Nano Mechanic

Biochemist Gerald Audette is at the cutting edge – sometimes literally – of work with cellular proteins.

BY DAVID FULLER

PHOTOGRAPHY BY LINDSAY LOZON

HE DOESN'T WEAR COVERALLS or skin his knuckles reefing on lug nuts, but you could call Gerald Audette a kind of high-end mechanic. He spends hours taking sophisticated machines apart to see how they work. The difference between Audette, a professor in York's Faculty of Science & Engineering, and those in the automotive fraternity is the size of the mechanisms they work on: his are microscopic – and alive. Welcome to the world of bionanotechnology, where lean protein machines are the stars inside your body's cells, meeting, greeting and passing on DNA in an endless dance that few have ever seen close up.

Using a process called X-ray crystallography, Audette and his lab team are making detailed studies of how proteins, the engines of cellular processes, work and how that might point the way to new methods of treating disease. By understanding the physical structure of proteins, Audette says, researchers can learn about processes such as how bacteria transfer DNA to other cells. Then they can design more specific drug treatments for cancer or the new superbug bacteria and viruses. "You need to know the nuts and bolts of what's going on," Audette explains, looking through his collection of 3D protein portraits.

Audette's research was the basis for a successful $1.6-million joint application to the Canada Foundation for Innovation with York biology professor and fellow crystallographer Vivian Saridakis, whose study of a specific protein and its biological function requires the same equipment. The two found out in June last year that their proposal for an X-ray diffractometer, the first one at York, and a cryocooling system to keep their crystal samples safely chilling at -180 C had been accepted. "This brings us onto a level playing field with other researchers," Audette explains.

The method he and Saridakis use involves purifying a protein so it can be turned into a crystal that will reveal its component parts when X-rayed. By combining visual clues from the resulting images with computer models of protein structure, Audette can locate the individual pieces of hardware on each protein and discover how it physically transfers DNA to adjacent cells. "It's like building a 3D puzzle and the image is our guide," says Audette.

Once scientists understand how proteins work, he explains, drugs can be developed to suppress or modify a protein's function and reduce cell damage from cruder, less discriminating drug compounds. The process can also help speed up the development of therapeutic drugs by eliminating a lot of trial and error. "By having a structure to guide our design, it allows us to rapidly zero in on what kinds of compounds we need to synthesize. Instead of screening 100,000 compounds, you're now screening a hundred," he says.

Like any mechanic with a creative flair, however, Audette wasn't content to leave the proteins the way he found them. He wanted to customize a few to see what would happen. As a post-doctoral researcher at the University of Alberta, he once suggested cutting a tail-like section off one protein, to see if it would help with a related problem of producing enough sample for study. The result was a classic "eureka" moment when he discovered the section rapidly began growing longer, much longer, after being cut. That set him on his second research path – developing biological nano "wires" or tubing that could replace carbon filaments used in the manufacture of nanotechnology. "Everything nano has carbon nanotubes in some variety or other," Audette explains. "The problem is, as we branch out into more biological applications for these things, we're finding that carbon nanotubes, which are made of soot, induce cell death – they are toxic. Our system is completely biological in origin."

His passion for science came naturally to Audette. As a boy in St. Albert, Alta., he helped his mother, a nurse, do blood-group testing. His father has a PhD in analytical inorganic chemistry and helped him find a place in graduate studies at the University of Saskatchewan in Saskatoon. His other passions, when he's not dismantling proteins, include the Japanese martial art of kendo – he's a third-degree black belt at his club in Mississauga – and playing with his young son. As an enthusiastic new faculty member (since 2006), Audette is equally excited to be at York in the early days of its degree program in biochemistry, launched in 2003. And once "Prairie Kendo Vagabond", as he's known to bloggers, gets all his new equipment installed, he can settle in to some serious tinkering in his tiny garage.