'Motorized' DNA opens door to autonomous molecular experiments

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(PhysOrg.com) -- Using the same protein molecule that scientists have used for decades to copy genetic material, researchers have developed a molecular motor for propelling DNA.

The work, reported in the online edition of the Journal of the American Chemical Society, shows that RNA polymerase, an enzyme that scientists routinely use to copy DNA, can act as a propulsion system able to both move and direct molecules of DNA in specified ways.

The work demonstrates the ability to precisely control the motion of billions of DNA molecules at once and, through external stimuli, confer autonomous decision-making that sets the stage for massive, but greatly miniaturized experimental systems.

"This lays the basis for experiments that configure themselves and operate themselves," says David C. Schwartz, a University of Wisconsin-Madison genomicist and the senior author of the new study. "It will be possible to design intelligent systems to do billions of experiments" at once.

The new technology described by Schwartz and his colleagues could conceivably replace the armies of robots engaged in mundane and arduous lab work, but that are now essential for big science projects such as genome sequencing and analysis.

"Up until now, we've done this kind of work with robots," Schwartz explains. "Biotechnology robots dumbly move samples around. Here, we have intelligent agents that are single molecules — they can make decisions and they can evolve. We have something very new and powerful and miniature."

Such technology, Schwartz argues, can help address the pressing need in modern biology for new experimental systems capable of acquiring large, complex data sets. DNA molecules, hitched to their polymerase motors, he says, can be the basis for massive parallel assays where the souped-up molecules are regulated by different experimental factors and can reorganize themselves to become tiny, discrete experiments.

Billions of experiments could be conducted in a single test tube, Schwartz says. Such miniaturized and "intelligent" capacities address one of the key barriers to conducting the experiments required to answer some of biology's most pressing questions. For example, the technology could be put to work to comprehensively test millions of potentially therapeutic compounds to speed the development of new drugs, a process that now takes many years. It could also aid the development of DNA computing.

The motorized molecules steer themselves by sensing "fuel," a chemical nutrient that draws the molecule in, by temperature, or through nanoscale geometric patterns on the surface of a culture plate. "The molecules can make decisions based on the environment they find themselves in," Schwartz notes. "You can set them loose, but they sense and interact with their environment. And what makes it hugely scaleable is it is very simple."

Schwartz explains that scientists have for years been toying with such molecular complexes and have developed a bag of miniature tricks, the ability to attach cargo, for example, to make the molecules act like little burros.

But what no one bothered to explore, he says, was the apparent motion of the DNA molecule in free space as it was copied by the RNA polymerase. Schwartz and his colleagues, including fellow UW-Madison researchers Hua Yu, Kyubong Jo, Kristy L. Kounovsky and Juan de Pablo, found that the stiff rods of DNA created when a molecule is copied by RNA scoot like motorboats: "The RNA proteins act like little motors. The complex can then propel itself through space."

Once set in motion, the molecules can be sped along and directed by placing chemical nutrients in specified gradients. The DNA can sense the nutrient and is drawn toward the source as a form of fuel.

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