As the world of science becomes increasingly more complex, traditional methods of solving important problems are becoming inadequate, and the distinct borders between disciplines are blurring. No longer can one researcher with his or her limited knowledge and perspective adequately solve the challenges we face today. Collaboration, not only within one's field but also with disparate disciplines, is required. Professor Bruce Randall Donald's computer science laboratory exemplifies this sentiment.

The lab encompasses two areas of research. One area focuses on computational biology and chemistry, specifically structural genomics (also known as structural proteomics). The emphasis is on developing computational techniques (algorithms) in order to determine the structure of proteins and nucleic acids. Currently, it typically requires a number of years and possibly millions of dollars to determine the structure of a single protein. When one realizes that there are between 30,000 and 50,000 different proteins (not to mention the countless modifications that can occur to each protein that, inevitably, increases these numbers), it is obvious that a technique to expedite this process is urgently needed. According to Timothy Danford '01, a former undergraduate researcher in Donald's lab, "the amount of data is so great, and the interactions so complex, that computational techniques are necessary to make sense of it all." The goal of Donald's lab, therefore, is not only to automate the painstaking experimentation process and data analysis of structural determination but also to reduce the number of experiments needed by requiring less data. The hope is that hundreds of protein structures may be determined and analyzed within a single year with the aid of these new computational techniques. Simplifying this process would also allow the average researcher to perform a structural analysis, thus eliminating the need to hire an independent structural expert.

In order to develop better algorithms the scientists in Donald's lab work directly with experimental structural data from X-ray crystallography, nuclear magnetic resonance, and mass spectrometry experiments. In order to obtain these data, a great deal of collaboration with other biologists and chemists is required. Bruce Donald's lab, for example, works closely with Professor Rob McClung in the biology department, Professor Bernard Trumpower at the Dartmouth Medical School, and Professor Amy Anderson in the chemistry department on a number of projects. Using data acquired from other labs, Donald and his team are able to develop better computational techniques that facilitate and expand the work of these other labs. For example, Professor Anderson employs X-ray crystallography to determine the structures of proteins in order to answer questions of biochemical and biophysical interest. Using data supplied by Anderson's experiments, Donald and
his team are able to develop better computational techniques that facilitate and expand the experimental and interpretation processes. In this way, a truly symbiotic relationship is formed between these seemingly unrelated fields.

The second area of Donald’s lab is involved with physically altering enzymes of pharmacological interest in order to design better drugs, such as antibiotics and antivirals. If an enzyme that naturally synthesizes a given drug is able to be “rewired,” then it can be programmed to create a new drug. Ultimately, the goal is to make these enzymes nonspecific so that they can be used to make any drug that a researcher desires. Donald and his team work to design computational methods that explore the structure of enzymes and pinpoint the elements that will need to be altered. While this work can theoretically be done experimentally, it requires an inordinate amount of time. Computational tools, however, would make the implementation of this process a practical reality.

Interesting projects such as these are not beyond the reach of undergraduates. On the contrary, Professor Donald typically invites between four and eight undergraduates to work in his lab. Most students are introduced to Professor Donald and his lab while enrolled in one of the many classes he teaches in the computer science department. They typically begin working with Donald early on in their undergraduate career and continue to do so until graduation, culminating in a senior thesis or possibly even a published scientific paper. Such a commitment often produces many rewards as students can become intimately involved in projects and are able to make a real contribution. Working in such a multidisciplinary laboratory has other advantages. Undergraduates whose background is limited to the field of computer science are exposed to the teachings and viewpoints of the other disciplines. Brunn Roysden III ’04, an undergraduate who recently started working in Donald’s lab, has already discovered the reality of multidisciplinary work: “We start out discussing an improvement to an algorithm, but then completely switch gears and discuss the chemistry behind the biological process that we are studying or the engineering behind how the experimental data is actually collected.” Students also have the opportunity not only to work closely with Professor Donald but also with collaborators in the other disciplines. For all those involved, the result is a unique experience in a truly interdisciplinary laboratory.

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Do you work in or know of a lab that you would like to see in an issue of the DUJS? E-mail recommendations to dujs@dartmouth.edu