Abstract for GR-TR Conference on Statistical Mechanics and Dynamical Systems

Talk Invited Invited Talk

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The functional instability of native DNA

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With the discovery of the double helix structure of DNA, by Watson and Crick in 1953, the topological problem, arising from the need of the double helix to unwind in order to replicate, was recognised as an issue of primary concern. This point was resolved only 25 years later, with the advent of topoisomerases. Meanwhile, the great stability of DNA helix was documented, as a supercoil packed within the nucleosome structure in the chromosomes. At the same time a wide array of functional sites in the DNA topography were discovered, that need to undergo destabilization in order for the major cell functions to be accomplished. Such destabilisable sites are Origins of DNA replication and Promoters -enhancers-silencers of DNA transcription into RNA, that are the sites of actions for general or specific DNA binding proteins. Furthermore, it is currently understood that not only the genes that code for protein , rRNA and tRNA but almost the whole of the genome is transcribed.There is intergenic transcription as well as transcription for the production of a high number of small nuclear RNA molecules that are regulators of gene expression . This whole complex system poses a challenging task for the recognition of the destabilisable DNA sites that are involved in the regulation of transcription. Additionally, the regulation of transcription is only part of the regulation of gene expression program that specifies the cell type and developmental stage at which a gene is expressed (is allowed to produce the product that is coding for). The gene expression process is closely associated with the nuclear architecture and nuclear scaffold/matrix, through another type of destabilisable DNA site the so -called Scaffold and Matrix Attachement Regions (S/MAR). The functional instability of DNA sites like origins of replications, promoters and other transcription DNA elements and S/MARs often is not entirely a property of the site itself, but it also depends on other sequences along the same DNA molecule. The knowledge of the destabilization potential of these elements is of crucial importance for the experimental design of DNA structures, such as DNA plasmids and artificial chromosomes. Such DNA structures are used for the gene transfer into cells and are required to be able to direct their own DNA functions. The use of such elements will be discussed, within the context of formulating gene transfer vectors for gene therapy strategies.