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SIDDHARTH SINHA

Summary

An enthusiastic and dedicated researcher with expertise in cancer genomes, big data analytics, bioinformatics, drug design, and computational structural biology utilizing AI and machine learning techniques in conjunction with molecular biology. The scientific endeavors are marked by pioneering contributions in protein structure-based evaluation and statistical methods including Molecular Dynamics (MD) simulations, free energy estimation, ligand binding and conformational analysis. As a result of these techniques, we have been able to classify cancer genes as having deleterious or tolerated mutations (missense variants) based on their protein structure. Among my competencies are the analysis of large-scale biomedical data, utilizing computational methods for molecular simulation, statistical and drug target analysis using Homology & Pharmacophore modeling, Molecular Docking & Dynamics, and 3D & G-QSAR. In cancer genomics, I have experience with variant calling pipelines, next-generation sequencing, and sRNA-seq, while in molecular biology, I utilize techniques such as western blots, ELISAs, SDS-PAGE and PCRs. Currently, I am seeking a new opportunity that provides both professional development and growth.

Skills

- Biomedical Sciences
- Big Data Analytics
- R and Python
- Deep learning & neural network models in MD simulations (autoencoder)
- Pharmacophore studies
- Free Energy calculations
- WES, sRNA-seq, GATK
- AI & Machine Learning in Biological Sciences.
- Molecular Biology Techniques (Western Blot, ELISA, PCR)
- 3D/G-QSAR analysis
- Clinical Data
- QM/MM (semi-empirical)
- Molecular Dynamics (MD) Simulations (**all-atom & CG**)
- Variant Calling Pipeline
- Next Generation Sequencing
- High performance computing (HPCC).
- Cancer genomics
- Joint Genotyping.
- Molecular Docking Drug target Analysis

Research Experience

POSTDOCTORAL FELLOW 11/2017 – 04/2024
University of Macau, Macau, Macao S.A.R.

- Developed and executed a comprehensive research pipeline focused on the analysis of germline and somatic mutations in key cancer predisposition genes, including *BRCA1/2, PTEN, TP53, MLH1*, and *MSH2*, for the classification of missense variants (VUS).
- Utilized molecular dynamics (MD) simulations and enhanced sampling methods, such as Replica Exchange Molecular Dynamics (REMD), to investigate the free-energy landscape of PTEN catalytic core variants impacting the PI3K/AKT pathway.
- Performed advanced computational data mining across clinical cancer datasets, utilizing Whole Exome Sequencing, Targeted Amplicon Sequencing, and Whole Transcriptome Sequencing as well as gene expression analysis.
- Analyzed a range of biomolecules such as enzymes, ion channels, and receptors to design and develop tool compounds for drug targets with clinical relevance.

SENIOR RESEARCH FELLOW 02/2015 - 10/2017
Jawaharlal Nehru University (JNU), Delhi, INDIA

- Drug repurposing studies on Class IIa HDAC inhibitors towards neurological disorder Spinocerebellar Ataxia, enhancing understanding of therapeutic targets.
- Executed High throughput Screening (HTS) integrating pharmacophore modeling and QSAR analysis, designing two novel inhibitors, HIC and DHC validated on neurological cell lines SH5Y and IMR-32.
- Pioneered drug repurposing strategies targeting Mycobacterium Tuberculosis, contributing to innovative treatment approaches.
- Authored multiple scientific publications, disseminating research findings to the broader scientific community.

SENIOR PROGRAMMER 12/2012 - 07/2013
Bioinformatics Center, BIOTECH PARK, LUCKNOW, INDIA

- Utilized and validated bioinformatics software and algorithms.
- Proficient in multiple programming languages including Python, R, and C++.
- Delivered interactive training sessions and workshops to enhance user proficiency.

TRAINEE SCIENTIST 08/2008 - 10/2012
ACS bioINFORMATICS, LUCKNOW, INDIA

- Developed comprehensive course syllabi, aligning with industry standards.
- Project outsourcing initiatives, leveraging cross-institutional collaboration.
- Partnered with leading institutes and R&D centers to enhance project outcomes.
- Delivered expert-level training in bioinformatics and drug design for industrial applications.
- Conducted in-depth research on MMP9 inhibitors, contributing structural insights.
- Presented specialized lectures at bioinformatics workshops, sharing knowledge and expertise.

Education

Ph.D., Applied Health Sciences, 11/2018
TERI School of Advance Studies, New Delhi, INDIA
Ph.D., **Computational Structural Bioinformatics**; Supervisor: Associate Prof. Pallavi Somvanshi
Doctoral thesis focussed on the role of histone deacetylase (HDAC) towards neurological disorder spinocerebellar ataxia type 2 (SCA 2) employing various methodologies such as homology modelling, molecular docking, pharmaco-informatics, molecular dynamics, 3D-QSAR, G-QSAR as well as *invitro* validation of the *de-novo* synthesized HDAC inhibitors on neurological cell lines (SH5Y and IMR-32).

- Investigated spinocerebellar ataxia type-2 (SCA) through a thesis focusing on histone deacetylase (HDAC) modulation.
- Utilized homology modeling and molecular docking for structural analysis.
- Applied pharmaco-informatics for drug discovery insights.
- Conducted molecular dynamics simulations to assess protein-ligand interactions.
- Implemented 3D-QSAR and G-QSAR for quantitative structure-activity relationship studies.
- Performed *invitro* validation to corroborate computational findings.

B.Tech, Biotechnology, 01/2010
Amity University, Delhi (NCR) INDIA

Activities

Teaching Experience

University of Macau, Macau
Supervised 50+ dissertation thesis of M.Sc. students.
Teaching Fellow; Biomedical Statistics and Big Data Analysis in Cancer Biology (2019,2020,2022,2023)

TERI School of Advance Studies (TERI University) Delhi, India
Teaching Fellow; Bioinformatics lab session (Summer 2016, 2017)
Teaching Fellow; Lectures for 2nd Year M.Sc. (Fall 2015)

Professional Associations
Federation of European Neurosciences Society (FENS)
International Society for Computational Biology (ISCB)

Conferences (Oral and Poster)

1. Classification of PTEN missense VUS through exascale simulations. Advance Methods in MD workshop from 11th -12th December 2023 at Copenhagen, Denmark.
2. EMBO Workshop on Computational Structural Biology from 6th – 9th December 2023 at Heidelberg, Germany.
3. Identification of deleterious Variants of Uncertain Significance in BRCA2 BRC4 repeat through molecular dynamics simulations. Basel Computational Biology Conference from 13th-15th September 2021 at Basel, Switzerland.
4. Classification of variants of uncertain significance and unclassified variants in BRCA1 BRCT repeats using molecular dynamics simulations. 4th Symposium on Biomedical Sciences on 19th May 2020 at University of Macau, Macau.
5. Functional Computational Analysis of Disease-Associated Single Nucleotide Polymorphism in Human ATXN2 gene, 10th FENS forum of Neurosciences from 2nd – 6th July 2016 at Copenhagen, Denmark.
6. STRUCTURAL INSIGHTS OF HDAC INHIBITORS TOWARDS SPINOCEREBELLAR ATAXIA TYPE 2, 9th FENS forum of Neurosciences from 5th – 9th July 2014 at Milan, Italy.
7. In-silico analysis of histone deacetylase inhibitors (HDACi) towards frataxin protein: Insights into structural specificity of frataxin in Friedreich ataxia, Miptec 2012 Switzerland.
8. In-silico analysis of Topoisomerase Inhibitors towards Vascular Endothelial Growth Factor receptors: Insights into structural specificity of Vascular Endothelial Growth Factor receptors in lung adenocarcinoma, NIIT Rourkela, Orissa, INDIA 2010.
9. Molecular Docking and Dynamics Approach towards protein kinase PknB from Mycobacterium tuberculosis, MipTec, Switzerland, 2009.
10. Binding Patten Determination of Class of Antifungal Drugs, 2008, Basel, Switzerland, 2008.

Accomplishments

- Oral Speaker Honorable Mention - May 2020
- Silver Prize in Poster Presentation - April 2023
- National Eligibility Test (CSIR-NET); **Ph.D. Scholarship.** Govt. of INDIA.
- **24 Publications** in peer-reviewed scientific journals.
- 1st Prize in Poster Presentation - April 2013
- Post-doc projects (*BRCA1/2, PTEN, TP53, MLH1*) accepted for extramural funding.

Languages

English, Hindi First Language

French A1
Beginner

Cantonese A1
Beginner

Personal Details

- Father's Name: Mr. Dinkar Sinha
- Gender: Male
- Hobbies: Table Tennis, Basketball, Badminton, Hiking, Photography, Rowing (Indoor & Outdoor), Ancient & Medieval Indian History.
- Passport No: **Z4055925**

Profile Links

- https://scholar.google.co.in/citations?user=QiN-Z78AAAAJ&hl=en
- https://www.researchgate.net/profile/Siddharth-Sinha-7
- https://www.linkedin.com/in/siddharth-sinha-a30b939/
- https://orcid.org/my-orcid?orcid=0000-0003-3868-1967

**I hereby declare that all information furnished above is true to my knowledge and belief.*

(**Dr. Siddharth Sinha**)
(Ph.D.)

Publications

I. Publications in the field of Computational Structural Bioinformatics (enhanced sampling, free energy calculations, Deep learning neural network, statistical analysis).

1. Tam B, Lagniton PNP, Da Luz M, Zhao B, **Sinha S**, Lei CL, Wang SM. Comprehensive classification of TP53 somatic missense variants based on their impact on p53 structural stability. *Briefings in Bioinformatics*. **2024** Jul 25;25(5):bbae 400. (https://10.1093/bib/bbae400) (Impact Factor: 7.1)
2. Andaluz S, Zhao B, **Sinha S**, Lagniton PNP, Costa DA, Ding X, Brito M, Wang SM. Using Portuguese BRCA pathogenic variation as a model to study the impact of human admixture on human health. BMC Genomics. **2024** Apr 27;25(1):416. (https://10.1186/s12864-024-10311-4) (Impact Factor: 4.4)
3. Zhao B, Li J, **Sinha S**, Qin Z, Kou SH, Xiao F, Lei H, Chen T, Cao W, Ding X, Wang SM. Pathogenic variants in human DNA damage repair genes mostly arose in recent human history. BMC Cancer. **2024** Apr 4;24(1):415. (https://10.1186/s12885-024-12160-6) (Impact Factor: 3.4)
4. Tam B, Zhao B, **Sinha S**, Chon Lok Lei, and Wang SM. 2024. "Classification of MLH1 Missense VUS Using Protein Structure-Based Deep Learning-Ramachandran Plot-Molecular Dynamics Simulations Method" *International Journal of Molecular Sciences* **2024;** 25,: 850. (https://doi.org/10.3390/ijms25020850) (Impact Factor: 5.6)
5. **Sinha S**, Jiaheng Li, Benjamin Tam, San Ming Wang. Classification of PTEN missense VUS through Exascale Simulations. *Briefings in Bioinformatics,* **2023** Sep 22;24(6): bbad361. (https://doi.org/10.1093/bib/bbad361). (Impact Factor: 7.1)
6. **Sinha S**, Tam B, Wang SM. Applications of Molecular Dynamics Simulation in Protein Study. Membranes (Basel). **2022** Aug29; 12(9): 844. (https://doi.org/10.3390/membranes12090844) (Impact Factor: 3.6)
7. **Sinha S**, Qin Z, Tam B, Wang SM. Identification of deleterious Variants of Uncertain Significance in BRCA2 BRC4 repeat through molecular dynamics simulations. *Briefings in Functional Genomics* **2022.** (https://doi.org/10.1093/bfgp/elac003) (Impact Factor: 6.3)
8. **Sinha S**, Tam B, Wang SM. RBD Double Mutations of SARS-CoV-2 Strains Increase Transmissibility through Enhanced Interaction between RBD and ACE2 Receptor. *Viruses.* **2022**; 14(1):1. (https://doi.org/10.3390/v14010001) (Impact Factor: 4.7)
9. Tam B, **Sinha S**, Qin Z, Wang SM. Comprehensive Identification of Deleterious TP53 Missense VUS Variants Based on Their Impact on TP53 Structural Stability. *Int J Mol Sci*. **2021** Oct 20;22(21):11345. (https://doi.org/10.3390/ijms222111345) (Impact Factor: 5.6)
10. Tam B, **Sinha S**, Wang SM. Combining Ramachandran plot and molecular dynamics simulation for structural-based variant classification: Using TP53 variants as model. *Comput Struct Biotechnol J*. **2020** Dec 2; 18:4033-4039. (https://doi.org/10.1016/j.csbj.2020.11.041) (Impact Factor: 5.4)
11. **Sinha S**, Wang SM. Classification of VUS and unclassified variants in BRCA1 BRCT repeats by molecular dynamics simulation. Comput Struct Biotechnol J. **2020** Mar 21; 18:723-736. (https://doi.org/10.1016/j.csbj.2020.03.013) (Impact Factor: 5.4)
12. **Sinha S**, Verma S, Singh A, Somvanshi P, Grover A. Simulation Based Investigation of Deleterious nsSNPs in ATXN2 Gene and Its Structural Consequence Toward Spinocerebellar Ataxia. *J Cell Biochem.* **2018** Jan;119(1):499-510. (https://doi.org/10.1002/jcb.26209) (Impact Factor: 5.2)
13. Verma S, Singh A, Kumari A, Goyal S, Jamal S, **Sinha S**, Grover A. Dissecting the role of mutations in chymase inhibition: Free energy and decomposition analysis. *Gene.* **2017** Apr 20; 609:68-79. (https://doi.org/10.1016/j.gene.2017.01.030) (Impact Factor: 4.5)

II. Publications in the field of Drug Design & Its Planning Methods (computational protein-ligand binding, QSAR, MD simulations, ADME).

1. **Sinha S**, Tyagi C, Goyal S, Jamal S, Somvanshi P, Grover A. Fragment based G-QSAR and molecular dynamics based mechanistic simulations into hydroxamic-based HDAC inhibitors against spinocerebellar ataxia. J Biomol Struct Dyn. **2016** Oct; 34(10): 2281-95. (https://doi.org/10.1080/07391102.2015.1113386) (Impact Factor: 4.4)
2. **Sinha S**, Goyal S, Somvanshi P, Grover A. Mechanistic Insights into the Binding of Class IIa HDAC Inhibitors toward Spinocerebellar Ataxia Type-2: A 3D-QSAR and Pharmacophore Modeling Approach. Front Neurosci. **2017** Jan 10; 10:606. (https://doi.org/10.3389/fnins.2016.00606) (Impact Factor: 4.1)
3. Verma S, Singh A, Kumari A, Pandey B, Jamal S, Goyal S, **Sinha** S, Grover A. Insight into the inhibitor discrimination by FLT3 F691L. Chem Biol Drug Des. **2018** May;91(5):1056-1064. (https://doi.org/10.1111/cbdd.13169) (Impact Factor: 3.2)
4. Singh A, Grover S, **Sinha S**, Das M, Somvanshi P, Grover A. Mechanistic Principles Behind Molecular Mechanism of Rifampicin Resistance in Mutant RNA Polymerase Beta Subunit of Mycobacterium tuberculosis. J Cell Biochem. **2017** Dec;118(12):4594-4606. (https://doi.org/10.1002/jcb.26124) (Impact Factor: 3.3)
5. Tandon A, **Sinha S**. Structural insights into the binding of MMP9 inhibitors. Bioinformation. 2011 Jan 22;5(8):310-4. (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3046033/) (Impact Factor: 3.1)
6. Sehrawat A, **Sinha S**, Saxena A. Helicobacter pylori neutrophil-activating protein: a potential Treg modulator suppressing allergic asthma? Front Microbiol. 2015 Jun 1; 6:493. (https://doi.org/10.3389/fmicb.2015.00493) (Impact Factor: 5.2)

III. Publications in the field of cancer genomics (variant analysis, GATK, sRNA seq, WES).

1. Qin Z, Li J, Tam B, **Sinha S**, Zhao B, Bhaskaran SP, Huang T, Wu X, Chian JS, Guo M, Kou SH, Lei H, Zhang L, Wang X, Lagniton PNP, Xiao F, Jiang X, Wang SM. Ethnic-specificity, evolution origin and deleteriousness of Asian BRCA variation revealed by over 7500 BRCA variants derived from Asian population. Int J Cancer. **2023** Mar 15;152(6):1159-1173. (https://doi.org/10.1002/ijc.34359) (Impact Factor: 6.4)
2. Chian J, **Sinha S**, Qin Z, Wang SM. BRCA1 and BRCA2 Variation in Taiwanese General Population and the Cancer Cohort. Front. Mol. Biosci. **2021** 8:685174. (https://doi.org/10.3389/fmolb.2021.685174) (Impact Factor: 4.1)
3. Gupta H, Chandratre K, **Sinha S**, Huang T, Wu X, Cui J, Zhang MQ, Wang SM. Highly diversified core promoters in the human genome and their effects on gene expression and disease predisposition. BMC Genomics. **2020** Nov 30;21(1):842. (https://doi.org/10.1186/s12864-020-07222-5) (Impact Factor: 4.4)
4. Guo M, **Sinha S**, Wang SM. Coupled Genome-Wide DNA Methylation and Transcription Analysis Identified Rich Biomarkers and Drug Targets in Triple- Negative Breast Cancer. Cancers (Basel). **2019** Nov 4;11(11):1724. (https://doi.org/10.3390/cancers11111724) (Impact Factor: 5.2)
5. Bhaskaran SP, Chandratre K, Gupta H, Zhang L, Wang X, Cui J, Kim YC, **Sinha S**, Jiang L, Lu B, Wu X, Qin Z, Huang T, Wang SM. Germline variation in *BRCA1/2* is highly ethnic-specific: Evidence from over 30,000 Chinese hereditary breast and ovarian cancer patients. Int J Cancer. 2019 Aug 15;145(4):962-973. (https://doi.org/10.1002/ijc.32176) (Impact Factor: 6.8)

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