integrative variables and thousands or millions of connectivity variables (*24*) and perhaps integrative emergents yet to be discovered. The answers extend well beyond explanation by the neuron acting as a single functional unit.

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STRUCTURAL BIOLOGY

A Ribosomal Coup: *E. coli* at Last!

Peter B. Moore

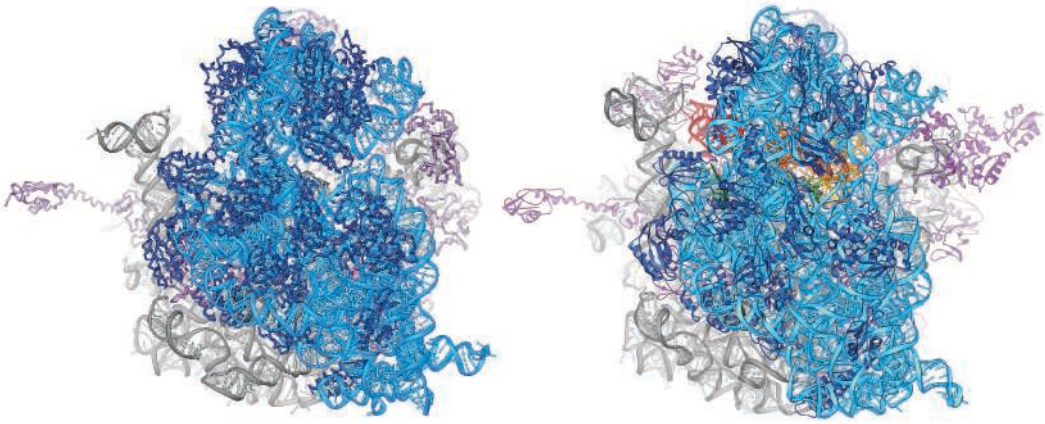
On page 827 in this week's issue, Schuwirth *et al.* (*1*) report an atomic resolution (3.5 Å) crystal structure for the 70*S* ribosome from the bacterium *Escherichia coli* (see the figure). More accurately, they report the atomic resolution for two such structures, because there are two, nonequivalent copies of the 70*S* ribosome per asymmetric unit in the crystals they have analyzed. The ribosome is the ribonucleoprotein enzyme that catalyzes messenger RNA–directed protein synthesis in all organisms, and the 70*S* ribosome, which is a 1:1 complex of a large and a small ribosomal subunit, is the particle that synthesizes proteins in prokaryotes. Because this enzyme plays a central role in gene expression, its structure has long been sought by molecular biologists.

The structures reported by Schuwirth *et al.* are by no means the first ribosomal crystal structures to appear. We already have a 2.4 Å resolution crystal structure for the large ribosomal subunit from *Haloarcula marismortui* (*2*), and a 3.1 Å resolution structure for the large ribosomal subunit from *Deinococcus radiodurans* (*3*). Two versions of the structure of the small ribosomal subunit from *Thermus thermophilus* have appeared, one at a resolution of 3.0 Å (*4*), and the other at a slightly lower resolution (*5, 6*). In addition, there is a structure for the 70*S* ribosome from *T. thermophilus* determined at 5.5 Å (*7*). Our sense of *déjà vu* is heightened by the impression that these new structures look very much like those that have appeared before (see the figure). Thus, we might wonder why these new structures should be considered noteworthy (which they are).

There are three reasons why these structures deserve attention. First, the structures that Schuwirth and colleagues have solved are that of the ribosome from *E. coli*. Since 1960, the *E. coli* ribosome has been the ribosome of choice for biochemists and molecular biologists; for no other ribosome is the information more complete. Observations made with the *E. coli* ribosome have been extensively used to interpret all the ribosome structures published previously, all of which came from other organisms. The argument has been that the extensive sequence homology that exists between ribosomes from different species justifies such cross-species comparisons. However, at some level, observations made on ribosomes from a mesophilic eubacterium like *E. coli* cannot be valid for ribosomes obtained from an extreme archaeal halophile like *H. marismortui*, or from an extreme eubacterial thermophile like *T. thermophilus.* These concerns can now be directly addressed.

Second, Schuwirth *et al.* are not the first investigators to attempt the crystallization of ribosomes from *E. coli*. For decades, laboratories all over the world have tried to obtain such crystals because of the obvious importance of the structures that might emerge from them. Schuwirth *et al.* are the first to obtain ribosomal crystals from this species that were worth analyzing, and that in itself is a coup. It should also be noted that the asymmetric unit of the crystals they have solved is gigantic; it contains roughly 5 megadaltons of macromolecular material. Determining structures this large is not trivial, even when much is known about them already, as was the case here.

Third, there is the matter of resolution. The resolution of the best 70*S* structure pub-



Structures of the 70*S* ribosome from two prokaryotes. (**Left**) *E. coli.* ribosome at 3.5 Å resolution [from (*1*)]. (**Right**) *T. thermophilus* ribosome at 5.5 Å resolution [from (*7, 9*)]. Both are oriented such that the small subunit [ribosomal RNA (light blue) and protein (dark blue)] is in the front.

The author is in the Department of Chemistry, Yale University, New Haven, CT 06520–8107, USA. E-mail: peter.moore@yale.edu

lished previously is 5.5 Å. In electron density maps in that resolution range, nucleic acid helices look like curved ribbons whose constituent nucleotides are often difficult to delineate, and protein density is hard to interpret at all. Nevertheless, a great deal was learned from those electron density maps because relevant structures that had been solved at higher resolution before could be fitted into them. The problem with the 70*S* model that emerged is that wherever its structure deviated from that of the structures being fit into its electron density maps, it was difficult to be sure what was going on. In 3.5 Å resolution electron density maps, such as those that led to the 70*S E. coli* structure reported by Schuwirth *et al.*, these ambiguities disappear because individual nucleotides are clearly visualized, and protein electron density is independently interpretable.

What has been learned? The structures presented by Schuwirth *et al*. are not the last word about the information contained in the particular crystals examined. Ribosomal proteins are not fully modeled at this point, and the structures are not fully refined. In addition, the crystals analyzed by Schuwirth *et al.* lack transfer RNAs or any of the other proteins, nucleic acids, or small molecules that interact with the ribosome during protein synthesis. Nevertheless, several themes clearly emerge. The structures of the bridges that hold the two subunits together are clear, which is important because the bridges are critical functionally: The two subunits of the ribosome not only communicate during protein synthesis, they also engage in coordinated, relative motions (*8*). In addition, the two 70*S* structures reported by Schuwirth *et al.* differ in the orientation of the head domains of their small subunits, and in neither is the head domain position the same as it is in the *T. thermophilus* 70*S* ribosome structure now available (*7*). Movements of the small subunit's head domain like the ones reported by Schuwirth *et al.* occur during protein synthesis [e.g., (*8*)]. It is now possible to understand how these motions occur at the molecular level, and to propose models for how they might be coupled to the events of protein synthesis. It remains to be seen what the small differences in conformation between the large ribosomal subunit of these *E. coli* ribosomes and the large ribosomal subunit structures of other organisms actually mean. Thus, the ribosome structures obtained by Schuwirth *et al*. really do advance our understanding of protein synthesis. Now that high-quality crystals are available for the *E. coli* 70*S* ribosome, the rate at which new information is obtained should increase.

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ATMOSPHERIC SCIENCE

Water Vapor Feedback in Climate Models

Robert D. Cess

General circulation models (GCMs) are the most detailed computer simulations available for projecting climate change caused by increasing greenhouse gases, as well as other anthropogenic changes. These numerical models contain numerous parameterizations of physical processes occurring within the climate system (that is, small-scale processes have to be described within the models). As a result, there is a need to devise ways of testing these parameterizations and processes within GCMs. On page 841 of this issue, Soden *et al*. (*1*) report an important reality check on one such process: the role of atmospheric water vapor in climate change.

It has long been known (*2*) that cloud-climate interactions constitute a major uncertainty in attempting to project future climate change with a GCM. As an illustrative example, if global cloud cover were to decrease because of climate warming, then this decrease reduces the infrared greenhouse effect due to clouds. Thus, the climate system is able to emit infrared radiation more efficiently, moderating the warming and so acting as a negative feedback mechanism. But there is a related positive feedback in this example that would increase the warming: The solar radiation absorbed by the climate system increases because the diminished cloud cover causes a reduction of reflected solar radiation by the atmosphere.

The situation is actually far more complicated than in this simple example, because changes in cloud cover will undoubtedly depend on cloud type and geographical location. Moreover, there would likely be associated changes in cloud altitude and cloud optical depth. One test of cloud-climate interactions within a GCM is to determine, relative to satellite observations, how well a GCM represents the radiative impact of clouds on the model's climate during the 5 years encompassing 1985 to 1989, and the top panel of the figure demonstrates that many models do rather poorly in this respect. And with regard to those models that do agree well with Earth Radiation Budget Satellite observations, it must be emphasized that this test is a necessary, but not sufficient, test of a model.

Another feedback mechanism is water vapor feedback. Water vapor is the atmosphere's dominant greenhouse gas, and a change in its concentration associated with a change in climate would alter the greenhouse effect of the atmosphere, thus producing a feedback mechanism. In 1967 it was proposed (*3*) that the atmosphere might conserve its relative humidity, and if so, this would lead to a positive feedback because a warmer atmosphere would contain more water vapor, thus amplifying the warming. And indeed, GCMs do tend to conserve global mean atmospheric relative humidity, as is shown for one such model in the bottom panel of the figure. But for more than a decade there has been considerable debate on this issue, with suggestions that water vapor feedback might actually be a negative feedback mechanism.

Soden *et al.* (*1*) present a very clever way of testing one aspect of water vapor feedback. As they point out, observed moistening trends in the lower troposphere have been linked to corresponding changes in surface temperature. But attempts to observe a moistening trend in the upper troposphere have proven to be unsuccessful, and this is the issue that Soden *et al.* address. They accomplish this by using clear-sky satellite radiance measurements from the High Resolution Infrared Radiometer Sounder channel centered at 6.7 μm (channel 12), which measures a portion of the 6.3-μm water vapor absorption band and therefore is sensitive to water vapor in the upper troposphere. They then compare the channel 12 observations of global mean blackbody temperature, for the

The author is at the Institute for Terrestrial and Planetary Atmospheres, Marine Sciences Research Center, State University of New York, Stony Brook, NY 11794, USA. E-mail: rcess@notes.cc.sunysb.edu