

The role of electrostatics in the transcription regulation in prokaryotes. DNA phenotype

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Physical properties of genome DNA define its shape in the functional space and influence its interactions with different proteins, esp. regulating transcription. DNA is a highly charged molecule and electrostatics contributes greatly to the subject. However, lack of methods to calculate the profile of electrostatic potential (EP) of large stretches of DNA, slow down researches of the problem. In our laboratory, such method has been developed and DEPPDB - database of electrostatic and other physical properties of all complete sequenced genomes – was built on its basis.

Negative EP has a nonuniform distribution along DNA molecule and correlates with the GC content, though does not correspond to it exactly, and strongly depends on both the sequence arrangement and its context (flanking regions). Binding frequency of RNA polymerase to DNA along the genome, measured in direct experiment, correlates to the calculated EP.

Transcription regulation areas have EP and other physical properties peculiarities. Binding sites of transcription factors of different protein families in different taxa are located in areas of high EP and possess its high value themselves. Promoters in average have high value and heterogeneity of EP profile. The transcription starting sites of prokaryotic genomes are characterized by extensive (hundreds of bp) zone of high EP and a series of peculiarities directly around TSS. This is associated with protein binding and formation of other physical properties, required for the transcription machinery. Specific details of the TSS EP architecture are similar in related taxa. Numerous data indicate that the third promoter determinant, the so-called up-element, has electrostatic nature.

Studies of the effects of electrostatics on genome functioning should consider also the formation of other physical properties of DNA, in particular - bending, thermal stability,

supercoiling. There are some evidences of the interactions of these properties and electrostatics in their formation, as well as in transcription regulation.

The data present suggest the importance and universality of the role of electrostatics in transcription regulation of prokaryotic genomes. The proposed mechanism affects the binding probability and positioning accuracy of proteins involved in transcription regulation. The universal nature of the regulatory impact of electrostatics suggests its importance to the process of horizontal gene transfer and the evolution of transcription regulation systems and contributes to understanding of high AT content of genome regulatory regions.

Principles of the physical properties formation on the basis of nucleotide sequence allow for a fresh look at several fundamental problems such as the Chargaff's second parity rule, redundancy of the genetic code, and neutrality of synonymous substitutions; and justify the fundamental idea of DNA phenotype, also defining the new principle of biophysical bioinformatics.

DEPPDB is available for academic use via the web interface at <http://deppdb.psn.ru> (or <http://electrodna.psn.ru>). The authors are grateful to the Institute of Mathematical Problems of Biology of RAS for hosting the Database.

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