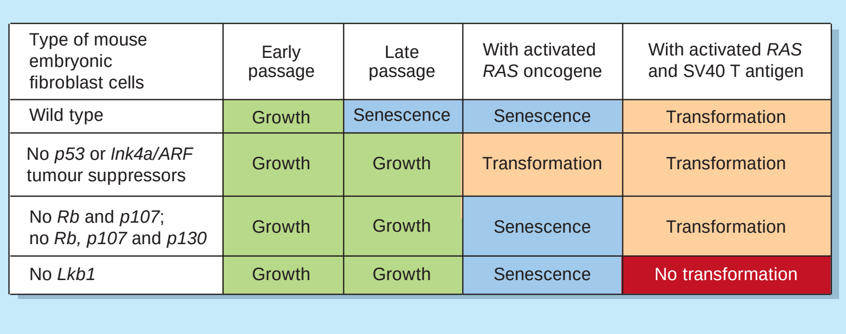

Type of mouse embryonic fibroblast cells	Early passage	Late passage	With activated *RAS* oncogene	With activated *RAS* and SV40 T antigen
Wild type	Growth	Senescence	Senescence	Transformation
No *p53* or *Ink4a/ARF* tumour suppressors	Growth	Growth	Transformation	Transformation
No *Rb* and *p107*; no *Rb, p107* and *p130*	Growth	Growth	Senescence	Transformation
No *Lkb1*	Growth	Growth	Senescence	No transformation

Figure 2 **A different type of tumour suppressor? The features of the mouse *Lkb1* gene are rather unusual, as seen here. *Rb, p107* and *p130* are tumour-suppressor genes of the *Rb* family. SV40 is simian virus 40. Senescence prevents indefinite cell growth (immortalization); transformation refers to processes by which cells become cancer cells. 'Early' and 'late' passage refers to the relative amount of time cells have spent in culture.**

stimuli, such as DNA damage, the expression of activated oncogenes (which promote cell growth), and stress induced by the tissue-culture process[8].

Bardeesy *et al.* found that their homozygous MEFs were resistant to tissue-culture-induced senescence, and thereby became immortal, but still underwent senescence induced by DNA damage or oncogenes. This suggests that a lack of *Lkb1* renders cells immortal by inhibiting or alleviating the culture-stress-induced activation of senescence. Importantly, however, these immortal MEFs also turned out to be resistant to transformation induced by potent combinations of oncogenes, such as activated *RAS* and SV40 large T antigen, which readily transform normal cells (Fig. 2). So, although the lack of *Lkb1* causes immortalization, the immortalized cells seem to be resistant to subsequent transformation.

So *Lkb1* deficiency is a double-edged sword, somehow promoting perpetual cell growth but preventing malignant transformation — and explaining why the polyps in PJS patients develop yet remain benign. But how does *Lkb1* loss in the intestinal epithelium promote the development of stromal-rich polyps? Bardeesy *et al.* examined the genes expressed in the homozygous MEFs and in polyps from heterozygous mice, and detected marked increases in the expression of various genes encoding components of the extracellular matrix and secreted signalling molecules. So perhaps factors such as these, produced by *Lkb1*-deficient epithelial cells, influence the stromal cells in PJS polyps. In keeping with this idea, the authors observed that homozygous MEFs, and the medium in which these cells were cultured, affected the expression of specific genes in normal MEFs.

An unanswered question is why PJS patients are more likely than usual to develop other types of cancer. This seems odd, given that a lack of *LKB1* prevents malignant transformation of intestinal polyps. Does this mean that *LKB1*-deficient cells are resistant to transformation by some activated oncogenes (such as members of the *RAS* pathway), but more susceptible to others? The low frequency of activating *RAS* mutations in tumours from PJS patients certainly hints at this possibility. Alternatively, the order of events may matter. For example, *LKB1* inactivation in normal intestinal epithelium might protect those cells from malignant transformation, resulting in benign polyps. But in cell types that have already acquired mutations in other cancer genes, *LKB1* loss might promote tumour progression. No doubt Bardeesy and colleagues' mouse model will prove valuable in addressing these and other issues. ■

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Ecology

Oceans under the macroscope

Andrea Belgrano and James H. Brown

Phytoplankton are marine algae that support all ocean life, so it is important to understand the processes that control their distribution, abundance and diversity. Macroecology offers a way to do so.

Increasingly, scientists are turning to the relatively new approach of macroecology to study the structure and dynamics of complex ecosystems. Macroecologists look for statistical patterns in the abundance, distribution, biomass and diversity of individual organisms or species, in an effort to understand why these patterns emerge and what processes govern the structure and dynamics of the ecosystem as a whole. At first, macroecology relied heavily on large data sets of quite well-studied terrestrial birds and mammals[1,2]. More recently, the approach and principles have been applied more widely — to fish, plants, molluscs and insects. Now, on page 154 of this issue, Li[3] takes a macroecological approach to biological oceanography.

One problem in understanding the ecology of the oceans is the enormous spatial and temporal variation that results largely from climatic and physical oceanographic fluctuations (see, for example, Fig. 1). How can this problem be overcome so as to discover general features that are due to fundamental organizing processes? This is where the macroecological approach of looking at the statistical patterns of ecosystem components is so useful. For instance, to understand the structure and function of marine ecosystems, it is crucial to determine which processes control the abundance, distribution and diversity of phytoplankton. These diverse, single-celled photosynthetic organisms, which convert solar energy into organic energy, are the primary producers that support the entire ocean food web — including commercially valuable fish stocks.

In his study, Li[3] used flow cytometry to measure precisely the number and size of phytoplankton cells, as well as the amount of chlorophyll (the main photosynthetic pigment), in sea water. This technique made it practical for Li to quantify billions of cells, in thousands of samples from 23 oceanographic cruises, across a large area of the North Atlantic Ocean over a 13-year period.

Two especially important insights emerge from Li's data and analyses. First, he finds a strong, negative, 'allometric' scaling relationship — scaling that follows some power of body mass — between phytoplankton abundance (cell density, N) and cell volume (body mass, M). Specifically, $N \propto M^{-3/4}$. So, given that the rate of energy use by whole organisms (metabolism, Q) scales with body size as $Q \propto M^{3/4}$, the energy used by all of the phytoplankton cells, no matter which species, that make up a given size class must be the same as that used by all the phytoplankton that make up other size classes: $NQ \propto M^{-3/4}M^{3/4} \propto M^0$.

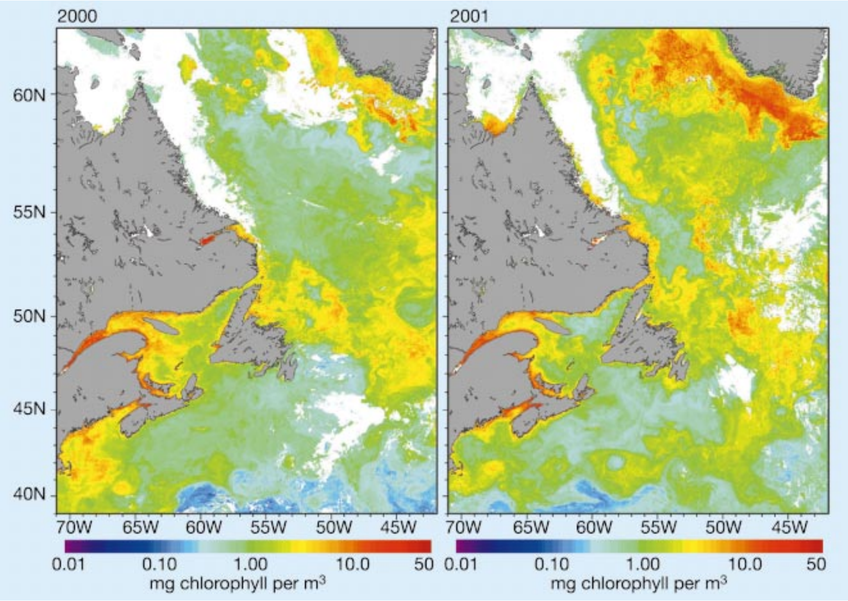

Figure 1 **Biomass of chlorophyll from phytoplankton in surface waters of the northwest North Atlantic Ocean, the area investigated by Li[3], in two-week periods in 2000 and 2001. The amount of chlorophyll is revealed by images produced from SeaWiFS data, collected by the OrbView-2 satellite, resolved to about 1.5 km per pixel. The images show broad similarities in chlorophyll concentration, as well as some significant differences, from year to year. They also show significant spatial heterogeneity. Li[3] has used macroecological principles to try to disentangle such broad patterns, which probably result from large-scale climatic and physical oceanographic events, from the organizing processes inherent to marine phytoplankton. (These images are composites for 16 May to 30 May in 2000 and 2001, and are available at http://oceanimage.mar.dfo-mpo.gc.ca)**

This extends to marine phytoplankton the 'energy equivalence rule' that has been demonstrated previously for other groups of organisms, including terrestrial animals and plants[4,5], suggesting that this rule is very general, if not universal. If all the individuals in a given size class do indeed use energy at the same rate as all the individuals that make up other size classes, this is an important feature of ecological organization that begs a mechanism. So far, it is not clear why organisms from different size classes should have access to, or be able to appropriate, equal quantities of energy.

Li's second important finding is that phytoplankton are most diverse at intermediate levels of chlorophyll concentration, and when the layers of the ocean water column are mixed to a degree somewhere between 'no mixing' and 'complete mixing'. Li obtained this result by measuring phytoplankton diversity not by tallying the number of species — as is traditional in ecology — but by creatively using flow cytometry to quantify the variety of phytoplankton types on the basis of their light-scattering properties. The results suggest that maximal diversity occurs when some intermediate degree of water mixing allows diverse functional types to coexist. (A high degree of mixing would allow one or a few species that can cope well with such disturbance to become dominant; likewise, no disturbance at all would foster competition, again allowing one or a few superior competitors to become dominant.)

More generally, Li's work[3] shows that, despite the enormous complexity and variety of marine phytoplankton, there are emergent features of phytoplankton abundance and diversity that are related to cell size and overall chlorophyll content, respectively. The implication is that it is possible to make mechanistic connections between the metabolism of individual organisms (in this case, phytoplankton) and the roles of those organisms in ecosystems (here, in the productivity and feeding dynamics of oceans). For example, a recent study[6] of marine food webs suggests how oceanographic and climatic events, through their effects on the abundance and productivity of phytoplankton, can cause fluctuations in commercial fish stocks.

Ecology has generally lacked unifying theories. Much of the emphasis has been on the seemingly large differences between different kinds of organisms and ecosystems, and on the extensive spatial and temporal variation within ecosystems. Now, however, there is increasing evidence that some macroecological patterns and mechanistic processes hold across diverse taxa and ecological systems. Such generality suggests exciting prospects for conceptual unification. ■

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Earth science

Baked Alaska

Peter Clift and Karen Bice

The warming of the Earth's climate more than 50 million years ago is as yet unexplained. Now the finger points to the heating of sediment in the Gulf of Alaska as an important source of the greenhouse gas methane.

Between about 58 and 52 million years ago, during the late Palaeocene and early Eocene epochs, the Earth's climate warmed considerably. What was the cause of this unusually long warming trend? Writing in *Geology*, Hudson and Magoon[1] put forward an idea that adds to thinking on the subject.

The marine geological record shows that Earth's climate has experienced swings of cooling and heating over various timescales. Change over thousands to hundreds of thousands of years seems to be related to orbital variations, but climate trends lasting millions of years have been harder to explain. The interval between the late Palaeocene and early Eocene has attracted particular interest, not only because of the exceptional warming but also because this was a time of widespread and intense tectonic activity at the Earth's surface.

Attempts to find out whether the two are connected have usually centred on the release of greenhouse gases, especially CO_2, generated by tectonic activity. In some models the CO_2 produced is related to volcanism, especially in the northeast Atlantic[2]. In others, the suggestion is that CO_2 was released from limestones originally deposited on the northern coast of the Indian subcontinent, which were buried, heated and then emitted CO_2 on a large scale when this landmass collided with the rest of Asia[3].

Hudson and Magoon[1] propose an alternative tectonic trigger for the global warming of 58–52 million years ago, one that invokes