bound to an aromatic, heterocyclic, aliphatic, or sugar scaffold (of type A), or appended to such a scaffold via a heteroatom, most frequently oxygen or nitrogen (leading thus to sulfamates and sulfamides, respectively) [25,26,27,28]. It interferes with PABA (p-aminobenzoic acid) in the biosynthesis of tetrahydrofolic acid, which is a basic growth factor essential for the metabolic process of bacteria.

## Swiss ADME studies

To be effective as a drug, a potent molecule necessarily reach its target in the body in sufficient concentration, and stay there in active form long enough for the expected biologic events to occur. Drug development involves assessment of ADME increasingly earlier in the discovery process, at a stage when considered compounds are numerous but access to the physical samples is limited. In that context, computer models constitute valid alternatives to experiments. Here, we present the new Swiss ADME web tool that gives free access to a pool of fast yet robust predictive models for physicochemical properties, pharmacokinetics, drug-likeness and medicinal chemistry

friendliness, among which in-house proficient methods such as the BOILED-Egg, iLOGP and Bioavailability Radar.

### Swiss ADME studies of Manganese Complex

To be effective as a drug, a potent molecule must reach its target in the body in sufficient concentration, and stay there in a bioactive form long enough for the expected biologic events to occur. Drug development involves assessment of absorption, distribution, metabolism and excretion (ADME) increasingly earlier in the discovery process, at a stage when considered

compounds are numerous but access to the physical samples is limited. In that context, computer models constitute valid alternatives to experiments. Here, we present the new Swiss ADME web tool that gives free access to a pool of fast yet robust predictive models for physicochemical properties, pharmacokinetics, drug-likeness and medicinal chemistry friendliness, among which in-house proficient methods such as the BOILED-Egg, iLOGP and Bioavailability Radar.

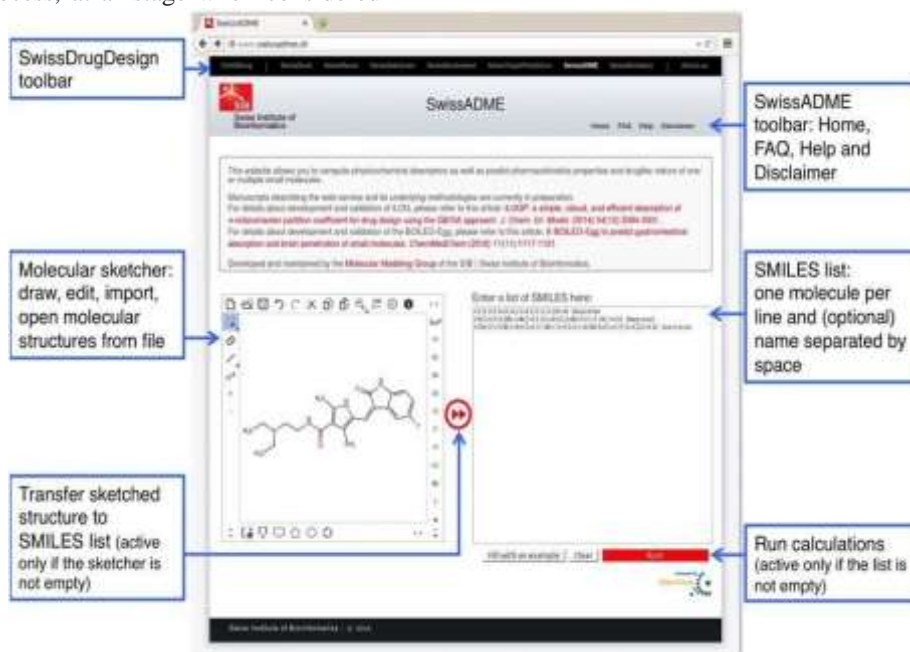


Figure 3: Web page allows the user to navigate within the different Swiss Drug Design tools

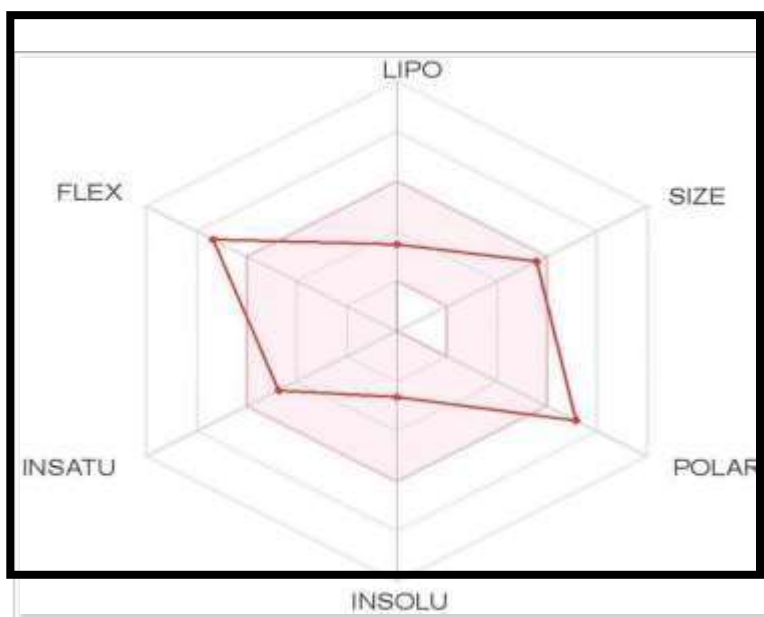


Figure 4: A physicochemical range on each axis was defined by descriptors adapted and depicted as a pink area in which the radar plot of the molecule has to fall entirely to be considered drug-like

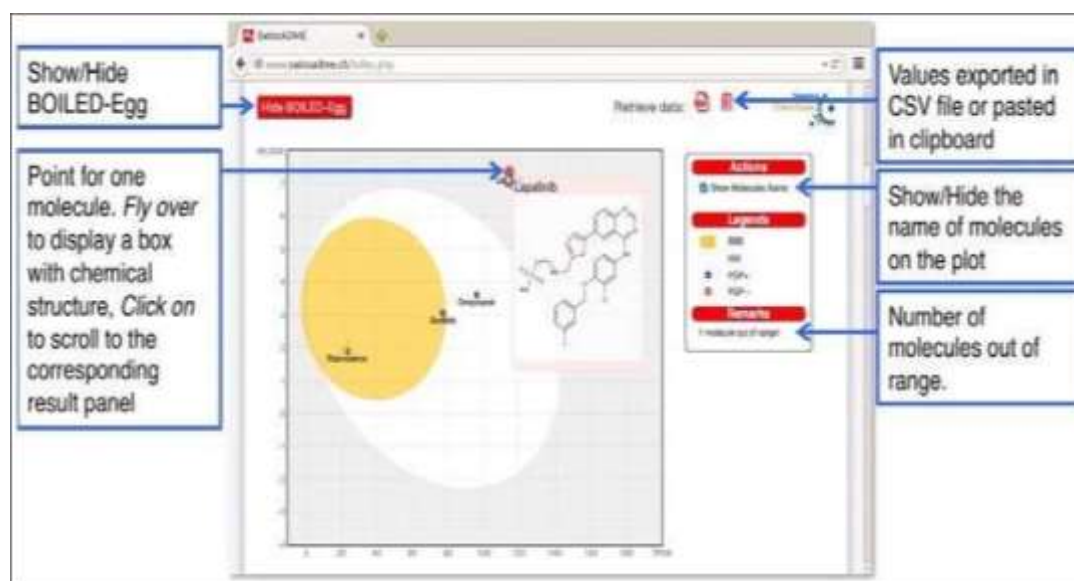


Figure 5: the “Show BOILED-Egg” red button appears below the sketcher to display the graphical output on the same page

Table.1 Tabular presentation of biophysical parameter of manganese metal complex

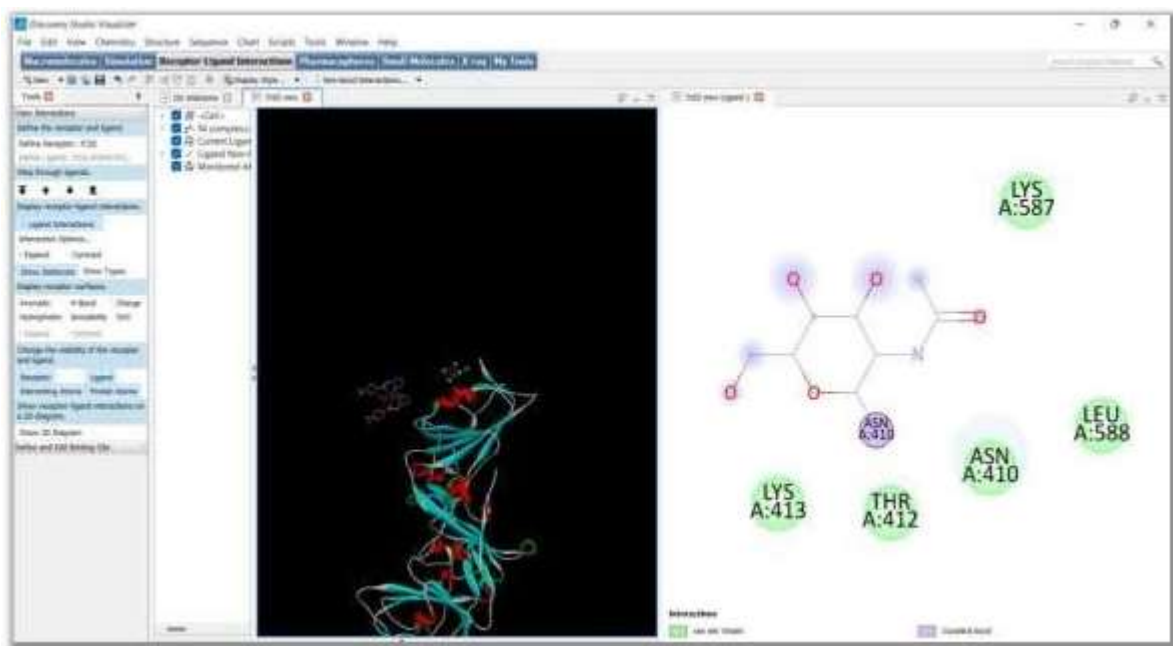
Physicochemical Properties	
<b>Formula</b>	C <sub>23</sub> H <sub>25</sub> MnN <sub>10</sub> O <sub>8</sub> S <sub>2</sub>
Molecular weight	688.57 g/mol
Num. heavy atoms	44
Num. arom. heavy atoms	24
Fraction Csp <sup>3</sup>	0.04
Num. rotatable bonds	13
Num. H-bond acceptors	13
Num. H-bond donors	3
Molar Refractivity	163.13
TPSA	292.78 Å <sup>2</sup>
<b>Lipophilicity</b>	
Log <i>P</i> <sub>o/w</sub> (iLOGP)	0.00
Log <i>P</i> <sub>o/w</sub> (XLOGP3)	2.64



Property	Model Name	Predicted Value	Unit
Absorption	Water solubility	-2.854	Numeric (log mol/L)
Absorption	Caco2 permeability	-0.017	Numeric (log Papp in 10 <sup>-6</sup> cm/s)
Absorption	Intestinal absorption (human)	8.034	Numeric (% Absorbed)
Absorption	Skin Permeability	-2.735	Numeric (log Kp)
Absorption	P-glycoprotein substrate	Yes	Categorical (Yes/No)
Absorption	P-glycoprotein I inhibitor	No	Categorical (Yes/No)
Absorption	P-glycoprotein II inhibitor	No	Categorical (Yes/No)
Distribution	VDss (human)	0.291	Numeric (log L/kg)
Distribution	Fraction unbound (human)	0.24	Numeric (Fu)
Distribution	BBB permeability	-2.204	Numeric (log BB)
Distribution	CNS permeability	-4.546	Numeric (log PS)
Metabolism	CYP2D6 substrate	No	Categorical (Yes/No)
Metabolism	CYP3A4 substrate	No	Categorical (Yes/No)
Metabolism	CYP1A2 inhibitor	No	Categorical (Yes/No)
Metabolism	CYP2C19 inhibitor	No	Categorical (Yes/No)
Metabolism	CYP2C9 inhibitor	No	Categorical (Yes/No)
Metabolism	CYP2D6 inhibitor	No	Categorical (Yes/No)
Metabolism	CYP3A4 inhibitor	No	Categorical (Yes/No)
Excretion	Total Clearance	2.321	Numeric (log ml/min/kg)
Excretion	Renal OCT2 substrate	No	Categorical (Yes/No)
Toxicity	AMES toxicity	No	Categorical (Yes/No)

Table no.2: Molecule properties:

Descriptor	Value
Molecular Weight	640.563
LogP	-0.711
#Rotatable Bonds	4
#Acceptors	15
#Donors	9
Surface Area	229.210



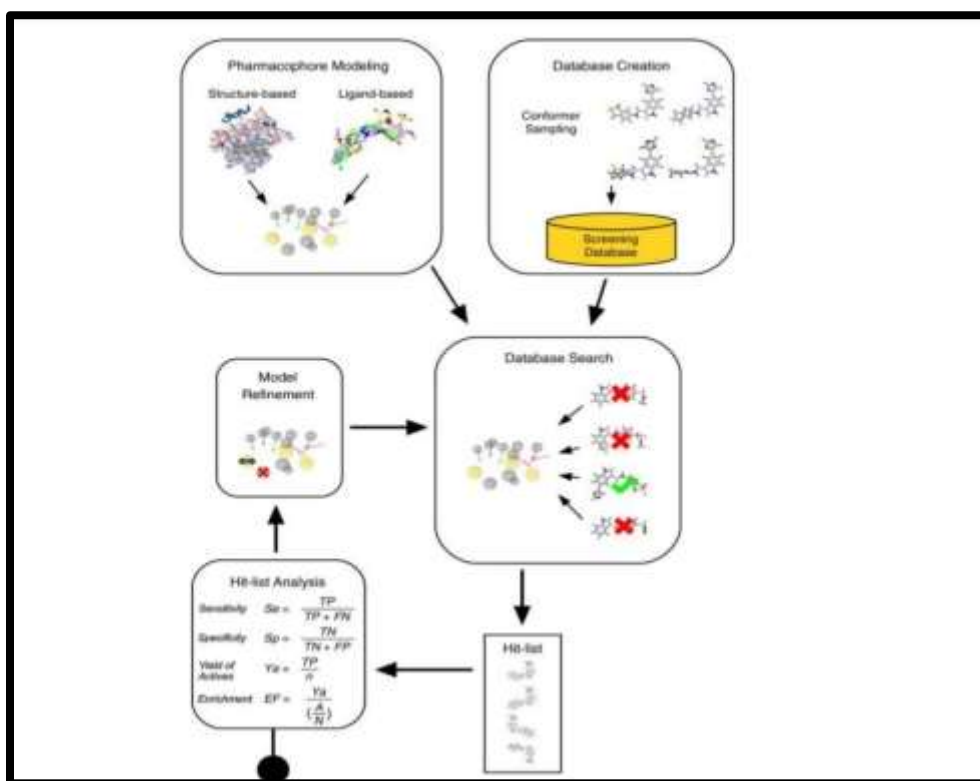
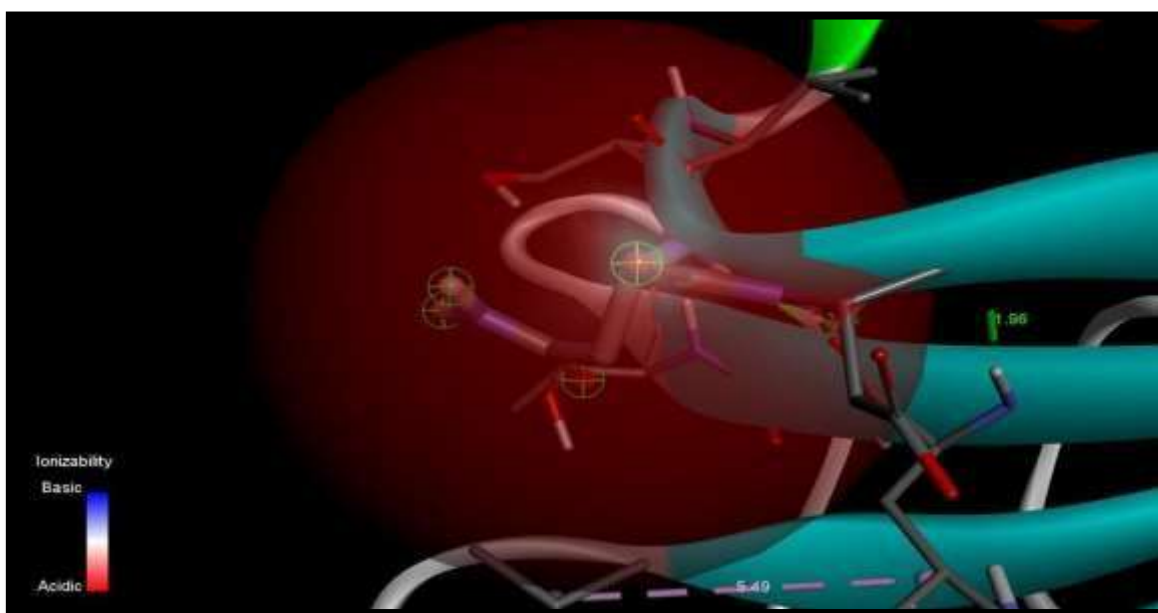


Fig.7 3D Pharmacophore-based virtual screening workflow.

### MOLECULAR DOCKING RESULTS

The protein structure and a database of ligands serve as inputs to a docking program. The success of a docking program depends upon the two components such as search algorithm and scoring function. Searching Conformational Space The search space consists of all possible orientations and conformations of the protein paired with ligand. With present computing resources, it is impossible to exhaustively explore the search space this would enumerating all possible distortions of each molecule and all possible rotational and translational

orientations of the ligand relative to the protein at a given level of granularity. Most docking programs in use account for flexible ligand, and several are attempting to model a flexible protein receptor. Each "snapshot" of the pair is referred as a pose. Scoring Functions The scoring function takes a pose as input and returns a number indicating the likelihood that the pose represents a favorable binding interaction. Most scoring functions are physics based molecular mechanics force fields that estimate the energy of the pose; a low (negative) energy indicates stable system and thus a likely binding interaction.



Drug complex dock with receptor pdb file 7c02 having certain types of results showing various graphical representation. In docking results showing maximum binding affinity of drug complex.

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