Towards a Molecular Model of Ribosome Assembly

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Abstract: An integrative whole-cell modeling approach aims at combining different main cellular processes such as metabolism, growth and cycle. Despite the success in constructing a whole-cell model for the parasitic bacterium Mycoplasma genitalium, full bottom-up (from molecules to function) modeling of a cell remains problematic. Translation of this approach from a parasitic bacterium to even a simple eukaryote such as the budding yeast Saccharomyces cerevisiae is bound to face significant challenges. In a recent publication, a coarse-grained model for the budding yeast is proposed, comprising metabolism, growth, and cycle modules.
It works as the scaffold model of the whole cell, into which functional modules of increasing molecular detail could be inserted individually or in combination.
This note paves the way for a model of ribosome assembly of Saccharomyces cerevisiae, possibly working as a molecular plug-in module of a coarse-grained model. Ribosomes are large RNA–protein complexes consisting of a Small and a Large SubUnit (40S-SSU and 60S-LSU, respectively). During protein synthesis, the small subunit binds to the large subunit onto the mRNA strand, with peptide-bond formation. Here, we present a new mathematical framework to account for the small/large subunits production. The roadmap to the building of a scaffold model detailing main processes involved are: (1) formation in the nucleolar compart of the SSU processome, including assembly factors and most ribosomal proteins complexed with the nascent rRNA precursor, which is co-transcriptionally processed; (2) after rRNA cleavage (yielding a 20S pre-rRNA), most assembly factors are released from the SSU processome (and some ribosomal proteins are added) in order to form the pre-40S particle which is translocated in the cy-toplasm; (3) in the cytoplasm, other assembly factors dissociate from the pre-40S, which in turn acquires other ribosomal proteins; (4) binding of the pre-40S to a mature 60S LSU (yielding a 80S-like particle) for the functional proofreading of the pre-40S: in case of positive check, the 60S LSU is released from the pre-40S particle, together with the remain-ing assembly factors, and the final cleavage of rRNA occurs, yielding the 18S rRNA included in the mature 40S SSU; in case of negative check, the 60S LSU is released and the pre-40S is degraded. All these points are conceived to be further extended to finer details, according to the modular Systems Biology philosophy that aims at integrating many and different molecular modules.