

30 January 2006

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Researchers Discover How to Detect Mutations

With the help of electric measurements

The human genome has 3 billion DNA bases. On average, mutations occur once in every 1000 DNA bases, although not every mutation has effects. Very specific information about mutations potentially has important medical applications in cancer research and the developing of highly personalized medication. It is also necessary for the understanding and prevention of diseases. The team's breakthrough relies on an intrinsic physical property of DNA: conductivity, or how well the molecule can carry an electrical current. Depending on the experimental conditions, DNA has been shown to act as a conductor and an insulator. How the current flows through the DNA molecule is still a subject of speculation. "We have developed a technology that allows us to wire single molecules into an electrical circuit," says Tao, a professor of electrical engineering in the Ira A. Fulton School of Engineering and also a researcher in the Center for Solid State Electronics Research. "We can now directly read the biological information in a single DNA molecule." "There are two things required to make a reliable measurement. One is that the DNA has to be tethered between two electrodes; the other is that it should be done in a slightly salty water environment to minimize any perturbations to the structure of the molecule." The technique involves the use of so called "chemical linker groups". These groups bond with gold electrodes and they also get attached to the ends of DNA. Thus, when a drop of a DNA solution is then placed between the two gold electrodes it sticks to the surface of the electrodes spontaneously. "We measure a small current through the molecules using a setup developed in our lab," Tao says. "It's a conceptually simple setup. You just bring two electrodes together, separate them apart, make the measurement and repeat." In order to prove the concept the team used DNA of 11 or 12 bases in length dissolved in a physiologically relevant saline solution. By measuring the conductance, the team was able to understand the sequence information in the DNA, and whether there was a mismatch in comparison to a normal DNA sequence. What they found was that just a single base pair mutation in a DNA molecule can cause a significant change in the conductance of the molecule. The measurement is extremely sensitive; the alteration of a single base in the DNA stack can either increase or decrease the conductivity of a DNA helix, depending on the type of mismatched base. The next goal of the research is to make the measurement steps easier and faster through automation, which will allow many different DNA sequences to be analyzed at once. Image credit: humandescent.com