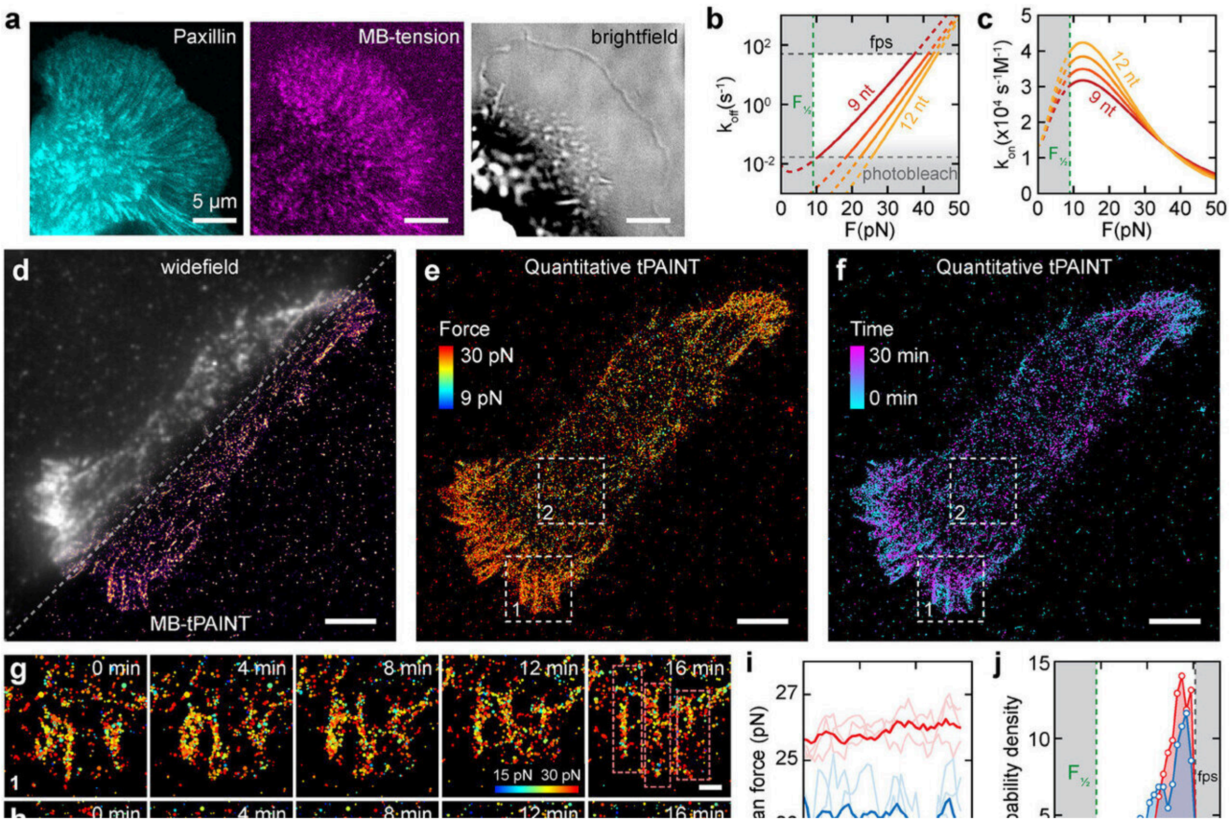
Molecular imaging tech measures forces in living cells with nanometer-level precision

August 7 2025, by Patty Wellborn



Live cell analysis using quantitative tension PAINT imaging. Credit: *Advanced Science* (2025). DOI: 10.1002/advs.202408280

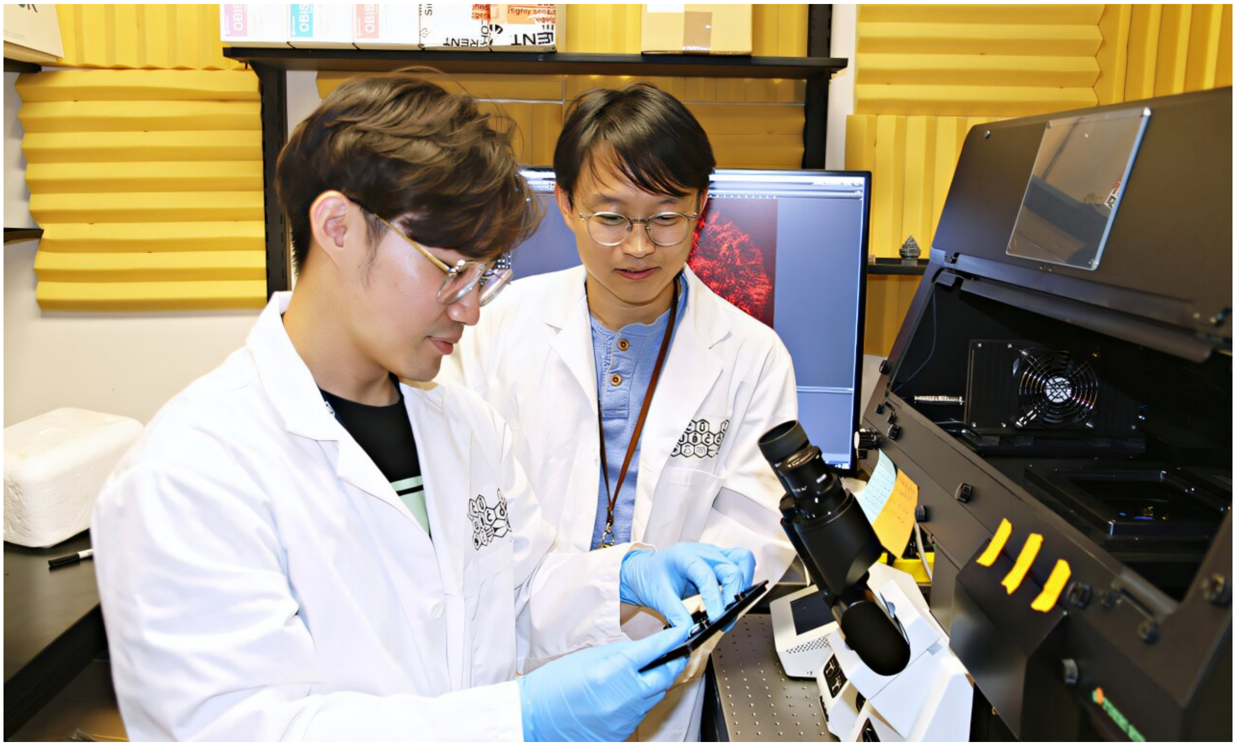
Researchers at UBC Okanagan have made two major discoveries that are set to revolutionize how scientists observe and measure molecular forces within living cells.

Published recently in two journals—*Advanced Science* and *Angewandte Chemie*—these discoveries significantly advance the field of molecular mechanobiology. These breakthroughs offer unprecedented precision and durability in force imaging, explains Dr. Isaac Li, Associate Professor of Chemistry with the Irving K. Barber Faculty of Science.

Led by Dr. Li, Canada Research Chair in Single-Molecule Biophysics and Mechanobiology, the research team created qtPAINT—a groundbreaking imaging technology.

qtPAINT is the first imaging method that can measure molecular forces with nanometer-level spatial precision and minute-scale time resolution. It works by combining DNA-based molecular tension probes with advanced microscopy, giving researchers a clearer view of how tiny mechanical forces behave inside living cells in real time.

"Tiny molecular forces drive many important functions in the body like fighting infections, healing wounds and cancer progression," explains Dr. Seongho Kim, lead author of the qtPAINT study. "Before qtPAINT, researchers could see where these forces were happening, but we couldn't measure how strong they were or how they changed over time."



UBCO master’s student Hongyuan Zhang and Dr. Isaac Li prepare decoy DNA samples as part of their latest research, work that explores the visualization and manipulation of nanoscale interactions within living systems. Credit: University of British Columbia

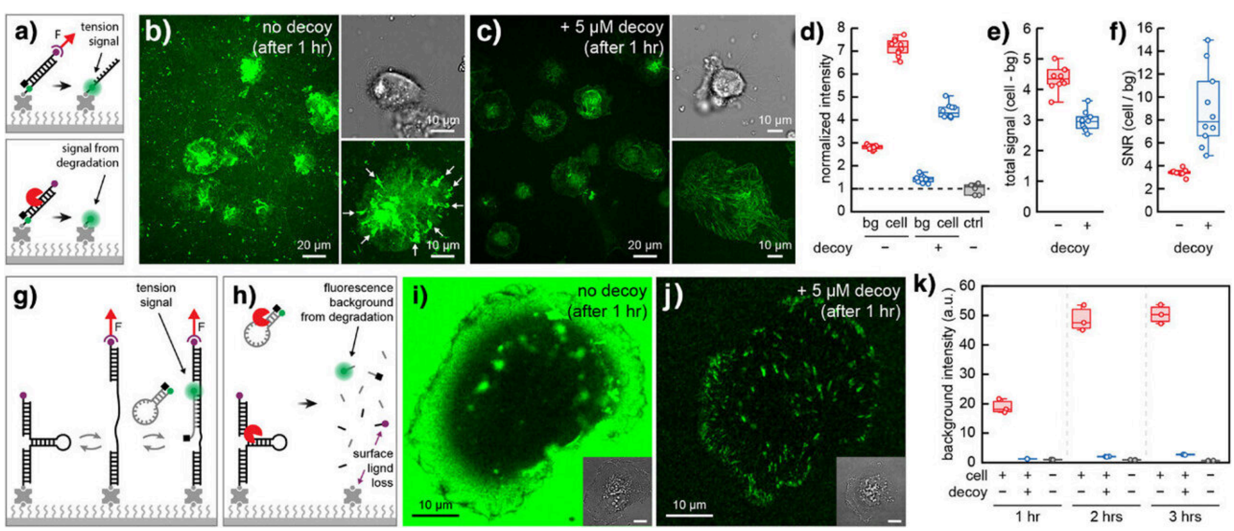
After the success of qtPAINT, Dr. Li's team tackled a long-standing challenge that limited the use of DNA-based tension probes: their rapid degradation by natural enzymes called DNases.

Dr. Li explains that the tension probes help scientists watch and measure these tiny mechanical forces taking place within cells in real time, revealing how they communicate and behave.

The team's second paper introduces a simple yet powerful solution called "decoy DNA," where extra strands of harmless DNA are added to experiments to act as sacrificial targets for DNases. This approach significantly extends the lifespan of functional tension probes from just a few hours to more than 24 hours, or even several days.

This approach greatly improves the stability and accuracy of cellular force measurements, says Hongyuan Zhang, lead author of the decoy DNA study.

"Rather than using complex and costly chemical modifications, our approach is more like distracting predators with these decoys," says Zhang. This protects our DNA probes and significantly improves the quality and duration of our measurements."



Decoy DNA enhances super-resolution and extends the duration of live-cell molecular tension imaging. Credit: *Angewandte Chemie International Edition* (2025). DOI: 10.1002/anie.202506590

Together, these two breakthroughs place UBCO researchers at the forefront of molecular force imaging and give scientists powerful and affordable tools to explore the mechanics of life.

"Longer-lasting, quantitative force imaging gives researchers the ability to delve deeper into complex biological systems, potentially driving new breakthroughs in cancer research, immunology and regenerative medicine," adds Dr. Li.

His lab specializes in single-molecule biophysics and mechanobiology, developing advanced methods to visualize and manipulate molecular forces within living cells. The research includes designing mechanosensitive DNA nanostructures—tiny DNA-based tools that respond to physical forces—to control how cells move and sense their environment, as well as developing high-throughput biophysical assays for use in drug screening and diagnostics.

The lab takes an interdisciplinary approach—combining cell biology, biochemistry, biophysics, nanotechnology and bioengineering—to create a unique platform for transformative scientific discoveries.

"Our goal has always been to develop effective and accessible tools," says Dr. Li. "These studies reflect our ongoing effort to develop technologies that support meaningful discoveries across many areas of science."

More information: Seong Ho Kim et al, Quantitative Super-Resolution Imaging of Molecular Tension, *Advanced Science* (2025). DOI: 10.1002/advs.202408280

Hongyuan Zhang et al, Decoy DNA Protects Molecular Tension Probes from DNase Degradation, *Angewandte Chemie International Edition* (2025). DOI: 10.1002/anie.202506590

Provided by University of British Columbia