

s1.m5.p1 **Symmetry at the active site of the ribosome: structure and function.** Ilana Agmon¹, ¹Structural Biology, Weizmann Institute, 76100 Rehovot, Israel. E-mail: agmon@actcom.co.il

Keywords: Ribosome; Peptide bond formation; 2-fold symmetrical region.

A sizable region of some 180 nucleotides obeying a local 2-fold symmetry was identified in and around the peptidyl transferase center (PTC), the active site of the large ribosomal subunit. The symmetry stems, most likely, from the need to pose the reacting amino acids facing each other, in order to obtain the favorable stereochemistry for the peptide bond formation. A rotatory mechanism [1,2], indicating a spiral rotation of the tRNA terminus from the A- to the P-site, is the main element of a unified mechanism explaining peptide bond formation, translocation on the large subunit and the advance of nascent chains into the exit tunnel. These three functional steps are controlled by the specifically designed environment of the PTC and particularly by structural elements deviating from the overall symmetry.

The ribosomal nucleotides in the PTC that accommodate the tRNA 3' ends carrying the amino acids, are related by a local screw axis rather than a 2-fold axis. This arrangement results in an optimal positioning of the peptide bond formation reacting groups, ensuring the polarity of the reaction and advancing the nascent chain towards the exit tunnel of the ribosome. Symmetry breaking nucleotides are responsible for shaping the arched void, which is the path designed to be taken by the 3' end from the A- to the P- site, and for anchoring the tRNA termini during translocation. Structural differences between the symmetry related A and P sites suggest that the substrate is firmly held at the P site and more loosely at the A site, maybe to permit the optimization of its nucleophilic attack. Indications are found that deviating elements may be involved in large scale flexibility of the upper rims of the PTC, presumably concerned with the accommodation of the tRNA 3' ends. Deviating nucleotides in the symmetrical region may also contribute to pathways that transmit signals between remote ribosomal locations. On the whole, the symmetrical region establishes a stable template, which carries local structural deviations from the symmetry, imperative for performing the function of the PTC.

s1.m5.p2 **Crystal structure of the RNA binding domain of NS2 from BTV.** Carmen Butan and Paul Tucker, European Molecular Biology Laboratory (EMBL) c/o DESY, Notkestrasse 85, D-22603 Hamburg, Germany. E-mail: butan@embl-hamburg.de

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The RNA binding domain of the non-structural protein 2 (NS2) from Bluetongue virus (BTV) has been crystallized and its structure determined and refined to a resolution of 2.4 Å. The structure reveals a three dimensional (3D) domain swapped dimer where the C-terminal segment (134-160) of each subunit is swapped into the major domain (8-134) of the other subunit. Three dimensional domain swapping has been described as a mechanism for forming oligomeric proteins from their monomers (1,2). Indeed, repetition of the monomer-monomer interactions, as previously described, gives rise to an infinite helical structure in the crystal with a pitch equal to the length of the c-axis (77.92 Å). We hypothesize that point mutations placed at the dimer interface will destabilized the monomer-monomer interactions and thus offer important insight into the mechanism of oligomerization.

- [1] Schlunegger, M.P., Bennett, M.J. & Eisenberg, D. *Adv. Protein Chem.* **50**, 61-122 (1997)
- [2] Bennett, M.J., Schlunegger, M.P. & Eisenberg, D. *Protein Sci.* **4**, 2455-2468 (1995)