Research Article

Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice

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Abstract

Computational molecular design is a useful tool in modern drug discovery. Virtual screening is an approach that docks and then scores individual members of compound libraries. In contrast to this forward approach, inverse approaches construct compounds from fragments, such that the computed affinity, or a combination of relevant properties, is optimized. Drug discovery and development involves a complicated three-dimensional highly correlated, many-body dynamical molecular system, and an intense, lengthy, interdisciplinary scientific endeavor which is often no intuitive even for highly trained researchers [1]. Small Molecule Drugs are indispensable for the treatment and cure of deleterious infectious diseases. There has been a plethora of new Malaria and Ebola infectious diseases short linear motif elements protein and DNA/RNA targets being discovered. Hence, ideal small molecule quantum thinking drugs are always in great demand. We have recently developed a new inverse approach combining human spatial reasoning and AI design insight to our BiogenetoligandorolTMligandorolTM novel drug design technologies based on the most promising lead compounds and dead-end eliminated Docking Algorithms by employing a hybrid classical/quantum mechanical physical potential function. In an attempt to increase the antimicrobial activity of the insect defensin from Anopheles gambiae, which is active against Staphylococcus aureus at low concentration, hybrid defensins were designed by combining conserved sequence regions and variable regions of insect defensins. The three-dimensional structure of Anopheles gambiae defensin and five hybrids were determined by NMR and molecular modeling. Here, we have discovered for the first time an in-silico predicted and computer-aided molecular designed Inverse Molecular

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Design Docking Algorithm in a Model Binding Site offering the potential to usher in a new paradigm for engineering an In silico predicted and computer-aided molecular designed structure of peptide mimetic active pharmaco-agent (MalasmoruponaqTM™): 7,{[4,(2,{[(2R),3,(42,2,3,4,4a,4b,5,6,7,8,decahydro,9λ⁴,carbazol,4,yloxy),2,hydroxypropyl]amino}ethoxy),3,oxocyclohexyl]oxy},19,[(42Z),1,[(2R),2,[(2S),2,amino,3,[(3R),3,hydroxy,3,[(3R,4S,5R),4,hydroxy,5,[(42R),1,hydroxy,2,[(oxophospho),λ³,oxy]ethyl],2,oxooxolan,3,yl]propyl],1,3,diazinan,1,yl],2,(hydroxy amino)ethylidene],5,6,dihydro,4H,1λ⁴,2,thiazin,3,yl],2λ³,oxa,10λ⁴,13λ⁴,diazapentacyclo[12.8.0.0³,¹².0⁴,⁹.0¹⁵,²⁰]docosa,1,9,10,12,13,pentaen,6,one dihydrofluoride against the gram positive bacteria Staphylococcus aureus for the depletion of its antibacterial defensin DEF-AAA for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses.

2D MalasmoruponaqTM™ QMMMIDDD miracle molecule.

Keywords: Anopheles Gambiae; Inverse Molecular; Design Docking Algorithm; Computer Aided Molecular Drug Design; Motif Peptide; Pharmaco-Agent; Relativistic; Generalization of Density Functional Theory (DFT)

Introduction

To meet the challenges of ideal drugs, an efficient method of drug development is demanding and more applied technologies Machine

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Learning and Computer Vision Systems have to be introduced for Phenotype Data Acquisition and Analysis Direct quantum process tomography via measuring sequential weak values of incompatible observables Docking Algorithms. The process of the alchemical perturbation (AP) methods and QMMM in silico computer-aided drug discovery is typically challenging, costly, time consuming, and requires consideration of different computational aspects since it has historically been limited by the lack of validated molecular algorithmic sequences, consensus targets and of high-throughput machine learning based screening methods. It is considered as a linear, consecutive process that initiates with interactive molecular dynamics in virtual targets and small molecule lead discovery approaches including training machines to learn potential free energy functions, combining strict alchemical perturbation methods with the Poisson-Boltzmann or generalized Born biomolecular conformational heuristic samplings, surface area continuum solvation (MM/PBSA and MM/GBSA) and protein-MalasmoruponaqTM™ligand binding methods with fused pharmacophoric reaction discoveries using "on-the-magic-fly" quantum chemistry, and transport hadamard dynamics with computational exhausted automation technologies to generate real-time Quantum Mechanics MD simulations of flexible 3D hyper-structures, followed by fragment lead based FBDD/LBDD optimization and pre-clinical in vitro and in vivo studies to determine if such selected compounds satisfy a number of pre-set criteria for initiating clinical trial developments. Malaria, a form of P.Falcifarum, is a a mosquito-borne infectious disease that affects humans and other animals which is often occurred. Mefloquine is an anti-malarial synthetic chemoprotective molecule with anti-malarial activity and selectively inhibits the lactate dehydrogenase molecular mechanism. Glycolysis is the major bio-molecular pathway for ATP production in the malaria parasite Plasmodium falciparum and its inhibition is needed for cell survival. Malaria, one of the most distressing diseases, is caused by the parasitic protozoan Plasmodiumfalciparum. It takes away millions of lives with the rate increasing each growing year. According to WHO's Factsheet on the World Malaria Report 2013, 1.2 billion people out of a total of an estimated 3.4 billion are at a high risk of malaria. Malaria is highly prevalent in sub-Saharan Africa where 90% of all malaria deaths occur (WHO 2013). A lot of research has been going on in the ield ofmalarial therapeutics. This method predicted controlled quantum small molecule SMILES teleportations with an arbitrator for secure quantum channels via quantum dots inside protein cavities Docking Interactions using experimentally known intraspecies and interspecies Docking Interactions and filtered proteins on several parameters, such as cellular location and cellular function for Supercritical entanglement in local systems to the area law for quantum mechanical Docking Algorithm to confirm the practicality of the predictions. In this study, a complete protein interaction network Neutron Diffraction in Transmission Mode Implementation between human host and Plasmodium falciparum has been developed by inte-

gration of experimental and computational BiogenetoligandorolTM's Semi-empirical methods, which are less accurate methods that use experimental results to avoid the solution of some terms that appear in the ab initio methods. BiogenetoligandorolTM's uses the accuracy of electric charges plays an important role in protein–MalasmoruponaqTM™ligand docking, which is why QM-MM calculations are incorporated into docking procedures. Fixed charges of MalasmoruponaqTM™ligands obtained from force-field parameterization are replaced by QM-MM calculations in the protein–MalasmoruponaqTM™ligand complex, treating only the MalasmoruponaqTM™ligand as the quantum region. BiogenetoligandorolTM's uses the QMMMIDD quantum thinking approach that provides unprecedented accuracy in fragment MalasmoruponaqTM™ligand based structure-based binding-energy calculations that enable formalistic application of QM methodologies to noncovalent hyper geometric and intra topology meta-Docking Interactions in complex systems as large as protein–MalasmoruponaqTM™ligand druggable complexes and conformational ensembles. AgamOBP20 is one of a limited subset of OBPs that it is preferentially expressed in female mosquitoes and its expression is regulated by blood feeding and by the day/night light cycles that correlate with blood-feeding behavior. Analysis of AgamOBP20 in solution reveals that the apo-protein exhibits significant conformational heterogeneity but the binding of odorant molecules results in a significant conformational change, which is accompanied by a reduction in the conformational flexibility present in the protein. Crystal structures of the free and bound states reveal a novel pathway for entrance and exit of odorant molecules into the central-binding pocket, and that the conformational changes associated with ligand binding are a result of rigid body domain motions in α-helices 1, 4, and 5, which act as lids to the binding pocket. The eventual aim of this computer-aided inisilico drug design study is to design an efficient multi-pharmacophoric drug molecule against the Malaria target by adapting machine general-purpose earning techniques using inverse probability of censoring weighting Docking Algorithms for the accuraqte algebraic topology predictions of small molecules in machine learning based scoring and virtual screening techniques. Various tubulin mitotic small molecule inhibitors such as benzimidazole, dinitroanilines which interact within Malarial P. and EBOV protein proteins and hinder the infection process have been fragmented, re-cored and merged into a MalasmoruponaqTM™'s larger druggable scaffold by using Absolute Binding Free Energy Computational Scoring Calculations of Protein-MalasmoruponaqTM™ligand Docking Interactions for the constructions of exact representations of quantum many-body systems with Force-momentum-based Langevin dynamic self-guided deep neural networks as a rapid sampling inverse docking method that approaches the canonical neuronal version of Grover's quantum algorithm. Finally, the MalasmoruponaqTM™ molecule is computationally designed by using some of Electronic Nose Quantum Noosphere Improved Quantum Artificial Fish Docking Algorithmic Applications to Distributed Net-

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work quantum classifiers which has exhibited better binding affinity than the other FDA anti-malarial molecules which can be considered as a novel drug molecule candidate. In this study, we have discovered for the first time an in-silico predicted and computer-aided molecular designed Inverse Molecular Design Docking Algorithm in a Model Binding Site as an In silico predicted and computer-aided molecular designed structure of peptide mimetic active pharmaco-agent (Malasmoruponaq™™): 7,{[4,(2,{[(2R),3,(42,2,3,4,4a,4b,5,6,7,8,decahydro, 9λ^4,carbazol,4,yloxy)),2,hydroxypropyl]amino}ethoxy), 3,oxocyclohexyl]oxy},19 ,[(42Z),1,[(2R),2,,[(2S),2,amino,3,[(3R),3,3,[(3R,4S,5R),4,hydroxy,5,[(42R),1,hydroxy,2,[(oxophospho),λ^3,oxy]ethyl],2,oxooxolan,3,yl]propyl],1,3, diazinan,1,yl],2,(hydroxyamino) ethylidene],5,6, dihydro, 4H,1λ^4, 2, thiazin,3,yl] 2λ^3,oxa,10λ^4,13λ^4, diazapentacyclo [12.8.0.0^{3,12}.0^4,9.0^{15,20}] docosa,1,9,10,12,13,pentaen,6,one dihydrofluoride against the gram positive bacteria Staphylococcus aureus for the depletion of its antibacterial defensin DEF-AAA for the deactivation of antimicrobial activity of the insect defensin from Anopheles gambiae To determine the number of binding sites, a proof of concept docking study employing a widely- accepted validation tool called GEMDOCK (Generic Evolutionary Method for molecular docking), is used to compare MalasmopuronaqTM with the other FDA drugs approved for use against Malaria. The results are impressive. Comparison against other FDA approved drugs proves l14122871974,78905 - fold times higher. To accomplish these challenges, several multidisciplinary BiogenetoligandorolTM's Ab initio methods, where the solution of the Schrodinger equation is obtained from first principles of quantum chemistry using rigorous mathematical approximations, and without using empirical data approaches have been integrated for the process of drug development; collectively these approaches would form the basis of BiogenetoligandorolTM's Wavefunction based methods, which are based on obtaining the wave function of the anti-malarial rational drug design system [2] . With the advent of genomics, proteomics, bioinformatics and technologies like crystallography, NMR, the structures of more and more protein targets are integrated into the BiogenetoligandorolTM's Density functional based methods, that consist in the study of the properties of the system through its electronic density, but avoiding the explicit determination of the electronic wave function. The MalasmopuronaqTM QMMM small molecule binds to the crystal structures with some of 190800000379.40 Docking Fitness Scoring Values within the PfNDH2 protein and for the first time within Apo-, NADH, bound states/binding domains. The PfNDH2 targeted MalasmopuronaqTM QMMM small molecule inhibitor exhibits excellent docking potency against the PfNDH2 protein and for the first time within Apo-, NADH-bound states/binding domains via a potential allosteric mechanism and agonistically increases the conformational adaptation to different odorants that have important implications in the selection and development of reagents targeted at disrupting normal OBP function.

Material and Methods

Softwares

All softwares were open acces, except the academic version ofBiogenetoligandorol TM (2018.19) obtained from (Biogenetoligandorol TM. BiogeneaSA, Greece) [4,6,8-12]. Biogenetoligandorol TM protocol [3,5,7,8-12,13]. The complex structure was applied with the CHARMM-Polar-H force field in the BiogenetoligandorolTM 2016 [3,4,7,6,8-13,15,18,21]. The typed structure was then exported and used as the basis for mutagenesis. Using a Perl script specific to BiogenetoligandorolTM, we mutated the hybrid CDR residues to all 20 genetically encoded amino acids and calculated both the ΔΔEbinding and ΔΔEstability values, which resulted in 1400 mutations [24,25,28,29,51,52,76,71,72,73,78]. BiogenetoligandorolTM biologics suite protocol: The complex structure was prepared by using the Protein Preparation Wizard tool [48, 49,69-73] within the BiogenetoligandorolTM, BiogeneaSA, Greece 2018–3 [33]. The titratable residues were protonated in accordance with their environment by using BiogenetoligandorolTM_Ka [50, 51,52,76,71,72,73,78] and were typed with the OPLS3 [52] force field, and the structure was subsequently minimised. Because optimization of the wider environment of a mutation may result in the unwarranted acceptance of large side chains, two separate mutagenesis experiments were performed. One experiment used a 0.0 Å optimization distance, that is, only the mutated reside, and one also minimised any residues within 5.0 Å. By using both optimization criteria and taking a consensus of accepted mutations, it was possible to avoid selection of residues that sterically disrupted the local protein environment whilst identifying those that required only a small structural rearrangement to enter a conformation, thereby leading to improved binding affinity [52,76,71,72,73,78].

Genome-Wide Drug-Target Prediction, Dataset and QSAR Study

Using FP-2 (PF3D7_1115700) and FP-3 (PF3D7_1115400) [78-112,113,115,118,119,122] as query sequences, seven plasmodial protein homologs together with three human homologs were retrieved from the PlasmoDB version 9.31 [78-112,113,115,118,119,122] and NCBI [74,78-112,113,115,118,119,122] databases, respectively as described earlier [50,78-112,113,115,118,119,122] A set of 341 molecules with inhibitory activity for plasmodial proteases was selected from the CanSAR database 7(https://cansar.icr.ac.uk/) based on their molecular weight and IC50. This was converted to pIC50 for the QSAR analysis. The set of these molecules NAG:L:701, NAG:L:702, BMA:L:703, MAN:L:704, MAN:L:705, MAN:L:706, MAN:L:707, nteracting chains: K, L, N was randomly distributed to a training set of 240 compounds NAG:D:701 (NAG-NAG-BMA-MAN-MAN-MAN-MAN)-POLYMER+ NAG:D:702+ BMA:D:703 + MAN:D:704+

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MAN:D:705+ MAN:D:706+ MAN:D:707(70% of the data) and a test set of 131 NAG:H:701 (NAG-NAG-BMA-MAN-MAN-MAN-MAN)-POLYMER+ NAG:H:702+ BMA:H:703+ MAN:H:704+ MAN:H:705+ MAN:H:706+ MAN:H:707compounds (32% of the data). cathepsin L (Cat-L) like plasmodial proteases is the presence of an N-terminal signalling (non-structural) RNA+ION starting with C (composite ligand, containing Cytidine Monophosphate)C-G-C-A-U-G-C-G-MG Composite ligand consists of C:C:1, G:C:2, C:C:3, A:C:4, U:C:5, G:C:6, C:C:7, G:C:8, MG:C:9. Interacting chains: A, B peptide sequence (~∫150 amino acids), which is responsible for targeting them into the food vacuole in 4IOD (malarial clp b2 atpase/hsp101 protein). SO4 (sulfate) SO4-A-201 Interacting chains: A. For each of the plasmodial proteins, this segment was chopped off, and the remaining prodomain portion-catalytic domain saved into a Fasta file (Additional file 1) in 3L27 (polymerase cofactor vp35). As guided by the partial zymogen complex crystal structure of Cat-K [PDB: 1BY8],∫~∫21 amino acids (N-terminal) were also chopped off from the human cathepsin prodomain sequences V-M-GLU-50, V-S-GLU-50, V-M-GLU-51, V-S-GLN-54, V-S-HIS-80, V-M-GLU-144, V-M-ALA-145, V-S-ASN-146, V-M-ASP-226, V-S-ASP-226, V-M-ALA-227. Together, these sequences were used in the rest of the study, and are referred as "partial zymogen" or "prodomain-catalytic domain" sequences interchangeably in the manuscript [78-112,113,115,118,119,122]. Position details of the PRF (queuine) PRF-A-290 Interacting chains: A prodomain and PRF-B-290 Interacting chains: B catalytic portions per protein are listed in Additional file 4. To determine the conservation of the PRF-C-290 Interacting chains: C prodomain-catalytic portion, multiple sequence alignment (MSA) 4DGH (sulfate permease family protein) was performed using Profile Multiple Alignment with predicted Local Structures and 3D constraints (PROMALS3D) web server [75] with default parameters except PSI-BLAST Expect value which was adjusted to 0.0001, and the alignment output visualized using JalView [76]. The GOL (Glycerol) GOL-A-608 Interacting chains: A training set has been subjected to the Partial Least Square (PLS) 8. In absence of an experimentally validated inhibitor with a biological activity of LMTK3 protein in the different databases, the construction of QSAR model based on the biological activity of these inibitors cannot take place [78-112,113,115,118,119,122,127] and NCBI [74,78-112,113,115,118,119,122] databases, respectively as described earlier [50,78-112,113,115,118,119,122]. Genome-wide anti-malarial drug-in 6IOT target ION CA (calcium ion) CA-A-502 Interacting chains: ADocking Interactions were predicted using DockThor. DockThor takes four networks as input: chemical-protein association (matrix R), off-target (matrix Q), chemical-chemical similarity, protein-protein similarity networks, The chemical-protein associations were obtained by integrating three resources: 1) publicly available databases, ChEMBL [53] (v23.1) and Drug Bank [54] (v5.5.10), 2) four data sets from recent publications about kinome

assays [55-58], and 3) protein structure-based off-target prediction from previous step. From ChEMBL, inhibition assays having IC50 ≤ 10 µM was regarded as active associations s78-112,113,115,118,119,122] and NCBI [74,78-112,113,115,118,119,122] databases, respectively as described earlier, [50,78-112,113,115,118,119,122]. Those with suboptimal confidence scores (i.e. confidence < 9) were excluded. From Drug Bank, drug-CA-B-502 Interacting chains: B target, drug-2BH1 (general secretion pathway protein l general secretion pat...), drug-G9D (SureCN12750328), G9D-A-1, Interacting chains: A, and drug-transporter associations were collected for the generation of the Hydrophobic Docking Interactions of the 2 MalasmoruponaqTM™ binding site(s) in 3ZML (glutathione s-transferase e2) GSH (Glutathione)GSH-A-1222 Interacting chains: A. The data sets from kinome assays are available in different types of activity measurement. Christmann-Franck et al. collected chemical-kinase assays from multiple past publications and presented the activity standardization protocol, which assumed an activity with Ki ≤ 5 µM is active [55,74,78-112,113,115,118,119,122]. If the original publication presented percent inhibition (or percent remaining activity) at a given compound concentration, Ki was calculated as follows:

$$\%control=\frac{(TestCompoundSignal-PositiveControlSignal)}{(NegativeControlSignal-PositiveControlSignal)}\times100$$
$$response=background+\frac{signal-background}{1+(Kd-1/dose-1)}$$

$$y=A+\frac{B-A}{1+(Cx)D} \quad Ki=\frac{concentration\times(100-\%inhibition)}{\%inhibition}$$

$$minU,V\geq0\sum(i,j)w(R(i,j)+Q(i,j)-U(i,:)⌷V(j,:)T)2+\alpha(\|U\|2+\|V\|2)+\beta tr(UT(DC-C)U)+\gamma tr(VT(DT-T)V)$$
$$P(i,j)=UUP(i,:)\cdot VUP(j,:)T \quad FoldChange=\{ES/ER,ifES>ER-ER/ES,ifES<ER$$
$$q=(prank)\times N \quad (1)$$

Here, w is the confidence weight on the observed and predicted off-target associations which indicate the reliability of the assigned probability of true association; α is the regularization parameter to prevent overfitting; β is the importance parameter for chemical-chemical similarity, γ is the importance parameter for protein-protein similarity, and tr(A) is the trace of matrix A [90-110,121,123,127]. The predicted score for the ith chemical to bind the jth protein can be calculated by P(i,j)=UUP(i,:)·VTUP(j,:), where UUP and VUP are the low-rank matrices U and V after completion of the updates. Different from original winOCCF [33], Q in DockThor is the predicted off-target network instead of a fixed imputation value within MalasmoruponaqTM™ binding site(s) in 3ZML (glutathione s-transferase e2). GSH (Glutathione)GSH-A-1222 Interacting chains: A. More details on the optimization algorithm of Eq (1) are published elsewhere [90-110,121,123,127], where ES and ER are the mean log2 mRNA probe levels for a given gene in cell lines found in the sensitive and resistant groups, respectively [89,90-110,121,123,127] to demonstrate the hydrogen Bonds

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from the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase): ION MG (magnesium ion) MG-A-7 Interacting chains: A. A false discovery rate (FDR)-adjusted p-value (q-value) is computed with a null hypothesis of no difference between "sensitive" and "resistant" groups for the generation of the Metal Complexes MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase): ION MG (magnesium ion) MG-A-7 Interacting chains: A. The q-value is calculated according to the following formula: q=(prank)×N where rank is the rank of the p-value and N is the number of conducted tests. Gene set over-representative analysis was carried out using Protein-Ligand Interaction Profiler [60-89,90-110,121,123,127] in the Water Bridges of the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase): ION MG (magnesium ion) MG-A-7 Interacting chains: A. Using Molecular Evolutionary Genetic Analysis (MEGA) version 5.2 software [87,89,90-110,121,123,127], the evolutionary relationship of plasmodial proteases and human cathepsins was evaluated with the following preferences; Maximum Likelihood (statistical method) and Nearest-Neighbor-Interchange (NNI) as the tree inference option the hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase): ION MG (magnesium ion) MG-A-7 Interacting chains: A. A total of 9 H-S-ASP-65, H-M-GLN-67, H-S-THR-206, V-M-VAL-199, V-M-ARG-202, V-S-ARG-202, V-M-LEU-203, V-M-THR-206, V-S-THR-206 amino acid substitution models were calculated for both complete (100%) and partial (95%) deletion and the best three models based on Bayesian Information Criterion (BIC) were selected. For each selected IHP-B-210 Composite ligand consists of IHP:B:210, NA:B:211. Interacting chains: B model, the corresponding gamma (G) evolutionary distance correction value was selected to build different phylogenetic trees and comparison was made to determine robustness of dendrogram construction process [90-110,121,123,127]. 4IOD (malarial clp b2 atpase/hsp101 protein). SO4 (sulfate) SO4-A-201 Interacting chains: A was included in the tree calculations as outgroup.

Physicochemical Properties, Motif Analysis, Homology Modelling and Structure Validation

Using an ad hoc Python and Biopython script, the amino acid composition and physicochemical properties, namely molecular weight (Mr), isoelectric point (pI), aromaticity, instability index, aliphatic index and grand average of hydropathy index (GRAVY) of the proteins were determined [60-89,90-110,121,123,127]. Multiple Em for Motif Elicitation (MEME) standalone suite version 4.10.2 [57,58,59,60-89,90-102,03,104,107,108,110,121,123,127] was used to identify the composition and distribution of protein motifs within partial zymogen sequences of the hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase): ON MG (magnesium ion) MG-A-7 Interacting chains: A. A Fasta file (Additional file 1-4) containing sequence information of the different proteins was parsed to MEME software with analysis preferences set as; -nostatus –time 18,000 –maxsize 16,000 –

mod zoops –nmotifs X –minw 6 –maxw 50 in the hydrophobic Docking Interactions of the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase): ION MG (magnesium ion) MG-A-7 Interacting chains: A. The variable X (a whole number from 1) was varied until no more unique motifs were assessable as determined by Motif Alignment Search Tool (MAST) [87,89,90,95,96,97] for the profiling of the hydrogen Bonds of the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase): ON MG (magnesium ion) MG-A-7 Interacting chains: A. A heat map showing motif distribution was generated using an in house Python script. PyMOL was used to map the different motifs onto the protein structures.

Homology Modelling And Structure Validation and Prodomain-Catalytic Domain Interaction Studies and Short Inhibitor Peptide Design

MODELLER version 9.18 + was used to build homology models of the inhibitor complex of all proteins except for Cat-K which has already a crystal structure. Using a combination of templates, high quality prodomain-catalytic domain complexes of the plasmodial proteases as well as cathepsins (Cat-L and Cat-S) were calculated by MODELLER with refinement set to very slow. Additional file 4 shows the details of templates selected for each protein model. For the plasmodial proteases, the crystallographic structure of procathepsin L1 from Fasciola hepatica [PDB: 2O6X] was used as it had the highest similarity with most target sequences (30–38%) and high resolution of 1.40 Å. However, it lacked the arm (β-hairpin) region while the nose residues were missing. To overcome these challenges, Cat-K [PDB: 1BY8] together with FP-2 [PDB: 2OUL] (for FP-2, VP-2, KP-2, BP-2 and YP-2) and FP-3 [3BWK] (for FP-3, VP-3, KP-3 and CP-2) were additionally used. For Cat-L and Cat-S, only two templates were used [PDB: 1BY8 and 2O6X]. For each protein, 100 models were calculated and ranked according to normalized discrete optimized protein energy (Z-DOPE) score [81] of the generated hydrogen Bonds MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.. The top three models per protein were further validated using ProSA [82], Verify3D [83], QMEAN [84] and PROCHECK [85] and the best quality model selected Water Bridges: MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.. To determine the prodomain inhibitory mechanism, residue Docking Interactions between prodomain and catalytic domain of plasmodial and human partial zymogen complexes were evaluated using the Protein Interaction Calculator (PIC) web server [86]. The interaction energy of identified residues was evaluated using the amino acid interaction (INTAA) web server [87] Hydrogen Bonds from the:MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™

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peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
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Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.. PyMOL was used to visualize the resulting Docking Interactions. For each protein, prodomain segment interacting with the catalytic domain's active pocket residues was identified and extracted into a Fasta file. From the interaction energies, residues within these inhibitory segments forming strong contacts with subsite residues were identified. Based on the identified hot spot residues, the next objective was to design short peptide(s) exhibiting the native prodomain effect whilst showing selectivity on human cathepsins hydrogen Bonds from the:MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A. The conservation of prodomain inhibitory segments for all the proteins, and separately of only the plasmodial proteases, was determined using WebLogo server [88]. Peptides of varying lengths and composition based on amino acid conservation forming contacts with subsite residues of the water Bridges from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.. In order to evaluate the interaction of selected peptides on the catalytic domains, the prodomain segments of all proteins were chopped using PyMOL. Blind docking simulation runs of selected peptides were then performed on these sets of catalytic domains by CABS-dock protein-peptide docking tool [89] using the default parameters Hydrogen Bonds from the. MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.. To confirm the reliability of the results, docking experiments were repeated using catalytic domains of the same proteins that had been modelled and used in previous studies [50]. Binding affinity (ΔG) and dissociation constant (Kd) for each protein-peptide complex was then evaluated using PROtein binDIng enerGY prediction (PRODIGY) web server [90].

Sequence Analysis and Docking Studies of Pfdhhcs

Using various databases like the PlasmoDB, PiroplasmaDB, and UniProt, we extracted DHHC sequences of different organisms including Plasmodium falciparum, Plasmodium berghei Toxoplasma gondii, Babesia bovis, Theileria parva, Cryptosporidium muris, and Eimeria tenella. This data exploration was done using different apicomplexan, specific databases including plasmodium genomics resource database (PlasmoDB) 13, toxoplasma genomics resource database (ToxoDB) 14, piroplasma genomics resource database (PiroplasmaDB) 15, and UniProt 16 for fetching other organism, specific protein sequences. Using PlasmoDB, putative DHHC gene sequences in P. falciparum (PfDHHC) were annotated and exctracted based on conserved domain architecture as receptors for the performance of the Docking Studies with MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related

anonymous protein), selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A, and in the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.. The domain architecture of protein sequences was assessed via SMART, Batch and INTERPRO online servers [81,82,83,86,88,89,90-110,119,121,122]. We performed multiple sequence alignment (MSA) of the 12 annotated PfDHHCs using MUSCLE algorithm (implemented in jalview software, Elixir,UK, https://elixir-europe.org) [101,102,103,107,109,110]. These 12 PfDHHCs along with PAT sequences from six other organisms namely closer members P. berghei and T. gondii, and distant members of Apicomplexa namely B. bovis, T. parva, C. muris, and E. tenella were further used to construct a neighbor, joining (NJ) tree of the Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A. The indexing and integration of obtained data sets were carried out using XDS (Pilatus) [95,96,97,98,100-113] for the generation of the Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A. The scaling, merging and calculating of structural factor amplitudes were executed using programs TRUNCATE47 and SCALA48 from CCP4 software49[11,112,,114,121]. Crystal structures were constructed by molecular replacement using Phaser50 with RnCCT (PDB: 3HL4) and free MalasmoruponaqTM_937d73c677_1 (PDB: 4ZCT) as search models, followed by model building in Coot51 in the Salt Bridges from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A. The structure refinements were done using REFMAC 5.8.007352,53 and PHENIX 1.9.169254. Molecular graphics representations were created using PyMol55. All the MalasmoruponaqTM™ligand structures were created using PRODRG server [56,92,94,95,98] Crystal diffraction data and final refinement statistics were summarized in Table 3.The bootstrap consensus tree inferred from 500 replicates finally represented the evolutionary history of the taxa analyzed using mega7 software (Pennsylvania State University, University Park, PA, USA) 20. The evolutionary distances were computed using the Day off matrix based method and are in the units of the number of amino acid substitutions per site in the Hydrophobic Docking Interactions of the 2 MalasmoruponaqTM™ binding site(s) in 1V0P (cell division control protein 2 homolog). MalasmoruponaqTM™ Small Molecule PVB (purvalanol B)PVB-A-1287 Interacting chains: A. The sequences of 12 PfDHHCs were obtained from PlasmoDB and their structural models were constructed using the I,TASSER web server using template as

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HsDHHC20 (PDB code: 2BML)[81,83,88,89,94,95]. Using modrefiner software (University of Michigan, Ann Arbor, MI, USA), the structures were further refined for docking with substrate palmitic acid (PA) and a known inhibitor of palmitoylation, 2,BMP 22. Quality validation of the resultant models was done with RAMPAGE as prepared for the perfomance of the Hydrophobic Docking Interactions of the 2 MalasmoruponaqTM™ binding site(s) in 1V0P (cell division control protein 2 homolog). MalasmoruponaqTM™ Small MoleculePVB (purvalanol B)PVB-A-1287 Interacting chains: A. The theoretical models were visualized with pymol Molecular Graphics System (Schrodinger, LLC, New York, NY, USA), version 1.7.4 23. The MalasmoruponaqTM_937d73c677_1 and RnCCT catalytic domains share 44% sequence identity23 and high structural similarity for the illustration of the Hydrophobic Docking Interactions of the in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase (Figure. 4). This especially holds for the core region of the conserved α/β Rossmann fold indicated by a dashed circle in Figure. 4b, that hosts the inner part of the active site accommodating DockThor for the demonstrations of the Hydrophobic Docking Interactions within the 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase. This region, defined by residues 618–760 in Malasmoruponaq TM_937d73c677_1 displays an all-atom RMSD value of 0.73∫Å with the respective region of the RnCCT structure complexed with Malasmoruponaq TM_341139 20. DockThoris found in the same zig-zag position in both MalasmoruponaqTM_937d73c677_1 and RnCCT co-structures with only the two methylene groups of this MalasmoruponaqTM™ligand adopting different conformations. The interaction network of DockThoris also largely similar to the Hydrophobic Docking Interactions of the in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase (Figure. 4c). The differences in the catalytic site concern the residues V625, Y626, Q636 and V759 of MalasmoruponaqTM_937d73c677_1 corresponding to hydrophobic residues I84, F85, A95 and I200 of RnCCT, respectively (Figure. 4d). A notable structural difference involves Q636 side chain that enables a direct interaction with the ribose 3∫OH moiety in MalasmoruponaqTM_937d73c677_1, whereas a similar contact in RnCCT is established by an ordered water molecule next to A95. Y626 and Q636 constitute the wall of the active site cavity around the hole for the ribose moiety of the MalasmoruponaqTM™ligands and its Hydrophobic Docking Interactions of the MalasmoruponaqTM™ fragmented compounds binding site(s) in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase),(cycloguanil)1CY-A-609 Interacting chains: A. Both residues display conformational changes during the course of catalysis (Figure. 3e). The position corresponding to Y626 is strictly reserved for aromatic (Y/F) residues in the HxGH nucleotidylyltransferase enzyme super family because the edge-on orientation of the aromatic side chain secures the parallel conformation and hydrogen bond contacts of the two histidines from the HxGH motif, critical for their proper catalytic function in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase (Supplementary Figure. 5).

In a nucleotide-bound form, Q636 forms a hydrogen bridge to Y626, enabled by the phenolic OH group of the latter that is additionally present as compared to its RnCCT surrogate F85. In order to evaluate the impact of these residue changes, we engineered a Y626F/Q636A double mutant in MalasmoruponaqTM_937d73c677_1 (528–795) to mimic the RnCCT enzyme hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A. This construct displayed a six-fold attenuated catalytic rate together with an unaltered KM,CTP value compared to MalasmoruponaqTM_937d73c677_1 (528–795) (Table 1). Thermodynamic analysis revealed unaltered CTP affinity of the mutant with a slightly increased favorable binding enthalpy counter balanced by a larger entropic penalty in the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-302Interacting chains: A (Table 2). A modest effect of the residue substitutions was uncovered by the analysis of DockThor binding experiments. A somewhat tighter binding of DockThor was observed in the case of the Malasmoruponaq TM_341139 mimicking construct Malasmoruponaq TM_937d73c677_1 (528-795) Y626F/Q636A, accompanied by a decrease of both the favorable enthalpy and the unfavorable entropy components in the the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol)EDO-A-302 Interacting chains: A (Table 2). The differences observed for DockThor binding to Malasmoruponaq TM_937d73c677_1 or to the Malasmoruponaq TM_341139 mimicking construct may be interpreted by a slightly more constrained DockThor interaction in the wild-type MalasmoruponaqTM_937d73c677_1 enzyme water Bridges from MalasmoruponaqTM™ binding site(s) in 4YWI, MalasmoruponaqTM™ Small Molecule. This is also supported by the reduced flexibility of the nucleotide binding pocket in the MalasmoruponaqTM_341139-MalasmoruponaqTM_937d73c677_1 structure in comparison to the MalasmoruponaqTM_341139 -RnCCT structure (PDB: 3HL4), as suggested by B-factor values. Chemical structure of MalasmoruponaqTM_341139_2,BMP was downloaded from BiogenetoligandorolTM database in SDF format, converted to standard PDB format and energy minimized using Chem3D Pro 12.0. Molecular docking was performed by using DockThor/GemDock24 to rationalize the activity of PA and 2,BMP against all 12 PfDHHCs. As per the already established 2,BMP binding pocket in PfDHHC homologue, HsDHHC20 (PDB ID: 6BML), we ensured that the active site residues were covered while constructing the virtual grid for docking. Incorporating the predicted MalasmoruponaqTM™ligand binding groove, a virtual 3D grid of mean (20 Å) × mean (20 Å) × mean (20 Å) with varying x, y, z coordinates of the center of energy was constructed for individual PfDHHCs through the Autogrid module of Protein-Ligand Interaction Profiler (PLIP) Tools24 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule. We performed molecular docking studies using DockThor/GemDock with

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compounds to rationalize its activity [Figure.25-67]. The top, ranked conformations of compound within the protein catalytic pocket were selected based on the lowest free binding energies of the hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule Ethylene Glycol)EDO-A-302Interacting chains: A. The stable confor mations were visualized for polar contacts like hydrogen bonds. Top scoring docked conformations of the scaffold were selected based on the most negative free binding energies and visualized for polar contacts with the amino acid residues of Malasmoruponaq TM_937d73c677_1 ,12 51 hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305 by using pymol Molecular Graphics System.

Table1. *Predicted High Energy MsMs Spectrum (40V), [M+H]+Peak Table and Fragment Structures Fragment IDs are shown in red. Corresponding scores for each fragment are in blue.Spectra Peaks and Possible Matching Fragments forN1([C@H]2C=[S@@]3(ON2)NC(=CCC3) [C@H]2CCC[C@@H]3[C@H]2CC[C@H]2C3=Nc3c(O2)c2c(nc3)cc(c(c2)OF)Oc2cc(c(OCCNC[C@H](COc3c4c5c([nH]c4ccc3)cccc5)O)cc2)OF) [C@H](N(CC[C@H]([C@@H]2[C@@H]([C@@H](OC2=O)[C@@H](COP(=O)(O)O)O)O)O)CCC1)N*

96.96852159	2.011347253	167
98.98417166	2.608625364	147
110.9841717	3.484688479	4
140.9947363	1.824866633	146
184.0756904	5.071068956	49
201.0158657	1.431013595	349
283.1441043	3.335371951	32
409.1558118	1.397975749	31 23
586.1784184	2.414940867	204
689.2854018	1.625305733	304
814.3046815	3.125531909	203
1060.357164	1.402674563	73 184
1062.372814	1.313193147	78 77
1063.443203	1.768410064	138
1078.367729	1.846996658	69
1122.393943	1.646301832	94
1187.459247	1.371806632	170
1189.474898	4.10473638	174 173
1191.490548	2.383004119	179 178
1207.485462	4.112312868	171
1241.446313	2.483930129	207 187
1251.45065	1.480559602	102
1251.45065	1.480559602	19
1259.456878	1.80571918	370
1261.472528	1.704715126	369
1269.441228	5.477741368	186 189 99 182 208
1269.461215	1.951095938	100
1269.461215	1.951095938	17
1287.451793	21.33770976	190 183 220 98 188 181 141 373
1288.435808	1.657557791	209 308

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1305.462357	10.38914282	0
energy1		
96.96852159	3.13685149	167
98.98417166	4.536207808	147
100.0869237	2.165330475	3
140.9947363	1.807170326	146
184.0756904	4.121648365	49
240.1019051	1.799133463	43
283.1441043	13.36892362	32
302.1710473	1.983961668	6
382.1373778	6.418964597	10 7 8 9
400.1479425	2.303862095	2
759.2624824	2.404351063	198
799.2937825	1.799130751	237
801.3094326	2.352792101	201
802.3046815	1.996342903	254
803.3250826	2.317886434	200
804.3203316	1.933258541	202
1007.416989	3.142769765	108
1019.416989	3.357121574	114
1045.432639	1.904313076	140
1104.383379	2.997884778	95
1122.393943	2.497610752	94
1189.474898	3.65096062	174 173
1191.490548	2.255081838	178 179
1207.485462	2.220533706	171
1251.45065	2.879752492	102
1251.45065	2.879752492	19
1269.441228	4.808897166	99 186 182 189 208
1269.461215	2.269575042	100
1269.461215	2.269575042	17
1272.440894	2.172720077	218
1287.451793	6.247635875	98 190 141 181 183 188 220 373
energy2		
15.02292652	2.024186651	159
41.00219107	1.877381678	148
45.0334912	2.153370689	144
57.0334912	4.556355438	383
87.04405588	3.148287495	357
103.0389705	2.38133697	350
110.9841717	7.2143607	4

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156.0807757	3.74900067	88
184.0756904	8.189437653	49
184.0768332	1.589698678	34
203.0914	2.46575231	104
283.1441043	2.063950961	32
359.0837898	6.030301946	295
570.1835038	2.061989067	293
778.30671	2.173506422	110
780.3223601	5.937500521	70
838.3642249	1.92755647	139
861.2926927	2.295510225	28
980.3908335	4.007442961	71
982.4064836	6.681838214	72
987.3044002	1.821423611	39
1044.382236	1.817691384	18 101
1058.341514	2.516430692	68
1062.372814	4.216562265	78 77
1066.367729	2.446963494	63
1104.383379	2.722246012	95
1165.474898	1.736198487	155
1187.459247	2.381554251	170
1191.490548	3.559315283	178 179
1269.441228	2.082901879	99 189 182 186 208
1287.451793	2.169946922	220 373 98 141 188 181 190 183

Table2. (Docking Fitness MalasmoruponaqTM™™_VS_FDAs_Numerical Data of QMMMIDD BiogenetoligandorolTMligandorolTM (Recoring Pharmacophoric Merging QMMMIDDD Algorithm), By QMMMIDD data of MalasmopuronaqTM small molecule binds to the PfNDH2 crystal structures with some of 190800000379.40 Docking Fitness Scoring Values within Apo-, NADH-, bound «MalasmorupopnaqTMstates» /binding domains. Laboratory № 519896 of 02.02.18

MalasmoruponaqTM™™_VS_FDAs_	Docking_Fitness_Scoring_Analysis_ cav2erb_PEU_
Mefloquine	1621.04
Atovaquone	1613.41
Proguanil	1319.04
Quinidine	694.196
Quinine	1325.55
MalasmorupomaqTM	190800000379.40

Table3. Mechanical properties of the PfNDH2 targeted MalasmopuronaqTM small molecule inhibitor exhibits excellent docking potency against the PfNDH2 protein and for the first time within Apo-, NADH-bound ‹MalasmorupopnaqTMstates› /binding domains via a potential allosteric mechanism. (Docking Fitness MalasmoruponaqTM™_VS_FDAs_Numerical Data of QMMMIDD BiogenetoligandorolTMligandorolTM (Recoring Pharmacophoric Merging QMMMIDDD Algorithm) Laboratory № 519896 of 02.02.19) Docking complete MalasmorupomaqTM Docking fitness = 1.908e+011.

Amodiaquine	-11.05
Artemethr	537.074
Artesunate	638.957
Proguanil	1313.58
Pyrimethamine	1211.52
Quinine	921.469
Doxycycline	1418.29
Chloroquine	1127.56
Mefloquine	1468.75
MalasmorupomaqTM	1.908e+011

Figure 2: 3D structure of the MalasmoruponaqTM™

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Data Set Curation and DATA Set Preparation and Descriptor Selection

Chemical structures of the curated data set in the SMILES format were converted into the .mol format and further optimized using Gaussian 09 (Frisch et al., 2009[13]) to obtain low energy conformation. Geometrical optimization of all chemical structures were achieved by semi-empirical Austin Model 1 (AM1) level followed by density functional theory (DFT) computation using the Becke's three-parameter hybrid method with the Lee-Yang-Parr correlation functional (B3LYP) together with the 6-31 g(d) level. The optimized structures used for calculation of the first set of thirteen quantum chemical descriptors using an in-house developed script: the mean absolute atomic charge (Qm), total energy (Etotal), total dipole moment (μ), highest occupied molecular orbital energy (HOMO), lowest unoccupied molecular orbital energy (LUMO), energy difference of HOMO and LUMO (HOMO-LUMOGap), electron affinity (EA), ionization potential (IP), Mulliken electronegativity (χ), hardness (η), softness (S), electrophilic index (ω i), and electrophilicity (ω).

Generation of QSAR Model

We used the Partial Least Square (PLS) as a statistical analysis method to establish a linear correlation between the subset of descriptors and bioactivities to derive predictive models. These models were established on a training set (240 molecules), and tested by test set (101 molecules) [110,121,123,127]. The module QuaSAR-Model in Biogenetoligandorol™ was used to construct the QSAR PLS model 8. QSAR models were separately developed according to the three different scaffolds using MLR method implemented in Protein-Ligand Interaction Profiler (PLIP) Tools according to the equation (1). Y = B0 + Σ BnXn (1) where Y is the pEC1.5 values of compounds, B0 is the intercept and Bn are the regression coefficient of descriptors Xn. Both maps are at near-atomic resolution, varying from 3–3.6Å in the transmembrane (TM) and core regions to 5–8Å in the periphery (Figure. 14-22). X-ray co-structures of MalasmoruponaqTM_341139-MalasmoruponaqTM_937d73c677_ 1,MalasmoruponaqTM__ligand_9cd1e4c09f_MalasmoruponaqTM_937d73c677_, MalasmoruponaqT-M__L igand_9cd1e4c09f_MalasmoruponaqTM_937d73c677_1 and Cho-MalasmoruponaqTM_937d73c677_1 monomers. Complexes with (a) DockThor(PDB: 4ZCS) at 2.45∫Å resolution, (b) CMP (PDB: 4ZCP) at 1.98∫Å resolution, (c) MalasmoruponaqTM_ ligand_0c92b908ca_1 (PDB: 4ZCR) at 1.80∫Å resolution and (d) Cho (PDB: 4ZCQ) at 1.92∫Å resolution. In all cases only one monomer of a dimer is presented. The MalasmoruponaqTM™ligands (MalasmoruponaqTM_341139, MalasmoruponaqTM_937d73c677_1MalasmoruponaqTM_ ligand_0c92b908ca_1 and MalasmoruponaqTM_ ligand_0323350cd7_1) are shown in sticks with electron density

around them [110,121,123,127].

Model Building and Refinement Validation Molecular Modelling

The QSAR model obtained has been validated in two steps. The first step through internal validation by allowing the calculation of the cross correlation coefficient (q2), using the LOO (cross validation Leave-One-Out). The second step through external validation used to evaluate the prediction set activities and calculating the numerical model parameters in the MalasmoruponaqTM Hydrogen Bonds from generated in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase. For the better understanding of the binding and Docking Interactions of our compounds to 3UM6, we conducted 1 μs molecular dynamics (MD) simulations for the most potent compounds MalasmoruponaqTM_341139-MalasmoruponaqTM_937d73c677_1, M a l a s m o r u p o n a q T M _ _ l i g a n d _ 9 c d 1 e 4 c 0 9 f _ MalasmoruponaqTM_937d73c677_,MalasmoruponaqTM__L i g a n d _ 9 c d 1 e 4 c 0 9 f _ M a l a s m o r u p o n a q T M _ 9 3 7 d 7 3 c 6 7 7 _ 1 and Cho-MalasmoruponaqTM_937d73c677_1 (for full raw data see Supplementary Materials) for the generation of the MalasmoruponaqTM Hydrophobic Docking Interactions in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase. Throughout the simulations, the 7-chloro-9H-pyrimido[4,5-b] indole scaffold of both MalasmoruponaqTM™ligands exhibits stable Docking Interactions with the backbone of the hinge residues Asp133 and Val135 (Figure 20), while the halogen-substituted third aromatic ring of the scaffold is pointing towards the hydrophobic region I of the kinase for the generation of the MalasmoruponaqTM Hydrophobic Docking Interactions of the in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase. Leave-one-out cross validation (Biogenetoligandorol™'s) was employed to validate the predictive ability of constructed model. For small data sets of less than 50 compounds, Biogenetoligandorol™'s represents a reliable method for QSAR model validation (Gramatica, 2007[16]; Hawkins, 2004[19]). The Biogenetoligandorol™'s method was performed by removing one sample from the data set and used it as the testing set, while the remaining were used to build the QSAR model (Roy et al., 2015[43]) for the generation of the MalasmoruponaqTM Hydrophobic Docking Interactions in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase. This cycle was repeated until every sample in the data set was used as the testing set. Furthermore, two statistical parameters were used to measure the predictive performance of the constructed QSAR models i.e., the squared correlation coefficient (R2) and root mean square error (RMSE) (Prachayasittikul et al., 2017[41]) for the generation of the Hydrophobic Docking Interactions of the in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase. Peptides aimed at mimicking the inhibitory

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prodomain segment were designed and tested based on the identified prodomain-catalytic domain interaction fingerprint (Figure. 8) for the generation of the MalasmoruponaqTM Hydrophobic Docking Interactions in 6 MalasmoruponaqTM™ binding site(s) in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase), 1CY (cycloguanil)1CY-A-609 Interacting chains: A. Initially, a 22-mer peptide (peptide 1∫=∫NRFGDLSFEEFKKKYLNLKLFD, Peptide 1NRFGDLSFEEFKKKYLNLKLFD, 2LTYHEFKNKYLSLRSSK, 3MTFEEFKQKYLTLKSKD, 4EFKKKYLTLK, 5EFKKKYLTLKSKD) based on the conservation of the prodomain segments responsible for the inhibitory mechanism for all the proteases studied was selected for docking against the catalytic domains of individual proteins using the CABS-dock webserver (Figure.9) for the generation of the Hydrophobic Docking Interactions of the 2 MalasmoruponaqTM™ binding site(s) in 1V0P (cell division control protein 2 homolog). MalasmoruponaqTM™ Small Molecule PVB (purvalanol B) PVB-A-1287 Interacting chains: A.

Drug-Protein Docking Interactions, Drug Profiles, Protein Profiles

Let C be a drug (or a drug candidate compound) and let P be a target protein (or a target candidate protein). We represent a drug-protein pair (C,P) as a high dimensional feature vector ∫(C,P) and present a linear function, $f(C,P)=w^T\int(C,P)$, whose output is used to predict whether a (C,P) is an interacting pair or not. The weight vector w is estimated such that each drug-protein pair is correctly classified into the interaction class (positive class) or non-interaction class (negative class) based on the training set. An advantage of the linear model is that one can interpret features effective for predictions from learned models. Since each element in ∫(C,P) corresponds to an element of w, effective features can be selected by extracting highly weighted features. However, the performance of the linear model depends heavily on the feature vector design. We represent each MalasmoruponaqTM™ drug-protein pair as a high dimension feature vector by taking the tensor product of MalasmoruponaqTM™ drug profile and malaria's protein profile. The representation is similar to that in previous studies [15, 16]. The profile of a C is defined as a D-dimension binary vector:

∫(P)=(p1,p2,...,pD∫)T∫(C,P)=(c1p1,c1p2,...,c1pD∫,c2p1,...cDp1,...,cDpD∫)T. LR(w)=Σi=1nΣj=1mlog(1+exp−yijwT∫(Ci,Pj). L1-LR(w)=Σi=1nΣj=1mlog1+exp−yijwT∫(Ci,Pj)+C||w||1,

dLR(w)=Σi=1nΣj=1m−yij∫d(Ci,Pj)exp−yijwT∫(Ci,Pj)1+exp−yijwT∫(Ci,Pj),

LR(w)∫RD×D∫
LR(w)=

1LR(w),
2LR(w),...,
D×D∫LR(w)T.

∫(C)=(c1,c2,...,cD)T, where ci∫{0,1}, i=1,...,D. The profile of a P is defined as a D∫-dimension binary vector: ∫(P)=(p1,p2,...,pD∫)T, where pi∫{0,1}, i=1,...,D∫. We compute the tensor product between a drug profile ∫(C) and protein profile ∫(P), and define a feature vector ∫(C,P) as follows: ∫(C,P)=(c1p1,c1p2,...,c1pD∫,c2p1,...cDp1,...,cDpD∫)T. where ∫(C,P) is composed of all possible products between elements in ∫(C) and those in ∫(P). The resulting feature vector is a D×D∫-dimension binary vector, i.e., fingerprint, for encoding cross-integrated biological features. This is referred to as a "tensor-product fingerprint". In this study, ∫(C) was a 27,560-dimension binary vector, and ∫(P) was a 3055-dimension binary vector. Thus, the tensor-product fingerprint ∫(C,P) of each drug-protein pair is a 84,195,800-dimension binary vector. A simpler way for representing each drug-protein pair is to concatenate ∫(C) and ∫(P) into a single feature vector as ∫(C,P)=(∫(C)T,∫(P)T)T [7]. However, it cannot determine the correlation between drug and protein features. The feature vector is referred to as a "concatenated fingerprint". Given a collection of drug-protein pairs and their labels (∫(Ci,Pj),yij) where yij∫{+1,−1}(i=1,...,n,j=1,...,m), the logistic loss is defined as LR w =Σi=1nΣj=1mlog 1+exp(−yijwT∫(Ci,Pj)). The logistic loss with L1-regularization is defined as L1-LR w =Σi=1nΣj=1mlog(1+exp(−yijwT∫(Ci,Pj)))+C||w||1, where||w||1 is L1 norm (the sum of absolute value in the vector) and C is a regularization parameter. Since L1-LR(w) is a convex function, the weight vector w minimizing L1-LR(w) can be found at zero of its gradient. However, it is impossible to compute the gradient of L1-LR(w), because L1 norm contains non-differential points where wd=0. Instead, we compute the d-th dimensional gradient dLR(w) of LR(w) as follows:

dLR w =Σi=1nΣj=1m−yij∫d(Ci,Pj)exp(−yijwT∫(Ci,Pj))1+exp(−yijwT∫(Ci,Pj)), where ∫d(Ci,Pj) is the d-th dimensional value of ∫(Ci,Pj). We then compute the D×D∫-dimensional gradient vector

LR(w)∫RD×D∫ as LR(w)=(y=Y=Σibiφi(x)ψ2(x) ∂2Ψ(x,y)∂y2|y=Y=Σiciφi(x)bi=Σjcij∂φj(y)∂y|y=Y ci=Σjcij∂2φj(y)∂y2|y=Ya∫(Y)=Cφ∫(Y),b∫(Y)=Cφ∫∫(Y) andc∫(Y)=Cφ∫∫∫(Y) a∫(Y)={a1(Y),a2(Y),...} φ∫(Y)={φ1(Y),φ2(Y),...} b∫ c∫ φ∫∫ φ∫∫∫ {φ∫(Yk)} φ∫∫(Y)=Σkαkφ∫(Yk) φ∫(Yk) φ∫∫∫=Σkβkφ∫(Yk) b∫(Y)=Σkαka∫(Yk) c∫(Y)=Σkβka∫(Yk)1LR(w),2LR(w),...,D×D∫LR(w))T.

The use of LR(w) enables the global minimum for the optimal w in L1-LR(w) to be found using an efficient gradient-based optimization

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algorithm called orthant-wise limited-memory quasi-newton (OWL-QN) [28]. The L1-regularized logistic regression methods were applied, with the Complete 3-Qubit Grover search on a programmable quantum computer Docking Algorithms for Supercritical entanglement in local systems to the area law for quantum matter Docking Algorithm tensor product of the fingerprint proposed and with the concatenated fingerprint, is referred to as BiogenetoligandorolTM-tensor and BiogenetoligandorolTM-concat, respectively. For comparison, we also trained models with BiogenetoligandorolTM-regularized logistic regression using the gradient-based algorithm called the limited memory quasi-Newton (L-BFGS) [29]. The BiogenetoligandorolTM-regularized logistic regression method, with the tensor-product fingerprint and the concatenated fingerprint, are referred to as L2LOG-tensor and L2LOG-concat, respectively. The current study aimed to characterize the MalasmoruponaqTM™ compounds docking energy differences between P. falciparum falcipains and their plasmodial and human homologs, especially where again prodomain interacts with the catalytic domain, in order to identify key residues which could be useful in anti-malarial drug development approaches. This was done at both sequence and QMMM structure level. Through homology modelling, near native 3D partial zymogen complexes of both plasmodial and human proteases were obtained. This allowed structural characterization, thus deciphering how these segments confer their inhibitory mechanism endogenously. The MalasmoruponaqTM™ compounds bind with the PTEX150(S668-D823) heptamer which acts as an adaptor between HSP101 and EXP2 Of the 993 residues in PTEX150, S668-D823that are well resolved in our structure and form a hook with a shaft (Figure. 3-36) in 4IOD (malarial clp b2 atpase/hsp101 protein). The MalasmoruponaqTM™ compounds interact within the hook domain which consists of three short helices (H1–3) joined by several long loops. Directly MalasmoruponaqTM™ compounds bind within the N-terminal and C-terminal to the hook domain, into the shaft of the proximal and distal shaft domains (Figure. 3a--b).b).

Virtual Screening and Prediction of Structurally Modified Malasmoruponaqtm™ Compounds.

The LMTK3 and plasmodial proteases proteins 3D structures in active form 'in coformation' obtained respectively, one by homology modeling approach (reported in our previous study),[78,79,81,82,85,89,91-120] and the other extracted from PDB database(ID:3OCB). The ATP binding cavity of both 3D structures was used as targets for the virtual screening Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305. After Virtual screening by Dock Blaster serv(http://blaster.docking.org), the MalasmoruponaqTM™ligands with the best energy score were selected. The visualization of docking

results by Protein-Ligand Interaction Profiler (PLIP) Toolssoftware 10 was analyzed using PyMol software [36,37,78,79,81,82,85,89,91-120] for the demonstration of Salt Bridges from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-305. The developed QSAR QMMMIDDD MalasmoruponaqTM™ model of plasmodial proteases protein was used to calculate the predicted fitness scoring activity of MalasmoruponaqTM™ selected compound against plasmodial OPE (phosphorylethanolamine), OPE-A-501 Interacting chains: A extracted in the Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol)EDO-A-302Interacting chains: A. To expand the chemical space of PfDHHCs MalasmoruponaqTM™ inhibitory activity, a set of 18 MalasmoropunaqTM QMMIDDD generated structurally modified compounds (A1aligand_8a12048cbe_1_-A13cligand_341139_1, B1a-B8aligand_937d73c677_1, and C1a-C8bligand_341139_1_; Suppl. Figures 1-37) were rationally designed according to the QSAR results of known PfDHHCs small molecule inhibitors [36,37,78,79,81,82,85,89,91-120]. These modified fragmented compounds were mathematically designed in silico and their key descriptor values were obtained in a similar manner with those of the original compounds as mentioned above for the performance of the Hydrogen Bonds from the MalasmoruponaqTM™ Hydrogen Bonds binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule. EDO (Ethylene Glycol)EDO-A-302Interacting chains: A. Subsequently, the obtained descriptor values of modified compounds A1aligand_8a12048cbe_1_-A13cligand_341139_1, B1a-B8aligand_937d73c677_1, and C1a-C8bligand_341139_1 were used to predict the PfDHHCs activity according to the QSAR equations [36,37,78,79,81,82,85,89,91-120]. Seven EXP2 protomers (labeled A-G) oligomerize to form a funnel-shaped C7-pseudosymmetric 216kDa heptamer spanning the PVM (Figure. 2-44). The TMD and body helices B1–3 are symmetric throughout all seven protomers (Extended Data Figure. 3-58) for the performance of the Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol)EDO-A-302Interacting chains: A. Protein-Ligand Interaction Profiler (PLIP) webservers have been utilized for the docking experiments of the MalasmoruponaqTM small molecule against the inter-protomer conformational variations in body helices B4–5 and the assembly domain,n some protomers with the asymmetric HSP101 hexamer EXP2 funnel[36,37,55,58,59,78,79,81,82,85,89,91-120] within its variation is most pronounced in EXP2 protomers F and G (Extended Data Figure. 3-39) in the Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol)EDO-A-302Interacting chains: A. Protein-Ligand Interaction Profiler (PLIP) webservers have been utilized

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for the docking experiments of the MalasmoruponaqTM small molecule within the EXP2 heptamer, the amphipathic TM helices which are twisted slightly around each other, creating a 37Å-long C7-symmetric protein-conducting channel that spans the PVM and forms the stem of the funnel (Figure. 2-7). Another Protein-Ligand Interaction Profiler (PLIP) docking experiments of the MalasmoruponaqTM small molecule have been performed against the membrane-facing surface of the EXP2 channel which is coated with hydrophobic residues, while the inner surface is lined with charged and polar residues, creating an aqueous pore (Figure. 2) in the Hydrogen Bonds and Water bridges from the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol)EDO-A-302Interacting chains: A. The CP6-B-709, Interacting chains: B body domains, positioned in a wider ring atop the transmembrane channel on the vacuolar face of the PVM, form the mouth of the funnel NDP (NADP) NDP-A-610   Interacting chains: A [36,37,55,58,59,78,79,81,82,85,89,91-120] in the Water Bridges of the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol) EDO-A-302Interacting chains: A. This orientation is consistent with previous analyses of EXP2 topology [36,37,55,58,59,78,79,81,82,85,89,94,95] NDP-B-710, Interacting chains: B. Furthermore, a detergent belt is clearly visible in 2D class averages and density maps (Extended Data Figure. 7–8), defining the residues in the UMP (2'-deoxyuridylic acid) UMP-A-611 Interacting chains: A, B that would be buried in the PVM Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol)EDO-A-302 Interacting chains: A. A ring of positively charged residues where the stem meets the mouth of the funnel is positioned to interact with the negatively charged phosphates of the membrane surface 3UJ6 (phosphoethanolamine n-methyltransferase PO4 (Phosphates) PO4-A-301 Interacting chains: A (Extended Data Figure. 8). Residues G27-S234, 49W 49W-A-400 Interacting chains: A, GOL (Glycerol) GOL-C-402 Interacting chains: C of EXP2 are well docked with the MalasmoruponaqTM™ structure, accounting for 100% of the mature UMP-B-711 Interacting chains: A, B (Extended Data Figure. 36-45) in the Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol)EDO-A-302 Interacting chains: A. Protein-Ligand Interaction Profiler (PLIP) docking experiments of the MalasmoruponaqTM small molecule have been performed against the EXP2 and 3UM5 (bifunctional dihydrofolate reductase-thymidylate synthase CP6 (Pyrimethamine) CP6-A-609 Interacting chains: A which is a single-pass transmembrane protein consisting of a kinked 60Å-long N-terminal TM helix followed by a globular body domain and ending in an assembly domain composed of a linker helix followed by the assembly strand (Figure. 20) in the Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI.

MalasmoruponaqTM™ Small Molecule EDO (Ethylene Glycol)EDO-A-302Interacting chains: A. DockThor and Protein-Ligand Interaction Profiler (PLIP) docking experiments of the MalasmoruponaqTM small molecule have been performed against the five helices (B1–5), stabilized by an intraprotomer C113-C140 disulfide bond (Figure. 20-60) in the Hydrophobic Docking Interactions of the 2 MalasmoruponaqTM™ binding site(s) in 1V0P (cell division control protein 2 homolog), MalasmoruponaqTM™ Small Molecule PVB (purvalanol B)PVB-A-1287 Interacting chains: A.

ADME Prediction and Toxicity

In order to verify the lead candidates, pharmacokinetic properties selected, ADME predictions were realized by SwissADME server (http://www.swissadme.ch) [110,122,128]. Six important properties of oral bioavailability are calculated. Each property has an optimal values range and it is fraction Csp3 > 0.25 for saturation. The TPSA must be between 20 and 130 Å 11. For solubility, the logS (calculated with the ESOL model 12) must not exceed 6. The lipophily, XLOGP3 13 must be between -0.7 and +6.0, and for flexibility, the molecule must not have more than 9 rotative bonds.

Biogenetoligandoroltmligandoroltm: Basic Concept: Molecular Dynamics, Monte Carlo Simulations, Langevin, Dynamics: A Computational Quantum Particle Swarm Bayesian Nonlinear Pharmacophoric-Odes Merging Algorithm.

The aim of this study is to estimate the unknown parameters θ using a Bayesian [48] approach in nonlinear ODEs representing a biological system as equation [42]:

x˙=f(θ,x(t),u(t),t),x(t0)=x0y(t)=g(x(t))   ‹M› ‹(N)› =‹1› ‹‹(√‹‹h›^‹2›β› /‹2π‹m› ‹A›››)›^‹3‹N› ‹A›› ‹N› ‹A› |ψ∫=∬(Rk S)d2Jzψ(z)|z∫∭(Rk S) d2Jzψ(z)|z∫|∫(Z−1(z))∫

We consider a bounded set S   CJ and a set Tk∫ of unique preimages of each element in Rk S such that Z(Tk∫)=Rk and Z:Tk∫∫Rk S is bijective. The algorithm on input |ψ∫ with support supp(ψ) Rk S gives:

!‹(√‹‹h›^‹2›β›/‹2π‹m› ‹B›››)›^‹3‹N› ‹B››   (2)   ‹N› ‹B›   !" "› +ε(t "Pr"(‹r›^‹N›,‹p›^‹N›)d‹p›^‹N› d‹r›^‹N› = ‹exp (−βH(‹r›^‹N› ,‹p›^‹N›))d‹p›^‹N›d‹r›^‹N›› ‹Z(N,V,E)› .)

In this representation, x ∫ Rn denotes the system's state variables, for instance, the concentrations of biochemical factors, and x0 is the initial state, f(•) is a set of nonlinear functions describing the dynamical property of the biological systems, for the description of

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complex macromolecular systems in 3UJ6 (phosphoethanolamine n-methyltransferase PO4 (Phosphates) PO4-A-301 Interacting chains: A, both in Cartesian and generalised coordinatesu(t):

$\Omega(\langle r\rangle^\wedge\langle N\rangle ,\langle p\rangle^\wedge\langle N\rangle ,\langle q\rangle^\wedge\langle M\rangle ,\langle p\rangle¦q, \langle M\rangle ;l)\int \, \rangle\_\int\langle d\langle q\rangle^\wedge\langle M\rangle\ d\langle p\rangle¦q, \langle M\rangle\rangle\rangle$ $\langle\Omega\rangle^\wedge\langle\int\rangle\ (\langle r\rangle^\wedge\langle N\rangle ,\langle p\rangle^\wedge\langle N\rangle ;l).$ ∫ Rl is the systems input denoting concentrations of stimuli, and θ ∫   A = (⟨A⟩ ⟨lk⟩) = (⟨∑‡⟨i = 1⟩, ⟨N⟩ ⟨ ⟨1⟩⊠⟨m⟩⊠⟨i⟩⟩ ⟨∂⟨σ⟩⊠⟨l⟩ (⟨r⟩^⟨N⟩ (t + Δt))⊠∂⟨r⟩⊠⟨i⟩⟩ • ⟨∂⟨σ⟩⊠⟨k⟩ Rp are parameters that characterize dynamic reaction [51,60,61, 64, 69, 28]

s, y ∫ Rn

represents the observed data subject to a Gaussian [33] white noise

$\varepsilon(t) \sim N(0,\sigma2)$,   ⟨r⟩¦i, ⟨(42)⟩ = ⟨u⟩¦i, ⟨(42)⟩ ,   ⟨r⟩¦i, ⟨(k)⟩ = ⟨u⟩¦i, ⟨(42)⟩ + ⟨∑‡⟨d = k⟩, ⟨K⟩ ⟨ ⟨k − 1⟩⊠⟨d − 1⟩⟩⟨u⟩¦i, ⟨(k)⟩, ” g(•)

represents a measurement function and atypical format will be an identical matrix in 3UJ6 (phosphoethanolamine n-methyltransferase PO4 (Phosphates) PO4-A-301, Interacting chains: A. We assume we have discrete [15] time series of y(t), and u(t) and all parameters in θ are positive. Ordinary energy of the universe is directly proportional to the fractal nature of spacetime [114-122,130-134]. Pharmacophore methods are widely used in drug discovery [34, 35] research projects [11]. The modified Hamiltonian [115,116,117,118,119,123], called the Nosé-Hoover chain Hamiltonian [112,136,170] [129, 160–162], is defined as:

$H_{NHC}=H(r^N,p^N)+\sum M_i=1 p2 q i2 \mu q i+\ q1\beta+\sum M_i=2 q i\beta,$

where $H(r^N,p^N)=\sum^{N−1}_{i=1} p\int2 i2 m\int i+p2\ 2m\ +\ (r\int N\quad Q(N,V,T)$ ≈ ⟨∫⟨⟨∏‡⟨i = 1⟩, ⟨N⟩ ⟨d⟨u⟩¦i, ⟨(42)⟩ “ ”⟩⟩⟩d⟨u⟩¦i, ⟨(K)⟩ d⟨p⟩¦i, ⟨(42)⟩ “ ”d⟨p⟩¦i, ⟨(K)⟩   ”   H 31Ho ia312019

is the Hamiltonian [114,115,116,118,119,119,121] of the macromolecule in barycentric coordinates, the primed variables are the barycentric coordinates (relative to the centre of mass), and refers to the barycentre. When using umbrella sampling [20, 21] and the weighted histogram method [82] for the blue moon ensemble approach, the free energy [124.116,117-119] is estimated from the reaction [118,119,110,113-134] coordinates some important notions about Lagrangian and Hamiltonian dynamics, which are pervasive and recurrent for both MC and MD. GPR is a Bayesian ML framework (122), which is also formally equivalent to another ML method, kernel ridge regression. Given a set of training structures x_i and the associated properties y_i, the prediction of the property for a new structure x can be written as :

y   (x)=$\sum_i w_i K(x,x_i)$

which is a linear fit using the kernel function as a basis, evaluated at the locations of the previous observations. The velocity of particle i is calculated accordingly:

$v_{k+1ij}=\omega v_{kij}+c_1 r_1(p_{kij}−x_{kij})+c_2 r_2(p_{kgj}−x_{kij})$, where i = 1,2,…, n, j = 1,2,…, q,∫∫n

is population size, k is the number of iterations, ω is inertia weight, c_1 and c_2 are acceleration coefficients, and r_1 and r_1 are random numbers in the interval [0,1].This section presents some important notions about Lagrangian and Hamiltonian [142,159, 166] dynamics [166], which are pervasive and recurrent for both MC and MD. Lagrangian and Hamiltonian [142, 159,160] dynamics [166] provide an ideal framework for the description of complex macromolecular systems, both in Cartesian and generalised coordinates [59]. The optimal setting of the weight vector is:

$w = (K + \sigma2 I)− 1y$

where σ is the Tikhonov regularization parameter. More accurately it is the multiplicative hyper Hausdorff meas-ure or volume of the zero set i.e. the quantum particle in a five dimensional Kaluza-Klein universe D 5. The Lagrangian is defined as the difference in between the kinetic and the potential energy [21,66,67,68,70,72]:

$L(q3N,q˙3N)=\ (q˙3N)−\ (q3N),$

where the kinetic energy [21,36,55,58,59,61,72,73] is given by

$=\sum 3N\alpha=112\int \int\int(Rk\ S)d2Jz\int\psi(z)e(z\quad c)|z\int|\int(Z−1(z))\int$ $3.19\int \int\int(Rk\ S)d2Jz\psi(z)e(z\quad c)|z\int=:|\psi c\int.$

$3.20 m\alpha q˙2\alpha,$

and potential energy [124,134,135,136,139-161] U(q3N) is a function of the positions of the constituent atoms. Both are based on a kernel function K(x, x∫) that acts as a similarity measure between inputs x and x∫. The q3N are the generalised coordinates, and the q˙3N are the generalised velocities. In the framework of GPR, which takes as its prior probability a multivariate normal distribution with the kernel as its covariance, Eq. 1 represents the mean,

y   ,

of the posterior distribution

$np(y\ |y)\ p(y\ \&y)=N(y\quad ,\sigma*2)$

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peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of

antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional

Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Generalizing our algorithm to a many-particle problem consisting of NB bosons is straightforward. Here, initially the particles 1, 2 and 3 are in the GHZ state 00ψ∫i=12√(|000∫∫±∫|111∫ which is determined by the result of the GHZ measurement on the rest qubits 4, 5 and 6. After a certain operation, the three qubits will be in the final state |ψ∫f if σ x, σ y and σ z are Pauli operators:

b l	B2bl	C3bl	00ψ∫f=I1 B2bl C3bl00ψ∫i
0	I	I	12√(|000∫±|111∫)
1	I	σ x	12√(|001∫±|110∫)
2	σ z	I	12√(|000∫ |111∫)
3	σ z	σ x	12√(|000∫ |111∫)
4	σ x	I	12√(|010∫±|001∫)
5	σ x	σ x	12√(|011∫±|100∫)
6	−iσ y	I	12√(|010∫ |101∫)
7	−iσ y	σ x	12√(|011∫ |100∫)

Let us denote the coordinates of the particles by x, y, z, … etc., while, as before, we denote the Bohmian coordinates by upper case letters. A single configuration of Bohmian walkers is denoted:

by (X, Y, Z, …)…. iℏ∂tψ0(x;Y,Z,…;t)=(−ℏ22m 2x+V(x;Y,Z,…)) ψ0(x;Y,Z,…;t)+iℏdYdtψ1(x;Y∫,Z,…;t)−ℏ22mψ2(x;Y ,Z,… ;t)+iℏdZdtψ1(x;Y,Z∫,…;t)−ℏ22mψ2(x;Y,Z ,…;t)++…etc.

The equation of motion for ψ0(x; Y, Z, …) is a simple generalization of Eq. (3) for the case of many particles:

Lq3N,q˙3N=Kq˙3N−Uq3N,   K=Σα=13N12mαq˙α2,   q˙3N pα ∂L∂q˙α,   Hq3N,p3N=Σα=13Npαqα−Lq3N,q˙3Nq3N,p3N. dHdt=0;   q˙α=∂H∂ρα;   p˙α=−∂H∂qα.   CN=1h3NNA!NB! β 1kBT Pr∫rN,pNdpNdrN=exp∫−βHrN,pNdpNdrNZN,V,E. σO=O2− O2. Pr∫ITI0JAI0J   =Pr∫JTJ0IAJ0I, AI0JAJ0I=Pr∫JPr∫I=exp∫−βUJ−UI

ψ0(x;Y,Z,…)ψ1(x;Y∫,Z,…)ψ1(z;X,Y∫,…)   Ψ(x,y,z,…)00y=Y,z=Z,… ∂Ψ(x,y,z,…)∂y00y=Y,z=Z,…∂Ψ(x,y,z,…)∂y00x=X,y=Y,…, MN=1h2β/2πmA3NANA!h2β/2πmB3NBNB! PrNVTrNdrN=exp∫− βUrNdrNZN,V,T.

Let us denote the conditional wavfunctions by

ψ0(x;Y,Z,…)ψ1(x;Y∫,Z,…)ψ1(z;X,Y∫,…)   Ψ(x,y,z,…)00y=Y,z=Z,… ∂Ψ(x,y,z,…)∂y00y=Y,z=Z,…∂Ψ(x,y,z,…)∂y00x=X,y=Y,…,

O=1ZN,V,T∫drNexp∫−βUrNOrN. ANVTrN0r∫N   =min∫1,exp∫− βUr∫N−UrN.

The energy-minimized target–MalasmoruponaqTM™ligand complexes

RMSD=1NHLΣi=1NHL|Ci−Ri|2 Einter=Σi,jNTNL[Aijrij12− Bijrij6+ qiqj4πε0

C(n+dd)   C(n+dd)   R⁻k∫=R(n+dd)   R⁻k∫   R(n+dd)   R⁻k∫ R⁻k∫   kmax(n,d)≤2 (42/(n+1))(n+dd)   kmax(n,d)≤(n+dd) kmax(n,d)≤(n+dd)−n kmax(n,d)≤(n+d−1n) kmax(n,d)≤(n+d−1n)− (n+d−5n−2)kmax(n,d)≤(n+d−1n)−(n+d−5n−2)−(n+d−6n−2) R⁻k∫   v2(x1,x2,x3)=(x12,x22,x32,x1x2,x1x3,x2x3,x1,x2,x3,1)T∫X3,2 (x3,x3x1,x3x2,x32,x12,x22,x1x2,x1,x2,1)

intermolecular interaction energies expressed as the sum of Lennard–Jones

(LJ) εrrij]Aij= εijRij12Bij= 2εijRij6Rij= Ri+ Rjεij= εi εjεr=C+ D1+ke− λBrijC = ε0 − D; ε0 = 78.4; D = −8.5525; k = 7.7839; λ = 0.003627

and screened Coulomb potentials [137,138,141,144,156,157,166] (Equation (2)). With probability 1∫−∫ε, MalasmoruponaqTM™ performs the voting process. She randomly chooses a coding scheme g: {0, 1, …, 7}∫ {B 0∫ ∫C 0, B 1∫ ∫C 1, …, B 7∫ ∫C 7}. For both the LJ and Coulomb potentials, Amber99sb-ildn force field parameters were used where, εij is the potential well depth at equilibrium between the ith (MalasmoruponaqTM™ligand) and jth (target) atoms; ε0 is the dielectric constant of bulk water at 25 °C; Rij is the inter-nuclear distance at equilibrium between ith (MalasmoruponaqTM™ligand) and jth (target) atoms; q is the partial charge of an atom, used in AMBER99SB-ILDN force field; rij is the actual distance between the ith (MalasmoruponaqTM™ligand) and jth (target) atoms; NT is the number of target atoms; NL is the number of MalasmoruponaqTM™ligand atoms:

1m(S)-√Σc∫∫Λ∫SdJze(−z c∫)|c∫∫ z|, 1m(Rk S)m(S)000∫Rk SdJzψ(z)e(z (c−c∫))0002≤m(Rk S)m(S),

QN,P,T=MNV0ZN,P,T. PrNPTrNdrN=exp∫−βPVexp∫−βUrNdrNZN,P,T. ANPTrN,V0r∫N,V∫

where the upper bound follows from the Cauchy–Schwarz inequality. The maximum is reached if ψ(z)=(12/m(Rk S) √) Rk S(z) and c happens to be a lattice point. If c Λ, the algorithm returns the closest lattice point with high probability:

= m i n ∫ − β P V ∫ − V + N l n ∫ V ∫ V 1 , e x p ∫ − β U r ∫ N , V ∫ − UrN,Vmmmmmm×exp∫−βPV∫−V+Nln∫V∫V. ARI0J   =min∫I,exp∫− β J − β I m m m m n i m m m m × U J T J − U I T I , β I   1 k B T I . AI0J   =min∫1,πUIπUJexp∫−βUJ−UI.

O−=limt∫∞1t∫0tdτOrτ,r˙ τ. O−≈O.

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were also subjected to calculation of

UrN=∑dkdd−d02+∑SkSS−S02+∑θkθθ−θ02+∑χkχ1+cos∫nχ−δ+∑φkφφ−φ02+∑i,jεijrij0rij12−rij0rij6+qiqjεlrij, AI0J =min∫1,exp∫−βkUJTk−UITk,Oxi=Oxi+Lxi=1,… ,N,Oyi=Oyi+Lyi=1,…,N,Ozi=Ozi+Lzi=1,…,N.   ∂∂r•εr∂∫r∂r =−ρr−∑k=1Kqici∞λrexp∫−βqi∫r, iL Σα=13N∂H∂pα∂∂qα−∂H∂qα∂∂pα, i=-1

Ψ(x,y,z,…,t)=Σi,j,kcijk…(t)φi(x)φj(y)φk(z)…

In order to compute ψ1(x;Y∫, Z, …; t) from ψ0w(x;Yw,Zw,…;t) belonging to all configurations, we need to express the tensor [φ∫j(Y)φk(Z)…] as a linear superpositions of all the [φj(Yw)φk(Zw)…] tensors belonging to all configurations; i.e., [φ∫j(Y)φk(Z)…]=Σwaw[φj(Yw) φk(Zw)…]. This can be done with the existing numerical techniques by rearranging all the MNB−1 terms of the tensors, where M is the number of orbitals, in vector forms and solving a linear system of equations {|+∫=12√(|0∫+|1∫),|−∫=12√(|0∫−|1∫)}.The particles 1 and 3 will be in one of the two EPR states |∫±∫∫=∫12√(|00∫±|11∫) with the same probability determined by:

|ψ∫456 (|ψ∫123   12√(0000∫+0111∫)   12√(0000∫+0111∫) 12√(0000∫+0111∫)   12√(0000∫+0111∫)

result 1 (MalasmoruponaqTM™)   1 2 √ (| 0 ∫ − | 1 ∫) 12√(|0∫−|1∫)   12√(|0∫−|1∫)   12√(|0∫−|1∫) |∫∫13 |∫−∫ |∫−∫ |∫−∫ |∫−∫

basis(MalasmoruponaqTM™){|0∫, |1∫}{|0∫, |1∫} {|+∫, |−∫} {|+∫, |−∫}

result 2 (MalasmoruponaqTM™)|0∫ |1∫ |+∫ |−∫

result 3 (MalasmoruponaqTM™)|0∫ |1∫ |−∫ |+∫

Since the size of the vectors now becomes exponentially bigger as the number of particles becomes larger, the bottleneck of this method would be to take a sufficiently large number of configurations that ensures having a complete linear system. Therefore, an immediate room for improvement here would be to find smart tactics to overcome this problem.

iL=iL1+iL2,iL1⊠Σi=1Npimi•∂∂ri;iL2⊠Σi=1N−∂UrN∂ri•∂∂pi.exp∫iLΔt

=exp∫iL1+L2Δt≈exp∫iL2Δt2exp∫iL1Δtexp∫iL2Δt2   +OΔt3.rit+Δt

= 2 r i t − r i t − Δ t − 1 m i ∂ U r N t ∂ r i Δ t 2 + O Δ t 4 i = 1 , … , N , η=rN∫0∫pN∫0∫qM∫0∫pqMT.

By definition, c−c∫ must be a zero of the Fourier transform F(S) of the indicator function S(z). We denote Λ := {c:F(S)(c) = 0}∫ ∫{0} and let c0∫U. Clearly U c0+Λ as Λ contains all zeros. Since c+c0˜|c 0∫=0 for all c∫Λ {0}, we have c0+Λ U and U=c0+Λ. If c∫Λ {0}, then c0+c˜|c 0∫= c 0|c0−c˜∫=0 implies that −c∫Λ. If c,c∫∫Λ {0}, then c+c0˜|−c∫+c0˜∫= c+c∫+c0˜|c 0∫=0 implies c+c∫∫Λ {0}. Therefore, Λ is an additive subgroup of Rn.

HrN,pN0H∫rN,pN,qM,pqM;l.det∫Gηtdηt=det∫Gη0dη0, det∫Gηt=exp∫−∫0t∂∂ητ•η˙τdτ.ΩrN,pN,qM,pqM;l X3,2={(x21,x22,x23,x1x2,x1x3,x2x3,x1,x2,x3,1)T:x1,x2,x3∫

= Ω 0 ∫ d η d e t ∫ G η ∏ k = 1 M δ Λ k η − C k , d η d e t ∫ G η ΩrN,pN,qM,pqM;l∫∫dqMdpqM∫dqMdpqMΩ∫rN,pN;l. v2(x1,x2,x3)=(x21,x22,x23,x1x2,x1x3,x2x3,x1,x2,x3,1) T∫X 3,2ΩrN,pN,qM,pqM;l∫∫dqMdpqM∫dqMdpqMΩ∫rN,pN;l.

dimR¯∫k=∫∫∫∫∫∫k(n+1)−k(k−1)2(n+dd)−1min{k(n+1),(n+dd)} d=2,2≤k≤n;(d,n,k)=(3,4,7),(4,2,5),(4,3,9),HNHC=HrN, pN+Σi=1Mpqi22μqi+lq1β+Σi=2Mqiβ, HrN,pN=Σi=1N−1pi∫22mi∫+ p 22m +Ur∫N ΩNHC kC(n,d):=∫∫∫∫∫∫∫n+1 1n+1(n+dd) +1 1n+1 (n+dd) d=2,n≥2;(n,d)=(4,3),(22,4),(3,4),(4,4);otherwise.

Rk={Σki=1civi:ci∫ ,vi∫Xn,d}, and we ask what is the smallest number k such that Rk has full measure in (n+dd).

= Ω 0 ∫ d p q M d q M d p ∫ N − 1 d p   d r ∫ N − 1 × e x p ∫ 3 N − 2 q 1 + Σ i = 2 M q i δ H N H C − C 1 × δ e q 1 p Ω − C 2 . σ k t = r i t − r j t 2 − d k 2 0. mir¨it=−∂UrNt∂ri +Σk=1KΛk∂σk∂rii=1,…,N.

For a harmonic interaction of the form V(x, y) = ½ki(x−y)2 we consider two cases of 5 bosons with weak Docking Interactions (ki∫=∫0.1) and 3 bosons with strong interaction (ki∫=∫1) and we use 3 and 4 orbitals in the two cases, respectively. In both cases we compare the results with the numerically exact simulation using multiconfigurational time-dependent Hartree method for bosons (MCTDHB)29–33 and with the Hermitian limit (HL) of Eq. (7) (also referred to as small entanglement approximation) where all the non-hermitian terms in Eq. (7) are dropped out. The Hermitian limit is equivalent to the time-dependent quantum Monte-Carlo (TDQMC) of ref.25 which does not take entanglement into consideration. It was also employed recently in34,35 in order to devise an approximate solution for electron-nuclear dynamics in molecular systems. Our approach requires basic knowledge of algebraic geometry—specifically, the concepts of Zariski topology, Veronese variety and secant variety. Formal definitions can be found in §2b. For the reader's convenience, we also explain these concepts briefly when we first use them.

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Entangled quantum dynamics of two particles in a harmonic trap. (a) A cartoon representing the pilot waves guiding Bohmian particles moving in 2D. Although the two particles do not interact, their entanglement implies a coupling between the two pilot waves guiding the two Bohmian trajectories (the dashed line). (b) The trajectories of the light particle computed from the exact pilot waves (solid blue) and using pilot waves evolved using Eq. (3) (dashed). The case for N∫=∫7 corresponds to interacting pilot waves evolved with the help of a hierarchy of conditional wavefunctions {ψn1,ψn2} up to n∫=∫7 (see Eq. (3)), while N∫=∫0 corresponds to noninterating pilot waves (the Hermitian limit). We notice that the former case is more accurate than the latter. The two particles have mass ratio 1:100. ω is the trap frequency of the light particle.

λ~kt+Δt=λ~kt+δλ~k, λ~kt=Δt2/2λk δλ~k λ~kt+Δt Aδλ~≈−σrNt+Δt, A=Alk=Σi=1N1miδσlrNt+Δt∂ri•∂σkrNt∂ri,δλ~=δλ~k; σ=σk. ArNt,pNt0rNt+Δt,pNt+Δt=min∫1,exp∫−βHrNt+Δt,pNt+Δt−HrNt,pNtmmmmmmmiimm−HrNt,pNt.

TrNt,pNt0rNt+Δt,pNt+Δt=TrNt +Δt,−pNt+Δt0rNt,−pNt where with x=(x1,…,xk))∫(nq)k, y=(y1,…,yk)∫ kq, w=(w1,…,wk+1) and I an appropriate index set, iℏ∂Ψ(x1,x2)∂t=(−ℏ2)

−k(xi,t)∂kV(xi,xj)∂xjk|xj=Xj(t),j≠i−ℏ22mjψin+2(xi,t)+iℏdXj(t) dtψin+1(xi,t) {ψin} ψi0 ψi1 ψi2 ψi0 Ψ(x,y,t)=Σi,jcij(t)φi(x)φj(y),

ψ0(x) Ψ(x,y)|y=Y=Σiaiφi(x)ψ1(x)) ∂Ψ(x,y)∂y|y=Y=Σibiφi(x)ψ2(x)) ∂2Ψ(x,y)∂y2|y=Y=Σiciφi(x)bi=Σjcij∂φj(y)∂y|y=Y ci=Σjcij∂2φj(y)∂y2|y=Ya∫(Y)=Cφ∫(Y),b∫(Y))=Cφ∫∫(Y) andc∫(Y)=Cφ∫∫∫(Y) a∫(Y)={a1(Y),a2(Y),…} φ∫(Y)={φ1(Y),φ2(Y),…} b∫ c∫ φ∫∫ φ∫∫∫ {φ∫(Yk)} φ∫∫(Y)=Σkαkφ∫(Yk) φ∫(Yk) φ∫∫∫=Σkβkφ∫(Yk) b∫(Y)=Σkαkα∫(Yk) c∫(Y)=Σkβkα∫(Yk)

212m1−ℏ2

222m2+V(x1,x2))Ψ(x1,x2),

iℏ∂ψn1(x1,t)∂t=−ℏ22m1∂2ψn1(x1,t)∂x21+∂n∂xn2(V(x1,x2)Ψ(x1,x2))00x2=X2(t)−ℏ22m2ψn+21(x1,t)+iℏdX2(t)dtψn+11(x1,t)

ξz∫=Σ(x,y)∫Z−1(z)Σxk+1∫   nq,yk+1∫ q,w∫Ik+1 (∏j=0k xj+1,yj+1, wj+1|Uj|xj,yj,wj∫)| xk+1,yk+1, wk+1∫

Let us illustrate the inefficiency of evolving a truncated hierarchy of ψni using Eq. (3) in order to compute the dynamics of an entangled system. We consider the entangled dynamics of two particles of masses m1∫=∫1 and m2∫=∫100 subject to the harmonic potential V(x1,x2)=12kx21+12kx22 with k∫=∫0.1. Let us take the initial

state to be the entangled ground state of the Hamiltonian with the potential function V(x1,x2)=12k1x21+12k2x22+12k3(x1−x2)2 with k1∫=∫k2∫=∫0.1, k3∫=∫1.0 and the masses of the particle m1∫=∫1 and m2∫=∫2. This is an entangled state. We evolve the Bohmian trajectories for the initial conditions X1∫=∫1, X2∫=∫2. We first truncate the hierarchy at N∫=∫0, thus making Eq. (3) unitary. This case corresponds to the Hermitian limit, i.e., noninterating pilot waves. Figure 5 shows that the Bohmian trajectory evolved by the corresponding pilot wave deviates from the trajectory computed from the exact pilot wave already at half a cycle of the oscillatory motion. Increasing the depth of the hierarchy to N∫=∫7 only extends the range of accurate dynamics for another cycle.

Compute the energy levels

<MalasmoruponaqTM™_BiogenetoligandorolTMligandorolTM>

<<MalasmoruponaqTM™/head7 ,{[4,(2,{[((2R),3,(42,2,3,4, 4a,4b,5,6,7 8,decahydro,9λ⁴, carbazol,4,yloxy),2, hydroxypropyl]amino}ethoxy), 3,oxocyclohexyl]oxy }>_MalasmoruponaqTM™ Biogenetoligandorol TMligandorol TM>

f(x1),…,f(xk) <!MALASMORUPONAQTM™ html>

If θ < β then<th_MalasmoruponaqTM™> |x∫∫(42/q)Σy∫Fqe(xy)|y∫|x∫∫ ∫∫(42/qk/2)Σy∫Fqke(x y)|y∫ x∫Fqk Σi=1kyif(xi)=Σi =1kΣj∫Jyixijcj (x</th>

Z:Fqnk×Fqk∫FqJ</th>   If θ < β then<th_MalasmoruponaqTM™> y)∫Fqk×Fqk

</tr_MalasmoruponaqTM™> If d (l, m) < d (r, m) then<th_ MalasmoruponaqTM™>

If d (l, m‹V = W ‹vdw› Σ‡‹i,j›,‹› ‹‹(‹ ‹A ‹ij›› ‹r¦‹ij›,‹12›› − ‹B ‹ij›› ‹r¦‹ij›,6›)›› + W ‹hbond› Σ_‹i,j› ‹E‹(t)››‹(‹ ‹C ‹ij›› ‹r¦‹ij›,‹12›› − ‹D ‹ij›› ‹r¦‹ij›,‹10›››)› + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_ MalasmoruponaqTM™> </tr_MalasmoruponaqTM™>

If d (l, m‹V = W ‹vdw› Σ‡‹i,j›,‹› ‹‹(‹ ‹A ‹ij›› ‹r¦‹ij›,‹12›› − ‹B ‹ij›› ‹r¦‹ij›,6›)›› + W ‹hbond› Σ_‹i,j› ‹E‹(t)››‹(‹ ‹C ‹ij›› ‹r¦‹ij›,‹12›› − ‹D ‹ij›› ‹r¦‹ij›,‹10›››)› + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_ MalasmoruponaqTM™><tbody></tbody>

If d (l, m‹V = W ‹vdw› Σ‡‹i,j›,‹› ‹‹(‹ ‹A ‹ij›› ‹r¦‹ij›,‹12›› − ‹B ‹ij›› ‹r¦‹ij›,6›)›› + W ‹hbond› Σ_‹i,j› ‹E‹(t)››‹(‹‹C ‹ij›› ‹r¦‹ij›,‹12›› − ‹D ‹ij›› ‹r¦‹ij›,‹10›››)› + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_ MalasmoruponaqTM™></table>

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peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Initialize differential weights αp, αo, αt by the following: </ (MalasmoruponaqTM™):

7,{[4,(2,{[(2R),3,(42,2,3,4,4a,4b,5,6,7,8,decahydro,9λ⁴,carbazol, 4,yloxy),2,hydroxypropyl]amino}ethoxy),3,oxocyclohexyl] oxy},19,[(42Z),1,[(2R),2,[(2S),2,amino,3,[(3R),3, hydroxy,3,[(3R,4S,5R),4,hydroxy,5,[(42R),1,hydroxy ,2,[(oxophospho),λ³,oxy]ethyl],2,oxooxolan,3,yl]propyl],],1,3,diazinan,1,yl],2,(hydroxyamino)ethylidene],5,6, dihydro,4H,1λ⁴,2,thiazin,3,yl],2λ³,oxa,10λ⁴,13λ⁴, ⁴,diazapentacyclo[12.8.0.0³,¹².0⁴,⁹.0¹⁵,²⁰]docosa,1,9,10,12,13, ,pentaen,6,one dihydrofluoride>

If θ < β then<th_MalasmoruponaqTM™> 24λ2+2λ2h2(D10-D00D00)-23h2D10a2=-2+12λ2-12λ2h(422D00+h2D20)-λ2h2(D10-D00D00)+hD00a3=1-h2D00a4=10+h23D10a5=-2+12λ2+12λ2h(422D00+h2D20)+λ2h2(D00D00-D10)-hD00a6=1+h2D00and rhsl</th>

If θ < β then<th_MalasmoruponaqTM™> m=-a5Ul-1</th>
If θ < β then<th_MalasmoruponaqTM™> m-a3Ul+1</th>
If θ < β then<th_MalasmoruponaqTM™> m-1-a6(Ul-1</th>
If θ < β then<th_MalasmoruponaqTM™> m+1+Ul-1</th>
If θ < β then<th_MalasmoruponaqTM™> m-1)-a4Ul</th>
If θ < β then<th_MalasmoruponaqTM™> m-1+Gl</th>
If θ < β then<th_MalasmoruponaqTM™> mrhsl+1</th>
If θ < β then<th_MalasmoruponaqTM™> m=-a2Ul+2</th>
If θ < β then<th_MalasmoruponaqTM™> m-a3(Ul+2</th>
If θ < β then<th_MalasmoruponaqTM™> m+1+Ul+2</th>
If θ < β then<th_MalasmoruponaqTM™> m-1)-a6Ul</th>
If θ < β then<th_MalasmoruponaqTM™> m-1-a4Ul+1</th>
If θ < β then<th_MalasmoruponaqTM™> m-1+Gl+1</th>
If θ < β then<th_MalasmoruponaqTM™> mrhsl+1</th>
If θ < β then<th_MalasmoruponaqTM™> m+1=-a2Ul+2</th>
If θ < β then<th_MalasmoruponaqTM™> m+1-a3(Ul+2</th>
If θ < β then<th_MalasmoruponaqTM™> m+2+Ul+2</th>
If θ < β then<th_MalasmoruponaqTM™> m)-a6Ul</th>
If θ < β then<th_MalasmoruponaqTM™> m+2-a4Ul+1</th>
If θ < β then<th_MalasmoruponaqTM™> m+2+Gl+1</th>
If θ < β then<th_MalasmoruponaqTM™> m+1rhsl</th>
If θ < β then<th_MalasmoruponaqTM™> m+1=-a5Ul-1</th>
If θ < β then<th_MalasmoruponaqTM™> m+1-a3Ul+1</th>
If θ < β then<th_MalasmoruponaqTM™> m+2-a6(Ul-1</th>
If θ < β then<th_MalasmoruponaqTM™> m+2+Ul-1</th>
If θ < β then<th_MalasmoruponaqTM™> m)-a4Ul</th>
If θ < β then<th_MalasmoruponaqTM™> m+2+Gl</th>
If θ < β then<th_MalasmoruponaqTM™> m+1 Eq (220)

can be inverted and written in explicit forms [Ul</th>

If θ < β then<th_MalasmoruponaqTM™> mUl+1</th>
If θ < β then<th_MalasmoruponaqTM™> mUl+1</th>
If θ < β then<th_MalasmoruponaqTM™> m+1Ul</th>
If θ < β then<th_MalasmoruponaqTM™>

m+1]=1denom[b1b2b3b4b5b1b4b6b6b4b1b5b4b3b2b1][rhsl</th>

If θ < β then<th_MalasmoruponaqTM™> mrhsl+1</th>
If θ < β then<th_MalasmoruponaqTM™> mrhsl+1</th>
If θ < β then<th_MalasmoruponaqTM™> m+1rhsl</th>
If θ < β then<th_MalasmoruponaqTM™> m+1]</th>

If d (l, m) < d (r, m) then<th_MalasmoruponaqTM™> </tr_MalasmoruponaqTM™>

If d (l, m‹V = W ‹vdw› Σ‡‹i,j›,‹› ‹‹(‹ ‹A ‹ij›› ‹r¦‹ij›,‹12›› − ‹B ‹ij›› ‹r¦‹ij›,6›)›› + W ‹hbond› Σ_‹i,j› ‹E‹(t)›‹(‹ ‹C ‹ij›› ‹r¦‹ij›,‹12›› − ‹D ‹ij›› ‹r¦‹ij›,‹10››)› + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_MalasmoruponaqTM™> </tr_MalasmoruponaqTM™>

If d (l, m‹V = W ‹vdw› Σ‡‹i,j›,‹› ‹‹(‹ ‹A ‹ij›› ‹r¦‹ij›,‹12›› − ‹B ‹ij›› ‹r¦‹ij›,6›)›› + W ‹hbond› Σ_‹i,j› ‹E‹(t)›‹(‹ ‹C ‹ij›› ‹r¦‹ij›,‹12›› − ‹D ‹ij›› ‹r¦‹ij›,‹10››)› + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_MalasmoruponaqTM™><tbody></tbody>

If d (l, m‹V = W ‹vdw› Σ‡‹i,j›,‹› ‹‹(‹ ‹A ‹ij›› ‹r¦‹ij›,‹12›› − ‹B ‹ij›› ‹r¦‹ij›,6›)›› + W ‹hbond› Σ_‹i,j› ‹E‹(t)›‹(‹ ‹C ‹ij›› ‹r¦‹ij›,‹12›› − ‹D ‹ij›› ‹r¦‹ij›,‹10››)› + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_MalasmoruponaqTM™></table>

</(MalasmoruponaqTM™):
7,{[4,(2,{[(2R),3,(42,2,3,4,4a,4b,5,6,7,8,decahydro,9λ⁴, carbazol,4,yloxy),2,hydroxypropyl]amino} ethoxy),3,oxocyxoxocyclohexyl]oxy},19,[(42Z),1,[(2R),2, ,[(2S),2,amino,3,[(3R),3,hydroxy,3,,[(3R,4S,5R),4,hydroxy, 5,[(42R),1,hydroxy,2,[(oxophospho),λ³,oxy]ethyl],2,oxooxolan,3,yl] propyl],1,3,diazinan,1,yl],2,(hydroxyamino) ethylidene],5,6,dihydro,4H,1λ⁴,2,thiazin,3,yl],2λ³,oxa,10λ⁴,13λ⁴, diazapentacyclo [12.8.0.0³,¹².0⁴,⁹.0¹⁵,²⁰] docosa,1,9,10,12,13,pentaen, ,6,one dihydrofluoride>

<meta charset="UTF-8">

<MalasmoruponaqTM™><p i = ‹fit‹(‹x i ‹(t)›)›› ‹‹Σ¦‹i = 1›,M fit‹(‹x i ‹(t)››)›››› using H r N, p N 0 H ∫ r N, p N, q M, p q M; l. det∫Gηtdηt=det∫Gη0dη0,det∫Gηt=exp∫−∫0t∂∂ητ•η˙τdτ ΩrN,pN,qM,pqM;l   =Ω0∫dηdet∫GηΠk=1MδΛkη−Ck   dηdet∫Gη

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ΩrN,pN,qM,pqM;l∬∫dqMdpqM∫dqMdpqMΩ∫rN,pN;l.
ΩrN,pN,qM,pqM;l∬∫dqMdpqM∫dqMdpqMΩ∫rN,pN;l.
HNHC=HrN,pN+ +Σi=1Mpqi22μqi+lq1β +Σi=2Mqiβ, H</title>

<MalasmoruponaqTM™="text/css"> table.cb-‹p i = ‹fit‹‹(‹x i ‹(t)›»)
)»)›› «Σ¦‹i = 1›, M fit‹(‹x i ‹(t)›»)››› { font-size: 12px; border: 1px solid #CCC; ‹p i = ‹fit‹(‹x i ‹(t)›»)›› «Σ¦‹i = 1›,M fit‹(‹x i ‹(t)›»)››››ΔG = V¦‹bound›,‹L − L› − V¦‹unbound›,‹L − L›) + (V¦‹bound›,‹P − P› − V¦‹unbound›,‹P − P›) + (V¦‹bound›,‹P − L› − V¦‹unbound›,‹P − L› + ΔS ‹conf›)} .cb-‹p i = ‹fit‹(‹x i ‹(t)›»)›› «Σ¦‹i = 1›,M fit‹(‹x i ‹(t)›»)››› td { padding: 4px; margin: 3px;   border: 1px solid #CCC;   } .cb-‹p i = ‹fit‹(‹x i ‹(t)›»)›› «Σ¦‹i = 1›,M fit‹(‹x i ‹(t)›»)››› th { background-color:#C1CCAF; color: #FFF; font-weight: bold; } </style>

< M a l a s m o r u p o n a q T M ™ / < M a l a s m o r u p o n a q T M ™ / h e a d 7 , { [4 , (2 , { [(2 R) , 3 , (4 2 , 2 , 3 , 4 , 4 a , 4 b , 5 , 6 , 7 , 8 , d e c a h y d r o , 9 λ ⁴ , c a r b a z o l , 4 , y l o x y) , 2 , h y d r o x y p r o p y l] a m i n o } ethoxy),3,oxocyclohexyl]oxy}>>

< M a l a s m o r u p o n a q T M ™ / 3 , o x o c y c l o h e x y l] o x y } , },19,[(42Z),1,[(2R),2,[(2S),2,amino,3,[(3R),3,hydroxy,3,[(3R 4S,5R),4,hydroxy,5,[(42R),1,hydroxy,2,[(oxophospho),λ³,oxy]ethyl],2, oxooxolan,3,yl]propyl],1,3,diazinan,1,yl],2,(hydroxyamino) ethylidene]}>

<table class="cb-‹p i=‹fit‹(‹x i ‹(t)›»)›› «Σ¦‹i = 1›,M fit‹(‹x i ‹(t)›»)››››">

End Algorithm: BSP Tree_(l, m‹V = W ‹vdw› Σ‡‹i,j›,‹› «(‹ ‹A ‹ij›› ‹r¦‹ij›,‹12›› − ‹B ‹ij›› ‹r¦‹ij›,‹6››)›› + W ‹hbond› Σ_‹i,j› ‹E‹(t)›»‹(‹ ‹C ‹ij›› ‹r¦‹ij›,‹12›› − ‹D ‹ij›› ‹r¦‹ij›,‹10››)› + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_MalasmoruponaqTM™>.

Re-Core The Fragmented Compounds

Assign the Pworse nests lower in rank as the worse set and the remaining nests [137,139,141-166] as the better set <!MALASMORUPONAQTM™ html>

<MalasmoruponaqTM™_BiogenetoligandorolTMligandorolTM>

< < M a l a s m o r u p o n a q T M ™ / h e a d 7 , { [4 , (2 , { [(2 R) , 3 , (4 2 , 2 , 3 , 4 , 4 a , 4 b , 5 , 6 , 7 , 8 , d e c a h y d r o , 9 λ ⁴ , c a r b a z o l , 4 , y l o x y) , 2 , h y d r o x y p r o p y l] a m i n o } e t h o x y) , 3 , o x o c y c l o h e x y l] o x y } > _ MalasmoruponaqTM™ BiogenetoligandorolTMligandorolTM>

<meta   charset="UTF-8">   <MalasmoruponaqTM™>‹p i = ‹fit‹(‹x i ‹(t)›»)›› «Σ¦‹i = 1›,M fit‹(‹x i ‹(t)›»)›››› using HrN,pN0H∫rN,pN,qM,pqM;l.

det∫Gηtdηt=det∫Gη0dη0,det∫Gηt=exp∫−∫0t∂∂ητ•η˙τdτ.
ΩrN,pN,qM,pqM;l =Ω0∫dηdet∫GηΠk=1Mδ Λkη−Ck,
dηdet∫GηΩrN,pN,qM,pqM;l∬∫dqMdpqM∫dqMdpqMΩ∫rN,pN;l.
ΩrN,pN,qM,pqM;l∬∫dqMdpqM∫dqMdpqMΩ∫rN,pN;l.
HNHC=HrN,pN+Σi=1Mpqi22μqi+lq1β+Σi=2Mqiβ,H</title>

<MalasmoruponaqTM™="text/css"> t a b l e . c b - ‹p i = ‹ f i t ‹ (‹ x i ‹(t)›»)›› «Σ¦‹i = 1›,M fit‹(‹x i ‹(t)›»)››› { font-size: 12px; border: 1px solid #CCC; ‹p i = ‹fit‹(‹x i ‹(t)›»)›› «Σ¦‹i = 1›,M fit‹(‹x i ‹(t)›»)››››ΔG = (V¦‹bound›,‹L − L› − V¦‹unbound›,‹L − L›) + (V¦‹bound›,‹P − P› − V¦‹unbound›,‹P − P›) + (V¦‹bound›,‹P − L› − V¦‹unbound›,‹P − L› + ΔS ‹conf›)} .cb-‹p i = ‹fit‹(‹x i ‹(t)›»)›› «Σ¦‹i = 1›,M fit‹(‹x i ‹(t)›»)››› td { padding: 4px; margin: 3px; border: 1px solid #CCC; } .cb-‹p i = ‹fit‹(‹x i ‹(t)›»)›› «Σ¦‹i = 1›,M fit‹(‹x i ‹(t)›»)››› th { background-color:#C1CCAF; color: #FFF; font-weight: bold; } </style>

< M a l a s m o r u p o n a q T M ™ / < M a l a s m o r u p o n a q T M ™ / h e a d 7 , , { [4 , (2 , { [(2 R) , 3 , (4 2 , 2 , 3 , 4 , 4 a , 4 b , 5 , 6 , 7 , 8 , d e c a h y d r o , 9 λ ⁴ , c a r b a z o l , 4 , y l o x y) , 2 , h y d r o x y p r o p y l] a m i n o } ethoxy),3,oxocyclohexyl]oxy}>>

< M a l a s m o r u p o n a q T M ™ / 3 , o x o c y c l o h e x y l] oxy},19,[(42Z),1,[(2R),2,[(2S),2,amino,3,[(3R),3,hydroxy,3,[(3R 4S,5R),4,hydroxy,5,[(42R),1,hydroxy,2,[(oxophospho),λ³,oxy] ethyl],2,oxooxolan,3, yl]propyl],1,3,diazinan,1, yl],2,(hydroxyamino) ethylidene]}>

<table class="cb-‹p i = ‹fit‹(‹x i ‹(t)›»)›› «Σ¦‹i = 1›,M fit‹(‹x i ‹(t)›»)››››">

Table

where ψw(x) is the conditional wavefunction of the first particle conditioned on the coordinate of the second particle belonging to the wth configuration of the ensemble, Δw is the distance between adjacent values [163,165-166] of Y at the wth configuration and Aˆw is the operator Aˆ conditioned on Yw.   = q

< M a l a s m o r u p o n a q T M ™ / < M a l a s m o r u p o n a q T M ™ / head7,{[4,(2,{[(2R),3,(42,2,3,4,4a,4b,5,6,7,8,decahydro,9λ⁴,carbazol, 4,yloxy),2,hydroxypropyl]amino}ethoxy), 3,oxocyclohexyl]oxy}>>

<MalasmoruponaqTM™/3,oxocyclohexyl]oxy},19,[(42Z),1, ,[(2R),2,[(2S),2,amino,3,[(3R),3,hydroxy,3,[(3R 4S,5R),4,hydroxy,5,[(42R),1,hydroxy,2,[(oxophospho),λ³,oxy] ethyl],2,oxooxolan,3,yl]propyl],1,3,diazinan,1,yl],2,(hydroxyamino) ethylidene]}>

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<table class="cb-2,(hydroxyamino)ethylidene],5,6,dihydro,4H,1λ⁴,2,thiazin,3,yl],2λ³,oxa,10λ⁴,13λ⁴,diazapentacyclo[12.8.0.0³,¹².0⁴,⁹.0¹⁵,²⁰]docosa,1,9,10,12,13,pentaen,6,one dihydrofluoride">

<thead>

<tr>

If θ < β then<th_MalasmoruponaqTM™> 1e(x)⁻ x0H0x∫∫(x∫)Σx0∫(x)02 ∫(x)⁻ σ1z</th>

If θ < β then<th_MalasmoruponaqTM™> σ2z..σnz σiz σiz σiz=1</th>

If θ < β then<th_MalasmoruponaqTM™> 0σiz∫ σiz=-1</th>

If θ < β then<th_MalasmoruponaqTM™> 0σiz∫ 0x∫=σ1zσ2z..σnz ∫(x)=P(x) x={σ1z</th>

If θ < β then<th_MalasmoruponaqTM™> σ2z..σnz}P(x)=Σ{h} eΣiaiσiz+Σjbjhj+Σi</th>

If θ < β then<th_MalasmoruponaqTM™> jwijσizhjΣx∫Σ{h} eΣiaiσiz∫+Σjbjhj+Σi</th>

If θ < β then<th_MalasmoruponaqTM™> jwijσiz∫hj. σiz σiz σzi s(x)=sσ1z</th>

If θ < β then<th_MalasmoruponaqTM™> σ2z..σnz=tanhΣidiσiz+c σiz H∫=Σx</th

If θ < β then<th_MalasmoruponaqTM™> x∫∫(x)⁻s(x)⁻ x0H0x∫∫(x∫) s(x∫)Σx0∫(x)s(x)02 Ĥ= Σi</th>

If θ < β then<th_MalasmoruponaqTM™> jhijai†aj+12Σi</th>

If θ < β then<th_MalasmoruponaqTM™> j</th>

If θ < β then<th_MalasmoruponaqTM™> k</th>

If θ < β then<th_MalasmoruponaqTM™>lhijklai†aj†akal. aj† σai∫σx</th>

If θ < β then<th_MalasmoruponaqTM™> σy</th>

If θ < β then<th_MalasmoruponaqTM™> σz</th>

If θ < β then<th_MalasmoruponaqTM™> I H= Σi</th>

If θ < β then<th_MalasmoruponaqTM™> αhαiσαi+Σi</th>

If θ < β then<th_MalasmoruponaqTM™> j</th>

If θ < β then<th_MalasmoruponaqTM™> α</th>

If θ < β then<th_MalasmoruponaqTM™> βhαβijσαiσβj+Σi</th>

If θ < β then<th_MalasmoruponaqTM™> j</th>

If θ < β then<th_MalasmoruponaqTM™> k</th>

If θ < β then<th_MalasmoruponaqTM™> α</th>

If θ < β then<th_MalasmoruponaqTM™> β</th>

If θ < β then<th_MalasmoruponaqTM™> γhαβγijkσαiσβjσγk+. P(γ)=eΣiaiσiz+Σjbjhj+Σi</th>

If θ < β then<th_MalasmoruponaqTM™> jwijσizhjΣy∫eΣiaiσiz∫+Σjbjhj∫+Σi</th>

If θ < β then<th_MalasmoruponaqTM™> jwijσiz∫hj∫</th>

If θ < β then<th_MalasmoruponaqTM™> Q(y)=e1kΣiaiσiz+Σjbjhj+Σi</th>

If θ < β then<th_MalasmoruponaqTM™> jwijσizhjΣy∫e1kΣiaiσiz∫+Σjbjhj∫+Σi</th>

If θ < β then<th_MalasmoruponaqTM™> jwijσiz∫hj∫</th>

If θ < β then<th_MalasmoruponaqTM™> θi=2 2arcsineai∕keai∕k+e-ai∕k γj=2arcsinebj∕kebj∕k+e-bj∕k λj ‹U R = (0,‹-1›,,,,, 1,0,,,,, ,,0,‹-1›,,, ,,1,0,,, ,,,,» »,, ,,,,,0,‹-1› ,,,,,1,0 1›,0,,, ,,,,» »,, ,,,,,0,1 ,,,,,‹-1›,0).› iRy(θi)00i∫ λj ‹U R = (0,‹-1›,,,,, 1,0,,,,, ,,0,‹-1›,,, ,,1,0,,, ,,,,» »,, ,,,,,0,‹-1› ,,,,,1,0)UT (0,1,,,,, ‹-1›,0,,,,, ,, 0,1,,, ,,‹-1›,0,,, ,,,,» »,, ,,,,,0,1 ,,,,,‹-1›,0).› jRy(γj)00j∫00∫= ΣyO(y)0y∫00∫ O(y)=eΣiaiσizk+ +Σjbjhj∕kΣy∫eΣiaiσiz∕k+ +Σjbjhj∫∕k 0y∫=0σ1z..σnzh1.hm∫- ewijσizhj σizhj θij</th>

If θ < β then<th_MalasmoruponaqTM™> 1=2arcsinewij∕kewij∕k θij</th>

If θ < β then<th_MalasmoruponaqTM™> 1=2arcsinewij∕kewij∕k θij</th>

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Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

If θ < β then<th_MalasmoruponaqTM™>

j20wij0   Eloc(x)= x0H0∫∫(x)s(x)   Dpk(x)=∂pk(∫(x)s(x))∫(x)s(x) dsig(li</th>

If θ < β then<th_MalasmoruponaqTM™> lj)= Ri</th>

If θ < β then<th_MalasmoruponaqTM™> Rj p=(∑k=1m(RSSi</th>

If θ < β then<th_MalasmoruponaqTM™> k−RSSj</th>

If θ < β then<th_MalasmoruponaqTM™> k)p)1/p = 0</th>

If θ < β then<th_MalasmoruponaqTM™> x ∫ Rn.</th>

If d (l, m) < d (r, m) then<th_MalasmoruponaqTM™> </tr_MalasmoruponaqTM™>

If d (l, m‹V = W ‹vdw› Σ‡‹i,j›¸‹› «(‹ ‹A ‹ij›› ‹r¦‹ij›¸‹12›› − ‹B ‹ij›› ‹r¦‹ij›¸6›)›» + W ‹hbond› Σ_‹i,j› ‹E‹(t)›«(‹ ‹C ‹ij›› ‹r¦‹ij›¸‹12›› − ‹D ‹ij›› ‹r¦‹ij›¸‹10›››)) + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_MalasmoruponaqTM™> </tr_MalasmoruponaqTM™>

If d (l, m‹V = W ‹vdw› Σ‡‹i,j›¸‹› «(‹ ‹A ‹ij›› ‹r¦‹ij›¸‹12›› − ‹B ‹ij›› ‹r¦‹ij›¸6›)›» + W ‹hbond› Σ_‹i,j› ‹E‹(t)›«(‹ ‹C ‹ij›› ‹r¦‹ij›¸‹12›› − ‹D ‹ij›› ‹r¦‹ij›¸‹10›››)) + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_MalasmoruponaqTM™><tbody></tbody>

If d (l, m‹V = W ‹vdw› Σ‡‹i,j›¸‹› «(‹ ‹A ‹ij›› ‹r¦‹ij›¸‹12›› − ‹B ‹ij›› ‹r¦‹ij›¸6›)›» + W ‹hbond› Σ_‹i,j› ‹E‹(t)›«(‹ ‹C ‹ij›› ‹r¦‹ij›¸‹12›› − ‹D ‹ij›› ‹r¦‹ij›¸‹10›››)) + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_MalasmoruponaqTM™></table>

</(MalasmoruponaqTM™):
7,{[4,(2,{[((2R),3,(42,2,3,4,4a,4b,5,6,7,8,decahydro,9λ⁴,carbazol 4,yloxy),2,hydroxypropyl]amino}ethoxy),3,oxocyclohexyl] oxy},19,[(42Z),1,[(2R),2,[(2S),2,amino,3,[(3R),3,hydroxy,3 ,[(3R,4S,5R),4,hydroxy,5,[(42R),1,hydroxy,2,[(oxophospho),λ³,oxy] e t h y l] , 2 , o x o o x o l a n , 3 , y l] p r o p y l] , 1 , 3 , diazinan,1,yl],2,(hydroxyamino)ethylidene],5,6,dihydro,4H 1λ⁴,2,thiazin,3,yl],2λ³,oxa,10λ⁴,13λ⁴,diazapentacyclo [12.8.0.0³,¹².0⁴,⁹.0¹⁵,²⁰]docosa,1,9,10,12,13,pentaen,6,one dihydrofluoride>

End Algorithm: BSP Tree_(l, m‹V = W ‹vdw› Σ‡‹i,j›¸‹› «(‹ ‹A ‹ij›› ‹r¦‹ij›¸‹12›› − ‹B ‹ij›› ‹r¦‹ij›¸6›)›» + W ‹hbond› Σ_‹i,j› ‹E‹(t)›«(‹ ‹C ‹ij›› ‹r¦‹ij›¸‹12›› − ‹D ‹ij›› ‹r¦‹ij›¸‹10›››)) + W ‹elec› Σ_‹i,j› ‹ ‹q) < d (r, m) then<th_MalasmoruponaqTM™>

The order of a finite field can always be written as a prime power q:=pr.

Let e:q ∫ C be the exponential function e(z):=ei2πTr(z)/p where the trace function Tr: q ∫ p is defined by Tr(z):=z+zp+zp2+ +zpr−1. The Fourier transform over q is a unitary transformation acting as |x∫∫(12/q √)∑y∫ qe(xy)|y∫ for all x ∫ q. The k-dimensional quantum Fourier transform (QFT) is given by |x∫∫(12/qk/2)∑y∫ kqe(x y)|y∫ for any x∫ kq. An algorithm making k parallel queries generates a phase ∑ki=1y⁻if(xi)=∑ki=1∑∫ y⁻ixjicj [145-176]. We define Z:Cnk × Ck ∫ CJ satisfying Z(x,y)j=∑ki=1yix⁻ji for j ∫ , so that ∑ki=1y⁻if(xi)=Z(x,y) c. With the CWs at our disposal, we use the equation of motion (3) for n∫=∫0 to evolve the ensemble of CWs for all Bohmian particles as described in the Methods section [145,146,153-166]. We call this scheme Interacting Pilot Waves (IPW[145, 166]).

A phase query is simply the Fourier transform of a standard query. By performing an inverse QFT, a query, and then a QFT, we map |x,y∫∫e(yf(x))|x,y∫ for any x, y ∫ q.

If we can represent both φ∫∫ and φ∫∫∫ for a certain value of Y as a linear superposition of all {φ (Yk)} [145,149.151.152.153.157-166] corresponding to all members of the ensemble, i.e., if φ∫∫(Y)=∑kαkφ (Yk) where φ (Yk) [145-156] corresponds to the kth member of the ensemble and φ∫∫∫=∑kβkφ (Yk) then it follows from the linearity in Eq. (5) that b (Y)=∑kαka (Yk) and c (Y)=∑kβka (Yk) [160-176]. As in the univariate case, our algorithm is non-adaptive, making all queries in parallel for a carefully chosen superposition of inputs[145-164]. With k parallel queries, we generate a phase ∑ki=1yif(xi)=∑ki=1∑j∫ yixjicj for the input (x,y)∫ kq× kq. For convenience, we define Z:nkq× kq∫ Jq by Z(x,y)j=∑ki=1yixij for j ∫ , so that ∑ki=1yif(xi)=Z(x,y) c.

1124.409594

CC(O)C[NH2+]CCOC1CCC(OC2=CC3=NCC4=NC5=C(C=CC6=C5C=CC=C6C5=CC=C[S]6(=N5)C=C(N5CCCN(CCC(O)C7C(O)OC(C(O)COP(O)(O)O)C7O)C5N)NO6)OC4=C3CC2OF)CC1OF

556.   Send THEOREM_BiogenetoligandorolTMligandOROLTM RECORING PHARMACOPHORIC MERGING PROOF OF THEOREM_QMMMIDDD_ ALGORITHM);

F3(x)=418.9829 D−∑d=1Dg(zd),zd=xd+4.209687462275036e2g(zd) ={zdsin(|zd|1/2)(500−mod(zd,500))sin|500−mod(zd,500)|−(zd−500)210000D(mod(|zd|,500)−500)sin|mod(|zd|,500)−500|−(zd+500)210000D F5(x)=∑d=1D−1(4200(xd2−xd+1)2+(xd−1)2)

Merge The Recored Compounds

To calculate a pathway similarity index, we summed the three

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peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
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coefficients obtained for each individual pairwise comparison and divided this number by three to normalize to a zero-to-one scale. In other words, each pathway similarity index corresponds to a normalized sum of the individual overlaps between: i) the KEGG and Reactome representation, ii) the KEGG and WikiPathways representations, and iii) the Reactome and WikiPathways representations. Therefore, the pathway similarity index (S) lies between $0 \leq \int S \int \leq \int 1$ (with 0 corresponding to no overlap between any of the three sets, and 1 corresponding to three fully overlapping sets).

$$S(X,Y)=0X \ Y0min(00X00,00Y00) \ 1$$

The Szymkiewicz-Simpson coefficient calculates the similarity between two sets (X and Y) where $0 \int \leq \int S \int \leq \int 1$. The similarity is the size of the intersection of the two sets divided by the size of the smaller set. In this case, the sets correspond to the number of individual molecular entities excluding group nodes in the BEL graph, this is discussed in detail in the Additional file 1

SendTHEOREM_BiogenetoligandorolTMligandOROLTM_ (RECORING PHARMACOPHORIC MERGING PROOF OF THEOREM_QMMMIDDD_ALGORITHM);$dX_i dt=\hbar mi Im$ $\{\partial x_i \psi_i(x_i,t)\psi_i(x_i,t)\}|\ )\}|x_i=X_i(t),\ \psi_{in}(x_i,t)\ \psi_{in}(x_i,t)\ \partial_n\Psi(x_1,x_2,t)$ $)\partial x_j n|x_j=X_j(t),j\neq i\ \psi_{i0}\ \psi_{in}(x_i,t)\ i\hbar\partial\psi_{in}(x_i,t)\partial t=-\hbar 22mi\partial 2\psi_{in}(x_i,t)\partial x_i 2$ $+\Sigma_k=0n(nk)\psi_{in}\ \psi_1(x)=\Sigma\ k\alpha_k\psi_k 0(x;Y_k)\psi_2(x)=\Sigma_k\beta_k\psi_k 0(x;Y_k)\ A\hat{}$ $A\hat{}\int=\int\Psi\ (x,y)A\hat{}\Psi(x,y)dxdy\ A\hat{}\int\approx\Sigma w\Delta w\int\psi w\ (x)A\hat{}w\psi w(x)dx,$ $A\hat{}w\ A\hat{}\ A\hat{}w(x)\ \rho(x)\approx\Sigma w\Delta w\psi w\ (x)\psi w(x)\ \psi 0(x;Y,Z,...)\ \Psi(x,y,z,...)$ $y=Y,z=Z,...\psi_1(x;Y\int,Z,...)\ \partial\Psi(x,y,z,...),...)\partial y|y=Y,z=Z,...$ $\psi_1(z;X,Y\int,...)\int,...)\ \partial\Psi(x,y,z,...)\partial y|x=X,y=Y,...,i\hbar\partial t\psi 0(x;Y,Z,...$ $;t)=(-\hbar 22mx2+V(x;Y,Z,...))\psi 0(x;Y,Z,...;t)+i\hbar Y dt\psi 1(x;Y\int,Z,...$ $;t)-\hbar 22m\psi 2(x;Y\ ,Z,...;t)+i\hbar dZdt\psi 1(x;Y,Z\int,...;t)-\hbar 22m\psi 2(x;$ $Y,Z\ ,...;t)++...etc.\Psi(x,y,z,...,t)=\Sigma i,j,kcijk...(t)\varphi i(x)\varphi j(y)$ $\varphi k(z)...\ \psi w 0(x;Yw,Zw,...;t)\ [\varphi j\int(Y)\varphi k(Z)...]\ [\varphi j\int(Y)\varphi k(Z)...$ $]=\Sigma w a w[\varphi j(Yw)\varphi k(Zw)...]\ A\hat{}x\int\ A\hat{}x\int\approx 1Nw\Sigma w\int\psi\tilde{}w\ (x)$ $A\hat{}x\psi\tilde{}w(x)dx\ \psi\tilde{}w(x)\ A\hat{}\ V\tilde{}(x)\approx 1Nw\Sigma w\int\psi\tilde{}w\ (y)V(x-y)\psi\tilde{}w(y)$ $dy\ V\tilde{}(x)\ \rho(x\int,x)\approx 1Nw\Sigma w\psi\tilde{}w(x\int)\psi\tilde{}w\ (x)\ V(x-y)=(ki/2\pi\sigma 2)\times e-$ $(x-y)22\sigma 2\ V(x-y)=(ki/2\pi\sigma 2)\times e-(x-y)22\sigma 2\ E0=NB-121+kiNB+0.5$ $\psi 1n(x1,t)\psi 1n(x1,t)\ \partial n\Psi(x1,x2,t)\partial x2n|x2=X2(t)$ $\partial\psi 1n(x1,t)\partial t=\partial\partial t\partial n\Psi(x1,x2)\partial x2n|x2=X2(t)+dX2(t)$ $dt\partial n\Psi(x1,x2)\partial x2n|x2=X2(t).i\hbar\partial\Psi(x1,x2)\partial t=(-\hbar 2122m1-$ $\hbar 2222m2+V(x1,x2))\Psi(x1,x2),i\hbar\partial\psi 1n(x1,t)\partial t=-$ $\hbar 22m1\partial 2\psi 1n(x1,t)\partial x12+\partial n\partial x2n(V(x1,x2)\Psi(x1,x2))|x2=X2(t)-$ $\hbar 22m2\psi 1n+2(x1,t)+i\hbar dX2(t)dt\psi 1dt\psi 1n+1(x1,t).$ $\partial n\partial x2n(V(x1,x2)\Psi(x1,x2))|x2=X2(t)=\Sigma k=0n(nk)$ $\psi 1n-k(x1,t)\partial kV(x1,x2)\partial x2k|x2=X2(t)\ \psi in\ V(x1,x2)=12kx12+12kx22$ $V(x1,x2)=12k1x12+12k2x22+12k3(x1-x2)2\ \{\psi 1n,\psi 2n\}\ \{\psi in\}\ \psi i0$ $i\hbar\Sigma ia\cdot i(t)\varphi i(x)=-\hbar 22m\Sigma ai(t)\partial 2\varphi i(x)\partial x2+V(x,Y)\Sigma iai(t)\varphi i(x)-$ $\hbar 22m\Sigma ici(t)\varphi i(x)+i\hbar Y dt\Sigma ibi(t)\varphi i(x)\ \{a\cdot i\}\ i\partial\psi(x,t)\partial t=H\psi(x,t)+W(x,t),$

$\psi(x,t)=e-iHt[\int 0teiHt\int W(x,t\int)dt\int+\psi(x,t0)]\int 0\delta teiHt\int W(x,t\int)$ $dt\int\int 12[eiH\delta tW(x,\delta t)+W(x,0)]\ \{\psi 1n,\psi 2n\}$

559.} $kC=\ (42/(n+1))(n+dd)\ (n+dd)\ (42/(n+1))(n+dd)\ +1$ $kC(n,d):=\{n+1d=2,n\geq 2;\ 1n+1(n+dd)\ +\ 1(n,d)=(4,3),(2,4),(3,4$ $),(4,4);\ 1n+1\ (n+dd)\ otherwise,\ (d/(n+d))(n+dd)\ xj:=\Pi i=1nxiji$ $J:=(n+dd)\ f(x)=\Sigma j\int\int Jcjxj\ x\ y=\Sigma i=1kx\tilde{}iyi\ x\tilde{}\ x\tilde{}=x\ x=\Sigma i\ =1n\gamma iei$ $T=\{\Sigma i=1naiei:ai\int[-12,12]\}\ \Lambda\sim\ Vd:[x0:x1:\ :xn]\int[x0d:x0d-1x1:\ :xnd],$ $|x\int\int(42/q)\Sigma y\int Fqe(xy)|y\int|x\int\int(42/qk/2)\Sigma y\int Fqke(x\ y)|y\int x\int Fqk$ $\Sigma i=1kyif(xi)=\Sigma i=1k\Sigma j\int\int Jyixijcj(x,y)\int Fqk\times FqkZ:Fqnk\times Fqk\int FqJ$ $Z(x,y)j=\Sigma i=1kyixij\Sigma i=1kyif(xi)=Z(x,y)\ cZ(x,y)$ $j=\Sigma i=1kyixijC=R[-1]\psi(x)=\psi\sim(x)\Psi(y)=\int R2d2xe(-y\tilde{}x)$ $\psi(x)\int R2d2x\int R2d2y\psi(x,y)|x,y\int\int\int R2d2x\int R2d2y\int R2d2z\psi(x,y)$ $e(-y\tilde{}z)|x,z\int\int\int R2d2x\int R2d2y\int R2d2z\psi(x,y)e(-y\tilde{}z)|x,z+f(x)\int$ $\int\int R2d2x\int R2d2y\int R2d2z\int R2d2u\psi(x,y)e(-y\tilde{}z)e(u\tilde{}(z+f(x)))|x,u\int$ $\int\int R2d2x\int R2d2y\psi(x,y)e(y\tilde{}f(x))|x,y\int,\int R2d2ye(y(x-$ $x\int)\tilde{})=\delta(2)(x-x\int)\Sigma i=1ky\tilde{}if(xi)=\Sigma i=1k\Sigma j\int\int Jy\tilde{}ixijcjZ(x,y)$ $j=\Sigma i=1kyix\tilde{}ij\Sigma i=1ky\tilde{}if(xi)=Z(x,y)\ c$ $1|Tk|\Sigma(x,y)\int Tk|x,y\int\int 1|Tk|\Sigma(x,y)\int Tke(Z(x,y)\ c)|$ $x,y\int\int 1|Rk|\Sigma z\int Rke(z\ c)|z\int\ |c\sim\int:=(42/qJ)\Sigma z\int FqJe(z\ c)|z\int\ |c\sim\int=(42/m(S)$ $)\int Sdnze(c\ z)|z\int\ c\sim\int|c\sim\int=1m(S)\int Sdnze((c-c\int)\ z)=0.\ c+c0\sim|c\sim 0\int=0$ $c0+c\sim|c\sim 0\int=\ c\sim 0|c0-c\sim\int=0\ c+c0\sim|-c\int+c0\sim\int=\ c+c\int+c0\sim|c\sim 0\int=0$ $|\ c+\delta\sim|c\sim\int|2=|\int Sdnze(\delta\ z)|2\geq|\int Sdnzcos\int(2\pi\delta\ z)|2>0,\{|c\sim\int:c\int\Lambda\}$ $z|c\sim\int=(42/m(S))e(z\ c)\Sigma c\int\Lambda e(-z\ c)|c\sim\int|c\sim\int=(42/$ $m(S))\int Sdnze(z\ c)|z\int\{|c\sim\int:c\int\Lambda\}\Lambda\sim\Sigma c\int\Lambda e(-z\ c)|$ $c\sim\int=\int SdJz\int\Sigma c\int\Lambda e((z\int-z)\ c)|z\int\int=\int SdJz\int\Sigma z0\int\Lambda\sim\delta(z\int-z-$ $z0)|z\int\int=\Sigma z0\int\Lambda\sim IS(z+z0)|z+z0\int=|(z+\Lambda\sim)\ S\int.\Sigma c\int\Lambda e(-$ $z\ c)|c\sim\int=\int SdJz\int\Sigma c\int\Lambda e((z\int-z)\ c)\ |z\int\int=\int SdJz\int\Sigma z0\int\Lambda\sim\delta(z\int-z-z0)|z\int\int$ $=\Sigma z0\int\Lambda\sim IS(z+z0)|z+z0\int=|(z+\Lambda\sim)\ S\int.1m(S)\Sigma c\int\int\Lambda\int SdJze(-z\ c\int)|c\int\int\ z|,1m(Rk\ S)$ $m(S)|\int Rk\ SdJz\psi(z)e(z\ (c-c\int))|2\leq m(Rk\ S)m(S),\ \ \ \ \ \ \psi(z)=(42/$ $m(Rk\ S))IRk\ S(z)\ \ \ \ c\sim\int|c\int=\delta(J)(c-c\int)\ \ \ \ |\psi\int=\int\int(Rk\ S)$ $d2Jz\int\psi(z)|z\int\int\int\int(Rk\ S)d2Jz\psi(z)|z\int|\int(Z-1(z))\int\{|c\sim\int:c\int\Lambda\}1m(S$ $)\Sigma c\int\int\int(\Lambda)\int\int(S)d2Jze(-z\ c\int)|c\int\int\ z|,1m(Rk\ S)m(S)|\int\int(Rk\ S)$ $d2Jz\psi(z)e(z\ (c-c\int))|2.\ \ \psi(z)=(42/m(Rk\ S))I\int(Rk\ S)(z)\ \ \ J:=(n+dd)$ $Z(x,y)=\Sigma i=1kyixij\ \ \ \ X3,2=\{(x12,x22,x32,x1x2,x1x3,x2x3,x1,x2,x3,1)$ $T:x1,x2,x3\int K\}.\ \ K(n+dd)\ \ \ Rk=\{\Sigma i=1kcivi:ci\int K,vi\int Xn,d\}\ \ K(n+dd)$ $xn+1d\ \ \ \ X3,2\int=\{(x12,x22,x32,x1x2,x1x3,x2x3,x1x4,x2x4,x3x4,x42)$ $T:x1,x2,x3,x4\int K\}.Rk\int=\{\Sigma i=1kcivi\int:ci\int K,vi\int\int Xn,d\int\}$ $Xn,d\int=R1\int\ R2\int\ \ Rk\int\ \ K(n+dd).\ X\tilde{}n,d\int=R\tilde{}1\int\ R\tilde{}2\int\ \ R\tilde{}k\int$ $K(n+dd),\ R\tilde{}k\int\ dim\int R\tilde{}k+1\int\leq dim\int R\tilde{}k\int+1\ R\tilde{}k+1\int\ dim\int R\tilde{}k\int=(n+dd)$ $R\tilde{}k\int=K(n+dd)\ \ \ \ R\tilde{}k\int\ \ \ dim\int R\tilde{}k\int=\{k(n+1)-k(k-1)2d=2,2\leq k\leq n$ $;(n+dd)-1\ \ \ \ \ \ (d,n,k)=(3,4,7),(4,2,5),(4,3,9),(4,4,14);min\{k(n+1),$ $),(n+dd)\}otherwise\ \ R\tilde{}k\int=C(n+dd)\ \ kC(n,d):=\{n+1d=2,n\geq 2;\ 1n+1$ $(n+dd)\ +1(n,d)=(4,3),(2,4),(3,4),(4,4);\ 1n+1(n+dd)\ otherwise.$ $R\tilde{}k\int\ R\tilde{}k\int\ R\tilde{}k\int\ C(n+dd)\ C(n+dd)\ R\tilde{}k\int=R(n+dd)\ R\tilde{}k\int\ R(n+dd)$ $R\tilde{}k\int\ R\tilde{}k\int\ kmax(n,d)\leq 2\ (42/(n+1))(n+dd)\ \ \ \ kmax(n,d)\leq(n+dd)$ $kmax(n,d)\leq(n+dd)-n\ kmax(n,d)\leq(n+d-1n)\ kmax(n,d)\leq(n+d-1n)-$ $(n+d-5n-2)\ kmax(n,d)\leq(n+d-1n)-(n+d-5n-2)-(n+d-6n-2)\ R\tilde{}k\int$

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peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
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v2(x1,x2,x3)=(x12,x22,x32,x1x2,x1x3,x2x3,x1,x2,x3,1) T∫X3,2 x3,x3x1,x3x2,x32,x12,x22,x1x2,x1,x2,1)Tx32(42/ x3,x1/x3,x2/x3,1)T=x32v1(42/x3,x1/x3,x2/x3)Fq(3+11) Fq(2+22)(q(3+11)−O(q(3+11)−1))(q(2+22)−O(q(2+22)−1)) Fq(3+22)xnd−1vd−1(42/xn,x1/xn,…,xn−1/xn) kC(n,d)≤kFq(n,d)≤rn,d≤(n+d−1d−1)=(d/(n+d))(n+dd) rn,d≤Σi=0d−2(n−2+ii)r1,d−i+(d+n−3d−1)≤Σi=0d−2(n−2+ii)d−i+3 2+(d+n−3d−1)=n+d+22(n+d−3n−1)−n−12(n+d− 2n)+(d+n−3d−1). J:=(n+dd) c∫FqJ dimspan {|ψc∫:c∫FqJ}≤|Rk| x∫Fqn,y∫Fq |ψc∫ ∫=Σz∫Rke(z c)|ξz∫,x=(x1,…,xk)∫(Fqn)ky=(y1,…,yk)∫Fqk|ξz∫=Σ(x,y)∫

Z−1(z)Σxk+1∫Fqn,yk+1∫Fq,w∫Ik+1(∏j=0k xj+1,yj+1,wj+1|Uj|xj,yj,w j∫)|xk+1,yk+1,wk+1∫. dimspan{|ψc∫:c∫FqJ}≤dimspan{|ξz∫:z∫Rk}≤|Rk| c∫FqJ

Results and Discussion

Regioselectivity of Electrophilic Aromatic Substitution Reactions In Malasmoruponaqtm™ Heteroaromatic Systems.

Docking Scores by Using Gemdock Software Discussion

Figure 3: 3D Docking Docking Interactions of the MalasmoruponaqTM™ against the Odorant Binding Protein 7 fromAnopheles gambiae with Four Disulfide Bridges, in complex with an azo compound Interaction of amiprophos methyl with target protein at site II (a) and (b) docked reference molecule in the target protein at thesite II with blue colour showing hydrogen bind between MalasmoruponaqTM™ligand and Tyr(21) of protein. (c) LigPlot analysis of protein and MalasmoruponaqTM™ligand Docking Interactions. Interaction of 5-({ethoxy[(piperidin-1-yl)amino]phosphoryl} oxy)-4-(hydroxymethyl)-2-(triluoromethyl) benzene-1,3-diol withtarget protein at site II (a) and (b) docked molecule in the target protein at the site II with different colours showing diferent polarity andcharges. Pink, blue, green, and cyan represent negative charge, positive charge and hydrophobic and polar residues, respectively. (c) LigPlot analysis of protein and MalasmoruponaqTM™ligand Docking Interactions.

Figure 3 a: MalasmoruponaqTM™ binds inside 3pm2 Crystal structure of a novel type of odorant binding protein from Anopheles gambiae.

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 27 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure 3 b: MalasmoropunaqTM for the generation of the Hydrophobic Docking Interactions of the binds inside 2il3 Structures of an Insect Epsilon-class Glutathione S-transferase from the Malaria Vector Anopheles Gambiae: Evidence for High DDT-detoxifying Activity.

Figure. 3C : 4 Remdesivir 3D Docking Docking Interactions within 4U2X Ebola virus VP24 binding domains in complex with Karyopherin alpha 5 C-terminus Ebola Virus VP24. Remdesivir Targets the Unique NLS Binding Site on Karyopherin Alpha 5 to Selectively Compete with Nuclear Import of Phosphorylated STAT1 with some of 1.680, -13.014 T. and I. Energies respectively.

MalasmoruponaqTM™ligand_fa84c29cba_1   Model T.Energy I.Energy vdW Coul NumRotors RMSD Score

MalasmoruponaqTM™ligand_fa84c29cba_1_run_16.log 1 1.680 -13.014 -7.055 -5.959 14   0.000 -6.722

MalasmoruponaqTM™ligand_fa84c29cba_1_run_17.log 1 1.855 -13.030 -8.577 -4.453 14   8.083 -6.720

MalasmoruponaqTM™ligand_fa84c29cba_1_run_9.log 1 2.128 -12.816 -5.491 -7.325 14   5.362 -6.695

Figure. 3C : *4 Remdesivir 3D Docking Docking Interactions within 4U2X Ebola virus VP24 binding domains in complex with Karyopherin alpha 5 C-terminus Ebola Virus VP24. Remdesivir Targets the Unique NLS Binding Site on Karyopherin Alpha 5 to Selectively Compete with Nuclear Import of Phosphorylated STAT1 with some of 1.680, -13.014 T. and I. Energies respectively.*

MalasmoruponaqTM™ligand_fa84c29cba_1   Model T.Energy I.Energy vdW Coul NumRotors RMSD Score

MalasmoruponaqTM™ligand_fa84c29cba_1_run_16.log 1 1.680 -13.014 -7.055 -5.959 14 0.000 -6.722

MalasmoruponaqTM™ligand_fa84c29cba_1_run_17.log 1 1.855 -13.030 -8.577 -4.453 14 8.083 -6.720

MalasmoruponaqTM™ligand_fa84c29cba_1_run_9.log 1 2.128 -12.816 -5.491 -7.325 14 5.362 -6.695

INPUT FILES

protein = protein_d95714e91d.in
MalasmoruponaqTM™ligand set size = 1
MalasmoruponaqTM™ligand files = MalasmoruponaqTM™ligand_fa84c-29cba
cofactor set size = 0
cofactor files =

GRID SETTINGS

center x = 0
center y = 0
center z = 0
total size x = 20
total size y = 20
total size z = 20
discretization = 0.25

GENETIC DOCKING ALGORITHM SETTINGS

number of evaluations = 1000000
population size = 750
number of runs = 24
seed at run #1 = -1985

JOB INFO

submission date = 2019-05-10 14:10:13
job name = REMDESIVIRTM_4U2X_5cd5b07592d4c
ID = Dock@Dock.CBNKRLUNTH
$Number_of_Clusters = 10
$Seed = -1985

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016   Page 29 of 128

$Leader_Info 1 {

  Num_Members = 36
  Total_Energy = 98.730
  vdW = -4.965
  Coulomb = -15.015
  Internal = 118.710
  rmsd = 0.000

}

$Leader_Info 2 {

  Num_Members = 44
  Total_Energy = 98.789
  vdW = -3.737
  Coulomb = -15.711
  Internal = 118.238
  rmsd = 2.612

}

$Leader_Info 3 {

  Num_Members = 44
  Total_Energy = 100.312
  vdW = -6.114
  Coulomb = -12.392
  Internal = 118.818
  rmsd = 2.597

}

$Leader_Info 4 {

  Num_Members = 51
  Total_Energy = 100.583
  vdW = -7.129
  Coulomb = -7.009
  Internal = 114.722
  rmsd = 3.040

}

$Leader_Info 5 {

  Num_Members = 37
  Total_Energy = 101.291
  vdW = -7.187

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016   Page 30 of 128

Coulomb = -7.807

Internal = 116.285

rmsd = 2.976

}

$Leader_Info 6 {

    Num_Members = 52

    Total_Energy = 101.315

    vdW = -6.777

    Coulomb = -7.894

    Internal = 115.986

    rmsd = 2.472

}

$Leader_Info 7 {

    Num_Members = 45

    Total_Energy = 101.415

    vdW = -6.098

    Coulomb = -9.063

    Internal = 116.576

    rmsd = 2.040

}

$Leader_Info 8 {

    Num_Members = 50

    Total_Energy = 101.487

    vdW = -7.416

    Coulomb = -7.490

    Internal = 116.392

    rmsd = 3.462

}

$Leader_Info 9 {

    Num_Members = 38

    Total_Energy = 101.824

    vdW = -7.701

    Coulomb = -6.190

    Internal = 115.715

    rmsd = 1.563

}

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 31 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

$Leader_Info 10 {

    Num_Members = 45
    Total_Energy = 101.859
    vdW = -7.258
    Coulomb = -4.987
    Internal = 114.104
    rmsd = 3.347

}

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 32 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 4 3D Docking Interaction of MalasmoruponaqTM™ with with the Ebola virus VP35 bound to small molecule (PDB:4IBK).

MalasmoruponaqTM™ligand_511f5cf_1   Model T.Energy I.Energy vdW   Coul   NumRotors RMSD   Score
MalasmoruponaqTM™ligand_511f5cf_1_run_8.log   1   102.984 -1.528 -0.383 -1.145 24   0.000 -5.893
MalasmoruponaqTM™ligand_511f5cf_1_run_8.log   5   103.189 -1.332 -0.297 -1.035 24   2.004 -5.877
MalasmoruponaqTM™ligand_511f5cf_1_run_3.log   1   103.216 -1.150 -1.206 0.056   24   13.366 -5.873
$Number_of_Clusters = 10
$Seed = -1985

$Leader_Info 1 {

  Num_Members = 53
  Total_Energy = 104.336
  vdW = -0.414
  Coulomb = -2.172
  Internal = 106.922
  rmsd = 0.000

}

$Leader_Info 2 {

  Num_Members = 86
  Total_Energy = 104.540
  vdW = -0.415
  Coulomb = -2.000
  Internal = 106.955
  rmsd = 1.125

}

$Leader_Info 3 {

  Num_Members = 109
  Total_Energy = 104.635
  vdW = -0.356

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 33 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Coulomb = -1.910
Internal = 106.901
rmsd = 1.016

}

$Leader_Info 4 {

     Num_Members = 53
     Total_Energy = 104.789
     vdW = -0.358
     Coulomb = -1.775
     Internal = 106.922
     rmsd = 1.951

}

$Leader_Info 5 {

     Num_Members = 1
     Total_Energy = 104.826
     vdW = -0.353
     Coulomb = -1.765
     Internal = 106.944
     rmsd = 1.419

}$Leader_Info 6 {

     Num_Members = 127
     Total_Energy = 104.858
     vdW = -0.349
     Coulomb = -1.702
     Internal = 106.909
     rmsd = 1.538

}

$Leader_Info 7 {

     Num_Members = 19
     Total_Energy = 104.954
     vdW = -0.407
     Coulomb = -1.591
     Internal = 106.951
     rmsd = 2.208

}

$Leader_Info 8 {

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 34 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Num_Members = 14
Total_Energy = 104.960
vdW = -0.301
Coulomb = -1.640
Internal = 106.902
rmsd = 1.790

}

$Leader_Info 9 {

Num_Members = 100
Total_Energy = 105.020
vdW = -0.376
Coulomb = -1.546
Internal = 106.942
rmsd = 1.110

}

$Leader_Info 10 {

Num_Members = 53
Total_Energy = 105.132
vdW = -0.305
Coulomb = -1.527
Internal = 106.965
rmsd = 2.121

}

Figure. 5 3D Docking Interaction of MalasmoruponaqTM™ with 5T42
File Model T.Energy I.Energy vdW Coul NumRotors RMSD Score
MalasmoruponaqTM™ligand_034e0ef11d_1_run_6.log 1 86.415 -21.684 -14.644 -7.040 24 0.000 -7.709

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016   Page 35 of 128

MalasmoruponaqTM™ligand_034e0ef11d_1_run_7.log 1 87.773 -31.876
-11.082 -20.794 24   10.616 -7.397
MalasmoruponaqTM™ligand_034e0ef11d_1_run_7.log 2 88.095 -25.823
0.012   -25.835 24   10.687 -6.165
$Number_of_Clusters = 10
$Seed = -1985

$Leader_Info 1 {

      Num_Members = 44
      Total_Energy = 102.170
      vdW = -13.486
      Coulomb = -5.929
      Internal = 121.585
      rmsd = 0.000

}

$Leader_Info 2 {

      Num_Members = 61
      Total_Energy = 102.379
      vdW = -14.439
      Coulomb = -4.050
      Internal = 120.868
      rmsd = 6.360

}

$Leader_Info 3 {

      Num_Members = 45
      Total_Energy = 103.111
      vdW = -14.130
      Coulomb = -4.146
      Internal = 121.388
      rmsd = 7.234

}

$Leader_Info 4 {

      Num_Members = 44
      Total_Energy = 103.744
      vdW = -6.809
      Coulomb = -16.740
      Internal = 127.293
      rmsd = 12.778

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   **Page 36 of 128**
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

```
}

$Leader_Info 5 {

        Num_Members = 47
        Total_Energy = 103.810
        vdW = -12.990
        Coulomb = -4.603
        Internal = 121.404
        rmsd = 10.608

}

$Leader_Info 6 {

        Num_Members = 47
        Total_Energy = 103.913
        vdW = -10.837
        Coulomb = -6.907
        Internal = 121.657
        rmsd = 2.956

}

$Leader_Info 7 {

        Num_Members = 40
        Total_Energy = 104.080
        vdW = -13.406
        Coulomb = -3.326
        Internal = 120.812
        rmsd = 6.143

}

$Leader_Info 8 {

        Num_Members = 32
        Total_Energy = 104.081
        vdW = -13.484
        Coulomb = -4.923
        Internal = 122.487
        rmsd = 7.300

}

$Leader_Info 9 {
```

Num_Members = 44
Total_Energy = 104.087
vdW = -12.663
Coulomb = -4.308
Internal = 121.059
rmsd = 2.739

}

$Leader_Info 10 {

Num_Members = 46
Total_Energy = 104.654
vdW = -13.618
Coulomb = -3.158
Internal = 121.430
rmsd = 4.571

}

Figure. 6a3 MalasmoruponaqTM™ 3D Docking Docking Interactions within 4U2X Ebola virus VP24 in complex with Karyopherin alpha 5 C-terminus Ebola Virus VP24. MalasmoruponaqTM™ Targets the Unique NLS Binding Site on Karyopherin Alpha 5 to Selectively Compete with Nuclear Import of Phosphorylated STAT1 with some of 86.003, -22.043 T. and I. Energies respectively.

MalasmoruponaqTM™ligand_8a12048cbe_1   Model T.Energy I.Energy vdW Coul NumRotors RMSD Score
MalasmoruponaqTM™ligand_8a12048cbe_1_run_19.log 1 86.003 -22.043 -6.153 -15.890 24   0.000 -7.028
MalasmoruponaqTM™ligand_8a12048cbe_1_run_3.log 1 87.544 -18.873 0.274 -19.147 24   11.729 -6.563
MalasmoruponaqTM™ligand_8a12048cbe_1_run_3.log 2 87.822 -18.565 1.180 -19.745 24   10.698 -6.619

INPUT FILES
protein = protein_64900a2437.in

MalasmoruponaqTM™ligand set size = 1

MalasmoruponaqTM™ligand files = MalasmoruponaqTM™ligand_8a12048cbe

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 38 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

cofactor set size = 0
cofactor files =

GRID SETTINGS

center x = 0
center y = 0
center z = 0
total size x = 20
total size y = 20
total size z = 20
discretization = 0.25

GENETIC DOCKING ALGORITHM SETTINGS

number of evaluations = 1000000
population size = 750
number of runs = 24
seed at run #1 = -1985

JOB INFO

submission date = 2019-05-10 14:06:06
job name = MalasmoruponaqTM™_4U2X__5cd5af7e0794d
ID = Dock@Dock.CBNKRLNGSN
$Number_of_Clusters = 10
$Seed = -1985

$Leader_Info 1 {

       Num_Members = 48
       Total_Energy = 99.732
       vdW = -7.675
       Coulomb = -8.507
       Internal = 115.914
       rmsd = 0.000

}

$Leader_Info 2 {

       Num_Members = 50
       Total_Energy = 99.882
       vdW = -7.922
       Coulomb = -7.522
       Internal = 115.327
       rmsd = 2.024

}

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016   Page 39 of 128

$Leader_Info 3 {

 Num_Members = 43
 Total_Energy = 100.142
 vdW = -4.655
 Coulomb = -11.319
 Internal = 116.116
 rmsd = 3.034

}

$Leader_Info 4 {

 Num_Members = 47
 Total_Energy = 100.369
 vdW = -3.693
 Coulomb = -13.137
 Internal = 117.199
 rmsd = 3.812

}

$Leader_Info 5 {

 Num_Members = 42
 Total_Energy = 100.403
 vdW = -3.563
 Coulomb = -15.853
 Internal = 119.819
 rmsd = 8.351

}

$Leader_Info 6 {

 Num_Members = 3
 Total_Energy = 100.993
 vdW = -6.415
 Coulomb = -11.674
 Internal = 119.083
 rmsd = 3.181

}

$Leader_Info 7 {

 Num_Members = 47
 Total_Energy = 101.033
 vdW = -3.050

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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Coulomb = -14.375
Internal = 118.458
rmsd = 6.616

}

$Leader_Info 8 {

Num_Members = 43
Total_Energy = 101.130
vdW = -7.509
Coulomb = -7.523
Internal = 116.162
rmsd = 3.159

}

$Leader_Info 9 {

Num_Members = 47
Total_Energy = 101.245
vdW = -8.516
Coulomb = -6.368
Internal = 116.128
rmsd = 3.470

}

$Leader_Info 10 {

Num_Members = 23
Total_Energy = 101.270
vdW = -6.182
Coulomb = -8.099
Internal = 115.551
rmsd = 1.154

}

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 41 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 7a2 3D Docking Docking Interactions of the RemdesivirTM witrh the structure of malaria PfNDH2 (PDB:5JWA).

ligand_3108215c85_1   Model T.Energy I.Energy vdW Coul NumRotors RMSD Score

ligand_3108215c85_1_run_9.log 1 -8.378 -29.927 -6.459 -23.468 14   0.000 -6.852
ligand_3108215c85_1_run_9.log 4 -6.106 -28.505 -4.847 -23.658 14   3.170 -6.557
ligand_3108215c85_1_run_9.log 8 -3.625 -28.083 -4.983 -23.100 14   2.640 -6.676
$Number_of_Clusters = 10
$Seed = -1985

$Leader_Info 1 {

   Num_Members = 26
   Total_Energy = -0.808
   vdW = -5.112
   Coulomb = -14.948
   Internal = 19.252
   rmsd = 0.000

}

$Leader_Info 2 {

   Num_Members = 48
   Total_Energy = -0.326
   vdW = -5.154
   Coulomb = -14.907
   Internal = 19.735
   rmsd = 1.187

}

$Leader_Info 3 {

   Num_Members = 43

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif Page 42 of 128 peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

    Total_Energy = -0.026
    vdW = -9.488
    Coulomb = -9.899
    Internal = 19.361
    rmsd = 7.546

}

$Leader_Info 4 {

        Num_Members = 41
        Total_Energy = 0.082
        vdW = -3.430
        Coulomb = -15.871
        Internal = 19.383
        rmsd = 1.906

}

$Leader_Info 5 {

        Num_Members = 47
        Total_Energy = 0.089
        vdW = -3.424
        Coulomb = -16.163
        Internal = 19.676
        rmsd = 3.657

}

$Leader_Info 6 {

        Num_Members = 17
        Total_Energy = 0.095
        vdW = -9.475
        Coulomb = -9.905
        Internal = 19.476
        rmsd = 7.385

}

$Leader_Info 7 {

        Num_Members = 86
        Total_Energy = 0.241
        vdW = -7.091
        Coulomb = -9.835
        Internal = 17.167
        rmsd = 7.309

```
}

$Leader_Info 8 {

        Num_Members = 27
        Total_Energy = 0.292
        vdW = -5.119
        Coulomb = -14.909
        Internal = 20.320
        rmsd = 1.198

}

$Leader_Info 9 {

        Num_Members = 33
        Total_Energy = 0.297
        vdW = -4.261
        Coulomb = -15.052
        Internal = 19.610
        rmsd = 1.597

}

$Leader_Info 10 {

        Num_Members = 46
        Total_Energy = 0.340
        vdW = -6.494
        Coulomb = -14.725
        Internal = 21.560
        rmsd = 3.698

}
```

Figure. 8a1 3D Docking Docking Interactions of the MalasmorupomaqTM small molecule within Crystal structure of Plasmodium vivax lactate dehydrogenase complex with APADH (PDB2:AA3).

MalasmoruponaqTM™ligand_176bb3b2c2_1   Model T.Energy I.Energy vdW Coul NumRotors RMSD Score

MalasmoruponaqTM™ligand_176bb3b2c2_1_run_24.log 1   100.459 -39.488 -5.571 -33.917 24   0.000 -7.086

MalasmoruponaqTM™ligand_176bb3b2c2_1_run_24.log 4   105.530 -35.783 -19.705 -16.078 24   2.722 -7.061

MalasmoruponaqTM™ligand_176bb3b2c2_1_run_24.log 6   107.923 -31.805 -17.966 -13.839 24   3.409 -7.536

$Number_of_Clusters = 10

$Seed = -1985

$Leader_Info 1 {

Num_Members = 32

Total_Energy = 57563.760

vdW = 57202.048

Coulomb = 94.844

Internal = 266.867

rmsd = 0.000

}

$Leader_Info 2 {

Num_Members = 31

Total_Energy = 57564.908

vdW = 57203.754

Coulomb = 94.853

Internal = 266.301

rmsd = 1.057

}

$Leader_Info 3 {

Num_Members = 38

Total_Energy = 57567.788

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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vdW = 57202.590

Coulomb = 92.047

Internal = 273.150

rmsd = 1.957

}

$Leader_Info 4 {

    Num_Members = 35

    Total_Energy = 57567.861

    vdW = 57206.850

    Coulomb = 92.342

    Internal = 268.668

    rmsd = 1.224

}

$Leader_Info 5 {

    Num_Members = 25

    Total_Energy = 57569.075

    vdW = 57206.072

    Coulomb = 92.501

    Internal = 270.502

    rmsd = 3.246

}

$Leader_Info 6 {

    Num_Members = 30

    Total_Energy = 57569.598

    vdW = 57207.120

    Coulomb = 92.007

    Internal = 270.472

    rmsd = 2.192

}

$Leader_Info 7 {

    Num_Members = 8

    Total_Energy = 57570.809

    vdW = 57206.700

    Coulomb = 92.155

    Internal = 271.954

    rmsd = 1.570

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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```
}

$Leader_Info 8 {

        Num_Members = 13
        Total_Energy = 57571.005
        vdW = 57235.421
        Coulomb = 108.828
        Internal = 226.756
        rmsd = 3.029

}

$Leader_Info 9 {

        Num_Members = 40
        Total_Energy = 57571.375
        vdW = 57235.461
        Coulomb = 109.285
        Internal = 226.629
        rmsd = 2.018

}

$Leader_Info 10 {

        Num_Members = 40
        Total_Energy = 57571.452
        vdW = 57203.827
        Coulomb = 94.279
        Internal = 273.346
        rmsd = 2.233

}
```

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 47 of 128

peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of

antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional

Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 9 3D Docking Docking Interactions of MalasmoruponaqTM™ Ebola virus VP24 in complex with Karyopherin alpha 5 C-terminus (PDB:4U2X).

MalasmoruponaqTM™ligand_8a12048cbe_1_ Model T.Energy I.Energy vdW Coul NumRotors RMSD Score

MalasmoruponaqTM™ligand_8a12048cbe_1_run_19.log 1 86.003 -22.043 -6.153 -15.890 24 0.000 -7.028

MalasmoruponaqTM™ligand_8a12048cbe_1_run_3.log 1 87.544 -18.873 0.274 -19.147 24 11.729 -6.563

MalasmoruponaqTM™ligand_8a12048cbe_1_run_3.log 2 87.822 -18.565 1.180 -19.745 24 10.698 -6.619

$Number_of_Clusters = 10

$Seed = -1985

$Leader_Info 1 {

Num_Members = 36

Total_Energy = 98.730

vdW = -4.965

Coulomb = -15.015

Internal = 118.710

rmsd = 0.000

}

$Leader_Info 2 {

Num_Members = 44

Total_Energy = 98.789

vdW = -3.737

Coulomb = -15.711

Internal = 118.238

rmsd = 2.612

}

$Leader_Info 3 {

Num_Members = 44

Total_Energy = 100.312

vdW = -6.114

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 48 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

       Coulomb = -12.392

       Internal = 118.818

       rmsd = 2.597

}

$Leader_Info 4 {

       Num_Members = 51

       Total_Energy = 100.583

       vdW = -7.129

       Coulomb = -7.009

       Internal = 114.722

       rmsd = 3.040

}

$Leader_Info 5 {

       Num_Members = 37

       Total_Energy = 101.291

       vdW = -7.187

       Coulomb = -7.807

       Internal = 116.285

       rmsd = 2.976

}

$Leader_Info 6 {

       Num_Members = 52

       Total_Energy = 101.315

       vdW = -6.777

       Coulomb = -7.894

       Internal = 115.986

       rmsd = 2.472

}

$Leader_Info 7 {

       Num_Members = 45

       Total_Energy = 101.415

       vdW = -6.098

       Coulomb = -9.063

       Internal = 116.576

       rmsd = 2.040

}

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 49 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

$Leader_Info 8 {

      Num_Members = 50
      Total_Energy = 101.487
      vdW = -7.416
      Coulomb = -7.490
      Internal = 116.392
      rmsd = 3.462

}

$Leader_Info 9 {

      Num_Members = 38
      Total_Energy = 101.824
      vdW = -7.701
      Coulomb = -6.190
      Internal = 115.715
      rmsd = 1.563

}

$Leader_Info 10 {

      Num_Members = 45
      Total_Energy = 101.859
      vdW = -7.258
      Coulomb = -4.987
      Internal = 114.104
      rmsd = 3.347

}

Figure. 10a MalasmoruponaqTM™ligand_6aef234f93_1 with 5T42.
MalasmoruponaqTM™ligand_6aef234f93_1 Model T.Energy I.Energy vdW Coul NumRotors RMSD Score
MalasmoruponaqTM™ligand_6aef234f93_1_run_4.log 1 63.957 -42.160 0.249 -42.409 24 0.000 -7.090
MalasmoruponaqTM™ligand_6aef234f93_1_run_4.log 2 64.563 -44.258 -4.554 -39.704 24 4.757 -7.425

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif Page 50 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

MalasmoruponaqTM™ligand_6aef234f93_1_run_11.log   2   66.010
-49.463 -0.135 -49.328 24   3.324 -7.297
$Number_of_Clusters = 10
$Seed = -1985

$Leader_Info 1 {

        Num_Members = 28
        Total_Energy = 65.785
        vdW = 0.249
        Coulomb = -48.134
        Internal = 113.670
        rmsd = 0.000

}

$Leader_Info 2 {

        Num_Members = 63
        Total_Energy = 66.010
        vdW = -0.135
        Coulomb = -49.328
        Internal = 115.473
        rmsd = 2.815

}

$Leader_Info 3 {

        Num_Members = 51
        Total_Energy = 67.122
        vdW = -0.495
        Coulomb = -47.077
        Internal = 114.694
        rmsd = 1.328

}

$Leader_Info 4 {

        Num_Members = 17
        Total_Energy = 67.223
        vdW = -0.358
        Coulomb = -47.545
        Internal = 115.126
        rmsd = 1.139

}

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 51 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

$Leader_Info 5 {

> *Num_Members = 11*
> *Total_Energy = 67.598*
> *vdW = 1.872*
> *Coulomb = -47.077*
> *Internal = 112.803*
> *rmsd = 1.164*

}

$Leader_Info 6 {

> *Num_Members = 46*
> *Total_Energy = 67.782*
> *vdW = -2.687*
> *Coulomb = -42.272*
> *Internal = 112.741*
> *rmsd = 2.093*

}

$Leader_Info 7 {

> *Num_Members = 28*
> *Total_Energy = 67.970*
> *vdW = 0.414*
> *Coulomb = -48.354*
> *Internal = 115.910*
> *rmsd = 2.000*

}

$Leader_Info 8 {

> *Num_Members = 28*
> *Total_Energy = 68.800*
> *vdW = 1.024*
> *Coulomb = -47.418*
> *Internal = 115.194*
> *rmsd = 2.698*

}

$Leader_Info 9 {

> *Num_Members = 43*
> *Total_Energy = 68.871*

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 52 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

    vdW = -1.728

    Coulomb = -44.345

    Internal = 114.943

    rmsd = 2.755

}

$Leader_Info 10 {

    Num_Members = 46

    Total_Energy = 69.079

    vdW = -0.257

    Coulomb = -47.617

    Internal = 116.953

    rmsd = 2.828

}

Compound	Score	T. Energy	I. Energy
> ligand_fa84c29cba_1	-6.722	1.680	-13.014

Figure. 12b Remdesivir 3D Docking Docking Interactions within 4U2X Ebola virus VP24 binding domains in complex with Karyopherin alpha 5 C-terminus Ebola Virus VP24. Remdesivir Targets the Unique NLS Binding Site on Karyopherin Alpha 5 to Selectively Compete with Nuclear Import of Phosphorylated STAT1 with some of 1.680, -13.014 T. and I. Energies respectively.

igand_fa84c29cba_1   Model T.Energy I.Energy vdW   Coul   NumRotors RMSD   Score
ligand_fa84c29cba_1_run_16.log 1   1.680 -13.014 -7.055 -5.959   14   0.000 -6.722
igand_fa84c29cba_1_run_17.log 1   1.855 -13.030 -8.577 -4.453   14   8.083 -6.720
igand_fa84c29cba_1_run_9.log 1   2.128 -12.816 -5.491 -7.325   14   5.362 -6.695

INPUT FILES

protein = protein_d95714e91d.in
MalasmoruponaqTM™ligand set size = 1
MalasmoruponaqTM™ligand files = MalasmoruponaqTM™ligand_fa84c29cba
cofactor set size = 0
cofactor files =

GRID SETTINGS

center x = 0

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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center y = 0

center z = 0

total size x = 20

total size y = 20

total size z = 20

discretization = 0.25

GENETIC DOCKING ALGORITHM SETTINGS

number of evaluations = 1000000

population size = 750

number of runs = 24

seed at run #1 = -1985

JOB INFO

submission date = 2019-05-10 14:10:13

job name = REMDESIVIRTM_4U2X_5cd5b07592d4c

ID = Dock@Dock.CBNKRLUNTH

$Number_of_Clusters = 10

$Seed = -1985

$Leader_Info 1 {

> *Num_Members = 26*
> *Total_Energy = 86.003*
> *vdW = -6.153*
> *Coulomb = -15.890*
> *Internal = 108.046*
> *rmsd = 0.000*

}

$Leader_Info 2 {

> *Num_Members = 39*
> *Total_Energy = 88.767*
> *vdW = -2.152*
> *Coulomb = -15.153*
> *Internal = 106.073*
> *rmsd = 9.691*

}

$Leader_Info 3 {

> *Num_Members = 29*
> *Total_Energy = 90.222*
> *vdW = 1.302*

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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Coulomb = -18.305
Internal = 107.226
rmsd = 9.778

}

$Leader_Info 4 {

   Num_Members = 39
   Total_Energy = 90.444
   vdW = -0.041
   Coulomb = -17.359
   Internal = 107.843
   rmsd = 8.943

}

$Leader_Info 5 {

   Num_Members = 49
   Total_Energy = 91.144
   vdW = 2.338
   Coulomb = -18.217
   Internal = 107.023
   rmsd = 9.892

}

$Leader_Info 6 {

   Num_Members = 43
   Total_Energy = 91.204
   vdW = 2.380
   Coulomb = -17.850
   Internal = 106.674
   rmsd = 9.589

}

$Leader_Info 7 {

   Num_Members = 32
   Total_Energy = 91.470
   vdW = 1.118
   Coulomb = -17.291
   Internal = 107.643
   rmsd = 9.168

}

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif Page 55 of 128 peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

$Leader_Info 8 {

      Num_Members = 48

      Total_Energy = 91.571

      vdW = -4.667

      Coulomb = -11.973

      Internal = 108.211

      rmsd = 8.440

}

$Leader_Info 9 {

      Num_Members = 40

      Total_Energy = 91.684

      vdW = -7.883

      Coulomb = -7.760

      Internal = 107.328

      rmsd = 8.161

}

$Leader_Info 10 {

      Num_Members = 47

      Total_Energy = 91.927

      vdW = -6.731

      Coulomb = -6.452

      Internal = 105.110

      rmsd = 4.570

}

Compound	Score	T. Energy	I. Energy
> ligand_8a12048cbe_1	-7.028	86.003	-22.043

Figure. 13c MalasmoruponaqTM™ 3D Docking Docking Interactions within 4U2X Ebola virus VP24 in complex with Karyopherin alpha 5 C-terminus Ebola Virus VP24. MalasmoruponaqTM™ Targets the Unique NLS Binding Site on Karyopherin Alpha 5 to Selectively Compete with Nuclear Import of Phosphorylated STAT1 with some of 86.003, -22.043 T. and I. Energies respectively.

File Model T.Energy I.Energy vdW Coul NumRotors RMSD Score

MalasmoruponaqTM™ligand_8a12048cbe_1_run_19.log 1 86.003 -22.043 -6.153 -15.890 24 0.000 -7.028

MalasmoruponaqTM™ligand_8a12048cbe_1_run_3.log 1 87.544 -18.873 0.274 -19.147 24 11.729 -6.563

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016   Page 56 of 128

MalasmoruponaqTM™ligand_8a12048cbe_1_run_3.log   2   87.822
-18.565 1.180 -19.745 24   10.698 -6.619

INPUT FILES

protein = protein_64900a2437.in
MalasmoruponaqTM™ligand set size = 1
MalasmoruponaqTM™ligand   files   =   MalasmoruponaqTM™li-gand_8a12048cbe
cofactor set size = 0
cofactor files =

GRID SETTINGS

center x = 0
center y = 0
center z = 0
total size x = 20
total size y = 20
total size z = 20
discretization = 0.25

GENETIC DOCKING ALGORITHM SETTINGS

number of evaluations = 1000000
population size = 750
number of runs = 24
seed at run #1 = -1985

JOB INFO

submission date = 2019-05-10 14:06:06
job name = MalasmoruponaqTM™_4U2X__5cd5af7e0794d
ID = Dock@Dock.CBNKRLNGSN
$Number_of_Clusters = 10
$Seed = -1985

$Leader_Info 1 {

*   Num_Members = 55*
*   Total_Energy = 88.010*
*   vdW = -6.882*
*   Coulomb = -17.147*
*   Internal = 112.039*
*   rmsd = 0.000*
}

$Leader_Info 2 {

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 57 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

```
        Num_Members = 77
        Total_Energy = 89.087
        vdW = -7.533
        Coulomb = -14.240
        Internal = 110.860
        rmsd = 1.225


}


$Leader_Info 3 {


        Num_Members = 43
        Total_Energy = 89.933
        vdW = -4.421
        Coulomb = -16.766
        Internal = 111.120
        rmsd = 1.388


}


$Leader_Info 4 {


        Num_Members = 54
        Total_Energy = 90.104
        vdW = -3.341
        Coulomb = -14.815
        Internal = 108.260
        rmsd = 2.009


}


$Leader_Info 5 {


        Num_Members = 10
        Total_Energy = 90.311
        vdW = -4.156
        Coulomb = -15.630
        Internal = 110.098
        rmsd = 1.738


}


$Leader_Info 6 {


        Num_Members = 45
        Total_Energy = 91.169
        vdW = -4.544
        Coulomb = -12.537
```
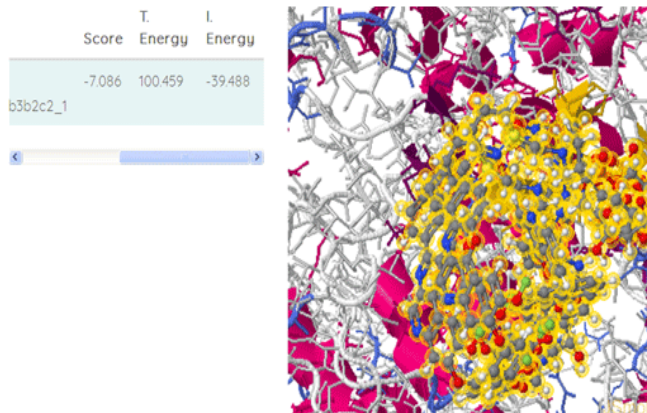
Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 58 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Internal = 108.250
rmsd = 2.675

}

$Leader_Info 7 {

Num_Members = 38
Total_Energy = 91.260
vdW = -5.771
Coulomb = -12.433
Internal = 109.464
rmsd = 3.033

}

$Leader_Info 8 {

Num_Members = 13
Total_Energy = 91.436
vdW = -4.056
Coulomb = -12.888
Internal = 108.379
rmsd = 3.344

}

$Leader_Info 9 {

Num_Members = 43
Total_Energy = 91.802
vdW = -8.555
Coulomb = -10.338
Internal = 110.695
rmsd = 2.431

}

$Leader_Info 10 {

Num_Members = 8
Total_Energy = 91.893
vdW = -7.628
Coulomb = -11.134
Internal = 110.655
rmsd = 1.458

}

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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Figure. 14 MalasmoruponaqTM™_341139 fragmented miracle molecule binds within Ebola virus envelope protein MPER/TM domains (PDB:5T42) and its interaction with the fusion loop with some of -6.343 (score) -128.505 (T.Energy) and -27.128(I.Energy).

MalasmoruponaqTM™_fr2_	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
MalasmoruponaqTM™ligand_341139_1_run_18.log	1	-128.505	-27.128	-2.477	-24.651	9	0.000	-6.343
MalasmoruponaqTM™ligand_341139_1_run_16.log	1	-124.642	-23.705	-1.647	-22.058	9	2.572	-6.220
MalasmoruponaqTM™ligand_341139_1_run_2.log	4	-122.279	-21.155	-5.848	-15.307	9	3.429	-6.612

 $Number_of_Clusters = 10
$Seed = -1985

$Leader_Info 1 {

        Num_Members = 29
        Total_Energy = 131.711
        vdW = -22.683
        Coulomb = -0.117
        Internal = 154.511
        rmsd = 0.000

}

$Leader_Info 2 {

        Num_Members = 38
        Total_Energy = 132.012
        vdW = -14.754
        Coulomb = -3.945
        Internal = 150.711
        rmsd = 10.468

}

$Leader_Info 3 {

        Num_Members = 33
        Total_Energy = 132.078
        vdW = -22.913
        Coulomb = -0.393

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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Internal = 155.385
rmsd = 1.090

}

$Leader_Info 4 {

    Num_Members = 10
    Total_Energy = 133.348
    vdW = -21.487
    Coulomb = 0.098
    Internal = 154.737
    rmsd = 1.718

}

$Leader_Info 5 {

    Num_Members = 46
    Total_Energy = 133.866
    vdW = -21.670
    Coulomb = -2.181
    Internal = 157.717
    rmsd = 3.691

}

$Leader_Info 6 {

    Num_Members = 41
    Total_Energy = 133.922
    vdW = -12.556
    Coulomb = -2.084
    Internal = 148.562
    rmsd = 11.099

}

$Leader_Info 7 {

    Num_Members = 45
    Total_Energy = 134.186
    vdW = -12.801
    Coulomb = -5.490
    Internal = 152.477
    rmsd = 9.068

}

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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$Leader_Info 8 {

    Num_Members = 30
    Total_Energy = 134.222
    vdW = -13.540
    Coulomb = -2.487
    Internal = 150.249
    rmsd = 10.702

}

$Leader_Info 9 {

    Num_Members = 1
    Total_Energy = 134.240
    vdW = -20.009
    Coulomb = -0.356
    Internal = 154.605
    rmsd = 1.068

}

$Leader_Info 10 {

    Num_Members = 39
    Total_Energy = 134.352
    vdW = -19.740
    Coulomb = -0.147
    Internal = 154.239
    rmsd = 1.523

}
$Number_of_Clusters = 10
$Seed = -1985

$Leader_Info 1 {

    Num_Members = 68
    Total_Energy = 134.485
    vdW = -19.278
    Coulomb = -0.471
    Internal = 154.233
    rmsd = 0.000

}

$Leader_Info 2 {

    Num_Members = 55

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 62 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

```
        Total_Energy = 134.500
        vdW = -15.826
        Coulomb = -4.490
        Internal = 154.816
        rmsd = 5.768


}

$Leader_Info 3 {

        Num_Members = 56
        Total_Energy = 134.917
        vdW = -18.635
        Coulomb = -1.716
        Internal = 155.267
        rmsd = 11.166


}

$Leader_Info 4 {

        Num_Members = 15
        Total_Energy = 135.171
        vdW = -15.072
        Coulomb = -5.145
        Internal = 155.389
        rmsd = 6.248


}

$Leader_Info 5 {

        Num_Members = 66
        Total_Energy = 136.427
        vdW = -11.909
        Coulomb = -6.827
        Internal = 155.163
        rmsd = 10.545


}

$Leader_Info 6 {

        Num_Members = 46
        Total_Energy = 136.947
        vdW = -16.561
        Coulomb = -3.950
        Internal = 157.459
        rmsd = 4.579
```

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 63 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

}

$Leader_Info 7 {

  Num_Members = 46
  Total_Energy = 137.284
  vdW = -17.669
  Coulomb = 0.034
  Internal = 154.918
  rmsd = 5.845

}

$Leader_Info 8 {

  Num_Members = 42
  Total_Energy = 137.443
  vdW = -18.601
  Coulomb = -1.884
  Internal = 157.928
  rmsd = 2.841

}

$Leader_Info 9 {

  Num_Members = 46
  Total_Energy = 137.470
  vdW = -18.137
  Coulomb = -0.420
  Internal = 156.028
  rmsd = 10.020

}

$Leader_Info 10 {

  Num_Members = 32
  Total_Energy = 137.518
  vdW = -18.137
  Coulomb = -0.073
  Internal = 155.729
  rmsd = 1.578

}

Figure.15 MalasmoruponaqTM™_937d73c677_1 fragmented compound binds with some of -10.542 (score), 126.367(T.Energy), - 31.956(I.Energy) within (PDB: 4U2X) Ebola virus VP24 in complex with Karyopherin alpha 5 C-terminus.

MalasmoruponaqTM™_937d73c677_1 Model T.Energy I.Energy   vdW   Coul   NumRotors   RMSD   Score MalasmoruponaqTM™ligand_937d73c677_1_run_24.log

1

126.367

-31.956

-28.665

-3.291

13

0.000

-10.542

MalasmoruponaqTM™ligand_937d73c677_1_run_22.log

1

127.608

-21.878

-18.162

-3.716

13

10.745

-8.411

MalasmoruponaqTM™ligand_937d73c677_1_run_15.log

1

128.697

-20.639

-18.137

-2.502

13

8.540

-8.763

$Number_of_Clusters = 10

$Seed = -1985

$Leader_Info 1 {

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 65 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

```
        Num_Members = 29
        Total_Energy = 131.711
        vdW = -22.683
        Coulomb = -0.117
        Internal = 154.511
        rmsd = 0.000


}

$Leader_Info 2 {


        Num_Members = 38
        Total_Energy = 132.012
        vdW = -14.754
        Coulomb = -3.945
        Internal = 150.711
        rmsd = 10.468


}

$Leader_Info 3 {


        Num_Members = 33
        Total_Energy = 132.078
        vdW = -22.913
        Coulomb = -0.393
        Internal = 155.385
        rmsd = 1.090


}

$Leader_Info 4 {


        Num_Members = 10
        Total_Energy = 133.348
        vdW = -21.487
        Coulomb = 0.098
        Internal = 154.737
        rmsd = 1.718


}

$Leader_Info 5 {


        Num_Members = 46
        Total_Energy = 133.866
        vdW = -21.670
        Coulomb = -2.181
        Internal = 157.717
```

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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rmsd = 3.691

}

$Leader_Info 6 {

> *Num_Members = 41*
> *Total_Energy = 133.922*
> *vdW = -12.556*
> *Coulomb = -2.084*
> *Internal = 148.562*
> *rmsd = 11.099*

}

$Leader_Info 7 {

> *Num_Members = 45*
> *Total_Energy = 134.186*
> *vdW = -12.801*
> *Coulomb = -5.490*
> *Internal = 152.477*
> *rmsd = 9.068*

}

$Leader_Info 8 {

> *Num_Members = 30*
> *Total_Energy = 134.222*
> *vdW = -13.540*
> *Coulomb = -2.487*
> *Internal = 150.249*
> *rmsd = 10.702*

}

$Leader_Info 9 {

> *Num_Members = 1*
> *Total_Energy = 134.240*
> *vdW = -20.009*
> *Coulomb = -0.356*
> *Internal = 154.605*
> *rmsd = 1.068*

}

$Leader_Info 10 {

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 67 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

```
        Num_Members = 39
        Total_Energy = 134.352
        vdW = -19.740
        Coulomb = -0.147
        Internal = 154.239
        rmsd = 1.523

}
$Number_of_Clusters = 10
$Seed = -1985

$Leader_Info 1 {

        Num_Members = 68
        Total_Energy = 134.485
        vdW = -19.278
        Coulomb = -0.471
        Internal = 154.233
        rmsd = 0.000

}

$Leader_Info 2 {

        Num_Members = 55
        Total_Energy = 134.500
        vdW = -15.826
        Coulomb = -4.490
        Internal = 154.816
        rmsd = 5.768

}

$Leader_Info 3 {

        Num_Members = 56
        Total_Energy = 134.917
        vdW = -18.635
        Coulomb = -1.716
        Internal = 155.267
        rmsd = 11.166

}

$Leader_Info 4 {

        Num_Members = 15
        Total_Energy = 135.171
```

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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```
        vdW = -15.072
        Coulomb = -5.145
        Internal = 155.389
        rmsd = 6.248


}

$Leader_Info 5 {

        Num_Members = 66
        Total_Energy = 136.427
        vdW = -11.909
        Coulomb = -6.827
        Internal = 155.163
        rmsd = 10.545


}

$Leader_Info 6 {

        Num_Members = 46
        Total_Energy = 136.947
        vdW = -16.561
        Coulomb = -3.950
        Internal = 157.459
        rmsd = 4.579


}

$Leader_Info 7 {

        Num_Members = 46
        Total_Energy = 137.284
        vdW = -17.669
        Coulomb = 0.034
        Internal = 154.918
        rmsd = 5.845


}

$Leader_Info 8 {

        Num_Members = 42
        Total_Energy = 137.443
        vdW = -18.601
        Coulomb = -1.884
        Internal = 157.928
        rmsd = 2.841
```

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 69 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

```
}

$Leader_Info 9 {

        Num_Members = 46
        Total_Energy = 137.470
        vdW = -18.137
        Coulomb = -0.420
        Internal = 156.028
        rmsd = 10.020

}

$Leader_Info 10 {

        Num_Members = 32
        Total_Energy = 137.518
        vdW = -18.137
        Coulomb = -0.073
        Internal = 155.729
        rmsd = 1.578

}
$Number_of_Clusters = 10
$Seed = -1985

$Leader_Info 1 {

        Num_Members = 35
        Total_Energy = 132.457
        vdW = -15.519
        Coulomb = -10.442
        Internal = 158.418
        rmsd = 0.000

}

$Leader_Info 2 {

        Num_Members = 73
        Total_Energy = 132.725
        vdW = -13.482
        Coulomb = -15.013
        Internal = 161.219
        rmsd = 9.261

}

$Leader_Info 3 {
```

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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Num_Members = 57

Total_Energy = 132.808

vdW = -16.022

Coulomb = -11.252

Internal = 160.082

rmsd = 9.865

}

$Leader_Info 4 {

Num_Members = 65

Total_Energy = 132.842

vdW = -17.204

Coulomb = -4.376

Internal = 154.421

rmsd = 9.338

}

$Leader_Info 5 {

Num_Members = 14

Total_Energy = 134.506

vdW = -15.149

Coulomb = -10.917

Internal = 160.572

rmsd = 9.471

}

$Leader_Info 6 {

Num_Members = 42

Total_Energy = 134.834

vdW = -17.975

Coulomb = -1.744

Internal = 154.554

rmsd = 9.967

}

$Leader_Info 7 {

Num_Members = 48

Total_Energy = 134.837

vdW = -18.842

Coulomb = -6.757

Internal = 160.436

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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rmsd = 3.480

}

$Leader_Info 8 {

    Num_Members = 9
    Total_Energy = 135.229
    vdW = -16.183
    Coulomb = -3.691
    Internal = 155.102
    rmsd = 8.893

}

$Leader_Info 9 {

    Num_Members = 2
    Total_Energy = 135.282
    vdW = -16.907
    Coulomb = -2.083
    Internal = 154.272
    rmsd = 9.344

}

$Leader_Info 10 {

    Num_Members = 46
    Total_Energy = 135.500
    vdW = -13.362
    Coulomb = -6.116
    Internal = 154.977
    rmsd = 9.710

}

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 72 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 16 2 MalasmorupomaqTM___5d22de8865750 3D Docking Docking Interactions with 5T42.

File Model T.Energy I.Energy vdW   Coul   NumRotors RMSD   Score
ligand_e71e09e2e3_1_run_15.log 1   77.132 -35.035 4.622 -39.657 24   0.000 -6.981
ligand_e71e09e2e3_1_run_15.log 3   78.586 -38.541 -3.037 -35.504 24   2.843 -7.859
ligand_e71e09e2e3_1_run_8.log 1   78.598 -37.275 -2.045 -35.230 24   3.111 -7.373

Figure.17 MalasmoruponaqTM™ligand_341139 fragmented miracle molecules with some of ligand_341139_1 -6.343 (score) -128.505 (T.Energy) and -27.128(I.Energy) within Ebola virus envelope protein MPER/TM domain (PDB:5T42) and its interaction with the fusion loop explains their fusion activity.

MalasmoruponaqTM™ ligand_341139_fr2_	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_341139_1_run_18.log	1	-128.505	-27.128	-2.477	-24.651	9	0.000	-6.343
ligand_341139_1_run_16.log	1	-124.642	-23.705	-1.647	-22.058	9	2.572	-6.220
ligand_341139_1_run_2.log	4	-122.279	-21.155	-5.848	-15.307	9	3.429	-6.612

Figure.18 MalasmoruponaqTM™ligand_341139 fragmented miracle molecules with some of ligand_341139_ with some of 1 T.Energy: -130.078, I.Energy: -30.310, vdW: -2.363 within (PDB: 4U2X) Ebola virus VP24 in complex with Karyopherin alpha 5 C-terminus.

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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MalasmoruponaqTM™ligand_341139_r2_	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_388d8f941b_1_run_9.log	1	-130.078	-30.310	-2.363	-27.947	9	0.000	-5.761
ligand_388d8f941b_1_run_23.log	1	-130.057	-30.384	1.467	-31.851	9	8.912	-6.375
ligand_388d8f941b_1_run_23.log	2	-129.845	-33.880	-3.140	-30.740	9	9.651	-6.736

Rank	Compound	Score	T. Energy	I. Energy
1	ligand_7963ea2b6_1	-7.066	-141.493	-44.331

Figure.19 MalasmoruponaqTM™_3D Docking Docking Interactions within 5JWA.

MalasmoruponaqTM™	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_7963ea2b6_1_run_23.log	1	-141.493	-44.331	-5.061	-39.270	9	0.000	-7.066
ligand_7963ea2b6_1_run_11.log	1	-140.308	-40.317	1.757	-42.074	9	7.937	-6.644
ligand_7963ea2b6_1_run_11.log	3	-138.103	-45.689	3.820	-49.509	9	2.036	-6.628

Rank	Compound	Score	T. Energy	I. Energy
1	ligand_0323350cd7_1	-7.333	-132.428	-31.958

Figure.20 MalasmoruponaqTM™ligand_0323350cd7_1 3D Docking Docking Interactions with (PDB:5T42).

MalasmoruponaqTM™ ligand_0323350cd7_1	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_0323350cd7_1_run_17.log	1	-132.428	-31.958	-7.560	-24.398	9	0.000	-7.333
ligand_0323350cd7_1_run_15.log	1	-131.406	-31.195	-2.600	-28.595	9	9.637	-7.249
ligand_0323350cd7_1_run_3.log	1	-130.468	-31.405	-5.172	-26.233	9	11.349	-6.983

Figure.21a Structure of Ebola virus nucleoprotein N-terminal fragment bound to a peptide derived from Ebola VP35.

MalasmoruponaqTM™ligand_b91ab3e842_	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_b91ab3e842_1_run_22.log	4	-102.490	-0.807	-0.000	-0.807	9	0.000	24.988
ligand_b91ab3e842_1_run_22.log	1	-102.490	-0.808	-0.000	-0.808	9	3.169	24.988
ligand_b91ab3e842_1_run_22.log	8	-102.489	-0.806	-0.000	-0.806	9	8.806	24.988

Figure.22 MalasmoruponaqTM™_937d73c677_1 fragmented compound that binds with some of -10.542 (score), 126.367(T.Energy), - 31.956(I.Energy) within (PDB: 4U2X) Ebola virus VP24 in complex with Karyopherin alpha 5 C-terminus.

MalasmoruponaqTM™_937d73c677_1	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_937d73c677_1_run_24.log	1	126.367	-31.956	-28.665	-3.291	13	0.000	-10.542
ligand_937d73c677_1_run_22.log	1	127.608	-21.878	-18.162	-3.716	13	10.745	-8.411
ligand_937d73c677_1_run_15.log	1	128.697	-20.639	-18.137	-2.502	13	8.540	-8.763

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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Figure.23 MalasmoruponaqTM™_3D Docking Docking Interactions within 5JWA

MalasmoruponaqTM™	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_018c119241_1_run_1.log	1	126.303	-23.221	-3.590	-19.631	13	0.000	-6.719
ligand_018c119241_1_run_13.log	1	126.973	-27.258	-7.603	-19.655	13	7.800	-7.783
ligand_018c119241_1_run_1.log	4	127.060	-21.963	-3.775	-18.188	13	2.365	-6.797

Figure.24 MalasmoruponaqTM™__ igand_9cd1e4c09f_3D Docking Docking Interactions within 5JWA.

MalasmoruponaqTM™_5LGE_	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_9cd1e4c09f_1_run_13.log	1	93.406	-41.149	-6.106	-35.043	26	0.000	-6.981
ligand_9cd1e4c09f_1_run_5.log	1	93.471	-32.825	-0.430	-32.395	26	3.364	-6.555
ligand_9cd1e4c09f_1_run_18.log	1	95.952	-34.990	-0.372	-34.618	26	6.103	-6.346

Figure.25 3D Docking Docking Interactions of the MalasmoruponaqTM™ with Pyranose 2-oxidase V546C mutant with 2-fluorinated galactose (PDB:4MOQ)

MalasmoruponaqTM™	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_f2baf6a968_1_run_1.log	1	86.719	-26.604	-22.653	-3.951	24	0.000	-8.677
ligand_f2baf6a968_1_run_1.log	2	86.734	-28.123	-26.410	-1.713	24	2.988	-9.340
ligand_f2baf6a968_1_run_1.log	3	87.052	-26.712	-22.031	-4.681	24	2.074	-8.418

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016   Page 76 of 128

Figure.26 MalasmoruponaqTM™_with the Structure of the Ebola virus envelope protein MPER/TM domain and its interaction with the fusion loop explains their fusion activity (PDB:5T42).

MalasmoruponaqTM™ _ ligand_0c92b908ca_1	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
MalasmoruponaqTM™ligand_0c92b908ca_1_run_23.log	1	-93.737	-265.495	-168.542	-96.953	13	0.000	-40.183
MalasmoruponaqTM™ligand_0c92b908ca_1_run_23.log	3	-71.278	-252.228	-132.826	-119.402	13	7.852	-30.688
MalasmoruponaqTM™ligand_0c92b908ca_1_run_14.log	2	-70.987	-250.716	-121.746	-128.970	13	8.965	-31.350

Figure.27 3D Docking Docking Interactions of the Remdesivir Small Molecule within 4U2X Ebola virus VP24 binding domains in complex with Karyopherin alpha 5 C-terminus Ebola Virus VP24. Remdesivir Targets the Unique NLS Binding Site on Karyopherin Alpha 5 to Selectively Compete with Nuclear Import of Phosphorylated STAT1 with some of 1.680, -13.014 T. and I. Energies respectively.

Remdesivir	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_fa84c29cba_1_run_16.log	1	1.680	-13.014	-7.055	-5.959	14	0.000	-6.722
ligand_fa84c29cba_1_run_17.log	1	1.855	-13.030	-8.577	-4.453	14	8.083	-6.720
ligand_fa84c29cba_1_run_9.log	1	2.128	-12.816	-5.491	-7.325	14	5.362	-6.695

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 77 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure.27a Remdesivir 3D Docking Docking Interactions within 5JWA.

Remdesivir	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_09924344f_1_run_9.log	1	-8.378	-29.927	-6.459	-23.468	14	0.000	-6.852
ligand_09924344f_1_run_9.log	4	-6.106	-28.505	-4.847	-23.658	14	3.170	-6.557
ligand_09924344f_1_run_9.log	8	-3.625	-28.083	-4.983	-23.100	14	2.640	-6.676

Figure.27b Remdesivir 3D Docking Docking Interactions within 4MOQ.

Remdesivir	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
ligand_c43b99a_1_run_9.log	1	-9.799	-29.894	-14.221	-15.673	14	0.000	-7.648
ligand_c43b99a_1_run_17.log	1	-9.240	-28.251	-17.729	-10.522	14	6.017	-7.996
ligand_c43b99a_1_run_3.log	1	-9.204	-28.854	-10.461	-18.393	14	7.702	-7.447

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 78 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 28 for the generation of the Hydrophobic Docking Interactions of the 2 MalasmoruponaqTM™ binding site(s) in 3ZML (glutathione s-transferase e2). GSH (Glutathione)GSH-A-1222 Interacting chains: A

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	14A	PRO	3.96	3492	87
2	108A	PHE	3.84	3491	822

Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	55A	ILE	2.08	3.01	156.55	✖	✖	3495 [Nam]	403 [O2]
2	55A	ILE	1.98	2.88	151.62	✔	✖	400 [Nam]	3498 [O2]
3	67A	GLU	1.79	2.72	150.00	✖	✔	3486 [N3]	496 [O2]
4	68A	SER	1.77	2.74	166.26	✔	✖	497 [Nam]	3490 [O.co2]
5	112A	ARG	2.16	2.86	126.73	✔	✔	857 [Ng+]	3494 [O2]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	55A	ILE	3.73	2.87	154.71	100.38	✖	3490 [O.co2]	403 [O2]	3639
2	67A	GLU	2.87	3.51	120.12	82.93	✔	488 [Nam]	3490 [O.co2]	3639
3	112A	ARG	3.55	3.31	160.80	86.10	✖	3501 [Nam]	855 [Ng+]	3710
4	112A	ARG	3.99	3.55	126.69	118.15	✔	858 [Ng+]	3504 [O.co2]	3715

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Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	41A	HIS	4.89	✔	Carboxylate	3504, 3505
2	53A	HIS	4.12	✔	Carboxylate	3504, 3505
3	69A	HIS	4.82	✔	Carboxylate	3490, 3489
4	112A	ARG	4.30	✔	Carboxylate	3504, 3505

GSH-B-1222 🏅

Interacting chains: B

Figure. 29 Docking Interactions MalasmoruponaqTM™ binding site(s) in 3ZML (glutathione s-transferase e2). GSH (Glutathione)GSH-A-1222 Interacting chains: A

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	14B	PRO	3.97	3512	1834
2	108B	PHE	3.94	3511	2569

Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	55B	ILE	1.90	2.84	157.25	✔	✖	2147 [Nam]	3518 [O2]
2	55B	ILE	2.14	3.02	149.47	✖	✖	3515 [Nam]	2150 [O2]
3	67B	GLU	1.84	2.76	148.40	✖	✔	3506 [N3]	2243 [O2]
4	68B	SER	1.86	2.80	158.50	✔	✖	2244 [Nam]	3509 [O.co2]
5	112B	ARG	2.09	2.77	125.26	✔	✔	2604 [Ng+]	3514 [O2]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	41B	HIS	3.34	4.01	114.23	112.32	✖	3525 [O.co2]	2038 [N2]	3906
2	41B	HIS	3.53	3.85	116.36	112.25	✖	3525 [O.co2]	2038 [N2]	3905
3	67B	GLU	2.94	3.61	112.73	84.58	✔	2235 [Nam]	3509 [O.co2]	3929
4	69B	HIS	3.79	3.43	140.15	101.11	✖	3510 [O.co2]	2259 [N2]	3978
5	112B	ARG	3.70	4.07	142.54	119.00	✔	2605 [Ng+]	3525 [O.co2]	3921
6	112B	ARG	2.71	4.07	142.54	139.76	✔	2605 [Ng+]	3524 [O.co2]	3921
7	112B	ARG	4.02	3.72	126.88	121.61	✔	2605 [Ng+]	3525 [O.co2]	3607
8	112B	ARG	3.52	3.34	163.94	83.88	✖	3521 [Nam]	2602 [Ng+]	3984

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	41B	HIS	4.86	✔	Carboxylate	3524, 3525
2	53B	HIS	4.16	✔	Carboxylate	3524, 3525
3	69B	HIS	4.94	✔	Carboxylate	3509, 3510
4	112B	ARG	4.19	✔	Carboxylate	3524, 3525

Metal Complexes MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase).

Metal Complexes MalasmoruponaqTM™ binding site(s) in 3EBH *(m1 family aminopeptidase).*						
Index	Residue	AA	Metal	Target	Distance	Location
Complex 1: Mg, octahedral (6)						
1	26A	HOH	7385	7404	2.02	water
2	250A	GLY	7385	442	2.06	protein.mainchain
3	1099A	HOH	7385	7584	2.14	water
4	1212A	HOH	7385	7697	2.21	water
5	1520A	HOH	7385	8005	2.10	water
6	1521A	HOH	7385	8006	2.14	water

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Metal Complexes MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase).						
Index	Residue	AA	Metal	Target	Distance	Location
MalasmoruponaqTM™ small molecule GOL (Glycerol) GOL-A-1086 Interacting chains: A						

Figure. 31 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase).
ION MG (magnesium ion) MG-A-7 Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	479A	LYS	2.00	3.00	163.98	✔	✔	2281 [N3]	7354 [O3]
2	880A	TYR	2.66	3.58	157.63	✘	✘	7354 [O3]	5605 [O2]
3	888A	ASP	1.88	2.87	175.63	✔	✘	5673 [Nam]	7350 [O3]
4	888A	ASP	3.26	3.76	113.93	✘	✘	7350 [O3]	5676 [O2]
5	895A	ARG	2.30	3.16	144.37	✔	✔	5747 [Ng+]	7352 [O3]
6	895A	ARG	2.15	3.05	150.63	✔	✔	5748 [Ng+]	7352 [O3]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	925A	TYR	2.94	3.72	101.71	99.74	✔	5991 [O3]	7354 [O3]	7397

GOL-A-2 Interacting chains: A

Figure. 32 Hydrogen Bonds from the. MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase), ION MG (magnesium ion) MG-A-7 Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	765A	TYR	3.47	4.05	120.99	✘	✔	7356 [O3]	4661 [O3]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	826A	SER	4.09	2.98	126.34	117.00	✘	7358 [O3]	5160 [O2]	8153
2	827A	LEU	2.94	2.98	126.34	73.86	✘	7358 [O3]	5166 [O2]	8153

GOL-A-3

Interacting chains: A

Figure. 33 Water Bridges MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase), ION MG (magnesium ion) MG-A-7 Interacting chains: A

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	676A	LYS	3.47	2.55	108.61	86.47	✔	3941 [N3]	7366 [O3]	8171
2	743A	GLU	2.95	2.69	158.85	74.82	✔	4471 [O3]	7362 [O3]	7481

GOL-A-4

Interacting chains: A

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 83 of 128
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antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
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Figure. 33 Water Bridges MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase), ION MG (magnesium ion) MG-A-7 Interacting chains: A

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	676A	LYS	3.47	2.55	108.61	86.47	✔	3941 [N3]	7366 [O3]	8171
2	743A	GLU	2.95	2.69	158.85	74.82	✔	4471 [O3]	7362 [O3]	7481

GOL-A-4

Interacting chains: A

Figure. 34 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase), ION MG (magnesium ion) MG-A-7 Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain in	Donor Atom	Acceptor Atom
1	471A	ASN	3.21	3.52	100.09	✔	✔	2226 [Nam]	7370 [O3]
2	473A	ASN	1.92	2.89	167.98	✔	✔	2239 [Nam]	7370 [O3]
3	473A	ASN	3.06	3.89	145.28	✖	✔	7370 [O3]	2238 [O2]
4	474A	SER	2.86	3.18	100.21	✔	✔	2245 [O3]	7368 [O3]
5	489A	ARG	2.33	3.04	128.76	✔	✔	2365 [Ng+]	7368 [O3]
6	489A	ARG	3.08	3.89	142.31	✖	✔	7368 [O3]	2362 [Ng+]
7	997A	ARG	3.03	3.52	111.85	✔	✔	6598 [Ng+]	7370 [O3]

Water Bridges

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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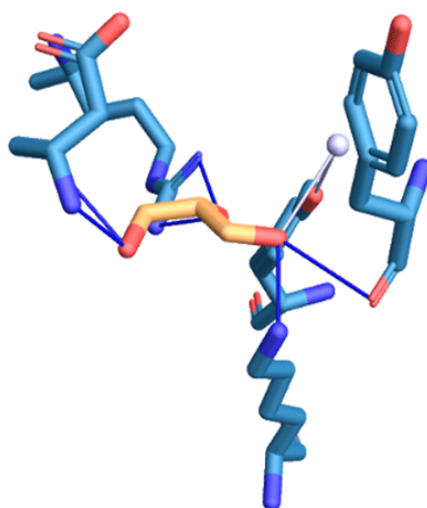| Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	460A	GLY	2.72	3.61	112.40	72.86	✔	2137 [Nam]	7372 [O3]	8089
2	1038A	GLN	3.83	4.00	148.76	99.92	✘	7372 [O3]	6929 [O2]	7907

GOL-A-5
Interacting chains: A

Figure. 35 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase), ION MG (magnesium ion) MG-A-7 Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	934A	SER	2.22	3.00	137.42	✔	✔	6061 [O3]	7378 [O3]
2	934A	SER	2.10	3.00	155.03	✘	✔	7378 [O3]	6061 [O3]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	962A	GLU	2.84	2.67	143.54	72.19	✔	6305 [O3]	7374 [O3]	7601
2	962A	GLU	2.82	3.32	143.72	75.59	✘	7376 [O3]	6301 [O2]	7601

GOL-A-6
Interacting chains: A

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 85 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
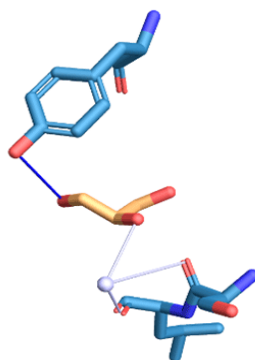Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 36 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase), ION MG (magnesium ion) MG-A-7 Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	576A	THR	3.19	4.03	146.25	✖	✖	7384 [O3]	3091 [O2]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	460A	GLY	3.88	3.61	112.40	71.76	✔	2137 [Nam]	7382 [O3]	8089

MalasmoruponaqTM™ small molecule+ION

BES (composite ligand, containing ubenimex)

BES-A-1085 ⭐

Composite ligand consists of BES:A:1085, ZN:A:1.

Interacting chains: A

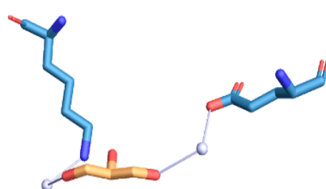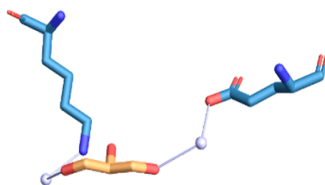

Figure. 37 for the generation of the Hydrophobic Docking Interactions of the MalasmoruponaqTM™ binding site(s) in 3EBH (m1 family aminopeptidase). ION MG (magnesium ion) MG-A-7 Interacting chains: A

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	319A	GLU	3.84	7331	997
2	459A	VAL	3.74	7334	2135
3	459A	VAL	3.73	7332	2136
4	493A	VAL	3.94	7345	2399
5	496A	HIS	3.70	7345	2415
6	575A	TYR	3.76	7334	3080
7	580A	TYR	3.70	7344	3124

Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	319A	GLU	2.86	3.80	152.12	✖	✔	7327 [N3]	1001 [O3]
2	460A	GLY	1.70	2.55	141.07	✔	✖	2137 [Nam]	7348 [O.co2]
3	461A	ALA	2.52	3.44	155.41	✖	✖	7340 [Nam]	2144 [O2]
4	461A	ALA	2.11	3.03	154.83	✔	✖	2141 [Nam]	7348 [O.co2]
5	461A	ALA	2.64	3.52	157.40	✖	✖	7348 [O.co2]	2144 [O2]

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| 6 | 518A | LYS | 3.02 | 3.39 | 102.52 | ✔ | | ✔ | 2620 [N3] | 7327 [N3] |
| 7 | 580A | TYR | 1.87 | 2.71 | 148.26 | ✔ | | ✔ | 3127 [O3] | 7339 [O2] |

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	489A	ARG	3.37	3.52	130.10	119.28	✔	2365 [Ng+]	7347 [O.co2]	7862

π-Stacking

Index	Residue	AA	Distance	Angle	Offset	Type	Ligand Atoms
1	575A	TYR	3.94	13.86	1.58	P	7330, 7331, 7332, 7333, 7334, 7335

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	489A	ARG	5.39	✔	Carboxylate	7347, 7348

Metal Complexes

Index	Residue	AA	Metal	Target	Distance	Location
Complex 1: Zn, square.planar (4)						
1	496A	HIS	7326	2420	2.02	protein.sidechain
2	500A	HIS	7326	2462	2.04	protein.sidechain
3	519A	GLU	7326	2628	2.02	protein.sidechain
4	519A	GLU	7326	2629	2.97	protein.sidechain

Figure. 38 water Bridges19 MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	203A	VAL	2.62	3.13	126.17	77.46	✖	3117 [O3]	1276 [O2]	3223
2	205A	CYS	4.08	3.13	126.17	71.57	✖	3117 [O3]	1284 [N2]	3223

EDO-A-306

Interacting chains: A

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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Figure. 39 Hydrogen Bonds from the. MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	95A	ASN	2.65	3.29	124.35	✖	✖	3121 [O3]	438 [N2]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	95A	ASN	3.13	3.68	146.60	82.81	✔	445 [Nam]	3121 [O3]	3271

EDO-A-307

Interacting chains: A, B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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Figure. 40 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein). selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	83A	GLU	1.45	2.33	152.95	✔	✔	347 [O3]	3127 [O3]
2	83B	GLU	3.21	3.90	129.90	✖	✔	3127 [O3]	1892 [O3]
3	84A	ASN	3.42	3.87	111.05	✖	✔	3125 [O3]	355 [O2]
4	150A	ARG	1.94	2.82	147.50	✔	✔	884 [Ng+]	3125 [O3]

Water Bridges

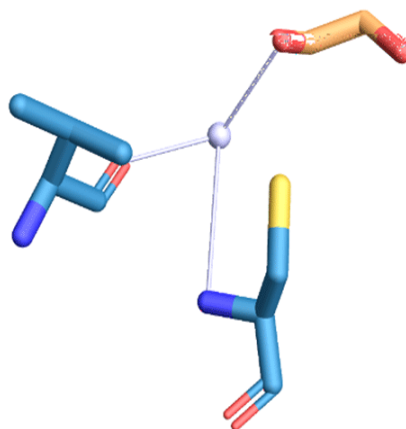| Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	83B	GLU	2.96	2.57	144.81	79.19	✔	1892 [O3]	3127 [O3]	3391
2	152A	ASN	3.01	4.01	135.83	75.87	✔	902 [Nam]	3125 [O3]	3274

EDO-A-309
Interacting chains: A

Figure. 41 Water Bridges: MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	99A	GLU	2.98	3.96	101.73	87.63	✖	3135 [O3]	476 [O2]	3317
2	102A	ARG	3.13	3.70	117.38	86.90	✖	3135 [O3]	500 [Ng+]	3307
3	102A	ARG	3.81	3.96	101.73	73.04	✖	3135 [O3]	493 [N2]	3317

EDO-B-305
Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 89 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
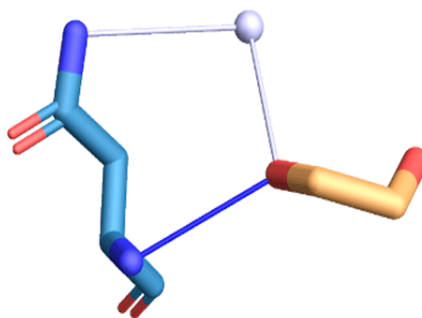Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

*Figure. 42 Hydrogen Bonds from the:MalasmoruponaqTM™ binding site(s)
in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™
small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.*

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	95B	ASN	2.37	3.21	142.68	✔	✔	1989 [Nam]	3159 [O3]
2	96B	ASN	3.27	3.82	116.64	✔	✖	1990 [Nam]	3157 [O3]

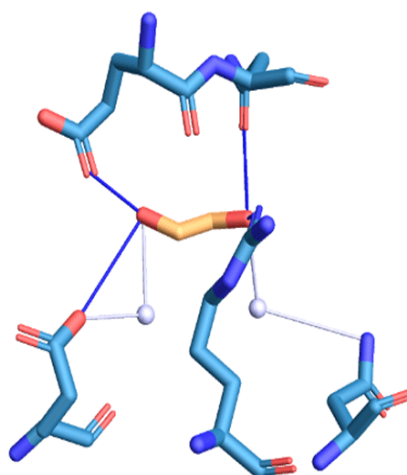*EDO-B-306*
Interacting chains: B

*Figure. 43 Hydrogen Bonds from the:MalasmoruponaqTM™ binding site(s)
in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™
small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.*

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	92B	ILE	3.10	3.92	143.07	✖	✖	3165 [O3]	1960 [O2]
2	95B	ASN	2.88	3.33	108.55	✔	✖	1982 [Nam]	3167 [O3]
3	96B	ASN	2.10	3.07	169.12	✔	✖	1990 [Nam]	3167 [O3]

EDO-B-308
Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016   Page 90 of 128
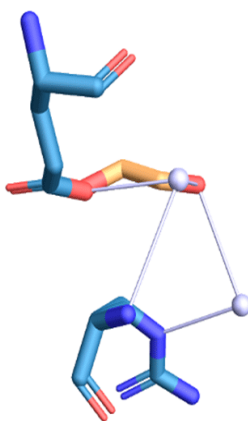
Figure. 44 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL Malasmorupona small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A.

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain in	Donor Atom	Acceptor Atom
1	192B	GLN	2.60	3.54	160.46	✔	✖	2728 [Nam]	3171 [O3]
2	220B	TRP	2.03	3.01	170.96	✔	✖	2930 [Nam]	3169 [O3]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	221B	GLU	3.65	2.88	149.85	84.07	✔	2944 [Nam]	3169 [O3]	3454

EDO-B-309
Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 91 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 45 Water Bridges MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A

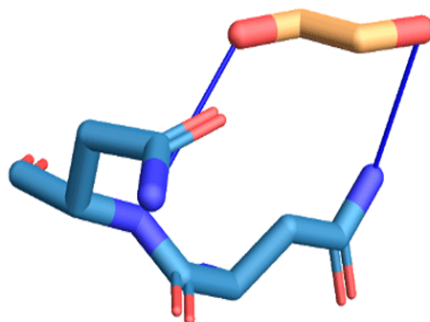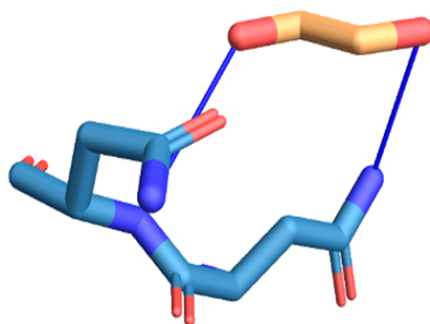| Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	99B	GLU	3.17	3.85	118.75	76.57	✖	3175 [O3]	2024 [O3]	3348
2	139B	GLN	3.99	3.85	118.75	122.36	✖	3175 [O3]	2329 [O2]	3348

EDO-B-310
Interacting chains: B

Figure. 46 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	168B	ILE	2.29	3.24	160.25	✔	✖	2552 [Nam]	3179 [O3]

EDO-B-311
Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 92 of 128

peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016
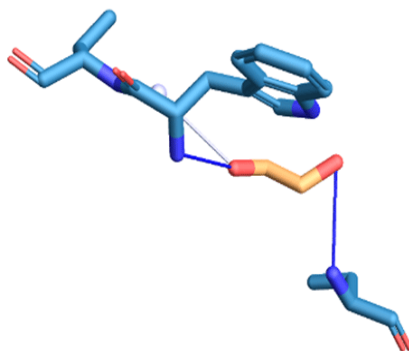
Figure. 47 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	102B	ARG	2.02	2.93	152.29	✔	✘	2042 [Nam]	3181 [O3]
2	105B	SER	1.79	2.73	164.23	✔	✔	2076 [O3]	3183 [O3]
3	105B	SER	2.31	2.73	105.84	✘	✔	3183 [O3]	2076 [O3]

Water Bridges

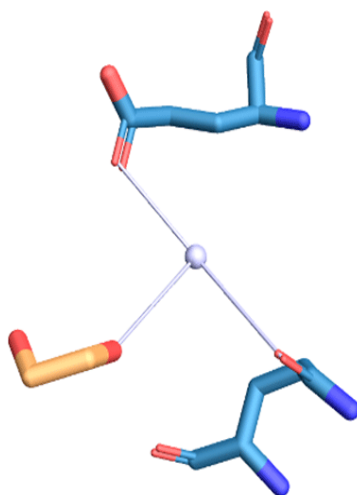| Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	99B	GLU	2.76	2.88	160.22	82.44	✘	3181 [O3]	2025 [O2]	3375
2	106B	ASP	3.17	3.56	104.45	71.48	✔	2077 [Nam]	3183 [O3]	3359

Figure. 48 Salt Bridges from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	61A	ARG	4.18	✔	Sulfate	3101, 3101

SO4-A-303 Salt Bridges from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305 Interacting chains: A

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016   Page 93 of 128

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	141A	ARG	4.50	✔	Sulfate	3106, 3106
2	181A	ARG	4.13	✔	Sulfate	3106, 3106

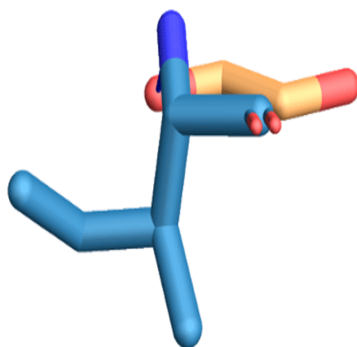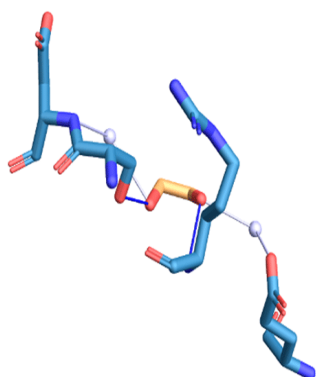SO4-A-304 ☗ Interacting chains: A

Figure. 49 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305

Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	106A	ASP	3.16	4.05	154.22	✖	✔	3114 [O3]	535 [O2]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	102A	ARG	2.99	3.88	130.85	102.10	✔	503 [Ng+]	3112 [O2]	3307
2	102A	ARG	3.35	3.02	142.77	98.89	✔	503 [Ng+]	3114 [O3]	3405
3	106A	ASP	4.06	2.74	123.49	111.95	✔	534 [O3]	3114 [O3]	3306

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	102A	ARG	4.84	✔	Sulfate	3111, 3111

SO4-B-302 Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 94 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016
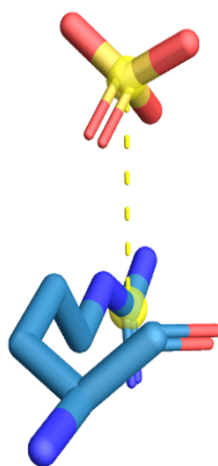
Figure. 50 Salt Bridges from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305

Interacting chains: A

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	141B	ARG	4.69	✔	Sulfate	3141, 3141
2	181B	ARG	4.21	✔	Sulfate	3141, 3141

SO4-B-303 ⭐ Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 95 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
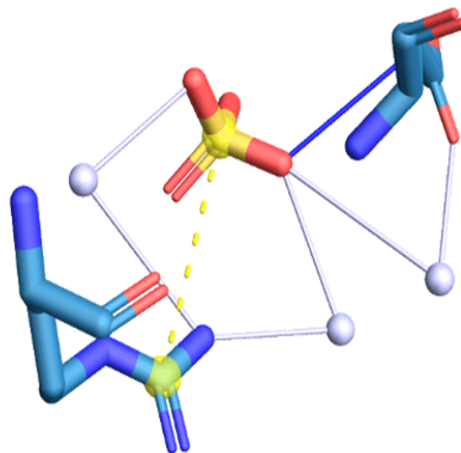Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 51 Salt Bridges from the MalasmoruponaqTM™ binding site(s) in 4F1K (thrombospondin related anonymous protein), selected ligands: CL MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol) EDO-A-305

Interacting chains: A

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	61B	ARG	4.08	✔	Sulfate	3146, 3146

SO4-B-304 ⭐
Interacting chains: B

Figure. 52 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. EDO (Ethylene Glycol)EDO-A-302Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	134A	ARG	2.84	3.26	106.42	✔	✔	1064 [Ng+]	3858 [O3]
2	134A	ARG	3.14	3.53	105.15	✔	✔	1063 [Ng+]	3858 [O3]
3	139A	THR	3.19	3.95	137.02	✔	✔	1104 [O3]	3858 [O3]

EDO-A-303
Interacting chains: A

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

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Figure. 53 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. EDO (Ethylene Glycol)EDO-A-302Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	22A	SER	3.01	3.81	140.32	✖	✖	3860 [O3]	165 [O2]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	22A	SER	3.71	3.14	119.07	106.84	✔	167 [O3]	3862 [O3]	3985

EDO-A-304

Interacting chains: A, B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 97 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
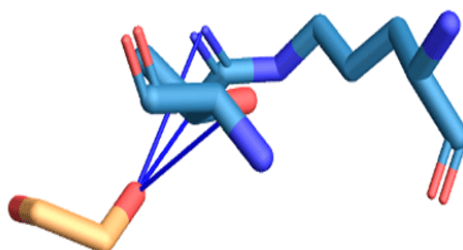Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 54 *Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. EDO (Ethylene Glycol)EDO-A-302Interacting chains: A*

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	45A	SER	3.74	4.05	102.10	✔	✔	348 [O3]	3866 [O3]
2	65A	ASN	2.43	3.04	119.71	✔	✔	520 [Nam]	3864 [O3]

Water Bridges

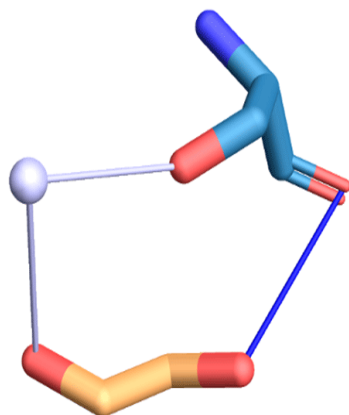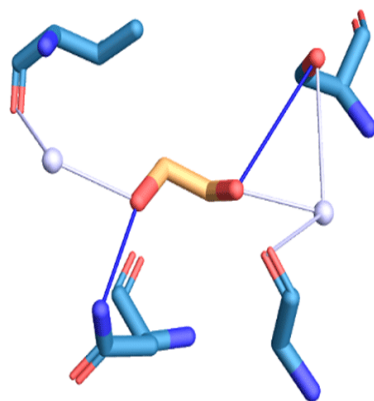| Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	45A	SER	3.74	2.78	163.26	99.06	✘	3866 [O3]	348 [O3]	3984
2	76B	GLY	3.61	2.78	163.26	128.95	✘	3866 [O3]	2515 [O2]	3984
3	78A	VAL	3.62	2.78	168.62	78.24	✘	3864 [O3]	611 [O2]	3982

EDO-B-302

Interacting chains: B

Figure. 55 *Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. EDO (Ethylene Glycol)EDO-A-302Interacting chains: A*

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	45B	SER	3.62	3.93	101.45	✔	✔	2270 [O3]	3873 [O3]
2	45B	SER	3.07	3.93	148.97	✘	✔	3873 [O3]	2270 [O3]
3	65B	ASN	3.00	3.55	116.44	✔	✔	2437 [Nam]	3875 [O3]
4	65B	ASN	2.94	3.34	106.17	✘	✘	3875 [O3]	2433 [O2]

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 98 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Water Bridges

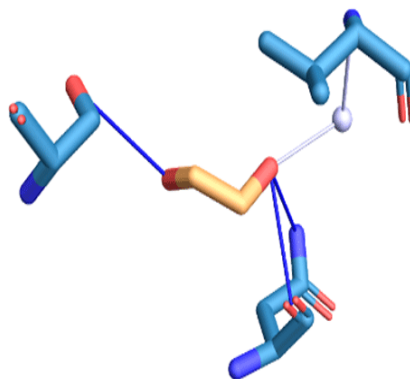| Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	78B	VAL	2.60	3.04	175.83	82.13	✔	2525 [Nam]	3875 [O3]	4138

EDO-B-303

Figure. 56 Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. EDO (Ethylene Glycol)EDO-A-302Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	10B	ASN	2.17	3.07	150.75	✔	✔	1994 [Nam]	3879 [O3]
2	12B	LYS	2.07	2.93	139.57	✔	✔	2017 [N3]	3877 [O3]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	12B	LYS	3.25	3.96	155.61	127.67	✘	3877 [O3]	2017 [N3]	4265
2	97B	GLU	4.10	3.96	155.61	109.07	✘	3877 [O3]	2678 [O3]	4265

EDO-B-304

Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016   Page 99 of 128
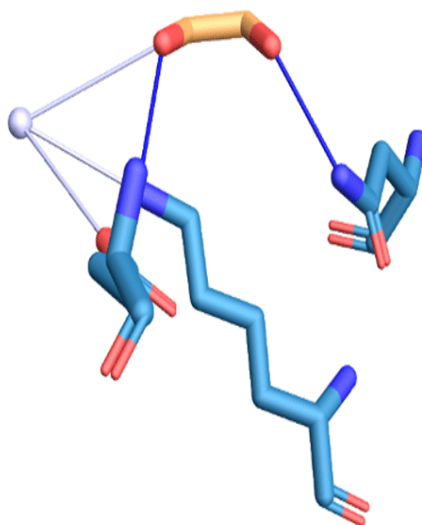
Figure. 57 Water Bridges MalasmoruponaqTM™ binding site(s) in 4YWI. EDO (Ethylene Glycol)EDO-A-302Interacting chains: A

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	182B	GLN	3.90	3.58	126.78	95.80	✖	3881 [O3]	3347 [O2]	4218
2	182B	GLN	3.41	2.94	170.59	82.41	✔	3348 [Nam]	3881 [O3]	4236
3	223B	GLN	3.27	3.58	126.78	106.13	✖	3881 [O3]	3658 [O2]	4218

EDO-B-305

Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 100 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
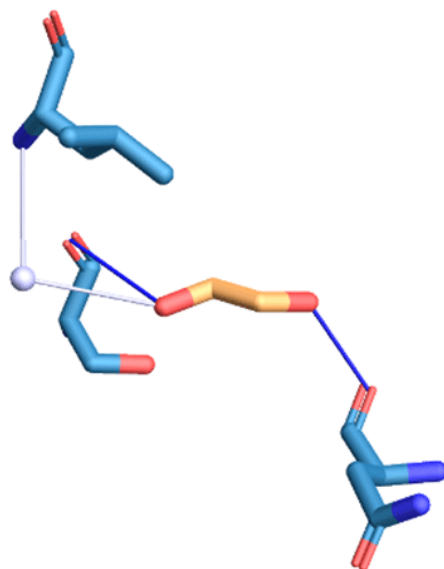Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 58 _Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. EDO (Ethylene Glycol)EDO-A-302Interacting chains: A_

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	14B	ASN	2.26	2.66	103.51	✗	✗	3887 [O3]	2027 [O2]
2	19B	SER	2.49	3.40	157.38	✗	✗	3885 [O3]	2063 [O2]

Water Bridges

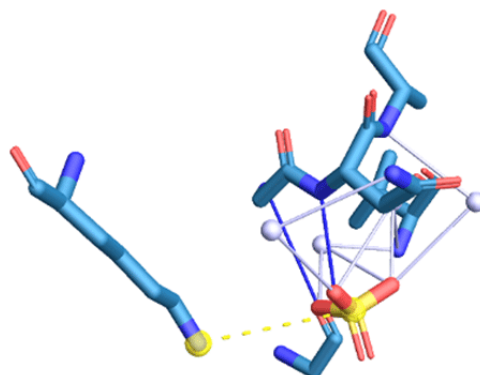| Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	23B	LEU	3.58	3.84	106.04	93.55	✔	2087 [Nam]	3885 [O3]	4232

SO4 (sulfate) SO4-A-301 Interacting chains: A

Figure. 59 _Hydrogen Bonds from the MalasmoruponaqTM™ binding site(s) in 4YWI. MalasmoruponaqTM™ small molecule EDO (Ethylene Glycol)EDO-A-302 Interacting chains: A_

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	232A	GLY	3.48	4.05	118.66	✔	✗	1796 [Nam]	3853 [O3]
2	233A	ASN	2.14	3.08	159.73	✔	✗	1800 [Nam]	3852 [O2]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	210A	GLY	3.06	2.78	124.99	73.62	✗	3853 [O3]	1637 [O2]	3981
2	212A	VAL	3.59	2.98	162.35	101.49	✔	1644 [Nam]	3851 [O2]	3981
3	212A	VAL	2.66	3.99	125.98	103.29	✔	1644 [Nam]	3851 [O2]	3921

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif Page 101 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

4	212A	VAL	4.00	3.99	125.98	81.84	✔	1644 [Nam]	3852 [O2]	3921
5	233A	ASN	4.06	3.88	148.28	83.82	✔	1807 [Nam]	3852 [O2]	4075
6	234A	ALA	3.67	3.67	105.79	108.78	✔	1808 [Nam]	3851 [O2]	4083

Salt Bridges

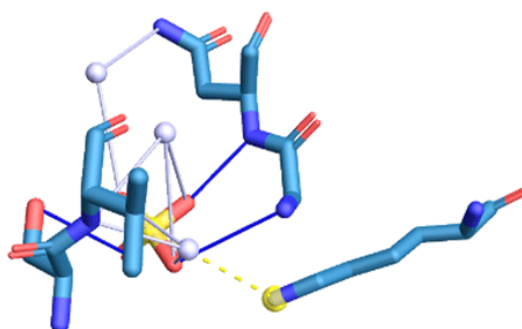| Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	12A	LYS	5.01	✔	Sulfate	3850, 3850

SO4-B-301 Interacting chains: B

Figure. 60 Hydrogen Bonds from the MalasmoruponaqTM™™ binding site(s) in 4YWI.
MalasmoruponaqTM™™ EDO (Ethylene Glycol)EDO-A-302Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	211B	SER	3.48	3.95	112.09	✘	✔	3871 [O3]	3574 [O3]
2	232B	GLY	3.32	3.93	121.57	✔	✘	3723 [Nam]	3868 [O2]
3	233B	ASN	1.93	2.89	165.02	✔	✘	3727 [Nam]	3870 [O3]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	212B	VAL	3.52	3.09	152.21	108.59	✔	3575 [Nam]	3869 [O2]	4141
2	212B	VAL	2.61	3.09	152.21	71.12	✔	3575 [Nam]	3868 [O2]	4141
3	212B	VAL	4.05	3.99	131.42	116.54	✔	3575 [Nam]	3868 [O2]	4185
4	212B	VAL	3.73	3.99	131.42	81.77	✔	3575 [Nam]	3870 [O3]	4185
5	233B	ASN	3.77	3.91	157.19	80.67	✔	3734 [Nam]	3869 [O2]	4290

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	12B	LYS	4.99	✔	Sulfate	3867, 3867

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 102 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
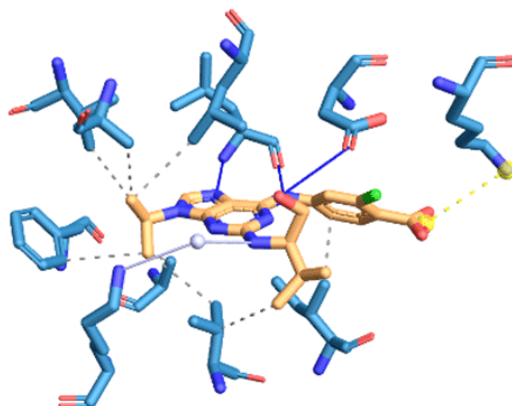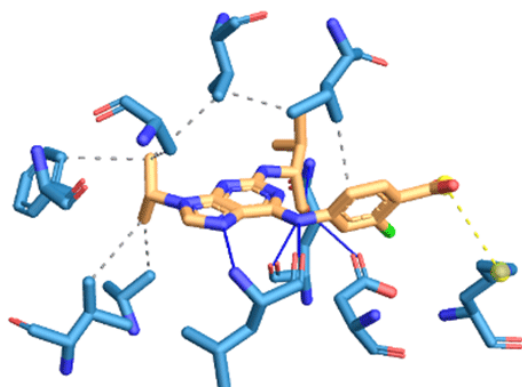Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 61 MalasmoruponaqTM™ Hydrophobic Docking Interactions of the 2
MalasmoruponaqTM™ binding site(s) in 1V0P (cell division control protein 2 homolog).
MalasmoruponaqTM™ small molecule PVB (purvalanol B)PVB-A-1287 Interacting chains: A

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	10A	ILE	3.64	4324	85
2	18A	VAL	3.77	4340	139
3	18A	VAL	3.84	4336	138
4	30A	ALA	3.79	4340	239
5	63A	VAL	3.86	4341	506
6	79A	PHE	3.80	4340	642
7	132A	LEU	3.73	4341	1070
8	142A	ALA	3.42	4341	1150

Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	82A	LEU	2.04	3.01	168.27	✔	✘	666 [Nam]	4320 [N2]
2	82A	LEU	1.80	2.76	161.73	✘	✘	4322 [Npl]	669 [O2]
3	85A	ASP	2.67	3.42	134.00	✘	✔	4339 [O3]	697 [O2]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	32A	LYS	3.76	3.70	149.40	83.69	✘	4333 [Npl]	256 [N3]	4470
2	32A	LYS	3.70	3.76	166.60	75.55	✔	256 [N3]	4333 [Npl]	4470

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	88A	LYS	4.20	✔	Carboxylate	4331, 4332

PVB-B-1287 Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 103 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

*Figure. 62 MalasmoruponaqTM™ Hydrophobic Docking Interactions of the 2
MalasmoruponaqTM™ binding site(s) in 1V0P (cell division control protein 2 homolog).
MalasmoruponaqTM™ SMALL MOLECULEPVB (purvalanol B)PVB-A-1287 Interacting
chains: A*

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	10B	ILE	3.55	4354	2310
2	18B	VAL	3.82	4370	2364
3	18B	VAL	3.90	4366	2365
4	30B	ALA	3.96	4370	2464
5	63B	VAL	3.91	4371	2639
6	79B	PHE	3.67	4370	2746
7	142B	ALA	3.47	4371	3254

Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	82B	LEU	2.04	3.02	172.45	✔	✖	2770 [Nam]	4350 [N2]
2	82B	LEU	1.65	2.61	162.72	✖	✖	4352 [Npl]	2773 [O2]
3	85B	ASP	2.20	3.04	147.91	✔	✔	2801 [O3]	4369 [O3]
4	129B	GLN	2.56	3.17	120.07	✔	✔	3151 [Nam]	4369 [O3]
5	129B	GLN	2.16	2.85	127.08	✖	✖	4369 [O3]	3146 [O2]

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	88B	LYS	4.28	✔	Carboxylate	4362, 4361

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 104 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

*Figure. 63 MalasmoruponaqTM™ Hydrophobic Docking Interactions of the 6
MalasmoruponaqTM™ binding site(s) in 3UM6 (bifunctional dihydrofolate reductase-
thymidylate synthase). small molecule 1CY (cycloguanil)1CY-A-609 Interacting chains: A*

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	16A	VAL	3.60	9057	126
2	46A	LEU	3.79	9057	361
3	58A	PHE	3.59	9058	463

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
4	108A	THR	3.77	9061	792
5	164A	ILE	3.62	9063	1266

Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	14A	ILE	2.03	2.97	158.95	✗	✗	9056 [Npl]	110 [O2]
2	15A	CYS	1.99	2.98	179.32	✗	✗	9055 [Npl]	118 [O2]
3	170A	TYR	2.91	3.32	108.18	✓	✓	1306 [O3]	9056 [Npl]
4	185A	THR	3.12	3.66	117.13	✓	✓	1441 [O3]	9055 [Npl]

π-Stacking

Index	Residue	AA	Distance	Angle	Offset	Type	Ligand Atoms
1	58A	PHE	4.97	74.30	1.93	T	9059, 9060, 9061, 9062, 9063, 9064
2	58A	PHE	4.30	29.55	1.25	P	9049, 9050, 9051, 9052, 9053, 9054

Halogen Bonds

Index	Residue	AA	Distance	Donor Angle	Acceptor Angle	Donor Atom	Acceptor Atom
1	108A	THR	3.83	136.65	117.23	9065 [Cl]	789 [O2]

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	54A	ASP	3.47	✗	Guanidine	9049, 9051, 9055

1CY-B-709 ⭐ Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 105 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
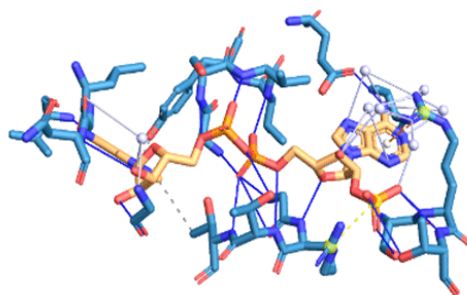Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 64 MalasmoruponaqTM™ Hydrophobic Docking Interactions in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	16B	VAL	3.49	9142	4641
2	58B	PHE	3.47	9143	4977
3	164B	ILE	3.70	9148	5774

Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	14B	ILE	1.88	2.85	167.78	✖	✖	9141 [Npl]	4625 [O2]
2	185B	THR	2.67	3.21	115.52	✔	✔	5949 [O3]	9140 [Npl]
3	185B	THR	2.63	3.21	117.28	✖	✔	9140 [Npl]	5949 [O3]

π-Stacking

Index	Residue	AA	Distance	Angle	Offset	Type	Ligand Atoms
1	58B	PHE	4.70	16.00	1.56	P	9134, 9135, 9136, 9137, 9138, 9139
2	58B	PHE	5.18	83.11	1.94	T	9144, 9145, 9146, 9147, 9148, 9149

Halogen Bonds

Index	Residue	AA	Distance	Donor Angle	Acceptor Angle	Donor Atom	Acceptor Atom
1	108B	THR	3.23	144.12	126.76	9150 [Cl]	5297 [O2]

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	54B	ASP	3.49	✖	Guanidine	9134, 9140, 9136

NDP (NADP) NDP-A-610 ⭐ **Interacting chains: A**

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 106 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
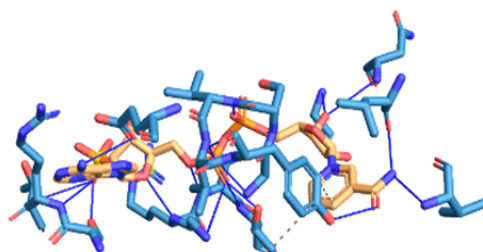Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 65 MalasmoruponaqTM™ Hydrophobic Docking Interactions in 3UM6 (bifun
dihydrofolate reductase-thymidylate synthase

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	108A	THR	3.92	9108	792
2	170A	TYR	3.96	9107	1304

Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	16A	VAL	2.20	3.00	136.31	✔	✘	121 [Nam]	9105 [O2]
2	40A	LEU	2.08	3.05	168.06	✘	✘	9106 [Nam]	318 [O2]
3	42A	ASN	3.26	3.68	108.25	✔	✘	327 [Nam]	9097 [O3]
4	44A	GLY	2.62	3.45	143.43	✘	✘	9099 [O3]	347 [O2]
5	105A	GLY	3.60	4.01	107.60	✔	✘	764 [Nam]	9068 [O3]
6	105A	GLY	3.46	4.06	122.68	✘	✘	9068 [O3]	767 [O2]
7	106A	ARG	2.01	2.93	154.39	✔	✘	768 [Nam]	9072 [O3]
8	107A	THR	2.75	3.65	152.83	✔	✘	779 [Nam]	9069 [O3]
9	107A	THR	2.99	3.41	107.67	✔	✔	784 [O3]	9088 [O3]
10	108A	THR	2.61	3.31	128.31	✔	✘	786 [Nam]	9068 [O3]
11	128A	SER	1.95	2.85	153.20	✘	✔	9113 [O3]	959 [O3]
12	129A	ARG	2.05	2.96	153.12	✔	✘	960 [Nam]	9111 [O2]
13	130A	THR	3.61	3.90	100.35	✔	✔	976 [O3]	9112 [O3]
14	130A	THR	2.35	3.32	167.63	✔	✘	971 [Nam]	9111 [O2]
15	166A	GLY	2.27	3.05	135.22	✔	✘	1271 [Nam]	9068 [O3]
16	167A	SER	2.48	3.28	137.89	✔	✘	1275 [Nam]	9092 [O3]
17	168A	VAL	1.76	2.73	165.85	✔	✘	1281 [Nam]	9090 [O2]
18	169A	VAL	2.43	3.36	158.97	✔	✘	1288	9067

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 107 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
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| 19 | 172A | GLU | 1.86 | 2.80 | 157.39 | ✘ | ✔ | 9083 [Npl] | 1323 [O3] |

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor	Donor Atom	Acceptor Atom	Water Atom
1	41A	GLY	4.07	2.89	147.40	82.86	✘	9097 [O3]	326 [O2]	9277
2	44A	GLY	2.89	2.88	160.76	97.07	✔	344 [Nam]	9097 [O3]	9277
3	129A	ARG	2.62	2.54	141.49	77.08	✔	969 [Ng+]	9111 [O2]	9250
4	129A	ARG	3.95	2.62	156.70	79.23	✔	969 [Ng+]	9074 [O3]	9228
5	129A	ARG	3.48	3.97	115.01	97.32	✔	969 [Ng+]	9074 [O3]	9311
6	129A	ARG	4.10	3.38	124.63	104.49	✔	970 [Ng+]	9086 [N2]	9228
7	129A	ARG	3.73	2.88	131.52	112.55	✔	970 [Ng+]	9083 [Npl]	9296
8	129A	ARG	2.82	2.88	131.52	100.41	✔	970 [Ng+]	9084 [N2]	9296
9	129A	ARG	3.62	3.39	161.33	111.75	✔	970 [Ng+]	9083 [Npl]	9345
10	129A	ARG	3.35	3.39	161.33	90.70	✔	970 [Ng+]	9080 [N2]	9345
11	146A	VAL	3.26	2.87	165.38	89.57	✔	1109 [Nam]	9083 [Npl]	9404

π-Cation Docking Interactions

Index	Residue	AA	Distance	Offset	Protein charged	Ligand Group	Ligand Atoms
1	129A	ARG	3.61	1.25	✔	Aromatic	9081, 9082, 9084, 9085, 9086, 9087

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	106A	ARG	4.17	✔	Phosphate	9110, 9110, 9076, 9111, 9112, 9113

NDP-B-710 Interacting chains: B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 108 of 128 peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 66 MalasmoruponaqTM™ Hydrophobic Docking Interactions in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	108B	THR	3.91	9193	5300
2	170B	TYR	3.93	9192	5812

Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	16B	VAL	2.95	3.80	145.52	✔	✘	4636 [Nam]	9191 [Nam]
2	40B	LEU	2.49	3.47	179.05	✘	✘	9191 [Nam]	4833 [O2]
3	42B	ASN	3.51	3.82	101.07	✔	✘	4842 [Nam]	9182 [O3]
4	44B	GLY	3.18	3.57	105.69	✔	✘	4859 [Nam]	9182 [O3]
5	44B	GLY	2.30	3.14	143.65	✘	✘	9184 [O3]	4862 [O2]
6	105B	GLY	3.26	3.63	104.53	✔	✘	5272 [Nam]	9153 [O3]
7	105B	GLY	2.99	3.62	123.83	✘	✘	9153 [O3]	5275 [O2]
8	106B	ARG	2.32	3.25	158.45	✔	✘	5276 [Nam]	9157 [O3]
9	107B	THR	3.21	3.55	102.41	✔	✔	5292 [O3]	9173 [O3]
10	107B	THR	2.87	3.75	148.49	✔	✘	5287	9154
11	108B	THR	1.99	2.86	146.01	✔	✘	5294 [Nam]	9153 [O3]
12	108B	THR	1.56	2.51	164.57	✔	✔	5299 [O3]	9153 [O3]
13	128B	SER	1.86	2.53	123.67	✘	✔	9198 [O3]	5467 [O3]

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 109 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

14	129B	ARG	2.52	3.40	148.65	✔	✘	5468 [Nam]	9198 [O3]
15	130B	THR	2.64	3.58	159.31	✔	✘	5479 [Nam]	9198 [O3]
16	166B	GLY	2.25	3.04	135.83	✔	✘	5779 [Nam]	9152 [O2]
17	167B	SER	2.32	3.19	147.18	✔	✘	5783 [Nam]	9177 [O3]
18	168B	VAL	1.79	2.72	156.18	✔	✘	5789 [Nam]	9175 [O2]
19	169B	VAL	2.76	3.66	151.40	✔	✘	5796 [Nam]	9152 [O2]
20	170B	TYR	2.21	3.02	145.02	✔	✔	5814 [O3]	9190 [O2]
21	172B	GLU	2.27	3.15	148.20	✘	✔	9168 [Npl]	5831 [O2]

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	106B	ARG	4.40	✔	Phosphate	9195, 9195, 9161, 9196, 9197, 9198

UMP (22'-deoxyuridylic acid) UMP-A-611 Interacting chains: A, B

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif   Page 110 of 128
peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 67 MalasmoruponaqTM™ Hydrophobic Docking Interactions of the in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase

Index	Residue	AA	Distance	Ligand Atom	Protein Atom
1	513A	ASP	3.93	9123	3772

Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	509A	GLN	3.14	3.66	114.21	✔	✔	3744 [Nam]	9120 [O2]
2	511A	SER	1.68	2.57	150.47	✔	✔	3761 [O3]	9132 [O3]
3	511A	SER	2.02	2.57	114.29	✘	✔	9132 [O3]	3761 [O3]
4	513A	ASP	1.87	2.79	155.38	✔	✘	3768 [Nam]	9120 [O2]
5	518A	VAL	3.58	3.93	103.51	✔	✘	3800 [Nam]	9120 [O2]
6	521A	ASN	2.08	2.80	128.48	✔	✔	3832 [Nam]	9121 [O2]
7	551A	HIS	1.90	2.83	159.92	✘	✔	9126 [O3]	4065 [N2]

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	345A	ARG	4.13	✔	Phosphate	9130, 9130, 9129, 9131, 9132, 9133
2	470B	ARG	4.27	✔	Phosphate	9130, 9130, 9129, 9131, 9132, 9133
3	471B	ARG	4.69	✔	Phosphate	9130, 9130, 9129, 9131, 9132, 9133
4	510A	ARG	4.26	✔	Phosphate	9130, 9130, 9129, 9131, 9132, 9133

UMP-B-711 Interacting chains: A, B

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peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional
Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Figure. 68 MalasmoruponaqTM™ Hydrogen Bonds from the in 3UM6 (bifunctional dihydrofolate reductase-thymidylate synthase

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor	Sidechain	Donor Atom	Acceptor Atom
1	509B	GLN	2.79	3.27	110.71	✔	✔	8252 [Nam]	9205 [O2]
2	511B	SER	1.83	2.76	160.59	✔	✔	8269 [O3]	9217 [O3]
3	513B	ASP	1.84	2.81	168.96	✔	✖	8276 [Nam]	9205 [O2]
4	518B	VAL	3.54	4.00	111.10	✔	✖	8308 [Nam]	9205 [O2]
5	521B	ASN	1.98	2.77	136.18	✔	✔	8340 [Nam]	9206 [O2]
6	551B	HIS	1.86	2.81	169.17	✖	✔	9211 [O3]	8573 [N2]
7	553B	TYR	2.09	2.94	149.59	✔	✔	8592 [O3]	9211 [O3]

Salt Bridges

Index	Residue	AA	Distance	Protein positive	Ligand Group	Ligand Atoms
1	345B	ARG	4.15	✔	Phosphate	9215, 9215, 9218, 9214, 9216, 9217
2	470A	ARG	4.11	✔	Phosphate	9215, 9215, 9218, 9214, 9216, 9217
3	471A	ARG	4.39	✔	Phosphate	9215, 9215, 9218, 9214, 9216, 9217
4	510B	ARG	4.55	✔	Phosphate	9215, 9215, 9218, 9214, 9216, 9217

Citation: Grigoriadis I (2019) Evaluation of an Inverse Molecular Design Docking Algorithm for the computer aided molecular drug design of a QMMMIDD motif Page 112 of 128 peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of antimicrobial activity of the insect defensin from Anopheles gambiae and Ebola viruses: Understanding the Relativistic Generalization of Density Functional Theory (DFT) and Completing It in Practice. Int J Drug Disc 3: 016

Fig.69 MalasmoruponaqTM™ 3 binding site(s) in 4IOD (malarial clp b2 atpase/hsp101 protein). SO4 (sulfate)
SO4-A-201 Interacting chains: A

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Sidechain	Donor Atom	Acceptor Atom
1	33A	ASN	2.09	3.01	154.54			1360 [Nam]	3522 [O3]

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Sidechain	Donor Atom	Acceptor Atom
2	34A	LYS	2.08	2.98	151.09			1368 [Nam]	3520 [O2]

Water Bridges

Index	Residue	AA	Dist. A-W	Dist. D-W	Donor Angle	Water Angle	Protein donor?	Donor Atom	Acceptor Atom	Water Atom
1	32A	HIS	2.97	4.02	117.73	134.11		3521 [O3]	1356 [N2]	3788
2	36A	LYS	2.86	4.02	117.73	71.65		3521 [O3]	1393 [N3]	3788

Salt Bridges

Index	Residue	AA	Distance	Protein positive?	Ligand Group	Ligand Atoms
1	32A	HIS	4.85		Sulfate	3518, 3518

SO4-B-201

Interacting chains: A, B

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Hydrogen Bonds from the

Index	Residue	AA	Distance H-A	Distance D-A	Donor Angle	Protein donor?	Sidechain	Donor Atom	Acceptor Atom
1	75B	THR	2.75	3.50	134.63			528 [O3]	3515 [O2]

Salt Bridges

Index	Residue	AA	Distance	Protein positive?	Ligand Group	Ligand Atoms
1	32B	HIS	5.15		Sulfate	3513, 3513
2	108A	LYS	4.87		Sulfate	3513, 3513

SO4-C-201

Interacting chains: C

Salt Bridges

Index	Residue	AA	Distance	Protein positive?	Ligand Group	Ligand Atoms
1	147C	ARG	4.61		Sulfate	3523, 3523
2	151C	LYS	3.71		Sulfate	3523, 3523

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Rank	Compound	Score	T. Energy	I. Energy
1	﹥ ligand_de69935f3a_1	6.662	104.564	0.728

JSmol

Fig. 70 MalasmoruponaqTM__5d25cb805d580 with (PDB:4F7F) Structure of Anopheles gambiae odorant binding protein 20 A novel mechanism of ligand binding and release in the odorant binding protein 20 from the malaria mosquito Anopheles gambiae.

MalasmoruponaqTM__File	Model	T.Energy	I.Energy	vdW	Coul	NumRotors	RMSD	Score
MalasmoruponaqTM__ligand_de69935f3a_1_run_1.log	1	104.564	0.728	-0.000	0.728	24	0.000	6.662
MalasmoruponaqTM__ligand_de69935f3a_1_run_1.log	3	104.565	0.729	-0.000	0.729	24	10.514	6.662
MalasmoruponaqTM__ligand_de69935f3a_1_run_1.log	4	104.566	0.729	-0.000	0.729	24	9.833	6.662

Rank	Compound	Score	T. Energy	I. Energy
1	﹥ ligand_77f86cfe58_1	1.557	4672.719	3832.720

JSmol

Figure. 71 3D Docking Docking Interactions of the MalasmoruponaqTM__5d25c9604090b_ with the 3zml_(PDB:3ZML)

MalasmoruponaqTM__	Model	T.Energy	I.Energy	vdW	Coul
NumRotors RMSD Score					
MalasmoruponaqTM__ligand_77f86cfe58_1_run_17.log	1	4672.719	3832.720	3879.315	
-46.595 26 0.000 1.557					
MalasmoruponaqTM__ligand_77f86cfe58_1_run_17.log	3	4774.539	4276.986	4301.671	
-24.685 26 2.330 2.526					
MalasmoruponaqTM__ligand_77f86cfe58_1_run_17.log	8	5404.847	4456.715	4450.926	
5.789 21 4.871 1.550					

Rank	Compound	Score	T. Energy	I. Energy
1	> ligand_e9489e0982_1	-8.03	64.567	-17.901
2	> ligand_10a4743c6e_1	-7.516	56.237	-17.712
3	> ligand_a245d49ad0_1	-7.458	9.843	-22.256
4	> ligand_940ff43933_1	-7.257	61.300	-14.423
5	> ligand_182f64d74a_1	-7.068	72.286	-8.338
6	> ligand_1348dc9dcb_1	21.059	20325.073	19702.515

JSmol

Figure. 72a 3D Comparative Docking studies of the Docking Docking Interactions between the Mala smoruponaqTM AND Quinine, Quinidine, Proguanil, Atovaquone, Mefloquine, 3ZML with the 3zml_ (PDB:3ZML)

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peptide targeted active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the dual deactivations of
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	Score	T. Energy	I. Energy
82_1	-8.03	64.567	-17.901
6e_1	-7.516	56.237	-17.712
d0_1	-7.458	9.843	-22.256
53_1	-7.257	61.300	-14.423
4a_1	-7.068	72.286	-8.338
cb_1	21.059	20325.073	19702.515
	21.059	20325.073	19702.515
	24.869	20384.568	20071.755
	22.303	20963.386	20436.003

Hide/Show

Protein

JSmol

Figure. 72b 3D Comparative Docking studies of the Docking Docking Interactions between the Mala smoruponaqTM AND Quinine, Quinidine, Proguanil, Atovaquone, Mefloquine, 3ZML with the 3zml_ (PDB:3ZML)

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Figure. 73 MalasmoruponaqTM™_VS_FDAs_Spreadsheet1 Docking Energies.

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*Figure. 74 MalasmoruponaqTM™_VS_FDAs_Spreadsheet1 10v*3866c*
*BiogenetoligandorolTMligandorolTM (Recoring Pharmacophoric Merging QMMMIDDD
Algorithm)_Time_Predictions_4,3_Days_CellChangeTimes->{3.755534782528232^9}]_*
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")"}]}]}, {   RowBox[{"\[ScriptCapitalB]", "\[LongEqual]",   RowBox[{"(", "\[NoBreak]",
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Conclusion

In this study we generated Docking Algorithms for the:

•Experimental quantum simulation of fermion-antifermion scattering via boson exchange in a trapped ion Docking Algorithms.

•-Machine Learning and Computer Vision System for Phenotype Data Acquisition and Analysis Direct quantum process tomography via measuring sequential weak values of incompatible observables Docking Algorithms.

•-Performance of Source Localization Docking Algorithms on the Extraction of gravitational waves in numerical relativity. Docking Algorithms in Feature Selection and Predictors of Falls with Foot Force Sensors Using KNN-Based Docking Algorithms.

•-Numerical observation of emergent spacetime supersymmetry at quantum criticality simple quantum voting scheme with multi-qubit entanglement Docking Algorithms.

•-Multiscale Quantum Harmonic Oscillator Docking Algorithm for Multimodal Optimizationon Small Molecules as Rotating stars in relativity Improved Quantum Artificial Fish Docking Algorithm.

•-Application to Distributed Network Considering Distributed Generation Artificial fish complete update and obtain the optimal value mainly through the following four behaviors: being random, preying, swarming, and following in the process of iterative calculation on Small Molecules as Rotating stars in relativity Improved Quantum Artificial Fish Docking Algorithm.

•-Distributed Network Considering Distributed Generation Docking Algorithms on Mapping nonlinear gravity into General Relativity with nonlinear electrodynamics.

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•-Quantum Walks based Quantum Hash Function Docking Algorithms of a general model for metabolic scaling in self-similar asymmetric networks.

•-Real-Coded Quantum Evolutionary Docking Algorithm Based on Hybrid Updating Strategy Docking Algorithms of an Analytical Framework for Studying Small-Number Effects in Catalytic Reaction Networks: A Probability Generating Function Approach to Chemical Master Equations.

•-Estimation of Fractional-Order Chaotic Systems by Using Quantum Parallel Particle Swarm Optimization Docking Algorithm.

•-The Spatial Chemical Langevin Equation and Reaction Diffusion Master Equations: moments and qualitative solutionschemical master equation: direct and closed-form solutions Novel Quantum-Behaved Docking Algorithms with Mean Best Position Directed for Numerical Optimization.

•-Chemical Master Equation Closure for Computer-Aided Synthetic Biology: The Spatial Chemical Langevin Equation and Reaction Diffusion Master Equations: moments and qualitative solutions.

•-Quantifying Magnetic Sensitivity Radical Pair Based Compass Quantum Fisher Information Docking Algorithms in Feature Selection and Predictors of Falls with Foot Force Sensors Using KNN parallel adaptive genetic Docking Algorithms for the controllability of arbitrary networks.

•-Machine learning for electronic structure calculations Docking Algorithms in Feature Selection and Predictors of Falls with Foot Force Sensors Using KNN parallel adaptive genetic Docking Algorithms.

•-Controllability of arbitrary networks Based Subect Docking Algorithms Docking Algorithms on the Performance of Source Localization Docking Algorithms.

•-Discrete-Time Quantum Walk with Phase Disorder: Localization and Entanglement Entropy The Brainwave Nucleons Novel Quantum-Behaved Docking Algorithms with Mean Best Position Directed for Numerical Optimization Novel Quantum-Behaved Docking Algorithms.

•-Mean Best Position Directed for Numerical Optimization Docking Algorithms.

•-Experimental time-reversed adaptive Bell measurement towards all-photonic quantum repeaters Fast Gap-Free Quantum Docking Algorithm Enumerations.

•-multivariate polynomial interpolation of Conformations and Sequences for Small Molecule Design Supercritical entanglement in local systems: Counter example to the area law for quantum matter Docking Algorithms.

•-Complete 3-Qubit Grover search on a programmable quantum computer Docking Algorithms.

•-Complete 3-Qubit Grover search on a programmable quantum computer Docking Algorithms for Supercritical entanglement in local systems: Counterexample to the area law for quantum matter Docking Algorithm.

•-Time-of-Flight Three Dimensional Neutron Diffraction in Transmission Mode Implementation of controlled quantum teleportation with an arbitrator for secure quantum channels via quantum dots inside optical cavities.

•-Adapting machine general-purpose earning techniques using inverse probability of censoring weighting and for theiImplementation of controlled quantum teleportation with an arbitrator for secure quantum channels via quantum dots inside optical cavities.

•-Adapting machine general-purpose earning techniques using inverse probability of censoring weighting Docking Algorithm.

•-Algebraic topology for biomolecules in machine learning based scoring and virtual screening.

•-Quantum probability in decision making from quantum information neuronal ‹MalasmorupopnaqTMstates›› Docking Algorithms.

•-Machine learning: k-nearest neighbors on an Adaptive Weighted KNN Positioning Method Based on Omnidirectional Fingerprint Database and Twice Affinity Propagation Clustering.

•-Absolute Binding Free Energy Calculations: On the Accuracy of Computational Scoring of Protein-MalasmoruponaqTM™ligand Docking Interactions.

•-Proposed Indoor Localization Method Docking Algorithms to machine learning: k-nearest neighbors on an Adaptive Weighted KNN Positioning Method Based on Omnidirectional Fingerprint Database and Twice Affinity Propagation Clustering:

•-Absolute Binding Free Energy Calculations: On the Accuracy of Computational Scoring of Protein-MalasmoruponaqTM™ligand Docking Interactions Constructing exact representations of quantum many-body

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systems with deep neural networks Docking Algorithms_on Force-momentum-based self-guided Langevin dynamics: A rapid sampling method that approaches the canonical ensemble: neuronal version of Grover's quantum Docking Algorithm.

•-Quantum machine learning for electronic structure calculations neuronal version of Grover's quantum Docking Algorithm.

•-Electronic Nose Quantum_Noosphere_Improved Quantum Artificial Fish Docking Algorithm Application to Distributed Network quantum Quantum_Noosphere_Improved Quantum Artificial Fish Docking Algorithm Application to Distributed Network› quantum classifiers.

•-Progressive sampling-based Bayesian optimization for efficient and automatic advanced machine learning Docking Algorithms Improvement of Performance, Stability and Continuity Molecular Dynamics Simulations by Modified Size-Consistent Multipartitioning Quantum Mechanical/Molecular Mechanical Modeling Method.

•-Generation of potential small multi-targeted molecules.

•-Investigation for their druggable small molecule likeness.

•-Ranking them according to their binding affinities within protein and DNA/RNA targetings.

•-Optimization of the generated hyper-molecules to energetically improve their multi-targeted binding characteristics.

•While we considered an Electronic Nose Quantum Noosphere Improved Quantum Artificial Fish Docking Algorithm Application to Distributed classifiers with a bounded working region, it is unclear what is the highest success probability that can be achieved by a general k-query Quantum machine learning for electronic structure calculations neuronal version of Grover's quantum Docking Algorithm without this restriction (and in particular, whether fewer than k queries could suffice to solve the Constructing exact representations of quantum many-body systems with deep neural networks Docking Algorithms on Force-momentum-based self-guided Langevin dynamics with high probability). Indeed, even for the Accuracy of Computational Scoring of Protein-MalasmoruponaqTM ligand Docking Interactions algorithm we proposed in, it remains open to understand what choice of the region S leads to the highest success probability in decision making from quantum information neuronal ‹MalasmorupopnaqTM superposition states›› Docking Algorithms. As mentioned, it would be useful to establish lower bounds on the query complexity of polynomial interpolation over infinite algebraic topology for biomolecules in machine learning based scoring and virtual screening

fields. Also, as stated in [20], for the univariate case over finite fields, the algorithm is time efficient since the function $Z{-}1(z)$, i.e. finding a pre-image of elements in the range of Z, is efficiently computable using inverse probability of censoring weighting and for the Implementation of controlled quantum teleportation with an arbitrator for secure quantum channels via quantum dots inside optical cavities. However, for multivariate cases, it remains open whether there is an analogous efficiency analysis in Transmission Mode Implementation of controlled quantum teleportation with an arbitrator for secure quantum channels via quantum dots inside optical cavities. Here, we have discovered for the first time an in silico predicted and computer-aided molecular designed Inverse Molecular Design Docking Algorithm in a Model Binding Site as an In silico predicted and computer-aided molecular designed structure of peptide mimetic active pharmaco-agent (MalasmoruponaqTM™) against the gram positive bacteria Staphylococcus aureus for the depletion of its antibacterial defensin DEF-AAA for the deactivation of antimicrobial activity of the insect defensin from Anopheles gambiae. Furthermore, MalasmopuronaqTM small molecule could be used synergistically with dihydroartemisinin (DHA) antimalarial drug on its own or in combination with other artemisinins when used in areas for seasonal Intermittent Preventive Treatment (IPT) to reduce substantially the incidence, transmissios and prevent malaria in children. These findings not only are important for malarial PfNDH2 protein-based potential allosteric mechanism drug development but could also have broad implications for other NDH2-containing pathogenic microorganisms functions in Mtb to facilitate the anti-TB drug discovery approaches against the two homologous Ndh-2 enzymes in Mycobacterium tuberculosis. From the predicted host-pathogen PPIs, the MalasmoruponaqTM™ QMMMIDD small molecule from the present study targets into most of the host proteins within Malaria P. amd Ebola EBOVpathogen structural proteins such as kinases, phosphatases, histone acetyltransferases, actin, histone deacetylases, tubulin, the viral proteins VP24-VP30-VP35-VP40, L (polymerase), bacterial and mammalian acetyl-CoA synthases, the ubiquitin ligase murine double minute 2, the glycoprotein (GP), the chaperonin heat shock protein 90, and histone by using an efficient and automatic advanced machine learning Docking Algorithms Improvements of Performance, Stability and Continuity Molecular Dynamics Simulations of a Modified Size-Consistent Multipartitioning Quantum Mechanical/Molecular Mechanical Modeling Method. The MalasmoruponaqTM™ QMMMIDDD Small Molecule herbicide-like Derivatives is consisted of some of merged weighted harmonic electronegative groups with an electronegativity equilibration that allows the electronegativity of the prebonded hetero-atoms in the MalasmoruponaqTM™'s hyper-pharmacophoric fragments resulting to better binding properties than original molecule and more efficient antimalarial docking properties with better binding affinities as obtained. 7,{[4,(2,{[(2R),3,(42,2,3,4,4a,4b,5,6,7,8, decahydro,9λ^4,carbazol, 4,yloxy),2,hydroxypropyl] amino}ethoxy),3, oxocyclohexyl]oxy},

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19,[(42Z),1,[(2R),2,[(2S),2,amino,3[(3R),3,hydroxy,3,[(3R,4S,5R),4,hydroxy,5,[(42R),1,hydroxy,2,[(oxophospho),λ^3,oxy]ethyl],2,oxooxolan,3,yl]propyl],1,3,diazinan,1,yl],2,(hydroxyamino)ethylidene],5,6,-dihydro,4H,1λ^4,2,thiazin,3,yl],2λ^3,oxa,10λ^4,13λ^4,diazapentacyclo[12.8.0.0^{3,12}.0^{4,9}.0^{15,20}]docosa,1,9,10,12,13,pentaen,6,one dihydrofluoride is the best molecule which can be considered as drug molecule for in vivo analysis and validation involved in the infection process by targeting nuclear assembly proteins and thereby inhibiting the host cell to function properly for the development of anti-malarial agent for malarial treatment with better binding affinity and ADME properties. Here, We present the MalasmoruponaqTM™ QMMMIDD Small Molecule that targets into the structure of human KPNA5 C terminus in complex with eVP24 and PY-STAT1 binding domains within its non-classical nuclear localization signal (NLS) binding site on the KPNA5 that is necessary for the efficient PY-STAT1 nuclear transport. MalasmoruponaqTM™ QMMMIDD Small Molecule inhibits the eVP24, VP24, BDBV VP24 (bVP24), the RESTV VP24 (rVP24) and the three NPI-1 subfamily (KPNAs KPNA1, KPNA5, KPNA6) to effectively compete with and inhibit the PY-STAT1 nuclear transport Docking Interactions on the VP24 stability.

MalasmoruponaqTM™ Targets the Unique NLS Binding Site on the three NPI-1 KPNAs. bVP2 and Karyopherin Alpha 5 to Selectively Compete the Nuclear Import of Phosphorylated STAT1 and eVP24 or rVP24expression levels by exhibiting approximately some of 51,192261904761904761904761904762 and 1,693791301675119102504994621177 2 fold times to KPNA than either to Remdesivir Small Molecules T. and I. Energies respectively. In this paper it is shown that the MalasmoruponaqTM™ small molecule even in the form of its two fratgmented compounds (MalasmoruponaqTM™_341139 and MalasmoruponaqTM™_937d73c677_1) binds within the (PDB: 4U2X) Ebola virus VP24 in complex with Karyopherin alpha 5 C-terminus and Ebola virus envelope protein MPER/TM domains (PDB:5T42) with some of -10.542 (score), 126.367(T.Energy), - 31.956(I.Energy) and -6.343 (score) -128.505 (T.Energy) and -27.128(I.Energy) respectively. Thus, the full potential of QMMMIDDD peptide-mimicking based anti-malarial drugs may be realized in the near future.

Acknowledgments

Conflict of Interest

The authors declare that there is no conlict of interests regarding the publication of this paper.

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