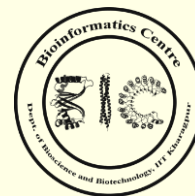




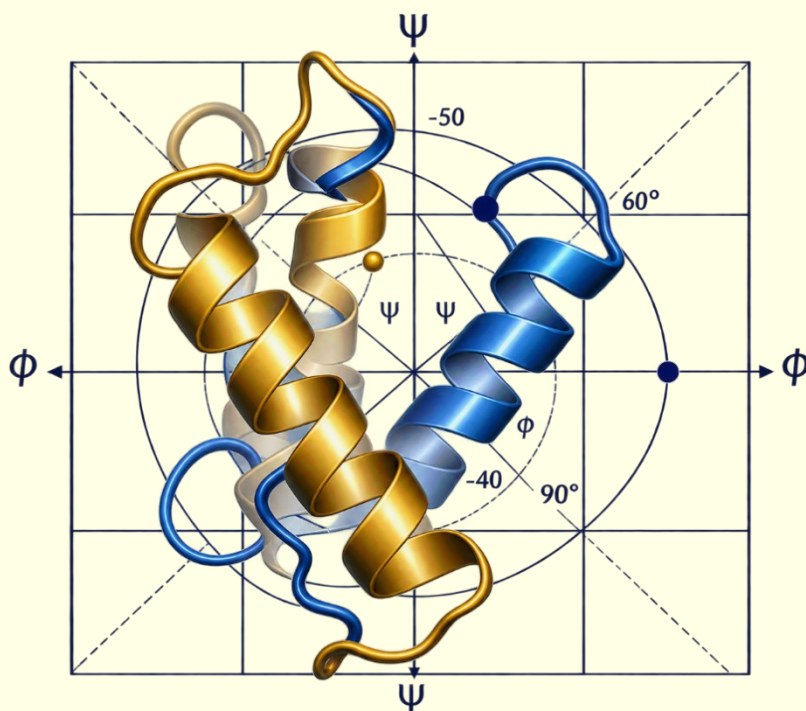
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on

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G. N. Ramachandran and His Impact on Protein Science and Structural Biology.

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Abstract: This talk will trace the path that G.N.Ramachandran took during his stellar career, beginning in optics and crystallography during his early days in the Physics department at the Indian Institute of Science, achieving the peak of his career at Madras University and finally his return to Bangalore and his creation of the Molecular Biophysics Unit. Collagen and the Ramachandran Map form the dominant themes of this presentation. The impact of his work on the field of polypeptide and protein conformations, central to the biological activity of these molecules, will be assessed.

PPCheck: Energy calculations and objective measure of strength of protein-protein interactions

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Abstract: Protein-protein interactions regulate various biological processes. It is important to understand the strength of these interactions since few types are transient and others are permanent. Inspired by the Ramachandran map, we have used similar energy calculations to measure the total energy at the site of protein-protein interactions. Total energy is viewed as the sum of Van der Waals, electrostatic, hydrogen bond interactions. These calculations are identical to the ones employed in the historic Ramachandran map calculations. I will share few examples where these calculations can enable better understanding of selectivity of quaternary structures and preferred orientations.

Computational approaches for understanding and predicting binding affinities of protein complexes and their mutants

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Abstract: The interactions of proteins with other molecules are important for several biological functions (1). The strength of these interactions is accounted with binding affinity. Further, mutation of amino acids in the interfaces of protein complexes alter their structure, binding affinity and function, and some of them lead to diseases (2). The binding affinities of protein complexes are related with sequence and structural features of residues at the interface. We have developed thermodynamic databases (3,4) for protein-protein, protein-nucleic acid, protein-carbohydrate and protein-peptide complexes and derived several parameters including contact potentials, interaction energies and solvent accessibility to relate with binding affinity (5). Based on the insights gained from this analysis, we have developed computational tools for predicting the binding affinity of protein-protein, protein-DNA, protein-RNA and protein-carbohydrate complexes (6,7). Further, we have elucidated the features important for the binding affinity change upon mutation and developed algorithms for predicting the change in binding affinity (8-10). These resources help to relate the binding affinity with disease-causing mutations, and designing therapeutic strategies for diseases.

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- K. Harini ... M.M. Gromiha (2026) *Int. J. Biol. Macromol.* (in press)

Seeing the Invisible: Structural Insights into the Survival Machinery of *Mycobacterium tuberculosis*

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Abstract: Sophisticated molecular mechanisms are employed by *Mycobacterium tuberculosis* (Mtb) to adapt, persist, and survive under diverse environmental stresses. In this talk, structural biology, biophysical, biochemical, computational, and cellular approaches will be presented to elucidate molecular mechanisms underlying mycobacterial survival and persistence.

The fatty acid synthase type II (FAS-II) pathway will be discussed, with particular emphasis on the β -hydroxyacyl-ACP dehydratases HadAB and HadBC. Structural, biochemical, and biophysical studies have revealed the molecular basis of their differential interactions with acyl carrier protein and have provided insights into the regulatory roles of flexible structural elements. The role of EthA in the activation of Thiacetazone (TAC) and its analogue will also be presented. The molecular mechanism of non-homologous end joining (NHEJ), a critical DNA repair pathway during Mtb dormancy, will further be described. Cryo-EM structures of mycobacterial Ku (mKu), complemented by biochemical and cellular studies, have revealed the molecular basis of DNA binding, Ku oligomerization, and DNA synapsis during double-strand break repair.

Collectively, structural and mechanistic insights into lipid metabolism, antimycobacterial drug activation, and DNA repair will be presented, highlighting fundamental molecular strategies employed by *M. tuberculosis* for survival, adaptation, and persistence.

AI-assisted Medical Image Interpretation: Insights from Pathology and Ophthalmology

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Abstract: Interpreting biomedical images is not always straightforward. Differences between disease categories can be subtle, and even experienced clinicians may disagree. Can AI help make sense of these difficult cases—and where does it still fall short? In this talk, I will share lessons from our work at ICGEB, New Delhi, in collaboration with clinicians at AIIMS, focusing on thyroid pathology and glaucoma imaging.

In thyroid pathology, we explore a staged deep learning approach to distinguish closely related thyroid neoplasms, including non-invasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP). I will discuss what these models can learn from tissue architecture and nuclear features, alongside an important limitation: recognizing patterns in small image patches cannot replace the assessment of tumor invasion needed for diagnosis.

In glaucoma imaging, we investigate whether a combination of deep learning models can identify abnormalities in the eye's drainage angle from anterior segment optical coherence tomography images. Comparisons with expert assessments and images from patients with glaucoma-associated mutations help us explore the clinical relevance of the predictions. Explainable AI offers further clues about which anatomical regions influence the models' decisions.

Through these two studies, I will reflect on both the promise of AI and the practical challenges of working with limited, carefully annotated clinical data. The central question is not whether AI can replace clinical expertise, but how it might support it—and what evidence we need before these tools can become a reliable part of everyday care.

Protein- Protein interactions that influence the breast cancer transcriptome

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Abstract: Breast cancer is a highly heterogenous disease and deep genomic data analysis has identified very few actionable mutations and aberrations that are common to more than 10% of the cases studied. In contrast, transcriptome data from same tumors have accurately classified not only the disease at diagnosis but also elaborated breast cancer gene signatures for estimating progression and response to therapy. The best target for therapy is Estrogen receptor, a ligand activated transcription factor, that is expressed in about 70% of diagnosed cases. However, therapy resistance occurs in ER+ cases suggesting that alternate cancer promoting transcriptional programs need to be explored. Such a program may also serve in combating ER negative disease. Towards this goal, we performed an siRNA screen and discovered that high expression of an epitranscriptomic regulator, JMJD6, is consistently associated with adverse survival outcome in breast cancer patients. We will discuss our current understanding of how it regulates cancer-related gene expression by interacting with select transcription factors.

Allostery and Inhibition: Mechanistic Insights from Computation

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Abstract: Allostery, i.e. the mechanical process of remote communication within a biological macromolecular structure, is often linked to its functional activation and/or deactivation. Allosteric changes are triggered by various types of stimuli, e.g. binding to another macromolecule, or post-translational modification etc. The allosteric machinery can also be activated by appropriate small molecule which would thus become a potential lead compound or an allosteric inhibitor to combat a disease. Molecular dynamics simulations of macromolecular structures are increasingly giving insights into the mechanism of allosteric changes including the underlying thermodynamics. This presentation will show some examples of applications made in recent time, e.g. tubulin-microtubule dynamics in the context of cell proliferation, kinases and its activation, etc. Our recent success on applications of machine learning based methods to identify the allosteric communication channels and the capacity to take context dependent judgement will also be discussed.

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ST-01

Investigating conformational transitions in intrinsically disordered regions upon binding to proteins and nucleic acidsPrachi Bhargava¹, Paramveer Yadav¹, Madhabendra Mohon Kar¹, Amita Barik^{1*}¹*Department of Biotechnology, National Institute of Technology Durgapur 713209, India**Email ID: abarik.bt@nitdgp.ac.in

Abstract: Intrinsically disordered regions (IDRs) lack stable three-dimensional folds and are frequently observed as missing residues in experimental structures. Here, we study conformational changes in IDRs upon protein binding to other macromolecules. We analyse a non-redundant dataset comprising 356 protein-protein (PP) and 228 protein-nucleic acid (PNA) complexes, along with their unbound proteins, and classify IDR transitions into three classes: Disordered-to-Ordered (D-O), Disordered-to-Partially Ordered (D-PO), and Disordered-to-Disordered (D-D). In both PP and PNA, the IDRs in D-O class predominantly adopt coils (77%), followed by helices and sheets. Helix formation is more common in PNA (20%) than in PP (15%), while sheets are higher in PP (8% vs 4% in PNA). Though a majority of IDR residues are solvent-exposed, a significant number are present at the interface and form polar bonds. Interface IDRs prefer more hydrogen bond (H-bond) formation with phosphates (50%) in DNA, while bases are preferred more in RNA (43%). Sugars contribute least, with ribose forming more H-bonds (25%) than deoxyribose (4%). Aromatic residues contribute more to the PP interface IDRs, whereas charged residues predominate in PNA. We also report ordered-to-disordered transitions in IDRs upon complexation, indicating that conformational changes can occur in either direction depending on the functional requirements.

Keywords: *intrinsically disordered regions, protein-nucleic acid complexes, protein-protein complexes, transitions, interfaces, hydrogen bonds*

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ST-02

Reinventing the Golden Alkaloid: Altered Formulations for Ancient Therapeutics

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Abstract: Berberine (Daruharidra) is an Ayurvedic isoquinoline alkaloid, extracted from *Berberis aristata*, *Coscinium fenestratum*, *Berberis asiatica*, etc. It exhibits diverse pharmacological activities such as antidiabetic, antimicrobial, hepatoprotective, hypolipimedic, etc. Its clinical translation however, is constrained by unfavorable pharmacokinetic properties and toxicological concerns. To investigate the obstacles limiting the bench to bedside advancement of berberine, an integrated computational framework combining metabolomics, toxicological profiling, quantum chemical modeling and molecular interaction studies were employed and subsequently utilized to propose rational structural redesign strategies aimed at mitigating safety concerns and improving therapeutic and translational potential of berberine. Cytochrome P450 1A2-mediated biotransformation modeling identified metabolites, among which BTMR0052 exhibited the most pronounced toxicological risk profile. In contrast, BTMR1071 retained close structural homology to the parent compound, positioning it as a promising scaffold for future analogue development. We also attempted to propose targeted structural modifications to enhance aqueous solubility, and preserve biological activity of berberine. The predictions in the study were corroborated by experimental validation in a HepG2 cell line and zebrafish model, which demonstrated hepatotoxic and neurotoxic effects. It establishes a comprehensive, multidimensional framework for the rational optimization of natural products and offers a practical roadmap for the development of safer, more efficacious berberine-based therapeutics.

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ST-03

**Role of ligand-dependent conformational modulation of TNPO3
HEAT-repeat solenoid in nuclear import**Sonali Chatterjee¹, Atanu Maity² and Ranjit Prasad Bahadur^{1,2*}¹*Computational Structural Biology Laboratory, Department of Bioscience and Biotechnology, Indian Institute of Technology Kharagpur, Kharagpur-721302, India*²*Bioinformatics Center, Department of Bioscience and Biotechnology, Indian Institute of Technology Kharagpur, Kharagpur-721302, India*

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Abstract: Transportin-3 (TNPO3) is a HEAT-repeat nuclear transport receptor that mediates nuclear import of serine/arginine-rich (SR) proteins and interacts with Ran GTPase during nuclear transport cycle. Although structures of several TNPO3 complexes are available, how ligand binding modulates the conformational landscape of the receptor remains poorly understood. Here, we combine microsecond-scale molecular dynamics simulations with umbrella sampling free-energy calculations to investigate how SR cargo binding, Ran nucleotide state and cargo phosphorylation regulate TNPO3 conformational dynamics. Equilibrium simulations show that apo TNPO3 samples a broad conformational ensemble, while ligand binding substantially reshapes the conformational landscape. SR cargo protein stabilizes a partially extended solenoid architecture and introduces an energetic penalty to prevent further opening. Ran binding favours compact conformations of TNPO3 scaffold. Among these states, Ran-GTP produces the strongest confined conformational ensemble, while Ran-GDP allows broader structural variability. State-resolved structural analysis indicates that these energetic differences arise from ligand-dependent modulation of interface packing and hydrogen-bond networks. The modulation propagates across the HEAT-repeat array and alters global solenoid curvature. Reduction in phosphorylation of SR cargo weakens binding and increases conformational heterogeneity, highlighting the role of phosphorylation in stabilizing the TNPO3-cargo interface. These findings support a ligand-dependent conformational pathway, in which TNPO3 shifts from a flexible apo ensemble to an SR-bound extended state. This is followed by a structurally compatible intermediate shared with Ran-GTP-bound form before reaching compact Ran-GTP-stabilized state associated with cargo release. Together, these results provide a quantitative framework for understanding how ligand binding reshapes TNPO3 conformations during nuclear transport cycle.

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Chatterjee S, Maity A, Bahadur R Role of ligand-dependent conformational modulation of TNPO3 HEAT-repeat solenoid in nuclear import *Biophysical Journal*, 2026, <https://doi.org/10.1016/j.bpj.2026.09.036>

ST-04

Weighted Gene Co-expression Network Analysis of Transcriptomic Drivers of Organ-Specific Metastasis in Breast Cancer

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Abstract: Despite advances in breast cancer genomics, the transcriptional regulatory architecture which dictates organ-specific metastatic tropism remains under-resolved, as most primary studies are limited to single-gene or bulk differential expression analyses that overlook coordinated gene network dynamics. A genome-wide systems biology perspective is therefore needed to identify the regulatory modules and hub genes that govern organ-specific colonization. High-throughput transcriptomic data pose several challenges of dimensionality, noise, imbalance, especially the feature space can vastly exceed sample volume. The proposed work utilizes weighted Gene Co-expression Network Analysis (WGCNA) on the super-series transcriptomic dataset GSE14020 to deconvolute bulk microarray matrices into discrete, highly synchronized transcriptional modules following pre-processing that retained only the top 25% highest-variance probes. The WGCNA applies soft-thresholding to the Pearson correlation matrix to construct a scale-free topological network. Further, through singular value decomposition the dominant expression variance across all genes within a module is identified. Supervised module-trait correlation analysis across four metastatic sites identified ME_Module_26 as the dominant lung-associated module ($r = 0.60$, $P = 9.8 \times 10^{-5}$), with no comparable association to bone, brain, or liver that may show lung-specific organotropism. The top ten hub genes were ranked by intramodular connectivity i.e. module membership (kME), which shows a tightly co-regulated cluster of probe sets led by 211644_x_at with a Module Membership score of 0.978.

ST-05

Uncovering the landscape of functional transition in the tumor microenvironment with cancer progression

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Abstract: The tumor microenvironment (TME) harbors multiple cell-types whose functional contributions collectively determine the overall tumor phenotype and intra-tumor heterogeneity. These cell types undergo functional and phenotypic transitions that have role in cancer progression and therapy response (1). Intra-tumor functional plasticity has been mapped primarily within individual cell types and these studies, across different cancers, have identified common as well as cancer-specific programs (2). However, our understanding of less frequent transitory cell states within the TME and their role in cancer progression remains limited. In addition, the landscape of functional plasticity among different cell types within a tumor remains largely unexplored. In the present work, by analyzing tumor functional states in lung adenocarcinoma and colorectal cancer, we uncover the occurrence of transitory functional states in myeloid cell populations. These transitory myeloid states occurred preferentially in tumor samples compared to adjacent normal samples and were associated with signatures of immune suppression. We also observed widespread functional plasticity within the TME as different cell types converged to similar functional states across different patients. Taken together, our work illustrates the landscape of functional transitions and plasticity within the TME. The discovery of transitory myeloid cell states could have important implications for cancer progression and immunotherapy.

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ST-06

Multi Omics Deep Learning Identifies *MAOB* and *ANO1* as Prognostic Biomarkers and Prioritizes Voglibose in Hepatocellular Carcinoma

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Abstract: Hepatocellular carcinoma (HCC) remains difficult to manage because molecular heterogeneity limits biomarker-guided treatment. We developed a multi-omics deep-learning framework to nominate prognostic biomarkers and repurposable therapeutic candidates. **Methods:** More than 7,000 HCC-associated molecular and pharmacological profiles from TCGA, CCLE/DepMap, and GDSC were integrated through modality-specific autoencoders and cross-omics neural embeddings. Perturbation-based attribution prioritized candidates, followed by survival modelling, protein-protein interaction and pathway analyses, proteomic validation, ADMET screening, molecular docking, MM-GBSA, and QSAR. **Results:** Forty-eight high-confidence drug-target interactions linked 28 genes to 46 compounds were identified. *MAOB* and *ANO1* were independently associated with poorer overall survival in TCGA-LIHC, while a four-gene panel (*MAOB*, *ANO1*, *EGFR*, *VPS13D*) showed potential for risk stratification. Network analysis identified *MUC16*, *EGFR*, *ALB*, *CTNNB1*, *LRP1*, *MUC2*, *RYR2*, *DMD*, *HSPG2*, and *FASN* as hubs in PI3K/AKT/mTOR, AMPK, insulin, and HCC-related programmes; multiple hubs displayed tumour-associated protein-level changes. Voglibose achieved the most favourable convergent multi-target profile, supported by ADMET, docking, MM-GBSA, and QSAR evidence. **Conclusion:** This framework prioritizes *MAOB* and *ANO1* for prospective validation as biomarkers and positions voglibose as a testable HCC repurposing hypothesis.

PP-01

How IDR Phosphorylation Regulates Bcl-xL: Mechanistic and Thermodynamic Insights

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Abstract: Bcl-xL, an anti-apoptotic Bcl-2 protein, contains a structured region and a ~60-residue intrinsically disordered region (IDR). While the structured region governs function through conformational transitions and partner interactions, phosphorylation at specific IDR sites is known to influence these processes. However, the mechanism by which IDR dynamics, both in the wild-type and phosphorylated states, modulate the structured domain, particularly when the transmembrane domain (TMD) occupies the binding site, remains unclear. This investigation combines molecular dynamics (MD) simulation (~7.5 μ s total) of phosphomimetic mutations (PMMs) and true post-translational modifications (PTMs) to explore their effects. PMMs enhance coupling between the IDR, TMD, and binding site, reducing accessibility and hindering TMD release. Reversal mutation partially restored wild-type behaviour. Conformational thermodynamics and dynamic network analyses reveal that mutations reduce conformational entropy and induce long-range communications. PTM simulation grossly agrees with PMM results, with subtle interaction differences. These findings reveal how IDR modifications act as conformational rheostats that can revise the thermodynamic signature of the protein to tune Bcl-xL function.

Benchmarking of computational predictors of protein intrinsic disorder and Genome-wide prediction of intrinsic disorder in *E. Coli*.

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Abstract: Intrinsically Disordered Proteins (IDPs) are those proteins which lack a stable tertiary structure under native conditions but still perform important functions within the cell and have also been linked to numerous neurodegenerative diseases and cancers. [1] Approximately 9% of proteins listed in UniProt contain long disordered regions. [2] Since IDPs keep changing their conformation with time and adopt a range of different conformations, this makes the prediction of their exact structure challenging using standard biophysical methods. Therefore, there is a necessity to develop computational tools to predict intrinsic disorder propensity based on their sequences. Existing tools use either energy/physics-based calculations or, more recently, protein language models. In this work, we developed and benchmarked two predictors: (i) a sliding-window predictor based on physicochemical properties of residues, and (ii) a deep learning predictor that generates per residue embeddings using the ESM2 protein language model [3] and processes them through a convolutional neural network (CNN) layer to capture local sequence context. We evaluated both models against IUPred3 [4] and other established predictors on the CAID3 [5] benchmark dataset. Additionally, we also performed proteome-wide disorder prediction on all protein-coding sequences derived from open reading frames of the *E. coli* K-12 genome and developed a disorder map of the *E. coli* proteome.

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Investigation of the intrinsically disordered regions in macromolecular assemblies using computational approaches

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Abstract: Intrinsically disordered proteins (IDPs) and intrinsically disordered regions (IDRs) within folded proteins lack a well-defined three-dimensional structure under physiological conditions and are abundant in macromolecular assemblies. We curate 1136 non-redundant IDPs from the RCSB PDB, verified against DisProt, and compare their 1886 IDRs across six assemblies: ribosomes, spliceosomes, chaperonins, nucleosomes, nuclear pore complexes (NPCs) and G protein-coupled receptors (GPCRs). Across all assemblies, short IDRs are most abundant (46-57%), followed by intermediate (25-36%) and long IDRs (15-24%); long IDRs are most frequent in spliceosomes and least in GPCRs. The majority of IDRs residues adopt a coil conformation (84-89%), followed by helices (9-13%) and strands (1-3%) across all six groups. Although the abundance of dipeptide and tripeptide repeats varies, the SP, EE, and EEE are the most abundant repeats in all assemblies. Biophysical parameters (FCR, NCPR, kappa, hydropathy, aromatic and disorder-promoting fractions) show consistent assembly-dependent trends. IDRs in spliceosomes and nucleosomes have the highest FCR (~34%) and are the most hydrophilic and disorder-prone, whereas those in chaperonins and GPCRs have a lower FCR (~30-31%), are more hydrophobic, and least disorder-prone. Together, the studied features provide a basis for the identification and prediction of IDRs across diverse macromolecular assemblies.

Keywords: Intrinsically Disordered Proteins, Intrinsically Disordered Regions, Macromolecular Assemblies, Physicochemical Properties, Dipeptides, Tripeptides

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Identification of phytochemical inhibitors against SARS-CoV-2 NSP10 using computational approaches

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Abstract: Non-structural protein 10 (NSP10) of SARS-CoV-2 is an essential co-activator of the viral methyltransferases NSP14 and NSP16. When interacting with these enzymes, it mediates mRNA cap methylation and viral replication, which makes it a viable antiviral target. In this study, we screen various phytochemicals against the isolated NSP10 subunit (PDB ID: 7BQ7, Chain B) using an integrated computational approach. A library of 195 Lipinski-compliant phytochemicals is docked using PyRx, yielding binding affinities between -5.13 and -7.42 kcal/mol. The pharmacokinetic and toxicity profiling through SwissADME, pkCSM and ProTox-II narrowed this pool of 195 compounds to 16 drug-like lead candidates. Further, 100 ns molecular dynamics simulations using GROMACS 2025.4 with the CHARMM36m force field are performed to determine the conformational stability, structural dynamics, and binding behaviour of the selected compounds with NSP10. Complexes with Bergenin, Eupalitin, Eupatorin, and Gallocatechin are observed to be the most stable ones, with comparatively lower RMSD, RMSF, Rg, and SASA values. The minimum-distance analysis and the deeper energy funnels from FEL analysis further reflect their thermodynamically stable conformations. Unlike other complexes, the persistent hydrogen bonding with NSP10 throughout all the simulations shows lower fluctuations, indicating the potential of these four phytochemicals as good drugs for NSP10.

Keywords: NSP10; phytochemicals; ADMET; molecular docking; molecular dynamic simulation

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Comparative Evaluation of Mitochondria-Targeted Antioxidants for Ulcerative Colitis

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Abstract: Ulcerative colitis (UC), an inflammatory bowel disease, is associated with chronic intestinal inflammation & tissue injury due to oxidative mitochondrial dysfunctioning. Existing therapies target inflammation, overlooking oxidative stress related injuries. This accentuates the need for a more strategic therapeutic alternative, directly addressing the underlying cause. Mitochondria-targeted antioxidants emerging as a promising possibility, with MitoQ surfacing as a potential contender. MitoTEM, on the flip side, is relatively new and unexplored. To ascertain the better candidate for UC treatment, the current investigation was attempted. Antioxidant potential and redox characteristics of both were compared through computational predictions, whereas viability assays established optimal concentrations. Subsequently, competitive analysis of mitochondrial respiratory-chain complex activities, membrane potential and ATP generation also provided insights on their capacities and proficiencies. Evaluation of mitochondrial bioenergetics, cardiolipin integrity, oxidative stress, nitrite, 3-nitrotyrosine and caspase activation employing DSS-induced UC-murine model further generated better understanding of their therapeutic efficacy. Moreover, in silico predictions of pharmacokinetic indicators, molecular fate, SAR & QSAR analysis, toxicological constraints and underlying electronic behavior offered additional comparative clarity. This study aimed at establishing a rational framework involving mechanistic-oriented antioxidant screening for selecting superior and safer next-generation mitochondrial drug and therapeutic development for UC.

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Machine learning and network topology reveal key host proteins driving *candida albicans* infection in immunodeficiency

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Abstract: While a robust immune system suppresses *Candida albicans* (*C. albicans*), immunodeficiency allows its transition from a benign yeast to an invasive, often fatal, hyphal form which leads to systemic candidiasis with high mortality rate. The specific host factors driving this susceptibility remain largely unknown. To uncover the molecular differences between these conditions, blood-associated proteins from the NDEx database and differentially expressed genes from GEO datasets of immunocompetent and immune-deficient individuals infected with *C. albicans* were analysed. We isolated 539 deregulated proteins exhibiting inverse expression patterns between the two groups. By mapping these onto a blood-associated protein-protein interaction network, we identified 45 hubs and 11 immunologically relevant MCODE modules. Network topology analysis pinpointed 13 core host molecules as central players. To validate these findings, we developed a machine learning model (Accuracy: 81%, Precision: 85%, Recall: 92%, F1-score: 89%), which robustly linked 11 of these 13 proteins to fungal co-infections in immunodeficient patients. Our findings highlight crucial host proteins that maintain immune homeostasis. Disruption of these molecules, particularly those driving T-reg cell proliferation and M2 macrophage polarization weakens defense mechanisms and promotes systemic candidiasis. Pending experimental validation, these proteins represent highly promising therapeutic targets for immunocompromised patients.

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In Silico Identification of Druggable Hub Proteins in Mycobacterium tuberculosis Drug Resistance Pathways via Protein-Protein Interaction Network and Molecular Docking Analysis.

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Abstract: Emergence of multi-drug-resistant (MDR) and extensively drug-resistant (XDR) strains of *Mycobacterium tuberculosis* poses a major challenge to global TB control, with resistance to first-line drugs primarily driven by mutations in *rpoB*, *katG*, *inhA*, *gyrA*, *gyrB*, *embB*, *pncA*, and *rpsL*. This study constructed a protein-protein interaction (PPI) network of these eight resistance-associated genes using the STRING database (8 nodes, 28 edges; PPI enrichment $p\text{-value}=3.33 \times 10^{-16}$) and analyzed network topology in Cytoscape v3.10.4. Hub proteins were ranked by degree centrality using the cytoHubba plugin, identifying RpoB, GyrB, EmbB, RpsL, and PncA as the top five hubs. RpoB, the established rifampicin target, emerged as a central node, supporting the biological validity of this network-based prioritization. The crystal structure of the RpoB β -subunit (PDB ID: 5UHC, chain C) was retrieved from RCSB PDB, and preliminary molecular docking at the rifampicin-binding pocket was performed using AutoDock Vina via SwissDock, yielding a binding affinity of approximately 5.1 kcal/mol. These findings indicate that RpoB occupies a structurally accessible, druggable position within the resistance interactome, providing a rational foundation for future virtual screening of FDA-approved drugs as repurposing candidates against drug-resistant tuberculosis.

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PP-08

Drug Resistance Prediction in Cancer using Interpretable Machine Learning

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Abstract: Cancer chemotherapy resistance is the innate and/or acquired ability of cancer cells to escape the effects of chemotherapeutics, and is one of the most concerning obstacles in cancer therapy. Artificial Intelligence (AI) and Machine Learning (ML) are increasingly being applied to address cancer drug resistance by identifying effective therapies and resistance mechanisms. Recent studies have focused on using omics data and ML models to predict drug response in cancer cells. Most of the recent drug resistance prediction (DRP) pipelines have predicted drug response from gene expression data in spite of genetic alterations representing some of the earliest and most fundamental drivers of drug resistance. Common genetic changes include acquired driver mutations, gene amplifications, fusions, and deletions. Several mutations in tumor are known to contribute to drug resistance such as BRCA1 and BRCA2 mutations in breast cancer is known to decrease the efficacy of chemotherapy. Here we present a ML pipeline that can predict drug responses of patients/cell lines to drugs using genomic data. Using Interpretable ML, we can identify which genes are contributing to resistance and these genes can be further targeted. Mutation data alone, however, proved insufficient for accurate prediction (AUC ~0.4-0.7), likely because of the tumor microenvironment (TME) which mutation profiles cannot capture. The TME plays a substantial role in modulating resistance. To benchmark against existing approaches, we incorporated gene expression data into the same pipeline and found performance comparable to established expression-based models, proving that mutation data alone cannot fully predict drug resistance. For some drugs (where AUC~0.7), mutation only features still captured meaningful signal for the primary response, suggesting they retain diagnostic value even where they fall short of full predictive power.

Bonding Biology and Data: AI Driven Advances in Stem Cell Research

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Abstract: Stem cell-based therapies represent a central component of regenerative medicine owing to their capacities for self-renewal, multilineage differentiation, and disease modelling. However, their clinical translation remains hindered by biological heterogeneity, inconsistent differentiation outcomes, safety concerns, and limitations in scalability. Simultaneously, high-throughput experimental platforms have produced large, complex datasets that challenge conventional analytical methodologies. This study synthesises current literature addressing the application of artificial intelligence (AI), including machine learning and deep learning approaches, in stem cell research and therapy. Emphasis is placed on computational strategies for stem cell identification, characterisation, differentiation analysis, and cell fate prediction, drawing from studies integrating imaging and multi-omics data. Accumulating evidence indicates that AI-driven frameworks substantially enhance the accuracy, reproducibility, and efficiency of stem cell analyses. These approaches enable automated interpretation of high-dimensional datasets, facilitate prediction of lineage commitment, and improve quality assessment of cellular populations. AI methodologies further contribute to experimental optimisation and the development of predictive models supporting regenerative applications. Artificial intelligence is reshaping stem cell research by addressing longstanding analytical and biological challenges. Although technical, regulatory, and ethical limitations persist, continued advancements in AI integration are expected to accelerate the development of robust, scalable and personalised regenerative therapies.

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Competitive Inhibition of the Nipah Virus Matrix Protein by Conivaptan: From Binding Pocket Dynamics to Protein-Membrane

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Abstract: The recurrent outbreaks of Nipah virus since its first emergence have intensified efforts to identify effective antiviral therapeutics. The matrix protein is a key structural protein that maintains virion architecture and plays a crucial role in anchoring the virus to the host plasma membrane. Binding of phosphatidylinositol-4,5-bisphosphate (PIP2) to the matrix protein promotes conformational changes that facilitate membrane association and initiate viral assembly. Therefore, an effective small-molecule inhibitor should not only compete with PIP2 for binding to the Nipah virus matrix protein (NiVM) but also disrupt its interaction with the host membrane. Using virtual screening of FDA-approved drugs combined with ensemble docking, we identified Conivaptan as a potential inhibitor of the Nipah virus matrix protein. The multivalent interactions of Conivaptan establish stable binding within the PIP2-binding pocket while simultaneously rewiring protein-membrane interactions. In the presence of PIP2, NiVM anchors to the membrane through multiple charged residues, resulting in pronounced local bilayer deformation, an early signature of membrane remodeling. In contrast, Conivaptan binding weakens membrane anchoring and preserves a more ordered and compact bilayer, thereby suppressing membrane deformation. Together, these findings identify Conivaptan as a promising repurposable inhibitor of the Nipah virus matrix protein and provide a mechanistic framework for targeting virus-membrane interactions during viral assembly.

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From Braak Staging to Blood Biomarkers: A Transcriptomics and Machine Learning Framework for Parkinson's Disease Progression

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Abstract: Parkinson's disease (PD), the second most prevalent neurodegenerative disorder, is characterized by dopaminergic neuron-loss and α -synuclein-aggregation. While Braak staging based on Lewy-body stratifies disease progression, clinical variability persists, underscoring the need for stage-specific molecular signatures to develop effective progressive biomarkers. In this study, we integrated pathology midbrain transcriptomic data from microarray, bulk-RNA-seq, and snRNA-seq platforms, and applied a three-layered approach combining PPI-networks, shortest-path analysis, and ModuLand-based module detection to identify key molecular drivers of disease progression. By mapping gene interactions within and across Braak stages, we identified core module genes influencing network topology and disease advancement. Braak stage transition analysis revealed key genes significantly enriched in ubiquitin-mediated proteolysis, cytokine signaling, and neurodegenerative pathways. ElasticNet-regression short-listed candidate biomarkers with strong predictive power ($AUC \geq 0.80$), and ML models further identified biomarkers with robust predictive and diagnostic potential, validated across independent transcriptomic and clinical datasets. Blood transcriptome validation supported their utility as non-invasive biomarkers, while survival analysis of PPMI data highlighted their prognostic significance as risk-associated genes in PD. Additionally, a key regulatory axis involving lncRNA-miRNA interactions was identified, offering mechanistic insight into disease progression. These findings provide a systems-level perspective on PD pathogenesis and highlight promising candidates for early diagnosis and therapeutic targeting.

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Comparative exploration of plant non-coding genomes uncovers conserved miRNA regulatory networks and potential cross-kingdom interactions with human mRNAs and lncRNAs

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Abstract: Plant genomes consist of a large number of non-coding sequences along with the protein coding sequences. The non-coding sequences include microRNAs (miRNAs), long non-coding RNAs (lncRNAs), circular RNAs, transposable elements and repeat sequences. In this study we compared the non-coding genome of three different families namely Brassicaceae, Fabaceae, Poaceae and Solanaceae. We took total 14 economically important species from these Viridiplantae families for the comparison work with respect to miRNAs, lncRNAs and their target genes. By analyzing the mRNA targets of miRNA families from the fourteen species, we annotated specific function for selected miRNA families namely miR156, miR159, miR160, miR164 and miR166, miR171, miR172, miR395, miR396 and miR397. We also studied the interaction between plant-derived miRNAs are human mRNAs and lncRNAs. We found that the target human mRNAs are involved in different types of cancer, neurological disorder, auto-immune disorder and immune deficiency disorder and the lncRNAs are involved in various diseases including cancer, neurological disorder and immune disorder. Plant miRNA-mRNA-lncRNA interaction database (PMMLID) is designed by combining all our findings of plant miRNAs containing information about their targets on plant and human mRNAs (mode of inhibition, biological processes, molecular functions and cellular components). We believe the findings of this study will certainly enhance the existing knowledge of non-coding genome of the representative plant species and their roles in post-transcriptional gene regulation. The cross-kingdom interaction among plant-derived miRNAs and human mRNAs and lncRNAs may illuminate the knowledge of nutrigenetics and nutrigenomics.

Database [URL:http://www.csb.iitkgp.ac.in/databases/miR_details/details.html](http://www.csb.iitkgp.ac.in/databases/miR_details/details.html)

Keywords: microRNA, miRNA family, long non-coding RNA, Viridiplantae, cross-kingdom interaction.

PP-13

Decoding Cardiac Muscle Disease at Atomic Resolution: Molecular Mechanisms of Cardiomyopathy and Therapeutic Modulation

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Abstract: Cardiomyopathies arise from disease-associated mutations in cardiac sarcomeric proteins that disrupt the molecular mechanisms governing muscle contraction. However, how a single amino-acid substitution propagates through large multiprotein assemblies to alter their conformational dynamics and functional regulation remains incompletely understood. Our research combines molecular dynamics simulations, enhanced-sampling techniques, free-energy calculations, and multiscale modeling to investigate the molecular mechanisms underlying cardiac muscle disease. We have investigated mutation-induced allosteric effects in the cardiac thin filament and β -myosin, focusing on disease-associated mutations in tropomyosin, troponin T, and myosin. In the cardiac thin filament, simulations revealed that mutations can alter protein flexibility, inter-protein interactions, and the free-energy landscape of functionally important conformational transitions. Studies of β -myosin further demonstrated that cardiomyopathy-associated mutations remodel conformational dynamics and reduce the free-energy barriers associated with key mechanochemical transitions, including the recovery stroke and ATP-dependent processes. Beyond understanding disease mechanisms, our work explores computational approaches for therapeutic modulation. In the D230N tropomyosin mutant, we investigated the action of the small molecule Z06 (4-hydroxy duloxetine β -D-glucuronide). Enhanced-sampling simulations showed that Z06 reshapes the conformational free-energy landscape and restores features of the mutant system toward a wild-type-like state, providing a molecular framework for understanding small-molecule-mediated rescue. Together, these studies establish an atomistic framework connecting cardiomyopathy-associated mutations to altered conformational dynamics, allosteric communication, and functional free-energy landscapes, while demonstrating how computational approaches can contribute to the mechanistic development of targeted therapeutic strategies.

Comprehensive analysis of lncRNA-miRNA-mRNA network in neurodegenerative disorders

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Abstract: Neurodegenerative diseases are complex disorders characterised by progressive neuronal loss and widespread transcriptomic dysregulation; however, the coordinated interactions among coding and non-coding RNAs that contribute to disease progression remain incompletely understood. In this study, RNA-Seq datasets from disease-relevant neuronal populations and brain regions representing Alzheimer's disease (AD), Parkinson's disease (PD) and amyotrophic lateral sclerosis (ALS) were analysed using an integrative network-based framework. Differential expression analysis and weighted gene co-expression network analysis (WGCNA) were combined to identify disease-associated modules and prioritise highly connected hub genes, which were subsequently integrated with curated RNA interaction databases to construct candidate lncRNA-miRNA-mRNA regulatory networks. Functional enrichment and UTR variant analyses were further incorporated to connect the regulatory network framework with biological processes and potential sequence-level changes. The novelty of the present study lies in the systematic integration of transcriptomic, co-expression, post-transcriptional regulatory, functional and sequence-level analyses within a single comparative framework across AD, PD and ALS, enabling the identification of disease-specific and shared regulatory features and linking candidate regulatory interactions with potential UTR sequence alterations. Across eight tissue-specific studies, 163 hub genes and 4,869 candidate lncRNA-miRNA-mRNA interactions were identified, together with 414 UTR variants associated with the hub genes. These results provide a quantitative resource for prioritising candidate regulatory relationships and potential sequence-level insights for future experimental investigation.

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Molecular Dynamics Insights into Dual-Surface RNA Recognition and Conformational Dynamics of the Hfq Hexamer

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Abstract: The Hfq protein is a host factor for Q β phage RNA replication in *Escherichia coli* and functions as an RNA chaperone involved in various cellular stress responses. Hfq forms a homohexameric, ring-like structure with 6-fold symmetry, characteristic of Sm-like proteins found in bacteria similar to *Staphylococcus aureus*. The protein exhibits distinct RNA binding preferences at its proximal and distal surfaces, with U-rich small RNAs preferentially interacting with the proximal face, whereas A-rich mRNAs interact with the distal face. In the present study, molecular dynamics simulations were performed to investigate the structural dynamics and RNA-binding behavior of Hfq in different functional states. Trajectory-based analyses reveal distinct conformational behavior among the simulated systems, while residue-level fluctuations indicate changes in protein flexibility associated with RNA binding and the Y24W substitution. Hydrogen-bond analysis identifies persistent interactions between RNA nucleotides and residues located on the corresponding Hfq surfaces. Overall, we provide a comparative overview of Hfq–RNA recognition and characterize how RNA binding, the Y24W substitution at the distal face, and simultaneous occupation of both RNA-binding surfaces influence the conformational dynamics and interaction patterns of the Hfq hexamer.

Distinct Roles of Biomolecular Condensates in Protein Aggregation and Purine Metabolism

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Abstract: Biomolecular phase separation provides a mechanism for organizing proteins into compartments whose composition can influence aggregation and metabolic function. Here, we investigate the regulation of condensates in two systems: an amyloidogenic prion protein variant and enzymes involved in de novo purine biosynthesis. The truncated prion protein variant Y145X forms liquid-like droplets that subsequently undergo aggregation. The molecular chaperone Ydj1 partitions into these droplets and suppresses their aggregation, supporting a protective role for heterotypic interactions within condensates. These observations demonstrate how chaperone recruitment can alter the fate of an aggregation-prone protein after condensation. In a complementary study, we examine the co-condensation of purine-biosynthetic enzymes and its response to metabolites. Fluorescence imaging reveals enzyme colocalization within shared condensates, while cryo-electron microscopy provides complementary structural information. Metabolite-dependent changes in assembly indicate feedback regulation of condensation, and cellular imaging reveals punctate enzyme organization consistent with compartmentalized assembly. Together, these studies highlight condensate composition as a means of regulating protein behavior across distinct biological contexts. Chaperone recruitment suppresses pathological aggregation, whereas enzyme co-condensation offers a framework for investigating the spatial organization of purine biosynthesis. The findings motivate further investigation of how molecular interactions couple condensate formation to protein homeostasis and metabolic regulation.

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Directed Modelling of G γ Subunit C-terminal Using Random Conformer Search Based on Neighbour-Dependent Ramachandran Distribution

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Abstract: G-protein subunits G α , G β , and G γ form a heterotrimeric complex (G $\alpha\beta\gamma$). This complex interacts with the transmembrane G protein-coupled receptor (GPCR) on the cytoplasmic plane of the plasma membrane (Calebiro et al., 2021). The G γ subunit is recognised for its role in determining the effector specificity of the G $\beta\gamma$ complex (Kankanamge et al., 2022; Tennakoon et al., 2021). To investigate whether the G γ subunit directly interacts with GPCRs, an analysis of 890 available PDB structures of the GPCR-G $\alpha\beta\gamma$ complex was performed. Analysis of interactions between GPCR and G γ subunits reveals that the distances between GPCR and the G γ subunit were always greater than the maximum essential distance required for interaction, i.e., 6 Å. In most cases, the distances ranged from 15 to 25 Å. It is hypothesised that the NPF domain of the G γ subunit interacts with the Helix 8 and TM1 regions of the GPCR (McIntire, 2022). To test this hypothesis, an ensemble of 10 million G γ chain C-terminal (residue 48-68) conformations was generated by sampling ϕ and ψ torsional angles from the Neighbour-Dependent Ramachandran distribution (NDRD) (Ting et al., 2010). 25 sampled G γ C-terminal conformations were found to approach the NPF-binding domain of the GPCR.

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***In Silico* Design and Molecular Docking Studies of 4-Aminoquinoline-Chalcone Hybrids Targeting the DNA Gyrase A C-Terminal Domain of *Salmonella typhi* as Potential Antibacterial Agents**

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Abstract: The rise of antimicrobial resistance in *Salmonella typhi* has led to a demand for novel antibacterial drugs for treating typhoid (Manjunathaiah *et al.*, 2026). Quinoline and chalcone are significant pharmacophores in biology, and their combination presents a hopeful approach for discovering antibacterial drugs (Tidke *et al.*, 2026). This research involved the computational design of seventy 4-aminoquinoline-chalcone hybrids, with their structures created using ChemDraw. Molecular docking was performed on the C-terminal domain of Gyr-A from *S. typhi* (**PDB ID: 5ZTJ**) utilizing Maestro 14.2.1 (Schrödinger) (Mohammed *et al.*, 2023). SwissADME was utilized to assess drug-likeness and forecast ADMET characteristics. Twelve designed compounds exhibited superior docking scores compared to **ciprofloxacin (-5.030 kcal/mol)** and **moxifloxacin (-4.755 kcal/mol)**. Compound **22** exhibited the top docking score (**-6.528 kcal/mol**), succeeded by compounds **9d (-6.100)**, **10 (-5.615)**, **12 (-5.545)**, **21 (-5.473)**, and **19 (-5.386 kcal/mol)**. Compound 22 established hydrogen bond interactions at GLU629, ILE631, VAL733, ASP573, and VAL834, hydrophobic interactions at pi interaction at ARG630, ARG580 and halogen bond interaction at ARG580. The developed hybrids showed good molecular docking scores as well as interactions and anticipated pharmacokinetic profiles, reinforcing their potential as lead antibacterial.

Keywords: 4-Aminoquinoline-chalcone hybrids, DNA gyrase A, *Salmonella typhi*, Molecular Docking

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An atlas of non-redundant sequences and structures of transcription factor assemblies across domains of life

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Abstract: Transcription factors (TFs) regulate gene expression by controlling the recruitment of transcriptional machinery to regulatory regions of the genome. Nearly 10% of the human genome encodes TFs, making them one of the largest protein families. Despite their central roles in gene regulation, TFs are historically considered challenging therapeutic targets due to their complex interactions with DNA, RNA and associated proteins. Although recent progress in studying TFs both at molecular and structural level excels our understanding on their function, yet a universal rule decoding their recognition process remains elusive. Here, we present a curated non-redundant dataset of TFs with 3,570 sequences and 377 structures. We further characterize “unique interfaces” by quantifying interface identity across interacting chains in TF assemblies. Surprisingly, our data shows that the “unique interfaces” have optimal size ranging from 2000 Å² to 4000 Å² irrespective of their quaternary assembly. To understand the functional diversity, we integrate sequence motifs, structural domains, subcellular localization and functional enrichment of TFs. We have also catalogued association of TFs with various human diseases. Our dataset provides a comprehensive platform to perform large scale analysis of TF-assemblies and aid in computational methods for their prediction across domains of life.

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Explainable Multimodal AI for Dimensional Assessment of Dyslexia and Comorbid Conditions Using Physiological and Behavioral Signals

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Dyslexia, a multidimensional neurodevelopmental disorder, is diagnosed largely through categorical cut-offs. It often leaves comorbid conditions attentional, socio-emotional, motor-coordination and behavioral disorders that are largely unexamined, even though they shape both the presentation of dyslexia and intervention outcomes. Multiple-deficit models of developmental disorders have long argued that such co-occurrence does not imply a principled causal link between the deficits. Extending our earlier conceptual model, this work grounds dyslexia assessment in a computational-biology perspective. As bioinformatics pipelines fuse genomic, transcriptomic and proteomic layers through early, intermediate or late integration strategies to model complex phenotypes, this framework integrates physiological signals from wearable sensors, behavioral data, and caregiver/school-environment input into a single multimodal model, interpreted through XAI and adaptive feedback. Building on recent multimodal dyslexia-screening systems, the framework further proposes incorporating genomic biomarkers reported in the dyslexia-genetics literature, particularly DCDC2 and KIAA0319, including population-specific variants documented in Indian cohorts, as an additional input layer linking behavioral phenotypes to genetic predisposition. This direction is being discussed with clinical institutions for future validation. Thus, the framework aims to strengthen detection accuracy, optimize intervention strategies and support emotional and cognitive well-being of an individual.

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Molecular driver that leads to the heterogeneity across immune cell population and sub population in Tumor Microenvironment (TME)

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Abstract: The tumor microenvironment (TME) is a dynamic and complex ecosystem in which immune cells act as a double-edged sword, capable of eliminating malignant cells as well as promoting tumor progression. The success of antitumor immunity depends on the proportion, phenotype, and functional state of infiltrating immune cells, particularly cytotoxic CD8⁺ T cells. However, chronic exposure to tumor antigens, together with epigenetic remodelling, drives these cells into a dysfunctional, exhausted state. Exhaustion is characterized by sustained expression of inhibitory receptors such as PD-1 and TIM-3 and by a reduced capacity to produce effector cytokines, including IL-2, TNF- α , and IFN- γ . Transcription factors such as TOX have been identified as key regulators that establish and maintain this exhausted program. Single-cell RNA sequencing (scRNA-seq) and advanced bioinformatic tools have transformed the study of intra-tumor heterogeneity. Pan-cancer analyses reveal extensive diversity among tumor-infiltrating T cells and other immune lineages, including distinct subpopulations with different functional states. Despite this progress, the regulatory programs that drive such heterogeneity remain incompletely understood. Conventional methods for inferring gene regulatory networks (GRNs) from scRNA-seq data often rely solely on gene co-expression metrics. Although these statistical approaches identify genes that are activated together, they cannot distinguish direct regulatory interactions from indirect transcriptional cascades, in which a primary transcription factor activates a secondary factor that in turn regulates downstream targets. Co-expression-based models therefore tend to yield noisy networks that misclassify indirect interactions and statistical coincidences as direct connections. Approaches that incorporate cis-regulatory information, such as transcription factor motif enrichment and chromatin accessibility, have been developed to prune such false-positive links and to improve the identification of true regulators [9–11]. Applying these approaches to the TME can help uncover the molecular drivers underlying immune cell heterogeneity and may reveal new therapeutic targets for reinvigorating antitumor immunity.

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***In silico* Design and Molecular Docking Studies of Some Novel Isatin-4-Aminoquinoline Hybrids Targeting Human Estrogen Receptor alpha (ER- α) as Potential Anticancer Agents**

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Abstract: Cancer is a one of the most important public health problems (Singh *et al.*, 2022). *In silico* approach was employed to design and evaluate a series of novel Isatin–4-Aminoquinoline hybrids as potential ER- α -targeting (Alshams *et al.*, 2025) anticancer candidates. Sixty compounds were designed by combining two pharmacophores, Isatin and 4-aminoquinoline, with systematic structural modifications. Molecular docking studies were performed against the Human Estrogen Receptor alpha (ER- α) ligand-binding domain (PDB ID: 3OS8) using the *Schrödinger Maestro* molecular modelling suite. All designed Isatin-4-aminoquinoline hybrids exhibited good molecular docking scores and interactions. Out of 60 designed compounds, the 15 compounds showed best favorable docking scores and interactions against ER- α pockets i.e. compound A28 (-7.81 kcal/mol), B14 (-7.27 kcal/mol), C16 (-6.98 kcal/mol), D11 (-6.94 kcal/mol), A12 (-6.21 kcal/mol), compared to the reference ligands tamoxifen (-5.4 kcal/mol) and raloxifene (-4.9 kcal/mol). The compound A12 showed hydrogen bond interaction at Arg 372, pi cation interaction at LYS and Halogen interaction at LYS 467 within the ER- α ligand-binding pocket, supporting its potential as a promising scaffold for further investigation.

Keywords: Anticancer agents, *In-silico*, Isatin–4-Aminoquinoline hybrids, Human Estrogen Receptor alpha, Molecular Docking.

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Estimation of Spatial Abundance of Microbiota Coexisting with Host Cells in the Tumour Microenvironment

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Intratumoral bacteria are now recognised as functional residents of the tumour microenvironment, capable of altering host metabolism, immune signalling and therapeutic response. Spatial transcriptomics makes it possible to place these organisms in their tissue context, since every captured transcript carries a positional barcode, yet the non-host reads in such libraries are usually discarded as contamination. We developed a pipeline that recovers these reads while preserving their spatial coordinates. Host-unmapped reads from 10x Visium libraries were classified using GATK PathSeq, separated into rRNA and mRNA fractions with RiboDetector and SortMeRNA, assembled *de novo*, and converted into a depth-based abundance estimate for each spot. Applied to colorectal (CRC) and oral squamous cell carcinoma (OSCC) sections, the pipeline resolved bacteria as discrete clusters at defined tumour locations rather than a diffuse background, and host expression was consistently reduced in and around colonised spots. Community structure differed sharply between the two tumours: CRC was dominated by *Fusobacterium* sp. CM1 (60% of positive spots), whereas OSCC carried an even community with no taxon exceeding 4%. A brain tumour section processed identically yielded no microbial signal, supporting specificity. These spatially resolved abundances now seed community-scale metabolic models of host–microbe exchange within the tumour.

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Computational Approaches for Predicting Non-coding RNAs in Legumes: A Cost-Effective Alternative to Lab-Based Experiments

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Abstract: Legumes serve as a basis for ensuring global food safety since they provide protein, biological nitrogen fixation, and soil fertility recovery to billions of people. However, the regulatory role of ncRNAs in legumes has not been well-studied yet. The majority of existing prediction tools are based on mammalian or Arabidopsis datasets and do not work well on other genomes, hence creating a gap between the volume of legume sequence data and the ability to identify its regulatory content. In the current review, we analyze the history of the development of ncRNA prediction in three methodological periods: homology/structure-based search, classical machine learning methods, and deep learning approaches. We describe major classes of ncRNAs (with focus on miRNA, lncRNA), their biological functions and the importance in legumes for nitrogen fixation, and resistance to abiotic stress. We compare the predictive performance of three widely-used tools (PLncPRO, P-TarPmiR, miRDeep2) for different legume species including soybean, chickpea, common bean, and pigeon pea. We identify four main issues which appear during comparison: poor cross-species generalization of the model which was trained on other organisms, significant imbalance of hairpins between real, background noises like transposable elements, and lack of legume-specific benchmark datasets. Finally, we discuss the prerequisites for developing a legume-specific miRNA, LncRNA prediction framework and possible solutions, such as using RNA language models, pan-genomic studies.

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G. N. Ramachandran: A Jewel in the Crown of Indian Science

Professor G.N. Ramachandran was one of the most brilliant scientists with an intelligently gifted mind in post-independence India. Born on 8th of October 1922, he received his primary and secondary education in the erstwhile princely state of Cochin. With undergraduate and postgraduate degrees in Physics, Prof. G.N. Ramachandran received his doctoral degree from Cambridge University, UK in the field of X-ray diffraction. After completing doctoral degree, Prof. G.N. Ramachandran joined the Department of Physics of Indian Institute of Science as an Assistant Professor of Physics in 1949. He was in charge of the X-ray Diffraction Laboratory that he was instrumental in building as a student. After spending about two years at the Indian Institute of Science, he shifted to Madras University, where he and his group made lasting contributions to the field of Biophysics. Prof. G.N. Ramachandran and his peerless postdoctoral fellow, Dr. Gopinath Kartha proposed the triple helical structure of collagen in 1954. Several studies on the structure and conformation of proteins and peptides resulted in the development of the eponymous "Ramachandran Plot", which was published in the Journal of Molecular Biology in 1963 and has become a gold standard for studying the protein conformations.

About the Department

The Indian Institute of Technology Kharagpur (IIT Kharagpur) is the First IIT established by the Government of India in 1951. It is recognized as an Institute of National Importance and recently, as an Institute of Eminence by the Government of India. The Institute was established with a mandate to produce world class engineers and scientists after our independence in 1947. IIT Kharagpur launched M. Tech. program in Biotechnology & Biochemical Engineering way back in 1986. Wide appreciation of our program in the country and abroad led to introduction of an UG program in Biotechnology & Biomedical Engineering in 1994. Subsequently, the Department of Bioscience and Biotechnology (<http://www.bt.iitkgp.ac.in>) was established in 1999 to run the UG and PG programs independently. Presently, the Department is running 4-Year B. Tech, 5-Year dual degree (B. Tech & M. Tech), 2-Year M. Tech and Ph.D. programs in Biotechnology & Biochemical Engineering. The department also runs 2-Year M.Sc program in Chemical Biology. The faculty members are involved in research and development in emerging areas of basic biological science and their applications in various domains along with Industry-institute participation.

About Bioinformatics Centre

The DBT supported Bioinformatics Centre (BIC) was set up in 2022 at the Department of Bioscience and Biotechnology IIT Kharagpur. The mission of this centre is to provide a national level facility and expertise in Bioinformatics and Computational Biology by pursuing cutting edge research and development along with the focused man-power training in various fields of Bioinformatics and Computational biology. Faculty members involved in this centre has significant contributions in the areas of Structural Bioinformatics, Biomolecular simulations, Big-data analysis in genomics, proteomics and systems level metabolomics analysis. As a mark of respect, honoring and remembering scientific contributions made by Prof. G.N. Ramachandran, the Bioinformatics Centre, Department of Bioscience and Biotechnology, IIT Kharagpur is organizing the G.N. Ramachandran lecture series on 12th and 13th of October 2026.

