THE AUTHOR FILE

Wesley P. Wong

Brainstorming leads to an invention that makes a lab workhorse gallop.

"I love the process of brainstorming and coming up with lots of different and interesting ideas without being critical or worrying about practical constraints," says Wesley Wong, a biophysicist at Boston Children's Hospital, Harvard Medical School and the Wyss Institute for Biologically Inspired Engineering at Harvard University. Some of his most useful ideas, he says, arise while playing with ideas in the company of friends or at lunch with lab members.

Heidi Shin

Wesley P. Wong

A past creative brainstorm was about making single-molecule manipulation with optical tweezers more accessible and faster. It led to a microscope that spins like a centrifuge and that makes many simultaneous single-molecule measurements without lasers and at a relatively low price.

Next, Wong wondered how researchers might study molecular interactions in higher throughput and in an instrument-free way. The result, which he now presents, harnesses gel electrophoresis to deliver a more quantitative and sensitive readout on molecular interactions, transforming a lab workhorse into a galloping racehorse with a comely name: DNA nanoswitch.

With DNA nanoswitches, molecules whose interaction a scientist wants to study are tethered to a strand of DNA, and the interaction between these tethered molecules is converted into a shape change. When the molecules bind, the DNA strand will form a closed loop; when the bond breaks, the DNA strand is open and linear. Looped and unlooped DNA migrate differently through a gel, which lets researchers measure the fraction of DNA nanoswitches that are open or closed and track their changes over time.

The result is a wealth of biochemical data such as the rate at which bonds are formed or ruptured and various thermodynamic properties.

Wong and his team used DNA nanoswitches not only to measure a single pair of interacting molecules but also to capture the kinetics of a four-body interaction, which helps in understanding molecular complexes and is hard to do with current methods. The researchers also managed to study interactions both between molecules tethered to the DNA scaffold and between molecules in solution and tethered molecules.

Wong is originally from Peterborough in Ontario, Canada. He was an undergraduate at the University of British Columbia and completed his PhD in physics at Harvard University.

Instead of a postdoctoral fellowship, Harvard gave him his own lab as a Rowland junior fellow. After that fellowship, he garnered his current Harvard faculty post. It was the second time Wong stocked an empty lab. "An empty lab can certainly be exciting—ripe with possibility, like a blank page to a painter or a writer," he says.

In his eight-member lab, Wong fosters group-wide conversations about work accomplished and next week's strategies because "we like to solve problems together." He helps his students and postdocs find projects that are meaningful to them. "This is not always an easy thing to do and requires honest exploration and perhaps a little soul-searching," he says. "But it can also be fun, if one is willing to take some risks and try new things."

Wong has tried plenty of unfamiliar activities: for example, he helped to produce a children's public television science series. "I make a pretty good camera and sound guy," he says about the work that took him to a Vermont maple sugar farm and to Cairo's streets. He travels more locally now with his wife and young daughter. His daughter, whom he calls a little scientist, tries to figure out how everything works, such as through dinnertime gravity experiments.

"I love the process of brainstorming."

At first glance, Wong may appear filled with a child's starry-eyed curiosity, says Donald Ingber, who directs Harvard's Wyss Institute. But in conversation, "it quickly becomes clear that he is one of the deepest thinkers in the field of molecular biophysics today."

"Wesley is a magician when it comes to devising new methods to attack and solve long-standing problems," says Ingber. Instead of developing a new mega-instrument that will cost hundreds of thousands of dollars, he says, Wong finds solutions that are simpler, less expensive and more likely to be carried out by a lone investigator using existing equipment.

At the University of British Columbia, Wong was in a special multidisciplinary program called Science One. "Embrace your ignorance" is its motto. "I think this is great advice," he says. "Being able to recognize and be honest about what you know and what you don't know is an important step to learning new things and, ultimately, making new discoveries and inventions."

Vivien Marx

Koussa, M.A., Halvorsen, K., Ward, A. & Wong, W.P. DNA nanoswitches: a quantitative platform for gel-based biomolecular interaction analysis. *Nat. Methods* **12**, 123–126 (2015).