that the AMO does not exist, in the sense that the temperature variations concerned are neither intrinsically oscillatory nor purely multidecadal.

Another implication concerns hurricanes. As noted earlier, quiescent and active periods of Atlantic hurricane activity have been linked[2] to the AMO. These swings in hurricane frequency and intensity might therefore be the regional response to variations in the concentration of pollutant aerosols against a background of global warming, and thus completely man-made. Similarly, human activity might have caused periods of drought within the Sudano-Sahel region of Africa and in northeastern Brazil.

As we try to predict the climate in a warming world, an increasing body of work suggests that aerosols may have regional effects as great as those caused by the global increase in atmospheric carbon dioxide. Booth and colleagues' work[3] underscores the importance of understanding the diverse pathways by which humans alter the climate. ■

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GENE EXPRESSION

Running to stand still

Transcription factors regulate the expression of genes by binding to certain DNA sequences. But the outcome can be markedly different, depending on whether the binding is stable or short-lived. SEE LETTER P.251

TOMMY KAPLAN & NIR FRIEDMAN

To reproduce, differentiate or even just respond to changes in their surroundings, cells need to control the expression of thousands of genes. One way of doing this is to use transcription factors — proteins that bind to regulatory regions on their target genes and either activate or repress the transcription of DNA into RNA. Over the past decade, researchers have analysed the binding sites of hundreds of these proteins on the genomes of many organisms and cell types, and measured the gene-expression patterns within the same cells. In such studies, the overall degree of occupancy by a transcription factor at a regulatory region is commonly interpreted as an indication of the protein's ability to control the expression of the gene. However, transcription factors also bind to thousands of genes in a weak, and probably non-functional, manner[1]. On page 251 of this issue, Lickwar *et al.*[2] illuminate this matter by reporting the results of a systematic, genome-wide study of the binding dynamics of a particular transcription factor. The authors find that transcription levels have a stronger link to the kinetics of binding than to the total occupancy of the factor.

The DNA-binding sites of the transcription factor Rap1 along the genome of the yeast *Saccharomyces cerevisiae* were mapped more than a decade ago[3]. The mapping used a genome-wide protein–DNA binding assay, known as chromatin immunoprecipitation (ChIP)-on-chip, or ChIP-seq, which identifies the genomic locations of a transcription factor over a huge number of live cells and therefore averages the transcription-factor occupancy over a large population. This is still the method of choice in similar genome-wide studies. However, a high occupancy of a transcription factor at a specific site — as detected by this technique — can mean either that the factor is constantly bound to this DNA location in some of the cells, or that it is transiently bound in many cells.

To distinguish between the two possibilities, Lickwar *et al.*[2] adapted a strategy, previously used to measure the turnover of DNA-bound proteins[4–6], to address the question of transcription-factor binding stability. The authors created yeast cells that produced two Rap1 variants, Rap1–Flag and Rap1–Myc, each one with a 'tag' consisting of a specific peptide that could be recognized by antibodies. Furthermore, Rap1–Flag was produced constantly, whereas Rap1–Myc's expression was experimentally inducible. The authors then measured the binding of each Rap1 variant to the yeast genome in a dense time series after Rap1–Myc induction. Although the inducible protein quickly outcompeted Rap1–Flag at

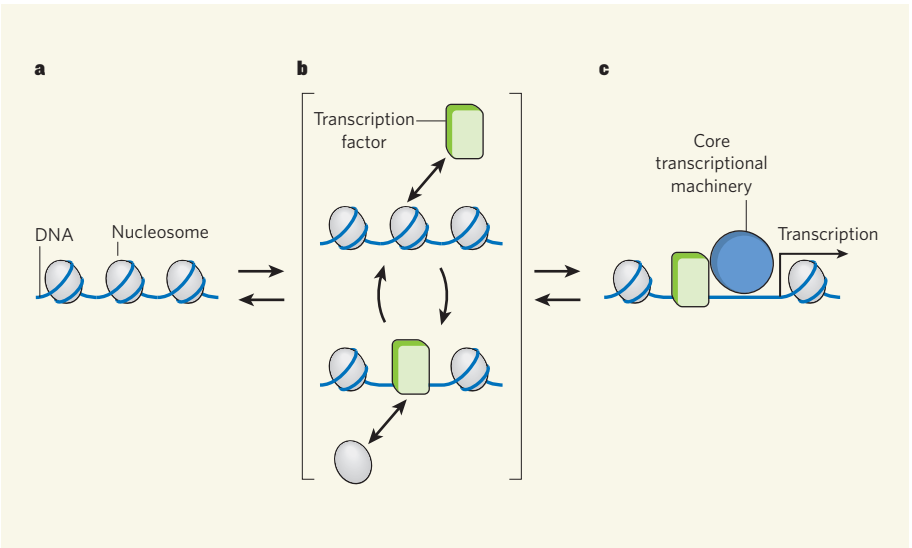

Figure 1 | Well-balanced gene expression. Transcription factors can activate the expression of genes by binding to certain regulatory regions on the genome. Lickwar *et al.*[2] studied, at the genomic scale, the binding dynamics of one of these proteins, and propose the following model for transcription-factor function. **a**, Most of the genome is wrapped around histone proteins to form nucleosomes, the basic units of DNA packaging into chromatin. **b**, Nucleosomes and transcription factors compete for binding to some regulatory regions. Transcription-factor binding to these regions occurs in short pulses, which are not sufficient for efficient transcription of the gene into RNA. **c**, When the transcription factor binds to its target site for longer periods, it recruits the core transcriptional machinery required to start transcription, leading to high transcription rates.

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some genomic sites, it was slowly incorporated into other sites, which suggested that Rap1 binding to the first sites was less stable than to the other sites.

The researchers then applied a mathematical model[5] to estimate the rate of Rap1 turnover at more than 400 target genes. They found that, among genes with high Rap1 occupancy, those with slower Rap1 turnover showed higher transcription levels than those with faster Rap1 turnover. That is, the transcription level depended on how long Rap1 remained bound. Of note, the genomic sites that exhibited fast Rap1 turnover in this analysis[2] have previously been reported[5,6] to have fast turnover rates of nucleosomes (protein complexes around which DNA is packaged) and of the general transcription factor TBP (which facilitates the binding of the core transcriptional machinery). Overall, the results are consistent with those of other studies[7,8] that showed that transcription factors and nucleosomes compete for some genomic sites and that this competition leads to inefficient transcription.

Lickwar *et al.* suggest a model for the binding dynamics of transcription factors that activate transcription (Fig. 1). In this model, on binding to a target site, the factor has to recruit the core transcriptional machinery. This process takes some time. Therefore, if the factor's binding to the DNA site is unstable, it will not lead to productive transcription. Indeed, it has been shown[9] that short, repeated pulses of Msn2 — another transcription factor — into the cell nucleus do not activate target genes, whereas longer pulses do. Therefore, for transcription factors to be effective activators, they require stable binding to their target DNA.

Moreover, the researchers speculate that a constant turnover or 'treadmilling' of nucleosomes and transcription factors acts as a distinct mechanism for transcriptional regulation. Unlike static gene repression[10], in which transcription is prevented by the nucleosome's protection of DNA, a site that has a treadmilling transcription factor is poised for activation. When, somehow, the nucleosome is removed or its affinity for DNA is decreased, the factor can quickly achieve stable binding to its target sequence and so activate the gene's transcription. Several mechanisms would allow for the targeted eviction of nucleosomes, including chromatin-remodelling enzymes (which move nucleosomes on DNA), chemical modifications of histones (the protein components of nucleosomes) or the replacement of certain histones with specific variants.

Lickwar and colleagues' study[2] explains how different regulatory regions can present similar levels of transcription-factor occupancy and different transcriptional levels. But it also raises further exciting questions. Do the different turnover rates of transcription factors play a key part in gene regulation? Or do they just reflect some other aspects of the transcriptional process, such as stabilization of protein–DNA binding by interactions with the transcriptional machinery? Are nucleosomes the only competition for factor binding to DNA, or is competition with other transcription factors important too?

To fully understand how transcription factors work, we should consider not only their overall binding occupancy, but also their binding dynamics. This line of research will form the basis for a much-needed quantitative understanding of transcription regulation kinetics. ■

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ASTROPHYSICS

Fresh light on stardust

Ageing stars produce elements vital for life and disperse them into space on stellar winds. The discovery of large dust grains in the vicinity of cool giant stars sheds light on the mechanisms that drive such winds. SEE LETTER P.220

SUSANNE HÖFNER

Chemical elements that are crucial for building Earth-like planets and living organisms have their origin in ageing stars and stellar deaths. The nuclear processes that create these elements are well understood, but the mechanisms that transport them to the stellar surfaces and out into interstellar space are still a matter of intensive research. On page 220 of this issue, Norris *et al.*[1] report the detection of silicate particles about 600 nanometres in diameter in the immediate vicinity of several cool giant stars. This result confirms the predictions of models[2] that explain how gas can escape stellar gravity and become part of the cosmic-matter cycle.

Stellar explosions known as supernovae have considerable input into the production and dispersion of heavy elements (those heavier than helium), but they are not the sole contributors. Stars, including the Sun, release continuous outflows of gas, called stellar winds, for most of their lives. As stars evolve into cool giants and supergiants, stellar winds become increasingly effective in transporting matter out of stellar-gravity wells, enriching the surrounding interstellar medium with newly produced chemical elements. Winds of ageing low- and intermediate-mass stars, such as those observed by Norris *et al.*[1], lead to a runaway mass-loss process that eventually stops the stars' nuclear processes and turns them into white dwarfs.

The mechanisms that drive gas away from stars differ, depending on a star's surface temperature, mass, luminosity, chemical composition and magnetic field. Winds of cool, luminous giants are presumably triggered by radiative acceleration of dust grains that form in the extended stellar atmospheres. Momentum is transferred from the photons emitted by the star to the dust grains through photon absorption and scattering, and is subsequently redistributed to the more numerous gas particles by collisions with the dust grains (Fig. 1). Because the star's photons are predominantly directed away from the stellar surface, the flow of gas and dust also follows this pattern.

Although the physical principles of dust-driven winds are reasonably well understood, there is currently no consensus on which types of grain are driving the outflows. However, some basic features are known. First, the mass of the gas that is pushed outwards by the dust is more than 100 times higher than the collective mass of the dust particles. This requires grains made from abundant materials that have large radiative cross sections to drive the winds. Second, the grains have to form close to the star to trigger the outflows. This distance is limited by how far shock waves, caused by pulsation and convection in the stellar interiors, can lift gas above the stellar surface, at

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