of microorganisms an infected phagocyte contains. The model was then used to investigate the origin of variability in host-cell response to infection, reaching the conclusion that stochastic rather than intrinsic differences between cells offered the best fit for the observational data.

Finally, using these insights into intra- and intercellular infection dynamics, the authors explored the effects of medical intervention. Using the model, the authors could demonstrate that inhibiting intracellular bacterial replication reduces the number of infective bacteria that trigger host-cell lysis and are released into the extracellular environment. In terms of therapy, an intriguing prediction from this analysis is that the efficacy of common extracellular antibiotics will be enhanced by the use of molecules that slow intracellular bacterial division.

David O'Connell

ORIGINAL RESEARCH PAPER Brown, S. P. *et al.* Intracellular demography and the dynamics of *Salmonella enterica* infections. *PLoS Biol.* 17 Oct 2006 (doi:10.371/journal.pbio.0040349)

of VOCs, Sandhu *et al.* directly measured phenol degradation by natural phyllosphere communities. Leaves were collected from trees growing in an area that was known to be high in VOCs. Unsterilized and surface-sterilized leaves were then exposed to radiolabelled phenol in closed chambers for 24 hours and the amount of phenol degradation was compared. The phenol degradation by the non-sterilized leaves was significantly greater than the degradation by the sterilized leaves, indicating that degradation of this VOC was enhanced by the presence of the phyllosphere communities.

This work indicates that plant leaves can accumulate phenol, which is subsequently available to bacteria in the phyllosphere for degradation. The authors are planning future studies to further probe the role of phylloremediation in the attenuation of natural airborne pollutants.

Sheilagh Molloy

ORIGINAL RESEARCH PAPER Sandhu, A., Halverson, L. J. & Beattie, G. A. Bacterial degradation of airborne phenol in the phyllosphere. *Environ. Microbiol.* 04 Oct 2006 (doi:10.1111/j.1462-2920.2006.01149.x)

NETWORK BIOLOGY

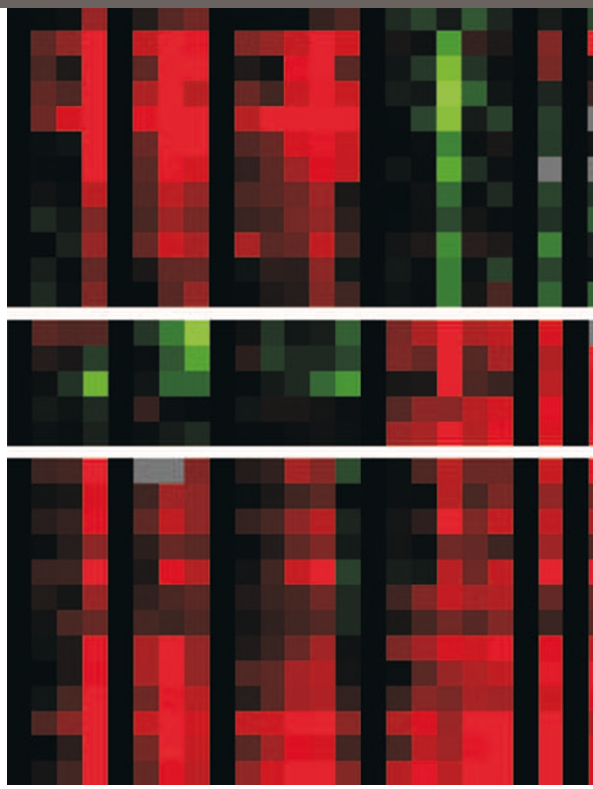
Wiring with a difference

The fact that changes in transcriptional logic bring about adaptive changes — as might occur when developmental modules are rearranged — is no longer front page news. Now, a study of mating type in two divergent yeast species shows the opposite principle: that phenotypes might stay the same during evolution, while the transcriptional logic is sometimes completely rewired.

The ascomycete yeasts *Candida albicans* and *Saccharomyces cerevisiae* each come in two varieties, **a** and α, depending on which allele they express at the mating-type (MAT) locus. Each mating type expresses a set of specific genes, which allows mating only between **a** and α types. In this respect the two yeast species are identical — however, they differ radically in how they regulate the expression of these antigens. In *C. albicans*, **a**-type genes are 'off' by default, and are turned 'on' in **a**-type cells; in *S. cerevisiae*, **a**-type genes are 'on' by default, and need to be repressed in α-type cells. The end result is the same — **a**-type genes are 'on' in **a** cells and 'off' in α cells — but the two yeasts use opposite means of achieving this pattern of expression. How did this transition take place, in the 200–800 million years since the two species shared a common ancestor? By combining microarrays (see image) and other bench experiments with comparative genomics in modern yeasts, Annie Tsong, Brian Tuch and colleagues have identified the *cis* and *trans* elements that were in place at the transition, and have traced the order in which the events took place.

A phylogenetic survey shows that the *C. albicans* style of activation is the ancestral state: in *C. albicans* and its ancestors, **a**-type genes are induced by an activator (**a**2) that is encoded by MAT**a**. The challenge is to explain how this activator was lost in the *S. cerevisiae* lineage and replaced by a repressor — α2, which is encoded by MATα.

The authors started out by identifying the **a**-type genes that were specifically activated in the *Candida* lineage and then characterizing the *cis*-regulatory motifs that allowed **a**-type activation. By combining this information with knowledge of the mating-type circuitry in *S. cerevisiae* and the genome sequence of 16 ascomycete yeasts, the authors concluded that the transition from activator to repressor occurred as follows. First, regulation of **a**-type genes became independent of **a**2; in the ancestral state, Mcm1 (a protein in the MADS-box family) required **a**2 to activate **a**-type genes, but this dependence was lost owing to sequence changes in the *cis*-elements, which allowed Mcm1 to operate on its own. As Mcm1 is constitutively active, **a**-type genes would have been inappropriately expressed in α cells: this situation would have favoured a second step, in which α2 stepped in as an Mcm1 cofactor, thereby allowing the evolution of α2-mediated repression. This step would have required the conversion of a *cis*-sequence that recognizes **a**2 to one that recognizes α2, which the authors think could have occurred simply through changes both in *cis* and in *trans*.



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Beyond the immediate implications for the wiring of yeast mating systems, this study stands out because of the molecular resolution at which it has defined an evolutionary transition. Importantly, proper gene regulation seems to be maintained at all steps during the transition. Large evolutionary transitions can be ordered, stable affairs, as long as they involve coordinated interactions between proteins, and between proteins and DNA that do not compromise fitness.

Tanita Casci Senior Editor,
Nature Reviews Genetics

ORIGINAL RESEARCH PAPER Tsong, A. E., Tuch, B. B. *et al.* Evolution of alternate transcriptional circuits with identical logic. *Nature* **443**, 415–420 (2006)