

Detailed study of living cells challenges classic gene regulation model

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In all living organisms, genes are regulated by proteins called transcription factors. The established model states that a gene is switched off as long as a repressing transcription factor is bound to the DNA. For the first time ever, researchers at Uppsala University, Sweden, have been able to study the process in living cells, showing that it may be more complex than previously thought.

The study is published in the online edition of *Nature Genetics* today.

"The relation between transcription factor concentrations and [gene expression](#) is at the heart of biology since it describes how the concentration of proteins sets the rate of change in protein concentrations. Its position in biology is much like Newton's law of motion in classical physics. Getting this basic relation right is very important for understanding biological systems", says Johan Elf, professor of physical biology at Uppsala University.

Researchers in Johan Elf's group were able to test the relation directly in living cells by measuring both the binding and dissociation rates for a transcription factor to an individual binding site in the bacterial chromosome, and compare those measurements to the independently measured repression of the same gene.

"The assumptions behind the model are so deeply rooted that it may seem like we are measuring the same thing in two different ways", says Johan Elf.

The researchers did however find small but clearly significant differences between the measurements for specific regulatory DNA sequences. This opens a large number of new possibilities for how genes are regulated in living cells.

"One interpretation of our results is that the active transcription initiation keeps the regulatory system out of equilibrium. This is fun because it means that we need to start thinking about gene regulation beyond the simple picture given by equilibrium statistical mechanics", says Dr. Petter Hammar one of the key researchers behind the study.

It is at present unclear how the finding generalizes to other genes and organisms, but the fact that the researchers find interesting deviations in the first system they look at implies that it is not unlikely that it is important in many cases. The single molecule method developed by the Uppsala researchers can be used to explore also these cases.

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