Industry Day Theme
SUSTAINABLE MEDICAL TECHNOLOGIES

Application of Computational Techniques in Biopharma

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Abstract
"Biotherapeutics" have emerged as an important therapeutic molecules in last couple of decades. It consist almost 50% of total drugs approved by FDA. However, there is only 18% are free from all development challenges. Computational biology can play a big role in improving the molecule stability and bioactivity. We showcase here our work where we used computational biology to assist biotherapeutics discovery, manufacturing and storage.

Introduction
Biotherapeutic molecule is exponentially capturing the drug market. Among these different biologics, protein as therapeutic molecule has special stand. These molecules are high in activity but at the same time they are difficult to handle due to their size and diversity. Computational techniques are being used to address and solve key concerns in biotherapeutic domain. **Biological activity** and **Biophysical Stability** are two major aspects for any drug molecule. Computational biology, in conjugation with machine learning methods can be used to improve activity and stability. Bioengineering of therapeutic protein can be approached from computational methods. This would allow to cover large sample space which is not possible in experiments otherwise. Bioengineering can enhance activity or solubility, although both these are trade-off. **Toxicity Prediction** of molecule is also another area which is continuously being addressed using high end
ML algorithm.

Here, we discuss some of our projects that have been performed using computational techniques and further they were validated in experiments using biological and bioanalytical methods. We also portray, how these ideas and scientific approaches can be commercialized. Recently, a startup – "Growdea Pvt. Ltd." is spin-off from our laboratory where we focus on computational techniques to assist biological and biopharma sector.

Materials and Methods
We used computational methods to achieve different goals, they are: (i) Protein-Protein Docking (ii) Binding Energy Estimation (iii) Molecular Dynamic Simulation (iv) Machine learning (v) Protein modeling (vi) Pharmacophore generation (vii) Virtual Screening (viii) Ligand Design.
In addition we also used different experimental techniques to validate out computational finding, they are: (i) Size-exclusion chromatography (ii) Isothermal titration calorimetry (iii) Surface Plasmon Resonance (iv) Enzyme assay (v) Cell assay (vi) Animal Testing.

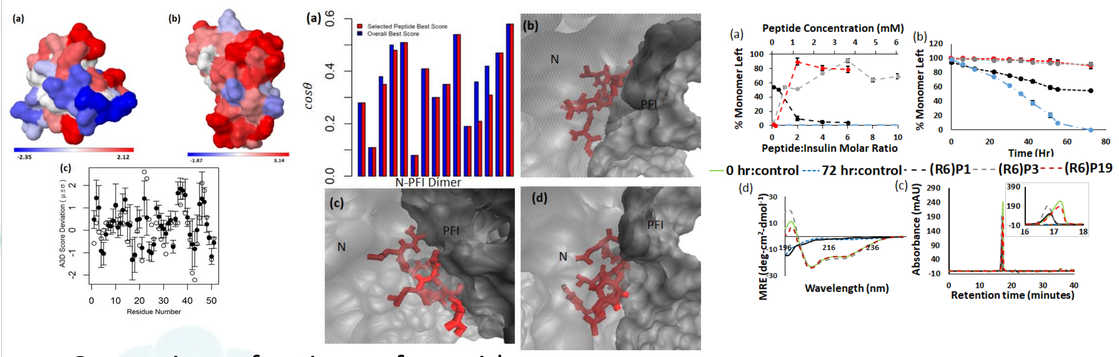
Conclusions
Computational techniques can be used to catalyze biotherapeutic and drug discovery domain. It can explore large possibility virtually and can report the best, that be tested experimentally. It has huge potential of saving time and cost in pharmaceutical research.

Industrial Significance
We started a computational biology based start-up from our lab – "Growdea Technology". Our motive is to facilitate experimentalist with meaningful prior prediction in order to reduce time and effort.

Technology Readiness Level:
We validated our protocol.
Filed patent for excipient against insulin aggregation.

Results

Arrest Insulin Aggregation

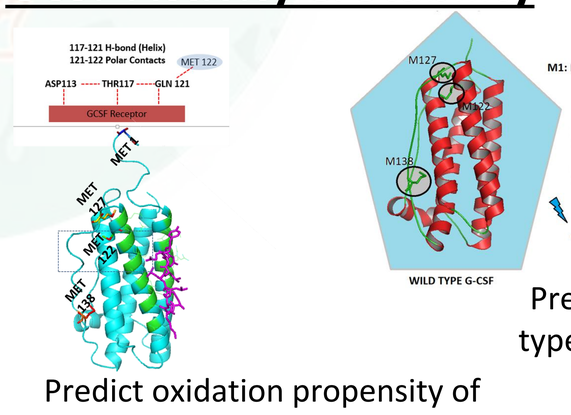


Comparison of native surface with partially folded structure. "Propensity for Aggregation"

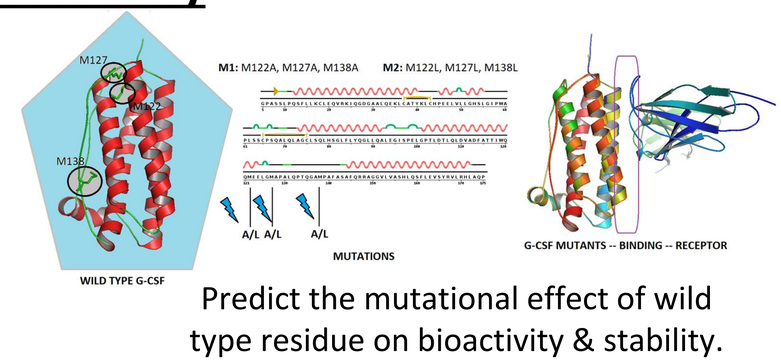
Design small peptide to inhibit native-partially folded complex, that propagates to aggregation. "Percentage Monomers"

Indian Application No.: 201711030494 Date of filing: August 29, 2017
Title of Invention: "POLYPEPTIDE SEQUENCE AND COMPOSITION THEREOF"
Applicant: INDIAN INSTITUTE OF TECHNOLOGY DELHI

GCSF Activity & Stability

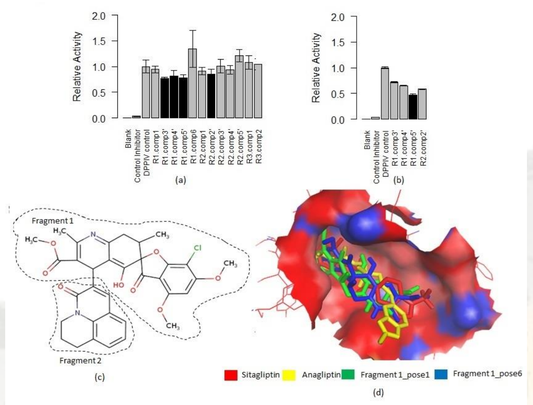


Predict oxidation propensity of methionine residues



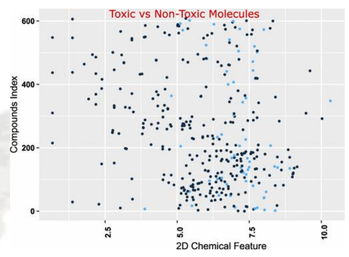
Predict the mutational effect of wild type residue on bioactivity & stability.

Design DPP-4 Inhibitor



Design & Test new Inhibitors against DPP-4, a potential drug target for Diabetes.

Toxicity Prediction



Neural Network & Decision Tree predict-nuclear receptor (NR), stress response (SR), ames mutagenicity (AM), *Tetrahymena pyriformis* IGC50, oral rat LD50, 96 h fathead minnow LC50 data set (LC50 set), 48 h Daphnia magna LC50 data set (LC50-DM set), toxicity.

References
- Abdul Karim,Avinash Mishra, M. A. Hakim Newton, Abdul Sattar, Efficient Toxicity Prediction via Simple Features Using Shallow Neural Networks and Decision Trees, ACS Omega, 2019.
- Avinash Mishra*, Megan Cross, Andreas Hofmann, Mark J. Coster, Abdul Karim, and Abdul SattarIdentification of a Novel Scaffold for Inhibition of Dipeptidyl Peptidase-4, J. Computational Biology, 2019.

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