go to fixation — that is, each individual will become homozygous for this allele — thus implying widespread bisexuality.

This theoretical framework[3] is an advance in evolutionary biology and studies of human behaviour because it generates several testable predictions: for example, if a gene influencing homosexuality is linked to the X chromosome, then it would support the sexual-antagonism hypothesis rather than overdominance. The framework will be used to guide research on the genetic basis of male and female homosexuality, and will help in resolving the 'Darwinian paradox of male homosexuality'[2]. But it is of course theory only. Tasks for the future are to establish more precisely the costs and benefits of such behaviour in natural populations[1]. Such knowledge will help fine-tune these models of sexual orientation and show whether overdominance or antagonistic selection has been operating in mammals and throughout human history. ■

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OCEANOGRAPHY

A marine nitrogen cycle fix?

Douglas G. Capone and Angela N. Knapp

Some of our suppositions about the marine nitrogen cycle may be wrong. An innovative analysis of nutrients at the ocean's surface reveals a feedback mechanism that might hold the whole cycle in balance.

The flow of nitrogen compounds between the oceans and the atmosphere is central to life, as nitrogen is a fundamental component of biomass and is essential for many biological processes. Although we have learned much about the nitrogen cycle of the oceans, two burning questions remain unanswered: is the marine nitrogen budget currently in balance, and are the processes that add and remove nitrogen to and from the seas closely linked? On page 163 of this issue, Deutsch *et al.*[1] provide evidence that the primary process responsible for putting nitrogen compounds into the sea — biological nitrogen fixation — is intimately associated, both geographically and temporally, with marine nitrogen removal. Furthermore, their work implies that the ratio of nitrogen to phosphorus in sea water may be the central factor that regulates nitrogen fixation.

Biological nitrogen fixation — the enzyme-catalysed reduction of nitrogen gas (N_2) — continually adds nitrogen to the sea in the form of compounds that can be used as nutrients. Nitrogen fixation is commonly associated with certain cyanobacteria that inhabit the warm, sunlit surface waters of low-latitude oceans[2]. These photosynthetic bacteria can tap the immense reservoir of dissolved N_2 gas in sea water, but their growth is often limited by the scarcity of other nutrients such as phosphorus and iron[2].

Fixed nitrogen is eventually converted to nitrate by nitrifying bacteria. Ultimately, the loss of nitrogen from the ocean occurs by denitrification, a process that converts nitrogen compounds such as nitrate back to N_2. Denitrification occurs mostly at depths of 200–700 metres in the 'oxygen minimum zones' (OMZs) of the ocean — that is, in the eastern tropical north Pacific, the eastern tropical south Pacific and the Arabian Sea — and in marine sediments[3–5].

Nitrogen fixation and denitrification are generally assumed to dominate the flows of nitrogen into and out of the ocean[3,4,6]. Some estimates suggest that the rate of marine denitrification substantially exceeds that of nitrogen fixation[3,4]. However, if this is the case, the ocean would be progressively depleted of biologically available nitrogen, which is not supported by geochemical evidence[5]. If we accept that, in the oceanic nitrogen cycle, sources need to balance sinks[5,6], then either the inputs are underestimated or the outputs are overestimated.

For the inorganic compounds dissolved in deep ocean water, the ratio of nitrogen to phosphorus is expected to be about 16:1, as noted by the oceanographer Alfred Redfield[7] in the early 1930s. Several of Deutsch's co-authors have previously analysed inorganic nutrients in oceanic subsurface waters, using a parameter N* to discern areas with nitrogen-to-phosphorus ratios higher or lower than the 'Redfield' ratio[8]. They discovered large regions that have elevated nitrogen-to-phosphorus ratios, particularly in the north Atlantic, and speculated that these nutrient patterns resulted from the subsurface

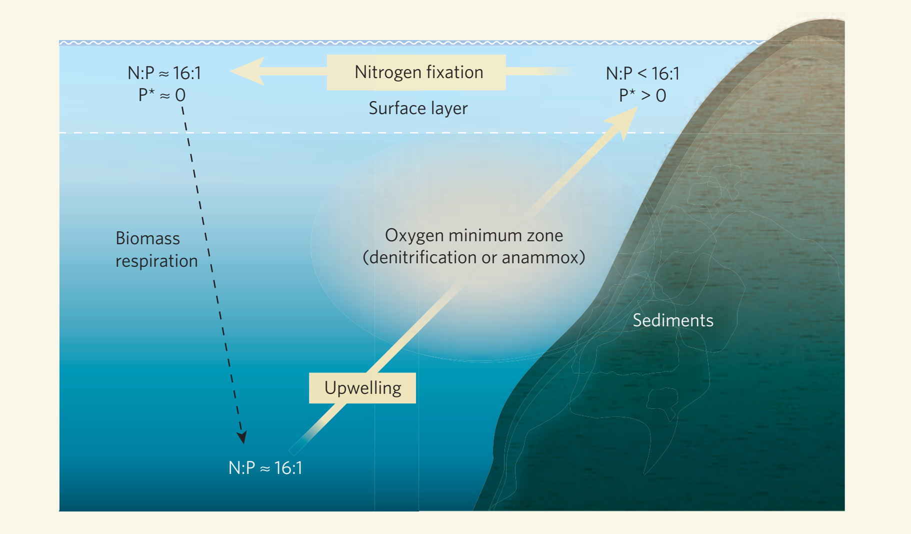

Figure 1 | Coupling between marine nitrogen fixation and denitrification zones. Nitrogen enters the marine nitrogen cycle by 'fixation' when microbes at the ocean's surface convert nitrogen gas (N_2) into biomass. This biomass may then release nitrogen compounds into the ocean. Denitrification and 'anammox' processes remove nitrogen from the sea by converting inorganic nitrogen compounds into N_2; this occurs in the 'oxygen minimum zones' (OMZs) of deeper waters and in marine sediments. The expected ratio of nitrogen to phosphorus in the deep ocean is about 16:1. Deutsch *et al.*[1] define a parameter P* that identifies deviations of relative phosphorus levels from this ratio. In upwelling waters in contact with OMZs, the nitrogen-to-phosphorus ratio is less than 16:1, and surface waters over the OMZs have an excess P* (P* > 0). As these surface waters flow offshore, the 'excess' of phosphorus decreases back to the expected ratio (P*≈ 0), presumably as nitrogen fixers extract phosphorus without absorbing any nitrogen compounds. Residual nitrogen and phosphorus compounds are used by phytoplankton, which redeliver some of these compounds, with a nitrogen-to-phosphorus ratio of about 16:1, to the deep sea.

degradation of nitrogen-fixer biomass carried down from overlying waters. Such biomass typically has a nitrogen-to-phosphorus ratio greater than 16:1 (ref. 9). These authors[8] also proposed that the geochemically inferred high rates of nitrogen fixation in the north Atlantic were a result of unusually high growth rates of nitrogen-fixers, stimulated by the high flux of iron-bearing dust that is blown into this basin from northwest Africa. Although nitrogen fixation rates based on the value of N* were estimated for the north Atlantic, nitrogen fixation rates in the Pacific were obscured by higher net rates of denitrification[1,8].

On the basis of field observations of nitrogen fixation[2,10] and these N* distributions[2,8], the dominant sites of nitrogen fixation and denitrification seemed to be geographically removed from each other and were presumably coupled only over the timescales of ocean circulation (thousands of years). But recent modelling efforts have led to the conclusion that nitrogen fixation and denitrification must be more closely linked than this, and that nitrogen fixation provides a strong negative feedback that stabilizes the marine nitrogen cycle[5,6], as originally hypothesized by Redfield[7].

Deutsch *et al.*[1] now define a parameter P* that discerns excesses or deficiencies of phosphorus relative to the canonical 16:1 ratio of nitrogen to phosphorus in sea water, and use this to examine nutrient fields at the ocean's surface. They note that, downstream of OMZs, surface waters that initially carry a surplus of phosphorus because of subsurface denitrification gradually lose this excess (Fig. 1). They attribute this effect to nitrogen fixation restoring the system to a 'Redfieldian' balance.

Deutsch and colleagues' analysis creates a very different view of the distribution of nitrogen fixation in the ocean and of the extent of its coupling to denitrification. The highest rates of fixation are not in the tropical Atlantic with its large inputs of iron-rich dust, as was previously surmised, but downstream from OMZs in the Pacific Ocean — despite the lower supply of airborne iron to these regions. So a supply of iron-rich dust may not exert as much influence on marine nitrogen fixation as is currently assumed[11]. These findings also indicate that, on a global scale, nitrogen fixation should compensate for denitrification, so balancing the marine-nitrogen books[5,6].

Deutsch and colleagues' proposed distribution of nitrogen fixation[1] is supported by other evidence. For example, the distribution of nitrogen isotopes[12] — and, in some cases, that of oxygen isotopes[13] — in nitrate samples collected above the eastern tropical north Pacific and Arabian Sea OMZs is consistent with nitrogen-fixation inputs to these regions. Furthermore, the occurrence of dense surface accumulations of the nitrogen-fixing *Trichodesmium* cyanobacteria[14], mapped by satellite, is strikingly similar to the P* distributions presented by Deutsch *et al.*[1].

As with any method, there are limits to the uses of P*. The authors note that P* would underestimate nitrogen fixation by microbes that have both an unusually high nitrogen-to-phosphorus ratio and a very high export efficiency — that is, the capacity to sink rapidly into deep waters. Nitrogen-to-phosphorus ratios are highly variable in *Trichodesmium*[9], but are unknown for other marine nitrogen-fixers. With regard to export efficiency, in some regions nitrogen fixation can occur in symbiotic groups of cyanobacteria and diatom algae[10]; these associations have a greater potential for gravitational sinking and export than free-living nitrogen fixers. Furthermore, surface P* distributions do not take into account nitrogen fixation that may occur in environments that are uncoupled from the ocean's surface, such as deep-sea-floor methane seeps and hydrothermal vents[15].

This re-evaluation of nitrogen fixation[1] arrives at the same time as other bombshells about the marine nitrogen cycle, including recognition that nitrogen-fixing microbes are more diverse than was thought[2], and the apparent importance in several OMZ studies[16] of the anaerobic ammonia oxidation or 'anammox' pathway for nitrogen removal (as opposed to conventional denitrification). Recent evidence also shows that Archaea microbes, which are distinct from bacteria, also have leading roles in the marine nitrogen cycle, as they predominate in nitrification[17] and may be involved in nitrogen fixation[15]. All things considered, it may soon be time to start rewriting the textbooks. ■

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BIOINFORMATICS

Industrializing neuroscience

Henry Markram

The project for producing a genome-wide atlas of gene expression in the mouse brain shows how, with advancing technology, huge volumes of data can be collected and made accessible through the Internet.

It took until the beginning of the twenty-first century for the Industrial Revolution to reach life science, an event marked by the sequencing of the human genome[1,2]. The wave of industrialization is sweeping on, not least in neuroscience, where it is especially evident in the Allen Institute for Brain Science's effort to map the 'transcriptome' of the entire mouse brain — the brain locations where each of 21,500 genes is activated. Following online publication last month, results from the project appear on page 168 of this issue[3].

The project essentially involved building 21,500 three-dimensional brain atlases, plus a reference atlas — a task that would probably take a single researcher a century to complete. The Allen Institute[4], however, decided to complete this task in a couple of years by industrializing the work flow. The brains of mice were sectioned into 25-μm-thick slices and stained for an activated gene using a technique called *in situ* hybridization[5]. To obtain the three-dimensional locations of all 21,500 activated genes, more than 6,000 brains were sectioned and processed — a total of 1 million sections were finally used.

The sections were fed into a pipeline for automated staining that processes more than 16,000 sections per week. Every micrometre of each section was then photographed at low and high magnifications using automated microscopy and image capture. Operating continuously, this system produced a total of 85 million images, which were dumped onto storage servers at a rate of a terabyte (a trillion bytes) of data per day during full production, to end with more than 600 terabytes of data. The next pipeline screened the quality of the data to