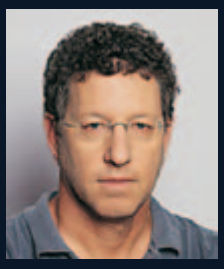
# DNA-based biomolecular computing

Scientists at the Weizmann Institute in Israel are using a Freedom EVO® platform to control DNA-based biomolecular computing.

Tom Ran



Ehud Shapiro

The Weizmann Institute in Rehovot, Israel, uses a Freedom EVO platform to develop sophisticated DNA-based biomolecular computing systems capable of answering molecular 'questions'. The team, led by Tom Ran, a PhD student, and Professor Ehud Shapiro, has previously developed DNA-based computing systems to detect cancerous RNA in a test tube and release a molecule to destroy it , but the current approach is different. Professor Shapiro explained: "We are using more sophisticated biochemistry and implementing simple logic programs, similar to programming electronic computers."

The Weizmann Institute's molecular computing system uses DNA associated with a fluorescent molecule bound to a quencher, which prevents fluorescence. The computation is activated by a specialized enzyme that recognizes the part of the molecule signifying the correct answer, removing the quencher and allowing the fluorescent light to shine.

Using the Freedom EVO system, facts and rules are imported as a computer file, and turned into the DNA starting products of a query. This allows the Weizmann Institute scientists to use the DNA computer to answer basic questions. The team tested the system with simple logic problems, feeding the computer a molecular rule, such as 'all men are mortal', and a molecular fact, 'Socrates is a man', before asking the question 'Is Socrates mortal?' The DNA computer was able to answer this type of question correctly, and the team went on to ask more complex questions involving multiple rules and facts.

Tom Ran explained: "We wanted to enable somebody who knew nothing about biology to operate the biomolecular computer, and this has been very successful." Programs are written in normal sentences, which are translated into an assembly order for the Freedom EVO. Strands of DNA are placed in 96-well microplates, and the workstation dispenses the correct reagents into dedicated wells, compiling the molecular program. The plate is transferred to a microplate reader, where the reader's injector adds the enzyme necessary to activate the computing system. Fluorescence output is monitored, and the computer arrives at the answer based on the observed fluorescence. If fluorescence is seen, the answer is yes, otherwise the answer is no.

Only the computation is done on a molecular level, so a regular user can write and use a basic program. The system can also be programmed to answer more complex questions that require something other than a simple yes or no answer. In these cases, several questions are asked in just one well of the 96-well plate, with the plate reader's monochromators using several wavelengths to read the various different fluorophores and answer the questions.

Tom added: "We chose Tecan because the system has open architecture, which allows us to develop our in-house language, and we could modify the scripts to suit our application." The fully automated system used by the Weizmann Institute consists of two Freedom EVOs which are connected to each other, one for liquid handling, the other for centrifugation and more complicated operations for real-time PCR. These are fully integrated with microplate readers, shakers, an incubator, a centrifuge and an electrophoresis machine."

Professor Shapiro concluded: "The development of the DNA computer involved a vast number of experiments and, without robotic support, we would not have finished this in our lifetime."

To find out more on Tecan's Freedom EVO, visit **www.tecan.com/freedomevo**