the STM so that the probe could respond to the general attractive/repulsive forces between atoms (for example, van der Waal interactions), a new generation of scanning probe microscope, called the atomic force microscope (AFM), was born[2].

Atomic force microscopy has an advantage over other microscope techniques in that samples can be imaged under water or in aqueous buffer solutions. Thus, the structural details of biological molecules can be investigated under physiological conditions. Much of the pioneering work for this important development was performed in the laboratory of Paul Hansma at the University of California, Santa Barbara. While the early AFM images of biological molecules were at low resolution, one particular example of an application of this technique revealed the potential of the instrument: a series of AFM images captured the clotting of human fibrinogen in progress[3].

Since its invention ~15 years ago, the AFM has become the predominant scanning probe microscope in use. In recent years, the applications of atomic force microscopy range from imaging static structures to providing snapshots of kinetic processes to studying the mechanical properties of biological molecules. As studies of single molecules become increasingly important, this versatile technique has emerged as a powerful tool in structural research. *Hwa-ping Feng*

1. Binnig, G., Rohrer, H., Gerber, Ch. & Weibel, E. *Phys. Rev. Lett.* **49**, 57 (1982).
2. Binnig, G., Quate, C.F. & Gerber, Ch. *Phys. Rev. Lett.* **56**, 930 (1986).
3. Drake *et al. Science* **243**, 1586–1589 (1989).

Four easy pieces

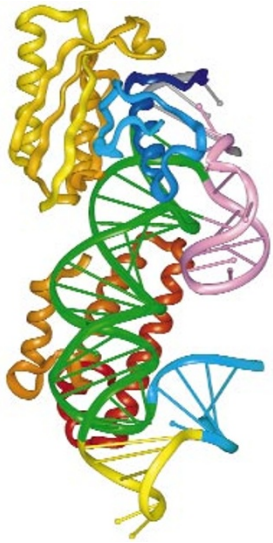
Recent low resolution structures of the bacterial ribosome, which is a 70S particle made up of small (30S) and large (50S) subunits, have generated much excitement. For the first time we can 'see' the large, complex machine that translates messenger RNA into protein at near atomic resolution.

Researchers are now in a position to address key questions about the mechanism of protein synthesis. For example, how does the ribosome 'read' the genetic code, how does transfer RNA bind, how does the peptidyl transferase reaction occur and how does the messenger RNA move through the ribosome during translation? In addition to the business of protein synthesis, there is an equally important question: how the 50 or so ribosomal proteins assemble with three ribosomal RNAs to form a functional ribonucleoprotein particle (RNP)?

While we look forward to atomic resolution structures of the entire ribosome some time in the near future, high resolution pieces of this complex RNP keep coming. The latest is the crystal structure of the central domain of the 30S subunit that consists of a 104 nucleotide fragment of 16S rRNA and the ribosomal proteins S15, S6 and S18 (*Science* **288**, 107–112).

The 30S subunit is the site of the codon–anticodon interaction between the messenger RNA and the transfer RNA substrates. S15 binds to 16S rRNA early in the process and is required for assembly of the 30S subunit. The new structure provides insights into this assembly process as well as RNA–protein recognition. S15 (orange) interacts with the backbone of the lower three-helix junction (green, yellow and blue) and with nucleotides in the adjacent minor groove of the RNA. This protein–RNA interface is almost identical to that observed in the crystal structure of a 57 nucleotide fragment of 16S rRNA and the S15 protein (*Nature Struct. Biol.* **7**, 273–277). In the S15,S6,S18–rRNA complex, the proteins S6 (yellow) and S18 (blue) bind across the upper three-helix junction (green, gray and pink) of the RNA.

While the exact functions of these RNAs and proteins in translation remain unknown, these structures, together with previous biochemical and biophysical experiments, suggest the following scenario for assembly of the central domain of



the 30S particle. Binding of S15 stabilizes the tertiary structure in the upper three-helix junction that is required for subsequent binding of proteins S6 and S18, and induces a conformational change in the lower three-helix structure that is necessary for further assembly of the other 16S rRNA helices. This model emphasizes the importance of an ordered and sequential assembly of RNA helices and proteins that could turn out to be a general feature of the assembly of large RNPs. *Boyana Konforti*