DNA nanoswitches reveal how life's molecules connect

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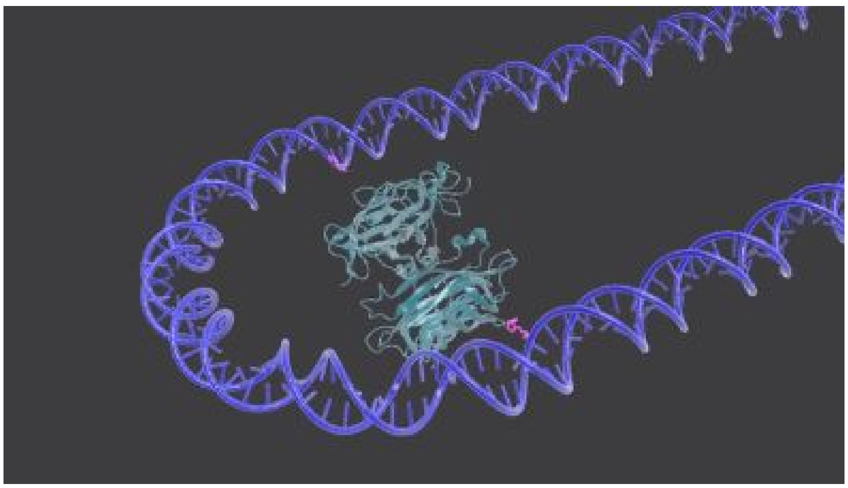

A complex interplay of molecular components governs almost all aspects of biological sciences - healthy organism development, disease progression, and drug efficacy are all dependent on the way life's molecules interact in the body. Understanding these bio-molecular interactions is critical for the discovery of new, more effective therapeutics and diagnostics to treat cancer and other diseases, but currently requires scientists to have access to expensive and elaborate laboratory equipment.

Now, a new approach developed by researchers at the Wyss Institute for Biologically Inspired Engineering, Boston Children's Hospital and

Harvard Medical School promises a much faster and more affordable way to examine bio-molecular behavior, opening the door for scientists in virtually any laboratory world-wide to join the quest for creating better drugs. The findings are published in February's issue of *Nature Methods*.

"Bio-molecular interaction analysis, a cornerstone of biomedical research, is traditionally accomplished using equipment that can cost hundreds of thousands of dollars," said Wyss Associate Faculty member Wesley P. Wong, Ph.D., senior author of study. "Rather than develop a new instrument, we've created a nanoscale tool made from strands of DNA that can detect and report how molecules behave, enabling biological measurements to be made by almost anyone, using only common and inexpensive laboratory reagents."

Wong, who is also Assistant Professor at Harvard Medical School in the Departments of Biological Chemistry & Molecular Pharmacology and Pediatrics and Investigator at the Program in Cellular and Molecular Medicine at Boston Children's Hospital, calls the new tools DNA "nanoswitches".

Nanoswitches comprise strands of DNA onto which molecules of interest can be strategically attached at various locations along the strand. Interactions between these molecules, like the successful binding of a drug compound with its intended target, such as a protein receptor on a cancer cell, cause the shape of the DNA strand to change from an open and linear shape to a closed loop. Wong and his team can easily separate and measure the ratio of open DNA nanoswitches vs. their closed counterparts through gel electrophoresis, a simple lab procedure already in use in most laboratories, that uses electrical currents to push DNA strands through small pores in a gel, sorting them based on their shape

"Our DNA nanoswitches dramatically lower barriers to making traditionally complex measurements," said co-first author Ken Halvorsen, formerly of the Wyss Institute and currently a scientist at the RNA Institute at University of Albany. "All of these supplies are commonly available and the experiments can be performed for pennies per sample, which is a staggering comparison to the cost of conventional equipment used to test bio-molecular interactions."

To encourage adoption of this method, Wong and his team are offering free materials to colleagues who would like to try using their DNA nanoswitches.

"We've not only created starter kits but have outlined a step-by-step protocol to allow others to immediately implement this method for research in their own labs, or classrooms" said co-first author Mounir Koussa, a Ph.D. candidate in neurobiology at Harvard Medical School.

"Wesley and his team are committed to making an impact on the way bio-molecular research is done at a fundamental level, as is evidenced by their efforts to make this technology accessible to labs everywhere," said Wyss Institute Founding Director Donald Ingber, M.D., Ph.D., who is also the Judah Folkman Professor of Vascular Biology at Boston Children's Hospital and Harvard Medical School and a Professor of Bioengineering at Harvard SEAS. "Biomedical researchers all over the world can start using this new method right away to investigate how biological compounds interact with their targets, using commonly-available supplies at very low cost."

More information: *Nature Methods*, www.nature.com/nmeth/journal/v … /abs/nmeth.3209.html

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