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ECOLOGY

Neutral theory tested by birds

Annette Ostling

A continental-scale analysis of habitat and bird distribution in South America provides the latest challenge for neutral theory — a controversial idea in ecology about what determines the make-up of communities.

How do different species end up living together in communities? Do they coexist only when each finds a different niche, or simply when they happen to disperse to the same habitable region? Debate over these questions intensified not long ago with the introduction of 'neutral theory'[1], a stochastic theory of community properties whose predictions have proven stubbornly robust, despite its disregard of the niches that many ecologists hold dear. Writing in *Proceedings of the National Academy of Sciences*, however, Graves and Rahbek[2] point out continental-scale patterns in the bird communities of South America that neutral theory may not be able to explain.

The dominant view in ecology is that species live together in communities only when they differ from one another. Species competing for the same nutrient or food source cannot coexist because one species will always be more efficient than the others and will quickly drive the rest to extinction[3]. Species that coexist must differ from one another in the resource they use most efficiently or in the environmental conditions to which they are best adapted — that is, they must have different niches. This view is often called 'niche-assembly'.

The contrary viewpoint is that communities are primarily shaped by historical accidents that influence where species disperse (a beetle floating to a distant island on flotsam, for example, or the uplift of a mountain range that blocks the flight of seeds between nearby forests). This view has deeper roots in evolutionary biology, where history is at centre stage, than in ecology, which concentrates on short-term interactions between species. The idea behind it is that, rather than being quickly outcompeted, species that are less efficient at using a resource evolve to be as efficient as their competitors. The main criterion for coexistence is dispersal to the same habitable region. This view is sometimes called 'dispersal-assembly'.

The neutral theory tested by Graves and Rahbek[2] is the modern synthesis of dispersal-assembly into a mathematical framework. It models a community as a finite collection of individuals that have identical probabilities of reproduction, death and dispersal. This yields predictions for community properties in terms of parameters that govern the stochastic changes that the community undergoes — for example the immigration or dispersal rate, the speciation rate, and the size of the community. Despite its simplicity, neutral theory's predictions have proven robust. Claims that it has been falsified[4] have been followed by persuasive counter-arguments[5].

Graves and Rahbek mount a new line of attack on neutral theory by testing it at the scale of an entire continent. Armed with an impressive bird-distribution database amassed from the collections of over 30 museums in 20 countries, as well as a global land-cover map created from satellite data, they quantify the correlation between the distribution of habitat (or land-cover type) and the distribution of birds across South America at the resolution of 1° latitude by 1° longitude grid cells.

Put simply, Graves and Rahbek find that birds in more widespread habitats tend to be more wide-ranging. In particular, birds present in the lowland regions of the continent to the east of the Andes, where elevation changes slowly and habitats are widespread, are on average an order of magnitude more wide-ranging than those on the western side of the Andes, where topographic relief is at a maximum and habitat changes quickly in space (Fig. 1a). Furthermore, as one looks outwards from various locations on the continent, the change in bird-community composition is asymmetric and mimics the underlying changes in habitat (Fig. 1b).

Graves and Rahbek conclude that there is a strong causal influence of birds' habitat requirements on their spatial distribution across South America. They argue that this influence contradicts neutral theory, which ignores species differences in habitat requirements.

It is worth pointing out that the first of Graves and Rahbek's results, a correlation between habitat extent and species' spatial extents, could arise from a source other than habitat influence, a source that is instead consistent with neutral theory. The Andes act as a physical barrier to the dispersal of both birds and the flora that cover the landscape. This barrier, combined with the very different land areas available to dispersing species to the west and east of it, could alone explain the observed correlation.

But there are no dispersal barriers to explain the relationship between community composition and the distribution of riverside habitat evident in Fig. 1b. And further study of the

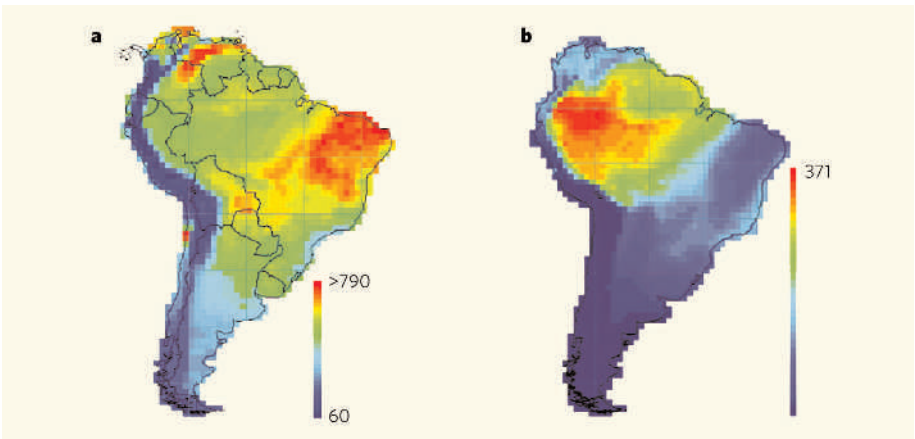

Figure 1 | Summary of Graves and Rahbek's results[2]. **a**, Bird species in the lowland regions of South America, where habitat types are more widespread, are more wide-ranging than those on the western edge of the continent, where the Andes create quick changes in elevation and habitat type. Colours indicate median range-size in units of 1° latitude × 1° longitude cells. **b**, The composition of bird communities changes asymmetrically as one looks outwards from a location in the Amazon basin (here 1–2° S, 69–70° W), mimicking the underlying distribution of riverside habitat. Colours indicate the number of species in common with the focal location whose coordinates are listed. Neutral theory may be consistent with **a** but Graves and Rahbek are correct that it cannot predict the ecological importance of habitat evident in **b**. The theory may still be relevant at smaller scales, however, and species differences in habitat requirements can evolve under dispersal-assembly on a heterogeneous landscape. (Figures reproduced from ref. 2.)

bird and land-cover databases would surely yield quantitative evidence of the influence of habitat. Practically all ecologists agree that species have habitat requirements that limit where they can live — tropical trees cannot survive on the Arctic tundra. Graves and Rahbek are correct that neutral theory cannot predict the resulting influence of habitat on community composition because it ignores species differences entirely.

But does the importance of habitat disagree with the letter or the intent of neutral theory? In other words, does it contradict the overall principle of dispersal-assembly?

Not necessarily. The idea of dispersal-assembly is not that differences between species do not exist — they are the inevitable result of disparate evolutionary histories. Rather, the idea is that species similarities, not their differences, lead them to find the same region habitable and to coexist. Neutral theory applies only in that realm of intermingling, where species are similar.

Habitat influence on species' distributions at any scale does indicate a role for niche-assembly, which has implications for ecological dynamics. The species that differ in the habitat they do best in cannot out-compete each other. Their differences allow them to coexist stably in the landscape.

However, unless habitat and species change in lock-step, habitat effects do not rule out a simultaneous role for dispersal-assembly. As Graves and Rahbek acknowledge, their observations limit only the spatial scale and groups of species within which neutral theory's unstable ecological dynamics may apply. Furthermore, differences between species in habitat requirements can arise from sources that are consistent with dispersal-assembly in a heterogeneous landscape over evolutionary timescales, such as from local selection for capabilities on a par with those of competitors. Selection for the avoidance of competition (or niche-assembly) may not be the evolutionary origin of these differences.

More empirical work is needed to distinguish between niche-assembly and dispersal-assembly on both ecological and evolutionary timescales. We also need to understand the implications of this distinction, and more refined ones, for judging the robustness and resilience of communities in the face of anthropogenic change. ■

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CANCER

Crime and punishment

Norman E. Sharpless and Ronald A. DePinho

Cellular senescence stops the growth of cells. This process, first glimpsed in cell culture, is now confirmed by *in vivo* evidence as a vital mechanism that constrains the malignant progression of many tumours.

Societies have traditionally taken three approaches to handling recidivist criminals: exile, execution and lifetime imprisonment. It seems that human cells use similar strategies to prevent rogue cells harbouring dangerous mutations from turning into fully fledged cancers. Epithelial tissue, such as that lining the airways and intestines, continuously renews and sloughs off, thereby sentencing some precancerous cells to extra-corporeal exile. There is also a cellular version of the death penalty — apoptosis, a well-established anticancer mechanism. And in this issue, four groups[1–4] report striking *in vivo* evidence that the body can subject potential cancer cells to the equivalent of a life-sentence: cellular senescence.

Senescence is a specific form of stable growth arrest provoked by diverse stresses, including the enforced expression of cancer-promoting genes in cultured cells. This 'oncogene-induced senescence' (OIS)[5] is linked to known cancer pathways in cultured cells, notably the ARF–p53 and $p16^{INK4a}$–RB pathways (Fig. 1). But whether OIS is an authentic anticancer process *in vivo*, or simply an artefact of enforced oncogene expression in cells experiencing culture shock[6], has been controversial.

This issue is settled by the new papers[1–4], which show that OIS occurs *in vivo* in several diverse precancerous tissues from both human and mouse. In addition, the work identifies much-needed markers of senescence, and further delineates the molecular underpinnings of this key tumour-suppressing process. A compelling feature of these studies is the consistency of OIS in response to a variety of cancer-causing mutations in different human tumour types and mouse-model systems. At the same time, the reports reveal that the molecular circuitry of OIS may be wired differently among tumour types.

Michaloglou *et al.* (page 720)[1] worked with cultures of human melanocytes (pigmented skin cells) and nevi (skin moles, the benign precursors of malignant melanoma). They found that nevi harbouring mutations of the BRAF protein (mutations that are frequently found in melanomas) have robust expression of senescence markers and do not seem to proliferate. In melanoma cells, however, senescence is extinguished and proliferation accelerated.

Curiously, the tumour suppressor $p16^{INK4a}$ — a known activator of senescence that is deleted in melanoma cells — showed spotty expression in nevi, and experimental depletion of $p16^{INK4a}$ failed to increase BRAF-induced senescence in melanocyte cultures. Mutated BRAF in melanocytes also failed to induce the ARF and p53 tumour suppressors, two proteins integral to the activation of senescence in many systems. These results expose serious gaps in our understanding of the genes and pathways that function to constrain the transformation of nevi into lethal melanomas.

Exploring the evolution of prostate cancer, Chen *et al.* (page 725)[2] discovered senescence in early-stage prostate abnormalities in humans and in mice engineered to sustain prostate-specific deletion of the PTEN tumour-suppressor gene. However, in contrast to the situation in melanocytes, prostate OIS is dependent on p53, and co-deletion of PTEN and p53 cancelled senescence, promoting full-blown prostate cancer. Parallel studies using mouse models to dissect the role of the *Ras* oncogene in the lung and pancreas[3] and in lymphoid cells[4] reinforced similar principles. So, although previous work has established that the role of p53 as a tumour suppressor depends on its ability to mediate apoptosis, these papers emphasize that p53 can also mediate senescence in primary tumours.

Collado *et al.* (page 642)[3] address a crucial need for better *in vivo* markers of OIS. So far, the gold standard has been the detection of an enzymatic activity associated with senescence (that of SA-β-gal)[7]. Although SA-β-gal has been used successfully to analyse human and mouse samples, this marker is not molecularly well-defined and demonstrates background activity in certain organs. Collado *et al.* employed an ingenious microarray screen to identify a small set of genes, the expression of which correlates strongly with senescence induced by the ERK protein. (ERK mediates the effects of certain cancer-causing mutations.) The correlations with gene expression are not seen when ERK is induced in the absence of senescence. These markers of OIS include protein-encoding genes and at least three RNA-encoding genes that are relevant to mouse tumour models of different tissues. These markers might predict OIS in precancerous abnormalities in humans.

Braig *et al.* (page 660)[4] provide a penetrating biochemical view of senescence. Their experiments were guided by the observation of unusual foci of tightly packed DNA in senescent cells[8]. These foci possessed features of a form of silenced DNA called heterochromatin,