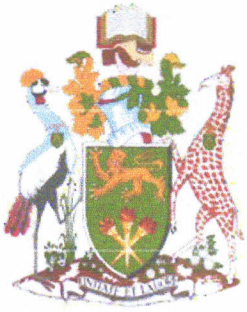
Structure of the 40S ribosomal subunit from *Plasmodium falciparum* By Homology and *De novo* modeling



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ABSTRACT

Generation of the three dimensional structures of macromolecules using *in silico* structural modeling technologies such as homology and *de novo* modeling has improved dramatically and increased the speed in which tertiary structures of organisms of interest can be generated. This is especially the case if a homologous crystal structure is already available. High resolution structures can be rapidly created using only their sequence information as input and thus increasing the speed of scientific discoveries. In this study, a host of homology modeling and structure prediction tools such as RNA123 and SWISS –MODEL among others, were used to generate the 40S subunit from *Plasmodium falciparum.* This structure was modeled using the published crystal structure from *Tetrahymena Thermophila*, a homologous eukaryote X-ray structure. In the absence of any information from the solved *Plasmodium falciparum* 40S ribosomal crystal structure, the model accurately depicts a global topology, secondary and tertiary connections, and gives an overall RMSD value of 3.9 Å relative to the templates crystal structure. The model accuracy is even better than prior hypothesis, though deviations are modestly larger for areas that had no homology between the templates. These results lay ground work for using this approach for larger and more complex eukaryotic ribosomes, as well for still larger RNAs, RNA-protein complexes and entire ribosomal subunits. The model created will provide a scaffold onto which *in silico* ligands screening can be performed with the ultimate goal of developing new classes of anti-malarial compounds.

Keywords: Ribosome; 40S subunit; RNA; structure; comparative analysis; three-dimensional modelling; RMS