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ment of the flight time and the deflection of the ions enables their kinetic energy and charge state (Xe^{q+}) to be determined.

These results confirmed the presence of the highly stripped, very energetic ions observed previously for clusters with about 2000 atoms (5) and also provided additional information on the acceleration mechanism. In the case of the Coulomb explosion, the energy of repulsion is expected to scale as the square of the ionic charge, whereas, in the case of hydrodynamic explosions, the energy is purely thermal and scales linearly as the ionic charge and the electron temperature. The studies by Lezius *et al.* of argon clusters that contained typically 10^5 atoms indicated that the dominant mechanism was Coulombic but that for xenon clusters that each contained about 10 times more atoms, lower charge states ($q < 6$) were Coulombic but the majority of the higher charge states ($q > 10$) were produced by a hydrodynamic expansion. These results for xenon ions of up to $q = 30$ are summarized in the figure and show the transition in mechanism as the ionic charge and the kinetic energy increase. However, the most energetic ions with energies approaching 1 MeV appear to be produced by Coulomb explosion.

By the elegant adaptation of a simple experimental technique, Lezius *et al.* have demonstrated the complexity of the processes responsible for the dissociation of clusters. Further progress will require more detailed theoretical models to be developed to elucidate further the physical mechanisms responsible.

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OCEANOGRAPHY

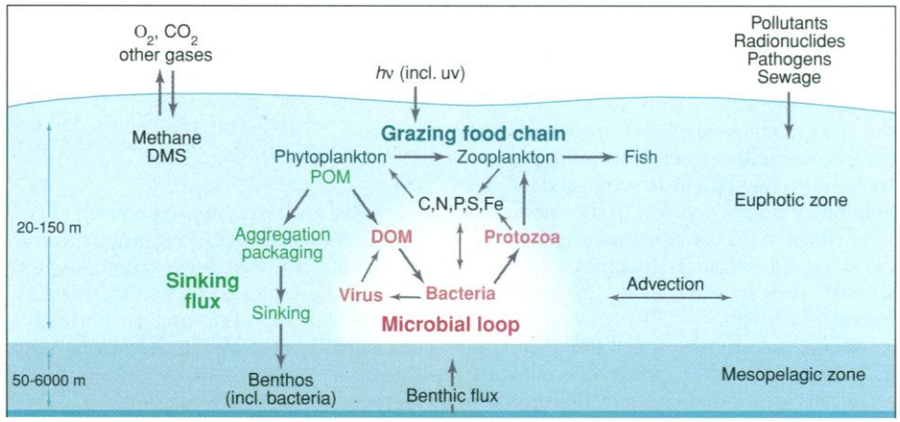
Microbial Control of Oceanic Carbon Flux: The Plot Thickens

Farooq Azam

Photosynthesis fixes carbon into organic matter in the ocean. Biological forces then paint intricate flux patterns for carbon in ocean space and in time, as it flows through the food web, becomes stored in the sediments and exchanged with the atmosphere. Predicting how these carbon flux patterns might respond to global change (or to human manipulation) is a primary reason for learning more about the workings of the ocean's carbon cycle. The flux patterns are a result of intricate interactions of a diverse biota with a physically and chemically complex pool of organic matter. It now seems that things will get even more complicated before they get simpler. New fundamental findings on the roles of microbes in the fate of organic matter and, recently, on the nature of the organic matter itself (*1–4*) must be properly assimilated before we can hope to construct ecosystem models to predict the patterns of carbon flux. This impetus could lead to a powerful new synthesis.

What biological forces act on photosynthetically produced organic matter in the ocean? Historically, the paradigm has been that essentially all primary production stays within the particle phase (*5*), it is eaten by herbivores, and the fate of carbon is determined by the "grazing food chain" (see the diagram in the figure below). Little dissolved organic matter is spilled for bacteria to use. It had, therefore, been implicitly assumed to be safe to ignore bacteria, protozoa, and viruses in studying the fate of organic matter—they were too sparse and not active enough (*5*). This is now changed (*5–8*): Major fluxes of organic matter, often eclipsing the grazing food chain in quantity, move via dissolved organic matter into bacteria and the "microbial loop" (*7, 8*) (figure below). Previous methods had missed >99% of microorganisms and had grossly underestimated their metabolism. Now we know from extensive field studies that in most of the ocean, organic matter flux into bacteria is a major pathway; one-half of oceanic primary production on average is channeled via bacteria into the microbial loop (*7, 8*)—a major biological force in the ocean.

Ocean basin–scale biogeochemical studies now routinely quantify organic matter fluxes into bacteria in conjunction with other major flux pathways: grazing food chain, sinking flux, and dissolved organic matter "storage." The fraction of primary production used by bacteria (F_b) is highly variable over various time and space scales (*7–10*). The magnitudes and variability of the fluxes are large enough to cause variability in flux partitioning between competing pathways (see figure below)—the microbial loop, the grazing food chain, sinking fluxes, and storage of dissolved organic matter (*8, 9*). Fish production in the eastern Mediterranean was diminished by a dominant microbial loop ($F_b = 0.85$) (*11*). In an earlier study (*12*), the richness of the fishery in



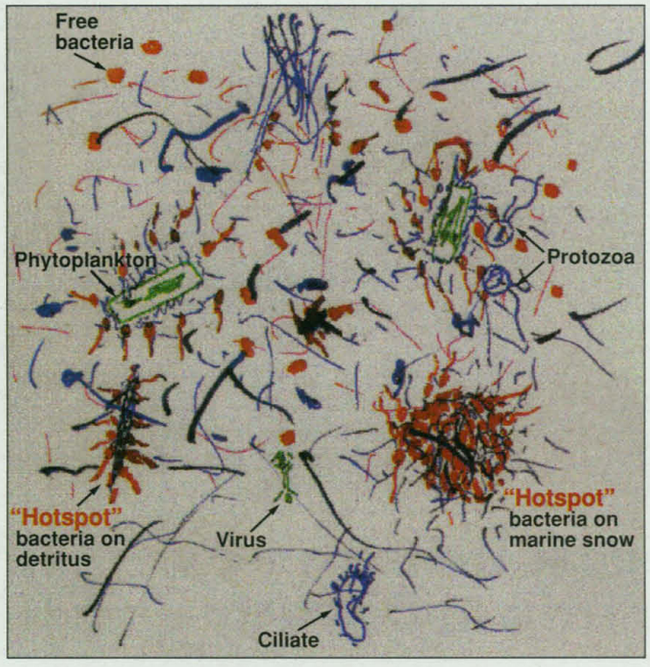
The microbial loop: classical version. Modern view of the pelagic food web, emphasizing the microbial loop as a major path for organic matter flux. Competition between the three main flux paths—grazing food chain, microbial loop, and sinking—significantly affects oceanic carbon cycle and productivity. DOM, dissolved organic matter; DMS, dimethylsulfide.

The author is at the Scripps Institution of Oceanography, University of California, La Jolla, CA 92093, USA. E-mail: fazam@ucsd.edu

coastal Newfoundland was ascribed to uncoupling of bacteria from primary production during the spring bloom. These are tantalizing but rare success stories where descriptive studies lead to interesting insights into the bacterial control of organic matter fluxes and ecosystem dynamics.

However, we lack a conceptual framework to predict variation in organic matter flux into bacteria and how it fits into the overall oceanic flux picture (for example, how the flux partitioning will respond to global change). This requires elucidating the causes and mechanisms of variability of organic matter flux into bacteria. How do bacteria interact with organic matter, and what regulates the flux of organic matter into them?

It is generally thought that pelagic bacteria passively receive dissolved organic matter leaking from the grazing food chain and diffused homogeneously. However, recent studies on the complex nature of the organic matter field (*1–4*, *13*) and behavioral strategies of bacteria (*14*) have suggested (*2*) that bacteria do not use only preformed dissolved organic matter; they also attack all organic matter, even live organisms, thus liberating dissolved organic matter. Hence, bacterial attack can profoundly modify the biogeochemical behavior of organic matter in ways not inferred from measuring cumulative organic matter fluxes into bacteria. Recognition of such "modification interactions" could add important new variables in biogeochemical models.



The microbial loop: impressionist version. A bacteria-eye view of the ocean's euphotic layer. Seawater is an organic matter continuum, a gel of tangled polymers with embedded strings, sheets, and bundles of fibrils and particles, including living organisms, as "hotspots." Bacteria (red) acting on marine snow (black) or algae (green) can control sedimentation and primary productivity; diverse microniches (hotspots) can support high bacterial diversity.

Our view of the organic matter in seawater has changed dramatically. The traditional dichotomy of particulate organic matter versus dissolved organic matter is being replaced by the concept of an organic matter continuum (*2*). Several new classes of abundant colloids, submicrometer particles, and transparent polymer particles have been discovered (*1*, *4*, *13*). This oceanic "dark matter" ranges in size from 20 nm to hundreds of micrometers. It has been proposed (*2*, *3*) that pelagic bacteria experience a gel-like polymeric matrix with colloids and particles embedded as suprapolymeric "hotspots" (*8*) (see the lower part of the figure). The interaction of bacteria with the organic matter continuum, and their behavioral response to its heterogeneity, creates microscale features—activity hotspots—with distinctive natures and intensities of biogeochemical transformations. Patchiness may also support high bacterial diversity. An important recent study by Chin *et al.* (*1*) demonstrated that polymers in seawater indeed form a gel.

Do bacteria respond to the structure of the organic matter field? Large bacterial populations can develop on hotspots—for example, marine snow, dead and even living algae—and in association with the "dark matter." [In one study, 24 to 68% of bacteria were on transparent particles (*13*)]. Oceanic bacteria (*14*) exhibit sophisticated behavior—swimming speeds of hundreds of micrometers per second, unusual swimming (run reversals), and chemosensing. The organic matter field is dominantly polymeric and suprapolymeric, so most pelagic bacteria have a diverse repertoire of surface-bound enzymes (proteases, glucosidases, lipases, phosphatases, nucleases) to cause its hydrolysis (*15*). Small-scale variation of species composition can significantly change the distributions of enzyme activities (*16*). Pelagic bacteria also have multiphasic permeases for nutrient uptake (*17*), with nanomolar to millimolar half-saturation constants, suggesting their adaptations to life in a patchy environment. Considering the intimate contact of their "digestive system" with the organic matter gel, motile bacteria are the "ultimate swimming stomachs" (*18*). They cannot avoid interacting with and changing organic matter.

Bacterial action on components of the organic matter field can modify its character in varied ways without necessarily involving large organic matter fluxes into bacteria. Two examples illustrate this point. In a study of bacterial activity on marine snow (*19*), the colonizing bacteria grew slowly but expressed large amounts of ectohydrolases, which solubilized particulate organic matter; however, because of the low carbon demand of these bacteria, most hydrolysate diffused out ("uncoupled solubilization"), thus reducing the sinking flux. Also, enzyme action was thought to increase the efficiency of the oceanic carbon pump; protease and phosphatase activities were much higher than those of α- and β-glucosidases, and this would cause preferential nitrogen and phosphate retention compared with carbon in the photic layer where it supports more carbon fixation and export. Thus, bacteria influenced the fate of carbon without a significant carbon demand. Bacterial interaction with live diatoms was examined in a mesocosm (*20*). Bacteria colonized the diatoms, grew rapidly, and expressed large amounts of ectohydrolase. Experiments suggested that ectohydrolases of attached bacteria "prune" mucus from the surface of diatoms, thereby controlling diatom stickiness and inhibiting aggregation. Bacterial modification of algal surfaces, a microscale process, could increase the persistence and intensity of algal blooms, as well as influence the sinking flux, with profound ecological and biogeochemical implications. Attached bacteria could also expose the alga to high microscale concentrations of remineralized nutrients, thus enhancing carbon fixation. Partial hydrolysis of complex polysaccharides by bacterial attack could produce slow-to-degrade dissolved organic matter, resulting in carbon storage (high bacterial activity could actually produce more slow-to-degrade dissolved organic matter). This could be used by bacteria at a different place and time (for example, dissolved organic matter accumulating in Antarctic waters during summer could support the food web during winter). These and other examples show that the ecosystem-level consequences of bacteria–organic matter interactions may be pervasive in ways not currently being quantified, or even recognized, in ocean basin–scale biogeochemical studies.

Thus, behavioral and metabolic responses of bacteria to the complex and heterogeneous structure of the organic matter field at the microscale influence ocean basin-scale carbon fluxes in all major pathways: microbial loop, sinking, grazing food chain, carbon storage, and carbon fixation itself. However, studying such varied influences of bacteria on organic matter, and their spatial-temporal variations, in piecemeal fashion will only result in a conceptual patchwork without a unifying framework or predictive power. A unifying theme should derive from applying robust principles of biochemical adaptation in a realistic microenvironmental context. Biogeochemical variability could then be considered as a consequence of adaptive responses to (micro)environmental variations. This approach should also serve as a framework to understand the maintenance of microbial diversity and to make predictions on the survival of specific bacterial species, including human pathogens such as *Vibrio cholerae*, in response to ecosystem perturbations (*21*). This framework, which includes bacteria-algae interactions, should also be relevant to the prediction of algal blooms, including toxigenic species. Powerful new approaches are enabling us to study microbial ecology, including consortial activities, in an ecosystem context. New techniques allow multiple interrogations—phylogeny, metabolism, growth—at the individual cell level. These ideas and approaches should lead to a synthesis of bacterial adaptation, evolution, ecology, and biogeochemistry, and should form a basis for integrating the roles of bacteria in predictive biogeochemical models.

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BIOMEDICINE

Triplet-Repeat Transcripts: A Role for RNA in Disease

Robert H. Singer

A set of baffling human diseases—including myotonic dystrophy and Huntington's disease—are caused by expansion of a repeated sequence of three nucleotides within almost a dozen genes identified to date (*1*). With each generation, these repeats are replicated and the sequence gets longer, eventually compromising the function of the gene. The effect is dominant—only one of the two alleles of the gene need be expanded to result in the full pathology. Furthermore, the severity of the disease can be proportional to the length of the repeat expansion.

Unlike most genetic diseases, which are a result of a mutation that impairs or eliminates a gene product, the triplet-repeat diseases are likely caused by a "gain of function," in which a new function arises from the genetic defect. The new function is most easily understood when the expansion of the triplet CAG, which encodes the amino acid glutamine, occurs within the coding frame of a gene and creates a new protein with a polyglutamine tract. Huntington's disease is one example of such an expansion and is typical in that it exhibits a central nervous system pathology, as do all the polyglutamine diseases. Normal individuals can withstand a few repeats of glutamine at this position in their genes. As the polyglutamine expands, however, it disrupts the protein and affects cellular functions, possibly due to the high charge density of the expanding repeat. The new, gain-of-function protein can wreak havoc on cellular processes such as nuclear export, RNA and DNA binding, or membrane transport.

Expansions of these triplet repeats can also occur outside the coding region, but in these instances new proteins are not produced. Within this group of disorders, myotonic dystrophy is a particular curiosity. In this disease, the expansion occurs in the untranslated region of the transcript, after protein coding has occurred, and can increase the mRNA by 6 kilobases or more. As this expansion gets progressively larger in one of the alleles, the resulting pathology of the disease becomes proportionately more severe. This behavior begs for a new model of molecular cytopathology. Such a model is provided by Philips, Timchenko, and Cooper on page 737 of this issue. They propose that the gain of function in myotonic dystrophy is at least in part a result of disrupted activity of a CUG-binding protein induced by the repeats in the RNA, which prevents it from doing its normal job of splicing a certain family of genes.

The new proposal is not the first; various models have been readily forthcoming since the first description of these diseases. None has been sufficient to explain the molecular etiology. The expansion most likely occurs initially in the germ cells or early embryos, where the DNA polymerase may "stutter" on the repeats and, in doing so, expand them. Some models rely on DNA-based mechanisms to explain the pathology of these diseases—changes in chromatin organization because of nucleosome positioning, stalling of the RNA polymerase, or suppression of other genes nearby. But these models cannot explain the trans-dominant effect of the allele, the effect of one abnormal gene on the functioning of the whole cell.

Another DNA mechanism is possible.

The author is in the Department of Anatomy and Structural Biology and Cell Biology, Institute for Molecular Medicine, Albert Einstein College of Medicine, Bronx, NY 10461, USA. E-mail: rhsinger@aecom.yu.edu