ules—groups of nodes (for example, proteins and metabolites) that are responsible for discrete cellular functions (*6*). These modules are nested in a hierarchical fashion and define the cell's large-scale functional organization (*8*).

The papers by Lee *et al.* (*2*) and Milo *et al.* (*3*) offer key support for the cellular organization suggested by the complexity pyramid (see the figure). Using 106 tagged transcription factors of the budding yeast *Saccharomyces cerevisiae*, Lee *et al.* have systematically identified the genes to whose promoter regions these transcription factors (regulators) bind. After establishing transcription factor binding at various confidence levels, they uncovered from 4000 to 35,000 genetic-regulatory interactions, generating the most complete map of the yeast regulatory network to date. The map allows the authors to identify six frequently appearing motifs, ranging from multi-input motifs (in which a group of regulators binds to the same set of promoters) to regulatory chains (alternating regulator-promoter sequences generating a clear temporal succession of information transfer). A similar set of regulatory motifs was recently uncovered in the bacterium *Escherichia coli* by Alon and co-workers (*9*). In their new study, Milo, Alon and colleagues provide evidence that motifs are not unique to cellular regulation but emerge in a wide range of networks, such as food webs, neural networks, computer circuits, and even the World Wide Web (*3*). They identified small subgraphs that appear more frequently in a real network than in its randomized version. This enabled them to distinguish coincidental motifs from recurring significant patterns of interconnections.

An important attribute of the complexity pyramid is the gradual transition from the particular (at the bottom level) to the universal (at the apex). Indeed, the precise repertoire of components—genes, metabolites, proteins—is unique to each organism. For example, 43 organisms for which relatively complete metabolic information is available share only ~4% of their metabolites (*7*). Key metabolic pathways are frequently shared, however, and—as demonstrated in this issue (*2, 3*) and elsewhere (*9*)—so are some of the motifs. An even higher degree of universality is expected at the module level; although quantitative evidence is lacking, it is generally believed that key properties of functional modules are shared across most species. The hierarchical relationship among modules, in turn, appears to be quite universal, shared by all examined metabolic (*8*) and protein interaction networks. Finally, the scale-free nature (*7*) of the network's large-scale organization is known to characterize all intracellular relationships documented in metabolic, protein interaction, genetic, and protein domain networks. The Milo *et al.* study now raises the possibility that the complexity pyramid might not be specific only to cells. Indeed, scale-free connectivity with embedded hierarchical modularity has been documented for a wide range of nonbiological networks. Motifs are now known to be abundant in networks as different as ecosystems and the World Wide Web.

These results highlight some of the challenges systems biology will face in the coming years. Lately, we have come to appreciate the power of maps—reliable depositories of molecular interactions. Yet existing maps are woefully incomplete; key links between different organizational levels are missing. For example, we lack the systematic tools to map out lipid-protein or metabolite–transcription factor interactions in vivo. The topological relationships among pathways, motifs, modules, and the full network will also have to be studied in much more detail. Most important, maps must be complemented with detailed measurements of cellular dynamics, recording the timing of processes that take place along the links. This topic is increasingly studied within isolated motifs and modules (*10*) but has received relatively scant attention at the whole-network level. Despite all of these recent challenges, an initial framework offering a rough roadmap appears to have been established. As we seek further insights, we increasingly understand that our quest to capture the system-level laws governing cell biology in fact represents a search for the deeper patterns common to complex systems and networks in general. Therefore, cell biologists, engineers, physicists, mathematicians, and neuroscientists will need to equally contribute to this fantastic voyage.

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PERSPECTIVES: ARCHAEOLOGY

Climate and Human Migrations

Tom D. Dillehay

Archaeological records are affected by a variety of natural and cultural processes at a variety of spatial and temporal scales (*1*). A given cultural phenomenon may appear across a broad range of environments, or may be limited to a narrow range of environments and time periods. Paleoecological studies can help to discriminate between these cases. But most reconstructions of early human ecosystems are based on the excavation and interpretation of individual archaeological sites. Paleoecological studies of long-term climatic change are also often limited in scope (*2*).

Integrative studies of multiple sites, multiple records, and larger areas over long time periods can dramatically change the interpretation (*3–7*). On page 821of this issue, Núñez *et al.* (*8*) demonstrate the power of such a comprehensive approach. They closely integrate paleoecological and archaeological analysis to study the long-term interaction between hunter-gatherers and changing environments over the last 15,000 years in the Atacama desert of northern Chile.

The authors examine why initial human occupation occurred about 2000 years later in this hyperarid region than in more humid forested regions in south central Chile (*9*), and several centuries later than in less arid areas in the central and southern Andes. They also ask why a long "Silencio Arqueologico" (a cultural hiatus in the archaeological record) took place between 9500 and 4500 calendar years before the present (cal yr B.P.).

The possible reasons for these variations in human presence considered by Núñez *et al.* include migration lags, inhospitable late Pleistocene environments, biased survey and visibility, and rapid and long-term abandonment of the region. The study illustrates the importance of integrating local environmental and archaeological information in studying regional human ecosystems and in comparing the findings with other regions at a larger scale.

The authors assume that high-altitude ancient lakes (paleolakes), mid-altitude grasslands (puna), and low-altitude wetlands best indicate changes in habitat ex-

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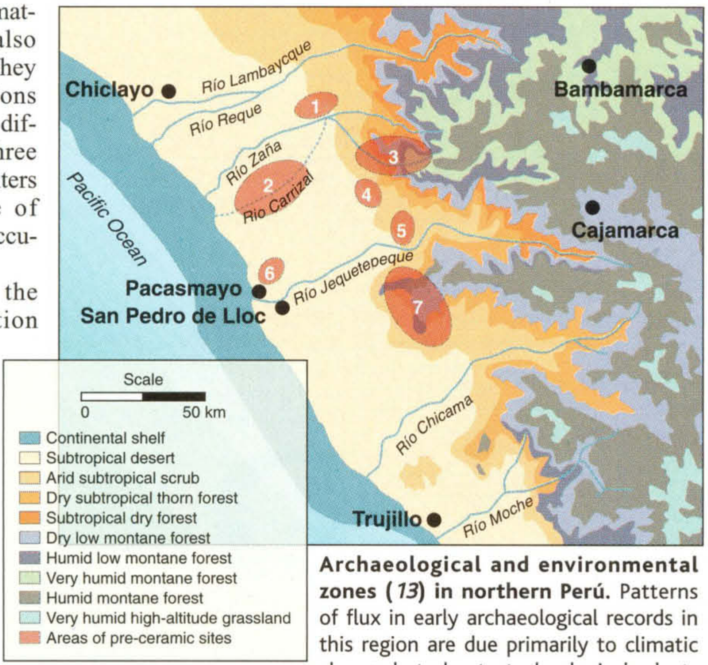
ploitation due to regional climatic change. Although they also examined open campsites, they concentrated their excavations on caves and rock shelters at different elevations in these three settings. Caves and rock shelters usually contain evidence of long-term cycles of human occupation and abandonment.

Núñez *et al.* show that the reason for human occupation fluctuations and the Silencios Arqueologicos was climatic change. When vegetation and animal life were abundant, mobile hunters moved into higher elevations between 11,800 and 10,500 cal yr B.P. They practiced seasonal migrations between the higher paleolakes and lower wetlands between 9900 and 8800 cal yr B.P. Around 9000 cal yr B.P., the paleolakes dried up and were abandoned until about 4500 cal yr B.P., when human reoccupation occurred along the shorelines of reduced lake levels. At this time, movement between paleolakes and wetlands was reestablished.



Archaeological and environmental zones (*13*) in northern Perú. Patterns of flux in early archaeological records in this region are due primarily to climatic change but also to technological adaptability, resource availability, and social organization (*14*). People were always present in the area from at least 11,000 cal yr B.P., but during periods of increased aridity they primarily occupied spring-fed wetlands at different elevations between the coastal plains and foothills. Zones 2 and 6 were inhabited only between ~11,000 and 9000 cal yr B.P. Zones 1, 4, and 5 reveal human activity between 11,000 and 5000 cal yr B.P. Zone 3 was occupied primarily between 11,000 and 7000 cal yr B.P. Since the late Holocene, all areas have been inhabited intermittently.

The findings lend support to the hypothesis that some of the first people in the Atacama region focused on favorable, humid habitats such as lakes, springs, and streams during periods of decreased aridity. During periods of increased aridity, people were absent at the higher elevations, especially during the long Silencio from 9000 to 4500 cal yr B.P. Núñez *et al.* point out that in more humid conditions such as central Chile (*10*) and the central highlands of Peru, the Silencio does not exist or is reduced in time and space to "micro-Silencios."

Around 14,600 cal yr B.P., when people occupied the rainforests of south central Chile, there is no evidence of human occupation anywhere in the Atacama region. When favorable climatic conditions and biotic regimes were established between 10,000 and 9000 cal yr B.P., people colonized these previously inhospitable environments within a few hundred years, indicating that they lived nearby and perhaps occasionally probed and explored the edges of the region.

Late Pleistocene archaeological site. In the foreground is a dense scatter of stone artifacts and hearths of a campsite dating around 10,300 cal yr B.P. The site is located 8 km from and 800 m above the fog-covered valley floor of the Zaña River in the background. Although no late Pleistocene sites appear on the valley floor, they are present near springs in the distant hills of zone 3.

Such exploratory behavior may account for the extremely low human activity observed by Núñez *et al.* in some environments during periods of extreme climatic stress. Although fluctuations in aridity levels appear to be the primary factor influencing continuities and hiatuses in the human presence, the authors also recognize that sampling bias and visibility may account for occupational fluxes in certain places at certain times.

The study raises other questions with important implications. It is clear that for climatic, social, and other reasons, people disappear from the archaeological record from time to time (see the figures). Patterns of presence and absence need to be factored in when making claims about early human migration and in extrapolating local site-specific findings from one region to another. If other early human ecosystems in the Americas varied across time and space as they did in the Atacama, then initial human colonization could not have been a blitzkrieg movement (*11, 12*) but was likely a stutter-step, characterized by hesitancy followed by rapid transience through or around inhospitable environments and slow migration through hospitable ones.

The report by Núñez *et al.* illustrates that our understanding of past ecosystems and early human migration and strategies of land use is enhanced by asking specific questions about specific habitat changes during reduced time periods. By going beyond the comparison of local records and performing integrative research, we can shed light on the relation between human societies and climate change.

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