The Map of the Cell is in the Chromosome

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Abstract

Contrary to an intuitive idea there is often no predictable link between structure and function in biological objects. Observing biases in features which would be thought to be unbiased, is the hallmark of some selection pressure. Because the genetic code is redundant, coding sequences can be studied by analysing their codon usage. It has long been observed in Escherichia coli that genes could be split into three classes according to the way they use codons. The same is true for *Bacillus subtilis*. These biases could reflect a bias in the concentration of some tRNAs, but if a tRNA gene had a strong promoter, spontaneous mutations would tend to lower its efficiency, making transcription of this particular tRNA similar to its other counterparts. This is true, unless there is selection pressure for the converse. The cytoplasm of a cell is not a tiny test tube, there must be some kind of organisation of transcription, translation and replication so that mRNA molecules and DNA are not mixed up together all the time. One should therefore consider translating ribosomes as attractors of a certain pool of tRNA molecules. With this view, the cytoplasm is a ribosome lattice, moving slowly with respect to local diffusion of small molecules as well as macromolecules. This provides an efficient selection pressure leading to adaptation of the codon usage of the translated message as a function of its position in the cell's cytoplasm. If the codon usage changes from mRNA to mRNA, this indicates that these different molecules do not see the same ribosomes in the usual life cycle of the organism. In particular if two genes have very different codon usage this indicates that the corresponding mRNAs are not made from the same part of the cell. Messenger RNA threads are pulled off DNA by the lattice of ribosomes, going from one ribosome to the next one, as does a thread in a wiredrawing machine. Polycistronic operons ensure that proteins having related functions are co-expressed locally, permitting channelling of the corresponding substrates and products. If ribosomes act as attractors of tRNA molecules, this implies a local coupling between these molecules and the codons they can use in the message they read. This requires that a given ribosome translates mRNAs having similar codon usage. But this has the

consequence that as one goes away from a strongly biased ribosome, there is less and less availability of the most biased tRNAs. In turn this creates selection pressure for a gradient of codon usage as one goes away from the most biased messages and ribosomes. With this view transcripts are nested around central core(s), formed of transcripts for highly biased genes. We shall show that this fits with what is seen of the general organisation of genes in the chromosome. In particular this agrees with the observation that the distance between E. coli genes oriented in the same direction on the chromosome is positively correlated to the expression level of the downstream genes. Furthermore the chromosome must separate from each other and migrate in each of the daughter cells : there must exist a repulsive force that pushes DNA strands away from each other. Continuous synthesis of ribosomes between the replicating forks provides the required mechanical stress. If ribosome sources are organisers of the cell, mRNA for genes highly expressed under exponential growth conditions should be located near the center of these organisers, while other mRNAs should be translated in nested layers, all the way to the ribosomes that are located near the cytoplasmic membrane, and that would be involved in cotranslational membrane protein localisation. Organisation of the genes in the chromosome should therefore show regularities that are linked to this architecture. Work will be presented, using E. coli and B. subtilis as models, consistent with this emerging picture of a cell organised around a kind of celluloculus.