Computational Approach to Molecular Catalysis by 3d Transition Metals: through 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 moleMnles, is used to prepare complex substances called sciff 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 pair wise interaction energies are calculated . Both approaches are outlined below. Shape c/ 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 pair wise 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 moleMnles, 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.

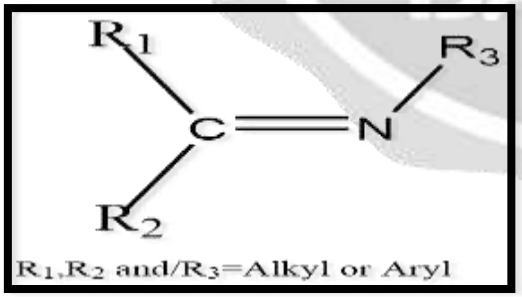


Fig.1 General Structure of Schiff base

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 themetabolic 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 ocMnr. 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.

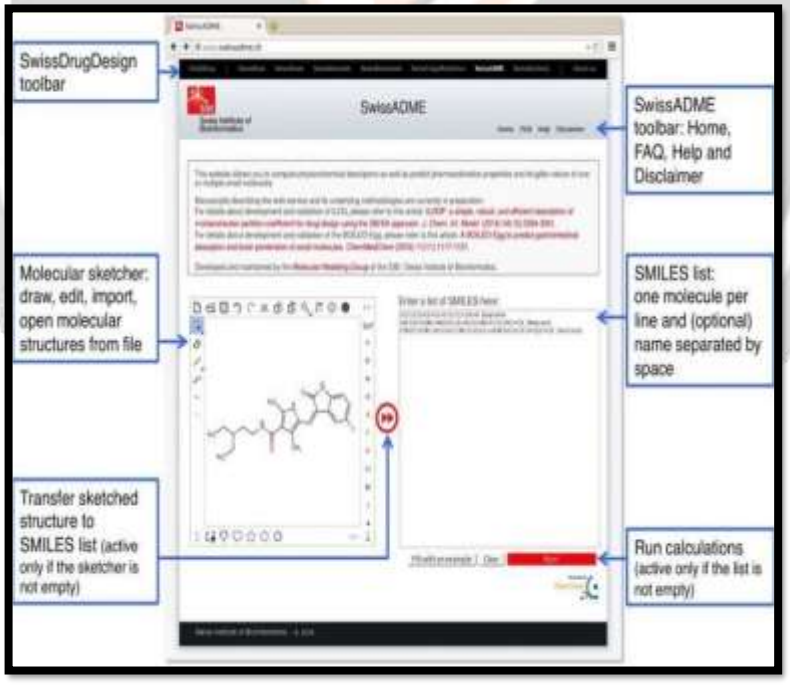


Figure 3: Web page allows the user to navigate within the different Swiss Drug Design tools

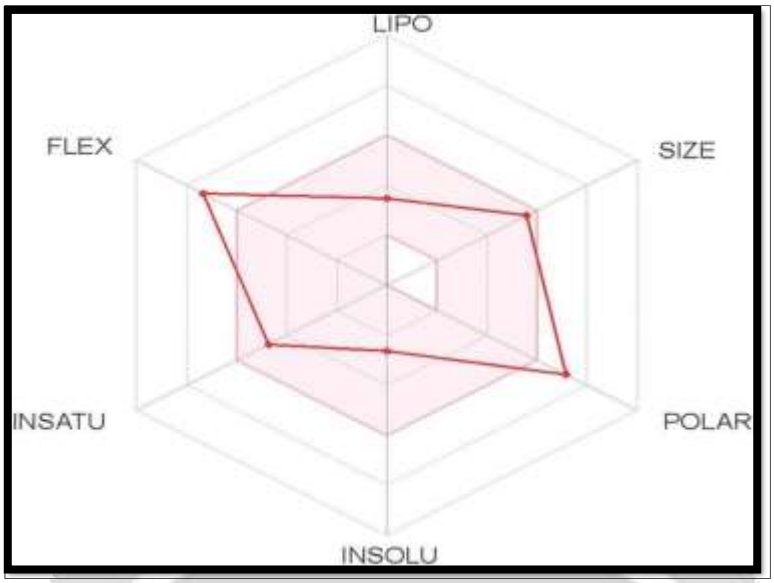


Figure 4: A physicochemical range on each axis was defined by descriptors adapted and depictedas a pink area in which the radar plot of the molecule has to fall entirely to be considered drug-like

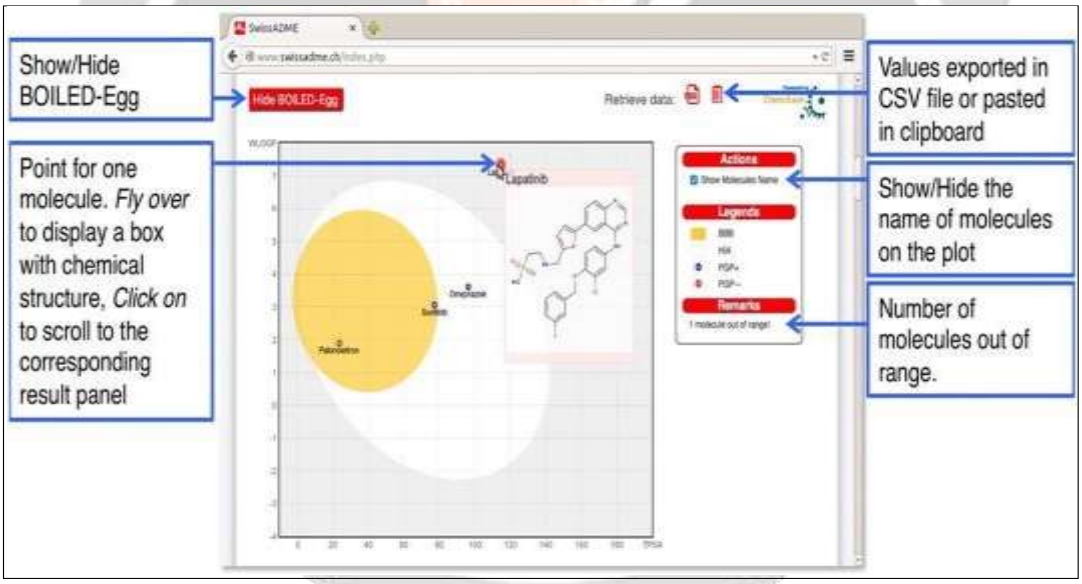


Figure 5: the "Show BOILED-Egg" red button appears below the sketcher to display the graphical output on the same page

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

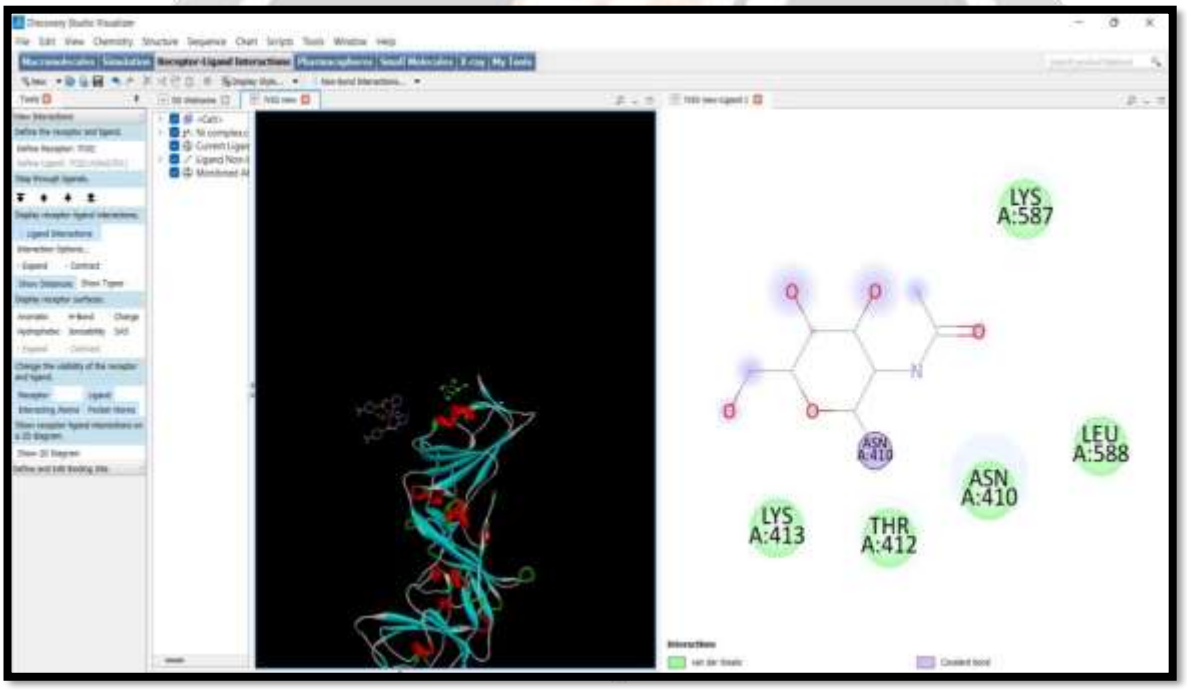
Physicochemical Properties	
Formula	C23H25MnN10O8S2
Molecular weight	688.57 g/mol
Num. heavy atoms	44
Num. arom. heavy atoms	24
Fraction Csp3	0.04
Num. rotatable bonds	13
Num. H-bond acceptors	13

Num. H-bond donors	3
Molar Refractivity	163.13
TPSA	292.78 Å²
Lipophilicity	
Log $P_{O/W}$ (iLOGP)	0.00
Log $P_{O/W}$ (XLOGP3)	2.64
Log $P_{O/W}$ (WLOGP)	1.77
Log $P_{O/W}$ (MLOGP)	-3.05
Log $P_{O/W}$ (SILICOS-IT)	-7.67
Consensus Log $P_{O/W}$	-1.26
Water Solubility	
Log *S* (ESOL)	-5.32
Solubility	3.31e-03 mg/ml ; 4.81e-06 mol/l
Class	Moderately soluble
Log *S* (Ali)	-8.44
Solubility	2.51e-06 mg/ml ; 3.64e-09 mol/l
Class	Poorly soluble
Log *S* (SILICOS-IT)	-4.00
Solubility	6.85e-02 mg/ml ; 9.95e-05 mol/l
Class	Moderately soluble
Pharmacokinetics	
GI absorption	Low
BBB permeant	No
P-gp substrate	Yes
CYP1A2 inhibitor	No
CYP2C19 inhibitor	No
CYP2C9 inhibitor	Yes
CYP2D6 inhibitor	No
CYP3A4 inhibitor	Yes
Log K_p (skin permeation)	-8.63 cm/s
Druglikeness	
Lipinski	No; 2 violations: MW>500, NorO>10
Ghose	No; 2 violations: MW>480, MR>130
Veber	No; 2 violations: Rotors>10, TPSA>140
Egan	No; 1 violation: TPSA>131.6
Muegge	No; 3 violations: MW>600, TPSA>150, H-acc>10
Bioavailability Score	0.11

Medicinal Chemistry	
PAINS	0 alert
Brenk	3 alerts: aniline, oxygen-nitrogen_single_bond, thiocarbonyl_group
Leadlikeness	No; 2 violations: MW>350, Rotors>7
Synthetic accessibility	5.55

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



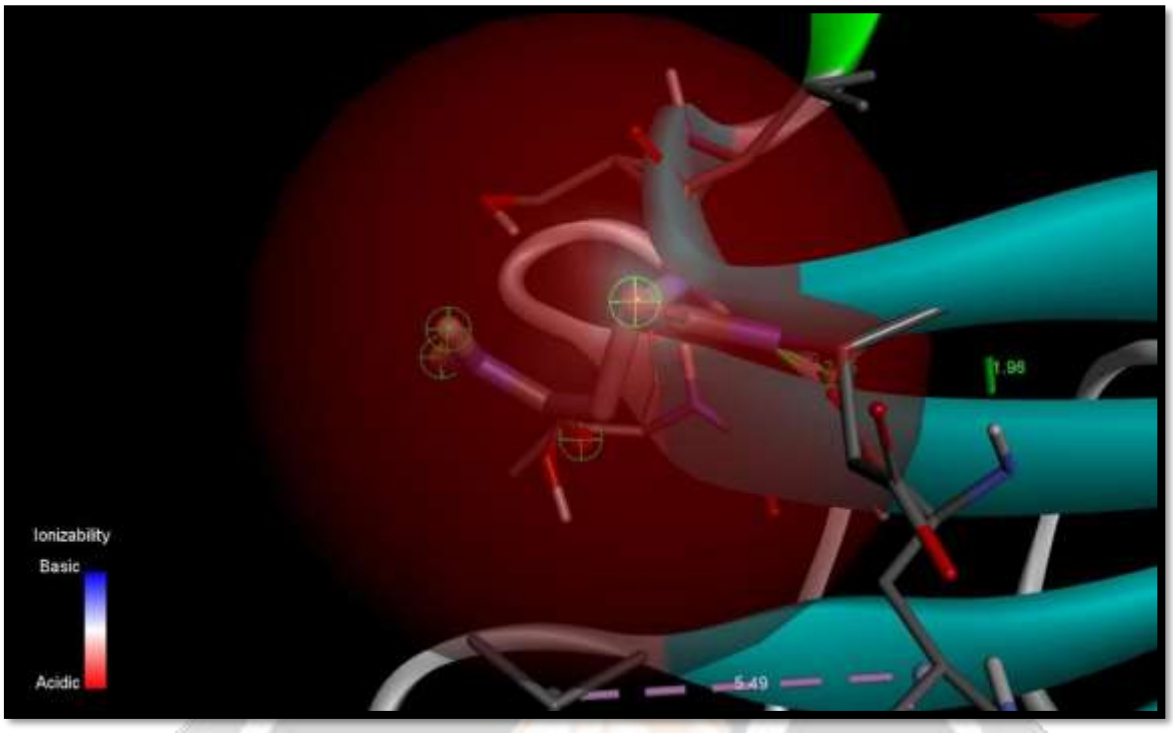


Figure 6 & 7: Molecular docking

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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