Cooperation among circadian oscillators. Circadian oscillators in the SCN and in the forebrain regulate rhythms of locomotor activity, sleep, and feeding. In the SCN, CLOCK (C, orange) and BMAL1 (B, blue) form heterodimers that influence rhythmic transcription of target genes, such as per and cry. In the forebrain, rhythmic transcription is regulated by NPAS2 (N, yellow), which forms heterodimers with BMAL1. Light acts on heterodimers that influence rhythmic transcription of target genes, such as SCN and in the forebrain regulate rhythms of locomotor activity, sleep, and feeding are decoupled by the forebrain clock, whereas the daily light/dark cycle acts primarily on the SCN. It is probable that the forebrain and the SCN, responding to different inputs, together regulate normal entrainment of circadian behavior to diverse temporal signals in the environment.

The circadian phenotype of NPAS2-deficient mice is perhaps more subtle than those of mice carrying other circadian mutations or gene deletions that abolish rhythmicity entirely or dramatically change its period. The new phenotype is nonetheless instructive. Its very subtlety emphasizes the importance of painstaking analysis of whatever assay is being used to measure rhythmicity. In previous studies, little attention has been paid to the fine structure of locomotor behavior patterns, and important findings may have been missed. More importantly, the work of Dudley et al. reveals the first tissue-specific specialization within the circadian molecular machinery in mammals. It seems unlikely that this is the only such variation on the circadian molecular theme. Oscillators in other areas of the central nervous system and in the periphery may well vary in subtle ways that affect their tissue-specific functions or their coupling to the rest of the circadian system. The findings of Dudley et al. represent an important step in what will be a difficult but rewarding analysis of the system that has been called the "biological clock" but might be better characterized as the "circadian temporal program."

References

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Snapshots of Water at Work
William H. Robertson, Eric G. Diken, Mark A. Johnson

The molecular structure of water is simple. But compared to most molecular liquids, the degree of deformation of the H2O molecule changes dramatically as it fluctuates in and out of the cooperative hydrogen bonds afforded by extended networks. Add an ion, which can further distort the sheath of water surrounding it, and you have a seriously complex situation.

Two reports in this issue address the dynamical aspects of how water responds to the presence of a charged solute and how the mechanism of a chemical reaction between two negatively charged reactants depends on their initial separation in solution. On page 347, Omta et al. (1) use ultrafast lasers to establish the unique character of water molecules in the hydration shell around an anion. And on page 349, Rini et al. (2) show how the hydration shell participates in a photoinitiated acid-base reaction by shuttling the proton between reaction partners. Both studies demonstrate the power of time-resolved infrared spectroscopy to isolate the contribution of different regions of the solvation to bulk behavior (in this case viscosity and reaction rate, respectively).

Omta et al. (1) call into question the meaning of the traditional notion (3) that some aqueous ions are “structure makers” while others are “structure breakers.” To quantitatively address the issue of solute-imposed structure on water, they argue that a measurable quantity related to structure is the viscosity. The viscosity usually controls diffusive motions, including orientational diffusion. Hence, interrogation of the orientational relaxation of water molecules as a function of distance from an ion—in this case, ClO4−—should reveal variations in the local structure.

By carrying out this measurement in the infrared region of the OH stretching vibrations, Omta et al. selectively probe water molecules that reside either in the primary hydration shell or in the more distant bulk water. For water molecules near the ClO4− ion, the relaxation times are long, as one might expect for molecules that are strongly anchored to the anion. Surprisingly, however, for all other water molecules detected in the experiment (away from the ion), the rate is found to be identical to that of the pure liquid and independent of the concentration of the solute.

The dominant effect of the ion on water structure thus appears to be restricted to the immediate vicinity of the ion, rather than propagated into the fabric of the surround-
ing liquid. But the ClO$_4^-$ ion is known to increase the macroscopic viscosity of aqueous solutions. This paradox is resolved by noting that a larger effective radius of the ions would account for the increased viscosity (4). The required radius corresponds nicely to the size of the ion and its associated hydration shell. Thus, the hydration shell seems to act like a chemically distinct species whose overall size controls the macroscopic viscosity.

The localized character of the hydration shell around a solute anion naturally raises the important question of its molecular structure. Recent studies (5) of ions surrounded by a controlled number of water molecules have shed light on this issue. For example, Robertson et al. (6) have identified the intrinsic structures of the hydration shells around the hydroxide and fluoride ions, and have started to map how water interacts with complex anions such as acetate (see the figure) (7). These organic species are more challenging because they possess both hydrophilic and hydrophobic domains (3).

Water structure also plays a key role in the kinetics of acid-base reactions. Rini et al. (2) present an elegant ultrafast study of a photoinitiated proton transfer between an anionic proton donor and the acetate-ion proton acceptor. With a universal infrared probe, the authors can independently monitor the decay of the photo-acid and the rise of both its conjugate base and the acetic acid product. They thus provide an unusually complete picture of how all species in the reaction evolve.

The resulting time profiles clearly differentiate between reactions that occur through initially hydrogen-bonded reactant pairs and those that occur by diffusion of the reactants to form a collision complex. At low concentration, Rini et al. observe a third pathway, in which the photo-acid donates a proton to the water molecules in the hydration shell to form the hydronium ion. This species then migrates to find and neutralize the acetate ion long after the appearance of the photo-acid’s conjugate base. Water thus plays an integral role in the reaction by shuttling the proton between the reaction partners.

Water in action. Schematic illustration of how the hydration shell around the anionic part of the acetate ion participates in the reaction with H$_2$O$^+$. Rini et al. (2) provide evidence for this proton shuttle mechanism. Omta et al. (7) show that the effect of an anion on water structure is highly localized.

References

PERSPECTIVES

The two studies (1, 2) illustrate how detailed mechanistic insights into aqueous processes can be obtained with ultrashort time resolution, which allows researchers to look beneath the averaging inherent in bulk measurements. Together with cluster studies, these ultrafast techniques provide rigorous tests of widely accepted molecular-level pictures (8, 9).

One of the longstanding challenges in aqueous chemistry, raised by the work of Rini et al., is the molecular-level mechanism of proton transport (8, 10, 11). An important step toward this goal is to extend the ultrafast infrared methods demonstrated in the bulk studies reported here (1, 2) to the cluster regime. The advantages of the small systems are that the reactions can be initiated with precisely controlled energy and starting geometry, and the dynamics can be treated with the powerful theoretical tools refined in the study of molecular photochemistry.

PALEONTOLOGY

Making the Best of a Patchy Fossil Record

Andrew B. Smith

Paleontologists have been striving to document the history of species diversity through geological time for nearly 150 years. Until recently, the favored method involved nothing more complex than counting the fossils recorded from each time interval, and a great effort has gone into compiling taxonomic and stratigraphic data to quantify diversity trends through time.

However, this simple approach comes with a price: It is only valid if each time interval has been sampled to the same extent. On page 358 of this issue, Crampton et al. (1) show that this may not be the case. Working from a massive database of fossil marine molluscs and fossil localities in New Zealand covering the past 60 million years, they point out that sampling effort is far from uniform. Furthermore, sampling effort correlates with the amount of rock that crops out at the surface.

Paleontologists have long been aware that the more thoroughly a rock unit is sampled, the more specimens are found. This, in turn, leads to higher recorded diversity: All other things being equal, if only a small amount of rock is present at outcrop, then the total diversity recorded is likely to be much lower than if a large area of outcrop is available for sampling.

Rarefaction, a statistical technique that uses subsampling to reduce populations to the same size, can be used to remove such bias. Initial large-scale studies with this approach (2) suggest that global biodiversity patterns may indeed be substantially biased by unequal sampling. However, rarefaction requires more data than are generally available in global taxonomic compilations. Hence, more indirect ways of estimating sampling levels are required. Two have recently been used.

First, estimates of how extensively a time interval has been sampled have been based on the number of named geological formations (that is, mappable units of rock laid down in a distinct past environmental setting). The more geological formations that are recorded in a time interval, the greater the range of environments that exist to be