

## OCEANOGRAPHY

## A bigger nitrogen fix

Nicolas Gruber

**Biologically useful nitrogen is delivered to the upper ocean from the depths by vertical transport processes — or such was the received wisdom. In fact, bacteria that convert atmospheric nitrogen may be just as crucial.**

Next to light, nitrogen is the main factor that limits the biological productivity of primary producers in the sea. All photosynthetic organisms need nitrogen to grow, yet most cannot use it in its simplest form, molecular  $N_2$ . But biologically useful, 'fixed' forms of nitrogen are scarce over much of the illuminated upper ocean. Writing in *Global Biogeochemical Cycles*, Capone *et al.*<sup>1</sup> highlight a little-considered mechanism for supplying the upper ocean with nitrogen — bacteria that fix molecular nitrogen from the atmosphere.

The scarcity of fixed nitrogen in the illuminated ocean results from a continuous loss of nitrogen to the dark, abyssal ocean, resulting primarily from the sinking of organic nitrogen (Fig. 1). If this lost nitrogen were not recycled to the upper ocean, primary production in the sea would plummet within a few years. So identifying and quantifying the replenishment mechanism is essential for understanding marine productivity. Furthermore, as the biologically induced cycling of nitrogen is closely coupled to the cycling of carbon, these processes are also of prime relevance for understanding the oceanic carbon cycle, and hence atmospheric carbon dioxide levels.

Over much of the ocean, upward mixing and transport of nitrate ( $NO_3^-$ ) constitutes the primary supply pathway (Fig. 1). Nitrate is the dominant form of fixed nitrogen and is

generated in the dark ocean from the mineralization of sinking organic nitrogen. In most regions of the tropical and subtropical ocean, however, vertical transport is insignificant, and mixing tends to be inefficient. Surprisingly, biological productivity in these regions is often much higher than might be expected from the poor vertical supply of nitrate, implying the involvement of other, unidentified nitrogen sources<sup>2</sup>. One candidate source was the biological fixation of molecular  $N_2$  from the atmosphere, but based on the measurements then available, this was generally considered unimportant.

Capone and colleagues<sup>1</sup> now demonstrate, in the most exhaustive and comprehensive study so far, that over large regions of the tropical and subtropical Atlantic, biological  $N_2$  fixation is indeed substantial. In fact, it provides the ecosystem of the illuminated ocean with a source of nitrogen that rivals the vertical supply of nitrate. The contribution cements a paradigm shift that has been occurring over the past decade in models of marine nitrogen cycling (see ref. 3 for an example).

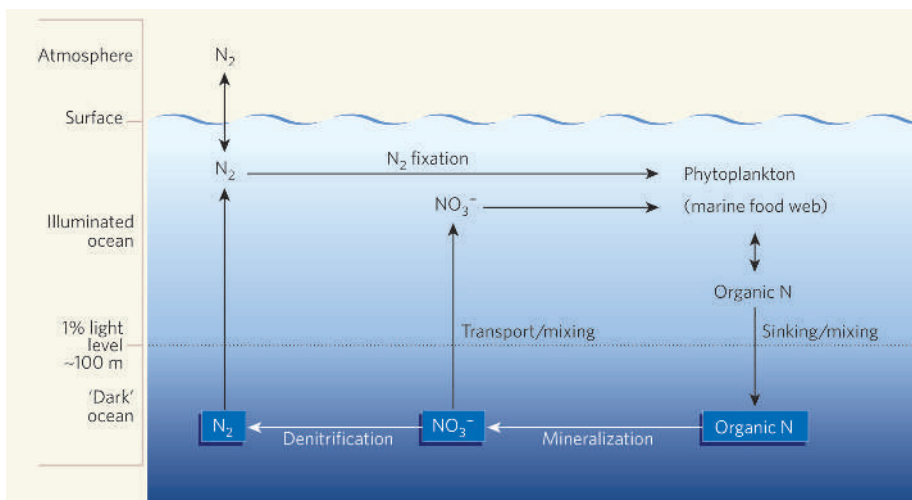
The authors focused<sup>1</sup> on the contribution of *Trichodesmium*, a cyanobacterium that is the most conspicuous and best-studied marine  $N_2$  fixer. In a painstaking effort, they measured the  $N_2$  fixation rates of gently collected colonies of *Trichodesmium* at more than 150 stations during six cruises to the tropical and

subtropical Atlantic. Averaged over all stations and integrated over the depth of the upper ocean at each station, the annual  $N_2$  fixation rate was  $87 \pm 14$  millimol of N per square metre. This value is of the same order of magnitude as the vertical flux of nitrate into the upper ocean in the region studied.

What makes Capone and colleagues' study particularly compelling is that they estimated  $N_2$  fixation rates using an array of independent methods, each with their own strengths and weaknesses. This results in an unprecedented level of confidence in the estimates obtained. In particular, the authors used measurements of the ratio of the two stable isotopes of nitrogen,  $^{14}N$  and  $^{15}N$ , to confirm that about half of the organic nitrogen in the surface ocean stems from atmospheric  $N_2$  (Fig. 1).

Assuming that their estimate of the biological  $N_2$  fixation rate is representative of most of the tropical and subtropical North Atlantic, Capone *et al.* estimate<sup>1</sup> that *Trichodesmium* annually adds between 1.6 and 2.4 teramol (a teramol is  $10^{12}$  mol) of fixed nitrogen to this region, almost an order of magnitude larger than earlier estimates of  $N_2$  fixation over the whole Earth<sup>4</sup>. This extrapolation is consistent with several indirect geochemical estimates<sup>5-7</sup> of the biological fixation rate that are based on anomalies in the relative abundance of nitrate and phosphate ( $PO_4^{3-}$ ); these ranged, with one exception<sup>7</sup>, from 2 to 6 teramol of nitrogen per year. As these estimates are integrated explicitly over time and space, they are less prone to the difficulties associated with extrapolating local rate measurements. They are, however, based on a number of assumptions — some of which, such as the exact amount of nitrogen and phosphorus required by primary producers that do not fix  $N_2$  — are difficult to verify.

Capone *et al.* also show that their extrapolation is broadly consistent with the value inferred from a region-wide analysis of the  $^{15}N$ -isotopic mass balance. To determine the rate of  $N_2$  fixation, they combine their estimate derived from the nitrogen isotopic ratio — that some 50% of the organic nitrogen in the upper ocean comes from atmospheric  $N_2$  — with an estimate for the turnover rate of organic nitrogen. This value is in fact somewhat larger than the value the authors find based on *Trichodesmium*. But the discrepancy might be explained by the fact that mass-balance analysis includes all sources of  $N_2$  fixation, including recently discovered single-cell cyanobacteria<sup>8</sup> and a cyanobacterium that



**Figure 1 | The marine nitrogen cycle.** Some of the organic nitrogen fixed by phytoplankton (primary producers), and then cycled through the food web of the upper ocean, is lost to the dark ocean by sinking and mixing. Over most of the ocean this loss is compensated by the upward transport and mixing of nitrate that is generated from the mineralization of the sinking organic nitrogen. Capone *et al.*<sup>2</sup> show that in certain regions, such as the tropical and subtropical North Atlantic, biological  $N_2$  fixation can supply as much nitrogen to the upper ocean as vertical nitrate transport, and can compensate for the fixed nitrogen lost through denitrification.

lives symbiotically within a marine diatom<sup>9</sup>.

Not only does N<sub>2</sub> fixation provide a pathway for adding new nitrogen to the illuminated ocean, but it is also the main source of fixed nitrogen to the ocean as a whole. On long timescales, this source could compensate for the effects of denitrification, a respiratory process that converts fixed nitrogen back to N<sub>2</sub> (Fig. 1). It has been suggested<sup>10</sup> that past estimates of the loss of fixed nitrogen from the ocean need to be revised substantially upwards. If the rate of N<sub>2</sub> fixation is as low as was estimated two decades ago, this would imply that the present-day marine nitrogen budget is seriously out of balance. The much higher estimates of N<sub>2</sub> fixation proposed on the basis of geochemical methods had brought the budget back to near-balance<sup>5</sup>, but without direct measurements that conclusion

remained tentative. The new convergence of estimates for the Atlantic provides good evidence that N<sub>2</sub> fixation in the ocean may occur on a large enough scale to balance losses of fixed nitrogen.

A fascinating corollary is the question of how marine N<sub>2</sub> fixation and denitrification are coupled. With both processes occurring at such high rates, the residence time of fixed nitrogen in the ocean can be only a few thousand years. This would require a well-established balance between the two processes in order to avoid large swings in the biological productivity of the oceans. Because all organisms need phosphorus as well as nitrogen to survive, the marine phosphorus content almost certainly plays an important role here. Room for surprises in the marine nitrogen cycle remains, but one conclusion is clear: that

cycle is much more dynamic than was thought only a few years ago. ■

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CANCER

# Two in one

Anton Berns

**As cancer develops, at least two cell processes are disrupted — cell growth is promoted, and cell death inhibited. It seems that mutated versions of the notorious cancer-promoting protein MYC can accomplish both at once.**

The MYC gene is one of the classic cancer-promoting ‘oncogenes’. It is overexpressed in many types of tumour, and the MYC protein it encodes causes a surge in the proliferation of cells. But it has another effect: it enhances programmed cell death, or ‘apoptosis’. So under normal circumstances, the extra cell divisions MYC causes when overexpressed are cancelled out by a rise in cell fatalities. In MYC-associated tumours, however, there is usually a mutation in an ancillary protein that disrupts the apoptosis pathway, releasing the brakes on cell proliferation. In this issue, Hemann *et al.* (page 807)<sup>1</sup> report that MYC does not need to rely on a partner-in-crime to cause tumours — it can itself be mutated in a way that interferes with its apoptotic function.

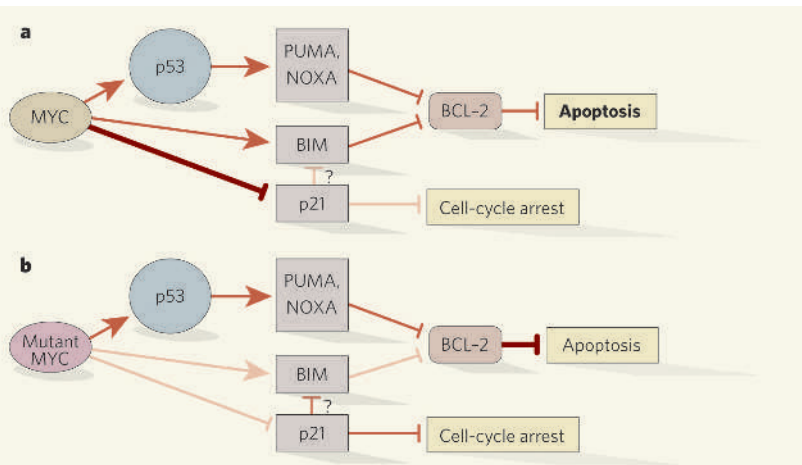
The authors examined MYC function in Burkitt’s lymphoma, a malignancy of immune cells called B cells, which normally produce immunoglobulins in response to an immune attack. The cancer is characterized by gross overexpression of MYC because the position of the MYC gene is swapped with that of the immunoglobulin gene. As this latter gene is often switched on in B cells, and as the ‘translocated’ MYC gene is slotted in next to the regulatory sequences for the immunoglobulin gene (the ‘promoter’), it too is switched on. Translocated MYC genes often harbour specific point mutations that tend to result in altered amino acids in a specific part of the MYC protein (the amino-terminal domain). This clustering of mutations led to the suspicion

that they augment the tumorigenic potential of MYC. However, *in vitro* assays with these mutants failed to show either enhanced cancer-promoting activity or reduced apoptosis<sup>2</sup>.

To assess the cancer-promoting potential of MYC mutants, the authors used mice that had been irradiated to permit reconstitution of their immune system. They reconstituted these cells from progenitor cells, called

haematopoietic stem cells (HSC), that had been manipulated to express either normal (wild-type) or mutated MYC, and then followed the formation of tumours. When HSC expressing wild-type MYC were used, lymphomas developed in a small fraction of the mice only after a long period. By contrast, most of the mice grafted with HSC carrying mutant MYC quickly developed tumours, indicating that the MYC mutants are far more tumorigenic than wild-type MYC.

To identify the mechanism underlying this difference, the authors checked whether the gene mutants had different effects on the apoptotic signalling pathways induced by MYC overexpression. They found that the ARF-p53 pathway, a known target of MYC, was induced equally by wild-type and mutant MYC. However, the apoptosis-promoting protein BIM, which is part of a different pathway, was



**Figure 1 | The machinations of MYC.** The pathways induced by wild-type (a) and mutant (b) MYC. Arrows indicate activation, and T-bars indicate inhibition, with the depth of colour showing signal intensity. Hemann *et al.*<sup>1</sup> find that mutant MYC fails to induce BIM. BIM acts through BCL-2, a key player in protecting cells from programmed cell death (apoptosis). If BIM is not induced, apoptosis is prevented. The same result is observed if wild-type MYC is overexpressed in cells in which either the p53 or the BIM pathway is disabled by targeted disruption of BIM or p53. The signalling through these pathways seems to be additive, and therefore partial inactivation of either one might lead to a similar outcome. Question marks indicate speculative connections.