Computer Scientist in Profile: **Bruce R. Donald**

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Of all the undergraduate majors that might steer someone towards an accomplished scientific career and prolific research in Artificial Intelligence, Robotics, and Computational Structural Biology, you would have a hard time circling 'Russian Language and Literature.' Yet, that is exactly how Bruce's journey started at Yale. Bruce fondly recalls his famous English and Literature professors, such as Harold Bloom and Victor Ehrlich, who left a deep impression on him and played no small part in Bruce eventually graduating *summa cum laude* in 1980. "The connection with Computer Science was there all along," says Bruce, "though I did not obtain any formal training in CS. I had been a hacker in high school, and I did take some LOGO and Fortran classes at MIT. I hung out with a group of programmers in school and had a job programming and selling one of the first personal computers, the MITS Altair 8800." He recalls that despite his interest in programming, at Yale he almost exclusively took only Humanities courses. The only other courses outside Humanities were a Physics, Calculus, and Artificial Intelligence course.

During the better half of his undergraduate studies and four years afterwards, Bruce was also a Research Analyst in the Laboratory for Computer Graphics and Spatial Analysis at the Harvard University Graduate School of Design, where he worked on Geographical Information Systems (GIS) and computer-aided architectural design. "In 1978 I just walked into the Harvard Graduate School of Design and convinced them I could program." They hired him. At first he was mostly attracted to the design, art, and visual connections. However, there was rigorous computer science that got him interested in theory. The lab was a hotbed of algorithms, GIS, graphics, and geometry. Eventually the administration urged Bruce to go back to graduate school. He was not quite sure what he wanted to do. So, he did the next logical thing.

Bruce simultaneously applied to Oxford in Russian literature and MIT in Computer Science. He was accepted to both. "MIT offered a stipend, whereas Oxford asked me to pay a lot, thousands of pounds." He goes on, "I do not know why MIT admitted me, but I was lucky to find a great advisor who trained me, Tomás Lozano-Pérez." In 1982, Bruce began working under the direction of Lozano-Perez at the MIT Artificial Intelligence Laboratory. He received the S.M. degree in Electrical Engineering and Computer Science, soon followed by a Ph.D. degree in Computer Science in 1987. His officemate at MIT, Mike Erdmann, urged Bruce to also study Mathematics. As a result, Bruce minored in Topology during his graduate studies, which he notes he still uses in his work today.

The next leg of the journey landed Bruce in Ithaca, N.Y., where he joined the Computer Science faculty at the Cornell University. At Cornell, Bruce also held a joint appointment in Applied Mathematics and co-founded the Cornell Robotics and Vision Laboratory. He got an early sign of the impact of his research when he received a National Science Foundation Presidential Young Investigator Award in 1989. He rose through the ranks of tenure by 1993.

Bruce spent more than a decade at Cornell before joining the Computer Science Department at Dartmouth in 1997. As if anticipating my question, he proceeds to tell me that the move happened organically. After obtaining tenure in 1993, he stayed in Ithaca an extra year to run the Masters Program, which he expanded from 6 to 80 students. Afterwards he took a sabbatical at Stanford as a visiting professor from 1994 to 1996. "I was very lucky to have a visiting position in Computer

Science and to work at Paul Allen's Company, Interval Research Corporation," he says. Bruce worked in Palo Alto, CA from 1995 to 1997. During this time, he became co-inventor of Embedded Constraint Graphics (ECG). Most importantly, he also met his wife, then a Neurobiology postdoctoral fellow at Stanford. They got married and looked for jobs. He hoped they could go back to Cornell or find positions in the West Coast. After spending one more year at Cornell trying to figure out how to solve the two-body problem, he got a surprise. Daniela Rus had just gone to Dartmouth as an Assistant Professor and helped Bruce and his wife find the right positions at Dartmouth. "That is how I ended up at Dartmouth," he says.

At Dartmouth, Bruce was named the Joan and Edward Foley Professor in 2003. During his time at Dartmouth, Bruce made significant contributions to robotics, including numerous scientific papers. "It was at Dartmouth that I started getting results in computational molecular biology," he recalls. The analogies with robotics gave Bruce a fresh perspective on computational problems involving molecular structures and some very exciting research directions. Indeed, in 2001, he was awarded a Guggenheim Fellowship for his advancement of algorithmic research on Structural molecular biology and proteomics. Since then, Bruce's research has advanced advanced protein design, molecular nanotechnology, and their biomedical applications. He has developed transformative algorithms for positive and negative protein design. He has extended the boundaries of what is possible with provable algorithms, in a series of end-to-end studies going from mathematics to novel algorithms to software to prospective experimental validation including binding, kinetics, stability, in vivo assays, and both NMR structures and crystal structures.

"I have been very lucky to have amazing collaborators with whom I have co-supervised students. That makes for the best science."

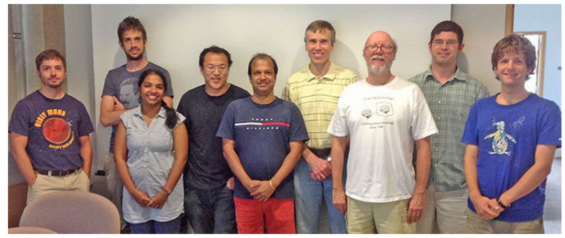
Bruce is now James B. Duke Professor of Computer Science at Duke University and Professor of Biochemistry in the Duke University Medical Center. He is a Fellow of the ACM and the IEEE for contributions in robotics, microelectromechanical systems, and computational molecular biology. In 2011, Bruce published a seminal book with MIT Press, "Algorithms in Structural Molecular Biology."

Bruce's efforts have significantly advanced computational structural biology. His algorithms have been experimentally demonstrated to have remarkable accuracy and predictive power. His algorithms have been applied prospectively to systems of significant biochemical and pharmacological interest. Seminal work includes reprogramming an antibiotic-producing enzyme (*PNAS 2009*), predicting MRSA resistance mutations to a new inhibitor (*PNAS 2010*), developing allosteric inhibitors of oncogenic protein-protein interactions (PPIs) in leukemia (*Chemistry & Biology 2007*), designing competitive inhibitors of PPIs to combat cystic fibrosis (*PLoS Comp. Biol. 2012*), designing molecular probes to selectively pull down broadly neutralizing antibodies against HIV-1 from donor sera (*Retrovirology 2012*), and designing a new antigenic MPER trimer for examining immunogenic responses to the HIV-1 viral coat protein gp41 (PDB id: 2m7w).

It is worth noting that Bruce is behind many structures deposited to the Protein Data Bank, which is a remarkable feat for a computer scientist. Bruce has developed breakthrough algorithms for structure determination from X-ray crystallography and NMR data, specifically for difficult systems including large proteins, symmetric proteins, and membrane proteins. For example, he has used his algorithms to solve challenging protein structures central in Cryptosporidosis (PDB id: 1QZF), cardiac calcium cycling (PDB id: 2HYN), and HIV (PDB id: 2M7W). Finally, he has developed biomedical microtechnology, including the world's smallest untethered controllable microrobots (*J.MEMS 2006, 2008*), massively-parallel distributed micromanipulation and microassembly, and carbon nanotube neural probes for intracellular recording in freely behaving animals (*PLoS 2013*).

With such a remarkably diverse and high-impact research contributions in molecular biology, it seems appropriate to pause and ask. "How does someone arrive at this point?" Bruce credits two sources to his success. First, a diverse and accomplished research portfolio in Artificial Intelligence. “The second is my colleagues,” he says. “My experimental collaborators have been instrumental to my ability to chart new paths in my scientific career and be successful. I have been lucky to co-supervise outstanding students with my collaborators.”

Bruce is exceptionally proud of the accomplishments of his former Ph.D. and postdoctoral students. He tells me that many of them have gone to impressive positions and accomplishments as independent scientists with successful laboratories of their own. Perusing the detailed list he maintains on his lab’s website, I realize I recognize many of them.



A recent photo of the Donald Lab.

“So, what is next?” I cannot resist to ask him. He shares with me his firm belief that his algorithms can revolutionize therapeutic treatment. “Our algorithms could enable the design of proteins and other molecules to act on today’s undruggable proteins and tomorrow’s drug-resistant diseases,” he says. In the next few years, Bruce plans to develop novel protein design algorithms and software. He notes, “My goal is to use to them to (1) predict future resistance mutations to new drugs in pathogens responsible for deadly nosocomial and community-acquired infections; (2) design inhibitors of protein-protein interactions that address the underlying genetic defect in cystic fibrosis patients and alleviate their symptoms; and (3) discover, improve, and design broadly neutralizing antibodies against Human immunodeficiency virus (HIV).”

As we are approaching the end, it occurs to me that as a student of Literature, Bruce would have ideas of his own on how to bring the profile to a close and probably also have no trouble doing so in Russian. “How should I end?” I ask him. He seems prepared. “At a cartoon level, there are five major themes in Russian intellectual history: messianism, nationalism, anarchism, eschatologism, and socialism,” he says. “If you perhaps morph ’nationalism’ to ’disciplinary exceptionalism,’ these are essentially the same figurative arteries in the heart of every successful biomedical laboratory and department.”