SCHOOL OF COMPUTER SCIENCE
Faculty Candidate

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Identifying Combinations of Driver Mutations in Cancer

Large cancer genome sequencing efforts have provided new opportunities for breakthroughs in cancer research, but also revealed key computational challenges in cancer genomics. Consortia such as The Cancer Genome Atlas have led this effort, taking advantage of rapid advances in DNA sequencing technology to measure the somatic mutations in thousands of cancer genomes. One major goal of these consortia has been to distinguish the handful of driver mutations that cause cancer from the multitude of passenger mutations that play no role in cancer. Identifying driver mutations has important clinical implications, including opening new avenues for and improving the personalization of cancer treatments. However, the new wealth of cancer genomics data also has revealed a major computational hurdle for the discovery of driver mutations: each tumor is a "snowflake" with a different combination of mutations, such that some driver mutations may be observed in only a handful of tumors, even in large cohorts.

In this talk, I present several methods I have developed for identifying combinations of driver mutations in cancer. One explanation for the observed heterogeneity of mutations across tumors is that driver mutations target key cancer signaling pathways, each of which include multiple genes and can be perturbed in numerous ways. Thus, I have developed multiple algorithms for discovering the key pathways targeted by driver mutations, including the Combinations of Mutually Exclusive Alterations and HotNet2 algorithms, which utilize techniques from graph theory, statistics, and combinatorial optimization. I will show the methods identify combinations overlapping known cancer pathways and make novel predictions when applied to genome-scale datasets with hundreds of tumor samples. I also describe the Mutation Annotation and Genome Interpretation (MAGI) web application, which displays interactive visualizations as well as crowd-sourced and text-mined mutation annotations in order to help prioritize likely driver mutations.

Bio:
Mark (Max) Leiserson is a Ph.D. candidate in computational biology and computer science and NSF Graduate Research Fellow in the lab of Professor Benjamin Raphael at Brown University. His research focus is on developing and using computational techniques to advance understanding of the genetics of disease, and he has developed and applied computational methods to cancer genomics to identify the somatic mutations within a tumor cohort that contribute to cancer. Max's interests include graph algorithms, statistics, combinatorial optimization, and data visualization. Max received his M.Sc. in computer science from Brown and his B.Sc. in computer science at Tufts University, where he analyzed yeast genetic interaction networks under the supervision of Drs. Benjamin Hescott and Lenore Cowen.

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Host: Russell Schwartz