# Biochemists create computer controlled feedback loop with yeast

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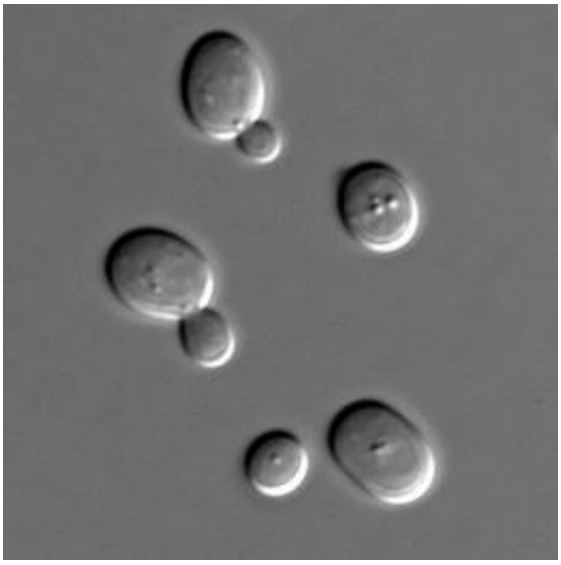

Sacharomyces cerevisiae cells in DIC microscopy. Credit: Wikipedia.

(PhysOrg.com) -- Scientists of many varied backgrounds have been hard at work in recent years trying to figure out a way to control the intricate processes that go on in cells so as to allow them to manipulate them to do their bidding. Much of that work has involved trying to code the genes at the outset. Now a joint team of American and Swiss researchers, working out of ETH Zurich, has taken a completely different approach. As they describe in their paper published in *Nature Biotechnology*, they have figured out a way to create a feedback loop between a computer and yeast cells (*Saccharomyces cerevisiae*), to control the production of

proteins.

Their discovery rests on the fact that yeast cells have a molecule in them called phytochrome that serves as a sort of switch, causing changes within the genetic structure that turns on a protein producing process, when a red light is shined on it. Interestingly, a darker red light causes the opposite effect; in its presence, the yeast cells go back to their original genetic structure and stop making the protein. Thus, using just two kinds of light the researchers can cause protein production to start or stop at their whim.

What would be more interesting though is if the protein production process could be controlled through a feedback loop. To make this happen, the team introduced a so-called reporter molecule into the yeast cells that turn on (go fluorescent) when protein is being produced. Unfortunately, cell processes can't be made to do their thing within certain constraints, such as say, turn on or off at specific time rates or intervals. To get around this problem, the team built a computer model to figure out how long light pulses should last in order for the yeast cells to produce the proteins when they wanted them too. They then set the whole process to working.

What they constructed was a process that starts with a computer telling a red light when to shine, thus setting the yeast cells into action. The computer then monitors the reporter cells to note first when they come on, indicating proteins are being made. When just the right amount of time has elapsed, the computer then commands the red light to cease and the darker light to go on to cause the protein production to cease. The whole process can go on and on automatically because of the feedback loop, with a constant amount of proteins being produced all the while. And that's the beauty of the whole thing, because if researchers can control yeast cells in such a manner, other applications quickly spring to mind, such as making drugs or creating biofuels. Though it may take

time, this new process could very well revolutionize the way biological processes are manipulated.

**More information:** In silico feedback for in vivo regulation of a gene expression circuit, *Nature Biotechnology* (2011) doi:10.1038/nbt.2018


## Abstract

We show that difficulties in regulating cellular behavior with synthetic biological circuits may be circumvented using in silico feedback control. By tracking a circuit's output in Saccharomyces cerevisiae in real time, we precisely control its behavior using an in silico feedback algorithm to compute regulatory inputs implemented through a genetically encoded light-responsive module. Moving control functions outside the cell should enable more sophisticated manipulation of cellular processes whenever real-time measurements of cellular variables are possible.