principles underlying metabolic networks provides a template for gene therapy and other strategies to treat metabolic diseases, exploiting principles revealed in simpler, better controlled systems.

An important opportunity is provided by the network features of cellular signaling pathways. Although previously studied in isolation, these pathways are now known to interact with one another (cross-talk): One ligand may regulate the expression of more than one gene, or the expression of a single gene may be affected by more than one ligand (*12*). Technologies—such as DNA microarrays, quantitative proteomics, and improved metabolite measurement methods—that quantify important classes of intracellular variables are proving invaluable for deciphering this cross-talk. The main challenge ahead is the development of computational methods to integrate and make optimal use of such technologies for the elucidation of cell physiology at scales comparable to those now attainable at the gene expression level. Metabolic engineering will be pivotal in this endeavor while continuing its pursuit of cellular property improvement for industrial and medical applications.

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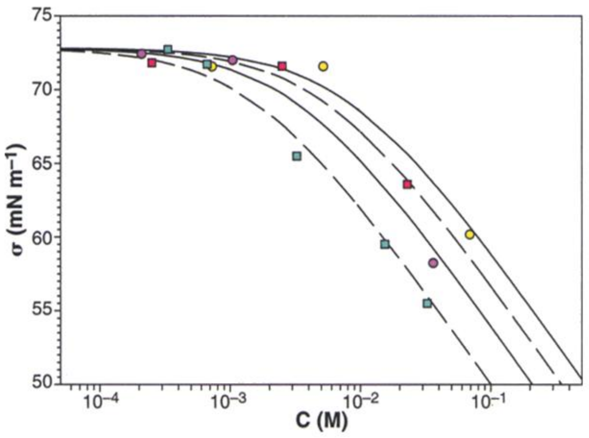
PERSPECTIVES: ATMOSPHERIC SCIENCE

Reshaping the Theory of Cloud Formation

Robert J. Charlson, John H. Seinfeld, Athanasios Nenes, Markku Kulmala, Ari Laaksonen, M. Cristina Facchini

Droplet clouds are the most important factor controlling the albedo (reflectivity) and hence the temperature of our planet. Man-made aerosols have a strong influence on cloud albedo, with a global mean forcing estimated to be of the same order (but opposite in sign) as that of greenhouse gases (*1*), but the uncertainties associated with the aerosol forcing are large. Recent studies indicate that both the forcing and its magnitude may be even larger than anticipated.



Surface tension lowering by organics in cloud water. Surface tension decrease with respect to pure water as a result of water-soluble organic carbon in cloud water (expressed as moles per liter of carbon). Data from Tenerife (Spain) and Po Valley (Italy) taken by one of the authors (M.C.F.).

Cloud optical properties are controlled by the sizes and numbers of the droplets in the cloud, which are, in turn, governed by the availability of atmospheric particles that serve as cloud condensation nuclei. Twomey (*2*) suggested that an increase in atmospheric aerosols from anthropogenic emissions would lead to smaller cloud droplets because the same amount of cloud liquid water is distributed among more condensation nuclei. For the same liquid water content, a cloud with more numerous, but smaller, drops has a higher albedo than one with fewer, larger drops. This phenomenon, termed the first indirect climatic effect of aerosols, could constitute a major climate forcing (*1*). But current estimates of indirect aerosol radiative forcing or of its uncertainty (*1*) do not include the combined influences of some recently identified chemical factors, each of which leads to additional negative forcing (cooling) on top of that currently estimated.

Estimates of the indirect climatic effect of aerosols are based on the theory of cloud droplet formation advanced by the Swedish scientist Hilding Köhler in the 1920s and 1930s (*3*, *4*). Köhler assumed that clouds consist of "activated" water droplets that grow spontaneously after they have reached a critical size corresponding to a critical value of the supersaturation of water vapor. Köhler further assumed that the aerosol is composed of a completely soluble salt and that the particles are in thermodynamic equilibrium until the point of spontaneous growth. Indeed, it is still generally assumed that a cloud forms only in a supersaturated water environment with all the solute coming from the particle. It has recently become clear, however, that soluble gases (*5*, *6*), slightly soluble solutes (*7*), and surface tension depression by organic substances (*8*) also influence the formation of cloud droplets, in a manner unforeseen by Köhler.

Nitric acid (HNO_3) is perhaps the most important highly soluble trace gas in the atmosphere. Ample data establish the prevalence of nitrate as a constituent of cloud and fog water in polluted air (*9–11*). In the presence of a water-soluble trace gas such as HNO_3, the critical supersaturation for that droplet is lowered as the gas condenses into a growing droplet. Depending on how it is dispersed over the aerosol population, a minute amount of soluble gas can exert a profound effect on the number of activated droplets. A striking consequence of the presence of a soluble trace gas is that clouds or fogs with micrometer-sized droplets may exist even though the droplets have not undergone traditional activation and even though the ambient relative humidity never exceeds 100% (*5*, *6*). Such "pollution clouds" have a higher droplet number concentration and a broader droplet size distribution than "clean clouds" (*12*).

Highly soluble gases are not the only compounds that can affect aerosol activation. The importance of carbonaceous compounds as components of atmospheric aerosols is well established. A variety of measurements have shown that between 20 and 60% of the carbon mass in fine (diameter <1 μm) atmospheric aerosols consists of

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R. J. Charlson is in the Department of Atmospheric Sciences and Department of Chemistry, University of Washington, Seattle, WA 98195, USA. J. H. Seinfeld is in the Department of Chemical Engineering and the Division of Engineering and Applied Science, California Institute of Technology, Pasadena, CA 91125, USA. A. Nenes is in the Department of Chemical Engineering, California Institute of Technology, Pasadena, CA 91125, USA. M. Kulmala is in the Department of Physics, University of Helsinki, 00014 Helsinki, Finland. A. Laaksonen is in the Department of Applied Physics, University of Kuopio, 70211 Kuopio, Finland. M. C. Facchini is at the Instituto di Scienze dell' Atmosfera e dell' Oceano-CNR, via Gobetti 101, 40129 Bologna, Italy. E-mail: seinfeld@caltech.edu

partially soluble organic compounds (*13–16*). A partially soluble aerosol component adds solute to the aqueous phase as the droplet grows, decreasing the critical supersaturation of the particle. Many of these organic compounds are surface active (see the figure) (*8*); if, in addition, surface tension is lowered as the substance dissolves, the critical supersaturation is further lowered, and the number of particles that can activate increases even more. In general, the lowering of surface tension associated with a dissolving substance has a stronger effect on cloud properties than the fact that the substance itself is only partially soluble, given that most water-soluble organic compounds are surface active.

As predicted by Köhler some 80 years ago, droplet activation places an upper limit on the supersaturation of water vapor that can be reached in the atmosphere. Given sufficient solute or enough depression of surface tension, or a combination of the two, the supersaturation in a given situation will decrease. At high aerosol and soluble trace gas concentrations and for low cooling rates, strict activation is not necessary for formation of a visible cloud; indeed, a continuum exists from ambient aerosol to wetter and wetter particles to unactivated clouds to activated ones. What is seen as "cloud" can, in reality, be a collection of droplets ranging from fully activated to unactivated.

By affecting cloud optical properties, these chemical phenomena may lead to nonnegligible global negative forcing (*17*) and may be as important regionally as the Twomey effect itself. To assess the importance of the indirect climatic effect of aerosols, one seeks a robust connection between cloud droplet population and a prognostic variable from global aerosol models. How that link might depend upon chemical cloud activation effects, including variations in aerosol chemical composition, solute water solubility, solute surface tension lowering, and condensation of trace gases, remains to be determined. Lack of global data on these activation effects poses additional uncertainty beyond that already recognized by the Intergovernmental Panel on Climate Change (*1*), making the largest uncertainty in estimating climate forcing even larger.

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17. Preliminary simulations of cloud albedo differences relative to a baseline case, in which the cloud is formed from an aerosol composed exclusively of soluble salt, show that the presence of surface tension–lowering substances or a soluble gas (HNO_3) leads to an increase in the number of activated droplets and cloud albedo that, if applied globally, is of a climatological significance.

PERSPECTIVES: PLANETARY SCIENCE

Life Without Photosynthesis

Christopher F. Chyba and Kevin P. Hand

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Recent planetary exploration has shown that oceans of liquid water appear to be common in our solar system. Galileo spacecraft measurements of induced magnetic fields suggest that Jupiter's large icy moons—Europa, Ganymede, and Callisto—all harbor salty oceans beneath the surface ice (*1*). This is exciting news for extraterrestrial biology because life as we know it requires liquid water.

But life also requires energy. Life that does not harvest sunlight directly obtains that energy from chemical disequilibrium in the environment. On Earth, photosynthesis, coupled with organic carbon burial, has produced oxidizing surface conditions that provide chemical disequilibria for biology to exploit. Sunlight cannot, however, penetrate kilometers of ice. The chemical energy available in the form of disequilibrium concentrations of redox reactants is therefore substantially less, raising the specter of entropic death for subsurface oceans—be they within icy satellites or on an earlier "snowball Earth" (*2*). All is not lost, however, because nonphotosynthetic sources of molecular oxygen (O_2) and other oxidants are available even to subsurface oceans. Here we estimate these for Europa (see the figure).

Europa's surface is continuously bombarded with charged particles accelerated in Jupiter's magnetic field. They produce H_2O_2, O_2, and other oxidants at Europa's surface (*3*), as well as hydrogen, which mostly escapes into space. The radiation products are mixed to a depth of 1 m through impact "gardening" (the slow overturning of Europa's surface by meteorite impacts) (*4*). Spectral observations of H_2O_2 only probe the upper ~0.1 mm of the surface, where some H_2O_2 is destroyed photolytically (*3*). These observations therefore give a lower limit to H_2O_2 concentrations in the upper meter.

It is not known whether the top of Europa's ice shell mixes with the ocean on geological time scales. If it does, and if H_2O_2 production is not limited by the quantity of H_2O available in the upper meter of Europa's surface (*4*), up to $\sim 10^{12}$ mol year^{-1} equivalent O_2 (*5*) could reach Europa's ocean (*3, 4*). A lower limit may be estimated by assuming that the H_2O_2 concentration observed at Europa's surface holds throughout the upper 1 m of gardening depth (*4*). In this case, $\sim 10^9$ mol year^{-1} equivalent O_2 could mix into the ocean. These limits straddle Earth's abiotic source of O_2 (7×10^9 mol year^{-1}) owing to photolysis of water vapor and loss of H_2 to space (*6*).

Were there no sinks, 10^{12} mol year^{-1} equivalent O_2 could produce a ~20 mM oceanic O_2 concentration over the estimated ~50-million-year resurfacing time scale of Europa's crust (*3*). Some deep-ocean macrofauna on Earth live at concentrations as low as 20 to 40 μM (*4*). These considerations suggest that if suitable carbon compounds were available in the ocean, substantial biomass production—10^{10} to 10^{14} g year^{-1}, depending on O_2 production and microbial growth efficiencies—could be achieved (*4, 7*).

On Earth, photosynthesis produces about 10^{16} mol year^{-1} O_2, but this is nearly balanced by the sinks of respiration and decay (*6*). What sinks might be present on Europa? Hydrothermal activity levels have been estimated based on calculations of internal heating. According to these highly uncertain estimates, $\sim 10^{10}$ liters year^{-1} of hydrothermal fluid may be generated at Europan hydrothermal vents (*8–10*). If reductants such as H_2S, H_2, CH_4, and Fe are present in this fluid at concentrations of around 50 mM (*9*), about 10^9 mol year^{-1} of reductants would enter the ocean from this source. O_2 input could at least match this potential sink, suggesting that Europa's ocean could have become oxidizing over time.

It is unknown how much carbon Europa may have incorporated at the time of its for-

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C. F. Chyba is at the Center for the Study of Life in the Universe, SETI Institute, Mountain View, CA 94404, USA; the Center for International Security and Cooperation (CISAC), Stanford University, Stanford, CA 94305, USA; and in the Department of Geological and Environmental Sciences, Stanford University, Stanford, CA 94305, USA; e-mail: chyba@seti.org. K. P. Hand is in CISAC and the Department of Mechanical Engineering, Stanford University, Stanford, CA 94305, USA.