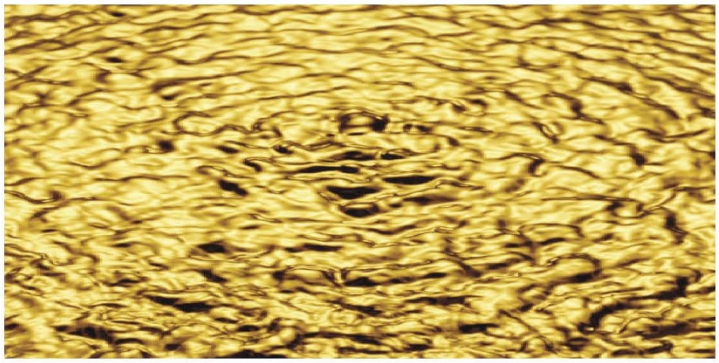

URLs

SYSTEMS BIOLOGY

Noise is golden

Our understanding of gene interactions, and our ability to exploit their properties in building synthetic circuits, relies on modelling not only what happens in a population but also what goes on inside individual cells. Two complementary studies now use synthetic gene networks in single cells to model how signals are transmitted, heralding a welcome quantitative turn in the field of network biology.

Reduced to its bare bones, gene expression involves the presence of a transcription factor that, by binding to a promoter, eventually leads to the production of a protein or its suppression. But how do we describe the dynamic properties of this simple relationship? Also, what type of noise affects these properties, and how?

To address these questions, Nitzan Rosenfeld and colleagues built an artificial gene network, in *Escherichia coli*, in which they could quantify the concentration of an engineered phage λ-transcriptional repressor and the rate at which its target protein is produced. Measuring this fundamental relationship — known as the gene regulation function (GRF) — reveals a lot. First, it shows, in molecular terms, how transcription factors control the expression of target genes and therefore provides the basis for modelling cellular networks. Second, the experiments reveal how other processes that occur in the cell influence the GRF; for example, the GRF varies significantly both between cells and over time. The differences between cells can be put down to noise, such as fluctuations in molecules, like polymerases, that have a widespread impact on gene expression. The paper also shows how such 'extrinsic' noise can be effectively incorporated into the modelling and design process.

The second study also relies on the input–output relationships of artificial gene circuits in *E. coli*, but examines how the connectivity of a circuit affects the propagation of noise through its components. This time, the engineered circuit consists of three members of a regulatory cascade that are separated by two regulatory steps. By chemically perturbing the two levels of regulation, Pedraza and van Oudenaarden show that the regulation step between gene 1 and gene 2 has a different effect on the expression of gene 2 than on that of gene 3. Gene 3 responds more sharply to the perturbation, almost like a switch. Elowitz's group previously revealed that noise is transmitted from a regulatory gene to its target, and indeed that this is the most prevalent type of noise. The novel value of this study lies in bringing these observations together into a single model in which the noise levels can be measured and related quantitatively to the connectivity of the network.

The results presented here, derived from just a few genes and using bacterial cells, should be universally applicable, for understanding both more sophisticated networks and more complex organisms. They will also help in the construction of artificial networks in which noise can either be compensated for or exploited.

Tanita Casci

References and links

ORIGINAL RESEARCH PAPERS Rosenfeld, N. *et al.* Gene regulation at the single-cell level. *Science* **307**, 1962–1965 (2005) | Pedraza, J. M. & van Oudenaarden, A. Noise propagation in gene networks. *Science* **307**, 1965–1969 (2005)
FURTHER READING Isaacs, F. J. *et al.* Signal processing in single cells. *Science* **307**, 1886–1888 (2005)
WEB SITES
Michael Elowitz's laboratory: http://biology.caltech.edu/Members/Elowitz
Alexander van Oudenaarden's laboratory: http://web.mit.edu/biophysics