Ribosomes are the protein synthesis machines in the cell. They read out the genetic information encoded in messenger RNA (mRNA) molecules and translate it into proteins. In prokaryotes, these molecular machines are assembled from 3 RNA and ~50 protein molecules, forming a small subunit (30S) where recognition and decoding of mRNA takes place, and a large subunit (50S) where peptide bond formation is catalyzed. Understanding the molecular mechanism of protein synthesis requires the high resolution structure of the ribosome, which has been a long sought-after goal of many structural biologists.

Last year, we were treated to the structures of both 30S and 50S subunits at atomic resolution (for a review, see Puglisi et al. Nature Struct. Biol. 7, 855–861), which provided clear evidence that the ribosome is indeed a ribozyme—that is, peptide bond formation is most likely catalyzed by the RNA component of this machine. However, a ribosome is a dynamic machine with many moving parts, and static structures of the subunits do not provide a complete picture of the protein synthesis process. Therefore, structural characterization of the ribosome in various functional states would further our understanding of its mechanism.

One important step in protein synthesis is the initiation process, which requires correct recognition of the start codon on the mRNA by the initiator transfer RNA (tRNA) at the peptidyl-tRNA binding site (P-site). In prokaryotes, this task involves the formation of a dynamic complex containing the 30S subunit and three initiation factors, IF1–3. To define the molecular interactions that may be important in the initiation process, Carter et al. (Science, in the press, 2001) have determined the crystal structure of the 30S subunit in complex with IF1.

The structure of the 30S–IF1 complex (overview (top right panel) and closeup view (top left panel)) shows that IF1 (purple) binds to a region near an RNA duplex known as helix 44 (H44; cyan) and a small subunit ribosomal protein S12 (orange), occluding the aminoacyl-tRNA binding site (A-site). The overall structure of IF1 is not substantially altered from that in solution; however, IF1 binding induces small but significant changes in the 30S structure. First, two bases that are implicated in the decoding process — A1492 and A1493 (marked by asterisks) — are flipped out from the H44 duplex and become buried in pockets between IF1 and S12 and in IF1, respectively. Second, one strand in the H44 duplex moves toward the proteins, resulting in disruption of base pairing in parts of H44 (for example, between bases A1413 and G1487 in the top left panel; compare with the same region in the 30S structure alone in the bottom panel). The local structural changes are propagated to the head domain directly connected to H44, resulting in a change in the relative position of certain domains in the 30S subunit — the overall effect of IF1 binding is that the head, platform and shoulder (see overview for these landmarks) of the 30S subunit rotate toward the A-site. Such a concerted movement of the domains may be an important feature of 30S function.