Understanding Ribosomal Structural Differences Between Bacteria and Archaea Using Network Graphs

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THE RIBOSOME AS A NETWORK

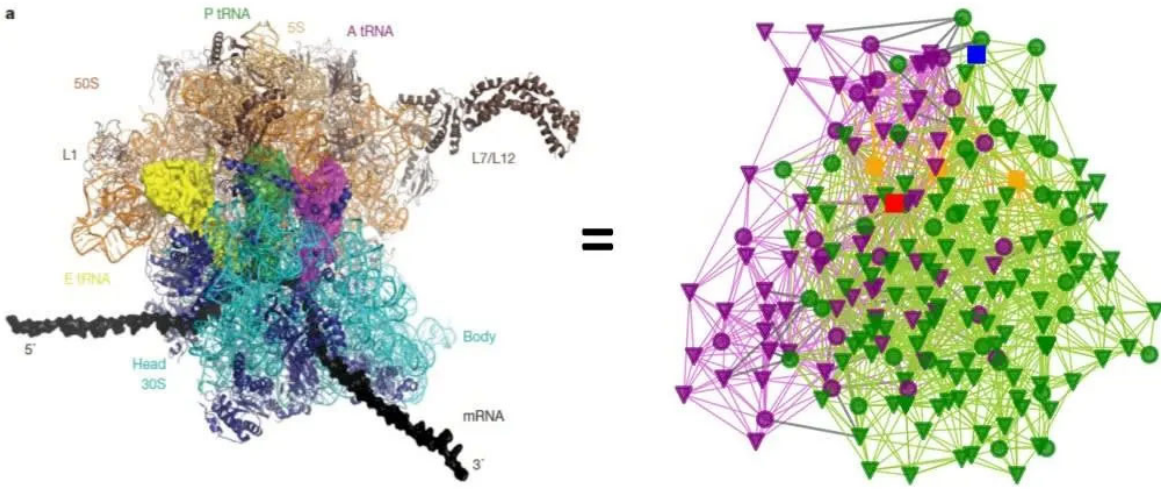
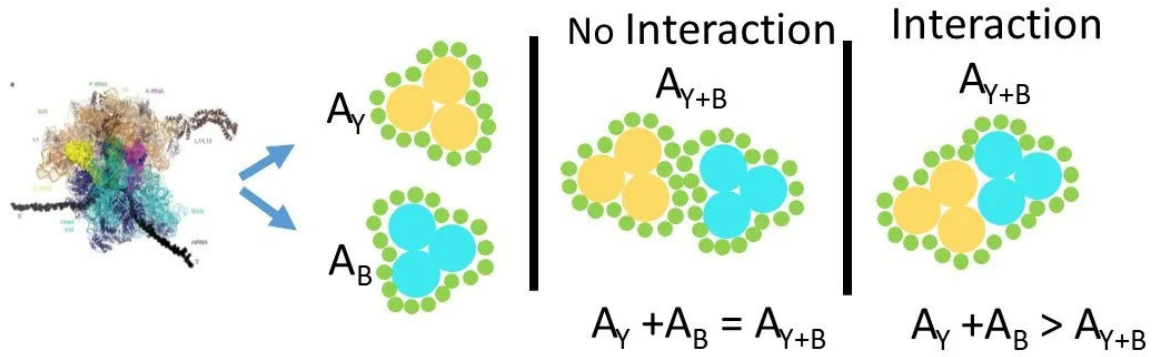


Image from T.M. Schmeing and V. Ramakrishnan Nature **461** 1234 (2009)

The first near-atomic resolution crystal structures of the ribosome were published over twenty years ago, hearlding in a new era for understanding the systematic relationship between ribosome function and structure. However, there is not a mathematical representation that is able to succintly describe ribosome structure. Such a framework would enhance the use of physical modeling, bringing a new understanding of translation and also enable insights into the evolution of life. This research focuses on developing a mathematical model of the ribosome based based on the interactions of its elements.An example of the result for T. *thermophilus* is shown in the figure above with the structrual file (left) transformed into a mathematical network (right). The nodes are placed at the center of mass of the coordinates found in the structural file and the lines connecting the different represent the interactions between them.

DETERMINING INTERACTIONS



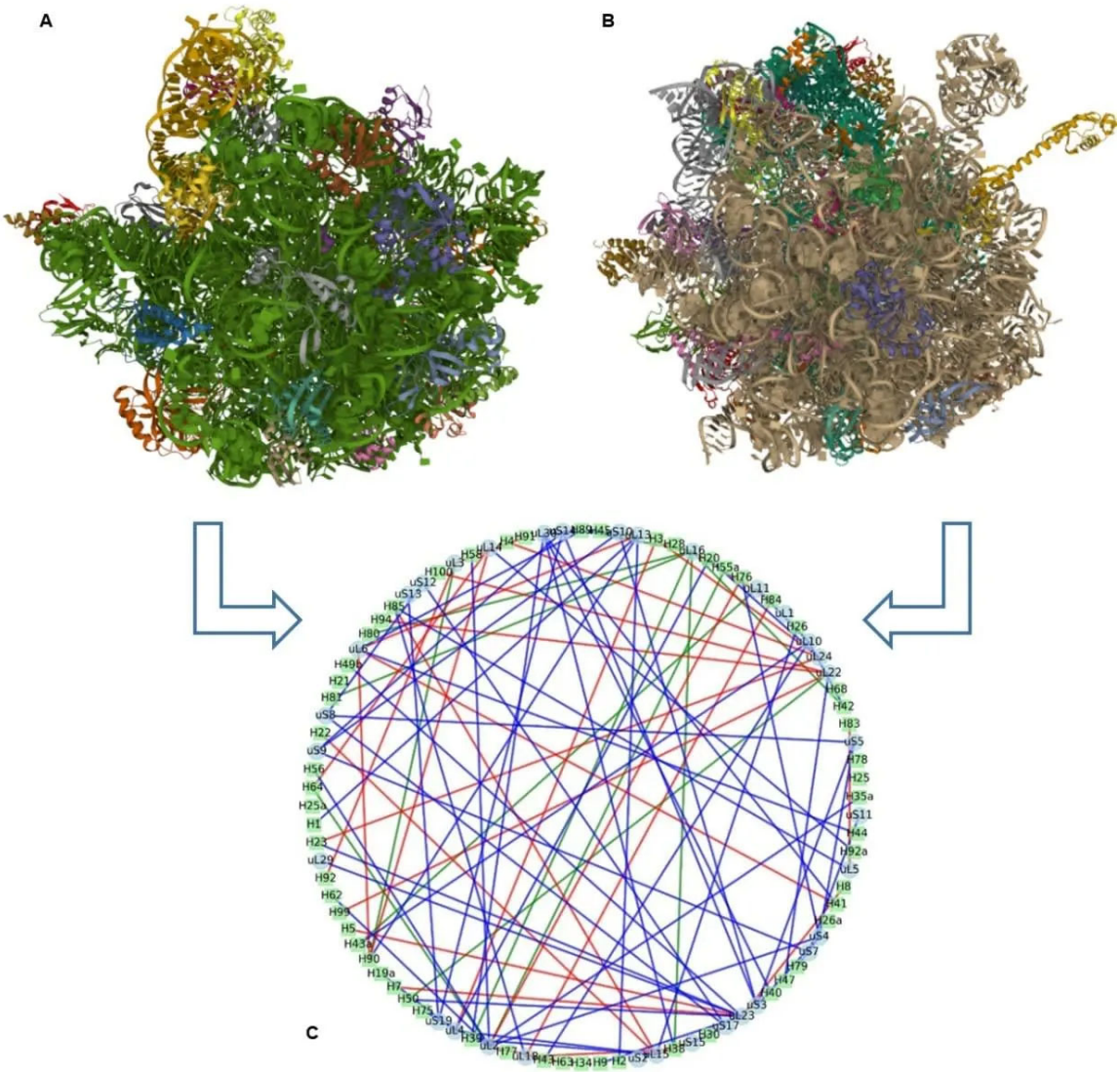
A physical based method is used to determine the interactions, which is independent of the chemistry of the molecules.Each element in the ribsoome is isolated from the main structured and the Solvent Accessible Surface Area (SASA) is determined using the Shrake Rupley method [1]. Then, each two elements are isolated from the ribosome structure and the SASA of the two elements together is calculated. If the SASA of the two elements isolated together is smaller than the SASA of the sum of the two elements in isolation, then an interaction is found. The solvent is taken as the radius of a water molecule at 1.4 Angstroms.

GRAPH PROPERTIES OF E. COLI AND H MARISMORTUI

	E. coli	*H. marismortui*
size (number of nodes)	136	135
order(number of edges)	653	681
isolated	0	0
pendant	0	0
ave degree	4.80	5.04
diameter	7	7
ave path length	3.10	3.02
cluster coefficient	0.490	0.506
density	0.071	0.075
assortativity	0.292	0.188
max_deg_name	H74, uL15	H35, uL2, H74, uL15
max_degree_value	21	20
max_betw_name	H74	H42
max_betw_value	0.107	0.099
max_clos	H74	H74
max_clos_value	0.458	0.451
number modular groups	5	4

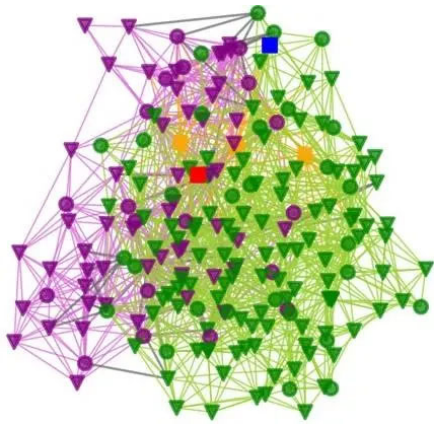
This table compares the graphs properties of the large subunit of *E. coli* and *H. marismortu*i. It can be compared with previous work looking at the graph properties of the bacterial ribosome [4], where the rRNAs were accounted for by domain as opposed to helices. Here we find that two maximally connected element in both ribosomes are uL15 and H74: the latter forming an important region of the peptidyl transferase center (PTC). This is striking because the previously it was found that domain II of the 23S formed the larged number of connections. Here, the connections of H74 are dominated by interactions within the 23S, connecting with just 4 rproteins: uL2, uL4, uL15 and uL28. Note further that this interconnectivity between important nodes is captured in the positive assortativity value. The increased connectivity of uL2 is due to new connections with eukaryotic rproteins in H. marismortui, mostly notably with eL37.

COMPARISON OF E. COLI AND H MARISMORTUI



(A) The Refined Crystal Structure of the H. marismortui LSU at 2.4 Å [5] where 5S rRNA is golden yellow and 23S rRNA is green, PDB ID: 3CC2 (X-ray diffraction). (B) High-resolution structure of the E. coli ribosome [6]. Resolution: 2.10 Å with 5S rRNA in silver grey, 16S rRNA in green and 23S rRNA in light yellow, PDB ID: 4YBB (X-ray diffraction). (C) Circle representation showing the changes in the interactions of the pivot points [7,8] between the LSU of H. marismortui LSU [9] and E. coli [6]. In brief, the interactions of each file were calculated as described in Calvet et al [4]. Interactions between elements common to both ribosomes are drawn in green, interactions present in E. coli but not H. Marismortui are drawn in blue, and those present in H. marismortui but not E. coli are drawn in red. (A) and (B) images were created using pymol [10]. Calculations and layout in (C) done using python.

WHICH ELEMENTS TO USE?



The ribosome is broken into constituent elements in the following way. First, rproteins (circles) are considered as single elements. The smaller RNAs, such as the mRNA (red square), the 5S rRNA (blue square) and the tRNAs (orange squares) are considered as single elements.The larger rRNAs, notably the 23S and the 16S are divided into secondary structure using the enumeration on the Ribovision website [11].To distiguish the large and small subunits, the elements are depicted respectively in green and purple. Interactions bridging the two are drawn in grey. The positions of the elements are the center of mass of their coordinates in the structural file.

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Future work will focus on improving the methodology to take into account the resolution of the structural file. This will faciliate comparisons between files.We will continue to explore how we can understand changes in different speices using a network description

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ABSTRACT

The ribosome is a universal molecular machine (comprised of RNA and proteins) which translates the message from the genome into proteins (polymers of amino acids) in biology. **Similar to how Flight and Cockpit voice recorders record and preserve an aircraft's flight history, the ribosome has recorded signatures of its evolution. Tapping this resource is important for understanding the origins of life.**

The electrostatic properties/net positive charge(s) of ribosomal proteins (RPs) stabilize interactions with the negatively charged ribosomal RNA (rRNA) and influence the assembly and folding of ribosomes. A high percentage of RPs from extremely halophilic archaea are known to be acidic/negatively charged. Recently the net charges (at pH 7.4) of the RPs from a highly conserved cluster of RPs were found to have an inverse relationship with the halophilicity/halotolerance (ability to survive under salt conditions) levels in bacteria and archaea. In non-halophilic bacteria, these RPs are generally basic, contrasting with the acidic proteomes of the extreme halophiles. We explore the use of a new mathematical modeling technique based on interaction graphs to provide a systematic understanding of the structural differences in the Large Subunit (LSU) of the bacterium *Escherichia coli* and that of the extremely halophilic archaeon *Haloarcula marismortui*.