

NEWS AND VIEWS

PERSPECTIVE

How *Prochlorococcus* bacteria use nitrogen sparingly in their proteins

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Organisms use proteins to perform an enormous range of functions that are essential for life. Proteins are usually composed of 20 different kinds of amino acids that each contain between one and four nitrogen atoms. In aggregate, the nitrogen atoms that are bound in proteins typically account for a substantial fraction of the nitrogen in a cell. Many organisms obtain the nitrogen that they use to make proteins from the environment, where its availability can vary greatly. These observations prompt the question: can environmental nitrogen scarcity lead to adaptive evolution in the nitrogen content of proteins? In this issue, Gilbert & Fagan (2011) address this question in the marine cyanobacteria *Prochlorococcus*, examining a variety of ways in which cells might be thrifty with nitrogen when making proteins. They show that different *Prochlorococcus* strains vary substantially in the average nitrogen content of their encoded proteins and relate this variation to nitrogen availability in different marine habitats and to genomic base composition (GC content). They also consider biases in the nitrogen content of different kinds of proteins. In most *Prochlorococcus* strains, a group of proteins that are commonly induced during nitrogen stress are poor in nitrogen relative to other proteins, probably reflecting selection for reduced nitrogen content. In contrast, ribosomal proteins are nitrogen rich relative to other *Prochlorococcus* proteins, and tend to be down-regulated during nitrogen limitation. This suggests the possibility that decaying ribosomal proteins act as a source of nitrogen-rich amino acids during periods of nitrogen stress. This work contributes to our understanding of how nutrient limitation might lead to adaptive variation in the composition of proteins and signals that marine microbes hold great promise for testing hypotheses about protein elemental costs in the future.

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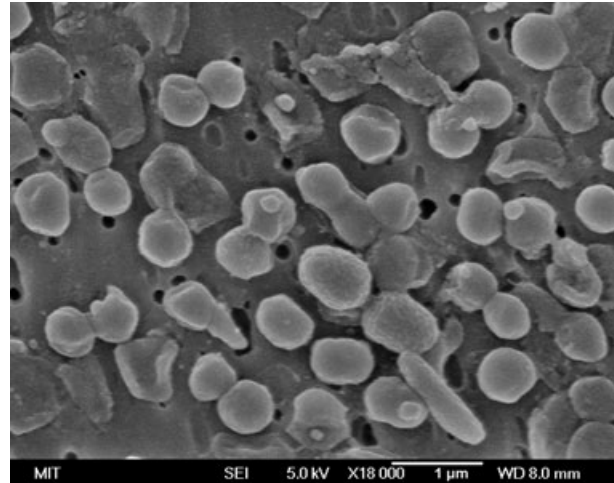


Fig. 1 Electron micrograph of cells from a culture of *Prochlorococcus* strain MIT9215. Image credit: Anne Thompson, Chisholm Lab, MIT.

Prochlorococcus are tiny cyanobacteria (0.5–1 μm diameter; Fig. 1) that are highly abundant (often exceeding 10^5 cells/mL) in areas of the open ocean where the water column is stratified and nutrients are drawn down to very low concentrations in surface waters that are lit by the sun (Partensky *et al.* 1999). *Prochlorococcus* thrive under these conditions and exhibit traits that reduce their demands for limiting nutrients, including striking adaptations in the elemental composition of cells and metabolites (e.g. Van Mooy *et al.* 2006). Within the *Prochlorococcus* genus, there are a number of strains that are phenotypically adapted to the environmental conditions that prevail in subtly different open ocean habitats, including the high light levels in the upper layers of stratified waters ('high light strains') and the low light levels of greater depths ('low light strains') (Moore & Chisholm 1999). Gilbert & Fagan (2011) use the rich history of environmental adaptation in *Prochlorococcus* and published information on *Prochlorococcus* genome sequences and transcriptional responses to various nutrient limitations, to investigate a range of different ways in which *Prochlorococcus* might be thrifty with nitrogen when making proteins.

This study provides compelling evidence for adaptive bias in the nitrogen content of a group of *Prochlorococcus* proteins that are commonly induced in response to low nitrogen availability—many of which function in nitrogen uptake or assimilation. These proteins contain significantly fewer nitrogen atoms (per amino acid side chain) than other proteins, in most of the 12 *Prochlorococcus* strains that were studied (Gilbert & Fagan 2011). This probably reflects selection for reduced use of nitrogen-rich amino acids in proteins whose function is critical to survival during episodes of nitrogen limitation, similar to observations for

carbon and sulphur assimilatory proteins in yeast and *Escherichia coli* (Baudouin-Cornu *et al.* 2001). In an extended analysis of two *Prochlorococcus* strains whose transcriptional responses to nitrogen stress have been measured experimentally (Tolonen *et al.* 2006), genes up-regulated in response to nitrogen stress encoded proteins that were poor in nitrogen (relative to other proteins) in one strain (MIT9313), but not in the other strain (MED4).

Another group of proteins exhibiting unusual nitrogen content are ribosomal proteins (Acquisti *et al.* 2009). Ribosomal proteins are rich in nitrogen relative to other *Prochlorococcus* proteins, and genes encoding ribosomal proteins tend to be down-regulated during nitrogen (but not phosphorus) stress in *Prochlorococcus* strain MED4 (Gilbert & Fagan 2011). This could be advantageous from the perspective of nutrient relations if the degradation of ribosomal proteins during nitrogen stress releases nitrogen-rich amino acids that can be used in the synthesis of new proteins (Acquisti *et al.* 2009). However, it is also pointed out that nitrogen-rich amino acids might be used in ribosomal proteins as a result of constraints that are imposed by protein function (Acquisti *et al.* 2009; Gilbert & Fagan 2011).

At a broader scale, Gilbert & Fagan (2011) compare the average nitrogen content of proteins encoded by different *Prochlorococcus* strains. They show that the proteins of high light strains tend to be poorer in nitrogen than the proteins of low light strains and suggest this might be an adaptation to low levels of available nitrogen in the upper layers of the water column where high light strains are dominant, building on a previous study by Lv *et al.* (2008). However, Gilbert & Fagan (2011) also find that protein nitrogen content is strongly associated with genomic base composition (GC content) among *Prochlorococcus* strains (reflecting a pattern observed across diverse prokaryotes, Bragg & Hyder 2004). This raises the possibility that variation among strains in average protein nitrogen content is influenced substantially by evolutionary processes that change genomic base composition, and might not reflect environmental nitrogen availability (Gilbert & Fagan 2011). This observation is important—the identification (and testing) of different potential explanations for variation in protein nitrogen content will be necessary for a clear picture to emerge of when and how nitrogen availability directly influences the evolution of protein nitrogen content.

Over the course of decades, evidence has accumulated showing that the composition of proteins can respond to the availability of their constituent elements in the environment (Knight & Hardy 1966; Cuhel *et al.* 1981; Mazel & Marlière 1989). More recently, genomic information has provided novel opportunities to study biases in the elemental composition of proteins from an ecological and evolutionary perspective (e.g. Baudouin-Cornu *et al.* 2001; Elser *et al.* 2006). A key remaining challenge for this field is to find consistencies among observations of adaptive bias in protein elemental content and to identify any general principles that might determine when and where selection can act on protein composition directly in response to nutrient availability (Bragg & Wagner 2009). Gilbert & Fagan (2011) make two major con-

tributions towards these goals. First, they show how environmental nitrogen availability has influenced the nitrogen content of *Prochlorococcus* proteins and, in particular, proteins whose expression is induced during nitrogen stress. Second, their study highlights the enormous potential for using marine microbes to generate and to test hypotheses about the evolution of protein elemental content in relation to environmental pressures.

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JGB studies links between the genomes and environments of photosynthetic organisms.

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