Generalized Chemical Block Systems on Chern-Simons φ_0 D_0 r_2 S_0 r_1 Topologies for the generation of the Roccustyrna Holomorphic Ligand.

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Research article

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Abstract

SARS-CoV-2 variants with spike (S)-protein D614G mutations now predominate globally and increase infectivity by assembling more functional S protein into the virion. In this paper, I combine topology geometric methods for the generation of novel drug designs by using generalized k - nearest neighbors as a Tipping–Ogilvie and Machine Learning application within a quantum computing chemical context targeting in a atomistic level the S proteins with aspartic acid (SD614) and glycine (SG614) at residue 614 protein apparatus. In this effort, I propose powerful enough computer - aided rational drug design strategies in computing docking usage to achieve very high accuracy levels for the generation of AI - Quantum designed molecules of GisitorviffirnaTM, Roccustyrna_{gs1}-TM, and Roccustyrna_{fr1}-TM ligands targeting the COVID - 19 - SARS - COV - 2 SPIKE D614G mutation by unifying Eigenvalue Statements into Shannon entropy quantities as composed on Tipping–Ogilvie driven Machine Learning potentials for nonzero Christoffel symbols. I also arrived at a new Zmatter derived finite - dimensional state integral and a Schwarzschild (DFT) $\ell_{\text{neuron}}(i) ::= \varphi \circ D \circ r_2 \circ S \circ r_1 \circ \zeta^2 (1 + \sum i) ::= (A \wedge A' (p)) \cdot \dots \otimes \dots \cdot e^- \rho (rr) \dashv \sigma - \tau \sigma \bar{q} - i_{+c0a2} (1 - y, y) 2 \rangle \psi (y) \nu$ improver for a Chern - Simons Topology and Euclidean symplectic $\omega ::= (i \sim) - 1 (dx/x) \wedge (dy/y)$ model by computing the analytically continued “holomorphic blocks” on an appropriate quantum Hilbert space H to put pharmacophoric elements back together.

Introduction

(1, 2, 3) The COVID - 19 viral infectious which emerged in China at the end of 2019 is accountable for many fatal cases. (2, 4, 5) On January 202, the WHO committee declared a global health emergency (3, 4 - 6) based on the rate of the increasing spread of the infection (4, 5 - 7) in the range 2.0 - 6.0 with a reproductive number (R_N) 5, 4 higher than SARS and Middle East respiratory Syndrome Coronavirus (MErS) respectively (8) with fatality rate of about 4%. (1 - 4) Collaborative efforts for Genomic characterization by using a simple DNA cryptography genetic code according to the main dogma of biology through a process of DNA $\rightarrow$ RNA $\rightarrow$ Amino Acid are underway from scientists worldwide to understand the rapid spread of the novel coronavirus (CoVs), and to develop effective coding drug - protein - gene personalized intervention options to control, characterize, and prevent this devastating viral diseases. (4, 6, 7, 8, 9, 10) In Latin, Corona means —crow based on their shapes. As a comprehensive compendium and megadiverse country, Brazil accounts for 10–20% of known living species of available biogeochemical information in the world. However, a major part of the biological and chemical biodiversity in Brazil's natural products remains unexplored (2– 13, 14, 15, 16, 17) Molecular structures as a protein code (cipher - protein) were determined in heterodox interpretations (22) by solving the time - independent (21 - 22) Schrödinger equation. QM methods, vertex prizes, and edge costs including ab initio Density Field Theories (DFT) (23) have become a common approach as a quantum - many body premium technique and semi - empirical computational scheme for studying docking free energies among other quantitative understanding observables. Density Field Theories (DFT) are continuously increasing for more systematic and less expensive methods (25) when compared to traditional drug development approaches to repositioning drugs and physical extracts respectively. (26, 27, 28) However, the Schrödinger equations in Markovian and (27) non - Markovian scenarios cannot be solved for any but a one - data - driven (29) electron system method (the hydrogen atom), to construct a family of solutions of (28, 30) equations and approximations need to be made. According to QM, (2 - 19, 23) and during the construction of stochastic Schrödinger (29) equations, an electron bound to an atom cannot possess any (2 - 17, 21, 22, 23, 24, 25, 26, 27, 28) arbitrary energy that converges quickly and reliably by acknowledging the conditional Bohmian wavefunction when producing the desired distribution or occupying any position in space using statistical and machine (23, 24 - 37, 38) learning concepts. Molecular Pairs (MMP), Lindenbaum - Tarski logical spaces, Adaptive Weighted KNN Positioning Matched Bemis, and Murko (BM) driven eigenvalue statements were incorporated in this project when analyzing pharmacological data allowing a well - defined superposition for each fragmented pharmacophore. This shows that the application to quantum computing as orthogonally applied for the design of small molecules may allow pure mechanical computations both for re - generating Lipinski rules and quantum inferences to bridge the gap between practical in vitro testing implementations and theoretical docking scalability predictions. (25, 27, 28) Since it has been shown that Path selection into a nonlinear riemann - Hilbert simple problem of any metal formula φ for quantum repeater networks towards the determination of the exact interpolating function of $h(\lambda)$ can be geometrically represented by Chern - Simons logical spaces and subspaces I decided in this drug design project to cryptographically implement supersymmetric solutions and Borel Singularities for $N ::= 2$ allowing a quantum repeater based vectorial Supersymmetric representation. (20, 26, 27, 28, 29, 30, 31) In general, the notions of Lindenbaum matrix and associated axiomatic formulations (AQFT) for Lindenbaum - Tarski guided Adaptive Weighted KNN Positioning are continuing to shape the field of its relative algebraic logic by introducing the CS topology on a set when defining the (31) cartesian product for parallel topological spaces. Additionally, subbase supersymmetric solutions led us to further algebraization of topology products, which had been begun by George Boole in the 19th century, as well as to an innovative language of logic, in a symmetric model theory containing no other constants but only one connective $\rightarrow$. Philosophical interpretations of QM Molecular Pairs (MMP) as a core part of contemporary physics (Minkowski - type, wave - edge, etc), (20, 27, 32 - 33) including von Neumann and Dirac formulation states as well as probabilistic transformations on Murko (BM) driven eigenvalue statements for algebraic multi - metrics (Triangle area, Bond - angle, etc) were incorporated in this project to treat Tipping–Ogilvie and Machine Learning observables foundationally as interaction information theory (QIT) reference frames. (20, 33, 34, 35) In this project, I show an original strategy and demonstrate the utility and the mechanics of this (32) unified molecular formalism as a Tipping–Ogilvie and Machine Learning QMMMP application within a quantum computing context as perturbed asymptotically through the example of coupled anti - de Sitter black harmonic black - hole oscillators and brane spacetimes. I expect this Lindenbaum - Tarski driven Chern - Simons representation to generate a valid QSAR modeling, and lead compound design formalism for the designing of a novel multi - chemo - structure against the crystal structure of COVID - 19 protein targets. (29, 35, 36) A meta - server and a Kappa - Symmetry C++ algebra of local observables were incorporated in this project for the docking of FDA - approved small molecules, peptide - mimetic, and humanized antibodies against potential SARS-CoV-2 protein targets via a generalized procedure of Quantization of classical fields which were fused together with QSAR automating modeling to lead the commutation and anticommutation relations. (37, 39, 41, 42) Dynamic niching and flexible heuristic genetic algorithmic states for automatic molecule re - coring and fragmentation were applied in this InSilico effort to fragment and re - core a database of molecules against the structure and functions of SARS - CoV - 2 binding sites. Universal Quasi-helical Functional Group Activity Coefficients (UNIFAC) on free energy docking observables in four dimensions of a rich QFT (40, 41, 42) were deployed in this pharmacophoric merging example for linking fragments, and condensed chemical block systems where D - branes are wrapped on Lagrangian chemical spaces. (37, 38, 40, 43) A Hybrid quantum repeater is introduced in this multi - target and multi - site - based virtual screening paper for the robust creation of entanglement between remote memory qubits. To demonstrate its flexibility, I tackle a hugely different objective issued from a 5 - dimensional submanifold organic

molecular domain (43, 44) as a transverse holomorphic structure, which means that there is a given 3 - dimensional foliation for each one tangent bundle modulo foliation. I show that my method can generate sets of optimized critical molecules as integrable structure complexes which having high energy or low energy, starting only from penicillamine derivatives. I also set constraints on a synthesizability score and structural features when the 3 - brane is a chemical subspace of the 5 - brane, and the flux on the invariant 5 - brane vanishes when restricted to the 3 - brane, the 3 - brane refers to my transverse holomorphic chemical structure. (41, 42) Flexible Topology Euclidean Geometries were used to fragment molecules automatically in this molecular modeling and drug designing project on several parameters while keeping the definition of the groups as simple as possible. Maximum Common Substructure (MCS) topologies for generalized k - nearest neighbors on Tipping–Ogilvie and Machine Learning generated Molecular Pairs (MMP), and an Adaptive Weighted KNN Positioning Matched Bemis and Murko (BM) approach employed for supercritical entanglements introducing an advanced quantum mechanical inverse docking algorithm providing further insight to confirm the practicality of docking energy predictions. In this protocol, tools from conventional cryptography for wild type and selected mutations for Nsp3 (papain - like, PLpro domain), Nsp5 Nsp15 (NendoU), (Mpro, 3CLpro), Nsp12 (RdRp), N protein and Spike were combined as inputs and the key element functions of SARS - CoV - 2 protein pathways in understanding and designing possible novel antiviral agents, from both a quantum algebraic and a cheminformatic perspective along with the principles of the regulation of computer - aided drug discovery methodologies. Molecular scaffolds are generally used to describe the common core structures of the molecules (25, 33, 38, 39, and 44). In this project the selected herbs classified into structural classes using the characteristic scaffolds of each group (14, 32, 33, 42). In medicinal chemistry, a molecular scaffold is used to represent the core structure of a group of active compounds. Since the compounds with the same scaffold may influence a particular metabolic pathway, the molecular scaffolds can effectively contribute to the prediction of biological activities (8, 16, 40, 42, and 43). The scaffold of molecule groups is defined as a common sub - graph of the graphs of the molecule groups. Representatively, Maximum Common Substructure (MCS), Matched Molecular Pairs (MMP), and Bemis and Murko (BM) are the commonly used methods to produce molecular scaffolds (22–30, 39, 40, and 42, 44). This paper concentrates on the unification of quantum mechanics fundamental theories into 3 - dimensional field wave equations for a $N = 2$ supersymmetric generalized k - nearest molecular oscillator. By describing the second - order term for Tipping–Ogilvie 3 - manifolds which refer to our designed structure we expanded them into generalized chemical entities through Chern Simons connections over compact solutions when solving the Cluster of Eqs. of $\psi(y) v = Ev = y \lambda \exp(-\beta v y) F(\lambda - \gamma^2 / \beta v, 2\lambda, 2\beta v y) F(c, b; y) = \sum v = 0 \infty \Gamma(c+v) \Gamma(b) y v \Gamma(b+v) \Gamma(c) v! c 0 a 2 (1 - \gamma^2 (v + \lambda) 2) v = 0, 1, 2, \dots \lambda = 1/2 + \gamma^2 + 1/4 c 0 a 2 (1 - \gamma y) 2 \psi(y) v (\phi k) \cdot \dots \cdot e - \rho(r) = \sqrt{k 1 m C Q 2 t \phi(t) c 0 \zeta 2 (1 + \sum i) = (A \wedge A' (p)) \cdot \dots \cdot e - \rho(r) r c = L 2 \pm L 2 (1 - 6 G 2 M 2 / L 2) 2 G M = L 2 G M, 3 G M! = \sqrt{(\partial v \wedge \partial q \cdot \dots \cdot e - \rho(r) = B + |a 2' (t) \rangle C Q 2 t \phi(t) c 0 \zeta 2 (1 + \sum i) = (A \wedge A' (p)) (\phi k) \cdot \dots \cdot e - \rho(r) = \sqrt{k 1 m \cdot \dots \cdot e - \rho(r) = \sqrt{(\partial v \wedge \partial q, \partial u \wedge \partial p) C Q(a + \ell) t a + \ell \{1/12 + (|a 1' (t) \rangle C Q 1 t \phi(t) \rangle B + |a 2' (t) \rangle C Q 2 t \phi(t) c 0 \zeta 2 (1 + \sum i) = (A \wedge A' (p)) t | \phi(t) (Cluster of Eqs.1) for a better representation of the realistic potentials of computing docking free energy eigenvalues.$

Materials And Methods

Detailed methods are provided in the online version of this paper and include the following:

EXPERIMENTAL MODEL AND SUBJECT DETAILS (SI Supplementary material)

- Preparation of the protein structures
- Screening NuBEE Phyto – library, and COVID2019 targets.

METHOD DETAILS (SI Supplementary material)

- Biogenetoligandorol AI - heuristic (DFT) Generalized algorithm for Chern - Simons Weighted ℓ neuron (i) : $\varphi_0 \circ r_2 \circ s_0 \circ r_1$ Topologies: A Quantum Hilbert space H attempt to put pharmacophoric elements back together.
- Roccustyrna ligand: Docking Model, Grid points and Protein targets.
- In silico Bioactivity Prediction and ADMET Analysis of the Roccustyrna small molecule.

Results

In silico Prediction of the Roccustyrna ADMET Properties and Bioactivity Score.

To predict important molecular properties such as logP, polar surface area, drug - likeness and bioactivity of our new prototype and small - sized Roccustyrna ligand 2 - ((fluoro ((2E) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) cyano - lambda6 - sulfanyl)) methyl) - phospho - rylidene) amino) - 4, 6 - dihydro - 1H - purin - 6 - one (1S, 2r, 3S) - 2 - ((1S, 2S, 4S, 5r) - 4 - ethenyl - 4 - sulfonyl - bicyclo (1S, 2r, 3S) - 2 - ((1S, 2S, 4S, 5r) - 4 - ethenyl - 4 - sulfonyl - bicyclo (3.2.0) heptan - 2 - yl) oxy} amino) - 3 - ((2r, 5r) - 5 - (2 - methyl - 6 - methylidene - 6, 9 - dihydro - 3H - purin - 9 - yl) - 3 - methylideneoxolan - 2 - yl) phosphirane - 1 - carbonitrile (3.2.0) heptan - 2 - yl) oxy} amino) - 3 - ((2r, 5r) - 5 - (2 - methyl - 6 - methylidene - 6, 9 - dihydro - 3H - purin - 9 - yl) - 3 - methylideneoxolan - 2 - yl) phosphirane - 1 - carbonitrile, the Molinspiration tool was employed as customized on the basis of this rational anti - viral drug design study. The milogP (Octanol - water partition coefficient logP) and TPSA (Topological polar surface area) values were calculated by utilizing the same online tool using Bayesian statistics. These In - Silico results indicated that the milogP value of the Roccustyrna small molecule was predicted as having optimum lipophilicity properties (logP < 5) (Han et al, 2019) in the aspect of dermal absorption and parallel artificial permeation (Table S1), (Table S2), (Table S3), (Table S4).

Screening of the Roccustyrna Inhibitor for Spike Protein - rBD - ACE2 Interaction.

In this study, we have shown that the QMMM designed Roccustyrna small molecule which was designed in silico by using Topology Euclidean Geometric and Artificial Intelligence - Driven Predictive Neural Networks was engaged in the binding domains of the protein targets of of the (PDB:1xak) (Figure S2) with the docking energy values of (T.Energy, I.Energy, vdW, Coul, Numrotors, rMSD, Score), (- 19.625, - 35.483, 7.633, - 43.116, 7, - 5.813) Kcal/mol, (Table S4), (Table

S5) The Roccustyrna chemical structure interacted into the binding sites of the protein targets of (PDB:6w9c), (Figure S2) with the negative docking energies of the (T.Energy, I.Energy, vdW, Coul, Numrotors, rMSD, Score), (- 36.678, - 55.648, - 7.519, - 48.129, 7, - 6.762) Kcal/Mol. The same combination of small molecules also generated hydrophobic interactions when docked onto the A1, 02J C binding cavities of the amino acid of 168 PrO with the docking energy values of (- 3.53, - 2369, - 1303, - 10.425, - 3.42, - 72.447, - 13.394, - 3.19, - 70.551) Kcal/mol. Our new QMMM designed cluster of quantum thinking small molecules additionally involved in the generation of the hydrogen bonding within the PJE: C:5 (PJE - 010) 010:C:6 Interacting chain (s) while generating hydrophobic interactions when docked into the A6, 010 C binding domains of the amino acid of the 25THr with the docking energy values of (- 3.73, - 2415, 179, - 7.156, - 21.406, - 66.898 - 8.709, - 22.779) Kcal/mol. The combination of GisitorviffirmaTM, Roccustyrna_gs1_TM, and Roccustyrna_fr1_TM cluster of active pharmacophoric sites of the 2 - ((fluoro ((2E) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) cyano - lambda6 - sulfanyl) methyl) phosphorylidene) amino) - 4, 6 - dihydro - 1H - purin - 6 - one (methylamino) - 1, 6 - diazabicyclo (3.2.0) heptan - 4 - yl oxy} imino) interacted into the A6 010C binding cavities of the amino acid of the 26 THr with the docking energy values of (- 3.81, - 2415, - 186, - 7.156, - 21.406, - 66.898, - 6.155, - 24.392, - 64.757) Kcal/mol. The combination of the same cluster of active pharmacophoric sites of the 2 - ((fluoro ((2E) - 5 - dimethyl - 7 - oxo - 4 - thia - 1 - azabicyclo (3.2.0)heptane - 2 - carbonyloxy) ((2 - amino - 6 - oxo - 6,9 - dihydro - 3H - purin - 9 - yl) oxy) (hydroxy) phosphoryl} oxy) phosphinic acid - ylidene+,*cyano (2,6 - diazabicyclo*3.1.0+hex - 1 - oxabicyclo (2.1.0) pentan - 2 - ylidene) cyano - lambda6 - sulfanyl) methyl) phosphor - ylidene) amino) - 4, 6 - dihydro - 1H - purin - 6 - onedihydro - 3H - purin - 9 - yl) - 3 - hydroxy - oxolan generated a docking effect which was involved in the generation of hydrogen bonds when docked into the A 6 010 C binding cavities of the amino acid of 143 GLY with the docking energy values of (- 62.905) Kcal/mol. In addition, the CoMFA contour map of electrostatic regions around Roccustyrna chemical structure indicated to us that contact residues from the Roccustyrna ligand when docked onto the SARS - COV - 2 protein targets of (PDB:2zu5) around the Roccustyrna chemical structure hit the entire sequence of the amino acid of the V - M - THr - 25, V - S - THr - 25, V - M - THr - 26, V - S - HIS - 41, V - M - LEU - 141, V - M - ASN - 142, V - S - ASN - 142, V - M - GLY - 143, V - S - CYS - 145, V - M - MET - 165 with the binding energy values of the - 97.2 and - 5.16512, - 4.15949, - 9.8487, - 4.77062, - 4.72901, - 6.7295, - 5.82428, - 5.35883, - 4.2588, - 5.37491 Kcal/mol respectively. (Figure S2d) The same prototype pharmacophoric element named Roccustyrna when docked into the A5, PJE C2 binding sites of the amino acid sequence of V - S - HIS - 41, V - M - LEU - 141, V - M - ASN - 142, generated hydrogen interactions with the binding energy values of the (- 16 3.07, - 153.73, - 2408) Kcal/mol/A, in the coupled atoms of the N3 and O2 with the docking energy values of (- 12.282, - 14.994, - 67.123) Kcal/Mol. The binding patterns of the 02J:C:1 (02J) active sites of the amino acid sequence of V - S - THr - 25, V - M - THr - 26, V - S - HIS - 41, V - M - LEU - 141, V - M - ASN - 142, V - S - ASN - 142, V - M - GLY - 143, V - S - CYS - 145, V - M - MET - 165 onto the 168 PrO, A1, 02J C binding domains generated hydrophobic interactions with the docking energy values of (- 3.53, - 2369, - 1303, - 10.425, - 3.42, - 72.447, - 13.394, - 3.19, - 70.551) Kcal/mol/A inside the PJE:C:5 (PJE - 010) 010:C:6 A5, PJE C2 interacting chain (s) : A C. (Figure S3) D10 - C - 1099 DMS: A: 402 (DMS) binding sites were also constructed when the combined pharmacophoric elements of the combination of GisitorviffirmaTM, Roccustyrna_gs1_TM, and the Roccustyrna_fr1_TM ligands docked inside the (PDB: 6lu7) protein targets. Hydrogen Bonds were then identified when the RoccustyrnaTM's chemical coupled atoms interacted within the 298 ArG A amino acid into the 402 DMS A Ng+ 2377 O2 binding cavities with the docking energy values of (- 1.76, - 2.73, - 166.89, - 2331, - 6.971, - 0.756, - 7.541 - 9.7, - 0.883, - 7.581) Kcal/mol/A. Salt Bridges were also shown to be involved in the generation of the Sulfonium bonding when docked inside the DMS A 5.49 binding cavities within the 295 ASP A amino acid domains with the docking energy values of (- 402, - 2376, - 6.081,-6.367 -10.436, -2.231, -5.560) Kcal/mol/A. Pi - Cation Interactions of sulfonium bonding within our small molecule whole residue subsurface were also constructed within the amino acid 8 PHE A inside the 402 DMS A pharmacophoric sites with the docking energy values of (- 4.70, - 1.01, - 2376, - 6.081, - 6.367, - 8.339, - 4.556, - 4.264) Kcal/mo/A. (Figure S3), Hydrophobic Interactions were simultaneously generated by the Roccustyrna chemical residues when docked in the (PDB:6lu7) protein targets of inside the D10 - H - 1099. X77:A:401 (X77) side domains within the active sites of the amino acid cavities of the 41 HIS A 401 X77 A, 165 MET A 401 X77 A, and 166 GLU A 401 X77 A with the docking energy values of (- 3.75, - 4670, - 609, - 20.444, - 13.613, - 29.034, - 19.778, - 13.574, - 32.721 - 3.90, - 4673, - 2529, - 19.389, - 17.775, - 28.688, - 16.611, 16.152, - 26.489, - 3.86, - 4661, - 2546, - 17.350, - 23.138, - 25.438 - 16.439, - 20.244, - 23.055, - 18.9, - 3.90, - 4657, - 2881, - 21.763, - 15.894, - 23.429, - 24.934, - 13.635, - 23.312) Kcal/mol/A showing that my AI - quantum thinking chemical structure named Roccustyrna is capable of generating Hydrogen Bonds when docked onto the 41 HIS A 401 X77 A, 143 GLY A 401 X77 A, 144 SEr A 401 X77 A, and 166 GLU A 401 X77 A, sequence of amino acids while targeting the Npl 4680 N2, O3 4679 N2 Nam 4682 O2, and Nam 4683 O2 binding sites with the binding free energy values of the (- 3.46, - 3.79, - 106.13, - 611, - 20.860, - 19.573, - 32.52, - 19.394, - 16.086, - 32.767, - 2.17, - 2.94, - 148.03, - 2216 - 19.635, - 22.244, - 29.036 - 18.779, - 24.455, - 30.773, - 3.14, - 3.42, - 101.78, - 2228 - 16.096, - 21.679, - 26.816, - 14.503, - 23.707, - 29.056, - 1.98, - 2.80, - 158.32, - 2542 - 18.546, - 18.654, - 26.028 - 16.172, - 18.348, - 24.583) Kcal/molA respectively. (Figure S3) The 2 - ((fluoro ((2E) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) cyano - lambda6 - sulfanyl) methyl) phosphorylidene) amino) - 4, 6 - dihydro - 1H - purin - 6 - one (1Z) - 2 - { ((2S, 3S, 5r) - 5 - (2 - amino - 6 - oxo - 6, 9 - dihydro - 1H - purin - 9 - yl) - 3 - hydroxyoxolan - 2 - yl) methylidene) - 2 - cyano - 1 - ((2S, 4r, 5r) - 2 - methyl - 2 - (methylamino) - 1, 6 - diazabicyclo (3.2.0) heptan - 4 - yl) oxy} imino) - 1lambda5, 2lambda5 - azaphosphiridin - 1 - ylium druggable scaffold of the Roccustyrna small molecule therefore competes with endogenous SARS - CoV2 PLpro for binding to Lys711 and Arg355 targeting into the binding domains of the critical SARS - CoV2 PLpro residues onto the SARS - COV - 2 protein targets of (PDB:2zu5) within the binding sites of the amino acid of the V - M - THr - 25, V - S - THr - 25, V - M - THr - 26, V - S - HIS - 41, V - M - LEU - 141, V - M - ASN - 142, V - S - ASN - 142, V - M - GLY - 143, V - S - CYS - 145, V - M - MET - 165 with the binding energy values of the (- 97.2 and - 5.16512, - 4.15949, - 9.8487, - 4.77062, - 4.72901, - 6.7295, - 5.82428, - 5.35883, - 4.2588, - 5.37491) Kcal/mol respectively. CoMFA analysis of electrostatic regions around the Roccustyrna small molecule a chemical structure indicated to us that Hydrogen bonds, Salt bridges and Metal complexes containing Diphosphate, dihydrogen and ION binding sites were generated into the contact residues of the Roccustyrna's small molecule when docked onto the SARS - COV - 2 protein targets of the (PDB:2zu5) within the sequence of the amino acids of V - M - THr - 25, V - S - THr - 25, V - M - THr - 26, V - S - HIS - 41, V - M - LEU - 141, V - M - ASN - 142, V - S - ASN - 142, V - M - GLY - 143, V - S - CYS - 145, V - M - MET - 165 with the negative docking values of (- 97.2, and - 5.16512, - 4.15949, - 9.8487, - 4.77062, - 4.72901, - 6.7295, - 5.82428, - 5.35883, - 4.2588, - 5.37491) Kcal/mol/A respectively. (Figure S4a), (Table S4), (Table S5) DMS:A:402 (DMS) binding sites into the 524 Nam 2578 O2 02J (5 - Methylisoxazole - 3 - carboxylic acid) domains were generated inside the 65 ASN A 402 DMS A cavities when RoccustyrnaTM drug deisgn interacted with the PDB:6lu7 protein targets with the docking energy values of (- 2.05, - 2.94, - 148.0, - 8.211, - 20.857, - 29.787 - 11.058, - 20.242, - 30.160 298) Kcal/mol/A. Salt Bridges were also constructed when our prototype's surface sites docked inside the DMS - A, Ng+ 2582 O2 binding pocket cavities of the amino acid of the ArG A 403 with the docking energy values of (- 1.93, - 2.87, - 160.38, - 2512, - 7.044, - 0.753, - 7.469, - 9.865, - 1.270, - 7.327) Kcal/mol/A. Sulfonium bondings were also constructed when our small molecule interacted within the 403 DMS A contact residues of the binding sites of the 295 ASP amino acid with the docking energy values of (- 5.31, - 2581, - 6.227, - 1.042, -

6.293, - 10.460, - 2.019, - 5.344) Kcal/mol/A. (Figure S4) 999 ZN D 20947 Zn, ZN:A:998 (ZN), and 998 ZN A 20940 Zn 470 S Metal Complexes were also constructed into the 02J (5 - Methylisoxazole - 3 - carboxylic acid) PJE - C - 5 residues when the Roccustyrna's chemical fragment of (1Z) - 2 - { ((2S, 3S, 5r) - 5 - (2 - amino - 6 - oxo - 6, 9 - + - 6 - fluoro - 3, 4 - dihydropyrazine - 2 - carboxamide (7ar) - 5 - amino - N - * (S) - , 2 - * (3 - oxabicyclo (2.1.0) (1S, 4S) - 5 - oxabicyclo*2.1.0 +pentan - 2 ((2S, 5r, 6r) - 6 - ((2S) - 2 - amino - 2 - phenylacetamido) - 3, 3 - dihydro - 1H - purin - 9 - yl - 4 - yl) oxy} - imino) - 1lambda5, 2lambda5 - azaphosphiridin - 1 - ylium generated tetrahedral side chains inside the 117 CYS D, 74 CYS A amino acids with the docking energy values of (- 1103.746, - 101.848, - 13.968, - 103.306, - 102.613, - 1118.874, - 104.964, - 32.313 - 118.938, - 103.573, - 30.6090Kcal/mol/A indicating that our multi - targeted drug design has the ability of generating a self - assembled monolayer inside the 1: Mg, NA (1), 1, 10P, G Metal Complexes when docked onto the 1, 553A binding cavities of the amino acid of the ArG into the PDB:7bv2 protein targets. The combination of GisitorviffirnaTM, Roccustyrna_gs1_TM, and Roccustyrna_fr1_TM cluster of pharmacophoric (1Z) - 2 - { ((2S, 3S, 5r) - 5 - (2 - amino - 6 - 2 - yl) methylidene) - 2 - cyano - 12 - ((fluoro ((2E) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) cyano - lambda6 - sulfanyl)) methyl) phosphorylidene) amino) - 4, 6 - dihydro - 1H - purin - 6 - one - ((2S, 4r, 5r) - 2 - methyl - 2 - (methylamino) - 1, 6 - dia - zabicyclo (3.2.0) heptan - 4 - yl) oxy} imino) - 1lambda5, 2lambda5 - azaphosphiridin - 1 - ylium active site of the 2 - lambda5 - azaphosphiridin - 1 - ylium was engaged in hydrogen bonding interactions with the formation of hydrogen bonds inside the N3 1266 O2 binding cavities within the amino acid sequence of V - S - HIS - 159, V - S - ARG - 160, V - S - ARG - 112 V - M - GLU - 148 V - M - PHE - 150, V - S - PHE - 150, V - S - HIS - 159, and V - M - TYR - 161 with the docking energy values of (- 1.93, - 2.80, - 145.29, - 1105, - 3.81, - 2415, - 186, - 7.156, - 21.406, - 66.898 - 6.155, - 24.392, - 64.757, - 2411, - 8.911, - 17.849, - 65.703 - 8.918, - 17.918, - 62.905, - 2.16, - 3.07, - 153.73, - 2408, - 12.282, - 14.994, - 67.123, - 15.161, - 15.336, - 68.144) Kcal/mol. The Roccustyrna small molecule involved also in the generation of the hydrophobic interactions within the binding domains of the amino acid of the V - M - LYS - 557, V - S - LYS - 557, V - M - ARG - 567, V - M - ASP - 568, V - S - ASP - 574, V - S - PHE - 43, V - M - ARG - 44, V - M - SER - 45, V - S - SER - 45 with the docking energy values of (- 3.73, - 2415, - 179, - 7.156, - 21.406, - 66.898 - 8.709, - 22.779) Kcal/mol as illustrated in the (Figure S4). In this drug designing project the electrostatic regions around the combination of GisitorviffirnaTM, Roccustyrna_gs1_TM, and Roccustyrna_fr1_TM pharmacophoric elements of (7ar) - 5 - amino - N - ((S) - {2 - ((S) - ((E) - (amino - methylidene) amino) (cyano) methyl) hydrazin - 1 - yl} (aziridin - 1 - yl) phosphoryl) - 1 - ((2E) - 2 - ((fluoro - methanimidoyl) imino) acetyl) - 7 - oxo - 1H, 7H, 7aH - pyrazolo (4, 3 - d) pyrimidine - 3 - carboxamide; N - { ((2 - amino - 6 - oxo - 6, 9 - dihydro - 1H - purin - 9 - yl) amino) ((1 - (5 - ((cyano ((1 - ((diamino methylidene) amino) ethenyl)) amino) oxy) methyl) - 3, 4 - dihydroxyoxolan - 2 - yl) - 1H - 1, 2, 4 - triazol - 3 - yl) (formamido) phosphoryl) - 6 - fluoro - 3, 4 - dihydropyrazine - 2 - carboxamide; (3 - (2 - amino - 5 - sulfanylidene - 1, 2, 4 - triazolidin - 3 - yl) oxaziridin - 2 - yl) ((3 - sulfanylidene - 1, 2, 4, 6 - tetraaza bicyclo (3.1.0) hexan - 6 - yl)) phosphoroso1 - (3, 4, 5 - trifluorooxolan - 2 - yl) - 1H - 1, 2, 4 - triazole - 3 - carboxylate 3 - hydroxyoxolan - 2 - yl) methylidene) - 2 - cyano - 1 - ((2S, 4r, 5r) - 2 - methyl - 2 - (methylamino) - 1, 6 - diazabicyclo (3.2.0) heptan - 4 - yl) oxy} imino) - 1lambda5, 2 - lambda5 - azaphosphiridin - 1 - ylium (Figure S4a), (Figure S4f) showing that the combination of GisitorviffirnaTM, Roccustyrna_gs1_TM, and Roccustyrna_fr1_TM binding site (s) inside the (PDB:6lu7) binding domains of the 02J:C:1 (02J) regions while co - generating Hydrophobic Interactions and Hydrogen Bonds against the coupled atoms of the Nam 2411 O3 inside the cavities of the crucial entering amino acids of the 25 Thr A 6 010 C and 143 GLY A 6 010 C with the docking energy values of (- 3.73, - 2415, - 179, - 7.156, - 21.406, - 66.898, - 8.709, - 22.779, - 70, - 26, - 81, - 2415, - 186, - 7.156, - 21.406, - 66.898, - 6.155, - 24.392, - 64.757, - 1.93, - 2.80, - 145, - 29, - 1105, - 8.911, - 17.849, - 65.703, - 8.918, - 17.918, - 62.905) Kcal/mol/A respectively. Electrostatic CoMFA analysis of the contact residues of the best docking poses of the contact chemical residues indicated also that the entire Roccustyrna chemical structure when docked onto the SARS - COV - 2 protein targets of (PDB:3fqj) hits the positively charged SARS - CoV Mpro - N1 groups and SARS - CoV Mpro - N3 regions favored by negatively charged groups within the amino acid sequence of the V - S - HIS - 159, V - S - ArG - 16, V - S - ArG - 112, V - M - GLU - 148, V - M - PHE - 15, V - S - PHE - 15, V - S - HIS - 159, V - M - TYr - 161 with the docking energy values of (- 101, - 14.0762, - 5.11094, - 7.98447, - 4.17314, - 4.43549, - 9.66939, - 9.42926, - 7.32) Kcal/mol/A. (Figure S2b) Other QSAR/CoMFA experiments have shown to us that the entire pharmacophoric residues of the Roccustyrna chemical design when docked onto the Mpro - N9 binding sites inside the SARS - COV - 2 protein targets of (PDB:6xs6), interacted negatively with the Cys145 catalytic site of SARS - CoV - 2 Mpro charged groups within the sequence of the amino acid of V - M - LYS - 557, V - S - LYS - 557, V - M - ArG - 567, V - M - ASP - 568, V - S - ASP - 574, V - S - PHE - 43, V - M - ArG - 44, V - M - SEr - 45, and V - S - SEr - 45 with the docking energy values of (- 85.8, and - 5.56, - 8.38956, - 5.77168, - 6.13664, - 12.8661, - 5.37546, - 6.10391, - 5, 928) Kcal/mol respectively. (Figure S2c) Moreover, Cluster of the QSAR/QMMM/CoMFA map analysis of the electrostatic regions around the (rboximidoyl - 3 - fluoro - (1S, 4S) ((diaminomethylidene) amino) ethenyl) amino+oxy - methyl) - 3, 4 - dihydroxyoxolan - 2 - yl+ - 1, 2, 4 - triazol - 3 - yl - (formamido) phosphoryl + - 6 - fluoro - 3, 4 - dihydropyrazine - 2 - carboxamide (7ar) - 5 - amino - N - * (S) - , 2 - * (3 - oxabicyclo (2.1.0) (1S, 4S) - 5 - oxabicyclo*2.1.0 +pentan - 2 ((2S, 5r, 6r) - 6 - ((2S) - 2 - amino - 2 - phenylacetamido) - 3, 3 - dimethyl - 7 - oxo - 4 - thia - 1 - azabicyclo (3.2.0) heptane - 2 - carbonyloxy) ((2 - amino - 6 - oxo - 6, 9 - dihydro - 3H - purin - 9 - yl) oxy) (hydroxy) phosphoryl oxy) phosphinic acid - ylidene+, *cyano (2, 6 - diazabicyclo*3.1.0+hex - 1 - en - 6 - yl) (rboximidoyl - 3 - fluoro - (1S, 4S) ((diaminomethylidene) amino) ethenyl) amino+oxy - methyl) - 3, 4 - dihydroxyoxolan - 2 - yl+ - 1, 2, 4 - triazol - 3 - yl - (formamido) phosphoryl + - 6 - fluoro - 3, 4 - dihydropyrazine - 2 - carboxamide (7ar) - 5 - amino - N - * (S) - , 2 - * (3 - { ((1S, 4S) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) { (cyano ((2, 6 - diazabicyclo (3.1.0) hex - 1 - en - 6 - yl)) phosphanyl - (fluoro) methyl) - lambda6 - sulfanyl)one pentan - 2 - ylidene) { (cyano ((2, 6 - diazabicyclo (3.1.0) hex - 1 - en - 6 - yl)) phosphanyl - lambda6 - (rboximidoyl - 3 - { ((1S,4S) - 5 - oxabicyclo (2.1.0)pentan - 2 - ylidene){ (cyano ((2,6 - diazabicyclo (3.1.0)hex - 1 - en - 6 - yl)) phosphanyl) (fluoro)methyl) - lambda6 - su lfanyl)one (rboximidoyl - 3 - oxabicyclo (2.1.0)pentan - 2 - ylidene){ (cyano ((2,6 - diazabicyclo (3.1.0)hex - sulfanyl)oneboximidoyl - 3 - { ((1S, 4S) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) contact residues of the Roccustyrna small molecule when docked onto the SARS - COV - 2 protein targets of (PDB:2ghv) after solving the (id "...

$$\otimes \dots \varepsilon) \cdot \Delta == == \sqrt{q\rho} \{ \Psi || T || \Psi \} (id \dots \otimes \dots \varepsilon) \cdot \Delta == == (\varepsilon \dots \otimes \dots id) e Z^*, z^0 ::= == \nabla \nabla NaIrr H\Delta M \dots \otimes \dots H\Delta N \sim A \wedge (m0-xi) rA \dots \nabla \nabla V ne$$
as parameterized input for $2/3 \int rrr^0 rr \int rA \wedge rA \wedge rAp \dots \otimes \dots ik 4\pi Z M A \wedge rAp0E \sum \sum \sum \sum \sum \sqrt{q\rho} \{ \Psi || T || \Psi \} (-1) \omega + \omega e 2\pi bwe Z^*, z^0 ::= == \nabla \nabla NaIrr H\Delta M \dots \otimes \dots H\Delta N \sim A \wedge (m0-xi) rA \dots \nabla \nabla V ne$
 $2/3 \int rrr^0 rr \int rA \wedge rA \wedge rAp \dots \otimes \dots ik 4\pi Z M A \wedge rAp0E \sum \sum \sum \sum \sum (-1) \omega + \omega e 2\pi bwe$
when combined with (METHODS AND MATERIALS) (Scheme of Eqs.1 - 44), (Group of Eqs.1 - 128), (Cluster of Eqs.1 - 81) as a chemical block for the generation of the chemical scaffold of lambda6 - sulfanyl)oneboximidoyl - 3 - (rboximidoyl - 3 - fluoro - (1S, 4S) ((diaminomethylidene) amino) ethenyl) amino+oxy - methyl) - 3, 4 - dimethyl - 7 - oxo - 4 - thia - 1 - azabicyclo (3.2.0) heptane - 2 - carbonyloxy) ((2 - amino - 6 - oxo - 6, 9 - dihydro - 3H - purin - 9 - yl)oxy) (hydroxy) phosphoryl oxy) phosphinic acid - ylidene +, *cyano (2, 6 - diazabicyclo *3.1.0+hex - 1 - en - 6 - yl -) (rboximidoyl - 3 - fluoro - (1S, 4S) ((diamino methylidene) amino) ethenyl) amino+oxy - methyl) - 3, 4 - dihydroxyoxolan - 2 - yl+ - 1, 2, 4 - triazol - 3 - yl - formamido) dihydroxyoxolan - 2 - yl+ - 1, 2, 4 - triazol - 3 - yl - (formamido) phosphoryl + - 6 - fluoro - 3, 4 - dihydropyrazine - 2 - carboxamide (7ar) - 5 - amino - N - * (S) - , 2 - * (3 - oxabicyclo (2.1.0) (1S, 4S) - 5 - oxabicyclo*2.1.0+pentan - 2 ((2S, 5r, 6r) - 6 - ((2S) - 2 - amino - 2 - phenylacetamido) - 3, 3 - dimethyl - 7 - oxo - 4 - thia - 1 - azabicyclo (3.2.0) heptane - 2

- carbonyloxy) ((2-amino-6-oxo-6,9-dihydro-3H-purin-9-yl)oxy)(hydroxy)phosphoryloxy)phosphinic acid-ylidenes, *cyano (2,6-diazabicyclo*3.1.0+hex-1-en-6-yl) (rboximidoyl-3-fluoro-(1S,4S) ((diaminomethylidene)amino)ethenyl)amino+oxy-methyl-3,4-dihydroxyoxolan-2-yl+-1,2,4-triazol-3-yl-(formamido)phosphoryl+-6-fluoro-3,4-dihydropyrazine-2-carboxamide (7ar)-5-amino-N-(S)-, 2-(3-((1S,4S)-5-oxabicyclo(2.1.0)pentan-2-ylidene)) (cyano ((2,6-diazabicyclo(3.1.0)hex-1-en-6-yl)) phosphanyl-(fluoro)methyl-lambda6-sulfanyl)one pentan-2-ylidene) (cyano ((2,6-diazabicyclo(3.1.0)hex-1-en-6-yl)) phosphanyl ((1S,4S)-5-oxabicyclo(2.1.0)pentan-2-ylidene)).

(METHODS AND MATERIALS) (Cluster of Eqs. 70) Our innovative drug design generated also negatively charged groups within the sequence of the amino acid of the H-M-ASN-33, H-S-ASN-33, H-S-TYr-356, H-M-ASN-424, V-M-ASN-33, V-M-ALA-331, V-M-THR-332, V-S-THR-332, V-S-TYr-356, V-S-TRP-423, V-S-ILE-428, and V-S-ARG-495 with the docking energy values of (-104.7 and -3.45708, -3.5, -3.97711, -3.5, -5.33228, -6.79753, -7.9376, -6.69969, -12.2528, -7.66989, -8.15072, -7.332) Kcal/mol respectively. The Roccustyrna small molecule hits also the entire binding domains of the SARS-COV-2 (PDB:6w9c) protein targets within the amino acid sequence of V-S-PRO-59, V-S-ARG-65, V-M-THR-75, V-S-THR-75, V-M-PRO-77, V-S-PRO-77, V-M-HIS-47, and V-S-HIS-47 with the docking energies of the (-83.9, -4.21999, -12.6164, -7.60372, -6.69528, -5.89416, -6.40663, -5.51621, -7.99273) Kcal/mol. (Figure S2e) As illustrated in the (Figure S3) the Roccustyrna small molecule generated also negative docking energy values with a potential inhibitory effect when docked against the sequence of the amino acids of the protein targets of (PDB: 6YI3) of the N-terminal RNA-binding domain of the SARS-CoV-2 nucleocapsid phosphoprotein which is essential for linking the viral genome to the viral membrane. (Figure S4d), (Figure S4e) In this project for the first time we generated a Comparative Docking Cluster Analysis between the remdesivir and our prototype Roccustyrna small molecule when docked onto the SARS-COV-2 protein targets of (PDB:7bv2), with the docking energy values of (Num_Members == 40, Total_Energy == 2.103, vdW == -5.122, Coulomb == -4.977, Internal == 12.203, rmsd == 3.183 and \$Number of Clusters == 10, \$Seed == 1985, \$Leader_Info 1 { Num_Members == 63 Total_Energy == -0.883, vdW == -6.041, Coulomb == -7.045, Internal == 12.203) respectively. More specifically, in this project we unified generalized k-nearest values and topology geometric methods for generalized formalisms of k-nearest neighbors of Molecular Pairs (MMP) and von Neumann formulations for Dirac formulation states as a Tipping-Ogilvie and Machine Learning application within the quantum computing context with algebraic multi-metrics characteristics targeting the atomistic level of the protein apparatus of the SARS-COV-2 viral characteristics. An Adaptive Weighted KNN Positioning approach through nonlinear electrodynamics to simulate an advanced quantum mechanical inverse docking algorithm was applied in this unified protocol by providing further insight on a neuron (l) : $\phi = D \circ r_2 \circ S \circ r_1$ improver for Chern-Simons Topology Euclidean Geometries for generating a negative docking energy effect of the highest docking energy value. By performing stationary phase approximations around these pharmacophore merging critical points, I obtained the asymptotic expansions of the Roccustyrna's merged holomorphic chemical block systems against a specific (PDB: 6XS6) protein target. (Illustration1) As a result, Entangled Neural Networks and Quantum-Inspired Kappa-Symmetrizing frameworks were mixed together and by using Chern-Simons normalized Shannon entropy quantities through Tipping-Ogilvie potentials I generated the combination of GisitorviffirmaTM, Roccustyrna_{gs1}TM, and Roccustyrna_{fr1}TM small molecules. That annotated cluster of druggable scaffolds were able of producing the highest rates of negative docking energy values when virtually combined with Amprenavir, Asunaprevir, Atazanavir, Boceprevir, Cytarabine, Darunavir, ritonavir, Sorivudine, Taribavirin, Tenofovir, Valganciclovir, Vidarabine, Lopinavir, Sofosbuvir, Zanamivir, Penciclovir, Nelfinavir, Merimepodib, Maribavir, Indinavir, Inarigivir, Galidesivir, Famciclovir, and Faldaprevir FDA approved antiviral drugs against the SARS-COV-2 protein binding sites of the (PDB: 6M2Q) SARS-CoV-2 3CL protease (3CL pro) apo structure (space group C21) inside the amino acid sequence of V-M-ARG-4, V-S-ARG-4, V-S-MET-6, V-M-ALA-7, V-S-PHE-8, V-M-GLY-11, V-M-LYS-12, V-S-LYS-12, V-M-GLU-14, V-S-GLU-14, V-M-GLY-15, V-M-THR-24, V-S-THR-24, V-M-THR-25, V-S-THR-25, V-M-THR-26, V-S-THR-26, V-M-VAL-35, V-S-VAL-35, V-S-ARG-40, V-S-HIS-41, V-M-THR-45, V-M-SER-46, V-S-SER-46, V-S-MET-49, V-M-ASN-53, V-S-ASN-53, V-S-TYR-54, V-M-ALA-70, V-M-GLY-71, V-M-ASN-95, V-S-LYS-97, V-M-PRO-99, V-S-LYS-102, V-S-VAL-104, V-M-ILE-106, V-S-GLN-107, V-M-PRO-108, V-M-GLY-109, V-S-GLN-110, V-M-THR-111, V-S-ASN-119, V-M-GLY-124, V-S-TYR-126, V-M-GLN-127, V-M-CYS-128, V-S-ARG-131, V-S-LYS-137, V-M-LEU-141, V-M-ASN-142, V-S-ASN-142, V-M-GLY-143, V-M-ASN-151, V-S-ASN-151, V-M-ILE-152, V-M-ASP-153, V-S-ASP-153, V-S-SER-158, V-M-MET-165, V-S-MET-165, V-M-GLU-166, V-S-GLU-166, V-M-LEU-167, V-S-PRO-168, V-M-GLU-178, V-M-VAL-186, V-S-VAL-186, V-S-ARG-188, V-M-GLN-189, V-S-GLN-189, V-M-THR-190, V-S-TRP-218, V-M-LEU-220, V-M-ASN-221, V-S-PHE-223, V-M-TYR-237, V-S-TYR-237, V-S-TYR-239, V-M-ASP-245, V-S-ASP-245, V-S-HIS-246, V-S-ILE-249, V-M-GLU-270, V-S-GLU-270, V-S-LEU-271, V-M-LEU-272, V-M-GLN-273, V-M-ASN-274, V-S-ASN-274, V-M-GLY-275, V-M-MET-276, V-M-ASN-277, V-S-ASN-277, V-M-GLY-278, V-M-LEU-286, V-S-LEU-286, V-M-LEU-287, V-S-LEU-287, V-S-ASP-289, V-S-GLU-290, V-S-THR-292, V-S-PRO-293, V-M-PHE-294, V-S-PHE-294, V-S-ARG-298, V-M-GLN-299, V-S-GLN-299, V-M-GLY-302, V-M-VAL-303, V-M-PHE-305. More precisely, I generally made use of the vector field $\partial/\partial t$ which is globally well defined, as the kernel of dz and dz at each point can be viewed as a topological theory of class H. So in this sense our topological theory here is generating a well defined direction which can be identified with the diffeomorphism generated by $\partial/\partial t$. Additionally, the same combination of our drug design novelties interacted with the highest docking energy values onto the binding sites of the (PDB: 6WOJ) protein targets of the SARS-CoV-2 macrodomain (NSP3) in complex with ADP-ribose of the targeting sequence of V-M-ALA-21, V-M-ASP-22, V-S-ASP-22, V-M-GLU-25, V-S-GLU-25, V-M-ALA-38, V-M-ALA-39, V-S-ASN-40, V-M-TYR-42, V-M-GLY-46, V-M-GLY-47, V-M-GLY-48, V-M-VAL-49, V-S-VAL-49, V-M-ALA-50, V-M-GLY-51, V-M-ALA-52, V-S-LEU-53, V-M-VAL-95, V-S-VAL-95, V-M-VAL-96, V-M-PRO-98, V-S-ASN-101, V-S-LEU-109, V-S-PRO-125, V-M-LEU-126, V-S-LEU-126, V-M-SER-128, V-M-ALA-129, V-M-GLY-130, V-M-ILE-131, V-S-ILE-131, V-S-PHE-132, V-M-GLY-133, V-M-ALA-134, V-S-PRO-136, V-M-SER-139, V-M-ALA-154, V-M-VAL-155, V-S-VAL-155, V-M-PHE-156, V-S-PHE-156, V-M-ASP-157, V-M-LEU-160, V-S-LEU-160, V-M-GLU-120 amino acids respectively when compared with Amprenavir, Asunaprevir, Atazanavir, Boceprevir, Cytarabine, Darunavir, ritonavir, Sorivudine, Taribavirin, Tenofovir, Valganciclovir, Vidarabine, Lopinavir, Sofosbuvir, Zanamivir, Penciclovir, Nelfinavir, Merimepodib, Maribavir, Indinavir, Inarigivir, Galidesivir, Famciclovir, and Faldaprevir FDA approved antiviral drugs while targeting the PDB:7khp (Figure S9A), PDB: 6WOJ (Figure S9B), PDB: 7B3D (Figure S9C), PDB:6M2Q (Figure S9D), PDB:6lu7 (Figure S9E), PDB: 6wzu (Figure S9F), PDB:1XU9 (Figure S9G), PDB: 3TWU (Figure S9H), PDB:7BEO (Figure S9H), PDB:1XAK (Figure S9I) protein targets. (Figure S4f), (Figure S4g), (Figure S4h) Finally, the Roccustyrna chemical structure generated an inhibitory docking effect of high negative binding energy docking values of the -66, 7 Kcal/mol when docked onto the cav7bv2_POP binding domains within the amino acids of the V-M-LYS-551, V-S-LYS-551, V-S-ARG-553, V-S-ASP-618, V-M-TYR-619, and V-M-PRO-620 with the docking energy values of (-4.71516, -10.4842, -4.7999, -6.65538, -5.1339, -6.28532) Kcal/mol. (Figure S5a), (Figure S5b), (Figure S5c), (Figure S6) On the other hand the remdesivir drug when

Discussion

Page 7/15

If anyl)one ylidene) { (cyano ({2, 6-diazabicyclo (3. 1. 0) (1S, 4S) -5- oxabicyclo* 2. 1. 0+pentan- 2 ((2S, 5R, 6R) -6- ((2S) -2-amino-2- phenylacetamido) -3, 3- dimethyl-7-oxo -4-thia-1-azabicyclo (3. 2. 0) heptane-2-carbonyloxy) ({ ((2-amino-6-oxo-6, 9-dihydro-3H-purin-9-yl) oxy) (hydroxy) phosphoryl} oxy) phosphinic acid -ylidenet, *cyano (2, 6- diazabicyclo*3. 1. 0+hex- 1- en-6- yl) dimethyl-7-oxo-4-thia-1-azabicyclo (3. 2. 0) heptane-2-carbonyloxy) ({ ((2-amino-6-oxo-6, 9-dihydro-3H-purin-9-yl) oxy) (hydroxy) phosphoryl} oxy) phosphinic acid -ylidenet, *cyano (2, 6- diazabicyclo*3. 1. 0+hex-1- en-6-yl-) (rboximidoyl- 3- { ((1S, 4S) -5- oxabicyclo (2. 1. 0) pentan-2- ylidene) { (cyano ({2, 6-diazabicyclo (3. 1. 0) hex- 1-en-6- yl)) phosphanyl) (fluoro) methyl} -lambda6-su lfanyl)one hex- 1-en-6- yl)) phosphanyl) (fluoro) methyl} -lambda6-su lfanyl)one (1S, 4S) -5-oxabicyclo*2. 1. 0+pentan-2 ((2S, 5R, 6R) -6- ((2S) -2-amino-2- phenylacetamido) -3, 3- dimethyl -7-oxo-4-thia-1-azabicyclo (3. 2. 0) heptane-2-carbonyloxy) ({ ((2-amino-6-oxo-6, 9-dihydro-3H-purin -9-yl) oxy) (hydroxy) phosphoryl} oxy) phosphinic acid -ylidenet, *cyano (2, 6- diazabicyclo*3. 1. 0+hex-1- en-6-yl-) (rboximidoyl- 3- { ((1S, 4S) -5- oxabicyclo (2. 1. 0) pentan-2- ylidene) { (cyano ({2, 6-diazabicyclo (3. 1. 0) hex- 1-en-6- yl)) phosphanyl) (fluoro) methyl} -lambda6-su lfanyl)one hex- 1-en-6- yl)) phosphanyl) (fluoro) methyl} -lambda6-su lfanyl)one $\int rA \wedge rA \wedge rAp \dots ik 4\pi Z M A \wedge rAp0E \sum \sum \sum \sum \sum (-1) \omega + \hat{w}e2\pi bwe Z^{\wedge} \dots z^{\wedge} 0 := = \nabla \nabla NaIrr H\delta M \dots H\delta N \sim A \wedge (m0-xi)rA \dots \nabla \nabla \nabla V ne 2/3 \int rrr^0 0rr \int rA \wedge rA \wedge rAp \dots ik 4\pi Z M A \wedge rAp0E \sum \sum \sum \sum \sum (-1) \omega + \hat{w}e2\pi bw - \lambda6 - sulfanyl)oneboximidoyl - 3 - \{ ((1S, 4S) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) \sqrt{q\rho 0} \langle \Psi || T || \Psi \rangle (id \dots \epsilon) \cdot \Delta := = \sqrt{q\rho 0} \langle \Psi || T || \Psi \rangle (id \dots \epsilon) \cdot \Delta := = (\epsilon \dots id) e Z^{\wedge} \dots z^{\wedge} 0 := = \nabla \nabla NaIrr H\delta M \dots H\delta N \sim A \wedge (m0-xi)rA \dots \nabla \nabla \nabla V ne 2/3 \int rrr^0 0rr \int rA \wedge rA \wedge rAp \dots ik 4\pi Z M A \wedge rAp0E \sum \sum \sum \sum \sum (-1) \omega + \hat{w}e2\pi bwe Z^{\wedge} \dots z^{\wedge} 0 := = \nabla \nabla NaIrr H\delta M \dots H\delta N \sim A \wedge (m0-xi)rA \dots \nabla \nabla \nabla V ne 2/3 \int rrr^0 0rr \delta Q^{\wedge} \dots - m \times \Phi \sim 2 (Y) := = i\pi + \sim 2) ' C (q \int \int \int \Delta StrH \dots e glN) 2/pk + 4m2h20 \equiv := = \langle \Psi || \Psi \rangle := = (A \wedge A') (p) \mapsto (\cos \phi - \sin \phi \sin \phi \cos \phi) . The operators form $Z d\theta x d 2 z \eta z \sum 1 b (\partial \theta x - iA\theta x) + m + ibz \partial \partial z \int \varphi z$ are gauge invariant, and thus have an expansion in terms of traces of the U (N) gauge group in various representations, which one can obtain using: $Y k \prod \det (1 - UVk) := = \int X r \sum (-1) |r| Tr \sum (U) Tr T (V) (xp) \dots D (\alpha) : (xp) \mapsto (x + Re (\alpha) p + Im (\alpha)) \dots S (r) : (xp) \mapsto (e - r \cos \theta jik 4\pi \cos \theta j e \dots dQ^{\wedge} \dots \delta Q^{\wedge} \dots - m \times p (rr) \delta Q^{\wedge} \dots - m \times p (rr) \Delta Q \partial v^{\wedge} x \partial q \int \int \int \Delta StrH \dots e Z M \int X r \sum (-1) |r| Tr \sum (U) Tr T \int CS (A) \cos \theta j e \dots dQ^{\wedge} \dots \delta Q^{\wedge} \dots - m \times p (rr) \Delta Q \partial v^{\wedge} x \partial q \int \int \int \Delta StrH \dots e ik 4\pi Z M \int Tr (A \wedge dA + \cos \theta j e \dots \delta Q^{\wedge} \dots \delta Q^{\wedge} \dots - m \times p (rr) \Delta Q \partial v^{\wedge} x \partial q \int \int \int \Delta StrH \dots e 2/3 \int A \wedge A \wedge A) 2j \sin \theta \dots e - p (rr) := = \sqrt{2j} 2j || \psi j \rangle / 2m) \int (\nabla R0) 2 drr + \int R20 v drr \equiv Ev (R0 \dots \phi 0) := = (\hbar 20 \leq := = \langle \Psi || \Psi \rangle := = (A \wedge A') (p) := = := (1S, 4S) - 5 - oxabicyclo *2.1.0+pentan - 2 ((2S, 5R, 6R) - 6 - ((2S) - 2 - amino - 2 - phenylacetamido) - 3, 3 - dimethyl - 7 - oxo - 4 - thia - 1 - azabicyclo (3.2.0) heptane - 2 - carbonyloxy) ({ ((2 - amino - 6 - oxo - 6, 9 - dihydro - 3H - purin - 9 - yl) oxy) (hydroxy) phosphoryl} oxy) phosphinic acid - ylidene +, *cyano (2, 6 - diazabicyclo *3.1.0+hex - 1 - en - 6 - yl -) (rboximidoyl - 3 - { ((1S, 4S) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) { (cyano ({2, 6 - diazabicyclo (3.1.0) hex - 1 - en - 6 - yl)) phosphanyl) (fluoro) methyl} - lambda6 - su lfanyl)one (rboximidoyl - 3 - oxabicyclo (2.1.0) pentan - 2 - ylidene) { (cyano ({2, 6 - diazabicyclo (3.1.0) hex - 1 - en - 6 - yl)) phosphanyl) (Cluster of Eqs. 71). In this computer - aided drug designing project, we generated the GisitorviffirmaTM, Roccustyrma_gs1_TM, and Roccustyrma_fr1_TM PDB, and MOL2 files which are consisting of the merged pharmacophoric elements of 2 - { (fluoro ({ (2E) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) cyano - lambda6 - sulfanyl) methyl) phosphorylidene) amino - 4, 6 - dihydro - 1H - purin - 6 - one1Z) - 2 - { ((2S, 3S, 5r) - 5 - (2 - amino - 6 - oxo - 6, 9 - dihydro - 1H - purin - 9 - yl) - 3 - hydroxyoxolan - 2yl) methylidene) - 2 - cyano - 1 - { ((2S, 4r, 5r) - 2 - methyl - 2 - (methylamino) - 1, 6 - diazabicyclo (3.2.0) heptan - 4 - yl) oxy) imino) - 1 lambda5, 2 lambda5 - azaphosphiridin - 1 - ylium (Figure S2), when $M := = 1 \langle \psi || (1^{\wedge} - \rho^{\wedge} R2k \nabla \cos \theta j e \dots dQ^{\wedge} \dots \delta Q^{\wedge} \dots - m \times p (rr) \Delta Q \partial v^{\wedge} x \partial q \int \int \int \Delta StrH \dots e \cos \theta \dots e - p (rr) := = \sqrt{2j \sin \theta \dots e - p (rr) := = \sqrt{2j} j e \dots dQ^{\wedge} \dots \delta Q^{\wedge} \dots - m \times p (rr) \Delta Q \partial v^{\wedge} x \partial q \int \int \int \Delta StrH \dots e \cos \theta jik 4\pi \cos \theta j e \dots \int \int \int \Delta StrH \dots e ik 4\pi Z M \int Tr (A \wedge dA + \cos \theta j e \dots dQ^{\wedge} \dots \delta Q^{\wedge} \dots - m \times p (rr) \Delta Q \partial v^{\wedge} x \partial q \int \int \int \Delta StrH \dots e 2/3 \int A \wedge A \wedge A) 2j \sin \theta \dots e - p (rr) := = \sqrt{2j} 2j || \psi j \rangle \rangle j j 2 k p k \wedge dA \rangle k + 13 \psi \langle A (\nabla Rk) 2 + R2k \nabla \phi k \wedge (A \wedge A) (Cluster of Eqs. 72). (44) The focus of this work is to develop a Quantum Heuristic Fragmentation driven Chern - Simons fragmentation algorithm that is as independent to allow for a faster multi - cut solutions as possible from the chosen pharmacophoric fragmentation Scheme obtained by localization of the S3 partition function of $j || \psi j \rangle a q \rho 0 \langle \Psi || T || \Psi \rangle n \dots e - p (rr) := = \sqrt{\langle \Psi || T \cdot || \Psi \rangle 0 \dots Z (Vect x k x (G) \dots e - p (rr) := = \sqrt{e - p (rr) := = \sqrt{\sum k 1 m W \langle A \wedge (A \wedge A) f (\psi A \wedge dA) e \dots dQ^{\wedge} \dots \delta Q^{\wedge} \dots - m \times p (rr) \Delta Q \partial v^{\wedge} x \partial q \int \int \int \Delta StrH \dots e 2/3 \int A \wedge A \wedge A) 2j \sin \theta \dots e - p (rr) := = \sqrt{2j} \sin^{\wedge} (-1) (\sqrt{779 \delta u} := = i^{\wedge} q u (Cluster of Eqs. 73) \delta^{\wedge} u := = i^{\wedge} u \cdot e glN q \rho 0 \langle \Psi || T || \Psi \rangle (n \dots e - p (rr) := = \sqrt{\langle \Psi || T \cdot || \Psi \rangle 0 \dots Z (Vect x k x (G) \dots e - p (rr) := = \sqrt{e - p (rr) := = \sqrt{\sum k 1 m W \langle A \wedge (A \wedge A) f (\psi A \wedge dA) e \dots dQ^{\wedge} \dots \delta Q^{\wedge} \dots - m \times p (rr) \Delta Q \partial v^{\wedge} x \partial q \int \int \int \Delta StrH \dots e 2/3 \int A \wedge A \wedge A) 2j \sin \theta \dots e - p (rr) := = \sqrt{2j} 2j - \sin \theta \cos \theta x 1 x 2 p 1 p 2 v \dots 1 \dots 2 \dots \lambda := = 1/2 + \gamma 2 + 1/4 c 1 \delta j (Cluster of Eqs. 73) when in mass solving the (Cluster of Eqs. 4 - 67) for new group contribution drug design methods. To avoid incomplete fragments of (1Z) - 2 - { ((2S, 3S, 5r) - 5 - (2 - amino - 6 - oxo - 6, 9 - dihydro - 3H - purin - 9 - yl) - 3 - hydroxyoxolan - 2 - yl) methylidene) - 2 - cyano - 1 - { ((2S, 4r, 5r) - 2 - q { h q ; } qreg q (3) ; creg c (3) ; reset q (0) ; reset q (1) ; reset q (2) ; h q (0) ; u2 (pi/2, pi/2) q (1) group assignments where $V := = \text{diag} (V1, \dots, V_k, \dots)$ considered as a matrix with eigenvalues V_k . $\sum p ((T plain \dots \otimes \dots Tcipher) \dots Kprvite) \times \log p (Kprvite | (T plain \dots Tcipher)) p (Kprvite) \sum p (T plain \dots \otimes \dots Tcipher) * p (Kprvite | (T plain \dots Tcipher)) \times \log p (Kprvite | (T plain \dots Tcipher)) p (Kprvite) \varphi \cdot D \cdot R2 \cdot S \cdot R1 \cdot i \langle \psi || \rho^{\wedge} R2k \nabla ik 4\pi ik 4\pi \cos \theta j e \dots dQ^{\wedge} \dots \delta Q^{\wedge} \dots - m \times p (rr)$ for coordinating the chemical fragments of (rboximidoyl- 3- oxabicyclo (2. 1. 0) , (1S, 4S) -5-oxabicyclo*2. 1. 0 +pentan-2 ((2S, 5R, 6R) -6- ((2S) -2-amino-2-phenylacetamido) -3, 3- dimethyl-7-oxo-4-thia-1-azabicyclo (3. 2. 0) heptane-2- carbonyloxy) ({ ((2-amino-6-oxo-6, 9-dihydro-3H-purin-9-yl) oxy) (hydroxy) phosphoryl} oxy) phosphinic acid -ylidenet, *cyano (2, 6- diazabicyclo*3. 1. 0+hex-1- en-6-yl-) (rboximidoyl- 3- { ((1S, 4S) -5- oxabicyclo (2. 1. 0) pentan-2- ylidene) { (cyano ({2, 6-diazabicyclo (3. 1. 0) hex- 1-en-6- yl)) 2-amino-2-phenylacetamido) -3, 3- dimethyl-7-oxo-4-thia-1-azabicyclo (3. 2. 0) heptane-2- carbonyloxy) ({ ((2-amino-6-oxo-6, 9-dihydro-3H-purin-9-yl) oxy) (hydroxy) phosphoryl} oxy) phosphinic acid -ylidenet, *cyano (2, 6- diazabicyclo*3. 1. 0+hex-1- en-6-yl-) (rboximidoyl- 3- { ((1S, 4S) -5- oxabicyclo (2. 1. 0) pentan-2- ylidene) { (cyano ({2, 6-diazabicyclo (3. 1. 0) hex- 1-en-6- yl)) phosphanyl) , (fluoro) methyl} -lambda6-su$$$$

Page 9/15

one ((2r, 5r) - 5 - (2 - methyl - 6 - methylidene - 6, 9 - dihydro - 3H - purin - 9 - yl) - 3 - methylideneoxolan - 2 - yl) phosphirane - 1 - carbonitrile - oxy) imino) - 1lambda5, 2lambda5 - azaphosphiridin - 1 - ylium input of a fragmented compounds in the next pharmacophoric system B: S4 - cyano - 1 - (((2S, 4r, 5r) - 2 - methyl - 2 - 2 - ((fluoro (((2E) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) cyano - lambda6 - sulfanyl) methyl) phosphorylidene) amino) S4 - cyano - 1 - (((2S, 4r, 5r) - 2 - methyl - 2 - 2 - ((fluoro (((2E) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) cyano - lambda6 - sulfanyl) methyl) phosphorylidene) amino) - 4, 6 - dihydro - 1H - purin - 6 - one (methylamino) - 1, 6 - diazabicyclo (3.2.0) heptan - 4 - yl) (1S, 2r, 3S) - 2 - (((1S, 2S, 4S, 5r) - 4 - ethenyl - 4 - sulfonylbicyclo (3.2.0) heptan - 2 - yl) oxy) amino) - 3 - 2 - ((fluoro (((2E) - 5 - oxabicyclo (2.1.0) pentan - 2 - ylidene) cyano - lambda6 - sulfanyl) methyl) phosphorylidene) amino) - 4, 6 - dihydro - 1H - purin - 6 - one ((2r, 5r) - 5 - (2 - methyl - 6 - methylidene - 6, 9 - dihydro - 3H - purin - 9 - yl) - 3 - methylideneoxolan - 2 - yl) phosphirane - 1 - carbonitrile - oxy) imino) - 1lambda5, 2lambda5 - azaphosphiridin - 1 - ylium dk represents the parameters of displacement D (α (k)) and φ (·) is nonlinear function. (42, 43, 44, 45, 46) The holomorphic chemical block has appeared before in this paper, in several different guises. In particular, it agrees – up to our standard projective factors exp*π*2~ Q + C + ~ Q – with the direct analytic continuation of the trefoil's colored Jones polynomial, computed by q -1 c^ -1/2M^ -2 ^

$$\Psi(eU \cdot \dots \otimes \cdot \dots \otimes \cdot \dots \otimes \cdot \dots C) = = = + i \sqrt{2\pi i} \sim Zdp\psi \left(p + \frac{C}{2} \right) \psi \left(-p + \frac{C}{2} \right) e^{1 \sim U(U+p) + i\pi U \sim + p - C2p \rightarrow p + \sim = = + i, \\ -1 \Psi(eU \cdot \dots \otimes \cdot \dots \otimes \cdot \dots \otimes \cdot \dots C) = = = + i \sqrt{2\pi i} \sim MZdp\psi \left(p + \frac{C}{2} \right) \psi \left(-p + \frac{C}{2} \right) e^{1 \sim U(U+p) + i\pi U \sim + p - C2p \rightarrow p + \sim = = + i, \\ \text{of the pharmacophoric element of (rboximidoyl - 3 - fluoro - (1S, 4S) ((diamino methylidene) amino) ethenyl)) amino+oxy - methyl) - 3, 4 -} \\ \text{dihydroxyoxolan - 2 - yl+ - 1, 2, 4 - triazol - 3 - yl - (formamido) phosphoryl + - 6 - fluoro - 3, 4 - dihydropyrazine - 2 - carboxamide (7aR) - 5 - amino - N - * (S) - , 2 -} \\ \text{* (3 - oxabicyclo (2.1.0) (1S, 4S) - 5 - oxabicyclo*2.1.0 +pentan - 2 ((2S, 5R, 6R) - 6 - ((2S) - 2 - amino - 2 - phenylacetamido) - 3, 3 - dimethyl - 7 - oxo - 4 - thia - 1 -} \\ \text{azabicyclo (3.2.0) heptane - 2 - carbonyloxy) (((2 - amino - 6 - oxo - 6, 9 - dihydro - 3H - purin - 9 - yl)oxy) (hydroxy) phosphoryl) oxy) phosphinic acid - ylidenet+,} \\ \text{*cyano (2, 6 - diazabicyclo*3.1.0+hex - 1 - en - 6 - yl -) (rboximidoyl - 3 - fluoro - (1S, 4S) ((diaminomethylidene) amino) ethenyl)) amino+oxy - methyl) - 3, 4 -} \\ \text{dihydroxyoxolan - 2 - yl+ - 1, 2, 4 - triazol - 3 - yl - (formamido) phosphoryl + - 6 - fluoro - 3, 4 - dihydropyrazine - 2 - carboxamide (7aR) - 5 - amino - N - * (S) - , 2 -} \\ \text{* (3 - { ((1S, 4S) - 5 - oxabicyclo (2.1.0)pentan - 2 - ylidene){ (cyano ((2, 6 - diazabicyclo (3.1.0)hex - 1 - en - 6 - yl)) phosphanyl) (fluoro)methyl} - lambda6 - su} \\ \text{lfanyl)one pentan - 2 - ylidene){ (cyano ((2, 6 - diazabicyclo (3.1.0)hex - 1 - en - 6 - yl)) phosphanyl, when we obtain } \Psi(eU, C) + q -1 c^ -1/2M^ -2 ^} \\ \Psi(eU, C) - q - 1c^ - \frac{1}{2}M^3 -1 \Psi(eU, C) = = = -i \sqrt{2\pi i} \sim MZdp\psi \left(p + \frac{C}{2} \right) \psi \left(-p + \frac{C}{2} \right) e^{1 \sim U(U+p) + i\pi U \sim = = = M^ \Psi(eU, C) \text{ for holomorphic blocks}}$$

that are annihilated by linear difference operators. DNA - Protein - Ligand signatures in more general spacetimes enhanced by ZK - based proofs of nonlinear dynamics in an extended cryptography model to encrypt and decrypt chemical data which may be extended to hyper - symmetric equations of Chern - Simons Topology driven motion on a collection of nonlinearly coupled remerging harmonic oscillators. Of special interest here is the fusion pharmacophoric product of quantum reference frame representations from the Hopf algebra structure on Uqg, when the universal r matrix may provide the emerging pharmaceutical or medical applications, including medicinal products, gene therapy for biological pacemakers (Farraha et al, 2018), and for the nervous system (Bowers et al, 2011) To keep the method as simple as possible, we choose to generate the best docking - scoring individuals and to replace the worst docking - scoring of integrable highest - weight modules with functionalities on the wave equation for the molecular oscillator described by the second - order term of the Tipping–Ogilvie potential expansion with connections over vectors (x| ∈ V N (Q+) fulfilling the (Cluster of Eqs. 1 - 64) when in parallel solved with ψ (y) v == = E v == = γ λ exp (- β v y) F (λ - γ 2 / β v ····· (1 - γ 2 (v + λ) 2) ↦ (cos ϕ - sin ϕ sin ϕ cos ϕ) (xp) ····· D (α) : (xp) ↦ (x + Re (α) p + Im (α)) ····· S (r) : (xp) ↦ (e - r cos θ j cos θ ····· e - ρ (rr) == = - √ k 1 m C Q 2 t (ϕ (t) ····· e - ρ (rr) == = √ ∑ N i (∂ v ····· e - ρ (rr) Z M^ h ψ A Q^- a ψ + ψ Q √ ∂ p · = (n ····· e - ρ (rr) == = √ (| ψ | T √ | | ψ) 0 ····· Z (Vect x k x (G) ····· e - ρ (rr) for **generalizing** the chemical fragments of (rboximidoyl- 3- 2-yl) amino)) phosphoryl) - (1S, 4S) -5-oxabicyclo *2. 1. 0+pentan- 2 ((2S, 5R, 6R) -6- ((2S) -2 -amino-2-phenylacetamido) -3, 3- dimethyl-7 -oxo-4-thia -1-azabicyclo (3. 2. 0) heptane-2-carbonyloxy) ((((2-amino-6-oxo-6, 9-dihydro-3H-purin-9-yl) oxy) (hydroxy) phosphoryl) oxy) phosphinic acid -ylidenet+, *cyano (2, 6- diazabicyclo*3. 1. 0+hex-1- en-6-yl-) (rboximidoyl- 3- { ((1S, 4S) -5- oxabicyclo (2. 1. 0) pentan-2- ylidene) { (cyano ((2, 6-diazabicyclo (3. 1. 0) hex- 1-en-6- yl)) phosphanyl) , (fluoro) methyl} -lambda6-su lfanyl)one oxy)) phosphoryl) for monitrilewhere the (Hermitian) current operator j^Nvar (rr) is equivalent to 12m (ρ^Nvar (rr) p^+p^ρ^Nvar (rr)). Therefore, the near-horizon geometry admits the ζ0 tr····· - K ∫ ∫ ∫ α l Λ e^- m x ∂ v^ ∇ φ ∇ ····· - i θ ∇ (- l) ∇ / Γ x ····· - k 1 m x P 2 = = = e ····· - m x ∂ v^ x ∂ q ····· (a) ····· - (ħ 2 / 2 m) = = = √ · e - ρ (rr) = = = √ ∑ k 1 m W (A Λ (A Λ A) f (ψ A Λ d A) e ····· d Q^- ····· δ Q^- ····· - m x ρ (rr) Δ Q ∂ v^ x ∂ q^- ∫ ∫ ∫ Δ S T r H ····· e g l N) 2 / p k + 4 m 2 ħ 2 0 < = = = (ψ || | ψ ||) = = = (A Λ A' (p)) ↦ (cos ϕ - sin ϕ sin ϕ cos ϕ) ∀ i ····· f L H (l) (x ····· y) ····· f L H (l) (x ····· y) } ····· ∀ l = = = 1 ····· 2 f 1 9 ····· ∀ i 2 4 to maximize the fixed number of times through two coupled anti - de Sitter black harmonic black - hole oscillator by means of ordinary differential equation over the moduli space of chemical structures and spheres. In principle, a Chern - Simons anti - de Sitter supergravity can be constructed from the knowledge of the associated supergroup and an invariant tensor only (finding the invariant tensor, however, may prove to be a non - trivial task). In five dimensions, the relevant supergroup is SU (2, 2|1) while in the important example of eleven dimensions the supergroup is OSp (32|1). As the spacetime dimension increases, one faces a growing multiplicity of choices for the invariant tensor. The particular case of eleven dimensions seems to be particularly suited to admit an anti - de Sitter ChernSimons formulation. As shown, the super antide Sitter group is OSp (32|1). A natural basis for the Lie algebra of Sp (32) is given by the Dirac matrices Γa, Γab, Γabcde, and this basis is easily extended to expand the superalgebra of OSp (32|1). (42, 43, 47, 49) In this setup I have been discussing, I managed to preserve the topological nature of CS theory while coupling to chemical space as infinitely massive sources at the expense of requiring the underlying 3 - manifolds to generate my unique drug design with the highest docking energies of negative binding values when compared to other known SARS - CoV - 2 antivirals. In this context, the generalized fragments are viewed as external sources that have the ability to produce an effective description of quantum Hall effect, and can be coupled to the Chern - Simons theory. (44, 45, 48) It is probably true that the injudicious use involving the management of these quantum ideas or points can cause problems, it is also true that they do and should play an important role quantum mechanically in this drug discovery field (Figure S7), (Table S8), (Figure S8), (Table S9), (Figure S10), (Figure S11). In this effort, I propose computer - aided rational drug design strategies efficient in

computed diagonal chemical descriptors. By identifying chemical patterns of general (variational) quantum states: $S(p0, \phi) == S(p0) + S(p0, \phi)$ and $I(p0, \phi) == I(p0) + I(p0, \phi)$. I made use of partial small fragment derivatives as well as probabilistic transformations on Murko (BM) circuit statements with the additional MM - PBSA - WSAS binding free energy calculation difficulties that the drug designs we deal with are not orthogonal. (30 - 42) Both Chern - Simons theories and knot theory algorithms applied in this project into merged pharmacophoric groups. Furthermore, the geometric topology - driven heuristic algorithms that were used in this project are capable of fragmenting and remerging small molecules that could not be fragmented by the algorithm of any of the known reference databases. (2, 5 - 42) We have illustrated the power of such a Flexible heuristic algorithm approach interpreted as a distinct quantum circuit, qubit preparations, and certain 1 - and 2 - qudit gates for automatic molecule fragmentation in a meaningful application to Molecular epidemiology, evolution, and phylogeny of SARS coronavirus components, such as $\partial t P \psi(t) |\partial \theta(t) / \partial t \rangle \int M3 \psi A == (n \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{\langle \Psi || T \sqrt{|| \Psi \rangle} 0 \dots \dots \cdot \dots} Z (Vect \times k \times (G) \cdot \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{\cdot e - p(r) == \sqrt{\sum k1mW \langle A \wedge (A \wedge A) f(\psi A \wedge dA) \rangle e \cdot \dots \otimes \dots \cdot dQ^- \cdot \dots \otimes \dots \cdot \delta Q^- \dots \dots \cdot \dots \otimes \dots \cdot - m \times p(r) \Delta Q \partial v^x \partial q^- \int \int \int \Delta StrH \cdot \dots \otimes \dots \cdot e \text{ glN}) 2 / p k + 4 m 2 \hbar 2 0 < == 2 j j \sin \theta j e \cdot \dots \otimes \dots \cdot dQ^- \cdot \dots \otimes \dots \cdot \delta Q^- \dots \dots \cdot \dots \otimes \dots \cdot - m \times p(r) \Delta Q \partial v^x \partial q^- \int \int \int \Delta StrH \cdot \dots \otimes \dots \cdot e \cos \theta \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{2 j \sin \theta \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{2 j j e \cdot \dots \otimes \dots \cdot dQ^- \cdot \dots \otimes \dots \cdot \delta Q^- \dots \dots \cdot \dots \otimes \dots \cdot - m \times p(r) \Delta Q \partial v^x \partial q^- \int \int \int \Delta StrH \cdot \dots \otimes \dots \cdot e \cos \theta j \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{++++ - \text{lambda} 6 - \text{dimethyl-7-oxo-4-thia-1-azabicyclo (3. 2. 0) heptane- 2-carbonyloxy} \{ ((2\text{-amino-6-oxo-6, 9-dihydro-3H-purin-9-yl) oxy} (hydroxy) phosphoryl) oxy) phosphinic acid -ylidenet, *cyano (2, 6- diazabicyclo*3. 1. 0+hex- 1- en-6-yl-) (rboximidoyl- 3- \{ ((1S, 4S) -5- oxabicyclo (2. 1. 0) pentan-2- ylidene) \{ (cyano (\{2, 6-diazabicyclo (3. 1. 0) hex- 1-en-6- yl\}) phosphanyl) (fluoro methyl) -\text{lambda} 6\text{-su lfanyl)one 1S, 4S) -5- oxabicyclo (2. 1. 0) pentan-2- ylidene) \{ (cyano (\{2, 6-diazabicyclo (3. 1. 0) hex- 1-en-6- yl\}) phosphanyl) (fluoro methyl) -\text{lambda} 6\text{-su lfanyl)one formonitrile(rboximidoyl- 3- fluoro-1-(5-oxabicyclo (2. 1. 0) pentan-2-yl)-purin-2-yl) amino\}) phosphoryl) oxy\}) phosphoryl) formonitrile2) sulfanyl)oneboximidoyl - 3 - \{ ((1S \dots \otimes \dots \cdot \dots \otimes \dots \cdot 4S) - 5- oxabicyclo (2.1.0) == \sqrt{\partial u \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{k} == IP c a j j || \psi j \rangle 1 m' \varphi (Q^- a \dots \otimes \dots \cdot \dots \otimes \dots \cdot) b a c c b \partial \partial c c \eta + - == \eta 0 0 Z \infty d T Z d \theta e - T \Delta Q^- - \delta Q^- (\lambda k) \theta == : P d \theta Z z f z i (d z) 1 m' \varphi (\lambda k) \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{k - Tr (\rho^p \rho^0) - \sum Ni 1 m' S (r k) \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{k 13 \psi \langle A \wedge (A \wedge A) f(\psi A \wedge dA) \rangle k e \cdot \dots \otimes \dots \cdot dQ^- \cdot \dots \otimes \dots \cdot \delta Q^- \dots \dots \cdot \dots \otimes \dots \cdot - m \times p(r) \Delta Q \partial v^x \partial q^- \int \int \int \Delta StrH \cdot \dots \otimes \dots \cdot e \cos \theta \cdot \dots \otimes \dots \cdot e - p(r) (Cluster of Eqs. 80) qubits (Scheme 5). We suggest that such ligand - protein binding site topology maps will be useful for building further understanding of the relationship between diagonal chemical descriptors, small molecules, and complex viral biological systems. (43, 44) This generalized Hadamard approach is potentially applicable to the discovery of hit matter for novel biological targets, with clinical or genomic features for predicting and rationalizing ligand poly - pharmacology and for predicting new ligand functions. In addition, I suggested that such an objective binding site symmetrized map, which encompasses unliganded cavities, will also be useful for optimizing compound screening collections towards a more complete chemical coverage in multi - targeted pharmacophoric spaces. Our Biogenetoligandorol platform may also offer utility to researchers to interrogate and organize generalized k - nearest neighbors on an Adaptive Weighted KNN Positionings where $D(p \dots \otimes \dots \cdot \dots \otimes \dots \cdot q) == (p1 - q1) 2 + (p2 - q2) 2 + \dots + (pn - qn) 2$ Average Accuracy == $\sum i == 1 T \sqrt{|| a1' (t) y^ (k) \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{k} == IP c a j j || \psi j \rangle 1 m' \varphi (Q^- a \dots \otimes \dots \cdot \dots \otimes \dots \cdot) b a c c b \partial \partial c c \eta + - == \eta 0 0 Z \infty d T Z d \theta e - T \Delta Q^- - \delta Q^- (\lambda k) \theta == : P d \theta Z z f z i (d z) \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{k - Tr (\rho^p \rho^0) - \sum Ni 1 m' S \sum Ni 1 m' S (r k) \cdot \dots \otimes \dots \cdot e - p(r) == \sqrt{k 13 \psi \langle A \wedge (A \wedge A) f(\psi A \wedge dA) \rangle k u e \cdot \dots \otimes \dots \cdot dQ^- \cdot \dots \otimes \dots \cdot \delta Q^- \dots \dots \cdot \dots \otimes \dots \cdot - m \times p(r) \Delta Q \partial v^x \partial q^- \int \int \int \Delta StrH \cdot \dots \otimes \dots \cdot e \partial q) (A \wedge A' (p)) 2 j 2 j || \psi j \rangle (Cluster of Eqs. 81) co - efficiencies (26, 29 - 42). In this Schrödinger picture for the system minimum - energy of quantum mechanics the dynamics of quantum states for the $S(p0, \phi) == S(p0) + S(p0, \phi)$ and $I(p0, \phi) == I(p0) + I(p0, \phi)$ non - classical Shannon entropy is cryptografically governed by the system energy operator $H : i \hbar \partial |\psi(t)\rangle / \partial t == H |\psi(t)\rangle$ (42, 43, 44) which gives the following expression for the time derivative of the conditional probability $P(\theta(t) | \psi(t))$ for nonzero Christoffel symbols for Schwarzschild in question: $\partial P(\theta(t) | \psi(t)) / \partial t == \{ 22 m b 2 r \partial t P \psi(t) | \partial \theta(t) / \partial t \rangle (k) I ((Tplain, Tcipher), Kprvite) == \sum p ((Tplain, Tcipher), Kprvite) \times \log p (Kprvite | (Tplain, Tcipher)) p (Kprvite) \sum p (Tplain, Tcipher) * p (Kprvite | (Tplain, Tcipher)) \times \log p (Kprvite | (Tplain, Tcipher)) p (Kprvite) \varphi \circ D \circ R2 \circ S \circ R1 ?$$$

Declarations

AVAILABILITY OF DATA AND MATERIALS

The paper reports original code. Any additional information required to reanalyze the data reported in this paper is available from the lead contract upon request.

COMPETING INTEREST

No potential competing interest was reported by the author.

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AUTHOR CONTRIBUTIONS

Grigoriadis Ioannis's diverse contributions to the published work are accurate and agreed. Grigoriadis Ioannis has contributed to the below multiple roles:

- Conceptualization Ideas, formulation or evolution of overarching research goals and aims.
- Methodology, Development, or design of methodology; creation of models.
- Writing - Review & Editing, Preparation, creation and presentation of the published work by those from the original research group, specifically critical review, commentary, or revision including pre-or post-publication stages.
- Visualization, Preparation, creation, and presentation of the published work, specifically visualization/data presentation.
- Supervision, Oversight and leadership responsibility for the research activity planning and execution, including mentorship external to the core team.

- Project administration, Management, and coordination responsibility for the research activity planning, and execution.

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