Swanson School of Engineering

Undergraduate Summer Research Program

2016

Welcome to the 2016 Issue of the Swanson School of Engineering (SSOE) Summer Research Abstracts!

Every year the SSOE invites all undergraduates to propose a research topic of interest to study for the summer and to identify a faculty mentor willing to serve as a mentor and sponsor for their project. In this way, students get to work on cutting edge research with leading scientists and engineers while spending their summertime at SSOE. The students, however, were not restricted to the Swanson School of Engineering or even the University of Pittsburgh. The world has been provided to them! As a result, eight students spent their internship in Singapore at the National University of Singapore and Nanyang Technological University. One student traveled to Israel to study at the Israel Institute of Technology and another student studied at Politecnico di Milano in Italy. Stateside we had one student at John Hopkins University and another student at the Dana-Farber Institute at Harvard Medical School.

There are multiple programs that offer summer research opportunities to the SSOE undergraduates, the largest of these being the Summer Internship Program jointly sponsored by the Swanson School and the Provost. This year, the program was able to fund over 60 students, with generous support from both the SSOE and the Office of the Provost. Additional support was provided by a generous gift from the PPG Foundation for students selected as PPG Fellows. The Swanson School study abroad program assisted with the students who participated in international internships.

The following individual investigators also provided support: Kevin M. Bell, David M. Brienza, Bryan N. Brown, Lance A. Davidson, Richard E. Debski, Bryan M. Hooks, Karl J. Johnson, Jung-Kun Lee, Colleen A. McClung, Micahel M. Modo, Ian A. Sigal, Matthew A. Smith, George D. Stetten, Jonathan Vande Geest, and Götz Veser.

As part of the requirements of the internship, students submitted poster abstracts to *Science 2016 –Game Changers!* in September. Nearly all of these students were selected to present posters in a special undergraduate student research session at Science 2016, with Engineering making up 70% of the undergraduate posters at the conference!

SSOE provides other opportunities in addition to the internship program. Interns and other summer students were invited to submit an abstract to be considered for expansion into a full manuscript for consideration for the third issue of *Ingenium: Undergraduate Research in the Swanson School of Engineering.* This provides undergraduates with the experience of writing manuscripts and graduate students – who form the Editorial Board of *Ingenium* – with experience in peer-review and editing.

We hope you enjoy this compilation of the innovative, intellectually challenging research that our undergraduates took part in during their tenure at SSOE. In presenting this work, we also want to acknowledge and thank those faculty mentors who made available their laboratories, their staff, and their personal time to assist the students and further spark their interest in research.

Larry J. Shuman, Senior Associate Dean for Academic Affairs
David A. Vorp, Associate Dean for Research

Student	Student Department	Mentor(s)	Mentor Primary Department(s) All mentors are faculty at the University of Pittsburgh unless otherwise noted.	Title (*abstract witheld)
Julie L. Hartz	Chemical Engineering	Götz Veser	Chemical and Petroleum Engineering	*CELL RECOVERABILITY AFTER EXPOSURE TO COMPLEX ENGINEERED NANOPARTICLES*
Kenny L. To	Chemical Engineering	Götz Veser	Chemical and Petroleum Engineering	*ASSESSING TOXICITY OF COMPLEX ENGINEERED NANOPARTICLES*
Meghan J. Wyatt	Bioengineering	Sing Yian Chew	Chemical and Biomedical Engineering, Nanyang Technological University, Singapore	*INFLUENCING DIFFERENTIATION AND GROWTH OF NEURAL PROGENITOR CELLS WITH GENE SILENCING AND LAMININ*
Laura B. Fulton	Mechanical Engineering	Jeffrey J. Gray	Chemical and Biomolecular Engineering, Johns Hopkins University	*IMPROVEMENT OF ROSETTA BIOCOMPUTING SOFTWARE FOR CANONICAL ANTIBODY CDR LOOP PREDICTION*
Nicole E. Cimabue	Civil Engineering	Kyle J. Bibby	Civil and Environmental Engineering	*PERSISTENCE OF EBOLA SURROGATE AT VARIOUS TEMEPERATURES AND NEUTRAL PH*
Carolyn M. Wehner	Civil Engineering	Andrew P. Bunger	Civil and Environmental Engineering	*WELL PLUGGING WITH ABSORBANT CLAY: STUDYING BENTONITE PELLET DESCENT IN BOREHOLES*
Brandon Contino	Electrical Engineering	David V.P. Sanchez	Civil and Environmental Engineering	*AN EVALUATION OF CARBON ELECTRODES FOR ANTI-FOULING IN THE ELECTRO-FENTON PROCESS*
Swaroop Akkineni	Computer Engineering	Samuel J. Dickerson	Electrical and Computer Engineering	*SPIWAVE: AUTOMATED SPIRAL EVALUATION FOR PARKINSONIAN PATIENTS USING WAVELETS*
Michael P. Urich	Electrical Engineering	Zhi-Hong Mao	Electrical and Computer Engineering	*IT'S ALL IN YOUR HEAD- BRIDGING NEUROLOGICAL SIGNALS TO THE PHYSICAL WORLD THROUGH EEG*
Mark D. Littlefield	Bioengineering	Young Jae Chun	Industrial Engineering	*MODELING AND EXPERIMENTAL ANALYSIS OF THE TEMPORARY, FULLY-RETRIEVABLE STENT FOR TRAUMATIC HEMORRHAGE CONTROL*
Rithika D. Reddy	Industrial Engineering	Paul W. Leu	Industrial Engineering	*NITROGEN DOPING CARBON NANOTUBES*

IMPROVEMENT OF ROSETTA BIOCOMPUTING SOFTWARE FOR CANONICAL ANTIBODY CDR LOOP PREDICTION

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INTRODUCTION

Computational modeling of protein structures and protein-protein interactions is an increasingly important method for molecular biophysics research as well as for applied research for drug design. Experimental protein structure prediction is often labor intensive, time consuming, and costly, involving techniques for obtaining structures such as X-ray crystallography and NMR [1, 2]. At Johns Hopkins University, the Gray laboratory is developing computational tools for antibody structure prediction and antibody docking as part of the Rosetta Commons biocomputing software suite to tackle real world problems [3, 4].

Antibodies, with their high affinity and specificity to target antigens, are of particular interest as potential therapeutics for the prevention and treatment of infectious diseases. They are Y-shaped glycoproteins that consist of a constant region and a fragment variable (Fv). Antibody specificity is located in the Fv, which contains the antigen-binding site that is comprised of six complementary determining region (CDR) loops [1, 2]. The six CDRs consist of variable regions of light (VL) and heavy (VH) chains. CDR loops (L1, L2, L3, H1, H2, H3) are immunoglobulin (Ig) hypervariable domains responsible for antigen recognition and specific antibody (Ab) binding [1].

In order to create a homology model of an antibody variable domain, Rosetta biocomputing software splits the antibody sequence into heavy and light chain framework regions and six CDR loops. For each of these regions, a template is picked from a set of antibody crystal structures based on sequence similarity using a BLAST search [5]. The six CDR loops are then grafted onto the framework regions.

Previous research conducted in the Gray laboratory indicates that template selection using BLAST does not always lead to the lowest possible energy as assessed by the Rosetta score function. Alternative templates that were manually selected lead to substantially lower energies in some cases. "A New Clustering of Antibody CDR Loop Conformations" published in the Journal of Molecular Biology demonstrates clustering of conformations of the five non-H3 CDR loops [1]. For each of the clusters, one representative median structure is identified [1]. Research in the Gray laboratory has suggested that the selection of these median conformations as templates for the non-H3 CDR loops can yield lower energy structures than selection of a template based on sequence similarity.

The goal this research focuses on improving accuracy of CDR loop prediction and contributing to the ongoing goal of improving protein prediction. To improve selection, median protein CDR loop conformations were incorporated into the antibody prediction algorithm, a python script was written that parsed for PDBs and their clusters, and C++ code was added for proline filtering for the CDR loops. This research will contribute to an improved prediction of antigen binding sites that is highly relevant for antibody docking applications and design strategies based on homology models.

METHODS

Part 1: CDR cluster identification was obtained from "A New Clustering of Antibody CDR Loop Conformations." Information for structures and their median PDB ids was recorded in a hash table. As part of cluster identification, positioning of prolines for clusters was noted and rules drafted for proline filtering. Proline filtering occurred for H1 and L3 clusters. For the H1 cluster sequence, filtering is possible only when the sequence length is 13 and there also exists a proline (P) at position 9 of the sequence. For L3, sequence length is checked and if the length is 8, 9, or 10 filtering is possible. For lengths 8 or 9 a proline must be present in position 6 for filtering and for length 10 prolines must be present at positions 6 and 7 for filtering to occur.

Part 2: A python script was written to parse the Rosetta antibody database. The script identified

the PDBs and corresponding heavy (H1-H3) and light (L1-L3) chains. This information was organized and piped to a file for later use. Cases where chain information was missing for PDBs were also noted and this data and related error messages were piped to a CDR failures file for debugging.

Figure 1: Flow of parsing for PDBs

Part 3: To improve protein prediction for the CDR loops, proline filtering was added. C++ code was written to filter protein sequences for L1 and H3 clusters based on sequence length and proline positioning. For example, based on CDR cluster identification rules obtained in Part 1, a L3 sequence of length 8 with a proline at position 6 would be filtered out whereas an L3 sequence of length 8 lacking a proline at position 6 would remain unfiltered.

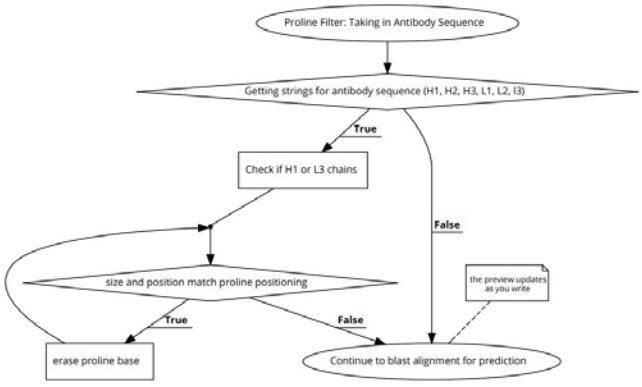

Figure 2: Filtering by Prolines

RESULTS AND DISCUSSION

This research to improve prediction of antibody CDR looping contributes to the goal of the Rosetta Commons Biocomputing software to better understand and improve protein structure prediction methods to solve practical problems. Using documented rules helped structure how filtering occurs, improving antibody selection. Parsing the Rosetta antibody database was a key step in identifying PDBs and obtaining chain information. By identifying CDR clusters, it was then possible to write filtering rules involving median cluster id and prolines to improve accuracy of antibody CDR loop prediction. Understanding antibody looping will help researchers better target diseases caused by misfolded proteins – type II diabetes, Alzheimer's, Parkinson's, Huntington's, sickle cell - to develop genetic and therapeutic medical cures.

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5. Definition: BLAST. U.S. National Library of Medicine, NCBI National Center for Biotechnology Information.

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