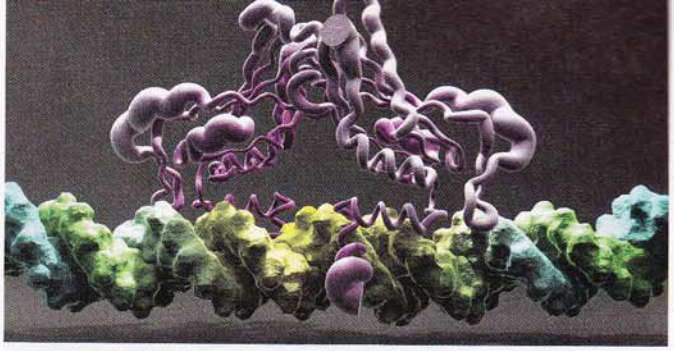

HOT PAPER IN MOLECULAR GENETICS

Lac on, lac off

The paper:
J. Elf et al., "Probing transcription factor dynamics at the single-molecule level in a living cell," *Science*, 316:1191-94, 2007. (Cited in 65 papers)

The findings:
Using fluorescence imaging, a Harvard team led by Sunney Xie quantified the kinetics of the *lac* operon repressor protein in *Escherichia coli* in real time. They showed that the protein spends a few milliseconds weakly and nonspecifically bound to DNA, diffusing along the chromosome, then dissociates for a fraction of a millisecond. This cycle of unbinding and rebinding various DNA segments repeats for a few minutes until the protein encounters its specific target.

The background:
Xie's team used a pair of techniques—developed in-house in 2006—to track fluorescently labeled proteins in living cells. In their method, DNA-bound proteins glow like bright dots, while the fluorescence of proteins diffusing in cytoplasm gets lost in the background. Xie's group also visualized nonspecific DNA binding using short laser pulses.

The impact:
The Hot Paper reported the first direct observation of transcription factor dynamics in a living cell, and directly confirmed predictions made by in vitro work, says Peter von Hippel, a molecular biologist at the University of Oregon. "The whole field of looking at single living cells in a microscopic way is taking off."

The follow-up:
Last year, Xie's group used the technique to show that *lac* operon induction depends on whether the repressor dissociates partially or completely from its operator—a single-molecule stochastic event (*Science*, 322:442-46, 2008). In addition, Xie says, "we are working on experiments to make [the technique] possible in mammalian cells"—more complicated because of the added geometry of chromatin.

—Alla Katsnelson

Quantifying *lac* repressor kinetics

3D diffusion rate in cytoplasm: 3 $\mu m^2/s$
1D diffusion rate along DNA: 0.046 $\mu m^2/s$

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